

Marit Synnøve Skrove

**Emotional symptoms, lifestyle
and somatic aspects in
adolescence**

- The importance of resilience factors

Thesis for the degree of Philosophiae Doctor

Trondheim, September 2015

Norwegian University of Science and Technology
Faculty of Medicine
Regional Centre for Child and Youth Mental Health
and Child Welfare



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Emosjonelle symptomer, livsstil og somatiske aspekter i ungdomstiden. Betydningen av resilience faktorer

Symptomer på angst og depresjon forekommer hyppig hos ungdom og kan være assosiert med livsstil og somatiske aspekter som kronisk smerte, pubertet og fedme. Resilience faktorer som sosial støtte fra familie og venner er assosiert med lavere forekomst av emosjonelle symptomer hos ungdom. Det er lite kunnskap om effekten av resilience faktorer på assosiasjonene mellom emosjonelle symptomer og livsstil, så vel som somatiske aspekter, hos ungdom. Formålet med denne studien var å undersøke nærmere assosiasjonene mellom emosjonelle symptomer og livsstil, kronisk smerte, pubertet og kroppsmasse hos jenter og gutter i ungdomstida, samt å undersøke den mulige effekten av resilience faktorer på disse assosiasjonene. Studien er basert på data fra den tredje Helseundersøkelsen i Nord-Trøndelag (HUNT 3) som ble gjennomført i tidsperioden 2006 til 2008. Ungdom i alderen 13 til 18 år med som hadde svart på de aktuelle spørsmålene for studien ble inkludert og dette ga en studiepopulasjon på 7639 ungdommer i artikkel I og III og 7070 ungdommer i artikkel II.

Emosjonelle symptomer ble rapportert av 19 % av jentene og 6 % av guttene i studiepopulasjonen. Røyking, bruk av alkohol eller å ha prøvd narkotika, så vel som lav fysisk aktivitet var assosiert med høyere forekomst av emosjonelle vansker. Kronisk smerte forekom oftere hos ungdom med høyt nivå av emosjonelle eller atferdsmessige vansker sammenlignet med ungdom med lavt nivå. Subjektiv oppfatning av pubertet og vekt var sterkere assosiert med emosjonelle symptomer enn objektive mål. Assosiasjonene mellom emosjonelle symptomer og livsstil, så vel som mellom emosjonelle symptomer og kronisk smerte ble svekket ved justering for resilience faktorer. Resilience faktorer hadde også en modererende effekt på sammenhengen mellom emosjonelle symptomer og subjektiv oppfatning av pubertet, samt subjektiv oppfatning av vekt. Assosiasjonen mellom tidlig pubertet og emosjonelle symptomer var avhengig av nivå av ensomhet hos jenter, mens sammenhengen mellom emosjonelle symptomer og sein pubertet eller fedme var sterkere for gutter med lavt nivå av resilience faktorer sammenlignet med gutter med høyt nivå av resilience faktorer.

Emosjonelle symptomer var vanlig hos ungdom, spesielt hos jenter. Det var sterke assosiasjoner mellom emosjonelle symptomer og livsstil, så vel som mellom emosjonelle symptomer og kronisk smerte, subjektiv oppfatning av pubertet og vekt. Nytt i denne studien er betydningen av ungdommens egen vurdering av kroppslige faktorer, så vel som betydningen av positive relasjoner med familie og venner for sammenhengen mellom emosjonelle vansker, livsstil og somatiske aspekter i ungdomstida. Studien understreker derfor viktigheten av å utrede kronisk smerte, kroppoppfattelse og tilgangen på sosial støtte i forebygging og behandling av emosjonelle symptomer i ungdomstida.

Navn kandidat: Marit S Skrove

*Institutt: Regionalt kunnskapssenter for barn og unge – Psykisk helse og barnevern,
Det medisinske fakultet*

Veiledere: Marit S Indredavik, Pål Romundstad, Stian Lydersen

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Marit Synnøve Skrove

Abbreviations

ACTH	Adrenocorticotrophic Hormone
ADHD	Attention-Deficit/ Hyperactivity Disorder
BDNF	Brain-Derived Neurotrophic Factor
BMI	Body Mass Index
CD	Conduct Disorder
CI	Confidence Intervals
CRF	Corticotropin-Releasing Hormone
DALY	Disability-Adjusted Life Years
DNA	Deoxyribonucleic Acid
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders - IV
fMRI	Functional Magnetic Resonance Imaging
FSH	Follicle-Stimulating Hormone
GR	Glucocorticoid Receptor
HPA	Hypothalamic-Pituitary-Adrenal
5-HTTLPR	5-HydroxyTryptamine Transporter Gene-Linked Polymorphic Region/ Serotonin transporter gene promoter region
HUNT	The Nord-Trøndelag Health Study
ICD-10	International Statistical Classification of Diseases and Related Health Problems -10
INF	Interferon

MAO	Mono-Amino-Oxidase
OR	Odds Ratio
PDS	Pubertal Development Score
READ	Resilience Scale for Adolescents
RSE	Rosenberg Self-Esteem Scale
SCL	Hopkins Symptom Checklist
SES	Socioeconomic Status
SPAI-C	Social Phobia and Anxiety Inventory for Children
WHO HBSC	World Health Organization Health Behaviour in School-aged Children

List of papers

Paper I

Resilience, lifestyle and symptoms of anxiety and depression in adolescence: the Young-HUNT study

Marit Skrove, Pål Romundstad, Marit S. Indredavik

Social Psychiatry and Psychiatric Epidemiology 2013; 48:407-16.

Paper II

Chronic multisite pain in adolescent girls and boys with emotional and behavioural problems: the Young-HUNT study

Marit Skrove, Pål Romundstad, Marit S. Indredavik

European Child and Adolescent Psychiatry 2014 Aug. [Epub ahead of print].

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Paper III

Pubertal timing, body mass, emotional symptoms and the moderating effect of resilience factors during adolescence: The Young-HUNT study

Marit Skrove, Stian Lydersen, Marit S. Indredavik

Submitted.

Summary

Symptoms of anxiety and depression occur frequently among adolescents and are associated with an unfavourable lifestyle and bodily factors such as chronic pain, off-time pubertal development and high body mass. Few scholars have reported on the frequency of chronic multisite pain in adolescents with emotional or behavioural problems. Resilience factors such as social support from family and friends are associated with reduced levels of emotional symptoms in adolescence. However, there is little knowledge about the effects of resilience on the associations between emotional symptoms and lifestyle and somatic aspects in adolescence.

This study aimed to explore the associations between emotional symptoms and lifestyle, chronic pain, pubertal timing and body mass in adolescent girls and boys and to investigate the possible effects of resilience factors on these associations. The study uses data from a large cross-sectional health survey conducted in Norway between 2006 and 2008; the Nord-Trøndelag Health Study (HUNT 3). Adolescents aged 13 to 18 years old with complete measures on the outcome variables were included, yielding a study population of 7639 adolescents in papers I and III and 7070 adolescents in paper II.

Emotional symptoms were reported by 19% of girls and 6% of boys in the study population. Smoking, use of alcohol, having tried drugs and infrequent physical activity were associated with higher levels of anxiety and depression (odds ratios ranging from 2.1 to 4.0). Chronic multisite pain was more prevalent among adolescents with high levels of emotional or behavioural symptoms (22.8-31.0% for girls, 8.8-19.0% for boys) compared to adolescents with low levels of symptoms (3.4-8.8% for girls, 1.5-2.5% for boys). Perceived pubertal timing and perceived body mass were more strongly associated with symptoms of anxiety and depression than actual pubertal timing and body mass. Resilience factors substantially attenuated the associations between

emotional symptoms and unfavourable lifestyle, as well as between emotional symptoms and chronic pain. Additionally, resilience factors also moderated some of the associations between emotional symptoms and perceived pubertal timing or perceived body mass: Whereas the association between early perceived pubertal timing and emotional symptoms was dependent on coexistent loneliness in girls, the associations between late perceived pubertal timing, as well as perceived obesity, and emotional symptoms were stronger for boys with low levels of resilience factors than for boys with high levels of resilience factors.

Emotional symptoms were common in adolescence, particularly among girls. There were strong associations between emotional symptoms and lifestyle or bodily factors such as chronic pain, perceived pubertal timing and body mass. Some of the new findings in the current study were the importance of the adolescents' own evaluation of their body, as well as the importance of positive relationships with family and friends, for the associations between emotional symptoms, lifestyle and somatic aspects in adolescence. The findings in this thesis expand our knowledge on these associations and underscore the importance of exploring possible co-existence of chronic pain, perceptions of body and availability of social support in the treatment and prevention of emotional symptoms in adolescence.

1. Introduction

This thesis explores how emotional symptoms, primarily symptoms of anxiety and depression, are related to lifestyle and somatic aspects in adolescence. The topic is examined by cross-sectional analyses, using data from a large population-based health study: the Nord-Trøndelag Health Study (HUNT 3) (www.ntnu.edu/hunt). There are two main themes: 1) the associations between emotional symptoms and lifestyle, chronic pain, puberty and body mass in adolescence and 2) the possible influence of resilience factors on these associations.

1.1 Rationale

The inter-relationship between somatic and psychological factors has been given varying attention throughout history. Although it is a common experience that psychological strain increase susceptibility to infections and physical illness may trigger psychological change [1], this perspective is not always taken into account in clinical practice [2-4]. Emotional symptoms and disorders are considered a major public health problem worldwide, and their prevalence increases rapidly during adolescence [5-8]. Approximately 25% of adolescent girls and 10% of boys report emotional symptoms in population-based studies [9, 10]. The development of emotional symptoms and the increasing prevalence in adolescence appear to be caused by an interaction between genetic and environmental factors [11]. In the last few decades, increasing attention has been given to the inter-relationship between somatic or bodily factors and emotional symptoms. An unfavourable lifestyle and bodily factors such as chronic pain, pubertal timing and body mass have been found to be related to emotional symptoms in adolescence [12-16]. The underlying mechanisms for these associations are complex and not fully understood. Research may extend our understanding of these associations and increase the awareness of clinicians who work with adolescents troubled by emotional symptoms. Furthermore, the associations between emotional symptoms and lifestyle and somatic aspects are not universal. Not every individual with an unfavourable lifestyle or who is suffering from chronic pain develops emotional symptoms. Resilience factors are factors that may buffer the negative effects of

experienced stressors and are associated with reduced levels of emotional symptoms in adolescence. However, there is little knowledge about the effect of these factors on the relationship between emotional symptoms, lifestyle and somatic aspects. The HUNT study offers a unique possibility to examine these relationships in a large population of non-selected adolescents. This thesis provides data on the relationship between emotional symptoms and lifestyle, as well as somatic aspects, in adolescence and explores the influence of resilience factors on these relationships. Thus, this thesis extends the knowledge of key factors for adolescents' mental health.

1.2 Concepts and delimitations

This thesis is based on data from a large epidemiological health survey using self-report questionnaires. It therefore considers only self-reported emotional symptoms and associated factors and does not include emotional disorders or functional somatic conditions that require a clinical assessment for diagnosis. Consequently, in this thesis, emotional symptoms refer to self-reported symptoms of anxiety and depression.

Paper II also examines symptoms of social anxiety and behavioural problems. In this thesis, behavioural symptoms refer to self-reported symptoms of attention problems or conduct problems. Because emotional symptoms constitute the main theme in the thesis, behavioural symptoms will be discussed more briefly.

Symptoms of anxiety may include feelings of fear, panic or nervousness, uncontrollable worry, an inability to be still or calm, often accompanied by heart palpitations, muscle tensions, shortness of breath, cold or sweaty hands or feet, and sleep disturbance [17]. The symptoms may be present across situations (generalized anxiety) or may be related to specific situations such as social interaction (social phobia). Symptoms of depression typically include lowered mood or irritability, loss of interest or pleasure, decreased energy, loss of self-confidence, self-devaluation, suicidal thoughts, concentration problems, sleep disturbances and decreased psychomotor activity or appetite [17]. In

severe forms symptoms of anxiety may be diagnosed as anxiety disorders (such as generalized anxiety disorder) and depressive symptoms as depressive disorders (such as major depressive disorder or depressive episodes). Symptoms of anxiety and depression often co-occur in the same patient, and anxiety and depressive disorders have common risk factors and considerable symptomatic and diagnostic overlap [18-21]. Some even argue that anxiety and depression are different expressions of the same disorder, as anxiety frequently precedes depression [20, 22, 23]. Anxiety and depression are therefore often studied together [9, 18, 19].

Attention problems are characterized by symptoms of inattentive, hyperactive and impulsive behaviours and severe symptoms are diagnosed as hyperkinetic disorder (ICD-10) or attention-deficit/hyperactivity disorder (ADHD) (DSM-IV) [17, 24]. Conduct problems are characterized by excessive aggression and violation of major rules or societal norms; in severe forms these behaviours are diagnosed as conduct disorder (CD) [25].

In this thesis, lifestyle includes the adolescents' reports of smoking, use of alcohol or having tried illegal drugs, and frequency of physical activity.

Somatic aspects refer to bodily factors, and in this thesis somatic aspects include chronic pain, body mass and pubertal timing; i.e. the adolescent's pubertal status compared to others' of same age and sex.

Resilience is a complex concept with several definitions [26-31]. It is generally understood as the ability to bounce back from adversities [31]. In this study, resilience is understood as factors at the individual, familial and external social level that contribute to a good psychological outcome in spite of the presence of risk factors [27, 29]. Hence, in this thesis, social competence and self-esteem are included as measures

of resilience factors at the individual level, family cohesion and relations to parents are included as measures of resilience factors at the familial level, while loneliness and number of friends are included as measures of resilience factors at the external social level.

Adolescence refers to the age period of 13 to 18 years.

1.3 Theoretical approach

The interplay between the body and mind or between somatic and psychological processes has been described in several models, including the biopsychosocial model [32], the bio-ecological model [33] and the nature-nurture model [34]. According to Rutter, these models have some common general principles, as follows: 1) Individuals differ in their reactivity to their environment, 2) there is a reciprocal relationship between individuals and their environments, and this relationship should be considered in an ecological framework, and 3) individuals actively process their experiences and act on their environment to shape and select their experiences [34]. In addition, individual characteristics may change over time. These models offer a theoretical framework for exploring the associations between emotional symptoms and their associations with lifestyle and somatic aspects that includes biological, psychological and social processes and will constitute the theoretical basis for this thesis. Biological aspects may include structural or functional deficits or alterations in the body or brain, as well as genetic or epigenetic effects. Psychosocial aspects may include cognitions, inter-personal relations and environmental experienced traumas such as physical or sexual abuse.

1.4 Aetiology

1.4.1 Neuroanatomy and neural circuitry

Neurological correlates of emotional symptoms and disorders include structural and functional brain deficits or dysfunctions. Anxiety is associated with changes in the amygdala, the ventrolateral prefrontal cortex and the anterior cingulate cortex [21]. The amygdala is the structure that generates the central fear response, and adolescents with generalized anxiety disorder demonstrated increased amygdala size [21]. Functional magnetic resonance imaging (fMRI) studies have shown increased activity in the amygdala and ventrolateral prefrontal cortex in youth with anxiety, particularly in response to fearful facial expressions [21, 35].

Depression is associated with changes in the prefrontal and cingulate cortex, hippocampus, striatum, amygdala and thalamus [36]. Post-mortem and neuroimaging studies of depressed patients have shown reduced gray matter and glial density in the prefrontal cortex and hippocampus, whereas fMRI has shown strong correlations between activity in the amygdala and the cingulate cortex and sadness in both healthy and depressed individuals [37]. The function of these regions under normal conditions suggests their contribution to depressive symptoms: the neocortex and hippocampus may mediate the cognitive aspects of depression such as memory impairment, feelings of hopelessness, worthlessness and guilt. The striatum and amygdala are important in emotional memory and may mediate anhedonia and anxiety, whereas the hypothalamus may be involved in the regulation of sleep and appetite [36, 37].

The prefrontal cortex, caudate and cerebellum have been described as the primary areas that show deficits in attention problems and ADHD [38]. Patients with ADHD are reported to have slower maturation of the prefrontal cortex and a smaller volume or reduced activity of the caudate or cerebellum [38]. Children and adolescents with CD are reported to have reduced right temporal lobe and right temporal grey matter volume [39].

Hence, several areas within the frontal and temporal regions of the brain, as well as the limbic structures are thought to be involved in the development of emotional and behavioural symptoms. However, as highlighted in two reviews, caution should be made to attribute specific functions to specific structural locations [36, 37].

1.4.2 Genetic and epigenetic mechanisms

Twin studies report that genetic factors account for a moderate to substantial amount of variance in emotional and behavioural symptoms [35, 36, 40-42]. However, even if many genetic variants are detected and examined, for most genetic variants the effect sizes are small, and few findings concerning specific genes that may increase vulnerability for emotional symptoms are replicated [41, 43]. For the transmission of depression, the presence of two short alleles in the promoter region of the human serotonin transporter gene (5-HTTLPR) and a polymorphism in the brain-derived neurotrophic factor (BDNF) gene have been suggested [44-46]. However, study results are inconsistent, and the genetic contribution to emotional symptoms most likely reflects combinations of genes that are expressed in different ways at different points in life [47]. There is also scientific support for the hypothesis that a set of genes is globally associated with all forms of child and adolescent psychopathology [48]. In addition, the individual's genetic equipment will affect personal traits such as intelligence and temperament, which, in turn, could contribute to the vulnerability for developing psychological symptoms [35, 49]. According to a longitudinal study, children who were inhibited, socially reserved and easily upset at age three had higher levels of depressive disorders at age 21 than children who did not demonstrate these characteristics [50]. Genes may also contribute to our environment as an inherited tendency to enter adverse surroundings [51]. For example, individuals who are shy and introverted will seek different social experiences than those who are more extroverted [52].

Environmental factors may influence genetic expression via epigenetic mechanisms [53]. Epigenetic mechanisms include alterations in the chromatin structure, such as histone acetylation or DNA methylation, and changes in secondary structures formed by DNA and histones (nucleosomes) [54]. These processes influence the accessibility or activation state of gene regulatory elements and mediate the effects of the environment on the transcriptional regulation of specific genes [55]. In a post-mortem study, suicide victims with a history of child abuse had increased methylation of the promoter region of the gene coding for the glucocorticoid receptor (GR) in the hippocampus compared to non-abused suicide victims or non-suicide controls [56]. Increased promoter methylation is thought to decrease GR expression and increase responsivity of the hypothalamic-pituitary-adrenal (HPA) axis, thereby contributing to increased vulnerability for depression [56].

1.4.3 Molecular mechanisms

For several decades, depression was hypothesized to be caused by decreased monoamines in the brain. This hypothesis originated from clinical observations of the anti-depressant effects of drugs that enhance serotonin or noradrenaline transmission or inhibit enzymes catabolizing monoamines such as monoamine oxidase (MAO) [36, 57]. Furthermore, the monoaminergic systems are extensively distributed throughout the brain regions and neural circuits that are thought to be involved in anxiety and depression. Alterations in the serotonergic and noradrenergic systems are associated with emotional symptoms. However, monoamines are currently thought to be involved as mediating rather than causal factors [57].

The immune and endocrine systems and interactions between these systems and the brain are probably very important in the development of emotional symptoms and disorders [1]. One of the brain's reactions to stress is the activation of the HPA axis: corticotropin-releasing hormone (CRH) is secreted from neurons in the hypothalamus and stimulates the synthesis and secretion of adrenocorticotrophic hormone (ACTH) from the pituitary, which, in turn, stimulates the secretion of cortisol from the adrenal

cortex [36]. The stress-response is beneficial in protecting the individual from injury and adjusting the individual to future adverse situations [1]. However, chronic uncontrollable stress results in the sustained hyperactivity of the stress axis with hyper-secretion of cortisol and hyper-activity of the sympatho-adrenal system. This may cause both symptoms of anxiety and depression and physical changes such as diabetes, hypertension and inflammatory changes [1]. Hyper-secretion of cortisol initiates changes in the serotonergic system. Whereas acute stress is associated with an increased turnover of serotonin, chronic stress is associated with decreased serotonin turnover. Decreased serotonin turnover is thought to contribute to the development of emotional symptoms [1].

The immune system is affected by acute and chronic stress, and the immune system, the brain and the endocrine system reciprocally influence each other. Changes in the immune system with an increase in the pro-inflammatory and a decrease in the anti-inflammatory parts are reported in both anxiety and depression [58, 59]. Cytokines, the signaling molecules of the immune system, activate specific receptors on neurons and glial cells and thereby directly influence brain function [1]. Cytokines also affect brain function by activating the hypothalamus and the HPA axis and by modulating the release of monoamines. Increased levels of pro-inflammatory cytokines are associated with impaired sleep, anorexia, decreased libido and social interaction, which are common symptoms of emotional disorders [1]. Furthermore, it is reported that patients who are treated with the pro-inflammatory cytokine interferon (INF) α for hepatitis or cancer may develop symptoms of anxiety and depression, anorexia and impaired sleeping [1, 60].

The hypercortisolism and inflammatory changes associated with chronic stress may cause secondary changes in the structure of the brain [1]. Chronic elevated levels of cortisol damage hippocampal neurons, which could explain the volumetric decreases in the hippocampus that are frequently observed in depressed individuals [36]. Pro-inflammatory cytokines contribute to structural changes by mediating

neurodegeneration and by reducing the synthesis of neurotrophic factors such as BDNF, leading to reduced neuronal repair [1].

It is hypothesized that the symptoms of ADHD may be related to disturbances in the dopamine and noradrenaline systems in the prefrontal cortex [38]. Both conduct problems and attention problems have been linked to low responsiveness in the HPA axis and the autonomic nervous system, as indicated by low cortisol levels, low heart rate and low heart rate variability [11, 61].

1.4.4 Environmental factors

Stress may be defined as any internal or external environmental change that disturbs homeostasis [1]. While mild to moderate stress may enhance functioning, severe stress is an accepted risk factor for emotional symptoms [52]. Stressors may be physical as well as psychosocial. An example of a physical stressor is maternal smoking during pregnancy, which affects the physical environment of the foetus and is associated with increased anxiety and depression in adolescence [62, 63]. Preterm birth, prenatal exposure to smoking, alcohol or substance misuse or environmental toxins such as organophosphate pesticides and lead are associated with attention and behavioural problems and cognitive difficulties [42, 64].

Psychosocial events that are associated with an increased risk for developing emotional symptoms and disorders include a wide range of factors such as emotional neglect, sexual or physical abuse, the death of parents or parental conflicts and divorce [44]. Exposure to multiple risks may be particularly harmful [65]. In a retrospective study, childhood adversities were estimated to account for approximately 30 % of all adolescent emotional disorders [66]. Furthermore, children of parents with depressive or anxiety disorders have a substantially increased rate of emotional disorders compared to children of healthy parents [35, 44, 67]. In addition to genetic inheritance, non-inherited environmental factors may contribute to this increased risk. This can apply to the

parent's modelling of anxious or depressive behaviour, affect and cognition or more negative parenting behaviour with less responsiveness [68].

Individuals may have different vulnerabilities to the potential pathological effects of adverse life events. Gene-environment interactions occur when the effect of an environmental risk factor is moderated by variation in specific genes [52]. An example of this was first shown by Caspi et al. These researchers found that individuals who had one or two copies of the short allele of 5-HTTLPR had more depressive symptoms, diagnosable depression and suicidality in relation to stressful life events than individuals with two long alleles [45]. There was no main effect of the genotype without the environmental stressor, and there was only a small main effect of the environmental stressor without the genotype. Individuals who have experienced earlier episodes of depression may have an increased vulnerability in that less stress is required to trigger a new episode of depression [55]. Expanding this hypothesis, early childhood adverse events also may sensitize the individual to later stress [55]. This relationship may be mediated by epigenetic effects. The findings of increased levels of pro-inflammatory cytokines and the down-regulation of GR expression associated with adverse life events in childhood support this hypothesis [69]. Some developmental phases are likely more sensitive to environmental influences than others, such as the pre- and neonatal periods and adolescence [70].

Cognitive theories on depression suggest that individuals with negative cognitions will have a tendency to attribute negative events to stable and global causes, to assume future negative consequences and to view the negative event as an indication of lowered self-worth [71, 72]. This theory suggests an interaction between stress and a negative cognitive style that leads to depressive symptoms [71, 72].

Interpersonal theories emphasize the importance of a secure child-parent attachment. Insecure attachment is associated with symptoms of anxiety and depression in

adolescence [73]. Emotional symptoms in adolescence are associated with adolescent-parent communication problems and conflicts and certain parenting styles (overprotection, coldness or rejection) [35, 74]. However, this may be a bidirectional relationship as depressed adolescents may themselves contribute to conflicts in interpersonal relationships [74]. Rejection by family or peers and bullying also represent psychosocial stressors that are associated with increased levels of emotional symptoms in adolescents [68, 74, 75].

Low socioeconomic status at birth is one of the strongest and most consistent risk factor for conduct problems in adolescence [40]. In addition, a parent-child relationship with minimal involvement, maltreatment, having a parent convicted of a crime, low peer popularity and few social activities are associated with conduct problems [49, 67], while maltreatment and extreme early deprivation are associated with ADHD [67].

Hence, a wide range of psychosocial stressors may contribute to the development of emotional symptoms in adolescence. Previously experienced stressors as well as genetic differences may make some individuals more vulnerable than others.

1.5 Prevalence of emotional symptoms in adolescence

Anxiety disorders and depression are two of the most common psychiatric disorders in adolescence, with a point prevalence of 11% and 6 % respectively, according to diagnostic interviews [76]. The prevalence of anxiety and depression is typically higher when subclinical symptoms are included [77]. Subclinical disorders may be understood as milder versions on a continuum of symptoms rather than qualitatively different conditions [35, 78, 79]. Indeed, subthreshold anxiety and depression was associated with a substantial burden and suicide risk [77]. Subthreshold depression was found to have the same risk factors as major depressive disorder in two recent reviews [80, 81]. The prevalence of self-reported symptoms of anxiety and depression was 13.2% and 14.2 %, respectively, in a population of Australian adolescents [9]. Other studies have

shown even higher rates of adolescents reporting symptoms above the cut-off point for clinically significant emotional symptoms [10, 82]. In a study of Norwegian adolescents, 8.8-13.1% of boys and 25.8-33.8% of girls reported symptoms of anxiety and depression [10].

ADHD and CD, including oppositional defiant disorder were estimated to occur in approximately 3-4% of adolescents in a review by Costello et al [76]. In more recent review, the global prevalence in the ages 5-19 years was 2.2% for boys and 0.7% for girls for ADHD and 3.6% for boys and 1.5% for girls for CD [83].

1.5.1 Sex and age differences

The prevalence of emotional symptoms increases with increasing age during adolescence [6-8]. While symptoms of anxiety are more common in girls than in boys even at an early age, depressive symptoms and disorders occur at approximate the same rate in preadolescent boys and girls [11]. However, during early to middle adolescence, the rate of depressive symptoms and disorders in girls rises by two to three times that of boys, resulting in a female:male ratio of 2:1 that continues throughout adult life [8, 11, 74, 84, 85]. Attention and conduct problems typically have a childhood onset and show a male preponderance, with 3-4 times as many boys as girls being affected [11, 39].

Several theories have been proposed to explain the sex difference and the marked increase in the prevalence of emotional symptoms and disorders in adolescence. Adolescence is characterized by the pubertal transition involving rapid physical, intellectual, hormonal and social changes. The individual must cope with the pressure of forming an identity, separating from parents, handling emerging sexuality and making important decisions about education and future careers [86]. All these events could serve as stressors for the individual and increase his/her risk of developing emotional symptoms [86]. During adolescence, the brain must adjust to hormonal changes with a dramatic increase in androgens, such as testosterone for boys; and oestrogens, such as

oestradiol and progesterone, for girls [11, 85]. Oestrogen increases the stress response in the prefrontal cortex in animals, whereas androgens inhibit CRH production in the hypothalamus and thereby decrease the stress response in males [85, 87]. Evidence of an increased cortisol response to CRH with increasing Tanner stages in girls, but not in boys, suggests that a similar mechanisms may be present in humans [88]. Oestrogen may also modulate mood by affecting the brain's neurotransmitter systems, for example, by regulating the concentration of serotonin [85].

According to psychosocial theories, girls are more cognitive vulnerable to depression than boys [84]. Girls are more prone than boys to doubt themselves and their problem-solving abilities and hence view their problems as insolvable [84, 89]. Different ways of reacting to stress, such as girls' more frequent use of rumination and boys' more frequent use of distraction, have also been suggested to account for the gender difference; rumination leads to reflection on depressive symptoms, whereas distraction leads to avoidance of exploring these feelings [86]. It has also been suggested that girls more frequently experience negative life events such as sexual abuse or negative social experiences than boys and therefore are more prone to develop depressive symptoms [90]. Additionally, the Western idealization of a slim body may be a psychosocial stressor for adolescent girls, who tend to increase in weight and body shape during adolescence, whereas boys more often become taller and thinner during puberty. Body dissatisfaction has been found to be associated with depression in numerous studies [8, 91, 92].

The same environmental stressor may also affect boys and girls differently. Maternal depression is reported to have a long-term effect on the later development of depression in girls, but not in boys [93]. Girls more often develop depression when exposed to family conflicts or interpersonal conflicts than do boys [11]. It is likely that the rising prevalence and profound sex difference in psychiatric symptoms in adolescence can be explained by a combination of hormonal changes, psychosocial factors and epigenetic mechanisms.

1.5.2 Time trends

Due to changes in assessment methods, it is difficult to make conclusions concerning trends in the prevalence of symptoms of anxiety and depression over time [67]. In a meta-analysis by Costello et al. [94], there was no evidence of an increase in depressive disorders among adolescents between 1965 and 1995. However, more recent comparisons using identical instruments that measure emotional symptoms suggest an increase in prevalence and a decrease in age at onset of symptoms [95-98]. In Iceland, symptoms of anxiety and depression increased significantly among girls over the period from 1997 to 2006 [97], whereas in Great Britain the prevalence of emotional symptoms doubled from 1986 to 2006 [96]. In a recent systematic review, five of eight studies reported an increase in internalizing symptoms in adolescent girls, whereas the findings for boys were mixed [99].

1.6 Consequences of emotional symptoms in adolescence

Adolescents' emotional symptoms may be associated with significant distress, with social and economic consequences for the individuals, their families and society [74, 100]. For the individual, symptoms of anxiety and depression may be associated with problems in interpersonal relationships and academic achievement [74, 101]. Both emotional symptoms and disorders increase the risk for later occurrence of anxiety and depressive episodes [35, 102]. Depression is a major risk factor for suicide, which is the third leading cause of death among adolescents and young adults [103]. In addition, anxiety and depression have a high comorbidity with other psychiatric disorders, such as CD, substance use disorder and eating disorders, which may further increase the burden on the individual [74].

There are few studies on the burden that the parents or siblings of adolescents with emotional symptoms face. In general, caregivers of those who are mentally ill may experience both objective burden related to daily tasks and subjective burden such as

reduced well-being and worries [104]. As expected, the level of symptoms and degree of impairment are associated with perceived parental strain [104].

In 2010, mental and substance use disorders accounted for 7.4% of all disability-adjusted life years (DALYs) worldwide, which are calculated as the sum of the years of life lost because of premature mortality and the years lived with disability [105]. Anxiety disorders accounted for 14.6% of these DALYs, whereas depressive disorders accounted for 40.5%. The highest portion of total DALYs caused by mental and substance use disorders was in the age group between 10 and 29 years [105]. In contrast to adult mental disorders, the economic burden of mental health problems in childhood or adolescence is sparsely studied [100]. The costs associated with mental problems in adolescence include medical costs, special education or needs, burdens to the criminal justice system and social services [74]. Because emotional symptoms in adolescence may indicate life-long morbidity, the economic costs for the society in terms of the loss of work and need for health services are large.

ADHD often has a chronic course, with 30% to 50% of affected individuals reporting ADHD symptoms as adults [106]. Attention problems in adolescence are associated with poorer academic achievement, school drop-out, problems in social relationships, and substance abuse [38, 107]. Longitudinal studies have shown that conduct problems and CD are associated with crime, anti-social personality disorder, alcohol or drug abuse, unemployment, domestic violence and unstable marital relationships [108].

1.7 Lifestyle, somatic aspects and emotional symptoms in adolescence

1.7.1 Smoking, alcohol and substance use

Associations between anxiety and depression and smoking, alcohol or substance use have been reported in a number of cross-sectional and prospective studies in the last decades [16, 109-115]. According to some studies, smoking, alcohol and substance use

precedes the development of anxiety and depression in adolescence [111, 116-120]. According to others, smoking, alcohol and substance use arise as consequences of emotional symptoms [112, 114, 121, 122]. Others have suggested a reciprocal relationship [110, 123, 124].

The “self-medication hypothesis” suggests that emotional symptoms may lead to smoking or use of alcohol because of the relieving effect of these behaviours on psychological distress [112, 113, 124]. Cigarette smoke is reported to inhibit brain MAO-A, and this could explain an anti-depressant effect of smoking [125]. Further, nicotine may induce elevated mood by activating nicotinic receptors [126]. Other researchers have suggested that smoking and the use of alcohol or drugs may cause emotional symptoms, because the active substances may change monoamine transmission or reward mechanisms associated with mood regulation [109, 110, 127]. Evidence suggests that serotonin levels are inversely related to smoking in individuals with a depressive disorder [128]. Increased HPA activity and alterations in the immune system have also been suggested as a common underlying mechanism of emotional symptoms and substance use [129, 130]. Psychosocial theories emphasize that adolescents with emotional symptoms may be more prone to pressure from peers who smoke or drink or that smoking may ease social interaction with peers [111, 112]. Other scholars have argued that the associations between emotional symptoms and smoking, alcohol or drugs may be a function of underlying shared environmental or genetic risk factors [123, 131, 132].

There are few studies on the relationships between resilience factors and smoking, alcohol and substance use in adolescence. Structured style, parental supervision and family cohesion were associated with a lower probability of smoking and substance use [133, 134], whereas social competence was associated with an increased risk of smoking and the use of cannabis [134]. In a Chinese study, adolescents with high family cohesion were less likely to smoke, even if they reported higher levels of anxiety or depression, suggesting that resilience factors may attenuate the association [135].

1.7.2 Physical activity

Several studies have found that frequent physical activity is correlated with lower levels of anxiety and depression among adolescents [136-142]. However, there are also contradictive findings, with some studies reporting an association for boys only [143] or no association at all [144-146]. In a systematic review, Larun et al. concluded that physical activity appeared to have a reducing effect on anxiety and depression, but there was little evidence for the use of exercise as prevention or treatment for emotional disorders in adolescents [147].

The underlying mechanisms for the association between physical activity and symptoms of anxiety and depression are not fully understood [148]. Because depressive symptoms may include decreased energy, reduced physical activity could be a consequence of depression. It is speculated that physical activity may increase levels of neurotransmitters and thus relieve depressive symptoms or that physical activity contributes to improved mastery and physical self-worth, resulting in improved self-esteem, and consequently, decreased levels of emotional symptoms [148]. Additionally, an inverse association was reported between levels of physical activity and levels of inflammation markers such as C-reactive protein (CRP) and IL-6 [149].

Few scholars have explored the effect of resilience factors on the association between emotional symptoms and physical activity. One study found that vigorous physical activity was associated with enhanced social functioning [144]. In a study of Icelandic adolescents, individuals who attended a sports club displayed lower levels of symptoms of anxiety and depression than individuals who participated in individual sports [150]. The authors suggested that the social benefits of participating in a group, rather than the physical activity per se, may contribute to improved mental health [150]. Thus, the possible effect of resilience factors on the relationship between physical activity and emotional symptoms in adolescents should be further explored.

1.7.3 Chronic pain

Psychiatric symptoms are associated with the existence of chronic pain in adolescence [14, 151-157]. Most studies have explored the relationship between pain and emotional symptoms, but there is also evidence for an association with behavioural problems [152, 153, 158]. Although earlier studies tended to focus on specific pains (headaches, stomach pain or back pain) and their relation to emotional or behavioural symptoms, more recent research suggests that the associations rather depend on the coexistence of multiple pains [14, 159].

Emotional distress may predispose an individual for pain, be a modulating or perpetuating factor or be a consequence of pain [160]. Several studies found that emotional or behavioural symptoms preceded chronic pain in adolescents [14, 159, 161, 162]. Evidence suggests that unpleasant emotions may exacerbate the experience of pain and decrease tolerance to pain [160]. In addition, negative emotions may, through autonomic reactivity, increase muscle tension and physiological arousal, contributing to the exacerbation of symptoms and persistence of pain [163]. However, chronic pain may also lead to emotional or behavioural symptoms; adolescents with chronic pain may be anxious about having a severe disease or may be frustrated because of experiences with reduced function in daily activities [160]. This anxiety or frustration may result in depressive symptoms or aggressive behaviour and conduct problems. Pain symptoms may also interfere with the adolescent's ability to concentrate at school.

The neurobiological linkages between the brain, the spinothalamic tract, the dorsal horn and peripheral nerves provide a physiological pathway by which negative emotions and stress can amplify and prolong pain [163]. The amygdala, anterior cingulate cortex and anterior insula are involved in the pathophysiology of emotional symptoms and the perception of pain and pain unpleasantness [163]. In addition, evidence suggests that the HPA axis is involved in several aspects of pain [164] and the HPA axis is, together with

the inflammation system and the monoamine systems, suggested to be common underlying mechanisms of the co-occurrence of chronic pain and depression [165, 166]. Cytokines may interact with the HPA axis, while noradrenergic and serotonergic neurons are hypothesized to be involved in a pain-modulating circuit including the amygdala, periaqueductal grey and rostroventral medulla [166]. Additionally, antidepressants acting through both noradrenergic and serotonergic receptors have been shown to be effective in relieving pain in clinical settings [167].

Chronic pain may have a large effect on adolescents' everyday functioning and emotional symptoms are found to increase functional disability in adolescents with chronic pain [168-170]. Because most studies on the association between chronic pain and psychiatric symptoms do not include measures of the degree to which pain interferes with daily functions, the frequency of chronic pain with high disability among adolescents with emotional and behavioural symptoms has not been reported.

Evidence from some studies suggests that social support from parents and peers, together with high self-esteem and having friends, are associated with lower presence of chronic pain in adolescents [171-174]. In a study on children and adolescents with recurrent abdominal pain, social support from teachers and classmates was associated with lower levels of depressive symptoms [175]. However, there is little research on the influence of resilience factors on the association between emotional or behavioural symptoms and chronic pain in unselected populations of adolescents.

1.7.4 Pubertal timing

Pubertal timing refers to pubertal development compared to same sex and same aged peers. Early pubertal timing is associated with higher levels of emotional symptoms in adolescence for both boys and girls [13, 176, 177]. Studies have suggested that girls with early pubertal timing have an elevated risk for depressive disorder also in young adulthood [178, 179]. For late pubertal timing, the findings are more inconsistent. Some

studies suggest that adolescents with late pubertal timing have a higher occurrence of emotional symptoms than those with average pubertal timing, whereas others find this to be true only for boys [13]. Pubertal timing can be measured as *actual* timing, referring to the adolescent's physical development (measured by self-report or clinical examination) compared to peers of the same sex and age, or as *perceived* timing, referring to the adolescent's own perception of pubertal status compared to others. Most studies of the association between pubertal timing and emotional symptoms have only included one measure of pubertal timing. Actual measures do not always agree with perceived measures, which may explain some of the inconsistencies in previous research [180].

In explaining the association between off-time pubertal timing and emotional symptoms, some scholars emphasize the mismatch between physical and emotional or cognitive development in adolescents with early pubertal timing [61, 176, 181]. In adolescence, the individual must handle new social expectations and experiences, and early timers must address these stressors before they are emotionally or cognitively ready to do so [176]. Others have suggested that the feeling of being different from peers leads to psychological distress and causes symptoms of depression and anxiety [176]. The hormonal influences of puberty may cause the adolescent to be more sensitive to social and emotional experiences, resulting in disproportionate increases in negative feelings. Adolescents with off-time pubertal timing must address these feelings when the majority of their peers do not experience the same sensitivity, and this may lead to interpersonal difficulties and conflicts [176]. Social context is suggested to be critical for determining the emotional effect of pubertal timing. In a study on girls in competitive ballet schools, in which maturation typically occurs later than in the general population, girls who matured on time perceived themselves as early developers and had a higher risk for psychopathology [182].

Biological theories suggest that the steep rise in adrenal or gonadal hormones at puberty, together with age-decreasing hormone-sensitivity in the brain, may contribute

to the increased occurrence of emotional symptoms in adolescents with early or late pubertal timing [13, 176]. There is evidence that early maturing girls have higher levels of follicle-stimulating hormone (FSH) and estradiol than later maturing girls and that these hormonal differences persist into adulthood [183, 184]. In addition, a selection effect may contribute; girls with early pubertal timing have a higher risk for early pregnancies, lower education, lower income and more adverse environments [181]. Because pubertal timing is partly heritable, this selection effect causes children with earlier timing to grow up in more adverse environments. Such environments are often characterized by chronic stress, parental conflict, harsh parenting and socioeconomic adversity, and it is suggested that these factors may account for the positive association between early pubertal timing and emotional symptoms in adolescence [176, 181].

Socio-contextual factors may influence the association between pubertal timing and emotional symptoms. Experiences of early dating (girls), deviant peer affiliation (boys) and perceived parental rejection were found to increase the associations between early pubertal timing and depressive symptoms in a recent study by Benoit et al. [185]. Similarly, pubertal timing (early in girls and late in boys) was associated with concurrent or later depression only when peer relations were problematic [186]. In addition, earlier pubertal timing more strongly predicted depressive symptoms in adolescents exposed to maternal depression or to familial environments characterized by high levels of stress, than in adolescents without these risks [187]. However, as most previous studies only included actual pubertal timing, there is little knowledge about possible moderators of the associations between perceived pubertal timing and symptoms of anxiety and depression in adolescence.

1.7.5 Body mass

Although it appears to be a consistent finding that obese adults have a higher risk for emotional symptoms or disorders, findings for children and adolescents are less clear [15, 188]. Whereas some studies have reported an association [189, 190], others have found an association for girls only [191-193] or no association [194]. The mixed

findings may be a result of methodological weaknesses because most studies used self-reported weight and height rather than clinical measurements [195]. In addition, actual measures of body weight are not strongly associated with an adolescents own opinion about his or her body mass [196, 197]. Perceived body mass is repeatedly found to be more closely linked to emotional symptoms in adolescents, than actual body mass [196-198].

The association between obesity and emotional symptoms appears to be bidirectional [15, 199]. Inflammation is associated with both obesity and symptoms of anxiety and depression and is suggested to be a possible mediator of the association [200, 201]. Other scholars suggest that elevated inflammation is a consequence rather than a precursor of depression in adolescence [200]. Obesity might cause dysregulation of the HPA axis, which is also commonly found in depressed patients [201]. Dysregulation of the HPA axis may increase obesity because cortisol, in the presence of insulin, inhibits lipid-mobilizing enzymes [15]. Additionally, a genetic vulnerability to both depression and obesity has been suggested [202]. Furthermore, adverse childhood experiences as neglect or abuse are associated with both emotional symptoms and obesity [202]. In addition, depression may lead to reduced physical activity, resulting in weight gain [201], or the use of antidepressants may contribute to excess body weight [15]. Because thinness is considered the beauty ideal in Western countries, being overweight may negatively affect an individual's self-esteem and lead to emotional symptoms [15]. Obese adolescents may experience stigmatization and social isolation [203, 204].

Poor family functioning was associated with an increased risk for overweight and obesity in children and adolescents in a recent systematic review [205]. Poor communication, poor family cohesion, high levels of conflict and low familial hierarchy were aspects of family functioning that were associated with increased weight in children and adolescents. Few studies have explored the effect of resilience factors on the association between body mass and emotional symptoms in adolescents. In a study of obese children and adolescents, social support was an important predictor of

psychosocial functioning, as measured by weight-related quality of life [206]. The role of resilience in relation to perceived body mass and emotional symptoms in unselected populations of adolescents has been sparsely studied.

1.8 Resilience

1.8.1 Individual level

Resilience factors at the individual level may include factors such as intelligence, adaptive temperament, personal talent or skills, social competence and self-esteem [27, 29, 207, 208]. Social competence refers to the perceptions of one's own ability to engage in effective social interactions [71]. High social competence is found to be associated with fewer interpersonal conflicts [71] and lower levels of emotional symptoms in adolescents [71, 209, 210].

Self-esteem refers to an individual's general sense of worth or abilities and is consistently reported to be inversely associated with emotional symptoms in a number of studies [211-214]. Several theories attempt to describe the inter-relationship between depression and self-esteem; indeed, low self-esteem or feelings of worthlessness is one of several criteria that is used to diagnose depression [17, 24]. Depressive episodes may damage close relationships or social networks that play an important role in developing a positive self-esteem [215]. Other scholars suggest that individuals with low self-esteem may excessively seek reassurance from others and thereby increase their risk of being rejected [215]. Additionally, individuals with low self-esteem may seek negative feedback to confirm their own negative self-concept, or they may avoid social interaction or engage in anti-social behaviour [215]. Rejection, negative feedback and poor interpersonal relations may all lead to emotional symptoms. Some researchers have suggested that self-esteem and depression are one common construct. However, moderate correlations, varying stabilities across life-span and diverse genetic influences contradict this hypothesis [215]. Resilient adolescents are observed to have higher

levels of self-esteem than less resilient adolescents, and several authors include self-esteem as a measure of resilience factors at the individual level [27, 134, 216, 217].

1.8.2 Familial and external social level

Whereas, resilience factors at the familial level may include positive parent-child attachments, positive relationships with parents and family cohesion, resilience factors at the external social level may include positive relationships with teachers or peers or characteristics of the school or neighbourhood [27, 29, 207, 208]. Social support, defined as the support that is accessible to an individual through social ties with other individuals, groups and the larger community, appears to be a particularly important resilience factor and may be measured both at the familial and external social levels [218].

Family cohesion refers to a feeling of connectedness and togetherness in the family [219] and high levels of family cohesion is related to resilience and lower levels of emotional symptoms in adolescents [29, 219-222]. Having a stable living situation, and living with both parents are also related to resilience [223]. As emphasized in a review by Olsson et al., the family remains the primary social arena for many adolescents and appears to be important for adolescents' resilience [29]. In fact, for adolescent girls, a lack of parental support was found to predict depression even in the presence of peer support [71]. Ge et al. found that closeness with mothers, but not with fathers, moderated the effects of both personal and family negative life events on subsequent depressive symptoms in adolescents [224].

Positive relationships and social support from peers, as well as seldom feeling lonely are associated with lower levels of emotional symptoms in adolescents [211, 225-229]. Loneliness may be a marker of perceived inadequate social relations [230] and thus, may be used as an indirect measure of external social support. There has been increasing interest in research which may contribute to understand the effect of social

support on medical and psychiatric morbidity and the neurobiological mechanisms involved in these processes. Kaufman et al., showed that social support buffered the increased risk for depression in maltreated children with the short allele of 5-HTTLPR [231]. Evidence from animal research shows that social bonding may buffer stress-induced activation of the HPA axis and the immune system [232]. It is suggested that oxytocin facilitates social bonding and may suppress the HPA axis reactivity to stressors in humans [218]. Furthermore, social support was found to attenuate the increase of CRP associated with adverse childhood experiences [233]. Finally, social support contributes to better coping strategies when facing a stressor [234, 235].

1.9 Socioeconomic status

Socioeconomic status (SES) is a combined measure of an individual's or family's position in relation to others concerning work experience, economy and social position; and it is typically measured according to an individual's income, occupation and/or education. In a recent review, 52 of 55 studies found an inverse relationship between SES and mental health problems in children and adolescents [236].

In Nordic countries, the social differences are less pronounced. However, according to studies in Finland and Sweden, low parental education, parental manual occupation and low social position were associated with increased emotional symptoms in adolescence, suggesting that this association is present even in countries with small social differences such as Norway [237, 238].

The effect of low SES is proposed to be caused by chronic stress due to economic difficulties, adverse environment and family disruption [74]. In addition, low SES may decrease parents' ability to afford, demand and receive good health care for their children [238].

2. Aims of the thesis

The overall aim of this thesis was to explore the associations between emotional symptoms and lifestyle, as well as somatic aspects in adolescent girls and boys. A second aim was to explore the possible effects of resilience factors on these associations. More specifically, the main aims of this thesis were as follows:

Paper I:

- To assess the prevalence of symptoms of anxiety and depression according to sex and age in a large population of non-clinical adolescents.
- To explore the associations between emotional symptoms and lifestyle factors such as smoking, use of alcohol, having tried illegal drugs and frequency of physical activity.
- To explore the associations between emotional symptoms and resilience factors such as social competence, family cohesion, relationships with family members and number of friends.
- To investigate whether resilience factors such as social competence and family cohesion attenuated the associations between emotional symptoms and lifestyle factors.

Paper II:

- To assess the prevalence of chronic multisite pain with high disability in adolescent girls and boys with symptoms of anxiety and depression, social anxiety, conduct or attention problems.
- To assess the prevalence of chronic multisite pain according to resilience factors such as social competence, self-esteem, family cohesion and loneliness.
- To explore whether resilience factors could attenuate the associations between emotional or behavioural symptoms and chronic multisite pain.

Paper III:

- To explore the associations between actual and perceived pubertal timing and symptoms of anxiety and depression.
- To explore the associations between actual and perceived body mass and emotional symptoms.
- To explore the possible moderating effect of resilience factors such as social competence, family cohesion and loneliness on the associations between emotional symptoms and pubertal timing and body mass.

3. Material and methods

3.1 Data material

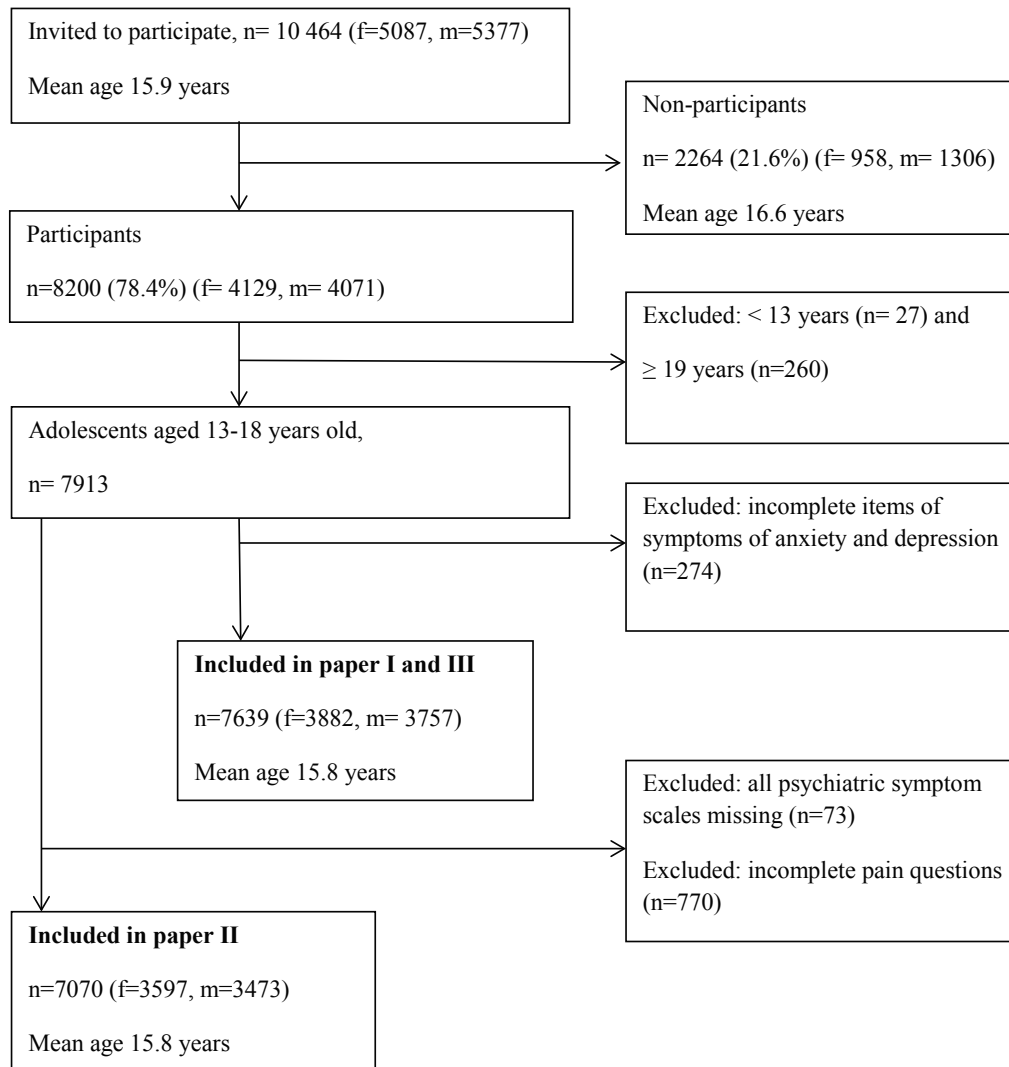
The papers included in the thesis are all based on data from the youth part of the third survey of the Nord-Trøndelag Health Study (Young-HUNT 3). In all papers we included additional data on parents' income and education, as provided by Statistics Norway.

3.1.1 Study design

The Nord-Trøndelag Health study (HUNT) is a large cross-sectional population based health study in the county of Nord-Trøndelag, Norway. This county is situated in the middle of Norway and has a stable population of approximately 134 000 inhabitants. The county is mostly rural, without large cities, but is fairly representative of Norway regarding demographic variables [239]. The HUNT study consists of three surveys that were conducted in 1984-86 (HUNT 1), 1995-97 (HUNT 2) and 2006-08 (HUNT 3) [240]. HUNT 1 included only adults aged 20 years or older, whereas HUNT 2 and 3 also included adolescents aged 13 to 18 years in a youth part of the study: Young-HUNT. The Young-HUNT 3 study was conducted between October 2006 and June 2008, and all adolescents aged 13 to 18 years old in the county were invited to participate. The adolescents completed a questionnaire on health- and lifestyle-related issues during a school hour in an exam-like situation. Within a month after the questionnaire, the adolescents underwent a clinical examination that included measurements of weight, height, waist and hip circumference, heart rate and blood pressure and buccal smears for genetic analyses. Adolescents who were absent from school on the day of the questionnaire were encouraged to complete it on the day of the clinical examination performed by nurses in each school. Adolescents who did not attend school received a letter of invitation and the questionnaire by post.

3.1.2 Study population

Of the 10 485 adolescents invited to participate in the Young-HUNT 3 study, 8200 (78.4%) completed the questionnaire and 7716 (73.7%) also underwent the clinical examination. The main reasons for not participating in the survey were being absent from school, failing to return a written consent from parents or not wanting to participate. The adolescents who did not participate in the study were older (mean age 16.6 versus 15.9 for participants) and more often boys (57.7% versus 49.6%) than those who participated [239]. In the papers of the thesis, adolescents younger than 13 years and older than 19 years were excluded because of their low numbers (n= 27 and n=260). Adolescents with missing or incomplete outcome variables were also excluded. Thus, the study population for papers I and III consisted of 7639 adolescents, and the study population for paper II consisted of 7070 adolescents. This is illustrated in the flow chart in Figure 1.



f = female, m = male

Figure 1. Flow chart of adolescents included in Paper I-III

3.2 Study measures

3.2.1 Emotional and behavioural symptoms

Symptoms of anxiety and depression

The questionnaire included a five-item shortened version of the Hopkins Symptom Checklist (SCL-25), a commonly used instrument to measure symptoms of anxiety and depression. The five-item version, SCL-5, has been translated and validated in a Norwegian population from the age of 16 [241]. The SCL-5 has been shown to correlate well ($r=0.92$) with the SCL-25 [241]. The SCL-5 consists of five phrases: “During the last 14 days; I have been constantly afraid and anxious; I have felt tense or uneasy; I have felt hopeless about the future; I have felt dejected or sad; I have worried too much about various things”. There are four responses ranging from “not bothered” (1) to “very much bothered” (4). A mean cut-off value of SCL-5 > 2.0 indicates adolescents with symptoms of anxiety and depression in a clinical range, i.e. those who have the highest probability of having a clinical diagnosis of anxiety and depression [242]. The internal consistency of the SCL-5, as measured by Cronbach’s alpha, was 0.83 in the present study.

Social anxiety

Symptoms of social anxiety were measured by a six-item version of the Social Phobia and Anxiety Inventory for Children, SPAI-C. The original SPAI-C consists of 26 items and has adequate validity, internal consistency and reliability [243]. The six items included in the HUNT questionnaire were: “How often do you experience these reactions; I feel anxious and don’t know what to do in an embarrassing situation; I feel anxious when I am with others and I have to do something while they watch me do it (ex. be in a play, play music, sports); I feel anxious when I have to speak or read aloud in front of a group of people, Before I go someplace where I’m going to be with people (ex. a party, school, football game) I sweat, my heart beats fast and/or I get a headache or stomach ache; Before I go to a party or someplace with other people I think about what could go wrong (ex. that I make mistakes, seem dumb and/or... what if they see how frightened I am!); I feel anxious and don’t know what to do when I’m in a new

situation”. The responses were “never” or “hardly never” (0), “sometimes”/ “most of the time” (1) or “always” (2). The Cronbach’s alpha for the SPAI-C in this study was 0.84.

Attention and conduct problems

The questionnaire included 16 items on school-related functioning that were designed by the Norwegian Institute of Public Health and have been used in several previous studies [244-246]. A principal component analysis with an oblique rotation was performed and identified “conduct problems” and “attention problems” as two independent factors. Attention problems included the following items: “have difficulties concentrating in class”; “skip school”; “cannot manage to be calm or sit still during class”; and “become bored or dissatisfied”. Conduct problems included the following items: “argue with the teacher”; “have fistfights”; and “am reprimanded by the teacher”. All the items had four alternative responses ranging from “never” (1) “to very often” (4). The Cronbach’s alpha value was 0.69 for both conduct problems and attention problems.

Categorization

In paper II the four groups of psychiatric symptoms (symptoms of anxiety and depression, social anxiety, attention and conduct problems) were categorized into four levels according to the distribution of responses in the study population. Because the cut-off value for SCL-5 (mean value >2.0) corresponded to above the 85th percentile, we defined a high scorer group in each category of psychiatric symptoms as the mean value $>85^{\text{th}}$ percentile. Below the 85th percentile, we set two cut-off points for the purpose of obtaining a substantial number of observations in each category, resulting in four levels of symptoms: 0-45, 46-60, 61-85 and > 85 percentiles.

3.2.2 Lifestyle

Smoking

The questionnaire included several items on smoking. The items used in our study included “Have you tried smoking?” (response alternatives “no” or “yes”) and “Do you smoke?” (“no, I don’t smoke”, “no, not anymore, but previously I smoked daily”, “no, not anymore, but previously I smoked occasionally”, “yes, I smoke occasionally, but not daily” and “yes, I smoke daily”). Adolescents were categorized as “current smokers” if they reported to smoke daily or occasionally. Adolescents who reported that they had never tried to smoke, that they did not smoke or that they had smoked previously, but not now were categorized as “non-smokers” in line with previous studies using these smoking variables [247, 248].

Alcohol

Items on alcohol included “Have you ever tried drinking alcohol?” (response alternatives “no”, “yes” and “don’t know”), “If yes, do you sometimes drink alcohol now?” (“no” or “yes”) and “Have you ever drunk so much alcohol that you felt intoxicated (drunk)?” (“no, never”, “yes, once”, “yes, 2-3 times”, “yes, 4-10 times”, “yes 11-25 times and “yes, more than 25 times”). Adolescents who reported that they sometimes drank alcohol presently were categorized as “current alcohol users”, while those that reported that they never had tried alcohol or that they did not drink alcohol presently were categorized as “non-users of alcohol”. The number of self-reported alcohol intoxications was categorized in three levels, in line with previous studies [246, 249]: “never been drunk”, “been drunk 1-10 times” and “been drunk 11 times or more”.

Drugs

The questionnaire included one item regarding illegal drugs: “Have you ever tried hash, marijuana or other drugs?” (response alternatives “no” or “yes”).

Physical activity

Physical activity was recorded with the following question: “Not during the average school day: How many days a week do you play sports or exercise to the point where you breathe heavily and/or sweat?” (response alternatives: “never”, “less than once a month”, “less than once a week”, “1 day a week”, “2-3 days a week”, “4-6 days a week” and “everyday”). The question was adopted from the World Health Organization Health Behaviour in School-aged Children study (WHO HBSC) [250] and is shown to correspond well with cardiorespiratory fitness among adolescents [251]. As in previous studies the responses were grouped into three levels of physical activity: once a week or less, 2-3 days a week and 4 days a week or more [247, 249, 252].

3.2.3 Pain

Adolescent pain

In the questionnaire the adolescents were asked about headache/migraine, abdominal pain and musculoskeletal pain in the following locations: neck/shoulder, upper back, low back/buttocks, chest, upper and/or lower extremities. The pain should not be related to any known disease or injury. Response alternatives were “never/seldom”, once a month”, “once a week”, “more than once a week” and “almost every day”. The pain questions were adapted from Mikkelsen et al. [253] and have shown adequate validity and reliability [156, 253]. Chronic non-specific pain was defined as pain not related to any known disease or injury, for at least once a week, during the last three months [254].

Disability

An adapted form of the subjective disability index by Mikkelsen et al. [254] was included in the questionnaire to measure in which extent the pain restricted the adolescent’s daily life. The adolescents were asked to respond to the following four phrases: “Pain makes it difficult to fall asleep and/or pain disturbs my sleep at night”; “Pain makes it difficult to sit in class”, “Pain makes it difficult for me to walk more than

one kilometer”; “Because of pain I have problems in gym class”. In the HUNT questionnaire the fifth statement in the original disability index, “pain disturbs my hobbies”, was converted to a question: “All things considered, has pain made it difficult to do daily activities in leisure time?” All items had alternative responses “no” or “yes”. The subjective disability index was calculated by summing the responses to the four statements and the fifth additional question, and was categorized in three levels: low (0), moderate (1-2) and high (3-5) disability [249, 255, 256]. The adapted form of the disability index has been approved for use by Mikkelsen.

Chronic multisite pain

We defined chronic multisite pain as chronic non-specific pain in three or more locations with a high disability index.

Use of pain relieving medicine

The adolescents were asked how often in the last three months they had taken non-prescription medicine for headache, muscle/joint pain, back pain, stomach pain or other pain. The answer alternatives were “never”, “1 day a week or more”, “2 days a week or more”, “3 days a week or more” and “4 days a week or more”. We summed the responses to all locations of pain and categorized the response in two levels according to the frequency of use of non-prescribed pain killers: “never to once a week” and “twice a week or more”.

3.2.4 Pubertal timing

Actual pubertal timing was measured by four questions from the Pubertal Development Score (PDS) [257]. The PDS is a widely used measure of secondary sex characteristics and has demonstrated adequate reliability and validity [257, 258]. All adolescents were asked to rate themselves regarding growth spurts and pubic hair growth. Girls were asked about menarche and breast development, whereas boys were asked about changes in voice and facial hair growth. One of the questions of the original PDS concerning

skin changes was not included in the questionnaire. The assessment of skin changes has been found to be a less reliable measure of pubertal onset than other maturational characteristics [257]. For all the items in the PDS, the responses ranged from “have not begun” (1) to “development completed” (4), except for menarche, which had response alternatives of “no” (1) and “yes” (4). A total PDS-score was obtained by summing the responses from all four items. The PDS-scores were categorized according to an age- and sex-specific distribution, and adolescents in the lower quintile were classified as “late” and the adolescents in the upper quintile were classified as “early” [259]. Adolescents with PDS-scores between the 20th and the 80th percentiles were classified as “on time”.

Perceived pubertal timing reflected the adolescents’ own evaluation of his or her pubertal development compared to others of same age and sex, and was measured by the following question, as recommended and validated by Dubas et al. and used in several previous studies [180, 259, 260]: “When you look at yourself, do you think that you are physically maturing/have physically matured earlier or later than others your own age?”. The seven alternative responses were categorized into three groups: “early” (“much earlier”, “early”, “a little bit earlier”), “the same as others” and “late” (“a little bit later”, “later”, “much later”).

3.2.5 Body mass

Actual body mass, or body mass index (BMI), was calculated as weight in kilograms divided by the squared value of height in meters (kg/m^2). Height and weight were measured by trained nurses using internally standardized meter measures and weight scales. The participants wore light clothes and no shoes. The BMI cut-off points for being thin ($\text{BMI} \leq 18.5$ at age 18), overweight ($\text{BMI} \geq 25$ to 30 age 18) and obese ($\text{BMI} \geq 30$ age 18) were defined according to international cut-off points for age and sex [261, 262]. For example, the cut-off point for obesity at age 13 was 26.84 for boys and 27.76 for girls [261].

Perceived body mass was assessed by the following question, which has been used in several previous studies [197, 263]: “Do you consider yourself very thin, thin, about the same as others, chubby or very fat?” In the regression analysis the responses were categorized into three levels: “thin” (very thin and thin), “as others” and “fat” (chubby and very fat).

3.2.6 Resilience

Social competence and family cohesion

Eight items from the Resilience Scale for Adolescents (READ) were included in the questionnaire. The READ is developed and validated by Hjemdal et al., and consists originally of 28 items measuring five factors: personal competence, social competence, structured style, family cohesion and social resources [27]. The HUNT questionnaire included items from social competence and family cohesion. Social competence was measured by the following four statements: “I easily make others feel comfortable around me”; “I easily find new friends”; “I am good at talking to new people” and “I always find something good to talk about”. Family cohesion was measured by the four statements: “In my family we share views of what is important in life”; “I feel comfortable with my family”; “My family view the future as positive, even when very sad things happen” and “In my family we support each other”. Each item had five alternative responses ranging from “I totally disagree” (1) to “I totally agree” (5). Cronbach’s alpha was 0.82 for social competence and 0.86 for family cohesion in this study population.

Self-esteem

Self-esteem was measured by four items from the Rosenberg Self-Esteem scale (RSE) [264]. The RSE is one of the most widely used instruments measuring self-esteem [265]. It originally consists of ten items and has shown adequate validity and reliability [265]. The following phrases were included in the HUNT questionnaire: “I take a

positive attitude toward myself”, “I certainly feel useless at times”, “I feel I do not have much to be proud of”, “I feel that I am a person of worth, at least on an equal plane with others”. The alternative responses ranged from “strongly disagree” to “strongly agree”, (valued from 1 to 4). Cronbach’s alpha was 0.77 for the self-esteem items.

Loneliness

Loneliness was measured by the question “Do you often feel lonely?” with the following response alternatives: “very often”, “often”, “sometimes”, “seldom” and “very seldom/never”.

Relationships

The HUNT questionnaire also included questions about relationships with family and friends. Adolescents’ number of friends was measured by the question “About how many close friends do you have?” with alternative responses “none”, “one” and “two or more”. Family relationships were assessed with the question “How good is the relationship you have with your immediate family?” with separate responses for father, mother and siblings ranging from “very bad” (1) to “very good” (4). Adolescents’ living situation was recorded with the question “Who do you currently live with?” (response alternatives “mother”, “father”, “1-2 siblings”, “3 or more siblings”, “mothers new husband/father”, “father’s new wife/partner”, “foster parents”, “adoptive parents”, “grandparents/other”, “spouse/partner”, “friends” and “alone/in a rented room”) and classified as “living with both parents” or “not living with both parents”.

3.2.7 Socioeconomic status

Socioeconomic status was assessed by the gross income of both parents and the total years of education of mother and father. All HUNT data is linked with the unique personal identification number given to all Norwegians at birth. This made it possible to link the adolescents’ response on the questionnaire with parental data on education and income, provided by Statistics Norway. Gross income (summed income of mother and

father) and total years of education for mother and father (separate variables) were included separately as continuous variables in the analysis.

3.3 Ethics

Participation in the Young-HUNT study was voluntary and all participants signed a written informed consent to take part in the study. For adolescents less than 16 years of age, parents also gave their written consent. The consent included acceptance of linking the data from the questionnaires with data from other national registers. The Young-HUNT study was approved by the Norwegian Data Inspectorate, the Regional and National Committees for Medical and Health Research Ethics, and the Norwegian Directorate of Health. The study protocol and the use of data in the present study were approved by the Regional and National Committees for Medical and Health Research Ethics and the Norwegian Data Inspectorate (N.ref 4.2007.2258).

3.4 Statistical methods

In paper I, descriptive statistics were reported for the SCL-5 scores in relation to age, gender and resilience and lifestyle factors. To investigate the factor structure of the school adjustment items, a principal component analysis (oblique rotation) was used. The associations between lifestyle factors and SCL-5 scores were analysed using a multiple logistic regression with high/low SCL-5 scores as the dependent variable. We adjusted the analyses for the potential confounders of age and parental SES. In the second regression-model, we also adjusted for READ social competence and READ family cohesion to investigate the possible attenuating effect of these variables. In paper II, a descriptive analysis was performed for the prevalence of pain in relation to emotional or behavioural symptoms and resilience factors. The associations between emotional/behavioural symptoms and chronic multisite pain were analysed using a multiple logistic regression with chronic multisite pain with high disability as the dependent variable. We adjusted the analyses for age and SES. In the second regression model, we first separately included READ social competence, READ family cohesion, self-esteem and loneliness, and then all resilience factors together, to investigate the

potential attenuating effects of these variables. We finally included a total regression model with all the covariates to investigate the possible coexistence of emotional/behavioural symptoms. In paper III, we used linear regression models with SCL-5 scores as dependent variables, and actual and perceived measures of pubertal timing and body mass were included separately as categorical covariates. The moderating roles of social competence, family cohesion and loneliness were examined by including product terms with pubertal timing and body mass. For all papers, separate analyses were conducted for boys and girls. The data were analysed with SPSS for Windows (SPSS Inc., Chicago, IL) 19 (paper I and II) and 21 (paper III). For the estimation of exact confidence intervals for the proportion of participants with high scores on SCL-5 in relation to lifestyle (paper I) or chronic pain in relation to emotional/behavioural symptoms (paper II), we used STATA for Windows, version 11 (STATA Corp, College Station, TX).

4. Main results

Paper I: Resilience, lifestyle and symptoms of anxiety and depression in adolescence: the Young-HUNT study.

The prevalence of symptoms of anxiety and depression above the threshold value was 13% for the total population: 19% for girls and 6% for boys. The prevalence increased substantially with age, and the sex difference remained at all ages.

High levels of social competence or family cohesion, living with both parents, having a good/very good relationship with parents or having two or more friends were associated with a lower prevalence of symptoms of anxiety and depression, with odds ratios (ORs) ranging from 0.2 to 0.6. Current smokers and adolescents who reported drinking alcohol or having ever tried illegal drugs had a higher occurrence of emotional symptoms than adolescents who did not use these substances, with ORs ranging from 1.2 to 4.0.

Adjusting for socioeconomic factors moderately attenuated the associations. Additional adjusting for social competence strengthened the associations for both girls and boys, whereas adjusting for family cohesion had the opposite effect and attenuated the associations. Low levels of physical activity were associated with an increased prevalence of symptoms of anxiety and depression: OR for girls, 1.7 (95% CI: 1.3-2.1); OR for boys, 1.8 (95% CI: 1.2-2.5). Adjusting for social competence and family cohesion had an attenuating effect, and when adjusting for these resilience factors together, the associations were attenuated to a non-significant level for both girls and boys. In conclusion, our findings suggest that emotional symptoms frequently occur in adolescents, unfavourable lifestyle factors are associated with increased levels of emotional symptoms and resilience factors have substantial effects on these associations.

Paper II: Chronic multisite pain in adolescent girls and boys with emotional and behavioural problems: the Young-HUNT study.

The prevalence of chronic multisite pain with high disability increased with increasing scores of emotional or behavioural problems. High levels of symptoms of anxiety and depression were associated with the highest prevalence of chronic multisite pain, which affected 31.0 % of girls and 19.0% of boys in these groups. For adolescents with high levels of social anxiety, conduct problems or attention problems, the prevalence of chronic multisite pain ranged from 22.8% to 30.9% for girls and 8.8% to 12.8% for boys. The prevalence of multisite pain was found to increase with an increasing total score of emotional and behavioural problems (range 4-16), reaching a prevalence of 44.1% in girls and 21.6% in boys for a total symptom score greater than 9.

High levels of social competence, family cohesion, self-esteem and never/seldom feeling lonely were associated with a lower prevalence of chronic multisite pain. The OR for chronic multisite pain was 12.8 (95% CI 8.7-18.9) among girls and 15.4 (95% CI 8.8-27.0) among boys with high levels of symptoms of anxiety and depression. For adolescents with high levels of social anxiety, conduct or attention problems, the OR for chronic multisite pain ranged from 3.6 to 8.4 for girls and from 3.6 to 9.6 for boys compared to adolescents with low symptom scores. Separate analyses for each resilience factor showed a particularly strong attenuating effect of never/seldom feeling lonely. When adjusting for all resilience factors, the associations between emotional or behavioural symptoms and chronic pain were substantially attenuated, and for symptoms of anxiety and depression or attention problems the ORs were reduced by more than 50%. When including all psychiatric symptom groups in the model, the associations were further attenuated. However, all high score groups remained significantly associated with chronic pain, except for conduct problems in girls and attention problems in boys. In conclusion, chronic multisite pain with high disability was frequently occurring in adolescents with high scores of emotional and behavioural symptoms. The results suggest that resilience factors may possibly protect adolescents from experiencing chronic pain.

Paper III: Pubertal timing, body mass and the moderating effect of resilience factors during adolescence: the Young-HUNT study.

Perceived pubertal timing and actual and perceived body mass were associated with emotional symptoms in adolescent boys and girls. Symptoms of anxiety and depression increased with increasing actual body mass. For perceived pubertal timing and perceived body mass, a u-shaped relationship with emotional symptoms was identified. After adjusting actual and perceived measures for one another, only the perceived measures remained significantly associated with symptoms of anxiety and depression.

Early and late perceived pubertal timing was significantly associated with increased levels of emotional symptoms. For girls, an interaction effect was found between early pubertal timing and feeling lonely: early pubertal timing was associated with emotional symptoms only for girls who often/very often felt lonely. For boys, an interaction effect was found between late pubertal timing and social competence as well as family cohesion: the association between late pubertal timing and emotional symptoms was stronger for boys who reported low levels of social competence or family cohesion.

Perceived body mass as thin/very thin or as chubby/fat, was significantly associated with increased levels of emotional symptoms in girls and boys. For girls, none of the resilience factors had an interaction effect on the association between perceived body mass and emotional symptoms, whereas all the resilience factors had an interaction effect on this association for boys. The association between perceiving oneself as chubby/fat and emotional symptoms was stronger for boys with low levels of social competence and family cohesion and for boys who often felt lonely than for boys with high levels of these resilience factors. In conclusion, we found that perceived measures of pubertal timing and body mass were more strongly associated with emotional symptoms in adolescence than actual measures and that resilience factors had sex-specific moderating effects on these associations.

5. Discussion

5.1 Main findings

This thesis, which examines data from an almost complete adolescent population, extends knowledge on the associations between emotional symptoms and lifestyle as well as somatic aspects in adolescence, with a special focus on the possible effect of resilience on these associations. Our findings confirmed that emotional symptoms are prevalent in a general population of adolescents and are more common in girls than in boys. An unfavourable lifestyle, assessed by smoking, consume of alcohol or experiences of being drunk, having tried illegal drugs and infrequent physical activity, was associated with increased prevalence of emotional symptoms in both girls and boys. While family cohesion had an attenuating effect on all these associations, social competence strengthened the associations between emotional symptoms and smoking, the use of alcohol and illegal drugs.

A considerable proportion of adolescents with high symptom levels of anxiety/depression, social anxiety, conduct problems or attention problems reported having chronic pain in three or more locations and high pain-related disability scores. Nearly one in three girls and one in five boys with high levels of symptoms of anxiety and depression reported chronic multisite pain. The prevalence increased with the increasing frequency of co-occurring psychiatric symptoms. Adjusting for resilience factors attenuated the associations between emotional and behavioural symptoms and chronic multisite pain.

Perceived measures of pubertal timing and body mass were more strongly associated with symptoms of anxiety and depression than actual measures. Perceiving oneself as early or late in pubertal timing or as thin or fat in body mass was associated with increased symptom scores of anxiety and depression compared to perceiving oneself as similar to others. Moderating effects of resilience factors were found for some of these associations. For girls, the association between early pubertal timing and emotional

symptoms was stronger in combination with loneliness. For boys, the associations between late pubertal timing and emotional symptoms, and between feeling fat and emotional symptoms, were stronger for boys with low levels of resilience factors.

5.2 Methodological considerations

The main strength of the study was the large number of subjects from a general population. The participation rate was high resulting in data from nearly an entire population of unselected adolescents. Weight and height were measured in standardized clinical examinations, and socioeconomic data were provided by objective measures of the parents' education and income.

The study in this thesis was an observational study with a cross-sectional design. In cross-sectional studies, all variables are assessed simultaneously and there is no information about the temporal relationships between the variables. This makes it difficult to make inferences about causality [266]. However, findings from cross-sectional studies may add knowledge that generates hypotheses about mechanisms and mediating pathways that may be examined in longitudinal studies.

Before evaluating the study findings, possible errors should be considered. Statistical analyses in epidemiological studies are based on the assumption that observations can be made on a sample of subjects and then inferences can be drawn about the total population of all such subjects [267]. However, if the sample is not representative or there have been errors in the estimation, the estimates may be misleading. Research errors in observational epidemiological studies are classified as random (lack of precision) or systematic (lack of internal validity) [268].

5.2.1 Precision

Random errors represent variability in the data that we cannot explain [269]. Such errors may be caused by random variations in sampling or by factors that randomly affect the measurements. A common measure of random variation is the variance of the estimates. The precision of the estimate is often described as the inverse of the variance. Confidence intervals (CI) are used to indicate the precision of the study sample estimates as population values. A wide CI indicates low precision of the estimate while a narrow CI indicates high precision. The width depends on the sample size; larger sample sizes result in higher precision and narrower CIs. The width also depends on the variability of the characteristic being studied; as the variability decreases, the estimate becomes more precise and the CIs become narrower [267].

In paper I, a large study population and overall narrow CIs indicated the high precision of estimates. In paper II, the associations between high symptom scores of psychiatric groups, particularly anxiety and depression, and chronic multisite pain had wider CIs. This indicates larger random variation. However, the CIs of the ORs were far from one, indicating that the associations were strong, even if the true OR may be smaller or larger than the estimate. In paper III, p-values and standard errors of estimates, rather than CIs, are included in the tables. Statistical significance testing with p-values typically uses the null hypothesis that there is no association in a “super-population” from which the observations were sampled [270]. The p-value is the probability that the data in the study would demonstrate an association as far from the null hypothesis as was observed, assuming that the null hypothesis is true. A p-value of 0.05 or less is typically used as a measure of statistical significance. For the associations between early perceived pubertal timing, as well as feeling fat or thin, and symptoms of anxiety and depression, the p-values were smaller than 0.001, indicating that the associations observed would be extremely unlikely if the null hypothesis was true. For the association between late perceived pubertal timing and symptoms of anxiety and depression in girls, the p-value was larger and we cannot exclude chance findings.

5.2.2 Internal validity

Internal validity refers to the degree to which the results are representative of the particular population being studied. In observational studies, the internal validity depends on the degree of systematic error or bias. Unlike random errors, systematic errors are not reduced when the size of the study is increased. Bias may be classified into three broad categories: selection bias, information bias and confounding.

Selection bias

Selection bias results from procedures that are used to select participants or from factors that influence the study participation [271]. Selection biases occur when the relationship between exposure and outcome is different for those who participate and for those who do not participate in the study. Nearly 80% of the adolescent population in the county of Nord-Trøndelag participated in the Young-HUNT 3 study. The high attendance rate reduces the probability of selection bias. However, selection bias cannot fully be ruled out. Because the survey was conducted at school, non-participation was mainly a result of absence on the day of study sampling [239]. Symptoms of anxiety and depression may be more prevalent among those with school absence. Some may be absent from school because of emotional symptoms, or because of associated factors such as an unfavourable lifestyle or chronic pain. Non-responders were more often boys, older and attendees of vocational, rather than academic, classes [239]. The participation rate among adolescents who had dropped out of school was particularly low. One might suspect a higher frequency of emotional symptoms, chronic pain and unhealthy lifestyle factors in this population. However, the proportion of adolescents not attending school constituted less than 5% of the total population [239]; thus we do not expect our results to be substantially influenced by selection bias.

In paper I, the number of adolescents who answered the question about alcohol intoxication was much lower than the number who answered the other questions, including the question about current alcohol use. However, the proportion of

adolescents with and without emotional symptoms who answered this question was similar; thus we do not expect that the missing answers greatly affected the results.

Information bias

Information bias refers to systematic errors in the measurement of an effect as a result of incorrect information collected about or from the study participants. For discrete variables, measurement errors are typically called classification errors or misclassifications [271]. Misclassification that depends on the actual value of other variables is called differential misclassification. Another form of differential misclassification is recall bias. Typically, individuals with a disease will report true exposures differently than healthy individuals simply because the disease serves as a stimulus to recall and report all events that may have contributed to the development of the disease. The bias caused by differential misclassification can either exaggerate or underestimate an effect [271]. Misclassification is non-differential if it is unrelated to the exposure or presence of disease [268]. Non-differential misclassification tends to produce estimates that are diluted [268].

The questionnaires in the Young-HUNT 3 survey were self-reported; and thus, information bias cannot be excluded. Adolescents may have underreported their frequency of smoking, drinking alcohol or using drugs or over-reported their frequency of physical activity because they wanted to appear more socially desirable. However, there is no special reason why this should be different for those with symptoms of anxiety and depression than for those without emotional symptoms, leading to a differential misclassification. In addition, height and weight were measured by specially trained nurses. Compared to measured values, self-reported weight tends to be underestimated and height to be over-estimated among adolescents [196, 272, 273]. It has been suggested that self-reported height and weight may be differently biased in depressed and non-depressed adolescents, because depressed individuals are more prone to negative self-perceptions and thus may perceive their height and weight differently

than non-depressed [195]. This may have caused a differential information bias in the association between perceived body mass and symptoms of anxiety and depression.

It is possible that adolescents with emotional symptoms report different resilience factors than adolescents without emotional symptoms. For example, it is possible that adolescents with emotional symptoms report lower scores of family cohesion or social competence than adolescents without emotional symptoms, because they perceive themselves and their environment in a more negative view. This may have introduced a differential information bias that lead to an overestimation of the association between resilience and emotional symptoms.

Confounding

Confounding refers to the mixing of effects and occurs when the association between study variables is actually mediated through a third variable that is associated with both the exposure and the outcome [268]. For example, age may be a confounder of the association between emotional symptoms and smoking, because increased age is associated with an increased frequency of emotional symptoms as well as increased frequency of smoking. A confounder must not be an effect of the exposure or a consequence of the outcome; thus, causal intermediates are not confounders. Two methods that are often used to address confounding in data analysis are stratification and regression modelling. However, there is always a possibility that unmeasured confounders that could bias the results.

In order to control for confounding, the analyses in paper I were stratified for sex and adjusted for age and SES. Further, the analyses of the associations between smoking and emotional symptoms were adjusted for alcohol use and the analyses of the associations between alcohol use and emotional symptoms were adjusted for smoking. However, it cannot be excluded that emotional symptoms and unfavourable lifestyle factors were associated because of a common unmeasured factor.

Additionally, although analyses conducted in paper II were stratified by sex and adjusted for age and SES, confounding cannot be excluded as a possibility. Parental pain is reported to be associated with both emotional symptoms and chronic pain in adolescents, and may thus have constituted a confounder that we were unable to control for [244, 274].

The analyses in paper III were stratified by sex and adjusted for SES. For actual pubertal timing and actual body mass, the percentiles were specific to sex and age. Age was included as a part of the questions on perceived pubertal timing and body mass, and was therefore not included as a covariate in the analyses in paper III. However, also in this study there is a possibility for unmeasured confounders. One might presume that perception of body mass may be influenced by bullying from peers, which is also associated with emotional symptoms.

Measures

The instruments used in this study consisted of few items, and for some of these instruments, only a selection of items from the original instrument was included. Resilience factors were measured by social competence, self-esteem, family cohesion and loneliness. As self-esteem is closely related to depression, it was considered to be inappropriate to adjust for self-esteem in the analyses where emotional symptoms were the outcome variable. Only two factors from the original READ scale were included in the Young-HUNT questionnaire, and there were no measures of resilience in the external social level. To seldom or never feel lonely may be considered a perception of access to social support, and loneliness was therefore in this thesis used as an indirect measure of resilience on the external social level.

The main outcome measure was self-reported symptoms of anxiety and depression rather than clinically assessed diagnoses. High symptom burden was categorized according to a predefined cut-off value. Although symptom-based instruments are

common in population studies, it may be appropriate to question the reliability (consistency) and validity (accuracy) of the instruments. For some of the measures, there are no data on reliability or validity of the selection of items that were included in the HUNT survey. However, the internal consistency of all instruments was high, and the reliability and validity of main outcome, the SCL-5, has been evaluated in another Norwegian population-based study of individuals aged 16 years and older [241, 242].

5.2.3 External validity- generalizability

Whereas the internal validity of a study expresses whether the results apply to the population being studied, external validity expresses whether the results are applicable to people and populations outside the study population [271]. A high degree of external validity indicates that inferences drawn from the current study may also apply to the general population of adolescents in Norway or adolescent populations in other countries. This may only be achieved if the study population is representative of the total population.

This study used data from a large population of adolescents in Norway. Nord-Trøndelag is a rural county, and the average education and income are slightly lower than those in the rest of Norway [239]. In addition, immigrants constitute a smaller proportion of the population than in other parts of the country. However, in regard to geography, economy, industry, sources of income, age distribution, morbidity and mortality, the county is considered nationally representative [239]. Thus, the results are fairly representative for the adolescent population in Norway. Because other nations will differ regarding more urban areas and larger cities, socioeconomic conditions, education, culture and health services, caution should be taken when generalizing to other countries.

5.3 Interpretation of main findings

In this section, some of the main themes of the thesis will be discussed in relation to previous literature, and theoretical frameworks.

5.3.1 Sex differences

The prevalence of symptoms of anxiety and depression was reported as 13% in the total population and 19% for girls and 6% for boys, which is in line with previous reports from comparable populations [9, 10, 98]. Boyd et al. examined a population of Australian adolescents and found a prevalence of symptoms of anxiety or depression ranging from 13.2-14.2% in the total sample; 17.5-18.8% in girls and 8.5-9.3% in boys [9]. In Finland, the prevalence of depressive symptoms in nationwide samples of 14 to 16 year-old adolescents in the time period between 2000 and 2011 was 15.7- 18.1% in girls and 7.7- 8.4% in boys [98]. In a longitudinal study of adolescents in Oslo, Norway, Lien et al. reported a prevalence of symptoms of anxiety and depression of 25.8% in girls and 8.8% in boys at age 15 and 33.8% in girls and 13.1% in boys at age 18 [10]. The prevalence reported in the Norwegian study was higher than that in the present study, possibly because of the older age of the adolescents in their sample or because of a higher prevalence in urban areas. However, comparisons of the prevalence of emotional symptoms measured by different self-report questionnaires are of limited value as differences may be a result of the instruments themselves. In the present study, the prevalence was higher in girls than in boys, and the increase with age was steeper for girls than for boys. This finding supports previous research [6, 8], as well as theories that suggest that females are more vulnerable to developing emotional symptoms than males: the sex differences may be a result of hormonal differences and a greater tendency for girls to doubt themselves or to ruminate [85, 86].

For the associations between emotional symptoms, lifestyle and somatic aspects explored in this thesis, few sex differences were identified. However, some aspects must be considered. The OR for having high levels of emotional symptoms was higher in boys who reported high levels of alcohol intoxication or having tried illegal drugs. In a study by Veleska et al., negative self-esteem was associated with cannabis use and

regular cigarette smoking in adolescent boys but not in girls [134]. One might speculate that boys with low self-esteem or emotional problems smoke or drink alcohol as an attempt to cope or self-medicate more often than girls. The OR for chronic multisite pain was higher in boys than in girls who had high anxiety/depression or conduct problems scores. For social anxiety the opposite was true; the OR for chronic multisite pain was higher for girls with high versus low levels of social anxiety compared to boys. In previous studies chronic pain has typically been more strongly associated with internalizing symptoms in girls and with externalizing symptoms in boys [152, 153, 159]. Egger et al. found that headache, stomach ache and musculoskeletal pain were associated with generalized anxiety disorder and social anxiety disorder in girls but not in boys [153]. Headache was associated with CD in boys but not in girls [152]. Kröner-Herwig et al. found that internalizing symptoms were predictors of multiple pains only in girls, whereas externalizing symptoms were influential risks only in boys [159]. No previous studies have presented the prevalence of multisite pain with high disability in relation to psychiatric problems; therefore it is difficult to make comparisons.

Associations between early and late perceived pubertal timing, as well as feeling thin or fat, and symptoms of anxiety and depression were found both in girls and boys. Early perceived pubertal timing and feeling fat appeared to be more strongly associated with emotional symptoms in girls, whereas late perceived pubertal timing appeared to be more strongly associated with emotional symptoms in boys. For girls in Western countries, which have a slim body ideal, changes of body shape and weight gain during puberty may be particularly difficult and may lead to psychological distress, decreased self-esteem and emotional symptoms [8, 197, 275]. For boys, the ideal body type is muscular, and because later maturing boys will have smaller and less muscular bodies than their peers, this could explain the higher levels of emotional symptoms for boys with late pubertal timing [197, 275].

Overall, girls had a higher occurrence of emotional symptoms in adolescence, whereas the associations between emotional symptoms and lifestyle, chronic pain, pubertal timing and body mass showed mainly similar patterns for girls and boys. However, as the prevalence of emotional symptoms was substantially higher in girls than in boys, the

absolute risk of the associated factors was higher for girls than for boys, even if the ORs were at a similar level.

The main effect of adjusting the associations between lifestyle factors and emotional symptoms for resilience factors was similar in girls and boys. This was also true when the associations between emotional or behavioural symptoms and chronic pain were adjusted for resilience factors. However, when investigating the moderating effects of resilience on the associations between emotional symptoms and pubertal timing, as well as body mass, sex differences were found. The association between early perceived pubertal timing and emotional symptoms was stronger for girls who often felt lonely, and the association between late perceived puberty and emotional symptoms was stronger for boys with low levels of social competence or family cohesion. These findings could indicate that resilience factors may buffer the risk for emotional symptoms in those who perceive themselves as maturing early or late. The association between feeling fat and emotional symptoms was stronger for boys with low levels of resilience, whereas resilience did not affect this association in girls. This finding may indicate that for boys with low levels of social support, feeling fat is particularly emotionally distressing. It may be that boys with less support in their surroundings experience more negative comments about their weight compared to boys with high levels of social support. For girls, the results indicate that feeling fat is associated with increased emotional symptoms, even in those with high resilience. This finding supports the theory that the Western body ideal of a slim female body contributes to the substantial psychological stress of girls who feel that they have excess body weight. To our knowledge, these sex-specific moderating effects of resilience factors have not been reported previously.

5.3.2 Resilience

The present findings are well in line with previous reports suggesting that adolescents with high levels of resilience factors have a substantially lower prevalence of emotional symptoms [26, 71, 211, 226, 228]. The results in this thesis add new information about the influence of resilience on the associations between emotional symptoms and

lifestyle, as well as chronic multisite pain, pubertal timing and body mass. The associations between smoking and the use of alcohol or drugs and emotional symptoms were increased when social competence was taken in account, whereas the associations were attenuated by high levels of family cohesion. This could suggest that adolescents with high levels of social competence have higher risks for smoking or using substances, supporting findings from a previous study [134]. It is possible that more socially competent adolescents are more likely to be in settings where cigarettes, alcohol or drugs are available. Adolescents with high levels of family cohesion, on the contrary, may be less exposed to social opportunities to smoke or drink alcohol.

When adjusting for social competence and family cohesion, the association between low frequency of physical activity and emotional symptoms was substantially attenuated. In a previous study, adolescents who attended a sports club had lower levels of emotional symptoms than individuals who performed individual sports [150]. Hence, social competence could possibly have a mediating effect: adolescents who exercise more frequently may feel more socially competent because of their social relationships in their sports club or football team, and higher social competence may contribute to lower levels of emotional symptoms. If the social aspects of physical exercise are more important for reducing the frequency of emotional symptoms than the physical activity itself, this may explain why some previous studies have failed to provide evidence for physical activity as an effective treatment for anxiety and depression [146, 147, 276]. It is also possible that adolescents with high levels of resilience exercise more; for example, one may hypothesize that in families with a high level of family cohesion and low levels of conflicts, parents have a greater capacity to encourage physical activity than families with low levels of resilience. However, because the data were based on a cross-sectional survey, the temporal relationships between lifestyle, emotional symptoms and resilience could not be explored; therefore, theories about mediating effects are only speculations.

Resilience factors were associated with lower levels of pain, which is in line with previous findings of a low prevalence of chronic pain in youth who report high levels of social support [172, 173]. In the present study, the associations between emotional or

behavioural symptoms and chronic multisite pain were attenuated after adjusting for resilience factors, particularly seldom feeling lonely. A confounding effect of resilience factors may be involved in that resilience was associated with both lower levels of emotional symptoms and lower levels of chronic pain. In a study on adults, perceived social support was associated with less depressed mood, lower pain intensity and less passive coping strategies [277]. Moreover, social support may contribute to less attention to pain, whereas loneliness could have the opposite effect. In a study of children and adolescents with juvenile rheumatic disease, the association between pain and depressive symptoms was stronger for those who reported high levels of peer rejection [278]. However, resilience could also be negatively affected by chronic pain as pain with high disability could reduce the adolescents' self-esteem or affect their relationships with family and friends. The attenuating effect of resilience factors in the present study may indicate that adolescents with high scores for resilience factors are less likely to experience chronic multisite pain, even if they have emotional or behavioural problems.

The strong association between resilience factors and low levels of anxiety and depression reported in this thesis supports previous theories of the buffering effects of resilience on emotional symptoms. Social support was shown to reduce the risk for depression in children who experienced maltreatment and had the short allele of the serotonin transporter gene [231]. Social support is also hypothesized to cause epigenetic changes associated with decreased HPA reactivity and stress-resilient individuals [54]. Social support from others may contribute to better coping strategies when facing stressors such as experiencing chronic pain or perceiving oneself as different from peers or societal ideals in regard to pubertal development or body mass. Exposure to stress is not always associated with negative consequences for the individual, and exposure to the same event may be experienced as stressful by some individuals and not by others. Lower levels of stress are thought to result in adaptive biological changes and may lead to reduced HPA activation and better emotional regulation in response to later stressors [52]. Previous experiences of stress may thus lead to increased resilience. The extent to which the stressor is perceived as "controllable" is suggested to determine whether a

situation is considered stressful [52]. The choice of coping strategy has been shown to contribute to differences in both neuroendocrine responses and psychological outcomes of stressful experiences [279, 280]. It may be suggested that resilience factors such as having close friends and good relationships with parents may increase the chance that the adolescent will perceive the stressor as “controllable” and to choose a more functional coping strategy to handle the stressful experience.

Studies of gene-environment interactions have shown that some individuals are more vulnerable to the potential negative effects of adverse events than others (such as having the short serotonin transporter allele compared to having the long allele). This may lead to the assumption that individuals with the “less vulnerable” genotype are more resilient. However, a more recent theory suggests that individuals with “the vulnerable” genotype may rather be perceived as more sensitive to both positive and negative development [281]. According to this theory, these individuals will, under positive environments, do better than individuals with the “resilient” allele. This also suggests that those who are at the greatest risk for developing emotional problems when exposed to adverse events are also those who are more likely to benefit from positive environments such as social support [52]. Thus, the evaluation of resilience factors such as social support is of great relevance for clinicians working with adolescents with emotional symptoms.

5.3.3 Body and mind

The findings in this thesis endorse prior research that suggests a strong interrelationship between bodily factors and emotional symptoms in adolescents. Associations were found between emotional symptoms and smoking, the use of alcohol, having tried drugs and low levels of physical activity. These findings suggest that an unfavourable lifestyle is associated with increased levels of anxiety and depression in adolescence. Because the data were cross-sectional, conclusions cannot be drawn regarding the direction of the relationships. Additionally, lifestyle factors may appear in clusters [133], and adolescents who smoke may possibly have a higher risk for additional use of alcohol or

drugs. To exclude the possibility that the association between emotional symptoms and alcohol was mainly mediated through smoking or that the association between smoking and emotional symptoms was mediated through alcohol, we mutually adjusted these factors. Only smaller attenuations in the associations were found.

The present study provides new knowledge about the prevalence of chronic multisite pain with high disability in adolescents with emotional or behavioural symptoms. Previous studies have mainly focused on the prevalence of mental disorders in adolescents with chronic pain, and few have included a measure of functional disability, even though this is associated with a worse prognosis and higher risks for emotional problems [151, 154, 170, 256, 282]. Luntamo et al. reported the prevalence of headache and abdominal pain in relation to emotional, hyperactivity-inattention or conduct problems [158]. However, that study did not include the presence of multisite pain and did not present the prevalence of pain separately for boys and girls. In the present study, a large sex difference in the prevalence of pain was present. One-fourth to one-third of girls with high scores on emotional or behavioural problems reported chronic multisite pain, compared to one-fifth to one-tenth of boys. This is important knowledge for clinicians, who should be particularly cautious in investigating chronic pain in adolescent girls with emotional or behavioural problems. Moreover, adolescents with a higher frequency of co-occurring emotional or behavioural symptoms had an even higher prevalence of chronic multisite pain, indicating that a higher psychiatric burden may constitute an additional risk for experiencing chronic pain.

Actual pubertal timing was not associated with emotional symptoms in either boys or girls, although for boys, the association was nearly significant. This is contrary to most previous studies [13, 181, 283]. The discrepancy may be a result of different methods of classifying early and late pubertal timing. Furthermore, some of the effects of pubertal timing found in earlier studies may have been mediated by perceived pubertal timing. Perceived measures of pubertal timing and body mass were shown to be more strongly associated with emotional symptoms than actual measures. This is in line with some previous studies: Conley and Rudolph found that perceived pubertal timing among adolescent girls and boys was more strongly associated with depression than actual

pubertal timing [186]. Similarly, ter Bogt et al. showed that perception of body mass was more closely linked to internalizing and externalizing symptoms than BMI [197]. Together with these studies, the present results suggest that one's self-perception is a potential stressor that impacts the development of emotional symptoms. Self-perception and particularly perceiving one-self as different from peers, may be an underestimated risk for emotional psychopathology.

Adverse life events and childhood experiences may be a common contributor to the associations between emotional symptoms and bodily factors found in the present study. Childhood adversities are associated with an increased occurrence of obesity and chronic pain, and involve a severe risk for emotional symptoms and disorders [284, 285]. Adverse life events may induce epigenetic modifications that alter the expression of genes involved in the regulation of the HPA axis, immune system and serotonin transporter gene, influencing future stress responses and vulnerability to emotional symptoms and disorders [52, 54]. Both HPA hyper- and hypo-reactivity have been associated with psychiatric disorders and it is suggested that the homeostasis of the set-point of the HPA axis is decisive for maintaining health [52].

The clustering of covariates may possibly increase the associations with emotional symptoms. Body mass may be related to an unfavourable lifestyle with less physical activity and a higher prevalence of smoking and the use of alcohol [286]. Chronic pain is reported to be associated with lifestyle factors and adiposity [249]. Increased body mass is associated with earlier pubertal timing in girls, and possibly later pubertal timing in boys [287, 288]. Furthermore, early pubertal timing is associated with less frequent physical activity and higher prevalence of smoking and alcohol use [259, 289, 290].

The results of this thesis may well be understood within a theoretical framework that includes biological, psychological and social processes. All the associations that were explored in this thesis may be bidirectional, possibly with the exception of pubertal timing. Common underlying mechanisms may be involved in the development and course of the emotional, somatic and life style factors. As described previously,

increased levels of both cortisol and pro-inflammatory cytokines were associated with emotional symptoms, substance use, chronic pain and adiposity [130, 149, 164, 200]. In a study of 151 adolescents, Rao et al. found that elevated cortisol was associated with the onset of substance use disorder [291]. The relationship between depression and substance use disorder was attenuated when HPA dysregulation and stressful experiences were taken into account, suggesting that the associations may partly be explained by these factors [291]. Additionally, smoking, use of alcohol or drugs, low levels of physical activity and adiposity have been associated with increased levels of pro-inflammatory cytokines [130, 149, 200]. Furthermore, nociceptive stimuli are shown to activate the HPA axis, and various components of the HPA hormone cascade have been implicated in the pain response [166], whereas dysregulation of the HPA axis has been shown to increase obesity [15]. One hypothesis suggests that elevated pro-inflammatory cytokine levels in response to a stressor induce both depressive symptoms and HPA activation. Genetic variants of cytokines or previously epigenetic moderations of GR may increase individuals' vulnerability for depressive symptoms [292]. The inflammation system is activated in the presence of stress, regardless of whether it is a biological (actual obesity or chronic pain) or a psychosocial stressor (perceived off-time puberty or perceived obesity). Interacting endocrine and immune systems may be involved in linking the body and mind and are thus relevant for all the associations explored in this thesis.

6. Conclusion

This thesis adds some pieces to the puzzle of the reciprocal relationship between emotional symptoms and somatic factors, and the importance of social relationships and support. Emotional symptoms were common in adolescence, and the prevalence was much higher in girls than in boys. Adolescents with high levels of emotional symptoms reported a less healthy lifestyle and a higher prevalence of chronic multisite pain than adolescents with low levels of emotional symptoms. Perceived measures of pubertal timing and body mass were more strongly associated with emotional symptoms than actual measures. Resilience factors substantially attenuated the associations between emotional symptoms and lifestyle, as well as chronic pain, and moderated some of the associations between emotional symptoms and perceived pubertal timing and body mass. The results of the current study expand our knowledge of the relationship between emotional symptoms, lifestyle and somatic aspects in adolescence and underline the importance of one's perception of one's own body and the availability of social support.

7. Clinical implications and future perspectives

This study confirms the importance of bearing a broad perspective when encountering the adolescent patient. It is essential to include the adolescents' physical symptoms, lifestyle and perception of his/her body in the assessment of emotional symptoms in adolescence. Having tried illegal drugs was associated with a higher frequency of emotional symptoms, even after adjusting for resilience factors. Reducing the frequency of substance use is a major health concern and should be included in public health measures that aim to improve adolescents' mental health. Involvement in physical activity should include participation in a social setting because this could be an important aspect of the positive effect of exercise on mental health in adolescence. Moreover, clinicians should be aware of the high frequency of chronic multisite pain in adolescents with emotional or behavioural symptoms. Chronic pain is associated with a worse prognosis of psychiatric symptoms, and the assessment and treatment of chronic pain should therefore be included in the management of emotional symptoms in adolescents.

Social relationships with family and friends may be crucial for adolescents' ability to cope with psychosocial or environmental stressors. The findings of this study underline the importance of resilience and of including these factors in the assessment, prevention and treatment of emotional symptoms in this age group.

Emotional symptoms in adolescence may cause life-long morbidity and lead to reduced education and ability to work and social and relational problems for the individual and economic costs for society. Increased knowledge of the factors that are associated with emotional symptoms may increase our understanding of the underlying mechanisms and be of importance in prevention and treatment. Because this study was based on data from a cross-sectional health survey, hypotheses about causal effects or mediating factors could not be tested. However, the results provide a basis for generating hypotheses that can be tested in future research. Studies should aim to include repeated assessments to evaluate the temporal relationships between the variables that were explored in this study. In addition, data on prior adverse life events would be relevant. Future waves of the HUNT survey will make it possible to follow the adolescents into

adult age and explore if, and how, their self-perception changes during development. Moreover, it will be possible to explore whether positive relationships with others in adolescence are of significance for the development of emotional symptoms in young adulthood, and whether social relationships and resilience factors change over time. The inclusion of complete instruments for the assessment of psychiatric symptoms will provide a better basis for comparisons with other studies.

It has been hypothesized that epigenetic effects and alterations in the inflammation and immune system are underlying mechanisms of the associations in this study. Future research on emotional symptoms, somatic aspects and resilience may explore biomarkers that are related to the endocrine and immune systems as well as epigenetic effects and may possibly reveal the specific mechanisms for the close interplay between the body and mind.

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Paper I

Resilience, lifestyle and symptoms of anxiety and depression in adolescence: the Young-HUNT study

Marit Skrove · Pål Romundstad · Marit S. Indredavik

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Abstract

Purpose This study investigated the symptoms of anxiety and depression in adolescence, their associations with lifestyle and resilience and the possibility that resilience factors can attenuate the associations between unhealthy lifestyle and symptoms of anxiety and depression.

Methods Adolescents ($n = 7,639$) aged 13–18 years completed a questionnaire regarding lifestyle and health. Symptoms of anxiety and depression were measured by the SCL-5, a five-item shortened version of the Hopkins Symptom Checklist. Resilience factors included questions on friends and family relations and two sub-scales of the Resilience Scale for Adolescents; Family cohesion and Social competence.

Results Of the total population, 13 % reported symptoms of anxiety and depression. Resilience characteristics were associated with lower symptom levels (ORs ranging from 0.2 to 0.6), and substance use and infrequent physical activity with higher symptom levels (ORs ranging from 2.1 to 4.0). The associations with substance use were

strengthened by social competence, but attenuated by family cohesion. The association with physical activity was attenuated by both social competence and family cohesion.

Conclusion Symptoms of anxiety and depression were frequent in adolescents and were associated with unhealthy lifestyle factors as substance use and low physical activity. Resilience characteristics seemed to protect against symptoms and markedly influenced the associations between lifestyle factors and symptoms of anxiety and depression. The importance of family and other supportive relationships should be emphasized in treatment and prevention of anxiety and depression in adolescence.

Keywords Resilience · Anxiety · Depression · Physical activity · Substance use

Introduction

Symptoms of anxiety and depression are frequently occurring mental health problems among adolescents [6, 10]. Prevalence rates of 6.1 % for anxiety and 10.7 % for depression were reported in a recent review [9]. Slightly higher prevalence rates have been found in studies using self-reported symptom scales [1, 6, 12, 22]. Anxiety and depressive disorders are closely related conditions and are therefore often studied together [3, 27, 50].

Unhealthy lifestyle factors have been associated with symptoms of anxiety and depression in adolescence [4, 39]. Smoking was associated with symptoms of anxiety and depression in cross-sectional and longitudinal studies [15, 28, 34, 39, 48]. The direction of the relationship and the underlying mechanisms for this association are, however, unclear [13, 48], and more research on possible mediating or confounding factors is needed [13, 28, 30]. Adolescents

M. Skrove (✉) · M. S. Indredavik
Department of Neuroscience, Faculty of Medicine,
RBUP, NTNU, 7489 Trondheim, Norway
e-mail: marit.s.skrove@ntnu.no

M. S. Indredavik
e-mail: marit.s.indredavik@ntnu.no

M. Skrove · M. S. Indredavik
Department of Child and Adolescent Psychiatry,
St Olav's University Hospital, Trondheim, Norway

P. Romundstad
Department of Public Health and General Practise,
Faculty of Medicine, Norwegian University of Science and
Technology, Trondheim, Norway
e-mail: pal.romundstad@ntnu.no

who used alcohol or other substances had a higher level of anxiety and depression than those who did not use substances [39]. Anxiety preceded substance use in a recently published longitudinal study [14], while an association between anxiety and depression and frequent intoxication of alcohol in girls was reported in a cross-sectional study [44]. Physical activity has been negatively associated with anxiety and depression in adolescence in several cross-sectional studies [19, 23, 42, 49], but findings from longitudinal studies are less clear. Adolescents with high levels of physical activity had lower risk for depressive symptoms in some longitudinal studies [40, 45], but not in others [11, 37]. The role of exercise in prevention and treatment is unknown because the evidence base is sparse [4, 25].

Resilience is defined in terms of factors that contribute to good psychological outcomes in spite of the presence of risk factors [38]. Resilience factors are often divided into three categories: individual resources, family support and supportive external social networks [7, 17]. High self-esteem, social support from family and friends, and living with both parents are all associated with lower levels of depressive symptoms or psychological distress [8, 24, 26, 36]. In a recent study, social support from friends and spending time with friends during leisure hours were the strongest protective factors against symptoms of anxiety and depression in adolescents [31]. Still, knowledge on the effects of resilience is incomplete. A structured life and family support seem to be negatively associated with substance use and low physical activity in adolescents [2, 29, 51], while social competence may have the opposite effect and increase the risk of smoking and use of cannabis [51]. Few studies have evaluated the role of resilience on the association between anxiety and depression and substance use and physical activity.

The aims of this study were to estimate the prevalence of symptoms of anxiety and depression in a large adolescent population and to explore the association of these symptoms with lifestyle factors (such as smoking, use of alcohol and illegal drugs and physical activity), and resilience factors (such as social competence, family cohesion, number of friends and relations to family members). Furthermore, we wanted to investigate whether resilience factors attenuated the association between unhealthy lifestyle factors and symptoms of anxiety and depression.

Methods

Study design

This study uses data from a large cross-sectional population-based study in Norway, the Nord-Trøndelag Health Study (HUNT 3). Data were collected from 2006 to 2008,

and all inhabitants aged 13 years or older in the county of Nord-Trøndelag were invited to participate. Nord-Trøndelag has a stable population of approximately 132,000 inhabitants [32]. Students in junior high and high schools aged 13–19 years were included in the youth part of the study called Young-HUNT 3. The Young-HUNT 3 study was carried out at school, where the adolescents completed a self-administered questionnaire regarding lifestyle and health, which was supplemented with measurements of blood pressure, weight and height.

Study population

The total number of adolescents invited to participate in the Young-HUNT 3 study was 10,485. Of these, 8,200 (78.2 %) completed the questionnaire. Adolescents less than 13 or older than 19 years were excluded from the present study due to low numbers ($n = 27$ and 260, respectively). Adolescents with incomplete information on symptoms of anxiety and depression ($n = 274$) were also excluded from the study. Thus, 7,639 adolescents constituted the present study population, of which 3,882 (51 %) were girls and 3,757 (49 %) were boys.

Measures

The original questionnaire and its English translation can be downloaded from the HUNT website [20].

Symptoms of anxiety and depression were measured by the SCL-5, a five-item shortened version of the Hopkins Symptom Checklist (SCL-25). The SCL-25 is a commonly used instrument designed to measure symptoms of anxiety and depression. The SCL-5 has been shown to correlate well ($r = 0.92$) with the SCL-25 [46]. The SCL-5 scale consists of five phrases (During the last 14 days: I have been constantly afraid and anxious; I have felt tense or uneasy; I have felt hopeless about the future; I have felt dejected or sad; I have worried too much about various things) with four alternative responses, ranging from “not bothered” (1) to “very much bothered” (4). Participants were excluded from the study if one or more responses to this questionnaire were missing. A cut-off point at >2.0 was used to determine if adolescents were troubled with symptoms of anxiety and depression [43]. Cronbach’s alpha for the SCL-5 was 0.83 in this study.

“Current smokers” were identified as adolescents who answered that they were daily or occasional smokers, while adolescents who answered that they had never tried smoking or that they had smoked previously but not now, were classified as “non-smokers”. Adolescents who reported that they sometimes drank alcohol now were classified as “current alcohol users” while adolescents who reported that they had never tried alcohol or that they did

not drink alcohol now, were classified as “non-users of alcohol”. Adolescents were also asked if they had ever felt intoxicated (drunk). Answers were categorized into three groups: “never been drunk”, “been drunk 1–10 times” and “been drunk 11 times or more” [44]. Adolescents were also asked if they had ever tried hash, marijuana or other drugs; response alternatives were “yes” and “no”. Physical activity was measured by the World Health Organization Health Behaviour in Schoolchildren Survey Questionnaire (WHO HBSC). The questionnaire includes one question about the duration and one question about the frequency of vigorous activity. The frequency question was “Outside school hours: How often do you usually exercise in your free time so that you get out of breath or sweat?” Answers were categorized into three categories: “low activity” (1 day a week or less), “moderate activity” (2–3 days a week) and “high activity” (4 days a week or more) [35].

Resilience factors were measured with 8 of 28 items in the Resilience Scale for Adolescents (READ) [18]. The original READ addresses five factors: personal competence, social competence, structured style, family cohesion and social resources. In the HUNT questionnaire, two of these factors were included: social competence (I easily make others feel comfortable around me; I easily find new friends; I am good at talking to new people; I always find something fun to talk about) and family cohesion (In my family we share views of what is important in life; I feel comfortable with my family; My family view the future as positive, even when sad things happen; In my family we support each other). Each item had five alternative responses, ranging from “I totally disagree” (1) to “I totally agree” (5). In the current study, Cronbach’s alpha was 0.82 for the READ social competence items and 0.86 for the READ family cohesion items. Adolescent’s current living situation was recorded and classified as “living with both parents” or “not living with both parents”. Adolescent’s number of friends was measured with the question, “About how many close friends do you have?” Response alternatives were “none”, “one” or “two or more”. Family relationships were measured with the question, “How good is the relationship you have with your immediate family?” The questionnaire asked for separate responses pertaining the adolescents’ mother, father and sibling(s) and the responses were scored from very good (1) to bad (4).

Socioeconomic data for the adolescents were measured in terms of total years of education and gross income (NOK) of parents. This information was provided by Statistics Norway.

Statistical analysis

The data were analyzed with SPSS 19 for Windows (SPSS INC., Chicago, IL). A descriptive analysis was carried out for the SCL-5 scores in relation to age, gender and resilience

and lifestyle factors. *P* values <0.01 were required for statistical significance. Exact confidence intervals were calculated using STATA for Windows, version 11 (STATA Corp, College Station, TX). Multiple logistic regression was used to estimate odds ratios for the associations between lifestyle factors and SCL-5 scores above 2. We adjusted the associations for age and parental socioeconomic status, and, in the second regression-model, we also included READ social competence and READ family cohesion to investigate the possible attenuating effect of these variables.

Ethics

Participation in the study was voluntary. Each participant signed a written consent form to take part in the study, and the parents of adolescents less than 16 years of age also gave their written consent. The Regional Committee for Medical and Health Research Ethics and the Norwegian Data Inspectorate approved the study protocol for HUNT 3 and the current study (N.ref 4.2007.2258).

Results

Characteristics of the study population

Characteristics of the study population are summarized in Table 1. The mean age was 15.8 years (SE 0.03). Whereas the mean SCL-5 score was higher for girls than for boys (1.65 vs. 1.34), the mean scores for the resilience factors READ social competence and READ family cohesion were lower for girls than for boys (Table 1).

Prevalence of symptoms of anxiety and depression

Of 7,639 adolescents, 988 adolescents (13 %) reported symptoms of anxiety and depression. The prevalence was significantly higher for girls than for boys (19 vs. 6 %, $p < 0.001$). The prevalence increased substantially with age, and the sex difference remained significant at all ages. The increase started at younger age and was steeper for girls than for boys (Fig. 1).

Resilience factors

Living with both parents, having good/very good relationships with family members and having two or more friends were associated with lower levels of symptoms of anxiety and depression (Table 2). Among adolescents with good/very good relationships with their mother 17 % of girls and 6 % of boys reported symptoms of anxiety and depression, compared to 51 % of girls and 23 % of boys with not so good/bad relationships with their mothers (Table 2).

Table 1 Characteristics of the study population

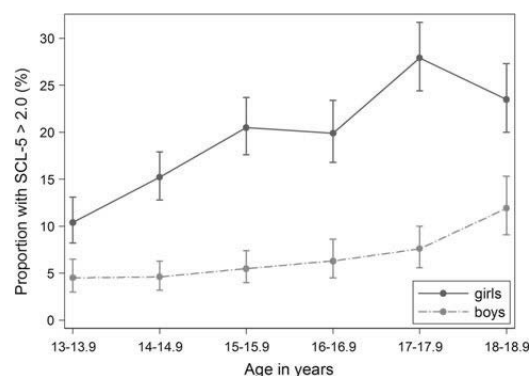
Characteristics	Girls	Boys
Participants, <i>n</i> (%)	3,882 (51)	3,757 (49)
Age, years ^a	15.8 (0.03)	15.8 (0.03)
Living with <i>n</i> (%)		
One parent	468 (12)	445 (12)
Both parents	2,521 (65)	2,582 (69)
Parent and step-parent	573 (15)	480 (13)
Other adult	43 (1)	38 (1)
Without adult	250 (6)	184 (5)
SCL-score ^a	1.65 (0.01)	1.34 (0.01)
READ social competence ^a	3.77 (0.01)	3.96 (0.01)
READ family cohesion ^a	4.15 (0.01)	4.27 (0.01)
Number of close friends, <i>n</i> (%)		
0	34 (1)	68 (2)
1	123 (3)	112 (3)
≥2	3,599 (96)	3,380 (95)
Smoking <i>n</i> (%)		
Non smoker	3,300 (86)	3,254 (89)
Current smoker	532 (14)	420 (11)
Alcohol use <i>n</i> (%)		
No alcohol use	1,687 (45)	1,810 (50)
Current alcohol use	2,071 (55)	1,803 (50)
Alcohol intoxication <i>n</i> (%)		
Never been drunk	1,358 (42)	1,329 (44)
Been drunk 1–10 times	1,059 (33)	866 (29)
Been drunk 11 times or more	828 (25)	806 (27)
Illegal drugs <i>n</i> (%)		
Never used illegal drugs	3,750 (97)	3,563 (96)
Ever used illegal drugs	97 (3)	147 (4)
Physical activity <i>n</i> (%)		
High activity (≥4 days/week)	1,396 (36)	1,712 (46)
Moderate activity (2–3 days/week)	1,474 (38)	1,189 (32)
Low activity (≤1 day a week)	970 (25)	825 (22)
Gross income parent 1,000 NOK ^a	787 (6.4)	779 (6.4)
Years of education father ^a	13.5 (0.04)	13.5 (0.04)
Years of education mother ^a	14.0 (0.04)	14.0 (0.05)

^a Values are expressed as mean (SE)

Increasing levels of social competence and family cohesion were associated with lower odds of having symptoms of anxiety and depression for both girls and boys (Table 3). Adjusting for age and socioeconomic status had little effect on the associations between resilience characteristics and symptoms of anxiety and depression (Table 3).

Lifestyle factors

Current smokers and adolescents who used alcohol or had ever tried illegal drugs had higher frequency of symptoms of anxiety and depression than adolescents who did not use

**Fig. 1** Proportion of adolescents with SCL-5 score > 2.0 by age

these substances (Table 2). Adolescents who had been drunk 11 times or more had an odds ratio of 2.6 (95 % CI 1.9–3.6) among girls and 3.4 (95 % CI 2.1–5.7) among boys for reporting symptoms of anxiety and depression (Tables 4, 5). Girls and boys who had used illegal drugs had an odds ratio of 3.2 (95 % CI 2.1–4.9) and 4.0 (95 % CI 2.5–6.3) for anxiety and depression compared to girls and boys who had never used illegal drugs. Adjusting for age and socioeconomic status moderately attenuated the association between smoking, alcohol and illegal drugs and symptoms of anxiety and depression. Additional adjusting for social competence strengthened the associations. Adjusting for family cohesion substantially attenuated the associations in both girls and boys, although the associations were still significant (Tables 4, 5). Mutual adjustment for smoking and alcohol intoxication attenuated the associations, but the effect of adjusting for resilience factors remained (data not shown).

The odds ratio for having symptoms of anxiety and depression was higher for girls and boys who reported low levels of physical activity compared to girls and boys who reported high levels [OR girls 1.7 (95 % CI 1.3–2.1), OR boys 1.8 (95 % CI 1.2–2.5)]. These associations were attenuated to a non-significant level when adjusting for social competence and family cohesion together (Tables 4, 5).

Discussion

In this study, we found that symptoms of anxiety and depression are frequent in adolescence, especially among girls. Resilience characteristics seemed to protect adolescents against symptoms of anxiety and depression, and markedly influenced the associations between lifestyle factors and symptoms of anxiety and depression. While the association with low physical activity was reduced to a non-significant level, substance use remained associated

Table 2 Resilience and life style factors according to symptoms of anxiety and depression

Resilience and life style factors	Girls SCL5 >2.0			Boys SCL5 >2.0		
	<i>n</i>	%	95 % CI	<i>n</i>	%	95 % CI
Total (<i>n</i> = 7,639)	748	19	18–21	240	6	6–7
Living with both parents (<i>n</i> = 7,586)						
Yes	400	16	14–17	128	5	4–6
No	348	26	23–28	112	10	8–11
Relationship with mother (<i>n</i> = 7,217)						
Good/very good	576	17	16–18	186	6	5–6
Not so good/bad	145	51	45–57	35	23	16–30
Relationship with father (<i>n</i> = 7,143)						
Good/very good	472	15	14–17	160	5	4–6
Not so good/bad	235	40	36–44	57	19	15–24
Relationship with sibling (<i>n</i> = 7,086)						
Good/very good	577	17	16–19	177	6	5–7
Not so good/bad	134	40	35–45	43	13	10–18
Number of close friends (<i>n</i> = 7,316)						
≥2	668	19	17–20	196	6	5–7
1	43	35	27–44	13	12	6–19
0	17	50	32–68	17	25	15–37
Smoking (<i>n</i> = 7,506)						
Non-smoker	552	17	16–18	182	6	5–6
Current smoker	188	35	31–40	57	14	10–17
Alcohol (<i>n</i> = 7,371)						
Non-user of alcohol	212	13	11–14	74	4	3–5
Current alcohol user	514	25	23–27	157	9	7–10
Alcohol intoxication (<i>n</i> = 6,246)						
Never been drunk	169	12	11–14	52	4	3–5
Been drunk 1–10 times	249	24	21–26	60	7	5–9
Been drunk 11 times or more	231	28	25–31	94	12	10–14
Illegal drugs (<i>n</i> = 7,557)						
Never used illegal drugs	696	19	17–20	206	6	5–7
Ever used illegal drugs	43	44	34–56	32	22	15–29
Physical activity (<i>n</i> = 7,566)						
High activity (≥4 days/week)	215	15	14–17	85	5	4–6
Moderate activity (2–3 days/week)	274	19	17–21	72	6	5–8
Low activity (≤1 day a week)	245	25	23–28	81	10	8–12

For all items $p < 0.001$ for both girls and boys

with symptoms of anxiety and depression after adjusting for resilience factors as social competence and family cohesion.

The high prevalence (13 %) of symptoms of anxiety and depression among adolescents in the present study is supported by findings of earlier studies [1, 6, 12, 22]. An Australian cross-sectional study of 1,299 adolescents found an overall prevalence of anxiety and depression of 13.2 and 14.2 %, respectively [6]. Other studies of Norwegian adolescents using self-report questionnaires have found similar prevalence rates [12, 28, 45]. Consistent with other

studies, the prevalence of symptoms of anxiety and depression was higher in girls than in boys and the increase with age was larger for girls than for boys [16, 53].

In the current study, resilience characteristics as having a good/very good relationship with parents or having a high number of friends showed a major attenuating tendency on the presence of symptoms of anxiety and depression. These findings supplement emerging research on resilience [8, 21, 24, 26, 31, 36]. In a review on the social determinants of health in adolescence, family connectedness was found to be one of the most important factors to protect against poor

Table 3 Odds ratio for SCL5 score by resilience characteristics

Resilience characteristics	Girls			Boys		
	Crude	Adjusted for age ^a and socioeconomic status ^b		Crude	Adjusted for age ^a and socioeconomic status ^b	
	OR	OR	95 % CI	OR	OR	95 % CI
READ social competence (range 1–5) ^c	0.5	0.5	0.5–0.6	0.5	0.4	0.4–0.5
READ family cohesion (range 1–5) ^c	0.4	0.4	0.4–0.4	0.4	0.4	0.3–0.5
Living with both parents (<i>n</i> = 7,586)						
No	1.0	1.0	(ref)	1.0	1.0	(ref)
Yes	0.6	0.6	0.5–0.7	0.5	0.5	0.4–0.7
Relationship with mother (<i>n</i> = 7,217)						
Not so good/bad	1.0	1.0	(ref)	1.0	1.0	(ref)
Good/very good	0.2	0.2	0.1–0.2	0.2	0.2	0.1–0.3
Relationship with father (<i>n</i> = 7,143)						
Not so good/bad	1.0	1.0	(ref)	1.0	1.0	(ref)
Good/very good	0.3	0.3	0.2–0.3	0.2	0.2	0.2–0.3
Relationship with sibling (<i>n</i> = 7,086)						
Not so good/bad	1.0	1.0	(ref)	1.0	1.0	(ref)
Good/very good	0.3	0.3	0.2–0.4	0.4	0.4	0.2–0.5
Number of close friends (<i>n</i> = 7,316)						
0	1.0	1.0	(ref)	1.0	1.0	(ref)
1	0.4	0.4	0.2–0.9	0.5	0.5	0.2–1.0
≥2	0.2	0.2	0.1–0.3	0.2	0.2	0.1–0.4

^a Adolescent age

^b Parental income and educational level

^c Included in the model as continuous variable

health, including mental health, across countries [52]. The adolescence is a crucial time of each individual's development, involving both pubertal processes, establishing a more secure identity and separating from the original family. Parental factors such as maternal warmth, parental monitoring and school involvement are found to be crucial in development of self-regulatory strategies, while peer relations can promote a sense of belonging and feelings of self-worth [5, 47]. These are all important factors for a healthy development in adolescence.

Adolescents who smoked or used alcohol or illegal drugs were more likely to have symptoms of anxiety and depression than adolescents who did not use substances, even after adjusting for resilience factors. These findings are supported by several previous studies [39, 41]. One possible explanation to these associations is that adolescents might be self-medicating [33]. There is also a possibility that substance use precedes the onset of anxiety and depression, due to a shared vulnerability to both substance use and anxiety and depression or to mutual neurobiological factors [48]. There were almost no differences between girls and boys in the associations between smoking and use of alcohol and symptoms of anxiety and

depression. However, as the prevalence of symptoms of anxiety and depression was much higher in the female population, the increase in absolute risk of these factors seems to be higher for girls than boys.

Adjusting for social competence strengthened the associations between substance use and symptoms of anxiety and depression, while adjusting for family cohesion attenuated the associations. This could indicate that social competence might increase the likelihood of adolescents being in a setting where cigarette smoke, alcohol or illegal drugs are available, while adolescents with a supportive family are less likely to use substances. This is well in line with studies reporting social competence to be positively, and family cohesion to be negatively, associated with adolescents' substance use [51]. We consider the attenuating effect of resilience factors on the associations between substance use and symptoms of anxiety and depression as a novel and important finding.

As expected, a low frequency of physical activity was associated with increased prevalence of symptoms of anxiety and depression [19, 23, 42, 49]. When adjusting for family cohesion and social competence, the association was attenuated to a non-significant level. These results suggest

Table 4 Odds ratio for SCL5 score by life style, girls

Life style factors	Crude		Adjusted for age ^a and socioeconomic status ^b		Adjusted for READ social competence ^c		Adjusted for READ family cohesion ^c		Adjusted for READ social competence + READ family cohesion ^c	
	OR	OR	95 % CI	OR	95 % CI	OR	95 % CI	OR	95 % CI	
Smoking										
Non-smoker	1.0	1.0	(ref)	1.0	(ref)	1.0	(ref)	1.0	(ref)	
Current smoker	2.8	2.3	1.9–2.9	2.5	2.0–3.2	1.7	1.3–2.2	2.1	1.6–2.6	
Alcohol										
Non-user of alcohol	1.0	1.0	(ref)	1.0	(ref)	1.0	(ref)	1.0	(ref)	
Current alcohol user	2.3	2.0	1.5–2.5	2.1	1.7–2.7	1.4	1.1–1.8	1.7	1.3–2.2	
Alcohol intoxication										
Never been drunk	1.0	1.0	(ref)	1.0	(ref)	1.0	(ref)	1.0	(ref)	
Been drunk 1–10 times	2.2	2.1	1.6–2.7	2.3	1.8–3.0	1.6	1.2–2.1	1.9	1.4–2.5	
Been drunk 11 times or more	2.8	2.6	1.9–3.6	3.1	2.1–4.2	1.8	1.3–2.5	2.3	1.7–3.2	
Illegal drugs										
Never used illegal drugs	1.0	1.0	(ref)	1.0	(ref)	1.0	(ref)	1.0	(ref)	
Ever used illegal drugs	3.9	3.2	2.1–4.9	3.5	2.2–5.5	2.1	1.3–3.4	2.7	2.2–5.7	
Physical activity										
High activity (≥ 4 days/week)	1.0	1.0	(ref)	1.0	(ref)	1.0	(ref)	1.0	(ref)	
Moderate activity (2–3 days/week)	1.2	1.2	1.0–1.5	1.1	0.9–1.3	1.1	0.9–1.4	1.0	0.8–1.3	
Low activity (≤ 1 day a week)	1.9	1.7	1.3–2.1	1.4	1.1–1.7	1.3	1.0–1.7	1.2	0.9–1.5	

^a Adolescent age^b Parental income and educational level^c Also adjusted for adolescent age and parental income and educational level

that adolescents with supportive families may be more likely to exercise frequently. The findings could also indicate that some of the protective effect of frequent physical activity might be attributed to the social aspect of exercise. The crucial factor may well be participation in a social setting rather than physical activity itself. If this is true, it may explain why previous studies have failed to provide evidence for physical activity as an effective treatment for anxiety and depression in adolescents [11, 25, 37].

Clinical implications

The importance of family and other supportive relationships may have been underestimated in the treatment and prevention of anxiety and depression in adolescents. Our results indicate that clinicians who work with youngsters with symptoms of anxiety and depression should concentrate on supporting their family and social environment, in addition to specific treatment of anxiety and depression. Substance use in the present study confirmed to be associated with higher frequency of symptoms of anxiety and depression, even after adjusting for resilience factors. Reducing the frequency of substance use should therefore be included in public health measures that aimed to improve mental health in adolescents. Our results also

indicate that family factors may protect adolescents from engaging in risky behaviour, suggesting that supporting a positive family environment is important in preventive health interventions. Involvement in physical activity should include participating in a social environment, as this could be an important aspect of the positive effect of exercise on mental health.

Strengths and limitations

The major strengths of the current study are the large sample size and the precision of the estimated associations, which make chance an unlikely explanation for the observed results. An entire population was included and the participation rate was high, reducing the possibility of selection bias. We were able to adjust for age and socioeconomic status, which are possible confounders of the relationships between substance use and physical activity and symptoms of anxiety and depression. One major limitation of the study is that it relied only on self-report, which can be prone to recall bias, especially concerning lifestyle items. We did not use a diagnostic tool or interview to evaluate mental health problems. The measure of the outcome variable was a shortened version of the original screening instrument, and has been proven reliable in

Table 5 Odds ratio for SCL5 score by life style, boys

Life style factors	Crude		Adjusted for age ^a and socioeconomic status ^b		Adjusted for READ social competence ^c		Adjusted for READ family cohesion ^c		Adjusted for READ social competence + READ family cohesion ^c	
	OR	95 % CI	OR	95 % CI	OR	95 % CI	OR	95 % CI	OR	95 % CI
Smoking										
Non-smoker	1.0		1.0		1.0		1.0		1.0	
Current smoker	2.6	1.5–3.1	2.2	1.4–2.9	2.5	1.4–2.9	1.7	1.2–2.5	2.0	1.4–2.9
Alcohol										
Non-user of alcohol	1.0		1.0		1.0		1.0		1.0	
Current alcohol use	2.4	1.4–3.0	2.1	1.2–2.5	2.2	1.2–2.5	1.5	1.0–2.2	1.8	1.2–2.5
Alcohol intoxication										
Never been drunk	1.0		1.0		1.0		1.0		1.0	
Been drunk 1–10 times	2.0	1.3–3.2	2.0	1.5–3.7	2.3	1.5–3.7	1.4	0.9–2.2	1.8	1.1–2.8
Been drunk 11 times or more	3.5	2.1–5.7	3.4	2.7–7.4	4.4	2.7–7.4	2.0	1.2–3.4	2.9	1.7–4.8
Illegal drugs										
Never used illegal drugs	1.0		1.0		1.0		1.0		1.0	
Ever used illegal drugs	4.8	2.5–6.3	4.0	2.2–5.7	4.6	2.2–5.7	2.7	1.6–4.3	3.5	2.2–5.7
Physical activity										
High activity (≥ 4 days/week)	1.0		1.0		1.0		1.0		1.0	
Moderate activity (2–3 days/week)	1.3	0.9–1.8	1.3	0.8–1.6	1.1	0.8–1.6	1.2	0.8–1.7	1.1	0.8–1.6
Low activity (≤ 1 day a week)	1.9	1.2–2.5	1.8	0.9–1.9	1.3	0.9–1.9	1.4	1.0–2.0	1.2	0.9–1.8

^a Adolescent age^b Parental income and educational level^c Also adjusted for adolescent age and parental income and educational level

other studies [43, 46]. Another limitation is that the cross-sectional design limits suggestions about the direction of causality between lifestyle and resilience factors and symptoms of anxiety and depression.

Conclusions

In this study, we found that symptoms of anxiety and depression were frequently occurring in adolescence, especially among girls. Resilience characteristics as having a good relation to parents and a high number of friends seemed to protect against such symptoms, while substance use and low physical activity were associated with a higher symptom burden. The novel finding of this study is the substantial effect of resilience factors on the association between unhealthy lifestyle factors and symptoms of anxiety and depression in adolescents, underlining the importance of these factors in preventive measures and treatment.

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Paper II

Chronic multisite pain in adolescent girls and boys with emotional and behavioral problems: the Young-HUNT study

Marit Skrove · Pål Romundstad · Marit S. Indredavik

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Abstract The aim of this study was to assess the prevalence of chronic multisite pain with high disability in relation to emotional or behavioral problems and resilience factors in adolescence. A second aim was to investigate if resilience factors could attenuate the associations between psychiatric symptoms and chronic multisite pain. The study was based on a large cross-sectional study carried out in Norway between 2006 and 2008 and included 7,070 adolescents aged 13–19 years. Chronic multisite pain was defined as pain at least once a week during the last 3 months, scoring high on a disability index, and occurring in three or more locations. Chronic multisite pain was prevalent among adolescents with high scores (>85 %) for anxiety/depression, social anxiety, conduct or attention problems (22.8–31.0 % for girls, 8.8–19.0 % for boys). Several coexistent psychiatric symptoms increased the prevalence of chronic multisite pain for both girls and boys. Resilience factors, including high self-esteem, seldom feeling lonely, and high scores for family cohesion or

social competence, were associated with a lower prevalence and markedly attenuated the association between psychiatric symptoms and chronic multisite pain. Psychiatrists should be careful to assess and treat comorbid chronic pain in adolescents with emotional or behavioral problems.

Keywords Chronic pain · Anxiety · Depression · Conduct problems · Attention problems · Resilience

Introduction

The biopsychosocial model offers a useful theoretical framework for understanding the relation between psychiatric symptoms and chronic pain. In the light of this model, an individual's perception of pain is influenced by interacting physical, psychological and social factors [1, 2]. In this perspective, it is highly relevant to explore the associations between psychiatric symptoms and chronic pain and possible influencing psychosocial factors. Psychiatric symptoms are associated with unexplained chronic pain in both clinical and unselected populations of children and adolescents [3–11]. Headache has been reported more than twice as frequently in adolescents with depression or anxiety disorders compared to healthy individuals [11]. In a Finnish study, headaches and abdominal pain were reported more often by adolescents with high scores for psychiatric symptoms compared to those with lower scores (20–36 vs. 11–12 % and 12–16 vs. 5 %) [10]. Psychiatric symptoms have been found to be associated with persistent chronic pain in children and adolescents [8, 12], and comorbid chronic pain has been reported to be associated with a worse prognosis of psychiatric disorders [7]. Therefore, new knowledge on factors influencing the association

M. Skrove (✉) · M. S. Indredavik
Regional Centre for Child and Youth Mental Health and Child Welfare (RKBU), Faculty of Medicine, NTNU,
7489 Trondheim, Norway
e-mail: marit.s.skrove@ntnu.no

M. S. Indredavik
e-mail: marit.s.indredavik@ntnu.no

M. Skrove · M. S. Indredavik
Department of Child and Adolescent Psychiatry, St Olav's
University Hospital, Trondheim, Norway

P. Romundstad
Department of Public Health and General Practise, Faculty
of Medicine, Norwegian University of Science
and Technology, Trondheim, Norway
e-mail: pal.romundstad@ntnu.no

between psychiatric symptoms and pain could be of great clinical significance.

Although the majority of adolescents with chronic pain report pain in more than one location [13, 14], few studies have examined the relationship between psychiatric symptoms and chronic pain in multiple locations [8, 9, 15, 16]. Larsson and Sund [8] argued that the association between psychiatric symptoms and pain depends on the frequency and coexistence of multiple pains rather than the type or localization of pain, and that the presence of multiple pains should be included as an outcome in future studies. The importance of studying multiple, rather than single site pain, was also supported by a recent German study on risk factors for recurrent pain in children and adolescents [16].

Chronic pain may have a large impact on everyday functioning and may cause adolescents to rely on medications to reduce pain [6, 13]. The adolescent's own perception of pain's interference with daily activities may have a strong predictive value for the persistence of pain [17]. Comorbid internalizing symptoms were associated with functional disability in a study of children and adolescents with chronic pain [18]. Still, measures of functional disability are not included in most studies exploring associations between psychiatric symptoms and chronic pain. Moreover, the frequency of chronic pain with high disability among adolescents with psychiatric symptoms has not been reported.

Psychosocial factors may reduce the presence of both chronic pain and psychiatric symptoms [10, 19–21]. High levels of perceived support by parents and teachers were associated with a lower prevalence of chronic pain in several studies [10, 20, 22]. In a recent systematic review, chronic pain was associated with having few friends and being isolated [23]. In addition, low self-esteem was reported to precede headaches in adolescent girls [24]. Parental or peer support, as well as high self-esteem, is also shown to be protective factors in relation to psychiatric symptoms and is often referred to as resilience factors [19, 21, 25]. There is some evidence that social support is associated with fewer depressive symptoms in children with chronic pain [26]. However, research on the influence of protective psychosocial factors on the association between psychiatric symptoms and chronic multisite pain is sparse in unselected populations. The HUNT study offers a unique possibility to investigate the relationship between psychiatric symptoms, chronic pain and resilience factors in a large non-clinical population of adolescents.

The aim of the present study was to assess the prevalence of chronic multisite pain with high disability in adolescent girls and boys with emotional or behavioral problems and to assess the prevalence of multisite pain according to resilience factors. Furthermore, we wanted to

explore if resilience factors could attenuate the associations between psychiatric symptoms and chronic multisite pain in adolescence.

Methods

Study design

This study uses data from a large cross-sectional population-based study in Norway, the Nord-Trøndelag Health Study (HUNT 3) [27]. Data were collected from 2006 to 2008, and all inhabitants aged 13 years or older in the county of Nord-Trøndelag were invited to participate. This county is situated in the middle of Norway. It is mostly rural and sparsely populated, the largest of six small towns has a population of 21,000. The population of Nord-Trøndelag (134,000 residents) is stable and homogenous, making it suitable for epidemiological studies. Adolescents aged 13–19 years were included in the youth part of the study called Young-HUNT 3. A questionnaire regarding lifestyle and health was completed at school in an exam-like situation. This was supplemented with measurements of blood pressure, weight and height.

Study population

Of the 10,464 invited adolescents, 8,200 (78.4 %) participated in the Young-HUNT 3 study. For the present study, adolescents less than 13 years of age or older than 19 years of age were excluded due to low numbers ($n = 27$ and 260, respectively). Adolescents with missing responses on pain questions ($n = 770$) or with missing responses to all psychiatric symptom scales ($n = 73$) were also excluded from the study. A total of 7,070 adolescents (67.6 % of invited, 86.2 % of participants) constituted the present study population, of which 3,597 (50.9 %) were girls and 3,473 (49.1 %) were boys. The mean age was 15.8 years (SD 1.6).

Measures

The original questionnaire and its English translation can be downloaded from the HUNT website: <http://www.ntnu.edu/hunt/data/que>.

Pain variables

Pain was measured by questions of whether the adolescent had experienced pain, not related to any known disease or injury, during the last 3 months. There were separate questions for pain in different locations (headache/migraine, abdominal pain, pain in neck/shoulder, upper

back, low back/buttocks, chest, upper and/or lower extremities) [14, 28]. Response alternatives included “never/seldom”, “once a month”, “once a week”, “more than once a week” or “almost every day”. The validity and the reliability of the pain questions have been shown to be good [28, 29]. Chronic non-specific pain was defined as pain not related to any known disease or injury, for at least once a week during the last 3 months [14]. An adapted form of the subjective disability index was included to measure the extent to which pain disturbed the adolescent’s everyday life [14, 30]. The subjective disability index included five items: “I have difficulties falling asleep and/or pain disturbs my sleep”, “because of pain I have difficulties sitting during a lesson”, “pain disturbs me if I walk more than 1 kilometre”, “pain disturbs me during physical exercise class” and “pain makes it difficult to do daily activities in leisure time”. All items were answered “yes” (1) or “no” (0). The subjective disability index was calculated by summing the five responses and was categorized into three groups: low (0), moderate (1–2) and high disability (3–5) [14, 17]. Chronic multisite pain was defined as chronic pain with high disability, in three or more locations [31]. Use of pain relieving medicine was measured by one question “How often in the last 3 months have you taken non-prescription medicine, for any of the below listed: headache, muscle pain, back pain, stomach pain, other?”. In this study, we dichotomized the answers in “never to once a week” and “twice a week or more”.

Psychiatric symptom variables

Responses to the four different measures of psychiatric symptoms used in this study were categorized into four groups according to the distribution of responses in the study population. For SCL-5, mean score values >2.00 are defined as clinical range [32], and the cut-point at 2.00 corresponds to the 85 % percentile. We subsequently set the upper cut-point corresponding to this percentile for the other measures of psychiatric symptoms. Below the 85 % percentile, we set two cut-points for the purpose of obtaining a substantial number of observations in each category. Hence, the included percentiles (p) for each group are as follows: 0–45 p, 46–60 p, 61–85 p, and >85 p.

Symptoms of anxiety and depression were measured by the SCL-5, a five-item shortened version of the Hopkins Symptom Checklist (SCL-25). The SCL-5 has been shown to correlate well ($r = 0.92$) with the SCL-25 [33]. The SCL-5 scale consists of five phrases regarding symptoms on anxiety and depression with four alternative responses, ranging from “not bothered” (1) to “very much bothered” (4). The mean score values for the four SCL-5 groups were:

1.00–1.20, 1.21–1.60, 1.61–2.00, >2.00 . Cronbach’s alpha for the SCL-5 was 0.83 in this study.

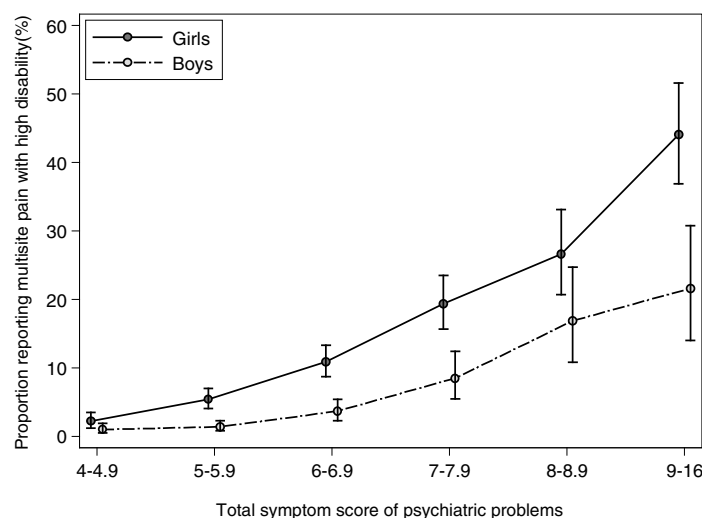
Symptoms of social anxiety were measured by six items from the SPAI-C, the Social Phobia and Anxiety Inventory for Children (original 26 items) [34]. The SPAI-C has adequate validity, internal consistency and reliability [35]. The scale uses three alternative responses: “never” or “hardly never” (0), “sometimes” (1) and “most of the time” or “always” (2). The mean score values for the four SPAI-C groups were: 0.00–0.07, 0.08–0.16, 0.17–0.33, and >0.33 . The Cronbach’s alpha for the SPAI-C was 0.84.

Conduct problems and attention problems were measured by questions regarding the adolescent’s school functioning as reported in previous studies [36–38]. A factor analysis with an oblique rotation was performed and identified conduct problems (highest loading item “I am reprimanded by my teacher”) and attention problems (highest loading item “I have problems concentrating in class”) as two independent factors. All items had four alternative responses from “never” (1) to “very often” (4). The mean score values for the four groups of conduct problems were 1.00–1.32, 1.33–1.66, 1.67–1.68, and >1.68 . The mean score values for the four groups of attention problems were 1.00–1.50, 1.51–1.75, 1.76–2.25, and >2.25 . The Cronbach’s alpha was 0.69 for both conduct problems and attention problems in this study population.

Resilience variables

Resilience factors were measured by eight items from the Resilience Scale for Adolescents (READ) [39]. The original READ addresses five factors: personal competence, social competence, structured style, family cohesion and social resources. In the HUNT questionnaire, two of these factors were included: social competence (“I easily make others feel comfortable around me”; “I easily find new friends”; “I am good at talking to new people”; “I always find something fun to talk about”) and family cohesion (“in my family we share views of what is important in life”; “I feel comfortable with my family”; “my family views the future as positive, even when sad things happen”; “in my family we support each other”). Each item had five alternative responses, ranging from “I totally disagree” (1) to “I totally agree” (5). In the present study, the responses were categorized into three equally large groups. The values for the READ social competence were: 20–18, 17–15 and 14–4. The values for the READ family cohesion were: 20–19, 18–17, and 16–4. In the current study, Cronbach’s alpha was 0.82 for the READ social competence items and 0.86 for the READ family cohesion items.

Fig. 1 Proportion of adolescents with multisite pain according to total symptom score of psychiatric symptoms. Total symptom score of psychiatric symptoms: Total sum of mean score of SCL-5 (Hopkins symptom checklist), SPAI-C (Social Phobia and Anxiety Inventory for Children), conduct problems and attention problems (all range 1–4)



Self-esteem was measured by four items from the Rosenberg self-esteem scale (RSE) (original 10 items) [40]. All items had four response alternatives from “strongly agree” to “strongly disagree” (range 1–4) with high total scores indicating high self-esteem. In the present study, the responses were categorized into three equally large groups (16–14, 13–12, 11–4). Cronbach’s alpha was 0.77 for the self-esteem items.

Loneliness was measured by the question “do you often feel lonely” with response alternatives: “very often”, “often”, “sometimes”, “seldom”, or “very seldom or never”.

Socioeconomic variables

To obtain socioeconomic data on the adolescents, information related to the total years of education and gross income (NOK) for both parents was collected from Statistics Norway.

Statistical analysis

The data were analyzed with SPSS 19 for Windows (SPSS INC., Chicago, IL, USA). Separate analyses were conducted for girls and boys. A descriptive analysis was carried out for the prevalence of pain in relation to psychiatric symptoms and resilience factors. p values <0.05 were required for statistical significance. Exact confidence intervals were calculated using STATA for Windows, version 11 (STATA Corp, College Station, TX, USA). To summarize the four different psychiatric measurements, the SPAI-C scores were transformed from a 0–2 scale to a 1–4

scale by multiplying by 3/2 and adding 1 (used in Fig. 1). Multiple logistic regression analysis was applied to estimate the odds ratios (ORs) for the associations between psychiatric symptoms and chronic multisite pain. We adjusted the associations for age and socioeconomic status. In the second regression model, we first included READ social competence, READ family cohesion, self-esteem and loneliness separately, and then all resilience factors together, to investigate the potential attenuating effects of these variables. We finally included a total regression model with all the covariates to investigate possible coexistence of psychiatric symptoms. Only participants with complete datasets on the items used in the analyses were included in the multiple logistic regression analyses.

Ethics

The study was approved by the Norwegian Data Inspectorate and the Regional Committee for Medical and Health Research Ethics (N.ref 4.2007.2258). Participation in the study was voluntary. A written consent was obtained from each participant. For adolescents younger than 16 years of age, written consent was obtained from both the participant and the parents.

Results

The prevalence of chronic multisite pain with high disability increased with increasing scores for psychiatric symptoms and was higher for girls than for boys in all four symptom groups ($p < 0.001$) (Table 1). For adolescents

Table 1 Prevalence of chronic multisite pain in adolescent girls and boys according to emotional and behavioral symptoms

		Girls				Boys			
		Total	Chronic multisite pain			Total	Chronic multisite pain		
		<i>n</i>	<i>n</i>	%	95 % CI	<i>n</i>	<i>n</i>	%	95 % CI
Total		3,597	409	11.4	10.4–12.5	3,473	131	3.8	3.2–4.5
Anxiety/depression (SCL-5 ^a)	1.00–1.20	1,192	41	3.4	2.5–4.6	2,046	32	1.6	1.1–2.2
	1.21–1.60	1,078	78	7.2	5.8–8.9	829	32	3.9	2.7–5.4
	1.61–2.00	622	80	12.9	10.3–15.8	340	26	7.6	5.1–11.0
	>2.00	670	208	31.0	27.6–34.7	210	40	19.0	14.0–25.0
	Missing	125	–	–	–	128	–	–	–
Social anxiety (SPAI-C ^b)	0.00–0.07	1,140	61	5.4	4.1–6.8	1,717	42	2.5	1.8–3.3
	0.08–0.16	637	60	9.4	7.3–12.0	636	15	2.4	1.3–3.9
	0.17–0.33	1,130	136	12.0	10.2–14.1	735	41	5.6	4.0–7.5
	>0.33	619	141	22.8	19.5–26.3	283	29	10.3	7.0–14.4
	Missing	71	–	–	–	102	–	–	–
Conduct problems	1.00–1.32	2,055	180	8.8	7.6–10.1	1,366	23	1.7	1.1–2.5
	1.33–1.66	719	86	12.0	9.7–14.6	740	25	3.4	2.2–5.0
	1.67–1.68	440	71	16.1	12.8–19.9	576	22	3.8	2.4–5.7
	>1.68	166	42	25.3	18.9–32.6	512	45	8.8	6.5–11.6
	Missing	217	–	–	–	279	–	–	–
Attention problems	1.00–1.50	1,445	74	5.1	4.0–6.4	1,338	20	1.5	0.9–2.3
	1.51–1.75	831	77	9.3	7.4–11.4	792	20	2.5	1.5–3.9
	1.76–2.25	744	115	15.5	12.9–18.3	701	30	4.3	2.9–6.1
	>2.25	366	113	30.9	26.2–35.9	368	47	12.8	9.5–16.6
	Missing	211	–	–	–	274	–	–	–

Pain at least once a week for at least 3 months, in three or more locations, scoring high on a disability index

CI confidence interval

^a Hopkins symptom checklist

^b Social Phobia and Anxiety Inventory for Children

with high scores (>85 %) for symptoms of anxiety/depression, social anxiety, conduct or attention problems, the prevalence of chronic multisite pain ranged from 22.8 to 31.0 % for girls and from 8.8 to 19.0 % for boys. In both girls and boys, high scores for anxiety/depression were associated with the highest prevalence of pain (Table 1).

The proportion of adolescents with chronic multisite pain increased with increasing total psychiatric symptom scores (all four psychiatric measurements summarized, range 4–16), reaching a prevalence of 44.1 % of girls and 21.6 % of boys with a total symptom score of 9 or more (Fig. 1). Girls had a higher prevalence of chronic multisite pain than boys at all symptom scores, although this trend was not statistically significant at a total score of 4–4.9 ($p = 0.073$).

The prevalence of chronic high disability pain *occurring daily*, in any location, was higher in adolescents with high scores for psychiatric symptoms compared to adolescents with low scores. Among girls with high scores for anxiety/depression symptoms or attention problems, 21.8 %

(151/693) and 21.5 % (82/382), respectively, reported pain occurring daily, compared to 3.1 % (38/1,225) and 3.7 % (54/1,472), respectively, of girls with low symptom scores ($p < 0.001$). The corresponding prevalence rates for boys were 12.4 % (27/218) and 10.5 % (40/382) in the high score groups for anxiety/depression and attention problems, respectively, compared to 1.3 % (27/2,092) and 1.8 % (25/1,360), respectively, in the low score groups ($p < 0.001$). Similar significant, but slightly smaller, differences in prevalence of daily pain were also found between high and low scorer groups of social anxiety and conduct problems.

Adolescents with high scores for psychiatric symptoms reported a more frequent use of analgesics than adolescents with low scores for psychiatric symptoms. For girls with high scores for anxiety/depression symptoms, 33.4 % (210/628) reported using pain relieving medicine twice a week or more compared to 8.9 % (101/1,140) of girls with low symptom scores. The corresponding values for boys were 23.4 % (46/197) and 5.7 % (113/1,976). Of girls with high

Table 2 Prevalence of chronic multisite pain in adolescent girls and boys according to resilience characteristics

		Girls				Boys				
		Total	Chronic multisite pain			Total	Chronic multisite pain			
		<i>n</i>	<i>n</i>	%	95 % CI	<i>n</i>	<i>n</i>	%	95 % CI	
Total		3,597	409	11.4	10.4–12.5	3,473	131	3.8	3.2–4.5	
READ ^a social competence	4–14	1,346	181	13.5	11.7–15.4	994	49	4.9	3.7–6.5	
	15–17	1,220	133	10.9	9.2–12.8	1,203	41	3.4	2.5–4.6	
	18–20	907	82	9.0	7.3–11.1	1,148	35	3.1	2.1–4.2	
	Missing	125	–	–	–	128	–	–	–	
READ ^a family cohesion	4–16	1,303	229	17.6	15.5–19.8	1,096	71	6.5	5.1–8.1	
	17–18	834	77	9.2	7.4–11.4	832	24	2.9	1.9–4.3	
	19–20	1,331	87	6.5	5.3–8.0	1,398	30	2.2	1.5–3.1	
	Missing	130	–	–	–	147	–	–	–	
Rosenberg self-esteem	4–11	1,526	269	17.6	15.7–19.6	797	64	8.0	6.2–10.1	
	12–13	1,158	85	7.3	5.9–9.0	1,142	32	2.8	1.9–3.9	
	14–16	776	41	5.3	3.8–7.1	1,417	30	2.1	1.4–3.0	
	Missing	71	–	–	–	102	–	–	–	
Pain at least once a week for at least 3 months, in three or more locations, scoring high on a disability index	Feeling lonely	Often/very often	416	112	26.9	22.7–31.5	201	34	16.9	12.0–22.8
		Sometimes	956	147	15.4	13.1–17.8	603	28	4.6	3.1–6.6
		Never/seldom	2,093	129	6.1	5.2–7.3	2,442	56	2.3	1.7–3.0
		Missing	133	–	–	–	229	–	–	–

CI confidence interval

^a Resilience Scale for Adolescents

scores for conduct problems or attention problems, 32.5 % (50/154) and 30.8 % (104/338), respectively, reported using analgesics twice a week or more. The corresponding values for boys were 11.3 % (54/479) and 15.1 % (52/345). When adjusting for chronic pain, the associations were attenuated but remained significant for all high score groups for psychiatric symptoms, with the exception of conduct problems in boys (data not shown).

The prevalence of chronic multisite pain decreased with increasing scores for resilience factors for both girls and boys (Table 2). Adolescents with high scores on the READ family cohesion scale had a significantly lower prevalence of pain compared to adolescents with low scores: 6.5 vs. 17.6 % among girls and 2.2 vs. 6.5 % among boys. The lowest prevalence of chronic multisite pain was found in individuals with high self-esteem, while the highest prevalence was found in adolescents feeling lonely (Table 2). Girls and boys who reported to feel lonely (often/very often) had a higher odds ratio for chronic multisite pain than those who did not report loneliness: OR 5.4 (95 % CI 4.1–7.3) among girls, OR 8.1 (95 % CI 5.0–12.8) among boys.

Adolescents with high scores for anxiety/depression had an OR of 12.8 (95 % CI 8.7–18.9) among girls and 15.4 (95 % CI 8.8–27.0) among boys for having chronic multisite pain compared to adolescents with low symptom scores (Table 3). Adjusting for age and socioeconomic factors had small effects on the associations between

psychiatric symptoms and chronic multisite pain in all four symptom groups. Separate analyses for each resilience factor showed a particularly strong attenuating effect of being seldom/never lonely (Model 2, Table 3). When adjusting for all resilience factors, the associations between psychiatric symptoms and chronic pain were substantially reduced for both girls and boys. However, the attenuating effect of adjusting for resilience factors was most evident for anxiety/depression and attention problems. The OR for having chronic multisite pain for high scorers versus low scorers was reduced more than 50 %. We found no statistically significant interaction between sex and psychiatric symptom score in these analyses. When including all psychiatric symptom groups in the regression model, the associations were further attenuated (Model 3, Table 3). Still, all high score groups remained significantly associated with chronic multisite pain except for conduct problems in girls and social anxiety in boys.

Discussion

In the present study, chronic multisite pain was highly prevalent among adolescents with emotional or behavioral problems. The prevalence increased with increasing psychiatric symptom scores. One out of three girls and one out of five boys with high scores for emotional or behavioral problems had chronic multisite pain. This was true not only

Table 3 Odds ratio for chronic multisite pain by psychiatric symptoms in adolescent girls and boys

Adolescent girls														
Crude	Model 1 SES and age		Model 2a READ family		Model 2b READ social		Model 2c Self-esteem		Model 2d Loneliness		Model 2e All resilience		Model 3 All covariates	
	OR	95 % CI	OR	95 % CI	OR	95 % CI	OR	95 % CI	OR	95 % CI	OR	95 % CI	OR	95 % CI
Anxiety/depression (SCL-5^a)														
1.00-1.20	1.0	(ref)	1.0	(ref)	1.0	(ref)	1.0	(ref)	1.0	(ref)	1.0	(ref)	1.0	(ref)
1.21-1.60	2.0	1.3-3.1	2.0	1.4-3.1	2.3	1.5-3.4	1.9	1.3-2.9	2.1	1.4-3.1	1.7	1.1-2.6	1.5	0.9-2.3
1.61-2.00	4.0	4.0-6.1	3.7	2.4-5.6	4.0	2.6-6.0	3.5	2.3-5.4	3.7	2.4-5.7	2.8	1.8-4.4	2.3	1.4-3.7
>2.00	12.8	8.7-18.9	10.4	7.1-15.2	12.9	8.9-18.8	10.3	6.9-15.4	9.4	6.2-14.3	6.3	4.0-10.0	4.9	3.0-7.9
Social anxiety (SPALC^b)														
0.00-0.07	1.0	(ref)	1.0	(ref)	1.0	(ref)	1.0	(ref)	1.0	(ref)	1.0	(ref)	1.0	(ref)
0.08-0.16	2.0	1.3-2.9	1.8	1.2-2.7	2.0	1.4-2.9	1.7	1.2-2.5	1.7	1.1-2.5	1.4	1.2-2.6	1.4	0.9-2.2
0.17-0.33	2.6	1.8-3.5	2.2	1.6-3.1	2.6	1.8-3.6	1.9	1.3-2.6	1.9	1.4-2.7	1.3	1.3-2.7	1.3	0.9-1.9
>0.33	5.3	3.7-7.5	4.0	2.8-5.6	5.6	3.9-8.1	3.5	2.5-5.0	2.9	2.1-4.3	1.7	1.9-4.2	1.7	1.1-2.6
Conduct problems														
1.00-1.32	1.0	(ref)	1.0	(ref)	1.0	(ref)	1.0	(ref)	1.0	(ref)	1.0	(ref)	1.0	(ref)
1.33-1.66	1.4	1.1-1.9	1.4	1.1-1.9	1.5	1.1-1.9	1.3	1.0-1.7	1.4	1.0-1.8	1.2	0.9-1.6	1.0	0.7-1.4
1.67-1.68	2.0	1.4-2.7	1.6	1.2-2.2	1.8	1.3-2.5	1.7	1.2-2.3	1.6	1.2-2.2	1.4	1.0-2.0	1.1	0.8-1.6
>1.68	3.6	2.4-5.5	2.5	1.6-3.8	3.2	2.1-4.8	2.7	1.7-4.0	2.7	1.8-4.1	2.1	1.3-3.3	1.3	0.8-2.1
Attention problems														
1.00-1.50	1.0	(ref)	1.0	(ref)	1.0	(ref)	1.0	(ref)	1.0	(ref)	1.0	(ref)	1.0	(ref)
1.51-1.75	2.1	1.5-3.0	1.9	1.3-2.7	2.0	1.4-2.9	1.9	1.3-2.7	1.8	1.3-2.6	1.7	1.2-2.5	1.6	1.1-2.3
1.76-2.25	3.7	2.6-5.0	3.0	2.2-4.2	3.4	2.4-4.7	2.9	2.1-4.0	2.7	1.9-3.7	2.2	1.5-3.1	1.8	1.2-2.6
>2.25	8.4	5.9-12.0	6.5	4.6-9.3	7.9	5.6-11.1	6.6	4.6-9.4	5.5	3.9-7.9	4.0	2.7-5.9	3.1	2.1-4.8
Explained variance	0.12-0.31		0.19-0.32		0.14-0.31		0.19-0.32		0.25-0.32		0.28-0.34		0.37	
Adolescent boys														
Crude	Model 1 SES and age		Model 2a READ family		Model 2b READ social c		Model 2d RSE		Model 2e Loneliness		Model 2f All resilience		Model 3 All covariates	
	OR	95 % CI	OR	95 % CI	OR	95 % CI	OR	95 % CI	OR	95 % CI	OR	95 % CI	OR	95 % CI
Anxiety/depression (SCL-5^b)														
1.00-1.20	1.0	(ref)	1.0	(ref)	1.0	(ref)	1.0	(ref)	1.0	(ref)	1.0	(ref)	1.0	(ref)
1.21-1.60	2.3	1.3-3.9	2.3	1.4-3.9	2.6	1.5-4.4	2.3	1.4-3.8	2.2	1.2-3.8	1.8	1.0-3.1	1.5	0.9-2.8
1.61-2.00	5.4	3.1-9.8	5.1	2.9-8.9	5.8	3.3-10.1	4.3	2.4-7.7	4.6	2.5-8.4	3.4	1.8-6.4	2.9	1.5-5.6
>2.00	15.4	8.8-27.0	12.4	7.1-21.5	15.7	9.1-27.0	11.3	6.4-20.2	10.9	5.8-20.5	6.6	3.2-13.5	5.3	2.6-10.8

Table 3 continued

Adolescent boys														
Crude	Model 1 SES and age		Model 2a READ family		Model 2b READ social c		Model 2d RSE		Model 2e Loneliness		Model 2f All resilience		Model 3 All covariates	
	OR	95 % CI	OR	95 % CI	OR	95 % CI	OR	95 % CI	OR	95 % CI	OR	95 % CI	OR	95 % CI
Social anxiety (SPAI-C ^b)														
0.00–0.07	1.0	(ref)	1.0	(ref)	1.0	(ref)	1.0	(ref)	1.0	(ref)	1.0	(ref)	1.0	(ref)
0.08–0.16	1.0	0.5–1.8	0.9	0.5–1.6	1.0	0.5–1.8	0.9	0.5–1.6	0.8	0.4–1.5	0.7	0.4–1.4	0.8	0.4–1.5
0.17–0.33	2.2	1.3–3.4	1.9	1.2–3.1	2.3	1.4–3.6	1.8	1.1–2.9	1.4	0.9–2.3	1.3	0.8–2.2	1.0	0.6–1.8
>0.33	3.8	2.1–6.2	2.9	1.7–5.0	3.9	2.3–6.8	2.6	1.5–4.4	1.7	1.0–3.1	1.6	0.8–3.2	1.1	0.6–2.2
Conduct problems														
1.00–1.32	1.0	(ref)	1.0	(ref)	1.0	(ref)	1.0	(ref)	1.0	(ref)	1.0	(ref)	1.0	(ref)
1.33–1.66	1.9	1.1–3.6	1.7	0.9–3.0	2.0	1.1–3.7	1.9	1.0–3.4	1.8	1.0–3.2	1.6	0.9–3.0	1.3	0.7–2.5
1.67–1.68	2.5	1.3–4.6	2.0	1.1–3.7	2.4	1.3–4.4	2.1	1.1–3.8	2.2	1.2–3.9	1.9	1.0–3.5	1.4	0.7–2.7
>1.68	6.3	3.5–10.3	4.5	2.6–7.6	5.8	3.4–9.9	4.6	2.7–8.0	4.3	2.5–7.4	3.7	2.1–6.5	2.5	1.3–4.7
Attention problems														
1.00–1.50	1.0	(ref)	1.0	(ref)	1.0	(ref)	1.0	(ref)	1.0	(ref)	1.0	(ref)	1.0	(ref)
1.51–1.75	1.9	1.0–3.7	1.7	0.9–3.2	1.8	0.9–3.4	1.7	0.9–3.3	1.7	0.9–3.2	1.8	0.9–3.5	1.5	0.7–2.9
1.76–2.25	3.0	1.6–5.4	2.4	1.3–4.4	2.8	1.5–5.1	2.4	1.3–4.4	2.3	1.3–4.2	2.0	1.0–3.7	1.4	0.7–2.7
>2.25	10.5	5.4–17.1	6.9	3.9–12.2	8.9	5.1–15.6	7.2	4.0–13.0	6.5	3.7–11.5	4.9	2.7–9.1	2.9	1.5–5.9
Explained variance														
	0.15–0.26		0.17–0.26		0.15–0.26		0.18–0.26		0.21–0.29		0.23–0.30		0.37	

Pain at least once a week for at least 3 months, in three or more locations, scoring high on a disability index

Model 1: OR adjusted for age and parental education and income

Model 2: OR adjusted for age, parental education and income and resilience factors (2a) READ (Resilience Scale for Adolescents) social competence, (2b) READ family cohesion, (2c) self-esteem and (2d) all resilience factors

Model 3: OR adjusted for age, parental education and income, resilience factors and all psychiatric symptom groups (all covariates)

Explained variance: Pearson correlation of observed outcome with estimated probability

CI confidence interval, OR odds ratio

^a Hopkins symptom checklist

^b Social Phobia and Anxiety Inventory for Children

for adolescents with symptoms of anxiety/depression, but also for those with social anxiety, attention problems and conduct problems. Coexistent psychiatric symptoms further increased the prevalence of chronic multisite pain. Resilience factors were associated with a lower prevalence of pain and markedly attenuated the association between psychiatric symptoms and chronic multisite pain.

Few previous studies have reported on the prevalence of chronic multisite pain in unselected populations of adolescents with emotional or behavioral problems. In a study by Luntamo et al. [10], 20.4–36.0 % of adolescents with high scores (≥ 90 %) for emotional, hyperactivity-inattention or conduct problems reported weekly headaches, and 12–15.6 % reported abdominal pain. However, this study did not include separate analyses for boys and girls or the presence of coexistent or multisite pain; thus, a direct comparison of the prevalence between studies is difficult. In the current study, adolescents with higher psychiatric total symptom scores had an even higher prevalence of chronic pain and, when adjusting for other psychiatric groups, the associations between psychiatric symptoms and chronic pain were attenuated. These findings indicate that a higher psychiatric burden may increase the vulnerability for adolescents to experience chronic pain.

High scores for anxiety/depression were associated with the highest frequency of chronic multisite pain in both girls and boys. This finding is supported by previous studies that demonstrated a strong association between anxiety and depressive symptoms and pain in specific locations [3, 5, 6, 11]. Symptoms of social anxiety have seldom been included in studies of chronic pain. However, the associations we found between social anxiety and chronic multisite pain are in line with a recent study demonstrating that chronic migraine was strongly associated with a high social anxiety score [41].

Only two previous studies on multisite pain have explored associations with both internalizing and externalizing psychiatric symptoms in adolescence [8, 16]. The frequency and the number of reported pains were positively related to the levels of internalizing and externalizing problems in an unselected sample of 2,360 adolescents [8]. In the same sample, depressive symptoms predicted multiple pains 1 year later. In another study, both internalizing and externalizing symptoms were found to predict multiple pains, although sex and former pain were more important explanatory variables [16]. However, none of these studies included disability in their definition of chronic pain. Neither did they report the prevalence rates of chronic multisite pain among adolescents with psychiatric symptoms. In our study, we wanted to include only chronic pain that had a significant effect on the adolescent's everyday life, and we, therefore, defined chronic multisite pain as only pain causing high disability. Our results illustrate that

a high proportion of adolescents with various psychiatric symptoms also are troubled with chronic pain that interferes with their daily life activities.

As expected, girls reported a higher frequency of chronic multisite pain than boys. This finding is consistent with previous reports [8, 14, 16, 42] and may be the result of hormonal differences [8] or differences in coping mechanisms between boys and girls [43]. In a recent review, the authors conclude that the sex differences emerge or become larger around puberty [44]. Sex hormones may influence the central nervous system in multiple ways, including effects on the endogenous opioid systems, the dopaminergic or the serotonergic activities [44]. Sex differences in coping strategies could also explain the higher prevalence of pain in girls. A study on pain-related coping in adolescents reported that girls used more social support, positive statements and internalizing/catastrophizing, while boys used behavioral distraction, of which internalizing/catastrophizing was found to mediate the relationship between sex and pain [43].

According to the biopsychosocial model, the relationship between psychiatric symptoms and chronic pain may go in both ways and the explanations for this relationship are wide ranging and multifactorial. Physical, psychological and social factors all need to be considered. Chronic pain may lead to psychiatric symptoms [1]. Individuals with chronic pain may experience despair from being unable to participate in activities with friends and family. This despair may result in depressive symptoms or aggressive behavior and conduct problems. Pain symptoms may interfere with the adolescent's concentration at school and result in attention problems. Additionally, adolescents with chronic pain may be anxious about having a severe disease [1]. However, psychiatric symptoms may also influence chronic pain. Several studies have reported that psychiatric symptoms precede chronic pain in adolescents [8, 12, 16, 42]. Emotional distress may predispose adolescents to experience pain or may contribute to the persistence of chronic pain [1]. Evidence from research on adult populations suggests that unpleasant emotions may exacerbate and pleasant emotions may inhibit the experience of pain [45]. The neurobiological linkages between the brain, the spinothalamic tract, the dorsal horn and the peripheral nerves provide a physiologic pathway by which negative emotions and stress can amplify and prolong pain [46]. In addition, negative emotions can through autonomic reactivity cause contraction of muscle tissue (that may be perceived as painful spasms) or cardiovascular autonomic responses (that may reduce the perceived control over pain) [46]. Further, negative emotions can lead to releasing of proinflammatory cytokines and the stress hormone cortisol which will enhance nociception. Negative emotions are also associated with increased activity in the amygdala,

anterior cingulate cortex and anterior insula, brain structures that are important nodes of the pain neuromatrix that tune attention toward pain and intensify pain unpleasantness [46]. Other researchers have argued that common predisposing factors, such as negative life events [47] or a shared neurobiological dysfunction, could be possible explanations for the association between psychiatric symptoms and pain [1, 48].

Evidence suggests that adolescents with chronic pain use more pain killers than their healthy peers [6, 49]. In this study, we found an increased risk for using analgesics twice or more a week in adolescents with high scores for psychiatric symptoms, even after adjusting for the presence of chronic pain. We cannot exclude the possibility that these associations would be attenuated to a non-significant level if we had adjusted for pain that occurred more seldom. However, our finding is supported by Egger et al. [4] who reported that depressed girls with headaches took medication for their headaches significantly more often than non-depressed girls with headaches and could indicate that adolescents use pain killers to relieve psychological distress [50]. Adolescents with psychiatric symptoms could also use analgesics more often because of poorer strategies to cope with their pain, as psychiatric symptoms have been found to be associated with maladaptive coping styles [51].

In the current study, resilience factors, including high family cohesion, social competence and high self-esteem, were associated with a reduced frequency of chronic multisite pain in both girls and boys. This finding is supported by other studies reporting that low self-esteem precedes chronic pain and that parent and teacher support may be protective [20, 22, 24, 42]. The association between resilience factors and chronic pain may be explained by several mechanisms, with high resilience reducing the adolescent's experience of pain. In a study on adults, social support was associated with lower pain intensity and less passive coping strategies [52]. High levels of social support from family and friends may contribute to improved coping mechanisms by means of distraction, self-encouragement or an ability to control the pain. Pain is perceived as more intense when attention is focused on the pain or when the pain is perceived as overwhelming and uncontrollable, while it is experienced as less intense when attention is distracted from pain or when pain is perceived as controllable [46]. On the other hand, resilience could be negatively affected by chronic pain, as pain with high disability could reduce the adolescents' self-esteem or affect relations to family and friends.

Resilience factors are shown to be protective factors in relation to psychiatric symptoms, with high resilience being associated with lower levels of anxiety and depression in adolescents [19, 21, 53]. However, there have been few studies exploring the influence of resilience factors on

the association between psychiatric symptoms and chronic pain. In the present study, those who reported loneliness had a high prevalence of chronic multisite pain. Loneliness may contribute to paying more attention to pain, thereby increasing the adolescent's experience of pain. We found a strong attenuating effect of being seldom/never lonely on the associations between psychiatric symptoms and chronic pain. This could be due to a confounding effect of loneliness, as loneliness may be associated with both higher levels of psychiatric symptoms and higher levels of pain. However, loneliness could also be a moderating factor in the association between chronic pain and psychiatric symptoms. In a study on children and adolescents with juvenile rheumatoid arthritis, social rejection was found to exacerbate the impact of pain on depressive symptoms, while social support was associated with fewer depressive symptoms in a study on children with recurrent abdominal pain [26, 54]. The attenuating effect of resilience factors found in this study may indicate that adolescents with high scores for resilience factors are less likely to experience chronic multisite pain, even if they have psychiatric symptoms.

Clinical implications

Clinicians working with adolescents with psychiatric symptoms should be aware of the high frequency of chronic multisite pain among these patients. It is essential for the clinician's understanding and choice of treatment to know about the existence and degree of pain symptoms and their possible interference with the adolescents' daily life activities. As chronic pain worsens the prognosis of psychiatric symptoms, adequate pain treatment should supplement the treatment of psychiatric symptoms. While there has been an increase in the awareness of the coexistence of pain and psychiatric symptoms among pediatricians [3] and clinicians working in pain clinics, this coexistence may be underestimated by psychiatrists. Our results show that resilience factors, including social competence, family cohesion, high self-esteem and not feeling lonely, may protect an adolescent from experiencing pain. This finding underscores the importance of supporting the adolescent's self-esteem and his/her relationships with friends and family.

Strengths and limitations

The strengths of the present study are the inclusion of a large unselected population of adolescents with a high participation rate, reducing the possibility that the findings could be due to chance or selection bias. We used a strict

definition of chronic pain that included only chronic pain in multiple locations and with a high level of disability, which strengthens the validity of our results. We also adjusted for the possible confounding effects of age and socioeconomic factors. The limitations include the cross-sectional design that limits the identification of the direction of causality between psychiatric symptoms and chronic pain. As the study only relies on self-report, we cannot exclude any halo-effect or recall-bias in the adolescents' completion of the questionnaires. However, adolescents have been found to report valid information on pain symptoms [55]. As the biggest city in the county of Nord-Trøndelag has only 21,000 inhabitants, the results might not without reservations be generalized to adolescents living in more urban areas. However, the county does not differ considerably from other counties in Norway with regard to demographic factors, geography and industry. We did not use a diagnostic tool or interview to evaluate mental health problems, and because the young-HUNT study was designed to cover a broad range of issues, only a selection of items were used for some of the psychiatric scales. However, the measures of psychiatric symptoms selected have been used in several previous studies [36, 53] and two of the measures consisted of shortened versions of screening instruments with proven reliability [32, 33, 35].

Conclusions

In this study, we found that chronic multisite pain was prevalent among adolescents with emotional or behavioral symptoms. The prevalence was higher among girls and among adolescents with several coexistent psychiatric symptoms. Resilience factors such as family cohesion, self-esteem and seldom/never feeling lonely markedly attenuated the associations between psychiatric symptoms and chronic multisite pain. Our findings underscore the significance of these factors and the importance of assessing and treating chronic pain among adolescents with emotional or behavioral problems.

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Conflict of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

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Paper III

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