

Doctoral thesis

Doctoral theses at NTNU, 2022:25

Kari Skulstad Gårdvik

# Psychiatric morbidity and associated factors over three years in an adolescent psychiatric population

A prospective cohort study

**NTNU**  
Norwegian University of Science and Technology  
Thesis for the Degree of  
Philosophiae Doctor  
Faculty of Medicine and Health Sciences  
Department of Mental Health



Norwegian University of  
Science and Technology



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Trondheim, February 2022

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# Norsk sammendrag

## Psykiatrisk sykkelighet og assosierte faktorer over tre år i en ungdomspsykiatrisk populasjon

I overgangen fra ungdomsalder til voksenlivet er det en økning i forekomsten av psykiske lidelser. Samtidig er somatiske tilstander og spesielt kroniske smerter vanlige i ungdomsårene. Formålet med denne studien var å få kunnskap om psykisk helsestatus i en ungdomspsykiatrisk populasjon etter tre år, og undersøke mulige sammenhenger med somatiske tilstander, rusmiddelbruk, negative livshendelser og mottatt behandling hos jenter og gutter. Resiliens, av mange beskrevet som styrke til å tåle påkjenninger, ble også undersøkt. Studien har brukt data fra Helseundersøkelsen i Barne- og ungdomspsykiatrisk klinikk ved St. Olavs hospital (Hel-BUP).

Nesten tre av fire ungdommer hadde fortsatt en psykisk lidelse etter tre år, og en av tre rapporterte opplevde symptomer i klinisk eller klinisk grenseområde. Kroniske smerter, røyking og det å ha prøvd ulovlige rusmidler var sterkt forbundet med psykiatrisk sykkelighet tre år senere. Jentene hadde en høyere sykkelighet enn guttene, med økt andel angstlidelser, fem ganger høyere forekomst av depressive lidelser og fem til ti ganger hyppigere kroniske smerter. Det var sammenheng mellom psykiske vansker, generell fungering og frafall i skolen. Selvmordstanker og selvmordsatferd var ikke uvanlig hos de jentene som fortsatt hadde en psykisk lidelse etter tre år. Mange negative livshendelser, spesielt eksponering for vold, var assosiert med selvmordstanker og selvmordsatferd eller skolefrafall, hvilket tyder på en kompleks symptombyrde, spesielt blant jentene i dette utvalget.

Behandlingstiltakene var omfattende og besto særlig av psykoterapi hos jentene og medisinerings hos guttene. Selvrappert resiliens var lavest blant de med depressive lidelser, høyest hos de med ADHD, og lavere hos jenter enn hos gutter. Jo høyere personlige og sosiale ressurser, jo mindre var de psykiske plagene etter tre år, noe som kan tyde på en beskyttende effekt av slike faktorer.

Studien understreker viktigheten av å gjennomføre grundig utredning av psykiske helseproblemer og sentrale risikofaktorer hos ungdomspasienter. Å kartlegge selvmordstanker og selvmordsatferd, livshendelser og fungering i skolen er helt sentralt for å sette inn riktige tiltak og hindre negativ utvikling. Det hører også med å spørre om smerter, særlig hos jenter, likeså røykevaner og bruk av narkotika. Studien fremhever betydningen av beskyttelsesfaktorer og målrettede tiltak for ungdom med psykiske lidelser, likeså et behov for videre forskning for å finne de mest effektive behandlingstiltakene.

<b>Institutt:</b>	Regionalt kunnskapssenter for barn og unge - psykisk helse og barnevern (RKBU Midt-Norge), Institutt for psykisk helse, Fakultet for medisin og helsevitenskap
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Kari Skulstad Gårdvik

## List of papers

- Paper I:** Gårdvik KS, Rygg M, Torgersen, T, Lydersen S, Indredavik MS. **Psychiatric morbidity, somatic comorbidity and substance use in an adolescent psychiatric population at 3-year follow-up.** *Eur Child Adolesc Psychiatry.* 2021 Jul;30(7):1095-1112. doi:10.1007/s00787-020-01602-8. Epub 2020 Jul 15. PMID: 32671493; PMCID: PMC8295167.
- Paper II:** Gårdvik KS, Torgersen T, Rygg M, Lydersen S, Indredavik MS. **Suicidality, function and associated negative life events in an adolescent psychiatric population at 3-year follow-up.** *BMC Psychiatry.* 2021 Feb 18;21(1):109. doi:10.1186/s12888-021-03100-w. PMID: 33602162; PMCID: PMC7893950.
- Paper III:** Gårdvik KS, Rygg M, Torgersen T, Wallander JL, Lydersen S, Indredavik MS. **Association of treatment procedures and resilience to symptom load three-years later in a clinical sample of adolescent psychiatric patients.** *BMC Psychiatry.* 2021 Aug 19;21(1):411. doi:10.1186/s12888-021-03417-6. PMID: 34412609; PMCID: PMC8377856.



## Abbreviations

<b>ACT-codes:</b>	Anatomical Therapeutic Chemical codes
<b>ADHD:</b>	Attention Deficit Hyperactivity Disorder
<b>ASD:</b>	Autism Spectrum Disorder
<b>CAMELS:</b>	Child/Adolescent Anxiety Multimodal Extended Long-Term Study
<b>CAMHS:</b>	Child and Adolescent Mental Health Services
<b>CAP Survey:</b>	Health Survey undertaken at the Department of Children and Youth, Clinic of Mental Health Care, St. Olavs hospital, Trondheim University Hospital, Norway
<b>CBT:</b>	Cognitive Behavioural Therapy
<b>CGAS:</b>	Children's Global Assessment Scale
<b>CI:</b>	Confidence Interval
<b>DAWBA:</b>	Development and Well-Being Assessment
<b>DSM-IV-TR:</b>	Diagnostic and Statistical Manual of Mental Disorders IV Text revision
<b>GAD:</b>	Generalized Anxiety Disorder
<b>GBD:</b>	Global Burden of Disease
<b>HUNT:</b>	Trøndelag Health Study
<b>ICD-10:</b>	International Statistical Classification of Disease and Related Health Problems, 10 <sup>th</sup> Revision
<b>K-SADS:</b>	Kiddie SADS: Schedule for Affective Disorders and Schizophrenia for School-Age Children
<b>NCS-A:</b>	The National Comorbidity Survey Adolescent Supplement
<b>OCD:</b>	Obsessive Compulsive Disorder
<b>PTSD:</b>	Post-Traumatic Stress Disorder
<b>READ:</b>	Resilience Scale for Adolescents
<b>RD:</b>	Risk Difference

**SES:** Socioeconomic Status

**SD:** Standard Deviation

**SSRI:** Selective Serotonin Reuptake Inhibitor

**WHO:** World Health Organization

**YSR:** Achenbach System of Empirically Based Assessment - Youth Self Report



## Summary

In the transition from adolescence to adulthood, there is an enlargement in overall rates of psychiatric disorders, also an increase in psychiatric comorbidity and suicidal symptoms. At the same time, somatic conditions and especially chronic pain are common during adolescence, and strong associations have been found between chronic pain and psychiatric disorders. The overall aim of this thesis was to obtain knowledge on the course of psychiatric morbidity over three years in a clinical adolescent population, and investigate possible associations with somatic conditions, substance use, experiences of negative life events, resilience factors and received treatment procedures, also exploration of gender differences. The study was part of the Health Survey in Department of Children and Youth, Clinic of Mental Health Care, St. Olavs hospital (The St. Olav CAP Survey).

Almost three out of four adolescents still had a psychiatric disorder after three years, and one out of three reported symptom load in the borderline/clinical range. Chronic pain, smoking and having tried illicit drugs at baseline were factors strongly associated with psychiatric morbidity three years later. Girls had a higher morbidity than boys, with an increased frequency of anxiety disorders, a five times higher prevalence of mood disorders, and a five to ten times higher prevalence of chronic pain. One out of four girls with a psychiatric disorder at follow-up had suicidal ideations, and one out of three had a previous history of suicidal behaviour. Furthermore, girls had lower psychosocial functioning, higher rates of school dropout and more experiences of negative life events than boys. Negative life events, especially exposure to interpersonal violence, were associated with suicidal ideation, suicidal behaviour, or school dropout, indicating a complex symptom burden, especially among the girls in this sample.

Treatment procedures were extensive and consisted especially of psychotherapy for girls and medication for boys. Self-reported resilience was lowest among those with depressive disorders, highest among those with ADHD, and lower among girls than among boys in all diagnostic groups. The higher the personal and social resources, the less mental symptoms after three years, suggesting a protective potential.

This thesis underlines the importance of performing a comprehensive assessment of mental health problems and risk factors in adolescent patients. To ask about suicidal ideation and suicidal behaviour, experiences of negative life events and school functioning is essential in order to reveal any such risks, provide interventions and prevent negative development. The results of this study should also encourage to investigate presence of pain, especially among girls, and to uncover smoking habits and illicit drug use. This thesis emphasizes the importance of resilience factors and targeted interventions for adolescents with psychiatric disorders to enhance optimal function, and it also accentuate the importance of continuous research to find the most effective interventions and facilitating factors.

# **1. Introduction**

## **1.1 Topic of the thesis**

The principal topic of this thesis is adolescent psychiatric morbidity and associated areas of function in a three-year follow-up perspective. The thesis examines the course of psychiatric disorders, somatic co-morbidity, substance use and psychosocial functioning in a clinical adolescent population three years after referral to Child and Adolescent Mental Health Services (CAMHS). The occurrence of suicidality and school dropout are given special focus, and their associations with negative life events. Furthermore, the significance of resilience factors and treatment procedures for subsequent symptom load at three-year follow-up are investigated.

## **1.2 Motivation and rationale of the thesis**

Adolescence is a period of pronounced change, both physically and emotionally, and involves a shift in the social environment (1). Emerging adulthood represents a particularly vulnerable time for the initiation of mental health problems (2, 3), and adolescence is the time at which a high burden of disease develop from mental disorders (4). Through my work in the CAMHS for more than 25 years, I have met a large number of adolescents with severe mental health problems, extensive functional impairment, and major challenges in their everyday lives. This has often led to many thoughts and questions about how these adolescents develop further, and how they cope in life as young adults. The opportunity to get some answers to these questions and to follow the development of a number of former patients, has been given through the Health Survey in Department of Children and Youth, Clinic of Mental Health Care, St. Olavs hospital (The St. Olav CAP Survey). This prospective longitudinal cohort study of psychiatric morbidity in an adolescent clinical population has provided a unique database with extensive information on lifestyle, personal and family histories, and psychiatric diagnostic assessment of adolescent patients referred to the CAMHS in Mid-Norway in 2009-2011. The baseline register (T<sub>1</sub>) provides a broad basis for examining factors associated with psychiatric disorders, and follow-up data after 3 years (T<sub>2</sub>) makes it possible to study developmental course of disorders and associated factors in the defined population.

Despite the fact, that suffering from a psychiatric disorder in adolescence is a potent risk factor for having a psychiatric disorder in adulthood (5, 6), the frequency of psychiatric disorders is naturally expected to decline in a clinical follow-up, due to treatment, individual maturation, and situational factors. However, knowledge is scarce on the developmental course of psychiatric morbidity in a clinical adolescent cohort, as well as its interaction with co-occurring somatic disorders, chronic pain, and substance use. Information about how negative life events affect psychiatric symptoms and functioning later in adolescence in a general clinical adolescent population is also limited. Furthermore, resilience factors may influence mental health, but as research on these factors in relation to psychiatric symptoms are primarily carried out in the general population or in specific diagnostic groups, knowledge is restricted on the significance of resilience factors in a general clinical population of adolescents. Such insight is greatly wanted in clinical practice, as a necessary basis for the choice of interventions and specific treatment.

### **1.3 Adolescence – a time of change**

Adolescence is a period of life in which major changes occur with biological maturation and social role transitions (7). According to the World Health Organization (WHO), the age of adolescence is defined as the period between 10 and 19 years (8), but the definition of adolescence has in recent years been suggested to include the years between 10 to 24 years, to adjust to the more modern patterns of changes and development during this life phase (7). Arnett defined the period from 18 to 25 years as emerging adulthood (9), a period of life when the person has left the dependency of childhood and adolescence, into a period characterized by possibilities in life direction, work and love, but not yet having the responsibilities as are normal among adults. The term *emerging* catches the dynamic and inconstant character of this period.

The biological changes occurring during puberty affect the risk of developing psychiatric symptoms (10), and include both pubertal hormonal changes and maturation of the brain. The hormonal changes are found to play a part in the risk for mood and anxiety disorders (10, 11). The adolescent brain undergoes neurodevelopmental processes, as the prolonged maturation of the prefrontal cortex and parietal lobes occurs, with an extended pruning of neuronal axons which entails thinning of cortical grey matter, and a simultaneous increase in neuronal

myelination (12). The maturational process of the prefrontal cortex constitutes the growing control of behaviour. In adolescents this maturation has not yet reached the point of adequate risk assessment and safeguarded control, providing the adolescent-typical behaviour characterized by impulsivity, risk-taking and sensation seeking (12, 13). This behaviour may increase the risk of mental illness. The active state of maturation during adolescence makes the adolescent brain structurally and functionally vulnerable to not only risky behaviour, but also substance use and environmental stress (14). This transitional period of life is also a time of emotional insecurity and uncertainty, since the lives of adolescents are very unsettled (15). The changes in social environment are for many adolescents positive and easy to adapt to, but can for some be stressful and unpleasant, and contribute to vulnerability and poor mental health (1).

## **1.4 Psychopathology in adolescence**

### **1.4.1 Psychiatric diagnoses**

Epidemiological studies have shown large variations in prevalence of mental disorders in children and adolescents (16). The worldwide prevalence of mental disorders in this age group was 13.4% in 2015 (17), with anxiety disorders as the most frequent disorder (6.5%). The reported prevalence has been lower in Norway; 8% met the criteria for a psychiatric disorder requiring treatment in 2009 according to the Norwegian Institute of Public Health (18, 19). Although the proportion with diagnosed disorder was low, 15-20% of children and adolescents aged 3-18 years had reduced function due to symptoms of psychiatric disorders (18-20). A national investigation among adolescents in Norway (Ungdata), has during the last years showed a marked increase in self-reported depressive symptoms, especially among girls (21). Still, the global prevalence of psychiatric disorders in adolescents has not increased over the past two decades (22, 23).

Psychiatric diagnoses differ with age and gender. Before puberty, more boys than girls are diagnosed, and attention deficit hyperactivity disorder (ADHD) and conduct disorder dominate, while after puberty, the diagnoses and gender predominance shift to anxiety, depression and eating disorders among girls (3, 24). The incidence of depression in girls rises sharply after puberty, indicating adolescent depression being more closely linked to female hormonal changes than chronological age (25).

In the transition from adolescence to adulthood, there is an increase in overall rates of psychiatric disorders for both genders (24, 26). Psychiatric disorders occurring frequently in adolescence are often precursors and strong predictors of similar disorders in young adulthood (24, 27, 28). A 14-year prospective cohort study found that 65% of female adolescents and 47% of male adolescents with a psychiatric disorder had at least one further episode in young adulthood (27), and for those with a persistent disorder from adolescence, the rate of disorder continuation increased to 70% among girls and 55% among boys. A developmental follow-back of a prospective longitudinal cohort showed that among those who met criteria for a major Diagnostic and Statistical Manual of Mental Disorders (DSM) diagnosis at 26 years, half had a disorder at age 11-15 years, and three out of four before 18 years (29).

Adolescent depression has been found to increase the risk for adult depression regardless of comorbidity (30, 31), and recurrence in young adulthood was reported by the majority in the developmental follow-back of a prospective longitudinal cohort (32). Anxiety disorder has been found to be a predictor of depression in adolescence (33), and in a meta-analysis of longitudinal studies, anxiety and depression were found to bidirectionally predict one another (34). In a previous study of the developmental course of anxiety and depression from adolescence to young adulthood in the current clinical cohort, heterotypic continuity was more common than homotypic continuity, and depression predicted later anxiety disorder (35).

#### **1.4.2 Psychiatric comorbidity**

Psychiatric comorbidity refers to two or more psychiatric diagnoses present at the same time of assessment (36). Comorbidity of psychiatric disorders is common in children and adolescents and increases by age (37, 38), more marked in girls than in boys (37). Approximately 40% of the participants in the adolescent supplement of the National Comorbidity Survey (NCS-A) in USA with one class of psychiatric disorder also met criteria for another class of lifetime disorder (38). Among adults with psychiatric disorders, almost half have more than one disorder, and comorbidity continues to be more frequent in females (39).

Anxiety disorders in children and adolescents often coexists with other psychiatric disorders, and one anxiety disorder frequently co-occur with another anxiety disorder (40-42). In a recent study of generalized anxiety disorder (GAD) investigating prevalence, predictors, and comorbidity in children and adolescents, 57.6% of those with GAD met the diagnostic criteria for another anxiety disorder (43). Depression is also frequently occurring together with anxiety disorders in children and adolescents (37, 44, 45). In a former review study, about 25-50% of depressed adolescents had a comorbid anxiety disorder, and about 10-15% of the adolescents with an anxiety disorder also had depression (45).

Major depressive disorder was associated with other classes of psychiatric disorders in 63.7% of all 12-month cases in the NCS-A (46). The strongest associations were with anxiety disorders, conduct disorder and oppositional defiant disorder, followed by ADHD and substance use disorder. Due to the common comorbidity between depression and other psychiatric disorders, it is referred to as the rule rather than the exception (47), and found in both community and clinical settings (48). The high degree of comorbidity between depression and other psychiatric disorders can be partly explained by shared risk factors for numerous disorders, but could also emerge given that comorbid disorders are risks or consequences of depressive disorder (25).

Comorbidity in children and adolescents with ADHD is broadly studied, as for example in a large Danish study which aimed to identify the full range of psychiatric disorders comorbid to ADHD in children and adolescents diagnosed in Danish psychiatric hospitals between 1995 and 2010 (49). The researchers found that 52% of the patients had at least one psychiatric disorder comorbid to ADHD, 26% had two or more comorbid disorders, and the most frequent coexisting disorders were conduct disorders (16.5%), followed by specific developmental disorders of language, learning and motor development (15.4%) and autism spectrum disorders (ASD) (12.4%) (49). In an Italian study of children and adolescents with ADHD, 66% of the patients had one or more comorbid psychiatric disorder, with specific learning disorder as the most frequent co-occurring disorder (56%) (50). A recent review article investigating comorbidity between ADHD and anxiety disorders across the lifespan (51), points out that ADHD and anxiety disorders are among the most common psychiatric disorders with a 25% comorbidity rate with each other, and that the prevalence of anxiety

disorders in children with ADHD increases after puberty, primarily owing to increased rates of anxiety disorders among females.

Other psychiatric disorders also have high prevalence of psychiatric comorbidity, as for example ASD (52), eating disorders (53), and conduct disorder (54).

### **1.4.3 Suicidal ideation and behaviour**

Suicidal symptoms increases during adolescence (55-57) with a shift from suicidal ideation to suicidal behaviour (56, 58, 59), and an estimated lifetime prevalence of suicidal ideation and suicide attempts of 12.1% - 33% and 4.1% - 9.3%, respectively (56, 60). The prevalence of self-harm, regardless of motivation and intention to die, has increased among Norwegian adolescents from 4.1% to 16.2% between 2002 and 2018 (61). Second to road accidents, suicide is the most common cause of death among young people worldwide, rare before 15 years of age, but the frequency increases through adolescence (57, 62-64). The prevalence across all ages, gender and countries is 3.77/100 000, and in Norway 3.00/100 000 (63). Overall, suicides are the reason for 1.4% of early deaths worldwide (65).

Suicidal ideation and behaviour are common in patients with psychiatric disorders (24, 56, 57) and are more than three times more frequent in clinical samples of youth than in the general population (58, 66). The increase of suicidal thoughts and behaviour through adolescence coexists with increasing frequencies of psychiatric disorders and related psychopathology that by itself provide higher suicide risk, as for example depression, substance use, some anxiety disorders and first episode of psychosis (24, 56, 58, 67). The majority of suicides and attempts are related to psychiatric disorders and occur at least ten times more often among psychiatric patients than in the general population (65). Depression, substance use disorders and schizophrenia are among the disorders with the highest risk for suicide (65). According to a meta-review investigating risk of all-cause and suicide mortality in psychiatric disorders, also borderline personality disorder, bipolar disorder and anorexia nervosa had substantially increased rates of suicide compared to the general population (68). Another meta-analysis and systematic review of longitudinal studies of psychiatric disorders as risk factors for suicidal behaviour in young people, showed that psychiatric disorders



significantly increase the risk of suicide attempts, and particularly of completed suicide in adolescents and young adults aged 12 to 26 years (69).

Comorbidity increases the risk of suicide (65, 70), and a strong association was found between psychiatric disorders and suicidal attempts when psychiatric comorbidity was present (69). It applies to all classes of psychiatric disorders, with combinations with psychotic disorders involving the highest risk, followed by mood disorders (65). A population-based prospective longitudinal study of the impact of anxiety disorders in suicidal ideation and suicidal behaviour, showed that the presence of any anxiety disorder in combination with a mood disorder was associated with a higher probability of suicide attempts compared with having a mood disorder alone (71). The prevalence of suicide attempts and suicides is also increased in the context of physical health problems, as are shown for a large group of chronic diseases and injuries, regardless of comorbidity with psychiatric disorders (65). Chronic pain is entitled to a special mention, as the frequency of suicide attempts is high (72, 73), and it remains high even when the comorbid psychiatric disorders are adjusted for (73, 74).

Suicide characteristics differ by gender (57, 63, 64, 75, 76), with girls having higher rates of suicidal ideation and behaviour, whereas boys have the highest rates of committed suicide. In the NCS-A, the lifetime prevalence of suicide attempts was three times higher in girls than in boys (6% versus 2%) (56). Gender differences are furthermore found in the risk factors for suicidal ideation; anxiety disorders were among the major risk factors for girls, whereas mood disorders were the only common psychiatric disorders at risk for both genders (76). The factors that increased the risk for suicidal behaviour only among girls were eating disorders, post-traumatic stress disorder (PTSD), bipolar disorder and depressive symptoms, whereas among boys, disruptiveness and hopelessness were the factors with significant associations to suicide attempts (75).

#### **1.4.4 Symptom load**

The high degree of continuity of psychopathology from adolescence into young adulthood implies that the perceived symptom load may be considerable (3, 27). According to a Lancet report in 2011, psychiatric disorders are the most prominent reason for the global burden of

disease in young people (4). The WHO describes depression as the leading cause of disability, measured by years lived with a disability (77). In the Global Burden of Disease (GBD) Study 2013, depression was rated as the second largest contributor to the global burden of disease among adolescents and adults between 15 and 44 years of age, when measured by disability-adjusted life years (78).

## **1.5 Somatic morbidity in adolescence**

### **1.5.1 Somatic conditions**

Somatic conditions are common in young age and approximately one in ten adolescents suffer from a chronic somatic condition or disability that limits their daily activities (79, 80). Number of adolescents with chronic somatic conditions are rising (80, 81), due to medical advances and improvements in survival of former fatal conditions of childhood such as for example preterm birth with very low birthweight, congenital heart disease, and to an increasing incidence in adolescence of other conditions as for example diabetes and cancer, with better outcomes of many types of cancer (80, 82).

There are challenges in coping with chronic conditions in childhood and adolescence (83), since chronic conditions during these years cause significant stress in everyday life affecting educational and social participation. Despite the various challenges associated with each somatic disorder, there is a large degree of similar experiences across diagnoses (84). Long-term health problems when growing up can involve an increased risk of being bullied compared to healthy peers (85, 86), academic challenges and school dropout (87, 88), reduced physical and social well-being (81), and the children are more likely to show internalising symptoms than healthy controls (79). Previous research also indicates that adolescents with chronic somatic conditions are as likely or even more likely to engage in risky behaviours and substance use than their healthy fellows (80, 89). A possible explanation is that adolescents with chronic conditions may feel a need of acceptance from their healthy peers, and that participation in risk behaviours demonstrate their normality, or that the higher rate of emotional distress is a risk factor for the behaviours (89).

Adolescents with chronic somatic conditions have a double inconvenience, since chronic somatic conditions can affect adolescent development, and adolescent development, especially engaging in risky behaviours, can influence the condition and potentially give adverse health outcomes (79, 80). The somatic conditions may also affect entering and coping with adulthood. As stated by previous research, becoming an adult today means being able to support themselves and learning to be an independent person (15). However, many adolescents with somatic conditions experience limitations in their possibilities to become independent and report barriers to being a normal participant and contributor to society (90).

### **1.5.2 Comorbidity between psychiatric and somatic disorders**

Chronic somatic conditions is frequent in adults with psychiatric disorders, as presented in a comprehensive review of comorbidity of mental disorders and somatic conditions in adults (91). Among adults with a psychiatric disorder, more than 68% had at least one somatic condition. Previous research has confirmed an explicit relationship between somatic symptoms and psychiatric disorders (92) and that psychiatric disorders of all types are associated with an increased risk of onset of a broad range of somatic conditions (93). The connections between psychiatric disorders and somatic conditions are most often compound and bidirectional (91). One example is that somatic conditions with high symptom burden can lead to major depression (94) and simultaneously, major depression is a risk factor for somatic conditions (95). Another aspect is the fact that many of the common medical treatments for psychiatric diseases may actually worsen the comorbid somatic condition, such as weight gain and risk for metabolic changes and diabetes when using antipsychotic medication (96).

The prevalence of anxiety disorders in adolescents with chronic somatic conditions is higher than in the general population (97), and previous research have found anxiety disorders to be positively associated with somatic disorders even after adjusting for mood disorders, substance use disorders, and sociodemographic characteristics (98). A systematic review displayed that in adolescence there was a strong positive association between anxiety and depressive disorders and chronic somatic disorders (99). Another systematic review found that in children and adolescents with ASD and ADHD, somatic conditions were extensive and manifested across different medical areas, such as gastroenterology, neurology and

immunology (100). In a recent population-based Swedish study, children with psychiatric disorders were found to have a high risk for concurrent somatic conditions, across all ages and across many types of conditions (101). In the Neurodevelopmental Genomics Cohort Study, the pervasive comorbidity between the full range of psychiatric disorders and clinically diagnosed somatic conditions were documented (102), and direct associations were found between the severity of the somatic condition and most classes of psychiatric disorders. Chronic somatic conditions are also associated with increased risk for the onset of suicidal thoughts and behaviours (103).

Previous research indicates that the comorbidity between psychiatric disorders and somatic disorders with a neurological basis are high among adolescents, suggesting this is mainly caused by these conditions' impact on brain structure and neural chemistry (99). Longitudinal studies have found that in the months before the first epileptic seizure, children and adolescents have experienced marked changes in mood and behaviour (104). ADHD, primarily the inattentive type, is reported in 28-70% of children and adolescents with epilepsy (105), and children with ADHD were 2.7 times more likely to evolve epilepsy than children without ADHD (105, 106). The ADHD symptoms are frequently observed at the time prior to the first seizure, and compared with patients with epilepsy alone, those with comorbid epilepsy and ADHD are younger at onset and have more frequent seizures (106). Children and adolescents with ASD are also more plausible to have epilepsy than those without neurodevelopmental disorders (105).

Comorbid psychiatric disorders are challenging to assess and treat, especially in combination with co-existing somatic symptoms or disease (102). All these study findings point to the importance of placing focus on the associations between psychiatric and somatic symptoms in disease development.

### **1.5.3 Chronic pain**

Chronic pain is common during adolescence across countries, and as many as 44.2% of the adolescents in 42 countries reported chronic weekly pain during the last six months (107). Similar high prevalence was found among Norwegian adolescents (108). Gender and age were strongly associated with chronic multisite pain, with higher prevalence among girls and

in older age groups (107-109). Gender differences are found in pain tolerance after reaching puberty, with a decreased pain threshold among girls (110). Research has documented the effects on pain endurance by positive self-instruction and pain-related self-efficacy for both genders, with no gender differences in adolescents related to the pain endurance (110).

Pain symptoms in adolescence involves an increased risk for mental distress in young adulthood (111-113), with a linear relationship between number of pain sites and later mental distress (111). Chronic multisite pain was prevalent among adolescents with emotional or behavioural symptoms in a large population sample of adolescents, and higher among girls and among those with several coexistent psychiatric symptoms (114). In the current sample of interest, consisting of former young adolescent patients with psychiatric disorders, higher rates of chronic pain were found than the rates reported for the general adolescent population (108, 115).

Strong associations are reported between chronic pain and especially anxiety and depression (116, 117), and a bidirectional relationship is found between pain and depressive symptoms in adolescents (118). Functional imaging studies propose that shared neural mechanisms contribute to the bidirectional relationship between chronic pain and psychiatric disorders (119). Brain structures as amygdala, anterior cingulate cortex, and anterior insula, mediate the processing of emotions, and are also the structures involved in perception of pain and pain unpleasantness (120). A review has demonstrated that many of the same hormones, cytokines, neurotransmitters and genes have been involved in chronic pain, anxiety, depression and PTSD, and that they are inextricably connected to one another, either directly or through the hypothalamic-pituitary-adrenal (HPA) axis (121). Another recent review has proposed a conceptual framework of the bidirectional interplay between depression and chronic pain, based on the assumption that the individual and contextual factors are interacting with one another and connected in dynamic and compounded ways (122). The individual child-specific factors in this framework includes neurobiological, cognitive, behavioural, and affective factors, and the contextual elements include parental factors such as their pain status, mental health, and behaviour.

Therefore, pain seems to be a common symptom and part of the complexity in many psychiatric disorders, especially in anxiety and depressive disorders. Also, having chronic pain in adolescence has been found to be associated to an increased probability of lifetime history of anxiety and depressive disorders in adulthood (123). Chronic pain is a leading contributor to the global morbidity and disability burden as described in The GBD 2013 study, where low back pain is the worldwide leading cause of years lived with disability (78). The high prevalence of chronic pain among adolescents makes them vulnerable, especially with comorbid psychiatric symptoms and disorders, as this combination increases the prevalence of multisite pain (114, 115) and functional disability (115, 124).

## **1.6 Substance use**

Adolescence is the period of life when substance use is usually initiated (125). One reason may be the neurobiological changes in the complex developmental processes of the adolescent brain (125). Other reasons may be that the adolescents are in a period of being undetermined and experimental, characterized by environmental changes and increasing access to substances. Adolescents seem to be more prone to experience negative effects of substance use than older age groups (14). In the USA, the most commonly used substance among 18 years old adolescents is alcohol, with a lifetime prevalence of 59%, followed by marijuana (44%), and cigarette use (24%) (126). Cigarette use has declined, whereas e-cigarette use vaping nicotine has become prevalent (34%) the last couple of years (126). Boys are still more likely to have higher rates of substance use than girls, but the gender differences has changed within the different substance groups during the period of 1975-2018, as for example nearly closing the gender gap in annual marijuana use in 2018 and narrowing the difference between genders in alcohol use considerably (126).

There are differences in prevalence of substance use across countries, and Norway appears to be a low-prevalence country when it comes to substance use in the general adolescent population in comparison with other European countries (127). In the European countries participating in the European School Survey Project on Alcohol and Other Drugs (ESPAD), the average lifetime prevalence reported by students were 80% of alcohol use, 46% of cigarette smoking, and 18% of having tried illicit drugs at least once (127). The Norwegian figures were lower; alcohol use 57%, cigarette smoking 28%, and illicit drug use 7% (127).

Boys reported higher rates than girls in illicit drug use (10% versus 4%) and cigarette smoking (29% versus 26%), whereas girls reported slightly higher rates than boys of alcohol use (58% versus 56%) (127).

In a Lancet article about substance use in young people (128), those with mental health problems are described having higher rates of substance use, dependence, and experiences of adverse effects of use than those without such disorders. Furthermore, for young people with previous mental health problems, substance use might worsen or trigger a recurrence of symptoms (128). A previous study comparing the current clinical sample of adolescents with the general adolescent population, displayed high frequency of alcohol intake in both samples, while the clinical sample had a higher prevalence of smoking, and four times higher odds of having tried illicit drugs compared to the general population (129). Similar results were reported in a recent population-based survey linked with data from National Patient Registry in Norway, which showed that adolescents receiving specialist mental health care reported more frequent alcohol use, drug use and problems compared to adolescents not receiving this service (130). The same study reported that all investigated psychiatric diagnoses, except autism, were associated with some measure of hazardous alcohol/drug use, with highest odds among adolescents with conduct disorders, trauma-related disorders, and depression (130). Harmful alcohol consumption combined with depression and anxiety is commonly observed (131, 132), and adolescent substance use predicts internalizing disorders in adulthood among females (133). The observational follow-up of the Multimodal Treatment Study of Children with ADHD (MTA) investigated substance use through adolescence into early adulthood, and the findings were no differences in alcohol use with the comparison group, but the ADHD group had higher rates of weekly marijuana users and daily cigarette smokers (134). Substance use, especially cannabis use, has been found to be frequent among those with first-episode psychosis and may trigger early psychosis in vulnerable patients (135).

Use of a single substance is rare, whereas use of multiple substances is more common (136), and early initiation of substance use and using multiple substances, are both powerful predictors of later substance use problems and disorders (137). Although, most adolescents who use substances do not develop addiction, the NCS-A in USA displayed high prevalence

of substance use disorders by the age of 18 years, where 15% meet the diagnostic criteria for alcohol abuse and 16% for drug abuse (138). Substance use represents major public health challenges and is closely related to increased mental and somatic comorbidity and mortality. The GBD 2013 study implies that the burden attributable to substance use increases considerably in adolescence and young adulthood, as alcohol and illicit drug use are liable for 14% of total health burden among men aged 20-24 years (78).

## **1.7 Negative life events**

It is common to have experienced negative or stressful life events or adversities from childhood to young adulthood (139-141). A systematic review and minimum estimates of the global prevalence of past-year violence, defined as physical, sexual, emotional, or multiple types, showed that globally over half of all children (1 billion children, ages 2-17 years) experienced such violence (142). In Norway, studies of childhood abuse in the general population have shown prevalence numbers of physical abuse of 5-6% (both genders) and of sexual abuse of 10-14% among girls and 3-4% among boys (143-145). Similar prevalence rates of sexual abuse are found in European countries (146). Childhood abuse is more frequent in clinical psychiatric samples of children and adolescents than in the general population, as shown in a study of a Norwegian child and adolescent outpatient setting (147). This study reported prevalence of physical abuse of 33.9%, sexual abuse of 28.8% and neglect of 28.1%, and the rate of reported sexual abuse was significantly higher in girls versus boys (37.2% vs. 6.3%) (147). A large Swedish study reporting on multiple types of lifetime victimization and current health, showed that victimization was more common in adolescence than in childhood, and to be victimized recurrently rather than a single time occurred more frequently among both girls and boys (148).

Experiencing negative life events during demanding developmental periods in childhood and adolescence may increase vulnerability to mental distress by inducing biological changes with long-term effects on nervous, endocrine, and immune systems (149, 150), and may even cause genetic modifications of DNA (150-153). An annual research review of neurobiological effects of childhood abuse and neglect (154) described that childhood abuse was found to be associated with changes in brain structure and function, with a clear dose-response relationship between exposure severity and extent of the neurobiological findings.



Furthermore, the review suggested that the maltreatment-related findings have the appearance of neuroplastic adaptive responses, and stated that the type of maltreatment, age of exposure and gender matter. Thus, negative life events may increase the risk for psychiatric symptoms, including suicidal behaviour in vulnerable individuals (143, 149).

In a recent study (155), the number of stressful life events was found to associate with both internalizing and externalizing psychopathology, indicating that stressful life events are a transdiagnostic risk factor of psychopathology. Previous research has found strong associations between childhood adversities and the onset of psychiatric disorders in adolescence (141), and that exposure to more than one type of adversity and negative life event increases the risk of psychiatric disorders and symptoms (148, 156, 157). An umbrella review including 68 systematic reviews and meta-analyses (158), demonstrated that exposure to at least one adverse childhood experience, and to specific types such as child maltreatment, bullying, and maladaptive parenting behaviours, doubled the risk of anxiety disorders, depression or suicidality. Former studies have found associations between negative life events and a number of psychiatric disorders, such as anxiety disorders (148, 156, 159), depression (156, 157, 159, 160), PTSD (148, 157), eating disorders (156, 159), bipolar disorders (156), psychosis (161-163), and behavioural disorders (159, 164). Experiences of childhood adversities increases the risk of recurrent psychiatric disorders throughout life (28). Furthermore, previous research has also given evidence suggesting causal relationship between negative life events and drug use (148, 156, 159), and especially when poly-victimization is present (148, 156).

Different negative life events are also found to be associated with suicidal symptoms in adolescents (149, 165, 166), such events may include being exposed or witnessed to violence, sexual trauma, or other injury and trauma (140). In a systematic review, young people with attempted suicide were more likely to have experienced stressful life events than those with suicidal ideation (149). A meta-analysis presented strong evidence that early exposure to any interpersonal violence increased the risk of suicide attempts (167). Many other negative life events have shown associations to suicidal ideation, behaviour or committed suicide, as for example death of a parent or a loved one (168, 169), experiences of disasters or accidents (169), peer victimization (170) and multiple other family factors (171, 172).

## **1.8 Functioning**

### **1.8.1 Psychosocial function**

Psychosocial functioning plays an important role in the conceptualization of psychopathology as a diagnostic criterion, and is widely used in defining the severity of a psychiatric disorder and in evaluation of treatment outcome (173). It contains descriptions across important life domains, measuring the impact of the symptoms in these domains, including personal, family, social, and academic functioning. Psychosocial function is assessed by clinicians in CAMHS, being an objective measure of the function.

Adolescents with anxiety disorders may experience being impaired in various life domains crucial for the developmental period of emerging adulthood, and adolescent anxiety compared to childhood anxiety, was found to be associated with more adverse psychosocial outcomes at age 30 years (174). A systematic review of the impact of social cognitive deficits in major depressive disorder showed associations with poor psychosocial functioning in domains of cognitive functioning and quality of life (175). Another recent systematic review and meta-analysis has investigated adolescent depression and the long-term psychosocial outcome, demonstrating that adolescent depression is associated with a great number of adult psychosocial outcomes which may lead to difficulties through the lifespan (176).

In a 6-year follow-up study of children and adolescents with ADHD, almost one out of two was still functionally impaired in late adolescence and young adulthood (177). In another recent study, ADHD with comorbid disorders was associated to low level of psychosocial functioning compared to ADHD only (178). There is support in the literature that psychosocial functional impairment is highly present in severe psychiatric disorders. In early-onset psychosis, predictors of worse functional outcome are a positive history of premorbid difficulties, greater symptom severity at baseline, especially negative symptoms, and longer duration of untreated psychosis (67). These are all common factors when adolescents develop a severe psychotic disorder. Among adolescents diagnosed with a bipolar disorder, those with persistent mood symptoms had worse psychosocial functioning compared to the others (179). Exposure to childhood trauma and negative life events are common experiences in a clinical sample, and may also have longstanding effects on psychosocial functioning for adolescents and young adults (180).

Associations between psychiatric disorders and unfavourable functional outcomes has been found to increase with higher clinical severity at baseline (181). Previous research has shown gender differences in psychosocial functioning related to different psychiatric symptoms and disorders, as one study reported lower psychosocial functioning among boys with symptoms of anxiety and depression, compared to girls (182). Another recent study showed that boys with depression had higher risk of low psychosocial functioning compared to girls (183).

### **1.8.2 School dropout**

School dropout is a major concern in countries all over the world (184-186). In the Young-HUNT1 Study, a population-based study in Central Norway, 17% was registered as being high school dropouts, as reported at age 24 (184), and more boys than girls were found to be non-completers in another Norwegian population-based survey (185). There are many risk factors for school dropout (187), and the reasons vary widely (186). A meta-analytic review of risk factors for school absenteeism and dropout described significant associations to having problems at or with the school, physical and mental health problems, adverse childhood experiences, parenting difficulties and family problems (187). Negative or stressful life events are found to be associated with intentions of and actual dropout (188), including conflicts with authorities for boys, and relational problems for girls (189). In a recent study, high school students exposed to severe acute stressors were immediately vulnerable to dropping out (190).

According to WHO, education and health are strongly linked (191). Mental health problems in early years influence academic functioning and may subsequently lead to increased risk of dropping out of school (176) and receiving unemployment benefits or social insurance support (184). School dropout was associated with poor mental health in a Danish population-based study (192), and school dropout involve heavy and enduring individual and social costs (190). A study of childhood determinants of adult psychiatric disorders, described that poor school performance and low levels of educational achievement in adolescence were associated with a two or three times increased risk of adult anxiety and depression (28).

A recent systematic review and meta-analysis investigating adolescent depression and the long-term psychosocial outcome, showed that adolescent depression was associated with

higher odds of failure to complete secondary school (176). Another recent systematic review of social and academic functioning in adolescents with anxiety disorders, reported that adolescents with anxiety disorders felt impaired at school, had higher risk for school rejection and started higher education less often (193). Previous research has found links between suicidal symptoms and school functioning. According to a systematic review with meta-analysis of longitudinal studies, adolescents and young adults with school failure were at higher risk of suicide attempts (194).

## **1.9 Factors related to outcome**

### **1.9.1 Treatment procedures**

Psychosocial, pharmacological and brain stimulation options are accessible as treatment procedures of many psychiatric disorders in children and adolescents. However, what should be the first choice of treatment methods, based on efficacy and acceptability, remains uncertain according to a recent umbrella review (195). Focusing on 20 different outcomes in 15 psychiatric disorders or groups of disorders, this comprehensive review has given a thorough meta-analytic view of the evidence base concerning the efficacy, acceptability and other relevant outcomes of psychiatric treatment in children and adolescents (195). It provides important knowledge about both medication and psychotherapy recommended for different psychiatric disorders in children and adolescents. In addition to psychotherapy and medication, it will always be of great importance and relevance to have other treatment interventions in CAMHS, such as family therapy, counselling parents, and counselling municipal services.

#### **1.9.1.1 Psychotherapy**

Psychotherapy is often recommended as the first-line treatment for adolescents suffering from specific psychiatric disorders. A multilevel meta-analysis synthesizing five decades of aggregated knowledge on effects of youth psychotherapy, states that the impact of therapy differs markedly by target problem, showing larger treatment effects for anxiety than for other problems, and most unsatisfying effects for depression (196). As an example of a psychotherapy method widely used for adolescents, cognitive behavioural therapy (CBT) has been a recommended treatment for anxiety disorders, with many studies showing positive

effect (195, 197, 198). However, a Cochrane review from 2020 concluded that CBT was no more effective than non-CBT active control treatments or treatment as usual (199). Results from the Child/Adolescent Anxiety Multimodal Extended Long-Term Study (CAMELS) found that treatment type was not associated with remission status across the follow-up (200). Likewise, even though many new treatment methods have been developed for depression during the past decades, their effectiveness has not improved over time (201), according to a meta-analysis of 13-year follow-up of psychotherapy effects on youth depression (202). Whereas for obsessive compulsive disorder (OCD), CBT with exposure and response prevention has shown to be effective and is recommended as the first-line treatment (195, 203). Finally, we must also have in mind the therapist's effects, an often ignored but critical factor, since the therapist's qualities have an impact on the treatment outcome (204).

As comorbidity of psychiatric disorders is frequent in adolescence (37, 38), especially in clinical samples (48, 49), treatment often needs to involve compound procedures. Also, severe disorders require comprehensive treatment interventions (205-207). Some transdiagnostic psychotherapy methods have been developed and designed to address symptoms of different diagnostic clusters (208, 209). These have been found to exceed effects of standard manualized treatments with clinically referred adolescents (210).

### **1.9.1.2 Pharmacotherapy**

Pharmacotherapeutic principles are the same for children and adolescents as for adults, but with stricter guidelines. ADHD is the most common disorder for which medication is recommended, using amphetamine and methylphenidate (195, 211, 212), which are showing good efficacy and tolerability for children and adolescents (213). Moreover, antidepressants are often used for mood and anxiety disorders, with selective serotonin reuptake inhibitors (SSRI) as the preferred treatment for children and adolescents (214). The differences in effect between psychotherapy and antidepressant medication are found to be small to non-existent in the treatment of adult depression and anxiety disorders (215). A combination of psychotherapy and pharmacotherapy is the treatment of choice for patients with adult depression (205, 216), but the evidence is limited for children and adolescents (217-219). For OCD, medication with SSRI has shown to be effective and should be considered the first-line

pharmacological treatment when indicated (195). For schizophrenia spectrum disorders, antipsychotic medication is the cornerstone of treatment, also for adolescents (195).

When using psychotropic medication in the treatment of children and adolescents, we have to bear in mind the adverse effects, which are especially important in these developmentally sensitive periods of life (220). A recent large systematic meta-review of 78 adverse effects focused on the safety of 80 antidepressants, antipsychotics, anti-ADHD medication and mood stabilizers in children and adolescents with psychiatric disorders, contributing with important knowledge to the clinical practice (220).

### **1.9.1.3 Research on treatment interventions**

Research on the course of symptoms and treatment outcome is mainly conducted on patient groups recruited to treatment studies with specific psychiatric disorders without comorbidity, whereas in clinical populations, comorbidity of psychiatric disorders is more the rule than the exception. Also, most evidence is accessible for monotherapy versus placebo or non-treatment, although combination of treatments interventions, including both medication and psychosocial treatment modalities, are frequently used in clinical practice (195). Study design and characteristics of both illness and participants often differ considerably between pharmacological and non-pharmacological trials, and thus effect sizes must be interpreted critically (195). We also need to have in mind that most meta-analytic evidence of treatment interventions involve the acute and short-term treatment effects, and future research is required to investigate the efficacy and safety of long-term treatment, and also interventions to prevent relapses of psychiatric disorders in adolescents (195).

### **1.9.2 Resilience factors**

Resilience can be referred to as positive adaptation to risk exposure (221) and a more positive psychological outcome than would be expected in case of high levels of environmental adversities (222). It is a dynamic process where psychological and physical functioning are maintained normal despite stress and adversity (223, 224). The neurobiology of resilience has been investigated (223), and resilience is found to be a multidimensional and compound construct (224). Genetic, epigenetic, and neurochemical factors are all important contributors

to the development of resilience together with the developmental and psychosocial factors (224).

Factors that promote resilience may be categorized into positive individual factors, such as personal and social competence, and may include cognitive factors such as intelligence, personal skills, adaptive temperament, and self-esteem (225-227). Resilience factors can also be contributed at the familial and external social levels, such as family cohesion and support, and social resources and supportive environment outside the family (225-227). These factors may influence developmental courses of psychiatric disorders, have implications for the course of treatment and contribute to a better outcome (228-230).

Previous research has demonstrated that patients with higher baseline resilience scores showed less severe psychiatric symptoms after psychotherapeutic interventions (231-233). As previously found in a group of youth with ADHD in the present clinical population, personal resilience characteristics were associated with better psychosocial functioning and less depression and anxiety (234). In another study of adolescents, higher resilience scores predicted lower scores on levels of depression, anxiety, and obsessive-compulsive symptoms (235), and optimal outcomes of child and adolescent psychiatric disorders were predicted by a combination of personal characteristics and environmental support (236).

### **1.9.2.1 Personal competence**

Personal competence is related to the constructs of self-esteem and self-efficacy (237). It refers to a person's sense of worth and capabilities, and several studies report an inverse relationship between self-esteem and emotional symptoms (182, 238-240). In fact, low self-esteem is one of the diagnostic criteria of depression (241), demonstrating the strong correlation between depression and self-esteem. A large meta-analysis including 85 longitudinal studies (240), concluded that the effect of low self-esteem on depression and anxiety is substantial in the general population, and this association has also been reported in clinical samples (234, 242). Decrease in self-esteem has been found to play a crucial role in the associations between depression and social phobia (243).

Higher personal competence has been shown to significantly relate to lower levels of anxiety, depression, and obsessive compulsive symptoms (235, 244), also protecting adolescents with ADHD from coexisting emotional problems (245). The perception of self was found to be the strongest predictor of fewer psychiatric symptoms over time (232), and the high correlation of the Personal Competence factor to internalizing psychological problems underlines the significance of this factor for psychological health (227). Previous research has shown gender differences in personal competence, as boys compared to girls have reported higher personal competence (226, 227, 244, 246).

### **1.9.2.2 Social competence**

Social competence can be described as the ability to accomplish social goals by using the cognitive, behavioural, and emotional resources available in the child (247). In a recent systematic review investigating social competence and psychopathology in early childhood, social competence was defined as showing prosocial behaviour by fulfilling the needs of others on the one hand, and taking social initiative by fulfilling own needs on the other (248). Social competence has been found to have an essential effect on healthy development and adaptive social functioning, and a causal role in the evolution of internalizing and externalizing symptoms in the future (248). The review demonstrates that deficits in social competence are related to psychiatric disorders as anxiety, depression, ADHD, or conduct disorders in later childhood and adolescence.

Previous research has shown that increasing levels of social competence were associated with lower odds of having symptoms of anxiety and depression (228), and adolescents with ADHD and higher levels of social competence were more protected from coexisting emotional problems (245) and anxiety disorders in young adulthood (234). Furthermore, boys compared to girls have reported higher social competence (227, 228).

### **1.9.2.3 Structured style**

Structured style is related to how a person performs executive functions, which are cognitive processes that integrate information from working memory with context information in order to choose optimal action (249). These functions include the ability to planning, problem



solving, inhibitory control, emotional regulation, attention capacities and goal orientation. Executive weaknesses and dysfunction are a common problem among children and adolescents with ADHD (249), but have been associated with other psychiatric disorders as well (250), such as symptoms of anxiety and depression (251), OCD (252), and conduct disorder (253). Comorbidity among adolescents with ADHD is frequent and increases the difficulties within executive functions, especially when comorbid disorders are anxiety or conduct disorders (250).

Compared with the other four resilience factors, structured style showed lower correlations to symptoms of anxiety and depression in a previous study, which may indicate that the structured lifestyle is less protective for mental health problems than the other resilience factors (227). In the same study, structured style showed high correlation with school grades for girls, suggesting that a structured way of working may present a resilience factor for girls in the academic area.

#### **1.9.2.4 Family cohesion**

Family cohesion is related to how the family is functioning as a unit, with characteristics including stability, emotional support, parental warmth, encouragement and assistance, togetherness and caring relations within the family (225, 227). Although adolescents turn their focus towards the peer group, family remains the primary social support also for many adolescents and is important for their resilience (225).

Family connectedness has been found to be one of the most important factors to protect against poor health outcome in adolescents across countries, including mental health (254). High levels of family cohesion are positively related to resilience and lower levels of psychiatric symptoms, such as anxiety, depression, and obsessive-compulsive symptoms, and demonstrated in many studies (228, 235, 255, 256). A review of resilience factors in adolescents with ADHD showed that some of the strongest evidence for promotive and protective factors was found among family-level factors (229). In another study of ADHD patients in the present sample, better family functioning was associated with fewer emotional and conduct problems (245). Former research has shown gender differences in reported

family cohesion, as boys have scored higher on perceived family cohesion than girls (227, 228, 244, 246).

#### **1.9.2.5 Social resources**

Social resources are described as supportive environment outside the family, characterized by the neighbourhood, school and accessible social support and positive role models (227). Supportive and positive influence from peers and teachers are found to be positively linked to resilience in adolescents (225), indicating the importance of the school environment and broader social environment (225, 257). Previous research has shown that adolescents reporting low family and overall support had increased probability of psychological distress than those reporting high support (258). A meta-analysis has suggested a less likely development of trauma-related psychopathology in children and adolescents with high levels of social support, and that this appears across diagnoses (259).

In a review of factors improving resilience in adolescents with ADHD, the presence and quality of friendship, with peer acceptance, was a protective factor shown to buffer against negative outcomes (229). Higher levels of social support has been found to be connected with lower levels of anxiety (244), and having a high number of friends with reduced symptoms of anxiety and depression (228). Previous research has found gender differences in the reporting of social resources, as girls have reported more access to social resources than boys, including both supportive family and friends (226, 227, 246).

#### **1.9.2.6 Interventions promoting resilience**

Interventions promoting resilience can be addressed within three broad areas; individual-level, family-level, and social environment interventions (225, 257). A recent systematic review and meta-analysis of resilience training programs shows that interventions based on a combination of mindfulness techniques and CBT seem to have a positive impact on individual resilience (260). Strengthening home and school environments promotes resilience in children and adolescents as shown in a recent literature review (261). This research underscores that resilience can be improved through interventions, which thereby may impact mental health among children and adolescents.

## 2. Aims of the thesis

The overall aim of this thesis was to obtain knowledge on the course of psychiatric morbidity, somatic co-morbidity, and function over three years in a clinical adolescent population. The intention was to have a special focus on factors that could possibly affect status of mental health and further development of psychiatric disorders, as resilience factors, experiences of negative life events, substance use and received treatment procedures, and to explore gender differences in these aspects.

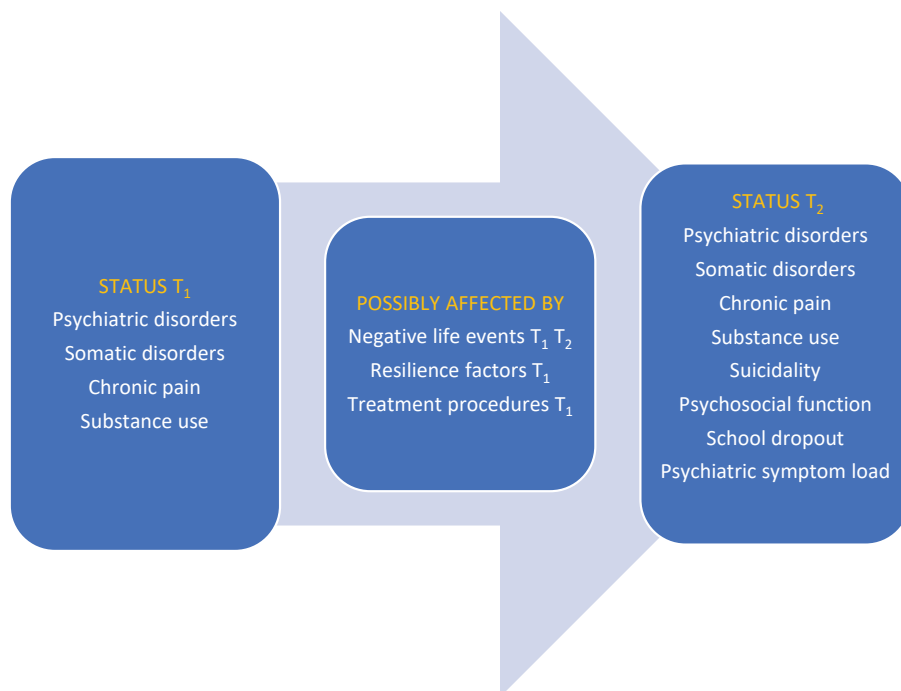


Figure 1. Illustration of topics related to aims of the thesis

The aims were examined in three separate papers, with hypotheses stated based on present literature, and were as follows:

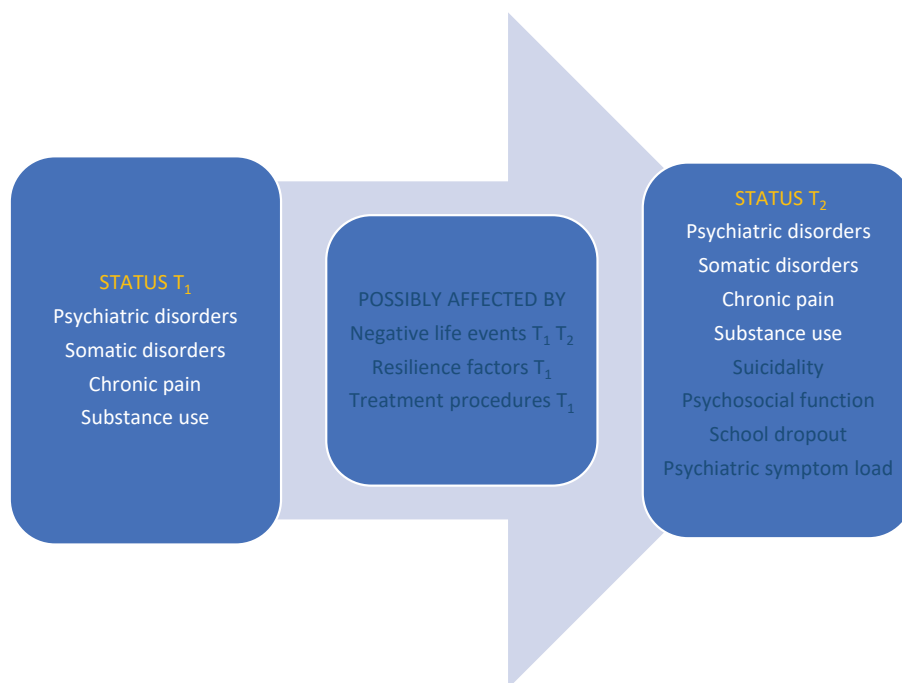
### Paper I:

The primary aim of this paper was to investigate any changes during 3-year follow-up in the frequency of psychiatric disorders, comorbidities with other psychiatric or somatic disorders, chronic pain, and substance use. The assessments were made for the overall sample, by

diagnostic groups, and separately for girls and boys. The secondary aim was to study if somatic disorders, chronic pain, and substance use were associated with persisting psychiatric disorders, overall, by diagnostic groups, and separately for girls and boys.

The hypotheses were that:

- the frequency of psychiatric disorders declined over the three years
- continuity of a psychiatric disorder was associated with concurrent comorbid disorders, chronic pain, and substance use at baseline
- there would be a different pattern of morbidity for girls and boys



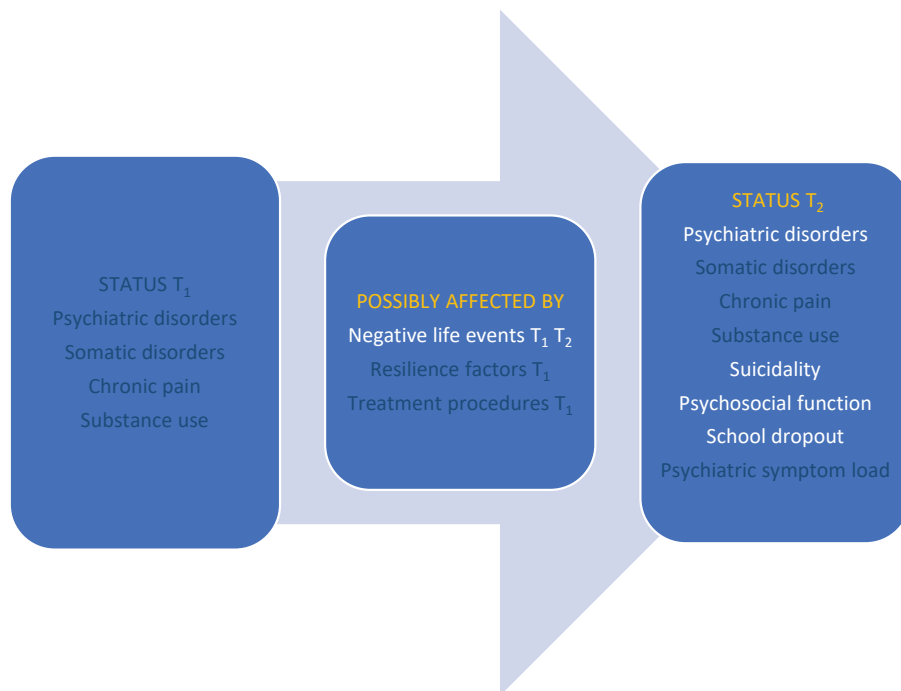
**Figure 2. Illustration of topics related to aims of paper I**

## **Paper II:**

The objective of this paper was to examine suicidality and functioning three years after referral to CAMHS. We aimed to assess psychosocial function, suicidal ideation, suicidal behaviour, and school dropout, in the total sample and specified by psychiatric disorders, and furthermore to investigate associations with negative life events. We set out to specify analyses for girls and boys and explore gender differences.

The hypotheses were that:

- present suicidal symptoms and school dropout were associated with co-occurring exposure to negative life events
- frequencies differed between girls and boys, with girls having higher rates of suicidal symptoms and boys more school dropout



**Figure 3. Illustration of topics related to aims of paper II**

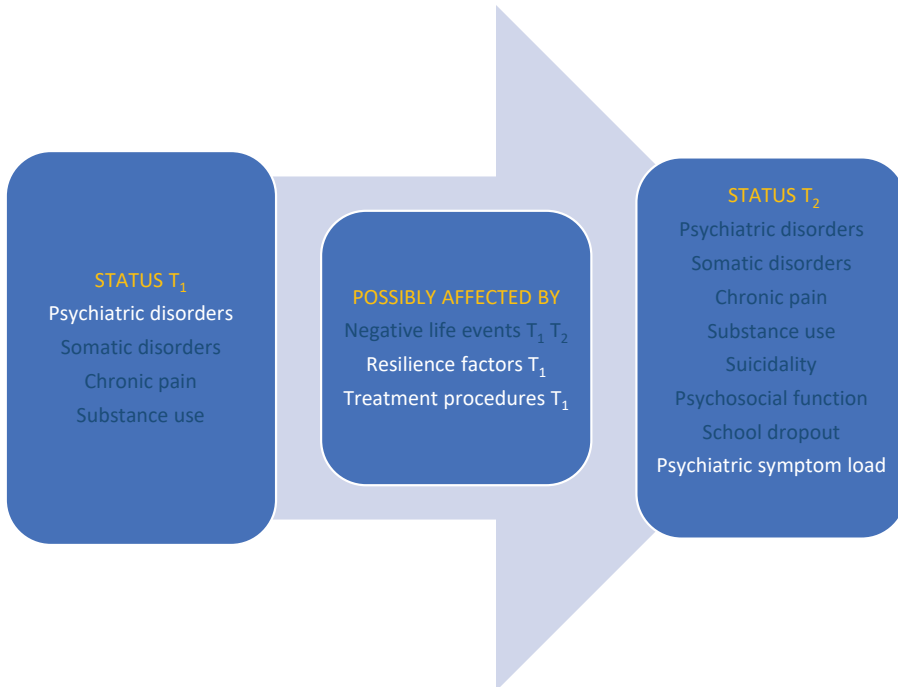
### **Paper III:**

The overriding aim of this paper was to examine whether psychiatric symptom load three years later was related to the treatment procedures received and the resilience factors upon first presenting at CAMHS. Characteristics of treatment received in standard adolescent mental health care and symptom load three years later were described, as were the self-reported resilience measures at baseline.

The hypotheses were that:

- symptom load remained substantial and that disorder specific treatment procedures were analogues for girls and boys

- having received more psychotherapy sessions or medication was associated with higher symptom load three years later, indicating the larger burden of initial symptoms in this subgroup of former patients
- higher resilience factors at baseline was associated with lower symptom load three years later
- boys would report higher resilience factors in personal and social competence domains, whereas girls would report higher social resources



**Figure 4. Illustration of topics related to aims of paper III**

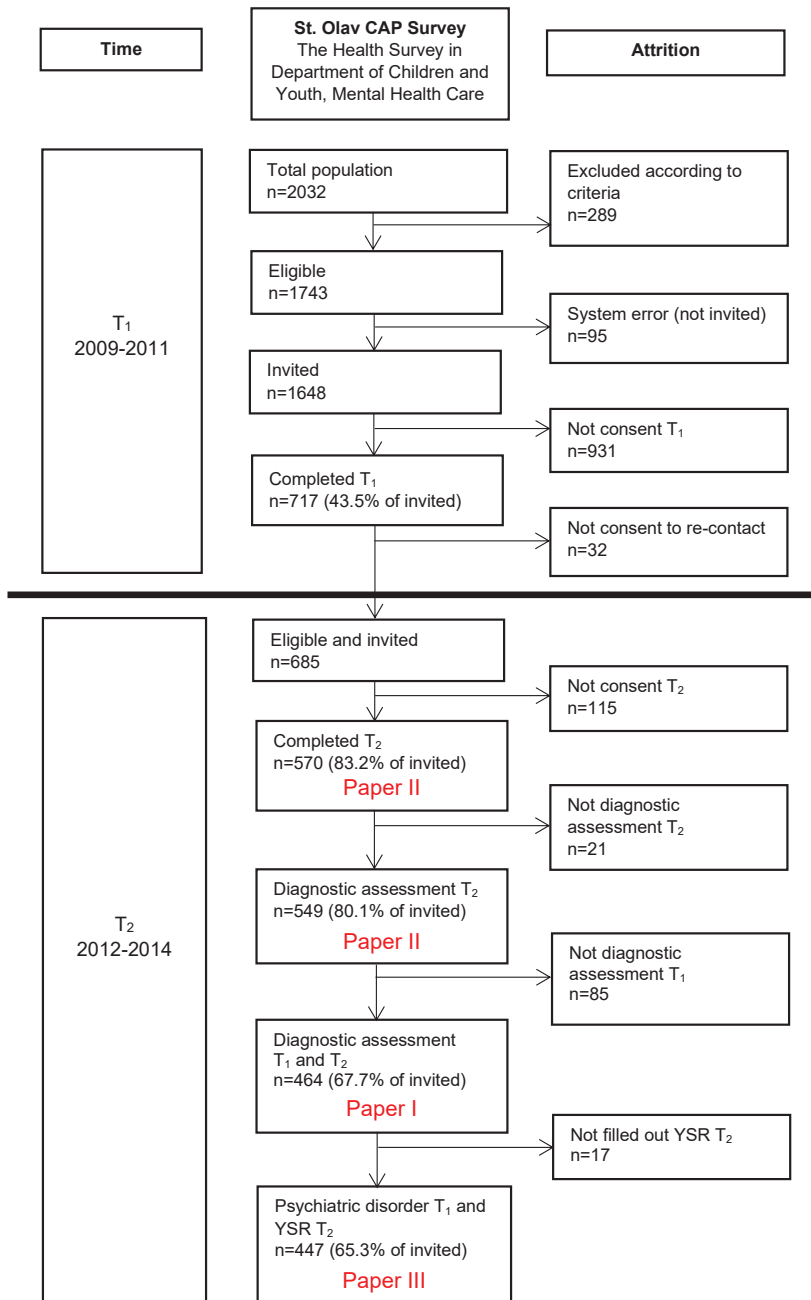
### **3. Material and methods**

#### **3.1 Study design**

The study is part of the St. Olav CAP Survey, a prospective longitudinal cohort study of a defined clinical population assessed at two time points. At time point 1 (T<sub>1</sub>), data were collected at inclusion in a cross-sectional study of adolescent patients, at time point 2 (T<sub>2</sub>) data were collected at a 3-year follow-up. At T<sub>1</sub> (2009-2011), all patients aged 13-18 years who visited the Department of Children and Youth at least once over a 2-year period, received both oral and written invitations at their first attendance. The exclusion criteria were difficulties in answering the survey due to low cognitive function, visual impairments, insufficient language skills, or an unstable psychiatric state. Emergency patients were invited to take part once they entered a stable phase. The participants and their parents received standard application of services. They gave written informed consent to extract diagnostic data from clinical charts and respond to an electronic survey. At T<sub>2</sub> (2012-2014), age 16-21 years, data were collected from the T<sub>1</sub> enrolled sample and their parents, by an electronic survey and a diagnostic telephone interview performed by trained professionals with graduate degree in medicine or psychology.

#### **3.2 Participants**

In the T<sub>1</sub> study period, 2032 adolescent patients had at least one attendance at the Department of Children and Youth. Figure 5 demonstrates the participant flow in each stage of the survey. At T<sub>1</sub>, n = 717 participated (393, 54.8% girls), of whom n = 597 had a complete diagnostic assessment. At T<sub>2</sub>, all T<sub>1</sub> participants who previously consented to further inquiry were invited (eligible n = 685), of whom 570 (83% of eligible) completed the follow-up questionnaire (324, 56.8% girls), and 549 (80%) completed the diagnostic interview (308, 56.1% girls). These 570 and 549, respectively, were included in Paper II. In Paper I, participants with complete diagnostic assessment at both T<sub>1</sub> and T<sub>2</sub> were included (n = 464, 256 (55.2%) girls). In Paper III, the 447 (65.3% of invited) participants who had a psychiatric disorder at T<sub>1</sub> and had filled out YSR at T<sub>2</sub> (254, 56.8% girls) were included. Background characteristics of age, gender, and SES in the three papers are shown in Table 1. There were more girls than boys participating, and the girls were older than the boys (p < 0.001) in all three papers (Table 1).



**Fig 5. Flowchart of participants**



**Table 1. Background characteristics of participants and non-participants in the three studies**

	Participants		Non-participants	
	Girls Mean (SD)	Boys Mean (SD)	Girls Mean (SD)	Boys Mean (SD)
<b>Paper I</b>	<b>Diagnostic assessment at T<sub>1</sub> and T<sub>2</sub> (n=464)</b> n=256 (55.2%)      n=208 (44.8%)		<b>Diagnostic assessment at T<sub>1</sub>, not at T<sub>2</sub> (n=133)</b> n=65 (48.9%)      n=68 (51.1%)	
Age T <sub>1</sub>	16.0 (1.7)	15.3 (1.6)	16.0 (1.7)	15.4 (1.6)
Age T <sub>2</sub>	19.0 (1.6)	18.3 (1.6)		
SES T <sub>1</sub>	4.9 (1.7)	4.8 (1.7)	4.5 (1.1)	4.7 (2.0)
<b>Paper II</b>	<b>Questionnaire completed at T<sub>2</sub> (n=570)</b> n=324 (56.8%)      n=246 (43.2%)		<b>No questionnaire completed at T<sub>2</sub> (n=147)</b> n=69 (46.9%)      n=78 (53.1%)	
Age T <sub>1</sub>	16.0 (1.7)	15.3 (1.6)	15.7 (1.7)	15.4 (1.6)
Age T <sub>2</sub>	19.0 (1.7)	18.3 (1.6)		
SES T <sub>1</sub>	4.9 (1.7)	4.8 (1.8)	4.3 (1.9)	4.3 (1.5)
<b>Paper II</b>	<b>Diagnostic assessment at T<sub>2</sub> (n=549)</b> n=308 (56.1%)      n=241 (43.9%)		<b>No diagnostic assessment at T<sub>2</sub> (n=168)</b> n=85 (50.6%)      n=83 (49.4%)	
Age T <sub>1</sub>	15.9 (1.7)	15.3 (1.6)	15.9 (1.6)	15.4 (1.6)
Age T <sub>2</sub>	19.0 (1.7)	18.3 (1.6)		
SES T <sub>1</sub>	4.9 (1.7)	4.8 (1.8)	4.5 (1.1)	5.1 (2.2)
<b>Paper III</b>	<b>Psychiatric disorder at T<sub>1</sub> (n=447)</b> n=254 (56.8%)      n=193 (43.2%)		<b>Diagnostic assessment at T<sub>1</sub>, no disorder (n=150)</b> n=67 (44.7%)      n=83 (55.3%)	
Age T <sub>1</sub>	16.0 (1.7)	15.3 (1.6)	15.8 (1.7)	15.3 (1.7)
Age T <sub>2</sub>	19.0 (1.7)	18.3 (1.6)		
SES T <sub>1</sub>	4.9 (1.7)	4.8 (1.7)	4.3 (1.8)	4.3 (1.5)

*Age is given in years and SES is measured by the mothers' highest level of education, divided into eight categories (1 lowest, 8 highest).*

### 3.2.1 Participants vs. Non-participants

To explore the representativeness of the study population at T<sub>1</sub>, anonymous information about the total clinical population was collected from annual reports from the Department of Children and Youth during the period 2009-2011. All adolescents in the study period (n = 2032) minus those excluded (n = 289) were defined as reference population (n = 1743). The main reason for referral, age and gender were similar between participants (n = 717, 41.1%) and non-participants (n = 1026, 58.9%). Participants were 0.27 (95% CI 0.10-0.45) years older (Mean (SD) 15.7 (1.7) vs. 15.4 (2.0), p = 0.002), and there were more girls among the participants (393 (54.8%) vs. 509 (49.6%), p = 0.032).

In all three present papers, comparing participants versus non-participants, the proportion of girls was higher among participants, while age at T<sub>1</sub> was similar (Table 1). SES was similar for participants and non-participants in paper I and III, and also in paper II with completed questionnaire (n = 570), but not in paper II with diagnostic assessment (n = 549), which may be due to few non-participants with information on SES in this group. There was diagnostic

assessment of n = 597 at T<sub>1</sub>, and the frequencies of any psychiatric disorder were similar among participants and non-participants at T<sub>2</sub> (94.8% vs. 95.5%, Table 2).

**Table 2. Diagnoses at T<sub>1</sub> of participants and non-participants at T<sub>2</sub>**

Diagnoses at T <sub>1</sub>	Participants T <sub>2</sub>			Non-participants T <sub>2</sub>		
	Girls (n=256) n (%)	Boys (n=208) n (%)	Total (n=464) n (%)	Girls (n=65) n (%)	Boys (n=68) n (%)	Total (n=133) n (%)
<b>Any psychiatric disorder</b>	245 (95.7)	195 (93.8)	440 (94.8)	62 (95.4)	65 (95.6)	127 (95.5)
<b>Anxiety disorder</b>	96 (37.5)	51 (24.5)	147 (31.7)	23 (35.4)	18 (26.5)	41 (30.8)
<b>Mood disorder</b>	82 (32.0)	17 (8.2)	99 (21.3)	22 (33.8)	10 (14.7)	32 (24.1)
<b>ADHD</b>	83 (32.6)	121 (58.2)	204 (44.0)	23 (35.4)	35 (51.5)	58 (43.6)
<b>Other psychiatric disorder</b>	52 (20.3)	68 (32.7)	120 (25.9)	13 (20.0)	30 (44.1)	43 (32.3)

### 3.3 Measures

An overview of the measures used in this thesis is given in Table 3.

**Table 3. Overview of measures used in the thesis**

Measures	Data collection tools and sources						Paper
	Medical records	K-SADS	CGAS	ASEBA	READ	Web survey	
<b>Psychiatric diagnoses</b>	T <sub>1</sub>	T <sub>2</sub>				T <sub>1</sub> T <sub>2</sub>	Papers I-III
<b>Suicidality</b>			T <sub>2</sub>				Paper II
<b>Somatic diagnoses</b>	T <sub>1</sub>	T <sub>2</sub>				T <sub>1</sub> T <sub>2</sub>	Paper I
<b>Pain</b>						T <sub>1</sub> T <sub>2</sub>	Paper I
<b>Substance use</b>	T <sub>1</sub>	T <sub>2</sub>				T <sub>1</sub> T <sub>2</sub>	Paper I
<b>Treatment history</b>	T <sub>1</sub>						Paper III
<b>Psychotropic medication</b>	T <sub>1</sub>						Paper III
<b>Resilience</b>					T <sub>1</sub>		Paper III
<b>Negative life events</b>						T <sub>1</sub> T <sub>2</sub>	Paper II
<b>Psychosocial function</b>		T <sub>2</sub>	T <sub>2</sub>				Paper II
<b>School dropout</b>						T <sub>2</sub>	Paper II
<b>Psychiatric symptom load</b>					T <sub>2</sub>		Paper III
<b>Maternal socioeconomic status</b>	T <sub>1</sub>					T <sub>1</sub>	Papers I-III

*K-SADS (T<sub>2</sub>):* Schedule for Affective Disorders and Schizophrenia for School-Age Children, a semi-structured interview designed to assess current and past psychopathology (DSM-IV-TR).

*CGAS (T<sub>2</sub>):* The Children’s Global Assessment Scale is a numerical scale (1 – 100) used to rate the general psychosocial functioning. A score above 80 denotes good functioning.

*ASEBA-YSR (T<sub>2</sub>):* Achenbach System of Empirically Based Assessment – Youth Self Report, provides three competence scales, eight syndrome scores and three composite scales.

*READ (T<sub>1</sub>):* The Resilience Scale for Adolescents: Personal competence, social competence, social support, family cohesion, structured style; 28 items, 5-point Likert scale.

*Web survey (T<sub>1</sub>, T<sub>2</sub>):* Validated scales and questions on somatic symptoms and pain, substance use, life events, school dropout.

### **3.3.1 Baseline measures**

#### **3.3.1.1 Psychiatric diagnoses**

All psychiatric diagnoses were set in ordinary clinical practice according to the International Statistical Classification of Disease and Related Health Problems (ICD-10) multi-axial diagnostics (axes I-VI) (241). The diagnostic process followed standardized procedures for assessment and diagnosis of common adolescent psychiatric disorders, requiring a thorough developmental history and interviews with the adolescents and their parents. In some cases, the semi-structured Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS) (262) was used, in others The Development and Well-Being Assessment (DAWBA) (263), and various rating scales suitable for the presenting problem. The diagnoses were set by a child and adolescent psychiatrist, or a clinical psychologist based on all available clinical information, after consensus with other professionals from the multi-disciplinary team. The assessments were supplemented with somatic examination if indicated, and possible coexisting disorders were explored.

In the present study, disorders were grouped into the following categories, based on ICD-10 diagnoses at T<sub>1</sub> with equivalent DSM-IV diagnoses in parentheses; Any psychiatric disorder, Anxiety disorders ICD-codes F40-F44, F48, F93 (DSM-codes 300, 308, 309), Mood disorders ICD-codes F31-F34, F38, F39 (DSM-codes 296, 300.4, 311), ADHD ICD-code F90 (DSM-code 314) and Other ICD-codes F10-F19, F20-F21, F28-F29, F50, F54, F59-F60, F84, F91-F92, F94-F95, F98 (DSM-codes 291, 292, 295, 298, 299, 301, 303, 304, 305, 307, 312, 313, 316). Due to few participants in some diagnostic groups, for example autism and eating disorders, and especially when examining various symptoms or factors in the three papers, we chose to merge these diagnoses into one larger group of “Other psychiatric disorders”.

Psychiatric diagnoses at T<sub>1</sub> were used in Paper I and Paper III.

#### **3.3.1.2 Somatic diagnoses**

Somatic diagnoses were registered according to ICD-10 Axis 4, set by the medical doctor based on anamnestic information, the entire medical records, including paediatrics, or by clinical investigation. All patients reporting somatic symptoms or disorders had an evaluation

by a medical doctor. Somatic comorbidity was defined as having a psychiatric disorder with a co-occurring somatic disorder requiring regular clinical follow-up.

Somatic diagnoses at T<sub>1</sub> were used in Paper I.

### **3.3.1.3 Chronic Pain**

Chronic Pain was defined as pain not related to any known disease or injury, occurring at least once a week in the last 3 months. The test-retest reliability of questions of pain occurrence at least once a week for the last three months has shown to be good (116, 264). As in previous studies, adolescents were asked to fill in a questionnaire and specify if they had experienced headaches, abdominal pain or musculoskeletal pain (e.g. pain in the neck, shoulder, upper and lower extremities, upper back, lower back/seat or chest), accompanied with an illustration of the different locations (108, 116). Multisite pain was defined as having chronic pain in three locations or more (108, 116). The same questions were used in the Young-HUNT3 study (<https://www.ntnu.edu/hunt/data/que>).

Chronic Pain at T<sub>1</sub> was used in Paper I.

### **3.3.1.4 Substance Use**

Substance Use was registered by self-report as smoking, alcohol use and drug use. “Current smokers” included daily or occasional smokers. “Current alcohol users” included participants who answered “yes” to the following question: “Do you sometimes drink alcohol presently?”. “Drug use” was indicated by answering “yes” to the question: “Have you ever tried hash, marijuana, or other illicit drugs?” The questions were similar to those used in the Young-HUNT3 study (<https://www.ntnu.edu/hunt/data/que>).

Substance Use at T<sub>1</sub> was used in Paper I.

### **3.3.1.5 Treatment procedures**

Treatment given at T<sub>1</sub> was registered in medical records by type (cognitive, neurobiological, psychodynamic, psychoeducational, social-relational, medication), participant (individual, group, parent, family), number of sessions, duration of treatment, in-patient or out-patient, indirect patient work by counselling municipal services, giving consultations to service

agencies already engaged with the patient. Treatment was provided according to guidelines for specific diagnosis. In this study, we classified treatment procedures into psychotherapy (specified or unspecified, and divided into numbers of sessions given; <10, 10-30, >30), medication according to Anatomical Therapeutic Chemical (ATC) codes, counselling parents/family therapy and counselling municipal services, all classified as present or not (Yes/No).

Treatment procedures given at T<sub>1</sub> were used in Paper III.

### **3.3.1.6 Resilience factors**

Resilience factors were reported using the Resilience Scale for Adolescents (READ), a self-report questionnaire measuring the ability to manage stress and negative experiences (226). READ is a 28-item scale with positively formulated items organized in five subscales: Personal Competence, Social Competence, Structured Style, Family Cohesion and Social Resources. READ is based on the Resilience Scale for Adults (265) and was developed in Norway in 2006 with a 5-point Likert-type response scale from 1 = Totally Disagree to 5 = Totally Agree. Higher scores on the READ indicate higher level of resilience. The READ scale is widely used in research and has shown good psychometric properties in validation studies (227, 246). In this study, we used mean item scores for each scale (values between 1 and 5). Internal consistency measured as Cronbach's alpha for the subscales was .89 (Personal Competence), .84 (Social Competence), .73 (Structured Style), .91 (Family Cohesion), and .84 (Social Resources), which would generally be considered to be in the range from acceptable to excellent (266).

Resilience factors at T<sub>1</sub> were used in Paper III.

### **3.3.1.7 Negative life events**

Negative life events were registered by self-report. The following questions were asked: "Have any of the following things happened to you?"; "That someone in your family has been seriously ill", "Death of a loved one", "A catastrophe (fire, avalanche, tidal wave, hurricane, etc.)", "A serious accident (ex: a very serious car accident)", "Been violently hurt (beaten or injured)", "Seen others violently hurt", "Been put in sexually uncomfortable/abusive situations by someone about your age", "Been put in sexually

uncomfortable/abusive situations by an adult”, “Been threatened or physically harassed by other students at school for a long time”, “Received painful or frightening treatment at the hospital while being treated for an illness or injury”. These items were also used in the Young-HUNT3 study (<https://www.ntnu.edu/hunt/data/que>). The answering opportunities were: “No”, “Yes, last year” and “Yes, in my life”.

Negative life events at T<sub>1</sub> were used in Paper II.

### **3.3.1.8 Socioeconomic status**

Socioeconomic status (SES) was measured by the mothers’ highest level of education, divided into eight categories: (1) less than 9-year primary school; (2) completed 9-year primary school; (3) one or two years in high school; (4) completed high school; (5) completed high school and one-year education/training after high school; (6) academy/university for up to and including four years; (7) academy/university for five years or more; (8) academy/university including PhD.

SES at T<sub>1</sub> were used in Paper I, Paper II and Paper III.

## **3.3.2 Follow-up measures**

### **3.3.2.1 Psychiatric diagnoses**

Psychiatric diagnoses were set using the K-SADS (262) according to the Diagnostic and Statistical Manual of Mental Disorders IV Text revision (DSM-IV-TR) (267). Psychometric properties of K-SADS, including reliability and validity, are found to be excellent (262). The K-SADS is designed for children and adolescents under 18 years, but was in this study used for all participants, also those above the age of 18 years. The interview has previously been applied to populations in young adulthood (268, 269). The interviews were performed with the adolescents by telephone by trained interviewers, all with graduate degree in medicine or psychology and experience in child and adolescent psychiatric assessment. They met regularly with a supervisor, an experienced child and adolescent psychiatrist, to assure the quality of the diagnostic assessment. All were blinded to T<sub>1</sub> diagnoses. Inter-rater reliability was assessed using second ratings for 28 of the taped telephone interviews. Because of weaknesses of kappa as measure of agreement (270), positive and negative agreement were

used as measurement. Positive agreement, as defined by van de Vet et al, varied from 0.615 to 1.000 and, negative agreement varied from 0.884 to 1.000 (271).

In the present study, disorders were grouped into the following categories, based on DSM-IV diagnoses at T<sub>2</sub> with equivalent ICD-10 diagnoses in parentheses; Any psychiatric disorder, Anxiety disorders DSM-codes 300, 308, 309 (ICD-codes F40-F44, F48, F93), Mood disorders DSM-codes 296, 300.4, 311 (ICD-codes F31-F34, F38, F39), ADHD DSM-code 314 (ICD-code F90) and Other DSM-codes 291, 292, 295, 298, 299, 301, 303, 304, 305, 307, 312, 313, 316 (ICD-codes F10-F19, F20-F21, F28-F29, F50, F54, F59-F60, F84, F91-F92, F94-F95, F98). The reason for merging diagnoses into one larger group of “other psychiatric disorders”, is described in section 3.3.1.1.

Psychiatric disorders at T<sub>2</sub> were used in Paper I and Paper III.

### **3.3.2.2 Somatic disorders**

Somatic disorders were recorded as part of the K-SADS interview, and with the same definition of somatic comorbidity as at T<sub>1</sub>.

Somatic diagnoses at T<sub>2</sub> were used in Paper I.

### **3.3.2.3 Chronic Pain**

Chronic Pain was measured by self-report using the same definition and the same questions as used at T<sub>1</sub>.

Chronic Pain at T<sub>2</sub> was used in Paper I.

### **3.3.2.4 Substance Use**

Substance Use was registered by self-report as smoking, alcohol use and drug use. “Current smokers” included daily or occasional smokers. “Current alcohol users” included participants who answered “yes” to the following question: “Have you drunk alcohol during the last four weeks?”. “Drug use” was indicated by answering “yes” to the question: “Have you ever tried hash, marijuana, or other illicit drugs?”.

Substance Use at T<sub>2</sub> was used in Paper I.

### 3.3.2.5 Negative life events

Negative life events were registered by self-report with the same questions as at T<sub>1</sub>, but with a supplementary question: “Been seriously ill or injured”. The answering opportunities were: “No”, “Yes, last year” and “Yes, last three years”. In the present study, negative life events defined as “last 3 years” were events measured at T<sub>2</sub> only, and negative life events defined as “ever” were measured at T<sub>1</sub> or T<sub>2</sub>.

Negative life events at T<sub>2</sub> were used in Paper II.

### 3.3.2.6 Psychosocial function

The Children’s Global Assessment Scale (CGAS) (272) was used to rate general psychosocial functioning on a scale from 1 (extremely impaired, needs constant supervision) to 100 (superior functioning), based on the K-SADS interview. The CGAS is designed for children in age group 4-16 years, but has been applied to older age groups in previous studies (269, 273, 274). The assessment scale was in this study used for all participants. The inter-rater reliability for CGAS in terms of intraclass correlation coefficient (ICC) was 0.835, based on second ratings for 28 of the taped telephone interviews (275).

CGAS at T<sub>2</sub> was used in Paper II.

### 3.3.2.7 Suicidal ideation and behaviour

Suicidal ideation and behaviour were measured by asking the following questions during K-SADS interview:

**Suicidal ideation:** “Sometimes children who get upset or feel bad think about dying or even killing themselves. Have you ever had such thoughts? How would you do it? Did you have a plan?” Assessed and scored as; 0; No information, 1; Not at all, 2; Infrequent or vague thoughts of suicide (e.g., less than once per month), or 3; Recurrent thoughts of suicide. As measure of **Suicidal ideation**, we used “infrequent or vague thoughts” (2) or “recurrent thoughts of suicide” (3), presently at T<sub>2</sub>.

**Suicidal acts or attempts:** “Have you actually tried to kill yourself? When? What did you do? Any other things? Did you really want to die? How close did you come to doing it? Was anybody in the room? In the apartment? Did you tell them in advance? How were you found?”



Did you really want to die? Did you ask for any help after you did it?" Assessed and scored as; 0; No information, 1; No attempt, 2; Preparations with no actual intent to die (e.g., held pills in hand) or planned attempt but did not follow through, 3; Self injurious behaviour with any suicidal intent. There was one more assessment; "Ever attempted suicide", scored as yes or no. In the present study, **Suicidal behaviour** included "preparations or planned attempt" (2) or "self-injurious behaviour with any suicidal intent" (3), presently at T<sub>2</sub>, or yes to the question: "Ever attempted suicide".

Suicidal ideation and suicidal behaviour at T<sub>2</sub> were used in Paper II.

### **3.3.2.8 School dropout**

School dropout was self-reported based on answering "yes" to the following question: "Have you cancelled your education (dropped out)?"

School dropout at T<sub>2</sub> was used in Paper II.

### **3.3.2.9 Psychiatric symptom load**

Psychiatric symptom load was investigated using the Achenbach System of Empirically Based Assessment – Youth Self Report (YSR) (276). This is a screening instrument for emotional and behavioural symptoms, designed to assess a broad array of psychopathological manifestations in adolescents, consisting of both a competence scale and a problem scale. For the purpose of this study, the latter was used, consisting of 103 problem items, rated on a 3-point scale (0 = not true; 1 = somewhat or sometimes true; 2 = very true or often true), during the past six months. In this study, Total problems T-score was used as the measure of symptom load, with cut-off at scores  $\geq 60$  as borderline/clinical range, and  $< 60$  as normal. The scale has shown good psychometric properties and is widely used in research and clinical services in different populations (277, 278).

Psychiatric symptom load at T<sub>2</sub> was used in Paper III.

### 3.4 Statistical methods

Statistical analyses were conducted using SPSS versions 25 and 27, and STATA versions 15 and 16. Some calculations were made in Excel. We reported 95% confidence intervals where relevant, and two-sided p-values  $<0.05$  were considered statistically significant.

In paper I, the change in point prevalence from  $T_1$  to  $T_2$  was based on paired dichotomous data, with Newcombe hybrid score confidence intervals and the McNemar asymptotic test, as recommended by Fagerland, Lydersen and Laake (279). We used binary linear regression with psychiatric disorder at  $T_2$  as dependent variable and relevant variables at  $T_1$ , one at a time, to study their associations. Effects of age and SES as possible confounders were explored.

In paper II, we compared proportions using the Newcombe hybrid score confidence intervals, as recommended (279), and the Pearson Chi squared test. Confidence intervals and tests for differences in psychosocial functioning between girls and boys were based on Student's t-test for independent samples. We used binary linear regression with suicidal ideation, suicidal behaviour, or school dropout at  $T_2$  as dependent variables and negative life events reported at  $T_1$  and  $T_2$  as covariates, one at a time, to study their associations. The coefficients in binary linear regression represent risk differences. These regression analyses were carried out unadjusted and adjusted for SES as a possible confounder where relevant. Some estimates including suicidal behaviour could not be computed when adjusting for SES due to non-convergence of the calculations.

In paper III, confidence intervals and tests for differences in age, SES, symptom load and resilience measures between girls and boys were based on Student's t-test for independent samples. We compared proportions of treatment procedures between girls and boys by using the Newcombe hybrid score confidence intervals, as recommended (279), and the Pearson Chi squared test. Linear regression was used with symptom load at  $T_2$  as dependent variable and resilience and treatment procedures reported at  $T_1$  as covariates, one at a time, to study their associations. These regression analyses were accomplished adjusted for age and SES as possible confounders.

### **3.5 Ethics**

The Norwegian Regional Committee for Medical and Health Research Ethics of Central Norway approved the Health Survey in Department of Children and Youth, Clinic of Mental Health Care, St. Olavs hospital, Trondheim University Hospital (St. Olav CAP Survey) with reference numbers T<sub>1</sub>: 4:2008.1393 and T<sub>2</sub>: 2011/1435/REK Midt. The Norwegian Social Science Data Services, The Data Protection Official for Research, gave permission to use the variables “age”, “gender” and “main reason for referral” to investigate the representativeness of the study at T<sub>1</sub> (reference number: 19976).

The present study using T<sub>1</sub> and T<sub>2</sub> data, was approved by the regional committee with reference number 2017/589/REK Midt. Written informed consent was obtained prior to inclusion at T<sub>1</sub> from adolescents and parents if the participant was younger than 16 years, and from the adolescents at T<sub>2</sub> according to study procedures. The studies have been performed in accordance with the ethical standards in the Declaration of Helsinki from 1964 and later amendments.

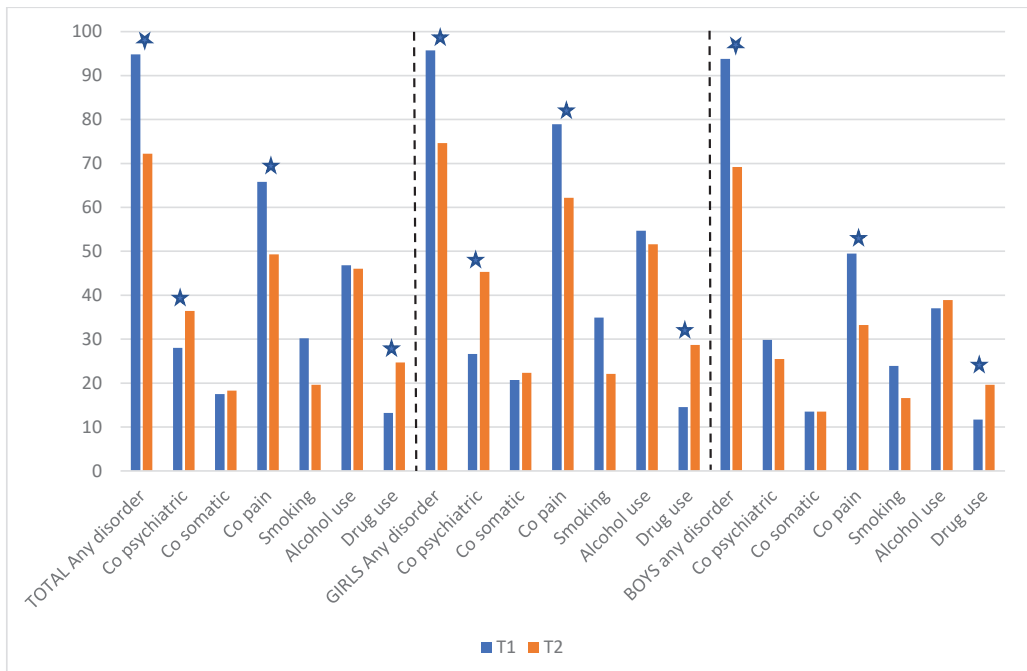


## 4. Results

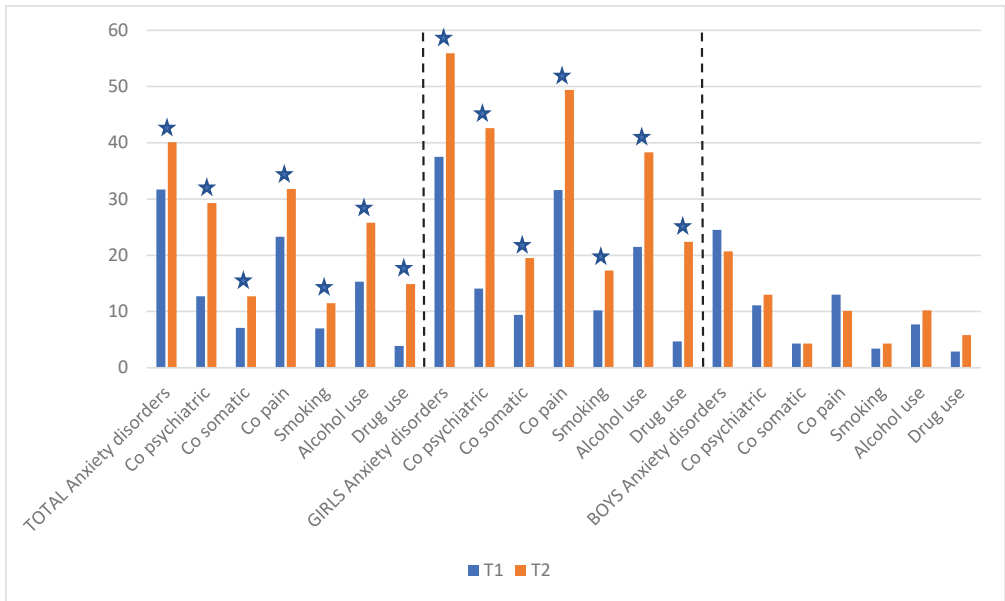
### 4.1 Paper I

#### *Psychiatric morbidity, somatic comorbidity and substance use in an adolescent psychiatric population at 3-year follow-up.*

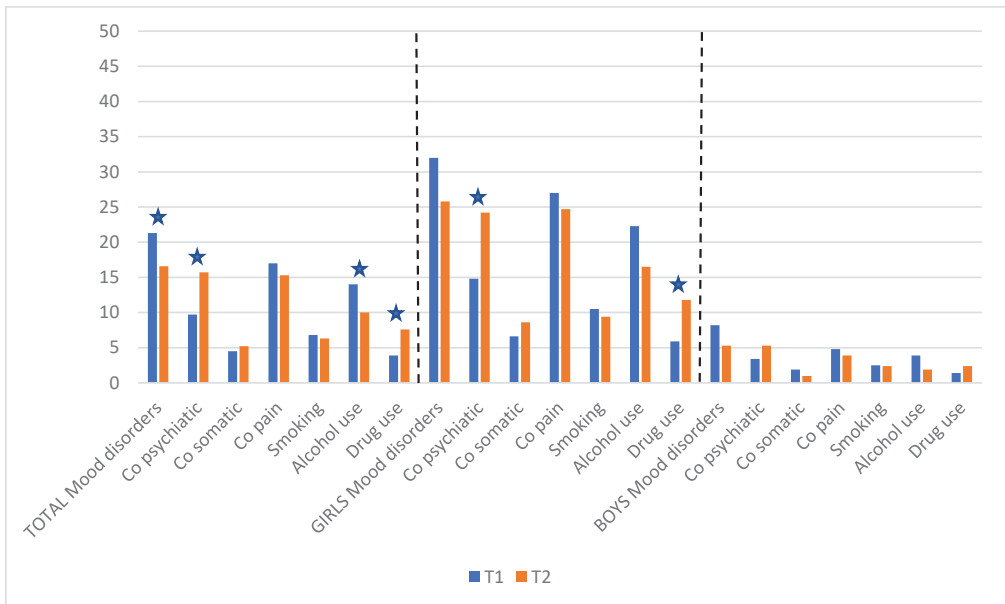
The overall rate of psychiatric diagnoses decreased from 94.8% at T<sub>1</sub> to 72.2% at T<sub>2</sub> ( $p < 0.001$ ) (Paper I  $n = 464$ ) (Figure 6), and the change was present in both genders. However, the frequency of anxiety disorders increased in the total sample, but among girls only (37.5% T<sub>1</sub> to 55.9% T<sub>2</sub>,  $p < 0.001$ ) (Figure 7). Psychiatric comorbidity increased from 26.6% at T<sub>1</sub> to 45.3% at T<sub>2</sub> ( $p < 0.001$ ) for girls with any psychiatric disorder. The increase in psychiatric comorbidity in the total sample was statistically significant in anxiety disorders (Figure 7), mood disorders (Figure 8) and ADHD (Figure 9), and for girls in all diagnostic subgroups, but not for boys.



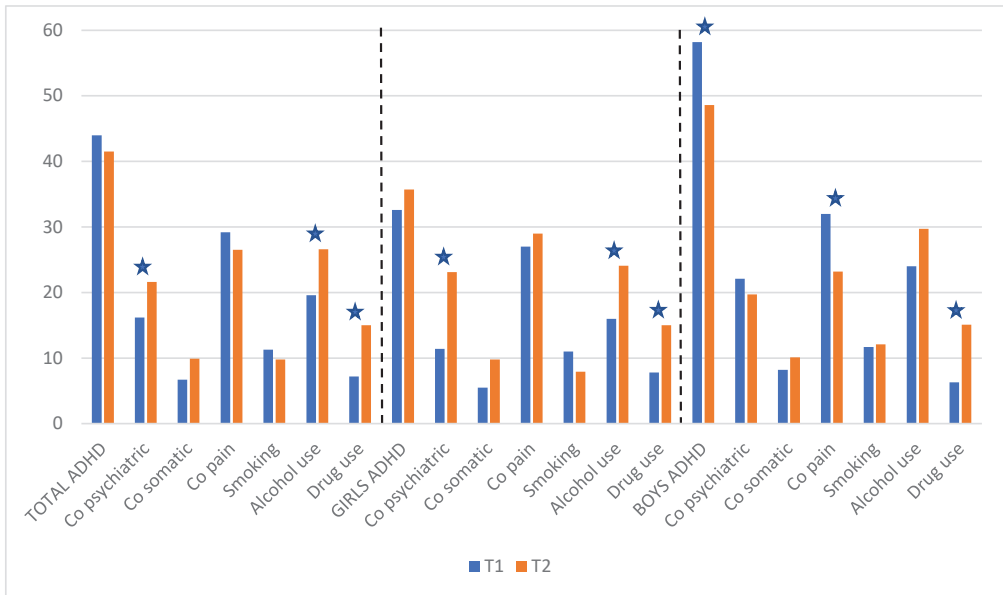
**Fig 6.** Frequency (%) of Any psychiatric disorder at the two time points for the total sample, girls and boys, with comorbid psychiatric or somatic disorders, chronic pain, and substance use.  $P$ -values  $< 0.05$  are marked.



**Fig 7. Frequency (%) of Anxiety disorders at the two time points for the total sample, girls and boys, with comorbid psychiatric or somatic disorders, chronic pain, and substance use. *P*-values <0.05 are marked.**



**Fig 8. Frequency (%) of Mood disorders at the two time points for the total sample, girls and boys, with comorbid psychiatric or somatic disorders, chronic pain, and substance use. *P*-values <0.05 are marked.**



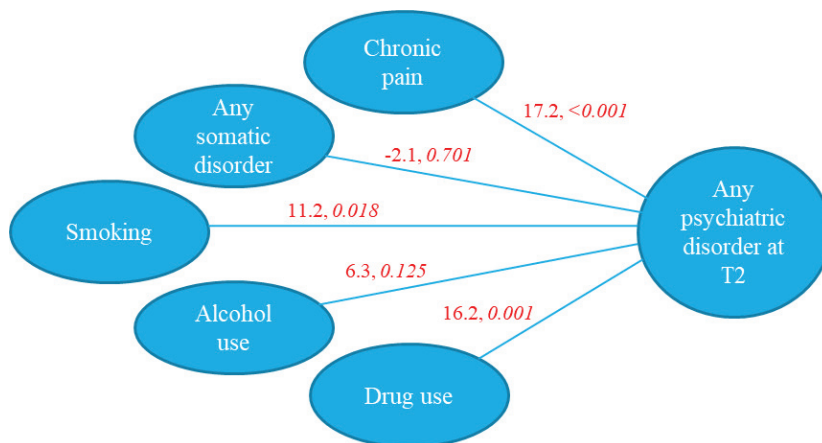
**Fig 9. Frequency (%) of ADHD at the two time points for the total sample, girls and boys, with comorbid psychiatric or somatic disorders, chronic pain, and substance use. *P*-values <0.05 are marked.**

Somatic comorbidity remained unchanged in the total sample for any psychiatric disorder and all diagnostic groups except for the anxiety disorder group where it increased in frequency, but among girls only (9.4% T<sub>1</sub> to 19.5% T<sub>2</sub>, *p* = 0.001). The prevalence of chronic pain in the cohort was still high after three years but decreased overall in the total sample (65.8% T<sub>1</sub> to 49.3% T<sub>2</sub>, *p* < 0.001) for all diagnostic groups except for the anxiety disorder group. However, this increase in the anxiety disorder group was present among girls only (31.6% T<sub>1</sub> to 49.4% T<sub>2</sub>, *p* < 0.001). At T<sub>2</sub>, girls with anxiety disorders had a higher rate of chronic pain than boys with these disorders (88.7% vs. 48.8%), and a higher rate of multisite pain (66.2% vs. 20.9%). The diagnostic group with highest frequencies of chronic pain was mood disorders for both girls (96.9%) and boys (72.7%). The frequencies of multisite pain were also highest in this diagnostic group.

The amount of substance use changed during the 3-year follow-up. There was a non-significant reduction in smoking in the total sample, but it increased for girls with anxiety disorders (10.2% T<sub>1</sub> to 17.3% T<sub>2</sub>, *p* = 0.001). Alcohol use increased in the total sample for anxiety disorders (15.3% T<sub>1</sub> to 25.8% T<sub>2</sub>, *p* < 0.001) and ADHD (19.6% T<sub>1</sub> to 26.6% T<sub>2</sub>, *p* < 0.001), and among girls with these disorders. Trying illicit drugs increased overall, in both

genders, and in all diagnostic subgroups for girls, with highest increase in the anxiety group (4.7% T<sub>1</sub> to 22.4% T<sub>2</sub>,  $p < 0.001$ ). Among boys, an increase was seen in the ADHD group (6.3% T<sub>1</sub> to 15.1% T<sub>2</sub>,  $p < 0.001$ ) and in the group of other psychiatric disorders.

Associations were found between chronic pain at T<sub>1</sub> and persisting psychiatric disorder for the total sample of participants with any psychiatric disorder ( $n = 440$ ) (Figure 10). Furthermore, smoking and trying illicit drugs were associated with persisting psychiatric disorders, but only among girls. Age and SES showed no association with persistence of psychiatric disorder, i.e. no confounding effects were found either in the total sample or separately for each gender.



**Fig 10.** Associations between chronic pain, somatic disorders, and substance use at T<sub>1</sub> and persisting psychiatric disorder at T<sub>2</sub> for the total sample ( $n=440$ ). The numbers are risk difference (%) and *p-values*.

## 4.2 Paper II

### *Suicidality, function and associated negative life events in an adolescent psychiatric population at 3-year follow-up.*

At T<sub>2</sub>, the psychosocial functioning CGAS score in the total sample (Paper II  $n = 549$ ) was mean 71.3, and girls had lower CGAS score than boys (mean 68.2 vs. 75.2). Specified by psychiatric disorder, girls had lower CGAS than boys in all diagnostic groups.



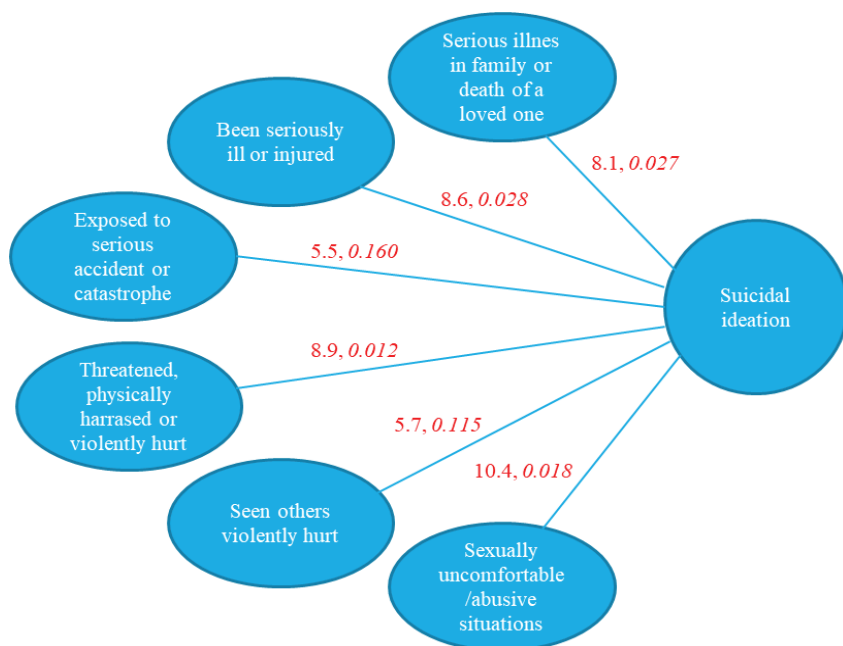
The frequency of suicidal ideation was 12.4% in the total sample (Paper II n = 549), whereas the frequency of suicidal behaviour was 18.2%. There was a significant difference between girls and boys for suicidal ideation (17.9% vs. 5.4%), and similar gender difference was found in suicidal behaviour, where girls had the highest frequencies of suicidal attempts ever (25.0% vs. 9.5%). Girls had higher frequencies of suicidal measures than boys in all diagnostic groups. Among those with any psychiatric disorder at T<sub>2</sub>, suicidal ideation was higher among girls (24.8%), and suicidal behaviour even higher (30.0%), with significant gender differences for both suicidal ideation and suicidal behaviour (18.0% and 18.3%, respectively). The frequencies of suicidal ideation and behaviour were highest in mood disorders and lowest in ADHD.

School dropout was present among 18.5% of the participants (Paper II n = 570), and more frequent for girls than boys (22.5% vs. 13.2%). When specifying by psychiatric disorders, gender difference was only found among patients with ADHD, with highest frequencies among girls (24.7% vs. 13.5%).

Negative life events were common experiences in this cohort (Paper II n = 570). Having serious illness of someone in family or death of a loved one, were the most common negative life events (57.7% last three years and 85.7% ever), with higher frequencies among girls than boys only for the last three years. Having been seriously ill, injured or received painful or frightening treatment in hospital were more frequent among girls than boys both for the last three years and ever, as was ever been exposed to a serious accident or catastrophe. There were highly significant differences between girls and boys in having been put into sexually uncomfortable or abusive situations, both during the last three years and ever (23.5% vs. 2.9%, and 44.4% vs. 7.9%, respectively).

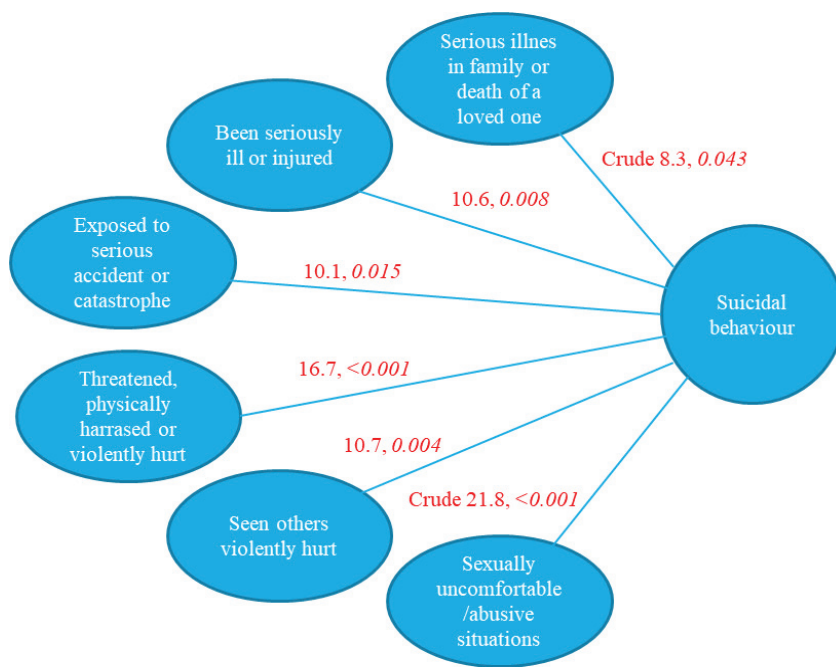
Associations were found between several negative life events and suicidal ideation (Figure 11). After adjustment for SES, the strongest associations were for having been threatened, physically harassed, or violently hurt and having been put into sexually uncomfortable or abusive situations. Gender-specific analyses, adjusted for SES, showed associations with experiencing serious illness of someone in the family or death of a loved one, and being

threatened, physically harassed, or violently hurt for girls, but no associations were present for boys.



**Fig 11. Associations between the experience of negative life events and suicidal ideation at T<sub>2</sub> for the total sample (n=549). The numbers are risk difference (%) and *p*-values.**

Suicidal behaviour was associated with been seriously ill or injured, exposure to a serious accident or catastrophe, and been threatened, physically harassed, or violently hurt (Figure 12). Having seen others violently hurt was associated with suicidal behaviour in girls only. Some estimates could not be adjusted for SES due to non-convergence of the calculations. Thus, the association with having been put into sexually uncomfortable or abusive situations could not be adjusted for SES, neither could the corresponding association that was present only for girls. Having been threatened, physically harassed, or violently hurt was related to suicidal behaviour for both girls and unadjusted for boys. There was an association between SES and suicidal behaviour ( $p = 0.005$ ), and specified by diagnostic groups, associations with suicidal behaviour were highly significant for mood disorders and anxiety disorders ( $p < 0.001$ ) and the group of other disorders ( $p = 0.007$ ), adjusted for SES.



**Fig 12. Associations between the experience of negative life events and suicidal behaviour at T<sub>2</sub> for the total sample (n=549). The numbers are risk difference (%) and *p*-values.**

School dropout was associated with having seen others been violently hurt, after adjusting for SES (Figure 13), but only among girls. An association found between suicidal behaviour and school dropout was attenuated after adjustment for SES in the total sample.

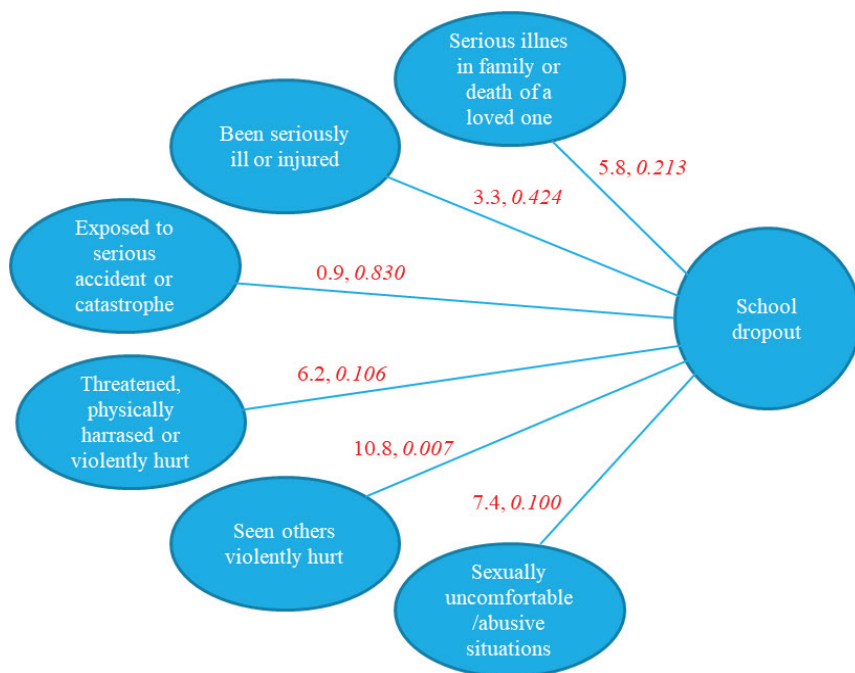


Fig 13. Associations between the experience of negative life events and school dropout at T<sub>2</sub> for the total sample (n=570). The numbers are risk difference (%) and *p-values*.

### 4.3 Paper III

#### *Association of treatment procedures and resilience to symptom load three-years later in a clinical sample of adolescent psychiatric patients.*

In the total sample (Paper III n = 447), 93.0% received individual treatment. The frequency of psychotherapy sessions varied by disorder group: Among patients with ADHD, 50.5% received less than 10 sessions, while patients with mood disorders and anxiety disorders received the highest number of sessions; 19.8% and 19.7% respectively received more than 30 sessions. Medication was most frequent in the ADHD group (81.2%). The rates of parent counselling or family therapy were between 60.8% and 76.5% in the total sample, with the highest rate for anxiety disorders, with no difference between genders. Counselling municipal services was provided for 49.1% in the total sample.

Gender differences were found in receiving treatment procedures. Psychotherapy was more frequent among girls overall (RD = 18.9), as well as in all groups of psychiatric disorders, with the largest gender difference occurring in the group of other psychiatric disorders. Medication was significantly less common for girls versus boys overall (RD = -18.4) and in the group of other psychiatric disorders. There was no gender difference for ADHD medication.

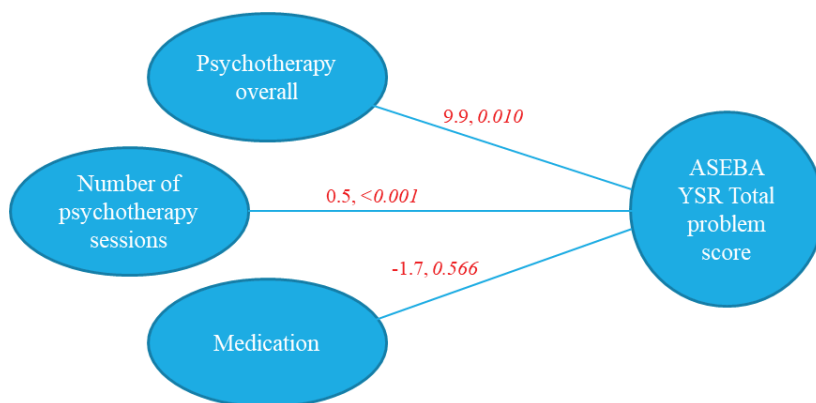
Resilience factors measured by READ showed a Total READ mean value of 3.5 (SD 0.8) for patients with any psychiatric disorder, ranging from 3.0 (SD 0.7) for patients with mood disorders to 3.7 (SD 0.7) for patients with ADHD. Girls had lower total READ mean values than boys for any disorder and for all disorder groups except for mood disorders. The subscale Personal Competence showed the largest gender differences, with statistically significantly higher mean values for boys than girls, in all diagnostic groups.

The YSR Total Problem mean T-score at T<sub>2</sub> ranged from 48.6 (SD 26.3) to 62.7 (SD 28.0) across the diagnostic groups. The highest symptom scores were for those with mood disorders at T<sub>1</sub>, of whom 48.6% had T-scores in the borderline/clinical range ( $\geq 60$ ) three years later. Comparing the T-scores for participants with and without a diagnosis at T<sub>2</sub> ( $n_{\text{diagnosis}} = 314$ ,  $n_{\text{no diagnosis}} = 108$ ), the mean T-scores were 55.5 (SD 26.8) versus 34.0 (SD 18.3), respectively. The YSR scores were significantly higher among girls than among boys in all diagnostic groups, especially in the groups of mood disorders and other psychiatric disorders, also when comparing participants with and without a diagnosis at T<sub>2</sub>.

Older age and lower SES were significantly associated with higher symptom load at 3-year follow-up in the total sample, but for girls only. Linear regression analysis with YSR Total Problem T-score at T<sub>2</sub> as dependent variable and treatment procedures as covariates were therefore performed adjusted for age and SES.

There was a statistically significant positive association between having received psychotherapy at T<sub>1</sub> and symptom load three years later for the total sample for any psychiatric disorder (Figure 14). When increasing the number of psychotherapy sessions in

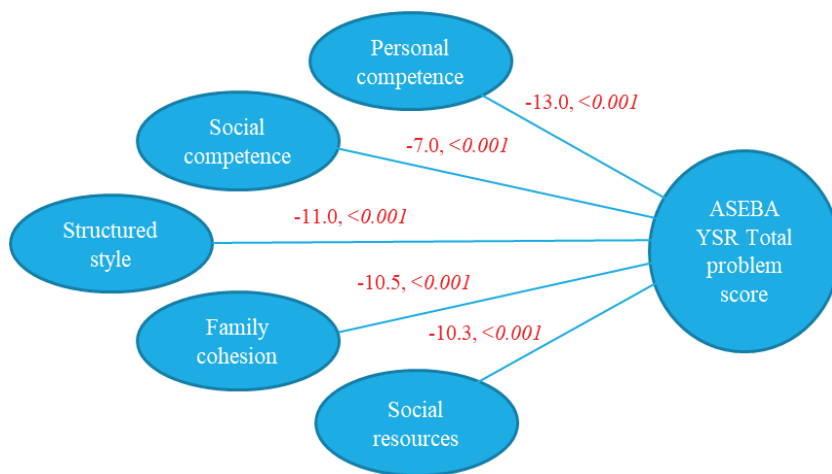
the total sample by 1 session, the YSR Total Problems T-score increased with 0.5 units. This association was present only for participants with a diagnosis at T<sub>2</sub>. The significant associations were found in all diagnostic groups except for mood disorders. The significant associations were found for girls with anxiety disorders and ADHD, as well as any psychiatric disorders.



**Fig 14. Associations between treatment procedures and symptom load at T<sub>2</sub> for the total sample (n=447). Numbers are regression coefficients and *p*-values.**

Medication prescribed at T<sub>1</sub> was not statistically significantly associated with symptom load three years later for the total sample. For boys only, medication was associated with an increased YSR Total Problem T-score of over 7 at follow-up for any psychiatric disorder ( $\beta = 7.4, p = 0.032$ ), but no statistically significant associations were found when specifying by psychiatric disorders. No statistically significant associations were found between counselling parents or counselling municipal services and symptom load at follow-up.

READ resilience scale scores were associated with YSR Total Problem T-score, with significant negative associations for Total READ and for all subscale scores, adjusted for age and SES (Figure 15). Increasing the Total READ score by 1 unit (scale 1-5), the YSR Total Problems T-score decreased by 15.7 units. Associations were present both for participants with and without a diagnosis at T<sub>2</sub>. The subscale Personal Competence was associated with the lowest Total Problem score for both genders.



**Fig 15. Associations between READ resilience scores and symptom load at T<sub>2</sub> for the total sample (n=447). Numbers are regression coefficients and *p*-values.**

Including the five READ subscales simultaneously in the analyses, showed that Personal Competence and Family Cohesion remained associated with a decrease in Total Problem score, but for girls only. When differentiating between psychiatric disorder groups, there were significant negative associations for Total READ in all disorder groups, except for boys with mood disorders.





## **5. Discussion**

### **5.1 Main findings**

This thesis investigated the course of psychiatric morbidity, somatic co-morbidity, and function over three years in a clinical adolescent population. Psychiatric morbidity decreased, including for mood disorders, but nevertheless, almost three out of four still had a psychiatric disorder. Chronic pain, smoking and having tried illicit drugs at baseline were factors strongly associated with psychiatric morbidity three years later. Adolescent girls seemed to have a higher morbidity than adolescent boys, with an increased frequency of anxiety disorders after three years, a five times higher prevalence of mood disorders than boys, and a five to ten times higher prevalence of chronic pain. Furthermore, one out of four girls with a psychiatric disorder at follow-up had suicidal ideations, and one out of three had a previous history of suicidal behaviour. Girls had lower psychosocial functioning and higher rates of school dropout and experiences of negative life events than boys. Negative life events, especially exposure to interpersonal violence, were associated with suicidal ideation, suicidal behaviour, or school dropout, indicating a complex symptom burden especially among the girls in this sample.

One out of three former patients reported symptom load in the borderline/clinical range after three years. Girls had highest symptom load, especially those with previous mood disorders. Treatment procedures were extensive in form and duration and consisted especially of psychotherapy for girls and medication for boys. Nine out of ten had received individual treatment. Resilience measures were reported lowest among patients with mood disorders and highest among ADHD patients, and lower among girls than among boys in all diagnostic groups. Higher self-reported personal and social resources were associated with lower symptom load after three years, suggesting a protective potential.

### **5.2 Methodological considerations**

The main strength of this study is inclusion of a large clinical sample, reassessed after three years with a high retention rate providing good precision in the analyses and results. Despite a considerable attrition rate in the initial recruitment, the participants at T<sub>1</sub> did not differ in age, gender or reason for referral compared to non-participants. The psychiatric diagnoses

were classified by clinicians at both time points, according to the current diagnostic classification system. Suicidal ideation and behaviour were assessed in-depth by clinicians during the diagnostic interview at follow-up and were not only based on self-report measures of symptoms, which may involve the limitations of less accuracy in establishing psychopathology. Another strength of this study is the broad mapping of somatic disorders and chronic pain, in combination with mental health status, as it is important to put the spotlight on connections between mental and somatic health. The use of validated questionnaires in this mapping also strengthens the study findings. Furthermore, it is a strength that the study includes a broad mapping of functioning, experiences of negative life events, substance use, but also resilience factors that can positively affect outcome.

Before discussing the study-findings related to previous research, possible methodological limitations must be considered. It is always desirable for the sample in an observational study to be representative of the population of interest, and the sample should be chosen to be as similar as possible to the relevant population (280, 281). In epidemiological studies, statistical analyses are based on the assumption that we can draw inferences about the total population of specific subjects by making observations on a sample of such subjects (282). Still, errors can occur, and estimates may be deceptive if the sample is not representative or there have been miscalculations. The two types of errors that cause trouble to epidemiological studies, are random errors that affects the precision (283), and systematic errors also called biases (284).

### **5.2.1 Precision**

Random error is variability in the data that cannot be readily explained and are also referred to as chance (283). These random variations may be caused by an incidental process in sampling the data, or that different factors can affect the measurements causally. This may lead to the fact that different samples will produce different results. These differences are called sampling error, and two possible sampling errors can appear; Type I or Type II error (285). If we achieve a significant result, and reject the null hypothesis, when the null hypothesis is in fact true, it is called a Type I error. This may be considered as a “false positive” result. On the other hand, we may get a non-significant result when the null hypothesis is not true, which is called a Type II error and can be referred to as a “false

negative” finding. Type II error depends upon the sample size. By increasing the sample size, the dispersion gets smaller, and the mean of the distribution is closer to the population mean (Central Limit Theory) (286).

The sample sizes in our study were substantial, but some of the subgroups of psychiatric disorders were small, and this limited subgroup analyses, as well as increased the risk of Type 2 errors. However, the numbers were acceptable for the most common disorders as ADHD, anxiety disorders, and mood disorders. A total of 447 to 549 adolescents in the three papers constitute an acceptable sample for a variety of analyses with sufficient power.

*Statistical Power* was calculated in the study protocol:  $n=550$  with diagnostic information, if the risk of outcome is 20% in a group of 150 subjects and the risk is 10% in a group of 400 subjects, the power is 84% (two-sided,  $\alpha=0.05$ ).

Using the scale of original measurement to present study findings directly has definite advantages over just giving p-values alone commonly dichotomized into “significant” or “non-significant”. At the same time, information on the inherent inaccuracy due to sampling variability is shown. This is the rationale for using confidence intervals (282, 287), and the main intention is to point out the precision of the estimates in the sample study as population values. The calculated interval provides values in an area within which we can have a chosen confidence of it containing the true value. The wider the CI the less the precision, while a narrow CI indicates less random errors and higher precision. The width depends mainly on three different factors (282). It depends on the sample size, in that the larger the sample size is, the narrower the CI becomes, and the results are more precise. The width also relies upon the variability of the characteristics being studied, if the variability decreases, the narrower the CI becomes indicating the more precise estimates. The width also depends on the degree of confidence prescribed, since the more confidence chosen, the wider the interval. The most common degree of confidence presented is 95% (287), and the 95% CI was used as a more informative measure of the precision in the present study, supplementing the reported p-values.

## **5.2.2 Internal validity**

Internal validity refers to the degree to which the study findings precisely reflect the population from which the participants are recruited, and is defined by how well a study can rule out alternative explanations for its findings (281, 288). It is important to strive for as high internal validity as possible, by collecting, analysing, and interpreting data correctly. This can be done by using reliable measures and minimizing errors, such as random errors due to chance and systematic errors due to bias or confounding. Definitions of these errors will be elaborated in the following. A study can be biased because of the way in which subjects have been selected, the way the study variables are measured, or some confounding factor that is not completely controlled for (284). Although random errors can be reduced to zero if a study population became infinitely large, systematic errors are not affected by increasing the size of the sample. Before concluding that the associations presented in this thesis most probably are real and not attributed to some other circumstances, the factors contributing to systematic errors must be considered.

### **5.2.2.1 Selection bias**

Selection bias is a systematic error causing an imbalanced study sample that may have its cause in the procedures used to select subjects or from factors that affect study participation (289). The implication of selection bias is that the participants in the study sample will differ systematically from the population sample they are selected from. In the St. Olav CAP-study, the main reason of referral was not different in the initial recruitment of participants and non-participants, nor was age or gender, as described in section 3.2.1. Still, participation is a decision that may correlate with conditions concerning social, educational and health status. These conditions could again correlate with risk factors for study outcome, and we cannot rule out bias due to baseline selective participation (290, 291). The clinical population of all patients aged 13-18 years who visited the Department of Children and Youth at least once over a 2-year period, from whom the selection of participants was done, may differ in social, educational and health conditions. As non-participants did not consent to take part in research, ethical restraints hindered any further comparison with participants, other than the analyses approved by The Data Protection Official for Research (age, gender and main reason for referral, cf. section 3.5).

This thesis is based on data from two time points in this longitudinal cohort study. One possible systematic error is therefore selection bias due to loss to follow-up, which may represent a threat to the internal validity of estimates (290). The retention rate was high from T<sub>1</sub> to T<sub>2</sub>, as described in section 3.2. Analyses comparing the participants at follow-up with those who did not participate at follow-up, showed no differences in age or diagnosed psychiatric disorders at T<sub>1</sub>. There was though a difference in gender at the two time points, with more girls than boys among participants compared to non-participants at T<sub>2</sub>, indicating that we may have lost either boys with good function or some of the boys with psychiatric disorders, high symptom load or impaired function.

#### **5.2.2.2 Information bias**

Systematic error in a study can emerge because of incorrect collected information about or from study subjects (292). Such faulty information is often referred to as misclassification and may lead to a person being placed in an incorrect category. A common type of information bias is *recall bias*, which occurs when a subject is interviewed to achieve exposure information after disease has occurred. The same could apply to remembering what one has experienced back in time. Another type of information bias is *interviewer bias*, as when the information is evoked or interpreted differently by researchers or research assistants. One way of avoiding recall and interviewer bias is by using information from medical records instead of interview information. In our study, information about disorders and treatment procedures were obtained from medical records at T<sub>1</sub>, which may have helped providing more accurate information.

At both time points in this thesis, self-report was used as a method of obtaining additional characteristics, and information bias cannot be excluded for these variables. Adolescents may have answered the questionnaires incorrectly, leading to an under- or overestimation of symptoms, functioning or experiences. This applies to the measurements of chronic pain, substance use, negative life events, school dropout and symptom load. The same consideration applies to the self-reported resilience measures where social desirability may lead to reporting better competences and resources. School dropout was reported by only one question. Additional information would have strengthened the measure, either by using several questions or information from other sources, supplemented by asking about the

subjective reasons for the respective school dropout. Trying illicit drugs was also reported only by one question, and although the same question was used at both time points, this topic may be especially prone to information bias.

### **5.2.2.3 Measurement bias**

When selecting instruments for research, it is crucial to use reliable and valid instruments, and to use standardized procedures. In our study, two different classification systems for psychiatric diagnoses were used at the two time points, which may have affected prevalence rates and is a possible limitation. Research has shown that the concordance between the two systems can differ across the range of disorders, and with varying concordance within the anxiety disorders (293). Furthermore, the diagnostic criteria for Hyperkinetic disorder in ICD-10 are stricter than the criteria for ADHD in DSM-IV. This may have contributed to a higher increase in ADHD diagnosis at follow-up. Beyond that, the ICD-10 and DSM-IV are widely harmonized, and mood disorders as depression and dysthymia, showed high levels of concordance in an investigation of ICD-10 versus DSM-IV (294).

The diagnostic methods and procedures were different at the two time points; based on all available clinical information using multi-disciplinary team at T<sub>1</sub>, and by telephone interview at T<sub>2</sub>, using the acknowledged K-SADS semi-structured interview (262). This may also have affected the diagnostic accuracy. K-SADS assesses all psychiatric disorders systematically, which could have led to reporting more comorbid disorders at T<sub>2</sub>, even though secondary disorders were stated also at T<sub>1</sub>, based on thorough assessment. It is reasonable to assume that some differences in diagnoses over time might be explained by the different methods and diagnostic procedures between the two time points. Another possible limitation was the use of K-SADS for participants above 18 years, although such use has been conducted in earlier research. To ensure that the assessments made by the clinicians using K-SADS were carried out as similar as possible, inter-rater reliability was assessed and found to be good, as described in section 3.3.2.1. The inter-rater reliability was also assessed to ensure similar ratings of psychosocial functioning using CGAS and was found to be satisfactory, as reported in section 3.3.2.6.

There is no well-established definition of chronic pain in children, but the definitions of chronic pain and multisite pain used in paper I are widely used in other epidemiologic pain studies, and have been used in a general population study from the same area; The Young-HUNT3 study (108, 116), as described in section 3.3.1.3. The questions used to ask about substance use (paper I) and negative life events (paper II) were also the same questions asked in The Young-HUNT3 study, as reported in sections 3.3.1.4 and 3.3.1.7.

Treatment plausibly impacts the course of suicidal ideations or behaviour, general psychosocial function and school dropout, and more detailed information on treatment procedures would have strengthened the analyses in paper II. Self-report questionnaire was used to measure symptom load at T<sub>2</sub> in paper III and should preferably be supplemented by proxy reports. Although YSR is a widely used and validated instrument (276, 278), some information bias cannot be excluded when using self-report. The same consideration can be made when it comes to the self-reported resilience measures, but to ensure the best possible measurements, the validated questionnaire READ was used in the study (226, 227).

Using level of maternal education to indicate socioeconomic status may not enclose the complete concept of socioeconomics, and furthermore, this information was accessible for a reduced sample, which may not accurately reflect the total study population. Also, the reduced sample resulted in reduced power in the association analyses. Nevertheless, parental education is an important measure that shows the strongest differences in inequality of socioeconomics in children and adolescents (295).

#### **5.2.2.4 Confounding factors**

A simple definition of confounding is confusion of effects, meaning that the effect of one variable is mixed with the effect of another variable, leading to a bias (296). This blending of effects may contribute to misleading estimates of relationships between two variables. To control for confounding in the present study, analyses were adjusted for common potential confounders, such as age, gender, and SES.

Diagnoses of psychiatric disorders differ by age and gender. As described in section 1.4.1, the prevalence of psychiatric disorders may change over time, and thereby be affected by the age of the participant (17, 24, 27). The age at assessment was examined as a possible confounder in both paper I and paper III, with no confounding effect found in paper I, but a possible confounding effect was detected in paper III and therefore adjusted for in this paper. Since gender plays an important role in the prevalence of psychiatric disorders during childhood and adolescence, and since there were more girls than boys among participants at both time points in our study, the analyses were performed separately for girls and boys.

Earlier research has clarified the relationship between SES and psychiatric disorders (297), and studies investigating this relationship in children and adolescents have found that lower SES gives a higher risk of mental health problems (295). For children and adolescents, the inequalities are found to be stronger for income or parental education than parental occupation. In our thesis, SES was measured by maternal education, and because of its possible confounding effect, all analyses were adjusted for SES.

### **5.2.3 External validity**

External validity is the extent to which the results of a study can be generalized to other corresponding populations than the study population (281, 288). Since there were more girls than boys among participants compared to non-participants in this study, we may have lost some of the boys with psychiatric disorders, high symptom load or impaired function. Both severity of symptoms and types of treatment may have played a role in the continuity of a disorder and for participation at follow-up. Also, the number of participants were low for some diagnostic groups, requiring us to merge some diagnoses into one larger group, which limited the generalizability of the results for these disorders. All taken into consideration, the study holds an acceptable external validity to emphasize the results as important for clinical focus and for well-funded hypotheses in research elaborating the long-term trajectories of adolescent psychiatric disorders.



## **5.3 Discussion of main results**

### **5.3.1 Psychiatric morbidity and symptom load after three years**

The frequency of psychiatric disorders and the level of symptoms were substantial three years after referral to CAMHS. The numbers at follow-up may involve continuity of the T<sub>1</sub> diagnosis, relapse after temporary recovery or shift to other diagnoses. The reasons for the high rates of persisting morbidity may be diverse, both depending on the treatment given and the general vulnerability in the adolescents in this clinical population, who have a high disease burden. There is an increase in overall rates of psychiatric disorders in the transition from adolescence to adulthood (24, 26). Common psychiatric disorders in adolescence are often forerunners and strong predictors of similar disorders in young adulthood, and most young adults with episodes of a psychiatric disorder have had episodes during their teenage years (5, 6, 24, 27, 28). The higher frequency among girls overall, and especially in girls with anxiety disorders, is comparable with earlier research (38, 298). Results from the CAMELS study found that despite receiving high-quality evidence-based treatments for anxiety, only 22% were in stable remission across all four years they were assessed, 30% were chronically ill, and 48% experienced relapses (200). In the CAMELS study, male gender was associated with increased probability of being in the remission group compared to the relapse group, supporting our finding that it went better with boys, whereas girls had a higher morbidity. The decreased frequency of mood disorders at follow-up may be due to an under-registration in this study. As the course of such disorders is fluctuating, present status may not reflect struggling with periodic disorders.

Psychiatric comorbidity increased from T<sub>1</sub> to T<sub>2</sub>. The female patients seemed to be more prone to develop co-occurring psychiatric disorders, corresponding well with previous studies reporting more comorbidity in girls than boys (37, 299). In our sample, girls had very high rates of psychiatric comorbidity at follow-up, in all diagnostic groups. The rate was highest among those with mood disorders, where more than nine out of ten had an additional psychiatric disorder. All boys with mood disorders also had a comorbid psychiatric disorder, but since there were few boys with mood disorders, the change in frequencies were small.

The prevalence of suicidal ideation and behaviour at 3-year follow-up was high and comparable with earlier research on clinical samples (58, 66). The frequent occurrence of

suicidal attempts may reflect that this is a follow-up of former patients, with high rates of psychiatric disorders, and the results correspond well with earlier research describing that the majority of youth with suicidal behaviours have pre-existing mental disorders (56). Still, the reasons for the high rates of suicidal ideation and behaviour may be diverse, both depending on the persistence of psychiatric disorders, treatment given and the general vulnerability of the adolescents in this clinical population. There were large gender differences with girls having much higher rates than boys of both suicidal ideation and behaviour, in line with earlier research (56), and especially described in the systematic review of 67 population-based longitudinal studies with focus on gender differences in suicidal behaviour in adolescents and young adults (75). In our study, almost one out of two girls with mood disorders had both suicidal ideation and suicidal behaviour, whereas less than one out of four boys with mood disorders had the same symptoms. Boys with ADHD or other psychiatric disorders had the lowest frequencies of suicidal ideation or behaviour. This underscores the large gender differences and added risk for girls when it comes to suicidal symptoms.

The considerable symptom load three years after referral was as expected substantially higher than in the general population (278), and corresponds well with the reported symptom load in other studies of outpatient child and adolescent mental health services (300, 301). Analyses comparing the T-scores for participants with or without a psychiatric diagnosis at T<sub>2</sub>, showed as anticipated highest symptom scores among the participants with a T<sub>2</sub> diagnosis. Girls had significantly higher symptom load than boys in all diagnostic groups, and the participants with the highest symptom scores were those with mood disorders or in the group of other psychiatric disorders (e.g., eating disorders, psychotic disorders, ASD). We do not know if the high symptom load in patients with mood disorders was due to persistence of the mood disorder at T<sub>1</sub> or relapse, but research shows that both persistence rates and relapse rates are high for mood disorders (302).

The main feature of treatment characteristics was that patients in all diagnostic groups received extensive interventions, as roughly nine out of ten received some type of individual treatment. Disorder specific features were also observed in that those with anxiety and mood disorders at T<sub>1</sub> had received the highest number of psychotherapy sessions, whereas ADHD and other disorders had the highest rate of medication, both indicating a high disease burden

at T<sub>1</sub>. The different treatment methods depend naturally on recommended treatment guidelines, as medication has been long established as an effective treatment for ADHD. Furthermore, choice of treatment depends on additional disorder specific features, for example verbal deficits and problems with emotion processing often present with ADHD (50, 303). When investigating treatment procedures given to the participants in this study, we should also keep in mind the high degree of comorbidity at T<sub>1</sub>. Nearly one out of three had comorbid disorders in addition to their primary disorder, which may render necessary more than one treatment procedure.

Treatment characteristics showed distinct gender differences, as girls received significantly more psychotherapy sessions than boys in all diagnostic groups. More than one in two girls compared with about one in four boys received ten or more psychotherapy sessions. We need to be mindful that the girls in this sample were older (0.7 years at both time points) than the boys when participating in the study. This may have an impact on the findings related to the use of psychotherapy among girls, because higher age may imply higher maturity to utilize the benefits of psychotherapeutic approaches. The opposite pattern was found for medication, where boys were more likely to receive medication compared with girls. Even though more boys than girls had ADHD, for which medication is the treatment of choice, the gender difference was present also for this disorder.

Positive associations were found between the number of psychotherapy sessions and symptom load for girls only, overall and in the groups of anxiety disorders and ADHD, possibly because these groups had a high and complex symptom pattern in the first place, resulting in longer treatment duration, as also described in the CAMELS study (200). The positive association between receiving medication at baseline and higher symptom load at follow-up were found only in boys. As a counterintuitive result, this warrants replication in future studies. One might speculate that this could have been due to gender-specific differences in initial diagnoses and symptom load, or less additional psychotherapy in boys. When analysing the participants with or without a psychiatric diagnosis at T<sub>2</sub>, we found that the associations between the number of psychotherapy sessions and symptom load was only present in the subgroup with a psychiatric diagnosis at T<sub>2</sub>. This fits with the assumption that this is the presumed group with most symptom burden.

This three-year follow-up of a large clinical population provides a picture of clinical reality. It is therefore worrying that such a large proportion of former adolescent patients in CAMHS, especially girls, struggle with mental illness and symptom burden after three years. This provides concern prognostically and may indicate the importance of necessary follow-up of adolescent patients to improve future outcomes.

### **5.3.2 Co-occurring chronic pain or somatic disorders**

Overall, there was a decrease in chronic pain for the total sample after three years, but an increase among those with anxiety disorders, not surprisingly since chronic pain may be regarded as part of the anxiety disorder. We found large differences in frequency of pain between the genders at T<sub>2</sub>. Nearly nine out of ten girls and five out of ten boys with anxiety disorders had chronic pain, and the frequency of multisite pain was more than three times as high in girls with anxiety disorders compared to boys. A systematic review investigating the epidemiology of chronic pain in children and adolescents from the general population, found that pain prevalence was generally higher in girls and increased with age for most pain types (109). In our study, girls were older than boys at follow-up, which may be one of the reasons girls reported higher frequency of chronic pain than boys after three years. Previous research has also demonstrated gender differences in responses to pain, showing that female participants experiences greater pain sensitivity, increased pain facilitation and reduced pain inhibition compared to male participants (304), and that adolescent girls have a decreased pain threshold after puberty (110).

A study using data from a large Norwegian population survey, the Young-HUNT3 Study, demonstrated higher prevalence of chronic multisite pain among adolescent girls and boys with increasing number of psychiatric symptoms, but with highest rates among girls (114). In the St. Olav CAP Survey at T<sub>1</sub>, 70% of the patients reported chronic pain in addition to a psychiatric disorder (115). This was a higher frequency than the 44% reported in the general adolescent population in many countries (107) and in our region (115) and underlines the importance of assessing chronic pain among adolescents with psychiatric symptoms and disorders.

Somatic comorbid diagnoses became more frequent at T<sub>2</sub> for female patients with anxiety disorders. An increased risk of somatic disorders is reported in patients with anxiety disorders (98), independent of gender. Furthermore, adolescents who experience chronic somatic health conditions, are found to be at risk of elevated physiological anxiety symptoms in mid-adolescence (305). The higher frequency of girls than boys with anxiety disorders in our sample may have influenced the finding of a significant increase only among female patients. Still, the results show consistently that the burden of disease was most prominent among girls.

We also need to have in mind that functional somatic syndromes, with impaired functioning and the absence of physical pathological findings, are common in adolescents (306). Patients with these syndromes are known to have a high prevalence of psychiatric disorders, particularly emotional disorders (307, 308), but are also found to have a higher number of somatic conditions compared to the general population (309). A recent cohort study of children and adolescents with psychogenic nonepileptic seizures demonstrated a higher risk of a broad variety of psychiatric disorders compared to children and adolescents with epilepsy and controls in good health (310). In our study, there were few patients diagnosed with functional somatic syndromes, but bearing in mind the high prevalence of chronic and multisite pain among the participants, there may have been some adolescents with undetected functional somatic syndromes.

The connection between somatic symptoms and psychiatric disorders goes both ways. Having somatic symptoms or disorders increases the risk of developing psychiatric symptoms in adolescence, indicating a strong relationship between somatic factors and psychiatric symptoms and disorders (91, 101, 102), as the findings in this study supports. We found a significant association between having chronic pain at T<sub>1</sub> and persisting psychiatric disorder after three years for the total sample, and strongest in the female group. Earlier studies have demonstrated associations between pain in adolescence and mental health problems in young adulthood (111, 112). There is a complex interplay between genetic, epigenetic, neuronal, chemical, and environmental factors that may collaborate synergistically to affect the expansion and maintenance of chronic pain and mental health conditions in adolescents (121, 122). It is also essential to have in mind the parent-child relational context and the powerful

role of parental factors (121). Presence of chronic pain in adolescents with psychiatric disorders, especially among girls, is therefore important to assess, since these patients seem to be vulnerable for persistent and even increasing psychiatric morbidity.

### **5.3.3 Substance use**

Norway appears to be a low-prevalence country when it comes to substance use in the general adolescent population in comparison with other European countries (127). At T<sub>1</sub>, the adolescents reported a higher intake of alcohol, a higher prevalence of smoking, and a four times higher ratio of having tried illicit drugs compared to the general population (129). In our sample, smoking tended to decrease during follow-up, with no gender differences, whereas alcohol use did not change substantially overall, but increased for anxiety disorders and ADHD in the total sample and for girls. A higher rate was expected, since the age of participants shifted from 13-18 years to 16-21 years, and drinking alcohol is more common at these latter ages. Also, in Norway it is not allowed to buy alcohol before 18 years. Finding the highest increase among girls with anxiety disorders corresponds well with earlier Norwegian studies (132, 311).

The more surprising result was the significantly increased level of having tried illicit drugs in all diagnostic categories, and especially in the female sample. Getting correct information by using self-report on behaviour that may be shameful or illegal, may be a challenge.

Therefore, the reports on drug use must be interpreted critically. During adolescence, there is a general increased use of illicit drugs and a possible heightened tolerance, which can contribute to an increased incidence three years later (128). Still, associations with the specific psychiatric disorders are relevant. We found highest rates among girls with anxiety disorders, in this group one out of five had tried illicit drugs. There are inconsistent findings on the association between anxiety disorders and alcohol/drug use in previous studies, some indicating a positive association (312), and other demonstrating negative associations (313). Opposite to our finding, a former review demonstrated that self-medication with alcohol or drugs for mood and anxiety disorders was associated with male gender (314). A recent population-based study showed gender-specific substance use patterns among Portuguese adolescents (315). In this study, family structure as not living with both parents and poor parent-adolescent communication were associated with more problematic substance use

among girls only. Additionally, higher psychological distress was associated with higher odds of being frequent alcohol and tobacco users, specifically in female adolescents. We found an association between smoking or having tried illicit drugs and persistence of psychiatric morbidity in girls. Furthermore, we found increasing rates of illicit drug use among patients with ADHD for both genders, which corresponds with recent findings from the MTA longitudinal study (134). Our results and the inconsistent findings between studies, indicate the need for further research on gender and disorder-specific substance use in a clinical population, and the impact and effect of substance use on psychiatric morbidity in adolescence.

#### **5.3.4 Negative life events and associations with suicidality and school dropout**

The frequencies of experiencing negative life events in this sample were in accordance with earlier research reporting associations between psychiatric disorders and earlier negative life events or childhood adversities (180, 316, 317). The most common experiences, in both genders, were serious illness of someone in the family or death of a loved one, reported for eight to nine out of ten adolescents. These events are naturally occurring in the life-course. More worrying is that almost half of the adolescents had been threatened, physically harassed, or violently hurt, or had seen others violently hurt. There were no gender differences in experiencing these events, whereas exposure to sexually uncomfortable or abusive situations were far more common for girls than for boys. Less than one out of ten boys had such experiences, but almost one out of two girls were exposed. The prominent gender difference in exposure to sexual uncomfortable or abusive situations, was larger in our study than in earlier findings in European countries (146) and in a former study of a Norwegian child and adolescent outpatient setting (147). This may be because the participants in our study were not only asked about experiences of sexual abuse, but also posed a broader question of exposure to sexual uncomfortable situations. Nevertheless, these former adolescent patients had a large degree of exposure to negative life events, with the stress and burden such events provide.

We examined possible associations between suicidal ideation and behaviour at follow-up and negative life events, and earlier studies have demonstrated such relationships (149, 165). In our study, we found associations between suicidal behaviour and all the negative life events

in the total sample, whereas suicidal ideation was associated with four of the negative life events. The associations were strong between suicidal ideation and behaviour and having been threatened, physically harassed, or violently hurt in the total sample, and for suicidal behaviour it was found in both genders, whereas suicidal ideation was only associated for girls. These findings strengthen the proposed relationship demonstrated in previous research (167). Among adolescents, victimization by peers is highly prevalent and is related to increased risk of suicidal attempts, and the longer history of victimization, the greater risk (170). For girls only, suicidal behaviour was related to having seen others violently hurt, as also reported in earlier research (169).

Suicidal ideation and behaviour were furthermore associated with exposure to sexually uncomfortable or abusive situations in the total sample, but after gender-specific analyses, the connection persisted only for suicidal behaviour among girls. Sexual abuse or violence has been found to be strongly associated to suicide attempts and behaviour (169) and contributing the most to suicide attempts in youths and young adults together with bullying (167).

Losing a loved one by death may be a very stressful event for children and adolescents, and a systematic review and meta-analysis found that stressful life events increased the risk of both reported suicidal ideation and behaviour (318). Opposite to suicidal ideations, suicidal behaviour was associated with serious illness of someone in the family or death of a loved one for boys only. This relation has been found in earlier research (168, 169), but not specified by gender. Having been seriously ill, injured or received painful or frightening treatment in hospital, was associated with suicidal behaviour in the total sample, in line with the meta-analysis of 50 years of research (165). In the WHO World Mental Health Surveys, a cross-national analysis of the associations between traumatic events and suicidal behaviour were investigated, and accidents and disasters were associated with suicidal behaviour (169), as also found in our study. The study results in this thesis, with the high frequency of negative life events and suicidal symptoms, underscores the importance of assessing suicidality in follow-up of adolescent patients in clinical practice and also being aware of this relationship in former adolescent patients.



In our clinical sample, a negative association was found between suicidal behaviour and SES, for both girls and boys. The risk of having suicidal behaviour decreased for the total sample with 2.3% per unit increase in level of mothers' education. This indicates that SES does influence the presence of suicidal behaviour, and that higher maternal education may be a protective factor for development of these symptoms. A large national register-based study showed strong relationship between SES and suicidal risk (319). Furthermore, a systematic review of population-based studies (318), found that suicidal phenomena in adolescents were associated with female gender, mental health problems, negative life events and poor family functioning, corresponding well with our findings.

School dropout was more frequent among girls than boys in our study, opposite to what we expected to find. Dropping out of school is related to many different risk factors. A meta-analytic review (187) described 23 risk domains with significant overall effect on school dropout, where mental health problems of the child and adverse childhood experiences were two of these domains. In our sample, we found associations between school dropout and having seen others been violently hurt, among girls only, which adds to the knowledge base. A recent systematic review and meta-analysis of longitudinal studies (194) showed that adolescents and young adults who had school failure were at higher risk of a suicide attempt.

The results in our study underline the importance of assessing negative life events and associated factors among adolescents with psychiatric symptoms and disorders to reveal any such risks and functional consequences, give proper measures and treatment and if possible, prevent further traumatic events.

### **5.3.5 The presence of resilience factors and their effect on symptom load**

The self-reported resilience factors showed a well-known pattern across subscales (227), but overall, the levels of these factors were fairly low, indicating the vulnerability typical in a clinical sample. When differentiating by psychiatric disorders, patients with mood disorders had the lowest levels of resilience factors in the total sample and for both genders.

We found gender differences in resilience factors corresponding to results from earlier research (226, 227), especially concerning the subscale Personal Competence. The considerably higher scores for boys in this subscale are consistent with research showing boys to report higher levels than girls on constructs such as general self-esteem and self-efficacy (237). We hypothesized based on previous research that girls would report higher scores than boys on Social Resources (226, 227, 246), but this was not verified as girls reported lower levels for all resilience factors. One reason for the lower scores among girls may be their higher prevalence of mood disorders compared to boys, and that especially depression possibly had a negative impact on resilience scores reported at the same time among girls, which may have biased the findings (320).

Resilience factors were associated with symptom scores, across all subscales and both genders. We found that higher levels of resilience factors at baseline were linked to lower symptom severity three years later, overall and in all diagnostic groups, except for mood disorders among boys. When performing analyses of the participants with or without a psychiatric diagnosis at T<sub>2</sub>, the associations were present in both groups. Resilience factors are of great importance for mental health. Having high levels of resilience factors may lead to a better psychosocial functioning and reduction of psychiatric symptoms, especially emotional symptoms as depression and anxiety (234, 235), and may improve the outcome of psychotherapeutic interventions (231-233). Even though our clinical sample is characterized by its high symptom burden after three years, resilience factors appear to be important contributors for better functioning. The findings in this study are not only similar to earlier research, but also strengthen previous findings, and may propose that personal and social resources can have a protective potential.

### **5.3.6 Treatment challenges in CAMHS**

As this thesis describes, adolescent patients in CAMHS have a complex symptomatology and need interventions addressing many different domains. Former research has shown that the effects of psychotherapy for adolescents differ by psychiatric disorders (196) and may not be as effective as wanted (199, 202). It is challenging to implement high quality and targeted treatment since the burden of comorbid psychiatric disorders is substantial during adolescence (37, 38). Treatment methods designed to encompass more than one specific

psychiatric disorder reflects the quest to achieve treatment benefits beyond what is produced by single disorder therapies (202). There are few such transdiagnostic treatment options available today (202), but one example is the Modular Approach to Therapy for Children with Anxiety, Depression, Trauma, or Conduct Problems (MATCH) (208). Another aspect is that effect sizes for therapies in children and adolescents have been found to be significantly smaller than for adults (201, 321). We surmise that in our study those with the highest symptom burden at baseline received the most extensive treatment procedures. Therefore, this observational follow-up study is not intended to evaluate effect of the treatment provided, as this would require randomized controlled trial methods. Furthermore, it is important to investigate how to use the resources in CAMHS in the best possible way, and to find the optimal scope of psychotherapy for adolescent psychiatric patients.

The results in this thesis have shown that somatic cofactors increase the risk of persistent psychiatric disorders in adolescents. Therefore, beside treatment given in CAMHS, it is also well grounded to implement interventions aimed at these cofactors, especially chronic pain, in order to reduce the risk of maintenance of psychiatric disorders (121). It is uncertain whether this will be an effective treatment procedure, as chronic pain may be just another expression of psychiatric symptom load. Still, it would be interesting to combine psychotherapy with physical exercise in the form of specific muscle training (e.g., physiotherapy, cardio training), especially to those who report chronic pain at baseline, and evaluate if this affects the persistence of psychiatric symptoms or disorders.

Interventions promoting resilience in children and adolescents may also be of importance to improve the mental health of adolescents. In our clinical sample, resilience turns out to be a very important factor, and CAMHS may not have integrated this perspective sufficiently. A recent systematic review and meta-analysis of resilience training programs and interventions shows that interventions based on a combination of mindfulness techniques and CBT seem to have a positive impact on individual resilience (260). Also, a recent literature review showed that resilience was promoted in children and youth by strengthening home and school environments (261). This research highlights that resilience can be built through interventions among children and adolescents, which in turn may affect their mental health status.



## **6. Conclusion**

This thesis aimed to access new knowledge on the course of psychiatric morbidity, somatic comorbidity, and functioning in a clinical adolescent population over three years. The high frequency of psychiatric and somatic comorbidity, including suicidal symptoms, indicates a substantial burden of symptoms and disease in this group of former patients, especially for girls. The results highlight that chronic pain is part of the complexity of psychiatric disorders. Smoking and having tried illicit drugs at baseline were also factors strongly related to persistent psychiatric morbidity. The high frequency of suicidal symptoms, school dropout and experiences of negative life events, indicates a considerable burden of challenges in functioning.

Although some differences in diagnoses over time might be explained by the different methods and diagnostic procedures between the two time points, the results indicate the need for addressing these symptoms and the associated factors and include them in a comprehensive follow-up of psychiatric disorders in this age group. The thesis also provides new information regarding resilience factors in the clinical adolescent population, suggesting that personal and social resources can have a protective potential. The results accentuate the importance of continuous research to find the most effective interventions and facilitating factors for adolescents with psychiatric disorders to enhance optimal function.



## **7. Clinical implications and future research perspectives**

The results of this study bring an important message to clinical practice. Even though clinicians know about mental health challenges in adolescence, the persistence of psychiatric morbidity over three years from early to late adolescence should be an extra eye-opener, and especially the increased rate of anxiety disorders and comorbidities among girls. The self-reported high symptom load and rates of suicidal attempts in this group of former female patients, should also be an extra reminder, as should the high rates of school dropout.

Development and persistence of psychiatric disorders is prone to impact function in school and socialization, with possible long-term consequences, although resilience factors hold the potential to protect and enhance benefit from adaptive measures and treatment. It is therefore crucial to break the cycle at an early stage and hinder maintenance of problems.

This thesis illustrates the sad fact that psychiatric disorders become chronic in many patients already in adolescence and shows that the treatment offered may not prevent long-term and, in some cases, a severe course. This is a challenge for all levels of health care in our society, not only for CAMHS. By being very diagnostic- and treatment-focused, a timely reflection is whether some important focus areas are not addressed properly.

The burden of mental health problems in adolescence must be acknowledged, also the implication of exposure to negative life events. Comprehensive assessment of mental health problems should of course include important risk factors, and asking adolescent patients about suicidal ideation and behaviour, experiences of negative life events and school functioning is important, in order to reveal any such risks and prevent further traumatic events. The results of this study should also encourage asking adolescent patients about pain, uncover smoking habits and illicit drug use, which seems to be important factors for risk of persistence of psychiatric problems, especially among girls.

The results accentuate the importance of targeted interventions for adolescents with psychiatric disorders to enhance optimal function. Also, focus on factors that can improve outcome is of special significance. Despite clinical interventions that were intended to address presenting disorders, the high symptom load reported in our study by girls, and by

those with mood disorders, is especially noteworthy. This points to the importance of focusing on this vulnerable group of patients at the transition from youth to young adulthood. The burden of mental health problems in adolescence must motivate the search for more effective interventions, either targeted or transdisciplinary, as providing standard clinical care may not be enough. The protective potential of personal resources should be utilized. Research on how to promote resilience and whether this leads to reduced symptom load several years later is of importance. Furthermore, long-term clinical follow-up should be considered for adolescents with risk factors identified in this study.

This thesis based on a three-year follow-up can generate essential hypotheses for future research. Longitudinal studies over more years are needed to provide further knowledge on the developmental course of psychiatric disorders in adolescents entering young adulthood. But hopefully, results from this thesis can indicate some preventive measures, upgrade clinical practice, and guide public health policy to the benefit of young people.



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# Appendix



## Appendix 1. Overview of instruments used in this thesis

Instrument	Description	Target group	Conditions	Scoring	Psychometric properties	Commentary and use	References
Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS-PL) Revised version 2009	Psychiatric diagnoses based on the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) (present and lifetime)  Used in clinical and unselected populations	6-18 years	Semi-structured psychiatric interview (child/adolescent and parents), performed by trained interviewer	Diagnoses are scored as: - Definite - Probable (≥ 75% of criteria) - Not present	Inter-rater reliability: 98% (range 93-100%) agreement Test-retest reliability (Cohen's kappa): .63 (ADHD) to 1.0 (Any Bipolar disorder)  High concurrent validity when compared with questionnaires on anxiety, depression, ADHD, and behavioural problems	Applied to older age-groups: Miller et al., 2008: age 16-22 years Lund et al., 2011: age 19-20 years Psychiatric diagnoses at T <sub>2</sub> : Paper I-III  Suicidal ideation and behaviour at T <sub>2</sub> : Paper II	<b>Kaufman</b> , J. et al. Schedule for affective disorders and schizophrenia for school-age children-present and lifetime version (K-SADS-PL): initial reliability and validity data. <i>J. Am. Acad. Child Adolesc. Psychiatry</i> 36, 980–988 (1997). <a href="https://doi.org/10.1097/00004583-199707000-00021">https://doi.org/10.1097/00004583-199707000-00021</a> <b>Miller</b> , C.J., Miller, S.R., Newcorn, J.H. et al. Personality Characteristics Associated with Persistent ADHD in Late Adolescence. <i>J Abnorm Child Psychol</i> 36, 165–173 (2008). <a href="https://doi.org/10.1007/s10802-007-9167-7">https://doi.org/10.1007/s10802-007-9167-7</a> <b>Lund</b> L.K, Vik T, Skranes J, Brubakk AM, Indredavik MS. Psychiatric morbidity in two low birth weight groups assessed by diagnostic interview in young adulthood. <i>Acta Paediatr.</i> 2011;100(4):598–604. <a href="https://doi.org/10.1111/j.1651-2227.2010.02111.x">https://doi.org/10.1111/j.1651-2227.2010.02111.x</a>
Resilience Scale for Adolescents (READ)	Rating of 5 protective factors; personal competence, social competence, structured style, family cohesion and social resources	13-18 years	Self-report questionnaire for adolescents	28 items with a 5-point Likert-type response scale (1=Totally Disagree to 5=Totally agree)  Higher scores reflect higher degrees of resilience	Factor analyses provided acceptable psychometric properties (Von Soest et al., 2010 and Askeland et al., 2020)  In this study internal consistency (Cronbach's alpha) for the subscales was in the range .73 to .91	Applied to older age-groups: Von Soest et al., 2010: age 18-20 years Askeland et al., 2020: age 16-19 years  Paper III	<b>Hjemdal</b> O, Friborg O, Stiles TC, Martinussen M, Rosenvinge JH. A new scale for adolescent resilience: Grasping the central protective resources behind healthy development. <i>Measurement and evaluation in Counseling and Development.</i> 2006;39(2):84-96. <a href="https://doi.org/10.1080/07481756.2006.11909791">https://doi.org/10.1080/07481756.2006.11909791</a> <b>Von Soest</b> T, Mossige S, Stefansen K, Hjemdal O. A validation study of the resilience scale for adolescents (READ). <i>Journal of Psychopathology and Behavioral Assessment.</i> 2010;32(2):215-25. <a href="https://doi.org/10.1007/s10862-009-9149-x">https://doi.org/10.1007/s10862-009-9149-x</a> <b>Askeland</b> KG, Hysing M, Sivertsen B, Breivik K. Factor structure and psychometric properties of the resilience scale for adolescents (READ). <i>Assessment.</i> 2020;27(7):1575-87. <a href="https://doi.org/10.1177/1073191119832659">https://doi.org/10.1177/1073191119832659</a>
Children's Global Assessment Scale (CGAS)	Index of psychosocial functioning  Used in research and clinical settings	4-16 years	Lowest level of functioning last month  In this study rated by clinicians	Scoring 1-100: From lowest 1-10 (needs 24-hour care) to highest 91-100 (superior functioning)	Inter-rater reliability (ICC): .84 Test-retest stability (ICC): .69 to .95  Discriminant validity: significantly lower scores for inpatients than outpatients, and distinguish cases from non-cases	Applied to older age-groups: Weissman et al., 1990: age 0–23 years  **The theoretical reason for choosing 16 years as an upper age limit for CGAS is not documented. Several studies have used the scale up to ages 18, 20, 21 or 23 years without reducing inter-rater reliability.**  Paper II	<b>Shaffer</b> D, Gould MS, Brasic J, et al. A Children's Global Assessment Scale (CGAS). <i>Arch Gen Psychiatry.</i> 1983;40(11):1228–1231. doi:10.1001/archpsyc.1983.01790100074010 <b>Weissman</b> MM, Warner V, Fendrich M. Applying impairment criteria to children's psychiatric diagnosis. <i>J Am Acad Child Adolesc Psychiatry</i> 1990; 29: 789–95. <a href="https://doi.org/10.1097/00004583-199009000-00019">https://doi.org/10.1097/00004583-199009000-00019</a> <b>Schorre</b> , B.E.H, Vandvik I.H. Global assessment of psychosocial functioning in child and adolescent psychiatry. <i>European Child &amp; Adolescent Psychiatry</i> 13, 273–286 (2004). <a href="https://doi.org/10.1007/s00787-004-0390-2">https://doi.org/10.1007/s00787-004-0390-2</a>

Instrument	Description	Target group	Conditions	Scoring	Psychometric properties	Commentary and use	References
Achenbach System of Empirically Based Assessment (ASEBA) – Youth Self Report (YSR)	Ratings of behavioural and emotional problems and adaptive functioning Used in research and clinical settings	11-18 years	Self-report questionnaire for adolescents Problem scores refer to the past 6 months Adaptive scores refer to present situation	Problem scores: 112 problem items rated “Not true” (0), “Somewhat or sometimes true” (1), “Very true or often true” (2) Eight Syndrome Profiles Two composite scales; Internalizing Problems and Externalizing Problems, and a Total Problem Score Higher scores indicate more problems	Mean test-retest reliability for problem scales (Pearson's correlation), .82 Internal consistency (Cronbach's alpha): .71 to .95 Analyses of validity showed significant ( $p < .01$ ) discrimination between referred and non-referred adolescents	In this study, Total problems T-score was used as the measure of symptom load at follow-up. Cut-off was set at scores $\geq 60$ as borderline/clinical range, and $< 60$ as normal range, as recommended in the manual. Paper III	Achenbach, T.M., Rescorla L. Manual for the ASEBA school-age forms & profiles: An integrated system of multi-informant assessment: Burlington, VT University of Vermont, Research Center for Children, Youth & Families; 2001
Other	Measure of Chronic pain, Substance use, Negative life events and School dropout	13-19 years	Self-report questionnaire for adolescents	Different number of questions in the various domains	Psychometric properties of questionnaire are rated in the Young-HUNT3 study	Chronic pain and Substance use: Paper I Negative life events and School dropout: Paper II	The Young-HUNT3 study: <a href="https://www.ntnu.edu/hunt/young-hunt">https://www.ntnu.edu/hunt/young-hunt</a> <a href="https://www.ntnu.edu/hunt/data/que">https://www.ntnu.edu/hunt/data/que</a>









# Psychiatric morbidity, somatic comorbidity and substance use in an adolescent psychiatric population at 3-year follow-up

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## Abstract

Knowledge is scarce on the course of psychiatric disorders in adolescence. We aimed to assess changes in the frequency of psychiatric disorders, somatic disorders, pain, and substance use in a clinical psychiatric cohort from adolescence to young adulthood. This study is part of the Health Survey in Department of Children and Youth, St. Olavs Hospital, Norway. At age 13–18 years, 717 (43.5% of eligible) participated in the first study visit ( $T_1$ ) in 2009–2011, 549 were reassessed 3 years later with telephone interview ( $T_2$ ), and 464 had diagnostic evaluation at both time points. Data included: ICD-10 diagnoses ( $T_1$ ), DSM-IV diagnoses ( $T_2$ ), self-reported pain and substance use ( $T_1$  and  $T_2$ ). The overall rate of psychiatric disorders decreased ( $T_1$  vs.  $T_2$ : 94.8% vs. 72.2%,  $p < 0.001$ ); while, an increased rate of anxiety disorders was marked among girls (37.5% vs. 55.9%,  $p < 0.001$ ), with accompanying raised frequencies of psychiatric comorbidity (14.1% vs. 42.6%,  $p < 0.001$ ), somatic comorbidity (9.4% vs. 19.5%,  $p = 0.001$ ), chronic pain (31.6% vs. 49.4%,  $p < 0.001$ ), smoking, alcohol use and trying illicit drugs. Chronic pain, smoking and trying illicit drugs were associated with persisting psychiatric disorders, with highest risk differences for girls (RD = 25.4%,  $p = 0.002$ , RD = 15.6%,  $p = 0.008$ , RD = 18.0%,  $p = 0.001$ , respectively). Three out of four adolescents still had a psychiatric disorder after 3 years. Unlike boys, girls had an increasing rate of anxiety disorders and comorbidities. Chronic pain, smoking and trying illicit drugs were associated with persisting psychiatric disorders. Despite methodological limitations, these findings emphasize the importance of early targeted intervention for adolescents with psychiatric disorders.

**Keywords** Mental disorders · Adolescent · Pain · Comorbidity · Longitudinal study

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## Introduction

An increasing focus on mental disorders in children and adolescents has revealed large variations in prevalence between nations [1]. The worldwide prevalence of mental disorders in this age group was 13.4% in 2015 [2], with anxiety

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disorders as the most frequent disorder (6.5%). In Norway, the reported prevalence is lower; 8% met the criteria for a psychiatric disorder requiring treatment in 2009 [3, 4]. Still, 15–20% of children and adolescents aged 3–18 years had reduced function due to symptoms of mental disorders [3–5]. Diagnoses differ with age and gender. Before puberty, more boys than girls are diagnosed, and conduct disorder and attention deficit/hyperactivity disorder (ADHD) dominates; while after puberty, the diagnoses and gender predominance shift to anxiety, depression and eating disorders among girls [6, 7]. For both genders, emerging adulthood represents a particularly vulnerable time for the initiation of mental health problems, including substance use [6, 8], and adolescence is the time at which a high burden of disease emerges from mental disorders [9].

Comorbidity of psychiatric disorders is common in children and adolescents, and increases by age [10, 11]. Presence of co-occurring disorders is more marked in girls than in boys [10]. Among adults with psychiatric disorders, almost half have more than one disorder, and comorbidity continues to be more frequent in females [12]. Comorbid psychiatric disorders are challenging to assess and treat, especially in combination with co-existing somatic symptoms or disease [13]. Earlier research have found strong evidence for a relation between somatic symptoms and psychiatric disorders [14] and that psychiatric disorders of all types are associated with an increased risk of onset of a broad range of somatic conditions [15]. A systematic review demonstrated a strong positive association between chronic somatic disorders in adolescence and anxiety and depressive disorders [16]. A recent population-based Swedish study reported a high risk for concurrent somatic disorders in children with psychiatric disorders, across all ages and across many types of conditions [17].

Pain symptoms in adolescence involves an increased risk for mental distress in young adulthood [18, 19], and strong associations are reported between chronic pain and especially anxiety and depression [20]. Therefore, pain seems to be a common symptom and part of the complexity in many psychiatric disorders, especially in anxiety and depressive disorders. In the current sample of interest, when patients with psychiatric disorders were young adolescents, higher rates of chronic pain were found compared to the general adolescent population [21, 22]. In adults with psychiatric disorders, it is well known that chronic somatic conditions are frequent [23]. Still, knowledge is scarce on the longitudinal effect of psychiatric–somatic comorbidity from adolescence to adult age in a clinical psychiatric sample.

Co-existing substance use is another factor contributing to the complexity of mental disorders. Adolescent psychiatric patients have increased risk of substance use [24]. Harmful alcohol consumption combined with depression and anxiety is commonly observed [25, 26]. A recent population-based

survey linked with data from National Patient Registry in Norway, found that all investigated psychiatric diagnoses, except autism, were associated with some measure of hazardous alcohol/drug use, with highest odds among adolescents with trauma-related disorders, depression and conduct disorders [27].

Although having a psychiatric disorder in adolescence is a potent risk factor for having a psychiatric disorder in adulthood [28, 29], the frequency of psychiatric disorders is intuitively expected to decline in a clinical follow-up, due to treatment, individual maturation and other factors. However, knowledge is limited on the developmental course of psychiatric morbidity in interplay with co-occurring disorders and substance use in a clinical adolescent cohort. Such knowledge is highly wanted in clinical practice, as a necessary basis for intervention and specific treatment.

The objective of the present study was to examine the prevalence and associations of disorders in a clinical psychiatric cohort over a 3-year period from adolescence to young adulthood. The primary aim was to investigate any changes in the frequency of psychiatric disorders, comorbidities with other psychiatric or somatic disorders, chronic pain, and substance use, overall, by diagnostic groups, and separately for girls and boys. The secondary aim was to study if somatic disorders, chronic pain and substance use were associated with persisting psychiatric disorders, overall, by diagnostic groups, and separately for girls and boys. We hypothesized that the frequency of psychiatric disorders, i.e., anxiety, mood, ADHD and other psychiatric disorders (grouped) declined over the 3 years, and that continuity of a psychiatric disorder was associated with concurrent comorbid disorders, chronic pain and substance use at baseline. We further hypothesized that there would be a different pattern of morbidity for girls and boys.

## Methods

### Study design

The Health Survey in Department of Children and Youth, Division of Mental Health Care, St. Olavs hospital, Trondheim University Hospital, Norway (St. Olav CAP Survey), is a prospective longitudinal cohort study of a defined clinical population assessed at two time points. At time point 1 ( $T_1$ ), data were collected at inclusion in a cross-sectional study of adolescent patients; at time point 2 ( $T_2$ ) data were collected at a 3-year follow-up.

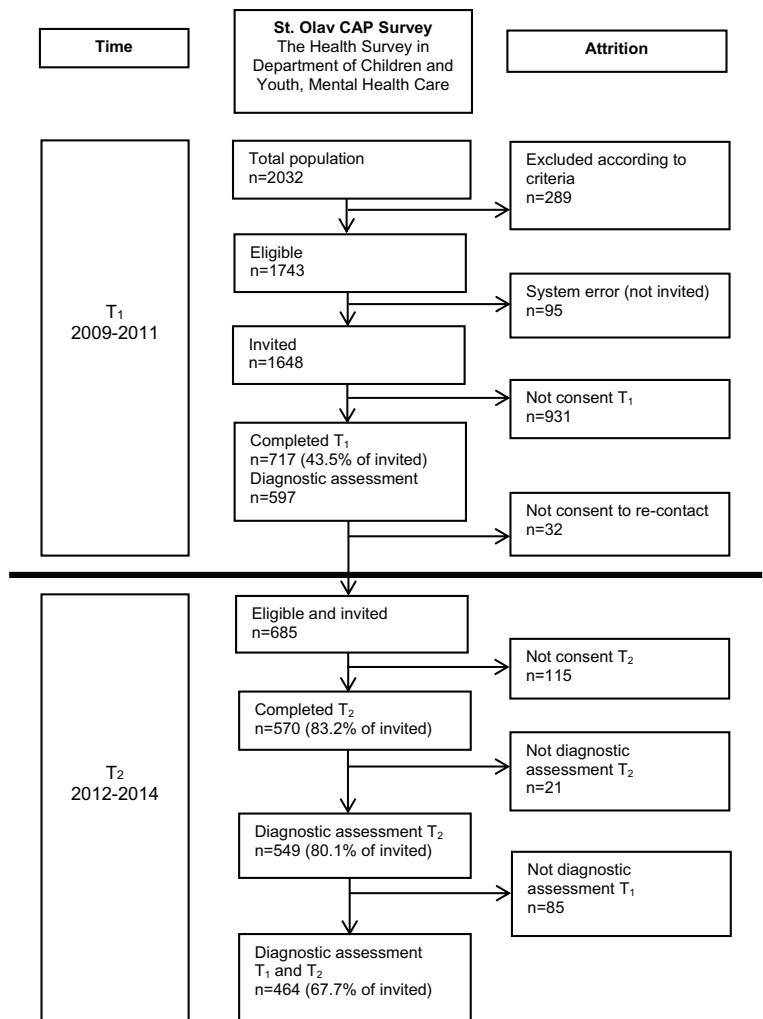
At  $T_1$  (2009–2011), all patients aged 13–18 years who visited the Department of Children and Youth (hereafter: CAP clinic) at least once over a 2-year period received both oral and written invitations at their first attendance during the study period. The exclusion criteria were difficulties in

answering the survey due to an unstable psychiatric state, low cognitive function, visual impairments, or insufficient language skills. Emergency patients were invited to take part once they entered a stable phase. The participants and their parents received standard application of services. They gave written informed consent to extract diagnostic data from clinical charts and respond to an electronic survey. At  $T_2$  (2012–2014), age 16–21 years, data were collected from the  $T_1$  enrolled sample and their parents, by an electronic survey and a diagnostic telephone interview performed by trained professionals.

### Participants

In the  $T_1$  study period, 2032 adolescent patients had at least one attendance at the CAP clinic. Figure 1 demonstrates the participant flow in each stage of the survey. At  $T_1$ ,  $n = 717$  participated (393 (54.8%) girls), of whom  $n = 597$  had a complete diagnostic assessment. At  $T_2$ , all  $T_1$  participants who previously consented to further inquiry were invited (eligible  $n = 685$ ), of whom 570 (83% of eligible) completed the follow-up questionnaire, and 549 (80%) completed the diagnostic interview (308 (56.1%) girls). The present study included participants with complete diagnostic assessment at both  $T_1$  and  $T_2$  ( $n = 464$ , 256 (55.2%) girls), with mean age

**Fig. 1** Flow-chart of the recruitment and attrition in the present study



at  $T_1$ : 15.7 (range 13.0–20.5), and at  $T_2$ : 18.7 (16.0–23.5) years (Table 1).

**Participants vs. non-participants**

To explore the representativeness of the study population at  $T_1$ , anonymous information about the total clinical population was collected from annual reports from the CAP clinic, 2009–2011. All adolescents in the study period ( $n=2032$ ) minus those excluded ( $n=289$ ) were defined as reference population ( $n=1743$ ). The main reason for referral, age and gender were similar between participants ( $n=717$ , 41.1%) and non-participants ( $n=1026$ , 58.9%) (data not shown). Participants were 0.27 years older: mean (SD) 15.7 (1.7) vs. 15.4 (2.0), and there were more girls among the participants: 393 (54.8%) vs. 509 (49.6%). Among those with complete diagnostic assessment at  $T_1$ , there were 464 participants and 133 non-participants at  $T_2$ . Attrition analyses are given in Supplementary Material (Tables S1, S2 and S3). Age, socio-economic status and frequencies of any psychiatric disorder were similar among participants and non-participants; while, the proportion of girls was higher among participants.

**Measures**

Psychiatric diagnoses at  $T_1$  were set in ordinary clinical practice according to the International Statistical Classification of Disease and Related Health Problems (ICD-10) multi-axial diagnostics (axes I–VI) [30]. The diagnostic process followed standardized procedures for assessment and diagnosis of common adolescent psychiatric disorders, requiring a thorough developmental history and interviews with the adolescents and their parents. For some participants, the semi-structured Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS) [31] was used, for others the Development And Well-Being Assessment (DAWBA) [32], and various rating scales suitable for the presenting problem. The diagnoses were set by a child and adolescent psychiatrist or a clinical psychologist based on all available clinical information, after consensus with other professionals from the multi-disciplinary team. The assessments were supplemented with somatic examination if indicated, and possible coexisting disorders were explored. At  $T_2$ , diagnoses were set using the K-SADS [31] according to the Diagnostic and Statistical Manual of Mental Disorders IV Text revision (DSM-IV-TR) [33]. The interviews were performed with the adolescents by telephone by trained interviewers, all with a graduate degree in medicine or psychology and experience in child and adolescent psychiatric assessment. They met regularly with a supervisor, an experienced child and adolescent psychiatrist, to assure the quality of the diagnostic assessment. All were blinded to  $T_1$  diagnoses. Inter-rater reliability was assessed using second

**Table 1** Age of participants in diagnostic groups at  $T_1$  and  $T_2$

	Any psychiatric disorder		Anxiety disorders		Mood disorders		ADHD		Other psychiatric disorders	
	$T_1$	$T_2$	$T_1$	$T_2$	$T_1$	$T_2$	$T_1$	$T_2$	$T_1$	$T_2$
Total ( $n=464$ )										
Age (years)	15.7	18.7	15.8	19.0	16.4	19.0	15.4	18.5	15.5	18.8
Mean (SD)	(1.7)	(1.7)	(1.7)	(1.6)	(1.6)	(1.5)	(1.5)	(1.7)	(1.7)	(1.6)
Girls ( $n=256$ )										
Age (years)	16.0	19.0	16.0	19.2	16.5	19.0	15.9	18.8	16.1	19.3
Mean (SD)	(1.7)	(1.7)	(1.6)	(1.6)	(1.5)	(1.5)	(1.4)	(1.9)	(1.7)	(1.6)
Boys ( $n=208$ )										
Age (years)	15.3	18.3	15.4	18.5	15.9	18.8	15.2	18.2	15.1	18.3
Mean (SD)	(1.6)	(1.6)	(1.6)	(1.6)	(1.7)	(1.6)	(1.8)	(1.5)	(1.6)	(1.6)

ratings for 28 of the taped telephone interviews. Because of weaknesses of kappa as measure of agreement [34], positive and negative agreement were used as measurement. Positive agreement, as defined by van de Vet et al., varied from 0.615 to 1.000 and, negative agreement varied from 0.884 to 1.000. Details are given in Supplementary Material (Tables S4 and S5).

In the present study, disorders were grouped into the following categories, based on ICD-10 diagnoses at  $T_1$  and DSM-IV diagnoses at  $T_2$ ; any psychiatric disorder, anxiety disorders (ICD-codes F40-F44, F48, F93/DSM-codes 300, 308, 309), mood disorders (ICD-codes F31-F34, F38, F39/DSM-codes 296, 300.4, 311), ADHD (ICD-code F90/DSM-code 314) and other (ICD-codes F10-F19, F20-F21, F28-F29, F50, F54, F59-F60, F84, F91-F92, F94-F95, F98/DSM-codes 291, 292, 295, 298, 299, 301, 303, 304, 305, 307, 312, 313, 316). As there were few participants in some diagnostic groups, for example autism and eating disorders, and especially when examining comorbidity, we chose to merge children with these diagnoses into one larger group of other psychiatric disorders for the purpose of this manuscript.

Somatic disorders at  $T_1$  were registered according to ICD-10 axis 4, set by the medical doctor based on anamnestic information, the entire medical records, including pediatrics, or by clinical investigation. All patients reporting somatic symptoms or disorders had an evaluation by a medical doctor. At  $T_2$ , somatic disorders were recorded as part of the K-SADS interview. Somatic comorbidity was defined as having a psychiatric disorder with a co-occurring somatic disorder requiring regular clinical follow-ups.

Chronic pain ( $T_1$  and  $T_2$ ) was defined as the pain not related to any known disease or injury, occurring at least once a week in the last 3 months. The test–retest reliability of questions of pain occurrence at least once a week for the last 3 months has shown to be good [20, 35]. As in previous studies, adolescents were asked to fill in a questionnaire and specify if they had experienced headaches, abdominal pain or musculoskeletal pain (e.g., pain in the neck, shoulder, upper and lower extremities, upper back, lower back/seat or chest), accompanied with an illustration of the different locations [20, 22]. Multisite pain was defined as having chronic pain in three locations or more [20, 22].

Substance use was registered by self-report as smoking, alcohol use and drug use. “Current smokers” included daily or occasional smokers ( $T_1$  and  $T_2$ ). “Current alcohol users” included participants, who answered “yes” to the following questions:  $T_1$ : “Do you sometimes drink alcohol presently?”, and  $T_2$ : “Have you drunk alcohol during the last four weeks?”. “Drug use” was indicated by answering “yes” to the question: “Have you ever tried hash, marijuana, or other illicit drugs?” ( $T_1$  and  $T_2$ ).

Socioeconomic status (SES) was measured at  $T_1$  by the mothers’ highest level of education, divided into eight categories: (1) less than 9-year primary school; (2) completed 9-year primary school; (3) 1 or 2 years in high school; (4) completed high school; (5) completed high school and 1-year education/training after high school; (6) academy/university for up to and including 4 years; (7) academy/university for 5 years or more; and (8) academy/university including PhD.

## Statistical analyses

The change in point prevalence from  $T_1$  to  $T_2$  was based on paired dichotomous data, with Newcombe confidence intervals and the McNemar asymptotic test, as recommended by Fagerland, Lydersen and Laake [36]. We used binary linear regression with psychiatric disorder at  $T_2$  as dependent variable and relevant variables at  $T_1$ , one at a time, to study their associations. Effects of age and SES as possible confounders were explored. We reported 95% confidence intervals (CI) where relevant, and two-sided  $p$  values  $< 0.05$  were considered statistically significant. Binary regression was performed in Stata 15, Newcombe CI and McNemars test were calculated in Excel, and the rest in SPSS 25.

## Ethics

Written informed consent was obtained from adolescents and parents prior to inclusion at  $T_1$ , and from the adolescents at  $T_2$ , according to study procedures. Study approval was given by the Regional committee for Medical and Health Research Ethics (reference numbers CAP survey  $T_1$ : 4.2008.1393,  $T_2$ : 2011/1435/REK Midt, and present study using  $T_1$  and  $T_2$  data: 2017/589/REK Midt). The Norwegian Social Science Data Services, The Data Protection Official for Research, gave permission to compare the main reason for referral, age and sex between participants and non-participants in connection with inclusion at baseline (reference number CAP survey: 19976).

## Results

### Psychiatric disorders and comorbidity

The overall rate of diagnoses decreased from 94.8% at  $T_1$  to 72.2% at  $T_2$ . The change [risk difference; RD = - 22.6%, CI (- 26.9, - 18.5),  $p < 0.001$ ] was present in both genders (Table 2). However, the frequency of anxiety disorders increased in the total sample [31.7% vs. 40.1%, RD = 8.4%, CI (2.7, 14.0),  $p = 0.004$ ], but among girls only [37.5% vs. 55.9%, RD = 18.4%, CI (10.1, 26.3),  $p < 0.001$ ]. Psychiatric comorbidity increased in any psychiatric disorder [28.0% vs. 36.4%, RD = 8.4%, CI (2.8, 13.9),  $p = 0.003$ ], but for

**Table 2** Changes in frequencies of psychiatric disorders and comorbid psychiatric disorders from  $T_1$  to  $T_2$

	Any psychiatric disorder			Anxiety disorders			Mood disorders			ADHD <sup>a</sup>			Other psychiatric disorders		
	$T_1$	$T_2$	RD <sup>b</sup> % (95% CI) <i>p</i> value	$T_1$	$T_2$	RD <sup>b</sup> % (95% CI) <i>p</i> value	$T_1$	$T_2$	RD <sup>b</sup> % (95% CI) <i>p</i> value	$T_1$	$T_2$	RD <sup>b</sup> % (95% CI) <i>p</i> value	$T_1$	$T_2$	RD <sup>b</sup> % (95% CI) <i>p</i> value
<b>Total (<math>n=464</math>)</b>															
<b>Psychiatric disorder</b>															
$n/n_{total}^c$ (%)	440/464 (94.8)	335/464 (72.2)	-22.6 (-26.9, -18.5) <0.001	147/464 (31.7)	186/464 (40.1)	8.4 (2.7, 14.0) 0.004	99/464 (21.3)	77/464 (16.6)	-4.7 (-9.1, -0.4) 0.031	204/463 (44.0)	192/463 (41.5)	-2.5 (-6.8, 1.7) 0.230	120/464 (25.9)	107/464 (23.1)	-2.8 (-7.2, 1.6) 0.209
<b>Comorbid psychiatric disorder</b>															
$n/n_{disorder}^d$ (%)	130/440 (29.5)	169/335 (50.5)		59/147 (40.1)	136/186 (73.1)		45/99 (45.5)	73/77 (94.8)		75/204 (36.8)	100/192 (52.1)		70/120 (58.3)	86/107 (80.4)	
$n/n_{total}^e$ (%)	130/464 (28.0)	169/464 (36.4)	8.4 (2.8, 13.9) 0.003	59/464 (12.7)	136/464 (29.3)	16.6 (11.6, 21.1) <0.001	45/464 (9.7)	73/464 (15.7)	6.0 (2.0, 10.1) 0.004	75/463 (16.2)	100/463 (21.6)	5.4 (1.0, 9.8) 0.020	70/464 (15.1)	86/464 (18.5)	3.4 (-0.7, 7.6) 0.100
<b>Girls (<math>n=256</math>)</b>															
<b>Psychiatric disorder</b>															
$n/n_{total}$ (%)	245/256 (95.7)	191/256 (74.6)	-21.1 (-26.7, -15.8) <0.001	96/256 (37.5)	143/256 (55.9)	18.4 (10.1, 26.3) <0.001	82/256 (32.0)	66/256 (25.8)	-6.2 (-13.1, 0.7) 0.077	83/255 (32.6)	91/255 (35.7)	3.1 (-2.1, 8.4) 0.238	52/256 (20.3)	50/256 (19.5)	-0.8 (-6.6, 5.0) 0.789
<b>Comorbid psychiatric disorder</b>															
$n/n_{disorder}$ (%)	68/245 (27.8)	116/191 (60.7)		36/96 (37.5)	109/143 (76.2)		38/82 (46.3)	62/66 (93.9)		29/83 (34.9)	59/91 (64.8)		23/52 (44.2)	45/50 (90.0)	
$n/n_{total}$ (%)	68/256 (26.6)	116/256 (45.3)	18.7 (10.5, 26.6) <0.001	36/256 (14.1)	109/256 (42.6)	28.5 (20.8, 35.8) <0.001	38/256 (14.8)	62/256 (24.2)	9.4 (2.8, 15.9) 0.005	29/255 (11.4)	59/255 (23.1)	11.7 (5.9, 17.7) <0.001	23/256 (9.0)	45/256 (17.6)	8.6 (3.2, 14.1) 0.002
<b>Boys (<math>n=208</math>)</b>															
<b>Psychiatric disorder</b>															
$n/n_{total}$ (%)	195/208 (93.8)	144/208 (69.2)	-24.6 (-31.1, -18.0) <0.001	51/208 (24.5)	43/208 (20.7)	-3.8 (-11.2, 3.5) 0.302	17/208 (8.2)	11/208 (5.3)	-2.9 (-7.7, 1.8) 0.201	121/208 (58.2)	101/208 (48.6)	-9.6 (-16.3, -2.7) 0.007	68/208 (32.7)	57/208 (27.4)	-5.3 (-12.0, 1.5) 0.124

**Table 2** (continued)

	Any psychiatric disorder			Anxiety disorders			Mood disorders			ADHD <sup>a</sup>			Other psychiatric disorders			
	<i>T</i> <sub>1</sub>	<i>T</i> <sub>2</sub>	RD <sup>b</sup> % (95% CI) <i>p</i> value	<i>T</i> <sub>1</sub>	<i>T</i> <sub>2</sub>	RD % (95% CI) <i>p</i> value	<i>T</i> <sub>1</sub>	<i>T</i> <sub>2</sub>	RD % (95% CI) <i>p</i> value	<i>T</i> <sub>1</sub>	<i>T</i> <sub>2</sub>	RD % (95% CI) <i>p</i> value	<i>T</i> <sub>1</sub>	<i>T</i> <sub>2</sub>	RD % (95% CI) <i>p</i> value	
Comorbid psychiatric disorder																
<i>n</i> / <i>n</i> <sub>disorder</sub> (%)	62/195	53/144		23/51	27/43		7/17	11/11		46/121	41/101		47/68	41/57		
<i>n</i> / <i>n</i> <sub>total</sub> (%)	(31.8)	(36.8)		(45.1)	(62.8)		(41.2)	(100)		(38.0)	(40.6)		(69.1)	(71.9)		
	62/208	53/208	- 4.3	23/208	27/208	1.9 (- 3.6, 7.5)	7/208	11/208	1.9 (- 2.3, 6.3)	46/208	41/208	- 2.4	47/208	41/208	- 2.9	
	(29.8)	(25.5)	(- 11.4, 2.8)	(11.1)	(13.0)	0.480	(3.4)	(5.3)	0.346	(22.1)	(19.7)	(- 9.0, 4.1)	(22.6)	(19.7)	(- 9.2, 3.5)	
			0.233													0.366

Newcombe confidence intervals and McNemar asymptotic *p* values are based on paired data displayed in Supplemental Material Table S6

Psychiatric disorder includes both primary and additional diagnoses, based on only complete case (diagnostic assessment at both *T*<sub>1</sub> and *T*<sub>2</sub>)

Comorbid psychiatric disorder includes all patients with more than one psychiatric disorder

<sup>a</sup>In ADHD group there is 1 missing among girls

<sup>b</sup>RD is risk difference, the difference between the proportions of patients with psychiatric disorder or comorbid psychiatric disorder at *T*<sub>2</sub> compared with *T*<sub>1</sub>

<sup>c</sup>*n*/*n*<sub>total</sub> means that there are (*n*) numbers of patients with psychiatric disorder among the total sample of patients

<sup>d</sup>*n*/*n*<sub>disorder</sub> means that there are (*n*) numbers of patients with comorbid psychiatric disorder among the patients with the actual psychiatric disorder

<sup>e</sup>*n*/*n*<sub>total</sub> means that there are (*n*) numbers of patients with comorbid psychiatric disorder among the total sample of patients



girls only [26.6% vs. 45.3%, RD = 18.7%, CI (10.5, 26.6),  $p < 0.001$ ]. The increase in psychiatric comorbidity in the total sample was statistically significant in anxiety disorders, mood disorders and ADHD, and in all diagnostic subgroups for girls, but not for boys (Table 2).

### Somatic comorbidity and chronic pain

Somatic comorbidity increased in frequency in the anxiety disorder group [7.1% vs. 12.7%, RD = 5.6%, CI (2.0, 9.3),  $p = 0.003$ ], but only among girls [9.4% vs. 19.5%, RD = 10.1%, CI (4.3, 16.1),  $p = 0.001$ ] (Table 3). For other psychiatric disorders, somatic comorbidity remained unchanged in both genders. The prevalence of chronic pain in the cohort was high, but decreased overall in the total sample [65.8% vs. 49.3%, RD = -16.5%, CI (-21.0, -11.0),  $p < 0.001$ ], and for both girls and boys. However, chronic pain increased among patients with anxiety disorders [23.3% vs. 31.8%, RD = 8.5%, CI (3.1, 13.7),  $p = 0.002$ ], but the increase was found only among girls [31.6% vs. 49.4%, RD = 17.9%, CI (9.5, 25.4),  $p < 0.001$ ]. At  $T_2$ , girls with anxiety disorders had a higher rate of chronic pain than boys with these disorders (88.7% vs. 48.8%), and also a higher rate of multisite pain (66.2% vs. 20.9%). The diagnostic group with highest frequencies of chronic pain was mood disorders for both girls (96.9%) and boys (72.7%). The frequencies of multisite pain were also highest in this diagnostic group.

### Substance use

The amount of substance use changed during the 3-year follow-up (Table 4). There was a non-significant reduction in smoking [30.3% vs. 19.6%, RD = -10.6%, CI (-10.4, 0.5),  $p = 0.074$ ] in the total sample, but smoking increased for anxiety disorders [RD = 4.5%, CI (2.0, 9.2),  $p = 0.002$ ], and only among girls. Alcohol use increased for anxiety disorders and ADHD in the total sample [RD = 10.5%, CI (6.3, 16.3),  $p < 0.001$ , and RD = 7.0%, CI (3.6, 13.1),  $p < 0.001$ , respectively], and among girls with these disorders. Trying illicit drugs increased overall, in both genders, and in all diagnostic subgroups for girls, with the highest increase in the anxiety group [4.7% vs. 22.4%, RD = 17.7%, CI (12.8, 23.7),  $p < 0.001$ ]. Among boys, an increase was seen in the ADHD group [6.3% vs. 15.1%, RD = 8.8%, CI (5.6, 15.1),  $p < 0.001$ ] and in the group of other psychiatric disorders.

### Analysis of associations

Binary linear regression including age or SES as covariate showed no association with persistence of psychiatric disorder, i.e., no confounding effects were found either in the total sample or separately for each gender (Table 5).

There was an association between having chronic pain at  $T_1$  and persisting psychiatric disorder for the total sample [RD = 17.2%, CI (7.9, 26.6),  $p < 0.001$ ], and most evident for girls [RD = 25.4%, CI (9.6, 41.2),  $p = 0.002$ ] (Table 4). Associations were also found between smoking and trying illicit drugs and persisting psychiatric disorders among girls [RD = 15.6%, CI (4.1, 27.0),  $p = 0.008$ , and RD = 18.0%, CI (7.3, 28.6),  $p = 0.001$ , respectively].

## Discussion

This study is one of the few surveys studying the development of psychiatric disorders and comorbidity over time, following a general clinical psychiatric population of adolescents who received standard clinical care. While the general psychiatric morbidity decreased in the course of 3 years, including mood disorders, the rate of anxiety disorders increased, and having more than one psychiatric disorder became more frequent. Altogether, three out of four still had a psychiatric disorder. The most prominent finding was the marked increase of anxiety disorders among girls, accompanied by more psychiatric comorbidity, somatic comorbidity and chronic pain; whereas boys had decreased morbidity overall. Substance use was prevalent among girls with anxiety disorders, while trying illicit drugs clearly involved the most marked increase in both genders. Chronic pain, smoking and trying illicit drugs at the first visit were associated with persisting psychiatric disorders, with highest risk difference for girls.

The reasons for the high rates of persisting disorders may be diverse, both depending on the treatment given and the general vulnerability in the adolescents in this clinical population, who have a high disease burden. In a study of Copeland et al., investigating the cumulative prevalence of psychiatric disorders in young adulthood among 1420 participants assessed between ages 9 and 21, they found that 61.1% met DSM criteria for a well-specified psychiatric disorder by 21 years of age, indicating that many struggle with mental health problems in young adulthood [37]. There is an increase in overall rates of psychiatric disorders in the transition from adolescence to adulthood [7]. Common psychiatric disorders in adolescence are often forerunners and strong predictors of similar disorders in young adulthood, and most young adults with episodes of a psychiatric disorder have had episodes during their teenage years [7, 8, 28, 29], which is in accordance with the findings by Ranøyen et al. in the CAP Survey [38]. Kim-Cohen et al. found that among those who met criteria for a major DSM diagnosis at 26 years, half had a disorder at age 11–15 years, and three out of four before 18 years [39]. The higher frequency among girls overall, and especially in girls with anxiety disorders, is comparable with the earlier research [11, 40]. Results from the



**Table 3** Changes in frequencies of psychiatric disorders with comorbid somatic disorders and pain from  $T_1$  to  $T_2$

	Any psychiatric disorder			Anxiety disorders			Mood disorders			ADHD			Other psychiatric disorders		
	$T_1$	$T_2$	RD <sup>a</sup> % (95% CI) <i>p</i> value	$T_1$	$T_2$	RD % (95% CI) <i>p</i> value	$T_1$	$T_2$	RD % (95% CI) <i>p</i> value	$T_1$	$T_2$	RD % (95% CI) <i>p</i> value	$T_1$	$T_2$	RD % (95% CI) <i>p</i> value
<b>Total (<math>n=464</math>)</b>															
<b>Comorbid somatic disorder</b>															
$n/n_{\text{disorder}}$	81/440	85/335		33/147	59/186		21/99	24/77		31/203	46/192		20/120	27/107	
$n/n_{\text{total}}$	(18.4)	(25.4)		(22.5)	(31.7)		(21.2)	(31.2)		(15.3)	(24.0)		(16.7)	(25.2)	
	81/464	85/464	0.8 (-3.8, 5.5) 0.713	33/464	59/464	5.6 (2.0, 9.3) 0.003	21/464	24/464	0.7 (-2.0, 3.3) 0.612	31/463	46/463	3.2 (-0.2, 6.7) 0.059	20/464	27/464	1.5 (-1.3, 4.4) 0.274
<b>Chronic pain<sup>d</sup></b>															
$n/n_{\text{disorder}}$ (%)	304/438	225/330		108/147	147/185		79/99	71/76		135/202	122/188		74/120	70/106	
$n/n_{\text{total}}$ (%)	(69.4)	(68.2)		(73.5)	(79.5)		(79.8)	(93.4)		(66.8)	(64.9)		(61.7)	(66.0)	
	304/462	225/456	-16.5 (-21.0, -11.0) <0.001	108/463	147/463	8.5 (3.1, 13.7) 0.002	79/464	71/463	-1.7 (-5.8, 2.3) 0.400	135/462	122/461	-2.7 (-7.2, 2.0) 0.261	74/464	70/463	-0.9 (-4.6, 3.3) 0.745
<b>Multisite pain<sup>e</sup></b>															
$n/n_{\text{disorder}}$ (%)	171/435	141/329		68/145	103/185		56/99	51/76		71/201	67/187		39/120	45/106	
$n/n_{\text{total}}$ (%)	(39.3)	(42.9)		(46.9)	(55.7)		(56.6)	(67.1)		(35.3)	(35.8)		(32.5)	(42.5)	
	171/459	141/455	-6.3 (-13.3, -2.1) 0.008	68/462	103/463	7.6 (3.1, 12.1) 0.001	56/464	51/463	-1.1 (-4.7, 2.5) 0.553	71/461	67/462	-0.9 (-4.5, 3.1) 0.732	39/464	45/463	1.3 (-1.7, 4.3) 0.386
<b>Girls (<math>n=256</math>)</b>															
<b>Comorbid somatic disorder</b>															
$n/n_{\text{disorder}}$ (%)	53/245	57/191		24/96	50/143		17/82	22/66		14/83	25/91		11/52	18/50	
$n/n_{\text{total}}$ (%)	(21.6)	(29.8)		(25.0)	(35.0)		(20.7)	(33.3)		(16.9)	(27.5)		(21.2)	(36.0)	
	53/256	57/256	1.6 (-5.1, 8.2) 0.642	24/256	50/256	10.1 (4.3, 16.1) 0.001	17/256	22/256	2.0 (-2.3, 6.3) 0.353	14/255	25/255	4.3 (-0.2, 9.0) 0.056	11/256	18/256	2.7 (-1.1, 6.8) 0.144
<b>Chronic pain</b>															
$n/n_{\text{disorder}}$ (%)	202/245	158/189		81/96	126/142		69/82	63/65		69/83	74/89		42/52	41/50	
$n/n_{\text{total}}$ (%)	(82.5)	(83.6)		(84.4)	(88.7)		(84.2)	(96.9)		(83.1)	(83.2)		(80.8)	(82.0)	
	202/256	158/254	-16.7 (-46.8, -21.5) <0.001	81/256	126/255	17.8 (9.5, 25.4) <0.001	69/256	63/255	-2.3 (-9.0, 4.3) 0.486	69/256	74/255	2.0 (-3.4, 7.3) 0.466	42/256	41/256	-0.4 (-5.9, 5.1) 0.886
<b>Multisite pain</b>															

**Table 3** (continued)

		Any psychiatric disorder			Anxiety disorders			Mood disorders			ADHD			Other psychiatric disorders		
$T_1$	$T_2$	RD* % (95% CI)	$T_1$	$T_2$	RD % (95% CI)	$T_1$	$T_2$	RD % (95% CI)	$T_1$	$T_2$	RD % (95% CI)	$T_1$	$T_2$	RD % (95% CI)	$p$ value	
$n/n_{\text{total}}$ (%)	$n/n_{\text{total}}$ (%)	$p$ value	$n/n_{\text{total}}$ (%)	$n/n_{\text{total}}$ (%)	$p$ value	$n/n_{\text{total}}$ (%)	$n/n_{\text{total}}$ (%)	$p$ value	$n/n_{\text{total}}$ (%)	$n/n_{\text{total}}$ (%)	$p$ value	$n/n_{\text{total}}$ (%)	$n/n_{\text{total}}$ (%)	$p$ value		
131/243 (53.9)	114/189 (60.3)		56/94 (59.6)	94/142 (66.2)		53/82 (64.6)	47/65 (72.3)		46/83 (55.4)	49/89 (55.1)		23/52 (44.2)	34/50 (68.0)			
131/254 (51.6)	114/254 (44.9)	-6.7 (-17.6, 0.8)	56/254 (22.1)	94/255 (36.9)	<0.001	53/256 (20.7)	47/255 (18.4)	14.8 (7.7, 22.1)	46/256 (18.0)	49/255 (19.2)	-2.3 (-8.6, 3.9)	23/256 (9.0)	34/256 (13.3)	4.3 (-0.2, 8.9)	0.055	
Boys ( $n = 208$ )																
Comorbid somatic disorder																
28/195 (14.4)	28/144 (19.4)		9/51 (17.6)	9/43 (20.9)		4/17 (23.5)	2/11 (18.2)		17/121 (14.0)	21/101 (20.8)		9/68 (13.2)	9/57 (15.8)			
28/208 (13.5)	28/208 (13.5)	0 (-6.4, 6.4)	9/208 (4.3)	9/208 (4.3)	1	4/208 (1.9)	2/208 (1.0)	0 (-4.0, 4.0)	17/208 (8.2)	21/208 (10.1)	-0.9 (-4.0, 1.8)	9/208 (4.3)	9/208 (4.3)	0 (-4.3, 4.3)	1	
Chronic pain																
102/193 (52.9)	67/141 (47.5)		27/51 (52.9)	21/43 (48.8)		10/17 (58.8)	8/11 (72.7)		66/119 (55.5)	48/99 (48.5)		32/68 (47.1)	29/56 (51.8)			
102/206 (49.5)	67/202 (33.2)	-16.3 (-29.0, -9.3)	27/208 (13.0)	21/208 (10.1)	0.355	10/208 (4.8)	8/208 (3.9)	-2.9 (-9.1, 3.3)	66/206 (32.0)	48/206 (23.3)	-0.9 (-5.2, 3.2)	32/208 (15.4)	29/207 (14.0)	-1.4 (-6.8, 4.9)	0.739	
Multisite pain																
40/192 (20.8)	27/140 (19.3)		12/51 (23.5)	9/43 (20.9)		3/17 (17.7)	4/11 (36.4)		25/118 (21.2)	18/98 (18.4)		16/68 (23.5)	11/56 (19.6)			
40/205 (19.5)	27/201 (13.4)	-6.1 (-7.4, -0.4)	12/208 (5.8)	9/208 (4.3)	0.029	3/208 (1.4)	4/208 (1.9)	-1.5 (-6.0, 3.0)	25/205 (12.2)	18/207 (8.7)	0.5 (-2.5, 3.6)	16/208 (7.7)	11/207 (5.3)	-2.4 (-6.6, 1.5)	0.197	

Newcombe confidence intervals and McNemar asymptotic  $p$  values are based on paired data displayed in Supplementary Material Table S7

Psychiatric disorder includes both primary and additional diagnoses, based on only complete case (diagnostic assessment at both  $T_1$  and  $T_2$ )

Comorbid somatic disorder includes all patients with somatic disorders that require regular controls

\*RD is risk difference, the difference between the proportions of patients with psychiatric disorder or comorbid psychiatric disorder at  $T_2$  compared with  $T_1$

<sup>b</sup> $n/n_{\text{disorder}}$  means that there are ( $n$ ) numbers of patients with comorbid somatic disorder among the patients with the actual psychiatric disorder

<sup>c</sup> $n/n_{\text{total}}$  means that there are ( $n$ ) numbers of patients with comorbid somatic disorder among the total sample of patients

<sup>d</sup>Chronic pain was defined as pain occurring at least once a week in the last 3 months, not related to any known disease or injury

<sup>e</sup>Multisite pain was defined as having chronic pain in three locations or more

**Table 4** Changes in frequencies of psychiatric disorders with comorbid substance use from  $T_1$  to  $T_2$

	Any psychiatric disorder			Anxiety disorders			Mood disorders			ADHD			Other psychiatric disorders		
	$T_1$	$T_2$	RD <sup>a</sup> % (95% CI) <i>p</i> value	$T_1$	$T_2$	RD % (95% CI) <i>p</i> value	$T_1$	$T_2$	RD % (95% CI) <i>p</i> value	$T_1$	$T_2$	RD % (95% CI) <i>p</i> value	$T_1$	$T_2$	RD % (95% CI) <i>p</i> value
<b>Total (<math>n=464</math>)</b>															
Smoking <sup>b</sup>	99/304	90/330		29/97	53/185		30/75	29/76		46/147	45/188		25/76	35/106	
$n/n_{\text{disorder}}$ <sup>c</sup>	(32.6)	(27.3)		(29.9)	(28.7)		(40.0)	(38.2)		(31.3)	(23.9)		(32.9)	(33.0)	
$n/n_{\text{total}}$ <sup>d</sup>	99/328	90/459	- 10.6 (- 10.4, 0.5)	29/414	53/463	4.5 (2.0, 9.2)	30/440	29/463	- 0.5 (- 3.0, 2.6)	46/407	45/460	- 1.5 (- 4.4, 2.9)	25/420	35/463	1.6 (- 1.2, 4.7)
(%)	(30.2)	(19.6)	0.074	(7.0)	(11.5)	0.002	(6.8)	(6.3)	0.882	(11.3)	(9.8)	0.680	(6.0)	(7.6)	0.228
Alcohol use <sup>e</sup>	217/440	207/321		71/147	118/180		65/99	46/75		91/204	121/183		58/120	63/102	
$n/n_{\text{disorder}}$ <sup>c</sup>	(49.3)	(64.5)		(48.3)	(65.6)		(65.7)	(61.3)		(44.6)	(66.1)		(48.3)	(61.8)	
$n/n_{\text{total}}$ <sup>d</sup>	217/464	207/450	- 0.8 (- 8.1, 6.9)	71/464	118/458	10.5 (6.3, 16.3)	65/464	46/462	- 4.0 (- 7.8, 0.3)	91/464	121/455	7.0 (3.6, 13.1)	58/464	63/459	1.2 (- 2.6, 5.1)
(%)	(46.8)	(46.0)	0.875	(15.3)	(25.8)	<0.001	(14.0)	(10.0)	0.033	(19.6)	(26.6)	<0.001	(12.5)	(13.7)	0.518
Drug use <sup>f</sup>	61/437	113/329		18/147	69/185		18/99	35/76		33/201	69/187		15/120	45/105	
$n/n_{\text{disorder}}$ <sup>c</sup>	(14.0)	(34.4)		(12.2)	(37.3)		(18.2)	(46.1)		(16.4)	(36.9)		(12.5)	(42.9)	
$n/n_{\text{total}}$ <sup>d</sup>	61/461	113/458	11.5 (8.3, 16.5)	18/464	69/463	11.0 (7.8, 14.7)	18/464	35/463	3.7 (0.8, 6.6)	33/461	69/459	7.8 (5.1, 11.6)	15/464	45/462	6.5 (3.6, 9.6)
(%)	(13.2)	(24.7)	<0.001	(3.9)	(14.9)	<0.001	(3.9)	(7.6)	0.011	(7.2)	(15.0)	<0.001	(3.2)	(9.7)	<0.001
<b>Girls (<math>n=256</math>)</b>															
Smoking	66/178	56/189		23/66	44/142		25/65	24/65		26/63	20/89		14/39	20/50	
$n/n_{\text{disorder}}$ <sup>c</sup>	(37.1)	(29.6)		(34.9)	(31.0)		(38.5)	(36.9)		(41.3)	(22.5)		(35.9)	(40.0)	
$n/n_{\text{total}}$ <sup>d</sup>	66/189	56/254	- 12.8 (- 14.8, 0.6)	23/226	44/255	7.1 (3.6, 14.9)	25/239	24/255	- 1.1 (- 5.2, 4.4)	26/236	20/254	- 3.1 (- 8.0, 1.1)	14/243	20/256	2.0 (- 1.8, 5.6)
(%)	(34.9)	(22.1)	0.069	(10.2)	(17.3)	0.001	(10.5)	(9.4)	0.873	(11.0)	(7.9)	0.131	(5.8)	(7.8)	0.297
Alcohol use	140/245	130/187		55/96	97/140		57/82	42/64		41/83	61/88		34/52	39/50	
$n/n_{\text{disorder}}$ <sup>c</sup>	(57.1)	(69.5)		(57.3)	(69.3)		(69.5)	(65.6)		(49.4)	(69.3)		(65.4)	(78.0)	
$n/n_{\text{total}}$ <sup>d</sup>	140/256	130/252	- 3.1 (- 15.5, 6.4)	55/256	97/253	16.8 (10.7, 26.7)	57/256	42/254	- 5.8 (- 12.4, 0.6)	41/256	61/253	8.1 (3.3, 15.1)	34/256	39/256	1.9 (- 3.5, 7.4)
(%)	(54.7)	(51.6)	0.414	(21.5)	(38.3)	<0.001	(22.3)	(16.5)	0.071	(16.0)	(24.1)	0.002	(13.3)	(15.2)	0.484

**Table 4** (continued)

	Any psychiatric disorder			Anxiety disorders			Mood disorders			ADHD			Other psychiatric disorders		
	$T_1$	$T_2$	RD <sup>a</sup> % (95% CI) <i>p</i> value	$T_1$	$T_2$	RD % (95% CI) <i>p</i> value	$T_1$	$T_2$	RD % (95% CI) <i>p</i> value	$T_1$	$T_2$	RD % (95% CI) <i>p</i> value	$T_1$	$T_2$	RD % (95% CI) <i>p</i> value
Drug use $n/n_{\text{disorder}}$ (%)	37/244 (15.2)	73/189 (38.6)		12/96 (12.5)	57/142 (40.1)		15/82 (18.3)	30/65 (46.2)		20/82 (24.4)	38/89 (42.7)		8/52 (15.4)	29/50 (58.0)	
$n/n_{\text{total}}$ (%)	37/255 (14.5)	73/254 (28.7)	14.2 (9.7, 21.7) <0.001	12/256 (4.7)	57/255 (22.4)	17.7 (12.8, 23.7) <0.001	15/256 (5.9)	30/255 (11.8)	5.9 (1.0, 10.6) 0.016	20/255 (7.8)	38/254 (15.0)	7.2 (2.5, 11.8) 0.002	8/256 (3.1)	29/256 (11.3)	8.2 (3.6, 10.9) <0.001
<b>Boys (<math>n = 208</math>)</b>															
Smoking $n/n_{\text{disorder}}$ (%)	33/126 (26.2)	34/141 (24.1)		6/31 (19.4)	9/43 (20.9)		5/10 (50.0)	5/11 (45.5)		20/84 (23.8)	25/99 (25.3)		11/37 (29.7)	15/56 (26.8)	
$n/n_{\text{total}}$ (%)	33/138 (23.9)	34/205 (16.6)	- 7.3 (-10.1, -5.7) 0.578	6/177 (3.4)	9/208 (4.3)	0.9 (-3.3, 5.5) 0.593	5/201 (2.5)	5/208 (2.4)	- 0.1 (-2.6, 2.6) 1	20/171 (11.7)	25/206 (12.1)	0.4 (-3.1, 9.3) 0.317	11/177 (6.2)	15/207 (7.3)	1.1 (-3.4, 6.6) 0.513
Alcohol use $n/n_{\text{disorder}}$ (%)	77/195 (39.5)	77/134 (57.5)		16/51 (31.4)	21/40 (52.5)		8/17 (47.1)	4/11 (36.4)		50/121 (41.3)	60/95 (63.2)		24/68 (35.3)	24/52 (46.2)	
$n/n_{\text{total}}$ (%)	77/208 (37.0)	77/198 (38.9)	1.9 (-6.2, 13.7) 0.460	16/208 (7.7)	21/205 (10.2)	2.5 (-2.6, 8.6) 0.289	8/208 (3.9)	4/208 (1.9)	- 2.0 (-5.3, 1.3) 0.206	50/208 (24.0)	60/202 (29.7)	5.7 (-0.6, 15.3) 0.069	24/208 (11.5)	24/203 (11.8)	0.3 (-5.5, 6.6) 0.866
Drug use $n/n_{\text{disorder}}$ (%)	24/193 (12.4)	40/140 (28.6)		6/51 (11.8)	12/43 (27.9)		3/17 (17.7)	5/11 (45.5)		13/119 (10.9)	31/98 (31.6)		7/68 (10.3)	16/55 (29.1)	
$n/n_{\text{total}}$ (%)	24/206 (11.7)	40/204 (19.6)	7.9 (3.4, 15.2) 0.002	6/208 (2.9)	12/208 (5.8)	2.9 (-0.8, 7.0) 0.109	3/208 (1.4)	5/208 (2.4)	1.0 (-1.8, 4.0) 0.414	13/206 (6.3)	31/205 (15.1)	8.8 (5.6, 15.1) <0.001	7/208 (3.4)	16/206 (7.8)	4.4 (0.2, 9.0) 0.039

Newcombe confidence intervals and McNemar asymptotic *p* values are based on paired data displayed in Supplementary Material Table S8

Psychiatric disorder includes both primary and additional diagnoses, based on only complete cases (diagnostic assessment at both  $T_1$  and  $T_2$ )

<sup>a</sup>RD is risk difference, the difference between the proportions of patients with psychiatric disorder and comorbid substance use at  $T_2$  compared with  $T_1$

<sup>b</sup>Smoking included daily or occasional smokers ( $T_1$  and  $T_2$ )

<sup>c</sup> $n/n_{\text{disorder}}$  means that there are (*n*) numbers of patients with comorbid substance use among the patients with the actual psychiatric disorder

<sup>d</sup> $n/n_{\text{total}}$  means that there are (*n*) numbers of patients with comorbid substance use among the total sample of patients

<sup>e</sup>Alcohol use was indicated by answering “yes” to the following questions:  $T_1$ : “Do you sometimes drink alcohol presently?”, and  $T_2$ : “Have you drunk alcohol during the last four weeks?”

<sup>f</sup>Drug use was indicated by answering “yes” to the question: “Have you ever tried hash, marijuana, or other illicit drugs?” ( $T_1$  and  $T_2$ )

**Table 5** Binary linear regression with psychiatric disorder at  $T_2$  as dependent variable, and the listed covariates one at a time

Co-variable at $T_1$	<i>n</i>	Any psychiatric disorder $T_2$					
		Co-variable $T_1$ NO <i>n</i> (%)	Co-variable $T_1$ YES <i>n</i> (%)	RD <sup>a</sup> %	95% CI for RD		<i>p</i> value
					Lower	Upper	
Total sample	440						
Chronic pain	438	84/134 (62.7) <sup>b</sup>	243/304 (79.9)	17.2	7.9	26.6	<0.001
Any somatic disorder	440	269/359 (74.9)	59/81 (72.8)	– 2.1	– 12.8	8.6	0.701
Smoking	304	151/205 (73.7)	84/99 (84.8)	11.2	1.9	20.5	0.018
Alcohol use	440	160/224 (71.4)	168/216 (77.8)	6.3	– 1.8	14.5	0.125
Drug use	437	272/376 (72.3)	54/61 (88.5)	16.2	7.0	25.4	0.001
Age	440			0.105 <sup>c</sup>	– 2.39	2.60	0.934
SES	326			0.012 <sup>d</sup>	– 2.82	2.80	0.993
Girls	245						
Chronic pain	245	24/43 (55.8)	164/202 (81.2)	25.4	9.6	41.2	0.002
Any somatic disorder	245	149/192 (77.6)	39/53 (73.6)	– 4.0	– 17.3	9.3	0.553
Smoking	178	81/112 (72.3)	58/66 (87.9)	15.6	4.1	27.0	0.008
Alcohol use	245	78/105 (74.3)	110/140 (78.6)	4.3	– 6.5	15.1	0.437
Drug use	244	153/207 (73.9)	34/37 (91.9)	18.0	7.3	28.6	0.001
Age	245			0.200	– 3.21	3.61	0.908
SES	177			0.797	– 4.58	2.98	0.680
Boys	195						
Chronic pain	193	60/91 (65.9)	79/102 (77.5)	11.5	– 1.2	24.2	0.076
Any somatic disorder	195	120/167 (71.9)	20/28 (71.4)	– 0.4	– 18.5	17.7	0.963
Smoking	126	70/93 (75.3)	26/33 (78.8)	3.5	– 13.0	20.1	0.677
Alcohol use	195	82/119 (68.9)	58/76 (76.3)	7.4	– 5.3	20.1	0.253
Drug use	193	119/169 (70.4)	20/24 (83.3)	12.9	– 3.5	29.4	0.124
Age	195			0.881	– 4.78	3.01	0.657
SES	149			0.944	– 3.24	5.13	0.659

<sup>a</sup>RD is risk difference, the difference between the proportions of patients with persistent psychiatric disorder and co-variable present at  $T_1$  compared with patients with persistent psychiatric disorder without present co-variable at  $T_1$

<sup>b</sup>The numbers in this table, for example 84/134 (62.7) and 243/304 (79.9), indicate that among the 134 patients with a psychiatric disorder and no chronic pain at  $T_1$ , 84 had a psychiatric disorder at  $T_2$ , and among the 304 patients with a psychiatric disorder and chronic pain at  $T_1$ , 243 had a psychiatric disorder at  $T_2$

<sup>c</sup>The risk of having a persistent psychiatric disorder increases with 0.105% per one year increase of age

<sup>d</sup>The risk of having a persistent psychiatric disorder increases with 0.012% per one unit change in level of mothers education

Child/Adolescent Anxiety Multimodal Extended Long-Term Study (CAMELS) found that despite receiving high-quality evidence-based treatments for anxiety, only 22% were in stable remission across all 4 years they were assessed, 30% were chronically ill, and 48% experienced relapses [41]. In this study, male gender was associated with increased probability of being in the remission group compared to the relapsing group, supporting our finding of higher morbidity among girls. Mood disorders had decreased at follow-up and may have been under-registered in this study. As the course of such disorders is fluctuating, present status may not reflect struggling with periodic disorders.

The female patients seemed to be more prone to develop co-occurring psychiatric disorders. This corresponds well with the previous studies reporting more comorbidity in

girls than boys [10, 42]. In our sample, girls had very high rates of psychiatric comorbidity at follow-up, in all diagnostic groups, and highest among those with mood disorders, where more than nine out of ten had an additional psychiatric disorder. All boys with mood disorders also had a comorbid psychiatric disorder, but since there were few boys with mood disorders, the change in frequencies were small. Also, somatic comorbid diagnoses became more frequent for female patients with anxiety disorders. An increased risk of somatic disorders is reported in patients with anxiety disorders [43], independent of gender. Furthermore, adolescents who experience chronic somatic health conditions, are found to be at risk of elevated physiological anxiety symptoms in mid-adolescence [44]. The higher frequency of girls than boys with anxiety disorders in our sample may have

influenced the finding of a significant increase only among female patients. Still, the results show consistently that the burden of disease was most prominent among girls.

Overall, there was a decrease in chronic pain for the total sample after 3 years, but an increase among those with anxiety disorders, not surprisingly since chronic pain may be regarded as part of the anxiety disorder. We found large differences in frequency of pain between the genders at  $T_2$ . Nearly, nine out of ten girls and five out of ten boys with anxiety disorders had chronic pain, and the frequency of multisite pain was more than three times as high in girls with anxiety disorders compared to boys. A systematic review investigating the epidemiology of chronic pain in children and adolescents from the general population found that pain prevalence was generally higher in girls and increased with age for most pain types [45]. Using data from a large Norwegian population study, Skrove et al. demonstrated higher prevalence of chronic multisite pain among adolescent girls and boys with increasing number of psychiatric symptoms, but with highest rates among girls [46]. In the St. Olav CAP Survey at  $T_1$ , 70% of the patients reported chronic pain in addition to a psychiatric disorder [21]. This was a higher frequency than the 44% reported in the general adolescent population in many countries [47] and in our region [22], and underlines the importance of assessing chronic pain among adolescents with psychiatric symptoms and disorders.

Norway appears to be a low-prevalence country when it comes to substance use in the general adolescent population in comparison with other European countries [48]. At  $T_1$ , the adolescents reported a higher intake of alcohol, a higher prevalence of smoking, and a four times higher ratio of having tried illicit drugs compared to the general population [24]. In our sample, smoking tended to decrease during follow-up, with no gender differences; whereas, alcohol use did not change substantially overall, but increased for anxiety disorders and ADHD in the total sample and for girls. Some increase was expected, since the age of participants increased from 13–18 years to 16–21 years, and drinking alcohol is more common at these ages. Also, young adults are allowed to buy alcohol in Norway from 18 years. Finding the highest increase among girls with anxiety disorders corresponds well with earlier Norwegian studies [26, 49].

The more surprising result was the significantly increased level of having tried illicit drugs in all diagnostic categories, and especially in the female sample. Getting correct information using self-report on behavior that may be shameful or illegal, may be a challenge. Therefore, the reports on drug use must be interpreted with caution. During adolescence, there is a general increased use of illicit drugs and a possible increased tolerance, which can contribute to an increased incidence 3 years later [50]. Still, associations with the specific psychiatric disorders are relevant. We found highest rates among girls with anxiety disorders; in this group,

one out of five had tried illicit drugs. There are inconsistent findings on the association between anxiety disorders and alcohol/drug use in previous studies, some indicating a positive association [51], and other demonstrating negative associations [52]. Opposite to our finding, Turner et al. demonstrated in a review that self-medication with alcohol or drugs for mood and anxiety disorders was associated with male gender [53]. A recent population-based study showed gender-specific substance use patterns among Portuguese adolescents [54]. We found increasing rates of illicit drug use among patients with ADHD for both genders, which corresponds with recent findings from the MTA longitudinal study [55]. Our results and the inconsistent findings between studies indicate the need for further research on gender and disorder-specific substance use in a clinical population.

We examined the possible risk factors associated with the persistence of psychiatric disorders. There was a significant association between having chronic pain at  $T_1$  and persisting psychiatric disorder over 3 years for the total sample, and strongest in the female group. Earlier studies have demonstrated associations between pain in adolescence and mental health problems in young adulthood [18, 19]. Presence of chronic pain in adolescents with psychiatric disorders, especially among girls, is, therefore, important to assess, since these patients seem to be vulnerable for persistent and even increasing psychiatric morbidity. There was also an association between smoking or having tried illicit drugs and persistence of psychiatric morbidity in girls. Socioeconomic status as measured by maternal level of education could not explain the persistence of disorders or the effect of these risk factors, nor could participants' age.

The strength of the present study is the inclusion of a large clinical sample, providing a high degree of precision in the estimates, and the response rate from  $T_1$  to  $T_2$  was high. Although the attrition rate was high in the initial recruitment, the  $T_1$  sample did not differ in age, gender or reason for referral compared to non-participants. This high attrition rate may still have affected the results, and both severity of symptoms and types of treatment may have played a role in the continuity of a disorder and for participation at follow-up. The number of participants was low for some diagnostic groups which probably limits the generalizability of the results. Furthermore, due to few participants in some diagnostic groups, especially when examining comorbid chronic pain, somatic disorders and substance use, we chose to merge children with these diagnoses into one larger group.

The psychiatric diagnoses were classified by clinicians, according to the current diagnostic classification systems, and not based on the self-report measures which involves the limitations of less accuracy in establishing psychopathology. However, two different classification systems were used at the two time points, which may have affected prevalence rates and is a possible limitation. Research has shown that

the concordance between the two systems can differ across the range of disorders, and with varying concordance within the anxiety disorders [56], and also the diagnostic criteria for hyperkinetic disorder in ICD-10 are more strict than the criteria for ADHD in DSM-IV. In particular, this may have contributed to a higher increase in ADHD diagnosis at follow-up. Beyond that, the ICD-10 and DSM-IV are widely harmonized. The classification process differed between the two time points; At  $T_1$ , diagnoses were based on all available clinical information collected by the multi-disciplinary team, and at  $T_2$ , the acknowledged K-SADS semi-structured interview was performed as telephone interview. This may also have affected the diagnostic accuracy. K-SADS assesses all psychiatric disorders more systematically, which could have led to reporting more comorbid disorders at  $T_2$ , even though secondary disorders were stated on the basis of thorough assessment also at  $T_1$ . It is also reasonable to assume that some differences in diagnoses over time might be explained by the different methods and diagnostic procedures between the two time points. There is no well-established definition of chronic pain in children, but the definitions of chronic pain and multisite pain used in this study are widely used in other epidemiologic pain studies, and have been used in the general population in studies from the same area [20, 22]. Still, some information bias cannot be excluded when using self-reports, which could lead to an under- or overestimation of chronic pain and substance use. There was different wording in the question about alcohol use at the two time points. Trying illicit drugs was reported only by one question, and although the same question was used at both time points, this topic may be especially prone to information bias. Using level of maternal education to indicate socioeconomic status may not encircle the entire concept of SES, and furthermore, the SES information was available in a reduced sample, which may not reflect the total study population. Treatment plausibly impact the course of morbidity, and the lack of treatment assessment in this study is a limitation. Since there were more girls than boys among participants compared to non-participants in this study, we may have lost some of the boys with psychiatric disorders.

### Clinical implications

The results of this study bring an important message to clinical practice. Even though clinicians know about mental health challenges in adolescence, the persistence of psychiatric disorders over 3 years from early to late adolescence should be an extra eye-opener, and especially the increased rate of anxiety disorders and comorbidities among girls. The burden of disease in this age group must be acknowledged. In-depth assessment of mental health problems should of course include important risk factors, and asking adolescent patients about pain, uncover smoking habits and illicit drug

use seems to be essential, especially for female patients. Providing standard clinical care may not be enough, as these risk factors point to the need for intensified psychiatric treatment to prevent persistence of the psychiatric disorders. Furthermore, long-term clinical follow-up should be considered for adolescents with risk factors.

### Conclusions

Psychiatric morbidity decreased over 3 years in this adolescent clinical sample, including mood disorders, but nevertheless, almost three out of four still had a psychiatric disorder. The high frequency of psychiatric and somatic comorbidity, and chronic pain, indicates generally a high burden of disease, and chronic pain may be seen as part of the complexity of psychiatric disorders, especially anxiety disorders. Female adolescents seemed to have a higher morbidity than male adolescents, with an increased frequency of anxiety disorders after 3 years, and a five–ten times higher prevalence of chronic pain than boys. Chronic pain, smoking and having tried illicit drugs at baseline were factors strongly associated with persistent psychiatric morbidity. Although some differences in diagnoses over time might be explained by the different methods and diagnostic procedures between the two time points, the results indicate the need for addressing the associated factors and include them in a comprehensive follow-up of psychiatric disorders in this age group.

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### Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethical approval** This study has been approved by the Regional committee for Medical and Health Research Ethics of Central Norway and



comply with the ethical standards in the Declaration of Helsinki from 1964 and later amendments.

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## Supplementary Material

**Table S1. Age, gender and SES of participants at T<sub>2</sub> and non-participants at T<sub>2</sub>**

		Participants T <sub>1</sub> (n=717)		Participants T <sub>2</sub> (n=570)		Non-participants T <sub>2</sub> (n=147)	
Age (years)	Mean (SD)	15.7	(1.7)	15.7	(1.7)	15.5	(1.6)
Gender	Girls n (%)	393	(54.8)	324	(56.8)	69	(46.9)
	Boys n (%)	324	(45.2)	246	(43.2)	78	(53.1)
SES	Mean (SD)	4.7	(1.7)	4.8	(1.7)	4.3	(1.7)

**Table S2. Age, gender and SES of participants and non-participants in present sample**

		Diagnostic assessment at T <sub>1</sub> (n=597)		Participants (n=464)		Non-participants (n=133)	
Age (years)	Mean (SD)	15.7	(1.7)	15.7	(1.7)	15.7	(1.7)
Gender	Girls n (%)	321	(53.8)	256	(55.2)	65	(48.9)
	Boys n (%)	276	(46.2)	208	(44.8)	68	(51.1)
SES	Mean (SD)	4.7	(1.7)	4.8	(1.7)	4.4	(1.6)

**Table S3. Diagnoses T<sub>1</sub> of participants and non-participants in present sample**

Diagnoses at T <sub>1</sub>	Participants (n=464)			Non-participants (n=133)		
	Girls (n=256) n (%)	Boys (n=208) n (%)	Total (n=464) n (%)	Girls (n=65) n (%)	Boys (n=68) n (%)	Total (n=133) n (%)
Any psychiatric disorder	245 (95.7)	195 (93.8)	440 (94.8)	62 (95.4)	65 (95.6)	127 (95.5)
Anxiety disorder	96 (37.5)	51 (24.5)	147 (31.7)	23 (35.4)	18 (26.5)	41 (30.8)
Mood disorder	82 (32.0)	17 (8.2)	99 (21.3)	22 (33.8)	10 (14.7)	32 (24.1)
ADHD	83 (32.6)	121 (58.2)	204 (44.0)	23 (35.4)	35 (51.5)	58 (43.6)
Other psychiatric disorder	52 (20.3)	68 (32.7)	120 (25.9)	13 (20.0)	30 (44.1)	43 (32.3)

### Study of agreement of diagnostic classification:

The study of agreement between first and second rater was designed as follows: Seven of the interviewers were used as second opinion raters for taped telephone interviews. Each of these seven re-scored four interviews performed by four of the other six interviewers. Hence, the number of re-scored patients were 7x4=28. The design was constructed as shown in Table S4, to be as balanced as possible.

**Table S4. Design of agreement study**

		Second rater									
		B	C	E	D	F	G	A			Sum
First rater	B		1	1	1	1	0	0			4
	C		1	1	1	0	1	0			4

	E		0	0		1	1	1	1		4
	D		1	1	0		0	1	1		4
	F		1	0	0	1		1	1		4
	G		0	1	1	0	1		1		4
	A		1	1	1	0	1	0			4
	Sum		4	4	4	4	4	4	4		28

The diagnostic group variables Depressive, Bipolar, Psychotic, Anxiety, ADHD, and Other were coded as 1(not present), 2 (Partly in remission), and 3 (Present). For the variable Bipolar, the code 2 (partly in remission) was not used. A diagnostic group variable “Any diagnosis” was coded equal to the maximum of the aforementioned codes. A separate variable “suicidal” was coded as “not present” versus “present”.

For each diagnostic group, we quantified the inter-rater reliability between rating 1 and 2 using negative agreement and positive agreement, as recommended by (1). The positive (negative) agreement is the probability that the second rater classifies the patient as with diagnosis (without diagnosis), given that the first rater diagnosed the patient as with diagnosis (without diagnosis). In this setting, we merged “partly” with “no” diagnosis.

Crosstables for diagnostic groups for rating 1 versus rating 2 are shown in Table S5. Negative agreement was generally high, varying from 0.88 to 1.00 for the different disorders. This would be regarded as good to excellent agreement in most settings. The negative agreement was 0 for bipolar and psychotic disorder, and varied from 0.57 to 1.00 for the rest of the disorders.

**Table S5. Interrater reliability for diagnostic groups**

First rater (rows) and second rater (columns)

					Specific agreement, Partly merged with No	
					Positive agreement	Negative agreement
Depressive disorder presently	No	Partly	Yes		1,000	1,000
	No	23	0	0		
	Partly	3	0	0		
	Yes	0	0	2		
Anxiety	No	Partly	Yes		0,615	0,884
	No	15	2	1		
	Partly	2	0	1		
	Yes	2	1	4		
ADHD	No	Partly	Yes		0,941	0,974
	No	15	1	0		
	Partly	1	2	0		
	Yes	1	0	8		
Other	No	Partly	Yes		0,667	0,960
	No	22	1	0		
	Partly	1	0	0		

	Yes	2	0	2		
Any	No	7	4	0	0,929	0,929
	Partly	1	1	0		
	Yes	0	2	13		

1. de Vet HC, Mokkink LB, Terwee CB et al. Clinicians are right not to like Cohen's kappa. BMJ 2013; 346: f2125.

**Table S6. Paired data of the presence of disorders and psychiatric comorbidity at T<sub>1</sub> and T<sub>2</sub>**

	Disorder/comorbidity T <sub>1</sub> NO		Disorder/comorbidity T <sub>1</sub> YES	
	Disorder/co-morbidity T <sub>2</sub> NO	Disorder/co-morbidity T <sub>2</sub> YES	Disorder/co-morbidity T <sub>2</sub> NO	Disorder/co-morbidity T <sub>2</sub> YES
<b>Total sample (n=464)</b>				
Any psychiatric disorder	17	7	112	328
Anxiety disorder	207	110	71	76
Mood disorder	324	41	63	36
ADHD	215	44	56	148
Other psychiatric disorder	297	47	60	60
Any psychiatric disorder and comorbid psychiatric disorder	226	108	69	61
Anxiety disorder and comorbid psychiatric disorder	292	113	36	23
Mood disorder and comorbid psychiatric disorder	359	60	32	13
ADHD and comorbid psychiatric disorder	322	66	41	34
Other psychiatric disorder and comorbid psychiatric disorder	339	55	39	31
<b>Girls (n=256)</b>				
Any psychiatric disorder	8	3	57	188
Anxiety disorder	76	84	37	59
Mood disorder	141	33	49	33
ADHD	145	27	19	64
Other psychiatric disorder	177	27	29	23
Any psychiatric disorder and comorbid psychiatric disorder	104	84	36	32
Anxiety disorder and comorbid psychiatric disorder	125	95	22	14
Mood disorder and comorbid psychiatric disorder	169	49	25	13
ADHD and comorbid psychiatric disorder	181	45	15	14
Other psychiatric disorder and comorbid psychiatric disorder	197	36	14	9
<b>Boys (n=208)</b>				
Any psychiatric disorder	9	4	55	140
Anxiety disorder	131	26	34	17
Mood disorder	183	8	14	3

ADHD	70	17	37	84
Other psychiatric disorder	120	20	31	37
Any psychiatric disorder and comorbid psychiatric disorder	122	24	33	29
Anxiety disorder and comorbid psychiatric disorder	167	18	14	9
Mood disorder and comorbid psychiatric disorder	190	11	7	0
ADHD and comorbid psychiatric disorder	141	21	26	20
Other psychiatric disorder and comorbid psychiatric disorder	142	19	25	22

**Table S7. Paired data of the presence of disorders and somatic comorbidity at T<sub>1</sub> and T<sub>2</sub>**

Total sample (n=464)	Comorbidity T <sub>1</sub> NO		Comorbidity T <sub>1</sub> YES	
	Comorbidity T <sub>2</sub> NO	Comorbidity T <sub>2</sub> YES	Comorbidity T <sub>2</sub> NO	Comorbidity T <sub>2</sub> YES
Any psychiatric disorder and comorbid somatic disorder	322	61	57	24
Anxiety disorder and comorbid somatic disorder	381	50	24	9
Mood disorder and comorbid somatic disorder	424	19	16	5
ADHD and comorbid somatic disorder	393	39	24	7
Other psychiatric disorder and comorbid somatic disorder	420	24	17	3
Any psychiatric disorder and chronic pain	119	37	110	188
Anxiety disorder and chronic pain	257	98	59	49
Mood disorder and chronic pain	343	41	49	30
ADHD and chronic pain	274	51	63	71
Other psychiatric disorder and chronic pain	349	41	44	29
Any psychiatric disorder and multisite pain	241	41	69	99
Anxiety disorder and multisite pain	320	73	38	30
Mood disorder and multisite pain	374	33	38	18
ADHD and multisite pain	352	37	40	30
Other psychiatric disorder and multisite pain	397	27	21	18
<b>Girls (n=256)</b>				
Any psychiatric disorder and comorbid somatic disorder	164	39	35	18
Anxiety disorder and comorbid somatic disorder	189	43	17	7
Mood disorder and comorbid somatic disorder	222	17	12	5
ADHD and comorbid somatic disorder	219	22	11	3
Other psychiatric disorder and comorbid somatic disorder	230	15	8	3
Any psychiatric disorder and chronic pain	119	37	110	188
Anxiety disorder and chronic pain	94	80	35	46
Mood disorder and chronic pain	152	34	40	29
ADHD and chronic pain	160	26	21	48
Other psychiatric disorder and chronic pain	190	24	25	17
Any psychiatric disorder and multisite pain	241	41	69	99
Anxiety disorder and multisite pain	132	65	27	29

Mood disorder and multisite pain	173	29	35	18
ADHD and multisite pain	183	27	23	22
Other psychiatric disorder and multisite pain	211	22	11	12
<b>Boys (n=208)</b>				
Any psychiatric disorder and comorbid somatic disorder	158	22	22	6
Anxiety disorder and comorbid somatic disorder	192	7	7	2
Mood disorder and comorbid somatic disorder	202	2	4	0
ADHD and comorbid somatic disorder	174	17	13	4
Other psychiatric disorder and comorbid somatic disorder	190	9	9	0
Any psychiatric disorder and chronic pain	82	20	51	47
Anxiety disorder and chronic pain	163	18	24	3
Mood disorder and chronic pain	191	7	9	1
ADHD and chronic pain	114	25	42	23
Other psychiatric disorder and chronic pain	159	17	19	12
Any psychiatric disorder and multisite pain	150	9	21	18
Anxiety disorder and multisite pain	188	8	11	1
Mood disorder and multisite pain	201	4	3	0
ADHD and multisite pain	169	10	17	8
Other psychiatric disorder and multisite pain	186	5	10	6

**Table S8. Paired data of the presence of disorders and substance use at T<sub>1</sub> and T<sub>2</sub>**

	Substance use T <sub>1</sub> NO		Substance use T <sub>1</sub> YES	
	Substance use T <sub>2</sub> NO	Substance use T <sub>2</sub> YES	Substance use T <sub>2</sub> NO	Substance use T <sub>2</sub> YES
<b>Total sample (n=464)</b>				
Any psychiatric disorder and smoking	193	32	48	50
Anxiety disorder and smoking	344	40	17	12
Mood disorder and smoking	387	22	23	7
ADHD and smoking	333	25	28	17
Other psychiatric disorder and smoking	368	26	18	7
Any psychiatric disorder and current alcohol use	161	80	82	127
Anxiety disorder and current alcohol use	301	88	39	30
Mood disorder and current alcohol use	367	30	49	16
ADHD and current alcohol use	302	66	32	55
Other psychiatric disorder and current alcohol use	356	46	40	17
Any psychiatric disorder and drug use	328	67	15	45
Anxiety disorder and drug use	386	59	8	10
Mood disorder and drug use	414	31	14	4
ADHD and drug use	380	44	8	24
Other psychiatric disorder and drug use	408	39	9	6
<b>Girls (n=256)</b>				
Any psychiatric disorder and smoking	102	19	32	34
Anxiety disorder and smoking	170	32	11	12
Mood disorder and smoking	194	19	20	5
ADHD and smoking	198	10	18	8
Other psychiatric disorder and smoking	215	14	9	5
Any psychiatric disorder and current alcohol use	70	44	52	86
Anxiety disorder and current alcohol use	130	69	26	28

Mood disorder and current alcohol use	170	27	42	15
ADHD and current alcohol use	179	34	13	27
Other psychiatric disorder and current alcohol use	194	28	23	11
Any psychiatric disorder and drug use	173	43	8	29
Anxiety disorder and drug use	194	49	4	8
Mood disorder and drug use	213	27	12	3
ADHD and drug use	209	24	7	13
Other psychiatric disorder and drug use	223	25	4	4
<b>Boys (n=208)</b>				
Any psychiatric disorder and smoking	91	13	16	16
Anxiety disorder and smoking	174	8	6	0
Mood disorder and smoking	193	3	3	2
ADHD and smoking	135	15	10	9
Other psychiatric disorder and smoking	153	12	9	2
Any psychiatric disorder and current alcohol use	91	36	30	41
Anxiety disorder and current alcohol use	171	19	13	2
Mood disorder and current alcohol use	197	3	7	1
ADHD and current alcohol use	123	32	19	28
Other psychiatric disorder and current alcohol use	162	18	17	6
Any psychiatric disorder and drug use	155	24	7	16
Anxiety disorder and drug use	192	10	4	2
Mood disorder and drug use	201	4	2	1
ADHD and drug use	171	20	1	11
Other psychiatric disorder and drug use	185	14	5	2



# Paper II



RESEARCH ARTICLE

Open Access

# Suicidality, function and associated negative life events in an adolescent psychiatric population at 3-year follow-up



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## Abstract

**Background:** We aimed to examine psychosocial function, suicidality and school dropout in a clinical psychiatric population over a 3-year period from adolescence to young adulthood and explore associations with negative life events.

**Methods:** This study is part of the Health Survey in Department of Children and Youth, St. Olavs hospital, Norway. In the first study visit (T<sub>1</sub>), 717 (43.5% of eligible) participated, aged 13–18 years (2009–2011), and 3 years later (T<sub>2</sub>), 570 answered a questionnaire (school functioning and negative life events), and 549 completed Kiddie SADS as telephone interview assessing DSM-IV diagnoses, psychosocial functioning and suicidality.

**Results:** Suicidal ideation was more frequent among girls (17.9%) than among boys (5.4%) (risk difference; RD = 12.5%, CI (7.2 to 17.7),  $p < 0.001$ ), as was suicidal behavior (25.0% vs. 9.5%, RD = 15.5%, CI (9.2 to 21.4),  $p < 0.001$ ). Girls had lower psychosocial functioning than boys (Children's Global Assessment Scale; Mean score 68.2 vs. 75.2, Mean difference = -7.0, CI (-9.4 to -4.7),  $p < 0.001$ ), and more school dropout (22.5% vs. 13.2%, RD = 9.3%, CI (2.8 to 15.5),  $p = 0.006$ ). For those with a psychiatric disorder, 24.8% of girls had suicidal ideation and 30.0% suicidal behavior, which was larger than for boys (RD = 18.0%, CI (10.8 to 24.7),  $p < 0.001$ , and RD = 18.3%, CI (10.2 to 25.8),  $p < 0.001$ , respectively). Exposure to negative life events was frequent for both genders, but more girls had experienced sexually uncomfortable or abusive situations, the last 3 years (23.5% vs. 2.9%, RD = 20.6%, CI (15.4 to 25.7),  $p < 0.001$ ), and ever (44.4% vs. 7.9%, RD = 36.5%, CI (29.9 to 42.7),  $p < 0.001$ ). Suicidal behavior was associated with having been threatened, physically harassed or violently hurt (RD = 16.7%, CI (9.5 to 23.9),  $p < 0.001$ ), and for girls been put into sexually uncomfortable or abusive situations (RD = 20.1%, CI (10.4 to 29.9),  $p < 0.001$ ) and seen others violently hurt (RD = 14.6%, CI (3.4 to 25.8),  $p = 0.011$ ).

**Conclusions:** The high frequency of suicidality and school dropout confirms the severity of adolescent psychiatric disorders, especially among girls. Specific life events were associated risk factors and should be target points for prevention and intervention.

**Keywords:** Suicidal ideation, Suicidal behavior, School dropout, Adolescent, Negative life event, Longitudinal study

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## Background

Adolescence is the period for transitioning into young adulthood and is usually a time of life characterized by good physical health [1]. However, the majority of mental disorders develop during adolescence and contribute to reduced psychosocial function [1–3]. Suicidal symptoms increase during this developmental period [4–6], with a rapid shift from suicidal ideation to suicidal behavior [5, 7, 8], and an estimated lifetime prevalence of suicidal ideation and suicide attempts of 12.1–33% and 4.1–9.3%, respectively [5, 9]. The prevalence of self-harm, defined broadly regardless of motivation and intention to die, has increased among Norwegian adolescents from 4.1 to 16.2% between 2002 and 2018 [10]. Second to road injury, suicide is the most common cause of death among young people worldwide, uncommon before 15 years of age but the frequency increases through adolescence [6, 11–13]. The prevalence across all ages, countries and gender is 3.77/100000, and in Norway 3.00/100000 [12]. Suicide characteristics differ by gender [6, 12–15], with girls having higher rates of suicidal thoughts and behavior, and boys highest rates of committed suicide. Suicidal ideation and behavior are common in patients with psychiatric disorders [5, 6, 16] and are more than three times more frequent in clinical samples of youth than in the general population [7, 17]. Accordingly, the rise of suicidal thoughts and behavior through adolescence coexists with increasing frequencies of psychiatric disorders and related psychopathology that by itself provide higher suicide risk, as for example depression, substance use and some anxiety disorders [5, 7, 16].

It is common to have experienced negative or stressful life events or adversities from childhood to young adulthood [18, 19]. Many different life events are found to be associated with youth suicidal symptoms [20–22]. Such events may include being exposed or witnessed to violence, sexual trauma, or other injury and trauma [19], which are more frequent in clinical psychiatric samples than in the general population [23, 24]. In a systematic review, young people with attempted suicide were more likely to have experienced stressful life events than those with suicidal ideation [20]. A meta-analysis provided strong evidence that early exposure to any interpersonal violence increased the risk of suicide attempts [25]. Many other negative life events have shown associations to suicidal ideation, behavior or committed suicide, as for example death of a parent or a loved one [26, 27], experiences of disasters or accidents [27], peer victimization [28] and multiple other family factors [29, 30]. Experiencing negative life events during demanding developmental periods in childhood and adolescence may increase vulnerability to mental distress by inducing biological changes with long-term effects on nervous, endocrine and immune systems [20, 31]. Thus, negative

life events may increase the risk for psychiatric symptoms, including suicidal behavior in vulnerable individuals [20, 32].

Psychiatric disorders and comorbidities in early years influence academic functioning, and may subsequently lead to increased risk of dropping out of school [33] and receiving unemployment benefits or social insurance support [33]. In a population-based study in Central Norway, 17% was registered as being high school dropouts at age 24 [33], and more boys than girls were found to be non-completers in another Norwegian population-based survey [34]. According to World Health Organization, education and health are strongly linked [35]. School dropout was associated with poor mental health in a Danish population-based study [36], and school dropout involve heavy and enduring individual and social costs [37]. The link between suicidal symptoms, psychosocial and school function seems to be bidirectional; Adolescent self-harm or suicidal behavior are found to be associated with later mental health disorders and worse long-term functioning in young adulthood [38, 39]. According to a systematic review with meta-analysis of longitudinal studies, adolescents and young adults with school failure were at higher risk of suicide attempts [40]. There are many risk factors for school dropout [41], and reasons for leaving school vary widely [42]. Negative or stressful life events are found to be associated with intentions of and actual dropout [43], including conflicts with authorities for boys, and relational problems for girls [44]. High school students exposed to severe acute stressors are immediately vulnerable to dropping out [37].

The objective of the present study was to examine suicidality and functioning 3 years after referral to Child and Adolescent Mental Health Services. We aimed to assess psychosocial function, suicidal ideation, suicidal behavior, and school dropout, in the total sample and specified by psychiatric disorders, and furthermore to investigate associations with negative life events. We set out to specify analyses for girls and boys and explore gender differences. Hypotheses were that present suicidal symptoms and school dropout were associated with co-occurring exposure to negative life events, and furthermore, that frequencies differed between girls and boys, with girls having higher rates of suicidal symptoms and boys more school dropout.

## Method

### Study design

The Health Survey in Department of Children and Youth, Division of Mental Health Care, St. Olavs hospital, Trondheim University Hospital, Norway (St. Olav CAP Survey), is a prospective longitudinal cohort study of a defined clinical population assessed at two time

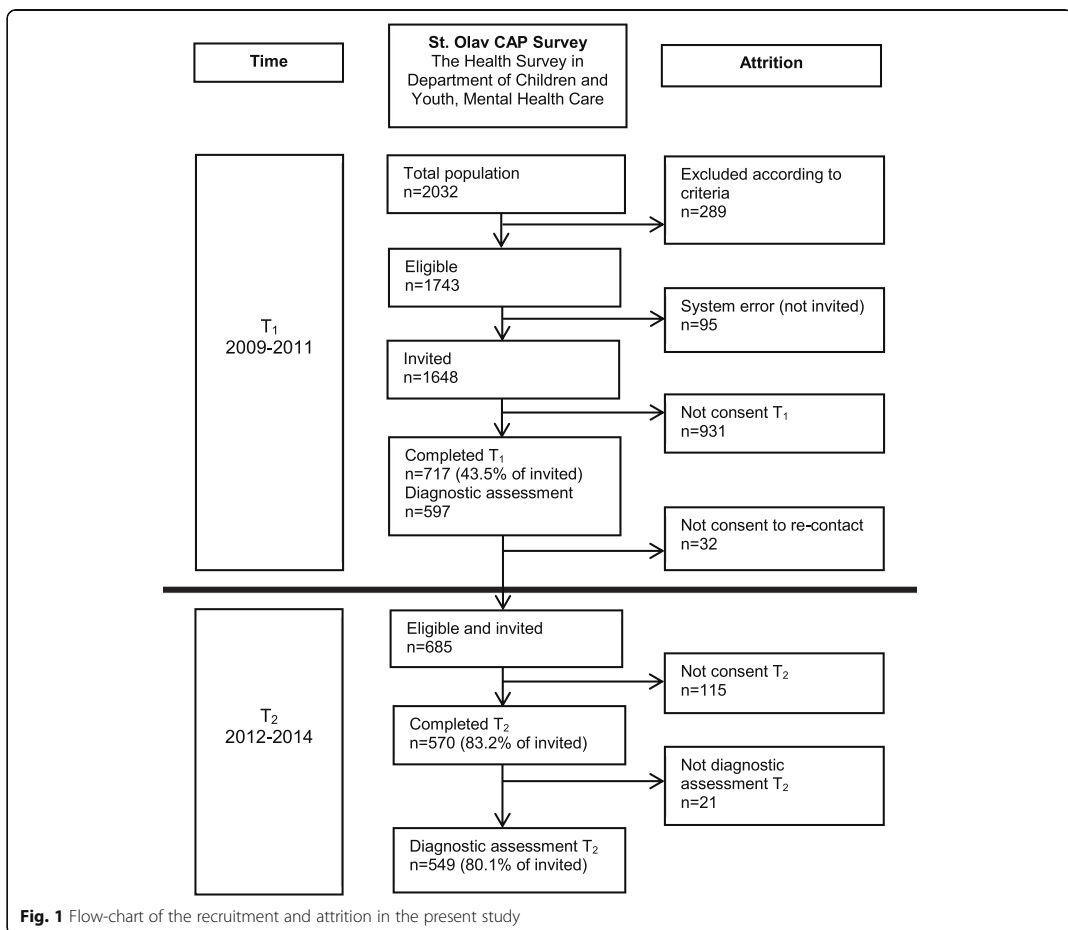
points. Design and procedures are thoroughly described in former publications [45, 46]. At time point 1 (T<sub>1</sub>) (2009–2011), all patients aged 13–18 years who visited the Department of Children and Youth at least once over a 2-year study period, received oral and written invitations at their first attendance. The exclusion criteria were difficulties in answering the survey due to low cognitive function, visual impairments, insufficient language skills, or an unstable psychiatric state. Emergency patients were invited to take part once they entered a stable phase. The participants and their parents received standard application of services. They gave written informed consent to extract diagnostic data from clinical charts and respond to an electronic survey. At 3-year study follow-up (T<sub>2</sub>) (2012–2014), age 16–21 years, data were collected from the T<sub>1</sub> enrolled sample and their parents, by an electronic survey and a diagnostic telephone interview performed by trained professionals.

**Participants**

In the T<sub>1</sub> study period, 2032 adolescent patients had at least one attendance in the Department of Children and Youth [45, 46]. Figure 1 shows the participant flow in each stage of the survey. At T<sub>1</sub>, n = 717 participated (393 (54.8%) girls). At T<sub>2</sub>, all T<sub>1</sub> participants who previously consented to further inquiry were invited (eligible n = 685), of whom 570 (83% of eligible) completed the follow-up questionnaire (324 (56.8%) girls), and 549 (80%) completed the diagnostic interview (308 (56.1%) girls).

**Participants vs. non-participants**

To explore the representativeness of the study population at T<sub>1</sub>, anonymous information about the total clinical population was collected from annual reports from the Department of Children and Youth, 2009–2011, as previously published [45, 46]. All adolescents in the



study period ( $n = 2032$ ) minus those excluded ( $n = 289$ ) were defined as reference population ( $n = 1743$ ). The main reason for referral, age and gender were similar between participants ( $n = 717$ , 41.1%) and non-participants ( $n = 1026$ , 58.9%) (data not shown). Participants were 0.27 years older: Mean (SD) 15.7 (1.7) vs. 15.4 (2.0), and there were more girls among the participants: 393 (54.8%) vs. 509 (49.6%). Among those with participation at  $T_1$ , there were 570 participants and 147 non-participants at  $T_2$ . In depth attrition analyses are reported in a former publication [46]. Age and socioeconomic status were similar among participants and non-participants.

### Measures

**Psychiatric Diagnoses** at  $T_2$  were set using the semi-structured Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS) [47] according to the Diagnostic and Statistical Manual of Mental Disorders IV Text revision (DSM-IV-TR) [48]. Psychometric properties of the K-SADS, including reliability and validity, are found to be excellent [47], and the interview has previously been applied to populations in young adulthood [49, 50]. Adolescents were interviewed by telephone by trained interviewers, all with graduate degree in medicine or psychology and experience in child and adolescent psychiatric assessment. The interviewers met regularly with a supervisor, an experienced child and adolescent psychiatrist, to assure the quality and harmonization of the diagnostic assessment. All were blinded to  $T_1$  diagnoses. Inter-rater reliability in terms of negative agreement and positive agreement as recommended by van de Vet et al. [51], was assessed using second ratings for 28 of the taped telephone interviews. Positive agreement varied from 0.615 to 1.000, and negative agreement varied from 0.884 to 1.000 [46]. The underlying contingency tables showing agreement are previously reported [46].

In the present study, disorders were grouped into the following categories, based on DSM-IV diagnoses at  $T_2$ : Any psychiatric disorder, Anxiety disorders (DSM-codes 300, 308, 309), Mood disorders (DSM-codes 296, 300.4, 311), ADHD (DSM-code 314) and Other (DSM-codes 291, 292, 295, 298, 299, 301, 303, 304, 305, 307, 312, 313, 316). Due to few participants in some diagnostic groups, for example autism and eating disorders, and especially when examining suicidality and school dropout, we chose to merge children with these diagnoses into "other psychiatric disorders" for the purpose of this manuscript.

**The Children's Global Assessment Scale (CGAS)** [52] was used to rate general psychosocial functioning on a scale from 1 (extremely impaired, needs constant supervision) to 100 (superior functioning), based on K-

SADS interview. The CGAS is designed for children under 18 years, but was in this study used for all participants, also those above the age of 18 years. The inter-rater reliability for CGAS in terms of intraclass correlation coefficient (ICC) was 0.835, based on second ratings for 28 of the taped telephone interviews. Details are given in the [Supplementary material](#) (Table S1).

**Suicidal ideation or behavior** were measured at  $T_2$  by asking the following questions during K-SADS interview:

**Suicidal ideation**; "Sometimes children who get upset or feel bad think about dying or even killing themselves. Have you ever had such thoughts? How would you do it? Did you have a plan?" Assessed and scored as; 0; No information, 1; Not at all, 2; Infrequent or vague thoughts of suicide (e.g., less than once per month), or 3; Recurrent thoughts of suicide. As measure of **Suicidal ideation**, we used "infrequent or vague thoughts" (2) or "recurrent thoughts of suicide" (3), presently at  $T_2$ .

**Suicidal acts or attempts**; "Have you actually tried to kill yourself? When? What did you do? Any other things? Did you really want to die? How close did you come to doing it? Was anybody in the room? In the apartment? Did you tell them in advance? How were you found? Did you really want to die? Did you ask for any help after you did it?" Assessed and scored as; 0; No information, 1; No attempt, 2; Preparations with no actual intent to die (e.g., held pills in hand) or planned attempt but did not follow through, 3; Self injurious behavior with any suicidal intent. There was one more assessment; "Ever attempted suicide", scored as yes or no. In the present study, **Suicidal behavior** included "preparations or planned attempt" (2) or "self injurious behavior with any suicidal intent" (3), presently at  $T_2$ , or yes to the question: "Ever attempted suicide".

**School dropout** was self-reported at  $T_2$  based on answer "yes" to the following question: "Have you canceled your education (dropped out)?"

**Negative life events** were registered by self-report at both  $T_1$  and  $T_2$ . At  $T_1$ , the following questions were asked: "Have any of the following things happened to you?"; "That someone in your family has been seriously ill", "Death of a loved one", "A catastrophe (fire, avalanche, tidal wave, hurricane, etc.)", "A serious accident (ex: a very serious car accident)", "Been violently hurt (beaten or injured)", "Seen others violently hurt", "Been put in sexually uncomfortable/abusive situations by someone about your age", "Been put in sexually uncomfortable/abusive situations by an adult", "Been threatened or physically harassed by other students at school for a long time", "Received painful or frightening treatment at the hospital while being treated for an illness or injury". These items were also used in the Young-HUNT3 study (<https://www.ntnu.edu/hunt/data/que>).

At T<sub>2</sub>, the same questions were asked, and with a supplementary question: “Been seriously ill or injured”.

The answering opportunities were at T<sub>1</sub>; “No”, “Yes, last year” and “Yes, in my life”, and at T<sub>2</sub>; “No”, “Yes, last year” and “Yes, last three years”. In the present study, negative life events defined as “last 3 years” were events measured at T<sub>2</sub> only, and negative life events defined as “ever” were measured at T<sub>1</sub> or T<sub>2</sub>.

**Socioeconomic Status (SES)** was measured at T<sub>1</sub> by the highest level of mothers’ education, divided into eight categories: 1) less than 9-year primary school; 2) completed 9-year primary school; 3) one or two years in high school; 4) completed high school; 5) completed high school and one-year education/training after high school; 6) academy/university for up to and including 4 years; 7) academy/university for 5 years or more; 8) academy/university including PhD.

### Statistical analyses

We compared proportions using the Newcombe hybrid score confidence intervals, as recommended by Fagerland, Lydersen and Laake [53], and the Pearson Chi squared test. Confidence intervals and tests for differences in psychosocial functioning between girls and boys were based on Student’s t-test for independent samples. We used binary linear regression with suicidal ideation, suicidal behavior or school dropout at T<sub>2</sub> as dependent variables and negative life events reported at T<sub>1</sub> and T<sub>2</sub> as covariates, one at a time, to study their associations. The coefficients in binary linear regression represent risk differences. These regression analyses were carried out

unadjusted and adjusted for SES as a possible confounder where relevant. Some estimates including suicidal behavior could not be computed when adjusting for SES due to non-convergence of the calculations. We report 95% confidence intervals (CI) where relevant, and two-sided *p*-values < 0.05 were considered statistically significant. Binary linear regression and the Newcombe CI were performed in Stata 16, and the other in SPSS 25.

## Results

### Suicidal measures and functioning

At T<sub>2</sub>, psychosocial functioning CGAS score was mean 71.3 (standard deviation 14.5) (Table 1). Girls had lower CGAS score than boys (mean 68.2 vs. 75.2, mean difference = -7.0, CI (-9.4 to -4.7), *p* < 0.001). The frequency of suicidal ideation was 12.4%, girls 17.9% and boys 5.4% (risk difference; RD = 12.5%, CI (7.2 to 17.7), *p* < 0.001) (Table 1). Similar gender differences were found in suicidal behavior, were girls had the highest frequencies of suicidal attempts ever (25.0% vs. 9.5%, RD = 15.5%, CI (9.2 to 21.4), *p* < 0.001). School dropout was more frequent for girls than boys (22.5% vs. 13.2%, RD = 9.3%, CI (2.8 to 15.5), *p* = 0.006). Among those with a psychiatric disorder, suicidal ideation was higher among girls (24.8%), and suicidal behavior even higher (30.0%), RD for gender differences 18.0%, CI (10.8 to 24.7), *p* < 0.001, and 18.3%, CI (10.2 to 25.8), *p* < 0.001, respectively (Table 2). Specified by psychiatric disorder, girls had lower CGAS and higher frequencies of suicidal measures than boys in all diagnostic groups. The frequencies of suicidal ideation and behavior were highest in mood

**Table 1** Clinical characteristics, psychosocial functioning, suicidal measures and school dropout at 3-year follow up

Follow-up (T <sub>2</sub> )	Total		Girls		Boys		Girls versus Boys					
	n	Mean	(SD)	n	Mean	(SD)	n	Mean	(SD)	Mean difference	95% CI <sup>a</sup>	<i>p</i> -value <sup>a</sup>
Age (years)	570	18.7	(1.7)	324	19.0	(1.7)	246	18.3	(1.6)	0.7	(0.4 to 0.9)	< 0.001
SES	404	4.8	(1.7)	221	4.9	(1.7)	183	4.8	(1.8)	0.1	(-0.3 to 0.4)	0.714
CGAS	549	71.3	(14.5)	308	68.2	(15.5)	241	75.2	(12.0)	-7.0	(-9.4 to -4.7)	< 0.001
		<b>Proportion (%)</b>		<b>Proportion (%)</b>		<b>Proportion (%)</b>		<b>Risk difference (%)</b>		<b>95% CI<sup>b</sup></b>	<b><i>p</i>-value<sup>c</sup></b>	
Suicidal ideation <sup>d</sup>	549	68/548	(12.4)	308	55/307	(17.9)	241	13/241	(5.4)	12.5	(7.2 to 17.7)	< 0.001
Suicidal behavior	549	100/549	(18.2)	308	77/308	(25.0)	241	23/241	(9.5)	15.5	(9.2 to 21.4)	< 0.001
- Suicidal attempts presently	549	9/549	(1.6)	308	9/308	(2.9)	241	0/241	(0.0)	2.9	(0.8 to 5.5)	0.007
- Suicidal attempts ever	549	100/549	(18.2)	308	77/308	(25.0)	241	23/241	(9.5)	15.5	(9.2 to 21.4)	< 0.001
School dropout <sup>e</sup>	570	101/546	(18.5)	324	70 <sup>f</sup> /311	(22.5)	246	31/235	(13.2)	9.3	(2.8 to 15.5)	0.006

**Note:** SES Socioeconomic status, SD Standard Deviation, CGAS Children Global Assessment Scale (psychosocial functioning) (1–100, 1 = worst, 100 = best)

<sup>a</sup> Confidence intervals and tests for differences between girls and boys were based on Student’s t-test for independent samples

<sup>b</sup> Newcombe hybrid score

<sup>c</sup> Pearson Chi squared test

<sup>d</sup> Suicidal ideation is defined as suicidal thoughts occasionally or often

<sup>e</sup> School dropout includes patients answering yes to the question “Have you canceled your education (dropped out)?”

<sup>f</sup> Of these, 6 had given childbirth

**Table 2** General psychosocial functioning, suicidal ideation or behavior and school dropout at 3-year follow up, specified by psychiatric disorders

	Total (n = 549)		Girls (n = 308)		Boys (n = 241)		Girls versus Boys		
<b>Any psychiatric disorder<sup>a</sup></b>	<b>n = 385</b>		<b>n = 223</b>		<b>n = 162</b>				
	<b>Mean</b>	<b>(SD)</b>	<b>Mean</b>	<b>(SD)</b>	<b>Mean</b>	<b>(SD)</b>	<b>Mean difference</b>	<b>95% CI<sup>d</sup></b>	<b>p-value<sup>d</sup></b>
CGAS	66.8	(14.0)	63.3	(14.4)	71.6	(12.0)	-8.3	(-10.9 to -5.6)	< 0.001
	<b>n</b>	<b>(%)</b>	<b>n</b>	<b>(%)</b>	<b>n</b>	<b>(%)</b>	<b>RD (%)</b>	<b>95% CI of RD<sup>e</sup></b>	<b>p-value<sup>f</sup></b>
Suicidal ideation <sup>b</sup>	66/384	(17.2)	55/222	(24.8)	11/162	(6.8)	18.0	(10.8 to 24.7)	< 0.001
Suicidal behavior <sup>c</sup>	86/385	(22.3)	67/223	(30.0)	19/162	(11.7)	18.3	(10.2 to 25.8)	< 0.001
School dropout	77/361	(21.3)	53/211	(25.1)	24/150	(16.0)	9.1	(0.5 to 17.1)	0.037
<b>Anxiety disorders</b>	<b>n = 218</b>		<b>n = 168</b>		<b>n = 50</b>				
	<b>Mean</b>	<b>(SD)</b>	<b>Mean</b>	<b>(SD)</b>	<b>Mean</b>	<b>(SD)</b>	<b>Mean difference</b>	<b>95% CI of Difference</b>	<b>p-value</b>
CGAS	61.6	(13.3)	60.5	(13.9)	65.2	(10.4)	-4.7	(-8.2 to -1.0)	0.012
	<b>n</b>	<b>(%)</b>	<b>n</b>	<b>(%)</b>	<b>n</b>	<b>(%)</b>	<b>RD (%)</b>	<b>95% CI of RD</b>	<b>p-value</b>
Suicidal ideation	48/218	(22.0)	43/168	(25.6)	5/50	(10.0)	15.6	(2.7 to 24.7)	0.019
Suicidal behavior	64/218	(29.4)	55/168	(32.7)	9/50	(18.0)	14.7	(0.3 to 25.8)	0.045
School dropout	50/205	(24.4)	42/159	(26.4)	8/46	(17.4)	9.0	(-5.7 to 20.1)	0.209
<b>Mood disorders</b>	<b>n = 98</b>		<b>n = 80</b>		<b>n = 18</b>				
	<b>Mean</b>	<b>(SD)</b>	<b>Mean</b>	<b>(SD)</b>	<b>Mean</b>	<b>(SD)</b>	<b>Mean difference</b>	<b>95% CI of Difference</b>	<b>p-value</b>
CGAS	55.8	(11.3)	54.5	(11.4)	61.4	(9.6)	-6.9	(-12.7 to -1.2)	0.018
	<b>n</b>	<b>(%)</b>	<b>n</b>	<b>(%)</b>	<b>n</b>	<b>(%)</b>	<b>RD (%)</b>	<b>95% CI of RD</b>	<b>p-value</b>
Suicidal ideation	42/98	(42.9)	38/80	(47.5)	4/18	(22.2)	25.3	(-0.0 to 42.4)	0.050
Suicidal behavior	39/98	(39.8)	36/80	(45.0)	3/18	(16.7)	28.3	(3.5 to 43.7)	0.026
School dropout	30/90	(33.3)	23/73	(31.5)	7/17	(41.2)	-9.7	(-34.4 to 13.0)	0.446
<b>ADHD</b>	<b>n = 211</b>		<b>n = 99</b>		<b>n = 112</b>				
	<b>Mean</b>	<b>(SD)</b>	<b>Mean</b>	<b>(SD)</b>	<b>Mean</b>	<b>(SD)</b>	<b>Mean difference</b>	<b>95% CI of Difference</b>	<b>p-value</b>
CGAS	69.2	(13.6)	65.9	(14.9)	72.1	(11.6)	-6.2	(-9.9 to -2.6)	0.001
	<b>n</b>	<b>(%)</b>	<b>n</b>	<b>(%)</b>	<b>n</b>	<b>(%)</b>	<b>RD (%)</b>	<b>95% CI of RD</b>	<b>p-value</b>
Suicidal ideation	22/210	(10.5)	16/98	(16.3)	6/112	(5.4)	10.9	(2.6 to 20.0)	0.010
Suicidal behavior	41/211	(19.4)	27/99	(27.3)	14/112	(12.5)	14.8	(4.0 to 25.5)	0.007
School dropout	37/197	(18.8)	23/93	(24.7)	14/104	(13.5)	11.3	(0.3 to 22.3)	0.043
<b>Other psychiatric disorders</b>	<b>n = 120</b>		<b>n = 59</b>		<b>n = 61</b>				
	<b>Mean</b>	<b>(SD)</b>	<b>Mean</b>	<b>(SD)</b>	<b>Mean</b>	<b>(SD)</b>	<b>Mean difference</b>	<b>95% CI of Difference</b>	<b>p-value</b>
CGAS	63.2	(14.5)	57.7	(14.2)	68.4	(12.9)	-10.7	(-15.7 to -5.8)	< 0.001
	<b>n</b>	<b>(%)</b>	<b>n</b>	<b>(%)</b>	<b>n</b>	<b>(%)</b>	<b>RD (%)</b>	<b>95% CI of RD</b>	<b>p-value</b>
Suicidal ideation	27/120	(22.5)	20/59	(33.9)	7/61	(11.5)	22.4	(7.5 to 36.4)	0.003
Suicidal behavior	31/120	(25.8)	23/59	(39.0)	8/61	(13.1)	25.9	(10.2 to 40.1)	0.001
School dropout	31/114	(27.2)	19/57	(33.3)	12/57	(21.0)	12.3	(-4.1 to 27.8)	0.141

**Note:** SD Standard Deviation, CGAS Children Global Assessment Scale (general psychosocial functioning) (1–100, 1 = worst, 100 = best), RD Risk difference

<sup>a</sup> Psychiatric disorder includes both primary and additional diagnoses

<sup>b</sup> Suicidal ideation is defined as suicidal thoughts occasionally or often

<sup>c</sup> Suicidal behavior is defined as suicidal acts or attempts, presently at T<sub>2</sub> or ever, also suicidal acts and attempts with suicidal thoughts

<sup>d</sup> Confidence intervals and tests for differences between girls and boys were based on Student's t-test for independent samples

<sup>e</sup> Newcombe hybrid score

<sup>f</sup> Pearson Chi squared test

disorders and lowest in ADHD. For school dropout, gender difference was only found among patients with ADHD, with highest frequencies among girls (24.7% vs. 13.5%, RD = 11.3%, CI (0.3 to 22.3), p = 0.043).

**Negative life events**

Having serious illness of someone in family or death of a loved one, were the most common negative life events in this study (57.7% last 3 years and 85.7% ever), with



higher frequencies among girls than boys only for the last 3 years (63.2% vs. 50.4%, RD = 12.8%, CI (4.5 to 20.8),  $p = 0.002$ ) (Table 3). Having been seriously ill, injured or received painful or frightening treatment in hospital were more frequent among girls than boys both for the last 3 years and ever (26.5% vs. 16.5%, RD = 10.0%, CI (3.1 to 16.6),  $p = 0.005$ , and 38.0% vs. 27.0%, RD = 11.0%, CI (7.6 to 22.5),  $p < 0.001$ , respectively). Ever been exposed to a serious accident or catastrophe, were more frequent among girls (37.0% vs. 24.0%, RD = 13.0%, CI (5.4 to 20.4),  $p = 0.001$ ). There were highly significant differences between girls and boys in having been put into sexually uncomfortable or abusive situations, both during the last 3 years and ever (23.5% vs. 2.9%, RD = 20.6%, CI (15.4 to 25.7),  $p < 0.001$ , and 44.4% vs. 7.9%, RD = 36.5%, CI (29.9 to 42.7),  $p < 0.001$ , respectively).

### Associations

Binary linear regression with suicidal ideation as dependent variable and negative life events as covariates showed associations for several life events (Table 4). After adjustment for SES, the strongest associations were for been threatened, physically harassed or violently hurt (RD = 8.9%, CI (2.0 to 15.9),  $p = 0.012$ ) and having been put into sexually uncomfortable or abusive situations (RD = 10.4%, CI (1.8 to 19.0),  $p = 0.018$ ). Gender-specific analyses adjusted for SES, showed associations with

having serious illness of someone in the family or death of a loved one, and being threatened, physically harassed or violently hurt for girls, but no associations were present for boys.

With suicidal behavior as dependent variable, adjusted associations were present for been seriously ill or injured (RD = 10.6%, CI (2.8 to 18.4),  $p = 0.008$ ), exposure to a serious accident or catastrophe (RD = 10.1%, CI (1.9 to 18.3),  $p = 0.015$ ), and been threatened, physically harassed or violently hurt (RD = 16.7%, CI (9.5 to 23.9),  $p < 0.001$ ) (Table 5). Having seen others violently hurt was associated with suicidal behavior in girls only (RD = 14.6%, CI (3.4 to 25.8),  $p = 0.011$ ). Some estimates could not be adjusted for SES due to non-convergence of the calculations. Thus, the association with having been put into sexually uncomfortable or abusive situations (RD = 21.8%, CI (13.6 to 29.9),  $p < 0.001$ ) could not be adjusted for SES, neither could the corresponding association that was present only for girls (RD = 20.1%, CI (10.4 to 29.9),  $p < 0.001$ ). Having been threatened, physically harassed or violently hurt was related to suicidal behavior for both girls (RD = 17.6%, CI (6.9 to 28.3),  $p = 0.001$ ) and unadjusted for boys (RD = 12.0%, CI (3.8 to 20.2),  $p = 0.004$ ). There was an association between SES and suicidal behavior (RD = -2.3%, CI (-4.4 to -0.8),  $p = 0.005$ ). Specified by diagnostic groups, associations with suicidal behavior were highly significant for Mood

**Table 3** Negative life events at 3-year follow up

Self-reported questionnaire (T <sub>1</sub> and T <sub>2</sub> ) <sup>a</sup>	Total (n = 570)		Girls (n = 324)				Boys (n = 246)				Girls versus Boys					
	Last 3 years <sup>b</sup>		Ever <sup>b</sup>		Last 3 years		Ever		Last 3 years		Ever		Last 3 years		Ever	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	95% CI <sup>c</sup>	p <sup>d</sup>	95% CI	p
Serious illness of someone in family or death of a loved one	326/565	(57.7)	485/566	(85.7)	204/323	(63.2)	284/323	(87.9)	122/242	(50.4)	201/242	(83.1)	(4.5 to 20.8)	0.002	(-0.9 to 11.0)	0.080
Been seriously ill or injured, received painful or frightening treatment at hospital	126/566	(22.3)	178/566	(31.4)	86/324	(26.5)	123/324	(38.0)	40/242	(16.5)	55/242	(22.7)	(3.1 to 16.6)	0.005	(7.6 to 22.5)	< 0.001
Exposed to a serious accident or catastrophe	74/566	(13.1)	178/566	(31.4)	45/324	(13.9)	120/324	(37.0)	29/242	(12.0)	58/242	(24.0)	(-3.9 to 7.4)	0.506	(5.4 to 20.4)	0.001
Been threatened, physically harassed or violently hurt	124/566	(21.9)	262/566	(46.3)	77/324	(23.8)	160/324	(49.4)	47/242	(19.4)	101/242	(41.7)	(-2.6 to 11.0)	0.216	(-0.6 to 15.8)	0.088
Seen others violently hurt	131/566	(23.1)	241/566	(42.6)	65/324	(20.1)	140/324	(43.2)	66/242	(27.3)	101/242	(41.7)	(-14.4 to -0.2)	0.044	(-6.7 to 9.6)	0.726
Been put in sexually uncomfortable/abusive situations	83/566	(14.7)	163/566	(28.8)	76/324	(23.5)	144/324	(44.4)	7/242	(2.9)	19/242	(7.9)	(15.4 to 25.7)	< 0.001	(29.9 to 42.7)	< 0.001

**Note:** <sup>a</sup> Same questions at both T<sub>1</sub> and T<sub>2</sub>, except for question "Been seriously ill", which was only asked at T<sub>2</sub>

<sup>b</sup> Negative life events defined as "last 3 years" were events measured at T<sub>2</sub> only, and negative life events defined as "ever" were measured at T<sub>1</sub> or T<sub>2</sub>

<sup>c</sup> Newcombe hybrid score

<sup>d</sup> Pearson Chi squared test

**Table 4** Binary linear regression with suicidal ideation at 3-year follow up as dependent variable, and negative life events as covariates

Suicidal ideation <sup>a</sup> at T <sub>2</sub>												
Negative life events	No Neg. life event		Neg. life event		Crude				Adjusted for SES			
	n	n (%)	n (%)	%	RD <sup>b</sup>	95% CI for RD		p value	RD	95% CI for RD		p value
					Lower	Upper		Lower	Upper			
<b>Total sample</b>	549											
Serious illness of someone in family or death of a loved one	535	3/73 <sup>c</sup> (4.1)	63/462 <sup>c</sup> (13.6)	9.5	4.0	15.1	0.001	8.1	0.9	15.2	0.027	
Been seriously ill or injured, received painful or frightening treatment at hospital	536	39/367 (10.6)	27/169 (16.0)	5.3	-1.0	11.7	0.100	8.6	0.9	16.3	0.028	
Exposed to a serious accident or catastrophe	536	40/365 (11.0)	26/171 (15.2)	4.2	-2.0	10.5	0.184	5.5	-2.2	13.3	0.160	
Been threatened, physically harassed or violently hurt	536	26/287 (9.1)	40/249 (16.1)	7.0	1.4	12.7	0.015	8.9	2.0	15.9	0.012	
Seen others violently hurt	536	32/306 (10.5)	34/230 (14.8)	4.3	-1.4	10.1	0.139	5.7	-1.4	12.7	0.115	
Been put in sexually uncomfortable/abusive situations	536	36/383 (9.4)	30/153 (19.6)	10.2	3.3	17.2	0.004	10.4	1.8	19.0	0.018	
SES	385			0.2 <sup>d</sup>	-1.7	2.2	0.820					
<b>Girls</b>	308											
Serious illness of someone in family or death of a loved one	304	2/35 (5.7)	52/269 (19.3)	13.6	4.6	22.6	0.003	12.7	0.8	24.5	0.037	
Been seriously ill or injured, received painful or frightening treatment at hospital	305	30/188 (16.0)	24/117 (20.5)	4.6	-4.5	13.6	0.322	8.4	-2.7	19.6	0.138	
Exposed to a serious accident or catastrophe	305	31/192 (16.2)	23/113 (20.4)	4.2	-4.9	13.3	0.364	7.2	-4.3	18.7	0.221	
Been threatened, physically harassed or violently hurt	305	21/153 (13.7)	33/152 (21.7)	8.0	-0.5	16.5	0.067	11.1	0.2	21.9	0.045	
Seen others violently hurt	305	25/170 (14.7)	29/135 (21.5)	6.8	-2.0	15.5	0.129	9.1	-2.0	20.2	0.109	
Been put in sexually uncomfortable/abusive situations	305	27/170 (15.9)	27/135 (20.0)	4.1	-4.6	12.8	0.354	6.1	-4.9	17.0	0.277	
SES	210			-0.4	-3.6	2.8	0.806					
<b>Boys</b>	241											
Serious illness of someone in family or death of a loved one	231	1/38 (2.6)	11/193 (5.7)	3.1	-3.0	9.1	0.321	0.9	-6.8	8.6	0.821	
Been seriously ill or injured, received painful or frightening treatment at hospital	231	9/179 (5.0)	3/52 (5.8)	0.7	-6.4	7.9	0.838	3.9	-4.9	12.7	0.387	
Exposed to a serious accident or catastrophe	231	9/173 (5.2)	3/58 (5.2)	0.0	-6.6	6.6	0.993	3.0	-8.8	2.8	0.308	
Been threatened, physically harassed or violently hurt	231	5/134 (3.7)	7/97 (7.2)	3.5	-2.6	9.6	0.261	3.6	-3.5	10.7	0.317	
Seen others violently hurt	231	7/136 (5.2)	5/95 (5.3)	0.1	-5.7	6.0	0.969	0.8	-5.9	7.4	0.820	
Been put in sexually uncomfortable/abusive situations	231	9/213 (4.2)	3/18 (16.7)	12.4	-5.0	29.9	0.163	3.2	-11.0	17.4	0.659	
SES	175			1.1	-0.1	2.4	0.072					

**Note:** Binary linear regression is based on paired data displayed in Supplemental Material Table S2. SES Socioeconomic status

<sup>a</sup> Suicidal ideation includes suicidal thoughts occasionally or often

<sup>b</sup> RD is risk difference, the difference between the proportions of patients with suicidal thoughts or behavior and negative life events compared with patients with suicidal thoughts or behavior without negative life event

<sup>c</sup> The numbers in this table, for example 3/73 (4.1) and 63/462 (13.6), indicate that among the 73 patients with no negative life event, 3 had suicidal ideation at T<sub>2</sub>, and among the 462 patients with the negative life event, 63 had suicidal ideation at T<sub>2</sub>

<sup>d</sup> The risk of having suicidal ideation increases with 0.2% per one unit increase in level of mothers education

**Table 5** Binary linear regression with suicidal behavior at 3-year follow up as dependent variable, and negative life events as covariates

Suicidal behavior <sup>a</sup> at T <sub>2</sub>												
Negative life events	No Neg. life event		Neg. life event		Crude				Adjusted for SES			
	n	n (%)	n (%)	%	RD <sup>b</sup>		p value	RD			p value	
					Lower	Upper		Lower	Upper			
<b>Total sample</b>	549											
Serious illness of someone in family or death of a loved one	536	8/73 <sup>c</sup> (11.0)	89/463 <sup>c</sup> (19.2)	8.3	-0.2	16.3	0.043	- <sup>d</sup>	-	-	-	-
Been seriously ill or injured, received painful or frightening treatment at hospital	537	50/368 (13.6)	48/169 (28.4)	14.8	7.2	22.5	< 0.001	10.6	2.8	18.4	0.008	
Exposed to a serious accident or catastrophe	537	52/365 (14.2)	46/172 (26.7)	12.5	5.0	20.0	0.001	10.1	1.9	18.3	0.015	
Been threatened, physically harassed or violently hurt	537	28/287 (9.8)	70/250 (28.0)	18.2	11.7	24.8	< 0.001	16.7	9.5	23.9	< 0.001	
Seen others violently hurt	537	37/306 (12.1)	61/231 (26.4)	14.3	7.6	21.1	< 0.001	10.7	3.4	18.1	0.004	
Been put in sexually uncomfortable/abusive situations	537	46/383 (12.0)	52/154 (33.8)	21.8	13.6	29.9	< 0.001	-	-	-	-	
SES	386			-2.3 <sup>e</sup>	-4.4	-0.8	0.005					
<b>Girls</b>	308											
Serious illness of someone in family or death of a loved one	305	7/35 (20.0)	68/270 (25.2)	5.2	-9.1	19.4	0.476	-	-	-	-	
Been seriously ill or injured, received painful or frightening treatment at hospital	306	37/189 (19.6)	39/117 (33.3)	13.8	3.5	24.0	0.009	7.4	-3.5	18.3	0.184	
Exposed to a serious accident or catastrophe	306	39/192 (20.3)	37/114 (32.5)	12.1	1.8	22.5	0.021	6.3	-5.1	17.6	0.280	
Been threatened, physically harassed or violently hurt	306	22/153 (14.4)	54/153 (35.3)	20.9	11.5	30.3	< 0.001	17.6	6.9	28.3	0.001	
Seen others violently hurt	306	27/170 (15.9)	49/136 (36.0)	20.1	10.4	29.9	< 0.001	14.6	3.4	25.8	0.011	
Been put in sexually uncomfortable/abusive situations	306	27/170 (15.9)	49/136 (36.0)	20.1	10.4	29.9	< 0.001	-	-	-	-	
SES	211			-3.6	-6.5	0.6	0.017					
<b>Boys</b>	241											
Serious illness of someone in family or death of a loved one	231	1/38 (2.6)	21/193 (10.9)	8.3	1.5	15.0	0.016	-	-	-	-	
Been seriously ill or injured, received painful or frightening treatment at hospital	231	13/179 (7.3)	9/52 (17.3)	10.0	-0.9	21.0	0.073	-	-	-	-	
Exposed to a serious accident or catastrophe	231	13/173 (7.5)	9/58 (15.5)	8.0	-2.1	18.1	0.122	11.1	-0.4	22.7	0.152	
Been threatened, physically harassed or violently hurt	231	6/134 (4.5)	16/97 (16.5)	12.0	3.8	20.2	0.004	-	-	-	-	
Seen others violently hurt	231	10/136 (7.4)	12/95 (12.6)	5.3	-2.7	13.3	0.196	5.1	-2.8	13.0	0.206	
Been put in sexually uncomfortable/abusive situations	231	19/213 (8.9)	3/18 (16.7)	7.7	-9.9	25.4	0.390	15.7	-5.8	37.2	0.152	
SES	175			-1.7	-3.4	-0.0	0.047					

Note: Binary linear regression is based on paired data displayed in Supplemental Material Table S3. SES Socioeconomic status

<sup>a</sup> Suicidal behavior includes suicidal acts or attempts, presently at T<sub>2</sub> or ever, also suicidal acts and attempts with suicidal thoughts

<sup>b</sup> RD is risk difference, the difference between the proportions of patients with suicidal thoughts or behavior and negative life events compared with patients with suicidal thoughts or behavior without negative life event

<sup>c</sup> The numbers in this table, for example 3/73 (4.1) and 63/462 (13.6), indicate that among the 73 patients with no negative life event, 3 had suicidal ideation at T<sub>2</sub>, and among the 462 patients with the negative life event, 63 had suicidal ideation at T<sub>2</sub>

<sup>d</sup> Estimates could not be computed due to non-convergence of the calculations

<sup>e</sup> The risk of having suicidal behavior decreases with 2.3% per one unit increase in level of mothers education

disorders and Anxiety disorders ( $p < 0.001$ ) and the group Other disorders ( $p = 0.007$ ), adjusted for SES (data not shown).

There were associations between school dropout and having seen others been violently hurt or been put in sexually uncomfortable/abusive situations, but after adjusting for SES, the associations only persisted for having seen others been violently hurt (RD = 10.8%, CI (2.9 to 18.8),  $p = 0.007$ ), and only among girls (RD = 11.7%, CI (0.5 to 22.9),  $p = 0.041$ ) (Table 6). Results were mainly unchanged when excluding those who gave childbirth ( $n = 6$ ) (data not shown). An association found between suicidal behavior and school dropout was attenuated after adjustment for SES in the total sample (RD = 7.0%, CI (- 3.9 to 17.9),  $p = 0.209$ ).

## Discussion

This study is one of few surveys following a general clinical psychiatric population of adolescents who received standard clinical care, studying symptoms and function over time. Reassessed after 3 years, suicidal ideation and suicidal behavior were frequent, especially among girls, and across all subgroups of psychiatric disorders. Girls had lower psychosocial functioning than boys, and more school dropout. Associations were found between negative life events and suicidal ideation and behavior. Most marked were the associations between suicidal behavior and having been exposed to interpersonal violence for both girls and boys. For girls only, sexually uncomfortable or abusive situations were also related to suicidal ideation and suicidal behavior, as was having seen others been violently hurt. Furthermore, having serious illness of someone in family or death of a loved one were also associated with suicidal ideation for the total sample, and SES was linked to suicidal behavior for both girls and boys. School dropout was associated with having seen others be violently hurt among girls with ADHD.

In our sample assessed 3 years after referral for psychiatric disorders, the prevalence of suicidal ideation and behavior were similar to earlier research on clinical samples [7, 17]. The frequent occurrence of suicidal attempts may reflect that this is a follow up of former patients, with high rates of psychiatric disorders [46], and the results correspond well with earlier research describing that the majority of youth with suicidal behaviors have pre-existing mental disorders [5]. Still, the reasons for the high rates of suicidal ideation and behavior may be diverse, both depending on the persistence of psychiatric disorders [46], treatment given and the general vulnerability of the adolescents in this clinical population. There were large gender differences with girls having much higher rates than boys of both suicidal ideation and behavior, in line with earlier research [5], and especially described in the systematic review of 67

population-based longitudinal studies with focus on gender differences in suicidal behavior in adolescents and young adults [14]. In our study, almost one out of two girls with mood disorders had both suicidal ideation and suicidal behavior, whereas less than one out of four boys with mood disorders had the same symptoms. Boys with ADHD or other psychiatric disorders had the lowest frequencies of suicidal ideation or behavior. This follow up of former adolescent patients underscores the large gender differences and added risk for girls when it comes to suicidal symptoms.

Psychosocial function as measured by CGAS with values in the sub-normal range, indicated better functioning than expected in a clinical sample with frequent comorbidity. The inter-rater reliability was tested and shown to be good. CGAS was lower among girls than among boys, corresponding with earlier findings by Gårdvik et al. [46], showing that female participants had higher rates of psychiatric disorders and seemed to be more prone to develop co-occurring psychiatric disorders and a higher burden of disease. School dropout was also significantly higher among girls compared to boys, which may once again reflect a higher burden of disease among girls in this sample. Earlier research has showed that poor health, and especially mental health, has been significantly associated with dropout of school among adolescents, most marked for boys in higher education [33, 36]. Development and persistence of psychiatric disorders is prone to impact function in school and socialization, with possible long-term consequences [2]. It is therefore crucial to break the cycle at an early stage and hinder maintenance of problems.

The frequencies of experiencing negative life events are in accordance with earlier research reporting associations between psychiatric disorders and earlier negative life events or childhood adversities [54–56]. The most common experiences, in both genders, were serious illness of someone in the family or death of a loved one, reported for eight to nine out of ten adolescents. Almost half of the adolescents had been threatened, physically harassed or violently hurt, or seen others violently hurt, with no gender differences, whereas there were large gender differences in exposure to sexually uncomfortable or abusive situations. Less than one out of ten boys had such experiences, but almost one out of two girls were exposed. The results underline the importance of assessing negative life events among adolescents with psychiatric symptoms and disorders, in order to reveal any such risks, give proper treatment and if possible, prevent further traumatic events.

We examined possible associations between suicidal ideation at follow-up and negative life events. There was a significant association between suicidal ideation and having been threatened, physically harassed or violently

**Table 6** Binary linear regression with school dropout at 3-year follow up as dependent variable, and negative life events as covariate

School dropout <sup>a</sup> at T <sub>2</sub>													
Negative life events	n	No Neg. life event		Neg. life event		Crude			Adjusted for SES				
		n	(%)	n	(%)	RD <sup>b</sup>	95% CI for RD		p value	RD	95% CI for RD		p value
						%	Lower	Upper		%	Lower	Upper	
<b>Total sample</b>	570												
Serious illness of someone in family or death of a loved one	541	9/74 <sup>c</sup>	(12.2)	91/467 <sup>c</sup>	(19.5)	7.3	-1.0	15.6	0.083	5.8	-3.3	15.0	0.213
Been seriously ill or injured, received painful or frightening treatment at hospital	542	67/376	(17.8)	34/166	(20.5)	2.7	-4.6	9.9	0.472	3.3	-4.8	11.4	0.424
Exposed to a serious accident or catastrophe	542	65/371	(17.5)	36/171	(21.0)	3.5	-3.7	10.8	0.339	0.9	-7.1	8.9	0.830
Been threatened, physically harassed or violently hurt	542	43/289	(14.9)	58/253	(22.9)	8.0	1.4	14.7	0.017	6.2	-1.3	13.8	0.106
Seen others violently hurt	542	40/312	(12.8)	61/230	(26.5)	13.7	6.9	20.5	< 0.001	10.8	2.9	18.8	0.007
Been put in sexually uncomfortable/abusive situations	542	59/386	(15.3)	42/156	(26.9)	11.6	3.8	19.5	0.004	7.4	-1.4	16.3	0.100
SES	404					-1.1 <sup>d</sup>	-3.2	1.1	0.319				
<b>Girls</b>	324												
Serious illness of someone in family or death of a loved one	310	5/35	(14.3)	64/275	(23.3)	9.0	-3.7	21.6	0.164	8.2	-5.7	22.2	0.247
Been seriously ill or injured, received painful or frightening treatment at hospital	311	42/195	(21.5)	28/116	(24.1)	2.6	-7.1	12.3	0.600	3.1	-8.1	14.3	0.588
Exposed to a serious accident or catastrophe	311	44/195	(22.6)	26/116	(22.4)	-0.2	-9.8	9.5	0.976	-1.7	-12.6	9.1	0.756
Been threatened, physically harassed or violently hurt	311	30/156	(19.2)	40/155	(25.8)	6.6	-2.7	15.8	0.165	2.2	-8.4	12.7	0.688
Seen others violently hurt	311	28/177	(15.8)	42/134	(31.3)	15.5	6.0	25.1	0.001	11.7	0.5	22.9	0.041
Been put in sexually uncomfortable/abusive situations	311	34/173	(19.7)	36/138	(26.1)	6.4	-3.0	15.9	0.181	3.7	-7.2	14.6	0.505
SES	221					-1.5	-4.8	1.7	0.351				
<b>Boys</b>	246												
Serious illness of someone in family or death of a loved one	231	4/39	(10.3)	27/192	(14.1)	3.8	-6.9	14.5	0.487	2.5	-9.2	14.2	0.674
Been seriously ill or injured, received painful or frightening treatment at hospital	231	25/181	(13.8)	6/50	(12.0)	-1.8	-12.1	8.5	0.731	0.6	-10.8	11.9	0.923
Exposed to a serious accident or catastrophe	231	21/176	(11.9)	10/55	(18.2)	6.3	-5.0	17.5	0.278	1.8	-10.1	13.6	0.770
Been threatened, physically harassed or violently hurt	231	13/133	(9.8)	18/98	(18.4)	8.6	-0.6	17.8	0.067	9.4	-1.5	20.4	0.092
Seen others violently hurt	231	12/135	(8.9)	19/96	(19.8)	10.9	1.6	20.2	0.022	9.3	-1.5	20.1	0.091
Been put in sexually uncomfortable/abusive situations	231	25/213	(11.7)	6/18	(33.3)	21.6	-0.7	43.8	0.057	10.2	-11.7	32.0	0.362
SES	183					-0.7	-3.3	2.0	0.621				

Note: Binary linear regression is based on paired data displayed in Supplemental Material Table S4. SES Socioeconomic status

<sup>a</sup> School dropout includes patients answering yes to the question "Have you canceled your education (dropped out)?"

<sup>b</sup> RD is risk difference, the difference between the proportions of patients with school dropout and negative life events compared with patients with school dropout without negative life event

<sup>c</sup> The numbers in this table, for example 9/74 (12.2) and 91/467 (19.5), indicate that among the 74 patients with no negative life event, 9 had school dropout at T<sub>2</sub>, and among the 467 patients with a negative life event, 91 had school dropout at T<sub>2</sub>

<sup>d</sup> The risk of having school dropout decreases with 1.1% per one unit increase in level of mothers education

hurt in the total sample, but in gender-specific analyses, the association was present only for girls. Suicidal ideation was also associated with exposure to sexually uncomfortable or abusive situations for the total sample, corresponding with earlier research described in the meta-analysis of 50 years of research by Franklin et al. [21]. Furthermore, we found that suicidal ideation was associated with having serious illness of someone in the family or death of a loved one, but only for girls. Losing a loved one by death may be a very stressful event for children and adolescents, and a systematic review and meta-analysis by Howarth et al., found that stressful life events increased the risk of both reported suicidal ideation and behavior [22].

Earlier studies have demonstrated associations between suicidal behavior in adolescents and experiences of negative life events, as described in the systematic review by Serafini et al. [20]. In our study, we found associations between suicidal behavior and all negative life events. There was a strong association between suicidal behavior and having been threatened, physically harassed or violently hurt, for the total sample and for both girls and boys, which is in line with previous research, as described in the meta-analysis by Castellví et al. [25]. Among adolescents, victimization by peers is highly prevalent and associated with increased risk of suicidal attempts, and the longer history of victimization, the greater risk [28]. For girls only, suicidal behavior was related to having seen others violently hurt, as reported in earlier research [27]. Suicidal behavior was furthermore associated with exposure to sexually uncomfortable or abusive situations for girls only. Sexual abuse or violence has been found to be strongly associated to suicide attempts and behavior [27], and contributing the most to suicide attempts in youths and young adults together with bullying [25]. Opposite to suicidal ideations, serious illness of someone in the family or death of a loved one, was associated with suicidal behavior for boys only. This association has been found in earlier research [26, 27], but not specified by gender. Having been seriously ill, injured or received painful or frightening treatment in hospital, was associated with suicidal behavior in the total sample, in line with the meta-analysis of 50 years of research [21]. In the WHO World Mental Health Surveys, a cross-national analysis of the associations between traumatic events and suicidal behavior were investigated, and accidents and disasters were associated with suicidal behavior [27], as also found in our study. A systematic review of population-based studies by Evans et al. [57], found that suicidal phenomena in adolescents were associated with female gender, mental health problems, negative life events and poor family functioning, corresponding well with our findings.

In our clinical sample, an association was found between suicidal behavior and SES, for both girls and boys. The risk of having suicidal behavior decreased for the total sample with 2.3% per unit increase in level of mothers' education. This indicates that SES does have an effect on the presence of suicidal behavior at follow-up, and that higher maternal education may be a protective factor for development of these symptoms. A large national register-based study showed strong associations between SES and suicidal risk [58].

School dropout is related to many different risk factors. A meta-analytic review by Gubbels et al. [41] described 23 risk domains with significant overall effect on school dropout, where mental health problems of the child and adverse childhood experiences were two of these domains. In our sample, we found associations between school dropout and having seen others been violently hurt, among girls only. A recent systematic review and meta-analysis of longitudinal studies by Castellví et al. [40] showed that adolescents and young adults who had school failure were at higher risk of a suicide attempt. In our clinical sample, the association found between suicidal behavior and school dropout in the crude analysis, did not withstand adjustment for SES. Therefore, SES may be a confounding factor for associations between suicidal behavior and school dropout, but may as well reflect larger *p*-values due to lower number of participants with SES information, or that the attrition was not random, i.e. that those with SES information were not representative for the entire sample.

One strength of the present study is the inclusion of a large clinical sample receiving standard clinical care, assessed after 3 years with a high response rate from T<sub>1</sub> to T<sub>2</sub>. Furthermore, suicidal ideation and behavior were assessed in-depth by clinicians during the diagnostic interview, and not based on self-report measures which involves the limitations of less accuracy in establishing psychopathology. Some limitations need to be considered. The attrition rate was high in the initial recruitment, and even though the T<sub>1</sub> sample did not differ in age, gender or reason for referral compared to non-participants, we cannot exclude that this high attrition rate may have affected the results. Since there were more girls than boys among participants compared to non-participants in this study, we may have lost some of the boys with psychiatric disorders, suicidality symptoms and impaired function. Life events and school dropout were measured by self-report only. School dropout was reported by one question, and additional information would have strengthened the measure, either by using several questions or information from other sources, supplemented by asking about the subjective reasons for the respective school dropout. Family characteristics including unemployment and low socioeconomic status

influence mental health in off-spring [59], and may have important influence on many of the negative life events measured in this study, and their associations with suicidal measures or school dropout. Using level of maternal education to indicate socioeconomic status may not enclose the complete concept of socioeconomics, and furthermore, this information was accessible for a reduced sample, which may not reflect the total study population. Also, the reduced sample resulted in reduced power in the association analyses. The fact that some estimates including suicidal behavior could not be computed due to non-convergence of the calculations, was a statistical limitation. Treatment plausibly impact the course of suicidal ideations or behavior, also both general psychosocial function and school dropout, and information on treatment measures would have strengthened this study.

### Clinical implications

The results of this study bring an important message to clinical practice. Even though clinicians know about increasing symptoms of suicidal ideation and behavior during adolescence, the self-reported high rates of suicidal attempts in this patient group should be an extra reminder, also the high rates of school dropout, especially among girls. The burden of exposure to negative life events must also be acknowledged. Comprehensive assessment of mental health problems should of course include important risk factors, and asking adolescent patients about suicidal ideation and behavior, experiences of negative life events and school functioning seems to be important, especially for female psychiatric patients, in order to reveal any such risks and prevent further traumatic events.

### Conclusion

In this clinical sample reassessed after 3 years, one out of four adolescent girls with a persisting psychiatric disorder had suicidal ideations, and one out of three had a previous history of suicidal behavior. Girls had lower psychosocial functioning and higher rates of school dropout and experiences of negative life events than boys. Negative life events, especially exposure to interpersonal violence, were associated with suicidal ideation, suicidal behavior or school dropout. The high frequency of suicidal symptoms, school dropout and experiences of negative life events, indicates a high burden of challenges in functioning. The results reinforce the need to include these symptoms and associated factors in an extensive follow-up of psychiatric disorders in this age group.

### Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12888-021-03100-w>.

**Additional file 1: Table S1** Design matrix for the re-scoring of telephone interviews. **Table S2** Suicidal ideation T<sub>2</sub> and Negative life events. **Table S3** Suicidal behavior T<sub>2</sub> and Negative life events. **Table S4** School dropout T<sub>2</sub> and Negative life events

### Abbreviations

K-SADS: Kiddie SADS: Schedule for Affective Disorders and Schizophrenia for School-Age Children; DSM-IV-TR: Diagnostic and Statistical Manual of Mental Disorders IV Text revision; ADHD: Attention Deficit Hyperactivity Disorder; CGAS: Children's Global Assessment Scale; SES: Socioeconomic status; RD: Risk difference; CI: Confidence interval

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### Authors' contributions

KSG reviewed the literature, drafted and revised the manuscript, performed and interpreted statistical analyses, with substantial contribution by MSI in the entire process. SL contributed to performing and interpreting the statistical analyses, in addition to being involved in revising the manuscript. TT and MR participated in designing the study and made substantial contributions in revising the manuscript critically. All authors read and approved the final manuscript.

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### Availability of data and materials

The datasets analyzed during the current study are not publicly available due to privacy policy, but they are available from the corresponding author on reasonable request.

### Ethics approval and consent to participate

Written informed consent was obtained from adolescents and parents participating at T<sub>1</sub> and T<sub>2</sub>, according to study procedures. Study approval was given by the Regional Committee for Medical and Health Research Ethics of Central Norway (REK Midt) (reference numbers CAP survey T<sub>1</sub>: 4.2008.1393, T<sub>2</sub>: 2011/1435/REK Midt, and present study using T<sub>1</sub> and T<sub>2</sub> data: 2017/589/REK Midt). The Norwegian Social Science Data Services, The Data Protection Official for Research, gave permission to compare the main reason for referral, age and sex between participants and non-participants at baseline (reference number CAP survey: 19976). The research followed the agreement of the ethical standards in the Declaration of Helsinki from 1964 and later amendments, and we confirm that all methods were performed in accordance with relevant guidelines and regulations.

### Consent for publication

Not applicable.

### Competing interests

The authors declare that they have no competing interest.



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## Supplementary Material

### Inter-rater reliability for the CGAS ratings:

The IRR study was designed as follows: Seven of the interviewers were used as second opinion raters for taped telephone interviews. Each of these seven re-scored four interviews performed by four of the other six interviewers. Hence, the number of re-scored patients were  $7 \times 4 = 28$ . The design was constructed as shown in Table S1, to be as balanced as possible.

**Table S1 Design matrix for the re-scoring of telephone interviews**

		Second rater							Sum
		B	C	E	D	F	G	A	
First rater	B		1	1	1	1			4
	C	1		1	1		1		4
	E				1	1	1	1	4
	D	1	1				1	1	4
	F	1			1		1	1	4
	G		1	1		1		1	4
	A	1	1	1		1			4
	Sum	4	4	4	4	4	4	4	28

The CGAS score is a continuous variable. We used a mixed effect model with rating number (first or second opinion) as fixed effect, and with individual and rater as random factors, to estimate the intraclass correlation coefficient (ICC). In this design, the raters are crossed with individuals (not nested within individuals), as illustrated in (Rabe-Hesketh & Skrondal 2012) page 98 (1). ICC analyses were carried out using Stata 13.

In the mixed effect model, the average CGAS score for rating number 1 was 74.07. For rating 2, the average score was 1.43 ( $p=0.31$ ) higher. There are 3 variance components (given the fixed effect of rating number):

Individual to be rated:  $187.0117 = 13.675^2$

Rater:  $9.789 = 3.129^2$

Residual:  $27.120 = 5.208^2$

The total variance is

$187.0117 + 9.789 + 27.120 = 223.9209 = 14.964^2$

It follows (Rabe-Hesketh & Skrondal 2012, page 437-441) that the between rater, within individual intraclass correlation estimate is

$13.675^2 / 14.964^2 = 0.835$

The variance between the raters was not statistically significant (Likelihood ratio test  $p=0.19$ ). That is, there was no evidence that some raters tended to give systematically higher scores than others with respect to CGAS.

1. Rabe-Hesketh S, Skrondal A. Multilevel and longitudinal modeling using Stata: STATA press; 2008.

**Table S2 Suicidal ideation (SI) T<sub>2</sub> and Negative life events (NLE)**

	Negative life events	n	No SI and No NLE	Yes SI and No NLE	No SI and Yes NLE	Yes SI and Yes NLE
<b>Total (n=549)</b>	Serious illness of someone in family or death of a loved one	535	70	3	399	63
	Been seriously ill or injured, received painful or frightening treatment at hospital	536	328	39	142	27
	Exposed to a serious accident or catastrophe	536	325	40	145	26
	Been threatened, physically harassed or violently hurt	536	261	26	209	40
	Seen others violently hurt	536	274	32	196	34
	Been put in sexually uncomfortable/abusive situations	536	347	36	123	30
	<b>Girls (n=308)</b>	Serious illness of someone in family or death of a loved one	304	33	2	217
Been seriously ill or injured, received painful or frightening treatment at hospital		305	158	30	93	24
Exposed to a serious accident or catastrophe		305	161	31	90	23
Been threatened, physically harassed or violently hurt		305	132	21	119	33
Seen others violently hurt		305	145	25	106	29
Been put in sexually uncomfortable/abusive situations		305	143	27	108	27
<b>Boys (n=241)</b>		Serious illness of someone in family or death of a loved one	231	37	1	182
	Been seriously ill or injured, received painful or frightening treatment at hospital	231	170	9	49	3
	Exposed to a serious accident or catastrophe	231	164	9	55	3
	Been threatened, physically harassed or violently hurt	231	129	5	90	7
	Seen others violently hurt	231	129	7	90	5
	Been put in sexually uncomfortable/abusive situations	231	204	9	15	3

**Table S3 Suicidal behavior (SB) T<sub>2</sub> and Negative life events (NLE)**

	Negative life events	n	No SB and No NLE	Yes SB and No NLE	No SB and Yes NLE	Yes SB and Yes NLE
<b>Total (n=549)</b>	Serious illness of someone in family or death of a loved one	536	65	8	374	89
	Been seriously ill or injured, received painful or frightening treatment at hospital	537	318	50	121	48
	Exposed to a serious accident or catastrophe	537	313	52	126	46
	Been threatened, physically harassed or violently hurt	537	259	28	180	70
	Seen others violently hurt	537	269	37	170	61
	Been put in sexually uncomfortable/abusive situations	537	337	46	102	52
	<b>Girls (n=308)</b>	Serious illness of someone in family or death of a loved one	305	28	7	202
Been seriously ill or injured, received painful or frightening treatment at hospital		306	152	37	78	39
Exposed to a serious accident or catastrophe		306	153	39	77	37

	Been threatened, physically harassed or violently hurt	306	131	22	99	54
	Seen others violently hurt	306	143	27	87	49
	Been put in sexually uncomfortable/abusive situations	306	143	27	87	49
<b>Boys (n=241)</b>	Serious illness of someone in family or death of a loved one	231	37	1	172	21
	Been seriously ill or injured, received painful or frightening treatment at hospital	231	166	13	43	9
	Exposed to a serious accident or catastrophe	231	160	13	49	9
	Been threatened, physically harassed or violently hurt	231	128	6	81	16
	Seen others violently hurt	231	126	10	83	12
	Been put in sexually uncomfortable/abusive situations	231	194	19	15	3

**Table S4 School dropout (SD) T<sub>2</sub> and Negative life events (NLE)**

	Negative life events	n	No SD and No NLE	Yes SD and No NLE	No SD and Yes NLE	Yes SD and Yes NLE
<b>Total (n=570)</b>	Serious illness of someone in family or death of a loved one	541	65	9	376	91
	Been seriously ill or injured, received painful or frightening treatment at hospital	542	309	67	132	34
	Exposed to a serious accident or catastrophe	542	306	65	135	36
	Been threatened, physically harassed or violently hurt	542	246	43	195	58
	Seen others violently hurt	542	272	40	169	61
	Been put in sexually uncomfortable/abusive situations	542	327	59	114	42
<b>Girls (n=324)</b>	Serious illness of someone in family or death of a loved one	310	30	5	211	64
	Been seriously ill or injured, received painful or frightening treatment at hospital	311	153	42	88	28
	Exposed to a serious accident or catastrophe	311	151	44	90	26
	Been threatened, physically harassed or violently hurt	311	126	30	115	40
	Seen others violently hurt	311	149	28	92	42
	Been put in sexually uncomfortable/abusive situations	311	139	34	102	36
<b>Boys (n=246)</b>	Serious illness of someone in family or death of a loved one	231	35	4	165	27
	Been seriously ill or injured, received painful or frightening treatment at hospital	231	156	25	44	6
	Exposed to a serious accident or catastrophe	231	155	21	45	10
	Been threatened, physically harassed or violently hurt	231	120	13	80	18
	Seen others violently hurt	231	123	12	77	19
	Been put in sexually uncomfortable/abusive situations	231	188	25	12	6

# Paper III



RESEARCH

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# Association of treatment procedures and resilience to symptom load three-years later in a clinical sample of adolescent psychiatric patients



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## Abstract

**Background:** We aimed to examine symptom load in a clinical adolescent population at three-year follow-up and explore associations with standard care treatment procedures and resilience factors upon first presenting at Child and Adolescent Mental Health Services.

**Methods:** This study is part of a prospective longitudinal cohort study: The Health Survey in Department of Children and Youth, St. Olavs hospital, Norway. A clinical population of 717 (43.5% of eligible) adolescents aged 13–18 years participated in the first study visit (T<sub>1</sub>, 2009–2011). Of these, 447 adolescents with psychiatric disorders, with treatment history from medical records and self-reported resilience factors (Resilience Scale for Adolescents; READ) at T<sub>1</sub>, reported symptom load (Achenbach System of Empirically Based Assessment - Youth Self Report; YSR) three years later aged 16–21 years (T<sub>2</sub>).

**Result:** At T<sub>1</sub>, 93.0% received individual treatment. The frequency of psychotherapy and medication varied by disorder group and between genders. Overall, psychotherapy was more frequent among girls, whereas medication was more common among boys. Total READ mean value (overall 3.5, SD 0.8), ranged from patients with mood disorders (3.0, SD 0.7) to patients with Attention Deficit Hyperactivity disorder (3.7, SD 0.7), and was lower for girls than boys in all diagnostic groups. At T<sub>2</sub>, the YSR Total Problem mean T-score ranged across the diagnostic groups (48.7, SD 24.0 to 62.7, SD 30.2), with highest symptom scores for those with mood disorders at T<sub>1</sub>, of whom 48.6% had T-scores in the borderline/clinical range ( $\geq 60$ ) three years later. Number of psychotherapy sessions was positively associated and Total READ score was negatively associated with the YSR Total Problems T-score (regression coefficient  $\beta = 0.5$ , CI (0.3 to 0.7),  $p < 0.001$  and  $\beta = -15.7$ , CI (-19.2 to -12.1),  $p < 0.001$ , respectively). The subscale Personal Competence was associated with the lowest Total Problem score for both genders.

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**Conclusions:** Self-reported symptom load was substantial after three years, despite comprehensive treatment procedures. Higher self-reported resilience characteristics were associated with lower symptom load after three years. These results highlight the burden of adolescent psychiatric disorders, the need for extensive interventions and the importance of resilience factors for a positive outcome.

**Keywords:** Mental disorders, Adolescent, Treatment, Resilience, Symptom load

## Background

In the transition from adolescence to adulthood, there is an expansion in overall rates of psychiatric disorders [1, 2]. Frequently occurring psychiatric disorders in adolescence are often precursors and strong predictors of comparable disorders in young adulthood [1, 3]. The high degree of continuity of psychopathology from adolescence into young adulthood indicates that the perceived symptom load may be substantial [3, 4]. According to a Lancet report in 2011, psychiatric disorders are the most prominent reason for the global burden of disease in young people [5]. Targeted treatment of psychiatric disorders among adolescents is therefore crucial, and treatment outcomes of standard clinical care is consequently of great interest.

Psychotherapy is often recommended as the first choice of treatment for young people suffering from specific psychiatric disorders. A multilevel meta-analysis synthesizing five decades of cumulative knowledge on effects of youth psychotherapy, states that the impact of therapy differs markedly by target problem, showing larger treatment effects for anxiety than for other problems, and most disappointing effects for depression [6]. As an example of a psychotherapy method widely used for adolescents, cognitive behavioral therapy (CBT) has been a recommended treatment for anxiety disorders, with many studies showing positive effect [7, 8]. However, a Cochrane review from 2020 concluded that CBT was no more effective than non-CBT active control treatments or treatment as usual [9]. Results from the Child/Adolescent Anxiety Multimodal Extended Long-Term Study (CAMELS) found that treatment type was not associated with remission status across the follow-up [10]. Likewise, even though many new treatment methods have been developed for depression during the past decades, their effectiveness has not improved over time [11], according to a meta-analysis of 13-year follow-up of psychotherapy effects on youth depression [12].

As comorbidity of psychiatric disorders is frequent in adolescence [13, 14], especially in clinical samples [15], treatment often needs to involve compound procedures. Also, severe disorders require comprehensive treatment interventions [16–18]. Some transdiagnostic psychotherapy methods have been developed designed to address symptoms of different diagnostic clusters [19, 20]. These have been found to exceed effects of standard

manualized treatments with clinically referred youths [21]. The medications for psychiatric disorders are in principle the same for children and adolescents as for adults, but with stricter guidelines. Attention Deficit Hyperactivity disorder (ADHD) is the most common disorder for which medication is recommended [22–24], showing good efficacy and tolerability for children and adolescents [25]. Moreover, antidepressants are often used for mood and anxiety disorders, with selective serotonin reuptake inhibitors (SSRI) as the preferred treatment for children and adolescents [26]. The differences in effect between psychotherapy and antidepressant medication have been found to be small to non-existent in the treatment of adult depression and anxiety disorders [27]. A combination of psychotherapy and pharmacotherapy is the treatment of choice for patients with adult depression [16, 28], but the evidence is limited for children and adolescents [29, 30].

Resilience factors may have implications for the course of treatment, as previous research has found that patients with higher baseline resilience scores, showed less severe psychiatric symptoms after psychotherapeutic interventions [31–33]. Resilience can be referred to as positive adaptation to risk exposure [34] and a more positive psychological outcome than would be expected in case of high levels of environmental adversities [35]. Factors that promote resilience may be categorized into positive individual factors, such as personal and social competence, and may include cognitive factors such as intelligence, personal skills, temperament, and self-esteem [36–38]. Resilience factors can also be contributed at the familial and external social levels, such as family cohesion and support, and social resources and supportive environment outside the family [36–38]. These factors may affect developmental courses of psychiatric disorders and contribute to a better outcome [39, 40]. As previously found in a group of youth with ADHD in the present clinical population, personal resilience characteristics were associated with better psychosocial functioning and less depression and anxiety [41]. In another study of adolescents, higher resilience scores predicted lower scores on levels of depression, anxiety, and obsessive-compulsive symptoms [42], and optimal outcomes of child and adolescent psychiatric disorders are predicted by a combination of personal characteristics and environmental support [43].



Resilience factors may differ between girls and boys in adolescence. Boys compared to girls have reported higher personal competence [36, 38, 44, 45] and social competence [38, 40], whereas girls have reported more access to social resources, which includes supportive family and friends [36, 38, 45]. Furthermore, boys have scored higher on perceived family cohesion than girls [38, 40, 44, 45]. These studies have investigated gender differences in resilience factors in the general population.

The motivation for the present study was to advance knowledge on the progress of psychiatric symptoms in a clinical adolescent population who had received standard care either in out- or inpatient setting in the Child and Adolescent Mental Health Services (CAMHS). Earlier research on the course of symptoms and treatment outcome is mainly conducted on patients with selected psychiatric disorders, recruited to treatment studies. As the impact of therapy differs markedly by target problem [6], research on symptom development must be differentiated by psychiatric disorders. Furthermore, resilience factors may affect psychiatric outcome, but as research on these factors in relation to psychiatric symptoms are primarily carried out in the general population or in specific diagnostic groups, knowledge is scarce about the significance of resilience factors in a general clinical population of adolescents.

The overriding aim of this study was to examine whether psychiatric symptom load three years later was related to the treatment procedures received and resilience factors upon first presenting at mental health clinics for adolescents. We describe characteristics of treatment received in standard adolescent mental health care and symptom load three years later. We hypothesized that symptom load remained substantial and that disorder specific treatment procedures were analogues for girls and boys. Additionally, we hypothesized that having received more psychotherapy sessions or medication was associated with higher symptom load three years later, indicating the large burden of symptoms in this group of former patients. Further, we describe self-reported resilience measures at baseline, specified by psychiatric disorders and gender. We hypothesized that higher resilience factors at baseline was associated with lower symptom load three years later and that boys would report higher resilience factors in personal and social competence domains, whereas girls would report higher social resources.

## Method

### Study design

The study is part of the Health Survey in Department of Children and Youth, Clinic of Mental Health Care, St. Olav's hospital, Trondheim University Hospital, Norway

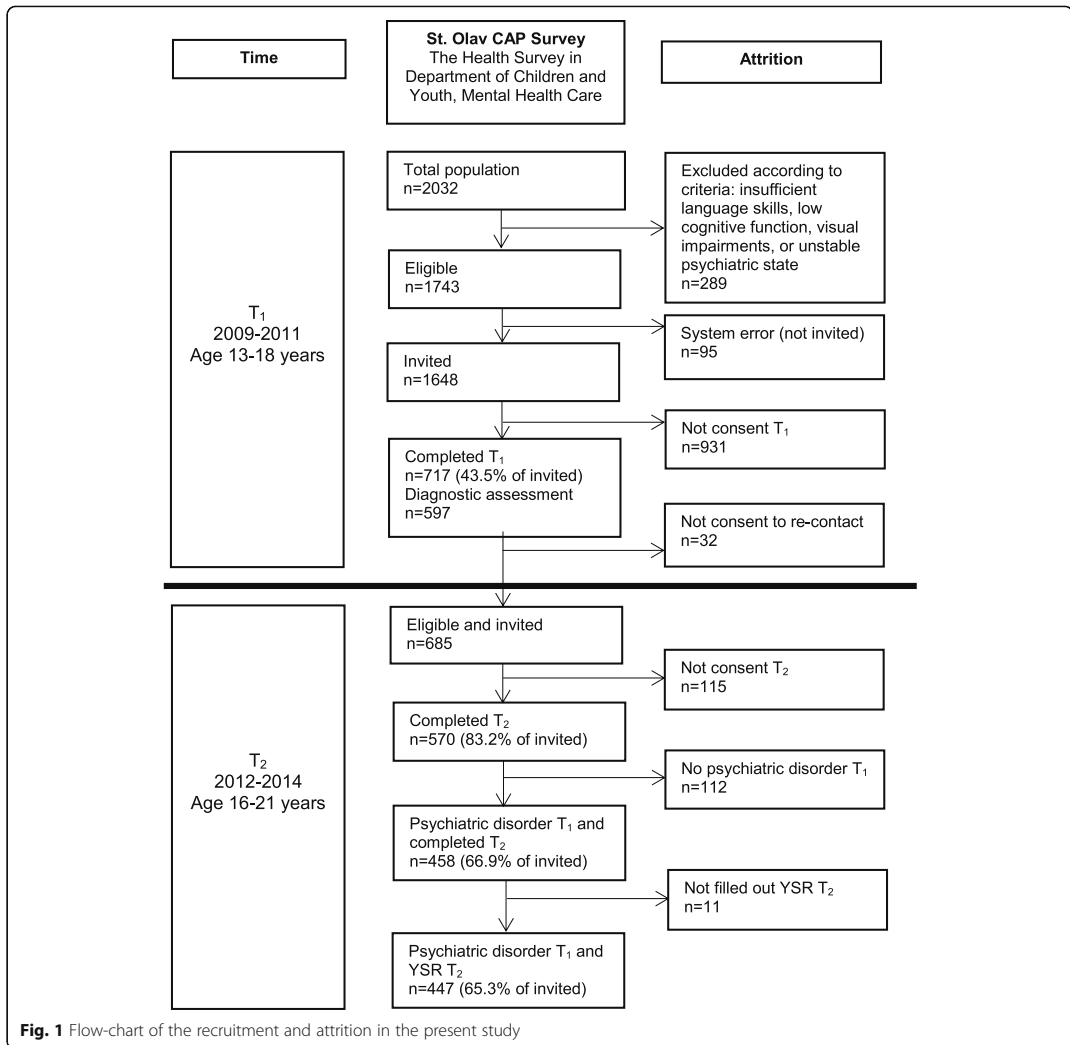
(St. Olav CAP Survey), a prospective longitudinal cohort study of a defined clinical population assessed at two time points. At time point 1 ( $T_1$ ) (2009–2011), all patients aged 13–18 years who visited the Department of Children and Youth at least once over a 2-year period were invited at their first attendance. The exclusion criteria were difficulties in answering the survey due to insufficient language skills, low cognitive function, visual impairments, or unstable psychiatric state. Emergency patients were invited to take part once they entered a stable phase. The study design is detailed in a previous publication [15]. The participants and their parents received standard application of mental health services. At 3-year follow-up ( $T_2$ ) (2012–2014), age 16–21 years, data were collected from the  $T_1$  enrolled sample and their parents, by an electronic survey and a diagnostic telephone interview performed by trained professionals.

### Participants

In the  $T_1$  study period, 2032 adolescent patients had at least one attendance in the Department of Children and Youth. Figure 1 illustrates the participant flow in each stage of the survey. Among the possible participants in the study period ( $n = 2032$ ),  $n = 289$  were excluded, and  $n = 1743$  were eligible. Since  $n = 95$  were lost to registration (missing),  $n = 1648$  (81.1%) were invited. Of these,  $n = 717$  (43.5%) participated (393, 54.8% girls), and  $n = 931$  (56.5%) declined or did not respond to the invitation. The representativeness of the study population at  $T_1$  has been investigated in a previous publication, including in depth attrition analyses [15]. Of the  $T_1$  participants,  $n = 597$  had completed diagnostic assessment investigating the reason for referral. The number of participants by single-year age-groups were: 13 years:  $n = 79$  (17.7%), 14 years:  $n = 87$  (19.5%), 15 years:  $n = 80$  (17.9%), 16 years:  $n = 83$  (18.6%), 17 years:  $n = 82$  (18.3%), 18 years:  $n = 36$  (8.0%). At  $T_2$ , all  $T_1$  participants who previously consented to further inquiry were invited (eligible  $n = 685$ ), and 570 (83% of eligible) completed the follow-up questionnaire (324, 56.8% girls). The present study included the 447 (65.3% of invited) participants who had a psychiatric disorder at  $T_1$  and had filled out YSR at  $T_2$  (254, 56.8% girls). Comparing participants versus non-participants at  $T_2$ , the proportion of girls was higher among participants, while age and socioeconomic status were similar.

### Measures

**Psychiatric Diagnoses** at  $T_1$  were set in ordinary clinical practice according to the International Statistical Classification of Disease and Related Health Problems (ICD-10) multiaxial diagnostics (axes I–VI) [46]. The diagnostic process followed standardized procedures for assessment and diagnosis of common adolescent



psychiatric disorders, depending upon a comprehensive developmental history and interviews with the adolescents and their parents. The semi-structured Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS) [47] was used in some cases, and in others The Development And Well-Being Assessment (DAWBA) [48] and diverse rating scales appropriate for the presenting problem were used. The diagnoses were set by a clinical psychologist or a child and adolescent psychiatrist, both of which are qualified to set diagnoses in CAMHS in Norway, based on all accessible clinical information, after consensus discussion with other professionals from the multi-disciplinary team. Somatic

examinations were added to the assessments if indicated, and possible coexisting disorders were investigated.

In the present study, disorders were grouped into the following categories, based on ICD-10 diagnoses at T<sub>1</sub>; (1) Any psychiatric disorder, (2) Anxiety disorders (ICD-codes F40-F44, F48, F93), (3) Mood disorders (ICD-codes F31-F34, F38, F39), (4) ADHD (ICD-code F90) and (5) Other (ICD-codes F10-F19, F20-F21, F28-F29, F50, F54, F59-F60, F84, F91-F92, F94-F95, F98). Due to few participants in some diagnostic groups, for example autism and eating disorders, we chose to merge these diagnoses into one larger group of “other psychiatric disorders”.

**Treatment** given at T<sub>1</sub> was registered in medical records by type (cognitive, neurobiological, psychodynamic, psychoeducational, social-relational, medication), participant (individual, group, parent, family), number of sessions, duration of treatment, in-patient or out-patient, indirect patient work by counselling municipal services, giving consultations to service agencies already engaged with the patient. In this study, we classified treatment procedures into psychotherapy (specified or unspecified, and divided into numbers of sessions given; < 10, 10–30, > 30), medication according to Anatomical Therapeutic Chemical (ATC) codes, counselling parents/family therapy and counselling municipal services, all classified as present or not (Yes/No). Treatment were provided according to guidelines for specific diagnosis.

**Resilience** factors were measured at T<sub>1</sub> using the Resilience Scale for Adolescents (READ), a self-report questionnaire measuring the ability to manage stress and negative experiences [36]. READ is a 28-item scale with positively formulated items organized in five subscales: Personal Competence, Social Competence, Structured Style, Family Cohesion and Social Resources. READ is based on the Resilience Scale for Adults [49] and was developed in Norway in 2006 with a 5-point Likert-type response scale from 1 = Totally Disagree to 5 = Totally Agree. Higher scores on the READ indicate higher level of resilience factors. The READ scale is widely used in research and has shown good psychometric properties in validation studies [38, 45]. In this study, we used mean item scores for each scale (values between 1 and 5). Internal consistency measured as Cronbach's alpha for the subscales was .89 (Personal Competence), .84 (Social Competence), .73 (Structured Style), .91 (Family Cohesion), and .84 (Social Resources), which would be generally regarded in the range from acceptable to excellent [50].

**Psychiatric symptom load** at T<sub>2</sub> was investigated using the Achenbach System of Empirically Based Assessment – Youth Self Report (YSR) [51]. This is a screening instrument for emotional and behavioral symptoms, designed to assess a broad array of psychopathological manifestations in adolescents, consisting of both a competence scale and a problem scale. For the purpose of this study, the latter was used, consisting of 103 problem items, rated on a 3-point scale (0 = not true; 1 = somewhat or sometimes true; 2 = very true or often true), during the past six months. In this study, Total problems T-score was used as the measure of symptom load at T<sub>2</sub>, with cut-off at scores  $\geq 60$  as borderline/clinical range, and  $< 60$  as normal range, as recommended in the manual [51]. The scale has shown good psychometric properties and is widely used in research and clinical services in different populations [52, 53].

**Socioeconomic Status (SES)** was measured at T<sub>1</sub> by the mothers' highest level of education, categorized in eight levels: (1) less than 9-year primary school; (2) completed 9-year primary school; (3) one or two years in high school; (4) completed high school; (5) completed high school and one-year education/training after high school; (6) academy/university for up to and including four years; (7) academy/university for five years or more; (8) academy/university including PhD.

#### Statistical analyses

In this study, distributions were checked for normality using Q-Q Plots. Confidence intervals and tests for differences in age, SES, symptom load and resilience measures between girls and boys were based on Student's *t*-test for independent samples. We compared proportions of treatment measures between girls and boys by using the Newcombe hybrid score confidence intervals, as recommended [54], and the Pearson Chi squared test. Linear regression was used with symptom load at T<sub>2</sub> as dependent variable and resilience and treatment procedures reported at T<sub>1</sub> as covariates, one at a time, to study their associations. These regression analyses were accomplished adjusted for age at T<sub>1</sub> and SES as possible confounders. We have reported 95% confidence intervals (CI) where relevant, and two-sided *p*-values  $< 0.05$  were considered statistically significant. However, due to testing multiple hypotheses and thus the possibility of Type I error, *p*-values between 0.01 and 0.05 should be interpreted critically. The Newcombe CI were calculated in Stata 16, and the other calculations in SPSS 27.

#### Ethics

Written informed consent was obtained from adolescents and parents prior to inclusion at T<sub>1</sub>, and from the adolescents at T<sub>2</sub>, according to study procedures. The Norwegian Social Science Data Services, The Data Protection Official for Research, gave permission to investigate the representativeness of the study at T<sub>1</sub> (reference number: 19976). Study approval was given by the Regional committee for Medical and Health Research Ethics of Central Norway (reference numbers CAP survey T<sub>1</sub>: 4.2008.1393, T<sub>2</sub>: 2011/1435/REK Midt, and present study using T<sub>1</sub> and T<sub>2</sub> data: 2017/589/REK Midt).

## Results

### Descriptive information

The 447 participants had mean age at T<sub>1</sub>: 15.7 years (SD 1.7) and T<sub>2</sub>: 18.5 years (SD 1.6). Girls were significantly older than boys at both time points (16.0 years (SD 1.7) vs 15.3 years (SD 1.6),  $p < 0.001$ , and 19.0 years (SD 1.7) vs 18.3 years (SD 1.6),  $p < 0.001$ , respectively). SES was measured at T<sub>1</sub> ( $n = 327/447$ ): Mean 4.9 (SD 1.7), for girls ( $n = 181/254$ ) 4.9 (SD 1.7) and boys ( $n = 146/193$ )

4.8 (SD 1.7). At  $T_1$ , ADHD was the most frequent diagnostic group (46.3%) in the total sample, followed by anxiety disorder (33.8%) and mood disorder (23.9%), when both primary and additional diagnoses were included. Anxiety disorder (40.5%) was the most frequent diagnostic group among girls, and ADHD (62.2%) was among boys (Table 1). Comorbid psychiatric disorders were found among 30.2% of the participants, with no gender differences (data not shown).

### Treatment procedures

Frequency of different treatment procedures are presented in Table 1. In the total sample, 93.0% received individual treatment. The frequency of psychotherapy sessions varied by disorder group: Among patients with ADHD, 50.5% received less than 10 sessions, while patients with mood disorders and anxiety disorders received the highest number of sessions; 19.8 and 19.7% respectively received more than 30 sessions. Medication was most frequent in the ADHD group (81.2%). The rates of parent counselling or family therapy were between 60.8 and 76.5% in the total sample, with the highest rate for anxiety disorders, with no difference between genders. Counselling municipal services was provided for 49.1% in the total sample.

Gender comparisons in treatment procedures are shown in Table S2. Psychotherapy was more frequent among girls overall (RD = 18.9, CI (11.2 to 26.4),  $p < 0.001$ ), as well as in all groups of psychiatric disorders, with the largest gender difference occurring in the group of other psychiatric disorders. Medication was significantly less common for girls versus boys overall (RD = -18.4, CI (-27.3 to -9.1),  $p < 0.001$ ) and in the group of other psychiatric disorders. There was no gender difference for ADHD medication.

### Resilience factors

As shown in Table 2, Total READ mean value was 3.5 (SD 0.8) for patients with any psychiatric disorder, ranging from 3.0 (SD 0.7) for patients with mood disorders to 3.7 (SD 0.7) for patients with ADHD. Girls had lower total READ mean values than boys for any disorder and for all disorder groups except for mood disorders. The subscale Personal Competence showed the largest gender differences, with statistically significantly higher mean values for boys than girls, in all diagnostic groups (Table S3).

### Psychiatric symptom load after three years

In the total sample, the YSR Total Problem mean T-score at  $T_2$  ranged from 48.6 (SD 26.3) to 62.7 (SD 28.0) across the diagnostic groups. The highest symptom scores were for those with mood disorders at  $T_1$ , of whom 48.6% had T-scores in the borderline/clinical

range ( $\geq 60$ ) three years later (Table 3). Comparing the T-scores for participants with and without a diagnosis at  $T_2$  ( $n_{\text{diagnosis}} = 314$ ,  $n_{\text{no diagnosis}} = 108$ ), the mean T-scores were 55.5 (SD 26.8) versus 34.0 (SD 18.3), respectively. The YSR scores were significantly higher among girls than among boys in all diagnostic groups, especially in the groups of mood disorders and other psychiatric disorders (Mean difference 24.8, CI (6.7 to 11.6),  $p < 0.001$  and 25.2, CI (14.2 to 36.2),  $p < 0.001$ , respectively) (Table 3). The gender differences were present when comparing the T-scores for participants with or without a diagnosis at  $T_2$ , with girls ( $n_{\text{diagnosis}} = 182$ ,  $n_{\text{no diagnosis}} = 57$ ) having mean T-scores of 64.5 (SD 26.4) versus 38.6 (SD 18.2), and boys ( $n_{\text{diagnosis}} = 132$ ,  $n_{\text{no diagnosis}} = 51$ ) mean T-scores 43.1 (SD 21.9) versus 28.7 (SD 17.0), respectively.

### Associations between treatment characteristics and symptom load 3 years later

Older age and lower SES were significantly associated with higher symptom load at 3-year follow-up in the total sample (Age  $T_2$ : regression coefficient  $\beta = 2.5$ , CI (1.1 to 4.0),  $p = 0.001$ ; SES:  $\beta = -2.1$ , CI (-3.7 to -0.5),  $p = 0.012$ ), and for girls only (Age  $T_2$ :  $\beta = 2.2$ , CI (0.2 to 4.2),  $p = 0.033$ ; SES:  $\beta = -2.9$ , CI (-5.3 to -0.6),  $p = 0.014$ ). Linear regression analysis with YSR Total Problem T-score at  $T_2$  as dependent variable and treatment procedures as covariates were therefore performed adjusted for age and SES.

There was a statistically significant positive association between having received psychotherapy at  $T_1$  and symptom load three years later for the total sample for any psychiatric disorder ( $\beta = 9.9$ , CI (2.4 to 17.4),  $p = 0.010$ ). When increasing the number of psychotherapy sessions in the total sample by 1 session, the YSR Total Problems T-score increased with 0.5 units ( $\beta = 0.5$ , CI (0.3 to 0.7),  $p < 0.001$ ) (Table 4). This association was present only for participants with a diagnoses at  $T_2$  ( $n_{\text{diagnosis}} = 314$ ,  $\beta = 0.6$ , CI (0.4 to 0.9),  $p < 0.001$ ), ( $n_{\text{no diagnosis}} = 108$ ,  $\beta = 0.1$ , CI (-0.2 to 0.4),  $p = 0.519$ ). The significant associations were found in all diagnostic groups except for mood disorders (Table 4). The significant associations were found for girls with anxiety disorders and ADHD, as well as any psychiatric disorders.

Medication prescribed at  $T_1$  was not statistically significantly associated with symptom load three years later for the total sample (Table 4). For boys only, medication was associated with an increased YSR Total Problem T-score of over 7 at follow-up for any psychiatric disorder ( $\beta = 7.4$ , CI (0.7 to 14.2),  $p = 0.032$ ), but no statistically significant associations were found when specifying by psychiatric disorders. No statistically significant associations were found between counselling parents or counselling municipal services and symptom load at follow-up (data not shown).

**Table 1** Outpatient treatment procedures at T<sub>1</sub> differentiated by psychiatric disorders, including comorbid disorders at T<sub>1</sub>, overall and separately for girls and boys

Psychiatric disorders <sup>a</sup> T <sub>1</sub>		Outpatient treatment procedures T <sub>1</sub>														
		Individual treatment procedures										Counselling				
		Any individual treatment		Psychotherapy <sup>b</sup>						Medication <sup>c</sup>		Parents/family therapy		Municipal services		
		n	(%)	< 10 sessions		10–30 sessions		> 30 sessions		n	(%)	n	(%)	n	(%)	
<b>Total sample</b>																
Any psych disorder	447		414/445	(93.0)	177/424	(41.7)	120/424	(28.3)	53/424	(12.5)	236/445	(53.0)	295/438	(67.4)	214/436	(49.1)
Anxiety disorders	151/447	(33.8)	139/150	(92.7)	46/142	(32.4)	58/142	(40.8)	28/142	(19.7)	56/150	(37.3)	114/149	(76.5)	76/149	(51.0)
Mood disorders	107/447	(23.9)	99/106	(93.4)	28/101	(27.7)	45/101	(44.6)	20/101	(19.8)	52/106	(49.1)	71/105	(67.6)	42/105	(40.0)
ADHD	207/447	(46.3)	199/207	(96.1)	99/196	(50.5)	35/196	(17.9)	14/196	(7.1)	168/207	(81.2)	131/203	(64.5)	116/203	(57.1)
Other psych disorders	99/447	(22.1)	89/99	(89.9)	35/93	(37.6)	28/93	(30.1)	15/93	(16.1)	46/99	(46.5)	59/97	(60.8)	48/95	(50.5)
<b>Girls</b>																
Any psych disorder	254		239/253	(94.5)	88/242	(36.4)	87/242	(36.0)	44/242	(18.2)	114/253	(45.1)	172/250	(68.8)	117/248	(47.2)
Anxiety disorders	103/254	(40.5)	96/102	(94.1)	28/96	(29.2)	41/96	(42.7)	23/96	(24.0)	36/102	(35.3)	76/101	(75.3)	50/101	(49.5)
Mood disorders	88/254	(34.6)	83/88	(94.3)	21/83	(25.3)	39/83	(47.0)	18/83	(21.7)	44/88	(50.0)	58/87	(66.7)	33/87	(37.9)
ADHD	87/254	(34.3)	84/87	(96.5)	40/84	(47.6)	20/84	(23.8)	13/84	(15.5)	66/87	(75.9)	60/87	(69.0)	54/87	(62.1)
Other psych disorders	49/254	(19.3)	45/49	(91.8)	13/44	(29.6)	18/44	(40.9)	11/44	(25.0)	16/49	(32.7)	28/47	(59.6)	20/45	(44.4)
<b>Boys</b>																
Any psych disorder	193		175/192	(91.1)	89/182	(48.9)	33/182	(18.1)	9/182	(5.0)	122/192	(63.5)	123/188	(65.4)	97/188	(51.6)
Anxiety disorders	48/193	(24.9)	43/48	(89.6)	18/46	(39.1)	17/46	(37.0)	5/46	(10.9)	20/48	(41.7)	38/48	(79.2)	26/48	(54.2)
Mood disorders	19/193	(9.8)	16/18	(88.9)	7/18	(38.9)	6/18	(33.3)	< 5/18		8/18	(44.4)	13/18	(72.2)	9/18	(50.0)
ADHD	120/193	(62.2)	115/120	(95.8)	59/112	(52.7)	15/112	(13.4)	< 5/112		102/120	(85.0)	71/116	(61.2)	62/116	(53.4)
Other psych disorders	50/193	(25.9)	44/50	(88.0)	22/49	(44.9)	10/49	(20.4)	< 5/49		30/50	(60.0)	31/50	(62.0)	28/50	(56.0)

Note: <sup>a</sup> Psychiatric disorders include both primary and additional diagnoses

<sup>b</sup> Psychotherapy include both specified and unspecified psychotherapy

<sup>c</sup> Medication includes medication for psychiatric disorders; according to Anatomical Therapeutic Chemical (ATC) codes Yes/No. Supplementary Material Table S1 shows the medication given for primary diagnoses differentiated by ATC-codes

**Associations between resilience factors and symptom load 3 years later**

Linear regression analysis with YSR Total Problem T-score at 3-year follow up as dependent variable and READ resilience scale scores as covariates showed significant negative associations for Total READ and for all subscale scores, adjusted for age and SES (Table 5). Increasing the Total READ score by 1 unit (scale 1–5), the YSR Total Problems T-score decreased by 15.7 units ( $\beta = -15.7$ , CI  $(-19.2$  to  $-12.1)$ ,  $p < 0.001$ ). Associations

were present both for participants with and without a diagnosis at T<sub>2</sub> ( $n_{\text{diagnosis}} = 226$ , Total READ  $\beta = -17.9$ , CI  $(-22.1$  to  $-13.7)$ ,  $p < 0.001$ ), ( $n_{\text{no diagnosis}} = 84$ , Total READ  $\beta = -7.1$ , CI  $(-12.3$  to  $-1.9)$ ,  $p = 0.008$ ). READ Personal Competence was the subscale associated with the largest decrease in Total Problem score for both genders (girls:  $\beta = -11.8$ , CI  $(-15.9$  to  $-7.6)$ ,  $p < 0.001$  and boys:  $\beta = -9.4$ , CI  $(-13.5$  to  $-5.2)$ ,  $p < 0.001$ ) (Table 5). Linear regression analysis including the five READ subscales simultaneously, showed that Personal

**Table 2** Resilience scales at T<sub>1</sub> differentiated by psychiatric disorder groups, overall and separately for girls and boys

Psychiatric disorders <sup>a</sup> T <sub>1</sub>	n	(%)	Personal competence		Social competence		Structured style		Family cohesion		Social resources		Total READ		Total READ Girls versus Boys		
			Mean	(SD)	Mean	(SD)	Mean	(SD)	Mean	(SD)	Mean	(SD)	Mean	(SD)	Diff.	95% CI <sup>b</sup>	p-value <sup>b</sup>
<b>Total sample</b>																	
Any psychiatric disorder	447		3.3	(1.0)	3.7	(0.9)	3.1	(0.9)	3.5	(1.0)	4.1	(0.8)	3.5	(0.8)			
Anxiety disorders	151/447	(33.8)	3.1	(0.9)	3.6	(0.9)	3.0	(0.9)	3.5	(1.1)	4.0	(0.9)	3.5	(0.8)			
Mood disorders	107/447	(23.9)	2.5	(0.9)	3.2	(0.9)	2.6	(0.8)	3.0	(0.9)	3.6	(0.9)	3.0	(0.7)			
ADHD	207/447	(46.3)	3.5	(0.9)	3.8	(0.9)	3.2	(0.9)	3.7	(0.9)	4.2	(0.7)	3.7	(0.7)			
Other psychiatric disorders	99/447	(22.1)	3.3	(0.9)	3.7	(0.9)	3.1	(0.9)	3.7	(1.0)	4.2	(0.7)	3.6	(0.7)			
<b>Girls</b>																	
Any psychiatric disorder	254		2.9	(0.9)	3.6	(0.9)	2.9	(0.9)	3.4	(1.1)	4.0	(0.9)	3.3	(0.7)	-0.5	-0.6 to -0.3	< 0.001
Anxiety disorders	103/254	(40.5)	2.9	(0.9)	3.5	(0.9)	2.9	(0.9)	3.3	(1.1)	4.0	(0.9)	3.3	(0.8)	-0.5	-0.7 to -0.2	< 0.001
Mood disorders	88/254	(34.6)	2.4	(0.8)	3.2	(0.8)	2.6	(0.7)	3.0	(0.9)	3.6	(0.9)	2.9	(0.6)	-0.3	-0.6 to 0.0	0.080
ADHD	87/254	(34.3)	3.1	(1.0)	3.7	(1.0)	2.8	(0.9)	3.5	(1.0)	4.1	(0.8)	3.4	(0.7)	-0.5	-0.7 to -0.3	< 0.001
Other psychiatric disorders	49/254	(19.3)	2.9	(0.7)	3.6	(0.9)	2.9	(0.9)	3.5	(1.1)	4.1	(0.7)	3.4	(0.7)	-0.4	-0.6 to -0.1	0.013
<b>Boys</b>																	
Any psychiatric disorder	193		3.7	(0.8)	3.9	(0.9)	3.4	(0.9)	3.8	(0.9)	4.3	(0.7)	3.8	(0.7)			
Anxiety disorders	48/193	(24.9)	3.6	(0.7)	4.0	(0.8)	3.3	(0.8)	3.8	(0.8)	4.3	(0.7)	3.8	(0.6)			
Mood disorders	19/193	(9.8)	3.0	(0.9)	3.4	(1.0)	2.8	(0.9)	3.2	(1.1)	3.9	(1.0)	3.2	(0.8)			
ADHD	120/193	(62.2)	3.8	(0.8)	4.0	(0.9)	3.5	(0.9)	3.9	(0.8)	4.3	(0.7)	3.9	(0.7)			
Other psychiatric disorders	50/193	(25.9)	3.7	(0.8)	3.8	(1.0)	3.3	(0.9)	3.8	(0.9)	4.2	(0.7)	3.8	(0.7)			

Note: Resilience measures using READ = Resilience Scale for Adolescents, based on a 5-point Likert scale (1 = Totally Disagree to 5 = Totally Agree, higher scores indicate higher level of resilience factors), SD = Standard Deviation, CI = Confidence Interval

<sup>a</sup> Psychiatric disorders include both primary and additional diagnoses

<sup>b</sup> Confidence intervals and tests for differences between girls and boys were based on Student's t-test for independent samples

Competence and Family Cohesion remained associated with a decrease in Total Problem score, but for girls only (Table S4). When differentiating between psychiatric disorder groups, linear regression analysis with YSR Total Problem T-score as dependent variable and Total READ scale as covariate showed significant negative associations for Total READ in all disorder groups, except for boys with mood disorders (Table S5).

**Discussion**

This is one of few longitudinal surveys studying the potential impact of standard care and resilience factors on subsequent symptom level in a general clinical

psychiatric outpatient population of adolescents. The symptom load three years after referral was substantial, where one out of three reported symptoms that places them in the borderline/clinical range. Differentiated by psychiatric disorders, the former patients with ADHD reported the lowest symptom load, whereas those with mood disorders, especially girls, reported the highest symptom load. One main finding was that patients with mood disorders, and especially girls, had received the highest number of psychotherapy sessions, and yet had the highest symptom load after three years. One out of five patients with mood as well as with an anxiety disorder received more than 30 psychotherapy sessions. In

**Table 3** Symptom load at T<sub>2</sub> differentiated by psychiatric disorders at T<sub>1</sub>, overall and separately for girls and boys

Psychiatric disorders <sup>a</sup> T <sub>1</sub>	YSR Total Problem T-Score at T <sub>2</sub>				Girls versus Boys				
	n	(%)	n	(%)	Mean	(SD)	Mean difference	95% CI <sup>c</sup>	p-value <sup>c</sup>
<b>Total sample</b>									
Any psychiatric disorder	447		137/447	(30.6)	50.5	(26.5)			
Anxiety disorder	151/447	(33.8)	46/151	(30.5)	50.1	(24.0)			
Mood disorder	107/447	(23.9)	52/107	(48.6)	62.7	(28.0)			
ADHD	207/447	(46.3)	57/207	(27.5)	48.6	(26.3)			
Other psychiatric disorder	99/447	(22.1)	33/99	(33.3)	52.9	(30.2)			
<b>Girls</b>									
Any psychiatric disorder	254		103/254	(40.5)	58.7	(27.0)	18.9	14.3 to 23.4	< 0.001
Anxiety disorder	103/254	(40.5)	37/103	(35.9)	54.1	(23.4)	12.8	4.8 to 20.9	0.002
Mood disorder	88/254	(34.6)	49/88	(55.7)	67.1	(27.1)	24.8	6.7 to 11.6	< 0.001
ADHD	87/254	(34.3)	34/87	(39.1)	59.3	(28.9)	18.6	11.4 to 25.8	< 0.001
Other psychiatric disorder	49/254	(19.3)	24/49	(49.0)	65.6	(29.7)	25.2	14.2 to 36.2	< 0.001
<b>Boys</b>									
Any psychiatric disorder	193		34/193	(17.6)	39.8	(21.6)			
Anxiety disorder	48/193	(24.9)	9/48	(18.7)	41.3	(23.2)			
Mood disorder	19/193	(9.8)	3/19	(15.8)	42.3	(22.7)			
ADHD	120/193	(62.2)	23/120	(19.2)	40.8	(21.2)			
Other psychiatric disorder	50/193	(25.9)	9/50	(18.0)	40.4	(25.3)			

Note: Symptom load is measured by using Youth Self Report (YSR, Achenbach System of Empirically Based Assessment), Total Problem T-score, with scores  $\geq 60$  as borderline and clinical range, and  $< 60$  as normal range. SD = Standard Deviation, CI = Confidence Interval

<sup>a</sup> Psychiatric disorders include both primary and additional diagnoses

<sup>b</sup> Borderline/clinical range

<sup>c</sup> Confidence intervals and tests for differences between girls and boys were based on Student's t-test for independent samples

contrast, patients with ADHD, and especially boys, received the fewest psychotherapy sessions and had the largest rate of medication as their treatment. Medication given at baseline was marginally associated with higher symptom scores after three years for boys only. Resilience factors were reported to be lowest among patients with mood disorders and highest among ADHD patients. In all diagnostic groups, self-reported resilience factors were lower among girls than boys. Reporting higher resilience factors was associated with lower symptom load after three years, suggesting a protective potential for personal resources.

Our findings of a considerable symptom load three years after referral were similar to the reported symptom load in other studies of outpatient child and adolescent mental health services [55, 56]. The prevalence of borderline/clinical range symptoms of 30.6% for any psychiatric disorder and 48.6% for mood disorders, were as expected substantially higher in this clinical sample than is reported in the general population (mean YSR Total Problems scores 35.3) [52]. Girls had significantly higher symptom load than boys in all diagnostic groups. It must be taken into account that our sample was a follow-up of former outpatients with a high degree of comorbidity

and complex symptom patterns [15, 57]. This is quite different from patients with a specific disorder without comorbidity as recruited to most treatment studies [6, 58]. The participants with the highest symptom scores in our study were girls with mood disorders and those in the group of other psychiatric disorders (e.g., eating disorders, psychotic disorders, autism spectrum disorders). We do not know if the high symptom load in patients with mood disorders was due to persistence of the mood disorder at T<sub>1</sub>, or relapse, but research shows that both persistence rates and relapse rates are high for mood disorders [59]. We have previously reported a high degree of comorbidity after three years among girls in this sample [15], as well as high rates of suicidal ideation and behavior [57], which may contribute to the higher symptom scores compared with boys. Explorative analyses of the T-scores for participants with or without a psychiatric diagnosis at T<sub>2</sub>, showed as expected highest symptom scores among the participants with a diagnosis, and highest scores among girls.

The main feature of the analysis of treatment characteristics was that patients in all diagnostic groups received extensive interventions, as roughly nine out of ten received some type of individual treatment. Disorder



**Table 4** Linear regression analysis with YSR Total Problems T-score at 3-year follow up as dependent variable and treatment procedures as covariates one at a time, adjusted for age and SES, differentiated by psychiatric disorders

Psychiatric disorders T <sub>1</sub> <sup>a</sup>	n	(%)	Treatment procedures	YSR Total Problems T-score at T <sub>2</sub>				
				Adjusted for age T <sub>1</sub> and SES				
				n	%	β	95% CI	p-value
<b>Total sample</b>								
Any psychiatric disorder	447		Psychotherapy <sup>b</sup>	299/424	(70.5)	0.5	0.3 to 0.7	< 0.001
			Medication <sup>c</sup>	236/445	(53.0)	-1.7	-7.4 to 4.0	0.566
Anxiety disorders	151/447	(33.8)	Psychotherapy	95/150	(63.3)	0.5	0.1 to 0.8	0.007
			Medication	56/150	(37.3)	9.0	-0.6 to 18.7	0.067
Mood disorders	107/447	(23.9)	Psychotherapy	60/106	(56.6)	0.3	-0.1 to 0.8	0.169
			Medication	52/106	(49.1)	-2.1	-16.6 to 12.4	0.773
ADHD	207/447	(46.3)	Psychotherapy	146/207	(70.5)	0.7	0.4 to 1.0	< 0.001
			Medication	168/207	(81.2)	-5.7	-16.1 to 4.6	0.275
Other psychiatric disorder	99/447	(22.1)	Psychotherapy	72/99	(72.7)	0.6	0.1 to 1.0	0.011
			Medication	46/99	(46.5)	-6.9	-20.5 to 6.7	0.313
<b>Girls</b>								
Any psychiatric disorder	254		Psychotherapy	165/242	(68.2)	0.4	0.2 to 0.7	0.002
			Medication	114/253	(45.1)	-1.7	-10.0 to 6.6	0.692
Anxiety disorders	103/254	(40.6)	Psychotherapy	59/102	(57.8)	0.6	0.2 to 1.0	0.007
			Medication	36/102	(35.3)	7.4	-5.6 to 20.3	0.260
Mood disorders	88/254	(34.7)	Psychotherapy	51/88	(58.0)	0.2	-0.3 to -0.7	0.414
			Medication	44/88	(50.0)	0.4	-14.7 to 15.4	0.960
ADHD	87/254	(34.3)	Psychotherapy	62/87	(71.3)	0.7	0.3 to 1.2	0.002
			Medication	66/87	(75.9)	-9.6	-25.4 to 6.1	0.226
Other psychiatric disorder	49/254	(19.3)	Psychotherapy	36/49	(73.5)	0.5	-0.1 to 1.0	0.103
			Medication	16/49	(32.7)	12.0	-11.3 to 35.3	0.304
<b>Boys</b>								
Any psychiatric disorder	193		Psychotherapy	134/182	(73.6)	-0.1	-0.4 to 0.3	0.780
			Medication	122/192	(63.5)	7.4	0.7 to 14.2	0.032
Anxiety disorders	48/193	(24.9)	Psychotherapy	36/48	(75.0)	-0.2	-0.9 to 0.4	0.451
			Medication	20/48	(41.7)	12.9	-0.5 to 26.3	0.059
Mood disorders	19/193	(9.8)	Psychotherapy	9/18	(50.0)	-0.9	-3.2 to 0.4	0.141
			Medication	8/18	(44.4)	-9.8	-34.0 to 14.5	0.347
ADHD	120/193	(62.2)	Psychotherapy	84/120	(70.0)	0.0	-0.5 to 0.6	0.972
			Medication	102/120	(85.0)	5.7	-7.3 to 18.7	0.385
Other psychiatric disorder	50/193	(25.9)	Psychotherapy	36/50	(72.0)	-0.1	-0.9 to 0.6	0.767
			Medication	30/50	(60.0)	-0.9	-16.7 to 15.0	0.913

Note: Symptom load is measured by using Youth Self Report (YSR, Achenbach System of Empirically Based Assessment), Total Problem T-score, SES = Socioeconomic Status measured by level of mothers' education (1 = lowest level of education, 9 = highest level of education), β = Regression Coefficient, CI = Confidence Interval

<sup>a</sup> Psychiatric disorders include both primary and additional diagnoses

<sup>b</sup> Psychotherapy by number of sessions: 1 session as the measurement unit

<sup>c</sup> Medication includes medication for psychiatric disorders; according to Anatomical Therapeutic Chemical (ATC) codes Yes/No

specific features were also observed in that those with anxiety and mood disorders at T<sub>1</sub> had received the highest number of psychotherapy sessions, whereas ADHD and other disorders had the highest rate of medication, both indicating a high disease burden at T<sub>1</sub>. The

different treatment methods could furthermore depend on disorder specific features, for example verbal deficits and problems with emotion processing often present with ADHD [60, 61]. Moreover, medication has been long established as an effective treatment for ADHD.



**Table 5** Linear regression analysis with YSR Total Problems T-score at 3-year follow up as dependent variable and resilience factors as covariates one at a time, adjusted for age and SES, overall and separately for girls and boys

Resilience measures	n	YSR Total Problems T-score at T <sub>2</sub> Adjusted for age T <sub>1</sub> and SES		
		$\beta$	95% CI	p-value
<b>Total sample</b>	447			
Total resilience	444/447	-15.7	-19.2 to -12.1	< 0.001
Personal competence	446/447	-13.0	-15.7 to -10.2	< 0.001
Social competence	444/447	-7.0	-10.1 to -4.0	< 0.001
Structured style	445/447	-11.0	-14.0 to -8.0	< 0.001
Family cohesion	444/447	-10.5	-13.3 to -7.8	< 0.001
Social resources	444/447	-10.3	-13.6 to -6.9	< 0.001
<b>Girls</b>	254			
Total resilience	253/254	-14.7	-19.8 to -9.6	< 0.001
Personal competence	254/254	-11.8	-15.9 to -7.6	< 0.001
Social competence	253/254	-5.1	-9.5 to -0.7	0.022
Structured style	254/254	-10.3	-14.9 to -5.7	< 0.001
Family cohesion	253/254	-10.5	-14.1 to -7.0	< 0.001
Social resources	253/254	-9.2	-13.6 to -4.9	< 0.001
<b>Boys</b>	193			
Total resilience	191/193	-10.8	-15.7 to -6.0	< 0.001
Personal competence	192/193	-9.4	-13.5 to -5.2	< 0.001
Social competence	191/193	-6.1	-9.9 to -2.3	0.002
Structured style	191/193	-7.4	-11.2 to -3.6	< 0.001
Family cohesion	191/193	-6.6	-10.7 to -2.5	0.002
Social resources	191/193	-7.7	-12.6 to -2.9	0.002

Note: Symptom load is measured by using Youth Self Report (YSR, Achenbach System of Empirically Based Assessment), Total Problem T-score, Resilience measures using READ = Resilience Scale for Adolescents, based on a 5-point Likert scale (1 = Totally Disagree, 5 = Totally Agree, higher scores indicate higher level of resilience factors), SES = Socioeconomic Status measured by level of mothers education (1 = lowest level of education, 9 = highest level of education),  $\beta$  = Regression Coefficient, CI = Confidence Interval

When investigating treatment procedures given to the participants in this study, we should also keep in mind that there was a high degree of comorbidity at T<sub>1</sub>, as nearly one out of three had comorbid disorders in addition to their primary disorder.

Treatment characteristics were not found to be analogues for girls and boys. More than one in two girls compared with only about one in four boys received ten or more psychotherapy sessions. Moreover, girls received significantly more psychotherapy sessions than boys in all diagnostic groups. We need to be mindful that the girls in this sample were significantly older than the boys when participating in the study. This may have an impact on the findings related to the use of psychotherapy among girls, because higher age may imply higher maturity to utilize the benefits of psychotherapeutic

approaches. The opposite pattern was found for medication, where boys were more likely to receive medication compared with girls. The differences in treatment provided may reflect that more boys than girls had ADHD, for which medication is the treatment of choice. Nonetheless, even when having the same diagnosis of ADHD, there were still some gender differences. Consistent with our results, previous research has found that girls with ADHD are less likely to be prescribed medication unless they have prominent externalizing problems [62].

Positive associations were found between the number of psychotherapy sessions and symptom load for girls only, overall and in the groups of anxiety disorders and ADHD, possibly because these groups had a high and complex symptom pattern in the first place, resulting in longer treatment. Results from the CAMELS study found that despite receiving evidence-based treatments for anxiety, only 22% were in stable remission across all four years when they were assessed, 30% were chronically ill, and 48% experienced relapse [10]. Furthermore, the positive association between psychotherapy sessions and symptom load for girls with ADHD may reflect both the high symptom load for these girls and that fewer girls than boys received medication for this disorder. The positive association between receiving medication at baseline and higher symptom load at follow-up were found only in boys. As a counterintuitive result, this warrants replication in future studies. One might speculate that this could have been due to gender-specific differences in initial diagnoses, less additional psychotherapy in boys, or possibly gender-specific differences in initial symptom load. When performing explorative analyses for the participants with or without a psychiatric diagnosis at T<sub>2</sub>, we found that the associations between the number of psychotherapy sessions and symptom load was only present in the subgroup with a psychiatric diagnosis at T<sub>2</sub>. This fits with the assumption that this is the presumed group with most symptom burden.

Beyond this, no associations were found between treatment characteristics at baseline and symptom load at follow-up, whether for counselling parents nor municipal services. This may be due to the complexities in classifying outpatient treatment, symptom patterns, and comorbidity in this sample. It is challenging to implement high quality and targeted treatment in adolescence, if the burden of comorbid psychiatric disorders is high [13, 14]. There are few transdiagnostic treatment options available today, which could expand treatment benefits beyond what is produced by therapies for any single disorder [12]. One example of a transdiagnostic approach is the Modular Approach to Therapy for Children with Anxiety, Depression, Trauma, or Conduct Problems (MATCH) [19]. Another aspect is that effect sizes for

therapies in children and adolescents have been found to be significantly smaller than for adults [11, 63]. We surmise that in our study those with the highest symptom burden at baseline received the most extensive treatment procedures. Therefore, this observational follow-up study is not intended to evaluate effect of the treatment provided, as this would require randomized controlled trial methods. Furthermore, it is important to investigate how to use the resources in CAMHS in the best possible way, for example to find the optimal scope of psychotherapy for adolescent psychiatric patients.

Factors that positively can influence outcomes for adolescent patients are of great interest and importance. The concept of resilience may point to such factors, yielding more positive psychological outcome than would be expected based on risk exposure. The fact that higher self-reported personal and social resources may have a protective potential in relation to adolescents' symptom load, may be due to a variety of factors including cognitive level. The self-reported resilience factors found in this clinical sample showed a pattern across subscales similar to previous research within a general population [38]. Overall, the levels of resilience factors were fairly low, indicating the vulnerability typical in a clinical sample. This vulnerability may also partly explain the high symptom load after three years [15, 57]. When differentiating by psychiatric disorders, patients with mood disorders had the lowest levels of resilience factors for both genders. We cannot exclude that the presence of a mood disorder, particularly depression, may have had a negative impact on resilience scores reported at the same time, and possibly biased the findings. Consistent with our hypothesis, resilience factors were associated with symptom scores, across all subscales and both genders. We found that higher levels of resilience factors at baseline were linked to lower symptom severity three years later, overall and in all diagnostic groups, except for mood disorders among boys. When performing explorative analyses for the participants with or without a psychiatric diagnosis at T<sub>2</sub>, the findings were present in both groups.

We found gender differences in resilience factors that were similar to results from earlier research [36, 38], especially concerning the subscale Personal Competence. The considerably higher scores for boys in this subscale are consistent with research showing boys to report higher levels than girls on constructs such as general self-esteem and self-efficacy [64]. A large meta-analysis including 85 longitudinal studies [65] concluded that the effect of low self-esteem on depression and anxiety is substantial in the general population, and this association has also been reported in studies with clinical samples [41, 66]. We hypothesized based on previous research that girls would report higher scores than boys

on Social Resources [36, 38, 45]. This was not verified as girls reported lower levels for all resilience factors. One reason for the lower scores among girls may be their higher prevalence of mood disorders compared to boys, and that especially depression has affected the self-reported scores among girls [67]. The results for boys were in accordance with previous studies [36, 38, 40, 44, 45] and our hypotheses that they had higher resilience scores than girls in Personal and Social Competences.

Previous studies have investigated interventions promoting resilience in children and adolescents. A recent systematic review and meta-analysis of resilience training programs and interventions shows that interventions based on a combination of mindfulness techniques and CBT seem to have a positive impact on individual resilience [68]. Also, a recent literature review showed that resilience was promoted in children and youth by strengthening home and school environments [69]. This research highlights that resilience can be improved through interventions among children and adolescents.

Strengths of the present study include a large clinical sample receiving standard psychiatric clinical care, with reassessment after three years with a high retention rate. Another strength is that the psychiatric diagnoses at T<sub>1</sub> represent clinical practice as they were classified by clinicians within a multi-disciplinary team, according to the current diagnostic classification system and based on all available clinical information. The diagnoses were not only based on self-report measures of symptoms. Associations were examined when adjusted for age and SES as possible confounders. Some limitations need to be taken into consideration. At the initial recruitment, the rate of enrollment was less than ideal [15, 70], and this may have biased the results. However, the participants at T<sub>1</sub> did not differ in age, gender or reason for referral compared to non-participants. We may have lost especially patients with high symptom load and impaired function at baseline, as is typical, especially boys since they were underrepresented among participants. Also, the number of participants was low for some diagnostic groups, requiring us to merge some diagnoses into one larger group, which limited the generalizability of the results for these disorders. Association analyses between resilience and symptom load for boys with mood disorders may have been affected by low numbers and therefore low power. Another limitation is that the assessment of psychiatric disorders of study participants at T<sub>1</sub> were not done by using the same structured procedure, rather reflecting clinical practice influenced by patient presentation and clinical preferences. Self-report was used to measure symptom load at T<sub>2</sub> and should ideally be supplemented by clinical interview and proxy report. Although YSR is a widely used and validated instrument, some information bias cannot be excluded when using

only self-report. As different informants may have different standards for rating problems, adding proxy reports from parents using the Child Behavior Check List (CBCL) could have balanced the information [51]. Low agreement between self-report (YSR) and parent-report (CBCL) may appear, depending on subjective factors of both respondents [71]. Furthermore, social desirability may lead to self-reported better competences and resources. This study did not have data from YSR available at  $T_1$ , which would have strengthened the study and made it possible to compare resilience scores with symptom load at different times.

### Clinical implications

The results of this study bring an essential message to clinical practice. Despite clinical interventions that were intended to address presenting disorders, the high symptom load reported by girls, and by those with mood disorders, is especially noteworthy. Even though clinicians know about the increase of psychiatric disorders during adolescence, the self-reported high symptom load in this sample of former patients should be an additional reminder. The results point to the importance of focusing on this vulnerable group of patients at the transition from youth to young adulthood. The burden of mental health problems in adolescence must be acknowledged and motivate the search for more effective interventions, either targeted or transdisciplinary. Systematic use of validated screening measures will increase the likelihood that symptoms are properly recognized. Higher reported resilience factors were associated with lower symptom load after three years, suggesting the protective potential of personal resources. Future research needs to expand knowledge on how resilience factors can be developed or enhanced through intervention and whether this leads to reduced symptom load several years later.

### Conclusions

In this clinical sample of adolescents reassessed after three years, one out of three had symptom loads in the borderline/clinical range. Girls had the highest symptom load, especially those with previous mood disorders. Treatment were extensive in form and duration for large portions and nine out of ten had received individual treatment. Self-reported resilience factors appeared lowest among patients with mood disorders and highest among ADHD patients, and lower among girls than boys in all diagnostic groups. Higher self-reported personal and social resources were associated with lower symptom load after three years, suggesting that they can have a protective potential. The results accentuate the importance of continuous research to find the most effective interventions and facilitating factors for adolescents with psychiatric disorders to enhance optimal function.

### Abbreviations

ADHD: Attention Deficit Hyperactivity Disorder; ATC-codes: Anatomical Therapeutic Chemical codes; CAMELS: Child/Adolescent Anxiety Multimodal Extended Long-Term Study; CAMHS: Child and Adolescent Mental Health Services; CBT: Cognitive Behavioral Therapy; CI: Confidence interval; DSM-IV-TR: Diagnostic and Statistical Manual of Mental Disorders IV Text revision; K-SADS: Kiddie SADS: Schedule for Affective Disorders and Schizophrenia for School-Age Children; MATCH: Modular Approach to Therapy for Children with Anxiety, Depression, Trauma, or Conduct Problems; READ: Resilience Scale of Adolescents; RD: Risk difference; SES: Socioeconomic status; YSR: Achenbach System of Empirically Based Assessment - Youth Self Report

### Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12888-021-03417-6>.

**Additional file 1: Table S1.** Medication differentiated by primary psychiatric disorders at  $T_1$ . **Table S2.** Treatment procedures at  $T_1$  differentiated by psychiatric disorders. **Table S3.** Resilience measures at  $T_1$  differentiated by psychiatric disorders. **Table S4.** Linear regression analysis with YSR Total Problems T-score at 3-year follow up as dependent variable and resilience factors as covariates with all subscales simultaneously. **Table S5.** Linear regression analysis with YSR Total Problems T-score at 3-year follow up as dependent variable and Total READ as covariate, differentiated by psychiatric disorders.

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### Authors' contributions

KSG was responsible for reviewing the literature, drafting and revising the manuscript, with substantial contribution by MSI in the entire process. KSG performed and interpreted statistical analyses with contribution by SL and MSI, and SL was involved in revising the manuscript in relation to analyzes and statistics. MR, TT and JLW participated in designing the study and made comprehensive contributions in revising the manuscript critically. All authors have read and approved the final manuscript.

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### Availability of data and materials

The datasets analyzed during the current study are not publicly available due to privacy policy, but they are obtainable from the corresponding author on acceptable request.

### Declarations

#### Ethics approval and consent to participate

According to study procedures, written informed consent was obtained from adolescents and parents participating at  $T_1$  and  $T_2$ . Study approval was given by the Regional committee for Medical and Health Research Ethics of Central Norway (reference numbers CAP survey  $T_1$ : 4.2008.1393,  $T_2$ : 2011/1435/REK Midt, and present study using  $T_1$  and  $T_2$  data: 2017/589/REK Midt). The

Norwegian Social Science Data Services, The Data Protection Official for Research, gave approval to compare the main reason for referral, age and sex between participants and non-participants at baseline (reference number CAP survey: 19976). The research performed in accordance with the ethical standards in the Declaration of Helsinki from 1964 and later amendments. We affirm that all methods were accomplished in agreement with relevant guidelines and regulations.

#### Consent for publication

Not applicable.

#### Competing interests

The authors declare that they have no competing interest.

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## Supplementary Material

Table S1 Medication differentiated by primary psychiatric disorders at T1, overall and separately for girls and boys

Psychiatric disorders <sup>a</sup> T1	Medication																			
	n	(%)	n	(%)	Antidepressants <sup>c</sup>	n	(%)	Psycholeptics <sup>d</sup>	n	(%)	Psychostimulants <sup>e</sup>	n	(%)	Antiepileptics <sup>f</sup>	n	(%)	Medication for sleeping problems <sup>g</sup>	n	(%)	
<b>Total sample</b>																				
Any psych disorder	445 <sup>h</sup>		236	(53.0)	55	(12.4)	14	(3.1)	166	(37.3)	7	(1.6)	21	(4.7)						
Anxiety disorders	116	(26.1)	34	(29.3)	26	(22.4)	<5 <sup>i</sup>		7 <sup>j</sup>	(6.0)	<5		5	(4.3)						
Mood disorders	68	(15.3)	26	(38.2)	19	(27.9)	<5		<5		<5		6	(8.8)						
ADHD	172	(38.7)	137	(79.7)	5	(2.9)	<5		133	(77.3)	<5		<5							
Other psych disorders	87	(19.6)	39	(44.8)	5	(5.7)	9	(10.3)	24	(27.6)	<5		6	(6.9)						
<b>Girls</b>																				
Any psych disorder	253		114	(45.1)	41	(16.2)	5	(2.0)	64	(25.3)	7	(2.8)	16	(6.3)						
Anxiety disorders	79	(31.2)	22	(27.8)	17	(21.5)	0		<5		<5		5	(6.3)						
Mood disorders	56	(22.1)	21	(37.5)	15	(26.8)	<5		<5		<5		<5							
ADHD	77	(30.4)	58	(75.3)	5	(6.5)	0		55	(71.4)	<5		<5							
Other psych disorders	40	(15.8)	13	(32.5)	<5		<5		<5		<5		<5							
<b>Boys</b>																				
Any psych disorder	192		122	(63.5)	14	(7.3)	9	(4.7)	102	(53.1)	0		5	(2.6)						
Anxiety disorders	37	(19.3)	12	(32.4)	9	(24.3)	<5		<5		0		0							
Mood disorders	12	(6.3)	5	(41.7)	<5		0		<5		0		<5							
ADHD	95	(49.5)	79	(83.2)	0		<5		78	(82.1)	0		0							
Other psych disorders	47	(24.5)	26	(55.3)	<5		6	(12.8)	20	(42.6)	0		<5							

**Note:** <sup>a</sup> Psychiatric disorder includes **only primary diagnoses**

<sup>b</sup> Medication includes medication for psychiatric disorders; according to Anatomical Therapeutic Chemical (ATC) codes Yes/No

<sup>c</sup> Antidepressants ATCN06A - B03, B04, B06, B10, X03 and X16

<sup>d</sup> Psycholeptics ATCN05 - AH04, AX08 and AX12

<sup>e</sup> Psychostimulants ATCN06B - A01, A04 and A09

<sup>f</sup> Antiepileptics ATCN03 - AD01 and AX09

<sup>g</sup> Medication for sleeping problems: Psycholeptics ATCN05 - CF01 and CH01, and Antihistamins ATCR06 including AD01

<sup>h</sup> Information about medication was missing from 2 participants

<sup>i</sup> Numbers below 5 are not given

<sup>j</sup> All 7 patients had ADHD as additional diagnosis

**Table S2 Treatment procedures at T<sub>1</sub> differentiated by psychiatric disorders, including comorbid disorders at T<sub>1</sub>, comparing girls versus boys**

Psychiatric disorders <sup>a</sup> T <sub>1</sub>	Treatment procedures T <sub>1</sub>						Medication <sup>c</sup>					
	Psychotherapy <sup>b</sup>			Girls versus Boys			Boys		Girls		Girls versus Boys	
	Girls n (%)	Boys n (%)	RD (%)	RD (%)	95% CI <sup>d</sup>	p <sup>e</sup>	n (%)	n (%)	n (%)	n (%)	RD (%)	95% CI
<b>Any psych disorder</b>	224/242 (92.5)	134/182 (73.6)	18.9	11.2 to 26.4	<0.001	114/253 (45.1)	122/192 (63.5)	122/192 (63.5)	114/253 (45.1)	-18.4	-27.3 to -9.1	<0.001
<b>Anxiety disorders</b>	93/96 (96.9)	40/46 (87.0)	9.9	1.0 to 22.7	0.023	36/102 (35.3)	20/48 (41.7)	20/48 (41.7)	36/102 (35.3)	-6.4	-22.8 to 9.7	0.452
<b>Mood disorders</b>	81/83 (97.6)	15/18 (83.3)	14.3	1.9 to 36.9	0.011	44/88 (50.0)	8/18 (44.4)	8/18 (44.4)	44/88 (50.0)	5.6	-18.6 to 27.9	0.667
<b>ADHD</b>	73/84 (86.9)	77/112 (68.7)	18.2	6.3 to 28.8	0.003	66/87 (75.9)	102/120 (85.0)	102/120 (85.0)	66/87 (75.9)	-9.1	-20.4 to 1.6	0.097
<b>Other psych disorders</b>	43/44 (97.7)	36/49 (73.4)	24.3	10.2 to 38.1	0.001	16/49 (32.7)	30/50 (60.0)	30/50 (60.0)	16/49 (32.7)	-23.3	-40.6 to -3.6	0.006

**Note:** RD = Risk Difference, CI = Confidence Interval, p = p-value

<sup>a</sup> Psychiatric disorders include both primary and additional diagnoses

<sup>b</sup> Psychotherapy includes both specified and unspecified psychotherapy, measured by Yes/No

<sup>c</sup> Medication includes medication for psychiatric disorders; according to Anatomical Therapeutic Chemical (ATC) codes Yes/No

<sup>d</sup> Newcomb hybrid score

<sup>e</sup> Pearson Chi squared test



**Table S3 Resilience measures at T1 differentiated by psychiatric disorders, including comorbid disorders at T1, comparing girls versus boys**

Psychiatric disorders <sup>a</sup> T1	Resilience measures - Girls versus Boys																	
	Personal competence			Social competence			Structured style			Family cohesion			Social resources			Total READ		
	Diff	95% CI	p	Diff	95% CI	p	Diff	95% CI	p	Diff	95% CI	p	Diff	95% CI	p	Diff	95% CI	p
Any psychiatric disorder	-0.8	-1.0 to -0.7	<0.001	-0.3	-0.5 to -0.1	0.001	-0.5	-0.7 to -0.4	<0.001	-0.4	-0.6 to -0.3	<0.001	-0.3	-0.4 to -0.1	<0.001	-0.5	-0.6 to -0.3	<0.001
Anxiety disorders	-0.7	-1.0 to -0.5	<0.001	-0.5	-0.8 to -0.2	0.003	-0.4	-0.7 to -0.1	0.014	-0.5	-0.8 to -0.2	0.003	-0.3	-0.6 to -0.0	0.029	-0.5	-0.7 to -0.2	<0.001
Mood disorders	-0.6	-1.0 to -0.2	0.007	-0.2	-0.6 to 0.3	0.388	-0.2	-0.6 to 0.2	0.361	-0.2	-0.7 to 0.3	0.405	-0.3	-0.8 to 0.1	0.146	-0.3	-0.6 to 0.0	0.080
ADHD	-0.7	-1.0 to -0.5	<0.001	-0.3	-0.5 to 0.0	0.057	-0.7	-0.9 to -0.4	<0.001	-0.4	-0.6 to -0.1	0.002	-0.2	-0.4 to -0.0	0.022	-0.5	-0.7 to -0.3	<0.001
Other psychiatric disorders	-0.8	-1.1 to -0.5	<0.001	-0.2	-0.6 to 0.2	0.335	-0.4	-0.8 to -0.1	0.019	-0.3	-0.6 to 0.2	0.227	-0.4	-0.4 to 0.2	0.587	-0.4	-0.6 to -0.1	0.013

**Note:** Resilience measures using READ = Resilience Scale for Adolescents, based on a 5-point Likert scale (1 = Totally Disagree to 5 = Totally Agree, higher scores indicate higher level of resilience factors), Diff = Difference Girls versus Boys, CI = Confidence Interval, p = p-value

<sup>a</sup> Psychiatric disorders include both primary and additional diagnoses

**Table S4 Linear regression analysis with YSR Total Problems T-score at 3-year follow up as dependent variable and resilience factors as covariates with all subscales simultaneously, adjusted for age and SES, overall and separately for girls and boys**

Resilience measures	n	YSR Total Problems T-score at T <sub>2</sub> Adjusted for age T <sub>1</sub> and SES		
		$\beta$	95% CI	p-value
<b>Total sample</b>	447			
Personal competence	446/447	-11.4	-16.1 to -6.7	<0.001
Social competence	444/447	2.9	-1.0 to 6.7	0.146
Structured style	445/447	-0.7	-5.0 to 3.6	0.759
Family cohesion	444/447	-4.8	-9.1 to -0.6	0.026
Social resources	444/447	0.1	-5.0 to 5.2	0.960
<b>Girls</b>	254			
Personal competence	254/254	-8.6	-15.7 to -1.4	0.019
Social competence	253/254	2.8	-2.6 to 8.1	0.307
Structured style	254/254	0.4	-6.2 to 7.1	0.897
Family cohesion	253/254	-7.6	-13.2 to -1.9	0.009
Social resources	253/254	0.3	-6.3 to 6.9	0.929
<b>Boys</b>	193			
Personal competence	192/193	-6.8	-14.1 to 0.5	0.067
Social competence	191/193	0.5	-5.3 to 6.2	0.873
Structured style	191/193	-2.9	-8.1 to 2.3	0.268
Family cohesion	191/193	-0.6	-7.1 to 5.9	0.859
Social resources	191/193	-0.8	-8.9 to 7.3	0.849

**Note:** Symptom load is measured by using Youth Self Report (YSR, Achenbach System of Empirically Based Assessment), Total Problem T-score, Resilience measures using READ = Resilience Scale for Adolescents, based on a 5-point Likert scale (1 = Totally Disagree, 5 = Totally Agree, higher scores indicate higher level of resilience factors), SES = Socioeconomic Status measured by level of mothers education (1 = lowest level of education, 9 = highest level of education),  $\beta$  = Regression Coefficient, CI = Confidence Interval

**Table S5 Linear regression analysis with YSR Total Problems T-score at 3-year follow up as dependent variable and Total READ as covariate, adjusted for age and SES, differentiated by psychiatric disorders**

Psychiatric disorders T <sub>1</sub> <sup>a</sup>	Total READ		YSR Total Problems T-score at T <sub>2</sub> Adjusted for age T <sub>1</sub> and SES					p-value
	n (%)	n %	n	%	$\beta$	95% CI		
<b>Total sample</b>								
Any psychiatric disorder	447	444/447 (99.3)	326/444	(73.4)	-15.3	-18.8 to -11.9	<0.001	
Anxiety disorders	151/447 (33.8)	151/151 (100)	106/151	(70.2)	-16.4	-21.5 to -11.2	<0.001	
Mood disorders	107/447 (23.9)	106/107 (99.1)	68/106	(64.2)	-23.3	-33.0 to -13.5	<0.001	
ADHD	207/447 (46.3)	205/207 (99.0)	159/205	(77.6)	-13.2	-18.1 to -8.2	<0.001	
Other psychiatric disorder	99/447 (22.1)	98/99 (99.0)	77/98	(78.6)	-18.5	-27.2 to -9.8	<0.001	
<b>Girls</b>								
Any psychiatric disorder	254	253/254 (99.6)	180/253	(71.1)	-14.2	-19.1 to -9.2	<0.001	
Anxiety disorders	103/254 (40.6)	103/103 (100)	68/103	(66.0)	-15.7	-22.4 to -9.0	<0.001	
Mood disorders	88/254 (34.7)	88/88 (100)	58/88	(65.9)	-20.8	-31.3 to -10.3	<0.001	
ADHD	87/254 (34.3)	86/87 (98.8)	66/86	(76.7)	-11.7	-20.3 to -3.2	0.008	
Other psychiatric disorder	49/254 (19.3)	49/49 (100)	39/49	(79.6)	-15.9	-30.4 to -1.4	0.033	
<b>Boys</b>								
Any psychiatric disorder	193	191/193 (99.0)	146/191	(76.4)	-11.4	-16.2 to -6.6	<0.001	
Anxiety disorders	48/193 (24.9)	48/48 (100)	38/48	(79.2)	-15.3	-26.6 to -4.1	0.009	
Mood disorders	19/193 (9.8)	18/19 (94.7)	10/18	(55.6)	-9.1	-33.6 to 15.4	0.398	
ADHD	120/193 (62.2)	119/120 (99.2)	93/119	(78.2)	-10.6	-16.7 to -4.5	0.001	
Other psychiatric disorder	50/193 (25.9)	49/50 (98.0)	38/49	(77.6)	-15.0	-23.9 to -6.0	0.002	

**Note:** Symptom load is measured by using Youth Self Report (YSR, Achenbach System of Empirically Based Assessment), Total Problem T-score, Resilience measures using READ = Resilience Scale for Adolescents, based on a 5-point Likert scale (1 = Totally Disagree, 5 = Totally Agree, higher scores indicate higher level of resilience factors), SES = Socioeconomic Status measured by level of mothers education (1 = lowest level of education, 9 = highest level of education),  $\beta$  = Regression Coefficient, CI = Confidence Interval

<sup>a</sup> Psychiatric disorders include both primary and additional diagnoses

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