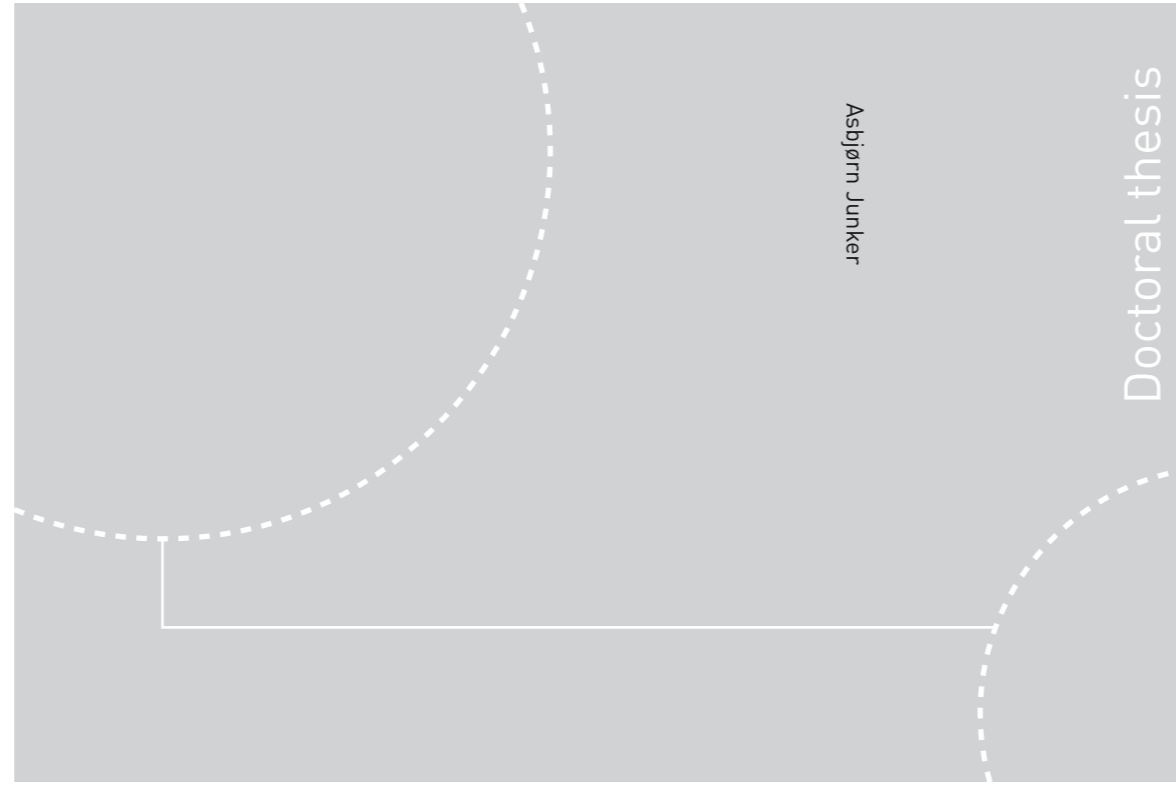


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The Young-HUNT Study, Norway

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Risikofaktorer for sykehusinnleggelse grunnet villet egenskade hos ungdom og unge voksne

Ung-HUNT, Helseundersøkelsen i Nord-Trøndelag

Villet egenskade er utfordrende og påvirker både personen som skader seg selv, venner og familie, helsevesenet, og samfunnet som helhet. Villet egenskade er en av de viktigste årsakene til sykehusinnleggelse blant unge, og er sterkt knyttet til risiko for senere selvmord. Manglende enighet blant forskere og klinikere om hvordan atferden best kan defineres og klassifiseres, gjør det vanskelig å etablere et omforent kunnskapsgrunnlag – noe som er essensielt for å kunne overvåke, studere, forebygge og behandle villet egenskade på en hensiktsmessig og effektiv måte.

Nesten 9000 ungdommer deltok i Helseundersøkelsen i Nord-Trøndelag i 1995-97 (Ung-HUNT1). Vi fulgte ungdommene i opptil 15 år ved å koble data fra Ung-HUNT1 med informasjon fra pasientjournaler, og undersøkte hvordan ulike faktorer blant tenåringer i Nord-Trøndelag påvirket risikoen for senere sykehusinnleggelse på grunn av villet egenskade. Resultatene er presentert i tre vitenskapelige artikler.

Sannsynligheten for sykehusinnleggelse på grunn av villet egenskade påvirkes av mange ulike faktorer i ungdomstiden. Mobbing, ensomhet og negative livshendelser er eksempler på faktorer som kan medvirke til villet egenskade, enten direkte eller via utvikling av angst- og depresjonsplager – som også er tett knyttet til søvnplager. Vi fant at omtrent en av ti tenåringer har ofte søvnproblemer, som regel vansker med å sovne om kvelden. Slike søvnproblemer er assosiert med økt risiko for senere sykehusinnleggelse på grunn av villet egenskade. Sammenhengen kan imidlertid delvis forklares av samtidige symptomer på angst og depresjon – som i seg selv påvirker risikoen for villet egenskade og en rekke andre helseutfordringer. Videre fant vi at opplevd ensomhet og mobbing medfører en selvstendig økning i risiko for villet egenskade. Dessuten kan fysiske sykdommer, deriblant migrene og epilepsi, samt andre kroppslige smerter og ubehag, øke sannsynligheten for senere sykehusinnleggelse på grunn av villet egenskade. Personlighetstrekk er i stor grad utviklet og relativt stabile allerede i ungdomsårene, og påvirker hvordan en person oppfatter seg selv og verden rundt seg, og hvordan man reagerer på ulike former for stress og påkjenninger. Ungdom med en personlighet preget av nevrotiske eller psykotiske trekk, har ifølge våre funn høyere risiko for å bli innlagt på sykehus på grunn av villet egenskade. En personlighet preget av ekstrovertsjon og høy selvfølelse ser derimot ut til å virke beskyttende.

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Appendix

Papers I – III

Original developed methods manual

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Bodø, January 2018

Asbjørn Junker

Abbreviations

AJ	Asbjørn Junker
BMI	Body Mass Index
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, 5 th version
EPQ-18	Eysenck's Personality Questionnaire, 18-item version
HR	Hazard Ratio
HUNT	Nord-Trøndelag Health Study
ICD	International Classification of Diseases
ID	Identification
PAS	Patient Administrative System
REK	Regional Committee for Medical and Health Research Ethics
SCL-5	Hopkins Symptom Checklist, 5-item version
UK	United Kingdom
US	United States
Young-HUNT	The adolescent part of HUNT, participants aged 13 – 19 years

List of papers

- Paper I Junker A, Bjørngaard JH, Gunnell D, Bjerkeset O.
Sleep problems and hospitalization for self-harm: a 15-year follow-up of 9000 Norwegian adolescents. The Young-HUNT study
Sleep 2014;37(3):579-585
- Paper II Junker A, Bjørngaard JH, Bjerkeset O.
Adolescent health and subsequent risk of self-harm hospitalisation: a 15-year follow-up of the Young-HUNT cohort
Child and Adolescent Psychiatry and Mental Health 2017;11:25
- Paper III Junker A, Nordahl HM, Bjørngaard JH, Bjerkeset O.
Adolescent personality traits, low self-esteem and self-harm hospitalisation: a 15-year follow-up of the Norwegian Young-HUNT1 cohort
(Manuscript submitted to European Child & Adolescent Psychiatry)

1 Introduction

This thesis presents findings from three studies investigating how various self-reported indicators of adolescent health are related to the risk of in-patient admission to hospital because of a self-harm episode (onwards referred to as self-harm hospitalisation).

1.1 Terminology

1.1.1 Age

According to World Health Organization, “... *onset of adolescence is usually associated with the commencement of puberty and the appearance of secondary sex characteristics*”, while the more vaguely described end of adolescence includes having developed full sexual and reproductive maturity, adult cognitive and emotional patterns, and individual relative socioeconomic independence [1]. This development generally occurs during the age range of 10 – 19 years, yet 10 – 24 years is used as a pragmatic approach in order to encompass the United Nations definition of “youth”, being 15 – 24 years [2]. Young adulthood is even less clearly defined, but usually encompasses a period including life’s second and third decades – for example defined as 18 – 35 years [3].

1.1.2 Self-harming behaviour

Self-harm has been defined as any intentional self-injury or self-poisoning, irrespective of motivation or suicidal intent [4]. It is usually precipitated by suicidal ideation – i.e. thoughts, fantasies, ideas and plans concerning death by suicide. Suicidal ideation is common among adolescents, and often seen together with self-harm [5]. Self-harm is a frequent reason for hospitalisation among young people, and constitutes a large burden both in terms of costs related to health service utilization [6], and increased morbidity and mortality [7]. Research on the epidemiology and aetiology of self-harming behaviour is challenging because of inconsistent terminology, including various labels, classification methods and definitions [8]. Ambiguity and variations in level of suicidal intent and heterogeneous motives complicate matters further, making it difficult to

compare study results, do systematic meta-analyses and establish a solid base of knowledge – needed to create good surveillance programs and evaluate treatment and prevention. Among the names and terms used to describe self-injurious behaviour are self-injury or deliberate self-harm, yet the adjective “deliberate” has been decreasingly used because of negative reactions from self-harm patient groups, particularly in the United Kingdom (UK). Other examples are self-inflicted violence, intentional self-harm, parasuicide, self-mutilation, suicidal behaviour, suicide attempt, self-wounding, or the umbrella term suicidal phenomena [9, 10]. Evidently, no definitions of self-harm have reached global acknowledgement yet, even though various suggestions have been proposed.

In the Child & Adolescent Self-Harm in Europe (CASE) Study, the researchers assessed self-harm among adolescents in seven countries and developed a self-harm definition similar to what we have applied in our studies. They used the following criteria: *“An act with a non-fatal outcome in which an individual deliberately did one or more of the following: Initiated behaviour (for example, self-cutting, jumping from a height), which they intended to cause self-harm. Ingested a substance in excess of the prescribed or generally recognised therapeutic dose. Ingested a recreational or illicit drug that was an act that the person regarded as self-harm. Ingested a non-ingestible substance or object.”* [11]

There is a principal difference between severe self-harm and a suicide attempt, in terms of the underlying intention of the act. A *suicide attempt* is an act with a principal intent (explicit or inferred) to die, but the outcome is non-fatal [12]. Suicidal intent can be assessed for example with Beck Suicide Intent Scale [13]. Episodes with presence of suicidal intent are associated with increased risk of future death by suicide, but while providing valuable information for clinical risk assessment, scale results cannot reliably predict which individual patients will ultimately die by suicide [14]. Similar to suicide attempts, *self-harm* episode outcomes are non-fatal. Within a European context, *self-harm* includes any act of self-poisoning or self-injury, regardless of associated motivation and intent [15], but suicide intent is often present. However, the amount of intent may vary, and death may not be wanted as much as a temporary break from a problem [16]. The intention behind self-harming behaviour may actually not involve a

death wish at all, in which the behaviour in literature from the United States (US) often is referred to as (non-suicidal) self-injury [17, 18]. It is difficult (and impossible within the framework of this thesis) to reliably distinguish self-harm without suicidal intention from suicide attempts. As mentioned above, and according to the literature [4], this thesis will use the terms self-harm and self-harming behaviour to describe and include any behaviour or act of self-injury or self-poisoning, independent of presence or amount of suicidal intent.

1.2 Epidemiology

Self-harm is associated with a multitude of health adversities: first and foremost suicide, but also premature death by natural causes related to circulatory and gastrointestinal organ systems [19]. Furthermore, self-harm represents a major health concern due to psychiatric comorbidities such as affective, anxiety or personality disorders, as well as maladaptive functioning in later life [10, 20]. Various life problems, such as partner and relationship difficulties, mental health issues and alcohol problems, are commonly co-occurring in hospital-presenting self-harm patients [21], and often trigger self-harm behaviour directly. Self-harm in offspring puts a great strain on parents' wellbeing [22, 23], and affects both parental behaviour and perceived parenting [24, 25]. In addition to the impact on single individuals and their closest families and friends, self-harm constitutes a substantial economic burden on the society in general, and health care institutions in particular [6, 26].

In terms of self-harm methods, self-cutting is a commonly reported method in community samples [11]. However, most of these episodes never reach the attention of health care personnel [27-29]. Self-poisoning and overdoses constitutes the majority of hospital-presenting self-harm episodes [29], and adolescents discharged from hospital after self-poisoning are at greatly increased risk of suicide and other causes of premature death many years later [30]. Apart from self-harm methods and differences in associated potential harm, chance of presentation to health services after self-harm is also affected by geography, personality, gender, and presence or absence of a supporting social network. While no substantial differences were found regarding help-seeking after self-harm with suicide intent, the likelihood of using health services after

self-harm without suicidal intent was four times higher in urban than suburban or rural areas [31].

Self-harm is rare before 12 years of age [32], but those who self-harm at this young age are likely to do so in adolescence also [33]. Incidence of self-harm rapidly increases and peaks between the age 15 and 25, followed by a slow decline [34]. English data indicate small overall differences in self-harm incidence from 2000 to 2012, except from a noted increase in the latest years of follow-up [35]. Evidence of gender differences is abundant, and females are clearly overrepresented in early adolescence. However, gender differences tend to decline with age, at least when it comes to self-harm presenting to hospital. One study reported the female-to-male ratio to be 6.3:1 at 12 – 14 years old and reduced to 1.2:1 at 22 – 25 years old [36]. Another study reported a total ratio at 1.5:1 for all ages pooled, but 8:1 in 10 – 14-year-olds, 3.1:1 in 15 – 19-year-olds, 1.6:1 in 20 – 24-year-olds, around 1.3:1 in 25 – 49-year-olds, and 0.8:1 in people 50 years and older [37].

A few studies have examined occurrence of self-harm and suicide attempts among Norwegian adolescents [38] and adults (15 years and above) [39, 40]. Reported lifetime prevalence of self-harm with and without suicidal intention was 3 % in the adolescent group, and 1-year incidence of suicide attempts was 0.9 %. Nationally, estimated yearly incidence rate of self-harm hospitalisation was 120 per 100 000 person years, with highest incidence found in women aged 20 – 24 years [39]. Data from the Stavanger region, Norway, demonstrated person-based incidence rates at 176 and 178 per 100 000 males and female person years, respectively. Corresponding episode-based rates were 214 and 208 per 100 000 person years, and at least one repetition occurred in 25 % within 5 years [40]. Another national register study assessed hospital admissions and readmissions for self-poisoning with medications in Norwegian adolescents [41], where female-to-male ratio was 3.2:1, and 18.4 % were hospitalised again for medication self-poisoning during the four-year observation period.

A small proportion of all patients who self-harm can be classified as high-volume repeaters. Using data from a multi-centre study in England, authors defined high-volume repeaters as patients with at least 15 attendances within 4 years to emergency departments, and these patients (0.6 %) accounted for 10 per cent of all self-harm

admissions to emergency departments [42]. The risk of repeated self-harm is highest during the first months after the initial episode [43]. Yet, prediction of repeated self-harm is challenging as no scale in common use provides such reliable information [44]. Within 5 years after the index episode of self-harm presenting to hospital, a fatal repetition (suicide) happens to 1 in 25 patients, and a non-fatal repetition to 1 in 6 patients [45]. A Canadian study reported three hospitalisations for self-inflicted injuries per registered suicide [46]. Globally, there are 20 – 25 nonfatal suicide attempts per completed suicide [47], differing by country, region, age and gender. Higher ratios are found in females, and in young adults (18 – 30 years old) [48]. Among adolescents who self-harm, risk of death by suicide in males is also substantially higher than in females [49], as males tend to choose more violent methods associated with increased lethality, possibly because of differences in motivation and intention underlying the act.

1.3 The Norwegian health care system

With the National Strategy for Suicide Prevention in 1995, Norway was one of the first countries to establish and implement national recommendations regarding care of suicide attempters [50]. Systematic in-hospital assessment of psychosocial and suicide risk was one of the main components that were recommended. Research indicates that non-assessed self-harm patients who were discharged directly from the emergency department were twice as likely to present again with another episode of self-harm during the following year, as compared to those who did receive such assessment [51]. In England, only around half of patients presenting to hospital emergency departments with a self-harm episode receive psychosocial specialist assessment, even fewer are admitted to a hospital ward [52]. To our best knowledge, there has not been any systematic assessment of the corresponding situation in emergency departments in Norway so far, but two thirds of Norwegian general hospitals with emergency departments reported that more than 90 % of their hospitalised self-harm patients were provided with in-hospital psychiatric assessment [53]. Previous recommendations [50] were established as national quality standards in Norway in 2001 [54], and an updated plan of action was released in 2014 [55]. Guidelines have also been established for suicide prevention specifically among patients in psychiatric specialist healthcare [56].

The health care system in Norway is built on the Scandinavian welfare model principle of universal and equal access to services independent of social class, financial resources or geographical factors. Health care is provided at two main levels: *primary care level* provided by the municipalities, where general practitioners have the main role and functions as gatekeepers referring patients in need of more complex care at the *specialized health care level*, constituted by hospitals owned by regional health authorities and their hospital trusts [57]. Health care is divided into public and private sector, where the public sector mainly is funded by the government via the health department, and the private sector mostly rely on out-of-the-pocket payments.

Pre-hospital emergency medical services are provided by in-office general practitioners during regular work hours, and on-call general practitioners outside work hours. Contact rates to out-of-hours services for episodes of self-poisoning are increasing in Norway for all groups except small children, and women between 15 and 25 years present most frequently (785 per 100 000 inhabitants) [58]. If there might be urgent need of specialized or complex healthcare exceeding what can be provided pre-hospital, patients may be referred to accident and emergency departments at the nearest hospital providing emergency care. There, a specialized nurse triage the patient (i.e., assesses the severity of the condition and determines what priority the patient's treatment should have), before a physician decides whether or not the patient should be hospitalised. Patients with inconclusive conditions can as an alternative be monitored in observational units, with less resources than ordinary hospital units. Outpatient appointments constitute the majority of treatment provided in Norwegian hospitals, and around 90 % of these appointments are planned activities. The distribution is opposite for in-patient stays, where almost 70 % of over-night hospitalisation episodes (for example heart disease episodes, injuries and poisoning) are emergency related [59].

Aetiology and mechanisms underpinning self-harm behaviour is complex and, unfortunately, evidence of effective treatment and interventions is scarce and weak, both for youth [60] and adults [61, 62]. Despite positive qualities in previously published literature, many of the existing longitudinal studies have limitations; few participants, low participation, and the use of self-report measures for self-harm behaviours are common shortcomings. In addition, baseline exposure data are often

limited - an unfortunate feature concerning the complexity of mechanisms underlying self-harm.

1.4 Suicide intent, motives and function of self-harm

Self-harm may function as an externally directed cry for help, or an internally oriented cry of pain [63], in other words attempting to evoke reaction in others, or to regulate or modulate own feelings and emotions. Both dimensions can be viewed as ways of handling emotional distress. Young adolescents often self-harm “to get relief from a terrible state of mind”, while interpersonal reasons such as “to frighten someone” is less common [64]. In those presenting to hospital with self-harm, wanting to escape from a problem was more often endorsed in combination with high suicide intent, while those reporting lower intent more often wanted to appeal to others or get a temporary break from their problem [16].

Self-harm without suicidal intention (non-suicidal self-injury) is often explained as a coping mechanism, or emotional regulation, a way to get relief from mind states that in the moment seem unbearable [65]. Similar to human behaviour in general, non-suicidal self-injury is also affected and maintained by variants of reinforcement, for example by reducing or distracting from negative feelings (negative intrapersonal reinforcements) [66]. Reported non-suicidal reasons for self-harm may also be positive, and include self-validation or achieving a personal sense of mastery, in addition to dealing with distress and exerting interpersonal influence [67].

Negative life events are important contributing factors to self-harm, as self-harm is used to regulate distress and emotional difficulties. Few studies have assessed life events immediately precipitating self-harm, yet reported examples of such events include relationship difficulties, economic and financial problems, and death of a significant other [68]. In early adolescence, relationship problems usually relate to parents, while perceived problems related to a partner or spouse is more common in later adolescence and young adulthood [21]. These relationship problems are often perceived as insoluble, and thus, often accompanied by hopelessness [69].

In the stress-diathesis model of suicidal behaviour [70], diathesis is a constitutional increased vulnerability to develop a disorder (such as suicidal behaviour), in response to perceived stress caused by adverse life events. Self-blame and other non-productive coping strategies is associated with self-harming, while productive strategies (for example consulting significant others for support), is likely to reduce perceived stress, and thus lower the risk of self-harm [71]. Various biopsychosocial factors exert force on each side of the lever, and more stress can be tolerated when protective forces are available. Yet again other models focus on cognitive, clinical or neurobiological pathways to suicidal behaviour. The concept of psycho-neuro-endocrino-immunology [72] encompasses the mind and body as one unity – and holds promise for a more holistic understanding of the self-harm phenomenon.

1.5 Factors associated with self-harm

Numerous study designs have been applied to identify risk factors for self-harm, and as a consequence, findings diverge. Unfortunately, many studies assessing youth provide low level of evidence, especially for factors associated with suicide attempts and suicidal ideation [73]. Still, aggregated results have identified several risk factors for self-harm, including various psychiatric and psychological factors (for example symptomatic or diagnosed depression and other affective disorders, eating disorder, low self-esteem, impulsivity), negative individual factors (parental divorce or death, bullying, exposure to childhood trauma, relationship problems and other adverse life events), as well as sociodemographic factors (female gender, poor socioeconomic status) [21, 27, 74-77]. Completed suicide and non-fatal self-harm share many characteristics, and many suicide risk factors are also associated with self-harm [27]. In the following, we will focus on self-harm related factors appearing in adolescence, both intra- and interpersonal difficulties, as well as physiological, physical and psychiatric conditions.

1.5.1 Sleep problems

The concept of physiological homeostasis was initially presented almost 100 years ago [78], and describes the tendency to maintain stable internal conditions even if external conditions vary. The human organism needs homeostasis for optimal functioning, and compromised homeostatic integrity initiates counteractive measures, to return to equilibrium. Sleep homeostasis and the circadian cycle are two core factors responsible for regulating the sleep-wake cycle [79]. Adequate nocturnal sleep is a fundamental need for general health [80], and sleep problems cause disruptions in psycho-neuro-immunologic homeostasis [79].

Growing evidence upholds that associations exist between sleep problems and multiple adverse outcomes, including poor academic performance, cognitive and emotional dysfunction, early onset use of alcohol and other illicit drugs, and psychiatric illness, self-harm and suicide [81-88]. Sleep disturbances increase levels of endogenous proinflammatory cytokines such as CRP and IL-6 [89]. Moreover, inflammation is bi-directionally linked with depression [90], thus providing a plausible pathway from sleep problems to self-harm.

Few large, population-based longitudinal studies have assessed how sleep problems influence risk of self-harm. Most published studies arise from the US, reporting associations between sleep problems and decreased self-esteem, depression symptoms and -diagnosis, and future suicidal thoughts and attempts [91-94]. Moreover, results from a Japanese twin study suggested a causal relationship between sleep habits and self-harm [95], and a dose-response relationship between sleep problems and risk of self-harm was reported in a longitudinal study assessing Norwegian adolescents [96]. Further research is warranted to better understand which mechanisms are involved in the relationship between sleep problems and self-harm behaviour.

1.5.2 Mental and physical health factors

An increasing literature base underlines the many and strong associations between self-harm and other mental health issues [10, 20, 27]. Previous self-harm, anxiety disorders, unipolar depression and bipolar disorder, and borderline personality disorder, are

overrepresented among people who have self-harmed in clinical samples, as well as in population-based studies. Childhood trauma in form of physical or sexual abuse is also frequently identified [97, 98], and results from a study of non-suicidal self-injury in Italian adolescents indicated that sexual abuse in childhood was associated with both presence and severity of the behaviour [99].

Self-harm behaviour is frequently found to be comorbid to borderline personality disorder [100] and mood disorders [101], including subthreshold symptoms of depression [102]. Mood disorders seem to be the strongest predictors of suicide attempts in developed countries, while issues regarding impulse-control, substance use, and post-traumatic stress disorders better predict suicide attempts in developing countries [103].

A growing interest is emerging around the interplay between self-harm and physical ailments, and associations between self-harm and various illnesses and functional impairment have been reported [104-106]. Physical illness can be accompanied by pain, and pain can occur by itself too – often with non-malignant musculoskeletal cause. Chronic musculoskeletal pain is a common health problem in adolescence, and associated with perceived stress [107], symptoms of anxiety and depression [108], and reduced sleep quality [109]. International data describing adolescents indicate that different pain subtypes coexist more often than occurring in isolation, that pain is more prevalent in females, and that pain prevalence increase throughout adolescence [110]. Suffering adolescents might experience feelings of hopelessness and helplessness related to their chronic pain. Combined with poor problem-solving abilities, these psychological processes likely contribute to the enhanced risk of suicidal thoughts, suicide attempts and completed suicides reported [111]. Furthermore, presence of various self-reported chronic illnesses (for example asthma, high blood pressure, migraine, diabetes, epilepsy, bowel disease) in Canadian youth (15 – 30 years) increased odds of suicidal thoughts, plans and attempts [112].

While self-harm and suicide attempt rates decline after a peak in adolescence and young adulthood, numbers increase again later in life. Among additional reasons, the heightened risk of attempted and completed suicide observed among older adults is related to the perceived elevated burden caused by pain and physical disease [113]. In a

recent study encompassing the entire Danish population aged 65 years or more, adjusted results display substantially increased suicide risk associated with multiple diseases, including various cancers, cerebrovascular disease, heart disease, gastrointestinal disease, epilepsy, cataract and more [114]. Comorbid depression might explain some, but not all of the elevated risk conveyed by physical illnesses, as UK results also indicate solid associations in women with asthma, diabetes, back pain, epilepsy, or hypertension – even when adjusting for depression [115].

Migraine and other severe type headaches are associated with unipolar and bipolar disorders, and also with increased risk of suicidal ideation and suicide attempts [116]. Dysfunctions in neural serotonergic systems are related both to suicidality, depression and migraine, and may in part explain the underlying comorbidity between these conditions. Interestingly, migraine with aura – but not migraine without aura – was associated with high suicidal risk in a sample of Taiwanese adolescents, when controlling for age, gender, anxiety and depression [117].

Further, people with epilepsy are at increased risk of suicide, and have been found presenting to hospital with self-harm at twice the rate compared to people without epilepsy [118]. It has been indicated in single studies that suicidal behaviour and epilepsy may share common gene polymorphisms related to serotonin transmission, but a meta-analysis could not confirm these findings [119]. Moreover, the proposed association between epilepsy and self-harm has also been challenged, by community-based studies failing to find substantial or lasting associations between childhood epilepsy and suicidal ideation or suicide attempt [120].

In sum, there are multiple pathways and mechanisms involved in both physical and mental illnesses, creating a complex and entangled network of risk factors for self-harm. On top – or perhaps at the bottom of it all, individual personality factors influence how we cope with distress, illness and disease, and how we interact with others.

1.5.3 Personality

A long history of personality studies have provided valuable insights into how personality impact on several short- and long-term outcomes related to health and

function [121]. Numerous theoretical paradigms emphasize distinct facets (psychoanalytic, behavioural, trait, biologic, or social-cognitive) when used to define personality and how it is developed [122]. All theories build on a general consensus that we are born with temperament, i.e. an individual biologically dependent predisposition of how to act and react on stimuli from the environment. Consequently, such predisposition features in childhood are described as temperamental traits, while personality is the adult, more complex and developed equivalent to temperament. Temperament and personality are continuous constructs, with a temporary overlap as childhood is followed by adolescence. The earliest temperamental traits encompass fear, anger or frustration, positive affect and approach, activity level and attentional persistence [123]. These traits evolve and new dimensions (e.g. shyness, impulsivity) emerge as childhood passes, adding further complexity to the picture. Based on factor analyses, three broad factors (surgency or extraversion, negative affectivity, and effortful control) emerge among 3 – 8 year old children [124]. These factors bear some resemblance to factors of extroversion and neuroticism from Eysenck [125], or extraversion and negative affectivity from Goldberg's big-five factor model [126]. Some previous reports suggest that temperamental traits that emerge in childhood are relatively stable, and persists into adult age [127, 128]. Other studies claim that most pronounced changes of the five-factor personality traits occur in the beginning and end of life, and that these changes are likely to result from both genes and environmental events [129].

Adult personality traits are associated with both body size perception [130] and sleep quality [131], and increasing amounts of evidence indicate that personality and psychological factors affect the risk of self-harm and suicidal behaviour. Neuroticism is associated to suicidal behaviour and suicide attempts in both youth and adults, while extroversion is lower among suicide attempters than non-attempters [132]. Authors found a gender difference when comparing suicide attempters and completers, with higher extroversion in male suicide completers than attempters, and the opposite result for females [133]. Further, hopelessness is commonly experienced among patients who self-harm, and this psychological phenomenon exacerbate the risk-increasing effect of other factors on self-harm and suicide [134]. People with a history of non-suicidal self-

injury display higher neuroticism, openness to experience, and lower conscientiousness than those without such history [135]. Moreover, there are data indicative of a relationship between personality, function of the self-injury, and number of methods used to self-injure [136]. A less studied feature is psychoticism [137], which has suffered critique and controversies. For instance, rather than describing a continuum from normal to higher risk of developing psychosis, some claim that personality traits of psychoticism relate more to a variety of features involving constraint, including impulsivity, recklessness and poor socialization skills. Investigators have reported elevated psychoticism traits among adolescent self-harmers [138].

Available knowledge about the interplay between personality and self-harming behaviour is increasing. Nonetheless, only a minority of previous studies has applied longitudinal designs within adolescent community populations, leaving a gap we attempt to fill with the present study.

2 Objectives

The main objective of this thesis was to examine associations between a range of self-reported factors related to demography, health and personality in adolescence, and risk of later self-harm hospitalisation. Potential effect measure modification by caseness symptoms of anxiety and depression (paper I), gender (papers I and II), and age (paper II) was also examined. The overall objective was investigated and reported in three separate studies with the following specific aims:

Paper I: To study the association between sleep problems in adolescence and risk of later self-harm hospitalisation.

Paper II: To investigate how mental and physical illnesses and health conditions in adolescence impact on future self-harm hospitalisation risk.

Paper III: To examine the associations between adolescent self-esteem, traits of neuroticism, extroversion and psychoticism, and risk of later self-harm hospitalisation.

3 Material and methods

3.1 The Nord-Trøndelag Health Study (HUNT)

Norway had a population of 5 258 317 persons per 1 January 2017 [139], equating an average population density of 14 persons per km².



Figure 1. Norway with Nord-Trøndelag County marked ¹

Nord-Trøndelag County was one of 19 administrative regions in Norway. From 1 January 2018, Nord- and Sør-Trøndelag Counties merged as Trøndelag County, resulting from a political region reform [140]. Geographically located in central Norway, Nord-Trøndelag covers approximately 22 400 km², and had 136 399 inhabitants by the beginning of 2016 [141]. The county is mainly rural and lacks large cities. Population numbers in town centres per 1 January 2016 were: Steinkjer 12 466, Stjørdal 11 934, Levanger 9745 and Namsos 8322, but some municipality towns (Steinkjer, Stjørdal) exceed 20 000 inhabitants in total. Nord-Trøndelag is considered

¹ Map basis: Norwegian Mapping Authority (Creative Commons Attribution ShareAlike 3.0)

fairly representative of Norway as a whole, and adolescents (13 – 19 years) accounts for almost 10 500 people [142].

The Nord-Trøndelag Health Study (HUNT – www.ntnu.edu/hunt) is a large health study covering the entire population in Nord-Trøndelag aged 13 and above. For adults 20 years and above, three study waves have been conducted so far: HUNT1 (1984 – 86), HUNT2 (1995 – 97), and HUNT3 (2006 – 08). All adolescents (13 – 19 years old, i.e. pupils attending lower or upper secondary school) were invited to the Young-HUNT Study (www.ntnu.edu/hunt/young-hunt) [142]. Young-HUNT1 (1995 – 97) was the first of three waves so far, and data from 8983 participants serve as baseline measure in this study. The later follow up studies Young-HUNT2 and Young-HUNT3 were carried out in 1999 – 2000 and 2006 – 08, respectively.

Principals at all schools in Nord-Trøndelag County consented to school participation in Young-HUNT. Data collection consisted of a self-report questionnaire administered by teachers and completed by pupils present in class during a school-hour long test-like setting. Within one month later, specially trained nurses visited the schools for structured interviews and clinical health examinations of the participants. On the same occasion, initially absent invitees were invited to complete their questionnaire.

In total, 10 202 adolescents were invited to take part in Young-HUNT1. Of these, 8983 persons (88%) completed the questionnaire, and 8439 (83%) completed both the questionnaire and the health examination. Non-responders were mainly pupils absent from school on the participation day. Questionnaire items covered e.g. physical and mental health, physical activity, quality of life, pubertal staging, eating disorders and psychosomatic disorders, tobacco and alcohol habits and reading/writing difficulties. The clinical examination included measurements of blood pressure, pulse, weight, height, waist and hip circumference. English translations of original questionnaires are available in full text online (www.ntnu.edu/hunt/data/que) [143].

The HUNT Study is a collaboration between HUNT Research Centre, the Faculty of Medicine and Health Sciences at the Norwegian University of Science and Technology, the Norwegian Institute of Public Health, Nord-Trøndelag County Council,

and the Central Norwegian Regional Health Authority. Participation in the Young-HUNT Study was encouraged, but voluntary, and participants were not given any financial or other incentives.

3.2 Study variables

Baseline data used in this thesis are from Young-HUNT1 and Statistics Norway (highest attained parental educational level), and endpoint data from our own recording of self-harm hospitalisation episodes at Levanger and Namsos Hospitals – the only two hospitals covering the HUNT catchment area (Nord-Trøndelag County).

3.2.1 Endpoint measurement: first episode of self-harm hospitalisation

Primary end point in all three papers was the index self-harm hospitalisation episode, i.e. the first hospitalisation due to a self-harm episode among participants in Young-HUNT1. Since participants mainly were recruited when attending regular school, no complete official invitation list with unique 11-digit national ID number (*fødselsnummer*, similar to Social Security number in the US and National Insurance number in the UK) for Young-HUNT1 invitees exist – like it does for adult HUNT participants. First, we developed an algorithm describing how to identify self-harm incidents in hospital-based patient records within the Young-HUNT1 age cohort, and how to collect information about these episodes from the record entries. Then, a list of all hospitalisations in this cohort was generated from the patient administrative system (PAS) at Levanger and Namsos Hospitals. This list covered the period from 1 January 1995 to 31 December 2010, and consisted of every acute hospitalisation for every inhabitant within the Young-HUNT1 participation age range.

Each admission in the PAS list contained patient name and national ID number, date of admission and what department the patient was admitted to, ICD-9 or -10 diagnosis codes (given at hospital discharge by the physician in charge) and a free text field filled in by a nurse in the emergency department, describing main cause of patient presentation (e.g. “chest pain,” “fever and vomiting,” “intoxication,” “suicide attempt”). This tentative diagnosis may in retrospect to various degrees be correct, but gives a

good estimate of the main reason for admission. We created a list of search terms/ criteria based on other studies [144-146] and our clinical knowledge of possible reasons, symptoms, and mechanisms associated with self-harm. The method developed in this project (Appendix) displayed excellent sensitivity of incident self-harm ending with admission to hospital. One major obstacle impeded a direct and quick identification of all self-harm hospitalisation episodes: specific ICD-codes for self-harm (in ICD-10: X6n, Intentional self-harm) were only occasionally used in the episodes that eventually were identified and confirmed as self-harm hospitalisations. Consequentially, self-harm hospitalisation statistics are likely to suffer from large underestimation. Similar results are reported from the UK, where approximately 40 % was identified using standard hospital episode statistic data [147], and Norway, where an ICD self-harm diagnosis was given only to half of all patients experiencing a self-harm induced somatic admission after a previous discharge from psychiatric hospital [148]. Further, many self-harm episodes involving superficial cutting present to accident and emergency departments, and are thereafter sent back home or admitted as an inpatient instead of being internally referred to an emergency surgical outpatient-appointment. We identified one study that developed and tested an algorithm to identify intentional self-harm where E-codes (external cause of injury, used in ICD-9) were absent or incompletely reported [149]. The algorithm produced excellent specificity, good positive predictive value and adequate sensitivity, but we could unfortunately not use this algorithm in our studies because of differences between ICD-9 and ICD-10 systems, and that the majority of our outcome data was ICD-10 coded.

Together with three specially trained nurses, the author (AJ) searched the patient administrative system list for relevant text strings and ICD-codes (see Appendix to paper I) and manually inspected patient records that were positive in the search results. Of nearly 6000 patients, almost 1700 were positive in the screening search. Two thirds of these were false positives (high sensitivity/low specificity search, e.g. the search term “cut” returned “**acute** appendicitis”), and approximately 50% of the remaining were hospitalised for other reasons than intentional self-harm. This left 273 patients with confirmed first-time self-harm hospitalisations, of which 175 persons had not participated in Young-HUNT1. Finally, we excluded 9 out of the 98 remaining because

they experienced their first self-harm hospitalisation prior to the date of Young-HUNT1 participation. Due to an inadvertence, the nine patients who experienced self-harm hospitalisation before they participated in Young-HUNT1 were included in descriptive statistics in Table 1 in paper I. The corresponding number of self-harm cases presented in Table 2 in paper I also reads 98. However, the nine patients were censored from regression analyses due to the analysis setup, meaning that regression analyses actually included 89 patients. Hence, reported main results (regression analyses) were correct, and there were only insignificant (decimal level) errors in descriptive statistics.

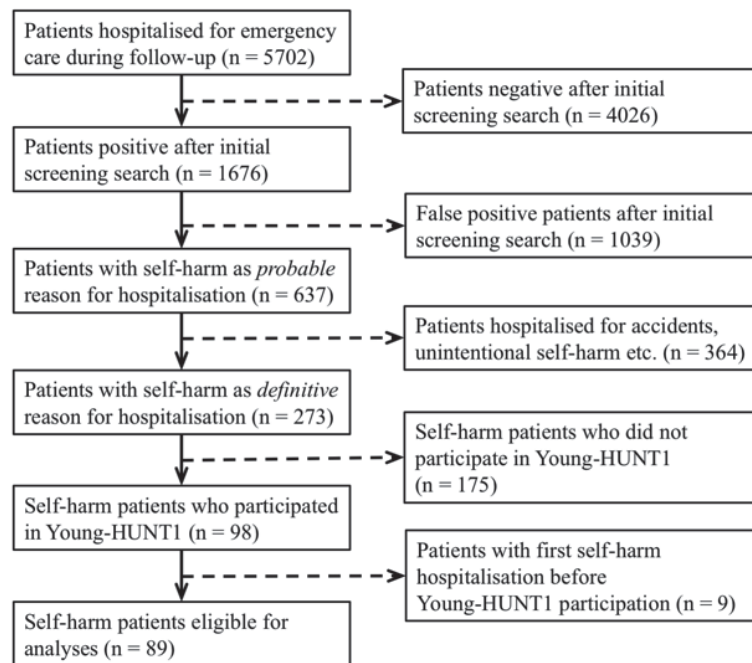


Figure 2. Identification and inclusion of first time self-harm hospitalisation patients

We then included all patients admitted to hospital due to intentional self-poisoning or self-injury, irrespective of motive and extent of suicidal intent. Altogether, we identified 89 persons from the Young-HUNT1 cohort who were hospitalised after a self-harm episode during the follow-up time. We recorded data on date and time of self-harm, self-harm method(s), type of psychiatric care offered or provided to the patient, somatic

or psychiatric comorbidity, and presence of any subsequent admissions due to self-harm, where applicable. A research technician at HUNT Research Centre provided linkage of the recorded endpoint data and Young-HUNT1 data. Linked participant data were de-identified and assigned new, project-specific identification numbers, before data were returned to AJ.

3.2.2 Adjustment variables from Statistics Norway

Statistics Norway has the overall responsibility for official statistics in Norway, and maintains several databases. We obtained data from Statistics Norway on highest attained educational level for Young-HUNT1 participants' biological parents. These data are recorded only once per person, on 1 October the year they turn 16 years old. National ID numbers enabled linkage of data from Young-HUNT and Statistics Norway, and we used these data in papers II and III as a marker of socioeconomic status.

3.2.3 Baseline data from Young-HUNT1

For questionnaire items that we recoded from nominal categorical into binary, new recoded values can be inferred based on the following legend:

Original options in italic: 0 / Low / Non-caseness / No

Original options in bold italic: 1 / High / Caseness / Yes

3.2.3.1 Age

We adjusted for age in all Cox regression analyses by using attained age as time axis. In paper I, we stratified participants into two age groups (< 16 years old and ≥ 16 years old), and looked for any potential age-related differences in sleep problem prevalence. The chosen cut-off corresponds well with median and mean attained participant age at baseline (15.9 and 16.0 years, respectively).

3.2.3.2 Alcohol use

We included alcohol use as an adjustment variable in paper I, and used it as a main exposure variable in paper II. In both papers, we recoded the originally categorical variable into a binary version (0 / 1) and set cut-off at 10 times. This definition has the advantage of being reasonably valid and reliable, both on a population and individual level [150], and has been applied in previous studies on this cohort [151, 152]. Missing responses were recoded as 0.

Questionnaire item:

Have you ever drunk so much alcohol that you felt intoxicated (drunk)?

Response options (choose one):

*No, never / Yes, once / Yes, 2-3 times / Yes, 4-10 times / **Yes, more than 10 times***

3.2.3.3 Anxiety and depression

Anxiety and depression symptoms during the two last weeks were assessed with a five-item version of the Hopkins Symptom Checklist (SCL-5) [153, 154].

Questionnaire items:

Below is a list of some problems. Have you been bothered by any of these in the last 14 days?

Been constantly afraid and anxious

Felt tense or uneasy

Felt hopelessness when you think of the future

Felt dejected or sad

Worried too much about various things

Response options (choose one):

*Not at all / A little / **Quite a bit** / **Very***

In paper I, we calculated an average scale score (range 1 – 4, calculated only when maximum two out of five item responses were missing), created a new binary variable and defined an average SCL-5 score above 2.00 to indicate caseness symptoms of anxiety and depression [153]. In paper II, we also created binary versions of all five single SCL-5 items. These binary single items were included in Cox regression analyses, together with the binary variable indicating caseness anxiety and/or depression symptoms (average SCL-5 score > 2.00).

3.2.3.4 Body mass index

Body mass index (BMI; kg/m²) was calculated from height and weight measurements recorded by specially trained nurses at baseline. In order to retain as much information as possible, we calculated age- and sex- specific Z-scores (number of standard deviations deviating from the group mean BMI) and used BMI Z-score as a continuous variable in paper I to adjust for possible confounding. In paper II, we used BMI as a categorical variable in order to increase readability and ease of inference. We applied international age- and gender specific cut-off values proposed by Cole et al. [155, 156], and assigned participants to BMI categories of underweight (BMI < 18.5), normal weight (BMI 18.5 – 25), overweight (BMI 25 – 30) and obesity (BMI > 30).

3.2.3.5 Bullying

We included being victim to bullying as one of the markers of mental health in paper II. The question was originally created for a Norwegian Institute of Public Health study covering child sexual abuse [157]. The item lacks psychometric validation, but has been used in multiple studies [158, 159]. We recoded the variable from categorical to dichotomous.

Questionnaire item:

Does it happen or has it previously happened that you are teased or harassed by other students at school?

Response options (choose one):

Never / From time to time / Often / Very often

3.2.3.6 Cohabitation situation

We included this covariate in paper II by creating a binary variable that indicated whether or not a participant lived together with both his or her parents.

Questionnaire item:

Are your parents separated or divorced, or have they lived separately for more than one year?

Response options (choose one):

No / Yes, they lived separately or were separated, but they later moved back together again / Yes, they were divorced or permanently separated

3.2.3.7 Gender

Extensive literature describes gender differences in self-harm prevalence and choice of method. Thus, we adjusted for centrally registered gender in all analyses, and used male gender as reference (because self-harm is assumed more common among females in the age group analysed), or stratified by gender, whenever appropriate.

3.2.3.8 Loneliness

Loneliness was one of the dependent variables we assessed in paper II. The questionnaire item was created specifically for HUNT. Coherent with previous literature [160], we recoded original response options into a binary alternative.

Questionnaire item:

Do you feel lonely?

Response options (choose one):

Very seldom or never / Seldom / Sometimes / Often / Very often

3.2.3.9 Personality

In paper III we examined associations between adolescent personality traits and later self-harm risk. In Young-HUNT1, personality traits were assessed with a short-version of Eysenck's Personality Questionnaire (EPQ-18) [125]. The dimensions measured is extroversion (often described as extroversion-introversion axis), neuroticism (often also described as emotional instability) and psychoticism.

Questionnaire items:

Are you a relatively lively person?

Would you be upset by seeing a child or animal suffer?

Do you like meeting new people?

Are your feelings easily hurt?

Do you often feel that you lose interest?

Do you like to tease people even though it may hurt them?

Are you often worried?

Are good manners and cleanliness important to you?

Do you worry that terrible things might happen?

Do you usually take the first step to make new friends?

Are you mostly quiet when you are around other people?

Do you like to be on time for appointments?

Do you often feel tired and indifferent/unmotivated without reason?

Do many people try to avoid you?

Are you a life-of-the-party type person?

Are you bothered by an embarrassing experience long after it happens?

Do you like to have a lot of life and excitement around you?

Do people tell you a lot of lies?

Response options:

Yes / No

Previous studies using Eysenck's Personality Questionnaire have identified personality-related associations to self-harming behaviour and suicide attempts [161, 162], cocaine use [163], and axis I and II comorbidity among patients with major depressive disorder [164]. The Young-HUNT1 version included 18 items (six items per sub-dimension), with wording slightly modified from the original to better suit the youngest participants. Score increased with 1 point per positive response, so all participants scored from 0 to 6 on each subscale (6 indicating highest trait exposure). This subscale sum score was included as a categorical variable (7 values) in the analyses, along with all single items as binary variables. A reliability generalization study noted considerable variation in score reliability across subscales (poorest performing by psychoticism), but higher reliability with student samples compared to samples of other individuals [165]. Accordingly, Cronbach's alpha values in this study were 0.60, 0.65 and 0.34 for extroversion, neuroticism and psychoticism subscales, respectively.

3.2.3.10 Somatic symptoms

Twelve-month prevalence of somatic symptoms has been analysed in previous studies of the Young-HUNT cohort, for example assessing later receipt of social health insurance benefits [166], suicidal thoughts [167], or welfare dependence [168]. In paper I, we included headache, neck- and shoulder pain, muscle or joint pain, stomach pain, nausea, constipation, diarrhoea and heart palpitations, and dichotomised each sub-item. We created two sub-groups of items (related to pain, and gastrointestinal disturbance), and in addition kept heart palpitations by itself. In paper II, we analysed stomach pain and headache by themselves as dependent variables.

Questionnaire items:

Have you had any of these ailments in the past 12 months?

Headache (without known medical cause)

Neck or shoulder pain

Joint or muscle pain

Stomach pain

Nausea

Constipation

Diarrhoea

Heart palpitations

Response options (choose one):

*Never / Seldom / **Sometimes** / Often*

3.2.3.11 Self-esteem

Self-esteem was assessed with a four-item version of the Rosenberg Self-Esteem Scale [169] (items 5, 6, 7 and 10 in the original version). The Norwegian version is previously validated in an adolescent sample [170], and the four-item version correlation to the original version is estimated at 0.95, with an alpha reliability at 0.78 [171]. In addition to include each item as categorical variables, we created one additional variable by summing responses to single items into one total self-esteem score, if no responses were missing. We included these five categorical self-esteem variables as dependent variables in paper III.

Questionnaire items:

I take a positive attitude toward myself.

I certainly feel useless at times.

I feel I do not have much to be proud of.

I feel that I'm a person of worth, at least on an equal plane with others.

Response options (choose one):

Strongly disagree / Disagree / Agree / Strongly agree

3.2.3.12 Sleep problems

We included sleep problems as independent variables in paper I. Previous research assessing the same population indicates a dose-response relationship between insomnia symptoms and later high school drop-out [172]. Original response options were dichotomised, and we also created two additional, binary variables. One was coded positive if one, or the other, or both original items were positive. The other was coded positive only if both original items were positive.

Questionnaire items:

During the last month have you:

Had difficulty falling asleep?

Woke up too early and not been able to fall asleep again?

Response options (choose one):

*Never / Sometimes / **Often** / **Almost every night***

3.2.3.13 Smoking

We classified smoking status similar to previous studies of this cohort [108, 173], as present non-smoker, or present smoker. We controlled for smoking status in paper I, and included smoking as an independent variable in paper II. We did not account for number of cigarettes or smoking years.

Questionnaire item:

[If yes, ever tried smoking]: At present, do you smoke?

Response options (choose one):

Yes, I smoke daily** / **Yes, I smoke occasionally, but not daily** / **No, not anymore, but previously I smoked once in a while** / **No, not anymore, but I previously smoked daily** / **No, I don't smoke

3.2.3.14 Physical illnesses

The Young-HUNT1 questionnaire contained multiple items assessing presence of physical illnesses. We adjusted for physical illnesses in paper I, and included presence of diagnosed asthma, epilepsy, diabetes, migraine, pulmonary disease, or other diseases lasting more than three months, in our categorisation of physical health status. Similar to previous studies [166, 172], participants were scored 1 if at least one of these conditions were present, 0 if not. In order to shed more light on associations between physical illnesses and self-harm, we analysed five conditions separately in paper II (allergy, skin rash, diagnosed epilepsy, migraine and asthma). Items covering presence of asthma, allergy and skin rash were adapted from the ISAAC core questionnaire [174].

Questionnaire items:

Has a doctor said that you have:

Diabetes?

Epilepsy?

Migraine?

If yes [asthma ever]: Has a doctor said that you have had asthma?

[If yes, other sicknesses which lasted more 3 months]: Which?

Pulmonary disease

Allergies

Other disease/illness

Have you ever had an itchy rash which was coming and going for at least 6 months?

Response options:

Yes / No

3.3 Statistical analyses

All data were analysed using Stata software (Stata Corp., College Station, Texas), version SE 12.0 for Mac (paper I) and version SE 12.1 for Mac (papers II and III).

3.3.1 Cox Proportional Hazards regression

The main method of statistical analysis was Cox proportional hazards regression [175]. Effect estimates were reported as hazard ratios (HR), with 95 % confidence intervals (CI). We tested the assumption of proportional hazards by assessing Schoenfeld residuals [176, 177] for all independent variables in our analyses. No results indicating violation of the proportional hazards assumptions were detected.

Follow-up period was defined as starting on the date each person completed the Young-HUNT1 questionnaire. Study participants were followed until the first occurring of the following alternatives: participant moved out of Nord-Trøndelag County or were otherwise lost to within-county follow-up; participant died; participant experienced their first self-harm hospitalisation; or the date 31 December 2010 was reached.

We applied Cox regression analyses with a varying extent of adjustment for potentially confounding factors. There will be a considerable overlap between different markers of adolescent vulnerability. Consequently, primary intention was not to establish precise estimates of independent effects, but to do explorative analyses with adjustment for possible confounders, in order to identify important factors influencing risk of future self-harm behaviour.

In paper I, we initially adjusted for attained age and gender only. While acknowledging the fact that comorbidities with sleep problems are difficult to disentangle with multivariable adjustment, we added adjustments for potential confounding by physical illnesses and BMI, and finally for any confounding (or possibly mediating) effect of various somatic symptoms, symptoms of anxiety and depression, smoking, and alcohol use.

In paper II, we investigated several dimensions of mental states and physical health in adolescence, and subsequent self-harm hospitalisation risk. Each variable was

initially analysed with adjustment for age only, generating a crude association to later self-harm hospitalisation risk. The final model included additional adjustment for possible confounding by gender, cohabitation situation and parental educational level.

When we assessed associations of personality traits and self-esteem with risk of self-harm hospitalisation in paper III, crude results were obtained by age-adjusted analyses. In the main regression model, we included additional adjustments for confounding caused by gender and parental educational level. In an alternative model, we controlled for symptoms of anxiety and depression, and alcohol use – as these factors also might influence associations between personality, self-esteem and self-harm.

3.3.2 Statistical interaction

We examined whether the effect measures of different exposure variables on self-harm hospitalisation risk differed according to caseness symptoms of anxiety and depression (paper I), gender (papers I and II), or age (paper II).

3.3.3 Missing observations and complete case analyses

Information concerning parental educational level was missing for twenty study participants, and additional information was missing for various participants on various Young-HUNT1 questionnaire items. We recoded missing responses to items assessing somatic illnesses as non-missing (No / 0) in paper I, assuming absence of the disease or disorder if participants did not respond to the relevant item. Missing responses to any of the five items covering symptoms of anxiety and depression were not recoded directly. Instead, we calculated mean SCL-5 score only in participants with responses to minimum three out of five items, by dividing total SCL-5 score by the number of items answered. Participants were excluded from Cox regression analyses if there were missing observations on any other main variable to be analysed or controlled for in the adjusted models.

3.3.4 Additional analyses

Self-harm hospitalisation incidence rates were estimated for all participants, and stratified by gender. In order to assess possible reverse causality in paper II, we estimated hazard ratios for all predictor variables after excluding the first five months of all participants' respective follow-up.

3.4 Ethics

All Young-HUNT1 participants provided written, informed consent for using their data in future research projects (<https://www.ntnu.no/hunt/deltaker/brev>), which could be withdrawn at any time without giving any reason or explanation. Additional consent was obtained from parents or guardians in participants younger than 16 years. The Regional Committee for Medical and Health Research Ethics in Central Norway (REC Central) approved this project (2010/1924-3), included using data on parental educational level obtained from Statistics Norway (papers II and III, 2010/1924-16).

4 Summary of results

In total, we identified 273 persons within the specified age range who during observation time experienced at least one self-harm hospitalisation episode in one of two hospitals covering the Young-HUNT catchment area. Of these, 89 persons (32.6 %) experienced their first episode and had previously participated in Young-HUNT1. Without a complete list containing personal identification numbers of invitees, it is uncertain how many of the remaining 184 persons that were invited to Young-HUNT1, but did not participate. Assumedly, some were not invited to participate because they were too old or too young. Also, one third of the 273 persons ($n = 97$) was not registered with a home address in Nord-Trøndelag at the time of their first self-harm hospitalisation. Quite a few may have moved to Nord-Trøndelag as students some time during Young-HUNT1 or the follow-up period. In the period 1995 – 2010, between 3000 and 5000 university college students were dispersed on four campuses (Levanger, Namsos, Stjørdal and Steinkjer). Many students in Norway do not update national registers with their temporary study address, which probably explain the majority of those without a registered home address in Nord-Trøndelag. Some patients may also simply have visited or passed by the area on travel elsewhere. In addition, approximately 17 % of the non-participation self-harm patients were (international) migrants, asylum seekers, or refugees (registered place of birth outside Norway).

4.1 Results across papers

The final Young-HUNT1 cohort of 8965 adolescents included in our analyses comprised 4451 (49.7%) females, with mean baseline age of 16 years for both genders. Further baseline characteristics of the study population are presented in tables in each paper (Appendix).

There was a substantial migration out of the study region during follow-up. It is plausible that many participants moved in order to attend university or university college studies, or to work elsewhere after finished studies in Nord-Trøndelag. There were, however, few differences between those who moved (42.5 %) and those who stayed in the county, yet lower parental education was more common among those who

moved (11.7 % primary education) compared to those who did not (4.4 % primary education).

Average follow-up time was 11.9 years (range 0.02 – 16.0 years), during this period 89 (1.0 %) Young-HUNT1 participants were hospitalised after a self-harm episode. Twenty-six (29 %) were males, 54 (61 %) experienced only one self-harm hospitalisation, whereas the remaining 35 patients (39 %) were admitted to hospital after self-harm more than once during follow-up. Mean age at index self-harm hospitalisation was 22.6 years for males and 20.9 years for females. Self-poisoning (n = 72, 81 %) and laceration (n = 13, 15 %) were the most frequently used self-harm methods; eight of these patients both cut and intoxicated themselves in the same episode. In total, over half of all self-harm patients (n = 47, 53 %) were under influence of alcohol at the time of self-harm. Alcohol influence occurred in half of those who self-poisoned with medications (n = 35, 49 %), but was percentwise more common in those who cut themselves (n = 9, 69 %). The estimated incidence rate of hospitalisation for self-harm for the entire follow-up period was 84 (95 % CI 67.9 – 102.8) per 100 000 person years; 121 (95 % CI 94.5 – 154.8) per 100 000 person years for females, and 48 (95 % CI 32.5 – 70.1) per 100 000 person years for males.

4.2 Paper I

In this study, we investigated the risk of future self-harm hospitalisation associated with self-reported sleeping problems in adolescence. We adjusted for attained age, sex, symptoms of anxiety and depression, body mass index, somatic illnesses, symptoms of pain, gastrointestinal disturbance and heart palpitations, smoking status and excessive alcohol use.

Ten per cent of participants reported difficulties initiating sleep, 4 % reported early morning wakening. Eighty-nine participants (71 % females) were hospitalised following a self-harm episode during follow-up. Difficulties initiating sleep and/or early morning wakening was associated with increased risk of self-harm hospitalisation (HR 2.11, 95 % CI 1.29 – 3.46, sex- and age-adjusted) compared with no problems, yet coexistent symptoms of combined anxiety and depression explained most of the

association (fully adjusted HR 1.19, 95 % CI 0.66 – 2.16). Hazard ratio for difficulties initiating sleep and early morning waking combined, was significantly different between those with anxiety and depression symptoms at baseline, and those without (P interaction = 0.03). In participants without caseness symptoms of anxiety and depression, HR was 5.58 (95 % CI 2.02 – 15.40), while corresponding HR in those with caseness symptoms of anxiety and depression was 0.82 (95 % CI 0.19 – 3.44).

4.3 Paper II

The purpose of this study was to examine associations between nine markers of adolescent mental and physical health (symptoms of anxiety and depression, loneliness, bullying, headache, stomach pain, body mass index, somatic illnesses, smoking and alcohol use) and risk of later self-harm hospitalisation. We adjusted for age, gender, cohabitation situation and parental education level.

Caseness symptoms of anxiety and depression (HR 3.52, 95 % CI 2.18 – 5.67), loneliness (HR 3.31, 95 % CI 1.91 – 5.73) and being subject to bullying (HR 3.30, 95 % CI 1.33 – 8.16) were all associated with a 3–4-fold increased risk of future self-harm hospitalisation. Stomach pain (HR 2.23, 95 % CI 1.42 – 3.52) and headache (HR 2.17, 95 % CI 1.36 – 3.46) were also substantially associated with increased risk. Epilepsy (HR 3.97, 95 % CI 1.25 – 12.63) and migraine (HR 2.34, 95 % CI 1.08 – 5.10) were both associated with increased self-harm risk comparable to those of caseness symptoms of anxiety and depression, and female gender (HR 2.50, 95 % CI 1.56 – 4.01). In contrast, asthma, allergy and skin rashes in adolescence did not alter self-harm risk substantially. Current smoking (HR 1.82, 95 % CI 1.11 – 2.98), and high alcohol consumption (HR 1.23, 95 % CI 0.76 – 2.00) were associated with increased risk of self-harm hospitalisation. We also found a substantially increased risk related to obesity (BMI > 30, HR 3.06, 95 % CI 1.39 – 6.73). Other weight categories merely affected self-harm hospitalisation risk at all.

4.4 Paper III

The principal aim was to examine associations between future self-harm hospitalisation and perceived self-esteem and personality traits in adolescence. We adjusted for age, gender and parental educational level, as well as anxiety and depression symptoms and alcohol use.

Results demonstrated increased risk of self-harm hospitalisation associated with one-unit increases on subscales (0 – 6) for neuroticism (HR 1.29, 95 % CI 1.14 – 1.47) and psychoticism (HR 1.30, 95 % CI 1.03 – 1.63). All single neuroticism trait items were associated with increased risk. As were most psychoticism items, yet one item (regarding being on time for appointments) indicated reduced risk (HR 0.69, 95 % CI 0.32 – 1.50). All extroversion characteristics but one (usually initiating new friendships, which indicated 35 % increased risk), were inversely associated with self-harm hospitalisation. Correspondingly, results indicated reduced risk associated with one-unit increases on extroversion subscale (HR 0.89, 95 % CI 0.77 – 1.04). Self-esteem was inversely associated with risk of self-harm hospitalisation, consistently indicated by single self-esteem items, and self-esteem subscale too (HR 0.74, 95 % CI 0.68 – 0.82).

The majority of associations were substantially attenuated with additional adjustments for anxiety and depression symptoms and alcohol use. Subscale neuroticism (HR 1.13, 95 % CI 0.96 – 1.32) and psychoticism (HR 1.07, 95 % CI 0.82 – 1.40) results were most affected, but also extroversion results (HR 0.96, 95 % CI 0.80 – 1.14) were diminished. Conversely, self-esteem estimates remained largely unchanged (HR 0.78, 95 % CI 0.70 – 0.87). Hence, symptomatic anxiety and depression and/or alcohol use explained much of the risk increase associated with specific personality traits, while influence on self-esteem was minor.

5 Discussion

5.1 Main findings

In three studies, we assessed how sleep problems, physical and mental issues, and personality features in adolescence were related to risk of self-harm hospitalisation later in adolescence or young adulthood.

In order to explore these associations, we developed a method to identify self-harm hospitalisation episodes among teenage participants in Young-HUNT1 – a large, Norwegian population-based health study.

Our main findings are:

- Consistent with previous research [27, 35, 41, 46]; women were overrepresented (female-to-male ratio 2.5:1) in the self-harm hospitalisation group.
- Co-existent symptoms of anxiety and depression explained much of the association we identified between sleep problems and self-harm hospitalisation: However, those with extensive sleep problems, but low anxiety and depression problems, were at markedly increased risk of later self-harm hospitalisation.
- Several health conditions in adolescence were associated with increased self-harm hospitalisation risk. Symptoms of combined anxiety and depression, bullying, and loneliness expectedly increased the probability of later self-harm hospitalisation, about 2–3-fold. Of particular interest, physical issues such as epilepsy, migraine and obesity in adolescence might increase self-harm hospitalisation risk to a similar degree as mental health problems.
- Personality traits and self-esteem in adolescence were associated with later self-harm hospitalisation. High neuroticism and psychoticism conveyed an increased risk, while higher extroversion might reduce risk of self-harm hospitalisation. Notably, coexistent anxiety and depression, and alcohol use, seemed to explain much of these associations. Still, high self-esteem was distinctively associated with reduced risk, largely independent of adjustments.

5.1.1 Strengths and limitations

This thesis has several strengths, one of the main being the longitudinal design, with almost 15 years' follow-up at the most. This enabled us to assess risk of self-harm hospitalisation over time, and examine how participant age influenced this risk. The long follow-up time covered the age range before, during, and after most frequent self-harm hospitalisation onset age. Our study findings are further strengthened by the large sample size and high attendance rate (88 %), which increases the validity of our results. Superior to self-reported information about self-harm, we have collected outcome data from validated sources, and the reliability of these data is high.

Nevertheless, reported findings must be considered in the light of both strengths and limitations, and this balance is further elaborated in the following sections.

5.2 Internal validity

5.2.1 Random error

When testing a hypothesis, the test statistic's p-value informs the tester of the probability of getting the same result or more extreme, by random/chance, given that the null-hypothesis was true. P-values (often chosen as statistically significant when ≤ 0.05) are influenced by both the strength of the association, and the study size (number of participants).

Conversely, confidence intervals encompass an effect estimate, and give information both on strength of the association and the precision (high precision with narrow confidence intervals and low precision with wide confidence intervals). In good epidemiological tradition, we relied on confidence intervals when interpreting effect measure estimates in our study [178]. We used p-values in cases to a priori test the presence of statistical interaction. Our studies included almost 9000 study participants, however only 89 people experienced one or more episodes of self-harm hospitalisation during follow-up. Although we found many strong statistical associations, the low number of people hospitalised for self-harm reduced the precision of our effect estimates and resulted in wide confidence intervals.

5.2.2 Confounding

Confounding is a mixture of effects that arises from a common cause of the exposure and the outcome [179]. Ideally, confounding is best handled with a randomized trial. In observational studies, where randomization is not possible, a conventional approach is to use prospective data and adjust for possible confounding factors. It is important to note that confounding only can be evaluated based on substantive knowledge about the outcome and previous evaluations of the same or related research questions, and not by statistical tests alone [179]. Furthermore, it is important to differentiate between confounding and mediating factors. *Mediating factors* are consequences of the exposure also affecting the outcome, and such factors should not be adjusted for when assessing the putative causal effect of an exposure on an outcome. In our studies, we have adjusted for several potentially confounding factors, based on a priori selection of possible factors. Nonetheless, we cannot rule out the possibility of residual confounding. Also, it is challenging to accurately identify the effect of single health-measures, because of overlap and mixture of confounding and mediating between factors, exemplified by sleep problems and depression.

5.2.3 Bias

Selection bias arises where relations between exposure and outcome are different for those who actually participate and those who theoretically was eligible to the study. Almost 90 % of the eligible adolescents participated in the Young-HUNT1 Study, giving their informed consent to use their data in future research before they had experienced the outcome (longitudinal design), which reduces the risk of selection bias.

A non-responder study in the adult HUNT 3 showed that nonparticipants had lower socioeconomic status and higher mortality than participants, in addition to higher prevalence of common chronic diseases [180]. Data from another Norwegian population study indicated similar findings, with poorer health and more mental disorders among nonparticipants. They concluded that participation bias is threatening the validity in prevalence studies more than in studies of associations between exposures and outcomes [181].

Since we used patient records from local hospitals, people who emigrated out of Nord-Trøndelag County (e.g. for higher education) and had one or more self-harm hospitalisations in other parts of Norway were lost to follow-up. This is perhaps the most important limitation regarding outcome. However, we believe that our censoring of individuals when they moved out of the catchment area counteracts much of this challenge, as these people only contributed with observation time as long as they lived in the county.

Information bias originates from erroneous measures of a variable, which may lead to non-differential misclassification (misclassification of the exposure is not related to the outcome values and/or vice versa) or differential misclassification (misclassification of the exposure is related to the outcome values and/or vice versa). All papers in this thesis were based on prospective data, with outcome data collected from hospital registry data. Hence, differential misclassification is unlikely. Non-differential exposure misclassification generally results in more conservative estimates (towards the null), although there are exceptions for categorical exposures with more than two categories. Further, we used validated clinical outcome measurements, which stands in contrast to most previous studies relying on self-reported self-harm behaviour. Based on the method we used to identify and include self-harm hospitalisation episodes, we assume that the self-harm hospitalisation positive predictive value (the number of true positive self-harm hospitalisations divided by the number of episodes indicated being self-harm hospitalisations) is high.

Yet, we cannot rule out the influence of non-differential misclassification on the exposure variables. All baseline variables (except height and weight used to calculate BMI) were based on self-report, and the participants were of different age (from 13 to 19 years old) when completing the questionnaire. First, this makes direct comparison of results to studies using diagnostic categories of anxiety and depression, or polysomnography to measure sleep quality, difficult. Second, all baseline variables were only measured once, yet some of these might have fluctuated considerably during follow-up. Finally, the Young-HUNT questionnaire contains in part short versions of longer original instruments and scoring systems. Ambiguous wording and different

participant age may have influenced interpretation of questionnaire items and response to these.

5.3 External validity and generalisability

External validity can be described as the reliability of conclusions drawn from a study, when applied to a population outside the actual study population. In biomedical research, a multitude of different biological factors' effects may make a finding valid only in populations that share qualities and circumstances of the study population [182]. Nevertheless, sampling a study population to match the population of interest too closely, will lead to a fail in generalisability outside this group.

The HUNT catchment area, which is fairly representative for the general Norwegian population, covers mainly rural communities and a few towns but no large cities. Inhabitant number exceeds 20 000 in Steinkjer and Stjørdal town municipalities [141]. A study from the UK [183] suggest that self-harm rates, especially among the young, are considerably higher in urban than rural areas. As a consequence, estimates of incident self-harm hospitalisation reported here are possibly somewhat lower than corresponding incidence for Norway in total.

Generalisability also varies considerably dependent on type of exposure variable. For instance, sleep patterns change during the adolescence transition [184]. This process is driven both by factors such as delaying bedtime because of an increasing amount of homework, or leisure activities in the evening, and by physiological changes in brain matter and biochemical signalling. Different sleep patterns among children and elderly as compared to adolescents therefore reduces the generalisability to people outside this age group. Now, loneliness is approximately equally prevalent throughout life and across genders [185], which indicates that generalisability for our findings concerning loneliness is higher than for sleep problem findings. Moreover, bullying is unfortunately prevalent in workplaces as well as in schools, and may precede suicidal ideation in adults [186] as well as adolescents.

The majority of self-harm episodes never present to hospital, and our analyses were restricted to hospital admitted self-harm patients. Hence, our findings are not

generalisable to every patient who self-harm, yet they provide important information about people who self-harm severe enough to require hospital admission.

5.4 General discussion

5.4.1 Terminology

The definition of self-harm encompasses behaviour along a spectrum of acts, resulting in none or a minimum of bodily harm on one end, to the other end where possibly only coincidence kept a person attempting suicide alive. In this study, we assess risk factors present in adolescence, and outcome behaviour resulting in hospitalization in the first 15 years after Young-HUNT1. The occurrence and patterns of less severe self-harm behaviours (not requiring hospitalisation for treatment) are therefore not known in this study.

Two of the most prominent conceptualisations of self-harm behaviour today differ regarding whether self-harm consists along a continuum of suicidal intent, or rather should be categorised as either non-suicidal or suicidal behaviour. Some decades ago, self-harming was described only as a behavioural characteristic typical for borderline type personality disorder. Existing diagnose code systems failed to acknowledge an increasing group of people who did not fulfil criteria for borderline personality disorder, yet still injured themselves without suicidal intent. There is evidence supportive of the continuum theory [187, 188]. At the same time, empirical evidence and qualitative studies provide evidence of substantial differences in underlying motivation, functions and patterns, encouraging to discern between non-suicidal self-injury and attempted suicide [189]. Non-suicidal self-injury has been an increasingly used term during the first decade of this millennium – especially in the US, and is defined as the intentional destruction of body tissue without suicidal intent and for purposes not socially sanctioned [190]. A group of researchers proposed to include non-suicidal self-injury disorder as a new diagnostic entity in the fifth version of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) in 2009. However, due to a lack of reliability of diagnostic criteria in clinical trials, non-suicidal self-injury was instead included as a condition that needs further study. The gap between American and

European researchers concerning naming and definition conventions has become noticeable, but there are both similarities and differences between the two ways of defining self-harm. For example, meta-analyses revealed that women were 1.5 times more likely than men to report engaging in non-suicidal self-injury, but as a contrast to hospital-presenting self-harm, female overrepresentation was not significantly different between age groups [191]. Further, reported prevalence estimates are highly incongruous. Ranging from a few per cent meeting criteria for non-suicidal self-injury disorder, to over 50 % with a life-time prevalence of single episode non-suicidal self-injury, a recent meta-analysis reported that more than half of this variation could be explained by methodological differences [192].

Implementing a separation of these two major conceptualisations will still not escape one considerable conundrum; if presence or absence of suicidal intent is critical for a self-harm diagnosis, with whom should the right to decide about intention lie - health personnel treating the patient, or the patient? Intentions may fluctuate and be ambiguous – also during one single act. At what time should the decision about intention be taken? An impulse to self-harm or attempt suicide increases, and fades, with varying speed. Except for those characterised as chronic suicidal, most people experience these impulses as transient and passing. When we recorded outcome data from patient records, a clear suicidal intent was often described in the initial admission entry, yet less or none actual suicidal intent in records from later entries, e.g. from psychiatric assessment the day after. This challenge, in addition to evidence indicating that non-suicidal self-injury and self-harm with suicidal intent often co-occur and share many risk factors and predisposing elements, tips the weight in favour of studying non-suicidal self-injury and suicidal behaviour as partly overlapping entities along the same continuum [193].

5.4.2 Sleep problems and self-harm

We found that sleep problems are common among Norwegian adolescents. Few previous studies have examined longitudinal associations between sleep problems and self-harm in adolescents and young adults. We identified four US studies [91, 92, 94, 194], two Norwegian studies (based on the same data material) [96, 195] and one

Japanese twin study [95]. Also, one study assessed Swedish adults (18 – 65 years old) [196]. In spite of differences in participant selection, size, and outcome measurements, all studies reported a positive association between various sleep problems and subsequent suicidal ideation, self-harm or suicide attempts. Several cross-sectional studies have identified sleep problems as a risk factor for self-harm [91, 197-200]. This relationship might be mediated by depression and low self-esteem [93], but also impaired cognitive judgment and impulse control, possibly leading to increased impulsiveness and increased risk of self-harm [201, 202].

Accordingly, we found that coexistent symptoms of anxiety and depression influenced the strong associations between sleep problems and self-harm hospitalisation markedly, indicating that this might be the key pathway determining risk. As measures of sleep problems and mental health were recorded at the same time, causality is still inconclusive, but a bidirectional relationship between sleep and anxiety and depression is likely [203]. In sub-analyses among those without symptoms of anxiety and depression, results revealed a strong association between combined problems of initiating sleep and early morning waking with self-harm hospitalisation risk. This observation could indicate that having serious sleep problems in adolescence might be an early prospective marker of subsequent development of mental health problems (especially anxiety and/or depression), which is in line with previously proposed mechanisms [94, 204]. However, prevention of adolescent sleep problems, anxiety and depression – all modifiable risk factors, seem to be of particular importance in order to reduce and prevent self-harm behaviours and hospitalisation.

5.4.3 Mental and physical health factors and self-harm

We identified several associations between adolescent health vulnerability indicators and later self-harm hospitalisation. These associations were particularly strong for anxiety and depression symptoms, loneliness, and bullying, but also for physical conditions such as epilepsy, stomach pain and headache.

Our results suggest a threefold increased risk of baseline depressive symptoms in self-harm hospitalisation patients. These findings are in keeping with clinical studies

of both adolescent [205] and adult [206] self-harmers presenting at the emergency unit; around 90 % fill the criteria of one or more psychiatric disorder(s), and about 7 out of 10 patients have an affective disorder. Some authors question the validity of stating that mental disorders play a significant role in at least 90 % of suicide cases [207], and have noted methodological weaknesses in studies supporting such numbers. Other reasons for suicide may be equally important or more, and the picture behind a case of suicide is complex [207]. In general, previous studies report considerably lower rates of mental disorders and psychological distress in those who self-harm and attempt suicide, than in those who die by suicide [206].

Although anxiety and depression often overlap [208], the role of anxiety in suicidal behaviours still remains inconclusive. Our findings indicate that symptoms of fear, tension and general anxiety, might be even closer linked to future self-harm risk than symptoms of lowered mood and depression. This is supported by results from the prospective population based Netherlands Mental Health Survey and Incidence Study, reporting that lifetime diagnoses of all anxiety disorders (social phobia, simple phobia, generalized anxiety disorder, panic disorder, agoraphobia, obsessive-compulsive disorder) were associated with suicidal ideation and attempts both at baseline and during follow-up [209]. Nonetheless, in a case-control study of 129 young people presenting with medically serious suicide attempts [205], anxiety disorders occurred in only 1 of 7 patients while antisocial disorders (35 %), substance use disorders (39 %) and affective disorders (70 %) were much more prevalent. However, follow-up studies of the adult HUNT population showed that those with mixed anxiety and depressive symptoms, compared to single conditions, were at the greatest risk for future death by suicide [210].

Loneliness was associated with a fourfold increased self-harm hospitalisation risk in our study. This is in line with results from a large study of Norwegian teenagers in the nineteen nineties [211], reporting that loneliness was substantially associated with suicidal behaviour – even when adjusted for use of different intoxicants and familial factors. A replication study 10 years later arrived at similar conclusions [212]. In an Icelandic population-based study of 9th and 10th graders [213], results revealed that breakup with a friend was positively associated with suicide attempts. Furthermore,

among Hong Kong secondary school students [214], perception of poor peer acceptance was associated with suicidal ideation among girls, but not boys.

We found a strong association between baseline report of being bullied, and risk of subsequent self-harm hospitalisation. This is in keeping with results from a 10 year follow-up of Australian adolescents [215], and it has been repeatedly reported that bullying is a strong risk factor for suicide [216]. Furthermore, a 2006 review [217] indicated that bullying of obese adolescents was linked to the development of self-harm behaviour. In our study, obesity (BMI > 30) increased the self-harm hospitalisation risk threefold. At the same time, corresponding risk was almost identical between the reference (normal weight, BMI 18.5 – 25) and overweight group (BMI 25 – 30). Although underweight (BMI < 18.5) seemed to increase the risk of self-harm hospitalisation somewhat, this estimate was imprecise due to low group numbers and might as well be a result of chance. If not, eating disorders such as anorexia might in part explain the association.

Previous studies have reported associations between physical illness (especially chronic and severe conditions in older adults) and increased suicide risk [218]. Accordingly, reduced functioning and autonomy, somatic problems and physical pain were often reported reasons for attempted suicide in a Swedish senior sample [113]. Nonetheless, reasons applicable also to young people, such as the desire to escape, depression, perceived burdensomeness and thwarted belongingness or other social problems, were also reported. This implies that some core mechanisms underlying a suicide attempt might be independent of age. In a US study of children and adolescents with chronic health conditions [219], youth with chronic physical conditions alone (n = 12 554) only had a slight increased risk for self-harm, suicidal ideation and suicide. However, those with co-existing chronic physical and mental conditions, and those with chronic mental conditions had 2–3-fold increased risks. Another multinational population-based study including 38 000 people [220] linked a wide range of pre-existing physical conditions to suicidal ideation, plans, and attempts. Epilepsy, physical conditions occurring early in life, and increasing number of physical conditions were especially predictive of future suicidality, and adjustment for co-existing mental disorders altered the results marginally.

We found several associations between indicators of physical health problems and risk of self-harm hospitalisation. Both diagnosed migraine and other symptomatic headaches were associated with much the same elevated risk of self-harm hospitalisation. This is somewhat surprising as one might assume diagnosed migraine to cause heavier symptom load and bigger impairment than other headache, thus raising self-harm risk more. However, the migraine point estimate has low precision due to few patients, and satisfactory migraine treatment might leave less symptoms compared to other headaches without proper treatment. Another possible explanation could be that increased risk of self-harm hospitalisation might rather be related to suffering from a chronic and recurrent pain issue, more than to the specific kind of headache.

Further, symptomatic stomach pain was in our study associated with an increased risk of self-harm hospitalisation, to the same amount as headache problems. In keeping with these results, a previous systematic review [221], showed that both irritable bowel syndrome (IBS), and other non-IBS abdominal pain syndromes, independently predict suicidal behaviour. Also, abdominal pain [222, 223] and headache [223, 224] are commonly coexisting symptoms of perceived stress among pupils and students, thus indicating that these conditions reflect a state of mental vulnerability in adolescence.

The previously proposed causal link between smoking and elevated risk of mental health problems and suicide has been questioned [225, 226]. A more likely explanation for the association we found between smoking and self-harm hospitalisation is the strong relationship between adolescent cigarette smoking and factors predisposing to mental health problems and other adverse behaviours, rather than being a causal factor in itself.

Definition of what should be considered high alcohol use depends on age. The risk associated with having been drunk more than 10 times is not equivalent for a 13-year-old and an 18-year-old. Around 30 % of all our included participants were defined as having high alcohol use, which is comparable to estimated lifetime prevalence of diagnosed alcohol use disorder among US adults [227]. Corresponding prevalence among adolescents, however, is only 6 % [228], and the weak association identified in our study may in part be explained by dilution because of our high-sensitive measure.

Additional post-hoc analyses with age stratification (younger than 16 years, versus 16 years and older) displayed a somewhat larger HR among the youngest (HR 1.72, 95 % CI 0.76 – 3.90) compared to the oldest participants (HR 1.46, 95 % CI 0.69 – 3.11), but point estimates were imprecise. In sum, we cannot rule out chance as the explaining factor. Alcohol use disorder is associated with a threefold higher probability of suicide attempt according to a meta-analysis [229], and to premature mortality in general. Further, a cross-sectional study of more than 30 000 US pupils and students between the ages of 11 and 19 years [230] found that heavy episodic drinking was associated with doubled risk for self-reported suicide attempt in the last year, and those drinking at a very young age (aged 13 years and younger) were at greatest risk.

In sum, the distribution of self-harm hospitalisation events across a wide range of different symptoms and behavioural ranges underlines the need for both individual and population strategies in the prevention and treatment of self-harm.

5.4.4 Personality traits and self-harm

Our findings were supportive of a relationship between trait neuroticism and self-harm hospitalisation among young adults. A similar link was also demonstrated for psychoticism, while high self-esteem and extroversion seemed to reduce the self-harm hospitalisation risk. In other words, assessing personality and self-esteem in adolescence can potentially unveil important predictive information about later self-harming behaviour. However, most associations were markedly diminished when we adjusted for coexisting symptomatic anxiety and depression, and alcohol use, meaning that these factors need to be considered. Self-esteem was an important exception, and differed from the other factors as the inverse association remained substantial, independent of adjustments.

High neuroticism increases the likelihood of developing symptoms of anxiety and depression, insomnia and other sleep problems. In case of a causal pathway from neuroticism to self-harm, controlling for intermediate anxiety and depression should be considered overadjustment and bias results towards null [231]. Conversely, if anxiety and depression simultaneously influence responses to personality items and self-harm

hospitalisation risk, this confounds the apparent association between those two, and adjustments should be made. The current study holds insufficient information to confirm any of the two, and there is a large likelihood of both alternatives being true in some degree, which makes it especially difficult to disentangle effects and associations.

People endorsing higher amounts of psychoticism traits are likely to be more reckless, impulsive, aggressive and hostile than their peers, and according to Eysenck, more prone to developing psychosis. Separately, and particularly in combination, these psychoticism traits seem to increase the chance self-harm, for example via increased interpersonal conflict, lack of social support, more negative emotions, and a more disorganised way of coping with stress and negative experiences [138]. Impulsivity is a concept that has both intellectual or cognitive, and affective or mood-based facets, and is related to psychoticism [232], but is also associated with neuroticism and extroversion. This could perhaps explain the attenuation of associations between trait psychoticism and self-harm hospitalisation. Psychoticism and neuroticism have also been reported associated with cocaine-use, but via different mechanisms [163]. Elevated traits of psychoticism correlated with higher levels of cocaine dosage, perhaps influenced by higher impulsivity in these individuals. Further, elevated neuroticism was indirectly linked to frequency of cocaine-use via hormonal stress reactivity [163]. Possible explanations could include some similarity in the use of cocaine and self-harm as anxiety-reducing agents, or as coping mechanisms to temporarily escape from problems.

Utilising food as another remedy to deal with emotional distress is not uncommon – either by binge eating or by restricting food intake. Lifetime prevalence of DSM-5 anorexia nervosa among women is perhaps as much as 4 %, while bulimia nervosa and binge eating disorder is approximately 2 % [233]. However, symptoms of disordered eating are alarmingly common among adolescents, for example found in over half of all high school students in a Norwegian sample [234]. There is a substantial correlation between eating disorders and self-harm [106], yet no particular associations were identified between personality traits and underweight, overweight or obesity among Norwegian adolescents [235]. Personality may still impact on how adolescents react to weight-related bullying, and mediate risk of self-harm that way.

We found an association indicating that extrovert personality could potentially reduce risk of later self-harm. One possible explanation might be the higher likelihood of contacting and talking to others, thereby increasing the probability of a large and well-functioning social network. In turn, less loneliness, higher probability of support and help from friends and family, might help individuals to cope with their problems by other means than self-harm [71, 236]. The attenuation caused by controlling for coexisting symptoms of anxiety and depression suggests some relationship between extroversion and such symptoms. Yet, we were unable to make solid conclusions regarding directions and magnitudes of these effects. There is also evidence describing how extrovert and emotionally stable individuals experienced higher self-esteem than their peers, at multiple assessment points from 14 to 30 years of age [237]. Longitudinal data from New Zealand showed that extroversion was moderately associated with higher overall rate of later mental health problems including drug and alcohol dependence and depression, but not anxiety or suicidality. Simultaneously, associations with higher self-esteem, better life satisfaction and relationship quality were also evident [238]. Extroversion thus seems to affect multiple outcomes, more for positive outcomes than for negative ones.

Because personality is a mix of several traits expressed to various degrees, the interplay between these factors is complex and it is difficult to isolate single trait effects. In community samples, prevalence of any personality disorder is estimated around 10 %, with specific prevalence of borderline personality disorder around 1 % [239]. Being diagnostic criteria in both DSM-5 [240] and ICD-10 [241], negative affectivity (neuroticism) and disinhibition (impulsivity) are characteristic features in patients diagnosed with borderline (emotionally unstable) personality disorder. Another characteristic feature among these patients is frequent suicidal threats and self-harming behaviour. In a longitudinal study assessing initial inpatients aged 18 – 35 years with borderline personality disorder, over 70 % reported multiple methods and multiple episodes of non-suicidal self-injury during their lifetime, 60 % reported multiple suicide attempts, and 31 % reported corresponding lifetime prevalence of attempted suicide by multiple methods [242].

Typical features and symptoms of borderline personality disorder appear in adolescence [243], yet clinical principles has advised against diagnosing personality disorders until there are clear and long-standing deviations from average levels. Personality disorders have thus, for a long time, been diagnosed first when patients have reached adulthood. Now, there is emerging evidence that supports the validity of diagnosing personality disorders earlier in adolescence [244]. Valid diagnoses at younger age are likely to facilitate new important research, thus providing novel insights into the development and aetiology of borderline personality disorder. This is an important aspect, because the evidence base for the effective treatment of personality disorders is limited [245]. Borderline personality disorder is studied most widely, and long-term (12 – 18 months) dialectical behaviour therapy show promising results for this patient group [246]. Although they are relatively stable, personality traits continue to develop, change and accommodate to match environmental influences throughout life [247]. The effects of personality traits are only a few of many aspects that must be addressed in order to properly assess and understand risk of self-harm hospitalisation and other self-harm behaviour. Personality traits, and self-esteem in particular, may provide valuable information about adolescents with higher risk, who would benefit from closer monitoring and earlier interventions. Future longitudinal studies are needed to assess the effectivity of interventions directly targeting these traits.

5.4.5 Incidence rate estimates

We reported incidence rate estimates of self-harm hospitalisation in papers I and II. Multiple factors contribute to estimates smaller than what is reported elsewhere [39, 43, 248, 249], yet diverse terminology, non-identical frameworks – and perhaps most important – different endpoints, prevent comparison on equal grounds. It is important how an outcome is measured, and self-reporting rarely provides results identical to objective measurements based on diagnostic criteria. Among the most comparable studies found, one used Norwegian patient register data on participants older than 15 years, and included deliberate self-poisonings treated in hospital [39]. Another study retrospectively recorded self-harm episodes in adults treated in an outpatient and hospital setting in south-west Norway in 1992 [40]. Incidence rate estimates in our

study sample were lower than reported in both these studies. Partial explanation of the difference includes a lower age in our patient group, which also did not include outpatient episodes. In addition, older data from Oslo [250] and Trondheim [251] indicate a reduced incidence the recent decades. With approximately 80 % self-poisoning in our data material, findings are relatively comparable with regard to outcome and methodological aspects. Presentation to primary care out-of-hours services because of intoxication increased in Norway the last 10 years, particularly in young women, and especially at night and during weekends [252]. This contradiction might for example indicate that an increasing number of episodes is managed with prehospital treatment only. For comparison, nationwide Danish registers comprising inpatient hospital contacts (hospitalisations), as well as contacts to emergency department and outpatient facilities from 1995 onward, showed average incident rates of deliberate self-harm at 130.7 and 86.9 per 100 000 person years for women and men, respectively [249].

5.5 Concluding remarks and implications for future research

Sleep problems represent a highly prevalent transdiagnostic challenge in youth, and they are associated with elevated risk of later self-harm hospitalisation. Symptoms of anxiety and depression are equally common. These symptoms modify the association between sleep problems and self-harm, and are strongly associated with increased risk of self-harm as well. Anxiety disorders and symptoms are important long-term risk factors [209, 210, 253], and probably essential in the transition from suicide ideation to self-harm and suicide attempts [254]. Increased risk of self-harm hospitalisation was also identified for loneliness and being bullied. Moreover, we have presented evidence indicating increased risk associated with obesity, common neurological disorders, headache and stomach pain. We identified strong associations with elevated self-harm hospitalisation risk for high neuroticism and psychoticism traits. Self-esteem in particular, but also extroversion trait, were inversely associated with self-harm, indicating protective effects. Comorbid presence of anxiety and depression symptoms explained much of these associations, and are likely to represent important components on pathways including adolescent personality traits and later self-harm. Associations

between self-esteem and self-harm hospitalisation risk, however, were largely unchanged after these adjustments.

Adequate prevention of self-harm behaviour requires initiatives focused on high-risk groups, and population strategies aimed at the society and youth in general [27]. Sleeping problems, symptomatic anxiety and depression, loneliness and bullying are examples of modifiable factors readily available for risk-reducing interventions. With paramount focus shifting from long-term, to improving short-term prediction [255], the Suicide Crisis Syndrome (an acute negative affect state) has been proposed as an indicator of imminent suicide risk, mediating relationships between several long-term risk factors and suicidal behaviour [256]. This novel viewpoint holds promise for better identification of high-risk individuals in need of considerable follow-up. Finally, a comprehensive, national register would provide an essential fundament for surveillance, research and treatment of self-harming behaviour, and establishing such a register is greatly encouraged. Until then, healthcare personnel in both primary and specialist care are encouraged to use relevant classification codes for self-harming behaviour, when appropriate.

6 References

1. World Health Organization. Young people's health--a challenge for society. Report of a WHO Study Group on young people and "Health for All by the Year 2000". World Health Organ Tech Rep Ser. 1986;731:1-117.
2. United Nations Department of Economic and Social Affairs (UNDESA). Definition of youth [Available from: <http://www.un.org/esa/socdev/documents/youth/fact-sheets/youth-definition.pdf>].
3. McCauley CO, McKenna HP, Keeney S, McLaughlin DF. Concept analysis of recovery in mental illness in young adulthood. *J Psychiatr Ment Health Nurs*. 2015;22(8):579-89.
4. Hawton K, Harriss L, Hall S, Simkin S, Bale E, Bond A. Deliberate self-harm in Oxford, 1990-2000: a time of change in patient characteristics. *Psychol Med*. 2003;33(6):987-95.
5. Kidger J, Heron J, Lewis G, Evans J, Gunnell D. Adolescent self-harm and suicidal thoughts in the ALSPAC cohort: a self-report survey in England. *BMC Psychiatry*. 2012;12(1):69.
6. Sinclair JM, Gray A, Hawton K. Systematic review of resource utilization in the hospital management of deliberate self-harm. *Psychol Med*. 2006;36(12):1681-93.
7. Hawton K, van Heeringen K. Suicide. *Lancet*. 2009;373(9672):1372-81.
8. World Health Organization. Practice manual for establishing and maintaining surveillance systems for suicide attempts and self-harm 2016 [Available from: http://www.who.int/mental_health/suicide-prevention/attempts_surveillance_systems/en/].
9. Evans E, Hawton K, Rodham K, Deeks J. The prevalence of suicidal phenomena in adolescents: a systematic review of population-based studies. *Suicide Life Threat Behav*. 2005;35(3):239-50.
10. Skegg K. Self-harm. *Lancet*. 2005;366(9495):1471-83.
11. Madge N, Hewitt A, Hawton K, de Wilde EJ, Corcoran P, Fekete S, et al. Deliberate self-harm within an international community sample of young people: comparative findings from the Child & Adolescent Self-harm in Europe (CASE) Study. *J Child Psychol Psychiatry*. 2008;49(6):667-77.
12. O'Carroll PW, Berman AL, Maris RW, Moscicki EK, Tanney BL, Silverman MM. Beyond the Tower of Babel: a nomenclature for suicidology. *Suicide Life Threat Behav*. 1996;26(3):237-52.
13. Beck AT, Schuyler D, Herman I. Development of suicidal intent scales. In: Beck AT, Resnick HL, Lettieri DJ, editors. *The Prediction of Suicide*. Oxford, England: Charles Press Publishers; 1974. p. 249.
14. Harriss L, Hawton K. Suicidal intent in deliberate self-harm and the risk of suicide: the predictive power of the Suicide Intent Scale. *J Affect Disord*. 2005;86(2-3):225-33.
15. Townsend E. Self-harm in young people. *Evid Based Ment Health*. 2014;17(4):97-9.
16. McAuliffe C, Arensman E, Keeley HS, Corcoran P, Fitzgerald AP. Motives and suicide intent underlying hospital treated deliberate self-harm and their association with repetition. *Suicide Life Threat Behav*. 2007;37(4):397-408.
17. Klonsky ED. The functions of deliberate self-injury: a review of the evidence. *Clin Psychol Rev*. 2007;27(2):226-39.
18. Wilkinson P. Non-suicidal self-injury. *Eur Child Adolesc Psychiatry*. 2013;22 Suppl 1:S75-9.
19. Bergen H, Hawton K, Waters K, Ness J, Cooper J, Steeg S, et al. Premature death after self-harm: a multicentre cohort study. *Lancet*. 2012;380(9853):1568-74.
20. Portzky G, van Heeringen K. Deliberate self-harm in adolescents. Current opinion in psychiatry. 2007;20(4):337-42.

21. Townsend E, Ness J, Waters K, Kapur N, Turnbull P, Cooper J, et al. Self-harm and life problems: findings from the Multicentre Study of Self-harm in England. *Soc Psychiatry Psychiatr Epidemiol.* 2016;51(2):183-92.
22. Arbuthnott AE, Lewis SP. Parents of youth who self-injure: a review of the literature and implications for mental health professionals. *Child and adolescent psychiatry and mental health.* 2015;9:35.
23. Whitlock J, Lloyd-Richardson E, Fisseha F, Bates T. Parental Secondary Stress: The Often Hidden Consequences of Nonsuicidal Self-Injury in Youth. *J Clin Psychol.* 2017.
24. Baetens I, Claes L, Onghena P, Grietens H, Van Leeuwen K, Pieters C, et al. Non-suicidal self-injury in adolescence: a longitudinal study of the relationship between NSSI, psychological distress and perceived parenting. *J Adolesc.* 2014;37(6):817-26.
25. Baetens I, Claes L, Onghena P, Grietens H, Van Leeuwen K, Pieters C, et al. The effects of nonsuicidal self-injury on parenting behaviors: a longitudinal analyses of the perspective of the parent. *Child and adolescent psychiatry and mental health.* 2015;9:24.
26. Sinclair JM, Gray A, Rivero-Arias O, Saunders KE, Hawton K. Healthcare and social services resource use and costs of self-harm patients. *Soc Psychiatry Psychiatr Epidemiol.* 2011;46(4):263-71.
27. Hawton K, Saunders KE, O'Connor RC. Self-harm and suicide in adolescents. *Lancet.* 2012;379(9834):2373-82.
28. Ystgaard M, Arensman E, Hawton K, Madge N, van Heeringen K, Hewitt A, et al. Deliberate self-harm in adolescents: comparison between those who receive help following self-harm and those who do not. *J Adolesc.* 2009;32(4):875-91.
29. Hawton K, Rodham K, Evans E, Harriss L. Adolescents Who Self Harm: A Comparison of Those Who Go to Hospital and Those Who Do Not. *Child and Adolescent Mental Health.* 2009;14(1):24-30.
30. Finkelstein Y, Macdonald EM, Hollands S, Hutson JR, Sivilotti ML, Mamdani MM, et al. Long-term outcomes following self-poisoning in adolescents: a population-based cohort study. *Lancet Psychiatry.* 2015;2(6):532-9.
31. Fadum EA, Stanley B, Rossow I, Mork E, Tormoen AJ, Mehlum L. Use of health services following self-harm in urban versus suburban and rural areas: a national cross-sectional study. *BMJ Open.* 2013;3(7).
32. Hawton K, Fagg J, Simkin S. Deliberate self-poisoning and self-injury in children and adolescents under 16 years of age in Oxford, 1976-1993. *The British journal of psychiatry : the journal of mental science.* 1996;169(2):202-8.
33. Sourander A, Aromaa M, Pihlakoski L, Haavisto A, Rautava P, Helenius H, et al. Early predictors of deliberate self-harm among adolescents. A prospective follow-up study from age 3 to age 15. *J Affect Disord.* 2006;93(1-3):87-96.
34. Moran P, Coffey C, Romaniuk H, Olsson C, Borschmann R, Carlin JB, et al. The natural history of self-harm from adolescence to young adulthood: a population-based cohort study. *Lancet.* 2012;379(9812):236-43.
35. Geulayov G, Kapur N, Turnbull P, Clements C, Waters K, Ness J, et al. Epidemiology and trends in non-fatal self-harm in three centres in England, 2000-2012: findings from the Multicentre Study of Self-harm in England. *BMJ Open.* 2016;6(4):e010538.
36. Diggins E, Kelley R, Cottrell D, House A, Owens D. Age-related differences in self-harm presentations and subsequent management of adolescents and young adults at the emergency department. *J Affect Disord.* 2017;208:399-405.
37. Hawton K, Harriss L. The changing gender ratio in occurrence of deliberate self-harm across the lifecycle. *Crisis.* 2008;29(1):4-10.
38. Larsson B, Sund AM. Prevalence, course, incidence, and 1-year prediction of deliberate self-harm and suicide attempts in early Norwegian school adolescents. *Suicide Life Threat Behav.* 2008;38(2):152-65.

39. Kopjar B, Dieserud G, Wiik J. [Deliberate self-poisonings treated in hospitals]. *Tidsskr Nor Laegeforen*. 2005;125(13):1798-800.
40. Engeland A, Wiik J, Lande G. [Registration of parasuicide at hospitals and emergency units]. *Tidsskr Nor Laegeforen*. 2001;121(9):1033-7.
41. Fadum EA, Stanley B, Qin P, Diep LM, Mehlum L. Self-poisoning with medications in adolescents: a national register study of hospital admissions and readmissions. *Gen Hosp Psychiatry*. 2014;36(6):709-15.
42. Ness J, Hawton K, Bergen H, Waters K, Kapur N, Cooper J, et al. High-Volume Repeaters of Self-Harm. *Crisis*. 2016;37(6):427-37.
43. Perry IJ, Corcoran P, Fitzgerald AP, Keeley HS, Reulbach U, Arensman E. The incidence and repetition of hospital-treated deliberate self harm: findings from the world's first national registry. *PLoS One*. 2012;7(2):e31663.
44. Quinlivan L, Cooper J, Davies L, Hawton K, Gunnell D, Kapur N. Which are the most useful scales for predicting repeat self-harm? A systematic review evaluating risk scales using measures of diagnostic accuracy. *BMJ Open*. 2016;6(2):e009297.
45. Carroll R, Metcalfe C, Gunnell D. Hospital presenting self-harm and risk of fatal and non-fatal repetition: systematic review and meta-analysis. *PLoS One*. 2014;9(2):e89944.
46. Skinner R, McFaull S, Draca J, Frechette M, Kaur J, Pearson C, et al. Suicide and self-inflicted injury hospitalizations in Canada (1979 to 2014/15). *Health Promot Chronic Dis Prev Can*. 2016;36(11):243-51.
47. World Health Organization. Preventing suicide - A global imperative. Geneva 2014.
48. Crosby AE, Han B, Ortega LAG, Parks SE, Gfroerer J. Suicidal Thoughts and Behaviors Among Adults Aged ≥18 Years --- United States, 2008-2009. Centers for Disease Control and Prevention; 2011.
49. McMahon EM, Keeley H, Cannon M, Arensman E, Perry IJ, Clarke M, et al. The iceberg of suicide and self-harm in Irish adolescents: a population-based study. *Soc Psychiatry Psychiatr Epidemiol*. 2014;49(12):1929-35.
50. Retterstol N, Ekeberg O, editors. The Norwegian National Plan for Suicide Prevention. XVIII International Association of Suicide Prevention Congress Suicide, Disease, Disadvantage: a holistic approach Venice; 1995.
51. Hickey L, Hawton K, Fagg J, Weitzel H. Deliberate self-harm patients who leave the accident and emergency department without a psychiatric assessment: a neglected population at risk of suicide. *J Psychosom Res*. 2001;50(2):87-93.
52. Gunnell D, Bennewith O, Peters TJ, House A, Hawton K. The epidemiology and management of self-harm amongst adults in England. *J Public Health (Oxf)*. 2005;27(1):67-73.
53. Mork E, Ekeid G, Ystgaard M, Mehlum L, Holte A. Psychosocial follow-up after parasuicide in Norwegian general hospitals. *Tidsskr Nor Laegeforen*. 2001;121(9):1038-43.
54. Helsetilsynet. Rutiner for registrering, behandling og oppfølging av pasienter innlagt i norske sykehus etter parasuicid. Oslo 2001.
55. Helsedirektoratet. Handlingsplan for forebygging av selvmord og selvskading 2014-2017. Oslo 2014.
56. Sosial- og Helsedirektoratet. Nasjonale retningslinjer for forebygging av selvmord i psykisk helsevern. Oslo 2008.
57. Ringard A, Sagan A, Sperre Saunes I, Lindahl A. Norway: Health system review. . *Health Systems in Transition*. 2013;15(8).
58. Sandvik H, Hunskaar S. Contacts with out-of-hours services because of poisonings in Norway 2006 – 15. *Tidsskr Nor Laegeforen*. 2017.

59. Statistics Norway. 7 000 000 treatments in Norwegian hospitals <http://www.ssb.no2017/> [Available from: <https://www.ssb.no/en/helse/artikler-og-publikasjoner/7-000-000-treatments-in-norwegian-hospitals>].
60. Hawton K, Witt KG, Taylor Salisbury TL, Arensman E, Gunnell D, Townsend E, et al. Interventions for self-harm in children and adolescents. The Cochrane database of systematic reviews. 2015(12):CD012013.
61. Hawton K, Witt KG, Taylor Salisbury TL, Arensman E, Gunnell D, Hazell P, et al. Pharmacological interventions for self-harm in adults. The Cochrane database of systematic reviews. 2015(7):CD011777.
62. Hawton K, Witt KG, Taylor Salisbury TL, Arensman E, Gunnell D, Hazell P, et al. Psychosocial interventions for self-harm in adults. The Cochrane database of systematic reviews. 2016(5):CD012189.
63. Scoliers G, Portzky G, Madge N, Hewitt A, Hawton K, de Wilde EJ, et al. Reasons for adolescent deliberate self-harm: a cry of pain and/or a cry for help? Findings from the child and adolescent self-harm in Europe (CASE) study. *Soc Psychiatry Psychiatr Epidemiol*. 2009;44(8):601-7.
64. Rasmussen S, Hawton K, Philpott-Morgan S, O'Connor RC. Why Do Adolescents Self-Harm? *Crisis*. 2016;37(3):176-83.
65. Nock MK. Self-injury. *Annu Rev Clin Psychol*. 2010;6:339-63.
66. Nock MK. Why do People Hurt Themselves? New Insights Into the Nature and Functions of Self-Injury. *Curr Dir Psychol Sci*. 2009;18(2):78-83.
67. Edmondson AJ, Brennan CA, House AO. Non-suicidal reasons for self-harm: A systematic review of self-reported accounts. *J Affect Disord*. 2016;191:109-17.
68. Joubert L, Petrakis M, Cementon E. Suicide attempt presentations at the emergency department: outcomes from a pilot study examining precipitating factors in deliberate self-harm and issues in primary care physician management. *Soc Work Health Care*. 2012;51(1):66-76.
69. Milnes D, Owens D, Blenkiron P. Problems reported by self-harm patients: perception, hopelessness, and suicidal intent. *J Psychosom Res*. 2002;53(3):819-22.
70. van Heeringen K. Stress-Diathesis Model of Suicidal Behavior. In: Dwivedi Y, editor. *The Neurobiological Basis of Suicide*. Frontiers in Neuroscience. Boca Raton (FL)2012.
71. Guerreiro DF, Figueira ML, Cruz D, Sampaio D. Coping strategies in adolescents who self-harm. *Crisis*. 2015;36(1):31-7.
72. Getz L, Kirkengen AL, Ulvestad E. The human biology--saturated with experience. *Tidsskr Nor Laegeforen*. 2011;131(7):683-7.
73. Christiansen E, Larsen KJ, Agerbo E, Bilenberg N, Stenager E. Risk factors and study designs used in research of youths' suicide behaviour-an epidemiological discussion with focus on level of evidence. *Nord J Psychiatry*. 2014;68(8):513-23.
74. Evans E, Hawton K, Rodham K. Factors associated with suicidal phenomena in adolescents: a systematic review of population-based studies. *Clin Psychol Rev*. 2004;24(8):957-79.
75. McMahon EM, Reulbach U, Corcoran P, Keeley HS, Perry IJ, Arensman E. Factors associated with deliberate self-harm among Irish adolescents. *Psychol Med*. 2010;40(11):1811-9.
76. Fliege H, Lee JR, Grimm A, Klapp BF. Risk factors and correlates of deliberate self-harm behavior: a systematic review. *J Psychosom Res*. 2009;66(6):477-93.
77. Christiansen E, Larsen KJ, Agerbo E, Bilenberg N, Stenager E. Incidence and risk factors for suicide attempts in a general population of young people: a Danish register-based study. *Aust N Z J Psychiatry*. 2013;47(3):259-70.
78. Cannon WB. ORGANIZATION FOR PHYSIOLOGICAL HOMEOSTASIS. *Physiol Rev*. 1929;9(3):399-431.

79. Irwin MR. Why sleep is important for health: a psychoneuroimmunology perspective. *Annu Rev Psychol.* 2015;66:143-72.
80. Banks S, Dinges DF. Behavioral and physiological consequences of sleep restriction. *J Clin Sleep Med.* 2007;3(5):519-28.
81. Baglioni C, Battagliese G, Feige B, Spiegelhalder K, Nissen C, Voderholzer U, et al. Insomnia as a predictor of depression: a meta-analytic evaluation of longitudinal epidemiological studies. *J Affect Disord.* 2011;135(1-3):10-9.
82. Beebe DW. Cognitive, behavioral, and functional consequences of inadequate sleep in children and adolescents. *Pediatr Clin North Am.* 2011;58(3):649-65.
83. Carskadon MA. Sleep's effects on cognition and learning in adolescence. *Prog Brain Res.* 2011;190:137-43.
84. Crum RM, Storr CL, Chan YF, Ford DE. Sleep disturbance and risk for alcohol-related problems. *The American journal of psychiatry.* 2004;161(7):1197-203.
85. Fairholme CP, Nosen EL, Nillni YI, Schumacher JA, Tull MT, Coffey SF. Sleep disturbance and emotion dysregulation as transdiagnostic processes in a comorbid sample. *Behav Res Ther.* 2013;51(9):540-6.
86. McCall WV. Insomnia is a risk factor for suicide-what are the next steps? *Sleep.* 2011;34(9):1149-50.
87. Wolfson AR, Carskadon MA. Understanding adolescents' sleep patterns and school performance: a critical appraisal. *Sleep Med Rev.* 2003;7(6):491-506.
88. Wong MM, Brower KJ, Fitzgerald HE, Zucker RA. Sleep problems in early childhood and early onset of alcohol and other drug use in adolescence. *Alcohol Clin Exp Res.* 2004;28(4):578-87.
89. Gimeno D, Kivimaki M, Brunner EJ, Elovainio M, De Vogli R, Steptoe A, et al. Associations of C-reactive protein and interleukin-6 with cognitive symptoms of depression: 12-year follow-up of the Whitehall II study. *Psychol Med.* 2009;39(3):413-23.
90. Kiecolt-Glaser JK, Derry HM, Fagundes CP. Inflammation: depression fans the flames and feasts on the heat. *Am J Psychiatry.* 2015;172(11):1075-91.
91. Wong MM, Brower KJ, Zucker RA. Sleep problems, suicidal ideation, and self-harm behaviors in adolescence. *J Psychiatr Res.* 2011;45(4):505-11.
92. Wong MM, Brower KJ. The prospective relationship between sleep problems and suicidal behavior in the National Longitudinal Study of Adolescent Health. *J Psychiatr Res.* 2012;46(7):953-9.
93. Fredriksen K, Rhodes J, Reddy R, Way N. Sleepless in Chicago: tracking the effects of adolescent sleep loss during the middle school years. *Child Dev.* 2004;75(1):84-95.
94. Roane BM, Taylor DJ. Adolescent insomnia as a risk factor for early adult depression and substance abuse. *Sleep.* 2008;31(10):1351-6.
95. Matamura M, Tochigi M, Usami S, Yonehara H, Fukushima M, Nishida A, et al. Associations between sleep habits and mental health status and suicidality in a longitudinal survey of monozygotic twin adolescents. *J Sleep Res.* 2014;23(3):290-4.
96. Hysing M, Sivertsen B, Stormark KM, O'Connor RC. Sleep problems and self-harm in adolescence. *Br J Psychiatry.* 2015;207(4):306-12.
97. Gratz KL. Risk factors for and functions of deliberate self-harm: an empirical and conceptual review. *Clinical Psychology: Science and Practice.* 2003;10(2):192-205.
98. Fergusson DM, Beautrais AL, Horwood LJ. Vulnerability and resiliency to suicidal behaviours in young people. *Psychol Med.* 2003;33(1):61-73.
99. Di Pierro R, Sarno I, Perego S, Gallucci M, Madeddu F. Adolescent nonsuicidal self-injury: the effects of personality traits, family relationships and maltreatment on the presence and severity of behaviours. *Eur Child Adolesc Psychiatry.* 2012;21(9):511-20.

100. Black DW, Blum N, Pfohl B, Hale N. Suicidal behavior in borderline personality disorder: prevalence, risk factors, prediction, and prevention. *J Pers Disord.* 2004;18(3):226-39.
101. Beautrais AL, Joyce PR, Mulder RT, Fergusson DM, Deavoll BJ, Nightingale SK. Prevalence and comorbidity of mental disorders in persons making serious suicide attempts: a case-control study. *The American journal of psychiatry.* 1996;153(8):1009-14.
102. Fergusson DM, Horwood LJ, Ridder EM, Beautrais AL. Subthreshold depression in adolescence and mental health outcomes in adulthood. *Arch Gen Psychiatry.* 2005;62(1):66-72.
103. Nock MK, Hwang I, Sampson N, Kessler RC, Angermeyer M, Beautrais A, et al. Cross-national analysis of the associations among mental disorders and suicidal behavior: findings from the WHO World Mental Health Surveys. *PLoS Med.* 2009;6(8):e1000123.
104. Fassberg MM, Cheung G, Canetto SS, Erlangsen A, Lapierre S, Lindner R, et al. A systematic review of physical illness, functional disability, and suicidal behaviour among older adults. *Aging Ment Health.* 2015:1-29.
105. Mitchell R, Draper B, Harvey L, Brodaty H, Close J. The association of physical illness and self-harm resulting in hospitalisation among older people in a population-based study. *Aging Ment Health.* 2015:1-10.
106. Singhal A, Ross J, Seminog O, Hawton K, Goldacre MJ. Risk of self-harm and suicide in people with specific psychiatric and physical disorders: comparisons between disorders using English national record linkage. *J R Soc Med.* 2014;107(5):194-204.
107. Osteras B, Sigmundsson H, Haga M. Perceived stress and musculoskeletal pain are prevalent and significantly associated in adolescents: an epidemiological cross-sectional study. *BMC Public Health.* 2015;15:1081.
108. Hoftun GB, Romundstad PR, Rygg M. Factors associated with adolescent chronic non-specific pain, chronic multisite pain, and chronic pain with high disability: the Young-HUNT Study 2008. *J Pain.* 2012;13(9):874-83.
109. Karaman S, Karaman T, Dogru S, Onder Y, Citil R, Bulut YE, et al. Prevalence of sleep disturbance in chronic pain. *Eur Rev Med Pharmacol Sci.* 2014;18(17):2475-81.
110. Swain MS, Henschke N, Kamper SJ, Gobina I, Ottova-Jordan V, Maher CG. An international survey of pain in adolescents. *BMC Public Health.* 2014;14:447.
111. Tang NK, Crane C. Suicidality in chronic pain: a review of the prevalence, risk factors and psychological links. *Psychol Med.* 2006;36(5):575-86.
112. Ferro MA, Rhodes AE, Kimber M, Duncan L, Boyle MH, Georgiades K, et al. Suicidal Behaviour Among Adolescents and Young Adults with Self-Reported Chronic Illness. *Can J Psychiatry.* 2017;62(12):845-53.
113. Van Orden KA, Wiktorsson S, Duberstein P, Berg AI, Fassberg MM, Waern M. Reasons for attempted suicide in later life. *Am J Geriatr Psychiatry.* 2015;23(5):536-44.
114. Erlangsen A, Stenager E, Conwell Y. Physical diseases as predictors of suicide in older adults: a nationwide, register-based cohort study. *Soc Psychiatry Psychiatr Epidemiol.* 2015;50(9):1427-39.
115. Webb RT, Kontopantelis E, Doran T, Qin P, Creed F, Kapur N. Risk of self-harm in physically ill patients in UK primary care. *J Psychosom Res.* 2012;73(2):92-7.
116. Pompili M, Di Cosimo D, Innamorati M, Lester D, Tatarelli R, Martelletti P. Psychiatric comorbidity in patients with chronic daily headache and migraine: a selective overview including personality traits and suicide risk. *J Headache Pain.* 2009;10(4):283-90.
117. Wang SJ, Juang KD, Fuh JL, Lu SR. Psychiatric comorbidity and suicide risk in adolescents with chronic daily headache. *Neurology.* 2007;68(18):1468-73.

118. Meyer N, Voysey M, Holmes J, Casey D, Hawton K. Self-harm in people with epilepsy: a retrospective cohort study. *Epilepsia*. 2014;55(9):1355-65.
119. Yang K, Su J, Hu Z, Lang R, Sun X, Li X, et al. Serotonin transporter (5-HTT) gene polymorphisms and susceptibility to epilepsy: a meta-analysis and meta-regression. *Genet Test Mol Biomarkers*. 2013;17(12):890-7.
120. Baldin E, Hesdorffer DC, Caplan R, Berg AT. Psychiatric disorders and suicidal behavior in neurotypical young adults with childhood-onset epilepsy. *Epilepsia*. 2015;56(10):1623-8.
121. Friedman HS, Kern ML. Personality, well-being, and health. *Annu Rev Psychol*. 2014;65:719-42.
122. Engler B. *Personality Theories*: Cengage Learning; 2008.
123. Rothbart MK, Ahadi SA, Evans DE. Temperament and personality: origins and outcomes. *J Pers Soc Psychol*. 2000;78(1):122-35.
124. Rothbart MK, Ahadi SA. Temperament and the development of personality. *J Abnorm Psychol*. 1994;103(1):55-66.
125. Eysenck HJ, Eysenck SBG. *Manual of the Eysenck Personality Questionnaire (junior and adult)*: Hodder and Stoughton; 1975.
126. Goldberg LR. An alternative "description of personality": the big-five factor structure. *J Pers Soc Psychol*. 1990;59(6):1216-29.
127. Markey PM, Markey CN, Tinsley BJ. Children's behavioral manifestations of the five-factor model of personality. *Pers Soc Psychol Bull*. 2004;30(4):423-32.
128. Shiner R, Caspi A. Personality differences in childhood and adolescence: measurement, development, and consequences. *J Child Psychol Psychiatry*. 2003;44(1):2-32.
129. Specht J, Egloff B, Schmukle SC. Stability and change of personality across the life course: the impact of age and major life events on mean-level and rank-order stability of the Big Five. *J Pers Soc Psychol*. 2011;101(4):862-82.
130. Hartmann C, Siegrist M. A longitudinal study of the relationships between the Big Five personality traits and body size perception. *Body Image*. 2015;14:67-71.
131. Hintsanen M, Puttonen S, Smith K, Tornroos M, Jokela M, Pulkki-Raback L, et al. Five-factor personality traits and sleep: evidence from two population-based cohort studies. *Health Psychol*. 2014;33(10):1214-23.
132. Brezo J, Paris J, Turecki G. Personality traits as correlates of suicidal ideation, suicide attempts, and suicide completions: a systematic review. *Acta Psychiatr Scand*. 2006;113(3):180-206.
133. Hirvikoski T, Jokinen J. Personality traits in attempted and completed suicide. *Eur Psychiatry*. 2012;27(7):536-41.
134. Steeg S, Haigh M, Webb RT, Kapur N, Awenat Y, Gooding P, et al. The exacerbating influence of hopelessness on other known risk factors for repeat self-harm and suicide. *J Affect Disord*. 2016;190:522-8.
135. Mullins-Sweatt SN, Lengel GJ, Grant DM. Non-suicidal self-injury: the contribution of general personality functioning. *Personal Ment Health*. 2013;7(1):56-68.
136. Robertson CD, Miskey H, Mitchell J, Nelson-Gray R. Variety of self-injury: is the number of different methods of non-suicidal self-injury related to personality, psychopathology, or functions of self-injury? *Arch Suicide Res*. 2013;17(1):33-40.
137. Eysenck HJ. The definition and measurement of psychoticism. *Personality and Individual Differences*. 1992;13(7):757-85.
138. Buresova I, Vrbova M, Cernak M. Personality characteristic of adolescent self-harmers. *Procd Soc Behv*. 2015;171:1118-27.
139. Statistics Norway. Key figures for the population 2017 [updated 1 June 2017]. Available from: <https://www.ssb.no/en/befolkning/nokkeltall/population>.

140. Kommunal- og moderniseringsdepartementet. Meld. St. 22 (2015-2016) Nye folkevalgte regioner - rolle, struktur og oppgaver. 2016.
141. Statistics Norway. Folkemengde og befolkningsendringar, 1. januar 2016 2016 [Available from: <https://ssb.no/befolkning/statistikker/folkemengde/aar-per-1-januar/2016-02-19?fane=tabell&sort=nummer&tabell=256001>].
142. Holmen TL, Bratberg G, Krokstad S, Langhammer A, Hveem K, Midthjell K, et al. Cohort profile of the Young-HUNT Study, Norway: a population-based study of adolescents. *Int J Epidemiol*. 2014;43(2):536-44.
143. HUNT Research Centre. Questionnaires from the HUNT studies [Available from: <https://www.ntnu.edu/hunt/data/que>].
144. Evans J, Johnson C, Stanton R, Morgan HG. How to establish case registers: II. Non-fatal deliberate self-harm. *Psychiatric Bulletin*. 1996;20(July):403-5.
145. Horrocks J, House A, Owens D. Establishing a clinical database for hospital attendances because of self-harm *Psychiatric Bulletin*. 2004;28(April):137-9.
146. Carroll R, Gunnell D. Annual report 2011 - Bristol Self-Harm Surveillance Register. University of Bristol; 2011.
147. Clements C, Turnbull P, Hawton K, Geulayov G, Waters K, Ness J, et al. Rates of self-harm presenting to general hospitals: a comparison of data from the Multicentre Study of Self-Harm in England and Hospital Episode Statistics. *BMJ Open*. 2016;6(2):e009749.
148. Mellesdal L, Kroken RA, Lutro O, Wentzel-Larsen T, Kjølby E, Oedegaard KJ, et al. Self-harm induced somatic admission after discharge from psychiatric hospital - a prospective cohort study. *Eur Psychiatry*. 2014;29(4):246-52.
149. Patrick AR, Miller M, Barber CW, Wang PS, Canning CF, Schneeweiss S. Identification of hospitalizations for intentional self-harm when E-codes are incompletely recorded. *Pharmacoepidemiol Drug Saf*. 2010;19(12):1263-75.
150. Lintonen T, Ahlstrom S, Metso L. The reliability of self-reported drinking in adolescence. *Alcohol Alcohol*. 2004;39(4):362-8.
151. Strandheim A, Holmen TL, Coombes L, Bentzen N. Alcohol intoxication and mental health among adolescents--a population review of 8983 young people, 13-19 years in North-Trøndelag, Norway: the Young-HUNT Study. *Child and adolescent psychiatry and mental health*. 2009;3(1):18.
152. Strandheim A, Holmen TL, Coombes L, Bentzen N. Alcohol use and physical health in adolescence: a general population survey of 8,983 young people in North-Trøndelag, Norway (the Young-HUNT study). *Subst Use Misuse*. 2010;45(1-2):253-65.
153. Strand BH, Dalgard OS, Tambs K, Rognerud M. Measuring the mental health status of the Norwegian population: a comparison of the instruments SCL-25, SCL-10, SCL-5 and MHI-5 (SF-36). *Nordic journal of psychiatry*. 2003;57(2):113-8.
154. Tambs K, Moum T. How well can a few questionnaire items indicate anxiety and depression? *Acta Psychiatr Scand*. 1993;87(5):364-7.
155. Cole TJ, Bellizzi MC, Flegal KM, Dietz WH. Establishing a standard definition for child overweight and obesity worldwide: international survey. *BMJ*. 2000;320(7244):1240-3.
156. Cole TJ, Flegal KM, Nicholls D, Jackson AA. Body mass index cut offs to define thinness in children and adolescents: international survey. *BMJ*. 2007;335(7612):194.
157. Tambs K. Undersøkelse av seksuelle overgrep mot barn. Oslo: Statens institutt for folkehelse. 1994.
158. Stensland SO, Thoresen S, Wentzel-Larsen T, Dyb G. Interpersonal violence and overweight in adolescents: the HUNT Study. *Scand J Public Health*. 2015;43(1):18-26.

159. Mykkestad I, Roysamb E, Tambs K. Risk and protective factors for psychological distress among adolescents: a family study in the Nord-Trøndelag Health Study. *Soc Psychiatry Psychiatr Epidemiol.* 2012;47(5):771-82.
160. Jeppesen E, Bjelland I, Fossa SD, Loge JH, Sorebo O, Dahl AA. Does a parental history of cancer moderate the associations between impaired health status in parents and psychosocial problems in teenagers: a HUNT study. *Cancer Med.* 2014;3(4):919-26.
161. Liang SG, Yan J, Zhu CZ, Situ MJ, Du N, Fu XY, et al. [Personality traits of Chinese adolescents with non-suicidal self injury and suicide attempt]. *Sichuan da xue xue bao Yi xue ban = Journal of Sichuan University Medical science edition.* 2014;45(6):970-3.
162. Kumar PN, Rajmohan V, Sushil K. An exploratory analysis of personality factors contributed to suicide attempts. *Indian journal of psychological medicine.* 2013;35(4):378-84.
163. Prisciandaro JJ, McRae-Clark AL, Moran-Santa Maria MM, Hartwell KJ, Brady KT. Psychoticism and neuroticism predict cocaine dependence and future cocaine use via different mechanisms. *Drug Alcohol Depend.* 2011;116(1-3):80-5.
164. Jylha P, Melartin T, Isometsa E. Relationships of neuroticism and extraversion with axis I and II comorbidity among patients with DSM-IV major depressive disorder. *J Affect Disord.* 2009;114(1-3):110-21.
165. Caruso JC, Witkiewitz K, Belcourt-Dittloff A, Gottlieb JD. Reliability of Scores from the Eysenck Personality Questionnaire: A Reliability Generalization Study. *Educational and Psychological Measurement.* 2001;61(4):675-89.
166. de Ridder K, Pape K, Krokstad S, Bjorngaard JH. Health in adolescence and subsequent receipt of social insurance benefits - The HUNT Study. *Tidsskr Nor Laegeforen.* 2015;135(10):942-8.
167. Strandheim A, Bjerkeset O, Gunnell D, Bjornelv S, Holmen TL, Bentzen N. Risk factors for suicidal thoughts in adolescence--a prospective cohort study: the Young-HUNT study. *BMJ Open.* 2014;4(8):e005867.
168. Pape K, Bjorngaard JH, Westin S, Holmen TL, Krokstad S. Reading and writing difficulties in adolescence and later risk of welfare dependence. A ten year follow-up, the HUNT Study, Norway. *BMC Public Health.* 2011;11:718.
169. Rosenberg M. The association between self-esteem and anxiety. *J Psychiatr Res.* 1962;1(2):135-52.
170. Ystgaard M. Sårbar ungdom og sosial støtte: en tilnærming til forebygging av psykisk stress og selvmord: Senter for sosialt nettverk og helse; 1993.
171. Sandanger I, Sørensen T, Nordkyst p, Universitetet i O. Ubevisst sjeleliv og bevisst samfunnsliv : psykisk helse i en sammenheng : festskrift til Tom Sørensen på hans 60-årsdag. Oslo: Universitetet i Oslo Nordkyst psykiatri; 2004.
172. De Ridder KA, Pape K, Johnsen R, Holmen TL, Westin S, Bjorngaard JH. Adolescent health and high school dropout: a prospective cohort study of 9000 Norwegian adolescents (the Young-HUNT). *PLoS One.* 2013;8(9):e74954.
173. Mangerud WL, Bjerkeset O, Holmen TL, Lydersen S, Indredavik MS. Smoking, alcohol consumption, and drug use among adolescents with psychiatric disorders compared with a population based sample. *J Adolesc.* 2014;37(7):1189-99.
174. Asher MI, Keil U, Anderson HR, Beasley R, Crane J, Martinez F, et al. International Study of Asthma and Allergies in Childhood (ISAAC): rationale and methods. *Eur Respir J.* 1995;8(3):483-91.
175. Cox DR. Regression models and life-tables. *Journal of the Royal Statistical Society Series B.* 1972;34(2):187-220.
176. Grambsch PM, Therneau TM. Proportional hazards tests and diagnostics based on weighted residuals. *Biometrika.* 1994;81(3):515-26.

177. Schoenfeld D. Partial residuals for the proportional hazards regression model. *Biometrika*. 1982;69(1):239-41.
178. Rothman KJ, Greenland S, Lash TL. *Precision and Statistics in Epidemiologic Studies*. Modern Epidemiology. 3rd ed: Lippincott Williams & Wilkins; 2008.
179. Hernan M, Robins J. Causal Inference [PDF]. 2017 [Available from: https://cdn1.sph.harvard.edu/wp-content/uploads/sites/1268/2017/03/hernanrobins_v1.10.32.pdf].
180. Langhammer A, Krokstad S, Romundstad P, Heggland J, Holmen J. The HUNT study: participation is associated with survival and depends on socioeconomic status, diseases and symptoms. *BMC Med Res Methodol*. 2012;12:143.
181. Knudsen AK, Hotopf M, Skogen JC, Overland S, Mykletun A. The health status of nonparticipants in a population-based health study: the Hordaland Health Study. *Am J Epidemiol*. 2010;172(11):1306-14.
182. Rothman KJ, Greenland S, Lash TL. *Validity in Epidemiologic Studies*. Modern Epidemiology. 3rd ed: Lippincott Williams & Wilkins; 2008.
183. Harriss L, Hawton K. Deliberate self-harm in rural and urban regions: a comparative study of prevalence and patient characteristics. *Soc Sci Med*. 2011;73(2):274-81.
184. Colrain IM, Baker FC. Changes in sleep as a function of adolescent development. *Neuropsychol Rev*. 2011;21(1):5-21.
185. Nicolaisen M, Thorsen K. Who are lonely? Loneliness in different age groups (18-81 years old), using two measures of loneliness. *Int J Aging Hum Dev*. 2014;78(3):229-57.
186. Nielsen MB, Nielsen GH, Notelaers G, Einarsen S. Workplace Bullying and Suicidal Ideation: A 3-Wave Longitudinal Norwegian Study. *Am J Public Health*. 2015;105(11):e23-8.
187. Brausch AM, Gutierrez PM. Differences in non-suicidal self-injury and suicide attempts in adolescents. *Journal of youth and adolescence*. 2010;39(3):233-42.
188. Kapur N, Cooper J, O'Connor RC, Hawton K. Non-suicidal self-injury v. attempted suicide: new diagnosis or false dichotomy? *Br J Psychiatry*. 2013;202(5):326-8.
189. Andover MS, Morris BW, Wren A, Bruzzese ME. The co-occurrence of non-suicidal self-injury and attempted suicide among adolescents: distinguishing risk factors and psychosocial correlates. *Child and adolescent psychiatry and mental health*. 2012;6:11.
190. Klonsky ED, Muehlenkamp JJ. Self-injury: a research review for the practitioner. *J Clin Psychol*. 2007;63(11):1045-56.
191. Bresin K, Schoenleber M. Gender differences in the prevalence of nonsuicidal self-injury: A meta-analysis. *Clin Psychol Rev*. 2015;38:55-64.
192. Swannell SV, Martin GE, Page A, Hasking P, St John NJ. Prevalence of nonsuicidal self-injury in nonclinical samples: systematic review, meta-analysis and meta-regression. *Suicide Life Threat Behav*. 2014;44(3):273-303.
193. Grandclerc S, De Labrouhe D, Spodenkiewicz M, Lachal J, Moro MR. Relations between Nonsuicidal Self-Injury and Suicidal Behavior in Adolescence: A Systematic Review. *PLoS One*. 2016;11(4):e0153760.
194. Bernert RA, Hom MA, Iwata NG, Joiner TE. Objectively Assessed Sleep Variability as an Acute Warning Sign of Suicidal Ideation in a Longitudinal Evaluation of Young Adults at High Suicide Risk. *J Clin Psychiatry*. 2017;78(6):e678-e87.
195. Nrugham L, Larsson B, Sund AM. Specific depressive symptoms and disorders as associates and predictors of suicidal acts across adolescence. *J Affect Disord*. 2008;111(1):83-93.
196. Sjostrom N, Hetta J, Waern M. Persistent nightmares are associated with repeat suicide attempt: a prospective study. *Psychiatry Res*. 2009;170(2-3):208-11.
197. Bernert RA, Joiner TE. Sleep disturbances and suicide risk: A review of the literature. *Neuropsychiatr Dis Treat*. 2007;3(6):735-43.

198. Liu X, Buysse DJ. Sleep and youth suicidal behavior: a neglected field. *Current opinion in psychiatry*. 2006;19(3):288-93.
199. Fitzgerald CT, Messias E, Buysse DJ. Teen sleep and suicidality: results from the youth risk behavior surveys of 2007 and 2009. *J Clin Sleep Med*. 2011;7(4):351-6.
200. Liu X, Chen H, Bo QG, Fan F, Jia CX. Poor sleep quality and nightmares are associated with non-suicidal self-injury in adolescents. *Eur Child Adolesc Psychiatry*. 2017;26(3):271-9.
201. Conner KR, Meldrum S, Wiczorek WF, Duberstein PR, Welte JW. The association of irritability and impulsivity with suicidal ideation among 15- to 20-year-old males. *Suicide Life Threat Behav*. 2004;34(4):363-73.
202. Evans J, Reeves B, Platt H, Leibenau A, Goldman D, Jefferson K, et al. Impulsiveness, serotonin genes and repetition of deliberate self-harm (DSH). *Psychol Med*. 2000;30(6):1327-34.
203. Gregory AM, Sadeh A. Sleep, emotional and behavioral difficulties in children and adolescents. *Sleep Med Rev*. 2012;16(2):129-36.
204. Roberts RE, Roberts CR, Chen IG. Impact of insomnia on future functioning of adolescents. *J Psychosom Res*. 2002;53(1):561-9.
205. Beautrais AL, Joyce PR, Mulder RT. Psychiatric illness in a New Zealand sample of young people making serious suicide attempts. *The New Zealand medical journal*. 1998;111(1060):44-8.
206. Hawton K, Houston K, Townsend E. Psychiatric and personality disorders in deliberate self-harm patients. *Br J Psychiatry*. 2001;178(1):48-54.
207. Hjelmeland H, Dieserud G, Dyregrov K, Knizek BL, Rasmussen ML. Suicide and mental disorders. *Tidsskr Nor Laegeforen*. 2014;134(14):1369-70.
208. Tyrer P. The case for cothymia: mixed anxiety and depression as a single diagnosis. *Br J Psychiatry*. 2001;179:191-3.
209. Sareen J, Cox BJ, Afifi TO, de Graaf R, Asmundson GJ, ten Have M, et al. Anxiety disorders and risk for suicidal ideation and suicide attempts: a population-based longitudinal study of adults. *Arch Gen Psychiatry*. 2005;62(11):1249-57.
210. Mykletun A, Bjerkeset O, Dewey M, Prince M, Overland S, Stewart R. Anxiety, depression, and cause-specific mortality: the HUNT study. *Psychosom Med*. 2007;69(4):323-31.
211. Rossow I, Wichstrom L. Parasuicide and use of intoxicants among Norwegian adolescents. *Suicide Life Threat Behav*. 1994;24(2):174-83.
212. Rossow I, Groholt B, Wichstrom L. Intoxicants and suicidal behaviour among adolescents: changes in levels and associations from 1992 to 2002. *Addiction*. 2005;100(1):79-88.
213. Bjarnason T, Thorlindsson T. Manifest predictors of past suicide attempts in a population of Icelandic adolescents. *Suicide Life Threat Behav*. 1994;24(4):350-8.
214. Stewart SM, Lam TH, Betson C, Chung SF. Suicide ideation and its relationship to depressed mood in a community sample of adolescents in Hong Kong. *Suicide Life Threat Behav*. 1999;29(3):227-40.
215. Lereya ST, Winsper C, Heron J, Lewis G, Gunnell D, Fisher HL, et al. Being bullied during childhood and the prospective pathways to self-harm in late adolescence. *J Am Acad Child Adolesc Psychiatry*. 2013;52(6):608-18 e2.
216. Kim YS, Leventhal B. Bullying and suicide. A review. *Int J Adolesc Med Health*. 2008;20(2):133-54.
217. Robinson S. Victimization of obese adolescents. *The Journal of school nursing : the official publication of the National Association of School Nurses*. 2006;22(4):201-6.
218. Qin P, Webb R, Kapur N, Sørensen HT. Hospitalization for physical illness and risk of subsequent suicide: a population study. *J Intern Med*. 2013;273(1):48-58.

219. Barnes AJ, Eisenberg ME, Resnick MD. Suicide and self-injury among children and youth with chronic health conditions. *Pediatrics*. 2010;125(5):889-95.
220. Scott KM, Hwang I, Chiu WT, Kessler RC, Sampson NA, Angermeyer M, et al. Chronic physical conditions and their association with first onset of suicidal behavior in the world mental health surveys. *Psychosom Med*. 2010;72(7):712-9.
221. Spiegel B, Schoenfeld P, Naliboff B. Systematic review: the prevalence of suicidal behaviour in patients with chronic abdominal pain and irritable bowel syndrome. *Aliment Pharmacol Ther*. 2007;26(2):183-93.
222. Hjern A, Alfvén G, Ostberg V. School stressors, psychological complaints and psychosomatic pain. *Acta Paediatr*. 2008;97(1):112-7.
223. Alfvén G, Ostberg V, Hjern A. Stressor, perceived stress and recurrent pain in Swedish schoolchildren. *J Psychosom Res*. 2008;65(4):381-7.
224. El Ansari W, Oskrochi R, Labeeb S, Stock C. Symptoms and health complaints and their association with perceived stress at university: survey of students at eleven faculties in Egypt. *Cent Eur J Public Health*. 2014;22(2):68-79.
225. Bjørngaard JH, Gunnell D, Elvestad MB, Davey Smith G, Skorpen F, Krokan H, et al. The causal role of smoking in anxiety and depression: a Mendelian randomization analysis of the HUNT study. *Psychol Med*. 2013;43(4):711-9.
226. Davey Smith G, Phillips AN, Neaton JD. Smoking as "independent" risk factor for suicide: illustration of an artifact from observational epidemiology? *The Lancet*. 1992;340(8821):709-12.
227. Grant BF, Goldstein RB, Saha TD, Chou SP, Jung J, Zhang H, et al. Epidemiology of DSM-5 Alcohol Use Disorder: Results From the National Epidemiologic Survey on Alcohol and Related Conditions III. *JAMA Psychiatry*. 2015;72(8):757-66.
228. Clark DB, Bukstein O, Cornelius J. Alcohol use disorders in adolescents: epidemiology, diagnosis, psychosocial interventions, and pharmacological treatment. *Paediatr Drugs*. 2002;4(8):493-502.
229. Darvishi N, Farhadi M, Haghtalab T, Poorolajal J. Alcohol-related risk of suicidal ideation, suicide attempt, and completed suicide: a meta-analysis. *PLoS One*. 2015;10(5):e0126870.
230. Aseltine RH, Jr., Schilling EA, James A, Glanovsky JL, Jacobs D. Age variability in the association between heavy episodic drinking and adolescent suicide attempts: findings from a large-scale, school-based screening program. *J Am Acad Child Adolesc Psychiatry*. 2009;48(3):262-70.
231. Schisterman EF, Cole SR, Platt RW. Overadjustment bias and unnecessary adjustment in epidemiologic studies. *Epidemiology*. 2009;20(4):488-95.
232. Eysenck SB, Eysenck HJ. The place of impulsiveness in a dimensional system of personality description. *Br J Soc Clin Psychol*. 1977;16(1):57-68.
233. Smink FR, van Hoeken D, Hoek HW. Epidemiology, course, and outcome of eating disorders. *Curr Opin Psychiatry*. 2013;26(6):543-8.
234. Torstveit MK, Agedal-Mortensen K, Stea TH. More than half of high school students report disordered eating: a cross sectional study among Norwegian boys and girls. *PLoS One*. 2015;10(3):e0122681.
235. Bjørnelv S, Nordahl HM, Holmen TL. Psychological factors and weight problems in adolescents. The role of eating problems, emotional problems, and personality traits: the Young-HUNT study. *Soc Psychiatry Psychiatr Epidemiol*. 2011;46(5):353-62.
236. Evans E, Hawton K, Rodham K. In what ways are adolescents who engage in self-harm or experience thoughts of self-harm different in terms of help-seeking, communication and coping strategies? *J Adolesc*. 2005;28(4):573-87.
237. Erol RY, Orth U. Self-esteem development from age 14 to 30 years: a longitudinal study. *J Pers Soc Psychol*. 2011;101(3):607-19.

238. Newton-Howes G, Horwood J, Mulder R. Personality characteristics in childhood and outcomes in adulthood: findings from a 30 year longitudinal study. *Aust N Z J Psychiatry*. 2015;49(4):377-86.
239. Urnes O. [Self-harm and personality disorders]. *Tidsskr Nor Laegeforen*. 2009;129(9):872-6.
240. American Psychiatric Association. *Diagnostic and statistical manual of mental disorders (DSM-5®)*: American Psychiatric Pub; 2013.
241. World Health Organization. *The ICD-10 classification of mental and behavioural disorders: clinical descriptions and diagnostic guidelines*: World Health Organization; 1992.
242. Zanarini MC, Frankenburg FR, Reich DB, Fitzmaurice G, Weinberg I, Gunderson JG. The 10-year course of physically self-destructive acts reported by borderline patients and axis II comparison subjects. *Acta Psychiatr Scand*. 2008;117(3):177-84.
243. Stepp SD. Development of borderline personality disorder in adolescence and young adulthood: introduction to the special section. *J Abnorm Child Psychol*. 2012;40(1):1-5.
244. Winsper C, Lereya ST, Marwaha S, Thompson A, Eyden J, Singh SP. The aetiological and psychopathological validity of borderline personality disorder in youth: A systematic review and meta-analysis. *Clin Psychol Rev*. 2016;44:13-24.
245. Bateman AW, Gunderson J, Mulder R. Treatment of personality disorder. *Lancet*. 2015;385(9969):735-43.
246. Stoffers JM, Vollm BA, Rucker G, Timmer A, Huband N, Lieb K. Psychological therapies for people with borderline personality disorder. *The Cochrane database of systematic reviews*. 2012(8):CD005652.
247. Roberts BW, Walton KE, Viechtbauer W. Patterns of mean-level change in personality traits across the life course: a meta-analysis of longitudinal studies. *Psychol Bull*. 2006;132(1):1-25.
248. Hawton K, Hall S, Simkin S, Bale L, Bond A, Codd S, et al. Deliberate self-harm in adolescents: a study of characteristics and trends in Oxford, 1990-2000. *Journal of child psychology and psychiatry, and allied disciplines*. 2003;44(8):1191-8.
249. Reuter Morthorst B, Soegaard B, Nordentoft M, Erlangsen A. Incidence Rates of Deliberate Self-Harm in Denmark 1994-2011. *Crisis*. 2016;37(4):256-64.
250. Jacobsen D, Frederichsen PS, Knutsen KM, Sorum Y, Talseth T, Odegaard OR. A prospective study of 1212 cases of acute poisoning: general epidemiology. *Hum Toxicol*. 1984;3(2):93-106.
251. Rygnestad T, Fagerhaug O. [Acute deliberate self-poisonings in the area of Trondheim, 1978-2002]. *Tidsskr Nor Laegeforen*. 2004;124(21):2736-9.
252. Sandvik H, Hunskar S. Contacts with out-of-hours services because of poisonings in Norway 2006 - 15. *Tidsskr Nor Laegeforen*. 2017;137(12-13):876-80.
253. Boden JM, Fergusson DM, Horwood LJ. Anxiety disorders and suicidal behaviours in adolescence and young adulthood: findings from a longitudinal study. *Psychol Med*. 2007;37(3):431-40.
254. Galynker I, Yaseen Z, Briggs J. Assessing Risk for Imminent Suicide. *Psychiatr Ann*. 2014;44(9):431-6.
255. Glenn CR, Nock MK. Improving the short-term prediction of suicidal behavior. *Am J Prev Med*. 2014;47(3 Suppl 2):S176-80.
256. Cohen LJ, Ardalan F, Yaseen Z, Galynker I. Suicide Crisis Syndrome Mediates the Relationship Between Long-term Risk Factors and Lifetime Suicidal Phenomena. *Suicide Life Threat Behav*. 2017.

Paper I

Sleep Problems and Hospitalization for Self-Harm: A 15-Year Follow-Up of 9,000 Norwegian Adolescents. The Young-HUNT Study

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Objectives: To investigate the association between sleeping problems in adolescence and subsequent hospital admission for self-harm (SH).

Design: Prospective cohort study, linking health survey information on sleep problems to hospital-based patient records.

Setting: Residents of Nord-Trøndelag County, Norway, aged 13-19 years in 1995-97.

Patients or Participants: 10,202 adolescents were invited to participate in the Young-HUNT study; 8,983 (88%) completed the health survey.

Measurements and Results: 10% of participants reported difficulties initiating sleep, 4% reported early morning wakening. Ninety-eight participants (27% male) were hospitalized following SH over a mean 12 years follow-up. Difficulties initiating sleep/early morning wakening were associated with increased risk of SH (HR 2.11, 95% CI 1.29-3.46, sex- and age-adjusted) compared with no problems, yet coexistent symptoms of combined anxiety/depression explained most of the association with sleep problems (fully adjusted HR 1.19, 95% CI 0.66-2.16). The HR of combined difficulties initiating sleep/early morning wakening differed in those with and without anxiety/depression at baseline (P interaction = 0.03); among those without caseness symptoms of anxiety/depression it was 5.58 (95% CI 2.02-15.40), while in those with caseness symptoms of anxiety/depression it was 0.82 (95% CI 0.19-3.44).

Conclusions: Sleep problems are common among Norwegian adolescents. The strong association between sleep problems and subsequent hospitalization for self-harm could mainly be related to coexistent symptoms of anxiety and depression. Prevention of adolescent sleep problems, anxiety and depression should be targeted when seeking to reduce and prevent self-harm.

Keywords: Difficulties initiating sleep, early morning wakening, self-harm, anxiety and depression, cohort study, adolescents

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INTRODUCTION

Self-harm (SH) is one of the most frequent reasons for hospitalization in people under 30 years of age¹ and is the strongest risk factor for suicide.² Approximately 7% of those hospitalized following non-fatal SH die by suicide over the following nine years or longer.³

The etiology of SH is complex.⁴⁻⁶ Its incidence peaks at age 15-24 and occurs more frequently in females than males. Data from the UK indicate an annual incidence of hospital presentation following self-harm in 15- to 24-year-olds of 0.3% for males and 0.7% for females⁷; figures from a cohort study of 14- to 19-year-old Norwegian high school students indicates that the 5-year incidence of suicide attempts was 3.2% (0.6% per year).⁸ The literature is difficult to interpret, as many cases of self-harm do not present to medical services, and of those cases that do, many are not admitted to a hospital bed. Key risk factors for SH include depression symptoms and other psychiatric disorders,^{9,10} drug/alcohol misuse,⁵ stressful life events,^{11,12} and socioeconomic disadvantages.⁹ There is growing interest in the role sleep disturbance may play both in the etiology of psychiatric disorders and in suicidal behavior.¹³ Sleep difficulties have been reported as being associated with a twofold increased

risk of depression,^{14,15} and a range of other psychiatric disorders including anxiety, addictions, and psychosis. Moreover, the trans-diagnostic nature of sleep disturbances and emotional dysregulation in the etiology and maintenance of symptoms and functional disabilities of several psychiatric disorders have been emphasized.¹⁶⁻¹⁸ In keeping with this a growing body of literature has indicated that disturbed sleep is associated with an increased risk of suicidal thoughts, SH, and suicide¹⁹⁻²²; yet these symptoms still remain among the least explored in this field.

Problems such as difficulties initiating sleep and/or early morning wakening, as well as irregular sleep schedules (especially between schooldays and weekends) and daytime sleepiness are often reported among adolescents.²⁰ Poor sleep in adolescence is linked to several unfavorable outcomes, such as cognitive and behavioral deficits, increased risk of obesity, depressed mood, depressive symptoms, and decreased self-esteem.^{20,23} Furthermore, sleep problems in early childhood have been associated with early onset of alcohol and other substance misuse,²⁰ both of which are associated with an increased risk of SH and suicide.⁹

Large population-based prospective studies investigating the association between sleep problems in adolescence and adolescent SH and/or suicidal behavior are rare, and outcomes are typically based on self-report. Studies from US and Norway have suggested substantial associations between sleep problems and subsequent suicidal thoughts and attempts in adolescence and young adulthood.^{21,24-26} However, the results from these studies were based on interview/self-report registered SH, and it is difficult to evaluate whether these results also are valid for more severe (i.e., hospital presenting) SH.

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In the current study, we examined the association between self-reported sleep problems in almost 9,000 adolescents and the risk of hospitalization following SH in the subsequent 15 years.

METHOD

Study Population and Setting

In 1995-97, all 10,202 adolescents aged 13 to 19 years in Nord-Trøndelag County, Norway, were invited to take part in the Young-HUNT 1 Study (www.ntnu.edu/hunt). Altogether, 8,983 participants (88%) completed the questionnaire used for this study, and 8,439 participants (83%) completed the questionnaire and the health examination.

The questionnaires were administered to all pupils by teachers at each school and completed during school time in about 45 minutes. Invitees missing from school on the day of Young-HUNT were all invited to participate when they returned to school. Those 285 not attending regular school (i.e., home-schooling, dropouts), were sent the questionnaires by regular mail for completion at home. The questionnaires included 114 and 125 items in total for participants in middle or secondary school, respectively. Questionnaire items covered physical and mental health, physical activity, quality of life, pubertal staging, eating disorders and psychosomatic disorders, tobacco and alcohol habits and reading/writing difficulties. All instruments are available in full text on <http://www.ntnu.edu/hunt/data/que>. After completing the questionnaire, participants attended a clinical examination, performed by especially trained nurses. Overall, 89% of all 13- to 19-year-olds in Nord-Trøndelag County attended the study. Non-responders were mainly those who were absent from school that day.

All participants gave their written informed consent to use the data for medical research. Parental consent was also obtained for participants under 16 years of age.

Outcome: Hospital Admissions Due to SH (1995-2010)

Any SH episode that required hospitalization was registered in this study. A list with all acute admissions for all persons within the age group eligible for Young-HUNT 1 from January 1, 1995, to December 31, 2010, was generated from the patient administrative system (PAS) at Levanger and Namsos hospitals, the two hospitals serving the catchment area for Young-HUNT 1.

Each admission is recorded on the PAS file by means of ICD diagnosis codes and a free text field completed by the nurse in the emergency unit describing how the patient presents at admission (e.g. "chest pain," "fever and vomiting," "intoxication," "suicide attempt"). We created a list of search terms/criteria based on other studies²⁷⁻²⁹ and our clinical knowledge of possible reasons, symptoms, and mechanisms associated with SH. To identify the index episode of all SH admissions, the first author (AJ) and 3 specially trained nurses searched the PAS file for relevant text strings and ICD-codes (see Appendix), and reviewed the patient records for search-positive SH cases. SH has been defined as intentional self-poisoning or self-injury, irrespective of type of motive or the extent of suicidal intent.³⁰ We used the same definition and included all hospital-admitted SH cases. We found that 98 persons from the Young-HUNT 1

cohort had subsequently been admitted to hospital following SH. We recorded data on date and time of SH, SH method(s), what kind of psychiatric care the patient received or was offered, somatic or psychiatric comorbidity, and possible subsequent admissions due to SH. These data were merged with the baseline Young-HUNT data by a technician at the HUNT Research Centre and anonymized before they were delivered to the research group.

Exposure: Sleep Problems in Young-HUNT 1 (1995-97)

Sleep problems were assessed with 2 main items in the Young-HUNT questionnaire—one addressing difficulties initiating sleep: "*In the last month, have you had difficulties falling asleep?*" and one addressing early morning waking: "*In the last month, have you woken up too early and not been able to fall asleep again?*" There were 4 response options to these items: never/occasionally/often/almost every night. We dichotomized each of these items, so 0 answered to responses never/occasionally, and 1 to responses often/almost every night. Based on these 2 single sleep problem items, we created 2 new variables (difficulties initiating sleep and/or early morning waking, and combined difficulties initiating sleep and early morning waking). Analyses were performed with each single item separately and the combinations of the two.

One to two percent of the Young-HUNT participants had missing data on the first, the second, or both original sleep questionnaire items, respectively.

Covariates

We investigated the impact on sleep-SH associations of the following factors measured at baseline.

- a. Symptoms of combined anxiety and depression during the last 2 weeks were assessed with a short, 5-item version of the Hopkins Symptom Checklist (SCL-5).^{31,32} The questions are *In the last 14 days, have you...*
 1. *been constantly afraid and anxious?*
 2. *felt tense or uneasy?*
 3. *felt hopelessness when you think of the future?*
 4. *felt dejected or sad?*
 5. *worried too much about various things?*Each question had 4 response options, from "not bothered" to "very much bothered." An average scale score ranging from 1 to 4 was calculated, and a cutoff value > 2 was set to indicate caseness of symptoms of anxiety and depression.³²
- b. Body mass index (BMI; weight/height²) was calculated from height and weight measurements recorded by a specially trained nurse. We calculated age- and sex-specific Z-scores (number of standard deviations above or below the mean BMI for the group) and used BMI Z-score as a continuous variable.
- c. Somatic illnesses (diagnosed asthma, epilepsy, diabetes, migraine, pulmonary disease, and other diseases lasting > 3 months) were dichotomized into having none/having one or more somatic illnesses.
- d. Symptoms of
 1. pain
 2. gastrointestinal disturbance
 3. heart palpitations

- e. Smoking status was categorized as nonsmoker/smoker (those who reported daily or occasional cigarette smoking).
- f. Alcohol use was categorized as having felt drunk > 10 times, or not/less.

Statistics

We analyzed the data using Cox proportional hazard regression with age as the time axis, using STATA version 12 (www.stata.com). The follow-up period ranged from the date each person completed the Young-HUNT survey and to the date when they moved out of the county (county-based registers), died, experienced their first hospital admission for SH, or until December 31, 2010—whichever occurred first. On average, follow-up time was 11.9 years.

At first (Model 1), we investigated the association of (a) difficulties initiating sleep, (b) early morning waking, (c) difficulties initiating sleep and/or early morning waking, and (d) difficulties initiating sleep and early morning waking with SH, adjusting for age and sex. In Model 2, we adjusted for the possible confounding effect of somatic illnesses and BMI. In Model 3, we also adjusted for the possible mediating or confounding effect of different psychosomatic symptoms during the last year, presence of baseline symptoms of combined anxiety and depression, smoking, and alcohol use—variables that both could be causing sleeping problems but also could be caused by sleeping problems. Hazard ratios (HR) were reported with 95% confidence intervals (95% CI). We found no indications of violation of the proportional hazards assumptions on the basis of Schoenfeld residuals.

We carried out tests for effect measure modification to investigate whether the impact of sleeping problems on SH differed in males versus females, and in those with and without caseness symptoms of anxiety and depression.

RESULTS

Characteristics of the study population are shown in Table 1. Approximately equal numbers of males and females participated in Young-HUNT, and the mean age of participants at baseline was 16 years for both genders.

Sleep problems were relatively common; 10% reported difficulties initiating sleep, and 4% reported early morning waking often or almost every night. Two percent reported both difficulties initiating sleep and early morning waking often or almost every night. The prevalence of difficulties initiating sleep (23%) and early morning waking (8%) among SH patients was twice as high as in the overall study group. Altogether, 175 (2%) participants had both difficulties initiating sleep and early morning waking; 7 (4%) of this group self-harmed.

Sleep problems were more common among participants with caseness symptoms of anxiety/depression and who reported lifetime suicidal thoughts, versus similar participants not reporting suicidal thoughts. For difficulties initiating sleep, the prevalence was 111 (40%) versus 69 (25%), for early morning waking 52 (44%) versus 20 (17%), and for both of these sleep problems combined 36 (48%) versus 15 (20%).

Baseline mean scores for caseness symptoms of combined anxiety and depression (SCL-5) were 1.9 (SD 0.8) and 1.5

Table 1—Descriptive baseline characteristics of the study population

	Total cohort	
	SH	Non-SH
Sex, N (%)		
Men	26 (27)	4,494 (51)
Women	72 (73)	4,391 (49)
Age, mean (SD)	16.0 (1.8)	16.0 (1.8)
Difficulties initiating sleep, N (%)		
No	75 (76)	7,870 (89)
Yes	22 (23)	877 (10)
Missing	1 (1)	138 (1)
Early morning waking, N (%)		
No	85 (87)	8,305 (93)
Yes	8 (8)	372 (4)
Missing	5 (5)	208 (2)
SCL-5 score, mean (SD)	1.9 (0.8)	1.5 (0.5)
Somatic illnesses, N (%)		
None	75 (76)	7,063 (79)
One or more	23 (24)	1,822 (21)
BMI, mean (SD)	21.8 (3.9)	21.4 (3.3)
Psychosomatic symptoms, mean (SD)		
Pain	1.6 (1.2)	1.0 (1.1)
Gastrointestinal disturbance	0.6 (1.0)	0.3 (0.7)
Heart palpitations	0.1 (0.3)	0.1 (0.2)
Smoking, N (%)		
Non-smoker	57 (58)	7,024 (79)
Smoker (occasionally/daily)	41 (42)	1,861 (21)
Alcohol, N (%)		
Been drunk ≤ 10 times	62 (63)	6,317 (71)
Been drunk > 10 times	36 (37)	2,568 (29)
Total	98	8,885

SH, self-harm; SCL-5, Hopkins Symptom Checklist, 5-item version; BMI, body mass index.

(SD 0.5) for self-harmers and non-self-harmers, respectively. The prevalence of sleep problems at baseline was higher in older than younger participants. Among all participants younger than 16 years, 346 (8%) reported difficulties initiating sleep often or almost every night, 193 (4%) reported early morning waking often or almost every night, and 70 (2%) reported both of these sleep problems combined. The corresponding prevalence among participants aged ≥ 16 years was 553 (13%), 187 (4%), and 108 (3%).

There was a strong association between sleep disturbance and symptoms of combined anxiety and depression at baseline. The odds of having symptoms of combined anxiety and depression above caseness level was 5.4 (95% CI 4.6-6.3) times higher among those having difficulties initiating sleep than those with no problems, and 4.6 (95% CI 3.6-5.8) higher for those troubled by early morning waking compared with those without difficulties.

Sleep and Self-Harm (SH)

Over an average follow-up period of 11.9 years (range 0.02-16.0 years) 98 (1.1%) participants were hospitalized following SH. Twenty-six (27%) were males and 60 (61%) had only one

Table 2—Hazard ratios for self-harm according to baseline adolescent sleeping problems

	N	Model 1		Model 2		Model 3	
		SH	HR 95% CI	HR 95% CI	HR 95% CI	HR 95% CI	
No difficulties initiating sleep	75	1.00	Ref.	1.00	Ref.	1.00	Ref.
Difficulties initiating sleep	22	2.53	(1.53-4.17)	2.43	(1.43-4.12)	1.39	(0.75-2.56)
No early morning waking	85	1.00	Ref.	1.00	Ref.	1.00	Ref.
Early morning waking	8	1.82	(0.84-3.95)	1.65	(0.72-3.81)	1.25	(0.53-2.95)
No difficulties initiating sleep and/or early morning waking	74	1.00	Ref.	1.00	Ref.	1.00	Ref.
Difficulties initiating sleep and/or early morning waking	23	2.11	(1.29-3.46)	2.03	(1.21-3.41)	1.19	(0.66-2.16)
Difficulties initiating sleep and early morning waking	7	3.28	(1.43-7.52)	2.92	(1.18-7.24)	1.93	(0.75-4.99)

Model 1: adjusted for sex, age (time variable) at baseline. Model 2: adjusted for sex, age (time variable) BMI, somatic illnesses at baseline. Model 3: adjusted for sex, age (time variable) BMI, somatic illnesses, psychosomatic symptoms, anxiety and depression, smoking, and alcohol use at baseline. SH, self-harm; HR: hazard ratio.

SH hospitalization, while 38 (39%) were hospitalized twice or more during follow-up. The mean age at time of hospital-presenting SH index episode was 22.7 for males and 20.3 years for females. The most frequently used methods of SH were self-poisoning (n = 80, 82%) and laceration (n = 14, 14%); 8 of these patients used both cutting and self-poisoning in the same episode. The estimated incidence hospitalization for SH per 100,000 person years for the entire follow-up period was 84 (95% CI 67.9-102.8); 121 (95% CI 94.5-154.8) for females, and 48 (95% CI 32.5-70.1) for males.

Table 2 presents hazard ratios (HR) for SH hospitalization according to baseline sleeping problems. The sex and age adjusted (Model 1) HR for the association of difficulties initiating sleep with SH was 2.53 (95% CI 1.53-4.17). Early morning waking was associated with SH, with an adjusted HR of 1.82 (95% CI 0.84-3.95); in those with both difficulties initiating sleep and early morning waking, the HR was 3.28 (95% CI 1.43-7.52). Additional adjustment for BMI and somatic illnesses at baseline (Model 2) somewhat weakened the effect of both difficulties initiating sleep and early morning waking.

In Model 3, the association between difficulties initiating sleep and SH was markedly attenuated when we adjusted for different psychosomatic symptoms, symptoms of combined anxiety and depression, smoking, and alcohol use (fully adjusted HR 1.39, 95% CI 0.75-2.56). The same pattern was seen regarding the association between early morning waking and SH (fully adjusted HR 1.25, 95% CI 0.53-2.95). Most of the attenuation of the sleep-SH association could be explained by adjustment for symptoms of combined anxiety and depression (Model 4, not presented in table). With adjustment for symptoms of combined anxiety and depression only, the HR of SH among those reporting difficulties initiating sleep was 1.66 (95% CI 0.97-2.86) and for those reporting early morning waking it was 1.25 (95% CI 0.57-2.77).

We did not find any indications of effect measure modification by sex either with regard to difficulties initiating sleep (P interaction = 0.3) or early morning waking (P interaction = 0.5). Nor did we find any indications of effect measure modification with sex and (a) difficulties initiating sleep and/or early morning waking (P interaction = 0.4), or (b) combined difficulties initiating sleep and early morning waking

(P interaction = 0.3). Further, we found no evidence of effect measure modification by caseness symptoms of anxiety and depression either with regard to (a) difficulties initiating sleep (P interaction = 0.3), (b) early morning waking (P interaction = 0.2), or (c) difficulties initiating sleep and/or early morning waking (P interaction = 0.5). There was, however, evidence of statistical interaction between caseness symptoms of anxiety and depression and combined difficulties initiating sleep and early morning waking (P interaction = 0.03). The age- and sex-adjusted HR of combined difficulties initiating sleep and early morning waking among those without caseness symptoms of anxiety and depression (n = 175 [2%]) was 5.58 (95% CI 2.02-15.40), while the same association in those with caseness symptoms of anxiety and depression was 0.82 (95% CI 0.19-3.44).

DISCUSSION

Our results indicate that sleeping problems in adolescence, and in particular difficulties initiating sleep, is associated with a more than two-fold elevated risk of subsequent admission to hospital due to SH. However, much of this association was explained by coexisting symptoms of combined anxiety and depression. Even so, it seems that adolescents having combined difficulties initiating sleep and early morning waking, but no symptoms of anxiety and depression, may be at a substantially higher risk of getting hospitalized for SH at a later point in life.

Previous Findings and Possible Mechanisms

Sleep disturbance is acknowledged as an important risk factor for suicidal thoughts and behavior, and, therein, SH.³³ There are few comparable studies, if any, that have reported SH rates using similar inclusion criteria to those we used in the current study. Most previous studies have been based on self-reported self-harm^{8,34} or hospital attendance for self-harm.³⁰ Our incidence estimates are lower than those in these studies as (a) most cases of self-harm do not seek medical help (< 15% in one recent analysis³⁴; figures are likely to be even lower in rural Norway); and (b) many of those cases that do present to hospital are not admitted. As mentioned above, only a few large studies have prospectively examined the sleep-SH association in adolescents/young adults. Two studies were based on the same data material: 6,500 representative American adolescents

followed for six to seven years.^{25,26} Another American study examined 400 adolescents from a community sample of high-risk alcoholic families,²¹ following them for three years, and one Norwegian study analyzed data from 265 adolescents from a representative sample of Norwegian school students, with a follow-up of six years.²⁴ In spite of differences in participant selection, size, and outcome measurements, all four studies reported a positive association of sleep problems with subsequent suicidal ideation and SH. Only one study investigated gender differences in the association of insomnia symptoms with self-harm—this reported that the prevalence rate of insomnia symptoms was significantly related to sex ($P = 0.019$), and that females with insomnia were 2.31 to 5.5 times more likely to have attempted suicide during the past year than were females without insomnia ($P < 0.001$), and that insomnia was not a significant risk factor for males.²⁵ None of the four studies examined possible statistical interaction between symptoms of anxiety/depression and sleep problems, as we have in the current study.

In a cross-sectional study among Chinese adolescents, nightmares were associated with suicidal ideation also after adjusting for depression, while symptoms of insomnia were not.³⁵ A review combining data from adults and adolescents also indicated a close association between nightmares and suicide risk¹⁹ but underscored that the mechanisms linking insomnia and suicidality remain unclear. In addition, insomnia was, in a study of American adolescents, reported to be more common in depressed suicidal youths than in depressed non-suicidal youths,³⁶ which is in line with results found in the current study.

Previous studies emphasize sleep problems as a risk factor for SH,^{19,21} and several mechanisms have been suggested. Poor sleep is associated with depressed mood, depressive symptoms and low self-esteem,³⁷ which are all linked to SH behavior. Sleep disturbance may also impair cognitive judgement and impulse control, possibly leading to increased impulsiveness and increased risk of SH.^{38,39} Low serotonin function seems to be a vulnerability among female adolescents for engaging in SH due to an impulsive response style when in emotional distress.⁴⁰

In the current study, adjustment for symptoms of combined anxiety and depression attenuated the sleep-SH associations markedly, which indicate that this might be the key pathway determining risk. The measures of sleep disturbance and mental health were recorded at the same time, which makes it difficult to determine whether sleep problems led to raised SCL-5 scores or vice versa, or whether the sleep disturbance was simply a feature of preexisting mental illness. A bidirectional relationship between sleep and anxiety and depression is likely.⁴¹ It is also possible that poor sleep and sleep problems may increase the influence from other risk factors on self-harm and self-harm behavior. However, we did not find statistical evidence for an effect measure modification between anxiety and depression symptoms and difficulties initiating sleep and/or early morning wakening. In sub-analyses among those without symptoms of anxiety and depression, results revealed a substantial association of problems in both initiating sleep and early morning wakening with risk for hospital admission for SH. This observation could indicate that having serious sleep problems in adolescence might be an early prospective marker of subsequent development of mental health problems (especially

anxiety/depression), which is in line with previously proposed mechanisms.^{25,42}

Strengths and Limitations

This is, to our best knowledge, the first study linking a large population-based cohort sample to hospital admissions due to SH in adolescents and young adults. The main strengths of this study are the prospective design, long follow-up time, large sample size, and validated clinical outcome measurements. Most previous studies have relied on self-reported SH behaviors. There are, however, also limitations to this study. Sleeping problems were only measured once (at baseline), yet these symptoms might have fluctuated considerably during the follow-up period. In addition, problems of nocturnal awakenings may have been underestimated due to the wording in the questionnaire item assessing early morning wakening. In our study, 10% reported difficulties initiating sleep, while 4% reported early morning wakening. The difference between those reporting difficulties initiating sleep versus early morning wakening may be dependent on the definition of sleep maintenance problems, which include early morning wakening, but not nocturnal awakenings within sleep period time. Examples of previous research have reported rates of 10.8% versus 6.3% for sleep initiation⁴³ and 12.4% versus 9.2% for sleep maintenance,⁴⁴ respectively. Further, our analysis was restricted to hospital admitted SH patients, and results cannot be generalized to other and milder forms of SH, not leading to hospitalization. Since we used local hospital records, people who emigrated out of the catchment area and were hospitalized in other parts of Norway were lost to follow-up.

CONCLUSION

Sleeping problems were highly prevalent among adolescents in the general population in Norway and were associated with a twofold increased risk of subsequent severe SH requiring hospitalization. Most of the association between sleep problems and SH could be explained by coexisting symptoms of combined anxiety and depression. Sleeping problems, anxiety, and depression are all possible modifiable risk factors, yet often tend to a chronic course when left untreated. Therefore, special attention should be given to these symptoms in prevention and treatment programmes among adolescents, both online services and school-based programs should be offered. Still, more research—in the form of large, prospective studies with repeated measures of sleep disturbance and mood—is warranted to further understand the underlying mechanisms and causal pathways between sleep problems and SH.

ABBREVIATIONS

- BMI, body mass index
- CI, confidence interval
- HR, hazard ratio
- HUNT, The Nord-Trøndelag Health Study
- ICD, International Classification of Diseases
- NIHR, National Institute for Health Research
- PAS, patient administrative system
- SCL-5, Hopkins Symptom Checklist, 5-item version
- SD, standard deviation
- SH, self-harm

UK, United Kingdom
 US, United States of America
 Young-HUNT, the adolescent part of HUNT including participants aged 13-19 years.

APPENDIX

Free text search criteria and terms used for case identification from PAS (translated from Norwegian)

- | | | |
|----------------|--------------|---------------|
| • accident | • firearm | • poison |
| • acid | • gas | • psych |
| • affect | • gun | • razor blade |
| • alcohol | • hang | • rope |
| • anxiety | • high | • self |
| • attempt | • i*x | • self-harm |
| • bleed | • impuls | • shoot |
| • burn | • inhal | • slash |
| • car | • innhal | • slit |
| • carbondiox | • intoks | • stab |
| • cut | • intox | • strangul |
| • deliberate | • jump | • suicid |
| • depr | • knife | • swallow |
| • drain opener | • mc | • tabl |
| • drown | • medicament | • tbl |
| • etch | • moped | • traffic |
| • exit road | • motorcycle | • transfusion |
| • fall | • overdose | • unconc |
| • fire | • pills | |

Codes used for case identification from PAS

ICD-9

- E850 - E869; Accidental poisoning by drugs, medical substances, and biologicals
- E950 - E959; Suicide and self-inflicted injury
- E980 - E989; Injury undetermined whether accidentally or purposely inflicted

ICD-10

- X40 - X49; Accidental poisoning by and exposure to noxious substances
- X60 - X84; Intentional self-harm
- Y10 - Y34; Event of undetermined intent
- Y87.0 and Y87.2; Sequelae of intentional self-harm, and of undetermined event
- Y90 - Y91; Evidence of alcohol involvement determined by blood alcohol level, and level of intoxication
- Z72.8; Problems related to lifestyle, self-damaging behavior
- Z91.5; Personal history of risk factors, history of self-harm

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REFERENCES

1. Gunnell DJ, Brooks J, Peters TJ. Epidemiology and patterns of hospital use after parasuicide in the south west of England. *J Epidemiol Community Health* 1996;50:24-9.
2. Hawton K, van Heeringen K. Suicide. *Lancet* 2009;373:1372-81.
3. Owens D, Horrocks J, House A. Fatal and non-fatal repetition of self-harm. Systematic review. *Br J Psychiatry* 2002;181:193-9.
4. Nock MK. Self-injury. *Annu Rev Clin Psychol* 2010;6:339-63.
5. Hawton K, James A. Suicide and deliberate self harm in young people. *BMJ* 2005;330:891-4.
6. Hawton K, Saunders KE, O'Connor RC. Self-harm and suicide in adolescents. *Lancet* 2012;379:2373-82.
7. Hawton K, Harriss L, Hall S, Simkin S, Bale E, Bond A. Deliberate self-harm in Oxford, 1990-2000: a time of change in patient characteristics. *Psychol Med* 2003;33:987-95.
8. Wichstrom L. Predictors of non-suicidal self-injury versus attempted suicide: similar or different? *Arch Suicide Res* 2009;13:105-22.
9. Skegg K. Self-harm. *Lancet* 2005;366:1471-83.
10. Moran P, Coffey C, Romaniuk H, et al. The natural history of self-harm from adolescence to young adulthood: a population-based cohort study. *Lancet* 2012;379:236-43.
11. de Wilde EJ, Kienhorst IC, Diekstra RF, Wolters WH. The relationship between adolescent suicidal behavior and life events in childhood and adolescence. *Am J Psychiatry* 1992;149:45-51.
12. Madge N, Hawton K, McMahon EM, et al. Psychological characteristics, stressful life events and deliberate self-harm: findings from the Child & Adolescent Self-harm in Europe (CASE) Study. *Eur Child Adolesc Psychiatry* 2011;20:499-508.
13. McCall WV. Insomnia is a risk factor for suicide-what are the next steps? *Sleep* 2011;34:1149-50.
14. Riemann D, Voderholzer U. Primary insomnia: a risk factor to develop depression? *J Affect Disord* 2003;76:255-9.
15. Baglioni C, Battagliese G, Feige B, et al. Insomnia as a predictor of depression: a meta-analytic evaluation of longitudinal epidemiological studies. *J Affect Disord* 2011;135:10-9.
16. Harvey AG, Murray G, Chandler RA, Soehner A. Sleep disturbance as transdiagnostic: consideration of neurobiological mechanisms. *Clin Psychol Rev* 2011;31:225-35.
17. Fairholme CP, Nosen EL, Nillni YI, Schumacher JA, Tull MT, Coffey SF. Sleep disturbance and emotion dysregulation as transdiagnostic processes in a comorbid sample. *Behav Res Ther* 2013;51:540-6.
18. Talbot LS, Stone S, Gruber J, Hairston IS, Eidelman P, Harvey AG. A test of the bidirectional association between sleep and mood in bipolar disorder and insomnia. *J Abnorm Psychol* 2012;121:39-50.
19. Bernert RA, Joiner TE. Sleep disturbances and suicide risk: A review of the literature. *Neuropsychiatr Dis Treat* 2007;3:735-43.
20. Liu X, Buysse DJ. Sleep and youth suicidal behavior: a neglected field. *Curr Opin Psychiatry* 2006;19:288-93.
21. Wong MM, Brower KJ, Zucker RA. Sleep problems, suicidal ideation, and self-harm behaviors in adolescence. *J Psychiatr Res* 2011;45:505-11.
22. Bjorgaard JH, Bjerkeset O, Romundstad P, Gunnell D. Sleeping problems and suicide in 75,000 Norwegian adults: a 20 year follow-up of the HUNT I study. *Sleep* 2011;34:1155-9.
23. Nielsen LS, Danielsen KV, Sorensen TI. Short sleep duration as a possible cause of obesity: critical analysis of the epidemiological evidence. *Obes Rev* 2011;12:78-92.
24. Nruham L, Larsson B, Sund AM. Specific depressive symptoms and disorders as associates and predictors of suicidal acts across adolescence. *J Affect Disord* 2008;111:83-93.
25. Roane BM, Taylor DJ. Adolescent insomnia as a risk factor for early adult depression and substance abuse. *Sleep* 2008;31:1351-6.

26. Wong MM, Brower KJ. The prospective relationship between sleep problems and suicidal behavior in the National Longitudinal Study of Adolescent Health. *J Psychiatr Res* 2012;46:953-9.
27. Evans J, Johnson C, Stanton R, Morgan HG. How to establish case registers: II. Non-fatal deliberate self-harm. *Psychiatr Bull* 1996;20:403-5.
28. Horrocks J, House A, Owens D. Establishing a clinical database for hospital attendances because of self-harm. *Psychiatric Bulletin* 2004;28:137-9.
29. Carroll R, Gunnell D. Annual report 2011 - Bristol Self-Harm Surveillance Register: University of Bristol, 2011.
30. Hawton K, Hall S, Simkin S, et al. Deliberate self-harm in adolescents: a study of characteristics and trends in Oxford, 1990-2000. *J Child Psychol Psychiatry* 2003;44:1191-8.
31. Tambs K, Mowm T. How well can a few questionnaire items indicate anxiety and depression? *Acta Psychiatr Scand* 1993;87:364-7.
32. Strand BH, Dalgard OS, Tambs K, Rognerud M. Measuring the mental health status of the Norwegian population: a comparison of the instruments SCL-25, SCL-10, SCL-5 and MHI-5 (SF-36). *Nordic J Psychiatry* 2003;57:113-8.
33. Pigeon WR, Pinquart M, Conner K. Meta-analysis of sleep disturbance and suicidal thoughts and behaviors. *J Clin Psychiatry* 2012;73:e1160-7.
34. Kidger J, Heron J, Lewis G, Evans J, Gunnell D. Adolescent self-harm and suicidal thoughts in the ALSPAC cohort: a self-report survey in England. *BMC Psychiatry* 2012;12:69.
35. Liu X. Sleep and adolescent suicidal behavior. *Sleep* 2004;27:1351-8.
36. Barbe RP, Williamson DE, Bridge JA, et al. Clinical differences between suicidal and nonsuicidal depressed children and adolescents. *J Clin Psychiatry* 2005;66:492-8.
37. Fredriksen K, Rhodes J, Reddy R, Way N. Sleepless in Chicago: tracking the effects of adolescent sleep loss during the middle school years. *Child Dev* 2004;75:84-95.
38. Conner KR, Meldrum S, Wieczorek WF, Duberstein PR, Welte JW. The association of irritability and impulsivity with suicidal ideation among 15- to 20-year-old males. *Suicide Life Threat Behav* 2004;34:363-73.
39. Evans J, Reeves B, Platt H, et al. Impulsiveness, serotonin genes and repetition of deliberate self-harm (DSH). *Psychol Med* 2000;30:1327-34.
40. Fikke LT, Melinder A, Landro NI. The effects of acute tryptophan depletion on impulsivity and mood in adolescents engaging in non-suicidal self-injury. *Hum Psychopharmacol* 2013;28:61-71.
41. Gregory AM, Sadeh A. Sleep, emotional and behavioral difficulties in children and adolescents. *Sleep Med Rev* 2012;16:129-36.
42. Roberts RE, Roberts CR, Chen IG. Impact of insomnia on future functioning of adolescents. *J Psychosom Res* 2002;53:561-9.
43. Liu X, Uchiyama M, Okawa M, Kurita H. Prevalence and correlates of self-reported sleep problems among Chinese adolescents. *Sleep* 2000;23:27-34.
44. Ohayon MM, Roberts RE, Zully J, Smirne S, Priest RG. Prevalence and patterns of problematic sleep among older adolescents. *J Am Acad Child Adolesc Psychiatry* 2000;39:1549-56.

Paper II

RESEARCH ARTICLE

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Adolescent health and subsequent risk of self-harm hospitalisation: a 15-year follow-up of the Young-HUNT cohort

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Abstract

Background: Self-harm is associated with increased suicide risk, and constitutes a major challenge in adolescent mental healthcare. In the current study, we examined the association between different aspects of adolescent health and risk of later self-harm requiring hospital admission.

Methods: We linked baseline information from 13 to 19 year old participants (n = 8965) in the Norwegian Young-HUNT 1 study to patient records of self-harm hospitalisation during 15 years of follow-up. We used Cox regression to estimate risk factor hazard ratios (HR).

Results: Eighty-nine persons (71% female) were admitted to hospital because of self-harm. Intoxication/self-poisoning was the most frequent method (81%). Both mental (anxiety/depression, loneliness, being bullied) and somatic (epilepsy, migraine) health issues were associated with up to fourfold increased risk of self-harm-related hospital admission.

Conclusions: Several health issues during adolescence markedly increased the risk of later self-harm hospitalisation. Current findings should be incorporated in the strive to reduce self-harming and attempted suicides among young people.

Keywords: Self-harm, Hospitalisation, Adolescence

Background

Self-harm behaviours constitute a large health burden, both in terms of health service utilization costs [1], and of increased morbidity and mortality, particularly from suicide [2]. It has been defined as any intentional self-poisoning or self-injury, irrespective of motivation or suicidal intent [3]. The etiology of self-harm is complex [4, 5], and its incidence peaks between 15 and 24 years, occurring most frequently in females [6, 7]. Anxiety and depression are strong risk factors for self-harm behaviour [5, 8]. Further, both internalizing and externalizing disorders and substance use disorders are commonly found comorbidities to self-harm [9]. Also, there is evidence to suggest an association between self-harm risk and drug/

alcohol misuse, stressful life events, and socioeconomic disadvantages [5, 8]. Sleep problems have been associated with self-harm in two Norwegian studies [10, 11]. Motivations for self-harm, and associated predictors are overlapping in different sub-populations and the general population, albeit with some differences. For example, among adolescents in the juvenile justice system, externalising disorders and substance use or disorder appear to have limited predictive value [12], perhaps because these conditions are highly prevalent in this population. Patients with psychiatric illness as a group [13], and those with borderline personality disorder in particular [14, 15], are at increased risk of self-harm. There is also emerging evidence of increased risk in relation to autism spectrum disorder in adults [16]. The existing literature has mostly addressed relations between poor mental health and risk of self-harm. Even though associations have been reported between self-harm and physical illnesses

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such as epilepsy, migraine, asthma, diabetes and eczema [13], evidence is limited—especially among adolescents and young adults. The majority of psychiatric research, and that of North American origin in particular, has used classification criteria from the Diagnostic and Statistical Manual of Mental Disorders (DSM) [17]. Hence, potential associations between physical illnesses and a range of psychiatric disorders including self-harm might not have been as easily studied and identified, since the DSM is a system for psychiatric disorders only, while the ICD system covers all areas of health.

Unfavorable health conditions in adolescence often present with a wide range of physical and psychological symptoms, and their relations to self-harm have often been studied separately. Additionally, few prospective studies have investigated the extent to which risk factors present in adolescence are associated with the self-harm risk in early adulthood. Most studies are also based on self-reported self-harm; limited by non-response and misreporting, and possible underestimation of self-harm prevalence [18].

With the present study, we sought to fill some of these gaps by investigating associations between several dimensions of self-reported physical and mental health symptoms in a community cohort of almost 9000 adolescents, and the risk of self-harm related hospitalisation during 15 years of follow-up. The outcome ascertainment was based on validated outcome data on self-harm recorded from hospital-based patient records.

As previously defined, we investigated self-harm that resulted in hospital admission, without assessing the presence or degree of suicidal intent. However, research indicates that most people whose self-harm leads to hospitalisation carry out the act with at least some degree of suicidal intent [19, 20].

Methods

Study population and setting

The Young-HUNT 1 Study [21] was conducted in 1995–97, and all 13–19 year old adolescents ($n = 10,202$) in Nord-Trøndelag County, Norway, were invited to participate. The Young-HUNT questionnaire was completed by 8983 participants (88%). A total of 114 and 125 questions/items for middle and secondary school, respectively, covered a wide range of aspects of physical and mental health, quality of life, and lifestyle factors (such as alcohol and tobacco use as well as physical activity). Questionnaires were completed during school time, and although non-present invitees on the day of Young-HUNT were invited to take part in the study when they returned, the latter group covered the bulk of non-responders. Two hundred and eighty-five adolescents not attending regular school were mailed the questionnaires

at home. Especially trained nurses performed a clinical examination after questionnaire completion.

We excluded 18 persons because their respective Young-HUNT participation date occurred after they experienced their first self-harm hospitalisation ($n = 9$), or after the date they were registered as lost to follow-up in Nord-Trøndelag County ($n = 9$).

All participants gave written informed consent for the use of data for medical research (for those <16 years of age, parental consent was also obtained). The study was approved by the Regional Committee for Medical and Health Research Ethics (2010/1924-3).

Outcome: hospital admissions due to self-harm (1995–2010)

The registration of outcome data has been described in more detail previously [10]. We registered all self-harm episodes that required hospitalisation from 1 January 1995 to 31 December 2010, based on a list of all acute admissions for persons eligible for Young-HUNT 1, at the two hospitals serving the catchment area for the study. The list contained both ICD diagnostic codes and a free text field with the nurses' description of the reason for admission. We searched this free text field for terms and criteria associated with self-harm ([10], see Appendix). All search-positive patient records were inspected thoroughly, to include or exclude the event as a self-harm episode. Accidental self-harm and events resulting in bodily damage, but without evidence of such an intention, were excluded from further analyses. Examples would include cutting accidents in the kitchen, injuries from sports and games, or the unintended alcohol intoxication at a party. In confirmed self-harm events, we recorded a range of relevant information from patient records, such as date and time for the first self-harm related hospital admission, method(s) used to self-harm, mental and psychiatric comorbidities. The recorded outcome data was merged to the same persons' baseline data from Young-HUNT by a research technician at HUNT Research Centre, anonymized and returned to the principal investigator (AJ).

Exposures in Young-HUNT 1 (1995–97)

We included variables from the Young-HUNT 1 questionnaire based on established or proposed associations to self-harm and suicide attempts. Loneliness and being bullied are often accompanied by anxiety and depression, which again may present as psychosomatic symptoms like headache or stomach pain. The burden of various somatic illnesses increases with age, and are known to increase self-harm risk among seniors. We included some somatic illnesses in adolescence to see how this affected the risk of self-harm hospitalisation.

Symptoms of anxiety and depression during the last two weeks were assessed with a five-item version of the Hopkins Symptom Checklist (SCL-5) [22]; “In the last 14 days, have you...”: 1... been constantly afraid and anxious? 2... felt tense or uneasy? 3... felt hopelessness when you think of the future? 4... felt dejected or sad? 5... worried too much about various things? All items had four response options, which we grouped as “not at all/a little” (scored as zero) and “quite a bit/very” (scored as one). We calculated an average scale score ranging from one to four, created a dummy variable where average SCL-5 value >2.00 indicated high mental distress (caseness level), and used single items and the dichotomized SCL-5 variable in the different Cox analyses. Average SCL-5 value variable was analysed for trend measure.

Loneliness was assessed with the item “Do you feel lonely?” Five response options from “very often” to “seldom or never” were dichotomized into “very often/often”, and the remaining options.

Bullying was assessed with one of several items regarding school events, originating from a Norwegian Institute of Public Health survey on child sexual abuse [23]; “Does it happen or has it previously happened at school: you are teased/harassed by other students”. Four response options ranging from “never” to “very often” were dichotomized into “never/sometimes” and “often/very often”.

Two items assessing each of the somatic symptoms stomach pain and headache during the last 12 months (without known medical reason) had four response options that we dichotomized into “never/seldom”, and “sometimes/often” for both symptom items.

Body mass index ($\text{weight}/\text{height}^2$) was calculated from height and weight measurements recorded by a specially trained nurse. We categorized each participant’s body mass index into underweight (BMI <18.5), normal weight (BMI $18.5\text{--}25$), overweight (BMI $25\text{--}30$) or obesity (BMI >30), based on international age-and-gender specific cut-off values [24, 25].

Somatic illnesses included five binary variables (yes/no); epilepsy, migraine, asthma, allergy, and ever having had intermittent skin rashes for at least 6 months. The questions assessing asthma, allergy and skin rash were adapted from the ISAAC core questionnaire [26].

Smoking status was categorized as non-smoker/smoker (those who reported daily or occasional cigarette smoking).

Alcohol use was categorized in keeping with previous studies on this cohort [27] as having felt drunk >10 times during their lives, or not/less.

Covariates

Self-harm incidence differs between age groups and genders. Parental conflict, and an unstable family situation

may adversely affect the health and wellbeing in children and adolescents, and increase mental distress. Socioeconomic status is another factor well-known for influencing various aspects and outcomes regarding health. To control for potential confounding by these factors, we used information on age and gender of participants, parental cohabitation situation (whether the participants lived together with non-divorced mother and father, or not) and socioeconomic status (highest educational level for mother or father or both—categorized as primary, intermediate or tertiary. Data on parental educational level were obtained from a national database held by Statistics Norway (SSB) [28], after the end of the follow-up period. Parental educational level refers to parents’ highest education on 1 October the year the offspring turns 16 years old.

Statistics

With attained age as the time axis, we applied Cox proportional hazard regression analyses, using STATA version 12 for Mac [29]. We performed person-based analyses where the follow-up period covered the time between each participant’s survey completion date and the date when they moved out of the county, died, experienced their first self-harm related hospital admission, or until 31 December 2010—whichever occurred first.

First, we investigated the association of baseline score on (a) caseness symptoms of anxiety and depression (mean SCL-5 score >2.00), (b) each single SCL-5 item, (c) loneliness, (d) bullying, (e) stomach pain, (f) headache, (g) epilepsy, (h) migraine, (i) asthma, (j) allergy, (k) skin rashes, (l) smoking, (m) alcohol use and (n) body mass index with subsequent hospitalisation for self-harm. Each variable was analysed only adjusting for age (as time axis). Analyses were then repeated, adjusted for gender, age, cohabitation situation and socioeconomic status. Hazard ratios (HR) were reported with 95% confidence intervals (95% CI). We used the Schoenfeld residuals test to test the proportional hazard assumption in the Cox analysis [30]. Based on Schoenfeld residuals, we found no indications of violation of this assumption. In order to assess possible reverse causality, we did an additional analysis removing the first 5 months of follow up. We investigated the possibility of statistical interaction between gender and the included health measures, and tested for effect measure modification to see whether an effect measure of a certain variable on self-harm hospitalisation risk was different in males and females. In addition, we examined whether age modified the effect of smoking and alcohol on self-harm risk, by testing for effect measure modification when participants were categorised in middle school (13–16 years old) and secondary school (16–19 years old). Using the STATA add

on package—punafcc—[31], we calculated individual population attributable fractions (PAF) for the variables assumed most plausible to have a causal effect on self-harm hospitalisation risk. PAF is an estimate of a specific risk factor's contribution to the disease burden in a population; how large the reduction in disease or mortality would be if exposure to a risk factor was reduced to a defined, lower level. In the current study setting, PAF would translate to: how many self-harm hospitalisations would be prevented if none of the participants experienced caseness symptoms of anxiety and depression? We chose not to estimate PAFs for factors where direct causality is unlikely (smoking, body mass index), or where an exposure reduction is impossible or difficult to obtain (gender, age, socioeconomic status).

Results

In this cohort of 8965 adolescents, 4451 (49.7%) were female, and mean age at baseline was 16 years for both genders. Baseline characteristics of the study population are presented in Table 1.

Over the follow-up period 3813 participants (42.5%) emigrated out of the study region. Those lost to follow-up in this way were broadly similar to those who remained; e.g. caseness anxiety and depression was 10.2% in those moving and 9.6% in those who remained in Nord-Trøndelag. However, those who migrated tended to have a less well-educated parents (11.7% primary education) compared to those who remained (4.4% primary education).

Average follow-up period was 11.9 years (range 0.02–16.0 years), during this period 89 (1.0%) participants were hospitalised after a self-harm episode in one of the two County Hospitals. Twenty-six (29%) were males, 54 (61%) experienced only one self-harm hospitalisation, and the remaining patients ($n = 35$) were admitted to hospital after self-harm more than once during follow-up. Mean age at self-harm index episode was 22.6 for males and 20.9 years for females. Self-poisoning ($n = 72$, 81%) and laceration ($n = 13$, 15%) were the most frequently used self-harm methods; eight of these patients both cut and intoxicated themselves in the same episode. The estimated incidence rate of hospitalisation for self-harm for the entire follow-up period was 84 per 100,000 person years [95% confidence interval (CI) 67.9–102.8]; 121 per 100,000 person years (95% CI 94.5–154.8) for females, and 48 per 100,000 person years (95% CI 32.5–70.1) for males.

Among the 89 self-harm patients, $n = 37$ (42%) were under current psychiatric treatment at the time of self-harm index episode. The majority ($n = 22$) were in an outpatient setting, four were admitted to a psychiatric department, and 11 received combined outpatient and inpatient psychiatric treatment. Most patients ($n = 59$)

had not previously been in contact with psychiatric specialist healthcare.

In the self-harm patients under current psychiatric treatment at index episode, mood (affective) disorders (F30–39 in ICD-10) and neurotic, stress-related and somatoform disorders (F40–49) were equally common, found in over 50% ($n = 20$). Second most common was disorders of adult personality and behaviour (F60–69, $n = 13$), followed by mental disorders due to psychoactive substance use (F10–19, $n = 11$). There were no cases of self-harm (independent of psychiatric treatment status) that had a diagnosis of autism spectrum disorder (F84).

Mental health measurements and self-harm hospitalisation

As summarized in Table 2, we found several indicators of psychological distress to be strongly associated with increased risk of self-harm. Frequently feeling tense and uneasy, or afraid and anxious, increased the risk of self-harm hospitalisation over four times. Caseness symptoms of anxiety/depression, often feeling lonely, or being bullied, were also associated with more than three times the self-harm risk compared to less symptoms and psychological distress.

Adjusted population attributable fractions (PAFs) are presented in Table 3. Caseness symptoms of anxiety and depression PAF was 22.4%, with single item PAFs ranging from 10.1 (often afraid) to 18.3% (often tense/uneasy). Being bullied and feeling lonely was associated with approximately the same risk increase, but due to higher prevalence, loneliness PAF was three times the PAF of being bullied.

Physical health problems and self-harm hospitalisation

Diagnosed epilepsy and migraine at baseline increased the self-harm hospitalisation risk almost four, and over two times, respectively. However, these estimates were subject to poor precision due to small number of people in the exposed groups. With regard to psychosomatic symptoms, people reporting frequent stomach pain or headache had twice the risk of self-harm hospitalisation, compared to those experiencing a lesser symptom burden. Stomach pain PAF was 22.8%, and headache PAF was estimated to be 34.6%.

Daily or occasionally smoking was associated with a nearly doubled risk of self-harm hospitalisation. High alcohol consumption resulted in a small risk increase, but the estimate was not precise enough to leave out chance as a possible explanation. Asthma, allergy and skin rashes were not substantially associated with self-harm hospitalisation, neither were underweight or overweight compared to normal-weight. However, obesity increased the risk substantially.

Table 1 Descriptive baseline characteristics of the study population

	Total cohort			
	Self-harm		Non-self-harm	
	N (%)	Mean (SD)	N (%)	Mean (SD)
Gender				
Male	26 (29.2)		4488 (50.6)	
Female	63 (70.8)		4388 (49.4)	
Parental socioeconomic status				
Primary education	9 (10.1)		661 (7.5)	
Secondary education	14 (15.7)		2198 (24.8)	
Tertiary education	66 (74.2)		5997 (67.5)	
Missing	0 (0)		20 (0.2)	
Age (in years)		15.9 (1.9)		16.0 (1.8)
Anxiety and depression (SCL-5)				
SCL-5 score		1.9 (0.8)		1.5 (0.5)
Missing	3 (3.4)		174 (2.0)	
Non-caseness symptom level	58 (65.2)		7845 (88.3)	
Caseness symptom level	28 (31.4)		857 (9.7)	
Missing	3 (3.4)		174 (2.0)	
(SCL-5 single items)				
Not felt constantly afraid and anxious	73 (82.0)		8469 (95.4)	
Felt constantly afraid and anxious	13 (14.6)		233 (2.6)	
Missing	3 (3.4)		174 (2.0)	
Not felt tense or uneasy	64 (71.9)		8223 (92.7)	
Felt tense or uneasy	21 (23.6)		445 (5.0)	
Missing	4 (4.5)		208 (2.4)	
Not felt hopelessness thinking of the future	65 (73.0)		7818 (88.1)	
Felt hopelessness thinking of the future	21 (23.6)		877 (9.9)	
Missing	3 (3.4)		181 (2.0)	
Not felt dejected or sad	67 (75.3)		7954 (89.6)	
Felt dejected or sad	19 (21.3)		691 (7.8)	
Missing	3 (3.4)		231 (2.6)	
Not worried too much about things	62 (69.6)		7703 (86.8)	
Worried too much about things	24 (27.0)		981 (11.0)	
Missing	3 (3.4)		192 (2.2)	
Loneliness				
No	68 (76.4)		8227 (92.7)	
Yes	18 (20.2)		509 (5.7)	
Missing	3 (3.4)		140 (1.6)	
Bullied at school				
No	76 (85.4)		8475 (95.5)	
Yes	6 (6.7)		173 (2.0)	
Missing	7 (7.9)		228 (2.5)	
Body mass index (kg/m ²) ^a				
Underweight (BMI <18.5)	6 (6.7)		401 (4.5)	
Normal-weight (BMI 18.5–25)	59 (66.3)		6485 (73.1)	
Overweight (BMI 25–30)	11 (12.4)		1191 (13.4)	
Obesity (BMI >30)	7 (7.9)		246 (2.8)	
Missing	6 (6.7)		553 (6.2)	
Epilepsy				
No	79 (88.7)		8467 (95.4)	

Table 1 continued

	Total cohort			
	Self-harm		Non-self-harm	
	N (%)	Mean (SD)	N (%)	Mean (SD)
Yes	3 (3.4)		95 (1.1)	
Missing	7 (7.9)		314 (3.5)	
Migraine				
No	76 (85.4)		8313 (93.7)	
Yes	7 (7.9)		302 (3.4)	
Missing	6 (6.7)		261 (2.9)	
Asthma				
No	77 (86.5)		7691 (86.7)	
Yes	12 (13.5)		1044 (11.8)	
Missing	0 (0)		141 (1.6)	
Allergy				
No	65 (73.0)		5863 (66.1)	
Yes	23 (25.9)		2882 (32.5)	
Missing	1 (1.1)		131 (1.5)	
Skin rash				
No	67 (75.3)		6913 (77.9)	
Yes	21 (23.6)		1785 (20.1)	
Missing	1 (1.1)		178 (2.0)	
Stomach pain				
No	52 (58.4)		6818 (76.8)	
Yes	33 (37.1)		1743 (19.6)	
Missing	4 (4.5)		315 (3.6)	
Headache				
No	31 (34.8)		5186 (58.4)	
Yes	55 (61.8)		3474 (39.2)	
Missing	3 (3.4)		216 (2.4)	
Smoking				
Non-smoker	31 (34.8)		3086 (34.8)	
Smoker (occasionally/daily)	36 (40.5)		1859 (20.9)	
Missing	22 (24.7)		3931 (44.3)	
Alcohol				
Been drunk ≤ 10 times	45 (50.6)		4669 (52.6)	
Been drunk >10 times	30 (33.7)		2564 (28.9)	
Missing	14 (15.7)		1643 (18.5)	
Total	89		8876	

Results are reported as numbers and percentages [N (%)] except for the continuous variables where mean and standard deviation [Mean (SD)] is reported
 SCL-5 Hopkins Symptom Checklist, 5-item version

^a Age-and-gender specific body mass index categories based on international cut-off values

Sensitivity analysis

Tests for effect measure modification revealed no statistically significant differences between males and females (all interaction p values >0.05). Nor did we find any evidence of statistically significant age differences with regard to smoking or alcohol use (interaction p values 0.519 and 0.775, respectively). After excluding incident

cases in the first 5 months of follow-up, results were nearly identical to the main results (Table 4).

Discussion

The results from this 15-year follow-up study of 8965 adolescents displayed strong associations between psychological distress and some somatic illnesses and

Table 2 Hazard ratios for self-harm according to indicators of adolescent mental and physical health in the study population (crude and adjusted models)

	No. SH ^a	Crude ^b HR (95% CI)	Adjusted ^c HR (95% CI)
Gender			
Male	24	1.00	1.00
Female	60	2.55 (1.59–4.10)	2.50 (1.56–4.01)
Parental socioeconomic status			
Primary education	8	1.00	1.00
Secondary education	13	0.47 (0.20–1.14)	0.43 (0.18–1.05)
Tertiary education	63	0.83 (0.40–1.73)	0.73 (0.35–1.53)
Cohabitation status			
Parents live together	51	1.00	1.00
Parents separated/divorced	33	2.59 (1.67–4.01)	2.54 (1.63–3.94)
Anxiety/depression (SCL-5)			
SCL-5 mean score	83	2.98 (2.22–4.00)	2.51 (1.84–3.43)
Non-caseness symptoms anxiety/depression	57	1.00	1.00
Caseness symptoms anxiety/depression	26	4.46 (2.80–7.10)	3.52 (2.18–5.67)
(SCL-5 single items)			
Not felt constantly afraid and anxious	72	1.00	1.00
Felt constantly afraid and anxious	11	5.78 (3.06–10.90)	4.21 (2.21–8.02)
Not felt tense or uneasy	63	1.00	1.00
Felt tense or uneasy	19	5.95 (3.56–9.95)	4.75 (2.82–8.01)
Not felt hopelessness when thinking of the future	64	1.00	1.00
Felt hopelessness when thinking of the future	19	2.88 (1.73–4.81)	2.49 (1.49–4.18)
Not felt dejected or sad	66	1.00	1.00
Felt dejected or sad	17	3.21 (1.88–5.47)	2.46 (1.43–4.25)
Not worried too much about various things	61	1.00	1.00
Worried too much about various things	22	3.01 (1.85–4.89)	2.44 (1.49–4.00)
Loneliness			
Sometimes/less seldom	68	1.00	1.00
Very often/often	16	3.99 (2.32–6.89)	3.31 (1.91–5.73)
Bullied at school			
Never/sometimes	75	1.00	1.00
Very often/often	5	3.39 (1.37–8.38)	3.30 (1.33–8.16)
Body mass index (kg/m ²) ^d			
Underweight (BMI <18.5)	5	1.47 (0.59–3.67)	1.46 (0.59–3.65)
Normal-weight (BMI 18.5–25)	56	1.00	1.00
Overweight (BMI 25–30)	11	1.06 (0.56–2.03)	0.99 (0.52–1.89)
Obesity (BMI >30)	7	3.15 (1.44–6.92)	3.06 (1.39–6.73)
Epilepsy			
No	75	1.00	1.00
Yes	3	3.82 (1.21–12.13)	3.97 (1.25–12.63)
Migraine			
No	72	1.00	1.00
Yes	7	2.72 (1.25–5.91)	2.34 (1.08–5.10)
Asthma			
No	73	1.00	1.00
Yes	11	1.13 (0.60–2.12)	1.09 (0.58–2.05)
Allergy			
No	62	1.00	1.00

Table 2 continued

	No. SH ^a	Crude ^b HR (95% CI)	Adjusted ^c HR (95% CI)
Yes	22	0.73 (0.45–1.19)	0.71 (0.43–1.15)
Skin rash			
No	64	1.00	1.00
Yes	20	1.21 (0.73–1.99)	1.04 (0.63–1.73)
Stomach pain			
Seldom/never	47	1.00	1.00
Sometimes/often	33	2.73 (1.75–4.26)	2.23 (1.42–3.52)
Headache			
Seldom/never	29	1.00	1.00
Sometimes/often	52	2.68 (1.70–4.22)	2.17 (1.36–3.46)
Smoking			
Non-smoker	30	1.00	1.00
Smoker (occasionally/daily)	34	2.01 (1.23–3.29)	1.82 (1.11–2.98)
Alcohol			
Been drunk ≤10 times	45	1.00	1.00
Been drunk >10 times	28	1.30 (0.80–2.10)	1.23 (0.76–2.00)

SH self-harm, HR hazard ratio, SCL-5 Hopkins Symptom Checklist, 5-item version

^a Total number of self-harm patients vary due to complete case analyses with varying number of missing observations

^b Adjusted for age (as time axis)

^c Adjusted for age (as time axis), gender, cohabitation situation and socioeconomic status/parental education level at baseline

^d Age-and-gender specific body mass index categories based on international cut-off values

symptoms in adolescence, and subsequent risk of self-harm hospitalisation. Symptoms of anxiety and depression, loneliness and being subject to bullying were all strongly associated with the risk of self-harm hospitalisation. Self-reported stomach pains and headaches were associated with self-harm hospitalisation, as were epilepsy and migraine. Underweight or overweight altered the risk only marginally, but obesity was associated with a substantial risk increase. Smoking and alcohol consumption were also associated with increased risk, yet less than the indicators of mental and physical health. Asthma, allergy and skin rashes were not substantially associated with self-harm hospitalisation.

The incidence rates estimated in our study are lower than might be expected in this age group. A Norwegian study [7] using national patient register data including patients older than 15 years, found an incidence rate for deliberate self-poisonings treated in hospitals at 120 per 100,000 person years, higher among women (144 per 100,000 person years) than men (94 per 100,000 person years). That study was incidence based, which implies that each patient could contribute with repeated hospitalisations, while patients in our study were censored when they experienced their first self-harm related hospitalisation. This could in part explain our lower incidence rates, given that almost 40% of our patients were hospitalized more than once during follow-up, combined with

high repetition rates in this patient group [32]. Perhaps more important, Young-HUNT non-participants are as a group presumably at higher risk of self-harm hospitalisation compared to those who participated. In addition, people are lost to follow-up from the date they move out of Nord-Trøndelag county. Over 42% (n = 3813) moved—and were therefore censored—before 31 December 2010, and may have been hospitalised outside our catchment area.

Strengths and limitations

This is one of the first studies linking a large population-based cohort sample to hospital admissions due to self-harm in adolescents and young adults. The main strengths of this study are the prospective design, long follow-up time, large sample size, and validated clinical outcome measurements, with minimal misclassification. Most previous studies have relied on self-reported self-harm behaviours. Additionally, the Young-HUNT survey makes it possible to investigate and compare the effect of a broad variety of risk factors, among self-harm patients and controls from the same large, representative community population.

There are, however, important limitations to this study. Baseline variables were only measured once, yet some of these might have fluctuated considerably during the 15-year follow-up period. Endpoint-data were

Table 3 Population attributable fractions for self-harm hospitalisation according to indicators of adolescent mental and physical health in the study population

	No. SH ^a	PAF % ^b (95% CI)
Anxiety/depression (SCL-5)		
Caseness symptoms anxiety/depression (SCL-5 single items)	26	22.4 (18.1–26.6)
Felt constantly afraid and anxious	11	10.1 (8.1–12.1)
Felt tense or uneasy	19	18.3 (15.7–20.8)
Felt hopelessness when thinking of the future	19	13.7 (8.8–18.3)
Felt dejected or sad	17	12.2 (7.5–16.6)
Worried too much about various things	22	15.6 (10.1–20.9)
Loneliness		
Very often/often	16	13.3 (10.1–16.4)
Bullied at school		
Very often/often	5	4.4 (2.6–6.1)
Epilepsy		
Yes	3	2.9 (1.8–4.0)
Migraine		
Yes	7	5.1 (2.1–8.0)
Stomach pain		
Sometimes/often	33	22.8 (13.9–30.8)
Headache		
Sometimes/often	52	34.6 (19.2–47.0)

SH self-harm, SCL-5 Hopkins Symptom Checklist, 5-item version

^a Total number of self-harm patients vary due to complete case analyses with varying number of missing observations

^b Adjusted for age (as time axis), gender, cohabitation situation and socioeconomic status/parental education level at baseline

registered by four different persons. Based on measures such as introductory training, a guiding algorithm document and discussing difficult cases with the first author, we expect the inter-rater reliability to be acceptable. Nevertheless, no analyses to quantify the exact value were carried out. Further, our analysis was restricted to self-harm hospitalisation, and results cannot be generalized to other and milder forms of self-harm, not leading to hospitalisation. In addition, our study does not explicitly differentiate non-suicidal self-injury (NSSI) from suicidal self-harm (suicide attempts). Previous studies indicate that a high proportion of people admitted to hospital following self-harm have self-harmed with suicidal intent [20].

Moreover, measures of anxiety and depression were based on self-report in this study, which makes direct comparison of results to studies using diagnostic categories difficult. The other measures of symptoms and health conditions were also based on self-report. A diagnostic screening could, therefore, have provided more valid information. However, given the prospective nature of

our study, it is likely that possible misclassification would be non-differential. Non-differential misclassification would, with some exceptions for categorical exposures, give more conservative estimates.

Although the study was based on a large sample, self-harm hospitalisation is a rare event and only 89 individuals experienced their first self-harm hospitalisation during follow up, limiting our power to detect small, but potentially clinically important associations. We may have missed some participants, for instance due to moving outside Nord-Trøndelag county while studying, and thereby experiencing their first self-harm hospitalisation in other hospitals. Also, in remote, rural areas of Nord-Trøndelag, people may also have sought primary care or no care at all, rather than travelling large distances to receive hospital care. Nevertheless, the positive prediction value is likely to be high based on the rigorous approach of outcome ascertainment. Additionally, premises for valid PAF estimates includes a causal, non-confounded association with the outcome, and this may not be the case for some or all of the associations investigated.

Adolescent mental health

Overall, the majority of previous studies report considerably lower rates of mental disorders and psychological distress in those who self-harm and attempt suicide, than in those who die by suicide [33]. Nevertheless, clinical studies of both adolescents [34] and adults [33] who self-harm and present to the emergency department, confirm that around 90% fulfil the criteria of one or more psychiatric disorder(s), and that about 7 out of 10 patients have an affective disorder.

We found a more than 2.5 times increased risk for self-harm with caseness symptoms of anxiety and depression, yet most admissions (65%) occurred among participants with low or normal anxiety and depression scores, which highlights the dilemma of individual versus population-based approach in self-harm and suicide prevention. Calculated population attributable fraction for caseness anxiety/depression was 22.4%, suggesting a noticeable decrease in self-harm hospitalisation numbers if it was possible to reduce mental distress among adolescents to a minimum. Although anxiety and depression often overlap [35], the role of anxiety in suicidal behaviours remain somewhat unclear. In a case-control study of 129 young people presenting with medically serious suicide attempts [34], anxiety disorders occurred in only a seventh of patients. In contrast, results from the prospective, population based Netherlands Mental Health Survey and Incidence Study, lifetime diagnoses of all anxiety disorders (social phobia, simple phobia, generalized anxiety disorder, panic disorder, agoraphobia,

Table 4 Hazard ratios for self-harm according to indicators of adolescent mental and physical health in the study population (crude and adjusted models)

	No. SH ^a	Crude ^b HR (95% CI)	Adjusted ^c HR (95% CI)
Gender			
Male	24	1.00	1.00
Female	57	2.42 (1.50–3.90)	2.37 (1.47–3.82)
Parental socioeconomic status			
Primary education	7	1.00	1.00
Secondary education	13	0.54 (0.21–1.34)	0.49 (0.20–1.23)
Tertiary education	61	0.91 (0.42–1.99)	0.80 (0.37–1.76)
Cohabitation status			
Parents live together	49	1.00	1.00
Parents separated/divorced	32	2.61 (1.67–4.08)	2.56 (1.63–4.00)
Anxiety/depression (SCL-5)			
SCL-5 mean score	80	2.80 (2.06–3.81)	2.36 (1.71–3.27)
Non-caseness symptoms anxiety/depression	56	1.00	1.00
Caseness symptoms anxiety/depression (SCL-5 single items)	24	4.25 (2.63–6.86)	3.37 (2.06–5.52)
Not felt constantly afraid and anxious	70	1.00	1.00
Felt constantly afraid and anxious	10	5.43 (2.80–10.54)	4.00 (2.04–7.84)
Not felt tense or uneasy	62	1.00	1.00
Felt tense or uneasy	17	5.48 (3.20–9.38)	4.40 (2.55–7.59)
Not felt hopelessness when thinking of the future	63	1.00	1.00
Felt hopelessness when thinking of the future	17	2.65 (1.55–4.53)	2.31 (1.34–3.96)
Not felt dejected or sad	65	1.00	1.00
Felt dejected or sad	15	2.91 (1.55–5.10)	2.25 (1.27–3.99)
Not worried too much about various things	60	1.00	1.00
Worried too much about various things	20	2.80 (1.69–4.65)	2.29 (1.37–3.83)
Loneliness			
Sometimes/less seldom	66	1.00	1.00
Very often/often	15	3.88 (2.22–6.80)	3.24 (1.84–5.70)
Bullied at school			
Never/sometimes	73	1.00	1.00
Very often/often	5	3.45 (1.40–8.55)	3.37 (1.36–8.35)
Body mass index (kg/m ²) ^d			
Underweight (BMI <18.5)	4	1.22 (0.44–3.36)	1.21 (0.44–3.35)
Normal-weight (BMI 18.5–25)	54	1.00	1.00
Overweight (BMI 25–30)	11	1.10 (0.58–2.11)	1.02 (0.53–1.96)
Obesity (BMI >30)	7	3.28 (1.49–7.22)	3.18 (1.45–7.01)
Epilepsy			
No	72	1.00	1.00
Yes	3	3.99 (1.26–12.68)	4.08 (1.28–12.98)
Migraine			
No	69	1.00	1.00
Yes	7	2.85 (1.31–6.19)	2.45 (1.13–5.35)
Asthma			
No	70	1.00	1.00
Yes	11	1.18 (0.62–2.23)	1.13 (0.60–2.14)
Allergy			
No	60	1.00	1.00

Table 4 continued

	No. SH ^a	Crude ^b HR (95% CI)	Adjusted ^c HR (95% CI)
Yes	21	0.73 (0.44–1.20)	0.70 (0.43–1.15)
Skin rash			
No	63	1.00	1.00
Yes	18	1.10 (0.65–1.86)	0.96 (0.57–1.62)
Stomach pain			
Seldom/never	46	1.00	1.00
Sometimes/often	31	2.62 (1.66–4.14)	2.16 (1.36–3.45)
Headache			
Seldom/never	29	1.00	1.00
Sometimes/often	49	2.53 (1.60–4.00)	2.06 (1.29–3.31)
Smoking			
Non-smoker	29	1.00	1.00
Smoker (occasionally/daily)	33	2.08 (1.26–3.43)	1.89 (1.14–3.13)
Alcohol			
Been drunk ≤10 times	45	1.00	1.00
Been drunk >10 times	26	1.28 (0.78–2.10)	1.21 (0.73–2.00)

Excluding self-harm hospitalisations occurring within 5 months after participation in Young-HUNT

SH self-harm, HR hazard ratio, SCL-5 Hopkins Symptom Checklist, 5-item version

^a Total number of self-harm patients vary due to complete case analyses with varying number of missing observations, and start of follow-up postponed 5 months (152 days) from Young-HUNT participation date

^b Adjusted for age (as time axis)

^c Adjusted for age (as time axis), gender, cohabitation situation and socioeconomic status/parental education level at baseline

^d Continuous age- and gender-specific residuals of standard deviation from mean group body mass index

obsessive–compulsive disorder) were associated with suicidal ideation and attempts both at baseline and during follow-up [36].

Our findings (also stemming from a population-based study) indicate that symptoms of fear, tension and general anxiety, might be even closer linked to future self-harm risk than common symptoms of lowered mood and depression. In accordance with this observation, follow-up studies of the adult HUNT population showed that while depression alone predicted mortality in nearly all causes of death, only combined anxiety and depression predicted death by suicide [37]. Keeping in mind that the information from single items is limited, it is interesting that positive responses to the SCL-5 items regarding anxiety symptoms displayed larger risk increase than the depression-related ones. This might be explained by the typical age distribution difference, where anxiety often presents at younger age (during teen years) while depression more often begins around 30 years of age [38].

Elevated risk of self-injury among adults with autism spectrum disorder (ASD), compared to those without, has been reported [16]. Unfortunately, we did not have information on ASD symptoms or diagnosis at baseline, and could therefore not estimate the specific association

between this disorder and risk of self-harm hospitalisation. Higher rates of self-injury as reported in adolescents and young adults with ASD [39] could arise from using “stereotypical and habitual” self-harm methods: often medically less serious, thus with lower likelihood of presenting to hospital for treatment. Also, the distress following an increasing awareness of social differences and isolation is likely to augment the risk of suicide attempts among adolescents with higher-functioning ASD.

Loneliness, social and family factors

In a large study of Norwegian teenagers [40], loneliness was associated with suicidal behaviour even when adjusted for use of different intoxicants and familial factors. An Icelandic population-based study of 9th and 10th graders [41] found that breakup with a friend was associated with suicide attempts. Findings from the current study points in a similar direction, with a substantial risk increase for reported loneliness, and an estimated population attributable fraction of 13.3%.

A previous Norwegian population based study [42] indicated that not living with both biological parents, and a diagnosis of any depressive disorder were associated

with future self-harm among young and older adolescents. This is in accordance with our results, indicating that not living with both parents (due to separation/divorce) was associated with a more than doubled self-harm risk.

Results from an Australian study following adolescents for 10 years stated that being bullied during childhood increases the risk of self-harm both directly, and indirectly via depression symptoms in early adolescence [43]. Our findings support these results, as we found a more than threefold increased risk of self-harm hospitalisation in those who reported being bullied at baseline. Furthermore, obesity (BMI >30) was associated with substantially increased risk.

Somatic health and illness

In a US study of children and adolescents with chronic health conditions [44], youth with chronic physical conditions alone ($n = 12,554$) only had a slight increased risk for self-harm, suicidal ideation and suicide. However, those with co-existing chronic physical and mental conditions, and those with chronic mental conditions had 2–3-fold increased risk. In contrast, another multinational population-based study of 38,000 people [45] linked a wide range of pre-existing physical conditions to suicidal ideation, plans, and attempts. Epilepsy, physical conditions occurring early in life, and increasing number of physical conditions were especially predictive of future suicidality, and adjustment for co-existing mental disorders altered the results only marginally.

We found strong associations between diagnosed epilepsy, migraine and symptomatic headache without known medical reason, and risk of self-harm hospitalisation. This goes along with a British study reporting twice the rate of hospital-presenting self-harm among patients with, compared to people without, epilepsy [46], and a recent Canadian population-based study where migraine headache was prospectively associated with self-harm [47]. In a lifetime perspective, migraine is a common comorbidity to both manic and depressive episodes [48], yet the majority of children and adolescents with migraine do not have a comorbid psychiatric disorder [49]. In addition, recent findings do not suggest a substantial or lasting association between childhood epilepsy and psychiatric disorders and suicidal behaviour [50].

We also found symptomatic abdominal pain to increase the risk of future self-harm hospitalisation, which complies with a review showing that abdominal pain syndromes, both IBS and non-IBS syndromes [51], served as independent predictors for suicidal behaviour.

Estimated PAFs for stomach pain and caseness anxiety and depression were nearly identical. However, an even higher PAF was estimated for headache without known

medical reason. Hazard ratios for symptomatic headache and diagnosed migraine were almost the same, but symptomatic headache was much more prevalent. Stomach pain and headache are common and often coexistent somatic symptoms in adolescence, and PAF estimates may not be valid due to confounding. Nonetheless, the high numbers call for possible explanations, of which one could include a bidirectional association between pain symptoms and mental distress caused by various reasons, mediating the disposition to self-harm.

There is evidence suggestive of a link between asthma and suicidal ideation and suicide attempts [52], yet we found no such association in our dataset. This might be explained by ours being a younger study population, with less advanced or serious disease. Similar to asthma, neither skin rashes nor allergy altered the risk substantially.

Daily smoking and excess alcohol use

In a cross-sectional study of more than 30,000 pupils and students aged 11–19 years [53], results indicated that heavy episodic drinking was associated with doubled risk for self-reported suicide attempt in the last year, and those drinking at a very young age (aged 13 years and younger) were at greatest risk. Our results also indicated that excess alcohol use was associated with elevated risk of future self-harm hospitalisation, similar to results presented in a prospective study of Australian adults [54]. Still, even though our results do indicate an association, we cannot rule out chance as the explaining factor.

Smoking is strongly associated with mental illness, but the causal link has been questioned [55]. Our results indicated an increased risk of self-harm hospitalisation caused by smoking, yet it is likely that this association have arisen due to a strong association between adolescent cigarette smoking and factors predisposing to mental health problems rather than being a causal exposure in itself.

The evidence that smoking and alcohol use act as risk factors for self-harm in our study might be limited, since the prevalence of alcohol and smoking is highly age dependent. However, we did not find support for any evidence of statistical interaction between age and alcohol or age and smoking on subsequent self-harm risk—a result indicating that these behaviours operate as risk factors across adolescence and young adulthood.

Conclusions

Our results indicated strong associations between several indicators of adolescent health vulnerability and subsequent risk of self-harm hospitalisation. Associations were strongest for indicators of poor mental health, anxiety symptoms in particular. The distribution of self-harm events across the whole symptom score scales for

anxiety and depression underlines the need for both individual and population strategies in the prevention and treatment of self-harm behaviour. Most admissions for self-harm occurred among participants reporting low symptom levels on the different analysed factors. This result underscores the limitations of targeted approaches in self-harm and suicide prevention. Though uncertain, epilepsy apparently increased self-harm hospitalisation risk more than caseness anxiety and depression did, and new studies attempting to replicate the results are needed to clarify this further. Additional investigations might provide better understanding of the increased self-harm risk apparently related to headache and stomach pain. Self-harm prevention is a complex matter, as many factors contribute to increased risk. From a population-based point of view, our results indicate that drug administration safety and prescription patterns need further attention. In a clinical setting, extra care should be taken when dealing with young people reporting loneliness or being bullied at school, especially if they also display signs of anxiety or depression, and if they report suicidal thoughts.

Abbreviations

SCL-5: Hopkins Symptom Checklist, 5-item version; PAF: population attributable fraction; ASD: autism spectrum disorder; SSB: Statistics Norway.

Authors' contributions

AJ contributed to design of study, collected/recorded outcome data, analysed and interpreted data and drafted manuscript. JHB contributed to analysis and interpretation of data, and critically revisions of the manuscript. OB contributed to conception and design of study, interpretation of data and critically revisions of manuscript. All authors read and approved the final manuscript.

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Competing interests

The authors declare that they have no competing interests.

Availability of data and materials

Informed consent for publication of raw patient data not obtained, and dataset could in theory pose a threat to confidentiality. Not possible to obtain consent for publication of raw data by practical reasons.

Baseline data that support the findings of this study are available from HUNT Research Centre and Statistics Norway, but restrictions apply to the

availability of these data, which were used under license for the current study, and so are not publicly available. In addition, outcome data (recorded from patient records) may pose a threat to confidentiality, and so are not publicly available. Data may however be available from HUNT, Statistics Norway, and the authors, respectively, upon reasonable request and with relevant ethical approval.

Ethics approval and consent to participate

This study was approved by the Regional Committee for Medical and Health Research Ethics (2010/1924-3). All Young-HUNT1 participants gave written informed consent for the use of data for medical research (for those <16 years of age, parental consent was also obtained).

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References

- Sinclair JM, Gray A, Rivero-Arias O, Saunders KE, Hawton K. Healthcare and social services resource use and costs of self-harm patients. *Soc Psychiatry Psychiatr Epidemiol*. 2011;46:263–71.
- Hawton K, van Heeringen K. Suicide. *Lancet*. 2009;373:1372–81.
- Hawton K, Harriss L, Hall S, Simkin S, Bale E, Bond A. Deliberate self-harm in Oxford, 1990–2000: a time of change in patient characteristics. *Psychol Med*. 2003;33:987–95.
- Nock MK. Self-injury. *Annu Rev Clin Psychol*. 2010;6:339–63.
- Hawton K, Saunders KE, O'Connor RC. Self-harm and suicide in adolescents. *Lancet*. 2012;379:2373–82.
- Madge N, Hewitt A, Hawton K, de Wilde EJ, Corcoran P, Fekete S, et al. Deliberate self-harm within an international community sample of young people: comparative findings from the Child and Adolescent Self-harm in Europe (CASE) Study. *J Child Psychol Psychiatry*. 2008;49:667–77.
- Kopjar B, Dieserud G, Wiik J. Deliberate self-poisonings treated in hospitals. *Tidsskr Nor Laegeforen*. 2005;125:1798–800.
- Skegg K. Self-harm. *Lancet*. 2005;366:1471–83.
- Nock MK, Joiner TE Jr, Gordon KH, Lloyd-Richardson E, Prinstein MJ. Non-suicidal self-injury among adolescents: diagnostic correlates and relation to suicide attempts. *Psychiatry Res*. 2006;144:65–72.
- Junker A, Bjørngaard JH, Gunnell D, Bjerkeset O. Sleep problems and hospitalization for self-harm: a 15-year follow-up of 9000 Norwegian adolescents. *The Young-HUNT Study*. *Sleep*. 2014;37:579–85.
- Hysing M, Sivertsen B, Stormark KM, O'Connor RC. Sleep problems and self-harm in adolescence. *Br J Psychiatry*. 2015;207:306–12.
- Stokes ML, McCoy KP, Abram KM, Byck GR, Teplin LA. Suicidal ideation and behavior in youth in the juvenile justice system: a review of the literature. *J Correct Health Care*. 2015;21:222–42.
- Singhal A, Ross J, Seminog O, Hawton K, Goldacre MJ. Risk of self-harm and suicide in people with specific psychiatric and physical disorders: comparisons between disorders using English national record linkage. *J R Soc Med*. 2014;107:194–204.
- Kolla NJ, Eisenberg H, Links PS. Epidemiology, risk factors, and psychopharmacological management of suicidal behavior in borderline personality disorder. *Arch Suicide Res*. 2008;12:1–19.
- Black DW, Blum N, Pfohl B, Hale N. Suicidal behavior in borderline personality disorder: prevalence, risk factors, prediction, and prevention. *J Pers Disord*. 2004;18:226–39.
- Maddox BB, Trubanova A, White SW. Untended wounds: non-suicidal self-injury in adults with autism spectrum disorder. *Autism*. 2016. doi:10.1177/1362361316644731.

17. Lopez-Munoz F, Garcia-Garcia P, Saiz-Ruiz J, Mezzich JE, Rubio G, Vieta E, Alamo C. A bibliometric study of the use of the classification and diagnostic systems in psychiatry over the last 25 years. *Psychopathology*. 2008;41:214–25.
18. Mars B, Cornish R, Heron J, Boyd A, Crane C, Hawton K, et al. Using data linkage to investigate inconsistent reporting of self-harm and questionnaire non-response. *Arch Suicide Res*. 2016;20:113–41.
19. Groholt B, Ekeberg O, Haldorsen T. Adolescents hospitalised with deliberate self-harm: the significance of an intention to die. *Eur Child Adolesc Psychiatry*. 2000;9:244–54.
20. Haw C, Casey D, Holmes J, Hawton K. Suicidal intent and method of self-harm: a large-scale study of self-harm patients presenting to a general hospital. *Suicide Life Threat Behav*. 2015;45:732–46.
21. Holmen TL, Bratberg G, Krokstad S, Langhammer A, Hveem K, Midtthjell K, et al. Cohort profile of the Young-HUNT Study, Norway: a population-based study of adolescents. *Int J Epidemiol*. 2014;43:536–44.
22. Strand BH, Dalgard OS, Tamsb K, Rognerud M. Measuring the mental health status of the Norwegian population: a comparison of the instruments SCL-25, SCL-10, SCL-5 and MHI-5 (SF-36). *Nord J Psychiatry*. 2003;57:113–8.
23. Tamsb K. Undersøkelse av seksuelle overgrep mot barn. Oslo: Statens institutt for folkehelse; 1994.
24. Cole TJ, Flegal KM, Nicholls D, Jackson AA. Body mass index cut offs to define thinness in children and adolescents: international survey. *BMJ*. 2007;335:194.
25. Cole TJ, Bellizzi MC, Flegal KM, Dietz WH. Establishing a standard definition for child overweight and obesity worldwide: international survey. *BMJ*. 2000;320:1240–3.
26. Asher MI, Keil U, Anderson HR, Beasley R, Crane J, Martinez F, et al. International Study of Asthma and Allergies in Childhood (ISAAC): rationale and methods. *Eur Respir J*. 1995;8:483–91.
27. Strandheim A, Holmen TL, Coombes L, Bentzen N. Alcohol intoxication and mental health among adolescents—a population review of 8983 young people, 13–19 years in North-Trøndelag, Norway: the Young-HUNT Study. *Child Adolesc Psychiatry Ment Health*. 2009;3:18.
28. Statistics Norway. Education: level of education. <https://ssb.no/en/utdanning?de=Level+of+education>. Accessed 01 Feb 2017.
29. StataCorp LLC. STATA. Data analysis and statistical software. 2016. <http://www.stata.com/>. Accessed 01 Feb 2017.
30. Grambsch PM, Therneau TM. Proportional hazards tests and diagnostics based on weighted residuals. *Biometrika*. 1994;81:515–26.
31. Newson R. Scenario comparisons: How much good can we do? (Report). In United Kingdom Stata Users' Group Meetings. 2012. <https://ideas.repec.org/p/boc/usug12/01.html>. Accessed 11 May 2016.
32. Carroll R, Metcalfe C, Gunnell D. Hospital presenting self-harm and risk of fatal and non-fatal repetition: systematic review and meta-analysis. *PLoS ONE*. 2014;9:e89944.
33. Haw C, Hawton K, Houston K, Townsend E. Psychiatric and personality disorders in deliberate self-harm patients. *Br J Psychiatry*. 2001;178:48–54.
34. Beautrais AL, Joyce PR, Mulder RT. Psychiatric illness in a New Zealand sample of young people making serious suicide attempts. *N Z Med J*. 1998;111:44–8.
35. Tyrer P. The case for cothymia: mixed anxiety and depression as a single diagnosis. *Br J Psychiatry*. 2001;179:191–3.
36. Sareen J, Cox BJ, Afifi TO, de Graaf R, Asmundson GJ, ten Have M, et al. Anxiety disorders and risk for suicidal ideation and suicide attempts: a population-based longitudinal study of adults. *Arch Gen Psychiatry*. 2005;62:1249–57.
37. Mykletun A, Bjerkeset O, Dewey M, Prince M, Overland S, Stewart R. Anxiety, depression, and cause-specific mortality: the HUNT study. *Psychosom Med*. 2007;69:323–31.
38. Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry*. 2005;62:593–602.
39. Hannon G, Taylor EP. Suicidal behaviour in adolescents and young adults with ASD: findings from a systematic review. *Clin Psychol Rev*. 2013;33:197–204.
40. Rossow I, Groholt B, Wichstrom L. Intoxicants and suicidal behaviour among adolescents: changes in levels and associations from 1992 to 2002. *Addiction*. 2005;100:79–88.
41. Bjarnason T, Thorlindsson T. Manifest predictors of past suicide attempts in a population of Icelandic adolescents. *Suicide Life Threat Behav*. 1994;24:350–8.
42. Nruham L, Larsson B, Sund AM. Predictors of suicidal acts across adolescence: influences of familial, peer and individual factors. *J Affect Disord*. 2008;109:35–45.
43. Lereya ST, Winsper C, Heron J, Lewis G, Gunnell D, Fisher HL, et al. Being bullied during childhood and the prospective pathways to self-harm in late adolescence. *J Am Acad Child Adolesc Psychiatry*. 2013;52(608–18)e2.
44. Barnes AJ, Eisenberg ME, Resnick MD. Suicide and self-injury among children and youth with chronic health conditions. *Pediatrics*. 2010;125:889–95.
45. Scott KM, Hwang I, Chiu WT, Kessler RC, Sampson NA, Angermeyer M, et al. Chronic physical conditions and their association with first onset of suicidal behavior in the world mental health surveys. *Psychosom Med*. 2010;72:712–9.
46. Meyer N, Voysey M, Holmes J, Casey D, Hawton K. Self-harm in people with epilepsy: a retrospective cohort study. *Epilepsia*. 2014;55:1355–65.
47. Colman I, Kingsbury M, Sareen J, Bolton J, van Walraven C. Migraine headache and risk of self-harm and suicide: a population-based study in Ontario, Canada. *Headache*. 2016;56:132–40.
48. Nguyen TV, Low NC. Comorbidity of migraine and mood episodes in a nationally representative population-based sample. *Headache*. 2013;53:498–506.
49. Gelfand AA. Psychiatric comorbidity and paediatric migraine: examining the evidence. *Curr Opin Neurol*. 2015;28:261–4.
50. Baldin E, Hesdorffer DC, Caplan R, Berg AT. Psychiatric disorders and suicidal behavior in neurotypical young adults with childhood-onset epilepsy. *Epilepsia*. 2015;56:1623–8.
51. Spiegel B, Schoenfeld P, Naliboff B. Systematic review: the prevalence of suicidal behaviour in patients with chronic abdominal pain and irritable bowel syndrome. *Aliment Pharmacol Ther*. 2007;26:183–93.
52. Goodwin RD, Eaton WW. Asthma, suicidal ideation, and suicide attempts: findings from the Baltimore epidemiologic catchment area follow-up. *Am J Public Health*. 2005;95:717–22.
53. Aseltine RH Jr, Schilling EA, James A, Glanovsky JL, Jacobs D. Age variability in the association between heavy episodic drinking and adolescent suicide attempts: findings from a large-scale, school-based screening program. *J Am Acad Child Adolesc Psychiatry*. 2009;48:262–70.
54. Moller CI, Tait RJ, Byrne DG. Self-harm, substance use and psychological distress in the Australian general population. *Addiction*. 2013;108:211–20.
55. Bjorngaard JH, Gunnell D, Elvestad MB, Davey Smith G, Skorpens F, Krokan H, et al. The causal role of smoking in anxiety and depression: a Mendelian randomization analysis of the HUNT study. *Psychol Med*. 2013;43:711–9.

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Paper III

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