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# Substance Use in Swedish Adolescents

*The Importance of Co-occurring Psychiatric  
Symptoms and Psychosocial Risk*

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### Abstract

Lövenhag, S. 2015. Substance Use in Swedish Adolescents. The Importance of Co-occurring Psychiatric Symptoms and Psychosocial Risk. *Digital Comprehensive Summaries of Uppsala Dissertations from the Faculty of Medicine* 1110. 85 pp. Uppsala: Acta Universitatis Upsaliensis. ISBN 978-91-554-9263-2.

**Aims: Study I:** Identify substance use disorders (SUDs), psychiatric disorders, and psychosocial risk (PSR) in adolescence, to predict SUD after 5 years in 147 adolescents who sought treatment at a misuse-clinic. **Study II:** Identify alcohol risk use (ARU) and its association with psychiatric symptoms and PSR in 960 adolescents who sought treatment in general psychiatric care. **Study III:** Examine the effect of antisocial behavior (ASB) on the association between inattention, hyperactivity, impulsivity, and alcohol use in 3,864 adolescent students. **Study IV:** Examine the veracity of drug use reports comparing responses in questionnaires, in-depth interview, and hair analysis in 200 adolescent students.

**Results: Study I:** SUDs in adolescence persisted into early adulthood. Predictors for SUD: girls who had mothers with alcohol use disorder, victimization, criminality, SUD, or SUD treatment. **Study II:** Prevalence of ARU was 20%. ARU increased with the number of psychiatric symptom domains. Probability of psychiatric symptoms increased with ARU. Most ARU was found in: ASB and sexual abuse. Most common in ARU: symptoms of ADHD, depression, and anxiety. **Study III:** ASB reduced association between inattention, hyperactivity, impulsivity, and alcohol use for boys, and hyperactivity and impulsivity for girls. Girls' inattention continued to affect alcohol use despite the presence of ASB. **Study IV:** Twice as many participants reported drug use in interviews compared to questionnaires. Questionnaires and hair-analysis showed low sensitivity and high specificity. Responses from participants in less privileged socioeconomic circumstances were less reliable.

**Conclusions: Study I:** Treatment-as-usual experienced difficulties preventing the persistence of SUD. Participants' comorbidity and PSR must be attended to. **Study II:** ARU in general psychiatric care is prevalent and associated with other psychiatric symptoms, and all symptoms must be attended to simultaneously. **Study III:** ASB should be screened for when symptoms of ADHD are present. Inattention in girls might require special attention to prevent alcohol use. **Study IV:** Interviews might be an alternative to questionnaires. Hair analysis was less useful in this population, but a physical measure might function as a pipeline procedure. Responses from participants in less privileged circumstances might be interpreted with caution.

*Keywords:* Alcohol, illicit drug, psychiatry, measures, validity, ADHD, antisocial behaviors, depression, anxiety

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# List of Papers

This thesis is based on the following papers, which are referred to in the text by their Roman numerals.

- I Hodgins, S., Lövenhag, S., Rehn, M., & Nilsson, K. W. (2013). A 5-year follow-up study of adolescents who sought treatment for substance misuse in Sweden. *European Journal of Child and Adolescent Psychiatry*, 23(5):347–360
- II Lövenhag, S., Larm, P., Åslund C., & Nilsson, K. W. (2015). Adolescent alcohol risk use co-occurrence with psychiatric symptoms in Swedish general psychiatric care. *Submitted manuscript*.
- III Lövenhag, S., Larm, P., Åslund, C., & Nilsson, K. W. (2015). Antisocial behavior reduces the association between ADHD subdimensions and alcohol use in a large population-based sample of adolescents. *Scandinavian Journal of Psychology*. Accepted.
- IV Lövenhag, S., Kronstrand, R., Åslund, C., & Nilsson, K. W. (2015). Reports of adolescent illicit drug use: in what and whom can we trust? Investigating the congruency of questionnaires, in-depth interviews, and hair analysis. *Submitted manuscript*.

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# Abbreviations

ADHD	Attention deficit hyperactivity disorder
ARU	Alcohol risk use
ASB	Antisocial behavior
ASRS-A	ADHD Self-Report Scale- Adolescent version
AUD	Alcohol use disorder
AUDIT-C	Alcohol Use Identification Test (first three questions)
CD	Conduct disorder
DSM	Diagnostic Manual of Mental Disorders
DSRS	Depression Self-Rating Scale
DUD	Drug use disorder
EPIQ	Electronic Psychiatric Intake Questionnaire
K-SADS-PL	Kiddie-Schedule for Affective Disorders and Schizophrenia for School-Aged Children – Present and Lifetime Version
ODD	Oppositional defiant disorder
PSR	Psychosocial risk
SALVe	Survey of Adolescent Life in Västmanland
SCAS	Spence Child Anxiety Scale
SCID	Structured Clinical Interview for DSM-IV Axis I Disorders
SUD(s)	Substance use disorder(s)



# Background

The use of mind-altering substances has been documented in paintings and writings since the beginning of human time [1]. Sedative beverages and inebriating herbs have been used throughout history to induce euphoria, for religious purposes, to celebrate joyful life events, to smooth social interactions, to enhance the taste of the Sunday roast, to increase artistic creativity, to ease mind and tension, to take the edge off setbacks or just to make everyday life less painful to endure.

According to the WHO World Drug report 2014, 39% and 6% of the adult world population use alcohol and illicit drugs, respectively [2]. Approximately 16% of alcohol users engage in heavy episodic drinking, and 0.6% of the individuals who reported illicit drug use in the past year are considered to be problem drug users [2]. The greater proportion of the world's population is hence abstainers, and the lion's share of alcohol and drug use is non-problematic. However, the substances used do cause vast individual, interpersonal, and financial costs, and across times and cultures, great efforts have been invested in restricting and banning elements considered to be harmful to humans. An early attempt to forbid the use of alcohol was made in China, by Emperor Yu the Great, around 2000 BCE. The entire country stayed compulsorily sober until the emperor's death, when his son Qi immediately lifted the ban. In 600 CE, the Koran prohibits all intoxicants saying "[...] their sinfulness far outweighs their benefit" 2:219 premise [3]. In Sweden, the use of alcohol was monitored and restricted by the use of ration books until the 1950s, and even today, alcoholic beverages are sold only in specialized stores monitored by the governmental Swedish Alcohol Retailing Monopoly.

The war against drugs has been fought throughout the centuries; the Chinese government battled the immense British importation of opium that threatened to defeat great parts of the Chinese population in the 19<sup>th</sup> century. In the 1960s, after the first UN Convention on Narcotic Drugs [4], US President Richard Nixon declared war on drugs, labeling drug abuse public enemy number one [5].

Nevertheless, despite the painfully acquired extensive knowledge of the harmful effects of alcohol and narcotics, the use of these substances seems to

be impossible to discard. Alcohol use is currently allowed worldwide, with the exception of 12 countries [6]. According to the UN, the general public perceive cannabis to be the least harmful illicit drug, and the use of the substance is now legal in Jamaica, the Netherlands, and Uruguay, and in the US states of Washington, Colorado, Oregon and Alaska, with political opinion makers in other countries, such as Sweden [7-9] pleading the benefits of legalization.

I work as a clinical psychologist at a child and adolescent psychiatric outpatient clinic. It is the rule, rather than the exception, that the patients I meet present with several psychiatric conditions, often including problematic substance use. The treatment outcome for a patient with such a combination of difficulties is worse than for a patient without substance use [10, 11]. The use of mind-altering substances has obviously charmed, but also challenged, the individual user and society at large since the beginning of time. The challenge will remain and is ours to take on, accept and master. Some individuals do it easily and some do not, and with this thesis I would like to make an attempt to facilitate the challenge of the latter ones.

# Introduction

Substance use contributes significantly to the burden of disease among young people, causing the loss of lives and healthy productive years in Western societies [12]. Globally, alcohol misuse is the leading factor for disability and premature death among individuals aged 15–49 [13].

It has been proposed that the strongest association with problematic substance use in adolescence and later dependence in adulthood is early initiation of substance use [14]. Adverse patterns of substance use established in adolescence tend to persist throughout early adulthood [15], and it is therefore possible to infer that many adult problem substance users started their use at an early age [16].

It is well established that the younger the age of substance use onset, the worse the outcome [17]. In a longitudinal community study of 808 boys and girls, Hawkins et al. concluded that early onset of alcohol consumption predicted binge drinking, drunk driving, and other related problems at ages 17–18 years, with the youngest initiators reporting the greatest number of problems [18]. In recognition of the early onset factor, much effort has been spent preventing and treating problematic substance use prior to adulthood [15].

Substance use among young people is not a new phenomenon. However, few studies have investigated the impact of problematic substance use in youth over longer periods. A research team at the Karolinska Institute in Sweden studied a cohort of 1,992 men and women who had been treated in the late 60s at a large clinic for adolescents with substance problems in Stockholm [19]. These individuals were compared with a control group matched for sex, age, and place of birth. The research team analyzed information about participants from six national records and saw that the young people who sought treatment for substance use were affected by premature death, physical and mental illness, substance use disorder (SUD), crime, and poverty to a much greater extent in adult life [20]. In addition, the substance use problems tended to persist from adolescence into adulthood, despite treatment [19].

In 2002, Armstrong and colleagues conducted a review study examining the existing adolescent community literature on co-occurring substance use disorder and other psychiatric diagnoses. The results revealed comorbidity in about 60% of cases [21]. The authors concluded that adolescents presenting with SUD “are not, on the whole, just normal adolescents who happen to be experimenting with substances but, in many cases, are youths with other, and remediable, problems” [21]. The co-occurrence of psychiatric and SUDs contributes significantly to the total burden of disease and accounts for 22.9% of all years lost as a result of disabilities globally [22]. Coexisting substance use and psychiatric symptoms are associated with greater severity of illness, worse disability, poorer response to treatment, and worse prognosis [10, 11]. There is a lack of information regarding the prevalence of co-occurrence of psychiatric conditions in Swedish adolescents treated for substance use problems and vice versa; however, the studies conducted indicate a clear overlap [19, 23].

## Substance use

### Risk use

The WHO use the term “harmful use” when discussing heavy or dependent consumption of alcohol or illicit drugs [2]. The Swedish Health and Human Services Department and the Swedish Council for Information on Alcohol and Other Drugs (CAN) use the terms “risk free use of alcohol” versus “alcohol risk use.” [24, 25]. The use of drugs are considered to be a risk behavior in itself and therefore drug use is labeled as episodic (irregular) or heavy (injection use/daily use/almost daily use) [24]. The risk use concept relates to epidemiological studies indicating a lower risk of physical damage if consumption is kept below a certain quantity [26].

The 2013 Swedish Health and Human Services Departments’ *Disease Prevention in the Swedish Healthcare System: Health situation, national guidelines and implementation* defined alcohol risk use as a high average consumption or intensive drinking at least once a month [27]. High average consumption is defined as more than 14 standard servings a week for men, and nine for women. Intense consumption is defined as five standard servings or more at one time for men, and four or more for women [27]. To consume a standard serving, which, according to the guidelines, is 12 grams of alcohol, one of the bottle or glass amounts in Figure 1 should be poured [27]. For obvious reasons, there are no adolescent recommendations. However, to identify adolescent risk use, the adult measures of amount and frequency can be applied.



Medium-strong beer,	Strong beer/cider	Table wine	Fortified wine	Liquor
50 cl/3.5%	33 cl/5%	12cl/12%	8 cl/17%	4 cl/40%

Figure 1. Each bottle or glass corresponds to a standard serving containing around 12g of alcohol.

### Substance use disorders (SUDs)

In the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), SUDs were classified as either abuse or dependence. Abuse was characterized by the negative psychological and social consequences caused by the use of the substance [28]. To meet the criteria for dependence, strong psychological and physiological symptoms of addiction should be present [29]. In the fifth edition of the DSM (DSM-5), the social and physiological negative consequences of substance use are no longer treated separately but are merged into a single dimension, with the consequences of use described as mild, moderate, or severe. The criterion of substance-related legal problems has been removed, and an item asking about craving has been added [30]. The differences between the DSM-IV and DSM-5 are shown in Table 1. The same criteria apply for both underage and adult populations, but there is ongoing debate over whether there is a need for a child- and adolescent-adapted diagnostic measure [31].

Table 1. Similarities and differences between DSM-IV diagnosis of substance abuse and dependence and DSM-5 diagnosis of substance use disorder.

<b>Criterion</b>	<b>DSM-IV Substance abuse</b>	<b>DSM-IV Substance dependence</b>	<b>DSM-5 Substance use disorder</b>
Substance-related legal problems	✓		
Substance-related failures to fulfill obligations	✓		✓
Recurrent use of substance in hazardous situations	✓		✓
Continued use despite problems	✓		✓
Tolerance		✓	✓
Withdrawal		✓	✓
Used more/more often than intended		✓	✓
Unable to quit/cut back		✓	✓
Spent a lot of time using/recovering		✓	✓
Give up important activities due to use		✓	✓
Continued use despite consequences		✓	✓
Craving			✓

## Adolescent substance use

Adolescence is a sensitive and challenging period, both physically and mentally. The identity of the individual develops and the young person tries to find a place in life [32]. Substance use is usually initiated during this period in life, peaks in early adulthood, and thereafter gradually decreases [33]. For some young people, however, the use does not decrease, and the substance use leads to psychological and physical impairment, social or school complications, or failure to perform the other duties that are expected of youths [12, 34]. Adolescent substance use is associated with several physiological negative effects. Although the health problems associated with alcohol use are not as frequent or severe as in the adult population, adolescent alcohol use has been proven to affect normal brain development, growth, the endocrine system, and the function of the liver [35].

The Swedish Council for Information on Alcohol and Other Drugs (CAN) has monitored the alcohol and drug use habits in Swedish students since 1971. In 2014, there were statistically significant more 16-year-old female students (50%), compared with male students (43%) reporting having been drunk at least once, while 10% of all students reported alcohol risk use. [36]. This is the lowest prevalence numbers since 1971 and it is the first time girls' consumption exceeds the boys' [36]. Among 18 year old, the numbers

were 76% and 82%. Although the adolescent prevalence of alcohol use in Sweden is historically low, and also low compared with other European countries, Swedish adolescents who use alcohol report more frequent use, and in greater quantities, than their European drinking peers [37]. In 2009, 8% of the ninth-grade students and 16% of the second-year students in secondary schools in Sweden reported using illicit drug at least once [37].

In 2009, approximately 3000 patients between 10 and 19 years were treated for a substance-use-related diagnosis in Swedish inpatient care—a 30% increase on 1999 levels [38]. Substance use treatment data are recorded in the Swedish patient register; however, the information is limited, and international studies assume that substance-related disorders are underdiagnosed in adolescent psychiatric care facilities [39].

## Etiology of adolescent SUDs

### Co-occurrence with psychiatric symptoms

Presenting with both SUD and other psychiatric symptoms makes the conditions more severe, worsens the disability, weakens the response to treatment, and impairs the prognosis [10, 11]. Co-occurring psychiatric symptoms among adolescents with SUDs are the norm rather than the exception [21, 40]. Etiological models have been suggested to explain the vast co-occurrence of psychiatric symptoms and substance use problems. Table 2 presents an overview [40, 41].

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Table 2. Three common models explaining the etiology of substance use disorders (SUD) and psychiatric symptoms.

<b>Model</b>	<b>Pathway</b>
Secondary SUDs	Psychiatric disorders cause SUDs
Secondary psychiatric disorders	SUDs cause the development of psychiatric disorders
Common factor	Shared underlying risk factors predispose to both the foundation of SUDs and other psychiatric conditions

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### Secondary SUDs versus secondary psychiatric disorders

Psychiatric externalizing disorders in childhood, such as ADHD, conduct disorder (CD), and oppositional defiant disorder (ODD) often precede substance use [42, 43]. This temporal order might, however, be explained by

the fact that symptoms of these externalizing disorders often begin in the early school years, when substance use is still rare. Internalizing disorders such as depression and anxiety, with a wider onset range, are regarded in some studies as precursors to substance use [44] and in others as consequences of the use [45].

However, much evidence does support the secondary SUDs model, suggesting that mental disorders often precede SUDs in young individuals. Results from the American National Comorbidity Study showed that the median age of onset for a mental disorder was 11, while substance abuse disorders normally developed 5–10 years later [46, 47]. Eighty-three percent of the adolescents in the comorbidity study presenting with comorbid SUD and psychiatric disorders reported onset of at least one mental disorder prior to substance use problems [47].

### **Common factor model**

The common factor model suggests that high rates of comorbidity are the result of shared risk factors. The common factor model indicates that both SUDs and psychiatric symptoms in adolescence are attributable to similar underlying risk factors, including environmental factors, such as malfunctioning family environment [48] or victimization in the peer group [49]. Individual factors, such as genetic predisposition, [50-53], co-occurring psychiatric disorders [42, 43], disruptive behavior, and behavioral dysregulation characterized by sensation seeking, risk taking, and impulsive behavior [40, 50] are also suggested as common factors for the development of SUDs and other mental illnesses.

### *Behavioral dysregulation*

According to the common factor theory of behavioral dysregulation, genetic vulnerability for substance use problems is expressed by impaired behavioral disinhibition, which is characterized by high levels of impulsivity. Behavioral disinhibition is distinguished by reacting with boldness and spontaneity to new events and experiences, exhibiting low self-control, thrill-seeking behavior and fearlessness in dangerous situations [54]. The theory suggests that externalizing behavioral disorders such as antisocial behavior, ADHD and substance use problems are rooted in a common underlying dimension of a lack of ability to manage and control behavior [50-53]. The other side of the behavioral dysregulation coin, also associated with substance use, is behavioral inhibition, which is characterized by fear and anxiety, and avoidance of novel stimuli, reflecting a lower threshold for stress [54]. Behavioral inhibition is associated with internalizing conditions such as anxiety and other affective disorders [54].

## **Externalizing symptoms**

### *Symptoms of attention deficit hyperactivity disorder (ADHD)*

Alongside antisocial behaviors, symptoms of ADHD are the most common comorbid psychiatric condition with SUDs [21]. ADHD is characterized by persistent and pervasive symptoms of inattention and/or hyperactivity/impulsivity [30]. Review studies estimate the prevalence of ADHD in children and adolescents to be 5–9% [55-57]. Analyses of sex differences say that boys exhibit more symptoms of hyperactivity/impulsivity [58], while girls report more problems with inattention [59]. Furthermore, girls with ADHD exhibit higher rates of comorbidity with depression and anxiety than both the general population of girls [60, 61], and boys with ADHD [58, 62, 63].

Several pathways to SUDs involving the role of ADHD have been suggested: 1) The traditional model, regarding ADHD as an independent significant developmental risk factor for substance use problems, which was recently confirmed in a meta-analysis of 13 international studies [64]; 2) a cumulating model, suggested by the review by Lee and coworkers, where ADHD in combination with antisocial behaviors increases the risk of developing SUD, compared with presenting with only one of the conditions [65]; and 3) a model viewing antisocial behaviors as a major developmental risk factor for the progress of SUDs, diminishing the role of ADHD symptoms [66].

The symptoms defining the ADHD construct are not uniform in their manifestation; for example, inattention (“Often has trouble organizing tasks and activities”) and impulsivity (“Often interrupts or intrudes on others”) are vastly different behaviors. Analyzing the subdimensions of ADHD (inattention and hyperactivity/impulsivity) separately from each other, in relation to substance use, might explain the inconsistencies attached to substance use that have been reported in the literature. Symptoms of inattention, hyperactivity, and impulsivity have been explained as expressions of different underlying neurocognitive impairments that influence substance use, such as cigarette smoking, in various ways [67]. Furthermore, comorbidity patterns have been shown to differ between ADHD subdimensions with increased levels of depression in patients with inattentive and combined subtype, and increased antisocial behaviors in the hyperactive/impulsive subtype [68]. Although the results from these studies are not consistent, the results of two publications have indicated that inattentiveness, but not hyperactivity/impulsivity, was related to alcohol problems [69, 70]. A small number of studies has analyzed hyperactivity and impulsivity separately from each other, thus creating three analyzable dimensions of ADHD, and has found that impulsivity, but not hyperactivity,

was related to abuse in the family [71] and increased psychosocial difficulties [72].

### *Antisocial behaviors*

Antisocial behaviors often begin in childhood, starting with ODD characterized by a negative, hostile, and defiant behavior, and proceeding to CD in adolescence with violent and/or abusive behavior [30]. The prevalence in the population is estimated to be close to 13% for ODD and 7% for CD [56]. In Armstrong and Costello's community review, antisocial behaviors were observed in almost one-half of the adolescents with SUDs and were often seen preceding the substance use [21].

In the third model of ADHD pathways to substance use, Flory et al. suggest that antisocial behavior is an independent risk factor for SUDs [66]. However, a twin study by Edwards and Kendler reported a genetic correlation between ADHD, antisocial behavior, and alcohol-related problems in youth [73], supporting the common factor explanation of behavioral disinhibition.

## **Internalizing symptoms**

### *Symptoms of depression*

The main symptoms of depression are depressed mood, irritability, and/or loss of interest [30]. The prevalence of major depression or dysthymia sometime during adolescence is estimated to be about 11% [56]. According to the Armstrong and Costello community study review, 20–30% of adolescents with a diagnosis of substance abuse suffer from some form of mood disorder [21]. Depression is believed to increase the risk of substance use among adolescents [74, 75], and it has been suggested that self-medication with alcohol or drugs is used as a coping strategy to alleviate depressive symptoms and to regulate negative affect [76, 77]. The high rate of comorbidity has also been explained by the common factor theory, which hypothesizes that depression and substance use problems are associated with the same risk factors and that some individuals have inherited vulnerability to both conditions [62, 63].

### *Symptoms of anxiety*

Anxiety is characterized by a wide range of negative emotions, including unease, worry, fear, or panic [30]. It has been proposed that individuals with feelings of anxiety, as in the case of depression, might self-medicate their condition with substances [77]. Anxiety disorders are one of the most common psychiatric conditions in children and adolescents [78], and review studies argue that the prevalence in adolescents extends to 32% [56]. About one-third of young people with anxiety disorders also meet the criteria for

depression [79], and the overlap is hypothetically explained by the common factor theory [62, 80], relating to behavioral inhibition as illustrated by avoidance of novel stimuli, fear, and anxiety reflecting a lower threshold for stress, and activation of the sympathetic nervous system [54].

## Co-occurrence with psychosocial risk

The common factor model suggests that SUDs and psychiatric conditions in adolescence are attached to similar underlying risk factors, including environmental factors, such as factors within the family, socioeconomic status, and victimization. Specific vulnerability factors are seldom strongly associated with problem behavior alone but play an important role when they interact [81]. Dube and colleagues found that experience of aversive psychosocial events, such as physical, psychological, and sexual abuse, mental disorders in the family, parental SUDs and criminality, or family conflict increased the likelihood for illicit drug use. Each additional aversive experience in childhood increased the likelihood of drug use before the age of 14 years by 2–4 times and elevated the risk of addiction later in life fivefold. Young people with experience of five or more aversive events were 7–10 times more likely to report illicit drug use than individuals without experience of aversive childhood conditions [82].

### **Family factors**

Children of parents with substance use problems are thought to be 2–10 times more likely to develop the same difficulties themselves [48, 83]. Parents with substance use problems constitute a genetic risk and at the same time offer their youth a psychosocially unfavorable environment where the use of alcohol and drugs is normalized and parenting ability might be insufficient [84, 85]. Socioeconomic factors, such as ethnicity, social status, form of housing, level of education, employment type, income, and poverty have been presented as risk factors for the development of substance use problems [86-89]. However, there is some disagreement about the role of socioeconomic factors for the establishment and maintenance of substance problems, and some study overviews indicate a nonexistent correlation [90, 91].

### **Victimization**

It has been suggested that children and adolescents who suffered physical and/or psychological abuse in the family exhibit an increased risk of heavy episodic alcohol intake [92] and increased risk of developing substance use problems [49, 93]. Experience of sexual abuse has also been proposed as a risk factor for problematic substance use [94]. Furthermore, being victimized by peers and being the perpetrator of bullying have both been associated with substance problems [95]. Bullying may be characterized as a one-way

exposure of harassment but can also be a two-way exposure, attributed to individuals exhibiting antisocial traits and creating conflict around themselves.

## Gene–environment interaction

Genes interact with the environment that they are expressed in; both unfavorable genes and environment increase the risk of developing SUDs. Specific genotypes have been shown to interact with high levels of maltreatment and maladaptive family relations [96-98], sexual abuse [99], and negative life events [100] affecting substance use. However, recent studies have found that genetic variants previously shown to confer vulnerability for delinquency and disruptive behaviors, including alcohol and drug risk use, were associated with the lowest delinquency scores in interaction with a positive child–parent relationship [101]. The theory of genetic plasticity suggests that risk genes confer susceptibility to the environment, and depending on the positive or negative characteristics in the environment, the risk genes provide either protection or vulnerability against deviant behavior including SUDs [102, 103]. Thus, underlying genetic risk factors might be reduced and even turned into positive factors in the presence of favorable environmental conditions.

## Assessment

Psychiatric assessment of children and adolescents is often complicated, because the degree of development strongly influences what is normal or abnormal [104]. Furthermore, it may be difficult to determine whether the child or young person’s symptoms are caused by, for example, a neurological disorder or a dysfunctional home or school environment [105].

To identify, describe, and interpret SUDs and the factors affecting their establishment and maintenance, a systematic mapping of the patient’s symptoms is essential. Clinical interviewing—talking to the patient and evaluating the information using clinical experience, without using diagnostic tools such as structured interviews and questionnaires—is an unreliable but widely employed method for assessing psychiatric conditions [106-108]. The practice of structured diagnostic interviews improves perceptiveness to comorbidity, enhances adherence to DSM criteria, and increases inter-rater reliability of the evaluation of symptoms [39, 107-110].

However, Martin and colleagues argue that little is known about the validity of DSM SUD criteria when applied to adolescents [31]. No matter how strictly the clinician adheres to the DSM criteria, the nosology will not be

useful if the criteria do not really grasp the essence of adolescent substance use. Some symptoms are less prevalent in clinical groups and may be limited in their use. For example, withdrawal and alcohol-related medical problems generally surface after many years of heavy drinking and are not typically experienced by adolescent problem drinkers [31]. Furthermore, in an earlier study, Martin and coworkers found that tolerance occurred at relatively moderate drinking levels in most adolescents, irrespective of the presence of alcohol use disorder [111]. In short, the difficulty in specifying what adolescent substance use actually *is* makes it understandably hard to measure.

Nevertheless, clinicians and researchers naturally use various approaches to assess alcohol and drug problems in adolescents. The breadth and depth of the evaluation depends on the purpose of the assessment; screening in a first-line health care facility and diagnostic measurement in a specialized psychiatric clinic demand different techniques. Self-reports such as questionnaires and interviews are common methods, providing direct information about a person's substance use and associated problems that is most often not possible to extract from official records or from biological tests [112].

It is common to analyze biological materials such as blood, urine, saliva, or hair to document traces of substances. Biological measurements can, however, be perceived as both invasive and unfavorable to the individual [112]. The technology called head space solid-phase microextraction/ gas chromatography –mass spectrometry (HS-SPME/GC –MS) is a method commonly used to detect drug use in hair. The method is pain free and provides the opportunity to evaluate the use for a much longer period than is possible with other biological materials [113]. The method has been found to have good sensitivity and specificity [113-116]. As well as assessing traces of consumed substances in biological material, biochemical analysis can also be used as a validator of answers given in self-reports and as a pipeline procedure (i.e., an additional procedure used to increase the motivation to self-report substance use more accurately). If the respondent is aware that his/her answers will be compared with a biological key, reflecting the “truth,” the respondent might be more disposed to admit actual use [117].

## Treatment

In Sweden today, adolescents with substance use problems are primarily treated by social services, while adolescents with psychiatric symptoms are referred to child and adolescent psychiatric care facilities. In cases where adolescents present with both substance use problems and psychiatric

symptoms, collaboration and joint actions by these two caregivers are demanded.

In 2002, the U.S. Department of Health and Human Services reported that 1.4 million American adolescents met the criteria for alcohol abuse or dependence, but only 227,000 actually received any treatment for these problems [35]. The same pattern is reflected in the Swedish 2005 Government Official Report, *People with heavy abuse. Incentives for better care and treatment*, which states that a great proportion of the individuals with SUD neither ask for nor receive the care to which they are entitled and that people with comorbid substance use and psychiatric disorders suffer the greatest difficulties attaining the help needed [118]. In a Swedish study of individuals at an adolescent substance misuse clinic, patients presented with an average of three mental disorders, but the majority of patients had not received treatment for their comorbid conditions [23].

Young people do not always respond to treatment strategies developed for the adult population. Therefore, interventions tailored for the conditions of the adolescent user are essential [38]. Until the 2014 publication of the Swedish Health and Human Services Departments' revised *National guidelines for substance abuse and dependence treatment*, there existed no official recommendations for the treatment of adolescent substance use in Sweden [119]. The 2011 Swedish Government Official Report, *Better interventions for abuse and dependence—the individual, the knowledge and the reasonability*, strongly criticized the lack of national guidelines and evidence-based work in the Swedish municipalities and county councils, underlining the gravity of the nearly nonexistent praxis of treatment of coexisting adolescent substance use and other psychiatric symptoms. The 2015 *National guidelines for treatment and support in abuse and dependence* recommendations for adolescent substance use treatment consist of motivation enhancement, learning behavioral and cognitive skills for the abstaining and prevention process, and a range of family therapeutic strategies aiming to enhance communication and problem-solving skills in the family while eliminating antisocial behaviors [120].

There are no recommendations for the treatment of coexisting adolescent substance use and psychiatric disorder in the guidelines, as a result of a lack of studies in the field [120]. There are, however, guidelines for psychotherapeutic intervention for adults with alcohol use disorder in combination with depression, posttraumatic stress disorder, and severe mental disorder (not further specified in the report) [120]. The Swedish Health and Human Services Department highlights the importance of integrated treatment in cases of comorbidity, recommending the treatment to address both the patients' substance use and his/her mental illness. This form

of treatment is based on the recognition that the conditions should be treated simultaneously to increase the chance of both reducing the abuse or dependence and increasing the psychosocial functioning level [68, 120].

## Rationale for the thesis

Given the high co-occurrence of adolescent substance use problems and psychiatric symptoms, it is valuable to study this interplay in the groups in which it occurs: at a substance misuse clinic and in general psychiatric care facilities. At the misuse clinic, there is a need for longitudinal studies investigating the importance of psychiatric disorders and psychosocial adversities in childhood and adolescence with regard to the development of substance disorders in early adulthood. It has been suggested that psychiatric symptoms often precede SUDs, and it is therefore necessary to attend to indicators of substance risk use in general psychiatric care facilities. The extent of co-occurrences of psychiatric symptoms and alcohol risk use in general psychiatric care facilities in Sweden is in need of attention and further knowledge is vital.

There is a high co-occurrence of externalizing psychiatric symptoms, such as ADHD and antisocial behaviors, and substance use. The interplay has not been thoroughly investigated, and there is a need for further clarification, especially regarding the individual contributions of the subdimensions of ADHD symptoms, in relation to antisocial behaviors.

Furthermore, discrepancies between self-reported and biologically detected drug use have been documented for many years [121-123], challenging the validity of self-reports and possibly undermining epidemiological research findings [124, 125]. There is a need to investigate the veracity of measures, in order to be able to provide both reliable study reports and proper clinical interventions.

# Aim

## General aim

The general aim of the thesis was to contribute to a further understanding of adolescent substance use and its interplay with psychiatric and psychosocial risk factors.

## Study-specific aims

### Study I

To examine the prevalence of alcohol use disorders and drug use disorders in early adulthood, and to identify psychiatric comorbidity and psychosocial risk measured in adolescence that predicted these disorders, separately for boys and girls, among 147 adolescents who sought treatment for substance misuse.

### Study II

To examine the prevalence of alcohol risk use and its co-occurrence and association with psychiatric symptoms and psychosocial risk, separately for boys and girls, among 960 adolescents who sought treatment for psychiatric symptoms in general psychiatric care facilities.

### Study III

To examine the possible reducing effect of antisocial behavior on the association between three ADHD subdimensions (inattention, hyperactivity, and impulsivity) and alcohol use, separately for boys and girls, in a cross-sectional population-based sample of 3,864 adolescent students.

### Study IV

To examine the veracity of reports of illicit drug use among adolescents, by comparing responses to questionnaires, in-depth interviews, and hair analysis, separately for boys and girls, in a cross-sectional population-based sample of 200 adolescent students.

# Method

## Participants

### Study I

#### **Baseline**

During a 19-week period in the spring of 2004, 742 adolescents aged 13–18 years sought treatment for alcohol and drug misuse at the only adolescent substance misuse clinic in Stockholm. The clinic offered integrated treatment provided by the county council and social services in cooperation. Fifty percent (373) of the adolescents, and their parents, were invited to join the study. Of these, 180 adolescents (81 boys and 99 girls) agreed to participate (Figure 2). The mean age of the participants was 17 years. Comparison of 61 of the adolescents who agreed to participate in the study with 61 who declined indicated that the sample was representative of the clinic population [10].

#### **Five-year follow-up**

In 2009, five years after the initial assessments in 2004, all participants from the baseline measures were invited to partake in a follow-up study. Of the initial sample of 180 adolescents, 147 (82%) agreed to participate. The mean age of the participants at follow-up was 22 years, and the mean follow-up time was 67 months.

Comparison of the participants who completed the 5-year follow-up and those who did not, indicated that there were no significant differences between them on baseline characteristics: parents' SUDs, criminality, maltreatment by parents, family poverty, participants' mental disorders, experience of victimization by peers, experience of sexual abuse, treatment, and age at first contact with the clinic. However, the adolescents who declined to participate in the follow-up were more likely to be boys, to have one or both parents born abroad, and to have official and/or self-reports of nonviolent and violent crime at baseline.

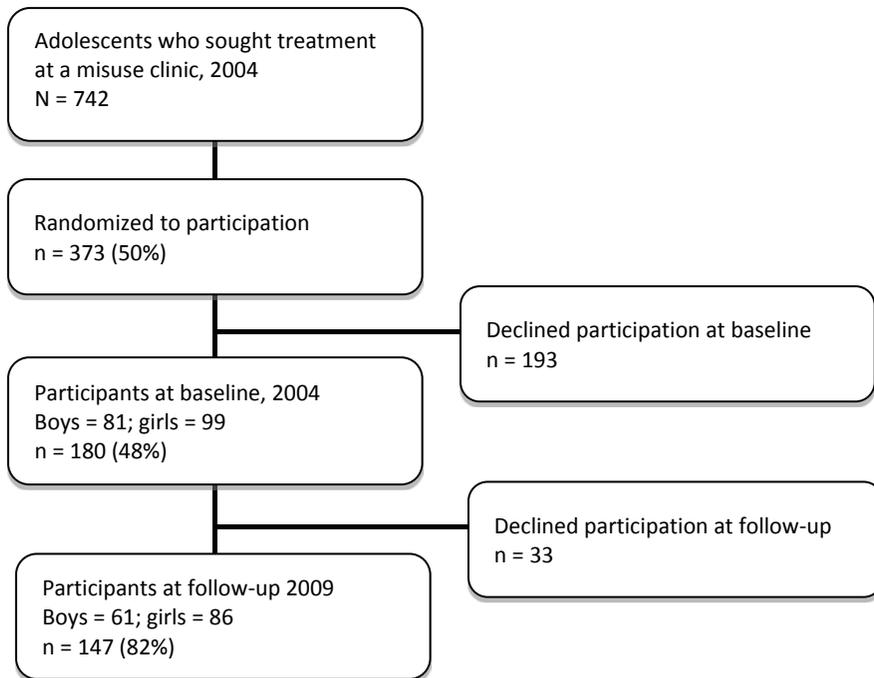


Figure 2. Flowchart of the study population in study I.

## Study II

During the period from 1 August 2010 to 30 April 2014, 1,792 adolescents aged 13–18 years sought treatment for psychiatric symptoms at three child and general adolescent psychiatric care facilities in the Swedish county of Västmanland. Adolescents entering the clinics underwent the standard intake routine, completing an electronic psychiatric intake questionnaire (EPIQ), an instrument including details about alcohol use, psychiatric symptoms, psychosocial factors and demographic variables. Due to reorganizations at the clinics during the period for the study, 129 adolescents entered the clinics alongside the standard intake routine, and were unfortunately not invited to complete the EPIQ and another 260 adolescents that completed the EPIQ was never asked to participate in the study. The eligible population of 1663 adolescents was invited to complete the EPIQ. Out of these, 1487 completed the EPIQ and 960 adolescents (406 boys and 554 girls) agreed to partake in the study, giving a participation rate of 58% (Figure 3). The mean age of the participants was 16 years. There was no significant difference between participants and nonparticipants in the study regarding sex and age distribution.

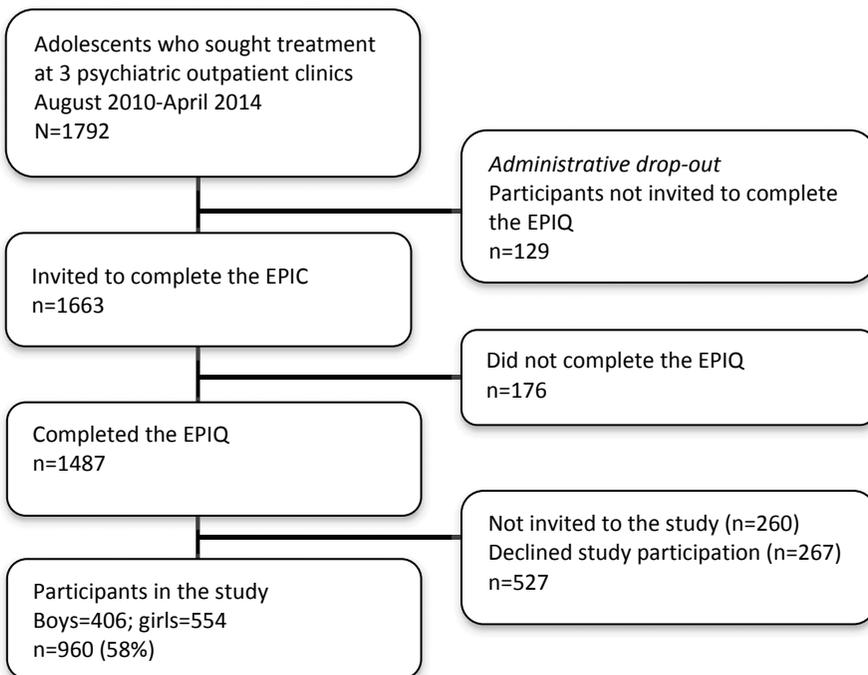


Figure 3. Flowchart of the study population in study II.

### Study III

In 2010, 6,790 individuals were registered as students in the 2<sup>nd</sup> and 9<sup>th</sup> grades in primary and secondary schools in Västmanland. All students attending class at the time of the survey were invited to participate. Students at special schools were not invited to participate in the study (n = 26). Thus, 5,211 students constituted the eligible population, and 4,140 completed the questionnaire. Responders who gave inadequate answers (n = 250) or did not state their sex (n = 13), were excluded from the analyses. The final sample consisted of 3,864 students (74%) (see Figure 4). Comparison of students who completed the questionnaire on the initial occasion with students who were absent at that time and completed the questionnaire up to three months later revealed no differences in antisocial behavior or alcohol use. However, the late responders presented higher levels of ADHD symptoms.

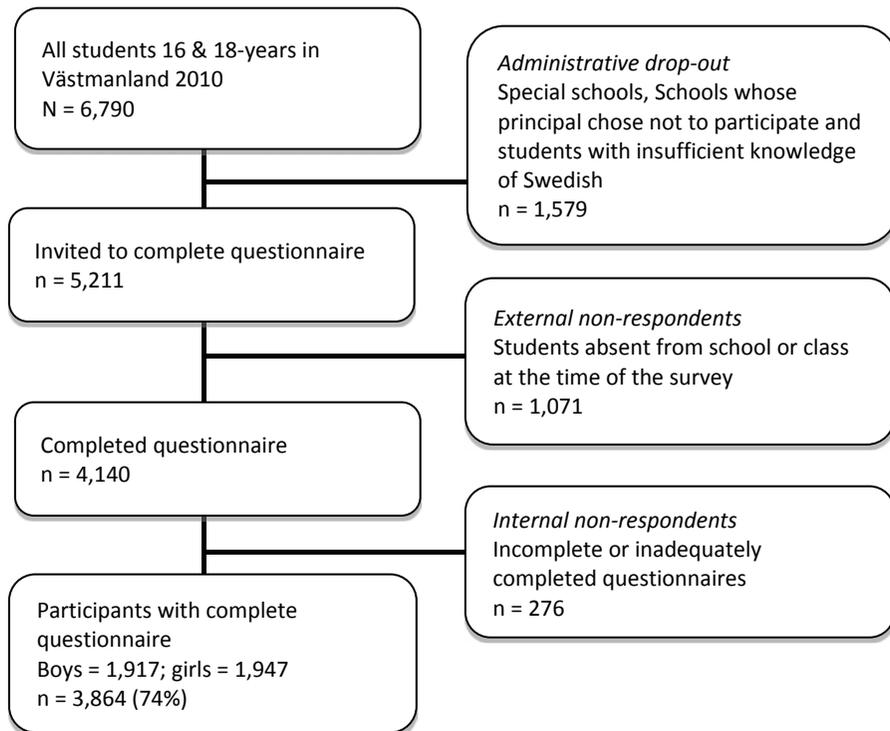


Figure 4. Flowchart of the study population in study III.

## Study IV

### **Step 1: Questionnaire**

In 2001, 5,542 individuals were registered as students in the 9<sup>th</sup> and 3<sup>rd</sup> grades in primary and secondary schools in Västmanland. All students attending class at the time of the survey were invited to participate. Students at special schools and schools in which the principal did not allow participation were not invited to participate in the study (n = 369). Thus, 5,173 students constituted the eligible population, and 4,260 (82%) completed the questionnaire (Figure 5).

### **Steps 2 and 3: In-depth interview and hair analysis**

Before completing the questionnaires in the classrooms, all students were invited to participate in a subsequent in-depth interview about drug habits and drug screening on a later occasion. The students willing to participate (n = 785) marked their interest by signing their personal code number on the questionnaire.

The participants answers were classified according to a risk index, based on alcohol- and drug-consumption risk behavior, and antisocial behavior, such as property and violent offences, as reported in the questionnaire. The students were categorized as exhibiting “high-,” “medium-,” or “low-risk” behavior. The risk index was created to ensure that those participants exhibiting low-risk behaviors were represented in the sample as well as those exhibiting high risk.

From the 785 students who marked their interest to participate in the forthcoming in-depth interview and hair analysis, 400 students, matched for age, sex, and weighted risk index behavior, were randomly selected. A stratification based on the risk behavior index was made within each age and sex group (hence four groups) by computer sampling software, inviting 33 individuals from < q1 (comprising the 25% in the lowest-risk group); 34 individuals from q1–q3 (comprising the 50% in the medium-risk group); and 33 individuals from > q3 (comprising the 25% in the highest-risk group). Of these, 81 boys and 119 girls agreed to participate in the interview and to give hair samples for drug screening. Hair samples were obtained for 193 individuals (44%).

Comparison of students who responded to the initial questionnaire, those who indicated their interest in being interviewed, and those who finally volunteered, indicated no significant differences in the risk index. Thus, the randomized individuals did not differ from the population in frequency and magnitude of risk behavior within each risk group. There was, however, an

overrepresentation of high-risk girls, compared with low- and medium-risk girls, in the final sample.

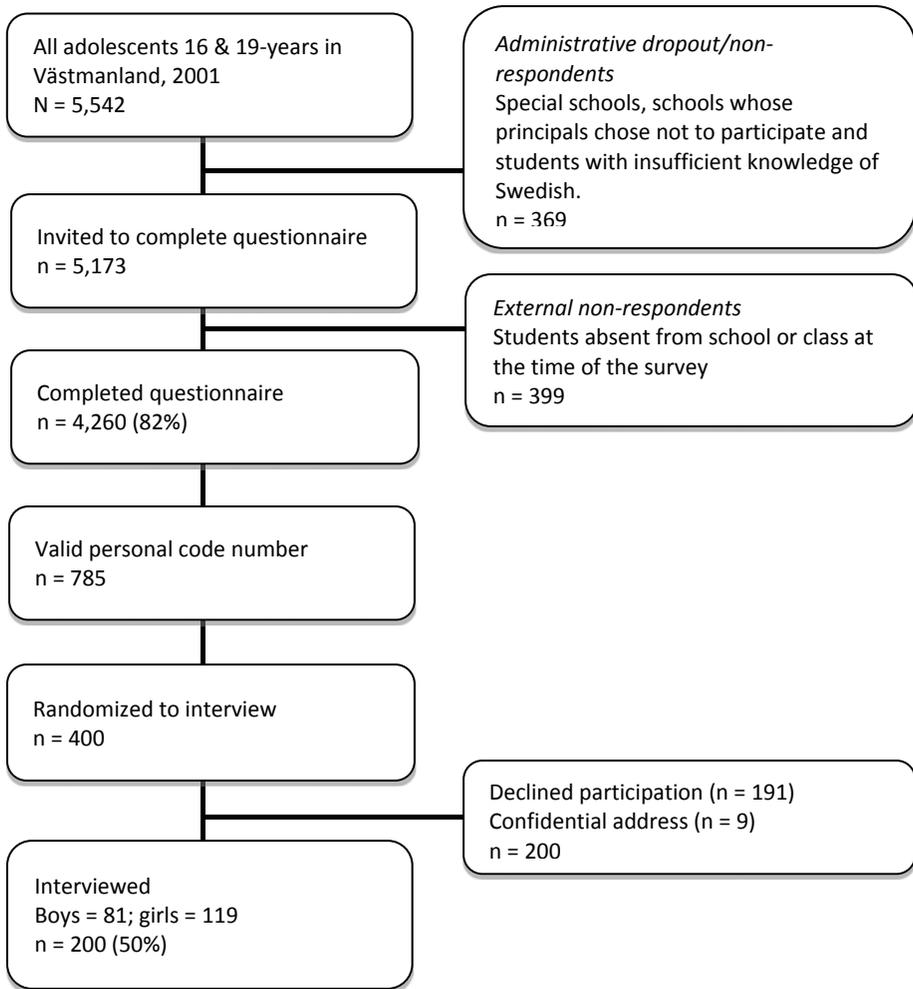


Figure 5. Flowchart of the study population in study IV.

## Procedure

### Study I

#### **Baseline**

One-half of the adolescents entering the misuse clinic during the 19-week period in 2004 were randomly selected and invited to participate in the study. The adolescents and their parents were informed about the study, and the families who agreed to participate, signed consent forms agreeing to share the information on health care, criminal convictions, and social insurance from national registers with the research team. Individual interviews were conducted individually with adolescents and each parent by two psychologists. All participants were guaranteed confidentiality of the information that they provided, with the exception of intentions to hurt themselves or others, or current experience of maltreatment. The participants and their parents were given a gift certificate worth 500 and 300 SEK, respectively, at a department store as compensation for their time and cooperation.

#### **Five-year follow-up**

In 2009 and 2010, approximately five years after the initial assessment, the participants were contacted by telephone and asked to participate in the follow-up study. Those who accepted signed consent forms again, agreeing to complete the questionnaires and interviews. The participants were given a gift certificate worth 500 SEK at a department store as compensation for their contribution.

### Study II

All adolescents who entered the three general psychiatric facilities between 2010 and 2014 completed the EPIQ. The patients and their parents were informed about the study by mail before their first visit and were reformed about the procedure during their appointment. The adolescent and each parent signed consent forms agreeing to complete the questionnaire and authorizing the research team to handle the information.

The EPIQ was distributed by a psychologist, a psychiatric social worker, a psychiatric nurse, or a psychiatrist specially trained for the procedure. The questionnaire took approximately 30–120 minutes to complete. All participants were guaranteed confidentiality of the information that they provided, with the exception of current experience of maltreatment, or intentions to hurt themselves or others.

## Study III

The students were asked to complete a mental and psychosocial health screening questionnaire, the Survey of Adolescent Life in Västmanland (SALVe). The questionnaire, information about the study, and instructions about how to complete the forms were sent to the schools by mail and then distributed to the students by their teachers during school hours. The teacher ensured that the questionnaire was filled out in private and not under the influence of peers. All students were informed that participation was optional and were guaranteed confidentiality of the information that they provided. Students who were absent from school on the initial distribution occasion were given the opportunity to complete the questionnaire up to three months later. All questionnaires were sent back to the SALVe study administration by the administrating teacher.

## Study IV

### **Step 1: Questionnaire**

The SALVe questionnaires were distributed to the students during school hours by a specially trained research assistant from the Centre for Clinical Research. The research assistant made sure that the questionnaire was filled out in private and not under influence of peers. All students were informed that their participation was optional and were guaranteed confidentiality of the information that they provided. The research assistant also informed them about the possibility of participating in the subsequent interview and hair analysis. Students who were absent from school on the initial distribution occasion were given the opportunity to complete the questionnaire up to three months later. Questionnaires from late responders were sent back to the Centre for Clinical Research by the student's teacher.

The 400 students who were invited to participate in the in-depth interview and hair analysis were contacted by a research assistant 3–6 months after completing the questionnaire. The 200 students who agreed to participate were again asked for informed consent at the interview appointment, consistent with the recommendations of the Human Ethical Committee of the Medical Faculty at Uppsala University

### **Step 2: In-depth interview**

All but two interviews were conducted by a PhD student from the Centre for Clinical Research, Västerås, Sweden. An interview guide was used, but the interview design was semistructured and permitted improvisation and specific follow-up questions. To facilitate participation and to accommodate the participants' needs for easy access and availability, the interviews were

held either in the school nurse's office or another community health department. The interviews were tape-recorded.

Two raters listened to 10% of the sample of audiotaped in-depth interviews. The inter-rater reliability was 1.0 (Cohen's  $\kappa$ ) for: used illicit drugs at the time of the questionnaire, and used any type of illicit drugs five times or more. Cronbach's alpha for number of times hashish/marijuana was used, number of times drugs other than hashish/marijuana were used, and time in months since last drug use was 1.0; and for quality of relation within the family 0.7.

### **Step 3: Hair analysis**

To perform the HS-SPME/GC-MS, the participants were asked by the interviewer to leave three small hair samples from different areas of the skull and were told that these would be analyzed for drug content. The crown of the head was used as the first site, and samples were then taken from behind the left ear and the middle of the neck. The sampling was guided and supervised by the interviewer. Five participants had no hair on their skull, but one of those had a long beard that was used for the sampling. A total of 196 participants gave hair samples. The hair samples were individually wrapped in aluminum foil, sealed, and forwarded to the National Board of Forensic Medicine, Department of Forensic Toxicology, University Hospital, Linköping, Sweden. However, three samples were of poor quality, and together with the four participants with no hair, a total of seven participants (3.5%) were excluded from hair analysis.

## **Measures**

### **Study I**

SUDs and other psychiatric disorders were assessed at baseline using the Kiddie-Schedule for Affective Disorders and Schizophrenia for School-Aged Children-Present and Lifetime Version (K-SADS-PL) [126] and the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) [127]. In addition, psychosocial variables were measured. At five-year follow-up, SUD and treatment for substance use and other mental problems were assessed.

### **Study II**

Alcohol risk use, psychiatric symptoms, and psychosocial variables were assessed using the EPIQ. Data were transformed into dichotomous units

based on clinical cutoffs. Psychiatric symptom domains and psychosocial risks were coded as present if they exceeded the cutoff.

### Study III

Alcohol use, symptoms of ADHD, and antisocial behavior were assessed using the SALVe and were transformed into a summation index. In addition, symptoms of depression and psychosocial variables were measured.

### Study IV

In step 1, illicit drug use and psychosocial variables were assessed using the SALVe. In step 2, illicit drug use was reported during the in-depth interview, and in step 3, traces of illicit drugs in the hair were examined with HS-SPME/GC-MS analysis.

### Substance use

#### **SUDs**

In study I, alcohol use disorder, drug use disorder and combined alcohol and drug use disorders in participants 17 years or younger were assessed using the K-SADS, while participants 18 years or over were assessed using the SCID.

#### **Alcohol risk use**

In study II, the first three items in the Alcohol Use Disorders Identification Test (AUDIT-C) self-report questionnaire [128] were used to measure alcohol risk use:

1. How often, during the last three months, have you had a drink containing alcohol?
2. How many units of alcohol do you drink on a typical day when you are drinking?
3. How often do you have 6 or more units on a single occasion?

Adolescent alcohol use differs from the use patterns of adults. To catch better the adolescent pattern of use, the answer alternatives were slightly modified, by adding an extra answer alternative to the first and last questions: once every two months or more seldom. The three items generate a range of 0–14 points. Compared with the full 10-item form, the adolescent version of AUDIT-C has previously generated reports of Cronbach's alpha coefficient of .95 and a Spearman's  $r$  correlation coefficient of .96, plus a high correlation ( $r=.733$ ) with alcohol-related problem behavior [129-131].

As suggested by Kelly et al. [132], alcohol risk use was defined as present if symptoms exceeded a cutoff point of six for males and five for females.

### **Alcohol use**

In study III, as in study II, the degree of alcohol consumption was measured using the first three questions on the modified version of AUDIT-C. A summation index with a range of 0–15 was created.

### **Drug use**

In study IV, the participants were asked the following questions in the questionnaire in step I:

1. Have you ever used narcotics?
2. How many times have you used hashish/marijuana?
3. How many times have you used other narcotics?
4. What narcotics have you ever tested/used?

Possible answers for question (1) were yes/no. For questions (2) and (3), the answer alternatives were: never, once, 2–4 times, 5–10 times, 11–20 times, 21–50 times, and more than 50 times. For question (4), the answer alternatives were: have never used narcotics, have used hashish/marijuana, amphetamine, cocaine, morphine/heroin, ecstasy, and others.

In step 2, in the in-depth interview, the participants were given a list with the formal and street names of the most commonly used illicit drugs in Sweden at that time. Two questions were posed to all participants:

1. Have you ever heard of any of these drugs?
2. Have you ever used any of them?

The interview protocol had not defined specific follow-up questions in advance. However, if the participant admitted illicit drug use during the interview, the interviewer was obligated to try to retrieve information about the time of the first use, the frequency of use, and the time since last use.

In step 3, hair analysis was used to detect illicit drug use. To examine possible traces of illicit drug accumulated in the hair, the interviewer sent the hair samples to the Department of Forensic Toxicology in Linköping for analysis with the HS-SPME/GC–MS. The analysis for hashish/marijuana was performed as previously described by Nadulski and Pragst [133], while analysis for amphetamine, cocaine, morphine/heroin, and ecstasy was performed as previously described by Kronstrand et al. [116].

### **Substance misuse in family**

In study I, parental SUDs were assessed using the SCID-I. In cases where one parent did not participate in the study, the other parent reported (14 fathers, and 78 mothers) on the absent parent's SUDs using the Family Interview for Genetic Studies [134]. In study III, substance misuse in the family was defined as the participant's reporting that anyone in the family had ever experienced a problem with alcohol or narcotics.

## Psychiatric symptoms

### **Psychiatric disorders**

In study I, presence of mood, anxiety, or conduct disorder in participants 17 years or younger was measured using the K-SADS-PL. Fifteen interviews were rated by another clinical psychologist, and inter-rater reliability ranged from  $\kappa=.76$  to  $.92$ . Disorders in participants over 18 years were assessed using the SCID-I. Inter-rater reliability, analyzed on 12 cases, ranged from  $\kappa=.82$  to  $1.0$ .

### **Symptoms of ADHD**

In studies II and III, the Swedish version of the World Health Organization ADHD Self-Report Scale for Adolescents (ASRS-A) was used to measure symptoms of ADHD during the previous six months [135]. The ASRS-A consists of 18 items and is composed of two subscales: inattention and hyperactivity-impulsivity. As recommended by Kessler et al. [136], a cutoff point of  $\geq 9$  was used in study II. This cutoff has previously generated a sensitivity of 79% and a specificity of 60% in an adolescent clinical population [135]. To analyze separately the subdimension of ADHD in study III, the symptom reports were summed as follows: inattention (range 0–36 points), hyperactivity (range 0–20 points), and impulsivity (range 0–16 points).

### **Symptoms of depression**

In studies II and III, an adolescent version of the Depression Self-Rating Scale (DSRS) [137] was used to measure symptoms of depression during the previous two weeks. The DSRS (22 items, range 0–19 points) is based on the DSM-IV criteria A and C for major depression [137]. Depression in adolescence is defined as either irritable or dysphoric mood [127], and as in previous studies [138], an additional question about irritability was built in. Earlier studies of the DSRS have reported instrument sensitivity of 86.3% and specificity of 75.0% for major depression in an adult psychiatric population [137]. In study III, a summation index with a range of 0–19 was created for the number of symptoms.

### **Symptoms of anxiety**

In study II, the Spence Children Anxiety Scale (SCAS) was used to measure current symptoms of anxiety, (45 items, range 0–135 points) [139]. To detect clinically significant levels of anxiety symptoms in the study population, a cutoff score of 33 was applied for both sexes. The cutoff was based on receiver operating characteristic analysis using scores from adolescent patients in general psychiatric care facilities in Västmanland and generated both sensitivity and specificity measures of 90% [140].

### **Symptoms of eating disorders**

In study II, present symptoms of anorexia nervosa were measured by three questions (range 0–3 points). If at least two of the following criteria were met, the anorexia nervosa symptom domain was defined as present:

1. Are you trying to weigh less than others your age that are as tall as you?
2. Do you have an intense fear of becoming fat even though you weigh too little?
3. Is your weight or body shape more important for your self-esteem than other things in life?

Present symptoms of bulimia nervosa were measured by four questions (range 0–4 points). If at least two of the following criteria were met, the bulimia nervosa symptom domain was defined as present:

1. Is your weight or body shape more important for your self-esteem than other things in life?

Have you, at least twice a week for three months:

2. Had periods of binge eating, eating too much, and losing control?
3. Vomited, or used laxatives or other medications because you ate too much?
4. Fasted or exercised excessively because you ate too much?

### **Antisocial behaviors**

#### **Criminality**

In study I, information on criminal convictions of the adolescents and their parents was obtained from records at the Swedish National Council for Crime Prevention (Brottsförebyggande rådet). Violent crime was defined as having a conviction for: attempted or completed homicide or manslaughter, criminal negligence causing death, assault or aggravated assault, arson or aggravated arson, robbery or aggravated robbery, kidnapping or stalking, harassment, unlawful threats, rape or aggravated rape, sexual assault, sexual

molestation or sexual abuse of minors, incest, or procuring and child pornography crimes. Nonviolent crime was defined as having a conviction for any other felony in the Swedish penal code.

### **Antisocial behaviors**

In studies I, II and III violent and nonviolent antisocial behavior was measured using a self-rating questionnaire [141]. Participants were asked about the frequency of delinquent and violent behavior. The answers were coded as: never (0), once (1), 2–4 times (2), 5–10 times (3), and more than 10 times (4). The questionnaire is similar to other validated self-reports [142] and is used in other studies [88, 101]. The choice of questions differs slightly between the studies, and an asterisk (\*) indicates the studies in which the specific question was included.

Have you:

1. taken goods in a store, shop, or kiosk without paying; (\*I,II,III)
2. been caught by the police for something that you did; (\*I,II,III)
3. deliberately smashed or wrecked windows, streetlights, benches, gardens, etc.; (\*I,II,III)
4. without permission painted graffiti on, or scrawled on, for example, a public wall; (\*I,II,III)
5. stolen a bike; (\*I,II,III)
6. threatened or forced someone to give you money, cigarettes, or anything else; (\*I,II,III)
7. been involved in a fight; (\*I,II,III)
8. carried tear gas, pepper spray, or similar items at school, or during your leisure time; (\*I,II,III)
9. carried a weapon (knuckle-duster, baseball bat, knife, switchblade, or similar) at school or during your leisure time; (\*I,II,III)
10. stolen a car; (\*I,II,III)
11. stolen a moped, motorbike, or motor scooter; (\*I,II,III)
12. hit or kicked someone so hard that he/she needed medical attention; (\*I,II,III)
13. deliberately hurt someone with a knife, switchblade, knuckle-duster, or similar; (\*I,II,III)
14. by yourself coerced another person to do something that he/she did not want to do; (\*I, II, III)
15. avoided paying (at the cinema, in a coffee chop, train, bus, or similar); (\*I,II,III)
16. stolen something from a car; (\*I,II,III)
17. entered a home, store, kiosk, storage, or other building with the intention to steal something; (\*I,II)
18. bought or sold something that you knew or believed was stolen; (\*I,II)
19. stolen something from someone's pocket or bag; (\*I,III)

20. played with fire and started a real outbreak of fire; <sup>(\*II)</sup>
21. played violently with animals where the animal got hurt; <sup>(\*II)</sup>
22. together with others coerced another person to do something that he/she did not want to do; <sup>(\*II)</sup>
23. driven a moped, motorbike, or car while drunk; <sup>(\*II, III)</sup>
24. had sex with someone against his/her will; <sup>(\*III)</sup>
25. taken money at home that did not belong to you? <sup>(\*III)</sup>

## Treatment

In study I, treatment for substance use and for other mental problems was measured using the SCID-I and the semistructured Life History Calendar interview [143]. Participants reported on treatment for substance use problems and other mental disorders received since baseline measures.

## Victimization

### **Physical abuse by parents**

In study I, physical abuse by parents was measured using the Conflict Tactics Scales: Parent–Child [144, 145]. The questionnaire was individually completed by the adolescent and each parent. If one parent chose not to participate in the study, the other parent reported on the absent parent's behaviors. Physical abuse during the participant's lifetime was defined as present if any of the following were reported: hit with a fist or kicked hard, hit on a part of the body other than the bottom with a hard object, thrown or knocked down, grabbed around the neck and choked, beaten up, hit repeatedly very hard, burned, or threatened with a gun or knife. In studies II, III and IV, physical abuse was defined as the participant's reporting that any form of violence, including pushing and beating, was inflicted by parents on the participant.

### **Psychological abuse**

In study I, psychological abuse at any time in life was defined as the participant's reporting being: left at home alone when inappropriate, not provided with adequate emotional support, not provided with food or medical assistance when needed, or parent being too drunk or high to provide supervision or assistance. In studies III and IV psychological abuse by parents was defined as the participant's reporting on psychological maltreatment, including being taunted or scorned by parents.

## Experience of sexual abuse

In study I, experience of sexual abuse was measured with the questionnaire Sexual Experience Survey [146] and was defined as either a parent's or the adolescent's reporting any experience in which a participant was forced to have sex against her/his will by a person in position of authority, by offering alcohol or drugs, or by physical violence. In study II, sexual abuse was defined as present if the question "Has anyone ever had sexual intercourse (vaginal, oral, or anal) with you, against your will" was answered affirmatively.

## Victimization by peers

In study I, victimization was defined as the participant's reporting being attacked unprovoked, kicked in the head while lying on the ground, threatened with weapons, forced to hand over money, a cell phone, cigarettes, or other things, called bad things, made fun of or teased, assaulted, or ostracized by peers within six months prior to the interview. In study III, victimization was defined as the participant's reporting being hit, kicked, exposed to other violence, called bad names, lied about, backbitten, or ostracized by peers at least once a year.

## Family factors

### **Ethnicity**

Studies III and IV: Was the participant or at least one parent born outside Scandinavia?

### **Separated parents**

Studies II, III and IV: Did the participant's parents live together?

### **Family finances**

Study I: Did the participant's family receive income support? Poverty was defined as the participant's family having received social welfare payments for at least 3 months during the period 1990–2004, because of low income. Information on payments was obtained from the Swedish Social Insurance Administration. Study IV: Did the participant rate his/her family's financial economy as good, or stretched?

### **Family socioeconomic status**

Study III: How did the participant rate his/her family's socioeconomic status? The participant was asked to compare his/her family with the rest of society and to rate the family's socioeconomic status on a seven-point Likert

scale. Ratings one standard deviation below the mean defined the socioeconomic status of the family as low.

### **Family residence**

Studies III and IV: Did the participant live in a single-family or multifamily house?

### **Parental employment**

Study III: Was at least one parent unemployed during the past year?

### **Parental verbal conflict**

Study III: Did the participant report severe, heartrending quarrels between his/her parents, at least once every month?

### **Parental physical conflict**

Study III: Did the participant report any form of violence, including pushing and beating, between his/her parents, at least once a year?

### **Family functioning**

Study IV: Did the participant report the presence or absence of traumatic family conflict?

### **Parental education**

Study IV: Had the participant's parents attended comprehensive school or upper secondary school or higher?

## **Statistics**

### **Study I**

Analyses were completed in three steps. In the first step, univariate logistic regressions were run to identify possible associations between predictors assessed at baseline and alcohol use disorder, drug use disorder, and combined alcohol and drug use disorders at follow-up. Predictors with significant associations were entered into a multivariate logistic regression model. One model included family factors, another model the individual factors, and a final model included the significant variables from the two preceding models, thereby identifying baseline factors that were independently associated with outcomes. Interaction of each factor with sex was tested.

In the second step, the final model was adjusted for baseline alcohol use disorder, drug use disorder, and combined alcohol and drug use disorder, and

in the third step, the final model was adjusted for treatment for SUDs and treatment for other mental disorders during the follow-up period.

## Study II

Multivariate binary logistic regression was performed to identify possible associations between the number of psychiatric symptom domains and alcohol risk use. The distribution of data was severely skewed; therefore, the associations between alcohol risk use and number of psychiatric symptom domains were analyzed using negative binomial regression. Comparisons of alcohol risk use, psychiatric symptom domains, and psychosocial risk between boys and girls were calculated with chi-square significance tests.

## Study III

Initially, univariate associations between covariates, ADHD subdimensions, antisocial behavior, and the dependent variable of alcohol use were calculated with ordinary least square linear regression analyses to determine their relevance to alcohol use.

These analyses were followed by a two-step multivariate regression model where the first step analyzed independent associations between inattention, hyperactivity, and impulsivity adjusted for covariates, and in the second step, these associations were additionally adjusted for antisocial behavior. The two-step multivariate regression analysis was performed to evaluate whether the associations between ADHD subdimensions and alcohol use changed when antisocial behavior was adjusted for.

Indirect analysis was conducted to test statistically for change in the two-step regression. The indirect effect of antisocial behavior for the association between each ADHD subdimension and alcohol use was evaluated, while covariates and the other ADHD subdimensions were adjusted for. Finally, moderating effects presented as interaction term effects between ADHD subdimensions and antisocial behavior in relation to alcohol use were calculated.

## Study IV

Chi-square significance tests were used to analyze differences between the answers in the questionnaire and the hair analysis, in relation to the in-depth interview, and disagreements in answers in relation to sociodemographic factors. To measure the degree of agreement between the different methods of measuring drug consumption, Cohen's kappa was applied. To investigate the relation of answers within subjects, taking similar and dissimilar pairs

into account, Gamma correlation was used. Sensitivity and specificity were also calculated.

## Ethics

In all four studies, participation was voluntary, and the participants were informed about the possibility of dropping out at any stage without further explanation. The patients in clinical studies I and II were assured that withdrawing would not affect their care and treatment in any way.

All four studies asked about private and possibly sensitive matters. Questions about sexual abuse, victimization, neglect, and suicidal behavior might have affected the participants in a negative and offensive way. In clinical studies I and II, the participants were in the hands of experienced professionals who had both the time and the opportunity to give adequate support or to direct the participants to appropriate help, including access to psychiatric emergency facilities. In studies III and IV, the questionnaire was completed during school hours under the supervision of a teacher and a research assistant, respectively. In these cases, traumatized individuals were not given opportunity to vent their emotions within the research protocol. In study IV, the interview situation in step 2 gave participants the opportunity to explore possible harm to themselves and others, and to discuss unfavorable home conditions. In one case, contact was initiated with health care professionals regarding care for a participant with suicidal tendencies.

### Study I

Each wave of data collection was approved by the Karolinska Institute Research Ethics Committee Nord and the Regional Board for Research Ethics in Stockholm. (Diary number: 2008/1934-31/3).

### Study II

The study was approved by the Regional Ethical Review Board at Uppsala University. (Diary number: 2008-214).

### Study III

The study followed the Swedish Guidelines for Social Sciences and Humanities Studies in accordance with the ethical principles of the Helsinki Declaration of 1975, as revised in 1983.

## Study IV

The study was approved by the Human Ethics Committee of the Faculty of Medicine of Uppsala University (Diary number: 2000-325).

# Results

## Study I

Five major findings emerged from the present study: (1) SUDs present in mid-adolescence were highly comorbid with psychiatric disorders and psychosocial risk factors; (2) SUDs present in mid-adolescence were in most cases also present in early adulthood; (3) despite extensive clinical assessments, there were few factors in mid-adolescence associated with SUDs five years later; (4) treatment displayed limited effect on curbing the SUDs; and (5) there were few gender differences.

(1) In the sample of adolescents who sought treatment at the misuse clinic in 2004, 90% of the girls and 81% of the boys presented with at least one mental disorder, and on average, the adolescents were diagnosed with three mental disorders. Notably, most of these disorders preceded the substance misuse. Among the adolescents who participated in the follow-up study, mood disorders were reported by 13% of the boys and 19% of the girls, and 10% of the boys and 42% of the girls were diagnosed with anxiety disorders, while conduct disorder was present in almost 50% of the boys and 31% of the girls. Furthermore, reports of psychosocial adversities were frequent; 48% of the boys and 52% of the girls reported physical abuse by parents, and 10% of the boys and 45% of the girls reported experiences of sexual abuse. Violent offences were reported by 68% of the boys and 45% of the girls.

(2) Five years after seeking treatment for substance misuse, SUDs were present in about one-half of the participants. When comparing the prevalence of disorders in mid-adolescence with disorder presence in early adulthood, there was little difference. Table 3 shows the persistent nature of the disorders at a group level. However, analyzing the participants presenting with SUDs only at baseline, but not at the five-year follow up, a treatment success rate of 35% emerged.

Table 3. Alcohol use disorder (AUD), drug use disorder (DUD) and combined alcohol and drug use disorder (AUD+DUD) in boys and girls at first contact with the clinic and at five-year follow-up.

Substance use disorder	Boys n(%)		Girls n(%)	
	Baseline	Follow-up	Baseline	Follow-up
AUD	29 (47.5)	28 (45.9)	36 (41.9)	35 (40.7)
DUD	18 (29.5)	29 (47.5)	24 (27.9)	21 (24.4)
AUD+DUD	14 (23.0)	19 (31.1)	13 (15.1)	15 (17.4)

Figure 6 presents the numbers of participants with SUDs at follow-up as a function of the disorders present at baseline. The figure shows that only 20 of the 60 participants with alcohol use disorder at follow-up, 14 of the 50 with drug use disorder at follow-up, and 8 of the 34 with combined alcohol and drug use at follow-up had not presented with SUD at baseline.

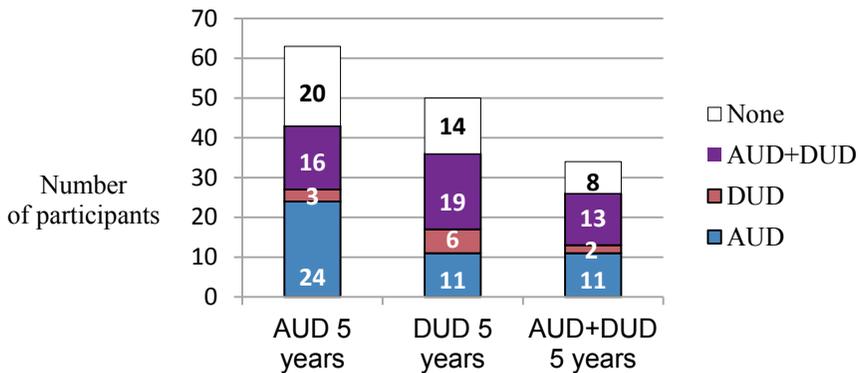


Figure 6. Number of participants presenting with alcohol use disorder (AUD), drug use disorder (DUD) and combined alcohol and drug use disorder (AUD+DUD) five years after first contact with the clinic, as a function of substance use disorders at baseline.

(3) Boys presenting with alcohol use disorder in mid-adolescence had a ninefold increase in the risk of developing an alcohol use disorder five years later (OR = 9.37, 2.91–30.16), but this did not hold for females (OR = 2.38, 0.98–5.75). Having a drug use disorder in mid-adolescence was associated with a fourfold increased risk of DUD five years later among boys (OR = 4.39, 1.32–14.60), and an almost sixfold increase among girls (OR = 5.89, 2.02–17.13). Having combined alcohol and drug use disorder in mid-adolescence was associated with a fourfold increase in risk for the same

disorders five years later among both boys (OR = 4.36, 1.24–15.32) and girls (OR = 3.94, 1.07–14.47).

Besides the predicting influence of baseline SUD, there was a more than eightfold increased risk for girls with mothers with alcohol use disorders to present with the same disorder themselves after five years (OR = 8.37, 1.90–36.99). See the interaction by sex explained in Figure 7. Experience of victimization by peers increased the risk by almost three times for alcohol use disorder (OR = 3.86, 1.71–8.68). Committing nonviolent crime was marred by a fourfold increased risk for alcohol use disorder (OR = 4.07, 1.18–14.05) and by an eightfold increased risk for combined alcohol and drug use disorder (OR = 8.07, 1.04–62.85) at follow-up.

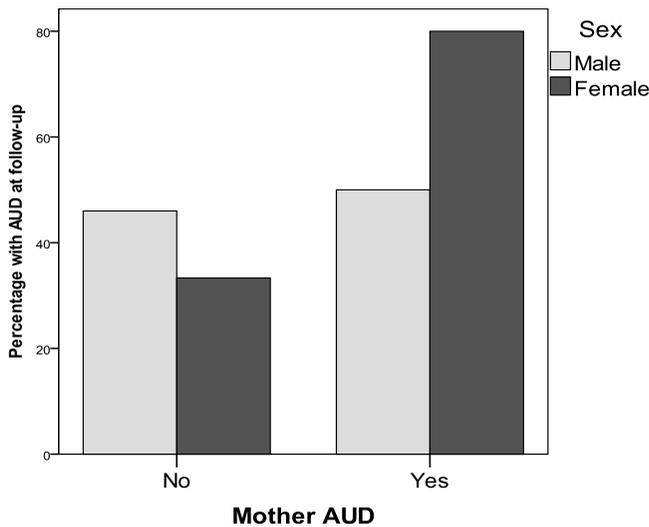


Figure 7. Comparison of percentages of boys and girls presenting with alcohol use disorder at five-year follow-up as a function of mother's alcohol use disorder.

(4) Fifty-two percent ( $n = 76$ ) of participants received treatment for SUDs, and 71% ( $n = 85$ ) received treatment for other psychiatric symptoms during the follow-up period. However, prediction models detected no positive effect of treatment in limiting the persistence of these disorders. In fact, receiving treatment for SUD increased the risk for drug use disorder at follow-up by six times (OR = 6.34, 2.79–14.43) and increased the risk for presenting with combined alcohol and drug use by 2.5 times (OR = 2.46, 1.07–5.63).

## Study II

The study generated four main results: (1) Alcohol risk use was presented by one-fifth of the participants, making it the fourth most common symptom domain; (2) prevalence and probability of presenting alcohol risk use increased with the presented number of symptom domains; (3) prevalence of alcohol risk use was highest among participants that reported antisocial behaviors and experience of sexual abuse; and (4) among participants reporting alcohol risk use, the psychiatric symptom domains of depression, anxiety, and ADHD were the most prevalent.

(1) Alcohol risk use was reported by 177 participants (19.7%), making it the fourth most common psychiatric condition in the sample. Depression and anxiety were the most frequent psychiatric symptom domains, followed by symptoms of ADHD. There was no difference in alcohol risk use between boys and girls. However, girls reported more psychiatric symptoms and a higher incidence of sexual abuse than boys, while boys reported higher frequencies of antisocial behaviors.

(2) As seen in Figure 8, alcohol risk use increased with the reported number of symptom domains. Among participants reporting no symptom domains, 8% reported alcohol risk use, whereas all of the participants reporting six symptom domains reported alcohol risk use.

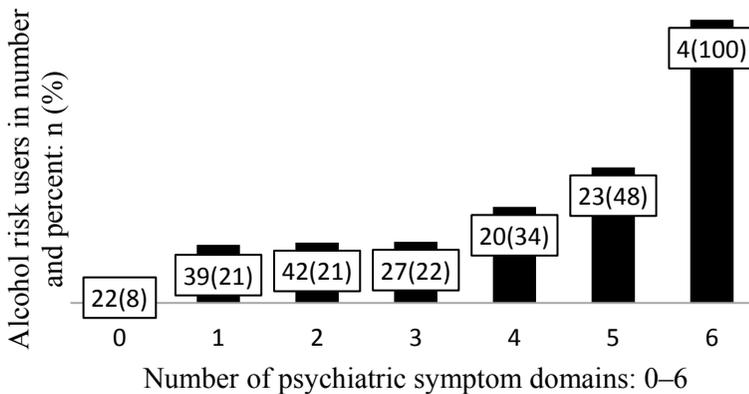


Figure 8. Frequency and prevalence of alcohol risk use among participants in relation to the number of psychiatric symptom domains.

The strength of the observations displayed in Figure 8 was analyzed with binomial logistic regression, which partially confirmed the observed pattern. Table 4 shows that the probability of presenting with alcohol risk use increased as a function of the number of symptom domains. Furthermore, turning the model around to treat the number of symptom domains as a dependent variable and alcohol risk use as the predictor in negative binomial regression analysis indicated that the presence of alcohol risk use increased the probability of reporting symptom domains (OR = 1.505, 1.225–1.854).

Table 4. Binomial logistic regression model analyzing associations between the number of psychiatric symptom domains and alcohol risk use. Standardized regression coefficient, *p*-value, and explained variance are displayed in the model, adjusted for psychosocial risks.

Number of symptom domains	<i>p</i>	OR	95% CI	
			Lower	Upper
1	≤ .001	2.848	1.618	5.013
2	≤ .001	2.881	1.645	5.045
3	.002	2.693	1.441	5.031
4	≤ .001	5.215	2.579	10.545
> 5	≤ .001	9.122	4.430	18.781
Nagelkerke, R <sup>2</sup> = .149				

(3) As seen in Figure 9, among participants reporting antisocial behaviors, 60% also reported alcohol risk use, while only 30% of the participants with alcohol risk use reported antisocial behaviors. The same pattern applied for the experience of sexual abuse.

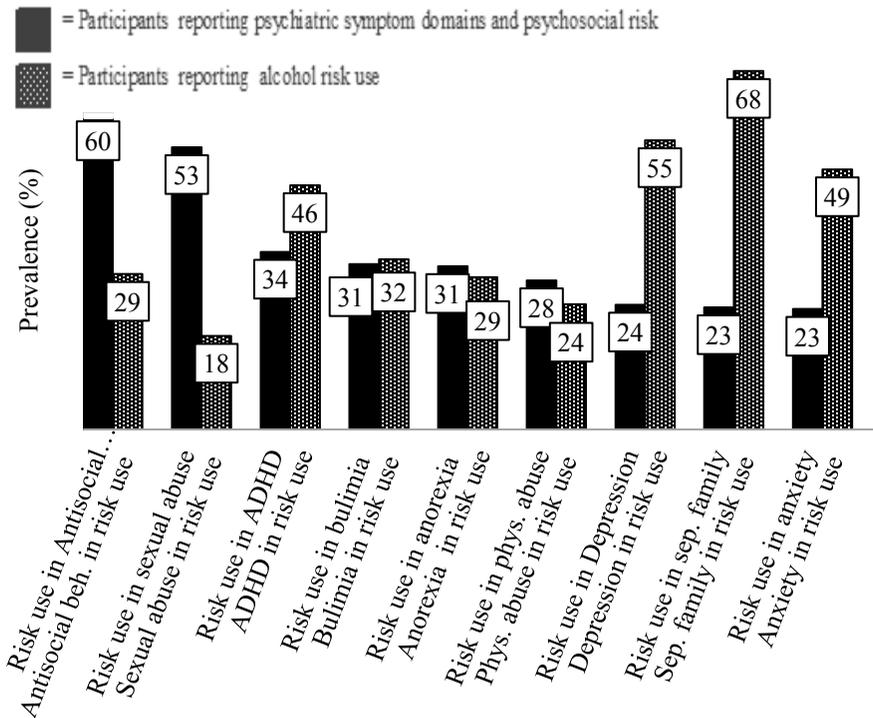


Figure 9. Frequency of alcohol risk use among participants with psychiatric symptom domains and psychosocial risk, compared with frequency of psychiatric symptom domains and psychosocial risk among participants with alcohol risk use.

The majority of participants with alcohol risk use also presented with depressive symptoms, while only 25% of the depressed participants reported concurrent risk use (Figure 10). The same pattern applied for the anxiety and ADHD symptom domains.

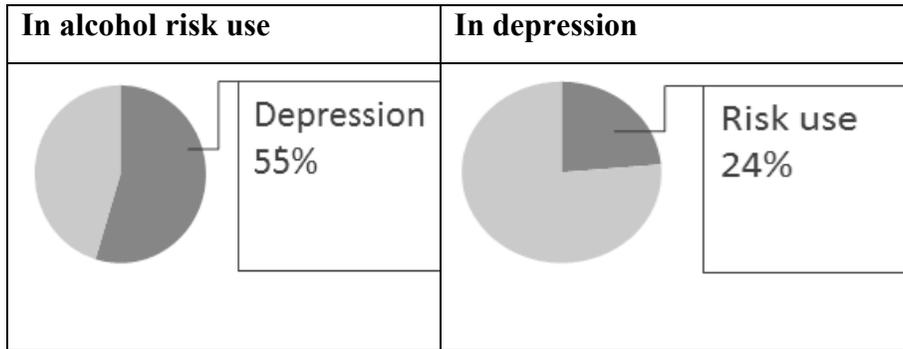


Figure 10. Proportion of participants with alcohol risk use who reported depression, and proportion of participants with depression who reported alcohol risk use.

### Study III

There were four main findings for this study: (1) Except for girls' symptoms of inattention, subdimensions of ADHD symptoms were not associated with alcohol use when antisocial behavior was accounted for; (2) the associations that became non-significant between hyperactivity, impulsivity, and alcohol use for boys and girls when antisocial behavior was adjusted for, indicated an overlap between hyperactivity, impulsivity, and antisocial behavior; (3) a moderating effect of antisocial behavior on the association between impulsivity and alcohol use was found among boys, suggesting a weaker association between impulsivity and alcohol use among those with high levels of antisocial behavior; and (4) symptoms of inattention displayed independent association with alcohol use among girls even when antisocial behavior was adjusted for, pointing to a direct pathway between symptoms of inattention and alcohol use in girls.

(1, 2, & 4) Multivariate regression analysis was performed in two steps as displayed in Table 5. The first step analyzed associations between inattention, hyperactivity and impulsivity, and alcohol use, adjusted for covariates. In the second step, these associations were adjusted for antisocial behavior. For boys, in the first step, inattention and impulsivity displayed positive associations with alcohol use, but after including antisocial behaviors in the model, these associations disappeared. For girls, in the first

step, all three subdimensions of ADHD symptoms were positively associated with alcohol use, but after adjusting for antisocial behavior, only effect of inattention symptoms remained significant.

Table 5. Multivariate regression models analyzing associations between symptoms of ADHD subdimensions and alcohol use. Standardized regression coefficients,  $p$ -values and explained variance are displayed first unadjusted, and then adjusted for antisocial behavior.  $\beta$  values with significant associations are presented in bold.

Symptoms	Boys' alcohol use				Girls' alcohol use			
	Un-adjusted		Adjusted for antisocial behavior		Un-adjusted		Adjusted for antisocial behavior	
	$R^2=$		$R^2=$		$R^2=$		$R^2=$	
	$\beta$	$p$	$\beta$	$p$	$\beta$	$p$	$\beta$	$p$
Inattention	.045	.139	.040	.160	<b>.096</b>	.001	<b>.086</b>	.002
Hyperactivity	<b>.096</b>	.002	.055	.062	<b>.087</b>	.003	.140	.142
Impulsivity	<b>.064</b>	.022	.043	.103	<b>.067</b>	.007	.030	.210
Antisocial behavior	–	–	<b>.357</b>	.000	–	–	<b>.336</b>	.000

(3) Antisocial behavior not only reduced the strength in associations between alcohol use and the subdimensions of ADHD symptoms but likewise moderated the associations. The results of the interaction analysis are presented in Table 6. In boys, antisocial behavior moderated the association between symptoms of impulsivity and alcohol use, proposing weaker associations among boys with high antisocial behavior, compared with boys presenting with low antisocial behavior.

Table 6. Interaction term effects between ADHD subdimensions and antisocial behavior in relation to alcohol use. Standardized regression coefficients, *p*-values, and explained variance are displayed.  $\beta$  values with significant interaction term effects are presented in bold.

Symptoms	Boys' alcohol use		Girls' alcohol use	
	$\beta$	<i>p</i>	$\beta$	<i>p</i>
Inattention × Antisocial behavior	.019	.543	-.038	.239
Hyperactivity × Antisocial behavior	-.011	.742	-.034	.368
Impulsivity × Antisocial behavior	<b>-.096</b>	<b>.001</b>	-.047	.096
<i>R</i> <sup>2</sup> change	0.8%	< <b>.001</b>	0.7%	< .001

## Study IV

There were three main findings for study IV: (1) Twice as many participants reported illicit drug use in the in-depth interview as in the questionnaire; (2) both questionnaires and in-depth interviews showed low sensitivity and high specificity; and (3) greater disagreement in answers between questionnaire and in-depth interview, and between hair analysis and in-depth interview, was detected among participants from less privileged socioeconomic circumstances.

(1) As shown in Table 7, out of the 46 participants who reported illicit drug use in the in-depth interview, only 24 admitted use in the questionnaire. Cohen's  $\kappa$  was low ( $\kappa = 0.559$ ,  $p < 0.001$ ). In contrast, out of the 24 participants who admitted illicit drug use in the questionnaire, 22 also reported their use in the in-depth interview. Analyses with Gamma correlation ( $\gamma$ ), which takes skewness into account, gave an association of 92% ( $\gamma = 0.972$ ,  $p < 0.001$ ), indicating a strong correlation with severe underreporting.

Traces of illicit drugs were detected in the hair of eight of the 18 participants who admitted using drugs during the last six months in the in-depth interview, and in seven of those who admitted no drug use ( $\kappa = 0.371$ ,  $p < 0.001$ ;  $\gamma = 0.860$ ,  $p = 0.011$ ). This indicates that the in-depth interview method, compared with both questionnaire and hair analysis, provided a better reporting rate in this sample.

Table 7. Frequencies of: (A) self-reported lifetime drug use in the questionnaire in relation to self-reported drug use in the in-depth interview; and (B) hair analysis in relation to self-reported drug use during the last six months in the in-depth interview.

Used	(A)		(B)	
	Questionnaire	In-depth interview	Hair analysis	In-depth interview
	n(%)	n(%)	n(%)	n(%)
Any illicit drugs	24 (12)	46 (23)	15 (8)	18 (9)
Hashish/marijuana	21 (11)	40 (20)		
Amphetamine	4 (2)	8 (4)		
Cocaine	1 (0.5)	1 (0.5)		
Morphine/heroin	2 (1)	0 (-)		
Ecstasy	1 (0.5)	6 (3)		

(2) As seen in the left column of Table 8, the sensitivity of the questionnaire compared with the in-depth interview for the use of any illicit drugs varied between 0.166 and 1.0 for the different classes of substances. For the use of cocaine, there was a full match between the two instruments, but this match was based on the data from only one participant. Conversely, the specificity was high, for both the use of all different classes of substances and for the use of any illicit drugs; the affirmative reports of illicit drug use in the in-depth interview were, to a large extent, also reported in the questionnaires. This indicated that the questionnaire resulted in accurate reports but was subject to underreporting. Comparison of the hair analysis and the in-depth interview regarding reports of any use of illicit drugs, generated low sensitivity and high specificity for the hair analysis. This suggests that the hair analysis did not erroneously classify negative findings of illicit drug use as positive but did miss cases of actual illicit drug use.

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Table 8. Frequencies of: (A) self-reported lifetime drug use in the questionnaire in relation to self-reported drug use in the in-depth interview; and (B) hair analysis in relation to self-reported drug use during the last six months in the in-depth interview.

<b>Used</b>	<b>(A) Questionnaire</b>		<b>(B) Hair analysis</b>	
	Sensitivity	Specificity	Sensitivity	Specificity
Any illicit drugs	0.478	0.987	0.389	0.953
Hashish/marijuana	0.475	0.988		
Amphetamine	0.375	0.995		
Cocaine	1.0	1.0		
Morphine/heroin	–	0.995		
Ecstasy	0.166	1.0		

(3) A higher proportion of participants reporting illicit drug use had a father who had attended only comprehensive school ( $p = 0.019$ ), a mother who had attended only comprehensive school ( $p = 0.002$ ), were living in a multifamily house ( $p < 0.001$ ), reported being financially stretched ( $p = 0.002$ ), and had experienced traumatic conflicts within the family ( $p < 0.001$ ). As shown in Table 9, there was also a sociodemographic pattern in the proportion of disagreement in reports of illicit drug use between the questionnaire and the in-depth interview, and between the hair analysis and the in-depth interview. Participants from less privileged sociodemographic circumstances had higher proportions of disagreement between their answers.

Table 9. Disagreement (percentages and  $p$ -values) between self-reported drug use in the in-depth interview and (A) self-reported drug use in the questionnaire; and (B) hair analysis, in relation to sociodemographic factors.

Sociodemographic factors	(A) In-depth interview/ Questionnaire		(B) In-depth interview/ Hair analysis	
	%	$p$	%	$p$
Scandinavian	13.4		24.1	
Non-Scandinavian	10.7	0.698	14.8	0.268
Father; $\geq$ upper secondary school	10.5		19.0	
Father; comprehensive school	20.8	0.068	34.8	<b>0.026</b>
Mother; $\geq$ upper secondary school	9.0		15.8	
Mother; comprehensive school	23.2	<b>0.007</b>	40.7	<b>&lt; 0.001</b>
Single family house	10.1		18.2	
Multifamily house	21.6	<b>0.035</b>	36.0	<b>0.010</b>
Nuclear family	8.2		15.1	
Separated parents	20.5	<b>0.012</b>	35.1	<b>0.001</b>
Non-stretched finances	11.9		18.7	
Stretched finances	18.8	0.291	48.1	<b>0.001</b>
No traumatic family conflict	8.9		12.3	
Traumatic family conflict	18.8	0.053	35.6	<b>&lt; 0.001</b>
No maltreatment in family	11.7		22.0	
Maltreated by family member	25.0	0.093	30.0	0.417

# Discussion

## Strengths and limitations

### Participants

#### **Selection, attrition and generalizability**

Studies I and II focused on participants in clinical settings. Study I invited participants from an adolescent substance misuse clinic in Stockholm, and study II participants were recruited at general adolescent psychiatric care facilities in the county of Västmanland. Using clinical populations from two different settings allows exploration of the phenomenon of comorbidity in a unique way, enabling a wide-angle perspective on the characteristics of adolescent substance use. Furthermore, study II recruited participants from general psychiatric care facilities in three different sites, generating a large number of participants (n = 960) displaying a broad range of psychiatric symptoms and psychosocial risk.

Study I had a relatively small sample of 180 participants at baseline and 147 at follow-up. The rather few significant associations between risk factors measured in adolescence, and the outcome of SUDs after five years, might be attributable to the small sample size causing a type II error of failing to detect a possible association. Another limitation of study I relates to the lack of information about whether treatment was an alternative to criminal prosecution or not.

It was not possible to say anything about the adolescents who chose not to participate in study II, as information about these individuals was not registered within the research protocol. It might be that the adolescents with the most severe problems did not participate in the study, and the results might not be completely generalizable to the entire spectrum of patients in psychiatric care facilities. Furthermore, the fact that the participants were recruited in a clinical setting might have affected their symptom reports. An individual who finally received a consultation at a substance use clinic or in a general psychiatric care facility might exaggerate his/her symptoms to ensure that he/she received the care needed. However, this behavior would be present among patients in the general clinical population and would therefore not affect the generalizability of results.

Studies III and IV recruited participants from schools in a county considered to be representative of Sweden, regarding distribution of rural and urban regions, and spread of educational, income and employment levels [147]. Consequently, the results generated in these large samples give an opportunity to generalize to other adolescent community populations in other parts of Sweden. However, adolescents that do not attend school might be the ones displaying the highest risk behaviors, including substance use [148]. Using a school sample might miss the experiences of these adolescents, which affects generalizability.

Study IV enrolled participants in three steps, and the attrition rate might be considered to be high. Of the 4,260 who completed the initial survey and were invited to participate in the study, 785 expressed an interest. Of these, 51% (n = 400) were invited to undergo interviews and hair analysis, and 200 agreed to participate. The attrition rate is considerable. However, there was never any intention to interview all 4,260 students who filled out the questionnaire, or to include all students who expressed an interest in participating in the interviews. After performing 200 interviews, no new information appeared, and thereby saturation was achieved. Furthermore, comparing those who responded to the initial questionnaire, those who marked their interest to participate in the interview, and those who finally participated in the in-depth interview and hair analysis study, there were no differences in the risk index; neither for drug or alcohol consumption, nor for any other antisocial behavior. This suggests that there was no major systematic bias introduced by the participants in the study.

## Design

Study I was not designed to have a comparison group, and it is therefore not possible to determine the nature of the relationship that these patients may have had with alcohol and drugs had they not received treatment at all. The treatment might have been lifesaving, but the only observable factor was that the number of SUDs in the sample was about as high as at first contact with the clinic.

The designs of studies II and III were cross-sectional and did not allow analysis of causality or conclusions about the direction of associations. Furthermore, these studies were based on data of symptoms, disallowing conclusions about disorders. Nevertheless, despite these limitations, important insights and conclusions related to diagnostic entities might be reached.

## Measures

### **The DSRS**

The DSRS was used in clinical study II and in community study III. Although the DSRS has not yet been validated in Swedish adolescent clinical or community populations, it has been used in adolescent populations [138], and shows good psychometric properties in adult clinical trials [137].

### **Symptoms of eating disorders**

In study II, present symptoms of anorexia nervosa were investigated using only three questions, and bulimia nervosa by four questions. These are relatively small numbers of questions for exploring such complex conditions, and the psychometric properties of the questions are unknown. Results from these measures should be interpreted with caution.

### **ASRS-A**

The ASRS-A was used in clinical study II and in community study III. Sonnby et al. used a cutoff point of  $\geq 9$ , as recommended by Kessler et al. [149] and found sensitivity of 77% and specificity of 60% in an adolescent population in general psychiatric care [135]. Despite the absence of documented psychometric properties described for adolescent community populations, the ASRS-A is widely used in such samples. Furthermore, the ASRS-A were not evaluated for differentiating between ADHD subdimensions, which might increase the risk of misclassification.

Furthermore, symptoms of depression and ADHD might be captured by both the ASRS-A and the DSRS, because of an overlapping clinical picture. In study III, there was an association between symptoms of inattention and alcohol use in girls, even after adjusting for antisocial behaviors. According to the literature of common co-occurring symptoms of ADHD and depression, the association might be due to symptoms of depression rather than symptoms of ADHD. However, symptoms of depression measured with the DSRS were adjusted for in the analyzes.

### **Cutoffs**

In study II, the term “symptom domain” was defined as a patient reporting a sum of symptoms over a clinically significant level. The clinically significant level was decided by cutoffs described in earlier works (i.e., the ASRS-A and the SCAS), or by symptom cutoffs (i.e., the symptom domain of depression where A and C criteria had to be met). The scales are attached with varying psychometric properties—for example, the SCAS had reported sensitivity and specificity of 90% [140], while the ASRS-A had sensitivity of 77% and specificity of 60% [135]—but in study II, they were considered

to have equivalent capacity to find and exclude individuals with and without clinically significant symptom levels.

### **Antisocial behaviors**

The instrument measuring antisocial behaviors has not yet been validated. However, the questionnaire is used before, and the internal consistency is good [88, 101]. The questions were based upon the DSM-IV criteria for conduct disorder and strongly resemble these criteria [127].

### **Hair analysis**

In the hair analysis, a maximum of six centimeters of hair was used, limiting the window of time for analysis to approximately six months. Of the 46 participants who admitted illicit drug use in the in-depth interview, only 18 reported using within the past six months. The low prevalence of admitted drug use within the six-month time-frame, caused a severely underpowered statistical comparison of detection rates between the different methods, and therefore none of the measures could be considered as a gold standard. However, the in-depth interview was used as a reference in the analyses, given the practice of the pipeline procedure that were added to it. The low amount of drugs found with the hair analysis method limits the opportunity to draw conclusions, and the study might be referred to as a pilot work, providing a foundation for further examination.

## **A persistent challenge at the misuse clinic**

The young people seeking treatment for substance use problems in study I displayed extensive psychiatric and psychosocial difficulties at baseline measures. Over 90% of girls and 80% of boys exhibited at least one other psychiatric disorder. On average, patients presented with three diagnosable psychiatric conditions, which in many cases preceded the substance use problems. The results from this sample confirm the etiology model [40, 41] regarding psychiatric symptoms as a risk factor for developing SUDs (Table 1). Comorbid mood, anxiety, and conduct disorders were common. Over 50% of the girls and almost half of the boys reported severe abuse by parents, and 45% of the girls reported experiencing sexual abuse, a number four times as high as that reported in a Swedish general population sample of the same age. This is a much burdened group of adolescents, who require a broad range of efforts addressing substance use, psychiatric symptoms, and psychosocial adversities. It is of great importance that information should be shared between authorities and institutions such as the social services, child and adolescent psychiatric care facilities, the police, and schools, and that they should cooperate to tailor proper treatment programs.

Approximately one-half of the study I sample presented with an SUD at baseline, and over one-half of the sample received treatment for SUDs during the follow-up period. In addition, 71% received treatment for other mental disorders. Although having received treatment during the follow-up period was one of the predictors for presenting with SUD after five years. However, the association can be partly explained by the fact that treatment was probably given to the most severe cases. In studies investigating treatment outcomes in samples with SUDs, the relapse rate usually vary between 60% during the first three months after treatment [150], to around 80% after one year [151]. However, the treatment given at the misuse clinic in study I displayed a success rate of 35%, despite the persistent nature of the disorders and the vast comorbidity. This indicates that the working method of integrated treatment is an important step in the right direction.

Interaction by sex analysis in study I indicated that girls, but not boys, who had a mother who presented with alcohol use disorder were eight times more likely to present with the same disorder themselves after five years. This is consistent with the results from review studies of Johnsson and Leff, and Lieberman, which claimed that children of parents with substance use problems are 2–10 times more likely to develop the same difficulties themselves [48, 83]. The interaction can be explained both by unfavorable environmental factors, such as acceptance of adolescent substance use or inadequate parenting styles, and by genetic predisposition [84, 85]. However, in study I, girls seemed to be especially vulnerable to maternal alcohol use. This is important, because more than 25% of the female participants had become mothers themselves by the five-year follow-up. Thus, given the fact that substance use, antisocial behavior, and other psychiatric symptoms often co-occur in families because of both shared genetic and environmental settings, prevention and treatment policies that adopt a multigenerational perspective might be useful.

## Alcohol risk use in general adolescent psychiatric care facilities

In study II, every fifth adolescent participant who sought treatment for psychiatric problems in general psychiatric care facilities reported alcohol risk use. Compared to normal population, the risk use prevalence was twice as high [36]. Prevalence and probability of presenting alcohol risk use increased with the reported number of psychiatric symptom domains. Conversely, the probability of presenting psychiatric symptoms increased among participants with alcohol risk use. The majority of participants with alcohol risk use also reported high prevalence of symptoms of depression,

anxiety, and ADHD. When analyzing the presence of alcohol risk use in these symptom groups, the prevalence was substantially lower. However, among adolescents reporting antisocial behaviors and experience of sexual abuse, the prevalence of alcohol risk use was high, compared with the prevalence of these conditions among adolescents with alcohol risk use. In sum, alcohol risk use is considerably comorbid with other psychiatric symptom domains, but the co-occurrence is not homogeneous. For example, features common among alcohol risk users, such as internalized symptoms of depression and anxiety, do not necessarily imply that alcohol risk use is common in these symptom clusters.

In study II, there was an overlap of alcohol risk use and sexual abuse among girls. The majority of the girls who reported experiencing sexual abuse also reported alcohol risk use, a pattern previously observed longitudinally in adolescent Norwegian girls [152]. However, in the group of girls who reported alcohol risk use, only 18% also reported being sexually abused. Study II used a cross-sectional design, so it was not possible to draw any conclusions about causality, but it was concluded that alcohol risk use and sexual abuse among girls co-occur frequently. This co-occurrence is important to address when treating trauma in psychiatric care facilities.

However, adolescent reports of substance risk use indicate co-occurring symptoms of depression, anxiety, and ADHD, and these conditions should then be screened for. Conversely, the results of study II indicate that when adolescents report antisocial behaviors or experiences of sexual abuse, they may also have co-occurring alcohol risk use. The screening procedure should occur regardless of the clinical setting; social services and general adolescent psychiatric care facilities should be able to provide the same basic tools for detection. The 83% of adolescents at the misuse clinic who reported having received treatment for psychiatric conditions other than substance use during the follow-up period probably received that treatment in facilities such as first-line psychiatric care, with the school psychologist or in general child and adolescent psychiatric care clinics. With further integrated treatment models, this comorbidity might be possible to hinder at an earlier stage.

## Special attention to externalizing behaviors

Antisocial behavior was reported by the vast majority of the participants in study I, and a similar pattern emerged in study II, where 60% of the adolescents who presented with alcohol risk use also reported antisocial behaviors. In study II, 46% of the clinical sample of adolescents with alcohol risk use also presented with clinically significant levels of ADHD symptoms. Almost 50% of the boys and 30% of the girls at the substance misuse clinic

were diagnosed with conduct disorder, which is unusually high compared with the prevalence in the general population (6.8%).

The results of study III showed that antisocial behaviors reduced the association between alcohol use and symptoms of inattention, hyperactivity, and impulsivity among boys, and symptoms of hyperactivity and impulsivity among girls. There was an association between alcohol use and inattention in girls, even in the presence of antisocial behaviors. Flory and coworkers suggested that ADHD symptoms seldom affected substance use on its own but almost always through the presence of antisocial behaviors [66], and the results of the present study are consistent with this suggestion, with the exception of girls reporting inattention problems. The etiology of substance use in relation to symptoms of ADHD and antisocial behaviors is complex, and different pathways to substance use have been suggested. For example, a study of adolescent tobacco use proposed that adolescents with different subtypes of ADHD reported different expectancies of substance use, implying that girls with inattentive symptoms perceived fewer possible negative consequences than did boys and girls with predominantly hyperactive/impulsive subtypes [67]. The authors' explained the differences in expectations by inferring that the ADHD subdimension were attached to different underlying neurocognitive impairments, affecting substance use such as cigarette smoking, in various ways [67].

Furthermore, girls with symptoms of inattention often exhibit concurrent symptoms of depression and anxiety [62, 63], which in some cases might be considered to be secondary effects of ADHD symptoms [76, 77]. The association could be explained by theories of self-medication of negative consequences, such as failures in school, low social status, or symptoms of depression and anxiety associated with the inattention symptoms [59, 76]. The results of the present study underline the importance of a differential diagnosis procedure, mapping all comorbidity, psychosocial adversities, and their interconnections to enable the right interventions.

## The common factor model—different expressions of a common underlying structure

The theory of behavioral disinhibition suggests that externalizing behavioral disorders, such as antisocial behavior, ADHD, and substance use, emerge from a common underlying dimension of difficulties of controlling behavior [50-53]. Kendler and coworkers, and Røysamb and coworkers, investigated the comorbidity of common axis I and axis II disorders in Norwegian twins, revealing internalizing and externalizing genetic and environmental

dimensions of these disorders. According to the results, alcohol abuse or dependence shared the most environmental risk with internalizing axis I disorders such as depression and anxiety. However, SUDs shared genetic risk with the axis I externalizing disorders, docking in a cluster together with disorders reflecting antisocial behaviors, and cluster B personality disorders, implying that these disorders are somewhat different expressions of the same underlying liability structure [153, 154]. The Kendler and Røysamb results indicate that the high prevalence of conduct disorders in participants with SUDs in study I, the high rate of alcohol use in participants with antisocial behaviors, and symptoms of ADHD in participants with alcohol risk use in study II might be due to a clustering of externalizing symptoms with a shared underlying genetic structure.

Furthermore, the overlapping nature of symptoms of hyperactivity and impulsivity with antisocial behaviors in relation to alcohol use in study III might also be explained by the suggested clustering of externalizing symptoms sharing a genetic structure that features behavioral disinhibition. The frequent reports of depression and anxiety in alcohol risk users in study I, and the inattentive symptoms in girls who displayed an intact relation to alcohol use regardless of the presence of antisocial behaviors, might be explained by the same theory, linking the association to underlying structures clustering internalized conditions characterized by behavioral inhibition. In study II, symptoms of depression and anxiety were prevalent in around one-half of the alcohol risk users, but alcohol risk use was present in one-quarter of participants with symptoms of depression and anxiety. Study II used a cross-sectional design, and causal conclusions cannot be drawn, but it is tempting to apply the etiology model regarding SUDs as a developmental risk factor for psychiatric conditions to these results, indicating that alcohol use nurtures these symptoms.

### Implications of a common underlying structure

Studies I and II were performed in clinical settings, where psychiatric comorbidity was the rule, rather than the exception. Farchione and coworkers are supporters of the common factor approach, suggesting that different expressions of internalized disorders such as social phobia, panic attacks, and anhedonia might just be individual variations in the manifestation of a broader underlying syndrome [155]. Today's professionals are facing the needs of patients who suffer from comorbid conditions, and treatment protocols for single disorders are blunt tools for operating on these patient groups. If this hypothesis is also applicable to SUDs, it is of great importance to develop strategies targeting the underlying syndrome, rather than specific variations in the expression of this structure. What these treatment protocols of screening and treatment should address,

and how, are questions for future research, but as van Emmerik–van Oortmerssen and colleagues concluded in their work on comorbid ADHD and substance use -further integration of addiction treatment facilities with general mental health services would be a good start [68].

## Barriers to effective screening and treatment

Hallfors and Van Dorn evaluated barriers to effective screening and treatment of coexisting adolescent psychiatric symptoms and substance use problems in US primary care and attributed shortcomings to lack of knowledge and tested screening tools, and limited skills and confidence, flanked by financial limitations [14]. The analysis of the American barriers is very much applicable to Swedish conditions, according to the 2015 Swedish Health and Human Services Department report on the needs of professionals in the social services [156].

The adolescents at the misuse clinic in study I exhibited widespread psychiatric and psychosocial difficulties, and one-fifth of the young patients in the general psychiatric care facilities in study II reported alcohol risk use. The mean age was 16 and 17 years in the samples when first contact with the respective clinic was initiated. It is most likely that the prelude to the sad tones of harsh psychosocial conditions, germinating psychiatric symptoms and the initiation of alcohol and drug use, began at a younger age. The treatment outcomes in study I might be a consequence of that treatment was given too late. Consequently, if the patients in general psychiatric care facilities receive proper differential diagnostic evaluation and treatment tailored accordingly, alcohol risk use might be nipped in the bud, preventing future stays at substance use clinics. However, this is speculation. Further treatment studies, designed with matched comparison groups, are needed. The results do however say that what is done today could be done differently to further prevent aversive outcomes. To begin with, effective strategies for screening and assessment methods are needed.

## Difficulties of adolescent substance use assessment

The validity of self-reports has been discussed for many years [157-159]. When comparing answers in self-report questionnaires and interviews with results from biological testing such as HS-SPME/GC–MS, discrepancies that indicate underreporting in self-reports have emerged [121-123]. There are several explanations for these inconsistencies. In addition to the evident purpose of hiding the truth about a criminal act, respondents might deliver distorted responses because of a lack of insight [31], or a low reading level

may hinder understanding of the question [31, 160]. The use of alcohol and drugs generally impairs cognitive function, and adolescents with substance use problems sometimes present with delayed cognitive, social, and emotional development, possibly affecting their understanding of the extent and nature of their problems, and their willingness and ability to describe them [31].

However, Maisto and colleagues reviewed the field of literature and provide some support for the validity of adolescent self-reports of substance use, concluding that adolescents in substance use treatment tend not to fake answers (i.e., they do not respond positively to the use of factitious drugs, etc.); the answers from adolescents in normal populations generally correspond to information obtained from parents, schools, and other records; and the answers often remain consistent over time [161]. Although these results are far from unchallenged, other study findings report that most mothers underreport alcohol use in their adolescent offspring [162] and that adolescents sometimes report greater past substance use and associated problems at the end of treatment than at treatment entry [163], consistent with the notion that substance use that has occurred recently is often omitted from self-reports [164, 165].

Study IV dealt with the difficulties of adolescent substance use assessment. The results showed that twice as many adolescents admitted illicit drug use in an in-depth interview than in an anonymous questionnaire survey. The answers in the interview were compared with the analysis of traces of drugs in hair by the HS-SPME technique. The hair analysis was performed at the same time as the interview and functioned as a pipeline procedure (i.e., a measure presented as a form of validator of truth). The participants were implicitly told that the method was very good at tracking drugs and that it was more or less pointless to withhold any information about use in the interview, because it would be revealed in the hair analysis later on.

The questionnaire and the hair analysis showed high specificity and low sensitivity, indicating that if use was admitted in any method, the answer was most probably trustworthy, and inversely a denial/negative hair test did not necessarily imply abstinence. Furthermore, there was a sociodemographic pattern in the proportion of disagreement in reports of illicit drug use between the questionnaire and the in-depth interview, and between the hair analysis and the in-depth interview. Participants from less privileged sociodemographic circumstances presented higher proportions of disagreement. The discrepancy might be explained by considering that individuals growing up in less privileged contexts might develop a low social trust (i.e., experience less confidence in authorities) [166, 167]. Low

trust might have influenced the decision to withhold sensitive information in the questionnaires.

Regardless of the source of these documented discrepancies, from a clinical perspective, they are highly problematic, as information about substance use is fundamental, not only for the treatment of the substance use itself but also because the substance use might affect assessment and treatment of other comorbid psychiatric symptoms [23]. Furthermore, differences between the responses in questionnaires, interviews, and biological investigation imply that the validity of adolescent substance self-reports can be questioned, which could undermine epidemiological research findings [124, 125], including the findings of this thesis. In Study I, data were collected by the use of the semistructured interviews K-SADS and SCID-I, self-assessment questionnaires, and register data on criminal activity. Here, the extraction of criminal offences might be regarded as a pipeline procedure, enhancing the motivation to answer more truthfully, because the participants knew that their statements about criminality would be verified by registry data. In studies II and III, all data were assembled by the use of self-report questionnaires, and the questionnaire in study II was completed in the presence of the participant's parents. This might have undermined the trustworthiness of symptom reporting, especially on the sensitive items regarding substance use. Neither interviews nor elements of register data extracts or biological testing that could serve as a pipeline procedure were included in the design. However, as mentioned before, the sensitivity might be low for these measures, but the specificity remains high, indicating that the confirmative reports of sensitive information that this work is built upon can be considered to be reliable.

# Conclusions

## Study-specific conclusions

### Study I

Treatment-as-usual provided by the psychiatric service for adolescents with substance misuse in a large urban center in Sweden experienced difficulties preventing the persistence of substance misuse. Despite extensive clinical assessments of the clients and their parents, few factors assessed in mid-adolescence were associated with substance misuse disorders five years later. This is a much burdened group of young individuals requiring evidence-based treatments for each of their disorders and protection from maltreating parents and other abusive experiences, at an earlier stage.

### Study II

Alcohol risk use in general adolescent psychiatric care facilities is highly prevalent and highly comorbid with other psychiatric symptoms. The more psychiatric symptoms -the greater the probability of alcohol risk use, and vice versa. Alcohol risk use in relation to psychiatric comorbidity should be investigated properly and treated in general psychiatric care facilities.

### Study III

The reduced associations between hyperactivity, impulsivity, and alcohol use for boys and girls after adjusting for antisocial behavior suggest a considerable overlap between hyperactivity, impulsivity, and antisocial behavior. The direct pathway between inattention and alcohol use among girls suggests that girls with inattention symptoms are at risk of alcohol use regardless of antisocial behavior. Special attention should be given to these girls. Accounting for antisocial behavior reduced the relation between ADHD subdimensions and alcohol use, and antisocial behaviors should therefore be screened for when symptoms of ADHD are present.

## Study IV

The fact that reports of illicit drug consumption were twice as frequent in the in-depth interviews as in the questionnaires casts doubt on the validity of data retrieved by self-report questionnaires. Hair analysis could function as a pipeline procedure, increasing the validity of reports in this population. Moreover, respondents from less privileged socioeconomic circumstances reported illicit drug use less accurately, which is also an issue of validity. Results indicate that in-depth interviews in combination with a pipeline procedure could be considered as a complement or alternative to questionnaires and that answers from respondents from less privileged circumstances might be interpreted with greater caution.

## General conclusions

The adolescents who sought treatment for substance use problems at the misuse clinic in study I reported substantial co-occurring mental illness, as well as maltreatment and several forms of abuse. These young people, like those described in the literature, challenge the traditional clinical and social services. The adolescents who sought treatment for mental illness in general child and adolescent psychiatric care facilities in study II reported co-occurring alcohol risk use, as well as maltreatment and several forms of abuse.

The two groups of patients were treated in two different facilities, but their characteristics in terms of treatment needs were partly comparable. Assessment and treatment are traditionally given predominantly by social services for the first group, and by psychiatric care facilities for the other group. The Swedish Health and Human Services Department highlighted the importance of integrated treatment interventions in cases of comorbidity, based on the recognition that the conditions should be treated simultaneously to reduce abuse or dependence and to increase psychosocial functioning level [119].

The substantial co-occurrence of multiple substance use and numerous mental illnesses portrays underlying syndromes with different variations in the expressions of its structure. Comorbid externalizing symptoms might share etiological grounds, possibly founded in behavioral disinhibition, while internalizing disorders in relation to substance use might share the impairments of behavioral inhibition. Awareness about the structure of common psychiatric and psychosocial risk factors for substance use is crucial at all levels in adolescent health care organizations, for the understanding, assessment, and treatment of substance use in young patients.

Furthermore, the difficulties of measuring sensitive, private, and illegal matters of this kind should be kept in mind, and protocols should be designed to maximize the motivation for patients or respondents to report their actual use.

In short, there is major comorbidity in clinics for substance-abusing adolescents, and in child and adolescent outpatient clinics. Working with young individuals having these complex problems requires extensive knowledge about the nature of both adolescent substance use and child and adolescent psychiatry, and the need for expertise is once again stressed.

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