

From the Department of Clinical Neuroscience
Karolinska Institutet, Stockholm, Sweden

CANNABIS USE IN ADOLESCENCE: STUDIES OF TRENDS, CORRELATES AND ADVERSE MENTAL HEALTH CONSEQUENCES

Isabella Gripe



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Cannabis use in adolescence: Studies of trends, correlates and adverse mental health consequences

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By

Isabella Gripe

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Principal Supervisor:

Professor Mats Ramstedt
Karolinska Institutet
Department of Clinical Neuroscience

Co-supervisor(s):

Associate professor Anna-Karin Danielsson
Karolinska Institutet
Department of Global Public Health

Professor Thor Norström
Stockholm University
Swedish Institute for Social Research

Opponent:

Senior researcher Anne Line Bretteville-Jensen
Norwegian Institute of Public Health

Examination Board:

Associate professor Mats Anderberg
Linnaeus University
Department of Social Work

Associate professor Ylva Brännström
Almquist
Stockholm University
Department of Public Health Sciences

Associate professor Charlotte Borg Skoglund
Uppsala University
Department of Medical Sciences

Popular science summary of the thesis

Cannabis use is associated with several negative health and social consequences. Cannabis use typically begins during adolescence and is more common among young people than adults. Starting early in life increases the risk of negative outcomes and cannabis may be particularly harmful to adolescents, whose brains are not yet fully developed. Adolescence is also a period of change when one starts to find a direction in life. Using cannabis during this period may, in addition to the health risks, have consequences for a person's future prospects. Thus, it is not surprising that adolescent cannabis use is a public health concern.

This thesis focuses on three aspects of the epidemiology of cannabis use among adolescents where previous research is missing or inconclusive:

- If cannabis and alcohol acts as substitutes (one replaces the other) or complements (use of one substance is accompanied by use of the other)
- If there are socioeconomic differences in cannabis use
- If there is an association between cannabis use and mental distress

The overall aim of the thesis was to contribute with new knowledge on these three topics using data from population samples of adolescents in Sweden and Norway. Whether changes in cannabis use is related to changes in alcohol use is important knowledge for understanding trends in adolescence substance use. To know if they act as substitutes or complements are also valuable from a policy perspective, since this affects the implications of substance-specific prevention strategies. To what extent there are socioeconomic differences in cannabis use among adolescence is essential given the numerous risks associated with cannabis use. This question is especially relevant for identifying risk groups for cannabis use and related harm but also for assessing if cannabis use may contribute to the reproduction of socio-economic differences in life chances. One major risk of cannabis use is mental health problems and numerous studies have addressed this issue. Still, previous research is inconclusive and the importance of cannabis use is still debated.

The results from the thesis show that alcohol and cannabis act neither as complements nor substitutes in the general population of Swedish 15–16-year-olds. Moreover, 17–18-year-olds with at least one parent with higher education are at *higher* risk of ever having used cannabis, but at *lower* risk of frequent cannabis use. The latter association is explained in part by higher occurrence of cannabis-related risk factors among those whose parents lack higher education. The results also show that academic orientation is associated with frequent cannabis use: pupils from introductory and vocational programs had a higher risk of having used cannabis frequently compared with pupils in higher education preparatory programs. In this case, the association is fully explained by higher prevalence of cannabis-related risk factors among pupils in introductory and

vocational programs. Lastly, the results show that males who increase their cannabis use during adolescence and young adulthood have higher risk of increased symptoms of anxiety, depression, and suicidal ideation. Increased cannabis use in females is associated with an increased risk for anxiety and suicidal ideation.

A major conclusion is that cannabis and alcohol act neither as complements nor as substitutes among Swedish adolescents. Thus, prevention strategies aimed at either substance are unlikely to affect use of the other. Evidence was also found for the idea that cannabis use in adolescence and young adulthood is associated with adverse mental health consequences. The thesis also revealed differences in cannabis use depending on both parental education level and one's own academic orientation. Adolescents whose parents lack higher education and those who attend a vocational or introductory program at upper secondary school have an increased risk of using cannabis more frequently. Overall, the results indicate that young people's cannabis use is an important public health issue and that it is important to try to prevent cannabis use. The thesis also highlights that there are groups that are particularly vulnerable where targeted efforts may be needed to reduce the use of cannabis.

Populärvetenskaplig sammanfattning

Att använda cannabis är förknippat med både sociala och hälsomässiga risker. De flesta som börjar med cannabis gör det under tonåren. Det är också vanligare bland unga än bland vuxna att använda cannabis. Det har visat sig särskilt skadligt att börja med cannabis tidigt i livet. Att använda cannabis under tonåren kan, utöver hälsoriskerna, även få konsekvenser för en persons framtidsutsikter eftersom det kan påverka skolprestationer och den sociala utvecklingen. Mot den här bakgrunden är det lätt att förstå varför ungas cannabisanvändning är en viktig folkhälsofråga.

I den här avhandlingen ligger fokus på tre områden där tidigare kunskap om ungdomars cannabisanvändning saknas eller behöver kompletteras:

- Om cannabis och alkohol fungerar som substitut (till exempel att cannabis ersätter användning av alkohol) eller komplement till varandra (till exempel att användning av alkohol kompletteras med cannabis)
- Om det finns socioekonomiska skillnader i cannabisanvändning
- Om det finns samband mellan cannabisanvändning och psykisk ohälsa

Det övergripande syftet med avhandlingen är att, med hjälp av data från befolkningsundersökningar av svenska och norska ungdomar, öka kunskapen om ungas cannabisanvändning inom dessa områden. Om förändringar i cannabisanvändning hänger ihop med förändringar i alkoholanvändning är en viktig fråga för att bättre förstå trender i ungdomars substansbruk. Är det så att de fungerar som substitut kan insatser som exempelvis minskar alkoholkonsumtionen få som önskad effekt att cannabisanvändningen ökar. Fungerar de som komplement kan det istället innebära att insatser som minskar alkoholkonsumtionen även minskar konsumtion av cannabis. I vilken utsträckning det finns socioekonomiska skillnader i cannabisanvändning bland ungdomar är en viktig fråga för att identifiera riskgrupper. Det är viktigt eftersom cannabisanvändning innebär risker. Det är också viktigt att bättre förstå sambandet mellan cannabisanvändning och psykisk ohälsa, något som fortfarande inte är helt klarlagt.

Resultaten visar att alkohol och cannabis varken fungerar som komplement eller substitut bland svenska 15–16-åringar. Resultaten visar också att 17–18-åringar med minst en förälder med högre utbildning har *högre* risk för att någon gång ha testat cannabis men en *lägre* risk för att använda cannabis frekvent. Det sistnämnda sambandet förklarades delvis av andra riskfaktorer, exempelvis skolk och föräldrarnas inställning till cannabis. Resultaten visar också att gymnasieinriktning har betydelse för risken att använda cannabis ofta. Elever från introduktions- och yrkesprogram hade en högre risk för att ha använt cannabis frekvent, jämfört med elever på högskoleförberedande program. Det här sambandet kunde förklaras av andra riskfaktorer, till exempel om man hade börjat med alkohol, tobak eller droger när man var

yngre än 14 år. Slutligen visade resultaten att det fanns ett samband mellan att öka sin cannabiskonsumtion under ungdomsåren och en ökad risk för psykisk ohälsa.

En viktig slutsats är att cannabis och alkohol varken fungerar som substitut eller komplement bland svenska ungdomar. Det är därför osannolikt att riktad prevention som syftar till att minska användningen av antingen alkohol eller cannabis kommer att påverka användningen av den andra substansen. Resultaten från avhandlingen stärker också bilden av att cannabisanvändning under tonåren och tidiga vuxenåren är förknippat med ökad risk för psykisk ohälsa. Avhandlingen belyser också att både ungdomar vars föräldrar saknar högre utbildning och ungdomar som går ett yrkes- eller introduktionsprogram på gymnasiet har en ökad risk att använda cannabis frekvent. Sammantaget pekar resultaten på att ungas cannabisanvändning är en viktig folkhälsofråga och att det är viktigt att försöka förebygga cannabisanvändning. Avhandlingen belyser också att det finns grupper som är särskilt utsatta där det kan behövas riktade insatser för att minska användningen av cannabis.

Abstract

Background: Cannabis is currently the most commonly used illicit psychoactive substance. Cannabis use is typically initiated during adolescence and is more common among young people than among adults. Cannabis use is associated with negative health and social consequences and early initiation increases the risk of negative outcomes. Cannabis may be particularly harmful to individuals whose brain is not yet fully developed.

Overall aims: The overall aim was to improve our understanding of various aspects of the epidemiology of cannabis use among adolescents. The four studies within the thesis highlight the following main research questions regarding adolescents: (I) Are trends in cannabis use related to trends in drinking? (II) Is socioeconomic status (SES) related to cannabis use? (III) Do pupils in introductory programs (IPs) have an increased risk of cannabis use compared with pupils in national programs? (IV) Is there an association between cannabis use and mental distress?

Data and methods: Data for three of the four studies came from a nationally representative, self-reported, and anonymous school survey conducted annually by the Swedish Council for Information on Alcohol and Other Drugs. The survey is cross-sectional and the sample consists of Swedish 9th grade pupils (15–16 years of age) and pupils in year 2 in upper secondary school (17–18 years of age). To assess whether trends in cannabis use were related to trends in drinking, autoregressive integrated moving average (ARIMA) time-series analysis was used (Study I). To assess the association between self-reported cannabis use and socioeconomic status (SES) and academic orientation, respectively, multi-level mixed-effects Poisson regression with robust standard errors was used. Because the pupils were clustered in school classes, the assumption of independence between observations was not met. Hence, data were analyzed with a random intercept for the school/school class level (Studies II and III).

In the fourth study, data stemmed from the Young in Norway Longitudinal Study. The study covered a broad range of topics and followed a cohort of young people prospectively over 13 years. The cohort was assessed in 1992, 1994, 1999, and 2005. Only those who participated in all four waves and who were aged 11–18 years in 1992 were included in the analysis ($n = 1,988$). The within-person association between increased cannabis use and mental distress was assessed using fixed-effects modeling.

Results: Alcohol and cannabis consumption functioned neither as complements nor as substitutes in the general population of Swedish 15–16-year-olds. Among cannabis users, there was a positive association between consumption of alcohol and cannabis use. However, this association had become weaker over time, suggesting that alcohol and cannabis used to be complements, but no longer are (Study I).

Childhood SES was associated with cannabis use. Those who had at least one parent with higher education were at *higher* risk of lifetime cannabis use, but had a *lower* risk of frequent (51+ times) cannabis use. Truancy, risk assessment of cannabis, and parental attitude attenuated the latter association (Study II).

Academic orientation was associated with frequent (21+ times) cannabis use. Pupils from IPs and vocational programs had an increased risk of having used cannabis 21+ times compared with pupils in higher education preparatory programs. However, the association was attenuated and no longer significant when SES, truancy, school dissatisfaction, and early onset of substance use were adjusted for. Moreover, including pupils from IPs when calculating the prevalence of cannabis use did not alter the national estimate of cannabis use among Swedish adolescents aged 17–18 years (Study III).

Changes in cannabis use during adolescence and young adulthood were associated with increased risk of anxiety, symptoms of depression, and suicidal ideation among males. In females, increased cannabis use was associated with an increased risk of anxiety and suicidal ideation (Study IV).

Conclusion: Cannabis and alcohol act neither as complements nor as substitutes among Swedish adolescents. Hence, prevention strategies aimed at either substance are unlikely to affect use of the other. Moreover, the findings strengthen the assumption that cannabis use in adolescence and young adulthood is associated with adverse mental health consequences. The thesis also shows SES differences in cannabis use, related to both parental education level and academic orientation. Adolescents whose parents lack higher education and those who attend a vocational program or IP at upper secondary school have an increased risk of using cannabis more frequently. Overall, the results indicate that young people's cannabis use is an important public health issue and that it is important to try to prevent cannabis use. The thesis also highlights that there are groups that are particularly vulnerable where targeted efforts may be needed to reduce the use of cannabis.

List of scientific papers

- I. Gripe, I., Danielsson, A. K., Ramstedt, M. (2018) Are changes in drinking related to changes in cannabis use among Swedish adolescents? A time-series analysis for the period 1989–2016. *Addiction*, 2018;Apr 21 doi:10.1111/add.14244.
- II. Gripe, I., Danielsson, A. K., Karlsson, P., Thor, S., Ramstedt, M. (2021) Are the well-off youth in Sweden more likely to use cannabis? *Drug and Alcohol Review*, 40 (1), 126–134 doi: 10.1111/dar.13139. Epub 2020 Aug 10. PMID: 32776657
- III. Gripe, I., Ramstedt, M., Karlsson, P., Thor, S. Academic orientation and cannabis use – Findings from a population-based study of Swedish adolescents in upper secondary school. Manuscript.
- IV. Gripe, I., Pape, H., Norström, T. Association between cannabis use and mental distress in young people: a longitudinal study. Submitted.

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List of abbreviations

ARIMA	Autoregressive Integrated Moving Average
CAN	The Swedish Council for Information on Alcohol and Other Drugs
CI	Confidence Interval
DSH	Deliberate Self-Harm
FE	Fixed Effects
HEP	Higher Education Preparatory Programs
IP	Introductory Programs
IRR	Incidence Rate Ratio
RR	Risk Ratio
SCB	Statistics Sweden
SES	Socioeconomic Status
THC	Δ 9-Tetrahydrocannabinol
VP	Vocational Programs

1 Introduction

Humans have always experimented with psychoactive substances and drug use is by no means a modern phenomenon. Cannabis is now the most commonly used illicit psychoactive substance, with an estimated past 12-month prevalence globally of 4% in 2020. It is more common to use cannabis among young people and it is more common for men than women to use cannabis (1). There are large variations between countries, with the highest past 12-month prevalence of cannabis use found in North America (17%) (1), whereas the estimated prevalence in Sweden was approximately 3% in 2021 (2).

Using cannabis entails a risk of negative health and social consequences (3, 4). These consequences can be divided into *acute* effects (occurring in direct relation to use) and *long-term* effects (occurring later in life). Acute effects include anxiety and panic reactions (3) as well as reduced reaction capacity, which is why driving under the influence of cannabis increases the risk of motor vehicle accidents (5) especially in combination with alcohol (6). In 2017, the National Academies of Sciences, Engineering, and Medicine published a comprehensive report on the current evidence of the health effects of cannabis. The authors investigated a wide range of long-term negative health effects of cannabis use and found evidence for an association between cannabis use and testicular cancer, worse respiratory symptoms, and low birthweight in offspring (4).

Cannabis is considered an illicit drug in most countries. The starting point for an international regulation of cannabis was the Second International Opium Convention in 1925 (7). In Sweden, use of cannabis (and other narcotics) was criminalized in 1988. In 1993, penalties were increased to include imprisonment (8). Hence, not only can the consumption of cannabis have negative consequences, in Sweden the illegal status of cannabis use means that users commit an offence, with associated risks of adverse social and judicial consequences.

The main psychoactive substance in cannabis is Δ^9 -tetrahydrocannabinol (THC), which causes the “high” and potentially causes addiction (9). Cannabis also contains cannabidiol, which has been suggested to suppress the acute effect of THC (10). In recent decades, the concentration of THC in cannabis has increased (11, 12). This is a concern, as a higher THC level increases the risk of several negative health outcomes. For instance, the risk of regular use and dependence becomes higher (13), as does the risk of psychosis (14).

Cannabis use among adolescents is an important research area for several reasons. Cannabis use is typically initiated during adolescence (15) and early initiation of cannabis use increases the risk of later harmful cannabis use patterns (4). Moreover, cannabis may be particularly harmful to individuals whose brains are still developing (16).

Using cannabis in adolescence is associated with greater risks of long-term negative health consequences such as psychosis and cannabis dependence (17).

Furthermore, adolescence is a period of change when individuals start to find a direction to shape their life (18). Using cannabis during this period may, in addition to the health risks, have consequences for a person's future possibilities. In a country like Sweden, where cannabis is illegal, there are also possible legal consequences that may affect future prospects. Moreover, several studies have shown that cannabis use in adolescence is a risk factor for negative educational outcomes (19–21) and for ending up outside the labor market (22, 23).

Thus, it is not surprising that adolescent cannabis use is viewed as a public health concern and is included in the Swedish government's strategy to reduce illicit drug use (24). Obtaining more knowledge of the epidemiology of cannabis use in the adolescent population is a prerequisite for developing prevention strategies and health interventions.

There has been a lively international debate about the legal status of cannabis which has given rise to concerns about the public health consequences of increased cannabis use in the population (25). Although there is currently no political support for decriminalization or legalization of cannabis in Sweden (26), the international debate has the potential to stimulate a discussion about the legal status of cannabis use in Sweden. It is important that such discussions are based on research, such as studies of the epidemiology of cannabis use among adolescents.

The point of departure for the present thesis is cannabis use in the general youth population, with the overarching aim to improve our understanding of various aspects of the epidemiology of cannabis use among adolescents. The main focus will be on trends in use, socioeconomic differences, and the association between cannabis use and mental health.

2 Background

The following chapter will give an overview of epidemiological research on adolescent cannabis use. It begins with a description of prevalence and trends in adolescent cannabis use, with a focus on Sweden. This is followed by a presentation of current knowledge regarding socioeconomic differences in cannabis use. An overview of negative consequences associated with cannabis use among adolescents is also given.

2.1 Cannabis use in the adolescent population

Sweden, like many other countries, has a long tradition of monitoring adolescent cannabis use through school surveys (27–29). Based on these surveys, it is known that cannabis use is more common in men, among older adolescents and, in the Swedish perspective, that cannabis use is more common in urban areas (27).

Cannabis use is generally more common among young people than adults, and the prevalence is subject to large national variations (1). In the US, 24% of 10th graders (age 15–16 years) reported lifetime use of cannabis in 2021 (29). Among European 15–16-year-olds, the prevalence ranges from 3 percent in Kosovo to 28 percent in Czechia (lifetime use). Compared with the European average of 16 percent, cannabis use in Sweden is relatively low (28). The Swedish Council for Information on Alcohol and Other Drugs (CAN) annually conducts school surveys among Swedish 9th graders (15–16 years old) and pupils in year 2 in upper secondary school (17–18 years old). In 2022, 6 percent of the Swedish 9th graders reported lifetime use of cannabis, and among adolescents in year 2 in upper secondary school, the corresponding figure was 14 percent (27).

2.2 Trends in adolescent substance use

Since the mid-nineties, the prevalence of cannabis use has been more or less unchanged among Swedish 15–16-year-olds. The same trend has been observed in other European countries (28) and in the US (29). However, there are indications of an increase in use frequency among Swedish cannabis-using adolescents. In 1996, around 7% of cannabis users reported use more than 20 times; in 2022, the corresponding figure was 23% (27).

In parallel with this development, alcohol consumption has declined markedly among Swedish adolescents (27), a decrease observed at all drinking levels (30, 31). This development is by no means unique for Sweden, similar trends are observed in many high-income countries (32, 33). The discrepancy in trends between alcohol and cannabis is surprising and has raised the question of whether the trend seen for alcohol is somehow related to the trend in cannabis use among adolescents.

2.2.1 Cannabis and alcohol – complements or substitutes?

Previous research shows that compared with non-users, cannabis users tend to drink larger amounts of alcohol and to drink more often (34, 35). Cannabis users are also at greater risk of developing alcohol dependence (36). Moreover, it is common among adolescents to use cannabis simultaneously with alcohol (37–39). Hence, at the individual level, previous research suggests an association between alcohol consumption and cannabis use among adolescents. Simultaneous use of alcohol and cannabis is usually defined as use of the two substances at the same time (40). Simultaneous use would also indicate that the two substances act as complements (38) and that reduced levels of drinking would be followed by decreased levels of cannabis use (38, 41).

However, the recent trends with decreased alcohol consumption and stable cannabis use challenge the idea that alcohol and cannabis act as complements among adolescents. Instead, it has been suggested that alcohol consumption has partially been replaced by cannabis use among adolescents, and that the substances thus act as substitutes. According to this line of reasoning, the possible substitution of alcohol with cannabis could explain the diverging trend, a suggestion that has been made in the public debate (42, 43). There is some support for the idea of substitution in previous research, based mainly on studies of changes in access to alcohol in the US (44, 45). However, according to the most recent review, the evidence is inconclusive, showing support for both substitution and complementary effects (46). Furthermore, most research on both substitution and complementarity between alcohol and cannabis originates from the US, which is evident from some of the systematic reviews of the matter (47, 48).

A better understanding of the association between alcohol and cannabis use among adolescents could aid the development of prevention strategies. If cannabis and alcohol work as complements among adolescents, it is likely that measures that reduce alcohol consumption will also reduce cannabis consumption. On the other hand, if cannabis and alcohol act as substitutes, methods aiming at reducing the use of one substance may have the opposite effect on the use of the other (48). Yet another possibility is that there is no association between alcohol and cannabis consumption. Insight into this would also be of importance for understanding young people's consumption of alcohol and cannabis and to what extent substance-specific policy measures are warranted. Epidemiological research on whether alcohol and cannabis acts as complements or substitutes is scarce, especially outside the US. Hence, one of the aims of the thesis is to investigate this further in the Swedish context.

2.3 Socioeconomic differences in cannabis use

Studying adolescent cannabis use in relation to other substances, such as alcohol, is one way to increase our understanding of cannabis use in the adolescent population. Another important issue to disentangle is if there are certain groups of adolescents at greater risk of cannabis use. Considering the well-known adverse consequences of cannabis use (3, 4), it is of interest to assess whether there is a socioeconomic difference in the use of cannabis, as the existence of such a difference would strengthen and reproduce socioeconomic differences in life chances.

The term socioeconomic status (SES) refers to the position that an individual (or a group) has on the socioeconomic scale within a society. SES is measured by a number of economic and social indicators, such as income, level of education, and occupation (49) and is critical for understanding the social stratification within a society. Among adults, low SES has been linked to higher risks of health problems and negative health behaviors (50), for instance illicit substance use (51). The major suggested mechanisms behind socioeconomic inequalities in health are differential exposure and differential vulnerability. Differential exposure refers to an uneven distribution of risk factors for ill health between SES groups whereas differential vulnerability refers to differences in the effects of risk factors between SES groups (52, 53). A stressful life situation, limited access to health care (50) or disadvantaged living environment (54), are examples of suggested explanations of why there is a more detrimental effect of risk factors in lower SES-groups.

Regarding the association between SES and cannabis use in adolescence, previous findings are mixed. A study of adolescents in several European countries found no association between parental education level and cannabis use (55). This is in line with the conclusions drawn in a previous review by Hanson and Chen (56). However, other studies found evidence for an association between low childhood SES and later cannabis use (57). Moreover, Gerra and colleagues (2020) looked at other dimensions of SES and found that low SES (in terms of how well-off the adolescent perceived their family to be compared with other families) increased the risk of frequent cannabis use. Other studies suggest the opposite: that high childhood SES is linked to more cannabis use (58–60). However, some of these studies found that heavy and more problematic use of cannabis was associated with lower childhood SES (59) and that the risk of going from experimental use to daily cannabis use was greater among adolescents with low SES (61).

Against this background, it seems safe to say that previous research on the association between SES and cannabis use in adolescents is inconclusive and more research is needed. There are some possible explanations for the inconsistency in previous research. An important issue concerns how SES is defined. This was illustrated by Gerra

et al. (2020), who found that results varied with SES indicator (55). Childhood SES is an important factor and has been included in most previous studies, albeit measured in different ways (56–61).

2.3.1 School characteristics and academic orientation

The influence of the family diminishes in adolescence and peer social status becomes more important during this period of transition (56). Since young people spend a lot of time in school, the characteristics of the school are of interest in relation to health behaviors. There are some previous findings that suggest an association between school characteristics and hazardous health behaviors, such as cannabis use (62). The social composition at the school may shape a young person's health behaviors (63). However, just as for childhood SES, the gradient of the association is not fully established, and there are findings indicating that pupils in more advantaged schools are at greater risk of use of cannabis and other substances (64). In line with this, a report from the Swedish National Council for Crime Prevention showed that adolescents from affluent areas in Stockholm reported higher prevalence of illicit substance use (65).

Yet another dimension of SES in adolescence is linked to the path in life that a young person chooses; the term “socioeconomic position of destination” (here called SES of Destination) has been used to describe this phenomenon (66). Some previous studies of SES differences in alcohol and substance use have used academic orientation as a measure of SES of destination among older adolescents (66, 67).

In Sweden, children leave compulsory school when they are 16 years old. After compulsory school, they can attend a 3-year, free-of-charge, upper secondary school education. The upper secondary education has three tracks of academic orientation:

- Vocational programs (VPs)
- Higher education preparatory programs (HEPs)
- Introductory programs (IPs)

The VPs and HEPs are so-called national programs and lead to a degree. The IP is for those who lack qualifications to enter a VP or HEP and does not lead to a degree. Pupils in IPs made up approximately 8.5% of all upper secondary school pupils in 2021 (68). The pupils enrolled in IPs are there for various reasons, but all have incompleteness of compulsory school in common. Previous reports have found that these pupils are characterized by lower motivation for school, early onset of substance use, more often are boys, and report higher levels of truancy and lower levels of school enjoyment compared with other pupils (69). These factors are also associated with cannabis use (70–72).

As previously mentioned, academic orientation can be a useful tool when investigating social differences in cannabis use among adolescents. Despite this, only a few studies

have investigated the association between academic orientation and substance use. Results from these studies indicate that hazardous health behaviors, such as drinking and substance use, are significantly higher among pupils in VPs compared with in HEPs (66, 67).

Furthermore, previous studies of the association between academic orientation and substance use have only included pupils in the national programs. It is well-known that a significant proportion of adolescents are not qualified to enter the national programs and this group has grown in recent years. In 2020, about 14% lacked qualifications to enter the national programs (73). Hence, a relatively large group of adolescents has not been included in previous studies of academic orientation and substance use. Moreover, they are not included in the national estimates of cannabis use in Sweden. This is not unique to Sweden; although educational systems differ between countries, adolescents leaving school before they should is a universal problem. In 2021, within the European Union, just under 10 percent of adolescents left school before they were supposed to (74). Thus, in countries using school surveys to monitor trends in adolescent substance use, it is likely that adolescents who are not able to continue to upper secondary school are excluded. This is problematic if they make up a risk group for cannabis use.

However, in Sweden, most of these adolescents are enrolled in an IP, which means that adolescents who fail compulsory school are still present within the Swedish school system. To our knowledge, no previous research has included adolescents from IPs. Hence, there is a lack of knowledge regarding both their cannabis use habits and how the national estimates are affected if this group is included. One aim of this thesis is to investigate this further.

2.4 Adverse effects of cannabis use in adolescence

Adolescence is a period of cognitive and social development (18) and previous research suggests that adolescents are particularly vulnerable to cannabis use (4, 16, 17).

Approximately one in ten regular cannabis users tends to develop dependence, but if cannabis use is initiated during adolescence, which is common (18), that figure is one in six users (3, 75).

Another area of interest has been how and if cannabis use in adolescence affects cognition. However, this remains unclear. There are studies suggesting an association between frequent cannabis use in adolescence and impaired cognition later in life (3, 76). One of the more influential is Meier et al. (2012), which indicated that adolescents who started using cannabis before age 18 years and who had a documented substance abuse at age 38 years showed a decline in IQ (8 points in average) compared with those not using cannabis (77). However, a more recent twin study, also by Meier et al. (2018), testing the associations between cannabis use in youth and decline in IQ, found that short-term adolescent cannabis use was not associated with a decline in IQ by age 18

years (78). Similar results, with weak support for a causal relationship between cannabis use and impaired cognition, have been found in other twin studies (79, 80).

An area related to cognition is school performance. Since school performance is an important foundation for a person's future prospects (52, 81, 82), it is not surprising that the relationship between cannabis use and school performance is an area of interest for research. Several studies suggest that adolescent cannabis users are at greater risk of school failure in terms of both poor educational performance and school drop-out (19, 20, 75, 83). However, it is not yet fully established if these associations are causal (19) or if there are shared risk factors, such as low parental support or other family factors, for cannabis use and, e.g., school failure (84).

2.4.1 Adolescent cannabis use and mental health

A growing field of research studies whether cannabis use is associated with negative mental health consequences. As early as 35 years ago, Andréason et al. (1987) showed that cannabis use was a risk factor for schizophrenia among men (85). Since then, numerous studies have demonstrated that cannabis use is related to mental illness, notably schizophrenia and other psychotic disorders (86, 87). However, results are mostly based on observations in the adult population (4, 88, 89). Associations between cannabis use and subclinical levels of mental health problems in adolescence have been less extensively studied. Some previous research suggests that cannabis use in adolescence and young adulthood is associated with various types of mental distress, such as suicidal behaviors, symptoms of depression and anxiety (for a review, see (90)). For example, adolescent cannabis users are at greater risk of suicide ideation (91-93) and some studies indicate that these relationships are of a dose-response character (92, 93). Furthermore, there are indications that age matters for the association between cannabis use and suicidal behaviors, with younger regular users of cannabis being at greater risk of suicidal behaviors than older ones (91).

Regarding the relationship between cannabis use in adolescence and symptoms of depression and anxiety, previous research shows mixed results (4). In a recent review, Xue et al. (2021) concluded that cannabis use is likely to increase the risk of anxiety. However, other studies have found no association between adolescent cannabis use and later anxiety (90). Likewise, studies of the association between adolescent cannabis use and depression show inconclusive results. Some studies have found a relationship between cannabis use in adolescence and later depressive disorders (94, 95), with a stronger association for heavy cannabis use (96, 97).

Various mechanisms underlying the association between cannabis use and mental health problems have been suggested. From a neurophysiological perspective, it has been argued that intake of THC affects brain functions in a way that increases the risk of mental health symptoms (98). Another possible explanation is common risk factors, for

example family background or parental mental health-problems, affecting both cannabis use and mental distress through either genetics or environment (99). Hence, studying the association between cannabis use and mental distress using techniques that can account for such stable common risk factors is important. Another potential mechanisms is that cannabis use is indirectly linked to mental distress through social mechanisms (92) such as difficulties in the labor market (22) or school failure (19). According to this line of reasoning, mental distress would emerge from these types of social problems, which are also related to cannabis use. Since the association between adolescent cannabis use and mental health remains unclear, additional studies of this association are warranted.

2.5 Rationale for the thesis

A deeper understanding of the epidemiology of cannabis use among adolescents is important in many respects, in particular as cannabis use in adolescence is a risk factor for adverse consequences that affect a person's future prospects in life.

There are some previous studies of how drinking and cannabis use are associated, and whether alcohol and cannabis act as substitutes or complements. Such information is useful in the development of prevention strategies, as the strategy would differ depending on the nature of the association. However, most such research has been carried out in the US. Insights into the relationship between adolescent alcohol and cannabis consumption in a Swedish context are also important, particularly in light of the recent development with decreasing alcohol consumption and increased prevalence of more frequent cannabis use.

Another important issue is to disentangle whether certain groups of adolescents are at higher risk of cannabis use. One area where previous findings are mixed is the association between SES and cannabis use among adolescents. This is important to investigate further as a socioeconomic gradient in cannabis use could strengthen and reproduce socioeconomic differences in life chances. Moreover, there are groups of youths previously overlooked in research on adolescent cannabis use, e.g., the relatively large group of adolescents not eligible for the national programs in upper secondary school in Sweden. Hence, there is a lack of knowledge regarding both their cannabis use and how the national estimates are affected if this group were included in national youth surveys on cannabis use. Furthermore, the association between adolescent cannabis use and the risk of negative mental health consequences is not fully disentangled. Hence, there is a need for more research in this area using adequate statistical approaches. The studies included in this thesis aim to fill some of the knowledge gaps in this research area, e.g., by exploring if cannabis and alcohol act as complements or substitutes, if there is an association between socioeconomic status and cannabis, and how cannabis use is related to mental health.

3 Research aims

The overarching aim of this thesis was to improve our understanding of various aspects of cannabis use among adolescents, with a focus on trends in use, correlates and associated adverse mental health consequences. The four studies within the project highlight the following main research questions regarding adolescents: (I) Are trends in cannabis use related to trends in drinking? (II) Is socioeconomic status related to cannabis use? (III) Do pupils in introductory programs have an increased risk of cannabis use compared with pupils in national programs? (IV) Is there an association between cannabis use and mental distress?

Study I The aim was to examine if changes in alcohol consumption were associated with changes in cannabis use among Swedish adolescents in a period of diverging trends, and to investigate if cannabis and alcohol act as complements or substitutes.

Study II The aim was to examine the association between childhood SES and lifetime and frequent cannabis use, respectively, adjusted for SES of school environment and academic orientation among Swedish upper secondary school pupils.

Study III The aim was to build on Study II and further examine the association between academic orientation and frequent cannabis use among Swedish adolescents in upper secondary school and include pupils from IPs, a large group previously overlooked in research on adolescent cannabis use. A second aim was to assess if the inclusion of this hard-to-reach group modified the national estimates of cannabis use in Sweden.

Study IV The aim was to analyze the within-person association between changes in cannabis use and various types of mental distress, in terms of symptoms of depression, anxiety, suicidal ideation, and deliberate self-harm (DSH) during adolescence and young adulthood.

4 Materials and methods

In the following section, a description of data sources, measures, and statistical analyses are presented. An overview for the different studies is given in Table 1.

Table 1. Overview of design, main outcome, main exposure, potential confounders and mediators, and main statistical analysis in the four studies.

	Study I	Study II	Study III	Study IV
Design	Swedish cross-sectional school survey (n = 149,603). Years 1989–2016	Swedish cross-sectional school survey (n = 9,497). Years 2014–2016	Swedish cross-sectional school survey (n = 4,980). Year 2021	Norwegian prospective cohort study (n = 1,988). Years 1992 (T1), 1994 (T2), 1999 (T3), and 2005 (T4)
Main outcome	Mean frequency of cannabis use	Lifetime cannabis use, frequent cannabis use (51+ times)	Frequent cannabis use (21+ times)	Depressive mood, anxiety, suicidal ideation, deliberate self-harm (DSH)
Main exposure/predictor	Mean alcohol consumption in liters of 100% alcohol per year	Childhood SES, SES of school environment, academic orientation	Academic orientation	Cannabis use
Main analysis	Time-series analysis (ARIMA)	Multi-level mixed-effects Poisson regression with robust standard errors, including random intercept for the school/school class level	Multi-level mixed-effects Poisson regression with robust standard errors, including random intercept for the school/school class level	Fixed-effects (FE) modeling
Confounders & mediators		Gender, truancy, risk assessment, parental permissiveness	Gender, childhood SES, truancy, school dissatisfaction, early onset of substance use	Heavy episodic drinking (HED)

4.1 Data sources

The analyses in this thesis are based on data from three cross-sectional Swedish school surveys and one Norwegian longitudinal study. The datasets for each respective study are described below.

4.1.1 The Swedish national school survey

Studies I–III were based on multiple waves of the Swedish national school survey, a cross-sectional study, conducted by CAN. CAN has conducted school surveys on alcohol and drug habits among Swedish 9th grade pupils (15–16 years of age) annually since 1971 and among pupils in year 2 in upper secondary school (17–18 years of age) since 2004. The sampling procedure is stratified in two steps, to ensure that all regions in Sweden are represented. In the first step, the number of pupils in each grade, each year, determines the likelihood to be included in the sample. If a pupil is selected, all pupils in that school are included in the first step of the sample procedure. The first step is performed by Statistics Sweden (SCB). In the second step, a pupil is randomly selected (within each of the selected schools from the first step) and the whole class in which the randomly selected pupil belongs participates in the survey. The sampling method used in both steps is Pareto πps sampling (100). The survey is anonymous and completed in the classroom. Before 2018, the questionnaire was filled out with pen-and-paper, in 2019 and 2020, school could choose to participate digitally and as of 2021 only a digital option is offered.

The annual samples comprise about 5,000 individuals (with an equal number of boys and girls) representative of each grade. Before analyzing the material, incomplete or obviously exaggerated responses are excluded (about 1–2%) (27).

4.1.1.1 Data for Study I

In Study I, data stemmed from the surveys among Swedish 9th grade pupils (15–16 years old) for the years 1989–2016. The participation rate among the sampled classes was 86% (range: 80–96%). At the individual level (i.e., pupils who were present and willing to participate), the participation rate was 85% (range: 83–90%). The sample was weighted by region and gender (27). The total sample include 149,603 individuals (with an equal number of boys and girls) representative of 9th grade pupils in Sweden. In the sample, a total of 8,261 individuals were lifetime users of cannabis. Those who were missing on the variable “lifetime use of cannabis” were excluded from the analysis ($n = 1,076$).

4.1.1.2 Data for Study II

In Study II, data stemmed from the survey among Swedish pupils in year 2 in upper secondary school (17–18 years old). Data from three waves were used, covering the years 2014–2016. The participation rate among the sampled classes was 80%. At the

individual level, the participation rate was 82%. The sample was weighted by region and gender (27). The total sample consisted of 12,096 pupils and the analytical sample included 9,497 pupils (48% boys), representative of pupils in year 2 in upper secondary school in Sweden.

4.1.1.3 Data for Study III

In Study III, data stemmed from two cross-sectional studies carried out in 2021. The first dataset (Dataset 1) came from the 2021 wave of the Swedish national school survey in year 2 in upper secondary school (age 17–18 years). The response rate among the sampled classes was 74%. At the individual level, the response rate was 81%. The sample was weighted by region and gender (27).

The second dataset (Dataset 2) came from a cross-sectional study targeting the IPs in Sweden. The sampling was performed by Statistics Sweden (SCB) using the same method as for the national survey. To avoid too small survey units, which could risk pupils' anonymity, only schools with at least 20 pupils enrolled in the IP were included in the sampling frame. The survey was offered to all pupils in the randomly selected IPs. The additional survey in IPs was designed to generate results comparable to those of the yearly Swedish national school survey (Dataset 1). The sample was weighted by gender. The response rate at the class level was 56% and that at the individual level was 67% (69).

The total sample included 5,239 pupils (3,289 in HEPs, 1,060 in VPs, and 890 in IPs). Only pupils who completed all survey items were included in the analysis (95% of the total sample): 3,151 pupils in HEPs, 1,010 pupils in VPs, and 819 pupils in IPs.

4.1.2 The Young in Norway study

In Study IV, data stemmed from the Young in Norway Longitudinal Study. The study covered a broad range of topics and followed a cohort of young people prospectively over 13 years (101). The cohort was assessed in 1992 (T1), 1994 (T2), 1999 (T3), and 2005 (T4). The survey at T1 included 8th to 13th graders in 67 schools, and the sample was selected to generate a national representative cross-section of this pupil population. The response rate was 97%. At T2, pupils who had left their original school received postal questionnaires, while those who were still at their original school filled in questionnaires in the classroom, in the presence of a supervising teacher. Only the latter group achieved a high response rate (92%). Therefore, the subsequent follow-ups were restricted to pupils who had attended the same school at T1 and T2 (i.e., 8th and 11th graders at T1). The vast majority (91%) of these pupils consented to be traced for future participation in the study, with 84% responding at T3 and 82% at T4. The cumulative response rate was 60%. Only those who participated in all four waves and who were 11–18 years at T1 were included in the analysis ($n = 1,988$).

4.2 Measures

In the following section, the most central measures in each study are described. More detailed descriptions are found in the articles included in the thesis.

4.2.1 Measures in Study I

Cannabis use was measured using the question: “Have you ever used drugs?”. Those who answered “yes” were asked to choose which type(s) of illicit drug(s) they had used from a list. Those who selected at least one of the options marijuana, hashish, cannabis oil, or cannabis were classified as using cannabis.

Mean frequency of cannabis use was measured using the question “On how many occasions have you used hashish or marijuana?”, with the response options 0, 1, 2–4, 5–10, 11–20, 21–50, and more than 50 times. To examine the development of frequency of cannabis use over time, a mean was created using the category midpoints. For the highest category (> 50), the frequency was set to 51.

Alcohol consumption was measured using beverage-specific questions (including medium strong beer, strong beer, cider, wine, and spirits) regarding quantity and frequency and converted into a measure of alcohol consumption in liters of 100% alcohol per year.

4.2.2 Measures in Study II

Lifetime cannabis use was measured using the question “On how many occasions have you used hashish or marijuana?” with the response options 0, 1, 2–4, 5–10, 11–20, 21–50, and more than 50 times. Those who answered 1 time or more were defined as lifetime users of cannabis.

Frequent cannabis use was derived from the same question. In order to investigate the most advanced group of users, those who reported use more than 50 times were defined as frequent users.

Childhood SES was created from two questions: “Has your father studied at a university or college?” and “Has your mother studied at a university or college?”. The questions were combined and coded into two categories. Those who reported that at least one parent studied at university or college were coded as having at least one parent with higher education. Those who reported that neither parent studied at university or college or reported no higher education for one parent alongside not knowing or not answering for the second parent, were coded as not having a parent with higher education.

SES of school environment was measured through information on the proportion of pupils with at least one parent with university or collage education among pupils in year

2 in each upper secondary school, each year (i.e., 2014, 2015, and 2016). The information was gathered from Statistics Sweden and schools were divided into 3 equal categories based on this variable.

Academic orientation was measured through information collected from the participating schools; classes were coded as either VPs or HEPs.

4.2.3 Measures in Study III

Frequent cannabis use was measured using the question “On how many occasions have you used hashish or marijuana?”, with the response options 0, 1, 2–4, 5–10, 11–20, 21–50, more than 50 times. Those who reported use more than 20 times were defined as frequent users in Study III. The cut-off was set to capture a high frequency of use, taking into account the distribution in the sample.

Academic orientation was measured through information collected from the participating schools. In Dataset 1, the school classes were coded as either VP or HEP, whereas Dataset 2 included only IPs.

4.2.4 Measures in Study IV

Depressive mood was measured as an additive index based on six items from the Depressive Mood Inventory (102): The question was: “During the past week, have you not been bothered at all, a little bit bothered, pretty much bothered, or very much bothered by some of these things?:” (1) Felt too tired to do things; (2) Had trouble sleeping; (3) Felt unhappy, sad, or depressed; (4) Felt hopeless about the future; (5) Felt tense or keyed up; and (6) Worried too much about things. There were four response options: Not bothered at all (coded 0), A little bit bothered (1), Quite bothered (2), and Extremely bothered (3).

Anxiety was measured as an additive index based on the following three items from the Hopkins Symptom Checklist (103): The question was: “During the past week, have you not been bothered at all, a little bit bothered, pretty much bothered, or very much bothered by some of these things?:” (1) Suddenly scared for no reason; (2) Constantly scared or worried; and (3) Nervousness or shakiness inside. The reference period was the preceding week, and the same four response options as for Depressive mood were used.

Suicidal ideation was measured using the item (with the same opening question as for depressive mood and anxiety): “Had thoughts of ending your life”. The reference period was the preceding week, and the same four response options as for Depressive mood were used.

Deliberate self-harm (DSH) was measured through the question: “Have you ever on purpose taken an overdose of pills or in another way tried to hurt yourself?”. Those who

responded affirmatively were asked how long it had been since the (most recent) episode of DSH. Based on the responses, a variable on past-year incidence of DSH (yes/no) was constructed. This measure captures both suicide attempts and non-suicidal self-inflicted injuries and has been used previously (104).

Cannabis use was measured by the following question: "During the past 12 months, have you used hashish or marijuana?". There were six response options: never, once, 2 to 5 times, 6 to 10 times, 11 to 50 times, and more than 50 times. The responses were coded into a three-level measure: Never, 1–10 times, and 11 times or more.

4.3 Statistical analyses

The statistical analyses were chosen based on the research questions and the structure of the data in each particular study. In Study I, an autoregressive integrated moving average (ARIMA) time-series analysis was used to estimate the association between cannabis and alcohol use. Data were differenced in order to make the series stationary. In Studies II and III, multi-level mixed-effects Poisson regressions with robust standard errors, including random intercept for the school/school class level, were used. As the pupils were clustered in school classes, the assumption of independence between observations was not met. Therefore, data were analyzed with a random intercept for the school/school class level. Poisson regression provides intuitively interpreted results in terms of incidence rate ratios and can be used for dichotomous variables. However, results tend to be conservative, which is why robust standard errors were used (105). In Study IV, my coworkers and I analyzed the within-person association between increased cannabis use and mental distress by applying fixed-effects (FE) modeling. The FE-technique eliminates the risk for bias caused by covariates that are stable within individuals across time. However, it does not remedy confounding due to time-varying factors that affect the outcome as well as the explanatory variable. The design can thus be strengthened by including time in the model, in order to eliminate bias from unobserved variables that change over time but are constant over individuals (106). We controlled for time by including assessment year in our analysis.

4.4 Ethical considerations

The purpose of investigating cannabis use among adolescents was to improve our understanding of various aspects of cannabis in this population and to contribute to the research field with new knowledge that can hopefully be of use for policymakers and practitioners. Still, even with the best intentions, unintentional damage may be done. Therefore, it is important to carefully consider the ethical aspects of each research project.

In Studies I–III, data came from the annual national school survey compiled by CAN. The survey is anonymous and is conducted in school years 9 and 11, which means that the pupils are aged 15–16 years or 17–18 years. Hence, they are considered old enough to decide for themselves if they want to participate (107). However, the fact that the survey is conducted in the classroom with peers and a teacher present can be perceived as causing peer pressure. In order to avoid that pupils feel pressured to participate, it is clearly stated to both the teacher and the pupils that participation is voluntary.

Moreover, the questionnaire includes questions that can be perceived as private or unpleasant to answer. Questions regarding cannabis use, which is illegal, can be perceived as particularly sensitive. Respondents are informed that they can skip individual questions if they want to or feel uncertain about answering them.

Unlike in Studies I–III, participants in Study IV did not participate anonymously. However, we gained only restricted access to anonymized data. All data were stored securely in a server hosted by Tjenester for Sensitive Data (TSD), Universitetets senter for informasjonsteknologi, at Oslo University. The longitudinal Norwegian study upon which Study IV was based received ethical approval from Norwegian authorities.

Moreover, the thesis was based on data that had already been collected. This means that the research was cost-effective. Furthermore, the studies included in the thesis did not require any additional effort from the respondents.

Studies I and II were part of a larger research project which was subject to ethical vetting and approved by the Central Ethical Review Board in Stockholm (dnr 2018/1804–31/5). Studies III and IV were evaluated by the Swedish Ethical Review Authority, which made an advisory statement declaring that it had no ethical objections to the projects (dnr 2020–04829 and 2022–06254–01).

5 Results

5.1 Complements or substitutes?

The aim in Study I was to examine if changes in alcohol consumption were associated with changes in cannabis use among Swedish adolescents, in order to establish if cannabis and alcohol act as complements or substitutes.

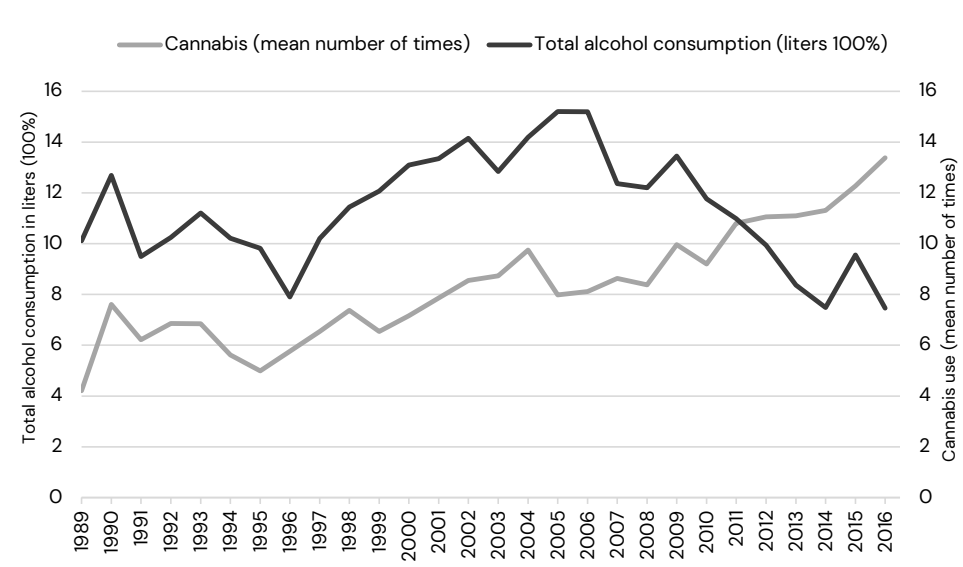
The results from Study I showed that up to the year 2000, trends in alcohol consumption and mean frequency of cannabis use developed in parallel. After that, alcohol consumption decreased, whereas mean frequency of cannabis use increased (Figure 1). In 1989, mean alcohol consumption was 2.2 liters. In 2016, it was 1.1 liters. The mean number of times that adolescents had used cannabis increased from 0.1 to 0.7 during the same period.

Figure 1. Total alcohol consumption (liters 100% per capita) and mean frequency of cannabis use among all adolescents during the period 1989–2016.



The analysis restricted to cannabis users revealed that alcohol consumption was higher among cannabis users. However, drinking dropped in this group as well, from 10.1 to 7.5 liters between 1989 and 2016 (Figure 2). The mean number of times cannabis-using adolescents had used cannabis increased from 4.2 to 13.4 times between 1989 and 2016.

Figure 2. Total alcohol consumption (liters 100% per capita) and mean frequency of cannabis use among cannabis users during the period 1989–2016.



In analyzing all adolescents, we found no significant association between changes in alcohol consumption and changes in mean frequency of cannabis use. Among cannabis users, on the other hand, our analysis of the period 1986–2016 revealed a significant and positive association between changes in alcohol consumption and changes in mean frequency of cannabis use. The results suggested that a 1-liter increase in mean alcohol consumption was associated with a 0.28 increase in mean frequency of cannabis use ($p = .010$). When the period was divided into before and after the year 2000, the result for the first period showed that a 1-liter increase in mean alcohol consumption was associated with a 0.52 increase in mean frequency of cannabis use ($p = .003$). When the most recent period (2000–2016) was analyzed, the association was not significant ($p = .735$).

5.2 Childhood socioeconomic status, academic orientation, and cannabis use

The aim of Study II was to examine how childhood SES was associated with cannabis use adjusted for SES of school environment and academic orientation. Study III was based on Study II, exploring the association between academic orientation and frequent cannabis use and included pupils from IPs, who had not previously been included in research on adolescent cannabis use.

First, the analysis showed that adolescents with at least one parent with higher education had a 17% (incidence rate ratio (IRR): 1.17, 95% confidence interval (CI): 1.03–

1.33) significantly ($p = .014$) *higher* risk of lifetime use of cannabis compared with those whose parents had no higher education, in the fully adjusted model (Model 1, Table 2). Second, we found that cannabis users with at least one parent with higher education had a 28% (IRR 0.72, 95% CI: 0.52–1.00) significantly ($p = .049$) *lower* risk to have used cannabis more than 50 times (Model 2, Table 2), compared with those whose parents had no higher education. The results of Study II also revealed that adolescents in VPs had an increased risk of lifetime cannabis use compared with adolescents in HEPs.

Table 2. Association between childhood SES and cannabis use, fully adjusted models (multi-level mixed-effects Poisson regression), years 2014–2016.

	Model 1. Risk of lifetime cannabis use among all pupils (n = 9,497)				Model 2. Risk of frequent (> 50 times) cannabis use among cannabis users (n = 1,491)			
	IRR	P> z	95% conf. interval		IRR	P> z	95% conf. interval	
			Lower	Upper			Lower	Upper
Girls (ref. boys)	0.83	0.000	0.76	0.91	0.60	0.001	0.45	0.81
<i>Childhood SES, individual level</i>								
Neither mother nor father studied at university/college	ref	ref	ref	ref	ref	ref	ref	ref
At least one parent studied at university/college	1.17	0.003	1.05	1.30	0.72	0.033	0.53	0.97
<i>Control variables, school class level</i>								
Proportion with tertiary education among parents								
Schools with <u>lowest</u> proportion	ref	ref	ref	ref	ref	ref	ref	ref
Schools in the middle category	0.95	0.513	0.83	1.10	0.85	0.398	0.58	1.24
Schools with <u>highest</u> proportion	1.03	0.716	0.88	1.20	0.86	0.467	0.57	1.29
Academic orientation								
Higher education preparatory program	ref	ref	ref	ref	ref	ref	ref	ref
Vocational program	1.23	0.004	1.07	1.41	1.33	0.135	0.92	1.92
<i>Control variables, individual level</i>								
Truancy once a month or more often	2.41	0.000	2.20	2.64	1.44	0.008	1.10	1.90
Considers cannabis use 1–2 times NOT harmful	4.47	0.000	3.94	5.07	2.84	0.000	1.69	4.75
Thinks parents accept use of cannabis	1.48	0.000	1.30	1.69	2.62	0.000	1.89	3.63

IRR, incidence rate ratio; SES, socioeconomic status. Statistically significant associations are **bolded**.

When the association between academic orientation and cannabis use was further analyzed in Study III, the analysis showed an increased risk of cannabis use 21 times or more among adolescents in both IPs and VPs compared with those in HEPs. Adolescents in IPs had a 2.45 times higher risk of cannabis use 21 times or more compared with those

in HEPs (IRR 2.45, 95% CI 1.28–4.66); for adolescents in VPs the risk was 82% higher (IRR 1.82, CI 95% 1.09–3.04) compared with those in HEPs. However, when adjusting for childhood SES, truancy, school satisfaction, and early onset of substance use, the associations between academic orientation and cannabis use 21 times or more were attenuated and no longer significant. Furthermore, results from Study III showed that the inclusion of adolescents from IPs did not alter the national estimates of cannabis use in Sweden. The combined total differed by just 0.2 percentage points compared with the total for national programs only.

5.3 Cannabis use and mental distress

In Study IV, the aim was to examine the within-person association between changes in cannabis use and various types of mental distress. Among males, increased cannabis use was significantly related to all outcomes except DSH. For example, in males who went from no cannabis use to use 11+ times, the increase was significantly associated with increased risk of anxiety (risk ratio (RR): 1.72, $p = .009$), depressed mood (RR: 1.49, $p < .001$), and suicidal ideation (RR: 3.43, $p = .012$). Among females, on the other hand, increased cannabis use was only significantly associated with anxiety and suicidal ideation. Females who went from no cannabis use to use 11+ times had a 38% increased risk of anxiety (RR: 1.38, $p = .023$) and 2.47 higher risk for suicidal ideation (RR: 2.47, $p = .002$).

6 Discussion

6.1 Main findings

The overarching aim of the thesis was to improve our understanding of various aspects of the epidemiology of cannabis use among adolescents. The main focus was to investigate trends in use, socioeconomic differences in cannabis use, and the association between cannabis use and mental distress. The context was Nordic, with three studies based on data from adolescents in Sweden and one on data from adolescents in Norway.

The studies showed that alcohol and cannabis were neither complements nor substitutes in the general population of Swedish 15–16-year-olds. Among cannabis users, however, my coworkers and I found a positive association between alcohol and cannabis use. This association had become weaker over time, suggesting that alcohol and cannabis used to be complements among cannabis users, but this was no longer the case. This finding indicates that the ongoing declining trend in youth drinking is not associated with the increase in frequency of cannabis use.

We also found an association between childhood SES and cannabis use and that the associations were different for lifetime use and frequent (51+ times) use. Adolescents who had at least one parent with higher education were at *higher* risk of lifetime cannabis use but at *lower* risk of frequent cannabis use, compared with those whose parents had no higher education. Truancy, risk assessment of cannabis, and parental attitudes towards cannabis attenuated the association between childhood SES and frequent cannabis use.

Moreover, my coworkers and I identified an association between academic orientation and cannabis use. Pupils from IPs and VPs had an increased risk of having used cannabis 21+ times compared with pupils in HEPs. However, the association was attenuated and no longer significant when SES, truancy, school dissatisfaction, and early onset of substance use were adjusted for. We also found that including pupils from IPs did not alter the national estimate of cannabis use among Swedish adolescents aged 17–18 years.

We observed an association between within-person changes in cannabis use and mental distress during adolescence and young adulthood. In males, increased cannabis use was associated with increased risk of anxiety, depressed mood, and suicidal ideation. In females, increased cannabis use was associated with an increased risk of anxiety and suicidal ideation. The associations between changes in cannabis use and mental distress were generally more pronounced among males.

6.2 Findings in a broader context

6.2.1 Are cannabis and alcohol complements or substitutes?

Information on whether cannabis and alcohol are complements or substitutes is useful in the development of prevention strategies, as it can indicate whether substance-specific prevention also have implications for use of other substances. This is especially important in light of the recent development with decreasing alcohol consumption and increased prevalence of more frequent cannabis use.

The question of substitution and complementarity between alcohol and cannabis has been studied previously and there are findings supporting both substitution (45, 108) and complementary use (33, 41). Our finding of complementary use among cannabis user during the first half of the period has some support in previous research. For instance, Williams et al. (2004) analyzed the years preceding the turn of the millennium and concluded that cannabis and alcohol had been complements for adolescents in Australia (41). A study of Norwegian adolescents, on the other hand, found support for complementary use based on data from after the turn of the millennium (2003–2006), which is not in line with our findings of no association after the turn of the millennium (33).

There are also several studies providing direct support for substitution between alcohol and cannabis among adolescents (44, 45, 109), and some indirect evidence showing that rising prices of alcohol are associated with increasing use of cannabis (110). However, recent reviews are inconclusive, as support is found for both substitution and complementary use (46, 47).

This inconsistency in findings may have several explanations. One recurring explanation in reviews is that the relationship between alcohol and cannabis is likely to vary across different populations. Subbaraman (2016) expanded this reasoning and suggested that complementarity may be more likely in settings prone to alcohol consumption and substitution more likely in settings with more liberal attitudes towards cannabis. This idea was based on studies of decriminalization of cannabis finding support for substitution (48). Our findings are in line with this reasoning, as Sweden has a low prevalence of cannabis use and strict legislation, while alcohol consumption is more widespread and socially accepted.

6.2.2 SES and academic orientation in relation to cannabis use

A better understanding of the association between SES and cannabis use is important as SES-differences in cannabis use could strengthen and reproduce SES-differences in life prospects. Previous research on the association between SES and cannabis use among adolescents has been inconclusive (55–60). Our finding of a higher risk of lifetime use of cannabis among adolescents with at least one parent with higher

education is in line with earlier studies showing that occasional cannabis use is more common among adolescents with high childhood SES (59, 60, 111). However, studies of the frequency of cannabis use among adolescents suggest that adolescents with low childhood SES have an increased risk of more frequent or extensive cannabis use (59, 61). Thus, our finding of a *lower* risk of frequent cannabis use among lifetime users of cannabis with high childhood SES are in line with these previous findings.

A possible explanation of the SES differences in cannabis use could be unequal exposure to risk factors for cannabis use, such as school commitment (70), parental attitudes (112, 113), and an adolescent's own risk assessment (114, 115). In Study II, we found that these factors did attenuate the association between childhood SES and frequent cannabis use among cannabis users but not the association between childhood SES and lifetime cannabis use among all adolescents. Hence, our findings suggest that truancy, parental permissiveness of cannabis use, and risk assessment of cannabis use among adolescents are of importance to understand the association between childhood SES and frequent cannabis use among adolescents but are not sufficient to explain it.

During adolescence, the influence of the family decreases and other factors become more important (56). Hence, it is of interest to elucidate other dimensions of SES relevant in adolescence. One such dimension is SES of destination, which is linked to the path in life that a young person chooses for themselves. Academic orientation can be used as a proxy for this (66). Only a few previous studies have used this possibility and researched the association between academic orientation and adolescent substance use. Results from these studies suggest an increased risk of negative health behaviors such as binge drinking (66, 67), tobacco use, and use of illicit substances (66) among pupils in VPs compared with those in HEPs. The results of Study II, showing an increased risk for cannabis use among pupils in VPs compared with those in HEPs, are in line with these results. Our findings from Study III add to previous findings and broaden the perspective further by including pupils from IPs.

In Study III, we found an increased risk of frequent (21+ times) cannabis use among pupils in both VPs and IPs compared with pupils in HEPs, with the highest risk among those in IPs. Our results lend further support to the idea that academic orientation may serve as an important predictor of negative health behaviors, including frequent cannabis use. In line with what we found in Study II, the association between academic orientation and frequent cannabis use was attenuated and no longer significant in the fully adjusted model. Thus, the increased risk of frequent cannabis use in VPs and IPs was by and large due to unequal exposure to risk factors such as truancy (71, 116) and early onset of substance use (71, 72).

6.2.3 Cannabis use and mental distress

The association between adolescent cannabis use and the risk of negative mental health consequences is not fully disentangled and previous findings are mixed (see, e.g., (4) for an overview). In Study IV, we assessed the within-person association between cannabis use and various types of mental distress during adolescence and early adulthood, using FE modeling.

The significant associations that we found between cannabis use and suicidal ideation for both males and females are generally in line with previous findings pertaining to the general youth population (90, 92). Regarding the association between cannabis use and anxiety, previous findings are inconclusive. Some recent studies of the association in question suggest no significant relationship between cannabis use and anxiety (90, 117), whereas other studies point in the same direction as our findings (118, 119). Moreover, previous findings from studies of the general youth population, indicate an association between cannabis use and DSH (92, 120), while our results did not give any support for such an association. A possible explanation for the inconsistency between our findings regarding anxiety and deliberate-self harm and some of the previous studies could be the different study designs and statistical approaches used. The association between cannabis use and depressive mood was the only one where we also found a significant difference in the estimates between males and females. This finding is consistent with previous conclusions from some US studies reporting gender-specific associations between cannabis use and symptoms of depression in males (119, 121).

It has been suggested that the association between cannabis use and mental distress can be attributed to THC, and that intake of THC affects brain functions in a way that increases the risk of mental distress (98). Moreover, it has been argued that adolescents are particularly vulnerable to the negative effects of cannabis use because their brains are not fully developed (16). Another suggested explanation is common risk factors, such as parental mental health problems, affecting both cannabis use and mental distress through either genetics or environment (99). Yet another possible explanation is that cannabis use is indirectly associated with mental distress through social mechanisms (92), such as difficulties in the labor market (22) or school failure (19). According to this line of reasoning, mental distress would emerge from these types of social problems, which are also related to cannabis use. However, it is not possible, based on the results in Study IV, to attribute the associations we found to either the effects of THC or social mechanisms. What can be established is that there seems to be an association between cannabis use and mental distress that is not explained by confounders that are stable within individuals over time, such as family background or genetics.

6.3 Methodological considerations

Three of the studies in this thesis (Studies I–III) are based on self-reported cross-sectional data. A well-known limitation of the cross-sectional design is that the outcome and predictor are measured at the same time, which prevents conclusions being drawn regarding causal relationships. One way to strengthen the approach when working with self-reported cross-sectional data is to avoid using self-reported data as both outcome and predictor. In Studies II and III, we therefore used information collected directly from the schools and from registers, which was therefore not sensitive to bias associated with self-reporting.

Furthermore, self-reported information may be affected by survey response bias. All four studies included in the thesis relied on self-reported information on cannabis use. Answering questions about a behavior that is illegal and presumably not socially desirable can lead to underreporting (122). However, the opposite can also occur among adolescents, and it cannot be ruled out that some respondents exaggerated their cannabis use. In order to prevent this type of bias, the surveys were filled out in the classroom, with the anonymity of the participants strongly emphasized. Furthermore, obviously exaggerated answers were removed in accordance with a standardized procedure (27). It is possible that the respondents had trouble remembering certain events, such as how many times they had used cannabis, this would lead to recall bias (122).

Another potential source of bias is non-response, which occurs when participants (pupils) do not take part in the survey. It is plausible that the pupils not present when the rest of the class answered the survey differed from those who were present (123). A Swedish study of non-responders found that those who were not present at the time of the survey reported higher levels of substance use. However, when they were included in the analysis, the overall results were only marginally affected (124). Furthermore, the Swedish national school survey, which was used in Studies I–III, has generally high response rates, both among the sampled classes and at the individual level. Another strength of the Swedish national school survey is its consistency over time. The same methodology has been used to collect data for several decades, with only minor modifications to the questions. This allowed us to examine whether cannabis and alcohol are complements or substitutes in Study I, using a time-series analysis methodology. Still, the number of datapoints ($n = 28$) was at the lower end of what is recommended for ARIMA modelling and future replications of the present findings with longer time series are warranted.

In Study IV, we used data from the Young in Norway Longitudinal Study, which has a relatively high cumulative attrition of 40%. A study analyzing the attrition in the Young in Norway Longitudinal Study found that, for example, being male, older age, having poor

grades, and suburban or urban residency predicted attrition between 1992 (T1) and 2005 (T4) [41]. Hence, it cannot be ruled out that the panel attrition of 40% may have led to an overrepresentation of adolescents with characteristics of importance for the analysis in Study IV. Moreover, the data in Study IV were collected between 1992 and 2005, when the concentration of THC was lower than it is today [2]. This means that the association between cannabis use and mental distress might have been stronger if the analysis had been based on more recent data. For instance, a recent study of US adults showed that the association between cannabis use and depression was strengthened markedly from 2005 to 2016 [39]. It is possible that cannabis use has grown in importance as a risk factor for mental distress since the time when the data for Study IV were collected.

Another important methodological issue concerns how cannabis use was measured. A crude measure of frequency of use was applied in all four studies. No data on the quantity of consumption were available. It has been suggested that the amount consumed is of importance, above and beyond the frequency of use (125).

However, our data allowed us to treat depressive mood, anxiety, and suicidal ideation as continuous conditions rather than as dichotomous outcomes. This is a strength, as dichotomization results in a loss of information and a decrease in statistical power (126). Another strength in Study IV is the statistical approach, where we analyzed within-person changes using FE modeling. This has the advantage of acting as a safeguard against bias due to confounders that are temporarily stable within a person, such as family background or genetics. Although the FE-technique eliminates the risk for bias caused by covariates that are stable within individuals across time, it does not remedy confounding that is due to time-varying factors that affect the outcome as well as the explanatory variable. The design can thus be strengthened by including time in the model, in order to eliminate bias from unobserved variables that change over time but are constant over individuals. We controlled for time by including assessment year in the model. Still, our estimates may be biased due to other time-varying factors affecting cannabis use or mental distress that we were unable to control for.

6.4 Implications and future directions

This thesis provides new knowledge regarding cannabis use in the general population of adolescents. An important finding was that cannabis and alcohol act neither as complements nor as substitutes among Swedish adolescents. This is valuable knowledge when shaping prevention strategies as it has been hypothesized that if alcohol and cannabis act as substitutes, policies reducing access to alcohol may lead to increased cannabis use (44, 45, 110). Further, it has been suggested that if alcohol and cannabis act as complements, preventive measures against youth drinking may also reduce cannabis use (38, 41, 127). None of these scenarios seems likely with regard to

Swedish adolescents aged 15–16 years, which is useful information for policymakers when planning preventive measures directed at use of alcohol and cannabis among adolescents. An area for future research is to assess whether this is true also for older adolescents, among whom use of alcohol and cannabis is more prevalent. It has been suggested that substitution or complementarity could vary between subgroups with different motives for use (128). Hence, further studies addressing this issue for adolescents stratified by motives for use are warranted, to understand the generalizability of our findings.

Furthermore, this thesis shows that cannabis use is unevenly distributed across SES groups among Swedish adolescents. As cannabis use is associated with increased risk for adverse consequences (3, 4), it is also likely that these consequences are unevenly distributed across SES groups. It is therefore important to further examine which factors are related to experimental cannabis use and which factors may relate to continued and more problematic use. Such knowledge is valuable for preventive efforts, to reduce cannabis use and the risk of negative consequences in general, but also for understanding the specific role of SES-differences in cannabis use and related problems in the youth population as a whole.

Additionally, the thesis sheds light on a previously overlooked group of adolescents in this context: pupils in IPs. In addition to using cannabis more frequently and having a greater number of risk factors for cannabis use, such as low motivation for school, truancy, and early onset of substance use (70–72), these pupils run a greater risk of not graduating from upper secondary school (125). School failure is related to worse future work opportunities and life prospects (81, 82), as well as drug abuse (126). From a social inequality perspective, this group of pupils, who struggle with multiple disadvantages, is important to reach with prevention efforts. Although pupils in IPs are not part of the national programs, they are enrolled in school and can thus be effectively reached through that channel. Previous research shows that a favorable school environment can have a mediating effect on risk factors related to alcohol use (129) and decrease the risk of gambling among adolescents (130). Hence, an important issue for future research is to investigate if this is valid also for cannabis use. Although including pupils from IPs in the national estimates of cannabis use did not have any effect on prevalence, it is important not to neglect this group in future research addressing risk groups for cannabis use.

Though the present thesis found support for the idea that cannabis use increases the risk of various types of mental distress among adolescents, further research in this area is warranted. This is particularly important in light of the recent reports of higher levels of THC in today's cannabis products (11, 12). Furthermore, our findings differed between males and females. Hence, an urgent task for future research is to determine what factors may account for this gender difference. Additionally, the finding of an

association between cannabis use and mental distress highlight that adolescent cannabis use is an important public health issue.

Another important area for the field of epidemiological cannabis research is how to measure and quantify cannabis use. A framework to accomplish this has been proposed, the *iCannToolkit* (131), but it is far from being implemented. Although it is desirable to strive towards harmonization in how to measure cannabis in surveys around the world, there are some challenges to this. Against the backdrop of the present thesis, it is important to ensure that such a framework can be used also among adolescents. Furthermore, it is important to preserve and gently improve the long time series on adolescents' cannabis use that exist around the world (27–29), as they are an invaluable source for future research.

6.5 Conclusions

This thesis shows that cannabis and alcohol act neither as complements nor as substitutes among Swedish adolescents. Hence, prevention strategies aimed at either substance is unlikely to affect use of the other. Moreover, the findings strengthen the assumption that cannabis use in adolescence and young adulthood is associated with mental distress. The thesis also shows SES differences in cannabis use, related to both parental education level and academic orientation. Adolescents whose parents lack higher education and those who attend a vocational or introductory program at upper secondary school have an increased risk of using cannabis more frequently. This finding also suggests that these groups are at higher risk of the negative consequences associated with cannabis use in adolescence. Overall, the results indicate that young people's cannabis use is an important public health issue and that it is important to try to prevent cannabis use. The thesis also highlights that there are groups that are particularly vulnerable where targeted efforts may be needed to reduce the use of cannabis.

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