



# Childhood Substance Use & Associated Adult Health Outcomes

## A Review of the Literature



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## INTRODUCTION

In September of 2015 Injury Free Nova Scotia engaged Sandstone Health Promotion to carry out a comprehensive review of the literature on the associations between a substance free childhood and health and/or injury outcomes in adulthood.

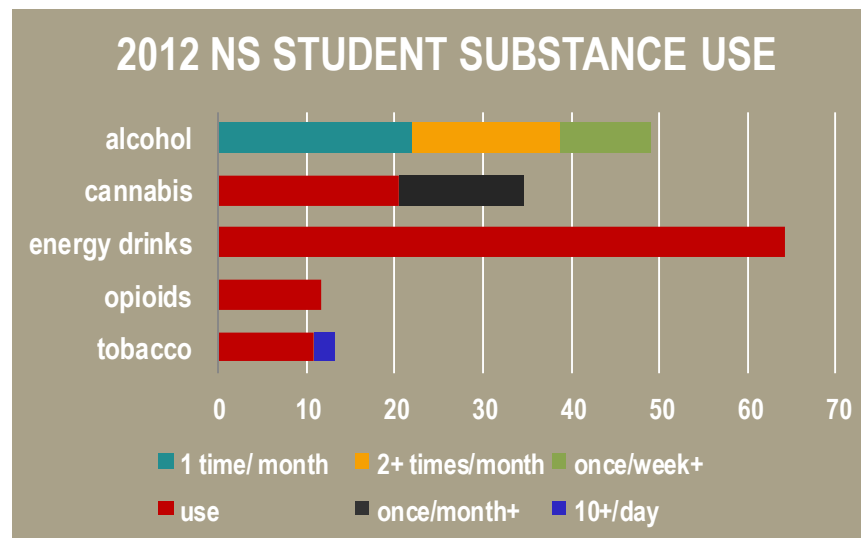
This review summarizes much of the published in English peer-reviewed evidence that exists surrounding the use of tobacco, alcohol, cannabis, non-prescribed opiates, and energy drinks by children and youth who are age 18 and under, and associated health and injury outcomes in adulthood (those that occur at age 19 years and beyond).

The focus of this review was to create an integrative and narrative document; one which attempts to find the common ideas and concepts around this topic and organizes them in a qualitative and structured way. As with any review of literature, all efforts were made to ensure the inclusion of a wide range of relevant, recent, credible and reliable peer-reviewed evidence; and to exclude any papers not meeting these criteria. A total of 150 peer-reviewed journal articles were considered and after exclusions 104 were used.

Adolescence is a life phase in which the opportunities for health are great, and future adult health patterns are established. (108) Health-related behaviours (i.e., behaviours that positively or negatively affect health) and health outcomes in adolescence have a sustained effect on future health. Many opportunities for prevention of a variety of health outcomes, including non-communicable diseases, mental disorders, and injuries in adults arise from a focus on risk processes that begin during or before adolescence. (93) Adolescence is a time of increased vulnerability to drug use; initiation of substance use typically occurs within this period. (118) Many health-related behaviours that usually start in adolescence, including substance use, contribute to the epidemic of non-communicable diseases, poor psychosocial and mental health, and increased rates of substance use and substance use disorders in adults. (93)

## Nova Scotia Student Substance Use Rates

The Nova Scotia Student Drug Use Survey 2012: Technical Report (2013) reports that the substances most commonly used by Nova Scotia students in 2012, as in prior years, were alcohol, cannabis and cigarettes. Almost half of all students consumed alcohol and more than a third used cannabis in the previous year. Cigarettes were used at the rate of 13.2%. The proportions of students using alcohol, cannabis and cigarettes were similar to those found in the 2007 survey. Also of note are energy drinks and non-prescription pain pills. Almost two thirds of students (64.3%) reported consuming energy drinks in the year prior to the survey. In 2012, 11.7% of students reported using pain pills that were not prescribed for them (such as Percocet, Percodan, Tylenol #3, Demerol, Oxycontin, or codeine). (130)



For cigarettes, alcohol and cannabis the period of highest risk for initiation peaks at age 18 and declines hereafter. (55)

## Important Aspects of the Literature

### Age of Onset of Use

Population based cohort study findings indicate that the timing of onset of substance use may be important. (23) Early onset of substance use during adolescence is often strongly associated with “developmental harm”, characterised by increased risks for the development of adverse health outcomes in late adolescence and early adulthood. (58)

Early onset of substance use (particularly under age 15) is associated with a higher rate of reporting symptoms of dependence both concurrently and even 20 years later, the progression to using multiple substances, and the onset of other psychiatric problems. It was also associated with longer substance use careers, longer histories of use before entering treatment, and longer treatment careers. Early use of tobacco, alcohol or cannabis in adolescence has also been associated with increased risk for later dependence, as well as other health problems in early adulthood. (25) (58)

Despite robust evidence for a link between early-onset substance use and the development of problem use or other psychopathology in late adolescence and early adulthood, the mechanisms that underlie such associations are not fully understood. (58) When it comes to age of onset, it may be more important in adult research where it serves as a retrospective marker of earlier vulnerability for a problem that has already occurred and appears to imply causality. (45)

### Brain Development

Adolescence is a key period of neuromaturation, with growing evidence that the adolescent brain may be more vulnerable to the effects of addictive substances than the adult brain. Substance use during adolescence can elicit altered sensitivity to later drug exposure, impair adult cognitive functioning, and even induce cortical damage. (59)

### Causality

A major caveat of human studies is the difficulty in demonstrating a causal relationship between adolescent substance use and subsequent health behaviour disturbances. This especially relates to the influence of confounding and mediating factors such as genetic, environmental, social, cultural and other factors; and other aspects such as such as trajectories of use and use of multiple substances. (50) Most, if not all, of the research stipulates that conclusion of a causal relationship is difficult, if not impossible, to prove. Most often an association can be concluded - an acknowledgement of a link; but proving that the substance directly causes the health outcome is very difficult. (11)

### Confounding

A confounding variable is an extraneous variable whose presence affects the variables being studied so that the results you get are not reflective of the actual relationship between the variables under investigation. The validity of the results of studies of substances is threatened by the possibility of residual uncontrolled confounding factors. A variable is considered a confounder if it is not intermediate in the pathway relating exposure to outcome but is associated with both the exposure and the outcome of interest, leading to a distortion of the true relationship.

For example, more recent studies have controlled for a wide range of factors that could confound the relation between cannabis and various outcomes—factors such as genotype, sex, age, psychosis before using cannabis, education, personality, IQ, affiliation with deviant peers, conduct and attention disorders, other substance use, social functioning, previous mental health, parental age, parental divorce, changes in parents, parental attachment, parental offending and substance use, socioeconomic factors, physical and sexual abuse, and childhood trauma. (34) However, it is often expressed that there is no way of knowing whether residual confounding factors exist.

## Dose Response Relationship

A dose response relationship is based on the premise that the more a substance is consumed, the more likely a health outcome (positive or negative) is to occur. Frequent substance use, especially in adolescence, is strongly associated with “developmental harm”, characterised by increased risks for the development of health problems, as well as a range of other adverse outcomes.

For example, an integrative analysis by Silins et al (2014) found clear and consistent associations and dose-response relations between the frequency of adolescent cannabis use and young adult outcomes. (98)

## Gateway Drugs

A *gateway drug* is one which the use of precedes the initiation and subsequent problematic use of other drugs. (64) The nature of these gateway effects is a matter of some debate. The original gateway hypothesis posited a progression in drug use beginning with tobacco and alcohol, moving onto cannabis, and then onto other illicit drugs. (7)

For example, research completed by Yamaguchi & Kandel in 1984 suggested that for men, the pattern of progression was one in which alcohol precedes marijuana; alcohol and marijuana precede the use of other prescribed psychoactive drugs. They found 87% of men were characterized by this pattern. For women the pattern of progression was one in which either alcohol or cigarettes preceded marijuana; alcohol, cigarettes, and marijuana precede other illicit drugs. Alcohol, cigarettes and marijuana precede prescribed psychoactive drugs; 86% of women shared this pattern. (117)

The evidence now demonstrates that alcohol, tobacco and cannabis all, to some degree, act as gateway drugs for one another, as well as for other licit and illicit drugs. It should be noted that research completed since the Yamaguchi and Kandel study has found more nuance in the pathways between various substances.

**Reverse gateway effect.** Sometimes the relationship is a reciprocal feedback loop involving simultaneous causation between two substances of one another, e.g. cannabis and tobacco; this is referred to as a reverse gateway effect.

## Generalisability

This is the question of whether study results are likely to apply, generally or specifically, in other study settings or samples; i.e., are the study results externally valid? An aspect of generalizability specific to this review is the inclusion of peer reviewed literature from Europe, Australia and New Zealand. Generally speaking, because rates of cannabis use in Australasia are similar to those in other high income countries (e.g. Canada, USA, and the UK), generalisability of findings to those setting is supported. (98)

## Psychosocial Development

This involves the stages through which a healthily developing human should pass from infancy to late adulthood. Numerous studies have linked substance use to psychosocial and behavioural problems during late adolescence and emerging adulthood. (108)

## Trajectories of Use

Many studies tracking substance use from childhood through to adulthood use a trajectory-based model to highlight developmental patterns which include: onset and duration of use, timing, the amount and number of substances used and any changes in these factors in relation to substance use.

Once these trajectories have been identified, they are used to track usage patterns and associated longitudinal health and other outcomes. Trajectories are useful in tracking long term outcomes of substance use, however, it should be noted that multiple trajectories of use can look the same, i.e. youth using cannabis do not necessarily look like ‘high risk’ users, especially early on in their use of a substance. It is often only retrospectively that we can see a higher risk trajectory. (108)

## Other Important Vocabulary

### Mediating Factors

A mediating relationship occurs when a third variable plays an important role in governing the relationship between the other two variables, e.g. between use of a substance and a specific health outcome, such as adult use of the substance.

### Sequelae

Sequelae refers to pathological conditions that are the consequences of a previous disease or injury.

### Substance Use

Substance use is when someone consumes alcohol or drugs (both licit and illicit). It does not necessarily mean that the use is harmful, or that it will lead to negative outcomes.

### Substance Use Disorder (SUD)

According to the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)* substance use disorders are defined as mild, moderate, or severe to indicate the level of severity, which is determined by the number of diagnostic criteria met by an individual. A person is considered to have a substance use disorder when the recurrent use of alcohol and/or drugs causes clinically and functionally significant impairment.

This term replaces the terms 'substance abuse' and 'substance dependence'. When specific to one substance, the substance name can be substituted for 'substance'; such as Nicotine Use Disorder (NUD), Tobacco Use Disorder (TUD), Alcohol Use Disorder (AUD), Caffeine Use Disorder (CUD) and Opioid Use Disorder (OUD).

## ALCOHOL

### Student Alcohol Use Rates in NS

According to the 2012 Nova Scotia Student Drug Use Survey: 22% of high school aged students reported drinking alcohol once a month or less, 16.7% consumed alcohol two or more times a month and 10.3% reported drinking at least once a week. (130) Alcohol use is comparable among male and female students in Nova Scotia. Alcohol use increased with higher grade level, with 10.7% of students reporting some use in grade 7, and more than three out of four students using alcohol by grade 12. (130)

### Binge Drinking

When asked about binge drinking, 26.6% reported at least one episode of heavy drinking in the previous month. The proportions of students who participated in this behaviour increased with grade level. (130)

### Age of First Drink

When asked about age of first drink: 29.4% of students reported never drinking alcohol. Among those students who had tried alcohol, the average age of first use was 13.4 years of age. This is slightly older than the age of first use in 2007(12.9 years). (130) Wagner and Anthony (2002) found that, with respect to risk of initiating use, estimated peak value for alcohol was found at age 18. (112)

## Dose Response Relationship

Use of alcohol demonstrates a linear relationship between the amount of alcohol consumed, the duration of alcohol use, and associated negative health outcomes. Patterns of chronic and late-onset heavy drinking in adolescence had negative consequences for later health. Compared with young adults who did not drink heavily during adolescence, chronic heavy adolescent drinkers had, at age 24, the most negative health profile of all drinkers, with increased risk for poor health and serious disease. (138)

## Energy Drinks + Alcohol

Adding energy drinks to alcohol does several things that complicate and/or enhance the effects of the alcohol. Carbonation tends to increase the rate of absorption of alcohol. Diluted concentrations of alcohol are emptied from the stomach into the faster absorbing small intestine more rapidly than high concentrations. (113)

Caffeine keeps one awake and blunts the sedative effects of the alcohol. Lengthened time awake theoretically allows greater alcohol intake before loss of consciousness. At low blood alcohol levels, caffeine appears to decrease some of the physical and mental impairment from the alcohol. At higher blood alcohol levels caffeine does not appear to have a modifying effect on either the physical or mental impairment induced by the alcohol. Energy drink ingredients give the consumer a greater false sense of physical and mental competence and decrease the awareness of impairment. (113)

## Physical Health

Early adolescent binge drinkers and those who steadily increased their binge drinking through adolescence, experienced poor physical health at age 23, as compared to abstainers, and those who moderately or heavily binge drank. (108)

## Cardiovascular Health

Chronic binge drinking is associated with cardiovascular health problems during emerging adulthood, such as hypertension and being overweight. (108) Compared with young adults who did not drink heavily during adolescence, chronic heavy drinkers during adolescence were three and a half to four times as likely to be overweight or obese, to have a high risk waist size and to have high blood pressure. (138) In a longitudinal study by Twisk et al. (1997) long term alcohol use was related to a high risk profile regarding hypercholesterolemia, an excess of cholesterol in the bloodstream. Alcohol use was inversely related to HDL (High-density lipoprotein), and positively to the TC (total cholesterol)/ HDL ratio. (109)

## Mental Health

### Neuropsychological Functioning

Clinical studies have revealed neurocognitive deficits evident years following adolescent alcohol use. A history of heavy alcohol use was associated with poorer cognitive and brain function, with residual affects seen for years thereafter. (100)

**Brain structure.** A number of studies have reported smaller hippocampal volumes amongst adolescents and young adults with alcohol use disorders (AUD) compared to healthy matched controls. In one of these studies, hippocampal volumes were positively correlated with age of first use and negatively correlated with duration of use. Adolescents with AUD have also been reported to have smaller prefrontal cortices and white matter volumes, with significant correlations noted between prefrontal cortical volumes and measures of alcohol consumption. Such structural abnormalities are in keeping with reported alcohol-related neurocognitive impairments amongst adolescent drinkers as well as recent functional imaging findings. (59)



**Dose-response.** At an average age of 24 years, greater cumulative lifetime alcohol experiences predicted poorer attention functioning as well as poorer working scores. (14) Heavy alcohol involvement during adolescence is associated with cognitive deficits that worsen as drinking continues into late adolescence and young adulthood. (14)

**AUD.** Brown and Tapert (2004) found in their longitudinal study that youths with AUD who continued alcohol involvement after treatment, and at any time experienced alcohol withdrawal symptoms, demonstrated poorer visuospatial functioning and neurocognitive outcomes at 4 years after treatment discharge; even after excluding youths who drank heavily and used other substances. (14)

### **Personality Disorders**

McGue et al. (2001) found that an early age of first drink is associated with antisocial personality and conduct disorder. (68)

## **Psychosocial Factors**

Adolescent binge drinking is related significantly to both prosocial and antisocial outcomes in adulthood. In particular, early high binge drinking predicted poor prosocial functioning at age 21; part of a cluster of problem behaviours resulting in fewer positive and more negative outcomes in young adulthood. (48)

### **Education**

McGue et al. (2001) found that an early age of first drink is associated with academic underachievement. (68) All adolescent binge drinkers experienced lower rates of college graduation at age 23, as compared to abstainers. (108)

### **Risk Taking**

**Sexual behaviour.** Growth in adolescent alcohol use was associated positively with young adult risky sex. Drinking may facilitate risky sexual involvement, either through the expectation that it will enhance sexuality or through the pharmacological effects of alcohol. A disinhibitory pattern, once established in adolescence, may extend into young adulthood. Early alcohol use predicted a higher level of, and a faster rate of increase in, adolescent drinking, which predicted, in turn, risky sex. (1)

**Driving.** Late onset adolescent drinkers were less likely to practice safe driving at age 24 compared to adolescents who did not drink heavily. (138)

### **Violence**

All groups of adolescent binge drinkers engaged in predatory violence (e.g. gang fighting, attacking someone) more at age 23, as compared to abstainers. (108)

### **Illegal Activity**

All adolescent binge drinkers experienced higher rates of selling drugs at age 23, as compared to abstainers. (108) Compared to adolescent non binge drinkers, early in adolescence high binge drinkers had higher rates of crime at age 21. (48)

## **Adult Substance Use**

All adolescent binge drinkers experienced significantly more drug problems at age 23, as compared to abstainers. (108) Compared to adolescent non binge drinkers, those who increasingly binge drank and those who did so a lot early in adolescence experienced far more alcohol abuse and dependence at age 21. (48)

## Adult Alcohol Use & Alcohol Use Disorder (AUD)

Adolescent onset of drinking poses an increased risk for lifetime alcohol related problems. (18) Heavy consumption in young people is common and persistence into young adulthood is much more likely than not. (24)

Moderate-risk adolescent alcohol use in the absence of weekly cannabis predicted an approximately threefold increased rate of high-risk drinking in young adulthood. (83) All adolescent binge drinkers experienced significantly more alcohol problems at age 23, as compared to abstainers. (108)

**Age of first drink.** Age of first drink is associated with increased likelihood of heavy drinking, and AUD. (68) The younger youth are when they start drinking, the more dependence criteria they develop later on. (14)

Research completed by Chou and Pickering in 1992 demonstrated that in youth who started drinking at age 15 or earlier there was a clear inverse relationship between age of first drink and the number of criteria for AUD. The prevalence rate of at least three criteria of AUD in early adulthood was 42.4%; with the exception of females who were 65 years or older, all age/ gender groups had a prevalence rate of at least 20%. (18)

Dewit and colleagues (2000) found that the incidence of life-time alcohol abuse and dependence is greatest for those who begin drinking between the ages of 11 & 14 years. Their research revealed a rapid progression to alcohol-related harm among those who reported having their first drink at ages 11–14.

After 10 years, 13.5% of the subjects who began to drink at ages 11 and 12 met the criteria for a diagnosis of alcohol abuse, and 15.9% had a diagnosis of dependence. Rates for subjects who began to drink at ages 13 and 14 were 13.7% and 9.0%, respectively. In contrast, rates for those who started drinking at ages 19 and older were 2.0% and 1.0%. Unexpectedly, a delay in progression to harm was observed for the youngest drinkers (ages 10 and under).

**Binge drinking.** In a 2013 study by Degenhart et al. 90% of male and 70% of female adolescent onset binge drinkers continued to binge in young adulthood. Adolescent binge drinking is a significant risk factor for adult binge drinking: Only 7% of the sample had binge drinking in adolescence but not young adulthood. (24)

Males with adolescent-onset binge drinking were more likely to continue binge drinking in adulthood than females: around 7 in 10 males reported doing so, compared to fewer than half of the females. Levels of adult heavy binge drinking (drinking more than 20 drinks on an occasion) did not differ markedly by sex among adolescent-onset binge drinkers; around 20–30% reported past-week heavy binge drinking at ages 20 and 24, with lower levels at 29 years. (24)

**AUD.** Adolescent alcohol use increases risk for young adult alcohol use disorders. (1) Adolescents who take their first drink of alcohol before the age of 15 are substantially more likely to become an 'alcoholic' than those whose first drink comes after the age of 20 years. (67) In a sample of more than 27,000 adults, the rate of lifetime alcohol dependence was four times higher among those who started to drink by age 14 years compared with those who had not started to drink until age 20 years or older. (68) Duncan and associates (2015) found that having an AUD in one development period significantly predicted having an AUD in the subsequent developmental period (youth, young adult, adult). (29)

The risk of becoming alcohol dependent persists for decades after first alcohol use. Cases of alcohol dependence continue to accumulate. (112) Some 12 – 13% of alcohol users had developed alcohol dependence within 10 years of first use. (112) Alex Mason et al. (2010) found that the level of alcohol use in middle adolescence was positively related only to AUDs in early adulthood. Early alcohol use was associated with a higher level of, and an accelerated increase in, adolescent alcohol use, both of which were associated, in turn, with elevated risk for young adult AUDs. (1)

**GLBT persons.** Gay and lesbian youth exhibited the fastest growth over time, which led them to transition from having normative levels of hazardous drinking during adolescence to reporting the highest levels of binge drinking and drunkenness among the groups during young adulthood. The levels of hazardous drinking among female sexual minority youth escalated into adulthood and neared or equalled levels among heterosexual males, for binge drinking and drunkenness, respectively. In contrast, disparities among men were delayed and did not emerge until young adulthood. (26)

### **Adult Tobacco Use & Tobacco Use Disorder (TUD)**

McGue et al. (2001) found that an early age of first drink is associated with increased rates of nicotine dependence. (68)

### **Adult Cannabis Use & Cannabis Use Disorder (CUD)**

Adolescent alcohol use and adult cannabis use are positively correlated. Moderate-risk adolescent alcohol use in the absence of weekly cannabis predicted an approximately threefold increased rate of daily cannabis use in young adulthood. (83)

**CUD.** Duncan and associates (2015) found youth AUD to be predictive of young adult CUD (ages 18 – 23.9). (29)

### **Adult Illicit Substance Use**

McGue et al. (2001) found that an early age of first drink is associated with illicit substance abuse. (68) Compared to adolescent non binge drinkers, those who increasing binge drank and those who did so a lot early in adolescence experienced more drug abuse and dependence at age 21. (48)

## **CANNABIS**

Youth is a very vulnerable period in life. Socially young people need to develop and mature, and to prepare themselves to meet demands in their adult life, such as completing education, and finding employment, choosing leisure activities, and finding partners and friends. Cannabis use, especially frequent use, impairs this development and reduces the likelihood that a young person will be able to establish a satisfactory adult life. (79)

The 2013 United Nations Children’s Fund study on the well-being of children found that Canadian adolescents (aged 11 to 15) have the highest rate of cannabis use among the 29 advanced economies of the world; an estimated 28% had used cannabis at least once in the past year. (129) The high rate of cannabis use is considered worrisome. Evidence shows lifelong, significant and substantial risks to persons who regularly use cannabis as youth. (101)

### **Student Cannabis Use Rates in NS**

Since 1996, cannabis use by Nova Scotia students has remained relatively consistent, with rates ranging from 32.1% to 37.7%. In 2012, 34.7% of students reported that they used cannabis in the past year; 14.2% of the students used cannabis more than once a month. Cannabis use increased significantly from grade 7 through to 12. The average age of first cannabis use among Nova Scotia students was 14.3 years. (130) With respect to risk of initiating cannabis use, risk peaks at age 18. (55)(112) Most adolescents who use cannabis use it infrequently (once a month or less). (23)

Current evidence raises a strong challenge to the widespread view that cannabis is a relatively harmless drug, and suggests that especially heavy use of cannabis may have significant and adverse consequences. (31) Adverse sequelae of adolescent cannabis use are wide ranging and extend into young adulthood. A significant amount of peer reviewed evidence has been published on the topic. Prevention or delay of cannabis use in adolescence is likely to have broad health and social benefits. (98)

## Early Onset of Use

A 2004 systematic review (Macleod et al.) of longitudinal, general population studies found that cannabis use at a younger age was consistently associated with greater subsequent problems. (60)

## Dose Response Relationship

Fergusson et al. (2008) noted that the results of their study suggested that the risk of adverse outcomes increases progressively with increasing levels of cannabis use. A large number of individuals in the cohort they studied used cannabis and experienced very few adverse consequences, and that outcomes for those using cannabis sparingly (fewer than 100 times) did not differ markedly from those who did not use cannabis at all. (31)

## Overall Health

Ellickson and her colleagues (2004) found that at age 29 all those who used cannabis more than three times per year had poorer overall health than abstainers; and those who were adolescent early high users fared significantly worse than all other groups of adolescent cannabis users. (30)

Macleod and his associates suggest that the association between cannabis use and physical harm may be linked to the fact that it is most often smoked along with tobacco; and that intermittent use, confined to adolescence, might have small effects. (60)

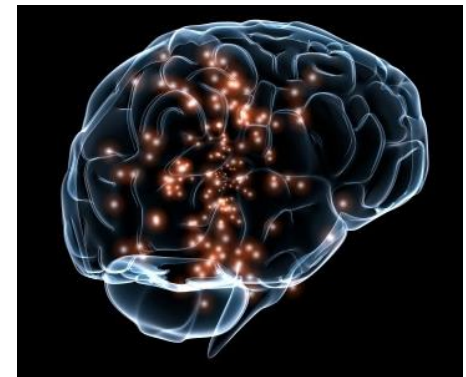
## Psychological Health

Overall, it is impossible to ignore the evidence that cannabis, and more specifically, Tetrahydrocannabinol, widely known as THC, is not harmless to the developing brain. (50)

It should be noted that in one small study of children raised in California during the 1970s children who experimented with cannabis were reportedly better adjusted psychologically than those who abstained until 18 years. (123) However, these study results were not replicated.

A few studies have found no significant connection between adolescent cannabis use and adult mental health. In 2004 Ellickson et al. found that the mental health at age 29 of adolescent cannabis users did not vary from adolescent abstainers. (30) In 2000, McGee and his colleagues found in their longitudinal review that there was no evidence that use of cannabis in adolescence was associated with an increased risk of later mental health problems. (65)

Many more lines of evidence do suggest a link between adolescent THC exposure and subsequent vulnerability to addiction and psychiatric risk. (50) Tucker and colleagues (2005) found that more persistent users of cannabis experienced poorer mental health than occasional and non-users. (108) The Dunedin (New Zealand) Multidisciplinary Health and Development Study demonstrated that cannabis use at age 18 elevated the risk of mental disorder at 21; this was especially true of externalizing conduct and antisocial disorders. (65)



## Directionality

Directionality of association in relation to negative mental health outcomes has been questioned. McGee et al. argue that the primary direction of risk lies from mental disorder to cannabis rather than the reverse. (65) However, the majority of the evidence presented in the following sections demonstrates a path leading from adolescent cannabis use to mental health problems and mental illness.

For example, Renard and colleagues (2014), conclude that the considerable body of evidence obtained from both human studies and animal models demonstrates that cannabis use during adolescence increases the risk of developing a psychiatric disorder in adulthood. (122)

## Multifactorial Causes

The psychiatric disorders discussed in this review are multifactorial in origin, and the transition from adolescent cannabis use to subsequent psychiatric illness may also involve both genetic factors and environmental factors. The developmental period of initiation, the frequency, and the duration of cannabis use, as well as any underlying psychiatric pathology, may all play a critical role in the development of a psychiatric disorder. In addition, compelling evidence suggests that some adolescents are more susceptible to the long-term effects of cannabis use than others, and this may be due to differences in genetic vulnerability. (122)

## Neuropsychological Functioning

In their research, Meier and associates found that when tested across various neuropsychological domains, impairment was found to be global in nature. (70) Other evidence, included below, provides more specific results. Of note: Cessation of cannabis by adolescents in one study included in the review by Meier et al. (2012) did not fully restore neuropsychological functioning among adolescent cannabis users. (70)

**Changes in brain structure.** The age at which regular cannabis use begins is a key factor in determining the severity of the resulting microstructural changes in white matter. (122) Young people who begin using cannabis before the age of 17 seem to be more vulnerable to cognitive impairments and show reduced brain grey matter. (59) Magnetic resonance imaging (MRI) and positron emission tomography (PET) studies have reported reduced overall cortical gray matter and increased white matter volume in adolescent cannabis users compared to users who began using cannabis in adulthood. (122)

**Attention.** Those who knew study participants well reported observing significantly more attention problems among those with more persistent cannabis use. (70)

**Learning and memory.** Studies suggest that chronic cannabis use during adolescence can cause long-term structural changes that are associated with decreased neuronal efficiency in brain regions that play a central role in learning and memory. (122)

**IQ.** In one longitudinal study included in the review by Meier et al. (2012), participants at age 38, who were diagnosed with dependence, persistent, and even infrequent use of cannabis at one or more points during their adolescence, had a decline in IQ of 6 – 8 points. Comparatively, adult onset cannabis users did not appear to experience IQ decline as a function of persistent cannabis use, and those who had never used cannabis experienced a slight increase in IQ, (70)

## Affective Disorders

'Affective disorders' is a term that most commonly refers to the diagnoses of depression and anxiety disorder. A significant amount of research has been published on the link between adolescent cannabis use and affective disorders in adulthood. Moore et al. found that the evidence that cannabis use leads to affective outcomes "is... of concern" (2007). (77)

Renard and colleagues (2014) conclude that a considerable body of evidence demonstrates that cannabis use during adolescence increases the risk of developing anxiety and depression in adulthood. (122) Scholes-Balog et al. (2016) found that marijuana-use was associated with an increased likelihood of experiencing internalizing symptoms of both depression and anxiety. (95)

Other research has found less/no connection between cannabis and anxiety, depression, or both. Degenhart and colleagues (2013) state that: "it is possible that early cannabis exposure causes enduring mental health risks in the general cannabis-using adolescent population". They, however, found that regular (particularly daily) adolescent cannabis use is associated consistently with anxiety, but not depressive disorder in adulthood. (132) A low/ lack of connection seemed especially common in studies looking at a low frequency use of the cannabis. In 1990, Shedler and Block found that continued *occasional* cannabis use was not related to later depression or anxiety. (123)

**Anxiety.** In reviewing research published about the effects of cannabis use, Renard and colleagues (2013) found that anxiety disorders are "the most common complications that arise from chronic heavy cannabis use". Whereas the lifetime prevalence for anxiety disorders in the general population is estimated around 6–17% this prevalence is increased in cannabis users with to prevalence up to 20%. Cannabis use during adolescence can double the risk of developing anxiety-related symptoms in adulthood, particularly if the onset of use was initiated before the age of 15. Moreover, girls are more likely than boys to develop these symptoms. (122)

A longitudinal study completed by Degenhart et al. (2013) looked at various adolescent cannabis use trajectories and anxiety at age 29. They found that: Heavy adolescent cannabis use was associated most consistently with anxiety, with a roughly twofold higher risk of the disorder at 29 years. Early regular cannabis use in adolescence increased risk of anxiety disorder at age 29 years. This connection remained even if they ceased using cannabis in adulthood. (132)

**Depression.** Renard et al. found, in their review of the literature, a variety of studies linking adolescent cannabis use to depression in adulthood. A study conducted among Australians between 13 and 17 years of age found that adolescents who use cannabis are three times more likely to meet the criteria for depression later in life compared to adolescents who never used cannabis. Another study found that 30% of adolescents who chronically use cannabis between the ages of 15 and 17 develop depressive symptoms by the age of 21. A third study confirmed this observation and also reported that regular/ frequent cannabis use and early onset of use both increase the risk of developing a depressive disorder later in life. (122) Ferguson, Horwood and Swain-Campbell (2002) found that the odds ratio for weekly cannabis users to experience depression was 1.7 times higher than for non-users. (125)

However, not all research has found such a connection. Some researchers suggest that both environmental factors and genetic predisposition play a role in this causal association. These studies put forward that pre-existing genetic factors may predispose an individual to depression, and that these factors may be revealed by early cannabis use. (122) An integrative analysis by Silins et al (2014) found that after adjusting associations between adolescent cannabis use and depression for confounding it was non-significant and negligible. (98)

### **Psychosis**

Significant epidemiological evidence has accumulated supporting the notion that adolescent cannabis use is associated with the development of psychosis. (21) National mental health surveys have repeatedly found more substance use, especially cannabis use, among people with a diagnosis of a psychotic disorder. (126) A series of longitudinal case controlled studies have all found increased rates of psychosis or psychotic symptoms in people using cannabis. (34)

Crocker & Tibbo (2015) reported that studies (that controlled for psychotic symptoms at the baseline) have reported increased risk of psychosis at age 26 associated with cannabis use between the ages of 15-18. (21) In a review by Fergusson and colleagues (2006) all studies found that the use of cannabis is associated with increased risks of psychosis or psychotic symptoms, the longitudinal studies they reviewed had odds ratios ranging from 1.77 to 10.9, with a median of 2.3. (34)

**Risk factor.** Not all teenagers who use cannabis will develop psychosis. (21) Given that the majority of cannabis users do not develop schizophrenia, the use of cannabis is not sufficient to develop full-blown disease onset, but rather cannabis use may contribute as an environmental risk in a specific population vulnerable to schizophrenia with genetic risks and/or other environmental factors (121) Having a first degree family member with schizophrenia increased the odds ratio of developing psychosis with cannabis use. (122)

**Age of first use.** Malone and colleagues (2010) found that earlier use at age 15 years conferred a greater risk of schizophrenia outcomes than later use. (62) In an Australian longitudinal cohort study ((McGrath et al., 2010) those participants who had started using cannabis at age 15 or younger were twice as likely to receive a diagnosis of nonaffective psychosis and four times more likely to have high scores on the Peters et al. Delusion inventory when tested at age 21 (compared to those who had not used cannabis). Longer duration since first cannabis use was associated with multiple psychosis related outcomes in young adults; an association that persisted when examined in sibling pairs, which reduced the chances of residual confounding factors. (66)

**Causal link.** Epidemiological research using longitudinal designs, augmented by a series of cross-sectional studies of large populations and high risk populations, produced suggestive evidence of a causal link between the use of cannabis and the development of psychosis or psychotic symptoms. (34) Malone, Hill & Rubine (2010) state that "despite some variable factors it appears that there is a causal link between adolescent cannabis use and the development of psychoses such as schizophrenia". (62)

According to Fergusson et al. (2008) this causal link has been shown to be "robust and resilient"; however, there is a solid amount of research published that questions the claims of causation after accounting for confounding. (34) The possibility that this association results from confounding factors or bias cannot be ruled out. (77)

Large and colleagues (2011) report that not all researchers agree that the association between cannabis use and earlier age at onset is causal. (126) Research they reviewed argued that the association between cannabis use and earlier age at onset could be explained by demographic variables. (21) McGrath et al. (2010) found that those individuals who were more vulnerable to psychosis (i.e. those with isolated psychosis symptoms) were more likely to commence cannabis use, which could then subsequently contribute to increased risk of conversion to a nonaffective psychiatric disorder. (66)

**Confounding.** In their 2007 meta-analysis, Moore and colleagues noted that after adjusting for various methodological issues in the studies they reviewed, there were often substantial reductions in the effect size between cannabis use and later psychosis-related outcomes; but the role of residual confounding cannot be discounted. (76) Sevy and associates (2010) also found that, although cannabis use precedes the onset of illness in most patients, there was no significant association between onset of illness and CUD that was not accounted by demographic and clinical variables. (128)

**Early onset psychosis.** A systematic meta-analysis completed by Large et al. (2011) found that cannabis use is associated with earlier onset of psychosis. Saito and his colleagues (2013) reported that the earlier the age of regular use (i.e. prior to 15) the more increased the risk of developing psychosis compared to minimally later use (between 15 & 18). (121) Adolescent cannabis use is linked to early onset, but not late onset, schizophrenia. (21) Large et al. (2011) also found in their meta-analysis that the use of cannabis and other illicit substances was associated with an earlier age at onset of psychotic disorders. (126)

**Schizophrenia.** A longitudinal study from Dunedin, NZ found that by age 26 those who had used cannabis as an adolescent, by age 15, and by age 18, had more 'schizophrenic' symptoms than controls (never used cannabis or had use cannabis 'once or twice'). (62) Large et al (2011) reported that their study demonstrated that cannabis use precipitates schizophrenia and other psychotic disorders. (126) It is speculated that the adolescent exposure to cannabinoids might tamper with normal developmental neuronal processes occurring in the still developing adolescent brain, thus leading to a predisposition to develop schizophrenia. (62)

**Self-medication.** Malone and colleagues explored the premise of 'self-medication.' They suggest that it is possible that some subjects who are prone to psychosis may seek out cannabis as a means of self-medication; however one study they reviewed demonstrated that increasing psychotic symptoms were not positively associated with increased rates of cannabis use. It is possible that for a small subset of patients with schizophrenia cannabis ingestion offers some relief of symptoms. However, there is overwhelming support in the literature for the lack of evidence for the self-medication hypothesis. (62) Renard et al. (2104) in their review found that here is overwhelming consensus within the literature citing a lack of evidence for the self-medication hypothesis, given that no relationship between early psychotic symptoms and an increased risk of later cannabis use has been reported. (122)

**Dose effect.** The systematic meta-analysis by Large et al. (2011) provides strong evidence that reducing cannabis use could delay or even prevent some cases of psychosis. (126) A systematic review by Moore et al. (2007) found a dose response effect was observed in all studies that examined the relation to increasing cannabis exposure. (77) Crocker & Tibbo (2015) found that studies demonstrated an increased risk of developing psychosis with a higher frequency of cannabis use, with up to a 6-fold increased risk for psychosis in heavy users (over 50 life time occasions by 18 years of age) compared to nonusers. (21)

## Suicide

A longitudinal study that was conducted in young Norwegians and followed over a 13-year period (from their early teens to their late teens) showed a dose-dependent relationship between chronic cannabis consumption and suicidal tendencies (i.e., thoughts and attempts) later in life. (122) In their 2004 study, Lynskey and colleagues found that those who initiated cannabis use before age 17 years had elevated rates of subsequent suicide attempt, at 3.5 times those who did not. (140)

## Psychosocial Factors

Cannabis use and particularly regular or heavy use are associated with increased rates of a range of adjustment problems in adolescence/young adulthood - other illicit drug use, crime, depression, and suicidal behaviours. (125)

A 25 year longitudinal study (Fergusson et al., 2008) completed in New Zealand, found that early, prior to age 18, cannabis use was associated with later adverse psychosocial outcomes by age 25. After extensive control/ adjustment for confounding factors, the frequency of cannabis use remained associated significantly with all six. (31) Brook et al. (2011) found that early onset adolescent cannabis users showed a higher frequency of negative psychosocial outcomes in adulthood as compared to the abstinent group. (12) Each marijuana-use trajectory group had greater adverse life-course outcomes than a non or low-use trajectory group. (95)

An Australian eight wave cohort study of 1520 students found that for psychosocial outcomes post-school qualifications, receipt of welfare, and depression/ anxiety, persistent weekly users (those using in adolescence and adulthood) had worse outcomes compared with those who had never used. (23)

Macleod et al. (2004) found that available evidence does not strongly support a causal relation between cannabis use by young people and psychosocial harm, but cannot exclude the possibility that such a relation exists.



The thought is that psychosocial problems may be more a cause than a consequence of cannabis use. (60) The confounding affect of tobacco for a number of cannabis related outcomes suggests possible mediating effects of underlying risk – taking behaviours in increasing risk for some adverse psychosocial outcomes that causes question about the cause. (23)

### **Life Satisfaction**

In one study of various marijuana use trajectories (Ellickson, 2004) all types of adolescent cannabis users were found to have less life satisfaction than abstainers. (30) A 25 year longitudinal study done in New Zealand (Fergusson et al., 2006), found that early, prior to age 18, cannabis use was associated with lower levels of overall life satisfaction (by age 25). (31)

### **Educational Attainment**

Multiple studies found that adolescent cannabis use was associated with lower levels of educational attainment. Occasional adolescent use was associated with lower educational attainment, but the association was significantly attenuated after adjustment for adolescent tobacco use. (23) A 2004 systematic review of longitudinal, general population studies found fairly consistent associations between cannabis use and lower educational attainment and reduced educational outcomes. (60)

Educational attainment appears to be effected by the dose-response concept. Ellickson et al. (2004) found that at age 29, early high users and stable light users had the lowest educational attainment of all; followed by stable light users, and occasional light users had higher educational attainment than all three other groups. (30)

**High school graduation.** An integrative analysis by Silins et al (2014) found that compared with individuals who had never used cannabis, those who were daily users before age 17 showed clear reductions in the odds of high school completion (0.37 – 63% lower) & degree attainment (0.38 – 62% lower). (98)

**Postsecondary education.** Adolescent cannabis users were less likely than non-users to have gained post school qualifications than non-users by 24 years. (23) (association remained after adjustment for background factors and adolescent use and depressive symptoms, but adjustment for adolescent cigarette smoking substantially reduced the association, as was the association between weekly cannabis use and government welfare. (23) A 25 year longitudinal study done in New Zealand, found that early, prior to age 18, cannabis use was associated with lower levels of degree attainment at age 25. (31) All types of cannabis users, even occasional light users of cannabis, differed from abstainers by having a lower rate of college graduation. (108)

### **Work, Earnings & Welfare Dependence**

Brook and colleagues (2013) found that trajectories of marijuana use were significant predictors of later work commitment and financial stability. Individuals in both the chronic and increasing marijuana user trajectory groups (compared to those in the none or low user trajectory group and the moderate marijuana user trajectory group) were more likely to be unemployed, and incapacitated at work. A member of the chronic user trajectory group was also more likely to be financially dependent. These findings are consistent with the conclusion that marijuana use may have a negative impact on work commitment. (120) Chronic marijuana users manifested greater difficulties in the work domain. (95)

Ellickson et al. (2004) found that at age 29 early high users fared significantly worse than all other groups of adolescent cannabis users on yearly earnings; followed by stable light users and steady increasers. Occasional light users did not differ from abstainers, and both groups had the highest earnings of all. (30) A 25 year longitudinal study done in New Zealand, found that early, prior to age 18, cannabis use was associated with later outcomes of higher welfare dependence and higher unemployment. (31)

### **Antisocial Behaviour & Illegal Activities**

A 2004 systematic review of 48 (16 of high quality) longitudinal, general population studies found cannabis use was inconsistently associated with antisocial or otherwise problematic behaviour. (60)

**Antisocial behaviour.** The Dunedin (New Zealand) Multidisciplinary Health and Development Study demonstrated that frequency of cannabis use at age 18 predicted a linear trend for subsequent antisocial behaviour. (65) Brook et al. (2011) found that early onset adolescent cannabis users showed a higher frequency of antisocial behaviour in young adulthood compared to both late onset cannabis users and the abstinent group. (12)

**Selling drugs.** Tucker and colleagues (2005) reported that all types of cannabis use increased the risk for selling drugs and having drug related problems by age 23. (108)

**Criminal behaviour.** The chronic marijuana-use trajectory group was highly associated with criminal behaviour. (95) Weekly adolescent cannabis users had rates of property and violent crime that were 1.7 times those of non-users at age 20-21. All types of cannabis users, even occasional light users of cannabis, differed from abstainers by having higher rates of delinquent behaviour (stealing, violence) and greater likelihood of having substance use problems. (108) They were also more likely to report poor physical health. (108)

**Violence.** Brook and colleagues (2013) followed a group of individuals from age 14 into their thirties and found that trajectories of marijuana use were significant predictors of the participant's report of the social environment including victimization. This research showed that those in the chronic and increaser marijuana user trajectory groups were more likely to experience violence from others than those in the none or low marijuana user trajectory group. (120)

In an earlier paper Brook and her colleagues (2011) also found that early onset adolescent cannabis users showed a higher frequency of violence in young adulthood compared to both late onset cannabis users and the abstinent group. (12)



## Adult Substance Use

There is compelling evidence of a continuing association between cannabis, licit and other illicit drug use well into young adulthood. (106) Substance use may be adolescent limited for some youth who mature out of regular use as they age into adulthood. Transitions to and among using two substances indicate life course persistent patterns of substance use. (74)

All adolescent cannabis use trajectories have risk for future drug use associated with them; especially as compared to non-users. Early and heavy cannabis use may be a particularly salient risk factor for the development and continuity of later substance use disorders. Early and continued occasional cannabis use did predispose to later drug use, even if it began and remained as occasional use, risks for drug use and drug use problems remained elevated. Those who maintained a stable occasional use pattern – the most populous group of adolescent onset users – were at risk of drug problems at age 24, than non-users and those who only began after adolescence. (23)

### Gateway Hypothesis

A major aspect of the debate regarding adolescent cannabis use is whether it increases the use of other addictive substances such as heroin and cocaine later in life, a phenomenon known as the gateway hypothesis. (50) The gateway hypothesis implicitly assumes a causal chain sequence in which (a) cannabis is used prior to the onset of other illicit drugs and (b) the use of cannabis increases the likelihood of using other illicit drugs. (32)

Altogether, the data suggest that use of 'heavy' drugs is almost systematically preceded by cannabis use, and that risk is correlated with the intensity of cannabis exposure. (50) It is not clear whether the predictive association between cannabis and other illicit drug use is causal or reflects confounding factors. (7) The results of a study by Fergusson et al. (2002) also suggest possible "gateway" effects in which use of cannabis may, by some unconfirmed route, encourage other forms of illicit drug use. (125)

### **Adult Cannabis Use & Cannabis Use Disorder (CUD)**

Adolescent use of cannabis has strong association with adult use of cannabis. Although, early marijuana use does not necessarily presage escalated use. (30) Brook et al. (2011) found that cannabis users showed a higher frequency of cannabis use and cannabis-related harms (compared to the abstinent group) in young adulthood. (12) Swift and associates (2008) found that is possible that adolescents who engage in regular cannabis use are particularly at risk for cannabis related problems up to 10 years later. (104) By age 24, occasional types of users were at three to four fold elevated risk of regular and dependent use compared to non-users, with weekly+ users at greatest risk of these outcomes. (105) Close to one in four moderate risk (weekly +) teenage cannabis users were later high-risk (daily) users as young adults. Weekly or more frequent cannabis use in teenagers predicted a sevenfold higher rate of daily cannabis use in young adults. (83)

**Dose-response relationship.** While cannabis dependence at age 18 strongly predicted later dependence, frequency of cannabis use at that age also predicted subsequent cannabis dependence in a linear fashion; the higher the level of use, the higher the risk of later dependency. (65) Adolescent onset cannabis users who were diagnosed with cannabis dependence before age 18 tended to become more persistent users in adulthood. (70)

The risk of both frequent and dependent cannabis use at 24 years increased with increasing levels of adolescent maximum use frequency. Those who commenced cannabis use before age 16 and those who used for more than 1.5 years were at between two and threefold elevated odds of frequent and dependent use outcome by age 24 relative to late cannabis started and those who used for only 6 months to one year, respectively. (104) Persistent, heavy and early onset cannabis users have high rates of problematic use. (104) Nearly one half of those reporting weekly+ adolescent use reported weekly+ use at age 24 as well. (104)

**Adult CUD.** An integrative analysis by Silins et al (2014) found that compared with individuals who had never used cannabis, those who were daily users before age 17 showed substantially increased odds of later cannabis dependence at 17.95 times those who abstained. (98) The transition to weekly use in adolescence may act as a critical threshold by providing sufficient drug exposure to initiate the early stages of cannabis dependence. (104, 105) Of those reporting weekly+ adolescent use 29% were dependent at age 24. (104)

For those who used marijuana at least once, the estimated cumulative probability of developing dependence on marijuana by age 54 was 10%. Some 8% of marijuana users had developed marijuana dependence within 10 years of first use, at which point risk drops to almost zero. (112) Duncan and associates (2015) found that having a CUD in one developmental period significantly predicted having a CUD in the subsequent developmental period (youth, young adult, adult). (29)

Some of the research provides a different perspective on the pathways between adolescent and adult CUDs. Duncan and associates (2015) found a significant negative relationship for women in the path from youth cannabis use disorder (CUD) to adult CUD: having a CUD in youth is related to not having a CUD in adulthood. (29)

### **Adult Alcohol Use & Alcohol Use Disorder (AUD)**

There is solid evidence of a link between adolescent cannabis use and adult alcohol use. Brook et al. (2011) found that both early onset and late onset adolescent cannabis users showed a higher frequency of alcohol harms in young adulthood compared to the abstinent group. (12) Weekly or more frequent cannabis use in the absence of moderate-risk alcohol use in teenagers predicted a twofold increase in high-risk alcohol use. (83)

**AUD.** The Dunedin (New Zealand) Multidisciplinary Health and Development Study demonstrated that frequency of cannabis use at age 18 predicted a linear trend for subsequent alcohol dependency. (65) Duncan and associates (2015) found that comorbidity of alcohol use disorders (AUDs) and cannabis use disorders (CUDs) was evident from youth through adulthood. Youth CUD had a significant correlation with adult (24 – 30 years) AUDs. (29)

### **Adult Tobacco Use & Tobacco Use Disorder (TUD)**

There is a strong connection in the peer reviewed evidence between cannabis and tobacco use. Daily adolescent users of cannabis had six times the rate of uptake of cigarette smoking than occasional cannabis users. (106) The prevalence of heavy tobacco smoking at age 35 was exactly the same as observed at age 18 years. There was an age related decline for all types of users and co-users, except for those who were heavy tobacco smokers only or heavy cannabis users only. (7)

**Gateway/ reverse gateway effect.** Cannabis is commonly used by adolescents before they move onto using substances other than nicotine. Evidence supports the notion of both gateway and reverse gateway effects in relation to the association between tobacco and cannabis use, which arises from a reciprocal feedback loop involving simultaneous causation between tobacco use disorder and cannabis use disorder. There are significant associations between extent of cannabis use and tobacco smoking and vice versa.

Increasing levels of tobacco smoking were associated with increasing levels of cannabis use, and vice versa. (7) Light cannabis users had approximately 5 times greater odds of being tobacco smokers than non-users, and vice versa for light tobacco smokers. The odds of co-use greatly increase in heavy users. (7) Part of this connection seems to be that biological mechanisms that modulating effect of the cannabinoid system on responses that are elicited by nicotine administration. Added to this is the combined use of tobacco and marijuana is a cross cultural phenomenon, e.g. blunts and joints. (11)

**Age of onset of cannabis use.** Brook et al. (2011) found that early onset adolescent cannabis users showed a higher frequency of cigarette use in young adulthood compared to both late onset cannabis users and the abstinent group. (12)

**TUD.** Brook and associates (2014) found that cannabis use is associated with an increased likelihood of nicotine dependence (11), even after controlling for earlier cigarette use. They used trajectory analysis to link various use patterns of cannabis to future use of tobacco. They found that those who did not, or used low amounts of cannabis has a 10% rate of adult TUD, while increasing (none at 14, at least monthly at ages 24 & 29) had a rate of 37% TUD, moderate cannabis use was connected to a rate of 24% TUD and those who used chronic marijuana use had a rate of 51% TUD. (11)

### **Other Adult Illicit Drug Use**

Fergusson et al. (2002) suggested that the strong associations between cannabis use and other illicit drug use after relatively comprehensive adjustments for confounding clearly suggests the possibility of a causal link between cannabis use and other illicit drug use. However, what remains unclear is the nature such a link, as the mechanisms that lead to these linkages between age and the impact of cannabis use on risks of illicit drug use are by no means clear. (125)

A 2004 systematic review of longitudinal, general population studies found that cannabis was consistently associated with the use of other drugs, and in particular, illicit drugs. (60) Brook et al. (2011) found that late onset adolescent occasional cannabis users reported a higher frequency illicit drug use in young adulthood compared to both early onset cannabis users and the abstinent group.

**Dose response.** The frequency of cannabis use was associated significantly with the use of other illicit drugs, other illicit drug abuse/ dependence and the use of a diversity of other drugs; the relationship is linear in fashion. (32)

Young people using cannabis at least once per week were at substantially increased risks of later illicit drug use, with 12 times the odds of other illicit drug use compared to non-users. (125)

An integrative analysis by Silins et al (2014) found that compared with individuals who had never used cannabis, those who were daily users before age 17 showed increased use of other illicit drugs at a rate of 7.8 times. (98) Compared with continuing occasional cannabis use weekly+ cannabis users had two to three times the rates of illicit drug use uptake. (106)

**Age of onset of cannabis use.** Starting to use cannabis before age 15 indicates a higher risk for using other illicit drugs. By age 29, all adolescent cannabis users, regardless of trajectory of usage, exhibited levels of hard drug use that were between two and nearly four times higher than those of abstainers. These results indicate that even low or experimental marijuana use, if consistent over time, is associated with an increased risk of involvement with other illicit drugs. (30) Delaying marijuana initiation does not necessarily protect young people from getting involved with hard drugs. (30)

## ENERGY DRINKS

Energy drinks are emerging as a public health threat and are increasingly, and in particular, consumed by youth and young adults. (86) (87) There is growing concern about the health effects of these beverages, which contain moderate to high concentrations of caffeine as well as taurine, vitamins, herbal supplements, and sugar and/or sweeteners. (5) (96) Energy drinks often contain additional amounts of caffeine through additives, including guarana, kola nut, yerba mate, and cocoa. (96)

Unfortunately, energy drink consumption has gone largely unnoticed in the scientific literature, but from a public health perspective, it is important to understand the potential impact energy drinks may have on the health and wellbeing of youth and young adults.

### NS Student Energy Drink Use Rates

In response to increasing sales of energy drinks and concerns about the use of such drinks by school-age children, the Nova Scotia Student Drug Use Survey 2012: Technical Report (2013) included asked respondents about their consumption of energy drinks such as Red Bull, Monster, Rockstar or Full Throttle. Almost two thirds of students (64.3%) reported consuming energy drinks in the year prior to the survey. (130) The proportion of students in grades 9 (67.4%), 10 (69.5%) and 12 (71.4%) who used energy drinks were much higher than the proportion in grade 7 (46.6%).

## Limited Research on Energy Drink Sequelae

Piotrowski (2014) completed a qualitative content analysis of 105 articles published about energy drinks. He found that research attention in the area of energy drinks is restricted to a limited range of subject areas. The main areas of focus have been combined energy- alcohol drinks in college populations; the deleterious effects of caffeine levels and the use of energy drinks in college athletics, and partying college students. (86)

Azagba, Langille and Asbridge (2013) highlight the need to further research the long-term effects of consumption of alcohol mixed with energy drinks in young people. (4) To date we lack the understanding of the prevalence of consumption of these drinks, related individual and social correlates of use, and the associated health and social burden, particularly among the most vulnerable – youth and adolescents. (4)

More research is needed regarding the health risks associated with energy drink use in young adults, including their possible role in the development of substance use problems.

**\* Due to the limited research available, all energy drink use, concurrent substance use, and their effects mentioned below are within the adolescent time frame.**

## Energy Drink User Profile

A survey of college students (Malinauskas et al., 2007) found that the majority of users consumed energy drinks for insufficient sleep (67%), to increase energy (65%), and to drink with alcohol while partying. (54%). Pettit and DeBarr (2011) found positive correlations existed between college students' perceived stress and energy drink consumption. (84) The majority of users consumed one energy drink to treat most situations although using three or more was a common practice to drink with alcohol while partying (49%). (61)

Frequent consumption of energy drinks may be a sign of high risk of health jeopardizing behaviour; frequent consumption of energy drinks may serve as a useful screening indicator to identify students at risk of substance use and/or other behaviour harmful to health, including an association with an increased risk of other substance abuses (alcohol, cigarettes). (39) Energy drink users tend to have greater involvement in alcohol and other drug use and higher levels of sensation-seeking, relative to non-users of energy drinks. (2)

## Energy Drinks + Alcohol

A number of studies point to the increasing use of alcohol mixed with energy drinks despite warnings to the contrary. There is an association between the heavy use of caffeine and the heavy use of alcohol. (91) Estimates are that between 15% and 85% of energy drink users mix them with alcohol, with the propensity to do so highest in youth and young adults. (4)

Ingesting alcohol and energy drinks together is associated with a decreased awareness of the physical and mental impairment caused by the alcohol without reducing the actual impairment. This is of particular concern for youth who have a baseline of less mature judgment. Adding energy drinks to alcohol tends to increase the rate of absorption through its carbonation and dilution of the alcohol, and keeps a person awake longer allowing ingestion of a greater volume of alcohol. At low blood alcohol levels, caffeine appears to decrease some of the impairment from the alcohol, but at higher blood alcohol levels, caffeine does not appear to have a modifying effect on either the physical or mental impairment induced by the alcohol. (113)

Energy drink and alcohol use together is associated with a number of alcohol related problems and complications in younger populations, including alcohol dependence, higher rates of binge drinking and an increase in the likelihood of alcohol related injuries and incidents. (5) Alcohol plus caffeine combinations have been associated with higher rates of alcohol related consequences, such as medical treatment, sexual assault, drunk driving and injury. (19) Compared to energy drink non-users, energy drink users had heavier alcohol consumption patterns, and were more likely to have used other drugs, both concurrently and in the preceding assessment. (2)

**AUD.** Energy drink consumption appears to be associated with an escalation of alcohol-related problems in young adults and college students in particular. High frequency energy drink users (weekly or daily energy drink consumption) were at significantly greater risk for alcohol dependence relative to both non-users and low-frequency users. Low-frequency energy drink users did not differ from non-users on their risk for alcohol dependence. (3)

**Sexual health.** Use of alcohol mixed with energy drinks was globally associated with at least some forms of sexual risk-taking. Alcohol mixed with energy drink users were more likely than nonusers to report intoxication and/or a casual partner at most recent sexual intercourse, even after accounting for the frequency of heavy episodic alcohol use. Women were significantly less likely to engage in indiscriminate sexual behaviour, and more likely to have unprotected sex, than their male peers. (73)

## Energy Drinks and Use of Other Substances

Evidence suggests a link between high caffeine consumption and other drug problems. A consistent finding is that students who consume energy drinks have higher rates of (alcohol and) other drug involvement. (4)

**SUD.** Heavy caffeine use, caffeine toxicity, and caffeine dependence have been shown to significantly increase the odds of developing a substance use disorder, including abuse or dependence on

cannabis, cocaine, or alcohol. (2) It seems likely that problems with caffeine dependence and withdrawal will also increase. (91)

Consumption of these drinks among Canadian high school students is substantial and can lead to many potential harms, both acute and long term (e.g. increased alcohol dependence). (4)

**Nicotine.** A link has also been observed between caffeine consumption and nicotine consumption with tobacco smokers consuming more caffeine than non-smokers. (2)

**Pain medications.** Prospectively, energy drink use has a unique relationship with nonmedical use of prescription stimulants and analgesics. (2)

## Potential Health Impacts (that *may* have long term effects)

Germany has tracked energy-drink-related incidents since 2002. Reported outcomes include liver damage, kidney failure, respiratory disorders, agitation, seizures, psychotic conditions, rhabdomyolysis (the breakdown of muscle tissue), tachycardia, cardiac dysrhythmias, hypertension, heart failure, and death. (96)

**Caffeine toxicity.** Over the long term caffeine toxicity could potentially impact various body systems, including: renal, cardiovascular, musculoskeletal, and the central nervous system. (6)

**Calcium deposition.** Early adolescence is the time of maximal calcium deposition in bone, and caffeine interferes with intestinal calcium absorption. (96)

**CUD.** There also exists potential for a caffeine use disorder, and if stopped, for symptoms of withdrawal. (6) The impact of newer, high caffeine energy drinks of sleep duration has not been sufficiently studied and has potential long term health effects. (15)

**Injury.** Traumatic brain injury (TBI) remains a disabling and common condition among adolescents and the consumption of

alcohol, energy drinks, and alcohol mixed with energy drinks further increase the odds of TBI among adolescents. (51)

Seifert and colleagues (2010) conclude after their review of the literature surrounding energy drink consumption in youth that: "Energy drinks have no therapeutic benefit, and both the known and unknown pharmacology of various ingredients, combined with reports of toxicity, suggest that these drinks may put some children at risk for serious adverse health effects." (96)

Seifert et al. (2010) also state that "interactions between compounds, additive and dose-dependent effects, long-term consequences, and dangers associated with risky behaviour in children remain to be determined." (96)

## NON-PRESCRIBED OPIOIDS

Opioids are medications that relieve pain. They reduce the intensity of pain signals reaching the brain and affect those brain areas controlling emotion, which diminishes the effects of a painful stimulus. Medications that fall within this class include hydrocodone (e.g., Vicodin), oxycodone (e.g., OxyContin, Percocet), morphine (e.g., Kadian, Avinza), codeine, and related drugs.

Physicians and other health care and public health professionals are concerned by what appears to be epidemic levels of prescription opioid abuse, misuse, and overdose (144) There has been considerable concern over adolescents' nonmedical use of prescription opioids, in particular because of its dramatic increase since the mid-1990s, and because it is highly correlated with excessive substance use, the risk of substance use disorders, and other adolescent problem behaviours. (146)

## NS Student Pain Relief Pill (Opioids) Non-Prescribed Use Rates

Students were asked about non-medical use of pain relief pills such as: Percocet, Percodan, Tylenol #3, Demerol, Oxycontin, and codeine. In 2012, 11.7% of students used pain pills that were not prescribed for them or without a doctor telling the student to take them. (130)

The proportion of students using nonmedical pain pills increased with grade level. In grade 7, 4% of students used non-medical pain pills compared to 11.3% in grade 9, 13.9% in grade 10 and 16.4% in grade 12. (130)

## Other Stats on Youth Use of Non Prescription Opioids

The literature reports that anywhere from 7% to 36% of adolescents in a normative sample had used a prescribed drug for a nonmedical reason. (17) In the U.S. 2005 National Survey on Drug Use and Health (Sung et al. 2005) 2.8 million adolescents self-reported lifetime prescription opioid misuse in 2002 compared to 240,000 in 1989. An estimated that 7.6% of adolescents, ages 12 to 17, reported nonmedical use of prescription type opioids in 2002. They found that although most drug related ER admissions are associated with heavy and poly drug use among young adults, the evidence of a rapid and simultaneous penetration of prescription opioid abuse in ER admissions among both young experimenters and career abusers signalled the onset of what appeared to be a new drug epidemic. (102) In their review of the same data set Schepis and Krishnan-Sarin (2008) found that among adolescents, 8.2% misused a medication and 3.0% endorsed symptoms of a substance use disorder related to prescription medication misuse in the past year. (94)



Gomes et al (2014) found the rate of dispensing high-dose opioid formulations increased 23.0%, from 781 units per 1000 population in 2006 to 961 units per 1000 population in 2011. One of the highest rates of high-dose hydromorphone dispensing specifically was found in Nova Scotia at 369 units per 1000 population. (149)

The sizeable and continuous growth in the lawful distribution of controlled prescription opioids, while beneficial to some, simultaneously raises concerns of abuse, since drug availability is consistent and powerful predictor of substance abuse among youth. (102)

Sung et al. (2005) found that when analyzed from a longitudinal retrospective perspective, incidence, and prevalence rates of youth opioid misuse displayed an epidemic character, with phases of incubation, expansion, plateau, and decline, similar with other drug abuse cycles. (102)

Sung et. Al (2005) also found that the most powerful correlate of youth opioid use was the use of other substances: Rates of prescription opioid misuse were considerably higher among users of alcohol and tobacco, and nearly endemic among users of illicit drugs (e.g. ecstasy, cocaine, or heroin) or misusers of other prescription drugs ( e.g. stimulants, tranquilizers, or sedatives. (102)

## **Risk Factors for Youth Using Non Prescription Medications**

Schepis and Krishnan-Sarin (2008) reported that rates of prescription misuse appear to be highest for the opioids, which are followed by the tranquilizers, stimulants and sedatives, but this has not been adequately evaluated. There is evidence that adolescents are at greater risk for prescription medication misuse than adults over 25 years of age and at roughly equal risk to young adults between the ages of 18 and 25.

The authors analyzed the 2005 U.S National Survey on Drug Use and Health data and found that the predictors of prescription medication misuse were:

- poorer academic performance with an odds ratio of 2.9
- past year Major Depression with an odds ratio of 3.1
- higher risk-taking levels with an odds ratio of 3.6
- past year use of alcohol with an odds ratio of 7.3
- cigarette use with an odds ratio of 8.6
- marijuana use with an odds ratio of 9.9, or
- past year use of cocaine or an inhalant with an odds ratio of 10.7

Predictors of abuse of or dependence among adolescent prescription medication misusers were:

- past year Major Depression with an odds ratio of 1.5
- past year cocaine or inhalant use with an odds ratio of 1.7, or
- ten or more episodes of past year prescription misuse with an odds ratio of 3.0

These risk factors could help clinicians identify those at risk for significant problems due to prescription misuse, allowing for prevention or early treatment in this population. (94)

## **Reasons for Using Non Prescribed Medications**

Quintero, Peterson and Young (2006) observed three categories of 'misuse' of prescription medications. The first was the use of pharmaceuticals to self-medicate. (89) Wu et al. (2008) found that adolescents perceiving their health as excellent had low odds of non-prescribed use of pain relievers, and health care utilization (emergency visits and inpatient hospitalizations) was associated with increased odds of non-prescribed use of pain relievers. Some adolescents may use pain relievers without a prescription mainly as a form of self-treatment for relieving pain, reducing anxiety or depression, coping with stress, or helping with sleep. (148) Medical users and nonmedical self treating users were best characterized by somatic complaints, anxiety/depressive symptoms, and history of sexual victimization. (146)

Two other categories of misuse are: the misuse of prescription drugs for recreational and academic purposes. Interviewees typically described recreational use in terms of getting high or having fun. Individuals reported the purposeful use of these medications in order to more effectively fulfill the role demands associated with being a college student. (89) Sensation seeking nonmedical users were best characterized by rule breaking and aggressive behaviours and possible substance dependence. (146)

Overall, prescription drugs are perceived to be safer and more socially acceptable than many other drugs. After all, medications are intentionally designed for specific purposes, and individuals, their families, and friends have used a number of prescription drugs throughout their lives. Some consider prescription drugs to be more attractive alternatives to other drugs that were previously used. (89)

## Adult Non-Prescription Drug Use

Cheng and Lo (2012) found that for adolescents in their sample lifetime nonmedical use of prescription medications was associated positively with the likelihood of current misuse of medications. (17) Wu et al. (2008) suggest that the very early onset of non-prescribed use of pain relievers in adolescent samples is noteworthy, given the potential risk of opioids' adverse interactions with other central nervous system depressants, overdose, and addiction. (148)

Early onset of time nonmedical use of prescription medications was a significant predictor of prescription drug abuse and dependence. (150) Schepis and Krishnan-Sarin (2008) found that earlier misuse of prescription medications increases the risk for the later development of abuse or dependence on a prescription medication, with a 5% drop in risk for each year misuse is delayed. (94)

McCabe et al. (2007) found that a higher percentage of individuals who began using prescription drugs non-medically at or before 13 years of age were found to have developed prescription drug abuse and dependence versus those individuals who began using at or

after 21 years of age. The odds of developing any life-time prescription drug abuse among nonmedical users was reduced by approximately 5% with each year non-medical use was delayed and that the odds of developing any lifetime prescription drug dependence were reduced by about 2% with each year onset was delayed. (150)

## Limited Evidence Regarding the Sequelae of Non Prescribed Opioids

To what extent early use of non-prescribed pain relievers is related to subsequent drug use and factors modifying the risk for adverse outcomes both requires and deserves investigation. (148) Additional research is warranted because several motivations for the nonmedical use of prescription medications seem associated with a greater likelihood of substance abuse problems. (147)

## TOBACCO

Cigarette/ tobacco smoking is a major health problem and considered one of the leading causes of preventable diseases and death worldwide. (22) Smoking has been linked to lower life satisfaction, higher negative affect, a high risk orientation, and engagement in problem behaviour. (108) In an article by Mathers et al. (2006) the authors reviewed studies on five cohorts and found that the patterns of tobacco use that have been implicated as patterns of adverse outcomes include experimental and frequent smoking at age 13; and from age 15 years, experimental, frequent, and daily patterns of cigarette use. (64)

Nicotine is a neuroteratogen that exerts long-term maturational effects at critical stages of brain development. Adolescence is a sensitive time for maturation of brain circuits that regulate cognition and emotion, with resulting vulnerability to the effects of nicotine and tobacco. (118)

Tobacco is often the first drug used by young people who later use alcohol, cannabis and other drugs, thus tobacco has been conceptualized a 'gateway drug,' a drug which precedes the initiation and subsequent problematic use of other drugs. (64)

## Tobacco Use Statistics

### NS Student Tobacco Use

The Nova Scotia Student Drug Use Survey 2012: Technical Report (2013) reports that in 2012, the average age for first smoking a whole cigarette was 13.7 years. In the past year, 13.2% of students in grades 7, 9, 10 and 12 reported any cigarette smoking with 2.5% smoking more than 10 cigarettes a day. (130)

### Other Stats

For cigarettes the period of highest risk for initiation peaks at age 18 and declines hereafter. (55)

Most tobacco users initiate and develop their smoking behaviour in adolescence, with very few people beginning their smoking habit as adults. (64) Statistics indicate that between 80 and 90% of smokers started before age 18. (43, 118) Patton et al. (2006) found that nicotine-dependent smokers at 24 years derived largely from those who had been daily smokers during the teens. (82)

Among smokers who first try smoking in their youth daily smoking may not develop until early adulthood, as a series of stages that may extend to age 25. Daily smokers are less likely to try their first cigarette after age 18. (43)

## Physical Health

All but occasional adolescent users of tobacco experienced more poor physical health at age 23 than non-smokers. (108) In an article by Mathers et al. (2006) the authors reported on several studies one of which found that daily smoking in childhood or early adolescence increased the odds at age 27 of self-reported physical health problems. (64)

## Cardiovascular Health

The origin of cardiovascular disease lies in childhood. (109) Cigarette smoking is a behaviour of adolescents that puts them at high risk for cardiovascular diseases later in adulthood. (116) Recent studies have highlighted the importance of preventing smoking and exposure to environmental tobacco smoke in children because of its direct association with cardiovascular disease risks. (97)

Smoking is a risk factor for coronary artery disease. (116) In a longitudinal study by Twisk et al. (1997) long term smoking behaviour was related to a high risk profile regarding hypercholesterolemia, an excess of cholesterol in the bloodstream. The relationship was inversely related to HDL (High-density lipoprotein), and positively to the TC (total cholesterol)/ HDL ratio. In the same study, smoking behaviour was inversely related to diastolic and systolic blood pressure. These relationships were found as early as adolescence. (109) Active smoking in young adulthood is associated with increased carotid intimal-medial thickness (CIMT) and decreased carotid artery elasticity in young adulthood. (97)

**Smokeless tobacco products.** Longer-range concerns of using smokeless tobacco products include potential nicotine-related health problems, including cardiovascular effects. Nicotine blood levels, which account for the highly addictive nature of tobacco products, are similar in smokers and ST users. (53)

**Second hand smoke.** Exposure to tobacco smoke from parents induces vascular damage in offspring in early adulthood. Environmental tobacco smoke in childhood has been linked with risk factors for and CVD processes in adulthood. (97)

## Pulmonary Health

Children who smoke are at high risk for increased morbidity and mortality during adulthood from lung diseases such as emphysema and chronic bronchitis. (116)

## Sexual Health

The fertility of young adults may be lowered by cigarette smoking. Woolf (1997) noted a dose-response inverse relationship between the number of cigarettes smoked per day, cumulative years of smoking, and body fluid (blood, urine, and semen) cotinine levels and sperm density, total count and motility. (116)

## Cancer

Lung cancer in adulthood has long been associated with smoking, with a dose-response risk related to the number of years of tobacco use. Those who initiate smoking earlier, in adolescence, are thus at greater risk for the cumulative toxic effects of cigarette smoke and the later development of lung cancer. (116)

Other types of cancer besides lung cancer are also more common in smokers. Nasopharyngeal, laryngeal, esophageal, gastric, pancreatic, bladder, and cervical have all been linked to long term smoking. (116) Epidemiological studies show smokeless tobacco or snuff use is linked to oral cancer. (53)

## Sleep Problems

In an article by Mathers et al. (2006) the authors reported on several studies, one of which found that experimental and frequent smokers at age 15 without sleep problems at baseline were found to exhibit occasional and frequent sleep problems at age 18.5. (64)

## Mental Health

Teen smokers are significantly more likely to develop psychiatric disorders than non-smokers. (118) The association between tobacco use and later mental health has been noted by several studies. (65) In an article by Mathers et al. (2006) the authors reported on studies of five cohorts and found that tobacco use may predict subsequent mental health problems. (64) Tobacco use is becoming increasingly concentrated among individuals with various mental disorders, such as depression and ADD; this study suggested that tobacco use may in fact lead to the disorder, rather than vice versa. (65) All but occasional adolescent users of tobacco

experienced mental health problems at age 23 than non-smokers. (108)

Patton et al. (2006) found moderately high rates of psychiatric morbidity were found in adults who were teen daily smokers. (82)

## Neuropsychological Function

One important aspect of adolescent nicotine exposure is the long lasting neurochemical and behavioural changes that result. (118) Biochemical studies have shown that chronic high dose nicotine exposure during adolescence results in altered indices of serotonin uptake function. Chronic nicotine exposure during adolescence also alters subsequent response of the serotonin system to nicotine later in life, suggesting that nicotine may elicit life-long detriments in serotonergic signalling. (118)

Chronic nicotine exposure during adolescence also has long term consequences on cognitive behaviour. Adolescent, but not post-adolescent exposure to nicotine has been shown to result in diminished cognitive function as adults with reduced attention span and enhanced impulsivity. (118)

## Depressive Disorders

Early onset smoking of is associated with increased rates of depressive disorders. (68) Nicotine and depression involve overlapping neurobiological underpinnings. (28) Hanna and Grant (1999) found that smokers who began between the ages of 14 and 16 were significantly more likely to have diagnoses of major depressive disorder than were late onset (after age 17) smokers and lifetime non-smokers. (44) In a paper by Yuan et al. (2015) adolescent, but not adult, nicotine exposure was found to result in a depression-like state in adulthood that is normalized by treatment with nicotine of anti-depressants. (118)

A study by Dierker et al. (2015) found that depression symptoms are positively and significantly associated with nicotine dependence. This was the first study to find that this association was consistent across time (i.e. from adolescence to young adulthood) and across lifetime smoking exposure. It is possible that an over-reliance on smoking to cope with depressive symptoms

may prevent acquisition of more effective coping responses to counteract mood disturbance. (28)

In an article by Mathers et al. (2006) the authors reported on several studies, one of which found that frequent tobacco use at age 16 years was linked with the emergence of major depression (MDD) at age 22. A second study they reported on found that tobacco use at age 15 years was associated with MDD at age 27. (64)

### **Anxiety**

Emotional responses exhibit long-term alterations following nicotine exposure, with enhanced anxiety and fear. (118) Heavy cigarette smoking during adolescence is associated with increased risk for agoraphobia, generalized anxiety disorder (GAD) and panic disorder during early adulthood. (54) In an article by Mathers et al. (2006) the authors reported on several studies, one of which found that frequent tobacco use at age 16 years was linked with the emergence of anxiety disorder at 22. (64)

### **Externalizing Disorders**

In an article by Mathers et al. (2006) the authors reported on several studies, one of which found that frequent tobacco use at age 16 years was linked with the emergence of antisocial personality disorder at age 22 years. (64)

## **Psychosocial Factors**

Smoking has been linked to lower life satisfaction, higher negative affect, a high risk orientation, and engagement in problem behaviour. (108)

### **Education**

All adolescent smokers, except those who only tried smoking, were less likely to graduate from college than abstainers. (108)

### **Risk Taking**

Teen smokers are significantly more likely to engage in high risk sexual behaviour than non-smokers. (118)

## **Involvement in Illegal Activities**

All but occasional adolescent users of tobacco showed more stealing and drug selling at age 23. (108)

### **Violence**

All but occasional adolescent users of tobacco engaged in more predatory violence (e.g. gang fighting, attacking someone) at age 23. (108)

## **Adult Substance Use**

Teen smokers are significantly more likely to use other drugs than non-smokers. (118) All adolescent users of tobacco showed an outcome of having a history of drug problems at age 23, as compared to abstainers. (108) Risk for drug dependence is greatest for those, regardless of gender and race, who begin smoking before age 16. (44)

### **Age of First Use**

Hanna and Grant (1999) found that the age of smoking onset was significantly and positively associated with lifetime drug use. The earlier one began smoking regularly, the greater his or her chances of reporting lifetime drug use. Relative to lifetime non-smokers, the odds of lifetime drug use were 7 times as great for those starting before age 13, 5 times as great for those starting between ages 14 and 16, and 2.5 times as great for those initiating regular smoking at age 17 or older. (44)

### **Adult Tobacco Use & Tobacco Use Disorder (TUD)**

Available evidence suggests a relationship between adult tobacco smoking as a consequence of tobacco use in adolescence. (64) Patton et al. (2006) found that the strongest predictors of adult smoking outcome were the initial pattern of smoking and the extent to which escalation to a high level of smoking took place in the teens. (82) Recent studies show that early smoking initiation will likely lead to long-lasting or even lifelong cigarette/ nicotine addiction. Nicotine exposure during adolescence causes acute and persistent effects in the developing brain which may result in an

increased probability of smoking continuation and relapse, even after long periods of abstinence. (22)

Among adolescents who had smoked fewer than 100 cigarettes, experiencing higher levels of overall nicotine dependence as well as individual symptoms at baseline predicted an increase in risk for daily smoking in young adulthood. (27) As well, maximum smoking levels, onset of daily smoking, duration of smoking, escalation time and duration of cessation during adolescence predicted later nicotine dependence. (110)

In research by Mathers et al. (2006) the authors found that being an experimenter or frequent smoker at 16 years more than doubled the odds of frequent smoking at age 18.5 relative to those who were not early experimenters. (64) Frequent smoking at age 13 related to daily and frequent smoking at age 18. Non-smoking and heavy daily smoking in the last year of high school maintained considerable stability through the post school years. (64)

**TUD.** Patton et al. (2006) found that nicotine-dependent smokers at 24 years derived largely from those who had been daily smokers during the teens. Two thirds of all nicotine dependent smokers had been earlier smokers, corresponding to a 17-fold higher odds than non-smokers. (82)

### **Adult Alcohol Use & Alcohol Use Disorder (AUD)**

In an article by Mathers et al. (2006) they found evidence that supports the view that tobacco use in adolescence increases the likelihood of initiating alcohol use or developing use problems. They found that tobacco use at age 17 years was related to alcohol use/ use disorder at age 24; and that tobacco use at age 15 was associated with alcohol dependence at age 27 years. A relationship was also found between experimental smoking at age 13 and binge drinking, frequent alcohol use, multiple alcohol problems and AUD at age 18. (64)

Research by Tucker et al. (2005) found that all but occasional adolescent users of tobacco were also more likely to have a history of alcohol problems at age 23. (108)

**AUD.** Early onset smoking of is associated with increased rates of AUD. (68) Patton et al. (2006) found moderately high rates of alcohol dependence were found in adults who were teen daily smokers. (82)

### **Cannabis Use & Cannabis Use Disorder (CUD)**

In an article by Mathers et al. (2006) the authors reported on several studies and drew a strong connection between adolescent tobacco use and adult cannabis use. Daily smoking at age 15 years predicted cannabis use at age 18 years; tobacco use at 17 years of age was related to cannabis abuse/ dependence at 24 years of age; and tobacco use and frequent use at age 15 years was related to cannabis use at age 25. (64)

Adolescent cigarette smoking was associated with a two to fourfold elevation in odds for subsequent weekly+ cannabis use and four to almost eightfold elevation in odds for cannabis dependence, accounted for only partially by the level of adolescent cannabis use. (104) There was an independent association between persistent adolescent smoking and problematic cannabis use, particularly dependence at age 24, persistent drinking was unrelated to subsequent cannabis use. (104)

**CUD.** Prince van Leeuwen et al. (2014) found that both early onset tobacco use and continued tobacco use in adolescence doubled the likelihood of developing a cannabis use disorder. (131) Patton et al. (2006) found a marked elevation in risk for cannabis dependence where adolescent daily smokers had a 27-fold increase in risk compared with non-smokers; 63% of all cases of cannabis dependent 24 year olds had been daily smokers as teenagers. (82) In a study by Prince van Leeuwen and colleagues (2014) early-onset tobacco use was associated with a higher likelihood of developing a cannabis use disorder; similarly, adolescents who reported continued use of tobacco were more likely to develop a cannabis use disorder, both by age 19. (131)

## Adult Illicit Drug Use

Early initiation of smoking is associated with increased rates of illicit drug abuse. (68) A series of studies investigating the 'gateway' effect of nicotine found that chronic nicotine exposure in mice sensitizes cocaine behavioural response and long term potentiation (persistent strengthening of synapses based on recent patterns of activity). (118)

In an article by Mathers et al. (2006) the authors reported on several studies, one of which reported that tobacco use at age 15 was related to illicit drug use for males but not for females at age 25 years, and that frequent tobacco use led to illicit drug use for both sexes. Another study they reported found a higher level of subsequent heroin use at age 32 years associated with early tobacco use. A third study they reported on found that experimental and frequent tobacco use at age 13 years was associated with hard drug use, polydrug use and multiple drug problems at 18 years. A final study they included reported that tobacco use at age 17 was linked to hard drug use and multiple drug use/ dependence at age 24 years. (64)

## E-Cigarettes

As explained above, teenage use of drugs containing nicotine may have potentially severe consequences for future addiction, cognition and emotional regulation. Thus, not only tobacco, but also e-cigarettes must be considered as serious threats to mental health. Even among current smokers, e-cigarettes increase the likelihood of perpetuating and increasing tobacco use. Teenagers who use e-cigarettes are also more likely to escalate to smoking tobacco. Current data demonstrates that nicotine disrupts normative limbic development and primes behavioural susceptibility to drugs of abuse. This research raises concerns for the impact of e-cigarettes on public health, and suggests that they may be a new gateway to both future tobacco use and substance abuse. (118)

## LIMITATIONS OF THE EVIDENCE

**Attrition.** Non response in longitudinal studies associated with drug use is fairly common; (23) and is often associated with and more likely in, people experiencing alcohol and drug use (24) and in those who develop mental health problems than in other participants. (77) It is possible that attrition/ non-participants are associated with different outcome patterns than those seen in participants. (104)

**Cannabinoid intake.** There is an almost certain large variation in biologically available cannabinoid concentrations; and varying intake practices, which influences the actual doses taken by participants in study cohorts. (77)

**Causation.** Most, if not all of the research stipulates that they cannot conclude a causal relationship; only association. It acknowledges a link, but cannot determine that the substance directly causes the health outcome. (11)

**Confounding.** A significant number of outcomes associated with substance use could potentially be impacted by other unaccounted for factors. An unknown third variable may exist, (70) indicative of residual unmeasured confounding. (31) Outcomes may reflect sources of confounding that have not been taken into account; (125) especially factors of a psychosocial nature. (60)

**Generalisability.** Typically, findings report on the experiences of a particular group of individuals born at a specific time and reared in a specific social context. (31) For example, several studies were based on a sample of urban Puerto Rican and African American youth, and it is questioned whether the findings generalizable to a more heterogeneous, or primarily Caucasian and/or rural population. (11) (120)

**Group size.** Statistical significance is difficult with the small size of some groups, especially after attrition of samples, and when looking at specific and not as common health outcomes. (23)

## PUBLIC HEALTH PERSPECTIVE

**Long term effects.** Little evidence exists regarding the long term impacts of injury and illness that take place/ begin in childhood in connection with substance use and endure into adulthood, e.g. injuries sustained from motor vehicle collisions due to alcohol consumption in childhood and their continued impacts in adulthood.

**Selection bias.** In one review substance use and experience of psychosocial problems were suggested be a selection and retention criteria, that could affect that apparent association between the two. (60) Another potential outcome is that substance use, particularly for those using most frequently, could be underrepresented. This makes it possible that the estimates presented in some/many studies may be somewhat conservative in nature. (31)

**Self report.** The majority of studies on the use of substances are longitudinal and cohort in design, data is based on self-report, which is typically retrospective self-assessment. (66) Almost always self-reports are not externally validated or corroborated. (11, 23, 60, 70) And thence will be subject to errors of reporting and reminiscence. (31) It is also a consideration that self-reports might be subject to socially desirable response bias (98). There is reasonable evidence that young people's reports of alcohol use are reliable and valid when they are made in a confidential manner and without any consequences for disclosing use (24)

**Statistical method.** Adequacy of the statistical methodology to capture the complexity of the processes being studied. It is likely that, given this complexity, the statistical models employed may give only an approximation to the true state of affairs. (125)

**Age of onset.** There is a strong case for allocating more resources to preventing early substance use among young people. (59) Increased efforts should be directed toward delaying or stopping the onset of substance use by young people, (70) as it may have more impact on the future use patterns of use than attempts to encourage overall use reduction. (105) This includes targeted early intervention programs; sophisticated health promotion campaigns that provide credible messages to youth in a persuasive manner that decreases the early initiation of all forms of drug use. (59)

**Adverse life situations.** Treatment programs for marijuana use should also directly address common adverse life-course outcomes which users may already be experiencing; that contribute to or are linked to cannabis use. (95)

**Community based prevention.** Given that occasional users are unlikely to present to specialised services this message might best be delivered through screening in primary care or community level health education. (23)

**Informed risk.** Appropriate messaging is needed about the risks of cannabis use, particularly those posed by increased exposure due to persistent and escalating use, e.g. there is a need for a renewed public health warning about the potential for cannabis use to bring on psychotic illness. (104) (126)

**Minimizing/ reducing cannabis dose.** Public health efforts to reduce the use of cannabis are important. Interventions to reduce escalation of cannabis and other drug use among occasional users are warranted. (23) Since individuals who use chronically or increasingly experienced the most adverse effects in each of the domains, interventions are indicated in order to decrease the likelihood of long-term morbidity.

**Overall prevention of use.** Preventing substance use uptake escalation remains a crucial health aim given the burden associated with cannabis, as well as cigarette, alcohol and illicit drug use. (106)



**Tobacco and cannabis.** Diminishing chronic, increasing and moderate marijuana use in youth (early use) may also reduce tobacco dependence in adulthood. (11) Marijuana cessation programs may be prudent to include incorporate prevention, assessment and cessation of tobacco use as part of their health promotion strategies. (11)

**Early intervention.** Age of first use was associated with longer substance use careers, longer histories of use before entering treatment, and longer treatment careers. The median time from first to last substance use was 27 years. The median time from first treatment episode to last use was 9 years. Years to recovery were significantly longer for people starting use under the age of 21 (particularly those starting under the age of 15). This suggests that while we want to delay the on-set of substance use through prevention as much as possible, outcomes are also likely to improve if we can proactively detect and intervene with people sooner in their substance use careers. (25)

**Treatment of connected conditions.** For many related conditions, i.e. depression, psychosis, there is a potential that early diagnosis and treatment of the condition could delay and/or prevent the uptake of substance use. (28)

**Policy around prescription and non-medical use of opioids.** When formulating policy decisions about prescription opioid non-medical use and abuse, a careful and balanced approach is needed, so that the risk management strategies developed to prevent and reduce diversion of prescription opioids do not deter physicians from prescribing high-efficacy opioids when those drugs are indicated. An overriding concern when formulating policies about prescription opioid non-medical use and abuse should be on the patients who need these opioids for adequate pain relief. Pain is still undertreated in this. (142)

## CONCLUSION

The literature is clear: substance use during childhood is directly associated with negative health outcomes in adulthood. There is a solid foundation of evidence regarding the significant and adverse sequelae of childhood alcohol, cannabis and tobacco use in regard to physical and psychological health, psychosocial development, and future substance use. Further research is required in regard to the long term effects of use of energy drinks, and non-medical prescription opioid drugs. As well is more in-depth exploration of the complexities of the relationship between childhood substance abuse and adult health outcomes so as to determine or eliminate causality.

It is our hope that this document will serve as a valuable source of information to those working to move our Nova Scotia toward a substance free childhood for all children and youth in our province, which in turn will lead to healthier children and adults.

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