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Substance Misuse in Adolescents: A Narrative Review

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Abstract

A review of recent literature on substance use and misuse in adolescents revealed a prevalence range of 4-88% in different countries that may relate to cultural differences and/or sampling different age groups as well as various types of substance use. Several negative effects have been noted including later substance use in adulthood, more serious substance use and several negative social and psychological problems including homelessness, posttraumatic stress disorder, depression, and suicide. Risk factors have been researched including attitudes about substance use, craving, and early initiation of substance use. Parental factors have included parental substance use and lack of parental monitoring adolescent use. Peer variables include peer misuse, racial discrimination, being a sexual minority, cyberbullying, and cyber victimization. Risk behaviors include excessive screen time and gambling. The only mechanism studies have cited reduced connectivity of different parts of the brain based on fMRI scans. The very few interventions (that probably relate to the significant decline in adolescents seeking intervention) have included youth electronic media messages, skill development, and supportive communities. Limitations of this literature include sampling and measurement variability and a paucity of longitudinal studies and intervention research.

1. Introduction

A review of recent literature on substance use and misuse in adolescents was conducted on PubMed and PsycINFO which involved entering the terms substance use in adolescents. The inclusion criteria were peer reviewed empirical and review papers. Exclusion criteria were case studies and non-English papers. Following these criteria, 46 papers could be classified as adolescent substance use studies including research on prevalence, negative effects, risk factors, and interventions. Many of the studies have been conducted in other countries where the prevalence of adolescent substance use has widely ranged from 4% to 88%. This variability may relate to cultural differences and/or different age groups and different types of substance use being surveyed. Several negative effects have been noted including later substance use in adulthood, more serious substance use and several negative social and psychological problems including homelessness, posttraumatic stress disorder, depression and suicide. Risk factors have been researched including attitudes about substance use, craving, and early initiation of substance use. Parental factors have included parental substance use and lack of parental monitoring of adolescent use, and peer variables include peer misuse, racial

discrimination, being a sexual minority, cyberbullying and cyber victimization. Risk behaviors include excessive screen time and gambling. The only mechanism studies have cited reduced connectivity of different parts of the brain based on fMRI scans. The few interventions have included youth media messaging, skill development and supportive communities. Limitations of this literature include variability on sampling and measurement and a limited number of longitudinal and intervention studies. This narrative review is accordingly divided into sections on prevalence data, negative effects, risk factors, potential underlying mechanisms and interventions for substance use in adolescents as well as limitations of this literature.

2. Prevalence of Substance Use

The prevalence of substance use has ranged widely between 4% and 88% depending on the type of substance use and the country that has surveyed the use (see Table 1). The recent literature on adolescent substance use can be divided into the types of substances including alcohol, marijuana, combined alcohol and marijuana, and opioids.

Table 1: Prevalence of Substance Misuse in Adolescents and First Authors.

Prevalence	First authors
Alcohol	
Los Angeles- 38%	Jacobs
Pakistan- 45%	Shahzad
Turkey- 88%	Yurtseven
ASEAN countries- 8% (pre-adolescents)	Pengp
Marijuana	
Arizona- 33%	Meier
U.S.- 20%	Marianos
Ghana- 5%	Oppong
Co-use Marijuana and Alcohol	
U.S.- Alcohol- 50% Marijuana- 25%	Watson
France- Alcohol- 35% Marijuana- 6%	Chau
Opioids	
U.S.- 14%	Barnett
U.S.- 4%	Han

2.1 Alcohol

Alcohol use in Hispanic/Latino students from Los Angeles (N= 781) has averaged 38% for the "past 30–day alcohol use" [1]. This use was associated with different factors for boys and girls. For boys, alcohol use was associated with intrapersonal (not qualifying for reduced lunch), interpersonal (mother's education and peer drinking) and institutional factors (alcohol–prone social club membership). For girls, alcohol use was associated with intrapersonal (academic achievement) and interpersonal factors (parent and peer alcohol use behaviors).

The alcohol use reported for Pakistani adolescents (N = 243) was higher at 45% of the sample reporting "lifetime alcohol use" [2]. These data are surprising given the strict prohibitions against alcohol use in Muslim countries. When using the stricter criteria of scores on the Alcohol Use Disorders Identification Test, 23% of the sample had high scores indicating

significant risk levels. When logistic regression analyses were conducted, lifetime alcohol use was related to depression and anxiety and risky use was associated with externalizing problems including aggressive and delinquent behavior. Both risk for and lifetime alcohol use were related to attention problems.

The prevalence rate was even higher for adolescents from Turkey at 88% for alcohol use and 95% for cigarette use [3]. This very high prevalence may relate to the adolescents being surveyed at an emergency department. Another contributing factor may be the ongoing civil unrest that was happening during this time period in Turkey. The data showed an increase in substance use from 13% in 2013 to 20% in 2014 to 30% in 2015 and 37% in 2018. The majority of substance users also used amphetamines (60%) and most of the substance users (61%) had neuropsychiatric complaints. The majority of the sample was also low income (59%) and came from single–parent families (54%).

Even though these prevalence rates are high, at least the prevalence of binge drinking (10 or more drinks per occasion) has declined among adolescents in recent years despite adolescents' greater propensity for risk–taking behaviors [4]. In another report on a survey called "Monitoring the Future", binge drinking among US adolescents (N=58,444) was noted to significantly decline from 1991 to 2018 [5]. In 1991, depressed adolescents had significantly greater odds of binge drinking, but by 2018, the strength of that association had declined by 24%.

Alcohol use during pre-adolescence (<12 years) has been significantly less prevalent at least in ASEAN countries (Indonesia, Laos, Philippines, Thailand and Timor-Leste) [6]. In that cross-sectional study (N=33,184), the prevalence was 8% pre-adolescent current alcohol use and 11% cigarette use. In a multinomial logistic regression analysis, pre-adolescent alcohol and cigarette use were associated with psychological distress including no close friends, loneliness, anxiety, suicidal ideation and suicide attempts, highlighting the risks of early onset alcohol use.

2.2 Marijuana Use

Marijuana use has also varied across countries. A large sample survey taken on Arizona adolescents in eighth, 10th and 12th grade from 245 schools (N= 47,142) revealed 33% lifetime cannabis users and 24% reported lifetime cannabis concentrate use [7]. Those who used concentrate were more likely to use other substances and have more substance use problems. A significantly lower prevalence has been reported by Hispanic adolescents on the National Survey on Drug Use and Health (N=3457) [8]. In this survey, 20% reported lifetime marijuana use, 15% past year use and 8% past month use. Those who used marijuana reported that parents seldom or never:

- checked on their homework;
- helped with their homework;
- limited their TV use;
- praised them for their work; and
- said they were proud of them.

There were no relationships between marijuana use and whether parents had their adolescents doing chores or limiting their time out on a school night. Authoritative parenting did limit marijuana use, although that protective effect decreased with age.

A lower prevalence has been reported for adolescents in Ghana (N=3632) [9]. The past month use of cannabis was 5% and the lifetime amphetamine use was 7%. Both cigarette smoking and number of close friends were related to past month cannabis use. Bullying, victimization and having been attacked, parental substance use, cigarette use and truancy were associated with lifetime amphetamine use.

Not surprisingly, marijuana use has also been associated with tobacco use in three samples of adolescents from California with 7-11% reporting past 30-day co-use [10]. The most common co-use patterns were combinations of E–cigarettes or cigarettes and combustible marijuana.

2.3 Co–Use of Alcohol and Marijuana

Although most of the recent surveys on substance use in adolescents have focused on one substance, those surveys that reveal co-use highlight the comorbidity of different substances used by adolescents. In a US sample on sexual and gender minority adolescents (N=11,129), a series of multivariate logistic regression models were used to assess whether substance use behaviors varied by sex assigned at birth and by gender identity [11]. More than 50% of the sample reported lifetime alcohol use and 25% cited lifetime marijuana use. Males assigned at birth had a greater prevalence of substance use than females assigned at birth. The greatest substance use occurred among transgender adolescents.

Multiple substance use was explored in a study on middle-school adolescents from France (N=1559) [12]. In this sample, alcohol was used by 35% of adolescents, tobacco by 11%, marijuana by 6% and other illicit drugs by 3%. The risk began in the early years in middle school which started mostly with alcohol/tobacco and then shifted to marijuana/other illicit drugs. The use of multiple substances was associated with socioeconomic factors, school grade repetition physical/verbal violence, sexual abuse, poor social support, depressive symptoms and suicide attempts.

2.4 Opioid Misuse

The prevalence of nonmedical prescription opioid use among older adolescents has been even higher at 14% based on the Youth Risk Behavior Survey in the US (N = 10,175) [13]. Surprisingly, opioid use was more likely among participants age 15 years (versus 16 years) but not surprisingly among American Indian/Alaska natives and those who reported being hopeless or sad. The use of opioids was three times more likely among alcohol users, two times more likely among cigarette and marijuana users and 1.5 times more likely among electronic vapor users. This study again highlights the co-use of substances by adolescents. Among a broader age range of adolescents (12–17 years) and a larger sample (N=41,579) taken from the National Survey on Drug Use and Health, the overall rate of opioid misuse was lower at 4% [14]. The differences between the results of these two surveys (4% versus 14%) may relate to the latter sample including younger middle school students (12–14-year-olds). As was recently reported in a review of statistics on the most commonly used substances in US adolescents, declines were noted on the use of cigarettes, alcohol and opioids, although they are still prevalent [15]. And, as the authors noted, new challenges are presented by newer practices including vaping and the legalization of marijuana.

3. Negative Effects of Substance Misuse

Several negative effects of substance misuse have been noted for adolescents in the recent literature (see Table 2). These include adolescent alcohol use leading to adult alcohol use, marijuana use leading to negative mood states, depression and suicide, marijuana and alcohol combined leading to negative developmental outcomes, substance use in general leading to PTSD and even alcohol use by others leading to depression and suicide.

Table 2: Effects of Substance Misuse and First Authors.

Effects	First authors
Adult substance misuse	Enstad
Heroin use	Kelley-Qaun
Negative mood states	Diaz-Geada
Major depressive disorder	Guyasyan
PTSD & homelessness	Davis
Poor academic performance	Karoly

In a study that combined data from two longitudinal studies including the Norwegian Tracking Opportunities and Problem Study (N=329) and the Australian International Youth Development Study (N=786), data were collected from mid-adolescence (14-16 years) to late adolescence/young adulthood (18–25 years) [16]. Both early onset drinking and early onset excessive drinking predicted increased risk of alcohol–related problems in late adolescence/young adulthood in both studies. Hazardous drinking was identified in 47% of young adults in Norway and 39% of young adults in Australia.

Nonmedical prescription opioid use has been predictive of subsequent heroin use in adolescents [17]. In this longitudinal cohort study conducted in 10 high schools in Los Angeles (N= 3298), eight semi-annual surveys were given from ninth through 12th grade. The data suggested that current nonmedical prescription opioid use predicted subsequent heroin use.

Negative mood states, depression and suicidal behavior have also resulted from substance misuse by adolescents. In a cross-sectional study from northern Spain (N=238), 11% of students experienced negative mood states (defined as feeling tired, sad, bored, hopeless, out of place, nervous or lacking sleep) [18]. The adolescents reported that having low perceived risk of marijuana use, having tried this at some point and having suffered bullying increased the risk of experiencing negative mood states. Results from the National Survey on Drug Use and Health in the US suggested that adolescents with any history of marijuana use had significantly greater rates of lifetime and past year major depressive disorder with severe role impairment as well as past year suicide attempts [19]. Surprisingly, heavy users had significantly lower prevalence of lifetime and past year major depressive disorder compared to those who used marijuana a year ago. The absence of a relationship between frequency of use and major depressive disorder was counter to the predicted result. PTSD and homelessness have also been associated with substance use during adolescence. In a study on a large sample of adolescents receiving substance use treatment in the US (N=20,069), greater substance use upon completion of treatment predicted greater PTSD symptoms and homelessness [20].

Mixed findings have been reported in a review on the effects of marijuana and alcohol co–use [21]. Some of the studies in this review, surprisingly, reported that the use of marijuana combined with alcohol during adolescence appeared to have a protective effect, yielding neuropsychological and structural brain outcomes that were better than for those adolescents who used only alcohol. Other studies, however, suggested that the co-use of marijuana and alcohol was associated with negative outcomes including poor academic performance and impaired driving.

Even alcohol use by others has been reported to have negative effects on adolescents [22]. In this Korea Youth Risk Behavior Survey (N=60,040), harmful effects due to alcohol use by others included being teased in public places (6%), sleep problems (6%), being scared of public places (34%) and fear of the safety of public places (40%). Increased risk of stress, depressive symptoms, suicidal ideation and suicide attempts were associated with being teased in public by people who drank alcohol, and mental health problems were associated with being afraid of public places and sleep problems.

4. Risk Factors/Predictors

Several risk factors/predictors for substance misuse in adolescents have appeared in the recent literature (see Table 3).

Table 3: Risk factors/Predictors of Substance Misuse and First Authors.

Risk factors	First authors
Substance misuse	
Tobacco use	Veliz
Belief that "marijuana is safe"	Chadi
Craving	Van Kampen
Unhealthy weight control	Lee
Related addictive behaviors	
Excessive screen time & gambling	Christodoulou
Family & friends factors	
Low maternal behavior control	Shek
Substance use in family & friends	Nalven
Peer substance use	Nalven
Cyberbullying roles	Yoon
Victimization	Davis
Cyber victimization	Rodriguez-Enriquez, Hong
Minority status	
Racial discrimination	Zapolski
Immigration/ documentation	Nieri
Sexual minority	Kolto
Alternative education students	Henderson

These include smoking, marijuana-related beliefs, craving, other addictions like screen time and gambling, cyberbullying and cyber victimization and minority status variables including racial discrimination, sexual minority and being a student in alternative education.

4.1 Substance Use Variables

In a survey on tobacco use and substance use in US adolescents (N=7595), multivariate analysis revealed that past 30–day cigarette use and other tobacco use were associated with increased current tobacco use disorder and substance use disorder symptoms [23]. Adolescents who converted to electronic cigarette use were at lower risk for tobacco use and substance use disorder symptoms.

In a study on marijuana use in adolescents 14-18 years (N=149), 30% reported past year marijuana use [24]. Perceived risk of marijuana was associated with lower rates of past–year use of marijuana. Greater marijuana use was associated with health beliefs that "marijuana is safe because it's natural" and "it can help adolescents focus on school" and less use was associated with beliefs that "it can affect you even after you don't feel high anymore" and "it can be addictive".

In an inpatient sample of adolescents diagnosed with cannabis use disorder, greater craving and less cognitive control were associated with more marijuana per day [25]. However, cognitive control did not have a moderating effect on the relationship between craving and marijuana use, suggesting that the underlying mechanism for marijuana use may differ from those of other substance disorders. A study that is potentially related reported a relationship between unhealthy weight control behavior and substance use patterns in Korean adolescents (N=27,284) [26]. In this article on unhealthy weight control behaviors, a fasting diet, pill use and purging were related to substance misuse including alcohol, cigarette smoking, electronic cigarette use and drug use. The use of these unhealthy weight control behaviors may have been attempts to compensate for cravings for drugs.

4.2 Related Addictive Behaviors

Other addictive behaviors include excessive screen time and gambling. In a study from the US on young adolescents (9-11 years) (N=709), excessive screen time was associated with substance use [27]. In a structural equations analysis, anhedonia (reduced capacity to experience pleasure) was noted to mediate the effects of screen time on substance use. As the authors suggested, adolescents may become desensitized and show a blunted response to the typically hedonic effects of screen time. An increase in anhedonia and greater risk for substance use may result from the need to compensate for the reduced experience of reward.

In a study on patterns of gambling and substance use initiation in adolescents, gender and ethnic differences were noted [28]. Gambling was a significant risk factor for the initiation of alcohol use for males and females and for White and African American adolescents. And, alcohol use was a risk factor for gambling in African American males only but marijuana use was a risk factor for gambling in both African American males and White females. As for most of the effects and risk factors for substance misuse, gambling and substance use had reciprocal effects.

4.3 Family and Friends Risk Factors

Several family and friends variables have been risk factors for substance misuse in adolescents. These include lack of maternal control and peer substance misuse as well as cyberbullying and cyber victimization. In a study on substance use among junior high school students in Hong Kong (N=2669), higher levels of maternal behavioral control and mother–adolescent relationship quality predicted less adolescent substance use [29]. The mother–adolescent

relationship was a robust longitudinal predictor of substance misuse. Surprisingly, fathers' behavioral control was only a concurrent predictor. In a review of data from an adolescent clinic in Uganda, substance use by adolescents was significantly correlated with maternal death, chronic illness and substance use among family members and friends [30].

In a study on American Indian adolescents (N= 3498), multilevel logistic regressions were used to explore the effects of peer, family and school–related risk factors for past month and lifetime opioid and heroin misuse [31]. Past month opioid misuse was predicted by peer substance use and less family disapproval for opioid use. Lifetime opioid misuse was predicted by peer substance use, less family disapproval of use and lower school performance. Peer substance use was the only risk factor for past month or lifetime heroin use.

Cyberbullying has been the focus of three recent studies on substance abuse in adolescents. In a study on adolescents in Los Angeles (N=2768 10th grade students), five mutually exclusive cyberbullying roles were identified including no involvement, witness only, witness and victim, witness and perpetrator and witness, victim and perpetrator [32]. The majority of students (52%) were involved in more than one cyberbullying role. All of the cyberbullying roles were associated with increased odds of substance and polysubstance use. Students who were involved in all three roles had greater odds of using several substances at a 12-month follow-up.

In a study on the effects of victimization on drug use, adolescents with substance use disorders (N= 5956) reported their drug use and their victimization experiences [33]. Females who experienced high rates of all victimization had a shorter latency to first illicit drug use. Comorbid conditions also lead to greater substance use. In a similar study in Spain, adolescents completed questionnaires on tobacco and alcohol consumption, personality traits and cyber victimization (N=305) [34]. As many as 40% reported being cyberbullied in the last year. Girls were more likely to be cyberbullied, and cyber victims had a significantly greater monthly alcohol consumption. They also had higher scores on extraversion and emotional instability as well as lower scores on conscientiousness. In a study on urban African American adolescents in Chicago (N=638), those who were bullied by peers were more likely to misuse substances [35]. In this case, internalizing problems mediated the effects of cyber victimization on substance use.

Minority status has also been a predictor variable for substance use in adolescents. These include racial discrimination, ethnic minority status, sexual minorities and students receiving alternative education. In a study on African American adolescents (N=500), attitudinal risk, intrapersonal risk, and racial discrimination risk were assessed for their predictive validity for initiation of alcohol, marijuana and cigarette use [36]. The results suggested that racial discrimination was the only variable that predicted initiation for all three substances.

In a survey on ethnic minority adolescents in Southern California, the effects of perceived discrimination at time one on substance use six months later were assessed [37]. Perceived discrimination was not based on ethnicity but on immigration or documentation status. Cultural socialization was negatively related to the likelihood of substance use.

Sexual minority youth are said to be at greater risk of substance use than heterosexual youth [38]. In that survey from eight European countries on 15-year-old adolescents (N=14,545), substance use was compared across same and both

gender attracted adolescents versus peers who reported opposite–gender attraction. The results suggested that both gender-attracted and to a lesser degree same–gender attracted adolescents were more involved than opposite-gender attracted adolescents in multiple substance use including smoking cigarettes, consuming alcohol, getting drunk and using marijuana during the last 30 days. Also, adolescents who had not been in love were less likely to use substances than all other adolescents. The authors suggested that their findings supported the minority stress and romantic stress theories that sexual minority stigma (and love on its own) contribute to greater substance use among adolescents.

In a cross–sectional self-report comparison of adolescents in mainstream (N=4024) and alternative education settings (N=219), self-report data on individual and polysubstance use were collected [39]. As would be expected, those adolescents in alternative education settings reported greater substance use including tobacco use, weekly drunkenness, using marijuana at least once a week and engaging in polysubstance use at least once a week. Those students also reported more frequent sexual health risk behaviors including earlier sexual activity and multiple sexual partners. The more frequent polysubstance use was noted for those adolescents even after adjusting for greater deprivation, lower parental monitoring, less school engagement and peer influence. It's not clear, however, whether these results are biased by the significantly unequal sample size of the two groups.

5. Interventions

Surprisingly few intervention studies have appeared in this recent literature on substance use in adolescents (see Table 4). This may relate to the decline in attendance at substance use prevention programs. In an examination of the last 15 years of data from The National Survey on Drug Use and Health, adolescents' participation in substance abuse prevention programs (especially school-based and community–based programs) decreased significantly from 48% in 2002 to 40% in 2016 [40]. These downward trends were observed in all demographic and drug involvement subgroups but especially among Latino youth and youth from rural areas and socio-demographically disadvantaged backgrounds. Another research group has noted that although unhealthy alcohol and drug use is common among adolescents, and evidence-based interventions are available, adolescents have rarely used them because of several barriers including lack of motivation to change, limited dissemination, lack of transportation and cost [41]. They further noted that there is a limited number of controlled trials that present a mixed picture in terms of the efficacy of interventions. In turn, they suggested that technology–delivered approaches may be more effective.

One technology that has been effective is adolescent–produced anti-substance use messaging [42]. These authors conducted a content analysis of 95 anti-substance use messages developed by 4–H club members across nine states. Posters and videos were content analyzed for their production elements, persuasion strategies, message content, message form, prevention goals and target substance. The data suggested that smoking was the most popular target substance and more adolescents developed messages with the goal of preventing substance use rather than stopping current use. They used slogans in the majority of the messages that contained information rather than narrative, statistical or persuasion strategies. The adolescents also used a variety of colors and fonts and font sizes in their messages.

Table 4: Interventions for Substance Misuse and First Authors.

Interventions	First Authors
Adolescent produced messaging	Pena-Alves
Education & community development	Snider
Community support for LGBQ	Eisenberg

Despite the paucity of intervention programs, at least two interventions have focused on minority groups including indigenous adolescents and lesbian, gay, bisexual and questioning adolescents. In a systematic review of the literature on preventing substance use among indigenous adolescents in the USA, Canada, Australia and New Zealand, 26 eligible studies were assessed for several components including program type, the setting, the type of delivery, the context and common components of the programs [43]. Reductions in substance use frequency were noted along with the intention to use substances. In addition, increased substance-related knowledge, improved attitudes and resistance strategies, and delay in substance use initiation were reported. The effective programs were focused on substance use education, skills development, cultural knowledge enhancement and community involvement in program development. The authors highlighted the importance of developing programs in partnership with the indigenous people.

High rates of substance use have also been noted in lesbian, gay, bisexual and questioning (LGBQ) adolescents as compared to their heterosexual peers [44]. In this large database on LGBQ students from 81 communities (N= 2454), multilevel models adjusting for student and school covariates suggested that those LGBQ adolescents who lived in communities with greater support had lower odds of frequent substance use, especially among females. The authors suggested that more LGBQ organizations and events such as the Pride Parade could be used to further reduce substance use by those adolescents.

6. Potential Underlying Mechanisms

Research on potential underlying mechanisms for substance misuse in adolescents is lacking as compared to recent literature on other addictive behaviors like Internet addiction [45], internet gaming addiction [46], sexting [47], Facebooking [48] and cell phone addiction [49]. The only two papers in the literature that were focused on potential underlying mechanisms for substance misuse in adolescents were a functional connectivity empirical study and a systematic review and meta-analysis. In the empirical study, 36 adolescents from a substance use disorder family who had used a substance before the age of 14 and had used at least two different types of substances at age 16 were considered high–risk [50]. They were compared to a group of adolescents who also had a family history of substance use but had not themselves used any substances (the resilient group). The high-risk group had less connectivity between the left dorsolateral prefrontal cortex and the left posterior cingulate cortex. The groups did not differ on connectivity between any other brain regions. The lesser connectivity in the high-risk group is perhaps not surprising given that those frontal striatal brain networks have been involved in inhibitory control of risk-taking behavior like substance misuse.

The focus of the systematic review and meta-analysis was on structural and functional neuroimaging studies that explored the treatment responses of adolescents with addictive disorders [51]. Unlike the previous study, the 18 studies

(N=354) that were included in this meta-analysis found connectivity associations in response to interventions across a broad array of cortical and subcortical brain regions and networks. Although there was significant heterogeneity in the methods used, activation clusters in most of the studies were localized to the anterior cingulate cortex, the inferior frontal gyrus, the supra marginal gyrus, the middle temporal gyrus, the precuneus and the putamen. The authors suggested that these data are consistent with adult data implicating those cortical and subcortical brain regions that are involved in cognition, emotion regulation, decision-making, and reward and are associated with treatment responses by addicted individuals.

7. Limitations of the Research

Several of the methodological limitations of the recent literature on substance misuse in adolescents are similar to those noted in the literature on other addictive behaviors in adolescents including internet addiction [45], gaming [46] and sexting [47]. These include sampling variability, different definitions for substance misuse, cross-sectional versus longitudinal research, self–report measures and different data analyses.

Sampling variability in part may relate to cultural differences which may explain the wide range of prevalence data (4-88% prevalence). Another potential factor is the source of sampling that has varied between large population surveys on representative samples of adolescents to minority samples (e.g. indigenous, African American and LGBQ) to clinical samples of adolescents who have been hospitalized or are being treated for substance misuse. The most frequent publications on adolescent substance use have been epidemiological studies focused on prevalence, effects and risk factors. Many of those studies are convenience samples that have not been randomly selected, thus limiting generalizability. Some of the studies are even limited to female or male adolescents. Others have been large age-range samples and have, for example, combined early adolescents with older adolescents in their data analyses despite the expected variability across age on the types of substance misuse well as the frequency of misuse. And, surprisingly, some studies have reported substance misuse as early as pre-adolescence.

The definitions of substance misuse have also varied including being defined as early initiation, binge drinking and co-use of multiple substances. The measures have typically been self-reported or parent-reported which appear to differ in their reliability as they are not always in agreement. And some have assessed current use while others have asked for past use. And, most studies have used frequency measures as opposed to standardized measures like the AUDIT. In addition, although there have been some studies that have measured co-use of multiple substances, the problems that are comorbid with substance misuse, like depression and externalizing behaviors, have rarely been studied.

The variability of sampling and measures has, in turn, limited the literature to very few meta-analyses. The most extensive research has been epidemiological studies focused on prevalence. Many of the prevalence studies have been conducted in other countries, although a few were multiple-country studies. Unlike other adolescent problems, for example, Internet addiction and sexting, substance use has not been studied in many cultures, possibly because parents need to give informed consent for their adolescents' participation and they may not be willing to acknowledge that their adolescents are misusing substances. They themselves may be misusing substances and have more tolerance or they

may not be closely monitoring their adolescents' substance use. And, the adolescents themselves may not want to acknowledge their substance use. These problems limit the representativeness and generalizability of the datasets.
As has been noted in research on other risky behaviors in adolescents, the primary measures have been self–reports which could result in over–reporting or under-reporting or questionable reliability. Most of the surveys have been online questionnaires and the adolescents have often been recruited at their schools. Even if they are anonymous surveys, adolescents (and their consenting parents) may feel embarrassed or ashamed to report substance misuse. This is exemplified by the relative absence of parental reports in this literature.

Further, most of the recent studies on substance misuse have been cross–sectional, making it impossible to determine causality or direction of effects. Although much of the research has focused on risk factors, those factors could also be considered effects, as most of the variables seem to be reciprocal, for example, alcohol leading to depression, in turn, leading to more alcohol. Longitudinal studies are needed to determine direction of effects to inform intervention research. They are also needed to trace and assess the reported developmental sequence of the use of alcohol leading to marijuana use, in turn, leading to the use of opioids.

The influences of parents, peers and teachers are notably absent in this literature given that peer pressure has been noteworthy in other adolescent addictions like gaming [46]. And media influences have also been absent from this literature, although they were apparent in the literature on internet addiction in adolescents [45].

In addition, very little research has focused on physiological measures that might suggest potential underlying mechanisms. Although the underlying mechanism studies suggest less connectivity in regions involving emotion regulation and reward, much like the adult studies on substance addiction, these studies are inconclusive and need replication. Surprisingly, heritability studies are also lacking. Craving has been considered a risk factor but its genetic predisposition and the effects of exposure to parents' substance use and peer pressure have not been assessed. Laboratory studies might help profile at-risk adolescents for prevention/intervention programs which are also rare. Surprisingly few interventions have been researched, including those that have been effective for other adolescent problems, e.g. cognitive behavior therapy. The paucity of intervention studies in this literature could relate to the significant decline in adolescents seeking intervention for substance misuse or the parents being more tolerant of the misuse.

Following these methodological limitations, future research might include longitudinal studies to determine direction of effects. Interview studies might help determine immediate precipitating factors as well as predisposing risks. Research on biochemical and physiological correlates such as neurotransmitter profiles and fMRI scans might also be informative as they have been for other addictive behaviors in adolescents like internet addiction [45] and sexting [47]. Similarities and differences might be noted for these addictive behaviors. Tapping a wider variety of variables might also help identify risk profiles. On the other hand, the absence of systematic reviews and meta-analyses might relate to excessive variability in sampling and measures that has precluded these types of research. And, more complex data analyses such as mediator/ moderator and structural equations models might be informative. Despite the

methodological limitations of recent research on substance misuse in adolescents, the studies on prevalence, effects and risk factors highlight the need for further research as well as prevention/intervention programs.

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