Investigation of the association between illicit substance use and suicidal behavior in schoolchildren: An integrative review of empirical data.

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Conflict of interest

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Association between illegal use of substances and suicidal behavior in school students: An integrative review of empirical data

ABSTRACT

Purpose: Investigation of the association between type of suicide behavior and type and frequency of illegal use of substances (IUS) among school students (aged between 12-18 years), with a focus on gender differences.

Design and Methods: A systematic review in PubMed, CINAHL, PsychINFO and Scopus was performed. Identified articles were published between 2007 and 2018.

Results: 20 empirical studies confirmed the association between IUS and suicidality, strongly differentiated between males and females, highlighting the importance of gender-specific mediating factors.

Conclusions: Mental health nurses need to document gender factors, frequency, and motivation of IUS when screening in adolescents experiencing suicidal behavior and IUS.

Key words: Suicidal behavior, substance use, adolescents, suicidality

INTRODUCTION

According to the World Health Organisation (WHO) suicide was expected to be a major cause of death in male and female adolescents (ages 15-29) worldwide by the end of the second decade of the 2000s (WHO, 2014). Indeed, in 2017 in the USA, suicide was reported as the second cause of death in ages 10-14 and ages 15-24 as well (Curtin, Warner, & Hedegaard, 2016; WISQARS, 2017). Globally in 2018, suicide was the second leading cause of death in ages 15-29 (WHO, 2018).

At the same time, it is well documented that the age when adolescents start substance use behaviors is constantly decreasing (WHO, 2014). Substance use is defined as the occasional consumption of alcohol or any other psycho-active substances, while substance use disorders arise when regular use of psych-active substances causes clinically and functionally significant impairment [American Psychiatric Association (APA), 2013]. Data show that 39.9% of school students in grades 9-12 have used marijuana at least once in their lifetime [Youth Risk Behavior Survey (YRBS), 2011]. Recent YRBS survey data indicate that illicit substance use was reported by 14% of high school students, use of injected illegal syubstances was reported by 1.5% and nearly one in seven reported misuse of prescripted opioids (YRBS, 2017). Additionally, data indicate an increase in the frequency of anxiety, depressive symptoms, and deaths related to substance use (WHO, 2014). Moreover, in the USA substance use-related suicide attempts increased by approximately 40% between 2004 and 2011 [Substance Abuse and Mental Health Services Administration (SAMHSA), 2013].

Suicidal behavior is one of many forms of deliberate self-injury (APA, 2013; Rodway et al. 2016). Deliberate self-injury ranges from no intention to end one's own life, which is termed non-suicidal self-injury (NSSI), to a strong intention to end one's own life, which corresponds to suicidal behavior (APA, 2013; Stewart et al. 2015). Consequently, suicidal behavior covers actions aimed at deliberately ending one's own life and includes suicidal

thoughts, suicide planning and suicide attempts (APA, 2013; Giletta et al. 2015). Suicidal ideation concerns thoughts about ending one's own life (suicide thoughts) and/or suicide planning, which involves making plans about how to kill oneself. Suicide attempts are the actions undertaken to achieve this goal.

Impaired impulse control, social impairment, and risky behavior are manifestations of substance use disorders. However, even occasional substance use in adolescents is associated with a wide variety of adverse phenomena, encompassing financial predicaments, unwanted and unsafe sexual experiences, dangerous driving, and self-injurious behaviors, including suicide (WHO, 2014). Although suicidal behavior in young people has been associated with clinical disorders (e.g. mood disorders) (Meza, Owens, & Hinshaw, 2016), its prevalence in non-clinical populations of school students has been increasing (Winsper, Lereya, Zanarini, & Wolke, 2012).

Several studies report that substance use disorders are strongly related to deaths by suicide, suicide ideation and suicide attempts (Castellví et al**.,** 2017; McManama O'Brien, 2013; Poorolajal, Haghtalab, Farhadi**,** & Darvishi**,** 2016**;** Ribeiro et al**.,** 2016). This may be attributed to neurophysiology; research demonstrates that substance use is linked with direct induction of serotonergic activity and subsequent dysfunction in the ventral prefrontal cortex, an area involved in the inhibition of impulsivity manifested in self-injurious behavior (Archer, Oscar-Berman, Blum, & Gold, 2012). Other researchers have shown that individuals facing mental distress related to depressive symptoms, such as hopelessness, suicidal ideation, or other kind of stressors (e.g. work-related pressure), may engage in substance use in an attempt to alleviate the severity of such experiences (Bolton, Robinson, & Sareen, 2009). The self-medication hypothesis may partially explain this phenomenon (Khantzian**,** 2003). According to this theoretical model, individuals who have not developed effective strategies to manage distress and everyday challenges, such as agony, hurt and loss,

suffering or frustration, may adopt substance use to recompense for the deficiency or absence of adaptive behavioral and cognitive schemas of coping.

The majority of the studies in adolescents conducted in the previous decade that have assessed the association between substance use and self-injurious behavior have not distinguished suicidal from non-suicidal self-injurious behavior (Dawes, Mathias, Richard, Hill-Kapturczak**,** & Dougherty 2008; Rossow, Hawton, & Ystgaard, 2009). Moreover, it is unclear whether the link between substance use and suicidal behavior is the same across different types of substances or in relation to the number of substances used, or even the type of suicidal behavior experienced, i.e. thoughts or attempts. For instance data on 10,203 adults from the National Survey on Drug Use and Health (NSDUH) in the USA confirmed a positive association between injection drugs, i.e. heroin, cocaine**,** and stimulants, and suicide attempts but not suicidal ideation (Cheek, Nestor, & Liu, 2016). Similar data in adolescents are limited (Liu, Case, & Spirito, 2014). In the majority of relevant studies, the type of substances assessed is not identified, nor compared with the type of suicidal behavior exhibited (Dervic et al., 2007). Additionally, studies underline the association between pre-teen initiation of substance consumption with suicidal behavior (Swahn, Bossarte, Ashby**,** & Meyers, 2010). Overall, the samples in which the association between substance use and suicidality is measured are not always consistent, thus comparison between different groups of adolescents is difficult (Esposito-Smythers & Spirito, 2004).

Moreover, a number of risk factors for substance use in adolescents seem to be gender specific, such as early onset of puberty in girls (Purper-Ouakil & Didillon**,** 2016), eating and weigh loss attitudes (Thomas et al.**,** 2018), perceived racial discrimination (Assari, Mistry**,** and Caldwell**,** 2018), subjective body image (Black, Sussman, Unger, Pokhrel**,** & Sun 2010), urbanization (Pitel, Geckova, van Dijk, & Reijneveld, 2011), or spirituality (Debnam, Milam, Mullen, Lacey**,** & Bradshaw 2018). Similarly, there are modifications in

the patterns of substance use between male and female adolescents, mainly in relation to the age of initiation and severity or duration of use (Campbell et al., 2018; Hawes, Trucco, Duperrouzel, Coxe, & Gonzalez, 2018). For instance, although in 2017 there was no statistically significant difference in the frequency of lifetime illicit substance use between male and female high school students in the USA, compared to females, a statistically significantly higher percentage of male students reported lifetime use of injected substances (YRBS, 2017). Additionally, data indicate that most of the times females use substances differently, respond to various substances differently, and may face distinctive obstacles to effective treatment [National Institute on Drug Abuse (NIDA), 2018]. For example, ecstasy seems to produce stronger hallucinatory effects in females compared to males; females may be more vulnerable to the rewarding effects of methamphetamine and cocaine compared to males and finally, compared to females, males are more likely to switch to another substance when they lack access to methamphetamine (NIDA, 2018).

Although research data show that the association between substance use and symptoms of mental health disturbances is differentiated by gender (Magidson et al., 2017; Wu et al., 2010), there is only limited evidence with regard to suicidal behavior. Nevertheless, the frequency of suicide attempts is twofold in female adolescents aged 15-24 years compared to male, while male adolescents die more frequently by suicide compared to female adolescents (Hawton, Saunders & O'Connor, 2012). Despite these differences, there are only limited data on the effects of various substances by gender regarding suicidal behavior. For instance, suicide from substance misuse is higher in females than among males (WISQARS, 2017).

AIMS

The present paper presents a synthesis of empirical data on the relationship between illegal use of substances (IUS) and suicidal behavior in non-clinical, community-based

school students with a mean age between 12 and 18 years. The main focus was on a) gender differences, b) type and frequency of illegal use of substances, c) type of suicidal behavior exhibited, and d) age at start of illegal use of substances

For the purpose of the present review we used the term "illegal use of substances" instead of "illicit substance use", with the aim of including substances which, although not illegal (e.g. glue or sedatives), their use by school students or within the school context is prohibited, or beyond medical provision. Also, they have been characterized as psycho-active agents.

METHOD

Study selection strategy

The Whittemore & Knafl (2005) guidelines for integrative reviews were applied. An advanced search in Medline, CINAHL, PsychINFO, Scopus and Cochrane Library was conducted between November 2016 and January 2018 by two researchers (MK & PZ) and validated by an expert librarian (KM). The following search words were employed singly and in combination: 'adolescent' or 'teenagers' or 'young' or 'schoolchildren' AND 'substance use' or 'misuse' or abuse' AND 'suicide attempt' or 'suicide' or 'suicide thoughts', or 'suicide plans' or "suicide ideation" AND 'depress*' AND 'marijuana' or 'cocaine' or 'ecstasy' or 'alcohol' or 'illicit drugs' AND 'dual diagnosis'.

Although the terms "self-harm" and "self-injury" are relevant to the topic under study, they were not included in the present search strategy. The reason behind this decision was that deliberate self-harm or self-injury includes a varied spectrum of behaviors, characterised by different levels of suicide intent and a changeability of motives (APA, 2013). Thus, deliberate self-harm ranges from no intention to end one's own life (NSSI) to strong intention to end one's own life (suicide attempt/suicide), and it is also possible for multiple motives to co-exist (e.g. aiming to send a message and at the same time to obtain

relief from suffering, or even die), where various ways to achieve this goal may be performed (APA, 2013). As the focus of the present study was solely on suicidal behavior, the terms "self-harm" or "self-injury" were not included in the search as it was expected that they would reveal studies with no clear distinction between suicidal and non-suicidal behavior.

The following inclusion criteria for the articles were set**:** (a) an empirical quantitative study (b) published in the English language, in a peer-reviewed journal between 2007 and 2018 (a timeframe set according to the date of publishing of previous reviews (Esposito-Smythers & Spirito, 2004; Vijayakumar, Kumar, & Vijayakumar, 2011). Studies were excluded if (a) their aim was to investigate the effectiveness of relevant interventions and (b) if they were dissertations (due to limited availability of data). Moreover, studies exploring self-injurious behavior without clarifying the respondents' intention to die were also excluded. In order to increase the generalizability of the present findings to the general population of school students, studies on vulnerable groups such as gays or lesbians, prisoners and clinical populations (undergoing treatment/hospitalized for mental disorders or substance use disorders) were also excluded, due to associated confounders (Pompili et al., 2014). Moreover, the inclusion of vulnerable populations at relatively high risk of both suicidal behavior and IUS might have increased the risk of selection bias. Additionally, data on the association of suicidal behavior with tobacco smoking and/or alcohol use were also excluded. Although the use of alcohol and tobacco is illegal among school students in many countries**, t**heir use outside the school context is socially accepted in many cultures (Quiroga et al.**,** 2018). Moreover, the profile of teenagers who solely smoke tobacco or/and consume alcohol occasionally, while not using any other substances differs from those who report tobacco and/or alcohol use, along with illegal substances or non-medical use of substances (Ganz & Sher**,** 2009; McKelvey, Ramo, Delucchi, & Rubinsteinc, 2017). Moreover, as the

focus of the present review was on substance use rather than substance abuse or dependence tobacco and alcohol were excluded because in the majority of studies it was not possible to differentiate between occasional and culturally accepted use of tobacco/ alcohol and problematic use or dependence on these substances (Adger & Saha, 2013). Furthermore, only one published manuscript from each study, strictly assessing data relevant to the present research questions was included. The stages of the selection procedure, which were in accordance with the PRISMA guidelines (Moher et al., 2014), are depicted in Figure 1.

< Please insert Figure.1 here>

Data extraction and critical appraisal

Each included study was independently reviewed by two of the researchers according to the variables presented in the Table 1 and Table 2, thus corresponding to the measures employed for the aim of the review, i.e., Context of IUS (school/ students), target population (school students with a mean age between 12-18 years), methods (study design; type of illicit substances; measures and tools employed), mediators in the association between IUS and suicidal behavior (gender; type and frequency of substance used; age at start of substance use), outcomes measured, and significant results. A specially designed extraction sheet was used for data collection purposes, while the reasons for excluding any study were documented. The Critical Appraisal Skills Programme (CASP) quality appraisal checklists for cross-sectional and cohort studies were used for the quality assessment of the methodological rigour of the included studies (Critical Appraisal Skills Programme, 2014). Studies meeting over 50% of CASP criteria were classified as being of moderate quality, those meeting 70% or more of the criteria were classified as high quality, while studies meeting 50% or less of these criteria were considered to be of low quality.

Data analysis and synthesis

Data were analyzed by all researchers in four steps (a) validation of the objectives of the review and relevant mediating variables in the association between type of suicidal behavior (suicidal ideation, suicide attempts) and type and frequency of substance use. i.e. gender and age at start of substance use; (b) description of the main methodological characteristics of the reviewed studies, including the main confounding factors and relevant limitations (c) organisation of the finding of the reviewed studies with special focus on mediating variables. In particular, the association between suicidal behavior and the substances used was reported separately for males and females, while the comparisons were reported in relation to their respective reference groups, i.e. male or female non-users. Regarding the variable "age at substance use initiation", the findings were grouped into the following two categories (i) substance use initiation before13 years and (ii) substance use initiation after 13 years.

The frequency of substance use was reported as current use and lifetime use, while the type of substance used was also reported in relation to the type of suicidal behavior exhibited, i.e. suicidal ideation or suicide attempt. Additionally, for the case in which the main illicit agents were not specified in the included studies, the term "Any Illicit Substance [AIS]" was applied here in to describe a group of substances including the main illicit psycho-active agents (cannabis, amphetamines, hallucinogens, crack, cocaine, heroin, ecstasy), assessed as a single variable (yes/no).

RESULTS

Two researchers (MK and PZ) independently screened the titles, abstracts and full texts of all retrieved papers for eligibility and resolved disagreements by consensus. Finally, 20 studies were included in the present review (Figure 1)(See Table 1). The methodological characteristics and the main results of the included studies are summarized in Table 1 and

Table 2. Seventeen out of the 20 included studies were of high quality and three were moderate (Afifi et al., 2007; Arenliu et al., 2014; Chin & Choi, 2015). Sample sizes ranged from 367 to 74,936 participants, and a total of 362,232 community-based school students with a mean age of 14.24 years (minimum age=9 years; maximum age 18 years) were assessed. Out of the twenty included studies, seven were conducted in the USA, six in European countries, one in New Zealand, one in Pacific Island Countries, one in Hong Kong, one in South Korea, two in Africa (Zambia, W.Africa-Benin), and two in Central America (Mexico, Peru). A cross-sectional design was used in the great majority of the studies, as only two were longitudinal (Roberts et al., 2010; Wong et al., 2008). Both convenience and random sampling methods were used in the cross-sectional studies. Only six out of the twenty studies reported separate results for males and females (Afifi et al., 2007; Arenliu et al., 2014; Chin & Choi, 2015; Cho et al., 2007; Epstein, & Spirito, 2010; Peltzer, & Pengpid, 2015; Swahn et al., 2012). Finally, three studies explored the association between suicidal behavior and age at onset of substance use (Epstein & Spirito, 2010; Peltzer & Pengpid, 2015; Swahn et al., 2012).

The reviewed studies conveyed a heterogeneity regarding the assessed prevalence of IUS, i.e. lifetime or current use. This variation was reported across the samples of the studies included in the present review. Herein, the term “current use” corresponds to the measure “substance use more than once in the past month”, while the term “lifetime use” corresponds to the measure “substance use more than once in one’s lifetime”. This is followed throughout the text and tables. Moreover, heterogeneity was reported in relation to the severity of suicidal thoughts, i.e. the presence or absence of actual plans in the majority of the reviewed studies.

Additionally, all but one of the studies describes confidence intervals (Chin & Choi, 2015). In this regard, Afifi et al. (2007) and Arenliu et al. (2014) reported large OR and very

broad confidence intervals, reflecting low-powered models that showed low-prevalence links between substance use behaviors and suicidality, thus their research results need to be interpreted with caution. Only statistically significant, adjusted scores are reported herein, as the association between IUS and suicidality is a phenomenon with a potentially high number of confounders. As a result, although we aimed to present the entire body of literature regarding the association between IUS and suicidality in school students, direct comparisons were not possible due to the diversity of the comparisons in the reviewed studies. However, although different confounders were included in each study, all of them encompassed the three main confounders, i.e. gender, anxiety**,** and depressive symptoms, thus allowing more generic conclusions regarding their findings. Overall, although the present review reports findings from studies investigating the same variables, due to the different methodological approaches applied, mainly with regard to the way possible covariates were controlled, a vast variance in the effect of the study variables has been noted with regard to the present research questions.

Table 2 mainly focuses on the main results of the reviewed studies/

Please insert Table 1 and Table 2 about here>

Findings from individual studies and synthesis

Association between the type of illegal use of substances, type of suicidal behavior and gender differences. Suicide attempts were 6-7.5 times higher amongst male current cannabis users compared to male non-users, while suicide attempts were 16 times higher in female current cannabis users compared to female non-users [OR 95% CI range: 6.17(1.41-15.54)-7.54(2.53-40.36)] (Afifi et al., 2007; Arenliu et al., 2014). Suicide ideation was 3.5 times higher amongst male current cannabis users compared to male non-users [3.51 (1.51-7.91)], while suicide ideation was almost 7 times higher in female current cannabis users compared

to female non-users [6.79 (1.67-25.39)] (Chin & Choi, 2015). Both studies report an OR with very broad confidence intervals.

With regard to Any Illicit Substance (AIS), as a group of psycho-active agents not otherwise specified, suicide attempts were 2 times higher in males reporting lifetime use of AIS compared to male non-users (OR: 1.94- CI not reported), as well as in females reporting lifetime use compared to female non-users (2.04-CI not reported) (Chin & Choi, 2015). Suicide ideation was slightly more than 2 times higher in females reporting current use of hard AIS compared to female non-users [OR(CI): 2.34 (1.0-5.4)], while suicide attempts were also five times higher amongst female current users of hard AIS compared to female non-users [5.03 (1.9-13.5)] (Cho et al., 2007). Suicide ideation was almost 5 times higher in males reporting lifetime use of amphetamine/hallucinogen/ecstasy compared to male non-users [4.78(2.15-10.18)] (Arenliu et al., 2014).

There was no statistically significant association between glue or solvent sniffing and suicide ideation/attempts in adjusted models for either male or female users compared to non-users. Suicide attempts were almost three times higher in males reporting lifetime, non-medical use of sedatives compared to male non-users [2.82 (0.95-7.40)]. Suicide attempts were almost five times higher in females reporting lifetime non-medical use of sedatives [4.69 (1.81-10.64)] (Arenliu et al., 2014). Suicide ideation was more than nine times higher in females reporting lifetime non-medical use of sedatives [9.39 (5.28-16.63)] (Arenliu et al., 2014). No statistically significant data were reported for males.

Age at initiation of substance use, suicidal behavior and gender differences. Suicide attempts were almost 3.5 times higher in males reporting the start of cannabis use before the age of 13 years compared to non-users [3.46 (2.22-5.38)] (Swahn et al., 2012), while this score was less than two times higher in males reporting the start of cannabis use

after the age of 13 years [1.61 (1.11-2.31)], compared to non-users (Swahn et al., 2012). Suicidal thoughts were almost double in males reporting the start of cannabis use before the age of 13 years compared to non-users [2.37 (1.55-3.62)], while there was no association between age of cannabis use initiation after the age of 13 years and suicidal thoughts. Suicide attempts among females reporting the start of cannabis use before the age of 13 years were more than two times higher [2.01 (1.15-3.51) to 3.37 (2.29-4.96)] compared to non-users (Swahn et al., 2012), while this score was almost identical among those reporting the start of cannabis use after the age of 13 years [2.12 (1.71-2.63) to 2.19 (1.51-3.20)] (Swahn et al., 2012). Suicidal thoughts were almost 1.5 times higher in females reporting the start of cannabis use either before [1.58 (1.02-2.46) to 1.67 (1.09-2.55)] or after the age of 13 years [1.60 (1.26-2.04)] (Swahn et al., 2012).

Suicide ideation was more than two times higher in males reporting the start of AIS use before the age of 13 years [2.55 (1.70–3.84)] compared to non-users. This score was slightly lower among males reporting the start of substance use after the age of 13 years [1.95 (1.32–2.88)]. Similar finding were reported in relation to suicide attempts. In particular, suicide attempts in males were more than two times higher in those reporting AIS use before the age of 13 years compared to non-users [2.39 (1.21–4.74)], as well as in those reporting the start of AIS use after the age of 13 years [2.07 (1.37–3.13)] (Peltzer & Pengpid, 2015). According to Peltzer and Pengpid (2015), suicide ideation was double in females reporting AIS use before the age of 13 years compared to non-users, and almost the same for females reporting AIS use initiation after the age of 13 years [1.90(1.09-3.70) to 1.82 (1.04-3.18)]. Suicide attempts in females reporting AIS use before the age of 13 years was almost three times higher [2.87(1.63-5.07)] compared to non-users, while this score was less than two times higher in those reporting the start of AIS use after the age of 13 years [1.84 (1.05-3.22)] (Peltzer & Pengpid, 2015).

DISCUSSION

To the best of our knowledge, this is the first systematic review on the association between IUS and suicidal behavior in secondary and high school students. Thus, the present findings add to existing literature by providing new evidence on the importance of gender-specific factors in this association and the need for gender-oriented interventions, as well as on the association between the frequency, type and age at the start of substance use and type of suicidal behavior experienced. Therefore, this study reveals specific challenges, in addition to data that can contribute to innovative interventions of importance for nurses caring for school students with adjustment and/or mental health problems in conjunction with substance use and suicidality. The findings also have implications for policy making aimed at prevention.

The research synthesis demonstrated that suicide attempts were more than seven times higher in male current cannabis users compared to non-users, even when controlled for anxiety and depressive symptoms. This score was sixteen times higher in female current cannabis users. The same pattern was noted in relation to suicide ideation, which was three times higher in male current cannabis users compared to non-users, while it was almost double, i.e. seven times higher, in female current users compared to female non-users. Although previous data show that males are more likely to use cannabis compared to females (APA, 2013), this stronger association between cannabis use and suicide attempts/ideation in females compared to male users may indicate that female school students are more vulnerable to the adverse effects of cannabis use on suicidal behavior, or that female school students use cannabis as a self-regulatory coping strategy against suicidality more frequently than males (Kokkevi et al., 2011; Seaman et al., 2014). Nevertheless, special focus on female school

student cannabis users regarding suicidality is needed in relation to policy making and the design of preventive interventions.

Moreover, although female cannabis users did not exhibit any difference in the frequency of suicidal behavior in relation to the age at which cannabis use started, i.e. before or after pre-adolescence, males reporting cannabis use before the age of 13 years reported more suicide attempts compared to those who reported starting cannabis use after pre-adolescence. Thus, targeted interventions regarding attempted suicide need to focus on male cannabis users who report starting use before the age of 13 years. Additionally, special focus is needed on females reporting any illicit substance use before the age of 13 years, as it was shown herein that females reporting any illicit substance use before the age of 13 years report suicide attempts more frequently than females reporting any illicit substance use after pre-adolescence.

The findings reported showing that current users of cannabis of both genders report a higher prevalence of suicide attempts compared to those reporting lifetime use of cannabis may indicate a time-based link between cannabis use and suicide attempts or that other factors related to the link between current cannabis use and suicidality are involved (e.g. school bullying victimization) (Winsper et al., 2012). For instance, exposure to severe negative experiences, i.e. bullying or sexual abuse, may lead to both current cannabis use and suicide attempts. Furthermore, previous data on adult users of cannabis show that repeated intoxication or experience of withdrawal symptoms may be associated with intense depressive symptoms, which although temporary, might be severe enough to trigger suicide attempts in those already experiencing suicidal thoughts (APA, 2013). Overall, the present finding suggest a different pathway in the association between cannabis use and suicidality in adolescents, supporting the hypothesis that additional factors, not only depressive symptoms, are needed to trigger an association between cannabis use and suicidal behavior/ideation

(Seaman et al., 2014; Sharmaet al., 2015). Additionally, this difference in the frequency of attempted suicide compared to thoughts about suicide in cannabis users of both genders may be attributed to the fact that the use of psycho-active substances might be associated with suicide attempts through a different neuro-biological pathway than suicidal ideation (Kokkevi et al., 2012a, 2012b; McManama O'Brien, 2013). At the same time, based on the findings by McManama O'Brien (2013) and Kokkevi et al., (2012a, 2012b) the present findings might also support the assumption that when suicide suicidal thoughts are present, a relationship between cannabis use and a suicide attempt develops more easily in both genders, with females showing greater vulnerability. Thus, suicide prevention strategies should place special focus on female school students who are current cannabis users. Increased vulnerability was also revealed in female school students who used any illicit substance before pre-adolescence.

The aforementioned patterns need to be further investigated, as it can be argued that females are more vulnerable to factors such as peer pressure for substance use or other life threatening behaviors and cultural norms linked with fluctuation in self-esteem and further expressed as suicidal ideation may differ between males and females (Chapman et al., 2017; WHO, 2014). Nevertheless, the motives behind illegal substance use need to be further explored in school students exhibiting suicidal behavior, and vice versa. Thus, gender-specific factors, such as cultural norms, impulsivity, motivation or hormonal profile need to be studied in more detail with regard to this association.

Only a limited number of studies were identified that aimed to explore the association between the use of individual illegal substances, i.e. amphetamine, hallucinogens, ecstasy, methamphetamine, and suicidal behavior in separate samples of males and females. However, they did not provide any statistically significant findings.

The prevalence of suicidal ideation was not associated with the age at the start of cannabis use in males or females, i.e. before or after pre-adolescence. In contrast, suicide attempts were almost 2 times higher in males reporting cannabis use before pre-adolescence compared to males reporting start of cannabis use after the age of 13 years. Regarding the age at which AIS use started, there was no difference in the prevalence of suicidal thoughts or suicide attempts in males, while suicide attempts were higher in females reporting AIS use before the age of 13 years compared to females reporting use after the age of 13 years. The above findings may suggest that a different cut-off point for age between males and females should be used in future studies, in order to capture significant associations between age at substance use initiation and adverse phenomena (e.g. suicidal behavior). Moreover, additional confounders related to the transitional period from pre-adolescence to adolescence, i.e. hormonal profile and relevant biomarkers, need to be included in future studies exploring this issue.

Limitations of the included studies

The present data need to be viewed in the light of the limitations of the included studies. The majority followed a cross-sectional pattern, thus assumptions on causality are not relevant. An additional limitation is that the samples included school students with a wide range of ages. Therefore, differences in the type and frequency of substances used may be present across different age clusters. Additionally, important confounding risks factors were not included in some of the studies reviewed, such as clinically relevant symptoms of depression or anxiety and adjustment problems. Indeed, research data indicate that a co-occurrence of mood and substance use disorders is most likely found in adolescents who died by suicide (Goldston, et al., 2009). In particular, it has been shown that substance use and clinically relevant depressive symptoms work synergistically and increase the risk of suicide attempts in clinical populations of this age group (Effinger & Stewart, 2012). Further

research exploring the mediating role of depressive or depressive-like symptoms in this association is needed, with special focus on gender differences. A lack of consistency in the way the frequency and severity of substance use was measured was identified in the reviewed studies. Most of the researchers used yes/no assessment measures. This type of item wording does not allow clear distinctions on the frequency, dose or even the type and number of the substances used, highlighting the need to address these limitations in future studies.

Regarding the controls included in the reviewed studies, only a limited number of them explored the mediating effect of a positive history of suicidal ideation or suicide attempts on the association between substance use and suicidal behavior, even in relation to gender differences, which is considered one of their main limitations. Data show that attempted suicide before the age of 19 years is the most significant predictor of a suicide attempt later in life, followed by alcohol use disorders and current mood disorder (Méan, Righini, Narring, Jeannin, & Michaud, 2005). Nevertheless, epidemiological data show a plethora of factors involved in the association between IUS and suicidality (Effinger & Stewart, 2012; Evans, Hawton, & Rodham, 2004; Méan et al., 2005; Ramchand, Griffin, Harris, Mcffrey, & Morral, 2008). The fact that the number and type of controls differed across the reviewed studies, may to some degree explain the differences in the effect size reported. Not surprisingly, studies including depressive symptoms, history of suicide attempts or impulsivity in the control variables reported lower risk scores compared to studies reporting un-adjusted scores or with a limited number of controls. Further studies including the above controls, as well as gender specific confounders when exploring relevant issues are proposed. The epigenetic mechanisms influencing the association between vulnerability to both substance use and suicidal behavior encompass many environmental

factors, such as social norms and parenting style, which are relatively different between males and females in many cultures (Archer et al., 2012; WHO, 2014).

Limitations of the present review

Although the aim of the present review could be more accurately explored through meta-analysis, due to the limited number of studies exploring gender differences in the association between IUS and suicidal behavior we solely applied a systematic investigation of the existing literature without proceeding to a meta-analysis. Thus, the results reported herein lack the accuracy of a meta-analysis approach, despite having been produced through a robust systematic approach that allows replication. Furthermore, caution is needed regarding the generalizability of the present findings.

Although many of the included studies are multi-centered, there is an under-representation of developing countries. However, despite the fact that seven out of the twenty studies were from the USA, the results of the studies from other countries do not contradict the rest of the findings, which may partially support their generalizability. Studies on vulnerable groups, i.e. prisoners, gays/lesbians or hospitalised populations were excluded, although these populations are at extremely high risk of suicidal behavior and illicit drug use, constituting an additional limitation (Cassidy, Yang, Kapczinski, & Passos, 2017; Smith, Armelie, Boarts, Brazil, & Delahanty, 2016). However, the inclusion of these groups might have jeopardized the generalizability of the present findings in community-based school students as additional or different confounders (e.g. self-stigma), may exist among them. Studies exploring the association between suicidal behavior and alcohol or tobacco use were within the scope of the present review and were not included; however not jeopardizing the novelty of the present findings regarding illegal substance use, as previous reports on the association of tobacco and alcohol use with suicidality have been published (Galaif, Sussman, Newcomb, & Locke, 2007; Li et al., 2012).

Implications for nursing practice

Based on the present findings, mental health nurses need to focus on particularly vulnerable school student populations during risk assessment for suicidal behavior and substance use (Esposito-Smythers et al., 2012). Furthermore, it is suggested that nursing interventions should be specifically designed not only according to the type/frequency of substance use and suicidal behavior, but to take account of gender differences as well. Nevertheless, the present data can inform both suicide and IUS prevention strategies in school students (Kim et al., 2011), as well as policy in relation to the provision of healthcare services for adolescents. The pattern of care in many healthcare systems is to treat both disorders, i.e. substance use disorders and mood disorders, separately, as well as to implement preventive strategies separately (Esposito-Smythers et al., 2012). This might be a reason why most of these care strategies fail to manage relevant symptoms.

Further research on the effectiveness of therapeutic approaches and preventive policies addressing both issues simultaneously is proposed, with special focus on younger age groups, i.e. individuals younger than 13 years old. Moreover, we propose specially developed therapeutic interventions for males and females, focused on different factors mediating the relationship between substance use and suicidal behavior. Interventional studies assessing the effectiveness of such therapeutic programs are also needed. Moreover, the association between suicidal behavior and the number of substances used needs to be further explored.

CONCLUSION

A difference between male and female school students regarding the association between IUS and suicidal behavior was reported. The onset of IUS before or after the age of 13 years must be viewed as an important mediating factor in relation to gender and the type of substance used. Relevant information may be important for mental health nurses to enable

them to carry out clinical assessment and implement preventive policies. Moreover, the study revealed the importance of the type and frequency of substances used by adolescents exhibiting suicidal behavior, as well as symptoms of suicidal behavior in those reporting substance use. During clinical assessment caregivers should consider additional risk factors prevailing in the transition from pre-adolescence to adolescence, such as the motives behind substance use and suicidal behavior or other gender-specific factors, such as hormonal profile or vulnerability to cultural norms. Overall, among school students who report ISU, male current cannabis users who report use before the age of 13 years are at increased risk of suicide attempts, as well as female current cannabis users and females who report use of any illicit substance before the age of 13 years. Thus, the above population needs to be the focus of interventional programs and policies.

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Figure 1 Selection strategy of the studies included in the present review according to the PRISMA flow chart (Moher, Liberty, Tetzlaff, Altmna, & the PRISMA Group 2009).

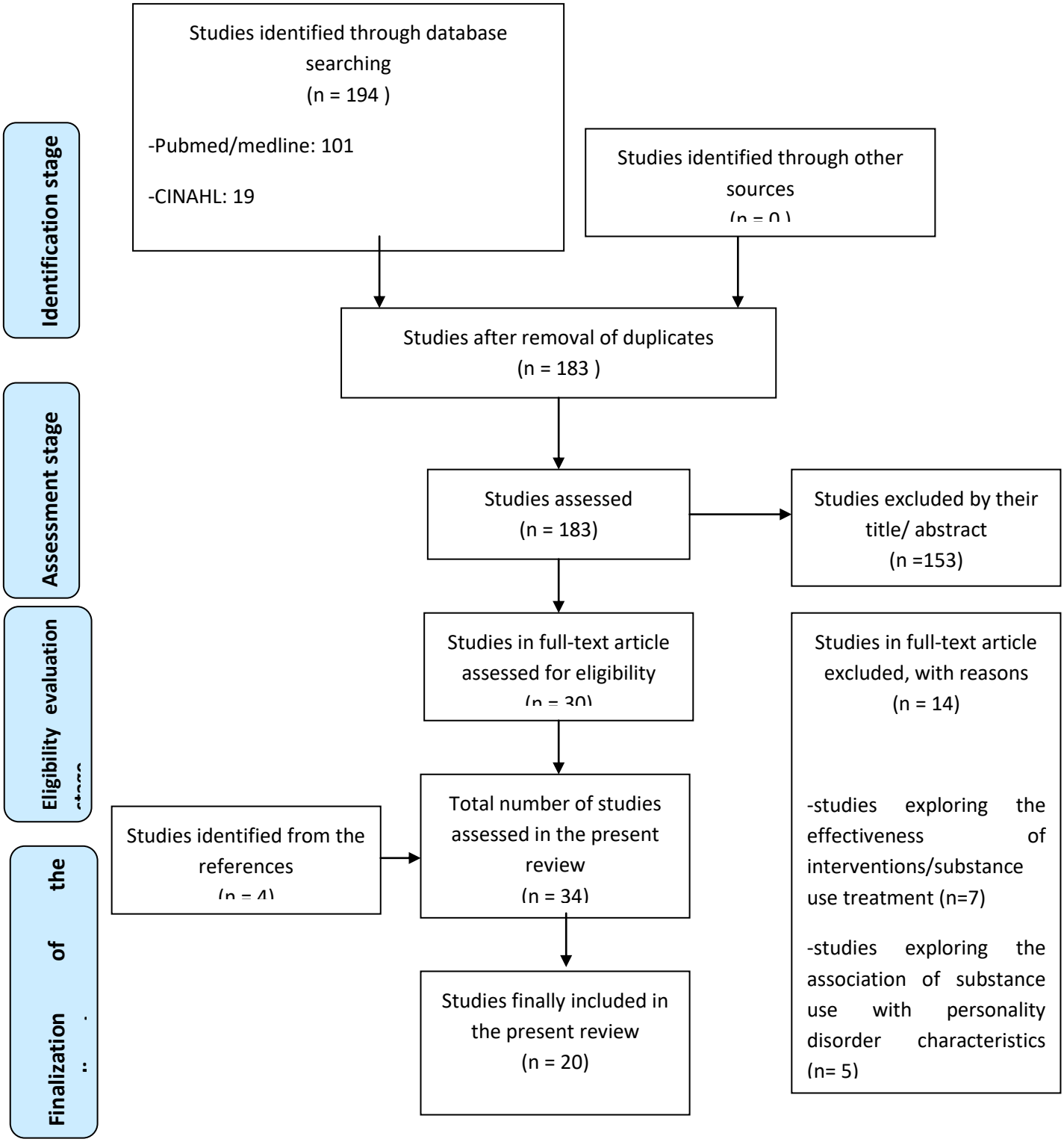

Table 1. Methodological characteristics of the studies in the present review.

Authors & year/Country	Study design	Sample	Measurement of the main variables (SBV/WSI-NSSI)	Confounding factors assessed	Limitations
Afifi et al. 2007/France	Cross-sectional, comparative & correlational study	Cluster sampling; mean age 12-13 years; n= 2090	Anonymous, self-reported questionnaires: yes/no questions & psychometric scales	Demographic data; anxiety & depressive symptoms; physical aggression & impulsivity; sexual intercourse	Self-reported data; no longitudinal data, thus the study cannot provide information about causality; no triangulation of data with other information sources; no assessment of lifetime suicidality, as well as important confounders, such as NSSI, sexual abuse, family history of suicide; large OR with very broad confidence intervals reported.
Arenliu et al. 2014 /Kossovo, Albania	Cross-sectional & correlational study	Random stratified sample; mean age 15.65 years; n= 4709	Anonymous, self-reported questionnaires: yes/no questions & psychometric scales	Demographic data; anomie; perceptions on substance use; anxiety & depressive symptoms; self-esteem	Self-reported data; the cross-sectional nature of the study does not allow assumptions on causality; no triangulation of data with other information sources; no assessment of important confounders, such as NSSI, sexual abuse, family history of suicide; large OR with very broad confidence intervals reported
Chin and Choi 2015/South Korea	Cross-sectional study	Stratified multistage cluster random sampling; age 12-13 years; n= 74936	Anonymous, self-reported web-distributed questionnaires: psychometric scales & yes/no questions	Demographic data; health risk behaviors; psychopathology; family & school related factors; depressive symptoms; happiness; health status	Retrospective, self-reported data; cross-sectional design, thus no conclusions on causality; 95%CI were not reported; no assessment of the frequency of suicidal behavior; no assessment of important confounders, e.g. NSSI, family history of suicide; self-esteem, impulsivity
Cho et al. 2007 /USA	Cross sectional & correlational study	Purposeful sampling; grades 9-11; n= 1252	Anonymous, self-reported questionnaires: psychometric scales & yes/no questions	Demographic data; depressive symptoms; perceptions & personal beliefs on suicidal behavior & substance use; substance use onset	Non representative sample (high-risk for school dropout sample); cross sectional design; no assessment of the quantity of substance abuse; no assessment of important confounders, e.g. NSSI, family history of suicide; self-esteem, impulsivity
Epstein & Spirito 2010/USA	Cross sectional & correlational,	Three stage cluster sample;	Anonymous self-reported questionnaires recorded electronically	Aggression; victimization; risky sexual behavior; gender	Self-reported data; risk factors were examined separately so it is unclear if associations were direct or indirect; race and ethnicity findings not

	exploratory study	grade 9-11; n= 13,917			reported; cross-sectional design, thus no conclusions on causality
Fleming et al. 2007/ New Zealand	Cross-sectional & correlational study	Random sample; mean age=11 years; n=9570	Anonymous, self-reported, electronically distributed questionnaires: Psychometric scales & yes/no questions	Age, gender, parental & family caring; depressive & anxiety symptoms; family dinners; sexual abuse; domestic violence; non-heterosexual orientation; trust in teachers, feeling safe at school	Self-reported data; no triangulation of data with other information sources; cross-sectional design, thus no conclusions on causality; important confounders were not assessed, i.e. self- esteem, impulsivity; genetic risk; coping strategies; NSSI
Kim et al. 2011/USA	Cross-sectional & correlational study	Random sample; mean age: NR; n=19,301	Personal interviews, using computers and including questionnaires: Psychometric scales and yes/no questionnaires	Age; gender; race/ethnicity; family income; residential instability; single parent family structure; communication with parents about serious problems; psychopathology (anxiety & depressive disorder symptoms; conduct disorder symptoms)	Self-reported data; no triangulation of data with other information sources; cross-sectional design, thus no conclusions on causality; not possible to fully control for the effects on ecstasy use only; no assessment of important confounders, such as NSSI, sexual abuse, family history of suicide, self-esteem
Kokkevi et al. 2011/Greece	Cross-sectional, comparative & correlational study	Nationwide, multistage stratified probability samples mean ag: NR	Anonymous, self-reported questionnaires: yes/no questions & psychometric scales	Age; gender; self-esteem; depressive mood; antisocial behavior; family structure; satisfaction from social and family relationships; socio-economic status	No triangulation of data with other information sources; no causality; no assessment of the severity of the attempted suicides; no assessment of important confounders, such as NSSI, sexual abuse, family history of suicide; assessment of the use of the main illicit drugs (cannabis, amphetamines, hallucinogenic, crack, cocaine, heroin, ecstasy) through a single variable (lifetime use; yes/no), thus findings do not differentiate among each substance
Kokkevi et al. 2012a/ 16European countries	Cross-sectional, comparative correlational study	Random samples; mean age: NR; n= 42,635	Anonymous, self-reported questionnaires: yes/no questions & psychometric scales	Age; gender; run away; self-harming; self-esteem; depressive mood; antisocial behavior; family structure; satisfaction from social and family relationships; parental socio-economic status	No triangulation of data with other information sources; no causality; no assessment of the severity of the attempted suicides; no assessment of important confounders, such as NSSI, sexual abuse, family history of suicide, social support; assessment of the use of the main illicit drugs (cannabis, amphetamines, hallucinogenic, crack, cocaine, heroin, ecstasy) through a single variable (lifetime use; yes/no), thus findings do not differentiate among each substance

Kokkevi et al. 2012b/ 17 European countries	Cross-sectional, comparativecorrelational study	Random sample; mean age 16 years; n= 3,881	Anonymous, self-reported questionnaires: open-ended questions & psychometric scales	Age; gender; run away; self-harming; self-esteem; depressive mood; antisocial behavior; family structure; satisfaction from social and family relationships; parental socio-economic status	No triangulation of data with other information sources; no causality; no assessment of the severity of the attempted suicides; no assessment of important confounders, such as NSSI, sexual abuse, family history of suicide, social support; assessment of the use of the main illicit drugs (cannabis, amphetamines, hallucinogenic, crack, cocaine, heroin, ecstasy) through a single variable (lifetime use; yes/no), thus findings do not differentiate among each substance
Miller et al. 2011/Mexico	Cross-sectional study	Multistage probability household survey; mean age: NR; n=3005	Personal interviews based on computer-assisted diagnostic instruments & yes/no/frequency questions	Gender; age; education, school attendance status; parental education; history of employment; marital status; having a child/ childbearing; psychiatric disorders (i.e. mood disorders, anxiety, impulse-control); substance use related disorders	Cross-sectional design; retrospective reports; limited response rate; no assessment of important confounders, e.g. NSSI, family history of suicide; self-esteem, impulsivity; negative life events and family psychopathology; urban population; adolescents who had died by suicide; skip pattern assessment of alcohol and substance use disorder
Muula et al. 2007/ Zambia	Cross-sectional, correlational study	Random sampling; mean age: NR; n= 1970	Anonymous, self-reported questionnaires: open-ended questions & psychometric scales	Socio-demographic characteristics; age; gender; depressive symptoms	Retrospective self-reporting data; cross-sectional design; questionnaires completed under supervision; no assessment of important confounders, e.g. NSSI, family history of suicide; self-esteem, impulsivity, etc.
Peltzer & Pengpid 2015/Pacific islands, Oceania	Cross-sectional, correlational study	Two-stage cluster random sampling; mean age: NR; n= 6540	Anonymous, self-reported questionnaires: open-ended & likert questions	Age; gender; psychological distress; bullying victimization; involvement in physical fight	No causality assessment; no clarification of the term “drug use”; no assessment of important confounders, e.g. NSSI, family history of suicide; self-esteem, etc.
Pena et al. 2008/USA	Cross-sectional & comparative study	Latino cluster from a national representative sample; mean age 15.3-16.0	Anonymous, self-reported questionnaires: open-ended questions & psychometric scales	Demographic data (age of drug use initiation, gender); immigrant generation status (country of origin; generation sequence) ; depressive symptoms; family structure; parental education & family socio-economic status;	No causality assessment; convenience sample; no assessment of important confounders, such as social support, traumatic experiences or life stressors, NSSI, family history of suicide, self-esteem, impulsivity; use of dichotomized substance use variables

		years; n= 3135			
Randall et al. 2014/ West Africa (Benin)	Cross-sectional study	Two stage cluster sample; mean age: NR; n= 2690	Anonymous, self-reported questionnaires: : yes/no questions & psychometric scales	Demographic data; gender; age; grade;, anxiety symptoms, loneliness, bullying victimization; number of close friends, food insecurity, parental support, truancy.	Cross-sectional design thus no conclusions on causality; self-reported data, responses in a socially desirable manner; considerable number of students did not answer the question regarding alcohol use, illicit drug use and bullying, thus were excluded from analysis; no assessment of important confounders, e.g. NSSI, family history of suicide; self-esteem, impulsivity
Roberts et al. 2010/USA	Longitudinal study	Stratified random sample; mean age: NR; n=4175 & 3134 (follow-up)	Diagnostic interviews & self-reported computerized questionnaires: yes/no questions & psychometric scales	Age, gender; ethnicity; self-esteem; family income; family structure; personal & family suicide attempt history; psychiatric disorder history; social stressors; personal & social resources/ coping strategies; traumatic events.	No triangulation of suicide data by the parents of the participants; no assessment of the frequency or severity of substance use; assessment of the use of the main illicit drugs (cannabis, amphetamines, hallucinogenic, crack, cocaine, heroin, ecstasy) through a single variable (lifetime use; yes/no), thus findings do not differentiate among each substance.
Sharma et al. 2015/Peru	Cross-sectional, comparative study	Purposively selected districts & stratified random sampling; median age: 15 years; n=916	Anonymous, self-reported questionnaires: yes/no questions & psychometric scales	Demographic data; exposure to fights; being insulted/attacked; parental understanding & quality of relationship with them; parental homework checking; school absenteeism; perceived body image; self-rate health status; perceived happiness. Sexual intercourse initiation, sexual abuse; condom use; psychological counselling sexual maltreatment; anxiety symptoms; depressive symptoms; withdrawn, aggressive & delinquent behavior; IQ	No assumptions on causality due to the cross-sectional design; no assessment of important confounders, e.g. NSSI, family history of suicide; self-esteem, impulsivity, life stressors, social support
Swahn et al. 2012/France & USA	Comparative, cross-sectional & study	Stratified, random samping; nean age:	Anonymous, self-reported questionnaires: dichotomous questions	Age; gender; current substance use; depressive symptoms; grade; involvement in fights; sexual assault; violence victimization	Self-reported data; no assumptions on causality due to the cross-sectional design; no assessment of important confounders in the analysis, i.e., history of substance use/ psychopathology, life stressors,

		NR; n_{YRBS}=15,136 & n_{ESPAD}=13,187			social support; parental characteristics & family structure, NSSI, self-esteem; low response rate
Wong et al. 2008/ Hong Kong	Longitudinal study	Purposeful sample; age 12-18 years; n=1099	Anonymous, self-reported questionnaires: yes/no questions & psychometric scales	Demographic data (gender, age, parental education); anxiety & depressive symptoms; environmental stressors; family relationships; exposure suicide attempt committed by others	Self-reported data; important confounders, such as family history of psychopathology, impulsivity or sexual abuse, NSSI, self-esteem, family history of suicide were not assessed; culturally specific results
Wong et al. 2013/ USA	Cross sectional survey	Nationally representative sample; High school students; n=73,183	Anonymous, self-reported questionnaire: yes/no questions & demographic data	Socio-demographic data (age, gender, ethnicity); interpersonal violence (sexual, fights); unsafe feelings, depressive symptoms; dieting habits; purging behavior; sexual behavior	Cross-sectional design; lack of assessment of other important confounders, i.e. psychopathology, childhood traumatic experiences, self-esteem, NSSI; variability or time trends of substance use during last decade not investigated

Table 2. Main results of the included studies*

Authors & Date (study acronym)	Aim	Study population	Main Results
Afifi et al. 2007 (National Longitudinal Survey of Children and Youth Study)	Exploration of the association between health risk behaviors, including substance use, and suicidal ideation and attempts in adolescents in the year prior to the study.	Community-based students (age range: 12-13 years); n= 2090; RR: NR.	Males: Smoking tobacco was associated with SI [OR (95% CI)]: 3.88(1.07-14.09), p<0.001, controlled for confounders Smoking tobacco was associated with SA[OR (95% CI)]: 6.08(1.25-29.09), p<0.001 Marijuana or hash was associated with SA[OR(95%CI)]: 7.54(1.41-40.36), p<0.01 Females: Smoking tobacco, marijuana or hash & alcohol use, glue or solvents use were all found to be strongly associated with both SI&SA in the unadjusted model, while none of these associations was noted had in the adjusted model.
Arenliu et al. 2014 (2011 European School Project on Alcohol and Drugs)	Examination of the association between substance use (tobacco, alcohol, cannabis; sedatives, amphetamine, hallucinogens, ecstasy) with self-reported suicidal behavior in Kosovar adolescents.	Community-based adolescents (age range: 18 years); n= 4709; RR: NR.	Males: Daily tobacco use was associated with SI[OR (95% CI)]: 2.88(1.39-5.66), p<0.05 Current alcohol use was associated with SI[OR (95% CI)]: 2.36(1.43-3.82), p<0.001 Current cannabis use was associated with SI[OR (95% CI)]: 3.51(1.51-7.91), p<0.05 Current amphetamine, hallucinogens, ecstasy use was associated with SI[OR (95% CI)]: 4.78(2.15-10.18), p<0.001 Current alcohol use was associated with SA[OR (95% CI)]: 2.90(1.51-5.45), p<0.05 Current Cannabis use was associated with SA[OR (95% CI)]: 6.17(2.53-15.54), p<0.001 Current Sedatives use was associated with SA[OR (95% CI)]: 2.82(0.95-7.40), p<0.01 Females: Current alcohol us was associated with SI[OR (95% CI)]: 3.24(1.93-5.28), p<0.0001 Current cannabis use was associated with SI[OR (95% CI)]: 6.79(1.67-25.39), p<0.05 Current sedatives use was associated with SI[OR (95% CI)]: 9.39(5.28-16.63), p<0.0001 Current alcohol use was associated with SA[OR (95% CI)]: 2.34(0.92-5.15), p<0.05 Current cannabis use was associated with SA[OR (95% CI)]: 16.05(3.69- 60.98), p<0.001 Current sedatives use was associated with SA[OR (95% CI)]: 4.69(1.81-10.64), p<0.001
Chin & Choi 2015 (2011 Korea Youth Risk Behavior Web-based Survey)	Exploration of the factors associated with suicide attempts in male and female Korean adolescents.	Community-based adolescents ; 12-18 years n= 74,936 RR:95,5%	Males Tobacco smoking was associated with SA[OR(95%CI)]:1.30(95%CI: NR), p<0.05 Substance use was associated with SA[OR(95%CI)]: 1.94(95%CI: NR), p<0.05 Females Tobacco smoking was associated with SA[OR(95%CI)]:1.78 (95%CI: NR), p<0.05 Substance use was associated with SA[OR(95%CI)]: 2.04(95%CI: NR), p<0.05
Cho et al. 2007 (Reconnecting	Exploration of the association between	Community-based adolescents 9-11	<u>Males</u> Current tobacco smoking was associated with SI[OR(95%CI)]: 1.36(1.1-1.7), p<0.01, controlled for alcohol & illicit

Youth Substance Use Prevention Program)	onset of substance use and suicide behavior indicators.	grade; n= 1252: 885 (RR 47%) & 367 (RR: 65%.	substance use Females Current alcohol use was associated with SI[OR(95%CI)]: 1.82(1.3-2.4), p<0.001-controlled for alcohol & illicit substance use Current alcohol use was associated with SA[(95%CI)]: 1.73(1.4-2.1), p<0.001 Current hard drug use was associated with SI[OR(95%CI)]: 2.34(1.0-5.4), p<0.05 Current hard drug use was associated with SA[OR(95%CI)]: 5.03(1.9-13.5), p<0.01
Epstein & Spirito 2010 (2005 Youth Risk Behavior Surveillance)		Community-based adolescents grades 9 to12; n=13,917; RR: 67%	Males Current tobacco use was associated with SI[OR(95% CI)]: 1.69(1.26-2.27), p<0.05 Lifetime sniffing glue use was associated with SI[OR(95%CI)]: 2.60(1.89-3.56), p<0.05 Lifetime injection of substances was associated with SI[OR(95%CI)]: 2.67(1.89-3.56), p<0.05 Sniffing glue was associated with SP[OR(95%CI)]:2.57(1.94-3.42), p<0.05 Lifetime substance injection was associated with SP[OR(95%CI)]:3.66(1.86-7.21), p<0.05 Having a first drink before the age of 13 was associated with SA[OR(95%CI)]:1.77(1.27-2.45), p<0.05 Lifetime glue sniffing was associated with SA[OR(95%CI)]:3.42(2.43-4.81), p<0.05 Lifetime substance injection was associated with SA[OR(95%CI)]:3.97(1.88-8.39), p<0.05 Females Current tobacco smoking was associated with SI[OR (95% CI)]: 2.01(1.53-2.64), p<0.05 Daily tobacco smoking was associated with SI[OR (95%CI)]: 1.45(1.04-2.04), p<0.05 First drink before 13 years was associated with SI[OR(95% CI)]:1.48(1.22-1.79),p<0.05 Sniffing glue was associated with SI[OR(95%CI)]:2.49(1.86-3.34), p<0.05 Lifetime substance injection was associated with SI[OR(95%CI)]: 2.47(1.26-4.85), p<0.05 Tobacco smoking before the age of 13 was associated with SA[OR(95%CI)]: 1.47(1.03-2.11), p<0.05 Current tobacco smoking was associated with SA[OR(95%CI)]: 2.06(1.58-2.69), p<0.05 First drink of alcohol before the age of 13 was associated with SA[OR(95%CI)]:1.49(1.19-1.86), p<0.05 Lifetime sniffed glue was associated with SA[OR(95%CI)]: 2.45(1.77-3.39), p<0.05 Lifetime substance injection was associated with SA[OR(95%CI)]: 4.75(2.07- 10.9), p<0.05 Current tobacco smoking was associated with SP[OR(95%CI)]: 2.05(1.73-2.44), p<0.05 Having the first drink of alcohol before the age of 13 was associated with SP[OR(95%CI)]:1.59(1.32-1.92), p<0.05 Lifetime glue sniffing was associated with SP[OR(95%CI)]:2.36(1.78-3.12), p<0.05 Lifetime substance injection was associated with SA[OR(95%CI)]:2.41(1.36-4.28), p<0.05
Fleming et al. 2007 (New Zealand Adolescent Health Survey)	Exploration of prevalence of suicide attempts in secondary school students in New Zealand, as well as	Community-based secondary school students 9-13 years; n= 9570; RR:NR	Mixed gender samples: Alcohol use was was associated with SA[OR (95% CI)]: 2.17(1.45-3.22), p=0.0002

	association with individual, family, school and social characteristics, including substance use.		
Kim et al. 2011 (2000 National Household Survey on Drug Abuse)	Exploration of the association between ecstasy use and both suicide ideation and attempts.	Community-based adolescents 12-17 years; n= 19,301; RR: NR	Mixed gender samples: Illicit substance use, except ecstasy, was associated with SI[OR (95% CI)]: 1.9(1.6- 2.2), p<0.001 & SA[OR(95% CI)]: 3.5(2.8- 4.3), p<0.001, Ecstasy use was associated with SI[OR(95% CI)]: 1.5(1.0- 2.1), p<0.05 & SA[OR(95% CI)]: 5.5(3.8- 8.1), p<0.001
Kokkevi et al. 2011 (European School Survey Project on Alcohol and Other Drugs 1984 & 2007-ESPAD)	Assessment of the psychosocial factors, including substance use, associated with the increased frequency of self-reported suicide attempts in adolescents in Greece in 2007 compared to 1984.	Community- based adolescents 14-18 years; n=9873(2007)& 10507 (1984); RR: 98.2%(2007) & 99% (1987)	1984 mixed gender samples: Daily tobacco use was associated with SA[OR (95% CI)]: 2.32(1.90-2.84), p<0.001 Frequent alcohol use was associated with SA[OR (95% CI)]: 1.90(1.37-2.65), p<0.001 Lifetime use of any illicit substance was associated with SA[OR (95% CI)]: 2.61(1.92-3.53), p<0.001 2007 mixed gender samples: Daily tobacco use was associated with SA[OR (95% CI)]: 1.72(1.48-2.00), p<0.001 Frequent alcohol use was associated with SA[OR (95% CI)]: 1.40(1.06-1.85), p<0.001 Lifetime use of any illicit substance was associated with SA[OR (95% CI)]: 1.43(1.15-1.78), p<0.001
Kokkevi et al. 2012a (European School Survey Project on Alcohol and Other Drugs 2007-ESPAD)	Exploration of the association between multiple substance use and self-reported suicidal behavior in adolescents in 16 European countries.	Community-based adolescents 15-16 years; n= 42,635; RR: 94.6%	Mixed gender samples: Daily tobacco use was associated with SA[OR (95% CI)]: 2.02(1.84-2.21), p<0.001 Frequent alcohol use was associated with SA[OR (95% CI)]: 1.47(1.32-1.63), p<0.001 Lifetime use of any illicit substance, except cannabis, was associated with SA[OR (95% CI)]: 2.41(2.14-2.70), p<0.001 Cannabis use was associated with SA[OR (95% CI)]: 1.37(1.18-1.58), p<0.001 Tranquilizers use (without prescription) was associated with SA[OR (95% CI)]: 3.34(3.00-3.71), p<0.001
Kokkevi et al. 2012b (European School Survey Project on Alcohol and Other Drugs 2007-ESPAD study)	Exploration of the association between legal/illegal substance use and suicidal behavior in 17 European countries.	Community-based adolescents 15-16 years; n=45806; RR: NR	Mixed gender samples: Daily tobacco use was associated with SA[OR (95% CI)]: 2.14(1.97-2.32), p<0.001 Frequent alcohol use was associated with SA[OR (95% CI)]: 1.49(1.34-1.66), p<0.001 Lifetime use of any illicit substance was associated with SA: OR[(95% CI)]: 2.22(2.02-2.43), p<0.001 Daily tobacco use was associated with frequent SI[OR (95% CI)]: 2.21(1.98-2.46), p<0.001 Frequent alcohol use was associated with SI[OR(95% CI)]: 1.43(1.25-1.62), p<0.001 Lifetime use of any illicit substance was associated with frequent SI[OR(95% CI)]: 1.73(1.55-1.94), p<0.001

Miller et al. 2011 (Mexican Adolescent Mental Health Survey 2005)	Exploration of the association between measures of suicidal behavior and substance abuse in adolescents.	Community-based adolescents 12-17 years old; n=3005; R.R:71%	Mixed gender samples: Alcohol use was associated with SI[OR(95%CI)]: 1.59(1.20–2.09), p<0.01 Alcohol use was associated with SI[OR(95%CI)]: 1.50(1.12–2.01), p<0.01, controlled for psychiatric disorders Alcohol use dependence was associated with SI[OR(95%CI)]: 4.91(1.99–12.15), p<0.01, controlled for psychiatric disorders Alcohol abuse dependence was associated with SI[OR(95%CI)]: 3.74(1.51–9.25), p<0.01, controlled for psychiatric& substance use related& tobacco use related disorder Alcohol use was associated with SI with plan [OR(95%CI)]: 2.62(1.61–4.25), p<0.01 Alcohol use was associated with SI with plan[OR(95%CI)]: 2.43(1.54–3.84), p<0.01, controlled for psychiatric disorder Alcohol use was associated with SI with plan[OR(95%CI)]: 1.85(1.18–2.90), p<0.01, controlled for psychiatric& substance use related& tobacco use related disorder Alcohol use was associated with SA[OR(95%CI)]: 2.43(1.51–3.90), p<0.05 Alcohol use was associated with SA[OR(95%CI)]: 2.27(1.39–3.73), p<0.05,controlled for psychiatric disorders Alcohol use was associated with SA[OR(95%CI)]: 1.66(1.01–2.73), p<0.05, controlled for psychiatric& substance use related& tobacco use related disorder Alcohol abuse dependence was associated with SA[OR(95%CI)]: 5.58(1.05–28.75), p<0.05 Illicit drug use/dependence was associated with SI[OR(95%CI)]: 3.73(1.09–12.79), p<0.05 Illicit drug use/dependence was associated with SI with plan[OR(95%CI)]: 7.14(1.84–27.69, p<0.01 Illicit drug use/dependence was associated with SI with plan[OR(95%CI)]: 5.52 (1.41–21.55), p<0.05, controlled for psychiatric disorder Illicit drug use/dependence was associated with SI with plan[OR(95%CI)]: 3.32 (1.05-10.48), p<0.0, controlled for psychiatric& substance use related& tobacco use related disorder Tobacco use was associated with SI[OR(95%CI)]: 2.39(1.82–3.14), p<0.01 Tobacco use was associated with SI[OR(95%CI)]: 2.27(1.74–2.96), p<0.01, controlled for psychiatric disorder Tobacco use was associated with SI[OR(95%CI)]: 2.16(1.66–2.81), p<0.01, controlled for psychiatric& substance use related& tobacco use related disorder Tobacco use dependence was associated with SI[OR(95%CI)]: 6.21(1.28–30.20), p<0.05 Tobacco use dependence was associated with SI[OR(95%CI)]: 4.93(1.04–23.35), p<0.05, controlled for psychiatric disorders Tobacco use dependence was associated with SI[OR(95%CI)]: 4.79(1.05-21.85), p<0.05, controlled for psychiatric& substance use related& tobacco use related disorder Tobacco use was associated with SI with plan[OR(95%CI)]: 2.78(1.61–4.81), p<0.01 Tobacco use was associated with SI with plan[OR(95%CI)]: 2.60(1.49–4.53), p<0.01 , controlled for psychiatric

			disorder Tobacco use as was associated with SI with plan[OR(95%CI)]: 2.20(1.25–3.87), p<0.05, controlled for psychiatric& substance use related& tobacco use related disorder Tobacco use was associated with SA[OR(95%CI)]: 6.67(2.72–16.35), p<0.01 Tobacco use was associated with SA[OR(95%CI)]: 5.66(2.28–14.09), p<0.01, controlled for psychiatric disorders Tobacco use was associated with SA[OR(95%CI)]: 5.74(2.45–13.43), p<0.01, controlled for psychiatric& substance use related& tobacco use related disorder Tobacco abuse was associated with SA[OR(95%CI)] 15.53(3.43–70.38), p<0.01 Tobacco use dependence was associated with SA[OR(95%CI)]: 13.00(3.12–54.25), p<0.01, controlled for psychiatric disorders Tobacco use dependence was associated with SA[OR(95%CI)]: 16.42(2.74-98.41), p<0.01, controlled for psychiatric& substance use related& tobacco use related disorder
Muula et al. 2007 (2004 Zambia Global School-Based Health Survey)	Exploration of the prevalence of suicidal ideation, as well as related factors in Zambian schoolchildren	Community-based adolescents 7-10 grade; n=1970; RR:75%	Mixed gender samples: Daily use of alcohol was associated with SI[OR(95% CI)]:1.28(1.27-1.29), p<0.01 Lifetime use of marijuana was associated with SI[OR(95% CI)]: 1.18(1.17-1.19), p<0.01
Peltzer & Pengpid 2015 (Global School-Based Health Survey)	Exploration of the association between early initiation of substance use and suicidal behavior.	Community-based schoolchildren 13-16 years; n= 6540; RR=72%-85%	Males: Tobacco smoking initiation in pre-adolescence was associated with SA[OR(95% CI)]:1.04(0.56-1.94),p<0.05 Alcohol use initiation in pre-adolescence was associated with SI[OR(95% CI)]: 3.37(2.16–5.27), p<0.001 Alcohol use initiation in pre-adolescence was associated with SA[OR(95% CI)]: 3.94(2.46–6.32), p<0.001 Alcohol use initiation after pre-adolescence was associated with SI[OR(95% CI)]: 1.88(1.14–3.10), p<0.05 Substance use initiation in pre-adolescence was associated with SI[OR(95% CI)]: 2.55(1.70–3.84), p<0.001 Substance use initiation in pre-adolescence was associated with SA[OR(95% CI)]: 2.39(1.21–4.74), p<0.05 Substance use initiation after pre-adolescence was associated with SI[OR(95% CI)]: 1.95(1.32–2.88), p<0.001 Substance use initiation after pre-adolescence was associated with SA[OR(95% CI)]: 2.07(1.37–3.13), p<0.01 Females: Tobacco smoking initiation in pre-adolescence was associated with SA[OR(95% CI)]:2.64(1.67-4.16),p<0.001 Tobacco smoking initiation in pre-adolescence was associated with SI[OR(95% CI)]:2.79(1.64-4.76),p<0.001 Alcohol use initiation in pre-adolescence was associated with SI[OR(95% CI)]: 3.12(1.95–4.90), p<0.001 Alcohol use initiation in pre-adolescence was associated with SA[OR(95% CI)]: 5.76(3.84–8.64), p<0.001 Alcohol use initiation after pre-adolescence was associated with SI[OR(95% CI)]: 2.12(1.34–3.34), p<0.01 Alcohol use initiation after pre-adolescence was associated with SA[OR(95% CI)]: 2.31(1.51–3.52), p<0.001 Substance use initiation in pre-adolescence was associated with SI[OR(95% CI)]: 1.90(1.09–3.70), p<0.05 Substance use initiation in pre-adolescence was associated with SA[OR(95% CI)]: 2.87(1.63–5.07), p<0.001

			Substance use initiation after pre-adolescence was associated with SI[OR(95% CI)]: 1.82(1.04–3.18), p<0.05 Substance use initiation after pre-adolescence was associated with SA[OR(95% CI)]: 1.84(1.05–3.22), p<0.05
Pena et al. 2008 (National Longitudinal Study of Adolescent Health)	Exploration of the association between immigrant generation status and suicidal behavior, as well as the mediating effect substance use and depressive symptoms in this association.	Community-based 7th to 12th grade Latino students; n= 3135; RR: NM	Mixed gender samples: Repeated other than marijuana substance use was associated with SA [Beta= 0.49 (p<0.001)]. Associations between SA and i) problematic alcohol use [r=0.28 (p<0.001)], and ii) repeated marijuana use [r=0.36 (p<0.001)] was reported, however strongly accounted for by strong associations with repeated other drug use [0.52 (p<0.001) and 0.71 (p<0.001)] and depressive symptoms [0.32 (p<0.001) and 0.28 (p< 0.001)].
Randal et al. 2014 (2009 Republic of Benin GSHS study)	Investigation of the prevalence of suicidal behavior, as well as related factors.	Community-based adolescents; junior and senior high school students 12-16 years; n= 2690; RR: 90%	Mixed gender samples: Illicit substance use was associated with SI[OR(95%CI)]:3.06(1.12–8.34), p=0.031 Illicit substance use was associated with SI with planning[OR(95%CI)]:1.69(1.05– 2.72), p=0.032 Illicit substance use was associated with a second SA[OR(95%CI)]: 5.73(2.99-11.0), p < 0.001 Alcohol use was associated with SI with planning [OR(95%CI)]:1.52(1.02–2.27), p=0.043
Roberts et al. 2010 (Teen Health 2000 study)	Exploration of the incidence of suicide attempts in youths, as well as associated risk and protective factors.	Community-based adolescents 11-17 years; n= 4.175 & 3134 (follow up); RR: 66%	Mixed gender samples: Marijuana use was associated with SA[OR(95% CI)]: 4.81(1.82-12.66), p<0.05
Sharma et al. 2015 (2010 Peruvian Student Health Survey & Global School-based Student Health Survey)	Exploration of the prevalence of suicide ideation & attempts, as well as related factors, including substance use.	Community-based secondary school students 15-18 years; n= 916; RR: 93.37%	Mixed gender samples: Tobacco smoking was associated with SI[OR(95% CI)]: 1.70(1.08-2.66), p<0.05 Alcohol use was associated with SI[OR(95% CI)]: 1.65(1.15-2.38), p<0.01 Alcohol use was associated with SA[OR(95% CI)]: 1.52(1.00-2.33), p<0.05 Illicit substance use was associated with SA[OR(95% CI)]: 2.91(1.51-5.61), p<0.01
Swahn et al. 2012 (2003 USA National Youth	Investigation of the association between the age of substance use initiation and suicidal	Community-based adolescents; YRBSS: grade 9-12, n= 15,136 &	YRBS (France) Mixed gender samples: Alcohol initiation<13 years was associated with SI[OR(95%CI): 1.41(1.10–1.80), p<0.05, controlled for heavy drinking, age, grade, depressive mood Tobacco smoking initiation<13 years was associated with SI[OR(95%CI)]: 1.54(1.27 -1.87), p<0.05, controlled for

Risk Bahavior Surveillance System & 2002 France European School Survey Project on Alcohol and Other Drugs)	behavior among students in France and the USA.	ESPAD: 11-19 years, n= 13,187; RR_{ESPAD}=91.0% & RR_{YRBSS}=67%	current smoking, age, grade, depressive mood Cannabis/marijuana use initiation<13 years was associated with SI[OR(95%CI)]: 1.80 (1.34–2.42), p<0.05, controlled for current cannabis use, grade, depressive mood Cannabis/marijuana use initiation>13 years as a risk factor for SI[OR(95%CI)]: 1.20 (1.00–1.45), p<0.05, controlled for current cannabis use, grade, depressive mood Alcohol initiation<13 years was associated with SA[OR(95%CI)]: 1.52 (1.17–1.97), p<0.05, controlled for heavy drinking, age, grade, depressive mood Tobacco smoking initiation<13 years as a risk factor for SA[OR(95%CI)]: 1.92 (1.55 -2.37), p<0.05, controlled for current smoking, age, grade, depressive mood Tobacco smoking initiation>13 years as a risk factor for SA[OR(95%CI)]: 1.41 (1.13 -21.77), p<0.05, controlled for current smoking, age, grade, depressive mood Cannabis/marijuana use initiation<13 years as a risk factor for SA[OR(95%CI)]: 2.90 (2.20–3.83), p<0.05, controlled for current cannabis use, grade, depressive mood Cannabis/marijuana use initiation>13 years as a risk factor for SA[OR(95%CI)]: 1.93 (1.61–2.31), p<0.05, controlled for current cannabis use, grade, depressive mood <u>Males</u> Cannabis/marijuana use initiation<13 years was associated with SI[OR(95%CI)]: 2.37(1.55–3.62), p<0.05, controlled for current cannabis use, grade, depressive mood Cannabis/marijuana use initiation<13 years was associated with SA[OR(95%CI)]: 3.46(2.22–5.38), p<0.05, controlled for current cannabis use, grade, depressive mood Cannabis/marijuana use initiation>13 years was associated with SA[OR(95%CI)]: 1.61(1.11–2.31), p<0.05, controlled for current cannabis use, grade, depressive mood <u>Females</u> Alcohol initiation<13 years was associated with SI[OR(95%CI)]: 1.40 (1.05–1.87), p<0.05, controlled for heavy drinking, age, grade, depressive mood Tobacco smoking initiation<13 years was associated with SI[OR(95%CI)]: 1.85 (1.43-2.38), p<0.05, controlled for current smoking, age, grade, depressive mood Cannabis/marijuana use initiation<13 years was associated with SI[OR(95%CI)]: 1.67-(1.09–2.55), p<0.05, controlled for current cannabis use, grade, depressive mood Alcohol initiation<13 years was associated with SA[OR(95%CI)]: 1.59 (1.18–2.15), p<0.05, controlled for heavy drinking, age, grade, depressive mood Tobacco smoking initiation<13 years was associated with SA[OR(95%CI)]: 2.28 (1.75-2.98), p<0.05, controlled for current smoking, age, grade, depressive mood Tobacco smoking initiation>13 years was associated with SA[OR(95%CI)]: 1.61 (1.23-2.11), p<0.05, controlled for current smoking, age, grade, depressive mood Cannabis/marijuana use initiation<13 years was associated with SA[OR(95%CI)]: 3.37-(2.29–4.96), p<0.05, controlled for current cannabis use, grade, depressive mood Cannabis/marijuana use initiation>13 years was associated with SA[OR(95%CI)]: 2.12-(1.71–2.63), p<0.05, controlled for current cannabis use, grade, depressive mood

YRBS (USA)

Mixed gender samples: Alcohol initiation<13 years was associated with SI[OR(95%CI)]: 1.50 (1.17–1.92), p<0.05, controlled for heavy drinking, age, grade, depressive mood

Alcohol initiation>13 years was associated with SI[OR(95%CI)]: 1.44 (1.13–1.83), p<0.05, controlled for heavy drinking, age, grade, depressive mood

Tobacco smoking initiation<13 years was associated with SI[OR(95%CI)]: 1.31 (1.04 -1.65), p<0.05, controlled for current smoking, age, grade, depressive mood

Tobacco smoking use initiation>13 years was associated with SI[OR(95%CI)]: 1.45 (1.18–1.78), p<0.05, controlled for current smoking, age, grade, depressive mood

Cannabis/marijuana use initiation>13 years was associated with SI[OR(95%CI)]: 1.40 (1.17–1.68), p<0.05, controlled for current cannabis use, grade, depressive mood

Tobacco smoking initiation<13 years was associated with SA[OR(95%CI)]: 1.53 (1.02 -2.28), p<0.05, controlled for current smoking, age, grade, depressive mood

Tobacco smoking initiation>13 years was associated with SA[OR(95%CI)]: 2.18 (1.69 -2.82), p<0.05, controlled for current smoking, age, grade, depressive mood

Cannabis/marijuana use initiation>13 years was associated with SA[OR(95%CI)]: 1.95 (1.41–2.71), p<0.05, controlled for current cannabis use, grade, depressive mood

Males

Alcohol use initiation<13 years was associated with SI[OR(95%CI)]: 1.51(1.01–2.22), p<0.05, controlled for heavy drinking, age, grade, depressive mood

Tobacco smoking initiation>13 years was associated with SA[OR(95%CI)]: 2.47 (1.19 -5.11), p<0.05, controlled for current smoking, age, grade, depressive mood

Females

Alcohol initiation<13 years was associated with SI[OR(95%CI)]: 1.56 (1.20–2.04), p<0.05, controlled for heavy drinking, age, grade, depressive mood

Alcohol initiation>13 years was associated with SI[OR(95%CI)]: 1.45 (1.02–2.07), p<0.05, controlled for heavy drinking, age, grade, depressive mood

Tobacco smoking initiation<13 years was associated with SI[OR(95%CI)]: 1.59 (1.15-2.20), p<0.05, controlled for current smoking, age, grade, depressive mood

Tobacco smoking initiation>13 years was associated with SI[OR(95%CI)]: 1.46 (1.15-1.86), p<0.05, controlled for current smoking, age, grade, depressive mood

Cannabis/marijuana use initiation<13 years was associated with SI[OR(95%CI)]: 1.58(1.02–2.46), p<0.05, controlled for current cannabis use, grade, depressive mood

Cannabis/marijuana use initiation>13 years was associated with SI[OR(95%CI)]: 1.60-(1.26–2.04), p<0.05, controlled for current cannabis use, grade, depressive mood

Tobacco smoking initiation<13 years was associated with SA[OR(95%CI)]: 1.83 (1.16-2.86), p<0.05, controlled for current smoking, age, grade, depressive mood

Tobacco smoking initiation>13 years was associated with SA[OR(95%CI)]: 2.09 (1.46-2.97), p<0.05, controlled for current smoking, age, grade, depressive mood

			Cannabis/marijuana use initiation<13 years was associated with SA[OR(95%CI)]: 2.01(1.15–3.51), p<0.05, controlled for current cannabis use, grade, depressive mood Cannabis/marijuana use initiation>13 years was associated with SA[OR(95%CI)]: 2.19(1.51–3.20), p<0.05, controlled for current cannabis use, grade, depressive mood
Wong et al. 2008	Investigation of the risk factors for repeated suicide attempts.	Community-based adolescents 15-16 years (10^{th} grade); n= 565; RR: 90.5%	Mixed gender samples: Illicit substance use was more frequent in suicide attempters compared to non-attempters (p<0.0001). Illicit substance use was independently associated with SA[OR (95% CI)]: 3.37(1.15-9.83), p<0.05, controlled for confounders, not including history of SA). SA was associated with Illicit substance use[OR(95% CI)]: 4.80(2.00-11.54), p<0.01
Wong et al. 2013 (2001-2009 Youth Risk Behavior Survey)	Exploration of the association between life time patterns of substance use and suicidal behavior in the year prior to the study.	Community-based high school students years; n= 73183; RR:	Mixed gender samples: Lifetime use of heroin was associated with SI[OR(95%CI)]: 1.9(1.5-2.3), p<0.001 Lifetime use of methamphetamine was associated with SI[OR(95%CI)]:1.9(1.7-2.1), p<0.001 Lifetime use of steroids was associated with SI[OR(95%CI)]:1.8(1.5-2.1), p<0.001)), Lifetime use of cocaine was associated with SI[OR(95%CI)]:1.7 (1.5-1.8), p<0.001 Lifetime use of inhalants was associated with SI[OR(95%CI)]: 2.0 (1.8-2.1), p<0.001 Lifetime use of hallucinogen was associated with SI[OR(95%CI)]: 1.8(1.6-2.1), p<0.001 Lifetime use of ecstasy was associated with SI[OR(95%CI)]:1.6(1.4-1.8), p<0.001 Lifetime use of alcohol was associated with SI[OR(95%CI)]:1.5(1.3-1.7), p<0.001 Lifetime use of tobacco was associated with SI[OR(95%CI)]:1.3(1.2-1.4), p<0.001 Lifetime use of marijuana was associated with SI[OR(95%CI)]:1.4(1.3–1.5), p<0.001 Lifetime use of heroin was associated with SA[OR(95%CI)]: 3.0(2.5–3.7), p<0.001 Lifetime use of methamphetamine was associated with SA[OR(95%CI)]: 2.3(2.0–2.7), p<0.001 Lifetime use of steroids was associated with SA[OR(95%CI)]: 2.5 (2.1–3.0), p<0.001 Lifetime use of cocaine was associated with SA[OR(95%CI)]: 2.3 (2.0–2.6), p<0.001 Lifetime use of inhalants was associated with SA[OR(95%CI)]: 2.2 (2.0–2.5), p<0.001 Lifetime use of hallucinogen was associated with SA[OR(95%CI)]: 2.1(1.8–2.4), p<0.001 Lifetime use of ecstasy was associated with SA[OR(95%CI)]: 1.9(1.7–2.2), p<0.001 Lifetime use of alcohol was associated with SA[OR(95%CI)]: 1.7 (1.4–2.1), p<0.001 Lifetime use of tobacco was associated with SA[OR(95%CI)]: 1.6 (1.5–1.8), p<0.001 Lifetime use of marijuana was associated with SA[OR(95%CI)]:1.6 (1.4–1.8), p<0.001 Lifetime use of heroin was associated with severe SA[OR(95%CI)]: 4.3(3.4–5.5), p<0.001 Lifetime use of methamphetamine was associated with severe SA[OR(95%CI)]: 3.2(2.6–3.9), p<0.001 Lifetime use of steroids was associated with severe SA[OR(95%CI)]: 2.7(2.1–3.5), p<0.001 Lifetime use of cocaine was associated with severe SA[OR(95%CI)]: 2.9(2.4–3.6), p<0.001 Lifetime use of inhalants was associated with severe SA[OR(95%CI)]: 2.5(2.1–2.9), p<0.001 Lifetime use of hallucinogen was associated with severe SA[OR(95%CI)]: 3.4(2.7–4.1),p<0.001

	Lifetime use of ecstasy was associated with severe SA[OR(95%CI)]: 2.9(2.4–3.6), p<0.001 Lifetime use of alcohol was associated with severe SA[OR(95%CI)]:1.4(0.99–2.0), p<0.001 Lifetime use of tobacco was associated with severe SA[OR(95%CI)]:1.9(1.5–2.3), p<0.001 Lifetime use of marijuana as a risk factor for severe SA[OR(95%CI)]:1.8(1.5–2.3), p<0.001

SI: Suicidal Ideation; SA: Suicidal Attempts; SP: Suicidal Plan; RR: Response Rate; n: number of participants; NR: Not Reported; ESPAD: European School Survey Project on Alcohol and Other Drugs; GSHS: Global School-based Student Health Survey

*Only adjusted scores, controlled for possible confounders are reported and findings from multivariate analysis.