The interplay between cannabis use and suicidal behaviours: epidemiological overview, psychopathological and clinical models

Summary

Objectives
The clinical and psychopathological relationships between substance use and suicidal behaviours are deserving growing attention. Understanding and identifying factors that may be associated with suicidal behaviours can help clinicians to early detect high-risk individuals.

Methods
We conducted a narrative review, summarising main epidemiological data from longitudinal studies, on the potential association between cannabis use and suicidal behaviours. In addition, we discuss possible psychopathological models that may explain and disentangle this clinical relationship.

Results
Individuals who use cannabis, the most common psychoactive drug apart from alcohol and nicotine, may have higher risk of suicidal behaviours. Despite the mixed findings, evidence seems to suggest that an early and heavy cannabis use may be associated with suicidal idea-tion, attempt, and completion.

Conclusions
Findings from our review show that it is likely that cannabis is associated with increased rates of suicidal behaviours. This relationship could be explained by the reciprocal influence of cannabis on severity of depression, psychotic features, and impulsivity. Cannabis may play a key role in the complex clinical pathways that link mental disorders and suicide-related behaviours. Nevertheless, various potential mechanisms and contributing factors to this association remain to be investigated.

Key words
Cannabis • Suicide • Epidemiology • Psychopathology

Introduction
According to the World Health Organization 1, suicide is a global phenomenon, representing the 17th leading cause of death in 2015. In the European Union, out of the 4.9 million deaths reported in 2014, 58,000 (1.2%) were due to intentional self-harm 2. In addition, evidence from the National Vital Statistics System show that between 1999 and 2014 age-adjusted suicide rates in the United States raised from 10.5 to 13.0 per 100,000 individuals in the general population 3. Thus, suicide represents a public health problem, and it seems correlated with different clinical, psychological, biological and environmental risk factors, although no effective predictive algorithms for clinical practice are available 4. Nevertheless, understanding and identifying factors that may be associated with suicidal behaviours could help clinicians to early detect high-risk individuals and assist them in screening for treatment 4.
In recent years, the possible relationship between substance use and suicidal behaviours has been investigated. Mood and substance use disorders are the most frequent mental disorders among suicide decedents worldwide. In addition, cannabis, following nicotine and alcohol, is the most commonly used psychoactive substance both in the United States and in Europe, with particularly high misuse rates among young people. Mixed results have been produced by studies analysing the possible detrimental effect of cannabis on health, making difficult to clarify whether, how, and to what extent cannabis is harmful. Negative effects are heterogeneous and may include a range of consequences in terms of brain development, mental disorders, use of other illicit drugs, school performance and lifetime achievement. In particular, cannabis misuse may explain a portion of the complex interplay between mental illness and suicidality. Individuals who have attempted suicide show structural and functional brain changes similar to those found in cannabis users. Moreover, high rates of cannabis use are common among individuals suffering from any mental disorders. For example, data from the NESARC study indicated that rates of cannabis use and cannabis use disorder among individuals with 12-month mental illness were 9.9 and 4.0%, respectively, as compared with 1.6 and 0.4% among individuals without any mental illness. In particular, the likelihood of having a cannabis use disorder for individuals with 12-month mental illness was over three times higher, after adjusting for sociodemographic characteristics and other substance use disorders. Potential effects of cannabis on suicidality have been analysed in different mental disorders, including major depression, anxiety, bipolar, and psychotic disorders. Consistently, toxicity reports have shown high cannabis rates amongst suicide decedents by non-overdose methods, and chronic, heavy cannabis use has been found to be associated with suicidal ideation, attempt, and completion. A relatively recent meta-analysis estimated that chronic cannabis use could predict suicidality. In particular, cannabis use was associated with any suicidal behaviours, including suicidal ideation (Odds ratio [OR] = 1.43; 95% Confidence Interval [CI]: 1.13-1.83), suicide attempts (OR = 2.23; 95% CI: 1.24-4.00), and suicide death (OR = 2.56; 95% CI: 1.25-5.27). Nevertheless, the lack of homogeneity in the measurement of cannabis exposure and, at least partially, of systematic controlling for known risk factors, temper these findings. Consistently, a systematic review of epidemiological evidence on adverse effects of cannabis use, has pointed out that it is still unclear whether a regular cannabis use may increase the risk of death, including it due to suicide. An epidemiological understanding is certainly required to clarify the nature of the clinical relationship between cannabis use and suicidal behaviours, as well as significance, consistency, and strength of this association. In particular, epidemiological research has attempted to establish whether a causal relationship may be postulated, clarifying the role of associated psychopathology, common among both cannabis users and suicidal individuals. In addition, it should be clarified whether certain mediators or moderators (the so-called third factors) might better explain the association between cannabis use and suicidal behaviours. These clinical, environmental, genetic factors may have an independent effect on both behaviours, thus confounding and influencing the association.

In this paper, we provide a narrative overview on the potential association between cannabis use and suicidal behaviours. In particular, we review findings of main longitudinal studies published in this field, discussing possible psychopathological models that may explain and disentangle this clinical relationship.

Methods

We conducted a narrative review including main population-based longitudinal studies. Studies had to analyse the direction of the association between cannabis use and any suicidal behaviours (suicidal ideation, attempts, completion), as well as the possible interplay of this relationship on individual psychopathological characteristics. We excluded studies selecting only special populations, such as individuals with mental disorders or those with substance use disorders. We searched on PubMed for articles written in English and indexed during the last 10 years (ranging from January 2008 to May 2018). Our search strategy included the following terms: ‘Cannabis’ or ‘Marijuana’ and ‘Suicide’ or ‘Suicidal’ and ‘Longitudinal’ or ‘Cohort’ or ‘Prospective’.

Results

Our search strategy identified a preliminary pool of 80 studies. Among these, seven longitudinal studies, analysing the association between cannabis use and different suicidal behaviours, met our inclusion criteria. We found that most of studies reported a significant association between cannabis use and subsequent suicidal behaviours. An integrative analysis of participant-level data from three large, long-running, longitudinal studies conducted in Australia and New Zealand, tested the association between the maximum frequency of cannabis use before the age 17 and various young adult psychosocial sequelae, including suicide attempts. After adjustment for confounders, daily cannabis users during adolescence had an increased odds of suicide attempts (adjusted OR = 6.83; 95% CI: 2.04 to 22.90), along with
other adverse outcomes, including reduction in school proficiency and risk of cannabis dependence or other illicit drugs use. Moreover, data from the Young in Norway longitudinal study 20, a population-based sample of 2,033 individuals followed up over a 13-year period, from their early teens to their late twenties, showed that exposure to cannabis by itself, though not leading to depression, was associated with later suicidal thoughts and attempts. Consistently, the Mexican Adolescent Mental Health Survey 21, estimating the prospective associations between substance use and incident suicide-related behaviours, showed that an early and a high frequency of cannabis use were associated with both suicide ideation and attempt. In addition, data gathered over the course of the Christchurch Health and Development Study, based on 938 individuals born in an urban region of New Zealand, estimated that using cannabis several times a week led to suicidal ideation in susceptible males, though, suicidal ideation did not lead to cannabis use in either males or females 22. Gender differences were found also from waves 1 and 2 of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) 23 based on 31,549 participants. This study showed that daily cannabis use was associated with an increased incidence of suicidality among men (adjusted OR = 4.28; 95% CI: 1.32 to 13.82), but not among women (adjusted OR = 0.75; 95% CI: 0.28-2.05). On the other hand, suicide ideation or attempts were associated with subsequent cannabis use among women (adjusted OR = 2.34; 95% CI: 1.42 to 3.87) but not among men (adjusted OR = 1.10; 95% CI: 0.57 to 2.15).

Other studies did not show any relationship between cannabis use and suicidal behaviours. The prospective cohort of the Collaborative Study of the Genetics of Alcoholism (COGA) 24, based on 3,277 individuals, reported that an early cannabis use was unrelated to the onset of suicidal ideation or suicide attempt. Similarly, no effect of suicidal ideation or suicide attempt on the onset of cannabis use was found. In addition, an important longitudinal study 25 investigating more than 50,000 men conscripted for Swedish military service, found 600 cases of suicides or deaths from undetermined causes at a 33-year follow-up. Findings showed that, despite a crude effect of cannabis use on risk of suicide was found (crude OR = 1.62; 95% CI: 1.28 to 2.07), this association was not confirmed after adjustment for relevant confounders (adjusted OR = 0.88; 95% CI: 0.65 to 1.20). The authors concluded that it is unlikely that cannabis use – either directly or because of mental health problems – may have a strong effect on completed suicide risk. Although there was a significant association between cannabis use and suicide, this relationship was likely to be attributable to correlated psychological and behavioural features.

Discussion

Summary and interpretation of findings

Over the years, epidemiological evidence has produced conflicting results, making it complex to identify a valid and reliable clinical model for subjects who use cannabis and have a greater risk of suicide ideation or attempt. In this narrative review, we pointed out that cannabis may be associated with increased rates of suicidal behaviours, despite mixed findings are available from different longitudinal studies. Heterogeneity of findings across studies could obviously involve methodological differences, in terms of study design, index population, follow-up duration, assessment methods. In addition, it should be considered that, in terms of toxicology, cannabis is a complex compound, with different active agents (phytocannabinoids) leading to various psychotropic effects. Delta-9-tetrahydrocannabinol (THC) explains most of the psychotropic and psychotomimetic effects of cannabis, while cannabidiol (CBD) may have anxiolytic, mood stabilizing, and antipsychotic effects 26. For this reason, future, prospective, cohort studies should benefit from specific biochemical analyses of different phytocannabinoids concentration to clearly characterize possible dose-response effects between cannabis use and adverse outcomes, including suicidality 27. Moreover, epidemiological research did not consider different methods for cannabis consumption, e.g., joints, bowls, bongs, edibles or drinks 28, despite these may potentially impact on related acute and chronic effects of cannabis, as well as on patterns of drug use 29. Thus, the lack of a sufficient amount of longitudinal studies taking into account cannabis potency and routes of administration does not allow estimating if these factors could influence the individual risk of suicide. Consistently, the possible role of cannabis legal status as an environmental factor that can prevent or shape life consequences for cannabis users should be considered 30. Country-level legalization or prohibition of cannabis represent key environmental factors that may influence outcomes of cannabis use, including those related to mental health and risk of suicide. Legislation changes in several countries may thus provide “natural” experiments on the effects of general population exposure to cannabis, giving the unique opportunity to monitor the related effects on mental health 31. Studies that attempted to analyse the relationship between country-level cannabis legalization/prohibition and rates of suicide, can be taken as an example of this approach. A relatively recent study 28 estimated the association between cannabis use and completed suicide, showing that the legalization of medical cannabis does not affect suicide rates. No association between the number of “medical cannabis” registrants (used
as a proxy measure of cannabis use) and completed suicide was found after controlling for multiple known, potential confounders. Consistently, relatively recent data from the National Vital Statistics System’s Mortality Detail Files, analysed pre- and post-legalization trends in US states where medical cannabis was legalized. After adjustment for economic conditions, state policies, and state-specific linear time-period trends, the association between legalizing medical cannabis and suicides was not statistically significant. However, suicide rates decreased after medical cannabis legalization as compared with states that did not legalize it. In particular, although estimates for women were less precise, legalization was associated with a significant suicide rate reduction among men aged 20 to 29 years and those aged 30 to 39 years, respectively.

**Psychopathological implications**

Despite epidemiological research produced mixed results and the lack of sufficient evidence to support the hypothesis of an independent role of cannabis on suicide risk, it is important to identify psychopathological models that may at least partially explain the perceived association found in crude models. Subjects misusing cannabis may have an increased risk of psychopathological conditions, possibly leading to a higher risk of suicidal behaviours (suicidal ideation, suicide attempt, completed suicide). On the other hand, cannabis use may be the consequence of pre-existing clinical conditions, independently correlated with increased suicidality. Cannabis, along with alcohol and other substances, may represent one of the facilitators of the clinical progression from non-structured suicidal thoughts to emergent suicide ideation and attempts. Recent findings actually support the hypothesis that cannabis users are vulnerable to perceived burdensomeness and thwarted belongingness, preliminarily confirming that difficulties in interpersonal functioning may serve as potential pathways through which daily cannabis use may lead to greater suicide risk.

From a clinical perspective, it should be considered that different psychopathological links may explain the interplay between cannabis use and suicidal behaviours (Fig. 1).

First, subjects experiencing depressive features, particularly those with pre-existing dysthymic traits or experiencing hopelessness, may use cannabis to relieve symptoms. This perspective is certainly consistent with the self-medication hypothesis, postulating that

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**FIGURE 1. Relationship between cannabis use and suicidal behaviours: psychopathological models.**

The association between cannabis use and suicidal behaviours may be explained by impairment on depressive symptoms, psychotic features, and impulsivity (continuous lines), which may have bidirectional links with cannabis use. In addition, personality traits (dotted lines) may independently cause both cannabis use and suicidal behaviours.
individuals may use illicit substances in order to relieve symptoms such as affective dysregulation, apathy, and anhedonia. According to this model, cannabis use would occur in a context of self-regulation vulnerability and individual difficulties in controlling subjective emotions, affects, relationships, and self-care. Moreover, a relationship between cannabis use and suicidal behaviours has been highlighted in subjects with additional risk factors, including stressful life events, interpersonal problems, poor social support, lonely lives, and feelings of hopelessness. This can represent the first step of a vicious circle in which cannabis use might impair, regardless of temporary improvement, depressive symptoms, increasing the degree of anhedonia and apathy. It has been reported that subjects with lifetime depression, under the influence of cannabis, more often experience sadness, anxiety and paranoia, being less likely to report happiness or euphoria. Consistently, negative symptoms are considered key features of depression in cannabis users, characterizing the so-called “amotivational syndrome”, which combines affective flattening and loss of emotional reactivity.

In particular, hopelessness may represent the most important clinical and psychopathological mediator of the complex interplay between depression, suicide risk and cannabis use. Nevertheless, evidence that cannabis use itself may independently trigger depressive symptoms are only partially convincing. For example, a three-year-follow-up longitudinal study, including 8,598 Swedish men and women, aged 20-64, did not show any association between cannabis use and incidence of depression/anxiety. Consistently, a recent longitudinal study showed that in mid-adolescence, anhedonia – an important psychopathological trait indicative of inability to experience pleasure and linked with suicide-related behaviors – might be correlated with subsequent increase of cannabis use, despite, conversely, cannabis use did not appear to be associated with subsequent anhedonia. On the other hand, a recent study reported that the monozygotic twin using cannabis was more likely to report both major depression and suicidal ideation, as compared with twin who used cannabis less frequently. Nevertheless, it has been argued that cannabis use is probably related to both depression and suicidal behaviours, through a constellation of mechanisms, involving genetic predisposition as well as social and environmental factors.

In particular, shared genetic influences seem to underlie the association of early-onset cannabis use with both depression and suicidality. Second, psychotic symptoms also play a role as potential mediators of the clinical association between cannabis use and suicidal behaviours. Both neurobiological models and epidemiological evidence support the role of cannabinoids as a possible risk factor for psychosis, showing that cannabis might influence, in a dose-dependent manner, the onset of schizophrenia and other psychotic disorders. A concomitant increase in the severity of positive symptoms can be expected as an acute and chronic effect of THC, inducing psychotomimetic symptoms, delusions and auditory hallucinations, which may be the core signal of suicidal risk in individuals suffering from psychotic disorders. Consistently, a relatively recent meta-analysis has shown that a continued cannabis use after the psychosis onset, may predict, along with other adverse outcomes, more severe positive symptoms as compared with individuals who discontinued cannabis use or never used it. In addition, cannabis can have an indirect effect on the overall symptoms’ severity and on the individual suicide risk, since cannabis use is one of main determinants of medication non-adherence. A third important element is the effect of cannabis on impulsivity. It is known that elevated impulsivity may facilitate the transition from suicidal thoughts to suicidal behaviours. Consistently, cannabis use is associated with changes in impulse control and hostility in daily life. Despite the unsolved issue as to whether impulsivity is a trait preceding cannabis consumption or, the other way, cannabis itself exacerbates impulsivity, reduced prefrontal volumes and differences in white matter integrity have been identified in cannabis users. This might explain the likelihood of impulsive and non-planned suicidal attempts in subjects with mental disorders misusing cannabis. Indeed, data from two community-based twin samples from the Australian Twin Registry showed that cannabis use is associated with unplanned suicide attempts, but not with planned ones, even after controlling for other substance use disorders. Finally, illicit substance use is common among subjects with personality disorders, especially antisocial and borderline ones. Recent cross-sectional data from the Norwegian Institute of Public Health Twin Study of Mental Health showed that subjects with antisocial or borderline personality disorders are more likely to use cannabis or suffering from a cannabis use disorder. In particular, it has been shown that the shared genetic risk between depression and cannabis dependence may be largely explained by genetic effects of antisocial personality disorder. Thus, the clinical relationship between cannabis use and suicidality in some personality disorders can be considered a false association, since both substance use and suicidal tendencies are likely to be direct consequences of individual traits, rather than linked through a causal or bidirectional relationship. In addition, it should be considered that individuals with personality disorders might be vulnerable to parasuicidal behaviours and manipulative/impulsive
suicidal threats and/or gestures, with low lethality and lack of medical consequences, rather than suicidal behaviours.\(^9\)\(^{60}\)\(^{61}\)

**Conclusions**

Over the years, disentangling psychopathological issues underlying the relationship between co-occurring substance use disorders and behaviours has represented a key challenge of research in psychiatry.\(^62\) Despite mixed findings deriving from main epidemiological evidence, our review shows that cannabis use may be clinically associated with an increased risk of suicide. However, the various mechanisms as well as contributing factors to this association remain to be clarified. Cannabis seems to have a role in the complex clinical pathways that link mental disorders and suicide-related behaviours. Cannabis may influence or trigger psychopathological features associated with increased suicidality. The association between cannabis use and suicidal behaviours may be due to an impairment on depressive symptoms, psychotic features, and impulsivity, which may have bidirectional links with cannabis use. In addition, personality traits and characteristics may independently cause both cannabis use and suicidal behaviours, thus determining a false association. Nevertheless, it is likely that the psychopathological relationship between cannabis use and suicidal behaviours cannot be explained by a single clinical model, even taking into account the possible role of overlapping genetic influences\(^45\). Future research should consider the possible association between increasing potency of cannabis and suicidality\(^31\), the potential anxiolytic, antidepressant, antipsychotic effects of CBD\(^26\), as well the possible influence of various routes for cannabis consumption\(^29\).

**Conflict of Interest**

The authors have no conflict of interest to declare.

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**References**


