

# Cannabis Abuse and Suicide in Non-Affective Psychosis: A Recent Literature Mini-Review

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## ABSTRACT

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## Introduction

Schizophrenia is a severe chronic psychiatric disorder characterized by delusions, hallucinations, disorganized thought and/or behavior and negative symptoms [1]. Compared to the general population, schizophrenic patients have an increased risk of suicide [2-4]. According to the WHO, suicide is the most common cause of death among patients affected by a psychotic disorder [5]. There is a close relationship between schizophrenia and suicide [6]. Bleuler defined suicidal impulse as "the most severe of schizophrenic symptoms" [5]. It has been reported that schizophrenia reduces overall life span by approximately 10 years. Suicide is the largest single contributor to this reduced life expectancy. Suicide is the most common cause of death among people with schizophrenia [5]. There is also a strong correlation between schizophrenia and substance abuse disorder (SUD), including cannabis. In fact, cannabis is the most common substance of abuse in the world, being easily available at low cost [7]. Substance use and psychosis appear to be linked by reciprocal interactions, in terms of the development, evolution, and severity of the disorders [8-10]. According to some studies, patients with schizophrenia have an increased risk of developing a substance use disorder [11]. On the other hand, substance use can represent a trigger for a psychotic episode, or a precipitating factor for an already florid psychosis [12-15].

According to the current evidence in the literature regarding cannabis use disorder (CUD) and synthetic cannabinoids (SCs), not only they seem to be a possible risk factor for the development of a psychotic disorder, but also are likely to be involved in the progression of the disease as well as determining the severity of symptoms [16-21]. Evidence also seems to suggest that the abuse of cannabis or synthetic cannabinoids may increase violent behaviors both directed towards others and themselves [22-24]. For this reason, we decided to conduct a literature search with the aim of better clarifying the existence of a possible relationship between suicide and cannabis use or abuse, as well as explaining and evaluating nature and characteristics of this correlation.

## Methods

### Data source

We searched the PubMed database from 2010 to November 2021 using the following search string: ("Suicide"[Mesh] OR suicide[tiab] OR "suicide attempt"[tiab] AND "suicidal behaviour"[tiab] OR suicidality[tiab] OR "suicidal ideation"[tiab] OR "self injurious behaviour"[tiab] OR "self-injurious behaviour"[tiab] OR "suicide idea" [tiab] OR "self harm"[tiab] OR "suicidal thought"[tiab] OR "suicidal thinking"[tiab] OR "self injur"[tiab] OR suicidality[tiab]) AND ("Schizophrenia Spectrum

and Other Psychotic Disorders"[Mesh] OR schizophrenia[tiab] OR "nonaffective psychos\*" [tiab] OR "non-affective psychosis" [tiab] OR "non affective psychosis"[tiab]) AND (Cannabis[tiab] OR "Cannabis use disorder\*" [tiab] OR Marijuana OR cannabinoid\* [tiab] OR endocannabinoid\* [tiab] OR CUD [tiab] OR "Cannabis" [Mesh] OR "Marijuana Abuse" [Mesh] OR "Endocannabinoids" [Mesh] OR "Cannabinoids" [Mesh] OR "Synthetic cannabinoid\*" [tiab]).

## Eligibility Criteria

For our mini review we focused on studies regarding patients diagnosed with schizophrenia or schizophrenic spectrum disorders or diagnosed with non-affective psychotic disorder induced by the use of SCs, who used cannabinoids and attempted suicide or had suicidal ideation. We included all studies that reported the effects of cannabis on suicide risk, including ideation or attempts. We excluded those regarding self-harm that did not have suicide as a goal. We included only reports written in English. Specifically, we included all articles that reported on the effects of cannabis in general, THC, CBD, and synthetic cannabinoids. We applied the following exclusion criteria: articles in which self-injurious acts were mentioned but without suicidal intent; articles in which patients were not diagnosed with schizophrenia or schizophrenic spectrum disorders or diagnosed with non-affective psychotic disorder induced after using SCs; articles that did not include specifically cannabinoids use but included drug abuse as a general category. Titles and abstracts were screened for inclusion by three researchers (A.C., E.C. and A.P.). A fourth investigator (V. R.) was assigned for those cases in which there was no agreement about whether the manuscript met the criteria for inclusion.

## Results

The research yielded a total of 49 articles which have been screened according to the inclusion criteria. Among these, 8 studies published between 2010 and 2021 were selected. Study designs distributed as follows: reviews (2), cohort studies (1), meta-analysis (1), cross-sectional analysis (2), systematic review (1); longitudinal studies (2); case reports (1). An Australian cross-sectional analysis ("Is cannabis a risk factor for suicide attempts in men and women with psychotic illness?"), performed on a sample of 1790 people diagnosed with schizophrenia or schizophrenia spectrum disorder, shows a positive correlation between cannabis use in adult males and suicide attempts. This study indicates a different gender susceptibility in response to cannabinoids regarding suicide risk, thus laying the foundations for further investigation to understand whether regular cannabis use has an influence on specific biological mechanisms that could explain the differences observed between men and women. However, the article concludes that there may be confounding factors and (depression, loneliness, homelessness and hallucinations) that need to be considered [25]. The Danish court

study "Associations between substance use disorders and suicide or suicide attempts in people with mental illness", performed on 35 patients, reports that cannabis is associated with an increased risk of suicide attempt in people with schizophrenia (HR: 1.11, 95% CI: 1.03-1.19).

As previously suggested, the associations between SUD and suicide attempts can be explained either by causal associations or by shared genetic and environmental vulnerabilities that predispose to both outcomes [26]. The longitudinal study "Suicidal behavior in first-episode nonaffective psychosis: Specific risk periods and stage-related factors" considers cannabis use, along with depressive symptoms, as the predominant risk factor for suicidal behavior over time. In particular, the article emphasizes the risk of cannabis use during first-episode psychosis (FEP), being this a phase characterized by a particular vulnerability to cannabis abuse, which appears to be an important risk for suicide attempts. Therefore, it would be important to assess the intervention on substance use during FEP as a valuable strategy to achieve the goal of reducing if not preventing suicidal risk [27]. The longitudinal study "Persistent cannabis use among young adults with early psychosis receiving coordinated specialty care in the United States" confirms the correlation between chronic cannabis use and increased suicidal ideation and risk. This article also underlines the importance of an intervention on the use of cannabis in the field of suicide risk prevention and quality of life [28]. In the Mendelian randomized study "Studying individual risk factors for self-harm in the UK Biobank: A polygenic scoring and Mendelian randomization study" polygenic scores (PSs) were generated to index 24 possible individual risk factors for self-harm, including suicide risk.

The results identify PSs, which appear to be predictors of self-injurious acts. Concerning lifetime cannabis use, the study shows that it actually is a predictor of risk for suicidal self-injurious acts [29]. The only selected study involving synthetic cannabinoids follows the same trend as the studies before mentioned. The cross-sectional analysis "Clinical characteristics of synthetic cannabinoid-induced psychosis in relation to schizophrenia: a single-center cross-sectional analysis of concurrently hospitalized patients" [22] specifically studying the effects of synthetic cannabinoids, states that a psychosis induced by this specific kind of drug exhibits a very high rate of suicidal ideation and acts. The two articles dealing exclusively with the CBD molecule show conflicting results. In the first study "The effects of cannabidiol (CBD) on cognition and the other symptoms in outpatients with chronic schizophrenia: a randomized placebo-controlled trial" [30], conducted by administering 600 mg/day of CBD for six weeks to schizophrenic patients stabilized with antipsychotics, no increase in suicidal risk was observed compared to the placebo-treated control group. Thus, this article found no association between CBD and increased

suicidal risk. On the other hand, the study “A Review of Human Studies Assessing Cannabidiol’s (CBD) Therapeutic Actions and Potential”<sup>14</sup>, aiming to test the efficacy and safety of CBD, proves that the impact of this substance requires further investigation. In particular, the authors emphasize the need to understand in a more detailed way the effects of CBD on suicidal ideation, which seems to be a rare but dangerous adverse event when used in combination with anticonvulsant drugs.

## Conclusion

From our review only few data have emerged regarding the correlation between cannabis use and suicide risk in patients with schizophrenia or other schizophrenia spectrum diseases, therefore we can’t draw definitive conclusions. Nonetheless these studies seem to point toward a positive correlation of cannabis use with increased suicide risk. It is not clear whether a single active component or rather a set of active metabolites is the explaining cause of the increased suicide risk, and unfortunately the data and the limited knowledge of the substance consumed by the patients included in the selected studies do not allow us to have a better understanding of the underlying phenomena. We think that greater clarification on these issues could be critical in reducing suicidal risk in patients with schizophrenia or schizophrenia spectrum disorders.

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