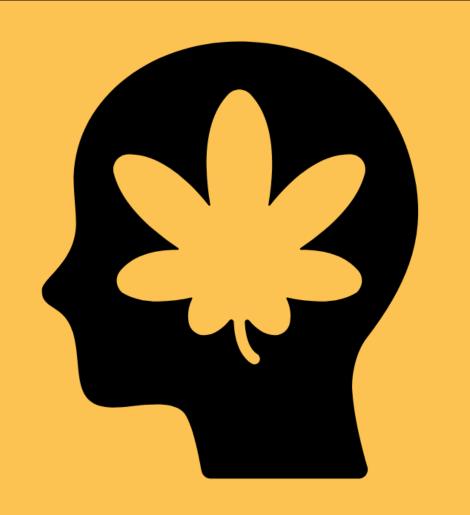


# A Systematic Review of Psychosis Risk and Cannabis Use:

## The Missing Direction

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#### Abstract

**Background:** The association between psychosis and cannabis is complex. The two phenomena are highly comorbid, but questions remain regarding the nature of this association. There are four primary theories that attempt to explain the interaction: 1) cannabis causes psychosis, 2) psychosis causes cannabis use, 3) the two phenomena function in both directions, and 4) the two phenomena share common risk factors. Most of the research in this area focuses on the first theory, while the opposite direction of effects has remained largely under investigated.

Objectives: The current study sought to systematically review the literature to understand the scope of research that has investigated psychosis risk as a predictor of cannabis use.

Methods: Adhering to PRISMA guidelines, we used the APA PsycInfo database to systematically search articles published from January 2000 to July 2022 that met the eligibility criteria of: (1) original empirical study (quantitative or mixed-methods research), and (2) addressed the psychosis—cannabis use pathway through direct tests.

<u>Results</u>: 18 studies met inclusion criteria. Overall, there was no consistent pattern of results: support was found for both directions of effects and for reciprocal effects in varying patterns across studies.

**Discussion:** Overall, the inconsistent findings indicate that the interaction between psychosis and cannabis is likely due to a complex synergy of directional effects, reciprocal effects, and/or shared etiology. Neither cannabis nor psychosis appear to be a necessary or sufficient causal factor of the other. Future efforts should focus on increasing early access to mental health treatment that includes targeted harm reduction and/or prevention efforts, rather than relying on cannabis-specific policy and/or intervention.

### Introduction

Four primary theories attempt to explain the association between cannabis and psychosis (see figure).

Each of the four theories are supported at least to some extent by existing research. However, most extant studies have focused on the unidirectional effects whereby cannabis use predicts psychosis.

The small corpus of literature that examines the opposite direction of effects has yet to be synthesized. To address this gap, this review summarizes the findings of studies that explicitly examined psychosis as a risk factor for cannabis use, whether unidirectionally or in the context of other tests that analyzed both directions of effects. The aim of this systematic review is to understand the scope of research investigating psychosis risk as a predictor of cannabis use (i.e., Theory 2 and Theory 3) to consolidate and evaluate its findings.

### Theory 1:

Cannabis use may lead to cascading biological effects that cause an increased risk for psychotic experiences

### Theory 3:

The two phenomena are bidirectional in nature

### Theory 2:

Those with psychosis may have vulnerability to cannabis use as a result of physiological factors and/or for self-medication

#### Theory 4:

Underlying common factors may increase the risk of cannabis use and psychosis

Study Citation	Cannabis use  Very Cannabis use  Psychosis risk	Psychosis risk  Cannabis use	Bidirectional
Bechtold, et al, 2016	Yes	No	Tested Not supported
Bourque et al., 2018	Yes	Yes	Yes
Buchy et al., 2015	Not tested	No	Not tested
Carey et al., 2016	Not tested	Yes	Not tested
Degenhardt et al., 2018	Yes	Yes	Yes
Ferdinand et al., 2005	Yes	Yes	Yes
Fergusson et al., 2005	Yes	No	Tested Not supported
Gage et al., 2017	Yes	Yes	Yes
Griffith-Lendering et al., 2013	Yes	Yes	Yes
Henquet et al., 2005	Yes	No	Tested Not supported
Hiemstra et al., 2018	Not tested	Mixed	Not tested
Hjorthøj et al., 2021	Not tested	Mixed	Not tested
Johnson et al., 2021	Yes	Yes	Yes
Mackie et al., 2013	No	No	Tested Not supported
Nesvåg et al., 2017	Yes	No	Tested Not supported
Pasman et al., 2018	No	Yes	Tested Not supported
Power et al., 2014	Not tested	Yes	Not tested
Verweij et al., 2017	Not tested	Yes	Not tested

### Results

#### 18 Studies Total

#### 8 Genetic Studies

The genetic studies included in this review all found support for the psychosis risk — cannabis use pathway, suggesting that genetic predisposition is a robust predictor of cannabis use.

#### 1 Twin Study

One twin study was included in this review which concurrently assessed genetic and environmental effects. Researchers found support *only* for the cannabis use — psychosis risk pathway and not the opposite.

#### 1 Cross-sectional Study

One cross-sectional observational study was included in this review. Researchers found more evidence for psychotic experiences predicting cannabis use than the opposite direction of effects.

#### 8 Longitudinal Studies

Patterns of results were inconsistent across longitudinal studies, with support for both directions of effects and reciprocal effects. The longitudinal studies included in this review specifically targeted adolescence and early adulthood, age ranges that were seemingly appropriate to investigate psychosis risk and cannabis use. Upon investigation however, no systematic findings emerged.

### Discussion

The current study systematically reviewed the literature to understand the scope of research on psychosis risk as a predictor of cannabis use. Results suggest a pattern of support for this direction of effects. However, 6 of the 18 studies did not find support for this pathway; there was no clear explanation that sufficiently rationalized the diverging patterns of results. There was evidence for the cannabis use — psychosis risk pathway (10 of the 12 studies found effects), but this does not necessarily represent the cannabis use — psychosis research at large, nor can it be concluded that this pattern of results would hold upon the inclusion of more studies.

Overall, there were no single pattern that explained which studies found significant results and which did not, nor were there obvious patterns of directional effects. This mixed pattern of results likely indicates an interplay between two or more of the four primary theories of the cannabis — psychosis association.

The mixed results found not only within this review, but also within the cannabis use — psychosis literature more broadly, strongly suggest that no one theory can consistently explain the association between psychosis and cannabis use.

It is likely that the high comorbidity of these phenomena represents a complex interaction of multiple etiologies. In fact, even amongst the studies whose primary aims were to establish either causation or bidirectionality, several studies noted that the interaction between cannabis and psychosis is very likely due to a combination of one of the four theories.