



## Review

## Cannabis use and mania symptoms: A systematic review and meta-analysis



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## ABSTRACT

**Background:** Whilst cannabis use appears to be a causal risk factor for the development of schizophrenia-related psychosis, associations with mania remain relatively unknown. This review aimed to examine the impact of cannabis use on the incidence of manic symptoms and on their occurrence in those with pre-existing bipolar disorder.

**Methods:** A systematic review of the scientific literature using the PRISMA guidelines. PsychINFO, Cochrane, Scopus, Embase and MEDLINE databases were searched for prospective studies.

**Results:** Six articles met inclusion criteria. These sampled 2391 individuals who had experienced mania symptoms. The mean length of follow up was 3.9 years.

Studies support an association between cannabis use and the exacerbation of manic symptoms in those with previously diagnosed bipolar disorder. Furthermore, a meta-analysis of two studies suggests that cannabis use is associated with an approximately 3-fold (Odds Ratio: 2.97; 95% CI: 1.80–4.90) increased risk for the new onset of manic symptoms.

**Limitations:** We were only able to identify a small number of studies of variable quality, thus our conclusions remain preliminary.

**Conclusions:** Our findings whilst tentative, suggest that cannabis use may worsen the occurrence of manic symptoms in those diagnosed with bipolar disorder, and may also act as a causal risk factor in the incidence of manic symptoms. This underscores the importance of discouraging cannabis use among youth and those with bipolar disorder to help prevent chronic psychiatric morbidity. More high quality prospective studies are required to fully elucidate how cannabis use may contribute to the development of mania over time.

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## Contents

1. Introduction . . . . .	40
2. Method . . . . .	40
2.1. Search strategy . . . . .	40
2.2. Inclusion and exclusion criteria . . . . .	40
2.3. Data extraction . . . . .	41
2.4. Quality assessment . . . . .	41
2.5. Data synthesis . . . . .	41
3. Results . . . . .	41
3.1. Description of studies . . . . .	41

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3.2.	Quality assessment of studies . . . . .	41
3.3.	Does cannabis use worsen mania symptoms in individuals with pre-existing bipolar disorder? . . . . .	43
3.4.	Does cannabis use increase the risk of onset of mania symptoms in those without pre-existing bipolar disorder? . . . . .	43
3.5.	Meta-analysis results . . . . .	44
4.	Discussion . . . . .	44
4.1.	Does cannabis use increase the occurrence of manic symptoms or mania in those with pre-existing bipolar disorder? . . . . .	44
4.2.	Does cannabis use induce mania symptoms specifically? . . . . .	45
4.3.	Potential mechanisms underlying the association between cannabis use and manic symptoms . . . . .	45
4.4.	Limitations . . . . .	45
4.5.	Implications for clinical and research practice . . . . .	46
	Role of funding source . . . . .	46
	Conflict of interest . . . . .	46
	Acknowledgements . . . . .	46
	References . . . . .	46

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## 1. Introduction

Cannabis is the most commonly used illegal substance in many countries, including the UK ([British Crime Survey, 2012](#)) and the USA ([NSDUH, 2011](#)). Cannabis use has been shown to produce transient, usually mild, psychotic and affective experiences in healthy individuals ([D'souza et al., 2004](#)). Symptoms which persist beyond, or occur independently of, intoxication effects are of greater concern ([Moore et al., 2007](#)). There is strong evidence that cannabis use contributes to the development of psychosis and results in a poorer prognosis for those with a pre-existing vulnerability to psychosis ([Arseneault et al., 2004; Van Os et al., 2002; Large et al., 2011; Smit et al., 2004](#)). What is less clear is whether cannabis use may also play a causal role in the development of manic affective symptoms and manic episodes specifically ([Van Laar et al., 2007; Gruber et al., 2012](#)). Although co-morbid cannabis use is more common in people experiencing bipolar disorder, the association between cannabis use and mania has not received the same degree of attention as that of cannabis use and schizophrenia ([Henquet et al., 2006](#)).

Bipolar disorder has the highest rate of substance use co-morbidity of any Axis I disorder ([Leweke and Koethe, 2008](#)) and a complex and somewhat reciprocal association between cannabis use and bipolar disorder has been noted ([Duffy et al., 2012; Salloum and Thase, 2000](#)). Anecdotal evidence suggests that bipolar patients may engage in 'self-medication' by using cannabis to moderate the symptoms of their illness ([Grinspoon and Bakalar, 1998](#)). Other studies indicate that cannabis use predates the advent of bipolar disorder and the reoccurrence of manic episodes ([Strakowski et al., 1998; Strakowski and Delbello, 2000](#)), which would suggest a potential causal association.

Bipolar disorder is a complex disease with extensive and diverse symptom clusters ([van Rossum et al., 2009](#)) including manic and depressive phases. In terms of cannabis use, associations with manic phases appear especially likely ([Strakowski and Delbello, 2000; Sarkar et al., 2003](#)). Manic symptoms are common in patients diagnosed with schizophrenia, and psychotic symptoms often occur in those with bipolar disorder ([Dunayevich and Keck, 2000; Henquet et al., 2006](#)). It has been suggested that mania and psychosis may share aetiological influences (e.g., cannabis use, and neuroticism) potentially underpinned by similar physiological mechanisms ([Murray et al., 2004](#)). For example, 'sensitisation' of the dopamine system may not only increase the risk of schizophrenia but also mania ([Henquet et al., 2006](#)); whether risk eventuates in psychotic or manic disorder is likely to depend on interactions between genetic vulnerability and environmental risk factors ([Murray et al., 2004](#)).

Due to the potentially overlapping aetiology between disorders, it is important to distinguish mania from co-occurring psychotic

symptoms when assessing associations between cannabis use and mania symptoms. The aim of this review is to assess the prospective associations between cannabis use and mania symptoms as distinct from psychosis symptoms. Specifically we consider:

- (1) Does cannabis use lead to increased occurrence of mania symptoms or manic episodes in individuals with pre-existing bipolar disorder?
- (2) Does cannabis use increase the risk of onset of mania symptoms in those without pre-existing bipolar disorder?

## 2. Method

### 2.1. Search strategy

We used the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) guidelines ([Moher et al., 2009](#)) as a framework for our review and reporting procedures. An extensive search of papers in the English language catalogued in PsychINFO, Cochrane, Scopus, Embase and MEDLINE data bases was conducted in June 2014. Search terms were used in three groups and included: cannabis, marijuana, delta-9-tetrahydrocannabinol, cannabinoids, cannabidiol, cannabinol, tetrahydrocannabivarin (group 1) AND bipolar disorder, manic depressive disorder, mania, hypomania, manic depression, bipolar spectrum (group 2) AND onset, trigger, induce,\* course (group 3). All MeSH terms (terms related to individual words) were also included within the search. In addition we examined the first 20 pages in Google Scholar using the terms 'cannabis AND cause AND mania'.

### 2.2. Inclusion and exclusion criteria

Studies were included if they were primary experimental, prospective, cohort, or longitudinal and if participants were diagnosed with bipolar disorder I or II (i.e., to explore prospective associations between cannabis use and mania in those with pre-existing bipolar disorder) or described as experiencing mania during the follow-up period (i.e., to explore whether cannabis use precedes the onset of mania in those without pre-existing illness). We included studies reporting on both sub-clinical mania symptoms and manic episodes (i.e., meeting criteria for a full manic episode). We selected prospective studies only so we could be more confident regarding the temporal ordering of exposure and outcome variables ([Schünemann et al., 2011](#)). Studies with participants primarily diagnosed with a psychotic disorder (e.g., schizophrenia, schizoaffective disorder) were excluded in order to help delineate potential causal associations between

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