International Platform of Registered Systematic Review and Meta-analysis Protocols

INPLASY

Cannabis Use and the Age of Onset of Bipolar Disorder

INPLASY202550049
doi: 10.37766/inplasy2025.5.0049
Received: 19 May 2025
Published: 19 May 2025

Stevens, C; Pincham, H; De Girolamo, G; Ratheesh, A; Large, M.

Corresponding author:
Matthew Large

mmclarge@gmail.com

Author Affiliation:
University of New South Wales.

ADMINISTRATIVE INFORMATION

Support - Nil.

Review Stage at time of this submission - Preliminary searches.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202550049

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 19 May 2025 and was last updated on 19 May 2025.

INTRODUCTION

Review question / Objective 1. Is cannabis use associated with an earlier age of onset of bipolar disorder?
2. Is the between-study heterogeneity in age of onset of bipolar disorder associated with cannabis use explained by depressive or manic phase, primary study mean age of onset, or indicators of severity of cannabis misuse?

Rationale It is known that cannabis use is associated with an earlier onset of schizophrenia but it is currently unclear whether this extends to bipolar disorder.

Condition being studied Bipolar disorder type I and II, which are common and severe mental disorders characterised by periods of mania and depression.

METHODS

Participant or population People of any age presenting with bipolar I/II who may or may not have indicators of cannabis use.

Intervention Independent variable is cannabis use, including lifetime use, current cannabis use and cannabis use disorder.

Comparator n/a.

Study designs to be included Cohort and case-control studies.

Eligibility criteria Inclusion criteria: Peer reviewed cohort or case-control studies with samples of patients with bipolar I/II that report age of onset according to cannabis use status. Proxies for age of onset, such as first hospitalisation, are included

if definition is consistent between cannabis and non-cannabis groups within a study.
Exclusion criteria: Studies reporting on non-affective psychosis or published in a language other than English.

Information sources Electronic databases (EMBASE, medline and psychINFO); contact with authors in cases of insufficient data.

Main outcome(s) Outcome of interest is the standardised mean difference and difference in means of the age of onset of bipolar disorder between cannabis and non-cannabis using groups.

Data management Data will be held by authors - all data used in this meta-analysis will be published as a supplementary file.

Quality assessment / Risk of bias analysis Modification of Newcastle-Ottowa scale consistent with previous literature on age of onset of schizophrenia. We will examine representativeness of the population (including measures of diagnosis of bipolar disorder and whether patients were drawn from an identified population group) and strength of reporting of independent variable (measures of cannabis use) and dependent variable (measures of age of onset of bipolar disorder).

Strategy of data synthesis A random-effects meta-analysis using CMA V4 software.

Subgroup analysis Mixed-effects meta-analysis and meta-regression for the polarity of onset (depression vs mania vs non-specified) and severity of cannabis use (e.g. cannabis use disorder). Measures of publication bias will be assessed using Egger's regression and trim-and-fill methods.

Sensitivity analysis Mixed-effects meta-analysis and meta-regression according to mean age of onset per study, overall study quality using dichotomised strength of reporting score, cohort vs case-control design and year of publication.

Country(ies) involved Australia and Italy.

Keywords bipolar disorder; mania; depression; cannabis; THC; marijuana; age of onset.

Contributions of each author

Author 1 - Carly Stevens.
Email: carly_stevens@outlook.com
Author 2 - Hannah Pincham.
Author 3 - Giovanni De Girolamo.
Author 4 - Aswin Ratheesh.
Author 5 - Matthew Large.