Marijuana Use and the Risk of Depression: A Systematic Review and Meta-Analysis

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Abstract

Given the cultural shift in medical and recreational marijuana use, we conducted a systematic review to help further understand this drug. Specifically, we asked whether marijuana use is associated with an increased risk of depression. **Methods**: The databases MEDLINE (PubMed), The Cochrane Library, CINAHL (EBSCO), PsychINFO, and Google Scholar were searched for the topics of marijuana use and depression. Cohort and case-control studies were evaluated using the Newcastle-Ottawa Quality Assessment Scale . Overall quality of evidence was determined using the GRADE methodology. The Bradford-Hill criteria were used to assess for causation.
Results: The quality of the evidence reviewed is low to very low. It does not meet Bradford-Hill criteria for causation. There is a slight positive correlation between marijuana use and depression. However, those studies included in the meta-analysis demonstrated a low overall pooled odds ratio (OR = 1.17; 95% CI = 1.06—1.29).
Conclusion: The evidence suggests a slight positive correlation between marijuana use and depression but is not sufficient to draw a conclusion. This evidence is generally of very low quality. It does not demonstrate a dose response, and is without a significant magnitude of effect.

Introduction

Marijuana use for medicinal purposes is currently legal in twenty-three states as well as the District of Columbia and is legal for recreational purposes in the states of Colorado, Washington, and Oregon. It is also the most commonly used illegal drug in the United States. Despite increasing cultural investment, its medical value and toxicities are largely unknown. It is evident that more knowledge about the drug is necessary to make an informed decision regarding its use.

In the state of Arizona, an annual petition process is in place to determine potential indications for medical marijuana. Such a review was submitted to evaluate the potential for marijuana to treat depression. During this process the reviewers found that although the evidence was insufficient to recommend marijuana as a treatment modality for depression, marijuana use may be associated with an increased risk of depression.

The purpose of this analysis is to systematically review the evidence available with respect to depression and marijuana and to understand if using marijuana is correlated with an increased risk of developing depression.

Methods

Inclusion Criteria: Randomized controlled trials, prospective cohort studies, case-control studies that addressed the key question, and were written in English. The studies had to specifically address the symptom of depression or major depressive disorder.
Exclusion Criteria: Case series or cross-sectional studies, animal studies, or did not address the key question. Studies were also excluded if they only addressed other psychological disorders including bipolar, schizoaffective, anxiety, suicidal ideation, and psychosis.
Database Search Strategy: Medline (PubMed), Cumulative Index to Nursing and Allied Health Literature (CINAHL), PsycINFO, and the Cochrane Library. The search string for Medline follows:

("Depression/etiology"[Mesh])) AND ((("Depression"[Mesh] OR "Depressive Disorder"[Mesh])) AND (("Cannabis"[Mesh] OR "Marijuana Abuse"[Mesh] OR "Marijuana Smoking"[Mesh]) OR "Tetrahydrocannabinol"[Mesh])). The other databases were searched using the keywords marijuana OR cannabis AND depression. References lists of each study found were also reviewed for additional studies.
Qualitative Analysis: Individual studies were rated as good, fair or poor based on scores achieved using a validated quality assessment tool: The Newcastle-Ottawa Scale (NOS). This allows the reviewer to assign scores based on (1) how well the study groups were selected, (2) how similar they are to each other, and (3) how exposure or outcomes were ascertained and monitored. The AMSTAR criteria (a measurement tool to assess systematic reviews) was used to evaluate systematic reviews. Once individual studies were assessed, the pooled information was evaluated using the GRADE criteria. This analytic tool allows the reviewer to assess the overall quality of the totality of evidence. The Bradford-Hill Criteria were used to assess causation.
Quantitative Analysis: Homogenous studies were pooled together for a meta-analysis. Random effects modeling was conducted to estimate an overall pooled odds ratio from individual odds ratios extrapolated from its respective paper. Heterogeneous studies were subject to qualitative analysis alone.

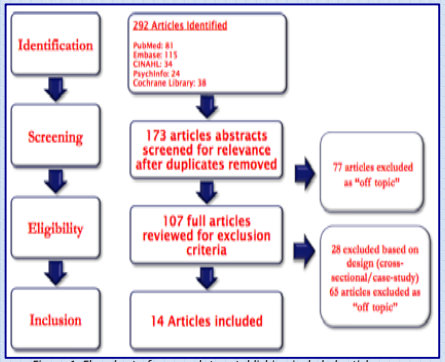

Figure 1: Flowchart of approach to establishing included articles

Results

Search Results: 292 articles reviewed. The Medline search resulted in 81 articles. The Embase search resulted in 115 articles. The CINAHL search resulted in 34 articles. The PsychINFO search resulted in 24 articles. The Cochrane Library search resulted in 38 articles.

After the articles were screened for obvious irrelevance and duplicates were removed, there were 107 articles that were fully reviewed for inclusion and exclusion criteria. From this list 28 studies were excluded due to cross-sectional or case-study design. 65 were excluded because they were off topic. Ultimately, 14 articles were consistent with the inclusion criteria.

These 14 articles included 13 observational studies and 1 systematic review. There were no randomized controlled trials.
Qualitative Analysis:
NOS results: See *Table 2*; AMSTAR Results: The single systematic review was of good quality and concluded that there was weak and insufficient evidence to correlated marijuana use with depression. The evidence did not reach Bradford-Hill Criteria for causation.

Newcastle Ottawa Scale: Quality assessment of observational studies

Author, Year	Representativeness of exposed cohort	Selection of non-exposed cohort	Method to ascertain exposure	Showed that outcome absent before study started?	Control for confounders / Comparability of cohorts	Outcome assessment	Appropriate duration follow-up	Adequate number of follow-ups	Total Score	Quality Rating
Bovasso et al., 2002	1	1	1	1	1	0	1	1	7	Good
Brook et al., 1998	1	1	0	0	1	0	1	1	5	Fair
Brook et al., 2002	1	1	0	0	1	0	1	1	5	Fair
Degenhardt et al., 2013	1	1	1	0	2	0	1	1	7	Good
Fergusson et al., 2002	1	1	1	1	2	0	1	1	8	Good
Harder et al., 2006	1	1	1	0	2	0	1	0	6	Poor
Harder et al., 2008	1	1	1	0	2	0	1	1	7	Good
Manique-Garcia et al., 2012	0	1	1	0	2	1	1	1	7	Good
[illegible]	1	1	0	1	0	0	0	1	4	Poor
Pedersen et al., 2008	1	1	0	0	2	0	1	1	6	Fair
Repetto et al., 2008	0	1	1	1	2	0	1	0	6	Fair
van Laar et al., 2007	1	1	1	1	2	0	1	1	8	Good
Windle et al., 2004	1	1	0	0	1	0	1	1	5	Fair

Figure 2: Newcastle Ottawa Scale of individual observational studies

Quantitative Analysis: 9 Studies were included in the meta-analysis (*Figure 3*). The I^2 value for these studies was 0.0% indicating homogeneity. The overall data demonstrated a pooled odds ratio (OR) of 1.17 (95% CI 1.06-1.29). This OR was not of a magnitude that was significant enough to increase the ranking of the quality of evidence.

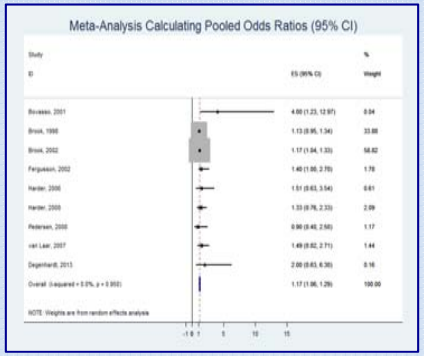

Figure 3: Forrest Plot of homogenous studies' odds ratios

Discussion and Conclusion

This study tested the hypothesis that marijuana use is positively correlated with the development of depression. The current body of evidence is insufficient to either reject or accept this hypothesis.

Of the 13 included observational studies 6 were considered good quality studies by Newcastle Ottawa Criteria. Of these 6, the Bovasso et al. study and the van Laar study both had a high risk of bias with respect to follow-up. The Bovasso study had only 15 exposed individuals from their follow-up cohort, which represented an over-sampling of an older population. The van Laar study failed to document the characteristics of those whom they followed-up with and accordingly had a high potential for bias. These 6 good quality studies demonstrated a mixed set of conclusions regarding the hypothesis that marijuana use is associated with depression. Bovasso et al. concluded there was an increased risk, OR 4.0, 95% CI: 1.23-12.97, again his follow-up sample was at high risk for bias.

The Degenhardt et al. study was compelling . This was a good study by the Newcastle Ottawa Scale criteria Degenhardt et al. concluded that marijuana dependence at age 29 and a baseline of marijuana abstinence was not association with depression at age 29, OR 2.0, 95% CI: 0.63–6.3. In this same study similar results were seen when observing patterns of depression in those with baseline weekly use who progressed to daily use and dependence, OR 1.6, 95% CI 0.47–5.2. This data suggests that those who consumed the highest levels of marijuana, when controlled for sex, non-metropolitan school location, low parental education, parental divorce/separation, concurrent alcohol or illicit drug use, baseline depression and anxiety, were not significantly different than their non-marijuana-using peers with respect to the development of depression. It is possible that if these individuals were followed for a long period of time they would develop depression, but the results at hand suggest otherwise.

Moore et al.'s systematic review was a high quality review according to AMSTAR criteria. It provided the strongest evidence on the topic. Their conclusion agreed with the data found in this study. Specifically, the evidence in the literature was generally low quality with contradictory results. They conclude there is insufficient evidence to draw a relationship between marijuana use and depression

In conclusion, the current evidence linking marijuana use to depression is of low quality and the overall pooled odds ratio is very low. Caution is urged with any claim that marijuana use causes depression.

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