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# Is Medical Marijuana the Answer for Epilepsy?

## Research Question

How effective is marijuana as a treatment of epilepsy and what are the associated negative side effects?

## Abstract

Medical marijuana, also known as medical cannabis, has become a topic of interest in the past decade, especially for the treatment of epilepsy. Epilepsy can be defined as a neurological disorder that is characterized by reoccurring and unpredictable seizures or loss of consciousness. Evidence from many studies suggests that cannabidiol (CBD), a non-psychoactive compound of cannabis, could potentially be beneficial in controlling seizures. By using reliable databases, 10 scholarly peer reviewed journal articles were found by restricting the years to be from 2010 to 2017 and searching keywords such as “marijuana AND epilepsy,” “epilepsy AND cannabis,” and “seizures AND cannabis.” The purpose of this systematic review is to discover the effectiveness of marijuana as a treatment of epilepsy and the associated negative side effects. The results found were that patients with epilepsy saw a decrease in seizures when using medical marijuana as a treatment, there are a few mild, negative side effects associated with this treatment, and that cannabis did not affect some individuals’ seizure load at all. Although factual information was found on medical cannabis as a treatment for epilepsy, more research will need to be done including secondary factors before a definite conclusion can be made.

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## Introduction

For close to 5000 years, cannabis has been used to treat medical conditions such as nausea, anorexia, pain, muscle spasticity, asthma, depression, and anxiety. Stories of cannabis's ability to reduce seizures has been around for almost 150 years, but the interest in the subject has increased dramatically within the last decade with help from legalization campaigns (Detyniecki & Hirsch, 2015). Epilepsy can be defined as a neurological disorder that is characterized by reoccurring and unpredictable seizures and loss of consciousness. Some of the first attempts of studying marijuana's effects on epilepsy date back to the nineteenth century when Reynolds and Gowers, well-known English neurologists, described anecdotal success. In 1842, William Brooke O'Shaughnessy discovered first signs of medical marijuana's beneficial use as he observed a decrease in the frequencies and intensities of infant seizures (Detyniecki & Hirsch, 2015). Since, it has been found that cannabidiol, a non-psychoactive compound of cannabis, is the factor that could potentially control seizures (Sirven). Dozens of companies in the United States, such as Healthy Oil, Dose of Nature, Natural Organic Solutions, and GW Pharma, have discovered different ways to produce and market cannabidiol such as being administered topically, through use of vaporizers, or ingested as food or oil. Roughly 30% of people with epilepsy do not have positive results with conventional treatments, so it is reasonable for them to consider cannabis. The Epilepsy Foundation provided information about studies of Epidiolex, a drug derived from cannabidiol, currently being performed in the United States. The 214 participants who completed 12 weeks or more of the drug reported a decrease in seizures by 54%. However, there were a few negative side effects reported, but nothing that was not mild and did not go away (Sirven). Although there has been a significant amount of success in

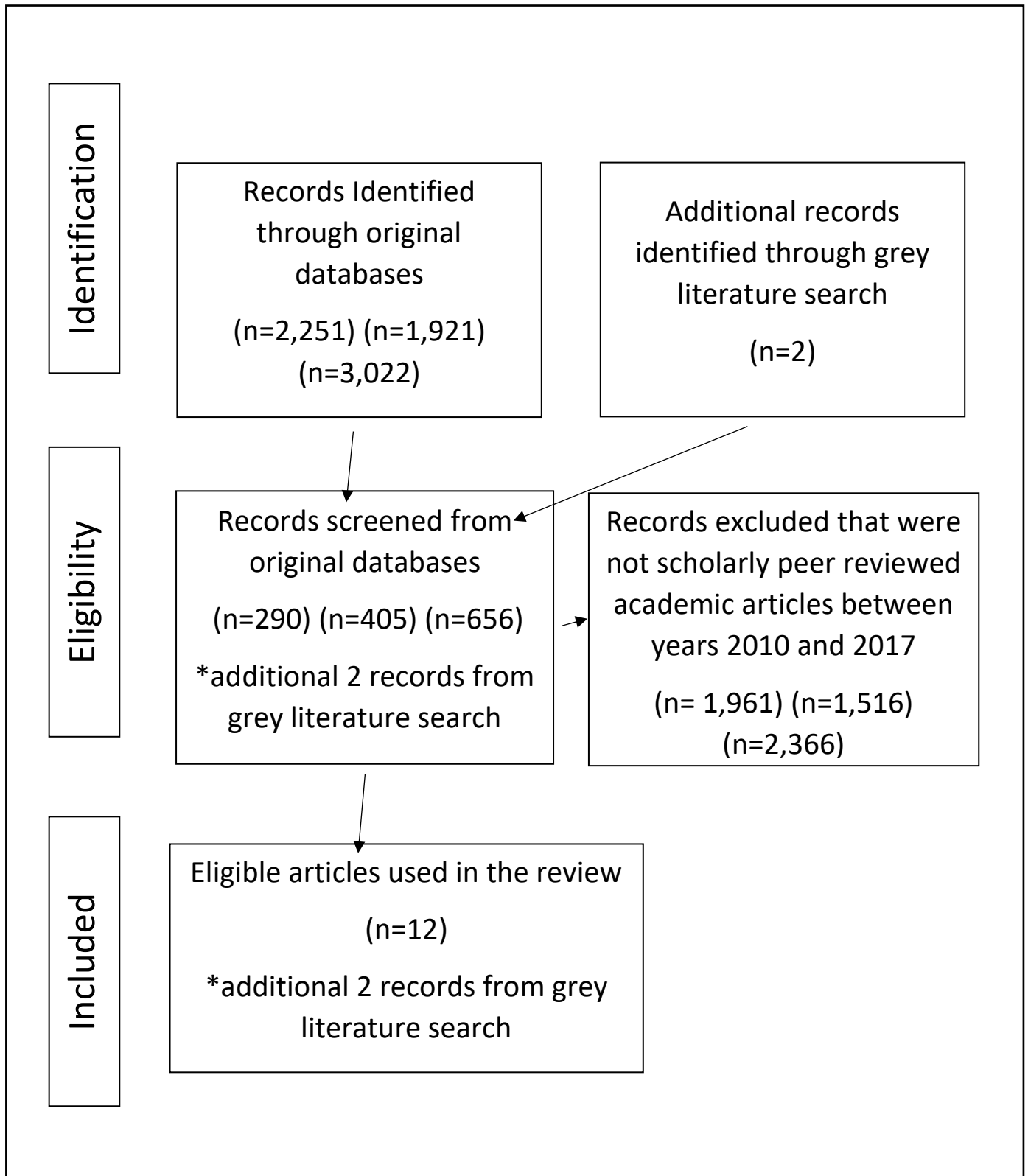
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treating epilepsy with medical marijuana, it is still illegal in 22 states and most countries around the world (Con). The purpose of this literature is to discover the effectiveness of marijuana as a treatment of epilepsy and the associated negative side effects for all populations globally.

## **Methods**

By searching databases such as the University of Georgia's Library's multi-search, the Epilepsy Foundation, Medline, CINAHL, and EMBASE, a systematic search was conducted to find studies that provide information regarding the potential benefits and risks associated with medical marijuana and epilepsy. Only scholarly peer reviewed academic journal articles published between 2010 and 2017 were considered. The University of Georgia's multi-search allows multiple keywords to be searched at once. Keywords used for this literature included "marijuana AND epilepsy," "epilepsy AND cannabis," and "seizures AND cannabis." Searching "marijuana AND epilepsy" resulted in 2,251 documents. After restricting to show only scholarly peer reviewed journals this number decreased to 290. Searching "epilepsy AND cannabis" resulted in 1,921 documents which was decreased to 405 when restricted, and searching "seizures AND cannabis" resulted in 3,022 documents which was decreased to 656 when restricted. Only articles that discussed medical cannabis as a treatment for epilepsy were used for this literature. Information regarding studies all over the world were also included. The geographical area was not narrowed down to a specific area because there have been many studies done globally that provide information necessary for this literature. All articles before

2010 or discussing medical marijuana as a treatment for other disorders were excluded. **Figure 1** explains how these articles were narrowed for the use of this literature.



**Figure 1.** Systematic review process

## Results

1. Patients with epilepsy saw a decrease in seizures with marijuana use.
  - a. Using cannabidiol as a treatment for epilepsy yielded a significant positive effect on seizure load. During a retrospective study on the effect of cannabidiol-enriched cannabis on children with epilepsy, 89% of the 74 patients reported reduction in seizure frequency. Improved behavior and alertness, language, communication, motor skills, and sleep was also seen (Tzadok et al., 2016). A Canadian study was able to conclude that of the 108 marijuana users studied, 84% saw overall improvement in their seizures (Massot-Tarrús & McLachlan, 2016). A similar study also done in Canada reported that their entire study population saw a reduction in seizure frequency and severity as well as improved mood, sleep quality, appetite, and general well-being (Ladino, Hernández-Ronquillo, & Téllez-Zenteno, 2014). In Colorado, patients were observed to see their reactions to oral cannabis extracts as a treatment to epilepsy. Of these 119 patients, 41% had relocated to Colorado to seek treatment using medical marijuana. Forty nine percent reported experiencing at least some improvement in seizures and 24% were considered to be responders to the oral cannabis treatment, which was defined as a >50% reduction in seizure load. Some non-seizure benefits were reported as well, including improved behavior and alertness in 46 patients (39%), improved motor skills in 9 patients (8%), and better sleep in 8 patients (7%) (Treat, Chapman, Colborn, & Knupp, 2016). Antiseizure effects



of cannabis in patients with epilepsy can also be supported with case reports. These reports also show exacerbation of seizures after abrupt discontinuation of the treatment (Friedman & Devinsky, 2015).

2. A few negative side effects resulted from the treatment using medical marijuana.
  - a. Some children showed somnolence, fatigue, gastrointestinal disturbances, and irritability (Tzadok et al., 2016). When using substances, side effects are inevitable. However, the rate and severity of most side effects seen with medical marijuana were mild. No allergic responses were seen. Some other side effects seen in other studies included drowsiness, dizziness, mouth dryness, increased appetite, tiredness, incoordination, and headaches. However, there was no differences in the side effects found between the participants who used marijuana for seizure control and those who used it for other reasons (Massot-Tarrús & McLachlan, 2016). A risk of dependence can also be found in long-term recreational use of cannabis. However, little is known regarding the potential of abuse of cannabidiol-based treatments administered in a clinical setting (Friedman & Devinsky, 2015).
3. Cannabis use does not seem to effect epilepsy.
  - a. A few studies used for this literature found contrasting results to the ones stated previously. A study conducted in Berlin, Germany found that 84% of their 310 epilepsy patients being studied reported no change in seizure load while using medical cannabis as a treatment. They also were able to conclude that frequent use of other drugs increases seizure risk (Hamerle, Ghaeni,

Kowski, Weissinger, & Holtkamp, 2014). An online survey was also conducted to seek opinions on the use of medical marijuana and cannabidiol for people with epilepsy. Of the 776 individuals who participated in the survey, 22% were epileptologists and general neurologists. When asked their opinion on the safety of the treatment, 66% said there was insufficient safety data. When asked if there was adequate efficacy data to use medical marijuana for epilepsy the results were essentially the same. Participants were then asked if they would advise patients with severe, catastrophic epilepsy who have not responded to other treatments to try medical marijuana. Of the epileptologists and general neurologists participating in this questionnaire, 52% said no (Mathern, Beninsig, & Nehlig, 2015).

Overall, every study used for this literature was able to provide information on each of these findings. Although some reported statistics that contrasted each other, each one stated that more research would need to be done before a final conclusion can be made. **Table 1** provides information on the scholarly peer reviewed articles used for this literature.

|          | <b>Author(s)</b>  | <b>Year</b> | <b>Article Title and Journal</b>   | <b>Purpose of article</b>   | <b>Sample info</b>                                      | <b>Type of Research</b>  | <b>Research Findings</b>  | <b>Limitations of article</b>  |
|----------|---|-------------|--|---|---|--|---|--|
| <b>1</b> | Ladino, L.D.<br>Hernandez-Ronquillo, L.<br>Tellez-Zenteno, J.F. | 2014        | Medical Marijuana for Epilepsy: A Case Series Study.<br><br><i>The Canadian Journal of Neurological Sciences.</i>                  | Investigating the sociodemographic and clinical characteristics of a group of patients with epilepsy with a formal prescription for medical marijuana and explore the potential clinical effects experienced by patients. | 18 patients, 12 men, 6 women, 89% Caucasian, Ages 19-50 | Retrospective review   | Medical marijuana has a potential positive effect on seizure activity   | Mainly based off self-reported effects of patients with no formal quantification of seizure frequency and severity, Lack of a control group, Small sample size   |
| <b>2</b> | Sulak, D.<br>Saneto, R.<br>Goldstein, B.                        | 2016        | The Current Status of Artisanal Cannabis for the Treatment of Epilepsy in the United States.<br><br><i>Epilepsy &amp; Behavior</i> | Discuss clinical consideration, including potential risks and benefits, challenges related to artisanal preparations, and cannabinoid dosing  | 272 patients from Washington state and California       | Retrospective chart review of clinical records from patients with epilepsy | 86% of the patients experienced some benefit from the use of artisanal cannabis preparations, 4% of patients had increased seizures, all other adverse effects were mild and well tolerated | Lack of control group, reliance upon parental report for seizure frequency and other characteristics, heterogeneous population, changes in concurrent treatment, variables inherent in artisanal botanical medicines |

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| 3 | Yap, M.<br>Easterbrook, L.<br>Connors, J.<br>Koopmans, L. | 2015 | Use of Cannabis in Severe Childhood Epilepsy and Child Protection Considerations<br><br><i>Journal of Paediatrics &amp; Child Health</i> | Identify the existing evidence for safety and efficacy of cannabis-derived products used in children with medically refractory epilepsy and to guide child protection physicians in their recommendations to Child Safety authorities regarding the potential risk or harm to children using such products | Articles addressing the use of cannabis or cannabis-derived product for recurrent seizures in children ages 0-18, English only publications | Systematic review                                 | Possible benefits from cannabis or cannabis-derived products for severe, refractor childhood epilepsy                             | Small study, selection bias, absence of controls, lack of objective measures   |
| 4 | Massot-Tarrus, A.<br>McLachlan, R.S.                      | 2016 | Marijuana Use in Adults Admitted to a Canadian Epilepsy Monitoring Unit.<br><br><i>Epilepsy &amp; Behavior</i>                           | Determine the prevalence and sociodemographic characteristics of marijuana users among patients admitted to their epilepsy monitoring unit (EMU), asses the perceived impact on seizures, evaluate the effects on stress and sleep, determine perceived adverse  | 310 patients, median age of 35, 57.2% female, 42.8% male  | Self-administered anonymous 27-item questionnaire | High rates of marijuana use in patients with uncontrollable epilepsy and a high perception of improvement in seizures as a result | Based on self-reports by patients, no formal quantifications of seizures or adverse effects, excluded patients with cognitive impairments which limited comparison with other studies, questionnaire |

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|   |   |      |  | effects of the drug   |  |                            |   | was not formally validated as it was designed for use only in this observational study   |
| 5 | Tzadok, M.<br>Uliel-Siboni, S.<br>Linder, I.<br>Kramer, U.<br>Epstein, O.<br>Menascu, S.<br>Nissenkorn, A.<br>Yosef, O.B.<br>Hyman, E.<br>Granot, D.<br>Dor, M.<br>Lerman-Sagie, T.<br>Ben-Zeev, B. | 2016 | CBD-enriched medical cannabis for intractable pediatric epilepsy. The current Israeli experience.<br><br><i>European Journal of Epilepsy</i> | Present the experience of four pediatric epilepsy units in Israel that treat children and adolescents diagnosed as having intractable epilepsy with enriched CBD medical cannabis | 74 patients, age 1-18, with intractable epilepsy resistant to >7 antiepileptic drugs | Retrospective study        | CBD treatment yielded a significant positive effect on seizure load. Most children (89%) reported reduction in seizure frequency. Five (7%) patients reported aggravation of seizures which led to CBD withdrawals. | Lack of a control group, no consistent rate of dosage elevation, reliance upon parental report on seizure frequency, short duration of the study and lack of long-term outcome, no EEG results and no measurement of other drug levels |
| 6 | Hamerle, M.<br>Ghaeni, L.<br>Kowski, A.<br>Weissinger, F.<br>Holtkamp, M.   | 2014 | Cannabis and other illicit drug use in epilepsy patients.<br><br><i>European Journal of Neurology</i>  | Assess the prevalence of cannabis and other illicit drug use among epilepsy patients, clinical variables associated with frequent cannabis consumption, and                       | 310 patients, age 18 or older, suffered from epilepsy for a year or more             | Semi-structured interviews | Cannabis use did not seem to affect epilepsy; however, frequent use of other drugs increases seizure risk   | Based on self-report   |

|   |   |      |   |  |  |                            |   |  |
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|   |   |      |   | effects of illicit drug use on epilepsy as experienced by patients   |  |                            |   |  |
| 7 | Treat, L.<br>Champman, K.E.<br>Colborn, K.L.<br>Knupp, K.G. | 2016 | Duration of use of oral cannabis extract in a cohort of pediatric epilepsy patients.<br><br><i>Epilepsia</i>  | Describe the duration of oral cannabis extracts (OCE) use as a reflection of perceived efficacy of the product, as well as to characterize the factors affecting duration of use of OCEs among pediatric epilepsy patients at a tertiary care center | 119 adults and children who were given OCEs for treatment of epilepsy        | Retrospective chart review | Majority patients found a reduction in seizure burdens  | Recall bias, retrospective methodology   |
| 8 | Mathern, G.W.<br>Beninsig, L.<br>Nehlig, A.                 | 2015 | Fewer specialists support using medical marijuana and CBD in treating epilepsy patients compared with other medical professionals and patients: Result of <i>Epilepsia's</i> survey | Summarize the results of an online survey seeking opinions about the use of medical marijuana and cannabidiol for people with epilepsy   | 776 participants, 58% patients, 22% epileptologists and general neurologists | Online survey              | Epileptologists and neurologists answered mostly no to questions regarding marijuana's safety, efficacy, and help while most patients answered yes. | Open access survey, responses were unaudited, trust that survey was honest and forthright in completing the poll's questions, also not sure if survey can represent the entire worldwide |

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|-----------|--------------------------------|------|---|---|--|-------------------|--|--|
|           |                                |      | <i>Epilepsia</i>  |   |  |                   |  | epilepsy community                                 |
| <b>9</b>  | Szaflarski, M.<br>Sirven, J.I. | 2017 | Social factors in marijuana use for medical and recreational purposes<br><br><i>Epilepsy &amp; Behavior</i> | Present and organize what is known about the social aspects of marijuana use  | Studies discussing the social, demographic, and historical variables that have led to the current opinions on cannabis therapy | Systematic review | Evolution of the sociocultural perspectives on cannabis use, trends in cannabis use for recreational/medical use and public views, current policy, legal, and economic issues, directions for research on social factors in cannabis use in epilepsy | Information from only a number of studies was used |
| <b>10</b> | Friedman, D.<br>Devinsky, O.   | 2015 | Cannabinoids in the Treatment of Epilepsy<br><br><i>The New England Journal of Medicine</i>                 | Address the current preclinical and clinical data that suggests that compounds found in cannabis have efficacy against seizures | Studies discussing preclinical and clinical data for cannabis  | Systematic review | Cannabidiol may be effective in the treatment of some patients with epilepsy but no conclusions can be drawn   | Information from only a number of studies was used |

**Table 1.**

## Discussion

The purpose of this literature was to discover the effectiveness of marijuana as a treatment of epilepsy and the associated negative side effects for all populations globally. The effects of medical cannabis on epilepsy are controversial. Most studies found report a beneficial effect and others report no clear effect of cannabis on seizures. During this review, it was found that majority patients found a decrease in seizure load when using medical cannabis, some mild negative side effects result as well, and some patients do not see any effect on seizures while using cannabis. These findings support the potential beneficial impact of treating epilepsy with medical cannabis but raises questions in regards to how much of the perceived effect is indirectly related to other factors such as decreased stress, mood stabilization, and improved sleep. These results are consistent with other literature in that they confirm what is already known about medical marijuana and epilepsy. The interest in marijuana has grown immensely in the past decade. Although many of the studies screened for this literature concluded that medical cannabis had positive effects on seizures, it is still illegal in 22 states in the United States. During a survey, the Pew Research Center asked Americans if they believed marijuana should be made legal or not. Fifty seven percent of American adults support legalizing marijuana versus 37% who do not, compared to 32% and 60% in 2006. The change in attitudes towards the legalization of marijuana is a result of the positive impacts on medical conditions using medical marijuana as a treatment (Szaflarski & Sirven, 2017). The limitations for this study include some restrictions on medical marijuana such as accessibility, religion and beliefs, and allergies. Medical marijuana is still illegal in 22 states in the United States as well as majority countries worldwide. For an individual with epilepsy living in these areas it is impossible to



obtain this treatment. This barrier requires these individuals to move to a new location where medical marijuana is legal or discover a different treatment that reduces seizure load. Beliefs can also be a barrier to this treatment. Religious individuals may see marijuana use as a sin, even for medical purposes. Personal beliefs may be similar. For an individual who has always thought of marijuana as an illegal drug, it may be difficult to see it as a positive impact on one's health. Although it was not seen in any of the studies used for this literature, allergies can also be a limitation. Another limitation for this study was that only 12 sources were used to gather this information. This topic is very new and more information will need to be discovered and studied in the future. Future studies on medical cannabis and epilepsy should not only focus on the effectiveness in reducing seizures but the safety as well. To date, there is no evidence on the safety, efficacy, and tolerability of cannabis products for the treatment of epilepsy. The lack of quality control in the manufacture of cannabis products makes it impossible to comment on safety for use, especially when the amount of active ingredient in each medical cannabis treatment is currently not regulated (Yap, Easterbrook, Connors, & Koopmans, 2015). A study of cannabis products available in Seattle, San Francisco, and Los Angeles found that of the 75 products examined, only 17% were accurately labeled while 60% contained lower concentrations than stated on the label and 23% contained higher concentrations (Sulak, Saneto, & Goldstein, 2016). Results from majority of these studies provide promising evidence that medical marijuana has a potential positive effect on reducing seizure load for people with epilepsy. However, there are some negative side effects that may result as well.

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