RELIAS MEDIA

Integrative Medicine

Evidence-based summaries and critical reviews on the latest developments in integrative therapies [ALERT]

Vol. 23, Issue 4, April 2020
ReliasMedia.com

CANNABIS

ABSTRACT & COMMENTARY

Cannabis in the Treatment of Headache and Migraine

By Ellen Feldman, MD

Altru Health System, Grand Forks, ND

Dr. Feldman reports no financial relationships relevant to this field of study.

SYNOPSIS: The authors of this observational study found nearly a 50% reduction in self-reported headache and migraine severity following use of inhaled medicinal cannabis.

SOURCE: Cuttler C, Spradlin A, Cleveland MJ, Craft RM. Short- and long-term effects of cannabis on headache and migraine. *J Pain* 2019. pii:S1526-5900(19)30848-X. doi:https://doi.org/10.1016/j.jpain.2019.11.001. [Epub ahead of print].

Cannabis is now legal for medicinal use in over half of the 50 U.S. states.[1] Multiple factors, including federal restrictions on funding cannabis research, have hindered the research necessary to provide evidence-based guidelines for use.[2]

Cuttler et al noted that 35% of medical cannabis users cite headache or migraine as a primary reason for medicinal cannabis use, but studies looking at the specifics of the responses are limited to one randomized, double-blind study in 30 outpatients.

With barriers limiting a traditional research protocol, Cuttler et al used an innovative approach to gather data for this study. Strainprint is a free, Canadian-based app developed to collect analytics regarding medical marijuana. All data are anonymous. Users register with basic information (gender and birth date), select a symptom or medical problem and rate severity, enter the cannabis strain and method of administration, and then are prompted to re-rate severity of symptoms within 20 minutes to four hours after cannabis use. Severity ratings are based on a scale of 0 to 10. In this way, patients can

Financial Disclosure: *Integrative Medicine Alert*'s Physician Editor Suhani Bora, MD; Peer Reviewer Eugene Lee, MD; Associate Editor Journey Roberts; Editor Jason Schneider; Relias Media Editorial Group Manager Leslie Coplin; and Accreditations Manager Amy M. Johnson, MSN, RN, CPN, report no financial relationships relevant to this field of study.

Integrative Medicine [ALERT]

Integrative Medicine Alert (ISSN 2325-2820) is published monthly by Relias LLC, 1010 Sync St., Ste 100, Morisville, NC 27560-5468. Periodicals postage paid at Morrisville, NC, and additional mailing offices. POSTMASTER: Send address changes to *Integrative Medicine Alert*, Relias LLC, 1010 Sync St., Ste. 100, Morrisville, NC 27560-5468.

GST Registration Number: R128870672.

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Summary Points

- Data for this study came from Strainprint, a free app designed for users of medical cannabis to track strains and doses of cannabis by rating symptoms at baseline and after use.
- Analysis of data covered 12,293 sessions of headache treatment and 7,441 sessions of migraine treatment with inhaled cannabis. Diagnosis was based solely on self-identification.
- Results for headache: Headache rating decreased in 89.9% of the sessions; men reported relief more frequently than did women; an average 47.3% decrease in severity was reported; a larger reduction in severity was noted with the concentrate form of cannabis (vs. flower); there appeared to be tolerance with use of the flower form.
- Results for migraine: Migraine rating decreased in 88.1% of the sessions; no gender differences were noted; an average 49.6% decrease in severity was reported; concentrate and flower form of cannabis appeared equally effective; there appeared to be a pattern of dose escalation over time.

track personal response to a specific strain of medical cannabis, while contributing information of use to researchers.[3]

Using Strainprint, Cuttler et al were able to analyze data from 1,306 medical cannabis users with headache (the app was used 12,293 times) and 653 medical cannabis users with migraines (the app was used 7,441 times). Eligibility criteria included using an inhaled form of medical cannabis, including smoking, vaping, and bubbler (edible and tincture users were excluded). The tetrahydrocannabinol (THC) and cannabidiol (CBD) content of the strain of cannabis also was documented; the app prepopulated this information for known strains sold by Canadian distributors.

Overall symptom reduction in all subjects with headaches was 89.9%. App users rated headache symptoms on a scale of 0 to 10 before and up to four hours following inhalation of medicinal cannabis. The mean reduction in severity was 47.3%. Statistical analysis showed significant individual variation in the extent of headache reduction following medicinal cannabis use; response to similar doses and strains was highly variable. There appeared to be a correlation between severe initial ratings of headaches and greater severity reduction post-use. Repeated use of cannabis was correlated with less of an effect on symptoms ($P = 0.010$), suggesting tolerance to the cannabis. The concentrate was associated with greater reduction in headache severity ($P < 0.001$) and no indication of tolerance; however, limited sessions with concentrate were available. (*See Table 1.*)

In app users with migraines, the overall symptom reduction was 88.1%. App users rated migraine symptoms on a scale of 0 to 10 before and up to four hours following inhalation of medicinal cannabis. Mean migraine rating reports decreased by 49.6% following cannabis use. Similar to headaches, there was significant variation in the extent of pain severity reported post-inhalation. Different than headaches, there was no correlation between severe initial ratings and greater migraine severity reduction, and no significant difference in migraine relief was associated with the use of concentrate vs. flower. As with headaches, there was a significant increase in the dose of inhaled cannabis with repeated use ($P = 0.0010$), suggesting tolerance. (*See Table 2.*)

■ COMMENTARY

California introduced legalization of medicinal cannabis to the United States in 1996. Since then, 33 states have followed suit. There is an urgent need to complete studies, understand the risks and benefits of medicinal cannabis, and develop evidence-based clinical guidelines for the use of medicinal cannabis. The strength

Table 1. Findings for Cannabis Users With Headache

	Women	Men	*P* value (men vs. women)
Reduction of Symptoms	89.1%	90.9%	***P* = 0.001**
Exacerbation of Symptoms	2.9%	1.8%	***P* < 0.001**
No change	8.1%	7.4%	*P* = 0.15

Significant *P* values are in bold.

Table 2. Findings for Cannabis Users With Migraine

	Women	Men	*P* value (men vs. women)
Reduction of Symptoms	88.6%	87.3%	*P* = 0.12
Exacerbation of Symptoms	3.2%	2.9%	*P* = 0.43
No change	8.2%	9.9%	***P* = 0.02**

Significant *P* values are in bold.

of this Cuttler et al work is rooted in the innovative approach and plethora of data. Yet, to understand and attempt to apply the results clinically, consideration of the origin of the data (self-reports from the Strainprint app) is essential.

The data were derived from 1,306 medicinal cannabis users with headache and 653 such users with migraine; both groups used the Strainprint app multiple times to rate response after cannabis use — 12,223 times for the headache group and 7,441 times for the migraine group. However, it is noteworthy that there are no data regarding medicinal cannabis users who do not use Strainprint, and no information regarding the frequency of app use per individual, or if any of the respondents stopped using Strainprint after an initial attempt.

Medicinal cannabis users who tended to use the app most frequently may represent those individuals who were most satisfied with the results of using medicinal cannabis. If so, this would bias the results. In addition, the lack of a control group and lack of blinding weakens the ability to generalize and use the results with clinical confidence.

Another feature of this study is that all of the subjects self-diagnosed and self-reported results. Thus, scales of pain severity were individualized, again leading to difficulty generalizing the results. Additionally, it would be useful to have external validation regarding the diagnosis of migraine and headache, as there do not appear to be any standard diagnostic criteria.

Cuttler et al found a slight but significant difference in gender response in the headache arm of the study, but not in the migraine arm. This is consistent with findings in a 2016 study, in which authors found inhaled cannabis to be a more powerful analgesic in men than in women. Future studies are necessary to determine any clinical significance to this finding.[4]

The headache results hint that concentrate was more effective than flower in pain reduction. Cuttler et al noted that the sample size of concentrate users was too small to draw conclusions (3.4% of subjects with headache used concentrate), but that this is an area ripe for exploration. Concentrate is a relatively newer form of cannabis with common names including "wax" and "dabs." This concentrated form of cannabis contains higher than typical amounts of THC; there are case reports of concentrate use resulting in neurotoxicity, psychosis, and cardiotoxicity.[5,6]

Strainprint encourages documenting responses to medical cannabis, but does not collect detailed information on adverse effects. This must be taken into consideration to put the results of this analysis into context.

Even with the clear limitations of this work, the results show marked promise for future investigation into the use of cannabis for headaches and migraines. There does appear to be an association of headache and migraine relief with the use of inhaled cannabis for some individuals. Future studies should help the medical field identify specific traits of the individuals and/or symptoms that best respond to this intervention.

For now, the primary care provider is on safe ground telling patients that although research is preliminary, this study points to the potential usefulness of medicinal cannabis in the treatment of headaches and/or migraine. The expectation of tolerance over time, as suggested by these results, should be included as part of an overall discussion. Cautionary notes include that there is not much information about side effects, effective dose, the effect of cannabis on any comorbid conditions, or cannabis interaction with pharmaceuticals or other substances. The hope is that with more robust and well-conducted studies, we will have clearer recommendations for patients in the future. ■

REFERENCES

1. Map of marijuana legality by state. DISA. 2020. https://disa.com/map-of-marijuana-legality-by-state

2. Challenges and Barriers in Conducting Cannabis Research. National Academies of Sciences, Engineering, and Medicine; Health and Medicine Division; Board on Population Health and Public Health Practice; Committee on the Health Effects of Marijuana: An Evidence Review and Research Agenda. The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research. National Academies Press (US); 2017.
3. Reports. Strainprint. 2020. Available at: https://strainprint.ca/
4. Cooper ZD, Haney M. Sex dependent effects of cannabis-induced analgesia. *Drug Alcohol Depen* 2016;167:112-120.
5. Cinnamon Bidwell L, YorkWilliams SL, Mueller RL, et al. Exploring cannabis concentrates on the legal market: User profiles, product strength, and health-related outcomes. *Addict Behav Rep* 2018;8:102-106.
6. Alzghari SK, Fung V, Rickner SS, et al. To dab or not to dab: Rising concerns regarding the toxicity of cannabis concentrates. *Cureus* 2017;9:e1676.

DIET

ABSTRACT & COMMENTARY

Incidence of Cardiovascular Disease and All-Cause Mortality: Does the Type of Meat Consumed Matter?

By Seema Gupta, MD, MSPH

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Dr. Gupta reports no financial relationships relevant to this field of study.

SYNOPSIS: Investigators found consuming more processed meat, unprocessed red meat, or poultry (but not fish) was closely connected to a higher risk for incident cardiovascular disease. Meanwhile, consuming processed meat or unprocessed red meat (but neither fish nor poultry) was strongly associated with a higher risk of all-cause mortality.

SOURCE: Zhong VW, Van Horn L, Greenland P, et al. Associations of processed meat, unprocessed red meat, poultry, or fish intake with incident cardiovascular disease and all-cause mortality. *JAMA Intern Med* 2020; Feb 3. doi: 10.1001/jamainternmed.2019.6969. [Epub ahead of print].

In the diet of U.S. adults, meat is a major source of protein and fat as well as minerals such as iron, zinc, and several vitamins (including B). The meat and poultry industry is the largest segment of U.S. agriculture, and Americans eat more meat annually than any other nation.[1]

Red meat often is processed to allow an improvement in shelf life as well as color and taste. Meat may be cured, salted, or smoked (e.g., ham or bacon). These processes add high amounts of ingredients known to be unhealthy, including salts, saturated fats, polycyclic aromatic hydrocarbons, and cholesterol. Therefore, eating too much processed meat could lead to an increased intake of these ingredients. Growing evidence reveals eating more red meat may lead to premature death, including death from cardiovascular disease (CVD) and cancer, but the results are not consistent.[2,3] The authors of several of these studies argued that plausible mechanisms for poor outcomes are available linking processed meat consumption and risk of chronic diseases, such as stroke, heart failure, CVD, diabetes mellitus, and cancer, at several sites, as well as mortality.[4] However, associations of poultry, fish, or unprocessed red meat consumption with CVD and mortality remain uncertain.

In their cohort study, Zhong et al analyzed individual-level data for approximately 30,000 U.S. adults from six prospective cohort studies. These included the Cardiovascular Health Study (CHS), the Atherosclerosis Risk in Communities (ARIC) study, the Framingham Heart Study (FHS), the Coronary Artery Risk Development in Young Adults (CARDIA) study, the Multi-Ethnic Study of Atherosclerosis (MESA), and Framingham Offspring Study (FOS).

The authors collected baseline diet data from 1985 to 2002. Study participants were followed up until mid-2016. The mean age of participants was 53.7 years, about 55% were women, and 69% of the total participants were non-Hispanic white (23% were non-Hispanic black). The researchers found that regular consumption of processed red meat (adjusted hazard ratio [HR], 1.07; 95% confidence interval [CI], 1.04 to 1.11), unprocessed red meat (adjusted HR, 1.03; 95% CI, 1.01 to 1.06), or poultry (adjusted HR, 1.04; 95% CI, 1.01 to 1.06) were significantly associated with incident CVD while fish intake was not (adjusted HR, 1.00; 95% CI, 0.98 to 1.02). Incident CVD included all fatal and nonfatal coronary heart

disease, fatal and nonfatal stroke, fatal and nonfatal heart failure, and other CVD deaths.

Additionally, intake of processed meat (adjusted HR, 1.03; 95% CI, 1.02 to 1.05) or unprocessed red meat (adjusted HR, 1.03; 95% CI, 1.01 to 1.05) was associated with significantly increased all-cause mortality, while poultry and fish consumption was not. However, researchers also found the strength of the association between the intake of processed meat and CVD decreased with age, according to whether participants were younger than age 45 years, age 45 to 64 years, or age 65 years or older.

■ COMMENTARY

Compared with previous research, Zhong et al harmonized diet and other data across six cohorts, which largely attenuated the heterogeneities from previous studies and found significant positive associations of processed meat or unprocessed red meat intake with incident CVD and all-cause mortality. Although the observed effect sizes were small, the potential effects on public health can be significant, since these findings highlight how modification of dietary preferences may lead to meaningful effects on individual health outcomes. Interestingly, the authors identified a significant positive association between poultry intake and incident CVD. Although we cannot state conclusively, this finding could be related to the intake of fried chicken; thus, it may be more of an adverse effect from frying than the poultry itself. Regardless, it is clear that certain meat choices are healthier than others.

It would be valuable to continue to advise patients to limit the intake of both processed and unprocessed red meats. Poultry, such as chicken and turkey, are leaner meats and are lower in saturated fats, which makes poultry a better protein choice than red meat. Of course, fish may be one of the healthiest options to recommend, since it is an excellent source of minerals, such as iron, zinc, iodine, magnesium, and potassium, as well as omega-3 fatty acids, vitamins, calcium, and phosphorus. The bottom line is that when fruits and vegetables are not sufficient, it may be poultry and fish that remain the healthiest options. ■

REFERENCES

1. Daniel CR, Cross AJ, Koebnick C, Sinha R. Trends in meat consumption in the USA. *Public Health Nutr* 2011;14:575-583.
2. Sinha R, Cross AJ, Graubard BI, et al. Meat intake and mortality: A prospective study of over half a million people. *Arch Intern Med* 2009;169:562-571.
3. Kappeler R, Eichholzer M, Rohrmann S. Meat consumption and diet quality and mortality in NHANES III. *Eur J Clin Nutr* 2013;67:598-606.
4. Wolk A. Potential health hazards of eating red meat. *J Intern Med* 2017;281:106-122.

CANNABIS

ABSTRACT & COMMENTARY

Cannabis for Mental Health Disorders: Follow the Evidence

By Ellen Feldman, MD

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Dr. Feldman reports no financial relationships relevant to this field of study.

SYNOPSIS: In a review of 83 eligible studies, researchers found little evidence to support the efficacy of cannabinoids to treat depressive disorders, anxiety disorders, or several other mental health disorders. There is low-grade evidence that pharmaceutical cannabis may help improve symptoms of anxiety in patients with a comorbid medical condition.

SOURCE: Black N, Stockings E, Campbell G, et al. Cannabinoids for the treatment of mental disorders and symptoms of mental disorders: A systematic review and meta-analysis. *Lancet Psychiatry* 2019;6:995-1010.

One of the most common reasons given for seeking medicinal cannabinoid use is for treatment of a mental health disorder. Medicinal cannabis currently is legal in 33 states; quality research regarding this substance is necessary to provide individuals with full clinical guidelines and risk profiles.[1]

Recognizing this need, Black et al conducted a meta-analysis of 83 eligible studies regarding medical cannabinoids and mental health disorders. In this study, the authors use "medicinal cannabinoids" to cover all plant-based and synthetic derivatives of the cannabis plant; "medicinal cannabis" refers to any part of the

Summary Points

- This meta-analysis included 83 studies involving medicinal cannabinoids in the treatment of one of the following mental health disorders (as a primary disorder or secondary to another medical condition): depression, anxiety, attention-deficit hyperactivity disorder, post-traumatic stress disorder, and psychosis.
- Low-quality evidence suggests an improvement in anxiety symptoms in participants with other medical conditions (such as multiple sclerosis and chronic, noncancer pain) when treated with pharmaceutical tetrahydrocannabinol (THC) with or without cannabidiol (CBD).
- Pharmaceutical THC with or without CBD is not associated with improvement in any of the mental health conditions reviewed; when compared with placebo, there is an association with adverse effects in 10 studies.

cannabis plant; "pharmaceutical cannabinoids" are extracts with defined tetrahydrocannabinol (THC) with or without cannabidiol (CBD); and "pharmaceutical CBD" refers to extractions of CBD alone.

Eligibility criteria included studies that used medicinal cannabinoids of any type and remission or change in symptoms in at least one of the following disorders: depression, anxiety, post-traumatic stress disorder (PTSD), attention deficit hyperactivity disorder (ADHD), Tourette syndrome, and psychosis. In all studies, the mental health disorder was either primary or secondary to another medical problem. Adverse effects and study withdrawals were included in the analysis.

Using standard tools — the Cochrane risk-of-bias tool[2] and the Grading of Recommendations, Assessment, Development and Evaluation (GRADE)[3] — researchers put the evidence from the controlled trials into one of four categories, ranging from "very low quality" to "high quality."

Within the 83 eligible studies, there were 50 randomized controlled trials (RCTs). The breakdown for each diagnosis is shown in Table 1.

The median sample size across all diagnoses for RCTs was 10 to 39 participants. Median length of the trials was four to five weeks. The most common substance investigated was pharmaceutical THC; the next most common was pharmaceutical CBD. The eligible studies that were not RCTs were observational and included prospective studies, chart reviews, and case studies.

Pharmaceutical THC (with or without CBD) was used in all but one RCT involving depression. In all studies, depression was not a stand-alone diagnosis but was secondary to a chronic medical problem (mainly chronic noncancer pain or multiple sclerosis [MS]). The pooled standardized mean difference (SMD) for a change in depressive symptoms associated with the use of pharmaceutical THC with or without CBD was 0.00 to 0.05 (95% confidence interval [CI], -0.20 to 0.17). Black et al explained that an SMD of 0.2 represents a small effect, 0.5 represents a medium effect, and 0.8 represents a large effect, meaning that pharmaceutical THC with or without CBD had very little affect on users with depression.

The one RCT that studied medicinal cannabis found no change in depressive symptoms in patients with chronic noncancer pain when compared to treatment with placebo.

Pharmaceutical THC with CBD beat placebo in a significant lowering of anxiety symptoms in seven studies involving patients with either chronic noncancer pain or MS. The SMD was -0.25 (95% CI, -.0.49 to -0.01). However, the evidence GRADE was very low because of several factors, including reporting bias and none of the respondents had a primary diagnosis of anxiety. Two studies looked at CBD alone vs. placebo in the treatment of social anxiety; there was no significant improvement in symptoms.

Symptoms of ADHD did not show a significant change in one RCT of pharmaceutical THC with CBD vs. placebo.

Two small RCTs compared pharmaceutical THC with CBD to placebo in treatment of Tourette syndrome and found no significant impact on symptoms.

One small study of 10 individuals with PTSD found that pharmaceutical THC with CBD vs. placebo was associated with improved global functioning and reduced nightmares (SMD = -1.3; 95% CI, -1.48 to -0.77).

One RCT of 24 individuals found no change in positive symptoms of psychosis (such as hallucinations) with the use of pharmaceutical THC with CBD vs. placebo, but a worsening of negative symptoms, such as social isolation and withdrawal; (SMD 0.36; 95% CI, 0.10 to 0.62).

The remaining five RCTs investigating psychosis used CBD vs. placebo. There was no significant

improvement noted in any primary outcomes, but one study involving 86 individuals reported an improvement in global functioning with an SMD of -0.62 (95% CI, -1.14 to -0.09).

Pooled results from all RCTs indicate that pharmaceutical THC with CBD was associated with significantly more adverse effects in 10 studies (odds ratio [OR] 1.99; 95% CI, 1.20 to 3.29) vs. placebo and significantly more study withdrawals in 11 studies vs. placebo (OR 2.78; 95% CI, 1.59 to 4.86). Adverse events were not recorded in this meta-analysis, but are known to be (from other literature) increased occurrence of depression, anxiety, and psychotic symptoms. The evidence GRADE for these findings was low to moderate. There were fewer studies examining adverse effects and study withdrawal when CBD (one study) or medicinal cannabis (three studies) was compared with placebo, but none of these resulted in a significant difference. The researchers also did not state whether cannabis was the only treatment participants were using for their conditions.

■ COMMENTARY

The most striking conclusion emerging from this comprehensive review and meta-analysis regarding cannabinoids for the treatment of mental health disorders is how little we know.

Standing in contrast to the lack of quality medical studies regarding mental health disorders and medical cannabinoids are high-quality, rigorous investigations regarding the use of this agent for chronic pain, neuropathic pain, and nausea and vomiting associated with chemotherapy, and spasticity associated with MS.[4]

In 2017, the National Academies of Sciences, Engineering, and Medicine released a comprehensive report reviewing and summarizing research since 1999 regarding recreational and medicinal cannabis use. The report summarizes the relevant medical literature and ranks evidence for efficacy as well as adverse effects when using medicinal cannabinoids for a specific medical condition. In regard to mental health, the study reports that there is "no evidence to support or refute a statistical association between cannabis use and changes in the course or symptoms of depressive disorder," and there is moderate evidence of increased social anxiety disorder associated with regular cannabis use.[5]

In addition, the report notes substantial evidence of development of schizophrenia with heavy cannabis use and moderate evidence of increased suicidal thoughts and attempts associated with heavy cannabis use.[5]

Table 1. Number of Studies per Diagnosis

	Total trials	Randomized controlled trials
Depression	42	23 (n = 2,551)
Anxiety	31	17 (n = 605)
Tourette syndrome	8	2 (n = 36)
Attention deficit hyperactivity disorder	3	1 (n = 30)
Post-traumatic stress disorder	12	1 (n = 10)
Psychosis	11	6 (n = 281)

The work of Black et al strongly supports the idea that there remains no strong evidence for medicinal cannabis to treat depression, anxiety, ADHD, Tourette syndrome, or psychosis. Of note, with the exception of PTSD and Tourette syndrome, most of these conditions are not on a list of conditions qualifying for medical cannabinoid use in any state. However, 23 states currently specify PTSD as an approved condition for medicinal cannabinoids and only five specify Tourette syndrome. In addition, in what appears to be a growing trend, at least six states allow physicians to certify a need for a dispensary card at the "discretion" of the provider.[6,7]

Given the strong probability that providers will be asked about medicinal cannabinoid use by patients looking for alternative treatment of a mental health disorder, it is useful to be armed with facts. There is currently no evidence that medicinal cannabinoid use helps mental health disorders, and there are concerns that heavy use can cause mental health problems. There is weak evidence that medicinal cannabinoid use is associated with a decrease in anxiety associated with a chronic health condition.

Many states have preemptively approved medicinal use of cannabinoids for specific diagnosis without waiting for rigorous studies or medical evidence to prove their efficacy. Efficacy of medicinal cannabinoids is well-studied and established for specific disorders, but there is not yet evidence of efficacy for treating mental health disorders. The downside to using medicinal cannabinoids for a mental health disorder may be considerable. The primary care provider is well-situated to aid patients in understanding the current state of knowledge regarding medicinal cannabinoid use in disorders of mental health. However, it is important to urge caution and patience until

enough evidence is gathered to reach firm conclusions. ■

REFERENCES

1. World Population Review. States with medical marijuana. 2020. http://worldpopulationreview.com/states/states-with-medical-marijuana/
2. Cochrane Methods Bias. RoB 2: A revised Cochrane risk-of-bias tool for randomized trials. 2020. https://methods.cochrane.org/bias/resources/rob-2-revised-cochrane-risk-bias-tool-randomized-trials
3. BMJ Best Practice. What is GRADE? 2019. https://bestpractice.bmj.com/info/us/toolkit/learn-ebm/what-is-grade/
4. Therapeutic Effects of Cannabis and Cannabinoids. National Academies of Sciences, Engineering, and Medicine; Health and Medicine Division; Board on Population Health and Public Health Practice; Committee on the Health Effects of Marijuana: An Evidence Review and Research Agenda. In: *The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research.* National Academies Press (US);2017. https://www.ncbi.nlm.nih.gov/books/NBK425767/
5. National Academies of Engineering, Science, and Medicine. The health effects of cannabis and cannabinoids: Committee's conclusions. 2017.https://www.nap.edu/catalog/24625/the-health-effects-of-cannabis-and-cannabinoids-the-current-state
6. Leafly. Qualifying conditions for marijuana by state. 2020. https://www.leafly.com/news/health/qualifying-conditions-for-medical-marijuana-by-state
7. Richter N. Qualifying conditions for medical cannabis (2020 update). Marijuana Break. Mar. 6, 2020. https://www.marijuanabreak.com/qualifying-conditions-for-medical-marijuana-2017

CME OBJECTIVES

Upon completion of this educational activity, participants should be able to:

- present evidence-based clinical analyses of commonly used alternative therapies;
- make informed, evidence-based recommendations to clinicians about whether to consider using such therapies in practice; and
- describe and critique the objectives, methods, results, and conclusions of useful, current, peer-reviewed, clinical studies in alternative medicine as published in the scientific literature.

CME QUESTIONS

1. In the study by Cuttler et al, medicinal cannabis use is associated with reduction of headache and migraine relief:
a. in more than 80% of the respondents in this double-blind, placebo-controlled study with volunteers from numerous headache clinics.
b. in more than 80% of the respondents in this observational study with volunteers using an anonymous app to record responses.
c. in just under half of the migraine respondents and close to 80% of those with headache, in this double-blind, placebo-controlled study with volunteers from numerous headache clinics.
d. in just under half of the headache respondents and close to 80% of those with migraine, in this observational study with volunteers using an anonymous app to record responses.

2. According to the study by Black et al, which of the following is true about medicinal cannabinoids?
a. There is evidence confirming efficacy in chronic pain, nausea and vomiting associated with chemotherapy, anxiety, and post-traumatic stress disorder, but not in any other mental health disorder.
b. There is evidence confirming efficacy in chronic pain, nausea and vomiting associated with chemotherapy, and spasticity in multiple sclerosis, but not in any disorder of mental health.
c. They are well-investigated for a range of disorders including multiple disorders of mental health.
d. They are approved for use in 33 U.S. states, despite no clear evidence of efficacy for any diagnosis.

3. Based on the study by Zhong et al, regularly consuming which of the following is not significantly associated with either incident cardiovascular disease or all-cause mortality?
a. Processed red meat
b. Unprocessed red meat
c. Fish
d. Poultry

[IN FUTURE ISSUES]

Black Elderberry (*Sambucus nigra*) and Upper Respiratory Infections

Relationship Between Social Media and Disordered Eating