BMJ Open

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Journal:	*BMJ Open*
Manuscript ID	bmjopen-2021-050831
Article Type:	Original research
Date Submitted by the Author:	08-Mar-2021
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Keywords:	QUALITATIVE RESEARCH, Pain management < ANAESTHETICS, GENERAL MEDICINE (see Internal Medicine)

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Values and preferences towards medical cannabis among people living with chronic pain: A mixed methods systematic review

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Abstract

Objective To explore values and preferences towards medical cannabis among people living with chronic pain.

Design Mixed methods systematic review.

Data sources We searched MEDLINE, EMBASE, and PsycInfo from inception to March 17, 2020.

Study selection Pairs of reviewers independently screened search results and included quantitative, qualitative and mixed methods studies reporting values and preferences towards medical cannabis among people living with chronic pain.

Review methods We analyzed data using meta-narrative synthesis (quantitative findings were qualitized) and tabulated review findings according to identified themes. We used the GRADE approach to assess certainty of evidence.

Results Of 1,838 initial records, 15 studies proved eligible for review. High to moderate certainty evidence showed that patient's use of medical cannabis for chronic pain was influenced by both positive (e.g. support from friends and family) and negative social factors (e.g. stigma surrounding cannabis use). Most patients using medical cannabis favored products with balanced ratios of tetrahydrocannabinol (THC) and cannabidiol (CBD), or high levels of CBD, but not high THC preparations. Many valued the effectiveness of medical cannabis for symptom management even when experiencing adverse events related to concentration, memory, or fatigue. Reducing use of prescription medication was a motivating factor for use of medical cannabis, and concerns regarding addiction, losing control or acting strangely were disincentives. Out-of-pocket costs were a barrier, whereas legalization of medical cannabis improved access and incentivized

use.

Low to very low certainty evidence suggested highly variable values towards medical cannabis among people living with chronic pain. Individuals with pain related to life-limiting disease were more willing to use medical cannabis, and preferred oral over inhaled administration.

Conclusions Our findings highlight factors that clinicians should consider when discussing medical cannabis. The variability of patients' values and preferences emphasize the need for shared decision making when considering medical cannabis for chronic pain.

Systematic review registration: The Open Science Framework (OSF) (https://osf.io/5d72w).

Word count: 3126

Strengths and limitations of this study

- Consideration of complementary bodies of evidence (qualitative, quantitative and mixed-methods) and use of the GRADE approach to assess the certainty of evidence provide greater confidence in the interpretation of results.

- Most eligible studies are from high-income countries, reflecting values and preferences of patients living in better health care service systems with health insurance coverage. The generalizability of our findings to other populations in uncertain.

- Studies eligible for this review failed to consistently report participants' socio-economic status, educational level, and religious beliefs, limiting exploration of the impact of these characteristics on values and preferences towards medical cannabis for chronic pain.

INTRODUCTION

Chronic pain is the major cause of non-fatal disease burden worldwide,[1] and is estimated to affect one in five adults in the general global population[2] and one in three in low and middle-income countries.[3] Opioids are commonly prescribed for chronic pain; however, increasing awareness of modest benefits and risks of addiction, overdose and death have generated interest for alternative management strategies. Medical cannabis, whose two most studied active ingredients are delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD), is one such therapeutic alternative.[4] Moreover, the legalization of medical cannabis among more than 30 countries[5] has increased access for people living with chronic pain who are considering this option. Accordingly, physicians are increasingly faced with questions from patients about the potential role of medical cannabis in managing their pain.[6]

Physicians who seek guidance from current clinical practice guidelines regarding medical cannabis for chronic pain will find recommendations to be inconsistent. As examples, the UK's National Institute for Health and Care Excellence (NICE) recommends against prescribing cannabis-related products for chronic pain, citing its high cost and inadequate supporting evidence.[7] The American Academy of Neurology (ANN) recommends an oral cannabis extract containing both THC and CBD as having the highest level of empirical support as a treatment for chronic pain associated with multiple sclerosis.[8] These guidelines, and others, have neglected to systematically identify and incorporate target patients' values and preferences, which may affect their findings.

Understanding patients' values and preferences, defined as patient-important desirable and undesirable consequences weighed when making a recommendation,[9]

can improve the trustworthiness of recommendations. Therefore, we conducted a systematic review investigating values and preferences towards the use of medical cannabis among people living with chronic pain. This systematic review is part of the BMJ Rapid Recommendations project, a collaborative effort from the MAGIC Evidence Ecosystem Foundation (www.magicevidence.org) and the British Medical Journal. This systematic review informed a parallel guideline published on bmj.com and MAGICapp (please insert link to guideline).[10]

METHODS

We registered and published our study protocol on the Open Science Framework (OSF) (https://osf.io/5d72w) and adhered to the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) statement.

Data source and Searches

We searched MEDLINE, EMBASE, and PsycInfo from inception to March 17, 2020, using a combination of search filters for retrieving studies on values and preferences towards cannabis use among people living with chronic pain (Appendix 1).[11] We reviewed reference lists of all included studies and relevant reviews to identify additional eligible studies.

Study selection

We included quantitative, qualitative (including survey research that only reported qualitative findings) and mixed-methods studies that reported values and preferences of people living with chronic cancer or non-cancer pain, or their carers, on: 1) relative values or importance of outcomes related to medical cannabis use (e.g. improvements in pain and function, side effects) for chronic pain (defined as pain lasting three months or longer); 2) formulation of medical cannabis (e.g. administration routes, ingestion methods, ratios of THC to CBD); or 3) factors that influence the decision to use medical cannabis. If studies enrolled both acute and chronic pain patients, we considered them eligible if they reported outcomes of chronic pain patients separate from others, or if at least 80% of patients were affected by chronic pain.

We excluded studies that: 1) did not elicit data from patients or carers directly (e.g. data elicited from health providers; information from databases of health records); 2) only reported health state values or quality of life of people living with chronic pain, not related to use of medical cannabis; 3) only reported correlation analyses of associations among demographic variables, other patient characteristics, and medical cannabis use for chronic pain; 4) case studies with less than 10 patients; 5) studies published in languages other than English, or 6) abstracts and literature reviews.

Before beginning each phase of the review process, we conducted calibration exercises in which reviewers assessed the same two articles and discussed any disagreements, leading to clarification and a common understanding of criteria and process. After calibration, six paired reviewers (LZ & XW, NK & SA, YS & MA) independently screened titles and abstracts of all retrieved references, and the full text of articles deemed potentially eligible. We resolved disagreements by discussion or consultation with an adjudicator (LL).

Data collection and risk of bias assessment

Three pairs of reviewers (LZ & XW, NK & SA, YS & MA) extracted data from eligible studies, independently and in duplicate, for research questions, population characteristics, design and methods of data collection, risk of bias or methodological limitations, and main findings (Appendix 2). For main findings, we selected two eligible articles per study design, identified key themes addressed in the studies, and then coded the themes as different categories for main findings in the data abstraction form (Appendix 2).[12] We resolved disagreements through discussion to

reach consensus, or in consultation with an adjudicator (LL).

For quantitative studies, we used GRADE (Grading of Recommendations Assessment, Development and Evaluation) guidance for studies of values and preferences to assess risk of bias of individual studies (Appendix 3).[13] For qualitative studies, we used the Critical Appraisal Skills Programme (CASP) checklist to assess methodological reporting quality of individual studies (Appendix 4).[14]

Data synthesis and analysis

Using an iterative process, we compared themes of the categories identified across all studies and developed analytic themes.[12] We applied critical meta-narrative synthesis, a modified form of critical interpretive synthesis, to transform quantitative into qualitative data using systematic profiles and critical questions that are asked to further extract narratives from the data. [15.16] To facilitate this transformation, we applied four types of profiles to transform the extracted quantitative data that had the potential to be qualitized, or converted into narratives (Table 1).[12,16] By using inductive content analysis we synthesized the qualitized findings to produce review findings which addressed the key themes.

Certainty of Evidence

For review findings from quantitative studies, we assessed the certainty of evidence according to the five GRADE domains (i.e. risk of bias, imprecision, inconsistency, indirectness, and small study effects)[13,17,18] For review findings from qualitative studies, we assessed the certainty of evidence according to the five GRADE-CERQual (Confidence in the Evidence from Reviews of Qualitative Research) domains (i.e.

methodological limitations, relevance, coherence, adequacy and dissemination bias).[19] We initially considered the certainty of evidence as high, and if serious or several minor or moderate concerns were detected in one or more domains, we rated down certainty of evidence by one or more levels to moderate, low or very low.

Patient and public involvement

We engaged three people living with chronic pain, one of whom used medical cannabis, to review our findings and advise if they were consistent with their experiences. Led by the MAGIC Evidence Ecosystem Foundation, a BMJ RapidRec panel of clinicians, methodologists and persons with lived experience of chronic pain were responsible for developing clinical practice recommendations for medical cannabis and chronic pain. Three patient partners were full members of the guideline panel and received training and support to optimise contributions throughout the guideline development process. The panel developed recommendations using the GRADE framework, available online through the MAGICapp (please insert link to guideline),[10] and considered evidence from systematic reviews on the effectiveness of medical cannabis, adverse events related to medical cannabis, opioid substitution with medical cannabis, and this review of patients' values and preferences regarding medical cannabis to manage chronic pain.

RESULTS

Our search retrieved 1,838 records, of which 102 were deemed potentially eligible based on titles and abstracts. After full text screening, 15 studies (reported in 16 articles) proved eligible for review, including nine quantitative studies, five qualitative studies and one mixed method study (Figure 1, Appendix 5,6) [20-35]

Study characteristics

Of the 15 studies, nine were conducted in the United States, two in the United Kingdom, two in Israel, one in Canada, and one in Australia. Four studies were conducted between 2000 and 2009, and 11 were conducted between 2010 and 2019. The number of participants ranged from 34 to 1,514 among quantitative studies, 18 to 150 in the qualitative studies, and 984 were enrolled in the mixed method study. All 15 studies included only chronic pain patients; no caregivers were enrolled. (Appendix 5)

Among the nine quantitative and one mixed method studies, four were at serious and one at critical risk of bias due to lack of valid representation of the outcomes (e.g. beneficial or harmful outcomes of medical cannabis), low response rate (less than 80%) and lack of reporting on how the authors confirmed participants' understanding of the measurement techniques (e.g. questionnaire) (Appendix 7). Among the five qualitative studies, only one was at serious risk of bias due to inadequate research design and data collection, and lack of reporting on whether the relationship between researchers and participants had been adequately considered (Appendix 8).

Findings

We identified two key themes: values and preferences towards medical cannabis for chronic pain (seven quantitative studies [2,185 participants]), three qualitative studies [95 participants], and one mixed method study [984 participants]) and factors that influenced patient's decisions regarding use of medical cannabis (seven quantitative studies [4,998 participants], five qualitative studies [263 participants], and one mixed method study [984 participants]). (Table 2, Appendix 9).

Use of medical cannabis for chronic pain

Low certainty evidence showed that patients had mixed levels of willingness to use medical cannabis and most patients who used medical cannabis reported positive attitudes toward its use. Most patients with advanced life-limiting illnesses were comfortable using cannabis for pain [25], while some other patients with chronic pain were unwilling or ambivalent about medical cannabis use[26] . Non-White patients with advanced illness were more concerned about medical cannabis compared to White patients, but they remained comfortable using medical cannabis [25]. People living with chronic pain who used medical cannabis believed it was effective for reducing their pain [25 27 31 34] and allowed them to reduce use of prescribed medications [27]. Two qualitative studies found similar results [22 28].

Medical cannabis vs. other pain medicines

Patients with histories of substance use preferred medical cannabis over prescription opioids (Low certainty).[23] Some patients endorsed that medical cannabis was safer than other analgesics, and such beliefs were more prevalent among non-Christians

and patients with colleges education or higher (Very low certainty).[25]

Different preparations of medical cannabis

Moderate certainty evidence showed that most people living with chronic pain preferred using a blend of indica and sativa to manage their condition.[21] There was no difference in the preference of cannabis strain between males and females, those who used cannabis for medical purposes only and those who endorsed medical and recreational use, or between novice and experienced users.[21]

Most patients preferred medical cannabis products with either balanced ratios of THC:CBD (37%) or high CBD formulations (46%), and only a minority (17%) preferred high THC products (Moderate certainty).[21 33] Specifically, women, novice users, or those who endorsed use of cannabis for medical purposes only were more inclined to choose products with low THC and high CBD ratios, while males, those endorsing use of cannabis for both medical and recreational purposes, and experienced users preferred products with equal ratios of THC:CBD.[21]

Sex, reason for use, and experience with cannabis influenced preference towards route of administration (Moderate certainty). [21 35] Compared to male patients, women preferred to use tinctures and topical preparations as opposed to vaporizing or smoking [21]. Patients who used cannabis both recreationally and medically preferred smoking most, while those who used cannabis medically only preferred vaporizing most. [21] Experienced cannabis users endorsed multiple routes of administration compared with novice users who preferred vaporizing.[21] Most patients with advanced life-limiting illness preferred oral formulations (non-inhaled) of medical cannabis. [25]

Factors influencing the decision to use medical cannabis

High to moderate certainty evidence showed that most people living with chronic pain used medical cannabis for symptom relief.[20 22 23 28 35] Specifically, patients viewed medical cannabis as an effective approach to managing pain[20 22 23 35], sleep, appetite, and nausea. [20, 35] Patients also reported that cannabis improved their emotional and mental well-being by reducing anxiety, depression and stress,[20 35] and increased their ability to focus and function[28]. Most patients reported that cannabis facilitated a state of relaxation in which pain remained present but was easier to tolerate [28].

Moderate certainty evidence showed that factors related to patients' unwillingness to use medical cannabis include major side effects (e.g. losing control or acting strangely) [20 23 26 27 31 34 35], addiction or tolerance [26 27 31 34 35], and negative social consequences (e.g. stigma)[25 26 31 34, 20 32 35]. Older age was associated with greater hesitancy to use medical cannabis, as was concerns about negative opinions from others which might lead to relationship problems or disagreements with loved ones [25 26 31 34]. Some patients reported that stigma affected their comfort in asking healthcare providers about cannabis as a treatment option, and their willingness to use medical cannabis in a public setting [32]. Moderate certainty evidence showed that cost, legal status, and accessibility of medical cannabis also influenced use[31 34 20 23-25 35].

Factors influencing the choice of different preparations of medical cannabis

Low certainty evidence suggested that most patients chose medical cannabis

products based on cannabinoid content (i.e. THC or CBD potency, ratio of THC and CBD), recommendations from dispensary employees, described effects (e.g. pain relief), strain of cannabis plant (i.e. sativa, indica, hybrid), smell, or varietal name.[21 22 23 28 30] A higher proportion of males selected cannabis products based on cannabinoid content, cannabis variety, visual properties, and smell, while a higher proportion of females consulted with a medical professional when choosing cannabis products (Moderate certainty). [21]

Patients who used cannabis both medically and recreationally were more likely to select cannabis products based on cannabinoid content, cannabis variety, described effects, visual properties, smell, recommendations from friends, and the product name, while those who only used cannabis medically were more likely to prioritize recommendations from dispensary employees or medical professionals (Moderate certainty). [21]

DISCUSSION

Values and preferences among patients with chronic pain towards the use of medical cannabis are highly variable. Improvement of symptoms and reduction of prescription medications are important factors that positively influence patients' decision to use medical cannabis, while concerns about addiction, losing control, acting strangely and negative social consequences are associated with unwillingness to use medical cannabis. Cost, legal status and accessibility are also important factors. Patients who endorsed use of cannabis for only medical reasons preferred high CBD or similar ratios of THC: CBD products, whereas those endorsing use of both medical and recreational purposes were more likely to use higher THC products. Further, patients with chronic pain endorsing both medical and recreational use were more likely to prefer smoking cannabis, versus patients who endorsed only medical use who preferred vaporizing. Our findings were consistent across bodies of evidence (quantitative, qualitative, and mixed method studies). The certainty of evidence for most findings was moderate, predominantly due to risk of bias or imprecision/ adequacy.

We asked three patient partners on the BMJ rapid recommendation panel for their comments on the findings of this systematic review. In particular, 1) whether our findings reflected their experiences, and 2) if some of the findings were different from their experience, what were possible reasons? The patient partners agreed that all except one of our review findings (Table 2) reflected their experiences with cannabis. Specifically, they suggested that patients who are using medical cannabis may not receive support from family or friends due to stigma and misinformation about cannabis use.

Our findings that some patients select medical cannabis based on properties that

dispensers attributed to strain type (indica or sativa), represents an opportunity for education. When these strains were originally characterized, sativa was shown to produce higher amounts of CBD whereas indica strains of cannabis produced high levels of THC. At present, however, commercially available cannabis plants and products have been extensively interbred to produce a multitude of unique strains. [36] As such, the only reliable way to determine the composition of any form of medical cannabis is through accurate reporting of the cannabinoid (e.g. THC, CBD) content.

We found important differences between patients who use cannabis for medical reasons only and those who report combined use (medical and recreational) in preferences regarding cannabis content and route of administration. Observational studies have shown that most consumers of cannabis endorse medical and recreational use, [37] [38] which presents a challenge to therapeutic use. Recreational users often prioritize cannabis with high THC concentrations, a psychotropic cannabinoid that is associated with greater harms than CBD.[39] [40] Patients that use cannabis for both medical and recreational purposes are also more likely to prefer inhaled forms of administration, which has a much faster onset and greater bioavailability than ingestion but also entails pulmonary risk factors due to inhalation of toxins and particulate matter.[41] Therapeutic use of cannabis should prioritize formulations supported by evidence, administered in a manner that prioritizes both safety and effectiveness.

Strengths and limitations of the review

Strengths of this review include explicit eligibility criteria, an extensive search strategy, and duplicate assessment of eligibility and risk of bias. The use of complementary

bodies of evidence (qualitative, quantitative and mixed-methods) and the use of the GRADE approach to assess the certainty of evidence allowed greater confidence in the interpretation of results.

This study also had limitations. Most of the eligible studies (13 out of 15 studies) are from high-income countries, reflecting values and preferences of patients living in better health care service systems with health insurance coverage. The generalizability of our findings to other populations in uncertain. In addition, we synthesized and reported patients' willingness to use medical cannabis despite the limitation that most studies did not provide participants with sufficient information about the benefits and harms of medical cannabis. Studies failed to consistently report participants' socio-economic status, educational level, and religious beliefs, limiting exploration of the effect of these characteristics on values and preferences.

Implications

Our findings have direct implications for clinicians attending people living with chronic pain who are considering use of medical cannabis. Benefits (effect on pain and reduction of prescription medications), harms (adverse effects), burdens (negative social consequences, cost) and accessibility (including legal status) of medical cannabis all appear to influence patients' decisions related to use. However, we did not identify any studies that considered how patients prioritized these factors. Subsequent research should address this issue. In addition, how patient characteristics (e.g. medical conditions, social economic status, religious beliefs) affect their values and preferences is another issue worth addressing in subsequent research.

CONCLUSIONS

There exists high variability of values and preferences towards medical cannabis among people living with chronic pain, particularly related to their willingness to use medical cannabis. These findings suggest that an individualized patient-centred approach, such as shared decision-making, should be emphasized for empowering patients to make choices that best suit their own values and preferences and accommodate their context.

Figure Legends

Figure 1: Evidence search and selection

Contributors

LZ, XW, NK, SA, YS and MAE identified and selected the studies. LZ, XW, NK, SA, YS and MAE collected the data. LZ, LL, XW, NK and SA analysed the data and assessed the certainty of the evidence. AFH, TA, GG and JWB provided advice at different stages. LZ, LL, XW, NK, SA drafted the manuscript. All authors revised the manuscript and approved the final version of the manuscript.

Funding

XW is supported by a post-doctoral fellowship from the Michael G. DeGroote Institute for Pain Research & Care.

Competing interests None

Ethical approval: Ethics approval for this study was not required.

Data sharing: Raw data are available on request from the corresponding author.

Acknowledgement We thank Rachel Couban (McMaster University) for performing the literature search; we thank Ray Zhang (McMaster University) for providing consult with the certainty of evidence rating; we thank Shelly-Anne Li (University of Toronto) for providing suggestions on data synthesis; we thank our patient partners for providing comments on review findings.

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Table 1 Critical meta-narrative synthesis: from quantitative data to narratives

Systematic profiles[a]			Critical questions
Technique	**Focus**	**Example**	
Modal profile	The most frequently occurring attributes	When asked to state the preference for route of administration: 86% (69/80) patients were comfortable with an oral form (pills, drops or added to food), while 15% (12/80) chose smoking . **This was qualitized as**: Most patients stated preference for oral formulations, while a minority preferred inhaled products.	What is this study trying to say about patients' values? Are patients' values and preferences explicitly identified? If so, what are they? How do participants' answers to the questions provide insight into patients' values and preferences, and their influence on the choice of treatment for chronic pain? How different (or similar) are patients' and carers' perspectives on medical cannabis for chronic pain? Are there other individual or contextual factors (e.g., age, gender, socioeconomic status) that influence patients' values and preferences towards medical cannabis for chronic pain?
Average profile	Average of the particular variables	Patients' concerns regarding medical cannabis using a 10-point scale (0 = not concerned, 10= extremely concerned) were, in order of important: side effects (mean = 7.0±2.9), addiction (6.6±3.2), tolerance (6.2±3.2), losing control or acting strangely (6.2±3.3), and what family and friends may think (3.9±3.8). **This was qualitized as:** Patients were generally most concerned about the side effects of medical cannabis, followed by addiction, tolerance, losing control or acting strangely, and what family and friends may think.	
Comparative profile	A comparison of key outcomes	Patients were asked to rate their values and concerns regarding use of cannabis (strongly agree, agree, disagree, strongly disagree and don't know). Significantly more males, vs. women, were concerned about cannabis being addictive (p =0.031), leading to the use of more harmful substances (p =0.036), and causing an inability to think clearly (p =0.008). **This was qualitized as:** Compared to females, significantly more males were concerned about cannabis being addictive, leading to the use of more harmful substances, and causing an inability to think clearly.	
Holistic profile	A combination of the modal, average and comparative profiles	Patients were asked to rate their willingness to use medical cannabis on a 0-10 point scale (0=extreme unwillingness to 10=extreme willingness). Greater unwillingness was associated with higher age (bivariate correlation coefficient [r]= 0.40; p=0.001), but not with pain intensity or duration, or sex. **This was qualitized as:** Higher age was related to more unwillingness to use medical cannabis.	

Note:
Abbreviation: SD: Standard deviation.
a. We used the following criteria when "qualitizing" quantitative into qualitative data:

"All or almost all": Reported by over 90% of patients; "Most": Reported by 75 to 90% of patients; "Majority": Reported by 50 to 75% of patients; "Minority": Reported by 25-50% of patients; "Some": Reported by10%-25% of patients; "None or almost none": Reported by 10% or less of patients (if the sample was 100 or less)

"Very few": Reported by 10% or less of patients (if the sample was >100). "Most common" and "least common" were used when factors were reported in groups, to denote the factors that patients agreed with the most vs. the least. The criteria above did not apply in these cases (e.g. "Recommendations from a medical professional was the least influential factor among patients when selecting cannabis.").

Table 2 Review findings and certainty of evidence

Review Findings [a]	Type of Research Evidence: Reference number	Certainty of Evidence
Values and preferences towards medical cannabis for chronic pain		
Use of medical cannabis for chronic pain		
Chronic pain patients had mixed levels of comfort or willingness to use medical cannabis.	Quantitative: 25,26,27	Low: Risk of bias and indirectness
	Qualitative: 22	Low: Minor concerns about relevance, serious adequacy concerns
Most patients who use medical cannabis had a positive attitude toward its use for pain relief.	Quantitative: 25,27, 29,31,34	Low: Risk of bias and indirectness
	Qualitative: 28	Moderate: Serious adequacy concerns
Medical cannabis over other pain medicines		
Patients with chronic pain and substance use histories preferred medical cannabis over prescription opioids.	Qualitative: 23	Low: Moderate methodological limitations and moderate adequacy concerns
Some patients believed that medical cannabis is safer than morphine and other strong pain killers.	Quantitative: 25	Very low: Risk of bias, indirectness and imprecision
Different preparations of medical cannabis		
Cannabis variety (i.e. sativa, indica, hybrid)		
Most patients preferred medical cannabis with a blend of indica and sativa, regardless of gender, reasons for use, and cannabis experience level.	Quantitative: 21	Moderate: Risk of bias
Cannabis content (i.e. THC or CBD potency, ratio of THC and CBD)		
A balanced ratio of THC:CBD was the most preferred preparation, but gender, reason for use, and cannabis experience level influenced patients' preference for cannabis ratio.	Quantitative: 21, 33	Moderate: Risk of bias

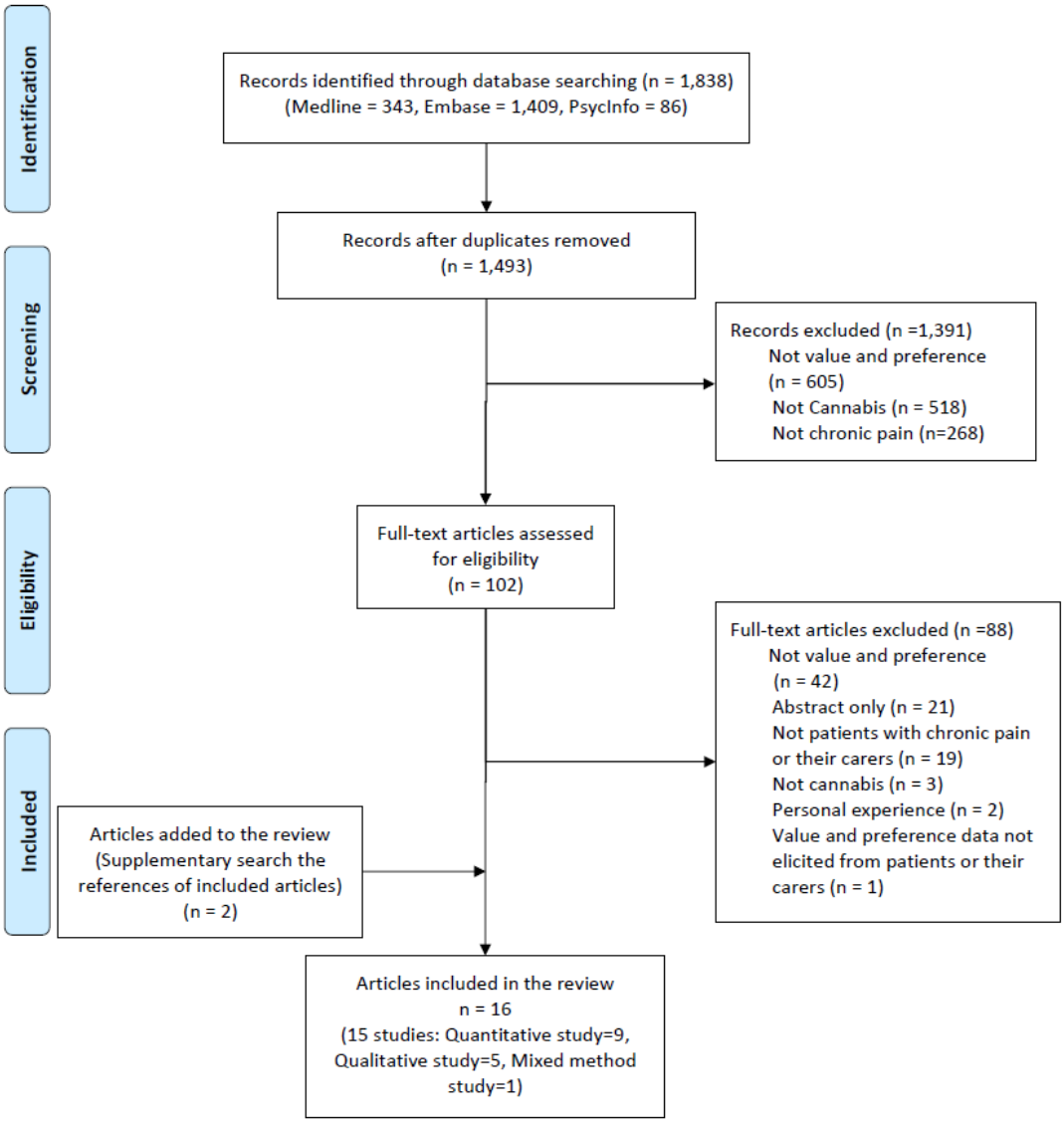
Cannabis administration route		
Gender, reason for use and cannabis experience level influenced patients' preferred cannabis administration routes.	Quantitative: 21 Mixed method: 35	Moderate: Risk of bias
Most patients with advanced life-limiting illness preferred an oral form (non-inhaled) of medical cannabis.	Quantitative: 25	Low: Risk of bias and imprecision
Factors that influenced patient's decision regarding use of medical cannabis		
Factors influenced the choice of medical cannabis use		
Most patients used medical cannabis because it improved symptoms associated with pain, mental health and other medical conditions.	Qualitative: 20,22,23,28	High
	Mixed method: 35	Moderate: Risk of bias
Most patients were motivated to use medical cannabis to reduce use of prescription medication.	Quantitative study: 27 Qualitative study: 22	Moderate: Risk of bias Moderate: Moderate adequacy concerns
The majority of patients expressed that their cannabis use was influenced by positive social consequences, such as social support from friends and family.	Quantitative: 25, 31,34	Moderate: Risk of bias
Most patients expressed concerns with using medical cannabis, and described a range of adverse effects.	Quantitative: 26, 27,31,34 Mixed method: 35 Qualitative : 20, 23	Moderate: Risk of bias Moderate: Moderate methodological concerns
Most patients expressed that their cannabis use was influenced by negative social consequences, such as stigma.	Quantitative: 25,26, 31,34 Mixed method: 35 Qualitative: 20, 32	Moderate: Risk of bias Moderate: Moderate methodological limitations
The cost, legal status, and accessibility of medical cannabis influenced patients' decisions to use medical cannabis.	Quantitative: 24,25, 31,34 Mixed method: 35 Qualitative: 20, 23	Moderate: Risk of bias Moderate: Moderate methodological limitations
Factors influenced the choice of different preparations of medical cannabis		

Patients chose medical cannabis products mainly based on cannabinoid content, recommendations from dispensary employees, described effects and side effects, strain of cannabis plant, smell, and flower appearance.	Quantitative: 21, 30	Low: Risk of bias and indirectness
	Qualitative: 22, 23, 28	Low: Moderate concerns about coherence and serious adequacy concerns
Gender, reason for use, and level of use experience were factors influencing patients' selection of cannabis products.	Quantitative: 21	Moderate: Risk of bias

Note:
Abbreviations: CBD: cannabidiol; THC: Delta-9-tetrahydrocannabinol.

a. We used the following criteria when "qualitizing" quantitative into qualitative data:
"All or almost all": Reported by over 90% of patients; "Most": Reported by 75 to 90% of patients; "Majority": Reported by 50 to 75% of patients; "Minority": Reported by 25-50% of patients; "Some": Reported by10%-25% of patients; "None or almost none": Reported by 10% or less of patients (if the sample was 100 or less)
"Very few": Reported by 10% or less of patients (if the sample was 101 or more). "Most common" and "least common" were used when factors were reported in groups, to denote the factors that patients agreed with the most vs. the least. The criteria above did not apply in these cases (e.g. "Recommendations from a medical professional was the least influential factor among patients when selecting cannabis.").

Figure 1 Evidence search and selection



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). *P*referred *R*eporting *I*tems for *S*ystematic Reviews and *M*eta-*A*nalyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

Appendix 1 Search strategies and results in MEDLINE, Embase and PsycInfo

March 17, 2020

MEDLINE

Database: OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

Search Strategy:

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1 Cannabis/ (8934)
2 exp cannabinoids/ or cannabidiol/ or cannabinol/ or dronabinol/ (13763)
3 Endocannabinoids/ (5620)
4 exp Receptors, Cannabinoid/ (9222)
5 (Cannabis or cannabinol or cannabinoid* or cannabidiol or bhang or cannador or charas or ganja or ganjah or hashish or hemp or marihuana or marijuana or nabilone or cesamet or cesametic or ajulemic acid or cannabichromene or cannabielsoin or cannabigerol or tetrahydrocannabinol or dronabinol or levonantradol or nabiximols or palmidrol or tetrahydrocannabinolic acid or tetrahydro cannabinol or marinol or tetranabinex or sativex or endocannabinoid*).mp. (54746)
6 or/1-5 (54746)
7 "marijuana use"/ or marijuana smoking/ (5304)
8 Marijuana Abuse/ (6168)
9 (epidiolex or gwp 42003p or gwp42003p or nabidiolex or dronabinol or thc or tetrahydrocannabinol* or ea 1477 or ea1477 or marinol or qcd 84924 or syndros or tetrabinex or tetranabinex or cesamet or nabilone or deltanyne or "abbott 40566" or namisol or dronabinolum or "QCD 84924" or "CCRIS 4726" or nabiximol? or "gw 1000" or gw1000 or "sab 378" or sab378 or sativex).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (11622)
10 or/7-9 (20972)
11 or/1-10 (55952)
12 *Attitude to Health/ (42364)
13 *Patient Participation/ (14355)
14 *Patient Preference/ (5009)
15 preference*.ti,ab. (148469)
16 choice.ti. (31408)
17 choices.ti. (6250)
18 value.ti. (124160)
19 health state values.ti,ab. (175)
20 valuation*.ti. (1523)

21 expectation*.ti,ab. (85695)
22 attitude*.ti,ab. (144860)
23 acceptab*.ti,ab. (174183)
24 knowledge.ti,ab. (676935)
25 point of view.ti,ab. (41412)
26 user participation.ti,ab. (243)
27 users participation.ti,ab. (49)
28 patient participation.ti,ab. (2134)
29 patients participation.ti,ab. (589)
30 patient perspective*.ti,ab. (3526)
31 patients perspective*.ti,ab. (5820)
32 user perspective*.ti,ab. (466)
33 users perspective*.ti,ab. (513)
34 patient perce*.ti,ab. (5165)
35 patients perce*.ti,ab. (9776)
36 health perception*.ti,ab. (2652)
37 user perce*.ti,ab. (351)
38 users perce*.ti,ab. (786)
39 user view*.ti,ab. (110)
40 users view*.ti,ab. (369)
41 patient view*.ti,ab. (546)
42 patients view*.ti,ab. (2807)
43 ((decision* and mak*).ti. or (decision mak* or decisions mak*).ti,ab.) and (patient* or user* or men or women).ti,ab. (73905)
44 discrete choice*.ti,ab. (1942)
45 decision board*.ti,ab. (45)
46 decision analy*.ti,ab. (7477)
47 decision-support.ti,ab. (13930)
48 decision tool*.ti,ab. (808)
49 decision aid*.ti,ab. (2976)
50 discrete-choice*.ti,ab. (1942)
51 *Decision Making/ and (patient* or user* or men or women).ti. (5869)
52 decision support techniques/ (19921)

53 (health and utilit*).ti. (1434)
54 gamble*.ti,ab. (4395)
55 prospect theory.ti,ab. (285)
56 preference score.ti,ab. (163)
57 preference elicitation.ti,ab. (179)
58 health utilit*.ti,ab. (2017)
59 utility value*.ti,ab. (1487)
60 utility score*.ti,ab. (1378)
61 Utility estimate*.ti,ab. (269)
62 health state.ti,ab. (4119)
63 feeling thermometer*.ti,ab. (68)
64 best-worst scaling.ti,ab. (202)
65 standard gamble.ti,ab. (832)
66 time trade-off.ti,ab. (1150)
67 TTO.ti,ab. (1026)
68 probability trade-off.ti,ab. (20)
69 utility score.ti,ab. (507)
70 preference based.ti,ab. (1291)
71 preference score*.ti,ab. (495)
72 multiattribute.ti,ab. (337)
73 multi attribute.ti,ab. (523)
74 EuroQol 5D.ti,ab. (1268)
75 EuroQol5D.ti,ab. (19)
76 EQ5D.ti,ab. (550)
77 EQ 5D.ti,ab. (7695)
78 SF6D.ti,ab. (32)
79 SF 6D.ti,ab. (753)
80 HUI.ti,ab. (1169)
81 15D.ti,ab. (1704)
82 or/12-81 (1494263)
83 (patient adj3 (value* or preference*)).ti,ab. (16093)
84 (patient* adj5 (report* or relate*) adj5 (outcome* or measure* or assess*)).mp. (41519)

85 patient participation/ or doctor patient relation/ or nurse patient relationship/ or patient attitude/ or patient preference/ or patient satisfaction/ or patient compliance/ or medication compliance/ or patient decision making/ or patient education/ or chronic patient/ or attitude to health/ or *"quality of life"/ or self care/ or self concept/ or self examination/ or adaptive behavior/ or coping behavior/ or coping.ab,ti. or needs assessment/ or personal autonomy/ or patient advocacy/ or life event/ (688791)
86 (patient* adj3 (prefer* or participat* or involve* or perspective* or view* or activat* or empower* or collaborate)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (154936)
87 (patient* adj2 (attitude* or decision* or needs*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (32381)
88 expert patient*.mp. (261)
89 (patient* and (centre* or center* or focus*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (726322)
90 patient*.mp. and (decision making/ or medical decision making/ or cooperation/ or distress syndrome/ or emotional stress/) [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (44808)
91 or/83-90 (1481530)
92 82 or 91 (2686916)
93 11 and 92 (6739)
94 (chronic adj4 pain*).mp. (68992)
95 Chronic Pain/ (13719)
96 exp Osteoarthritis/ (61921)
97 osteoarthrit*.mp. (88211)
98 osteo-arthrit*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (474)
99 exp Arthritis, Rheumatoid/ (111604)
100 exp Neuralgia/ (20041)
101 Diabetic Neuropathies/ (14472)
102 (neuropath* adj5 pain*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (24189)

103 neuralg*.mp. (26998)
104 zoster.mp. (20810)
105 Irritable Bowel Syndrome/ (7099)
106 IBS.mp. (8807)
107 Migraine Disorders/ (24884)
108 migraine*.mp. (38930)
109 Fibromyalgia/ (8287)
110 Fibromyalg*.mp. (11565)
111 complex regional pain syndromes/ or causalgia/ or reflex sympathetic dystrophy/ (5486)
112 Pain, Intractable/ (6166)
113 Phantom Limb/ (1855)
114 Hyperalgesia/ (11498)
115 exp back pain/ or failed back surgery syndrome/ or low back pain/ (38351)
116 radiculopath*.mp. (9283)
117 Musculoskeletal Pain/ (3090)
118 Headache/ (27380)
119 exp Headache Disorders/ (33884)
120 headache*.mp. (92254)
121 exp Temporomandibular Joint Disorders/ (17098)
122 whiplash.mp. (3942)
123 Whiplash Injuries/ (3216)
124 exp Cumulative Trauma Disorders/ (13612)
125 exp Peripheral Nervous System Diseases/dt, rh, th [Drug Therapy, Rehabilitation, Therapy] (29519)
126 Pain Measurement/de [Drug Effects] (6646)
127 (backache* or backpain* or dorsalgi* or arthralgi* or polyarthralgi* or arthrodyni* or myalgi* or fibromyalgi* or myodyni* or neuralgi* or ischialgi* or crps or rachialgi*).ti,ab. (44403)
128 ((noncancer* or non-cancer* or back or discogen* or chronic* or recurrent or persist* or bone or musculoskelet* or muscle* or skelet* or spinal or spine or vertebra* or joint* or arthritis or Intestin* or neuropath* or neck or cervical* or head or facial* or complex or radicular or cervicobrachi* or orofacial or somatic or non-malign* or shoulder* or knee* or hip or hips) adj3 pain).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (215471)
129 or/94-128 (633956)

Annotation: chronic pain and painful conditions
130 93 and 129 (343)

Embase
Database: Embase <1974 to 2020 March 16>
Search Strategy:
---
1 cannabis/ (33753)
2 exp cannabinoid/ (65425)
3 medical cannabis/ (2094)
4 exp cannabinoid receptor/ (14516)
5 exp endocannabinoid/ (8544)
6 (Cannabis or cannabinol or cannabinoid* or cannabidiol or bhang or cannador or charas or ganja or ganjah or hashish or hemp or marihuana or marijuana or nabilone or cesamet or cesametic or ajulemic acid or cannabichromene or cannabielsoin or cannabigerol or tetrahydrocannabinol or dronabinol or levonantradol or nabiximols or palmidrol or tetrahydrocannabinolic acid or tetrahydro cannabinol or marinol or tetranabinex or sativex or endocannabinoid*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (86218)
7 cannabis addiction/ (9661)
8 "cannabis use"/ or cannabis smoking/ (11097)
9 (epidiolex or gwp 42003p or gwp42003p or nabidiolex or dronabinol or thc or tetrahydrocannabinol* or ea 1477 or ea1477 or marinol or qcd 84924 or syndros or tetrabinex or tetranabinex or cesamet or nabilone or deltanyne or "abbott 40566" or namisol or dronabinolum or "QCD 84924" or "CCRIS 4726" or nabiximol? or "gw 1000" or gw1000 or "sab 378" or sab378 or sativex).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (19601)
10 or/1-9 (89571)
11 *attitude to health/ (55489)
12 *patient participation/ (9554)
13 *patient preference/ (4523)
14 preference*.ti,ab. (180987)
15 choice.ti. (36120)
16 choices.ti. (7375)
17 value.ti. (137715)
18 health state values.ti,ab. (233)

19 valuation*.ti. (2249)
20 expectation*.ti,ab. (106912)
21 attitude*.ti,ab. (179875)
22 acceptab*.ti,ab. (240808)
23 knowledge.ti,ab. (851427)
24 point of view.ti,ab. (57170)
25 user participation.ti,ab. (284)
26 users participation.ti,ab. (52)
27 patient participation.ti,ab. (2881)
28 patients participation.ti,ab. (830)
29 patient perspective*.ti,ab. (5558)
30 patients perspective*.ti,ab. (8635)
31 user perspective*.ti,ab. (564)
32 users perspective*.ti,ab. (624)
33 patient perce*.ti,ab. (8096)
34 patients perce*.ti,ab. (14350)
35 health perception*.ti,ab. (3709)
36 user perce*.ti,ab. (400)
37 users perce*.ti,ab. (902)
38 user view*.ti,ab. (169)
39 users view*.ti,ab. (469)
40 patient view*.ti,ab. (865)
41 patients view*.ti,ab. (3932)
42 ((decision* and mak*).ti. or (decision mak* or decisions mak*).ti,ab.) and (patient* or user* or men or women).ti,ab. (111434)
43 discrete choice*.ti,ab. (2789)
44 decision board*.ti,ab. (59)
45 decision analy*.ti,ab. (10602)
46 decision-support.ti,ab. (18317)
47 decision tool*.ti,ab. (1271)
48 decision aid*.ti,ab. (4097)
49 discrete-choice*.ti,ab. (2789)
50 *Decision Making/ and (patient* or user* or men or women).ti. (5671)

51 (health and utilit*).ti. (2083)
52 gamble*.ti,ab. (5213)
53 prospect theory.ti,ab. (286)
54 preference score.ti,ab. (241)
55 preference elicitation.ti,ab. (261)
56 health utilit*.ti,ab. (3331)
57 utility value*.ti,ab. (2815)
58 utility score*.ti,ab. (2530)
59 Utility estimate*.ti,ab. (494)
60 health state.ti,ab. (6770)
61 feeling thermometer*.ti,ab. (86)
62 best-worst scaling.ti,ab. (306)
63 standard gamble.ti,ab. (1081)
64 time trade-off.ti,ab. (1674)
65 TTO.ti,ab. (1635)
66 probability trade-off.ti,ab. (24)
67 utility score.ti,ab. (1024)
68 preference based.ti,ab. (1839)
69 preference score*.ti,ab. (654)
70 multiattribute.ti,ab. (376)
71 multi attribute.ti,ab. (721)
72 EuroQol 5D.ti,ab. (2064)
73 EuroQol5D.ti,ab. (39)
74 EQ5D.ti,ab. (1812)
75 EQ 5D.ti,ab. (14809)
76 SF6D.ti,ab. (110)
77 SF 6D.ti,ab. (1370)
78 HUI.ti,ab. (1774)
79 15D.ti,ab. (2541)
80 decision support system/ (21812)
81 or/11-80 (1879990)
82 (patient adj3 (value* or preference*)).ti,ab. (25871)

83 (patient* adj5 (report* or relate*) adj5 (outcome* or measure* or assess*)).mp. (73476)
84 patient participation/ or doctor patient relation/ or nurse patient relationship/ or patient attitude/ or patient preference/ or patient satisfaction/ or patient compliance/ or medication compliance/ or patient decision making/ or patient education/ or chronic patient/ or attitude to health/ or *"quality of life"/ or self care/ or self concept/ or self examination/ or adaptive behavior/ or coping behavior/ or coping.ab,ti. or needs assessment/ or personal autonomy/ or patient advocacy/ or life event/ (1037242)
85 (patient* adj3 (prefer* or participat* or involve* or perspective* or view* or activat* or empower* or collaborate)).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (234656)
86 (patient* adj2 (attitude* or decision* or needs*)).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (119435)
87 expert patient*.mp. (478)
88 (patient* and (centre* or center* or focus*)).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (1258089)
89 patient decision making/ (9864)
90 patient*.mp. and (decision making/ or medical decision making/ or cooperation/ or distress syndrome/ or emotional stress/) [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (180387)
91 or/82-90 (2444470)
92 81 or 91 (3858388)
93 10 and 92 (13785)
94 (chronic adj4 pain*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (113744)
95 chronic pain/ (59665)
96 exp osteoarthritis/ (124667)
97 osteoarthrit*.mp. (138729)
98 osteo-arthrit*.mp. (511)
99 degenerative arthrit*.mp. (1541)
100 exp rheumatoid arthritis/ (196173)
101 exp neuralgia/ (102320)
102 diabetic neuropathy/ (23303)
103 (neuropath* adj5 (pain or diabet*)).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (72882)
104 neuralg*.mp. (29911)

105 zoster.mp. (37512)
106 irritable colon/ (25493)
107 (irritable bowel syndrome or IBS).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (24789)
108 exp migraine/ (62395)
109 migrain*.mp. (69650)
110 fibromyalgia/ (19936)
111 fibromyalg*.mp. (21561)
112 reflex sympathetic dystrophy.mp. (2353)
113 complex regional pain syndrome.mp. (7426)
114 causalgia.mp. (1039)
115 intractable pain/ (4766)
116 phantom limb/ or phantom pain/ (2434)
117 agnosia/ (3053)
118 amputation stump/ (2062)
119 exp hyperalgesia/ (20518)
120 ((noncancer* or non-cancer* or chronic* or recurrent or persist* or non-malign*) adj3 pain).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (130063)
121 exp backache/ (106576)
122 radiculopathy/ or radiculopath*.mp. (13603)
123 exp bone pain/ (17842)
124 exp musculoskeletal pain/ (145426)
125 arthralgia/ (59500)
126 headache*.mp. (271974)
127 exp "headache and facial pain"/ (296382)
128 temporomandibular joint disorder/ (13611)
129 ((TMJ or TMJD) and pain*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (3753)
130 whiplash.mp. or whiplash injury/ (4884)
131 exp cumulative trauma disorder/ (20498)
132 or/94-131 (1089097)
133 93 and 132 (1409)

PsycInfo
Database: APA PsycInfo <1806 to March Week 2 2020>
Search Strategy:
---
1 exp cannabis/ or exp cannabinoids/ or tetrahydrocannabinol/ (12784)
2 (Cannabis or cannabinol or cannabinoid* or cannabidiol or bhang or cannador or charas or ganja or ganjah or hashish or hemp or marihuana or marijuana or nabilone or cesamet or cesametic or ajulemic acid or cannabichromene or cannabielsoin or cannabigerol or tetrahydrocannabinol or dronabinol or levonantradol or nabiximols or palmidrol or tetrahydrocannabinolic acid or tetrahydro cannabinol or marinol or tetranabinex or sativex or endocannabinoid*).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (26408)
3 marijuana laws/ or marijuana legalization/ or "cannabis use disorder"/ or marijuana usage/ (3594)
4 (epidiolex or gwp 42003p or gwp42003p or nabidiolex or dronabinol or thc or tetrahydrocannabinol* or ea 1477 or ea1477 or marinol or qcd 84924 or syndros or tetrabinex or tetranabinex or cesamet or nabilone or deltanyne or "abbott 40566" or namisol or dronabinolum or "QCD 84924" or "CCRIS 4726" or nabiximol? or "gw 1000" or gw1000 or "sab 378" or sab378 or sativex).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (3193)
5 or/1-4 (26475)
6 *health attitudes/ (8084)
7 *client participation/ (1678)
8 exp *client attitudes/ (17349)
9 preference*.ti,ab. (95876)
10 choice.ti. (21402)
11 choices.ti. (4602)
12 value.ti. (18077)
13 health state values.ti,ab. (77)
14 valuation*.ti. (983)
15 expectation*.ti,ab. (80049)
16 attitude*.ti,ab. (201050)
17 acceptab*.ti,ab. (38902)
18 knowledge.ti,ab. (290890)
19 point of view.ti,ab. (20482)
20 user participation.ti,ab. (282)
21 users participation.ti,ab. (46)

22 patient participation.ti,ab. (788)
23 patients participation.ti,ab. (264)
24 patient perspective*.ti,ab. (980)
25 patients perspective*.ti,ab. (1752)
26 user perspective*.ti,ab. (340)
27 users perspective*.ti,ab. (345)
28 patient perce*.ti,ab. (1343)
29 patients perce*.ti,ab. (3398)
30 health perception*.ti,ab. (1230)
31 user perce*.ti,ab. (393)
32 users perce*.ti,ab. (888)
33 user view*.ti,ab. (95)
34 users view*.ti,ab. (289)
35 patient view*.ti,ab. (210)
36 patients view*.ti,ab. (1022)
37 ((decision* and mak*).ti. or (decision mak* or decisions mak*).ti,ab.) and (patient* or user* or men or women).ti,ab. (21062)
38 discrete choice*.ti,ab. (960)
39 decision board*.ti,ab. (16)
40 decision analy*.ti,ab. (1133)
41 decision-support.ti,ab. (3235)
42 decision tool*.ti,ab. (169)
43 decision aid*.ti,ab. (1252)
44 discrete-choice*.ti,ab. (960)
45 *Decision Making/ and (patient* or user* or men or women).ti. (3428)
46 (health and utilit*).ti. (467)
47 gamble*.ti,ab. (5406)
48 prospect theory.ti,ab. (964)
49 preference score.ti,ab. (93)
50 preference elicitation.ti,ab. (134)
51 health utilit*.ti,ab. (532)
52 utility value*.ti,ab. (490)
53 utility score*.ti,ab. (334)

54 Utility estimate*.ti,ab. (103)
55 health state.ti,ab. (958)
56 feeling thermometer*.ti,ab. (58)
57 best-worst scaling.ti,ab. (109)
58 standard gamble.ti,ab. (210)
59 time trade-off.ti,ab. (279)
60 TTO.ti,ab. (190)
61 probability trade-off.ti,ab. (5)
62 utility score.ti,ab. (101)
63 preference based.ti,ab. (648)
64 preference score*.ti,ab. (402)
65 multiattribute.ti,ab. (531)
66 multi attribute.ti,ab. (567)
67 EuroQol 5D.ti,ab. (206)
68 EuroQol5D.ti,ab. (0)
69 EQ5D.ti,ab. (61)
70 EQ 5D.ti,ab. (1677)
71 SF6D.ti,ab. (10)
72 SF 6D.ti,ab. (284)
73 HUI.ti,ab. (445)
74 15D.ti,ab. (170)
75 decision support systems/ (3245)
76 or/6-75 (744950)
77 client attitudes/ or client satisfaction/ (21785)
78 values/ or personal values/ or social values/ (22591)
79 (patient* adj3 (prefer* or participat* or involve* or perspective* or view* or activat* or empower* or collaborate)).mp. (27273)
80 (patient* adj2 (attitude* or decision* or needs*)).mp. (23750)
81 or/77-80 (85433)
82 76 or 81 (783705)
83 5 and 82 (3282)
84 chronic pain/ (13151)
85 chronic illness/ and pain.mp. (916)

86 back pain/ (3813)
87 ((chronic* or persist* or refractor* or intract* or manag* or back) adj3 pain).mp. (34808)
88 or/84-87 (35275)
89 (chronic adj4 pain*).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (22123)
90 exp arthritis/ (4140)
91 osteoarthrit*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (2121)
92 osteo-arthrit*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (9)
93 degenerative arthrit*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (15)
94 exp Neuralgia/ (931)
95 exp Neuropathy/ (6243)
96 (neuropath* adj5 (pain or diabet*)).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (6749)
97 neuralg*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (3310)
98 zoster.mp. (577)
99 irritable bowel syndrome/ (1152)
100 (IBS or irritable colon or irritable bowel).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (2001)
101 exp headache/ (15176)
102 migrain*.mp. (12832)
103 fibromyalgia/ (1972)
104 fibromyalg*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (3408)
105 "complex regional pain syndrome (type i)"/ (152)
106 (complex regional pain syndrome* or causalgia).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (821)
107 somatosensory disorders/ (1367)
108 hyperalgesi*.mp. (5320)
109 exp Somatoform Disorders/ (15194)
110 ((noncancer* or non-cancer* or chronic* or recurrent or persist* or non-malign*) adj3 pain).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (23779)
111 radiculopath*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (351)
112 ((back or musculoskeletal) adj3 pain*).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (7604)
113 arthralgia.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (317)
114 headache*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (22401)
115 (backache* or backpain or dorsalgi* or arthralgi* or polyarthalgi* or arthrodyn* or myalgi* or fibromyalg* or myodny* or neuralg* or ischialg* or crps or

rachialgi*).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (8315)
116 ((back or discogen* or bone or musculoskelet* or muscle* or skelet* or spinal or spine or vertebra* or joint* or arthrit* or intestin* or neuropath* or neck or cervical* or head or facial* or complex or radicular or cervicobrach* or orofacial or somatic or shoulder* or knee* or hip or hips*) adj3 pain).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (20949)
117 or/84-116 (93580)
118 83 and 117 (86)
119 5 and 82 and 117 (86)

Appendix 2 Data extraction form

Researcher identification
Surname, name
Study identification
Study ID
Country
Funding
Study objectives or research questions
Study population
Description of patients
Response rate/ completion rate
Male %
Age
White %
Chronic pain %
Patients ever used cannabis %
Opioids use %
Aim intervention
Study design and methods
Study design
Sampling
Sample size
Data collection
Findings
Main findings (themes)
1. Values and preferences of outcome of medical cannabis 1.1 Relative value or importance patients put on outcomes of medical cannabis; 1.2 Tradeoff between benefits and harms or burdens of medical cannabis 2. Values and preferences towards medical cannabis 2.1 Values and preference for or against medical cannabis or choosing cannabis over

other medicines 2.2 Values and preferences of different preparations of medical cannabis (e.g. administration routes, ingestion method, ratio of THC to CBD) 3. Factors that influence the decision making regarding medical cannabis use 3.1 Factors that influence use or not use of medical cannabis 3.2 Factors that influence the choice of medical cannabis over other meds for pain management 3.3 Factors that influence the choice of different preparations of medical cannabis
Authors' interpretation
Authors' conclusions

Appendix 3 Tool and instructions for risk of bias assessment for quantitative studies

Domains	Participant selection	Completeness of data	Choice of measurement instrument	Administration of measurement instrument	Outcome/health state presentation	Participants' understanding of the measurement instrument	Data analysis	Overall risk of bias
Questions	Was the study sample selected in a manner to ensure the representativeness to the target population?	Was the attrition sufficiently low to minimize the risk of bias?	Was the choice of the methodology appropriate for addressing the study aim?	Was the instrument (or tools that was used to elicit values and preferences, e.g. questionnaire) administered in the intended way?	Was a valid representation of the outcome/health state (e.g. a state of pain relief - a beneficial outcome of medical cannabis, or an experience of coughing - a harmful outcome of medical cannabis) utilized?	Did the researchers check the understanding to the measurement techniques (e.g. questionnaire in a survey)?	Were the results analyzed appropriately?	
Instructions for questions	The sampling strategy solely does not determine the risk of bias; if there is a subset of the population more or less likely to be reached, the answer for "was the study sample selected in a manner to ensure the representativeness" is	Response rate for 80% or higher would be considered high for a cross-sectional study.	Consider yes or probably yes for the following methodologies: standard gamble, time trade off, visual analogue scale (or feeling thermometers), discrete choice,	-	If the researchers demonstrated they were using available evidence to support the health state presentation, the answer should be yes or probably yes.	If the methodology is simple, choosing "the investigators did not formally test the understanding, but the results suggested it was adequate"	To answer this question, reviewers also need to consider whether the adjustment, stratification, or model selection was appropriate.	· Low risk of bias= The study is classified as with low risk of bias across subdomains. · Moderate risk of bias= The study is classified as low (Yes -> low risk of bias) or moderate (Probably yes -> moderate risk

yes or probably yes.	treatment trade-off, willingness to pay	could be appropriate. If the researchers piloted the methodology, choosing “the investigators did not formally test the understanding, but the results suggested it was adequate” may also be appropriate.	This domain may not be applicable to all primary studies because not all studies will require controlled data analysis. Please check "NA" if not applicable.	of bias) risk of bias across subdomains. · Serious risk of bias= The study is classified as serious risk of bias (Probably no -> serious risk of bias) for at least one subdomain but not classified as critical risk of bias for any subdomain. · Critical risk of bias=The study is classified as critical risk of bias (No -> critical risk of bias) for at least one subdomain.	

Appendix 4 Tool and instructions for methodological limitation assessments for qualitative studies

Domains	Aim of the research	Qualitative methodology appropriateness	Research design	Appropriate recruitment strategy	Data collection	Investigator-participant relationship	Ethical issues	Data analysis	Findings	Value of the research	Overall methodological limitations
Questions	Was there a clear statement of the aims of the research?	Is a qualitative methodology appropriate?	Was the research design appropriate to address the aims of the research?	Was the recruitment strategy appropriate to the aims of the research?	Was the data collected in a way that addressed the research issue?	Has the relationship between researcher and participants been adequately considered?	Have ethical issues been taken into consideration?	Was the data analysis sufficiently rigorous?	Is there a clear statement of findings?	How valuable is the research?	
Instructions for questions	· what was the goal of the research · why it was thought important · its relevance	· If the research seeks to interpret or illuminate the actions and/or subjective experiences of research participants · Is qualitative research the right methodology for addressing the research goal	· if the researcher has justified the research design (e.g. have they discussed how they decided which method to use)	· If the researcher has explained how the participants were selected · If they explained why the participants they selected were the most appropriate to provide	· If the setting for the data collection was justified · If it is clear how data were collected · If the researcher has justified the methods chosen · If the	· If the researcher critically examined their own role, potential bias and influence during (a) formulation of the research questions (b) data collection, including sample	· If there are sufficient details of how the research was explained to participants for the reader to assess whether ethical standards were maintained · If the researcher has discussed issues raised by the study	· If there is an in-depth description of the analysis process · If thematic analysis is used. If so, is it clear how the categories/themes were derived from the data · Whether the researcher explains how the data presented	· If the findings are explicit · If there is adequate discussion of the evidence both for and against the researcher's arguments	· If the researcher discusses the contribution the study makes to existing knowledge or understanding (e.g. do they consider the findings in relation to current practice or policy, or relevant research-based literature · If they identify	· Serious = if more than 2 questions had "No". · Moderate = if 2 questions had "No". · No or minor = if less than 2 questions had "No".

access to the type of knowledge sought by the study · If there are any discussions around recruitment (e.g. why some people chose not to take part)	researcher has made the methods explicit · If methods were modified during the study. If so, has the researcher explained how and why · If the form of data is clear · If the researcher has discussed saturation of data	recruitment and choice of location · How the researcher responded to events during the study and whether they considered the implications of any changes in the research design	(e.g. issues around informed consent or confidentiality or how they have handled the effects of the study on the participants during and after the study) · If approval has been sought from the ethics committee	were selected from the original sample to demonstrate the analysis process · If sufficient data are presented to support the findings · To what extent contradictory data are taken into account · Whether the researcher critically examined their own role, potential bias and influence during analysis and selection of data for presentation	· If the researcher has discussed the credibility of their findings · If the findings are discussed in relation to the original research question	new areas where research is necessary · If the researchers have discussed whether or how the findings can be transferred to other populations or considered other ways the research may be used

Appendix 5 Characteristics of the included studies

Study ID	Country	Funding sources	Primary focus	Study design	Data collection methods	Sampling	Participants, n	Male Sex, %	Chronic pain, %	Chronic cancer pain, %	Prior use of cannabis, %	Risk of Bias/ Methodological Limitations
Bigand 2019	United States	Non-industry funding	To examine the perceived effects of medical cannabis among patients who are prescribed opioids for persistent pain conditions	Qualitative, Descriptive	Questionnaire	Convenience	150	31.3	100	NR	69.3	Serious
Boehnke 2019	United States	NR	To assess preferences towards medical cannabis products among medical cannabis users with chronic pain	Quantitative, Cross-sectional	Questionnaire	Convenience	1321	40.9	NR [a]	NR	100	Moderate
Bruce 2018	United States	Non-industry funding	To assess approaches to medical cannabis use vis-a-vis prescription medications among patients with chronic conditions	Qualitative, Descriptive	Semi-structured telephone interviews	Convenience	30	60.3	NR [b]	NR	100	No or minor
Cooke 2019	United States	Non-industry funding	To explore perspectives on the co-use of medical cannabis and opioids among clinicians, and	Qualitative, Modified grounded theory	Semi-structured in-person interviews	Purposive	46	45.6	100	0	45.7 [c]	Moderate

			patients with both chronic non-cancer pain and a history of substance use									
Degenhardt 2015	Australia	Non-industry funding	To investigate patterns and correlates of medical cannabis use among patients who are prescribed opioids for chronic non-cancer pain	Quantitative, Cross-sectional	Questionnaire, and diagnostic interview	Purposive	1514	44.4	100	0	43	Moderate
Gallagher 2003	Canada	NR	To survey willingness to try medical cannabis among patients with a known advanced life-limiting illness [d], and to assess this population's knowledge about medical cannabis	Quantitative, Cross-sectional	Discrete choice, VAS, Likert scales	Purposive	68	44.6	NR [e]	100 [d]	35.3	Critical
Gill 2001	United Kingdom	NR	To investigate beliefs about cannabinoids and the associations between those beliefs, beliefs about medication, and personal and pain variables in relation to willingness to try cannabinoids as analgesics, among	Quantitative, Cross-sectional	Questionnaire	Convenience	65	45	100	NR	NR	Serious

			patients with chronic pain who had interest in trying medical cannabis as an analgesic									
Heng 2018	United States	NR	To assess beliefs regarding using marijuana for medicine, post injury pain and speaking about marijuana to their health care providers, among patients who have a musculoskeletal injury in the last 1-6 months.	Quantitative, Cross-sectional	Questionnaire	Convenience	500	50	NR [f]	NR	60	Moderate
Lavie-Ajayi 2019	Israel	Non-industry funding	To explore and characterize the experience of using medical cannabis for chronic pain among patients receiving medical cannabis for at least three months	Qualitative, Phenomenological	Semi-structured in-person interviews	Purposive	19	52.6	100	5.3	100	No or minor
Notcutt 2004	United Kingdom	Non-industry funding	To evaluate the safety and tolerability of three CBMEs among patients with stable chronic pain, and poorly responsive to other modalities	Quantitative, RCT	NR	Convenience	34	32	100	NR	NR	Moderate

Piper 2017	United States	Non-industry funding	To survey perspectives of medical cannabis among legal members of medical cannabis dispensaries, and to examine the strengths and limitations of medical cannabis	Mixed Methods, Cross-sectional	Online survey, discrete choice, open-ended questions	Convenience and snowball	984	47.1	100 [g]	16.7	100	Serious
Rochford 2019	Ireland	NR	To evaluate attitudes towards medicinal cannabis among patients who attend chronic pain clinics	Quantitative, Cross-sectional	Questionnaire	Convenience	96	39.6	100	22.9	NR	Serious
Satterlund 2015	United States	Non-industry funding	To assess perceived risk, concern or overall stigma of marijuana use, and how this stigma may affect the health care among medical marijuana users [c]	Qualitative, Descriptive	Semi-structured interviews	Convenience and snowball	18	72	NR [h]	NR	100	Moderate
Sexton 2016	United States	Non-industry funding	To survey the patterns of use and perceived efficacy of medical cannabis among patients who have used medical cannabis in the last 90 days	Quantitative, Cross-sectional	Questionnaire	Convenience	1429	54.6	NR [i]	NR	100	Moderate
Zarrabi/Singh 2019	United States	Non-industry	To survey perceptions of the benefits and	Quantitative, Cross-	Questionnaire	Convenience	101	55.7	100	75.5	100	Serious

	funding	harms of medical cannabis, concerns about access to cannabis, and perceptions of support from family and health care providers, among patients with serious illness in APC	sectional

Note:

Abbreviation: APC: ambulatory palliative care, CBMEs: cannabis based medicinal extracts, CNCP: chronic non-cancer pain, NR: Not reported, RCT: Randomized controlled trial, US: United states, VAS: Visual Analogue Scale.

a Chronic overlapping pain conditions: back pain 58%, migraine 21%, fibromyalgia 15%, irritable bowel disease or Crohn's disease 14%, temporomandibular joint disorder 6%.

b Rheumatoid arthritis 23.3%, spinal cord disease or injury 20%, Chron's disease 20%, cancer 13.3%, hepatitis C 13.3%, post-traumatic stress disorder (PTSD) 13.3%, severe fibromyalgia 10%, other (chronic regional pain syndrome, epilepsy, HIV, MS, Parkinson's) 23.3%.

c Majority (≥80%) were patients with chronic and severe pain.

d Advanced life-limiting illnesses include malignancy, advanced cardiac, respiratory, liver or neurological diseases.

e The mean score of intensity of pain was 4.9 on a 0 to 10 VAS scale (0= absence of pain, 10=the worst pain intensity imaginable).

f Patients had experienced a musculoskeletal injury between 1 to 6 months before entry into the study.

g All the participants were legal members of medical cannabis dispensaries in the north-eastern US. Sixty-four percent of patients reported that they had been diagnosed with chronic pain by a medical professional.

h The authors stated "Maladies for which respondents used medical marijuana included migraine headaches, depression, chemotherapy and radiation treatment effects, chronic pain, and asthma, with the majority citing chronic and severe pain".

i Sixty-one percent of patients reported chronic pain, 35.5% had headache/migraine and the remaining 3.5% had other chronic pain conditions.

Appendix 6 Excluded studies and reasons for exclusion in full text screening

Study ID	Reason for exclusion
1. Aggarwal 2014	Not value and preference
2. Allan 2018	Not value and preference
3. Bekker 2018	Not value and preference
4. Cairns 2017	Not value and preference
5. Caplan B 2018	Not value and preference
6. Choo 2016	Not value and preference
7. Nickel 2018	Not value and preference
8. Djulus 2005	Not value and preference
9. Dowden 2019	Not value and preference
10. Gieringer 2003	Not value and preference
11. Harrison 2013	Not value and preference
12. Kepple 2016	Not value and preference
13. Kinnucan 2018	Not value and preference
14. Bachhuber 2018	Not value and preference
15. Zolotov 2016	Not value and preference
16. Lum 2019	Not value and preference
17. Martins-Welch 2017	Not value and preference
18. Naguib 2015	Not value and preference
19. Page 2015	Not value and preference
20. Parmar 2016	Not value and preference
21. Paut Kusturica2019	Not value and preference
22. Pearce 2014	Not value and preference
23. Pink 2012	Not value and preference
24. Piper 2018	Not value and preference
25. Reid 2013	Not value and preference
26. Reiman 2008	Not value and preference
27. Reisfield 2009	Not value and preference
28. Reynolds 2017	Not value and preference
29. Reynolds 2018	Not value and preference
30. Ste-Marie 2015	Not value and preference

31. Sutherland 2016	Not value and preference
32. Teigen 2019	Not value and preference
33. Toth 2015	Not value and preference
34. Volkow 2017	Not value and preference
35. Wallace 2015	Not value and preference
36. Wan 2017	Not value and preference
37. Ware 2010	Not value and preference
38. Wilsey 2015	Not value and preference
39. Winston-McPherson 2019	Not value and preference
40. Zaller 2015	Not value and preference
41. Ziadni 2018	Not value and preference
42. Zvolensky 2011	Not value and preference
43. Aggarwal 2018	Abstract only
44. Agornyo 2018	Abstract only
45. Bar-Sela 2014	Abstract only
46. Berg 2017	Abstract only
47. Burks 2016	Abstract only
48. Calvino 2017	Abstract only
49.Cofield 2015	Abstract only
50. Fitzcharles 2019	Abstract only
51.Galvin 2018	Abstract only
52. Gavigan 2019	Abstract only
53. Grella 2015	Abstract only
54.Gustavsen 2018	Abstract only
55.Kiszko 2017	Abstract only
56.Lee 2012	Abstract only
57. Mitra 2019	Abstract only
58. Muirhead 2015	Abstract only
59. Pires 2018	Abstract only
60. Rhyne 2019	Abstract only
61. Sabet 2014	Abstract only
62. Schnelle 1999	Abstract only

63. Wurtzen 2018	Abstract only
64.Grinberg 2018	Not patients with chronic pain or their carer
65. Iskedjian 2009	Not patients with chronic pain or their carer
66. Grotenhermen 2003	Not patients with chronic pain or their carer
67. LAU 2015	Not patients with chronic pain or their carer
68. Ishida 2019	Not patients with chronic pain or their carer
69. Lucas 2019	Not patients with chronic pain or their carer
70. Wan 2017	Not patients with chronic pain or their carer
71. Mendoza 2016	Not patients with chronic pain or their carer
72. Mendoza 2018	Not patients with chronic pain or their carer
73. Schenker 2019	Not patients with chronic pain or their carer
74. Sharon 2018	Not patients with chronic pain or their carer
75. St-Amant 2015	Not patients with chronic pain or their carer
76. Starrels 2018	Not patients with chronic pain or their carer
77. Starrels 2020	Not patients with chronic pain or their carer
78. Zolotov 2019	Not patients with chronic pain or their carer
79. Zolotov 2019	Not patients with chronic pain or their carer
80. Nouryan 2018	Not patients with chronic pain or their carer
81. Boehnke 2019	Not patients with chronic pain or their carer
82. Khelemsky 2017	Not patients with chronic pain or their carer
83. Vargas-Schaffer 2018	Not cannabis
84. Manchikanti 2008	Not cannabis
85. Mijatovic 2019	Not cannabis
86. Friedberg 2016	Personal experience
87. Greenberg 2019	Personal experience
88. Burke 2010	Value and preference data not elicited from patients or their carers

List of excluded studies at full text screening and reasons for exclusion

1. Not value and preference (n=42)

1. Aggarwal SK, Pangarkar S, Carter GT, Tribuzio B, Miedema M, Kennedy DJ. Medical marijuana for failed back surgical syndrome: A viable option for pain control or an uncontrolled narcotic? PM and R. 2014; 6: 363-72.
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3. Bekker A. Cannabis use and non-cancer chronic pain. The Lancet Public Health. 2018;3:e468.
4. Cairns EA, Kelly MEM. Why support a separate medical access framework for cannabis? Cmaj. 2017; 189: E927-E8.
5. Caulley L. Medical marijuana for chronic pain. New England Journal of Medicine. 2018; 379: 1575-7.
6. Choo EK, Ewing SWF, Lovejoy TI. Opioids Out, Cannabis in negotiating the unknowns in patient care for chronic pain. JAMA - Journal of the American Medical Association. 2016; 316: 1763-4.
7. Curtis Nickel J. Medical marijuana for urologic chronic pelvic pain. Canadian Urological Association Journal. 2018; 12: S181-S3.
8. Djulus J, Moretti M, Koren G. Motherisk update: Marijuana use and breastfeeding. Can Fam Physician. 2005; 51: 349-50.
9. Dowden A. Barriers to prescribing cannabis-based medicines. Prescriber. 2019; 30: 17-21.
10. Gieringer DH. The acceptance of medicinal marijuana in the U.S. Journal of Cannabis Therapeutics. 2003; 3: 53-65.
11. Harrison TE, Bruce BK, Weiss KE, Rummans TA, Bostwick JM. Marijuana and chronic nonmalignant pain in adolescents. Mayo Clinic proceedings. 2013; 88: 647-50.
12. Kepple NJ, Mulholland E, Freisthler B, Schaper E. Correlates of Amount Spent on Marijuana Buds During a Discrete Purchase at Medical Marijuana Dispensaries: Results from a Pilot Study. Journal of Psychoactive Drugs. 2016; 48: 50-5.
13. Kinnucan J. Use of medical cannabis in patients with inflammatory bowel disease. Gastroenterology and Hepatology. 2018; 14: 598-601.
14. Bachhuber MA, Arnsten JH, Starrels JL, Cunningham CO. Willingness to Participate in Longitudinal Research Among People with Chronic Pain Who Take Medical Cannabis: A Cross-Sectional Survey. Cannabis and Cannabinoid Research. 2018; 3: 45-53.

15. Zolotov Y, Baruch Y, Reuveni H, Magnezi R. Adherence to Medical Cannabis among Licensed Patients in Israel. Cannabis and Cannabinoid Research. 2016;1:16-21.

16. Lum HD. Medical Cannabis in Palliative Care: Meaningful Additions to the Research Evidence. Journal of Palliative Medicine. 2019;22:1173-4.

17. Martins-Welch D, Nouryan C, Kline M, Modayil S. Health providers' perspectives on medical marijuana use. Journal of Clinical Oncology. 2017;35 (31 Supplement 1):235.

18. Naguib M, Foss JF. Medical use of marijuana: Truth in evidence. Anesthesia and Analgesia. 2015;121:1124-7.

19. Page J, Ware M. Close the knowledge gap. Nature. 2015;525:S9.

20. Parmar JR, Forrest BD, Freeman RA. Medical marijuana patient counseling points for health care professionals based on trends in the medical uses, efficacy, and adverse effects of cannabis-based pharmaceutical drugs. Res Social Adm Pharm. 2016;12:638-54.

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6. Value and preference data not elicited from patients or their carers (n=1)

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Appendix 7 Risk of bias assessments for quantitative studies

Study ID (Reference number)	Was the study sample selected in a manner to ensure the representativeness to the target population?	Was the attrition sufficiently low to minimize the risk of bias?	Was the choice of the methodology appropriate for addressing the study aim?	Was the instrument (or tools that was used to elicit values and preferences, e.g. questionnaire) administered in the intended way?	Was a valid representation of the outcome/health state (e.g. a state of pain relief - a beneficial outcome of medical cannabis, or an experience of coughing - a harmful outcome of medical cannabis) utilized?	Did the researchers check the understanding to the measurement techniques (e.g. questionnaire in a survey)?	Were the results analyzed appropriately?	Overall risk of bias
Boehnke 2019 (21)	Probably yes	Probably yes	Probably yes	Yes	NA	Probably yes	Yes	Moderate
Degenhardt 2015 (24)	Probably yes	Yes	Yes	Yes	NA	Probably yes	Yes	Moderate
Heng 2018 (27)	Probably yes	Yes	Probably yes	Yes	NA	Probably yes	Yes	Moderate
Gill 2001 (26)	Probably yes	Yes	Yes	Probably yes	Probably no	Probably yes	Probably yes	Serious
Gallagher 2003 (25)	Probably yes	Probably no	Yes	Yes	Probably no	Probably no	Probably no	Critical
Piper BJ 2017 (35)	Yes	Probably no	Yes	Yes	NA	Yes	yes	Serious
Sexton 2016 (30)	Yes	Probably yes	Yes	Yes	NA	Yes	Yes	Moderate
Zarrabi 2020, Singh 2019 (31, 34)	Probably yes	Probably yes	Yes	Yes	Probably no	Probably no	Yes	Serious
Notcutt 2004 (33)	Probably yes	Probably Yes	Probably yes	Probably yes	NA	Probably yes	Probably yes	Moderate
Rochford 2019 (29)	Probably no	Probably yes	Probably yes	Probably yes	NA	Probably yes	Probably yes	Serious

Appendix 8 Methodological limitations assessments for qualitative studies

Study ID (Reference number)	Was there a clear statement of the aims of the research?	Is a qualitative methodology appropriate?	Was the research design appropriate to address the aims of the research?	Was the recruitment strategy appropriate to the aims of the research?	Was the data collected in a way that addressed the research issue?	Has the relationship between researcher and participants been adequately considered?	Have ethical issues been taken into consideration?	Was the data analysis sufficiently rigorous?	Is there a clear statement of findings?	How valuable is the research?	Overall methodological limitations
Bruce 2018 (22)	Yes	Yes	Yes	Can't tell	Yes	No	Yes	Yes	Yes	Yes	No or minor
Cooke 2019 (23)	Yes	Yes	Yes	Can't tell	Yes	No	Can't tell	Yes	No	Yes	Moderate
Bigand 2019 (20)	Yes	Yes	No	Can't tell	No	No	Yes	Yes	Yes	Yes	Serious
Lavie-Ajayi 2019 (28)	Yes	Yes	Yes	Yes	Yes	No	Can't tell	Yes	Yes	Yes	No or minor
Satterlund 2015 (32)	Yes	Yes	Yes	Can't tell	Yes	No	Yes	Yes	Yes	Yes	Moderate

Appendix 9 Evidence profile for review findings

Review finding	Explanation	Certainty assessment with GRADE/ GRADE CERQual							Certainty
		Study design (Reference number)	NO. of studies (participants)	Risk of bias/ Methodological limitations	Inconsistency/ Coherence	Indirectness/ Relevance	Imprecision/ Adequacy	Small effect bias	
1. Values and preferences towards medical cannabis									
1.1 Use of medical cannabis for chronic pain									
Patients had mixed levels of comfort or willingness to use medical cannabis.	[Quantitative] Most patients with advanced life-limiting illnesses were comfortable using cannabis for chronic pain and nausea (25), while other non-palliative patients with chronic pain were unwilling or ambivalent about medical cannabis use (26). Non-White patients with advanced illness were more concerned about medical cannabis compared to White patients, but they remained comfortable using medical cannabis (25). Chronic pain patients who use both medical cannabis and other prescription medications believed that medical cannabis was effective for managing	Quantitative (25,26,27)	3 (633)	Serious risk	Not serious	Serious	Not serious	Not serious	Low
	[Qualitative] Patients with a range of chronic medical conditions believed that medical cannabis was effective for pain (22).	Qualitative (22)	1 (30)	No or very minor concerns	NA	Minor concerns	Serious concerns	No or very minor concerns	Low

Most patients who use medical cannabis had a positive attitude toward its use for pain relief.	[Quantitative] Those using medical cannabis during their recovery believed that it reduced pain (25). Most individuals expressed positive aspects of medical cannabis use, such as pain reduction (27, 31, 34). The majority of participants with cancer in one study reported using cannabis products for a “cancer cure” (31). Some believed that cannabis should be legalized for medical purposes (29).	Quantitative (25,27,29,31,34)	4 (765)	Serious risk	Not serious	Serious	Not serious	Not serious	Low
	[Qualitative] Most individuals expressed use of medical cannabis for chronic pain was associated with a range of improved outcomes (e.g. better function, sleep, life changing etc.) (28).	Qualitative (28)	1 (19)	No or very minor concerns	NA	No or very minor concerns	Serious concerns	No or very minor concerns	Moderate
1.2 Medical cannabis over other pain medicines									
Patients with chronic pain and substance use histories preferred medical cannabis over prescription opioids.	[Qualitative] Patients with chronic pain and substance use histories preferred medical cannabis over prescription opioids to manage pain (23).	Qualitative (23)	1 (46)	No or very minor concerns	NA	Minor concerns	Serious concerns	No or very minor concerns	Low

Some patients believed that medical cannabis is safer than morphine and other strong pain killers.	[Quantitative] Some participants believed that because cannabis is a 'natural' product, it is safer than morphine and other strong pain killers (25). Non-Christians were more likely to believe that cannabis is safer than morphine (25). Those with high school education or less, were significantly less likely to believe that cannabis was safer than morphine (25).	Quantitative (25)	1 (68)	Very serious	Not serious	Serious	Serious	Not serious	Very low

1.3 Different preparations of medical cannabis

Cannabis variety (i.e. sativa, indica, hybrid)

Most patients preferred medical cannabis with a blend of indica and sativa, regardless of gender, reasons for use, and cannabis	[Quantitative] Most patients preferred using a blend of indica and sativa to manage chronic pain, followed by indica alone and sativa alone. There were no differences in cannabis variety preferences between males and females, those who use cannabis for medical purposes only and those who use for medical and recreational purposes, or novice and experienced users.(21)	Quantitative (21)	1 (1321)	Serious risk	Not serious	Not serious	Not serious	Not serious	Moderate

Cannabis content (i.e. THC or CBD potency, ratio of THC and CBD)

High THC and high CBD is the most preferred preparation, but gender, reason for use, and cannabis experience level influenced patients' preference for cannabis ratio.	[Quantitative] Females preferred low THC: high CBD, while males preferred equal ratios of THC: CBD. (21) Patients who use cannabis for medical purposes reported a greater preference for products with low THC: high CBD compared to individuals who use cannabis both medically and recreationally. (21) Both novice and experienced cannabis users preferred high CBD products most, and more novice users prefer low THC: high CBD while experienced users preferred high THC: high CBD.(21) Almost none preferred high THC and low CBD, low THC and low CBD, only CBD, or only THC.(21, 33)	Quantitative (21, 33)	2 (1355)	Serious risk	Not serious	Not serious	Not serious	Not serious	Moderate

Cannabis administration route

Gender, reason for use and cannabis experience level influenced patients' preferred cannabis administration routes.	[Quantitative] Females patients preferred to use tincture and topical preparations and less preferred to use vaporizing and smoking preparations compared with males. (21) Patients who used cannabis both recreationally and medically preferred smoking and vaporizing, while those who used cannabis medically only preferred smoking, vaporizing, tinctures, and edibles. (21) Experienced cannabis users preferred multiple administration routes compared with novice users. Smoking, vaporizing, and edibles were the most common preferred administration routes among both experience and novice users. (21) [Mixed] Among chronic pain patients who are legal members of medical cannabis dispensaries, a minority of participants preferred using a joint, pipe, or bong, while some preferred vaporizers, edibles, or tinctures; very few preferred concentrates or topicals. In addition, very few participants reported unpleasant routes of administration as what	Quantitative (21), Mixed (35)	2 (2305)	Serious risk	Not serious	Not serious	Not serious	Not serious	Moderate

Most patients who have an advanced life-limiting illness preferred an oral form of medical cannabis.	[Quantitative] Most patients who have an advanced life-limiting illness stated preference for an oral form (pill, droplets under the tongue, or droplets added to food) and only a minority preferred smoking. (25)	Quantitative (25)	1 (68)	Very serious	Not serious	Not serious	Serious	Not serious	Low

2. Factors that influenced patient's decision regarding use of medical cannabis

2.1 Factors influenced the choice of medical cannabis use

Most patients used medical cannabis because it improved the management of symptoms associated with pain, mental health and other medical conditions.	[Mixed] Some patients who were legal members of medical cannabis dispensaries preferred aspects of medical cannabis related to health and well-being, including pain relief, sleep benefits, limited addiction potential, improved quality of life, functionality, and relaxation, while others preferred general aspects of medical cannabis, like general improvement in the quality of life, functionality, cognitive aspects (35).	Mixed (35)	1(984)	Serious risk	Not serious	Not serious	Not serious	Not serious	Moderate

[Qualitative] Patients viewed medical cannabis as an effective approach to managing symptoms with or without other medications (20, 22, 23), including pain (20, 22, 23), disrupted sleep, poor appetite, and nausea (20). Patients reported that cannabis improved emotional and mental well-being by reducing anxiety, depression and stress (20). Patients also reported that cannabis allowed them to sleep, focus and function (28). Most patients reported that cannabis facilitated a state of relaxation in which pain could be dealt with in a more tolerable form (28). However, patients found that medical cannabis use sometimes made it difficult to manage their medication regimen (23).	Qualitative (20, 22, 23, 28)	4 (245)	Minor concerns	No or very minor concerns	No or very minor concerns	No or very minor concerns	No or very minor concerns	High

Most patients were motivated to use medical cannabis to reduce other prescription medications.	[Quantitative] Chronic pain patients who used both medical cannabis and prescription medications believed that medical cannabis was effective for pain relief and were motivated to use medical cannabis to decrease the amount of prescribed medications they used (27).	Quantitative (27)	1 (500)	Serious risk	Not serious	Not serious	Not serious	Not serious	Moderate

[Qualitative] Patients with a range of chronic medical conditions (22) believed that medical cannabis managed pain symptoms and were motivated to use medical cannabis to decrease the amount of prescribed medications they used (22).	Qualitative (22)	1 (30)	No or very minor concerns	NA	No or very minor concerns	Moderate concerns	No or very minor concerns	Moderate

The majority of patients expressed that their cannabis use was influenced by positive social consequences, such as social support from friends and family.	[Quantitative] A majority of patients agreed that cannabis for medical use would not cause disagreements or relationship problems with their loved ones (25). Most participants reported that their family members were supportive of their use, and the majority reported that their medical providers were supportive of their use (31,34).	Quantitative (25,31,34)	2 (2104)	Serious risk	Not serious	Not serious	Not serious	Not serious	Moderate

Most patients expressed concerns with using cannabis when describing a range of adverse effects from use of medical cannabis.	[Quantitative] Concerns about medical cannabis included concerns about side effects, addiction, tolerance, losing control or acting strangely, and were related to unwillingness to use cannabis (27). Patients who used cannabis to manage their pain had greater feelings of anxiety, and increased catastrophic thinking (26). Among those who were unwilling to use cannabis, increased age was related to more concerns about medical cannabis, including concerns of losing control (26). Increased age also impacted beliefs that cannabis was a useful medication to treat pain (27). Some patients reported that they were concerned about unpleasant physical or emotional symptoms suggestive of withdrawal after stopping medical cannabis use (31 , 34). Some patients were concerned about mental or physical dependence to medical cannabis; however, most did not perceive themselves as addicted to medical cannabis (31 , 34). Concerns about addiction were associated with unwillingness to use medical cannabis (26). [Mixed] Some patients who were legal members of medical cannabis dispensaries reported adverse physical, cognitive, and emotional effects of medical cannabis, as well as people's negative and stigmatizing values towards medical cannabis (35).	Quantitative (26, 27, 31, 34), Mixed (35)	4(1650)	Serious risk	Not serious	Not serious	Not serious	Not serious	Moderate

[Qualitative] Patients commonly reported lack of concentration, poor memory and sleepiness as consequences of medical cannabis use. Participants also reported minor consequence which included eating too much, coughing, and weight gain. Seizures and anaphylaxis from an allergic reaction were described as severe consequences from use (20). Some patients were concerned that, while medical cannabis helped with pain management, it might lead addiction (23). Patients with a history of addiction were concerned that medical cannabis use could pose a threat to their sobriety (23).	Qualitative (20, 23)	2 (196)	Moderate concerns	No or very minor concerns	No or very minor concerns	Minor concerns	No or very minor concerns	Moderate

Most patients expressed that their cannabis use was influenced by negative social consequences, such as stigma.	[Quantitative] Patients who were comfortable with their cannabis use for pain had a significant concern over the use of cannabis leading to relationship problems or disagreements with loved ones (25). Some patients agreed that medical cannabis would make them vulnerable to attack and theft by substance abusers. A minority of patients agreed that medical cannabis would cause problems with the law, and that they may be arrested or charged with possession of cannabis (25). Some patients expressed concerns about others' opinions towards their used of cannabis-related products (31,34).	Quantitative (25,26,31, 34), Mixed (35)	4 (3153)	Serious risk	Not serious	Not serious	Not serious	Not serious	Moderate

	[Qualitative] Commonly reported negative social consequences included judgment from others as a result of use and "stoner" or "pothead" stereotypes (20, 32). Some patients reported that stigma affected the way they asked healthcare providers about cannabis as a treatment option, the ability to seek out medical cannabis as a treatment option, the location at which they purchased cannabis, and their ability to use cannabis in public. Patients who reported these factors tended to take longer to seek out cannabis as a treatment option, conceal their use, and would not speak to healthcare providers about cannabis (32).	Qualitative (20, 32)	2 (168)	Moderate concerns	No or very minor concerns	No or very minor concerns	Minor concerns	No or very minor concerns	Moderate
The cost, legal status, and accessibility of medical cannabis influenced patients' decisions to use medical cannabis.	[Quantitative] Some patients were concerned about the cost of medical cannabis and some were concerned about the legal status and accessibility of medical cannabis (31). Some patients reported that they would use medical cannabis if they had access to it (24). When making decisions about medical cannabis, the majority of patients relied on information from doctors, followed by the internet and friends or family (31, 34). [Mixed] Some patients who were legal members of medical cannabis dispensaries were	Quantitative (24,31), Mixed (35)	3 (2599)	Serious risk	Not serious	Not serious	Not serious	Not serious	Moderate

[Qualitative] Some patients felt that the cost of medical cannabis was too high, potentially limiting their access (20), while some reported that the legalization of medical cannabis improved access and influenced their decisions to purchase medical cannabis for symptom relief (20). Other patients found changes in policies related to medical cannabis difficult to navigate and wanted assistance to access medical cannabis (23).	Qualitative (20, 23)	2 (196)	Moderate concerns	No or very minor concerns	No or very minor concerns	Minor concerns	No or very minor concerns	Moderate

2.2 Factors influencing the choice of different preparations of medical cannabis

Patients chose medical cannabis products mainly based on cannabinoid content, recommendations from dispensary employees, described effects and side effects, cannabis variety, smell, and flower appearance.	[Quantitative] Most patients selected medical cannabis products based on cannabinoid content (e.g. THC), recommendations from dispensary employees, described effects, and cannabis variety (i.e. indica vs. sativa). A minority of patients selected cannabis based on visual properties and smell, and some patients were guided by recommendations from a friend, or name of the product. Recommendations from a medical professional was the least common factor that patients would consider when selecting medical cannabis (21). When selecting medical cannabis products, patients consider the following factors: the most commonly factors were smell, delta 9-tetrahydrocannabinol (THC) content, hybrid indica/sativa species, indica species, how the flower looks (size, density of the flower, and/or trichome and shape, cannabidiol (CBD) content, and sativa species. Some patients reported varietal name as important factor for medical cannabis selection.(30)	Quantitative (21, 30)	2 (2750)	Serious risk	Not serious	Serious	Not serious	Not serious	Low

[Qualitative] One study reported that long lasting effect of medical cannabis positively influenced patients choice of medical cannabis product (22). Another two studies reported that patients' uncertain about how they could determine which species of cannabis might work best to manage their pain and side effects of medical cannabis (e.g. headaches, disorientation or the sensation of feeling "stoned," coughing) negatively influence patients choice of medical cannabis product (23, 28).	Qualitative (22, 23,28)	3 (95)	No or very minor concerns	Moderate concerns	No or very minor concerns	Serious concerns	No or very minor concerns	Low

Gender, reason for use, and level of use experience influenced the factors patients considered when selecting cannabis products.	[Quantitative] Selection of cannabis product were influenced by gender, reason for use (e.g., medical only vs. medical and recreational), and cannabis experience level (e.g., novice vs. experienced). (21) A higher proportion of males selected cannabis products based on cannabinoid content (i.e. THC or CBD potency, ratio of THC and CBD), cannabis variety (i.e. indica or sativa), visual properties, and smell. A higher proportion of females consulted with a medical professional when choosing cannabis products. (21) Patients who use cannabis both medically and recreationally were more likely to select cannabis products based on THC or other cannabinoid content, cannabis variety, described effects, visual properties, smell, recommendation from friends, and the product name, while those who use cannabis medically were more likely use recommendations from dispensary employees or a medical professional. (21) Novice users were more likely to select a cannabis product based on dispensary recommendation consult with a medical professional than experienced users, while experienced users chose products based on nearly all other selection factors including smell, visual properties, described effects, cannabinoid content (i.e. THC or CBD potency, ratio of THC and CBD), cannabis variety (i.e. indica or sativa) and name of medical cannabis product (21).	Quantitative (21)	1 (1321)	Serious risk	Not serious	Not serious	Not serious	Not serious	Moderate

Abbreviations: CBD = cannabidiol; THC = delta-9-tetrahydrocannabinol.

MOOSE Checklist for Meta-analyses of Observational Studies

Item No	Recommendation	Reported on Page No
Reporting of background should include		
1	Problem definition	5
2	Hypothesis statement	5,6
3	Description of study outcome(s)	6
4	Type of exposure or intervention used	6
5	Type of study designs used	6
6	Study population	6
Reporting of search strategy should include		
7	Qualifications of searchers (eg, librarians and investigators)	7,8
8	Search strategy, including time period included in the synthesis and key words	7 & Appendix 1
9	Effort to include all available studies, including contact with authors	7
10	Databases and registries searched	7
11	Search software used, name and version, including special features used (eg, explosion)	7,8
12	Use of hand searching (eg, reference lists of obtained articles)	7
13	List of citations located and those excluded, including justification	11 & Appendix 6
14	Method of addressing articles published in languages other than English	8
15	Method of handling abstracts and unpublished studies	8
16	Description of any contact with authors	n/a
Reporting of methods should include		
17	Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested	7,8
18	Rationale for the selection and coding of data (eg, sound clinical principles or convenience)	9
19	Documentation of how data were classified and coded (eg, multiple raters, blinding and interrater reliability)	9
20	Assessment of confounding (eg, comparability of cases and controls in studies where appropriate)	n/a
21	Assessment of study quality, including blinding of quality assessors, stratification or regression on possible predictors of study results	8,9
22	Assessment of heterogeneity	9,10
23	Description of statistical methods (eg, complete description of fixed or random effects models, justification of whether the chosen models account for predictors of study results, dose-response models, or cumulative meta-analysis) in sufficient detail to be replicated	9
24	Provision of appropriate tables and graphics	Figure 1, Tables 1 & 2, Supplementary File
Reporting of results should include		
25	Graphic summarizing individual study estimates and overall estimate	n/a
26	Table giving descriptive information for each study included	Table 1
27	Results of sensitivity testing (eg, subgroup analysis)	n/a

28	Indication of statistical uncertainty of findings	Table 2

Item No	Recommendation	Reported on Page No
Reporting of discussion should include		
29	Quantitative assessment of bias (eg, publication bias)	n/a
30	Justification for exclusion (eg, exclusion of non-English language citations)	18
31	Assessment of quality of included studies	16
Reporting of conclusions should include		
32	Consideration of alternative explanations for observed results	17,18
33	Generalization of the conclusions (ie, appropriate for the data presented and within the domain of the literature review)	18
34	Guidelines for future research	18
35	Disclosure of funding source	20

From: Stroup DF, Berlin JA, Morton SC, et al, for the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) Group. Meta-analysis of Observational Studies in Epidemiology. A Proposal for Reporting. *JAMA*. 2000;283(15):2008-2012. doi: 10.1001/jama.283.15.2008.

BMJ Open

Values and preferences towards medical cannabis among people living with chronic pain: A mixed methods systematic review

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2021-050831.R1
Article Type:	Original research
Date Submitted by the Author:	20-May-2021
Complete List of Authors:	Zeng, Linan; West China Second University Hospital, ; McMaster University, Lytvyn, Lyubov; McMaster University Wang , Xiaoqin ; McMaster University Kithulegoda, Natasha; Women's College Hospital Agterberg, Silvana; Yeshiva University Shergill, Yaad; McMaster University Esfahani, Meisam; McMaster University Heen, Anja; Innlandet Hospital Trust, Department of Medicine Agoritsas, Thomas; McMaster University, Department of Clinical Epidemiology and Biostatistics; University Hospitals of Geneva, Division of General Internal Medicine & Division of Epidemiology Guyatt, Gordon; McMaster University, Busse, Jason; McMaster University, Anesthesia
Primary Subject Heading:	General practice / Family practice
Secondary Subject Heading:	Patient-centred medicine, Qualitative research
Keywords:	QUALITATIVE RESEARCH, Pain management < ANAESTHETICS, GENERAL MEDICINE (see Internal Medicine)

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Values and preferences towards medical cannabis among people living with chronic pain: A mixed methods systematic review

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Abstract

Objective To explore values and preferences towards medical cannabis among people living with chronic pain.

Design Mixed methods systematic review.

Data sources We searched MEDLINE, EMBASE, and PsycInfo from inception to March 17, 2020.

Study selection Pairs of reviewers independently screened search results and included quantitative, qualitative and mixed methods studies reporting values and preferences towards medical cannabis among people living with chronic pain.

Review methods We analyzed data using meta-narrative synthesis (quantitative findings were qualitized) and tabulated review findings according to identified themes. We used the GRADE approach to assess certainty of evidence.

Results Of 1,838 initial records, 15 studies proved eligible for review. High to moderate certainty evidence showed that patient's use of medical cannabis for chronic pain was influenced by both positive (e.g. support from friends and family) and negative social factors (e.g. stigma surrounding cannabis use). Most patients using medical cannabis favored products with balanced ratios of tetrahydrocannabinol (THC) and cannabidiol (CBD), or high levels of CBD, but not high THC preparations. Many valued the effectiveness of medical cannabis for symptom management even when experiencing adverse events related to concentration, memory, or fatigue. Reducing use of prescription medication was a motivating factor for use of medical cannabis, and concerns regarding addiction, losing control or acting strangely were disincentives. Out-of-pocket costs were a barrier, whereas legalization of medical cannabis improved access and incentivized

use.

Low to very low certainty evidence suggested highly variable values towards medical cannabis among people living with chronic pain. Individuals with pain related to life-limiting disease were more willing to use medical cannabis, and preferred oral over inhaled administration.

Conclusions Our findings highlight factors that clinicians should consider when discussing medical cannabis. The variability of patients' values and preferences emphasize the need for shared decision making when considering medical cannabis for chronic pain.

Systematic review registration: The Open Science Framework (OSF) (https://osf.io/5d72w).

Word count: 3126

Strengths and limitations of this study

- Consideration of complementary bodies of evidence (qualitative, quantitative and mixed-methods) and use of the GRADE approach to assess the certainty of evidence provide greater confidence in the interpretation of results.

- Most eligible studies are from high-income countries, reflecting values and preferences of patients living in better health care service systems with health insurance coverage. The generalizability of our findings to other populations in uncertain.

- Studies eligible for this review failed to consistently report participants' socio-economic status, educational level, and religious beliefs, limiting exploration of the impact of these characteristics on values and preferences towards medical cannabis for chronic pain.

INTRODUCTION

Chronic pain is the major cause of non-fatal disease burden worldwide,[1] and is estimated to affect one in five adults in the general global population[2] and one in three in low and middle-income countries.[3] Opioids are commonly prescribed for chronic pain; however, increasing awareness of modest benefits and risks of addiction, overdose and death have generated interest for alternative management strategies. Medical cannabis, whose two most studied active ingredients are delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD), is one such therapeutic alternative.[4] Moreover, the legalization of medical cannabis among more than 30 countries[5] has increased access for people living with chronic pain who are considering this option. Accordingly, physicians are increasingly faced with questions from patients about the potential role of medical cannabis in managing their pain.[6]

Physicians who seek guidance from current clinical practice guidelines regarding medical cannabis for chronic pain will find recommendations to be inconsistent. As examples, the UK's National Institute for Health and Care Excellence (NICE) recommends against prescribing cannabis-related products for chronic pain, citing its high cost and inadequate supporting evidence.[7] The American Academy of Neurology (ANN) recommends an oral cannabis extract containing both THC and CBD as having the highest level of empirical support as a treatment for chronic pain associated with multiple sclerosis.[8] These guidelines, and others, have neglected to systematically identify and incorporate target patients' values and preferences, which may affect their findings.

Understanding patients' values and preferences, defined as patient-important desirable and undesirable consequences weighed when making a recommendation,[9]

can improve the trustworthiness of recommendations. Therefore, we conducted a systematic review investigating values and preferences towards the use of medical cannabis among people living with chronic pain. This systematic review is part of the BMJ Rapid Recommendations project, a collaborative effort from the MAGIC Evidence Ecosystem Foundation (www.magicevidence.org) and the British Medical Journal. This systematic review informed a parallel guideline published on bmj.com and MAGICapp (please insert link to guideline).[10]

METHODS

We registered and published our study protocol on the Open Science Framework (OSF) (https://osf.io/5d72w) and adhered to the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) statement.

Data source and Searches

We searched MEDLINE, EMBASE, and PsycInfo from inception to March 17, 2020, using a combination of search filters for retrieving studies on values and preferences towards cannabis use among people living with chronic pain (Appendix 1).[11] We reviewed reference lists of all included studies and relevant reviews to identify additional eligible studies.

Study selection

We included quantitative, qualitative (including survey research that only reported qualitative findings) and mixed-methods studies that reported values and preferences of people living with chronic cancer or non-cancer pain, or their carers, on: 1) relative values or importance of outcomes related to medical cannabis use (e.g. improvements in pain and function, side effects) for chronic pain (defined as pain lasting three months or longer); 2) formulation of medical cannabis (e.g. administration routes, ingestion methods, ratios of THC to CBD); or 3) factors that influence the decision to use medical cannabis. If studies enrolled both acute and chronic pain patients, we considered them eligible if they reported outcomes of chronic pain patients separate from others, or if at least 80% of patients were affected by chronic pain.

We excluded studies that: 1) did not elicit data from patients or carers directly (e.g. data elicited from health providers; information from databases of health records); 2) only reported health state values or quality of life of people living with chronic pain, not related to use of medical cannabis; 3) only reported correlation analyses of associations among demographic variables, other patient characteristics, and medical cannabis use for chronic pain; 4) case studies with less than 10 patients; 5) studies published in languages other than English, or 6) abstracts and literature reviews.

Before beginning each phase of the review process, we conducted calibration exercises in which reviewers assessed the same two articles and discussed any disagreements, leading to clarification and a common understanding of criteria and process. After calibration, six paired reviewers (LZ & XW, NK & SA, YS & MA) independently screened titles and abstracts of all retrieved references, and the full text of articles deemed potentially eligible. We resolved disagreements by discussion or consultation with an adjudicator (LL).

Data collection and risk of bias assessment

Three pairs of reviewers (LZ & XW, NK & SA, YS & MA) extracted data from eligible studies, independently and in duplicate, for research questions, population characteristics, design and methods of data collection, risk of bias or methodological limitations, and main findings (Appendix 2). For main findings, we selected two eligible articles per study design, identified key themes addressed in the studies, and then coded the themes as different categories for main findings in the data abstraction form (Appendix 2).[12] We resolved disagreements through discussion to

reach consensus, or in consultation with an adjudicator (LL).

For quantitative studies, we used GRADE (Grading of Recommendations Assessment, Development and Evaluation) guidance for studies of values and preferences to assess risk of bias of individual studies (Appendix 3).[13] For qualitative studies, we used the Critical Appraisal Skills Programme (CASP) checklist to assess methodological reporting quality of individual studies (Appendix 4).[14]

Data synthesis and analysis

Using an iterative process, we compared themes of the categories identified across all studies and developed analytic themes.[12] We applied critical meta-narrative synthesis, a modified form of critical interpretive synthesis, to transform quantitative into qualitative data using systematic profiles and critical questions that are asked to further extract narratives from the data. [15.16] To facilitate this transformation, we applied four types of profiles to transform the extracted quantitative data that had the potential to be qualitized, or converted into narratives (Table 1).[12,16] By using inductive content analysis we synthesized the qualitized findings to produce review findings which addressed the key themes.

Certainty of Evidence

For review findings from quantitative studies, we assessed the certainty of evidence according to the five GRADE domains (i.e. risk of bias, imprecision, inconsistency, indirectness, and small study effects)[13,17,18] For review findings from qualitative studies, we assessed the certainty of evidence according to the five GRADE-CERQual (Confidence in the Evidence from Reviews of Qualitative Research) domains (i.e.

methodological limitations, relevance, coherence, adequacy and dissemination bias).[19] We initially considered the certainty of evidence as high, and if serious or several minor or moderate concerns were detected in one or more domains, we rated down certainty of evidence by one or more levels to moderate, low or very low.

Patient and public involvement

We engaged three people living with chronic pain, one of whom used medical cannabis, to review our findings and advise if they were consistent with their experiences. Led by the MAGIC Evidence Ecosystem Foundation, a BMJ RapidRec panel of clinicians, methodologists and persons with lived experience of chronic pain were responsible for developing clinical practice recommendations for medical cannabis and chronic pain. Three patient partners were full members of the guideline panel and received training and support to optimise contributions throughout the guideline development process. The panel developed recommendations using the GRADE framework, available online through the MAGICapp (please insert link to guideline),[10] and considered evidence from systematic reviews on the effectiveness of medical cannabis, adverse events related to medical cannabis, opioid substitution with medical cannabis, and this review of patients' values and preferences regarding medical cannabis to manage chronic pain.

RESULTS

Our search retrieved 1,838 records, of which 102 were deemed potentially eligible based on titles and abstracts. After full text screening, 15 studies (reported in 16 articles) proved eligible for review, including nine quantitative studies, five qualitative studies and one mixed method study (Figure 1, Appendix 5,6) [20-35]

Study characteristics

Of the 15 studies, nine were conducted in the United States, two in the United Kingdom, two in Israel, one in Canada, and one in Australia. Four studies were conducted between 2000 and 2009, and 11 were conducted between 2010 and 2019. The number of participants ranged from 34 to 1,514 among quantitative studies, 18 to 150 in the qualitative studies, and 984 were enrolled in the mixed method study. All 15 studies included only chronic pain patients; no caregivers were enrolled. (Appendix 5)

Among the nine quantitative and one mixed method studies, four were at serious and one at critical risk of bias due to lack of valid representation of the outcomes (e.g. beneficial or harmful outcomes of medical cannabis), low response rate (less than 80%) and lack of reporting on how the authors confirmed participants' understanding of the measurement techniques (e.g. questionnaire) (Appendix 7). Among the five qualitative studies, only one was at serious risk of bias due to inadequate research design and data collection, and lack of reporting on whether the relationship between researchers and participants had been adequately considered (Appendix 8).

Findings

We identified two key themes: values and preferences towards medical cannabis for chronic pain (seven quantitative studies [2,185 participants]), three qualitative studies [95 participants], and one mixed method study [984 participants]) and factors that influenced patient's decisions regarding use of medical cannabis (seven quantitative studies [4,998 participants], five qualitative studies [263 participants], and one mixed method study [984 participants]). (Table 2, Appendix 9).

Use of medical cannabis for chronic pain

Low certainty evidence showed that patients had mixed levels of willingness to use medical cannabis and most patients who used medical cannabis reported positive attitudes toward its use. Most patients with advanced life-limiting illnesses were comfortable using cannabis for pain [25], while some other patients with chronic pain were unwilling or ambivalent about medical cannabis use[26] . Non-White patients with advanced illness were more concerned about medical cannabis compared to White patients, but they remained comfortable using medical cannabis [25]. People living with chronic pain who used medical cannabis believed it was effective for reducing their pain [25 27 31 34] and allowed them to reduce use of prescribed medications [27]. Two qualitative studies found similar results [22 28].

Medical cannabis vs. other pain medicines

Patients with histories of substance use preferred medical cannabis over prescription opioids (Low certainty).[23] Some patients endorsed that medical cannabis was safer than other analgesics, and such beliefs were more prevalent among non-Christians

and patients with colleges education or higher (Very low certainty).[25]

Different preparations of medical cannabis

Moderate certainty evidence showed that most people living with chronic pain preferred using a blend of indica and sativa to manage their condition.[21] There was no difference in the preference of cannabis strain between males and females, those who used cannabis for medical purposes only and those who endorsed medical and recreational use, or between novice and experienced users.[21]

Most patients preferred medical cannabis products with either balanced ratios of THC:CBD (37%) or high CBD formulations (46%), and only a minority (17%) preferred high THC products (Moderate certainty).[21 33] Specifically, women, novice users, or those who endorsed use of cannabis for medical purposes only were more inclined to choose products with low THC and high CBD ratios, while males, those endorsing use of cannabis for both medical and recreational purposes, and experienced users preferred products with equal ratios of THC:CBD.[21]

Sex, reason for use, and experience with cannabis influenced preference towards route of administration (Moderate certainty). [21 35] Compared to male patients, women preferred to use tinctures and topical preparations as opposed to vaporizing or smoking [21]. Patients who used cannabis both recreationally and medically preferred smoking most, while those who used cannabis medically only preferred vaporizing most. [21] Experienced cannabis users endorsed multiple routes of administration compared with novice users who preferred vaporizing.[21] Most patients with advanced life-limiting illness preferred oral formulations (non-inhaled) of medical cannabis. [25]

Factors influencing the decision to use medical cannabis

High to moderate certainty evidence showed that most people living with chronic pain used medical cannabis for symptom relief.[20 22 23 28 35] Specifically, patients viewed medical cannabis as an effective approach to managing pain[20 22 23 35], sleep, appetite, and nausea. [20, 35] Patients also reported that cannabis improved their emotional and mental well-being by reducing anxiety, depression and stress,[20 35] and increased their ability to focus and function[28]. Most patients reported that cannabis facilitated a state of relaxation in which pain remained present but was easier to tolerate [28].

Moderate certainty evidence showed that factors related to patients' unwillingness to use medical cannabis include major side effects (e.g. losing control or acting strangely) [20 23 26 27 31 34 35], addiction or tolerance [26 27 31 34 35], and negative social consequences (e.g. stigma)[25 26 31 34, 20 32 35]. Older age was associated with greater hesitancy to use medical cannabis, as was concerns about negative opinions from others which might lead to relationship problems or disagreements with loved ones [25 26 31 34]. Some patients reported that stigma affected their comfort in asking healthcare providers about cannabis as a treatment option, and their willingness to use medical cannabis in a public setting [32]. Moderate certainty evidence showed that cost, legal status, and accessibility of medical cannabis also influenced use[31 34 20 23-25 35].

Factors influencing the choice of different preparations of medical cannabis

Low certainty evidence suggested that most patients chose medical cannabis

products based on cannabinoid content (i.e. THC or CBD potency, ratio of THC and CBD), recommendations from dispensary employees, described effects (e.g. pain relief), strain of cannabis plant (i.e. sativa, indica, hybrid), smell, or varietal name.[21 22 23 28 30] A higher proportion of males selected cannabis products based on cannabinoid content, cannabis variety, visual properties, and smell, while a higher proportion of females consulted with a medical professional when choosing cannabis products (Moderate certainty). [21]

Patients who used cannabis both medically and recreationally were more likely to select cannabis products based on cannabinoid content, cannabis variety, described effects, visual properties, smell, recommendations from friends, and the product name, while those who only used cannabis medically were more likely to prioritize recommendations from dispensary employees or medical professionals (Moderate certainty). [21]

DISCUSSION

Values and preferences among patients with chronic pain towards the use of medical cannabis are highly variable. Improvement of symptoms and reduction of prescription medications are important factors that positively influence patients' decision to use medical cannabis, while concerns about addiction, losing control, acting strangely and negative social consequences are associated with unwillingness to use medical cannabis. Cost, legal status and accessibility are also important factors. Patients who endorsed use of cannabis for only medical reasons preferred high CBD or similar ratios of THC: CBD products, whereas those endorsing use of both medical and recreational purposes were more likely to use higher THC products. Further, patients with chronic pain endorsing both medical and recreational use were more likely to prefer smoking cannabis, versus patients who endorsed only medical use who preferred vaporizing. Our findings were consistent across bodies of evidence (quantitative, qualitative, and mixed method studies). The certainty of evidence for most findings was moderate, predominantly due to risk of bias or imprecision/ adequacy.

We asked three patient partners on the BMJ rapid recommendation panel for their comments on the findings of this systematic review. In particular, 1) whether our findings reflected their experiences, and 2) if some of the findings were different from their experience, what were possible reasons? The patient partners agreed that all except one of our review findings (Table 2) reflected their experiences with cannabis. Specifically, they suggested that patients who are using medical cannabis may not receive support from family or friends due to stigma and misinformation about cannabis use.

Our findings that some patients select medical cannabis based on properties that

dispensers attributed to strain type (indica or sativa), represents an opportunity for education. When these strains were originally characterized, sativa was shown to produce higher amounts of CBD whereas indica strains of cannabis produced high levels of THC. At present, however, commercially available cannabis plants and products have been extensively interbred to produce a multitude of unique strains. [36] As such, the only reliable way to determine the composition of any form of medical cannabis is through accurate reporting of the cannabinoid (e.g. THC, CBD) content.

We found important differences between patients who use cannabis for medical reasons only and those who report combined use (medical and recreational) in preferences regarding cannabis content and route of administration. Observational studies have shown that most consumers of cannabis endorse medical and recreational use, [37] [38] which presents a challenge to therapeutic use. Recreational users often prioritize cannabis with high THC concentrations, a psychotropic cannabinoid that is associated with greater harms than CBD.[39] [40] Patients that use cannabis for both medical and recreational purposes are also more likely to prefer inhaled forms of administration, which has a much faster onset and greater bioavailability than ingestion but also entails pulmonary risk factors due to inhalation of toxins and particulate matter.[41] Therapeutic use of cannabis should prioritize formulations supported by evidence, administered in a manner that prioritizes both safety and effectiveness.

Strengths and limitations of the review

Strengths of this review include explicit eligibility criteria, an extensive search strategy, and duplicate assessment of eligibility and risk of bias. The use of complementary

bodies of evidence (qualitative, quantitative and mixed-methods) and the use of the GRADE approach to assess the certainty of evidence allowed greater confidence in the interpretation of results.

This study also had limitations. Most of the eligible studies (13 out of 15 studies) are from high-income countries, reflecting values and preferences of patients living in better health care service systems with health insurance coverage. The generalizability of our findings to other populations in uncertain. In addition, we synthesized and reported patients' willingness to use medical cannabis despite the limitation that most studies did not provide participants with sufficient information about the benefits and harms of medical cannabis. Studies failed to consistently report participants' socio-economic status, educational level, and religious beliefs, limiting exploration of the effect of these characteristics on values and preferences.

Implications

Our findings have direct implications for clinicians attending people living with chronic pain who are considering use of medical cannabis. Benefits (effect on pain and reduction of prescription medications), harms (adverse effects), burdens (negative social consequences, cost) and accessibility (including legal status) of medical cannabis all appear to influence patients' decisions related to use. However, we did not identify any studies that considered how patients prioritized these factors. Subsequent research should address this issue. In addition, how patient characteristics (e.g. medical conditions, social economic status, religious beliefs) affect their values and preferences is another issue worth addressing in subsequent research.

CONCLUSIONS

There exists high variability of values and preferences towards medical cannabis among people living with chronic pain, particularly related to their willingness to use medical cannabis. These findings suggest that an individualized patient-centred approach, such as shared decision-making, should be emphasized for empowering patients to make choices that best suit their own values and preferences and accommodate their context.

Figure Legends

Figure 1: Evidence search and selection

Contributors

LZ, XW, NK, SA, YS and MAE identified and selected the studies. LZ, XW, NK, SA, YS and MAE collected the data. LZ, LL, XW, NK and SA analysed the data and assessed the certainty of the evidence. AFH, TA, GG and JWB provided advice at different stages. LZ, LL, XW, NK, SA drafted the manuscript. All authors revised the manuscript and approved the final version of the manuscript.

Funding

XW is supported by a post-doctoral fellowship from the Michael G. DeGroote Institute for Pain Research & Care.

Competing interests None

Ethical approval: Ethics approval for this study was not required.

Data sharing: Raw data are available on request from the corresponding author.

Acknowledgement We thank Rachel Couban (McMaster University) for performing the literature search; we thank Ray Zhang (McMaster University) for providing consult with the certainty of evidence rating; we thank Shelly-Anne Li (University of Toronto) for providing suggestions on data synthesis; we thank our patient partners for providing comments on review findings.

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Table 1 Critical meta-narrative synthesis: from quantitative data to narratives

Systematic profiles[a]			Critical questions
Technique	**Focus**	**Example**	
Modal profile	The most frequently occurring attributes	When asked to state the preference for route of administration: 86% (69/80) patients were comfortable with an oral form (pills, drops or added to food), while 15% (12/80) chose smoking . **This was qualitized as**: Most patients stated preference for oral formulations, while a minority preferred inhaled products.	What is this study trying to say about patients' values? Are patients' values and preferences explicitly identified? If so, what are they? How do participants' answers to the questions provide insight into patients' values and preferences, and their influence on the choice of treatment for chronic pain? How different (or similar) are patients' and carers' perspectives on medical cannabis for chronic pain? Are there other individual or contextual factors (e.g., age, gender, socioeconomic status) that influence patients' values and preferences towards medical cannabis for chronic pain?
Average profile	Average of the particular variables	Patients' concerns regarding medical cannabis using a 10-point scale (0 = not concerned, 10= extremely concerned) were, in order of important: side effects (mean = 7.0±2.9), addiction (6.6±3.2), tolerance (6.2±3.2), losing control or acting strangely (6.2±3.3), and what family and friends may think (3.9±3.8). **This was qualitized as:** Patients were generally most concerned about the side effects of medical cannabis, followed by addiction, tolerance, losing control or acting strangely, and what family and friends may think.	
Comparative profile	A comparison of key outcomes	Patients were asked to rate their values and concerns regarding use of cannabis (strongly agree, agree, disagree, strongly disagree and don't know). Significantly more males, vs. women, were concerned about cannabis being addictive (p =0.031), leading to the use of more harmful substances (p =0.036), and causing an inability to think clearly (p =0.008). **This was qualitized as:** Compared to females, significantly more males were concerned about cannabis being addictive, leading to the use of more harmful substances, and causing an inability to think clearly.	
Holistic profile	A combination of the modal, average and comparative profiles	Patients were asked to rate their willingness to use medical cannabis on a 0-10 point scale (0=extreme unwillingness to 10=extreme willingness). Greater unwillingness was associated with higher age (bivariate correlation coefficient [r]= 0.40; p=0.001), but not with pain intensity or duration, or sex. **This was qualitized as:** Higher age was related to more unwillingness to use medical cannabis.	

Note:
Abbreviation: SD: Standard deviation.
a. We used the following criteria when "qualitizing" quantitative into qualitative data:

"All or almost all": Reported by over 90% of patients; "Most": Reported by 75 to 90% of patients; "Majority": Reported by 50 to 75% of patients; "Minority": Reported by 25-50% of patients; "Some": Reported by10%-25% of patients; "None or almost none": Reported by 10% or less of patients (if the sample was 100 or less)

"Very few": Reported by 10% or less of patients (if the sample was >100). "Most common" and "least common" were used when factors were reported in groups, to denote the factors that patients agreed with the most vs. the least. The criteria above did not apply in these cases (e.g. "Recommendations from a medical professional was the least influential factor among patients when selecting cannabis.").

Table 2 Review findings and certainty of evidence

Review Findings [a]	Type of Research Evidence: Reference number	Certainty of Evidence
Values and preferences towards medical cannabis for chronic pain		
Use of medical cannabis for chronic pain		
Chronic pain patients had mixed levels of comfort or willingness to use medical cannabis.	Quantitative: 25,26,27	Low: Risk of bias and indirectness
	Qualitative: 22	Low: Minor concerns about relevance, serious adequacy concerns
Most patients who use medical cannabis had a positive attitude toward its use for pain relief.	Quantitative: 25,27, 29,31,34	Low: Risk of bias and indirectness
	Qualitative: 28	Moderate: Serious adequacy concerns
Medical cannabis over other pain medicines		
Patients with chronic pain and substance use histories preferred medical cannabis over prescription opioids.	Qualitative: 23	Low: Moderate methodological limitations and moderate adequacy concerns
Some patients believed that medical cannabis is safer than morphine and other strong pain killers.	Quantitative: 25	Very low: Risk of bias, indirectness and imprecision
Different preparations of medical cannabis		
Cannabis variety (i.e. sativa, indica, hybrid)		
Most patients preferred medical cannabis with a blend of indica and sativa, regardless of gender, reasons for use, and cannabis experience level.	Quantitative: 21	Moderate: Risk of bias
Cannabis content (i.e. THC or CBD potency, ratio of THC and CBD)		
A balanced ratio of THC:CBD was the most preferred preparation, but gender, reason for use, and cannabis experience level influenced patients' preference for cannabis ratio.	Quantitative: 21, 33	Moderate: Risk of bias

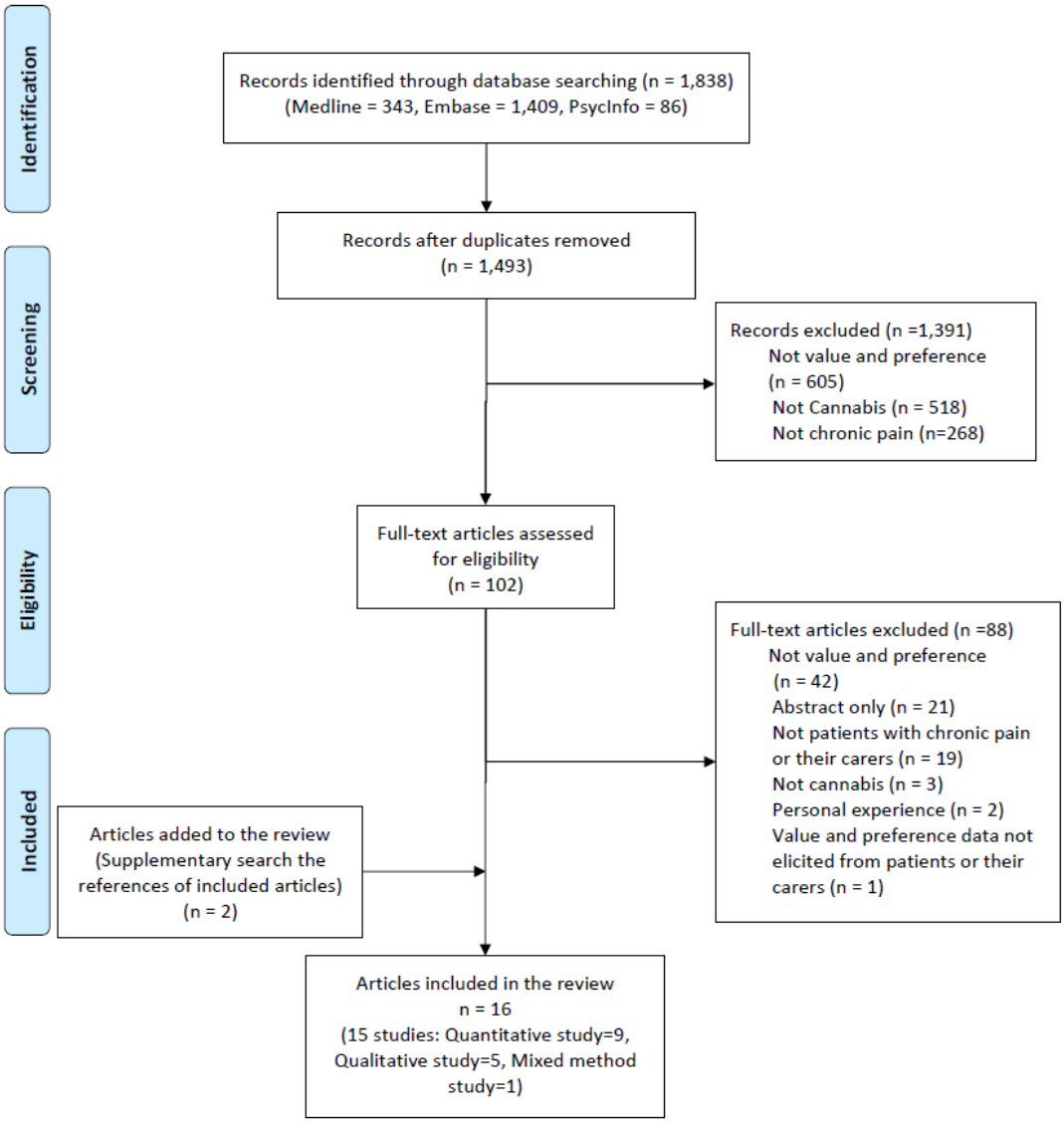
Cannabis administration route		
Gender, reason for use and cannabis experience level influenced patients' preferred cannabis administration routes.	Quantitative: 21 Mixed method: 35	Moderate: Risk of bias
Most patients with advanced life-limiting illness preferred an oral form (non-inhaled) of medical cannabis.	Quantitative: 25	Low: Risk of bias and imprecision
Factors that influenced patient's decision regarding use of medical cannabis		
Factors influenced the choice of medical cannabis use		
Most patients used medical cannabis because it improved symptoms associated with pain, mental health and other medical conditions.	Qualitative: 20,22,23,28	High
	Mixed method: 35	Moderate: Risk of bias
Most patients were motivated to use medical cannabis to reduce use of prescription medication.	Quantitative study: 27 Qualitative study: 22	Moderate: Risk of bias Moderate: Moderate adequacy concerns
The majority of patients expressed that their cannabis use was influenced by positive social consequences, such as social support from friends and family.	Quantitative: 25, 31,34	Moderate: Risk of bias
Most patients expressed concerns with using medical cannabis, and described a range of adverse effects.	Quantitative: 26, 27,31,34 Mixed method: 35 Qualitative : 20, 23	Moderate: Risk of bias Moderate: Moderate methodological concerns
Most patients expressed that their cannabis use was influenced by negative social consequences, such as stigma.	Quantitative: 25,26, 31,34 Mixed method: 35 Qualitative: 20, 32	Moderate: Risk of bias Moderate: Moderate methodological limitations
The cost, legal status, and accessibility of medical cannabis influenced patients' decisions to use medical cannabis.	Quantitative: 24,25, 31,34 Mixed method: 35 Qualitative: 20, 23	Moderate: Risk of bias Moderate: Moderate methodological limitations
Factors influenced the choice of different preparations of medical cannabis		

Patients chose medical cannabis products mainly based on cannabinoid content, recommendations from dispensary employees, described effects and side effects, strain of cannabis plant, smell, and flower appearance.	Quantitative: 21, 30	Low: Risk of bias and indirectness
	Qualitative: 22, 23, 28	Low: Moderate concerns about coherence and serious adequacy concerns
Gender, reason for use, and level of use experience were factors influencing patients' selection of cannabis products.	Quantitative: 21	Moderate: Risk of bias

Note:
Abbreviations: CBD: cannabidiol; THC: Delta-9-tetrahydrocannabinol.

a. We used the following criteria when "qualitizing" quantitative into qualitative data:
"All or almost all": Reported by over 90% of patients; "Most": Reported by 75 to 90% of patients; "Majority": Reported by 50 to 75% of patients; "Minority": Reported by 25-50% of patients; "Some": Reported by10%-25% of patients; "None or almost none": Reported by 10% or less of patients (if the sample was 100 or less)
"Very few": Reported by 10% or less of patients (if the sample was 101 or more). "Most common" and "least common" were used when factors were reported in groups, to denote the factors that patients agreed with the most vs. the least. The criteria above did not apply in these cases (e.g. "Recommendations from a medical professional was the least influential factor among patients when selecting cannabis.").

Figure 1 Evidence search and selection



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). *P*referred *R*eporting *I*tems for *S*ystematic Reviews and *M*eta-*A*nalyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

Appendix 1 Search strategies and results in MEDLINE, Embase and PsycInfo

March 17, 2020

MEDLINE

Database: OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

Search Strategy:

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1 Cannabis/ (8934)
2 exp cannabinoids/ or cannabidiol/ or cannabinol/ or dronabinol/ (13763)
3 Endocannabinoids/ (5620)
4 exp Receptors, Cannabinoid/ (9222)
5 (Cannabis or cannabinol or cannabinoid* or cannabidiol or bhang or cannador or charas or ganja or ganjah or hashish or hemp or marihuana or marijuana or nabilone or cesamet or cesametic or ajulemic acid or cannabichromene or cannabielsoin or cannabigerol or tetrahydrocannabinol or dronabinol or levonantradol or nabiximols or palmidrol or tetrahydrocannabinolic acid or tetrahydro cannabinol or marinol or tetranabinex or sativex or endocannabinoid*).mp. (54746)
6 or/1-5 (54746)
7 "marijuana use"/ or marijuana smoking/ (5304)
8 Marijuana Abuse/ (6168)
9 (epidiolex or gwp 42003p or gwp42003p or nabidiolex or dronabinol or thc or tetrahydrocannabinol* or ea 1477 or ea1477 or marinol or qcd 84924 or syndros or tetrabinex or tetranabinex or cesamet or nabilone or deltanyne or "abbott 40566" or namisol or dronabinolum or "QCD 84924" or "CCRIS 4726" or nabiximol? or "gw 1000" or gw1000 or "sab 378" or sab378 or sativex).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (11622)
10 or/7-9 (20972)
11 or/1-10 (55952)
12 *Attitude to Health/ (42364)
13 *Patient Participation/ (14355)
14 *Patient Preference/ (5009)
15 preference*.ti,ab. (148469)
16 choice.ti. (31408)
17 choices.ti. (6250)
18 value.ti. (124160)
19 health state values.ti,ab. (175)
20 valuation*.ti. (1523)

21 expectation*.ti,ab. (85695)
22 attitude*.ti,ab. (144860)
23 acceptab*.ti,ab. (174183)
24 knowledge.ti,ab. (676935)
25 point of view.ti,ab. (41412)
26 user participation.ti,ab. (243)
27 users participation.ti,ab. (49)
28 patient participation.ti,ab. (2134)
29 patients participation.ti,ab. (589)
30 patient perspective*.ti,ab. (3526)
31 patients perspective*.ti,ab. (5820)
32 user perspective*.ti,ab. (466)
33 users perspective*.ti,ab. (513)
34 patient perce*.ti,ab. (5165)
35 patients perce*.ti,ab. (9776)
36 health perception*.ti,ab. (2652)
37 user perce*.ti,ab. (351)
38 users perce*.ti,ab. (786)
39 user view*.ti,ab. (110)
40 users view*.ti,ab. (369)
41 patient view*.ti,ab. (546)
42 patients view*.ti,ab. (2807)
43 ((decision* and mak*).ti. or (decision mak* or decisions mak*).ti,ab.) and (patient* or user* or men or women).ti,ab. (73905)
44 discrete choice*.ti,ab. (1942)
45 decision board*.ti,ab. (45)
46 decision analy*.ti,ab. (7477)
47 decision-support.ti,ab. (13930)
48 decision tool*.ti,ab. (808)
49 decision aid*.ti,ab. (2976)
50 discrete-choice*.ti,ab. (1942)
51 *Decision Making/ and (patient* or user* or men or women).ti. (5869)
52 decision support techniques/ (19921)

53 (health and utilit*).ti. (1434)
54 gamble*.ti,ab. (4395)
55 prospect theory.ti,ab. (285)
56 preference score.ti,ab. (163)
57 preference elicitation.ti,ab. (179)
58 health utilit*.ti,ab. (2017)
59 utility value*.ti,ab. (1487)
60 utility score*.ti,ab. (1378)
61 Utility estimate*.ti,ab. (269)
62 health state.ti,ab. (4119)
63 feeling thermometer*.ti,ab. (68)
64 best-worst scaling.ti,ab. (202)
65 standard gamble.ti,ab. (832)
66 time trade-off.ti,ab. (1150)
67 TTO.ti,ab. (1026)
68 probability trade-off.ti,ab. (20)
69 utility score.ti,ab. (507)
70 preference based.ti,ab. (1291)
71 preference score*.ti,ab. (495)
72 multiattribute.ti,ab. (337)
73 multi attribute.ti,ab. (523)
74 EuroQol 5D.ti,ab. (1268)
75 EuroQol5D.ti,ab. (19)
76 EQ5D.ti,ab. (550)
77 EQ 5D.ti,ab. (7695)
78 SF6D.ti,ab. (32)
79 SF 6D.ti,ab. (753)
80 HUI.ti,ab. (1169)
81 15D.ti,ab. (1704)
82 or/12-81 (1494263)
83 (patient adj3 (value* or preference*)).ti,ab. (16093)
84 (patient* adj5 (report* or relate*) adj5 (outcome* or measure* or assess*)).mp. (41519)

85 patient participation/ or doctor patient relation/ or nurse patient relationship/ or patient attitude/ or patient preference/ or patient satisfaction/ or patient compliance/ or medication compliance/ or patient decision making/ or patient education/ or chronic patient/ or attitude to health/ or *"quality of life"/ or self care/ or self concept/ or self examination/ or adaptive behavior/ or coping behavior/ or coping.ab,ti. or needs assessment/ or personal autonomy/ or patient advocacy/ or life event/ (688791)
86 (patient* adj3 (prefer* or participat* or involve* or perspective* or view* or activat* or empower* or collaborate)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (154936)
87 (patient* adj2 (attitude* or decision* or needs*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (32381)
88 expert patient*.mp. (261)
89 (patient* and (centre* or center* or focus*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (726322)
90 patient*.mp. and (decision making/ or medical decision making/ or cooperation/ or distress syndrome/ or emotional stress/) [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (44808)
91 or/83-90 (1481530)
92 82 or 91 (2686916)
93 11 and 92 (6739)
94 (chronic adj4 pain*).mp. (68992)
95 Chronic Pain/ (13719)
96 exp Osteoarthritis/ (61921)
97 osteoarthrit*.mp. (88211)
98 osteo-arthrit*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (474)
99 exp Arthritis, Rheumatoid/ (111604)
100 exp Neuralgia/ (20041)
101 Diabetic Neuropathies/ (14472)
102 (neuropath* adj5 pain*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (24189)

103 neuralg*.mp. (26998)
104 zoster.mp. (20810)
105 Irritable Bowel Syndrome/ (7099)
106 IBS.mp. (8807)
107 Migraine Disorders/ (24884)
108 migraine*.mp. (38930)
109 Fibromyalgia/ (8287)
110 Fibromyalg*.mp. (11565)
111 complex regional pain syndromes/ or causalgia/ or reflex sympathetic dystrophy/ (5486)
112 Pain, Intractable/ (6166)
113 Phantom Limb/ (1855)
114 Hyperalgesia/ (11498)
115 exp back pain/ or failed back surgery syndrome/ or low back pain/ (38351)
116 radiculopath*.mp. (9283)
117 Musculoskeletal Pain/ (3090)
118 Headache/ (27380)
119 exp Headache Disorders/ (33884)
120 headache*.mp. (92254)
121 exp Temporomandibular Joint Disorders/ (17098)
122 whiplash.mp. (3942)
123 Whiplash Injuries/ (3216)
124 exp Cumulative Trauma Disorders/ (13612)
125 exp Peripheral Nervous System Diseases/dt, rh, th [Drug Therapy, Rehabilitation, Therapy] (29519)
126 Pain Measurement/de [Drug Effects] (6646)
127 (backache* or backpain* or dorsalgi* or arthralgi* or polyarthralgi* or arthrodyni* or myalgi* or fibromyalgi* or myodyni* or neuralgi* or ischialgi* or crps or rachialgi*).ti,ab. (44403)
128 ((noncancer* or non-cancer* or back or discogen* or chronic* or recurrent or persist* or bone or musculoskelet* or muscle* or skelet* or spinal or spine or vertebra* or joint* or arthritis or Intestin* or neuropath* or neck or cervical* or head or facial* or complex or radicular or cervicobrachi* or orofacial or somatic or non-malign* or shoulder* or knee* or hip or hips) adj3 pain).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (215471)
129 or/94-128 (633956)

Annotation: chronic pain and painful conditions
130 93 and 129 (343)

Embase
Database: Embase <1974 to 2020 March 16>
Search Strategy:
---
1 cannabis/ (33753)
2 exp cannabinoid/ (65425)
3 medical cannabis/ (2094)
4 exp cannabinoid receptor/ (14516)
5 exp endocannabinoid/ (8544)
6 (Cannabis or cannabinol or cannabinoid* or cannabidiol or bhang or cannador or charas or ganja or ganjah or hashish or hemp or marihuana or marijuana or nabilone or cesamet or cesametic or ajulemic acid or cannabichromene or cannabielsoin or cannabigerol or tetrahydrocannabinol or dronabinol or levonantradol or nabiximols or palmidrol or tetrahydrocannabinolic acid or tetrahydro cannabinol or marinol or tetranabinex or sativex or endocannabinoid*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (86218)
7 cannabis addiction/ (9661)
8 "cannabis use"/ or cannabis smoking/ (11097)
9 (epidiolex or gwp 42003p or gwp42003p or nabidiolex or dronabinol or thc or tetrahydrocannabinol* or ea 1477 or ea1477 or marinol or qcd 84924 or syndros or tetrabinex or tetranabinex or cesamet or nabilone or deltanyne or "abbott 40566" or namisol or dronabinolum or "QCD 84924" or "CCRIS 4726" or nabiximol? or "gw 1000" or gw1000 or "sab 378" or sab378 or sativex).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (19601)
10 or/1-9 (89571)
11 *attitude to health/ (55489)
12 *patient participation/ (9554)
13 *patient preference/ (4523)
14 preference*.ti,ab. (180987)
15 choice.ti. (36120)
16 choices.ti. (7375)
17 value.ti. (137715)
18 health state values.ti,ab. (233)

19 valuation*.ti. (2249)
20 expectation*.ti,ab. (106912)
21 attitude*.ti,ab. (179875)
22 acceptab*.ti,ab. (240808)
23 knowledge.ti,ab. (851427)
24 point of view.ti,ab. (57170)
25 user participation.ti,ab. (284)
26 users participation.ti,ab. (52)
27 patient participation.ti,ab. (2881)
28 patients participation.ti,ab. (830)
29 patient perspective*.ti,ab. (5558)
30 patients perspective*.ti,ab. (8635)
31 user perspective*.ti,ab. (564)
32 users perspective*.ti,ab. (624)
33 patient perce*.ti,ab. (8096)
34 patients perce*.ti,ab. (14350)
35 health perception*.ti,ab. (3709)
36 user perce*.ti,ab. (400)
37 users perce*.ti,ab. (902)
38 user view*.ti,ab. (169)
39 users view*.ti,ab. (469)
40 patient view*.ti,ab. (865)
41 patients view*.ti,ab. (3932)
42 ((decision* and mak*).ti. or (decision mak* or decisions mak*).ti,ab.) and (patient* or user* or men or women).ti,ab. (111434)
43 discrete choice*.ti,ab. (2789)
44 decision board*.ti,ab. (59)
45 decision analy*.ti,ab. (10602)
46 decision-support.ti,ab. (18317)
47 decision tool*.ti,ab. (1271)
48 decision aid*.ti,ab. (4097)
49 discrete-choice*.ti,ab. (2789)
50 *Decision Making/ and (patient* or user* or men or women).ti. (5671)

51 (health and utilit*).ti. (2083)
52 gamble*.ti,ab. (5213)
53 prospect theory.ti,ab. (286)
54 preference score.ti,ab. (241)
55 preference elicitation.ti,ab. (261)
56 health utilit*.ti,ab. (3331)
57 utility value*.ti,ab. (2815)
58 utility score*.ti,ab. (2530)
59 Utility estimate*.ti,ab. (494)
60 health state.ti,ab. (6770)
61 feeling thermometer*.ti,ab. (86)
62 best-worst scaling.ti,ab. (306)
63 standard gamble.ti,ab. (1081)
64 time trade-off.ti,ab. (1674)
65 TTO.ti,ab. (1635)
66 probability trade-off.ti,ab. (24)
67 utility score.ti,ab. (1024)
68 preference based.ti,ab. (1839)
69 preference score*.ti,ab. (654)
70 multiattribute.ti,ab. (376)
71 multi attribute.ti,ab. (721)
72 EuroQol 5D.ti,ab. (2064)
73 EuroQol5D.ti,ab. (39)
74 EQ5D.ti,ab. (1812)
75 EQ 5D.ti,ab. (14809)
76 SF6D.ti,ab. (110)
77 SF 6D.ti,ab. (1370)
78 HUI.ti,ab. (1774)
79 15D.ti,ab. (2541)
80 decision support system/ (21812)
81 or/11-80 (1879990)
82 (patient adj3 (value* or preference*)).ti,ab. (25871)

83 (patient* adj5 (report* or relate*) adj5 (outcome* or measure* or assess*)).mp. (73476)
84 patient participation/ or doctor patient relation/ or nurse patient relationship/ or patient attitude/ or patient preference/ or patient satisfaction/ or patient compliance/ or medication compliance/ or patient decision making/ or patient education/ or chronic patient/ or attitude to health/ or *"quality of life"/ or self care/ or self concept/ or self examination/ or adaptive behavior/ or coping behavior/ or coping.ab,ti. or needs assessment/ or personal autonomy/ or patient advocacy/ or life event/ (1037242)
85 (patient* adj3 (prefer* or participat* or involve* or perspective* or view* or activat* or empower* or collaborate)).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (234656)
86 (patient* adj2 (attitude* or decision* or needs*)).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (119435)
87 expert patient*.mp. (478)
88 (patient* and (centre* or center* or focus*)).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (1258089)
89 patient decision making/ (9864)
90 patient*.mp. and (decision making/ or medical decision making/ or cooperation/ or distress syndrome/ or emotional stress/) [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (180387)
91 or/82-90 (2444470)
92 81 or 91 (3858388)
93 10 and 92 (13785)
94 (chronic adj4 pain*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (113744)
95 chronic pain/ (59665)
96 exp osteoarthritis/ (124667)
97 osteoarthrit*.mp. (138729)
98 osteo-arthrit*.mp. (511)
99 degenerative arthrit*.mp. (1541)
100 exp rheumatoid arthritis/ (196173)
101 exp neuralgia/ (102320)
102 diabetic neuropathy/ (23303)
103 (neuropath* adj5 (pain or diabet*)).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (72882)
104 neuralg*.mp. (29911)

105 zoster.mp. (37512)
106 irritable colon/ (25493)
107 (irritable bowel syndrome or IBS).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (24789)
108 exp migraine/ (62395)
109 migrain*.mp. (69650)
110 fibromyalgia/ (19936)
111 fibromyalg*.mp. (21561)
112 reflex sympathetic dystrophy.mp. (2353)
113 complex regional pain syndrome.mp. (7426)
114 causalgia.mp. (1039)
115 intractable pain/ (4766)
116 phantom limb/ or phantom pain/ (2434)
117 agnosia/ (3053)
118 amputation stump/ (2062)
119 exp hyperalgesia/ (20518)
120 ((noncancer* or non-cancer* or chronic* or recurrent or persist* or non-malign*) adj3 pain).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (130063)
121 exp backache/ (106576)
122 radiculopathy/ or radiculopath*.mp. (13603)
123 exp bone pain/ (17842)
124 exp musculoskeletal pain/ (145426)
125 arthralgia/ (59500)
126 headache*.mp. (271974)
127 exp "headache and facial pain"/ (296382)
128 temporomandibular joint disorder/ (13611)
129 ((TMJ or TMJD) and pain*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (3753)
130 whiplash.mp. or whiplash injury/ (4884)
131 exp cumulative trauma disorder/ (20498)
132 or/94-131 (1089097)
133 93 and 132 (1409)

PsycInfo
Database: APA PsycInfo <1806 to March Week 2 2020>
Search Strategy:
---
1 exp cannabis/ or exp cannabinoids/ or tetrahydrocannabinol/ (12784)
2 (Cannabis or cannabinol or cannabinoid* or cannabidiol or bhang or cannador or charas or ganja or ganjah or hashish or hemp or marihuana or marijuana or nabilone or cesamet or cesametic or ajulemic acid or cannabichromene or cannabielsoin or cannabigerol or tetrahydrocannabinol or dronabinol or levonantradol or nabiximols or palmidrol or tetrahydrocannabinolic acid or tetrahydro cannabinol or marinol or tetranabinex or sativex or endocannabinoid*).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (26408)
3 marijuana laws/ or marijuana legalization/ or "cannabis use disorder"/ or marijuana usage/ (3594)
4 (epidiolex or gwp 42003p or gwp42003p or nabidiolex or dronabinol or thc or tetrahydrocannabinol* or ea 1477 or ea1477 or marinol or qcd 84924 or syndros or tetrabinex or tetranabinex or cesamet or nabilone or deltanyne or "abbott 40566" or namisol or dronabinolum or "QCD 84924" or "CCRIS 4726" or nabiximol? or "gw 1000" or gw1000 or "sab 378" or sab378 or sativex).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (3193)
5 or/1-4 (26475)
6 *health attitudes/ (8084)
7 *client participation/ (1678)
8 exp *client attitudes/ (17349)
9 preference*.ti,ab. (95876)
10 choice.ti. (21402)
11 choices.ti. (4602)
12 value.ti. (18077)
13 health state values.ti,ab. (77)
14 valuation*.ti. (983)
15 expectation*.ti,ab. (80049)
16 attitude*.ti,ab. (201050)
17 acceptab*.ti,ab. (38902)
18 knowledge.ti,ab. (290890)
19 point of view.ti,ab. (20482)
20 user participation.ti,ab. (282)
21 users participation.ti,ab. (46)

22 patient participation.ti,ab. (788)
23 patients participation.ti,ab. (264)
24 patient perspective*.ti,ab. (980)
25 patients perspective*.ti,ab. (1752)
26 user perspective*.ti,ab. (340)
27 users perspective*.ti,ab. (345)
28 patient perce*.ti,ab. (1343)
29 patients perce*.ti,ab. (3398)
30 health perception*.ti,ab. (1230)
31 user perce*.ti,ab. (393)
32 users perce*.ti,ab. (888)
33 user view*.ti,ab. (95)
34 users view*.ti,ab. (289)
35 patient view*.ti,ab. (210)
36 patients view*.ti,ab. (1022)
37 ((decision* and mak*).ti. or (decision mak* or decisions mak*).ti,ab.) and (patient* or user* or men or women).ti,ab. (21062)
38 discrete choice*.ti,ab. (960)
39 decision board*.ti,ab. (16)
40 decision analy*.ti,ab. (1133)
41 decision-support.ti,ab. (3235)
42 decision tool*.ti,ab. (169)
43 decision aid*.ti,ab. (1252)
44 discrete-choice*.ti,ab. (960)
45 *Decision Making/ and (patient* or user* or men or women).ti. (3428)
46 (health and utilit*).ti. (467)
47 gamble*.ti,ab. (5406)
48 prospect theory.ti,ab. (964)
49 preference score.ti,ab. (93)
50 preference elicitation.ti,ab. (134)
51 health utilit*.ti,ab. (532)
52 utility value*.ti,ab. (490)
53 utility score*.ti,ab. (334)

54 Utility estimate*.ti,ab. (103)
55 health state.ti,ab. (958)
56 feeling thermometer*.ti,ab. (58)
57 best-worst scaling.ti,ab. (109)
58 standard gamble.ti,ab. (210)
59 time trade-off.ti,ab. (279)
60 TTO.ti,ab. (190)
61 probability trade-off.ti,ab. (5)
62 utility score.ti,ab. (101)
63 preference based.ti,ab. (648)
64 preference score*.ti,ab. (402)
65 multiattribute.ti,ab. (531)
66 multi attribute.ti,ab. (567)
67 EuroQol 5D.ti,ab. (206)
68 EuroQol5D.ti,ab. (0)
69 EQ5D.ti,ab. (61)
70 EQ 5D.ti,ab. (1677)
71 SF6D.ti,ab. (10)
72 SF 6D.ti,ab. (284)
73 HUI.ti,ab. (445)
74 15D.ti,ab. (170)
75 decision support systems/ (3245)
76 or/6-75 (744950)
77 client attitudes/ or client satisfaction/ (21785)
78 values/ or personal values/ or social values/ (22591)
79 (patient* adj3 (prefer* or participat* or involve* or perspective* or view* or activat* or empower* or collaborate)).mp. (27273)
80 (patient* adj2 (attitude* or decision* or needs*)).mp. (23750)
81 or/77-80 (85433)
82 76 or 81 (783705)
83 5 and 82 (3282)
84 chronic pain/ (13151)
85 chronic illness/ and pain.mp. (916)

86 back pain/ (3813)
87 ((chronic* or persist* or refractor* or intract* or manag* or back) adj3 pain).mp. (34808)
88 or/84-87 (35275)
89 (chronic adj4 pain*).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (22123)
90 exp arthritis/ (4140)
91 osteoarthrit*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (2121)
92 osteo-arthrit*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (9)
93 degenerative arthrit*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (15)
94 exp Neuralgia/ (931)
95 exp Neuropathy/ (6243)
96 (neuropath* adj5 (pain or diabet*)).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (6749)
97 neuralg*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (3310)
98 zoster.mp. (577)
99 irritable bowel syndrome/ (1152)
100 (IBS or irritable colon or irritable bowel).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (2001)
101 exp headache/ (15176)
102 migrain*.mp. (12832)
103 fibromyalgia/ (1972)
104 fibromyalg*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (3408)
105 "complex regional pain syndrome (type i)"/ (152)
106 (complex regional pain syndrome* or causalgia).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (821)
107 somatosensory disorders/ (1367)
108 hyperalgesi*.mp. (5320)
109 exp Somatoform Disorders/ (15194)
110 ((noncancer* or non-cancer* or chronic* or recurrent or persist* or non-malign*) adj3 pain).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (23779)
111 radiculopath*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (351)
112 ((back or musculoskeletal) adj3 pain*).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (7604)
113 arthralgia.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (317)
114 headache*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (22401)
115 (backache* or backpain or dorsalgi* or arthralgi* or polyarthalgi* or arthrodyn* or myalgi* or fibromyalg* or myodny* or neuralg* or ischialg* or crps or

rachialgi*).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (8315)
116 ((back or discogen* or bone or musculoskelet* or muscle* or skelet* or spinal or spine or vertebra* or joint* or arthrit* or intestin* or neuropath* or neck or cervical* or head or facial* or complex or radicular or cervicobrach* or orofacial or somatic or shoulder* or knee* or hip or hips*) adj3 pain).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh] (20949)
117 or/84-116 (93580)
118 83 and 117 (86)
119 5 and 82 and 117 (86)

Appendix 2 Data extraction form

Researcher identification
Surname, name
Study identification
Study ID
Country
Funding
Study objectives or research questions
Study population
Description of patients
Response rate/ completion rate
Male %
Age
White %
Chronic pain %
Patients ever used cannabis %
Opioids use %
Aim intervention
Study design and methods
Study design
Sampling
Sample size
Data collection
Findings
Main findings (themes)
1. Values and preferences of outcome of medical cannabis 1.1 Relative value or importance patients put on outcomes of medical cannabis; 1.2 Tradeoff between benefits and harms or burdens of medical cannabis 2. Values and preferences towards medical cannabis 2.1 Values and preference for or against medical cannabis or choosing cannabis over

other medicines 2.2 Values and preferences of different preparations of medical cannabis (e.g. administration routes, ingestion method, ratio of THC to CBD) 3. Factors that influence the decision making regarding medical cannabis use 3.1 Factors that influence use or not use of medical cannabis 3.2 Factors that influence the choice of medical cannabis over other meds for pain management 3.3 Factors that influence the choice of different preparations of medical cannabis
Authors' interpretation
Authors' conclusions

Appendix 3 Tool and instructions for risk of bias assessment for quantitative studies

Domains	Participant selection	Completeness of data	Choice of measurement instrument	Administration of measurement instrument	Outcome/health state presentation	Participants' understanding of the measurement instrument	Data analysis	Overall risk of bias
Questions	Was the study sample selected in a manner to ensure the representativeness to the target population?	Was the attrition sufficiently low to minimize the risk of bias?	Was the choice of the methodology appropriate for addressing the study aim?	Was the instrument (or tools that was used to elicit values and preferences, e.g. questionnaire) administered in the intended way?	Was a valid representation of the outcome/health state (e.g. a state of pain relief - a beneficial outcome of medical cannabis, or an experience of coughing - a harmful outcome of medical cannabis) utilized?	Did the researchers check the understanding to the measurement techniques (e.g. questionnaire in a survey)?	Were the results analyzed appropriately?	
Instructions for questions	The sampling strategy solely does not determine the risk of bias; if there is a subset of the population more or less likely to be reached, the answer for "was the study sample selected in a manner to ensure the representativeness" is	Response rate for 80% or higher would be considered high for a cross-sectional study.	Consider yes or probably yes for the following methodologies: standard gamble, time trade off, visual analogue scale (or feeling thermometers), discrete choice,	-	If the researchers demonstrated they were using available evidence to support the health state presentation, the answer should be yes or probably yes.	If the methodology is simple, choosing "the investigators did not formally test the understanding, but the results suggested it was adequate"	To answer this question, reviewers also need to consider whether the adjustment, stratification, or model selection was appropriate.	· Low risk of bias= The study is classified as with low risk of bias across subdomains. · Moderate risk of bias= The study is classified as low (Yes -> low risk of bias) or moderate (Probably yes -> moderate risk

yes or probably yes.	treatment trade-off, willingness to pay	could be appropriate. If the researchers piloted the methodology, choosing “the investigators did not formally test the understanding, but the results suggested it was adequate” may also be appropriate.	This domain may not be applicable to all primary studies because not all studies will require controlled data analysis. Please check "NA" if not applicable.	of bias) risk of bias across subdomains. · Serious risk of bias= The study is classified as serious risk of bias (Probably no -> serious risk of bias) for at least one subdomain but not classified as critical risk of bias for any subdomain. · Critical risk of bias=The study is classified as critical risk of bias (No -> critical risk of bias) for at least one subdomain.	

Appendix 4 Tool and instructions for methodological limitation assessments for qualitative studies

Domains	Aim of the research	Qualitative methodology appropriateness	Research design	Appropriate recruitment strategy	Data collection	Investigator-participant relationship	Ethical issues	Data analysis	Findings	Value of the research	Overall methodological limitations
Questions	Was there a clear statement of the aims of the research?	Is a qualitative methodology appropriate?	Was the research design appropriate to address the aims of the research?	Was the recruitment strategy appropriate to the aims of the research?	Was the data collected in a way that addressed the research issue?	Has the relationship between researcher and participants been adequately considered?	Have ethical issues been taken into consideration?	Was the data analysis sufficiently rigorous?	Is there a clear statement of findings?	How valuable is the research?	
Instructions for questions	· what was the goal of the research · why it was thought important · its relevance	· If the research seeks to interpret or illuminate the actions and/or subjective experiences of research participants · Is qualitative research the right methodology for addressing the research goal	· if the researcher has justified the research design (e.g. have they discussed how they decided which method to use)	· If the researcher has explained how the participants were selected · If they explained why the participants they selected were the most appropriate to provide	· If the setting for the data collection was justified · If it is clear how data were collected · If the researcher has justified the methods chosen · If the	· If the researcher critically examined their own role, potential bias and influence during (a) formulation of the research questions (b) data collection, including sample	· If there are sufficient details of how the research was explained to participants for the reader to assess whether ethical standards were maintained · If the researcher has discussed issues raised by the study	· If there is an in-depth description of the analysis process · If thematic analysis is used. If so, is it clear how the categories/themes were derived from the data · Whether the researcher explains how the data presented	· If the findings are explicit · If there is adequate discussion of the evidence both for and against the researcher's arguments	· If the researcher discusses the contribution the study makes to existing knowledge or understanding (e.g. do they consider the findings in relation to current practice or policy, or relevant research-based literature · If they identify	· Serious = if more than 2 questions had "No". · Moderate = if 2 questions had "No". · No or minor = if less than 2 questions had "No".

access to the type of knowledge sought by the study · If there are any discussions around recruitment (e.g. why some people chose not to take part)	researcher has made the methods explicit · If methods were modified during the study. If so, has the researcher explained how and why · If the form of data is clear · If the researcher has discussed saturation of data	recruitment and choice of location · How the researcher responded to events during the study and whether they considered the implications of any changes in the research design	(e.g. issues around informed consent or confidentiality or how they have handled the effects of the study on the participants during and after the study) · If approval has been sought from the ethics committee	were selected from the original sample to demonstrate the analysis process · If sufficient data are presented to support the findings · To what extent contradictory data are taken into account · Whether the researcher critically examined their own role, potential bias and influence during analysis and selection of data for presentation	· If the researcher has discussed the credibility of their findings · If the findings are discussed in relation to the original research question	new areas where research is necessary · If the researchers have discussed whether or how the findings can be transferred to other populations or considered other ways the research may be used

Appendix 5 Characteristics of the included studies

Study ID	Country	Funding sources	Primary focus	Study design	Data collection methods	Sampling	Participants, n	Male Sex, %	Chronic pain, %	Chronic cancer pain, %	Prior use of cannabis, %	Risk of Bias/ Methodological Limitations
Bigand 2019	United States	Non-industry funding	To examine the perceived effects of medical cannabis among patients who are prescribed opioids for persistent pain conditions	Qualitative, Descriptive	Questionnaire	Convenience	150	31.3	100	NR	69.3	Serious
Boehnke 2019	United States	NR	To assess preferences towards medical cannabis products among medical cannabis users with chronic pain	Quantitative, Cross-sectional	Questionnaire	Convenience	1321	40.9	NR [a]	NR	100	Moderate
Bruce 2018	United States	Non-industry funding	To assess approaches to medical cannabis use vis-a-vis prescription medications among patients with chronic conditions	Qualitative, Descriptive	Semi-structured telephone interviews	Convenience	30	60.3	NR [b]	NR	100	No or minor
Cooke 2019	United States	Non-industry funding	To explore perspectives on the co-use of medical cannabis and opioids among clinicians, and	Qualitative, Modified grounded theory	Semi-structured in-person interviews	Purposive	46	45.6	100	0	45.7 [c]	Moderate

			patients with both chronic non-cancer pain and a history of substance use									
Degenhardt 2015	Australia	Non-industry funding	To investigate patterns and correlates of medical cannabis use among patients who are prescribed opioids for chronic non-cancer pain	Quantitative, Cross-sectional	Questionnaire, and diagnostic interview	Purposive	1514	44.4	100	0	43	Moderate
Gallagher 2003	Canada	NR	To survey willingness to try medical cannabis among patients with a known advanced life-limiting illness [d], and to assess this population's knowledge about medical cannabis	Quantitative, Cross-sectional	Discrete choice, VAS, Likert scales	Purposive	68	44.6	NR [e]	100 [d]	35.3	Critical
Gill 2001	United Kingdom	NR	To investigate beliefs about cannabinoids and the associations between those beliefs, beliefs about medication, and personal and pain variables in relation to willingness to try cannabinoids as analgesics, among	Quantitative, Cross-sectional	Questionnaire	Convenience	65	45	100	NR	NR	Serious

			patients with chronic pain who had interest in trying medical cannabis as an analgesic									
Heng 2018	United States	NR	To assess beliefs regarding using marijuana for medicine, post injury pain and speaking about marijuana to their health care providers, among patients who have a musculoskeletal injury in the last 1-6 months.	Quantitative, Cross-sectional	Questionnaire	Convenience	500	50	NR [f]	NR	60	Moderate
Lavie-Ajayi 2019	Israel	Non-industry funding	To explore and characterize the experience of using medical cannabis for chronic pain among patients receiving medical cannabis for at least three months	Qualitative, Phenomenological	Semi-structured in-person interviews	Purposive	19	52.6	100	5.3	100	No or minor
Notcutt 2004	United Kingdom	Non-industry funding	To evaluate the safety and tolerability of three CBMEs among patients with stable chronic pain, and poorly responsive to other modalities	Quantitative, RCT	NR	Convenience	34	32	100	NR	NR	Moderate

Piper 2017	United States	Non-industry funding	To survey perspectives of medical cannabis among legal members of medical cannabis dispensaries, and to examine the strengths and limitations of medical cannabis	Mixed Methods, Cross-sectional	Online survey, discrete choice, open-ended questions	Convenience and snowball	984	47.1	100 [g]	16.7	100	Serious
Rochford 2019	Ireland	NR	To evaluate attitudes towards medicinal cannabis among patients who attend chronic pain clinics	Quantitative, Cross-sectional	Questionnaire	Convenience	96	39.6	100	22.9	NR	Serious
Satterlund 2015	United States	Non-industry funding	To assess perceived risk, concern or overall stigma of marijuana use, and how this stigma may affect the health care among medical marijuana users [c]	Qualitative, Descriptive	Semi-structured interviews	Convenience and snowball	18	72	NR [h]	NR	100	Moderate
Sexton 2016	United States	Non-industry funding	To survey the patterns of use and perceived efficacy of medical cannabis among patients who have used medical cannabis in the last 90 days	Quantitative, Cross-sectional	Questionnaire	Convenience	1429	54.6	NR [i]	NR	100	Moderate
Zarrabi/Singh 2019	United States	Non-industry	To survey perceptions of the benefits and	Quantitative, Cross-	Questionnaire	Convenience	101	55.7	100	75.5	100	Serious

	funding	harms of medical cannabis, concerns about access to cannabis, and perceptions of support from family and health care providers, among patients with serious illness in APC	sectional

Note:

Abbreviation: APC: ambulatory palliative care, CBMEs: cannabis based medicinal extracts, CNCP: chronic non-cancer pain, NR: Not reported, RCT: Randomized controlled trial, US: United states, VAS: Visual Analogue Scale.

a Chronic overlapping pain conditions: back pain 58%, migraine 21%, fibromyalgia 15%, irritable bowel disease or Crohn's disease 14%, temporomandibular joint disorder 6%.

b Rheumatoid arthritis 23.3%, spinal cord disease or injury 20%, Chron's disease 20%, cancer 13.3%, hepatitis C 13.3%, post-traumatic stress disorder (PTSD) 13.3%, severe fibromyalgia 10%, other (chronic regional pain syndrome, epilepsy, HIV, MS, Parkinson's) 23.3%.

c Majority (≥80%) were patients with chronic and severe pain.

d Advanced life-limiting illnesses include malignancy, advanced cardiac, respiratory, liver or neurological diseases.

e The mean score of intensity of pain was 4.9 on a 0 to 10 VAS scale (0= absence of pain, 10=the worst pain intensity imaginable).

f Patients had experienced a musculoskeletal injury between 1 to 6 months before entry into the study.

g All the participants were legal members of medical cannabis dispensaries in the north-eastern US. Sixty-four percent of patients reported that they had been diagnosed with chronic pain by a medical professional.

h The authors stated "Maladies for which respondents used medical marijuana included migraine headaches, depression, chemotherapy and radiation treatment effects, chronic pain, and asthma, with the majority citing chronic and severe pain".

i Sixty-one percent of patients reported chronic pain, 35.5% had headache/migraine and the remaining 3.5% had other chronic pain conditions.

Appendix 6 Excluded studies and reasons for exclusion in full text screening

Study ID	Reason for exclusion
1. Aggarwal 2014	Not value and preference
2. Allan 2018	Not value and preference
3. Bekker 2018	Not value and preference
4. Cairns 2017	Not value and preference
5. Caplan B 2018	Not value and preference
6. Choo 2016	Not value and preference
7. Nickel 2018	Not value and preference
8. Djulus 2005	Not value and preference
9. Dowden 2019	Not value and preference
10. Gieringer 2003	Not value and preference
11. Harrison 2013	Not value and preference
12. Kepple 2016	Not value and preference
13. Kinnucan 2018	Not value and preference
14. Bachhuber 2018	Not value and preference
15. Zolotov 2016	Not value and preference
16. Lum 2019	Not value and preference
17. Martins-Welch 2017	Not value and preference
18. Naguib 2015	Not value and preference
19. Page 2015	Not value and preference
20. Parmar 2016	Not value and preference
21. Paut Kusturica2019	Not value and preference
22. Pearce 2014	Not value and preference
23. Pink 2012	Not value and preference
24. Piper 2018	Not value and preference
25. Reid 2013	Not value and preference
26. Reiman 2008	Not value and preference
27. Reisfield 2009	Not value and preference
28. Reynolds 2017	Not value and preference
29. Reynolds 2018	Not value and preference
30. Ste-Marie 2015	Not value and preference

31. Sutherland 2016	Not value and preference
32. Teigen 2019	Not value and preference
33. Toth 2015	Not value and preference
34. Volkow 2017	Not value and preference
35. Wallace 2015	Not value and preference
36. Wan 2017	Not value and preference
37. Ware 2010	Not value and preference
38. Wilsey 2015	Not value and preference
39. Winston-McPherson 2019	Not value and preference
40. Zaller 2015	Not value and preference
41. Ziadni 2018	Not value and preference
42. Zvolensky 2011	Not value and preference
43. Aggarwal 2018	Abstract only
44. Agornyo 2018	Abstract only
45. Bar-Sela 2014	Abstract only
46. Berg 2017	Abstract only
47. Burks 2016	Abstract only
48. Calvino 2017	Abstract only
49.Cofield 2015	Abstract only
50. Fitzcharles 2019	Abstract only
51.Galvin 2018	Abstract only
52. Gavigan 2019	Abstract only
53. Grella 2015	Abstract only
54.Gustavsen 2018	Abstract only
55.Kiszko 2017	Abstract only
56.Lee 2012	Abstract only
57. Mitra 2019	Abstract only
58. Muirhead 2015	Abstract only
59. Pires 2018	Abstract only
60. Rhyne 2019	Abstract only
61. Sabet 2014	Abstract only
62. Schnelle 1999	Abstract only

63. Wurtzen 2018	Abstract only
64.Grinberg 2018	Not patients with chronic pain or their carer
65. Iskedjian 2009	Not patients with chronic pain or their carer
66. Grotenhermen 2003	Not patients with chronic pain or their carer
67. LAU 2015	Not patients with chronic pain or their carer
68. Ishida 2019	Not patients with chronic pain or their carer
69. Lucas 2019	Not patients with chronic pain or their carer
70. Wan 2017	Not patients with chronic pain or their carer
71. Mendoza 2016	Not patients with chronic pain or their carer
72. Mendoza 2018	Not patients with chronic pain or their carer
73. Schenker 2019	Not patients with chronic pain or their carer
74. Sharon 2018	Not patients with chronic pain or their carer
75. St-Amant 2015	Not patients with chronic pain or their carer
76. Starrels 2018	Not patients with chronic pain or their carer
77. Starrels 2020	Not patients with chronic pain or their carer
78. Zolotov 2019	Not patients with chronic pain or their carer
79. Zolotov 2019	Not patients with chronic pain or their carer
80. Nouryan 2018	Not patients with chronic pain or their carer
81. Boehnke 2019	Not patients with chronic pain or their carer
82. Khelemsky 2017	Not patients with chronic pain or their carer
83. Vargas-Schaffer 2018	Not cannabis
84. Manchikanti 2008	Not cannabis
85. Mijatovic 2019	Not cannabis
86. Friedberg 2016	Personal experience
87. Greenberg 2019	Personal experience
88. Burke 2010	Value and preference data not elicited from patients or their carers

List of excluded studies at full text screening and reasons for exclusion

1. Not value and preference (n=42)

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4. Not cannabis (n=3)

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5. Personal experience (case study) (n=2)

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6. Value and preference data not elicited from patients or their carers (n=1)

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Appendix 7 Risk of bias assessments for quantitative studies

Study ID (Reference number)	Was the study sample selected in a manner to ensure the representativeness to the target population?	Was the attrition sufficiently low to minimize the risk of bias?	Was the choice of the methodology appropriate for addressing the study aim?	Was the instrument (or tools that was used to elicit values and preferences, e.g. questionnaire) administered in the intended way?	Was a valid representation of the outcome/health state (e.g. a state of pain relief - a beneficial outcome of medical cannabis, or an experience of coughing - a harmful outcome of medical cannabis) utilized?	Did the researchers check the understanding to the measurement techniques (e.g. questionnaire in a survey)?	Were the results analyzed appropriately?	Overall risk of bias
Boehnke 2019 (21)	Probably yes	Probably yes	Probably yes	Yes	NA	Probably yes	Yes	Moderate
Degenhardt 2015 (24)	Probably yes	Yes	Yes	Yes	NA	Probably yes	Yes	Moderate
Heng 2018 (27)	Probably yes	Yes	Probably yes	Yes	NA	Probably yes	Yes	Moderate
Gill 2001 (26)	Probably yes	Yes	Yes	Probably yes	Probably no	Probably yes	Probably yes	Serious
Gallagher 2003 (25)	Probably yes	Probably no	Yes	Yes	Probably no	Probably no	Probably no	Critical
Piper BJ 2017 (35)	Yes	Probably no	Yes	Yes	NA	Yes	yes	Serious
Sexton 2016 (30)	Yes	Probably yes	Yes	Yes	NA	Yes	Yes	Moderate
Zarrabi 2020, Singh 2019 (31, 34)	Probably yes	Probably yes	Yes	Yes	Probably no	Probably no	Yes	Serious
Notcutt 2004 (33)	Probably yes	Probably Yes	Probably yes	Probably yes	NA	Probably yes	Probably yes	Moderate
Rochford 2019 (29)	Probably no	Probably yes	Probably yes	Probably yes	NA	Probably yes	Probably yes	Serious

Appendix 8 Methodological limitations assessments for qualitative studies

Study ID (Reference number)	Was there a clear statement of the aims of the research?	Is a qualitative methodology appropriate?	Was the research design appropriate to address the aims of the research?	Was the recruitment strategy appropriate to the aims of the research?	Was the data collected in a way that addressed the research issue?	Has the relationship between researcher and participants been adequately considered?	Have ethical issues been taken into consideration?	Was the data analysis sufficiently rigorous?	Is there a clear statement of findings?	How valuable is the research?	Overall methodological limitations
Bruce 2018 (22)	Yes	Yes	Yes	Can't tell	Yes	No	Yes	Yes	Yes	Yes	No or minor
Cooke 2019 (23)	Yes	Yes	Yes	Can't tell	Yes	No	Can't tell	Yes	No	Yes	Moderate
Bigand 2019 (20)	Yes	Yes	No	Can't tell	No	No	Yes	Yes	Yes	Yes	Serious
Lavie-Ajayi 2019 (28)	Yes	Yes	Yes	Yes	Yes	No	Can't tell	Yes	Yes	Yes	No or minor
Satterlund 2015 (32)	Yes	Yes	Yes	Can't tell	Yes	No	Yes	Yes	Yes	Yes	Moderate

Appendix 9 Evidence profile for review findings

Review finding	Explanation	Certainty assessment with GRADE/ GRADE CERQual							Certainty
		Study design (Reference number)	NO. of studies (participants)	Risk of bias/ Methodological limitations	Inconsistency/ Coherence	Indirectness/ Relevance	Imprecision/ Adequacy	Small effect bias	
1. Values and preferences towards medical cannabis									
1.1 Use of medical cannabis for chronic pain									
Patients had mixed levels of comfort or willingness to use medical cannabis.	[Quantitative] Most patients with advanced life-limiting illnesses were comfortable using cannabis for chronic pain and nausea (25), while other non-palliative patients with chronic pain were unwilling or ambivalent about medical cannabis use (26). Non-White patients with advanced illness were more concerned about medical cannabis compared to White patients, but they remained comfortable using medical cannabis (25). Chronic pain patients who use both medical cannabis and other prescription medications believed that medical cannabis was effective for managing	Quantitative (25,26,27)	3 (633)	Serious risk	Not serious	Serious	Not serious	Not serious	Low
	[Qualitative] Patients with a range of chronic medical conditions believed that medical cannabis was effective for pain (22).	Qualitative (22)	1 (30)	No or very minor concerns	NA	Minor concerns	Serious concerns	No or very minor concerns	Low

Most patients who use medical cannabis had a positive attitude toward its use for pain relief.	[Quantitative] Those using medical cannabis during their recovery believed that it reduced pain (25). Most individuals expressed positive aspects of medical cannabis use, such as pain reduction (27, 31, 34). The majority of participants with cancer in one study reported using cannabis products for a “cancer cure” (31). Some believed that cannabis should be legalized for medical purposes (29).	Quantitative (25,27,29,31,34)	4 (765)	Serious risk	Not serious	Serious	Not serious	Not serious	Low
	[Qualitative] Most individuals expressed use of medical cannabis for chronic pain was associated with a range of improved outcomes (e.g. better function, sleep, life changing etc.) (28).	Qualitative (28)	1 (19)	No or very minor concerns	NA	No or very minor concerns	Serious concerns	No or very minor concerns	Moderate
1.2 Medical cannabis over other pain medicines									
Patients with chronic pain and substance use histories preferred medical cannabis over prescription opioids.	[Qualitative] Patients with chronic pain and substance use histories preferred medical cannabis over prescription opioids to manage pain (23).	Qualitative (23)	1 (46)	No or very minor concerns	NA	Minor concerns	Serious concerns	No or very minor concerns	Low

Some patients believed that medical cannabis is safer than morphine and other strong pain killers.	[Quantitative] Some participants believed that because cannabis is a 'natural' product, it is safer than morphine and other strong pain killers (25). Non-Christians were more likely to believe that cannabis is safer than morphine (25). Those with high school education or less, were significantly less likely to believe that cannabis was safer than morphine (25).	Quantitative (25)	1 (68)	Very serious	Not serious	Serious	Serious	Not serious	Very low

1.3 Different preparations of medical cannabis

Cannabis variety (i.e. sativa, indica, hybrid)

Most patients preferred medical cannabis with a blend of indica and sativa, regardless of gender, reasons for use, and cannabis	[Quantitative] Most patients preferred using a blend of indica and sativa to manage chronic pain, followed by indica alone and sativa alone. There were no differences in cannabis variety preferences between males and females, those who use cannabis for medical purposes only and those who use for medical and recreational purposes, or novice and experienced users.(21)	Quantitative (21)	1 (1321)	Serious risk	Not serious	Not serious	Not serious	Not serious	Moderate

Cannabis content (i.e. THC or CBD potency, ratio of THC and CBD)

High THC and high CBD is the most preferred preparation, but gender, reason for use, and cannabis experience level influenced patients' preference for cannabis ratio.	[Quantitative] Females preferred low THC: high CBD, while males preferred equal ratios of THC: CBD. (21) Patients who use cannabis for medical purposes reported a greater preference for products with low THC: high CBD compared to individuals who use cannabis both medically and recreationally. (21) Both novice and experienced cannabis users preferred high CBD products most, and more novice users prefer low THC: high CBD while experienced users preferred high THC: high CBD.(21) Almost none preferred high THC and low CBD, low THC and low CBD, only CBD, or only THC.(21, 33)	Quantitative (21, 33)	2 (1355)	Serious risk	Not serious	Not serious	Not serious	Not serious	Moderate

Cannabis administration route

Gender, reason for use and cannabis experience level influenced patients' preferred cannabis administration routes.	[Quantitative] Females patients preferred to use tincture and topical preparations and less preferred to use vaporizing and smoking preparations compared with males. (21) Patients who used cannabis both recreationally and medically preferred smoking and vaporizing, while those who used cannabis medically only preferred smoking, vaporizing, tinctures, and edibles. (21) Experienced cannabis users preferred multiple administration routes compared with novice users. Smoking, vaporizing, and edibles were the most common preferred administration routes among both experience and novice users. (21) [Mixed] Among chronic pain patients who are legal members of medical cannabis dispensaries, a minority of participants preferred using a joint, pipe, or bong, while some preferred vaporizers, edibles, or tinctures; very few preferred concentrates or topicals. In addition, very few participants reported unpleasant routes of administration as what	Quantitative (21), Mixed (35)	2 (2305)	Serious risk	Not serious	Not serious	Not serious	Not serious	Moderate

Most patients who have an advanced life-limiting illness preferred an oral form of medical cannabis.	[Quantitative] Most patients who have an advanced life-limiting illness stated preference for an oral form (pill, droplets under the tongue, or droplets added to food) and only a minority preferred smoking. (25)	Quantitative (25)	1 (68)	Very serious	Not serious	Not serious	Serious	Not serious	Low

2. Factors that influenced patient's decision regarding use of medical cannabis

2.1 Factors influenced the choice of medical cannabis use

Most patients used medical cannabis because it improved the management of symptoms associated with pain, mental health and other medical conditions.	[Mixed] Some patients who were legal members of medical cannabis dispensaries preferred aspects of medical cannabis related to health and well-being, including pain relief, sleep benefits, limited addiction potential, improved quality of life, functionality, and relaxation, while others preferred general aspects of medical cannabis, like general improvement in the quality of life, functionality, cognitive aspects (35).	Mixed (35)	1(984)	Serious risk	Not serious	Not serious	Not serious	Not serious	Moderate

[Qualitative] Patients viewed medical cannabis as an effective approach to managing symptoms with or without other medications (20, 22, 23), including pain (20, 22, 23), disrupted sleep, poor appetite, and nausea (20). Patients reported that cannabis improved emotional and mental well-being by reducing anxiety, depression and stress (20). Patients also reported that cannabis allowed them to sleep, focus and function (28). Most patients reported that cannabis facilitated a state of relaxation in which pain could be dealt with in a more tolerable form (28). However, patients found that medical cannabis use sometimes made it difficult to manage their medication regimen (23).	Qualitative (20, 22, 23, 28)	4 (245)	Minor concerns	No or very minor concerns	No or very minor concerns	No or very minor concerns	No or very minor concerns	High

Most patients were motivated to use medical cannabis to reduce other prescription medications.	[Quantitative] Chronic pain patients who used both medical cannabis and prescription medications believed that medical cannabis was effective for pain relief and were motivated to use medical cannabis to decrease the amount of prescribed medications they used (27).	Quantitative (27)	1 (500)	Serious risk	Not serious	Not serious	Not serious	Not serious	Moderate

[Qualitative] Patients with a range of chronic medical conditions (22) believed that medical cannabis managed pain symptoms and were motivated to use medical cannabis to decrease the amount of prescribed medications they used (22).	Qualitative (22)	1 (30)	No or very minor concerns	NA	No or very minor concerns	Moderate concerns	No or very minor concerns	Moderate

The majority of patients expressed that their cannabis use was influenced by positive social consequences, such as social support from friends and family.	[Quantitative] A majority of patients agreed that cannabis for medical use would not cause disagreements or relationship problems with their loved ones (25). Most participants reported that their family members were supportive of their use, and the majority reported that their medical providers were supportive of their use (31,34).	Quantitative (25,31,34)	2 (2104)	Serious risk	Not serious	Not serious	Not serious	Not serious	Moderate

Most patients expressed concerns with using cannabis when describing a range of adverse effects from use of medical cannabis.	[Quantitative] Concerns about medical cannabis included concerns about side effects, addiction, tolerance, losing control or acting strangely, and were related to unwillingness to use cannabis (27). Patients who used cannabis to manage their pain had greater feelings of anxiety, and increased catastrophic thinking (26). Among those who were unwilling to use cannabis, increased age was related to more concerns about medical cannabis, including concerns of losing control (26). Increased age also impacted beliefs that cannabis was a useful medication to treat pain (27). Some patients reported that they were concerned about unpleasant physical or emotional symptoms suggestive of withdrawal after stopping medical cannabis use (31 , 34). Some patients were concerned about mental or physical dependence to medical cannabis; however, most did not perceive themselves as addicted to medical cannabis (31 , 34). Concerns about addiction were associated with unwillingness to use medical cannabis (26). [Mixed] Some patients who were legal members of medical cannabis dispensaries reported adverse physical, cognitive, and emotional effects of medical cannabis, as well as people's negative and stigmatizing values towards medical cannabis (35).	Quantitative (26, 27, 31, 34), Mixed (35)	4(1650)	Serious risk	Not serious	Not serious	Not serious	Not serious	Moderate

[Qualitative] Patients commonly reported lack of concentration, poor memory and sleepiness as consequences of medical cannabis use. Participants also reported minor consequence which included eating too much, coughing, and weight gain. Seizures and anaphylaxis from an allergic reaction were described as severe consequences from use (20). Some patients were concerned that, while medical cannabis helped with pain management, it might lead addiction (23). Patients with a history of addiction were concerned that medical cannabis use could pose a threat to their sobriety (23).	Qualitative (20, 23)	2 (196)	Moderate concerns	No or very minor concerns	No or very minor concerns	Minor concerns	No or very minor concerns	Moderate

Most patients expressed that their cannabis use was influenced by negative social consequences, such as stigma.	[Quantitative] Patients who were comfortable with their cannabis use for pain had a significant concern over the use of cannabis leading to relationship problems or disagreements with loved ones (25). Some patients agreed that medical cannabis would make them vulnerable to attack and theft by substance abusers. A minority of patients agreed that medical cannabis would cause problems with the law, and that they may be arrested or charged with possession of cannabis (25). Some patients expressed concerns about others' opinions towards their used of cannabis-related products (31,34).	Quantitative (25,26,31, 34), Mixed (35)	4 (3153)	Serious risk	Not serious	Not serious	Not serious	Not serious	Moderate

	[Qualitative] Commonly reported negative social consequences included judgment from others as a result of use and "stoner" or "pothead" stereotypes (20, 32). Some patients reported that stigma affected the way they asked healthcare providers about cannabis as a treatment option, the ability to seek out medical cannabis as a treatment option, the location at which they purchased cannabis, and their ability to use cannabis in public. Patients who reported these factors tended to take longer to seek out cannabis as a treatment option, conceal their use, and would not speak to healthcare providers about cannabis (32).	Qualitative (20, 32)	2 (168)	Moderate concerns	No or very minor concerns	No or very minor concerns	Minor concerns	No or very minor concerns	Moderate
The cost, legal status, and accessibility of medical cannabis influenced patients' decisions to use medical cannabis.	[Quantitative] Some patients were concerned about the cost of medical cannabis and some were concerned about the legal status and accessibility of medical cannabis (31). Some patients reported that they would use medical cannabis if they had access to it (24). When making decisions about medical cannabis, the majority of patients relied on information from doctors, followed by the internet and friends or family (31, 34). [Mixed] Some patients who were legal members of medical cannabis dispensaries were	Quantitative (24,31), Mixed (35)	3 (2599)	Serious risk	Not serious	Not serious	Not serious	Not serious	Moderate

[Qualitative] Some patients felt that the cost of medical cannabis was too high, potentially limiting their access (20), while some reported that the legalization of medical cannabis improved access and influenced their decisions to purchase medical cannabis for symptom relief (20). Other patients found changes in policies related to medical cannabis difficult to navigate and wanted assistance to access medical cannabis (23).	Qualitative (20, 23)	2 (196)	Moderate concerns	No or very minor concerns	No or very minor concerns	Minor concerns	No or very minor concerns	Moderate

2.2 Factors influencing the choice of different preparations of medical cannabis

Patients chose medical cannabis products mainly based on cannabinoid content, recommendations from dispensary employees, described effects and side effects, cannabis variety, smell, and flower appearance.	[Quantitative] Most patients selected medical cannabis products based on cannabinoid content (e.g. THC), recommendations from dispensary employees, described effects, and cannabis variety (i.e. indica vs. sativa). A minority of patients selected cannabis based on visual properties and smell, and some patients were guided by recommendations from a friend, or name of the product. Recommendations from a medical professional was the least common factor that patients would consider when selecting medical cannabis (21). When selecting medical cannabis products, patients consider the following factors: the most commonly factors were smell, delta 9-tetrahydrocannabinol (THC) content, hybrid indica/sativa species, indica species, how the flower looks (size, density of the flower, and/or trichome and shape, cannabidiol (CBD) content, and sativa species. Some patients reported varietal name as important factor for medical cannabis selection.(30)	Quantitative (21, 30)	2 (2750)	Serious risk	Not serious	Serious	Not serious	Not serious	Low

[Qualitative] One study reported that long lasting effect of medical cannabis positively influenced patients choice of medical cannabis product (22). Another two studies reported that patients' uncertain about how they could determine which species of cannabis might work best to manage their pain and side effects of medical cannabis (e.g. headaches, disorientation or the sensation of feeling "stoned," coughing) negatively influence patients choice of medical cannabis product (23, 28).	Qualitative (22, 23,28)	3 (95)	No or very minor concerns	Moderate concerns	No or very minor concerns	Serious concerns	No or very minor concerns	Low

Gender, reason for use, and level of use experience influenced the factors patients considered when selecting cannabis products.	[Quantitative] Selection of cannabis product were influenced by gender, reason for use (e.g., medical only vs. medical and recreational), and cannabis experience level (e.g., novice vs. experienced). (21) A higher proportion of males selected cannabis products based on cannabinoid content (i.e. THC or CBD potency, ratio of THC and CBD), cannabis variety (i.e. indica or sativa), visual properties, and smell. A higher proportion of females consulted with a medical professional when choosing cannabis products. (21) Patients who use cannabis both medically and recreationally were more likely to select cannabis products based on THC or other cannabinoid content, cannabis variety, described effects, visual properties, smell, recommendation from friends, and the product name, while those who use cannabis medically were more likely use recommendations from dispensary employees or a medical professional. (21) Novice users were more likely to select a cannabis product based on dispensary recommendation consult with a medical professional than experienced users, while experienced users chose products based on nearly all other selection factors including smell, visual properties, described effects, cannabinoid content (i.e. THC or CBD potency, ratio of THC and CBD), cannabis variety (i.e. indica or sativa) and name of medical cannabis product (21).	Quantitative (21)	1 (1321)	Serious risk	Not serious	Not serious	Not serious	Not serious	Moderate

Abbreviations: CBD = cannabidiol; THC = delta-9-tetrahydrocannabinol.

MOOSE Checklist for Meta-analyses of Observational Studies

Item No	Recommendation	Reported on Page No
Reporting of background should include		
1	Problem definition	5
2	Hypothesis statement	5,6
3	Description of study outcome(s)	6
4	Type of exposure or intervention used	6
5	Type of study designs used	6
6	Study population	6
Reporting of search strategy should include		
7	Qualifications of searchers (eg, librarians and investigators)	7,8
8	Search strategy, including time period included in the synthesis and key words	7 & Appendix 1
9	Effort to include all available studies, including contact with authors	7
10	Databases and registries searched	7
11	Search software used, name and version, including special features used (eg, explosion)	7,8
12	Use of hand searching (eg, reference lists of obtained articles)	7
13	List of citations located and those excluded, including justification	11 & Appendix 6
14	Method of addressing articles published in languages other than English	8
15	Method of handling abstracts and unpublished studies	8
16	Description of any contact with authors	n/a
Reporting of methods should include		
17	Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested	7,8
18	Rationale for the selection and coding of data (eg, sound clinical principles or convenience)	9
19	Documentation of how data were classified and coded (eg, multiple raters, blinding and interrater reliability)	9
20	Assessment of confounding (eg, comparability of cases and controls in studies where appropriate)	n/a
21	Assessment of study quality, including blinding of quality assessors, stratification or regression on possible predictors of study results	8,9
22	Assessment of heterogeneity	9,10
23	Description of statistical methods (eg, complete description of fixed or random effects models, justification of whether the chosen models account for predictors of study results, dose-response models, or cumulative meta-analysis) in sufficient detail to be replicated	9
24	Provision of appropriate tables and graphics	Figure 1, Tables 1 & 2, Supplementary File
Reporting of results should include		
25	Graphic summarizing individual study estimates and overall estimate	n/a
26	Table giving descriptive information for each study included	Table 1
27	Results of sensitivity testing (eg, subgroup analysis)	n/a

28	Indication of statistical uncertainty of findings	Table 2

Item No	Recommendation	Reported on Page No
Reporting of discussion should include		
29	Quantitative assessment of bias (eg, publication bias)	n/a
30	Justification for exclusion (eg, exclusion of non-English language citations)	18
31	Assessment of quality of included studies	16
Reporting of conclusions should include		
32	Consideration of alternative explanations for observed results	17,18
33	Generalization of the conclusions (ie, appropriate for the data presented and within the domain of the literature review)	18
34	Guidelines for future research	18
35	Disclosure of funding source	20

From: Stroup DF, Berlin JA, Morton SC, et al, for the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) Group. Meta-analysis of Observational Studies in Epidemiology. A Proposal for Reporting. *JAMA*. 2000;283(15):2008-2012. doi: 10.1001/jama.283.15.2008.