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Complete List of Authors:	Wolfe, Dianna; Ottawa Hospital Research Institute, Ottawa Methods Centre Corace, Kimberly; University of Ottawa, Rice, Danielle Smith, Andra; University of Ottawa, Brain and Mind Research Institute Kanji, Salmaan; The Ottawa Hospital, Department of Pharmacy; University of Ottawa, Faculty of Medicine Conn, David; University of Toronto, Psychiatry Willows, Melanie; The Royal Ottawa Mental Health Centre, Substance Use and Concurrent Disorders Program Garber, Gary; Public Health Ontario, Infection Prevention and Control; University of Ottawa Faculty of Medicine, Medicine/infectious diseases Puxty, John; Queen's University, Faculty of Medicine Moghadam, Esther; Ottawa Public Health Skidmore, Becky; Independent Information Specialist Garritty, Chantelle; Ottawa Hospital Research Institute, Knowledge Synthesis Group; Ottawa Methods Centre, Ottawa Hospital Research Institut Thavorn, Kednapa; Institute for Clinical Evaluative Sciences, ICES @uOttawa; The Ottawa Hospital Research Institute, Moher, David; Ottawa Hospital Research Institute, Ottawa Methods Centre Hutton, Brian; University of Ottawa, Ottawa, Ontario, Canada,
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The effects of medical and non-medical cannabis use in older adults: protocol for a scoping review

Authorship List:

*Wolfe DM[1] (dwolfe@ohri.ca); *Corace K[1,2,3,4] (kim.corace@theroyal.ca); Rice DB[1,5] (danielle.rice@mail.mcgill.ca); Smith A[6] (andra.smith@uottawa.ca); Kanji S[1,7] (skanji@toh.ca); Conn D[8] (dconn@baycrest.org); Willows M[2,3,4] (melanie.willows@theroyal.ca); Garber G[9] (gary.garber@oahpp.ca); Puxty J[10] (puxtyj@providencecare.ca); Moghadam E[11] (esther.moghadam@ottawa.ca); Skidmore B[1] (bskidmore@rogers.com); Garritty C[1] (cgarritty@ohri.ca); Thavorn K[1,12] (kthavorn@ohri.ca); Moher D[1,12] (dmoher@ohri.ca); Hutton B[1,12] (bhutton@ohri.ca)

Affiliations

[1]Ottawa Hospital Research Institute, Ottawa, Canada
[2]University of Ottawa, Faculty of Medicine, Department of Psychiatry, Ottawa, Canada
[3]University of Ottawa Institute of Mental Health Research, Ottawa, ON, Canada
[4]The Royal Ottawa Mental Health Centre, Ottawa, ON, Canada
[5]McGill University Department of Psychology, Montreal, Canada
[6]University of Ottawa, Brain and Mind Research Institute
[7]The Ottawa Hospital, Department of Pharmacy, Ottawa, Canada
[8]University of Toronto, Department of Psychiatry
[9]Public Health Ontario, Toronto, Ontario
[10]Queen's University, Faculty of Medicine, Kingston, Canada
[11]Ottawa Public Health, Ottawa, Canada
[12]University of Ottawa, School of Epidemiology and Public Health, Ottawa, Canada

*denotes co-first authors; contributed equally to the planned research

Corresponding Author:
Dr. Brian Hutton
Center for Practice Changing Research
The Ottawa Hospital
501 Smyth Road, PO Box 201B,
Ottawa, ON, K1H 8L6
Email: bhutton@ohri.ca
Phone: 613-737-8899, ext 73842

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ABSTRACT

Introduction. With its legalization and regulation in Canada in 2018, the proportion of Canadians reporting cannabis use in 2019 increased substantially over the previous year, with half of new users being aged 45+ years. While use in older adults has been low historically, as baby boomers age, this demographic will progressively have more liberal attitudes, prior cannabis exposure and higher use rates. However, older adults experience slower metabolism, increased likelihood of polypharmacy, cognitive decline and chronic physical/mental health problems. There is a need to enhance knowledge of the effects of cannabis use in older adults. The following questions will be addressed using a scoping review approach: (1) What evidence exists regarding beneficial and harmful effects of medical and non-medical cannabis use in adults ≥50 years of age? (2) What is known about the beneficial and harmful effects of medical and non-medical cannabis use in older adults regarding: age, sex/gender, race/ethnicity, mental/physical comorbidities, use of other substances, consumption method, residential setting, employment status, marital status, accommodation status?

Methods and Analysis. Methods for scoping reviews outlined by Arksey & O'Malley and the Joanna Briggs Institute will be used. A librarian will design a systematic search of the literature for reviews, randomized trials, non-randomized trials, and observational studies of cannabis use. Eligibility criteria will be older adult participants, currently using cannabis (medical or non-medical), with studies required to report a cannabis-related health outcome to be eligible. Two reviewers will screen citations and full texts, with support from artificial intelligence. Two reviewers will chart data. Tables/graphics will be used to map evidence and identify evidence gaps.

Ethics and Dissemination. This research will enhance awareness of existing evidence addressing the health effects of medical and non-medical cannabis use in older adults. Findings will be disseminated through a peer reviewed publication, conference presentations and a stakeholder meeting.

Keywords: *medical cannabis; recreational cannabis; cannabis; elderly; seniors; scoping review; knowledge synthesis*

STRENGTHS AND LIMITATIONS OF THE STUDY

- This study will use a rigorous approach to scoping reviews to explore the health effects (both beneficial and harmful) of cannabis in the elderly, addressing a currently important knowledge gap for this population.
- The research is timely importance given emerging legalization of cannabis, and will address a large volume of literature which has not previously been synthesized.
- The proposal and protocol for this research have been designed by a broad group of experts in psychology, addiction medicine, mental health, knowledge synthesis, epidemiology, public health and knowledge translation, and will inform evidence needs for a range of vital knowledge users. Findings from the review will be discussed and interpreted collaboratively with team members holding a wealth of expertise and will help to prioritize future research.
- The final report will be prepared according to current best practices for reporting of scoping reviews, namely the PRISMA Extension Statement for scoping reviews.
- As this is a scoping review rather than a systematic review, formal quality assessments of all included studies will not be carried out.

INTRODUCTION

Until it was legalized in 2018, cannabis was the most widely used illicit substance in Canada [1]. However, many of the health impacts of cannabis, both positive and negative, have yet to be rigorously studied, given the ethics of conducting randomized controlled trials (RCTs) on illicit substances. Legalization has increased access to cannabis, resulting in potential benefits as well as potential harms to consumers, including, but not limited to increased risks of substance use disorder, accidents, injuries, and presentations to emergency departments [2,3]. These potential harms extend across all age groups. However, the effects of the aging process may mediate many cannabis-related harms in older adults that are not experienced in younger age groups. Although the proportion of middle-aged to older adults reporting cannabis use was relatively low prior to legalization in October 2018—9% amongst those 45 years and older, in early 2018 [4]—it has risen markedly in the months since legalization, to 14% in the first quarter of 2019 [4]. In addition to legalization, as the large baby boomer cohort ages, it brings with it more liberal attitudes, prior exposure to cannabis, and higher use rates [5]. Despite rising usage rates in this age group, the depth of available evidence regarding the health impacts of cannabis use in older adults is not known.

Cannabinoids are active at the endocannabinoid system (ECS), a series of neuromodulatory lipids and receptors located throughout the central and peripheral nervous systems, immune and hematopoietic systems, and many peripheral organs [6]. The presence of the ECS throughout the body implies the potential for widespread effects of cannabinoids, both beneficial and harmful. Delta-9 tetrahydrocannabinol (THC) and cannabidiol (CBD) are the predominant components of most cannabis products [7]. As well as some potential therapeutic benefits, THC is responsible for the intoxication and dependence associated with cannabis use and is the primary psychoactive

component of natural cannabis [7]. In contrast, CBD has no intoxicating effects or abuse liability, and because of its widespread activity in the ECS, it has been proposed to be beneficial therapeutically for a variety of health conditions [7]. Numerous potential therapeutic indications for medical cannabis have been evaluated in the literature, including but not limited to the control of nausea and vomiting associated with chemotherapy, relief of spasticity in multiple sclerosis patients, prevention of graft-versus-host disease in allogeneic hematopoietic stem cell transplantation, control of epilepsy and schizophrenia, ocular pressure reduction in glaucoma, HIV/AIDS-associated weight loss, and the control of central, peripheral, and chronic neuropathic pain of various etiologies [8,9]. As with many novel interventions, the results have varied by indication, with demonstrable benefits over harms for only some indications. Cannabis as a medical product became possible with the purification of whole plant extracts from *Cannabis sativa L.*, including the THC equivalent Tetrabinex, the CBD equivalent Nabidiolex, and nabiximols, a product containing THC and CBD in a 1:1 ratio [8]. Medical cannabis has been furthered through the development of various synthetic cannabinoids (e.g., the synthetic THC analogue, nabilone, and synthetic THC, dronabinol) [9]. Synthetic modification of the molecular structure of THC and CBD to create new synthetic molecules has the potential to widen the range of available cannabis products for medical and non-medical use and their effects on the body.

Generally, older adults suffer from more chronic medical and mental health conditions (e.g., chronic pain, insomnia) than younger adults, and the prevalence of anxiety disorders is high. Anecdotal reports suggest that older adults may be attracted to cannabis as a means to ameliorate symptoms of these chronic conditions [10]. As well, lifestyle changes that frequently occur in older adulthood, such as retirement or loss of a spouse, may lead to social isolation, increased leisure time, or loss of meaningful work, and contribute to increased cannabis use [10]. However, while

cannabis may be perceived by some patients to improve physical or mental health symptoms, older adults using cannabis either medically or recreationally may be unaware of changes that occur with age that may lead to varying and potentially harmful effects. Past research has demonstrated that cognitive function, attention, memory, and executive function—including abilities for impulse control, problem solving, and reasoning—are reduced with increasing age, and that consumption of drugs, including cannabis, has been associated with worsening and/or pronouncement of these deteriorations [11]. Aging is also associated with structural changes to both gray and white brain matter that correlate with brain function [12], and the use of cannabis can exacerbate these structural changes. Polypharmacy of prescription medications is widespread in the older adult population [13], and there is some evidence of negative drug interactions between cannabis and prescription and non-prescription medications [14–17], another important consideration for older adults. Finally, age-related alterations in the pharmacokinetics of drugs can have a direct impact on the psychoactive effects sought by recreational users, the beneficial health effects sought by medicinal users, and the harmful side-effects potentially experienced by both [11,18].

Age-related changes to the brain and pharmacodynamics suggest that there may be many important differences in the effects of cannabis in older adults compared to younger cohorts. However, the literature related to this research is diverse and vast. Although systematic and scoping reviews have been conducted on cannabis use in younger age groups [19–23], there remains a need for a collation and mapping of all research conducted on cannabis effects in older adults for the purposes of informing care, developing policy, and directing future research and synthesis efforts. A recent overview of systematic reviews evaluating the effectiveness of medical cannabis for any indication identified 73 relevant reviews [24], of which one was identified as highly relevant to older adults

[25]. In the planned research, we will conduct a scoping review of systematic reviews, RCTs, non-randomized studies (NRS) and observational studies to address the following research questions:

What sources and types of evidence exist regarding the beneficial and harmful effects of medical and non-medical cannabis use in older adults?

What is known from the existing literature about the beneficial and harmful effects of medical and non-medical cannabis use in older adults in the following sub-populations, concepts, and contexts:

- Age: 50–64 years, 65–74 years, 75+ years of age?
- Sex or gender?
- Race or ethnicity?
- Mental or physical comorbidities?
- Frailty?
- Use of other prescription or non-prescription drugs, alcohol, or illicit substances?
- Consumption method (i.e., smoking, vaporizing, oils, edibles, etc.)?
- Residential setting (e.g., community, retirement home, long-term care)?
- Employment status (e.g., working, retired) or income level?
- Marital status (e.g., single, married, widowed, divorced)?
- Accommodation status (i.e., alone, shared, homeless)?

METHODS AND ANALYSIS

This research will be undertaken using a scoping review approach, underpinned by the framework proposed by Arskey and O'Malley [26]. A scoping review maps the existing sources and types of evidence in a field of interest, and can be used to summarize and disseminate research findings to knowledge users [26]. Our methods will be guided by several resources, including the scoping

review methodology manual published by the Joanna Briggs Institute (JBI) [27] and other recent methods guidance [28–30].

Protocol and Registration

This protocol has been drafted to adhere to the Preferred Reporting Items for Systematic Reviews and Meta-analysis Protocols (PRISMA-P; **Appendix 1**). The protocol has been registered with the Open Science Framework. Given the reflexive and iterative nature of scoping reviews [26], amendments to the registered protocol are anticipated and will be described in the final study report.

Eligibility Criteria

Following the guidance of Arskey and O'Malley, our eligibility criteria will be adjusted as we develop familiarity and further expertise with the literature. We based our eligibility criteria on the PCC (Participants – Concept – Context) criteria [27] as follows:

- ***Participants***. Adults aged 50 years and older of any sex/gender or race, with current cannabis use.
    - **Age:** Studies or systematic reviews not explicitly reporting age data but evaluating patients with dementia/Alzheimer's disease, Parkinson's disease, or advanced or end-stage cancer will be included. In a recent review of cannabinoids in palliative medicine, included studies had age ranges >50 years when the population evaluated was patients with Alzheimer's disease or cancer-related pain, anorexia/cachexia, nausea and vomiting, or sleep disturbance [31]. More conditions specific to older adults may be identified as we progress through the review. Given that many studies will include patients both younger and older than 50 years of age, we will include studies that report age-stratified analyses for an age group of 50 years or older. If

age-stratified findings are not reported in a primary study, but 80% or more of the sample is 50 years of age or older, the study will be included. Similarly, if age data are not reported but patients with any of the health conditions identified above are included amongst patients with other health conditions, to be included, the study must have reported a condition-stratified analysis or 80–100% of the patients must have one of the identified conditions. ***For the purposes of this protocol, "older adult studies" are those in which (a) 80–100% of the sample is 50+ years of age, (b) if age data are not reported, 80–100% of the sample has dementia/Alzheimer's disease, Parkinson's disease, or advanced/end-stage cancer, or (c) an age- or condition-stratified analysis is reported for an age group over 50 years or one of the identified conditions.***

- **Current use:** The definition of "current use" will be variable across studies; however, we will not include studies evaluating use more than one year in the past. Older adults who are ex-users but are not currently using will not be of interest (e.g., those who used as adolescents). Patients with or without a mental or physical health comorbidity will be included. Studies and reviews evaluating younger as well as older adults will be included, if data have been reported for an age group of 50 years or older.
- **Comorbidities:** Examples of comorbidities include cancer (active or in remission), chronic pain, diabetes, anxiety, cognitive decline, dementia, depression, insomnia, post-traumatic stress disorder, and schizophrenia.

- ***Concept***. The concept of relevance for the review is characterized below in terms of both the interventions and outcomes of interest for this research, and are as follows:

- **Interventions**: Medical (i.e., either under the care of a medical professional or patient-defined) or non-medical cannabis, of any type, with any mode of consumption (e.g., smoking, vaporizing, oils, edibles), and any dosage will be included. All types of cannabis will be of interest, including whole-plant cannabis; purified whole-plant extracts from *Cannabis sativa L.* (e.g., Nabidiolex (purified CBD), Tetrabinex (purified THC), Sativex (purified 1:1 THC:CBD)); synthetic cannabinoids, such as synthetic THC (e.g., dronabinol, nabilone), CBD, and their derivatives, developed through modification of the molecular structure; and other cannabinoids, whether found in the cannabis plant or elsewhere, that are not THC or CBD but that interact with the ECS [32].
- **Outcomes**: Both beneficial and harmful effects of cannabis use on physical and mental health will be considered. These will include but not be limited to the following:
    - harmful physical health effects (e.g., falls, fractures, head injuries, emergency department visits, car accidents, cardiovascular effects, respiratory effects, non-adherence to other drugs);
    - beneficial physical effects (e.g., improvements in nausea, vomiting, pain, muscle spasticity, tremors, quality of life);
    - harmful mental health and behavioural outcomes (e.g., increased risky, manic, and suicidal behaviours; increased cannabis use disorder, cannabis abuse, cannabis dependence, or "problematic" cannabis use; increased or new anxiety, paranoia/psychosis, delirium, depression, sleep disturbance, reduced quality of life);

- beneficial mental health and behavioural outcomes (e.g., decreased risky, manic, and suicidal behaviours; decreased cannabis use disorder, cannabis abuse, cannabis dependence, or the word "problematic" or "problem" in juxtaposition to the phrase "cannabis use;" decreased anxiety, paranoia, delirium, depression, chronic pain, sleep, improved quality of life, improved post-traumatic stress disorder);
- physical brain outcomes (e.g., effects on gray matter, white matter integrity, functional connectivity, cortical thickness, total and regional volumes, surface morphometry/shape);
- pharmacokinetic impacts (e.g., comparative pharmacokinetics of cannabis in older vs younger adults, drug interactions between cannabis and other prescription/non-prescription/illicit drugs).

We will exclude single-arm studies that only report prevalence or incidence of cannabis use.

- ***Context***. Only studies focused on current cannabis consumption will be eligible. All settings are of interest in any geographic area. Consumption of other illicit or prescribed pharmaceuticals will be allowed. All periods of time and duration of follow-up will be eligible.
- ***Types of studies***. Systematic reviews, randomized controlled trials (RCTs), NRSs, and observational studies will be included. We will exclude diagnostic test accuracy studies, and studies developing or validating diagnostic criteria for cannabis use disorder or other cannabis-related mental health disorders. Editorials, letters, commentaries, abstracts, case reports, and narrative reviews will also be excluded. Only English and French publications

will be considered for reasons of timeliness and cost. Grey literature will not be reviewed given the anticipated volume of peer-reviewed literature to be screened (based on our preliminary search) as well as timeline and budget considerations.

We will define a systematic review as being a review with a clearly specified review question that incorporates a systematic search of two or more electronic literature databases, clearly defined eligibility criteria, systematic study selection and data collection by two or more reviewers, an appraisal of the risk of bias of included studies, and a synthesis of all information using a quantitative or qualitative approach. Review articles not meeting these criteria will be excluded. Non-randomized studies may include non-randomized, quasi-randomized, or single-arm trials (e.g., Phase I trials). Observational studies of any design will be included, except case reports and case series of fewer than 25 patients. Qualitative studies will be excluded.

Information Sources and Search Strategy

Preliminary basic searches of the literature identified an extremely high volume of references relevant to medical and non-medical cannabis (e.g., >120,000 records). We will work closely with an experienced information specialist to iteratively develop a search strategy that will balance the need for inclusivity with the need to yield a citation volume that will be manageable with current reference management software, within the budgetary and time constraints of the review. To balance these opposing needs, many alternative strategies will be considered, including restriction on date of publication, and application of filters for participant age (i.e., ≥50 years of age) or study designs of interest to the identified cannabis literature base.

Using the OVID platform, we will search Ovid MEDLINE®, including Epub Ahead of Print and In-Process & Other Non-Indexed Citations, Embase Classic+Embase, and PsycINFO. We will also search the Cochrane Library on Wiley.

Search strategies will utilize a combination of controlled vocabulary (e.g., "*cannabis,*" *"cannabinoids,*" "*marijuana use*") and keywords (e.g., "*marijuana,*" "*CBD,*" "*Sativex*"). Filters for the research designs of interest will be applied to the Ovid searches. Vocabulary and syntax will be adjusted across the databases searched as needed. When possible, animal-only, opinion pieces and case studies will be removed from the search results. Conference abstracts will be removed from Embase and Cochrane CENTRAL. Specific details regarding the strategies are provided in **Appendix 2**. The final search strategy will be peer reviewed by another senior information specialist using the Peer Review of Electronic Search Strategies (PRESS) Checklist [33].

Study Selection Process and Data Management

A sequential approach to study selection will be employed. We will prioritize screening and selection of systematic reviews first, given they are syntheses of findings from primary research studies, followed by NRSs and observational studies, and then RCTs. Non-randomized and observational studies will be prioritized for screening and selection above RCTs due to the expectation that (a) the majority of relevant recreational cannabis research will not be derived from RCTs, given the illegality of recreational cannabis throughout much of the world over the last 20 years; and (b) the expectation that much of the evidence pertaining to applications of medical cannabis from RCTs will be identified in included systematic reviews identified earlier in the study selection process. We will iteratively adjust our study selection based on the findings from each search result set, developing stop rules or refining terminology as needed. As noted earlier, any

adjustments will be noted in the final study report to maximize transparency in the research approach.

The online systematic review management software DistillerSR® will be used for database management and study selection (Evidence Partners Incorporated, Ottawa, Canada; www.evidencepartners.com). Generally, across the study design strata, two levels of reference screening will be conducted using a priori developed screening forms. A pilot exercise of a random sample of references will be conducted prior to starting each level to ensure high inter-rater reliability. Initially, titles and abstracts will be screened, with those references demonstrating potential relevance progressing to the next level, where their full texts will be assessed for relevance. At both levels, a liberal accelerated approach will be used: one reviewer will be required to include a paper, while agreement of two reviewers will be required to exclude [34]. Disagreements during title/abstract screening will result in a reference automatically progressing to the next level, where the full text will provide more information upon which to base a decision. At full-text screening, disagreements will be resolved by discussion or by the decision of a third reviewer.

Title/Abstract Screening

Initial screening will be designed to rapidly eliminate clearly irrelevant records. For each study design dataset, key word searches for terms related to adolescents and young adults will be conducted in the titles and abstracts, and the references identified by these searches as related to younger adults/adolescents will be split from the main dataset. Both datasets (i.e., the main dataset and the younger adult dataset) will be screened separately using the same methods described below.

Systematic review datasets will be screened with two levels of title/abstract screening: Level *1a* will screen for terms related to older age and current cannabis use, while Level *1b* will identify references with any cannabis-related outcomes. Primary study datasets (i.e., NRS/observational and RCT) will have a single level of title/abstract screening to identify references of relevance to older adults, current cannabis use, and any cannabis-related outcome.

Studies where relevance to older adults is unclear will be included to allow determination of age during full-text screening (i.e., if both younger and older patients are included, the reference will be included at title/abstract screening to determine if disaggregated results were reported in the full text). For title/abstract screening, the terms "psychedelic" and "hallucinogen" will be eligible; however, at full-text screening, cannabis use must be explicitly reported. Similarly, for title/abstract screening, any cannabis-related outcome will be eligible, where cannabis is the exposure/intervention (i.e., cannabis use should occur prior to the outcome). Case-control studies where a temporal association is not apparent will be included at title/abstract screening for further determination during full-text screening. Cannabis use as an outcome will not be eligible (e.g., studies evaluating associations between genes and cannabis use, evaluations of interventions to reduce cannabis use, single-arm studies reporting cannabis prevalence). However, cannabis use disorder (or similar) as an outcome will be eligible, where different types of cannabis use are compared as exposures/interventions. Diagnostic test accuracy evaluations and studies developing or validating diagnostic criteria for cannabis use disorder or other cannabis-related mental health disorders will be excluded.

Full-Text Screening

Full-text screening will follow a similar process for all study designs. Initially, references without full texts available in either English or French will be excluded. Subsequently, references that do not report results relevant to older adults will be excluded, followed by those that do not report a relevant cannabis-related outcome, and those in which cannabis use is not current. See the "Eligibility Criteria" section regarding definitions of "older adult study," "cannabis-related outcome," and "current cannabis use." The following criteria are study-design specific:

- Systematic reviews: must report **synthesized** results of older adult studies, whether in terms of a meta-analysis or narrative approach. If a narrative summary was used, it must include either quantitative results or a statement of the direction of effect cannabis use, with or without significance stated. Narrative summaries must appear in the Results section of the review, and not be limited to more general comments within the Discussion section. Reviews that by chance narratively summarize older adult studies, without acknowledging that the patient population was older, will be excluded because the inferences derived from the synthesis by the authors would not have been applied to the context of older adults. For final inclusion, systematic reviews must meet the definition of a systematic review described in the eligibility criteria. Systematic reviews reviewed in full text that reported relevant outcome data for one or more primary studies on older adults amongst many other primary studies on younger adults will be flagged to capture the citations of the older adult primary studies.

- Primary studies: must meet the definition of "older adult studies" as defined in the eligibility criteria.

Systematic reviews and primary studies focused strictly on adults over 50 years of age or, if age is not reported, on one of the eligible health conditions will have higher priority for subsequent data charting over studies that also include younger adults or other health conditions.

Use of Artificial Intelligence (AI) Software

Given the large number of anticipated search results, especially for the NRS and observational study stratum (>20,000 records), we will employ artificial intelligence (AI) methods available in DistillerSR software (Evidence Partners, Incorporated; Ottawa, Canada) where deemed feasible and reliable to inform the screening process. The available machine learning engines include both support vector machine (SVM) and Naïve Bayes classifiers. We will manually screen through the full text level a set of 300 or more references, which will be used to train the combined SVM and Naïve Bayes classifiers to generate a probability of relevance score valued at 0 (exclude), 0.5 (unclear) or 1 (include) for each reference in the database. These scores will be used to identify clearly non-relevant citations (i.e., those citations with a probability of 0). These citations will be grouped to be checked by a second human reviewer to confirm exclusion. The remaining studies that received probabilities of 0.5 or 1 will be sorted according to their relevance probability estimated by the empirical Naïve Bayes classifier, which is a continuous score between 0 and 1, to allow for prioritized screening. The Naïve Bayes classifier will be rerun and citations re-ordered after batches of 100 citations or more, depending on the size of the database and the inclusion rate. Prioritized screening will be performed using the liberal accelerated approach described earlier involving two reviewers, with the prioritized element allowing for earlier identification of eligible studies. A flow diagram will be presented in all reports to document the process of study selection.

Data Charting

Included studies will be prioritized for charting by study design. Systematic reviews will be charted first, followed by NRSs and observational studies, then RCTs. RCTs will be charted last, given that most will have already been captured in the data synthesized by the included systematic reviews. Using this approach, if, for example, a large volume of high-quality evidence is identified in systematic reviews related to applications of medical cannabis, it may provide rationale to limit the amount of data extraction from similarly focused RCTs.

A standardized data charting form will be developed in DistillerSR® (Evidence Partners Incorporated, Ottawa, Canada; www.evidencepartners.com) that will be refined during the data charting process as reviewers enhance their knowledge of the content area, in keeping with the iterative and reflexive nature of scoping reviews. Prior to data charting from references of a given study design, the charting form will be piloted by all reviewers who will chart data on a random sample of three articles [27]. Given the large number of anticipated included articles, we will (a) consider charting data in stages, starting with study-level data, then progressing to demographic/context data, then outcomes; and (b) have one reviewer chart study-level and demographic/context data, with a second reviewer verifying this information. To minimize errors of subjective interpretation of information that is critical to the review objectives, charting of the outcomes of each study will be conducted independently by two reviewers, followed by conflict resolution by discussion, with input from a third reviewer if necessary [35].

Items for data charting will include the following information:

- **Manuscript/study-level data**: study authors; year of publication; country of study or if not reported, country of first author; funding source; study design (i.e., systematic review,

RCT, NRS, observational study); objective; sample size. For systematic reviews, the number of included studies and patients will be charted.

- **Population demographics**: proportion of male/female/other participants, mean age/age distribution/age-related inclusion criteria, race/ethnicity distribution, employment status distribution, primary residence data (i.e., community, retirement home, long-term care facility), marital status data, accommodation status distribution (i.e., shared or alone), population data regarding mental health comorbidities (e.g., anxiety, depression, insomnia, schizophrenia) and physical health comorbidities (e.g., chronic pain, diabetes, cancer), data regarding co-use of other substances (yes/no, specify substances)
- **Type of cannabis consumption**: medical/non-medical/mixed, type of cannabis products consumed (e.g., whole plant/natural, synthetic, and names of strains/synthetic compounds evaluated), mode of consumption (e.g., smoking, vaporizing, edibles, oils), ratio of THC:CBD, concentration, dose.
- **Comparison evaluated**: no comparison (i.e., use-only single-arm studies) or comparisons of ***cannabis descriptors*** (e.g., use vs no use, frequencies of use, strain types, THC or CBD concentrations, THC:CBD ratios, modes of consumption) or ***participant descriptors*** (e.g., sexes/genders, age groups, races/ethnicities, employment statuses, primary residences (i.e., community, retirement home, long-term care facility), marital statuses, accommodation statuses (i.e., shared or alone), mental health comorbidities, physical health comorbidities, co-uses of other substances).
- **Outcomes**: For each outcome of interest reported (see eligibility criteria), the outcome definition, duration of follow-up, direction of effect, and significance will be charted.

Given this is a scoping review, all outcomes of interest will have equal priority. For systematic reviews, the authors' synthesized findings will be charted.

- Key findings identified by authors that are related to our review objectives.

Critical appraisal of included evidence sources

Quality appraisal of included systematic reviews will be conducted using the AMSTAR-2 tool [36] to identify evidence from high-quality reviews during synthesis. In keeping with scoping review methodology [27,37], formal assessment of the risk of bias in primary studies will not be undertaken.

Synthesis and presentation of the results

Mapping of the included evidence will be conducted in Microsoft Excel® (Microsoft Corporation, Seattle, Washington, USA), SmartDraw® (SmartDraw Software, LLC, San Diego, USA) and other software as needed, with results being presented using a combination of tabular, graphical, and narrative approaches. When presenting tabular data, we will group studies based upon underlying characteristics of interest, depending on the available data. These characteristics may include study design, analysis type, type of cannabis use (medical vs non-medical), or outcome type reported (i.e., mental health/behavioural, physical health, brain, and pharmacokinetic). Separate tables will be generated for each study design reviewed (e.g., systematic reviews, RCTs, NRSs and observational studies). Organizing data by outcome in tables may allow identification of comparisons across study design type, while also informing identification of contradictory results, if present. Visualization of results will be aided by using coloured table cells to indicate presence of subgroups. Similarly, outcome data will be presented with cell colour indicating direction of effect (e.g., studies with positive findings for an outcome would receive a green cell, negative findings a red cell, and non-significant findings a grey cell). Sample tables have been provided in

Appendix 3. Bar graphs, pie charts, geographic maps, bubble plots and other approaches will also be used to present trends of the evidence base in terms of characteristics such as year of publication, country of study, patient demographic traits (e.g., sex/gender, comorbidities). To augment tabular and graphical presentations, we will also provide structured descriptive summaries of study characteristics and outcomes to elaborate upon the evidence base and to identify topics associated with considerable information versus a current lack of primary research. Final reporting of the scoping review will follow the PRISMA extension for scoping reviews (PRISMA-ScR) [38].

Dissemination and Ethics

Scoping reviews involve the performance of reviewing and collecting data from publicly available information, and thus this research does not require ethics approval. Strategies for dissemination will include a peer reviewed publication, conference presentations and engagement with knowledge users as outlined in the Discussion section below.

Patient and Public Involvement

In planning this research, input was sought from patient organizations regarding elements of its design. Representatives from these organizations will also be part of a planned stakeholder meeting further described below that will inform prioritization of future research.

DISCUSSION

Knowledge translation strategies

Our review will use an integrated knowledge translation approach via the inclusion of our knowledge users (including representation from the Canadian Society of Addiction Medicine, the Canadian Coalition for Seniors' Mental Health, the National Initiative for the Care for the Elderly,

the Seniors Health Knowledge Network, the Community Addictions Peer Support Association, Public Health Ontario and Ottawa Public Health) as collaborators throughout the review process. Input on review questions and scope was sought in the design of this protocol to ensure that our work would inform current practice and policy needs. We will continue to consult with our knowledge user collaborators throughout the process of the review on questions of clinical and methodological importance. Manuscripts resulting from the review will be published in open-access journals chosen by the research team. Lay summaries and knowledge mobilization products for people with lived experience, the community, and decision makers will be developed for dissemination on our knowledge users' websites.

Implications

The findings from this review will form the foundation for a prioritization exercise with our knowledge users. Shortly after sharing our findings, we will present and discuss them with our knowledge users in a structured webinar. This will be followed by a survey of our knowledge users to establish their perspectives on future research priorities. Finally, an online Delphi process will further establish research priorities, as well as the appropriateness of designs for future research (i.e., the conduct of de novo primary research to address knowledge gaps vs the performance of full systematic reviews to synthesize evidence, where it already exists).

Potential limitations and mitigation strategies

This scoping review addresses a very broad topic and a considerable volume of information is anticipated to be retrieved by our search strategy. Using an unrestricted search strategy would result in a retrieved volume of records that would be unmanageable with current software (i.e., >120,000 references). We will mitigate this challenge in three ways: (1) imposing certain restrictions on the search strategy to reduce to volume of evidence, (2) using AI to aid in screening

a large volume of references, and (3) stratifying our approach to screening and data charting according to study design, focusing initial intensive efforts on higher levels of evidence [39].

Given the expected volume and heterogeneity of the charted evidence, we anticipate potential challenges in determining the most appropriate and useable method of reporting. We will maintain flexibility in the derivation of static tabular and graphical reporting methods, while communicating with our knowledge users regarding their needs. Provision of dynamic data options (i.e., Excel spreadsheets) will also be considered to allow greater usability of the data.

Conclusions

Recent legalization of cannabis in several jurisdictions worldwide has made a collation of the available evidence regarding the beneficial and harmful impacts of cannabis use on health imperative. Older adults are a population demonstrating increased levels of cannabis use; however, the natural aging process may put older adults at risk of adverse health effects from cannabis that may outweigh any benefits realized. The proposed scoping review will map the evidence base specific to older adults to inform decisions related to clinical care, policy, and future research directions.

FUNDING SOURCE

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CONTRIBUTIONS

BH, KC and DW designed the review. DW prepared the first draft of the manuscript. BS created and tested the search strategies to be used in the bibliographic databases. KC, DR, MW and AS provided clinical expertise, and BH and CG provided review expertise during protocol development. All authors reviewed, provided comment, and approved the protocol and manuscript. BH conceived of and is the guarantor of the review.

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APPENDICES TO:

The effects of medical and non-medical cannabis use in older adults: protocol for a scoping review.
Wolfe DM et al.

- Appendix 1: PRISMA-P Checklist
- Appendix 2: Search Strategy
- Appendix 3: Sample tables for presentation of findings

Appendix 1. PRISMA-P Checklist

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item	Page #
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	NA
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	23
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	8
Support:			
Sources	5a	Indicate sources of financial or other support for the review	23
Sponsor	5b	Provide name for the review funder and/or sponsor	23
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	23
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	4–7
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	7
METHODS			

Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	8–12
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	12–13
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	29–39
Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	14
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	13–17
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	18
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	18–20
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	10–11, 19–20
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	20
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	NA
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)	NA
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	NA
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	20–21, 40–45
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	NA
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	NA

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.

Appendix 2. Search Strategy

Cannabis
Final Strategy

Ovid Multifile

Database: Embase Classic+Embase <1947 to 2019 June 11>, Ovid MEDLINE(R) ALL <1946 to June 11, 2019>, PsycINFO <1806 to June Week 1 2019>
Search Strategy:
---

1 Cannabis/ (47483)
2 exp Cannabinoids/ (82151)
3 Marijuana Abuse/ (10406)
4 exp "Marijuana Use"/ (14185)
5 Marijuana Smoking/ (7532)
6 ("c.indica" or "c.sativa" or cannabi* or bhang or cannador or cbd or charas or eucannabinolide* or ganja or ganjah or hash or hashish or hemp or marihuana* or marijuana*).tw,kf. (136291)
7 (epidiolex or gwp 42003p or gwp42003p or nabidiolex).tw,kf. (165)
8 (dronabinol or thc or tetrahydrocannabinol* or ea 1477 or ea1477 or marinol or qcd 84924 or syndros or tetrabinex or tetranabinex).tw,kf. (24947)
9 (cesamet or nabilone).tw,kf. (979)
10 (deltanyne or "abbott 40566" or namisol or dronabinolum or "QCD 84924" or "CCRIS 4726").tw,kf. (27)
11 (nabiximol? or "gw 1000" or gw1000 or "sab 378" or sab378 or sativex).tw,kf. (1051)
12 (13956-29-1 or 19GBJ60SN5 or UNII-19GBJ60SN5 or ZYN002).rn,nm. (4791)
13 or/1-12 [CANNABIS] (170422)
14 exp Animals/ not (exp Animals/ and Humans/) (18640406)
15 13 not 14 [ANIMAL-ONLY REMOVED] (107451)
16 (comment or editorial or news or newspaper article).pt. (1925110)
17 (letter not (letter and randomized controlled trial)).pt. (2094822)
18 (case reports not (meta analysis or systematic review or controlled clinical trial or randomized controlled trial or pragmatic clinical trial or comparative study or observational study)).pt. (2003526)
19 (case report* or case study or case studies).ti. not (meta analysis or systematic review or controlled clinical trial or randomized controlled trial or pragmatic clinical trial or comparative study or observational study).pt. (663973)
20 15 not (16 or 17 or 18 or 19) [OPINION PIECES AND CASE REPORTS REMOVED] (100750)
21 limit 20 to yr="2000-current" (73251)
22 limit 21 to systematic reviews [Limit not valid in Embase; records were retained] (27329)
23 meta analysis.pt. (101732)
24 exp meta-analysis as topic/ (57757)
25 (meta-analy* or metanaly* or metaanaly* or met analy* or integrative research or integrative review* or integrative overview* or research integration or research overview* or collaborative review*).tw,kf. (390079)
26 systematic review.pt. (107850)
27 (systematic review* or systematic overview* or evidence-based review* or evidence-based overview* or (evidence adj3 (review* or overview*)) or meta-review* or meta-overview* or meta-synthes* or "review of reviews" or technology assessment* or HTA or HTAs).tw,kf. (463074)
28 exp Technology assessment, biomedical/ (24267)
29 (cochrane or health technology assessment or evidence report).jw. (38382)
30 (network adj (MA or MAs)).tw,kf. (22)

31 (NMA or NMAs).tw,kf. (4839)
32 indirect* compar*.tw,kf. (5074)
33 (indirect treatment* adj1 compar*).tw,kf. (743)
34 (mixed treatment* adj1 compar*).tw,kf. (1323)
35 (multiple treatment* adj1 compar*).tw,kf. (373)
36 (multi-treatment* adj1 compar*).tw,kf. (5)
37 simultaneous* compar*.tw,kf. (2469)
38 mixed comparison?.tw,kf. (69)
39 or/23-38 (799947)
40 21 and 39 (1997)
41 22 or 40 [SRs/MAs] (27931)
42 (controlled clinical trial or randomized controlled trial or pragmatic clinical trial).pt. (572176)
43 clinical trials as topic.sh. (187251)
44 exp Randomized Controlled Trials as Topic/ (288357)
45 (randomi#ed or randomly or RCT or placebo*).tw,kf. (2334678)
46 ((singl* or doubl* or trebl* or tripl*) adj (mask* or blind* or dumm*)).tw,kf. (420279)
47 trial.ti. (507909)
48 or/42-47 (2953906)
49 21 and 48 [RCTS] (5693)
50 controlled clinical trial.pt. (93106)
51 Controlled Clinical Trial/ or Controlled Clinical Trials as Topic/ (570170)
52 (control* adj2 trial*).tw,kf. (616820)
53 Non-Randomized Controlled Trials as Topic/ (10630)
54 (nonrandom* or non-random* or quasi-random* or quasi-experiment*).tw,kf. (132402)
55 (nRCT or nRCT or non-RCT).tw,kf. (710)
56 Controlled Before-After Studies/ (214313)
57 (control* adj3 ("before and after" or "before after")).tw,kf. (10168)
58 Interrupted Time Series Analysis/ (206520)
59 time series.tw,kf. (66339)
60 (pre- adj3 post-).tw,kf. (235905)
61 (pretest adj3 posttest).tw,kf. (18124)
62 Historically Controlled Study/ (224681)
63 (control* adj2 stud$3).tw,kf. (541007)
64 Control Groups/ (125963)
65 (control* adj2 group$1).tw,kf. (1235605)
66 trial.ti. (507909)
67 or/50-66 (3428538)
68 21 and 67 [NON-RCTS] (5249)
69 exp Cohort Studies/ (2337056)
70 cohort?.tw,kf. (1462096)
71 Retrospective Studies/ (1166307)
72 (longitudinal or prospective or retrospective).tw,kf. (3106077)
73 ((followup or follow-up) adj (study or studies)).tw,kf. (130193)
74 Observational study.pt. (62773)
75 (observation$2 adj (study or studies)).tw,kf. (252177)
76 ((population or population-based) adj (study or studies or analys#s)).tw,kf. (40902)
77 ((multidimensional or multi-dimensional) adj (study or studies)).tw,kf. (371)
78 Comparative Study.pt. (1831731)
79 ((comparative or comparison) adj (study or studies)).tw,kf. (263134)
80 exp Case-Control Studies/ (1156584)
81 ((case-control* or case-based or case-comparison) adj (study or studies)).tw,kf. (233233)

82 Cross-Sectional Studies/ (470673)
83 (cross-section* or crosssection*).tw,kf. (872615)
84 or/69-83 (8133205)
85 21 and 84 [OBSERVATIONAL STUDIES] (16552)
86 Qualitative Research/ (119259)
87 Interview/ (220812)
88 interview*.mp. (1208372)
89 (theme* or thematic).mp. (343144)
90 qualitative.af. (889955)
91 Nursing Methodology Research/ (30884)
92 questionnaire*.mp. (1946523)
93 ethnological research.mp. (29)
94 ethnograph*.mp. (49253)
95 ethnonursing.af. (363)
96 phenomenol*.af. (165043)
97 (grounded adj (theor* or study or studies or research or analys#s)).af. (78144)
98 (life stor* or women* stor*).mp. (6740)
99 (emic or etic or hermeneutic* or heuristic* or semiotic*).af. or (data adj1 saturat*).tw. or participant observ*.tw. (141504)
100 (social construct* or (postmodern* or post-structural*) or (post structural* or poststructural*) or post modern* or post-modern* or feminis* or interpret*).mp. (1234463)
101 (action research or cooperative inquir* or co operative inquir* or co-operative inquir*).mp. (17587)
102 (humanistic or existential or experiential or paradigm*).mp. (453321)
103 (field adj (study or studies or research)).tw. (43603)
104 human science.tw. (1161)
105 biographical method.tw. (103)
106 theoretical sampl*.af. (2386)
107 ((purpos* adj4 sampl*) or (focus adj group*)).af. (187736)
108 (account or accounts or unstructured or open-ended or open ended or text* or narrative*).mp. (1691731)
109 (life world or life-world or conversation analys#s or personal experience* or theoretical saturation).mp. (83460)
110 ((lived or life) adj experience*).mp. (67584)
111 observational method*.af. (4965)
112 content analys#s.af. (111618)
113 (constant adj (comparative or comparison)).af. (14795)
114 ((discourse* or discurs*) adj3 analys#s).tw. (13049)
115 narrative analys#s.af. (9134)
116 (heidegger* or colaizzi* or spiegelberg* or van manen* or van kaam* or merleau ponty* or husserl* or foucault* or (corbin adj2 strauss*) or glaser*).tw. (17480)
117 mixed method*.tw,kf. (59378)
118 or/86-117 (6729977)
119 21 and 118 [QUALITATIVE STUDIES] (18936)
120 41 or 49 or 68 or 85 or 119 [ALL STUDY DESIGNS] (51581)
121 120 use medall [MEDLINE RECORDS] (15274)
122 cannabis/ (47483)
123 exp cannabinoid/ (69089)
124 cannabis addiction/ (9169)
125 exp "cannabis use"/ (9827)
126 cannabis addiction/ (9169)

127 cannabis sativa/ (8702)
128 ("c.indica" or "c.sativa" or cannabi* or bhang or cannador or cbd or charas or eucannabinolide* or ganja or ganjah or hash or hashish or hemp or marihuana* or marijuana*).tw,kw. (137411)
129 (epidiolex or gwp 42003p or gwp42003p or nabidiolex).tw,kw. (165)
130 (dronabinol or thc or tetrahydrocannabinol* or ea 1477 or ea1477 or marinol or qcd 84924 or syndros or tetrabinex or tetranabinex).tw,kw. (25260)
131 (cesamet or nabilone).tw,kw. (993)
132 (deltanyne or "abbott 40566" or namisol or dronabinolum or "QCD 84924" or "CCRIS 4726").tw,kw. (27)
133 (nabiximol? or "gw 1000" or gw1000 or "sab 378" or sab378 or sativex).tw,kw. (1065)
134 (13956-29-1 or 19GBJ60SN5 or UNII-19GBJ60SN5 or ZYN002).rn. (4791)
135 or/122-134 [CANNABIS] (170167)
136 exp animal/ or exp animal experimentation/ or exp animal model/ or exp animal experiment/ or nonhuman/ or exp vertebrate/ (50765399)
137 exp human/ or exp human experimentation/ or exp human experiment/ (38848166)
138 136 not 137 (11918927)
139 135 not 138 [ANIMAL-ONLY REMOVED] (137727)
140 editorial.pt. (1097387)
141 letter.pt. not (letter.pt. and randomized controlled trial/) (2089753)
142 (case report* or case study or case studies).ti. not (meta-analysis/ or "systematic review"/ or randomized controlled trial/ or controlled clinical trial/ or controlled study/ or time series analysis/ or cohort analysis/ or retrospective study/ or longitudinal study/ or prospective study/ or exp comparative study/ or observational study/ or exp case control study/ or cross-sectional study/) (647181)
143 conference abstract.pt. (3430116)
144 139 not (140 or 141 or 142 or 143) [OPINION PIECES, CASE REPORTS AND CONFERENCE ABSTRACTS REMOVED] (119468)
145 limit 144 to yr="2000-current" (92402)
146 meta-analysis/ (270155)
147 "systematic review"/ (314772)
148 "meta analysis (topic)"/ (39946)
149 (meta-analy* or metanaly* or metaanaly* or met analy* or integrative research or integrative review* or integrative overview* or research integration or research overview* or collaborative review*).tw,kw. (393014)
150 (systematic review* or systematic overview* or evidence-based review* or evidence-based overview* or (evidence adj3 (review* or overview*)) or meta-review* or meta-overview* or meta-synthes* or "review of reviews" or technology assessment* or HTA or HTAs).tw,kw. (466451)
151 biomedical technology assessment/ (23156)
152 (cochrane or health technology assessment or evidence report).jw. (38382)
153 (network adj (MA or MAs)).tw,kw. (22)
154 (NMA or NMAs).tw,kw. (4857)
155 indirect* compar*.tw,kw. (5140)
156 (indirect treatment* adj1 compar*).tw,kw. (747)
157 (mixed treatment* adj1 compar*).tw,kw. (1347)
158 (multiple treatment* adj1 compar*).tw,kw. (379)
159 (multi-treatment* adj1 compar*).tw,kw. (5)
160 simultaneous* compar*.tw,kw. (2469)
161 mixed comparison?.tw,kw. (70)
162 or/146-161 (866096)
163 145 and 162 [REVIEWS] (3255)
164 randomized controlled trial/ or controlled clinical trial/ (1311919)
165 "clinical trial (topic)"/ (101825)

166 "randomized controlled trial (topic)"/ (161519)
167 (randomi#ed or randomly or RCT or placebo*).tw,kw. (2336720)
168 ((singl* or doubl* or trebl* or tripl*) adj (mask* or blind* or dumm*)).tw,kw. (420435)
169 trial.ti. (507909)
170 or/164-169 (3096931)
171 145 and 170 [RCTS] (8046)
172 controlled clinical trial/ (556323)
173 "controlled clinical trial (topic)"/ (10128)
174 (control* adj2 trial*).tw,kw. (620815)
175 (nonrandom* or non-random* or quasi-random* or quasi-experiment*).tw,kw. (132629)
176 (nRCT or nRCT or non-RCT).tw,kw. (711)
177 (control* adj3 ("before and after" or "before after")).tw,kw. (10173)
178 time series analysis/ (23336)
179 time series.tw,kw. (67114)
180 pretest posttest control group design/ (388)
181 (pre- adj3 post-).tw,kw. (235933)
182 (pretest adj3 posttest).tw,kw. (18127)
183 controlled study/ (6713848)
184 (control* adj2 stud$3).tw,kw. (542508)
185 control group/ (125963)
186 (control* adj2 group$1).tw,kw. (1235369)
187 trial.ti. (507909)
188 or/172-187 (8856567)
189 145 and 188 [NON-RCTS] (17004)
190 cohort analysis/ (714392)
191 cohort?.tw,kw. (1464380)
192 retrospective study/ (1537235)
193 longitudinal study/ (250984)
194 prospective study/ (1031600)
195 (longitudinal or prospective or retrospective).tw,kw. (3111465)
196 follow up/ (1448744)
197 ((followup or follow-up) adj (study or studies)).tw,kw. (132011)
198 observational study/ (231986)
199 (observation$2 adj (study or studies)).tw,kw. (252792)
200 population research/ (99974)
201 ((population or population-based) adj (study or studies or analys#s)).tw,kw. (48926)
202 ((multidimensional or multi-dimensional) adj (study or studies)).tw,kw. (372)
203 exp comparative study/ (3194802)
204 ((comparative or comparison) adj (study or studies)).tw,kw. (261543)
205 exp case control study/ (1156584)
206 ((case-control* or case-based or case-comparison) adj (study or studies)).tw,kw. (234698)
207 cross-sectional study/ (598245)
208 (cross-section* or crosssection*).tw,kw. (874654)
209 or/190-208 (10058649)
210 145 and 209 [OBSERVATIONAL STUDIES] (23782)
211 exp qualitative research/ (125102)
212 exp interview/ (285894)
213 interview*.mp. (1208372)
214 (theme* or thematic).mp. (343144)
215 qualitative.af. (889955)
216 nursing methodology research/ (30884)

217 questionnaire*.mp. (1946523)
218 ethnological research.mp. (29)
219 ethnograph*.mp. (49253)
220 ethnonursing.af. (363)
221 phenomenol*.af. (165043)
222 (grounded adj (theor* or study or studies or research or analys#s)).af. (78144)
223 (life stor* or women* stor*).mp. (6740)
224 (emic or etic or hermeneutic* or heuristic* or semiotic*).af. or (data adj1 saturat*).tw. or participant observ*.tw. (141504)
225 (social construct* or (postmodern* or post-structural*) or (post structural* or poststructural*) or post modern* or post-modern* or feminis* or interpret*).mp. (1234463)
226 (action research or cooperative inquir* or co operative inquir* or co-operative inquir*).mp. (17587)
227 (humanistic or existential or experiential or paradigm*).mp. (453321)
228 (field adj (study or studies or research)).tw. (43603)
229 human science.tw. (1161)
230 biographical method.tw. (103)
231 theoretical sampl*.af. (2386)
232 ((purpos* adj4 sampl*) or (focus adj group*)).af. (187736)
233 (account or accounts or unstructured or open-ended or open ended or text* or narrative*).mp. (1691731)
234 (life world or life-world or conversation analys#s or personal experience* or theoretical saturation).mp. (83460)
235 ((lived or life) adj experience*).mp. (67584)
236 observational method*.af. (4965)
237 content analys#s.af. (111618)
238 (constant adj (comparative or comparison)).af. (14795)
239 ((discourse* or discurs*) adj3 analys#s).tw. (13049)
240 narrative analys#s.af. (9134)
241 (heidegger* or colaizzi* or spiegelberg* or van manen* or van kaam* or merleau ponty* or husserl* or foucault* or (corbin adj2 strauss*) or glaser*).tw. (17480)
242 mixed method*.tw,kw. (59805)
243 or/211-242 (6739667)
244 145 and 243 [QUALITATIVE STUDIES] (23300)
245 163 or 171 or 189 or 210 or 244 [ALL STUDY DESIGNS] (50209)
246 245 use emczd [EMBASE RECORDS] (25229)
247 exp Cannabis/ (50168)
248 exp Cannabinoids/ (82151)
249 Marijuana Usage/ (2717)
250 ("c.indica" or "c.sativa" or cannabi* or bhang or cannador or cbd or charas or eucannabinolide* or ganja or ganjah or hash or hashish or hemp or marihuana* or marijuana*).tw. (135754)
251 (epidiolex or gwp 42003p or gwp42003p or nabidiolex).tw. (164)
252 (dronabinol or thc or tetrahydrocannabinol* or ea 1477 or ea1477 or marinol or qcd 84924 or syndros or tetrabinex or tetranabinex).tw. (24784)
253 (cesamet or nabilone).tw. (975)
254 (deltanyne or "abbott 40566" or namisol or dronabinolum or "QCD 84924" or "CCRIS 4726").tw. (26)
255 (nabiximol? or "gw 1000" or gw1000 or "sab 378" or sab378 or sativex).tw. (1040)
256 or/247-255 [CANNABIS] (167465)
257 limit 256 to yr="2000-current" (130951)

258 limit 257 to ("0830%2509%2509systematic review" or 1200 meta analysis or 1300 metasynthesis) [Limit not valid in Embase,Ovid MEDLINE(R),Ovid MEDLINE(R) Daily Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher,PsycINFO; records were retained] (111540)
259 meta analysis/ (270155)
260 (meta-analy* or metanaly* or metaanaly* or met analy* or integrative research or integrative review* or integrative overview* or research integration or research overview* or collaborative review*).tw. (388820)
261 "systematic review"/ (314772)
262 (systematic review* or systematic overview* or evidence-based review* or evidence-based overview* or (evidence adj3 (review* or overview*)) or meta-review* or meta-overview* or meta-synthes* or "review of reviews" or technology assessment* or HTA or HTAs).tw. (461287)
263 (network adj (MA or MAs)).tw. (22)
264 (NMA or NMAs).tw. (4824)
265 indirect* compar*.tw. (5052)
266 (indirect treatment* adj1 compar*).tw. (725)
267 (mixed treatment* adj1 compar*).tw. (1267)
268 (multiple treatment* adj1 compar*).tw. (360)
269 (multi-treatment* adj1 compar*).tw. (5)
270 simultaneous* compar*.tw. (2469)
271 mixed comparison?.tw. (69)
272 or/259-271 (811715)
273 257 and 272 (3419)
274 258 or 273 [REVIEWS] (111936)
275 limit 257 to "0300 clinical trial" [Limit not valid in Embase,Ovid MEDLINE(R),Ovid MEDLINE(R) Daily Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher; records were retained] (111666)
276 exp clinical trials/ (307124)
277 (randomi#ed or randomly or RCT or placebo*).tw. (2332689)
278 ((singl* or doubl* or trebl* or tripl*) adj (mask* or blind* or dumm*)).tw. (420183)
279 trial.ti. (507909)
280 or/276-279 (2730358)
281 257 and 280 (9191)
282 275 or 281 [RCTS] (112919)
283 (control* adj2 trial*).tw. (614352)
284 (nonrandom* or non-random* or quasi-random* or quasi-experiment*).tw. (132248)
285 (nRCT or nRCT or non-RCT).tw. (709)
286 (control* adj3 ("before and after" or "before after")).tw. (10162)
287 time series/ (23361)
288 time series.tw. (65880)
289 (pre- adj3 post-).tw. (235815)
290 (pretest adj3 posttest).tw. (18118)
291 (control* adj2 stud$3).tw. (540018)
292 experiment controls/ (907)
293 (control* adj2 group$1).tw. (1235251)
294 trial.ti. (507909)
295 or/283-294 (2833768)
296 257 and 295 [NON-RCTS] (7783)
297 limit 257 to ("0430 followup study" or "0450 longitudinal study" or "0451 prospective study" or "0453 retrospective study") [Limit not valid in Embase,Ovid MEDLINE(R),Ovid MEDLINE(R) Daily Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher; records were retained] (113931)
298 cohort?.tw. (1460179)

299 exp longitudinal studies/ (267415)
300 retrospective studies/ (1166307)
301 (longitudinal or prospective or retrospective).tw. (3101143)
302 followup studies/ (627480)
303 ((followup or follow-up) adj (study or studies)).tw. (128839)
304 exp observation methods/ (5724)
305 (observation$2 adj (study or studies)).tw. (251407)
306 ((population or population-based) adj (study or studies or analys#s)).tw. (40364)
307 ((multidimensional or multi-dimensional) adj (study or studies)).tw. (371)
308 ((comparative or comparison) adj (study or studies)).tw. (258365)
309 ((case-control* or case-based or case-comparison) adj (study or studies)).tw. (232321)
310 (cross-section* or crosssection*).tw. (871622)
311 or/298-310 (6229379)
312 257 and 311 (21156)
313 297 or 312 [OBSERVATIONAL STUDIES] (116189)
314 interview*.mp. (1208372)
315 thematic analysis/ (12832)
316 qualitative.af. (889955)
317 questionnaire*.mp. (1946523)
318 ethnological research.mp. (29)
319 ethnograph*.mp. (49253)
320 ethnonursing.af. (363)
321 phenomenol*.af. (165043)
322 grounded theory/ (10853)
323 (grounded adj (theor* or study or studies or research or analys#s)).af. (78144)
324 exp life experiences/ (51768)
325 (life stor* or women* stor*).mp. (6740)
326 (emic or etic or hermeneutic* or heuristic* or semiotic*).af. or (data adj1 saturat*).tw. or participant observ*.tw. (141504)
327 (social construct* or (postmodern* or post-structural*) or (post structural* or poststructural*) or post modern* or post-modern* or feminis* or interpret*).mp. (1234463)
328 (action research or cooperative inquir* or co operative inquir* or co-operative inquir*).mp. (17587)
329 (humanistic or existential or experiential or paradigm*).mp. (453321)
330 (field adj (study or studies or research)).tw. (43603)
331 human science.tw. (1161)
332 biographical method.tw. (103)
333 theoretical sampl*.af. (2386)
334 ((purpos* adj4 sampl*) or (focus adj group*)).af. (187736)
335 (account or accounts or unstructured or open-ended or open ended or text* or narrative*).mp. (1691731)
336 (life world or life-world or conversation analys#s or personal experience* or theoretical saturation).mp. (83460)
337 ((lived or life) adj experience*).mp. (67584)
338 observational method*.af. (4965)
339 content analys#s.af. (111618)
340 (constant adj (comparative or comparison)).af. (14795)
341 ((discourse* or discurs*) adj3 analys#s).tw. (13049)
342 narrative analys#s.af. (9134)
343 (heidegger* or colaizzi* or spiegelberg* or van manen* or van kaam* or merleau ponty* or husserl* or foucault* or (corbin adj2 strauss*) or glaser*).tw. (17480)

344 mixed method*.tw. (59032)
345 or/314-344 (6636676)
346 257 and 345 [QUALITATIVE STUDIES] (26698)
347 274 or 282 or 296 or 313 or 346 [ALL STUDY DESIGNS] (122411)
348 347 use medall,emczd (111415)
349 347 not 348 [PSYCINFO RECORDS] (10996)
350 121 or 246 or 349 [ALL STUDY DESIGNS - ALL DATABASES] (51499)
351 41 use medall [MEDLINE REVIEWS] (1327)
352 163 use emczd [EMBASE REVIEWS] (1765)
353 274 use medall,emczd (111415)
354 274 not 353 [PSYCINFO REVIEWS] (521)
355 351 or 352 or 354 [REVIEWS - ALL DATABASES] (3613)
356 remove duplicates from 355 (2316) [TOTAL UNIQUE REVIEWS]
357 356 use medall [MEDLINE UNIQUE REVIEWS] (1314)
358 356 use emczd [EMBASE UNIQUE REVIEWS] (853)
359 356 not (357 or 358) [PSYCINFO UNIQUE REVIEWS] (149)
360 49 use medall [MEDLINE RCTS] (2766)
361 171 use emczd [EMBASE RCTS] (4104)
362 282 use medall,emczd (111415)
363 282 not 362 [PSYCINFO RCTS] (1504)
364 360 or 361 or 363 [RCTS - ALL DATABASES] (8374)
365 limit 364 to yr="2012-current" (4981)
366 remove duplicates from 365 (2954)
367 364 not 365 (3393)
368 remove duplicates from 367 (2013)
369 366 or 368 [TOTAL UNIQUE RCTS] (4967)
370 369 use medall [MEDLINE UNIQUE RCTS] (2751)
371 369 use emczd [EMBASE UNIQUE RCTS] (1881)
372 369 not (370 or 371) [PSYCINFO UNIQUE RCTS] (335)
373 68 use medall [MEDLINE NRCTS] (2156)
374 189 use emczd [EMBASE NRCTS] (13613)
375 296 use medall,emczd (6496)
376 296 not 375 [PSYCINFO NRCTS] (1287)
377 373 or 374 or 376 [NRCTS - ALL DATABASES] (17056)
378 85 use medall [MEDLINE OBSERVATIONAL STUDIES] (9014)
379 210 use emczd [EMBASE OBSERVATIONAL STUDIES] (11318)
380 313 use medall,emczd (111415)
381 313 not 380 [PSYCINFO OBSERVATIONAL STUDIES] (4774)
382 378 or 379 or 381 [OBSERVATIONAL STUDIES - ALL DATABASES] (25106)
383 377 or 382 [NRCTS, OBSERVATIONAL STUDIES - ALL DATABASES] (35890)
384 limit 383 to yr="2018-current" (5258)
385 remove duplicates from 384 (3489)
386 limit 383 to yr="2016-2017" (5786)
387 remove duplicates from 386 (3556)
388 limit 383 to yr="2014-2015" (5227)
389 remove duplicates from 388 (3216)
390 limit 383 to yr="2012-2013" (4289)
391 remove duplicates from 390 (2631)
392 limit 383 to yr="2009-2011" (5305)
393 remove duplicates from 392 (3349)
394 limit 383 to yr="2005-2008" (5699)

395 remove duplicates from 394 (3749)
396 limit 383 to yr="2000-2004" (4326)
397 remove duplicates from 396 (2919)
398 385 or 387 or 389 or 391 or 393 or 395 or 397 [TOTAL UNIQUE NRCTS, OBSERVATIONAL STUDIES] (22909)
399 398 use medall [MEDLINE UNIQUE NRCTS, OBSERVATIONAL STUDIES] (10253)
400 398 use emczd [EMBASE UNIQUE NRCTS, OBSERVATIONAL STUDIES] (11250)
401 398 not (399 or 400) [PSYCINFO UNIQUE NRCTS, OBSERVATIONAL STUDIES] (1406)
402 119 use medall [MEDLINE QUALITATIVE STUDIES] (6892)
403 244 use emczd [EMBASE QUALITATIVE STUDIES] (9063)
404 346 use medall,emczd (18959)
405 346 not 404 [PSYCINFO QUALITATIVE STUDIES] (7739)
406 402 or 403 or 405 [QUALITATIVE STUDIES - ALL DATABASES] (23694)
407 limit 406 to yr="2017-current" (4897)
408 remove duplicates from 407 (3033)
409 limit 406 to yr="2014-2016" (5456)
410 remove duplicates from 409 (3388)
411 limit 406 to yr="2010-2013" (5531)
412 remove duplicates from 411 (3350)
413 limit 406 to yr="2005-2009" (4995)
414 remove duplicates from 413 (3056)
415 limit 406 to yr="2000-2004" (2816)
416 remove duplicates from 415 (1737)
417 408 or 410 or 412 or 414 or 416 [TOTAL UNIQUE QUALITATIVE STUDIES - ALL DATABASES] (14563)
418 417 use medall [MEDLINE UNIQUE QUALITATIVE STUDIES] (6877)
419 417 use emczd [EMBASE UNIQUE QUALITATIVE STUDIES] (3597)
420 417 not (418 or 419) [PSYCINFO UNIQUE QUALITATIVE STUDIES] (4089)

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Cochrane Library

https://www-cochranelibrary-com.proxy.bib.uottawa.ca/advanced-search/search-manager?search=3084048

Search Name: Cannabis - Final
Date Run: 13/06/2019 01:27:59
Comment: OHRI - 2019 Jun 12

ID Search Hits
#1 [mh Cannabis] 290
#2 [mh Cannabinoids] 731
#3 [mh "Marijuana Abuse"] 524
#4 [mh "Marijuana Use"] 284
#5 [mh "Marijuana Smoking"] 276
#6 ("c.indica" or "c.sativa" or cannabi* or bhang or cannador or cbd or charas or eucannabinolide* or ganja or ganjah or hash or hashish or hemp or marihuana* or marijuana*):ti,ab,kw 4028
#7 (epidiolex or gwp 42003p or gwp42003p or nabidiolex):ti,ab,kw 30
#8 (dronabinol or thc or tetrahydrocannabinol* or ea 1477 or ea1477 or marinol or qcd 84924 or syndros or tetrabinex or tetranabinex):ti,ab,kw 1387

#9 (cesamet or nabilone):ti,ab,kw 142
#10 (deltanyne or "abbott 40566" or namisol or dronabinolum or "QCD 84924" or "CCRIS 4726"):ti,ab,kw 16
#11 (nabiximol* or "gw 1000" or gw1000 or "sab 378" or sab378 or sativex):ti,ab,kw 167
#12 {or #1-#11} with Publication Year from 2000 to 2019, in Trials 3638
#13 {or #1-#11} in Cochrane Reviews, Cochrane Protocols 45
#14 #12 OR #13 3683

Reviews – 42
Protocols – 3
Trials – 3638

Appendix 3. Sample tables for presentation of findings

Table 1. Sample table depicting the presence/absence of demographic subgroups in observational studies.

Study	Age groups			Sex/gender			Race/ethnicity						Marital status					Employment status			Accommodation status			Residential setting			
	50–64	65–74	75+	Men	Women	Other	Caucasian	Black	Indigenous	Asian	Other	NR	Married	Single	Divorced	Widowed	NR	Retired	Working	NR	Alone	Shared	NR	Community	Retirement home	LTC	NR
Lee et al., 2012		■	■	■	■				■								■			■			■				
Smith et al., 2017	■			■			■								■			■			■			■			

Table 2. Sample table depicting the presence/absence of comorbidities and co-use in observational studies

Study	Mental health comorbidities							Physical comorbidities					Co-use			
	Anxiety	Depression	Insomnia	Schizophrenia	Cognitive decline	PTSD	NR	Cancer	Chronic pain	Diabetes	Multiple sclerosis	NR	Prescribed drugs	Illicit drugs	No co-use	NR
Lee et al., 2012									■							■
Smith et al., 2017		■											■	■	■	

Table 3. Sample table of types of cannabis use, products, and modes of consumption in observational studies

Study	Cannabis use				Cannabis product			Mode of consumption				
	Medical	Non-medical	Mixed	NR	Natural	Synthetic	NR	Smoking	Vaporizing	Edibles	Oils	NR
Lee et al., 2012	■	■	■		■			■	■	■	■	
Smith et al., 2017		■				■					■	

Table 4. Sample table of types of comparisons evaluated in primary studies

Study	Comparison evaluated					
	Use-only (single-arm study)	Use vs no use	Frequency of use	Strain type	Concentration of THC or CBD	Mode of consumption
Lee et al., 2012						
Smith et al., 2017						

Table 5. Sample table of all outcomes and direction of effects for observational studies. This table will likely be split into four, tables depending on outcomes reported: mental health/behavioural, physical health, brain, and pharmacokinetic outcomes. Green cells indicate a positive effect, red cells a negative effect, and grey cells a non-significant effect was found. Blank/white cells indicate an outcome was not measured.

Study and comparison (Reference group is listed second)	Mental health/behavioural						Physical health				Brain outcomes							Pharmacokinetic outcomes	
	Anxiety	Depression	Manic/ suicidal behaviour	Paranoia	Risky behaviour	New substance use disorder	Chronic pain	Car accidents	Falls	ED visits	Gray matter	White matter integrity	Functional connectivity	Cortical thickness	Total volume	Regional volumes	Surface morphometry/shape	Interactions with prescription drugs	Interactions with illicit drugs
Lee et al., 2012 Use vs no use																			
Lee et al., 2012 High vs low conc of THC																			
Lee et al., 2012																			

Study and comparison (Reference group is listed second)	Mental health/behavioural						Physical health				Brain outcomes							Pharmacokinetic outcomes	
	Anxiety	Depression	Manic/ suicidal behaviour	Paranoia	Risky behaviour	New substance use disorder	Chronic pain	Car accidents	Falls	ED visits	Gray matter	White matter integrity	Functional connectivity	Cortical thickness	Total volume	Regional volumes	Surface morphometry/shape	Interactions with prescription drugs	Interactions with illicit drugs
Smoking vs vaping																			
Smith et al., 2017 Daily vs weekly use																			
Smith et al., 2017 High vs low conc of THC																			

BMJ Open

The effects of medical and non-medical cannabis use in older adults: protocol for a scoping review

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2019-034301.R1
Article Type:	Protocol
Date Submitted by the Author:	13-Jan-2020
Complete List of Authors:	Wolfe, Dianna; Ottawa Hospital Research Institute Corace, Kimberly; University of Ottawa, Rice, Danielle; Ottawa Hospital Research Institute Smith, Andra; University of Ottawa, Brain and Mind Research Institute Kanji, Salmaan; The Ottawa Hospital, Department of Pharmacy; University of Ottawa, Faculty of Medicine Conn, David; University of Toronto, Psychiatry Willows, Melanie; The Royal Ottawa Mental Health Centre, Substance Use and Concurrent Disorders Program Garber, Gary; Public Health Ontario, Infection Prevention and Control; University of Ottawa Faculty of Medicine, Medicine/infectious diseases Puxty, John; Queen's University, Faculty of Medicine Moghadam, Esther; Ottawa Public Health Skidmore, Becky; Independent Information Specialist Garritty, Chantelle; Ottawa Hospital Research Institute Thavorn, Kednapa; The Ottawa Hospital Research Institute; Institute for Clinical Evaluative Sciences, ICES @uOttawa Moher, David; Ottawa Hospital Research Institute, Ottawa Methods Centre Hutton, Brian; Ottawa Hospital Research Institute; University of Ottawa, School of Epidemiology and Public Health
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Keywords:	PUBLIC HEALTH, EPIDEMIOLOGY, GERIATRIC MEDICINE

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The effects of medical and non-medical cannabis use in older adults: protocol for a scoping review

Authorship List:

*Wolfe D[1] (dwolfe@ohri.ca); *Corace K[1,2,3,4] (kim.corace@theroyal.ca); Rice D[1,5] (danielle.rice@mail.mcgill.ca); Smith A[6] (andra.smith@uottawa.ca); Kanji S[1,7] (skanji@toh.ca); Conn D[8] (dconn@baycrest.org); Willows M[2,3,4] (melanie.willows@theroyal.ca); Garber G[9] (gary.garber@oahpp.ca); Puxty J[10] (puxtyj@providencecare.ca); Moghadam E[11] (esther.moghadam@ottawa.ca); Skidmore B[1] (bskidmore@rogers.com); Garritty C[1] (cgarritty@ohri.ca); Thavorn K[1,12] (kthavorn@ohri.ca); Moher D[1,12] (dmoher@ohri.ca); Hutton B[1,12] (bhutton@ohri.ca)

Affiliations

[1]Ottawa Hospital Research Institute, Ottawa, Canada
[2]University of Ottawa, Faculty of Medicine, Department of Psychiatry, Ottawa, Canada
[3]University of Ottawa Institute of Mental Health Research, Ottawa, ON, Canada
[4]The Royal Ottawa Mental Health Centre, Ottawa, ON, Canada
[5]McGill University Department of Psychology, Montreal, Canada
[6]University of Ottawa, Brain and Mind Research Institute
[7]The Ottawa Hospital, Department of Pharmacy, Ottawa, Canada
[8]University of Toronto, Department of Psychiatry
[9]Public Health Ontario, Toronto, Ontario
[10]Queen's University, Faculty of Medicine, Kingston, Canada
[11]Ottawa Public Health, Ottawa, Canada
[12]University of Ottawa, School of Epidemiology and Public Health, Ottawa, Canada

*denotes co-first authors; contributed equally to the planned research

Corresponding Author:
Dr. Brian Hutton
Center for Practice Changing Research
The Ottawa Hospital
501 Smyth Road, PO Box 201B,
Ottawa, ON, K1H 8L6
Email: bhutton@ohri.ca
Phone: 613-737-8899, ext 73842

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ABSTRACT

Introduction. With its legalization and regulation in Canada in 2018, the proportion of Canadians reporting cannabis use in 2019 increased substantially over the previous year, with half of new users being aged 45+ years. While use in older adults has been low historically, as those born in the 1950s and 1960s continue to age, this demographic will progressively have more liberal attitudes, prior cannabis exposure and higher use rates. However, older adults experience slower metabolism, increased likelihood of polypharmacy, cognitive decline and chronic physical/mental health problems. There is a need to enhance knowledge of the effects of cannabis use in older adults. The following question will be addressed using a scoping review approach: What evidence exists regarding beneficial and harmful effects of medical and non-medical cannabis use in adults ≥50 years of age? Given that beneficial and harmful effects of cannabis may be mediated by patient-level (e.g., age, sex, race) and cannabis-related factors (e.g., natural vs synthetic, consumption method), subgroup effects related to these and additional factors will be explored.

Methods and Analysis. Methods for scoping reviews outlined by Arksey & O'Malley and the Joanna Briggs Institute will be used. A librarian designed a systematic search of the literature from database inception to June 2019. Using the OVID platform, Ovid MEDLINE® will be searched, including Epub Ahead of Print and In-Process & Other Non-Indexed Citations, Embase Classic+Embase, and PsycINFO for reviews, randomized trials, non-randomized trials, and observational studies of cannabis use. The Cochrane Library on Wiley will also be searched. Eligibility criteria will be older adult participants, currently using cannabis (medical or non-medical), with studies required to report a cannabis-related health outcome to be eligible. Two reviewers will screen citations and full texts, with support from artificial intelligence. Two reviewers will chart data. Tables/graphics will be used to map evidence and identify evidence gaps.

Ethics and Dissemination. This research will enhance awareness of existing evidence addressing the health effects of medical and non-medical cannabis use in older adults. Findings will be disseminated through a peer reviewed publication, conference presentations and a stakeholder meeting.

Keywords: *medical cannabis; recreational cannabis; cannabis; elderly; seniors; scoping review; knowledge synthesis*

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STRENGTHS AND LIMITATIONS OF THE STUDY

- This study will use a rigorous approach to scoping reviews to explore the health effects (both beneficial and harmful) of cannabis in the elderly, addressing a currently important knowledge gap for this population.
- The research will address a large volume of literature which has not previously been synthesized.
- This scoping review will include systematic reviews, randomized and non-randomized studies, and observational data.
- Grey literature will not be reviewed given the anticipated volume of peer-reviewed literature.
- This review will not formally assess the quality of included studies.

INTRODUCTION

Until it was legalized in 2018, cannabis was the most widely used illicit substance in Canada [1]. However, many of the health impacts of cannabis, both positive and negative, have yet to be rigorously studied, given the ethics of conducting randomized controlled trials (RCTs) on illicit substances with perceived harms. Legalization has increased access to cannabis, resulting in potential benefits as well as potential harms to consumers, including, but not limited to increased risks of substance use disorder, accidents, injuries, and presentations to emergency departments [2,3]. These potential harms extend across all age groups. However, the effects of the aging process may mediate many cannabis-related harms in older adults that are not experienced in younger age groups. Although the proportion of middle-aged to older adults reporting cannabis use was relatively low prior to legalization in October 2018—9% amongst those 45 years and older, in early 2018 [4]—it has risen markedly in the months since legalization, to 14% in the first quarter of 2019 [4]. In addition to legalization, as the cohort of individuals born in the 1950s and 1960s ages, it brings with it more liberal attitudes, prior exposure to cannabis, and higher use rates [5]. Despite rising usage rates in this age group, the depth of available evidence regarding the health impacts of cannabis use in older adults is not known.

Cannabinoids are active at the endocannabinoid system (ECS), a series of neuromodulatory lipids and receptors located throughout the central and peripheral nervous systems, immune and hematopoietic systems, and many peripheral organs [6]. The presence of the ECS throughout the body implies the potential for widespread effects of cannabinoids, both beneficial and harmful. Delta-9 tetrahydrocannabinol (THC) and cannabidiol (CBD) are the predominant components of most cannabis products [7]. As well as some potential therapeutic benefits, THC is responsible for the intoxication and dependence associated with cannabis use and is the primary psychoactive

component of natural cannabis [7]. In contrast, CBD has no intoxicating effects or abuse liability, and because of its widespread activity in the ECS, it has been proposed to be beneficial therapeutically for a variety of health conditions [7]. Numerous potential therapeutic indications for medical cannabis have been evaluated in the literature, including but not limited to the control of nausea and vomiting associated with chemotherapy, relief of spasticity in multiple sclerosis patients, prevention of graft-versus-host disease in allogeneic hematopoietic stem cell transplantation, control of epilepsy and schizophrenia, ocular pressure reduction in glaucoma, HIV/AIDS-associated weight loss, and the control of central, peripheral, and chronic neuropathic pain of various etiologies [8,9]. As with many novel interventions, the results have varied by indication, with demonstrable benefits over harms for only some indications. Cannabis as a medical product became possible with the purification of whole plant extracts from *Cannabis sativa L.*, including purified THC, CBD, and THC and CBD in a 1:1 ratio (nabiximols) [8]. Medical cannabis has been furthered through the development of various synthetic cannabinoids (e.g., the synthetic THC analogue, nabilone, and synthetic THC, dronabinol) [9]. Synthetic modification of the molecular structure of THC and CBD to create new synthetic molecules has the potential to widen the range of available cannabis products for medical and non-medical use and their effects on the body.

Generally, older adults suffer from more chronic medical and mental health conditions (e.g., chronic pain, insomnia, mood and cognitive disorders) than younger adults [10,11]. Anecdotal reports suggest that older adults may be attracted to cannabis as a means to ameliorate symptoms of these chronic medical conditions [12]. As well, lifestyle changes that frequently occur in older adulthood, such as retirement or loss of a spouse, may lead to social isolation, increased leisure time, or loss of meaningful work, and contribute to increased cannabis use [12]. However, while

cannabis may be perceived by some patients to improve physical or mental health symptoms, older adults using cannabis either medically or recreationally may be unaware of changes that occur with age that may lead to varying and potentially harmful effects. Past research has demonstrated that cognitive function, attention, memory, and executive function—including abilities for impulse control, problem solving, and reasoning—are reduced with increasing age, and that consumption of drugs, including cannabis, has been associated with worsening and/or pronouncement of these deteriorations [13–15]. Aging is also associated with structural changes to both gray and white brain matter that correlate with brain function [16], and the use of cannabis can exacerbate these structural changes. Polypharmacy of prescription medications is widespread in the older adult population [17], and there is some evidence of negative drug interactions between cannabis and prescription and non-prescription medications [18–21], another important consideration for older adults. Finally, age-related alterations in the pharmacokinetics of drugs can have a direct impact on the psychoactive effects sought by recreational users, the beneficial health effects sought by medicinal users, and the harmful side-effects potentially experienced by both [13,22].

Although systematic and scoping reviews have been conducted on cannabis use in younger age groups [23–27], age-related changes to the brain and pharmacodynamics suggest that there may be many important differences in the effects of cannabis in older adults compared to younger cohorts. Cannabis research literature is diverse and vast, which challenges systematic review methods. A scoping review would collate and map the available research on cannabis effects in older adults, demonstrating what topic areas may have sufficient evidence for future systematic review. As well, collation and mapping of the research evidence is a first step for the purposes of informing care, developing policy, and directing future primary research efforts. A recent overview of systematic reviews evaluating the effectiveness of medical cannabis for any indication identified

73 relevant reviews [28], of which one was identified as highly relevant to older adults [29]. In the planned research, we will conduct a scoping review of systematic reviews, RCTs, non-randomized studies (NRS) and observational studies to address the following research questions:

What evidence exists regarding the beneficial and harmful effects of medical and non-medical cannabis use in older adults?

What is known from the existing literature about the beneficial and harmful effects of medical and non-medical cannabis use in older adults in the following sub-populations, concepts, and contexts:

- Age: using older adult age groupings reported in the included literature?
- Sex or gender?
- Race or ethnicity?
- Mental or physical comorbidities?
- Frailty?
- Use of other prescription or non-prescription drugs, alcohol, or illicit substances?
- Consumption method (i.e., smoking, vaporizing, oils, edibles, etc.)?
- Residential setting (e.g., community, retirement home, long-term care)?
- Employment status (e.g., working, retired) or income level?
- Marital status (e.g., single, married, widowed, divorced)?
- Accommodation status (i.e., alone, shared, homeless)?

METHODS AND ANALYSIS

This research will be undertaken using a scoping review approach, underpinned by the framework proposed by Arskey and O'Malley [30]. A scoping review maps the existing sources and types of evidence in a field of interest, and can be used to summarize and disseminate research findings to

knowledge users [30]. Our methods will be guided by several resources, including the scoping review methodology manual published by the Joanna Briggs Institute (JBI) [31] and other recent methods guidance [32–34].

Protocol and Registration

This protocol has been drafted to adhere to the Preferred Reporting Items for Systematic Reviews and Meta-analysis Protocols (PRISMA-P; **Appendix 1**). The protocol has been registered with the Open Science Framework (DOI 10.17605/OSF.IO/5JTAQ). Given the reflexive and iterative nature of scoping reviews [30], amendments to the registered protocol are anticipated and will be described in the final study report.

Eligibility Criteria

Following the guidance of Arskey and O'Malley, our eligibility criteria will be adjusted as we develop familiarity and further expertise with the literature. We based our eligibility criteria on the PCC (Participants – Concept – Context) criteria [31] as follows:

- ***Participants***. Adults aged 50 years and older of any sex/gender or race, who currently use cannabis, with or without other substances (e.g., tobacco, alcohol, illicit drugs) will be of interest.
    - **Age:** Studies or systematic reviews not explicitly reporting age data but evaluating patients with dementia/Alzheimer's disease, Parkinson's disease, or advanced or end-stage cancer will be included. In a recent review of cannabinoids in palliative medicine, included studies had age ranges >50 years when the population evaluated was patients with Alzheimer's disease or cancer-related pain, anorexia/cachexia, nausea and vomiting, or sleep disturbance [35]. More conditions specific to older adults may be identified as we progress through the review. Given that many studies

will include patients both younger and older than 50 years of age, we will include studies that report age-stratified analyses for an age group of 50 years or older. If age-stratified findings are not reported in a primary study, but 80% or more of the sample is 50 years of age or older, the study will be included. Similarly, if age data are not reported but patients with any of the health conditions identified above are included amongst patients with other health conditions, to be included, the study must have reported a condition-stratified analysis or 80–100% of the patients must have one of the identified conditions. ***Therefore, for the purposes of this protocol, "older adult studies" are those in which (a) 80–100% of the sample is 50+ years of age, (b) if age data are not reported, 80–100% of the sample has dementia/Alzheimer's disease, Parkinson's disease, or advanced/end-stage cancer, or (c) an age- or condition-stratified analysis is reported for an age group over 50 years or one of the identified conditions.***

- **Current use:** The definition of "current use" will likely be variable across studies (e.g., daily, weekly, past-month, past-year); however, we will not include studies evaluating use more than one year in the past. Older adults who are ex-users but are not currently using will not be of interest (e.g., those who used as adolescents). Patients with or without a mental or physical health comorbidity will be included. Studies and reviews evaluating younger as well as older adults will be included, if data have been reported for an age group of 50 years or older.
- **Comorbidities:** Examples of comorbidities include cancer (active or in remission), chronic pain, diabetes, anxiety, cognitive decline, dementia, depression, insomnia, post-traumatic stress disorder, and schizophrenia.

- ***Concept***. The concept of relevance for the review is characterized below in terms of both the interventions and outcomes of interest for this research, and are as follows:
    - **Interventions**: Medical (i.e., either under the care of a medical professional or patient-defined) or non-medical cannabis, of any type, with any mode of consumption (e.g., smoking, vaporizing, oils, edibles), and any dosage will be included. All types of cannabis will be of interest, including whole-plant cannabis; purified whole-plant extracts from *Cannabis sativa L.* (e.g., purified THC, CBD, and 1:1 THC:CBD); synthetic cannabinoids, such as synthetic THC (e.g., dronabinol, nabilone), CBD, and their derivatives, developed through modification of the molecular structure; and other cannabinoids, whether found in the cannabis plant or elsewhere, that are not THC or CBD but that interact with the ECS [36].
    - **Outcomes**: Both beneficial and harmful effects of cannabis use on physical and mental health will be considered. These will include but not be limited to the following:
        - harmful physical health effects (e.g., falls, fractures, head injuries, emergency department visits, car accidents, cardiovascular effects, respiratory effects, non-adherence to other drugs);
        - beneficial physical effects (e.g., improvements in nausea, vomiting, pain, muscle spasticity, tremors, quality of life);
        - harmful mental health and behavioural outcomes (e.g., increased risky, manic, and suicidal behaviours; increased cannabis use disorder, cannabis abuse, cannabis dependence, or "problematic" cannabis use; increased or

new anxiety, paranoia/psychosis, delirium, depression, sleep disturbance, reduced quality of life);

- beneficial mental health and behavioural outcomes (e.g., decreased risky, manic, and suicidal behaviours; decreased cannabis use disorder, cannabis abuse, cannabis dependence, or the word "problematic" or "problem" in juxtaposition to the phrase "cannabis use;" decreased anxiety, paranoia, delirium, depression, chronic pain, sleep, improved quality of life, improved post-traumatic stress disorder);
- physical brain outcomes (e.g., effects on gray matter, white matter integrity, functional connectivity, cortical thickness, total and regional volumes, surface morphometry/shape);
- pharmacokinetic impacts (e.g., comparative pharmacokinetics of cannabis in older vs younger adults, drug interactions between cannabis and other prescription/non-prescription/illicit drugs).

We will exclude single-arm studies that only report prevalence or incidence of cannabis use.

- ***Context***. Only studies focused on current cannabis consumption will be eligible. All settings are of interest in any geographic area. Consumption of other illicit or prescribed pharmaceuticals will be allowed. All periods of time and duration of follow-up will be eligible.
- ***Types of studies***. Systematic reviews, randomized controlled trials (RCTs), NRSs, and observational studies will be included. We will exclude diagnostic test accuracy studies, and studies developing or validating diagnostic criteria for cannabis use disorder or other

cannabis-related mental health disorders. Editorials, letters, commentaries, abstracts, case reports, and narrative reviews will also be excluded. Only English and French publications will be considered for reasons of timeliness and cost. Grey literature will not be reviewed given the anticipated volume of peer-reviewed literature to be screened (based on our preliminary search (see Appendix 2)) as well as timeline and budget considerations.

We will define a systematic review as being a review with a clearly specified review question that incorporates a systematic search of two or more electronic literature databases, clearly defined eligibility criteria, systematic study selection and data collection by two or more reviewers, an appraisal of the risk of bias of included studies, and a synthesis of all information using a quantitative or qualitative approach. Review articles not meeting these criteria will be excluded. Non-randomized studies may include non-randomized, quasi-randomized, or single-arm trials (e.g., Phase I trials). Observational studies of any design will be included, except case reports and case series of fewer than 25 patients. Qualitative studies will be excluded.

Information Sources and Search Strategy

Preliminary basic searches of the literature identified an extremely high volume of references relevant to medical and non-medical cannabis (e.g., >120,000 records). We worked closely with an experienced information specialist to iteratively develop a search strategy that will balance the need for inclusivity with the need to yield a citation volume that will be manageable with current reference management software, within the budgetary and time constraints of the review (estimated completion date June 2020). To balance these opposing needs, alternative strategies will be considered, including restriction on date of publication, and application of filters for participant age (i.e., ≥50 years of age) or study designs of interest to the identified cannabis literature base.

Using the OVID platform, we will search Ovid MEDLINE®, including Epub Ahead of Print and In-Process & Other Non-Indexed Citations, Embase Classic+Embase, and PsycINFO. We will also search the Cochrane Library on Wiley. Databases will be searched from 1947 until June 11, 2019.

Search strategies will utilize a combination of controlled vocabulary (e.g., "*cannabis,*" *"cannabinoids,*" "*marijuana use*") and keywords (e.g., "*marijuana,*" "*CBD,*" "*Sativex*"). Filters for the research designs of interest will be applied to the Ovid searches. Vocabulary and syntax will be adjusted across the databases searched as needed. When possible, animal-only, opinion pieces and case studies will be removed from the search results. Conference abstracts will be removed from Embase and Cochrane CENTRAL. Specific details regarding the strategies are provided in **Appendix 2**. The final search strategy will be peer reviewed by another senior information specialist using the Peer Review of Electronic Search Strategies (PRESS) Checklist [37].

Study Selection Process and Data Management

A sequential approach to study selection will be employed. We will prioritize screening and selection of systematic reviews first, given they are syntheses of findings from primary research studies, followed by NRSs and observational studies, and then RCTs. Non-randomized and observational studies will be prioritized for screening and selection above RCTs due to the expectation that (a) the majority of relevant recreational cannabis research will not be derived from RCTs, given the illegality of recreational cannabis throughout much of the world over the last 20 years; and (b) the expectation that much of the evidence pertaining to applications of medical cannabis from RCTs will be identified in included systematic reviews identified earlier in the study selection process. We will iteratively adjust our study selection based on the findings from each

search result set, developing stop rules or refining terminology as needed. As noted earlier, any adjustments will be noted in the final study report to maximize transparency in the research approach.

The online systematic review management software DistillerSR® will be used for database management and study selection (Evidence Partners Incorporated, Ottawa, Canada; www.evidencepartners.com). Generally, across the study design strata, two levels of reference screening will be conducted using a priori developed screening forms. A pilot exercise of a random sample of references will be conducted prior to starting each level to ensure high inter-rater reliability. Initially, titles and abstracts will be screened, with those references demonstrating potential relevance progressing to the next level, where their full texts will be assessed for relevance. At both levels, a liberal accelerated approach will be used: one reviewer will be required to include a paper, while agreement of two reviewers will be required to exclude [38]. Disagreements during title/abstract screening will result in a reference automatically progressing to the next level, where the full text will provide more information upon which to base a decision. At full-text screening, disagreements will be resolved by discussion or by the decision of a third reviewer.

Title/Abstract Screening

Initial screening will be designed to rapidly eliminate clearly irrelevant records. For each study design dataset, key word searches for terms related to adolescents and young adults will be conducted in the titles and abstracts, and the references identified by these searches as related to younger adults/adolescents will be split from the main dataset. Both datasets (i.e., the main dataset

and the younger adult dataset) will be screened separately using the same methods described below.

Systematic review datasets will be screened with two levels of title/abstract screening: Level *1a* will screen for terms related to older age and current cannabis use, while Level *1b* will identify references with any cannabis-related outcomes. Primary study datasets (i.e., NRS/observational and RCT) will have a single level of title/abstract screening to identify references of relevance to older adults, current cannabis use, and any cannabis-related outcome.

Studies where relevance to older adults is unclear will be included to allow determination of age during full-text screening (i.e., if both younger and older patients are included, the reference will be included at title/abstract screening to determine if disaggregated results were reported in the full text). For title/abstract screening, the terms "psychedelic" and "hallucinogen" will be eligible; however, at full-text screening, cannabis use must be explicitly reported. Similarly, for title/abstract screening, any cannabis-related outcome will be eligible, where cannabis is the exposure/intervention (i.e., cannabis use should occur prior to the outcome). Case-control studies where a temporal association is not apparent will be included at title/abstract screening for further determination during full-text screening. Cannabis use as an outcome will not be eligible (e.g., studies evaluating associations between genes and cannabis use, evaluations of interventions to reduce cannabis use, single-arm studies reporting cannabis prevalence). However, cannabis use disorder (or similar) as an outcome will be eligible, where different types of cannabis use are compared as exposures/interventions. Diagnostic test accuracy evaluations and studies developing or validating diagnostic criteria for cannabis use disorder or other cannabis-related mental health disorders will be excluded.

Full-Text Screening

Full-text screening will follow a similar process for all study designs. Initially, references without full texts available in either English or French will be excluded. Subsequently, references that do not report results relevant to older adults will be excluded, followed by those that do not report a relevant cannabis-related outcome, and those in which cannabis use is not current. See the "Eligibility Criteria" section regarding definitions of "older adult study," "cannabis-related outcome," and "current cannabis use." The following criteria are study-design specific:

- Systematic reviews: must report **synthesized** results of older adult studies, whether in terms of a meta-analysis or narrative approach. If a narrative summary was used, it must include either quantitative results or a statement of the direction of effect cannabis use, with or without significance stated. Narrative summaries must appear in the Results section of the review, and not be limited to more general comments within the Discussion section. Reviews that by chance narratively summarize older adult studies, without acknowledging that the patient population was older, will be excluded because the inferences derived from the synthesis by the authors would not have been applied to the context of older adults. For final inclusion, systematic reviews must meet the definition of a systematic review described in the eligibility criteria. Systematic reviews reviewed in full text that reported relevant outcome data for one or more primary studies on older adults amongst many other primary studies on younger adults will be flagged to capture the citations of the older adult primary studies.

- Primary studies: must meet the definition of "older adult studies" as defined in the eligibility criteria.

Systematic reviews and primary studies focused strictly on adults over 50 years of age or, if age is not reported, on one of the eligible health conditions will have higher priority for subsequent data charting over studies that also include younger adults or other health conditions.

Use of Artificial Intelligence (AI) Software

Given the large number of anticipated search results, especially for the NRS and observational study stratum (>20,000 records), we will employ artificial intelligence (AI) methods available in DistillerSR software (Evidence Partners, Incorporated; Ottawa, Canada) where deemed feasible and reliable to inform the screening process. The available machine learning engines include both support vector machine (SVM) and Naïve Bayes classifiers. We will manually screen through the full text level a set of 300 or more references, which will be used to train the combined SVM and Naïve Bayes classifiers to generate a probability of relevance score valued at 0 (exclude), 0.5 (unclear) or 1 (include) for each reference in the database. These scores will be used to identify clearly non-relevant citations (i.e., those citations with a probability of 0). These citations will be grouped to be checked by a second human reviewer to confirm exclusion. The remaining studies that received probabilities of 0.5 or 1 will be sorted according to their relevance probability estimated by the empirical Naïve Bayes classifier, which is a continuous score between 0 and 1, to allow for prioritized screening. The Naïve Bayes classifier will be rerun and citations re-ordered after batches of 100 citations or more, depending on the size of the database and the inclusion rate. Prioritized screening will be performed using the liberal accelerated approach described earlier involving two reviewers, with the prioritized element allowing for earlier identification of eligible studies. A flow diagram will be presented in all reports to document the process of study selection.

Data Charting

Included studies will be prioritized for charting by study design. Systematic reviews will be charted first, followed by NRSs and observational studies, then RCTs. RCTs will be charted last, given that most will have already been captured in the data synthesized by the included systematic reviews. Using this approach, if, for example, a large volume of high-quality evidence is identified in systematic reviews related to applications of medical cannabis, it may provide rationale to limit the amount of data extraction from similarly focused RCTs.

A standardized data charting form will be developed in DistillerSR® (Evidence Partners Incorporated, Ottawa, Canada; www.evidencepartners.com) that will be refined during the data charting process as reviewers enhance their knowledge of the content area, in keeping with the iterative and reflexive nature of scoping reviews. Prior to data charting from references of a given study design, the charting form will be piloted by all reviewers who will chart data on a random sample of three articles [31]. Given the large number of anticipated included articles, we will (a) consider charting data in stages, starting with study-level data, then progressing to demographic/context data, then outcomes; and (b) have one reviewer chart study-level and demographic/context data, with a second reviewer verifying this information. To minimize errors of subjective interpretation of information that is critical to the review objectives, charting of the outcomes of each study will be conducted independently by two reviewers, followed by conflict resolution by discussion, with input from a third reviewer if necessary [39].

Items for data charting will include the following information:

- **Manuscript/study-level data**: study authors; year of publication; country of study or if not reported, country of first author; funding source; study design (i.e., systematic review,

RCT, NRS, observational study); objective; sample size. For systematic reviews, the number of included studies and patients will be charted.

- **Population demographics**: proportion of male/female/other participants, mean age/age distribution/age-related inclusion criteria, race/ethnicity distribution, employment status distribution, primary residence data (i.e., community, retirement home, long-term care facility), marital status data, accommodation status distribution (i.e., shared or alone), population data regarding mental health comorbidities (e.g., anxiety, depression, insomnia, schizophrenia) and physical health comorbidities (e.g., chronic pain, diabetes, cancer), data regarding co-use of other substances (yes/no, specify substances)
- **Type of cannabis consumption**: medical/non-medical/mixed, type of cannabis products consumed (e.g., whole plant/natural, synthetic, and names of strains/synthetic compounds evaluated), mode of consumption (e.g., smoking, vaporizing, edibles, oils), ratio of THC:CBD, concentration, dose.
- **Comparison evaluated**: no comparison (i.e., use-only single-arm studies) or comparisons of ***cannabis descriptors*** (e.g., use vs no use, frequencies of use, strain types, THC or CBD concentrations, THC:CBD ratios, modes of consumption) or ***participant descriptors*** (e.g., sexes/genders, age groups, races/ethnicities, employment statuses, primary residences (i.e., community, retirement home, long-term care facility), marital statuses, accommodation statuses (i.e., shared or alone), mental health comorbidities, physical health comorbidities, co-uses of other substances).
- **Outcomes**: For each outcome of interest reported (see eligibility criteria), the outcome definition, duration of follow-up, direction of effect, and significance will be charted.

Given this is a scoping review, all outcomes of interest will have equal priority. For systematic reviews, the authors' synthesized findings will be charted.

- Key findings identified by authors that are related to our review objectives.

Critical appraisal of included evidence sources

Quality appraisal of included systematic reviews will be conducted using the AMSTAR-2 tool [40] to identify evidence from high-quality reviews during synthesis. In keeping with scoping review methodology [31,41], formal assessment of the risk of bias in primary studies will not be undertaken.

Synthesis and presentation of the results

Mapping of the included evidence will be conducted in Microsoft Excel® (Microsoft Corporation, Seattle, Washington, USA), SmartDraw® (SmartDraw Software, LLC, San Diego, USA) and other software as needed, with results being presented using a combination of tabular, graphical, and narrative approaches. When presenting tabular data, we will group studies based upon underlying characteristics of interest, depending on the available data. These characteristics may include study design, analysis type, type of cannabis use (medical vs non-medical), or outcome type reported (i.e., mental health/behavioural, physical health, brain, and pharmacokinetic). Separate tables will be generated for each study design reviewed (e.g., systematic reviews, RCTs, NRSs and observational studies). Organizing data by outcome in tables may allow identification of comparisons across study design type, while also informing identification of contradictory results, if present. Visualization of results will be aided by using coloured table cells to indicate presence of subgroups. Similarly, outcome data will be presented with cell colour indicating direction of effect (e.g., studies with positive findings for an outcome would receive a green cell, negative findings a red cell, and non-significant findings a grey cell). Sample tables have been provided in

Appendix 3. Bar graphs, pie charts, geographic maps, bubble plots and other approaches will also be used to present trends of the evidence base in terms of characteristics such as year of publication, country of study, patient demographic traits (e.g., sex/gender, comorbidities). To augment tabular and graphical presentations, we will also provide structured descriptive summaries of study characteristics and outcomes to elaborate upon the evidence base and to identify topics associated with considerable information versus a current lack of primary research. Final reporting of the scoping review will follow the PRISMA extension for scoping reviews (PRISMA-ScR) [42].

Dissemination and Ethics

Scoping reviews involve the performance of reviewing and collecting data from publicly available information, and thus this research does not require ethics approval. Strategies for dissemination will include a peer reviewed publication, conference presentations and engagement with knowledge users as outlined in the Discussion section below.

Patient and Public Involvement

In planning this research, input was sought from multiple organizations representing individuals with lived experience during the preparation phase regarding elements of its design to ensure its findings would be of relevance to multiple groups including those with lived experience as well as stakeholders actively engaged in initiatives related to seniors' health. Representatives from these organizations will also be part of a planned stakeholder meeting further described below that will inform prioritization of future research.

DISCUSSION

Knowledge translation strategies

Our review will use an integrated knowledge translation approach via the inclusion of our knowledge users (including representation from the Canadian Society of Addiction Medicine, the Canadian Coalition for Seniors' Mental Health, the National Initiative for the Care for the Elderly, the Seniors Health Knowledge Network, the Community Addictions Peer Support Association, Public Health Ontario and Ottawa Public Health) as collaborators throughout the review process. Input on review questions and scope was sought in the design of this protocol to ensure that our work would inform current practice and policy needs. Based upon discussion amongst research team members, a scoping review approach (as opposed to a systematic review) was universally considered most appropriate based upon the current uncertainty regarding the availability and nature of evidence of cannabis use specific to the population of older adults. We will continue to consult with our knowledge user collaborators throughout the process of the review on questions of clinical and methodological importance. Manuscripts resulting from the review will be published in open-access journals chosen by the research team. Lay summaries and knowledge mobilization products for people with lived experience, the community, and decision makers will be developed for dissemination on our knowledge users' websites.

Implications

The findings from this review will form the foundation for a prioritization exercise with our knowledge users. Shortly after sharing our findings, we will present and discuss them with our knowledge users in a structured webinar. This will be followed by a survey of our knowledge users to establish their perspectives on future research priorities. An online Delphi process will further establish research priorities, as well as the appropriateness of designs for future research (i.e., the

conduct of de novo primary research to address knowledge gaps vs the performance of full systematic reviews to synthesize evidence, where it already exists).

Potential limitations and mitigation strategies

This scoping review addresses a very broad topic and a considerable volume of information is anticipated to be retrieved by our search strategy. Using an unrestricted search strategy would result in a retrieved volume of records that would be unmanageable with current software (i.e., >120,000 references). We will mitigate this challenge in three ways: (1) imposing certain restrictions on the search strategy to reduce to volume of evidence, (2) using AI to aid in screening a large volume of references, and (3) stratifying our approach to screening and data charting according to study design, focusing initial intensive efforts on higher levels of evidence [43]. The use of AI for screening in systematic reviews has become of considerable interest in recent years [44,45], particularly in the presence of large citation volumes [46], and we will employ a conservative approach wherein this tool will not be responsible for any final decisions as to the inclusion status of a study.

Regarding the minimum age criteria to be used for this review (50+ years), this value was selected by the research team following discussions wherein there was a consensus anticipation that there may exist limited data in adults aged 65+ years. A reduction in the minimum age criteria was considered to allow for a conservative approach to include more data related to the group of older adults.

To increase the transparency of our review methods, we will use the Open Science Framework to record any changes made to our protocol, as anticipated due to the iterative nature of scoping reviews.

Given the expected volume and heterogeneity of the charted evidence, we anticipate potential challenges in determining the most appropriate and useable method of reporting. We will maintain flexibility in the derivation of static tabular and graphical reporting methods, while communicating with our knowledge users regarding their needs. Provision of dynamic data options (i.e., Excel spreadsheets) will also be considered to allow greater usability of the data.

Recent legalization of cannabis in several jurisdictions worldwide has made a collation of the available evidence regarding the beneficial and harmful impacts of cannabis use on health imperative. Older adults are a population demonstrating increased levels of cannabis use; however, the natural aging process may put older adults at risk of adverse health effects from cannabis that may outweigh any benefits realized. The proposed scoping review will map the evidence base specific to older adults to inform decisions related to clinical care, policy, and future research directions.

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CONTRIBUTIONS

BH, KC and DW designed the review. DW prepared the first draft of the manuscript. BS created and tested the search strategies to be used in the bibliographic databases. KC, DR, MW and AS provided clinical expertise, and BH and CG provided review expertise during protocol development. All authors (DW, KC, DR, AS, SK, DC, MW, GG, JP, EM, BS, CG, KT, DM, BH) provided input in the planning of the study and also reviewed, provided comment, and approved the protocol and manuscript. BH conceived of and is the guarantor of the review.

COMPETING INTERESTS

BH has previously received honoraria from Cornerstone Research Group for methodologic advice related to the conduct of systematic reviews and meta-analysis. No other authors have any competing interests to declare.

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APPENDICES TO:

The effects of medical and non-medical cannabis use in older adults: protocol for a scoping review. Wolfe DM et al.

- Appendix 1: PRISMA-P Checklist
- Appendix 2: Search Strategy
- Appendix 3: Sample tables for presentation of findings

Appendix 1. PRISMA-P Checklist

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item	Page #
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	NA
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	23
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	8
Support:			
Sources	5a	Indicate sources of financial or other support for the review	23
Sponsor	5b	Provide name for the review funder and/or sponsor	23
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	23
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	4–7
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	7
METHODS			

Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	8–12
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	12–13
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	29–39
Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	14
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	13–17
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	18
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	18–20
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	10–11, 19–20
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	20
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	NA
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)	NA
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	NA
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	20–21, 40–45
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	NA
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	NA

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.

Appendix 2. Search Strategy

Cannabis
Final Strategy

Ovid Multifile

Database: Embase Classic+Embase <1947 to 2019 June 11>, Ovid MEDLINE(R) ALL <1946 to June 11, 2019>, PsycINFO <1806 to June Week 1 2019>
Search Strategy:
---

1 Cannabis/ (47483)
2 exp Cannabinoids/ (82151)
3 Marijuana Abuse/ (10406)
4 exp "Marijuana Use"/ (14185)
5 Marijuana Smoking/ (7532)
6 ("c.indica" or "c.sativa" or cannabi* or bhang or cannador or cbd or charas or eucannabinolide* or ganja or ganjah or hash or hashish or hemp or marihuana* or marijuana*).tw,kf. (136291)
7 (epidiolex or gwp 42003p or gwp42003p or nabidiolex).tw,kf. (165)
8 (dronabinol or thc or tetrahydrocannabinol* or ea 1477 or ea1477 or marinol or qcd 84924 or syndros or tetrabinex or tetranabinex).tw,kf. (24947)
9 (cesamet or nabilone).tw,kf. (979)
10 (deltanyne or "abbott 40566" or namisol or dronabinolum or "QCD 84924" or "CCRIS 4726").tw,kf. (27)
11 (nabiximol? or "gw 1000" or gw1000 or "sab 378" or sab378 or sativex).tw,kf. (1051)
12 (13956-29-1 or 19GBJ60SN5 or UNII-19GBJ60SN5 or ZYN002).rn,nm. (4791)
13 or/1-12 [CANNABIS] (170422)
14 exp Animals/ not (exp Animals/ and Humans/) (18640406)
15 13 not 14 [ANIMAL-ONLY REMOVED] (107451)
16 (comment or editorial or news or newspaper article).pt. (1925110)
17 (letter not (letter and randomized controlled trial)).pt. (2094822)
18 (case reports not (meta analysis or systematic review or controlled clinical trial or randomized controlled trial or pragmatic clinical trial or comparative study or observational study)).pt. (2003526)
19 (case report* or case study or case studies).ti. not (meta analysis or systematic review or controlled clinical trial or randomized controlled trial or pragmatic clinical trial or comparative study or observational study).pt. (663973)
20 15 not (16 or 17 or 18 or 19) [OPINION PIECES AND CASE REPORTS REMOVED] (100750)
21 limit 20 to yr="2000-current" (73251)
22 limit 21 to systematic reviews [Limit not valid in Embase; records were retained] (27329)
23 meta analysis.pt. (101732)
24 exp meta-analysis as topic/ (57757)
25 (meta-analy* or metanaly* or metaanaly* or met analy* or integrative research or integrative review* or integrative overview* or research integration or research overview* or collaborative review*).tw,kf. (390079)
26 systematic review.pt. (107850)
27 (systematic review* or systematic overview* or evidence-based review* or evidence-based overview* or (evidence adj3 (review* or overview*)) or meta-review* or meta-overview* or meta-synthes* or "review of reviews" or technology assessment* or HTA or HTAs).tw,kf. (463074)
28 exp Technology assessment, biomedical/ (24267)
29 (cochrane or health technology assessment or evidence report).jw. (38382)
30 (network adj (MA or MAs)).tw,kf. (22)

31 (NMA or NMAs).tw,kf. (4839)
32 indirect* compar*.tw,kf. (5074)
33 (indirect treatment* adj1 compar*).tw,kf. (743)
34 (mixed treatment* adj1 compar*).tw,kf. (1323)
35 (multiple treatment* adj1 compar*).tw,kf. (373)
36 (multi-treatment* adj1 compar*).tw,kf. (5)
37 simultaneous* compar*.tw,kf. (2469)
38 mixed comparison?.tw,kf. (69)
39 or/23-38 (799947)
40 21 and 39 (1997)
41 22 or 40 [SRs/MAs] (27931)
42 (controlled clinical trial or randomized controlled trial or pragmatic clinical trial).pt. (572176)
43 clinical trials as topic.sh. (187251)
44 exp Randomized Controlled Trials as Topic/ (288357)
45 (randomi#ed or randomly or RCT or placebo*).tw,kf. (2334678)
46 ((singl* or doubl* or trebl* or tripl*) adj (mask* or blind* or dumm*)).tw,kf. (420279)
47 trial.ti. (507909)
48 or/42-47 (2953906)
49 21 and 48 [RCTS] (5693)
50 controlled clinical trial.pt. (93106)
51 Controlled Clinical Trial/ or Controlled Clinical Trials as Topic/ (570170)
52 (control* adj2 trial*).tw,kf. (616820)
53 Non-Randomized Controlled Trials as Topic/ (10630)
54 (nonrandom* or non-random* or quasi-random* or quasi-experiment*).tw,kf. (132402)
55 (nRCT or nRCT or non-RCT).tw,kf. (710)
56 Controlled Before-After Studies/ (214313)
57 (control* adj3 ("before and after" or "before after")).tw,kf. (10168)
58 Interrupted Time Series Analysis/ (206520)
59 time series.tw,kf. (66339)
60 (pre- adj3 post-).tw,kf. (235905)
61 (pretest adj3 posttest).tw,kf. (18124)
62 Historically Controlled Study/ (224681)
63 (control* adj2 stud$3).tw,kf. (541007)
64 Control Groups/ (125963)
65 (control* adj2 group$1).tw,kf. (1235605)
66 trial.ti. (507909)
67 or/50-66 (3428538)
68 21 and 67 [NON-RCTS] (5249)
69 exp Cohort Studies/ (2337056)
70 cohort?.tw,kf. (1462096)
71 Retrospective Studies/ (1166307)
72 (longitudinal or prospective or retrospective).tw,kf. (3106077)
73 ((followup or follow-up) adj (study or studies)).tw,kf. (130193)
74 Observational study.pt. (62773)
75 (observation$2 adj (study or studies)).tw,kf. (252177)
76 ((population or population-based) adj (study or studies or analys#s)).tw,kf. (40902)
77 ((multidimensional or multi-dimensional) adj (study or studies)).tw,kf. (371)
78 Comparative Study.pt. (1831731)
79 ((comparative or comparison) adj (study or studies)).tw,kf. (263134)
80 exp Case-Control Studies/ (1156584)
81 ((case-control* or case-based or case-comparison) adj (study or studies)).tw,kf. (233233)

82 Cross-Sectional Studies/ (470673)
83 (cross-section* or crosssection*).tw,kf. (872615)
84 or/69-83 (8133205)
85 21 and 84 [OBSERVATIONAL STUDIES] (16552)
86 Qualitative Research/ (119259)
87 Interview/ (220812)
88 interview*.mp. (1208372)
89 (theme* or thematic).mp. (343144)
90 qualitative.af. (889955)
91 Nursing Methodology Research/ (30884)
92 questionnaire*.mp. (1946523)
93 ethnological research.mp. (29)
94 ethnograph*.mp. (49253)
95 ethnonursing.af. (363)
96 phenomenol*.af. (165043)
97 (grounded adj (theor* or study or studies or research or analys#s)).af. (78144)
98 (life stor* or women* stor*).mp. (6740)
99 (emic or etic or hermeneutic* or heuristic* or semiotic*).af. or (data adj1 saturat*).tw. or participant observ*.tw. (141504)
100 (social construct* or (postmodern* or post-structural*) or (post structural* or poststructural*) or post modern* or post-modern* or feminis* or interpret*).mp. (1234463)
101 (action research or cooperative inquir* or co operative inquir* or co-operative inquir*).mp. (17587)
102 (humanistic or existential or experiential or paradigm*).mp. (453321)
103 (field adj (study or studies or research)).tw. (43603)
104 human science.tw. (1161)
105 biographical method.tw. (103)
106 theoretical sampl*.af. (2386)
107 ((purpos* adj4 sampl*) or (focus adj group*)).af. (187736)
108 (account or accounts or unstructured or open-ended or open ended or text* or narrative*).mp. (1691731)
109 (life world or life-world or conversation analys#s or personal experience* or theoretical saturation).mp. (83460)
110 ((lived or life) adj experience*).mp. (67584)
111 observational method*.af. (4965)
112 content analys#s.af. (111618)
113 (constant adj (comparative or comparison)).af. (14795)
114 ((discourse* or discurs*) adj3 analys#s).tw. (13049)
115 narrative analys#s.af. (9134)
116 (heidegger* or colaizzi* or spiegelberg* or van manen* or van kaam* or merleau ponty* or husserl* or foucault* or (corbin adj2 strauss*) or glaser*).tw. (17480)
117 mixed method*.tw,kf. (59378)
118 or/86-117 (6729977)
119 21 and 118 [QUALITATIVE STUDIES] (18936)
120 41 or 49 or 68 or 85 or 119 [ALL STUDY DESIGNS] (51581)
121 120 use medall [MEDLINE RECORDS] (15274)
122 cannabis/ (47483)
123 exp cannabinoid/ (69089)
124 cannabis addiction/ (9169)
125 exp "cannabis use"/ (9827)
126 cannabis addiction/ (9169)

127 cannabis sativa/ (8702)
128 ("c.indica" or "c.sativa" or cannabi* or bhang or cannador or cbd or charas or eucannabinolide* or ganja or ganjah or hash or hashish or hemp or marihuana* or marijuana*).tw,kw. (137411)
129 (epidiolex or gwp 42003p or gwp42003p or nabidiolex).tw,kw. (165)
130 (dronabinol or thc or tetrahydrocannabinol* or ea 1477 or ea1477 or marinol or qcd 84924 or syndros or tetrabinex or tetranabinex).tw,kw. (25260)
131 (cesamet or nabilone).tw,kw. (993)
132 (deltanyne or "abbott 40566" or namisol or dronabinolum or "QCD 84924" or "CCRIS 4726").tw,kw. (27)
133 (nabiximol? or "gw 1000" or gw1000 or "sab 378" or sab378 or sativex).tw,kw. (1065)
134 (13956-29-1 or 19GBJ60SN5 or UNII-19GBJ60SN5 or ZYN002).rn. (4791)
135 or/122-134 [CANNABIS] (170167)
136 exp animal/ or exp animal experimentation/ or exp animal model/ or exp animal experiment/ or nonhuman/ or exp vertebrate/ (50765399)
137 exp human/ or exp human experimentation/ or exp human experiment/ (38848166)
138 136 not 137 (11918927)
139 135 not 138 [ANIMAL-ONLY REMOVED] (137727)
140 editorial.pt. (1097387)
141 letter.pt. not (letter.pt. and randomized controlled trial/) (2089753)
142 (case report* or case study or case studies).ti. not (meta-analysis/ or "systematic review"/ or randomized controlled trial/ or controlled clinical trial/ or controlled study/ or time series analysis/ or cohort analysis/ or retrospective study/ or longitudinal study/ or prospective study/ or exp comparative study/ or observational study/ or exp case control study/ or cross-sectional study/) (647181)
143 conference abstract.pt. (3430116)
144 139 not (140 or 141 or 142 or 143) [OPINION PIECES, CASE REPORTS AND CONFERENCE ABSTRACTS REMOVED] (119468)
145 limit 144 to yr="2000-current" (92402)
146 meta-analysis/ (270155)
147 "systematic review"/ (314772)
148 "meta analysis (topic)"/ (39946)
149 (meta-analy* or metanaly* or metaanaly* or met analy* or integrative research or integrative review* or integrative overview* or research integration or research overview* or collaborative review*).tw,kw. (393014)
150 (systematic review* or systematic overview* or evidence-based review* or evidence-based overview* or (evidence adj3 (review* or overview*)) or meta-review* or meta-overview* or meta-synthes* or "review of reviews" or technology assessment* or HTA or HTAs).tw,kw. (466451)
151 biomedical technology assessment/ (23156)
152 (cochrane or health technology assessment or evidence report).jw. (38382)
153 (network adj (MA or MAs)).tw,kw. (22)
154 (NMA or NMAs).tw,kw. (4857)
155 indirect* compar*.tw,kw. (5140)
156 (indirect treatment* adj1 compar*).tw,kw. (747)
157 (mixed treatment* adj1 compar*).tw,kw. (1347)
158 (multiple treatment* adj1 compar*).tw,kw. (379)
159 (multi-treatment* adj1 compar*).tw,kw. (5)
160 simultaneous* compar*.tw,kw. (2469)
161 mixed comparison?.tw,kw. (70)
162 or/146-161 (866096)
163 145 and 162 [REVIEWS] (3255)
164 randomized controlled trial/ or controlled clinical trial/ (1311919)
165 "clinical trial (topic)"/ (101825)

"randomized controlled trial (topic)"/ (161519)
(randomi#ed or randomly or RCT or placebo*).tw,kw. (2336720)
((singl* or doubl* or trebl* or tripl*) adj (mask* or blind* or dumm*)).tw,kw. (420435)
trial.ti. (507909)
or/164-169 (3096931)
145 and 170 [RCTS] (8046)
controlled clinical trial/ (556323)
"controlled clinical trial (topic)"/ (10128)
(control* adj2 trial*).tw,kw. (620815)
(nonrandom* or non-random* or quasi-random* or quasi-experiment*).tw,kw. (132629)
(nRCT or nRCT or non-RCT).tw,kw. (711)
(control* adj3 ("before and after" or "before after")).tw,kw. (10173)
time series analysis/ (23336)
time series.tw,kw. (67114)
pretest posttest control group design/ (388)
(pre- adj3 post-).tw,kw. (235933)
(pretest adj3 posttest).tw,kw. (18127)
controlled study/ (6713848)
(control* adj2 stud$3).tw,kw. (542508)
control group/ (125963)
(control* adj2 group$1).tw,kw. (1235369)
trial.ti. (507909)
or/172-187 (8856567)
145 and 188 [NON-RCTS] (17004)
cohort analysis/ (714392)
cohort?.tw,kw. (1464380)
retrospective study/ (1537235)
longitudinal study/ (250984)
prospective study/ (1031600)
(longitudinal or prospective or retrospective).tw,kw. (3111465)
follow up/ (1448744)
((followup or follow-up) adj (study or studies)).tw,kw. (132011)
observational study/ (231986)
(observation$2 adj (study or studies)).tw,kw. (252792)
population research/ (99974)
((population or population-based) adj (study or studies or analys#s)).tw,kw. (48926)
((multidimensional or multi-dimensional) adj (study or studies)).tw,kw. (372)
exp comparative study/ (3194802)
((comparative or comparison) adj (study or studies)).tw,kw. (261543)
exp case control study/ (1156584)
((case-control* or case-based or case-comparison) adj (study or studies)).tw,kw. (234698)
cross-sectional study/ (598245)
(cross-section* or crosssection*).tw,kw. (874654)
or/190-208 (10058649)
145 and 209 [OBSERVATIONAL STUDIES] (23782)
exp qualitative research/ (125102)
exp interview/ (285894)
interview*.mp. (1208372)
(theme* or thematic).mp. (343144)
qualitative.af. (889955)
nursing methodology research/ (30884)

217 questionnaire*.mp. (1946523)
218 ethnological research.mp. (29)
219 ethnograph*.mp. (49253)
220 ethnonursing.af. (363)
221 phenomenol*.af. (165043)
222 (grounded adj (theor* or study or studies or research or analys#s)).af. (78144)
223 (life stor* or women* stor*).mp. (6740)
224 (emic or etic or hermeneutic* or heuristic* or semiotic*).af. or (data adj1 saturat*).tw. or participant observ*.tw. (141504)
225 (social construct* or (postmodern* or post-structural*) or (post structural* or poststructural*) or post modern* or post-modern* or feminis* or interpret*).mp. (1234463)
226 (action research or cooperative inquir* or co operative inquir* or co-operative inquir*).mp. (17587)
227 (humanistic or existential or experiential or paradigm*).mp. (453321)
228 (field adj (study or studies or research)).tw. (43603)
229 human science.tw. (1161)
230 biographical method.tw. (103)
231 theoretical sampl*.af. (2386)
232 ((purpos* adj4 sampl*) or (focus adj group*)).af. (187736)
233 (account or accounts or unstructured or open-ended or open ended or text* or narrative*).mp. (1691731)
234 (life world or life-world or conversation analys#s or personal experience* or theoretical saturation).mp. (83460)
235 ((lived or life) adj experience*).mp. (67584)
236 observational method*.af. (4965)
237 content analys#s.af. (111618)
238 (constant adj (comparative or comparison)).af. (14795)
239 ((discourse* or discurs*) adj3 analys#s).tw. (13049)
240 narrative analys#s.af. (9134)
241 (heidegger* or colaizzi* or spiegelberg* or van manen* or van kaam* or merleau ponty* or husserl* or foucault* or (corbin adj2 strauss*) or glaser*).tw. (17480)
242 mixed method*.tw,kw. (59805)
243 or/211-242 (6739667)
244 145 and 243 [QUALITATIVE STUDIES] (23300)
245 163 or 171 or 189 or 210 or 244 [ALL STUDY DESIGNS] (50209)
246 245 use emczd [EMBASE RECORDS] (25229)
247 exp Cannabis/ (50168)
248 exp Cannabinoids/ (82151)
249 Marijuana Usage/ (2717)
250 ("c.indica" or "c.sativa" or cannabi* or bhang or cannador or cbd or charas or eucannabinolide* or ganja or ganjah or hash or hashish or hemp or marihuana* or marijuana*).tw. (135754)
251 (epidiolex or gwp 42003p or gwp42003p or nabidiolex).tw. (164)
252 (dronabinol or thc or tetrahydrocannabinol* or ea 1477 or ea1477 or marinol or qcd 84924 or syndros or tetrabinex or tetranabinex).tw. (24784)
253 (cesamet or nabilone).tw. (975)
254 (deltanyne or "abbott 40566" or namisol or dronabinolum or "QCD 84924" or "CCRIS 4726").tw. (26)
255 (nabiximol? or "gw 1000" or gw1000 or "sab 378" or sab378 or sativex).tw. (1040)
256 or/247-255 [CANNABIS] (167465)
257 limit 256 to yr="2000-current" (130951)

258 limit 257 to ("0830%2509%2509systematic review" or 1200 meta analysis or 1300 metasynthesis) [Limit not valid in Embase,Ovid MEDLINE(R),Ovid MEDLINE(R) Daily Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher,PsycINFO; records were retained] (111540)
259 meta analysis/ (270155)
260 (meta-analy* or metanaly* or metaanaly* or met analy* or integrative research or integrative review* or integrative overview* or research integration or research overview* or collaborative review*).tw. (388820)
261 "systematic review"/ (314772)
262 (systematic review* or systematic overview* or evidence-based review* or evidence-based overview* or (evidence adj3 (review* or overview*)) or meta-review* or meta-overview* or meta-synthes* or "review of reviews" or technology assessment* or HTA or HTAs).tw. (461287)
263 (network adj (MA or MAs)).tw. (22)
264 (NMA or NMAs).tw. (4824)
265 indirect* compar*.tw. (5052)
266 (indirect treatment* adj1 compar*).tw. (725)
267 (mixed treatment* adj1 compar*).tw. (1267)
268 (multiple treatment* adj1 compar*).tw. (360)
269 (multi-treatment* adj1 compar*).tw. (5)
270 simultaneous* compar*.tw. (2469)
271 mixed comparison?.tw. (69)
272 or/259-271 (811715)
273 257 and 272 (3419)
274 258 or 273 [REVIEWS] (111936)
275 limit 257 to "0300 clinical trial" [Limit not valid in Embase,Ovid MEDLINE(R),Ovid MEDLINE(R) Daily Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher; records were retained] (111666)
276 exp clinical trials/ (307124)
277 (randomi#ed or randomly or RCT or placebo*).tw. (2332689)
278 ((singl* or doubl* or trebl* or tripl*) adj (mask* or blind* or dumm*)).tw. (420183)
279 trial.ti. (507909)
280 or/276-279 (2730358)
281 257 and 280 (9191)
282 275 or 281 [RCTS] (112919)
283 (control* adj2 trial*).tw. (614352)
284 (nonrandom* or non-random* or quasi-random* or quasi-experiment*).tw. (132248)
285 (nRCT or nRCT or non-RCT).tw. (709)
286 (control* adj3 ("before and after" or "before after")).tw. (10162)
287 time series/ (23361)
288 time series.tw. (65880)
289 (pre- adj3 post-).tw. (235815)
290 (pretest adj3 posttest).tw. (18118)
291 (control* adj2 stud$3).tw. (540018)
292 experiment controls/ (907)
293 (control* adj2 group$1).tw. (1235251)
294 trial.ti. (507909)
295 or/283-294 (2833768)
296 257 and 295 [NON-RCTS] (7783)
297 limit 257 to ("0430 followup study" or "0450 longitudinal study" or "0451 prospective study" or "0453 retrospective study") [Limit not valid in Embase,Ovid MEDLINE(R),Ovid MEDLINE(R) Daily Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher; records were retained] (113931)
298 cohort?.tw. (1460179)

299 exp longitudinal studies/ (267415)
300 retrospective studies/ (1166307)
301 (longitudinal or prospective or retrospective).tw. (3101143)
302 followup studies/ (627480)
303 ((followup or follow-up) adj (study or studies)).tw. (128839)
304 exp observation methods/ (5724)
305 (observation$2 adj (study or studies)).tw. (251407)
306 ((population or population-based) adj (study or studies or analys#s)).tw. (40364)
307 ((multidimensional or multi-dimensional) adj (study or studies)).tw. (371)
308 ((comparative or comparison) adj (study or studies)).tw. (258365)
309 ((case-control* or case-based or case-comparison) adj (study or studies)).tw. (232321)
310 (cross-section* or crosssection*).tw. (871622)
311 or/298-310 (6229379)
312 257 and 311 (21156)
313 297 or 312 [OBSERVATIONAL STUDIES] (116189)
314 interview*.mp. (1208372)
315 thematic analysis/ (12832)
316 qualitative.af. (889955)
317 questionnaire*.mp. (1946523)
318 ethnological research.mp. (29)
319 ethnograph*.mp. (49253)
320 ethnonursing.af. (363)
321 phenomenol*.af. (165043)
322 grounded theory/ (10853)
323 (grounded adj (theor* or study or studies or research or analys#s)).af. (78144)
324 exp life experiences/ (51768)
325 (life stor* or women* stor*).mp. (6740)
326 (emic or etic or hermeneutic* or heuristic* or semiotic*).af. or (data adj1 saturat*).tw. or participant observ*.tw. (141504)
327 (social construct* or (postmodern* or post-structural*) or (post structural* or poststructural*) or post modern* or post-modern* or feminis* or interpret*).mp. (1234463)
328 (action research or cooperative inquir* or co operative inquir* or co-operative inquir*).mp. (17587)
329 (humanistic or existential or experiential or paradigm*).mp. (453321)
330 (field adj (study or studies or research)).tw. (43603)
331 human science.tw. (1161)
332 biographical method.tw. (103)
333 theoretical sampl*.af. (2386)
334 ((purpos* adj4 sampl*) or (focus adj group*)).af. (187736)
335 (account or accounts or unstructured or open-ended or open ended or text* or narrative*).mp. (1691731)
336 (life world or life-world or conversation analys#s or personal experience* or theoretical saturation).mp. (83460)
337 ((lived or life) adj experience*).mp. (67584)
338 observational method*.af. (4965)
339 content analys#s.af. (111618)
340 (constant adj (comparative or comparison)).af. (14795)
341 ((discourse* or discurs*) adj3 analys#s).tw. (13049)
342 narrative analys#s.af. (9134)
343 (heidegger* or colaizzi* or spiegelberg* or van manen* or van kaam* or merleau ponty* or husserl* or foucault* or (corbin adj2 strauss*) or glaser*).tw. (17480)

344 mixed method*.tw. (59032)
345 or/314-344 (6636676)
346 257 and 345 [QUALITATIVE STUDIES] (26698)
347 274 or 282 or 296 or 313 or 346 [ALL STUDY DESIGNS] (122411)
348 347 use medall,emczd (111415)
349 347 not 348 [PSYCINFO RECORDS] (10996)
350 121 or 246 or 349 [ALL STUDY DESIGNS - ALL DATABASES] (51499)
351 41 use medall [MEDLINE REVIEWS] (1327)
352 163 use emczd [EMBASE REVIEWS] (1765)
353 274 use medall,emczd (111415)
354 274 not 353 [PSYCINFO REVIEWS] (521)
355 351 or 352 or 354 [REVIEWS - ALL DATABASES] (3613)
356 remove duplicates from 355 (2316) [TOTAL UNIQUE REVIEWS]
357 356 use medall [MEDLINE UNIQUE REVIEWS] (1314)
358 356 use emczd [EMBASE UNIQUE REVIEWS] (853)
359 356 not (357 or 358) [PSYCINFO UNIQUE REVIEWS] (149)
360 49 use medall [MEDLINE RCTS] (2766)
361 171 use emczd [EMBASE RCTS] (4104)
362 282 use medall,emczd (111415)
363 282 not 362 [PSYCINFO RCTS] (1504)
364 360 or 361 or 363 [RCTS - ALL DATABASES] (8374)
365 limit 364 to yr="2012-current" (4981)
366 remove duplicates from 365 (2954)
367 364 not 365 (3393)
368 remove duplicates from 367 (2013)
369 366 or 368 [TOTAL UNIQUE RCTS] (4967)
370 369 use medall [MEDLINE UNIQUE RCTS] (2751)
371 369 use emczd [EMBASE UNIQUE RCTS] (1881)
372 369 not (370 or 371) [PSYCINFO UNIQUE RCTS] (335)
373 68 use medall [MEDLINE NRCTS] (2156)
374 189 use emczd [EMBASE NRCTS] (13613)
375 296 use medall,emczd (6496)
376 296 not 375 [PSYCINFO NRCTS] (1287)
377 373 or 374 or 376 [NRCTS - ALL DATABASES] (17056)
378 85 use medall [MEDLINE OBSERVATIONAL STUDIES] (9014)
379 210 use emczd [EMBASE OBSERVATIONAL STUDIES] (11318)
380 313 use medall,emczd (111415)
381 313 not 380 [PSYCINFO OBSERVATIONAL STUDIES] (4774)
382 378 or 379 or 381 [OBSERVATIONAL STUDIES - ALL DATABASES] (25106)
383 377 or 382 [NRCTS, OBSERVATIONAL STUDIES - ALL DATABASES] (35890)
384 limit 383 to yr="2018-current" (5258)
385 remove duplicates from 384 (3489)
386 limit 383 to yr="2016-2017" (5786)
387 remove duplicates from 386 (3556)
388 limit 383 to yr="2014-2015" (5227)
389 remove duplicates from 388 (3216)
390 limit 383 to yr="2012-2013" (4289)
391 remove duplicates from 390 (2631)
392 limit 383 to yr="2009-2011" (5305)
393 remove duplicates from 392 (3349)
394 limit 383 to yr="2005-2008" (5699)

395 remove duplicates from 394 (3749)
396 limit 383 to yr="2000-2004" (4326)
397 remove duplicates from 396 (2919)
398 385 or 387 or 389 or 391 or 393 or 395 or 397 [TOTAL UNIQUE NRCTS, OBSERVATIONAL STUDIES] (22909)
399 398 use medall [MEDLINE UNIQUE NRCTS, OBSERVATIONAL STUDIES] (10253)
400 398 use emczd [EMBASE UNIQUE NRCTS, OBSERVATIONAL STUDIES] (11250)
401 398 not (399 or 400) [PSYCINFO UNIQUE NRCTS, OBSERVATIONAL STUDIES] (1406)
402 119 use medall [MEDLINE QUALITATIVE STUDIES] (6892)
403 244 use emczd [EMBASE QUALITATIVE STUDIES] (9063)
404 346 use medall,emczd (18959)
405 346 not 404 [PSYCINFO QUALITATIVE STUDIES] (7739)
406 402 or 403 or 405 [QUALITATIVE STUDIES - ALL DATABASES] (23694)
407 limit 406 to yr="2017-current" (4897)
408 remove duplicates from 407 (3033)
409 limit 406 to yr="2014-2016" (5456)
410 remove duplicates from 409 (3388)
411 limit 406 to yr="2010-2013" (5531)
412 remove duplicates from 411 (3350)
413 limit 406 to yr="2005-2009" (4995)
414 remove duplicates from 413 (3056)
415 limit 406 to yr="2000-2004" (2816)
416 remove duplicates from 415 (1737)
417 408 or 410 or 412 or 414 or 416 [TOTAL UNIQUE QUALITATIVE STUDIES - ALL DATABASES] (14563)
418 417 use medall [MEDLINE UNIQUE QUALITATIVE STUDIES] (6877)
419 417 use emczd [EMBASE UNIQUE QUALITATIVE STUDIES] (3597)
420 417 not (418 or 419) [PSYCINFO UNIQUE QUALITATIVE STUDIES] (4089)

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Cochrane Library

https://www-cochranelibrary-com.proxy.bib.uottawa.ca/advanced-search/search-manager?search=3084048

Search Name: Cannabis - Final
Date Run: 13/06/2019 01:27:59
Comment: OHRI - 2019 Jun 12

ID Search Hits
#1 [mh Cannabis] 290
#2 [mh Cannabinoids] 731
#3 [mh "Marijuana Abuse"] 524
#4 [mh "Marijuana Use"] 284
#5 [mh "Marijuana Smoking"] 276
#6 ("c.indica" or "c.sativa" or cannabi* or bhang or cannador or cbd or charas or eucannabinolide* or ganja or ganjah or hash or hashish or hemp or marihuana* or marijuana*):ti,ab,kw 4028
#7 (epidiolex or gwp 42003p or gwp42003p or nabidiolex):ti,ab,kw 30
#8 (dronabinol or thc or tetrahydrocannabinol* or ea 1477 or ea1477 or marinol or qcd 84924 or syndros or tetrabinex or tetranabinex):ti,ab,kw 1387

#9 (cesamet or nabilone):ti,ab,kw 142
#10 (deltanyne or "abbott 40566" or namisol or dronabinolum or "QCD 84924" or "CCRIS 4726"):ti,ab,kw 16
#11 (nabiximol* or "gw 1000" or gw1000 or "sab 378" or sab378 or sativex):ti,ab,kw 167
#12 {or #1-#11} with Publication Year from 2000 to 2019, in Trials 3638
#13 {or #1-#11} in Cochrane Reviews, Cochrane Protocols 45
#14 #12 OR #13 3683

Reviews – 42
Protocols – 3
Trials – 3638

Appendix 3. Sample tables for presentation of findings

Table 1. Sample table depicting the presence/absence of demographic subgroups in observational studies.

Study	Age groups			Sex/gender			Race/ethnicity						Marital status					Employment status			Accommodation status			Residential setting			
	50–64	65–74	75+	Men	Women	Other	Caucasian	Black	Indigenous	Asian	Other	NR	Married	Single	Divorced	Widowed	NR	Retired	Working	NR	Alone	Shared	NR	Community	Retirement home	LTC	NR
Lee et al., 2012		■	■	■	■				■								■			■			■				
Smith et al., 2017	■			■			■								■			■			■			■			

Table 2. Sample table depicting the presence/absence of comorbidities and co-use in observational studies

Study	Mental health comorbidities							Physical comorbidities					Co-use			
	Anxiety	Depression	Insomnia	Schizophrenia	Cognitive decline	PTSD	NR	Cancer	Chronic pain	Diabetes	Multiple sclerosis	NR	Prescribed drugs	Illicit drugs	No co-use	NR
Lee et al., 2012									■							■
Smith et al., 2017		■											■	■	■	

Table 3. Sample table of types of cannabis use, products, and modes of consumption in observational studies

Study	Cannabis use				Cannabis product			Mode of consumption				
	Medical	Non-medical	Mixed	NR	Natural	Synthetic	NR	Smoking	Vaporizing	Edibles	Oils	NR
Lee et al., 2012	■	■	■		■			■	■	■	■	
Smith et al., 2017		■				■					■	

Table 4. Sample table of types of comparisons evaluated in primary studies

Study	Comparison evaluated					
	Use-only (single-arm study)	Use vs no use	Frequency of use	Strain type	Concentration of THC or CBD	Mode of consumption
Lee et al., 2012						
Smith et al., 2017						

Table 5. Sample table of all outcomes and direction of effects for observational studies. This table will likely be split into four, tables depending on outcomes reported: mental health/behavioural, physical health, brain, and pharmacokinetic outcomes. Green cells indicate a positive effect, red cells a negative effect, and grey cells a non-significant effect was found. Blank/white cells indicate an outcome was not measured.

Study and comparison (Reference group is listed second)	Mental health/behavioural						Physical health				Brain outcomes							Pharmacokinetic outcomes	
	Anxiety	Depression	Manic/ suicidal behaviour	Paranoia	Risky behaviour	New substance use disorder	Chronic pain	Car accidents	Falls	ED visits	Gray matter	White matter integrity	Functional connectivity	Cortical thickness	Total volume	Regional volumes	Surface morphometry/shape	Interactions with prescription drugs	Interactions with illicit drugs
Lee et al., 2012 Use vs no use																			
Lee et al., 2012 High vs low conc of THC																			
Lee et al., 2012																			

Study and comparison (Reference group is listed second)	Mental health/behavioural						Physical health				Brain outcomes							Pharmacokinetic outcomes	
	Anxiety	Depression	Manic/ suicidal behaviour	Paranoia	Risky behaviour	New substance use disorder	Chronic pain	Car accidents	Falls	ED visits	Gray matter	White matter integrity	Functional connectivity	Cortical thickness	Total volume	Regional volumes	Surface morphometry/shape	Interactions with prescription drugs	Interactions with illicit drugs
Smoking vs vaping																			
Smith et al., 2017 Daily vs weekly use																			
Smith et al., 2017 High vs low conc of THC																			