

# Medical Cannabis – Research Gaps

When Canadians want to know what the evidence says about drugs and medical devices, they turn to CADTH. Through our Rapid Response Service, we are able to help decision-makers stay on top of health technology research as it emerges.

With the increasing use of different forms of cannabis as a medical treatment for a wide variety of health conditions, questions arise about how well cannabis works with these conditions. Many of these questions have been brought to CADTH, where we searched for, critically appraised, and summarized the evidence. Knowing what the evidence says helps to inform decisions on the use of medical cannabis.

But in doing so, we've also revealed some significant gaps in the evidence – areas where evidence is needed but where little or no high-quality evidence can be found. Knowing where these gaps in the evidence exist can help researchers and research funding bodies better focus their efforts on cannabis research.

Following, you'll find a list of recent rapid reviews completed through our Rapid Response Service. For each report, the evidence found is listed and the gaps in research are highlighted. Some reports are listed more than once, as they fit into more than one category of evidence on medical cannabis.

Visit the [CADTH website](#) for more information on our evidence related to medical cannabis.

It is important to note that these gaps in evidence have been compiled from multiple CADTH reports from 2017 to 2020. For more details on each identified gap, consulting the full CADTH report is highly recommended. Depending on the date of the report, additional evidence may now be available that addresses the research gaps, as well as evidence from other organizations. And because of the methods used for rapid reviews, it is possible that evidence that could potentially address the research gaps may not have been included.

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# Cannabis for Pain

## Medical Cannabis for the Treatment of Chronic Pain (July 2019)

<https://cadth.ca/medical-cannabis-treatment-chronic-pain-review-clinical-effectiveness-and-guidelines-0>

### Evidence Requested for Decision-Making

- Clinical effectiveness of medical cannabis for the treatment of chronic pain
- Recommendations from evidence-based guidelines regarding medical cannabis for the treatment of chronic pain

### What We Found

- Low- or moderate-quality evidence suggests there may be some benefit with cannabis-based medicines for neuropathic pain compared to placebo; however, the benefits need to be weighed against harms.
- Findings are inconsistent for the effect of cannabis-based medicines in patients with fibromyalgia, musculoskeletal pain, Crohn disease, and multiple sclerosis compared to placebo.
- Four guidelines recommended that cannabis-based medicines may be considered as a treatment option for patients with neuropathic pain, but with some caveats.
- One guideline recommended that cannabis-based medicines may be a treatment option for patients with chronic non-cancer pain but with some caveats.
- One guideline recommended that cannabis-based medicines may be a treatment option for patients with chronic non-cancer, non-neuropathic pain, but with some caveats.
- Two guidelines recommended against the use of cannabis-based medicines for pain associated with fibromyalgia and back pain.
- One guideline recommended against the use of cannabis-based medicines for pain associated with headache, rheumatoid arthritis, and osteoarthritis.
- One guideline for pain management in patients with multiple sclerosis mentions that cannabis-based medicines may or may not be offered, depending on the type of cannabis-based medicine and patient condition.

*Based on four overviews, one systematic review of guidelines, and six evidence-based guidelines*

### Evidence Gaps

*What We Did Not Find*

High-quality research

Long-term studies

**Studies on the comparative clinical effectiveness of medical cannabis with other active comparators (e.g., pharmacologic treatment)**

# Cannabis for Pain

## Nabilone for Chronic Pain Management (November 2018)

<https://cadth.ca/nabilone-chronic-pain-management-review-clinical-effectiveness-and-guidelines-update>

### Evidence Requested for Decision-Making

- Clinical effectiveness of nabilone for the treatment of chronic pain due to any disease in adults
- Recommendations from evidence-based guidelines regarding the use of nabilone for the treatment of chronic pain due to any disease in adults

### What We Found

- Nabilone’s role in relieving chronic pain for patients with multiple sclerosis, fibromyalgia, or musculoskeletal pain remains unclear.
- Limited evidence suggests that cannabinoids are associated with more adverse events than placebo, though the majority of reported adverse events were non-serious.
- The identified evidence-based guidelines in general did not support the use of cannabinoids, including nabilone, for the treatment of chronic pain due to a lack of sufficient evidence. One guideline provides a weak recommendation that clinicians can consider cannabinoids as a third-line drug for neuropathic pain or palliative cancer pain when current therapies remain persistently problematic.

*Based on two systematic reviews and two evidence-based guidelines*

### Evidence Gaps

*What We Did Not Find*

High-quality studies

Adequately powered studies covering more clinical conditions

Long-term studies

Studies that control for concomitant treatments

# Cannabis for Pain

## Nabilone for Chronic Pain Management (August 2017)

<https://www.cadth.ca/nabilone-chronic-pain-management-review-clinical-effectiveness-and-guidelines-0>

### Evidence Requested for Decision-Making

- Clinical effectiveness of nabilone for the treatment of chronic pain due to any disease in adults
- Recommendations from evidence-based guidelines regarding nabilone for the treatment of chronic pain due to any disease in adults

### What We Found

- Low-quality evidence suggests some positive benefits and limited harms of nabilone compared with placebo or known analgesics.

*Based on one systematic review, one randomized controlled trial, and one observational study*

### Evidence Gaps

*What We Did Not Find*

High-quality research

Larger and longer-term studies

Recommendations from evidence-based guidelines

# Cannabis for Specific Conditions or Populations

## Medical Cannabis Use in Palliative Care – An Update (October 2019)

<https://cadth.ca/medical-cannabis-use-palliative-care-review-clinical-effectiveness-and-guidelines-update>

### Evidence Requested for Decision-Making

- Clinical effectiveness of medical cannabis for symptom control in adult patients receiving palliative care
- Recommendations from evidence-based guidelines regarding medical cannabis products for symptom control in adult patients receiving palliative care

### What We Found

- Medical cannabis for symptom control in adult patients receiving palliative care remains unclear as the evidence was of low or very low quality and was lacking in quantity.
- Limited evidence suggests that in patients with HIV, medical cannabis may be more effective than placebo for appetite and weight gain but increases the risk of psychiatric adverse events. Dronabinol may be less effective than megestrol for weight gain.
- Limited evidence suggests that in patients with cancer, dronabinol may be less effective than megestrol for improvements in appetite, weight gain, and health-related quality of life, and may increase risk of withdrawal due to adverse events.
- Limited evidence suggests that in patients with Alzheimer disease, dronabinol may be more effective than placebo for weight gain and negative affect, with no difference in caloric intake.
- One guideline recommended against the use of medical cannabis as a first- or second-line option for palliative cancer pain. The guideline suggests it may be considered in the case of refractory symptoms with careful consideration of the risks of adverse events.
- One guideline recommended that medical cannabis only be used in the palliative care setting when other treatments have failed and after consideration of the potential adverse events and drug interactions.

*Based on one systematic review and two evidence-based guidelines*

### Evidence Gaps

*What We Did Not Find*

#### High-quality research

Studies on the effectiveness of medical cannabis for palliative care populations other than terminal cancer, HIV, and Alzheimer disease.

Evidence-based guidelines that provide specific guidance on dosing and choice of medical cannabis product

# Cannabis for Specific Conditions or Populations

## Medicinal and Synthetic Cannabinoids for Pediatric Patients (October 2019)

<https://www.cadth.ca/medicinal-and-synthetic-cannabinoids-pediatric-patients-review-clinical-effectiveness-and-guidelines>

### Evidence Requested for Decision-Making

- Clinical effectiveness of medical cannabinoids in pediatric patients
- Clinical effectiveness of synthetic cannabinoids in pediatric patients
- Recommendations from evidence-based guidelines regarding the use of medical or synthetic cannabinoids in pediatric patients

### What We Found

- The clinical effectiveness of medicinal or synthetic cannabinoids in children remains unclear due to limited evidence.
- Limited quality evidence suggests cannabidiol and oral cannabis may be associated with a reduction in seizure frequency in pediatric patients with epilepsy.
- Limited quality evidence suggests the 5% oil formulation of cannabis (containing cannabidiol and tetrahydrocannabinol in either a 20:1 or a 6:1 ratio) may be associated with a reduction in spasticity, sleep difficulties, and pain, and an improvement in quality of life relative to baseline with rare occurrence of adverse events in pediatric patients with severe complex motor disorder.
- Limited quality evidence suggests dronabinol, a synthetic cannabinoid, may be associated with a reduction in seizure frequency in pediatric patients with epilepsy and a reduction in spasticity in patients with spasticity.

*Based on one systematic review and one randomized controlled trial*

### Evidence Gaps

*What We Did Not Find*

High-quality research

Adequately powered studies

Canadian studies

Studies on synthetic cannabinoid products that are available in Canada

Studies on the effectiveness of medical or synthetic cannabis for pediatric populations with medical conditions other than epilepsy and spasticity

Uniform dosing of cannabinoids

Recommendations from evidence-based guidelines

# Cannabis for Specific Conditions or Populations

## Medical Cannabis for the Treatment of Dementia (July 2019)

<https://cadth.ca/medical-cannabis-treatment-dementia-review-clinical-effectiveness-and-guidelines-0>

### Evidence Requested for Decision-Making

- Clinical effectiveness of medical cannabis for the treatment of dementia
- Recommendations from evidence-based guidelines regarding the use of medical cannabis for the treatment of dementia

### What We Found

- The clinical effectiveness of medical cannabis in patients with dementia remains unclear due to low-quality evidence.
- Low-quality evidence suggests that medical cannabis may be effective for treating agitation, disinhibition, irritability, aberrant behaviour, and nocturnal behaviour disorders as well as aberrant vocalization and resting care in patients with dementia.
- Low-quality evidence suggests medical cannabis may improve rigidity and cognitive scores in patients with dementia.

*Based on one systematic review and one non-randomized study*

### Evidence Gaps

*What We Did Not Find*

High-quality studies

Long-term efficacy and safety studies

Studies on botanical cannabis

Studies on medicinal cannabis administered via routes other than oral ingestion

Studies of patients under the age of 65 who have dementia

Studies on the comparative clinical effectiveness of medical cannabis with other active interventions

Recommendations from evidence-based guidelines

# Cannabis for Specific Conditions or Populations

## Nabilone for the Treatment of Nausea and Vomiting or Anorexia (February 2019)

<https://cadth.ca/nabilone-treatment-nausea-and-vomiting-or-anorexia-review-clinical-effectiveness-and-guidelines-0>

### Evidence Requested for Decision-Making

- Clinical effectiveness of nabilone for the treatment of nausea and vomiting or anorexia in adults and adolescents
- Recommendations from evidence-based guidelines regarding the use of nabilone for the treatment of nausea and vomiting, or anorexia in adults and adolescents

### What We Found

- Nabilone may not be more effective than conventional antiemetics or placebo for the reduction of nausea or vomiting induced by chemotherapy, radiotherapy, or occurring after a surgical operation.
- Nabilone was found to be associated with more safety concerns such as hallucination, drowsiness, dysphoria, and lack of muscle coordination.
- In patients with cancer diagnosed with anorexia, nabilone compared to placebo may increase daily caloric intake (with similar daily protein, fat, and iron intake).
- A Canadian guideline recommends against the use of medical cannabinoids for general nausea and vomiting in primary care and in pregnancy, due to the lack of evidence and known harms.
- The Canadian guideline also recommends against cannabinoids as the first- or second-line treatment of chemotherapy-induced nausea and vomiting; but recommends that nabilone can be considered as a third-line therapy for the treatment of refractory chemotherapy-induced nausea and vomiting.

*Based on one systematic review, three randomized controlled trials, and one evidence-based guideline*

### Evidence Gaps

*What We Did Not Find*

#### Adequately powered studies

Studies comparing cannabinoids to more recently approved antiemetics (such as 5-hydroxytryptamine 3 antagonists or neurokinin 1-receptor antagonists)

# Cannabis for Specific Conditions or Populations

## Nabilone for the Treatment of Post-Traumatic Stress Disorder (February 2019)

<https://cadth.ca/nabilone-treatment-post-traumatic-stress-disorder-review-clinical-effectiveness-and-guidelines-0>

### Evidence Requested for Decision-Making

- Clinical effectiveness of nabilone for the treatment of post-traumatic stress disorder (PTSD) in adults
- Recommendations from evidence-based guidelines regarding the use of nabilone for the treatment of PTSD in adults

### What We Found

- Further research is needed to understand the clinical effectiveness of nabilone for the overall PTSD condition.
- Limited evidence suggests that nabilone may improve PTSD-related symptoms (e.g., reduction of nightmares and improvements in sleep time and quality).
- Adverse events were described as mild or moderate in nature (e.g., dry mouth and headache), with the exception of individuals with a previous medical history of psychosis.

*Based on one randomized controlled trial and one non-randomized study*

### Evidence Gaps

*What We Did Not Find*

Adequate evidence for decision-making

Studies including the female population

Evidence for different subpopulations of patients with PTSD other than military personnel or institutionalized inmates

Studies on the comparative clinical effectiveness of nabilone with other active interventions

Recommendations from evidence-based guidelines

# Cannabis for Specific Conditions or Populations

## Cannabinoids for Behavioural Symptoms in Adults With Dementia (January 2018)

<https://www.cadth.ca/cannabinoids-behavioural-symptoms-adults-dementia-review-clinical-effectiveness-and-guidelines>

### Evidence Requested for Decision-Making

- Clinical effectiveness of cannabinoids for the treatment of behavioural symptoms in adults with dementia
- Recommendations from evidence-based guidelines on the use of cannabinoids for the treatment of behavioural symptoms in adults with dementia

### What We Found

- Limited studies of overall poor quality on dronabinol are consistent in reporting a reduction in behavioural symptoms.
- Adverse events reporting was limited, making the risk of adverse events uncertain.

*Based on two systematic reviews and two randomized crossover trials*

### Evidence Gaps

*What We Did Not Find*

High-quality studies

Longer-term studies

Larger studies

Canadian studies

Studies looking at subpopulations of adults with dementia

Recommendations from evidence-based guidelines

# Cannabis for Specific Conditions or Populations

## Medical Cannabis for Post-Traumatic Stress Disorder (January 2017)

<https://www.cadth.ca/medical-marijuana-post-traumatic-stress-disorder-review-clinical-effectiveness-and-guidelines-0>

### Evidence Requested for Decision-Making

- Clinical effectiveness of medical marijuana for post-traumatic stress disorder (PTSD) in adults
- Clinical effectiveness of synthetic cannabinoids for PTSD in adults
- Recommendations from evidence-based guidelines on the use of medical marijuana or synthetic cannabinoids in adults with PTSD

### What We Found

- There is evidence from very low-quality studies to support the efficacy of smoked marijuana, oral tetrahydrocannabinol, and nabilone in reducing some symptoms of PTSD.
- Side effects — such as light-headedness, forgetfulness, dizziness, and headache (described as mild to moderate) — were reported for only one retrospective chart review in which nabilone was discontinued in 28% of patients.

*Based on one systematic review, which included six studies*

### Evidence Gaps

*What We Did Not Find*

High-quality studies

Longer-term studies

Larger studies

Studies comparing medical cannabis to other treatments for PTSD

Studies that control for concomitant treatments

Evidence on adverse events

Evidence for different subpopulations of patients with PTSD

Recommendations from evidence-based guidelines

# Safety, Harms, and Misuse of Cannabis

## The Use of Medical Cannabis With Other Medications – An Update (September 2019)

<https://cadth.ca/use-medical-cannabis-other-medications-review-safety-and-guidelines-update>

### Evidence Requested for Decision-Making

- Clinical evidence regarding the safety of medical cannabis when used with other medications
- Recommendations from evidence-based guidelines regarding drug interactions between medical cannabis and other medications

### What We Found

- Low-quality evidence from two studies suggested oral cannabidiol increases serum levels of clobazam.
- Low-quality evidence from one study suggested oral cannabidiol may increase serum levels eslicarbazepine, topiramate, zonisamide, and rufinamide.

*Based on two non-randomized studies (for the comparisons of interest)*

### Evidence Gaps

*What We Did Not Find*

High-quality research

Long-term studies

Assessment of clinical outcomes

Additional data on the drug interactions of medical cannabis and other medications for conditions other than epilepsy

Studies on cannabis products available in Canada

Recommendations from evidence-based guidelines

# Safety, Harms, and Misuse of Cannabis

## Substance Use in Breastfeeding Parents (September 2018)

<https://cadth.ca/substance-use-breastfeeding-parents-review-safety-and-guidelines>

### Evidence Requested for Decision-Making

- Safety regarding the consumption of controlled and illicit substances by breastfeeding parents for the parent and infant
- Recommendations from evidence-based guidelines regarding the consumption of controlled or illicit substances by breastfeeding parents

### What We Found

- No relevant literature was identified on the consumption of cannabis by breastfeeding parents.

*None of the identified studies related to cannabis use*

### Evidence Gaps

*What We Did Not Find*

**Evidence on the safety of cannabis consumption by breastfeeding parents for the parent and infant**

**Recommendations from evidence-based guidelines**

# Safety, Harms, and Misuse of Cannabis

## The Use of Medical Cannabis With Other Medications

### (April 2017)

<https://www.cadth.ca/use-medical-cannabis-other-medications-review-safety-and-guidelines-0>

#### Evidence Requested for Decision-Making

- Clinical evidence regarding the safety of medical cannabis when used concurrently with other medications
- Recommendations from evidence-based guidelines regarding the use of medical cannabis with other medications

#### What We Found

- Medical cannabis (nabilone) may have additive depressant effects with diazepam when taken together with alcohol and codeine.

*Based on one systematic review of nabilone*

#### Evidence Gaps

*What We Did Not Find*

High-quality research

Additional data on the drug interactions of medical cannabis with other medications

Recommendations from evidence-based guidelines

# Using Cannabis in the Treatment of Other Substance Use Disorders

## Medical Cannabis in Residential Transition or Addiction Programs (April 2017)

<https://www.cadth.ca/medical-cannabis-residential-transition-or-addiction-programs-review-clinical-and-cost-effectiveness>

### Evidence Requested for Decision-Making

- Clinical effectiveness of medical cannabis for adults with addictions being treated in residential transition and addiction programs
- Cost-effectiveness of medical cannabis in adults with addictions being treated in residential transition and addiction programs
- Recommendations from evidence-based guidelines on cannabis in adults with addiction being treated in residential transition and addiction programs

### What We Found

- No relevant literature was identified.

*Zero included studies*

### Evidence Gaps

*What We Did Not Find*

Evidence on clinical effectiveness

Evidence on cost-effectiveness

Recommendations from evidence-based guidelines

# Using Cannabis in the Treatment of Other Substance Use Disorders

## The Use of Medical Cannabis With Other Medications (April 2017)

<https://www.cadth.ca/use-medical-cannabis-other-medications-review-safety-and-guidelines-0>

### Evidence Requested for Decision-Making

- Clinical evidence regarding the safety of medical cannabis when used concurrently with other medications
- Recommendations from evidence-based guidelines regarding the use of medical cannabis with other medications

### What We Found

- Nabilone may decrease the need for opioids, nonsteroidal anti-inflammatory drugs, tricyclic antidepressants, dexamethasone, and ondansetron when used concomitantly.

*Based on one systematic review on nabilone*

### Evidence Gaps

*What We Did Not Find*

High-quality research

Research on other types of medical cannabis beyond nabilone

Additional data on the drug interactions of medical cannabis with other medications

Recommendations from evidence-based guidelines

# Treatment of Cannabis Use Disorder

## e-Therapy Interventions for the Treatments of Substance Use Disorders and Other Addictions (June 2018)

<https://www.cadth.ca/e-therapy-interventions-treatments-substance-use-disorders-and-other-addictions-review-clinical>

### Evidence Requested for Decision-Making

- Clinical effectiveness of e-therapy for the treatment of patients with substance use disorders and other addictions

### What We Found

- Evidence consistently showed that therapist-guided e-therapy was superior to no treatment in reducing cannabis use.
- The effect was small.

*Based on four included studies, two systematic reviews, and two randomized controlled trials*

### Evidence Gaps

*What We Did Not Find*

Adequate evidence for decision-making

Details on the components of e-therapy strategies

Details on the amount and type of therapist support (e.g., telephone, email)

Studies of different patient populations

## Additional Reports From CADTH's Rapid Response Service

The following include Reference Lists and Summaries of Abstracts:

[Disposable Handheld Vaporization Devices for Inhalation of Medical Cannabis: Clinical Effectiveness and Cost-Effectiveness](#) (Reference List, March 2020)

[Peer Support Interventions for Substance Use Disorder: Clinical Effectiveness, Cost-Effectiveness, and Guidelines](#) (Summary of Abstracts, February 2020)

[Nabilone for the Treatment of Nausea and Vomiting, or Anorexia: Clinical Effectiveness and Guidelines – An Update](#) (Reference List, October 2018)

[Medical Cannabis Use in Palliative Care: Clinical Effectiveness and Guidelines](#) (Summary of Abstracts, September 2018)

[Medical Cannabis Use in the Elderly: Clinical Effectiveness and Guidelines](#) (Reference List, December 2017)

[Integrated Cessation Programs for Adults Who Smoke Cannabis and Tobacco: Clinical Effectiveness and Guidelines](#) (Reference List, September 2017)

[Pharmacological Interventions for the Prevention or Treatment of Cannabis Use: Clinical Effectiveness and Guidelines](#) (Reference List, September 2017)

[Psychological and Psychosocial Interventions for the Prevention or Treatment of Cannabis Use: Clinical Effectiveness and Guidelines](#) (Reference List, September 2017)

[Medical Cannabis or Cannabinoids for the Treatment of Insomnia Disorder in Adults: Clinical Effectiveness and Guidelines](#) (Summary of Abstracts, June 2017)

[Nabilone for the Treatment of Nausea and Vomiting, or Anorexia: Clinical Effectiveness and Guidelines](#) (Reference List, June 2017)

[Cannabis Use During Pregnancy: Safety](#) (Summary of Abstracts, April 2017)

[The Use of Medical Cannabis With Other Medications: Safety](#) (Reference List, February 2017)

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CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs and medical devices in our health care system.

CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

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**CADTH** Evidence Driven.

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