

Cannabis and cannabinoids: Cancer risk and use to manage cancer symptoms

Evidence summary, current as of January 30, 2023

Purpose

This document provides a brief evidence summary for healthcare providers, working in primary care and cancer care, on the cancer risk of cannabis and cannabinoids (medical and non-medical), and on using cannabis and cannabinoids to manage cancer symptoms.

Key messages

- The available evidence does not clearly show that using cannabis increases the risk of cancer; more research is required to address the limitations of current evidence.
- There is no evidence that cannabis or cannabinoids can be used to treat cancer.
- There is no evidence to recommend cannabis or cannabinoids as initial therapies for any health condition, including cancer-related symptoms.
- Consideration may be given to adding a pharmaceutical cannabinoid when managing the following cancer-related symptoms when they do not respond to standard therapies: pain in people with cancer receiving palliative care, neuropathic pain and chemotherapy induced nausea and vomiting.
- Healthcare providers should discuss risks and benefits with their patients before authorizing medical access to cannabis or cannabinoids.
- Cannabis and cannabinoids may be associated with short- and long-term health-related harms (e.g., respiratory symptoms when smoked or vaped, harmful mental health effects); the most effective way to reduce the risk of these harms is to not use cannabis.
- <u>Canada's Lower-Risk Cannabis Use Guidelines</u> and <u>Cannabasics</u> can help healthcare providers advise their patients and the general population on how to lower their risk of harms from cannabis use.

Approach

This summary is based on a limited number of sources that are deemed to be comprehensive and relevant. It was first released in January 2020, and included conclusions from *Cancer and the Health Effects of Cannabis and Cannabinoids: An Update of the Systematic Review by the National Academies of Sciences, Engineering, and Medicine (2017) Consensus Study Report, an evidence review by Ontario Health's (Cancer Care Ontario) Program in Evidence-Based Care, which was released in June 2020.¹ This summary was updated in January 2023, and reflects changes in the Health Canada approval status of Sativex®, along with updated data and references.*

Background

Cannabis refers to the plant, *Cannabis sativa*, and related plants, such as *Cannabis indica*.² Cannabis is used in a variety of ways such as by smoking its dried flowers, leaves, stems and seeds; inhaling it from a vaporizer; or eating or drinking the plant or its oils with other ingredients in prepared foods or teas.³

The Cannabis Act was passed in Canada in 2018, making it legal – with certain restrictions – for adults to buy and use cannabis in Canada.⁴ The minimum age for buying and using cannabis in Ontario is 19.⁵ Medical access regulations were first implemented in Canada in 2001 in response to a court decision, ruling that people with a medical need should have access to cannabis.⁶ Access to cannabis for medical purposes must be authorized by a medical or nurse practitioner.⁶ However, cannabis is not approved by Health Canada to treat diseases and health conditions.

Cannabinoids are a group of chemical compounds found in the cannabis plant.² They include delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD).² THC, but not CBD, is responsible for the psychoactive properties or intoxication (i.e., "high").³

Health Canada has authorized two pharmaceutical cannabinoids for marketing in Canada:

- Nabilone, a synthetic form of THC in capsule form, is authorized for managing severe nausea and vomiting associated with cancer chemotherapy.⁷
- Nabiximols (Sativex®), a buccal spray that contains equal amounts of standardized CBD and THC.⁸ It previously had conditional authorization to market for moderate to severe pain in adults with advanced cancer alongside standard pain treatment. Confirmatory clinical studies did not demonstrate a therapeutic advantage, therefore this indication was removed in 2020.⁹ Nabiximols is now only indicated for treatment-resistant spasticity in patients with multiple sclerosis.⁸

Synthetic cannabinoids are also used in products, such as those that simulate dried cannabis. These products are not authorized for importation and sale in Canada. Product names include "K2," "Spice" and "Brainfreeze Potpurri. Using these products can lead to severe health risks, including increased heart rate, vomiting, chest pain and kidney damage.

Cannabis use in Ontario

Cannabis use in Ontario has increased slightly since legalization in 2018. In people age 16 and older, 27 percent reported use in the past 12 months in 2021, compared to 24 percent in 2018. ^{11,12} A study published in 2021 finds that 34 percent of Canadian adults who stated that they had cancer in the 2015–2016 Canadian Community Health Survey reported cannabis use. ¹² In Ontario, 15 percent of respondents to the 2021 Canadian Cannabis Survey reported use for medical purposes in the past 12 months. ¹³



Cancer risk associated with cannabis use

The review by the Program in Evidence-Based Care found no conclusive or substantial evidence to support or exclude an association between cannabis use and increased or decreased cancer risk. The conclusions in the Program in Evidence-Based Care review related to cancer risk associated with cannabis use are the following:

- There is moderate evidence of no statistically significant association between:
 - Cannabis smoking and the incidence of lung cancer; and
 - Cannabis use and the incidence of head and neck cancers; smoking was the most common method of using cannabis in the nine case-control studies included in the meta-analysis that provides the basis for this conclusion.¹
- There is limited evidence of a statistical association between current, frequent or chronic cannabis smoking and non-seminoma-type testicular germ cell tumours.
- There is insufficient evidence to demonstrate an association between:
 - o Cannabis smoking and the incidence of esophageal cancer;
 - o Cannabis use and the incidence of other malignancies in adults; and
 - Maternal or paternal cannabis use in the months preceding birth and subsequent risk of children developing malignancies.

An additional systematic review on the association between cannabis use and bladder cancer published since the Program in Evidence-Based Care review, which found a small number of studies with contradictory findings.¹⁴

More research is needed to address the limitations in the studies conducted to date. For example, better control of simultaneous tobacco use, longer follow-up periods and biological validation of self-reported use would strengthen the evidence.² Investigating additional variables, such as mode, quantity and years of use, would also provide important information.¹

Cannabis and cannabinoids to manage cancer symptoms

The conclusions in the Program in Evidence-Based Care review¹ related to managing cancer symptoms with cannabis or cannabinoids are the following:

There is limited evidence that cannabis-based medicines may be an effective treatment for chronic pain in some people with cancer. Cannabis-based medicine is not supported by evidence for first- or second-line treatment, but it may be considered for third- or fourth-line treatment as an adjuvant therapy to other analgesics. It is important to weigh the benefits of cannabis-based medicine with the potential harms of adverse events, particularly among people with cancer who frequently have multiple comorbidities.



- There is conclusive evidence that oral cannabinoids are effective anti-emetics in the treatment of chemotherapy-induced nausea and vomiting, but there is insufficient evidence comparing oral cannabinoids with the currently available and most effective anti-emetics used in cancer care.
- There is insufficient evidence to support using cannabinoids or cannabis as a treatment for:
 - o Cancer-associated anorexia-cachexia syndrome and anorexia nervosa;
 - Spasticity in people with paralysis due to spinal cord injury, which may occur as a result of a cancer or cancer treatment; and
 - Cancer in general.¹

Findings from systematic reviews published since the Program in Evidence-Based Care review include one that finds the available evidence neither supports nor refutes the effectiveness of cannabis and cannabinoids for treating pain¹⁵ and two which suggest limited improvements for pain relief. A systematic review examining the effects of oral cannabinoid for chemotherapy-induced nausea and vomiting suggests that there may be a potential benefit, but the available evidence remains uncertain.

In March 2021, guidelines on prescribing pharmaceutical cannabinoids in primary care were published in *Canadian Family Physician* and endorsed by the College of Family Physicians of Canada.¹⁹ The guidelines provide practical recommendations and the following recommendations are relevant for managing cancer symptoms:

- Cannabis and cannabinoids are not recommended for treating most medical conditions, including cancer-related conditions, with potential exceptions for some types of pain and chemotherapy-induced nausea and vomiting.
- When standard therapies delivered in an optimal therapeutic fashion fail to produce adequate symptom relief, consideration could be given to adding a pharmaceutical cannabinoid to treat:
 - Pain in people with cancer who are receiving palliative care;
 - Neuropathic pain; and
 - Chemotherapy-induced nausea and vomiting.
- Pharmaceutical cannabinoids should be considered before cannabis for treating neuropathic pain and pain in people with cancer who are receiving palliative care.
- Cannabis in any form (smoked, oils or edibles) is not recommended for chemotherapy-induced nausea and vomiting.
- Healthcare providers should discuss the risks and benefits of cannabis and pharmaceutical cannabinoids with their patients.¹⁹

The authors of the guidelines note that the evidence for using pharmaceutical cannabinoids is limited.¹⁹



Additional potential acute and long-term health-related harms of cannabis use

In general, and for people with cancer, the most effective way to eliminate risks associated with using cannabis is to avoid use. 19,20

Using cannabis may lead to acute health-related harms, including psychosis, anxiety, increased heart rate, cognitive and psychomotor impairment, and injuries or fatalities due to psychomotor impairment (e.g., motor vehicle collisions).^{2,21}

Studies in Ontario have found increases in cannabis-related hospitalizations following legalization. In children age 0 to 9, the rate of emergency department visits due to unintentional ingestion of cannabis more than doubled from February 2020 to March 2021, compared to January 2016 to September 2018, following the legalization of edible cannabis products. In adults age 18 to 24, hospitalizations immediately following legalization in October 2018 increased by 38.5 and 77.8 percent in women and men, respectively. In women and men age 25 and older, this rate increased by 52.9 and 77.8 percent, respectively. Month-to-month changes from October 2018 to March 2020 ranged from 2.8 to 5.4 percent. However, hospitalizations did not further increase among adults following legalization of edible cannabis products and showed a slight month-to-month downtrend. In the contract of the cannabis products and showed a slight month-to-month downtrend.

Long-term and regular cannabis use may also lead to long-term health-related harms, including respiratory symptoms and more frequent episodes of chronic bronchitis (if cannabis is smoked or vaped), schizophrenia and psychoses, dependency or cannabis use disorder, and cannabinoid hyperemesis syndrome (cyclic vomiting).^{2,21} Long-term mental health effects likely increase when use begins before age 25.^{2,21}

Additional resources

More information and resources on the health effects of cannabis are available on the <u>Government of Ontario</u> and the <u>Government of Canada</u> websites.

For healthcare providers, <u>Canada's Lower-Risk Cannabis Use Guidelines</u>, ²⁰ which were developed by scientists at the Centre for Addiction and Mental Health, and <u>Cannabasics</u>, which is an information package from the Canadian Public Health Association, ²⁴ can help with advising patients and the general population on how to lower their risk of harms from cannabis use. The lower-risk use guidelines have been endorsed by several organizations, including the Canadian Medical Association, the Canadian Nurses Association and the Council of Chief Medical Officers of Health. ²⁰ In addition, the <u>College of Physicians and Surgeons of Ontario</u> has issued a detailed policy on authorizing access to cannabis for medical purposes. ²⁵



Acknowledgements

The original evidence summary was reviewed by the following experts whom we thank for their time and expertise:

Michelle Cotterchio, Gail Darling, Bill Evans, Ed Kucharski, Richard Steiner and Padraig Warde, Ontario Health (Cancer Care Ontario); Michael Chaiton, Centre for Addiction and Mental Health; Lisa Durocher and Sheila McNair, Ontario Health (Cancer Care Ontario) Program in Evidence-Based Care, McMaster University; Meredith Giuliani, Princess Margaret Cancer Centre; David Hammond, University of Waterloo; Pamela Leece, Public Health Ontario; Andrew Pipe and Bob Reid, University of Ottawa Heart Institute; Peter Selby, Centre for Addiction and Mental Health; Marissa Slaven, McMaster University; and Monica Staley-Liang, Erie St. Clair Regional Cancer Program.

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