

THE CANADIAN AIDS SOCIETY CLINICAL PRACTICE GUIDELINES ON THE USE OF CANNABIS AND CANNABINOID-BASED PRODUCTS

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The History of Cannabis

Cannabis has a long history of medicinal use. Perhaps the most famous example is that of Queen Victoria, whose physician JR Reynolds prescribed her cannabis for dysmenorrhea (BBC, 2020). In the AIDS era in the 1980s and 1990s, before the advent of combined antiretroviral therapy, many individuals were suffering from opportunistic infections and malignancies. Cannabis was a source of comfort due to its mood-uplifting, appetite-enhancing and pain-relieving effects (Fuller et al., 2004). During this era, strong HIV/AIDS advocates fought for the right to use cannabis as a medication and in 2001 cannabis was listed as a substance for medical use by Health Canada. However, unlike most medications, due to the time constraints cannabis did not undergo many of the formal studies most medications undergo.

In 2018, Canadian legislation approved the use of cannabis for recreational sale without a prescription. However, many individuals use cannabis to treat symptoms of a medical condition, but they obtain it themselves without a doctor's prescription (Costiniuk et al., 2019). The legalization of recreational cannabis has resulted in a surge of interest in understanding the potential benefits and risks associated with its use. Furthermore, in 2019 the *New England Journal of Medicine*, published a randomized clinical trial on the use of cannabidiol (CBD) to treat Lennox-Gastaut syndrome, a com-

plex childhood epilepsy disorder that is associated with drug-resistant seizures and a high mortality rate. According to the trial, CBD resulted in a greater reduction in convulsive-seizure frequency versus placebo.

Despite the positive aspects of cannabis use, there are also certain risks which must be considered, as with the use of any other medication. Cannabis continues to be surrounded by much stigma and uncertainty about its place amidst the spectrum of medicines (Melnikov et al, 2020). To address this concern, The Canadian AIDS Society (CAS) has spearheaded the creation of the "Canadian Clinical Practice Guidelines for the use of Cannabis and Cannabinoid-based Products for the Management of Chronic Pain and Co-occurring conditions." These guidelines will serve as a tool for clinicians and other health care providers when discussing cannabis and CBPs as part of a treatment regimen for pain and the conditions which frequently accompany it.

Why is cannabis research so difficult?

One of the most challenging aspects to conducting research is the regulatory classification of cannabis. Since recreational cannabis became legalized in 2018, additional approvals from Health Canada are required before one can embark on research in Canada, such as the need for a Cannabis Research License. However, these approvals take time to obtain and time trans-

lates into increased study costs. In the US it is classified as a Schedule 1 drug, making research difficult. For this reason, the Michael J. Fox Foundation for Parkinson's Research is advocating for reclassification of cannabis so that conducting research will be easier.

The best type of evidence is in the form of randomized, placebo-controlled double-blind clinical trials. However, such trials are very costly to run. For most pharmaceuticals, the drug company which has developed the drug will fund the clinical trials. However, cannabis companies do not have the same economic stability as pharmaceutical companies and often cannot invest as much money into research. Additionally, given the psychoactive effects of cannabis and some CBPs, masking a placebo from an active agent may be difficult if not impossible.

There still remain many unknowns with regards to pharmacokinetics of cannabis, meaning the absorption, distribution, metabolism, and secretion of drugs. Inter-person variability with regards to these parameters likely varies amongst individuals. There are many different formulations (oral capsules, oils, smoked). Variations in formulations and doses used between studies makes it challenging to extrapolate the use of medicinal cannabis. Sometimes patients may be tempted to use cannabis from outside of the study to address symptoms, which can confound the study results, and often there is not a clear way for investigators to detect this.

Stigma also hampers research. Stigma on the part of Health Care Providers (HCP), participants, their families, study staff, and the institution can render cannabis research challenging.

Who is writing the guidelines?

The guidelines committee is made up of various HCPs and researchers from across Canada, including physicians (family physicians, pain specialists, HIV specialists) in addition to nurses and cannabis researchers and community representatives representing patients. The committee is led by members of the CAS. Attempts to reduce bias include limiting steering committee membership to individuals without commercial affiliations.

How are the guidelines being assembled?

A systematic review protocol was created with the help of professional librarians. A task force, comprised of members of the steering committee, met regularly to develop the protocol for the systematic literature review. This protocol was published in *BMJ Open* in November 2019 and can be accessed at: <https://pubmed.ncbi.nlm.nih.gov/32448797/>

What will the guidelines look like?

This document will summarize the existing evidence, the strength of the evidence, and will provide recommendations so that HCPs and patients can make informed decisions about the use of cannabis and CBP for that unique individual.

The guidelines will have an introduction about the background of the guidelines, how they were made and then will list the strength and quality of the evidence, preferences and values, and practical tips. The guidelines also discuss the studies under the

various categories including HIV, multiple sclerosis, arthritis, fibromyalgia, chronic headache and migraine, nausea, sleeping problems appetite, post-traumatic stress disorder (PTSD), anxiety and depression. They will also discuss study limitations to give context to the recommendations.

The quality of the evidence will be measured using the Grading of Recommendations Assessment, Development and Evaluations (GRADE) system, which is a recognized scale for rating the quality of evidence.

The initial paragraph will be the guideline statement, providing specific recommendations on how to treat the condition. This is followed by the values and preferences which look at the rationale considering the adverse effects, etc. A practical tip will be added to allow for clinical judgment. The supporting information for all of this is provided in the body text of the document.

Where and when will the guidelines be published? Open Access

CAS aims to publish these guidelines in an Open Access journal, so that they can be accessed freely on the internet. The anticipated date of publication is in late 2020 or early 2021.

CAS and the Cannabis Guidelines Steering Committee sincerely hope that these guidelines will help reduce stigma about the topic of cannabis and encourage open dialogue between patients and their HCPs to help patients make informed choices regarding their health.

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Research and the Arthritis Society for their support.

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