

# Cannabis and Cannabinoids in Adults with Cancer

## ASCO Guideline

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Braun et al.

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# Background & Methodology

# Introduction

- Research suggests that adults with cancer use cannabis and/or cannabinoids for multi-symptom management (e.g., pain, nausea, vomiting, anorexia, cachexia, anxiety, depression, insomnia); cancer-directed therapy; and for its euphoric effects.<sup>1-10</sup>
- Socio-behavioral research indicates that many oncologists discuss medical cannabis and/or cannabinoids with patients, typically because adults with cancer & their caregivers raise the topic; however, less than a third of oncology clinicians feel confident to make clinical recommendations.<sup>11</sup>
- Adults with cancer using medical cannabis report receiving little clinical specification or guidance from their oncology team regarding safety and optimal use.
- Instead, they turn to non-medical sources, including cannabis dispensary personnel, for advice. These professionals consider themselves unevenly trained in cannabis therapeutics.<sup>2,12</sup>
- The purpose of this guideline is to guide clinicians, adults with cancer, caregivers, researchers, and oncology institutions on the medical use of cannabinoids, including synthetic cannabinoids and herbal cannabis derivatives; single, purified cannabinoids, combinations of cannabis ingredients, and full-spectrum cannabis.

# ASCO Guideline Development Methodology

- The ASCO Evidence Based Medicine Committee (EBMC) guideline process includes:
  - a systematic literature review by ASCO guidelines staff
  - an expert panel provides critical review and evidence interpretation to inform guideline recommendations
  - final guideline approval by ASCO EBMC
- The full ASCO Guideline methodology manual can be found at: [www.asco.org/guideline-methodology](http://www.asco.org/guideline-methodology)

# Clinical Questions

This clinical practice guideline addresses three clinical questions in adults with cancer:

1. How should clinicians and adults with cancer communicate about cannabis and/or cannabinoids?
2. Does use of cannabis and/or cannabinoids by adults improve cancer-directed treatment?
3. Does use of cannabis and/or cannabinoids by adults with cancer reduce treatment-related toxicities, palliate cancer symptoms, or improve QOL?

# Target Population and Audience

## Target Clinical Population

- Adults with cancer who use or are interested in using cannabis and/or cannabinoid products for medical purposes.

## Target Audience

- Clinicians providing care to adults with cancer; the health systems in which they work; adults with cancer and their caregivers; and researchers.

# 2

## Summary of Recommendations



# Summary of Recommendations

**Note.** In the United States, the Controlled Substance Act renders cannabis with >0.3% delta-9-tetrahydrocannabinol (THC) Schedule I. This status signifies that cannabis has no accepted medical use and a high potential for abuse.<sup>13</sup> The Schedule I designation creates frequent conflicts between federal and state laws, as 38 states now allow medical cannabis use by adults with qualifying conditions. In addition, the Schedule I designation creates challenges for cannabis and/or cannabinoid researchers who face sparse funding opportunities, scarce sources for trial products, regulatory barriers, and procedural obstacles. The designation also generates challenges for clinicians wishing to guide adults with cancer using or considering the use of cannabis and/or cannabinoids: insufficient evidence base, limited federal oversight of non-pharmaceutical cannabinoid product manufacturing, and theoretical legal liability.

# Summary of Recommendations

## Clinical Question 1

- How should clinicians and adults with cancer communicate about cannabis and/or cannabinoids?

### Recommendation 1.1

- Health systems and clinicians, in partnership, should provide adults with cancer unbiased, evidence-based cannabis and/or cannabinoid educational resources to facilitate clinical communication, informed decision-making, and systematized approaches to care.

Good Practice Statement

# Summary of Recommendations

## Recommendation 1.2

- Given the high prevalence of cannabis and/or cannabinoid use among adults with cancer, clinicians should routinely and non-judgmentally inquire about cannabis use (or consideration of use), and either guide care or direct adults with cancer to appropriate resources.

Good Practice Statement

**Note.** Clinicians should remain sensitive to cannabis regulations' disproportionate impacts on marginalized communities and work to omit cannabis-related and other biases (e.g., racial, ethnic, and socioeconomic) from clinical discussions about cannabis and/or cannabinoids. Table 1 (in the full guideline) offers suggestions for cannabinoid history-taking.

# Summary of Recommendations

## Recommendation 1.3

- When adults with cancer use cannabis and/or cannabinoids outside of evidence-based indications or clinician recommendations, clinicians should explore goals, educate, and seek to minimize harm.

Good Practice Statement

# Summary of Recommendations

## Clinical Question 2

- Does use of cannabis and/or cannabinoids by adults improve cancer-directed treatment?

### Recommendation 2.1

- Clinicians should recommend against use of cannabis and/or cannabinoids to augment cancer-directed treatment unless in the context of a clinical trial.

Evidence-based	
Evidence Quality	Strength of Recommendation
Very Low	Weak

# Summary of Recommendations

## Recommendation 2.2

- Clinicians should recommend against use of cannabis and/or cannabinoids in place of cancer-directed treatment.

**Note.** Cannabis and/or cannabinoids used as cancer-directed treatment may cause significant clinical (e.g., fatigue, confusion, feeling “high”) and financial toxicities without good quality evidence of clinical benefit.

Informal consensus	
Evidence Quality	Strength of Recommendation
Very Low	Strong

# Summary of Recommendations

## Clinical Question 3

- Does use of cannabis and/or cannabinoids by adults with cancer reduce treatment-related toxicities, palliate cancer symptoms, or improve QOL?

### Recommendation 3.1

- Adults with cancer who receive moderately or highly emetogenic antineoplastic agents with guideline-concordant antiemetic prophylaxis and experience refractory nausea or vomiting may augment their antiemetic regimen with dronabinol, nabilone, or a quality-controlled oral 1:1 THC:CBD extract.

Evidence-based	
Evidence Quality	Strength of Recommendation
Moderate for dronabinol and nabilone	Weak
Low for 1:1 THC:CBD extract	

# Summary of Recommendations

**Note for Recommendation 3.1.** Cannabis and/or cannabinoids are one of several pharmacologic options for adults with cancer experiencing refractory nausea and vomiting despite optimal prophylaxis. For such individuals, the 2020 ASCO antiemetics guideline<sup>14</sup> recommends the addition of olanzapine (if not already prophylactically administered); otherwise, the addition of an antiemetic from a different class (e.g., a neurokinin-1 receptor antagonist, dopamine receptor antagonist, benzodiazepine, or synthetic THC).



# Summary of Recommendations

## Recommendation 3.2

- Outside of a clinical trial, clinicians should not recommend that adults with cancer use 300 mg or more per day of oral CBD to manage symptom burden due to lack of proven efficacy and risk for reversible liver enzyme abnormalities.

**Note.** In adult and pediatric populations without cancer, reversible liver enzyme abnormalities primarily occurred in study participants taking 300 mg or more per day of oral CBD.<sup>15</sup>

Evidence-based	
Evidence Quality	Strength of Recommendation
Low	Weak

# Summary of Recommendations

## Recommendation 3.3

- Evidence remains insufficient to recommend for or against cannabis and/or cannabinoids in managing cancer treatment-related toxicities or symptoms (including cancer pain), aside from clinical settings addressed in Recommendations 3.1 and 3.2 or within the context of a clinical trial (see Table 2 in the guideline).

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Discussion

# Discussion

- Access to cannabis and cannabinoids has outpaced the science supporting evidence-based indications for their use.
- Simultaneously, anecdotal experience among adults with cancer using cannabis and/or cannabinoids continues to promote strong incentives for use despite an absence of objective evidence, creating ongoing clinical challenges and opportunities in the care of adults with cancer.
- Consequently, the Expert Panel believes addressing the lack of high-quality clinical evidence is critical.

# Potential Short- and Long-Term Risks

- While, with appropriate dosing and titration, cannabis and/or cannabinoids are well tolerated, adults with cancer considering their use should be aware of both common side effects, (e.g., dizziness, confusion, dry mouth, and fatigue) and more serious side effects (e.g., tachycardia, orthostatic hypotension, confusion, and paranoia).
- To minimize adverse effects, particularly in older adults and in those naïve to cannabis and/or cannabinoids, products should be started at a low dose and slowly increased until desired effect (e.g., antiemesis) is achieved.<sup>16</sup>
- Adults with cancer who ingest excessive cannabis and/or cannabinoids are not at risk for respiratory depression, as they might be with inappropriately dosed opioids. Nevertheless, cannabis and/or cannabinoid overdoses can be distressing and multiple poorly controlled acute symptoms may place an individual at high risk for falls and healthcare utilization.
- While free of many of THC's neuropsychiatric liabilities, cannabidiol presents risks for hepatotoxicity.

# Potential Short- and Long-Term Risks

- Clinicians, adults with cancer, and caregivers should understand the degree of risk for emergence of long-term side effects with cannabis and/or cannabinoid use.
- In addition to risk for long-term physical side-effects, chronic cannabis use carries long-term psychiatric risks, which may be correlated with cumulative exposure including age of first use.
- Ten percent of adults with chronic cannabis use may also develop cannabis use disorders,<sup>17</sup> associated with clinically significant impairment or distress, including using more cannabis than expected and difficulty in cutting back on use.<sup>18,19</sup>
- Cannabis users are also at higher risk of motor vehicle accidents.

# Patient and Clinician Communication About Medical Cannabis

- Cannabis and/or cannabinoid use continues to be addressed in stigmatizing ways within healthcare settings.
- To promote the safe, appropriate, and effective use of cannabis and/or cannabinoids, clinicians, adults with cancer, and their caregivers should engage in open, non-judgmental conversations about the potential risks and benefits of their use in cancer care.
- These conversations should omit pejorative terms commonly associated with substance use and reflect the language utilized by the adult with cancer and their caregiver.
- Clinicians should invite adults with cancer to express their knowledge, attitudes, and goals of care related to cannabis and/or cannabinoids, as well as prior and current history of use. The perceived effectiveness and side effects of cannabis and/or cannabinoids should also be explored.
- Clinicians may favor formally sourced cannabis products (e.g., from a medical dispensary) over those informally sourced. In many jurisdictions, the former will have undergone testing of key cannabinoid concentrations, as well as for the presence of heavy metals and contaminants.

# Patient and Clinician Communication About Medical Cannabis

- Clinicians should also provide recommendations to adults with cancer regarding driving or engaging in safety-sensitive work (e.g., working with vulnerable populations, operating heavy equipment) following the consumption of cannabis and/or cannabinoids when cognitive and physical impairment is likely (up to 12 hours, depending on the type of cannabis product).
- Given the varying legal status of medical and non-medical cannabis in different jurisdictions, it is prudent to discuss with adults with cancer and their caregivers how medical cannabis and/or cannabinoids are regulated in their region and how to access legal, quality-controlled sources to avoid interactions with law enforcement.
- For clinicians who lack knowledge and training related to medical cannabis or feel uncomfortable discussing the topic, a referral to a regional medical cannabis specialist or clinic may optimize comprehensive and informed care.
- Oncology clinicians should maintain ongoing communication with these clinical partners to ensure safe cannabis and/or cannabinoid use.



# Health Disparities

- When establishing the role of medical cannabis and/or cannabinoids in cancer care, certain societal disparities call for awareness by all members of multidisciplinary clinical oncology teams.
- First, state and federal cannabis laws impact minorities disproportionately. Though decriminalization and legalization of cannabis in many states resulted in fewer arrests for non-violent possession, African Americans are still 3.6 times more likely to be arrested for cannabis possession than their white counterparts despite the prevalence of cannabis use being approximately equal between the groups.<sup>20,21</sup>
- Second, the wide variability in cannabis laws across states has created many differences in which medical conditions qualify for medical cannabis, the types of cannabis products sold, permissible cannabis quantities, and the availability of dispensaries.
- These differences reflect structural barriers to accessing medical cannabis by adults with cancer.<sup>22</sup>
- Clinical teams must be aware of societal biases, stigma, and circumstances surrounding cannabis that may lead adults with cancer to underreport their cannabis use.<sup>23</sup>

# Barriers to Research

- The Expert Panel acknowledges barriers to the conduct of medical cannabis and/or cannabinoid research.
- The status of cannabis (containing >0.3% THC) as an illegal drug in most countries limits research funding and study drug access.
- In the US, the National Institute on Drug Abuse has funded the bulk of cannabis research and is understandably focused on the potential risks more than the potential benefits.<sup>24</sup> The University of Mississippi has served as the sole supplier of cannabis for research purposes since 1968, even following a 2016 announcement from the US DEA that licenses would be granted to other producers.<sup>25</sup>
- The University's product offerings are not nearly broad enough regarding potencies and formulations to reflect the cannabis products sourced formally or informally to adults with cancer.
- Numerous gaps in our understanding of cannabis and/or cannabinoid use by adults with cancer warrant further investigation. The Expert Panel details priorities for future research in the guideline.

# Additional Resources

- More information, including a supplement and clinical tools and resources, is available at [www.asco.org/supportive-care-guidelines](http://www.asco.org/supportive-care-guidelines)
- Patient information is available at [www.cancer.net](http://www.cancer.net)

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# Abbreviations

- ASCO, American Society of Clinical Oncology
- CBD, cannabidiol
- DEA, Drug Enforcement Administration
- EBMC, Evidence Based Medicine Committee
- QOL, quality of life
- THC, tetrahydrocannabinol
- US, United States

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