

# Let's Be Blunt: Can Cannabis and Opioids Play Nice in Pain Management?

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# Objectives

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- Summarize current perspectives on medical cannabis and opioid prescribing for pain management.
- Compare pharmacological mechanisms, efficacy, and safety profiles of cannabis versus opioids.
- Develop pain management strategies for transitioning patients between cannabis and opioids.
- Implement best practices for documentation and resources in co-prescribing or alternative therapy plans.

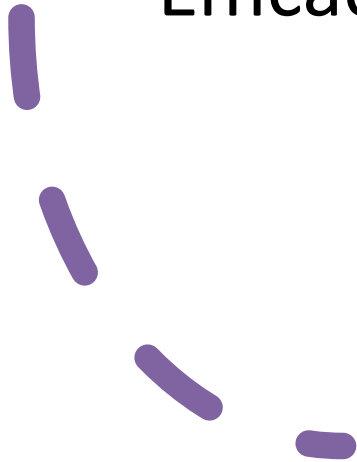
# Current Trends: Opioid and Medical Cannabis Prescribing for Pain Management

- **Widespread Legalization:** With over 37 states legalizing medical cannabis, patients across the U.S. have growing access to this alternative for pain management.
- **Reduced Opioid Dependency:** Studies consistently show that access to medical cannabis is associated with lower opioid prescriptions and overdose rates.
- **Positive Patient and Provider Reception:** Both patients and providers increasingly view medical cannabis as a safer, effective alternative to high-dose or long-term opioid use for chronic pain.



# Recreational vs. Medical Cannabis

## What's the difference?

- Potency
  - Labeling/Regulation
  - Availability
  - Efficacy for pain management
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# Cannabis: Mechanism of Action

## 1. Cannabinoid Receptors: CB1 and CB2

- *CB1 in CNS*: Modulates pain perception; THC (tetrahydrocannabinol) binds to CB1 receptors, producing analgesic & psychoactive effects
- *CB2 in Peripheral tissues and immune cells*: Modulate inflammation; CBD (cannabidiol) indirectly interacts with CB2 receptors, reducing inflammation without psychoactive effects.

## 2. Inhibition of Pain Signal Transmission

- Reduce glutamate and substance P.
- Dampens transmission of pain signals to the CNS → reduced pain perception.

## 3. Anti-Inflammatory Effects

- Suppressing pro-inflammatory cytokines like TNF-alpha and IL-6.
- Modulating immune cell activity to reduce chronic inflammation

# Cannabis: Mechanism of Action, continued

## 4. Modulation of Endocannabinoids

Cannabinoids in cannabis mimic the body's natural endocannabinoids:

- Anandamide binds to CB1 and CB2 receptors to regulate pain and mood.
- THC enhances anandamide by preventing its breakdown, leading to prolonged pain relief.

## 5. Interaction with Other Receptor Systems

- *TRPV1 Receptors (Vanilloid Receptors):*

- CBD activates TRPV1 receptors, which help detect and regulate pain and inflammation.
- Can lead to desensitization, reducing chronic pain over time.

- *Serotonin Receptors (5-HT1A):*

- CBD also interacts with serotonin receptors, to modulate the body's response to pain.

- *GABAergic and Glycinergic Systems:*

- Enhance effects of inhibitory neurotransmitters, which help dampen pain signals.

# Opioids: Mechanism of Action

## 1. Opioid Receptors

Binding with Mu ( $\mu$ ), Delta ( $\delta$ ), Kappa ( $\kappa$ ) Receptors produce analgesia and euphoria, but also respiratory depression, constipation, dependence.

## 2. Inhibition of Pain Signal Transmission

Opioids relieve pain through the following mechanisms:

*A. Presynaptic Action:* Reduce release of Substance P, Glutamate, CGRP

*B. Postsynaptic Action:* Hyperpolarize cell membrane, reduces the transmission of pain signals to the brain.

## 3. Activation of Descending Pain Modulation Pathways

Stimulate descending inhibitory pathways, including the periaqueductal gray (PAG) and the rostral ventromedial medulla (RVM), suppressing transmission of pain signals.

## 4. Effects on Pain Perception

Perceived as less intense, less distressing.

## 5. Reduction of Central Sensitization

Opioids dampen overactive neural circuits hypersensitized in chronic pain.

# Summary: Cannabis vs. Opioids

## Cannabis

**THC:** Provides pain relief and anti-inflammatory effects but has psychoactive properties, which may limit its use for some patients.

**CBD:** Offers anti-inflammatory and analgesic benefits without the high, making it suitable for a broader range of patients, including those who want to avoid psychoactive effects.

**Combination Therapy:** A balance of THC and CBD may enhance analgesic effects through synergistic interaction

## Opioids

**Analgesia:** Opioids are effective for nociceptive pain (e.g., post-surgical or inflammatory pain) and less so for neuropathic pain.

**Euphoria:** Activation of mu receptors in the reward pathway can lead to feelings of pleasure.

**Sedation:** Opioids often produce drowsiness, which can contribute to their pain-relieving effects by promoting rest.



# Side Effects: Cannabis vs. Opioids

Category	Cannabis Side Effects	Opioid Side Effects
<b>Neurological</b>	Dizziness	Drowsiness
	Impaired coordination	Sedation
	Psychoactive effects (e.g., euphoria, paranoia, anxiety with THC)	Euphoria (pleasurable feelings that may lead to misuse)
	Cognitive impairment (temporary memory, attention issues)	Cognitive slowing
	Rare risk of psychosis in predisposed individuals	Increased risk of tolerance and dependence
		Risk of addiction and withdrawal symptoms
<b>Respiratory</b>	Potential irritation of airways (if smoked)	Respiratory depression (life-threatening in high doses)
	Not linked to severe respiratory depression	Decreased responsiveness to carbon dioxide
<b>Gastrointestinal</b>	Dry mouth	Nausea and vomiting
	Increased appetite (often beneficial in certain conditions)	Constipation (common and severe with long-term use)

# Side Effects: Cannabis vs. Opioids

Category	Cannabis Side Effects	Opioid Side Effects
<b>Cardiovascular</b>	Tachycardia	Bradycardia
	Occasional BP fluctuations	Hypotension
		Risk of CV events (e.g., heart attack)
<b>Psychological/ Behavioral</b>	Anxiety or paranoia in THC-sensitive individuals	Depression and mood instability with long-term use
	Altered sensory perception	Reduced emotional responsiveness
		Hyperalgesia (increased sensitivity to pain)
<b>Immune System</b>	Anti-inflammatory effects	Immunosuppression
<b>Dependency Risk</b>	Low to moderate dependency potential (THC > CBD)	High dependency potential
	Risk of cannabis use disorder with chronic use	Severe withdrawal symptoms
<b>Other Notable Effects</b>	Red eyes	Increased tolerance over time
	Mild fatigue	Endocrine dysfunction (e.g., decreased testosterone levels)

# Medical Cannabis in Pain Management – What Works

Effectiveness varies by:

- Type of pain
- Composition of cannabis product (THC vs. CBD)
- Delivery method
- Individual patient factors

# FDA-Approved Cannabinoid Medications in the U.S.

Medication	Type	Brand Name(s)	Indications	Typical Dosing
Dronabinol	Synthetic THC	Marinol®, Syndros®	<ul style="list-style-type: none"><li>• CINV refractory to antiemetics</li><li>• Anorexia in AIDS</li></ul>	<ul style="list-style-type: none"><li>• CINV: 5 mg/m<sup>2</sup> pre-chemo, then q2–4h</li><li>• Anorexia: 2.5 mg BID, titrate to 5 mg BID</li></ul>
Nabilone	Synthetic cannabinoid	Cesamet®	<ul style="list-style-type: none"><li>• CINV unresponsive to other treatments</li></ul>	<ul style="list-style-type: none"><li>• 1–2 mg BID before chemo, continued for 48h post-chemo</li></ul>
Cannabidiol	Purified CBD (non-psychoactive)	Epidiolex®	<ul style="list-style-type: none"><li>• Seizures in Lennox-Gastaut, Dravet, Tuberous Sclerosis (≥1 yr old)</li></ul>	<ul style="list-style-type: none"><li>• Start 2.5 mg/kg BID; increase to 5 mg/kg BID; max 20 mg/kg/day</li></ul>

*Note: These are FDA-approved medications. Medical cannabis from dispensaries is not FDA-approved and varies in quality, content, and regulation.*

# Medical Cannabis in Pain Management

## Efficacy by Pain Type

### 1. Chronic Neuropathic Pain

- Effectiveness: Moderate effectiveness in reducing chronic neuropathic pain, which results from nerve damage and is often resistant to traditional painkillers.
- Studies: A 2015 systematic review published in *The Journal of the American Medical Association* (JAMA) found that medical cannabis provided significant pain relief for neuropathic pain patients compared to a placebo. Another review from *The Cochrane Library* found moderate evidence supporting cannabis-based medicines in reducing neuropathic pain by about 30% in a significant portion of patients.



***Recommendation: Cannabis can be a benefit, especially for patients who do not respond well to other medications like opioids or anticonvulsants.***

### 2. Cancer-Related Pain

- Effectiveness: Moderately effective for some patients in managing cancer-related pain, often when combined with other treatments.
- Studies: Research published in *The Journal of Pain and Symptom Management* suggests that cannabis can reduce pain in cancer patients and improve quality of life, particularly when added to a regimen that includes opioids. Another study from *The European Journal of Pain* noted that THC and CBD combinations might be particularly useful in managing cancer-related pain.



***Recommendation: Cannabis can be a supplement for cancer pain, helping to reduce opioid dosages and manage side effects.***

# Medical Cannabis Effectiveness, continued


## 3. Arthritis and Inflammatory Pain

- Effectiveness: Cannabinoids like CBD are reported to reduce inflammation, which may help with arthritis and other inflammatory pain, though evidence is mixed.
- Studies: A 2020 review in *Current Rheumatology Reports* found that while some arthritis patients report pain relief with CBD, high-quality clinical trials are limited. Animal studies show promising anti-inflammatory effects, but human studies are still in early stages.

 ***Recommendation: Cannabis may help with inflammatory pain, especially when inflammation is a primary pain driver, but more robust research is needed to confirm effectiveness.***

## 4. Fibromyalgia

- Effectiveness: Cannabis has shown some potential for relieving pain and improving sleep in patients with fibromyalgia, though responses vary widely.
- Studies: A study published in *Pain Research and Treatment* found that patients with fibromyalgia experienced pain relief, improved sleep, and enhanced quality of life with cannabis use. However, due to the complex nature of fibromyalgia, individual responses to cannabis can be inconsistent.

 ***Recommendation: Cannabis may benefit some fibromyalgia patients, particularly for improving sleep and quality of life, though it may not be effective for all.***

# Medical Cannabis Effectiveness, continued

## 5. Generalized Chronic Pain

- Effectiveness: Cannabis may provide mild to moderate pain relief for generalized chronic pain, though results vary.
- Studies: A 2017 *National Academies of Sciences, Engineering, and Medicine (NASEM)* report found substantial evidence that cannabis is effective for chronic pain in adults, particularly when pain is generalized or involves multiple systems.

 ***Recommendation: For generalized chronic pain, cannabis can be a useful adjunct, but its effectiveness may be less predictable than for specific pain types like neuropathic pain.***

## 6. Post-Surgical Pain

- Effectiveness: Evidence for cannabis in post-surgical pain is limited, and it is generally not recommended as a first-line treatment.
- Studies: Research has been inconclusive, with some studies showing no significant reduction in pain or opioid use for post-surgical patients using cannabis. Some researchers caution against its use in this context due to potential interactions with anesthetics and the unclear risk-benefit ratio.

 ***Recommendation: Cannabis is not widely recommended for acute post-surgical pain due to limited evidence and potential risks.***

# Medical Cannabis - Summary

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## Summary of Effectiveness

- **YES - Neuropathic Pain: Moderate evidence of effectiveness.**
- **YES - Cancer Pain: Moderate evidence, often used as a supplement to opioids.**
- **MAYBE - Inflammatory Pain:** Some potential, especially with CBD; more research needed.
- **MAYBE - Fibromyalgia:** Promising for some patients, but individual responses vary.
- **MAYBE - Generalized Chronic Pain:** Moderate effectiveness, helpful for some.
- **NO - Post-Surgical Pain:** Limited evidence; not widely recommended.


## Overall Recommendation:

Cannabis may be effective for certain types of chronic pain, especially neuropathic and generalized chronic pain, but results can vary significantly between individuals. It is often most effective as part of a multimodal pain management plan, rather than as a standalone treatment, and may allow for reduced opioid dosages in patients who respond well. However, more rigorous, large-scale studies are needed to confirm its effectiveness across broader pain categories





## Current Opioid Prescribing Guidelines

- CDC, AMA, AAFP guidelines on responsible opioid prescribing to patients taking cannabis
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# Key Guideline Takeaways (for opioid prescribing in general)

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1

Prioritize non-opioid treatments first

2

Prescribe the lowest effective dose

3

Closely monitor patients for side effects and/or signs of aberrant behavior

4

Refer to pain specialist when appropriate

# Impact of Cannabis on Opioid Efficacy

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# Cannabis and Opioid Interaction:

A help or a hinderance?



# Current Research

- It's mixed!
    - Variable results – helps short-term, not long-term
    - It helps
    - It interferes
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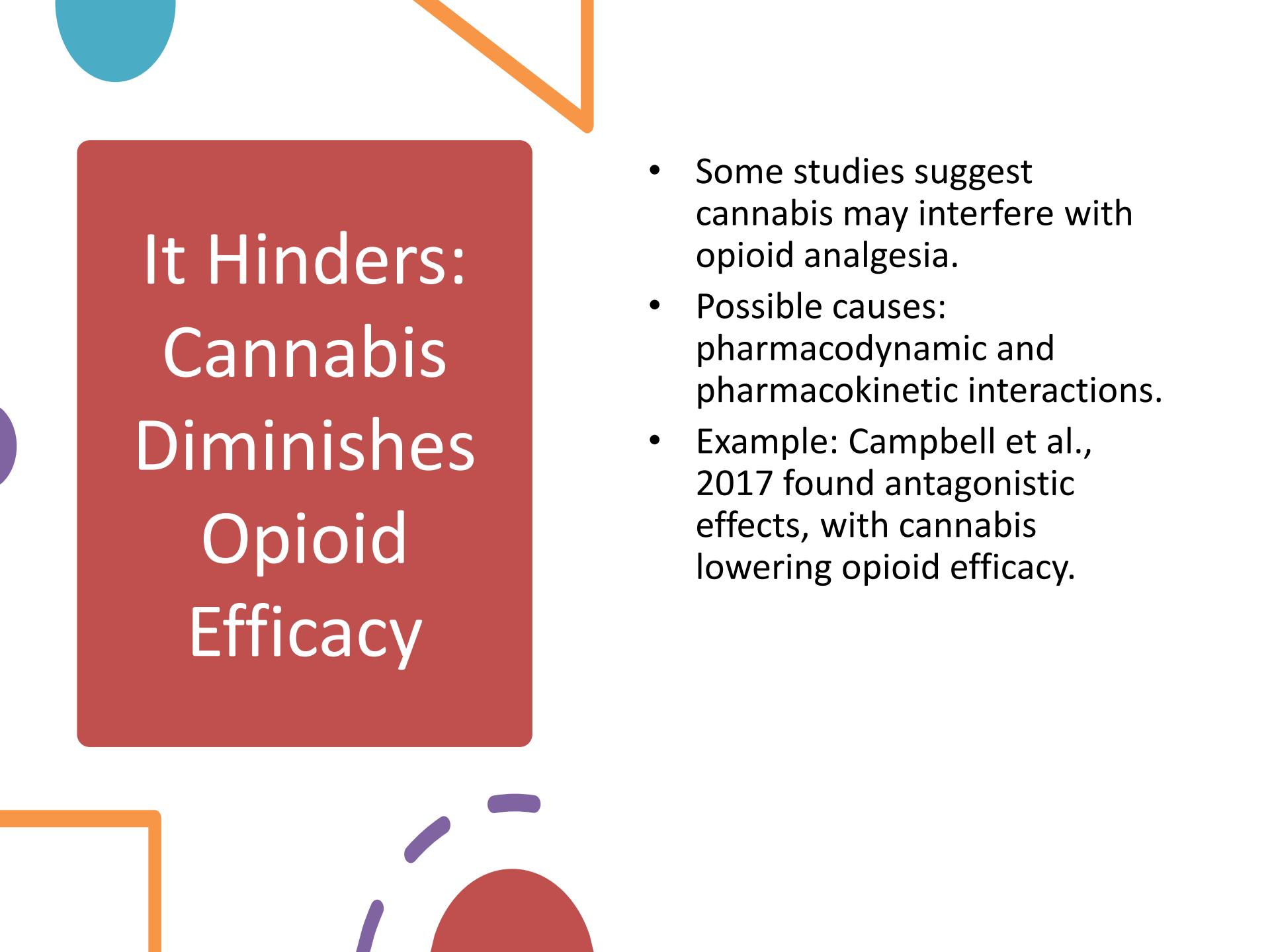
## Variable: Mixed Pain Outcomes

- Some studies report initial pain relief with cannabis, but effects can be short-lived.
- Pain scores varied based on cannabis formulation and dosing.
- Example: THC provided immediate pain relief but did not sustain opioid efficacy over time.
- Recommendation: Monitor patients closely for short-term relief vs. long-term impact.



## It Helps: Cannabis Enhances Opioid Analgesia

- Research from the *Journal of Pain* indicates that combining cannabis with opioids may enhance analgesic effects, allowing for lower opioid doses.
  - CBD may modulate pain pathways without significant psychoactive effects, potentially enhancing opioid effectiveness without exacerbating sedation or cognitive impairment.
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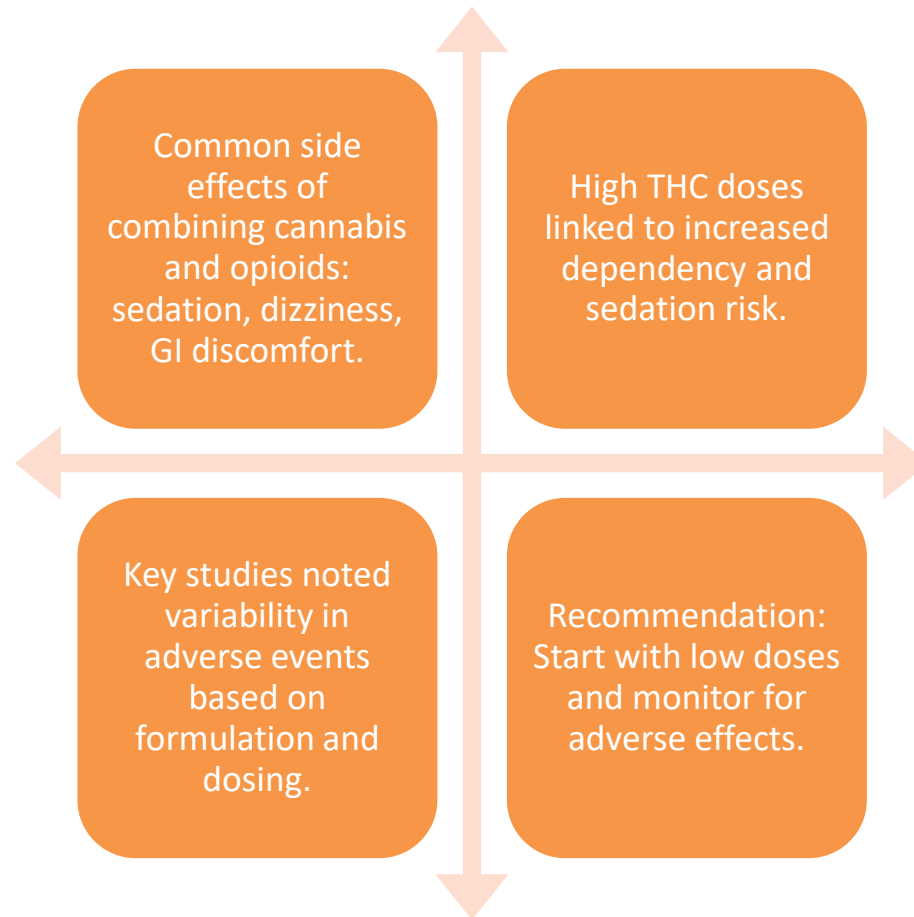


# It Hinders: Cannabis Diminishes Opioid Efficacy

- Some studies suggest cannabis may interfere with opioid analgesia.
- Possible causes: pharmacodynamic and pharmacokinetic interactions.
- Example: Campbell et al., 2017 found antagonistic effects, with cannabis lowering opioid efficacy.



# Adverse Events and Safety Concerns



# Summary of Findings

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Cannabis may offer initial relief, but sustained opioid efficacy varies.

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Possible diminished analgesic effect due to metabolic and interaction mechanisms.

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Adverse events should be monitored, particularly with high THC doses.

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Recommendation: Use personalized approaches and careful monitoring when combining therapies.

# Current perspectives/recommendations about combining Cannabis and Opioids

## 1. General Caution

- Lack of comprehensive research on long-term safety and potential drug interactions
- Increased risk of sedation
- Regulatory concerns

## 2. Potential Synergistic Effects

- May reduce opioid requirements
- Combining the two may offer a broader pain relief

## 3. Specific Contexts for Co-Prescribing May Be Appropriate

- Tapering Off Opioids
- Chronic Non-Cancer Pain
- Cancer Pain and Palliative Care

## 4. Clinical and Legal Challenges

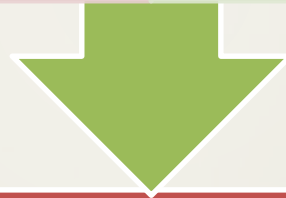
- Variable State Policies
- Insurance and Coverage

# Perspectives, continued

**Conclusion:** Co-prescribing opioids and cannabis is generally **not recommended** except in specific scenarios, such as:

**Tapering opioids** to manage withdrawal and provide an alternative for pain.

**Certain disease processes** like cancer or palliative care, where symptom management outweighs potential risks.



The decision to co-prescribe should involve careful consideration, close monitoring, patient involvement in shared decision making, and a thorough understanding of patient-specific factors.

# Managing Patients on Medical Cannabis for Pain

1. **Assessment:** Establish baseline - assess the form (THC vs. CBD), dosage, and frequency to understand patient's cannabis experience and tolerance.
2. **Go Slow:** Taper off slowly to minimize side effects and allow for careful observation of the patient's response.
3. **Use Cannabis to Reduce Opioids:** If cannabis effective, reduce opioid dose under close supervision to reduce opioid-related side effects and withdrawal
  - Document plan and the rationale for any opioid reduction based on patient-reported outcomes and objective pain measures, using a tapering plan that minimizes withdrawal risk.

# Managing Patients on Medical Cannabis for Pain, Continued

4. **Regular Monitoring and Follow-Up:** Closely monitor for side effects, functional changes, and any signs of misuse. Frequent follow-up visits, urine drug screening, and pain management contracts to ensure safe and effective use
5. **Individualized Treatment Plans:** No one-size-fits-all approach. Tailor the treatment plan based on the patient's pain type, response to opioids, and individual cannabis tolerance.
  - Multimodal approaches to manage chronic pain holistically.
  - Document each adjustment in the patient's plan, noting the clinical reasoning and any feedback from the patient on pain relief and side effects.
6. **Avoid Co-Prescribing for Acute Pain:** Use established multimodal analgesia options, such as NSAIDs, acetaminophen, and regional anesthesia, for acute pain management instead of co-prescribing opioids and cannabis.

# Managing Patients on Medical Cannabis for Pain, Continued

## **7. Educate Patients on Risks and Safe Usage:**

- Educate about the potential side effects of using opioids and cannabis together, including sedation, cognitive impairment, increased fall risk, driving.
- Provide written materials
- Document education provided

## **8. Consider Cannabinoid Ratios and Composition:**

For pain patients on opioids and cannabis, transition to cannabis products with higher CBD-to-THC ratios when possible

- Minimize psychoactive effects, sedation and cognitive impairment.

# Managing Patients on Medical Cannabis for Pain, Continued

## **9. Document and Monitor for Drug-Drug Interactions**

- Recognize that cannabis may interact with opioids at both pharmacokinetic and pharmacodynamic levels, which can synergistically influence pain and sedation.
- Review all patient medications and consider pharmacist or pain management specialist consultation for guidance on potential interactions, if the patient is on other CNS depressants in addition to opioids and cannabis.

## **10. Informed Consent and Documentation**

- Obtain informed consent, specifically addressing the risks and uncertainties of using both opioids and cannabis for pain.
- Include documentation in the patient's record showing that the risks, benefits, and alternatives were discussed, especially given the evolving legal landscape around cannabis.



# What Should You Document?

1. Thorough Initial Assessment
2. Rationale for Therapy Choices
3. Detailed Informed Consent
4. Regular Monitoring and Follow-Ups
5. Patient Education
6. Risk Mitigation Strategies
7. Objective Evidence and Justifications for Adjustments
8. Treatment Challenges and Patient Non-Compliance
9. Consultations and Referrals

## 2. Clearly Document the Rationale

- **Cite the specific guideline or study:** Mention the resource by name (e.g., “CDC guidelines recommend...” or “According to the AMA Task Force...”).
- **Detail the therapy choice and alternatives considered:** Specify why opioids, cannabis, or a combination were chosen, referring to evidence that supports their use for the patient's specific pain profile.
- **Outline the rationale:** Summarize why other options may not be appropriate (e.g., previous failure of NSAIDs or contraindications to non-opioid therapies) to illustrate the thoughtful selection of treatment.

# Documentation, Continued

- 3. Detailed Informed Consent
- 4. Regular Monitoring and Follow-Ups
- 5. Patient Education
- 6. Risk Mitigation Strategies
- 7. Objective Evidence and Justifications for Adjustments
- 8. Treatment Challenges and Patient Non-Compliance
- 9. Consultations and Referrals

# General Management Summary

- **Recommend CBD-dominant formulations:** CBD may be preferred to reduce psychoactive side effects when cannabis is used with opioids.
- **Gradual opioid reduction:** Where possible, use cannabis to reduce opioid dosages, monitored through close follow-up visits.
- **Patient education and consent:** Emphasize educating patients on safe practices and documenting their understanding of co-prescribing risks.
- **Frequent monitoring:** Ensure regular monitoring to detect any side effects, potential misuse, or need for dosage adjustments.
- **Comprehensive documentation!**



Thank you!

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