

# Evidence for THC versus CBD in cannabinoids

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## Clinical question

Do tetrahydrocannabinol (THC), cannabidiol (CBD), or THC-CBD combined have differing benefits or harms?

## Bottom line

Of 4 RCTs, 1 found THC-CBD superior to THC but this was inconsistent within the study and with other studies. Adverse events are prevalent with THC, CBD, and THC-CBD. While some early poor-quality research in healthy users suggests CBD attenuates some psychiatric effects of THC, better research in real patients is needed to verify any benefits of specific components.

## Evidence

Four RCTs compared THC, CBD, or both combined.

- One RCT (N=243 terminal cancer and weight loss patients) compared THC-CBD, THC, and placebo for 6 weeks.<sup>1</sup> There was no statistical difference in appetite or adverse events for THC-CBD versus THC.
- An RCT in 177 patients with refractory cancer pain taking strong opioids (about 270 mg of morphine) compared THC-CBD, THC, and placebo for 2 weeks.<sup>2</sup>
  - A pain reduction of 30% or more was seen in 38% of the THC-CBD group versus 21% in the THC group (number needed to treat=6). There was no difference for pain reductions of 10% or more or 50% or more.
  - There was no difference in adverse events with THC-CBD versus THC.
- An RCT in 48 patients with brachial nerve injury compared THC-CBD, THC, and placebo over 2 weeks.<sup>3</sup>
  - Baseline pain score was 7.5 of 10. The THC-CBD and THC groups' pain reduced by about 1.3 points, statistically significantly more than 0.6 points with placebo.
  - Adverse events were not significantly different between THC-CBD and THC.
- N of 1 studies in 34 chronic pain patients (24 completed) who benefited from THC-CBD compared THC-CBD, THC, CBD, and placebo over 8 weeks.<sup>4</sup>
  - Versus starting THC-CBD, patients' pain management was the same or better in 38% with repeat THC-CBD, 33% with THC, and 17% with CBD (no statistical difference).

## Context

- An RCT in 120 pediatric patients with Dravet syndrome showed CBD reduced seizure frequency by about 22% over placebo at 14 weeks.<sup>5</sup>

-Adverse events included somnolence (number needed to harm [NNH]=4), diarrhea (NNH=5), and appetite loss (NNH=5). A recent RCT of adults with Lennox-Gastaut (seizure) syndrome found similar results.<sup>6</sup>

- One guideline recommends low THC or a high CBD-to-THC ratio to reduce THC adverse events based on small studies of healthy volunteers (some with history of other drug use) examined with magnetic resonance imaging or short-term scale changes.<sup>7</sup>

## Implementation

A Canadian guideline recommends cannabinoids (pharmaceutically derived first) only in refractory neuropathic pain, palliative cancer pain, nausea and vomiting from chemotherapy, and spasticity.<sup>8</sup> Current guidance for smoked dried cannabis for pain recommends titrating up to 400 mg/d of 9% THC.<sup>9</sup> Health Canada permits patients with a prescription for medical cannabis to legally possess up to 150 g, a 1-month's maximum supply, equating to 5 g/d.<sup>10</sup> A content analysis of Canadian licensed producers found that 58% of THC-predominant products had concentrations of 15% THC.<sup>11</sup> Thus, patients might be using much higher doses than studied or recommended.

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**Competing interests**  
None declared

**The opinions expressed** in Tools for Practice articles are those of the authors and do not necessarily mirror the perspective and policy of the Alberta College of Family Physicians.

## References

1. Strasser F, Luftner D, Possinger L, Ernst G, Ruhstaller T, Meissner W, et al. Comparison of orally administered cannabis extract and delta-9-tetrahydrocannabinol in treating patients with cancer-related anorexia-cachexia syndrome: a multicenter, phase III, randomized, double-blind, placebo-controlled clinical trial from the Cannabis-in-Cachexia-Study-Group. *J Clin Oncol* 2006;24(21):3394-400.
2. Johnson JR, Burnell-Nugent M, Lossignol D, Ganae-Motan E, Potts R, Fallon M. Multicenter, double-blind, randomized, placebo-controlled, parallel-group study of the efficacy, safety, and tolerability of THC:CBD extract and THC extract in patients with intractable cancer-related pain. *J Pain Symptom Manage* 2010;39(2):167-79.
3. Berman JS, Symonds C, Birch R. Efficacy of two cannabis based medicinal extracts for relief of central neuropathic pain from brachial plexus avulsion: results of a randomised controlled trial. *Pain* 2004;112(3):299-306.
4. Notcutt W, Price M, Miller R, Newport S, Phillips C, Simmons S, et al. Initial experiences with medicinal extracts of cannabis for chronic pain: results from 34 'N of 1' studies. *Anaesthesia* 2004;59(5):440-52.
5. Devinsky O, Cross JH, Laux L, Marsh E, Miller I, Nabbott R, et al. Trial of cannabidiol for drug-resistant seizures in the Dravet syndrome. *N Engl J Med* 2017;376(21):2011-20.
6. Thiele EA, Marsh ED, French JA, Mazurkiewicz-Beldzinska M, Benbadis SR, Joshi C, et al. Cannabidiol in patients with seizures associated with Lennox-Gastaut syndrome (GWPCARE4): a randomised, double-blind, placebo-controlled phase 3 trial. *Lancet* 2018;391(10125):1085-96.
7. Fischer B, Russell C, Sabioni P, van den Brink W, Le Foll B, Hall W, et al. Lower-risk cannabis use guidelines: a comprehensive update of evidence and recommendations. *Am J Public Health* 2017;107(8):e1-12.
8. Allan GM, Ramji J, Perry D, Ton J, Beahm NP, Crisp N, et al. Simplified guideline for prescribing medical cannabinoids in primary care. *Can Fam Physician* 2018;64:111-20 (Eng), e64-75 (Fr).
9. Kahan M, Srivastava A, Spithoff S, Bromley L. Prescribing smoked cannabis for chronic noncancer pain. Preliminary recommendations. *Can Fam Physician* 2014;60:1083-90 (Eng), e562-70 (Fr).
10. Health Canada. *Controlled Drugs and Substances Act. Access to cannabis for medical purposes regulations*. Ottawa, ON: Government of Canada; 2016.
11. Mammen G, de Freitas L, Rehm J, Rueda S. Cannabinoid concentrations in Canada's regulated medical cannabis industry. *Addiction* 2017;112(4):730-2.

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