Medical Cannabis for Chronic Non Cancer Pain: A Systematic Review of Randomized Control Trials

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BACKGROUND

- Approximately 1 in 5 Canadians suffer from chronic non-cancer pain (CNCP)
- Opioids are commonly prescribed for CNCP, but are associated with addiction, overdose and death
- Medical cannabis is a potential alternative for CNCP, and the Canadian Pain Society has listed cannabinoids as a third line of treatment for neuropathic pain
- Prior reviews are limited by outdated searches, exclusion of trials from pooled analyses due to reporting of different outcomes across common domains, suboptimal presentation of results, and inadequate assessment of the overall quality of evidence.

OBJECTIVE

To assess the effect of cannabis on CNCP through a systematic review and meta-analysis of randomized clinical trials.

METHODS

Study Eligibility Criteria

- Patient: Patients with CNCP (must enroll ≥ 10 patients)
- Intervention: Any form of medicinal cannabis
- Control: Any non-cannabis control
- Outcome: All patient-important outcomes
- Timing: Minimum of 2 weeks' follow-up

Risk of bias assessment:

- Random sequence generation
- Allocation concealment
- Blinding of patients, personnel, outcome assessors and data analysts
- Incomplete outcome data

Data source: Up to Jan, 2017

- MEDLINE/PubMed
- EMBASE
- CENTRAL
- AMED
- CINAHL
- PsycInfo

Study Selection & Data Abstraction

- Pairs of reviewers, independently and in duplicate, screened titles and abstracts of identified citations, reviewed the full texts of potentially eligible trials, and extracted information from eligible studies.

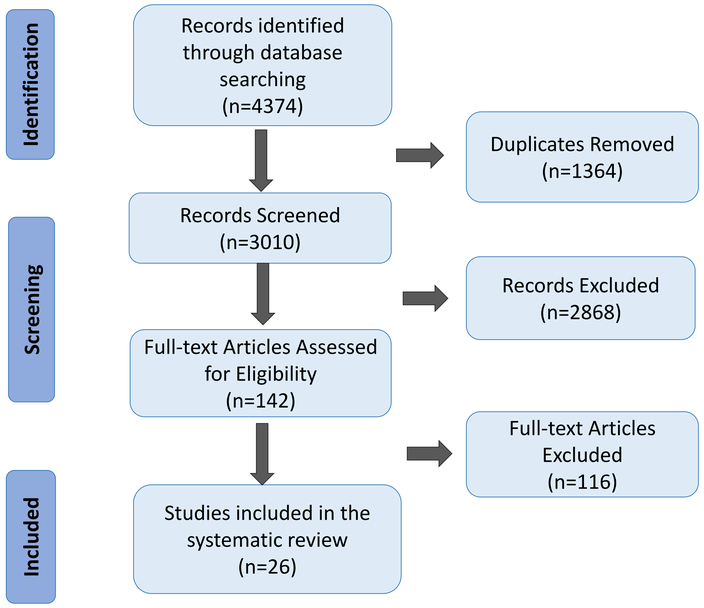
Meta-analysis

- Random effects models were used to pool data for each outcome across studies
- Continuous outcomes were reported as the weighted mean difference, after converting all outcomes reporting pain to a common scale
  - Results were also presented as the risk difference (RD) of achieving the minimally important difference (MID)
- Binary outcomes were reported as the relative risk (RR) of experiencing the event

PRELIMINARY RESULTS

- 26 trials, with a total of 1,915 patients
- Countries: Most trials in the UK (n=7) or Canada (n=5)
- Patient age: Median 50.1 years
- Duration of pain: Median 10.3 years
- Duration of follow-up : 28 days

Figure 1: Study flow diagram



Interventions

- THC+CBT (n=8)
- Nabilon (n=7)
- THC only (n=5)
- Dronabinol (n=2)
- Multiple Interventions(n=2)
- CBD only (n=1)
- CT-3 (n=1)

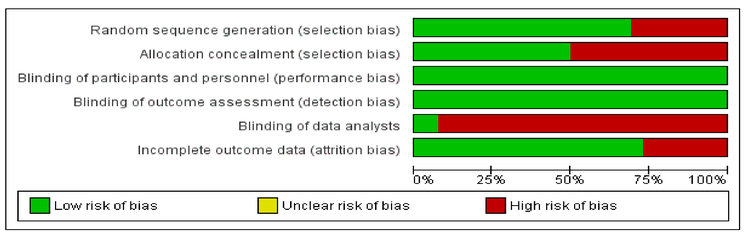
Mode of administration

- Pill (n=14)
- Spray (n=8)
- Smoke (n=4)

Control used

- Placebo (n=23)
- Amitriptyline (n=1)
- Dihydrocodeine (n=1)
- Ibuprofen (n=1)

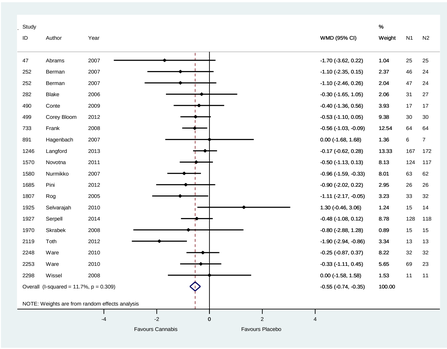
Figure 2: Risk of bias



Cannabis vs placebo

Figure 3: Pain

- 20 studies with 1,815 patients
- Follow-up: 14-98 days
- Medicinal cannabis vs placebo results in small but important pain relief
  - Baseline risk of achieving the MID (≥1cm pain reduction): 48%
  - RD: 12% more (95%CI 8% to 16% more) achieve a ≥1cm pain reduction
- MODERATE quality evidence



GRADE Evidence Profile for Pain Relief

No. of RCTs (# of Pts.)	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Risk Difference of achieving ≥1cm (95%CI)	Weighted Mean Difference (95%CI)	Quality of Evidence
Pain: Measured by 10 cm VAS Scale, Lower indicates better								
20 studies (1,815 pts.)	Serious	Not serious	Not serious	Not serious	Undetected; Symmetric funnel plot; Egger's test p =0.41	12% more (8% to 16% more) NNT=8	0.55 points lower (0.74 lower to 0.35 lower)	MODERATE

Figure 4: Drowsiness or Somnolence

- 19 studies with 1,830 patients
- Follow-up: 27-140 days
- Medicinal cannabis vs. placebo results in a moderate increase in drowsiness or somnolence
  - Baseline risk:7%
  - RD: 13% more (95%CI 10% to 18% more)
- MODERATE quality evidence

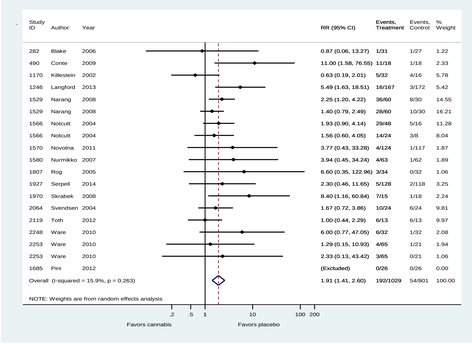
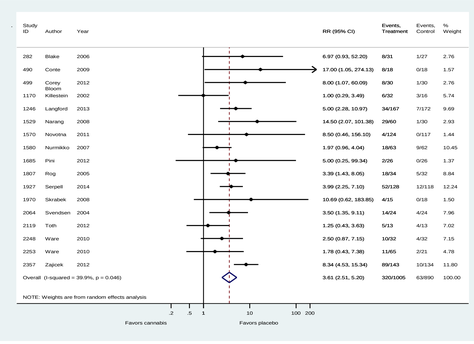


Figure 5: Dizziness or Vertigo

- 17 studies with 1,895 patients
- Follow-up: 27-140 days
- Medicinal cannabis vs. placebo results in a moderate increase in dizziness or vertigo
  - Baseline risk:7%
  - RD: 26% more (95%CI 18% to 37% more)
- MODERATE quality evidence



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SUMMARY

- Moderate quality evidence shows that cannabis provides small, but important pain relief versus placebo
- Moderate quality evidence shows that use of medicinal cannabis results in an increase in drowsiness and dizziness versus placebo
- Results are limited by short follow-up times
- We are updating our search and analyses to explore effects on all patient-important outcomes reported

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