

# Medical cannabis for symptom management in children with cancer: A systematic literature review and meta-analysis

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## Introduction

- Cannabis has a long history of being used to manage pain, nausea, vomiting, and other symptoms in patients with cancer
- Nabilone and dronabinol are synthetic cannabinoids approved for the treatment of the CINV in Canada (nabilone) and the United States (dronabinol and nabilone)
- However, their use in children is off-label due to a lack of controlled studies advocating their safety and efficacy
- Pediatric oncologists are understandably reluctant to authorize cannabis due to a lack of evidence advocating the safety and efficacy of cannabinoids in children with cancer

- A wide variety of cannabinoids were used for the management of the CINV in children with cancer including dronabinol, nabilone, cannabidiol, and unspecified cannabis herbal extracts.

**Table 2.** Summary of adverse events reported in children to cannabinoids and control in randomized controlled trials

Adverse events	No of studies	Events		Hetero I2	Test of association		
		Cannabinoids	Control		RR (95% CI)	Z	p
Withdrawal due to adverse events	2	5/123	1/123	0%	3.67 (0.61-21.89)	1.43	<0.0001
Somnolence	4	114/177	59/141	0%	1.51 (1.23-1.84)	4.03	<0.0001
Increase in appetite	2	7/50	0/50	0%	8 (1.03-61.84)	1.99	0.05
Development of high	3	67/221	7/221	0%	9 (4.38-18.48)	5.99	<0.0001
Dizziness	3	104/171	36/171	69%	5.47 (1.23-24.26)	2.23	0.03
Dry mouth	2	95/135	39/135	0%	2.42 (1.85-3.16)	6.48	<0.0001

**Table 3.** Summary of cannabis-related adverse events reported by included observational studies

Reported adverse effects	Anderson SP et al., 2021 (n= 1120)	Polito S et al., 2018 (n=110)
Drowsiness	2.5 %	20%
Dry mouth	2.2 %	NA
Fatigue	1.9%	NA
Increased appetite	1.5%	NA
Dizziness	1.3%	10%
Foggy Brain	1.3%	NA
Nausea	1.1%	NA
Headache	0.9%	2.7%
Euphoria	0.6%	3.6%
Lightheadedness	0.6%	NA
Constipation	NA	2 %
Abdominal Pain	NA	1.8%
Tachycardia	NA	1.8%
Others	NA	8.2%

- Six observational studies were of good quality, two were poor and one was the fair quality. In the case of RCTs, four studies were with a high risk of bias due to a lack of blinding in one study, and incomplete outcome data in three studies
- In the other three RCTs, there was an unclear risk of bias. Non-randomized controlled trials were of moderate quality, as both the studies were dose-finding studies without any control group

## Conclusion

- Cannabis products may have therapeutic applications for symptom management in children with cancer; however, there is a knowledge gap regarding their product composition, dose, short and long-term adverse events, and drug interactions.

## References

- Dupuis LL, et al. Optimizing symptom control in children and adolescents with cancer. *Pediatr Res.* 2019;86(5):573-8. 4.
- Rosenberg AR, et al. Quality of Life in Children With Advanced Cancer: A Report From the PediQUEST Study. *J Pain Symptom Manage.* 2016;52(2):243-53.

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## Methods

### Inclusion criteria

- Observational and Interventional studies
- Cannabinoids used as an intervention/ therapy
- Studies with at least one child < 18 years with cancer

### Database search

MEDLINE (Ovid), Embase (Ovid), The Cochrane Central Register of Controlled Trials (Ovid), Scopus, Web of Science, ClinicalTrials.gov, and the ICTRP Search Portal

### Data extraction

- Demographic details, characteristics of included studies, study participants, and intervention
- Data on serious adverse events, adverse events, and withdrawals

### Screening

- **First pass screening:** Title and Abstract Screening
- **Second Pass screening:** Full-text screening

### Data synthesis

- Descriptive synthesis in Microsoft excel,
- Pooling of adverse events data was done with a "meta-package" using R programming
- Heterogeneity assessed across included studies using  $\chi^2$  and I2 statistics

## Results

- 29,906 articles were reviewed and 19 unique studies (7 randomized controlled trials, 2 open-label studies, 8 treatment chart reviews, and 2 case reports) with 2,631 participants were included
- Nabilone (5/19, 26%), unspecified cannabis herbal extracts (5/19, 26%), delta-9 tetrahydrocannabinol (THC) (3/19, 16%), dronabinol (2/19, 11%), delta-8 THC (1/19, 5%), levonantradol (1/19, 5%), unspecified cannabinoids (1/19, 5%), cannabidiol (1/19, 5%) were used for the management of cancer symptoms in children

**Table 1.** Summary of cannabis-related adverse events reported by included observational studies

Indications	Number (n=19)
Chemotherapy Induced Nausea and Vomiting	11
Cancer-related symptoms	5
CNS tumor and leukemia	2
CNS tumor related epilepsy	1