

Medicinal cannabis in advanced cancer: Pot or panacea?

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Cannabis and cannabinoids

- **Cannabis plant : complex combination of >400 compounds (cannabinoids, flavonoids, terpenoids)**
- **Tetrahydrocannabinol (THC)- “psychoactive”, appetite stimulant, analgesia, anti-nausea, spasticity, sleep aid**
- **Cannabidiol (CBD) – anti-inflammatory, anti-epileptic, anti-psychotic, neuroprotectant, anxiolytic, antidepressant**

Legalisation

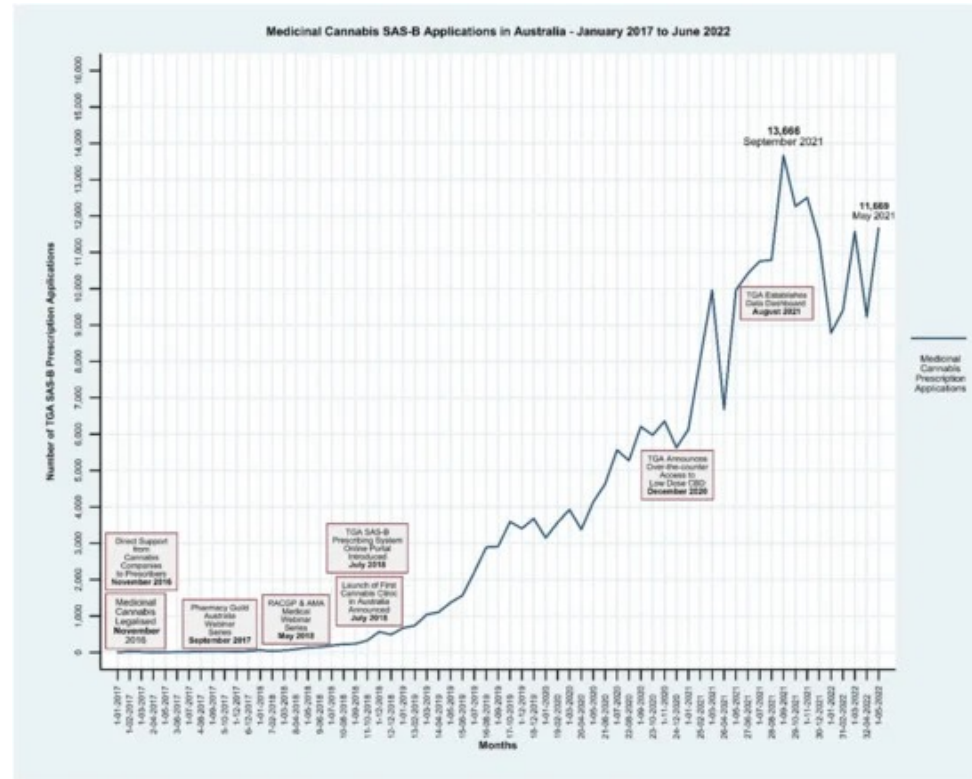
- robust public pressure
- Australian Govt legalised medicinal cannabis (MC) for the therapeutic management of specific indications November 2016
- pharmacoepidemiological data indicating potential benefit in epilepsy, nausea and vomiting, chronic pain, spasticity of MS, insomnia and “palliation”
- legislation allowed production and prescribing of MC for therapeutic and research purposes

Legalisation

- introduction was not underpinned by research evidence from clinical trials
- initial disjointed process of prescribing according to state jurisdiction
- July 2018, centralised national online portal for MC prescribing
- prescribing pathways: Authorised prescribing or Special Access Scheme
- progressive facilitation of prescribing process
- no systematic monitoring of efficacy, AEs or long-term effects

Medicinal Cannabis

Rise and rise*



Systematic review and meta-analysis of cannabinoids in palliative medicine

Mucke et al. J Cachexia, Sarcopenia and Muscle 2018

In cancer, no benefit for improving calorific intake, appetite, nausea/vomiting, decrease in pain or sleep

In HIV, superior in weight gain, appetite, but not nausea/vomiting

Cannabis in palliative care: a systematic review of current evidence

- **Doppen et al. JPSM 2022**
- **20 randomised , 32 non-randomised trials**
- **4786 patients (cancer, dementia, AIDS, spasticity)**
- **positive treatment effects for pain, N/V, appetite, sleep, fatigue**
- **quality of evidence low or very low**
- **no meta-analysis due to wide range of cannabis products and heterogeneity of outcomes**
- **no recommendations possible**

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REVIEW



Multinational Association of Supportive Care in Cancer (MASCC) guidelines: cannabis for psychological symptoms including insomnia, anxiety, and depression

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REVIEW



Multinational Association of Supportive Care in Cancer (MASCC) expert opinion/consensus guidance on the use of cannabinoids for gastrointestinal symptoms in patients with cancer

Bryony Alderman^{1,2} · David Hui³ · Sandip Mukhopadhyay⁴ · Carole Bouleuc⁵ · Amy A. Case^{6,7} · Koji Amano⁸ · Gregory B. Crawford^{9,10} · Giulia de Feo¹¹ · Andrea Sbrana¹² · Kimberson Tanco³ · Josephine To¹³ · Jessica Garsed¹⁴ · Mellar Davis¹⁵

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Medicinal Cannabis–Research program

STUDY PROTOCOL

Open Access

Oral medicinal cannabinoids to relieve symptom burden in the palliative care of patients with advanced cancer: a double-blind, placebo controlled, randomised clinical trial of efficacy and safety of cannabidiol (CBD)



Phillip Good^{1*} , Alison Haywood^{2,3}, Gauri Gogna⁴, Jennifer Martin^{5,6}, Patsy Yates^{7,8}, Ristan Greer⁹ and Janet Hardy¹⁰

Hardy et al. *Trials* (2020) 21:611
<https://doi.org/10.1186/s13063-020-04541-6>

Trials

JOURNAL OF PALLIATIVE MEDICINE
Volume XX, Number XX, 2019
Mary Ann Liebert, Inc.
DOI: 10.1089/jpm.2019.0540

Original Article

An Open-Label Pilot Study Testing the Feasibility of Assessing Total Symptom Burden in Trials of Cannabinoid Medications in Palliative Care

Phillip D. Good, MBBS, PhD,^{1–3} Ristan M. Greer, PhD,²
Georgina E. Huggett, RN,^{1,2} and Janet R. Hardy, BSc, MD^{1,2}

STUDY PROTOCOL

Open Access

Oral medicinal cannabinoids to relieve symptom burden in the palliative care of patients with advanced cancer: a double-blind, placebo-controlled, randomised clinical trial of efficacy and safety of 1:1 delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD)



Janet Hardy¹, Alison Haywood^{2,3}, Gauri Gogna⁴, Jennifer Martin^{5,6}, Patsy Yates^{7,8}, Ristan Greer³ and Phillip Good^{9*} 

Design

Interventions. Participant titrated CBD oil (100mg/ml) or matched placebo.

Main outcomes:

The primary outcome was ESAS total symptom distress score (TSDS) at day 14.

Response was defined as a decrease in TSDS by >6 from baseline to day 14.

Secondary outcome measures included: ESAS TSDS over time, physical and emotional ESAS sub-scores, individual symptom scores, patient determined effective dose, opioid use, Global Impression of Change, depression and anxiety, QoL and adverse events.



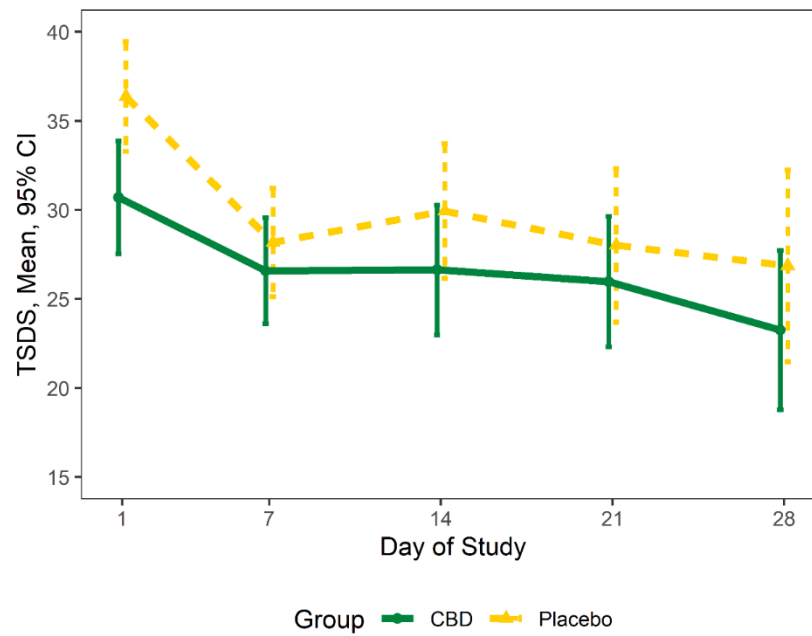
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MODIFIED EDMONTON SYMPTOM ASSESSMENT SYSTEM (m-ESAS-Can)

Please circle the number that best describes how you felt over the past 24hrs:

No pain	<u>0</u> 1 2 3 4 5 6 7 8 9 10	Worst possible pain
Not tired	<u>0</u> 1 2 3 4 5 6 7 8 9 10	Worst possible tiredness
Not nauseated	<u>0</u> 1 2 3 4 5 6 7 8 9 10	Worst possible nausea
No shortness of breath	<u>0</u> 1 2 3 4 5 6 7 8 9 10	Worst possible shortness of breath
Not drowsy	<u>0</u> 1 2 3 4 5 6 7 8 9 10	Worst possible drowsiness
Best appetite	<u>0</u> 1 2 3 4 5 6 7 8 9 10	Worst possible appetite
Not anxious	<u>0</u> 1 2 3 4 5 6 7 8 9 10	Worst possible anxiety
Not depressed	<u>0</u> 1 2 3 4 5 6 7 8 9 10	Worst possible depression
Best feeling of wellbeing	<u>0</u> 1 2 3 4 5 6 7 8 9 10	Worst possible wellbeing



Conclusion

What is already known:

- There is a strong public belief in the benefit of cannabinoids for a wide range of conditions including symptom control in cancer
- Multiple systematic reviews have highlighted the poor quality of studies assessing the benefit of medicinal cannabis and have failed to demonstrate meaningful benefit outside a few limited indications
- Cannabidiol (CBD) is one of the most common of the cannabinoids and is popular because of the perceived lack of psychotropic effect

What this study adds:

- CBD oil has no benefit over standard palliative care in relieving symptom burden in patients with advanced cancer
- CBD oil is well tolerated with minimal adverse events



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Talking MedCan



Most common reasons for wishing to take part

- **pain relief**
- **desire to get off opioids**
- **pressure from carers/relatives**
- **publicity/fear of losing out**
- **to help sleep, anxiety**
- **reassurance of approved product on trial**
- **cure for cancer**
- **altruism**
- **regular contact with research staff**

Most common barriers to recruitment

- wish to continue driving
- weekly visits (amendment post COVID)
- prior/recent use of cannabis
- performance status
- cost

Product registration

What is needed

- Efficacy
- Safety data
- High quality trials

Research Program

- MedCan-3 (CBD:THC 20:1)
- Sleep quality
- Anxiety/depression
- Carer perceptions
- “Happiness” scale
- Genomics
- Driving
- Inflammation
- Post trial use

Medicinal cannabis:

- remains an active area of research
- is very popular with consumers
- generally well tolerated
- apart from a few limited indications, it has been difficult to define an ideal product or indication for use
- unclear how cost subsidies can be justified at this stage
- ?role will be defined by the general public over time
- ?trial by social media

Teletrials

- **Refer to Mater**
- **Queensland Regional Clinical Trials Coordinating Centre (QRCCC)**
- **Local trials nurses**
- **MedCan 3 – THC/CBD 1:20 dose titration study**
- **28 days**
- **Primary outcome at 14 days**
- **Randomised, placebo controlled**



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Questions



