CANNABIDIOL FOR CANNABIS USE DISORDER

Will participants on cannabidiol reduce cannabis use compared to those on a placebo?

BACKGROUND

CANNABIDIOL (CBD)

- A non-psychoactive cannabinoid derived from *Cannabis Sativa* and *Cannabis Indica* plant (phytocannabinoid);
- Cannabinoids interact with the body's endocannabinoid system, and are vital in regulating mood, pain, inflammation, learning – i.e., physiological processes. CB_1 and CB_2. are primary cannabinoid receptors.

CANNABIS USE DISORDER (CUD)

- Problematic pattern of cannabis use causing significant clinical impairment or distress.
- It affects 9- 22% of cannabis users, with a higher risk among those who start in adolescence, using daily, or weekly, or combine cannabis with tobacco.

EPIDEMIOLOGY & HARMS

- Cannabis is the most widely used illicit drug worldwide
- In 2019, 11.7% of Australians aged ≥ 14, and 24% of Aboriginal and Torres Strait Island people aged ≥ 15, reported cannabis use in the past year; in 2021-22, cannabis was the third most common drug of concern people received treatment for in hospitals.
- Global estimate indicates that ~22.1 million people met the criteria for cannabis use disorder (CUD).
- In 2015/16 cannabis use in Australia resulted in a $4.5 billion societal cost, with harms across:

Mental Health | Physical Illness | Cognitive Impairment | Prenatal Exposure | Social harms

CANNABIDIOL & CUD

- Pharmacologically, CBD is a negative modulator of the CB_1 receptor – i.e., it lowers the binding ability of Tetrahydrocannabinol (THC) to CB_1 receptors, lowering THC's potency without blocking all CB_1 receptors.
- Clinical studies have suggested CBD plays a crucial role in the management of CUD, warranting further exploration in larger trials– i.e., this study!

STUDY DESIGN

This study is a double-blind, parallel group, Phase III Randomised Controlled Trial (RCT), summarised in Figure 1.

1. Recruitment
Via social media, posters, medical referrals, trial websites etc.

2. Initial Screening
Participants given PICF & pre-screened by Site-Coordinator (SC)

3. Medical Assessment
Formal assessment with Study Medical Officer (SMO); further investigations as required

4. Study Enrolment
Complete main study consent form, randomisation; and start Wk 1 D1

5A. Allocation to CBD
400 mg/day (4mL) of CBD

5B. Allocation to Placebo
4mL of Placebo

6. Study Intervention
Week 4, 7, 10, and 13 assessment completed by SMO and SC; counselling sessions as required

7. Study Follow-up
Week 25 activities with SMO and SC

Figure 1. **Study Overview**. Participants are screened via telephone following digital and traditional recruitment methods. Medical assessments are conducted to screen for eligibility. Successful participants (*n=250*) are randomised and allocated to Cannabidiol or Placebo (*n* =125/ condition); with an estimate of 20% of participants (*n* = 50) as Indigenous Australians. The 12-week study intervention will have five on-site visits every three weeks (±4 days), conducted with a Study Medical Officer (SMO) and Site Coordinator (SC).

STUDY MEASURES

HYPOTHESIS

In comparison to Placebo, CBD will lead to notable reductions in cannabis use, assessed through self-reported cannabis-free days and urinary THC-COOH levels in treatment-seeking patients with moderate-severe CUD.

Primary Outcome

- **Self-report cannabis use:**
  - Self-reported using the Timeline Follow back method
- **Biological cannabis use:**
  - Measured through urinary drug screening for THC and CBD-COOH (metabolites).

Secondary Outcome

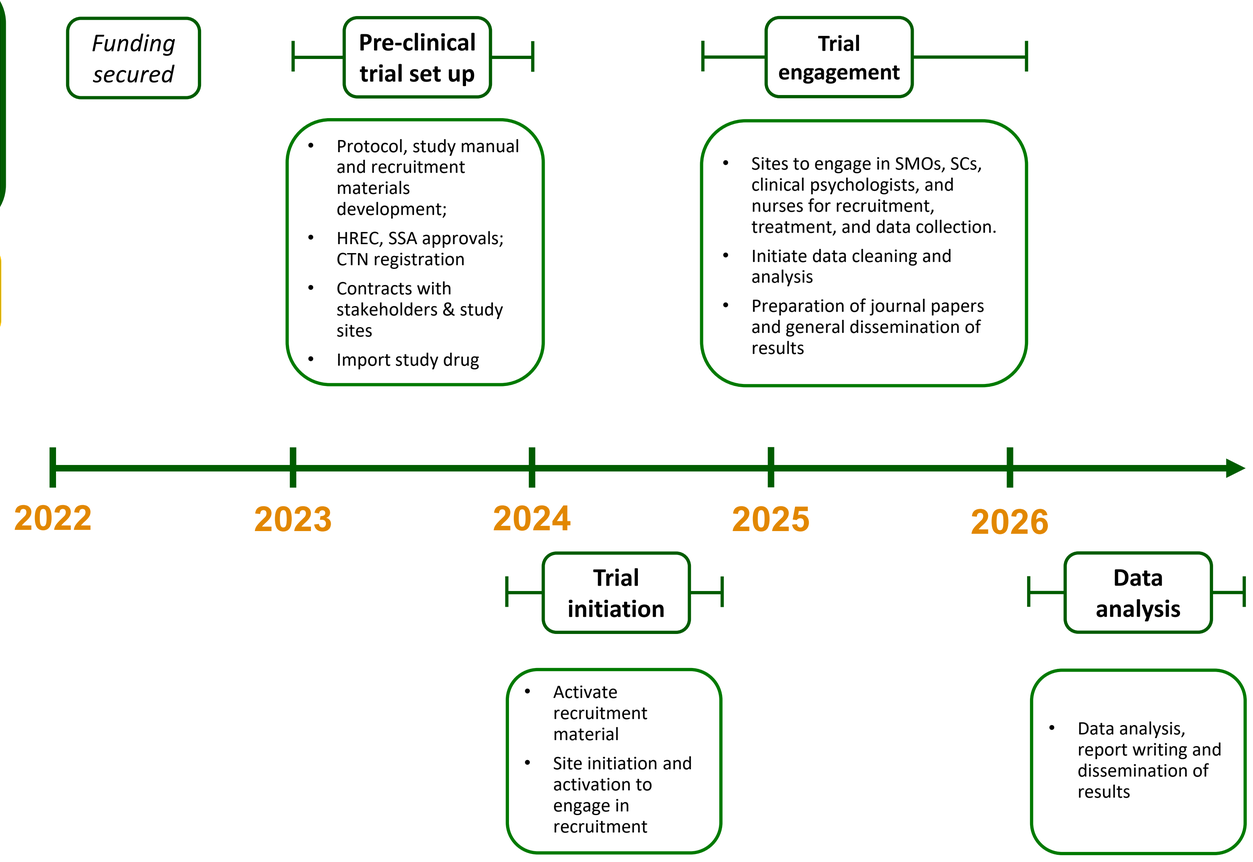
- **Cannabis associated measures**
  - Severity of CUD, withdrawals, cravings, quantity, related problems, motivation, abstinence
- **Health care**
  - Safety, quality of life, mental health state, treatment satisfaction, substance use
- **Cognitive function**
  - Cognitive tests

Aboriginal Focused Measures

- **Discrimination**: Modified everyday discrimination scale
- **Experience of treatment:** Semi-structured qualitative interviews

- Study drug provided by Jazz Pharmaceuticals Inc. (in-kind)
- Conducted across NSW (fives sites) and VIC (two sites)
- Four sessions of Cognitive Behavioural Therapy (CBT) based counselling
- 12-week post study follow-up
- Development of an Aboriginal Reference Group and a Consumer Advisory Group

TIMELINE & DISCUSSION



DISCUSSION

- Current treatments for CUD have modest outcomes. Current psychosocial treatments for CUD indicate that over 80% of patients relapse within 1-6 months of treatment. Pharmacological treatments are highly effective with other substance use disorders making CBD a promising candidate as a treatment for CUD due to its excellent safety profile, and potential efficacy for this indication.
- The anxiolytic, antipsychotic and neuroprotective effects of CBD may have added benefits by reversing many of the mental health and cognitive impairments seen with chronic cannabis use.

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CBD CUD Study

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