CANNABIDIOL YOUTH ANXIETY STUDY (CANCAN STUDY)

FREQUENTLY ASKED QUESTIONS

CLINICIAN INFORMATION

What does treatment resistant anxiety mean?

Anxiety disorders are among the most prevalent mental health conditions in young people, affecting 7% of adolescents in Australia. These include generalised anxiety disorder, social anxiety, panic disorder, specific phobia, agoraphobia, and separation anxiety disorder. Symptoms vary for different individuals, but can include feeling anxious, nervous, tense, or restless. People with an anxiety disorder may feel very sensitive to criticism or extremely self-conscious. They may worry about things that aren't likely to happen. These symptoms may cause them to become withdrawn or avoid difficult or new situations that make them anxious. They may have more difficulty than usual coping with work, school or relationships.

Current treatments for anxiety in young people include cognitive behavioural therapy and antidepressants. However, some young people do not respond well to these treatments. (2, 3).

A young person may be eligible to take part in this study if they meet DSM criteria for an anxiety disorder, and have not had clinically meaningful improvement in response to treatment as usual (TAU). TAU may include psychosocial therapy delivered by a mental health professional and/or antidepressant treatment. If after receiving treatment for at least two months the young person does not demonstrate a clinically meaningful improvement, they may be eligible for the trial.

For some people, symptoms of anxiety disorders can get worse without help. For others, symptoms may lessen or simply go away. Because of these varied outcomes it is important to be able to provide a range of effective treatments to young people.

What treatments are currently available for anxiety symptoms experienced by young people?

There are two main categories of evidence-based treatments available – pharmacological treatments (medicines) and psychological therapies such as cognitive behavioural therapy (CBT).

Why is Orygen running this trial?

Current treatments do not work for everyone, so Orygen is investigating a potential new treatment known as cannabidiol. Orygen's hope is that by testing potential new treatments we will be able to find effective treatments with limited side effects.

CANNABIDIOL

Is cannabidiol the same as cannabis or medical marijuana?

No. Cannabidiol is only one of many compounds found in the cannabis plant. Unlike other substances found in the cannabis plant (for example, tetrahydrocannabinol (THC)), cannabidiol does not make people 'high'.

Cannabidiol is extracted from the cannabis plant, purified and does not contain relevant quantities of THC.

Aren't there other drugs you can try? Why does it have to be cannabidiol?

Cannabidiol has been tested as a treatment for people with anxiety disorders and other illnesses such as epilepsy and psychotic disorders. Cannabidiol was found to reduce the severity of anxiety symptoms in young people and adults in several small studies, and it is important to test whether it is safe and effective in larger groups of young people.

Will the young people on the study get addicted to cannabidiol?

No. Unlike THC, cannabidiol is not addictive. In fact, it has been used to treat cannabis addiction in other research trials as it opposes some of the effects of THC.

None of the previous studies have indicated that cannabidiol may be addictive in young people or adults.

What amount of cannabidiol will you be giving participants?

Research participants will be randomly allocated to one of two groups:

- Group one will take 600mg–800mg daily of cannabidiol;
- Group two will take a placebo (no cannabidiol) each day for 12 weeks.

Orygen researchers decided on these doses based on previous studies testing cannabidiol in adult patients with psychosis, and studies testing cannabidiol in young people with anxiety and epilepsy.

How are you going to make sure participants don't take more than that?

Trial participants will receive only a certain number of cannabidiol capsules at each study visit, or as appropriate to prescribe for that individual. In addition, Orygen researchers will monitor the number of capsules taken as well as blood levels of cannabidiol.

Will participants know which group they're in?

No. Participants and researchers will not know which group each participant has been allocated to. Only the pharmacy will know this so they can provide the right medication. This means the results are less likely to be biased and the researchers can compare improvements within each group without making assumptions based on whether or not participants are taking CBD.

How will you know if the cannabidiol is working?

Researchers and clinicians will use a range of psychiatric measures, including a questionnaire, to evaluate the effectiveness of cannabidiol. These are well-established approaches that are used in clinical research to measure improvements in symptoms.

Will people on the study be smoking the cannabidiol?

No. The cannabidiol will be administered as a capsule and cannot be smoked or inhaled. Capsules are self-administered by the participant.

Where is Orygen getting the cannabidiol from?

The cannabidiol used in our study is a natural product extracted from cannabis plants and is distributed by a pharmaceutical company that is fully compliant with the quality and safety standards mandated in the industry.

Can someone continue using cannabidiol after the trial has concluded? If so, who will pay for it?

Cannabidiol can only be prescribed in Australia via a special access scheme and its cost is currently not subsidised by the Pharmaceutical Benefits Scheme. Trial participants who wish to access cannabidiol following the trial will need to cover the cost themselves. The research team encourages participants who are interested in continuing to take cannabidiol after the trial to speak to their GP.

CLINICAL TRIAL

What is a clinical trial?

Clinical trials are systematic research investigations where new treatments or other interventions are tested in patients under the strict surveillance of one or more ethics committees. This trial will be run under the guidance of a human ethics committee operated by the University of Melbourne.

How many people are going to be participating in the trial?

The research team is planning to enrol up to 180 participants in this trial.

How long will the trial go for?

Participants will take the study medicine (or placebo) for 12 weeks. In total, Orygen researchers expect the trial to run for about three years.

Trial preparations began in July 2022, with recruitment of participants from October 2024.

The trial will finish around October 2027.

Where is the trial being run?

Participants recruited from the community in metropolitan Melbourne and Perth.

The trial is being conducted at the following centres:

- Orygen Clinical Trials Unit in Parkville
- headspace Midland (Perth, Western Australia)
- headspace Osborne Park (Perth, Western Australia)
- headspace Joondalup (Perth, Western Australia)
- Youth Axis (Perth, Western Australia)
- UWA (Perth, Western Australia)
- headspace Craigieburn (Melbourne, Victoria)
- headspace Melton (Melbourne, Victoria)

- headspace Glenroy (Melbourne, Victoria)
- headspace Sunshine (Melbourne, Victoria)
- headspace Werribee (Melbourne, Victoria)

CLINICIANS AND TRIAL PARTICIPATION

How do clinicians refer clients to this trial?

To participate in this trial, eligible participants based in Melbourne or Perth can self-refer or be referred by their clinician.

A referral from the young person's regular GP will be required prior to starting the study treatment. If you have a client you believe would be appropriate for this trial, you can contact us directly on CANCANStudy@orygen.org.au.

What age does someone have to be to take part in the trial?

Young people aged between 12 and 25, inclusive, can participate in the study.

Aren't 12-year-olds too young to be having cannabidiol?

The age range of participants in this trial is similar to the age range of participants in other trials of cannabidiol (e.g., for epilepsy). It is important to know if this potential new treatment is effective for participants under the age of 18. Any participants aged under 18 will require the consent of their parent or guardian.

The client will be turning 26 soon, can they still be part of the trial?

Yes, if they are enrolled in the trial while still aged 25.

What happens if a participant begins the trial and decides they don't want to continue?

The study is voluntary, and all participants have the right to withdraw from the trial at any point. If a participant would like to withdraw, it is important for them to let the research assistant know to ensure the appropriate care can be provided.

What psychosocial support will a participant receive during the trial?

Participants will continue to receive treatment as usual with their current clinician. Participants who are not currently receiving psychosocial treatment can be connected with a mental health clinician through Orygen for the duration of the study treatment period.

How will risk be managed for participants who are no longer engaged with a mental health service or provider when follow-up interviews are completed?

Participants will be assessed for risk at all follow-up research time-points. Participants identified as being at-risk or in distress will be provided crisis numbers and encouraged to engage with their general practitioner and the appropriate mental health service.

What do I need to do as a clinician of a participant?

There is no extra work for clinicians. All appointments, medication and biological samples are organised by the research assistants. The trial medication will be prescribed by the study doctor who will monitor safety and any unexpected adverse events. Research assistants or the study doctor will liaise with you if there is any concern regarding risk to the participant. If you have any concerns regarding the trial participant, please contact the study team.

All enquiries about the trial should be forwarded to your local Research Assistant, or by emailing CANCANStudy@orygen.org.au.

CANCAN STUDY PARTICIPATION CRITERIA

INCLUSION AND EXCLUSION CRITERIA

Inclusion criteria

Eligible participants must:

- be aged 12–25 years, inclusive;
- be able to give informed consent (parent/guardian consent is required for those under 18 years);
- be fluent in English;
- have a diagnosis of a DSM-5 anxiety disorder (i.e., social anxiety disorder, panic disorder, separation anxiety disorder, specific phobia, agoraphobia, generalized anxiety disorder); and
- have anxiety symptoms and functional impairment despite receiving TAU for at least 2 months, indicated by a score of ≥10 on the OASIS, and a lack of clinically meaningful improvement (CGI-I score > 2).

Exclusion criteria

Participants are unable to participate in the study if:

- they have a prior sensitivity or allergy to CBD or any cannabis-derived product;
- they are having current treatment with anxiolytic medication e.g. benzodiazepines or beta blockers;
- they have been prescribed permitted psychotropic (e.g. antidepressant medication), and they have not been on a stable dose for a minimum of 4 weeks;
- they're pregnant, lactating or (if sexually active) not on effective contraception;
- clinical blood test findings might compromise participant safety or confound trial results;
- they have a history of DSM-5 schizophrenia spectrum, delusional, bipolar I disorder, or current substance/medication induced psychotic disorder
- they are experiencing an acute or unstable systemic medical disorder;
- they have a metabolic, endocrine or other physical illness, e.g. thyroid disease, with neuropsychiatric consequences which may compromise the safety of the participant or the conduct of the trial;

- they are experiencing acute suicidality (indicated by a score of 3 on QIDS -A17-C item 13) or severe depression (indicated by a score of >20 on the QIDS -A17-C);
- they are experiencing a severe disturbance, such that the person is unable to comply with either the requirements of informed consent or the treatment protocol.

DISCONTINUATION AND WITHDRAWAL

Voluntary discontinuation

Participants are free to withdraw their participation in the study at any time.

Participants who discontinue will be asked about the reason(s) for discontinuation and about the presence of any medical concerns. Any remaining medication will be returned and recorded.

Any medical concerns will be followed up until resolution, stabilisation or the participant is unable to be contacted.

Discontinuation criteria

A participant will be considered 'discontinued' from the study when they have stopped study medication. However, the participant may continue to complete other aspects as per the study schedule.

A participant will be discontinued when:

- they are not able to comply with study procedures, or develop exclusion criteria;
- an adverse event leads to a request for discontinuation by the participant or investigator;
- the randomisation code is broken;

Withdrawal criteria

A participant will be considered 'withdrawn' from the study in cases where all involvement is ceased.

Withdrawal from the trial will occur if consent is withdrawn either by the participant or their parent/guardian. Participants who withdraw from the study will be asked about the reason(s) for their withdrawal and about the presence of any medical concerns.

Medication will be ceased at the time of withdrawal from the study. Any remaining medication will be returned and recorded by the research assistant and pharmacy.

Participation in safety assessments with the study doctor will be offered to participants who withdraw from the study.