PLAIN LANGUAGE STATEMENT FORM

TO: The Participant

Plain Language Statement

Date: October 2022

Full Project Title: EndoCannED – Medicinal Cannabis for the reduction in emergency department presentations in people with endometriosis: a randomised, controlled feasibility study

Principal Researcher: Prof. Antonina Mikocka-Walus

Associate Researcher(s): Assoc. Prof. Mike Armour, Assoc. Prof. Subhadra Evans, Dr Marilla Druitt, Dr Jeremy Furyk, Prof. Jason Abbott, Prof. Jerome Sarris, Assoc. Prof. David Pate, Dr Cecilia Ng, Dr Allie Eathorne, Dr Karen Oldfield, Adj. Prof. Alex Semprini, Kat Stanley, Justin Sinclair, Susan Chesterman, Daniel Romano, Alex Martin

Dear Study Participant,

Thank you for considering participation in our study, which aims to better understand the feasibility, safety, and acceptability of two different medicinal cannabis interventions in people with endometriosis.

Why is this study important?

Endometriosis is a chronic inflammatory condition characterised by the presence of endometrial-like tissue outside of the uterus in the form of lesions. Endometriosis is incurable and its usual care – hormones and pain medications – has limited efficacy. Pain and poor quality of life are common in those with endometriosis, with greater than 50% reporting anxiety and/or depression. Due to poor pain control people with endometriosis often present to the emergency department (ED) with breakthrough pain.

Medicinal cannabis has received significant support in Australian surveys of the endometriosis population. In 2019, an Endometriosis Australia research priorities survey of 1,169 responses ranked medicinal cannabis the third highest research priority. In addition, since its use has been associated with reduced ED presentations in those with chronic pain, the usage of quality-controlled medicinal cannabis may reduce ED presentations in those with endometriosis and provide those affected by this condition with a new treatment option.

Since medicinal cannabis is available on prescription in Victoria, if the research shows it to be acceptable, safe, and effective, the guidelines for endometriosis treatment can be updated and the treatment offered more widely to Victorians with endometriosis.

Purpose

The purpose of this study is to determine the feasibility, safety, and acceptability of two different medicinal cannabis interventions in people with endometriosis. The study will also explore if the

tested interventions compared to placebo reduce the number of presentations to emergency department, or help with pelvic pain severity, fatigue, and improve quality of life.

Who can participate?
If you have a confirmed diagnosis of endometriosis, are aged 20 and over and live in Victoria, you may be eligible to participate.

How will this study be conducted?

You will be allocated randomly to one of the three study groups.

Group 1 will receive cannabidiol (CBD) oil (the dose will be individually titrated in the first 2 weeks of the trial).

Group 2 will receive CBD oil (the dose will be individually titrated in the first 2 weeks of the trial) + vapourised (i.e., inhaled) cannabis flower (10g of a moderate potency THC cannabis flower).

Group 3 will receive placebo oil (a colour-matched oil identical to the CBD oil provided to Group 1 and 2).

Each group will continue their usual care. All groups will receive the intervention for 12 weeks and will be followed up for a further 12 weeks. All participants will be asked to complete online questionnaires once recruited into the trial and informed consent provided, and throughout the intervention (active) and follow-up phases. An example question includes: 'How often, because of your endometriosis, have you been unable to go to social events because of the pain?'

You will be provided with links to the study questionnaires via your email. During the first week you will answer questions to establish your baseline scores across the different questionnaires being utilised. After this, over the next two weeks you will complete a log each evening, logging your daily dose, any adverse events (AEs), and a daily pelvic pain score. Once the two-week dose-finding period has passed, you will complete a log once per week which captures dosage (including use of vaporiser), pelvic pain severity, visits to the ED, AEs, and medication usage over the previous week. If any AEs are reported a member of the research team will follow up with a phone call within 72 working hours of receiving the diary. If an ED visit is reported, you will be asked to upload a copy of the electronic discharge summary or similar document which outlines the reason for the visit and outcome.

Risks of the study

This intervention has not been previously used in people with endometriosis and the present study will be the first to establish its safety in this population. In other groups, cannabis use has been associated with many adverse effects (AE). The most common include diarrhoea, changes in weight or appetite, tiredness, sedation, sleep disturbances, infection, and anaemia.

Cannabis is not safe for people with mental illness such as schizophrenia, psychosis, bipolar disorder, dissociative disorder, panic disorder, major depressive disorder, cannabis use disorder or obsessive- compulsive disorder. Cannabis is also not safe to people with major haematological, endocrine, cerebrovascular, cardiovascular, coronary, pulmonary, gastrointestinal, renal, or neurological disease. Cannabis should not be taken together with anticoagulant medication (e.g., warfarin, heparin, or supplements such as vitamin E, or *Gingko biloba*), immune modulators (e.g., cyclosporine), mood-altering drugs (e.g., lithium carbonate), monoamine oxidase inhibitors (e.g., selegiline, phenelzine), anti-arrhythmics (e.g., quinidine, disopyramide), hypoglycaemics (e.g., insulin), antiepileptics/anticonvulsants (e.g., phenytoin, valproic acid), anti-HIV drugs (e.g., saquinavir), antineoplastics (e.g., methotrexate), barbiturates, theophylline (1,3-dimethylxanthine), and cardiac glycosides (e.g., digoxin). Additionally, the present study will adhere to strict selection criteria to reduce the risk of AEs

due to cannabis use. Any AE will be closely monitored by the clinical investigators who are medical doctors – Dr Marilla Druitt, Dr Jeremy Furyk, Professor Jason Abbott, and Dr Karen Oldfield. Please do not hesitate to contact the Trial Manager via EndoCannED@deakin.edu.au to discuss any concerns regarding AEs.

Please note that if you are in the group taking CBD oil AND vapourised (inhaled) cannabis flower you will not be able to drive a car or operate heavy machinery for up to 4 months while participating in the study.

Further, answering questions about mental and physical health may make some people feel uncomfortable or emotional. If, at any stage of this study, you are concerned about the questions we ask, please do not hesitate to contact the study principal researcher: Professor Antonina Mikocka- Walus who is a Registered Psychologist. She can be contacted at mikocka@deakin.edu.au or via telephone +61 3 924 68575. You may also like to discuss your health with your GP or your endometriosis specialist.

Please remember your participation in this study is voluntary and you may withdraw from it at any time without any consequences. We will ask about your reasons for statistical purposes but answering this question is not compulsory. If you decide to withdraw, please let us know in writing if you would like us to withdraw all your data from our study.

Benefits of the study

Participation in this study may help you to manage symptoms of endometriosis. However, please be aware that since there are no previous similar studies of medicinal cannabis in endometriosis, there may be no direct benefit to you from participating in this study. While the intervention we are testing was found useful in other patient populations, there is no guarantee it will be effective in people with endometriosis. However, this project may benefit the wider endometriosis community. It is likely to provide necessary data to design better treatments for people with endometriosis.

How will your privacy and confidentiality be protected?

All information gathered in this study will be kept confidentially and stored securely following the Deakin University guidelines. All electronic information will be stored on secure servers at Deakin University. Identifiable information collected as part of this research project will be accessible only to the members of the research team. All stored survey information will be re-identifiable. This means that your name will not be recorded with the survey data. Instead, your survey information will be allocated and stored using a special code name. Only the research team will be able to match your name to your code name.

We will not share the identifiable data you will provide us with anyone outside this study's team.

Please be assured that only the researchers will have access to the raw data you provide. However, your data may be stored and used in other related projects for an extended period of time. This is normal University policy and in accordance with the Australian Code for the Responsible Conduct of Research. None of the data can be linked to you or reveal your identity in any way.

Monitoring of study conduct and declaration of interest

This project will be conducted by senior staff members of Deakin University in collaboration with Barwon Health, Western Sydney University, University of New South Wales, and Medical Research Institute of New Zealand.

The team will communicate monthly to oversee the study conduct and discuss any problems on an ongoing basis. We have no conflict of interest to report. This study is funded from the Victorian Medical Research Acceleration Fund (Award Number: TBA, approx. $100,000) and in-kind

contribution from Australian Natural Therapeutics Group PTY Ltd, EndoHelp Australia, and OnTracka Pty Limited.

Dissemination

We intend to publish the non-identifiable data resulting from the study in academic journals and present them at conferences. We may also share the raw data with other researchers and publishers (your name and identifying information will not be revealed) for an extended period of time. We also intend to provide a summary on the consumer organisations' websites and on request. If you are interested in receiving a summary via email please contact us via EndoCannED@deakin.edu.au.

Further information, queries or any problems

If you require further information or if you have any questions concerning this project, you can contact us on study email address or:

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Complaints

If you have any complaints about any aspect of the project, the way it is being conducted or any questions about your rights as a research participant, then you may contact:

> The Human Research Ethics Office, Deakin University, 221 Burwood Highway, Burwood, Victoria, 3125, tel. 03 9251 7129, research-ethics@deakin.edu.au

Please quote project number 2022: 342.