

# Cannabidiol for the treatment of patients at a high-risk of psychosis

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| <b>Submission date</b><br>01/08/2018   | <b>Recruitment status</b><br>No longer recruiting             | <input checked="" type="checkbox"/> Prospectively registered |
|  |   | <input type="checkbox"/> Protocol                            |
| <b>Registration date</b><br>31/08/2018 | <b>Overall study status</b><br>Completed                      | <input type="checkbox"/> Statistical analysis plan           |
|  |   | <input type="checkbox"/> Results                             |
| <b>Last Edited</b><br>21/02/2022       | <b>Condition category</b><br>Mental and Behavioural Disorders | <input type="checkbox"/> Individual participant data         |
|  |   | <input type="checkbox"/> Record updated in last year         |

## Plain English Summary

### Background and study aims

Psychotic disorders such as schizophrenia typically affect young people and rank as one of the most disabling conditions worldwide. They pose an enormous burden on those affected and their families. They also cost society a great deal. In England alone, the total cost to society for services caring for people with schizophrenia and from lost employment is estimated to be £11.8 billion per year. Estimates suggest that in England alone, around 15,763 people every year have early symptoms of psychosis. Around a third of such people who are clinically at high risk (CHR) of developing psychosis will do so over the next 3 years. CHR patients commonly experience low level anxiety and psychotic symptoms such as delusions (e.g. false beliefs) and hallucinations (e.g. hearing voices that are not there). Typically these experiences are short-lasting or less severe compared to when they develop frank psychosis. We would like to prevent young people from developing psychotic illnesses. However, this is not easy, as it is not possible to accurately predict which CHR person will later develop psychosis. Also, current treatments do not always work. The medications (such as antipsychotic drugs) that we have available were originally developed for those with frank psychosis, and only have a modest benefit and are not tolerated very well. As treatments have to be offered to all CHR patients and not just those who will later develop frank psychosis, this also raises ethical concerns. Hence, at the moment, most CHR patients typically receive practical help and support (e.g. for housing or vocational support) and help from clinicians to address current issues.

Cannabidiol (CBD), a naturally available chemical found in the extract of cannabis plant, has emerged as a promising candidate as it displays anti-anxiety and anti-psychotic like properties in animals and humans. It has also been tolerated very well in human studies. We have recently tested this in a small number of CHR patients by giving them a 600 mg capsule of CBD daily for a short period (3 weeks) and comparing it with a group of CHR patients who were given an inactive drug. Results from these small studies suggest that CBD may be useful in treating symptoms in CHR patients. CBD was also safe and tolerated well by CHR patients. However, we do not know whether CBD treatment will actually be useful in providing symptom relief in CHR patients. A large clinical trial comparing CBD to placebo is needed to test this. Therefore, we aim to test whether CBD treatment will actually be useful in providing symptom relief in CHR patients in a large clinical trial.

### Who can participate?

People aged 18-35 who have a diagnosis of a clinical high-risk state for psychosis with 'attenuated psychotic symptoms'

### What does the study involve?

Patients will be randomly allocated to receive one of two treatments. Half of them will receive the same dose of CBD (600 mg once a day) given in capsule form and the other half will receive placebo capsule. In this study, patients will receive the treatment for 6 months. Neither the researchers nor patients will know what they have been treated with during the study. At the end of treatment, we will compare whether those who received CBD were significantly better off in terms of the symptoms that they were experiencing before they started treatment compared to those who received placebo. We will also study a subgroup of people (50 of those receiving CBD and 50 of those receiving placebo) to study brain chemistry and function using brain scanning (MRI scanners) to understand how CBD may work.

### What are the possible benefits and risks of participating?

Patients taking part in the study may or may not receive any benefits from taking CBD as part of the study. CBD treatment might improve some of the psychological problems that patients may be experiencing. However, this is by no means certain, which is why we are conducting this study. Previous research has shown that the effects of CBD are very subtle. Apart from some mild sleepiness, mild diarrhea and nausea no adverse effects have been reported. Nevertheless, any unpleasant effects associated with taking part in the trial will be recorded throughout the study. The MRI scan procedure that will be employed is painless and safe and there are no known health risks. The MRI scanner makes loud noises while it is operating and participants will provide participants with headphones or earplugs to reduce the noise to safe levels. Some people find that being in an MRI scanner makes them feel anxious and/or claustrophobic, even if they have not experienced claustrophobia before. A member of staff will be in constant contact with participants via an intercom, and if they feel uncomfortable in any way the scanning can be stopped.

Further, the information we obtain from this study may help us to treat patients with mental health problems more effectively in the future.

### Where is the study run from?

Institute of Psychiatry, Psychology & Neuroscience of Kings College London (UK)

### When is the study starting and how long is it expected to run for?

July 2017 to May 2023

### Who is funding the study?

National Institute for Health Research Efficacy and Mechanism Evaluation Programme (EME) (UK)

### Who is the main contact?

Dr Sagnik Bhattacharyya  
sagnik.2.bhattacharyya@kcl.ac.uk

## Contact information

### Type(s)

Public

### Contact name

Dr Sagnik Bhattacharyya

### **Contact details**

Department of Psychosis Studies  
Institute of Psychiatry, Psychology & Neuroscience, KCL  
16 De Crespigny Park  
London  
United Kingdom  
SE5 8AF  
+44 (0)2078480002  
sagnik.2.bhattacharyya@kcl.ac.uk

## **Additional identifiers**

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

CANTOP-RCT

## **Study information**

### **Scientific Title**

CANnabidiol as a Treatment fOr clinical high-risk state Psychosis - a Randomised Clinical Trial (CANTOP-RCT)

### **Acronym**

CANTOP-RCT

### **Study hypothesis**

Efficacy/tolerability hypotheses:

1. CBD treatment will reduce the severity of attenuated psychotic symptoms in CHR patients as measured using established criteria compared to placebo
2. Greater proportion of patients treated with CBD will not meet the criteria for 'attenuated psychosis syndrome' compared to placebo
3. CBD will reduce distress associated with attenuated psychotic symptoms in CHR patients as measured using established criteria compared to placebo
4. CBD will reduce the severity of anxiety symptoms in CHR patients as measured using established rating scales compared to placebo
5. CBD will improve social and role functioning in CHR patients as measured using established rating scales compared to placebo
6. CBD will not be associated with greater incidence of side-effects compared to placebo

Mechanistic hypotheses:

7. CBD will modulate brain activation in the medial temporal cortex and basal ganglia as measured using fMRI while performing verbal paired memory and emotional (fear) processing tasks in CHR patients compared to placebo

8. CBD will modulate brain activation in the medial temporal cortex and basal ganglia as measured using arterial spin labeling in CHR patients compared to placebo
9. Cannabidiol will attenuate glutamate levels in the hippocampus as measured using proton magnetic resonance spectroscopy in CHR patients compared to placebo

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

Ethics approval pending with intention to submit by November 2018

**Study design**

Interventional pragmatic randomised placebo-controlled trial

**Primary study design**

Interventional

**Secondary study design**

Randomised controlled trial

**Study setting(s)**

Community

**Study type(s)**

Treatment

**Participant information sheet**

No participant information sheet available

**Condition**

Clinical high-risk for psychosis (CHR)

**Interventions**

Participants will be randomised into either the intervention or control group using block randomisation. Randomisation will be double-blind and stratified by site.

Participants both groups will receive treatment as usual (TAU), which is the standard clinical care provided to CHR psychosis patients in NHS early intervention services.

The intervention group will receive TAU and a single daily dose of cannabidiol (CBD) in capsule form for 6 months.

The control group will receive TAU and a placebo capsule to take daily for 6 months.

Both CBD and the placebo will be given as matched capsules.

Patients will be followed up for a period of 6 months.

**Intervention Type**

Drug

**Phase**

Phase II

**Drug/device/biological/vaccine name(s)**

Cannabidiol (CBD)

**Primary outcome measure**

Change in the severity of psychotic symptoms, assessed using the Comprehensive Assessment of At-Risk Mental States (CAARMS) questionnaire at the baseline and at the end of the study (day 182)

**Secondary outcome measures**

The following will be assessed at the baseline and at the end of the study (day 182):

1. Changes in the distress associated with psychotic symptoms, assessed using the Comprehensive Assessment of At-Risk Mental States (CAARMS) questionnaire
2. Changes in the severity of anxiety symptoms assessed using the Hospital Anxiety and Depression Scale (HADS) and in the level of global functioning (assessed using the social and role functioning scale)
3. Clinical remission, as defined as no longer meeting the criteria for a diagnosis of clinical high-risk: attenuated psychosis syndrome using the CAARMS questionnaire

**Overall study start date**

12/07/2017

**Overall study end date**

31/05/2023

**Eligibility****Participant inclusion criteria**

1. Aged 18-35
2. Diagnosed with a clinical high-risk state for psychosis (CHR)
3. 'Attenuated psychotic symptoms' sub-group (CHR-APS) as defined using the CAARMS (Comprehensive Assessment of At-Risk Mental States) criteria

**Participant type(s)**

Patient

**Age group**

Adult

**Lower age limit**

18 Years

**Upper age limit**

35 Years

**Sex**

Both

**Target number of participants**

300

**Participant exclusion criteria**

1. History of a previous psychotic or manic episode lasting 7 days or more
2. Neurological disorders (e.g. epilepsy) or severe intercurrent illness
3. Current treatment with psychotropic medication or previous treatment with antipsychotic medication for more than 7 days
4. IQ of less than 70
5. Females who are pregnant, lactating or not using contraception

**Recruitment start date**

01/09/2022

**Recruitment end date**

30/09/2022

## **Locations**

**Countries of recruitment**

England

United Kingdom

**Study participating centre**

**Institute of Psychiatry, Psychology & Neuroscience (IoPPN), KCL**

London

United Kingdom

SE5 8AF

**Study participating centre**

**University of Manchester**

Manchester

United Kingdom

M13 9PL

**Study participating centre**

**University of Birmingham**

United Kingdom

B4 7BD

**Study participating centre**

**University of Newcastle**

United Kingdom

NE1 7RU

**Study participating centre**

Cambridgeshire & Peterborough NHS Foundation trust/ University of Cambridge  
United Kingdom  
CB4 1PR

## Sponsor information

**Organisation**

King's College London and South London and Maudsley NHS Foundation Trust

**Sponsor details**

16 De Crespigny Park  
London  
England  
United Kingdom  
SE5 8AF

**Sponsor type**

Hospital/treatment centre

**ROR**

<https://ror.org/015803449>

## Funder(s)

**Funder type**

Not defined

**Funder Name**

Efficacy and Mechanism Evaluation Programme

**Alternative Name(s)**

NIHR Efficacy and Mechanism Evaluation Programme, EME

**Funding Body Type**

Government organisation

**Funding Body Subtype**

National government

**Location**

United Kingdom

# Results and Publications

## Publication and dissemination plan

Manuscripts from the study will be submitted for publication in peer-reviewed high impact journals and published in brief format on the IoPPN website. Dissemination of these findings to other professionals in the field will also be facilitated through existing close links with clinical services, some of which in turn have extensive links with organisations for young people (schools, universities, hostels, etc.). Press releases on the findings will be delivered to encourage public feedback/involvement and links to published manuscripts will be disseminated through the IoPPN Press Office, harnessing existing links of the Investigators with media outlets. Arrangements will be also be made to disseminate these results to the wider user community through links with websites of charities such as MIND and RETHINK that are accessed by service-users.

## Intention to publish date

## Individual participant data (IPD) sharing plan

The data sharing plans for the current study are unknown and will be made available at a later date

## IPD sharing plan summary

Not provided at time of registration