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A trial to investigate if psilocybin therapy is effective in improving outcomes for people with opioid use disorder

Submission date
30/11/2024

Recruitment status
Recruiting

Registration date
24/09/2025

Overall study status
Ongoing

Last Edited
27/02/2026

Condition category
Mental and Behavioural Disorders

[X] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Opioid addiction is a major public health challenge with rising death rates and over 140,000 people seeking treatment in the UK in 2023. Current treatments are limited, and many people relapse within a year after stopping using opioids. Research suggests that psilocybin (a compound in magic mushrooms) might be beneficial in treating addictions like alcohol and smoking. This study will investigate if psilocybin combined with psychological support ('psilocybin therapy') can be helpful in treating people recovering from opioid addiction and how it might work.

Who can participate?
Opioid-dependent individuals who have recently completed detoxification from all opioids, both illicit (e.g. heroin or opium) and prescribed opioid substitution therapy (e.g. methadone or buprenorphine). The study includes people aged 18-64 years of all sexes.

What does the study involve?
Stage 1 of the study will test three doses of psilocybin, and the best dose will be chosen for further testing in stage 2. Eligible participants will attend the Hammersmith Hospital clinic to receive a single dose of psilocybin, with guided support from a therapist/trained individual. Psychological support will also be provided at regular intervals before and for up to 3 months after receiving the psilocybin. Participants will be closely monitored throughout to understand the psychological effects and tolerability. At each study visit, the researchers will measure opioid use, cravings, mental health and well-being using questionnaires and interviews. To understand brain effects, they will perform brain MRI scans before, and 7 days after the psilocybin. They will also contact participants after 6 months to monitor progress.
The researchers are engaging individuals with lived experience of opioid addiction throughout the research process and within our team. This includes workshops for feedback on our research plan and study documents. Continuous feedback will help shape the study and ensure effective recruitment and communication of results.
Results will be shared with scientists, doctors, policymakers, and the public through scientific reports, policy documents, media, and healthcare discussions.

What are the possible benefits and risks of participating?
Taking part in this study may involve several potential disadvantages. Participation requires an increased number of visits to the study centre, which could be time-consuming. Some individuals may experience short-term anxiety related to taking psilocybin, the study drug. The psychological support sessions and clinical interviews will explore sensitive topics, such as the individual's upbringing, family life, substance use, and recovery plans, which may bring up challenging or upsetting feelings. Additionally, during the MRI cue-reactivity task, participants will be exposed to images or videos related to drug use to help researchers understand brain responses to such triggers. While this is an essential part of the study, it may evoke emotional discomfort or cravings. The study team has taken steps to ensure that participants receive appropriate support, including post-task discussions with therapists/trained individuals and access to the study medical team for ongoing assistance. While uncovering unknown medical conditions via the MRI scan is unlikely, if any are identified participants will be informed of any findings and this could potentially affect future medical insurance.
There are several potential advantages to participating in this study. Participants will have the unique opportunity to be part of one of the first clinical trials of psilocybin therapy in modern research. While we cannot guarantee therapeutic benefits, psilocybin therapy may be helpful for some individuals. As part of the study, participants will receive psychological support, which may provide psychological insights and emotional benefits. Furthermore, participants will contribute to advancing scientific understanding of how psilocybin therapy works and its potential as a treatment for opioid use disorder. The knowledge gained from this study could lead to improved treatments for others with opioid dependency and other addictions.

Where is the study run from?
Imperial College London (UK)

When is the study starting and how long is it expected to run for?
July 2024 to June 2027

Who is funding the study?
National Institute for Health and Care Research (NIHR) (UK) with Filament Health providing in-kind donation of drug

Who is the main contact?
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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
1010010

Protocol serial number
175297

Study information

Scientific Title
PsilOpioid: a proof of concept randomised controlled trial to investigate psilocybin therapy and brain reward mechanisms in opioid use disorder (OUD)

Acronym
PsilOpioid

Study objectives
Primary objective:
The overall objective is to conduct a Phase IIa trial to assess the feasibility, tolerability, proof-of-concept efficacy, and brain mechanisms of psilocybin therapy (PT) in a randomised, controlled and parallel groups design. The primary objective is to determine whether PT demonstrates superiority in reducing the return to opioid use, as compared to low dose, in people who have recently completed detox from all opioids. This includes detox from both illicit (e.g. heroin or opium) and prescribed opioid substitution therapy (e.g. methadone or buprenorphine).

Secondary objectives:
To assess changes in participants' substance use, health and wellbeing in the PT arm relative to low dose. Specifically, to determine:

1. Whether there are reductions in the frequency, severity, amount and/or duration of opioid use
2. Whether there are indications of improvement in clinical markers including self-reported measures of craving, quality of life, mood, recovery capital, social functioning and other substance use.
3. Whether psychedelic effects occur in response to the test doses of psilocybin in this population, and whether this is associated with clinical outcome(s).

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 23/04/2025, London - Fulham Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)207 104 8340; fulham.rec@hra.nhs.uk), ref: 26/LO/0001

Study design
Double-blind randomized controlled parallel-group trial

Primary study design
Interventional

Study type(s)
Other

Health condition(s) or problem(s) studied
Opioid use disorder

Interventions
This is a two-arm, single-dose, double-blind, randomised, controlled, Phase IIa trial investigating psilocybin therapy in participants with opioid use disorder (OUD) in early abstinence. Participants will be randomised to receive either psilocybin (intervention arm) or low-dose psilocybin (control arm) in two trial stages.

There are two trial stages:
Stage 1 (Ascending Dose-Finding Phase): Participants will be randomised to receive one of three psilocybin doses or low-dose psilocybin in an ascending dose design. This stage will identify the optimal dose for Stage 2.
Stage 2 (Full RCT): This will further test the dose selected from Stage 1, relative to low dose psilocybin.

Participants in the intervention arm and the control arm will receive a standardised psilocybin therapy package, including preparation, guided dosing sessions and post-session psychological integration. There will also be pre-dose and post-dose fMRI assessments.

Randomisation Process:
The randomisation list will be generated by an independent researcher. The trial will be double-blind, with both participants and investigators blinded to group allocation.

Follow-Up:
All participants in both arms will be followed up to 12 weeks post-dosing. There will be an out-of-trial follow-up at 6 months post-dosing.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Psilocybin (PEX010)

Primary outcome(s)
The primary endpoint is time to first opioid use within 3 months following psilocybin administration. This will be measured using the self-report modified Time Line Follow Back (mTLFB) between Investigational Medicinal Product (IMP) dosing and 3 months (12 weeks).

Key secondary outcome(s))
The frequency, amount, and/or duration of opioid use will be characterised using TLFB and summarised by dose. Specifically, the following measures will be used:
1. Total number of days using opioids between IMP dosing and 12-week primary endpoint summarised by type of opioid (either illicit opioid or prescribed OST).
2. Incidence of return to OST between IMP dosing and 12 weeks, where a return to OST is defined as any use of prescribed OST.
3. Number of lapses between IMP dosing and 12 weeks, where a lapse is defined as any use of illicit/street opioids (not including prescribed OST).
4. Number of relapses between IMP dosing and 12 weeks, where a relapse is defined as use of illicit/street opioids for 3 or more consecutive days (not including prescribed OST).
5. Average duration of lapse/relapse measured as number of consecutive days of illicit opioid use between IMP dosing and the 12-week primary endpoint
6. % of opioid free weeks, where an opioid-free week is defined as 7 consecutive days without the use of any opioid (illicit or prescribed OST) as measured using TLFB.

Improvements in health and wellbeing will be assessed using the following, summarised by dose:
1. Substance Use Recovery Evaluator (SURE) total score between baseline (Day -1) and the primary endpoint (12 weeks)
2. Craving, assessed using Opioid Craving Scale at baseline (day -1) and the 12-week primary endpoint
(Updated 21/10/2025, previously: Craving, assessed using Minnesota Craving Scale at baseline (day -1) and the 12-week primary endpoint)
3. Patient impression, assessed using Patient Reported Outcomes (PRO-I / S) collected at baseline (day -1) and the 12-week primary endpoint
4. Mental wellbeing (over last 2 weeks) using the Warwick-Edinburgh Mental Wellbeing Scale (WEMWBS) between baseline (Day -1), and 12-week primary endpoint
5. Assessment of Recovery Capital (ARC) total score between baseline (Day -1), and the primary endpoint at 12 weeks (Updated 02/02/2026, previously: Drug Abstinence Self Efficacy Scales (DASES) total score between baseline (Day -1), and the primary endpoint at 12 weeks)
6. Watts Connectedness Scale (WCS) total score between baseline (Day -1), and the primary endpoint at 12 weeks
7. Brief Experiential Avoidance Questionnaire (BEAQ) total score between Day -1 and the primary endpoint at 12 weeks

Acute psychedelic effects will be assessed using the following scales collected on Day 0, summarised by dose:

1. Mystical Experience Questionnaire (MEQ) score
2. Emotional Breakthrough Inventory (EBI) score

Completion date
30/06/2027

Eligibility

Key inclusion criteria
1. Current opioid use disorder of moderate to severe severity as diagnosed by an appropriate medical professional using DSM-5 diagnostic criteria
2. Within 3 months of detoxification or cessation from using opioids
3. Previously dependent on heroin or other illicit street opioids
4. Aged 18-64 years
5. Willing and able to comply with the requirements of the study
6. Able to read, comprehend and record information written in English
7. Capable of giving written informed consent, which includes compliance with the requirements and restrictions listed in the consent form
8. Be under the care of a primary care provider
9. People of childbearing potential and fertile males must be willing to use an adequate method of contraception from the time of enrolment until 28 days after dosing of the study drug
10. Willing to provide consent for authorised individuals to access their Summary Care Record and/or medical records to support the process of assessing eligibility

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
64 years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Current or previously diagnosed psychotic disorder or bipolar disorder I.
2. Immediate family member with a diagnosed psychotic disorder.
3. History of suicide attempts requiring hospital admissions or any suicidal ideation with intent within the past 6 months indicated by an answer “yes” to question 4 or 5 in the Columbia Suicide

Severity Rating Scale (C-SSRS) at screening, as well as clinician judgement.
4. Emotionally unstable personality, or other psychiatric problem that the screening clinician feels may jeopardise the therapeutic alliance and/or safe exposure to psilocybin.
5. Current ongoing moderate to severe (DSM-5) substance use disorder (including alcohol but excluding opioid, nicotine and cannabis). Lifetime history of dependence will be allowed given very high incidence of comorbidity.
6. Positive breath alcohol at screening visit, or at Day -1 or Day 0 (i.e. BAC above 0.08%). If positive on one of these visits, the visit may be rescheduled, at the discretion of the research team (updated 27/02/2026, previously: Positive breath alcohol at screening visit, or at Day -1 or Day 0 (i.e. BAC above 0.08%). If positive at screening, the screening may be rescheduled, at the discretion of the research team).
7. Positive urine drug screen for opioids on Day -1 or Day 0. If a urine drug screen is positive on one of these visits, the session may be rescheduled, at the discretion of the research team.
8. Psychedelic use in the past 6 months, at the discretion of the research team.
9. Clinically significant co-morbidities that would interfere with participant safety during the study, or with the integrity of the results such as current cardiac problems (e.g., ischemic heart disease, conduction defects, acute coronary syndrome or angina) or a clinically significant neurological condition (e.g. epilepsy, head injury) that in the opinion of the investigators, contraindicates their participation. Untreated hypertension – i.e., systolic blood pressure over 140, diastolic blood pressure over 90.
10. Tachycardia (heart rate >100 bpm)
11. Clinically significant abnormal biochemistry or haematological results on screening (e.g. hepatic or renal failure). Blood tests or other diagnostic tests will be undertaken, where it is deemed clinically necessary e.g., if a participant has a history of kidney/hepatic impairment that requires confirmation of current status. These can occur at the request of the clinical service or via the participant's GP, with their consent.
12. Clinically significant abnormality on ECG such that the QT measurement is not suitable (e.g., poorly defined termination of the T-wave) and/or presents other abnormalities which, in the opinion of the study physician, represent risk. If a participant has a QT interval corrected using Fridericia's formula (QTcF) value >440 ms for males and >470 ms for females, an exclusion decision will be made based on triplicate (3) ECG tracings obtained at least 1 minute apart. An average value for these 3 measurements will be used to determine if the participant has met the QTcF stopping criteria of >440 ms for males and >470 ms for females.
13. Current contraindications for MRI (e.g., claustrophobia, pacemaker, metal implants).
14. Known allergy or hypersensitivity to psilocybin.
15. Positive pregnancy test at screening or Day -1 or Day 0.
16. Currently breastfeeding.
17. Currently prescribed or using a medication, which might have an adverse interaction with the study drug e.g. 5HT2A agonists, mirtazapine, trazodone, analgesics that have serotonergic effects (tramadol), mood stabilisers (e.g., lithium, carbamazepine), MAOIs, antipsychotics with significant 5-HT2A receptor antagonist actions (risperidone, olanzapine and quetiapine), anticonvulsants, antihistamines with 5HT2A agonist activations (e.g., cyproheptadine).
18. Currently prescribed or using alcohol dehydrogenase, inhibitors, aldehyde dehydrogenase inhibitors, and UDG modulators.
19. Body Mass Index (BMI) <16 kg/m^2
20. Unable to endure the physical demands of dosing session (i.e., attend centre and remain in research facility for an extended period of time).
21. Any other reason judged by the study clinician as likely to impact on the ability of the participant to safely complete the trial.
22. Participant is in active withdrawal on Day –1 or Day 0, as assessed by the Clinical Opiate Withdrawal Scale. Active withdrawal on Day +7 may result in either rescheduling or exclusion from the MRI scan, at the discretion of the research team.

23. Intoxication on any study visits, as assessed by:
23.1. Difficulty in walking, the slurring of speech
23.2. Difficulty concentrating or drowsiness
23.3. The participant volunteers this information directly

N.B. This intoxication exclusion criteria would exclude a subject from that study day only and not the whole study, at the discretion of the research team.

Date of first enrolment
13/11/2025

Date of final enrolment
06/01/2027

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
NIHR Imperial Clinical Research Facility
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Sponsor information

Organisation
Imperial College London

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
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Funder Name
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Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

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National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Data sharing statement to be made available at a later date