

Psychedelic assisted therapy for Opioid Use Disorder – PATH-OUD trial

Frequently Asked Questions (clinician version)

What is the PATH-OUD study about?

This trial will examine whether psilocybin, administered as part of Psychedelic-Assisted Therapy, can improve clinical outcomes and neurocognitive functioning in individuals with OUD. The study also aims to identify cognitive and brain-based markers that predict treatment response. The findings will inform future approaches to OUD treatment and contribute to the growing evidence base for psychedelic-assisted therapy in Australia.

Who is eligible to participate?

We are exploring if patients who are on MATOD (methadone or buprenorphine), and who are also continuing to use non-prescribed opioids (on six or more days per month), might find benefit from Psilocybin-Assisted Therapy.

Inclusion and Exclusion criteria can be found at the end of this document.

What is Psychedelic Assisted Therapy (PAT)?

Psychedelic-assisted therapy is a form of treatment that combines controlled, clinically supervised use of psychedelic medicines with structured psychotherapy to help alleviate conditions such as depression, PTSD, and anxiety. There is emerging evidence for the use of PAT in treating addictions, including opioid use disorder. Not everyone responds to PAT, but for those who do, results are often seen in a much shorter time than therapy alone.

Two PAT-trained therapists work with the patient across 2 preparation sessions, during which the patient develops familiarity with the therapists, discuss what their intentions for the treatment are, and set expectations for the psychedelic journey.

During the Psilocybin dosing session, participants will be randomised to receive either a 30mg or 1mg dose of Psilocybin. The Psilocybin dosing session takes place across 6-8 hours, and the same two therapists sit with the patient, providing safety and guiding them in their experience as needed. During the Psilocybin dosing session, participants will be randomised to receive either a 30mg or 1mg dose of Psilocybin.

Two to three integration sessions take place after the dosing session, which allow the patient to consolidate and integrate the lessons drawn from their psilocybin journey.

There is plenty of information online about PAT, however the [Huberman Lab Podcast](#) has an accessible and evidence-based video about the subject.

What are the risks associated with Psilocybin-Assisted Therapy?

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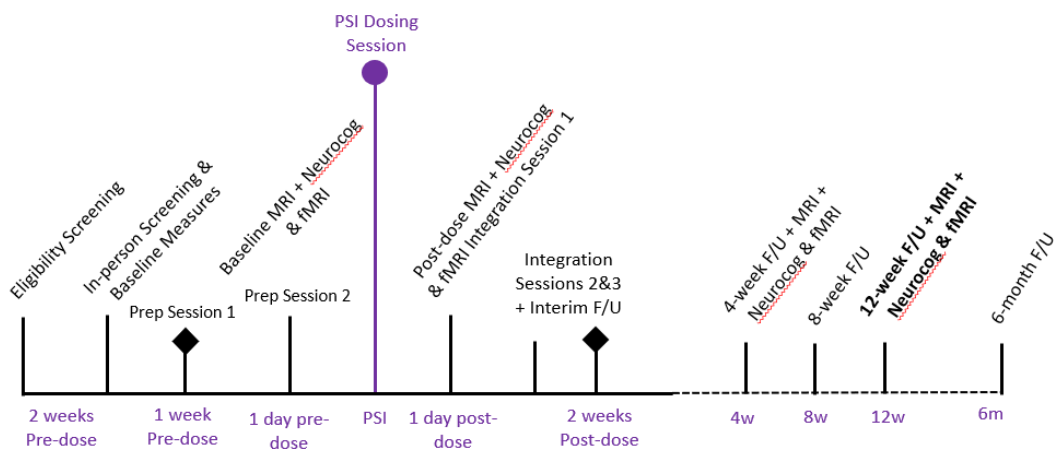
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PAT treatment is generally very low risk and in Australia there have been no reported adverse effects in two years of treatment. However, psychedelics come with a risk of increased anxiety and emotional dysregulation which is usually transient and managed by trained therapists. Hallucinogen Persisting Perception Disorder (HPPD), a rare condition where an individual has been exposed to a psychedelic substance continues to experience long term perceptual distortions after cessation of the psychedelic but the risk of HPPD after psilocybin administered in controlled settings is very low (Leistenschneider et al., 2024)¹.

For how long does the study run?

Participation in the study will take place across approximately six months, with the majority of patient involvement occurring in the first FOUR weeks. See the timeline below.

In addition to the PAT, participants will be asked – before and after the dosing session - to complete a series of well-validated surveys which measure aspects of their mental health and wellbeing. FOUR MRI scans will also take place – one prior to the dosing session, and three in the period after the dosing session. Tasks will be completed during the scan, and a set of validated neurocognitive activities will be run on the same days.



How do I refer one of my patients to the study?

If you have a patient that might be suitable for the study, they can be sent the study link below which will take them directly to the eligibility survey.

<https://redcap.helix.monash.edu/surveys/?s=DNDKWJFRPTD7RL8P>

You can also provide them with the participant information flyer for the study which accompanies this FAQ, as it contains a QR code which will link them to the eligibility survey.

¹ Leistenschneider, G., Majić, T., Reiche, S. *et al.* Neuropsychological profiles of patients suffering from hallucinogen persisting perception disorder (HPPD): A comparative analysis with psychedelic-using and non-using controls. *Sci Rep* **14**, 32159 (2024). <https://doi.org/10.1038/s41598-024-82216-x>

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If your patient consents to their information being passed on to the study team, you can send us their contact information at Path-OUD@monash.edu and the research team will get in touch with them.

Why do participants need to be on MATOD to be involved in this study?

There is growing evidence for the effectiveness of PAT in assisting individuals living with Substance Use Disorder, in particular nicotine and alcohol. This is a new field of research, and our trial is the first in Australia (there are similar trials running in other countries) to explore the potential for PAT who are living with Opioid Use Disorder.

Given the well-understood risks associated with using non-prescribed opioids on top of methadone or buprenorphine, a key inclusion criterion for study involvement is that the participant is able to provide the study investigators with consent to contact their MATOD prescriber.

Will I be notified if one of my patients is involved in this study? What do I need to do?

Once an individual has successfully completed the screening process and is deemed eligible for participation in the Path-OUD study, we will endeavour to contact their GP or pharmacotherapy prescriber to inform them of their participation.

Eligible participants will be asked to consent for the research team to obtain information about MATOD adherence from their pharmacist.

We assume that participants will continue on their MATOD upon return to their doctor, however if they change their dose drastically or change their pharmacotherapy medication, it may be necessary to wait until they are stabilised before engaging in Psychedelic-Assist Therapy. If you have any questions about this, our Head Therapist or Study Clinic would be happy to respond.

Please reach out to us should you have any further questions – you can contact us at Path-OUD@monash.edu

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Inclusion criteria	Exclusion criteria
1. Aged 18-60 inclusive.	1. Currently pregnant, planning pregnancy, or breastfeeding.
2. Meets DSM-5 criteria for Opioid Use Disorder, as assessed using QuickSCID-5.	2. Participation in clinical trial and receipt of investigational drug(s) during 30 days prior to the research study, except as explicitly approved by the study clinician.
3. Have been on a MATOD program for at least 2 months prior to screening interview.	3. Currently meets DSM-5 criteria for moderate to severe Substance Use Disorder (SUD) for substances other than opioids, alcohol, cannabis or nicotine. Patients with comorbid Alcohol Use Disorder (AUD) will be accepted if their AUD is not severe enough to require a medicated alcohol detoxification.
4. Methadone/buprenorphine average daily dose (or equivalent weekly/monthly dose in the case of long-acting injectable buprenorphine) has varied by no more than 20% in the 2 weeks prior to screening interview.	4. Any use of serotonergic psychedelics in the past 6 months or more than 50 uses of any serotonergic psychedelics in lifetime.
5. Willingness to remain on a stable dose of methadone/buprenorphine up to dosing day.	5. More than mild opioid withdrawal (COWS > 12).
6. Use of non-prescribed opioids more than 6 times on average across the 30-day period or at the judgement of the study clinician prior to screening interview.	6. Have a known allergy or hypersensitivity to psilocybin or any of the materials contained in the capsule used in the study.
7. Have a breath alcohol concentration less than or equal to 0.01% at screening - this may be re-evaluated during the study period, at the judgement of the study clinician.	7. Have an allergy, hypersensitivity, or other contraindication that would preclude safe treatment of acute hypertension, anxiety, or psychotic symptoms using standard medical interventions if necessary during or immediately after Psilocybin Dosing Session.

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<p>8. Agree to refrain from non-prescribed psychotropic substance or illicit drug use for at least 72 hours prior to Psilocybin Dosing Session, with the exception of moderate use of alcohol, cannabis, nicotine, and caffeine.</p>	<p>8. Meets current or lifetime DSM-5 criteria for schizophrenia or any psychotic disorder, or organic mental disorder, or has a first-degree family history of psychotic disorder. This includes hallucinogen-persistent perception disorder.</p>
<p>9. Agree to refrain from taking all non-prescription medications and supplements (nutritional and herbal) for at least 1 week prior to the Psilocybin Dosing Session unless approved by the study clinician.</p>	<p>9. Meets current or lifetime DSM-5 criteria for bipolar disorder or has first degree family history of bipolar disorder.</p>
<p>10. Are proficient in English, such that their literacy and comprehension is sufficient for understanding the consent form and study questionnaires, as evaluated by study staff obtaining consent.</p>	<p>10. Meets current DSM-5 criteria for severe Major Depressive Disorder (MDD); or current or lifetime DSM-5 criteria for MDD with psychotic features. Mild and moderate MDD as well as MDD in stable remission are allowed if no suicidal risk, in the clinical judgement of the study clinician.</p>
<p>11. Have the capacity to engage with, and consent to the study requirements and are able attend all study visits.</p>	<p>11. Have current serious suicide risk, as determined by responses to Columbia Suicide Severity Rating Scale (C-SSRS) and/or the clinical judgement of the study clinician or the treating team.</p>
<p>12. Must consent to the study investigators contacting their primary treating health practitioner(s) for the purpose of corroborating medical history and their MATOD dosing pharmacy for the purpose of cross-validation of self-reported MATOD adherence.</p>	<p>12. Presence of any other psychiatric condition that, in the opinion of the study clinician, may interfere with completion of the study or place the patient at heightened risk.</p>
<p>13. Have a family member or friend who can assist with transportation and activities of daily living after the Psilocybin Dosing Session.</p>	<p>13. Have a history of or have a current medical condition which – based on the judgement of the study clinician - would make a participant unsuitable for the study. This includes, but is not limited to, the following:</p>

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	<ul style="list-style-type: none"> a) Significant hepatocellular injury (except for patients with documented Gilberts syndrome) b) Significant renal injury c) Significant cardiovascular history/active cardiovascular conditions (e.g. high blood pressure, congenital long QT syndrome, coronary artery disease, cardiac ischemia, myocardial infarction, cardiac hypertrophy, congestive heart failure, tachycardia, ECG abnormalities, artificial heart valve) d) Significant pulmonary illness (e.g. COPD) e) Significant endocrine condition (e.g. insulin-dependent diabetes, hyperthyroidism) f) Significant gastrointestinal illness (e.g. Crohn's disease) g) Seizure disorder or history of seizures not related to drug or alcohol withdrawal (excluding childhood febrile seizure) h) History of serious head trauma or injury causing significant loss of consciousness and/or associate with skull fracture or intracranial bleeding or abnormal MRI i) Current HIV infection j) Weighs < 48kg or BMI < 17.
	<p>14. Participants who present with contraindications to MRI scanning (including, but not limited to, magnetically active implants or devices, significant claustrophobia, or non-removable skin patches) may be excluded from participation in the MRI component of the study, as determined by the study clinician or radiologist.</p>
	<p>15. Has received medication that could interact adversely with psilocybin (e.g. inhibitors of UGT1A9, UGT1A10, MAO and</p>

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	aldehyde or alcohol dehydrogenase) within the time of administration of study agent, based on the guidance of the study clinician.
	16. Current use of psychoactive medications that in the study clinician's judgement would meaningfully affect safety or effectiveness of trial medications (e.g. antipsychotics, mood stabilisers, stimulants). Antidepressants and PRN medications (e.g. short-acting benzodiazepines, z-drugs) may be permitted at the discretion of the study clinician, where safe and appropriate.