Informal study title: Psilocybin feasibility study

Formal study title: **Feasibility Study of the Effect of Psilocybin in Response to Brief Psychological Input with Psychological Flexibility as a Mediating Factor**

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Study site: University of Otago – Dunedin

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You are invited to take part in a feasibility study of psilocybin in response to brief psychological intervention. Psilocybin is a psychedelic which is the active ingredient of what is called "magic mushrooms". It has been used in traditional healing or ceremonial rituals and some people who have used psilocybin recreationally have said that it has helped them with their mood. Whether or not you take part is your choice. If you don't want to take part, you don't have to give a reason, and it won't affect the care you receive. If you do want to take part now, but change your mind later, you can pull out of the study at any time.

This Participant Information Sheet will help you decide if you'd like to take part. It sets out why we are doing the study, what your participation would involve, what the benefits and risks to you might be, and what would happen after the study ends. We will go through this information with you and answer any questions you may have. You do not have to decide today whether or not you will participate in this study. Before you decide you may want to talk about the study with other people, such as family, whānau, friends, or healthcare providers. Feel free to do this.

If you agree to take part in this study, you will be asked to sign the Consent Form on the last page of this document. You will be given a copy of both the Participant Information Sheet and the Consent Form to keep.

This document is 9 pages long, including the Consent Form. Please make sure you have read and understood all the pages.

VOLUNTARY PARTICIPATION AND WITHDRAWAL FROM THIS STUDY

Your participation in this study is entirely voluntary. You do not have to participate, and you may withdraw from this study at any time and without any disadvantage of any kind.

WHAT IS THE PURPOSE OF THIS STUDY?

Depression and anxiety are common experiences of people experiencing difficulties with mental health and wellbeing. With limited resources available, some people find that there are limitations around brief therapeutic interventions. Psilocybin has been known to produce a controllable change in a person's emotional and mental state, capacity for insight, and changes in psychological functioning. When administered alongside psychological therapy, it has been shown to have good effect in mood disturbance.

When looking at treatment in mental health services, it has been shown that different psychological factors may influence a person's response to treatment. For example, studies have shown that people with certain character traits, beliefs, thought processes etc may be more likely to respond to certain therapy or treatment more than others. Psilocybin has been shown to result in temporary changes in these mental processes that may create a change in the way a person receives and processes new information – such as psychological therapy. In this study all participants will receive psilocybin within two to four weeks after completion of therapy, and then changes in mood and cognition will be followed-up.

Previous trials of psilocybin with people showed that psilocybin was well tolerated, with some people experiencing improvements in their mood, and although some people's mood did not improve, no one experienced a worsening of their mood. This study will test whether psilocybin given after brief psychological intervention will improve mood and response to therapy, and if that is associated with any changes in thought processes and beliefs. In future we hope that being able to increase a person's likelihood of positive outcome to treatment may improve mental health outcomes and optimise the use of limited health resources.

Please note that psilocybin is not approved for use in New Zealand and is used as an unapproved drug for this study. This means that psilocybin's use for this study is not backed by a body of clinical trial data reviewed and approved by Medsafe. Medsafe is the NZ Medicines and Medical Devices Safety Authority. Medsafe is responsible for the regulation of therapeutic products (which includes medications) in NZ.

Psilocybin is an illegal Class A substance under the Misuse of Drugs Act 1975 but can be granted licences for research purposes.

WHO CAN TAKE PART IN THE STUDY?

You are being asked to participate in this study because you have indicated that you might be eligible for the study. To be eligible, you would need to be experiencing difficulties with depression or anxiety and have had brief psychological therapy recently with limited improvement. Brief psychological intervention/therapy here is defined as a short course of therapy by a psychologist of between 6 – 12 weeks which include some components of mindfulness, acceptance, values, goals, cognitions, and emotions.

The inclusion and exclusion criteria are listed below:

To take part in this study you must:

- Agree to the conditions of the study and provide written informed consent.
- Aged 25 – 60 years on the day of consent.
- Be in good health and pass the screening assessments.
- Experience mild to moderate anxiety or depression.
- Have recently completed brief psychological therapy.
- (For females) be on effective use of contraception within one week of dosing

You can't be in the study if you:

- Are or intending to become pregnant, or are lactating.
- Have any evidence of significant medical problems.
- Have any current severe, acute or chronic medical illnesses.
- Have a cardiovascular condition.
- Experience current active suicidal ideation.

- Have a history of schizophrenia, psychosis, bipolar disorder, or borderline personality disorder.
- Have a family history of schizophrenia, psychosis, and bipolar disorder.
- Current use of antidepressants, anxiolytics, MAOIs, thyroxine or stimulants (amphetamine/methyphenidate).
- Have had a substance use disorder within the last 6 months.
- Do not consent to us contacting your GP prior to the commencement of the study, about your medical history or after the study about any adverse results or reactions.
- Are not able to comply with the study restrictions or you do not understand the information or procedures or the study.

WHAT WILL MY PARTICIPATION IN THE STUDY INVOLVE?

The study will consist of:

- Informed consent and screening (Visit One)
- Visit two on Day 1 for dosing
- Visit three on Day 2 for 24hr check-in
- Visit four over Zoom for follow-up assessment at Week 6
- Visit five over Zoom for follow-up assessment at Week 12

Participants will receive a single Psilocybin 25mg capsule taken orally with water. After the dose, we will ask you about any side effects. We will monitor your vital signs.

Screening Procedures:

Before beginning the study you will undergo a number of procedures that will determine if you are eligible to participate in the study. **The screening procedures will take approximately 1 - 1.5 hours.** At your screening examination, a support person may be present with you if you wish. The screening procedures include:

- A medical practitioner will ask you about your medical history including current and previously taken medications and check the inclusion and exclusion criteria with you. The medical practitioner will discuss with you whether there is any possibility for drug interactions between your current medications and the study drug.
- Vital signs including blood pressure, respiratory rate, temperature, ECG, and heart rate measurements will be recorded.
- Other tests include urine and pregnancy.
- Psychological screening measures will include mood and trait scales: Depression Anxiety and Stress Scale (DASS-21), Becks Depression Inventory 2 (BDI-2), Becks Anxiety Inventory (BAI), the Acceptance and Action Questionnaire (AAQ-2), Brief Experiential Avoidance Questionnaire (BEAQ), and the NEO Personality Inventory-Revised (NEO-PI-R).

During the screening process we will explain to you the study and the procedures. As part of being accepted into the study we will ask you to give your consent to your GP being informed about your participation in the study. You will also be asked to identify a responsible adult who is available to monitor and support you overnight after dosing on the day.

If any of your screening results are abnormal or outside of the normal ranges you may be asked to repeat them. The results of these screening assessments may indicate that you are not able to take part in this study. If this happens, your results will be discussed with you and suggestions for treatment discussed, if applicable. Your GP will be informed of any important findings. You may also be referred to your GP for further follow-up.

Procedures for Day One - Visits 2 and 3.

You will be asked not to consume food on the day prior to dosing, and to come to the Fraser Building at approximately 8AM. Your time at the clinic for this visit will last approximately **8 hours** and will consist of the following:

- We will record your vital signs (blood pressure, temperature, heart rate, respiratory rate, ECG) and conduct a pregnancy test.
- You will be given 25mg of psilocybin capsule at approximately 8.30am, along with 100mL water.
- You will be in a quiet room and provided with eyeshades and headphones to use throughout the study. The room will be kept dark and there will be music playing through the headphones.
- You will be sitting upright in a comfortable chair for 2 hours after dosing.
- We will ask you about any side-effects you may be experiencing.
- We ask that you do not eat and drink for the first hour after dosing.
- After dosing we will continue to monitor and record your vital signs.
- At approximately hour 4 we will ask you about acute experiences using the Mystical Experiences Questionnaire (MEQ), Challenging Experiences Questionnaire (CEQ), and Psychological Insight Questionnaire (PIQ).
- For safety we ask you to stay in the research clinic for 8 hours after initial dosing. After this time you are free to leave the clinic.
    - If the intensity of the drug effect has not yet worn off within the 8-hour timeframe of the dosing day, the time may be extended depending on the effects of the drug.
- You will need to return to the clinic at approximately 9am the next day for a follow-up where vital signs will be measured, and you will be asked to fill in a few follow-up questionnaires about your mood (Depression Anxiety Stress Scale – 21 (DASS-21); Beck Depression Inventory (BDI-2); Beck Anxiety Inventory (BAI)) and experience (NEO Personality Inventory-Revised (NEO-PI-R); Acceptance and Action Questionnaire – 2 (AAQ-2); Brief Experiential Avoidance Questionnaire (BEAQ)). This appointment will take approximately **60 minutes**.
- We will set-up follow-up appointments for Week 6 & 12

Procedures for Week 6 & 12

You will be contacted via phone call and email to confirm a remote appointment via Zoom

- We will ask you about any effects you may be experiencing.
- We will ask you to complete some assessment forms around your mood, thought processes, and experiences with follow-up questionnaires mentioned above,
- This appointment will last approx. 1 – 1.5hrs
- You will be reimbursed a $50 supermarket voucher for your time.

Study Restrictions:

The following requirements must be adhered to during the study:

- You are required to refrain from food on the day prior to dosing, until one hour after the psilocybin dose.
- It is possible that psilocybin may affect your ability to drive a car. We request that on the dosing day (Visit 2) that you do not drive to the Fraser Building, and do not drive until the next day.
- You will need to return to the care of a responsible adult who is able to monitor and support you overnight of the dosing day (Visit 2).

- You need to be willing to commit to screening, dosing, and follow-up sessions, completing evaluation instruments, and all necessary telephone contact.
- You must agree to not participate in any other interventional clinical trials during the duration of this study.

WHAT ARE THE POSSIBLE EFFECTS OF TAKING PSILOCYBIN?

Psilocybin is called a 'psychedelic' drug and it can have a wide range of effects that depend on the individual person and their circumstances, so it's hard to predict how it will affect you personally. Some of psilocybin's effects will be unfamiliar or strange to people who have not experienced them before. The following effects may or may not happen to you:

1. Heightened emotions. Psilocybin can lead to heightened emotions of any kind, from bliss and ecstasy through to anxiety and, more rarely, panic or paranoia.
2. Vivid, dream-like experiences or memories whilst you are awake. This is a bit like daydreaming.
3. Visual disturbances such as vivid colours, textures, geometric patterns or illusions. Rarely, psilocybin causes visual hallucinations.
4. Changes in the sense of time. Time may seem to be passing slowly, quickly or may seem not to exist at all.
5. Changes in how your body feels. This can range from aches and pains or feeling the need to use the toilet to tickling/tingling sensations, or hot/cold sensations running through the inside or on the surface of your body.
6. Changes in your 'sense of who you are'. You may feel as though you 'no longer exist', that you have 'died' or been 'reborn'. This is called 'ego-dissolution'.
7. Other experiences that can have a deep personal significance for you (noetic), but which are hard to put into words (ineffable).

Most people feel back to their usual selves about 6-8 hours after taking psilocybin. Sometimes it takes up to 12 hours. We know that psilocybin has completely left the body after 24 hours. Psilocybin is not known to be toxic to the body. The most common after-effects of psilocybin are a feeling of mental 'exhaustion' and a headache. You should get plenty of rest after you have received the treatment. You can take simple painkillers like paracetamol for the headache if it is troublesome. Psilocybin is not known to stop you from sleeping.

Other potential side effects may include:

- Muscle weakness
- Pupil dilation
- Low blood oxygen
- High/low blood pressure
- Nausea/vomiting
- Abdominal pain
- Delusions
- Vertigo
- Urinary incontinence

And rare side effects such as:

- Renal failure
- Convulsions
- Psychotic-like symptoms

What are the possible benefits of taking part?

1. You will be helping with clinical research, which may help others in the future.
2. The treatment may induce positive feelings.
3. The treatment may help you see things differently.
4. This may help with your experience of anxiety or depression.

What are the possible risks of taking part?

1. Even after you sign up for this study, there is a chance you might not be able to participate. The team will only make the final call on whether you are a good fit for the study right before the treatment is supposed to happen. If they decide it is not the right treatment for you, they will not go ahead with it. While it is rare, finding out last minute that you cannot be part of the study could be a letdown and might make you feel worse. So please think about this before you decide to join.
2. There is no guarantee that the treatment will work for you. In some cases, people have felt worse or experienced new symptoms afterward.
3. Some people who have taken these psilocybin mushrooms recreationally have said they ended up with long-lasting changes in what they see, how they feel, and some discomfort, even after the drug has worn off. We do not know if this will happen when psilocybin is given in a clinical trial setting, however it has not happened to anyone in modern trials yet.

Following the dosing day, if you experience any severe side effects, please call Prof Glue at xxx-xxxxxxx; in an emergency call '111' or present at the Emergency Department for immediate help.

For questions, further support, and to report severe effects, contact Dr Valerie Tan at (03) 474 0999 ext 58943.

WILL IT SHOW UP ON A DRUG TEST?

Psilocybin itself is not typically detected on standard drug tests (such as those for employment, law enforcement, or probation), as most of these tests screen for common substances like THC, cocaine, opiates, amphetamines, and alcohol.

Psilocybin could theoretically be detected in the body and there are specialized tests available that can detect psilocybin or psilocin, such as a **hair test** or a **blood/urine test** specifically designed for detecting hallucinogens. However, these are not commonly used outside of specific legal or medical settings.

Urine: Psilocin may be detectable in urine for about 24 to 48 hours after ingestion.

Blood: Psilocin has a shorter detection window in blood, generally a few hours to a day.

Hair: Hair tests could theoretically detect psilocybin use for up to 90 days, though this type of testing for psilocybin is rare.

In summary, unless a test is specifically designed to look for psilocybin or psilocin, it is unlikely that psilocybin use will show up on a standard drug test.

WHERE IS PSILOCYBIN SOURCED FROM?

The psilocybin used in this study is sourced from Filament Health in Canada, and is an extract of the *Psilocybe cubensis* mushroom fruiting bodies.

WILL ANY COSTS BE REIMBURSED?

There will be no cost to you to participate in this study; all screening and treatment is without charge.

The study is being paid for with funds from the James Humes Bequest Trust.

We will compensate you $50 for time involved in each follow-up (Week 6 and Week 12), which will be provided as supermarket gift cards.

WHAT IF SOMETHING GOES WRONG?

If you were injured in this study, you would be eligible **to apply** for compensation from ACC just as you would be if you were injured in an accident at work or at home. This does not mean that your claim will automatically be accepted. You will have to lodge a claim with ACC, which may take some time to assess. If your claim is accepted, you will receive funding to assist in your recovery.

If you have private health or life insurance, you may wish to check with your insurer that taking part in this study won't affect your cover.

WHAT WILL HAPPEN TO MY INFORMATION?

During this study the study clinicians/research staff will record information about you and your study participation. This information includes the results of study assessments. You cannot take part in this study if you do not consent to the collection of this information.

Identifiable Information

Identifiable information is any data that could identify you (e.g. your name, date of birth, or address). The following groups may have access to your identifiable information:

- Study clinician and research staff (to complete study assessments)
- Ethics committees, or government agencies from New Zealand if the study or site is audited. Audits are done to make sure that participants are protected, the study is run properly, and the data collected is correct.
- Your usual doctor, if a study test gives an unexpected result that could be important for your health. This allows appropriate follow-up to be arranged.

Security and Storage of Your Information.

Your identifiable information is held securely in the Department of Psychological Medicine, Fraser Building during the study (in a locked room in a locked filing cabinet). When you enter the study we keep a one page document that contains your demographic details (name, address, phone number). When the study is completed, this page will be destroyed. At the start of the study you will be allocated a unique identifier (study number) and you will be identified by this number throughout the study documents. On completion of the study your information is stored securely in the Dept of Psychological Medicine for 10 years and then destroyed. All storage will comply with local data security guidelines.

Risks.

Although efforts will be made to protect your privacy, absolute confidentiality of your information cannot be guaranteed. Even with coded and anonymised information, there is no guarantee that you cannot be identified. The risk of people accessing and misusing your information (e.g. making it harder for you to get or keep a job or health insurance) is currently very small, but may increase in the future as people find new ways of tracing information.

Rights to Access Your Information.

You have the right to request access to your information held by the research team. You also have the right to request that any information you disagree with is corrected.

Please ask if you would like to access the results of your screening tests during the study.

If you have any questions about the collection and use of information about you, you should ask the study clinician.

What happens after the study or if I change my mind?

You may withdraw from the study at any time by letting the study clinician know.

If you withdraw from the study, your study participation will end, and the study team will stop collecting information from you.

If you agree, information collected up until your withdrawal from the study will continue to be used and included in the study. You may ask for it to be deleted when you withdraw, unless you withdraw after the study analyses have been undertaken.

Can I find out the results of the study?

We will provide you with a plain English summary of study results, if requested, within 3 months of completing all lab testing work.

This study has been registered online in a clinical trial registry, and can be accessed at the ANZCTR website https://www.anzctr.org.au/

The results of the study will be published in an international scientific journal. The data included in this publication will not be able to identify you.

Who is funding the study?

The study is being paid for with funds from the James Hume Bequest Trust.

Who Has Approved the study?

This study has been approved by an independent group of people called a Health and Disability Ethics Committee (HDEC), who check that studies meet established ethical standards. The HDEC has approved this study.

This study has also been approved by the Health Research Council's Standing Committee on Therapeutic Trials (SCOTT), who undertake scientific assessment of applications to conduct trials and makes recommendations to the Director-General of Health on whether or not trials should be approved.

Who do I contact for more information or if I have concerns?

If you have any questions, concerns or complaints about the study at any stage, you can contact:

Dr Valerie Tan, Dept of Psychological Medicine; tel (03) 474 0999 ext 58943. Email valerie.tan@otago.ac.nz

If you want to talk to someone who isn't involved with the study, you can contact an independent health and disability advocate on:

Phone:	0800 555 050
Fax:	0800 2 SUPPORT (0800 2787 7678)
Email:	advocacy@advocacy.org.nz
Website:	https://www.advocacy.org.nz/

For Māori health support:

For Māori cultural support you can contact Te Oranga Tonu Tanga by phoning 03 474 0999 extn. 5510 to make an appointment or speak to Te Oranga Tonu Tanga.

Location: Te Taiahoaho on the Wakari hospital site. Open 8.00am to 4.30pm, Monday to Friday, phone

You can also contact the health and disability ethics committee (HDEC) that approved this study on:

Email:	hdecs@health.govt.nz
Phone:	A callback can be requested via the Ministry of Health call centre on 0800 400 569

Consent Form

Feasibility Study of the Effect of Psilocybin in Response to Brief Psychological Input with Psychological Flexibility as a Mediating Factor

Please tick to indicate you consent to the following

I have read, or have had read to me in my first language, and I understand the Participant Information Sheet.
I have been given sufficient time to consider whether or not to participate in this study.
I have had the opportunity to use a legal representative, whanau/ family support or a friend to help me ask questions and understand the study.
I am satisfied with the answers I have been given regarding the study and I have a copy of this consent form and information sheet.
I understand that taking part in this study is voluntary (my choice) and that I may withdraw from the study at any time without this affecting my medical care.
I consent to the research staff collecting and processing my information, including information about my health.
If I decide to withdraw from the study, I agree that the information collected about me up to the point when I withdraw may continue to be processed.
I consent to my GP or current provider being informed about my participation in the study and of any significant abnormal results obtained during the study.
I understand that there may be risks associated with the treatment in the event of myself becoming pregnant. I undertake the responsibility for the prevention of pregnancy.
I agree to an approved auditor appointed by the New Zealand Health and Disability Ethics Committees, or any relevant regulatory authority or their approved representative reviewing my relevant medical records for the sole purpose of checking the accuracy of the information recorded for the study.
I understand that my participation in this study is confidential and that no material, which could identify me personally, will be used in any reports on this study.
I understand the compensation provisions in case of injury during the study.
I know who to contact if I have any questions about the study in general.
I understand my responsibilities as a study participant.
I wish to receive a summary of the results from the study. Yes ☐

Declaration by participant:

I hereby consent to take part in this study. Yes ☐

Participant's name:

Signature: Date:

Declaration by member of research team:

I have given a verbal explanation of the research project to the participant and have answered the participant's questions about it.

I believe that the participant understands the study and has given informed consent to participate.

Researcher's name:

Signature: Date: