

Mind Medicine Australia's

Submission to The Royal Commission into Victoria's Mental Health System



MIND MEDICINE
A U S T R A L I A

5th July 2019

"...My hope is that we will engage in mature, evidence-based discussions about how best to fund and deploy psychedelic-assisted psychotherapies to augment existing approaches to the treatment of mental illness. I hope that governments will have the courage to put the welfare of their citizens ahead of their fear of controversy – and that our politicians will deploy their considerable skills and positions of influence to nurture a balanced and objective understanding amongst the public."

– Dr Simon Longstaff AO, Leading Australian Ethicist
and Executive Director of The Ethics Centre



MIND MEDICINE
A U S T R A L I A

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5th July 2019

The Commissioners
The Royal Commission into Victoria's Mental Health System

Dear Commissioners

We live in one of the wealthiest countries and we have one of the best medical systems in the world. Yet despite the high calibre of our medical practitioners and institutions, and the enormous associated system costs, we also have one of the highest rates of mental illness in the world, and the situation appears to be getting worse. Simply doing more of the same, or making only incremental changes to the current system, is not going to solve this problem and relieve the suffering of so many Victorians.

To create positive change, we have to broaden the tools available to our medical practitioners and qualified therapists in this area.

Psychedelic-assisted treatments offer enormous potential in providing a very meaningful alternative to current modalities. This approach has already been given 'Breakthrough Therapy' designation by the Food and Drug Administration in the United States, and we have seen positive research trials taking place at many of the most prestigious universities in the world. Yet Australia will only be starting its first clinical psychedelic trial – conducted by PRISM and St Vincent's Hospital and part-funded by Mind Medicine Australia – later this year.

We are delighted to be able to brief you on the exciting potential of psychedelic-assisted psychotherapy for relieving the distress experienced by far too many sufferers of mental illness in Victoria, and to suggest tangible opportunities for the State of Victoria to become a world-leader in this exciting area.

We are, of course, available to answer any questions that you have, and we would be delighted to arrange for local and overseas experts in this field to be available to you.

Yours faithfully,

Peter Hunt AM
Chair

Tania de Jong AM
Deputy Chair

Dr Paul Liknaitzky
Executive Officer

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Introduction

Despite significant international investment and positive research outcomes for psychedelic treatments of mental illness (with 'Breakthrough Therapy' designation granted by the US Food and Drug Administration in the United States for both psilocybin- and MDMA-assisted treatments), Australia has barely participated in this highly prospective area of medicine. Esteemed researchers from leading universities such as Johns Hopkins, Harvard, Imperial College London, UCLA, and Yale have conducted well-controlled psychedelic treatment trials with remarkable results. Psilocybin-assisted psychotherapy for the treatment of depression and MDMA-assisted psychotherapy for the treatment of PTSD look set to become prescribable treatments in overseas jurisdictions as early as 2021, subject to positive Phase 3 trial results. In Australia, we have 39 universities, a large variety of brain and mind Institutes, Centres of Excellence in mental health, and numerous targeted psychiatric research facilities; we have some of the best mental health researchers in the world; and yet we are only just about to start our first psychedelic trial.

Mind Medicine Australia is proposing that a *Centre of Excellence in Psychedelic Medicine* be established in Victoria. This would be developed through a consortium with representation from universities, other relevant research establishments, industry, and Government and provide leadership, best practice development, research, information, and medical training in psychedelic-assisted treatments for mental illnesses, subject always to ongoing trial results and relevant regulatory approvals. The aim would be to develop a new modality for the treatment of mental illness which could offer substantial relief and support to a large number of people who have not found successful treatments in this State, and make Victoria a world-leader in this area.

We are also proposing that specific trials be conducted in this State, and seek support for the development of best practice therapist training courses to prepare for the potential implementation of this new paradigm.

A recent example of a world-leader in this area is the Centre for Psychedelic Research at Imperial College in London: <https://www.imperial.ac.uk/department-of-medicine/research/brain-sciences/psychiatry/psychedelics/> (please view the short video at this site for more information).

In this submission, we focus on the substantial impact that psychedelic-assisted therapies could have in the treatment of depression and PTSD. Also, we note that trials are being conducted or planned overseas to apply psychedelic therapy to other indications, such as addiction and anxiety disorders.

For the purposes of this submission, we use the term psychedelic-assisted therapy to refer to both psilocybin- and MDMA-assisted psychotherapy.

"There continues to be substantial untreated morbidity for many people with mental health problems; we urgently need to explore new treatment paradigms, and the promise of psychedelic medicines in terms of alleviation of suffering cannot be under-estimated."

– Prof David Castle, Psychiatrist at St Vincent's Hospital and the University of Melbourne

Mind Medicine Australia

Mind Medicine Australia (MMA) seeks to establish safe and effective psychedelic-assisted treatments for mental illness in Australia. As a registered charity (DGR-1 status), we seek to raise awareness through education, and support clinical research and development towards safe, regulatory-approved and evidence-based psychedelic-assisted therapies in this country. We provide a science-based nexus between medical practitioners, academia, government, regulatory bodies, philanthropists and other partners.

It is important to note that we do not advocate for non-clinical use of psychedelics or any other prohibited substances, nor do we advocate for any change to the law regarding non-clinical use.

The broad organisational approach of MMA can be found in Attachment 2, and our Frequently Asked Questions about MMA and about psychedelic-assisted therapy can be found in Attachment 3.

MMA's Board, Management team, Ambassadors, and Advisory Panel members consist of leading practitioners in the applied treatment of mental illness, psychedelic medical research, health strategy, ethics, and other relevant fields from both Australia and overseas, including:

- **Applied treatment of mental illness:** Professor David Castle (Professor of Psychiatry at The University of Melbourne); Dr Ben Sessa (adult and adolescent psychiatrist based in the UK, lead of psychedelic medical research team); Dr Nigel Strauss (practising psychiatrist).

- **Psychedelic medical research:** Professor David Nutt (Head of Neuropsychopharmacology at Imperial College London and lead on multiple clinical psychedelic trials); Dr Rick Doblin (Founder of the Multidisciplinary Association of Psychedelic Studies in the US, which is sponsoring the FDA-approved Phase 3 trials for MDMA therapy for PTSD); Professor Roland Griffiths (Research psychologist at the John Hopkins University School of Medicine, and leads on multiple clinical psychedelic trials); Dr Martin Williams (President of Psychedelic Research In Science and Medicine, Australia), Professor Jayashri Kulkarni (Professor of Psychiatry at The Alfred and Monash University); and Dr Robin Carhart-Harris (Director of the Centre for Psychedelic Research at Imperial College London).
- **Health Strategy:** Professor Jane Burns (Chair of the Centre for Mental Health at Swinburne University)
- **Ethics:** Dr Simon Longstaff AO (Executive Director of the Ethics Centre, and one of Australia's leading ethics practitioners).
- **Therapist Training:** Sean O'Carroll (Psychotherapist and psychotherapy course designer) and Dr Paul Liknaitzky (Research psychologist and Executive Officer of MMA).
- **Business and the Social Sector:** Peter Hunt AM (Investment Banker, Engaged Philanthropist, co-founder of MMA), Tania de Jong (Founder of Creative Universe, Creativity Australia, Creative Innovation Global, co-founder of MMA), and Monojit Ray (CEO and founder of ConnectAlex).

A full list of MMA's Board, Ambassadors, Advisory Panel Members, and Management Team can be found in Attachment 4.

Mind Medicine Australia's Purpose is to reduce mental ill-health in Australia. To achieve this, our Aims are to:

1. **Accelerate** the scientific exploration of psychedelic-assisted treatments for mental ill-health, and – *subject to adequate evidence* – regulatory approval, clinical training, and implementation.
2. **Develop and promote regulated best practice** in clinical psychedelic-assisted treatments for mental ill-health to enhance safety and effectiveness.
3. **Maximise accessibility** of psychedelic-assisted treatments for mental ill-health within medical centres of excellence, *subject to regulatory approval*.

For further detail about MMA's Approach and Principles, please see Attachment 1.

Terms of reference

This submission addresses the following Royal Commission into Victoria's Mental Health System (Royal Commission) terms of reference:

1. *How to most effectively prevent mental illness and suicide, and support people to recover from mental illness, early in life, early in illness and early in episode, through Victoria's mental health system, and in close partnership with other services.*
2. *How to deliver the best mental health outcomes and improve access to and the navigation of Victoria's mental health system for people of all ages, including through:*
 1. *best practice treatment and care models that are safe and person-centred;*
6. *Any other matters necessary to satisfactorily resolve the matters set out in paragraphs 1-5.*

Submission

Mind Medicine Australia submits that the Royal Commission recommend that the State of Victoria become a leader in the field of psychedelic-assisted treatment for mental illness through actively supporting:

1. The establishment of a *Centre of Excellence in Psychedelic Medicine* that positions Victoria as a global leader in the research and development of psychedelic assisted therapy for the treatment of mental illnesses.
2. Targeted randomised controlled trials testing the safety and long-term efficacy of psychedelic-assisted therapy in the person-centred treatment of depression and PTSD.
3. The establishment of Australia's first Psychedelic Therapist Training program.

The aim would be to position Victoria as a leader in the development and application of an alternative modality for the treatment of mental illness which could offer relief and support to a large number of people suffering from mental illness in this State.

MMA believes that it is crucial for the Victorian Government to be part of a funding consortium for these projects. MMA will contribute and seek philanthropic funding and support from other relevant stakeholders as part of this initiative.

Also, MMA would invite the opportunity to appear before the Royal Commission regarding this submission, and to make available expert witnesses to respond to Commissioners' questions regarding the safety and efficacy of psychedelic therapy.

A world-leading Centre of Excellence

The Centre of Excellence in Psychedelic Medicine, built on collaborative efforts, would bring together a consortium of Victorian leadership in clinical and research excellence, positioned on a world stage alongside other leading Research and Development centres across the United States, United Kingdom, and Europe. The *Centre* would be a world-leader in the exploration and development of psychedelic-assisted treatment, an approach that looks set to have a major impact on mental health treatment in the coming few years.

Victoria is uniquely positioned to take a leadership role in establishing a state-of-the-art *Centre of Excellence in Psychedelic Medicine*: the first clinical psychedelic trial is set to take place within Victoria this year; Mind Medicine Australia has established strong relationships internationally with experts and organisations at the forefront of psychedelic research and practice; a number of Victorian universities can support hospital-based trials and have experience with human-testing of Schedule 9 substances; and Victoria boasts the most extensive range of world-class research institutions in Australia, along with its exemplary clinical network. Consequently, it is the ideal Australian State to lead the development, understanding and application of psychedelic therapy in this country.

This would be trailblazing in Australia, and put Victoria on the global map for the development of psychedelic therapies to treat depression and PTSD.

Clinical Research Trials

Among the most prospective of psychedelic treatments, psilocybin-assisted psychotherapy for depression and MDMA-assisted psychotherapy for PTSD have achieved 'Breakthrough Therapy' designation from the FDA in the United States and are entering the final phase of clinical testing prior to their registration as prescribable medicines [see below for further detail].

Shockingly, one in seven Australians will experience depression in their lifetimesⁱ and one in 13 will experience PTSD.ⁱⁱ Current treatment options, including

pharmacotherapy and psychotherapy, help about 50% of sufferers, and often with nasty side effects and/or large economic and time burdens. And, in spite of a sustained global effort to understand and treat these mental illnesses, prevalence rates show that we are losing the battle. Novel and effective treatment options are needed if we are to have a substantial impact on mental health treatment. We therefore believe that Government, philanthropists and medical researchers need to support clinical trials that leverage off overseas work and focus on the development and evaluation of safe and effective outcomes in the Australian context.

Local clinical trials would use and refine best practice, comparing psychedelic-assisted psychotherapy to currently available combined pharmacotherapy and psychotherapy, and to a placebo with psychotherapy.

The approach we recommend will enable assessment of the long-term safety and efficacy for Australian patients in Australian conditions. Moreover, these trials would offer an opportunity to develop and test a viable service delivery framework, prepare clinicians, and afford a smooth transition to future service provision subject to regulatory approval.

Therapist Training Program

In order to adequately prepare for the availability of psychedelic-assisted therapies in Australia, qualified clinicians will require additional knowledge, skills, and experience in order to safely and successfully facilitate this treatment. Given the impressive early clinical evidence to date, and the near-term regulatory changes predicted in the US and EU subject to forthcoming data, an Australian therapist training program will play a major part in responsibly preparing the Australian context for likely regulatory changes in the coming years.

This first in Australia Therapist Training program will leverage off existing programs developed by our collaborators overseas, including the Multidisciplinary Association for Psychedelic Studies (MAPS) and the California Institute of Integral Studies (CIIS). Content for the training program will also be shaped to suit Australian applications and draw on local expertise.

The proposed program will incorporate theoretical, practical, and experiential modes of training, and will focus on all three stages of psychedelic-assisted psychotherapy: preparation, psychedelic session, and integration.

“Australia currently lags behind the international research and development community (Johns Hopkins, Imperial College London, Harvard, Stanford) in understanding the role that psychedelic medicine might play in the treatment of mental illness. A growing evidence base regarding psychedelic medicine and the importance of providing choice to consumers to access ‘the right care at the right time’ warrants careful consideration of the role that psychedelic medicine might play in supporting holistic mental health care in Australia.”

– Prof Jane Burns, Professor of Social Innovation,
Swinburne University

The need for new treatments for depression and PTSD

The Letters Patent establishing the Royal Commission state that:

Each year, one in five people in Victoria experience some form of mental illness.

Despite the number of people who experience mental illness in Victoria, only about half receive treatment.

Many people seeking help from Victoria’s mental health system...are not able to get the treatment and supports they need. For too many Victorians, the care they receive is far too late, when their mental health has deteriorated to the point of a serious crisis.

Mental health services are under significant pressure.

Every person living with mental illness deserves high quality care and treatment, so that every Victorian can have the opportunity to experience their best mental health, remain well and live a full life.

Depression is one of the most common mental illnesses in Australia. An estimated 5.8% of Australians (i.e. around 123,000 people) experience a major depressive episode in any year, while 30% of men and 40% of women will experience Major Depressive Disorder in their lifetime. Those suffering from severe and persistent depressive disorders live approximately 15 years less than other Victorians.ⁱⁱⁱ

Australia has one of the highest rates of antidepressant use (the most prevalent of which are the selective serotonin reuptake inhibitors; SSRIs). However, mounting evidence shows that these medications are substantially less effective than previously thought.^{iv} The effectiveness of commonly employed psychotherapies for

depression is modest too, and over-estimated.^v While better results are achieved using combined psychotherapy and pharmacotherapy, a high proportion of sufferers still do not respond, and the associated costs, high patient burden, and medication side-effects limit the ability for this approach to have substantial and sustained outcomes.

In fact, only 40 to 60% of depressed individuals respond to current pharmacotherapies or psychotherapies^{vi} (effect sizes of $d = 0.2$ are typical for high quality studies and meta-analyses), with the majority experiencing ongoing symptoms that fall below diagnostic thresholds, and between 50% and 80% relapse after treatment stops^{vii,viii,ix,x}. In addition, psychotherapy is often associated with high economic costs, and chemical therapies are usually associated with considerable side-effects.

Another debilitating disorder, Post-traumatic stress disorder (PTSD) will affect one in 13 Australians in their lifetimes.^{xi} Rates of PTSD among victims of sexual assault, childhood trauma, and veterans are as high as 50%.^{xii} More Australian soldiers commit suicide than have died in recent conflicts. PTSD commonly arises following exposure to traumatic events, and is often co-morbid with other disorders and illness, such as anxiety, depression, obesity, hypertension, and immune dysfunction.^{xiii}

PTSD is notoriously hard to treat, with current pharmacotherapy achieving relief from symptoms in about 20-30% of sufferers.^{xiv} For psychotherapy, PTSD sufferers exhibit very low retention rates, with around 30% of patients completing treatment. Therapeutic efficacy in PTSD may be limited by risks of re-traumatisation and substantial psychological discomfort associated with therapy.^{xv} Current treatments are ineffective for up to 50% of PTSD patients enrolled in clinical trials.^{xvi}

In addition to the devastating effect on quality of life, high rates of unresolved depression and PTSD produce a significant and ongoing economic burden on the healthcare system, and the economy more broadly: in 2017-18, working age Australians with a mental or behavioural illness were nearly twice as likely to be unemployed or not in the labour force as those without mental illness.

In spite of a vast global effort to understand and treat depression and PTSD, little appreciable advance in treatment outcomes has been made over the last 30 years, and treatment options remain inadequate. In this context of high prevalence, debilitating cost to human life and society, and inadequate treatment outcomes following decades of global research, *novel* and *effective* approaches are urgently needed. A substantial proportion of individuals diagnosed with depression or PTSD do not achieve remission following multiple treatment attempts. Variations on current treatment options, notwithstanding some positive advances, have not stemmed the tide.

Safety and effectiveness of psychedelic-assisted therapy

The last 15 years have seen a resurgence in psychedelic-assisted treatments for mental illness. Evidence is mounting for the safety and efficacy of psilocybin-assisted psychotherapy for depression, anxiety and addiction, and for MDMA-assisted psychotherapy in the treatment of Post-Traumatic Stress Disorder. A number of well-controlled Phase 2 trials that have shown excellent safety and remarkable treatment effect sizes. Indeed, many mental health experts are now paying close attention to this resurging field, in the hope that psychedelic-assisted psychotherapy may offer breakthroughs in mental health treatment.

Larger multi-site Phase 2b and Phase 3 clinical trials have commenced or are set to commence over the next year. Results from the preceding Phase 2 clinical trials have been so compelling that the Food and Drug Administration (FDA) in the United States recently designated both psilocybin- and MDMA-assisted psychotherapies as 'Breakthrough Therapies', expediting their transition to prescription medicines subject to positive outcomes within current trials. This designation highlights the FDA's anticipation that these therapies may offer substantial advantage over current treatments. If the results confirm these treatments are effective, MDMA-assisted treatment of PTSD may become prescribable as early as 2021, with psilocybin-assisted treatments for depression soon thereafter. Also, MDMA-assisted psychotherapy has recently been approved for advanced access (Compassionate Use) in Israel for patients who have not improved with available approaches. A similar program (Expanded Access) is pending approval in the USA.

Should the Commissioners wish to speak with the leads on currently active Phase 3 trials overseas, MMA would be happy to organise this. Also, please see statements attached from Dr Rick Doblin and Professor David Nutt, both actively leading this work (see Attachment 5).

Indeed, the resurgence in interest is palpable. About one hundred psychedelic research trials have recently been completed or are currently active. In many cases, the results have been remarkable in terms of the strength, speed, and the enduring nature of the treatment effect. Reductions in psychopathology symptoms within the modern trials have been substantially larger than what is typically found for other effective treatments, with statistically significant Cohen's *d* values ranging from 0.8 to 3.1, (i.e. a 'large effect')^{xvii}.

Preliminary and currently active trials are investigating additional applications, for example for obsessive-compulsive disorder, social anxiety associated with autism, and neurodegenerative disorders.

Overall across the clinical psilocybin trials for depression and anxiety, impressive and sustained improvements were found: about 80% of participants reported enduring positive effects six months after one psilocybin treatment session (longer follow-up data forthcoming). For example, in the well-controlled study at Johns Hopkins using psilocybin-assisted psychotherapy, 51 terminally-ill patients experiencing symptoms of depression and anxiety received one high-dose and one low-dose (i.e. “active placebo”) psilocybin session: following the high-dose session, 60% reported a drop in depression symptoms into the normal range, with sustained and further improved outcomes 6 months later (71% reporting remission into normal range).^{xviii}

As Prof David Nutt, Head of Neuropsychopharmacology at Imperial College states, *“The effect sizes of these psilocybin interventions are high, often greater in magnitude than those produced by other medicinal and psychological approaches. On the basis of these results there is a strong need to conduct further studies to confirm these present findings and establish the utility of psilocybin therapy in other countries and in other indications. If these are positive then I believe psilocybin will rapidly become an accepted treatment for mental illness.”* [See Attachment 5 for further detail].

Over the past decade, the Multidisciplinary Association for Psychedelic Studies (MAPS) completed six Phase 2 trials testing MDMA-assisted psychotherapy for the treatment of PTSD. Participants were 105 individuals with extremely severe PTSD ratings, an average duration of 18 years of PTSD, and multiple failed treatment attempts. These participants underwent a treatment program that included preparatory and follow-up psychotherapy sessions, along with two or three supervised MDMA (or placebo) sessions. The data across these trials was collated, showing that overall 54% of participants in the MDMA condition no longer met diagnostic criteria for PTSD, compared with 23% in the placebo group. It was also found that patients treated with MDMA-assisted therapy continued to improve, as observed in subsequent follow-ups a year later. These results are all the more remarkable given the severe and previously intractable nature of the diagnosis among most of these participants.

MDMA was well tolerated with only minor side effects reported in some cases. Over the 6 studies, 105 participants received MDMA without Serious Adverse Events. As Dr Rick Doblin, Director of MAPS, states, *“...psychedelics have been plagued by an incomplete and often inaccurate understanding of their risks and benefits. Extensive research since the 1950s, and in particular over the last two decades, shows that when done responsibly, psychedelic-assisted therapy and/or interventions are safe*

for humans and effective for the treatment of certain mental illnesses, including anxiety disorders, substance use disorders, and depression.” [See Attachment 5 for further detail].

As a result of the highly promising results, US-based MAPS is currently commencing a large multi-site international Phase 3 trial testing MDMA-assisted treatment for PTSD, and UK-based Compass Pathways is conducting a large multi-site Phase 2b and Phase 3 trial testing psilocybin-assisted treatment for depression.

In Australia, no research into the therapeutic benefits of psychedelics has yet been conducted.

The first Australian psychedelic trial will commence in September 2019, using psilocybin-assisted psychotherapy to treat severe anxiety and depression in 30 terminally-ill patients. This trial was developed and spearheaded by Psychedelic Research In Science and Medicine (PRISM), in collaboration with St Vincent’s Hospital in Melbourne. The trial will be conducted within the palliative care unit at St Vincent’s, and is part-funded by MMA.

Historical Context

It may be useful to place contemporary therapeutic research into an historical perspective.

Through the 1950s and 1960s, extensive studies of the psychotherapeutic effects of psychedelics were conducted in several countries. Over 1000 peer-reviewed clinical papers detailing the use of psychedelic compounds, involving over 40,000 participants, were published by the mid-60s.

The widespread and unregulated non-clinical use of hallucinogenic drugs through the 1960s caused concern in the US. This was a time when many young people were seeking more liberalised lives away from the conformity of the post war years. When coupled with the politics of a growing youth anti-Vietnam War protest movement, concern turned to prohibition. In 1971, the administration of US President Richard Nixon classified all psychedelics as prohibited substances.

Through international treaties, that prohibition was adopted in Australia, the UK, Europe, and many other countries. At that point, medical research ceased due to the nebulous legal framework and the increasing stigma associated with research that previously had been regarded as paradigm-changing. Classical psychedelics and MDMA remain categorised as Schedule 9 in Australia. Accordingly, administration and use of psychedelic substances within Australia are broadly prohibited by the

scheduling legislation, and importation and medical research are subject to the grant of appropriate licenses.

However, political motivations were central to the prohibition and scheduling of classical psychedelics as substances with no known medical benefit and high abuse potential (both not supported by the science). Decades later, John Ehrlichman (senior aide to Nixon) described the deliberate efforts of the Nixon White House to associate the anti-war left with psychotropic substance use in order to disrupt their efforts. In his words, *“Did we know we were lying about the drugs? Of course we did”*.

Since the early 2000s, there has been a steadily growing resurgence in research into this highly promising approach. To note, this research is being conducted by esteemed experts within highly regarded institutions such as UCLA, Johns Hopkins University School of Medicine, New York University, University of Zurich, and the Centre for Psychedelic Research within the Faculty of Medicine at Imperial College London. Research groups, including the Multidisciplinary Association for Psychedelic Studies (MAPS), the Heffter Research Institute, and the Beckley Foundation have built on the foundations set down half a century ago and, with the aid of modern brain imaging technology, we are now able to gain insights into how psychedelics influence the brain and how neuronal firing patterns are associated with clinical outcomes.

“Early stage clinical research has shown that when delivered safely and professionally, psychedelic therapy holds great promise for treating some very serious mental health conditions.”

– Dr Robin Carhart-Harris, Head of the Imperial Centre for Psychedelic Research, Imperial College London

What is psychedelic-assisted psychotherapy?

Psychedelic-assisted psychotherapy typically involves psychotherapy alongside the ingestion of a classical psychedelic such as psilocybin, or the compound MDMA. Three distinct phases of therapy have been described: preparation; active psychedelic session; and integration. The therapeutic context of this approach is essential for both safety and effectiveness. Approaches to preparation include practical aspects, patient symptoms and expectations, non-avoidance training, and the development of a therapeutic alliance. In clinical trials, therapy occurs in co-therapy teams. Participants will typically attend several psychotherapy sessions with the therapists, who will facilitate and provide support during their psychedelic session(s).

During the psychedelic session, 'set' and 'setting' are considered paramount. 'Set' refers to mind-set (e.g., expectations, mood, associations); 'setting' refers to the context in which the session takes place (e.g., comfort and aesthetic quality of the room, interpersonal context, medically safe environment). While many modern clinical trials occur within hospitals or research institutes, the session rooms are decorated in a way that is inviting and comfortable. The participant may sit or lie on a couch, they are often encouraged to wear eyeshades and listen to music compiled to help guide the experience. The active dose session will typically last about 6-8 hours. The therapeutic approach during psychedelic sessions is non-directive: attentive, with minimal direct inquiry, supporting the participant's emerging process. Trial protocols typically include between one and three psychedelic sessions.

Immediately after the psychedelic session and over the following weeks, a process of integration is facilitated by the therapists. During these integrative sessions, the participant can process, make sense of, and give meaningful expression to their psychedelic experience and any changes it has precipitated. The central aim is in sustaining the positive changes produced through the psychedelic sessions.

In clinical psychedelic sessions, classical psychedelics like psilocybin frequently produce profound personal or existential insights, feelings of empathy and self-compassion, and a sense of connection or unity with other people and the world in general. Research shows that these characteristics are correlated to therapeutic outcomes. The majority of patients report that their psychedelic experiences were among the most meaningful experiences of their lives. Classical psychedelics may help alleviate depressive, anxious, and addictive disorders by allowing the brain and mind to 'break out' of suboptimal, rigid styles of thinking, feeling, and behaving. Psychedelics temporarily create a labile brain state by de-coupling large-scale brain networks and increase connectivity between novel neural networks within the brain. These changes may help shift patients out of pathological patterns of habitual thought.

With respect to PTSD treatment, MDMA-assisted therapy has been found to increase feelings of safety and self-acceptance whilst decreasing fear and defensiveness, allowing patients to revisit traumatic memories and to address them. All memories are encoded by the brain with the emotional tone of the experience, which is re-encoded each time the memory is recalled. A key challenge for treating PTSD is that reactivating traumatic memories can induce fearful responses, increasing the risk of re-traumatisation. MDMA allows a substantial increase in a patient's ability to tolerate traumatic memories, and these memories are subsequently associated with an entirely different emotional state of ease and acceptance. In the words of Sergeant Jonathan Lubecky, a participant in a clinical MDMA trial for PTSD, *"The effect this treatment has had on my life has been nothing*

short of a miracle. Following my final treatment and integration sessions, I noticed my PTSD was almost entirely gone... Over the next 6 months, my suicidal ideation slowed and then stopped... I now lead a full and rich life... I am better today than I was before I left for Iraq.” [See Attachment 5 for further detail].



A psilocybin-assisted therapy session, Johns Hopkins University

Need for further research and development in Australia

Psychedelic-assisted therapies have shown strong early clinical results, and considerable international research is being conducted and planned to ensure appropriate levels of safety and to optimise clinical efficacy. Large multi-site international Phase 3 trials of both psilocybin and MDMA are already underway or set to commence in the next year. In line with standard medical research practice, these trials are essential to determine whether the promising results seen to date in the smaller Phase 2 trials will hold up in larger and more realistic clinical settings.

While classical psychedelics pose only negligible risks in terms of toxicity and potential for dependence, psychological risks need to be better understood and mitigated. To date, research trials have done well to select appropriate participants and conduct trials in such a way as to ensure impressive levels of safety; for example, potential participants who have, or are at risk of, psychotic or personality disorders have been excluded due to risk of exacerbating their condition. However, in order to offer these therapies to a much larger proportion of the population, more

work is needed to understand the psychological risks and how to maintain the currently low levels of adverse events.

Various theories have been put forward to explain why psychedelic-assisted therapies may be clinically effective, although none have been directly tested. More research into the therapeutic mechanisms of these approaches is essential in order to optimise the effective aspects while reducing any unhelpful aspects of the therapy, to understand why some people do not respond clinically, and to determine what works best for different mental health indications.

The impressive efficacy of psychedelic psychotherapy observed so far in the treatment of mood disorders suggests that it will be a viable and economical alternative to current first-line treatments, including psychotherapeutic approaches such as Cognitive Behavioural Therapy (CBT), and pharmacotherapeutic interventions such as antidepressant medications. The cost of psychedelic psychotherapy is likely to be cheaper than the cost of established treatment options. As the psychedelic drugs used are essentially generic medicines, and hence available at low cost, the primary costs associated with psychedelic psychotherapy are represented by therapist time, the total requirement for which is somewhat less than that associated with CBT and other psychotherapies. On the other hand, psychedelic psychotherapy typically involves a very small number of drug-assisted therapy sessions – usually only one or two – whereas pharmacotherapeutic treatments typically require daily administration of medicines for months, years, or even the rest of a patient’s life.

We submit that it is critical for Australian medical science to be active in this highly prospective and emerging approach to the treatment of mental illness. While the Australian population generally experiences comparable prevalence and similar types of mental illness to those of other Western countries, there are undoubtedly particular aspects of the Australian experience that would necessitate the optimisation of therapeutic approaches to meet local needs. Equally important, acceptance of psychedelic psychotherapy by the Australian medical practitioner community is likely to be substantially strengthened after its effectiveness and safety have been established in the local context. In the words of Dr Rick Doblin, Director of the Multidisciplinary Association for Psychedelic Studies (MAPS): *“Further research into the safety and efficacy of psychedelic therapy is needed. MAPS supports and encourages the Victorian and Australian governments to research the medical and therapeutic potential of psychedelic substances.”*

Conversely, foregoing the opportunity will mean that Australia will continue to fall behind the USA, the UK, Canada, Europe, and Israel in mental health research and treatment. Based on the increasingly well-founded prediction by many in the field that psychedelic psychotherapies will be approved for a range of mental health conditions in those countries in the next few years, it can be anticipated that patient

awareness and consequent demand will drive Australia in the same direction; however, a lack of focus locally will almost certainly lead to unreasonable delays in approval by regulatory authorities and adoption by the Australian medical community.

Indeed, we are seeing a surge of interest around the world, and large investments in further exploration of psychedelic-assisted research and therapy. This is an historic moment in mental health research and treatment. And it is time for Australia – led by the State of Victoria – to join in this exploration and implement the best solutions to ensure these therapies can be made accessible to all. We owe it to every person suffering with mental illness and their families to not be held hostage by historical prejudices, and to identify the best solutions available to alleviate the increasing suffering in our community.

“I would like to see psychedelics ... re-established as medicine... it's so important that we tell the truth about these drugs, because if we don't, we are losing an enormous amount of therapeutic potential”

– Professor David Nutt (speaking with Lynne Malcolm on All in the Mind, 2019)

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