To Mr Cain MLA, Dr Paterson MLA and Mr Davis MLA

Submission to the Select Committee on the Drugs of Dependence (Personal Use) Amendment Bill 2021[1]

Summary

Mind Medicine Australia supports the clinical use of psychedelic-assisted psychotherapy in medically controlled environments to treat major classes of mental illness such as treatment-resistant depression and treatment-resistant PTSD. These treatments use psychotherapy in combination with substances that are currently illegal irrespective of whether they are being used for medical purposes or for recreational purposes. Research trials have shown that these therapies are remarkably effective, lead to high remission rates, are safe to use in medically controlled environments and are non-addictive. This is of major significance as the scale of mental ill-health in Australia is staggering. Mental illness is a major reason people are drawn to illegally use psychedelic drugs in an effort to self-medicate. Allowing medically-approved psychedelic-assisted psychotherapy will mean that these people will be able to have this treatment option in a safe, medically controlled environment. We recommend conservative changes to ACT legislation so that medical practitioners that have received a specific approval from the TGA under the Special Access Scheme or Authorised Prescriber provisions of the Therapeutic Goods Act 1989 (Cth) can treat a treatment-resistant patient in the ACT with psychedelic-assisted psychotherapy.

Who is Mind Medicine Australia?

Mind Medicine Australia (MMA) is a registered charity (with DGR-1 status) founded by social entrepreneurs Tania de Jong AM and Peter Hunt AM to facilitate the introduction of safe, accessible and effective medicine-assisted psychotherapies in Australia. Our main focus is on the application of psilocybin-assisted therapy for depression and MDMA-assisted therapy for PTSD.

Our board includes: Admiral Chris Barrie AC (former Head of the Australian Armed Forces); The Honourable Andrew Robb AO (former federal Minister for Trade, Investment, and Tourism); Dr Simon Longstaff AO (Executive Director of the Ethics Centre); and Professor Jane Burns (a leading mental health consultant).

Our ambassadors and advisors include the heads of the two leading psychedelic therapy research centres in the world: Professor David Nutt (Imperial College, London and lead on multiple clinical research trials); and Professor Roland Griffiths (John Hopkins University and lead on multiple clinical research trials).

[1] This submission was written by Liron van Heerden, Mind Medicine Australia.

MMA operates as a nexus between medical practitioners, academics, governments, regulatory bodies, philanthropists, patients and other stakeholders in Australia's mental health system.

The remarkable results from psychedelic-assisted therapy

Considerable research was undertaken into psychedelic-assisted therapies in the 1950s and 1960s. The 'war on drugs' in the 1970s saw a crackdown on these substances because it failed to make a clear distinction between the medicinal use of medical grade psychedelics in a medically controlled environment as part of psychotherapy and the recreational use of these substances in an uncontrolled environment. Medical use of psychedelics was vilified without reference to scientific facts or data and research halted.

In the last 20 years research has restarted and slowly built up momentum. Today, scientists and psychotherapists using these treatments are more cautious in their screening of patients and research methods. Emphasis is placed on follow-up work to integrate the insights from psychedelic drugs into one's everyday life.

The research has had remarkable results which have been recognised in the last few years.

In 2017 and 2018 the US Food and Drug Administration granted "Breakthrough Status" to fast track trials of psilocybin-assisted psychotherapy for depression and major depressive disorder and MDMA-assisted psychotherapy to treat PTSD[2,3]. Breakthrough Status indicates that these therapies potentially offer a substantial improvement over existing treatments.

In March this year the Australian federal government announced that it will back psychedelic clinical trials with $15 million of funding[4].

In the last two years seven centres of excellence around the world have been set up at major universities to study psychedelic-assisted psychotherapy:

1. Imperial College London (UK),

2. Johns Hopkins (USA),

[2] Burns (2017). "FDA Designates MDMA as 'Breakthrough Therapy' For Post-Traumatic Stress". Retrieved from https://www.forbes.com/sites/janetwburns/2017/08/28/fda-designates-mdma-as-breakthrough-therapy-for-post-traumatic-stress/?sh=6ccff5f47460.
[3] Compass Pathways (2018). "COMPASS Pathways receives FDA Breakthrough Therapy designation for psilocybin therapy for treatment-resistant depression". Retrieved from https://compasspathways.com/compass-pathways-receives-fda-breakthrough-therapy-designation-for-psilocybin-therapy-for-treatment-resistant-depression/.
[4] The Hon Greg Hunt MP. "$15 million for development of innovative therapies for mental illness". Department of Health. Last modified 17 March 2021.

3. University of California Berkeley Centre for the Science of Psychedelics (USA),

4. New York University Langone Centre for Psychedelic Medicine (USA),

5. COMPASS Pathways with Sheppard Pratt for Advanced Diagnostics and Therapeutics (USA), and

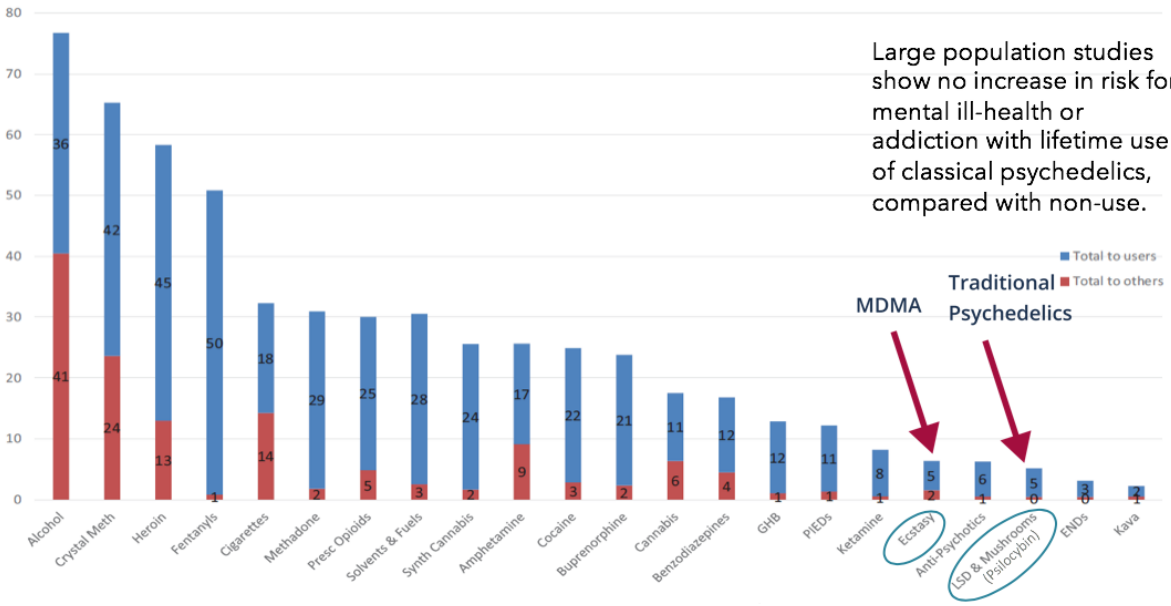
6. The Icahn School of Medicine at Mount Sinai Centre for Psychedelic Psychotherapy and Trauma Research (USA).

7. Harvard Medical School Centre/Massachusetts General Hospital for the Neuroscience of Psychedelics

There are over 160 current and recently completed research trials being conducted globally, including Australia's first clinical trial using psilocybin-assisted psychotherapy for end of life distress at St Vincent's Hospital in Melbourne. Apart from depression and PTSD, psychedelic-assisted psychotherapy has demonstrated remarkable promise for treating anxiety and addiction. Trials are also underway for dementia, anorexia and other eating disorders, obsessive-compulsive disorder, and cluster headaches.

Medicinal psilocybin (derived in its natural form) from certain mushrooms and medicinal MDMA (often confused with the street drug ecstasy which is usually adulterated rather than pure MDMA) have a strong safety record, with very low physiological toxicity and harm potential, when used in a medically controlled environment. These medicines are non-addictive and the patient will never be allowed to take these substances home. In the Australian drug harms study compiled by 25 leading experts which ranks the harm of recreational drugs ecstasy and psilocybin ranked near the bottom in terms of harm to user and harm to others in a

recreational context[5]. *Importantly, this is for their recreational use. When used in the medical setting the harm rate is negligible.* Street ecstasy in particular, is a mixture of MDMA and other substances, which can be harmful, and some ecstasy may contain no MDMA at all[6]. Unlike street MDMA, the medicinal use of MDMA as part of psychotherapy uses a pure, precisely dosed form of the substance, which is safe for human consumption when taken a limited number of times in moderate doses[7].



Nutt, D and Castle, D, et al. (2019) The Australian drug harms ranking study, Journal of Psychopharmacology, Vol 33, Issue 7.

Recent results

Current medicines for depression, such as antidepressants, require a daily dose and frequently have significant side effects, including insomnia, psychosis, blurred vision, weight gain, nausea etc. Despite this only 35% of suffers experience remission, and relapse is common (50-80%) when daily dosing stops[8]. Others are left with no viable treatment. When psychotherapy is used in combination with antidepressants, remission rates are little better - up to 40% at best[9,10]. The results from research trials of psychedelic-assisted therapy have been startlingly better.

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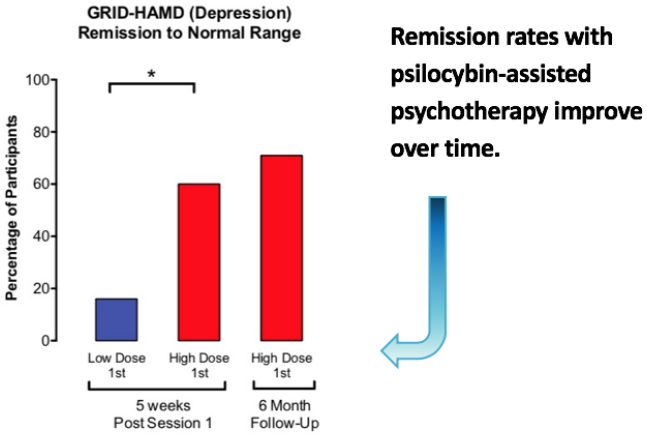
[5] Nutt, D and Castle, D, et al. (2019) The Australian drug harms ranking study, Journal of Psychopharmacology, Vol 33, Issue 7.
[6] Australian Institute of Health and Welfare. “Alcohol, tobacco & other drugs in Australia”. Last Modified 16 April 2021.
[7] Johansen & Krebs. "Psychedelics not linked to mental health problems or suicidal behaviour: A population study." Journal of Psychopharmacology 29.3 (2015): 270-279.
[8] De Maat et al (2006). Relative efficacy of psychotherapy and pharmacotherapy in the treatment of depression: A meta-analysis 16(5): 566-578.
[9] Holmes, E. A. et al. (2018) The Lancet Psychiatry Commission on psychological treatments research in tomorrow's science. Lancet Psychiatry, 5(3), pp. 237-286. (doi:10.1016/S2215-0366(17)30513-8).
[10] Cuijpers, P. (2017). Four decades of outcome research on psychotherapies for adult depression: An overview of a series of meta-analyses. *Canadian Psychology/psychologie canadienne*, *58*(1), 7.

In a psilocybin-assisted psychotherapy trial conducted at Johns Hopkins, 70% of participants improved on measures of depression and anxiety within a week of taking two doses of psilocybin and more than half were in remission within four weeks, showing that the effect of the medicine increased rather than dissipated which is what happens with most standard antidepressants[11].



Griffiths, R. R., Johnson, M. W., Carducci, M. A., Umbricht, A., Richards, W. A., Richards, B. D., ... & Klinedinst, M. A. (2016). Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial. *Journal of psychopharmacology*, *30*(12), 1181-1197.

Results recently published in one of the world's top medical journals (The New England Journal of Medicine) showed that in a Phase 2 trial conduced at Imperial College London, two sessions of psilocybin-assisted psychotherapy were as effective in treating moderate to severe depression over the course of six weeks as daily intake of a leading SSRI antidepressant (Escitalopram) combined with psychotherapy[12]. Psilocybin had quicker effects and was of greater magnitude in reducing depressive symptoms. Those who received psilocybin reported far fewer side effects and feelings of anxiety and suicidal ideation were also reduced significantly. Additionally, remission rates were twice as high in the psilocybin group as in the antidepressant group, 57% and 28%, respectively. Such encouraging results suggested that "psilocybin is as least as good – and probably better – than the gold standard treatment for depression"[13].

[11] Griffiths, R. R., Johnson, M. W., Carducci, M. A., Umbricht, A., Richards, W. A., Richards, B. D., ... & Klinedinst, M. A. (2016). Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial. *Journal of psychopharmacology*, *30*(12), 1181-1197.

& Klinedinst, M. A. (2016). Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial. *Journal of psychopharmacology*, *30*(12), 1181-1197.

[12] Carhart-Harris, R., Giribaldi, B., Watts, R., Baker-Jones, M., Murphy-Beiner, A., Murphy, R., ... & Nutt, D. J. (2021). Trial of Psilocybin versus Escitalopram for Depression. *New England Journal of Medicine*, *384*(15), 1402-1411.

[13] Sullivan, K. Psychedelic drugs worked for depression as well as common antidepressant, small trial finds. NBC News. Last modified 15 April 2021.

For those experiencing PTSD, the rate of recovery is even more dire. Only 20-30% of sufferers show some response to pharmacotherapy and only about 50% respond to any treatments at all. Remission rates remain as low as 5%[14]. The contrast between existing treatments for PTSD versus MDMA-assisted therapy is even greater than the results from psylocibin-assisted therapy for depression.

In a Phase 2 trial there were 105 participants, all with treatment-resistant PTSD (who on average had PTSD for 18 years). The results showed that MDMA assisted psychotherapy led to remission in 52% of patients immediately and in 68% at the 12-month follow up[15].

In a ground-breaking Phase 3 trial published in *Nature Medicine Journal* (May 2021), more than two-thirds of participants who took a dose of MDMA no longer qualified for a diagnosis of PTSD and 88% with more treatment-resistant forms of PTSD had their depressive symptoms significantly mitigated[16]. This pivotal Phase 3 trial treated 90 patients with severe, chronic PTSD caused by combat-related events, accidents, abuse, and sexual trauma, with an average PTSD duration of 14 years. These results replicated Phase 2 trials, were highly statistically significant, and exhibited an excellent safety record, suggesting MDMA-assisted therapy will be an effective treatment for severe, chronic PTSD.

Based on the results to date, MDMA-assisted therapy is expected to be registered as a therapy for widespread medical use as early at 2023 in the US and psilocybin-assisted therapy a year or two after that.

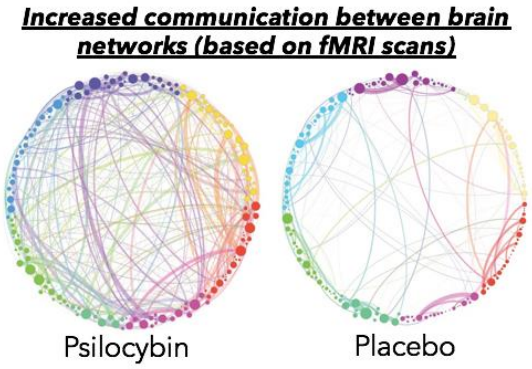
How the treatments work

These medicines are 'curative' not palliative; focusing on underlying causes rather than symptomatic treatment, which helps broaden our capacity to respond. Psilocybin-assisted therapy for depression alters communication between brain networks, such as the Default Mode Network (DMN), which is associated with many mental illnesses[17].

Using a fMRI scan (represented by the two circles below), the neural connectivity in a patient with depression following intervention with psilocybin vs. placebo was

[14] Morina, N., Wicherts, J. M., Lobbrecht, J., & Priebe, S. (2014). Remission from post-traumatic stress disorder in adults: a systematic review and meta-analysis of long-term outcome studies. *Clinical psychology review*, *34*(3), 249-255.
[15] Mithoefer, M. C., Feduccia, A. A., Jerome, L., Mithoefer, A., Wagner, M., Walsh, Z., ... & Doblin, R. (2019). MDMA-assisted psychotherapy for treatment of PTSD: study design and rationale for phase 3 trials based on pooled analysis of six phase 2 randomized controlled trials. *Psychopharmacology*, 1-11.
[16] Mitchell, J. M., Bogenschutz, M., Lilienstein, A., Harrison, C., Kleiman, S., Parker-Guilbert, K., ... & Doblin, R. (2021). MDMA-assisted therapy for severe PTSD: a randomized, double-blind, placebo-controlled phase 3 study. *Nature Medicine*, 1-9.
[17] Carhart-Harris, R. L., Roseman, L., Bolstridge, M., Demetriou, L., Pannekoek, J. N., Wall, M. B., ... & Nutt, D. J. (2017). Psilocybin for treatment-resistant depression: fMRI-measured brain mechanisms. *Scientific reports*, *7*(1), 1-11.

measured. In the placebo you can see the limited neural connections and repetitive loops of rigid, stuck thinking and negative rumination. Psilocybin on the other hand, showed massive neurogenesis of neural pathways and looser connection between brain networks, which then reintegrate. This is the brain's way of bypassing the DMN and 'resetting' itself on psilocybin by allowing parts of the brain to communicate that were not communicating. This appears to explain why this form of psychotherapy drives patients to rethink entrenched beliefs and break compulsive thought patterns and behaviours[18].



If common antidepressants dull emotions to help people cope, psilocybin works on our serotonin system to heighten emotional responses and encourage people to actively confront their depression, which can prompt enduring shifts in mindset.

MDMA is an empathogen that modulates emotional memory circuits by decreasing fear and defensiveness without blocking access to memories or preventing a deep and genuine experience of emotion[19]. By reducing activation in brain regions associated with fear- and anxiety-related behaviours, MDMA allows patients to revisit their trauma and emotional engagement without being retriggered and/or retraumatised. This promotes reprocessing of traumatic memories with increased equanimity without emotional numbing or dissociation.

Remarkably, in contrast to conventional treatments (which usually includes daily medications and/or weekly psychotherapy), only 2-3 dosage sessions in combination with a short program of psychotherapy is required. Even a single powerful experience, in a medically controlled setting, can lead to enduring changes in values and behaviours.
Three distinct therapy phases take place over several days: (1) preparation, screening and building rapport with the therapist, (2) the medicinal experience, and

[18] Schenberg, E. E. (2018). Psychedelic-assisted psychotherapy: a paradigm shift in psychiatric research and development. *Frontiers in pharmacology*, *9*, 733.
[19] Metzner, R. and S. Adamson, Using MDMA in healing, psychotherapy and spiritual practice, in Ecstasy, A Complete Guide: A Comprehensive Look at the Risks and Benefits of MDMA., J. Holland, Editor. 2001, Inner Traditions: Rochester VT. p. 182-207.

(3) integration[20,21]. *Importantly, the therapeutic elements of this approach are essential for both effectiveness and safety.*

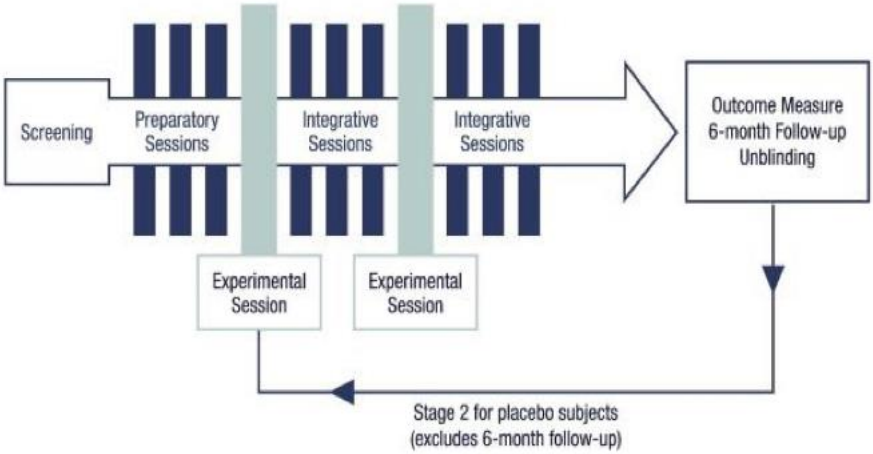


Figure: Medicine-assisted psychotherapy protocol (MAPS)

The results are unparalleled compared to existing medicines:

- Medicinal psilocybin-assisted psychotherapy and medicinal MDMA-assisted psychotherapy has demonstrated ongoing relief and remission in between 60-80% of cases.

- These therapies are comparable to decades of therapy, in just a few sittings.

Why medical psychedelic-assisted therapy is different from recreational use

While people can and do have beneficial healing experiences when using psychedelics in a non-medical setting, there are important differences between this and medical psychedelic psychotherapy. These differences mean that in a medical setting people are more likely to have a beneficial, healing experience, and less likely to have a negative one. These differences are:

1. The medical approach screens out participants for risk factors including a personal and family history of psychosis. The Mini Mental State Evaluation

[20] Mitchell, J. M., Bogenschutz, M., Lilienstein, A., Harrison, C., Kleiman, S., Parker-Guilbert, K., ... & Doblin, R. (2021). MDMA-assisted therapy for severe PTSD: a randomized, double-blind, placebo-controlled phase 3 study. *Nature Medicine*, 1-9.
[21] Mithoefer, M. C., Feduccia, A. A., Jerome, L., Mithoefer, A., Wagner, M., Walsh, Z., ... & Doblin, R. (2019). MDMA-assisted psychotherapy for treatment of PTSD: study design and rationale for phase 3 trials based on pooled analysis of six phase 2 randomized controlled trials. *Psychopharmacology*, 1-11.

(MMSE) is also used to determine mental state and competency to take part in trials[22,23].

2. The drugs are a known, safe quantity unlike substances bought on the street.

3. The emphasis on providing a beneficial mindset and environment ('set' and 'setting').

4. The emphasis placed on integration after the medicine event.

These later two points are worth further discussion.

'Set' and 'setting' are considered paramount. Psychotherapists have found that setting, intention, and expectancy are crucial for a positive outcome[24]. "Set" refers to the mindset of the individual (e.g., their intention, mind state, personality) and "setting" refers to factors outside the individual (e.g., presence of a therapist and the environment in which the substance is used). In preparatory sessions, the nature of the individual's struggle is explored. The therapist prepares the participant for the psychedelic session in a number of ways, with a particular emphasis on curiosity, and ways to remain open to challenging experiences. Challenging experiences are considered by many who work in the field to be integral to the therapeutic and personal benefits that follow. In contrast, so called 'bad trips' appear borne out of an attempt to avoid challenging experiences and can be mitigated by an open and curious mindset.

Immediately after the psychedelic session and in the following days, a process of integration is facilitated by the therapist. During these conversations, the participant has the opportunity to process, make sense of, and give meaningful expression to their psychedelic experience. This is considered important as many describe the experience as "overwhelming and transcendent", and most participants rate the experience as "among the 10 most meaningful experiences" in their lifetime[25].

Our huge hidden epidemic

[22] Multidisciplinary Association for Psychedelic Studies (MAPS): Kumar, S. Psilocybin-assisted Psychotherapy in the Management of Anxiety Associated with Stage IV Melanoma. Clinical Study Protocol. Retrieved from https://maps.org/research-archive/cluster/psilo-lsd/pca1protocol.pdf.
[23] Reiff, C. M., Richman, E. E., Nemeroff, C. B., Carpenter, L. L., Widge, A. S., Rodriguez, C. I., ... & Work Group on Biomarkers and Novel Treatments, a Division of the American Psychiatric Association Council of Research. (2020). Psychedelics and psychedelic-assisted psychotherapy. *American Journal of Psychiatry*, *177*(5), 391-410.
[24] Parrott, A. C. (2007). The psychotherapeutic potential of MDMA (3, 4-methylenedioxymethamphetamine): an evidence-based review. *Psychopharmacology*, *191*(2), 181-193.
[25] Reiff C. M. et al (2020) Psychedelics and Psychedelic-Assisted Psychotherapy, *The American Journal of Psychiatry, 177*(5), 391-410.

On average, one in five or 4.8 million Australian adults are currently experiencing mental ill-health every year and 1 in 2 will experience a serious mental illness in their lifetime.[26] Yet, there has been no improvement in treatment outcomes over the past 50 years.

This position is significantly worse for specific priority populations who are at higher risk, including Australian Defence Force veterans, first responders and Indigenous people[27].

	General Population*	ADF Veterans
Criteria (over 12 month period) for:	%	%
Mental Disorders	20	46
PTSD	6.4	17.7
Depression Episodes	4.1	11.2
Alcohol Disorder	4.3	12.9
Suicidal Ideation (Plans or Attempts)	2.2	21.7
Co-Morbidity	8.5	55.2

*above 16 years of age
Veterans Information- Mental Health Prevalence: Department of Veterans Affair 2018
General Population- 2007 National Survey of Mental Health & Wellbeing (ABS)

According to the Productivity Commission, the total cost of mental illness and suicide to the Australian economy is approximately $220 billion per year[28]. *This was around one tenth of Australia's total economic output in 2019.*

The Australian Productivity Commission (2020 final report)	
Direct costs of mental ill-health and suicide (a conservative estimate)	$43 - $70 billion per year
Diminished health & life expectancy for those living with mental illness	$150 billion cost per year
Total cost of mental illness and suicide to the Australian economy	~$200-220 billion cost per year

Productivity Commission, Mental Health, Final Report (November 2020)

Individuals with mental health issues are more likely to turn to illicit substances as a form of self-medication at a rate of 1.7 times (26% compared with 15.2%)[29]. There exists a surfeit of evidence showing those suffering from depression, bipolar disorder, and PTSD turn to cocaine, alcohol, and opiates respectively, as a way to cope with the devastating impacts of mental illness.

[26] Australian Bureau of Statistics 2018, National Health Survey First Results, cat. no. 4364.0.55.001, ABS, Canberra.
[27] Veterans Information- Mental Health Prevalence: Department of Veterans Affair 2018
General Population- 2007 National Survey of Mental Health & Wellbeing (ABS)
[28] Productivity Commission, Mental Health. "Productivity Commission Inquiry Report". 17 November 2020.
[29] Australian Institute of Health and Welfare. "Alcohol, tobacco & other drugs in Australia". Last Modified 16 April 2021.

As awareness grows of the potential for psychedelic treatment to cure mental illness it is to be expected that more people will self-medicate using psychedelics to treat their mental illness.

Recommendation

The Therapeutic Goods Administration (TGA) has recognised the very positive results from psychedelic-assisted therapy by allowing medical practitioners to treat patients who have been approved under its Special Access Scheme. In particular this allows treatment-resistant PTSD patients to receive MDMA assisted psychotherapy and treatment-resistant depression patients to receive psilocybin assisted psychotherapy. However, these treatments have not taken place because the States and Territories (other than Victoria) do not have legislated approval mechanisms whilst the use of these substances for medical purposes remains in Schedule 9 of the Poisons Standard. This includes the ACT. As such we recommend changes to ACT legislation to allow these TGA-approved treatments to take place. We recommend these changes because:

- Based on results to date, MDMA and psilocybin assisted psychotherapy are likely to dramatically change these patients' lives, reduce suicides and reduce the immense suffering and cost of mental ill health.

- Initially there would be a handful of practitioners treating a small number of treatment-resistant patients. However, it would also be a measured and significant step that would put the ACT at the forefront of the emerging field of psychedelic assisted psychotherapy. It is consistent with the ACT being an educated electorate that looks at the facts.

- The TGA allows treatment-resistant patients to be treated under its Special Access Scheme on compassionate grounds. The TGA recognises the long-term suffering of these patients, their 'all other options exhausted' nature and their serious risk of self-harm. *To argue against allowing this in the ACT, seems almost cruel and places you in disagreement with the TGA.* It also puts you in disagreement with the medical authorities of the US, Canada, Switzerland and Israel which have allowed similar access for similar reasons.

- *Nothing would take place that has not already been approved by the TGA.*

Based on legal advice from Greg Barns SC, we recommend changes to the *Medicines Poisons and Therapeutic Goods Act 2008* (ACT) (the Act) for the ACT Government to approve clinical use if the doctor has received approval from the TGA under Special Access Scheme – B. In particular we suggested amendment to section 20(3) of the Act to allow in relation to a prohibited substance, either;

1. The automatic issue of a license to a doctor if that doctor had first obtained an approval to use the substance from the TGA under the Special Access Scheme,

or the medical practitioner had been approved by the TGA to be an Authorised Prescriber in relation to that substance; or

2. The issue of a license in the same circumstances if approved by the Chief Medical Officer of the ACT.

The definition section of the Act would also be amended to include definitions of “Special Access Scheme-B” and “Authorised Prescriber” which would simply recognise that they have the meaning attributed to them in the TGA Act and Regulations.

The *Medicines, Poisons and Therapeutic Goods Regulations* 2008 (ACT) would need to be revised, and amended, to reflect s20(3) (c).