

PSILOCYBIN FOR TREATING DEPRESSION

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Depression can be fatal

Depression can be a fatal disease.

American novelist David Foster Wallace was one of its victims. He died of depression in September 2008.

A few years before that, he wrote something that might help us understand why someone would choose to take their life. He said that a depressed person doesn't choose this end because they find death suddenly appealing. Someone ends their life, he wrote, in 'the same way a trapped person will eventually jump from the window of a burning high-rise'. The terror of falling from a great height is easier to face than the terror of the fire's flames.

The 'trip' treatment

But there is a new treatment for depression that looks so promising, that some researchers are comparing this 'breakthrough' medical technology to the discovery of penicillin as an anti-biotic almost a century ago.

Psilocybin is the psychoactive substance found in certain kinds of mushroom species - what you will likely know as 'magic mushrooms' - and is amongst a family of naturally occurring psychedelics that people have been using for thousands of years, mostly for ceremonial and spiritual purposes.

Psychedelics' entry into the Western world came through the medical lab in the 1940s, when the psychiatric community in the United States first started investigating their potential to help understand the nature of the mind. There were at least three decades of research using psychedelic-assisted therapy (PAT) to treat conditions like depression, end-of-life anxiety, and alcoholism. In fact, Bill Watson, one of the founders of Alcoholics Anonymous (AA) had such a positive experience with LSD, which helped him with his own addiction, that he wanted this form of therapy used in the AA programme.

But then psychedelics escaped the lab, and made it into the recreational scene in the USA, where they became synonymous with the anti-war movement and hippie culture. The Nixon administration pressured the United Nations to declare psychedelics, including psilocybin, illicit substances under the 1971 UN Convention on Psychotropic Substances.

This shut down all the ongoing medical research overnight, and drove psilocybin and other psychedelics into the underground, where small communities have continued to use them recreationally and therapeutically ever since.

The 'renaissance'

There has been a resurgence of research in this field in the past two decades, where a number of internationally recognised medical research labs have been running clinical trials under licence from their governments, including Johns Hopkins University, Imperial College London, and New York University.

Some of these clinical trials involve using psilocybin-assisted therapy for treating depression, end-of-life anxiety in cancer patients, and alcohol and nicotine dependence.

The results are so promising that the Food and Drug Administration (FDA) in the USA is fast-tracking psilocybin through the medical licensing process, and it's expected to be legal for medical use there in about five years.

How psilocybin-assisted therapy (PAT) works

With anti-depressants like SSRIs, you need to take the medication daily, to keep the substance present in your body at a sustained level in order for it to work.

But psilocybin treatment involves occasional, supervised dosing sessions. Depending on the severity of a person's depression, for some, that may be four times a year, for others, maybe only once a year.



In session Two therapists supervise a patient during a psilocybin-assisted session at the Johns Hopkins medical school.

The clinical model:

The medical teams at universities like Johns Hopkins and Imperial College London put participants through a 12-week programme. The first few weeks involve normal talk therapy to prepare them for the dosing sessions. In the middle of the programme participants will have just two supervised psilocybin dosing sessions. These are then followed by the final weeks where patients have more talk therapy so that they can work through and integrate what they have experienced in the dosing sessions.



1 gram



2 grams



4 grams

Magic medicine A 'recreational' dose of psilocybin mushrooms might be up to a 1 gram or so. In the clinical trials, medical researchers use laboratory synthesised psilocybin for the first session, amounting to the equivalent of about 2 grams of dried mushrooms. The dose for the second session, usually a week later, is the equivalent of about 4 grams of dried mushrooms.

Dosing:

The medical teams use laboratory synthesised psilocybin. The first dose amounts to about 2 grams of dried *psilocybe* mushrooms per 70kg of body weight. The second dose amounts to about 4 grams of mushrooms, which gives a much more intense experience.

In the underground community, the ceremonial or therapeutic dose usually involves a 'flood dose' of 5 grams.

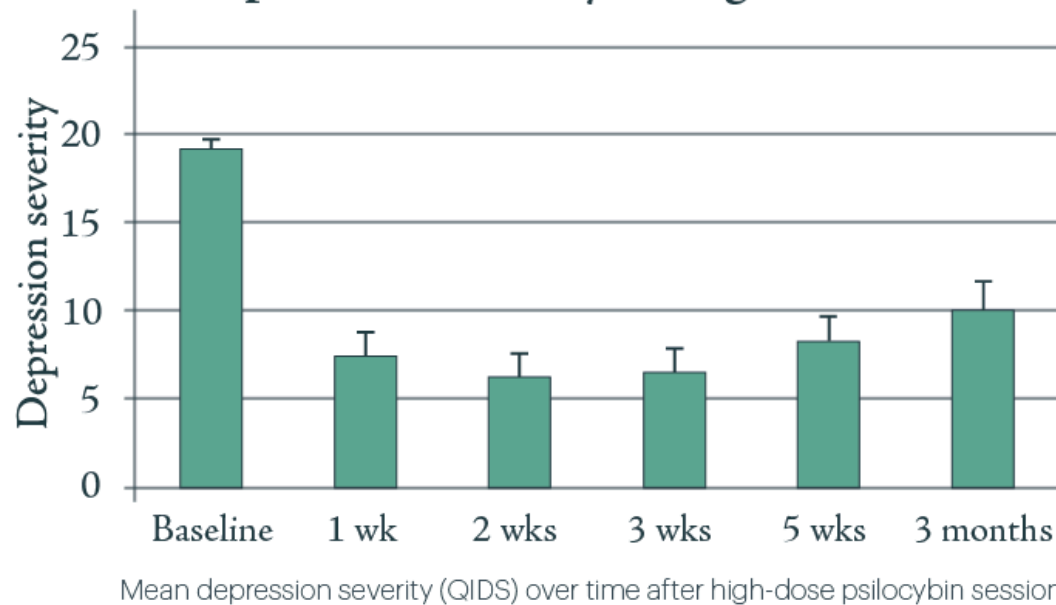
Promising results:

This graph (below) is from one of the earlier trials by the Imperial College team, where a small group of people with

treatment resistant depression went through the 12 week programme. The graph shows how their depression 'scores' dropped immediately after the treatment, and most were still showing signs of relief up to three months after the last dosing session.

Similarly, with the smoking cessation study done by the Johns Hopkins team, the psilocybin treatment looks like it is more effective for breaking the hold of nicotine than most current treatments.

Depression severity ratings over time



Carhart Harris et al. 2016. Psilocybin with psychological support for treatment-resistant depression: an open-label feasibility study. *Lancet Psychiatry*. 3: 619-27.

What's going on in the brain?

Two things are happening in the brain as a result of the psilocybin treatment, which might explain why people show positive mood and behaviour changes that last long after the substance has left the body, sometimes weeks, even months later.

The subjective experience during the session:

Unlike talk therapy, where you are externalising your 'narrative' and your therapist is helping you test and possibly rewrite that narrative, psilocybin is a deeply internal process. You are your own therapist. Many describe it as therapy on steroid; like years therapy in one night; the insights gleaned during dosing sessions go from being intellectual knowledge, to somehow becoming imbued with meaning and emotion, and therefore become more real and help reshape your personal narrative.

Quietens the ruminating mind:

Brain scans show that psilocybin operates on a part of the brain that's associated with locked-in patterns of thinking. This kind of rumination is often associated with depression and many habitual behaviours.

Think of the mind as a snowy hill, one researcher describes. Every time you respond to a trigger, it's like a sled running down that hill, cutting grooves into the snow.

Smoking cessation programmes and their abstinence rates after six months



Johnson, MW., Garcia-Romeu, A., Cosimano, MP. & Griffiths, RR. 2014. Pilot study of the 5-HT_{2A}R agonist psilocybin in the treatment of tobacco addiction. *Journal of Psychopharmacology*. Vol 28 (11): 983-992.

The more the brain reacts to the triggers, the deeper the grooves become, until the sled's runners are so stuck in those grooves that it can't respond any other way.

Researchers describe a psilocybin session as being like putting a fresh powder of snow over the hill, allowing the sled to track a new path. Using the plasticity of the brain, psilocybin seems to break those locked-in patterns of thinking and behaving.

It's the dual process of meaning-making during the session, and the plasticity of the brain responding to the substance, that might explain why people going through these trials show positive mood and behaviour changes that seem to last long after the substance has left the body.

Some of the depression study participants did say that they started to feel the depression begin to creep back after three to four months. This confirms what many in the underground psilocybin community report, where people take themselves for supervised dosing sessions every three to four months to manage their condition.

In the underground:

The substance is still illegal here in South Africa, which has driven people to look for this treatment through informal channels. These underground mushroom 'journeys' usually involve small groups of people getting

together in private homes, with experienced journey 'guides' to supervise them through the four to six hour sessions.

Mental wellbeing: like good oral hygiene

This isn't a magic bullet for treating depression. It's not a cure all. And it's not suited for people with psychosis or schizophrenia.

Taking care of your mental wellbeing is a bit like good oral hygiene. You need to brush and floss daily. You should visit the dentist from time to time. But every now and then you might need a root canal. Meditation, exercise, contemplative practice - these are the daily practices that can help brain-train yourself into a healthier state of mind. Occasionally, you might benefit from psychotherapy or some counselling. A psilocybin-session is like the root canal: a quick, intense surgical procedure to lance an abscess. It's a good complement to other therapies.

SSRIs are palliative: they relieve the pain of depression. But many people say that these drugs numb them,, or that it's like putting a plaster over a boil. A psilocybin dosing session goes directly to the cause of the pain, lancing the boil.

Harms and risks

The UK government's Independent Scientific Committee on Drugs published findings in the medical journal the *Lancet* in 2010, where they showed their findings of a study into the harms and risks associated with 20 most widely used substances.

They found that substances like alcohol, nicotine, cocaine, and cannabis are amongst the most harmful to individuals, and to society. In their multi-criteria ranking process, they found that psilocybin is the least harmful of them all.

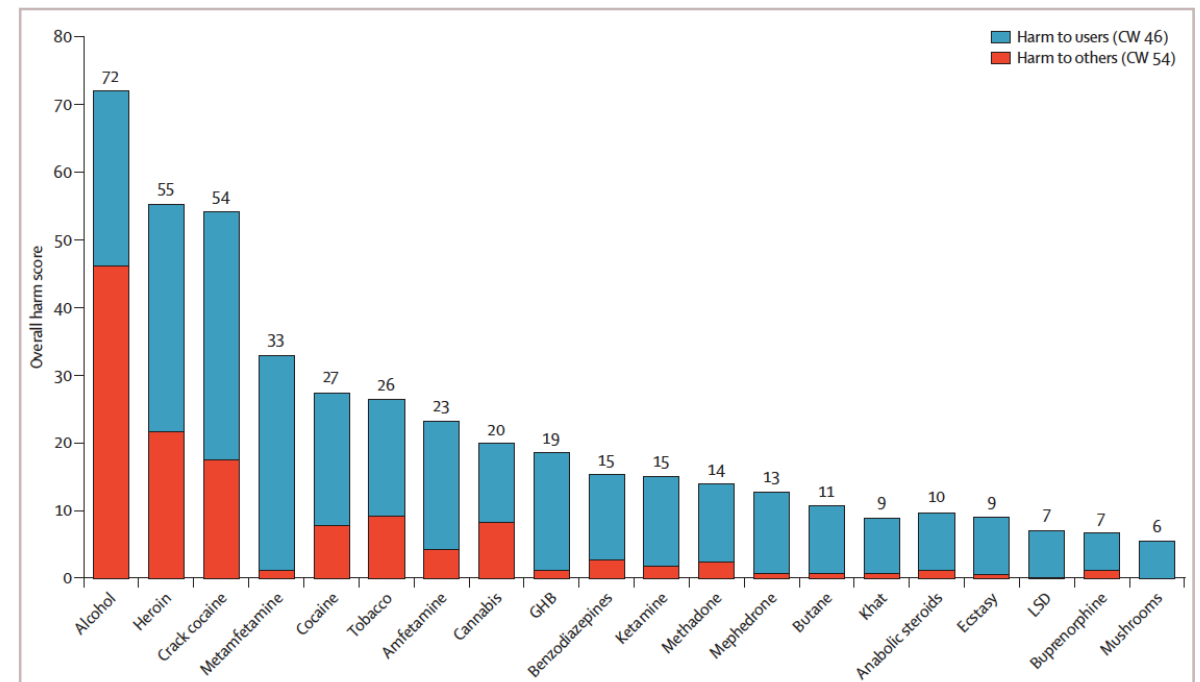
The United Nations' reason for making psilocybin illegal is because they argued that the substance is dangerous, addictive, and of no medical value.

This study, and anecdotal reports from decades of use in the underground community, show that psilocybin is not harmful, if used in the correct way. The clinical trials show that it does have medical value. But is it addictive?

Addiction risk:

Sugar is more addictive than psilocybin.

Substances like alcohol, nicotine, cocaine, and sugar work on pleasure-seeking dopamine system in the brain.



Nutt, DJ., King LA. & Phillips, LD. 2010. Drug harms in the UK: a multicriteria decision analysis. *Lancet*. Vol 376 (9752): 1558-1565.

Psychedelics like psilocybin work on the serotonin system in the brain, and is not associated with addictive behaviours.

What are the harms?

The main risk with larger doses of psilocybin is that a person might become distressed or agitated during a session, and might harm himself or someone else in the process. This is why trained supervision is key to successful therapy, and mitigates this sort of risk.

A psychedelic experience can be a bit like losing touch with reality for a while. Some find this distressing, and some don't. Researchers at Johns Hopkins found that about one in three people who have tried deep-dose psilocybin sessions, have described a 'difficult' or 'challenging' experience. But most of them also said that these were deeply meaningful experiences and explained their positive responses to the dosing session afterwards.

Non-Toxic:

It isn't possible to ingest enough of a psychedelic to have a toxic response. With too much alcohol, you have a toxic response to the substance: you will vomit, stop forming memories (the 'black outs'), and eventually pass out.

Taking a bigger dose of psilocybin just means a more intense psychological experience. It has no toxic impact on organs.

The side effects:

Some of the side effects of longer-term psychedelics use include: a tendency towards anti-establishment thinking (which is probably why they were so threatening to the Nixon administration's war agenda in the 1960s); heightened religiosity and meta-physical thinking; a tendency towards the evangelical.

It also comes with heightened empathy, a sense of connection with self, others, and the universe, and heightened compassion for others, humans and non-humans alike.

Opportunities for psilocybin-assisted therapy in South Africa

Psilocybin will be licensed for medical use in the United States in about five years. So it is coming to South Africa. The question is what our state regulators are doing to reschedule it for medical use. And is our medical community training itself up in how to administer this treatment. The answer to both of those questions is: no, not much, yet.

The South African Health Products Regulatory Authority (SAHPRA), formerly known as the Medicines Control Council of South Africa, is responsible for regulating medicines in this country.

Tightly restricted, or loosely restricted?

Psilocybin is a Schedule 7 substance at the moment. If SAHPRA re-schedules it to a Schedule 6 or 5 substance, this will likely mean that only lab synthesised psilocybin will be used in treatment. This will keep production of the medicine it in the realm of high-tech, well-resourced

pharmaceutical labs. It will make the drug much more expensive to roll out, and the processes of synthesising psilocybin will likely become tightly protected by intellectual property rights and patents.

This kind of scheduling is also likely to mean that only doctors can administer the therapy, which is good if the goal is to have strict best practice standards. But it might also make the supervision of the treatment process more expensive, meaning it is likely to only be accessible to people in the private health care sector.

A lower scheduling (Schedule 3 or 4) will allow people to use dried mushrooms. Even though this makes dosing less measurable and controllable, dosing doesn't need to be as precise as many other pharmaceuticals so the need for lab synthesised psilocybin doesn't need to be a bottle neck. Using dried mushrooms would mean the medicine can be grown, processed, distributed, and administered cheaply and easily. An entry-level dose of 2 gram of dried *psilocybe* mushrooms sells for about R160 to R200 at current prices, and 4 grams will cost you about R360 to R400. The greater cost will be for the therapist or counsellor who supervises the sessions.

The process does need to have medical doctors available to screen patients before treatment sessions, to make sure they're suited to it, and to see if they are on any mood

stabilising drugs that they should stop using for a few days leading up to the treatment. But the supervision of sessions themselves can easily be done by trained nurses, social workers, or even trained lay health people. The therapy sessions don't need to involve one-on-one sessions between therapist and patient. One person can supervise a larger treatment group during a dosing session, which again makes it more affordable.

In a country where about 2 out of 3 people who need mental health treatment from the state aren't able to get it, this may be a better way to roll it out at scale. With the right regulations and industry guidelines, it is possible to do this safely.

Psychedelic-assisted therapy is already here

There are already two forms of psychedelic-assisted therapies (PATs) that are legal for medical use here, and practiced by some psychiatrists and rehab clinics.

Legal psychedelic-assisted therapies (PATs):

Ketamine (Schedule 5) is an anaesthetic that's used every day in theatres around the country. But it's also used 'off label' by psychiatrists to treat severe depression and suicidality. Doctors administer this treatment using an IV infusion.

Ibogaine (Schedule 6) is a naturally occurring psychedelic that a few rehabilitation clinics use for treating substance dependence. This is a complicated story, and there isn't scope for expanding on it in this talk. But this treatment does need very careful medical screening and supervision. SAHPRA still has to draw up the regulations for how this substance is used, so there's an accountability grey area here which increases the risks associated with this treatment.

Soon-to-be-legal PATs:

Psilocybin will be legal for medical use as a depression treatment in the United States in about five years.

MDMA, what most people know as the party drug Ecstasy, isn't strictly a psychedelic, but its therapeutic potential is very similar to psilocybin, and clinical trials in the States have shown how effective it is for treating post traumatic stress disorder (PTSD). The FDA has declared this a 'breakthrough medical technology', meaning it is being fast-tracked through the regulatory process there and is likely to be legal for use in the US in about 3 years' time.

Other psychedelics which have similar therapeutic potential to psilocybin include DMT (administered as a form of tea known as ayahuasca, or smoked), and mescaline from the San Pedro cactus and peyote.



Civil disobedience and life-saving medicine

Here's a hypothetical scenario: you're walking down the street, and you find someone, a diabetic, who is in a medical emergency, and needs insulin urgently. There's a pharmacy nearby, but it's closed. Would you break into that pharmacy to get some insulin, even if you know you're breaking the law by doing so?

There's a small community here in South Africa who have answered this ethical conundrum for themselves. They believe that psilocybin is a life saving medicine, and that it's their moral responsibility to help people access it. So they are deliberately and wilfully breaking the law to do so. They see it as an act of responsible civil disobedience.

The Psychonauts is a serialised audio-book that I've been working on for the past two years, released chapter by chapter on a podcast platform. It brings together these stories in the underground psilocybin community here, weaves in the science from the clinical trials abroad, and

looks at what's happening on the legal front here that may eventually decriminalise or medicalise psilocybin in South Africa.

This article is the transcript of a 15 minute talk by science writer Leonie Joubert at the State of Dis-Ease conference held in Johannesburg from 25 to 28 March 2019. Leonie has spent the better part of two decades writing about climate change, energy policy, invasive species, and the hunger-obesity poverty-paradox in our cities. She's now turning her pen towards two new journalistic 'beats': the likely decline in mental health as communities face the existential threat of societal breakdown and climate-capitalism collapse, including how psilocybin-assisted therapy can help with this; and 'solutions' journalism, because she's tired of spending her days doing what feels like a doomsday audit as the climate emergency unfolds over the course of her lifetime. She is based in Cape Town, South Africa.