Scientific Research Publishing

Open Journal of Medical Psychology, 2023, 12, 150-171
https://www.scirp.org/journal/ojmp
ISSN Online: 2165-9389
ISSN Print: 2165-9370

Psychedelic Drug Therapy for Mental Disorders?

John R. Rossiter

School of Psychology, Charles Sturt University, Wagga Wagga, Australia
Email: jrrossiter14@gmail.com

How to cite this paper: Rossiter, J.R. (2023) Psychedelic Drug Therapy for Mental Disorders? *Open Journal of Medical Psychology*, **12**, 150-171.
https://doi.org/10.4236/ojmp.2023.123010

Received: March 29, 2023
Accepted: July 24, 2023
Published: July 27, 2023

Abstract

Objective: Psychedelic drug therapy is banned in all countries of the world except Australia, where the government regulatory watchdog, the Therapeutic Goods Administration, is planning to allow approved psychiatrists, as of July 1, 2023, to prescribe psilocybin to treat depression and MDMA to treat post-traumatic stress disorder, a move precipitated by the U.S. Food and Drug Administration's designation of these two drugs as "breakthrough therapy". The objective of the present article is to demonstrate that the evidence on which the FDA and then the TGA relied is irretrievably flawed and should be dismissed. **Method:** Expert review of psychedelic therapy clinical trials and specifically of the methodology and measures used. **Results:** The present review demonstrates that the studies the U.S. FDA and the Australian TGA relied on to approve these two psychedelic drugs for therapy are irretrievably flawed. All future trials will follow the same procedure and are therefore bound to be flawed as well. **Conclusions:** Psychedelic drug studies have so far provided no trustworthy evidence of their effectiveness for treating mental disorders and are not likely to produce this evidence in the future. Psychedelic drug therapy is in any event impractical because of its specialized training requirements and very high treatment costs. It is also dangerous because false publicity about its effectiveness will almost certainly lead to unsupervised self-dosing with drugs that not only are illegal but have an unacceptably high addiction rate.

Keywords

Psychedelic Drugs, Psychotherapy, Mental Disorders, Clinical Trials

1. Introduction

The psychedelic drug therapy movement is getting out of control in western societies. I will touch on the situation in the U.S. where the movement started but

focus mainly on my home country of Australia because it is about to become the world's first country to approve the use of certain psychedelic drugs to treat specific mental disorders. There was already a high level of usage of psychedelic drugs in both countries before the recent publicity about them (see Table 1). The single drug for which the U.S. has higher usage than in Australia is recreational marijuana, which has been legal to possess for personal use in Colorado and in the state of Washington since 2012, and is now, as of March this year, legal in 21 states plus Washington, D.C. [1]. The table shows the medical names as well as the common "street names" of the major psychedelic drugs. Although they are medically classified as either hallucinogens, psychostimulants, or anesthetic dissociatives, they are all in effect psychedelic because they can induce the hallucinatory perceptual experience known as "tripping".

Two major trends have coincided to produce the current situation. The first trend is the rise in depression and anxiety symptoms reported by adolescents, girls much more than boys, since 2011 when Internet-enabled phones became ubiquitous and social media became the largest information source among young people. In the U.S. by 2016, the percentage of 12 to 17-year-old boys diagnosed as having one or more depressive episodes in the past 12 months had risen to 6.5%, or about one in 15, whereas among adolescent girls the percentage had risen to 19.5%, or almost one in five [2]. The same trend, this time perceptual rather than diagnosed, was seen on college campuses where, in a 2014 survey, 27% of men and 33% of women reported experiencing at least one time in the past year where they felt so depressed that it was difficult to function, and

Table 1. Past year usage of psychedelic drugs in the U.S.A. and Australia in 2019. Figures are percentages for ages 12 and older in the U.S. and 14 and older in Australia.

Class and Type	Common Street Names[a]	U.S.A. (2019)[b]	Australia (2019)[c]
Hallucinogens			
Cannabis	Marijuana, Weed, Grass, Dope, Pot	17.5%	11.6%
Psilocybin	Magic Mushrooms, Mushrooms, Caps	0.9	1.6
LSD	Acid	0.9	1.6
Psychostimulants			
Cocaine	Coke, Crack, Rocks, Blow	2.0	4.2
Methamphetamine	Ice, Meth, Chrystal, Speed	0.7	1.3
MDMA	Ecstasy, E, Molly	0.9	3.0
Anesthetic Dissociatives			
Ketamine	K, Special K, Adam, Pills	0.9	0.9
PCP	Angel Dust, Purple Rain, Zombie	0.1	0.1

[a]Sources for street names: Addiction Center [65] and Newport Academy [66]; [b]Substance Abuse and Mental Health Services Administration [67]; [c]Australian Institute of Health and Welfare [68].

40% of men and 57% of women reported suffering from bouts of debilitating anxiety [3]. Australia underwent the same gender-skewed increase in perceived depression and anxiety from 2011 onwards, a wave of perceived mental illness that continues to overwhelm family physicians, school counselors, and other psychologists [4] [5] [6]. Even more shocking was the report that there had been "an alarming rise in children's self-diagnosing themselves as mentally ill via Google then competing with peers over who is worse off", with children as young as eight complaining of depression, anxiety, OCD, and ADHD, obviously without understanding what these terms medically mean [7].

The second and more recent trend is the overenthusiastic publicity circulating about psychedelic drugs as a treatment for mental disorders. This began early in 2019 with the news from the U.S., picked up immediately in Australia, the U.K., and Canada, that there is "emerging evidence" that psychedelic drugs administered with psychotherapy can alleviate or even cure mental disorders—especially those disorders that have failed to respond to conventional treatment [8] [9]. This claim, aside from being demonstrably false, as I will show in this review, ignores the reality of the horrific *addiction rate* of psychedelic drugs. Governments and the media tend to regard psychedelic drugs—unlike the so-called hard drugs such as heroin, methamphetamine, and cocaine—as relatively harmless. The reality is otherwise. Users of the most popular psychedelic drug, marijuana—so-called recreational cannabis, which contains the hallucinogen THC, as opposed to so-called medicinal cannabis, cannabidiol, which does not—face an addiction rate of 18%, while those who use others such as psilocybin, LSD, MDMA, and ketamine face at least a 12% addiction rate, the same as the addiction rate of alcohol (see **Table 2**). Addiction to almost any drug brings with it crushing treatment costs and often enormous familial distress. Against this backdrop, it is hard to see how anyone could be in favor of using psychedelic drugs to treat mental disorders.

Table 2. Estimated addiction[a] rates among users of various drugs (U.S.A., age 12+, 2004[b]).

Heroin[c]	68%	Pain relievers	12%
Cocaine	28	Alcohol	12
Marijuana	18	Hallucinogens	12
Sedatives	18	Tranquilizers	11
Stimulants	16	Inhalants	10

[a]Addiction is defined [26] as abuse (regular use in what medically would be regarded as a harmful drug dosage) or dependence (repeated use of the drug to overcome withdrawal symptoms, typically with the need for an ever-increasing dosage). [b]These user-based addiction figures are from the 2004 edition of the U.S. *National Survey of Drug Use and Abuse* reported in [26] and are valuable because in later years the survey changed to measuring addiction rates not among users but among the entire age 12 and older population. [c]Heroin is classified as an opiate rather than a psychedelic drug. However, heroin is quite frequently mixed by addicts with cocaine, a euphoric, in what is known as a "speedball" [65].

The surge in interest in psychedelic drug therapy arose because the U.S. Food and Drug Administration, in 2019, after assessing the studies reviewed later in the present article, decided to award what is called "breakthrough therapy" status to psilocybin (magic mushrooms) for treating resistant major depressive disorder, and MDMA (ecstasy) for treating resistant post-traumatic stress disorder, and to allow clinical trials of these two specific applications to proceed under the strict conditions that the trials be conducted in a clinical setting with a psychiatrist qualified in pharmacology and a psychologist qualified in psychotherapy present [10]. The U.S. Congress has introduced a bill urging the FDA to greatly extend the number of psychedelic drugs designated as "breakthrough therapies", but so far in the U.S. the above two, only, have been approved, and then only provisionally pending further evidence [11]. In Australia, however, the equivalent body to the FDA, the Therapeutic Goods Administration or TGA, has gone much further by issuing the ruling that, beginning July 1, 2023, psychiatrists who qualify via its Authorized Prescriber Scheme will be permitted to use these two psychedelic drugs, psilocybin and MDMA, to treat depression and post-traumatic stress disorder, respectively [12], with no requirement, by the way, that this treatment be accompanied by psychotherapy.

Researchers worldwide have not waited. According to the law firm King and Wood Mallesons, more than 600 psychedelic drug trials have been completed throughout the world and another 300 are reportedly underway [13]. In Australia alone there are apparently close to 30 psychedelic drug trials in progress – seven of them being funded, incredibly enough, by the very department to which the TGA reports, the Department of Health and Aging, through its Medical Research Future Fund [14], and another 20 or so being funded privately by venture capital groups to be conducted by the medical research company Ingenu [15]. These trials, government-funded and privately funded, go way beyond the two drugs and two disorders approved for trial by the FDA and being considered by the TGA. Australia is favored for these trials because, unlike in the U.S. with the FDA, there is no application fee payable to the TGA for the trial of new drugs and the approval process is comparatively fast. What could be behind this rush to support illegal drugs? As always, follow the money. As soon as the TGA's decision was announced, Australian investors reacted by driving up the stock prices of psychedelic drug companies by as much as 88% [16].

The practical purpose of the present article is to try to persuade the Royal Australian & New Zealand College of Psychiatrists, the principal body regulating psychiatrists in Australia and neighboring New Zealand, to step in and stop the trials and reverse the TGA's decision, which it could do by instructing its member psychiatrists not to participate. This will require some persuading because the RANZCP has already come out in favor of psychedelic drug trials. In July 2022, the RANZCP's Committee for Evidence-Based Practice and Committee for Research issued a clinical memorandum that tentatively accepted the early findings on psilocybin and MDMA while urging more research on these and other psychedelic drugs [17]. The present article should also serve as a warning to the

U.S. Food and Drug Administration to not go down the same path as the Australian TGA.

The academic purpose of this article, on the other hand, is to demonstrate to everyone, for the first time in the literature, that the evidence the FDA relied on to approve the psilocybin and MDMA trials is irretrievably flawed and should be dismissed. The new trials in Australia, and in the U.S. as well as in other westernized countries, will make the same methodological and measurement mistakes and should be stopped.

The arguments for stopping the trials are arranged under two main headings: firstly, dismissal of the key trials that the FDA relied on for approving psilocybin with psychotherapy for treating resistant depression and MDMA with psychotherapy for treating resistant post-traumatic stress disorder; and, secondly, the impracticality and questionable ethics of transferring such treatments to private practice.

2. Dismissal of the Two Key Trials of Psychedelic Drugs for Treating Mental Disorders

I am an expert in research methodology and measurement (see, e.g., [18] [19] and most recently my article in the OJMP [20] on the measurement of bipolar disorder). In reviewing the main published clinical trials of psychedelic drugs for the present article, I was struck by the inadequacy of the research knowledge that psychiatrists and psychologists must be receiving during their training. For a similar earlier claim, see [21]. The U.S. is usually considered to be the leader in curriculum design in psychology, and whereas 95% of U.S. doctoral programs in psychology offer coursework in multivariate statistics and 92% offer a course in research design, only 61% offer a course in psychological testing, needed to understand mental disorder diagnostic measures, and just 36% offer a course in survey research methodology, the type of coursework needed to understand the basics of sampling and interviewing as used in the clinical trials [22]. And the amount of training in research methods that physicians and psychiatrists receive would be minimal to none. It should not, therefore, be surprising, as I demonstrate in this article (also see [4] [5] [20] [23]), that the quality of research in psychiatry and in clinical psychology is appallingly low—as is, consequently, the ability of researchers to evaluate their own studies and those of others.

In the next two sections, I criticize the methodology and measures used in the trials the FDA relied on to award breakthrough status for psilocybin with psychotherapy for treating resistant depression, and MDMA with psychotherapy for treating resistant post-traumatic stress disorder. I have only to dismiss these two trials because other trials, no matter what the drug or the targeted disorder, are certain to use the same flawed methodology and repeat the same measurement mistakes that these two made. Alongside the criticisms, I offer constructive advice on what should have been done by way of correct methodology and measurement (this advice is placed in parentheses throughout).

2.1. Psilocybin with Psychotherapy for Treatment-Resistant Depression

The study that most influenced the FDA's decision to allow trials of psilocybin with psychotherapy for treating resistant depression was conducted by Imperial College London medical researchers Robin Carhart-Harris and colleagues [24], apparently under the guidance of the final author, outspoken U.K. psychiatrist and psychedelics advocate David Nutt [8]. My criticisms of the study are presented under the following subheadings: untested mechanism, incorrect placebo control, questionable psychotherapy, inappropriate sample, and the use of a non-valid outcome measure.

Untested mechanism

Psilocybin is an inactive plant-based compound found in about 200 species of mushrooms. Upon ingestion, psilocybin is quickly converted by the body to the chemical psilocin, an active compound that produces psilocybin's psychedelic effects [25] and lends it the street name "magic mushrooms" (see **Table 1**). The main active chemical in psilocin is serotonin, the same neurotransmitter that forms the basis of SSRIs, the most widely used antidepressant medication [26]. Therefore, the only mechanism through which psilocybin could prove to be superior to a serotonin-releasing antidepressant is one that does what an antidepressant cannot do, which is produce a state of euphoria, which in turn might block depression symptoms (see the account of response blocking in compound classical conditioning in [23]). The problem is that psilocybin does not always elicit euphoria, and among first-time users it is likely to result instead in panic and paranoia. Moreover, the euphoria would have to be shown to be experienced during the arousal of depression symptoms if it were to act as a depression blocker. Finally, note that blocking is not a cure and so the patient would have to continue to take the drug when depressive episodes arise.

Carhart-Harris *et al.* did not test the mechanism. To do this they would have had to record verbal protocols of exactly what went on for each participant during the psilocybin dosing sessions, then analyze the recordings to see whether, consistent with the hypothesized mechanism, depression symptoms arose and were blocked by euphoria. With only 12 participants in Carhart-Harris's study, this analysis would have been relatively easy to conduct. (None of the published reports on psychedelic drug trials that I have read has attempted to document and verify the mechanism. This type of mediating process test is standard practice in experimental social psychology and is necessary if other processes are to be ruled out and a causal case proven.)

Incorrect placebo control

The reason that Carhart-Harris *et al.*'s study should be described as a "study" rather than a clinical trial is that there was no placebo control group. Without a placebo control, researchers cannot know whether an apparently favorable effect of a drug on a mental disorder was due to the drug working chemically as a drug, or whether it was in whole or part due to it working psychologically as a

placebo, or even whether the effect was a "Hawthorne effect" due entirely to the extra attention that these patients received. (Strong placebo effects in placebo-controlled trials are the reason why most trials of psychiatric drugs fail, and why pharmaceutical companies these days are so reluctant to invest in developing new ones; see [20].)

Questionable psychotherapy

Another possibility is that any effect on depression in psychedelic drug therapy could be the result of the psychotherapy rather than the drug, or even the result of the mere presence of a psychotherapist. The mere presence explanation is the more likely in Carhart-Harris *et al.*'s study because psychotherapy was not provided in any usual sense. In Carhart-Harris *et al.*'s study, the two psychiatrists who were present throughout the psilocybin dosing sessions were instructed to adopt "a non-directive, supportive approach, allowing the patient to experience a mostly uninterrupted inner 'journey'" (p. 622) and although they were allowed from time to time to ask the patient how he or she was feeling, there were told not to comment on these feelings. Many would interpret this as social support or mere handholding rather than psychotherapy. (There is no evidence that psychotherapy—unless it is strictly controlled behavior therapy from a specialist in that field—works any more effectively than social support; see [23].)

Inappropriate sample

Major depressive disorder, MDD, either unipolar or as a phase of bipolar disorder, is characterized by major depressive episodes. Unlike so-called dysthymia in which there is a persistent low mood lasting for at least a year in children and adolescents and two years in adults, major depressive episodes, MDEs, are attack waves of depression that, according to the DSM-5 mental disorder diagnostic manual [27], need only last for two weeks. Between MDEs there are periods of virtually full recovery known as remission periods, which may last for several years, especially if the patient continues to take a maintenance dose of antidepressant medication [26]. In Carhart-Harris *et al.*'s study, it is most unlikely the participants were suffering from a major depressive episode. They were all outpatient volunteers well enough to attend the lengthy screening session, psychedelic drug briefing session, dosing sessions, and follow-up interviews, and at most could have been only moderately depressed. (Researchers should note here—see especially [4] —that a treatment-caused reduction in mild or even moderate symptoms does not mean that the treatment will alleviate *severe* symptoms. Rather, there seems to be a severity threshold whereby symptoms below it produce no or minimal dysfunction and those above it produce marked dysfunction. Consistent with this, note that the DSM-5 [27] requires the clinician to make a threshold yes-no judgment as whether the symptom is currently severe enough to cause dysfunction, and if it's not it should not be recorded as a symptom.)

Further invalidating Carhart-Harris's study is the realization that almost half of the participants, five out of the 12, stated during screening that they had *previously tried* taking psilocybin—apparently unsuccessfully (p. 623, their **Table**

1). Their inclusion not only lowers the study's chances of finding a favorable effect for psilocybin but also renders the sample inappropriate because it does not consist only of first-time triers. (Note that I am not criticizing the study for employing a small sample. As I hinted earlier with regard to testing the suspected mechanism, researchers can learn a lot from small samples if the patients are individually monitored, with their verbalized feelings recorded and a record kept of medication taken.)

From a research standpoint, it must emphasized that the above three problems are fatal flaws, any one of which invalidates Carhart-Harris *et al.*'s study. (What most researchers fail to understand is that you cannot compensate for a fatal flaw even if the other parts of the methodology are sound. As soon as you make the first mistake, the study is ruined.) However, the researcher could do everything right and then de-validate the study with the choice of a non-valid outcome measure, as explained next.

Non-valid outcome measure

Carhart-Harris *et al.* used four different depression measures at various stages of the study: two were clinician-rated, the Hamilton Rating Scale for Depression (HRSD, also called the HAM-D) and the Montgomery-Asberg Depression Rating Scale (MADRS), and two were patient-rated, the Beck Depression Inventory (BDI, version not stated) and the self-rated version of the Quick Inventory of Depressive Symptoms (QIDS-SR). Their use of multiple outcome measures represents a common failing in clinical trials. The use of multiple outcome measures leaves researchers vulnerable to accusations of conducting a "fishing expedition" and possible "p-hacking" for significant results. Indeed, this practice is encouraged in the case of psychedelic drug research by the fact that the FDA's "breakthrough therapy" designation requires merely a substantial improvement over available therapy on just *one* outcome measure (see [10], online p. 1). A related problem is that researchers mistakenly believe that all measures of a given construct that have been "psychometrically validated" are interchangeable and will produce the same finding. However, scores on depression measures correlate at an average of only about r = .65, a shared variance of just over 40%, which means that the almost 60% unshared variance will cause the scores from the measures to diverge substantially. (The only solution is to choose the measure whose content best fits the construct, and use only that one; see Rossiter [28].)

As it happens, none of the depression measures that Carhart-Harris *et al.* used is valid according to the core criteria for major depressive disorder in the DSM-5 (see [4] for a review of this and other problems with the first three of these measures, the HRSD, MADRS, and the original BDI, which differs from the newer version, the BDI-II). The fourth depression measure, the QIDS-SR [29], which the researchers said they chose as their primary outcome measure because at 16 items it was relatively brief and could be administered for follow-up purposes by phone (p. 622), also has fatal de-validating problems. Basically, the QIDS fails to properly measure the two essential-but-alternative symptoms of depression and at the same time it measures too many extraneous symptoms. A

more detailed criticism of the QIDS, here revealed by the present author for the first time in the literature, can be found in Table 3.

In summary, the evidence for the ability of psilocybin to alleviate major depressive disorder is not trustworthy and should be ignored. I note here that Carhart Harris *et al.*, again with David Nutt, conducted a further depression study [30] that compared psilocybin with an SSRI antidepressant, escitalopram in this case, but this study had the same mistakes as their 2016 study: use of the QIDS as the outcome measure, no testing of the mechanism, no placebo group, and invalidation of the study as a trial because some of the participants—8/30 in the psilocybin group and 8/29 in the SSRI group—were previous users of psilocybin.

2.2. MDMA with Psychotherapy for Treatment-Resistant Post-Traumatic Stress Disorder

The only study cited by the FDA in support of MDMA plus psychotherapy for treating resistant post-traumatic stress disorder, PTSD, is an amalgamation of six different trials in a meta-analysis conducted by Feduccia *et al.* [31]. This meta-analysis should be dismissed. (Meta-analysis cannot be trusted in the soft sciences such as psychology or psychiatry because the measures differ widely across studies and the results from methodologically poor studies are averaged in with those from better ones; see especially Eysenck [32].) Accordingly, I will

Table 3. Criticisms of the Quick Inventory of Depressive Symptomatology (QIDS). See Rush *et al.* [29] for the QIDS self-rated and clinician-rated questionnaires and details of scoring.

Commendable features
1) The QIDS asks about symptoms experienced "for the last seven days"—unlike the longer 2-week period in other depression measures such as the Hamilton, Beck, and the MADRS, and as specified in the DSM-5. The QIDS is therefore more likely to be able to capture an *ongoing* major depressive episode. 2) Easy to understand verbal-categories answer scales instead of the clinically meaningless numerical rating scales.
De-validating problems
1) The QIDS does not accurately measure the two essential but alternative DSM symptoms of a major depressive episode, MDE, which are severely depressed mood *or* persistent anhedonia. The QIDS uses "sadness" in place of depressed mood, and for anhedonia it uses "loss of interest" instead of loss of interest *and* enjoyment, which is the essential feature of anhedonia. 2) It measures the symptoms' frequency rather than their severity. 3) It fails to record whether the symptoms produce significant dysfunction. 4) It asks about 14 other symptoms that are not essential for depression, and it uses a complex scoring system in which only nine of the 16 items, mostly representing secondary and optional DSM depression symptoms, count toward the total score. This means, for example, that a fairly high score, such as the average 19 out of the maximum of 27 (nine items scored numerically from 0 to 3) reported at baseline in Carhart-Harris *et al.*'s study, could be obtained with high scores on the optional symptoms and zero or sub-threshold scores on the essential symptoms.

focus instead on the single most recent clinical trial. This was a clinical trial led by University of California, San Francisco psychiatry researcher Jennifer Mitchell [33]. Mitchell [34], writing in the February issue of *The Scientific American*, claimed this to be the first definitive "phase 3" —that is, fully valid and large-sample reliable—trial of MDMA for treating PTSD but, as I will show, it is far short of this. Her work is discussed below, using the same subheadings as previously.

Untested mechanism

MDMA, commonly known as "ecstasy" in pill form or "molly" in the less often used crystal form (again see **Table 1**), is a man-made, laboratory-synthesized amphetamine and hallucinogen widely used as a "party drug" because of its energizing and euphoric effects [35]. Ecstasy is rarely physically addictive [26] but a substantial number of young people become *psychologically* addicted, with many believing that they can't have a good time at dance clubs or rock music concerts without it, so that it is reportedly [36] the second most popular drug at these venues after recreational cannabis. However, its side effects—prevalent among first-time users of MDMA—include nausea, panic attacks, and paranoia, and just as with the highly addictive methamphetamine "ice", possible death from an overdose.

MDMA, like psilocin, releases serotonin in the same way that SSRI antidepressants do [35]. The hypothesized mechanism in taking MDMA while suffering from PTSD is that the release of serotonin allows "calm re-processing" of the traumatic memories in what would amount to the start of a "fear extinction" process; see Oehen *et al.* [37] and also see [5]. The problem is that there is little likelihood of trauma memories arising during the MDMA dosing unless they are actively prompted by the therapist, and the type of psychotherapy Mitchell *et al.* used does not allow prompting. Mitchell *et al.* did not take verbal records of the sessions and therefore could not prove that "calm re-processing of traumatic memories", let alone extinction of fear, took place.

Placebo control

Mitchell *et al.*, unlike Carhart-Harris *et al.* in the psilocybin study, did employ a placebo control group. We are not told what the placebo was, but it was probably lactose presented in the type of capsule used for the MDMA, because one of Mitchell's co-researchers was U.S. psychiatry researcher Michael Mithoefer, who used lactose as a control in the early trials included in Feduccia *et al.*'s meta-analysis. Moreover, the placebo was introduced correctly in that the control group received exactly the same instructions as the experimental group.

Questionable psychotherapy

Mitchell *et al.*'s study was accompanied by psychotherapy, as required by the FDA. However, the preparatory sessions for the psychotherapy could be seen to bias the study favorably. Firstly, the preparatory sessions were conducted to facilitate the formation of a "therapeutic alliance", a therapist-patient relationship that has been shown to increase the effectiveness of psychotherapy [38] but which

cannot be guaranteed to form in everyday clinical practice [39]. Secondly, the preparatory sessions predisposed the participants toward behaving in line with the researchers' expectations because they were "provided guidance on *how to respond* to the memories and feelings that could arise during treatment" (p. 1034, emphasis added). This preparatory advice predisposes the participants in the drug group and the placebo group toward reacting in the way that the researchers wanted them to. (It would be more realistic to omit the preparatory sessions and allow the participants to react naturally.)

Mitchell *et al.* employed 2-person teams of psychotherapists to deliver the psychotherapy (and presumably a physician was present as well in case any adverse reactions arose in the dosing sessions, although this was *not* stated in the methodology). The psychotherapists had taken part in Mithoefer's extensive training program on "MDMA-assisted psychotherapy", which consisted of an online course of 15 hours duration, a training program extending over five days, followed by three days of what was described as "experiential learning" —which might mean that the psychotherapists had to take the drug themselves, which would be a bad idea in general, though a good one from an educational standpoint—and one day of role-playing (p. 1035). It is highly unlikely that other researchers would be willing and able to duplicate this. (Methodology must be replicable, otherwise it is of no value.)

Inappropriate sample

A critical problem with the sample was that Mitchell *et al.* allowed almost a third of the participants to be previous users of MDMA. This not only means that these previous users would be much more likely than novice users to experience pleasant effects from MDMA but also, as with the two psilocybin studies, that the trial is not a valid trial for those who have tried the drug before.

Then there is a problem with sample exclusions. A "phase 3" clinical trial is supposed to have a sample size of at least 300 participants [40]. Mitchell *et al.* began with 345 voluntary participants who apparently met the DSM-5 criteria for current PTSD lasting for at least the past six months, but then excluded 214 of them, 178 of whom, or half the starting sample, because they had a prior diagnosis of psychotic depression, or bipolar disorder, or alcohol or substance abuse, or an eating disorder (see p. 1034 and their Figure 1 on p. 1027). These exclusions, besides causing the sample to fall below the 300 required for a phase 3 trial, would rule out just about everyone with serious PTSD. (Again, I would like to remind researchers that any one of the above flaws invalidates the study before we even consider the measures. Conversely, a study could be methodologically sound in all respects but be ruined by using a non-valid outcome measure.)

Non-valid outcome measure

Mitchell *et al.* employed two separate outcome measures to gauge the effectiveness of MDMA treatment of PTSD—the Clinician-Administered PTSD Scale for DSM-5 (CAPS-5 [41]) and the Sheehan Disability Scale (SDS [42]) —and therein lies another problem. The CAPS-5 is a clinical interview in which the clinician first must verify traumatic event exposure and then ask the patient

about 20 possible symptoms that may have been experienced since, whereas the SDS is a separate self-report measure that asks the patient to rate the extent to which the symptoms overall have disrupted work or schoolwork, social life and leisure activities, and family life and home responsibilities. However, Mitchell *et al.* analyzed the CAPS-5 and the SDS scores independently instead of combining them at the individual patient level, which would be necessary to show that symptom severity and dysfunction are related. This immediately invalidates the PTSD outcome assessment. (The correct method is to ask the patient about symptoms and then ask which symptoms, if any, caused dysfunction—as is done in the SCID-5-CV clinical interview for the DSM-5; see [43].)

The two measures in any case have fatal internal validity problems that are revealed here for the first time. The CAPS-5 questionnaire requires ratings of 20 symptoms (see **Table 4**). However, only three of them, called intrusion symptoms, are unique to PTSD—namely, intrusive memories of, or flashbacks of, or nightmares about, the event—and only *one* of these three symptoms experienced at a dysfunctional level is required for a DSM diagnosis of PTSD [27]. Thus, total CAPS-5 scores mean nothing because they represent the addition of severity scores across all 20 items, which could result in a high total score without the patient being rated as severe on one of the above-mentioned intrusion symptoms. (Researchers should note that the other widely used measure of PTSD symptoms, the PTSD Symptom Scale or PSS, has the same problem; see

Table 4. Criticisms of the clinically administered PTSD Scale, version 5 (CAPS-5).

Commendable features
None.
De-validating problems
1) There have now been seven different versions of the CAPS questionnaire—two based on the DSM-III (CAPS-1) and CAPS-2), three based on the DSM-IV (CAPS-DX, CAPS-SX, and CAPS-CA), and now the two based on the DSM-5 (CAPS-5 and a children's version, the CAPS-CA-5). These differ in their items and scoring and are *not* interchangeable, yet researchers treat them as though they give the same results. 2) The original 30-item CAPS-5 questionnaire is often used as a short 20-item version that does not verify traumatic event exposure as required by the DSM-5. 3) The CAPS-5 lacks the DSM-5 requirement that PTSD symptoms must be present for more than 1 month. 4) It also fails to ask about the effect of the symptoms on occupational functioning and social functioning, as required by the DSM-5. Instead, researchers typically and incorrectly use a separate measure such as Sheehan's (1983) Sheehan Disability Scale. 5) The 20 items include five symptom items labeled as *intrusions* but only one of the three (B1, B2, and B3) is required by the DSM-5. There are two avoidant behavior items, seven negative mood items, and six negative behavior items—but these are not specific to post-traumatic stress disorder and should not be counted. 6) The 20 symptoms' severity scores are added, which means that a person could have a high total score without having any of the three intrusion symptoms at a functionally severe level.

[5].) The Sheehan Disability Scale involves a similar mistake. Severity is totaled across all three areas of dysfunction when all that is required is marked dysfunction—which would be a score of 7 or higher out of maximum of 10—in one area.

In summary, the research on which MDMA was approved for treating resistant PTSD is hopelessly flawed and should be ignored. (This is also as good a place as any to point out that statistical tests applied to data from faulty measures are, for this very reason, meaningless and misleading. You should not even look at the statistics until you are convinced that both the methodology and the measures in the study are sound.)

2.3. Ketamine for Depression?

Ketamine, typical street names "K" or "Special K", is classified as a so-called anesthetic dissociative (again see **Table 1** earlier) but it is also a hallucinogen. At low doses it produces disinhibition, relaxation, and often euphoria. But at higher doses it can produce the trance-like state known as a "k-hole", characterized by a lasting out-of-body feeling and vivid dreams often described as a religiously toned "near-death" experience, which is why it is sometimes called "the God drug" [44]. Long-term use can lead to addiction, permanent damage to cognition and memory, and even death by overdose [45]. Ketamine can also interact negatively with conventional psychiatric drugs including MAOI antidepressants and Valium-type anti-anxiety medication [45], which many young people take on prescription. Not surprisingly, then, ketamine is prohibited in all countries for anything other than medical use as a painkiller or veterinary use as an anesthetic.

Unlike psilocybin, ketamine is not listed as a "breakthrough" drug for treating depression. But studies of ketamine for this purpose are going ahead anyway. The most recent that I have come across is a U.S. study by Oliver *et al.* [46], which is worth discussing in this article because it again reveals the fatal methodological and measurement mistakes that plagued the previous studies. These mistakes are briefly explained below.

Untested mechanism

It is vital to note that Oliver *et al.* used intravenous (*i.e.*, injected) ketamine, which has 100% absorption by the body, compared with 45% to 50% absorption by the FDA-approved esketamine nasal spray, and just 16% to 20% absorption when ingested in pill form, the most common recreational method of using ketamine [45]. Oliver *et al.*'s heavy dosing of participants with ketamine is unrealistic and basically rules out the study on external validity grounds alone. However, internal validity is also a concern because the chemical process by which ketamine is thought to operate is not well understood [45]. Then there is the psychological mechanism. For ketamine the mechanism should be the same as with psilocybin, whereby euphoria would have to emerge to block depression symptoms. However, euphoria is unreliably elicited by ketamine, especially if the ketamine taker is dissociative and halluci-

nating [45].

Oliver *et al.* did not check for either the arousal of depression symptoms or for the euphoria that had to follow.

Incorrect placebo control

In Oliver *et al.*'s study, as in Carhart-Harris *et al.*'s studies discussed earlier, there was *no* placebo control group. The researchers therefore could not possibly conclude that ketamine worked to reduce depression. In fact, if you look at their Figure 1 (p. 3) you will see that the reduction in depression scores could be entirely accounted for by patient dropout. Whereas depression symptoms a year after treatment had fallen by 30%, there were only 138 out of the original 432 patients, or 32%, left in the trial at the end—in other words, Oliver *et al.*'s ketamine study had a massive 68% dropout rate. It might be speculated that those who stayed in were likely to have been those for whom the treatment seemed to work, whereas those who dropped out may have experienced no change in, or even a worsening of, depression symptoms.

Questionable psychotherapy

There was no psychotherapy. This is despite psychotherapy—particularly the elaborate form known as cognitive behavior therapy, CBT—being claimed to be essential to ketamine therapy's success [47].

Inappropriate sample

The sample in Oliver *et al.*'s study comprised "ambulatory" outpatients (p. 2) able to attend the lengthy dosing sessions. This makes it unlikely they were suffering from a major depressive episode at the time. A further and almost incredible de-validating methodological step in Oliver *et al.*'s study was the inclusion requirement (see p. 2) that participants had to have had at least one infusion of ketamine *prior* to the start of the study. This means that it was not a trial for any of them.

Non-valid outcome measure

Oliver *et al.* used two outcome measures: the Brief Patient Health Questionnaire (specifically the 9-item PHQ-9 [48]) to measure depression, and the General Anxiety Disorder questionnaire (specifically the 7-item version known as the GAD-7 [49]) to measure anxiety, which was only of secondary interest in Oliver *et al.*'s study because the focus was on depression. These two measures, however, incorporate too many symptoms that are not specific to depression in the PHQ-9 or to anxiety in the GAD-7 (see **Table 5**). The two measures have since been shortened and combined to form a third measure called the PHQ-4 [50]) but there are major problems with all three measures. These are summarized in the lower half of the table. (Valid and much more efficient measures can be found in the present author's DEP-6 and ANX-8 questionnaires [4] [5].)

In summary, there is no credible evidence to show that ketamine – even when infused, a procedure that few clinicians are going to bother with – is effective in treating resistant depression.

Table 5. PHQ-9 and GAD-7 items and how they were combined and converted to the PHQ-4.

PHQ-9	GAD-7	PHQ-4
1) Depressed mood	1) Anxious	1) Depressed mood
2) Loss of interest	2) Uncontrollable worry	2) Loss of interest
3) Under- or over-sleeping	3) Worry about everything	3) Anxious
4) Lack of energy	4) Trouble relaxing	4) Uncontrollable worry
5) Under- or over-eating	5) Restless	
6) Low self-esteem	6) Irritable	
7) Trouble concentrating	7) Afraid	
8) Under- or over-active		
9) Suicidal thoughts		

Answer scale:

"Over the last *2 weeks*, how often have you been bothered by the following problems?"

Not at all	Several days	More than half the days	Nearly every day
0	1	2	4

Devalidating problems:

1) Only the first two items in the PHQ-9 and the GAD-7 are essential symptoms. The others are not unique to the disorder according to the DSM-5. Total scores on the PHQ-9 and the GAD-7 are therefore meaningless.
2) Functional impairment, required by the DSM-5, is not measured. "Bothered by" is not sufficient evidence of dysfunction.
3) The answer scale for all three measures records frequency instead of severity. The symptoms could be prevalent but subthreshold and mild.
4) The PHQ-4 is scored wrongly. The correct scoring is affirmative answers to Q1 *or* Q2 for depression, and to Q3 *and* Q4 for anxiety.

3. Impracticality, Expense, and Risk of Transferring Psychedelic Drug Treatment to Private Practice

Trials of psychedelic drugs for treating mental disorders *assume* that psychedelic drug treatment will be transferrable to private practice. If this is not likely, then one must ask why these drugs are being put into trials at all. There are several reasons why transfer to private practice will not be likely, namely, the impracticality of the transfer, the expense to practices in administering the treatments, the cost to patients, and the danger of patients self-dosing outside the clinical setting.

3.1. Impracticality

Psychedelic-assisted psychotherapy—which the reader should have realized by now is the *other way round*, with the psychotherapy assisting the *drug* treatment—is impractical. There are supposed to be at least two clinicians present

throughout—one a psychiatrist with pharmacological training and the other a psychologist with at least a master's degree and "clinical psychotherapy or mental health counseling experience" ([51], p. 8). The reality is, however, that in Australia very few psychiatrists and psychologists work together outside of occasional university research projects, and similar separation applies in the U.S. [52]. The long-standing rivalry between the two professions is well known. The American Psychiatric Association [53], for instance, for years has referred derogatively on its website to psychotherapy as simply "talk therapy" and I've heard Australian psychiatrists using the same description. On the other side of the ledger, judging by the mental health articles published in psychology journals, most psychologists seem to believe that mental disorders do not need medication and can be treated by psychotherapy alone—witness, for example, the Australian Psychological Society's and the Australian Association of Psychologists' objection to the government's recent cutting of subsidized psychotherapy sessions from 20 a year to 10 for treating even complex mental disorders; e.g. [54]. Given the rift, I cannot see collaboration between psychiatrists and psychologists happening widely in practice.

3.2. Cost

Twin factors to be considered here are the cost of providing psychedelic drug treatment on the supply side and the cost to the patient on the demand side.

On the supply side, there are enormous costs to cover. Carhart-Harris *et al.*'s psilocybin-for-depression study, for example, required paying two psychiatrists qualified in psychotherapy to be sitting either side of the patient's bed during the two 8-hour dosing sessions and to be available to answer patients' questions after the dosing and during the 3-month follow-up period, and Mitchell *et al.*'s MDMA-for-PTSD trial required even lengthier psychiatric and psychotherapeutic involvement and on a much larger scale. Then there are the required neurological and physical exams to be staffed and paid for. Few practicing clinicians, already swamped by ever-growing demand (see, e.g. [55]), would have the resources or time to participate.

Demand for psychedelic drug treatment would be limited to the wealthy. A report in *The Australian* [56] quotes an Edith Cowan University psychologist as estimating that psychedelic-assisted psychotherapy could cost the patient as much as $15,000 U.S. for a course of treatment. And the patient would have to pay the full fee because the government's medical rebate system, Medicare, does not cover psychedelic treatments and neither do the large private health insurance companies cover it (see HIF [57], the only insurance company in Australia that has said it would). Obviously, psychedelic drug treatment would unethically discriminate against public patients.

And what if the drug treatment seems to work? Note that no one apart from a few extremists is claiming that psychedelic drugs permanently cure mental disorders, so a medically supervised maintenance program would be necessary. Al-

so, there is a dangerous alternative, as discussed next.

3.3. Risk of Self-Dosing

Self-dosing with psychedelic drugs is likely to occur in two ways. First is the fallout from the psychedelic drug trials themselves. If psychedelic drug therapy alleviates but does not cure mental disorders then sufferers will have to *re-dose* continually, and this is likely to occur under uncontrolled and unsupervised conditions, even if the drugs themselves are purchased according to the clinician's prescription. Second is the increasing and totally uncontrolled phenomenon known as *micro-dosing*, which Lea *et al.* [58] define as self-administration of a small amount of the drug every three or four days or so, on average. Lea *et al.* conducted an international online survey of micro-dosers of either psilocybin or LSD and found that nearly all micro-dosing occurs without medical supervision and involves "street supply" of the drug, which in turn carries a very large risk of taking tablets that are mixtures, such as ketamine mixed with ecstasy [44], or of unknown strength. Almost half the *micro-dosers* had been medically diagnosed with a mental disorder, most often depression or anxiety, and others had simply heard about micro-dosing on social media or from friends. One in three micro-dosers reported experiencing hallucinations or visual distortions, which are indicative of a psychotic episode, and almost half reported dysfunctional anxiety or difficulty concentrating.

The one-sidedly favorable publicity surrounding psychedelic drug treatments at present seems very likely to encourage self-dosing. This will be a likely consequence if mental disorder sufferers come to believe that psychedelic drug therapy works.

The worst-case scenario is that psychedelic drugs become regarded as safe, in ignorance of the shocking addiction rates. It is well worth reminding readers just how easy it is to get hold of psychedelic drugs these days. In fact, you can order psychedelic drugs for delivery to your home merely by posting a request on *Facebook*! According to a recent report in *The Sunday Telegraph*, the most widely read newspaper in Australia, drug dealers—typically posing, of all things, as vegetable and fruit sellers—are openly trading on the popular social media website by using code names for various drugs [59]. For example, marijuana, the most requested drug, is often codenamed "broc" or "broccoli"; LSD is called "light salad dressing" or just "salad"; and methamphetamine often goes by the name "cold" rather than its well-known street name "ice". Apparently, users simply post the word "Need" on Facebook followed by the code name of the drug they want. Although Meta, the owner of Facebook, claims to have taken down millions of drug-offering posts and banned many seller groups, demand is so strong that others or renamed previous sellers spring up immediately.

4. Conclusions

The Royal Australian and New Zealand College of Psychiatrists, as the principal

organization of psychiatrists in Australia and New Zealand, should intervene to stop the psychedelic drug trials, which should never have been allowed to get as out-of-control as they are at present. So far, the RANZCP has not stepped in and has instead taken what I believe to be an irresponsible attitude toward the use of psychedelic drugs in therapy, probably because they do not understand the problems with the research and somehow believe that psychedelic drug therapy will not interfere with conventional pharmaceutical therapy for mental disorders. The other major medical organization, the Australian Medical Association, is already on record as opposing psychedelic drug therapy [60], one likely reason being that psychedelic drug therapy would not be covered by Medicare or by private health insurance. The other relevant parties, the Australian Psychological Society, the main organization of psychologists in Australia, and the Australian Association of Psychologists, Inc., which represents mainly practicing psychologists, are likely to support the use of psychedelic drug treatment because it could mean extra business for their members, but they cannot act without the cooperation of medical practitioners to prescribe the drugs. This leaves RANZCP *psychiatrists* as the only likely suppliers of psychedelic drug therapy, and thus I am appealing to them.

Remember, there is no credible evidence that psychedelic drugs—with or without psychotherapy—are effective for treating mental disorders (I went to great lengths in this article to point this out, at the same time doubting the ability of other researchers to do so). Many health professionals are calling for "more evidence" before they decide for or against psychedelic drugs, but this is senseless when it is realized that the future trials will be making the same methodological and measurement mistakes as the earlier trials, and so, like those earlier trials, should be ignored. Moreover, psychedelic drug treatment would have to be shown to be *much* more effective than standard treatments given the enormous time and expense it requires.

Finally, what is hard to understand is why the major *pharmaceutical companies* have not stepped in to oppose the trials. Only one of the more than 80 companies developing psychedelic drug treatments is owned by a major pharmaceutical company—namely, Johnson & Johnson, which owns Janssen Pharmaceuticals, the manufacturer of a brand of esketamine nasal spray [61]. And New Zealand also has a problem with backyard manufacturing of "party pills", which are close chemical imitations of drugs such as amphetamine, tryptamine, or fentanyl designed to avoid legal prohibition [62]. In the U.S., the FDA gets about 65% of its drug testing budget from the clinical trial application fees that pharmaceutical manufacturers are required to pay when they develop a new drug and want to bring it to market [63] and the manufacturers' contribution is even greater at 96% with the TGA in Australia. Also the reality is that doctors and psychiatrists receive large payments from the pharmaceutical companies for travel, conference attendance, running training courses, and conducting clinical trials [64]. They and the pharmaceutical companies stand to lose a lot if the psychedelics movement takes hold.

Conflicts of Interest

The author declares that there are no conflicts of interest with respect to the research, authorship and/or publication of this article. However, I have a serious conflict with the major psychiatric and psychological professional bodies in the U.S. and Australia, the editors of whose journals rejected earlier versions of this article. I suspect that this is partly because the editors and their chosen reviewers do not know how to properly evaluate research and partly because these organizations' practicing members stand to make money out of psychedelic drug therapy. I also have a conflict with the Australian government's Therapeutic Goods Administration to which I sent an earlier version immediately after reviewing the U.S. studies. The TGA acknowledged receipt of it then ignored it.

References

[1] Hansen, C., Alas, H. and Davis Jr., E. (2023) Where Is Marijuana Legal? A Guide to Marijuana Legalization. U.S. News. https://www.usnews.com/

[2] Lukianoff, G. and Haidt, J. (2018) The Coddling of The American Mind. Penguin Books, London.

[3] Henriques, G. (2014) The College Student Mental Health Crisis. Psychology Today. https://www.psychologytoday.com/sg

[4] Rossiter, J.R. (2022) The DEP-6: A Brief Multi-Diagnostic Measure of Depression. *Psychology*, **13**, 853-871. https://doi.org/10.4236/psych.2022.136058

[5] Rossiter, J.R. (2022) The ANX-8: A Brief Multi-Diagnostic Measure of Anxiety Disorders. *Psychology*, **13**, 1711-1726. https://doi.org/10.4236/psych.2022.1312107

[6] Cross, J. (2023) Fit for Their Future. The Sunday Telegraph, 18-19.

[7] Gusmaroli, D. (2021) Kids in a Race to See Who Is Sickest. The Daily Telegraph.

[8] Bilton, R. and Nutt, D. (2022) Psychedelic Drug Researcher. The Weekend Australian Magazine.

[9] Leckie, S. and de Jong, T. (2022) Drug of Choice: Support Is Growing for Greater Use of Psychedelic-Assisted Therapy. The Daily Telegraph.

[10] Center for Drug Evaluation and Research (2019) Fact Sheet: Breakthrough Therapies. Food and Drug Administration, Washington DC. https://www.fda.gov/

[11] Carboni, L.P., Patel, D. and Rosen, D.L. (2022) Psychedelic Drugs—Easing the Regulatory Hurdles for Development. Health Care Law Today. https://www.foley.com/en

[12] Therapeutic Goods Administration (2023) Change to Classification of Psilocybin and MDMA to Enable Prescribing by Authorized Psychiatrists. https://www.tga.gov.au/

[13] Dean, L. (2023) The People Getting Rich from the Psychedelic 'Renaissance.' Australian Financial Review, 1-3.

[14] Department of the Prime Minister and Cabinet, Ministers Media Centre (2021) $15 Million for Development of Innovative Therapies for Mental Illness. https://www.health.gov.au/ministers/the-hon-greg-hunt-mp/media/15-million-for-development-of-innovative-therapies-for-mental-illness

[15] Lynch, J. (2022) Psychedelic Studies Mushroom. The Australian.

[16] Boreham, T. (2023) Psychedelic Shares Edge Closer to Reality. The Daily Telegraph,

71.

[17] Royal Australian and New Zealand College of Psychiatrists (2022) Clinical Memorandum: Therapeutic Use of Psychedelic Substances. https://www.ranzcp.org/

[18] Rossiter, J.R. (2002) The C-OAR-SE Procedure for Scale Development in Marketing. *International Journal of Research in Marketing*, **19**, 305-335. https://doi.org/10.1016/S0167-8116(02)00097-6

[19] Rossiter, J.R. (2011) Measurement for the Social Sciences: The C-OAR-SE Method and Why It Must Replace Psychometrics. Springer, New York. https://doi.org/10.1007/978-1-4419-7158-6

[20] Rossiter, J.R. (2022) Aripiprazole and Cariprazine for Bipolar Disorder? *Open Journal of Medical Psychology*, **11**, 254-273. https://doi.org/10.4236/ojmp.2022.114019

[21] Dawes, R.M. (1994) House of Cards: Psychology and Psychotherapy Built on Myth. Free Press, New York. https://doi.org/10.1097/00005053-199509000-00011

[22] Aiken, L.S., West, S.G. and Millsap, R.E. (2008) Doctoral Training in Statistics, Measurement, and Methodology in Psychology: Replication and Extension of Aiken, West, Sechrest, and Reno's (1990) Survey of PhD Programs in North America. *American Psychologist*, **63**, 32-50. https://doi.org/10.1037/0003-066X.63.1.32

[23] Rossiter, J.R. (2022) Learning Theory Principles for Psychotherapy. *Psychology*, **13**, 743-766. https://doi.org/10.4236/psych.2022.135049

[24] Carhart-Harris, R.L., Bolstridge, M., Rucker, J., *et al.* (2016) Psilocybin with Psychological Support for Treatment-Resistant Depression: An Open-Label Feasibility Study. *The Lancet Psychiatry*, **3**, 619-627. https://doi.org/10.1016/S2215-0366(16)30065-7

[25] Wikipedia (2022) Psilocybin.

[26] Sadock, B.J. and Sadock, V.A. (2007) Kaplan & Sadock's Synopsis of Psychiatry. 10th Edition, Lippincott Williams & Wilkins, Philadelphia.

[27] American Psychiatric Association (2013) Diagnostic and Statistical Manual of Meental Disorders, Fifth Edition: DSM-5™. American Psychiatric Publishing, Washington DC. https://doi.org/10.1176/appi.books.9780890425596

[28] Rossiter, J.R. (2017) Optimal Standard Measures: Comment on Matthews *et al.* (2016). *American Psychologist*, **72**, 489-490. https://doi.org/10.1037/amp0000131

[29] Rush, A.J., Trivedi, M.H., Ibrahim, H.M., *et al.* (2003) The 16-Item Quick Inventory of Depressive Symptomatology (QIDS), Clinician Rating (QIDS-C), and Self-Report (QIDS-SR): A Psychometric Evaluation in Patients with Chronic Major Depression. *Biological Psychiatry*, **54**, 573-583. https://doi.org/10.1016/S0006-3223(02)01866-8

[30] Carhart-Harris, R., Giribaldi, B., Watts, R., *et al.* (2021) Trial of Psilocybin versus Escitalopram for Depression. *The New England Journal of Medicine*, **384**, 1402-1411. https://doi.org/10.1056/NEJMoa2032994

[31] Feduccia, A.A., Jerome, L., Yazar-Klosinski, B., *et al.* (2019) Breakthrough for Trauma Treatment: Safety and Efficacy of MDMA-Assisted Psychotherapy Compared to Paroxetine and Sertraline. *Frontiers in Psychiatry*, **10**, Article 650. https://doi.org/10.3389/fpsyt.2019.00650

[32] Eysenck, H.J. (1994) Meta-Analysis and Its Problems. *British Medical Journal*, **309**, 789-792. https://doi.org/10.1136/bmj.309.6957.789

[33] Mitchell, J.M., Bogenschutz, M., Lilienstein, A., *et al.* (2021) MDMA-Assisted Therapy for Severe PTSD: A Randomized, Double-Blind, Placebo-Controlled Phase 3 Study. *Nature Medicine*, **27**, 1025-1033.

https://doi.org/10.1038/s41591-021-01336-3

[34] Mitchell, J.M. (2022) A Psychedelic for Trauma. *Scientific American*, **326**, 56-61.

[35] Wikipedia (2022b) MDMA.

[36] Faculty of Medicine, University of Queensland (2021) More Australians Use Psychedelics to Self-Treat Mental Health. https://medicine.uq.edu.au/article/2021/03/more-australians-use-psychedelics-self-treat-mental-health

[37] Oehen, P., Traber, R., Widmer, V. and Schnyde, U. (2013) A Randomized, Controlled Pilot Study of MDMA-Assisted Psychotherapy for Treatment of Resistant, Chronic Post-Traumatic Stress Disorder (PTSD). *Journal of Psychopharmacology*, **27**, 40-52. https://doi.org/10.1177/0269881112464827

[38] American Psychological Association (2018) Understanding Psychotherapy and How It Works. https://www.apa.org/

[39] Muthukumaraswamy, S., Forsyth, A. and Sumner, R.L. (2022) The Challenges Ahead for Psychedelic 'Medicine.' *Australian & New Zealand Journal of Psychiatry*, **56**, 1378-1383. https://doi.org/10.1177/00048674221081763

[40] Wikipedia (2022) Phases of Clinical Research.

[41] Weathers, F.W., Bovin, M.J., Lee, D.J., *et al.* (2018) The Clinician-Administered PTSD Scale for DSM-5 (CAPS-5): Development and Initial Psychometric Evaluation in Military Veterans. *Psychological Assessment*, **30**, 383-395. https://doi.org/10.1037/pas0000486

[42] Sheehan, D.V. (1983) Sheehan Disability Scale (SDS). Although Copyrighted by Sheehan in 1983, This Measure Is Widely Available on the Internet. One of the Most Accurately Explained Versions Can Be Found on the Website for Stable Resources Toolkit. https://chk.static.cigna.com/assets/chcp/pdf/resourceLibrary/educationCenter/stableToolkit.pdf

[43] First, M.B., Williams, J.B.W., Karg, R.S. and Spitzer, R.L. (2016) Structured Clinical Interview for DSM-5, Clinician Version, SCID-5-CV. American Psychiatric Association Publishing, Arlington.

[44] PsychonautWiki (2023) Ketamine.

[45] Wikipedia (2023) Ketamine.

[46] Oliver, P.A., Snyder, A.D., Feinn, R., *et al.* (2022) Clinical Effectiveness of Intravenous Racemic Ketamine Infusions in a Large Community Sample of Patients with Treatment-Resistant Depression, Suicidal Ideation, and Generalized Anxiety Symptoms: A Retrospective Chart Review. *Journal of Clinical Psychiatry*, **83**, 1-7. https://doi.org/10.4088/JCP.21m14336

[47] Wikipedia (2023) Ketamine-Assisted Psychotherapy.

[48] Spitzer, R.L., Kroenke, K. and Williams, J.B.W. (1999) Validation and Utility of a Self-Report Version of PRIME-MD. *Journal of the American Medical Association* (*JAMA*), **282**, 1737-1744. https://doi.org/10.1001/jama.282.18.1737

[49] Spitzer, R.L., Kroenke, K., Williams, J.B.W. and Löwe, B. (2006) A Brief Measure for Assessing Generalized Anxiety Disorder: The GAD-7. *Archives of Internal Medicine*, **166**, 1092-1097. https://doi.org/10.1001/archinte.166.10.1092

[50] Kroenke, K., Spitzer, R.L., Williams, J.W. and Löwe, B. (2009) An Ultra-Brief Screening Scale for Anxiety and Depression: The PHQ-4. *Psychosomatics*, **50**, 613-621. https://doi.org/10.1016/S0033-3182(09)70864-3

[51] Australian Psychological Society (2021) Psychologists and Psychedelic-Assisted

Therapy. Australian Psychological Society, Melbourne.
https://aps.org.au/#gsc.tab=0

[52] Miller, P.F., Petterson, S., Burke, B.T., *et al.* (2014) Proximity of Providers: Co- Locating Behavioral Health in Primary Care and the Prospects for an Integrated Workforce. *American Psychologist*, **69**, 443-451. https://doi.org/10.1037/a0036093

[53] American Psychiatric Association (2018) What Is Psychotherapy?
https://www.psychiatry.org/

[54] Dudley, E. (2023) Psych Cuts 'Worst for Young Women.' The Australian.

[55] Dunlevy, S. (2022) Is Your Doctor Being Paid Big Bucks by Big Pharma? The Sunday Telegraph.

[56] Maddison, M. (2021) TGA to Rule on Psychedelic Drug Access to Mental Health Problems. The Australian.

[57] HIF: Health Insurance Fund (2022) Claiming MDMA on Health Insurance? It Could Become a Reality. https://www.hif.com.au/news

[58] Lea, T., Amada, N., Jungaberle, H., Schecke, H. and Klein, M. (2020) Microdosing Psychedelics: Motivations, Subjective Effects and Harm Reduction. *International Journal of Drug Policy*, **75**, Article ID: 102600.
https://doi.org/10.1016/j.drugpo.2019.11.008

[59] Holland, I. (2023) Too Easy to Buy Drugs on Facebook. The Sunday Telegraph.

[60] Down, R. (2021) AMA Cautions against Psychedelic Drugs. The Australian.

[61] Halford, B. (2022) Drug Companies Are Investing Big on Psychedelics, But Can They Engineer Out the Trip? Chemical & Engineering News.

[62] Johnson, C.S., Shadfar, Z., Allison, J.R., Walsha, K.A.J. and Partington, H.K. (2022) Controlling New Psychoactive Substances in New Zealand. *Australian Journal of Forensic Sciences*. https://doi.org/10.1080/00450618.2022.2067230

[63] U.S. Food and Drug Administration (2021) Fact Sheet: FDA at a Glance.
https://www.fda.gov/

[64] Dunlevy, S. (2023) Mentally Ill Who Can't Afford Help Forced to Call Police. The Australian.

[65] Addiction Center (2023) Drug Street Names.
https://www.addictioncenter.com/drugs/drug-street-names/

[66] Newport Academy (2021) Common Street Names for Drugs.
https://www.newportacademy.com/

[67] Substance Abuse and Mental Health Services Administration (2020) Key Substance Use and Mental Health Indicators in the United States: Results from the 2019 National Survey on Drug Use and Health.
https://www.addictioncenter.com/drugs/drug-street-names/

[68] Australian Institute of Health and Welfare (2022) The 2019 National Drug Strategy Household Survey. https://www.aihw.gov.au/