Psilocybin and Depression: Past Psilocybin Use Improving Future Depressive Symptom Management

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Abstract

In this study, I investigated whether individuals who have taken psilocybin in the past felt that their experience(s) helped them prevent or cope with depressive symptoms. This study was based on past research showing psilocybin-assisted psychotherapy's efficacy in treating depression. Three hundred seventy participants responded to the Survey on Psilocybin Use and Depressive Symptoms (SPUDS, created for this study) and Patient Health Questionnaire-9 (PHQ-9). The data was analyzed to determine associations between demographics, as well as correlations between how many times they ingested psilocybin, how much it helped, and their total depression scores. Data were also analyzed to determine any trends in the data from open-ended questions. While no associations with demographics were found with the amount of psilocybin ingested, how much psilocybin helped, or their total depression scores, there were weak but statistically significant correlations between age and how much they believe psilocybin helped, and how many times someone took psilocybin and how much they believed it helped. There were also several trends found in the open-ended responses, including what aspects of themselves psilocybin changed, or what dosages they preferred for the biggest changes. There was a skewness of the PHQ-9 scores, where more participants had more severe current depressive scores so that possibly affected the correlation strength between psilocybin ingestion and depression severity. I recommend more research be done on participants' past psilocybin experiences and their intentions, as well as more research focusing on why the most reported aspects of the psilocybin experience are both most common and if they correlate with changes found in the brain/behavior from other studies.

Keywords: psilocybin, depression, psychedelics, psychedelic research, depressive symptoms, psilocybin-assisted psychotherapy, psychedelic therapy.

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> *"Psychedelics, used responsibly and with proper caution, would be for psychiatry what the microscope is for biology and medicine, or the telescope is for astronomy"* (Grof, S., 2001, n.p.).

Psychedelic drugs have an extensive and varied history. There is evidence dating back millennia, from Mayans and other South American tribes using ayahuasca extracted from leaves on vines and psilocybin mushrooms, to possible Judeo-Christian–Islamic history of amanita mushroom use, ibogaine extracted from trees used by tribes in Africa, Native American consummation of the peyote cactus, and the list goes on and on. Their use has been seen in practically every culture that has been studied (Friedman, 2006; Smith, 2019). It can be seen in more modern usage of substances such as LSD and "magic mushrooms," of which psilocybin is the psychoactive agent, that counter cultures of the 1960s and 1970s heavily used, retreats to Peru for ayahuasca ceremonies, heavy use at music festivals around the world, and some substances' legalization or decriminalization in cities like Amsterdam, or states such as Oregon and Colorado. What these psychedelic substances have in common with each other is that they all alter consciousness and perception in some way after being ingested, often affecting the serotonin levels in the brain (Carhart-Harris & Goodwin, 2017).

Due to their effect on serotonin, early research in the 1950s and 1960s was promising in showing that psychedelics, especially psilocybin and LSD, were especially effective to add to psychotherapy for a much quicker and longer-lasting treatment for mental illnesses, such as depression and anxiety (Friedman, 2006). However, several factors such as the FDA's tightening control and requirements for pharmaceutical research and the halting of production of

psychedelics by the massive company Sandoz made these substances near impossible to study and then the war on drugs started and the Controlled Substances act made these substances illegal for both recreational and scientific use (Hall, 2021). Research in the US went into a hiatus until 1990, when the University of New Mexico conducted the first legal and approved psychedelic study on human participants since the 1960s (Friedman, 2006).

Recent studies in this field have continued to add to the promising research on using these substances to treat mental illness. One relationship showing strong results is using psilocybin to treat depression in numerous populations, such as those with treatment-resistant depression or depression related to terminal illness (Carhart-Harris et al., 2018; Griffiths et al., 2016). According to a study done by the National Institute of Mental Health in 2019, 7.8% of adults in the US (which is around 19.4 million people) had at least one major depressive episode, of which 68% said came with severe impairment to their daily life (NIMH, 2021). The criteria in their study for a major depressive episode came from the DSM-V, defining it as a minimum of two weeks with a severely depressed mood, loss of interest/pleasure in their daily activities, and a majority of other depressive symptoms listed, including low energy levels, sleeping problems, issues concentrating, low self-esteem, etc. (NIMH, 2021).

The present thesis study will aim to determine whether individuals who have used psilocybin in their past feel that their experience with the substance helped them deal with future depressive symptoms or potential depressive symptoms (if they feel it helped combat them entirely). The population of this study will include participants of any age, gender, race, or other demographics that have used psilocybin in the past. Since depression can affect anyone, regardless of their characteristics, it is necessary to cast a wide net in the hopes that the research can gather data from many diverse individuals (NIMH, 2021). Depression can also affect every

aspect of a person's life, from personal, familial, and romantic relationships to their jobs, overall quality of life, other aspects of their mental health or even physical health, and much more. Having depression can also greatly increase the risk of someone committing suicide, which is the 10th leading cause of overall death in the US, the 2nd leading cause in people ages 10 through 34, and the 4th leading cause between the ages of 35 and 54 ("Suicide", 2021).

Researchers and psychologists have put in vast amounts of effort, time, and other resources to figure out how to treat depression since it is so prevalent. Unfortunately, the treatment options do not have a one hundred percent success rate, with current treatments involving therapy and/or medications. Therapy can often be too costly, even with insurance, for many people to afford. It is not accessible depending on where they live or their ability to have extra time to dedicate to it. It may not fully help them with their mental illnesses. Medication can also often be too expensive for many people, does not always work, and can come with many side effects that can sometimes altogether be worse than the reason they started the medication in the first place (Penn & Tracy, 2012). Therefore, research needs to be focused on new types of treatments that are effective, short-acting, long-lasting, financially feasible, and readily available.

Research on using psilocybin-assisted psychotherapy to treat depression has shown it is highly effective, sometimes can be done in only one or two sessions, and can last for years after treatment (Carhart-Harris et al., 2018; Carhart-Harris et al., 2017; Davis et al., 2020; Griffiths et al., 2016; Lyons & Carhart-Harris, 2018; Ross et al., 2016; Vollenweider & Kometer, 2010; Wheeler & Dyer, 2020). The more research that can be done that shows more positive, evidence-based results to the effectiveness of this treatment will hopefully lead to this treatment becoming a more implemented option, therefore, potentially overcoming the financial and availability limitations of other treatments. This study will also ask participants what specific

aspects of their experience they felt were the most helpful in dealing with depressive symptoms. Future psilocybin-assisted psychotherapy sessions can be focused more on the aspects that generate the most positive and largest changes and therefore show even better results.

Literature Review

Overview of Safety of Psilocybin-Assisted Psychotherapy

One major hesitation many individuals have about hearing that psilocybin, or other psychedelic drugs, are being used in therapy to help treat mental illnesses is how safe they are to use on people. The reason for this concern often stems from the fact that psilocybin, LSD, and other psychedelics are considered a Schedule I (S1) drug per the Controlled Substances Act (CSA), which denotes that these substances have high abuse potential and no medical benefits whatsoever (Johnson et al., 2018). Though many studies showed strong evidence for both the high safety and efficacy of psilocybin, the media frenzy fueled by the war on drugs created an atmosphere of danger and overwhelming risk, leading to the small risks outweighing the huge benefits (Johnson et al., 2018).

According to the CSA, a review by Johnson et al. (2018) looked at psilocybin's history and characteristics to determine its true abuse potential. Evidence has been coming out since the 1970s that shows psilocybin has a very low prevalence of abuse and adverse reactions compared to other major drug classifications, yet, it remains S1. Their review cites that the CSA contains eight specific factors to determine a substance's potential for abuse, including the presence of withdrawal symptoms, reinforcement schedule, stimulus generalization, discriminative effects, etc..When they looked at past human and animal studies, they found no evidence of withdrawal symptoms, no or very weak rewarding effects, no or weak stimulus generalization to other substances that have shown high abuse-potential, and discriminative effects that do not

generalize to nor can be substituted with other addictive drugs like amphetamines. They found in these studies that individuals who use psilocybin, even those with an extensive history of use, do not use it compulsively, like how one would use methamphetamine. They also found that psilocybin does not have overdose toxicity. Overdose toxicity refers to a drug's effects on the respiratory, cardiovascular, or other systems that can lead to death. For example, heroin decreases a user's breathing rate, leading to the inability to breathe and possibly death. Studies have shown that psychedelics that act on serotonin have anti-inflammatory effects and help inflammatory diseases. While the researchers understand that a cost-to-benefit analysis needs to be done in full by the FDA, they are confident that the therapeutic benefits greatly outweigh the risks, especially with the administration of psilocybin in therapy being in highly controlled settings. This review concluded with the researchers recommending that while more research should be done, the CSA scheduling should be readdressed as psilocybin has shown in numerous studies to have therapeutic benefits and minuscule or no abuse potential.

Showing the safety of using psilocybin both in and out of therapy can help the potential benefits of a study more than outweigh the risks, especially when being reviewed or approved by the government, FDA, institutional review boards, etc. and can open the doors for more research and more facilities providing this type of therapy.

Underlying Mechanisms of Changes

Changes to Brain Function and Structure

A study by Carhart-Harris et al. (2017) sought to understand the mechanisms by which psilocybin-assisted psychotherapy works on the brain. Studies have shown that using psilocybin with therapy produces great results, but researchers do not fully understand why. Their study included 19 participants with treatment-resistant depression of varying ages, gender, and

ethnicities. The researchers wanted to use fMRI scans to measure the participant's brain activity and the 16-item Quick Inventory of Depressive Symptoms (QIDS-SR16) to measure depression levels and compare the differences between pre-treatment and one day post-treatment, as well as pre-treatment to five weeks post-treatment. In their first psilocybin-assisted therapy session, they were given 10mg, and in their second session one week later, they were given a dose of 25mg. The first fMRI scan and QIDS-SR16 test were before the first session, the second was done one day after their second session, and the third was given five weeks after the second session. The researchers looked for changes in cerebral blood flow and functional connectivity on the fMRI scans and depression scores on the QIDS-SR16 test.

Regarding the fMRI results, they found decreased cerebral blood flow to the temporal cortex, specifically the amygdala, which is correlated with decreased depressive symptoms (Carhart-Harris et al., 2017). They also found similar changes to the default mode network as some other therapies such as electroconvulsive therapy, which is a slight decrease and then increase back to normal levels; researchers consider this a sort of "system reset", which could explain why psilocybin-assisted psychotherapy is so effective. The results on the QIDS-SR16 measures were equally promising, with all 19 participants having significant decreases in their test scores and, therefore, depressive symptoms. The researchers noted that their sample size was limited. They did not have a control group, so they recommend more research on this topic to further understand how these substances work when being used to treat depression. In many studies looking at changes in brain functioning after psilocybin-assisted psychotherapy, the results have given us more information on how these substances generate such profound changes. Learning about these mechanisms can help us harness the benefits of using these substances to treat mental illness.

While much research has been done on the neural mechanisms of how psychedelic drugs travel the brain, there has not been the same attention given to the impact on the actual structure of the brain. Some studies looking at the functional changes have shown that psychedelics, which act as serotonin agonists, stimulate factors that influence the plasticity of the brain's synapses, to which Bouso et al. (2015) suggest that these substances could also prompt changes in the structures of brain tissue. Bouso et al. investigated this possibility in their study, looking at the differences in the thickness of the cortex in frequent users of psychedelic substances. They also wanted to study serotonin agonists' impact on personality (using the Temperament and Character Inventory), psychopathology (using the Symptom Check-List-90-Revised), and neuropsychological functioning (by testing working memory, executive functioning, and task switching). Their study included 22 control and 22 experimental participants who regularly consumed ayahuasca, which acts on the brain as a serotonin agonist like psilocybin. Regular use was defined as a minimum of 50 times within the past two years. They also screened participants for the history of psychiatric disorders and minimum usage of other drugs to lifetime use of 10-20 occasions or less to minimize the influence of other drugs substances. Both groups had MRI and CT scans and were tested on all the above measures, then their different structures and test results were compared to locate any potential differences.

Their scans showed significant differences in cortical thickness in midline brain structures, with the experimental group having thinning in the posterior cingulate cortex, a major part of the default mode network (Bouso et al., 2015). They also found that these structural changes correlated with more positive or increased scores than the control on the measures given, including self-transcendence, attention, internal mentation, openness, executive function, and a stronger sense of self. They say that the data gathered suggest that regular use of these

types of psychedelics could lead to changes in the brain structures that support "attentional processes, self-referential thought, and internal mentation" (p. 484), which could be responsible for the changes on their other test scores. Bouso et al. do note that this is a correlational study and therefore does not prove causation but did find results that were statistically significant and therefore should warrant more research. This study provides possible explanations for why therapy with these substances is both so long-lasting and effective.

If using these substances alone changes the brain positively, then including them with therapeutic interventions may create structural and functional changes that foster even more beneficial changes. The more we can learn about all the ways these substances affect the brain, the better we will be able to understand the underlying mechanisms of why they work so well when paired with therapy, and therefore be able to structure therapy sessions to maximize the benefits and use these substances to their fullest potential.

Since most of these psychedelic substances, such as psilocybin and LSD, work as agonists to serotonin, there has been a research interest to study the effects that process has, namely if psychedelics increase the spontaneity of neural activity, such as in a study by Herzog et al. (2020). The researchers noticed no mechanistic explanation for how this increase occurs and sought out to find an explanation. Delving deeper into how these changes occur would help explain why these substances are continually showing evidence of positive effects when used in therapy. According to the researchers, it could advance our knowledge of consciousness as a whole as well. The researchers created a computer model based on whole-brain activity using the Dynamic Mean-Field (DMF) model to simulate fMRI scans of brain activity during wakeful rest and under the influence of LSD. This model uses data from human participants on the human connectome (including excitatory and inhibitory neural populations and long-range connections)

and serotonin receptor expression obtained via positron emission tomography (PET) scans to simulate how the brain would operate under certain conditions. When they simulated this model, they found that entropy increased in some regions and decreased in others. The researchers suggested that serotonin receptor activation mediated a topographical reconfiguration in the brain and a change in connectivity. This change in the structural and functional aspects of the brain is potentially an explanation for why psilocybin or other psychedelic-assisted psychotherapies create such profound and lasting effects. The researchers recommend more studies looking at these mechanisms, as theirs was the first of its kind to understand even more about how these substances can produce such large and long-lasting changes. Again, the more we know about why these substances have been shown to work so well, the better we can harness them to use in therapy.

Raval et al. (2021) also wanted to study the underlying biological mechanisms behind psilocybin's antidepressant effects. Building off rodent studies that showed psilocybin and other serotonin agonists inducing structural neuroplasticity and altering the way certain proteins were expressed in the brain, they wanted to see if a single dose of psilocybin could create these changes. They took 24 pigs and gave half psilocybin (the amount given reflected the same ratio a human would take to produce effects) and the other half a saline solution. Those two groups were split again between being euthanized either one day or seven days post-injection, as evidence has shown one day after psilocybin can provide a window of time where therapy is very effective, and after seven days is when they found depressive scores as being reported to be the lowest. The researchers used in vitro autoradiography to measure the specific proteins SV2A, that reflects presynaptic density, and 5-HT2AR, a serotonin receptor. What they found was that in the psilocybin group, the SV2A levels were statistically significantly higher in the hippocampus in

both one and seven days post-injection and higher in the prefrontal cortex seven days post-injection. For the 5-HT2AR, they found a reduction in both the hippocampus and prefrontal cortex in the one-day post-injection group, but not the seven-day group. The researchers concluded that their data provides evidence that the psychedelic experience leads to increased formation of synapses (synaptogenesis), which is theorized to be the cause of the antidepressant effects found in humans. They found SV2A levels are increased and therefore 5-HT2AR density decreased after psilocybin use in the hippocampus and prefrontal cortex, whereas 5-HT2AR density is increased in individuals with major depression. The researchers make many recommendations for future studies. While we cannot have one hundred percent certainty that these results would generalize to humans, they note the SV2A density levels in the saline group are the same as post-mortem humans non-human primates so that it could be likely. Measuring specific levels of proteins, and therefore presynaptic density and serotonin receptors can uncover a possible way that psilocybin acts as an antidepressant similarly to other antidepressant methods, just in a possibly more effective way.

A meta-analysis conducted by Vollenweider and Kometer (2010) discussed the neurobiology of psychedelics and the numerous ways that research has found for how these substances produce their antidepressant effects. In looking at many studies using psilocybin to treat depression, anxiety, and obsessive-compulsive disorder, they found its therapeutic effects likely primarily come from its agonistic properties at 5-HT2A receptors in the cortex. Some studies suggest a very complex interaction between the serotonin and glutamate systems that modulates prefrontal cortex activity, more specifically psilocybin leading to a downregulation of prefrontal 5-HT2A receptors. These receptors may also lead to a modulation of subcortical structure-activity, such as in the amygdala. This is important as models of emotional regulation

show the prefrontal cortex has top-down control over our emotional and stress responses through its connection with the amygdala. Other studies have found evidence for psilocybin's effects on the dopaminergic system, though it is only a moderate contribution. They concluded that because the antidepressant effects of psilocybin or other psychedelic substances outlast the initial intake period and experience, they normalize different networks like serotonin and glutamate systems by increasing neuroplasticity. More evidence to support this comes from studies showing a deficit in neuroplasticity may play a role in the pathology of depression. The researchers believe that this finding that psilocybin can target neuroplasticity opens the way for this novel approach to treat these mental illnesses, especially since they are adaptations that generate long-lasting results. They also note that these substances might be especially clinically efficient when combined with psychotherapy, as their effects on neuroplasticity allow the brain to be more malleable by treatment plans. They propose more blind and controlled studies be conducted to test the different hypotheses on psilocybin's antidepressant mechanisms. Their potential to target these specific networks and brain processes may lead to potentially very promising novel treatment approaches.

Changes to Aspects of Depression

Suicidality. An unfortunate side effect of having major depressive disorder is a higher risk of suicide. Much research has gone into studying the relationships between suicide and depression, and psychedelic substances and depression. Still, not many studies have focused on the changes psychedelic-assisted psychotherapy has on suicidality levels (Hendricks et al., 2015b). In a study by Hendricks et al. (2015b), the researchers evaluated the relationship between classic psychedelic usage (to include dimethyltryptamine [DMT], psilocybin, ayahuasca, lysergic acid diethylamide [LSD], mescaline, and peyote) and suicidality levels. They

cited many studies showing these substances as targeting specific risk factors of suicide, such as affective disturbance, anxiety, substance misuse, impulsive-aggressive personality traits, early traumatic life events, increased 5-HT2A receptor density, reduced neuroplasticity, hyperactive default mode network, low openness, and nervous system inflammation, all of which these studies showed psilocybin significantly helping. The majority of these studies were done experimentally, but the researchers wanted to take a more generalized approach to gain a larger sample and assess subjects in the real world. Taking data from the last five years of the National Survey on Drug Use and Health, they pooled over 190,000 responses, controlled for many covariates, and looked at the correlations between psychedelic use and suicidality. What they found from their statistical analysis was that classic psychedelic use was significantly associated with decreased likelihoods of psychological distress, suicidal thinking, suicidal planning, and suicide attempts in the past year. They also found that lifetime use of other illicit, non-psychedelic substances was associated with either no change in suicidality, psychological distress, or increased odds. These correlation results align with past research on psychedelics to treat mental illness and suicidal risk factors. While this does not indicate direct causation, as other variables may be involved, it is data that supports other research on these topics showing that these psychedelic substances can alleviate many symptoms of depression and other mental illnesses.

Hendricks et al. (2015a) extended the analysis on this previous study by looking specifically only at lifetime psilocybin use's effects on past month psychological distress, and past year suicical thinking, suidical planning, and suicide attempts. Using the data from the National Survey on Drug Use and Health from 2008 through 2012, they isolated four specific groups to analyze: *psilocybin only* (lifetime use of psilocybin and no other psychedelics),

psilocybin and other psychedelics (lifetime use of both psilocybin and other psychedelics), *non-psilocybin psychedelics* (lifetime use of other psychedelics but no psilocybin), and *no psychedelic*s (no lifetime use of any psychedelics). They ran statistical analyses and controlled for a wide range of covariates including but not limited to age, gender, education, self reports on risky behavior engagement, and use of other illicit substances such as cocaine, heroin, sedatives, etc. What they found when comparing all four groups to one another was that the psilocybin only group showed significantly lower suicidality scores as compared to those who have never used any psychedelics. Past-year suicidal thinking and planning and psychological distress were lower in the psilocybin only group than the psilocybin and other psychedelics groups, and the non-psilocybin psychedelics group. The psilocybin only group and psilocybin and other psychedelics groups had decreased suicidality scores compared to the other two groups. The researchers note that these results suggest that psilocybin from the rest of the classic psychedelics class could provide the most potential for therapeutic purposes and could be especially protective against risk factors to suicidality. They conclude that psilocybin's effects on depression and suicidality factors, and the fact that it has been shown to have the most favorable safety reports as compared to other psychedelics, lends it to be a very promising, innovative intervention for those with mental illness. This conclusion provides paths for future research to focus on substances that will produce the greatest results and the least amount of harm to the participants or patients.

Increased openness. In research that examines personality, there is a large amount of evidence suggesting our core personality remains stable once we reach around 30 years old (MacLean et al., 2011). But, in research using psilocybin, many studies, including strict double-blind controlled trials, have shown that participant's experience with psilocybin has, in

many cases, led to long-term changes in their behavior, attitudes, and values (MacLean et al., 2011). When MacLean et al. (2011) noticed that there had not been a study, besides ones involving psilocybin or other psychedelics, that showed changes in personality after an "experimentally manipulated discrete event" (p. 1), they decided to test the effect of psilocybin on the Big 5 traits of personality: neuroticism, extroversion, openness, agreeableness, and conscientiousness. Their study included 52 participants who had never taken psychedelics and consisted of both male and female participants, who generally were educated and spiritually active. Participants completed between two and five 8-hour-long sessions that were separated by a minimum of 3 weeks. They were given either a moderate or a high dose during one of their sessions, but it was double-blind, so neither the participants nor session monitors knew when this would be. The participants were split between study 1 and study 2, study 1 consisting of two or three sessions, with participants receiving psilocybin in one session and a control drug in the others, and for study 2, each participant got 4 total doses of psilocybin in four sessions, either increasing or decreasing in dosage in subsequent sessions, with one control drug session added in a randomly assigned position. Personality measures were distributed at screening, 1-2 months after each drug session, and around 14 months after the last drug session, and included the NEO Personality Inventory (NEO-PI, measures the big 5 factors of personality and the facets that define each factor), States of Consciousness Questionnaire (SOCQ, measures phenomenological items during a person's altered-consciousness state), Mysticism Scale (assesses mystical experiences across a person's life), and APZ (assesses participant's altered state of consciousness).

When the researchers conducted a statistical analysis on their data, they found that participant's openness significantly increased between the screening and post-test measures, but

all other personality traits remained the same (MacLean et al., 2011). They found participant's results of those who had higher dosage sessions and rated their mystical experience as being substantial had significant correlation with the increase in openness. During their follow-up assessment given more than a year after participant's high-dose sessions, they found that participants who had a full mystical experience still had significantly higher openness levels than the screening assessment. While the researchers had statistically significant results, they do recommend replication studies using a larger sample size and more diverse baseline personality levels. This study's results go against the grain of how normal openness levels change as we age, as they usually decrease as we get older. It also shows significantly higher increases in openness than in studies testing antidepressants or counseling. This significant increase in openness could help those struggling with mental illness be more able to make the behavioral and cognitive changes necessary to overcome their illness.

Psilocybin-Assisted Psychotherapy

Used in General on Depression

In a recent study by Davis et al. (2020), they studied psilocybin-assisted therapy on participants who had major depressive disorder (MDD). They highlighted the need for more studies on psilocybin and depression due to the ineffectiveness of pharmacotherapy drugs that do not always work and often come with unwanted side effects. A total of 27 participants, ages 21-75, who have been diagnosed with MDD, were not currently taking antidepressants, and who did not have history of psychotic disorders, suicide attempts, or hospitalization were enrolled in the study. Participants were tested on the GRIDHamilton Depression Rating Scale (GRID-HAMD) to measure their depression scores pre- and post-treatment. Half of the participants got immediate treatment, and the other half got the treatment after an 8-week delay.

The psychotherapy sessions were otherwise the same for both groups, with the first session having a psilocybin dose of 20 mg/70 kg of body weight and the second session having a dose of 30 mg/70 kg. The results Davis et al. gathered heavily supported their hypothesis; in 71% of both groups, their first week post-treatment GRID-HAMD scores had statistically significant decreases of over 50%, and over half of both groups qualified for remission in their first week post-treatment. Davis et al. also noted that their effect sizes were 2.5 times greater than psychotherapy alone, and 4 times greater than psychopharmacological treatment alone, showing how effective psilocybin-assisted psychotherapy is compared to either traditional method of treatment. Both the absence of serious adverse effects of this treatment and its efficiency in working so well just after two sessions also support treatments that stray away from commonly prescribed antidepressants or traditional therapies.

Used in Specific Populations

Treatment-resistant Depression. One population that psilocybin-assisted psychotherapy is tested on frequently is individuals with treatment-resistant depression. After trying numerous types of therapies with no results, many seek to find other treatment paths, and research so far for these individuals has been promising.

A study conducted by Carhart-Harris et al. (2018) built off recent studies showing the short-term efficacy of psychedelic-assisted psychotherapy by testing the safety of this treatment and the long-term efficacy up to six months post-treatment. The study involved 20 participants, with 14 males and six females, aged 27-64. All participants had moderate-severe treatment-resistant depression, with no symptom improvements after completing two full courses of antidepressants for at least six weeks within their current depressive episode. After the participants were deemed eligible, the researchers documented the participants'

physical/mental backgrounds, diagnoses, blood work, ECG and MRI results, urine tests for drug use or pregnancy, and assessment results to establish baseline levels. The researchers used the following assessments: the Quick Inventory of Depressive Symptoms (QIDS-SR16) and a self-report of depressive symptoms, at baseline before the study, at weeks 1-3 and 5, and at three months and six months after the treatment session. The researchers also tested participants on their anxiety, suicidality, and sexual dysfunction. Participants had two sessions of psilocybin-assisted psychotherapy; in the first session, they received a 10mg dose, and in the second session, one week later, they received a 25mg dose. The results were positive, with depression, anxiety, suicidality, and sexual dysfunction scores all significantly less at the first post-treatment test through six months post-treatment, with many participants qualifying for remission. Also, not a single patient sought another treatment at least five weeks post-treatment. Carhart-Harris et al. concluded that this treatment is safe, considering the participants' psilocybin tolerance, it was highly efficient, both with large effect sizes and improvement of symptoms only after two sessions, and it was very effective with significant decreases through the six-month mark. This study shows just how useful psilocybin-assisted psychotherapy can be in treating individuals with treatment-resistant depression.

In many studies looking at psilocybin and depression, the measure of a participant's depression is based on a conglomerate score on a measure used to study depression in general. A study by Lyons and Carhart-Harris (2018) pieced apart the aspects of treatment-resistant depression that may be directly affected by psilocybin-assisted psychotherapy. There were 30 total participants, mostly White males, with half in the control group (mentally healthy participants who did not receive psilocybin) and half in the experimental group (individuals diagnosed with major depressive disorder who did receive psilocybin). Both groups were tested

on the Beck Depression Inventory (BDI) to measure their symptoms of depression and the Prediction of Future Life Events task (POFLE), which measures the belief that positive or negative events will happen in their lives within the following 30 days. This score is then compared after the thirty days to events that did or did not occur to get a final measure of pessimism versus optimism biases. The experimental group had two psilocybin-assisted psychotherapy sessions one week apart, the first a lower dose of 10mg and the second a higher dose of 25mg. The control group did not have any psychotherapy sessions as the researchers wanted to compare the experimental group's changes to potential base changes of healthy participants. Their results showed the experimental group had statistically significant decreases in their overall depressive symptoms (BDI scores) and pessimism bias (POFLE scores), which were also highly correlated with each other. The experimental group also had a significant increase in their accuracy of predicting future life events, again showing that their pessimism bias significantly decreased, as the researchers found no such change in the control group. Lyons and Carhart-Harris derived from their results that psilocybin-assisted psychotherapy can greatly improve an individual's outlook on life, and therefore their depressive symptoms as well.

Terminal Illness Patients. Another population that has been the subject of many studies on psilocybin-assisted psychotherapy is individuals with terminal illnesses, such as cancer. Because those facing the end of life can have such high levels of depression and anxiety, it is important to find a treatment method that works for them quicker than traditional therapy or medication can, and does not interfere with the medication or treatment plans for their illness.

A study done by Griffiths et al. (2016) wanted to find a way to help these individuals suffering from depression and anxiety surrounding a terminal illness. Building off previous studies showing that psilocybin has the potential to decrease depression and anxiety in cancer

patients, they created a randomized, double-blind study that included 51 participants who had both a life-threatening diagnosis as well as symptoms of depression and/or anxiety. The researchers wanted to see the difference between a very low dose versus a high dose of psilocybin on depression, anxiety, quality of life, and changes in the person's attitude or behaviors. The participants were split between getting the low, almost placebo-like dose first and the high dose of psilocybin second, and the second group had their first dose be the high amount and their second dose be the low amount. The first session was followed by the second session about 5 weeks later, and the assessments were distributed immediately after enrollment to get the participants' baseline scores, during and at the end of both sessions, 5 weeks after each session, and finally 6 months after the second session. These sessions were self-guided, with many participants wearing blindfolds to block external stimuli, and headphones to listen to music. Participants were only instructed to focus inward throughout the sessions.

Their results showed that the higher dose session was more effective than the lower dose at decreasing depression and anxiety and at increasing quality of life (Griffiths et al., 2016). The data produced showed large and statistically significant decreases in clinician/self-rated measures of depression, anxiety, and mood disturbance, as well as increases in quality of life, life meaning, death acceptance, and levels of optimism. The results also showed these significant changes at the 6 month mark with the majority of participants in symptom remission. These changes were also reported by friends, family, and coworkers of participants as another measure of changes to participant attitudes and behavior. Like many psilocybin studies, the researchers noted the small sample size, which is to be expected when working with a substance such as this, and recommended more research be done. This study provides more evidence to psilocybin's effectiveness in treating depression and anxiety, especially in more severe cases such as in those

with a terminal illness. It also shows that if future researchers or therapists want to achieve greater results with using psilocybin in therapy, the dosages given should be a higher milligram, rather than a "microdose." The results also add to the growing body of research showing that psilocybin-assisted psychotherapy produces not just significant results but also lasts for an extended period.

In another randomized, double-blind study, Ross et al. (2016) also looked at psilocybin's effect on depression and anxiety in participants who had been diagnosed with cancer. The researchers wanted to test how well psilocybin changes these measures compared to a control substance of niacin, a B vitamin, both added to psychotherapy. 29 mostly female, Caucasian cancer patients were randomly assigned to either group one who got the psilocybin first and then niacin, or group two who got the niacin first then psilocybin. The researchers gathered the participants' baseline assessment scores Then, the first session was 2-4 weeks later, and 7 weeks after that was session two. After the baseline scores were established, the measures were distributed again one day before session one, day of session one (7 hours post-dose), one day after session one, two and six weeks after session one, seven weeks after session one/1 day before session two, day of session two (7 hours post-dose), one day after session two, and then 6 and 26 weeks after session two.

While they primarily tested for anxiety (using the Spielberger State-Trait Anxiety Inventory) and depression (using the Hospital Anxiety and Depression Scale and Beck Depression Inventory) levels, they also had a secondary list of outcome measures on existential distress, quality of life, spirituality, and self-reported effects on their experience and any changes to their cognition, affect, and behavior using several different measures for each trait (Ross et al., 2016). On all of their primary outcome measures, they found significant differences between the

control and experimental group (before the crossover and after), with the psilocybin group "demonstrating immediate, substantial, and sustained...clinical benefits" (p. 1174) regarding the decrease in anxiety and depression symptoms, existential distress, and increases in quality of life and positive cognitive and behavioral changes. Like many of these studies, the researchers recommend more studies be done to confirm their results and add to the body of evidence supporting adding psilocybin to psychotherapy. It is important to see what populations can benefit the most from this treatment so it can be used to help those in need. Research like this study shows that even using only psilocybin once in therapy can lead to drastic positive outcomes that last a long time and with no significant side effects.

Understanding Recent Research to Look Ahead at Future Research

While research on psychedelics has had a bumpy road, there has been a resurgence in the past few decades to push to understand these substances' effects on mental illness more (Wheeler & Dyer 2020). In a meta-analysis conducted by Wheeler and Dyer (2020), they took data from psychedelic research from 1990-2020, a total of 43 studies, to evaluate the general clinical trials and results from research on substance use disorders, anxiety, depression, depression specifically in those with terminal illness, post-traumatic stress disorder (PTSD), and obsessive-compulsive disorder (OCD). They compared the studies' variables, including the mental illness being studied, the total number of participants, age, sex, design of study and therapy itself, times between assessments, and results. They found that most of the studies were recent (between 2017-2019). Many had small sample sizes, about half were randomized and controlled trials, used many different psychotherapy approaches, and about half were psilocybin studies. Most anxiety, depression, and the one OCD study used psilocybin, while the PTSD and substance use disorders used other psychedelics like MDMA or LSD. Their overall results showed these

psychedelic substances having a large, positive impact on mental health. This positive impact included methods that participants say increased their feelings of connectedness and acceptance, encouraged processing of emotions, which many said was the opposite from medications or some talk-therapy, including a feeling of disconnect, avoidance, and blunting of their emotions, forgiveness, self-compassion, more introspective awareness, and understanding, an increase in their motivation and commitment to make necessary changes, more positive worldviews, and change in perspective for those with substance use disorders and terminal illness regarding the substance of abuse and death acceptance, respectively. While they noted that positive results were abundant, many studies also had limitations that could help researchers on future studies, such as small sample sizes, limited diversity, not all studies being double-blind, a lack of the excruciating detail about the psychotherapeutic methods to allow for fully accurate replication studies, and that not all studies had extensive long-term follow up (about half of studies only assessed patients after 6 months post-treatment).

While it is crucial to look back on the progress made in psychedelic therapy, it is even more vital to learn from the limitations and look ahead towards future research and gather more, hopefully continuingly positive, evidence showing psychedelic's efficacy in the treatment of mental illness. When we learn more about how these substances work, how we can make them work better, and how we can make them work for a more generalized population by building stronger the foundation of evidence, they have increased potential to become a treatment option available for a wide range of issues.

Summary and Research Question

While there was a lull in research due to federal law, there has been a resurgence in the past few decades of research on psilocybin. Johnson et al. (2018) reviewed psilocybin's safety

and abuse potential and found psilocybin to have high safety and very low abuse potential as compared to other drugs both in the same and other schedule classification. Regarding how psilocybin affects the brain, Carhart-Harris et al. (2017) found changes to cerebral blood flow and the default mode network correlated with decreases in depressive symptoms. Bouso et al. (2015) found that psilocybin use changes actual structural components of the brain in ways that also correlate with decreases in depressive scores and increases in positive personality and behavior changes. Looking at mechanistic changes, Herzog et al. (2020) found in their study that psilocybin use changes both functional (serotonin receptors) and structural (reconfiguration of connections) systems. Raval et al. (2021) used pig brains to see if psilocybin could create changes to neuroplasticity and protein expression. In one dose, it can increase neuroplasticity and change receptor density, which correlates with brains in humans with major depression who are taking antidepressants. Vollenweider and Kometer (2010) did a meta-analysis on how psilocybin changes the brain to produce these large effects on depression. They found that it and other psychedelics normalize different brain systems and increase neuroplasticity.

There are also specific aspects of depression that are affected by psilocybin, as Hendricks et al. (2015b) found in their study showing psychedelic use correlating with decreased suicidality as compared to both individuals with no prior use or other non-psychedelic drug use. Hendricks et al. (2015a) expanded that study and looked at psilocybin specifically and found that psilocybin, out of all psychedelic substances, has the most promise to be used for therapeutic purposes and the best effects on suicidality scores. Psilocybin-assisted psychotherapy also greatly increases an individual's openness, as found in a study by MacLean et al., (2011), which correlates with decreased depressive scores. In a study by Davis et al. (2020), psilocybin-assisted psychotherapy was shown to decrease depression scores enough to put over half their subjects in

remission, and showed much larger effect sizes than therapy or medication treatment alone. Psilocybin-assisted psychotherapy is also used for individuals with treatment-resistant depression, as shown by results of a study by Carhart-Harris et al. (2018) that provided evidence of this therapy significantly decreasing depressive symptoms over an extended period of time. Lyons and Carhart-Harris (2018) looked at both overall depression scores and specific aspects of depression such as pessimism bias, and found psilocybin-assisted psychotherapy showed significant results in decreasing both general and specific depressive scores. Griffiths et al. (2016) wanted to study psilocybin-assisted psychotherapy on depression and anxiety in terminally ill participants. They found that there were significant positive changes to both, with the majority of participants qualifying for remission. Ross et al. (2016) also looked at participants with cancer who were experiencing depression and anxiety. Results showed significant improvements in both general scores and scores designed to measure specific aspects of other cognitive and behavioral changes. Wheeler and Dyer (2020) conducted a meta-analysis on psychedelic substances' effects on many mental illnesses and found many studies showing psychedelics had positive and large effects on mental health, especially as compared to therapy or medication treatments.

Studies on psilocybin alone have shown that it is both safe to use and can stand alone as an effective tool for depression and anxiety. The underlying mechanisms of why psilocybin is so effective are not understood in complete detail, but evidence showing changes to both the brain's structural and functional systems likely plays a role. Psilocybin has also been shown to work on specific factors leading to, or included in, the pathology of depression. Other studies have shown that coupling it with psychotherapy shows even greater and longer-lasting results than traditional treatment options, especially in individuals with severe illnesses like treatment-resistant

depression or terminal illness. The importance of finding a novel and effective treatment option for depression cannot be understated, as so many individuals still suffer from this often debilitating mental illness. If future studies continue to show evidence that psilocybin has such a positive and long-lasting effect, like in this literature review, it may not only provide another route to take for depressed individuals, it may help us learn more about depression, our brains, and mental health in general. More research must be done that includes larger sample sizes and looking at more ways psilocybin specifically affects depression both physically in brain structures and mentally in ways of thinking. This current study aims to address some of these concerns by including a large sample population and asking participants about their previous psilocybin experience and if it affected their depression, and if so, what specifically about their experience helped the most. Therefore, this present study asks: Do individuals who have used psilocybin feel their experience increased their ability to deal with depressive symptoms?

Method

This present study assessed whether people who have used psilocybin feel that the experience improved their ability to prevent or deal with depressive symptoms and what about their experiences had the most impact on their depressive symptoms. This study collected descriptive information from participants about their experiences and analyzed what aspects participants say were the most influential to help with depressive symptoms. This information can be then used in future psilocybin-assisted psychotherapy sessions to have the therapy focus on these factors to hopefully make the sessions more effective.

Participants

Participants were recruited online on sites including Facebook and LinkedIn that have groups related to the background of this study, such as groups for people to share their

experiences with psychedelics or groups for people who frequent music festivals, so, therefore, could provide a large pool of participants. There was no specific target demographic for the participants' age, sex, gender, ethnicity, race, or educational background; all demographics were welcome to participate, and would in fact were encouraged so as to get a more well-rounded participant pool. Since this survey is asking about past experience using psilocybin, those who have never taken the substance were not eligible to participate.

Potential participants learned about this study through posting of the research information on Facebook and LinkedIn, as well as by word of mouth to individuals I know who are involved in the psychedelic community (See Appendix A for Research Announcement). Participants saw this research announcement posted on my personal Facebook/LinkedIn page, as well as Facebook/LinkedIn groups that may have people who have used psilocybin in the past. Any group this announcement was posted in was not run by any official clinics or organizations and allowed such announcements to be posted, which was verified prior to sharing the link if it was not explicitly stated in the group rules. These groups on Facebook include: EntheoNation, neuro.circle, Illinois Psychedelic Society, Tipper Community, and Psychedelics, Sacred Medicines, Purpose & Business. On LinkedIn, the groups will include Psychedelic Leadership Development, Consilience - Psychedelics Networking, Psychedelic Profits, psychedelics, Psychedelic Opportunities, The Medicine: Science & Psychedelics, and Psychedelic Policy Forum.

Participants completed the questionnaire on any device that can access the internet, at a time and in a place that was most convenient for them. The answer forms were automatically saved through SurveyMonkey. The survey was open for 4 weeks to allow enough time to gather data. The participants had the option to provide their email address to be entered to win a $30

Amazon.com gift card. They did not have to participate if they wanted to be kept completely anonymous. If they did provide their email, it was kept confidential, as all email addresses were stored securely on an encrypted flash drive as well as an encrypted Excel spreadsheet file and were promptly deleted once the drawing for the giveaway was completed on the day the survey closed.

The Research Announcement was posted on the Facebook and LinkedIn pages of several open-access groups related to the background of this study and frequented by individuals who are more likely than the general population to have used psychedelics or dedicated to research announcements; see Appendix A for the announcement's text. Facebook's terms of service permit such research postings; see www.facebook.com/terms. LinkedIn's terms of service also permit such research postings; see https://www.linkedin.com/legal/l/service-terms. The Research Announcement remained on the social media sites for four weeks, and was reposted repeatedly to keep the announcement appearing in the news feed for the selected groups. Some Facebook/LinkedIn groups had moderators; others did not. Some groups included language in their terms disallowing posting on their pages for research and data collection. I only posted the Research Announcement on Facebook/LinkedIn pages whose terms allowed postings for research or data collection purposes.

The Research Announcement included a link to the survey, accessible via SurveyMonkey. The link took the subjects to SurveyMonkey, where the subject first saw and agreed to the Informed Consent; see Appendix B for the text of Informed Consent. If participants agreed to the Informed Consent, they automatically received access to the survey to complete online. If participants did not agree to the Informed Consent, they proceeded to a thank you page, and participation terminated at that point. Although it is unlikely, should participants have

experienced any emotional discomfort resulting from completing the survey, they could contact the Emotional Distress Hotline, a national mental health hotline, available 24/7 for free at 1-800-LIFENET. After 4 weeks, I closed the SurveyMonkey survey and analyzed the data.

Measures

The variables in this study include the independent variable of past psilocybin usage, and the dependent variable of effect on depressive symptoms. Psilocybin usage will be measured by asking participants how many approximate times in their life they have taken psilocybin. Effect on depressive symptoms will be measured by asking participants if they have ever had depressive symptoms, what effect psilocybin experiences had on those symptoms, and what about those experiences were most influential.

Demographics Questionnaire

The demographics questionnaire asks the participants about their race/ethnicity, gender, age, education level, and relationship status. This is to get an idea of the individuals who take the survey and see if there are any trends in the data. This can also be used to point out limitations to the research if the demographics were skewed in any direction, or did not include anyone of specific populations. Participants are not required to answer any of the questions in order to proceed with the rest of the survey.

Survey on Psilocybin Use and Depressive Symptoms (SPUDS)

Since the research question involves participants recounting their psilocybin use and both how much and how it affected their past/current depressive symptoms, and what aspects of their experience was the most salient, I developed a new survey since there was no existing measure looking at this specific topic. This survey asks participants about their past psilocybin use, their history or current dealings with depressive symptoms, and how much they felt their psilocybin

use helped them. It also asks about what parts of their experience(s) with psilocybin were the most influential. To assess whether someone has taken psilocybin and approximate lifetime usage, the survey asks whether they have ever ingested psilocybin and how many approximate times in their life they have partaken in this experience from several ranges of numbers, these are questions 1-2. To assess past or current depressive symptoms, question 3 asks if participants have ever experienced or are currently experiencing depressive symptoms or have been diagnosed with depression; another validated questionnaire (PHQ-9) is included after this survey to measure more in depth for current depressive symptoms. To assess their views on their psilocybin experiences affecting their depressive symptoms, participants are asked on question 4 using a Likert scale how much and what effect psilocybin had, from “made significantly worse” through “made significantly better”. Participants in the next question, question 5, can check all that apply from a list of common ways that psilocybin experiences help with depression, such as more openness, less fear of death, less worry about the future, etc. Following that question is question 6, an open-ended question where participants can describe in detail their experiences and what about them were most influential in coping with depressive symptoms. Participants are asked on question 7 if taking higher doses led them to have a more profound experience and if that led to a bigger effect on depression symptoms on a scale from none of the time to all of the time. There is also an open-ended question 8 that asks in detail what changed between the low and high dose experiences that was the most salient.

The survey was developed with several closed-ended questions to assess the participant’s history, and a question that is open-ended for participants to recount what was most influential about their psilocybin experience(s). Questions on the survey include both socio-demographics and key content related to the research question or suggested by the literature review. See

Appendix D for the full text of the survey. A doctoral-level researcher specializing in survey design reviewed and edited the survey, improving its face and content validity. Face validity suggests that the survey measures what it aims to measure based upon a simple reading of the questions. Content validity indicates that the instrument represents all key aspects of the construct it should measure; an expert appraisal can partially assess content validity (Miller & Lovler, 2015). Nevertheless, the new survey was developed for the present research and had no existing data on the reliability or validity of the questions or the instrument beyond the face and content validity.

The Patient Health Questionnaire-9 (PHQ-9)

In order to test participant's depression levels, they will be given the PHQ-9, which is a brief self-administered measure to test an individual's current depression severity (Kroenke et al., 2001). It contains 9 questions asking participants on a scale from "not at all" to "nearly every day" how often over the past two weeks have they been troubled with problems such as loss of interest, sleep issues, appetite changes, thoughts of self harm, and other indicators of depression It also asks a final question, that if the participant checked that they had any of the problems listed, to what extent did the problem(s) affect their daily responsibilities. Each problem and corresponding frequency is scaled so that the more severe the problem/depression, the higher the participant's score. The cutoffs for depression scores are 0-4 (none-minimal), 5-9 (mild), 10-14 (moderate), 15-19 (moderately severe), and 20-27 (severe). This measure was chosen because it is less lengthy than many other measures of depression so participants may be more willing to complete a shorter survey, as well as it showing both high validity and reliability when tested (Kocalevent et al., 2013; Kroenke et al., 2001). The measure showed high internal reliability, with Cronbach's α on several screenings between 0.86-.89 and test-retest reliability with a

correlation of 0.84 between self-reporting and clinician-given testing (Kroenke et al., 2001). The measure also has shown high criterion validity, with a ROC analysis of .95, indicating this test can discriminate very well between those with and without major depression. It also has shown high construct validity, with statistically significant correlations with other measures of depression, such as the SF-20 Health-related Quality of Life Scales.

Procedures

The first step in the procedure for this study is to distribute the survey to all potential pages and groups on Facebook and LinkedIn that may have people who have a background in using psilocybin. These can include groups that have members who frequent music festivals, who are part of groups that work on integrating psychedelic experiences into people's lives, who are involved in research on or advocacy for these substances, etc. The participants will open the survey, and those who do decide to participate will fill it out to the best of their ability. If they decide to also participate in the optional giveaway for the gift card, they can do so as well. Once the survey is closed after 4-5 weeks, all the data can be collected and transferred from SurveyMonkey into SPSS for analysis. Also after the survey closes and all emails are collected, the email addresses can be put into an encrypted Excel Spreadsheet. Using a random number generator, whatever number is generated should match a number corresponding with an email address on the Excel list, and that person will win the gift card. The gift card should be promptly sent to that email address. After the data has been transferred to SPSS, it must be analyzed to see the breakdown of demographics and both questionnaires to find trends in the data. The answers to open-ended questions will be analyzed to see if there are trends in what participants report as the aspects with the largest effects.

Data Management

To ensure the anonymity of the survey participants, in using SurveyMonkey, IP addresses will not be collected. For this study, I transferred the data from SurveyMonkey into an SPSS database for analysis. I presented all of the results in aggregate form to protect participants' identities. I had access to the data only in the form of physical completed surveys that they maintained on an encrypted flash drive, kept in a locked safe in my home. The thesis advisor and I were the only parties with access to the strong password that protected the SPSS dataset. The dataset will contain no coded identifiers and, as such, will be completely anonymous. The email addresses will be kept on a separate encrypted Excel file on a separate flash drive so that they cannot be matched with responses.

I will store all electronic data on an encrypted flash drive and not on any computer hard drive. I will retain the data set and related files for a minimum of five years after the study completion, in case questions arise about the analyses. After five years, I will destroy the data using the current Department of Defense data destruction standards. I will likely choose an affordable technique, such as encryption, pending technology at the time.

Results

For this study, I conducted a survey and gathered participants' responses. I exported the data from SurveyMonkey into IBM's SPSS statistical software, version 28.0 Standard. Using the data, I gathered descriptive statistics about their demographics and their SPUDS and PHQ-9 scores, including frequencies, mean, range, standard deviation, skewness, and kurtosis. I also ran a correlation analysis to determine any significant relationships between the scores on demographics, SPUDS, and PHQ-9.

Participant and Demographic Characteristics

There were a total of 403 individuals who participated in this study. Twenty-four individuals reported they had never taken psilocybin, and therefore were not included in the data. Seven participants only completed the SPUDS and not the PHQ-9, so they were also not included in the data. This may have been due to people running out of their free time to complete the survey, disinterest in completing the second survey, etc. The total number of participants after this was 370. For the demographic questions, two did not respond to age, four did not respond to race, two did not respond to their relationship status, and one did not respond to gender. Some were left blank and others chose the option "prefer not to say", and there could be a variety of reasons they did not feel comfortable disclosing this information. The rest of the questions were fully completed.

Of these total participants, the ages ranged from 19-70, with the mean age being 32. The majority of the participants were White/Caucasian (51.9%), with the second and third highest races reported being American Indian/Alaskan Native (17.2%) and Black/African American (16.1%). Most of the participants identified as men (48.4%), but women were a close second at 46.5%, and there were 3.5% who identify as transgender, and 1.3% as non-binary/non-conforming . Most participants were in a relationship whether married (46.2%) or not (18%), and most held bachelor's degrees (34.7%) or associate's degrees (21%). Table 1 in Appendix E summarizes participants' scores on the demographic questions.

Psilocybin Use

The first variable in this study is the participant's psilocybin use. 100% of the included respondents said they used psilocybin. Those who responded "no" to the question of whether they had ever taken psilocybin were not included and were sent to the end of the survey (as stated above, this was 24 respondents). There was also a question about how many total times in

their life they had taken psilocybin, with 14% saying once, 34.1% saying 2-3, 29.8% saying 4-8, 10.2% saying 8-12, and 11.8% saying 13+ times. This variable had a skewness of .483, with the majority of the participants taking psilocybin a smaller number of times. Participants were asked to rate how many of the common depressive symptoms they have experienced: No symptoms (9.7%), few symptoms (35.5%), moderate symptoms (28%), many symptoms (11.8%), and all symptoms/have been clinically diagnosed with depression (14.2%). On the question of what effect their psilocybin experience had on their potential depressive symptoms, 5.6% said it made them significantly worse, 25.3% responded slightly worse, 18.3% said it had no effect, 32.5% responded slightly better, and 18% said significantly better.

Of the list of most common positive aspects someone feels after their experience with psilocybin, the top four most reported were greater appreciation for life itself (47%), changes to ways of thinking (43.8%), feeling more connected to people and the world in general (40.1%), and stronger self of self (35.5%) (remaining aspect percentages are listed in Table 2). When asked how often a higher dose produces a more profound experience and bigger effects, the majority said either little of the time (33.1%) or neutral/some of the time (31.7%).

Table 2 summarizes all participants' scores on all the SPUDS questions except for the open ended questions. Table 3 lists out participants' responses to the two open-ended questions.

PHQ-9 Scores

The second variable in this study is respondents' PHQ-9 scores. On each of the questions, respondents were asked to rate how often they had been bothered by the specific problems over the past two weeks, including (0) Not at all, (1) Several days, (2) More than half the days, and (3) nearly every day. Each participants' scores were aggregated to get their individual total scores, and those scores were rated on the PHQ-9 scoring scale, ranging from 0-4

none/minimum, 5-9 mild, 10-14 moderate, 15-19 moderately severe, and 20-27 severe. On the depression severity, 5.6% were none/minimum, 20.4% were mild, 24.5% were moderate, 34.7% were moderately severe, and 14.8% were severe. The mean total score was 13.75, which is on the higher side of moderate, with a standard deviation of 5.758 and a skewness of -.309. Figure 1 below shows the skewness of the total score compared to a normal curve. When looking at the skewness of severity, we also see a skewness of -.278, shown in Figure 2 below as compared to a normal curve. The minimum score was zero (lowest score possible, none/min), and the highest score was 27 (highest score possible, severe). The last question on this survey asks participants how difficult the previous problems made doing work, taking care of things at home, and getting along with other people, to which 8.3% said not difficult at all, 44.6% said somewhat difficult, 26.6% said very difficult, 15.3% said extremely difficult, and 5.1% said none of the above.

Table 4 summarizes participants' scores on the PHQ-9.

Figure 1

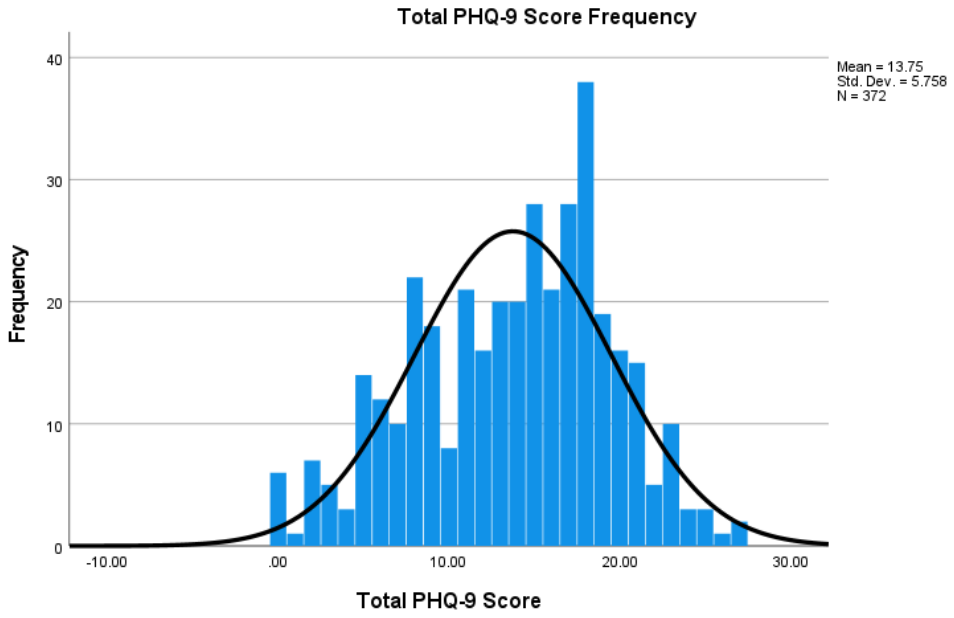
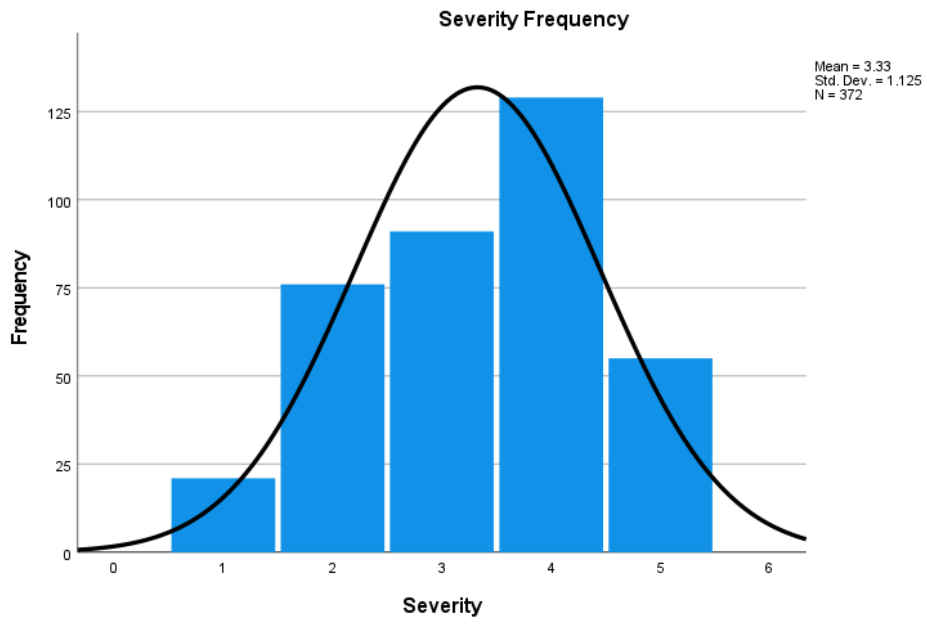


Figure 2



Statistical Analyses

An Eta Coefficient test was run to determine whether any demographic information was associated with changes on how many times participants ingested psilocybin, whether it helped their depression, and their total PHQ-9 scores. There were no high degree associations between any of these variables. Table 5 includes all the directional measures tables and Eta values.

A correlation analysis was run to determine relationships between the variables of age, how many times psilocybin was used, how much psilocybin helped from the SPUDS scores, and the total PHQ-9 scores. The analyses did not result in any high degree correlations between these variables. There were low correlations that were statistically significant between age and how much they reported psilocybin helping depressive symptoms (.212), with those who are older tending to slightly respond more that it helped them in a greater capacity, as well as times psilocybin was ingested and how much psilocybin helped (.229), with the more times psilocybin

was ingested tending to slightly correlate with more positive effects of psilocybin on depressive symptoms.

Tables 6-7 includes the full correlational tables between these variables.

SPUDS Open-Ended Questions

On the SPUDS questionnaire, there were two open-ended questions where participants could explain their answers in greater detail. Table 3 in Appendix E lists out all participants' responses on these questions. The first open-ended question was a follow-up to a checklist where participants could check all of the positive, common effects they may have experienced during their psilocybin trip(s). The question asked, "if you had any of those experiences, or others that were not listed, that helped prevent or cope with depressive symptoms, can you describe the most influential aspects in detail and what about them made such a large impact? If you did not experience any of these effects, please write N/A". 80 participants answered this question, but 27 responses were not included as they did not actually answer the question or the answer did not make sense, leaving a total of 53 responses. There seemed to be some trends in the answers, with 60% of participants responding that their experience(s) with psilocybin specifically changed parts of themselves, other than mood, for the better. Several responses stood out as quite meaningful:

- "The above mentioned experiences last for weeks/months after the trip. The experience itself is almost like resetting those negative thoughts."
- "Psilocybin established a deep love of nature in me. And connection to all people and animals. It also helped me love myself more which allowed me to quit drinking (2.5yrs now, a huge blessing) I believe it's made me a better father and husband."

- “The sense of self… feeling lost prior to but then being feeling brought back into my being and who I am.”
- “Gratitude for the beauty of nature, love for many people, animals, things… and connectedness with the world and the people in it. Feeling better about who I am, and more open and accepting of where I am at any given stage of my life. Realizing that no matter how sad or frustrated I feel, things could always be much worse.”
- “It's helped me to rebalance and rewire my brain after 7 years of taking SSRI medication for depression and anxiety.”
- “I learned to see myself not as a broken human being, but someone who has accomplished a lot, but had a temporary setback. There was hope for the future. I was able to see things from other points of view, which helped me grow personally.”
- “Feeling more connected to community, nature and myself has created the largest impact on my soul.... feeling like I am a part of the weaving of life. I felt like a ripple in the ocean and a star in the galaxy. divinely interconnected with all living beings... helped me realize we are all a part of each other's experiences. feeling so deeply led me to be more empathetic with everything and everyone.”
- “...It helped me get out of my head and into the present moment and connect with the world around me. It helped me recognize my inner fierceness and turn down the volume on my inner critic. With that kind of happiness I felt like the person I was supposed to be....”

Another trend, found in 40% of responses, was people reporting changes in their overall moods and increases in their happiness, as demonstrated by some of the below responses:

- “Each time I’ve experienced pure bliss, overall just super happy and intrigued/amazed/appreciative of everyday life and objects around me. specifically natural things. my perspective on life was widened in general.”
- “I realised I have the ability to be happy…”
- “...I felt free from my physical body and allowed to truly enjoy all the beautiful things life has to offer”
- “Less negative emotions, [more] confidence in life, personality has become a lot more cheerful.”
- “Depression is effectively resolved”
- “After the trip was over... it felt like I had died and came back completely cleaned and freed of my depression.”
- “I have experienced feeling connected and not alone in this world. The realization that everything is one helps me feel happy when I wake up in the morning. It helps me to look forward to the day and the future. I felt inspired to create my day and life fully. I have also felt very creative and started making art again.”

On the second open-ended question, participants were asked, “if you did find that the more psilocybin you ingested the bigger effect it had on you and your ability to prevent/deal with depressive symptoms, what was the biggest change(s) between your low and high dose experiences that led to these changes? Please write N/A if this did not apply to you”. There were 68 responses to this question, but 26 were not included as they did not answer the question, did not make sense, or answered with material they copied from an online source, leaving a total of 42 responses. There were several trends in the responses to this question as well. 69% of participants responded that the higher the dose they took, the better they felt, and the more the

experience affected their mental health or produced better and larger changes. Several responses are listed below that exemplified this well:

- “The mountains and valleys evened out. I stopped overreacting to bad experiences and wrote them off as the exception and not the rule. And that bad experiences happen to everyone. I was not unique in my suffering. It's the human condition.”
- “The high dose experience was so intense it made me question what I thought of as reality. This led to a radical shift in my thinking. Lower doses generally do not have such a profound effect on me, those are more of a recreational effect.”
- “At times a larger dose seemed to provide profound positive effects regarding internal existential conflicts and fears of death or changes in life. These particular effects have been more commonly noted after higher doses compared to lower doses.”
- “All the negative thoughts stopped and I was at peace with life and myself.”
- “Higher doses have a more dramatic and thorough examination and revelation of my inner self.”

There were also responses (24%) that said both high and low doses produced positive changes or said they use high and low dosages for different purposes:

- “Microdosing is life saving therapy for my depression. Macro dosing helps me tackle the big issues. So I can’t say [one] is better than the other.”
- “Microdosing is helpful for general sadness but bigger doses lead to more profound experiences that have changed truly changed the way I think and feel about certain things- for the better! I can honestly say without a doubt I [am] much happier in my life

than I was before ever trying mushrooms and while I won't say it's entirely because of them I will say they had a large part in helping me along the way."

- "Larger doses provided a deeper dig into the psyche… smaller doses were still markably uplifting but not as transformative."
- "Bigger doses tend to help me address more significant key details of my depressive symptoms (the root of the problem) whereas smaller doses I would take a few times a week and a couple days off in order to address aspects of my life that need to be changed in the present."

There was also a small percentage of respondents, 7%, that responded either that they had the same insights from low and high doses, have only microdosed, or have found that higher doses are not always more helpful.

Discussion

The research results gathered from this analysis support this study's original hypothesis that individuals who have used psilocybin feel that their experience(s) increased their ability to deal with depressive symptoms. However, the correlation, even though statistically significant, is not very strong. It seems that the consequences of using psilocybin that are most commonly experienced are greater appreciation for life itself, changes to ways of thinking, feeling more connected to people and the world in general, and stronger sense of self, which could be responsible for why psilocybin-assisted psychotherapy is so effective on depression. As to what effect the psilocybin experience had on depressive symptoms, "made it slightly better" was the highest chosen response. The amount of psilocybin does not necessarily affect depressive symptoms, as most said it only made it more profound either little or some of the time.

Implications

There are several important results of this study. First is that there is a correlation, albeit not strong, between psilocybin use and ability to cope with depressive symptoms. What parts of the psilocybin experience were most commonly felt was meaningful to learn, as well as that the amount of psilocybin taken does not necessarily matter. Finally, the participant's responses to the open-ended questions were significant to hear about the experiences from the participant's own words. It is possible that the most common aspects experienced can be focused on and tested in the future to see what about those aspects correlated with changes in depression or the brain. If the amount taken does not always matter, what is the key element of the experience that makes the changes? The participant's responses to the open-ended questions give insight as to what their experience(s) have done for them and their depression that quantitative data cannot give. There are many directions for future research based on the participants' responses and data analyses from this study to look into more of these aspects and more about the details of the psilocybin experience.

Similarities and Differences

There are some significant differences between this study and the work of others in this field. Most other work in this field is quantitatively gathered by performing experiments giving participants psilocybin coupled with therapy and measuring changes in depression scores. Whereas in this study, data was gathered qualitatively about past experiences with psilocybin that were likely not in therapeutic settings. This type of study was not feasible for this thesis due to legality of psilocybin in my residing state of Illinois, lack of funding, and inability to complete a study of this magnitude on my own with the time and resources available. Many of the quantitative studies have massive teams of people of various

professions working together over years to get results. What this study did address that these other studies do not is the qualitative data from participants' explaining in detail their experiences with psilocybin and how it affected their depression with their own words, rather than just being reported as changes in depression measures. I think this type of qualitative work can not only enhance the data gathered from quantitative studies, but can also help future quantitative studies focus the psilocybin-assisted psychotherapy sessions on specific salient aspects.

Limitations

This study did have several limitations. About half of the participants were white/caucasian and about two thirds had a college degree, so it is possible that the results may be different with a more diverse population. The survey was posted on Facebook and LinkedIn, which does have a large reach of people, but limits the population to those with internet access and those who have profiles on either website.

Another limitation is the skewness of the PHQ-9 scores in that there was a skew towards most of the scores being on the higher end of the depression severity scale. One major factor that could be behind this skewed distribution is the COVID-19 pandemic, as research has shown that this pandemic has significantly increased both anxiety and depression scores in individuals around the United States (Jia et al., 2021). This could account for the low correlation, as other research in this field, as previously discussed, shows statistically significant and high correlation between psilocybin-assisted psychotherapy and lowered depressive scores. The SPUDS survey did not ask when the participant's most recent experience with psilocybin was, so if a participant's most recent experience was well before the pandemic, the strength of the changes psilocybin made may not have been enough to

combat how powerful the pandemic was to exacerbating depression. It also did not ask if they took psilocybin for therapeutic purposes, or strictly for recreation, which could have changed how it affected their depressive symptoms if that was not the sought-after intent. Future iterations of this survey will be revised to account for these potentially confounding variables.

Conclusions

Based on the participant's responses to the most commonly experienced aspects of their psilocybin experience(s), more research should be conducted to focus on those specific aspects and what makes them the most common, and oftentimes the most life-changing. It is possible that these experiences can be correlated with the changes in the brain we see after psilocybin-assisted psychotherapy. In many of the quantitative studies in this field, the amount of psilocybin given to participants seems to affect how big of a change they see in their depressive symptoms, so it is interesting to see the participants in this study report that this has not always been the case for them. It could be that therapy, or taking psilocybin specifically with therapeutic intent, is the key ingredient to the higher doses consistently bringing about larger changes, but more research should be done to investigate this. The responses to the open-ended questions also leave a lot of room for more qualitative research on these experiences to get even more in-depth information as to an individual's subjective psilocybin experience. While those of us in research appreciate what numbers and statistics can show, oftentimes the general population responds more to stories such as those gathered from these questions, so this might be a helpful way to get more positive attention to the amazing results many of these studies in this field show. The biggest thing those of us who work in this field can do is continuing to do research and educating others on these

substances and what they can do for mental health based on the ever-growing field of positive evidence. There are a lot of decades of misinformation to undue and missed opportunities for research to make up for, so the more evidence that can be brought to light showing the effectiveness of these substances, the better it can be used to help people suffering from many different types of debilitating mental illnesses.

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Appendix A

Research Announcement

My name is Taylor Hansen.

I am conducting research through Purdue University Global to obtain a Master's Degree in Psychology.

The purpose of the research is to understand if individuals who have used psilocybin in the past feel that it increased their ability to prevent or cope better with symptoms of depression, and if so, what part of their experience had the most effect on these positive changes.

If you are interested in being a part of this study by taking the survey, please click here for more information: https://www.surveymonkey.com/r/67L8VHM

The survey will take about 10-15 minutes of your time.

There will be an **optional** part of the survey where you can include an email address if you would like to be entered to win a $30 Amazon.com gift card. You are **not** required to participate in this in order to participate in the study. If you *do not* include your email, then your responses will be anonymous, so no one will know that you were a participant and no one will ever be able to connect your answers to your identity. If you *do* wish to provide your email, it and your responses will be confidential, so your personal information will be protected securely according to all applicable laws and regulations.

Click here to participate! https://www.surveymonkey.com/r/67L8VHM

The research study is in no way sponsored, endorsed, administered by or associated with Facebook or LinkedIn. Participants release Facebook and LinkedIn of any responsibility or liability associated with participating in this research.

Appendix B

Purdue University Global
Consent for Participation in Research
"*Psilocybin and Depression: Past Psilocybin Use Improving Future Depressive Symptom Management*"

CONCISE SUMMARY

The purpose of this study is to assess whether past use of psilocybin can help prevent or mitigate the effects of depressive symptoms and what about the experience is the most influential in creating these changes. The total duration of participation in this study will be approximately 10-15 minutes. This study will require participants to fill out the survey to the best of their ability and will allow participants to be a part of studying this substance so it could potentially be used to help treat or combat depression. There are no significant risks to this study, but you will be asked to answer questions about past psilocybin use and past or current depressive symptoms. Please note participation in this study is completely optional and you can stop participation at any time. More details about all of this information can be found below.

Why am I being asked?

You are being asked to be a participant in a research study about whether past psilocybin use can help prevent or increase one's ability to deal with depressive symptoms and what parts of the experience were most influential. This research study is being conducted by Taylor Hansen, a Master's of Science in Psychology student at Purdue University Global. You have been asked to participate in the research because you are in a Facebook/LinkedIn group related to psychedelics and may be eligible to participate. We ask that you read this form and ask any questions you may have before agreeing to be in the research.

Your participation in this research is voluntary. Your decision whether or not to participate will not affect your current or future relations with Purdue University Global. If you decide to participate, you are free to withdraw at any time without affecting that relationship.

What is the purpose of this research?

The purpose of this research is:
To understand if past psilocybin use can prevent or help someone deal with symptoms of depression and what aspects of the experience participant's felt created the biggest effect.

What procedures are involved?

If you agree to be in this research, we would ask you to do the following things:

Fill out the following survey as accurately and to the best of your ability as you can.

Approximately 100 participants may be involved in this research at Purdue University Global.

What are the potential risks and discomforts?

The research will ask about:
-Past experiences when using psilocybin
-Potential symptoms of depression you may have felt or are feeling

If you think that these will be too sensitive of topics, you do not have to participate or you can cease participating during the study if it is too uncomfortable.

Are there benefits to taking part in the research?

A benefit to participating in this research is being able to contribute to the knowledge of psilocybin's effects on depression, which will hopefully turn into both more research on this subject as well as increasing the availability for this substance to be used therapeutically and to help people in need who have debilitating mental illnesses such as depression.

There is also the optional opportunity to be entered to win a $30 Amazon.com gift card.

What about privacy and confidentiality?

If you decide **not** to enter the giveaway for the gift card using your email address, no one will know that you are a research subject because this research is totally anonymous. No information about you, or provided by you during the research, can ever be disclosed to others because no information that can possibly identify you as an individual will be collected. When the research results are published or discussed in conferences, no information will be included that could ever reveal your identity.

If you **do** decide to enter the giveaway for the gift card using your email address, then the only people who will know that you are a research subject are members of the research team, and the only personally identifying information gathered will be your email address. No information about you, or provided by you during the research, will be disclosed to others without your written permission. When the results of the research are published or discussed in conferences, no information will be included that would reveal your identity.

Any information that is obtained in connection with this study and that can be identified with you will remain confidential and will be disclosed only with your permission or as required by law. Personal information, research data, and related records will be stored securely to prevent access by unauthorized personnel by being locked on a flash drive that only the researcher has access to

as well as being kept on an encrypted Excel spreadsheet. Once the study is complete and a winner is drawn for the gift card, the data sheet containing emails will be permanently deleted.

Will I be reimbursed for any of my expenses or paid for my participation in this research?
For this study, there will be an optional giveaway for a $30 Amazon.com gift card. Participating or not in this giveaway will have no bearing on the other survey data or any other situation. All emails will be kept securely as stated above and will be destroyed after the drawing is over.

If you win, the gift card will be sent to the email you provide so please make sure the email address is typed correctly and a valid email address. This gift card will be emailed the day the survey is scheduled to close.

Can I withdraw from the study?
You can choose whether to be in this study or not. If you volunteer to be in this study, you may withdraw at any time without consequences of any kind. You may also refuse to answer any questions you don't want to answer and still remain in the study.

Whom should I contact if I have questions?
The researcher conducting this study is Taylor Hansen. You may ask any questions you have now. If you have questions later, you may contact the researcher at:
Phone: 847-770-8889, Email: taytayhansen1144@gmail.com.
You may also contact the researcher's thesis adviser, Dr. Gabrielle Blackman PhD, at gblackman@purdueglobal.edu.

What are my rights as a research subject?
If you feel you have not been treated according to the descriptions in this form, or you have any questions about your rights as a research subject, you may contact the Institutional Review Board (IRB) at Purdue University Global through the following representative:

Susan Pettine, IRB Chair
Email: spettine@purdueglobal.edu

Remember: Your participation in this research is voluntary. Your decision whether or not to participate will not affect your current or future relations with Purdue University Global [or insert the names of any other cooperating institutions as well]. If you decide to participate, you are free to withdraw at any time without affecting that relationship.

You may keep a copy of this form for your information and your records.

Signature of Subject

I have read (or someone has read to me) the above information. I have been given an opportunity to ask questions and my questions have been answered to my satisfaction. I agree to participate in this research. I have been given a copy of this form.

- ☐ I agree to participating in this research.
- ☐ I do not agree to participating in this research.

Appendix C

Table 1.

Survey on Psilocybin Use and Depressive Symptoms (SPUDS) Development Plan

Objective	Operational Definition	Number and Type of Items
To assess whether someone has taken psilocybin or not	I define taking psilocybin as any method of mushrooms, tea, capsules	I will measure this objective with a simple yes/no response. This is Q1 of my survey.
To assess approximate lifetime usage	I define approximate lifetime usage as how many estimated times total in their life they took	I will measure this objective using a scale consisting of ranges of amounts of lifetime usage. This is Q2 of my survey
To assess depressive symptoms	I define depressive symptoms as persistent sadness or negative emotions, loss of pleasure/interest in daily activities, difficulty sleeping, changes in appetite, poor concentration, fatigue, feelings of worthlessness or guilt, thoughts of suicide or death	I will measure this objective using 5 Likert scale items ranging from no symptoms to all symptoms/a clinical depression diagnosis. This is Q3 of my survey.
To assess psilocybin helping depression	I define psilocybin helping depression as how much it helped the individual prevent or overcome depression and what aspects helped the most. Also if the higher the dose the more profound effect it had	I will measure this objective using 6 Likert scale items for how much effect psilocybin had on depression, a 10 item list of common aspects people can report as being most influential, an open-ended question about the aspects, and 6 Likert scale items for whether a higher dose led to a more profound experience or bigger effect. These are Q4-Q7 of my survey. Q8 of my survey asks participants to describe the changes between low/high doses on depressive symptoms.

Appendix D

Copies of All Measures

Measure 1.

Demographics Survey

1. What is your age? ___
2. What is your race/ethnicity?
    a. American Indian or Alaskan Native
    b. Asian/Pacific Islander
    c. Black or African American
    d. Hispanic
    e. White/Caucasian
    f. Multiple ethnicity/Other (please specify): _____
    g. Prefer Not to Answer
3. What is your gender identity?
    a. Woman
    b. Man
    c. Transgender
    d. Non-binary/non-conforming
    e. Other (please specify): _____
    f. Prefer Not to Answer
4. What is your relationship status?
    a. Single
    b. In a relationship (not married)
    c. Separated
    d. Married
    e. Widowed
    f. Other (please specify): _____
    g. Prefer Not to Answer
5. What is the highest level of education you have attained?
    a. Less than a high school degree
    b. High School degree or equivalent (GED)
    c. Some college, but no degree
    d. Associate degree
    e. Bachelor's degree
    f. Master's degree
    g. Doctoral degree
    h. Other (please specify):

Measure 2.

Survey on Psilocybin Use and Depressive Symptoms (SPUDS)

1. Have you ever taken psilocybin in any form, including, but not limited to, mushrooms, tea, capsules, etc.?
    a. Yes
    b. No
2. Approximately how many times total in your life?
    a. 1
    b. 2-3
    c. 4-8
    d. 8-12
    e. 13+
3. Have you ever experienced the following symptoms or have been diagnosed with depression? (persistent sadness or negative emotions, loss of pleasure/interest in daily activities, difficulty sleeping, changes in appetite, poor concentration, fatigue, feelings of worthlessness or guilt, thoughts of suicide or death)?
    a. No symptoms
    b. Few symptoms
    c. Moderate symptoms
    d. Many symptoms
    e. All symptoms/I have been clinically diagnosed with depression
4. How much do you feel like your experience(s) with psilocybin and what you learned from the experience(s) helped prevent or overcome any of the above depressive-like symptoms?
    a. Made it significantly worse
    b. Made it slightly worse
    c. Had no effect
    d. Made it slightly better
    e. Made it significantly better
5. If taking psilocybin did have a positive effect, did you experience any of the below common aspects of psilocybin ingestion? (Check all that apply)
    a. Greater openness
    b. Feeling more connected to people and the world in general
    c. No longer frightened by/worried about death
    d. Greater appreciation for life itself
    e. Changes to ways in thinking
    f. Stronger sense of self
    g. Less rumination on negative past events or worry about future events
    h. I did not experience any of these effects
6. If you had any of those experiences or others that were not listed, that helped prevent or cope with depressive symptoms, can you describe the most influential aspects in detail, and what about them made such a large impact? If you did not experience any of these effects, please write N/A.

_____

7. Did you find that the higher the dosage taken, the more profound the experience and the bigger the effect?
    a. None of the time
    b. Little of the time
    c. Neutral/Some of the time
    d. Most of the time
    e. All the time
8. If you did find that the more psilocybin you ingested, the bigger effect it had on you and your ability to prevent/deal with depressive symptoms, what was the biggest change(s) between your low and high dose experiences that led to these changes?

    _____

Measure 3.

Patient Health Questionnaire-9 (PHQ-9)

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

Not at all (0) Several days (1) More than half the days (2) Nearly every day (3)

1. Little interest or pleasure in doing things 0 1 2 3

2. Feeling down, depressed, or hopeless 0 1 2 3

3. Trouble falling or staying asleep, or sleeping too much 0 1 2 3

4. Feeling tired or having little energy 0 1 2 3

5. Poor appetite or overeating 0 1 2 3

6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down 0 1 2 3

7. Trouble concentrating on things, such as reading the newspaper or watching television 0 1 2 3

8. Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual 0 1 2 3

9. Thoughts that you would be better off dead or of hurting yourself in some way 0 1 2 3

FOR OFFICE CODING 0 + _____ + _____ + _____ =Total Score: _____

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all / Somewhat difficult / Very difficult / Extremely difficult

Developed by Drs. Robert L. Spitzer, Janet B.W. Williams, Kurt Kroenke and colleagues, with an educational grant from Pfizer Inc. No permission required to reproduce, translate, display or distribute.

Measure 4.

Giveaway Questionnaire

If you would like to participate in the <u>*optional*</u> giveaway of a $30 Amazon.com gift card for participating in this study, please include your email below.

<u>Please make sure it is typed in accurately and that this is a valid email address as the gift card will be sent when the survey closes if you win the giveaway.</u>

_____

Appendix E

Table 1.

Respondents' Sociodemographic Characteristics (N=370)

Measure	All Subjects
Age	
Range	51
Minimum	19
Maximum	70
Mean	32.48
Race and Ethnicity	
American Indian or Alaskan Native	17.2%
Asian/Pacific Islander	7.8%
Black or African American	16.1%
Hispanic or Latino	4.3%
White or Caucasian	51.9%
Multiple ethnicities/Other (please specify)	1.1%
Prefer not to say	1.1%
Marital Status	
Single	23.4%
In a relationship (not married)	18%
Married	46.2%
Divorced/Separated	9.4%

Widowed	2.4%
Other (specify)	0%
Prefer not to say	.3%
Gender	
Woman	46.5%
Man	48.4%
Transgender	3.5%
Non-binary/non-conforming	1.3%
Other (please specify): _____	0%
Prefer Not to Answer	.3%
Education Level	
Less than a high school degree	4.3%
High School degree or equivalent (GED)	10.2%
Some college, but no degree	19.1%
Associate degree	21%
Bachelor's degree	34.7%
Master's degree	8.6%
Doctoral degree	1.9%
Other (please specify):	.3%

Table 2.

SPUDS Responses (N=370)

Measure	All Subjects
Taken Psilocybin	
Yes	100%
No	0%
Lifetime Usage	
1	14%
2-3	34.1%
4-8	29.8%
8-12	10.2%
13+	11.8%
Depressive Symptoms	
No symptoms	9.7%
Few symptoms	35.5%
Moderate symptoms	28%
Many symptoms	11.8%
All symptoms/I have been clinically diagnosed with depression	14.2%
Psilocybin Effect on Depressive Symptoms	
Made it significantly worse	5.6%
Made it slightly worse	25.3%
Had no effect	18.3%
Made it slightly better	32.5%

Made it significantly better	18%
Common Aspects of Psilocybin Ingestion	
Greater openness	23.4%
Feeling more connected to people and the world in general	40.1%
No longer frightened by/worried about death	32.5%
Greater appreciation for life itself	47%
Changes to ways in thinking	43.8%
Stronger sense of self	35.5%
Less rumination on negative past events or worry about future events	32.3%
I did not experience any of these effects	6.2%
Higher Dosage Equaling Bigger Effect	
None of the time	10.8%
Little of the time	33.1%
Neutral/Some of the time	31.7%
Most of the time	17.5%
All the time	6.5%
Did not respond	.5%

Table 3.

Spuds Open-Ended Responses Q6 (N=53)

Question
Q6: *If you had any of those experiences, or others that were not listed, that helped prevent or cope with depressive symptoms, can you describe the most influential aspects in detail and what about them made such a large impact? If you did not experience any of these effects, please write N/A.*
-I prefer to share my daily life with others.
-Each time I've experienced pure bliss, overall just super happy and intrigued/amazed/appreciative of everyday life and objects around me. specifically natural things. my perspective on life was widened in general
-I realised I have the ability to be happy. During the "experiences" I was laughing at nature's beauty and the feeling carried on afterwards.
-I was tested for moderate depression including bipolar disorder, and tried many medications to control my depression Taking Psilocybin is just one of them
-Physical pain of depression (that "pit of the stomach" feeling, tense shoulders, occasional headaches) can cause more anxiety and depression. During peak psilocybin experiences, I felt free from my physical body and allowed to truly enjoy all the beautiful things life has to offer
-Being able to accept feelings as they are and not a reflection of my abilities. Also a greater sense of self led to less social anxiety. New perspectives on problems.

-Mushrooms, especially microdosing keeps me present. I'm way less focused on the past or future. Helps me to do what I need to do today

-Helped to cope with current events. Use was in microdosed amount usually 1-2 grams golden teacher type oral ingestion and alleviation of fear anxiety and sadness surrounding loss of family member breakup and job loss.

-I was able to see why I was stuck in life or to understand experiences that were blocked from me before.

-The above mentioned experiences last for weeks/months after the trip. The experience itself is almost like resetting those negative thoughts.

-It took me in a new direction with myself

-Less negative emotions, confidence in life, personality has become a lot more cheerful

-The mood opens up

-The biggest impact is that I don't worry too much about negative thoughts, and my mood is temporarily more comfortable

-Self-awareness, being able to see the best in yourself, trying to accept your imperfections

-I took a 7 gram dose in my sophomore year of college, and had an incredibly negative experience in the moment because of the environment and circumstances in which I chose to take such a dose. Afterwards, while coming down from the psilocybin, I spent a great deal of time reflecting on what I had experienced, and I can point at that as a moment when I really

reevaluated my life choices and began to make more positive choices for myself from that moment on.

-Open the door to a new world and have a different outlook on life

-I find it very effective in relieving me

-I feel more secure and not afraid of what I'm missing

-Ease

-Allow yourself to see different things and experience different feelings

-In me when I was at middle school I was very self-abased because of race, have the pessimistic mood, accompanied by family members to the hospital to do the inspection for major depression, began antidepressant, started taking a lot of hormone psychiatric drugs, after two years of medication and psychological therapy did not end the depression, I found the medication to be very effective during the treatment, forcing me to calm down, and taking Psilocybin was good for me, though it didn't make me fall into long-term fantasies.

-Use when in a slump…lightens me immediately

-Try to look on the bright side

-It made me more confident

-Relax your mind

-Reduce psychological burden

-Emotions are effectively controlled

-Depression is effectively resolved

-Mainly in terms of life, not so pessimistic

-Greater sense of my spiritual awareness and purpose.

-I used to be severely depressed, so I had to take it.

-It's essential to me

-Connect with people

-Less irritable, easier to laugh things off rather than let them make me mad or upset

-Overall the psilocybin has made me less critical of myself, especially my past actions. And it makes me realize that while what I do is important that I cannot control anyone else's life or decisions.

-Psilocybin established a deep love of nature in me. And connection to all people and animals. It also helped me love myself more which allowed me to quit drinking (2.5yrs now, a huge blessing) I believe it’s made me a better father and husband

-Reduce the thinking of the past negative events or worries about future events

-Feel the value of life

-The sense of self… feeling lost prior to but then being feeling brought back into my being and who I am

-I have experienced feeling connected and not alone in this world. The realization that everything is one helps me feel happy when I wake up in the morning. It helps me to look

forward to the day and the future. I felt inspired to create my day and life fully. I have also felt very creative and started making art again.

-During that particular trip, I wasn't able to concentrate on my experience, as a friend was having a difficult trip and I was mostly taking care of him. After the trip was over, I smoked weed and passed out, then when I came to, it felt like I had died and came back completely cleaned and freed of my depression

-Brighter mindset overall

-Gratitude for the beauty of nature, love for many people, animals, things… and connectedness with the world and the people in it. Feeling better about who I am, and more open and accepting of where I am at any given stage of my life. Realizing that no matter how sad or frustrated I feel, things could always be much worse.

-It's helped me to rebalance and rewire my brain after 7 years of taking SSRI medication for depression and anxiety.

-I learned to see myself not as a broken human being, but someone who has accomplished a lot, but had a temporary setback. There was hope for the future. I was able to see things from other points of view, which helped me grow personally.

-Realized that the things I was stressed about weren't that important in life overall, which made it so that I could approach those things more effectively with a calmer and healthier mind

-Feeling more connected to community, nature and myself has created the largest impact on my soul.... feeling like I am a part of the weaving of life. I felt like a ripple in the ocean and a star in the galaxy. divinely interconnected with all living beings... helped me realize we are all a part of

each other's experiences. feeling so deeply led me to be more empathetic with everything and everyone.

-Through many psilocybin experiences where my death was likely I can compare it to a more sober frame of mind. Essentially the thought being "if I didn't kill myself then I probably don't have to kill myself now."

-Had a powerful experience that is best described as summoning mother nature herself. Made me feel one with life + greater appreciation

-I'm more confident in my abilities than I was before

-feeling more connected and open to the past, present, and future

-I have only ever microdosed with psilocybin but it was enough to shift my perspective. I didn't get many visual disturbances characteristic of a classic trip, but its cerebral effects were noticeable and that's all I needed. It helped me get out of my head and into the present moment and connect with the world around me. It helped me recognize my inner fierceness and turn down the volume on my inner critic. With that kind of happiness I felt like the person I was supposed to be. It would have a positive ripple effect and enrich my everyday life and personal relationships for a short time.

-I was able to confront my father’s suicide for the first time after 10 years of refusing to address it.

-Shrooms opened my view on God.

-Psilocybin induces most of the aforementioned experiences for me when I consume it. It's difficult for me to simply choose one or two aspects of the experience as being the most

impactful, as they are all intertwined. I greatly value psilocybin for how it has allowed me to come to come to peace with negative events that have happened in the past, from childhood trauma to the deaths of loved ones. I also love how I feel as though I am cognitively firing on all cylinders for many days after consumption. The afterglow is wonderful.

-Changed perspectives, less anxiety, less negativity

Table 4.

Spuds Open-Ended Responses Q8 (N=53)

Question
Q8: *If you did find that the more psilocybin you ingested, the bigger effect it had on you and your ability to prevent/deal with depressive symptoms, what was the biggest change(s) between your low and high dose experiences that led to these changes?*
-I felt like the blissful and appreciative state is only increased when taking more. I have not taken what some would consider “a lot” though.
-The higher the dose the closer I got to being able to being able to relinquish control of my mind
-The mountains and valleys evened out. I stopped overreacting to bad experiences and wrote them off as the exception and not the rule. And that bad experiences happen to everyone. I was not unique in my suffering. It's the human condition.
-Microdosing is life saving therapy for my depression. Macro dosing helps me tackle the big issues. So I can’t say [one] is better than the other.
-Prefered to have some effects while in control for me personally id say 2-3g would be perfect for this need.
-When I use it a lot, MY mood will not be so low, and when I use it a little, I still have suicidal thoughts
-Microdosing is helpful for general sadness but bigger doses lead to more profound experiences that have changed truly changed the way I think and feel about certain things- for the better! I can honestly say without a doubt I [am] much happier in my life than I was before ever

trying mushrooms and while I won't say it's entirely because of them I will say they had a large part in helping me along the way.

-Make me more conscious

-Thinking about things differently

-It makes me feel more awake and comfortable

-Less negative emotions, more confidence in life, more cheerful personality, and the greater the dose, the more pronounced the effect

-Maybe it's the growing dependence on it, because it gives me relief, which is what I want

-Each experience is different, I can embrace the society and myself more

-The high dose experience was so intense it made me question what I thought of as reality. This led to a radical shift in my thinking. Lower doses generally do not have such a profound effect on me, those are more of a recreational effect.

-Made me more conscious, more comfortable, less desperate for life

-High dose used for transformation of negative patterns like drinking too much or stuck thinking…low dose on occasion for low mood times

-It makes me feel better. It doesn't make my life worse

-The more you use, the better you feel

-Change in mindset

-At times a larger dose seemed to provide profound positive effects regarding internal existential conflicts and fears of death or changes in life. These particular effects have been more commonly noted after higher doses compared to lower doses.

-All the negative thoughts stopped and I was at peace with life and myself

-The more you take, the better

-At low doses, there is some relief in the effect knowledge, and at high doses, there is more problem solving

-The larger the dose, the more pronounced the effect

-The bigger the dose makes me feel better

-The mood does not often become irritable

-It takes the edge off my nerves for a while

-When I use it a lot, I can control my emotions well, but when I use it less, I still get depressed

-Higher doses have a more dramatic and thorough examination and revelation of my inner self. Micro dosing hasn't had much of an effect so far but I'm just starting.

-The bigger the dosage, the more introspection

-The impact on ego and perception was much more significant at higher doses.

-At lower doses I can still control the experiences and mount my egoic defenses. At higher doses this is not possible.

-I'd say my typical dose is ~4-6g (not light, not heroic). I've found that when I take too much, I have fewer helpful insights/perspective shifts. And I feel like those things contribute to the alleviation of depression.

-More clarity about ultimate reality and our roles and power

-Larger doses provided a deeper dig into the psyche… smaller doses were still markably uplifting but not as transformative

- Feel that both kinds of doses are beneficial if you take the dose that you need in the moment. More isn't always better. When I use psilocybin I meditate on the mushroom and I ask how much to take. This always brings me the connection I need. And sometimes I get the response to microdose or not take any.

-The higher you go the less chance you have to fight the feeling of letting go; you are forced to. Fighting the trip always makes it worse for me and the sooner I can overcome that the quicker I can move on to an introspective state where I can work through issues.

-I've only microdosed. When I've microdosed with a higher than normal dosage, I definitely feel the healing effects more. The next few days after taking a heavier than normal dose are times of increased healing/purging/transmuting trauma.

-I paid attention to set/setting and prepared for my trips, so my usual 2g dose gave me roughly the same insight as my max 4g trip.

-High dose experiences force confrontation of emotional states, there is less ability to seek internal mental distraction

-Bigger doses tend to help me address more significant key details of my depressive symptoms (the root of the problem) whereas smaller doses I would take a few times a week and a couple days off in order to address aspects of my life that need to be changed in the present.

-As with most intoxicants, increasing the dosage tends to cause all of the experiences to become more intense, from the euphoria to the introspection. At a higher dose I find it's a lot more difficult to shut my mind down when trying to go to sleep, which causes me to spend more time analyzing anything and everything from all angles. This tends to be very beneficial, and I do experience epiphanies.

-The low dose didn’t do much for depression, and the high dose helped me communicate without too much fear

Table 5.

PHQ-9 Responses (N=370)

Measure	All Subjects
Depressive Aggregate Scores	
None/Min	5.6%
Mild	20.4%
Moderate	24.5%
Moderately Severe	34.7%
Severe	14.8%
Descriptive Statistics	
Mean	13.75
Standard Deviation	5.758
Skewness	-.309
Range	27
Minimum	0
Maximum	27
How Difficult Have Problems Made Life	
Not Difficult At All	8.3%
Somewhat Difficult	44.6%
Very Difficult	26.6%
Extremely Difficult	15.3%
None of the Above	5.1%

Table 6.

Association between Race x How Many Times Psilocybin Taken

Directional Measures

			Value
Nominal by Interval	Eta	Race Dependent	.307
		HowManyTimes Dependent	.289

Association between Race x How Much Psilocybin Helped

Directional Measures

			Value
Nominal by Interval	Eta	Race Dependent	.264
		HowMuchPsilocybinHelped Dependent	.334

Association between Race x Total PHQ-9 Score

Directional Measures

			Value
Nominal by Interval	Eta	Race Dependent	.344
		TotalScore Dependent	.143

Association between Gender x How Many Times Psilocybin Taken

Directional Measures

			Value
Nominal by Interval	Eta	Gender Dependent	.079
		HowManyTimes Dependent	.139

Association between Gender x How Much Psilocybin Helped

Directional Measures

			Value
Nominal by Interval	Eta	Gender Dependent	.114
		HowMuchPsilocybinHelped Dependent	.169

Association between Gender x Total PHQ-9 Score

Directional Measures

			Value
Nominal by Interval	Eta	Gender Dependent	.377
		TotalScore Dependent	.210

Association between Relationship Status x How Many Times Psilocybin Taken

Directional Measures

			Value
Nominal by Interval	Eta	Relationship Dependent	.200
		HowManyTimes Dependent	.152

Association between Relationship Status x How Much Psilocybin Helped

Directional Measures

			Value
Nominal by Interval	Eta	Relationship Dependent	.195
		HowMuchPsilocybinHelped Dependent	.205

Association between Relationship Status x Total PHQ-9 Score

Directional Measures

			Value
Nominal by Interval	Eta	Relationship Dependent	.206
		TotalScore Dependent	.176

Association between Education x How Many Times Psilocybin Taken

Directional Measures

			Value
Nominal by Interval	Eta	Education Dependent	.141
		HowManyTimes Dependent	.238

Association between Education x How Much Psilocybin Helped

Directional Measures

			Value
Nominal by Interval	Eta	Education Dependent	.172
		HowMuchPsilocybinHelped Dependent	.197

Association between Education x Total PHQ-9 Score

Directional Measures

			Value
Nominal by Interval	Eta	Education Dependent	.308
		TotalScore Dependent	.212

Table 7.

Correlations between Age x Times Psilocybin Ingested x Psilocybin Changes x Total PHQ-9 Score

		How Many Times Ingested	How Much Psilocybin Helped	Total Score
Age	Pearson Correlation	.116*	.212**	-.167**
	Sig. (2-tailed)	.026	<.001	.001

****. Correlation is significant at the 0.01 level (2-tailed).**

Table 8.

Correlations between Times Psilocybin Ingested x Psilocybin Changes x Total PHQ-9 Score

		How Many Times Ingested	How Much Psilocybin Helped	Total Score
How Many Times Ingested	Pearson Correlation	1	.229**	.086
	Sig. (2-tailed)	-	<.001	.098
How Much Psilocybin Helped	Pearson Correlation	-	1	-.178**
	Sig. (2-tailed)	-	-	<.001

****. Correlation is significant at the 0.01 level (2-tailed).**

Appendix F

Expedited Review – Final Approval

October 18, 2021

Ms. Taylor Hansen
Purdue University Global
taylorhansen1@student.purdueglobal.edu

Re:Protocol #21-**72** – **"Psilocybin and Depression: Past Psilocybin Use Improving Future Depressive Symptom Management."**

Dear Ms. Hansen:

Your proposed project was reviewed by the Purdue University Global Institutional Review Board (IRB) for the protection of human subjects under an Expedited Category. It was determined that your project activity meets the expedited criteria as defined by the DHHS Regulations for the Protection of Human Subjects (45 CFR 46), and is in compliance with this institution's Federal Wide Assurance 00010056.

Please notify the IRB immediately of any proposed changes that may affect the expedited status of your project. You should report any unanticipated problems involving risks to human subjects or others to the IRB.

If you have any questions or need additional information, please contact feel free to contact me at spettine@purdueglobal.edu. I wish you well with your project!

Sincerely,

Susan B. Pettine

Susan B. Pettine, Ph.D., CBM
IRB Chair
Purdue University Global