

Psilocybin for End -Of-Life

Psilocybin is a classic serotonergic psychedelic drug and is the primary psychoactive compound in magic mushrooms. Psychedelic drug's therapeutic potential were first investigated in the 1960s in numerous clinical studies but unfortunately, by the 1970s, clinical research with psychedelics was almost fully terminated and we are still experiencing the repercussions of this today. However, before that freeze out, studies into psychedelics pointed to a potential role for psilocybin and other classic psychedelics in cancer-associated or end-of-life-associated psychological distress (Reiche et al., 2018; Ross, 2018). Recently, after a long hiatus period of regulatory obstacles, interest in the clinical use of psilocybin for this patient population has resumed (George et al., 2020).

Individuals who have been diagnosed with a terminal illness may not only have physical suffering, but also significant emotional, spiritual, and social distress (Steinhauser et al., 2000). Anxiety and depression are some of the most common psychiatric symptoms of patients suffering with life threatening diseases, often associated with a low quality of life and a poor overall prognosis (Reiche et al., 2018). However, there are currently no pharmacologic interventions for existential distress (Bogenschutz and Ross, 2018) and available pharmacologic treatments for depressive symptoms in patients with cancer have not demonstrated superiority over placebo (Ostuzzi et al., 2018). Therefore, there remains a need for additional effective treatments for those conditions.

Today, there is a growing body of data has linked psilocybin-assisted psychotherapy with improved existential and spiritual well-being in patients with a terminal illness as well as improved quality-of life in the face of death, decreased depression, decreased hopelessness, decreased desire for hastened death, and increased gratitude (Breitbart et al., 2000, 2010; McClain et al., 2003; Nelson et al., 2002).

Present day clinical research with psychedelics involves a drug-assisted psychotherapy paradigm and psilocybin-assisted psychotherapy refers to the professionally guided use of psilocybin in combination with psychotherapy and differs greatly from the recreational use of psychedelics. In psilocybin-assisted psychotherapy, participants undergo just one or a small number of psilocybin sessions intended to produce a profound and temporary alteration of consciousness. "Set and setting"—a term which refers to the psychological, social, and cultural parameters which shape the response to psychedelic drugs, is highly influenced by factors such as expectancy, preparation, and intention (set), and physical or social environments (setting) (Hartogsohn, 2017) and are carefully managed by preparatory non-drug sessions and the creation of a safe, comfortable space for participants during drug treatment sessions. The presence of trained guides during drug treatment sessions is considered key, as are post-treatment non-drug integration sessions (Rosenbaum et al., 2019).

Randomized control trials utilizing psilocybin -assisted psychotherapy to treat psychological and existential distress associated with advanced or terminal cancer have resumed within the last 2 decades at the University of California Los Angeles (UCLA), Johns Hopkins University and New York University Langone Medical Center and have produced very promising results.

Two of the most recent studies with patients with life-threatening cancers as well as a range of psychiatric disorders in the mood and anxiety realms from Johns Hopkins University (Griffiths et al., 2016) and New York University (NYU) (Ross et al., 2016) have been very influential in the revival of psychedelic research. The Johns Hopkins University study included 51 patients and used a crossover design whereby each patient received both an experimental high dose of psilocybin and a low dose that served as an active placebo control. The NYU trial included 29 patients randomized to receive psilocybin or the active placebo niacin in a crossover design involving 1 drug session each. Both trials involved preparatory and post-treatment integration psychotherapy sessions,

Both studies demonstrated powerful, immediate, and lasting benefits based on standardized measures of anxiety and depression. Furthermore, both studies demonstrated a similarly robust safety profile of the experimental intervention in a medically ill population, with no serious adverse medical or psychological outcomes reported in either study. These findings are consistent with published work about the safety and risk profile of psychedelics, which can be appropriately mitigated both with careful screening of subjects who have an underlying risk of psychosis and with appropriate support by the psychotherapy team. (Gasser et al., 2014; Griffiths et al., 2016; Grob et al., 2011; Ross et al., 2016). There are also now positive preliminary reports on the safety and tolerability of psilocybin for clinical conditions such as obsessive compulsive disorder (Moreno et al., 2006) alcohol use disorders (Bogenschutz et al., 2015) tobacco addiction (Johnson et al., 2014) and for major depressive disorder (Carhart-Harris et al., 2021, 2016, 2012)

These milestone studies from Johns Hopkins University and NYU also suggested a central role of the psilocybin-occasioned mystical-type experience, which correlated significantly with therapeutic outcomes based on ratings using validated scales. Additionally, qualitative research from the NYU trial revealed several key themes identified by participants in their follow up psychotherapy sessions: reconciliation with death, acknowledgment of cancer's place in life, and emotional uncoupling from cancer (Swift et al., 2017). Indeed, participants reported that the psilocybin therapy helped them to reconnect to life, reclaim presence, and increase their confidence in the face of cancer recurrence.

These reports are also consistent with patient testimonials who have been treated with psilocybin for their end-of-life distress through TheraPsil. Thomas was one of the first patients to receive a legal exemption through TheraPsil and when asked how his perspective on life changed after his psilocybin treatment he says “It's really been very foreign for me dealing with this whole concept of anxiety. It's not a natural state for me. For some people, they deal with anxiety on a daily basis for years on end, and I just haven't had to deal with that. And as a result, I didn't really have a lot of good tools in my toolbox for dealing with that. Having the psilocybin has given me the chance to experience consciousness in a form that is ‘other’ from the way that I normally experienced it. [It] was a way of showing me that there are other elements to our reality and our existence that we're not aware of. And that perhaps the transition from living to not living could be as simple as the transition from waking to sleep. It's very comforting for me.”

In conclusion, there is now substantial evidence that psilocybin-assisted psychotherapy is effective in the treatment of mental health issues in patients with a life-threatening disease and is well tolerated. Moreover, there is clear evidence that psychedelic-induced mystical-type peak experiences mediate not only reduction of psychiatric symptoms in these patients but may also be helpful for these patients by improving disease coping and quality of life when facing a life-threatening condition. As more patients in palliative care report feeling uplifted, connected and hopeful a result of psilocybin-assisted psychotherapy and given the safety profile of psilocybin, this form of treatment is a very promising option— especially for patients where other approaches have been ineffective.

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