Psychedelics for psychological and existential distress in palliative and cancer care

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In recent years, there has been renewed scientific interest in, and associated media coverage of, psychedelics. A so-called psychedelic renaissance is underway, with research programmes at major academic institutions worldwide conducting basic and clinical research into the potential therapeutic effects of psychedelic medicines for a variety of psychiatric conditions. These compounds were first studied in the 1950s, but by the mid-to-late 1960s, clinical research began to be curtailed and was almost fully terminated by the mid-1970s. Before that freeze out, however, studies into psychedelics pointed to a potential role for those agents in the setting of cancer-associated or end-of-life-associated psychological distress (see Ross, 2018, and Reiche et al., 2018, for comprehensive reviews). Those early experiments and their contemporary counterparts invite the questions: Is there a role for psychedelics for treating patients in palliative medicine and cancer care today? And, if so, where?

The classic psychedelics include psilocybin (a naturally-occurring alkaloid found in several species of mushrooms), dimethyltryptamine (one of the primary psychoactive components of the Amazonian ayahuasca brew), and lysergic acid diethylamide. All are part of a group of psychoactive compounds that share serotonin 5-HT2A receptor agonist properties and which, at adequate doses, induce profound alterations in thought, perception, and emotion, together with experiences of ego dissolution or mystical-type experiences (see Nichols, 2016, for a comprehensive review).

Contemporary clinical research into psychedelics involves a drug-assisted psychotherapy paradigm whereby participants undergo just one or a small number of drug sessions intended to produce a profound and temporary alteration of consciousness. “Set and setting”—the concept that the drug response is highly influenced by factors such as expectancy, preparation, and intention (set), and physical or social environments (setting)—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.

The use of psychedelics in the fields of oncology and palliative care is intriguing for several reasons. First, many patients facing cancer or other life-threatening illnesses experience significant existential distress related to loss of meaning or purpose in life, which can be associated with hopelessness, demoralization, powerlessness, perceived burdensomeness, and a desire for hastened death. Those features are also often at the core of clinically significant anxiety and depression, and they can substantially diminish quality of life in this patient population. The alleviation of those forms of suffering should be among the central aims of palliative care. Accordingly, several manualized psychotherapies for cancer-related existential distress have been developed in recent years, with an emphasis on dignity and meaning-making (see Bauereiss et al., 2018, for a review). However, there are currently no pharmacologic interventions for existential distress per se, and available pharmacologic treatments for depressive symptoms in patients with cancer have not demonstrated superiority over placebo. There remains a need for additional effective treatments for those conditions.

Enter psychedelics. As reviewed by Ross and Reiche et al., psychedelic-assisted therapy for patients facing life-threatening illness appears to be a safe and potentially highly efficacious intervention for psychological and existential distress associated with such conditions. Contemporary double-blind placebo-controlled trials of psychedelics for depression and anxiety associated with cancer have produced very promising results. The two most recent and noteworthy of those studies were completed at Johns Hopkins University and New York University (NYU) and were published concurrently with eleven editorials from international experts in the fields of psychiatry, palliative medicine, and drug policy. The Johns Hopkins University study, which included 51 patients, used a crossover design whereby each patient, serving as their own control, received both an experimental high dose of psilocybin (22 mg or 30 mg/70 kg) and a low dose (1 mg or 3 mg/70 kg) that served as an active placebo control. The NYU trial included 29 patients randomized to receive psilocybin (0.3 mg/kg) or the active placebo niacin (250 mg) in a crossover design involving 1 drug session each. Both trials involved preparatory and post-treatment psychotherapy sessions, and both included patients with life-threatening cancers as well as a range of psychiatric disorders in the mood and anxiety realms. Both studies demonstrated robust, immediate, and—critically—lasting benefits (that is, out to 6 months or more after active...
treatment sessions in each case) based on standardized measures of anxiety and depression. Both studies demonstrated a similarly robust safety profile of the experimental intervention in a medically ill population. Medical symptoms were generally limited to transient elevations in blood pressure, with no serious adverse medical or psychological outcomes reported in either study.13,14. Those 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.15.

These landmark 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. Mystical-type experiences are characterized by core features of unity, a noetic quality (that is, the sense of encountering “ultimate reality”), sacredness, deeply felt positive mood, transcendence of space and time, and ineffability (that is, the sense that the experience cannot be adequately described using words). For a review of mystical-type experiences, including their neurobiologic correlates, see Barrett and Griffiths, 2018.16. Additionally, qualitative research from the NYU trial revealed several key themes identified by participants in their healing narratives: reconciliation with death, acknowledgment of cancer’s place in life, and emotional uncoupling from cancer.17. 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.

Psychological and existential distress associated with life-threatening illnesses including cancer represent unique and highly burdensome forms of suffering, for which available treatment options demonstrate limited efficacy. Recent clinical trials using rigorous methods have suggested a very promising potential role of psychedelic-assisted therapy in this clinical setting. The central import of the mystical-type experience and the themes emerging from participant reports of their psychedelic experiences point to the well-suitedness of this psychospiritual intervention to the unique and fundamental concerns of many people facing cancer and nearness to death. Barriers to conducting research involving psychedelics in Canada remain, including lasting stigma related to the methodologic and ethical shortcomings of certain research into psychedelics in the 1950s and 1960s, as well a potential dearth of traditional sources of research funding. However, given the methodologic rigour of contemporary clinical trials with psychedelics, together with published safety guidelines for human research involving psychedelics, we are hopeful that well-designed study protocols will be met with ethics approval from local research ethics boards, as well as from Health Canada and the Canadian Institutes of Health Research. We thus look forward to future randomized clinical trials that examine, in a Canadian context, the feasibility and effectiveness of psychedelic-assisted therapy for patients with cancer or at end of life.

CONFLICT OF INTEREST DISCLOSURES
We have read and understood Current Oncology’s policy on disclosing conflicts of interest, and we declare that we have none.

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REFERENCES