reunion
NEUROSCIENCE

Adjustment Disorder Associated With Medical Illness: Unmet Needs and Rationale for RE104 as a Novel Psychedelic Therapy

Mark H. Pollack, MD
Chief Medical Officer
Reunion Neuroscience, Inc.
mpollack@reunionneuro.com

04/07/2025

Reunion Neuroscience

Introduction

RE104 is a unique, proprietary, subcutaneously administered 4-hydroxy-N,N-diisopropyltryptamine (4-OH-DiPT) prodrug in development as a novel psychedelic investigational compound for the treatment of mental health conditions.

Preclinical and early phase 1 results suggest that RE104 induces a short and reproducible psychedelic experience comparable to psilocybin, which supports further investigation of RE104 in an ongoing phase 2 study in patients with postpartum depression (RECONNECT).[1,2] A randomized, double-blind phase 2 study is planned for the treatment of adjustment disorder in patients with cancer and other medical illnesses. The purpose of this resource is to review the significant unmet need of patients with adjustment disorder and to explain the rationale for exploring RE104 as a potential treatment for this population.

Table of Contents

Definition and Diagnosis of Adjustment Disorder

Adjustment disorder is a psychological condition characterized by the development of emotional or behavioral symptoms in response to an identifiable stressor; although these stress responses are natural, adjustment disorder is characterized by a response that is disproportionate to the severity or intensity of the stressor, or symptoms that cause functional impairment.[3] Symptoms vary between patients but may include constant rumination, feeling sad or hopeless, crying often, feeling anxious or irritable, having trouble sleeping or concentrating, social or occupational impairments, and withdrawing from family and friends.[3,4] Revisions to the definition of adjustment disorder in commonly used classification systems (eg, the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision [DSM-V-TR] and the International Classification of Diseases and Related Health Problems 11th Revision [ICD-11]) have provided much-needed guidance for diagnosis (Table 1).[3,5,6] Within adjustment disorder, there are 6 identified subtypes, including depressed mood, anxiety, mixed anxiety and depressed mood, disturbance of conduct, mixed disturbance of emotions and conduct, and unspecified.[3]

Adjustment disorder is one of the most frequently diagnosed stress-related psychiatric disorders, which also includes posttraumatic stress disorder, complex posttraumatic stress disorder, and acute stress disorder.[3,7-9] Conditions such as major depressive disorder, bereavement, or complex grief may share some symptoms but have distinct distinguishing features. The presence of an identifiable stressor contrasts with major depressive disorder, where depressive symptoms are variable and/or not tied to a specific stressor.[10] Additionally, while bereavement or complex grief can also impact patient daily functioning, they differ from adjustment disorder through the lack of a stress response to the precipitating or anticipated death.[3,11]

Stressors associated with development of adjustment disorder may be acute or chronic in nature.[12] Acute and chronic stressors include problems related to divorce, moving, death of a loved one, serious illness, financial difficulties, family conflicts, conflicts with neighbors, and concerns related to the health of one's self or a loved one.[12] Additional examples of stressors may include love affairs, domestic problems, education or work problems, and changes in residence or employment status.[3,13]

Table 1. Diagnostic Criteria for Adjustment Disorder[3]

DSM-V-TR	ICD-11
Onset of emotional or behavioral symptoms occurring in response to an identifiable stressor and within 3 months of the stressor	Presence of an identifiable psychosocial stressor, with symptoms emerging within 1 month of the stressor
Symptoms are clinically significant and marked by • Distress that is disproportionate to the severity or intensity of the stressor (accounting for cultural or other contextual factors) • Significant impairments in social, occupational, or other domains of functioning	Preoccupation related to the stressor or its consequences in the form of ≥1 of the following: • Excessive worry about the stressor • Recurrent and distressing thoughts about the stressor • Constant rumination about the implications of the stressor
Disturbance does not meet the diagnostic criteria for another mental disorder and is not an exacerbation of a pre-existing disorder	Failure to adapt to the stressor that causes significant impairment in personal, family, social, educational, or other important areas of functioning
Symptoms do not represent normal bereavement	Symptoms are not of sufficient specificity or severity to justify diagnosis of another mental or behavioral disorder
Symptoms do not last for more than 6 additional months after the stressor or its consequences have been resolved	Symptoms typically resolve within 6 months, unless the stressor persists for a longer duration

DSM-V-TR, Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision; ICD-11, International Classification of Diseases and Related Health Problems 11th Revision.

Epidemiology and Burden of Adjustment Disorder

Previous research suggests that the prevalence of adjustment disorder varies across settings, with rates in the overall population ranging from 0.5% to 2%, and up to 11.5% for patients presenting to outpatient psychiatric clinics.[3,6,13] Several unique populations may be at higher risk for adjustment disorder. For example, rates of adjustment disorder are higher among recently unemployed individuals (27%) and bereaved individuals (18%).[3] The prevalence of self-reported adjustment disorder increased with COVID-19 (18.2%) and was attributed to unique stressors, including restricted social contact, problems with work or childcare, fears of infection, and crisis management.[14] Socioeconomic characteristics such as young age, low educational attainment, marital status, and urban residence are all suggested risk factors for the development of adjustment disorder.[13] Notably, adjustment disorder may also impact younger patients, with estimates for prevalence of adjustment disorder in children and adolescent populations within the general population around 4%.[15] However, a formal diagnosis of adjustment disorder and other similar psychiatric diagnoses is more prevalent among patients over 10 years of age.[16]

In patients diagnosed with cancer, the prevalence of adjustment disorder ranges from 6% to 35%. Considering that approximately 2 million individuals received new cancer diagnoses in the United States in 2024, the known prevalence suggests that **hundreds of thousands of newly diagnosed cancer patients could be impacted by adjustment disorder each year in the United States alone.**

The diagnosis or progression of a medical illness is a well-known factor that may precipitate mental health challenges, leading to a high prevalence of adjustment disorder and other psychiatric disorders among patients with medical illnesses.[3,9,17,18] In patients diagnosed with cancer, the prevalence of adjustment disorder ranges from 6% to 35%.[19-25] Considering that approximately 2 million individuals received new cancer diagnoses in the United States in 2024,[26] the known prevalence suggests that hundreds of thousands of newly diagnosed cancer patients could be impacted by adjustment disorder each year in the United States alone.

Although formally diagnosed adjustment disorder is best characterized in individuals with cancer, other mental health concerns, such as depression and anxiety, are also common in those receiving other serious diagnoses, including multiple sclerosis (22%-31% of patients),

amyotrophic lateral sclerosis (10%-45%), Parkinson's disease (17%-40%), and idiopathic pulmonary fibrosis (24%-49%).[27-30] Prevalence of adjustment disorder in children and adolescent populations with chronic diseases, such as heart transplant recipients, those with end-stage renal disease, and diabetes, range from 14% to 60%.[15,31] Ultimately, patients with any serious illness involving a terminal diagnosis or palliative care may develop adjustment disorder and face a unique burden, as serious illness is a chronic stressor that does not usually resolve on its own.

Adjustment disorder and other psychiatric diagnoses in those with medical illnesses are associated with negative outcomes, including **reduced medication adherence, as well as higher healthcare resource utilization and costs.**

Individuals with adjustment disorder are more likely to develop other mental health problems compared with individuals without a psychiatric diagnosis,[3,17,32] and face a higher risk for suicide, experience lower quality of life, and have high rates of disability.[33] Although adjustment disorder generally resolves within 6 months of the stressor being removed (along with supportive therapy), adjustment disorder can persist if the stressor does not resolve (eg, serious illness, financial difficulties, family conflict).[3,7,12,17] In addition, individuals may experience multiple episodes of adjustment disorder over the course of their medical illness in reaction to different stressors (eg, initial diagnosis, negative impact on their family/social/work function, poor response to treatment, or discouraging prognosis). Individuals with adjustment disorder face substantial burden from their symptoms (eg, difficulty with daily activities, not going to work, or suicidal ideation).[4] Moreover, adjustment disorder and other psychiatric diagnoses in those with medical illnesses are associated with negative outcomes, including reduced medication adherence, as well as higher healthcare resource utilization and costs.[20,34] The psychological burden associated with medical illnesses, which includes shifting relationship dynamics, a fear of disease progression, reactions to physical changes, and uncertainty around possible medication side effects, adversely impacts the quality of life of patients. Therefore, effective treatment for adjustment disorder may help mitigate the development of other psychiatric diagnoses in addition to addressing the direct negative consequences of the disorder itself.[3,32]

Current Treatment Landscape for Adjustment Disorder

Despite the widespread nature of adjustment disorder, there is a gap in high-quality research evaluating treatments in populations with adjustment disorder and a corresponding lack of evidence-based treatment guidelines.[7,35] This is partially attributed to the potentially transient nature of the disorder (dependent on the duration of the stressor), symptoms that are also present in other psychiatric disorders, and, until recently, the lack of clear diagnostic criteria.[3,6,10] While adjustment disorder may resolve spontaneously in some patients, those with more severe or prolonged symptoms often require intervention and may experience persistent or chronic adjustment disorder.[7]

Pharmacotherapies approved for the treatment of depression and anxiety have been used **off-label** for adjustment disorder, but **supporting studies in populations with adjustment disorder have been prone to quality issues.**

Psychological interventions including support and psychotherapy are the most commonly recommended treatment options for adjustment disorder; however, there is limited evidence to support the use of any specific interventions; the majority of studies evaluating the efficacy of psychotherapy for adjustment disorder are of poor quality or have a high risk of bias.[7,36] Individuals experiencing adjustment disorder related to medical illness may also be unwilling to accept psychological treatment, as evidenced by studies demonstrating that up to half of patients experiencing psychological distress related to cancer diagnosis reject psychological intervention, although adherence among those accepting intervention is high (~90%).[19,37]

Pharmacotherapies approved for the treatment of depression and anxiety have also been used off-label for adjustment disorder, but studies evaluating the efficacy and safety of these therapies have been prone to the same quality issues that plague studies of psychotherapy in this population.[7,36] Benzodiazepines are the most commonly prescribed pharmacotherapy for adjustment disorder, but their undesirable side effects, including potential withdrawal symptoms after treatment cessation, may limit their suitability for long-term treatment.[33] Selective serotonin reuptake inhibitors (SSRIs) may also be used for treatment of adjustment disorder, although meta-analyses

have failed to demonstrate the superior efficacy of SSRIs over placebo.[38] The efficacy of SSRIs in patients with adjustment disorder may be counteracted by the presence of side effects, delayed onset of clinical benefits, and a need for ongoing daily treatment for months or longer to achieve and maintain a beneficial effect.[2,38,39] Pharmacotherapies for adjustment disorder related to medical illness may be particularly challenging, given the increased risk for drug interactions and potential consequences of adverse events.[34]

There ultimately remains an unmet need for effective, evidence-based treatments specifically for adjustment disorder, particularly for patients with chronic stressors such as serious medical illnesses that may hinder natural resolution of adjustment disorder.[40]

Psychedelics for Treatment of Adjustment Disorder Related to Medical Illness

Serotonergic hallucinogens have been considered for the treatment of psychological distress in patients with life-threatening illnesses since the 1960s, with early studies demonstrating sustained improvements in mood, as well as reduced anxiety.[41,42] While initial studies were intended to evaluate the analgesic effects of psychedelic drugs, specifically lysergic acid diethylamide (LSD), unexpected improvements in mood and reduced fear of death in LSD-treated patients prompted interest into the benefits of psychedelic-assisted psychotherapy on cancer-related psychological distress.[38,43]

The clinical potential of psychedelics for treating mental health disorders in individuals with serious medical conditions has recently re-emerged as a topic of interest.

Psychedelics induce their effects via activation of 5-HT2A receptors, leading to enhanced sensory perceptions, modified cognitive and emotional processing, and increased neuroplasticity.[44] Neuroimaging studies in patients receiving psychedelics have demonstrated improved functional connectivity within brain areas that are dysregulated in those with depression, anxiety, posttraumatic stress disorder, and chronic pain disorders, which may underlie some of the observed benefits of psychedelic therapy in those with psychiatric disorders.[44] From a psychological perspective, improvements in anxiety and depression following psychedelic therapy are typically attributed to mystical experiences associated with these agents, although the mechanism by which mystical or peak psychedelic experiences confer a therapeutic benefit is not fully understood.[42,44-46] Psychedelics have been demonstrated efficacious for the treatment of anxiety and depression.[47]

The clinical potential of psychedelics in treating mental health disorders has recently re-emerged as a topic of interest for individuals with serious medical conditions.[48] Initial studies demonstrate large reductions in anxiety and depression with psychedelic (psilocybin) treatment in patients with cancer (Table 2).[42,49,50] Randomized controlled trials of high-dose psilocybin for the treatment of depression and anxiety in patients with cancer demonstrated rapid and sustained improvements in mental health symptoms after a single dose.[40] In one

study, participants with life-threating cancer experiencing anxiety and depression reported decreases in hopelessness, improved spiritual well-being, and increased quality of life following psilocybin treatment.[41] Importantly, the use of classical psychedelics, including dipropyltryptamine (DPT), LSD, and psilocybin, has been well tolerated, with no adverse events observed beyond 1 day after treatment.[43]

Although the use of psychedelics for treatment of adjustment disorder in patients with medical illnesses has not been specifically explored, phenomenological and mechanistic similarities between adjustment disorder and other psychiatric conditions (eg, depression and anxiety) support the clinical potential of this intervention.[51]

Table 2. Psilocybin Treatment for Depression and Anxiety in Patients With Cancer

DSM-V-TR	Inclusion criteria	Patients, N	Efficacy	Adverse events
Agrawal et al.[49]	Adults diagnosed with cancer and major depression disorder	30	• MADRS scores reduced from baseline by 19.1 points (95% CI, -22.3 to -16.0; *P*<0.001) by Week 8 • Sustained response in 24 patients (80%) • Full remission of depressive symptoms in 15 patients (50%)	• No treatment-related SAEs or suicidality • Mild or expected AEs, including headache (n=24), nausea (n=12), altered mood (n=8), anxiety (n=7), and hallucinations (n=1)
Ross et al.[50]	Adults with life-threatening cancer or in remission, with a diagnosis of acute stress disorder, generalized anxiety disorder due to cancer, or adjustment disorder +/- depression	29	• Immediate, substantial, and sustained reduction of anxiety and depression as measured by HADS T, HADS A, HADS D, BDI, STAI S, STAI T	• No treatment-related SAEs • Most-common AEs included elevations in BP and HR (76%), headache/migraine (28%), anxiety (17%), and nausea (14%)
Grob et al.[42]	Adults with advanced-stage cancer and diagnosis of acute stress disorder, generalized anxiety disorder, anxiety disorder due to cancer, or adjustment disorder with anxiety	12	• Sustained improvement in anxiety (measured by STAI) and mood (BDI, POMS)	• Minor BP and HR elevations

AE, adverse event; BDI, Beck Depression Inventory; BP, blood pressure; CI, confidence interval; HADS, Hospital Anxiety and Depression Scale; HADS A, HADS anxiety subscale; HADS D, HADS depression subscale; HADS T, HADS total score; HR, heart rate; MADRS, Montgomery-Åsberg Depression Rating Scale; POMS, Profile of Mood States; SAE, serious AE; STAI S, State-Trait Anxiety Inventory; STAI T, State-Trait Anxiety Inventory-Trait version.

RE104 for Treatment of Adjustment Disorder in Patients With Cancer and Other Medical Illnesses

RE104 is a novel psychedelic compound with a shorter psychedelic duration than psilocybin, which may improve convenience and reduce monitoring requirements and costs.

RE104 is being investigated in a phase 2 study in individuals with adjustment disorder associated with cancer and other serious medical illnesses.

RE104 is a novel serotonergic and psychedelic prodrug of the synthetic tryptamine analog 4-OH-DiPT, which elicits a psychedelic state with a shorter duration than psilocybin.[1] This may improve convenience, as well as reduce monitoring requirements and corresponding costs.[1] RE104 was developed to facilitate subcutaneous administration and reduce pharmacokinetic variability associated with oral administration.[1] Preclinical studies have demonstrated a strong relationship between the pharmacokinetic profile of RE104 (and the active metabolite 4-OH-DiPT) and pharmacodynamic effects, and antidepressant effects have been observed in rodent models.[1]

In a recent phase 1 study in healthy adult volunteers with prior psychedelic experience, subcutaneously administered RE104 was generally well tolerated, with a safety profile similar to psilocybin.[2] Treatment with RE104 induced dose-dependent increases in psychoactive effects, with the majority of participants treated with ≥30 mg of RE104 experiencing a "complete mystical experience," supporting the potential clinical benefit of RE104. The peak effect of RE104 was reached in 1.2 hours, with a mean duration of 3.6 hours (ie, 50% shorter than what is typical of psilocybin), which supports improved convenience of clinical monitoring when combined with the favorable safety profile.

A phase 2 study is being initiated to evaluate the safety and efficacy of RE104 in treating adjustment disorder in participants with cancer and other medical illnesses. The trial will enroll male or female adult participants with adjustment disorder, as defined by DSM-V-TR and confirmed by the Structured Clinical Interview for DSM-5 - Clinical Trials Version (SCID-5-CT). Participants must identify cancer, amyotrophic lateral sclerosis, multiple sclerosis, Parkinson's disease, or idiopathic pulmonary fibrosis as the inducing stressor for adjustment disorder. The primary endpoint for this study is the change from baseline in the Montgomery-Åsberg Depression Rating Scale total score at Day 14 after RE104 treatment. Results from this trial are anticipated to further our knowledge about the clinical potential of RE104 for treatment of adjustment disorder associated with medical illness and to begin filling the gap related to lack of high-quality research in this underserved patient population.

Conclusion

Adjustment disorder is one of the most common psychiatric diagnoses in individuals with severe medical illnesses, but both patients and their healthcare providers currently have a major unmet need due to a lack of evidence-based treatment options. Investigation of RE104 may ultimately address this unmet need by providing a novel treatment option for effective and safe treatment of adjustment disorder related to medical illness.

References

1. Bryson N, Alexander R, Asnis-Alibozek A, Ehlers MD. RE104: Synthesis and activity of a novel serotonergic psychedelic prodrug of 4-hydroxy-N,N-diisopropyltryptamine. *ACS Chem Neurosci*. 2024;15(12):2386-2395.
2. Alexander R, Hocevar-Trnka J, Bryson N, Taylor B, Dossey M. A novel serotonergic psychedelic 4-OH-DiPT prodrug for treatment of postpartum depression. Poster presented at: Anxiety & Depression Association of America Annual Conference; April 11-14, 2024; Boston, MA.
3. O'Donnell ML, Agathos JA, Metcalf O, Gibson K, Lau W. Adjustment disorder: current developments and future directions. *Int J Environ Res Public Health*. 2019;16(14):2537.
4. Mayo Clinic. Adjustment disorders. https://www.mayoclinic.org/diseases-conditions/adjustment-disorders/symptoms-causes/syc-20355224#:~:text=Adjustment%20disorders%20affect%20how%20you,a%20part%20of%20your%20life. Accessed February 11, 2025.
5. Karatzias T, Shevlin M, Hyland P, Fyvie C, Grandison G, Ben-Ezra M. ICD-11 posttraumatic stress disorder, complex PTSD and adjustment disorder: the importance of stressors and traumatic life events. *Anxiety Stress Coping*. 2021;34(2):191-202.
6. Morgan MA, Kelber MS, Workman DE, Beech EH, Garvey Wilson AL, Edwards-Stewart A, et al. Adjustment disorders: a research gaps analysis. *Psychol Serv*. 2022;19(2):283-293.
7. Carta MG, Balestrieri M, Murru A, Hardoy MC. Adjustment disorder: epidemiology, diagnosis and treatment. *Clin Pract Epidemiol Ment Health*. 2009;5:15.
8. Reed GM, Mendonça Correia J, Esparza P, Saxena S, Maj M. The WPA-WHO Global Survey of psychiatrists' attitudes towards mental disorders classification. *World Psychiatry*. 2011;10(2):118-131.
9. Shevlin M, Hyland P, Ben-Ezra M, Karatzias T, Cloitre M, Vallières F, et al. Measuring ICD-11 adjustment disorder: the development and initial validation of the International Adjustment Disorder Questionnaire. *Acta Psychiatr Scand*. 2020;141(3):265-274.
10. Zapata-Ospina JP, Sierra-Muñoz JS, Martínez PM, Yepes-Delgado CE. The adjustment disorder is not a wastebasket diagnosis: a grounded theory study of psychiatrists' and psychologists' clinical reasoning. *Eur J Psychotraumatol*. 2024;15(1):2390332.
11. Osborn J, Raetz J, Kost A. Seasonal affective disorder, grief reaction, and adjustment disorder. *Med Clin North Am*. 2014;98(5):1065-1077.
12. Glaesmer H, Romppel M, Brähler E, Hinz A, Maercker A. Adjustment disorder as proposed for ICD-11: dimensionality and symptom differentiation. *Psychiatry Res*. 2015;229(3):940-948.
13. Yaseen YA. Adjustment disorder: prevalence, sociodemographic risk factors, and its subtypes in outpatient psychiatric clinic. *Asian J Psychiatr*. 2017;28:82-85.
14. Lotzin A, Krause L, Acquarini E, Ajdukovic D, Ardino V, Arnberg F, et al. Risk and protective factors, stressors, and symptoms of adjustment disorder during the COVID-19 pandemic - First results of the ESTSS COVID-19 pan-European ADJUST study. *Eur J Psychotraumatol*. 2021;12(1):1964197.
15. Casey P, Bailey S. Adjustment disorders: the state of the art. *World Psychiatry*. 2011;10(1):11.
16. Diaz I, Thurm C, Hall M, Auerbach S, Bearl DW, Dodd DA, et al. Disorders of adjustment, mood, and anxiety in children and adolescents undergoing heart transplantation and the association of ventricular assist device support. *J Pediatr*. 2020;217:20-24.e21.
17. Morgan MA, Kelber MS, Bellanti DM, Beech EH, Boyd C, Galloway L, et al. Outcomes and prognosis of adjustment disorder in adults: a systematic review. *J Psychiatr Res*. 2022;156:498-510.

References (cont)

18. Popkin MK, Callies AL, Colon EA, Stiebel V. Adjustment disorders in medically ill inpatients referred for consultation in a university hospital. *Psychosomatics*. 1990;31(4):410-414.
19. Van Beek F, Wijnhoven L, Custers J, Holtmaat K, De Rooij BH, Horevoorts NJE, et al. Adjustment disorder in cancer patients after treatment: prevalence and acceptance of psychological treatment. *Support Care Cancer*. 2022;30(2):1797.
20. Mitchell AJ, Chan M, Bhatti H, Halton M, Grassi L, Johansen C, et al. Prevalence of depression, anxiety, and adjustment disorder in oncological, haematological, and palliative-care settings: a meta-analysis of 94 interview-based studies. *Lancet Oncol*. 2011;12(2):160-174.
21. Mehnert A, Brähler E, Faller H, Härter M, Keller M, Schulz H, et al. Four-week prevalence of mental disorders in patients with cancer across major tumor entities. *J Clin Oncol*. 2014;32(31):3540-3546.
22. Unal D, Orhan O, Ozsoy SD, Besirli A, Eroglu C, Kaplan B. Effect of radiotherapy on psychiatric disorder in patients with head and neck cancer. *Indian J Cancer*. 2016;53(1):162-165.
23. van Beek FE, Wijnhoven LMA, Jansen F, Custers JAE, Aukema EJ, Coupé VMH, et al. Prevalence of adjustment disorder among cancer patients, and the reach, effectiveness, cost-utility and budget impact of tailored psychological treatment: study protocol of a randomized controlled trial. *BMC Psychol*. 2019;7(1):89.
24. Singer S, Meyer A, Wienholz S, Briest S, Brown A, Dietz A, et al. Early retirement in cancer patients with or without comorbid mental health conditions: a prospective cohort study. *Cancer*. 2014;120(14):2199-2206.
25. Miovic M, Block S. Psychiatric disorders in advanced cancer. *Cancer*. 2007;110(8):1665-1676.
26. Siegel RL, Giaquinto AN, Jemal A. Cancer statistics, 2024. *CA Cancer J Clin*. 2024;74(1):12-49.
27. Tzouvelekis A, Karampitsakos T, Kourtidou S, Bouros E, Tzilas V, Katsaras M, et al. Impact of depression on patients with idiopathic pulmonary fibrosis. *Front Med (Lausanne)*. 2020;7:29.
28. Heidari ME, Nadali J, Parouhan A, Azarafraz M, Tabatabai SM, Irvani SSN, et al. Prevalence of depression among amyotrophic lateral sclerosis (ALS) patients: a systematic review and meta-analysis. *J Affect Disord*. 2021;287:182-190.
29. Goodarzi Z, Mele B, Guo S, Hanson H, Jette N, Patten S, et al. Guidelines for dementia or Parkinson's disease with depression or anxiety: a systematic review. *BMC Neurol*. 2016;16(1):244.
30. Davis BE, Lakin L, Binns CC, Currie KM, Rensel MR. Patient and provider insights into the impact of multiple sclerosis on mental health: a narrative review. *Neurol Ther*. 2021;10(1):99-119.
31. Kaba D, Sarı BA, Taner HA. Adjustment disorder and its risk factors during the solid organ pre-transplant period for children: a retrospective analysis of the last 10 years. *Pediatr Transplant*. 2024;28(1):e14613.
32. Poremski D, Hariram J, Wong WK, Eu PW, Lee C. The longitudinal dispositions of people diagnosed with adjustment or severe stress disorders. *BMC Psychiatry*. 2024;24(1):457.
33. Constantin D, Dinu EA, Rogozea L, Burtea V, Leasu FG. Therapeutic interventions for adjustment disorder: a systematic review. *Am J Ther*. 2020;27(4):e375-e386.
34. Dai D, Coetzer H, Zion SR, Malecki MJ. Anxiety, depression, and stress reaction/adjustment disorders and their associations with healthcare resource utilization and costs among newly diagnosed patients with breast cancer. *J Health Econ Outcomes Res*. 2023;10(1):68-76.
35. Kazlauskas E, Zelviene P, Lorenz L, Quero S, Maercker A. A scoping review of ICD-11 adjustment disorder research. *Eur J Psychotraumatol*. 2017;8(sup7):1421819.

References (cont)

36. O'Donnell ML, Metcalf O, Watson L, Phelps A, Varker T. A systematic review of psychological and pharmacological treatments for adjustment disorder in adults. *J Trauma Stress*. 2018;31(3):321-331.
37. Brebach R, Sharpe L, Costa DS, Rhodes P, Butow P. Psychological intervention targeting distress for cancer patients: a meta-analytic study investigating uptake and adherence. *Psychooncology*. 2016;25(8):882-890.
38. Ross S. Therapeutic use of classic psychedelics to treat cancer-related psychiatric distress. *Int Rev Psychiatry*. 2018;30(4):317-330.
39. Johnson RJ, 3rd. A research study review of effectiveness of treatments for psychiatric conditions common to end-stage cancer patients: needs assessment for future research and an impassioned plea. *BMC Psychiatry*. 2018;18(1):85.
40. Blinderman CD. Psycho-existential distress in cancer patients: a return to "entheogens". *J Psychopharmacol*. 2016;30(12):1205-1206.
41. Dos Santos RG, Bouso JC, Hallak JEC. Serotonergic hallucinogens/psychedelics could be promising treatments for depressive and anxiety disorders in end-stage cancer. *BMC Psychiatry*. 2019;19(1):321.
42. Grob CS, Danforth AL, Chopra GS, Hagerty M, McKay CR, Halberstadt AL, et al. Pilot study of psilocybin treatment for anxiety in patients with advanced-stage cancer. *Arch Gen Psychiatry*. 2011;68(1):71-78.
43. Schimmers N, Breeksema JJ, Smith-Apeldoorn SY, Veraart J, van den Brink W, Schoevers RA. Psychedelics for the treatment of depression, anxiety, and existential distress in patients with a terminal illness: a systematic review. *Psychopharmacology (Berl)*. 2022;239(1):15-33.
44. Schipper S, Nigam K, Schmid Y, Piechotta V, Ljuslin M, Beaussant Y, et al. Psychedelic-assisted therapy for treating anxiety, depression, and existential distress in people with life-threatening diseases. *Cochrane Database Syst Rev*. 2024;9(9):CD015383.
45. Reiche S, Hermle L, Gutwinski S, Jungaberle H, Gasser P, Majić T. Serotonergic hallucinogens in the treatment of anxiety and depression in patients suffering from a life-threatening disease: a systematic review. *Prog Neuropsychopharmacol Biol Psychiatry*. 2018;81:1-10.
46. White CM, Weisman N, Dalo J. Psychedelics for patients with cancer: a comprehensive literature review. *Ann Pharmacother*. 2023;57(9):1062-1075.
47. Goldberg SB, Pace BT, Nicholas CR, Raison CL, Hutson PR. The experimental effects of psilocybin on symptoms of anxiety and depression: a meta-analysis. *Psychiatry Res*. 2020;284:112749.
48. Jing X, Hoeh NR, Menkes DB. Psychedelic medicines for end-of-life care: pipeline clinical trial review 2022. *Palliat Support Care*. 2023;21(4):697-704.
49. Agrawal M, Emanuel E, Richards B, Richards W, Roddy K, Thambi P. Assessment of psilocybin therapy for patients with cancer and major depression disorder. *JAMA Oncol*. 2023;9(6):864-866.
50. Ross S, Bossis A, Guss J, Agin-Liebes G, Malone T, Cohen B, et al. Rapid and sustained symptom reduction following psilocybin treatment for anxiety and depression in patients with life-threatening cancer: a randomized controlled trial. *J Psychopharmacol*. 2016;30(12):1165-1180.
51. Kumano H, Ida I, Oshima A, Takahashi K, Yuuki N, Amanuma M, et al. Brain metabolic changes associated with predispotion to onset of major depressive disorder and adjustment disorder in cancer patients--a preliminary PET study. *J Psychiatr Res*. 2007;41(7):591-599.

reunion
NEUROSCIENCE