A Global Population-Based Study on the Association Between Ketamine and Esketamine With Suicidality Using WHO VigiBase

Angela T. H. Kwan, MD(C), MSc; Moiz Lakhani, MD(C), BHSc; Joshua D. Rosenblat, MD, MSc, FRCPC; Rodrigo B. Mansur, MD, PhD; Taeho Greg Rhee, PhD; Kayla M. Teopiz, HBSc; Bing Cao, PhD; Roger Ho, MD, FRCPsych; Sabrina Wong, HBSc; Gia Han Le, HBSc; and Roger S. McIntyre, MD, FRCPC

Abstract

Background: Ketamine and esketamine have been reported to rapidly alleviate various parameters of suicidality, with antisuicidal effects that may be independent of their rapid-acting antidepressant effects. However, it remains unclear whether ketamine and/or esketamine are associated with the emergence or worsening of suicidality.

Methods: In this global observational pharmacovigilance cohort study, we analyzed suicidality reports associated with ketamine and esketamine using data from the World Health Organization's VigiBase, accessed from its inception through January 2024. Disproportionality was assessed using the reporting odds ratio (ROR), with significance defined as $P < .05$.

Results: Compared to lithium, esketamine exhibited higher disproportionality for suicidal ideation (ROR = 5.13, 95% CI, 4.48–5.87, $P < .0001$), while ketamine showed lower disproportionality for suicidal ideation (ROR = 0.76, 95% CI, 0.58–0.99, $P = .043$), suicide attempt (ROR = 0.17, 95% CI, 0.12–0.24, $P < .0001$), and completed suicide (ROR = 0.30, 95% CI, 0.22–0.40, $P < .0001$). Esketamine also had lower RORs for suicide attempt (ROR = 0.46, 95% CI, 0.39–0.54, $P < .0001$) and completed suicide (ROR = 0.36, 95% CI, 0.30–0.43, $P < .0001$). When fluoxetine was used as the reference, esketamine showed higher disproportionality for suicidal ideation (ROR = 3.34, 95% CI, 3.06–3.65, $P < .0001$), while ketamine had a lower ROR (ROR = 0.49, 95% CI, 0.39–0.63, $P < .0001$). For suicidal behavior, esketamine had a lower ROR (ROR = 0.37, 95% CI, 0.17–0.81, $P = .012$), and both ketamine (ROR = 0.15, 95% CI, 0.10–0.21, $P < .0001$) and esketamine (ROR = 0.39, 95% CI, 0.34–0.45, $P < .0001$) had lower RORs for suicide attempt. Both agents also had lower RORs for completed suicides (ketamine: ROR = 0.24, 95% CI, 0.18–0.32, $P < .0001$; esketamine: ROR = 0.29, 95% CI, 0.25–0.35, $P < .0001$).

Conclusion: Both increased and decreased RORs for suicidality parameters were observed with ketamine and esketamine, with similar results regardless of whether lithium or fluoxetine was used as the reference. However, causality between ketamine/esketamine use and changes in suicidality cannot be determined.

J Clin Psychiatry 2025;86(3):24m15534

Author affiliations are listed at the end of this article.

Ketamine and esketamine are well-established treatments for adults with treatment-resistant depression (TRD).[1,2] While both agents have demonstrated antisuicidal effects, concerns about the emergence or amplification of suicidality in psychiatric populations have not been ruled out and may pose a risk for select patients.[3–8] Given that individuals receiving ketamine and esketamine typically have TRD, which is differentially associated with suicidality, all patients should be closely monitored.[9] Although cases of suicide among individuals taking ketamine and esketamine have primarily been reported in case studies, randomized, placebo-controlled, and active-controlled trials have not shown a higher incidence of emergent or amplified suicidality compared to placebo-treated participants.[6,10–14] Further research is needed to identify subpopulations that may be at higher risk.

In addition to case reports of suicidality associated with these agents, there have been observations of an increased risk of self-harm or suicide in individuals with

Editor's Note
We encourage authors to submit papers for consideration as a part of our Focus on Suicide section. Please contact Philippe Courtet, MD, PhD, at psychiatrist.com/contact/courtet.

Clinical Points

- Treatment-resistant depression is associated with higher risk for suicide when compared to treatment-responsive depression.
- Concerns have been raised whether esketamine/ketamine are associated with amplification and/or emergence of suicidality when used to treat mental/medical disorders.
- Results from the WHO VigiBase do not provide causal evidence of worsening of suicidality in persons receiving esketamine/ketamine; mixed results of increased and decreased risk of suicidality were reported with both agents.

ketamine use disorders.[15] However, it is important to distinguish between medically supervised use and recreational misuse, as the contexts and associated risks differ significantly.

In this global population-based pharmacovigilance study, we sought to determine whether ketamine and esketamine are disproportionately associated with suicidality compared to reference agents prescribed to a similar patient population. We explored suicidality across several forms, including suicidal ideation, depression/suicidal, suicidal behavior, suicide attempts, completed suicides. Using real-world data from the World Health Organization (WHO) VigiBase, the largest pharmacovigilance database, our study aims to provide generalizable insights into the psychiatric safety profiles of ketamine and esketamine.

METHODS

We conducted a global retrospective observational analysis of real-world reports submitted to the WHO VigiBase from inception to March 2025.[16,17] VigiBase is the largest pharmacovigilance database in the world, collecting safety reports on medicines and vaccines from over 180 member countries of the WHO Programme for International Drug Monitoring, with more than 35 million adverse event entries to date.[16] Given that the data are publicly available and anonymized, our study did not require ethics approval and informed consent.

We identified suicidality-related parameters (ie, "suicidal ideation," "depression/suicidal," "suicidal behavior," "suicide attempt," and "completed suicide") associated with exposure to either ketamine or esketamine. These categories reflect the nomenclature used for adverse event reporting in the database, following the standardized Medical Dictionary for Regulatory Activities (MedDRA) terminology.[18] Lithium and fluoxetine were used as reference agents; lithium, shown in observational studies to have no risk and/or

Table 1.

Cases of Suicidality Associated With Ketamine and Esketamine: A VigiBase Analysis With Lithium as the Negative Control

	Number of cases (n)	Total cases of psychiatric disorders (N)	ROR	95% CI lower	95% CI upper	*Z* statistic	*P* value
Suicidal ideation							
Ketamine	68	2,260	0.76	0.58	0.99	2.02	.043
Esketamine	909	5,246	5.13	4.48	5.87	23.68	<.0001
Lithium (control)	303	7,718	1.00	–	–	–	–
Depression suicidal							
Ketamine	0	2,260	0	–	–	–	–
Esketamine	7	5,246	1.47	0.52	4.20	0.72	.47
Lithium (control)	7	7,718	1.00	–	–	–	–
Suicidal behavior							
Ketamine	2	2,260	0.53	0.12	2.33	0.85	.40
Esketamine	7	5,246	0.79	0.32	1.99	0.50	.62
Lithium (control)	13	7,718	1.00	–	–	–	–
Suicide attempt							
Ketamine	32	2,228	0.17	0.12	0.24	9.73	<.0001
Esketamine	194	5,246	0.46	0.39	0.54	9.25	<.0001
Lithium (control)	598	7,718	1.00	–	–	–	–
Completed suicide							
Ketamine	53	2,260	0.30	0.22	0.40	8.33	<.0001
Esketamine	148	5,246	0.36	0.30	0.43	10.90	<.0001
Lithium (control)	577	7,718	1.00	–	–	–	–

Table 2.

Cases of Suicidality Associated With Ketamine and Esketamine: A VigiBase Analysis With Fluoxetine as the Positive Control[a]

	Number of cases (n)	Total cases of psychiatric disorders (N)	ROR	95% CI lower	95% CI upper	*Z* statistic	*P* value
Suicidal ideation							
Ketamine	68	2,260	0.49	0.39	0.63	5.59	<.0001
Esketamine	909	5,246	3.34	3.06	3.65	26.80	<.0001
Fluoxetine (control)	1,527	25,875	1.00	–	–	–	–
Depression suicidal							
Ketamine	0	2,260	0	–	–	–	–
Esketamine	7	5,246	1.02	0.45	2.32	0.041	.97
Fluoxetine (control)	30	25,875	1.00	–	–	–	–
Suicidal behavior							
Ketamine	2	2,260	0.25	0.061	1.01	1.95	.051
Esketamine	7	5,246	0.37	0.17	0.81	2.50	.012
Fluoxetine (control)	92	25,875	1.00	–	–	–	–
Suicide attempt							
Ketamine	32	2,260	0.15	0.10	0.21	10.74	<.0001
Esketamine	194	5,246	0.39	0.34	0.45	12.36	<.0001
Fluoxetine (control)	2,323	25,875	1.00	–	–	–	–
Completed suicide							
Ketamine	53	2,260	0.24	0.18	0.32	10.06	<.0001
Esketamine	148	5,246	0.29	0.25	0.35	14.22	<.0001
Fluoxetine (control)	2,327	25,875	1.00	–	–	–	–

[a]Significant disproportionality was defined as $P < .05$.

reduction of suicidality, serves as a negative control, while fluoxetine, according to the US Food and Drug Administration, is associated with an increased risk of suicide in individuals under 25, acting as a positive control.

We comprehensively captured all adverse events, including the number of cases (n) and total cases of psychiatric disorders (N), reported to VigiBase (Table 1). We calculated the reporting odds ratio (ROR) to assess disproportionality in reporting between cases and non-cases using the frequency method with a fourfold table.[19–21] The ROR was determined using the formula: odds ratio = (odds of the event in the exposed group)/(odds of the event in the nonexposed group).[22] The upper and lower 95% confidence intervals (CIs) were calculated with an α risk of 5%, and disproportionate reporting was indicated when $P < .05$. Statistical analyses were performed using Microsoft Excel 2021 (Microsoft Corporation, Redmond, US) and R version 4.3.1 (R Core Team, Vienna, Austria).

RESULTS

In the WHO VigiBase, associated with lithium and fluoxetine, respectively, were a total of 303 and 1,527 reports of suicidal ideation; 7 and 30 reports of "depression/suicidal"; 13 and 92 reports of suicidal behavior; 598 and 2,323 reports of suicide attempts; and 577 and 2,327 reports of completed suicides (Tables 1 and 2; Figures 1 and 2).

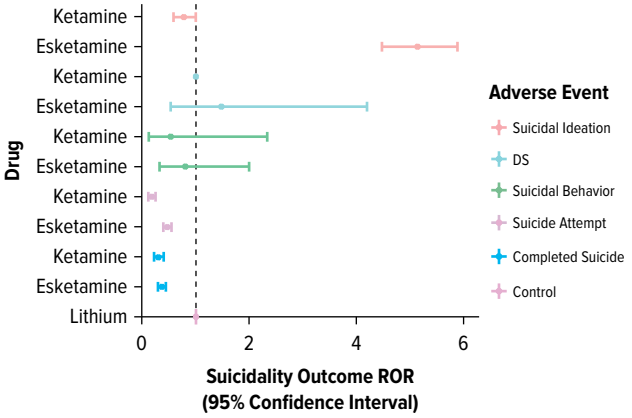
Comparison of Reports of Suicidality with Ketamine and Esketamine

Lithium as control. The RORs for suicidality-related parameters were as follows: for suicidal ideation, ketamine (ROR = 0.76, 95% CI, 0.58–0.99, $P = .043$) and esketamine (ROR = 5.13, 95% CI, 4.48–5.87, $P < .0001$); for "depression/suicidal," ketamine (ROR = 0) and esketamine (ROR = 1.47, 95% CI, 0.52–4.20, $P = .47$); for suicidal behavior, ketamine (ROR = 0.53, 95% CI, 0.12–2.33, $P = .40$) and esketamine (ROR = 0.79, 95% CI, 0.32–1.99, $P = .62$); for suicide attempts, ketamine (ROR = 0.17, 95% CI, 0.12–0.24, $P < .0001$) and esketamine (ROR = 0.46, 95% CI, 0.39–0.54, $P < .0001$); and for completed suicides, ketamine (ROR = 0.30, 95% CI, 0.22–0.40, $P < .0001$) and esketamine (ROR = 0.36, 95% CI, 0.30–0.43, $P < .0001$) (Figure 1).

Fluoxetine as control. When fluoxetine was used as the control, the RORs for most outcomes were directionally consistent with those observed with lithium. For suicidal ideation, the RORs were ketamine (ROR = 0.49, 95% CI, 0.39–0.63, $P < .0001$) and esketamine (ROR = 3.34, 95% CI, 3.06–3.65, $P < .0001$); for "depression/suicidal," ketamine (ROR = 0) and esketamine (ROR = 1.02, 95% CI, 0.45–2.32, $P = .97$); for suicidal behavior, ketamine (ROR = 0.25, 95% CI, 0.061–1.01, $P = .051$) and esketamine

Figure 1.

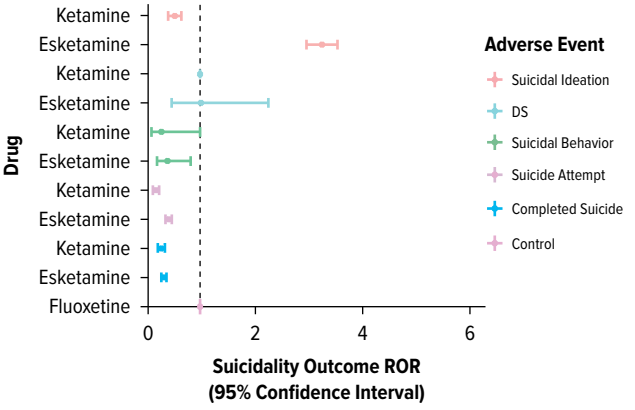
Reporting Odds Ratio (ROR) for Psychiatric Events With Ketamine and Esketamine Versus Lithium Control



Abbreviation: DS = depression suicidal.

Figure 2.

Reporting Odds Ratio (ROR) for Psychiatric Events With Ketamine and Esketamine Versus Fluoxetine Control



Abbreviation: DS = depression suicidal.

(ROR = 0.37, 95% CI, 0.17–0.81, $P = .012$); for suicide attempts, ketamine (ROR = 0.15, 95% CI, 0.10–0.21, $P < .0001$) and esketamine (ROR = 0.39, 95% CI, 0.34–0.45, $P < .0001$); and for completed suicides, ketamine (ROR = 0.24, 95% CI, 0.18–0.32, $P < .0001$) and esketamine (ROR = 0.29, 95% CI, 0.25–0.35, $P < .0001$) (Figure 2).

DISCUSSION

Overall, we observed a mixed pattern of RORs and suicidality parameters associated with ketamine and esketamine, assessed across multiple forms, including suicidal ideation, depression-related suicidal thoughts, suicidal behavior, suicide attempts, and completed suicides.[23] While some parameters did not show increased RORs, others demonstrated decreased RORs. Our findings of decreased RORs align with reports of the antisuicidality effects of ketamine and esketamine.[5] The mechanisms underlying the beneficial effects of ketamine and/or esketamine on suicidality remain unclear. Available evidence suggests that the antisuicidal effects of ketamine and esketamine are observed in specific subpopulations of individuals with depression rather than among all individuals with depression, highlighting the role of individual and disease-related factors on treatment response.[8]

The rapid alleviation of depressive symptoms is possibly a key mediator of the antisuicidal effects observed with ketamine and esketamine. It is a testable hypothesis that reductions in suicidality with ketamine and esketamine, partly mediated by factors independent of mood symptoms, may be explained by cognitive benefits associated with these treatments.[24–26] Studies suggest that ketamine and esketamine can improve anhedonia and cognitive dysfunction, both of which are commonly associated with TRD.[25,27] Specifically, improvements in anticipatory reward processing and impulse control, which are often impaired in individuals with TRD, may contribute to a reduction in suicidality by enhancing emotional regulation and decision-making.[25,27]

The WHO VigiBase has some limitations that affect the interpretation of our findings. VigiBase relies on spontaneous reporting of adverse events, which means it cannot be considered a comprehensive record of all drug-related events. Additionally, the available information for each reported case is insufficient to establish causality between ketamine and/or esketamine and suicidality. Moreover, our dataset does not allow us to determine whether ketamine or esketamine were used for on-label therapeutic purposes, off-label medical use, or recreational use. Another limitation is that VigiBase reports do not consistently provide information on whether patients were taking the medication prior to their suicidal behavior, limiting our ability to establish definitive temporal relationships. As a result, caution is warranted when interpreting findings related to suicidality.

Despite these limitations, our findings do not establish a consistent pattern of RORs related to parameters of suicide with either ketamine or esketamine. Persons who receive either one of these agents are typically being treated for disorders known to be associated with suicidality.[5,11,28] Clinicians implementing ketamine or esketamine as a standard of care should carefully monitor patients for suicidality and continue to assess any worsening of suicidality during treatment. Future research should focus on establishing a large safety database to capture data related to suicidality in all persons receiving ketamine or esketamine, rather than dependence on spontaneous reporting from pharmacovigilance databases.

Article Information

Published Online: July 7, 2025. https://doi.org/10.4088/JCP.24m15534

Submitted: January 11, 2025; accepted April 9, 2025.

To Cite: Kwan ATH, Lakhani M, Rosenblat JD, et al. A global population-based study on the association between ketamine and esketamine with suicidality using WHO VigiBase. *J Clin Psychiatry* 2025;86(3):24m15534.

Author Affiliations: Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada (Kwan, Lakhani); Brain and Cognition Discovery Foundation, Toronto, Ontario, Canada (Kwan, Lakhani, Rosenblat, Mansur, Teopiz, Wong, Le); Institute of Medical Science, University of Toronto, Toronto, Ontario, Canada (Teopiz); Department of Psychiatry, University of Toronto, Toronto, Ontario, Canada (McIntyre); Department of Pharmacology and Toxicology, University of Toronto, Toronto, Ontario, Canada (Rosenblat, Mansur, Wong, McIntyre); Department of Psychiatry, Yale School of Medicine, New Haven, Connecticut (Rhee); Department of Public Health Sciences, Farmington, Connecticut (Rhee); Key Laboratory of Cognition and Personality, Faculty of Psychology, Ministry of Education, Southwest University, Chongqing, P. R. China (Cao); Department of Psychological Medicine, Yong Loo Lin School of Medicine, National University of Singapore, Singapore (Ho); Institute for Health Innovation and Technology (iHealthtech), National University of Singapore, Singapore (Ho); Institute of Medical Science, University of Toronto, Toronto, Ontario, Canada (Le).

Corresponding Author: Roger S. McIntyre, MD, Departments of Psychiatry & Pharmacology and Toxicology, University of Toronto, 250 College St, 8th Floor, Toronto, ON M5T 1R8, Canada (roger.mcintyre@bcdf.org).

Drs Kwan and Lakhani share co-first authorship.

Author Contributions: All authors conceptualized, designed, and drafted the manuscript (ATH Kwan, JD Rosenblat, RB Mansur and RS McIntyre) as well as provided critical review for important intellectual concept and approved the final version to be published (Taeho Greg Rhee, Kayla Teopiz, Bing Cao, Sabrina Wong, Gia Han Le, Roger Ho). ATH Kwan analyzed and interpreted the data. All authors agree to be accountable for all aspects of the work.

Relevant Financial Relationships: Dr. McIntyre has received research grant support from CIHR/GACD/National Natural Science Foundation of China (NSFC) and the Milken Institute and speaker/consultation fees from Lundbeck, Janssen, Alkermes, Neumora Therapeutics, Boehringer Ingelheim, Sage, Biogen, Mitsubishi Tanabe, Purdue, Pfizer, Otsuka, Takeda, Neurocrine, Sunovion, Bausch Health, Axsome, Novo Nordisk, Kris, Sanofi, Eisai, Intra-Cellular, NewBridge Pharmaceuticals, Viatris, Abbvie, and Atai Life Sciences. **Dr. McIntyre** is a CEO of Braxia Scientific Corp. **Dr. Rosenblat** has received research grant support from the Canadian Institute of Health Research (CIHR), Physician Services Inc (PSI) Foundation, Labatt Brain Health Network, Brain and Cognition Discovery Foundation (BCDF), Canadian Cancer Society, Canadian Psychiatric Association, Academic Scholars Award, American Psychiatric Association, American Society of Psychopharmacology, University of Toronto, University Health Network Centre for Mental Health, Joseph M. West Family Memorial Fund, and Timeposters Fellowship and industry funding for speaker/consultation/research fees from iGan, Boehringer Ingelheim, Janssen, Allergan, Lundbeck, Sunovion, and COMPASS. **Dr. Mansur** has received research grant support from the Canadian Institutes of Health Research (CIHR), the Physicians' Services Incorporated (PSI) Foundation, and the Baszucki Brain Research Fund and support from an Academic Scholars Award from the Department of Psychiatry, University of Toronto. **Dr. Rhee** serves as a review committee member for Patient-Centered Outcomes Research Institute (PCORI) and Substance Abuse and Mental Health Services Administration (SAMHSA) and has received honoraria payments from PCORI and SAMHSA. **Dr. Rhee** has also served as a stakeholder/consultant for PCORI and received consulting fees from PCORI. **Dr. Rhee** serves as an advisory committee member for International Alliance of Mental Health Research Funders. **Dr. Rhee** is currently a co-Editor-in-Chief of *Mental Health Science* and has received honorarium payments annually from the publisher, John Wiley & Sons, Inc. The other authors report no relevant financial relationships.

Funding/Support: None.

Data Availability Statement: The data presented in this study are available on request from the corresponding author.

ORCiD: Angela T. H. Kwan: https://orcid.org/0000-0003-4013-1112; Moiz Lakhani: https://orcid.org/0009-0009-4603-826X; Joshua D. Rosenblat: https://orcid.org/0000-0002-4773-2191; Roger S. McIntyre: https://orcid.org/0000-0003-4733-2523

References

1. McIntyre RS, Rosenblat JD, Nemeroff CB, et al. Synthesizing the evidence for ketamine and esketamine in treatment-resistant depression: an international expert opinion on the available evidence and implementation. *Am J Psychiatry*. 2021;178(5):383–399.
2. McIntyre RS, Alsuwaidan M, Baune BT, et al. Treatment-resistant depression: definition, prevalence, detection, management, and investigational interventions. *World Psychiatry*. 2023;22(3):394–412.
3. Jollant F, Demattei C, Fabbro P, et al. Clinical predictive factors and trajectories of suicidal remission over 6 weeks following intravenous ketamine for suicidal ideation. *J Affect Disord*. 2024;347:1–7.
4. Krystal JH, Kavalali ET, Monteggia LM. Ketamine and rapid antidepressant action: new treatments and novel synaptic signaling mechanisms. *Neuropsychopharmacology*. 2024;49(1):41–50.
5. Xiong J, Lipsitz O, Chen-Li D, et al. The acute antisuicidal effects of single-dose intravenous ketamine and intranasal esketamine in individuals with major depression and bipolar disorders: a systematic review and meta-analysis. *J Psychiatr Res*. 2021;134:57–68.
6. Grunebaum MF, Galfalvy HC, Choo TH, et al. Ketamine for rapid reduction of suicidal thoughts in major depression: a midazolam-controlled randomized clinical trial. *Am J Psychiatry*. 2018;175(4):327–335.
7. Pan Y, Gorenflo MP, Davis PB, et al. Suicidal ideation and suicide attempt following ketamine prescription in patients with treatment-resistant depression: a nation-wide cohort study. *Res Sq*. 2023:rs.3.rs-3207199. doi:10.21203/rs.3.rs-3207199/v1.
8. O'Brien B, Lee J, Kim S, et al. Anti-suicidal effects of IV ketamine in a real-world setting. *Psychiatry Res*. 2024;331:115604.
9. Bell F. Acute suicidal ideation in the context of esketamine maintenance therapy. *Am J Psychiatry*. 2023;18(3):15–17.
10. Rayburn WF, Albright BB. Completed suicides and intranasal esketamine therapy: a case report and case series. *Psychiatry Res Case Rep*. 2023;2(1):100104.
11. Witt K, Potts J, Hubers A, et al. Ketamine for suicidal ideation in adults with psychiatric disorders: a systematic review and meta-analysis of treatment trials. *Aust N Z J Psychiatry*. 2020;54(1):29–45.
12. Wilkinson ST, Ballard ED, Bloch MH, et al. The effect of a single dose of intravenous ketamine on suicidal ideation: a systematic review and individual participant data meta-analysis. *Am J Psychiatry*. 2018;175(2):150–158.
13. Canuso CM, Singh JB, Fedgchin M, et al. Efficacy and safety of intranasal esketamine for the rapid reduction of symptoms of depression and suicidality in patients at imminent risk for suicide: results of a double-blind, randomized, placebo-controlled study. *Focus (Am Psychiatr Publ)*. 2019;17(1):55–65.
14. Fu DJ, Ionescu DF, Li X, et al. Esketamine nasal spray for rapid reduction of major depressive disorder symptoms in patients who have active suicidal ideation with intent: double-blind, randomized study (ASPIRE I). *J Clin Psychiatry*. 2020;81(3):19m13191.
15. Chai Y, Luo H, Wei Y, et al. Risk of self-harm or suicide associated with specific drug use disorders, 2004-2016: a population-based cohort study. *Addiction*. 2022;117(7):1940–1949.
16. Uppsala Monitoring Centre. About VigiBase. Accessed March 18, 2025. https://who-umc.org/vigibase/
17. Lindquist M. VigiBase, the WHO global ICSR database system: basic facts. *Drug Inf J*. 2008;42(5):409–419.
18. MedDRA. Accessed March 18, 2025. https://www.meddra.org/
19. Trillenberg P, Sprenger A, Machner B. Sensitivity and specificity in signal detection with the reporting odds ratio and the information component. *Pharmacoepidemiol Drug Saf*. 2023;32(8):910–917.
20. Rothman KJ, Lanes S, Sacks ST. The reporting odds ratio and its advantages over the proportional reporting ratio. *Pharmacoepidemiol Drug Saf*. 2004;13(8):519–523.
21. Szumilas M. Explaining odds ratios. *J Can Acad Child Adolesc Psychiatry*. 2010;19(3):227–229.
22. McIntyre RS, Mansur RB, Rosenblat JD, et al. The association between glucagon-like peptide-1 receptor agonists (GLP-1 RAs) and suicidality: reports to the Food and Drug Administration Adverse Event Reporting System (FAERS). *Expert Opin Drug Saf*. 2024;23(1):47–55.
23. Pompili M. On mental pain and suicide risk in modern psychiatry. *Ann Gen Psychiatry*. 2024;23(1):6.
24. McIntyre RS, Rosenblat JD, Rodrigues NB, et al. The effect of intravenous ketamine on cognitive functions in adults with treatment-resistant major depressive or bipolar disorders: results from the Canadian Rapid Treatment Center of Excellence (CRTCE). *Psychiatry Res*. 2021;302:113993.
25. Gill H, Gill B, Rodrigues NB, et al. The effects of ketamine on cognition in treatment-resistant depression: a systematic review and priority avenues for future research. *Neurosci Biobehav Rev*. 2021;120:78–85.
26. Lee Y, Syeda K, Maruschak NA, et al. A new perspective on the anti-suicide effects with ketamine treatment: a procognitive effect. *J Clin Psychopharmacol*. 2016;36(1):50–56.
27. Gillissie ES, Le GH, Rhee TG, et al. Evaluating Anhedonia as a risk factor in suicidality: a meta-analysis. *J Psychiatr Res*. 2023;158:209–215.
28. McIntyre RS, Berk M, Brietzke E, et al. Bipolar disorders. *Lancet*. 2020;396(10265):1841–1856.