#### LETTER

# Acute Effects of Intravenous Sub-Anesthetic Doses of Ketamine and Intranasal Inhaled Esketamine on Suicidal Ideation: A Systematic Review and Meta-Analysis: Letter in Response [Letter]

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### **Dear editor**

I have read the article written by Chen et al, "Acute Effects of Intravenous Sub-Anesthetic Doses of Ketamine and Intranasal Inhaled Esketamine on Suicidal Ideation: A Systematic Review and Meta-Analysis."<sup>1</sup> The authors provide an important analysis of the treatment of suicidal ideation with ketamine or esketamine, concluding that both may reduce suicidal ideation (SI) within 4-6 hours. This letter is not a rebuttal to the article but, rather, a response to further clarify a few points on the real-world use of ketamine and esketamine.

As the authors noted, esketamine was approved by the US Food and Drug Administration (FDA) as the first therapy for management of depressive symptoms in adults with major depressive disorder with acute SI or behavior<sup>2</sup> and thus has data establishing its use. The label is specific to the patient population. For example, esketamine nasal spray has the largest clinical randomized controlled trial program and the only registrational program for major depressive disorder with suicidal thoughts or actions (MDSI). The primary endpoint for these studies was reduction in depressive symptoms. Additionally, the esketamine US Risk Evaluation and Mitigation Strategies (REMS) program provides robust real-world safety data that are reported regularly.

The authors cite several safety concerns that have been raised about ketamine. Unlike the clinical trial environment, in which the trial drug quality is consistent and adverse events are captured regularly, real-world use of ketamine is subject to less rigorous oversight. The FDA issued a letter in February 2022 alerting health care professionals that "ketamine is not FDA-approved for the treatment of any psychiatric disorder", listing the safety concerns. As an approved product, the manufacturing and distribution practices of intranasal esketamine are carefully regulated, and the benefits, risks, and dosing have been established and approved by various regulatory agencies.<sup>3</sup> The SPRAVATO REMS program also provides guidance for the monitoring of patients and to ensure that it is dispensed and administered in health care centers, which is an additional safeguard against potential misuse and abuse.

I thank Chen et al for their article, which furthers the scientific literature and understanding of drug efficacy in crisis situations, an area of critical need for patients.

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