OSU – College of Osteopathic Medicine Assessment of the Harms Reporting in Systematic Reviews Focused on Hallucinogens: A Cross-Sectional Study

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INTRODUCTION

In recent years, hallucinogens have been studied and re-evaluated for several indications within psychiatry including treatment resistant mood, anxiety, and substance use disorders [1-3]. The clinical use of hallucinogens is historically controversial owing to the hallucinogenic effects associated with recreational use and their prohibition in the 1960s. Newer evidence is needed as research standards have changed over time. A recent systematic review (SR) of pre-prohibition studies evaluating the efficacy of LSD and psilocybin showed that 79% of patients treated with hallucinogens showed clinician-judged improvement. As the use of hallucinogens is continuously studied and introduced into practice, it is crucial that clinicians are equipped with high quality evidence and accurate reporting of benefits as well as harms when providing care to patients.

OBJECTIVES

A cross-sectional study was conducted to examine the reporting of harms in systematic reviews (SRs) focused on hallucinogen use. To better understand the use of therapeutic hallucinogens in various psychiatric conditions, we aimed to assess whether harms were consistently reported across SRs and the quality of harms reported across included studies using PRISMA guidelines.

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Figure 1. PRISMA Flow Diagram



Table 1. Mahady assessment for completion of harms reporting $(n=32)$	Yes	No
1. Are harms stated in title or abstract?	<u>11 (34.4)</u>	21 (65.6)
2. Are harms presented in the introduction?	<u>12 (37.5)</u>	<u>20 (62.5)</u>
3. Are harms listed and separately defined in the methods?	<u>3 (9.4)</u>	<u>29 (90.6)</u>
4. Are grades and/or severity scales used to classify harms in the methods?	2 (6.3)	30 (93.7)
5. Is there a method of harms data collection stated in the methods?	2 (6.3)	30 (93.7)
6. Is there a planned statistical analysis for harms stated in the methods?	2 (6.3)	30 (93.7)
7. Are the number of patients available for harms analyses stated in the results?	18 (56.3)	14 (43.7)
8. Are the number of treatment discontinuations in each arm reported in the results?	3 (9.4)	29 (90.6)
9. Are absolute figures for each harm in treatment and control groups presented in the results?	7 (21.9)	25 (78.1)
10. Were limitations of harms analyses discussed?	9 (28.1)	23 (71.9)
11. Is a balanced discussion of harms and benefits provided?	15 (46.8)	17 (53.1)
12. Did the authors discuss what future research would be needed to better clarify harms?	10 (31.3)	22 (68.7)
Systematic reviews completing 50% or more of items		
Completed 0% of harms items	5 (15.6)	
Completed 1 - 49.9% of harms items	23 (71.9)	
Completed 50% or more harms items	4 (12.5)	

in our study.

Figure 1. shows the PRISMA Flow Diagram visualising the screening process throughout the review.

Figure 2. Area of Reported Harms Overlap by the Paired Reviews Krebs et al. 2012 vs. Fuentes et al. 2021 Krebs et al.: nausea, vomiting; agitat[ion]; transient 'adverse reaction' • Overlapping reported outcome: acted bizarrely, transient moderate confusion Fuentes et al.: modest increase in blood pressure and heart rate; a tonic-clonic seizure Figure 2. shows the one of seven dyads within our study with a CCA \geq 50%. Krebs et al. 2012 reported four distinct harms that were listed as a primary or secondary outcome as a result of hallucinogen use, and Fuentes et al. 2021 had three distinct harms reported. Only one of the examined harms from each study was reported in both studies consistently. Of the remaining six studies with a CCA \geq 50% only one had harms reported with any identifiable overlap. The remaining five had no overlap in harms reported despite using many of the same

primary studies.





Table 1. shows the Mahady assessment for completion to determine the quality of harms reporting by reviews included



Figure 3. AMSTAR-2 Quality Assessment

Number of Studies with a Given AMSTAR-2 Rating

Figure 3. shows the AMSTAR-2 quality assessment results from the included systematic reviews, with or without a meta-analysis, within our study.



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METHODS

A search was conducted in May 2022 using MEDLINE, Embase, Epistemonikos, and Cochrane databases to retrieve SRs focused on the use of hallucinogens. Investigators screened the titles and abstracts from the search for study inclusion in a masked, triplicate fashion. Investigators analyzed the included SRs for reported harms linked to hallucinogen use via a pre-established harms reporting assessment. Methodological quality of SRs were graded using the A MeaSurement Tool to Assess Systematic Reviews-2 (AMSTAR-2) in a masked, duplicate manner. Study characteristics for each review were extracted in duplicate. Corrected covered area (CCA) was measured for SR dyads.

CONCLUSION

This study investigated the quality of harms reporting in SRs on hallucinogens, finding reporting deficiencies that could stand to be corrected. With increased funding to better understand their use, it will be important that harms are adequately and completely reported as publications are made available. Standardizing harms and using reporting guidelines is crucial to fully understand the potential risks of treatments.

1. Dos Santos RG, Bouso JC, Alcázar-Córcoles MÁ, Hallak JEC. Efficacy, tolerability, and safety of serotonergic psychedelics for the management of mood, anxiety, and substance-use disorders: a systematic review of systematic reviews. Expert Rev Clin Pharmacol 2018;11(9):889-902.

2. Thomas K, Malcolm B, Lastra D. Psilocybin-Assisted Therapy: A Review of a Novel Treatment for Psychiatric Disorders. J Psychoactive Drugs. 2017;49(5):446-455.

3. Reiff CM, Richman EE, Nemeroff CB, et al. Psychedelics and Psychedelic-Assisted Psychotherapy. Am J Psychiatry. 2020;177(5):391-410.