Review of: "Measuring the harms of psychotropic substance use and poly-use in the nightlife scene: a pilot application of poly-drug use indicators on Italian data collected within the ALAMA study"

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Thank you for the opportunity to review this study. Against the background of increasing use of the New Psychoactive Substance (NPS) in addition to the traditional addictive substance among young population, this manuscript makes a very important contribution with introducing the NPS into the construction of substance-related indicators in terms of harm-related and use-related. I read this paper with great interest and I would like to congratulate the authors for their astute observation of the urgent need for NPS indicators in social governance, and for following a well-established system of indicator construction to calculate these indicators. While I appreciate the aims of the study, my position on recommending this study for publication in Qeios is weakened by some key limitations presented in this version. I believe they should be addressed before it is published.

Major revision

- About the data inclusion, additional explanations could be added to justify the use of the Italian part of the ALAMA data. Furthermore, in page 3, additional explanations could be added to justify what are the particularities of the sub-population of nightlife substance users? How does it differ from the sub-population in Fabi and Rossi's (2023) study? What extra aspects of knowledge can be gained?
- About data visualization, I feel that the data visualization could be more concise and compact. As the main idea is to present the NPS using pattern among the participants, the distribution of the NPS using can be expanded while the other information should be shortened. For example, in page 5-8, the information in Figure 1 to Figure 4 and Table 1 could all be presented in a single table or even without the need for a diagram. In page 12 Table 2, the mean value of percentage of using (lifetime and past 12 months) and Delta and by two drug categories, i.e., the classical substance and the NPS, to show the discrepancy in drug using pattern between two drug categories. If available, authors could also add the statistical significance on those discrepancy between two drug categories. Above can also applied to the revision of Table 3.
- About the indicators construction, while the study applied well-established indicator approach, simple example can be added to illustrate the how the value of, such as F indicator.
- In the discussion section, What are the scenarios in which NPS-related indicators might be used and how can it enhance

future research? What is the limitation of current study, such as dose "experimental" data (page 20) would introduce some bias in the indicators?

- Overall, the authors have taken the NPS into the construction of key indicators. Though the team made convincing necessities of doing this and introducing the well-established approach, I'm left with a question that is this article being positioned as a research on methodology (indicator creation) or as an exploratory study exploring the association between indicators and other variables? Of course, both can exist at the same time. Regardless of the positioning, the authors need to add a more detailed description if based on either of two positions.

Minor revision

- The section name could be concise, such as shorten the "how to Assess the Harm-to-self and the Harm-to-others scores of new substances of interest."
- The location of the Table's name should be consistent.
- The line color and bar color in Figures could be consistent.
- Figure 8: Some yellow areas are blocked by blue areas.
- Figure 9: The total percentage value is 99%.
- Figures and Tables should add N=?.
- Figure 11 and Figure 12 can be merged into one figure.
- In page 19, please justify the sentence "Thus, in the studied population, the PDS self harm indicator seems the most indicative one in terms of harm prevention objectives."
- If possible, add the reference that illustrate the thresholds of "high" (PDS
self ≥ 0.35) group (page 19).
- If available, the results listed in the section "Possible Relation..." can be listed in cross-table with correspondent statistical significance to enhance the findings of some strong correlations.
- Figure 13: Figure 13 should present the distribution between F and occupation and between F and residence rather than the distribution between occupation and residence.