Methodological issues with "Public Supply of Addictive Drugs: A Rapid Review"

Assessing the methodological quality (AMSTAR-2) of "Public Supply of Addictive Drugs: A Rapid Review"

AMSTAR (Assessing the Methodological Quality of Systematic Reviews) – a well-established measurement tool to assess the methodological quality of reviews of randomized and non-randomized research

1. Did the research questions and inclusion criteria for the review include the components of PICO?	**Yes**
2. Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?	**No**
3. Did the review authors explain their selection of the study designs for inclusion in the review?	**No**
4. Did the review authors use a comprehensive literature search strategy?	**No**
5. Did the review authors perform study selection in duplicate?	**Yes**
6. Did the review authors perform data extraction in duplicate?	**No**
7. Did the review authors provide a list of excluded studies and justify the exclusions?	**No**
8. Did the review authors describe the included studies in adequate detail?	**Partial Yes**
9. Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review? RCT NRSI	 **No** **No**
10. Did the review authors report on the sources of funding for the studies included in the review?	**No**

11. If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results? RCT NRSI	 **0** **0**
12. If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?	**0**
13. Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?	**No**
14. Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?	**No**
15. If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?	**0**
16. Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?	**No**

Conclusion:

"*Public Supply of Addictive Drugs: A Rapid Review"* is a **critically low-quality review**.

Assessment Analysis

*Based on AMSTAR-2 assessment (https://amstar.ca/Amstar_Checklist.php), "Public Supply of Addictive Drugs: A Rapid Review" is a **critically low-quality review**. The following is a detailed assessment.*

1. Searching a single database is not recommended as it may lead to missing relevant publications. Recommended guidelines for conducting rapid reviews, such as those set by the Cochrane rapid review methods group (Garritty et al., 2021), suggest that at least three databases need to be searched for rapid reviews, including CENTRAL, MEDLINE, and Embase. The authors have only searched MEDLINE, which might partly explain why several relevant bodies of evidence are not captured in the review.

2. The authors' rationale for including specific study designs is unjustified and questionable. For example, Cochrane recommends that rapid reviews include previously published systematic reviews (Garritty et al., 2021); however, the authors have only included original research papers published in peer-reviewed journals. What is ironic is that the rapid review itself is not peer-reviewed. Additionally, the authors have failed to look for the relevant grey literature, which is not best practice based on Cochrane's recommendations. This approach has resulted in excluding an extremely relevant independent assessment of the pilot phase of safe supply interventions in Canada conducted by an arms-length consultant for CIHR (https://www.canada.ca/en/health-canada/services/opioids/responding-canada-opioid-crisis/safer-supply/early-findings-safer-supply-pilot-projects.html).

3. The eligibility criteria are vague and ill-defined. There is significant confusion around what studies were eligible to include, which has been reflected in the final types and numbers of included studies. See below for more details about the proposed population, intervention, comparator, and outcomes (PICO) framework.

***Population**:* The population of interest is "socially marginalized people who use illicit drugs," but there is no mention of how social marginalization is defined and assessed among the screened studies. Also not clear what is meant by "illicit drugs."

Intervention: The intervention of interest is "Public Supply of Addictive Drugs," which is not defined in the Methods but is mentioned on Page 4 and defined as "The provision of pharmaceutical opioids, heroin, crystal methamphetamine, cocaine, or other substances to people who are addicted to or dependent on these substances and who are at high risk for poisoning for witnessed or unwitnessed consumption." It is concerning that a large body of international evidence on heroin-assisted treatment trials, which fits the authors' definition of "Public Supply of Addictive Drugs", is omitted. Authors have briefly described and criticized the Canadian NAOMI and SALOME trials but surprisingly ignored the large body of international evidence on this issue and provided no justification for these inappropriate restrictions. For example, please see a few publications below on heroin-assisted treatment, including a seminal Cochrane systematic review.

E.g., 1. Smart, R, Reuter, P. Does heroin-assisted treatment reduce crime? A review of randomized-controlled trials. Addiction. 2022; 117: 518– 531. https://doi.org/10.1111/add.15601.

E.g., 2. Smart R. Evidence on the effectiveness of heroin-assisted treatment. RAND; 2018. https://www.rand.org/content/dam/rand/pubs/working_papers/WR1200/WR1263/RAND_WR1263.pdf.

E.g., 3. Ferri M, Davoli M, Perucci CA. Heroin maintenance for chronic heroin-dependent individuals. Cochrane Database of Systematic Reviews 2011, Issue 12. Art. No.: CD003410. https://doi.org/10.1002/14651858.CD003410.pub4.

Also missing from the review is the large body of evidence on psychostimulants for the treatment of stimulant use disorder. For example, see Tardelli VS, Bisaga A, Arcadepani FB, Gerra G, Levin FR, Fidalgo TM. Prescription psychostimulants for the treatment of stimulant use disorder: a systematic review and meta-analysis. Psychopharmacology. 2020; 237(8): 2233-55. https://doi.org/10.1007/s00213-020-05563-3.

More concerning is the confusion about whether a study is indeed about safer supply or not. For example, several publications included in the review are ineligible for inclusion based on the proposed eligibility criteria, given their lack of focus on safer supply (i.e., not meeting the intervention of interest criterion). However, they are still included because they have a single sentence in their Discussion section with the phrase "safer supply" or "safe supply." This is not how inclusion/exclusion criteria should be assessed in systematic reviews, given that it is misleading and significantly misrepresents the existing evidence (i.e., cherry-picking practice).

Outcomes: Lastly, the outcomes of interest are presented as "beneficial or adverse outcomes" associated with the safer supply interventions, but it is unclear how benefits or harms are examined or measured in the Methods. On page 4, the authors mention specific outcomes of interest as "Fatal and non-fatal poisoning; The health and safety of individuals or communities (e.g., crime, drug diversion); Any other benefits or consequences." This is vague and makes replicating the findings of this rapid review quite challenging.

4. Despite rapid review guideline recommendations (Garritty et al., 2021), the study's protocol was not registered or published in a peer-reviewed journal, which is poor methodological practice. If time had been of the essence, authors could have at least made their review's protocol available on free open-source websites or pre-print servers. Details of decisions to be made at each stage of the review process need to be transparent and published *a priori* which is not the case for this review.

5. No preferred reporting items for systematic reviews and meta-analyses (PRISMA) flowchart is presented, and reasons for excluding potentially relevant papers are not provided. It is unclear whether potentially relevant studies, including those about trials on heroin-assisted treatment, were not captured in their search strategy or captured but excluded based on the authors' judgement.

6. Another poor methodological practice is that despite Cochrane's recommendations, there is no mention or description of engaging with key stakeholders to help refine the rapid review's research question, inclusion/exclusion criteria, and outcomes of interest.

7. Although the authors have sought support from a librarian to create their search strategy, the presented version of the search strategy is imprecise and fails to follow recommended best practices, such as those presented in the PRESS guidelines (McGowan et al., 2016). Indeed, the search concepts are unclear, and the search strategy does not match the PICO. Moreover, the search strategy does not include any Subject Heading search terms (e.g., MeSH terms) and is limited to selected keyword searches that do not include spelling variants. **This is a major limitation** and would lead to missing relevant studies (i.e., unintended exclusions) as outlined below.

For example, adding the critical MeSH term of "Substance-Related Disorders" to their population of interest yields an additional 100,000+ to the search results presented in Table 1 of the rapid review report. Important to note that these key subject heading terms are closely related to the proposed PICO and should have been included. Similar issues can be detected in the rest of the search strategy. For example, the search box for looking for interventions of interest is not comprehensive and lacks terms related to heroin-assisted treatment while including keywords, such as "pharmaceutical opioid*."

As noted earlier, there is confusion regarding the inclusion of heroin-assisted treatment in this review. For example, the authors have searched for hydromorphone or diacetylmorphine but failed to incorporate the terms that include such interventions (i.e., heroin-assisted treatment). This could partly explain why the large body of international evidence on heroin-assisted treatment is absent from the review.

The authors' choice of keywords for outcomes is also poorly conceptualized and disorganized. While it includes several relevant outcomes, it ranges widely from overdose to social integration but surprisingly misses relevant keywords, such as "treatment adherence" or "relapse." Trying to limit the number of studies by creating a list of keywords and excluding relevant subject heading terms is problematic. Given the authors' interest in "beneficial or adverse outcomes" of safer supply interventions, a more sensitive search strategy could have left this section blank or involved a comprehensive list of keywords and subject headings to ensure that no relevant and important record is missing. These poor and haphazard decisions are reflected in the final number and type of studies included in the review.

Last but not least, the search strategy has not been updated after the initial search was done, limiting publications to Jan 15, 2022. This contradicts the recommended best practices that encourage rerunning or updating the search before submission for publication (Bramer & Bain, 2017; Lohr et al., 2021). This is particularly important in the context of the rapidly increasing evidence on safer supply interventions in Canada that requires keeping track of newly emerging evidence. The rationale for having this cut-off date may be understandable; however, had the authors updated their search before submitting their report, they would have been able to capture and include a considerable body of evidence on this topic that came out after Jan 15, 2022.

See below for a few examples:

E.g., 1. Young S, Kolla G, McCormack D, Campbell T, Leece P, Strike C, Srivastava A, Antoniou T, Bayoumi AM, Gomes T. Characterizing safer supply prescribing of immediate release hydromorphone for individuals with opioid use disorder across Ontario, Canada. International Journal of Drug Policy. 2022; 102: 103601. https://doi.org/10.1016/j.drugpo.2022.103601. **[Available online Feb 3, 2022]**

E.g., 2. Brothers, T. D., et al. (2022). Evaluation of an emergency safe supply drugs and managed alcohol program in COVID-19 isolation hotel shelters for people experiencing homelessness. Drug and Alcohol Dependence 235: 109440. https://doi.org/10.1016/j.drugalcdep.2022.109440.

[Available online as pre-print on Jan 17, 2022, and in Drug and Alcohol Dependence journal on Apr 7, 2022]

E.g., 3. Lew B, Bodkin C, Lennox R, O'Shea T, Wiwcharuk G, Turner S. The impact of an integrated safer use space and safer supply program on non-fatal overdose among emergency shelter residents during a COVID-19 outbreak: a case study. Harm Reduction Journal. 2022 Dec;19(1):1-6. https://doi.org/10.1186/s12954-022-00614-8. **[Available online Mar 21, 2022]**

E.g., 4. McNeil R, Fleming T, Mayer S, Barker A, Mansoor M, Betsos A, Austin T, Parusel S, Ivsins A, Boyd J. Implementation of Safe Supply Alternatives During Intersecting COVID-19 and Overdose Health Emergencies in British Columbia, Canada, 2021. American Journal of Public Health. 2022 Apr;112(S2):S151-8. https://doi.org/10.2105/AJPH.2021.306692. **[Available online Mar 29, 2022]**

8. The tool used for quality assessment is outdated and imperfect. Using valid risk of bias assessment tools specific to different study designs is recommended. It is also unclear how each study is scored on each bias criterion as the respective data is not presented. For example,

assuming that a qualitative study is of poor quality because it is not a randomized controlled trial represents a misunderstanding of the risk of bias and quality of evidence assessment.

REFERENCES

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Garritty, C., Gartlehner, G., Nussbaumer-Streit, B., King, V. J., Hamel, C., Kamel, C., Affengruber, L., & Stevens, A. (2021). Cochrane Rapid Reviews Methods Group offers evidence-informed guidance to conduct rapid reviews. *Journal of clinical epidemiology*, *130*, 13-22.

Lohr, A. M., Noah Van Gorden, D., Dubinsky, E., Gerald, L. B., Wilkinson-Lee, A., & Carvajal, S. C. (2021). Updating search strategies for literature reviews with OUR2D2: an open-source computer application. *Journal of the Medical Library Association: JMLA*, *109*(2), 317.

McGowan, J., Sampson, M., Salzwedel, D. M., Cogo, E., Foerster, V., & Lefebvre, C. (2016). PRESS peer review of electronic search strategies: 2015 guideline statement. *Journal of clinical epidemiology*, *75*, 40-46.