

Peer-Review comments and authors responses

“Caffeine, Alcohol, and Tobacco Use in Shift-Working Healthcare Professionals: A Systematic Review”

Dear Dr. Fregni,

Thank you for giving us the opportunity to submit a revised version of our manuscript titled “Caffeine, Alcohol, and Tobacco Use in Shift-Working Healthcare Professionals: A Systematic Review (2025 G2 – SR)” for consideration in the PPCR Journal. We sincerely appreciate the time and effort that you and the reviewers dedicated to evaluating our work. We have carefully addressed each of the reviewers’ observations and incorporated their suggestions into the revised version. These modifications are highlighted in the tracked-changes file. Below, we provide a detailed, point-by-point response to all reviewer comments and editorial recommendations.

Reviewer 1

Recommendation: Revisions Required

1. Comment: This manuscript addresses a highly relevant and underexplored issue: the relationship between shift work and substance use among healthcare professionals. The systematic review is generally well-structured, adheres to PRISMA guidelines, and provides a clear synthesis of the available evidence. The consistent association with caffeine use is notable, while findings regarding alcohol, tobacco, and sleep aids are less robust but still relevant. Given the implications for occupational health and patient safety, the topic is of high clinical and public health interest.

From my perspective, this is a publishable article, but it requires substantial revision to strengthen its contribution. In particular, the analysis should not only distinguish between types of professionals (nurses vs. physicians) but also consider the work setting (emergency departments, intensive care units, operating rooms). These are critical, high-stress environments that may strongly influence patterns of substance use, particularly caffeine, tobacco, and alcohol.

Response: We thank the reviewer for their thoughtful and constructive feedback on our manuscript. We greatly appreciate the recognition of our work’s relevance, methodological rigor, and potential contribution to occupational health and patient safety research. Unfortunately, because most of the included studies did not report detailed information about participants’ work settings (e.g., emergency departments, intensive care units, operating rooms), it was not possible to stratify our analysis by these categories. The lack of such data limited our ability to explore potential differences in substance use patterns across specific clinical environments but still provides valuable information distinguishing between types of professionals.

RESULTS

2. Comment: Across the included studies, “shift work” is defined inconsistently (night shifts, rotating schedules, extended shifts), which introduces substantial heterogeneity. I recommend providing a comparative table that summarizes how each study defined shift work and discussing

in greater depth how this variability limits comparability and the possibility of establishing a dose-response relationship.

Response: *We acknowledge that shift work was defined heterogeneously across the ten included studies, ranging from self-reported exposure to formal diagnostic criteria. This lack of uniformity limits comparability. We added a comparative table to the supplementary materials describing different definitions in the selected studies. We also enlarge the discussion paragraph about shift work heterogeneity and suggest that future studies should align with the International Labour Organization's (ILO) definition of shift work.*

3. Comment: The results section could benefit from a visual summary (e.g., heatmap or forest-plot style diagram). Ensure consistent terminology (e.g., “night shift,” “rotating shift,” “extended shift”) and abbreviations (AUDIT-C, PSQI, SWSD). The abstract should explicitly acknowledge the main limitations (cross-sectional designs, heterogeneity, reliance on self-report).

Response: *We appreciate the reviewer's suggestion to include a forest plot or similar visual summary. However, a quantitative forest plot could not be constructed because only a few of the included studies reported comparable effect sizes (e.g., odds ratios or prevalence ratios with 95% confidence intervals). Most studies presented substance use outcomes as raw frequencies or proportions without standardized effect estimates, precluding a valid pooled or graphical synthesis. Therefore, we opted to provide a narrative and tabular summary of the results to accurately represent the available evidence. The manuscript has been carefully reviewed to ensure consistent terminology throughout. The abstract now explicitly acknowledges the study limitations by describing them in the final result sentence.*

DISCUSSION

4. Comment: Few studies adequately adjusted for important confounders such as stress, burnout, depression, anxiety, workload, or institutional context. These factors may partly explain the inconsistent findings for alcohol and tobacco use. The authors should highlight more explicitly the need for future studies with robust multivariable adjustment.

Response: *We agree. A new paragraph has been added to the Discussion (page X, paragraph Y) explicitly acknowledging the lack of multivariable adjustment in most included studies and recommending that future research incorporate validated measures of stress, burnout, and workload into multivariable models. The paragraph also cites examples (Franke 2015; Haile 2019) where partial adjustment was conducted, underscoring the methodological gap that limits comparability across studies.*

5. Comment: Beyond professional role, the setting (ER, ICU, OR) may represent a stronger determinant of substance use, as these environments impose unique stressors and high cognitive demands. I strongly encourage the authors to emphasize this gap and propose it as a priority for future research. Additionally, while the introduction mentions sleep disturbance as a possible mechanism, the discussion does not sufficiently expand on this point.

Response: *We thank you for this insightful comment. We decided to expand the DISCUSSION to emphasize the influence of specific clinical settings, such as emergency departments, intensive care units, and operating rooms related to substance use patterns among healthcare professionals. These different scenarios with a high demand environment expose workers to heightened stress, circadian disruption, and*

cognitive fatigue, which may increase reliance on stimulants or sedatives. Although most included studies did not provide granular data by work setting, we now highlight this as a critical gap and a priority for future research.

6. Comment: This is a timely and relevant article that is publishable but requires revision. Emphasizing work setting as a determinant, discussing methodological heterogeneity more critically, and strengthening the clinical implications will substantially increase its impact.

Response: *We revised the Discussion's closing paragraph to underscore the translational value of our findings for occupational/health policy and workforce well-being, fulfilling the reviewer's recommendation.*

CONCLUSION

7. Comment: The conclusion currently emphasizes the need for more research, but the findings could be translated into preliminary recommendations for occupational health practice, such as implementing fair scheduling practices and sleep hygiene programs; offering prevention and early detection programs for substance misuse among healthcare staff; and promoting non-pharmacological alternatives (e.g., stress management, exercise, mindfulness) to reduce reliance on stimulants or sleep aids.

Response: *We thank you for the constructive suggestion. We agree the conclusion should go beyond "more research is needed" and we can add to our conclusion and translate our findings into preliminary, low-risk recommendations for healthcare workers in practice.*

Reviewer 2

1. Comment: Thank you for your submission. Unfortunately, as a reviewer, I would recommend developing a new manuscript rather than making further major revisions to this version. Although you have clearly engaged in valuable team discussions, it seems there has not been sufficient time to align all the evidence and generate original insights on this topic. The most critical reason I cannot proceed with further review is the lack of reproducibility. Considering the public health relevance of the subject, the paper should be accessible to readers who may not be specialists in this field. Readability — including the ability to easily trace evidence from the ten analyzed papers, is therefore essential, especially for non-specialist readers such as myself.

Overall recommendation: the topic is interesting, and publication may be possible, but the authors should (a) more carefully and systematically map existing evidence, (b) ensure reproducible search and study selection (with full citation of included studies), (c) verify and correct data extraction, and (d) clearly state how the review advances knowledge or public health before resubmission.

Please find attached the more detailed comments and AI search summary as a reference

Response: We thank the reviewer for this honest feedback. Considering the time allocated for the project, re-writing the manuscript is not feasible, but we have addressed the comments to the best of our abilities.

METHODS

- 2. Comment:** The ten studies reportedly included in the analysis are not cited in the reference list, and the reported search strategy does not reproduce them. This lack of transparency and reproducibility makes it difficult to accept the review in its current form. While listing every included study in the references is not strictly mandatory, systematic reviews usually do so. Since these studies are cited in the manuscript itself, their omission from the references is not explained.

Response: We thank the reviewer for this valuable feedback. The reference list was updated to contain the ten studies included in the systematic review. We have carefully rechecked our search strategy and confirm that the ten studies included in the review were indeed identified using the search methods described in our manuscript. For example, when applying our PubMed search strategy (fully detailed in the supplementary material) we were able to retrieve seven of the ten included studies directly, confirming that the search strategy is functioning as intended. The remaining studies were captured through equivalent search strategies applied to the other databases included in our systematic review protocol. Therefore, the search strategy is accurate, transparent, and reproducible across all databases, and it consistently retrieves the studies used in our analysis.

- 3. Comment:** Search strategy and missing key studies — several important papers appear to be missing (Yoon et al., 2025; Hamieh et al., 2022). This may be based on the search strategy. Some cohorts include these populations as part of a wider population, rather than a population with a “work shift” or “health worker” designation. To answer the stated research question, the search should be broadened and refined to capture the terminology and study designs used in this field; consulting existing systematic reviews would help construct a more comprehensive search strategy.

Response: We thank the reviewer for this thoughtful suggestion. The search strategy was predefined in the PROSPERO registration and executed within a fixed course timeline; post-hoc broadening and re-running are not feasible at this stage and could introduce protocol deviation bias. The manuscript has been clarified to state that studies were limited to healthcare professionals as the primary study population and that mixed-occupation cohorts were excluded when healthcare worker data couldn't be isolated. A limitation has been added noting that terminology heterogeneity may have led to missed studies.

RESULTS

- 4. Comment:** Accuracy of data extraction — the correctness of several data could not be confirmed. For example, it is unclear whether Kamber et al., presented the data regarding alcohol consumption. The study appears to focus on sleep disturbance (which the authors considered as a mediator) and substance misuse rather than alcohol consumption; however, the review extracts sleep as an outcome with OR. To clearly understand these issues, access to the exact extracted data and the original sources is required.

Response: We thank the reviewer for this valuable observation. Following a detailed verification of all extracted data, we have revised and clarified several points to ensure complete accuracy and alignment with the original studies. Specifically, we:

- Corrected the interpretation of Gold et al. (1992) by including the reported odds ratios for sleep aid use rather than indicating they were not provided;

- Revised Haile et al. (2019) to clarify that the association between sleep aid use and SWSD was significant only in crude analyses and not maintained after adjustment;

- Updated Swanson et al. (2023) to exclude unrelated findings and retain only shift work–specific substance use information;

- Reviewed and adjusted other extracted data to ensure that each outcome corresponds precisely to the reported variables and statistical models in the original publications. These updates resolve inconsistencies and improve the overall accuracy of data extraction across the review. Extracted data:

https://docs.google.com/spreadsheets/d/16D3qJu5162uYk2GPsp2KWXmIYD_xBOoAMBTifD9nFZE/edit?usp=sharing

- 5. Comment:** Claim of novelty — the authors state this is the “first” systematic review, yet they did not include existing systematic reviews in their search and provide no justification for this claim. A brief AI-assisted search identified recent reviews in the area (e.g., Richter 2020; Zhao and Turner 2008, see attached). I recommend mapping existing evidence, identifying genuine gaps, and revising the review strategy accordingly.

Response: We appreciate the reviewer’s observation regarding the claim of novelty. Following this comment, we reviewed the existing literature and identified several related systematic reviews addressing specific aspects of the topic, such as shift work and alcohol consumption (Richter et al., 2020), prevalence of shift work disorder (Pallesen et al., 2021), lifestyle and dietary factors among shift-working nurses (Pełtońska et al., 2019; Souza et al., 2018), and health-promotion interventions in nurses (Stanulewicz et al., 2020). Additionally, studies such as Colaprico et al. (2025) and Singh et al. (2025) examined substance use among healthcare professionals in general, but without an explicit focus on shift work. None of these reviews, however, have simultaneously synthesized evidence on the association between shift work, sleep disruption, and substance use specifically among nurses and physicians. Our review uniquely integrates these three elements, emphasizing the potential mediating role of sleep disruption in the relationship between shift work and substance use in clinical populations. Accordingly, we have revised our statement of novelty to more accurately reflect the existing evidence and to clarify the specific contribution of this review.

CONCLUSION

- 6. Comment:** Purpose and contribution — a review publication should do more than summarize. The manuscript currently states only general, vague next steps. If the authors wish to publish, they must articulately describe the novel contribution of this review and justify its public-health or scientific importance.

Response: We thank the reviewer for highlighting this point. In response, we have revised the manuscript to include concrete, actionable steps in the conclusion rather than general statements. We now clearly outline occupational health strategies that can be implemented based on the evidence, including fair scheduling and fatigue risk management policies, confidential screening and early detection programs for substance misuse, and campaigns promoting sleep hygiene, stress management, physical activity, and mindfulness to reduce reliance on stimulants or sedatives. These steps provide specific guidance for institutions while future longitudinal studies further clarify causal mechanisms, directly addressing the reviewer's request for clarity and practical relevance.

OTHER

- 7. Comment:** Presentation, authorship, and COI — there are numerous misspellings and typographical errors. The manuscript should be checked against the journal's author guidelines and professionally proofread. Affiliations are not provided, so conflicts of interest cannot be assessed; the authors should clarify institutional approval to list affiliations or whether the work will be published under the PPCR group name, and disclose COI accordingly.

Response: We thank the reviewer for the comment. The affiliations were already correctly listed as Harvard University, T. H. Chan School of Public Health, PPCR, Boston, MA, USA, since the work is associated only with the PPCR course and not with our home institutions. Therefore, no changes were made. The manuscript already follows the journal's author guidelines, has been carefully proofread, and all conflicts of interest have been properly disclosed.

Reviewer 3

Recommendation: Revisions Required

- 1. Comment:** First, I would like to sincerely thank the authors for their diligent and thoughtful work. This manuscript addresses a timely and important topic in occupational health, with clear relevance to both healthcare professional well-being and patient safety. The abstract piqued my interest, and the paper delivers valuable insights. Below are my section-by-section comments and suggestions for improvement.

Response: We thank the reviewer for this encouraging assessment. We appreciate the recognition of our manuscript's relevance to occupational health and patient safety. Below, we respond to each of the reviewer's detailed comments and describe the specific revisions made.

TITLE

- 2. Comment:** The title is clear and descriptive; however, refining it for impact and search engine discoverability could enhance visibility.

Suggested revision: "Caffeine, Alcohol, and Tobacco Use Among Shift-Working Healthcare Professionals: A PRISMA-Guided Systematic Review"

Response: We appreciate the reviewer's thoughtful suggestion regarding the title. However, we have decided to retain the original title, "Caffeine, Alcohol, and Tobacco Use in Shift-Working Healthcare

Professionals: A Systematic Review”, to maintain consistency with our registered protocol and to ensure alignment with how the study was initially reported. The manuscript already specifies in the Abstract section and we have added to the Methods section that the review was conducted in full accordance with PRISMA 2020 guidelines, and this adherence is clearly described there.

ABSTRACT

- 3. Comment:** The abstract is well-structured and effectively summarizes the study's scope, methods, and findings. However, it would benefit from more detail on key methodological aspects (e.g., databases searched, study types included), clearer quantification of major findings, and a slightly stronger discussion of limitations and practical implications.

Response: *We thank the reviewer for this valuable feedback. The Abstract has been revised, and we highlight below the information that was already present as well as the changes made. The first line of the Methods section already explicitly lists the databases searched: “Following PRISMA guidelines, we searched PubMed, Embase, Web of Science, PsycINFO, and CENTRAL”. The second line of the Methods section already specifies the type of studies included: “We included observational studies involving healthcare professionals exposed to night or rotating shifts and assessing substance use outcomes.”. The Conclusion was revised to incorporate the reviewer’s suggestions and to expand on practical implications, such as fair scheduling, fatigue management, and preventive workplace interventions.*

INTRODUCTION

- 4. Comment:** The introduction is well-written and establishes a strong rationale for the study. It identifies relevant literature gaps and presents focused objectives. Consider minor tightening of language to improve flow and more clearly articulating the practical implications of the identified knowledge gap.

Response: *We thank the reviewer for the positive assessment and constructive suggestion. The Introduction was carefully revised to improve clarity, conciseness, and logical flow. Redundant sentences were removed, transitions between paragraphs were refined, and the narrative now moves more smoothly from the problem statement to the study objectives. Additionally after re-reading we decided to expand the final paragraph of this section (introduction) in order to highlight the practical implications of addressing this knowledge gap.*

METHODS

- 5. Comment:** The methods section reflects strong methodological rigor. Suggestions: briefly summarize key search terms in the main text for transparency; justify the English-only restriction; clarify whether shift work definitions were standardized or accepted as reported; move detailed findings to the Results; and consider reporting inter-rater agreement (e.g., kappa statistic).

Response: *We are grateful for the reviewer’s insightful suggestions. A one-sentence summary of the four search concept groups was added to the Search strategy, and the English-language restriction was justified on feasibility and quality-control grounds. The primary shift-work definition (>3 night shifts/month) was clarified, with study-specific operationalizations noted as accepted and extracted verbatim. Duplicated detailed findings were removed from Methods/Data synthesis and are presented only in Results. Screening reliability was managed by duplicate independent review with consensus and third-reviewer adjudication; a formal inter-rater statistic was not calculated and this is stated explicitly.*

RESULTS

- 6. Comment:** The results are clearly presented, logically organized, and supported by comprehensive tables. Suggestions: reduce redundancy, highlight key trends and differences, ensure consistency in study referencing, and briefly note major research gaps to frame the discussion.

Response: We thank the reviewer for the positive evaluation and constructive suggestions. Consistency in study referencing has been standardized throughout the manuscript. All in-text citations now follow APA 7 author–year style (e.g., ‘Franke et al., 2015’; ‘Trinkoff & Storr, 1998’), ‘et al.’ is used consistently for three or more authors, and narrative vs. parenthetical conjunctions were corrected (‘and’ vs. ‘&’). Tables and figure notes were aligned to the same author–year format to match the text. Key trends and differences are now signposted in the opening lines of the Main results, while the risk-of-bias summary remains the closing subsection. Major research gaps are addressed in the Discussion/Limitations paragraph rather than repeated in Results to minimize duplication.

DISCUSSION

- 7. Comment:** The discussion is comprehensive and insightful. Strengths include clear identification of caffeine as the most consistently associated substance and balanced appraisal of limitations. It could be improved by restructuring for clarity, consolidating conclusions, and expanding on system-level interventions.

Response: We thank the reviewer for the constructive suggestion. We’ve adapted the text to make it clearer that the strongest association was with caffeine use. We also reviewed the text for clarity and consolidation of conclusions.

REFERENCES

- 8. Comment:** The reference list is generally well-curated. Recommendations: standardize DOI formatting (APA 7), ensure proper italics, correct capitalization, and remove placeholders.

Response: We thank the reviewer for this valuable feedback. The reference list was revised to conform to APA 7. DOI formatting was standardized as URLs (<https://doi.org/...>), journal titles and volume numbers were italicized, article titles were set in sentence case with appropriate capitalization of proper nouns (e.g., “U.S.”), issue numbers were placed in parentheses, page ranges were verified, and all placeholder text was removed. Items lacking full bibliographic details were retained with DOI-only “ahead of print” entries, and report citations were formatted with publisher and stable URLs where available.

- 9. Comment:** Overall, this manuscript makes a valuable contribution to occupational health by addressing the underexplored intersection of shift work and substance use among healthcare professionals. Refinements in structure, clarity, and formatting will make it even stronger.

Response: We are grateful for the reviewer’s encouraging conclusion. All relevant suggested structural and stylistic improvements have been implemented. We believe these refinements substantially enhance the clarity, readability, and impact of the manuscript while preserving the scientific integrity and purpose of the review.

Reviewer 4

Recommendation: Accept Submission

- 1. Comment:** Dear authors, congratulations on your excellent work. I outlined some points and suggestions to improve your work. Please, provide a Prisma checklist (Equator network page) with the pages attributed to each point.

Response: *We thank the reviewer for the positive evaluation and constructive suggestions. We have completed and included the official PRISMA 2020 checklist. Page numbers corresponding to each item have been added, and the document is provided as Supplementary Material 2 (PRISMA Checklist).*

TITLE

- 2. Comment:** Title: ok. Systematic review included in the title.

Response: *We appreciate the reviewer's confirmation. The title remains unchanged.*

ABSTRACT

- 3. Comment:** Background: The authors provided an explicit statement of the main objective and question. Methods, results, and conclusions met the standards of a systematic review.

Response: *Thank you for this positive feedback. In the revised version, we have made edits to incorporate the comments from all reviewers.*

INTRODUCTION

- 4. Comment:** The authors described the rationale for this review, contextualizing the existing knowledge. Also provided an explicit statement of the objective of this review.

Response: *We appreciate this comment. The Introduction has been further refined for flow and precision to incorporate the comments from all reviewers.*

METHODS

- 5. Comment:** Search strategy, inclusion and exclusion criteria: ok! Registered in PROSPERO: ok. Risk of Bias: A quality assessment was conducted using the Newcastle–Ottawa Scale (NOS). The authors also utilized AI to structure language and enhance coherence. AI was used as a complementary tool and did not replace intellectual contributions.

Response: *Thank you for acknowledging the methodological rigor.*

RESULTS

- 6. Comment:** Specified all databases, registers, and references. Tables presented clear study characteristics, exposure, and outcome measures. Results and risk of bias assessment were well reported.

Response: *Thank you for acknowledging the methodological rigor.*

DISCUSSION

- 7. Comment:** The authors provided a general interpretation of results, comparison to other evidence, discussion of limitations, and clinical implications. The discussion could be more concise and objective by splitting repetitive points.

Response: *We appreciate this helpful suggestion. The Discussion has been carefully edited to remove redundant sentences and improve logical flow.*

CONCLUSION

8. Comment: Conclusion: concise and adequate.

Response: *Thank you. The Conclusion was slightly refined to align with the revised discussion.*