PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Premenstrual syndrome and alcohol: a systematic review and meta-analysis.
AUTHORS	Takkouche, Bahi; Fernández, María del Mar; Saulyte, Jurgita; Inskip, Hazel

VERSION 1 – REVIEW

REVIEWER	Mahyar Etminan University of British Columbia/Canada
REVIEW RETURNED	12-Sep-2017

GENERAL COMMENTS	This systematic review tackles an important question. My comments are as follows; -Were databases such as papers first or proceedings first searched for any abstract/presentation on this topic in a scientific meeting which may have had useful data to include in this review? -The authors should describe a bit more what Ri is and how to interpret it. This is a similar parameter to I2 which many readers may be more familiar with as it has been used as a parameter to quantify between study heterogeneity for some time. It simply describes between study heterogeneity as a percentage between 0-100. I realize the Ri and I2 are virtually the same so the authors should either report the I2 or better explain how a reader can interpret the Ri in terms of percentage of between study heterogeneity and what Ri value presents high vs low heterogeneity -As there is substantial heterogeneity among the studies I suggest the authors discuss the types of biases that may be present in some of these studies. One is protopathic bias. In this case it is possible that some women may have used alcohol to treat symptoms related to the onset of PMS (anxiety) making it seem like PMS is the cause of PMS. This has to be discussed in the discussion section.

REVIEWER	Serena Houghton University of Massachusetts Amherst
REVIEW RETURNED	08-Oct-2017

GENERAL COMMENTS	While this was a well-written review, the reviewer has concerns related to the ORs reported for the individual studies. Methods should indicate that studies that examined PMDD were also included.

	Table 1 - It is unclear how the effect estimates were obtained in several of the studies. For example, the sample size reported for Bertone-Johnson refers to PMDD not PMS which was the outcome of interest. Secondly, even if the estimates were obtained for PMDD, the effect estimates do not appear to match those reported in Bertone-Johnson. In general, Bertone-Johnson reports non-significant estimates and non-significant inverse in the highest category- yet in Table 1 the any drinker and heavy drinker show significant positive associations. Another example is for Gold, these estimates appear to only be from a single symptom (anxiety) rather than PMS. The estimates for all papers should be checked. Table 1- Several of the confidence intervals are missing parentheses. Table 2 & 3 titles– Odds ratio is capitalized and the abbreviation shown is RR instead of OR as shown in the table. Figure 1 – is SPM supposed to be PMS? If not, the abbreviation needs to be defined.

REVIEWER	mark jones university of queensland, australia
REVIEW RETURNED	02-Nov-2017

GENERAL COMMENTS	Review of Premenstrual syndrome and alcohol BMJ open paper This study has a number of serious problems that would need to be fixed before it could be considered for publication. Specific comments follow. The following paper (not included in the study) reports on the association between alcohol use and premenstrual syndrome using a longitudinal cohort study: Hong Ju, Mark Jones, Gita Mishra. Illicit drug use, early age first use and risk of premenstrual syndrome: a longitudinal study. Drug and Alcohol Dependence, 2015 152:209-17. One of the eligibility criteria is that the study had to report estimates of odds ratios, etc. Sometimes in epidemiological studies only "significant" results are fully reported. Hence studies that find insufficient evidence of an association between alcohol and PMS may not report the odds ratio, etc. This could lead to reporting bias and to overestimates of associations in meta-analyses as the "non-significant" results are less likely to be reported. This is potentially an important limitation of the submitted study given that "The large majority of the articles retrieved initially were excluded because they did not provide any effect measure." It is concerning that the quality assessment tool was not implemented in its standard form. More explanation and justification is needed for why this has not been done. The implications of using this modified scale should be discussed. One issue is that "when the information on a specific item was not provided by the authors, we graded this item as 0." Surely an "unclear" grade should be made? Need to justify the statement that odds ratios are assumed to provide an unbiased estimate of relative risk particularly in the case of case-control studies and also studies where proportions of participants with PMS are > 15%. More details / justification is needed for how correlation coefficients were transformed into odds ratios. Also odds ratios corresponding to a 1 unit increase in alcohol intake may not be consistent with odds ratios corresponding to alcohol yes/no outcome. >1 standard drinks per day being classified as heavy intake seems excessive especially given alcohol guidelines generally suggest up

	to 2 drinks per day is acceptable. Why wasn't the standard Q test for heterogeneity used? 20 studies does not seem to be a small sample in terms of meta-analysis? Is there a protocol published for the study? Please provide a justification for the sensitivity analysis. Why does "this increase [in the risk of PMS] is more pronounced for heavy drinking" "favour a causal explanation of the relation between alcohol intake and PMS"? The paper mentions the "consistency" of results in multiple places but this does not seem accurate considering the huge heterogeneity between study results. Could estimates restricted to only those studies that adjusted for smoking be reported? I imagine smoking and alcohol use would be highly correlated hence it seems important that smoking should be appropriately taken into account in any estimates of association. Please explain why "The true OR is then even higher than the one we report in our meta-analysis". (pg13) The amount of heterogeneity found in this study is huge. It does not appear to be able to be explained by any of the subgroup analyses undertaken. It seems very debatable whether a meta-analysis should have been undertaken in the first place given the methodological diversity of the included studies. Would a descriptive study have been more appropriate? More information is needed on how PMS was defined for each study. More details on the 18 excluded studies should be provided including references.

VERSION 1 – AUTHOR RESPONSE

Dear Dr Gray,

Thank you for considering our manuscript entitled "Premenstrual syndrome and alcohol: a systematic review and meta-analysis" for publication. We are sending a revised version of the manuscript where the suggestions of the referees are taken into account. We would like to thank the editor and referees for their thorough reading of our manuscript and for the comments that will improve the quality of the paper.

We are sending a point-by-point answer to every comment made by the Editor and the 3 reviewers. As the format of the answer (italic type font for citations and underlined type font for emphasis) is lost when we paste the text in this box, we are sending this answer as a separate uploaded file, together with the revised version of the manuscript. If this causes any inconvenience, we would have no problem in using this box to provide our answer.

We would also like to mention that we have included the study proposed by reviewer #3, that we eliminated 2 studies that provided results under the form of correlation coefficients (please see the rationale in the answer to reviewer #3 below), and that we recalculated the pooled estimate of the study by Gold et al. as suggested by reviewer #2.

Consequently, we performed all analyses again including general pooling, subgroup analyses, publication bias with funnel plots, Egger's regression test and trim-and-fill procedure, quality scoring, flowchart, forest plots and sensitivity analyses. As one may observe, the results did not experience any substantial modification. The discussion and conclusions are then unchanged.

The data sharing statement is on page 17 of our manuscript. We now send the figures in the desired format and a track-changed version of the manuscript together with a clean version. All other queries of the Assistant Editor have been fulfilled.

Sincerely,

Bahi Takkouche MD, Ph.D
Professor of Preventive Medicine
University of Santiago de Compostela
Spain

VERSION 2 – REVIEW

REVIEWER	Mahyar Etmina University of British Columbia, Canada
REVIEW RETURNED	14-Dec-2017

GENERAL COMMENTS	I have no further comments on the revised version. I think all concerns have been addressed