Reviewer’s report

Title: Beverage Specific Alcohol Intake in a Population-Based Study: Evidence for a Positive Association between Pulmonary Function and Wine Intake

Authors:

Holger J Schunemann (hjs@buffalo.edu)
Brydon JB Grant (grant@buffalo.edu)
Jo L Freudenheim (jfreuden@buffalo.edu)
Paola Muti (muti@buffalo.edu)
Susan E McCann (mccann@buffalo.edu)
Deepa Kudalkar (deepapk@hotmail.com)
Malathi Ram (mram@buffalo.edu)
Tom Nochajski (tnochais@ria.buffalo.edu)
Marcia Russell (russell@prev.org)
Maurizio Trevisan (Trevisan@buffalo.edu)

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Reviewer: Dr Pat Cassano

Level of interest: A paper whose findings are important to those with closely related research interests

Advice on publication: Unable to decide on acceptance or rejection until the authors have responded to the compulsory revisions

Reviewer’s report on "Beverage Specific Alcohol Intake in a Population-Based Study: Evidence for a Positive Association between Pulmonary Function and Wine Intake"

I find this paper to be a well-written and straight-forward consideration of the hypothesis that alcohol is associated with pulmonary function. The question is an interesting one, and the finding that there are differential associations by type of alcohol consumed is important to know, both in terms of understanding past conflicting findings and in planning further research. The specific comments below are divided into major and minor points, and numbered within each category.

Major Points:
1. About 60% of the adults studied consume(d) multiple beverage types, making it difficult to disentangle the associations with specific beverage types. Is it possible to identify a subgroup drinking predominantly one type or another? Among the n=933 drinking various beverage types, what proportion are drinking wine? It is difficult to assess whether the wine-only drinkers are the main contributors to the wine-pulmonary function association, or whether the combined beverage group also contribute to these associations.

2. The authors are examining total lifetime alcohol consumption, but current vs. past consumption has not been considered explicitly. Do the findings for lifetime consumption mainly reflect current consumption, or is an independent effect of total consumption after current consumption is accounted for?
3. What is the postulated mechanism through which wine may be associated with FVC? If the proposed biological mechanism is via contributions to antioxidant levels, would we expect an effect on FVC? The authors mention that the Cohen paper (ref 18) uses the ratio of FEV1/FVC: the issue might be informed by a discussion of which outcome indicator(s) should be informative and why, based on the proposed biological mechanism.

4. Measurement of alcohol intake--The accurate and precise measurement of recent and lifetime alcohol consumption is central to the manuscript. The test-retest reliability of the lifetime measure has been mentioned, but is there any information on the validity of the measures? In the abstract it is stated that a validated questionnaire has been used, but it is not clear if this refers to the measurement of recent, lifetime or both, and it is also not clear which reference (is it reference 32?) provides information on validity (also not clear what type of validity has been demonstrated, eg, concurrent?)

5. If wine is postulated to contribute to antioxidant status, is there any possibility of over-control in adjusting the analysis for antioxidants measured in serum (and by the way seems to be in serum, not in diet as stated in paper on page 19, line 7). Also, given other publications by the same authors, we know that there are more complete data on antioxidants. If all the antioxidants are adjusted (rather than just he few that have statistically significant associations), it the effect size diminished?

6. How was the internal prediction equation developed (maximum R-squared?) and how does it compare to external standards that are in common use (eg., Hankinson et al 1999).

7. Did the Cohen paper (ref 18) find any trend in the same direction?

8. Ultimately, it would be helpful to put the results back into units that are more easily interpreted. Perhaps you could express the association of wine (from the best model) with FEV1 in terms of drinks per day of wine and %predicted FEV1?

9. In Table 3, since white wine is so much more strongly associated than red wine, why not try the simultaneous model with white and red wine as separate variables? Is multicollinearity a problem?

10. It might be helpful to provide some additional discussion of the lack of association of total alcohol with FEV1, which is brought about by associations in opposite directions for the sub-types of alcohol (at least in Table 4 for total alcohol intake).

11. The authors suggest that the stronger association of white wine is due to residual confounding by smoking. If the analysis is limited to the subgroup of nonsmokers (hence no residual confounding possible), is the effect of white wine still greater?

12. Given the proposed biological model, effect modification of the wine-pulmonary function association by cigarette smoking was considered. Small numbers of current smokers yields low power for such an analysis. Have the authors considered the subgroup of ex-smokers (as 43% are former smokers)? Are there data on time since quitting?

13. Page 15, line 16/17: Sentence reading "Alcohol from beer and liquor is significantly related to pulmonary function" doesn't fit with findings. Is this an error?

14. In looking at the various beverage types, are there consumers of all types across all ages, or is there a cohort effect such that heavy lifetime consumers of hard liquor are all older?
Minor Points:

1. pg 9, line 13: does "related to alcohol" mean the alcohol variables themselves? Are these log base 10 or natural log? Please provide some information for assessing the magnitude of the association as it is presented only for a unit change in the log-transformed variable (tables 3 and 4).

2. What are the numbers of subjects in the various regression models presented? Are all subjects in the regressions (n=1555?) regardless of single or multiple beverage type?

3. page 13, first paragraph: sentence beginning "There was some indication that hard liquor consumption was negatively associated...." Does this sentence refer to the finding in the simultaneous model in Table 3? If so, please clarify.

4. page 13, final sentence: Would it be simpler to say that beer had little or no association with pulmonary function?

5. page 13, lines 13-15: These data do not appear in table 4 which is being discussed here. It would be helpful to clarify that the data are not shown or to amend the table to show these findings.

6. page 14, paragraph: It would be helpful to have some idea of how the effect sizes compared when the top portion of the alcohol distribution was omitted.

7. page 15, line 3: Suggested wording change, as follows: "lifetime alcohol intake from wine" to "lifetime intake of wine (grams alcohol)"

8. page 15, line 6/7: Please clarify how residual confounding may explain the difference between the regression coefficient for red wine compared to the regression coefficient for white wine.

9. page 17, line 7: delete the word "did" from "did drank"

10. page 17, first sentence: Do the properties of flavonoids and other compounds refer to red wine specifically, or to both red and white wine?

11. page 18, last line: Suggest rewording to read, "this study is important in that it suggests the importance of beverage type in assessing the relation of alcohol to pulmonary outcomes."

12. Tables: as 3% are never drinkers, where do the n=219 come from in Table 2 (they are called no alcohol, and apparently classified by lifelong alcohol intake, but the numbers are not would be expected based on how I read Table 1)

13. Table 3. The asterisk indicates that 1.933 is statistically significant at p=0.05, but my calculation of the 95% confidence interval includes 0 (-0.08, 3.95) suggesting that this p value may be in error. The confidence intervals would be useful here, rather than the SE, although one can derive each from the other.
14. Table 3. What base is the log transformation?

**Competing interests:**

None declared.