Reviewer's report

Title: The Association of Alcohol Consumption with Mammographic Density in a Multiethnic Urban Population

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Reviewer: Rachel Denholm

Reviewer's report:

I think overall this is a well-written paper on an interesting study that uses a unique cohort to investigate alcohol intake and mammographic density. However, I think there are a couple of issues related to the appropriateness of this cohort to address the main aims of the manuscript. The small sample size means that the study does not have the power to investigate one of the main objectives of the paper: the association between alcohol and mammographic density in different ethnic groups. The use of a categorical variable to assess alcohol consumption resulted in a very small number of participants being classified as high alcohol consumers (>7 servings/week), and was then used as the main exposure measures in linear regression models. The main findings of the paper relate to the modification effect of BMI on the relationship between alcohol and mammographic density, which are only briefly touched on in the manuscripts introduction, aims, and objectives.

I think the manuscript needs to change its focus, highlighting the uniqueness of the cohort and opportunity to investigate the modification effect of BMI on the association between alcohol consumption and mammographic density, and investigate the relationship using a continuous measure of alcohol consumption.

Major Compulsory Revisions

o Categorisation of alcohol consumption – two methods are used to categorise alcohol consumption (grams of ethanol/week and number of weekly servings).
  # In the method section, what the definition of a weekly serving is, is not given.
  # Mean grams of ethanol/week is given for different subgroups, but its not used as an exposure variable in the linear regression models. Investigators could use the continuous measure of alcohol consumption and examine a linear trend in the association, especially as very few women (n=14) reported consuming the highest alcohol serving category. This was not clear made until the end of the manuscript and is inappropriate to use when examining the association in multiple subgroups due to low power to detect differences.

o Categorisation of different ethnic groups - is there a difference between Hispanic Caribbean and Hispanic Non-Caribbean, could the two groups be combined to form a Hispanic group?

o I think it would be important to investigate differences in drinking patterns
amongst Natives and Non-natives. The study categorised women who were born in the Caribbean or had at least one parent born in the Caribbean as ‘Caribbean’ but then described all Caribbean women as Caribbean-born – how many were not born in the US. Nativity would influence alcohol intake but also other risk factors which influence mammographic density, such as reproductive factors, thus should be further examined here.

- The outlier (African Caribbean women who reports drinking 70 servings of liquor/week) should be removed and analysis repeated as it is skewing the results.

- I wonder if using a change in estimate approach here, where there are three measures of the same outcome and different covariates are included in the three models, is appropriate as it is difficult for the reader to interpret. It is not clear if a forward or backward step-wise approach was used. Was there a large effect in the fully adjusted model?

- Table 1 should reflect the aims of the paper and thus I think it should be stratified by exposure (ever/never drinkers). Information on other confounding factors such as nativity, contraception, history of breast cancer, reproductive factors also needs to be included - was data complete for all confounding factors?

- Fully adjusted model for the BMI analysis is not presented – was there strong evidence of an association in the stratified analysis after accounting for other confounding factors?

- I don’t think this study, using the alcohol measures currently presented, is suitable to assess effect modification by ethnicity in the association between alcohol and mammographic density. The message in the paper is not consistent, for example in the results section (line 172/173) you state that no association was observed in African American women, in contrast to your comment in the discussion (line 251) where a positive association between alcohol intake and percent density in African American women is described. In Figure 2 there is little evidence of an association in African American women. Why are Hispanic Caribbean women included in the analysis when no participants report drinking >7 servings/week?

- In the discussion a new analysis is introduced (line 265-268) – this should be in the methods and results section.

- The discussion does not address why different associations were found in different measures of mammographic density (percent versus absolute dense area) and how this relates to BMI and other studies.

Minor Essential Revisions

- N to be included in Table 2 and Figure 2 and 3.
Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.