

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Prevalence and predictors of alcohol use during pregnancy: findings from international multi-center cohort studies
AUTHORS	O'Keeffe, Linda; Kearney, Patricia; McCarthy, Fergus; Khashan, Ali; Greene, Richard; North, Robyn; Poston, Lucilla; McCowan, Lesley; Baker, Philip; Dekker, Gus; Walker, James; Taylor, Rennae; Kenny, Louise

VERSION 1 - REVIEW

REVIEWER	Janna Skagerström Linköping University Sweden
REVIEW RETURNED	01-Sep-2014

GENERAL COMMENTS	<p>The references used are appropriate but a lot of recent relevant references are missing.</p> <p>One limitation that should be addressed is that the questions on alcohol are not posed in the same way in all cohorts. Also social desirability should be discussed.</p> <p>This is an interesting study that highlights the important question of validity and reliability of self reports of alcohol consumption during pregnancy. However, I have a few comments.</p> <p>The abstract would be clearer if you add the design of this study (not just the design of the included studies).</p> <p>In the introduction it is said that if prevalence is accurately reported, prevalence and predictors should be mostly consistent across studies. As table 1 show that the included cohorts are different with regard to sociodemography it would be interesting to control for these variables and make further analyses. This could give important information on how the different sampling methods in the study have impacted the results.</p> <p>Please specify grams of alcohol per unit under definitions on page 9.</p> <p>Are the results from all different cohorts reported elsewhere? If so, do your analyses add anything new? If not, please make this clearer.</p> <p>The discussion would be improved if you try to explain your results more. Do you think the differences between the cohorts are mainly due to methodological differences in the studies or due to sociodemographic differences between the cohorts?</p> <p>The discussion is virtually lacking comparance and references to earlier studies. For example studies comparing different modes of</p>
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	data collection and studies on predictors of drinking during pregnancy.
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REVIEWER	Camilla Nykjaer School of Food Science & Nutrition University of Leeds Leeds LS2 9JT UK
REVIEW RETURNED	04-Sep-2014

GENERAL COMMENTS	<p>The topic of the paper is very relevant and it is generally well written, although it could do with a thorough proof reading. There are several methodological issues that require attention</p> <p>Abstract: You have quoted OR but it is RR in the tables and text.</p> <p>Introduction: In the updated guidelines (2010) NICE emphasises the advice to avoid drinking alcohol in the first 3 months of pregnancy as this may be associated with an increased risk of miscarriage. So I wouldn't say they directly conflict with worldwide guidelines. In addition, another UK body, the Department of Health, recommends that pregnant women and women trying to conceive should avoid alcohol altogether and never drink more than 1–2 units once or twice a week.</p> <p>Methods: To make it clearer, the methods section would benefit from some subheadings such as "Study population"; "Assessment of alcohol"; "Assessment of participant characteristics" with the appropriate information attached.</p> <p>GUI: Eligibility criteria? How many women were approached for recruitment? SCOPE: How many women were approached? PRAMS: Please provide the numbers for exclusions. Studies approved by Ethics committee? Please provide ref number.</p> <p>For alcohol categories: How much ethanol is in one unit? This differ from country to country, was it taken into account? Were the categories based on any existing literature? If so please provide reference. Would be useful to add a non-drinking category.</p> <p>Statistical analysis: There are no continuous normally distributed variables so you can't have used t-test. The Kruskal-Wallis is the non-parametric alternative to the one-way ANOVA and is therefore not appropriate here where you are comparing characteristics between 2 groups only; drinkers and non-drinkers. Rather you should use the Mann-Whitney U-test as the majority of the variables you are testing are ordinal and then, as stated, the chi-squared test for the remaining categorical variables. Was Kruskal-Wallis used to compare alcohol use between the SCOPE centres? Please clarify.</p>
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	<p>Please justify why you chose to use log linear binomial regression instead of, for example, logistic regression and the choice of confounders.</p> <p>Results:</p> <p>Supplementary table 1: If possible, replace Table 1 with the supplementary Table 1 as this is much more interesting and reports results from your significance testing. Please add participant numbers to the drinking and non-drinking categories for each cohort. Also specify which period in pregnancy this refers to. It would be interesting to present these characteristics trimester specifically and not just averaged throughout pregnancy.</p> <p>Table 2: Please add a non-drinking category. For the median alcohol consumption, please report interquartile range rather than 95% CI.</p> <p>Table 3: Is it pre-pregnancy? In the text it refers to alcohol consumption during pregnancy. Please clarify.</p> <p>Table 4: See comments for table 2.</p> <p>Table 5: Add SCOPE to the table title. Add footnote from table 3.</p> <p>Discussion:</p> <p>p.22 liner 15: from what I gather the guideline is 1–2 units once or twice a week, meaning either 2 units in one sitting or 1 unit twice a week, making the maximum consumption 2 units per week.</p> <p>What are the guidelines for Ireland? Are they different to the UK? And how about Australia & New Zealand?</p> <p>A brief paragraph on the consequences of heavy alcohol consumption in pregnancy would be useful, including a translation of birth weight deficits to risk of other unwanted health outcomes in later life.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer Name Janna Skagerström

Institution and Country Linköping University

Sweden

Please state any competing interests or state 'None declared': None declared

The references used are appropriate but a lot of recent relevant references are missing.

RESPONSE: We agree with the reviewer and have now added a range of more up-to-date references where appropriate in the discussion of the text – see references page 32.

One limitation that should be addressed is that the questions on alcohol are not posed in the same way in all cohorts. Also social desirability should be discussed.

RESPONSE: Many thanks for this suggestion. We have added this in two locations in the discussion as it is, in fact, a major point which needs to be highlighted. See page 25-25 ¶ 375 -385 and page 29-30 ¶ 454-469.

This is an interesting study that highlights the important question of validity and reliability of self-

reports of alcohol consumption during pregnancy. However, I have a few comments.

RESPONSE: Many thanks – we address your further queries below.

The abstract would be clearer if you add the design of this study (not just the design of the included studies).

RESPONSE: We have now added the design of the study to the abstract as suggested. See page 2 ¶ 40.

In the introduction it is said that if prevalence is accurately reported, prevalence and predictors should be mostly consistent across studies. As table 1 show that the included cohorts are different with regard to sociodemography it would be interesting to control for these variables and make further analyses. This could give important information on how the different sampling methods in the study have impacted the results.

RESPONSE: We agree with the reviewer that controlling for socio-demographics is interesting since in Table 1, the included cohorts are different in this respect. We have now changed around our tables. Table 1 now details alcohol consumption over-all in each cohort. Table 2, which breaks down alcohol prevalence by the socio-demographics of each cohort was previously not in the main manuscript but reported in a supplemental file. This highlights variation in prevalence of alcohol use by socio-demographics across the cohorts. Subsequently, in Table 3 the reader can see predictors of alcohol use in each cohort for a specific factor of interest while controlling for other socio-demographic predictors.

Please specify grams of alcohol per unit under definitions on page 9.

RESPONSE: Thank you – this has now been added. See page 9-10 ¶ 213-216.

Are the results from all different cohorts reported elsewhere? If so, do your analyses add anything new? If not, please make this clearer.

RESPONSE: Yes, some crude prevalence estimates are reported elsewhere but the detail we present here has not been previously reported. This has now been highlighted in page 9 ¶ 212-213.

The discussion would be improved if you try to explain your results more. Do you think the differences between the cohorts are mainly due to methodological differences in the studies or due to sociodemographic differences between the cohorts?

RESPONSE: Thank you for this suggestion – we, in fact believe that it is an interaction of genuine population difference as well as reporting and measurement are likely to explain the findings and this is highlighted in the text – See page 25-25 ¶ 375 -385 and page 29-30 ¶ 454-469.

The discussion is virtually lacking comparance and references to earlier studies. For example studies comparing different modes of data collection and studies on predictors of drinking during pregnancy.

RESPONSE: We have added some more relevant and recent references to improve our discussion and reference to some recent evidence on predictors of alcohol use – see reference list for updated references.

For example, page 27-28 ¶ 417-421 refers to mode of collection and provides some discussion on that.

See page 29 ¶ 442-452 for more discussion and reference to other studies of predictors.

Reviewer Name Camilla Nykjaer
Institution and Country School of Food Science & Nutrition
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Leeds
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UK
Please state any competing interests or state 'None declared': None declared

COMMENTS TO THE AUTHOR:

The topic of the paper is very relevant and it is generally well written, although it could do with a thorough proof reading. There are several methodological issues that require attention

Abstract:

You have quoted OR but it is RR in the tables and text.

RESPONSE: Thank you and apologies for this – this has now been amended. See page 2 ¶ 55-56.

Introduction:

In the updated guidelines (2010) NICE emphasises the advice to avoid drinking alcohol in the first 3 months of pregnancy as this may be associated with an increased risk of miscarriage. So I wouldn't say they directly conflict with worldwide guidelines. In addition, another UK body, the Department of Health, recommends that pregnant women and women trying to conceive should avoid alcohol altogether and never drink more than 1–2 units once or twice a week.

RESPONSE: We have now changed the text to reflect your point above. See page 4 ¶ 89-92.

Methods:

To make it clearer, the methods section would benefit from some subheadings such as “Study population”; “Assessment of alcohol”; “Assessment of participant characteristics” with the appropriate information attached.

RESPONSE: We agree and have done as you suggest. See page 6 onward.

GUI: Eligibility criteria? How many women were approached for recruitment?

RESPONSE: This has now been added. See page 6 ¶ 132.

SCOPE: How many women were approached?

RESPONSE: This has now been added. See page 7 ¶ 149.

PRAMS: Please provide the numbers for exclusions.

RESPONSE: This has now been added. See page 8 ¶ 172-173.

Studies approved by Ethics committee? Please provide ref number.

RESPONSE: This has now been added. See page 12¶ 258-264.

For alcohol categories:

How much ethanol is in one unit? This differ from country to country, was it taken into account?

RESPONSE: This has been added to the text. See page 9-10 ¶ 213-214.

Were the categories based on any existing literature? If so please provide reference.

RESPONSE: Categories were not based on existing literature.

Would be useful to add a non-drinking category.

RESPONSE: Non drinking categories have now been added throughout, where relevant (see Table 2 and 4).

Statistical analysis:

There are no continuous normally distributed variables so you can't have used t-test.

RESPONSE: Apologies, this has now been removed.

The Kruskal-Wallis is the non-parametric alternative to the one-way ANOVA and is therefore not appropriate here where you are comparing characteristics between 2 groups only; drinkers and non-drinkers. Rather you should use the Mann-Whitney U-test as the majority of the variables you are testing are ordinal and then, as stated, the chi-squared test for the remaining categorical variables. Was Kruskal-Wallis used to compare alcohol use between the SCOPE centres? Please clarify.

REPOSENSE: Reference to use of Kruskal Wallis test is now removed from the text. Chi squared tests were used for all comparison of categorical variables both between non drinking and drinking in the different cohorts and in the SCOPE centres. Kruskal wallis test was used for comparing medians between SCOPE centres. This has been added as a footnote to Table 4 (page 14).

Please justify why you chose to use log linear binomial regression instead of, for example, logistic regression and the choice of confounders.

RESPONSE: Our reason for doing this has been added – “We used log linear binomial regression to examine the relative risk of alcohol consumption during pregnancy in relation to socio-demographic characteristics in each cohort and in each SCOPE country because when an outcome variable is common (>5%), logistic regression tends to over-estimate the association between our independent variable of interest and the outcome.” See page 11¶ 252-256.

Results:

Supplementary table 1: If possible, replace Table 1 with the supplementary Table 1 as this is much more interesting and reports results from your significance testing.

RESPONSE: As you advise, Table 1 has now been replaced with Supplementary Table 1.

Please add participant numbers to the drinking and non-drinking categories for each cohort. Also specify which period in pregnancy this refers to. It would be interesting to present these characteristics trimester specifically and not just averaged throughout pregnancy.

RESPONSE: The previous Table 1 is now Table 2 and participant numbers for the drinking and non-drinking categories are now added for each cohort as is the period in pregnancy to which it refers (see page 14-17).

We agree it would be interesting to present these characteristics by trimester specifically, however, having done so the difference between the trimester specific breakdown and overall breakdown is negligible. Therefore, adding trimester specific breakdown to the paper would considerably burden the paper without substantially adding anything new or interesting or indeed improving or adding to its message. We do take your point on board though, and are happy to provide these data to you upon request.

Table 2: Please add a non-drinking category. For the median alcohol consumption, please report interquartile range rather than 95% CI.

RESPONSE: Table 2 now becomes Table 1 given advice on moving Supplementary Table 1 into the manuscript. Both a non-drinking category and interquartile ranges for the median alcohol consumption have been added to this table – now Table 1, page 14.

Table 3: Is it pre-pregnancy? In the text it refers to alcohol consumption during pregnancy. Please clarify.

RESPONSE: Apologies, we refer here to alcohol consumption during pregnancy and this has now been clarified. See page 16.

Table 4: See comments for table 2.

RESPONSE: Both a non-drinking category and interquartile ranges for the median alcohol consumption have been added to Table 4, page 26.

Table 5: Add SCOPE to the table title. Add footnote from table 3.

RESPONSE: This has been added. Footnote also added from Table 3, page 21.

Discussion:

p.22 liner 15: from what I gather the guideline is 1–2 units once or twice a week, meaning either 2 units in one sitting or 1 unit twice a week, making the maximum consumption 2 units per week.

RESPONSE: As you highlight this has been clarified – see page 25 ¶ 360-361.

What are the guidelines for Ireland? Are they different to the UK? And how about Australia & New Zealand?

RESPONSE: We now refer to the guidelines for Ireland, Australia and New Zealand in the opening paragraph of the discussion - see page 25 ¶ 358-361.

A brief paragraph on the consequences of heavy alcohol consumption in pregnancy would be useful, including a translation of birth weight deficits to risk of other unwanted health outcomes in later life.

RESPONSE: A brief paragraph on this has now been added: see page 28-29 ¶ 435-442.

VERSION 2 – REVIEW

REVIEWER	Janna Skagerström Linköping University, Sweden
REVIEW RETURNED	27-Oct-2014

GENERAL COMMENTS	<p>The article has been greatly improved since the last version.</p> <p>Article summary: some of the discussion on the impact of mode of datacollection could be addressed here as well.</p> <p>Results: As you say in hte methods that you've "selected to examine the association between low birth weight and preterm birth ... and common confounders of these associations and alcohol use during pregnancy..." these results on low birth weight and preterm birth could be more highlited. This goes for the results as well as the discussion section.</p> <p>Table 2 - please look over the outline.</p> <p>Table 3: Why do you use different reference categories on BMI?</p>
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REVIEWER	Camilla Nykjaer University of Leeds Leeds LS2 9JT
REVIEW RETURNED	13-Nov-2014

GENERAL COMMENTS	<p>Much improved version. Below are a few technical comments.</p> <p>Methods: Statistical analysis: Appreciate the addition of footnote to table 4. But would advice to add it to the text here as well.</p> <p>Results: PRAMS: You state that all participant were included in the analysis (n=718) but in methods section state that 1,212 mother-infant pairs were sampled. Please clarify.</p> <p>Table 1 & 4: Please could you make it clear that the "severity of consumption categories" is the proportion of drinkers and not the whole cohort population.</p> <p>Now that you have changed your tables around and are presenting the characteristics table that was formerly in your supplementary material I would advice commenting on the results in this table rather than commenting on the one now added to your supplementary material (supplementary table 1). You may also consider whether it is more useful to present your results as row cumulative frequencies rather than columns cumulative frequencies, but again that will become clearer once you have commented on the results in this table.</p> <p>To follow the flow of the text I would recommend changing this</p>
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	<p>participant characteristics table to the first table in the article followed by the alcohol consumption table (currently table 1). In addition, please can you state what tests you used to obtain the P-values in footnotes below the participant characteristics table and please remove P< from p-value columns and either state actual P-values or just "<0.0001".</p> <p>Footnotes for table 2: I am unsure as to where the ** is in the table?</p> <p>Table 3: As you have commented in the text, age is significantly associated with drinking in GUI. As the association appears linear, and no P-value has been mentioned, it may be worth stating the P trend across the age categories in the text?</p> <p>Table 4: Please remove P< from p-value columns and either state actual P-values or just "<0.0001".</p>
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VERSION 2 – AUTHOR RESPONSE

Reviewer Name Janna Skagerström
Institution and Country Linköping University, Sweden
Please state any competing interests or state 'None declared': None declared

The article has been greatly improved since the last version.

Article summary: some of the discussion on the impact of mode of data collection could be addressed here as well.

Response: Thank you - we have now made reference to the potential impact of mode of administration in our article summary [page 5 ¶ 21-23].

Results: As you say in the methods that you've "selected to examine the association between low birth weight and preterm birth ... and common confounders of these associations and alcohol use during pregnancy..." these results on low birth weight and preterm birth could be more highlighted. This goes for the results as well as the discussion section.

Response: Thank you – we have discussed these results further in both the results and discussion sections; Results [page 19 ¶ 38-51] and Discussion [page 25 ¶ 57 – page 26 ¶ 1-11]

Table 2 - please look over the outline.

Response: Thank you – the formatting on this has been fixed [page 18].

Table 3: Why do you use different reference categories on BMI?

Response: Apologies – this is actually a mistake. The reference category is in fact the normal weight category group and this has been amended [page 18].

Reviewer Name Camilla Nykjaer
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University of Leeds
Leeds
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Please state any competing interests or state 'None declared': None declared

Much improved version. Below are a few technical comments.

Methods:

Statistical analysis:

Appreciate the addition of footnote to table 4. But would advise to add it to the text here as well.

Response: Thank you. This has been added to the text [page 21 ¶ 9-14].

Results:

PRAMS: You state that all participant were included in the analysis (n=718) but in methods section state that 1,212 mother-infant pairs were sampled. Please clarify.

Response: Thank you – we have added clarification on this to the text. 1212 women were sampled, 718 women responded and were included in the analysis [page 9 ¶ 54-57 - page 10 ¶3-6].

Table 1 & 4: Please could you make it clear that the “severity of consumption categories” is the proportion of drinkers and not the whole cohort population.

Response: Thank you – we have added a footnote to indicate this [page 16 and 22 respectively].

Now that you have changed your tables around and are presenting the characteristics table that was formerly in your supplementary material I would advise commenting on the results in this table rather than commenting on the one now added to your supplementary material (supplementary table 1).

Response: Thank you – we have now commented on the results on the table you refer to and not the supplementary table [page 17].

You may also consider whether it is more useful to present your results as row cumulative frequencies rather than columns cumulative frequencies, but again that will become clearer once you have commented on the results in this table.

Response: We think the column cumulative frequencies are intuitive – from glancing across the columns in table 2 – we can quickly decipher which cohorts have higher prevalence of use and severity of use. If it pleases the reviewer, we wish to retain these column frequencies.

To follow the flow of the text I would recommend changing this participant characteristics table to the first table in the article followed by the alcohol consumption table (currently table 1).

Response: Thank you – we have now done this [page 16].

In addition, please can you state what tests you used to obtain the P-values in footnotes below the participant characteristics table and please remove P< from p-value columns and either state actual P-values or just “<0.0001”.

Response: We have added this to the participant characteristics table (now Table 1) [page 16]. We have also removed the P< in each column as suggested [page 16].

Footnotes for table 2: I am unsure as to where the ** is in the table?

Response: Apologies – this is redundant and has been removed [now Table 1 page 16].

Table 3: As you have commented in the text, age is significantly associated with drinking in GUI. As the association appears linear, and no P-value has been mentioned, it may be worth stating the P trend across the age categories in the text?

Response: Thank you – we have added a p value for trend to the of text on Table 3 on [page 19 ¶ 31-36] as well as a line on this in the methods section [page 13 ¶ 51-54– page 14 ¶3]

Table 4: Please remove $P <$ from p-value columns and either state actual P-values or just “ <0.0001 ”
Response: Thank you – this has been completed – see page 22.