Author's response to reviews

Title: Past oral contraceptive use and high blood pressure in postmenopausal women: an observational cohort study

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Author's response to reviews: see over
To the Editors,

RE: MS: 1239366622124344

Thank you for reviewing our manuscript Past oral contraceptive use and high blood pressure in postmenopausal women: an observational cohort study. Our responses to each of the reviewer’s comments have been included on the following pages.

Yours sincerely,

Joanne Lind
Response to Reviewer

Title: Past oral contraceptive use and high blood pressure in postmenopausal women: an observational cohort study

We thank the reviewer for their comments. We have outlined below the changes we have made in response to these comments.

Abstract:

1. Methods: Need to provide number of participants and study location. ‘Adjusted odds ratio’, could the authors specify the variable adjusted for in the model. How was high BP defined?

The abstract has been updated to include the number of participants, the study location, and the variables adjusted for in the model. The definition of high blood pressure has also been included in the statement “current treatment for high blood pressure”.

2. Results: Need to provide statistics to support the interpretation, e.g. OR (95% CI), p value etc.

The results now contain the odds ratios, 99% confidence intervals, and p-value for each age group in the major analysis (association between hormonal contraceptive use and high blood pressure)

3. Conclusions; Being a cross-sectional study, authors should avoid the term ‘risk’ as risk can be assessed only in prospective studies. Suggest removing the last sentence as this kind of causal inference cannot be derived from a cross-sectional study.

The last sentence has been removed.

Background

4. Page 3, Last paragraph: Again, being a cross-sectional study, authors should avoid the terms, ‘incidence’, ‘risk’ etc. which are suggestive of prospective study.

The word incidence has been replaced with the “likelihood”.

Methods

5. Questions related to assessment of BP and other covariates such as smoking, alcohol and physical activity need to be provided. How was high BP defined? Was it same as hypertension?

These questions have now been provided in the methods section:

Pg 4, lines 87-89: “Women were identified as having high blood pressure if they answered “Yes” to the question “In the last month have you been treated for: high blood pressure”.

Pg 5, lines 97-104: For ‘Country of birth’, participants were classified according to whether they had been born in Australia or born in a country other than Australia. Physical activity levels were assessed using questions from the Active Australia Survey Vigorous activity as previously described [8]. Smoking was classified as current, past or never, according to the questions “Have you ever been a regular smoker?” and if yes, “Are you a regular smoker now?”. Consumption of alcohol was
classified into the groups shown in Table 1 based on the question “About how many alcoholic drinks do you have each week?”.

6. Was information on diabetes, BMI and antihypertensive medication available? If so, their relationship to OC use could be provided.

The authors did not have access to information on diabetes and antihypertensive medication. BMI was available and has been incorporated into Table 1. BMI was always accounted for in the other analyses of the paper and this is more clearly stated in the methods section and the footnotes of each of the tables.

7. How were variables for the multivariable model selected? Authors could provide a basic model without adjustment or adjusted for just age, in addition to the multivariable model. Authors could consider adjusting for variables that were significant in univariate models only, instead of adjusting for all variables (if this is the method adopted for the multivariable model).

All variables included in the model were significantly associated with current treatment for high blood pressure in univariate analysis. This has now been stated in the methods section:

Pg 5, lines 93-97: “Odds ratios were adjusted for demographic and lifestyle factors that were significantly associated with treatment for high blood pressure in univariate analysis. Namely, income, country of origin, BMI, smoking, alcohol, exercise, family history of high blood pressure, menopausal hormone therapy use, number of children, and age of menopause, with additional categories for missing values (Table 1).

Additionally, odds ratios, confidence intervals and p-values for all unadjusted models are now provided in Tables 2 and 3, stratified by age.

8. Line 93: Please provide P-interaction by age.

This has been included in the methods section:

Pg 5, line 108: “A significant interaction between age and past hormonal contraception use with having high blood pressure was observed (p<0.001).”

9. Suggest the authors provide a sensitivity analysis using 95% CI, instead of 99% CI.

As stated in the manuscript, 99% confidence intervals have been used to partially account for multiple testing. That is, a result is considered significant if p<0.01. If 95% confidence intervals were used then some other form of p-value adjustment would need to be applied due to the multiple tests performed in the analysis.

Results:

10. What was the prevalence of past OC users? What was the prevalence of ‘High BP’?

This information has now been included in the first sentence of the results section:
Pg 6, Line 115-116: “A total of 34,289 women were included in the study (Fig. 1) of which 75% reported past hormonal contraceptive use and 21% reported current treatment for high blood pressure.”

Tables:

11. Table 1: Information on ‘Age at menopause’ is missing in Table 1. It’s not clear why BP variable is not included in Table 1.

Age at Menopause has now been included in Table 1. BP is not included in Table 1 as this table is provided to show what variables are associated with hormonal contraceptive use, prior to investigating the relationship with HBP. The remainder of the paper investigates the relationship between HBP and hormonal contraceptive use.

12. Table 2: What is the rationale for the categorization of age as <58, 58-66 and >=66 etc. instead of conventional age groupings as <55, 55-65 >=65 or <60, 60-70, >=70 etc?

As stated in the paper the women were divided into tertiles so that each group was equally powered to identify significant differences. Statistically this is thought to be a sound stratification method.

13. Need to include a column to indicate % with high BP under each category.

This column has been included in Tables 2 and 3

Minor issues:

14. Methods, paragraph 3: Need to specify the demographic and life style factors adjusted in the model.

This has now been included:

Pg 5, lines 93-97: Odds ratios were adjusted for demographic and lifestyle factors that were significantly associated with treatment for high blood pressure in univariate analysis. Namely, income, country of origin, BMI, smoking, alcohol, exercise, family history of high blood pressure, menopausal hormone therapy use, number of children, and age of menopause, with additional categories for missing values (Table 1).

15. Table 2 and 3: Variables adjusted for in the multivariable model need to be provided in footnotes.

Footnotes have now been provided for the tables.