

Title: Hormonal Contraceptive Use and Women's Sexuality and Well-Being: Estimating Treatment Effects and Their Heterogeneity Based on Longitudinal Data

September 20<sup>th</sup>, 2023

Dear Prof. Dr. Evans, dear reviewers,

Thank you very much for the positive evaluation of our revised programmatic registered report stage 1 on heterogeneous effects of contraception and for the opportunity to revise and resubmit the manuscript to *Peer Community In - Registered Reports*.

We were pleased to hear that you and two reviewers were satisfied with our revisions included in the latest version of the manuscript. We appreciate your patience and the time you and the reviewers took to evaluate our manuscript. We are pleased to hear that you and the two reviewers are satisfied with the way we have addressed their previous feedback. Thank you again for your valuable feedback and for facilitating this review process. We look forward to the IPA for our manuscript and the start of the second phase of our registered report.

We appreciate the additional suggestions from reviewer #1 and have incorporated some of them into the revised manuscript. Although reviewer #1 explicitly stated that they did not need a response to their comments, we want to take the time to explain our decisions and thank you and the reviewers again for the helpful feedback in this review process.

We have made some additional minor changes throughout the manuscript to improve readability and to ensure consistency throughout the manuscript. We have again uploaded two versions of the manuscript. In one version, all changes from the first revised version of the manuscript are highlighted in blue to facilitate the review process. We would appreciate your consideration for a stage 1 acceptance.

Best regards,

Laura Botzet, on behalf of all co-authors

**Recommender's remarks:**

Thanks for resubmitting your RR and thank-you for your patience in awaiting a response. Two reviewers returned to consider the manuscript and as you can see below, they are content with the management of their previous feedback. One reviewer has a few additional comments to consider so before I 'accept' and grant IPA, I'd like to give you the opportunity to reflect upon their suggestion and action it as you see fit. Following your resubmission, I will not look to secure further reviewer feedback and will be aiming to provide IPA as swiftly as possible. I imagine this won't take long to action so I will be vigilant in awaiting and actioning your final revised Stage 1 submission.

Thanks and take care,

Dr Thomas Rhys Evans

**Reviewer #1's remarks:**

The authors did an excellent job of responding to comments and updating their registered report. I was really impressed with the revised report, and approve of the current version.

Thank you for your kind words and positive feedback on our revisions. We greatly appreciate your support and approval of the current version of our manuscript.

I had just had one actual note:

1. HCs are often prescribed to both homosexual women and women who are not sexually active. The assumption that women who have never had sex will not be using HCs seems a bit flawed - to me, this is just missing data. It is more likely that they are not using HCs, but not certain. The authors should consider treating this as missing data in the main analysis as opposed to just in a robustness analysis. In a related vein, perhaps a robustness analysis could also include homosexual women? I trust the authors to consider this feedback and adjust things if appropriate, and do not need a response to this comment.

We appreciate the reviewer's perspective on this issue and value their opinion. Regarding their concerns about including women who have never been sexually active as non-hormonal contraceptive users in our main analyses, we agree that this categorization is likely to introduce some errors. However, treating these women as "missing data" would also introduce bias due to sample selection (i.e., including only women who were sexually active). This is particularly important because PAIRFAM participants can be as young as 14 years old, making it more likely that girls or women included have never been sexually active. While we cannot provide a formal comparison of the magnitude of the error resulting from

the data analytic decision here—it would hinge on a lot of assumptions—we believe that including these women is preferable, on balance.

But this is an important limitation of the data. Therefore, we have explicitly highlighted this issue in footnote #3 in the manuscript: *In PAIRFAM, women who indicated that they had never been sexually active in their life were not asked about their contraceptive method. These women were coded as using no contraceptive method, i.e., a non-hormonal method (see the section about the variables for more information). This coding may introduce some errors as some women may use hormonal methods without being sexually active; we thus exclude them in an additional robustness analysis to ensure that this coding decision does not systematically affect results.*

Considering homosexual women, based on the previous comments R1.2. and R2.8. and this new comment from reviewer #1, we have decided to perform additional exploratory analysis only including homosexual women, if the relevant sample size is large enough (more than 200 homosexual women switching between hormonal and non-hormonal contraception at least once). We have added this information in the section *Methods - Exclusion Process and Participants*: *In addition to these robustness analyses, which focus on excluding specific women or waves that might bias the estimates of the main analyses, we would like to conduct exploratory subanalyses based only on women who reported being in a homosexual relationship or who have reported only homosexual relationships in the past (otherwise using the same exclusion criteria as in the main analyses). While we hope to gain some initial insight into the potential effects of hormonal contraceptives on sexuality and well-being of homosexual women, the sample size of these exploratory analyses is likely to be too small to draw any definitive conclusions (especially regarding exclusively homosexual women using hormonal contraceptives). If, after applying the exclusion rules, fewer than 200 exclusively homosexual women reported switching between hormonal and non-hormonal contraception at least once, we will not conduct these additional exploratory subanalyses.*

#### **Minor things I noticed in my read through:**

**1. Pg 1: missing commas here and there (e.g., between existed and which; after But); consider changing like to such as "...such as how HCs influence sexuality and well-being." I thought I saw a missing oxford comma too, but maybe I imagined that.**

We appreciate the mention of possible missing commas. We have added the suggested comma between “existed” and “which” on page 1 (the sentence now reads: *Before their invention, only so-called barrier methods existed, which prevent fertilization by blocking the union of egg and sperm (e.g., condoms, diaphragms, cervical caps, and chemical spermicides).*) but we decided not to add a comma after “But” as we thought this would be incorrect (see, for example, <https://www.grammarly.com/blog/comma-before-but/>; the sentence reads: *But a recent review by Both et al. (2019) found that only a minority of women reported changes in sexual functioning and concluded that the effects of hormonal contraceptives on sexual functioning – and sexual desire in particular – are understudied and therefore poorly understood.*). We also checked the rest of the manuscript for missing commas (including oxford commas) and added them where necessary.

We decided against changing “such as” to “like” but added a missing comma. The sentence now reads: *Experiments are considered the gold standard to answer causal research questions, such as the effects of hormonal contraceptives on sexuality and well-being.*

## **2. Pg 19: missing word of "...inform their decision OF which..."**

Thank you very much. We have added the missing word. The sentence now reads: *In addition, we want to investigate whether women’s individual treatment effects on sexuality and well-being inform their decision of which contraceptive method to use by investigating the correlation between estimated individual treatment effects and the number of years using hormonal contraceptives during the course of PAIRFAM.*

## **3. Pg 21: missing a space after ;**

We really appreciate the detailed feedback and have added the missing space. We have also made some minor changes to the rest of the sentence. The sentence now reads: *The data on which our analyses are based were already available and can be used for scientific purposes; the Leibniz Institute for the Social Sciences (GESIS) grants access to the scientific community.*

## **4. Table 3: check the header formatting, new column seems one character too small!**

We have checked the formatting of Table 3 and found no inconsistencies. The font used throughout Table 3 (including the "Conceptualization in Figure 1" column) is Arial, size 9.

### **Reviewer #2’s remarks:**

**I have gone through the authors' reply to reviewer comments in Round 1 and the new manuscript file with tracked changes. I believe the authors have sufficiently addressed the previous concerns and I did not see any additional concerns (ones that I have not raised before).**

Thank you for taking the time to review our revised manuscript and for your positive feedback. We greatly appreciate your thorough evaluation of our previous submission and your acknowledgement of our efforts to address the concerns raised in Round 1. Your feedback has been instrumental in improving the quality of our manuscript.