

Title: Positive Treatment Effects and High Heterogeneity of Hormonal Contraceptive Use on Women's Sexuality

Registered Report Stage 2 Based on a Programmatic Registered Report Stage 1

November 13th, 2024

Dear Prof. Dr. Evans, dear reviewers,

Thank you very much for the helpful and constructive feedback on our registered report stage 2 titled *Positive Treatment Effects and High Heterogeneity of Hormonal Contraceptive Use on Women's Sexuality* based on the programmatic registered report stage 1 titled *Estimating Average Treatment Effects and Treatment Heterogeneity of Hormonal Contraceptive Use on Women's Sexuality and Well-Being Based on Longitudinal Analyses*. We are grateful for the opportunity to revise and resubmit our stage 2 manuscript to the *Peer Community In Registered Reports*.

We greatly appreciate your and the reviewers' insightful comments and valuable feedback, which helped us improve the manuscript. We have carefully considered and responded to all points raised by you and the reviewers.

First, we replaced the term *waves* with *observations* where appropriate to avoid confusion (R1.2). Second, we expanded certain discussions, such as the analysis of individual treatment effects and contraceptive decisions (R1.3, R2.2), the decision to exclude women who had never been sexually active (R1.6), and which variables in future studies may be important for understanding the heterogeneity in individual treatment effects (R2.5). Finally, we added more detailed explanations and "hand-holding" throughout the manuscript to improve readability (R1.14, R2.3, R2.6), added subheadings to break up long sections (R1.9), and simplified complex sentences, while also addressing minor formatting issues as suggested by the reviewers (R1.4, R1.7, R1.10, R1.11, R1.12, R1.13). We have decided against implementing two suggested analyses that went beyond our in-principle accepted protocol from Stage 1 (R2.1, R2.4). We respond to each suggestion by you and the reviewers in more detail below.

Besides the excellent points raised by the reviewers, we also realized that our approach to estimate the correlations between individual treatment effects and other interindividual differences (including age, the Big Five personality dimensions, and the proportion of years using hormonal contraceptives) overestimated the shared variance between the two constructs. Therefore, instead of (1) summarizing individual treatment effects across draws and then (2) correlating them with interindividual differences weighted by the inverse standard error of the individual treatment effect estimates (we call this approach "average across draws, then correlate"), we (1) correlated the individual treatment effects and interindividual differences at draw level and then (2) summarized the correlations across draws (we call this approach "correlate, then average across draws"; Ly et al. (2017) for example use the term "plausible values"). In the manuscript, we focus on the "correlate, then average across draws" relationships, which appropriately take into account the estimation

uncertainty, and report the “average across draws, then correlate” relationships in the supplement.

In addition, we updated Figure S8, Figure S10, Figure S11, and Figure S12 displaying thin-plate spline effects of age on hormonal contraceptive use and the sexuality outcomes, because we discovered that our previous approach had exaggerated the uncertainty in these plots.

We uploaded two versions of the manuscript and the supplement, including one in which all changes are presented in blue font to ease the review process. We think that these changes have further strengthened our manuscript and would be grateful if you consider it for recommendation.

Best regards,

Laura Botzet, on behalf of all co-authors

Editor's remarks:

Thanks for submitting one of your Stage 2 reports. The work included is impressive and substantive and I thoroughly enjoyed learning more. I am also very grateful to our returning reviewers who have advised that only relatively minor changes are needed to help improve the clarity of your communication. I have no further feedback beyond their very helpful suggestions, so I encourage you to work through their comments systematically, providing a response to each to discuss if/how you have actioned and I will look forward to re-reading this shortly.

Congratulations, thanks, and take care,

Dr Thomas Rhys Evans

We really appreciate the positive feedback and the very helpful comments from the returning reviewers. We have revised our manuscript accordingly to address all concerns. Our specific responses and revisions are outlined below in response to the reviewers' remarks. To structure our responses, we have added numbering to the reviewers' comments whenever necessary (otherwise their comments remain unchanged).

Reviewer #1's remarks:

Here, the authors investigated the effect of hormonal contraceptive (HC) use on sexual outcomes using large, longitudinal dataset containing data from 5,401 women collected over the course of 14 waves. They also investigated the heterogeneity in women's responses to HC treatment and if women's treatment responses predict their future HC use. The authors found positive effects of HC use on sexual frequency and sexual satisfaction, and high heterogeneity in women's responses to HC use. Overall, the authors have done a great job with this registered report. I will be focused on new content as they have addressed previous comments well. This manuscript is well-written, the analyses very well planned and conducted, the results presented clearly, and the implications scientifically and practically important. I recommend it for publication after a very minor revision (point 2 is really the only one I think is critical to address), and hope that my below comments are helpful. I begin with major comments, and follow with minor comments, the latter of which are up to the author's discretion if they would like to address/respond to.

We really appreciate the positive feedback and the very helpful comments. We have responded to each one of them separately below.

Major comments:

R1.1 I was a bit unclear on how the two papers plan to use most of the same introduction – is the well-being paper still planning to use the same introduction? Is that ok in a registered report setting?

Yes, we plan to use a very similar *Introduction* section (and *Methods* section) for the second stage 2 article focusing on well-being, while shifting the focus to well-being and excluding all information about sexuality. Wherever appropriate, we will refer to the first stage 2 article focusing on sexuality.

The *Results* section of the second stage 2 article focusing on well-being will follow the same format as the *Results* section of the first stage 2 article focusing on sexuality with the aim to make them as comparable as possible. The *Discussion* section will of course differ between the two separate stage 2 articles.

As far as we understood the process from *Peer Community In Registered Reports* this is possible in the programmatic registered report format.

R1.2 The term waves is used throughout where it seems like the authors really mean observations. This is, the 14 waves of data collection include data from 5,401 women, surmising 23,130 individual observations. This was confusing to me in the abstract, on pg. 22, in Table 2, and in the results. I would suggest modifying the term waves to be observations where appropriate, or to better introduce the reason waves is being used here to mean both the sub-cycle of data collection and the number of total observations.

We really appreciate this comment and have changed *wave(s)* and *unit(s)* to *observation(s)* throughout the manuscript and the supplement, whenever we refer to single units of analysis. In line with the comment from the reviewer, we have decided to keep the term *wave(s)* whenever referring to the structure of the PAIRFAM dataset. In addition, we decided to keep the wording *previous wave* when referring to predictors measured in the last year to stress the fact that this information was based on the preceding year and not the last complete observation of this participant (which could potentially be years ago, if participants skipped waves).

These changes also affected minor parts of the already accepted Stage 1 protocol. As we agree with the reviewer, that the use of the term *wave(s)* was confusing, we believe that these changes improve the readability of our manuscript and are therefore justified.

In addition, we updated Figure 2, Figure 3, Figure 4, Figure 5, as well as Figure S3, Figure S4, Figure S5, and Figure S6 to reflect these changes.

R1.3 Pg 58: “Contraceptive Decisions and Individual Treatment Effects”. This was the only analysis that didn’t make sense to me/seemed a bit simplistic. Here, it seems like using the treatment effect estimates and correlating them with years of use is a bit lacking. To answer this question (“whether women guide their contraceptive method choices by deciding against hormonal contraceptive methods after experiencing adverse effects”), I would want to know if negative changes in sexual outcomes (an adverse effect) in preceding waves predicted discontinuation in subsequent waves. As the authors found that women reporting low sexual frequency/satisfaction were likely to switch in subsequent waves, these correlations here seem to add little to the story.

We agree with the reviewer that an ideal analysis of the highlighted question would look different, although we think the analysis proposed by the reviewer answers a slightly different question, because it focuses on generally low sexual frequency or low sexual satisfaction (which may or may not be attributable to contraception), not specific individual treatment effects on sexual frequency or sexual satisfaction.

With our question, we ran into the limitations of our dataset. We had noted this limitation in the section *Introduction - Estimands*:

In addition, we wanted to investigate whether women’s individual treatment effects on sexuality informed 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. Ideally, we would have sufficient data to instead estimate individual treatment effects (e.g., using all but the last observation of each participant) to predict individual behavior (e.g., contraceptive method in the very last observation of each participant). However, in the context of the available data, this would result in very low statistical power, and we thus decided on a different approach which would only provide very rough evidence for potential assortment based on experiences with contraceptive methods. Such an assortment based on experiences would result in the type of selective attrition explained above and may provide a partial explanation for the mixed evidence concerning effects of hormonal contraceptives on sexuality.

In addition, we changed the paragraph *Results - Contraceptive Decisions and Individual Treatment Effects* to remind the reader, why we are interested in this analysis:

We additionally wanted to investigate whether women guide their contraceptive choices based on their experiences. In fact, our analysis of predictors of hormonal contraceptive use already provided evidence pointing into that direction: women with higher sexual frequency and higher sexual satisfaction were more likely to stick with the method they were previously using. However, our registered analysis went further and asked whether the individual treatment effects (i.e., not just whether women are more or less sexually satisfied, but whether hormonal contraceptives have a negative or positive effect on their sexual satisfaction) correlated with the amount of time that women used hormonal contraceptives. Again, we used the “correlate, then average across draws” approach. That is, we correlated the individual treatment effects with the proportion of years of hormonal contraceptive use at draw level. Finally, these correlations were averaged across draws. None of the “correlate, then average across draws” relationships were significant (see the last column of Table 7).

We really appreciate the comment of the reviewer that the negative effects of sexual frequency and sexual satisfaction in the previous wave on hormonal contraceptive use in the current wave, may indicate switching behavior because of experienced adverse effects. Indeed, the results for the interaction effects of sexual frequency (sexual satisfaction) and hormonal contraceptive use at the previous wave on hormonal contraceptive use in the current wave might indicate switching behavior because of negative adverse effects on sexual frequency and sexual satisfaction (from the section *Results - Predictors of Hormonal Contraceptive Use*):

If a woman used non-hormonal contraceptives in the previous wave, for each increase of 1 on the scale for sexual frequency this corresponds to a decrease of -0.65% [-0.95%, -0.35%] in the probability to use hormonal contraception in the current wave. If a woman used hormonal contraceptives in the previous wave, for each increase of 1 on the scale for sexual frequency this corresponds to an increase of 1.17% [0.75%, 1.59%] in the probability to use hormonal contraception in the current wave.

[...]

If a woman used non-hormonal contraceptives in the previous wave, each increase of 1 on the scale for sexual satisfaction corresponds to a decrease of -0.25% [-0.40%, -0.09%] in the probability to use hormonal contraception in the current wave. If a woman used hormonal contraceptives in the previous wave, each increase of 1 on the scale for sexual satisfaction corresponds to an increase of 0.31% [0.10%, 0.51%] in the probability to use hormonal contraception in the current wave.

To discuss these results in light of the question whether women’s contraceptive decisions are guided by the experience of adverse effects, we have added a paragraph to the section *Discussion - Individual Treatment Effects*:

We also did not find significant correlations between the estimated individual treatment effects and the number of years of hormonal contraceptive use over the course of PAIRFAM, which we would interpret as preliminary evidence against potential assortment based on experiences with contraceptive methods. Again, the interpretability of this analysis is limited by the low reliability of the individual treatment effects. Furthermore, the analysis would have

at best provided indirect evidence for assortment. Another analysis we conducted can be used to answer a slightly different but related question, namely whether generally low sexual frequency or low sexual satisfaction (which may or may not be attributable to hormonal contraception) predict switches in contraceptive methods. This analysis provides another type of indirect evidence for assortment: In the models predicting hormonal contraceptive use in the current wave, women were more likely to switch their contraceptive method if they experienced lower levels of sexual frequency and sexual satisfaction. However, another recent study using a similar analysis found no support for women's experiences of lower levels of sexual frequency and sexual satisfaction predicting switches in contraceptive methods (Draxler et al., 2024). We believe that a better empirical test of the underlying idea would require more extensive longitudinal data. In such data, one could use all but the last observation per individual to estimate the individual treatment effect, and then test whether this effect predicts the contraceptive method reported in the last observation of the individual.

Minor comments:

R1.4 Pg 22: Consider adding a statement at the end of the paragraph that indicates that as criteria were not met, analyses were not conducted. (The authors do mention this in the paragraph, but should end on that note)

We appreciate the feedback and now end the paragraph with the sentence: *As the threshold of a sufficient number of exclusively homosexual women was not met, we did not perform the additional exploratory subanalyses based on this sample.*

R1.5 Remove unnecessary page breaks throughout.

We removed unnecessary page breaks throughout the manuscript but kept additional line breaks before every heading to structure the document and make it easier to read.

R1.6 Pg 30: "The new exclusion implies that we should not generalize our conclusions to women who start being sexually active and/or start using hormonal contraception." The authors should give a bit more explanation here. I was in agreement about the decision to use the exclusion, but then felt like I wanted more explanation of this statement. (Either here or in the discussion)

We appreciate that the reviewer agrees with our decision to exclude women who had never been sexually active. To elaborate a little bit more on the statement *The new exclusion implies that we should not generalize our conclusions to women who start being sexually active and/or start using hormonal contraception.* we added a new paragraph to the section *Methods - Deviations from Stage 1 Concerning the Analysis Sample*:

For women who are being sexually active for the first time, several factors may make their experience different from that of women who have been sexually active for a longer period of time. Initially, these women may be in the process of exploring and understanding their

sexual preferences, desires, and boundaries, which may influence their sexual frequency and satisfaction. These factors may result in a unique pattern of sexual behavior that differs from those with more established sexual routines and experiences. Women who begin using hormonal contraceptives without being sexually active may experience different dynamics than those who are already sexually active. For these women, the decision to use hormonal contraception may be driven by reasons other than birth control, such as managing menstrual cycles, reducing menstrual pain, or addressing hormonal imbalances. Without the context of sexual activity, their experience with contraception may be primarily focused on managing these health concerns.

R1.7 The CIs looked weird with semi-colons – don't they normally use commas? (e.g., pg 34: “[95% CI: .86; .87]” vs [95% CI: .86, .87])

In line with the comment from the reviewer and the 7th edition of the *Publication manual of the American Psychological Association* we have changed all the semicolons to commas to report the CIs throughout the manuscript and the supplement.

R1.8 I'm really impressed with the clear reporting of practical effects (i.e., corresponding to an X% increase) throughout the results.

Thank you very much for the positive feedback, we really appreciate it.

R1.9 Starting on pg 40: under “Predictors of Hormonal Contraceptive Use”, subheadings would be useful as this section is long. Future researchers will have an easier time finding the results they want to cite if subheadings are included.

Thank you for this really helpful suggestion. We have added four subheadings to the section *Results - Predictors of Hormonal Contraceptive Use*: (1) *Stability of Contraceptive Method Use*; (2) *Sexuality*; (3) *Relationship and Family Situation*; (4) *Income and Education* in the manuscript and the supplement.

R1.10 Figure 5: Stretch out header across all 3 panels

We stretched out the main heading in Figure 5 and Figure S6 across all 3 panels.

R1.11 Figure 7: What are the orange lines?

To clarify what the colors of the lines indicate, we have added the following sentence to the note of Figure 7 and Figure S7: *The green individual treatment effects do not differ significantly from zero, the orange individual treatment effects differ significantly from zero.*

R1.12 Pg 59: I don't think you need the word respectively at the end there.

We have removed the word respectively here.

R1.13 Pg 63: "discussed in the section before" discussed in the previous section

We have changed the sentence accordingly. The sentence now reads: *When women use hormonal contraceptives, they have a higher sexual frequency and a higher sexual satisfaction than when they use non-hormonal contraceptives, and these effects are robust to the inclusion of the potential confounding effects discussed in the previous section.*

R1.14 First paragraph on pg 64 doesn't read super well, I had to go over it more than once to understand the authors' points. Consider editing here somewhat.

We have revised the second paragraph on page 63 (referring to the clean version of the revised clean manuscript; originally the first paragraph on page 64 in the clean manuscript):

In contrast, our results are not consistent-with existing experimental evidence that hormonal contraceptive use negatively affects sexual functioning (e.g., Læssøe et al., 2014) and libido (e.g., Lee et al., 2017; Lundin et al., 2018; Zethraeus et al., 2016), as well as sexual activity, arousal, pleasure, orgasm, and lubrication (Smith et al., 2014). Therefore, based on the correlational data, we found no support for the hypothesis that the intervention in the endocrine system through the use of hormonal contraceptives (Stomati et al., 1998) negatively affects women's sexuality (Both et al., 2019).

Reviewer #2's remarks:

I enjoyed reading the Stage 2 manuscript! The authors did a good job using the data and following their registered plan of testing their hypotheses. I have several relatively minor comments on this version of the manuscript:

Thank you so much for the positive feedback, we really appreciate it.

From my understanding, in the PARFAIM dataset, if women were not sexually active they were given a code of non-hormonal contraceptive user even though they did not actually answer a question about their hormonal contraceptive use. This is indeed an issue because women who are not sexually active may be on HCs for a variety of other reasons. I agree that those women should be excluded from analyses because HC use cannot be ascertained. (I feel less strongly about the fact that they were given a 0 for sexual frequency.) Overall, I think this deviation from the Stage 1 plan is appropriate.

We are very happy that the reviewer agrees with our deviation from the accepted stage 1 submission.

R2.1 Though I am not sure about excluding women in lesbian relationships. Past research has found similar effects for the link between reproductive hormones and women's sexuality (e.g., sexual desire) among women who are in both heterosexual and homosexual relationships. I suggest this is added as a robustness analysis.

For our main analysis, only waves in which women indicated being in a homosexual relationship or only reported homosexual relationships in the past were excluded (section *Methods - Exclusion Process and Participants: In addition, we excluded all individual waves of data in which participants indicated being in a homosexual relationship or only reported homosexual relationships in the past [...]*). This means that e.g., women who had heterosexual and homosexual relationships in the past were indeed included. The reason for excluding these women in the first place was not that for them the link between reproductive hormones and women's sexuality might differ but that there is simply no need for them to use contraceptives to prevent pregnancies (see Table 2). To make this exclusion even more explicit, we adjusted Figure 2 and Figure 3 (changing *only homosexual relationships* to *only exclusively homosexual relationships*).

If the reviewer is referring to lesbian women, we agree that this subanalysis would have been extremely interesting. As explained in the section *Methods - Exclusion Process and Participants*, this subsample was unfortunately just too small to perform any meaningful analysis. Based on the comment R1.4. from reviewer #1, we have added a sentence that we were unable to perform subanalyses based on exclusively homosexual women because the sample size did not meet our registered threshold. The full paragraph now reads:

In addition to these robustness analyses, which focused on excluding specific women or waves that might bias the estimates of the originally registered main analysis, we would have liked 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 originally registered main analysis). While we hoped to gain some initial insight into the potential effects of hormonal contraceptives on sexuality of homosexual women, the sample size after applying our registered exclusion criteria was already too small to perform any meaningful analysis (n = 188, observations = 539). We had the information from the previous and the current wave that was necessary to perform the proposed models for only 62 exclusively homosexual women (213 observations). Of these, only three women reported a switch from non-hormonal to hormonal contraception and no women reported a switch from hormonal to non-hormonal contraception (compared to our registered threshold of 200 homosexual women reporting a switch between hormonal and non-hormonal contraception at least once). As the threshold of a sufficient number of exclusively homosexual women was not met, we did not perform the additional exploratory subanalyses based on this sample.

Including these 213 observations from 62 exclusively homosexual women in the main analysis, is very unlikely to affect our main results because the sample size is just so small. Therefore, we do not want to deviate from our registered and in-principle accepted protocol from stage 1.

R2.2 Overall, I found the analyses and results sound. With the exception of the final section (contraceptive decisions and individual treatment effects), because at this point I forgot what that model entailed.

Based on the comment R1.3 from reviewer #1, we have modified the section *Results - Contraceptive Decisions and Individual Treatment Effects*:

We additionally wanted to investigate whether women guide their contraceptive choices based on their experiences. In fact, our analysis of predictors of hormonal contraceptive use already provided evidence pointing into that direction: women with higher sexual frequency and higher sexual satisfaction were more likely to stick with the method they were previously using. However, our registered analysis went further and asked whether the individual treatment effects (i.e., not just whether women are more or less sexually satisfied, but whether hormonal contraceptives have a negative or positive effect on their sexual satisfaction) correlated with the amount of time that women used hormonal contraceptives. Again, we used the “correlate, then average across draws” approach. That is, we correlated the individual treatment effects with the proportion of years of hormonal contraceptive use at draw level. Finally, these correlations were averaged across draws. None of the “correlate, then average across draws” relationships were significant (see the last column of Table 7).

For a more detailed discussion on the analysis concerning contraceptive decisions and individual treatment effects please see our answer to comment R1.3 from reviewer #1 (including the addition of a paragraph to the section *Discussion - Individual Treatment Effects*).

R2.3 A general point is that I found the paper quite difficult to read. When there is so much going on, a reader will need a bit more hand-holding to follow the reasoning for all analyses. It is a lot to keep in one’s working memory without more written

guidance. I think adding some of that hand-holding and maybe simplifying some sentences to emphasize the central point better would go a long way.

We have simplified some sentences throughout the manuscript and added some handholding along the way, while trying not to add significantly to the length of the manuscript. All changes are indicated in blue font throughout the manuscript with tracked changes.

R2.4 Did the authors look at whether the big 5 influenced decisions to use HCs or more likely to stop and start use of HCs? That would be interesting.

As registered in the accepted stage 1 submission, we did not use the Big Five personality dimensions as predictors of hormonal contraceptive use. They were only measured in four waves (wave 2, 6, 10, and for the refreshment sample in wave 11), so we did not consistently have a Big Five measure preceding the first observed contraceptive choice (or we would have had to exclude large parts of our dataset).

Instead, we correlated the Big Five personality dimensions with the extracted individual treatment effects but no common pattern across the sexuality outcomes emerged (see sections *Heterogeneity in Treatment Responses, Estimands, Results - Predictors of Individual Treatment Effects, and Discussion - Individual Treatment Effects*). In the past, we have examined personality as a predictor of contraceptive use (Botzet al., 2021) and have found that more conscientious and less open women were more likely to use hormonal contraception, but that these factors were not very important predictors.

R2.5 In the discussion, I would like a bit more elaboration on

R2.5 (a) why specifically the one-year interval may be a limitation (and what interval may be better). Additionally maybe the reason for experimental studies' different effects might be with the time course of adjustment.

In the section *Discussion - Limitations* we discuss the question why the time interval might be problematic and which time interval might be better in some length:

And third, the time interval between observations (one year) was potentially too long to capture all of the switches in contraceptive methods that happened between waves. As we had no indicator of the time between switch and reporting of outcomes, we are unable to conclude whether the observed effects appear only shortly after changing contraceptive methods or after some time has passed. Diary studies (e.g., Blumenstock & Barber, 2022; Ott et al., 2008) investigating very short time frames found support for positive effects of hormonal contraceptive use on sexuality as well; more research focusing on an intermediate time frame (e.g., one month, one menstrual cycle) would be helpful to understand the effects of hormonal contraceptive use on sexuality further.

As we note there, in line with our results finding positive effects of hormonal contraceptive use on sexuality with a long time interval of one year, studies using longitudinal data with a short time interval of days or weeks (e.g., Blumenstock & Barber, 2022; Ott et al., 2008) also

found positive effects of hormonal contraceptive use on sexuality. Therefore, it is unlikely that the difference in time intervals between our study (one year) and experimental studies using a shorter time interval (months; e.g., Zethraues et al., 2016) can explain the difference in the reported results (positive effects of hormonal contraceptive use on sexuality or negative effects of hormonal contraceptive use on sexuality respectively).

R2.5 (b) a possible explanations for the negative association between HC use and income and education (including potentially biases from physicians)

We found significant effects of education and income on hormonal contraceptive use in only one of the three models and these effects were relatively small. Therefore, we decided not to speculate about potential explanations for these effects, besides the paragraph that was already included in the *Discussion* section:

We also found some non-robust evidence for negative effects of income and education on hormonal contraceptive use. These results potentially indicate that women with a higher income and more education were less likely to use hormonal contraceptives. As these effects are rather small and did not emerge across models, they need to be interpreted cautiously. It is quite possible that the effects of income and education on hormonal contraceptive use differ depending on the details of the health care system and how accessible it renders such contraceptives (e.g., is a prescription required? Does health insurance cover the cost of the necessary appointments and of the contraceptives?).

R2.5 (c) a greater discussion about what variables (beyond big 5 and age) in future studies may be important for understanding the heterogeneity individual treatment effects

We appreciate this suggestion and added a paragraph to the section *Discussion - Individual Treatment Effects*:

What could these markers of interindividual differences be? First, self-reported side effects (i.e., side effects mentioned by women) might be positively related to experienced side effects (i.e., individual treatment effects). This could provide a first test of whether interindividual differences in self-report questionnaires reflect individual treatment effects at all. Second, instead of a general measure of neuroticism, fear of unwanted pregnancy might be positively related to individual treatment effects, with women with a higher fear of unwanted pregnancy showing positive effects of hormonal contraceptives on sexual frequency and sexual satisfaction. Third, general attitudes toward the use of hormonal contraceptives might also be related to individual treatment effects, with women who are very skeptical about the use of hormonal contraceptives (but who still use them, e.g., for other health reasons) showing negative effects of hormonal contraceptives on sexual frequency and sexual satisfaction. Finally, we would hypothesize that hormone sensitivity (Kiesner, 2017) would be negatively related to individual treatment effects, with women with higher sensitivity experiencing more negative effects of hormonal contraceptives on sexual frequency and sexual satisfaction.

R2.6 Parts of the discussion also felt a bit sterile/clinical to me. Even if not measured in PARFAIM, it is easy to think about some psychological processes that might surround some of women's decisions to use or not use HCs depending on life events.

We hope that the changes based on the other comments from reviewer #1 and #2 make the discussion less sterile. Concerning life events, we aimed to capture these directly in our study by addressing predictors of hormonal contraceptive use like relationship situation (including relationship status, relationship duration, and whether a woman started a relationship during the last year or became single during the last year) and family situation (including whether fertility plans are completed and number of children). We found evidence for effects of these life events as discussed in the section *Discussion - Descriptive Patterns in Hormonal Contraceptive Use*.