Author's response to reviews

Title: Effects of a short individually tailored counselling session for HIV prevention in gay and bisexual men receiving Hepatitis B vaccination

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Author's response to reviews: see over
Dear editor,

Please find enclosed our revised manuscript entitled “Effects of a short individually tailored counselling session for HIV prevention in gay and bisexual men receiving Hepatitis B vaccination” by Mireille E.G.Wolfers et al. MS: 4894768723772115.

We much appreciate the reviewer’s comments and believe that these have helped us to further improve the manuscript. In this letter we give an account of how we have used the reviewer’s comments to adjust our manuscript. In order to reply on comment number 5 of Curtis Dolezal we have performed additional analysis, which led to a change in the results. We have rewritten the results section. The most important change is that some of the differences between sub groups of the experimental and control conditions are no longer significant, suggesting indeed a regression to the mean effect. We believe that although are conclusions are more modest now, they have become stronger.

Other changes in the manuscript are:

- We have added a paragraph in the methods section on the measures that we used to assess participants appreciation of the intervention, because we realised this was missing (page 12, line 8-15).
- In the history of test behaviour (pre-test behaviour) we changed a mistake in the numbers of respondents that are tested on HIV and STI on page 6, line 22-24. 37% had ever tested for STI (in stead of 22%), 3% in stead of 2% reported to be HIV positive. We added information on previous STI-testing: 21% ever tested positive on STI.
- We have also made language revisions.

We sincerely think that our manuscript improved and hope that our revised manuscript can be accepted for publication in your journal.

Reaction on comments of David L.B. Schwappach, major issues:

1. I would very much appreciate a simple table with descriptive reports on changes in UAI behaviour by control/intervention group.

We agree that a table on these descriptives would be useful, so we added table 5 with descriptives of scores on unprotected anal intercourse in the intervention and the control group, for steady and casual partner separately, on baseline and follow-up. From this table it can be seen that behaviour with steady partners in the control group was effected (more UAI especially in receptive AI) and that behaviour with casual partners in the intervention group
was effected, less UAI insertive AI). We have included this in the results section, page 9, line 18-21:

“To illustrate the changes across the four different behaviours that are used for calculating the UAI-index score, table 5 presents the scores for each behaviour in the experimental and control groups. It shows that behaviour with steady partners in the control group had changed (more UAI especially in receptive AI) and that behaviour with casual partners in the intervention group had changed, they had less insertive UAI.”

2. Please provide results on intervention effects after adjusting for differences between control and interventions subjects, in particular in terms of education and ethnicity.

We have presented the analysis of table 2 and 3 now with a correction for ethnic background (Dutch and non-Dutch) and level of education (lower vs higher education) and we have added information on this in the method section (page 5, line 21-24).

“Differences in risk behaviour change between experimental and control groups were then tested by analyses of covariance (ANCOVA), adjusted for educational level (higher versus lower education) and ethnic background (Dutch versus non-Dutch).”

Results are similar. We have decided to put table 2A,B,C in one table now (table 2).

3. Mr Schwappach suggests that we present the comparison of only those subjects that completed the study.

This is indeed what we have already presented in Table 1 (“Characteristics of participants at baseline who completed all study visits”). We have added an extra sentence on page 6, line 9-11 to make this point more clear:

“Table 1 presents a comparison of the demographic and behavioural characteristics of MSM in the experimental and control groups; only participants who completed pre-test and post-test assessments are included in this comparison.”

Since we have already presented the baseline measures of only those subjects that completed the study it can be seen that the effects in the intervention effects can’t be explained by the selective drop out, because we have not included those subjects that dropped out (and that had higher risks) in the analysis, so they can’t have caused the improvement by dropping out.

4. The sample sizes in some cells are very small (e.g., table 3). Did you calculate power for the many subgroup analyses you did? At least, I would mention this issue in the discussion.
We have calculated power, but we had a higher drop out, and less participants recruited than required, due to lower numbers of MSM that visited for vaccination during the intervention period, also the men had less risk behaviour then expected. The original power calculations were based on a risk level of 40%, less then 30% of the men were at risk (unsafe unprotected anal intercourse). We added a comment on this in the discussion, page 11, line 24-27:

“Secondly, the power of this study is lower then was calculated, since the recruitment of the men was less then expected. To obtain sufficient power, 216 men in each group were needed, with at least 40% risky behaviour (unsafe unprotected anal intercourse). We were able to recruit 472 men, but the large drop out reduced this number to 281, and less than 30% of the sample reported risk behaviour.”

5. The referent wonders about alternative explanations that could be discussed. He is right that we have not added al lot of discussion on this. Therefore we have discussed the following hypothesis at page 10, line 17-24.

“It could also be that the HBV vaccination itself has produced unwanted side-effects. Notably, men who received the vaccination may feel protected and perceive less risks when they have unprotected anal sex. The HIV prevention counselling may have protected men in the intervention group from this side-effect. Maybe risk perception regarding UAI in a steady relationship is stronger for HBV-infection risks than for HIV-infection, and that therefore men feel safer after the HBV vaccination to engage in sex without condoms. In the intervention group this has not occurred due to the protective effect of the counselling-intervention, which was specifically (but not exclusively) addressing HIV risks.”

6. To this referee, it is a substantial difference if the intervention was successful because controls worsened, or because men in the intervention improved:

We were not able to show that risk behaviour in the intervention group really decreased. The additional analyses on simple effects, re-running the models with the pre-test scores on UAI as additional covariate show that subgroup effects are not significant and a decrease that was shown in subgroups of unsafe men at pre-test in UAI is most probably due to a regression to the mean. In table 5 it shows that behaviour with casual partners in insertive anal sex seemed to have reduced in the experimental group, but in the ANCOVA’s no significance for this effect was reached.

Minor issues:

1. P7, first line “did attend the vaccination but did fill in....” We agree that this is a mistake, indeed the word ‘not’ is missing here. We have corrected this in the manuscript (page 6, line 30).

2. We did include an abstract with our submission.
Letter to editor, MS: 4894768723772115
Reaction on comments of Curtis Dolezal:

Major issues:

1. The referent states that the lack of randomisation is a limitation.

   We agree this weakness in the study design, and we have now added this as a third limitation of the study in the discussion on page 11, line 6-23.

   “A first limitation is related to the design of the study. Because of the quasi-experimental design the causality of the effect of HIV-prevention counseling relation on behavioural change must be interpreted with caution. A lack of randomisation may have resulted in regression to the mean effects, natural variation between pre-test and post-test may then be interpreted as a real change. However, we used analysis of covariance with the change between baseline and follow-up as the outcome variable. To adjust observed measurements for regression to the mean effects we run the models with the scores at pre-test as covariates. We found that a regression to the mean effect was unlikely to explain the observed difference in changes in the overall UAI-index score and the score with steady partners, but that changes in UAI with casual partners are most likely explained by a regression to the mean.”

   “Respondents in the experimental and control group were recruited in different cities in the Netherlands, but we chose cities that were all situated in major urban regions of the country. These cities have a rather comparable gay scene, with an easy accessible municipal health service situated in the city center which offered the free HBV vaccinations. We do not expect that the risk behaviour between the men living in the different cities varies substantially, as the Netherlands are not very large and men tend to travel to gay nightlife events. Also HIV prevention activities are comparable between the cities. In the Netherlands, HIV prevention aimed at risk groups, such as MSM, is carried out by the local municipal health services and is supported by a national organization on gay and lesbian health.”

2. The referent worries that we assessed sexual risk behaviour prior to the intervention, because the risk assessment covers a 6-month period, while the average follow-up period was 5.6 months.

   First we will explain the background of this discrepancy: This difference in time between assessment and follow-up is caused by the practical implications of using the contact moments of the vaccination for follow-up. The ideal time period is 5-6 months between the second and third vaccination, but the actual appointment for the third vaccination is not at the same time for everyone, making it difficult to define the precise recall period in terms of months or weeks that will be valid for everyone.

   We agree that the referent is right but we want to explain why we do not consider this as a large problem. If men had unprotected sex in these one or two weeks (0.4 month) before the intervention and they have started using condoms after the intervention, most of them would still be coded in the same category as a person who has not engaged at all in unprotected sex after the intervention, since the category ‘always or ‘almost always used a condom’ are taken together
in the same category coded ‘0’ (low risk). Only if he stopped sex completely but did engage in unprotected sex in this first one or two weeks, he could decide to choose the category ‘never used a condom in anal intercourse’ instead of indicating that he did not engage in anal sex. In this case he will be placed in the highest risk group coded ‘2’. In this situation, the risk behaviour of some men at follow-up is assessed as too high and this would mean that although they have become safer after the time of intervention this is not accounted for in the results. Nevertheless, this could have happened in both the experimental and the control group, and can have caused an overestimation of risk behaviour after the intervention for both groups.

Although we agree with the referent that he is correct on this point, we think that this is a theoretical issue, and that it would too much complicate things. Therefore we decided that we won’t raise this in the article.

3. The referent comments on the high attrition and asks about a comparison of those who dropped out to those who remained in the study. Actually, we did provide information on this, in the results section in the subsection ‘participants’ (page 7, top, in original manuscript, page 7, line 2-5 in current manuscript) And we also have discussed the matter in the discussion section. (page 18, line 8-13, current manuscript page 12 line 18-22). We have now changed the last paragraph under the subheading ‘participants’ in the results section. For the comparison of cultural background and educational level we have now reported comparisons between the ones that dropped-out and that retained within the experimental group and the control group seperately. This is consistent with the lines above in which we compare behaviour on pretest and follow-up: page 7, line 6-10.

“In the experimental group, those men who were retained were higher educated (62% versus 44%; \(\chi^2 = 7.50, p<0.01\)) and more often had a Dutch ethnic background than those who were lost to follow-up (87% vs 72%; \(\chi^2 = 7.51, p<0.01\)). In the control group no significant differences in educational level and ethnic background were found between men who were lost to follow-up or retained.”

4. The approach to a change in steady partner status is not very informative. Those who lost, gained, or changed a steady partner were all combined into one group. As a result, it is impossible to see how the type of relationship is related to behaviour change.

The referent raises a good point on the matter of the relationship change. It would be very interesting to see how the exact type of relationship change is related to behaviour change. But because numbers of participants with risk behaviour in the study group are small (n= 75), and 82% of the participants had no change in steady relationship status numbers are too small to find relationships between the different types of relationship change and behaviour change. In the discussion we have commented on this matter as a shortcoming of the study, page 11, line 23-28:

“Due to the small numbers of respondents we could not differentiate between the types of steady relationships change in our analyses. Unfortunately, it therefore remains unclear how steady
relationship change is related to a change in risk behaviour. For example, men who lose their steady relationship can become safer, because they do not practice UAI with their steady partner, but they can also become more unsafe because they engage in unsafe UAI with a new partner or casual partners.”

5. The referent believes that that from table 3 it can be concluded that the reported results are not to be interpreted as results, but basically as a regression to the mean, and that table 3 gives no interesting information.

We agree with the referent that regression to the mean (RTM) has to be considered as a possible cause of observed change. The major limitation in our study is the lack of randomisation, and randomisation can reduce the effect or RTM. To reduce the effects of RTM we have added the pre-test score as a covariate in the analysis of covariance. This technique and is recommended as a method to adjust observed measurements for RTM. It has high statistical power and adjusts each subject's follow-up measurement according to their baseline measurement (Twisk, 2003; Barnett, 2004). We describe this in the method section now, at page 5, line 24-27:

“To estimate whether changes in outcome measures could be contributed to a regression to the mean, models were re-run adding the UAI-index score at pre-test as a covariate, a method to adjust observed measurements for regression to the mean effects [28, 29].

We have completely rewritten the results section on the effects of the intervention (page 7 line 12, until page 9, line 29), reporting the analyses that adjust for RTM effects. The results show that indeed some of the effects are most likely due to this phenomenon RTM, this is described in the results section: page 9, line 17-24 in the paragraph on Table 3C, behaviour with casual partners.

“Significant main effects were found for study condition and risk behaviour at pre-test, but after adjusting for the pre-test UAI-index scores these effects did not remain significant, F(1,270)=0.36, p=0.55. This suggests that the observed difference in UAI-change score between study conditions reflects a regression to the mean effect. Also no significant interaction effect was produced between the experimental condition and the behaviour at pre-test, adjusted for pre-test UAI-index scores, suggesting that there were no changes in UAI-index score for the behaviour with casual partners within groups of men who were different in risk behaviour at pre-test, other than the natural variation.”

For the behaviour with steady partners, reported in table 3A and 3B, effects in subgroups of unsafe men are now no longer significant. This is reported at page 8, line 19-26 for table 3A.

“Adding the baseline UAI-index score as a covariate resulted in significant main effects again for study condition and steady relationship change, implying that a regression to the mean effect in the UAI change score is unlikely to explain these effects. The effect of sexual risk behaviour at baseline did not reach statistical significance anymore. Adjusted for pre-test UAI-index scores, a significant interaction between study condition and steady relationship change was found.
F(1,254)=4.00, p<0.05, but neither the interaction between study condition and sexual risk behaviour at baseline, nor the three-way interaction between study condition, steady-relationship change and sexual risk behaviour at baseline reached statistical significance."

For table 3B it is reported at page9, line 7-13; “After adjusting for the pre-test UAI-index score, significance was also found for the effect of steady-relationship change on UAI-change scores, F(1,255)=6.77, p<0.05, but not for sexual risk behaviour at baseline. A significant interaction between study condition and steady-relationship change, and a non-significant effect between study condition and sexual risk behaviour was found. A three-way interaction between study condition, steady-relationship change and sexual risk behaviour at pre-test did not reach statistical significance.”

We also comment on this matter in the discussion on page 11, line 1-10:

“A first limitation is related to the design of the study. Because of the quasi-experimental design the causality of the effect of HIV prevention counseling relation on behavioural change must be interpreted with caution. Randomnisation could have reduced possible effects of regression to the mean. The regression to the mean effect can have made the natural variation between pre-test and post-test look like a real change. However, we used analysis of covariance with the change between baseline and follow-up as the outcome variable. To adjust observed measurements for regression to the mean effects we-run the models with the scores at pre-test as covariates. We found that a regression to the mean effect was unlikely to explain the observed difference in changes in the overall UAI-index score, but that changes in UAI with casual partners are most likely explained by a regression to the mean. “

6. Throughout the discussion there are claims that the intervention reduced unsafe sex. This is really an overstatement as the reduction in risk across partner

We agree with the referent that intervention effects are modest and that our conclusions were too firm. We have removed the conclusion that the experimental group improved because we could not support this after we had performed the additional analyses. See page 10, line 4-8:

‘The results show that the intervention had a protective effect on sexual behaviour; six months after the time of the intervention, risk behaviour of men in the experimental group remained stable while it had increased by 0.27 in the control group. The intervention seemed mainly to have affected behaviour with steady partners.

Nevertheless, small significant effects are observed in the whole study group. We had a small study group, with low risk behaviour. In such a group it is difficult to observe behaviour change. We also suffered from a loss of power due to high drop out. That we have observed these small effects is due to the effects in small subgroups of men with behaviour risks. These are the men that are important to target with an intervention and therefore we think that this intervention, which is very feasible and well appreciated by the participants, shows promising results. UAI with steady
partners increased in the control group more than in the intervention group, a possible explanation could be that the HBV vaccination itself has produced unwanted side-effects, for example men who have received the vaccination feel more safe and perceive less risks when they have unprotected anal sex in the future, and therefore there engage in more unprotected sex. The counseling in the intervention group has protected the men the experimental group from this side-effect. We have added this comment in the discussion also. at page 10, line 17-24:

“It could also be that the HBV vaccination itself has produced unwanted side-effects. Notably, men who received the vaccination may feel protected and perceive less risks when they have unprotected anal sex. The HIV prevention counselling may have protected men in the intervention group from this side-effect. Maybe risk perception regarding UAI in a steady relationship is stronger for HBV-infection risks than for HIV-infection, as a result men feel safer after the HBV vaccination to engage in sex without condoms. In the intervention group this has not occurred due to the protective effect of the counselling-intervention.

7. If someone did not have a steady partner, were the coded as ‘no unprotected sex with steady partner’ or excluded from analyse?

It is indeed that they were coded as zero, see page 5, line 1-3

“For each sexual practice not engaging in the specific form of anal intercourse or using condoms always/most of the times was coded 0 (lowest risk),”

The numbers in table 2 are correct, for the measure in which the behaviour with steady partners is calculated, for three persons in both the experimental as the control group there were missing values for one or more of the variabled used to calculate the UAI-index score. W ehave added this comment now as a subscript at table 2:

# The number of respondents for the different behaviours are not equal, due to more missing values in the variables used to calculate the UAI-index score for UAI with steady partners than with casual partners

Reaction on comments of David Bimbi:

Introduction:

1. Page 2
   Paragraph 1
   last sentences, STIs instead of STI. We changed this in the manuscript on page 2, line 8

2. Paragraph 2
“(UAI) is the greatest risk...” is awkward, replace with “presents the greatest risk.” We changed this sentence on page 2, line 11-12:

“Among MSM, unprotected anal intercourse (UAI) is the major route of HIV transmission and the use of condoms is related to the relational status men have with their sexual partner.”

3. “Others also report more risk taking,” rephrase to make it clear that similar results were found in non-Dutch samples, e.g., “Similar findings in non-Dutch samples have been reported”. We have rephrased this whole alinea into:

“Among MSM, unprotected anal intercourse (UAI) is the major route of HIV transmission and the use of condoms is related to the relational status men have with their sexual partner. Studies have shown that UAI among MSM is more likely with steady partners than with casual partners, while new HIV infections are also more likely to occur within steady relationships than in casual contacts [11-13].” page 2, line 11-14.

4. “The majority of MSM in steady relationships...” This statement requires a scientific citation, if none is available, use a citation from the gay press. We added references of Dutch national surveys among MSM in 2003 and 2008, page 2, line 19.

5. In the Netherlands, an association between a decreased perception of HIV/AIDS threat...”sentence is awkward and should be rephrased for clarity. We have changed this sentence into:

“(…) and research among MSM in the Netherlands has shown that a decreased perception of HIV/AIDS threat not only prospectively predicts an increase in UAI, but is also related to STI incidence [18, 19] (page 2, line 22-24)

6. Page 3
“few studies showed...” rephrase, “several studies have demonstrated...”

We changed this in the manuscript on page 3, line 6

7. To offer MSM an individual counseling session...” ; Please clarify the focus/topic of the counselling session, it is unclear as written. At page 3, line 7-9. We changed this into:

“The introduction of a Hepatitis B vaccination campaign for MSM in the Netherlands created a unique opportunity to also offer MSM an individual counselling session on HIV prevention, which was provided by a skilled health professional as part of men’s series of consultation for HBV vaccination.”
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Methods:

8. Paragraph 1
   First sentence, replace “the quasi-experimental” with “this quasi-experimental”. We rephrased the whole sentence into “A quasi-experimental study using a pre-test post-test design was conducted in four Municipal Public Health Services (MPHS) in the Netherlands during a national campaign for free Hepatitis B vaccination among MSM” on page 3, line 15-17.

9. “Each gay and bisexual male…” Enrollment was indeed based upon sexual behaviour. Men with homosexual contacts are offered the free vaccination within the campaign. At intake the reason for attending the free service is assessed and registered. Only men who were registered in the risk group ‘men with homosexual contacts’ were asked to participate in the study. We added the sentence at page 3, line 19-21:

   “To be eligible for free HBV vaccination individuals had to identify as members of a population group at increased risk for HBV infection, including MSM; this information was obtained at intake.”

10. End parenthesis is missing. We rephrased these sentences, parentheses have disappeared now, see page 3, line 30 until page 4, line 3.

   “Based on previous research among Dutch MSM self-efficacy was considered a key factor shaping condom use in casual relationships, while partner norms were considered most influential in shaping men’s use of condoms within their steady relationships [11].”

11. To clarify the design we have rewritten the paragraph on page 4, line 13-16:

   “Participants in the experimental and control groups completed pre-test assessments after obtaining their first HBV vaccination (month 0); post-test assessments where obtained after men received their third and final vaccination (month 6). Men in the experimental condition received individual HIV prevention counselling after obtaining their second HBV vaccination (month 1).”

Results:

12. The authors indicate they “corrected for negotiated safety, but it is unclear how the remainder of this subsample is characterized, e.g., both HIV negative, but without HIV negative tests after the beginning of the relationship (which would not be negotiated safety… and unfortunately a situation that leads to many cases of transmission), or if the participant was in a sero-discordant relationship. Please clarify.

   We have replaced the wording “negotiated safety” with Risk reduction in steady relationships “

   In the methods section, page 5, line 4-6. We explain: Risk reduction in steady relationships was taken into account by attributing the value 0 when men engaged in UAI with a steady partner who had equally tested HIV-negative.
We have also explained this in the results section: ‘After correcting for mutually negative HIV status,’ Page 6, line 19-20.

13. Following the advice of one of the other reviewers we have performed new analyses, in which we adjusted for educational level and ethnicity. To answer a question of another referent regarding the effect of regression to the mean, we have also re-run the models to estimate whether changes in outcome measures could be contributed to a regression to the mean. Models were re-run adding the UAI-index score at pre-test as a covariate, a method to adjust observed measurements for regression to the mean effects. New results are presented in table 2 and results from both models are given. As a result, the behaviour with steady partners had now (just) reached significance at 0.05 level, but the behaviour with casual partners has a p-value from 0.61 with model 2. This suggest that a regression to the mean was a possible explanation for the change in scores between pre- and post-test. (see table 2, former table 2A, B and C combined in one table now).

Nevertheless, we have added a comment on the power issue in our discussion section on page 11, line 24-27:

“Secondly, the power of this study is lower then was calculated, since the recruitment of the men was less then expected. To obtain sufficient power, 216 men in each group were needed, with at least 40% risky behaviour (unsafe unprotected anal intercourse). We were able to recruit 472 men, but the large drop out reduced this number to 281, and less than 30% of the sample reported risk behaviour.”

14. Page 9

Last paragraph. Use of phrase “Christian name” is problematic, particularly since the study included non-Dutch persons who may not have “Christian” names.

Simply restate to say “first name.”

We agree with the referent on the names, so we have changed ‘christian name’ into ‘first name’, at page 12, line 11.

We sincerely hope you will find our revised manuscript suitable for publication in BMC Public Health, and we look forward to hearing your decision in the near future.

Yours sincerely,

Mireille Wolfers,
Letter to editor, MS: 4894768723772115

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