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Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Freeman D, Loe BS, Yu L-M, et al. Effects of different types of written vaccination information on COVID-19 vaccine hesitancy in the UK (OCEANS-III): a single-blind, parallel-group, randomised controlled trial. *Lancet Public Health* 2021; published online May 12. http://dx.doi.org/10.1016/S2468-2667(21)00096-7.

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Title: Covid-19 vaccination views: Oxford Coronavirus Explanations, Attitudes, and Narratives Survey (OCEANS III)

STATISTICAL ANALYSIS REPORT Version 0.5 08/28/2021

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Version History

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1. INTRODUCTION

This document details the analysis set out in **the statistical analysis plan (SAP) V0.4.pdf** dated **19 February 2021** for the OCEAN III randomised study to evaluate the effect of different information provision on willingness to be vaccinated. Subsequent analyses of a more exploratory nature will not be restricted to the methodology set out in the SAP, though they are expected to follow the broad principles described in the SAP.

The SAP will be made available when the principal papers are submitted for publication in a journal. Suggestions for further analysis by journal editors or reviewers will be considered carefully and carried out insofar as to the principles of the analysis strategy. The source of any suggestions, if reported, will be acknowledged.

This report is based on the **Statistical Analysis Plan – V0.4 pdf** dated **19 February 2021.** Any deviation from the statistical analysis plan will be described and justified in the trial report.

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1.1 VALIDATION

Validation of results presented In this report was conducted in R and Stata. Results from R and Stata output were checked for transcription errors.

1.2 SOFTWARE EMPLOYED

Analyses completed in R version 4.0.0. Emmeans R package version 1.5.2.1. Mice R package version 3.9.0. Lavaan R package version 0.6.7. semTools R package version 0.5.3. Analyses verified in Stata version SE 16.1.

2 METHODS

2.1 BACKGROUND INFORMATION

2.2 TRIAL DESIGN

OCEANS III is a single blind parallel groups randomised controlled design. A sample of 18,855 online participants will be recruited for this study. Participants will provide informed consent, complete an item for stratification for vaccine hesitancy level, provide socio-demographic information, randomised (1:1) to receive different vaccine information, and then complete measures of COVID-19 vaccine hesitancy and COVID-19 complacency and confidence beliefs.

Date of start of recruitment: 19th January 2021 Number recruited: 18,855 Date of end of recruitment: 18th February 2021

Target number of subjects: Originally 15,000, before amendment to increase size

Timing of trial procedures is provided in Appendix I.

2.3 OBJECTIVES

Primary Objectives

The outcome questions are:

- 1. Does adding information about; the collective benefit of vaccination from not getting ill, the collective benefit of vaccination from not spreading the virus, the personal benefit of getting vaccinated, the seriousness of the SARS-CoV-2, or why speed of development is not a problem (directly and indirectly), lead to lower levels of COVID-19 vaccine hesitancy than a simple statement that vaccination is efficacious and safe? [This is a test against condition 1 (control) of conditions 2, 3, 4, 5, 6, 7, 8.]
- 2. Does combining collective and personal benefits or combining collective and personal benefits with the seriousness of the virus and indirectly why the speed of development is not a problem lead to lower levels of COVID-19 vaccine hesitancy than a simple statement that vaccination is efficacious and safe? [This is a test against condition 1 (control) of conditions 9 and 10.]

The moderation question is:

1. Is the effect of information provision on COVID-19 vaccine hesitancy moderated by the three groupings of level of hesitancy (positive about vaccination, very unsure, strongly hesitant)?

Secondary Objectives

The outcome questions are:

- 1. Is emphasising collective benefit (i.e. leads to lower hesitancy) better than emphasising personal benefit? [This is a test of conditions 2 and 3 against 5].
- 2. Is emphasising why speed of development is not a problem better done directly or indirectly? [This is a test of condition 7 against 8.]
- 3. Is combining personal and collective benefits better than emphasising personal or collective benefits alone? [This is a test of condition 9 against conditions 4 and 5].
- 4. Is combining collective and personal benefits with the seriousness of the virus and indirectly why the speed of development is not a problem better than just combining collective and personal benefits? [This is a test of condition 10 against 9.]

The moderation question is:

1. Is the effect of information provision on COVID-19 vaccine hesitancy moderated by age, gender, ethnicity, income, region, or level of Covid-19 health risk?

The mediation question is:

1. If a significant relationship exists between randomised conditions and vaccine hesitancy, can that relationship be explained by COVID-19 vaccine views (the potential collective benefit, the likelihood of COVID-19 infection and the effectiveness of a vaccine, its side-effects, and concerns about the speed of vaccine development)?

2.4 TARGET POPULATION

Inclusion criteria

 \triangle Age \ge 18

Exclusion Criteria

None

2.5 INTERVENTIONS

2.6 OUTCOME MEASURES

Oxford Covid-19 Vaccine Hesitancy Measure (Freeman et al, 2020). This is a seven-item scale. Item specific response options (Saris, Revilla, Krosnick & Shaeffer, 2010), coded from 1 to 5, are used. A 'Don't know' option is also provided, which is excluded from scoring. The Cronbach's alpha is 0.97. Scores can range between 7 and 35, with higher scores indicating higher COVID-19 vaccine hesitancy.

2.6.1 PRIMARY OUTCOME

The overarching question addressed is: is there specific content about COVID-19 vaccination, above a simple statement of efficacy and safety, that may reduce hesitancy and/or consolidate existing positive views? We are most interested in the effects on those in the general population who are very unsure (approximately 16%) or strongly hesitant (approximately 12%) about a COVID-19 vaccination.

We are also interested in finding out whether the reduction in scores is moderated by different levels of vaccine hesitancy (positive about vaccination, very unsure, strongly hesitant). The vaccine hesitancy is calculated by adding together the scores for the 7 items. Each item ranging from 1 to 5, and the total score range between 0 to 35. Higher scores indicate greater vaccine hesitancy.

2.7 SAMPLE SIZE

Power calculation: This study is powered to detect a change in hesitancy level for each of the three levels of hesitancy level at baseline, i.e., positive, doubtful, and strongly hesitant. From our previous study, we estimated that there are 71.1% in the general population are positive hesitant with a mean (SD) score on the Oxford Hesitancy Scale of 10.8 (3.5); 16.6% doubtful with mean (SD) score 24.2 (5.8); and 11.7% are strongly hesitant with mean (SD) score 30.6 (3.5). Sample sizes of 96 and 254 will be able to detect a 3-point change in the strong and hesitant groups respectively at 90% power and a type I error at 0.5% (2-sided). For the positive groups, a sample size of 822 will be able to detect a 1-point change. This gives a total sample size of 1,172 is required for each condition. We intend to recruit a total of 15,000 participant to the study to adjust for multiple comparisons in the analysis.

This study is single blinded, as the participants are aware of which arm of the trial they are allocated to, but the researcher assessors are blinded to the study arm of the participant.

According to the original protocol, the target was aimed at 15,000 participants. However, halfway through data collection, vaccine hesitancy levels (as assessed by the stratification question) in the participants were lower than anticipated, and therefore we have planned to recruit approximately 3,500 additional participants who score for vaccine hesitancy (using the stratification question). The total sample is therefore likely to be closer to 18,500.

2.8 RANDOMISATION AND BLINDING IN THE ANALYSIS STAGE

Participants will be randomised equally across all conditions, stratified by three levels of vaccine hesitancy (positive, very doubtful, strongly hesitant). After agreeing to take part, participants will complete a single question: If the vaccine was available at my GP surgery I would: 1. Get it as soon as possible/2. Get it when I have time/3. Delay getting it/ 4. Avoid getting it for as long as possible/ 5. Never get it/ 6. Don't know. This item has a strong loading on the vaccine hesitancy latent factor (0.95) from our OCEAN-II study. The item is: The level of vaccine hesitancy is defined as, Positive=1 or 2, Doubtful=3 or 6, strong hesitant=4 or 5.

Participants are required to read their assigned information condition, and therefore they cannot be blinded to the fact they are given information, although they will be unaware of the other conditions. Participants complete the self-report outcome measures online and therefore the research team can be considered as blinded in relation to assessments. It is notable that all data will be collected by Lucid and the research team will not have any contact with research participants and will therefore be unable to bias the allocation or assessments.

2.9 DATA CLEANING

To ensure quality data is recorded at the end of the data collection process, data cleaning is conducted in real-time by the Lucid crowd sourcing platform. A description of the type of respondents removed is in Appendix II.

2.10 ANALYSIS FOR DATA MONTIORING COMMITTEE MEETINGS

The trial does not have a formal data monitoring committee and there are no planned interim analyses.

2.11 DEFINTION OF POPULATION FOR ANALYSIS

All data will be included in the analysis as far as possible. Participants will be analysed in the groups they were allocated.

The primary analysis included participants with complete response of the primary outcome

The sample size for multiple imputation analysis was different due to missing response from auxiliary variables. See Section 3.4 Numbers Analysed for more information.

2.12 DEVIATION FROM SAP

There were no deviations from the SAP.

3 RESULTS

3.1 REPRESENTATIVENESS OF STUDY SAMPLE AND PARTICIPANT THROUGHPUT

Appendix I provides the Consort Flow Diagram of the participants in the study. Table 1 shows baseline characteristics by randomised condition.

3.2 RECRUITMENT

Recruited started in 19th of January 2021 and carried on to the 5th of February 2021, after recruiting 15,014 participants. A protocol amendment was submitted to increase the sample size from 15,000 to 18,855, after it was determined that vaccine hesitancy levels (as assessed by the stratification question) in the participants were lower than anticipated. Therefore, recruitment continued to the $18th$ of February and we recruited approximately 3,855 additional participants who score for vaccine hesitancy (using the stratification question).

3.4 NUMBERS ANALYSED

Appendix I provides the total number of participants who participated in each of the study arm which were analysed in the primary and secondary analyses. Of the 18,855 participants enrolled (Table 1), (n=2400) who did not complete all items (i.e. used the 'don't know' option) in the Oxford Vaccine Hesitancy Scale were excluded from further analyses. Thus, the primary and secondary analyses included (n=16,455).

In the subgroup analyses, participants with missing data in both the Oxford Vaccine Hesitancy Scale and demographic characteristics were removed from further analyses. Therefore, the subgroup analyses included (n=15,735). Only complete cases were used in both mediation models (n=965, n=1011) to be consistent with the linear regression model.

Additionally, of the 18,855 participants who enrolled, (n=1413) had missing values in the auxiliary variables (gender and Covid-19 health risk levels). These participants were not included in the multiple imputation analysis. Thus (n=17,442) were included in the multiple imputation analysis.

As requested by the reviewer, the primary and secondary outcome analyses were repeated with only participants who have not been vaccinated (n=14,483).

3.3 BASELINE CHARACTERISTICS OF PARTICIPANTS

Table S1. Baseline characteristics

Region, n(%)

3.5 PRIMARY OUTCOME

3.5.1 Vaccine hesitancy

The primary outcome measure is Oxford Covid-19 Vaccine Hesitancy Measure (Freeman et al, 2020). This is a seven-item scale. Item specific response options (Saris, Revilla, Krosnick & Shaeffer, 2010), coded from 1 to 5, are used. A 'Don't know' option is also provided, which is excluded from scoring. Scores can range between 7 and 35, with higher scores indicating higher COVID-19 vaccine hesitancy.

We checked the assumptions of normality of the model residuals using graphical methods. The outcome residuals were strongly skewed to the right, but the model residuals were found to be sufficiently normally distributed to fit a linear model (Figure S1).

Figure S1. Histogram of residuals from linear regression model

3.5.2 Hesitancy scores between randomised conditions in primary and secondary objectives

The estimated marginal means in each randomised condition and their respective confidence intervals are reported in Table S2.

SE = Standard error

There were no significant differences across the randomised conditions (Table S3).

Table S3. Mean difference between marginal means across randomised conditions

* P values adjustment using False Discovery Rate method. C.I. = Confidence intervals. SE = Standard error

3.5.3 Impact of hesitancy vaccine levels on reduction of hesitancy scores between Condition 1 (Control) vs Conditions 2, 3, 4, 5, 6, 7, 8

The estimated marginal means in each randomised condition across the vaccine hesitancy groups and their respective confidence intervals are reported in Table S4.

Table S4. Estimated marginal means in each randomised condition across the vaccine hesitancy groups

SE = Standard error

There were significant differences between groups (Condition 5 vs 1) and (Condition 7 vs 1) in the strongly hesitancy group. Participants randomised to condition 5 showed significant reduced levels of hesitancy (mean differences (95% C.I.): -1.49 (-2.16;-0.82); adjusted p-value < 0.0001) compared to condition 1. Participants randomised to condition 7 showed significant reduced levels of hesitancy (mean differences (95% C.I.): -0.91 (-1.58; -0.23); adjusted p-value =0.0261) compared to condition 1 (Table S5).

There were no other significant differences in the strongly hesitant group and in the other vaccine hesitancy groups across the randomised conditions [Condition 1 (control) vs Conditions 2, 3, 4, 5, 6, 7, 8].

Table S5. Mean difference between marginal means across randomised conditions

Vaccine Hesitancy group - Willing

Randomised condition

* P values adjustment using False Discovery Rate method. C.I. = Confidence intervals. SE

= Standard error

3.5.4 Impact of hesitancy vaccine levels on reduction of hesitancy scores between Condition 1 (Control) vs Conditions 9 and 10

There was a significant difference between groups (Condition 10 vs 1) in the strongly hesitancy group. Participants randomised to condition 10 showed significant reduced levels of hesitancy (mean differences (95% C.I.): -0.86 (-1.53; -0.18); adjusted p-value = 0.0313) compared to condition 1 (Table S6).

There were no other significant differences in the strongly hesitant group and in the other vaccine hesitancy groups across the randomised conditions [Condition 1 (control) vs Conditions 9 and 10].

Table S6. Mean difference between marginal means across randomised conditions

* P values adjustment using False Discovery Rate method. C.I. = Confidence intervals. SE = Standard error

3.5.5 MODERATION ANALYSIS

SE = Standard error

3.6 SECONDARY OUTCOME

3.6.1 Impact of hesitancy vaccine levels on reduction of hesitancy scores between Condition 2 vs Conditions 3 and 5

There were significant differences between groups (Condition 5 vs 2) and (Condition 5 vs 3) in the strongly hesitancy group. Participants randomised to condition 5 showed significant reduced levels of hesitancy (mean differences (95% C.I.): -0.97 (-1.64; -0.30); adjusted p-value = 0.0165) compared to condition 2. Participants randomised to condition 5 showed significant reduced levels of hesitancy (mean differences (95% C.I.): -1.01 (-1.68; -0.35); adjusted p-value = 0.0150) compared to condition 3 (Table S8).

There were no other significant differences in the other vaccine hesitancy groups across the randomised conditions [Condition 5 vs Conditions 2 and 3].

Table S8. Mean difference between marginal means across randomised conditions

* P values adjustment using False Discovery Rate method. C.I. = Confidence intervals. SE

= Standard error

3.6.2 Impact of hesitancy vaccine levels on reduction of hesitancy scores between Condition 7 and Conditions 8

There were no significant differences in the vaccine hesitancy groups across the randomised conditions [Condition 7 vs Condition 8] (Table S9).

Table S9. Mean difference between marginal means across randomised conditions

Standard error

3.6.3 Impact of hesitancy vaccine levels on reduction of hesitancy scores between Condition 9 vs Conditions 4 and 5

There was a significant difference between groups (Condition 9 vs 5) in the strongly hesitancy group. Participants randomised to condition 9 showed significant increased levels of hesitancy (mean differences (95% C.I.): 1.12 (0.46; 1.79); adjusted p-value = 0.0068) compared to condition 5 (Table S10).

There were no other significant differences in the strongly hesitant group and in the other vaccine hesitancy groups across the randomised conditions [Condition 9 vs conditions 4 and 5].

Table S10. Mean difference between marginal means across randomised conditions

* P values adjustment using False Discovery Rate method. C.I. = Confidence intervals. SE = Standard error

3.6.4 Impact of hesitancy vaccine levels on reduction of hesitancy scores between Condition 9 and Condition 10

There were no significant differences in the vaccine hesitancy groups across the randomised conditions [Condition 10 vs condition 9] (Table S11).

Table S11. Mean difference between marginal means across randomised conditions

* P values adjustment using False Discovery Rate method. C.I. = Confidence intervals. SE = Standard error

SUBGROUP ANALYSES

Differences observed within subgroups should be interpreted with caution as sample sizes are small.

Figure S3. Subgroup analysis of Oxford Covid-19 Vaccine Hesitancy Score (Condition 3 vs Condition 1)

Figure S4. Subgroup analysis of Oxford Covid-19 Vaccine Hesitancy Score (Condition 4 vs Condition 1)

Figure S5. Subgroup analysis of Oxford Covid-19 Vaccine Hesitancy Score (Condition 5 vs Condition 1)

Figure S7. Subgroup analysis of Oxford Covid-19 Vaccine Hesitancy Score (Condition 7 vs Condition 1)

Figure S8. Subgroup analysis of Oxford Covid-19 Vaccine Hesitancy Score (Condition 8 vs Condition 1)

Figure S9. Subgroup analysis of Oxford Covid-19 Vaccine Hesitancy Score (Condition 9 vs Condition 1)

Figure S10. Subgroup analysis of Oxford Covid-19 Vaccine Hesitancy Score (Condition 10 vs Condition 1)

MEDIATION ANALYSIS

The results in the primary and secondary outcomes showed that a significant relationship existed between specific randomised conditions and vaccine hesitancy (Tables S5, S6, S8 & S10) in the strongly hesitant group. The primary outcomes that showed significant differences in vaccine hesitancy scores between randomised conditions were (Condition 7 vs Condition 1; Condition 5 vs Condition 1; Condition 10 vs Condition 1). The secondary outcomes that showed significant differences in vaccine hesitancy scores between randomised conditions were (Condition 5 vs Condition 2; Condition 5 vs Condition 3; Condition 5 vs Condition 9). Therefore, the objective of the mediation analysis was to assess whether the changes in the vaccine hesitancy scores for these conditions in the strongly hesitant group were explained by the COVID-19 vaccine views (Beliefs).

Two mediation analyses were performed given that the primary and secondary outcomes used different comparison groups. Condition 1 (control) was used as the reference group in the first mediation model and condition 5 was used as the reference group in the second mediation model. The following mediation analyses were performed according to the SAP version 0.4. dated 19th February 2021. That is, the mediation analyses were carried out under the structural equation modelling framework. Specifically, the factor scores of the Oxford Covid-19 Vaccine Hesitancy Measure will be the response variable with randomised group as the exposure and a higher order latent variable (beliefs) derived from the four subscales of the Oxford Vaccine Confidence and Complacency Scale as indicator will be the mediator variable. Age, gender, ethnicity, income, region and level of Covid-19 health risk were included in the models as controls. However, instead of allowing for missing data, we only used complete cases to be consistent with the linear regression model. The maximum likelihood (ML) estimation procedure with robust (Huber-White) standard errors and a scaled test statistic was employed to estimate the models due to non-normal data. The model's goodness of fit is considered acceptable when the root mean square error of approximate (RMSEA) and standardized root mean square residual (SRMR) are less than 0.08 (Kline, 2005). Additional fit indices included the comparative fit index (CFI) and Tucker-Lewis Index (TLI), all of which should exceed 0.90 (Kline, 2010), with RMSEA < 0.06, and CFI and TLI > 0.95 indicating good model data fit (Hu & Bentler, 1999).

Instead of testing a series of regression equations as proposed by Baron and Kenny (1986) to evaluate mediation, we applied a formal inferential test of the effects in the mediation model as suggested by Hayes & Preacher (2014). We employed the Monte Carlo (MC) method described by MacKinnon, Lockwood & Williams (2004) as it does not require the assumption of normality of the effect's sampling distribution. Using indirect effect as an example, this approach would randomly simulate values based on the parameters of the indirect effect and the associated standard errors, and estimate a confidence interval (CI). We used the proposed replication of 20,000 simulated values to generate the CIs for all the effects in the mediation models. Variables that do not have zero in the CI indicates a significant effect. The advantages of generating CIs for the effects in the mediation model using Monte Carlo are further described in Kristopher, Preacher & Selig (2012). We also applied an omnibus test (Wald test) to the indirect effects to evaluate the extent to which the coefficients are simultaneously equal to zero (null hypothesis). If the test fails to reject the null hypothesis, then it would indicate that there is no presence of any indirect effect.

Table S12 presents the mediation with SEM model that includes the unstandardised estimates for all relevant parameters for the randomised conditions in the primary outcomes. The sample size was (n=965). The indirect effects did not significantly mediate the paths between the randomised conditions and vaccine hesitancy score. The Wald statistic is 2.55 with df = 3 and $p = 0.47$, indicating that the null hypothesis was not rejected. The collective results indicated that there was no presence of a mediation effect. The model showed an acceptable model fit according to the SEM fit statistics and indices: robust *χ 2* (*df*=716) = 1418.87¹ , *p*≤0.001; Root Mean Square Error of Approximation (RMSEA)= 0.03; Standardised Root Mean Square Residual (SRMR) = 0.03; Comparative fit index (CFI)= 0.92; Tucker-Lewis index (TLI)= 0.91. The mediation with SEM model diagram with factor loadings and unstandardised effects are shown in Figure S11.

Table S12. Mediation with SEM model for primary outcomes

*Monte Carlo confidence interval. SE = Standard error

<u>.</u>

 1 The chi-square index is sensitive to sample size. Hence, an alternative method to evaluate model fit is the relative chi-square (x2/df), which is 1.98 in this case. There is no clear consensus of an acceptable ratio, though several researchers have recommended the ratio to be less than 2 to 5 as a general rule of thumb (Wheaton, Muthen, Alwin, & Summers, 1977; March & Hocevar, 1985; Byrne, 1989; Barrett, 2007).

Figure S11. Mediation with structural equation model for primary outcomes

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Note: *p < 0.01, **p < 0.01, ***p < 0.001
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IMP = collective importance; SPD = speed of development; WRK = vaccine will be effective; S.EF = side effects; VAC.HES = vaccine hesitancy; AND.COND = randomised condition The direct and indirect effects in the structural model are presented as *unstandardised* estimates. The factor loadings in the measurement model are presented as *standardised* estimates.

Table S13 presents the mediation with SEM model that includes the unstandardised estimates for all relevant parameters for the randomised conditions in the secondary outcomes. The sample size was (n= 1011). Similar to Table 10, the indirect effects did not significantly mediate the paths between the randomised conditions and vaccine hesitancy score. The Wald statistic is 0.44 with df = 3 and $p = 0.93$, indicating that the null hypothesis was not rejected. The collective results indicated that there was no presence of a mediation effect. The model showed an acceptable model fit according to the SEM fit statistics and indices: robust *χ²(df*=716) = 1573.58², *p*≤0.001; Root Mean Square Error of Approximation (RMSEA)= 0.03; Standardised Root Mean Square Residual (SRMR) = 0.03; Comparative fit index (CFI)= 0.91; Tucker-Lewis index (TLI)= 0.90. The mediation with SEM model diagram with factor loadings and unstandardised effects are shown in Figure S12.

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² The relative chi-square is 2.20.

Table S13. Mediation with SEM model for secondary outcomes

*Monte Carlo confidence interval. SE = Standard error

Note: *p < 0.01, **p < 0.01, ***p < 0.001 IMP = collective importance; SPD = speed of development; WRK = vaccine will be effective; S.EF = side effects; VAC.HES = vaccine hesitancy; RAND.COND = randomised condition

The direct and indirect effects in the structural model are presented as *unstandardised* estimates. The factor loadings in the measurement model are presented as *standardised* estimates.

3.7 SENSITIVTY ANALYSES 3.7.1 MISSING DATA MECHANIMS

Missing data measuring vaccine hesitancy at the item level was assumed to be missing at random (MAR) and thus, multiple imputation (MI) was used to impute missing values (Schafer, 1999). Predictive mean matching was used as the imputation algorithm which is appropriate for numeric data. The conditional predictive distribution of the item level responses required to be imputed was adjusted to account for the information from age, gender, and level of Covid-19 health risk, all of which were known to be significant predictors of vaccine hesitancy as described in OCEAN II (Freeman et al., 2020). Participants who answered 50% or more to the 'don't know' option in the Oxford Covid_19 Vaccine Hesitancy measure were removed. We only used complete cases for age, gender and level of covid-19 health risk. Participants that had missing values in either of the three variables were also removed. Hence, the sample size for MI was n=17,442.

MI was imputed 50 times at the item level, and the responses from each imputed dataset were summed to create total hesitancy scores. The regression model was estimated 50 times and the predictions were averaged based on Rubin's rules (Rubin, 1987) to calculate the estimated marginal means. Tables S14 and S15 shows the marginal means and the marginal mean differences between the conditions with imputed data respectively. The results from these tables were found to be comparable to those that used complete cases in the primary outcomes (Tables S4, S5 and S6). That is, only participants that were randomised to conditions 5, 7 and 10 in the strongly hesitant group showed significant reduced levels of hesitancy compared to condition 1 (control) (Table S14).

Table S14. Estimated marginal means in each condition across the vaccine hesitancy groups using multiple imputed data

Vaccine Hesitancy group - Doubtful

Randomised condition

SE = Standard error

Table S15. Mean difference between marginal means across randomised conditions using multiple imputed data

* P values adjustment using False Discovery Rate method. C.I. = Confidence intervals. SE

= Standard error

4 POST-HOC ANALYSIS

As requested by the reviewer, the primary and secondary outcome analyses were repeated with only participants who have not been vaccinated (n=14,483).

4.1 PRIMARY OUTCOME

4.1.1 Vaccine hesitancy

The primary outcome measure is Oxford Covid-19 Vaccine Hesitancy Measure (Freeman et al, 2020). This is a seven-item scale. Item specific response options (Saris, Revilla, Krosnick & Shaeffer, 2010), coded from 1 to 5, are used. A 'Don't know' option is also provided, which is excluded from scoring. Scores can range between 7 and 35, with higher scores indicating higher COVID-19 vaccine hesitancy.

We checked the assumptions of normality of the model residuals using graphical methods. The outcome residuals were strongly skewed to the right, but the model residuals were found to be sufficiently normally distributed to fit a linear model (Figure S13).

Figure S133. Histogram of residuals from linear regression model

4.1.2 Hesitancy scores between randomised conditions in primary and secondary objectives

The estimated marginal means in each randomised condition and their respective confidence intervals are reported in Table S16.

SE = Standard error

There were no significant differences across the randomised conditions (Table S17).

Contrast	Estimated mean difference (C.I.)	SE	Adjusted P-value*	
$2 - 1$	-0.02 $(-0.63; 0.60)$	0.31	0.9548	
$3 - 1$	0.05 (-0.56 ; 0.66)	0.31	0.9347	
$4 - 1$	$-0.16(-0.78; 0.45)$	0.31	0.9093	
$5 - 1$	-0.21 $(-0.83; 0.40)$	0.31	0.9093	
$5 - 2$	-0.19 $(-0.81; 0.42)$	0.31	0.9093	
$5 - 3$	-0.26 ($-0.87; 0.35$)	0.31	0.9093	
$6 - 1$	-0.08 (-0.69 ; 0.54)	0.31	0.9346	
$7 - 1$	-0.08 (-0.69 ; 0.54)	0.31	0.9346	
$8 - 1$	-0.19 ($-0.80; 0.42$)	0.31	0.9093	
$8 - 7$	-0.11 (-0.73 ; 0.50)	0.31	0.9346	
$9 - 1$	$0.18(-0.44; 0.80)$	0.31	0.9093	
$9 - 4$	0.34 (-0.27 ; 0.96)	0.31	0.9093	
$9 - 5$	0.39 (-0.22 ; 1.01)	0.31	0.9093	
$10 - 1$	-0.38 $(-0.99; 0.24)$	0.31	0.9093	
$10 - 9$	-0.56 $(-1.18; 0.06)$	0.31	0.9093	

Table S17. Mean difference between marginal means across randomised condition

* P values adjustment using False Discovery Rate method. C.I. = Confidence intervals. SE = Standard error

4.1.3 Impact of hesitancy vaccine levels on reduction of hesitancy scores between Condition 1 (Control) vs Conditions 2, 3, 4, 5, 6, 7, 8

The estimated marginal means in each randomised condition across the vaccine hesitancy groups and their respective confidence intervals are reported in Table S18.

Table S18. Estimated marginal means in each randomised condition across the vaccine hesitancy groups have not been vaccinated

SE = Standard error

There were significant differences between groups (Condition 3 vs 1), (Condition 4 vs 1), (Condition 5 vs 1), (Condition 7 vs 1) and (Condition 8 vs 1) in the strongly hesitancy group. Participants randomised to condition 3 showed significant reduced levels of hesitancy (mean differences (95% C.I.): -0.77 (-1.44; -0.11); adjusted p-value =0.0373) compared to condition 1. Participants randomised to condition 4 showed significant reduced levels of hesitancy (mean differences (95% C.I.): -0.98 (-1.64; -0.32); adjusted p-value =0.0088) compared to condition 1. Participants randomised to condition 5 showed significant reduced levels of hesitancy (mean differences (95% C.I.): -1.76 (-2.42; -1.09); adjusted p-value = 0.0002) compared to condition 1. Participants randomised to condition 7 showed significant reduced levels of hesitancy (mean differences (95% C.I.): -0.79 (-1.46; -0.11); adjusted p-value =0. 0373) compared to condition 1. Participants randomised to condition 8 showed significant reduced levels of hesitancy (mean differences (95% C.I.): -1.00 (-1.68; -0.33); adjusted p-value =0. 0088) compared to condition 1 (Table S19).

There were no other significant differences in the strongly hesitant group and in the other vaccine hesitancy groups across the randomised conditions [Condition 1 (control) vs Conditions 2, 3, 4, 5, 6, 7, 8].

Table S19. Mean difference between marginal means across randomised conditions

* P values adjustment using False Discovery Rate method. C.I. = Confidence intervals. SE = Standard error

4.1.4 Impact of hesitancy vaccine levels on reduction of hesitancy scores between Condition 1 (Control) vs Conditions 9 and 10

There was a significant difference between groups (Condition 10 vs 1) in the strongly hesitancy group. Participants randomised to condition 10 showed significant reduced levels of hesitancy (mean differences (95% C.I.): -0.96 (-1.63; -0.29); adjusted p-value = 0. 0107) compared to condition 1 (Table S20).

There were no other significant differences in the strongly hesitant group and in the other vaccine hesitancy groups across the randomised conditions [Condition 1 (control) vs Conditions 9 and 10].

Table S20. Mean difference between marginal means across randomised conditions

* P values adjustment using False Discovery Rate method. C.I. = Confidence intervals. SE

= Standard error

4.2 SECONDARY OUTCOME

4.2.1 Impact of hesitancy vaccine levels on reduction of hesitancy scores between Condition 2 vs Conditions 3 and 5

There were significant differences between groups (Condition 5 vs 2) and (Condition 5 vs 3) in the strongly hesitancy group. Participants randomised to condition 5 showed significant reduced levels of hesitancy (mean differences (95% C.I.): -1.15 (-1.81; -0.48); adjusted p-value = 0.0035) compared to condition 2. Participants randomised to condition 5 showed significant reduced levels of hesitancy (mean differences (95% C.I.): -0.98 (-1.64; -0.33); adjusted p-value = 0. 0088) compared to condition 3 (Table S21).

There were no other significant differences in the other vaccine hesitancy groups across the randomised conditions [Condition 5 vs Conditions 2 and 3].

Table S21. Mean difference between marginal means across randomised conditions

* P values adjustment using False Discovery Rate method. C.I. = Confidence intervals. SE = Standard error

4.2.2 Impact of hesitancy vaccine levels on reduction of hesitancy scores between Condition 7 and Conditions 8

There were no significant differences in the vaccine hesitancy groups across the randomised conditions [Condition 7 vs Condition 8] (Table S22).

intervals. SE = Standard error

4.2.3 Impact of hesitancy vaccine levels on reduction of hesitancy scores between Condition 9 vs Conditions 4 and 5

There was a significant difference between groups (Condition 9 vs 5) in the strongly hesitancy group. Participants randomised to condition 9 showed significant increased levels of hesitancy (mean differences (95% C.I.): 1.17 (0.51; 1.82); adjusted p-value = 0.0035) compared to condition 5 (Table S23).

There were no other significant differences in the strongly hesitant group and in the other vaccine hesitancy groups across the randomised conditions [Condition 9 vs conditions 4 and 5].

Table S23. Mean difference between marginal means across randomised conditions

* P values adjustment using False Discovery Rate method. C.I. = Confidence intervals. SE = Standard error

4.2.4 Impact of hesitancy vaccine levels on reduction of hesitancy scores between Condition 9 and Condition 10

There were no significant differences in the vaccine hesitancy groups across the randomised conditions [Condition 10 vs condition 9] (Table S24).

Table S24. Mean difference between marginal means across randomised conditions

SE = Standard error

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6. APPENDICES

Appendix I. CONSORT 2010 Flow Diagram

Appendix II. Data cleaning done by the crowd sourcing platform (LUCID)

Data Cleaning

Once data collection is underway, Lucid can provide data cleaning or scrubbing, which is the act of removing responses for gibberish, illogical, or fraudulent behavior. Data cleaning is conducted in real-time, while the survey is being fielded to ensure the final dataset is clean and ready for analysis once data collection is complete.

When Lucid is handling programming, the data should always be cleaned. Lucid PSMs can clean out obvious bad verbatims and speeders based on median LOI (removal of any cases that have completed the survey in less than 1/3 of the median LOI).

Below are the types of respondents removed:

- 1. Bad Verbatims: Respondents who type in gibberish, vulgar, or illogical responses to open ended questions
- 2. Straightliners/Flatliners: Respondents who answer grid questions in the same manner (i.e. all select "3") or create patterns in grids
- 3. Speeders: Respondents who speed through the survey. Completion time of 1/3 of the median LOI or below is the standard best practice.
- 4. Duplicates: Identification of respondents who have taken the survey multiple times IP Address, Cookie ID, etc.
- 5. Bots: Software created with the intention of gaming surveys for incentives. Identified by finding verbatim, demographic, attitudinal patterns, and geo-location data.

Belief	Group	n	Mean	SD	df	F	p- value
Collective	Willing	11156	8.23	2.29	2,14658	6792.63	< .001
Benefit*	Doubtful	1574	12.33	3.36			
	Strongly	1931	16.02	4.82			
	hesitant						
Risk and	Willing	9670	6.64	1.61	2, 14102	4948.93	< .001
efficacy*	Doubtful	1980	8.83	1.83			
	Strongly	2455	10.54	2.53			
	hesitant						
Speed of	Willing	11124	6.14	2.06	2,15404	4933.47	< .001
development*	Doubtful	1755	8.63	2.23			
	Strongly	2528	10.73	2.70			
	hesitant						
Side effects*	Willing	10883	5.25	1.72	2,15077	6185.20	< .001
	Doubtful	1842	8.05	2.24			
	Strongly	2355	9.92	2.75			
	hesitant						

Table S25. Beliefs about COVID-19 vaccination (Oxford Vaccine Confidence and Complacency Scale) by hesitancy stratification level.

* All group scores differ at p<.001.

Information conditions.

1. Control (sentences from NHS information provision)

The coronavirus (COVID-19) vaccines are safe and effective, and give you the best protection against coronavirus. They have been approved by the independent Medicines and Healthcare products Regulatory Agency (MHRA).

2. Collective benefit (a) (concerning benefit of not getting ill)

As we all know, coronavirus has had a dramatic effect on the UK, putting severe strain on families, health services, schools and universities, and businesses. Virtually every sector of our society and economy has been affected, bringing disruption and inconvenience to us all. Every case of COVID-19, whether it results in hospitalisation, long-term health issues, or simply a period of isolation, causes more problems. We're all eager to get back to the way things were before the pandemic struck. By making sure we're vaccinated -- and therefore less likely to become ill with COVID-19 -- we can play our part in helping the country to bounce back as quickly as possible.

The coronavirus (COVID-19) vaccines are safe and effective, and give you the best protection against coronavirus. They have been approved by the independent Medicines and Healthcare products Regulatory Agency (MHRA).

3. Collective benefit (b) (concerning benefit of not spreading virus)

The vaccines make it less likely that we'll pass on COVID-19 to other people. This means that by being vaccinated we're helping to protect each other: family, friends, neighbours, and colleagues. It's all the more important given that some of the people we meet may be especially vulnerable to the effects of the virus -- though we might not be able to tell just by looking at them.

The sooner we're all vaccinated, the sooner life will return to normal. The economy will be properly up and running again; children and young people will be able to attend school and university; and we can all get back to the activities we used to enjoy, like getting together with family and friends, going to the cinema or pub, or taking a holiday overseas. In fact, if we're all vaccinated cases of COVID-19 are expected to decline substantially, just like diseases such as smallpox, polio, and tetanus that used to kill or disable millions of people.

The coronavirus (COVID-19) vaccines are safe and effective, and give you the best protection against coronavirus. They have been approved by the independent Medicines and Healthcare products Regulatory Agency (MHRA).

4. Full collective benefits (combining a) and b))

The vaccines make it less likely that we'll pass on COVID-19 to other people. This means that by being vaccinated we're helping to protect each other: family, friends, neighbours, and colleagues. It's all the more important given that some of the people we meet may be especially vulnerable to the effects of the virus -- though we might not be able to tell just by looking at them.

The sooner we're all vaccinated, the sooner life will return to normal. The economy will be properly up and running again; children and young people will be able to attend school and university; and we can all get back to the activities we used to enjoy, like getting together with family and friends, going to the cinema or pub, or taking a holiday overseas. In fact, if we're all vaccinated cases of COVID-19 are expected to decline substantially, just like diseases such as smallpox, polio, and tetanus that used to kill or disable millions of people.

As we all know, coronavirus has had a dramatic effect on the UK, putting severe strain on families, health services, schools and universities, and businesses. Virtually every sector of our society and economy has been affected, bringing disruption and inconvenience to us all. Every case of COVID-19, whether it results in hospitalisation, long-term health issues, or simply a period of isolation, causes more problems. We're all eager to get back to the way things were before the pandemic struck. By making sure we're vaccinated -- and therefore less likely to become ill with COVID-19 -- we can play our part in helping the country to bounce back as quickly as possible.

The coronavirus (COVID-19) vaccines are safe and effective, and give you the best protection against coronavirus. They have been approved by the independent Medicines and Healthcare products Regulatory Agency (MHRA).

5. Personal benefit

Catching coronavirus can seriously disrupt your life. It can take you away from work, education, family, and friends. Even mild symptoms mean you'll be required to isolate for ten days, with all the inconvenience that brings. And you can't be sure, even if you're relatively young and fit, that you won't be seriously ill or struggle with long-term COVID-related problems: as many as one in five people are still unwell five weeks after contracting COVID-19; one in ten are still experiencing symptoms three months later. Vaccination minimises the chances of you falling ill with COVID-19, so you won't need to worry about what the virus might have in store for you.

The coronavirus (COVID-19) vaccines are safe and effective, and give you the best protection against coronavirus. They have been approved by the independent Medicines and Healthcare products Regulatory Agency (MHRA).

6. Seriousness

We shouldn't underestimate the seriousness of COVID-19. Even after months of lockdown restrictions, Public Health England has reported that by the first week of January 78,508 people in the UK had died from the illness and 297,000 had been hospitalised. Deaths from COVID-19 already far outstrip the annual average of 28,500 we've seen from flu and pneumonia over the last twenty years. The number hospitalised is already more than eight times what we'd expect per year with flu. For many of us, the effects of falling ill with COVID-19 stick around: as many as one in five people are still unwell five weeks after diagnosis; one in ten are still experiencing symptoms three months later.

The coronavirus (COVID-19) vaccines are safe and effective, and give you the best protection against coronavirus. They have been approved by the independent Medicines and Healthcare products Regulatory Agency (MHRA).

7. Safety/speed (addressing speed issues directly)

Some people may worry that the vaccines have been developed too quickly to be safe. The speed of development reflects exceptional commitment, investment, and co-operation from scientists, governments, public health organisations, pharmaceutical companies -- and tens of thousands of members of the public who volunteered to test the vaccines.

Some may be concerned that the vaccines haven't been tested for long enough. Decades of vaccine research show that side effects don't suddenly appear months and years after vaccination. Because of the way vaccines work -- quickly training the body's immune system to fight off a virus -- any issues arise within a month and usually much sooner. No serious problems have been reported by any of the thousands of people who have taken the COVID-19 vaccines so far. Any side effects are typically mild (for example a sore arm or headache), and last less than a week.

The speed of the vaccines' development hasn't affected the approval process: they have undergone the same rigorous, independent assessment as any other medicine.

The coronavirus (COVID-19) vaccines are safe and effective, and give you the best protection against coronavirus. They have been approved by the independent Medicines and Healthcare products Regulatory Agency (MHRA).

8. Safety/rigour (addressing speed issues indirectly)

The COVID-19 vaccines result from exceptional levels of commitment, investment, and cooperation from scientists, governments, public health organisations, pharmaceutical companies -- and tens of thousands of members of the public who volunteered to test them.

Decades of vaccine research have shown that side effects don't suddenly appear months and years after vaccination. Because of the way vaccines work -- quickly training the body's immune system to be ready to fight off a virus -- any issues show up within a month and usually much sooner. No serious problems have been reported by any of the thousands of people who have taken the COVID-19 vaccines so far. Any side effects are typically mild (for example a sore arm or headache), and last less than a week.

The vaccines have had to undergo the same rigorous, independent approval process as any other medicine. Large-scale clinical trials involving tens of thousands of people have shown that the vaccines will protect the vast majority of people from getting COVID-19.

The coronavirus (COVID-19) vaccines are safe and effective, and give you the best protection against coronavirus. They have been approved by the independent Medicines and Healthcare products Regulatory Agency (MHRA).

9. Collective and personal benefits (combining 4 and 5)

The vaccines make it less likely that we'll pass on COVID-19 to other people. This means that by being vaccinated we're helping to protect each other: family, friends, neighbours, and colleagues. It's all the more important given that some of the people we meet may be especially vulnerable to the effects of the virus -- though we might not be able to tell just by looking at them.

The sooner we're all vaccinated, the sooner life will return to normal. The economy will be properly up and running again; children and young people will be able to attend school and university; and we can all get back to the activities we used to enjoy, like getting together with family and friends, going to the cinema or pub, or taking a holiday overseas. In fact, if we're all vaccinated cases of COVID-19 are expected to decline substantially, just like diseases such as smallpox, polio, and tetanus that used to kill or disable millions of people.

As we all know, coronavirus has had a dramatic effect on the UK, putting severe strain on families, health services, schools and universities, and businesses. Virtually every sector of our society and economy has been affected, bringing disruption and inconvenience to us all. Every case of COVID-19, whether it results in hospitalisation, long-term health issues, or simply a period of isolation, causes more problems. We're all eager to get back to the way things were before the pandemic struck. By making sure we're vaccinated -- and therefore less likely to become ill with COVID-19 -- we can play our part in helping the country to bounce back as quickly as possible.

Catching coronavirus can seriously disrupt your life. It can take you away from work, education, family, and friends. Even mild symptoms mean you'll be required to isolate for ten days, with all the inconvenience that brings. And you can't be sure, even if you're relatively young and fit, that you won't be seriously ill or struggle with long-term COVID-related problems: as many as one in five people are still unwell five weeks after contracting COVID-19; one in ten are still experiencing symptoms three months later. Vaccination minimises the

chances of you falling ill with COVID-19, so you won't need to worry about what the virus might have in store for you.

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10. Full text (combining 6, 8, and 9)

The vaccines make it less likely that we'll pass on COVID-19 to other people. This means that by being vaccinated we're helping to protect each other: family, friends, neighbours, and colleagues. It's all the more important given that some of the people we meet may be especially vulnerable to the effects of the virus -- though we might not be able to tell just by looking at them.

The sooner we're all vaccinated, the sooner life will return to normal. The economy will be properly up and running again; children and young people will be able to attend school and university; and we can all get back to the activities we used to enjoy, like getting together with family and friends, going to the cinema or pub, or taking a holiday overseas. In fact, if we're all vaccinated cases of COVID-19 are expected to decline substantially, just like diseases such as smallpox, polio, and tetanus that used to kill or disable millions of people.

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We shouldn't underestimate the seriousness of COVID-19. Even after months of lockdown restrictions, Public Health England has reported that by the first week of January 78,508 people in the UK had died from the illness and 297,000 had been hospitalised. Deaths from COVID-19 already far outstrip the annual average of 28,500 we've seen from flu and pneumonia over the last twenty years. The number hospitalised is already more than eight times what we'd expect per year with flu.

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Decades of vaccine research have shown that side effects don't suddenly appear months and years after vaccination. Because of the way vaccines work -- quickly training the body's immune system to be ready to fight off a virus -- any issues show up within a month and usually much sooner. No serious problems have been reported by any of the thousands of people who have taken the COVID-19 vaccines so far. Any side effects are typically mild (for example a sore arm or headache), and last less than a week.

The vaccines have had to undergo the same rigorous, independent approval process as any other medicine. Large-scale clinical trials involving tens of thousands of people have shown that the vaccines will protect the vast majority of people from getting COVID-19.

The coronavirus (COVID-19) vaccines are safe and effective, and give you the best protection against coronavirus. They have been approved by the independent Medicines and Healthcare products Regulatory Agency (MHRA).