PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Associations between adverse childhood experiences, attitudes towards COVID-19 restrictions and vaccine hesitancy: a cross-sectional study
AUTHORS	Bellis, Mark; Hughes, Karen; Ford, Kat; Madden, Hannah; Glendinning, Freya; Wood, Sara

VERSION 1 – REVIEW

REVIEWER	Allington, Daniel King's College London
REVIEW RETURNED	20-Sep-2021

GENERAL COMMENTS	This paper reports on a important and well-designed study which I hope to see published soon. It is also very clearly written. I would like to raise two small issues which the authors may wish to address, at the editor's discretion. The first is I could not find any justification given for the analytical choice to transform both age and number of ACEs into ordinal variables for the sake of logistic regression. This transformation facilitates comparison with the bivariate analysis, and as such makes the findings easier to interpret, but I would still have preferred to see some discussion of the decision and its consequences. The second is that I would like to have seen some acknowledgement of the fact that the study appears to remain under-powered with regard to ethnicity *even after* collapse of all ethnic categories into a white / other-than-white binary. The discussion of limitations only acknowledges that the sample 'did not provide adequate numbers for any detailed analyses by ethnicity' (p. 18, l. 31-33), but there is more to be said than that. In particular, the authors state that 'Ethnicity was not related to vaccine hesitancy once ACEs, age and deprivation had been accounted for' (p. 15, l. 2-4), when in fact, the AOR appears to stand at 1.78. This means that ethnicity and vaccine hesitancy *are* associated in the data that were actually collected (for comparison, the AOR for an ACE count of 2-3 is 1.56, which is slightly lower). The association is statistically insignificant (p = .230), which means that we can't have much confidence in generalising it to the wider population, but -- given the tiny number of non-white respondents (n = 31) -- that is hardly surprising. I feel that this should be acknowledged in the discussion and perhaps also the conclusion. Given concerns about higher COVID mortality and lower vaccine uptake in some minority ethnic populations, it would seem important to note that the data by no means rule out the possibility that there is an association between ethnicity and

	vaccine hesitancy that is unexplained by other independent variables (on the contrary, they suggest -- albeit with low confidence -- that such an association may indeed exist).

REVIEWER	Moorhead, Steve Northumberland Tyne and Wear NHS Foundation Trust, St Georges Park
REVIEW RETURNED	12-Nov-2021

GENERAL COMMENTS	This is a tried and trusted methodology applied to a crucial question of our time and contributes to pushing forward effective public health policy. In discussion, it develops the findings in relation to childhood adversity to incorporate some basic personal psychological effects of this, how this may relate to the results and factors that may ameliorate this effect. I strongly recommend early publication. There are a number of minor considerations in my view that might strengthen the paper a little: P3 L15 - the period during which the research was performed covered several iterations of lockdown rules. While this does not fundamentally affect the research question and reference is made to the governmental timeline in the discussion section, it might be helpful to provide this fact as context, highlighting that this occurred during The Second Lockdown and maybe making reference to the range of intensity of restrictions during which data collection occurred. Later, in discussion, it might be helpful to provide some reassurance that there is no bias introduced by particular groups being interviewed during different stages of lockdown. P6 L5 - suggest rephrasing 'surrounding communities' - does this refer to the communities surrounding individuals or communities surrounding a kind of ghetto of such individuals? P8 Table 1: I had to go to appendices to work out how the percentages added up. The answer is that there is an intermediate 'yes a little' group left out from these analyses. It would be helpful to signpost this in the text or (I might be revealing some statistical naivity here) use a non-parametric correlation test that would include all data (think this might be a more powerful finding). Related to this is the statement that these are correlation findings (p8 L24) whereas they are, in fact, categorical tests that are reported. Table 2 shows that there is an approximate ratio of females:males of 7:4 participating in the study. This is worth noting, I think, and possibly commenting upon in the earlier description of sampling.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

1) The first is I could not find any justification given for the analytical choice to transform both age and number of ACEs into ordinal variables for the sake of logistic regression. This transformation facilitates comparison with the bivariate analysis, and as such makes the findings easier to interpret, but I would still have preferred to see some discussion of the decision and its consequences.

We have now included further text to explain the use of categorical data for age and ACEs in the Methods.

[Page 6] - Such categorisation has enabled: comparative examination of individuals exposed to lower, mid, and higher counts of ACEs; a more consistent approach to analyses between ACE studies; and combined analyses of findings from different studies.[7]

[Page 7] - For the purposes of anonymity and consistent with previous studies, respondents' age was collected in five-year age groups but combined into 10-year age categories (18-29, 30-39, 40-49, 50-59, 60-69, 70+) in order to ensure sufficient numbers in each category for analysis.

We have also included a line on this in the limitations.

[Page 17] - Analysis employed a categorical approach to variables including ACE count and age. Whilst this allowed non-ordinal comparisons between categories, potential differences between individuals within categories may have been obscured.

2) The second is that I would like to have seen some acknowledgement of the fact that the study appears to remain under-powered with regard to ethnicity *even after* collapse of all ethnic categories into a white / other-than-white binary. The discussion of limitations only acknowledges that the sample 'did not provide adequate numbers for any detailed analyses by ethnicity' (p. 18, l. 31-33), but there is more to be said than that. In particular, the authors state that 'Ethnicity was not related to vaccine hesitancy once ACEs, age and deprivation had been accounted for' (p. 15, l. 2-4), when in fact, the AOR appears to stand at 1.78. This means that ethnicity and vaccine hesitancy *are* associated in the data that were actually collected (for comparison, the AOR for an ACE count of 2-3 is 1.56, which is slightly lower). The association is statistically insignificant (p = .230), which means that we can't have much confidence in generalising it to the wider population, but -- given the tiny number of non-white respondents (n = 31) -- that is hardly surprising. I feel that this should be acknowledged in the discussion and perhaps also the conclusion. Given concerns about higher COVID mortality and lower vaccine uptake in some minority ethnic populations, it would seem important to note that the data by no means rule out the possibility that there is an association between ethnicity and vaccine hesitancy that is unexplained by other independent variables (on the contrary, they suggest -- albeit with low confidence -- that such an association may indeed exist).

We thank the reviewer for this important observation. We have added the word 'significantly' to our reporting on this in the results and have expanded our discussion of this issue in the paper.

[Page 17] - The sample did not provide adequate numbers for detailed analyses by individual ethnicity types, limiting analyses to just binary white and other categories. However, even with a low sample size and all black, Asian and other minority groups combined into a single category, odds of vaccine hesitancy, for instance, were substantially higher than in the white population (1.78, 95%CIs 0.69-4.56); although this failed to reach statistical significance (Table 3). Whilst the low level of ethnic minority participants reflects Wales having only 5.6% of adults from black, Asian and other minority ethnic groups,[47] this could be rectified in further studies with oversampling in such communities and may result in the identification of other important differences between ethnicities.

Reviewer: 2

1) P3 L15 - the period during which the research was performed covered several iterations of lockdown rules. While this does not fundamentally affect the research question and reference is made to the governmental timeline in the discussion section, it might be helpful to provide this fact as context, highlighting that this occurred during The Second Lockdown and maybe making reference to

the range of intensity of restrictions during which data collection occurred. Later, in discussion, it might be helpful to provide some reassurance that there is no bias introduced by particular groups being interviewed during different stages of lockdown.

In the methods we have included further information on dates for data collection and key changes in COVID-19 restrictions in Wales.

[Page 5] - A national telephone survey of Welsh residents aged 18 years and over was conducted between December 2020 and March 2021. Although pilot data were collected on 15th and 16th December, final survey data collection all occurred within a period of consistent national COVID-19 restrictions in Wales. Thus, a national lockdown including orders to stay at home and mandatory closure of non-essential retail, hospitality sectors and gyms was established 20th December 2020 with relaxation of restrictions beginning predominantly from 13th March 2021[19]. Mixing of two households indoors was permitted for just 25th December 2020 but no data collection occurred on this day.

We have also discussed the potential implications of the timing of data collection in the limitations.

[Page 17] - Finally, while the survey was conducted during a period of national lockdown, individuals' responses may have been affected by the timing of their interview (e.g. near the start or end of the lockdown period). However, individuals from all different socio-demographic groups were sampled throughout the entire data collection period.

2) P6 L5 - suggest rephrasing 'surrounding communities' - does this refer to the communities surrounding individuals or communities surrounding a kind of ghetto of such individuals?

We have changed surrounding communities to local communities throughout the paper.

3) P8 Table 1: I had to go to appendices to work out how the percentages added up. The answer is that there is an intermediate 'yes a little' group left out from these analyses. It would be helpful to signpost this in the text or (I might be revealing some statistical naivety here) use a non-parametric correlation test that would include all data (think this might be a more powerful finding).

The percentages in Table 1 do not add up to 100% as they show the percentage reporting outcomes within groups. To clarify this, we have added a line in the results describing one set of the figures in the Table. We have also added a footnote to Table 1 to clarify that the response described as 'no' for the outcome unfairly restricted a lot by government includes those responding both 'no' and 'yes, a little'.

4) Related to this is the statement that these are correlation findings (p8 L24) whereas they are, in fact, categorical tests that are reported.

We have changed the word correlations to associations.

5) Table 2 shows that there is an approximate ratio of females:males of 7:4 participating in the study. This is worth noting, I think, and possibly commenting upon in the earlier description of sampling.

We have now identified the sex ratio in the methods.

[Page 6] - Of those who agreed, 277 did not meet the age quota in their area and 2,326 completed the questionnaire, with 64.7% of respondents being female.

We have also commented on this in the limitations section.

[Page 17] - Whilst the survey included over 2,000 individuals, women were overrepresented in the final sample. However, sufficient data were available to include sex in all data models in order to identify differences between sexes and to control for sex-related differences when examining relationships between outcomes of interest and other independent variables.

VERSION 2 – REVIEW

REVIEWER	Moorhead, Steve Northumberland Tyne and Wear NHS Foundation Trust, St Georges Park
REVIEW RETURNED	03-Dec-2021

GENERAL COMMENTS	Thanks for addressing issues. Good luck with ongoing work.