Author’s response to reviews


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Author’s response to reviews:

Dear Professor Zhou,

Thank you for your review of our paper ‘Hepatitis B vaccination uptake in hard-to-reach populations in London: a cross-sectional study’. Please find below our responses to the single peer review that we received, as per our discussion with you. Our changes are tracked within the manuscript, apart from within the bibliography.

Please note that we have also included a form requesting a change in the order of the authors as part of our submission.

Reviewer 1

1) The authors report on a cross sectional study of hard to reach people recruited from day centres, homeless hostels and drug treatment centres across London, England. The cross sectional study was completed in preparation for a peer led intervention to improve links to health care within this group. The study aimed to describe the risk factors associated with incomplete vaccination for hepatitis B and the reasons for this being so. In addition to the risk factors the guideline for vaccination which includes recommendations for vaccination in four groups; those who have been imprisoned, people who have current or past IV drug use, liver disease, and/or HCV infection was also taken into account as a factor in likelihood of being vaccinated.
First, I would like to congratulate the authors on conducting this research in a very important population, and one that is often neglected. Also I recognise the challenges in researching these group of people.

Thank you for these positive comments.

2) Having said that there are some major issues in this paper which, when addressed will make it 1) much clearer, and 2) much more impactful.

The first issue is that of missing data. So a very typical marker of hard to reach people is just that - they don't know or are missing information - from both a health care standpoint and also from a health research standpoint. What may be very useful here is to give the reader as much description of these folks as possible so that they may be compared with the overall sample and most important with those whose vaccines are incomplete. To do that I would suggest reorganising Table 1 such that the columns show the percent of the 35 with unknown vaccine status clearly and they can be compared with others. You may find then that there are few differences between them and the ones who are under vaccinated and could even group them together. It looks as if this may be the case of the distribution of age groups and arrest/imprisonment status, where 61 or 46% of under vaccinated were imprisoned as were 40% of those with unknown vaccine status.

Thank you for your comment; we address the missing data component in detail under point 9. We include a version of table 1 with column rather than row percentages as a new Additional File and comment on this in the text (Additional File 2; line 176). The under- and unknown vaccination groups differ too much to warrant incorporation together.

3) The second thing I think is to set some context for the vaccine and the homeless population you are looking at. There are two reasons for this; one is to set the scene as to the need for HBV vaccine in this group, and for the reader to evaluate the current study which will have an impact on the peer intervention. So in North America for some time now, hepatitis B has been regarded as primarily sexually transmitted, and common also in household contacts of those who carry it, and universal vaccines were recommended in children routinely starting in the mid 1990's with a catch up program in teenagers. For this reason it would be helpful to contextualise the homeless folks a little better especially the women who if they sell sex may be at high risk of HBV infection. Of course injection drug users would be at very high risk of HBV and so they also would be a high priority to vaccinate. Also, people coming from other countries where HBV is endemic may expose other members of the general population so it would be helpful to have as high a vaccine rate as possible in the whole population. Another reason to contextualise the hard to reach population is so that we can better assess the reasons for not engaging in health care. Are there nurses or outreach workers who are out on the streets who provide medical care and counselling? What proportion of people who are on the street do not use the homeless facilities? What is the connection between sale and consumption of drugs, income, sex
work and/or survival sex? What kinds of offences and what programmes are offered to those who have been imprisoned? I notice that the article seems very short, so the authors may wish to expand a little here.'

We agree that this would be helpful for the international audience of this publication, thank you. This comment has been addressed in the background section (lines 56-80).

4) The second issue has to do with the logistic regression models. First it is not clear to me how you decide which variables are statistically significantly associated with your outcome of under vaccination; In Table 3 you have a p value of 0.03 with imprisoned and arrested, but the confidence levels overlap 1 in both categories. As far as I know this is impossible for a simple logistic regression so you need to consult a statistician. Later on also in the discussion you say that imprisonment/arrest is not associated, line 257, this contradicts line 189.

Thank you for this request for clarification. This is statistically possible and arises from the standard use in statistical software of Wald tests to derive confidence intervals for each strata of a variable versus likelihood ratio tests to derive pan-strata p-values, which can lead to an imperfect alignment. We agree, that the results as previously presented were confusing for the reader, however. To make things clearer, we have altered which strata of the imprisonment/arrested variable is the baseline in our model, which means that the largest strata is now the reference category for the analysis (Table 3). We agree, however, that the direct of effect in terms of the effect estimates is not biologically consistent and thus how refrain from highlighting this output in the text (lines 22, 220, 247, 302).

5) I know you say you checked for collinearity but this seems contradicted in Table 2 where you have some independent variables which seem to me may be collinear. One of these is high alcohol and homelessness, in which I can see that a much higher proportion of people who consume alcohol frequently may be homeless compared with those who don't. In table 3 it also seems to me that homelessness may have resulted from drug use, or imprisonment without sufficient rehabilitation supports. Last extreme alcohol use can result in liver disease, so I think it would be helpful to explain how these factors may be inter related so as to arrive at a better risk profile of those needing to be vaccinated.

Although we agree that the risk factors we assess are likely to be inter-related, this was not enough to cause statistical modelling issues in terms of inflated standard errors and issues with convergence. Our extended multivariable analysis (Table 3) treats these key variables separately and thus adjusts for the potential confounding effect of all of the factors on each exposure-outcome relationship, thus allowing for an unbiased assessment of each individual relationship.

6) I agree with all your conclusions and I think you can go further in some aspects. The criteria in the Green Book for HBV vaccine in those with HCV or liver disease may not
be useful in defining large populations who are under vaccinated because they are already in health care and are probably already they have been vaccinated.

Thank you for this positive comment. We have addressed this useful point on line 297.

7) Second thing, it is great that people who meet the Green book criteria are more likely to be vaccinated, but sad that women are less likely, for the reasons you mention. This is even more worrying as women usually are engaged in health care for reproductive needs and so have more contact with the health system than do men.

This is a good point; we have expanded on this in the discussion (line 300).

8) It is a pity that there is not more detail on why people are under immunised. I think it safe to be a little more assertive in emphasizing that 80% were not offered it, which indicated that health care is suboptimal. If providers do not know that the client's lifestyle puts them at risk that shows inadequate knowledge of the patient, and 2) non provision in itself is an indicator of inadequate health care.

This is an important point; we have expanded the discussion along these lines (line 277).

9) Line 160. Discuss the limitations of omitting non-responders from your analysis. Also explore use of multivariate missing imputation.

Thank you; this is now included at line 289 in the discussion. Given our comments about missingness in the outcome (point 2; 35/63 people) our data are not a good fit for multiple imputation, where missingness needs to be (completely) at random. This slightly limits the generalisability of our findings, rather than their validity.

10) Line 167. The text is confusing with regards to odds ratios of increased or decreased vaccination rates. I would standardise the test by saying that xx factor was associated with higher rate of vaccination, or lower rates compared to the reference group. Using a double negative like " 5 times decreased odds of an incomplete HBV vaccine" is difficult to interpret. So better to say that is was 5 times more protective against …" and then keep a consistent language.

This is a fair point; we have amended accordingly from lines 193-219 and in the abstract (lines 17 and 21).

11) Line 173 I wonder if smokers tend to have more health care visits than others and so are more likely to be given HBV vaccine.
This is possible, although less likely within this study population due to their generally limited engagement with healthcare services. We note that the average age of the population is young enough that many smoking-related conditions will not yet be at peak prevalence. The small sample size of participants with no smoking history means this result cannot be taken as conclusive.

12) Line 179 replace "… associated." with "associated with incomplete vaccination"

Thank you; this has now been amended (line 209).

13) Line 179, perhaps the reason that there was not an association with homelessness is that nearly all of the population were homeless.

We agree that this finding is set in the context of the population under study, which makes it less notable. We have thus removed it being highlighted within the text (line 199).

14) Line 188 the confidence limits cross over 1, so check that this statement and statistics are correct.

Please see response to point 4.

15) Line 201 and 216; compensation for child care and transportation are usual barriers, so it would have been great to have these reasons prelisted in the questionnaire.

The reviewer makes a good point when it comes to vaccination within the general population. Within our targeted population group, however, being a carer for a child is relatively uncommon (as that would result in rapid rehousing, removing individuals from the systems through which we approached people) and vaccination drives tend to be locally run in order to improve uptake.

16) Line 288 replace "includes" with "include"

Thank you; this sentence has been amended for clarity (line 26).

17) Line 241 Please given us a sentence on nurses' views from that study.

This sentence has now been edited to make the nurse’s views clearer (line 280).

18) I think the paper will be dramatically improved and very helpful once the changes have been made.
Thank you for this positive comment.

Thank you again for the opportunity to respond to the peer review comments. We are grateful for your continued consideration.

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