Author's response to reviews

Title: Epidemiology of hepatitis C virus infection among people receiving opioid substitution therapy (ECHO): study protocol

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Author's response to reviews: see over
Summary of responses to the peer reviewer’s comments

Title: Epidemiology of hepatitis C virus infection among people receiving opioid substitution therapy (ECHO): study protocol
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Dear Dr. Hilary Logan, Dear Dr. Jason Grebely,

On behalf of the authors of this paper, I would like to thank you for your comments. We have done our best to address them. Please find a summary of the responses to your comments below. Please note that the page numbers indicated by the reviewer do not correspond to the manuscript anymore, as the format has been corrected according to the guidelines of BMC Infectious Diseases. An English native speaker has improved the quality of written English.

We look forward to hearing from you.

Yours sincerely,
Lisa Strada
Corresponding author

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<tr>
<th>Major Compulsory Revisions</th>
<th>Accepted?</th>
<th>Description</th>
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| 1) Methods (Page 5, 2nd paragraph) – I would make it clear whether the plan is to take a blood sample at baseline or whether the HCV status will be just recorded from the participant’s chart. From reading later on, it seems as though the answer is the latter, but please clarify whether everyone will be required to have an HCV antibody and/or HCV RNA test performed at the baseline visit. Same for the second visit. Is HCV antibody and/or HCV RNA testing performed? | Yes       | Addressed this issue on page 6 (1st paragraph), page 14 (1st paragraph), page 15 (last paragraph):
‘At both baseline and follow-up, the HCV status will be recorded from the participant’s chart. Clinicians are reminded of the HCV treatment guidelines in Germany, which recommend yearly HCV testing in this high-risk population, to encourage them to perform HCV antibody and/or HCV RNA testing through the standard of care within the clinics.’ |
| 2) Methods (Page 5, 2nd paragraph) – Somewhat related to the above point, how will HCV incidence be monitored? Will you be relying on testing performed through the standard of care within the clinics? How will you ensure that there will be enough follow-up HCV antibody testing to measure incidence? | Yes       | See point/description 1. above:
We will rely on testing performed through the standard of care within the clinics and point out the HCV treatment guidelines to clinicians. |
3) Methods (Page 5, 2nd paragraph) – The measurement of incidence will rely on the fact that there will be a high proportion of those who return for follow-up. Will there be any potential for bias if only a small subset return for follow-up? If so, this really should be mentioned as a potential limitation in the discussion. Also, the sample size assumes a follow-up of 1 year for each individual (which is likely an overestimation). This should also be mentioned as a potential limitation.

Yes  
Addressed this issue in the limitations on page 18 (last paragraph):

‘The sample size calculation assumes a 1-year follow-up of all individuals and does not consider potential dropouts. Incidence estimates may be biased if only a small sub-sample returns for follow up. However, Germany has one of the highest retention rates of OST in the world [43]. The present study will provide first insights into HCV incidence among OST patients. All potential limitations will be discussed in following publications.’

4) Methods (Page 6, 2nd paragraph) – It would be useful to have a confidence interval around the estimate of HCV prevalence. This would be 66%, 70%, which is quite narrow and a strength of this study.

No  
We assume an HCV prevalence of 68% based on a previous study conducted among OST patients in Germany. We use this estimate of 68% to determine the sample size needed for our study.

We agree that a narrow confidence interval would be a strength of our study. However, since the number of 2500 patients is a result of our sample size calculation, it would not be correct to include the number of 2500 patients in a confidence interval, before the sample size of 2500 is determined.

Minor adjustment for clarification on page 7 (2nd paragraph): ‘Based on previous literature [33], we assume an HCV antibody prevalence of about 68% among OST patients in Germany. Therefore a sample size of 2500 patients is needed (32% corresponds to N = 800).’

**Minor Essential Revisions**

<p>| 1) Abstract and throughout manuscript - The term “opioid substituted patients” is somewhat odd. Perhaps people receiving opioid substitution therapy (OST) might be better. | Yes | Changed from ‘opioid substituted patients’ to ‘people receiving opioid substitution therapy (OST)’ |
| 2) Introduction (Page 3, 1st sentence) – Perhaps use injecting drug use instead of intravenous drug use. Drugs can be injected through means other than intravenously (e.g. intramuscular). | Yes | Changed from ‘intravenous’ to ‘injecting’ |</p>
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<tr>
<th>3) Introduction (Page 3, 1st sentence) – These are somewhat old references re: IDU as primary mode of transmission. I see you use Hajarizadeh Nat Rev Gastro Hepatol 2013 later on. That would be a more appropriate recent reference.</th>
<th>Yes</th>
<th>Reference changed: replaced Alter 2007 with Hajarizadeh 2013</th>
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<td>4) Introduction (Page 3, 2nd sentence) – I would use people who inject drugs (PWID) instead of injecting drug users (IDUs) as the field has moved towards this terminology to reduce stigmatization.</td>
<td>Yes</td>
<td>Changed from IDUs to PWID</td>
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<td>5) Introduction (Page 3, last paragraph, 1st sentence) – There is also a recent systematic review by Wiessing et al (PLoS One. 2014) which on HCV epidemiology among PWID in Europe which might be worth referencing.</td>
<td>Yes</td>
<td>Reference added</td>
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<td>7) Methods (Page 5, 1st paragraph) – I would highlight the proposed years of recruitment upfront in the first paragraph.</td>
<td>Yes</td>
<td>Text revised accordingly: added years of recruitment (page 5, last paragraph)</td>
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<td>8) Methods (Page 7, 1st paragraph) – In the last sentence, it says randomization. As there is no randomization in this study, is that meant to read “sampling”?</td>
<td>Yes</td>
<td>Changed from ‘randomization’ to ‘sampling’</td>
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