Author's response to reviews

Title: Cross Sectional Analysis of Respiratory Symptoms in an Injection Drug User Cohort: The Impact of Obstructive Lung Disease and HIV

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Author's response to reviews: see over
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Dear BMC Pulmonary Medicine Editorial Board,

Enclosed in this submission are the responses and revisions to the original research publication titled “Cross Sectional Analysis of Respiratory Symptoms in an Injection Drug User Cohort: The Impact of Obstructive Lung Disease and HIV” by M. Bradley Drummond, Gregory D. Kirk, Erin P. Ricketts, Meredith C. McCormack, J. Christian Hague, John F. McDyer, Shruti H. Mehta, Eric A. Engels, Robert A. Wise and Christian A. Merlo (Manuscript #2934825363421195). We appreciate the reviewers’ input and have addressed their specific comments as outlined below. We feel the changes have improved the quality of the manuscript. Specific comments have been itemized below and manuscript changes noted by section and paragraph.

Thank you for taking the time to consider the revisions of what we feel is an exciting and improved manuscript. Please do not hesitate to contact me with any questions.

M. Brad Drummond, MD MHS

Authors’ Responses:

Reviewer 1

C1: The manuscript is well written and explains the scope of the title of the study. Although it is beyond what would actually be required, it would be interesting if the authors explained the possible mechanisms whereby HIV virus by itself acted as a factor of respiratory diseases in HIV disease in the discussion section.
R1: We thank the reviewer for suggesting further commentary regarding potential mechanisms of HIV virus-mediated impact on respiratory diseases. We have added a paragraph to the discussion section (paragraph #4) briefly reviewing the potential mechanisms that HIV virus may act as a factor in the development of respiratory diseases.

C2: The tables lack proper explanatory headings.

R2: We have modified the titles of the tables to enhance their readability.

Reviewer 2

C1: This is a cohort of IDUs that could not represent the real population of IDU in the geographical area of the authors. Maybe these IDU subjects are those more compliant with medical care, or they have a better life habit, or whatever that could bias their attitude to develop a worse OLD. How are they enrolled in this cohort?

R1: We thank the reviewer for raising this important point and agree that participants who are involved in research studies often differ from the general population. The ALIVE study recruited participant in Baltimore City through community outreach efforts outside of any treatment center. Recruitment occurred primarily through distribution of flyers and word of mouth. Recruitment in this manner decreases, but does not fully eliminate, the likelihood of substantial differences between the study population and general population.

To address the reviewer’s concern, we have clarified the manner of recruitment in the methods section (“Setting and Participants” section) and added a statement regarding generalizability to the limitations paragraph (final paragraph) of the discussion section.

C2: The subpopulation of HIV infected individuals in this cohort is represented by individuals with a relatively high median CD4 count, that means that they are in better condition than other HIV+ IDUs not represented in this cohort. On the other side, only 54.6% were receiving HAART, while more than 55% had high HIV viremia levels. The authors should give more explanations on their immunological status.

R2: We thank the reviewer for indicating the ambiguities in our reporting of the immunological profiles of the HIV-infected participants. This confusion likely arose because we presented the
CD4 and viral load data without separating the cohort by HAART users and HAART non-users. To better describe the immunodeficiency profile of HIV-infected participants, we have modified the end of the first paragraph of the results section by stratifying the CD4 and undetectable viral load proportions by HAART users and HAART non-users.

C3: There is no description of cardiac conditions of these individuals. Of note, dyspnea could be related to pulmonary hypertension in HIV infected individuals. Has a cardiological evaluation been performed in these individuals?

R3: We agree with the reviewer that the role of cardiac conditions (pulmonary hypertension, HIV-associated cardiomyopathy) is an important consideration when evaluating dyspnea in this population. Currently, we do not have data on cardiac evaluations in this cohort. To highlight the importance of pulmonary hypertension in this population, we have added a discussion of pulmonary hypertension as a putative mechanism for virus-mediated dyspnea in the discussion section (paragraph #4). Additionally, given the lack of cardiac data, we have added this as a limitation in the limitations paragraph of the discussion.