Author's response to reviews

Title: Advancing Research and Practice in HIV and Rehabilitation: A Framework of Research Priorities in HIV, Disability and Rehabilitation

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Author's response to reviews: see over
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Dear Members of the BMC Infectious Diseases Editorial Team,

On behalf of my co-authors, we thank the journal and the reviewers for their review of the manuscript entitled: \textit{Advancing Research and Practice in HIV and Rehabilitation: A Framework of Research Priorities in HIV, Disability and Rehabilitation}.

We appreciate the time taken by the reviewers to review this manuscript and the invitation to revise and resubmit. Attached is a revised version of the manuscript with track changes and our responses to the reviewer comments are below.

This research was supported by the Canadian Institutes of Health Research (CIHR) HIV/AIDS Research Program. We have no competing interests to declare. This manuscript has not been published and is not under consideration for publication elsewhere.

Please do not hesitate to contact me if you require any further information. Thank you again for considering our manuscript for publication in \textit{BMC Infectious Diseases}. We look forward to hearing from you.

Sincerely,

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Referee #1
Reviewer: Lucette Cysique

1) **Authors should add the professional expertise of each of the participant as this certainly impact on the scope and angle of recommendations**

We thank the reviewer for her suggestion. All known information on the characteristics of participants were included in the manuscript including role and setting as it related to the field of HIV and rehabilitation. Given our invitations were primarily targeted through HIV and rehabilitation specific organizations such as the Canadian Working Group on HIV and Rehabilitation, and Canada-United Kingdom on HIV and Rehabilitation Research, the participants in this meeting were all stakeholders who possess clinical, research, experiential and/or community expertise in HIV and rehabilitation. We added a statement to the results section; given the nature of our recruitment was through collaborating organizations, participants were considered knowledgeable to the field of HIV and rehabilitation (Page 11).

2) **Overall, it is a very well written manuscript, methods, results and discussion are clearly exposed and limitations are acknowledged. It is informative for researchers who are entering the field as well as those who are more experienced. Of note some of the recommendations are already being implemented, but this paper has the advantage of providing an overall framework.**

We thank the reviewer for highlighting the readability of the manuscript and strength of providing the research recommendations in the form of a Framework.

Referee #2
Reviewer: Stephen Karpiak

This paper defines the state of the HIV epidemic in well-resourced countries including Canada which is the origin of this paper. The authors define/describe the issues/challenges which the enlarging aging HIV populations confront. Using a sample from a conference on HIV, qualitative data from a group of stakeholders was used to gather information that was employed to define a framework by which “rehabilitation” can optimally be used in order to achieve the best aging process for the HIV infected populations of older adults.

The scope of the effort is large which results in a manuscript that is at once far too broad in its statement of background and the definition of an operationalized framework. Too often it lacks needed detail.

We thank the reviewer for his detailed comments and participation in the meeting from which the priorities were derived. We agree that the scope is broad as the aim of the manuscript and research priorities are to describe research priorities applicable to people living with HIV at any age within the context of HIV and rehabilitation, rather than specific to aging and older adults with HIV. Although the Forum discussion largely focused on older adults living with HIV, participants also identified a need to consider research related to children, youth and young adults living with HIV. Aging across the lifespan is one of six research priorities within the larger framework.
Comments:
1) The paper is far too long and many sections are repetitions of prior concepts. It needs to be shortened and focused substantially.

We thank the reviewer and have revised the manuscript for clarity and succinctness. We welcome any additional suggestions on specific areas in which to further pare down the manuscript and as we would be happy to accommodate.

2) There is no context for this effort. No data – epidemiology – is used to describe the present status of the epidemic in Canada. In the US 70-80% of older adults with HIV are Medicaid dependent. Returning to work would jeopardize their health coverage and benefits. What about in Canada?

We added detail on the prevalence and incidence of HIV in Canada, United States and United Kingdom and the increasing number of people aging and prevalence of multi-morbidity (page 6). Given our manuscript did not focus on return to work and income support we chose to incorporate the prevalence of HIV and older adults living with HIV in the introduction (page 6). We also added detail on the presence of comorbidity and multi-morbidity (specifically as they relate to a given priority on concurrent health conditions) (page 8).

3) “Rehabilitation” must be defined and described.

We added a definition of rehabilitation in the context of HIV in the background section (page 6-7). We further describe rehabilitation, specifically physical therapy and occupational therapy and the ways in which they may address adverse effects of medication, fatigue, pain, cognitive impairments, and issues related to employment for people living with HIV.

4. Efforts to “rehabilitate” the HIV infected older adult with multi-morbidity is again stated without context. Have these long-term survivors been previously “rehabilitated” when they were younger? What percent work? What is/was their work history? And given the challenges of multi-morbidity what success with “rehabilitation” can be expected?

We appreciate the suggestion to further discuss the issue of access to rehabilitation and added more detail on the lack of access to formal rehabilitation services among people living with HIV (page 7). Because older adults, employment and long-term survivorship were not the focus of our inquiry, we added contextual information on the prevalence and impact of multi-morbidity as it relates to disability and rehabilitation for people with HIV (page 8). The field of HIV and rehabilitation is still emerging with a paucity of evidence to support the effectiveness of rehabilitation interventions. The aim of the Framework of Research Priorities is to ensure we focus future research on emerging issues of multi-morbidity, aging and other priorities related to HIV, disability and rehabilitation so that we can establish best evidence in which to document the impact of rehabilitation for people living with HIV.

5. The authors often blur purpose – Page 11 – line 204: “The Framework includes...”. After reading this section it seems that it includes all things and invokes concepts such as “knowledge translation”. The authors state they want to inform clinical practice, yet in the next paragraph (Line 210) they state that clinical practice informs the research. There is a need for CLARITY.
We thank the reviewer for this suggestion. Our conceptualization of research informing clinical practice and practice informing the research is derived from the process of evidence-based practice theory (Sackett DL, Straus SE, Richardson WS, et al, 2000). The steps to evidence-based practice involve a cyclical approach whereby clinical practice and research dually inform each other. This process is initiated with i) clinical question, ii) followed by tracking down and acquiring the best evidence to address the question, iii) critically appraising the evidence, iv) integrating the evidence in to clinical practice, and v) evaluating the impact of implementing the evidence and adjusting practice accordingly. This then informs the subsequent research question and feedback loop. We clarified this point in the manuscript stating that the Forum highlighted the important reciprocal relationship between research and practice. Specifically, clinical practice should inform research and subsequently, newly generated research evidence should be translated to inform the implementation of future clinical practice, programs and policy (Page 12). We further describe this cyclical relationship on page 20, whereby connecting research and practice emerged as a consistent theme throughout the Forum. Participants highlighted the need for research to be driven by the needs of the community and clinical practice and ensuring that research evidence is translated into appropriate programs and policy.

6. The authors are remiss to not allude to the extensive research priorities of NIH regards HIV and Aging that were generated by a diverse Working Group.

We thank the reviewer for highlighting the research priorities specific to HIV and aging by the National Institutes of Health. We introduce these priorities in the background (page 8) while building a rationale for the study. In the discussion, we specifically discuss how the priorities similarly relate to Priority 2 ‘aging across the lifespan’, Priority 3 ‘concurrent health conditions’ and Priority 6 ‘enhancing outcome measurement (Page 23 and 25). These priorities similarly addressed multi-morbidity and the need to emphasize maintenance of function, and the complexity (or uncertainty) of assessing effects of HIV, treatment effects, aging versus concurrent disease.

7. The authors need to explain how efforts to rehabilitate will be effective. Aren’t these older adults with HIV exhibiting the syndrome of Frailty? Can the syndrome be reversed? Is the goal to sustain functionality and independence?

We appreciate the reviewer’s request for further explanation of the effectiveness of rehabilitation. Given the paucity of research evidence on the effectiveness of rehabilitation; our aim is for this Framework to address this gap by highlighting a call for high level research to address the effectiveness of rehabilitation interventions (Priority 5). Specific interventions of importance include exercise, neurocognitive, mental health, self-management, and labour force and participation interventions. While the focus of rehabilitation is to enhance function and well-being our definition of rehabilitation is not specific to older adults or frailty. Hence, our description of Priority 5 broadly focuses on the call for evidence on rehabilitation interventions for people living with HIV. (Page 23-24)

8. The three primary themes and the 6 research priorities are logical elements/conclusions. But rehabilitation interventions (which really must be defined in some way – even if reliant on past experiences) seem to become the absolute focus of the framework defined by this effort. The authors have made this the a priori variable that will drive all other research efforts. Quite simply – what the authors mean by rehabilitation needs to be far better defined and described.
We agree with the reviewer that rehabilitation is the focus (or context) in which the research priorities were developed. Our aim was to establish a framework of research priorities in HIV, disability and rehabilitation. We added a definition of rehabilitation to the introduction to clarify the context (page 6). In the results, we specify that this Framework may be used by researchers, clinicians, students, people living with HIV, and the broader HIV community as a foundation to inform future HIV, disability, and rehabilitation research. (Page 13)

9. On page 12 Line 224 the authors categorize – physical, cognitive and mental health as separate domains. Are they?

Yes, physical, cognitive and mental health are considered separate dimensions of disability. Results from an exploratory factor analysis of health related consequences of HIV demonstrated that physical, cognitive and mental-emotional symptoms and impairments, along with uncertainty and challenges to social participation were distinct (albeit related) dimensions of disability (O’Brien KK, et al. 2008; O’Brien KK et al, 2014). http://www.ncbi.nlm.nih.gov/pubmed/25116628

10. The challenges are considerable for those living with multimorbidity. Episodic illnesses are not HIV specific - in fact are not most illnesses episodic? Why the emphasis on them? Examples are needed.

The theme exploring the episodic nature of disability and health over time emerged within the Priority 1 – Episodic Health and Disability. We agree with the reviewer that the experience of multi-morbidity adds further complexity to the health-related challenges living with HIV. We also agree that the experience of disability as episodic may not be unique to people living with HIV and may be similarly experienced by individuals living with other chronic and episodic illnesses including but not limited to mental health, arthritis, multiple sclerosis, or some forms of cancer. In the discussion we clarify that priorities related to episodic disability may be similarly experienced by individuals living with other chronic and episodic illnesses, followed by an example of how CWGHR has addressed issues of labour force and income support broadly among people living with episodic disabilities (Page 21). We also introduced the concept of episodic disability in the introduction with examples of factors that can exacerbate episodes of disability for people with HIV (Page 6).

11. Page 13 – line 254: again this is an example of the lack of care in being specific – what is the difference between concurrent health conditions and multi-morbidity?

We thank the reviewer for suggesting this point for clarification. Concurrent health conditions collectively may include co-morbidity (living with HIV and one other health condition) and multi-morbidity (described as the simultaneous occurrence of two or more conditions in addition to HIV). In the discussion we emphasized how increasing multi-morbidity and functional status impairment can lead to increased frailty, which is increasingly important to consider in the context of HIV clinical research (Page 23).

12. The authors rightly acknowledge that the arc of aging with HIV is complicated. But in fact Geriatrics and Gerontology have an extraordinary knowledge base/experience that can be used to address these complexities. That should be the starting point as one creates a model. There is an attempt to do this on page 17 line 340.
We thank the reviewer and agree that the field of geriatrics and gerontology have extraordinary expertise and knowledge from which the field of HIV and aging may build. We did not use this as our focal point in creating the research priorities given aging was not the specific focus of the model. Nevertheless, new partnerships and collaborations with the field of gerontology are integral to extending expertise to the HIV and rehabilitation agenda (Page 18).

13. At no point do the authors acknowledge that this effort is motivated by the fact that most HIV infected people have received care that emphasizes CD4 and Viral Load as the primary health care outcomes. The need to move from this siloed fragmented care model to one that is highly integrated is the impetus behind this paper’s effort. As the authors state health outcomes are now changing for the HIV infected population. This issue has now been engaged globally as UNAIDS lists NCDs (non-communicable diseases) as an added burden for the HIV aging populations worldwide.

We agree with the reviewer that this Framework addresses the shift from a medical model to considering the broader consequences of disease (disability) and the role for rehabilitation. In the discussion we emphasize that the Framework goes beyond the medical model focused on virological or immunological outcomes of health to emphasize the need to consider the consequences of disease (disability) and the role for rehabilitation in addressing disability (Page 26).

14. Page 18 Line 360. Contextual Factors. The language here is at best confusing and not focused. Which of these factors are structural and which are amenable to change in the short term?

We clarified the classification of non-modifiable versus modifiable factors. Personal attributes were considered non-modifiable such as gender, ethnocultural background whereas modifiable factors included extrinsic environmental factors such as stigma, social support which may be addressed through education or policy interventions (Page 20).

15. Page 21 Line 413 – exercise care when using terms like “successful aging” or “positive aging” – they are not the same descriptors (Butler’s definition of successful aging would never fit the HIV aging populations). What is “negative aging”? Again the language is too often imprecise in this paper.

We thank the reviewer for this comment and referring to Butler’s definition of successful aging and attention to adopting this terminology. Our conceptualization of successful aging relates to Baltes and Baltes’s definition that includes length of life, biological health, cognitive efficiency, mental health, social competence, productivity, personal control, and life satisfaction as discussed in the context of HIV by Vance et al. (2011). This terminology has subsequently been used by Emlet at al (2011) and Moore et al. (2013). As recommended we provide more detail on our recommendations for research to focus on interventions to promote these areas of successful aging in the context of HIV (page 22).

16. The one figure is not helpful – it needs to be rethought and recast.

We thank the reviewer for this comment. Frameworks by their nature are complex often comprised of multiple components demonstrating the multi-dimensional construct of interest. The construct in this study, research priorities in HIV, disability and rehabilitation research, is similarly complex and multi-dimensional comprised of research priorities and methodological considerations. Our aim with the
Framework is to comprehensively represent the multidimensional nature of the priorities. We made some minor revisions to the framework to enhance readability. We appreciate Reviewer 1 commenting the Framework was a useful way in which to articulate the priorities and we welcome specific suggestions as to if and how the Figure may be made more useful in articulating these priorities.

17. Was IRB approval needed?

We reviewed the need for ethics approval with the University of Toronto, HIV/AIDS Research Ethics Board prior to the meeting, who confirmed that given the nature of our consultation was the form of a meeting proceeding; this work did not require ethics approval. Please refer to the email exchange with the REB confirming no need for REB approval submitted with the manuscript submission (Page 9).