Author's response to reviews

Title: Specification of Implementation Interventions to Address the Cascade of HIV Care and Treatment in Resource Limited Settings: a Systematic Review

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See attached response letter for easier to read responses. Plain text point-by-point responses included below.

Reviewer #2: This is an improved version of the paper, and it reads well. Most comments are just for clarity.

Abstract

- Remove reference to PCA
- Where it reads "sought to assess... globally", you might want to change "globally" for in low to middle income countries

We have made both of the above changes.

**Background**

- Remove "to identify strategies" after "conceptualisation and reporting of implementation research" or clarify what you mean by "strategies"

We agree that this is unclear and have made the suggested change.

- Where you define implementation interventions as "improve use of ART in HIV-infected individuals" - is this not a bit too narrow to encompass what you then review? Would a more suitable definition recognise that you are not just looking at interventions that improve use in individuals, but as you say elsewhere that improve the uptake of HIV care and treatment at any point in the cascade?

We intended for ‘use of ART’ to include all of the necessary component steps required for delivery of ART, however your point that this is not clear is well taken. We have modified this statement to read: “We define an implementation intervention as any intervention that seeks to improve uptake or sustained delivery of HIV care and treatment across any step of the HIV cascade of care.” We think that this more effectively communicates the breadth of our definition of implementation interventions.

**Methods**

- In your search strategy, should you specify "implementation interventions" were the target rather than just "interventions"?

  Agreed. This change has been made.

- The idea of "semi-coded and coded form" is still not clear. I understand that you coded to Proctor domains and to your own intervention types and approaches, as you defined them. But what does the "semi-coded" part refer to? Is it clearer to state that somethings were coded to specific definitions, and others were extracted without any coding (e.g. author or country information)?

  You are correct that some data was coded and some was extracted without any coding. We have modified this statement to read “We captured both coded and unstructured data…” to clarify this point.

- "In turn, these behavioral targets are in general necessary but usually insufficient component causes of a cascade step." - is "causes" the right word here? The sentence is not currently clear.
I think what you mean is that these behavioural targets may be necessary to achieve the aims of that particular cascade step (e.g. retain people on treatment) but are not usually sufficient on their own to achieve the aim.

You are correct that we are suggesting that the behavioral targets are generally necessary but insufficient on their own to achieve the cascade step in question. The language we use here “necessary but usually insufficient component causes” refers to the concept in causation that there can be numerous component causes, some of which must be present for a particular event to happen, but that by themselves are insufficient as that event’s sole precipitant (see discussion of Rothman’s Causal Pies, there is a good explanation on the CDC’s website at https://www.cdc.gov/ophss/csels/dsepd/ss1978/lesson1/section8.html). So, when we say ‘cause’ we mean it in the above context, rather than in a linear cause-and-effect relationship. As such, if you agree, we would prefer to keep the existing language.

- Why do you say you "err towards inclusion" when things are not clear? Isn't it more typical to err towards exclusion"? Can you justify your choice, and what you mean by "erring towards inclusion" (do you mean in terms of including in the review or recording presence of a component rather than absence?)

We are referring to presence vs absence of a particular implementation component, though can see how this language may be confusing. We erred toward stating that a component was present because of the large variability in quality of reporting on each of these different components and the difficulty in drawing a clear line as to the degree of quality that was required to give a particular study ‘credit’ for reporting that component. Thus if a study made any mention of the component in question, we reported it as present. Our hope was that this would represent a bare minimum in reporting that should be present, though improvements in reporting quality above this minimum should of course be encouraged. We have now clarified this in the text.

Results

- in the sentence "in linear regression of reporting completeness..." I think it's clearer to say "by cascade step" rather than "on cascade step"

We have made this change, though generally speaking we think ‘on’ is the correct term to use when describing regression of a dependent variable on the independent variable.

Discussion

- It looks like you didn't change "substantially below 100%" as requested by reviewer 3

We have now made this change per the suggestion of reviewer 3.

- Where you write "a study in Kenya found", could you change it to "a study in Kenya, which found"
We have made this change.

- You use the word "positioning" a couple of times and it feels like "enabling" or "informing" might be better, e.g. "thus positioning scale up of this service" could be "thus informing scale up of this service" and "Mechanistic clarity positions results from one particular setting to inform expected results in a different" reads more clearly as "Clarity in terms of mechanisms enables results from one particular setting to inform expected results in a different setting"

We agree that the suggested changes clarify our meaning and have made both of them.

- The term "meta-scientific" is unnecessary and not clear

We have changed this to simply ‘scientific’.

- should this read "through" not "though" - "we extend the current meta-scientific discourse on reporting though empiric quantification of the reporting gap in a specific topical area"

Thanks for picking this up; we have made the change.

- you use the word "permits" but again "enables" would work better - "Specification also enables researchers to evaluate the intervention in a new setting and implementers to scale up the intervention (perhaps with adaptations)"

We have made this change.

Tables

- In the table defining the Proctor domains, the example given for "dose" and "temporality" is the same and actually the definition doesn't capture temporality well

We have now included the intended examples in this section. Thanks for picking up this oversight on our part.

- Table 1 has a small error in it - the word "is" is repeated in the action target example more than needed

We have removed the extraneous word

- Table 3 has 160 studies included, despite your repeated assertion of 157. Please clarify

The heading of Table 3 that referred to n=160 was an error (we initially had 160 studies before excluding some duplicates from the updated searches. The data displayed in the table is correct however (note that for study type, the numbers add up to 157). We have changed the heading to reflect the correct number of studies.
- Also, check the categories for table 3 all add up to the correct number of studies - you have accounted for the fact that a study might be done in more than one region, but it is less clear why there are only 156 studies with a positive or negative effect - is this because there was a study with no effect too?

Thanks for this pickup. One study had a missing value for study effect; we have now corrected this and included it in the table. We conducted checks for missing values for the variables included in our main analysis, but overlooked checking this variable.