Reviewer’s report

Title: The psychology of "cure" - unique challenges to consent processes in HIV cure research in South Africa

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Reviewer: Catherine Slack

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The psychology of cure - unique challenges to consent processes in HIV cure research in South Africa

Review

Thank you for the opportunity to read and review this manuscript. The manuscript reports on an empirical exploration with representatives from important stakeholder groups regarding the perceived ethical complexities in HIV cure research in South Africa.

HIV cure research is a key component in the spectrum of research into HIV. Empirical data from stakeholders with multiple forms of background expertise certainly comprises an important part of the 'puzzle' in understanding the complexity of such trials, and can illuminate key issues for affected groups planning and reviewing such trials. A manuscript setting out the perceived complexities of such research in South Africa is timely and important.

The manuscript itself would benefit from further development. To strengthen the manuscript the authors should:

Background

- Describe briefly what HIV cure research has already occurred in South Africa and is planned. At present, readers have to fill in these blanks.

- Describe briefly what it is about the South African context (or South African participants) in particular that might be especially complex for such trials. At present, these factors are hinted at in the paper, but it will help readers to have them set out more clearly. Presumably some of these factors will be shared in contexts outside of South Africa, which does not make them less interesting.
Make some brief reference to cure trials for other diseases. This will help contextualize the study and may help readers to evaluate whether the ethical challenges are really 'unique'. In my view, the issues in HIV cure research would not have to be positioned as 'unique' or 'unlike anything else' for them to be very demanding for research stakeholders, and worthy of considerable research, capacity building and guideline development. I would therefore recommend dropping the term 'unique'.

Methods

Reconcile the two slightly different formulations of the aims - in line 38/9 and line 45.

Provide some brief explanation and references for aspects of the methods section, in particular:

- purposive sampling
- external validity
- interpretive research and
- contextualised thematic approach.

Edit for clarity the paragraph lines 28-40. It is not clear what interviewers did with interviewees from this account - did they read a hypothetical scenario/vignette? Did they describe one?

Describe the domains of the interview (or focus group) schedule. What areas were covered? In what sequence? With what prompts?

Add the code list as a Table or a Text Box.

State the numbers of interviewees in each stakeholder group.

Clarify the following line - "Many of the respondents have international profiles which enhanced the external validity of the results".

Describe whether a 'between-stakeholder' analysis was conducted, and if not, why not. The authors have taken trouble to recruit interviewees from a broad range of stakeholders able to offer insights from diverse perspectives, but do not describe whether themes varied between
stakeholder groups. If this manuscript focuses only on themes shared across all stakeholders, then this should be made more explicit.

Results

- Use this section to describe data from interviews, and not to present observations from the literature, which are better reserved for the Discussion section. The 'voice' being described in the lines below seems to be that of the authors summarising important literature and not the 'voice' of the interviewees. For example:

  - On page 5 lines 53-59.
  - On page 6 lines 1-5 and lines 15-20 and lines 47-55.
  - On page 7 lines 3-12, and lines 23 to 35 and lines 49 - 56.
  - On page 9 lines 7-13, and 53 - 56.
  - On page 10 lines 1-9.

- State which stakeholder group is represented after each quote.

- Use conventions such as "all", "some", or "few" interviewees to give the reader a sense of the relative proportion of interviewees reporting various issues. At present, the reader has to intuit this - qualitative methodology notwithstanding.

Discussion

- Discuss each theme briefly in relation to the literature. Perhaps some of the lines above moved from the Results section would work well in this section.

- Clarify which specific 'aspects of the consent process are different', and different from what?

- Clarify which trials have 'minimal ethics requirements' that need to be surpassed in the case of HIV cure research?

- Elaborate on the 'level of protection and additional oversight' triggered by HIV cure studies.
Interpret lines 1-8 in terms of allowable levels of risk for beneficial and non-beneficial procedures set out in South African national ethics guidelines (DoH, 2015) and national regulations.

Make explicit concrete recommendations for RECs (apart from annual re-consent, and more frequent progress reporting/renewals, which are useful potential strategies). What would the authors have RECs do differently from what RECs already might do when they review other scientifically complex protocols enrolling participants, with multiple vulnerabilities drawn from communities with multiple vulnerabilities, into trials with experimental interventions that carry potential risks and uncertain benefits, and are targeted against stigmatized and stressful conditions?

For example, what should RECs do or specify to address the need for 'healing' and not just 'cure'?

Engage critically (with reference to literature or ethics guidance) with some of the recommendations perceived to be important by interviewees. The authors seem to present these suggestions instead of engaging critically with them. While the concerns behind some of the recommendations are not to be dismissed, it is not clear that these are the best remedies for concerns. For example,

That "a psychologist" should assess whether trial participants are able to make decisions about participation in HIV cure research.

That the "mental state" of participants in HIV cure research should be regularly assessed, and

That such research omit the term 'cure', because for example of the potential for participant or community misunderstanding that the 'cure' intervention is still experimental.

Make some observations about whether current ethics guidance for HIV cure research (or for other trials for that matter) offer helpful guidance for the contemporary difficulties raised by these stakeholders. For example, do current ethics guidelines offer any guidance for the ambivalence interviewees describe about HIV exceptionalism (Theme 1), or for the uncertainty interviewees describe regarding additional consent remedies (Theme 2) etc? This may provide important clues for those involved in guideline development or revision. How should current ethics guidelines be amended to be more responsive to actual concerns from the field described here? In my view, if this aspect of the paper were fully developed, this would contribute in no minor way to this field.

Thank you for the opportunity to review this paper.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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Please complete a declaration of competing interests, considering the following questions:

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