Author's response to reviews

Title: A comparison of linkage to HIV care after provider-initiated HIV testing and counselling (PITC) versus voluntary HIV counselling and testing (VCT) for patients with sexually transmitted infections in Cape Town, South Africa.

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Version: 2 Date: 18 September 2013

Author's response to reviews: see over
Dear Editor

A comparison of linkage to HIV care after provider-initiated HIV testing and counselling (PITC) versus voluntary HIV counselling and testing (VCT) for patients with sexually transmitted infections in Cape Town, South Africa.

This article was previously submitted to your journal and reviewed (ref no. MS: 129595406862873) and we appreciate the detailed and thorough reviews provided. Unfortunately we were not able to meet the deadline of the review period, for which we apologized in earlier correspondence. We have now attended to all the reviewer’s comments and would like to resubmit the article for your consideration. The responses to the reviewers’ comments are addressed in the table below in a point by point form.

The aim of expanded HIV testing strategies such as provider-initiated HIV testing and counselling (PITC), is not only to increase HIV test uptake, but to ultimately, through early detection of HIV and early linkage to care, to reduce morbidity and mortality as well as transmission of HIV. Research has focused mostly on studying HIV test uptake with less focus on the effect of PITC on linkage to care. Our article addresses this gap by investigating the effect of PITC on linkage to care for patient with sexually transmitted infection (STI) in the context of a controlled trial.

STI patients are a particularly vulnerable patient group for HIV infection and the main controlled trial assessed whether PITC increased HIV test uptake in 7 intervention clinics as compared to VCT in 14 control clinics in Cape Town [1]. The study examined linkage to care following a HIV-positive test for a nested cohort of 930 HIV-positive patients identified in the main trial, by tracking laboratory records for CD4 and viral load testing.

The study is of interest for BMC Health Services as it looks beyond the outcome of a HIV testing intervention, to the next stages in cascade of HIV care. The study was conducted in a routine operational setting and initiated by the health authorities themselves, rather than by researchers, factors that made it more likely for the findings to inform routine practice and policy.

We found that while the PITC intervention did not improve access or time to follow-on HIV CD4 count testing or viral load testing, patients eligible for antiretroviral treatment (ART) were able to access viral load testing approximately 2.5 months quicker than patients in the VCT arm. We identified major gaps in linkage to care, especially for ART-eligible patients, the majority of who did not have a record of viral load testing (and may not have been initiated on ART). Given the shift towards PITC in South Africa [2], the increased numbers of people testing via the National HIV Testing Campaign and the increased pressure on the health services to enrol patients on
antiretroviral treatment (ART), the findings of this study point to the limits of PITC in busy primary health care settings as well as to the potential it holds for improving linkage to care. We discussed how HIV strategies can contribute to increasing linkage to care. We make recommendations for further study, in particular, the need for larger studies to confirm the findings. To our knowledge, there are no studies where PITC and HIV follow-on care has been studied for STI patients in the context of a controlled trial, in a high HIV prevalence and low resource setting.

The authors declare that they do not have any competing interest.

Thanking you,

Sincerely

Natalie Leon (Dr)

### N Leon et al 2013: PITC and Linkage to care article

**Table: Response to the Reviewers’ comments, 18 September 2013**

<table>
<thead>
<tr>
<th>Reviewer comments</th>
<th>Author response- TBD</th>
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<tr>
<td><strong>Reviewer: B. Hensen</strong></td>
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<tr>
<td><strong>Major Compulsory Revisions</strong></td>
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<tr>
<td><strong>Background, Fifth paragraph</strong></td>
<td>1. Secondary aims are now introduced.</td>
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<tr>
<td>1. The aim of the study only describes the primary aim; the authors should also introduce the secondary study aims</td>
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<tr>
<td><strong>Study design, First paragraph</strong></td>
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<tr>
<td>1. The authors should state that the main controlled trial was non-randomised (also in final sentence of the background)</td>
<td>1. Reference to non-random allocation has now been stated.</td>
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<tr>
<td>2. Furthermore, as the intervention was allocated non-randomly at PHC-level, the lack of inclusion or discussion of potential cluster-level confounders is a limitation.</td>
<td>2. Non-random allocation is now discussed as a limitation.</td>
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<td>3. Baseline comparison used in the analysis of the main trial is reported on and Baseline table will be uploaded as an additional electronic file for information.</td>
<td>3. Baseline comparison used in the analysis of the main trial is reported on and Baseline table will be uploaded as an additional electronic file for information.</td>
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<tr>
<td>4. Potential confounders are now more clearly described as variables in the multiple regression analysis and with respect to baseline comparison.</td>
<td>4. Potential confounders are now more clearly described as variables in the multiple regression analysis and with respect to baseline comparison.</td>
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<tr>
<td>5. Cluster-level analysis now reported on (Rank sum and Weighted T-test) which do not change the main effect.</td>
<td>5. Cluster-level analysis now reported on (Rank sum and Weighted T-test) which do not change the main effect.</td>
</tr>
<tr>
<td>1. The authors state that their hypothesis is that PITC would offer more opportunity to link patients to care – they should define this numerically based on existing literature on linkage through standard VCT approaches. This hypothesis should then guide a power calculation.</td>
<td>1. We now discuss in the Limitations section that the study was underpowered due to being nested within a larger study. We did not perform a power calculation initially given the set sample size as well as the fact that estimates from the literature of the potential increased linkage we might have expected, were not available at the time. Given this, we would prefer not to provide a retrospective power calculation. If the reviewers think it useful/necessary, however, we could provide one using the differences found in this study or in more recent literature.</td>
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<tr>
<td><strong>Second paragraph</strong></td>
<td></td>
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<tr>
<td>1. The primary outcomes need to be more clearly defined rather than stating that the primary outcomes were “…proportion of HIV-positive patients who had accessed care, indicated by…” It would be clearer for the reader if they were numbered or highlighted e.g. the primary objectives were: 1. Proportion of… 2. Of these, the proportion…</td>
<td>1. Outcomes are now clarified by using numbering (see Study Design).</td>
</tr>
<tr>
<td>2. Sentence has now been moved.</td>
<td>2. Sentence has now been moved.</td>
</tr>
<tr>
<td>3. A clearer description of linkage to care differences can be found in prg 2, under the revised heading, The PITC intervention and HIV linkage to care. In addition, a new Table 1 has been inserted to better describe the...</td>
<td>3. A clearer description of linkage to care differences can be found in prg 2, under the revised heading, The PITC intervention and HIV linkage to care. In addition, a new Table 1 has been inserted to better describe the...</td>
</tr>
<tr>
<td><strong>The PITC intervention and follow-up care</strong></td>
<td>similarities and the differences between PITC and VCT as implemented in this study.</td>
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</table>
| First paragraph | 2. Move the last sentence to the section where the VCT approach is being described.  
3. Also it is not clear to me how the two HIV-testing strategies differ in how HIV-positive patients are linked to HIV care post-testing. It would be good for the reader to have a clear description of how the linkage to care differs in each arm. |
| Study population and sampling | 1. The description of the main study’s sample size has now been shortened. Please see comments above about the power calculation. |
| 1. The description of the sample size for the main study needs to be summarized. It is clear that the sample size for this study could not be influenced by the authors, but the paper should include a power calculation based on the available sample size and a hypothesised effect of the PITC intervention. |
| Data Collection | 1. The Data collection section has now been revised to improve clarity. It was not possible to use a unique patient identifier as this is not provided in either the clinic-based HIV testing register or the National Health Laboratory System (NHLS) electronic database.  
2-3. Yes it is possible that patients had a CD4 test done at other clinics. The searching of the province-wide database was able to capture CD4 and Viral load testing at other Cape Town or Western Province clinics which is discussed as strength of the study. It cannot capture testing for those who migrated out of the province and the implications are discussed in the limitations. |
| 1. In the description of how the patient records were searched – was it not possible to use clinic identifiers?  
2. Is it possible that the patients could have had their CD4 testing etc done at clinics other than the ones where they were tested for HIV?  
3. If so, any implications of this. |
| Results, Second paragraph | 1. All the changes regarding description of ‘known positives’ have been done. Additional explanation has been provided in the Methods section to improve clarity.  
2. The effect of removing ‘known positives’ are now discussed in the Discussion section.  
3. A table reporting the clinic based outcomes have now been included (See Table 3). |
| 1. The section where the removal of ‘known positives’ is described should be moved to the methods section.  
2. with the number of ‘known positives’ removed from the analysis by study arm kept in the results section.  
3. The sentences on the likely effect on removal of these individuals on the measure of effect on access to viral load testing should be moved to the discussion of the paper.  
2. It would be useful if the authors included a graph or table presenting outcomes by clinics in each study arm. This would allow the reader to explore variability in the outcomes across clinics and study arm. |
| CD4 Testing: | CD4 testing and viral load testing |

**Table 3**
1. The outcome should be discussed. This is not clear to the reader.
2. The authors should calculate the risk difference so that the difference is positive – at first glance readers may think that the proportion of patients tested for CD4 was lower in the PITC intervention clinics. Similarly for the results on viral load testing (second paragraph) and in the abstract.

| 1. | The results section has been revised to improve clarity. The CD4 and Viral load testing results are now reported together. |
| 2. | The analysis was redone to report on odds ratios rather than risk differences. |
| 3. | The corresponding changes have been made in the Abstract. |

### Viral Load Testing

1. I would suggest moving this section to before the HIV Disease Progression paragraph so that the results are presented in line with how the study objectives are presented.
2. It is not clear to me why additional data on ‘known positives’ is being presented. The paper states that the ‘known positives’ were excluded from the analyses (Results paragraph 2), why is it being repeated? Are these additional to the ones discussed earlier? If the earlier discussion refers to the exclusion of all known positives from the analysis this data does not need to be presented again

**HIV Follow-up Care, Second paragraph**

3. Details of the statistical analysis, including which confounders and interaction effects were considered a priori, need to be moved to the data analysis section.
4. All odds ratios should be presented with the 95% confidence intervals.

| 1. | Table 2 has now been split into two tables, Table 2 and Table 4. Table 2 is a description of the sample and Table 4 reports on the main outcomes. |
| 2. | Table 4 now reports both adjusted and unadjusted analysis. Cluster-level analysis was done for both CD4 and VL testing and this is now reported under CD4 testing and viral load testing in the Results section. |

### Third paragraph

1. It would be useful for the reader to see the unadjusted analysis as well as the adjusted effects presented in Table 2.
2. The authors should consider conducting cluster-level analysis for the effect of PITC on viral load testing. The trial has less than 15 clusters per arm so this could prove a more robust approach. The two stage process recommended for CRTs allows for the inclusion of individual-level covariates. Furthermore, it is not clear to the reader why the results are only presented for the effect on viral load testing?

| 1. | As reported above, the ‘Results’ section has been revised to improve the flow. And a new heading was created: CD4 testing and viral load testing |
| 2. | The duplication is now removed. The information retained in CD4 testing and Viral load testing 1st prg, is to indicate that that the size of the ‘known positives’ that were excluded, was equal in both arms, thus the analysis was not biased by its exclusion. If need be, this information can be excluded in the final paper. |
| 3. | Details of statistical analysis moved to data analysis. |
| 4. | All CIs for odds ratios are now provided. |

### Discussion, First paragraph

1. Where the authors state that ART was accessed sooner, they should emphasise that this is indicated by the fact that the individual had a viral load test. Also the sentence starting “The quicker access…” it would clearer for the reader if they restated to what the patients had quicker access to.

**Second paragraph**

2. The authors state that “…larger numbers of patients were diagnosed HIV-positive in the PITC intervention”. Figure 1 shows that a larger number of HIV-positive patients diagnosed through the VCT approach - even if the intervention arm were to have more

| 1. | The reference to ‘quicker access’ was revised to improve clarity, in the Results and Discussion sections |
| 2. | This discussion section was been revised extensively to improve clarity and relevance and this particular point was removed. Figure 1 is now removed to avoid duplication and confusion. |
| 3. | The Discussion section now offers possible reasons for the poor linkage to care, its implications for scale up and recommendations for improvement. |
clinics, the difference between the arms would be small. Perhaps rephrase this somewhat to state that if there were similar number of clinics, PITC is likely to identify more HIV-positive patients, as it may be unclear to the reader.

Fourth paragraph
3. Although the authors highlight that a high proportion of HIV positive patients did not have CD4 test and ART-eligible patients did not have a viral load test, more emphasis needs to be placed on why this could be and the implications of this. The push to scale-up PITC was to reduce missed opportunities for diagnosis and linkage to care, if there is still such a high loss to follow-up despite PITC this is a major short coming of the initiative – I think the discussion could be strengthened with more discussion on why there might be such poor linkage to care in PITC clinics and perhaps the implications of this in light of interest in expanding HTC beyond facility settings

Fifth paragraph
4 This discussion of ‘known positives’ should be expanded by including the discussion of how removal of these individuals could have underestimated effects on viral load testing (discussed in the results section)

| Strengths and limitations of the study | 1. The Strengths and Limitations section has been revised to address these concerns, including acknowledgement of the bias from non-randomising and attempts made to limit this bias through a baseline comparison of sites (done in the main trial).
2. Efforts to limit possible confounding effects (through the baseline comparison) are described in the Method and Limitations sections.

| Tables | 1. Table 2 has now been split into Table 2 (description of the sample) and Table 4 (main outcomes)

| Minor Essential Revisions | 1. This is now corrected by referring to prevention here as well as elsewhere in the text.
2. Details requested of these two studies are now provided.
3. The absence of a uniform definition of ‘linkage to care’ is now noted and more explanation is given on the cascade of care and what stages this study is focussed on.
4. Details of these SA studies are now provided.
5. See pt 1 above.

| Background, First paragraph | 1. The authors state that “The ultimate aim of approaches to expand HIV testing is improving access to HIV care...” The role of expanded HIV testing service delivery includes improving access to prevention, although the paper focuses on linkage to care I think it’s important to highlight here the role of HIV testing in prevention.
2. Two before-after studies are mentioned; the sentence “with increases in prevention of mother to child transmission (PMTCT) interventions...” is not clear. Please specify what

|  | 1. The possible effect of excluding ‘known positives’ is now dealt with in the Discussion section.

| Fourth paragraph | 1. The authors highlight some important limitations in this section. A major limitation of the study that is not discussed is that it is nested within a non-randomised study. In the absence of randomization, allocation of PITC could have been biased and the results subject to confounding.
2. However, the authors did not adjust for any cluster-level factors (see Table 2) nor did they discuss any possible confounding effects in their limitations.

|  | 1. The Strengths and Limitations section has been revised to address these concerns, including acknowledgement of the bias from non-randomising and attempts made to limit this bias through a baseline comparison of sites (done in the main trial).
2. Efforts to limit possible confounding effects (through the baseline comparison) are described in the Method and Limitations sections.

| Fifth paragraph | 4 This discussion of ‘known positives’ should be expanded by including the discussion of how removal of these individuals could have underestimated effects on viral load testing (discussed in the results section)
PMTCT interventions and that uptake of these increased.

Third paragraph
3. In describing the challenges in interpreting the evidence on linkage to care the authors could include that the definition of linkage to care is not uniform across studies.
4. In describing the two SA studies, could the authors state what population these studies were in, also are these studies comparison studies? This is not clear from the paragraph.

Fourth paragraph
5. The authors discuss the importance of linking STI patients to care following HIV detection; again I think they should highlight the role of HIV testing in HIV prevention.

Methods, Study design
1. Specify here that testing in 7 intervention clinics was compared with testing in control clinics PITC Intervention and HIV follow-up care.
2. The paragraph is written in both past and present, change all to past tense.

Data Collection paragraph
1. Change “…930 patients who tested for HIV…” to “…930 patients who tested positive for HIV…”
2. The sentence “The total number of potentially matching CD4 test records generated…” should be moved to the results section.
3. The detail on the number of patients with a CD4 and viral load test records identified should be moved to the results section.

Data Analysis
4. It would be useful for the reader to know how clustering was taken into account – this doesn’t require much detail, just stating for e.g. whether robust SE were calculated.

Data Analysis
1. The Data Collection section has been revised to improve clarity.
2. Corrected
3. Corrected

Results, CD4 Testing
1. The final sentence regarding the pooled data across study arms should be presented first.
2. The authors repeat the sentence “The quicker access to…” in two consecutive paragraphs, could this be emphasized differently or stated once.
3. Table 1. The *(p<0.05) should be moved to the footnotes of the table along with what test was used.
4. The row on numbers tested is missing the actual numbers.
Reviewer 2 Emily Hyle

<table>
<thead>
<tr>
<th>General</th>
<th>1. No response required</th>
<th>2. See responses to this below.</th>
<th>3. Revisions made see responses below</th>
<th>4. No response required</th>
<th>5. Discussion revised-see responses below.</th>
<th>6. Revision made-see response below</th>
<th>7. No response required</th>
<th>8. The title has been revised as per the reviewer’s suggestion.</th>
<th>9. The Conclusion in the text and Abstract has been revised to improve the clarity.</th>
<th>10. No response required.</th>
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</thead>
<tbody>
<tr>
<td>1. Is the question posed by the authors well defined?</td>
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<td></td>
<td>1. Please refine the vocabulary used throughout the manuscript regarding the cascade of</td>
<td>1. The terms in the manuscript is now defined and used consistently.</td>
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<tr>
<td>The research question is important and well-defined: Will patients who are diagnosed in a PITC setting experience better linkage to and retention in care when compared to patients who are diagnosed in a VCT setting?</td>
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<td>2. Are the methods appropriate and well described?</td>
<td>Improvements are needed; please see major compulsory revisions.</td>
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<td>3. Are the data sound?</td>
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<td>4. Does the manuscript adhere to the relevant standards for reporting and data deposition?</td>
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<td>5. Are the discussion and conclusions well balanced and adequately supported by the data?</td>
<td>Improvements are needed;</td>
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<td>6. Are limitations of the work clearly stated?</td>
<td>I suggest that the limitations be revised after the authors have had the opportunity to review comments by all reviewers. If some of the methodological concerns and suggestions cannot be implemented, then I suspect that the limitations (addressed in the discussion) will need to be expanded to address these issues.</td>
<td>Additional limitations: - only searched Western Cape; migration (especially to Eastern Cape) may result in a substantial number of people who transfer their care, which would not be accounted for in your methodology.</td>
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<td>7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished?</td>
<td>Yes.</td>
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<td>8. Do the title and abstract accurately convey what has been found?</td>
<td>Title: I suggest that this study design is a comparison of linkage to and retention in care after PITC vs. VCT, as a result, the current title (impact of PITC) is a bit misleading. I would suggest rephrasing.</td>
<td>9. Abstract: The “conclusion” is not yet clearly stated; please revise to clarify the meaning.</td>
<td>10. Is the writing acceptable?</td>
<td>Yes.</td>
<td>1. No response required</td>
<td>2. See responses to this below.</td>
<td>3. Revisions made see responses below</td>
<td>4. No response required</td>
<td>5. Discussion revised-see responses below.</td>
<td>6. Revision made-see response below</td>
</tr>
</tbody>
</table>
2. Given the complexity of the concepts that you are discussing, it will help your readers if you define your terms carefully regarding the steps in the care cascade (e.g., diagnosis, linkage, retention). A few examples in the current manuscript where this is not yet clear: “Follow-up care” (abstract), “gaps in linkage to care” (p5), “access to care” (p5) and “accessing CD4 testing and viral load testing” (p. 13).

Methods:
3. It took me several reviews of the methods section to understand the methods; revisions for clarity will be helpful.
4. Consider using the introduction to introduce the SA guidelines for linkage to care, ART-initiation, and pre-ART care, as well as retention in care;
5. a figure or flow diagram would be helpful. Because the study design and outcomes are introduced (p. 6) before the SA guidelines (p. 7), it is not yet clear
6. Please include a description for what the SA guidelines include regarding a protocol for pre-ART patients (not yet ART-eligible).
7. HIV disease progression” (p. 6): do you mean immune status at the time of diagnosis (and/or ART initiation)? This term is not yet clear to the reader.
8. Consider providing a table that outlines the differences in the PITC and VCT protocols (some description on p6, then on pp. 6-7)
9. Why did you choose to assess follow-up with CD4 test for only 6 months after HIV diagnosis? Given that you followed the data for 1 year, were there any examples of patients who had a CD4 > 6 months after initial diagnosis?
10. Why did you choose to assess ART initiation (and therefore retention in care) with HIV RNA test
11. Why did you not also verify a repeat CD4 count? Were there any patients who had a repeat CD4 count without having an HIV RNA test
12. Overall, you followed the subjects for different periods of time; if a subject was diagnosed in Jan 2007, there was 12 months of follow-up time; if a subject was diagnosed in June 2007; there were only 6 months of possible follow-up for CD4. You note this limitation (p. 8); why did you not censor your patients with the same amount of follow-up
13. Why did you limit your second stage search to those patients who had a CD4 test? This will exclude anyone started on ART for clinical reasons and I do not understand why you would include this selection bias.
14. I agree with removing those patients who had a CD4 test prior to HIV diagnosis in this
study; I would recommend excluding these subjects entirely (inclusion/exclusion criteria would be helpful in the methods) and removing them from the tables/figures.

15. Ideally, data would be double-extracted and double-entered for accuracy (p. 8).
16. At a minimum, please describe the method for the “independent check” (p. 8).

NHSL database.

13. We agree this is a limitation and it is discussed in the limitation section. It was not a clear decision to exclude those without CD4 counts, but rather related to our pragmatic limits to do the NHSLS searches. Data searches for CD4 testing and VL testing separately was done at different time periods and using different search tools.

14. The known positives are excluded from the analysis of proportions with access to viral load records and the timing of CD4 and viral load testing. The methods section was revised to improve the rationale for excluding them. The ‘known positives’ were included in the proportions with access to CD4 testing only if they also had a CD4 test after the HIV test date, thus increasing the chance that the CD4 test was related to this intervention. This fact was not described in the original version and we have now added it in to clarify the logic of including known positives for this particular outcome.

15. The data was not double-extracted and double-entered and this is acknowledged as a limitation.

16. The different levels of accuracy checks are now described more fully in the Methods section.

Discussion

1. How do you mean the evidence was “weaker” (p. 13)? Please clarify.
2. The last sentence of both paragraph 1 and 2 is redundant (p. 13).
3. You state “recent modeling of the effectiveness ... low as 20%” (p. 14); the connection of this statement to your results/conclusions is not yet clear. Please elucidate.
4. The details of linkage to and retention in care (last paragraph, p. 14) are very interesting; your study design does not address these specifics. Please revise this paragraph to relate to your overall data/conclusions or to suggest next steps in further investigation from this initial study.
5. Please discuss how subject death might play a role in your data, analysis, and conclusions.

4. Discussion:

1. Results and Discussion has been revised to improve clarity.
2. Revisions have now been done.
3. The Discussion has been revised to improve the connection to the study conclusions.
4. The Discussion section was revised to address these points, with recommendations for further investigation.
5. The effect of mortality is now discussed in the Strengths and limitations section, noting that mortality was not tracked in the routine health data used in this study, which means we could not determine its effect on our outcomes. We describe how a more recent study addressed this challenge.

5. Strengths and Limitations:

a. Please consider dividing this section into two paragraphs – the study has significant strengths that are not yet fully discussed.

1. The Strengths and limitations section has now been divided into two sections, with an expanded discussion of both strengths and weaknesses.
b. This study design has significant limitations (see Methods); also, please address
   generalisability of findings and possible impact of migration (dataset is from
   Western Cape only).

2. The generalisability of the study in now described at the end of the
   Discussion section.

| Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term,
  which the author can be trusted to correct) |
|---------------------------------------------|
| 1. Consider discussing how your inclusion criteria (viral load within 1 year of initial
   CD4 and assumed ART initiation) investigate only a brief time interval within
   “retention in care.” Have you considered extending the time interval (24 months,
   etc) to assess for consistency of retention in care? |
| 2. Have you considered assessing the pre-ART group (those who are diagnosed
   when not yet ART-eligible) in terms of follow-up for repeat CD4? |

| Discretionary Revisions (which are recommendations for improvement but which the
  author can choose to ignore) |
|-----------------------------|
| 1. Consider referencing HPTN 052 (NEJM) in discussion of how ART initiation can result in
   reductions in transmission (p. 5) |
| 2. Consider referencing the range of HIV prevalence in the Western Cape; at this time, you
   offer the mean and the highest rates (p. 6) |
| 3. Consider referencing Gardener et al CID 2011 in your description of the cascade of care
   (p. 12). |
| 4. The current ART initiation guidelines have changed since this data was collected (now
   ART-eligible at CD4 <= 350 cells/mm3); consider addressing how this might or might not
   change the implication of your results. |

<table>
<thead>
<tr>
<th>Editors request for formatting changes on 17 September 2013</th>
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<td>These have now been addressed as requested</td>
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1. The observation periods of follow-up care is now more clearly described
   in the Methods section. In the limitations section, we acknowledge that
   the observation period may still be too brief. The observation period for
   viral loads was minimum 18 month and maximum 24 months. We are
   not in a position to extend the search as for pragmatic reasons, we are
   not able to continue the research study.

2. We have not considered assessing this pre-ART group, other than
   including them as a sub-set of the total numbers who had accessed viral
   load tests (irrespective of their CD4 count). We make suggestions
   about this for further investigation.