Author’s response to reviews

Title: The impact of HIV status and antiretroviral treatment on TB treatment outcomes of new tuberculosis patients attending co-located TB and ART services in South Africa: a retrospective cohort study

Authors:

Mweete Nglazi (mweete.nglazi@gmail.com) (mweete.nglazi@mrc.ac.za)
Linda-Gail Bekker (linda-gail.bekker@hiv-research.org.za)
Robin Wood (robin.wood@hiv-research.org.za)
Richard Kaplan (Richard.Kaplan@hiv-research.org.za)

Version: 1 Date: 29 Sep 2015

Author’s response to reviews:

29 September 2015

The Editor,
BMC Infectious Diseases Journal

INFD-D-15-00103 "The impact of HIV status and antiretroviral treatment on TB treatment outcomes of new tuberculosis patients attending co-located TB and ART services in South Africa: a retrospective cohort study"

Dear Editor,

Thank you for your email of 3 September 2015 and for forwarding the reviewers’ comments. We thank the reviewers for the useful comments that we have used to revise and strengthen the manuscript. We copy the comments below in italics and respond in bold.

Reviewer #1

Reviewer: Baba Maiyaki Musa, MD

There is a disconnect between the narrative in the introduction, the set objectives and methodology. They said "......There are, however, relatively fewer studies on the impact of TB/HIV service integration on TB treatment outcomes among HIV-positive TB patients, and comparative studies of TB treatment outcomes under different models of integration". One would then expect that this is the gap in literature, and supposed intent of the study. Additionally
they said "Motivated by the paucity of research on the impact of integrated TB and HIV services on TB treatment outcomes and recent evidence from several trials on the survival benefit of early ART during TB treatment among HIV-positive patients [6-8], we introduced an ART service into a primary health care clinic with a TB service (i.e. co-located HIV and TB services) in Cape Town, South Africa and integrated adherence support and data management; and then examined TB treatment outcomes of new TB patients in relation to HIV status, ART status and CD4 count status." Reading these one would assume the natural sequence should be to study the impact of TB/HIV integration. This can be done by comparing data before and after the integration, or comparing data from center with integration against data from another center without integration. Better still it could be subjected to a cluster randomized control trial, with randomization of centers into arm with and without integration. It you want your conclusion to remain relevant then your narrative has to change.

We thank the reviewer for this important point and we have revised the manuscript as suggested. Please see below the amended text:

“Numerous studies from sub-Saharan Africa have examined the impact of HIV infection on TB treatment outcomes. These studies have yielded mixed results. Some studies have demonstrated poorer TB treatment outcomes in HIV-positive TB patients when compared to HIV-negative TB patients [15-20], while others found that TB treatment outcomes did not differ between the two groups [21, 22]. In addition, the benefit of ART on TB treatment outcomes has been demonstrated in results from the above-cited randomized controlled trials [6-8] and observational studies [23, 24, 19]. Also, a recent systematic review of studies conducted in sub-Saharan Africa and elsewhere showed the benefit of ART on TB mortality, and indicated a 44% to 71% reduction in TB mortality risk [25].

TB mortality among HIV-positive TB patients is one of the key indicators that measures the impact of collaborative TB/HIV activities [26]. With the advent of ART, it has become increasingly clear that HIV-positive TB patients are not a homogeneous group, and TB mortality during TB treatment will differ between HIV-positive TB patients on ART and those not on ART. However, to date, there has been no study on TB mortality in HIV-positive TB patients on ART relative to HIV-negative TB patients. Also, to date, there has been no study on TB mortality in HIV-positive TB patients not on ART relative to HIV-negative TB patients.

The aim of the study, therefore, was to establish whether there was a difference in the TB treatment outcomes (morality and treatment default) in HIV-positive patients on ART compared to HIV-negative TB patients and also among HIV-positive patients not on ART compared to HIV-negative TB patients attending co-located TB services in Cape Town, South Africa. In addition, we aimed to examine impact of ART status and CD4 status on TB treatment outcomes among HIV-positive TB patients.”

Reviewer #2

Reviewer: Hashem Bishara
The authors did not provide data regarding TB culture results or the distribution of drug resistant versus drug sensitive forms of TB in the study population. This is a study limitation that should also be addressed.

We thank the reviewer for this important point and have included this limitation as suggested. Please see below the added text:

“A further limitation of our study was that the routinely collected program data available did not have details regarding TB culture results or the distribution of drug resistant versus drug sensitive forms of TB in the study population. Therefore, the study could not determine the influence of these factors on TB treatment outcomes.”

We thank the reviewers for helping us to revise and strengthen this manuscript. We hope that this revised version is now acceptable for publication in BMC Infectious Diseases Journal. We look forward to your feedback in due course.

Yours sincerely,

Mweete D. Nglazi, on behalf of the all authors