INT J TUBERC LUNG DIS 15(12):1714–1715

Correspondence

The impact of antiretroviral treatment programs on tuberculosis notification rates

We read with interest the article in this *Journal* by Zachariah et al.[1] describing the impact of an antiretroviral treatment (ART) programme on tuberculosis (TB) notification rates in a Malawian community. In January we published a paper assessing the impact of a high coverage ART programme on TB notification rates in a peri-urban community in South Africa.[2]

Both of these studies provide an ecological assessment of standardised, community TB notification rates following the scale-up of high coverage ART programmes. The Zachariah paper reported TB notifications from 2002 to 2009, in a community where an ART programme was initiated in 2003. We assessed TB rates from 1997 to 2008 in a community where ART became available in 2003, although implementation was only scaled up in 2005. Both African communities had high TB rates, although the rates in the Malawian community were 10 times lower than those reported in our study community. In addition, the communities had a similar, high prevalence of human immunodeficiency virus (HIV) infection (>20%), and both rapidly achieved ART coverage of over 80% of those 'in need' during the period of observation ('in need' was defined as a CD4 count <200 cells/μl in the South African study;[3] no definition was provided in the Malawian study).

Our study reported a >20% reduction in community TB notification rates following the scale-up of the ART programme, and we were gratified to see that the Malawian study, performed in a larger study population, confirmed our findings.

There are a couple of differences worth noting between the two studies. First, TB rates reported over a longer pre-ART period in the South African study contextualised the impact of HIV on TB community rates prior to the implementation of the ART programme. Second, regular community censuses, together with repeated cross-sectional HIV prevalence surveys, have enabled us to develop an HIV and ART model of the population in the South African community,[3] and we were therefore able to analyse TB notification rates stratified by both HIV and ART status. This analysis showed that the decline in both overall and retreatment TB notification rates was due to a significant decline in TB rates among the HIV-infected population, and more specifically among patients receiving ART. This finding substantially strengthens the argument that the association between high coverage ART and declining TB notification rates is a causal relationship. Furthermore, we were able to exclude several important potential confounders or alternative explanations for the main study finding, including possible changes in infection control policies and practices, improved TB completion rates or increased mortality.

These two studies contribute to our understanding not only of the individual level benefit of ART, but also of the population benefits of high coverage ART programmes, and add weight to the ongoing call for the scale-up of ART in areas heavily affected by the dual epidemics of HIV and TB.

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In reply

We thank Keren Middelkoop and colleagues for underlining the individual and population level benefits of reducing tuberculosis (TB) case notification rates through scaling up antiretroviral treatment (ART). The total number of incident cases of TB worldwide rose to 9.4 million in 2009—the highest recorded in history.[1] About 12% (1.1 million cases) of this caseload was HIV-associated, with four of five new HIV-TB cases occurring in sub-Saharan Africa. Both the

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Malawi and South African studies showed considerable reductions in new TB notifications associated with ART scale-up. For new TB, this was 20% in South Africa and 33% in Malawi. The latter also reported a 25% reduction in recurrent TB associated with ART scale-up.[2,3]

Two additional points merit mention.

First, in the Malawi study, the population in need of ART was defined as those with CD4 cell counts < 200 cells/μl in 2003, with the ceiling raised to <250 cells/μl in 2006 and recently to <350 cells/μl.[4] It is well known that the cumulative lifetime risk of TB in HIV-infected individuals is a function of time spent at various CD4-defined levels of risk, both before and during ART. The lower the CD4 count at ART initiation, the higher the risk of incident TB. In both the Malawi and South African cohorts, patients received ART 'rather late', thereby negating the overall potential impact of ART on incident TB and subsequent TB notifications.

Second, there are now calls to raise the threshold for ART initiation to 500 cells/μl, as is done in the USA, or even to immediate ART, as this is likely to reduce both HIV transmission and the incidence of AIDS-related TB.[5] In this regard, Malawi is moving towards implementation of immediate start of ART for HIV-infected pregnant women as the first step towards a programme aimed at selected early and universal ART coverage.[6]

The take-home message from both the Malawi and South African studies is that while ART is a proven critical intervention for case management of HIV-associated TB, much of its preventive potential for TB control is currently being squandered because it is being started too late.[5] Moving towards earlier and universal ART coverage is the way forward to prevent HIV-associated TB.

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6 Schouten E J, Jahn A, Midiani D, et al. Prevention of mother-to-child transmission of HIV and the health-related Millennium Development Goals: time for a public health approach. Lancet 2011; 378: 282–284.

ERRATUM

IN THE ARTICLE entitled **'Early antiretroviral treatment reduces risk of bacille Calmette-Guérin immune reconstitution adenitis'** by H. Rabie, A. Violari, T. Duong, et al. (Int J Tuberc Lung Dis 2011; 15(9): 1194–1200; http://dx.doi.org/10.5588/ijtld.10.0721), the following acknowledgement was omitted: The authors and the CHER team thank GlaxoSmithKline and the Departments of Health of Western Cape and Gauteng provinces for donation of antiretroviral medication to infants in the study. [http://dx.doi.org/10.5588/ijtld.10.0721-e]

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Reviewers Volume 15, 2011

During 2011, the Editorial Board of *The International Journal of Tuberculosis and Lung Disease* received invaluable help from a number of experts in the fields of tuberculosis and respiratory health in the evaluation of manuscripts submitted for publication. Their names are listed below.

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