Reviewer's report

Title: Diabetes and tuberculosis: the impact of the diabetes epidemic on tuberculosis incidence

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Reviewer: Reinout R van Crevel

Reviewer's report:

The authors have addressed an important research question. The association between tuberculosis and diabetes was well-known in the past, but somewhat forgotten in the second half of the 20th century with the advent of widely available treatment for both diseases. Now, with the current global growth of diabetes, the link between the two diseases is re-emerging. The epidemic growth of diabetes especially occurs in developing countries, where tuberculosis is highly endemic. As a result, diabetes and tuberculosis will increasingly present together, and this calls for renewed interest in this topic.

The methods are appropriate and well-described, and provide sufficient detail to repeat the study. However, there is a concern with the data-source for relative risk for tuberculosis in diabetes, which was used for modeling. Kim et al (ref 17) indeed did the best longitudinal study on DM as a risk factor for TB. However, they only reviewed government employees (which may have biased prevalence of TB as well as DM), who had a blood glucose test in 1988 and 1990 (using cut-off points slightly different from WHO: higher for fasting, lower for post-prandial). Results from survey in 1988 and 1990 showed discrepancy with regard to diabetes diagnosis in 30%. It is unclear what causes this difference. More diabetes patients had bacteriological confirmation of TB, but this may have been biased by the fact that (diagnostic) management of diabetes patients was more thorough. The higher smear- or culture positivity in diabetic TB patients is no consistent finding in the literature. Some have reported higher smear-positivity (Singla 2006, Restrepo 2006), but a case control study in Turkey found the opposite (Bacakoglu, 2001), and fewer as well as more cavities have been associated with diabetes (Nissapatorn, 2005; Hendy 1983; Perez-Guzman 2001). Little can be said about females, as only 3 female diabetic pts in that study developed TB.

The manuscript adheres to the relevant standards for reporting and data deposition. The tables are helpful and clear.

The discussion and conclusions are well balanced and adequately supported by the data. The authors might refer to other studies which have examined the association between TB and DM, especially in less-developed settings like Tanzania (Mugusi, 1990) and Indonesia (Alisjahbana, 2006), and might comment on some of the shortcomings of Kim’s study.

The association between TB and DM has implications for public health, which the authors not fully address. Screening of patients with diabetes for tuberculosis and vice-versa may have significant health implications and has been advocated by some. To my knowledge, the impact of such interventions has not been formally examined. In a low TB-endemic setting, active screening and treatment of latent tuberculosis among diabetics, as advocated in different guidelines, will reduce the risk of active tuberculosis, but when TB is endemic, such a strategy may be less effective, or even detrimental, as INH-prophylaxis may induce drug-resistance in subjects who prove to have active, and not latent TB. From a practical point of view, screening might be targeted to pts over 30yrs of age or so. The authors should comment on this, referring tc guidelines. The recent international standard for TB-care, does not mention diabetes at all (Hopewell, Lancet Inf Dis 2006).

What next?: Accept after minor essential revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no interests