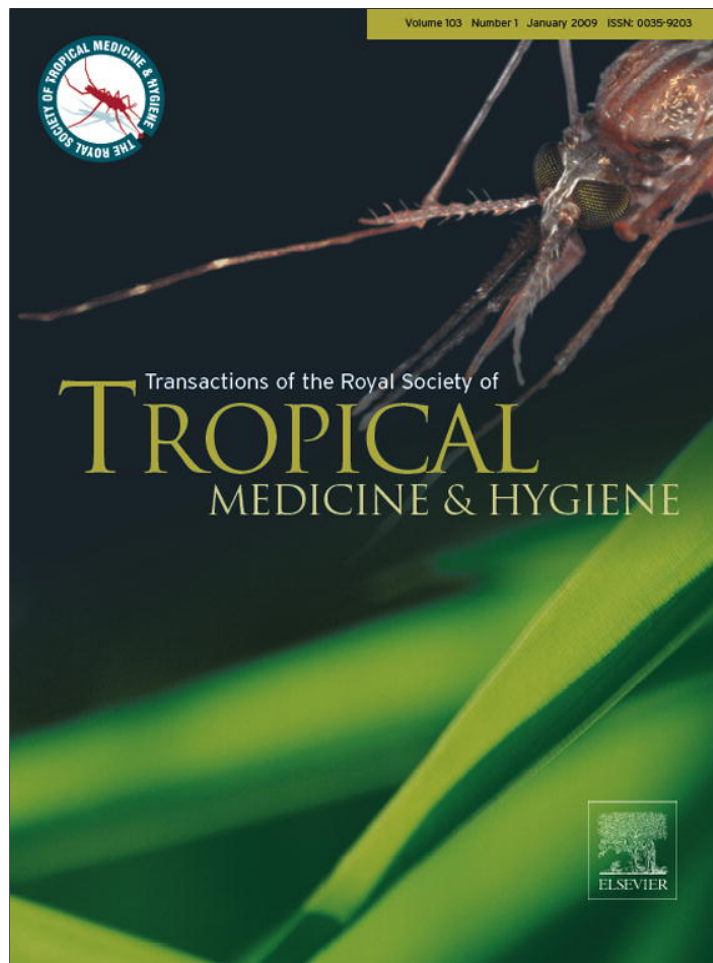


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## MINI-REVIEW

# Links between diabetes mellitus and tuberculosis: should we integrate screening and care?

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**Summary** Recent systematic reviews show that diabetes mellitus (DM) increases the risk and odds of developing tuberculosis (TB), especially in young people and in developing countries with a high background incidence of TB. There are no data showing that TB increases the risk of DM. The large dual burden of disease may make management of both conditions more difficult. High-quality implementation research is needed to assess the value and ways of screening for DM in patients with TB and vice versa, and to set up standardised systems of monitoring and evaluation based on the directly observed treatment, short-course (DOTS) model used for TB control.

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The global burden of disease from diabetes mellitus (DM) and tuberculosis (TB) is huge. In 2007, it was estimated that there were 246 million people living with DM, 6 million new cases and 3.5 million deaths. In the same year, it was estimated that there were 14.4 million people living with TB, 9.2 million new cases and 1.7 million deaths. While it is widely appreciated that 95% of TB patients live in the developing world, it is not so well known that 70% of DM patients also live in developing countries, especially in Southeast Asia and the Western Pacific. Are these two diseases connected, and if so, what should be done about it?

There are many risk factors for TB, which include HIV/AIDS, silicosis, malnutrition and smoking. While the link between DM and TB has been known about since Roman

times, it is only recently that unequivocal evidence has been gathered to show a strong association between the two diseases. A systematic review, using PubMed and EMBASE databases, identified 13 relevant, age-adjusted, quantitative observational studies and found that DM is associated with an increased risk of TB.<sup>1</sup> In the three cohort studies analysed, the relative risk of TB in patients with DM was 3.1 (95% CI 2.27–4.26), and in the case–control studies, the odds ratios of TB ranged from 1.16 to 7.83. The risks were higher in young people and in countries with a high background incidence of TB. Another search, using Medline and appraising studies published after 1995, found an increase in risk or odds of TB in patients with DM that ranged from 1.5 to 7.8.<sup>2</sup> In India, with an estimated 21 million adults with DM and 900 000 incident pulmonary tuberculosis (PTB) cases in 2000, DM accounted for nearly 15% of PTB and 20% of smear-positive PTB.<sup>3</sup>

DM therefore appears to increase the risk of active TB. This association is supported on biological grounds by some DM patients having evidence of impaired cell-mediated

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immunity, renal failure, micronutrient deficiency and pulmonary microangiopathy, all of which predispose to PTB. Reviews of clinical studies<sup>2</sup> show that DM patients with TB often present with lower lung infiltrates (similar to patients with HIV/AIDS), and may have worse treatment outcomes in terms of smear and culture conversion, case fatality and treatment failure. There are no data to show that TB increases the risk of DM, although as a chronic infectious disease TB may make the management of DM more difficult, and rifampicin (one of the key drugs in any anti-TB regimen) may have hyperglycaemic effects.

Should TB patients be screened for DM? A clinical study in Tanzania, where there was already a high threshold for recognising DM, showed that unless an oral glucose tolerance test was performed at the start of therapy, over half the cases with DM would have been missed.<sup>4</sup> It may therefore be of value to screen TB patients for DM, but how this is best done needs further evaluation. Should patients with DM be screened routinely for TB? Simple screening algorithms, which are currently used in HIV-infected patients in high HIV–TB burden countries, evaluate patients for cough, fever, night sweats, weight loss and chest pain. A positive response indicates the need for further assessment by sputum smear examination and chest radiography. The value of such screening tools in the diabetic clinics of developing countries is not known.

Finally, in most developing countries there are no systematic ways of monitoring or evaluating patients with non-communicable diseases (NCD). This has to change. The 'directly observed treatment, short-course' (DOTS) framework for TB control, developed by the International Union against Tuberculosis and Lung Disease and WHO, has allowed structured, well-monitored services to be delivered to millions of TB patients in some of the poorest countries in the world. In a resource-poor country such as Malawi, the DOTS model was successfully adapted for scaling up and monitoring antiretroviral therapy to AIDS patients. This model can be adapted for NCDs, such as DM.<sup>5</sup> With treatment cards and

registers, it would be feasible to do quarterly cohort reports on DM treatment outcomes, which include the monitoring and evaluation of co-morbidities such as TB.

The Millennium Development Goal 6, target 8, specifies that the incidence of infectious diseases such as TB should be halted and reversed by 2015. To succeed in achieving this target, it is important to focus in resource-poor countries not only on HIV/AIDS but also on the burgeoning epidemic of DM as a significant epidemiological risk factor. The link between TB and DM has been established; what is now needed is good-quality implementation research to screen for, care for and monitor this dual burden of disease.

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