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## Clinical management of concurrent diabetes and tuberculosis and the implications for patient services

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### Abstract

Diabetes triples the risk for active tuberculosis, thus the increasing burden of type 2 diabetes will help to sustain the present tuberculosis epidemic. Recommendations have been made for bidirectional screening, but evidence is scarce about the performance of specific tuberculosis tests in individuals with diabetes, specific diabetes tests in patients with tuberculosis, and screening and preventive therapy for latent tuberculosis infections in individuals with diabetes. Clinical management of patients with both diseases can be difficult. Tuberculosis patients with diabetes have a lower concentration of tuberculosis drugs and a higher risk of drug toxicity than

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See Online for appendix

#### Contributors

ALR, FP, JAC, and RvC did the literature review and wrote the first draft of the report. RA provided specific input for the section on pharmacokinetic interactions. All authors provided input to the report and approved the final version.

#### Declaration of interests

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tuberculosis patients without diabetes. Good glycaemic control, which reduces long-term diabetes complications and could also improve tuberculosis treatment outcomes, is hampered by chronic inflammation, drug-drug interactions, suboptimum adherence to drug treatments, and other factors. Besides drug treatments for tuberculosis and diabetes, other interventions, such as education, intensive monitoring, and lifestyle interventions, might be needed, especially for patients with newly diagnosed diabetes or those who need insulin. From a health systems point of view, delivery of optimum care and integration of services for tuberculosis and diabetes is a huge challenge in many countries. Experience from the combined tuberculosis and HIV/AIDS epidemic could serve as an example, but more studies are needed that include economic assessments of recommended screening and systems to manage concurrent tuberculosis and diabetes.

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## Introduction

Tuberculosis is a major global health problem. In 2012, 8.6 million people developed tuberculosis and 1.3 million died from the disease.<sup>1</sup> Diabetes increases the risk of developing active tuberculosis<sup>2,3</sup> and is associated with worse tuberculosis treatment outcomes.<sup>4</sup> Globally, 15% of tuberculosis cases are estimated to be attributable to diabetes.<sup>5</sup> The International Diabetes Federation predicts that the number of people worldwide with diabetes will increase by 55% during the next 20 years, with the largest increase expected in Africa (+109%).<sup>6</sup> Therefore, diabetes will make an increasingly important contribution to the tuberculosis epidemic. Whether screening for diabetes in patients with tuberculosis (and the converse) is feasible and cost effective, and how those identified with concurrent tuberculosis and diabetes can be best managed, are key research questions (panel 1).

In this Series paper, we focus on tuberculosis-endemic settings. We assess the epidemiology of tuberculosis and diabetes, screening for tuberculosis in patients with diabetes and the converse, and issues related to clinical management of concurrent tuberculosis and diabetes. We also discuss implications of the joint epidemic for health services and public health, and outline key questions for future research.

## Epidemiology

### Diabetes, tuberculosis, and evidence of an association between both diseases

Tuberculosis is caused by *Mycobacterium tuberculosis*, which is thought to latently infect a third of the global population, placing such individuals at a 5–10% average lifetime risk of progressing to the active form of the disease. Individuals with HIV are at a 12–20 times increased risk of developing tuberculosis. The prevalence and annual incidence of tuberculosis varies greatly geographically, as does laboratory capacity to test for this disease (figure 1). Tuberculosis requires treatment with multiple antituberculosis drugs for at least 6 months. Around 500 000 cases globally are of multidrug-resistant tuberculosis, which need to be treated with expensive second-line drugs and for long durations.<sup>7</sup>

Evidence shows that both type 1 and type 2 diabetes can increase tuberculosis risk. However, as type 2 diabetes accounts for 85–95% of global cases of diabetes the burden of comorbid disease from type 2 diabetes is much greater and thus the main focus of this paper. Diabetes