



**Figure** Chromatograms for drugs extracted from patient hair samples (Panel A) and MDR-TB drug panel (Panel B) showing multiple transitions monitored for each drug. PZA = pyrazinamide; LFX = levofloxacin; MFX = moxifloxacin; LZD = linezolid; KAN = kanamycin; DLM = delamanid; BDQ = bedaquiline; cps = counts per second; MDR-TB = multidrug-resistant tuberculosis.

(BDQ), delamanid (DLM), and kanamycin A (KAN) into this multi-analyte panel (Figure, Panel B), and patient hair extraction protocols for these drugs are in progress.

We developed assays to accurately and non-invasively determine long-term exposure to key second-line anti-tuberculosis drugs in hair within a single panel. Although various groups have published multi-TB drug panels in plasma,<sup>4–6</sup> to our knowledge this is the first report demonstrating a similar panel for MDR-TB drugs in hair. Further analytic validation of these hair assays and testing their utility in clinical settings is underway.

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#### References

- Zumla A I, Gillespie S H, Hoelscher M, et al. New antituberculosis drugs, regimens, and adjunct therapies: needs, advances, and future prospects. *Lancet Infect Dis* 2014; 14: 327–340.
- Research Excellence to Stop TB Resistance (RESIST-TB). DR-TB Clinical Trial Progress Report. [http://www.resisttb.org/?page\\_id=1602](http://www.resisttb.org/?page_id=1602). Accessed January 2015.
- Metcalfe J Z, O'Donnell M R, Bangsberg D R. Moving beyond directly observed therapy for tuberculosis. *PLoS Med* 2015; 12(9): e1001877.
- Kim H J, Seo K A, Kim H M, et al. Simple and accurate quantitative analysis of 20 anti-tuberculosis drugs in human plasma using liquid chromatography-electrospray ionization-tandem mass spectrometry. *J Pharm Biomed Anal* 2015; 102: 9–16.
- Song S H, Jun S H, Park K U, et al. Simultaneous determination of first-line anti-tuberculosis drugs and their major metabolic ratios by liquid chromatography/tandem mass spectrometry. *Rapid Commun. Mass Spectrom* 2007; 21: 1331–1338.
- Han M, Jun S H, Lee J H, Park K U, Song J, Song S H. Method for simultaneous analysis of nine second-line anti-tuberculosis drugs using UPLC-MS/MS. *J Antimicrob Chemother* 2013; 68: 2066–2073.

#### Screening for active tuberculosis in a diabetes mellitus clinic in Soweto, South Africa

People living with diabetes mellitus (DM) have a three times higher risk of developing tuberculosis (TB) than people without DM, as well as a five times

higher risk of death during TB treatment.<sup>1,2</sup> Although DM does not increase TB risk to the same magnitude as HIV/AIDS (human immunodeficiency virus/acquired immune-deficiency syndrome), DM is more prevalent and is a significant driver of the global TB epidemic. In South Africa, a country with an extreme TB epidemic, the synergistic effect of DM and TB could reverse recent gains against TB.

We performed a cross-sectional study to identify patients with active TB in the adult diabetes clinic at Chris Hani Baragwanath Academic Hospital in Soweto, South Africa. From June 2014 through January 2015, 672 eligible adults ( $\geq 18$  years of age with documented DM) were interviewed regarding demographics as well as TB history, risk factors, and symptoms (cough, fever, night sweats, or weight loss). Symptomatic participants provided a sputum sample for Xpert<sup>®</sup> MTB/RIF analysis (Cepheid, Sunnyvale, CA, USA). Anthropometrics, glycated hemoglobin (HbA1c) level, and DM treatment were abstracted from medical records.

The average age was 51 years, 61% were female, median body mass index (BMI) was 31.1 kg/m<sup>2</sup> (interquartile range [IQR] 26.0–35.9), and 72% had type II diabetes. Twenty-seven patients reported at least one TB symptom and provided a sputum sample, although no cases of active TB were diagnosed. Six participants (1%) reported a history of TB diagnosed after their initial DM diagnosis; these cases occurred at 4 months, 16 months, 5 years, 10 years, 11 years, and 15 years after DM diagnosis. Overall, 10% reported a lifetime history of TB.

Eighty-three per cent of our participants were living in houses, but 88% had a household monthly income of >1000 Rand (US\$70)/month (with 22% >5000 Rand [US\$345]/month), well below the average income, possibly due to the high proportion of pensioners in our sample. Eighty-nine per cent had more than primary education. However, our population had poorly controlled DM, as defined by elevated HbA1c (median 8.3, IQR 7–10.3), a risk factor for TB. This expected risk may be mitigated by other factors that may reduce TB risk in this sample, including high BMI, nearly universal receipt of insulin, low smoking prevalence (26% current; 32% ever), and few with comorbid HIV (48/672 participants, 7%).<sup>3</sup> However, we believe this DM clinic to be representative in this high TB incidence setting.

There are no prior reports of screening for TB in people with diabetes in South Africa, but meta-analyses have established an odds ratio of around three in other settings,<sup>1</sup> and the population attributable fraction of DM for TB in South Africa is currently estimated at 15%.<sup>3</sup> Epidemiologic and interventional research must continue in South Africa and elsewhere to measure the TB risk in disparate DM populations and detect when

DM prevalence reaches the critical level necessary to affect TB rates.<sup>4</sup> In addition, the cost-effectiveness of measures to detect and prevent TB in people with DM should be evaluated before uniform bi-directional screening<sup>5</sup> is implemented in South Africa.

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## References

- 1 Jeon C Y, Murray M B. Diabetes mellitus increases the risk of active tuberculosis: a systematic review of 13 observational studies. *PLOS MED* 2008; 5(7): e152.
- 2 Baker M A, Harries A D, Jeon C Y, et al. The impact of diabetes on tuberculosis treatment outcomes: a systematic review. *BMC Med* 2011; 9(1): 81.
- 3 Lönnroth K, Roglic G, Harries A D. Improving tuberculosis prevention and care through addressing the global diabetes epidemic: from evidence to policy and practice. *Lancet Diabetes Endocrinol* 2014; 2: 730–739.
- 4 Badawi A, Sayegh S, Sallam M, et al. The global relationship between the prevalence of diabetes mellitus and incidence of tuberculosis: 2000–2012. *Glob J Health Sci* 2014; 7(2): 183.
- 5 Kapur A, Harries A D, Lönnroth K, Wilson P, Sulistyowati L S. Diabetes and tuberculosis co-epidemic: the Bali Declaration. *Lancet Diabetes Endocrinol* 2016; 4: 8–10.