insight of drug susceptibility pattern in Mumbai, India.

Our centre is a tertiary referral centre for tuberculosis in Mumbai with a bias towards non-responders and relapse cases. We did a retrospective analysis of 1676 isolates from pulmonary and extrapulmonary tuberculosis samples received from June, 2015, to June, 2016, from a referral network of public and private health-care providers. All samples were tested in our accredited lab for phenotypic drug susceptibility testing using mycobacterium growth indicator tube as per WHO-recommended drug-critical concentrations. As in the original study,[1] moxifloxacin was tested at concentrations of 0·5 µg/mL and 2·0 µg/mL (table)

In agreement with previous studies,[2,3] this analysis also shows high incidence of rifampicin resistance and concomitant resistance to pyrazinamide and fluoroquinolones (table).

Notably low resistance to moxifloxacin at the critical concentration of 2·0 µg/mL has offered some respite. Moxifloxacin is considered as a cornerstone drug in management of multidrug-resistant tuberculosis, and is recommended by WHO in settings with high resistance to the earlier-generation fluoroquinolones. We believe that despite apparent resistance at 0·5 µg/mL, moxifloxacin could possibly be retained in the regimen at a higher dose[4] with regular QTc-interval monitoring on electrocardiogram.

We declare no competing interests.

*Shashank Ganatra, Zarir Udwadia, Camilla Rodrigues
shashankganatra11@gmail.com

Hinduja National Hospital and Medical Research Centre, Mahim, Mumbai 400016, India

	n	Pyrazinamide resistance (100 µg/mL)	Ofloxacin resistance (2·0 µg/mL)	Moxifloxacin resistance (0·5 µg/mL)	Moxifloxacin resistance (2·0 µg/mL)
All cases	1676	941 (56%)	805 (48%)	707 (42%)	123 (7%)
Rifampicin susceptible	578	20 (3%)	17 (3%)	13 (2%)	2 (0·3%)
Rifampicin resistance (1·0 µg/mL)	1098	921 (84%)	788 (72%)	694 (63%)	121 (11%)

MGIT=mycobacterium growth indicator tube. DST=drug susceptibility test.

Table: **Phenotypic MGIT DST patterns in 1676 cases from June, 2015, to June, 2016**

1 Zignol M, Dean AS, Alikhanova N, et al. Population-based resistance of *Mycobacterium tuberculosis* isolates to pyrazinamide and fluoroquinolones: results from a multi country surveillance projects. *Lancet Infect Dis* 2016; **16:** 1185–92.

2 Mullerpattan J, Udwadia Z, Shah K, Rodrigues C. Possible impact of the standardized category IV regimen on multidrug-resistant tuberculosis patients in Mumbai. *Lung India* 2016; **33:** 253.

3 Dalal A, Pawaskar A, Prabhudesai P, et al. Resistance patterns among multidrug-resistant tuberculosis patients in Greater Metropolitan Mumbai: trends over time. *PLoS One* 2015; **10:** e0116798.

4 Ganatra S, Udwadia Z, Rodrigues C, et al. High dose moxifloxacin for drug resistant tuberculosis; is 600mg the optimal dose in high resistance settings? *Am J Respir Crit care Med* 2016; **193:** A4570.

Predicting tuberculosis without knowing test specificity

In a recent paper by Jennifer Ho and colleagues,[1] a large study population was screened for tuberculosis with the Xpert MTB/RIF test. They calculated the specificity of this test on the basis of the positive predictive value and disease prevalence in Ca Mau province, Vietnam.

A broad range of patients who are known not to have the disease (eg, healthy people, patients with non-tuberculous lung diseases, and patients who have been cured of tuberculosis) should be included in the study to establish the specificity of the test.[2] The same is true for determining the sensitivity of a new test; one is inevitably in the need of a patient group who are known to have the disease.

Only after having found out the intrinsic properties (sensitivity and specificity) of a new test can we go further ahead to do field studies to determine the predictive values in different geographical settings, where disease prevalences might differ. To calculate the positive predictive value correctly, we need to know both of the sensitivity and specificity of a given test. This can be done in two ways: either the researchers use the previously determined sensitivity and specificity rates or they calculate them by incorporating the patients confirmed to have tuberculosis and patients who are known to not have tuberculosis into the study.

Since the study by Ho and colleagues did not include both of these patient groups, the specificity of the Xpert MTB/RIF test and the positive predictive value within the given population cannot be correctly calculated from this study.

Moreover, we hardly can be in accord with the calculated prevalence rate (169 of 43 435, 0·39%), since all Xpert MTB/RIF positive results were considered as true positives, which could falsely increase the observed prevalence. Another question about the given prevalence rate arises because of the probable verification bias that might lead to underdiagnosis;[2] by contrast with patients with positive Xpert MTB/RIF results (0·39%), those with negative results (53·01%) did not have the further tuberculosis investigations mentioned in the Article and those who could not produce sputum (46·6%) were not subjected to any tuberculosis investigation.

Considering the aforementioned points, the conclusions of this study should be interpreted cautiously.

We declare no competing interests.

*O Kaya Koksalan, Siran Keske, Yesim Yasin, Zeki Kilicaslan
okkoksalan@hotmail.com

Institute for Medical Experimental Research (DETAE), Istanbul University, Istanbul, Turkey (OKK); Department of Infectious Diseases, VKV American Hospital, Istanbul, Turkey (SK); Department of Public Health, School of Medicine, Acibadem University, Istanbul, Turkey (YY); and Department of Chest Diseases and Tuberculosis, Istanbul Medical Facility, Istanbul University, Istanbul, Turkey (ZK)

1 Ho J, Nguyen PT, Nguyen TA, et al. Reassessment of the positive predictive value and specificity of Xpert MTB/RIF: a diagnostic accuracy study in the context of community-wide screening for tuberculosis. *Lancet Infect Dis* 2016; **16:** 1045–51.
2 Ransohoff DF, Feinstein AR. Problems of spectrum and bias in evaluating the efficacy of diagnostic tests. *N Engl J Med* 1978; **299:** 926–30.

Authors' reply

We thank O Kaya Koksalan and colleagues for their correspondence about our study, which assessed the performance of Xpert MTB/RIF in the context of community-wide screening for tuberculosis.[1] We acknowledge that the concern regarding our approach to estimating sensitivity and specificity is a valid one. However, in the present study, we have not sought to estimate the sensitivity of Xpert.

What we have done, on a large scale, is to directly assess the positive predictive value of the Xpert test in the screening context. Positive predictive value is estimated only in people with positive test results; in this case the 169 people with a positive Xpert result. We have used a range of plausible criteria for establishing which of these people with a positive Xpert result were true positives and which were false positives. One of these criteria is the presence of a positive culture for *Mycobacterium tuberculosis*. An alternative criterion is the presence of an abnormal chest radiograph consistent with a radiological diagnosis of tuberculosis. We have acknowledged that this was not investigated in a blinded way and could overestimate the number of true positives. Nevertheless, we think it is reasonable to assume that the true positive rate lies somewhere between these two estimates (61–84%).

We then made a range of plausible assumptions about the sensitivity of Xpert, using data from a Cochrane review of 22 studies and almost 9000 individuals,[2] and the prevalence of tuberculosis in the population, using data from the present study and from a previous prevalence survey.[3] With these data, we have reverse-calculated what the specificity must have been to result in the observed positive predictive value. In our original Article, table 3 shows that, under a wide range of plausible assumptions, the specificity must have been at least 99·57% and was probably higher than this.

Although this is a novel approach, we stand by its validity. The reference standards used included a gold standard microbiological reference, and a composite reference that also included chest radiography. A study by Theron and others[4] done on 480 individuals suspected of having tuberculosis in South Africa, also suggested that a composite reference standard could be more appropriate to assess the diagnostic accuracy of molecular tests for tuberculosis, especially in settings where mycobacteria culture facilities can be overburdened and under-resourced.

Because of the many Xpert tests used in this study, we were able to estimate the positive predictive value and specificity of this test with more precision than previous studies combined.[2] Both the positive predictive value and specificity of Xpert for *M tuberculosis* detection were substantially greater than previous estimates.[2] Taken together with previous data on the sensitivity of the test, our data suggest that the accuracy of Xpert is adequate to support its role as a primary screening tool for detecting patients with tuberculosis in the context of community-wide screening in a moderate to high prevalence setting.

We declare no competing interests.

*Jennifer Ho, Guy B Marks
jennifer.ho@sydney.edu.au

Woolcock Institute of Medical Research, University of Sydney, Sydney, Australia (JH, GBM); South Western Sydney Clinical School, University of New South Wales, Sydney, Australia (JH, GBM); and Centre for Research Excellence in Tuberculosis (TB-CRE), University of Sydney, Sydney, Australia (JH, GBM)

1 Ho J, Nguyen PT, Nguyen TA, et al. Reassessment of the positive predictive value and specificity of Xpert MTB/RIF: a diagnostic accuracy study in the context of community-wide screening for tuberculosis. *Lancet Infect Dis* 2016; **16:** 1045–51.
2 Steingart KR, Schiller I, Horne DJ, Pai M, Boehme CC, Dendukuri N. Xpert(R) MTB/RIF assay for pulmonary tuberculosis and rifampicin resistance in adults. *Cochrane Database Syst Rev* 2014; **1:** CD009593.
3 Hoa NB, Sy DN, Nhung NV, Tiemersma EW, Borgdorff MW, Cobelens FG. National survey of tuberculosis prevalence in Viet Nam. *Bull World Health Org* 2010; **88:** 273–80.
4 Theron G, Peter J, van Zyl-Smit R, et al. Evaluation of the Xpert MTB/RIF assay for the diagnosis of pulmonary tuberculosis in a high HIV prevalence setting. *Am J Resp Crit Care Med* 2011; **184:** 132–40.

Prejudice and reality about infection risk among Syrian refugees

In their Personal View, Mishal Kahn and colleagues[1] propose that policy decisions about the risks of infectious diseases among migrants and refugees should be based on evidence for health risks and burdens to health systems, rather than prejudice or unfounded fears. Although the perception and generalisation that migrants and refugees carry a higher load of infectious diseases is questionable, it is undeniable that the Syrian conflict produced suitable conditions leading to the re-emergence of tuberculosis, cutaneous leishmaniasis, poliomyelitis, and measles.[2] In this Correspondence we aim to add data about infections in Syrian refugees.

As of July 20, 2016, Turkey hosts 2·7 million of 4·8 million Syrian refugees.[3] In Turkey, 10 689 refugees were screened for tuberculosis by the Ministry of Health in 2014–15 and the prevalence was 18·7 per 100 000, which is not higher than that in the Turkish population. Thereafter, Turkey