95   Effect of Xpert MTB/RIF On Early Mortality in Adults With Suspected TB: A Pragmatic Randomized Trial

Gavin Churchyard[1], Kerrigan McCarthy[1], Katherine L. Fielding[2], Wendy Stevens[3], Violet Chihota[1], Mark Nicol[4], Norbert Ndjeka[5], Alison D. Grant[2], David Mametja[5]

[1]*Aurum Institute, Houghton, South Africa*, [2]*London School of Hygiene and Tropical Medicine, London, United Kingdom*, [3]*National Health Laboratory Service, Sandringham, South Africa*, [4]*University of Cape Town, Cape Town, South Africa*, [5]*South African Department of Health, Pretoria, South Africa*

Background: South Africa has phased in Xpert MTB/RIF, replacing sputum smear microscopy in laboratories, as the first-line diagnostic test for tuberculosis (TB). In a pragmatic cluster randomized trial, we evaluated the effect of Xpert on early mortality in persons with suspected TB.

Methodology: 20 laboratories in 4 provinces were randomized to intervention (immediate Xpert implementation) or control (microscopy, with Xpert implementation deferred) arms. At 2 primary health clinics served by each laboratory, a systematic sample of adults with suspected TB, identified by clinic staff, was invited to participate; demographic and clinical data relevant to TB and mortality risk were collected. Vital status after 6 months was determined by interview of participants or relatives and using the National Vital Status Register. The intervention effect on mortality risk was estimated using methods appropriate for cluster randomized trials with small number of clusters. An adjusted analysis was conducted to control for baseline differences of individual-level factors by study arm.

Results: Between June to November 2012, 4,972 persons with suspected TB were screened for the study. 4,712 (94.8%) were eligible and 4,665 (99.0%) contributed to the analysis. Of 4,665 participants (median age 36 years, 62% female, 93% South African), 76% (3,551) knew their HIV status, 62% (2,212/3,551) reported being HIV positive with a median self-reported CD4 count of 311 cells/mm^3, 33% of whom reported ever being on ART, all similar by study arm. Participants in the intervention vs. control arm had lower socioeconomic indicators and were more likely to be asymptomatic (7.5% vs. 4.3%). Among 4,665 participants, 4,617 (99.0%) had known vital status at 6 months, with 208 deaths (4.5%). The 6 month mortality risk in the intervention and control arms were 3.9% (91/2,326) and 5.0% (117/2,339) respectively (risk ratio [RR] 0.86, 95% CI: 0.58, 1.27, p=0.42). After adjusting for age, sex, BMI, HIV status and factors imbalanced at baseline, the adjusted RR was 1.08 (95% CI: 0.73, 1.61; p=0.67). The 6 month mortality risk for self-reported HIV positive vs. -negative participants was 5.6% (124/2,212) and 1.9% (26/1,339) respectively (RR 2.63 (95%CI: 1.68, 4.12, p<0.001); and for HIV positive participants on vs. not on ART was 4.1% (30/730) and 6.3% (94/1,482) respectively (RR 0.63, 95% CI: 0.41, 0.97, p=0.03).

Conclusions: HIV prevalence and all-cause mortality were high among people with suspected TB, and mortality was not reduced by Xpert replacing smear microscopy in laboratories. Our data suggest that a sensitive diagnostic test needs to be supported by systems linking to appropriate care, particularly ensuring that people know their HIV status and those eligible, start ART promptly.