A Pilot RCT of GeneXpert MTB/RIF on a Mobile HIV Testing Unit in South Africa

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BACKGROUND

- Despite substantial investment in facility-based diagnosis and treatment of TB, TB control at the community level remains poor.
- Through early detection, active, mobile, community-based TB case finding may improve both individual outcomes and TB control at the population level.
- GeneXpert MTB/RIF, a rapid, automated molecular diagnostic tool, has great potential for intensified TB case finding at the community level.

OBJECTIVE

- To establish the feasibility of a Test & Treat TB Intervention that:
  1. Uses GeneXpert screening on a mobile testing unit, and
  2. Shortens time to TB treatment initiation compared to clinic-based referrals for TB, with the goal of increasing TB treatment completion rates.

METHODS

Study Setting and Participant Enrollment

- We conducted a pilot randomized trial to evaluate a Test & Treat TB intervention using GeneXpert MTB/RIF compared to usual care on a mobile HIV testing unit in Umlazi Township, South Africa.
- We enrolled English- or Zulu-speaking adults (≥18 years) waiting for HIV testing at the mobile HIV testing unit.
- All HIV-infected participants were eligible for TB screening, as well as HIV-uninfected participants having any TB symptoms.

Randomization (Usual Care vs Test & Treat TB)

- Randomization occurred by day.
- All patients seen at the mobile unit on a given day were exposed to the same arm to:
  - simplify logistical considerations, and
  - minimize the risk of participants interacting with the other study strategy.

Usual Care Arm

- Participants with TB symptoms were asked to produce a sputum sample on the mobile unit, which was sent for GeneXpert MTB/RIF testing at the provincial hospital.
- Participants were contacted ~7 days later with results and treatment referral.
- Symptomatic participants who could not produce a sputum were referred to a local clinic.

METHODS (CONTINUED)

Test & Treat TB Arm

- HIV-infected or HIV-uninfected/TB symptomatic participants were screened with GeneXpert on the mobile unit and received TB test results by SMS.
- A dedicated research nurse encouraged participants to use a nebulizer.
- GeneXpert-positive participants were provided:
  1. A TB treatment starter pack (3-week supply of medication and referral to a local clinic to continue treatment)
  2. Monthly SMS reminders for the duration of TB treatment
  3. Cashless incentives for retrieving starter pack, linking to TB care, and completing TB treatment

Outcomes

Primary Outcome

- The proportion of GeneXpert-positive individuals who completed 6 months in TB care.

Secondary Outcomes

- Secondary outcomes included:
  - Proportion of mobile testers screened for TB
  - Proportion of eligible participants able to produce sputum samples
  - TB prevalence among those tested
  - Distribution of TB symptoms
  - Return for TB test result
  - Linkage to TB care (first visit to a local clinic)
  - ART initiation for those HIV co-infected

Outcome Assessment

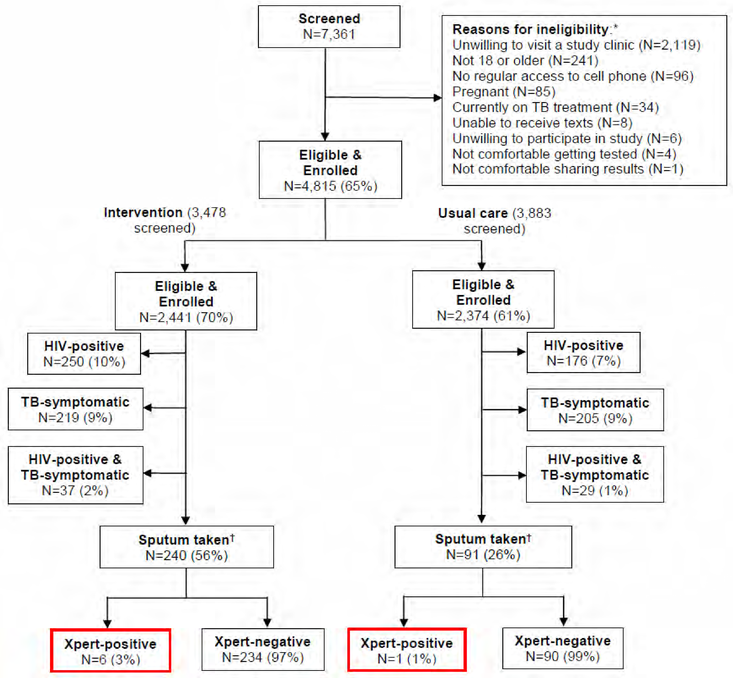
- Three weeks after enrollment, we contacted clinics to ascertain attendance at the first TB and/or HIV visit; we also contacted clinics at six months to assess retention in care.

Data Analysis

- We used an intent-to-treat approach to analyze participants in the group they were assigned.
- We compared rates of TB case identification between arms.
- We used Poisson regression to examine the effect of sex, age, number and type of TB symptoms, and HIV status on ability to produce a sputum sample.

RESULTS

Figure 1. Participant flow



- * Not mutually exclusive.
- † Denominator is participants who were only HIV-positive + participants who were only TB-symptomatic – participants who were both HIV-positive & TB-symptomatic.

Table 2. Factors affecting the likelihood of not providing a sputum sample (among all sputum-eligible participants)

Factor	Adjusted iRR (95% CI)	p-value
Clinical characteristics		
HIV-positive & no TB symptoms vs. HIV-positive & TB-symptomatic	2.01 (1.05, 3.85)	0.03
HIV-negative & TB-symptomatic vs. HIV-positive & TB-symptomatic	1.64 (0.85, 3.19)	0.14
Mobile testing location		
Mall/Other vs. Community area/Home	1.40 (1.00, 1.95)	0.05
Transit area vs. Community area/Home	1.11 (0.79, 1.57)	0.55
Cohort characteristics		
Age, per decade	1.15 (1.01, 1.31)	0.04

Table 1. Baseline characteristics of HIV-infected participants

	Intervention (n=2,441)	Usual care (n=2,374)	Overall (n=4,815)
Age, mean years (SD)	31 (13)	31 (13)	31 (13)
Sex			
Female n, (%)	1,206 (51)	1,109 (48)	2,315 (49)
Male n, (%)	1,181 (50)	1,200 (52)	2,381 (51)
Prior HIV testing			
Yes n, (%)	2,173 (95)	2,112 (95)	4,285 (95)
No n, (%)	104 (5)	121 (5)	224 (5)
HIV status			
Positive n, (%)	250 (9)	176 (7)	426 (9)
CD4 mean (SD)	435 (234)	498 (345)	440 (246)
CD4 median (IQR)	419 (264, 592)	413 (205, 769)	419 (259, 600)
TB symptoms			
Cough n, (%)	129 (5)	99 (4)	228 (5)
Weight loss n, (%)	84 (4)	89 (4)	173 (4)
Night sweats n, (%)	102 (4)	89 (4)	191 (4)
Fever n, (%)	82 (3)	56 (2)	138 (3)

KEY FINDINGS

- Seven participants tested GeneXpert-positive, six in the intervention and one in usual care; 71% were HIV-positive and 43% were TB symptomatic.
- Overall, only 42% of eligible participants could produce sputum (intervention: 56%; usual care: 26%).
- All 6 GeneXpert-positive participants in the intervention arm liked to care within 6 months, and 5 of 6 completed TB treatment.
- The single GeneXpert-positive participant in usual care did not like to TB care.

LIMITATIONS

- There was high ineligibility due to unwillingness to visit a prespecified clinic.
- Many eligible participants were not able to produce sputum on the mobile unit.
- Limited sensitivity of current GeneXpert MTB/RIF may have resulted in false negative diagnoses; sensitivity may improve with next generation assays.

CONCLUSIONS

- Screening for TB in the community using GeneXpert MTB/RIF is feasible and may assist in expanding access to TB testing and treatment completion.
- Yield for GeneXpert-positive TB was low, however the "Test & Treat TB" strategy led to high rates of TB treatment completion.
- The impact of a community-based Test & Treat TB program could be even greater with enhanced sputum induction techniques.