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MAJOR ARTICLE

Performance of GeneXpert MTB/RIF for Diagnosing Tuberculosis Among Symptomatic Household Contacts of Index Patients in South Africa

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Background. We describe the performance of GeneXpert MTB/RIF (Xpert) for diagnosing tuberculosis (TB) among symptomatic household contacts (HHCs) of rifampicin-resistant and drug-sensitive index cases.

Methods. We conducted a cross-sectional study among HHCs of recently diagnosed (<2 weeks) smear-positive and Xpert-positive index cases in the Bojanala District, South Africa. The HHCs were screened for TB symptoms; persons with ≥1 TB symptom provided 1 sputum for smear microscopy, Xpert, and mycobacterial growth indicator tube (MGIT) culture. Diagnostic test performance of Xpert was determined using MGIT as the reference standard.

Results. From August 2013 to July 2015, 619 HHCs from 216 index cases were enrolled: 60.6% were female, median age was 22 years (interquartile range, 9–40), and 126 (20.4%) self-reported/tested human immunodeficiency virus positive. A total of 54.3% (336 of 619) of contacts had ≥1 TB symptom (cough, fever, night sweats, weight loss), 297 of 336 (88.4%) of which provided a sputum; 289 (97.3%) had complete testing and 271 were included in the analysis. In total, 42 (6.8%) of 619 HHCs had microbiologically confirmed TB. The MGIT identified 33 HHCs as positive for *Mycobacterium tuberculosis*; of these, 7 were positive on Xpert resulting in a sensitivity of 21.2% (95% confidence interval [CI], 9.0–38.9), specificity of 98.3% (95% CI, 95.6–99.5), positive predictive value of 63.6% (95% CI, 30.8–89.1), and negative predictive value of 90.0 (95% CI, 85.7–93.4).

Conclusions. Among symptomatic HHCs investigated for TB, Xpert performed suboptimally compared with MGIT culture. The poor performance of Xpert for diagnosing TB suggests that a more sensitive test, such a Xpert Ultra or culture, may be needed to improve yield of contact investigation, where feasible.

Keywords. GeneXpert MTB/RIF; household contacts; mycobacterial culture; TB disease.

South Africa remains one of the highest tuberculosis (TB) burden countries in the world. The 2019 report from the World Health Organization (WHO) estimates the TB incidence is 520 per 100 000 population, suggesting that despite ongoing efforts, more directed strategies are required to curb the epidemic [1]. Recent initiatives such as "Find. Treat. All." recognize that scaling up the implementation of effective interventions by high-burden countries are required for us to realize the End TB strategy.

Active case-finding delivered through household contact tracing (HHCT) is a well established method for detecting and preventing TB [2–4] and has been recommended since 2012 [5, 6]. However, the adoption of HHCT has been mixed, likely due to the effort and cost required to conduct screening and variable TB disease yield among contacts [7–12]. Sputum-smear microscopy has been the mainstay of TB diagnosis in many resource-limited settings [13]; however, its inherently lower sensitivity compared with newer TB diagnostics undermines the value of HHCT when it is used. The introduction of the GeneXpert MTB/RIF (Xpert) assay, an automated molecular test for *Mycobacterium tuberculosis* (MTB) [14], has demonstrated significant improvements over existing TB diagnostics resulting in the WHO recommending its use as a first-line test for TB diagnosis [5, 6].

South Africa adopted Xpert as the initial diagnostic test for investigating persons with symptoms suggestive of TB in 2011 [15], primarily because of its shorter turnaround time when compared with mycobacterial culture and its ability to concurrently diagnose rifampicin-resistant TB (RR-TB). However, when bacterial burden within expectorated respiratory specimens is lower than the detection limit, Xpert may not be effective

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in diagnosing TB compared with mycobacterial culture [16]. A 2015 systematic review of Xpert for diagnosing pulmonary TB in children found that Xpert offers better sensitivity compared with smear microscopy; however, its sensitivity remains suboptimum compared with mycobacterial culture [17]. In addition, in the Gambia, among symptomatic household contacts (HHCs) <15 years old with induced sputum samples, Xpert returned a sensitivity of 42.9% (95% confidence interval [CI], 17.7–71.1) compared with mycobacterial culture [18]. In contrast, a pilot study from Tanzania evaluated the performance of Xpert for identifying undiagnosed TB among 5 culture-positive HHCs reported sensitivities of 60% (95% CI, 14.7–94.7) and 100% (95% CI, 47.8–100.0) for smear-microscopy and Xpert, respectively [19].

With a strong emphasis on identifying "missing TB patients" and scale-up of preventive therapy, particularly among HHCs, as well as the global adoption of Xpert for diagnosing TB in adults and children [20], it is imperative that we understand its performance for diagnosing TB among HHCs. We aimed to determine the yield and performance of Xpert in diagnosing TB compared with mycobacterial culture among symptomatics HHCs within a TB contact tracing program.

METHODS

Setting

This study was nested within The CDC-Aurum contact tracing study, a multicountry prospective cohort study (South Africa, Kenya, and China) with the primary aim of comparing the yield of active TB disease among HHCs of index patients with RR-TB to those with drug-susceptible TB (DS-TB).

Study Procedures

Index patients diagnosed with RR-TB or DS-TB were identified through routine case detection within the Bojanala District of the Northwest Province. According to the 2015/2016 District Health Barometer, the incidence of TB in Bojanala district was estimated at 419 per 100 000 population, with an estimated human immunodeficiency virus (HIV) coinfection rate among TB patients of 66.6% [21].

Pulmonary index patients were eligible if recently diagnosed (≤2 weeks), Xpert or MTB culture-positive, or smear-positive. Index patients and their HHCs provided written informed consent before study participation; an additional consent form was completed for children <18 years old by their respective guardians. The HHCs ≥5 years old were screened using a symptom screening questionnaire; any HHC reporting ≥1 symptom (cough ≥24 hours, night sweats, fever, or unintentional weight loss) was investigated. One spot sputum collected was sent to a single reference laboratory for quality-assured smear microscopy, Xpert, and mycobacterial growth indicator tube (MGIT) testing. The HHCs <5 years old were referred to their local health facility for further TB investigation and preventative therapy.

Each sputum specimen was decontaminated using NaOH-NALC-sodium citrate solution to a final (NaOH) of 1%. After centrifugation, the pellet was suspended in approximately 1.5–2 mL phosphate buffer pH 6.8. The sediment was split to perform all TB testing; an aliquot was taken first for MGIT testing as previously described [22] to prevent contamination followed by Xpert and then smear microscopy. A genotype MTBC test (HAIN Lifescience, Germany) was performed on all culture-positive samples to differentiate between MTB and non-TB mycobacteria. Individuals with positive TB test results were recontacted and provided with a referral letter to initiate treatment.

Human immunodeficiency virus counseling and testing was offered to all HHCs within the households if they reported an unknown or negative HIV status at the time of the visit. Any individual testing positive for HIV was referred to their local health facility for care.

Definitions and Statistical Analysis

A culture was positive if MTB was detected after being identified to species level; a negative culture was defined as the absence of MTB growth after 42 days. Time to culture positivity (TTCP), defined as the number of days it took for a positive culture result on the MGIT culture system, was used as a measure of mycobacterial burden.

Descriptive statistics were used to summarize demographic and socioeconomic characteristics of HHCs included in the analysis. Overall TB yield was defined as the proportion of TB cases diagnosed as positive on either MGIT culture or Xpert MTB/RIF or smear microscopy among those evaluated. Diagnostic yield was defined as the (no. of positive tests/total no. of tests performed) × 100. All CIs for proportions were exact. Comparison of proportions calculated from different samples (eg, sensitivity of Xpert among smear-positive vs smear-negative) were done using Fisher's exact test. Comparison of proportions calculated from the same sample (for example, sensitivity of Xpert compared with sensitivity of smear microscopy) was done using McNemar's test.

Xpert sensitivity, specificity, positive predictive value (PPV), and negative predicative value (NPV) were calculated using MGIT culture as the reference standard. Xpert assay cycle threshold values (C_T), which is defined as the number of polymerase chain reaction cycles completed after which each of the 5 probes is considered positive, was also documented. This provided a semiquantitative measure of bacillary burden in sputum, reported as high (<16 cycles), medium (16–22 cycles), low (23–28 cycles), and very low (>28 cycles) [23]. We excluded specimens that were culture-contaminated from the diagnostic performance analyses. Data was analyzed using Stata 13 (StataCorp, College Station, TX). A final HIV status for each

HHC was determined by combining the self-reported status with additional testing results obtained through testing that was conducted within the households.

Patient Consent Statement

All study participants provided written consent, and the study was approved by the ethics committees of the University of the Witwatersrand Human Research Ethics Committee, US Centers for Disease Control and Prevention, and the research committee of the North West Province, South Africa.

RESULTS

Index Patient Characteristics

From August 2013 to July 2015, we enrolled 216 index TB cases: 73 with RR-TB and 145 with DS-TB (Table 1). The median age was 36 years (interquartile range [IQR], 33–41) for RR-TB patients and 37 years (IQR, 35–40) for DS-TB patients. The median number of HHCs per index patient was 3 (IQR, 1–4) for both RR-TB and DS-TB patients.

Household Contact Characteristics

There were 619 HHCs included from the 216 index patients. Median age was 22 years (IQR, 9–40) (Table 2) and females comprised 60.6% of enrolled HHCs. Previous history of TB was reported among 42 (6.8%) HHCs. There were 336 (54.3%) HHCs who presented with at least 1 TB symptom; a cough ≥24 hours was the most common symptom, which was reported by 98.5% of symptomatic contacts. A sputum sample was collected from 297 (88.4%) symptomatic contacts representing 47.8% of all HHCs; 289 (97.3%) had complete results for all 3 diagnostic tests. One hundred seventeen (18.9%) contacts self-reported being HIV positive, and 291 (47.0%) contacts had an unknown or negative HIV status at enrollment; of these, 45 (15.5%) were tested for HIV, and 9 of these were HIV positive. The overall HIV prevalence was 20.4%.

Table 1. Characteristics of Index RR-TB and DS-TB Patients

Characteristic	MDR-TB (n = 73)	DS-TB (n = 145)
Gender, n (%)		
Male	39 (53.4)	78 (53.8)
Female	34 (46.6)	67 (46.2)
Age, n (%)		
18–29	17 (23.3)	30 (20.7)
30–39	26 (35.6)	52 (35.9)
40–49	21 (28.8)	47 (32.4)
≥50	9 (12.3)	16 (11.0)
Median (IQR)	36 (30–45)	37 (30–45)
Number of HHCs, n (%)		
1	21 (28.8)	38 (26.2)
2	15 (20.6)	26 (17.9)
3	9 (12.3)	28 (19.3)
4	13 (17.8)	20 (13.8)
≥5	15 (20.5)	33 (22.8)
HIV Status, n (%)		
Positive	62 (84.9)	100 (69.9)
Negative	11 (15.1)	43 (30.1)

Abbreviations: DS, drug susceptible; HHC, household contact; HIV, human immunodeficiency virus; IQR, interquartile range; MDR, multidrug resistant; TB, tuberculosis; RR, rifampicin resistant.

Comparison of Diagnostic Performance

Mycobacterial Growth Indicator Tube Culture and Smear Microscopy Testing

Figure 1 shows the results of Xpert and MGIT tests for the 289 specimens. The MGIT testing identified 33 (11.4%) patients as positive for MTB, 8 (2.8%) were non-TB mycobacteria, 18 (6.2%) were contaminated, and 230 (79.6%) were negative for any growth. The median TTCP among culture-positive contacts was 12 days (IQR, 9–22) with a range of 2–37 days (Figure 2). Among samples that were both MGIT culture- and Xpert-positive, the median TTCP was 6 days (IQR, 5–10), whereas among samples that were MGIT culture-positive and Xpert negative, the median TTCP was 18 days (IQR, 10–26).

Smear microscopy was performed on 289 samples, but 271 were included in the analysis; 5 were smear-positive and 266 were smear negative. Sensitivity of smear microscopy for detection of MTB, using MGIT culture as reference standard, was 3 of 33 (9.0%; 95% CI, 1.9–24.3) versus Xpert sensitivity of 21.2% overall ($P < .001$) (Table 3).

Table 2. Characteristics of HHCs and Culture-Positive TB Cases

Characteristic	All HHCs (N = 619)	Culture-Positive TB Cases (N = 33)
Gender, n (%)		
Male	244 (39.4)	16 (48.5)
Female	375 (60.6)	17 (51.5)
Age, n (%)		
<18	263 (42.5)	12 (36.4)
18–29	123 (19.9)	7 (21.1)
30–39	74 (12.0)	4 (12.1)
40–49	59 (9.5)	6 (18.2)
≥50	100 (16.1)	4 (12.2)
Median (interquartile range)	22 (9–40)	27 (14–42)
TB Symptoms, n (%)		
Cough ≥24 hours	331 (53.5)	33 (100.0)
Fever	20 (3.2)	3 (9.1)
Night sweats	18 (2.9)	2 (6.1)
Unintentional weight loss	30 (4.9)	5 (15.2)
≥1 TB symptoms	336 (54.3)	33 (100.0)
≥2 TB symptoms	41 (6.6)	5 (15.2)
≥3 TB symptoms	13 (2.1)	2 (6.1)
HIV Status, n (%)		
Positive	126 (20.4)	10 (30.3)
Negative	493 (79.6)	23 (69.7)
Previous history of TB, n (%)		
Yes	42 (6.8)	6 (18.2)
No	577 (93.2)	27 (81.8)

Abbreviations: HHC, household contact; HIV, human immunodeficiency virus; TB, tuberculosis.

Xpert Testing

Xpert testing identified 16 (5.5%) patients as positive for MTB. The Xpert quantitation results for the 16 sputa in which MTB was detected were "high" for 4 (25.0%), "medium" for 1 (6.3%), "low" for 6 (37.5%), and "very low" for 5 (31.2%). The mean C_T value among Xpert-positive contacts was 24.2 (95% CI, 20.8–27.8), the median was 24.9 (IQR, 17.3–30.6), and the range was 13.5–33.1. Four of the 16 Xpert-positive patients tested negative on MGIT culture; 2 were smear-positive (1+) and 2 were smear-negative.

Xpert performance characteristics, stratified by smear and HIV status, using MGIT culture as the reference standard are shown in Table 3. Overall, 271 (93.8%) sputa had an interpretable result for MGIT and Xpert; we excluded 18 specimens from this analysis that were contaminated in MGIT (5 Xpert-positive and 13 Xpert-negative). Xpert sensitivity was 21.2% (95% CI, 9.0–38.9), specificity was 98.3% (95% CI, 95.6–99.5), PPV was 63.6% (95% CI, 30.8–89.1), and NPV was 90.0 (95% CI, 85.7–93.4). Xpert sensitivity was higher for smear-positive specimens than for smear-negative specimens; 100% (3 of 3) for smear-positive vs 12.9% (4 of 30) for smear-negatives, $P = .06$.

Xpert sensitivity was higher for patients who were HIV-positive than for HIV-negative patients, although not statistically significant: 40.0% (4 of 10) for HIV-positive vs 13.0% (3 of 23) for HIV-negatives, $P = .21$. Similarly, there was no statistical evidence for a difference by HIV status in Xpert PPV (66.7% in HIV-positive vs 60.0% in HIV-negative; $P = 1.0$). Xpert specificity was 98.9% for HIV-negative vs 96.1% for HIV-positive ($P = .9$) or NPV (90.2% for HIV-negative vs 89.3% for HIV-positive; $P = 1.0$).

Among specimens with MTB detected by Xpert, rifampicin resistance was detected in 2 of 16 (12.5%). The 2 specimens that were rifampicin resistant on Xpert were contaminated on MGIT culture; therefore, phenotypic drug-susceptibility testing could not be performed.

Among the 42 TB cases identified through either MGIT culture, Xpert, or smear microscopy, 81% (34 of 42) were started on TB treatment; this was reported through patient record review at the referring health facility. Among TB cases diagnosed on culture (n = 33), 26 (79%) were successfully started on TB treatment, whereas among TB cases diagnosed on Xpert (n = 16), 12 (75%) were successfully started on TB treatment.

DISCUSSION

In evaluating Xpert diagnostic performance among HHCs, we found that it performed poorly in comparison to mycobacterial culture, diagnosing only 21.2% of all culture-confirmed cases, although still better than smear microscopy. Xpert diagnostic

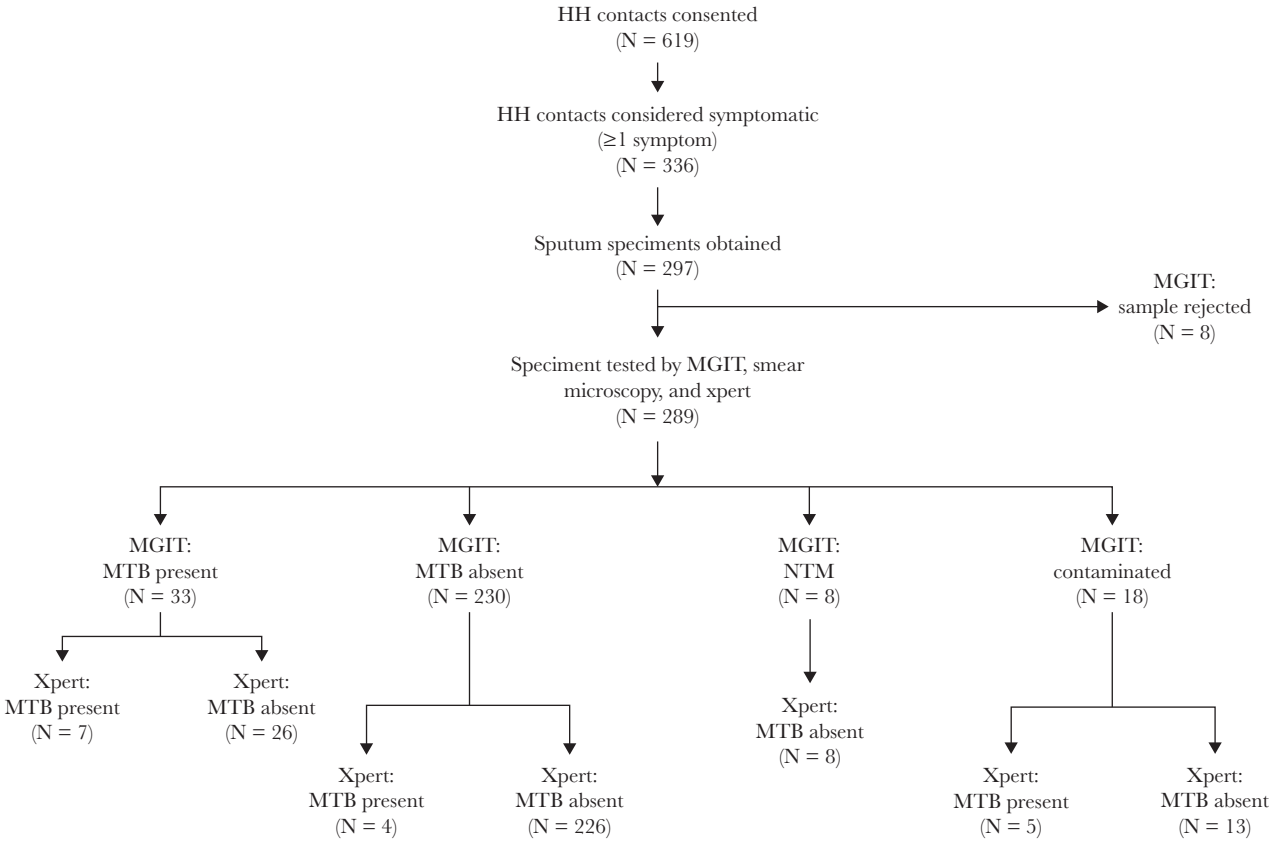

Figure 1. Flow diagram of Xpert MTB/RIF and mycobacterial growth indicator tube (MGIT) culture testing results. HH, household; MTB, *Mycobacterium tuberculosis*.

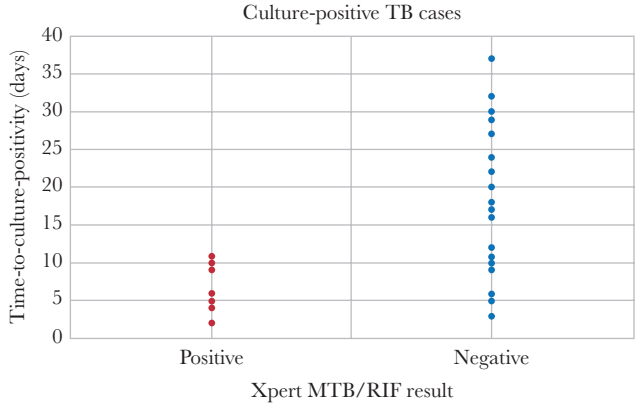

Figure 2. Distribution of time to culture positivity for each of the 33 culture-positive tuberculosis cases.

performance was possibly influenced by low bacillary burden, an expected consequence of active case finding that has important programmatic implications for TB elimination efforts. Our study, conducted among HHCs of RR-TB and DS-TB index patients, found a high microbiologically confirmed TB yield of 6.8% when testing a single spot sputum using either culture or Xpert.

Tuberculosis yield identified among HHCs in our study is consistent with other studies conducted in South Africa [11, 12], but double the 3.1% estimate from a meta-analysis conducted by Fox et al [24] in 2013. In addition, we demonstrated a higher microbiologically confirmed yield than a recent multicountry study conducted among contacts of multidrug-resistant TB index patients that reported a TB yield of 2% among bacteriologically confirmed cases [25]. The high yield highlights the importance of active case-finding strategies such as HHCT. These findings also emphasize the need for scaling-up TB preventive therapies to such high-risk groups, a strategy that has been shown to be highly effective among contacts exposed to infectious TB cases [26].

Our findings on Xpert performance contrast with a recent study conducted by Lebina et al [27] among HHCs, which found no significant difference in diagnostic yield between Xpert and culture. It is possible that differences in our study sample preparation and testing, ie, both culture and Xpert tests were conducted from 1 sample in our study, which differed from the Lebina et al [27] study, which used 2 separate samples for comparison, might explain the contrasting results. The sensitivity of Xpert varies in different settings, ranging from 58% to 100% [28]; however, there are few estimates of its performance for HHCT. One study from Tanzania reported a sensitivity of 100% among 5 culture-positive contacts, whereas another from the Gambia among 14 culture-positive children <15 years reported a sensitivity of 42.9% [18, 19]. We found no difference in sensitivity and specificity of Xpert by HIV status and a higher sensitivity among smear-positive pulmonary TB. Considering

Table 3. Performance Characteristics of the Xpert MTB/RIF Test Overall, and Stratified by Smear Microscopy Status and HIV Status, Using MGIT Culture as the Reference Standard

Performance characteristic		Overall (N = 271)[a]	Smear status		HIV Status	
			Positive (N = 5)[b]	Negative (N = 266)	Positive (N = 62)	Negative (N = 209)
Xpert MTB/RIF sensitivity	N/N	7/33	3/3	4/30	4/10	3/23
	% (95% CI)	21.2 (9.0–38.9)	100.0	13.3 (3.8–30.7)	40.0 (7.5–70.1)	13.0 (2.8–33.6)
Xpert MTB/RIF specificity	N/N	234/238	0/2	234/236	50/52	184/186
	% (95% CI)	98.3 (95.8–99.5)	0.0	99.1 (97.0–99.9)	96.1 (86.7–99.5)	98.9 (96.2–99.9)
Xpert MTB/RIF PPV	N/N	7/11	3/5	4/6	4/6	3/5
	% (95% CI)	63.6 (30.8–89.1)	60.0 (14.7–94.7)	66.7 (22.2–95.7)	66.7 (22.3–95.7)	60.0 (14.7–94.7)
Xpert MTB/RIF NPV	N/N	234/260	0/0	234/260	50/56	184/204
	% (95% CI)	90.0 (85.7–93.4)	0.0	90.0 (85.7–93.4)	89.3 (78.1–96.0)	90.2 (85.3–94.0)

Abbreviations: CI, confidence interval; HIV, human immunodeficiency virus; MGIT, mycobacterial growth indicator tube; NPV, negative predictive value; PPV, positive predictive value; TB, tuberculosis.

[a]Excluded from the analysis were 18 specimens that were contaminated in MGIT culture.

[b]Sensitivity of smear microscopy for detection of MTB, using MGIT culture as reference standard, was 3 of 33 (9.0%, [95% CI, 1.9–24.3] vs Xpert sensitivity of 21.2% overall ($P < .001$).

the limited evidence of Xpert performance in real-world conditions and our contrasting findings, national TB programs should consider selection of TB testing strategies based on their own operational research.

The poor sensitivity of Xpert from our study and previous studies [18, 19] have been explained by lower sputum bacillary burden present during early development of TB disease, demonstrated among HHCs or children [29]. A study that diagnosed TB in children <15 years old within a primary healthcare setting, reported an Xpert sensitivity of 43.3% when compared with culture [30]. Further evidence supporting a link to bacillary burden and reduced Xpert sensitivity can be found in TTCP; where there is a low sputum bacillary burden, TTCP is usually longer, which correlates with poorer sensitivity of Xpert [23, 31]. Our results show a similar trend; among culture-positive TB patients, median TTCP was shorter in Xpert-positive patients compared with Xpert-negative patients (6 vs 17 days), lending credibility to poorer Xpert sensitivity due to lower bacillary burden.

Our findings have important implications for Xpert use among HHCs, implying that in the absence of culture testing, substantial TB cases would have been missed, and therefore limiting the impact of contact tracing for TB control. The need for an improved diagnostic test among HHCs is compounded by high resources required for contact tracing [8, 32]; use of Xpert among HHCs would be an inefficiency of resources if only one fifth of cases are being identified according to our study. In our study, Xpert was also positive on an additional 9 patients; 4 were culture-negative and included in this analysis and 5 that were culture-contaminated and not included. Among the 4 Xpert-positive, culture-negative patients, 2 were smear-negative and 2 were-smear positive; the smear-negative TB patients also reported previous TB, which might explain the Xpert-positive result as a possible false-positive. However, the 2 smear-positive patients might be indicative of a false-negative culture result. Xpert-positive, culture-negative results have been reported elsewhere [33], and such results underscore the difficulties with Xpert interpretation. Additional long-term follow-up studies are required to understand their clinical outcomes [16].

Xpert yield in our study was higher than smear microscopy (2.6% vs 1.0%, respectively), a trend that is consistent with other studies [14, 18, 29, 32], and, more importantly, it did identify all smear-positive cases (3 of 3). Smear microscopy remains a mainstay of TB testing in many countries [29]; however, our findings emphasize the need for an alternate testing method. The extensive rollout of Xpert globally will likely replace smear microscopy as the initial TB test; however, given its poor diagnostic performance among presumptive TB contacts, further consideration should be given to identifying a suitable testing algorithm, especially the Xpert-negative pathway after initial testing. Although our study highlighted the poor diagnostic performance of Xpert compared with culture, its ease of implementation does counter its shortcomings for diagnosing TB. In particular, Xpert requires limited laboratory infrastructure and human resources, has a quicker turnaround for results, and minimizes the possibility of sample contamination, all of which are limitations associated with culture testing. Thus, microbiological testing among contacts may require a solution that balances the need for quicker results, minimal laboratory infrastructure, and costs but limits missed diagnoses. An algorithm that combines Xpert and culture testing may be possible, a strategy that has shown to improve yield [18].

We found no difference in the sensitivity and specificity of Xpert by HIV status, albeit with very low statistical power, consistent with a study from Tanzania where Xpert performance was not affected by HIV status [34]. Contradictory evidence suggests that the impact of HIV status on Xpert sensitivity decreased when adjusting for percentage smear-positive, suggesting that differences may be attributed to differences in smear status [28, 35]. In the context of HHCT, this issue maybe be important for countries with high HIV prevalence who opt for the exclusive use of Xpert; recent evidence evaluating the use of GeneXpert MTB/RIF Ultra among HIV-positive patients suggests that some of these trade-offs might be overcome [16]. Our study results affirm the importance of TB screening and testing of all HHCs to rule out TB disease regardless of HIV status; specifically, this will remove an important barrier to initiation and scale-up of TB preventive therapy.

The study has several strengths that make the findings relevant to national TB programs. First, this is one of the largest studies to evaluate Xpert performance for diagnosing TB among HHCs in "real-world" conditions. Second, we tested almost all HHCs investigated with smear microscopy, culture, and Xpert, making it appropriate to compare the yield and sensitivities. Third, laboratory testing was conducted by 1 laboratory to clinical trial standards. However, there are several limitations to our study. First, our small numbers of contacts and culture-confirmed TB cases limits the precision of our estimates. Second, we only requested a single spot sputum, and the quantity and quality of sample may have affected the yield of TB; however, our study showed a higher yield of TB compared with other studies. Third, using a single spot sputum for culture may have resulted in a lower Xpert PPV estimate because 5 samples that were positive on Xpert were contaminated on culture and excluded from the analysis.

CONCLUSIONS

Xpert may allow for a shorter time to diagnosis compared with mycobacterial culture as well as simultaneous detection of RR-TB [14]; however, its performance against culture in our study has been suboptimal. The Xpert Ultra assay, developed to overcome many inherent limitations of the original Xpert assay [16] with its lower limit of detection, has been touted to offer improved sensitivity for detecting TB. Among symptomatic HHCs, Xpert detected all smear-positives but only 13.3%

of the smear-negative culture-positive TB cases. The poor performance of Xpert for diagnosing TB among symptomatic HHCs suggests that consideration to a more sensitive test such a Xpert Ultra, in combination with mycobacterial culture, may be needed to optimize contact investigation.

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