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Using sputum and tongue swab specimens for in-home point-of-care targeted universal testing for tuberculosis of household contacts: an acceptability and feasibility analysis

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ABSTRACT

Introduction Effective strategies are essential for early tuberculosis (TB) detection. Reliance on passive case detection, symptom screening and collection of sputum results in delayed or undiagnosed TB, contributing to ongoing TB transmission. This study assessed the acceptability of in-home targeted universal TB testing (TUTT) using GeneXpert MTB/RIF Ultra at point-of-care (POC) during household contact investigations (HCIs) and the feasibility of using sputum and tongue swab specimens.

Methods The TB Home Study sought to evaluate the predictive value of different specimen types for use as a household-level triage test for TB. Household contacts of people with TB residing in the Buffalo City Metro Health District (Eastern Cape Province, South Africa) who received in-home POC TUTT through the TB Home Study were asked to complete a post-test acceptability survey. The survey assessed the level of comfort, confidence in the test results and perceived appropriateness of in-home POC TUTT. A feasibility framework was used to assess the feasibility of using sputum and tongue swab specimens for testing.

Results Of the 325 eligible household contacts, 281/325 (86.5%) provided consent. Of those contacts, 278/281 (98.9%) provided a tongue swab, and 50/281 (17.8%) could expectorate sputum. All specimens were successfully prepared for immediate in-home testing. Of the 172 tongue swab-based tests performed, 169 (98.3%) produced a valid result, whereas 47 of 49 (95.9%) sputum-based tests had a valid result. An immediate tongue swab-based test result was available for 274/278 (98.6%) clients compared with 47/49 (95.9%) sputum-based test results. The mean in-home POC TUTT acceptability score (5=highly acceptable) was 4.2/5 (SD=0.4).

Conclusion In-homePOC TUTT using sputum and tongue swab specimens was highly acceptable and feasible. Tongue swabs greatly increased the testing rates owing to the high sample collection yield. Combining sputum and tongue swabs for in-home POC testing offers a promising strategy to improve TB case detection and reduce diagnostic delays.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ TB transmission among household contacts of people with tuberculosis (TB) is a public health concern.
⇒ The delivery of community-based diagnostic testing for TB is challenging, and the reliance on sputum continues to hamper universal testing and result in diagnostic delay.
⇒ A large diagnostic gap remains globally, with an estimated 2.7 million of all suspected TB cases never being tested for TB.
⇒ Molecular testing of tongue swabs has high specificity and moderate sensitivity relative to sputum testing.

WHAT THIS STUDY ADDS

⇒ This is the first study to assess the acceptability of universal in-home point-of-care TB testing of household contacts during household contact investigations.
⇒ This study assesses the feasibility of different specimen types for immediate in-home point-of-care TB testing, including tongue swabs and sputum, by evaluating metrics associated with sample collection yield, processing, testing and notification rate.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Household contacts perceived in-home targeted universal TB testing to be highly acceptable, prompting the need for further investigation into the cost-effectiveness of such strategies to improve early case detection.
⇒ The use of tongue swabs as an additional or alternative sample type to sputum could increase testing and improve early case detection.

INTRODUCTION

Tuberculosis (TB) remains one of the world's leading infectious disease killers. Despite

being preventable, treatable and curable, it caused an estimated 1.25 million deaths in 2023.[1] Persistent gaps in the cascade of care include TB diagnosis, notification and linkage to treatment, all of which remain major contributors to TB burden, transmission and mortality.[2] Effective delivery of WHO-recommended rapid molecular diagnostic tests, such as GeneXpert MTB/RIF Ultra (Xpert Ultra, Cepheid, Sunnyvale, CA, USA), remains a key priority to meet the WHO goal of diagnosing 100% of people tested with WHO-recommended rapid tests.[1] Despite the introduction of rapid molecular diagnostic tests, such as Xpert Ultra, the global diagnostic gap is estimated to be 2.7 million of all suspected TB cases. Diagnosis remains the weakest link in the cascade of care.[1 3]

In 2021, the incidence of TB in South Africa was estimated to be 513 per 100 000 population, equating to appproximately 304 000 people living with TB, of which appproximately 120 000 were not tested, diagnosed or initiated on treatment.[4] Persistent gaps in testing are attributable to various factors including reliance on symptom presentation, limited access to testing and fragmented delivery of testing services.[5 6] Closing the diagnostic gap necessitates strategies that are patient-centred, can deliver testing at or near the point-of-care (POC) and are conducted in a single patient consultation.[3]

Active case finding strategies, including household contact investigations (HCIs) of people diagnosed with TB, have been shown to be cost-effective compared with passive case detection and form the cornerstone of TB programmes aimed at improving early case detection.[7] However, low uptake of clinic referrals and continued reliance on a hub-and-spoke model of sputum transportation and centralised testing (resulting in long test result turnaround) continue to hamper effective implementation of such strategies.[8] The use of portable, rapid molecular diagnostic platforms, such as the GeneXpert Edge (GX-Edge, Cepheid), has been shown to greatly improve access to immediate testing and improve treatment uptake when integrated into HCI.[6 9] However, reliance on symptom-based screening and sputum-based testing continues to limit case detection.[10]

Non-specific clinical symptoms, the paucibacillary nature of sputum and the challenge of collecting sputum have all been reported as barriers to effective diagnostic testing.[10] Furthermore, the high cost of Xpert Ultra testing severely limits its scalability in resource-constrained settings.[11] Recently, tongue swab specimens have been proposed as an alternative, less invasive sample, when sputum is not available, especially as sensitivity approaches that of sputum-based molecular tests.[12 13] Moreover, pooled testing of multiple sputum samples in a single Xpert Ultra cartridge has been shown to save up to 48% of the assay cost.[11] Combined, the collection of tongue swabs to increase sample collection yield and the pooling of samples to decrease cost may increase the scalability of HCI strategies adopting portable rapid molecular testing platforms.[14] Given the introduction of targeted universal testing for TB (TUTT) of household contacts of people with TB, irrespective of symptoms, there is an urgent need for rapid, affordable and accurate TB testing strategies.[15]

Exploration of the acceptability and feasibility of in-homePOC TUTT using tongue swab specimens is warranted. To make prudent decisions about adopting new technologies, decision-makers need well-executed studies assessing their acceptability and feasibility. Various contextual factors and patient preferences could ultimately determine the success of new healthcare interventions.[16] To this end, this study sought to assess the (1) acceptability of in-home POC TUTT of household contacts of people with TB using GX-Edge and (2) test the feasibility of using sputum and tongue swab specimens.

METHODS

Study design

This acceptability and feasibility assessment was nested within the larger TB Home Study. Data were collected between March and September 2024. The TB Home Study sought to evaluate the predictive value of individual and pooled tongue swab specimens vs sputum as a household-level triage test for TB during HCIs.[6] In brief, individuals with microbiologically confirmed TB were asked for permission to visit their homes and conduct an HCI. All consenting household contacts were asked to provide both sputum and tongue swabs for immediate in-home TB testing using the GX-Edge platform with Xpert Ultra. All household contacts were asked to complete an acceptability survey following the completion of in-home testing. The Theoretical Framework of Acceptability (TFA) guided the development of survey items designed to assess household contacts' experiences with in-home POC TB testing.[17] The metrics to assess the feasibility of rapid POC technologies framework was used to evaluate implementation outcomes associated with the feasibility of using sputum and tongue swab samples during in-home POC TUTT.[18]

Study setting

The TB Home Study was conducted in the Buffalo City Metro (BCM) Health District, Eastern Cape Province, South Africa. BCM has a population size of approximately 893 000, of which 86.7% are black. Approximately 45.3% of households are headed by women, and 24.9% of households reside in informal dwellings. Moreover, approximately 58.2% of people live in poverty, and 31.1% remain unemployed.[19] In 2019, BCM had an estimated TB incidence of 876 per 100 000 population.[20] In 2018, the last year in which data are available, BCM had a drug-susceptible TB treatment success rate of 71.2% (the lowest in South Africa), a loss-to-care rate of 17.6% (the second highest in South Africa) and approximately 40% of TB cases missed by the health system.[21] TB is the leading cause of death (18.4%) among the group aged 25–64 years in BCM.[19]

Household contact recruitment

Details regarding the HCI methods have been previously described.[22] Briefly, household and household contact information was obtained from people with microbiologically confirmed TB accessing services at collaborating public healthcare clinics. Contact investigation teams consisting of 2–3 trained lay community healthcare workers conducted up to three household visits to reach all household contacts listed. Household visits were conducted on weekdays between 8 am and 4 pm, during which the contact investigation team would conduct a household contact verification check, screen for study eligibility and introduce the study to all those present. Healthcare workers had to attend a 4-week training programme during which they were trained on the study protocol, research ethics and sample collection, preparation and testing. Household contacts were deemed eligible if they were (1) age ≥18 years, (2) not currently on TB treatment and (3) willing to provide informed consent. Study participation was voluntary, and no remuneration was provided. Once recruited into the study, participating household contacts were asked to respond to a series of survey questions and provide specimens for immediate in-home testing.

Specimen collection and testing

Details regarding the sample collection and testing have been previously reported.[23–25] Briefly, before sputum collection, community healthcare workers used Copan FLOQSwabs to collect tongue swab specimens from all study participants present at the time of the HCI. Study participants were instructed not to eat, drink, rinse their mouth or produce a sputum sample 30 min before swabbing and subsequent sputum collection as part of pretesting requirements. Tongue swabs were pooled from up to three individuals for immediate in-home testing using a single Xpert Ultra cartridge. If a household had more than three household contacts, the additional swabs were pooled and tested in a separate reaction. Pool sizes could be three, two or, in some cases, a single swab. Sputum samples were collected from all study participants while the tongue swab test was being conducted. Participants who were unable to expectorate sputum were referred to a clinic for further clinical evaluation. Sputum samples were individually prepared and tested immediately at home using Xpert Ultra with the GX-Edge platform. Samples were placed into a total solution volume of 3 mL of 1 mL Prime Store Molecular Transport Media and 2 mL of Xpert sample buffer. From the approximately 3 mL volume solution, 2 mL was taken out for processing in an Xpert Ultra cartridge. Up to three GX-Edge platforms were used simultaneously, allowing for testing of multiple samples concurrently, each taking approximately 90 min per test. Participants were referred for TB treatment based on positive sputum results.

Data collection and analysis

While Xpert testing was being conducted, a contact investigation team member collected basic socio-demographic and clinical history data from each participant. Descriptive statistics (median (IQR) for continuous variables and n [%] for categorical variables) were used to characterise distributions of study variables in the socio-demographic questionnaire (table 1). Data collected pre-testing and post-testing were analysed to assess the acceptability of in-home POC TUTT. Pre-test acceptability was assessed as the proportion of household contacts consenting to participate out of the eligible population to whom study participation was offered. Post-test acceptability was assessed using survey data collected following the conclusion of a household investigation. The development of the post-test acceptability survey was informed by the TFA framework and adapted specifically for this study.[17] This survey evaluated a respondent's level of acceptability of a healthcare intervention across eight different constructs using a 5-point Likert scale (table 2). Responses to two constructs with negatively framed questions (burden and opportunity costs) were reverse-coded before calculating the mean scores to ensure interpretability and consistency with the other acceptability constructs. SD is reported to represent the dispersion of responses around the mean score for each acceptability construct.

Implementation outcomes associated with sample collection and testing of sputum and tongue swab samples were captured and used to assess the feasibility of different testing methods and included the (1) type of sample collected, (2) success of sample collection, (3) processing and preparation of sample for testing, (4) outcome of test and (5) referral outcome. The final feasibility assessment was guided by elements of the metrics to assess the feasibility of rapid POC technologies framework, which was designed to assess the feasibility of rapid POC technologies during proof-of-concept studies.[18] This framework was used to select and define four metrics (table 3) to be included in the current assessment: (1) sample collection rate, (2) test processing rate, (3) test success rate and (4) client notification rate. The performance of both sputum and tongue swab testing methods against each metric was calculated and reported.

Ethical considerations

This study was conducted according to the ethical principles set forth in the Declaration of Helsinki, ICH-GCP, European Directive 2001/20/EC, US Code of Federal Regulations Title 21, South African Good Clinical Practice Guidelines and other local regulatory requirements. The study protocol was approved by the University of Pretoria Human Research Ethics Committee (HREC 391/2021) and the Boston University Institutional Review Board (H-44118).

Patient and public involvement

The study team engaged community advisory board mechanisms to ensure that household members of prospective

Table 1 Characteristics of household contacts who received in-home POC TUTT and completed the post-test acceptability survey

	TB symptomatic	Non-symptomatic	Overall
	n=88 (31%)	n=193 (69%)	n=281
Age (years) (median (IQR))	43 (27/55)	40 (27/55)	41 (27/55)
Provided sputum	23 (26%)	27 (14%)	50 (17.8%)
Provided tongue swab	88 (100%)	192 (99.5%)	280 (99.6%)
Race			
Black	73 (83.0%)	173 (89.6%)	246 (87.5%)
Coloured (mixed race)	14 (15.9%)	18 (9.3%)	32 (11.4%)
Indian	0 (0%)	1 (0.5%)	1 (0.4%)
Missing	1 (1.1%)	1 (0.5%)	1 (0.4%)
Employment status			
Unemployed	54 (61.4%)	104 (53.9%)	158 (56.2%)
Employed	18 (20.5%)	42 (21.8%)	60 (21.4%)
Other	15 (17.0%)	46 (23.8%)	61 (21.7%)
Missing	1 (1.1%)	1 (0.5%)	2 (0.7%)
Education			
None	5 (5.7%)	5 (2.6%)	10 (3.6%)
Less than grade 12	57 (64.8%)	120 (62.2%)	177 (63.0%)
Grade 12	22 (25.0%)	45 (23.3%)	67 (23.8%)
Tertiary	3 (3.4%)	20 (10.4%)	23 (8.2%)
Missing	1 (1.1%)	3 (1.6%)	4 (1.4%)
Income per month			
None	21 (23.9%)	47 (24.4%)	68 (24.2%)
Under R2000 ($114)	24 (27.3%)	39 (20.2%)	63 (22.4%)
R2000–5000 ($114–$284)	37 (42.0%)	83 (43.0%)	120 (42.7%)
R 5 000–10 000 ($284–$569)	3 (3.4%)	12 (6.2%)	15 (5.3%)
More than R10 000 ($569)	2 (2.3%)	11 (5.7%)	13 (4.6%)
Missing	1 (1.1%)	1 (0.5%)	2 (0.7%)
HIV status			
Negative	67 (76.1%)	153 (79.3%)	220 (78.3%)
Positive	16 (76.1%)	29 (15.0%)	45 (16.0%)
Did not want to disclose	4 (4.5%)	10 (5.2%)	14 (5.0%)
Missing	1 (1.1%)	1 (0.5%)	2 (0.7%)
TB history			
Never	67 (76.1%)	151 (78.2%)	218 (77.6%)
Yes, in the last 2 years	3 (3.4%)	5 (2.6%)	8 (2.8%)
Yes, more than 2 years ago	17 (19.3%)	36 (18.7%)	53 (18.9%)
Missing	1 (1.1%)	1 (0.5%)	2 (0.7%)

POC TUTT, point-of-care targeted universal tuberculosis testing; TB, tuberculosis.

study participants were approached in a manner that would not result in stigma. In addition, we collaborated with the Department of Health to streamline best practices for the delivery of all study-related activities, ensuring that these did not interfere with standard TB care and that effective linkage to care was maintained. Only individuals with a confirmed positive TB diagnosis were approached at clinics and introduced to the study. Permission was obtained from these individuals before initiating HCIs, thereby indirectly supporting potential study recruitment.

The study team prioritised the effective dissemination of findings by engaging key stakeholders at the

Table 2 Acceptability of in-home POC TUTT among household contacts during household contact investigations

Acceptability construct	Survey question	Mean score (SD)
Affective attitude	How comfortable did you feel with the home-based TB testing today?	4.4 (0.89)
Burden	How much effort did it take in order for you to be tested today?	1.4 (0.77)
Ethicality	How appropriate is it for healthcare workers to go to someone's household to provide TB testing services?	4.4 (0.75)
Perceived effectiveness	The delivery of home-based testing motivates me to go to a clinic for additional TB services when I need it.	4.3 (0.69)
Intervention coherence	It is clear to me how a positive test result would motivate someone to go to the clinic for TB treatment.	4.3 (0.52)
Self-efficacy	How confident are you in the test result you received today?	4.4 (0.60)
Opportunity costs	How did the home-based testing affect your other daily activities?	1.3 (0.69)
General acceptability	How acceptable was it to you for a healthcare worker to come to your house to offer TB testing?	4.5 (0.50)
General acceptability	How likely are you to recommend home-based TB testing to someone else?	4.5 (0.57)

POC TUTT, point-of-care targeted unirversal tuberculosis testing.

Department of Health, participating healthcare clinics and community-based representatives. A workshop was held where study staff presented key findings, and attendees were given the opportunity to ask questions and provide feedback.

RESULTS

Figure 1 provides a detailed summary of the number of household contacts listed, number of households reached and number of household contacts verified and screened for study eligibility. A total of 247 individuals with confirmed TB provided a household contact list with a combined total of 901 household contacts. The median household size was 3. Contact investigation teams conducted a total of 468 investigations, reaching 188 (76.1%) households and verifying the identification of a total of 68.5% (617/901) of all household contacts listed. Of 530 household contacts verified, 325 were eligible for enrolment.

All 281 participants completed the socio-demographics and clinical history questionnaire. The median age of the participants was 41 (IQR 27–55) years. The majority were black (87.5%, 246/281), 56.2% (158/281) were unemployed, and 89.3% (251/281) had a monthly income of less than R5,000 ($268). A quarter (21.7%, 61/281) had a previous bout of TB, and just less than one-fifth (16.0%, 45/281) were living with HIV (table 1). Almost a third of the participants (31.3%, 88/281) screened positive for TB using the WHO-recommended four-symptom screener.[26] Of those who screened positive for TB, 25%

Table 3 Performance of sputum and tongue swab specimens during in-home POC TUTT

		Sputum	Tongue swab			
Metric	Definition	Total	Total tongue swabs	Single swab	Two pooled swabs	Three pooled swabs
Sample collection rate	Proportion of participants able to provide a sample for testing	50/281 (17.8%)	278/281 (98.9%)	87/88 (98.9%)	128/130 (98.5%)	63/63 (100%)
Test processing rate	Proportion of tests for which all samples were prepared and processed successfully to conduct testing	49/49 (100%)	278/278 (100%)	87/87 (100%)	128/128 (100%)	63/63 (100%)
Test success rate	Proportion of tests that produced an actionable test result	47/49 (95.9%)	274/278 (98.6%)	85/87 (97.7%)	63/64* (98.4%)	21/21* (100%)
Client notification rate	Proportion of participants completing the test procedure who received an immediate result notification	47/49 (95.9%)	274/278 (98.6%)	85/87 (97.7%)	126/128 (98.4%)	63/63 (100%)

*The number of tests conducted is less than the number of samples collected, because samples were pooled into a single Xpert Ultra cartridge.
POC TUTT, point-of-care targeted universal tuberculosis testing.

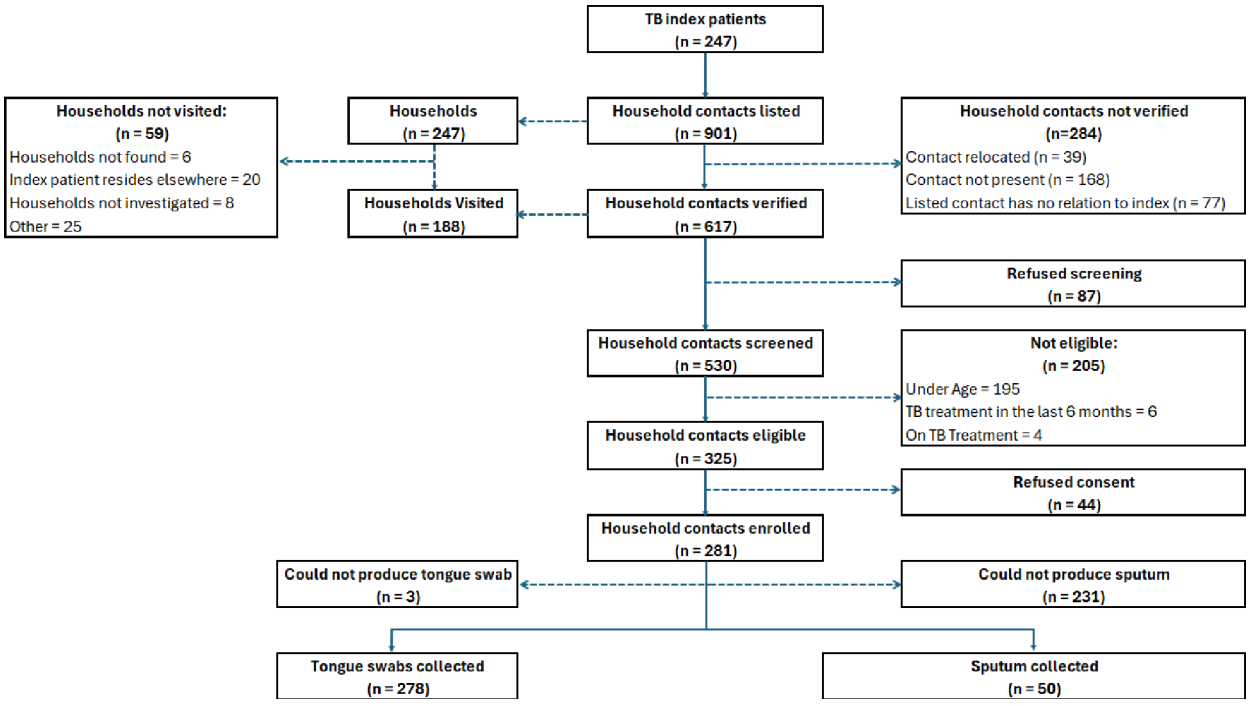

Figure 1 Flowchart of household contact investigations, verifications, screening and enrolment.

(22/88) were able to produce sputum compared with 14% (27/193) of those who screened negative.

Acceptability of in-home point-of-care targeted universal tuberculosis testing

Table 2 lists each of the eight acceptability constructs measured, associated survey question and its mean score. The associated SD has been included and represents the variability of responses around the mean score for each acceptability construct. Of the 325 household contacts that met all the study eligibility criteria, 86.5% (281/325) provided informed consent, suggesting a high level of acceptability for in-home POC TUTT before testing. A total of 274 (97.5%) participants completed the post-test acceptability questionnaire. The mean score for overall acceptability of in-home POC TUTT across all eight acceptability constructs was 4.2 (SD=0.4), with 5 representing the highest level of acceptability. All constructs measuring a positive attitude towards in-home TB testing had mean scores >4. The two constructs measuring negative attitudes toward in-home TB testing (ie, burden and opportunity cost) had mean scores of 1.4 and 1.3, respectively, with one representing the least negative response. When given the option to choose between sputum or tongue swabs for future in-home TB testing, 231/274 (84.3%) chose tongue swabs.

Feasibility of different sputum and tongue swab-based in-home point-of-care testing methods

Table 3 lists and defines the four metrics used to assess the feasibility of delivering in-home POC TB testing and the associated performance of different testing methods. Tongue swab-based testing had a higher s*ample collection rate* compared with sputum-based testing. A total of 278 (98.9%) study participants could provide a tongue swab for testing. The three participants who were unable to provide a tongue swab for testing failed to comply with the pre-sample collection requirements. Only 17.8% (50/281) of participants were able to successfully expectorate a sputum sample for testing. Contact investigation teams successfully prepared all samples for immediate POC testing during an HCI, irrespective of the sample type or number of tongue swab samples pooled. The *test processing rate* was consequently 100% for both specimen types. The t*est success rate* for tongue swab-based tests (98.6%, 274/278) was comparable to sputum (95.9%, 47/49). Two sputum-based and two tongue swab-based tests reported errors during testing. Table 4 summarises the test failure rate and associated error codes. Both error codes are due to complications associated with the Xpert Ultra reagent. All participants with actionable test results were immediately notified at the time of the household investigation. Given the higher *test success rate*, tongue swab-based tests had a higher *client notification rate* (98.6%), as 274 of the 278 participants received a valid in-home test result. Of the 49 participants able to provide a sputum, 47 (95.9%) received a valid, in-home test result. Among the various tongue swab-based testing methods, the pooling of three samples showed slightly better test and client notification rates compared with both two-sample pooling and individual tongue swab testing due to the absence of errors occurring during any of the 63 tests run using three tongue swabs.

DISCUSSION

To our knowledge, the TB Home Study is the first to examine in-home collection and testing of sputum and

Table 4 Failure rate and GeneXpert error codes associated with all in-home tests conducted and stratified by the specimen type

		Tongue swab tests (n=XX)			
	Sputum tests (n=XX)	Total tongue swab tests	Single swab	Two pooled swabs	Three pooled swabs
Successful tests	47	274	85	63	21
Test failures	2	3	2	1	–
Reasons for test failures					
Probe check failures (error code: 5006)	2	2	1	1	–
Probe check failures (error code: 5007)	–	1	1	–	–

tongue swabs for universal POC TB testing during HCIs. Our initial proof-of-concept study revealed that among household contacts with TB-related symptoms, in-home testing using sputum was both acceptable and feasible.[6 9] The current findings demonstrate high acceptability for in-home POC TB testing among household contacts, irrespective of symptom presentation. In addition to sputum, the collection, pooling and testing of tongue swab samples was highly feasible. The increased sample collection yield of tongue swab specimens (98.9%) compared with sputum (17.8%) highlights the benefit of collecting less invasive sample types for TB testing, supporting findings from previous research.[27]

Low sputum collection yield has widely been reported as a major barrier to TB testing, especially for children and individuals living with HIV.[28] The 17.8% sputum collection yield was far lower than that reported elsewhere, which ranges from 82% to 93%.[29] Of the 50 individuals who were able to produce sputum, 46.0% (23/50) had symptomatic TB, and 17.4% (8/46) of those willing to disclose were HIV-positive. In comparison, among those unable to produce sputum, 28.6% (66/231) had TB symptoms, and 16.9% (37/219) of those willing to disclose were HIV-positive. The low sputum collection yield may be a result of several factors, including collecting spot sputum samples at different times of the day, collection being done by lay healthcare workers with limited training or the fact that collection was done outside the traditional clinical setting without the option to offer induction.[30] Growing evidence highlights the potential of tongue swabs as a viable alternative to sputum for TB testing due to the increased sample collection yield and potentially higher probability of case detection.[27] A relatively low (31.3%) proportion of household contacts presented with symptoms, highlighting the large proportion that would not have received further clinical evaluation under routine conditions. TUTT of high-risk groups, such as household contacts, could increase case detection by as much as 17%.[10]

Although our findings support the acceptability and feasibility of in-home POC TUTT, the accuracy of tongue swab testing for TB remains a concern. Variability in accuracy could increase the probability of false negatives, thereby contributing to increased risk of transmission, or alternatively, false positives, resulting in misdiagnosis, followed by unnecessary treatment exposure. The optimal number of swabs and approach necessary to optimise DNA recovery during processing remains under investigation.[31] Similarly, although the pooling of sputum samples has been shown to be efficient at reducing costs while producing highly accurate results, uncertainty remains whether the same would hold true when pooling tongue swabs.[32] Although the sensitivity of tongue swabs for TB diagnosis remains variable, the specificity seems notably high, yielding an overall favourable diagnostic effect.[33] The high specificity of tongue swabs combined with the high sample collection yield makes them highly valuable for confirmatory testing alongside other diagnostics methods. Furthermore, high specificity can assist with minimising false positives, thereby assessing an individual's eligibility for TB preventive treatment.

The importance of our findings is supported by a growing recognition of the need for accurate tests that enable prompt linkage to care, are implementable at POC, by healthcare workers with minimal training and with results that are available in a single patient encounter. Consideration of the feasibility of collecting, processing and testing specimens outside of a traditional clinical setting is essential to estimating the true potential of using alternative sample types for TB testing during community-based active case finding. Despite the introduction of several new platforms, gaps in the current TB diagnostic pipeline remain.[29] Exploring the potential of new platforms, assays and testing methods that show promise for POC deployment across different use case scenarios plays an essential role in refining target product profiles.[31] Findings from this study can be used to inform new use case development as well as refine target product profiles aimed at delivering near-POC and POC TB testing.

A key strength of this study was the ability to employ lay community healthcare workers to conduct HCIs and deliver in-home POC TUTT. South Africa continues to face a severe shortage of qualified healthcare workers, which has resulted in task shifting to a range of lay healthcare workers. The delivery of TB services by community healthcare workers has been shown to enhance population coverage, increase testing and improve

early diagnosis and linkage to care.[34] Another strength is the use of a theory-informed instrument to measure acceptability. No standardised or validated healthcare intervention acceptability instruments currently exist.[17] Similar to most other evaluations, our previous work assessing the acceptability of in-home POC TB testing relied on behavioural measures of acceptability, such as study enrolment and/or dropout rate. However, several reasons other than low acceptability could explain why people decline or withdraw from a healthcare intervention, including the lack of motivation, distrust or privacy concerns, all of which are assessed when using the TFA framework. The TFA framework is innovative in that it provides conceptually distinct constructs that capture key dimensions of acceptability, allowing the assessment of complex healthcare interventions.[17]

This study had several limitations. The high level of pre-test acceptability of POC TB testing among household contacts might be an overestimation. The acceptability of TB testing might be higher among contacts of patients with TB compared with the general population due to increased perceived disease risk and awareness. Household contacts directly exposed to TB have a heightened understanding of the importance of early detection and treatment.[9] Furthermore, selection bias may account for the high post-test acceptability, as only household contacts who initially provided consent completed the post-test acceptability assessment. This analysis did not include a cost or cost-effectiveness analysis to estimate and compare the difference in cost and outcomes of each testing method. Pooling tongue swabs into a single Xpert Ultra cartridge aims to reduce the total number of cartridges required, often cited as a significant factor driving testing costs.[14] However, sputum remains the gold standard for TB testing due to its superior sensitivity over tongue swabs.[27] Future studies should explore the cost-effectiveness of these different testing methods to weigh potential cost savings with decreasing test accuracy, assessing the 'financial feasibility' and scalability of the proposed testing methods.[15] Testing was only offered to household contacts aged >18 years, even if approximately 12% of all suspected TB cases were reported as being children and young adolescents.[1] Effective TB diagnosis in children is hampered by several factors, including the paucibacillary nature of TB, its shared symptoms with other common childhood diseases and, most significantly, difficulties collecting samples for testing.[35] The collection of non-invasive samples, such as tongue swabs for TB screening among children, combined with the delivery of TB preventative treatment could have a significant public health effect. However, the low sensitivity of tongue swabs in children remains a major concern, limiting their use. Failing to optimise testing protocols that increase accuracy and prioritise children and adolescents in future studies will continue to stifle progress towards TB targets. No data were collected from the approximately 15% of household contacts who declined study participation. Evidence suggests that individuals who opt out of screening may be at higher risk for TB. Future studies should aim to further explore reasons for refusal, as it may hold valuable insights for intervention development. Lastly, study participants were required to adhere to strict pre-testing requirements, including no eating, drinking, mouth rinsing or producing a sputum sample before swab collection. The need for these precautions in ensuring optimal sample collection remains unclear and could well negatively affect the acceptability and feasibility of novel sample collection methods. The justification for such requirements should be further explored.

CONCLUSION

As novel platforms and diagnostics for decentralised molecular testing become more readily available, this study provides evidence to support their integration into existing strategies, including HCIs. Furthermore, these findings provide support for the expansion of in-home TB testing by minimally trained lay healthcare workers. The ability to integrate molecular POC testing into community-based strategies can reduce the workload of already overburdened laboratory and clinical facilities, improve client satisfaction and remove persistent barriers preventing equal access to services. In-home POC TUTT using either sputum or tongue swabs is highly acceptable and feasible. Rapid molecular TB testing with immediate result notification at POC reduces the burden placed on those at highest risk by offering testing services in a single consultation, improves access to testing and shows great potential for early case detection and result notification.

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