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"Something So Hard": A Mixed-Methods Study of Home Sputum Collection for TB Contact Investigation in Uganda

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Summary

Objective—Home sputum collection could facilitate prompt evaluation and diagnosis of tuberculosis(TB) among contacts of patients with active TB. We analyzed barriers to home-based collection as part of an enhanced intervention for household TB contact investigation in Kampala, Uganda.

Design—We conducted a convergent mixed-methods study to describe the outcomes of home sputum collection for 91 contacts and examine their context through 19 nested contact interviews and two focus-group discussions with lay health workers(LHWs).

Results—LHWs collected sputum from 35(39%) contacts. Contacts reporting cough were more likely to provide sputum than those with other symptoms or risk factors(53% vs 15%, RR: 3.6, 95%CI: 1.5–2.8, p<0.001). Males were more likely than females to provide sputum(54% vs 32%, RR: 1.7, 95%CI: 1.0–2.8, p=0.05). Contacts said support from the index patient and the convenience of the home visit facilitated collection. Missing containers and difficulty producing sputum spontaneously impeded collection. Women identified stigma as a barrier. LHWs emphasized difficulty procuring sputum and discomfort pressing contacts to produce sputum.

Conclusions—Home sputum collection by lay health workers entails different challenges from sputum collection in clinical settings. More research is needed to develop interventions to mitigate stigma and increase success of home-based collection.

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INTRODUCTION

Active case-finding for tuberculosis (TB) may expand detection of prevalent cases in high-burden settings and reduce incident cases by interrupting transmission.[1–6] The most common approach to active case-finding in the community is household contact investigation.[7–9] Contact investigation conventionally depends on a contact's ability and willingness not only to undergo screening for TB symptoms and risk factors[10], but also to complete TB evaluation by traveling to a clinic for testing if referred. In a previous study of contact investigation and clinical follow-up for household contacts of pulmonary TB patients, we showed that only 20% of symptomatic or high-risk contacts referred to clinics eventually completed TB evaluation.[11]

Home sputum collection could facilitate rapid identification of at-risk contacts with TB and linkage to care because it is perceived to be more convenient, more private, and less expensive for contacts.[12] In this study, we describe the rates, predictors, and context of successful home sputum collection delivered as part of an enhanced intervention for household TB contact investigation in Kampala, Uganda.

METHODS

Setting

The study took place in Kampala, Uganda from July 2016 to July 2017. The Uganda National TB and Leprosy Programme (NTLP) introduced household contact investigation in 2013.

Study design

This study employed a parallel-convergent mixed-methods design; quantitative and qualitative data were collected in parallel and interpreted together.[13] We collected quantitative data on outcomes of home sputum collection offered as part of the intervention arm of a household-randomized trial of enhanced contact investigation for TB. We performed qualitative interviews with a sub-sample of household contacts offered home sputum collection and focus group discussions (FGDs) with lay health workers (LHWs) who collected sputum specimens.

Study procedures

Trained LHWs visited the homes of index TB patients enrolled at six primary health centers and one hospital. During the home visit, LHWs screened household contacts[14] for TB symptoms and HIV. LHWs offered home sputum collection to contacts ≥5 years old identified as "at-risk" because they reported symptoms (cough ≥two weeks, subjective fever, night sweats, or weight loss) or living with HIV. LHWs were trained to collect sputum per NTLP guidelines; all routinely collected sputum in clinical settings.[15] LHWs were further trained provide standardized instructions for expectoration immediately prior to collection.[16] Laboratory personnel recorded sputum characteristics after delivery by LHWs, and performed smear microscopy or GeneXpert MTB/RIF testing. TB was confirmed by one positive GeneXpert or smear, and excluded by one negative GeneXpert or two negative

smears; a single negative smear was considered inconclusive. LHWs provided results by text message and/or telephone call.

Qualitative sub-sample

We purposively sampled adults offered home sputum collection according to whether or not they successfully provided sputum. The initial target of ten contacts per group was based on estimates of the sample size necessary to reach thematic saturation within a homogenous population.[17,18] Selected participants were contacted by phone and asked to participate in an in-depth interview (IDI) lasting approximately 30 minutes within one month following the home visit. After coding, we concluded that saturation had been reached and additional interviews were unnecessary. We invited all LHWs carrying out home sputum collection to participate in FGDs.

Qualitative data collection

The semi-structured IDI guide (Supplement S1) probed respondents about their experiences and outcomes of contact investigation in English or Luganda. All interviews were conducted by a bilingual, native Luganda-speaking researcher (JG). Responses were digitally recorded, transcribed, translated as necessary, and entered into Atlas.ti 8 (ATLAS.ti Scientific Software Development GmbH, Berlin, Germany) for analysis.

The FGD guide probed LHWs about attitudes and experiences related to collecting sputum during home visits. LHWs participated in English and Luganda; FGDs were facilitated by two bilingual researchers, recorded, summarized using a debriefing tool (Supplement S2), transcribed, translated, and entered into Atlas.ti.

Analysis

We analyzed the sputum collection and evaluation cascade using linked process measures[19]: sputum collection, sputum receipt at the laboratory, and completion of sputum analysis. We produced descriptive statistics for contacts offered home sputum collection, testing bivariate associations of successful sputum collection with sex, HIV status, and cough symptoms. We also stratified these analyses by cough symptoms. We assessed clustering by household by estimating the intra-class correlation (ICC). In a supplemental analysis, we fit a multivariable, population-averaged model using generalized estimating-equations with a robust covariance estimator to adjust standard errors for clustering by household.

We took a grounded-theory approach to the qualitative data[20] and used semi-structured content analysis to code for barriers to home sputum collection.[21] Excerpt blocks were fixed at the full response to a question. During open coding, codes were generated inductively from the responses. After discussion, open codes were iteratively refined into a codebook. Two researchers, a Ugandan (JG) and a non-Ugandan (MAH), applied codes and resolved differences by discussion. Codes were applied to whole excerpts; co-occurrence was permitted. We then linked the interviews to the quantitative data.

Human subjects

Each participant or parent/guardian provided written informed consent. Participants 8–17 years old also provided written assent. Institutional review boards at Makerere University, Uganda National Council for Science and Technology, and Yale University approved the study.

RESULTS

Study population

Of 471 contacts screened for TB symptoms and HIV, 91 (19%) were at risk of TB and ≥5 years old. All were offered home sputum collection. The 91 contacts included 33 (36%) children aged 5–15 years (Table 1). Sixty-three (69%) contacts were female, and 27 (30%) reported living with HIV, including one child.

Process evaluation

LHWs collected at least one sputum sample from 35 (39%) at-risk contacts (Figure 1). The laboratory received sputum for all 35 contacts and analyzed 34 (97%) initial specimens from 34 contacts. Sputum testing confirmed TB in one (3%) contact and excluded TB in 22 (65%) contacts. TB was neither confirmed nor excluded in the remaining 12 contacts.

Uptake of home sputum collection by sub-group

Success in sputum collection was weakly clustered among households (ICC for collection by household=0.12). Contacts reporting active cough (53% vs 15%, Risk ratio (RR): 3.6, 95%CI: 1.5–8.3, p<0.001) and males (54% vs 32%, RR: 1.7, 95%CI: 1.0–2.8, p=0.05) were more likely to provide sputum (Table 2). In multivariable models adjusting for household clustering (Table S1), males provided sputum significantly more often than females (adjusted RR: 5.8, 95%CI: 1.2–29.0, p=0.03). Among those who did not report coughing in a stratified analysis, men were significantly more likely to provide sputum (43% vs 7%, RR: 5.8, 95%CI: 1.2–28.2, p=0.02). Among those who reported coughing, there were no significant differences in successful sputum collection between men and women (57% vs 50%, RR: 1.1, 95%CI: 0.70–1.9, p=0.60) or adults and children (55% versus 50%, RR: 1.1, 95%CI: 0.67–1.8, p=0.70).

Age category was not significantly associated with sputum collection in bivariate or multivariable analyses. People living with HIV were less likely to provide sputum than those without HIV (22% vs 45%, RR: 0.49, 95%CI: 0.2–1.0, p=0.04). However, the effect of living with HIV was not significant after controlling for coughing in multivariable analyses. Sputum quality was similar among males and females (64% vs 61% salivary, RR: 1.1, 95%CI: 0.62–1.8, p=0.85) and among adults and older children (63% vs 62% salivary, RR: 1.0, 95%CI: 0.59–1.8, p=0.90).

Interviews with contacts

The 19 interview respondents ranged in age from 17 to 61 years. No contacts declined the invitation to interview; three contacts were not interviewed because they had left Kampala. About half (9, 47%) had not produced sputum during the home visit; the remainder gave at

least one sputum sample. Fourteen (74%) were women, reflecting the gender balance among household contacts.

Key themes from interviews

Support for (and from) the index patient—Contacts saw cooperation with contact investigation, including providing sputum, as a way of demonstrating support for their sick household member, the index patient. However, index patients were also a source of support for contacts asked to produce sputum themselves. A young mother explained,

> "I liked the fact that I was tested for TB because my partner, ever since he was diagnosed TB-positive, he has always wanted to take me for TB evaluation but I hadn't had the opportunity together with my baby. But as I was still planning I received a call that a [LHW] was coming to test us and we gave up on going to the clinic and we had it done from home." (female, provided sputum)

In this case, the index patient's prior experience with the logistics of TB diagnostic evaluation was also an asset. Having seen her husband complete evaluation for TB just a few days earlier, the idea of providing sputum was not new to this contact: "When [the LHW] requested me to do the same I did it and I never had worries around it."

Perception that home services are convenient—Many contacts who gave sputum cited the perception that home sputum collection was convenient—it saved them the time, money, and stress associated with visiting a clinic. Even respondents who did not successfully provide sputum emphasized its convenience:

> "It makes it convenient in a way that one doesn't have to use transport; you just have to wait for your results." (male, did not provide sputum)

Most contacts had negative perceptions of clinics and preferred to be spared the need to visit one. A few believed that home sputum collection would entitle them to home-based treatment services.

Lost or insufficient sputum-collection containers—Several contacts who did not provide sputum said they were not offered evaluation at home despite willingness to participate. Some said the LHW did not ask them to provide sputum, usually because there were an insufficient number of containers for the household. Others said the LHW left a sputum container at the home for later pickup, but that they subsequently lost it. For example,

> "[The LHW] actually tested us as well. You know, when she came on that day I had a cough and she provided a sputum mug to me which got lost..." (female, did not provide sputum)

In some cases, contacts did not understand that failing to provide a sputum for examination meant they never tested for TB.

Difficulty producing sputum—Producing sputum could be time-consuming even among contacts who reported a productive cough during screening, leading LHWs to leave a

sputum container for later pickup. Some contacts said they were simply unable to produce sputum:

> "[The LHW] asked for it but it wasn't productive. I cough in the morning but still I can't produce sputum." (female, did not provide sputum)

Contacts who said they had difficulty producing sputum also said the LHW left them a sputum-collection container, which they subsequently lost.

TB stigma—Several female contacts who did not give sputum described concern about TB stigma. For example, the woman who lost the sputum container said of being asked to provide sputum, "In a way, it felt shaming" (female, did not produce sputum). Another, who feared that neighbors might associate TB evaluation with HIV said, "We [stayed] inside the house and we never wanted our neighbors to know" (female, did not provide sputum). Even women who produced sputum mentioned stigma when asked about the most challenging aspect of the home visit:

> "It was the neighbors who were there. When I was told to go outside and collect sputum; they were asking 'What is going on? Why is it that everyone who moves out goes with a container?' then I told them that they just want sputum and they asked 'For what?' They kept on asking 'Are you all sick like [the index patient]?' and I told them that they were going to check and see if we are like [the index patient] or not. And they started isolating [the index patient] because he has tuberculosis." (female, provided sputum)

Only women expressed concerns about stigma.

FGDs with LHWs

Thirteen LHWs participated in two FGDs about home sputum collection, each lasting approximately 75 minutes. Eleven were women (85%). The median age was 34 (range 25–55). One completed primary-level education (8%), six (46%) ordinary secondary-level, two (15%) advanced secondary-level, two (15%) diplomas, and two (15%) bachelor's degrees. LHWs had a median of nine years' work experience (range 5–22).

Key themes from FGDs

Discomfort requesting sputum—Like household contacts, LHWs said that sputum collection could be unexpectedly difficult or time-consuming. They emphasized that even patients reporting a productive cough were often unable to produce sputum spontaneously:

> "Sometimes we ask them to take some warm water…we try all that we can to make sure they can produce the sputum sample but it is not something easy. A household contact might say that she has a cough and you give a container but then you have to wait for a very long time because she has failed to produce a sample and you have to try all that you can to make sure you get that sample."

> ***LHW-1***: "But there are some whom you provide with the container and they put something else like saliva and remember the tablet requires the sample and you have to give the results. So, in case you are not provided with the right sample it

then becomes a debt that you have to go back and collect the right sample. So, sometimes when it comes to sputum collection it is as though you are at gun point [*Laughter.*] You want to have it but is insisting that that is all he could provide."

LHW-2: "You feel you are forcing the person and they are getting disturbed."

LHWs felt uncomfortable pressing contacts for too long to provide sputum. In these cases, LHWs in both FGDs reported leaving a sputum container with the household, but said that most contacts would never return the containers for evaluation.

Risk associated with visit—LHWs emphasized that visiting homes to screen contacts and collect sputum put them at personal risk of infection:

"Remember we want to have these people get help to avoid infecting others but when we reach there, since we really want them, you do not want to put this person in a stigmatized condition by putting on a mask…so, there are many risks…"

LHWs also expressed discomfort with carrying sputum samples. They especially worried that carrying specimens home over the weekend when laboratories were not open increased the risk that their own children would be exposed to TB.

Disgust—Finally, LHWs said it took time to adjust to their sputum collection responsibilities:

LHW 1: "It is something so hard but we just get used to it. There is one of our colleagues who vomited after seeing a sputum sample."

LHW 2: "It is something hard that we only get used with time. What I usually do I give them a cotton and ask them to wrap it so that I do not have to look at it."

LHWs did not discuss the influence of their disgust with sputum collection on household contacts' ability or willingness to produce sputum.

DISCUSSION

Sputum collection is an important, yet under-studied, component of active case-finding in high-burden, resource-constrained settings like Uganda. Others have identified factors associated with successful sputum collection in clinical settings, showing that instruction can improve the quality of sputum collection[22–25], and demonstrating that LHWs can effectively escort symptomatic contacts to health facilities for evaluation.[26] However, the individual and contextual characteristics that facilitate or impede sputum collection by LHWs in community settings have not been well described. Our study linked quantitative data on characteristics associated with successful sputum collection to qualitative data on the perceptions of the LHWs collecting sputum and the household members asked to produce sputum. While we found major challenges to sputum collection by LHWs in household settings, we also identified factors that could be leveraged to improve success rates.

We found that fewer than half of household contacts eligible for home sputum collection contributed a sample, similar to previous studies of LHW-led collection.[27] Household members described their eagerness to cooperate with LHWs during contact investigation,

support from the index patient in their efforts to produce sputum, and the convenience of providing sputum at home instead of at a facility. However, when contacts did not produce sputum quickly, LHWs said they felt uncomfortable pressing them to keep trying. Though the incremental yield of second specimen evaluation is low[28], it is also notable that 35% of contacts who initially contributed sputum did not receive definitive results because the laboratory required a second sample, which the LHW did not procure.

Given the enthusiasm for home screening and evaluation, even among contacts who were unable to produce sputum during the visit, the low collection rate suggests a missed opportunity. Studies in which LHWs accompanied contacts to a clinic for sputum collection by trained laboratory personnel report substantially higher rates of sputum collection than we observed.[26] In the recent Uganda National TB Prevalence Survey, for which laboratory technicians supervised expectoration at community collection points, 94% of at-risk participants provided sputum.[29]

Efforts to improve home sputum collection should therefore focus on eliminating barriers that originate from LHW practices. In order to reduce losses during LHW-led sputum collection, we suggest that LHWs be provided clear guidelines regarding how much time should be allotted to collection and when participants should proceed to complete evaluation at the clinic. Moreover, LHWs should receive continuous training to bring their skills up to the standards of laboratory staff. Finally, equipment checklists might reduce attrition due to insufficient containers.

We also found that women were less likely to produce sputum at home than men. Studies from clinical settings in sub-Saharan Africa have found small or nonsignificant gender differences in ability to produce sputum, but substantial differences in the likelihood of being offered sputum collection by a health worker.[30–32] In a randomized trial in Pakistan, receiving standardized instruction significantly increased the proportion of women testing smear-positive for TB.[16] In our study, all participants received standardized instruction, and there was no difference between men and women in the quality of sputum produced. However, additional instruction targeted at women might improve the proportion of women who contribute sputum samples.

Finally, women repeatedly mentioned stigma when discussing sputum collection in interviews, while men did not. It is possible that stigma or negative associations with expectoration decrease the length of time or effort that women expend to produce sputum during the home visit, reducing the likelihood that a sputum sample is collected. Gender differences in experience or anticipation of TB stigma could explain why women were significantly less likely to produce sputum at home. While the home is often assumed to be more private than a clinic, household members are easily identified by neighbors if they step outside to produce sputum. In our study, most participants produced sputum outside rather than inside their homes in order to reduce risk of transmission.[15] Future research might explore the effect of offering sputum collection indoors or in peri-indoor locations like external water closets. Such strategies could reduce anticipated and experienced stigma for women.[33] Future research might also test the effectiveness of short educational videos[24] on

mobile devices to further standardize instruction, model expectoration, normalize TB evaluation, and address gender stereotypes.

This study has some limitations. First, the quantitative sample was relatively small, limiting the potential for multivariable analysis. While we found a statistically significant gender difference in home sputum production, future research should test the effect of gender in a larger sample. Furthermore, our study was not powered to test whether individuals without symptoms have a similar or lower prevalence of TB. While guidelines recommend sputum collection in individuals with risk factors but no symptoms, such individuals produced sputum at lower rates in our study. Future studies should assess the indications for sputum collection to optimize diagnostic yield, safety, and efficiency. The sample size also limited the opportunity for LHWs to acquire facility and experience collecting sputum in household settings. Finally, we did not prospectively collect quantitative data on missing or insufficient sputum containers, or on leaving sputum containers for later collection.

Our study also has several strengths. First, we fill a gap in the literature on sputum collection by analyzing associations between contact characteristics and successful home sputum collection by LHWs. Second, we triangulate quantitative and qualitative data from household contacts and the LHWs who offered them home sputum collection. We thereby provide a more complete picture of the reasons for low rates of home sputum collection from the perspectives of both contacts and LHWs. Finally, our study contributes to the understanding of gender disparities in TB evaluation by linking quantitative data showing gender differences in home sputum collection to qualitative data demonstrating gendered experiences of TB stigma in the same population.[34–38]

CONCLUSIONS

Home sputum collection entails different challenges than collection in a clinical setting, and LHW-led home sputum collection may be more difficult to implement than many anticipate. Sputum collection rates might be improved by addressing barriers identified by household contacts and LHWs. LHW discomfort with sputum collection, failure to carry containers, and misallocation of time for collection might be addressed through clear guidelines, equipment checklists, and continuous training. Anticipated or experienced stigma might be reduced by providing privacy during sputum collection or standardized instructional videos. More research is needed to design targeted, destigmatizing interventions that improve the uptake, patient-centeredness, and quality of TB contact investigation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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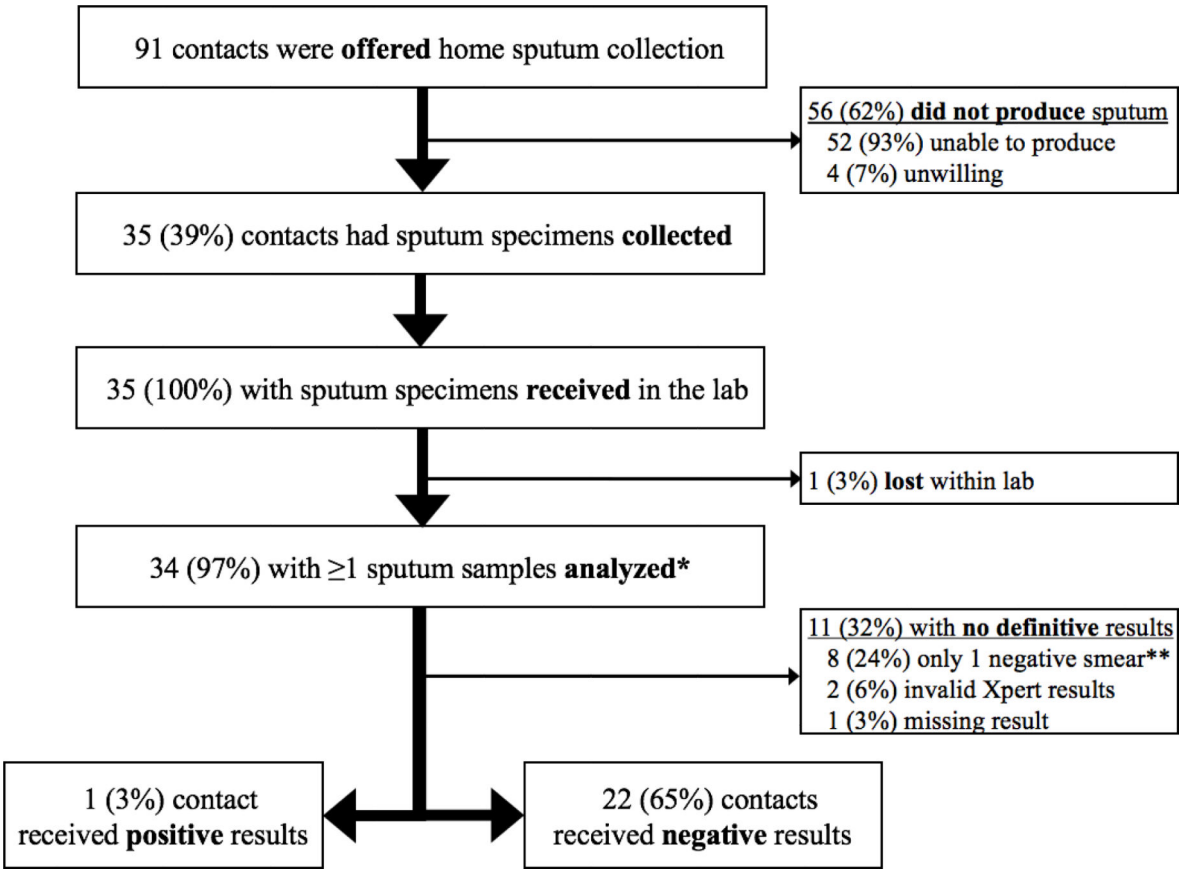

Figure 1. Flow diagram describing the sputum collection and evaluation cascade for at-risk household contacts

The figure presents the sputum collection and evaluation cascade for household contacts who were found to be at risk of TB during household contact investigation. All percentages were calculated as a proportion of the number of participants entering the previous step of the cascade. Initially, one sample was collected from each contact in the home. If possible, this single sample was evaluated by GeneXpert MTB/RIF. In some cases, GeneXpert was unavailable. In that case, the LHW attempted to return to the home to collect a second, early morning sputum sample for evaluation by smear microscopy. There were no statistically significant differences in characteristics between persons who gave one sample versus those who gave two samples.

* Of 34 initial samples, 25 (74%) were analyzed by GeneXpert, 10 (29%) by smear microscopy, and two (7%) by both.

** For 8 (24%) of the sputum samples, one sputum specimen was microscopically analyzed with a negative result but a second early morning sputum sample was not collected. Without a second negative smear, the results for these contacts are not definitive.

Abbreviation: TB, tuberculosis.

Table 1.

Characteristics of study participants

Characteristic	n (%) (n=91)
Age	
5 to 14 years old	32 (35%)
≥ 15 years old	59 (65%)
Female	63 (69%)
Persons living with HIV	27 (30%)
Cough of any duration	57 (63%)
Cough ≥2 weeks' duration	49 (54%)
Other TB symptoms *	16 (18%)

* Fevers, night sweats, weight loss. Characteristics of study participants by age group available in Table S2.

Abbreviation: TB, tuberculosis.

Table 2.

Association between participant characteristics and sputum collection

Characteristic	Sputum collected	Risk ratio (95%CI)	p-value
Cough of any duration			
Cough present (n=57)	30 (53%)	3.6 (1.5–8.3)	<0.001
Cough absent (n=34)	5 (15%)	--	
Sex			
Male (n=28)	15 (54%)	1.7 (1.0–2.8)	0.05
Female (n=63)	20 (32%)	--	
Age *			
≥ 15 years old (n=59)	20 (34%)	0.72 (0.43–1.2)	0.22
5 to 14 years old (n=32)	15 (47%)	--	
HIV status			
Living with HIV (n=27)	6 (22%)	0.49 (0.2–1.0)	0.04
No known HIV (n=64)	29 (45%)	--	

* Children under the age of five were not eligible for home sputum collection and were referred to a health center for sputum collection.