Title: Missed opportunities for tuberculosis investigation in a municipal hospital in Ghana: evidence from patient exit interviews

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Abstract

Background: We assessed coverage of symptom screening and sputum testing for tuberculosis (TB) in hospital outpatient clinics in Ghana.

Methods: In a cross-sectional study, we enrolled adults (≥18 years) exiting the clinics reporting ≥1 TB symptom (cough, fever, night sweats or weight loss). Participants reporting cough ≥2 weeks or cough of any duration plus ≥2 other TB symptoms (per national criteria) and those self-reporting HIV-positive status were asked to give sputum for testing with Xpert MTB/RIF.

Results: We enrolled 581 participants (median age 33 years [IQR: 24-48], 510/581 [87.8%] female). The most common symptoms were fever (348, 59.9%), chest pain (282, 48.5%) and cough (270, 46.5%). 386/581 participants (66.4%) reported symptoms to a healthcare worker, of which 157/386 (40.7%) were eligible for a sputum test per national criteria. Only 31/157 (19.7%) had a sputum test requested. 32 additional participants gave sputum among 41 eligible based on positive HIV status. In multivariable analysis, symptom duration ≥2 weeks (adjusted odds ratio [aOR] 6.99, 95% confidence interval [CI] 2.08-23.51) and previous TB treatment (aOR: 6.25, 95% CI: 2.24-17.48) were the strongest predictors of having a sputum test requested. 6/189 (3.2%) sputum samples had a positive Xpert MTB/RIF result.

Conclusion: Opportunities for early identification of people with TB are being missed in health facilities in Ghana.

Keywords: tuberculosis, screening practices, sputum request, missed diagnosis, healthcare workers, Ghana

Introduction

According to the World Health Organization (WHO), in 2018, an estimated 3 million TB cases were missed globally.[1] Missed or delayed diagnosis of TB can have negative implications for patients and the community. Treatment delays increase the duration of infectiousness among people with TB, which can lead to ongoing transmission in the community.[2, 3] Patients may also suffer increased ill-health, increased costs or mortality.[2]

The 2013 national TB prevalence survey in Ghana showed a higher prevalence than anticipated, (253/100 000 measured vs. 72/100 000 previously estimated) suggesting more missing cases than previously thought.[4, 5] The goal of the National TB Control Program (NTP) is to reduce TB prevalence by 25% by 2020 compared to 2013 baseline level of 253/100 000 population.[6] To achieve this goal, it is necessary to identify promptly people with active TB accessing care from health facilities and put them on treatment to reduce transmission. Moreover, Ghana's national standard operating procedures for TB case detection states that all adult patients attending outpatient departments and consulting rooms in clinics and hospitals, regardless of presenting symptoms, should be asked about cough by healthcare workers[7] and the criteria for requesting a sputum for TB testing are cough longer than two weeks or cough of any duration with at least two other TB-related symptoms (chest pain, weight loss, night sweat and fever). Patients who are HIV positive with cough of any duration, fever, weight loss or night sweat should also be asked to submit sputum for a TB test.[8]

Studies in Ghana have measured patient and health system delay in TB care but these recruited TB patients who were already on treatment.[9, 10] Much less is known about losses from the cascade of TB care prior to treatment in Ghana. We hypothesized suboptimal adherence to the national standard operating procedures for TB case detection in health facilities. We aimed to assess the coverage of TB symptom screening and sputum test-requesting practices among healthcare workers in a municipal hospital in Ghana.

Methods

Study setting

The study was conducted at outpatient clinics at the hospital in Ketu South Municipality of the Volta region, Ghana. In 2018, the municipality notified 172 TB cases out of a target of 546 estimated based on the 2013 national TB prevalence survey.[11] The municipality has eight health centres and one hospital. The hospital outpatient clinics provide several primary healthcare services. Persons identified in peripheral health centres as requiring further assessment or TB testing are referred to the hospital.[12] The hospital was chosen as the study site because it is the only testing centre for TB in the municipality with a laboratory that performs TB testing using Xpert MTB/RIF (Cepheid, Sunnyvale CA, USA). Tuberculosis diagnostic services are provided according to the national standard operating procedures for TB case detection.

Study design

We carried out a cross sectional study using exit interviews.

Study population

We recruited adults aged 18 years and above with at least one symptom suggestive of TB defined according to WHO criteria (cough, fever, night sweats or weight loss),[13] exiting the health facility after seeking care for their own health.

Sampling strategy and data collection procedure

Adults exiting the health facility on weekdays from September to November 2018, between 8am and 3pm, were approached by trained research assistants. Research staff attempted to approach consecutive adults; if the number of exiting adults exceeded the capacity of the research team to approach them, staff approached the closest individual. Those who reported seeking care for themselves were screened with a TB symptom questionnaire. Those who reported at least one symptom suggestive of TB were invited to be part of the study and those consenting were consecutively enrolled. A standardised questionnaire was used to collect data including socio-demographic characteristics; reason for clinic visit; TB-related symptoms, whether these symptoms were reported to the healthcare worker and whether a sputum test was requested. In line with national criteria, study staff

requested participants who reported a cough longer than two weeks; or cough of any duration plus at least two other TB-related symptoms to produce a single spot sputum sample for testing in the hospital laboratory using the Xpert MTB/RIF assay. In addition, those self-reporting HIV-positive status with any TB-related symptom were asked to produce sputum for laboratory testing. Research assistants coached participants who were eligible for a sputum test on how to produce quality sputum before a sputum container was given to them. Participants then went into a sputum booth to produce sputum on their own. Those who produced a sputum sample were informed of their test result and those with a positive test result were referred to the chest clinic for TB treatment. We crosschecked from the TB laboratory register at the hospital to find out if participants who reported having a sputum test requested by a healthcare worker did submit a sputum for testing. All data were collected electronically using Open Data Kit (ODK) and uploaded onto a secure server hosted by the London School of Hygiene & Tropical Medicine.

Primary outcome

The primary outcome was the proportion of participants who had a sputum test requested by a healthcare worker in the outpatient clinic, among individuals who met the criteria for a sputum test according to Ghana's national standard operating procedures for TB case detection.

Sample size

We assumed that 25% of patients reporting cough >2 weeks to a healthcare worker would be asked to submit sputum for a TB test;[4] to estimate the 95% confidence interval with 8% precision, the minimum target sample size was 450 participants.

Data management and statistical analysis

Characteristics of study participants were described, and comparisons made using chi-square test for categorical variables and t-test for continuous variables. Logistic regression analysis was used to identify associations between being asked to give a sputum sample as outcome variable and explanatory variables. Variables with likelihood ratio p-value <0.2 in univariable analysis were considered for inclusion in a multivariable model. However, adjusted analysis was limited by the relatively small number of outcomes and the multivariable model therefore included only covariates

most strongly associated with the outcome. Data were analysed using Stata v15 (Stata Corp, College Station TX, USA).

Results

A total of 2 516 people exiting the health facility were approached: 1 652 (65.7%) of them had sought care at the hospital of which 653/1652 (39.5%) were eligible for the study (Figure 1). The main reasons for ineligibility were not having any of the TB-related symptoms (865, 86.6%), being below 18 years (96, 9.6%) or already on TB treatment (32, 3.2%). Among these 653 eligible individuals, 581(89.0%) consented and were recruited. The main reasons for non-consent were not having time for the interview (53, 73.6%) and not interested in the study (19, 26.4%).

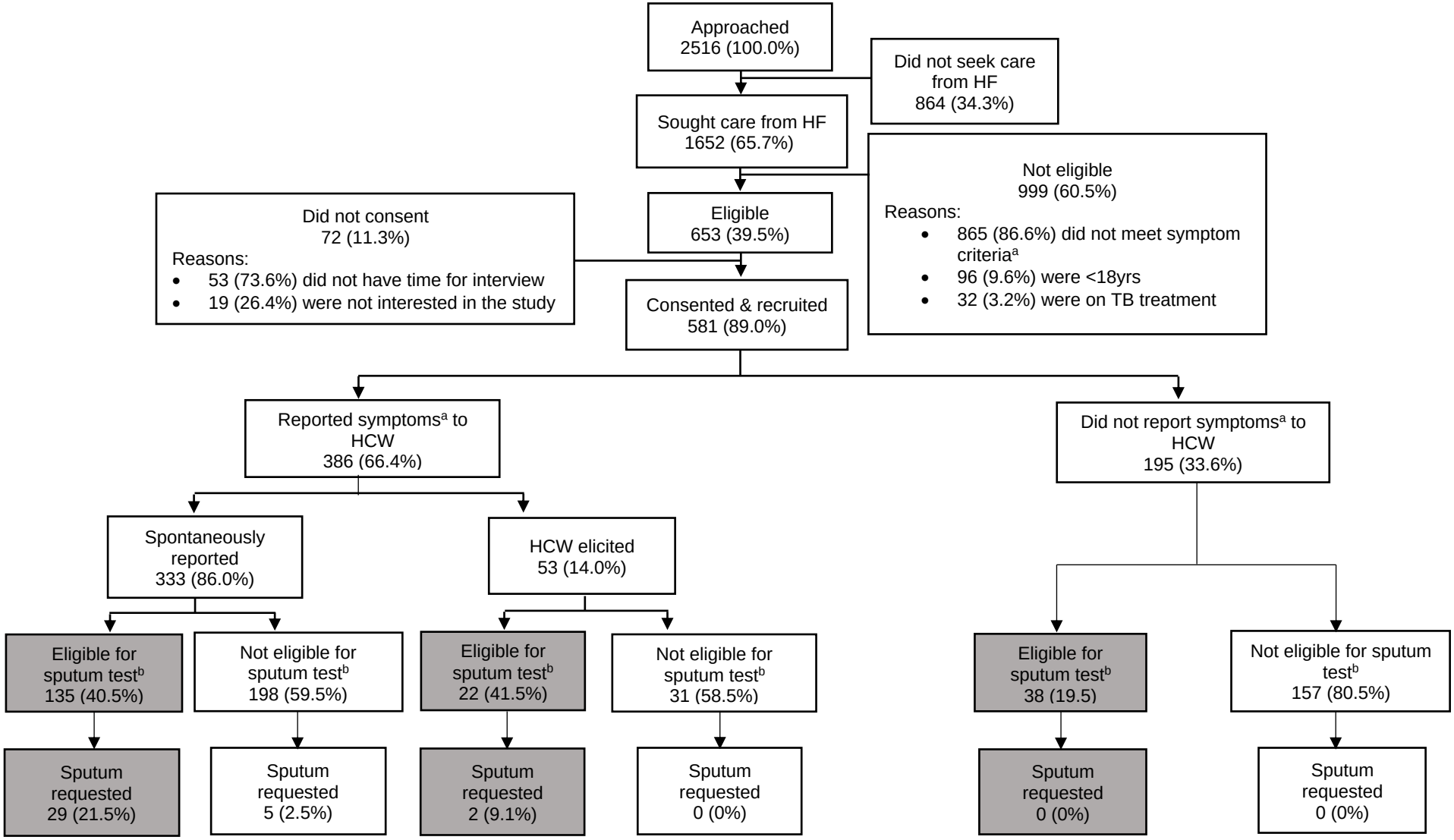

Figure 1: Flowchart of study recruitment of participants, reporting of symptoms and being asked to do a sputum test by HCW. HF: Health facility; HCW: Healthcare worker. [a] Symptoms considered suggestive of TB i.e. cough, fever, weight loss, night sweats. [b] Criteria for eligibility for sputum test= cough >2 weeks or cough of any duration plus at least two other TB-related symptoms (fever, weight loss, night sweats).

Characteristics of study participants

The median age among the 581 recruited participants was 33 years (interquartile range [IQR] 24-48), most were females (510/581, 87.8%) and the majority had attained primary level education (312/581, 53.7%), (Table 1). The most common TB-related symptoms were fever (348, 59.9%), chest pain (282, 48.5%) and cough (270, 46.5%). The main reason for visiting the hospital for most participants was for general medical care (237/581, 40.8%).There was strong evidence that those who reported symptoms to a healthcare worker had more TB-related symptoms (P <0.001) and longer duration of symptoms (P=0.01) compared to those who did not report their symptoms (Table 1).

Table 1: Characteristics of people exiting health facility and reporting at least one TB-related symptom in Ketu South Municipality, Ghana

Characteristics	Total N=581	Reported symptoms to HCW n=386		Did not report symptoms to HCW n=195	[a]P-value
	n (column %)	Spontaneously reported n=333 n (row %)	HCW elicited n=53 n (row %)	n (row %)	
Age, year, (IQR)	33 (24-48)	37 (25-51)	34 (22-48)	29 (22-39)	<0.001
Gender					0.28
Male	71 (12.2)	45 (63.4)	8 (11.3)	18 (25.4)	
Female	510 (87.8)	288 (56.5)	45 (8.8)	177 (34.7)	
Educational level					0.12
No formal education	148 (25.5)	97 (65.5)	8 (5.4)	43 (29.1)	
Primary/JHS	312 (53.7)	171 (54.8)	30 (9.6)	111 (35.6)	
Secondary/tertiary	121 (20.8)	65 (53.7)	15 (12.4)	41 (33.9)	
Symptoms (yes)[b]					
Cough	270 (46.5)	180 (66.7)	28 (10.4)	62 (23.0)	<0.001
Fever	348 (59.9)	220 (63.2)	32 (9.2)	96 (27.6)	0.001
Chest pain	282 (48.5)	186 (66.0)	29 (10.3)	67 (23.8)	<0.001
Excessive night sweat	163 (28.1)	88 (54.0)	14 (8.6)	61 (37.4)	0.47
Weight loss	214 (36.8)	113 (52.8)	28 (13.1)	73 (34.1)	0.03
Number of symptoms					<0.001
1	208 (35.8)	98 (47.1)	16 (7.7)	94 (45.2)	
2	165 (28.4)	99 (60.0)	13 (7.9)	53 (32.1)	
3	116 (20.0)	71 (61.2)	11 (9.5)	34 (29.3)	
≥4	92 (15.8)	65 (70.7)	13 (14.1)	14 (15.2)	
Duration of symptoms					0.01

<2 weeks	252 (44.4)	155 (61.5)	13 (5.2)	84 (33.3)	
≥2 weeks	315 (55.6)	174 (55.2)	39 (12.4)	102 (32.4)	
HIV status					0.19
Positive	63 (10.8)	40 (63.5)	3 (4.8)	20 (31.8)	
Negative	307 (52.8)	163 (53.1)	30 (9.8)	114 (37.1)	
Don't know	211 (36.3)	130 (61.6)	20 (9.5)	61 (28.9)	
Health histories (yes)[b]					
Diabetes	29 (5.0)	15 (51.7)	3 (10.3)	11 (37.9)	0.82
Hypertension	145 (25.0)	91 (62.8)	17 (11.7)	37 (25.5)	0.05
Ever treated for TB	22 (3.8)	13 (59.1)	3 (13.6)	6 (27.3)	0.67
Main reason for visit					<0.001
TB symptoms	96 (16.5)	92 (95.8)	4 (4.2)	0 (0.0)	
Routine ART clinic	40 (6.9)	26 (65.0)	3 (7.5)	11 (27.5)	
Antenatal care	129 (22.2)	54 (41.9)	10 (7.8)	65 (50.4)	
General medical care	237 (40.8)	133 (56.1)	30 (12.7)	74 (31.2)	
Other[c]	79 (13.6)	28 (35.4)	6 (7.6)	45 (57.0)	
Number of times ever sought care for TB symptoms					0.37
0	106 (18.2)	52 (49.1)	11 (10.4)	43 (40.6)	
1-2	408 (70.2)	240 (58.8)	35 (8.6)	133 (32.6)	
≥5	67 (11.8)	41 (61.2)	7 (10.5)	19 (28.4)	

ART: Antiretroviral therapy; HCW: Healthcare worker; HIV: Human immunodeficiency virus; JHS (12-14 years): Junior High School; TB: Tuberculosis

[a] P-value is for the comparison between those who reported their symptoms spontaneously, those a healthcare worker elicited their symptoms and those who did not report their symptoms at all

[b] Response is not mutually exclusive

[c] Diabetic clinic, hypertension clinic, mental health clinic, eye clinic and family planning unit

Practices of healthcare workers

Of the 581 recruited participants, 386/581 (66.4%) had reported their symptoms to a healthcare worker. Among those who reported their symptoms, 333/386 (86.0%) had spontaneously reported their symptoms while 53/386 (14.0%) only reported their symptoms when elicited by a healthcare worker (Figure 1). Overall, 195 (33.6%) participants of the 581 recruited were eligible for a sputum test according to Ghana's national standard operating procedures for TB case detection, but only 31/195 (15.9%) had a sputum test requested by a healthcare worker. Among those who spontaneously reported their TB-related symptoms, 135/333 (40.5%) were eligible for a sputum test, however, only 29/135 (21.5%) had a sputum test requested (Figure 1). Among the 53 participants whose symptoms were elicited by a healthcare worker, 22 (41.5%) were eligible for a sputum test, yet only 2/22 (9.1%) had a sputum test requested. Also, among participants who did not report their symptoms at all to a healthcare worker, 38/311 (19.5%) were eligible for a sputum test: none of them had a sputum test

requested (Figure 1). All participants who had a sputum test requested by a healthcare worker were confirmed in the laboratory register to have submitted sputum for the test.

Reasons for not reporting symptoms to a healthcare worker

For participants (195/581, 33.6%) who did not report their TB-related symptoms to the healthcare worker, the reasons given were that the TB-related symptoms were not the reason they visited the hospital (156/195, 80.0%), they did not think it was important to report (32, 16.4%) and other reasons such as forgetting to report (7, 3.6%).

Factors associated with having a sputum test requested by a healthcare worker

In univariable analysis, there was a higher odds of having a sputum test requested by a healthcare worker among people with longer duration of symptoms (≥2 weeks vs <2 weeks, OR: 9.71, 95% CI 2.94-32.06), previous TB treatment (OR 8.52, 95%CI 3.23-22.54), increasing number of symptoms (≥3 vs 1-2, OR 4.50, 95% CI 2.16-9.34), males (OR 3.56, 95% CI 1.67-7.59), attending for TB-related symptoms vs general medical care (OR 3.12, 95% CI 1.49-6.82) and older age (OR 2.82, 95% CI 1.17-6.84 and 1.74, 95% CI 0.79-3.80 for >60 and 40-60 vs 18-39 years respectively, Table 2). After adjusting for confounders in multivariable analysis, there remained strong associations between sputum being requested and duration of symptoms (adjusted OR [aOR] 6.99, 95%CI 2.08-23.51), previous TB treatment (aOR 6.25, 95%CI 2.24-17.46) and increasing number of symptoms (aOR 3.14, 95% CI 1.47-6.71), (Table 2). In addition, to explore any potential confounding effect of age and gender, a separate model was developed to assess the association of duration of symptoms with having a sputum test requested after adjusting for age and gender (data not shown). The strength of association was similar to that presented in table 2 thus not suggesting confounding by age or gender. Similar models were run for previous TB treatment and number of symptoms and similarly the strength of association remained the same (data not shown).

271 Table 2: Factors associated with being asked to submit sputum by a healthcare
272 worker, Ketu South Municipality, Ghana

Variable	N=581						
	Total (n)	Submitted sputum (n)	%	Univariable analysis		Multivariable analysis	
				OR (95%CI)	P	aOR (95%CI)	P
Gender					[a]<0.01		
Female	510	25	4.9	Reference			
Male	71	11	15.5	3.56 (1.67-7.59)	<0.01		
Age group (years)					[a]0.07		
18-39	371	17	4.6	Reference			
40-60	143	11	7.7	1.74 (0.79-3.80)	0.17		
>60	67	8	11.9	2.82 (1.17-6.84)	0.02		
Educational level					[a]0.19		
No formal education	148	14	9.5	Reference			
Primary/JHS	312	16	5.1	0.52 (0.25-1.09)	0.08		
Secondary/tertiary	121	6	5.0	0.50 (0.19-1.34)	0.17		
Number of symptoms					[a]<0.001		
1-2	373	11	3.0	Reference		Reference	
≥3	208	25	12.0	4.50 (2.16-9.34)	<0.001	[b]3.14 (1.47-6.71)	<0.01
Duration of symptoms					[a]<0.001		
<2 weeks	252	3	1.2	Reference		Reference	
≥2 weeks	315	33	10.5	9.71 (2.94-32.06)	<0.001	[b]6.99 (2.08-23.51)	<0.01
HIV status					[a]0.57		
Negative	307	16	5.2	Reference			
Positive	63	5	7.9	1.56 (0.55-4.45)	0.40		
Don't know	211	15	7.1	1.39 (0.67-2.88)	0.37		
Ever treated for TB					[a]<0.001		
No	559	29	5.2	Reference		Reference	
Yes	22	7	31.8	8.52 (3.23-22.54)	<0.001	[b]6.25 (2.24-17.46)	<0.001
Diabetes					[a]0.50		
No	552	35	6.3	Reference			
Yes	29	1	3.5	0.53 (0.07-3.99)	0.54		
Main reason for visit					[a]<0.001		
General medical care	237	14	5.9	Reference			
TB symptoms	96	16	16.7	3.12 (1.49-6.82)	<0.01		
Routine ART clinic	40	3	7.5	1.29 (0.35-4.71)	0.70		
Antenatal care	129	1	0.8	0.12 (0.02-0.96)	0.05		
Other[c]	79	2	2.5	0.41 (0.92-1.86)	0.25		
Number of times sought care for TB symptoms					[a]0.02		
0	106	7	6.6	Reference			
1-2	408	19	4.7	0.69 (0.28-1.69)	0.42		
≥3	67	10	14.9	2.48 (0.90-6.88)	0.08		

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274 ART: Antiretroviral therapy; HIV: Human immunodeficiency virus; JHS (12-14 years): Junior High School; P: P-value; TB:
275 Tuberculosis
276 [a] Log likelihood P-value
277 [b] In order to prevent overfitting of the adjusted model it was restricted to the three covariates with the strongest association with
278 the outcome
279 [c] Diabetic clinic, hypertension clinic; mental health clinic; eye clinic and family planning unit

Laboratory findings

A total of 236/581 (40.6%) participants were eligible according to study criteria to produce a spot sputum sample for laboratory testing using Xpert MTB/RIF (Figure 2). Among these, 195 met the national criteria for sputum testing, and an additional 41 met study criteria based on self-reporting HIV positive status who did not meet national criteria but reported any of cough, weight loss, fever or night sweats. Of those eligible, 189/236 (80.1%) produced a sputum sample for the test. The majority of the sputum samples (125/189, 66.1%) were salivary and 64/189 (33.9%) were mucopurulent. Test results showed 174/189 (92.1%) were negative, 6/189 (3.2%) were positive and 9/189 (4.8%) were invalid probably due to laboratory error (Figure 2). All positive results were without rifampicin resistance.

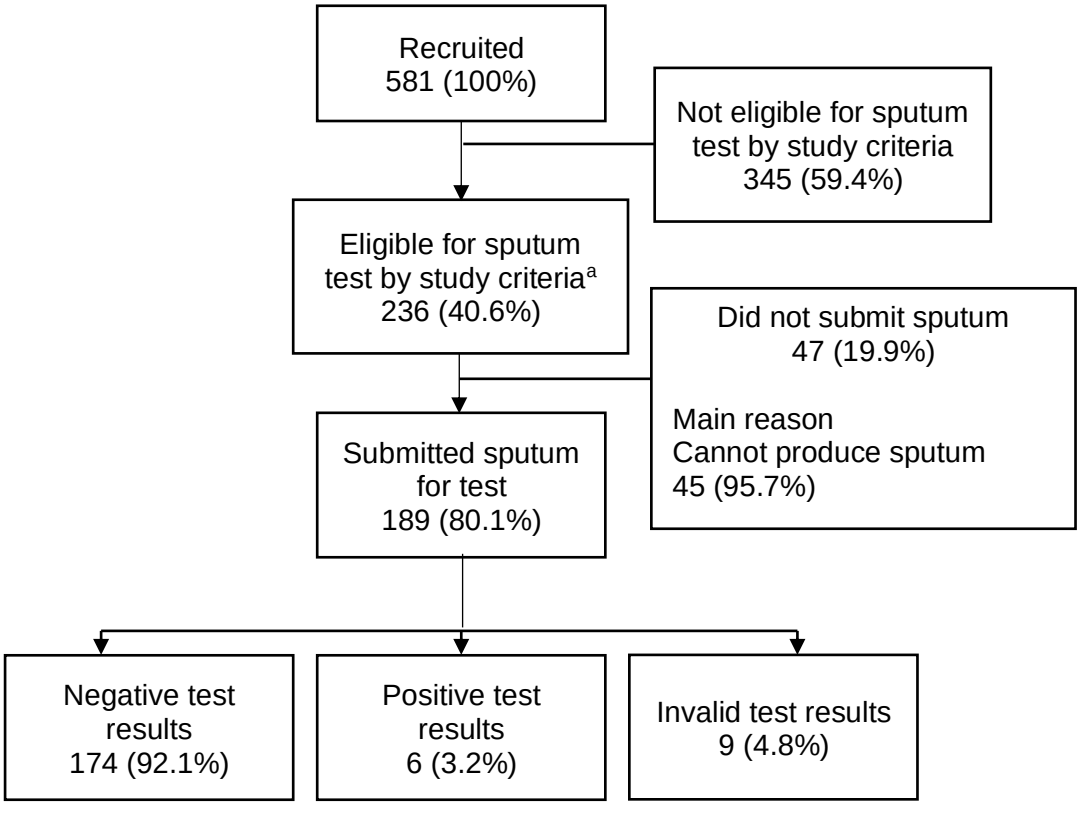

Figure 2: Flowchart for laboratory testing (Xpert MTB/RIF) using study criteria

[a] Eligibility for sputum test by study criteria= cough >2 weeks or cough of any duration plus at least two other TB-related symptoms (fever, weight loss, night sweats) or self-reporting HIV-positive status with any TB-related symptom

Discussion

Findings from this study show that patients with TB-related symptoms visiting outpatients' departments for primary health care services were not optimally screened for symptoms of TB even though the national standard operating procedure for TB case detection specifies that people attending outpatient departments of health facilities should be asked about TB-related symptoms. Even among patients who reported symptoms and were eligible for a sputum test, a large proportion of them never had the test requested by a healthcare worker. This shows there are missed opportunities for TB diagnosis in the health facility.

A study in Cape Town, South Africa in 2013, also showed that people with respiratory symptoms exiting primary health facilities were not asked about their symptoms and did not have a sputum test requested.[14] They recommended that intensified case finding should not be limited to only those who report their respiratory symptoms. Other studies have demonstrated missed opportunities for early TB diagnosis in health facilities due to non-adherence to diagnostic guidelines.[15-17] In a sub-study using exit interviews at clinics participating in a pragmatic cluster randomised trial evaluating programmatic roll-out of Xpert MTB/RIF in South Africa (XTEND), the change from sputum microscopy to Xpert MTB/RIF did not substantially influence healthcare workers' suboptimal practices in requesting sputum tests among patients presenting with TB symptoms.[18]

The main reason patients did not report their symptoms to a healthcare worker in our study was because they were not seeking care for these symptoms or did not find it important to report. The study in Cape Town conducted in primary health facilities also found that among study participants who tested positive for TB, none of them reported their symptoms to a healthcare worker when they visited the clinic.[14] Several other studies have shown patients delay in seeking care for their TB-related symptoms.[3, 19-21] It is imperative that we find ways to encourage patients to seek care early and to report all their symptoms when they visit a health facility.

Our study showed that persons with longer duration of symptoms or prior TB treatment were more likely to be asked to submit a sputum for a test. Studies in Uganda and South Africa have all shown that healthcare workers tend to request sputum tests in persons with longer duration of symptoms.[18, 22] However, a study conducted in the

Greater Accra region of Ghana from 2010 to 2013 showed that more TB cases were identified when screening was done using the new diagnostic guidelines of cough of any duration (>24 hours) and any other TB-related symptom compared to using just cough >2 weeks.[23] This confirms that using longer duration of symptoms to investigate for TB could lead to missed opportunities for early diagnosis. This however has high cost implications for diagnosis. Therefore, there is the need to find efficient and cost-effective strategies for diagnosis.

In this study, the majority of the participants were females, and this reflects the true outpatient department attendance where more women visit the outpatient department for care than men. This is supported by data from the district health information management system that shows from 2016 to 2019, 72.2% to 72.6% of outpatient department attendances were by women.[24]

There are some limitations to this study. We depended on participants' self-report of having reported or not reported their symptoms to a healthcare worker which we could not verify from clinic records. For those who said they had a sputum test requested, we cross-checked from the laboratory register to see if they submitted a sputum sample. However, the use of exit interviews was a robust way to reduce recall bias since patients were interviewed immediately after consultation with a healthcare worker. The low yield of TB cases among participants submitting a sputum sample to the study team could be as a result of poor quality of sputum samples since most of the samples were salivary. This highlights the need for staff to supervise patients to ensure good quality sputum samples. In addition, the study was conducted in only the municipal hospital, and only during working hours, so findings cannot necessarily be generalized to other health facilities in the municipality.

Conclusion

Opportunities to identify people with TB were missed in this health facility; both coverage of TB symptom screening and testing of those fulfilling criteria for testing were low. This shows suboptimal adherence to national guidelines by healthcare workers in the study setting. There is the need to improve the system to maximise early detection of TB among people attending health facilities.

Authors contribution: JD and ADG conceived and designed the study. Data capture tools were designed by JD, ADG, DG and CTN. Data collection was done by JD and CTN. Data analysis and interpretation were done by JD, DG, CTN and ADG. The first draft of the manuscript was written by JD. Critical comments were provided by ADG, DG, CTN and FB. All authors read and approved the final manuscript.

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Competing interest: None declared

Ethical approval: Ethical approval was obtained from the Ghana Health Service Ethics Review Committee and London School of Hygiene & Tropical Medicine Ethics Committee. Written informed consent was obtained from literate participants and for those who could not read and write, consent was documented with a thumbprint in the presence of a literate witness.

Data availability statement

The data underlying this article cannot be shared publicly due to sensitive patient information. The data will be shared on reasonable request to the corresponding author.

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