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Intensified tuberculosis case finding among HIV-infected persons using a WHO symptom screen and Xpert® MTB/RIF

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SUMMARY

SETTING—Human immunodeficiency virus (HIV) clinic in Addis Ababa, Ethiopia. The World Health Organization (WHO) recommends active tuberculosis (TB) case-finding among people living with HIV (PLHIV) in high-burden settings.

OBJECTIVE—To evaluate the effectiveness of combining a WHO-recommended symptom screen and the Xpert® MTB/RIF test to enhance TB case finding.

DESIGN—In this cross-sectional study, PLHIV were screened for TB using a WHO-recommended symptom-based algorithm (cough, fever, night sweats, weight loss). Those with a positive symptom screen (≥ 1 symptom) underwent diagnostic testing with smear microscopy, culture, and Xpert.

RESULTS—Of 828 PLHIV (89% on antiretroviral therapy), 321 (39%) had a positive symptom screen. In multivariate analysis, an unscheduled clinic visit (aOR 3.78, 95%CI 2.69–5.32), CD4 count <100 cells/μl (aOR 2.62, 95%CI 1.23–5.59) and previous history of TB (aOR 1.62, 95%CI 1.12–2.31) were predictors of a positive symptom screen. Among those with a positive symptom screen, 6% had active pulmonary TB. Smear microscopy sensitivity for TB was poor (30%) compared to culture and Xpert.

CONCLUSIONS—A positive symptom screen was common among PLHIV, creating a substantial laboratory burden. Smear microscopy had poor sensitivity for active TB disease. Given

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the high rate of positive symptom screen, substantial additional resources are needed to implement intensified TB case finding among PLHIV in high-burden areas.

Keywords

operational research; developing countries; Ethiopia; implementation science

Tuberculosis (TB) is the leading cause of death among people living with the human immunodeficiency virus (PLHIV) worldwide.^{1,2} Due to the high burden of TB-HIV co-infection, the World Health Organization (WHO) recommends intensified case finding for active TB among PLHIV in high-burden areas, including screening for TB at every health care encounter.¹ A meta-analysis determined that the absence of current cough, fever, night sweats, and weight loss has a 98% negative predictive value (NPV) for pulmonary TB among PLHIV in settings with 5% TB prevalence.³ The WHO recommends that those with a positive symptom screen (at least one of four symptoms) undergo further TB diagnostic testing.¹ However, TB diagnosis is limited by the diagnostic tests commonly available in resource-limited settings: smear microscopy has low sensitivity among PLHIV,⁴⁻⁷ and acid-fast bacilli (AFB) culture, the gold standard, is not widely available.^{8,9}

The Xpert[®] MTB/RIF assay (Cepheid, Sunnyvale, CA, USA) is a rapid TB molecular diagnostic test endorsed by the WHO in 2010 for use in resource-limited settings.^{7,10} In 2013, the WHO recommended Xpert as the initial diagnostic test for PLHIV with TB signs and symptoms in low- and middle-income countries.¹¹ Among PLHIV in a high TB prevalence area in South Africa, Xpert had a sensitivity of 73% when performed at a national reference laboratory (including both AFB smear-positive and smear-negative specimens) compared to 28% for smear microscopy.⁷ Despite promising results when performed in centralized facilities, the role of Xpert in enhancing TB case finding among PLHIV has not been well-defined in resource-limited health care facilities, especially outside South Africa.¹² Furthermore, data on the utility of combining the WHO symptom screen with Xpert in resource-limited settings are limited.

Ethiopia is one of the 22 high TB burden countries that account for >80% of global TB cases.¹³ There were an estimated 210 000 new TB cases in Ethiopia in 2013, and HIV co-infection is present in 10% of TB cases.¹³ Many patients in Ethiopia are treated empirically for TB, i.e., without microbiological confirmation, due to lack of laboratory infrastructure and the availability of smear microscopy alone in most areas.^{8,9,14,15} To inform clinical decisions regarding intensified TB case finding, including active TB screening for PLHIV and scale-up of Xpert as a diagnostic test in Ethiopia and other developing countries, we performed an implementation science/operational research study^{16,17} of implementing the WHO symptom-based screen for TB in combination with Xpert at a large HIV clinic in Addis Ababa, Ethiopia.

METHODS

Study setting and population

The study was conducted from July to October 2013 in Addis Ababa, Ethiopia, at the All Africa Leprosy Rehabilitation and Training Center (ALERT) Hospital HIV Clinic, which provides care for approximately 15 000 PLHIV. Before the study, the WHO TB symptom screen was the standard of care at the clinic, but was inconsistently applied. TB rates at the clinic were not well characterized, although a previous study reported on rates using 2007 WHO guidelines for smear-negative TB.^{14,18} PLHIV with CD4 count <500 cells/ μ l, active TB disease, or WHO clinical stage 3 or 4 HIV disease are started on antiretroviral therapy (ART).¹⁹

For this study, clinicians asked patients aged $\geq$ 18 years to participate; those who agreed and provided verbal consent were enrolled. PLHIV currently being treated for active TB disease were excluded. PLHIV were asked about the presence of four symptoms (cough, fever, night sweats, and weight loss) according to WHO guidelines.¹ Those with a positive symptom screen (at least one of the four symptoms) were asked to provide sputum samples. Because of laboratory capacity, the first five patients with a positive symptom screen were enrolled in the study each day. We also conducted a 20-day substudy where all PLHIV presenting to the HIV Clinic underwent the WHO-recommended TB symptom screen during clinic registration.

The study was approved by the Institutional Review Boards of Armauer Hansen Research Institute (AHRI), Addis Ababa; ALERT Hospital, Addis Ababa, Ethiopia; and Emory University, Atlanta, GA, USA.

Laboratory methods

PLHIV with a positive symptom screen were asked to provide three sputum specimens for diagnostic testing: 1) a 'spot' sputum specimen at the time of enrollment, 2) a 'morning' sputum specimen, and 3) an additional 'spot' sputum specimen when the morning specimen was returned. Data including demographic information, previous history of TB, HIV treatment and ART medication use, and laboratory results (including CD4 count) were abstracted from medical records.

AFB sputum smear microscopy was performed on all sputum samples at the ALERT Hospital Microbiology Laboratory using a direct Ziehl-Neelsen stain, as previously described.²⁰ In addition to smear microscopy, the morning sputum sample was used for AFB culture, which was performed at the AHRI TB Laboratory (located on the ALERT Hospital campus) using Löwenstein-Jensen solid media and standard diagnostic methods as previously described.¹⁴ A morning sputum specimen was also used for the Xpert test, performed at the Addis Ababa Regional Health Research Laboratory as previously described.²¹ Xpert results were reported as positive, negative, or indeterminate for *Mycobacterium tuberculosis*, and for the presence or absence of rifampin (RMP) resistance if *M. tuberculosis* was present. Only patients who submitted the first 'spot' sputum specimen were included in the analysis of smear microscopy results. A morning sputum specimen was required for analysis using Xpert and AFB culture. Laboratory results were communicated

verbally to the patient's primary clinician and recorded in the medical record; all management and treatment decisions were at the discretion of the clinician.

Data management and analysis

Data were entered into a password-protected electronic database (Research Electronic Data Capture [REDCap])²² and analyzed using SAS v9.4 (Statistical Analysis System Institute, Cary, NC, USA). Active pulmonary TB disease was defined as a positive Xpert result and/or positive AFB culture for *M. tuberculosis*. Univariable and multivariable logistic regression was performed to assess risk factors for a positive symptom screen and for TB disease. Risk factors with significance on univariable analysis and variables with biologic plausibility were included in the final multivariable model. $P = 0.05$ was considered statistically significant.

RESULTS

Patients

Among 850 PLHIV assessed for study eligibility, 22 were excluded due to current active anti-tuberculosis treatment and 828 were screened for TB with the WHO-recommended symptom screen (Figure). The mean age was 38.2 years (standard deviation [SD] ± 10.0), and 535 (65%) were female (reflecting the sex distribution in the clinic). The mean CD4 count was 420 cells/ μ l (SD ± 219); 730 (89%) were currently on ART, 272 (33%) had been treated for TB in the past, and 265 (33%) had presented for an unscheduled visit (Table 1).

WHO-recommended TB symptom screen

Among 828 PLHIV screened for TB using the WHO-recommended symptom screen, 321 (39%) had a positive symptom screen (one or more of the four symptoms): 280 (34%) reported cough, 172 (21%) night sweats, 159 (19%) fever, and 103 (13%) weight loss (Table 1). PLHIV with a positive symptom screen were more likely to make an unscheduled visit than those without symptoms (57% vs. 24%, odds ratio [OR] 4.11, 95% confidence interval [CI] 2.97–5.67, $P < 0.001$), be screened by a physician (56% vs. 19%, OR 4.89, 95% CI 3.15–7.60, $P < 0.001$), have a CD4 count < 100 cells/ μ l (8% vs. 3%, OR 3.17, 95% CI 1.62–6.18, $P < 0.001$), and not to be receiving ART (16% vs. 8%, OR 2.32, 95% CI 1.48–3.64, $P < 0.001$) (Table 2). In multivariable analysis, independent risk factors for a positive symptom screen included an unscheduled visit (adjusted OR [aOR] 3.78, 95% CI 2.69–5.32, $P < 0.001$), CD4 count < 100 cells/ μ l (aOR 2.62, 95% CI 1.23–5.59, $P = 0.01$), and previous history of treatment for active TB (aOR 1.62, 95% CI 1.12–2.31, $P < 0.01$) (Table 3).

TB diagnostic testing results

Among the 321 PLHIV with a positive symptom-based screen, 256 were referred for sputum collection (52 [16%] declined and 13 [4%] were not referred by their clinician). After referral, 39 of 256 patients (15%) did not provide a sputum sample for diagnostic testing. The remaining 217 patients provided sputum samples and had an Xpert and/or an AFB culture result. A total of 13/217 (6.0%, 95% CI 3.5–10.0) PLHIV had active TB disease based on a positive Xpert result and/or a positive AFB culture for *M. tuberculosis* (Figure). None of the eight Xpert-positive patients had RMP-resistant TB. Compared to the gold

standard of a positive Xpert and/or positive culture for *M. tuberculosis*, the sensitivity of smear microscopy was 30%.

No risk factor routinely assessed at clinic visits differed significantly between those with and those without active TB, including symptom screen results (Table 4). In univariable analysis, patients found to have active TB disease were younger (OR 0.94/year, 95%CI 0.88–1.01, $P = 0.08$), were diagnosed more recently with HIV (OR 0.98/month since diagnosis, 95%CI 0.97–1.00, $P = 0.09$), had CD4 counts <100 cells/ μ l (OR 3.29, 95%CI 0.61–17.68, $P = 0.16$), and were not currently on ART (OR 2.67, 95%CI 0.77–9.23, $P = 0.12$), but these differences were not statistically significant. Prior history of anti-tuberculosis treatment was not a risk factor for current active TB disease (OR 1.02, 95%CI 0.32–3.24, $P = 0.97$).

Symptom screening of all HIV clinic patients

PLHIV enrolled into our primary study represented a subset of patients seen at the ALERT HIV Clinic. Over a 20-day period, the WHO-recommended symptom screen was performed on all PLHIV at the time of clinic registration to assess the full impact of its implementation. During this period, of the 2687 PLHIV seen at the clinic and who underwent a symptom screen, 1410 had a positive symptom screen (52.5%, 95%CI 50.6–54.5). On average 134 patients visited the clinic per day, and 71 had a positive symptom screen.

DISCUSSION

TB remains the leading cause of death among PLHIV in sub-Saharan Africa and globally.^{2,23} The WHO therefore recommends enhanced TB case finding among PLHIV in high TB burden countries.¹ In this implementation science project, we evaluated the feasibility and efficacy of intensified TB case finding among PLHIV at a large HIV clinic in Addis Ababa, Ethiopia, by implementing the WHO-recommended TB symptom screen^{1,3} in combination with the Xpert assay. While both the symptom screen and Xpert are recommended by the WHO, data on the utility of combining these two interventions to enhance TB case finding among PLHIV, particularly outside South Africa, are limited. A high proportion of PLHIV (39%) in our primary study had a positive symptom screen (at least one of cough, fever, weight loss and night sweats). Among those with a positive symptom screen who provided a sputum sample, 6% had laboratory-confirmed pulmonary TB. Active pulmonary TB was thus common despite high ART coverage (89%) and a relatively high mean CD4 count (420 cells/ μ l). Smear microscopy, the standard of care diagnostic test in many resource-limited settings including the ALERT HIV Clinic, had low sensitivity (30%) compared to Xpert and/or culture. This suggests that Xpert can enhance TB case finding among PLHIV when used in combination with the WHO-recommended symptom screen. TB prevalence in our study was similar to that reported in previous studies in Ethiopia, although our cohort had a higher median CD4 count²⁴ and more ART coverage.^{14,24,25} A study by Balcha et al. reported a higher TB prevalence (17%), but the median CD4 count was substantially lower (172 cells/ μ l for PLHIV with active TB and 220 cells/ μ l for those without active TB).⁴

To facilitate TB screening, the WHO recommends the four-question symptom screen developed by Getahun et al. because of its high negative predictive value (NPV) of 98%.^{1,3} Despite the high sensitivity (90% in clinical settings) and the high NPV, the low specificity of the WHO symptom screen means that a large number of patients undergo follow-up diagnostic testing.^{3,26} Our study demonstrates the burden of this low specificity on the clinic's laboratory due to a high proportion of patients with a positive symptom screen. In our substudy, we assessed the impact of screening and diagnostic testing if all patients visiting the HIV Clinic undergo a symptom screen. During a 20-day period when we screened all patients presenting to the clinic, over half (52.5%) had a positive symptom screen. Based on the high patient volume, 71 patients per day would need to undergo TB diagnostic testing due to a positive symptom screen. The ALERT Hospital HIV Clinic and many other clinics in high-burden areas do not currently have the resources to fully implement intensified TB case finding.

In addition to low symptom screen specificity, a challenge in diagnosing TB in a resource-limited setting such as Ethiopia is the low sensitivity of smear microscopy (often the only available diagnostic test) among PLHIV. Similar to other studies, we found the sensitivity of smear microscopy was poor, at only 30%.⁴⁻⁷ Furthermore, the submission of three sputum samples for smear microscopy is burdensome and likely reduces adherence to this recommendation. Several patients declined to travel back to the clinic the following day to submit a morning sputum sample. Improved diagnostics such as Xpert are therefore needed to ensure higher TB case detection. The limitations of smear microscopy, combined with the poor specificity of the WHO-recommended symptom screen, make implementing the screen and further diagnostic testing unfeasible without substantial investments in laboratory and diagnostic testing. Ethiopian clinics would need additional funding from either the Federal Ministry of Health or outside donor organizations such as President's Emergency Plan for AIDS Relief or the Global Fund to scale up enhanced TB case finding through routine WHO-recommended TB screening in combination with improved diagnostics. Cost-effectiveness analyses are needed to assess the impact of implementing the symptom screen + Xpert given the costs associated with Xpert (US\$17 000 for the instrument, and approximately US\$10 per test cartridge).²⁷

Our study is subject to several limitations. First, because of limited laboratory capacity, only sputum samples from the first five patients with a positive symptom screen could be processed for AFB culture and Xpert daily. This might have biased our findings if more symptomatic patients arrived at the clinic earlier to ensure an appointment. Second, 16% of PLHIV with a positive symptom screen declined to provide sputum samples and 15% did not have specimens collected. Further interventions with protocol refinement are required to ensure that all patients with a positive symptom screen have specimens collected. In addition, 5/13 active TB cases did not undergo either Xpert or culture. Although this limited our ability to compare diagnostic tests, from an implementation standpoint it indicates that Xpert testing at an off-site facility is challenging due to specimen storage and transportation. Since the termination of the study, Xpert has been made available on site at ALERT. Using an on-site Xpert machine to test a single specimen collected at the time of visit will likely improve the rate of diagnostic testing due to reduced patient burden and increase the yield compared to three smear microscopy specimens.

CONCLUSION

In this operational research study conducted at a busy HIV clinic in Addis Ababa, Ethiopia, we evaluated the utility of combining two WHO recommendations (symptom screen and Xpert) to enhance TB case finding. Nearly 90% of patients were on ART, and a large proportion (39%) had a positive WHO-recommended symptom-based TB screen (one of cough, fever, night sweats, and weight loss). Of those with a positive symptom screen, 6% were diagnosed with laboratory-confirmed active pulmonary TB. Combining the WHO-recommended symptom screen with Xpert was an effective method of enhancing TB case finding among PLHIV, but will require substantial investment to implement fully. Further studies are needed to assess the cost-effectiveness of this approach.

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Figure.

Flow diagram of HIV-infected patients included in the primary study. Those patients included in the study underwent a WHO-recommended symptom screen, which included asking the patient about the presence of four symptoms (fever, cough, weight loss and night sweats), followed by diagnostic testing for TB on sputum if one or more symptoms were present. Active TB disease was defined as a positive Xpert result and/or a positive AFB culture for *M. tuberculosis*. TB = tuberculosis; + = positive; – = negative; HIV = human immunodeficiency virus; WHO = World Health Organization; AFB = acid-fast bacilli.

Table 1

Baseline demographic characteristics of HIV-infected patients screened for tuberculosis at the ALERT Hospital HIV Clinic in Addis Ababa, Ethiopia ($n = 828$)

Characteristic	<i>n</i> (%)
Age, years, mean $\pm$ SD	38.2 $\pm$ 10.0
Female sex	535 (65)
Unscheduled visit	265 (33)
Type of provider at study visit	
Nurse	402 (49)
Physician	276 (34)
Health officer	145 (18)
HIV history	
Time since HIV diagnosis, months, mean $\pm$ SD	64.8 $\pm$ 37.1
CD4 count, cells/ μ l, mean $\pm$ SD	420.1 $\pm$ 218.5
CD4 count, cells/ μ l	
<100	40 (5)
100–200	87 (11)
>200	683 (84)
Currently on ART	730 (89)
Duration of ART, months, mean $\pm$ SD*	57.0 $\pm$ 32.5
WHO HIV Stage	
I	430 (55)
II	150 (19)
III	148 (19)
IV	27 (3)
Unknown	73 (9)
TB history	
Past treatment for active TB	272 (33)
Type of previous TB [†]	
Pulmonary	212 (78)
Extra-pulmonary	35 (13)
Both	7 (3)
Unknown	18 (7)
WHO-recommended TB symptom screen results [‡]	
Any symptom (screen positive) [‡]	321 (39)
Cough	280 (34)
Night sweats	172 (21)
Fever	159 (19)
Weight loss	103 (13)
2 symptoms	222 (27)
3 symptoms	117 (14)

Characteristic	n (%)
All 4 symptoms	44 (5)

* Includes only patients currently on ART.

[†] Includes only patients treated for TB in the past.

[‡] According to the WHO, HIV patients in high-burden areas with at least one of the four listed symptoms have a positive symptom screen for TB.^{1,3}

HIV = human immunodeficiency virus; SD = standard deviation; ART = antiretroviral therapy; WHO = World Health Organization; TB = tuberculosis.

Table 2

Comparison of baseline characteristics between HIV-infected patients with a positive and negative WHO-recommended tuberculosis symptom screen

Risk factor	Symptom screen positive (<i>n</i> = 321, 39%)	Symptom screen negative (<i>n</i> = 493, 61%)	OR* (95%CI)	<i>P</i> value
	<i>n</i> (%)	<i>n</i> (%)		
Age, years, mean ± SD	38.0 ± 10.4	38.2 ± 9.7	1.00 (0.98–1.01)	0.74
Female sex	213 (68)	312 (64)	1.21 (0.90–1.63)	0.21
Unscheduled visit	157 (57)	107 (24)	4.11 (2.97–5.67)	<0.001
Clinician type				
Physician	179 (56)	92 (19)	4.89 (3.15–7.60)	<0.001
Nurse	99 (31)	295 (60)	0.84 (0.55–1.29)	0.43
Health officer	41 (13)	103 (21)	1	—
Months since HIV diagnosis, mean ± SD	62.2 ± 37.6	66.3 ± 36.9	1.00 (0.99–1.00) [†]	0.14
Current CD4 count, cells/μl, mean ± SD	410.9 ± 228.4	423.9 ± 211.9	—	0.41 [‡]
CD4 count status, cells/μl				
<100	26 (8)	14 (3)	3.17 (1.62–6.18)	<0.001
100–200	34 (11)	52 (11)	1.12 (0.70–1.77)	0.64
>200	248 (81)	423 (87)	1	—
Not currently on ART	51 (16)	39 (8)	2.32 (1.48–3.64)	<0.001
Duration of ART, months, mean ± SD [§]	55.0 ± 33.2	57.3 (32.4)	1.00 (0.99–1.00) [†]	0.38
WHO HIV Stage				
I	152 (50)	267 (57)	1	—
II	55 (18)	93 (20)	1.04 (0.71–1.53)	0.85
III	75 (25)	73 (16)	1.81 (1.24–2.64)	<0.01
IV	13 (4)	13 (3)	1.76 (0.79–3.89)	0.16
Past treatment for active tuberculosis	115 (36)	150 (31)	1.31 (0.97–1.76)	0.16

* Results of univariable analysis of risk factors for a positive symptom screen.

[†] ORs reflect change in odds for one unit increase in time.

[‡] Derived from a two-sample *t*-test.

[§] Includes only patients currently on ART.

HIV = human immunodeficiency virus; WHO = World Health Organization; OR = odds ratio; CI = confidence interval; SD = standard deviation; ART = antiretroviral therapy.

Table 3

Multivariable analysis of risk factors for a positive WHO-recommended tuberculosis symptom screen among HIV-infected patients

Characteristic	OR (95%CI)	P value
Age (per year)	1.01 (0.99–1.03)	0.41
Female sex	1.33 (0.92–1.92)	0.13
Visit type		
Unscheduled	3.78 (2.69–5.32)	<0.001
Scheduled	1.00	
CD4 count, cells/μl		
<100	2.62 (1.23–5.59)	0.01
100–200	1.18 (0.69–2.02)	0.54
>200	1.00	
No current ART	1.56 (0.89–2.74)	0.12
Past treatment for active tuberculosis	1.62 (1.12–2.31)	<0.01

WHO = World Health Organization; HIV = human immunodeficiency virus; OR = odds ratio; CI = confidence interval; ART = antiretroviral therapy.

Table 4

Comparison of baseline characteristics between HIV-infected patients with positive and negative tuberculosis diagnostic tests

Risk factor	TB positive (n = 13, 6%)	TB negative (n = 204, 94%)	OR* (95%CI)	P value
	n (%)	n (%)		
Age, years, mean $\pm$ SD	33.8 $\pm$ 8.1	39.2 $\pm$ 10.8	0.94 (0.88–1.01) [†]	0.08
Male sex	5 (38)	66 (33)	1.25 (0.39–3.97)	0.70
Unscheduled visit	8 (62)	88 (52)	1.47 (0.46–4.69)	0.51
Clinician type				
Doctor	7 (54)	101 (50)	0.83 (0.16–4.26)	0.83
Nurse	4 (31)	78 (38)	0.62 (0.11–3.57)	0.59
Health officer	2 (15)	24 (12)		
Symptom screen results				
Cough	12 (92)	169 (84)	2.27 (0.29–18.09)	0.44
Fever	5 (38)	95 (48)	0.69 (0.22–2.19)	0.53
Night sweats	5 (38)	111 (55)	0.51 (0.16–1.60)	0.25
Weight loss	6 (46)	63 (32)	1.87 (0.60–5.77)	0.28
2 symptoms	7 (54)	144 (71)	0.48 (0.16–1.51)	0.21
3 symptoms	7 (54)	74 (36)	2.05 (0.66–6.33)	0.21
4 symptoms	2 (15)	28 (14)	1.14 (0.24–5.43)	0.87
Time since HIV diagnosis, months, mean $\pm$ SD	44.2 $\pm$ 39.1	65.3 $\pm$ 37.7	0.98 (0.97–1.00) [†]	0.09
Current CD4 count, cells/ μ l, mean $\pm$ SD	360.1 $\pm$ 261.3	412.5 $\pm$ 224.2	—	0.48 [‡]
CD4 count status, cells/ μ l, mean $\pm$ SD				
<100	2 (20)	16 (8)	3.29 (0.61–17.68)	0.16
100–200	2 (20)	23 (12)	2.29 (0.44–12.03)	0.33
>200	6 (40)	158 (80)	1	—
No current ART	4 (31)	28 (14)	2.67 (0.77–9.23)	0.12
Duration of ART, months, mean $\pm$ SD [§]	62.5 $\pm$ 27.3	57.7 $\pm$ 34.2	1.00 (1.00–1.00) [†]	0.70
Past treatment for active TB [¶]	5 (38)	77 (38)	1.02 (0.32–3.24)	0.97

* Results of univariable analysis of risk factors for a positive symptom screen.

[†] ORs reflect change in odds for one unit increase in time.

[‡] Derived from a two-sample *t*-test.

[§] Includes patients currently on ART only.

[¶] Active TB disease was defined as having a positive Xpert results and/or positive AFB culture for *M. tuberculosis*.

HIV = human immunodeficiency virus; TB = tuberculosis; OR = odds ratio; CI = confidence interval; SD = standard deviation; ART = antiretroviral therapy.