NIH Public Access
Author Manuscript
Int J Tuberc Lung Dis. Author manuscript; available in PMC 2013 March 05.

Published in final edited form as:
Int J Tuberc Lung Dis. 2013 February ; 17(2): 214–220. doi:10.5588/ijtld.12.0395.

Prescribed and self-medication use increase delays in diagnosis of tuberculosis in the country of Georgia

A. S. Rabin[*], **G. Kuchukhidze**[†], **E. Sanikidze**[†], **R. R. Kempker**[*], and **H. M. Blumberg**[*,‡]

[*]Division of Infectious Diseases, Department of Medicine, Emory University School of Medicine, Atlanta, Georgia, USA

[†]National Center for Tuberculosis and Lung Diseases, Tbilisi, Georgia

[‡]Departments of Epidemiology and Global Health, Emory Rollins School of Public Health, Atlanta, Georgia, USA

Abstract

SETTING—Georgia has a high burden of tuberculosis (TB), including multidrug-resistant TB. Enhancing early diagnosis of TB is a priority to reduce transmission.

OBJECTIVE—To quantify delays in TB diagnosis and identify risk factors for delay in the country of Georgia.

DESIGN—In a cross-sectional study, persons with newly diagnosed, culture-confirmed pulmonary TB were interviewed within 2 months of diagnosis and medical and laboratory records were abstracted.

RESULTS—Among 247 persons enrolled, the mean and median total TB diagnostic delay was respectively 89.9 and 59.5 days. The mean and median patient delay was 56.2 and 23.5 days, while health care system delay was 33.7 and 14.0 days. In multivariable analysis, receipt of a medication prior to TB diagnosis was associated with increased overall diagnostic delay (adjusted odds ratio [aOR] 2.28, 95%CI 1.09–4.79); antibiotic use prior to diagnosis increased the risk of prolonged health care delay (aOR 4.16, 95%CI 1.97–8.79). TB cases who had increased patient-related diagnostic delay were less likely to have prolonged health care diagnostic delay (aOR 0.38, 95%CI 0.19–0.74).

CONCLUSION—Prolonged delays in detecting TB are common in Georgia. Interventions addressing the misuse of antibiotics and targeting groups at risk for prolonged delay are warranted to reduce diagnostic delays and enhance TB control.

Keywords

diagnostic delay; epidemiology; TB; former Soviet Union

INADEQUATE FUNDING, poverty, malnutrition, large numbers of internally displaced persons and collapse of the public health infrastructure following the breakup of the Soviet Union have all contributed to a resurgence of tuberculosis (TB) in the country of Georgia.[1] In 2010, the incidence rate of TB in Georgia remained high, at 107 cases per 100 000 population.[2] Georgia has also been designated one of the 27 high multidrug-resistant TB (MDR-TB) burden countries by the World Health Organization (WHO); in 2009, MDR-TB

Correspondence to: Alexander S Rabin, Emory University School of Medicine, 1648 Pierce Drive NE, Atlanta, GA 30322, USA. Tel: (+1) 508 308 8962. Fax: (+1) 404 727 5021. alexander.rabin@gmail.com.

NIH-PA Author Manuscript
NIH-PA Author Manuscript

prevalence in Georgia was 10% in newly diagnosed patients and 31% in patients previously treated for TB.[2] To enhance TB control, Georgia became one of the first middle-income countries to achieve universal access to diagnosis and treatment of TB, including MDR-TB, beginning in 2008. An assessment of the timely and proper utilization of these services is important to maximize their impact.

The early detection and diagnosis of TB have been identified as a major priority of global TB control efforts.[3] It is estimated that an untreated acid-fast bacilli (AFB) smear-positive TB case infects an average of 10 close contacts.[4] Delays in TB diagnosis result in patients being infectious for prolonged periods of time and further transmission of *Mycobacterium tuberculosis* among exposed susceptible contacts. Diagnostic delays of TB have been investigated in many parts of the world; however, total delays and risk factors for delay vary significantly from region to region, likely due to differences in culture and infrastructure.[4-6] No studies to date have evaluated delays in TB diagnosis in Georgia, and limited data exist on diagnostic delays from former Soviet republics. We sought to quantify delays in TB diagnosis and study risk factors for delays in an effort to target future public health interventions aimed at enhancing TB control in Georgia.

METHODS

Study setting and population

Using a cross-sectional study design, patients were enrolled from in-patient and out-patient facilities of the National TB Program (NTP) throughout Georgia between April and October 2011. The Georgian NTP provides all TB-related diagnostic services and treatment at no cost.[1] Inclusion criteria for the study included 1) recent (<2 months) culture-confirmed diagnosis of pulmonary TB (PTB), 2) first diagnosis of PTB (i.e., newly diagnosed case), and 3) age ≥16 years. Patients with positive AFB sputum smears were preferentially enrolled to increase the likelihood that those enrolled would subsequently have a positive culture for *M. tuberculosis*. All sputum cultures were performed at the Georgian National TB Reference Laboratory in Tbilisi, which follows standard protocols[7] and has undergone annual external quality assessment by the Antwerp WHO Supranational TB Reference Laboratory since 2005. Enrolled TB suspects who were subsequently found to have a negative sputum culture for *M. tuberculosis* were excluded from the study. Other exclusion criteria included those patients who could not be interviewed due to poor clinical condition and those who were retreatment cases.

Written informed consent in the patient’s native language was required for study participation.

Data collection

Each enrolled patient was interviewed using a standardized questionnaire adapted from a prior WHO survey of diagnostic and treatment delay in the Eastern Mediterranean Region (Appendix).[4*] All interviews were performed in either the Georgian language (Kartuli) or Russian. Data were collected on socio-demographic information; past medical history, including comorbidities; history of the patients’ TB disease, including symptoms; health care seeking patterns; and prior medication use. Medical chart abstraction was also performed to obtain further medical history and history of TB disease.

*The Appendix is available in the online version of this article.

Definitions

Patient delay was defined as time from first onset of any TB symptom (e.g., cough, fever, weight loss, night sweats and/or hemoptysis) until first presentation to the health care system. Health care delay was defined as time from first presentation to the health care system until diagnosis of TB. Total diagnostic delay was defined as the time from onset of first symptom until TB diagnosis (patient delay plus health care delay).[5,8] Treatment delay was defined as time from TB diagnosis until initiation of anti-tuberculosis treatment. The initial diagnosis of TB was defined by a positive AFB sputum smear, positive AFB sputum culture, and/or the clinical judgment of a TB specialist given compatible symptomatology and radiographic findings.[7] A medical comorbidity was defined as underlying cardiovascular, gastrointestinal, pulmonary, immunologic or malignant disease. Self-medication was defined as use of any medication not prescribed by a health care professional. Antibiotics and other medications are available at pharmacies in Georgia over the counter and without a prescription.

Data management and statistical analysis

Data were collected onto a standardized form and entered into an online REDCap (Research Electronic Data Capture, Vanderbilt University, Nashville, TN, USA) database.[9] All data analyses were performed using SAS version 9.3 (SAS Institute, Cary, NC, USA). Univariable and multivariable logistic regression analysis was used to evaluate risk factors for diagnostic delays. Median delays were used as a cut-off to define delay vs. non-delay. Variables included in the final model were chosen based on biological plausibility as well as statistical ($P \leq 0.1$) and epidemiological criteria according to the strategy of purposeful selection.[10] $P \leq 0.05$ was considered significant.

The study was approved by the Institutional Review Boards of Emory University and the Georgian National Center for Tuberculosis and Lung Disease.

RESULTS

Study participants

Of 289 patients considered for enrollment, 42 (15%) were excluded for the following reasons: 20 patients were not able to complete the survey, 8 were determined to be retreatment cases, 5 were diagnosed with TB >2 months prior to interview, 5 declined participation, 3 subsequently had negative sputum cultures and 1 had extra-pulmonary and no PTB. A final total of 247 patients with culture-confirmed PTB were enrolled in the study.

Patient demographics, symptoms and health care seeking behavior

The characteristics of the 247 study participants are detailed in Table 1. The median age was 33.5 years and 69% were male. Over half (53%) of the patients with newly diagnosed PTB were enrolled from outside the capital city of Tbilisi. Unemployment was high (68%), while median monthly household income was low (US$180). Many patients reported current or past tobacco (64%) and alcohol use (32%). A minority of patients (14%) reported the presence of chronic cough of at least 6 months' duration. The median number of symptoms experienced by patients prior to TB diagnosis was five. The most commonly reported symptoms included cough (84%), fever (81%), weight loss (73%) and night sweats (66%; Table 1). Eighty-three (34%) patients self-medicated prior to their diagnosis of TB, and 72 (29%) reported visiting a pharmacy or self-medicating as their first health seeking action. Of the 83 patients who self-medicated, 36 (43%) reported using antibiotics, including four patients who took anti-tuberculosis medications. One hundred and twenty patients (49%) presenting to a health care provider prior to diagnosis and enrollment in the Georgian NTP were prescribed medication and 104 were prescribed antibiotics (42%). A total of 127 (51%)

patients received over-the-counter antibiotics or were prescribed antibiotics by a physician prior to TB diagnosis; 92 (37%) patients were initially given a diagnosis of pneumonia, bronchitis or upper respiratory infection. The prevalence of isoniazid-resistant and MDR-TB was respectively 20.3% and 5.5% in the cohort of study patients (Table 1).

Diagnostic delays

The mean and median total TB diagnostic delay was respectively 89.9 and 59.5 days. The mean and median patient delay was respectively 56.2 and 23.5 days, while the health care system delay was 33.7 and 14.0 days (Figure).

Risk factors for TB diagnostic delay

Factors associated with an increased risk of TB diagnostic delays (patient, health care, and total delays) in univariable analysis are shown in Table 2. In multivariable analysis, risk factors that were positively associated with a prolonged patient component delay in the diagnosis of TB included chronic cough (adjusted odds ratio [aOR] 4.71, 95% confidence interval [CI] 1.75–12.69), tobacco use (aOR 3.13, 95%CI 1.31–7.48), female sex (aOR 3.03, 95%CI 1.24–7.40), hemoptysis (aOR 2.66, 95%CI 1.33–5.31), self-medication prior to diagnosis (aOR 2.53, 95%CI 1.32–4.86), and presence of a comorbidity (aOR 2.24, 95%CI 1.19–4.24; Table 3). Having been prescribed antibiotics prior to diagnosis was an independent risk factor for prolonged health care delay (aOR 4.16, 95%CI 1.97–8.79). Prolonged patient delay in TB diagnosis was associated with a shorter health care delay (aOR 0.38, 95%CI 0.19–0.74). Independent risk factors for total diagnostic delay included chronic cough (aOR 12.20, 95%CI 3.73–39.92), female sex (aOR 3.32, 95%CI 1.40–7.91), having been prescribed any medications in the pre-diagnosis period (aOR 2.28, 95%CI 1.09–4.79) and multiple first symptoms (aOR 0.41, 95%CI 0.21–0.78; Table 3).

DISCUSSION

The public health significance of TB diagnostic delays is important given that patients with long diagnostic delays remain infectious for prolonged periods of time and are thus more likely to transmit TB to a larger number of susceptible contacts. Reducing diagnostic delays is an important strategy in enhancing TB control. In this study in Georgia, we identified prolonged diagnostic delays. The overall median diagnostic delay was 59.5 days, which included a median patient delay component of 23.5 days and a health care delay component of 14 days. We found chronic cough (aOR 12.2), female sex (aOR 3.32), and prescribed medication use (aOR 2.28) to be significant risk factors for prolonged delays in diagnosis among patients with TB. We also found a previously unreported link between patient-factor and health care system delay: patients with prolonged patient delays had shorter health care system delays (aOR 0.38).

Although the ideal time to TB diagnosis is unknown, longer delays in diagnosis increase TB transmission and promote further spread of disease.[3] Lin et al. identified a significant increase in intra-household TB transmission beyond 30 days.[11] Our study is the first in Georgia to examine diagnostic delays in patients with TB, and only the second study to be reported from a former Soviet republic.[12] The median patient delay in our study in Georgia (23.5 days) was similar to that found in Ukraine (30 days),[12] the only other published study from the former Soviet Union to have examined patient-component delays in diagnosis. Other recent reports on diagnostic delays include Turkey (patient delay 30 days, health care delay 19 days),[13] Iran (patient delay 24 days, health care delay 42 days)[4] and Egypt (patient delay 12 days, health care delay 18 days).[4] While the median total diagnostic delay in Georgia (59.5 days) was similar to the delay found in prior studies, there was a wide range of delays in diagnosis, and the top quartile of patients had diagnostic delays >4 months (124 days). Patients who had a prolonged delay in diagnosis and were AFB smear-positive were likely to have transmitted the disease during this extended period without a diagnosis.

A striking and important finding from our study was that patients who received 'prescription-type' medications (available over the counter in Georgia without a prescription), including antibiotics, were at risk for prolonged total diagnostic delay. In multi-variable analysis, patients who had been prescribed medication by a health care provider were more than twice as likely (aOR 2.28) to have a total delay of >59.5 days. Furthermore, patients who self-medicated (frequently with antibiotics) had longer patient delays, while those who were prescribed antibiotics had longer health care system delays. Our findings are consistent with recent reports that have also demonstrated that any antibiotic use, regardless of class, is associated with longer TB diagnostic delays.[14-16] The basis for this delay is poorly understood; however, the delay is likely related to the time spent waiting for a clinical response to the antibiotic.[16]

Past studies in Georgia have identified the widespread availability of over-the-counter antibiotics, including both first- and second-line anti-tuberculosis drugs,[17] as well as other antimicrobial agents. Our study confirms that patients with symptoms of TB are taking these drugs: 51% received an antibiotic prior to TB diagnosis and 15% self-medicated with antibiotics without seeing a physician. One study patient example highlights the dangers associated with improper antibiotic use: the patient presented to an NTP facility in Gori, Georgia, with disseminated rifampin (RMP) resistant TB after a prolonged course of single-drug treatment (RMP) prescribed by a private cardiologist. The inappropriate use of antimicrobials resulting in prolonged diagnostic delays in a country with widespread drug-resistant TB is alarming. This new information emphasizes the need for public policy interventions to improve antimicrobial use, including the need for a prescription to obtain antibiotics and particularly anti-tuberculosis drugs, as well as measures to educate physicians and other health care providers about the diagnosis and treatment of TB.[18]

Other risk factors for prolonged delays in diagnosis in Georgia included patients with chronic cough and women. Patients with chronic cough may delay seeking care if they have a lack of knowledge about TB and do not associate worsening cough with symptoms of TB.[19] Data from earlier studies suggest that women subsequently found to have PTB delay seeking care due to health system barriers, familial caretaker obligations, stigma and financial insecurity.[20,21] Georgian women are not only at higher risk for delayed diagnosis: a prior investigation revealed that they also have an increased risk of MDR-TB.[22] It is not clear whether these two findings are related, and a follow-up study is necessary to identify resistance patterns and treatment outcomes among patients with a diagnostic delay.

The relationship between patient delay and health care system delay has never before been investigated. We found that patients who delayed seeking care had shorter subsequent health care system delays. This suggests that patients who wait longer to seek health care are easier to diagnose because their disease is at a more advanced and clinically apparent stage. If health care providers are diagnosing later stage disease, this finding suggests that public health awareness campaigns should be expanded to encourage patients with more non-specific symptoms, such as cough or fever, to seek care sooner.

There were some limitations to our study. First, we relied upon patient history to estimate date of onset of PTB disease. To limit recall bias, we cross-referenced chart data and directly questioned patients regarding discordant dates. Second, stigma and criminalization of injection drug use in Georgia may have led to underreporting of such use. Third, the prevalence of drug-resistant TB was likely underestimated due to limited access to patients on MDR-TB isolation wards. This may have led to an underestimation of diagnostic delays, as patients with drug-resistant TB may have been partially treated outside the health care system. Fourth, the study was conducted during the summer months, when historically fewer patients present to TB facilities; the seasonal impact on delays in diagnosis is not known. Fifth, smear-positive cases were preferentially included, leading to possible over-representation of patients with late stage disease and longer patient-factor delays. Lastly, our study only reflects diagnostic delays in the civilian population, as we did not enroll incarcerated persons with TB.

CONCLUSION

This is the first study of delays in diagnosis of TB in the country of Georgia and one of the first comprehensive studies of delay in the former Soviet Union, a region with unique challenges related to years of health system neglect and high rates of MDR-TB. Despite recent progress in TB control efforts in Georgia, our study found that diagnostic delays were common. This suggests an urgent need to develop policies that will improve the timely diagnosis of TB and reduce diagnostic delays.

First, we found that antibiotic misuse and inappropriate use of other ‘prescription drugs’ (that are freely available over the counter without a prescription) by both doctors and patients is common in Georgia and associated with an increased risk of TB diagnostic delay. To reduce TB diagnostic delays and further development and spread of TB disease, including both drug-susceptible and drug-resistant strains, governments should restrict the availability of over-the-counter antibiotics (including anti-tuberculosis drugs) and enhance efforts at educating practitioners and pharmacists about the potential harm of antibiotic overuse.[23] Second, we identified groups at increased risk for a delayed diagnosis of TB, including those with chronic cough (often in the setting of chronic tobacco use and tobacco-related lung disease) and women. While the Georgian NTP has carried out TB awareness campaigns, our study suggests the need to broaden these efforts to target these high-risk groups and further raise awareness about risk factors for prolonged diagnostic delays. Implementation of screening of high-risk groups for TB in established primary health centers is one strategy that may reduce time to diagnosis. Finally, our findings highlight the need to raise awareness about TB among public and private sector primary care providers and encourage early referral to health care facilities that have expertise in managing patients with TB. Further studies are necessary to quantify the relationship between antibiotic misuse prior to TB diagnosis and development of MDR-TB, and the effect of prolonged diagnostic delay on severity of disease and patient outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The authors thank the staff of the Georgian National TB Program/National Center for Tuberculosis and Lung Diseases for their assistance in patient recruitment. Research was supported in part by grants from the National Institutes of Health (NIH/FIC D43TW007124 and D43TW007124-06S and NIH/NCRR UL1 RR025008 [Atlanta Clinical and Translational Science Institute]), the Emory University Global Health Institute, Emory University School of Medicine Dean’s Office, and the Infectious Diseases Society of America.

References

1. Lomtadze N, Aspindzelashvili R, Janjgava M, et al. Prevalence and risk factors for multidrug-resistant tuberculosis in the Republic of Georgia: a population-based study. Int J Tuberc Lung Dis. 2009; 13:68–73. [PubMed: 19105881]

2. World Health Organization. WHO/HTM/TB/2011.16. Geneva Switzerland; WHO: 2011. Global tuberculosis control: WHO report 2011.
3. Lönnroth K, Castro KG, Chakaya JM, et al. Tuberculosis control and elimination 2010–50: cure care and social development. Lancet. 2010; 375:1814–1829. [PubMed: 20488524]
4. World Health Organization. WHO-EM/TDR/009/E. WHO; Geneva Switzerland: 2006. Diagnostic and treatment delay in tuberculosis: an in-depth analysis of the health-seeking behaviour of patients and health system response in seven countries of the Eastern Mediterranean Region.
5. Storla DG, Yimer S, Bjune GA. A systematic review of delay in the diagnosis and treatment of tuberculosis. BMC Public Health. 2008; 8:15. [PubMed: 18194573]
6. Sreeramareddy CT, Panduru KV, Menten J, van den Ende J. Time delays in diagnosis of pulmonary tuberculosis: a systematic review of literature. BMC Infect Dis. 2009; 9:91. [PubMed: 19519917]
7. World Health Organization, Regional Office for Europe/National Tuberculosis and Lung Diseases Research Institute (Poland). TB manual: national tuberculosis programme guidelines. WHO Regional Office for Europe; Copenhagen, Denmark: 2001.
8. Yimer S, Bjune G, Alene G. Diagnostic and treatment delay among pulmonary tuberculosis patients in Ethiopia: a cross-sectional study. BMC Infect Dis. 2005; 5:112. [PubMed: 16343350]
9. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform. 2009; 42:377–381. [PubMed: 18929686]
10. Hosmer, DW.; Lemeshow, S. Applied logistic regression. Wiley; New York, NY, USA: 2000. p. xii-373.
11. Lin X, Chongsuvivatwong V, Lin L, Geater A, Lijuan R. Dose-response relationship between treatment delay of smear-positive tuberculosis patients and intra-household transmission: a cross-sectional study. Trans R Soc Trop Med Hyg. 2008; 102:797–804. [PubMed: 18513768]
12. van der Werf MJ, Chechulin Y, Yegorova OB, et al. Health care seeking behaviour for tuberculosis symptoms in Kiev City, Ukraine. Int J Tuberc Lung Dis. 2006; 10:390–395. [PubMed: 16602402]
13. Okur E, Yilmaz A, Saygi A, et al. Patterns of delays in diagnosis amongst patients with smear-positive pulmonary tuberculosis at a teaching hospital in Turkey. Clinical Microbiol Infect. 2006; 12:90–92. [PubMed: 16460554]
14. Wang M, FitzGerald JM, Richardson K, et al. Is the delay in diagnosis of pulmonary tuberculosis related to exposure to fluoroquinolones or any antibiotic? Int J Tuberc Lung Dis. 2011; 15:1062–1068. [PubMed: 21740669]
15. Tattevin P, Che D, Fraisse P, et al. Factors associated with patient and health care system delay in the diagnosis of tuberculosis in France. Int J Tuberc Lung Dis. 2012; 16:510–515. [PubMed: 22325560]
16. Golub JE, Bur S, Cronin WA, et al. Impact of empiric antibiotics and chest radiograph on delays in the diagnosis of tuberculosis. Int J Tuberc Lung Dis. 2005; 9:392–397. [PubMed: 15832463]
17. Kobaidze K, Salakaia A, Blumberg HM. Over the counter availability of antituberculosis drugs in Tbilisi, Georgia, in the setting of a high prevalence of MDR-TB. Interdiscip Perspect Infect Dis. 2009; 2009:513609. [PubMed: 19543538]
18. Leung E, Weil DE, Raviglione M, Nakatani H. The WHO policy package to combat antimicrobial resistance. Bull World Health Organ. 2011; 89:390–392. [PubMed: 21556308]
19. Long Q, Li Y, Wang Y, et al. Barriers to accessing TB diagnosis for rural-to-urban migrants with chronic cough in Chongqing, China: a mixed methods study. BMC Health Services Res. 2008; 8:202.
20. Hu A, Loo E, Winch PJ, Surkan PJ. Filipino women's tuberculosis care seeking experience in an urban poor setting: a socioecological perspective. Health Care Women Int. 2012; 33:29–44. [PubMed: 22150265]
21. Marais BJ, Gupta A, Starke JR, El Sony A. Tuberculosis in women and children. Lancet. 2010; 375:2057–2059. [PubMed: 20488522]
22. Vashakidze L, Salakaia A, Shubladze N, et al. Prevalence and risk factors for drug resistance among hospitalized tuberculosis patients in Georgia. Int J Tuberc Lung Dis. 2009; 13:1148–1153. [PubMed: 19723406]

23. Morgan DJ, Okeke IN, Laxminarayan R, Perencevich EN, Weisenberg S. Non-prescription antimicrobial use worldwide: a systematic review. Lancet Infect Dis. 2011; 11:692–701. [PubMed: 21659004]

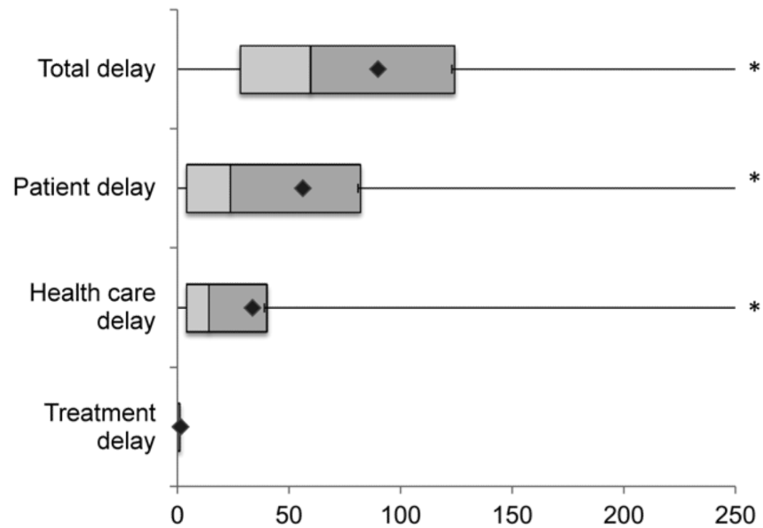

Figure.

Diagnostic and treatment delays in days. The mean total diagnostic delay was 89.9 days (median 59.5, IQR 28–124), including a patient component delay of 56.2 days (median 23.5, IQR 4–82) and health care system delay of 33.7 days (median 14.0, IQR 4–40). The mean treatment delay (time from diagnosis to initiation of treatment) was 1.45 days (median 0, IQR 0–1). ◆ Mean delay. * Outlier. Box represents IQR. IQR = interquartile range.

Table 1

Characteristics of study participants

	n (%)		*n* (%)
Male	170 (68.8)	Known TB contact	68 (27.5)
Age, years, median [IQR]	33.5 [25.2-49.3]	Lives with contact	41 (60.3)
Non-Tbilisi resident *	131 (53.0)	Symptoms prior to TB diagnosis	
West Georgia	54 (22)	Cough	208 (84.2)
East Georgia	53 (21.5)	Fever	200 (81.0)
Central Georgia	23 (9.4)	Weight loss	179 (72.5)
Rural location	56 (22.7)	Night sweats	163 (66.0)
		Chest pain	124 (50.2)
High school education or less	134 (54.3)	Loss of appetite	134 (54.3)
Unemployed	168 (68.0)	Difficulty breathing	100 (40.5)
Not married	105 (42.5)	Hemoptysis	74 (30.0)
		Other symptoms	33 (13.5)
History of incarceration	30 (12.2)	Total number of symptoms, median	5
Internally displaced person	11 (4.5)	First symptoms included cough	150 (61.0)
Household income, US$, median [IQR]	180 [60-301]	Multiple first symptoms ‡	168 (68.3)
Household members, *n*, median [IQR]	3 [2-5]	First health-seeking action	
Rooms per home, *n*, median [IQR]	2 [1-3]	Pharmacy/self-medicate	72 (29.2)
Any tobacco use	159 (64.4)	Primary care center/polyclinic	59 (23.9)
Current	81 (32.8)	Private clinic	47 (19.0)
Past	78 (31.6)	NTP TB facility	27 (10.9)
Any alcohol use	78 (31.6)	General hospital	18 (7.3)
Current	31 (12.6)	Emergency medical service §	13 (5.3)
Past	47 (19.0)	Other	10 (4.0)
		Traditional remedy	1 (0.4)
Injection drug abuse	8(3.2)	Number of HCF visits pre-diagnosis, median [IQR]	2 [1-5]
Any comorbidity	96 (38.9)		
Cardiovascular disease †	27 (10.9)	Total HCF visits pre-diagnosis, median [IQR]	3 [1-16]
Gastrointestinal ulcers	22 (8.9)	Treatment prior to TB diagnosis	
Seasonal allergies	21 (8.5)	Any antibiotic use	127 (51.4)
Diabetes	19 (7.7)	Self-medicated	83 (33.6)
Gastroesophageal reflux	16 (6.5)	Self-medicated with antibiotics	36 (14.6)
Hepatitis B or C	14 (5.7)	Prescribed medications	120 (48.6)
COPD/asthma	12 (4.9)	Prescribed antibiotics	104 (42.1)
HIV	1 (0.4)	Traditional remedy use ¶	16 (6.5)
Malignancy	1 (0.4)	Any of H, R, Z or E taken pre-diagnosis	5 (2.0)
Chronic cough (>6 months)	34 (13.8)	Took over-the-counter anti-tuberculosis drugs	4(1.6)
		Non-TB physician prescribed H, R, Z or E	4(1.6)
AFB smear status and DST			

	n (%)		*n* (%)
AFB smear-positive	229 (92.7)	Pre-TB diagnosis of pneumonia/bronchitis/URI	92 (37.2)
MDR-TB (n = 217)	12 (5.5)	Referred by self to NTP TB facility	75 (30.4)
INH-resistant TB (n = 217)	44 (20.3)	Travel from home (>1 week in last 3 months)	30 (12.2)
		Duration in days, median [IQR]	20 [14-60]
		>30 minutes travel time to nearest HCF	74 (30.0)

TB = tuberculosis; IQR = interquartile range; NTP = National Tuberculosis Program; HCF = health care facility; COPD = chronic obstructive pulmonary disease; HIV = human immunodeficiency virus; H, R, Z or E = first-line anti-tuberculosis drugs (rifampin, INH, pyrazinamide, ethambutol); AFB = acid-fast bacilli; DST = drug susceptibility testing; URI = upper respiratory infection; INH = isoniazid.

[*] Georgia was divided into four regions based upon geography and population: Tbilisi, West Georgia (Imereti, Guria, Samegrelo, Achara, Racha-Lechkhumi, Svaneti), Central Georgia (Shida Kartli, Kvemo Kartli, Samcxe-Javakheti) and East Georgia (Mtskheta-Mtianeti, Kakheti).

[†] Defined as hypertension, heart failure or history of myocardial infarction.

[‡] Multiple first symptoms defined as TB symptom reported at disease onset (e.g., cough and night sweats).

[§] Emergency medical service in Georgia refers to the visit of an ambulance service to the patient's home. Treatment is typically provided at home unless the patient requires transfer to a hospital.

[¶] Including honey, tea and herbal extracts.

Table 2

Univariable analysis of risk factors for delayed diagnosis

Risk factor	Prolonged patient delay (≥23.5 days)* OR (95%CI)	Prolonged health care delay (≥14 days) OR (95%CI)	Prolonged total delay (≥59.5 days) OR (95%CI)
Patient demographics			
Female	1.22 (0.71–2.10)	1.91 (1.10–3.31)†	2.1 (1.21–3.64)†
Age (per year)	1.01 (0.99–1.03)	1.01 (1.00–1.03)	1.02 (1.003–1.04)†
Age ≥5 years	1.32 (0.48–3.66)	4.45 (1.24–16.02)†	2.34 (0.79–6.94)
Non-Tbilisi resident	0.8 (0.62–1.02)	1 (0.78–1.27)	0.95 (0.74–1.21)
Rural location	0.7 (0.38–1.27)	1.23 (0.68–2.23)	0.92 (0.51–1.67)
High school education or less	1.16 (0.70–1.91)	0.83 (0.50–1.37)	1.02 (0.62–1.68)
Unemployed	0.95 (0.56–1.63)	0.9 (0.53–1.54)	1.61 (0.94–2.76)
Not married	1.05 (0.63–1.74)	0.94 (0.57–1.55)	0.92 (0.55–1.52)
History of incarceration	0.54 (0.25–1.20)	0.59 (0.27–1.29)	0.54 (0.25–1.20)
Internally displaced person	0.56 (0.16–1.97)	1.69 (0.48–5.93)	0.56 (0.16–1.97)
Household income ≤$180	1.72 (1.04–2.86)†	1.03 (0.62–1.71)	1.32 (0.80–2.19)
Travel from home >1 week	1.37 (0.63–2.96)	1.27 (0.59–2.75)	1.37 (0.63–2.96)
Drug use and comorbidities			
Any tobacco use	1.41 (0.83–2.38)	0.58 (0.34–0.98)†	0.74 (0.44–1.26)
Any alcohol use	1.27 (0.74–2.17)	0.74 (0.43–1.26)	0.81 (0.47–1.38)
Injection drug abuse	0.6 (0.14–2.55)	0.13 (0.02–1.06)	0.6 (0.14–2.55)
Any comorbidity	2.02 (1.20–3.40)†	0.91 (0.55–1.52)	1.63 (0.98–2.74)
Chronic cough >6 months	3.89 (1.68–8.98)†	1.07 (0.52–2.22)	9.68 (3.29–28.44)†
TB history/current presentation			
Known TB exposure	1.1 (0.63–1.92)	1.28 (0.73–2.25)	1.19 (0.68–2.08)
Symptoms			
Cough	1.35 (0.68–2.68)	1.65 (0.82–3.29)	1.73 (0.86–3.48)
Hemoptysis	1.49 (0.86–2.58)	0.49 (0.28–0.86)†	1.09 (0.63–1.88)
Weight loss	1.62 (0.92–2.84)	0.84 (0.48–1.48)	1.49 (0.85–2.61)
Fever	0.44 (0.23–0.85)†	1.55 (0.82–2.95)	0.76 (0.40–1.44)
Chest pain	1.82 (1.10–3.03)†	1.41 (0.85–2.32)	1.71 (1.04–2.83)†
Loss of appetite	1.84 (1.11–3.05)†	0.88 (0.55–1.46)	1.72 (1.04–2.85)†
Difficulty breathing	1.52 (0.91–2.53)	0.91 (0.55–1.51)	1.74 (1.04–2.91)†
Night sweats	1.32 (0.78–2.23)	1.17 (0.69–1.98)	1.64 (0.97–2.80)
Other symptoms	1.24 (0.59–2.58)	2.1 (0.95–4.45)	2.6 (1.18–5.73)†
First symptom included cough	0.47 (0.28–0.79)†	1.04 (0.62–1.74)	0.62 (0.37–1.04)
Multiple first symptoms	0.4 (0.23–0.69)†	1.38 (0.80–2.36)	0.37 (0.21–0.64)†

Risk factor	Prolonged patient delay (≥23.5 days)* OR (95%CI)	Prolonged health care delay (≥14 days) OR (95%CI)	Prolonged total delay (≥59.5 days) OR (95%CI)
Health seeking action			
First action was self-medication	3.33 (1.83–5.89)†	0.37 (0.21–0.65)†	1.33 (0.77–2.30)
Treatment before TB diagnosis			
Self-medicated	2.2 (1.28–3.78)†	0.42 (0.25–0.73)†	1.13 (0.67–1.91)
Self-medicated with antibiotics	2.3 (1.08–4.76)†	0.72 (0.35–1.47)	1.5 (0.73–3.06)
Prescribed medication	—	7.93 (4.49–14.01)†	1.5 (0.91–2.48)
Prescribed antibiotics	—	7.43 (4.15–13.28)†	1.42 (0.85–2.35)
Any antibiotic use	—	4.35 (2.55–7.41)†	1.66 (1.003–2.74)†
Traditional remedy use	3.23 (1.02–10.35)†	1.62 (0.57–4.62)	3.24 (1.02–10.35)†
First HCF visited			
Primary care center/polyclinic	1	1	1
Private clinic	0.74 (0.36–1.52)	0.79 (0.39–1.61)	0.68 (0.33–1.38)
NTP TB facility	1.57 (0.73–3.38)	0.27 (0.12–0.62)†	0.71 (0.33–1.51)
General hospital	1.59 (0.78–3.22)	0.78 (0.39–1.58)	1.22 (0.60–2.46)
Other	0.78 (0.31–1.95)	0.82 (0.33–2.03)	0.91 (0.37–2.25)
Pre-TB diagnosis of pneumonia/bronchitis/URI	—	5.47 (3.06–9.77)†	1.09 (0.65–1.82)
>30 min travel to nearest HCF	1.09 (0.63–1.88)	1.08 (0.62–1.86)	1.38 (0.80–2.38)
Patient delay	—	0.37 (0.22–0.61)†	—

OR = odds ratio; CI = confidence interval; TB = tuberculosis; HCF = health care facility; NTP = National Tuberculosis Program; URI = upper respiratory infection.

*Prolonged delay defined as delay greater than or equal to the median.

†Statistical significance at $P \leq 0.05$.

Table 3

Multivariable analysis of risk factors for delayed diagnosis

Risk factor	Prolonged patient delay (≥23.5 days)* aOR (95%CI)	Prolonged health care delay (≥14 days) aOR (95%CI)	Prolonged total delay (≥59.5 days) aOR (95%CI)
Female	3.03 (1.24–7.40)†	1.62 (0.65–4.01)	3.32 (1.40–7.91)†
Age (per year)	0.99 (0.97–1.01)	1.02 (0.99–1.05)	1.01 (0.99–1.04)
History of incarceration	—	0.65 (0.25–1.68)	0.63 (0.24–1.65)
Household income ≤US$180	1.81 (0.98–3.35)	1.11 (0.58–2.14)	1.19 (0.64–2.21)
Any tobacco use	3.13 (1.31–7.48)†	0.83 (0.36–1.95)	1.23 (0.54–2.81)
Any comorbidity	2.24 (1.19–4.24)†	0.87 (0.45–1.67)	1.36 (0.74–2.52)
Chronic cough >6 months	4.71 (1.75–12.69)†	1.5 (0.58–2.14)	12.20 (3.73–39.92)†
Hemoptysis	2.66 (1.33–5.31)†	0.58 (0.30–1.15)	1.45 (0.74–2.82)
First symptom included cough	0.36 (0.19–0.67)†	0.89 (0.46–1.71)	0.54 (0.29–1.00)
Multiple first symptoms	0.51 (0.27–0.97)†	1.24 (0.64–2.44)	0.41 (0.21–0.78)†
Self-medicated	2.53 (1.32–4.86)†	—	—
Prescribed medication	—	—	2.28 (1.09–4.79)†
Prescribed antibiotics	—	4.16 (1.97–8.79)†	—
Traditional remedy use	3.09 (0.80–11.89)	2.67 (0.70–10.24)	3.88 (0.96–15.65)
Pre-TB diagnosis of pneumonia/bronchitis/URI	—	2.1 (0.96–4.58)	0.68 (0.32–1.45)
Patient delay	—	0.38 (0.19–0.74)†	—

aOR = adjusted odds ratio; CI = confidence interval; TB = tuberculosis; URI = upper respiratory infection.

*Prolonged delay defined as delay greater than or equal to the median.

†Statistical significance at $P \leq 0.05$.