Loss to follow-up among patients receiving anti-tuberculosis treatment, Haiti, 2011–2015

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<http://dx.doi.org/10.5588/pha.18.0043>

Setting: Tuberculosis (TB) treatment facilities in Haiti.

Objective: To assess factors associated with loss to follow-up (LTFU) among patients receiving treatment for tuberculosis (TB) in Haiti.

Design: We analyzed Haiti's national surveillance data for patients started on anti-tuberculosis treatment from 2011 to 2015 to determine factors associated with LTFU using multivariable logistic regression and describe LTFU in terms of subnational units to target future intervention strategies. We also conducted a survival analysis to estimate hazard ratios of factors associated with time to LTFU.

Results: Of 81 490 TB cases reported, 7423 (9.1%) were LTFU during anti-tuberculosis treatment, increasing from 7.1% in 2011 to 10.3% in 2015. Six high-volume facilities had significantly higher rates of LTFU (14.3–31.9%) than the rest of the country, accounting for 18.8% of all TB cases reported, but 41.7% of all LTFU patients. Male sex, previous treatment history, and human immunodeficiency virus infection were associated with higher rates of LTFU. The median time to LTFU was 94 days.

Conclusion: A small number of facilities accounted for disproportionately high rates of LTFU. These results identify characteristics of facilities and individuals leading to concentrated interventions to reduce LTFU and improve treatment success.

Haiti has the highest burden of tuberculosis (TB) in the Western Hemisphere, with an estimated incidence of 188 cases per 100 000 population.¹ The devastating earthquake in 2010 threatened Haiti's TB prevention and care efforts, as massive physical destruction disrupted services and interrupted access to anti-tuberculosis treatment.^{2,3} Failure to complete treatment and poor adherence lead to prolonged infectiousness, drug resistance, and increased morbidity and mortality.⁴ Major TB-related activities have been strengthened in Haiti following the earthquake, including improved surveillance systems, diagnostic capacity, and implementation of the DOTS strategy.^{5–10} Active case-finding campaigns significantly improved case detection,^{11–13} although treatment success rates remained stable.⁹

The proportion of patients who successfully complete treatment is one of the priority indicators of TB program performance, with a target of $\geq 90\%$ defined by the World Health Organization's (WHO's) End TB Strategy.¹⁴ From 2011 to 2015, Haiti's treatment success rate ranged from 78% to 82%, while loss to follow-up (LTFU) rates steadily increased.

Improving TB treatment adherence to reverse this trend may be complex, as multiple dynamic factors influence adherence, including patient characteristics, socio-economic factors, health care system elements, and aspects of the treatment regimen.¹⁵ Some factors may be specific to certain settings or patient populations, making it difficult to broadly generalize interventions.¹⁶

We evaluated risk factors associated with LTFU at the national, subnational, and facility levels to help Haiti's National TB Control Program (*Programme national de Lutte contre la Tuberculose*, PNLT) develop strategies to address high LTFU rates and target interventions.

METHODS

Study design and population

Haiti's surveillance system captures $>75\%$ of the WHO-estimated total number of TB cases.¹⁷ We analyzed Haiti's national TB surveillance data from 2011 to 2015 to 1) describe demographic, clinical characteristics, and treatment outcomes of TB cases; 2) compare LTFU by geographic area, facility, age group, sputum smear status, and human immunodeficiency virus (HIV) status; 3) examine subnational units and facilities reporting the highest volume of TB cases; and 4) conduct a survival analysis of time to LTFU and associated factors to guide future intervention strategies. In addition, we visited nine high-volume facilities from 10 to 19 May 2017 to speak with TB staff about their perspectives of the challenges contributing to LTFU.

Data collection

The PNLT provided de-identified case-based data by year of all TB cases reported in the electronic TB surveillance system. This system does not include multi-drug-resistant TB cases, which are reported separately. The data included geographic subdivisions of Haiti's 10 departments (administrative provinces) and specific facilities at which patients received treatment, patient demographics, TB treatment history, sputum microscopy, chest radiography results, type of TB disease (pulmonary smear-positive, pulmonary smear-negative, or extra-pulmonary), HIV status, antiretroviral therapy (ART), and TB treatment outcome.

The PNLT selected a convenience sample of nine facilities in two high TB burden districts representing a spectrum of facilities with high and low LTFU rates. We interviewed health personnel at these facilities to determine staff perceptions related to LTFU at their facility and to identify successful interventions for improved TB treatment adherence. Interviews included

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ACKNOWLEDGEMENTS

The authors thank J B Koama for critical review of the manuscript. This work has been supported by the President's Emergency Plan for AIDS Relief (PEPFAR; Washington DC, USA) through the US Centers for Disease Control and Prevention (CDC). Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the CDC/ the Agency for Toxic Substances and Disease (Atlanta, GA, USA) Registry or funding agencies. Conflicts of interest: none declared.

KEY WORDS

TB; treatment default/LTFU; subnational analysis

Received 25 June 2018
Accepted 23 August 2018

PHA 2018; 8(4): 154–161
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an overview of care provided at each facility, staff insight related to factors associated with LTFU, including patient challenges, potential barriers, programmatic challenges, and strategies to reduce LTFU.

Data analysis

The primary outcome of interest was a reported treatment outcome of LTFU, defined as 'a TB patient who did not start treatment or whose treatment was interrupted for ≥ 2 consecutive months'.¹⁸ The remaining cases were categorized as not LTFU, including those with outcomes reported as cured, treatment completed, treatment failed, died, transferred, or not evaluated. The secondary outcome of interest was time to LTFU, defined as the number of days from treatment initiation to treatment outcome.

We used the χ^2 test to examine associations between potential predictor variables and LTFU. We calculated risk ratios (RRs) and 95% confidence intervals (CIs); statistical significance was defined at $P < 0.05$. To determine independent factors associated with LTFU, we used multivariable logistic regression, including in the model those variables with an epidemiologically or biologically plausible association that were statistically significant in descriptive analysis. A subnational analysis of the 10 facilities reporting the highest volume of TB cases by year was performed to identify facilities with high rates of LTFU and focus efforts for the greatest impact. All person-level analyses account for site-level clustering using the Survey family of procedures in SAS 9.4 software (Statistical Analysis System, Cary, NC, USA).

Time to outcome was estimated for cases reported from 2012 to 2015; cases reported in 2011 did not include date of treatment outcome and were thus excluded. Cases that were not LTFU were censored. We truncated follow-up time at the 1st and 99th percentiles to exclude outliers that were likely to be data entry errors. We used the Kaplan-Meier method to estimate survival probabilities and the log-rank test to determine statistical significance of categorical predictor variables. Independent predictors of LTFU were identified using Cox proportional hazards modeling. Hazard ratios (HRs) with 95% CIs were estimated for each variable. Proportional hazards assumptions were verified graphically; stratified Cox modeling was performed to control for variables that violated the proportional hazards assumption. We repeated Cox proportional hazards analysis using a shared frailty model to account for within-cluster correlation, incorporating cluster effects into the model as random variables. As the results were nearly identical, we report the results of the simpler model. Observations from the nine site visits and unstructured interviews were summarized in narrative form.

Ethical considerations

The Centers for Disease Control and Prevention (Atlanta, GA, USA) and the PNLTH, Port-au-Prince, Haiti, determined this project to be a public health program evaluation that did not require review by the Institutional Review Boards.

RESULTS

Descriptive characteristics of the study population, 2011–2015

Of 81 490 TB cases reported, 42 565 (52.2%) were male (Table 1). The median age was 29 years (interquartile range [IQR] 21–41), with the largest proportion aged 25–34 years (28.3%). The majority of the cases were new patients (94.5%); 5.0% of cases were previously treated. Of 79 332 cases with sputum smear microscopy results, 51 008 (64.3%) were smear-positive. Of 69 415 (85.2%)

cases with HIV status reported, 12 897 (18.6%) were HIV-positive. Among the TB-HIV co-infected patients, 6500 (50.4%) were on antiretroviral therapy (ART). The majority of the cases (90.7%) had a family member reported as their treatment supporter during anti-tuberculosis treatment.

Of 81 453 (99.95%) TB cases with a treatment outcome reported, 7423 (9.1%) were LTFU during treatment (Table 2). The proportion of LTFU cases steadily increased from 7.1% in 2011 to 10.3% in 2015 ($P < 0.0001$). Overall LTFU rates were highest in the West Department (12.3%), in out-patient clinics (10.9%), and in private not-for-profit facilities (16.6%) (Table 1). During this period, 284 facilities reported at least one TB case. The top 10 facilities in terms of numbers of patients varied year to year; 16 facilities made the top 10 at least once during the 5-year interval. These 16 facilities accounted for 41.7% of all cases and 55.6% of LTFU cases, with LTFU rates ranging from 0.2% to 31.9% (Table 3). The majority of these facilities are located in the West Department. Six of the facilities had significantly higher rates of LTFU (14.3–31.9%) than the rest of the country; these facilities accounted for 18.8% of all TB cases reported, but 41.7% of all patients who were LTFU. Two referral centers accounted for 29.2% of all LTFU cases.

Bivariate and multivariable analyses

Bivariate and multivariable analyses of facility-level factors indicated that the West Department, clinics, and private not-for-profit facilities were associated with significantly higher rates of LTFU (Table 4). Bivariate analyses of patient-level factors indicated that male sex (relative risk [RR] 1.17, 95%CI 1.12–1.23), history of previous anti-tuberculosis treatment (RR 1.48, 95%CI 1.36–1.61), negative sputum smear microscopy (RR 1.21, 95%CI 1.14–1.28), and HIV infection (RR 1.63, 95%CI 1.54–1.71) were associated with significantly higher rates of LTFU. The 25–34-year age group was also associated with significantly higher LTFU rates than other age groups. In multivariable analyses, male sex, previous treatment history, clinically diagnosed pulmonary TB, and HIV infection remained significant.

Time to LTFU analysis

Of 66 167 TB cases reported from 2012 to 2015, 59 569 (90.0%) had both date of treatment initiation and outcome reported. After excluding outliers, the calculated time to outcome for 58 404 cases ranged from 0 to 375 days. Kaplan-Meier analysis of the 5442 (9.3%) LTFU cases showed that the median time to LTFU was 94 days (IQR 62–152); >20% were lost to follow-up during the intensive phase, <60 days after treatment initiation (Figure). Factors associated with faster time to LTFU were similar to those associated with LTFU in general (Table 5). Stratified Cox proportional hazard modeling controlling for age, previous treatment history, department, type of facility, and facility category indicated that male sex (adjusted hazard ratio [aHR] 1.18, 95%CI 1.12–1.25), negative sputum microscopy (aHR 1.30, 95%CI 1.20–1.40), and HIV-positive status (aHR 1.70, 95%CI 1.59–1.83) were all significantly associated with a shorter time to LTFU (Table 6).

Tuberculosis staff interviews

The nine facilities visited were located in the West and Artibonite Departments, accounting for 27.6% of all reported cases and 38.9% of all LTFU cases nationally, ranging from 0.2% to 31.9% of LTFU cases (mean 11.1%). Seven of the nine facilities visited were included in the subnational analysis of high-volume facilities, indicated with an asterisk in Table 3. Three facilities (A, E, J) had LTFU rates higher than the national average (10.7–31.9%),

TABLE 1 Facility and patient characteristics of TB cases reported in Haiti TB surveillance system, 2011–2015

Characteristic	All reported (<i>n</i> = 81 490) <i>n</i> (%) [*]	LTFU (<i>n</i> = 7 423) <i>n</i> (%) [†]	Not LTFU (<i>n</i> = 74 030) <i>n</i> (%) [†]
Sex			
Male	42 565 (52.2)	4 174 (9.8)	38 372 (90.2)
Female	38 925 (47.8)	3 249 (8.4)	35 658 (91.6)
Age group, years			
0–4	4 431 (5.4)	493 (11.1)	3 935 (88.9)
5–14	4 568 (5.6)	357 (7.8)	4 208 (92.2)
15–24	20 027 (24.6)	1 885 (9.4)	18 131 (90.6)
25–34	23 068 (28.3)	2 280 (9.9)	20 778 (90.1)
35–44	12 930 (15.9)	1 096 (8.5)	11 830 (91.5)
45–54	8 364 (10.3)	708 (8.5)	7 652 (91.5)
55–64	4 735 (5.8)	339 (7.2)	4 395 (92.8)
≥65	3 367 (4.1)	265 (7.9)	3 101 (92.1)
Age, years, median [IQR]	29 [21–41]	29 [21–41]	28 [21–39]
Patient category			
New	76 972 (94.5)	6 821 (8.9)	70 144 (91.1)
Relapse	3 244 (4.0)	357 (11.0)	2 887 (89.0)
Failure	335 (0.4)	40 (11.9)	295 (88.1)
Resumption of treatment	455 (0.6)	132 (29.0)	323 (71.0)
Other	484 (0.6)	73 (15.1)	411 (84.9)
Sputum smear microscopy [‡]			
Positive	51 008 (64.3)	4 270 (8.4)	46 718 (91.6)
Negative	13 024 (16.4)	1 318 (10.1)	11 700 (89.9)
Not done	15 300 (19.3)	1 615 (10.6)	13 677 (89.4)
Chest radiography [§]			
Positive	20 425 (77.8)	2 270 (11.1)	18 144 (88.9)
Negative	349 (1.3)	28 (8.0)	321 (92.0)
Not done	5 475 (20.9)	464 (8.5)	5 008 (91.5)
TB disease type			
Pulmonary smear-positive	51 131 (62.7)	4 270 (8.4)	46 841 (91.6)
Pulmonary smear-negative	21 597 (26.5)	2 374 (11.0)	19 210 (89.0)
Extra-pulmonary	8 762 (10.8)	779 (8.9)	7 979 (91.1)
HIV testing done		Column %	Column %
Yes	68 181 (84.5)	6 145 (83.4)	62 018 (84.6)
No	12 553 (15.5)	1 226 (16.6)	11 313 (15.4)
HIV status [#]			
Negative	54 679 (78.8)	4 395 (8.0)	50 270 (92.0)
Positive	12 897 (18.6)	1 685 (13.1)	11 208 (86.9)
Indeterminate	1 839 (2.6)	244 (13.3)	1 595 (86.7)
ART status among HIV-positive			
On ART	6 500 (50.4)	850 (13.1)	5 649 (86.9)
Not on ART	3 501 (27.1)	410 (11.7)	3 090 (88.3)
Not reported	2 896 (22.5)	425 (14.7)	2 469 (85.3)
Year			
2011	15 323 (18.8)	1 082 (7.1)	14 204 (92.9)
2012	16 723 (20.5)	1 393 (8.3)	15 330 (91.7)
2013	17 040 (20.9)	1 672 (9.8)	15 368 (90.2)
2014	15 936 (19.6)	1 585 (9.9)	14 351 (90.1)
2015	16 468 (20.2)	1 691 (10.3)	14 777 (89.7)
Geographic department			
Artibonite	9 814 (12.0)	509 (5.2)	9 305 (94.8)
Center	4 360 (5.4)	301 (6.9)	4 059 (93.1)
Grand'Anse	3 648 (4.5)	247 (6.8)	3 401 (93.2)
Nippes	2 463 (3.0)	78 (3.2)	2 377 (96.8)
North	8 830 (10.8)	323 (3.7)	8 506 (96.3)
North-East	2 563 (3.1)	79 (3.1)	2 484 (96.9)
North-West	5 002 (6.1)	612 (12.2)	4 390 (87.8)
West	35 700 (43.8)	4 386 (12.3)	31 289 (87.7)
South	6 047 (7.4)	528 (8.7)	5 516 (91.3)
South-East	3 063 (3.8)	360 (11.8)	2 703 (88.2)
Type of facility ^{**}			
Hospital	46 989 (57.7)	3 676 (7.8)	43 289 (92.2)
Clinic	34 487 (42.3)	3 746 (10.9)	30 728 (89.1)
Category of facility ^{**}			
State facility (public)	36 954 (45.5)	2 382 (6.4)	34 551 (93.6)
Public/private (mixed)	12 228 (15.1)	979 (8.0)	11 244 (92.0)
Private, not-for-profit	20 303 (25.0)	3 374 (16.6)	16 922 (83.4)
Private for profit	11 712 (14.4)	664 (5.7)	11 044 (94.3)

^{*}Percentages of 'All enrolled' represents the column % of a given variable with no missing data.

[†]Percentages of LTFU and Not LTFU cases represent the row % of 'All enrolled TB cases' for a given variable stratum, with the exception of variable HIV testing done, which lists column %.

[‡]Missing baseline sputum smear microscopy results: 21 58 (2.6%) cases.

[§]Missing chest radiography results: 55 241 (67.8%) cases.

^{||}Missing HIV test results: 756 (0.9%) cases.

[#]Missing HIV status: 12 075 (14.8%) cases.

^{**}Missing type or category of facility: 293 (0.4%) cases.

TB = tuberculosis; LTFU = loss to follow-up; IQR = interquartile range; HIV = human immunodeficiency virus; ART = antiretroviral therapy.

TABLE 2 Sputum positivity, HIV testing, ART uptake, and treatment outcomes by year, Haiti, 2011–2015

Characteristic	All enrolled (<i>n</i> = 81 490) <i>n</i> (%)	2011 (<i>n</i> = 15 286) <i>n</i> (%)	2012 (<i>n</i> = 16 723) <i>n</i> (%)	2013 (<i>n</i> = 17 040) <i>n</i> (%)	2014 (<i>n</i> = 15 936) <i>n</i> (%)	2015 (<i>n</i> = 16 468) <i>n</i> (%)
Sputum smear microscopy						
Positive	51 008 (64.3)	8 904 (60.1)	9 863 (59.8)	10 324 (61.9)	10 408 (67.0)	11 509 (72.8)
Negative	13 024 (16.4)	2 996 (20.2)	1 863 (11.3)	2 554 (15.3)	2 944 (18.9)	2 667 (16.9)
Not done	15 300 (19.3)	2 923 (19.7)	4 771 (28.9)	3 789 (22.7)	2 187 (14.1)	1 630 (10.3)
HIV testing done*						
Yes	68 181 (84.5)	11 213 (76.1)	13 523 (80.9)	14 668 (86.2)	13 961 (88.4)	14 816 (90.0)
No	12 553 (15.5)	3 527 (23.9)	3 190 (19.1)	2 347 (13.8)	1 837 (11.6)	1 652 (10.0)
HIV status†						
Negative	54 679 (78.8)	8 666 (77.8)	10 755 (79.3)	11 692 (79.8)	11 280 (80.9)	12 286 (76.2)
Positive	12 897 (18.6)	2 320 (20.8)	2 705 (19.9)	2 857 (19.5)	2 588 (18.6)	2 427 (15.1)
Indeterminate	1 839 (2.6)	149 (1.3)	108 (0.8)	97 (0.7)	76 (0.5)	1 409 (8.7)
ART status of HIV-positive patients						
On ART	6 500 (50.4)	587 (25.3)	1 253 (46.3)	1 659 (58.1)	1 395 (53.9)	1 606 (66.2)
Not on ART	3 501 (27.1)	909 (39.2)	1 080 (39.9)	543 (19.0)	590 (22.8)	379 (15.6)
Not reported	2 896 (22.5)	824 (35.5)	372 (13.8)	655 (22.9)	603 (23.3)	442 (18.2)
Treatment outcome‡§						
Cured	37 300 (45.8)	6 491 (42.5)	7 444 (44.5)	7 563 (44.4)	7 153 (44.9)	8 649 (52.5)
Completed	28 111 (34.5)	6 016 (39.4)	6 185 (37.0)	6 257 (36.7)	5 194 (32.6)	4 459 (27.1)
LTFU	7 423 (9.1)	1 082 (7.1)	1 393 (8.3)	1 672 (9.8)	1 585 (10.0)	1 691 (10.3)
Transferred	2 844 (3.5)	784 (5.1)	641 (3.8)	497 (2.9)	525 (3.3)	397 (2.4)
Died	4 151 (5.1)	793 (5.2)	894 (5.3)	872 (5.1)	761 (4.8)	831 (5.0)
Failure	681 (0.8)	111 (0.7)	134 (0.8)	125 (0.7)	158 (1.0)	153 (0.9)
Not evaluated	943 (1.2)	9 (0.1)	32 (0.2)	54 (0.3)	560 (3.5)	288 (1.7)
Treatment success	65 411 (80.3)	12 507 (81.8)	13 629 (81.5)	13 820 (81.1)	12 347 (77.5)	13 108 (79.6)

*A total of 756 (0.9%) of 'All enrolled' cases had no information on the HIV test: 583 (3.8%) in 2011, 10 (0.1%) in 2012, 25 (0.1%) in 2013, 134 (0.9%), and 0 (0%) in 2015.

†A total of 12 075 (14.8%) cases had no information on HIV status: 4 188 (27.3%) in 2011, 3155 (18.9%) in 2012, 2394 (14.1%) in 2013, 1992 (12.5%) in 2014, and 346 (2.1%) in 2015.

‡37 (0.05%) cases did not have a treatment outcome reported. All of these cases were reported in 2011.

§Percentages represent the column % for a treatment outcome of a given year.

HIV = human immunodeficiency virus; ART = antiretroviral therapy.

TABLE 3 Top 16 facilities with the highest volume of reported TB cases and associated risk of LTFU for each facility as compared to the national LTFU rate, 2011–2015

Facility	Department	Type of facility	Facility category	Total cases <i>n</i>	LTFU cases <i>n</i> (%)	Bivariate analysis		Multivariable analysis	
						RR* (95%CI)	<i>P</i> value	OR* (95%CI)	<i>P</i> value
A†	West	Clinic	PNFP	7952	1717 (21.6)	2.78 (2.65–2.92)	<0.0001	2.90 (2.72–3.09)	<0.0001
B†	West	Hospital	State	3450	15 (0.4)	0.05 (0.03–0.08)	<0.0001	0.04 (0.03–0.07)	<0.0001
C	West	Hospital	State	2594	208 (8.0)	0.88 (0.77–1.00)	0.05	0.78 (0.68–0.91)	0.001
D†	West	Clinic	PNFP	2509	176 (7.0)	0.76 (0.66–0.88)	0.0002	0.89 (0.76–1.04)	0.15
E†	West	Hospital	Mixed‡	2153	231 (10.7)	1.18 (1.05–1.34)	0.01	1.34 (1.17–1.55)	<0.0001
F	West	Hospital	PNFP	1946	334 (17.2)	1.93 (1.74–2.13)	<0.0001	1.46 (1.29–1.67)	<0.0001
G†	Artibonite	Clinic	State	1666	3 (0.2)	0.02 (0.01–0.06)	<0.0001	0.02 (0.01–0.06)	<0.0001
H†	West	Hospital	State	1588	140 (8.8)	0.97 (0.82–1.13)	0.68	1.03 (0.86–1.22)	0.78
I	North	Hospital	State	1530	219 (14.3)	1.59 (1.40–1.80)	<0.0001	1.81 (1.56–2.10)	<0.0001
J†	West	Clinic	PNFP	1419	453 (31.9)	3.67 (3.39–3.97)	<0.0001	3.76 (3.31–4.27)	<0.0001
K	North-West	Hospital	State	1398	38 (2.7)	0.29 (0.22–0.40)	<0.0001	0.27 (0.19–0.37)	<0.0001
L	West	Hospital	PNFP	1293	189 (14.6)	1.62 (1.42–1.85)	<0.0001	1.70 (1.42–2.03)	<0.0001
M	Nippes	Clinic	PFP	1219	7 (0.6)	0.06 (0.03–0.13)	<0.0001	0.06 (0.03–0.13)	<0.0001
N	North-West	Hospital	PNFP	1159	185 (16.0)	1.77 (1.55–2.02)	<0.0001	2.10 (1.79–2.47)	<0.0001
O	Artibonite	Clinic	State	1133	103 (9.1)	1.00 (0.83–1.20)	0.98	1.02 (0.83–1.26)	0.84
P	Center	Hospital	State	995	109 (11.0)	1.21 (1.01–1.44)	0.04	1.45 (1.17–1.80)	0.0006

*Compared with all other facilities.

†Site visits and interviews with TB staff were conducted at these facilities.

‡Public/private mix.

TB = tuberculosis; LTFU = loss to follow-up; RR = risk ratio; CI = confidence interval; OR = odds ratio; PNFP = private not-for-profit; PFP = private for-profit.

TABLE 4 Bivariate and multivariable logistic regression and survey analyses of factors associated with LTFU

Characteristic	Bivariate analysis		Multivariable logistic regression		Multivariable logistic regression using Survey statistical methods	
	RR (95%CI)	P value	OR (95%CI)	P value	OR (95%CI)	P value
Sex						
Male	1.17 (1.12–1.23)	<0.0001	1.20 (1.14–1.26)	<0.0001	1.20 (1.12–1.28)	<0.0001
Female	Reference	Reference	Reference	Reference	Reference	Reference
Age group, years						
0–4	1.13 (1.03–1.23)	0.01	0.97 (0.87–1.09)	0.63	0.97 (0.72–1.31)	0.85
5–14	0.79 (0.71–0.88)	<0.0001	0.75 (0.67–0.85)	<0.0001	0.75 (0.63–0.90)	0.002
15–24	0.95 (0.90–1.01)	0.10	1.02 (0.95–1.09)	0.57	1.02 (0.96–1.09)	0.56
25–34	Reference	Reference	Reference	Reference	Reference	Reference
35–44	0.86 (0.80–0.92)	<0.0001	0.79 (0.73–0.85)	<0.0001	0.79 (0.72–0.86)	<0.0001
45–54	0.86 (0.79–0.93)	0.0002	0.79 (0.72–0.87)	<0.0001	0.79 (0.71–0.88)	<0.0001
55–64	0.72 (0.65–0.81)	<0.0001	0.71 (0.63–0.80)	<0.0001	0.71 (0.62–0.81)	<0.0001
≥65	0.80 (0.70–0.90)	0.0002	0.89 (0.78–1.02)	0.09	0.89 (0.76–1.04)	0.15
Patient category						
New	Reference	Reference	Reference	Reference	Reference	Reference
Previously treated*	1.48 (1.36–1.61)	<0.0001	1.50 (1.36–1.66)	<0.0001	1.50 (1.32–1.71)	<0.0001
Sputum smear microscopy						
Positive	Reference	Reference	Reference	Reference	Reference	Reference
Negative	1.21 (1.14–1.28)	<0.0001	1.14 (1.02–1.27)	0.02	1.14 (0.91–1.41)	0.25
Chest radiography						
Positive	Reference	Reference	Reference	Reference	Reference	Reference
Negative	0.72 (0.50–1.03)	0.07	0.95 (0.63–1.41)	0.78	0.95 (0.63–1.41)	0.78
Type of TB						
Pulmonary bacteriologically confirmed	Reference	Reference	Reference	Reference	Reference	Reference
Pulmonary clinically diagnosed	1.32 (1.26–1.38)	<0.0001	1.16 (1.09–1.24)	<0.0001	1.16 (1.01–1.34)	0.04
Extra-pulmonary	1.06 (0.99–1.15)	0.09	1.10 (1.01–1.19)	0.04	1.10 (0.90–1.33)	0.37
HIV status						
Negative	Reference	Reference	Reference	Reference	Reference	Reference
Positive	1.63 (1.54–1.71)	<0.0001	1.69 (1.58–1.80)	<0.0001	1.69 (1.50–1.90)	<0.0001
Indeterminate	1.65 (1.46–1.86)	<0.0001	1.57 (1.36–1.81)	<0.0001	1.57 (1.31–1.89)	<0.0001
ART status of HIV-positive patients†						
On ART	Reference	Reference	Reference	Reference	Reference	Reference
Not on ART	0.90 (0.80–1.00)	0.05	1.15 (1.00–1.31)	0.05	1.15 (0.99–1.35)	0.08
Not reported	1.13 (1.01–1.25)	0.04	1.16 (1.02–1.33)	0.03	1.16 (0.99–1.36)	0.06
Treatment supporter						
Family or friend	Reference	Reference	Reference	Reference	Reference	Reference
Health worker	1.36 (1.20–1.54)	<0.0001	1.18 (1.02–1.36)	0.03	1.18 (0.96–1.44)	0.13
Department						
Artibonite	0.42 (0.39–0.46)	<0.0001	0.58 (0.52–0.64)	<0.0001	0.58 (0.32–1.04)	0.07
Center	0.56 (0.50–0.63)	<0.0001	0.67 (0.59–0.78)	<0.0001	0.67 (0.34–1.32)	0.25
Grand'Anse	0.55 (0.49–0.62)	<0.0001	0.76 (0.66–0.88)	0.0002	0.76 (0.47–1.24)	0.27
Nippes	0.26 (0.21–0.32)	<0.0001	0.39 (0.31–0.49)	<0.0001	0.39 (0.13–1.19)	0.10
North	0.30 (0.27–0.33)	<0.0001	0.41 (0.36–0.47)	<0.0001	0.41 (0.27–0.63)	<0.0001
North-East	0.25 (0.20–0.31)	<0.0001	0.38 (0.30–0.48)	<0.0001	0.38 (0.17–0.88)	0.02
North-West	1.00 (0.92–1.08)	0.90	1.33 (1.21–1.47)	<0.0001	1.33 (0.86–2.06)	0.20
West	Reference	Reference	Reference	Reference	Reference	Reference
South	0.71 (0.65–0.77)	<0.0001	0.86 (0.79–0.95)	0.003	0.86 (0.58–1.28)	0.46
South-East	0.96 (0.86–1.06)	0.38	1.24 (1.10–1.41)	0.0006	1.24 (0.81–1.90)	0.31
Type of facility						
Hospital	Reference	Reference	Reference	Reference	Reference	Reference
Clinic	1.39 (1.33–1.45)	<0.0001	1.10 (1.04–1.17)	0.0005	1.10 (0.84–1.45)	0.48
Facility category						
State facility (public)	Reference	Reference	Reference	Reference	Reference	Reference
Public/private (mixed)	1.25 (1.16–1.34)	<0.0001	1.28 (1.18–1.39)	<0.0001	1.28 (0.93–1.77)	0.13
Private not-for-profit	2.58 (2.45–2.71)	<0.0001	2.12 (1.98–2.27)	<0.0001	2.12 (1.44–3.13)	0.0002
Private for-profit	0.88 (0.81–0.96)	0.002	1.06 (0.96–1.16)	0.23	1.06 (0.66–1.70)	0.81

*Previously treated includes the following patient categories: relapse, failure, and resumption of treatment.

†ART status among HIV-infected patients, $n = 1685$.

LTFU = loss to follow-up; RR = risk ratio; CI = confidence interval; OR = odds ratio; TB = tuberculosis; HIV = human immunodeficiency virus; ART = antiretroviral therapy.

FIGURE Kaplan-Meier curve of all LTFU patients indicating the duration of treatment before being LTFU, 2012–2015. LTFU = loss to follow-up.

while two facilities (B, G) reported very low LTFU rates (0.2–0.4%).

Staff consistently noted transportation costs as a major challenge for patients to reach the facilities. Transportation vouchers were not available for patients during anti-tuberculosis treatment. Additional challenges included food insecurity, TB- and HIV-associated stigma, lengthy waiting times at crowded facilities, medication side effects, and not understanding the consequences of interrupting treatment. Some patients believed in ‘supernatural’ causes for their illness, rather than bacteria, and sought alternative therapy through prayer or traditional healers. Occasional barriers to reaching the facilities for appointments included political instability or inclement weather making it unsafe to travel, and family emergencies or deaths.

Staff highlighted programmatic challenges with patient transfers and referrals between facilities. Patients who ‘self-transferred’ without proper documentation were often reported as LTFU. The proportion of successful vs. failed transfers is unknown. Apart from transfers, some patients are specifically referred to another facility closer to their home after being diagnosed. Patients who do not reach the destination facility to start treatment are never registered in the surveillance system and represent pre-treatment LTFU of unknown proportion. Communication between facilities in different geographic departments is poor.

To reduce LTFU, staff at all sites stressed the importance of continuous education throughout the course of TB treatment. They emphasized potential adverse consequences of incomplete treatment, including drug resistance, transmission to family members, and even death. The two facilities with the lowest LTFU rates (B, G) had implemented systems to immediately identify and contact patients who missed their appointment and utilize field workers if unable to reach them by telephone. Facility G, recognized consistently for its high TB treatment success rate, emphasized the importance of warmly welcoming patients and expressing genuine concern for their well-being. Facility G also reached out to local religious leaders and traditional healers, educating them about TB in the community and the importance of treatment completion.

TABLE 5 Bivariate Cox proportional hazards analysis of factors associated with time to LTFU

Characteristic	Pr > χ^2	HR (95%CI)
Sex		
Male	<0.0001	1.19 (1.13–1.26)
Female	Reference	Reference
Age group, years		
0–4	0.018	1.15 (1.02–1.29)
5–14	<0.0001	0.70 (0.61–0.81)
15–24	0.009	0.91 (0.85–0.98)
25–34	Reference	Reference
35–44	0.0002	0.85 (0.79–0.93)
45–54	0.001	0.85 (0.77–0.94)
55–64	<0.0001	0.69 (0.60–0.79)
≥65	0.004	0.80 (0.69–0.93)
Patient category		
New	Reference	Reference
Previously treated*	0.004	1.16 (1.05–1.29)
Sputum smear microscopy		
Positive	Reference	Reference
Negative	<0.0001	1.32 (1.22–1.42)
HIV status		
Negative	Reference	Reference
Positive	<0.0001	1.77 (1.66–1.89)
Department		
Artibonite	<0.0001	0.30 (0.27–0.34)
Center	<0.0001	0.46 (0.40–0.53)
Grand’Anse	<0.0001	0.54 (0.47–0.62)
Nippes	<0.0001	0.19 (0.14–0.25)
North	<0.0001	0.19 (0.16–0.23)
North-East	<0.0001	0.18 (0.13–0.23)
North-West	<0.0001	0.71 (0.63–0.79)
West	Reference	Reference
South	<0.0001	0.60 (0.53–0.67)
South-East	0.002	0.81 (0.71–0.92)
Type of facility		
Hospital	Reference	Reference
Clinic	<0.0001	1.59 (1.51–1.68)
Facility category		
State facility (public)	Reference	Reference
Public/private (mixed)	<0.0001	3.13 (2.94–3.33)
Private, not-for-profit	<0.0001	1.31 (1.20–1.44)
Private for-profit	0.890	0.99 (0.89–1.10)
Top 16 facilities†		
A	<0.0001	3.05 (2.87–3.24)
B	<0.0001	0.04 (0.02–0.07)
C	0.880	0.99 (0.84–1.16)
D	0.080	0.87 (0.74–1.02)
E	0.001	1.26 (1.09–1.46)
F	<0.0001	2.12 (1.86–2.41)
G	<0.0001	0.01 (0.00–0.05)
H	0.260	1.11 (0.93–1.33)
I	0.020	1.23 (1.03–1.47)
J	<0.0001	4.52 (4.10–4.98)
K	<0.0001	0.15 (0.08–0.28)
L	<0.0001	1.49 (1.25–1.78)
M	<0.0001	0.04 (0.01–0.11)
N	0.000	1.46 (1.19–1.79)
O	0.010	0.71 (0.55–0.92)
P	0.009	1.32 (1.07–1.63)

*Previously treated includes patient categories: relapse, failure, and resumption of treatment.

†The rest of the country was the reference group for these HRs, i.e., all other facilities. LTFU = loss to follow-up; HR = hazards ratio; CI = confidence interval; HIV = human immunodeficiency virus.

TABLE 6 Multivariable Cox proportional hazards analysis of predictors of time to LTFU controlling for age group, treatment history, department, and facility category*

Characteristic	aHR (95% HR confidence limits)	P value
Sex		
Male	1.18 (1.12–1.25)	<0.0001
Female	Reference	Reference
Sputum smear microscopy		
Positive	Reference	Reference
Negative	1.30 (1.20–1.41)	<0.0001
HIV status		
Negative	Reference	Reference
Positive	1.70 (1.59–1.83)	<0.0001
Type of facility		
Hospital	Reference	Reference
Clinic	1.00 (0.93–1.08)	0.97

*As age group, treatment history, department, and facility category violated the proportional hazards assumption, they were included as stratification variables, and it was not possible to calculate HRs for these variables.

aHR = adjusted hazards ratio; HIV = human immunodeficiency virus.

DISCUSSION

Since the earthquake in 2010, LTFU rates have risen steadily from 7.1% in 2011 to 10.3% in 2015. Independent risk factors for LTFU include male sex, age 25–34 years, previous treatment for TB, and HIV coinfection. HIV-positive status proved to be one of the strongest associations with LTFU in multivariable analyses. Other studies also found HIV-positive status to be associated with an increased risk for LTFU.^{19–23} Potential contributing factors include higher pill burden, more medication side effects, psychosocial stressors, stigma, and weak coordination between the TB and HIV programs.

Strategies to reduce LTFU include replicating practices at facilities with consistently low LTFU rates, including a team approach to TB care, continuous patient education, promptly identifying patients who miss appointments, and attempting to contact them by phone or field worker. However, not all facilities have field workers for TB activities and may engage treatment supporters. Some sites have developed new strategies and interventions in the past 2 years that were not reflected in the 2011–2015 surveillance data.

The subnational analysis identified high-volume facilities with disproportionately high rates of LTFU, mainly in the West Department, which also reports the highest proportion of TB case notifications.⁹ Patients may travel from distant sites to referral centers in the capital region that are recognized for their excellent care and expertise. Although the PNLT strongly encourages patients to seek care close to their home and avoid transferring during the initial 2 months of treatment,²⁴ many patients may self-transfer after treatment initiation and are subsequently recorded as LTFU. Targeted interventions, particularly at these high-volume referral centers, should focus on ensuring successful transfers and reducing LTFU among patients from outside the local area by improving communication between facilities. They should also consider the use of transportation vouchers.

Twenty per cent of LTFU patients were lost <60 days after starting treatment. As LTFU is defined as an interruption of at least 2 months, operationally, these patients were categorized as LTFU before meeting this criterion. Programmatically, this may

identify an early LTFU subgroup that may benefit from intensified treatment support and outreach following a missed appointment.

There were several limitations to the study. First, missing and inaccurate dates meant the exclusion of ~10% of cases from the survival analysis. Second, delayed reporting of treatment outcome²⁵ may have inflated the time to LTFU in this analysis. Third, the overall LTFU rate does not take into account patients who successfully self-transferred to another facility, although this is believed to represent a small proportion of cases. On the other hand, outcomes reported as ‘transferred’ or ‘not evaluated’ (4.7%) may include cases that in fact were ultimately LTFU.^{26,27} Patients diagnosed with TB who did not start treatment represent pre-treatment LTFU cases, and were not included in this analysis. The overall proportion of LTFU may therefore have been underestimated.^{28,29} Finally, statistical analyses were limited to programmatic data routinely collected through the national TB surveillance system. Patient-level variables, such as socio-economic status and substance use, were not available for this analysis.

Despite these limitations, the findings identify specific, actionable risk factors for LTFU at national, subnational, and facility levels. Strategies to reduce LTFU may include intensifying interventions among young men, patients previously treated for TB, and those co-infected with HIV. A small number of highly regarded facilities consistently reported excessive LTFU rates. Based on the present analysis, strategies and resources are being directed to these facilities. Furthermore, a few high-volume facilities consistently achieved high treatment success and low LTFU rates; their treatment approaches and interventions should be replicated. Future qualitative studies to query patients about their reasons for LTFU may identify potential remedies.^{28,30}

In conclusion, the subnational analysis revealed that a small number of facilities accounted for disproportionately high rates of LTFU. Providing this information to leadership at these facilities resulted in immediate steps to ensure treatment completion. More broadly, these results identify characteristics of facilities and individuals leading to focused interventions to reduce LTFU and improve treatment success.

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Contexte : Structures de traitement de la tuberculose (TB) en Haïti.

Objectif : Evaluer les facteurs associés à la perte de vue (LTFU) parmi les patients recevant un traitement de TB en Haïti.

Schéma : Nous avons analysé les données de surveillance nationale de Haïti pour les patients mis sous traitement de TB entre 2011 et 2015, afin de déterminer les facteurs associés aux LTFU grâce à une régression logistique multivariée, et nous avons décrit les LTFU par unités sous-nationales afin de cibler les stratégies d'intervention futures. Nous avons également réalisé une analyse de survie afin d'estimer les ratios de risque des facteurs associés au délai de LTFU.

Résultats : Sur 81 490 cas de TB rapportés, 7423 (9,1%) ont été perdus de vue pendant le traitement de TB, augmentant de 7,1% en

2011 à 10,3% en 2015. Six structures à haut débit de patients ont eu des taux de LTFU significativement plus élevés (14,3–31,9%) que le reste du pays, représentant 18,8% de tous les cas de TB rapportés, mais 41,7% de tous les patients perdus de vue. Le sexe masculin, des antécédents de traitement préalable, et une infection au virus de l'immunodéficience humaine ont été associés à des taux plus élevés de LTFU. Le délai médian de LTFU a été de 94 jours.

Conclusion : Un petit nombre de structures ont des taux disproportionnellement élevés de LTFU. Ces résultats identifient les caractéristiques des structures et des individus aboutissant à des interventions ciblées afin de réduire les LTFU et d'améliorer le taux de succès du traitement.

Marco de referencia: Establecimientos de tratamiento de la tuberculosis (TB) en Haïti.

Objetivo: Evaluar los factores que se asocian con la pérdida durante el seguimiento (LTFU) de los pacientes que reciben tratamiento antituberculoso en Haïti.

Método: Se analizaron los datos nacionales de vigilancia de los pacientes que iniciaron tratamiento antituberculoso del 2011 al 2015 en Haïti, con el objeto de determinar los factores asociados con la LTFU mediante modelos de regresión logística multivariante y se describieron estas pérdidas por unidades subnacionales, con el fin de orientar las futuras estrategias de intervención. Se practicó además un análisis de supervivencia con el fin de estimar los cocientes de riesgos instantáneos de los factores asociados con el tiempo transcurrido hasta la LTFU.

Resultados: De los 81 490 casos de TB notificados, se perdieron durante el seguimiento del tratamiento antituberculoso 7423 (9,1%)

y se observó un aumento del 7,1% en el 2011 al 10,3% en el 2015. En seis establecimientos con alta carga asistencial se encontraron tasas significativamente más altas de LTFU (14,3–31,9%) que en el resto del país y correspondieron al 18,8% de todos los casos de TB notificados, pero al 41,7% de todos los pacientes pérdidas. Los factores que se asociaron con tasas más altas de LTFU fueron el sexo masculino, el antecedente de tratamiento y la infección por el virus de la inmunodeficiencia humana. La mediana del lapso transcurrido hasta la LTFU fue 94 días.

Conclusión: Un número pequeño de establecimientos contribuyó con tasas desproporcionadamente altas de LTFU. Estos resultados ponen de manifiesto las características de las instalaciones y de las personas que deben orientar las intervenciones dirigidas, encaminadas a disminuir la LTFU y mejorar el éxito terapéutico.