ORIGINAL ARTICLE
TUBERCULOSIS

Predictors of loss to follow-up of tuberculosis cases under the DOTS programme in Namibia

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ABSTRACT

Background: In Namibia, one out of every 25 cases of tuberculosis (TB) is "lost to follow-up" (LTFU). This has impacted negatively on national efforts to end the disease by 2035. The aim of this study was to determine the trends and predictors of LTFU under the directly observed treatment short-course (DOTS) programme in Namibia.

Methods: The study involved a retrospective longitudinal analysis of a nationwide cohort of TB cases registered under the DOTS programme in Namibia from 2006 to 2015. The trends and predictors of LTFU among cases in the National Electronic TB Register of the National TB and Leprosy Program were respectively determined by interrupted time series and multivariate logistic regression analyses using R-Studio software.

Results: Out of 104 203 TB cases, 3775 (3.6%) were LTFU. A quarter (26%) of cases with poor outcomes were due to LTFU. The annual decline in cases of LTFU was significant between the first (2005–2010) and second (2010–2015) medium-term plan period for TB programme implementation (p=0.002). The independent predictors of LTFU were male sex (p=0.004), 15–24 years age group (p=0.03), provider of treatment (p<0.001), intensive phase (p=0.047) and living in border/transit regions (p<0.001). HIV co-infection and TB regimen were not significant predictors of LTFU.

Conclusions: There were declining trends in LTFU in Namibia. DOTS programmes should integrate socioeconomic interventions for young and middle-aged adult male TB cases to reduce LTFU.

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Loss to follow-up of tuberculosis patients is an important barrier to ending TB in high-TB-burden countries. The integration of social welfare among young and/or middle-aged men is critical in reducing loss to follow-up of TB patients. http://bit.ly/395WfBM

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Introduction

Tuberculosis (TB) has had a devastating impact on public health in Africa [1, 2]. In 2018, out of the 10.0 million cases notified, 24% were from the sub-Saharan countries [3]. Of concern is that the region accounts for 80% of the 1.8 million estimated annual deaths related to TB; this is a disproportionate impact in terms of mortality [4]. Namibia, with a case notification rate of 442 cases per 100 000, is ranked fifth among countries with highest burden of TB [5, 6]. However, the universal access to community-based TB care through the Stop-TB and End-TB strategies implemented since 2005 has improved case identification and treatment outcomes in Namibia [7].

Nevertheless, the gradual rise in incidence of drug-resistant TB (DR-TB) and poor treatment outcomes such as "lost-to-follow-up" (LTFU) (*i.e.* an interruption of TB treatment for at least two consecutive months) and death [7–10] are major barriers to ending TB in Namibia [3, 11–14]. For instance, the incidence of LTFU among notified cases in Namibia increased from 4% in 2014 to 10% in 2015. Studies in other low and middle-income countries (LMICs) such as India and Malaysia estimate higher incidences of LTFU at 19.2 and 24%, respectively [15, 16]. In addition, LTFU is an important risk factor for re-emergence of TB strains resistant to first-line anti-TB drugs [6]. In 2014, an estimated 300 000 cases of multidrug-resistant (MDR) TB (*i.e.* resistance to backbone first-line anti-TB medicines, rifampicin and isoniazid) were notified globally [17]. In the same year Namibia notified 137 MDR-TB and 6 extensively drug-resistant (XDR) TB (*i.e.* MDR-TB with resistance to second-line TB drugs, aminoglycosides and/or fluoroquinolones) cases [10].

The significance of risk factors of LTFU (*i.e.* patient demographics, socioeconomic status, directly observed treatment, short-course (DOTS) programme, clinical covariates, TB treatment regimen and HIV co-infection) on LTFU have been contested across countries [10, 14, 15, 18–24]. In Namibia, despite universal coverage of high-quality DOTS, little is known about the impact of these factors on poor treatment outcomes and, in particular, LTFU, hence, the current study intended to determine the prevalence and determinants of LTFU in the Namibian context.

Methods

Study design and population

The target population was all the new and retreatment cases with drug-sensitive TB initiated on first-line anti-tuberculosis DOTS regimens. The accessible population was TB cases registered in the National Electronic Tuberculosis Register (ETR) database over a 10-year period from 2006 to 2015. The study included all 104 300 TB cases registered in the ETR; 3775 of these were LTFU. A patient was considered LTFU if TB treatment was interrupted for 2 months or more [10, 17]. A retrospective cohort analysis for trends and predictors of LTFU was conducted. Quarterly trends in LTFU of TB cases in Namibia were analysed as a proportion of the total number of TB cases registered for each quarter. The main outcome measure was the effect size (*i.e.* odds ratio) for predictors for LTFU compared to TB cases that had a successful treatment outcome (*i.e.* cured or completed treatment). The study excluded all TB cases whose treatment outcome had not been registered in the ETR at the time of the study and patients with poor treatment outcome other than LTFU, (*i.e.* died, transferred out, treatment failure) (figure 1).

Medium-term plans for TB in Namibia

Since 2004, Namibia has implemented the DOTS strategy under a national strategic plan on TB implemented under 5-year medium-term plans (MTPs) to improve outcomes. The first MTP was implemented between 2004–2009, with the main goal of scaling up DOTS to all public health facilities in Namibia, with the main goal of achieving 85% treatment success rate from 65%, and to strengthen detection and management of TB cases. The second MTP-II was developed to address gaps in MTP-I and was implemented between 2015 and 2017 to meet the World Health Organization (WHO) and national targets for TB. This focused mainly on the expansion and enhancement of access to quality TB treatment, bacteriological testing and community-based interventions for reduction of cases LTFU. Thus, the difference in the interventions served as discriminates to assess the effectiveness the two mid-term policy strategies for time-series analysis [8, 9]

Procedure and data analysis

Data on treatment outcome, patient sociodemographic, clinical and treatment characteristics were extracted from the ETR and exported to R-Studio software (version 3.3.2) for quantitative analysis. The main outcome measures were an odds ratio of a TB case registered under DOTS programme getting LTFU relative to those with a successful treatment outcome (*i.e.* cured or completed). The covariates included in the model were patient characteristics, clinical/diagnostic, treatment and DOTS programmatic characteristics. The patient covariates were age, sex and region of residence. The clinical covariates were diagnostic or laboratory classification of the TB case, sputum conversion at 2 months and HIV

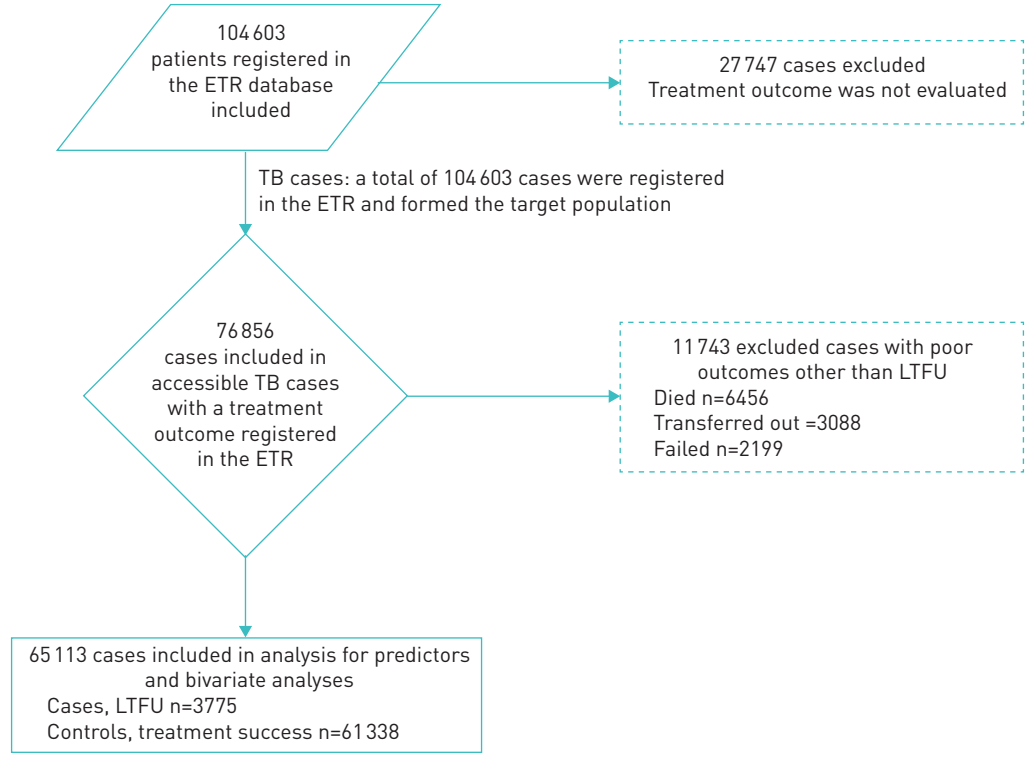

FIGURE 1 Flowchart for tuberculosis (TB) cases included in the analysis. ETR: electronic tuberculosis register; LTFU: lost to follow-up.

co-infection. The programmatic covariates were the TB strategies implemented (*i.e.* the first and second MTP for TB and leprosy), DOTS support category and level of health facility. Other clinical covariates pertained to the treatment regimens and therapy included the DOTS regimen initiated, anti-retroviral treatment (ART) regimen, type of DOTS provider, and previous prophylaxis with co-trimoxazole preventive therapy (CPT) and isoniazid preventive therapy (IPT). An interrupted time-series analysis was performed to determine the changes in level and trend of LTFU among TB cases registered in the DOTS programme during the implementation of MTP-I (2004–2009) and MTP-II (2010–2015) medium-term strategies for TB in Namibia. The following segmented regression model was used:

$$Y_t = \beta_0 + \beta_1 T + \beta_3 TX_t + e_t$$

Where, Y_t is the outcome (*i.e.* proportion of patients LTFU at time t), T is the time (in years) elapsed since the start of the study, X_t is a dummy variable indicating the pre-intervention period (coded 0) or the post-intervention period (coded 1); β_0 estimates the baseline outcome at T=0; β_1 is an estimate of the pre-intervention outcome trend (*i.e.* the change in outcome with time); β_2 is an estimate of the change in outcome immediately after the intervention (*i.e.* compared to the outcome at the end of the pre-intervention period); β_3 estimates the change in the post-intervention outcome trend compared to the pre-intervention outcome trend; e_t represents the random variability not explained by the model. Adjustment for serial autocorrelation was carried out by using the Durbin–Watson statistic and by including an autocorrelation parameter in the segmented regression model if necessary.

Bivariate analysis using Chi-squared test or crude odds ratios was used to identify factors associated with LTFU. Significant factors were subsequently included in the multivariate logistic regression analysis to adjust odds ratios for confounding for independent predictors for LTFU and to elaborate on the relationships between multiple variables. The level of significance for the bivariate and multivariate analyses for a 95% confidence interval was set at a type I error α of 0.05 and β of 0.20 (power 80%) to detect a significant odds ratio [18].

Ethics

The research and ethics committees of the Ministry of Health and Social Services (MoHSS) (17/3/3/ November 2015) and University of Namibia (SOM/114/2016) approved the study. The need for written

informed patient consent was waived as the study used retrospective records in the ETR database. Patient-specific identifiers, such as names, were anonymized or were not extracted or included from the dataset to ensure confidentiality.

Results

A significant decline in the quarterly trends in LTFU between 2006 and 2015 of 2.5 cases per quarter (R^2=0.45) was observed (figure 2 and table 2). There was a statistically significant decline in the cases of LTFU per quarter −0.23% (p<0.001) during MTP-I. The cases of LTFU increased slightly at start of MTP-II. The quarterly trend in LTFU significantly increased by 0.16% (p=0.044) during MTP-II relative to MTP-I (figure 2 and table 1).

Out of the 104 603 TB cases registered, 3775 (3.6%) were LTFU; this ranged between 6.7% and 34.4% by regions in Namibia. The prevalence of cases LTFU among patients with unsuccessful treatment outcomes was 24.3% (3775 of 15 518; table 2). The majority of patients LTFU were: male (66%), new TB cases (74.4%), aged between 25 and 34 years (31.7%), registered at primary healthcare (PHC) clinics (58.6%), with a diagnosis of pulmonary TB (82.4%), initiated on the standard 2HRZE/4HRE, *i.e* 2 months of isoniazid/rifampicin/pyrazinamide/ethambutol combination continued with 4 months of isoniazid/rifampicin/pyrazinamide/ethambutol regimen (73.6%), and registered during the implementation of the first MTP for TB (53.1%) (figure 3). One-third of cases of LTFU had TB/HIV co-infection (33.5%) and the majority of sputum smears of LTFU cases were either negative or not evaluated (55.0%) at the start of treatment. A higher number of patients who were LTFU had a guardian (*i.e.* family member/relative,

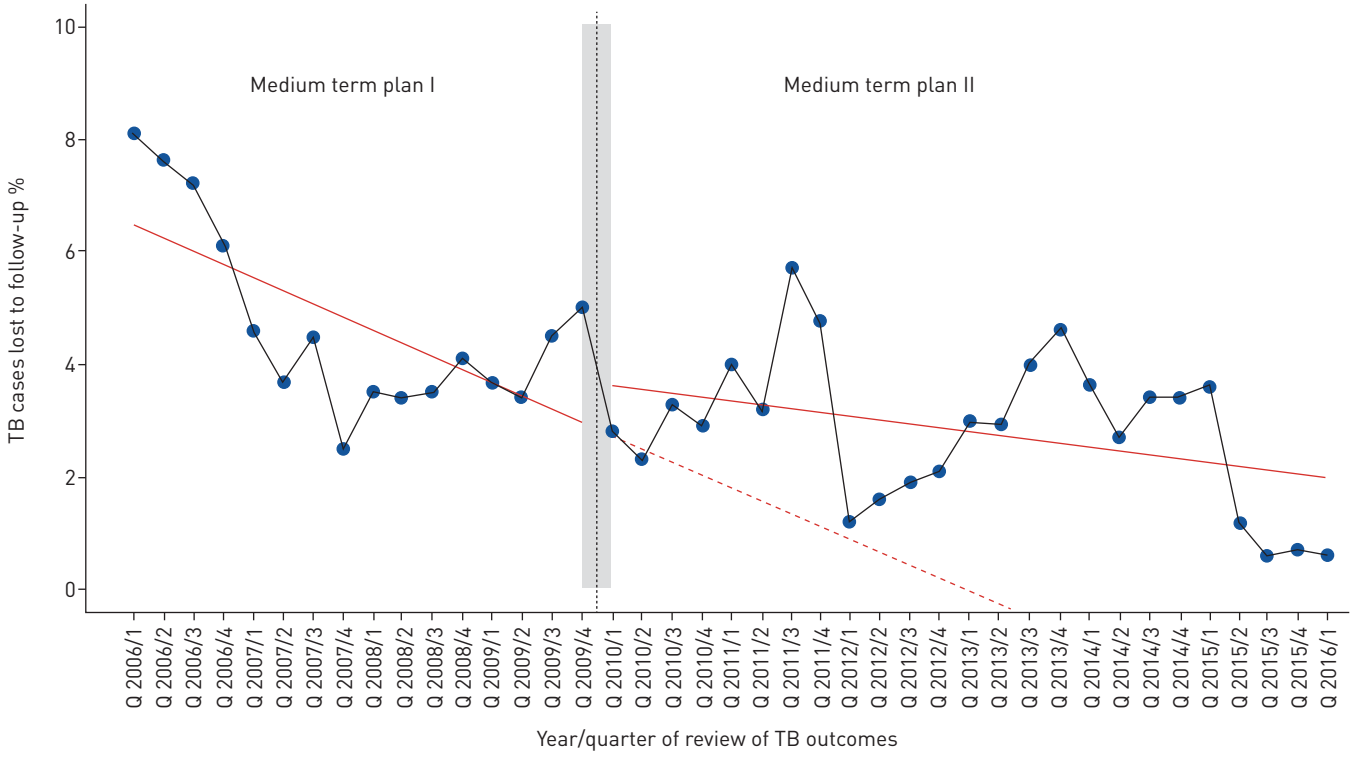

FIGURE 2 Trends of lost to follow-up cases in Namibia, 2006–2015. TB: tuberculosis; Q: quarter.

TABLE 1 Model for impact of medium-term plans (MTPs) on loss to follow-up (LTFU)

Coefficients	Estimate (95% CI)	SE	t-value	p-value
Level of LTFU at start of MTP-I (β_0)	6.67 (5.33–8.04)	0.67	9.93	0.0001*
Trend in LTFU in MTP-I (β_1)	−0.23 (−0.37– −0.09)	0.07	−3.32	0.002*
Level change in LTFU in MTP-II (β_2)	0.71 (−0.93–2.35)	0.81	0.88	0.385
Trend change in LTFU in MTP-II (β_3)	0.16 (0.004–0.32)	0.08	2.08	0.044*

*: p<0.05.

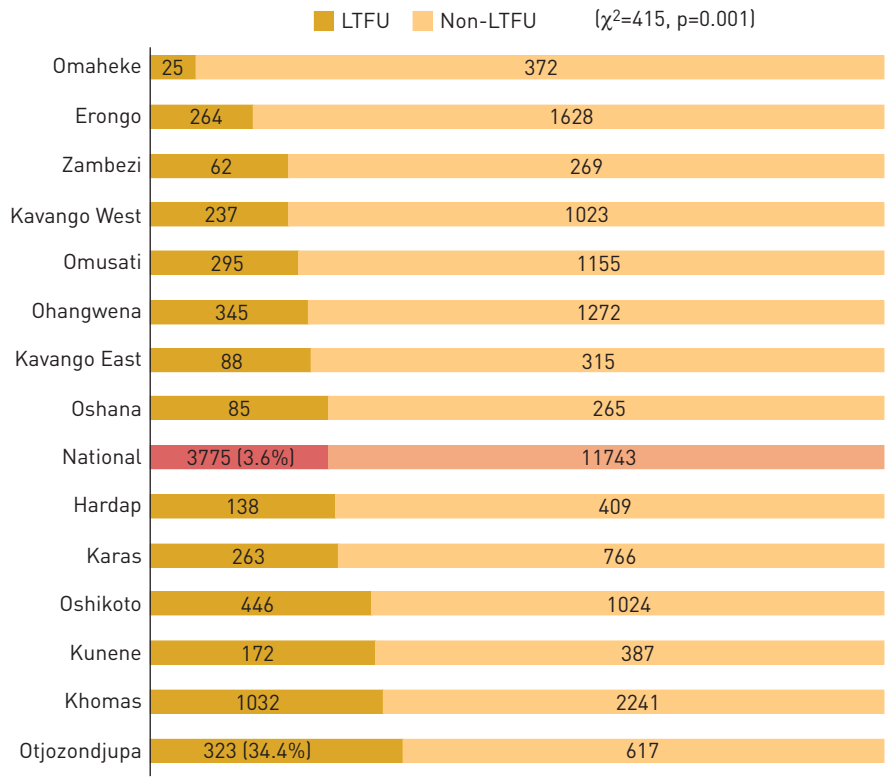

FIGURE 3 Prevalence of loss to follow-up (LTFU) among tuberuculosis cases by geographic region in Namibia.

neighbour) as the main DOTS provider (39.4%; table 2), were in the continuation phase of treatment (63.73%) and were not taking ART (83.9%). The cases of LTFU were significantly higher in regions with border, transit, and central business districts such as Khomas and Kunene (p=0.001, figures 3 and 4).

The univariate logistic regression analysis showed a significant association between percentage of cases of LTFU and young/middle-aged adult patients (15–45 years) (p=0.001), male sex (p=0.001) and region where TB care was received (p=0.001), known HIV status (p=0.001) and 2-month sputum conversion (p=0.001). The medicine-related characteristics associated with LTFU: ART (p=0.001), a relative being a

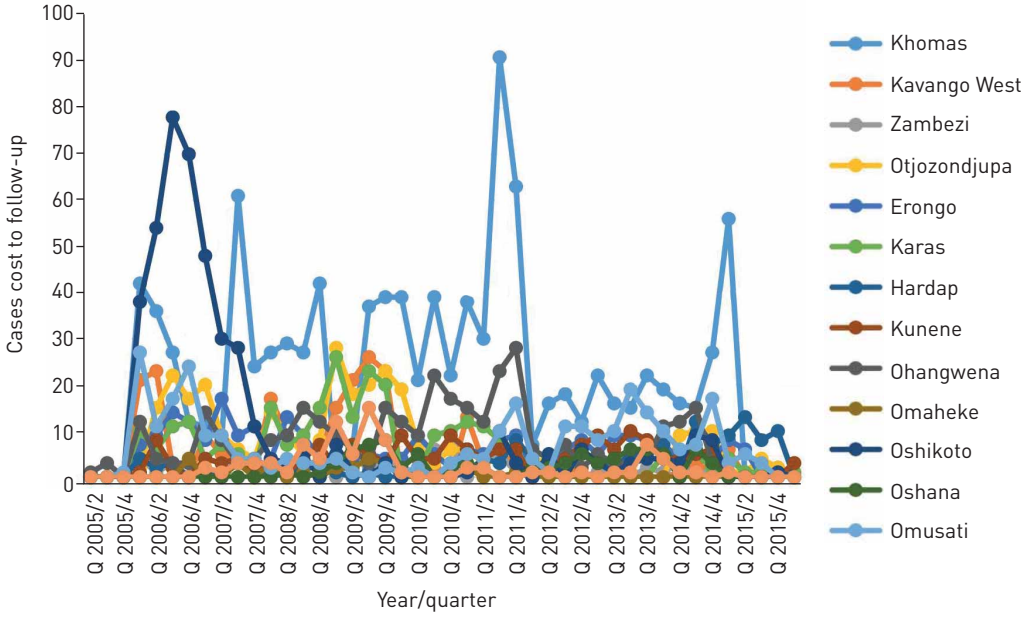

FIGURE 4 Absolute tuberculosis cases lost to follow-up by region in Namibia.

TABLE 2 Characteristics and factors associated with tuberculosis (TB) cases lost to follow-up (LTFU) in Namibia

Characteristic	Total	TB treatment outcome		df	cOR (95% CI)	p-value
		Successful	LTFU			
All TB cases	65 113 (100.0%)	61 338 (94.2%)	3775 (5.8%)			
TB strategy employed						
MTP-I	30 771 (100.0%)	28 766 (93.5%)	2005 (6.5%)	1	1.3 (1.2–1.4)	0.000*
MTP-II	34 342 (100.0%)	32 572 (94.8%)	1770 (5.2%)		1	
Region						
Khomas	13 137 (100.0%)	12 105 (92.1%)	1032 (7.9%)	13	1.1 (0.9–1.4)	0.000*
Kavango West	4572 (100.0%)	4335 (94.8%)	237 (5.2%)		0.7 (0.5–0.9)	0.410
Zambezi	2788 (100.0%)	2726 (97.8%)	62 (2.2%)		0.3 (0.2–0.4)	0.007*
Otjozondjupa	4021 (100.0%)	3698 (92.0%)	323 (8.0%)		1.1 (0.9–1.4)	0.000*
Erongo	7852 (100.0%)	7588 (96.6%)	264 (3.4%)		0.4 (0.3–0.6)	0.340
Karas	4122 (100.0%)	3859 (93.6%)	263 (6.4%)		0.9 (0.7–1.1)	0.000*
Hardap	2660 (100.0%)	2522 (94.8%)	138 (5.2%)		0.7 (0.5–0.9)	0.313
Kunene	2069 (100.0%)	1897 (91.7%)	172 (8.3%)		1.2 (0.9–1.5)	0.013*
Ohangwena	6248 (100.0%)	5903 (94.5%)	345 (5.5%)		0.8 (0.6–1.0)	0.251
Omaheke	2847 (100.0%)	2822 (99.1%)	25 (0.9%)		0.1 (0.1–0.2)	0.022*
Oshikoto	6331 (100.0%)	5885 (93.0%)	446 (7.0%)		0.9 (0.8–1.2)	0.000*
Oshana	1593 (100.0%)	1508 (94.7%)	85 (5.3%)		0.7 (0.5–1.0)	0.851
Omusati	5650 (100.0%)	5355 (94.8%)	295 (5.2%)		0.7 (0.5–0.9)	0.042*
Kavango East	1223 (100.0%)	1135 (92.8%)	88 (7.2%)		1	0.007*
Health facility						
Hospital	13 334 (100.0%)	12 348 (92.6%)	986 (7.4%)	2	1.4 (1.2–1.5)	0.000*
PHC clinic	41 454 (100.0%)	39 240 (94.7%)	2214 (5.3%)		1.0 (0.9– 1–1)	0.000*
Health centre	10 325 (100.0%)	9750 (94.4%)	575 (5.6%)		1	0.358
Sex						
Male	37 479 (100.0%)	34 986 (93.3%)	2493 (6.7%)	1	1.5 (1.4–1.6)	0.000*
Female	27 634 (100.0%)	26 352 (95.4%)	1282 (4.6%)		1	
Age years mean±SD	1.27	33.5±16.9	33.9±16.4			0.000*
Age categories years						
0–4	4420 (100.0%)	4191 (94.8%)	229 (5.2%)	7	0.9 (0.7–1.1)	0.000*
5–14	3901 (100.0%)	3729 (95.6%)	172 (4.4%)		0.7 (0.6–0.9)	0.202
15–24	8251 (100.0%)	7766 (94.1%)	485 (5.9%)		1.0 (0.8–1.2)	0.006*
25–34	18 760 (100.0%)	17 564 (93.6%)	1196 (6.4%)		1.1 (0.9–1.3)	0.976
35–44	15 447 (100.0%)	14 567 (94.3%)	880 (5.7%)		0.9 (0.8–1.1)	0.280
45–54	7734 (0%)	7292 (94.3%)	442 (5.7%)		0.9 (0.8–1.2)	0.718
55–64	3547 (100.0%)	3355 (94.6%)	192 (5.4%)		0.9 (0.7–1.1)	0.766
⩾65	3053 (100.0%)	2874 (94.1%)	179 (5.9%)		1	0.429
First-line TB regimen						
2 HRZE/4 HRE	49 226 (100.0%)	46 673 (94.8%)	2553 (5.2%)		0.7 (0.4–1.1)	0.000*
2 HRZES/1 HRZE/5 HRE	10 846 (100.0%)	9883 (91.1%)	963 (8.9%)	4	1.2 (0.8–2.0)	0.135
2 HRZS/1 HRZ/5 HR (children)	304 (100.0%)	288 (94.7%)	16 (5.3%)		0.7 (0.4–1.4)	0.360
2 HRZ/4 HR (children)	4475 (100.0%)	4251 (95.0%)	224 (5.0%)		0.6 (0.4–1.1)	0.329
Other regimens	262 (100.0%)	243 (92.7%)	19 (7.3%)		1	0.111
TB case registered						
New	53 956 (100.0%)	51 162 (94.8%)	2794 (5.2%)	5	0.7 (0.6–0.8)	0.000*
Failure	402 (100.0%)	370 (92.0%)	32 (8.0%)		1.2 (0.8–1.7)	0.000*
Other previously treated	2769 (100.0%)	2508 (90.6%)	261 (9.4%)		1.4 (1.2–1.6)	0.465
Readmission	842 (100.0%)	674 (80.0%)	168 (20.0%)		3.3 (2.7–4.0)	0.000*
Recurrent TB	1069 (100.0%)	974 (91.1%)	95 (8.9%)		1.3 (1.1–1.6)	0.000*
Relapse	6075 (100.0%)	5650 (93.0%)	425 (7.0%)		1	0.029
TB case						
New TB case	53 956 (100.0%)	51 162 (94.8%)	2794 (5.2%)	1	0.6 (0.5–0.6)	0.000*
Previously treated	11 157 (100.0%)	10 176 (91.2%)	981 (8.8%)		1	
Pulmonary TB case	52 454 (100.0%)	49 345 (94.1%)	3109 (5.9%)	1	1.1 (1.0–1.2)	0.004*
Extrapulmonary TB	12 659 (100.0%)	11 993 (94.7%)	666 (5.3%)		1	

Continued

TABLE 2 Continued

Characteristic	Total	TB treatment outcome		df	cOR (95% CI)	p-value
		Successful	LTFU			
Site of TB infection						
Pulmonary	52 273 (100.0%)	49 165 (94.1%)	3108 (5.9%)	6	0.9 (0.6–1.2)	0.000*
Lymph nodes	1806 (100.0%)	1732 (95.9%)	74 (4.1%)		0.6 (0.4–0.9)	0.347
Meningitis	731 (100.0%)	680 (93.0%)	51 (7.0%)		1.0 (0.7–1.6)	0.006*
Miliary	781 (100.0%)	740 (94.8%)	41 (5.2%)		0.8 (0.5–1.2)	0.928
Other sites	3509 (100.0%)	3295 (93.9%)	214 (6.1%)		0.9 (0.6–1.2)	0.211
Pleura	5400 (100.0%)	515 5(95.5%)	245 (4.5%)		0.6 (0.4–0.9)	0.476
Bones/joints	613 (100.0%)	571 (93.1%)	42 (6.9%)		1	0.011*
DOTS provider						
Guardian (relative/neighbour)	24 974 (100.0%)	23 482 (94.0%)	1492 (6.0%)	4	0.4 (0.3–0.6)	0.000*
Workplace	592 (100.0%)	566 (95.6%)	26 (4.4%)		0.3 (0.2–0.5)	0.000*
Health facility	22 577 (100.0%)	21 462 (95.1%)	1115 (4.9%)		0.4 (0.2–0.5)	0.000*
Community health worker	1262 (100.0%)	1230 (97.5%)	32 (2.5%)		0.2 (0.1–0.3)	0.000*
Other	295 (100.0%)	257 (87.1%)	38 (12.9%)		1	0.000*
Baseline sputum smear						
Smear negative	12 265 (100.0%)	11 544 (94.1%)	721 (5.9%)	2	1.0 (0.9–1.0)	0.005*
Smear positive	30 863 (100.0%)	29 165 (94.5%)	1698 (5.5%)		0.9 (0.8–1.0)	0.282
Smear not done	21 985 (100.0%)	20 629 (93.8%)	1356 (6.2%)		1	0.001
Sputum not converted						
Yes	36 769 (100.0%)	33 521 (91.2%)	3248 (8.8%)	1	5.1 (4.7–5.6)	0.000*
No	28 343 (100.0%)	27 816 (98.1%)	527 (1.9%)		1	
Sputum smear month 2						
Converted to smear negative	16 992 (100.0%)	16 73 5(98.5%)	257 (1.5%)	2	0.1 (0.10–0.13)	0.000*
Remaining smear positive	2043 (100.0%)	1971 (96.5%)	72 (3.5%)		0.3 (0.2–0.4)	0.000*
Defaulted+died+transferred+not available	11 829 (100.0%)	10 460 (88.4%)	1369 (11.6%		1	0.000*
On ART therapy						
No	8276 (100.0%)	7713 (93.2%)	563 (6.8%)	1	1.6 (1.4–1.8)	0.000*
Yes	13 793 (100.0%)	13 184 (95.6%)	609 (4.4%)		1	
Exposure to IPT						
Yes	8713 (100.0%)	8256 (94.8%)	457 (5.2%)	1	1.8 (0.9–3.7)	0.096
No	272 (100.0%)	264 (97.1%)	8 (2.9%)		1	
HIV CPT initiated						
No	4347 (100.0%)	4103 (94.4%)	244 (5.6%0	1	0.9 (0.8–1.1)	0.912
Yes	19 484 (100.0%)	18 382 (94.3%)	1102 (5.7%)		1	
HIV status						
Negative	22 719 (100.0%)	21 752 (95.7%)	967 (4.3%)	2	0.6 (0.5– 0.6)	0.000*
Positive	22 506 (100.0%)	21 243 (94.4%)	1263 (5.6%)		0.7 (0.6–0.8)	0.000*
Unknown	4012 (100.0%)	3713 (92.5%)	299 (7.5%)		1	0.000*

df: degrees of freedom; cOR: crude odds ratio; MTP: medium-term plan; PHC: primary healthcare; HRZE: isoniazid/rifampicin/pyrazinamide/ethambutol; HRE: isoniazid/rifampicin/ethambutol; DOTS: directly observed treatment short-course; ART: anti-retroviral treatment; IPT: isoniazid preventive therapy; CPT: co-trimoxazole preventive therapy. *: p<0.05.

DOTS provider (p=0.001), type of TB regimen type (p=0.044), MoHSS MTP-I strategic plan (p=0.001), and level of healthcare facility for TB care (p=0.002) (table 2).

Independent predictors of LTFU of the DOTS programme in Namibia

A multivariate logistic regression analysis was conducted to identify predictors of LTFU (table 3). A test of the full model against was statistically significant, indicating that the predictors as a set reliably distinguished between LTFU and non-LTFU outcomes (χ^2=36.6, p=0.001 with df=15). Nagelkerke's R^2 of 0.35 indicated a relationship between prediction and grouping by LTFU. Prediction success overall was 71.7% (60.8% for LTFU and 79.7% for non-LTFU). The Wald criterion demonstrated that MTP-I strategy implemented by the National TB and Leprosy Program, male sex [19], type of DOTS provider [20], a 2-month sputum conversion; the region in Namibia of DOTS implementation; particularly Otjozondjupa, Karas and Kunene regions; and the young/middle-age categories (*i.e.* 15–45 years of age) made a significant contribution to prediction of LTFU. However, there was no further significant association of LTFU with HIV status, regimen type and level of DOTS facility.

TABLE 3 Multivariate logistic regression for predictors of loss to follow-up in Namibia

Covariates	aOR (95% CI)	p-value
MTP for TB		
MTP period I	0.5 (0.30–0.96)	0.037*
MTP period II	1	
Region		
Karas	18.8 (4.9–73)	0.001*
Otjozondjupa	3.9 (1.0–15.6)	0.001*
Kunene	3.2 (1.0– 4.1)	0.048*
Khomas	1.7 (0.13–23)	0.043*
Kavango West	1.4 (0.5–4.0)	0.681
Zambezi	1.4 (0.5–4.0)	0.491
Erongo	0.4 (0.04–3.8)	0.443
Hardap	0 (0–10.4)	0.430
Ohangwena	0.6 (0.1–7.3)	1.000
Omaheke	1.6 (0.4–2.1)	0.641
Oshikoto	0 (0)	0.499
Oshana	0.7 (0.7)	0.999
Kavango East	1	0.537
Patient sex		
Male	2.2 (1.3–3.8)	0.004*
Female	1	
Patient age years		
0–4	0 (0–451)	0.025*
5–14	14.4 (0.5–281)	1.000
15–24	29.7 (3.1–194)	0.128
25–34	21.6 (2.4–110)	0.003*
35–44	12.2 (1.4–109)	0.006*
45–54	11.5 (1.2–71.6)	0.025*
55–64	6.2 (0.6–0.8)	0.033*
⩾65	1	0.140
DOTS regimen		
2 RHZE/4 RHE	1.0 (0.6–1.9)	0.748
Other regimens	1	
DOTS provider		
Guardian	1.0 (0.3–4.0)	0.001*
Workplace	0.8 (0.03–26.8)	0.886
Health facility	0.3 (0.08–1.2)	0.921
Community health worker	0 (0)	0.085
Other DOTS providers	1	0.999
2 month's sputum conversion		
Smear negative	1.6 (0.9–3.2)	0.047*
Smear positive	0.4 (0.2–1.2)	0.113
Smear not assessed	1	0.116
Anti-retroviral treatment		
No	1.9 (0.9–3.9)	0.052
Yes	1	
HIV status		
Negative	0.8 (0.2–3.0)	0.474
Positive	1.5 (0.4–6.2)	0.776
Unknown	1	0.563
Facility level		
Hospital	0.6 (0.2–1.9)	0.511
PHC clinic	0.6 (0.3–1.4)	0.437
Health centre	1	0.247
Constant	0	0.006

aOR: adjusted odds ratio; MTP: medium-term plan; TB: tuberculosis; DOTS: directly observed treatment, short-course; RHZE: rifampicin/isoniazid/pyrazinamide/ethambutol; RHE: rifampicin/isoniazid/ethambutol; PHC: primary healthcare. *: p<0.05.

Discussion

In the sample taken in this study, of all patients notified in Namibia that had a treatment outcome registered between 2006 and 2016, 1 out of every 25 TB cases registered was LTFU (table 2 and figure 2). Furthermore, one out of four patients with unsuccessful outcomes was a case of LTFU. The prevalence of LTFU varied widely between geographical regions in Namibia, 6.6% to 34%. These are higher than the national (2%) and global benchmarks for LTFU (0%). Studies in other LMICs in Africa and Asia report the prevalence of LTFU to range between 6% and 24% [15, 21]. This calls for national and regional specific strategies to be incorporated in the medium and long-term strategic plans for TB to reduce the burden of LTFU. The strategy should target building capacity in tracing and supporting patients at risk of LTFU, particularly those registered for DOTS services in border/transit points as well as regions with central business districts.

Multivariate logistic regression suggested that the TB patients most at risk of LTFU were male patients, young adults (<45 years), cases registered in the capital city, patients in transit and/or close to geographical border DOTS access points with high TB notification rates. Several studies have linked LTFU to patients initiated on therapy at immigration towns like borders and transit points. Similarly to our findings, studies associate higher LTFU rates among male patients [22–24], the youth or middle aged (34–44 years) [16, 23]. Contrary to our findings, Peltzer *et al.* [25] found no association between LTFU and male sex in a population in South Africa. Nonetheless, young adults in LMICs are a high-risk group for unemployment, HIV, alcohol and drug abuse, smoking, multiple sexual partners that predispose then to TB and poor outcomes, such as LTFU [12–15]. Secondly, the study demonstrated that the clinical risk factors for LTFU were new TB cases, a diagnosis of pulmonary TB *versus* extrapulmonary TB, and sputum conversion at 2 months (*i.e.* end of the intensive phase of treatment), but not HIV co-infection. Other studies found association of HIV [14] and regimen-related adverse drug reaction (ADR) [20] with LTFU among TB cases. Thirdly, the programmatic predictors of LTFU were interventions under the respective MTP strategy and DOTS support; MTP-II reduced LTFU by 50% ($p=0.037$). There was no association between the treatment regimen, ART and previous IPT exposure, HIV status and CPT prophylaxis and the occurrence of LTFU ($p>0.05$) (table 2).

Potential limitations of this study should be considered while interpreting the findings. Firstly, the retrospective data had missing information on the treatment outcome for several patients and were excluded from the analysis. In addition, we excluded cases with other poor treatment outcomes (*i.e.* death, transferred out and failure) and comparisons were made with patients who had a successful treatment outcome (*i.e.* cured and completed treatment). There may be many other factors which better explain LTFU that were not reported in the ETR database used. Nevertheless, the study utilises a nationwide dataset in a high-TB-burden country over a significant time period (10-year period). This nationwide study highlights the significance of improving socioeconomic welfare of TB patients to abate LTFU, as TB is a disease highly prevalent among patients of low socioeconomic backgrounds. Currently strategic goals of the TB programme in Namibia are mainly case identification and management with limited socioeconomic interventions among young adults in Namibia.

In conclusion, the study demonstrates a high prevalence LTFU among TB cases registered under the DOTS programme in Namibia, this is above the global target of 0%. The findings imply that main factors driving LTFU are related to socioeconomic welfare of young adults who seek temporary employment in regions that provide temporary working opportunities, including borders and capital towns. This age group is an important driver for HIV infection in Namibia. The study recommends the integration of socioeconomic interventions/incentives in DOTS programmes to support young adult TB cases in informal and/or temporary employments across all regions in Namibia. In addition, there is a need for integration of DOTS services in workplaces and institutions that provide temporary employment (*e.g.* construction sites) for mobile young male adults to enhance continuity of TB treatment and improve outcomes.

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