







Correlates of Unsuccessful Treatment among Persons Living with Tuberculosis in an Urban Setting in Northern Ghana

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Abstract

Background: Despite Tuberculosis (TB) being highly infectious, having equally high mortality rates, and being endemic in the northern region of Ghana, data on treatment evaluation is sparse. This novel study therefore sought to determine the correlates of unsuccessful treatment outcome of tuberculosis in the Tamale Metropolitan area in the Northern Region of Ghana.

Methods: Records of TB patients were retrospectively reviewed from January 2017 to December 2021. Demographic and other clinically important information were extracted from patients' folders in health facilities within the Tamale Metropolitan area. Binary logistic regression was used to assess the correlates of unsuccessful treatment at $p \leq 0.05$ and 95% Confidence Interval (CI).

Results: A total of 235 participants were sampled; 13.19% died, 5.96% of them defaulted treatment, 2.55% were lost to follow-up, and 0.43% experienced treatment failure. The unsuccessful treatment rate was found to be 22.12%. Human Immunodeficiency Virus (HIV) positive status [adjusted odds ratios (aOR) = 4.141, 95% (CI) = (1.28 - 13.36)] showed increased odds of resulting in unsuccessful treatment outcome, while visits by medical staff to patients on therapy [aOR = 0.043, 95% CI = (0.17 - 0.11)] resulted in lower odds of unsuccessful treatment outcome after adjusting for all other variables. **Conclusion:** In this novel study in the Tamale Metropolitan area, the unsuccessful treatment

rate was high. And so in order to achieve the 2035 “End TB strategy”, it’s imperative to improve the supervision of patients on therapy while scaling up the fight against TB/HIV coinfection both at the regional and national levels of Ghana.

Subject Areas

Infectious Diseases

Keywords

Unsuccessful Treatment, Northern Ghana, Tuberculosis, Treatment Outcome

1. Background

Among infectious diseases, Tuberculosis (TB) is the leading cause of mortalities globally, even ahead of the Human Immunodeficiency Virus (HIV) [1] [2]. Tuberculosis is estimated to have a global burden of roughly 10 million new cases with 1.5 million deaths per year [3] [4]. Though the global decline of TB incidence has been from 8.6 million in 1990 to 8.4 million in 2021 with a corresponding decrease in TB-related mortalities, the incidence rate is still comparatively higher in low-income and low-middle-income regions [5].

The TB situation is particularly sub-optimal in Sub-Saharan Africa. For instance, according to WHO, 16 of the 30 nations with the highest TB burden are in Sub-Saharan Africa and the WHO’s region of Africa accounted for 71% of all TB/HIV coinfections globally in 2019 [3] [6]. The estimated prevalence rate in Ghana is 282 per 100,000 people, with an estimated fatality rate of 36 per 100,000. One of the three people-centred goals of the global plan to end TB is to at least establish a 90% treatment success rate among those with TB diagnoses or those who are qualified for preventive treatment by 2030 [7]. However, the performance of the Ghanaian tuberculosis programme with regard to the “End TB Strategy” is currently 58%-77%-68% as against the 90%-90%-90% global target, suggesting that Ghana has less chance of achieving the benchmark target by the stipulated time if strong policy evaluation is not done [8].

The “End TB Strategy” primarily seeks to stamp out TB by controlling the incidence and prevalence to the barest minimum, as well as reducing the impact of TB infections in households of affected persons. These cannot be realised without improving the successful treatment levels and lowering mortalities in the country. Successful treatment has the dichotomous effect of forestalling incidence, subduing prevalence, and reducing mortalities [9]. Therefore, data on treatment outcomes and mortalities will have to be readily available so as to inform and direct policy [7]. This is however not the case in the northern region of Ghana. The only available data that attempts to present a treatment outcome and mortality status are the periodic TB reports from treatment centres. There is no intrinsic study attempt-

ing to determine associated factors of successful treatment and mortalities as might be unique to the geographic area and how to mitigate negative and improve positive ones in the metropolitan area and northern Ghana by extension. There is therefore a lack of evidence about correlates of unsuccessful treatment outcomes in the metropolitan area, the very objective of the Directly Observed Treatment Short-course (DOTS) programme of the National Tuberculosis Programme [10]. As a result, this study sought to determine the drivers of unsuccessful treatment in the Tamale metropolitan area of Ghana in order to evaluate the DOTS treatment regimen in the Metropolis.

2. Materials and Methods

2.1. Study Design and Setting

This was a cross-sectional retrospective study that included 235 TB patients in the Tamale Metropolitan area of the northern region of Ghana. The metropolis is endowed with a teaching hospital which serves as the referral centre for all five regions in the northern part of Ghana. There are also several hospitals, polyclinics and Community-based Health Planning and Service (CHPS) centres along with private health facilities. Literature has it that the incidence of pulmonary TB in the metropolis is 83.8 per 100,000 people [11] and beyond this, there is a paucity of data regarding the current prevalence of TB and the performance of the DOTS program in the Metropolis.

2.2. Study Population

All persons diagnosed with TB and who commenced treatment between 1st January 2017 and 31st December 2021 in the Tamale Metropolis formed the study population.

2.3. Sample Size Estimation

The sample size was estimated using Epi Info version 7.2.5.0 at 80% power, 95% confidence interval, and 5% margin of error assuming factors associated with successful tuberculosis treatment in the Tamale Metropolitan area were similar to those in Mogadishu, Somalia as reported by Ali, Karanja and Karama (2017) [12]. A sample size of 220 participants at a statistical power of above 80% was estimated in addition to a 10% non-response rate giving the total number of respondents recruited for the study to be 235.

2.4. Eligibility Criteria

2.4.1. Inclusion

The study included patients who had treatment results recorded in the TB registries within the treatment period under review.

2.4.2. Exclusion

Patients who were referred out of treatment area and those entries with undocu-

mented treatment outcome information were excluded.

2.5. Data Flow Chart

This chart is a flowchart (**Figure 1**) outlining the inclusion and exclusion criteria for the study involving participants spanning from the total number of patients available to how those included in the analysis were arrived at.

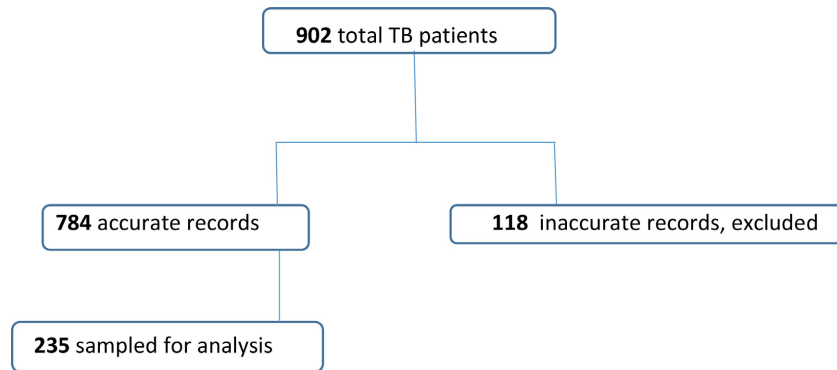


Figure 1. Flow chart.

2.6. Sampling Technique

A purposive sampling technique was used to select the TB treatment facilities based on the turnout of patients. Patients were randomly sampled within these TB treatment facilities. The patients within the TB register who fell within the study period were enumerated. The total number of TB cases in the TB observatory centres was 784 and thus, a directly proportional number of cases were selected from each centre to get an appropriate representation of the patient treatment outcome for the metropolis (sample size of 235 cases). These proportions of patients from each centre were chosen at random by the use of a research randomizer to meet the number required for each treatment centre.

2.7. Data Collection Techniques and Tools

A checklist was designed and pilot-tested in the TB Clinic of the Upper West Regional Hospital, Wa which provides similar services as the study site.

2.8. Study Variables

Outcome variable is unsuccessful treatment (see **Table 1**). This was obtained through the combination of patients who died, defaulted treatment, lost to follow-up, transferred out and failed treatment in accordance with the World Health Organisation's revised definitions and reporting framework for TB [13]. The independent variables in this study include socio-demographic characteristics: gender, age, pre-treatment weight, level of education, and marital status. For the other independent variables, the study looked at disease classification (pulmonary positive TB, pulmonary negative TB, extra pulmonary TB, MDR-TB), adverse drug reaction, income status, Smoking status, alcohol status, type of patient (new, relapse, transfer

in, failure, return after default, others) and periodic visit of medical staff to patients in their homes during treatment (home visits).

Table 1. Operational definitions.

Term	Definition
Completed treatment	A TB patient who finished treatment without experiencing treatment failure and without any proof that sputum smear or culture results in the final month of treatment or on at least one prior occasion were negative, either as a result of tests not being performed or as a result of results being unavailable.
Cured	A pulmonary positive patient who has finished the full course of treatment and who has tested negative for smear or culture in the final month of therapy and at least once before.
Failed treatment	Whether following the recommended treatment regimen or not, a TB patient who tests positive for sputum at month five or later in the course of treatment.
Died	A TB patient who passes away from any cause either before or during treatment.
Default	A patient who, after starting therapy, missed two or more consecutive treatment periods in a row.
Transferred in	A patient whose treatment outcome has not yet been determined but who has been relocated from a TB registry to continue treatment at another reporting and recording unit.
TB/HIV coinfection	A patient who has both Tuberculosis and Human Immuno-deficiency Virus infections.
HIV infection	A patient having first and second-line serologic evidence of Human Immunodeficiency Virus (HIV) infection.
Successful treatment	A combination of completed treatment and cure.
Unsuccessful treatment	Combination of treatment failure, death, and default.
Relapse	A previously treated patient declared cured or has completed treatment but is bacteriologically positive either through smear or culture.
New patient	A person who has never received TB treatment or who has only started taking anti-TB medications less than a month.
Failure	A person who is put back on TB medication after having failed an earlier round of treatment.
Treatment supporter	A person who helps the patient adhere to the TB treatment plan while it is being administered. It might be a family member or a professional.

2.9. Data Analysis

The data was exported to Stata version 16.0 for analysis. The study population was described using descriptive statistics, frequencies and percentages.

For the multiple logistic regression model, covariates with $p \leq 0.05$ at the bivariate level of analysis were taken into consideration. The logistic regression models were built using the forward stepwise regression approach, with 0.05 p-value serving as the cutoff point for keeping or removing a variable from the final model with the exception of variables whose p-values were above 0.05 but are clinically significant. In addition, the Variance Inflation Factor (VIF) was calculated to check multicollinearity. It showed no evidence of interaction among the predictor variables (see **Appendix I**). For the final models, $p \leq 0.05$ was regarded as statis-

tically significant, and confidence intervals were estimated at a 95% confidence level. The models were validated using the Hosmer-Lemeshow post-estimation goodness-of-fit test. The adjusted Odds Ratios (aOR) were used to explain the relationship between the outcome and predictor variables [14].

3. Results

Treatment Outcomes

The study found that majority of respondents (77.88%) had either completed their treatment successfully or were certified to be cured. The rest had unfavourable outcomes culminating in a 22.12% unsuccessful treatment success rate. As high as 13.19% of the patients died due to unsuccessful treatment and 5.96% defaulted in treatment by not following the prescribed uptake of the medication (see **Table 2**).

Table 2. Treatment outcome distribution.

Outcome	Frequency	Percentage (%)
Successful Treatment		
1) Cured	68	28.94
2) Completed treatment	115	48.94
Unsuccessful treatment		
1) Died	31	13.19
2) Treatment defaulted	14	5.96
3) Treatment failure	1	0.43
4) Transferred out	0	0.00
5) Lost to follow up	6	2.55

The chi-square test found the pretreatment weight, availability of treatment supporter for TB patients, HIV coinfection, supervisory visit by medical staff to patients on the DOTS treatment regimen, and combination of alcohol with anti-Koch's medications to be associated with unsuccessful treatment as can be seen in **Table 3** below.

Table 3. Socio-demographic and clinical characteristics TB patients and their association with unsuccessful treatment outcome.

Variable	Treatment outcome (N = 235)		X ² /F (p-value)
	Unsuccessful n (%)	Successful n (%)	
Gender			0.043 (0.386)
Female	21 (40.38)	71 (38.80)	
Male	31 (59.62)	112 (61.20)	
Age			3.823 (0.430)
≤30	11 (21.15)	47 (25.68)	
31 - 40	6 (11.54)	32 (17.49)	

Continued

41 - 50	12 (23.08)	38 (20.77)	
51 - 60	6 (11.54)	27 (14.75)	
≥61	17 (32.69)	39 (21.31)	
Pre-treatment weight			9.511 (0.050)
≤35	5 (9.62)	9 (4.97)	
36 - 45	13 (25.00)	19 (10.50)	
46 - 55	14 (26.92)	61 (33.70)	
56 - 65	11 (21.15)	52 (28.73)	
≥66	9 (17.31)	40 (22.10)	
Income level (GHC¹)			1.400 (0.497)
Low-income	34 (65.38)	104 (56.83)	
Lower middle-income	13 (25.00)	61 (33.33)	
Upper middle-income	5 (9.62)	18 (9.84)	
Occupation			2.128 (0.345)
Employed	5 (9.62)	31 (16.94)	
Self-employed	32 (61.54)	111 (60.66)	
Unemployed	15 (28.85)	41 (22.40)	
Marital status			2.740 (0.254)
Never married	10 (19.23)	46 (25.14)	
Married	34 (65.38)	122 (66.67)	
Others	8 (15.38)	15 (8.20)	
Education*			0.775
No formal education	23 (44.3)	64 (34.97)	
Primary	3 (5.77)	11 (6.01)	
Junior high	6 (11.54)	29 (15.85)	
Senior high	11 (21.15)	38 (20.77)	
Tertiary	9 (17.31)	41 (22.40)	
Address			0.472 (0.492)
Rural	20 (38.46)	61 (33.33)	
Urban	32 (61.54)	122 (66.67)	
Disease classification			0.337 (0.845)
Pulmonary positive	16 (30.77)	59 (32.24)	
Pulmonary negative	21 (40.38)	66 (36.07)	
Extra pulmonary	15 (28.85)	58 (31.69)	
Type of patient			0.002 (0.962)
New	47 (90.38)	165 (90.21)	
Retreatment	5 (9.62)	18 (9.84)	

Continued

Treatment supporter			6.931 (0.008)
No	14 (26.92)	22 (12.02)	
Yes	38 (73.08)	161 (87.98)	
Distance to treatment center			0.970 (0.325)
<10 km	27 (51.92)	109 (59.87)	
≥10 km	25 (48.08)	74 (40.44)	
Adverse drug reaction			0.050 (0.822)
No	39 (75.00)	140 (76.17)	
Yes	13 (25.00)	43 (23.50)	
HIV status			6.290 (0.012)
Negative	38 (73.08)	160 (87.26)	
Positive	14 (26.92)	23 (12.57)	
Visit by medical staff			68.905 (<0.001)
No	39 (75.00)	29 (15.85)	
Yes	13 (25.00)	154 (84.15)	
Alcohol consumption			4.795 (0.029)
No	41 (78.85)	165 (90.16)	
Yes	11 (21.15)	18 (9.84)	
Smoking			0.335 (0.563)
No	42 (80.77)	154 (84.15)	
Yes	10 (19.23)	29 (15.85)	

*Fisher exact test, **HIV** = Human Imuno-deficiency Virus, **X²** = chi-square, **N** = sample size, **n** = frequency **F** = Fisher's exact test.

Table 4 below documents the logistic regression of predictors of unsuccessful treatment outcome. It revealed that HIV positive status [OR = 2.320, 95% CI = (1.173 - 4.590)], alcohol consumption [OR = 2.460, 95% CI = (1.078 - 5.609)] and visit by medical staff [OR = 0.063, 95% CI = (0.030 - 0.132)] were statistically associated with unsuccessful treatment at the univariate level. At the multivariate level, being HIV positive [aOR = 4.141, 95% CI = (1.284 - 13.355)] has four-fold odds and visits by medical staff to patients on treatment [aOR = 0.043, 95% CI = (0.171 - 0.109)] have very low odds of having an unsuccessful treatment outcome after adjusting for other variables.

4. Discussion

Successful fight against TB and the subsequent achievement of the World Health Organisation's 2030 End TB strategy is greatly hinged on favourable outcomes because one of the targets of the global plan to end TB is the achievement of less than 10% treatment unsuccessful rate [7]. The results of this study demonstrate that the majority of TB patients either died, defaulted on treatment, or were lost

Table 4. Logistic regression analysis of drivers of unsuccessful treatment.

Variable	OR (95% CI)	p-value	aOR (95% CI)	p-value
Gender				
Female	Ref			
Male	0.940 (0.500 - 1.755)	0.836	0.961 (0.383 - 2.412)	0.932
Age (years)				
≤30	Ref			
31 - 40	0.801 (0.270 - 2.390)	0.691	1.228 (0.230 - 6.532)	0.811
41 - 50	1.350 (0.540 - 3.400)	0.525	1.466 (0.296 - 7.270)	0.640
51 - 60	1.000 (0.320 - 2.900)	0.927	1.416 (0.225 - 8.922)	0.711
≥61	1.862 (0.781 - 4.442)	0.161	4.325 (0.711 - 26.295)	0.112
Pretreatment weight				
≤35	Ref			
36 - 45	1.232 (0.335 - 4.524)	0.754	0.222 (0.192 - 2.580)	0.229
46 - 55	0.413 (0.120 - 1.425)	0.162	0.132 (0.122 - 1.430)	0.096
56 - 65	0.381 (0.107 - 1.359)	0.137	0.103 (0.008 - 1.422)	0.090
≥66	0.405 (0.110 - 1.502)	0.177	0.149 (0.010 - 2.141)	0.161
Income level (GHC)				
Low	Ref			
Lower-middle	0.652 (0.320 - 1.330)	0.240	-	-
Upper-middle	0.850 (0.300 - 2.462)	0.764	-	-
Occupation				
Employed	Ref			
Self-employed	1.787 (0.642 - 4.972)	0.266	-	-
Unemployed	2.268 (0.744 - 6.914)	0.150	-	-
Marital status				
Never married	Ref			
Married	1.282 (0.586 - 2.803)	0.534	-	-
Others	2.453 (0.819 - 7.350)	0.109	-	-
Education				
Junior high	Ref			
No education	1.737 (0.640 - 4.721)	0.279	-	-
Primary	1.318 (0.280 - 6.210)	0.727	-	-
Senior high	1.400 (0.463 - 4.228)	0.552	-	-
Tertiary	1.061 (0.340 - 3.308)	0.919	-	-
Address				
Rural	Ref			
Urban	0.80 (0.423 - 0.514)	0.493	-	-

Continued

Disease classification				
Extra pulmonary	Ref			
Pulmonary ⁻	1.230 (0.581 - 2.606)	0.588	0.830 (0.256 - 2.695)	0.755
Pulmonary ⁺	1.049 (0.475 - 2.315)	0.907	1.113 (0.385 - 3.218)	0.843
Type of patient				
New	Ref			
Retreatment	0.975 (0.344 - 2.766)	0.962	0.457 (0.102 - 2.050)	0.307
Treatment supporter				
No	Ref		-	
Yes	0.280 (0.017 - 4.558)	0.371	-	-
Distance to TC				
<10 km	Ref		-	-
≥10	1.364 (0.734 - 2.533)	0.326	-	-
Adverse drug reaction				
No	Ref			
Yes	0.872 (0.237 - 3.215)	0.838	0.432 (0.065 - 2.880)	0.386
HIV status				
Negative	Ref		Ref	
Positive	2.320 (1.173 - 4.590)	0.016	4.141 (1.284 - 13.355)	0.017
Visit by medical staff				
No	Ref		Ref	
Yes	0.063 (0.030 - 0.132)	<0.001	0.043 (0.109 - 0.17)	<0.001
Alcohol				
No	Ref		Ref	
Yes	2.460 (1.078 - 5.609)	0.032	0.6900 (0.243 - 1.953)	0.484
Smoke				
No	Ref			
Yes	1.264 (0.571 - 2.802)	0.563	-	-
Hosmer-Lemeshow post estimation test (p = 0.3509)				

to follow-up or defaulted treatment; as a result, the study area's rate of unsuccessful treatment outcome was 22.12%. Despite the fact that the majority of patients responded positively to the DOTS treatment regimen, the treatment unsuccessful rate fell short of the 12.3% national average [15]-[17] and findings from other studies in Ghana of 9.8% [18], 10% [19], and 17.5% [20] and in other parts of Africa [21]-[24]. The study period and relatively smaller sample size, considering the time and resources allocated to this study, could potentially account for the discrepancy in the unsuccessful treatment rate recorded in this study. The unsuc-

cessful treatment discovered in this study may also be due to quite an appreciable number of TB deaths recorded, a significant number of defaulters, and a marginal number of patients lost to follow-up as compared to that of previous studies [21] [22] [24]. This may be due to late treatment-seeking behaviour of patients within the metropolis, low follow-up treatment supervision on the part of health workers, or the lack of community sensitisation on TB as a disease and treatment available [25]. The remote possibility that those who failed treatment may have achieved that feat by developing resistance to the anti-Koch's medication is also valid [26]. The treatment outcome of this study is however in consonance with other studies conducted in settings that can be considered comparable, 21% [27] and 19.7% [28].

Patients aged 30 years and below had the highest case burden, while those aged 51 to 60 years had the lowest. This is consistent with a previous study in the Volta region of Ghana (20), in three teaching hospitals in Ghana [29], and in the Gambella regional state of Ethiopia [30]. This observation may be due to the higher tendency of younger individuals to find themselves in very crowded places with poor cough and other droplet hygiene etiquette like football centres, cinemas, and gaming centres among others. The implication, however, is that it is the active and most productive that are affected [31].

Also agreeing with several previous studies [18] [24] [29] [32]-[34], this study also found a positive association between HIV co-infection and unsuccessful treatment outcome. It could be due to the overloading of the immune system of such patients and poor access to anti-retroviral medications [35]. This could also be due to difficulty in combining medications for both medical conditions and having to deal with the side effects [36], which is another reason why follow-up supervision should be strengthened in the metropolis.

Visits by medical staff to patients in their homes in the course of their treatment were also found to be strongly associated with unsuccessful treatment outcomes, a finding consistent with existing literature [37]. This shows that those visited by medical staff to supervise their treatment regimen had lower odds of achieving an unsuccessful treatment outcome than their counterparts who were not visited by medical staff. This gives credence to the necessity of strengthening treatment supervision for more favourable treatment outcomes. Better still, authorities could consider adopting the tuberculosis treatment monitoring by Video Directly Observed Therapy (VDOT), which is proven to be 32% less expensive and 90% more effective than DOTS [38].

5. Conclusion

Findings from this novel study suggest that HIV positivity is a critical factor associated with poorer treatment success in this population and the importance of regular medical support and follow-up in improving treatment adherence and success rates. Future strategies should focus on increasing healthcare access and support for vulnerable populations to mitigate the risks of unsuccessful treatment

in the Tamale Metropolitan area.

Limitations

Authors allude to the fact that existing health facility records, which may introduce bias if certain groups of patients are more likely to be documented than others (e.g., those who are more compliant with treatment may have better documentation). The study may not account for all possible confounding variables that could influence treatment outcomes due to its limited scope. There is also the possibility of confounding effects of other health conditions or comorbidities with the association between unsuccessful treatment and HIV infection that were not considered in the analysis. Finally, findings of this study should be applied with caution since results may not be generalizable to populations with different socio-economic and healthcare contexts.

Statement of Ethical Approval

Approval for the conduct of this study was granted by the Kwame Nkrumah University of Science and Technology Committee on Human Research and Publication Ethics (KNUST-CHRPE) with reference CHRPE/AP/281/22. To protect patient privacy, patient path numbers were not recorded. It was highlighted that the information supplied in this study will exclusively be used for research purposes to help with patient management in the future.

Availability of Data and Materials

All data are fully available without restriction upon reasonable request.

Author Contributions

Conception and design: R. N. A., M. A., E. S., M. M. B.;

Analysis: R. N. A., E. S., M. M. B., R. D. N.;

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Drafting the article: R. N. A., E. S., M. M. B., D. O. A., A. I. S.;

Revising it critically for important intellectual content: R. N. A., E. S., M. A., M. M. B., A. M., R. D. N., D. O. A., M. A. Y.;

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Conflicts of Interest

The authors declare no conflicts of interest.

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Appendix I. Collinearity Test Result

Variable	VIF	1/VIF	R-squared
Age	1.29	0.7742	0.2258
Gender	1.10	0.9055	0.0945
Education	1.33	0.7539	0.2461
Occupation	1.17	0.8540	0.1460
Disease classification	1.10	0.9073	0.0927
Address	1.08	0.9217	0.0783
HIV status	1.08	0.9245	0.0755
Availability of treatment supporter	1.09	0.9171	0.0829
Adverse drug reaction	1.05	0.9548	0.0452
Smoke	1.28	0.7784	0.2216
Alcohol	1.35	0.7384	0.2616
Medication intake	1.03	0.9716	0.0284
Visit by medical staff	1.10	0.9061	0.0939
Mean VIF		1.16	

Appendix II. Abbreviations

aOR:	adjusted Odds Ration
CHPS:	Community-based Health Planning Services
CI:	Confidence Interval
DOTS:	Directly Observed Treatment Short-course
HIV:	Human Immunodeficiency Virus
MDR-TB:	Multidrug Resistant Tuberculosis
OR:	Odds Ratio
TB:	Tuberculosis
VIF:	Variance Inflation Factor
WHO:	World Health Organisation