Effect of missed clinic visits on treatment outcomes among people with TB: a quasi-experimental study utilizing instrumental variable analysis

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Short Communication

Effect of missed clinic visits on treatment outcomes among people with tuberculosis: a quasi-experimental study utilizing instrumental variable analysis

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ABSTRACT

Objectives: Missed clinic visits disrupt the continuity of care and potentially impact tuberculosis (TB) treatment outcomes negatively. We evaluated the effect of missed clinic visits on mortality and treatment success among people with bacteriologically confirmed pulmonary TB in rural eastern Uganda.

Methods: Using routine TB clinic data, we designed a quasi-experimental study and used instrumental variable analysis to estimate a cause-effect. The exposure was one or more missed clinic visit(s), the instrumental variable was patient residence in the same sub-county as the TB clinic, and the outcomes were mortality and treatment success. We performed a two-stage least squares logistic regression for causal analysis and reported the odds ratio (OR) and 95% confidence interval (CI).

Results: Of 762 participants with similar baseline characteristics, 186 (24.4%) missed ≥1 clinic visit(s), 342 (44.9%) resided in the same sub-county as the TB clinic, 61 (8.0%) had died, and 687 (90.2%) were successfully treated for TB. Missed clinic visits increased mortality (OR 2.88, 95% CI 1.36-6.13) and reduced TB treatment success (OR 0.41, 95% CI 0.20-0.82).

Conclusions: Missed clinic visits increase mortality and negatively impact treatment success among people with TB. The reasons for missed clinic visits should be identified and tackled through context-specific measures.

Background

Missed clinic visits disrupt care continuity and have the potential to impact treatment outcomes negatively among people with tuberculosis (TB). Few studies have examined missed clinic visits among people with TB. Among people with TB/HIV in South Africa, less than 20% had good adherence to clinic visits (>90% adherence to appointment visits) [1]. In Thailand, missed clinic visits were associated with a nearly sixfold increase in treatment clinical failure (sum of lost to follow-up, treatment failed, and treatment not evaluated) compared with treatment success [2].

Causal inference has a major strength in its ability to establish a cause-effect relationship between an exposure and an outcome [3]. To the best of our knowledge, no study has looked at the causal effect of missed clinic appointments on treatment outcomes among people with TB. Moreover, understanding the effect of missed clinic visits on treatment outcomes is critical in designing context-relevant measures that would improve treatment outcomes among people with TB. Therefore, we used a cause-effect analysis to evaluate the causal effect of missed clinic visits on mortality and treatment success among people with bacteriologically confirmed pulmonary TB (PTB) in rural eastern Uganda.

We hypothesized that people with TB who miss their clinic visit(s) have a higher mortality and lower TB treatment success than those who do not miss their clinic visit(s). The rationale for this hypothesis is based on a theory of change, suggesting that missed clinic visits disrupt medication pickups and treatment adherence, leading to ineffective TB care and, hence, increased mortality and reduced treatment success.

Methods and materials

Data source

The data analyzed have been described in previous studies [4–7]. Data are from an observational cohort of people with drug-susceptible, bacteriologically confirmed PTB across 10 TB clinics in rural eastern Uganda. The data source was the routine TB register. Participants who received a 6-month regimen [2 months of Rifampicin (R), Isoniazid (R), Pyrazinamide, and Ethambutol followed by 4 months of RH

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Table 1
Distribution of covariates and study outcomes by instrumental variable.

Variables	Levels	Residence in the same sub-county as the TB clinic		*P*-value
		Yes (n = 342)	No (n = 420)	
Age group (years)	15-34	152 (44.4)	191 (45.5)	0.947
	35-50	116 (33.9)	138 (32.9)	
	51 and over	74 (21.6)	91 (21.7)	
	mean (SD)	39.36 (15.67)	39.29 (15.97)	0.981
Sex	Male	228 (66.7)	274 (65.2)	0.736
	Female	114 (33.3)	146 (34.8)	
Type of person with TB	New	307 (89.8)	364 (86.7)	0.230
	Previously treated for TB	35 (10.2)	56 (13.3)	
Transferred-in	No	307 (89.8)	381 (90.7)	0.751
	Yes	35 (10.2)	39 (9.3)	
Tested for HIV	No	7 (2.0)	2 (0.5)	0.097
	Yes	335 (98.0)	418 (99.5)	
HIV test result	Negative	248 (72.5)	295 (70.2)	0.079
	Positive	87 (25.4)	123 (29.3)	
	Know HIV positive	7 (2.0)	2 (0.5)	
Had a child under 5 years in the household	No	205 (59.9)	225 (53.6)	0.091
	Yes	137 (40.1)	195 (46.4)	
Type of directly observed therapy short course	Facility	21 (6.1)	22 (5.2)	0.705
	Community	321 (93.9)	398 (94.8)	
Treatment supporter availability	No	48 (14.0)	61 (14.5)	0.930
	Yes	294 (86.0)	359 (85.5)	
Missed TB clinic visits	No	231 (67.5)	345 (82.1)	<0.001
	Yes	111 (32.5)	75 (17.9)	
Sputum smear microscopy monitoring				
At month 2/3	No	150 (43.9)	161 (38.3)	0.123
	Yes	192 (56.1)	259 (61.7)	
At month 5	No	229 (67.0)	232 (55.2)	<0.001
	Yes	113 (33.0)	188 (44.8)	
At month 6/8	No	235 (68.7)	215 (51.2)	<0.001
	Yes	107 (31.3)	205 (48.8)	
Sputum smear conversion[a]				
At month 2/3 (n = 451)	No	28 (14.6)	40 (15.4))	0.801
	Yes	164 (85.4)	219 (84.6)	
At month 5 (n = 301)	No	3 (2.7)	6 (3.2)	0.791
	Yes	110 (97.3)	182 (96.8)	
At month 6/8 (n = 312)	No	1 (0.9)	4 (2.0)	0.497
	Yes	106 (99.1)	201 (98.0)	
TB treatment outcome	Cured	174 (50.9)	239 (56.9)	0.101
	Treatment completed	138 (40.4)	136 (32.4)	
	Treatment failed	4 (1.2)	10 (2.4)	
	Dead	26 (7.6)	35 (8.3)	
Dead	No	316 (92.4)	385 (91.7)	0.814
	Yes	26 (7.6)	35 (8.3)	
Treatment success	No	30 (8.8)	45 (10.7)	0.440
	Yes	312 (91.2)	375 (89.3)	

TB, tuberculosis.
Note: [a]Data presented on sputum smear conversion are for participants who received sputum smear microscopy monitoring at months 2/3, 5, and 6/8.

(2RHZE/4RH)] required eight TB clinic visits (bi-weekly for 2 months and monthly for 4 months). Those who received the previous 8-month regimen [2 months of RHZE and Streptomycin (S), 1 month of RHZE, and 5 months of RHE (2RHZES/1RHZE/5RHE)] required 10 visits (bi-weekly for 2 months and monthly for 6 months). The parent study received approval from the Mbarara University of Science and Technology Research Ethics Committee (reference number 03/11-18) and the Uganda National Council for Science and Technology (reference number HS 2531). We received a waiver from the ethics committee to review, retrieve, and analyze the patient records. This study conformed to the principles of the Declaration of Helsinki.

Design and measurements

We designed a quasi-experimental study because a randomized trial would be not only impractical but also unethical. We used observational data and instrumental variable analysis (IVA) to estimate cause-effect, with one or more missed clinic visit(s) as the exposure, patient residence in the same sub-county as the TB clinic as the instrumental variable, and mortality and treatment success as the outcomes. The primary outcome was mortality, and TB treatment success (cure or treatment completion) was the secondary outcome, with all outcomes measured on a binary scale.

The instrumental variable created a counterfactual (unexposed group) that was identical to the exposed group because it was correlated with the exposure (relevance criterion), uncorrelated with measured covariates (exogeneity criterion), and correlated with the outcome through its effect on the exposure (exclusion restriction criterion). Fulfilling these criteria implied that selection bias and confounding associated with observational data have been removed, hence simulating a randomized trial.

Statistical analysis

Mean and SD were used to summarize numerical data, whereas frequencies and percentages were used to summarize categorical data. To verify whether the IVA criteria were met, (i) we considered an F-statistics of ≥10 between the instrumental variable and exposure for

Table 2
Effect of missed clinic visits on mortality and treatment success among people with TB in rural eastern Uganda using instrumental variable analysis.

		Missed clinic visits		Instrumental variable analysis
Variables	Levels	No (n = 576)	Yes (n = 186)	Odds ratio (95% confidence interval)
Dead	No	538 (93.4)	163 (87.6)	1
	Yes	38 (6.6)	23 (12.4)	2.88[a] (1.36-6.13)
Treatment success	No	47 (8.2)	28 (15.1)	1
	Yes	529 (91.8)	158 (84.9)	0.41[b] (0.20-0.82)
Sputum smear conversion[c]				
At month 2/3 (n = 451)	No	58 (14.9)	10 (16.1)	1
	Yes	33 (85.1)	52 (83.9)	1.02 (0.47-2.22)
At month 5 (n = 301)	No	5 (1.8)	4 (16.0)	1
	Yes	271 (98.2)	21 (84.0)	1.35 (0.13-13.68)
At month 6/8 (n = 312)	No	4 (1.4)	1 (3.3)	1
	Yes	278 (98.6)	29 (96.7)	2.31 (0.07-80.76)

Note: Odds ratios are the exponentiated coefficients; 95% confidence intervals are in brackets.
[a] P <0.01
[b] P <0.05
[c] Denotes data presented are for sputum smear conversion for participants who received sputum smear microscopy monitoring at months 2/3, 5, and 6/8.

the relevance criterion and (ii) distributional similarity in covariate and outcome stratified by the instrumental variable for the exogeneity and exclusion criteria, tested using the chi-square and Student's *t*-tests. For cause-effect estimation, we used the two-stage least squares regression approach. The first stage was a logit regression model for the exposure as a function of the instrumental variable and baseline covariates. The second stage was a logistic regression model for the outcomes as a function of the instrumental variable and the predicted value from the first stage. In the non-causal analysis, we analyzed the relationship between the outcomes and exposure with and without covariate adjustment. We reported the odds ratio (OR) and corresponding 95% CI intervals (CIs). The analysis was conducted in Stata version 15 and R version 4.2.1 (2022-06-23 ucrt) at a 5% significance level.

Results

The distribution of participant baseline characteristics stratified by residence is shown in Table 1. Of the 762 participants, 186 (24.4%) had one or more missed clinic visit(s), and 342 (44.9%) resided in the same sub-county as the TB clinic. The median number of missed clinic visits was two (interquartile range one to nine). We observed no differences in the distribution of participants' characteristics and study outcomes by residence (instrumental variable), as would be anticipated in a randomized trial, and residence was strongly correlated with missed clinic visits (F-statistics = 22.4, P <0.001).

Effect of missed clinic visits on mortality and treatment success among people with tuberculosis in rural eastern Uganda

In Table 2, participants with a missed clinic visit(s) had a higher proportion of mortality and a lower proportion of treatment success. The causal analysis showed that missed clinic visits increased mortality by nearly threefold (OR 2.88, 95% CI 1.36-6.13) and reduced TB treatment success by 59% (OR 0.41, 95% CI 0.20-0.82).

Discussion

We found that missed clinic visits increase mortality and reduce treatment success among people with bacteriologically confirmed PTB in rural eastern Uganda, in support of our hypothesis and theory of change. Our finding suggests a need to tackle missed clinic visits among people with TB to optimize treatment outcomes. People with TB miss clinic visits for several reasons, such as longer travel distances, inadequacies in patient education, forgetfulness, and lack of treatment support among others.

Therefore, in addition to identifying and addressing barriers to clinic visits, programs should explore proved interventions. Examples of these include improving patient education about clinic appointments and schedules, sending appointment reminders [8], providing incentives such as food vouchers or monetary rewards for attending clinic visits, mobile health services such as home-based anti-TB delivery by community-based health workers, and strengthening the health provider–patient relationship to build trust, and clarifying and strengthening treatment supporter roles [9].

Our study has strengths. Residence in the same sub-county as the TB clinic is logically correlated with missed clinic visits and the analysis also confirmed the strong correlation fulfilling assumptions for IVA. The analytic approach controlled for measured and unmeasured confounders, thus simulating a randomized trial. The study limitations include analysis of data from a rural setting that might not accurately depict the outcomes in an urban setting. Mortality was based on existing records and, hence, might not be accurate, although all deaths were verified by the TB clinic. The analysis focused on people with bacteriologically confirmed PTB and, hence, might not perfectly depict the treatment outcomes among people with other forms of TB disease. Distance from the TB clinic would be another good instrumental variable but was not measured in the routine data.

Conclusion and recommendation

Missed clinic visits increase mortality and negatively impact treatment success among people with TB. Therefore, reasons for missed clinic visits should be identified and tackled through context-specific measures in rural eastern Uganda and similar settings.

Declaration of competing interest

The authors have no competing interests to declare.

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Ethical approval statement

Mbarara University of Science and Technology Research Ethics Committee (reference number 03/11-18) and the Uganda National Council for Science and Technology (reference number HS 2531).

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Author contributions

JI, IKT, and FB: Conception and design of the study. JI: Acquisition of data. JI and FB: Analysis and interpretation of data. JI, IKT, and FB: Drafting of the article or revising it critically for important intellectual content. JI, IKT, and FB: Fnal approval of the version to be submitted.

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