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Effect of TB/HIV Integration on TB and HIV indicators in Rural Ugandan Health Facilities

Sarah M BURNETT^{1,2}, Stella ZAWEDDE-MUYANJA³, Sabine M HERMANS^{3,4}, Marcia R WEAVER⁵, Robert COLEBUNDERS⁶, and Yukari C MANABE^{3,7}

¹Africare, Washington, DC, USA; ²Department of Epidemiology and Social Medicine, Faculty of Medicine and Health Sciences, University of Antwerp, Antwerp, Belgium ³Infectious Diseases Institute, Makerere University College of Health Sciences, Kampala, Uganda ⁴Department of Global Health, Academic Medical Center, University of Amsterdam, Amsterdam Institute for Global Health and Development, the Netherlands ⁵Departments of Health Metrics Science and Global Health, University of Washington, 2301 Fifth Ave., Suite 600, Seattle, WA, 98121 ⁶Global Health Institute, Faculty of Medicine and Health Sciences, University of Antwerp, Universiteitsplein 1, 2610 Antwerp, Belgium ⁷Division of Infectious Diseases, Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD, USA

Abstract

Background—WHO recommends integrating services for patients co-infected with TB and HIV. We assessed the effect of TB/HIV integration on ART initiation and TB treatment outcomes among TB/HIV co-infected patients using data collected from 14 rural health facilities during two previous TB and HIV quality of care studies.

Methods—A facility was considered to have integrated TB/HIV services if TB/HIV patients had combined treatment for both illnesses by one provider or care team at one treatment location. We analyzed the effect of integration by conducting a cross-sectional analysis of integrated and non-integrated facility periods comparing performance on ART initiation and TB treatment outcomes. We conducted logistic regression, with the patient as the unit of analysis, controlling for other intervention effects, adjusting for age and gender, and clustering by health facility.

Results—From January 2012-June 2014, 996 TB patients were registered, 97% were tested for HIV and 404 (42%) were HIV positive. Excluding transfers, 296 patients were eligible for analysis with 117 and 179 from non-integrated and integrated periods, respectively. Being treated in a facility with TB/HIV integration was associated with lower mortality (adjusted odds ratio [aOR]=0.38, 95% confidence interval [CI]=0.18–0.77), but there was no difference in the proportion initiating ART (aOR=1.34, 95% CI=0.40–4.47), with TB treatment success (aOR=1.43, 95% CI=0.73–2.82), lost to follow-up (aOR=1.64, 95% CI=0.53–5.04), or failure (aOR=1.21, 95% CI=0.34–4.32).

Author contributions.YCM, SZM, SMB and SMH designed the study. SZM, the TB REACH team and the MENTORS teams gathered the data. SMB, SZM, SMH and YCM designed the analysis, interpreted the data and drafted the manuscript. All authors read and approved the final manuscript.

Conclusion—TB/HIV service integration was associated with lower mortality during TB treatment even in settings with suboptimal proportions of patients completing TB treatment and starting on ART.

Keywords

tuberculosis/HIV co-infection; anti-retroviral therapy initiation; tuberculosis treatment outcomes; mortality; Africa; south of the Sahara; Uganda

INTRODUCTION

Tuberculosis (TB) and human immunodeficiency virus (HIV) are among the top 10 causes of death in the world, resulting in nearly 2 million deaths in 2016. People living with HIV are more vulnerable to TB infection and have a higher risk of mortality during TB treatment compared to HIV-negative patients. These vulnerabilities have led to TB becoming the leading cause of death among people living with HIV, accounting for 37 percent of all AIDS-associated deaths. People living with HIV accounting for 37 percent of all AIDS-associated deaths. In 2012, the World Health Organization (WHO) released policy guidance on the implementation of collaborative TB/HIV activities, emphasizing the need to establish mechanisms for delivering integrated TB and HIV services, preferably at the same time and location. One model to achieve TB/HIV integration is the 'one-stop shop' approach where patients co-infected with TB and HIV are treated for both illnesses by one provider or care team during one visit at one treatment location. In addition to co-location, use of combined treatment plans, is another method for integrating care for HIV patients with multiple diagnoses.

Several studies have demonstrated the effects of TB/HIV integration on TB treatment outcomes or HIV-related indicators (isoniazid preventive therapy, ART uptake, time to initiation, mortality). ^{7–11} However, few have assessed both TB and HIV-related indicators in the same study, with fewer focusing on effects of integration on performance in rural health facilities. ^{4,12–14} This study utilized data from two evaluations of on-site support interventions conducted over three years in Uganda to determine whether TB treatment outcomes and ART initiation of TB/HIV co-infected patients are associated with TB/HIV integration status at rural health facilities.

METHODS

Study Design

This was a cross-sectional, retrospective study using data collected from 14 health facilities enrolled in two quasi-experimental studies conducted between January 2012 to June 2014. 15,16 Each health facility was classified based on their TB/HIV integration status prior to and during the interventions in the previously conducted studies. We compared integrated and non-integrated facility periods to determine the effect of integration on the following indicators: ART initiation TB treatment success, and mortality. The TREND checklist is available as Supplemental Table 1.

Setting, Participants and Eligibility

Fourteen rural health facilities that were part of the intervention arm for either the TB REACH or MENTORS program were included in this analysis. ^{15,16} Ten facilities received the TB REACH intervention and five received the MENTORS intervention as described below. One facility was included in both interventions, for a total of 14 facilities included in the analysis.

The health facilities were 13 health centers IV and one district hospital drawn from all regions of Uganda. Health Centers IV serve a catchment population of 100,000, providing outpatient and limited inpatient and surgical services for minor ailments, labor and delivery, and referral to district hospitals. During the interventions they were the lowest level health facility at which ART and TB treatment initiation services were available. All TB patients co-infected with HIV and not transferred in or out of the health facility for TB treatment were included in the analysis.

Description of interventions

For TB REACH, a team comprised of a clinical officer, a laboratory technician and a data manager conducted on-site support (OSS) visits for two days once per month over a ninemonth period (from January to October 2012) (Table 1). These visits included multidisciplinary and cadre-specific clinical sessions covering key areas of TB diagnosis and case management. 15 For MENTORS, two clinical officers trained as mentors conducted visits to each facility for one day every six weeks, over a nine-month period from October 2013 to June 2014. These visits focused on providing one-on-one clinical mentorship on HIV and TB care for four clinical officers, registered nurses and registered midwives at each facility. 16 As part of these visits in both interventions, program staff also worked with health facility staff to integrate TB/HIV services. Key strategies to foster TB/HIV integration included conducting trainings on the management of TB/HIV co-infected patients, moving TB drugs into the HIV clinic, and modifying TB and HIV clinic schedules so that clinics for both illnesses were held on the same day. To prevent nosocomial transmission, program staff helped to establish open air waiting areas and collaborated with health facility staff to develop systems to actively identify and separate coughing patients from other patients and fast track them through the patient care process.

Study Outcomes and Definitions

The primary outcomes for TB and HIV co-infected patients were (1) the proportion who started on ART during TB treatment, the proportion who (2) were cured or completed, (3) died, (4) were lost to follow-up, or (5) had treatment failure during TB treatment. The outcome indicator definitions are presented in Table 2. The data source for all three indicators was the National Tuberculosis and Leprosy Program (NTLP) Unit Register of the participating facilities.

During the time of the interventions, the guidelines on when to initiate ART and TB treatment regimens for co-infected patients changed (Table 1). From 2009–2013, the recommended time period to initiate ART ranged from starting after two weeks, if CD4 count was less than 250 cells/mm³ or patient had signs of stage 4 HIV, to starting after TB

treatment, if CD4 count was above 250 cells/mm³.¹⁷ In December 2013, the guidelines were changed to recommend starting patients on ART after two weeks, if the CD4 count was less than 50 cells/mm³, or after 8 weeks, if it was greater than 50 cells/mm³.¹⁸ During the same period, the guidelines for TB treatment changed from an eight-month to a six-month treatment regimen for new adult cases. Both regimens included a two-month initial phase of Isoniazid, Rifampicin, Pyrazinamide and Ethambutol. The six-month treatment regimen had a continuation phase of four months of Isoniazid and Rifampicin, compared to a six-month continuation phase of Isoniazid and Ethambutol under the eight-month regimen.

After implementation of the interventions, program managers who were involved in the TB REACH and MENTORS projects classified each health facility's TB/HIV integration status prior to (MENTORS) and during (MENTORS and TB REACH) the interventions. While data on TB outcomes and ART initiation was available for MENTORS for both time points, it was not available prior to the TB REACH intervention. Thus, each facility contributed between one to three time points that were integrated or not (integration periods), depending on whether they were enrolled in the TB REACH intervention (9 facilities, 1 integration period), MENTORS intervention (4 facilities, 2 integration periods), or both (1 facility, 3 integration periods) – for a total of 20 integration periods. TB/HIV integration was defined as TB patients infected with HIV being treated for both TB and HIV by one provider or care team using a combined treatment plan during one visit at one treatment location. The combined treatment plan included treatments for both diagnoses and took into consideration drug interactions and side-effects, as well as scheduling drug refills to coincide on a single visit when possible. Program managers were blinded to the study outcomes but not to overall facility performance when classifying the health facilities.

Sample Size

The number of facilities was based on the samples required for testing the effect of the TB REACH and MENTORS interventions. ^{15,16} For TB REACH, the sample size was calculated to detect a 50% change, from 15% to 65% in proportion of presumptive TB cases with a sputum smear, with a power of 80% and 5% level of significance. For MENTORS, the sample size was calculated to detect a 10% absolute difference in knowledge on HIV case scenarios with 80% power at a 5% level of significance.

Data Collection

Facility-based data entrants entered routinely collected patient data into electronic replicas of the NTLP Unit register during each project. For TB REACH, data was collected during the intervention from January to October 2012. Data entry personnel returned to the facilities in June 2013 to collect data on TB treatment outcomes for all patients who started TB treatment between January to October 2012. Data was not available for TB treatment outcomes prior to TB REACH. For MENTORS, data for January to September 2013 was entered retrospectively prior to the start of the intervention in October 2013 to create the time point prior to the intervention. Data entry personnel also entered data from October 2013 to June 2014 to create the time point during the intervention. Data entrants remained on-site from July 2014 to March 2015 following the intervention and collected TB treatment outcomes for all patients who started TB treatment between October 2013 to June 2014.

Statistical Methods

We analyzed the effect of integration by conducting a cross-sectional analysis assessing change in ART initiation, TB treatment outcomes (success, mortality, lost to follow-up and treatment failure), by TB/HIV integration status. We conducted bivariate analyses to compare patient demographics for the integrated and non-integrated health facility periods, using Student's t-tests for continuous and chi-square tests for categorical variables. Using the patient as the unit of analysis, we conducted logistic regression analysis with TB/HIV integration status as the independent variable, adjusting for age, gender, the introduction of the revised guidelines, and clustering by health facility. We controlled for other effects of the interventions and changes over time by including time (pre/post intervention) as a covariate. In addition to reporting the main effect of TB/HIV integration, we also report the effects of the change in guidelines on the outcomes. Sensitivity analyses were performed for the four TB outcomes, with two alternative assumptions about the missing observations: i) all missing values were interpreted as either having the outcome (treatment success or death) with a value of 1, or ii) not having the outcome and a value of 0. Data analysis was done using the statistical package Stata (version 14.2; StataCorp, College Station, TX).

Ethics Statement

Both studies were reviewed and approved by the Uganda National Council on Science and Technology. TB REACH was reviewed and approved by the Scientific Review Committee of the Infectious Diseases Institute and the Institutional Review Boards of Joint Clinical Research Center and Johns Hopkins University. MENTORS was reviewed and approved by the Institutional Review Boards of the Joint Clinical Research Center and the US Centers for Disease Control. The database used for analysis in this study did not contain identifying information on patients.

RESULTS

Characteristics of study population

For the 10 facilities included in TB REACH, eight of the facilities were integrated following the intervention (Table 3). For the five facilities included in MENTORS, none were integrated prior to the intervention and three were integrated post-intervention. Of the 20 TB/HIV integration periods assessed, health facilities were integrated in 11 (55%) periods, all occurring post intervention, and not integrated in 9 (45%) periods, 5 pre- and 4 post-intervention.

A total of 996 TB patients were registered for TB treatment; 966 (97%) were tested for HIV and 404 (42%) were HIV-positive. Of the 404 TB/HIV patients, 108 were transferred-in or transferred-out during their TB treatment, leaving 296 eligible patients - 117 and 179 during non-integration and integration periods, respectively. Of these 57.8% were male and the median age was 33 (IQR 26–40) (Table 4).

ART initiation

Of the 296 TB/HIV patients included in the study, 174 (58.8%) had not initiated ART prior to starting TB treatment and had their ART start date recorded when ART was initiated. In

this subset of patients, the difference in the proportion initiated on ART during integration periods compared to during non-integrated periods was not statistically significant (47.7% versus 33.8%; aOR=1.34 [95% CI=0.40–4.47]) (Table 5). There was no effect of the change in guidelines on ART initiation (S2 Table).

TB Treatment Outcomes

Of the 296 patients included in the study, 231 (78.0%) had TB treatment outcomes recorded. A similar proportion of TB/HIV patients were completed or cured in both arms, with 55.0% in the integration and 53.8% in the non-integration periods (adjusted odds ratio [aOR]: 1.43; 95% confidence interval [CI]=0.73–2.82) (Table 5). There was a smaller proportion of TB/HIV patients who died while on TB treatment during integrated facility periods (14.3%) compared to non-integrated facility periods (27.5%) (aOR=0.44; 95% CI=0.18–0.77). There were no differences in the patients lost to follow-up (29.2% vs. 17.6%; aOR=1.64; 95% CI=0.53–5.04) or the proportion with TB treatment failure (1.4% vs. 1.10%, aOR=1.21; 95% CI=0.34–4.32). There was no effect of the change in guidelines on any of the TB treatment outcomes (S2 Table).

In sensitivity analyses we imputed the 38 cases with missing data for the four TB treatment outcomes as equal to zero or one. The direction and significance of the effect estimates were the same, with one exception. The effect of TB/HIV integration on mortality was not statistically significant when it was assumed that all patients with missing treatment outcomes had died (aRR=0.48; 95% CI=0.21-1.11).

To assess the contribution of ART initiation to mortality, we compared the proportion of patients who died by their ART status. The proportion who died was similar among those on and not on ART (20% vs. 23%, χ^2 =0.0219, p=0.882).

DISCUSSION

Integration of TB and HIV services was associated with lower mortality in rural health facilities when compared with settings where TB and HIV services were not integrated. Integration of TB and HIV treatment services could lead to declines in mortality through several mechanisms, including ART initiation, earlier ART initiation, increased and earlier TB screening, and earlier initiation on TB treatment. ^{19–21} We found no evidence for an effect of TB/HIV integration on ART initiation and the proportion who died was similar among patients regardless of whether they were on ART. It is possible that integration of services led to earlier ART initiation among those who were initiated on ART during TB treatment. We were unable to reliably assess time to ART initiation in this study due to the small number of patients (n=62) in this group. Given the similar rates of survival regardless of ART initiation found in this study, mortality among those on ART could be due to late presentation with low CD4 counts. Several studies have documented higher mortality in the first few months of starting ART among patients with low CD4 counts. ^{22–24}

While data on the timeliness of TB treatment initiation was not available for this analysis, both Manabe et al. and Naikoba et al. reported an increase in TB screening among

outpatients when assessing the effect of the TB REACH and MENTORS interventions, and Naikoba et al. also reported high rates of TB screening among HIV patients. ^{15,16}

Through earlier identification of TB and HIV patients, and earlier initiation on both TB treatment and ART, facilities offering integrated TB/HIV services could likely reduce mortality. During TB REACH and MENTORS, facility staff implemented several interventions to improve TB/HIV integration that may have improved TB screening and initiation among HIV patients, such as taking more active measures to identify HIV patients with TB symptoms and moving TB drugs to the HIV clinic. At the same time, changes in national guidelines which recommended earlier initiation on treatment were also being implemented. Future studies on TB/HIV integration would benefit from further studying the components of TB/HIV integration to describe the pathways through which TB/HIV integration leads to reduction in mortality and which specific components of integration lead to the greatest improvement.

Overall, the proportion of TB/HIV patients initiated on ART during TB treatment (38.5%) and who were successfully treated for TB (54.5%) were low in this study, and the proportion of those who died was high (19.5%). Even during the integration periods, which had lower mortality than non-integration periods, 14.3% of patients died during TB treatment. These results suggest a lower level of quality of care than seen in several other studies of TB/HIV integration. 12,13,25-27 Three of these five similar studies were done in urban areas and most assessed outcomes two years following integration. This longer follow-up period may have allowed TB/HIV integration to become better established in these facilities and resulted in greater proportion of TB patients benefitting from the TB/HIV integration throughout their full treatment period. The outcomes in this study were assessed in rural facilities during the period when TB/HIV integration was implemented and followed for nine months. Some of the patients included in this analysis started their treatment prior to the TB/HIV integration which usually occurred a few months into the projects, and thus may have only partially benefitted from the TB/HIV integration during their treatment. This may have reduced our ability to assess the full effects of TB/HIV integration on our outcome indicators and resulted in lower overall performance.

Given the benefits of TB/HIV integration, as cited in this study and in others, TB/HIV integration should be further supported, particularly in areas with high burden of TB and HIV co-infection. In Uganda, the Ministry of Health is already supporting a country-wide approach to improving TB/HIV integration in all health facilities. ^{28,29} Operationally, there are many challenges to integrating TB and HIV services and rural facilities require special consideration. ⁵ Nurses and clinical officers are also less likely to have received regular training on updated guidelines for TB and HIV treatment than medical officers and physicians, and may be more reluctant to initiate ART due to fear of drug interactions and immune reconstitution syndrome. ³⁰ Regular supportive supervision can effectively improve the clinical skills of mid-level practitioners in providing HIV and TB care. Both the TB REACH and MENTORS studies helped to improve the quality of care over nine-month interventions, when compared with control facilities, while also improving TB/HIV integration. ^{15,16}

This study utilized existing datasets from two operational research interventions to draw conclusions regarding the effects of TB/HIV integration in rural settings. The NTLP Unit Register was a key data source for both interventions. Use of this standardized government register facilitated the analysis across the two projects. Both interventions also employed facility-based data entrants to review and verify the data as it was entered. Though this data was of higher quality data than routine health register data, there were still gaps in the data quality that affected the analysis. For example, sensitivity analyses were conducted to address missing data for TB outcomes. In addition, as this study was a secondary analysis some data that would have been useful, such as CD4 count and WHO clinical stage, were not collected for both interventions and thus could not be analyzed. This analysis was also limited to the sample size for the two interventions and may not have been large enough to show a difference in the intended outcomes. Future research should be powered with an adequate sample size. However, this analysis did allow us to gain further insight into TB/HIV integration in rural health facilities at little additional cost. Operational studies should collect data using existing national registers and make anonymized data publicly available for further analysis, taking into account best practices in responsible, ethical data sharing. ^{31,32} This is particularly important for low-resource settings where funding for operations research is limited to avoid waste and unnecessary duplication and to accelerate advancements in program implementation.³³

Our study had several limitations that should be considered when interpreting the findings. First, this was a cross-sectional study and was not randomized. Differences in mortality could have been influenced by factors other than the TB/HIV integration, including the effect of the two interventions (TB REACH and MENTORS), changes in ART guidelines during the study period, or other factors related to TB and HIV care and treatment, such as resources and infrastructure. Also, the TB/HIV integration status of the control facilities that did not receive the TB REACH and MENTORS interventions were not available so we were not able to use these facilities in the analysis. We attempted to control for the effects of these interventions and guidelines changes by using covariates to account for the time before and after the intervention and the change in guidelines as covariates in the model. We were unable to control for CD4 count, a main factor in determining timing of ART initiation for TB patients in both the previous and revised ART guidelines, as our data source was the NTLP Unit Register. Future research could link patient records across NTLP and ART registers. Second, eligibility criteria focused on subdistrict referral facilities within rural Uganda engaged in two TB and HIV interventions. However, to the extent that these facilities are similar to health facilities throughout sub-Saharan Africa, these results would be generalizable to TB/HIV integration in other rural settings. Third, program managers familiar with the two interventions classified each facility's integration status based on their knowledge of the facility. While they did not have access to the results by facility for these study outcomes, they may have been familiar with which facilities had higher performance in general, and it is possible they could have been biased in classifying higher performing sites as being more integrated. Finally, the effect of TB/HIV integration on mortality was not robust in sensitivity analyses when missing data on the TB treatment outcome was assumed to mean that the patient had died. However, this sensitivity analysis had a much higher proportion of deaths than seen in other studies.

CONCLUSION

TB/HIV service integration was associated with lower mortality on TB treatment even in a setting with suboptimal proportions completing TB treatment and starting on ART.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Timeline of Interventions and Guidelines

			2012	2			2013	3			2014	14	
		Jan-Mar	Apr-Jun	Jul-Sep	Oct-Dec	Apr-Jun Jul-Sep Oct-Dec Jan-Mar Apr-Jun		Jul-Sep	Oct-Dec	Jul-Sep Oct-Dec Jan-Mar	Apr-Jun Jul-Sep Oct-Dec	Jul-Sep	Oct-Dec
Pode Collegis	TB REACH	Interv	Intervention Study Period: Jan – Oct 2012	/ Period: 12	H Z	Follow-up Period *: Nov 2012-Jun 2013	iod *: 2013						
рага Сопесион	MENTORS					Baseline Jan-	Baseline Study Period: Jan-Sept 2013	:po	Interve	Intervention Study Period: Oct 2013- Jun 2014	Period:)14	Follow-up Period *: Jul 2014-Mar 2015	Follow-up Period *: Jul 2014-Mar 2015
Guidelines	ART		CD4 i	count < 250 nitiate ART CD4 countitiate ART	Ending Nov 2013 cells/mm3 or sign after 2 weeks of T t was above 250 center completion of	Ending Nov 2013 2D4 count < 250 cells/mm3 or signs of stage 4 HIV: initiate ART after 2 weeks of TB treatment CD4 count was above 250 cells/mm3: initiate ART after completion of TB treatment	ge 4 HIV: ment 13: 1tment			Starting Dec 2013 CD4 count < 50 cells/mm3: initiate ART after 2 weeks of TB treatment CD4 count > 50 cells/mm3: initiate ART after 8 weeks of TB treatment	Starting Dec 2013 CD4 count < 50 cells/mm3: ART after 2 weeks of TB tre CD4 count > 50 cells/mm3: ART after 8 weeks of TB tre	: 2013 :ells/mm3: s of TB trea ells/mm3: s of TB trea	ment ment
	TB] 2 mont	Ending Nov 2013 8-month regimen: 2 months HRZE, 6 months HE	2013 imen: months HE				S cont	Starting Dec 2013 6-month regimen: 2 months HRZE, 4 months HR	2013 men: months HR	

Outcomes for patients who started treatment during the intervention study period were collected during the follow-up period.

Abbreviations: Isoniazid (H), Rifampicin (R), Pyrazinamide (Z), Ethambutol (E)

Indicator Definitions

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Table 2.

	Indicators	Definition
-	Proportion of TB and HIV co-infected patients started on ART	Numerator: Number of TB patients who have a positive HIV test result, excluding transfer-ins and transfer-outs who had an ART number recorded in the NLTP Unit Register at a date later than TB treatment initiation. Denominator: Number of TB patients who have a positive HIV test result who were not started on ART prior to TB treatment initiation, excluding transfer-ins and transfer-outs.
2	Proportion of TB and HIV co-infected patients who were cured or completed TB treatment (out of all those with a treatment outcome recorded)	Numerator: Number recorded as either cured or completed TB treatment, excluding transfer-ins and transfer-outs Denominator: Number of TB patients who have a positive HIV test result and treatment outcome recorded (cured or completed, died, lost to follow-up, or treatment failure), excluding transfer-ins and transfer-outs.
8	Proportion of TB and HIV co-infected patients who died during TB Treatment (out of all those with a treatment outcome recorded)	Numerator: Number recorded as died during TB treatment, irrespective of cause, excluding transfer-ins and transfer-outs Denominator: Number of TB patients who have a positive HIV test result and treatment outcome recorded (cured or completed, died, lost to follow-up, or treatment failure), excluding transfer-ins and transfer-outs
4	Proportion of TB/HIV patients who were lost to follow-up during TB treatment	Numerator: Number recorded as lost to follow-up during TB treatment, excluding transfer-ins and transfer-outs Denominator: Number of TB patients who have a positive HIV test result and treatment outcome recorded (cured or completed, died, lost to follow-up, or treatment failure), excluding transfer-ins and transfer-outs
5	Proportion of TB/HIV patients who had TB treatment failure	Numerator: Number recorded as experiencing TB treatment failure during TB treatment, excluding transfer-ins and transfer-outs Denominator: Number of TB patients who have a positive HIV test result and treatment outcome recorded (cured or completed, died, lost to follow-up, or treatment failure), excluding transfer-ins and transfer-outs

Health facility Integration periods

	Total	Total Not integrated Integrated	Integrated
Number of health facility integration periods	20	9 (45.0%)	11 (55.0%)
Pre-intervention	S	5 (100.0%)	0 (0.0%)
TB REACH	0	0 (0.0%)	0 (0.0%)
MENTORS	S	5 (100.0%)	0 (0.0%)
Post-intervention	15	4 (26.7%)	11 (73.3%)
TB REACH	10	2 (20.0%)	8 (80.0%)
MENTORS	S	2 (40.0)	3 (60.0)

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Patient demographics

Table 4.

Not integrated Integrated P-value 0.806 0.735 0.182 102 (57.0) 77 (43.0) 33 (26, 39) 16.3 69 (59.0) 48 (41.0) 34 (28, 43) 14.6 117 125 (42.2) 171 (57.8) 33 (26, 40) Total 296 15.6 Average number of TB/HIV patients per facility Total TB/HIV patients enrolled Age (years); median (IQR) Sex; n (%) Female Male

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Table 5.

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Descriptive statistics and regression results of the comparison of healthcare facilities by TB/HIV integration level, adjusted for age, gender, intervention effects and change in guidelines, and clustering by healthcare facility

	TB/HIV Integration Status	ration Status		Regression Results	tesults		
	Total	Not integrated	Integrated	OR (95% CI) p-value	p-value	Adjusted OR (95% CI)	p-value
$\mathbf{ART} \ \mathbf{Indicator}^{+}$							
Proportion of TB/HIV patients started on ART	38.5% (67/174)	33.8% (24/71)	47.7% (43/103)	1.40 (0.33, 6.02)	0.648	1.34 (0.40, 4.47)	0.632
TB Indicators							
Proportion of TB/HIV patients with treatment success (completed or cured)	54.5% (126/231)	53.8% (49/91)	55.0% (77/140)	1.05 (0.47, 2.35)	0.910	1.43 (0.73, 2.82)	0.298
Proportion of TB/HIV patients who died during TB treatment	19.5% (45/231)	27.5% (25/91)	14.3% (20/140)	0.44*(0.26,0.73)	0.002	0.38*(0.18, 0.77)	0.008
Proportion of TB/HIV patients who were lost to follow-up during TB treatment $^{+++}$	24.7% (57/231)	17.6% (16/91)	29.2% (41/140)	1.94 (0.52, 7.30)	0.326	1.64 (0.53, 5.04)	0.386
Proportion of TB/HIV patients who had TB treatment failure	1.3% (3/231)	1.10% (1/91)	1.10% (1/91) 1.4% (2/140)	1.30 (0.18, 9.58)		0.794 1.21 (0.34, 4.32)	0.774
* p<0.01							

⁺ Of the 296 in the sample, 122 (41.2%) were not included in the analysis: 84 (68.9%) were already on ART prior to starting TB treatment, and thus were not eligible, 38 (31.1%) were missing ART start date and were excluded because it was unclear whether they started ART before or after TB treatment. Those missing comprised 18 (20.2%) of the non-integrated time period and 20 (16.3%) of the integrated time period samples.

⁺⁺ Of the 296 in the sample, 65 (22.0%) had outcomes missing - 26 (22.2%) of the non-integrated time period and 39 (22.2%) of the integrated time periods samples.

⁺⁺⁺