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Predictors of tuberculosis treatment outcomes among a retrospective cohort in rural, Central India

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ABSTRACT

Introduction: Programmatic design affects access to healthcare and can influence tuberculosis treatment outcomes. Potential predictors of tuberculosis treatment outcomes in one rural Indian setting were examined to improve outcomes with a focus on access to care.
Methods: Routinely collected tuberculosis treatment data from Jan Swasthya Sahyog, a community based healthcare system in rural Chhattisgarh, India were examined from 2003–2015. Predictors were analyzed for associations with death, loss to follow-up or failure in multivariable logistic regression models. The effect of distance from treatment on outcomes was graphed and Pearson's correlation coefficients (r^2) calculated. Descriptive time to event analyses were performed for all deaths and loss to follow-up from January 2010 to September 2015.
Results: 4979 patients with active TB were treated during the study period. Patients were mostly male, malnourished, diagnosed with pulmonary disease and many travelled lengthy distances. Positive treatment outcomes improved from 55% to 80% from 2003 to 2015 for all patients though positive treatment outcomes have been above 80% in the primary care setting since 2012. The annual case fatality rate was 4.4% with small yearly variation.Gender and site of treatment (primary versus secondary care facility) and also season of treatment initiation and travel time to care best predicted outcomes in both the complete model and model which included only patients with initial BMI data. No differences were found between primary and secondary care patients for initial BMI, percentage of sputum positivity among those with pulmonary disease and grade of sputum positivity among the sputum positive. Those who traveled the furthest to access care achieved the worst outcomes during the summer and, to a lesser degree, the monsoon. Distance from care was associated with treatment outcomes in a dose-response manner out to substantial distances. From 2010 to 2015, most patients who died or were lost to follow-up did so in the first week of treatment.
Conclusions: The provision of care through local facilities improves the treatment of tuberculosis in rural India. Interventions addressing death or loss to follow-up should focus on the newly diagnosed. Rural Indian physicians should be aware of how access issues affect TB treatment outcomes.

1. Introduction

The WHO mandates successful TB treatment outcomes of greater than 90% in developing nations and lower resource settings [1]. High proportions of successful TB treatment reported in higher resource settings [2,3] that serve TB patients from all over the world argue such goals are possible. Nonetheless, the realities of differences in public health resources to burden of TB patients can make such targets difficult to attain [4].

In 2017, India reported an incidence of 2.8 million new TB cases, accounting for approximately one-quarter of the world's new cases [5]. This includes 147,000 new cases of multi-drug resistance TB (MDRTB), also approximating a quarter of the world's total [5]. Excluding Human Immunodeficiency Virus (HIV), India reported 423,000 deaths due to TB. This number approximates a third of the world's total [5]. In India, TB care is coordinated by the Revised National Tuberculosis Control Programme (RNTCP). The RNTCP reports impressive treatment outcomes both nationwide [6] and in Chhattisgarh and Madhya Pradesh, the states from which the majority of our patient's live [5]. Independently published RNTCP data also estimate successful outcomes in about 85% of patients [7,8], though concerns exist about data inaccuracies [9]. Non-RNTCP Indian data report success in only

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50%–75% of diagnosed or enrolled patients [10–13]. While much is known about patient demographic and microbiologic data that affect TB outcomes in India [7,8,11,13–23], less studied are measures of healthcare access such as location of treatment [4], distance from care [24] and loss-to-follow-up before and during the treatment course [8,25–27].

At Jan Swasthya Sahyog, a team of health care providers treat rural Indian TB patients. In this retrospective cohort study, the objectives were to determine characteristics correlated with treatment outcomes, understand the effects of distance from care and season of treatment initiation on treatment outcomes and ascertain timing of deaths or loss to follow-up on treatment.

2. Methods

2.1. Setting

JSS is a community-based health care system operating in rural Chhattisgarh since 1999. JSS runs a secondary care hospital and three primary care clinics. TB care has been performed at all JSS sites since 1999 though has undergone multiple systems based modifications during that same time period. JSS primarily serves the rural Indian poor including tribal populations.

2.2. Design and data collection

JSS has maintained a database for all enrolled TB patients from early 2003, which includes demographic and clinical information recorded at diagnosis and throughout treatment. For most analyses, patient data were retrospectively reviewed from January 2003 to September 2015. For time-to-event (a) loss to follow-up and (b) death outcomes, a subset of patients from January 2010 to September 2015 were analyzed.

For distance from care analyses, patients provided their village name at treatment start. Community health workers (CHWs) serving each region provided information about each village's distance from care in both absolute distance (kilometers) and travel time (hours).

For data on loss to follow-up and death, patient charts were reviewed. For 2010 and 2011, data were extracted from paper charts and single entered in an Excel database. For 2012–2015, the Electronic Medical Record (Bahmni, ThoughtWorks, Bengaluru, India) was mined. The time from date of diagnosis to date of last clinical follow-up or death was recorded among those whose outcome was coded as 'loss to follow-up' or 'death' respectively.

2.3. Inclusion/exclusion criteria

All children and adults treated for active TB disease in both primary care clinic and secondary care hospital settings were included. Due to staffing shortages, there were periods (most of 2004 and September–December 2008) during which patient data were not collected.

2.4. Variable and outcome classification

Treatment outcomes were classified as follows: 'ongoing treatment' (at time of database closure), 'cured', 'completed', 'died', 'failed', 'lost to follow-up' or 'not evaluated/transferred care' (with unknown clinical endpoint). With the exception of 'ongoing treatment,' these definitions exactly mirror published WHO definitions [28]. The sum of cured and completed was defined as 'treatment success/positive outcomes,' also as per WHO definitions [28]. Cured referred to negative microscopy or culture (sputum or, if patient no longer producing sputum, saliva) at the end of treatment. Completed denoted patients who completed at least six months of consecutive treatment. Negative outcomes included patients who died, failed or were lost to follow-up. Patients who were still ongoing treatment at database closure or who were not evaluated/transferred care were considered uncertain outcomes and were not included in analyses.

Electronic scales were used to measure weight to the nearest tenth of a kilogram while height was measured to the nearest centimeter to calculate BMI. Analyses were performed using $< 16\,kg/m^2$, 16 to $< 18.5\,kg/m^2$ and $\geq 18.5\,kg/m^2$ as categories (based on WHO definitions [29]) due to the low number of patients who were normal weight, overweight or obese. Modifications in BMI cutoffs for Asian populations were not used because this population was predominantly underweight.

Site of disease was categorized as either pulmonary disease or extrapulmonary/disseminated disease. The former category included all patients with pulmonary TB; the latter category included all individuals with extrapulmonary disease and all disseminated disease. Those patients with both pulmonary and extrapulmonary involvement were categorized as pulmonary disease per WHO definitions [28]. AFB staining was graded per the standard 1+, 2+, and 3+ system [30]. For each patient, date of treatment start, site of treatment (secondary care hospital or primary care clinic), and previous treatment history ('new,' 'relapse,' 'treatment after failure,' and 'treatment after loss to follow-up') were recorded. Date of treatment start was categorized into season as monsoon (June–September), winter (October–February) or summer (March–May). Primary care clinics included three village-based clinics specializing in preventive and chronic care. The secondary care hospital was a single facility performing acute and emergency care and referrals.

The following data were recorded via patient self-report: gender, age and caste. For analyses, age was quantified as < 49 and ≥ 50 years old. Pediatric patients were defined as those individuals ≤ 18 years old at treatment start [31]. Data about human immunodeficiency virus (HIV) infection and diabetes status were not available for the duration of our retrospective analysis due to a period of systems optimization and so were not included in analyses.

2.5. Data analysis

All data were combined and transferred from Excel to STATA SE 14.1 for analyses.

Demographic characteristics were examined using descriptive techniques. Missing data were excluded from the calculation of all descriptive statistics and models.

A step-wise, multivariable analysis was conducted to determine relationships between demographic and clinical variables and treatment outcomes. Initially, univariate analyses of all variables of clinical interest were performed using Chi-squared testing. Variables demonstrating statistical significance ($p < 0.05$) in unadjusted analyses were checked for interactions. For significant interactions, a cutoff of $p \leq 0.15$ was used via analysis-of-variance (ANOVA) testing. Multiple significant interactions (all as dichotomous variables) were noted including gender and site of treatment, gender and absolute distance from care, site of treatment and season of treatment initiation, site of treatment and absolute distance from care, and season and both absolute distance and travel time from care. Finally, regression analyses were performed via generalized linear models including the following selected variables and interactions: gender and site of treatment (interaction), age (variable), treatment history (variable) and season of treatment initiation and travel time from care (interaction). Travel time from care was deemed more relevant than absolute distance from care (in the setting of longitudinal patient care) and was the variable of choice for regression analyses. Variables and interactions were removed from each model unless their removal demonstrated a significant likelihood ratio test for the reduced model compared to the full model ($p < 0.05$). Sensitivity analyses were also performed including BMI in these same models as BMI was not recorded for every patient at treatment initiation.

All patients commuting from similar absolute distances from care were aggregated into 25 km blocks while all patients commuting from similar travel times to care into one hour blocks to eliminate outliers. These aggregated outcome proportions were graphed for both loss to follow-up and positive outcomes and Pearson's correlation coefficients (r^2) determined.

For patients enrolled in care from January 2010 to September 2015 who were lost to follow-up or died, time-to-event graphs were drawn for descriptive purposes for each.

3. Ethics approval

This study involved de-identified retrospective data on standard of care TB treatment. Ethics Committee approval was received from Emmanuel Hospital Association (Protocol #146, Version #2, New Delhi) and was also approved by the Institutional Research Advisory Board of JSS. As this study involved de-identified retrospective data on standard of care TB treatment, informed consent was not performed. All research was performed in keeping with the *Helsinki Declaration.*

4. Results

Since 2003, men represented 64.7% and pediatric patients 18.4% of TB patients. 62.2% of patients had a BMI < 16 kg/m^2 while 12.2% had a normal or greater BMI. 67.9% of patients had pulmonary disease. Among this group, most were sputum positive at diagnosis (Table 1).

JSS diagnosed around 300–550 TB cases yearly. Most of these patients were treated at the secondary care hospital with only 10.8% treated in primary care settings. There were no differences in initial BMI (p = 0.52), pretreatment sputum status (p = 0.43) nor grade of sputum positivity (p = 0.19) between the secondary care hospital and primary care settings (data not shown). Many TB patients traveled lengthy distances to access care (Table 1).

Averaged over the 13 years of data collection, 51.5% of patients achieved a positive treatment outcome while 29.3% had a negative treatment outcome (Table 2). In recent years, the proportion has increased to 80% and has been above 80% in the primary care setting since 2012 (Fig. 1a and b). The annual case fatality rate averaged 4.4% with little yearly variation (Fig. 1c). There was no difference in outcomes (positive versus negative) for pretreatment sputum status (Table 3a, p = 0.69) or grade of sputum positivity (Table 3b, p = 0.17).

In multivariable analyses, removal of every single variable or interaction of interest (in the full model excluding BMI) demonstrated a significant change in outcomes. As such, all variables were included in the final model. Multivariable analyses showed interactions between gender and site of treatment and also season of treatment initiation and distance from care (in travel time). Men (RR = 0.56, 0.41–0.74) and women (RR = 0.59, 0.42–0.80) treated in primary care clinics achieved less negative outcomes than men treated at the secondary care hospital (Table 4). Those who traveled the furthest to access care achieved the worst outcomes during the summer and, to a lesser degree, the monsoon. Smaller effect sizes were seen linking older individuals (≥ 50 years old) and those previously treated for TB to negative outcomes (Table 4). Sensitivity analyses including BMI in multivariable models showed similar trends (data not shown).

Distance from care showed an inverse linear relationship with positive outcomes (Fig. 2a, r^2 = 0.54 for absolute distance from care; Fig. 2b, r^2 = 0.42 for travel time from care) and a direct linear relationship with loss to follow-up (Fig. 3a, r^2 = 0.50 for absolute distance from care; Fig. 3b, r^2 = 0.47 for travel time from care).

Most patients who died or were lost to follow-up on treatment did so immediately (Fig. 4). From 2010 to 2015, 75.8% (75/99) of deaths occurred during the first week while 83.8% (83/99) occurred by the end of the first month of treatment. Those who survived treatment initiation generally survived. Among individuals lost to follow-up, 69.8% (286/410) discontinued treatment in the first week while 77.3% (317/410) discontinued treatment by the end of the first month of treatment.

5. Discussion

In rural Indian TB patients, successful outcomes for self-administered therapy (SATs) approached ~80% after a decade of clinical quality improvement and community engagement in a high-risk

Table 1
Demographic characteristics, treatment details, distance from care and tuberculosis disease status at treatment initiation, 2003–2015.

Demographic characteristics	
Gender (n = 4979)	
Men	3220 (64.7%)
Women	1759 (35.3%)
Age (years, n = 4979)	
Unknown	4 (0.1%)
≤18	917 (18.4%)
19–29	1080 (21.7%)
30–39	977 (19.6%)
40–49	867 (17.4%)
50–59	545 (11.0%)
60–69	458 (9.2%)
70–79	118 (2.4%)
≥80	13 (0.3%)
BMI (kg/m^2, n = 4979)	
No data	1313 (26.4%)
< 16	1784 (35.8%)
16 to < 18.5	1278 (25.7%)
≥18.5	604 (12.2%)
Caste (n = 4979)	
Unknown	437 (8.8%)
Scheduled tribes	
Schedules castes	
Other backwards castes	
Upper caste	2046 (41.1%)
896 (18.0%)	
1451 (29.1%)	
149 (3.0%)	
Treatment details	
Season of treatment start (n = 4979)	
Unknown	25 (0.5%)
Winter (October–February)	1824 (36.6%)
Summer (March–May)	1434 (28.8%)
Monsoon (June–September)	1696 (34.1%)
Year of treatment start (n = 4979)	
Missing data	38 (0.8%)
2003	315 (6.3%)
2004	41 (0.8%)
2005	492 (9.9%)
2006	464 (9.3%)
2007	384 (7.7%)
2008	305 (6.1%)
2009	448 (9.0%)
2010	426 (8.6%)
2011	538 (10.8%)
2012	438 (8.8%)
2013	441 (8.9%)
2014	397 (8.0%)
2015	252 (5.1%)
Treatment site (n = 4979)	
Not recorded	19 (0.4%)
Secondary care hospital	4422 (88.8%)
Primary care clinic	538 (10.8%)
Treatment history (n = 4979)	
Unknown	90 (1.8%)
New	4444 (89.3%)
Treatment after loss to follow-up	254 (4.9%)
Relapse	110 (2.2%)
Previous treatment failure	81 (1.6%)
Distance from care	
Absolute distance (km) from care (n = 4979)	
Unknown	312 (6.3%)
≤20	1595 (32.0%)
21 to ≤40	842 (16.9%)
41 to ≤100	1141 (22.9%)
> 100	1089 (21.9%)
Travel time (hours) from care (n = 4979)	
Unknown	
312 (6.3%)	
≤0.75	1592 (32.0%)
> 0.75 to ≤ 1.5	1156 (23.2%)
> 1.5 to ≤4	930 (18.7%)
> 4	989 (6.3%)
Tuberculosis disease status	

(*continued on next page*)

Table 1 (*continued*)

Demographic characteristics	
AFB status among sputum positive	
(at presentation, n = 2235)	26 (1.2%)
Unknown	701 (31.4%)
1+	671 (30.0%)
2+	837 (37.4%)
3 +	
Site of disease (n = 4979)	
Pulmonary	3380 (67.9%)
Extrapulmonary/disseminated	1599 (32.1%)

BMI = Body Mass Index; kg = kilograms; m^2 = meters squared; km = kilometers; AFB = Acid Fast Bacilli.

Table 2
Summative tuberculosis treatment outcomes, 2003–2015.

Final treatment outcome (n = 4979)	
Cured†	1093 (22.0%)
Completed†	1468 (29.5%)
Died¶	219 (4.4%)
Failed treatment¶	2 (0.04%)
Lost to follow-up¶	1242 (24.9%)
Not evaluated/transferred care §	730 (14.7%)
Ongoing treatment§	255 (4.5%)

† Positive outcomes/treatment success.
¶ Negative outcomes.
§ Uncertain outcome.

population. Analyses showed many of the same clinical and demographic predictors seen in previous studies though these predictors had smaller effect sizes than variables related to access to care. Distance from care was correlated directly with loss to follow-up and inversely with positive treatment outcomes even out to substantial distances. Negative outcomes tended to occur very early during treatment.

These successful outcomes are lower than those published by the RNTCP [6–8]. Based on previous criticism of reported RNTCP data, however, it is difficult to know if the classification of patients enrolled in treatment in this setting is comparable [9].

Multiple different systems based changes likely explain the steady improvement in TB treatment success rates in both the primary and secondary care settings. In the inpatient setting, a dedicated TB Ward has been developed with its own staff. This ward is located in a well-ventilated and sunlight area of the hospital. Nutrition is heavily emphasized in this ward, with patients receiving two meals and one snack daily that is protein and calorie rich per recent recommendations concerning the nutritional care of the malnourished TB patient [32]. In the outpatient setting, patient wide counseling has been instituted at diagnosis which includes a description of what to expect during treatment, the follow-up schedule and explanation of common adverse reactions. There is a phone help line patients and family members can call at any time if any questions or concerns arise. Patients and a family member are provided with a drug organization box to help with organizing the pill burden and—where appropriate—family direct observed therapy (DOTs) is utilized. As possible, patients are provided nutritional support. When needed, financial support is given to cover the cost of transportation to and from the hospital. Those patients not following up are contacted by TB program staff who use phone or in-person contact to trace those patients lost to follow-up and reminder phone calls occur a few days before scheduled appointments. Those very malnourished patients who are particularly at risk of an early adverse drug reaction are often admitted in the TB Ward for three days to monitor the initiation of their care. For all patients, TB care also includes (at no additional cost, maximum 50 rupees/month) aggressive treatment of comorbid diseases that might affect ultimate treatment outcomes and quality of life. Narrow weight based bands for TB drug dosing are

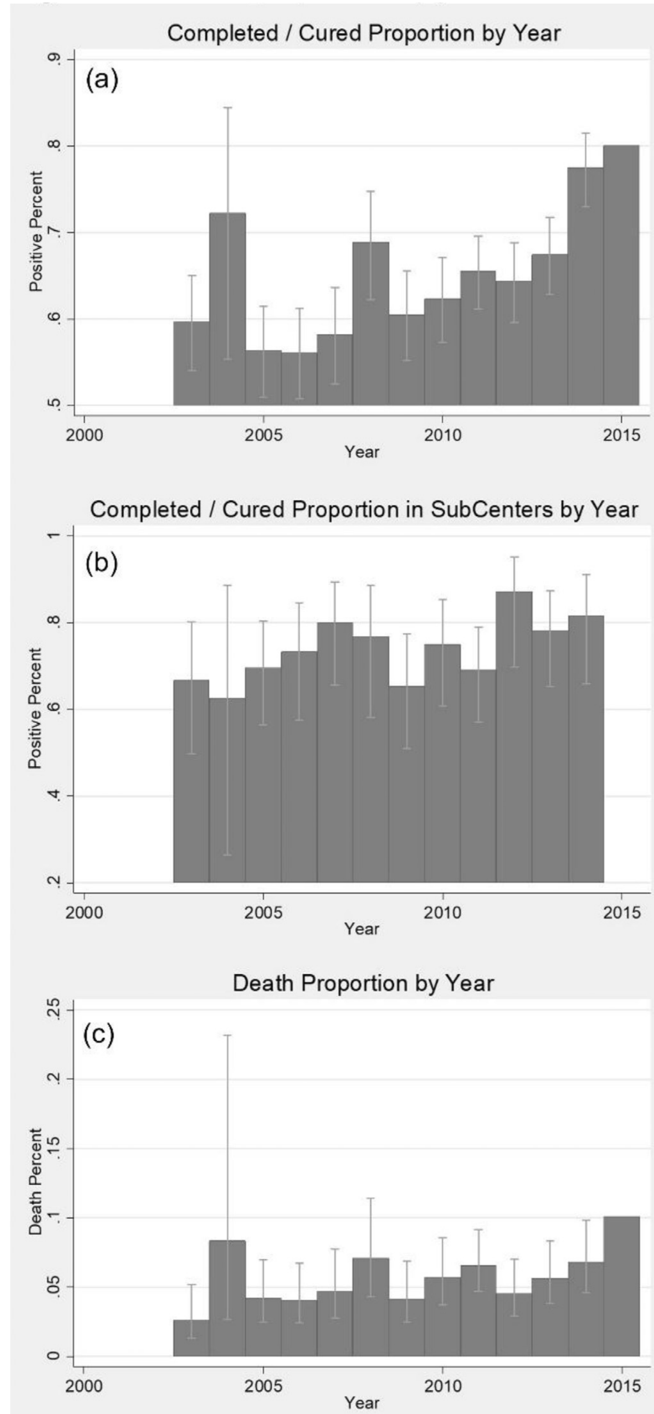

Fig. 1. Outcome proportions by year, legend: outcome proportions by year of treatment start (with 95% confidence intervals) for (a) all patients completing treatment or achieving cure, (b) all patients completing treatment or achieving cure in primary care settings and (c) all deaths, 2003–2015.

utilized to attempt to minimize adverse drugs reactions among the malnourished. Daily drug regimens have been used for many years, predating recent changes in Indian national treatment guidelines. We suspect the steady improvement in TB treatment success rates is multifactorial and due to the above outlined changes.

In multivariable analyses, the previously documented protective effects of female gender [11,15,33–35] and the negative effects of low BMI [36] on treatment outcome were seen. These effects were either not as large as healthcare access issues or modulated by them.

Table 3a
Outcomes by pretreatment sputum status (among patients with sputum samples), 2003–2015.

Pretreatment sputum status (*n* = 2607)	Positive outcome (cured or completed treatment)	Negative outcome (death, failure, LTFU)
Negative	549 (63.2%)	320 (36.8%)
Positive (any grade)	1112 (63.7%)	626 (36.0%)

$p = 0.69$.
LTFU = lost to follow-up.

Table 3b
Outcomes by pretreatment grade of sputum positivity (among the sputum positive), 2003–2015.

AFB grade (among sputum positive, *n* = 1714))	Positive outcome (cured or completed treatment)	Negative outcome (death, failure, LTFU)
1+	337 (64.2%)	188 (35.8%)
2+	367 (66.7%)	183 (33.3%)
3+	393 (61.5%)	246 (38.5%)

$p = 0.17$.
LTFU = lost to follow-up.

Table 4
Risk of negative treatment outcome without BMI in model (n = 3,642 individuals (73.1% of total)).

Variables	p-value	RR	95% CI
Gender / Site of Treatment &&			
• Male / Secondary Care Hospital	–	–	–
• Male / Primary Care Clinic	< 0.01	0.56	0.41 – 0.74
• Female / Secondary Care Hospital	< 0.01	0.77	0.66 – 0.90
• Female / Primary Care Clinic	< 0.01	0.59	0.42 – 0.84
Age (years) &			
• < 50	–	–	–
• ≥ 50	< 0.01	1.71	1.45 – 2.02
Treatment History &			
• No previous TB treatment	–	–	–
• Any previous TB treatment	0.05	1.28	1.00 – 1.63
Season / Distance from Treatment (travel time, hours) &&			
• Winter / ≤ 45 minutes	–	–	–
• Winter / > 45 minutes to ≤ 1.5 hours	0.93	1.01	0.75 – 1.37
• Winter / > 1.5 hours to ≤ 4 hours	0.08	1.31	0.96 – 1.78
• Winter / > 4 hours	0.43	1.13	0.83 – 1.55
• Summer / ≤ 45 minutes	0.05	1.33	1.00 – 1.77
• Summer / > 45 minutes to ≤ 1.5 hours	0.02	1.48	1.08 – 2.05
• Summer / > 1.5 hours to ≤ 4 hours	< 0.01	1.77	1.24 – 2.52
• Summer / > 4 hours	< 0.01	2.49	1.79 – 3.47
• Monsoon / ≤ 45 minutes	0.19	1.21	0.91 – 1.61
• Monsoon / > 45 minutes to ≤ 1.5 hours	0.86	1.02	0.75 – 1.40
• Monsoon / > 1.5 hours to ≤ 4 hours	0.13	1.30	0.93 – 1.81
• Monsoon / > 4 hours	0.06	1.35	0.99 – 1.85

RR = Relative Risk; CI = Confidence Interval; TB = Tuberculosis; Winter = October to February; Summer = March to May; Monsoon = June to September
& Variable; && Interaction

In the case of protection against negative outcomes, site of treatment was critical. It is unclear why TB patients treated in primary care settings achieved better outcomes. Primary care is generally cheaper than secondary hospital care (with lower travel costs). This may serve as an inducement. Many primary care patients live in communities served by a CHW who perhaps better monitored their care. Counseling may also be better in the primary care setting because of the less frenzied pace and potentially more private setting.

While the effects of distance from care affecting outcomes have been previously cited in other rural, low resource settings [37], there are less data on TB in India and these data pertain to loss to follow-up and delayed initiation of care only [24]. Further, these data only measure absolute distance and not travel time and only extends to a distance of 40 km [24], likely because it comes from a region (the Punjab) with more robust public health infrastructure than Chhattisgarh. This effect was documented out to an absolute distance of 200 km or a travel time of eight hours.

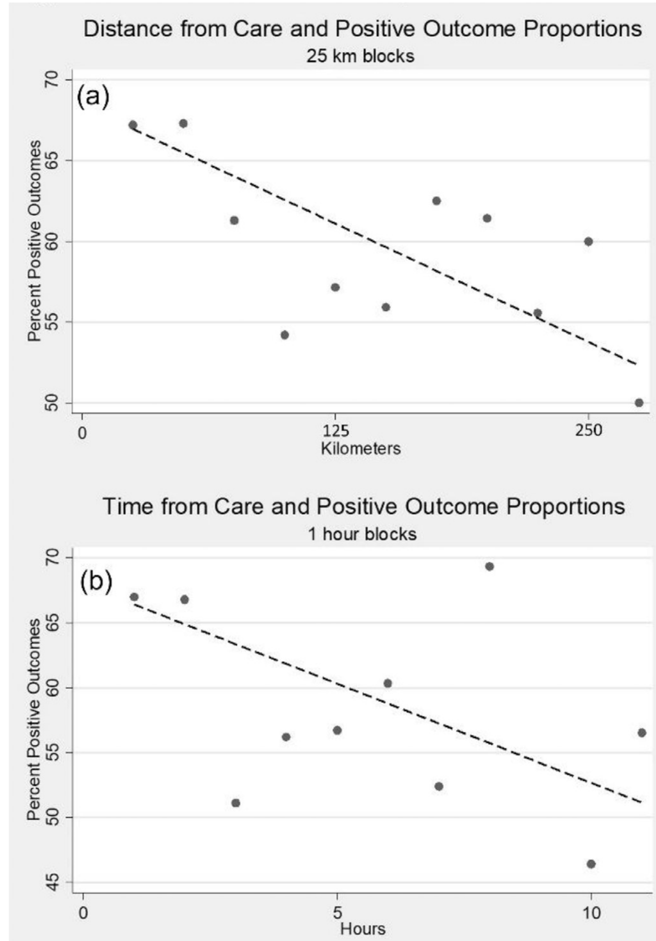

Fig. 2. Positive outcome proportions, legend: positive outcome (completing treatment or achieving cure) proportions for distance from care by (a) absolute distance (aggregated into 25 km blocks, $r^2 = 0.54$) or (b) travel time from care (aggregated into 1 h blocks, $r^2 = 0.42$), 2003–2015.

Further, in multivariable models, distance from care strongly interacted with season of treatment initiation. Monsoon or especially summer season of treatment initiation coupled with longer distances from care were the predictors most strongly correlated with negative outcomes. In Chhattisgarh, summer is the season of migrant labor while during the monsoon patients work their fields. Patients traveling from great distances during these months should be more carefully monitored due to increased risk of negative outcomes. During the monsoon, some of these patients may be candidates for primary care close to home.

Death occurred very early in treatment. This pattern was presumed secondary to delayed presentations of TB in this setting. However, this pattern could also reflect other intervenable disease processes like Immune Reconstitution Inflammatory Syndrome (IRIS) or Refeeding Syndrome. Loss to follow-up also occurred early in treatment. Efforts to retain patients should focus on the earliest treatment encounters.

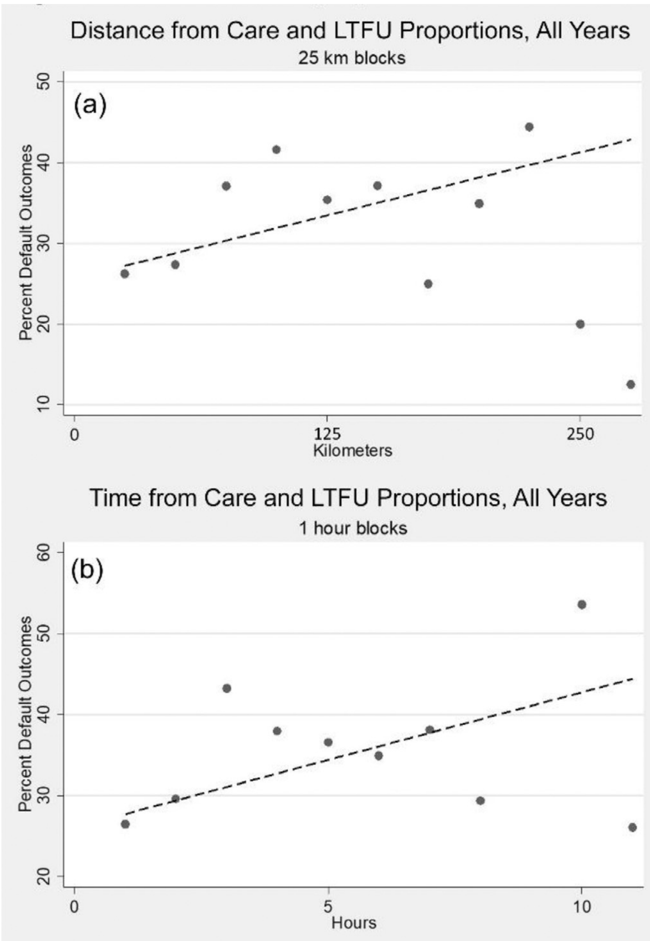

Fig. 3. LTFU outcome proportions, legend: loss to follow-up outcome proportions for distance from care by (a) absolute distance (aggregated into 25 km blocks, r^2 = 0.50) or (b) travel time from care (aggregated into 1 h blocks, r^2 = 0.47), 2003–2015. LTFU = loss to follow-up.

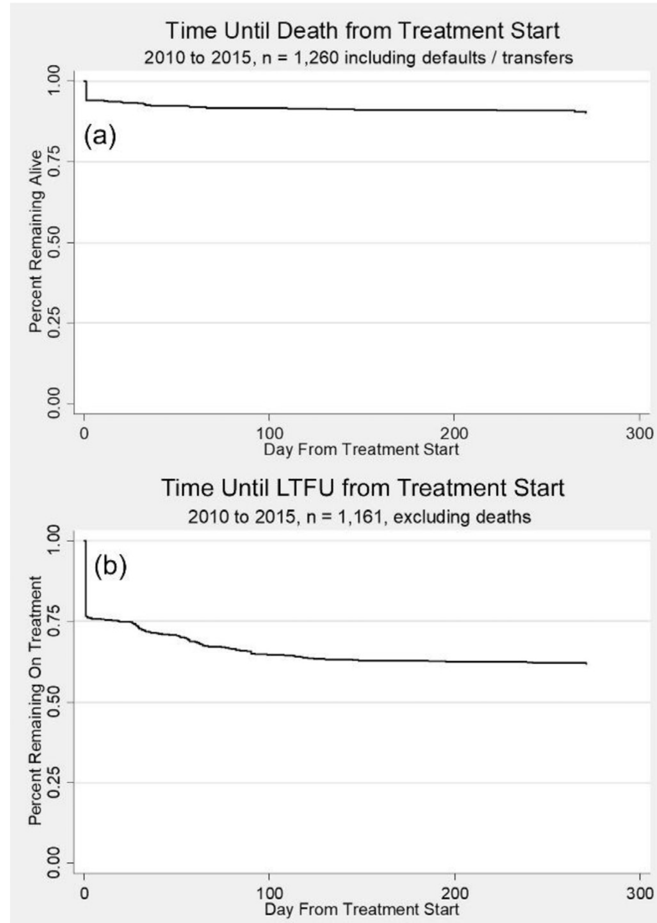

Fig. 4. Time to event graphs, legend: descriptive time-to-event graphs for time from treatment initiation until (a) death or (b), loss to follow-up, 2010–2015. LTFU = loss to follow-up.

5.1. Strengths

This study possessed several strengths. It included a large sample of TB patients over a lengthy period from one of the harder-to-study but most greatly-impacted TB prevalent zones in the world. It argues that persistence and system improvements can lead to positive TB treatment outcomes even in rural, low resource settings. It documents the effects of healthcare access issues on treatment outcomes and documents these same effects at greater distances than previously seen. It provides actionable information about when to intervene in the treatment course to prevent loss to follow-up in rural India and which patients are most at risk of a negative outcome.

5.2. Limitations

Nonetheless, there were several limitations. TB treatment outcomes are usually reported by drug sensitivity. Only recently was JSS able to perform drug sensitivity testing on all TB patients. These data were available for too few patients to be generalizable. As such, these outcomes are a summary measure of all TB patients without stratification by drug sensitivity or resistance. Similarly, diagnosis of HIV and diabetes was only consistently available for more recent patients. Due to missing data, the full multivariable model only included about three-quarters of the total patient population. While sensitivity analyses were performed showing very similar patterns, all models could be subject to selection bias. Finally, the reasons behind loss to follow-up could not be adjudicated. This requires further study.

6. Conclusions

While multiple factors were associated with treatment outcomes, healthcare access including site of treatment (primary versus secondary care), distance from care and season of treatment initiation demonstrated the largest effects. Interventions focused on providing TB care in a close to home, primary care setting should be encouraged. Two worrisome trends that require more examination but have great potential to improve treatment outcomes are the high rates of loss to follow-up and death in the first week of TB treatment.

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Competing interests statement

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