

# Treatment outcomes and associated factors among patients with drug-sensitive tuberculosis on daily fixed-dose combination drugs: A cohort study from Ahmedabad, India

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## ABSTRACT

**Background and Aim:** The National Tuberculosis Elimination Program (NTEP) has been progressive in addressing the issues related to tuberculosis (TB) control in the country, with constant programmatic changes based on evidence available from operational research. Our objectives were 1. to assess the sociodemographic and clinical characteristics, and the treatment outcomes of patients on fixed-dose combination (FDC) daily regimen and 2. to assess the factors associated with unsuccessful treatment outcomes among patients with DS-TB. **Materials and Methods:** A retrospective cohort study was conducted based on record review. The study population included all patients with drug-sensitive TB, registered and initiated on treatment under NTEP “new category” from January to June 2018 and under “previously treated category” from January to March 2018. Quantitative data downloaded from Nikshay in Excel format was imported. **Results:** A total of 8301 patients with DS-TB registered under NTEP. Mean (standard deviation [SD]) age of DS-TB patients was 35.3 + 16.9 years, and 63.2% were in the age group of 15–44 years. Also, 60.1% were male, 2.5% were human immunodeficiency virus (HIV) positive, 65.3% were pulmonary TB cases, and 70.4% obtained treatment from public providers. Proportion of “successful” and “unsuccessful” outcomes was 87.9% and 12.1%, respectively, in the new treatment category and 78.3% and 21.7%, respectively, in the previously treated category. Among the patients classified under new category, the unsuccessful treatment outcome remained significantly high after adjustments with known confounders among patients aged 45–54 years (adjusted relative risks [aRR] 1.59, 95% confidence interval [CI] 1.31–1.93) and 55–64 years (aRR 1.67, 95% CI 1.36–2.05) compared to patients aged <15 years. **Conclusion:** Unsuccessful treatment outcome was significantly high among patients aged 45–54 years. Various adherence mechanisms implemented can be evaluated for further upscaling and improving the program effectiveness.

**Keywords:** Drug-sensitive TB, fixed-dose combination, HIV, successful, treatment outcome

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## Introduction

Tuberculosis (TB) is the most common infectious cause of deaths globally.<sup>[1]</sup> India, a country with a high TB burden, shares nearly 2.7 million (27%) of the 10 million estimated global cases in 2017. Similarly, the country shares one-third of estimated deaths due to TB (excluding TB–human immunodeficiency virus [HIV]) globally. It is also one of the countries with a high burden of multidrug-resistant TB and TB–HIV cases.<sup>[2]</sup>

The National TB Elimination Program (NTEP), India, covered all the districts of the country for TB management by 2006.<sup>[3]</sup> Adopting the END TB strategy to achieve the Sustainable Development Goal (SDG) 3.3, a National Strategic Plan (NSP) for TB elimination 2017–2025 has been drafted and adopted by the country.<sup>[4]</sup> The NTEP has been continuously in addressing the issues related to TB control in the country with constant programmatic changes based on evidence available from operational research. With sputum smear microscopy and intermittent directly observed treatment short course (DOTS), the program consistently achieved 70% detection of pulmonary TB cases and 85% successful treatment outcome.<sup>[5]</sup> Owing to the high relapse rate and development of drug resistance with intermittent regimen, the Joint Monitoring Mission has recommended transition from intermittent to daily fixed-dose combination (FDC) regimen since October 2017.<sup>[5]</sup> Newer interventions like 99 DOTS (an innovative and low-cost intervention for ensuring medication adherence), Nikshay Poshan Yojana (financial assistance for nutritional support of the patient), universal drug sensitivity testing (DST), and strengthening adverse event surveillance and reporting have been rolled out in order to achieve the NSP goals by 2025.<sup>[5]</sup>

Conforming to these guidelines, Gujarat, a state in western India, has rolled out the daily FDC, 99 DOTS, and reporting of adverse drug events (ADEs) since October 2017. After the introduction of the above interventions, no study has systematically assessed the programmatic outcomes among newly diagnosed and previously treated categories of patients treated for drug-sensitive TB in India. A couple of studies done outside India have not shown any statistically significant difference between the treatment outcomes and medication policies of daily medication and thrice-weekly medication as described by the program.<sup>[6,7]</sup> The current NTEP guidelines suggest daily FDC to all diagnosed TB patients irrespective of the category of treatment. The present study was conducted to assess sociodemographic and clinical characteristics and the treatment outcomes of patients on FDC daily regimen. In addition, the study also assessed the factors associated with unsuccessful treatment outcomes among patients with drug-sensitive TB.

## Materials and Methods

### Study setting

#### General setting

The NTEP is an ongoing centrally sponsored scheme, being implemented under the umbrella of National Health Mission (NHM) in each state.<sup>[3]</sup> It was launched in the state

of Gujarat in 1993, and by 2004, the entire state was covered with implementation of DOTS chemotherapy strategy. A total of 306 TB units (TUs) in 33 districts and three municipal corporations (36 reporting units) and 1272 sanctioned designated microscopy centers (DMCs) are functional in Gujarat.<sup>[8,9]</sup>

#### Specific setting

Ahmedabad city is the seventh largest metropolis in India and the largest in Gujarat, located on the eastern bank of the river Sabarmati [Figure 1]. Revised national tuberculosis control programme (RNTCP) was implemented from March 24, 1999 in Ahmedabad Municipal Corporation (AMC). Under this program, the diagnosis (sputum microscopy/culture/cartridge-based nucleic acid amplification test [CBNAAT]) and treatment for TB is provided free of cost as per the guidelines.<sup>[10]</sup> The daily FDC therapy has been implemented since October 2017 in AMC. Currently, 99 DOTS has been implemented for all types of TB cases. The AMC population is divided into 23 TUs and 75 DMCs.

The principle of daily regimen is to administer daily FDCs of first-line antituberculosis drugs in appropriate weight bands.

Treatment regimen for drug sensitive (DS) - TB patients in 2018 is as follows: <sup>[11]</sup>

New cases: (2) HRZE treatment regimen in the intensive phase and (4) HRE in the continuous phase

Previously treated cases: (2) HRZES + (1) HRZE treatment regimen in the intensive phase and (5) HRE in the continuous phase

(prefix to the drugs stands for the number of months; H – isoniazid, R – rifampicin, Z – pyrazinamide, E – ethambutol, S – streptomycin)

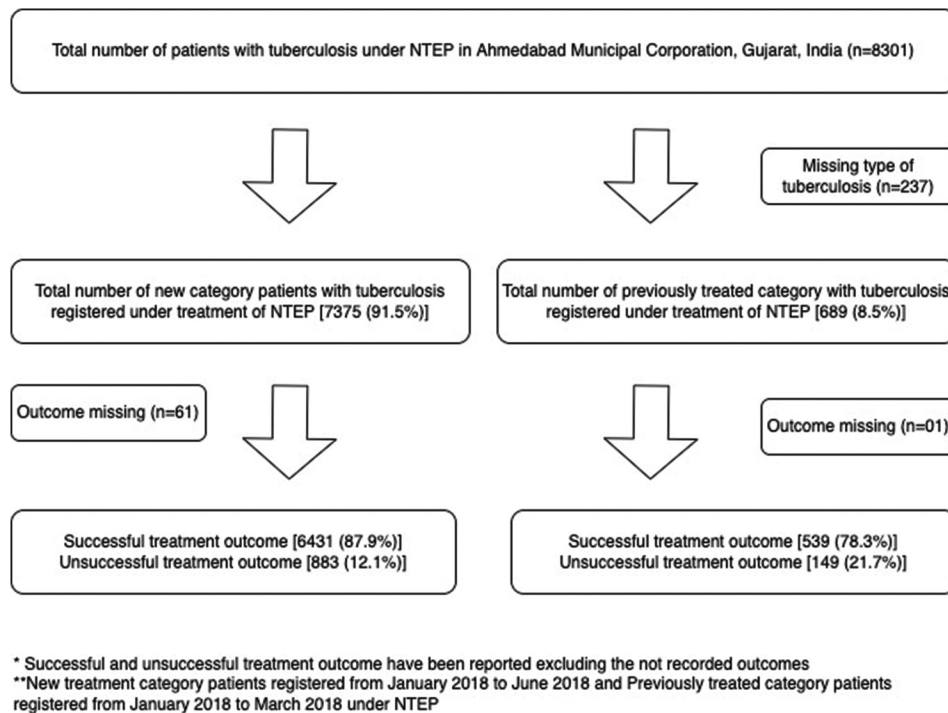
*Adherence technologies:* To improve TB treatment adherence, various interventions targeting the health system, social situation, and patients have been introduced. With the expansion of mobile and cellular access in high TB burden countries like India, digital adherence technologies (DATs) and information and communication technologies (ICT) may facilitate alternative approaches for improving treatment adherence of TB patients. These technologies range from short messaging service of cell phone to digital pillboxes to ingestible sensors namely electronic medication packing, medical event reminder monitor (MERM), video DOT, and 99 DOTS (phone-based adherence technology). DATs are being widely employed in efforts to help TB patients complete their treatment, which lasts for months or years.<sup>[12,13]</sup>

#### Study duration

From January 2018 to December 2019.

#### Study design

This was a retrospective cohort study based on record review from all the 75 DMCs, 23 TUs, and District TB Center under NTEP in AMC.



**Figure 1:** Flowchart of patients with drug-sensitive tuberculosis registered under “new category” and “previously treated category” of NTEP Ahmedabad Municipal Corporation in 2018 (Nikshay portal) NTEP = National Tuberculosis Elimination Program

### Sample size and sampling

The study population included all patients with drug-sensitive TB, registered and initiated on treatment under NTEP “new category” from January to June 2018 and under “previously treated category” from January to March 2018. The study duration for the two categories was selected purposively to enable us to study the outcomes at the end of the data collection period (March 2019). Patients diagnosed and referred for treatment initiation to other peripheral health institutions (PHIs) outside the study area were excluded. A total of 8301 patients with DS-TB registered under NTEP during the study period were included in the study.

Since a comprehensive sample was taken, no sampling was done.

### Data collection

A list of eligible drug-sensitive TB patients who underwent treatment (new category from January to June 2018 and previously treated category from January to March 2018) was downloaded from Nikshay. The principal investigator (PI) carried out the record review and data abstraction.

Below are the operational definitions for the type of case and standard TB treatment outcomes.<sup>[11,14]</sup>

New case is defined as a TB patient who has never had treatment for TB or has taken antituberculosis drugs for less than 1 month.

*Previously treated case* (recurrent TB case, treatment after failure, treatment after loss to follow-up, other previously treated patients) is defined as patients who have received 1 month or more of anti-TB drugs in the past.

*Microbiologically confirmed TB case* is defined as a presumptive TB patient with biological specimen positive for acid-fast bacilli (AFB) or positive for *Mycobacterium tuberculosis* on culture or positive for TB through quality-assured rapid diagnostic molecular test.

*Clinically diagnosed TB case* is defined as a presumptive TB patient who is not microbiologically confirmed, but has been diagnosed with active TB by a clinician on the basis of X-ray abnormalities, histopathology, or clinical signs, with a decision to treat the patient with a full course of anti-TB treatment.

*Cured patients* are microbiologically confirmed TB patients at the beginning of treatment, who were smear or culture negative at the end of the complete treatment.

*Treatment completed:* A TB patient who completed treatment without evidence of failure or clinical deterioration, but with no record to show that the smear or culture results of biological specimen in the last month of treatment was negative, either because the test was not done or the result was unavailable.

*Failure:* A TB patient whose biological specimen is positive by smear or culture at the end of the treatment.

*Lost to follow-up:* A TB patient who has taken treatment for a month or more, and whose treatment was interrupted for one consecutive month or more.

*Not evaluated:* A TB patient for whom no treatment outcome is assigned. This includes former “transfer-out” patients.

*Successful treatment outcomes:* A TB patient who is either cured or has undergone complete treatment is accounted in treatment success outcomes.

*Drug-sensitive TB:* Drug susceptible refers to patients who do not have evidence of infection with strains resistant to rifampicin (i.e., not rifampicin-resistant or multidrug-resistant TB).

### Data variables and source of data

Data variables were downloaded from Nikshay. The independent variables collected were age, gender, HIV status, treating facility, site of TB, type of case, basis of diagnosis, and method of adherence technology used. Date of diagnosis, treatment initiation, and treatment completion were also noted. The dependent variables were treatment outcomes grouped into successful and unsuccessful outcomes.

### Data analysis

#### Quantitative

Quantitative data downloaded from Nikshay in Excel format was imported and analyzed using EpiData analysis software version 2.2.2.182 (EpiData Association, Odense, Denmark). Descriptive statistics like number and proportion were calculated for demographic factors such as age (in group), sex, and clinical characteristics of the patients, namely, type of TB (pulmonary/extra pulmonary [EP]), category of TB (new/previously treated), basis of diagnosis (microbiologically confirmed/clinical TB), HIV status, and treatment outcome (categorized as successful and unsuccessful treatment outcomes). Mean (standard deviation [SD]) of age and median (interquartile range [IQR]) of duration of treatment were reported depending on normality of the data. Association of these variables with successful and unsuccessful outcomes was studied using bivariate log binomial regression. Adjusted relative risks (aRR) with 95% confidence interval were calculated using cluster-adjusted generalised linear model – Poisson regression which includes the factors with  $P < 0.2$  in bivariate log binomial regression for assessment of the association of demographic and clinical factors with TB treatment outcome. A  $P$  value of 0.05 was considered statistically significant. The findings have been reported by using Strengthening the Reporting of Observational studies in Epidemiology (STROBE) guidelines.<sup>[15]</sup>

#### Ethical issues

Ethics approval was obtained from the Institutional Ethics Committee of Gujarat Cancer Society (GCS) Medical College, Ahmedabad, India, and from the Ethics Advisory Group of the International Union Against Tuberculosis and Lung Disease, Paris, France. A waiver for informed consent was obtained from

the ethics committees as the study was based on secondary data and no patient contacts were made. Administrative permission was obtained from District TB Officer, Ahmedabad.

## Results

### Demographic and clinical characteristics of drug-sensitive TB patients

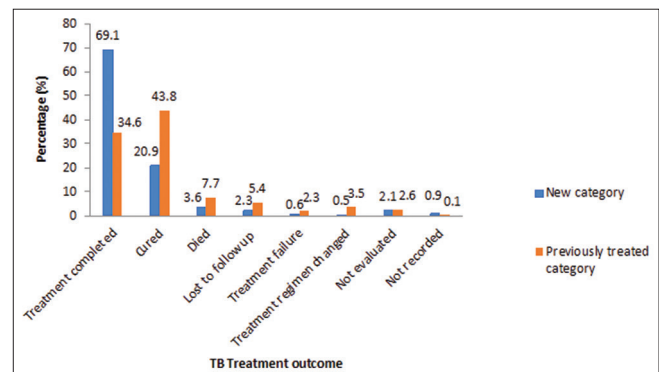
A total of 8301 patients with DS-TB registered under NTEP during the study period were included in the study [Figure 2]. Mean (SD) age of DS-TB patients was 35.3 + 16.9 years, and 63.2% were in the age group of 15–44 years. Of the 8301 patients, 4774 (60.1%) were male. Also, 195 (2.5%) were HIV positive, 5188 (65.3%) were pulmonary TB cases, and 5593 (70.4%) obtained treatment from public providers. The demographic and clinical characteristics have been described in Table 1. There were 7142 (89.9%) DS-TB patients registered under new category and 688 (8.7%) DS-TB patients registered under previously treated category. Data of 115 (1.4%) patients were missing in “type of TB,” which were excluded from adjusted analysis.

Median (IQR) time taken from TB diagnosis to treatment initiation, treatment initiation to treatment completed, diagnosis to treatment completed in new category patients with unsuccessful treatment outcome was 2 days (0–6), 38 days (6–106), and 62 days (26–133), respectively, and in previously treated category patients with unsuccessful treatment outcome was 2 days (1–9), 50.5 days (16.75–162.75), and 59 days (22–184), respectively (data not tabulated).

Among patients treated with daily FDC regimen, overall successful and unsuccessful treatment outcomes were 86.4% and 12.8%, respectively, while among 0.8% of patients, the outcomes were not recorded [Table 1].

### Treatment outcome among patients with drug-sensitive TB

Proportion of “successful” (cured and treatment completed) and “unsuccessful” (died, treatment failure, treatment changed,



**Figure 2:** Treatment outcome among patients with drug-sensitive tuberculosis who were initiated treatment as the “new category” and “previously treated category” under NTEP at Ahmedabad Municipal Corporation in 2018. NTEP = National Tuberculosis Elimination Program



**Table 1: Demographic and clinical characteristics of drug-sensitive TB patients registered as “new category” from January to June 2018 and as “previously treated category” from January to March 2018 in Ahmedabad Municipal Corporation**

Characteristics	Total	
	n	(%)
Total	8239	
Age group (in years)		
<15	458	(5.6)
15-24	2162	(26.2)
25-34	1932	(23.4)
35-44	1223	(14.8)
45-54	1100	(13.4)
55-64	794	(9.6)
≥65	570	(6.9)
Gender		
Male	4986	(60.5)
Female	3249	(39.4)
Others	3	(<0.1)
Not recorded	1	(<0.1)
HIV status		
Reactive	203	(2.5)
Nonreactive	4977	(60.4)
Unknown	3059	(37.1)
Not recorded	2	(<0.1)
Site of TB		
Pulmonary	5140	(62.4)
Extrapulmonary	2602	(31.6)
Not recorded	497	(6.0)
Type of TB		
New	7314	(88.8)
Previously treated	688	(8.4)
Not recorded	237	(2.9)
Treatment place		
Public	5828	(70.7)
Private	2411	(29.3)
Adherence method		
Conventional	8091	(98.2)
99 DOTS	148	(1.8)
Treatment outcome		
Successful	6970	(84.6)
Unsuccessful	1032	(12.5)
Not recorded	62	(0.8)

99 DOTS=directly observed treatment short course, HIV=human immunodeficiency virus, TB=tuberculosis

lost to follow-up, and not evaluated) outcomes was 87.9% and 12.1%, respectively, in the new treatment category and 78.3% and 21.7%, respectively, in the previously treated category [Tables 2 and 3, Figure 2].

### Association of demographic and clinical factors with TB treatment outcome of patients with drug-sensitive TB

Among patients classified under new category, the unsuccessful treatment outcome remained significantly high after adjustments with known confounders [Table 2] among patients aged

45–54 years (aRR 1.59, 95% confidence interval [CI] 1.31–1.93), 55–64 years (aRR 1.67, 95% CI 1.36–2.05), and ≥65 years (aRR 2.05, 95% CI 1.67–2.53) compared to patients aged <15 years. The unsuccessful treatment outcome was significantly higher among a) HIV-reactive status (aRR 1.73, 95% CI 1.16–2.57) and unknown HIV status (aRR 1.46, 95% CI 1.24–1.72) compared to HIV negatives, b) patients with pulmonary TB (aRR 1.68, 95% CI 1.41–2.01), and c) patients taking treatment from public health-care providers (aRR 2.16, 95% CI 1.85–2.54). However, unsuccessful treatment outcome was not influenced by any of the factors among patients treated as previously treated category, except age <15 years (aRR 2.48, 95% CI 1.41–5.40) [Table 2].

## Discussion

Daily regimen for NTEP along with FDC, as well as categorization of TB patients into new and previously treated categories was initiated in AMC in October 2017. These treatment guidelines were initially piloted for TB–HIV coinfecting patients.<sup>[3,16]</sup> Till date, quite a few studies have been done on outcomes with daily regimen and FDC in Gujarat, focusing more on 99 DOTS and TB–HIV patients. However, a few studies have been done so far to compare the treatment outcomes between the new and previously treated DS-TB patients in India, which has been attempted in the current study.<sup>[3,17]</sup>

### TB treatment outcome among different categories of patients

This study reported successful treatment outcomes (more than 7.90% and 78.3% in new and previously treated patients, respectively). Patients aged ≥45 years, HIV positives, pulmonary TB, and treatment in a public facility had higher rates of unsuccessful treatment outcomes among patients initiated on treatment under new category. Similar findings were also observed in another study conducted in Eastern Cape, South Africa.<sup>[18]</sup> However, the same factors did not affect unsuccessful treatment outcomes of patients in the previously treated category, except for age <15 years.

The age and gender precedence of the patients was in accordance with the epidemiology of TB.<sup>[19–21]</sup> Almost one-tenth of the patients in the new category and one-fifth of the patients in the previously treated category had unsuccessful treatment outcomes. Other studies related to TB treatment outcomes have shown an overall treatment success rate of 74%–95%.<sup>[22–25]</sup> A success rate of around 85% in our study reflects the effective functioning of NTEP in Gujarat. Further exploratory studies in this regard to understand the contextual factors for lower treatment success rates in previously treated category of patients and for identification of the subgroups may be undertaken.

We tried to focus on the factors associated with unsuccessful treatment outcomes to inform the program managers about possible areas of focus (related to patients’ demographic and clinical characteristics) during treatment initiation.

**Table 2: Association of demographic and clinical factors with TB treatment outcome of patients with drug-sensitive TB registered as “new category” from January to June 2018 in Ahmedabad Municipal Corporation**

Characteristics	Total		Unsuccessful treatment outcome		Unadjusted RR	Adjusted RR (7314 cases included)
	n	(%)	n	(%)		
	7314		883	(12.1)		
Age group (years)						
<15	441	(6.0)	44	(5.0)	1.21 (0.88-1.65)	1.32 (1.00-1.76)
15-24	1982	(27.1)	164	(18.6)	Ref.	Ref.
25-34	1700	(23.2)	193	(21.9)	1.37 (1.13-1.67)	1.26 (1.07-1.50)
35-44	1068	(14.6)	115	(13.0)	1.30 (1.04-1.63)	1.12 (0.92-1.37)
45-54	925	(12.6)	143	(16.2)	1.87 (1.51-2.31)	1.59 (1.31-1.93)
55-64	690	(9.4)	109	(12.3)	1.91 (1.52-2.39)	1.67 (1.36-2.05)
≥65	508	(6.9)	115	(13.0)	2.74 (2.20-3.40)	2.05 (1.67-2.53)
Gender						
Male	4342	(59.4)	602	(68.2)	1.47 (1.29-1.68)	1.15 (1.02-1.30)
Female	2969	(40.6)	280	(37.7)	Ref.	Ref.
Others	2	(<0.1)	1	(0.1)	3.53 (0.71-17.58)	3.52 (1.20-10.31)
HIV status						
Reactive	178	(2.4)	46	(5.2)	2.59 (2.00-3.38)	1.73 (1.16-2.57)
Nonreactive	4457	(60.9)	444	(50.3)	Ref.	Ref.
Unknown	2679	(36.6)	393	(44.5)	1.47 (1.30-1.67)	1.46 (1.24-1.72)
Site of TB						
Pulmonary	4510	(61.7)	448	(50.7)	1.53 (1.29-1.82)	1.68 (1.41-2.01)
Extrapulmonary	2468	(33.7)	160	(18.1)	Ref.	Ref.
Not recorded	336	(4.6)	275	(31.1)	12.62 (10.78-14.79)	13.11 (10.90-15.78)
Treatment place						
Public	5010	(68.5)	628	(71.1)	1.13 (0.99-1.30)	2.16 (1.85-2.54)
Private	2304	(31.5)	255	(28.9)	Ref.	Ref.
Adherence method						
Conventional	7188	(98.3)	848	(96.0)	2.35 (1.76-3.14)	2.11 (1.33-3.34)
99 DOTS	126	(1.7)	35	(4.0)	Ref.	Ref.

99 DOTS=directly observed treatment short course, HIV=human immunodeficiency virus, RR, relative risk, TB=tuberculosis

### HIV–TB correlation and TB treatment outcome

HIV-reactive and pulmonary cases showed higher unsuccessful outcome among both new (statistical significance among new category of patients) and previously treated DS-TB patients. The proportion of unsuccessful outcome was higher in new pulmonary DS-TB patients compared to previously treated DS-TB patients.

It is a known fact that overall unsuccessful outcome in TB–HIV coinfection is high.<sup>[18]</sup> Among unsuccessful outcome, HIV reactivity (positive) was 25.3% in new category and 33.3% in previously treated category. Similar findings were reported in other studies which showed higher proportion of unsuccessful outcomes in HIV-coinfected cases.<sup>[26,27]</sup> Our study findings may not be conclusive or generalizable since the HIV–TB infection rate was low in our study. Also, we have not studied the HIV–TB patients exclusively.

No evidence for higher risk of unsuccessful outcomes could be found in previously treated pulmonary TB cases. The reason could be treatment failure, development of drug resistance, and patient-related behavior.<sup>[28]</sup>

Various studies, including systematic reviews, have been carried out to know if daily regimen has a better impact on outcomes,

compared to intermittent therapy.<sup>[29]</sup> A couple of studies have found that daily regimen leads to higher rates of good treatment outcomes and lower incidence of acquired drug resistance.<sup>[30,31]</sup> One of the studies from Karnataka shows that daily regimen is not as effective as intermittent regimen (thrice weekly) in terms of outcomes.<sup>[32]</sup> A study showed that the new treatment category was less likely to have unsuccessful treatment outcome compared to the previously treated category on intermittent drug regimen.<sup>[33]</sup> Since the evidence base is limited and varied, this study gives an idea of early-stage implementation results of FDC daily regimen.

### Impact of adherence system on outcome

Few studies have been conducted to know the impact of adherence system (99 DOTS, MERM, manual) on treatment outcomes. However, in our study, this adherence mechanism was introduced at a later stage of study duration, and hence, association of the same with outcomes was not feasible. The same can be conducted in a future cohort to look for the impact of adherence mechanisms on treatment outcome in DS-TB patients.

Considering that studies on impact and treatment outcome of new cases and previously treated cases with FDC are scarce in the

**Table 3: Association of demographic and clinical factors with TB treatment outcome of patients with drug-sensitive TB registered as “previously treated category” from January to March 2018 in Ahmedabad Municipal Corporation<sup>a</sup>**

Characteristics	Total		Unsuccessful treatment outcome		Unadjusted RR
	n	(%)	n	(%)	
	688		149	(21.7)	
Age group (years)					
<15	8	(1.2)	1	(0.7)	Ref.
15-24	133	(19.3)	22	(14.8)	1.32 (0.20-8.61)
25-34	181	(26.3)	38	(25.5)	1.68 (0.26-10.74)
35-44	119	(17.3)	29	(19.5)	1.95 (0.30-12.53)
45-54	137	(19.9)	34	(22.8)	1.99 (0.31-12.71)
55-64	71	(10.3)	13	(8.7)	1.46 (0.22-9.77)
≥65	39	(5.7)	12	(8.1)	2.46 (0.37-16.34)
Gender					
Male	479	(69.6)	111	(74.5)	1.27 (0.92-1.77)
Female	209	(30.4)	38	(25.5)	Ref.
HIV status					
Reactive	13	(1.9)	5	(3.4)	1.73 (0.85-3.53)
Nonreactive	433	(62.9)	96	(64.4)	Ref.
Unknown	242	(35.2)	48	(32.2)	0.89 (0.66-1.22)
Site of TB					
Pulmonary	561	(81.5)	137	(91.9)	2.80 (1.56-5.01)
Extrapulmonary	126	(18.3)	11	(7.4)	Ref.
Not recorded	1	(0.1)	1	(0.7)	
Treatment place					
Public	658	(95.6)	144	(96.6)	1.31 (0.58-2.96)
Private	30	(4.4)	5	(3.4)	Ref.
Adherence method					
Conventional	666	(96.8)	144	(96.6)	0.95 (0.43-2.08)
99 DOTS*	22	(3.2)	5	(3.4)	Ref.

\*Indicates DOTS - Directly observed treatment strategy, HIV=human immunodeficiency virus, RR, relative risk, TB=tuberculosis. <sup>a</sup>Multivariate analysis was done for factors whose P value was <0.2 in above table

country, the results of this study may have several implications for policy and practice for the outcome-related factors. Knowing the factors associated with unsuccessful outcomes among new and previously treated cases of DS-TB in the initial cohort of daily regimen may help in focusing on patient-centric approaches and counseling strategies. Further focus on the impact of adherence mechanism and adverse events on outcomes with daily regimen may be undertaken.

Our findings do not show much difference in factors associated with outcomes in the new and previously treated categories. The current NTEP guidelines state same treatment regimen of daily FDC for new and previously treated categories. The underlying reason could be the same as reflected in our study, which may be one of the evidence for implementation of such newer guidelines.

### Strength of the study

Our study had the following strengths. To our knowledge, this is among a few studies reporting TB treatment outcomes among patients with DS-TB taking daily FDC regimen under existing programmatic setting. The study comprehensively included all the

patients enrolled for treatment in the study period and reported treatment outcomes.

### Limitation of the study

The study limitation was the record-based nature of the data variables. However, it is important to understand and study the factors influencing under routine programmatic settings, as in this study. It has also helped the investigators to report upon the “missing” or “not recorded” data in the Nikshay portal. The authors did not use any imputation method to include the missing data for adjusted analysis. It is important to note that the data were missing randomly (not tabulated). The study also missed to assess the effect of other potential confounders, especially the socioeconomic status and comorbidities.

### Conclusion

The low treatment success rate among patients with DS-TB in previously treated category can be further improved by studying the factors influencing the same comprehensively. Further efficient implementation of existing/new interventions related to HIV, poverty, and other social determinants should be researched upon. Various adherence mechanisms implemented can be evaluated for further upscaling and improving the program effectiveness.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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### Conflicts of interest

There are no conflicts of interest.

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