SenseDose Technologies

INDIAN INSTITUTE of PUBLIC HEALTH GANDHINAGAR

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Improving Adherence through Tuberculosis Medication Regimen using Tuberculosis Monitoring Encouragement Adherence Drive (TMEAD) Intervention in Nasik City of Maharashtra

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Abbreviations	Full Form
DAT	Digital Adherence Technology
DOT	Directly Observed Treatment
DSTB	Drug-Sensitive Tuberculosis
HBC	High Burden Countries
HIV	Human Papilloma Virus
ICT	Information and Communication Technology
MDR-TB	Multi-Drug Resistant Tuberculosis
MERM	Medication Event Reminder Monitoring
NTEP	National Tuberculosis Elimination Programme
PHC	Primary Health Center
QALYs	Quality Adjusted Life Years
RNTCP	Revised National Tuberculosis Control Programme
SDG	Sustainable Development Goals
TB	Tuberculosis
TBHVs	TB Health Visitors
TMEAD	Tuberculosis Monitoring Encouragement Adherence Drive
TU	Tuberculosis Units

Executive Summary

Medication adherence is one of the critical challenges to TB elimination in India. Poor medication adherence is associated with an increased risk of death, disease relapse, and the development of drug resistance. The digital adherence technologies (DAT) may have the potential to facilitate medication adherence and monitor adherence remotely. Among other DAT, the 99 DOTS, a cell phone-based DAT, has been implemented since 2015. Like any other technology, 99 DOTs, too, have certain challenges in the field practicum.

Thus, Tuberculosis Monitoring Encouragement Adherence Drive (TMEAD) is one of such modern DATs being piloted in one of the districts (Nasik) in Maharashtra from April 2020 to December 2021. This study had enrolled 400 DSTB patients, 200 each in the intervention and control arm. Overall, 261 patients completed treatment, 108 patients were on treatment, 15 patients died and 16 patients were defaulters over the study period. The study reported overall treatment adherence at 94% among those who completed treatment. Patient reported high levels of treatment adherence in the intervention group (99%) as compared to the Control group (90%). Adherence assessed through analysing trace of Rifampicin in urine sample for intervention arm was 84% compared to control arm (80%). Per beneficiary (discounted) cost for TMEAD was INR 6,573. Incremental cost effectiveness ratio of the intervention is INR 11,599 which shows the intervention is highly cost-effective.

This study concludes that, TMEAD could be an opportunistic DATs considering the above adherence, cost factors and could complement the national strategy of TB elimination by improving adherence to the treatment regimen in India.

Keywords: TMEAD, DAT, Adherence, Drug-sensitive Tuberculosis, cost-effectiveness, health technology assessment, India

Background

As per WHO report 2018, Tuberculosis (TB) is amongst the top 10 leading causes of mortality globally and one of the major killers among HIV-positive people. Approximately 10 million people have been infected with TB worldwide, and 1.6 million people died in 2017 [1]. The Sustainable Development Goals (SDG) envisages to ending TB by 2035 [2], while India aims to have it by 2025 [3].

India has a huge burden of TB accounting for roughly a quarter of the total global burden. WHO in 2015 came up with a concept of "high burden countries" (HBC) for TB, TB-HIV co-infection and Multi-Drug Resistant Tuberculosis (MDR-TB) wherein India was identified to have high burdens for all three of the TB [2]. The burden of TB in India is multifaceted, it not only deteriorates the people's health but also drains the country's economy. Evidence indicates that, the Indian Economy is predicted to bear a loss of $252.7 billion due to tuberculosis in the subsequent 15 years [4]. The economic burden laid by drug-resistant tuberculosis is nearly 10 times that of drug-sensitive tuberculosis [5].

On the one hand, the burden of tuberculosis varies within different regions of India as well. As per a systematic review, pooled prevalence estimates of DR TB and MDR TB from 2006-2015 were highest in Western India [6]. On the other hand, adherence to treatment is challenging, given the complexity, modest tolerability, and long duration of treatment regimens currently available for both drug-susceptible and -resistant TB. In turn, low adherence increases the risk of poor outcomes, including treatment failure, relapse, and development or amplification of drug resistance [7]. This double-edged challenge paves towards the unrealistic aim of eliminating TB by 2025 in the country.

To overcome such challenges, with the expansion of mobile phone and cellular access-digital adherence technologies (DATs) are facilitating as alternative approaches for improving adherence. These technologies range from cellphone short messaging service (SMS) texts, to

digital pillboxes, to ingestible sensors. DATs use cellular communication and other innovations to perform a variety of functions, including reminding patients to take medications, digitally observing doses taken and compiling dosing histories that can be used by healthcare providers (HCPs) to identify and intervene on non-adherence [8].

World Health Organisation (WHO) first pillar for TB elimination is to provide integrated, patient-centred care and prevention, various Information and Communication Technology (ICT) based strategies have been identified to improve the compliance of patients to treatment regimen [9]. To improve treatment regimen compliance, various DATs have been piloted in various parts of the world and found promising for scale-up.

Technology in Question

With an understanding of existing challenges of DATs, a Tuberculosis Monitoring Encouragement Adherence Drive (TMEAD) was piloted by a start-up in Maharashtra. TMEAD was designed and developed by SenseDose Technologies, a start-up venture supported through India Health Fund, an initiative of TATA Trust. TMEAD helps monitor and ensure patient compliance. It also creates a detailed, automated adherence dashboard of all patients for health workers and policymakers to prioritize their resources towards patient adherence [10]. The TMEAD device is a potential solution for both the patients and the TB control officers. Figure 1 provides an overview of the solution.

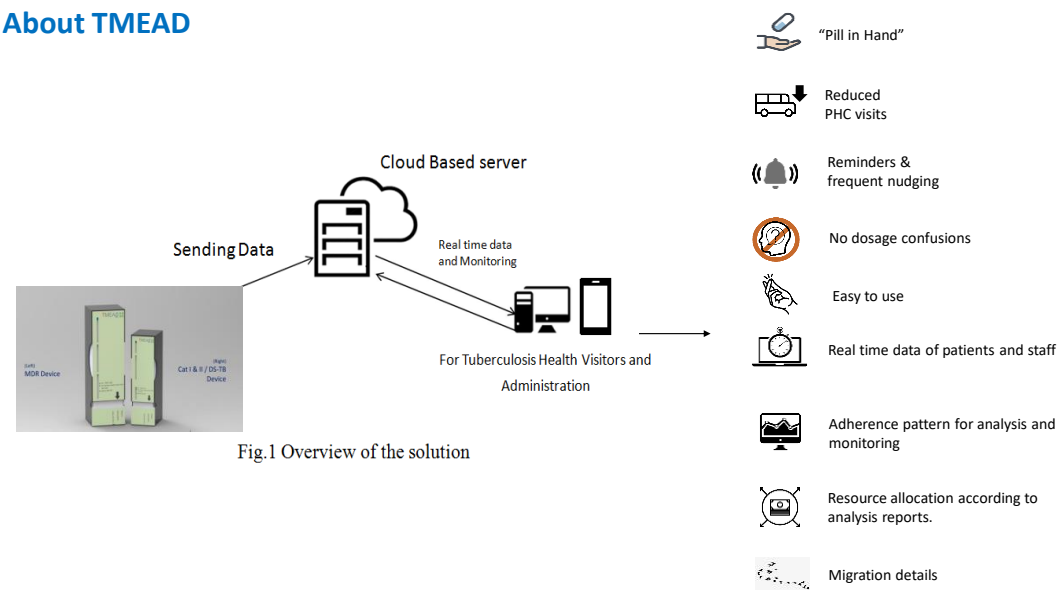

Fig.1 Overview of the solution

Figure 1:Overview of the solution

TMEAD platform includes:

- A physical device, is based on smart ICT technology that reminds, dispenses, and senses a patient's adherence to the RNTCP regime.
- A web-based application that provided real-time monitoring with daily updates and patient analytics to PHI and administration.
- Mobile application that provides instant update, quick view for the TBHVs when they are on the field.

Alternative Technology in Question (Comparator)

The usual care scenario includes the 99DOTS (another form of DATs) system for the purpose of monitoring the compliance of patients towards TB treatment. In 99DOTS, the patients are provided with an anti-TB blister pack is wrapped in a custom envelope, which includes hidden phone numbers that are visible only when doses are dispensed. After taking daily medication, patients make a free call to the hidden phone number, indicating that the dose has been taken. The 99DOTS patients receive a series of daily reminders (via SMS and automated calls). Missed doses trigger SMS notifications to care providers, who follow up with personal, phone-based counselling. Real-time adherence reports are also available on the web [11].

Rationale

As multiple DATs have been experimented with, there is currently insufficient evidence. There is currently insufficient evidence available on the clinical effectiveness and cost-effectiveness of using these digital health technologies to improve TB treatment adherence and outcomes. The paucity in evidence means that, at present, policymakers cannot make definitive evidence-based decisions regarding the wider implementation of these technologies.

Aims and Objectives

The study aims to assess the adherence (self-reported/digital/clinical) and cost effectiveness of the new DATs i.e. TMEAD, compared to the standard of care for the drug-sensitive tuberculosis (DSTB) patients residing in the urban geography of Nasik City in Maharashtra, India. The primary objective of the study is to measure treatment adherence with digital adherence technology (TMEAD). And the secondary objective of the study is to validate the adherence through urine rifampicin levels.

The specific objectives are-

1. To measure treatment adherence (self-reported/digital) of the TMEAD as compared to the standard of care
2. To validate the adherence (clinical) through urine rifampicin levels
3. To estimate the cost-effectiveness of the new DATs., i.e. TMEAD

PICOT

Participants: All patients detected and enrolled as per the definition of NTEP in selected TUs of Nasik Urban area

Intervention: Use of digital adherence technology as a reminder for adherence to treatment

Comparator: Standard treatment of Care

Outcome:

Primary Indicators

a) Daily dose adherence
b) Treatment completion rate

Secondary Indicators

Acceptability and feasibility for scale-up

Methods

Study settings

A prospective follow-up of new cases of TB as per NTEP residing in the urban geography of the city of Nasik was done from purposively selected non-contaminating TUs. Urban Nasik is spread across 5 TU, the TU were assigned into Two arms, ensuring that they are geographical apart and reducing the possibility of contamination. The participants were then divided randomly into two arms – intervention and control. Ethical permission for the study was obtained from the institutional ethics committee of Indian Institute of Public Health Gandhinagar prior to data collection. Permission from Nasik City TB office was also taken.

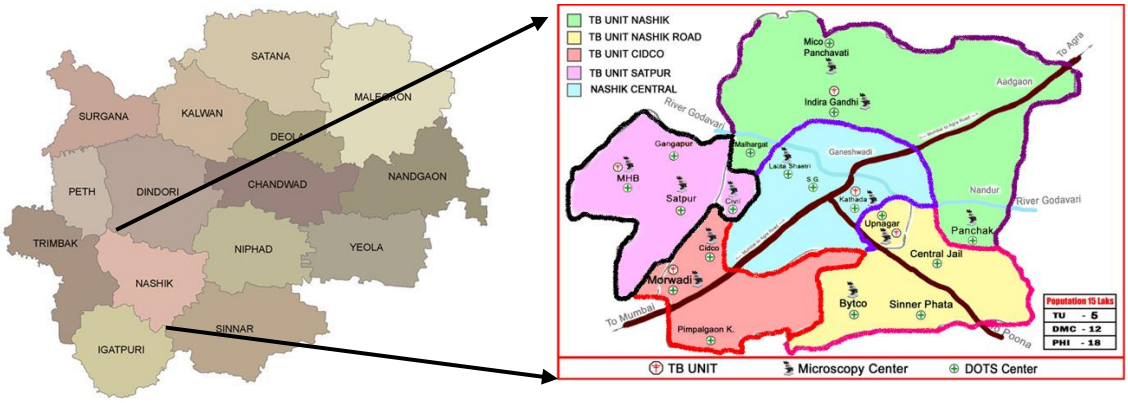

Figure 2: **Geographical distribution of TB unit of Nashik district, Maharashtra, India**

Study Type

Present study is a mixed-method (Primary & secondary) type of study which includes:

The primary component consists of

1. Quantitative Methods: A longitudinal follow up of the patients assigned to two arms Intervention and Control arm
2. Qualitative Methods: Key Informants interview and In-depth interviews of the family members and DOTS supporters to document the acceptance of technology and challenges if any.
3. Non-invasive urine sample collection for the rifampicin analysis

The secondary component consists of

4. Calculating cost of care and cost effectiveness.

Study sample & sampling

All newly diagnosed TB patients at selected TU as per the NTEP protocols.

Inclusion Criteria:

a) Newly diagnosed patients detected and enrolled as per the NTEP in selected TU.
b) More than 18 years of age
c) Giving consent to be a part of study and
d) Residing in the urban area of Nasik

Exclusion Criteria:

a) Seriously ill patients other than Category 1 TB, including any Drug-resistant TB patients
b) Not willing to provide consent to be part of the study

Sample size for Quantitative study

Sample sizes for Longitudinal follow up: Based on an assumption of an increase in the adherence to TB treatment from 80% (as cited from available literature to 95% (as desired under NTEP guideline) with 95% CI and 80% power and 20% of Drop Out / Non-response / Attrition, the sample size in each of the arm was 200.

Sample Size for Urine Analysis: Biological tests of drug ingestion (e.g., urine/serum testing for Isoniazid and Rifampicin content) with 20% of the sample in control and intervention arm each in 3 cycles was analysed.

Data Collection Methods

For Quantitative methods: The quantitative survey included the collection of patient's demographic details from the selected TUs, and ensured the baseline matching of the study participants in both the arms. Once the patients were enrolled in the Intervention Arm the TMEAD device was provided. A trained Research Staff engaged with the patient and the household member in explaining the mechanism of functioning of the box and also explained the finer details like when to charge, how to remove the tablet box from the TMEAD device, what if the medicine pill packets have not been removed and also the response mechanism is not removed. The patient in the intervention arm was also informed about the follow-up protocol. The control arm was to be followed up as per the national guidelines. As per the protocol, the study participants were followed for six months longitudinally from the start of their treatment to assess the outcome of treatment. The patients' treatment outcome was categorized into successful treatment, failure, which includes defaulters as well as treatment failure and death (if any). It was also proposed to document the adherence to the treatment in both the control as well the intervention arm in terms of the pill count. It was also proposed to validate the adherence and to validate the adherence for drug consumption beyond recall method i.e. 24 hrs Urine testing for Rifampicin content was proposed in both the control and intervention arm.

Operational Definitions

Adherence: Extent to which the patent's prescribed dosing regimen is followed; where the denominator comprises of the number of days into treatment (from treatment initiation date) and the numerator includes the number of days for which the prescribed number of doses are taken. WHO also defines adherence to medication as the extent to which patients take their

medications as prescribed with respect to dosage and intervals throughout the treatment period [12]. For present study, the level of adherence was defined as the patients who have completed 80% of the dose for treatment completion.

Treatment completion: Standards of evidence for treatment completion (DS-TB) need to be recorded for DS-TB patients only if a verifiable record is available. This can be any one of the following

- Refill dispensing of a minimum of 168 days of drugs within 240 days (8 months) from the treatment initiation date, without evidence of treatment interruption of 1 month or more.
- Total Adherence for DSTB Regimen reported at least 168 days of daily doses (manual or digital recording) within 240 days (8 months) from treatment initiation date without evidence of treatment interruption of 1 month or more

The recruitment was done after two weeks of enrolment. Research team followed up the patients weekly to document patient experience with treatment. Samples for Urine Rifampicin were processed in a Laboratory of a tertiary care Medical college and Hospital. The samples collected were send under standard protocols and alpha numeric codes were used to blind the samples send for lab testing.

Quantitative tool includes factors that influence TB treatment regimen adherence. Baseline score of socio-economic variables (e.g., age, gender, housing type and asset ownership, etc. to assess income level, occupation, education level, etc.) were compared to drug compliance level (including distance to the clinic, level of support from family members). Other set of variables included those related to challenges faced regarding use of Box. The deployment of TMEAD device for DS-TB patients was initiated from April 2020. The patient was enrolled for the study till sample size was achieved. The patient was followed up till 31 December 2021 and their outcomes were collected. During each of the follow up adherence was assessed.

For Urine Rifampicin estimation: Adherence was assessed by analysing trace of rifampicin in urine among 20% of patients enrolled from both arms. The Presence of rifampicin was considered a confirmation of the dose taken in the given time period. High-Performance Liquid Chromatography (HPLC) method was used for urine analysis among the DSTB patients. The

first sample of urine was collected within IP phase, the second sample within 1 month and the third sample within next 1 month of the second sample. Cut off value of 100 microgram was considered for reporting 24 hours adherence to medication. Results were reported for sample positivity in any round.

For Qualitative Methods: To document the acceptance, adherence and issues to the technology intervention, it was decided to undertake Key Informants interview and In-depth interviews. It was proposed to include

a) Household members (Male and Female)
b) DOTS supporters and
c) Patient (stratified across gender)

An open-ended tool/checklist to cover various domains regarding facilitators, inhibitors and challenges to the technology intervention were added. KII / IDI were audio-recorded after the formal consent and were continued till all the responses were saturated. Trained research assistant undertook the KII and IDI and thematic analysis was done.

Valuing of Health outcomes

Health-related quality of life (HRQoL) was assessed using the EQ-5D-5L tool at baseline and first follow-up. The tool has five domains, namely mobility, self-care, usual activities, pain/discomfort, anxiety/depression. Given score range from 1 to 5, with 1 being the worst and 5 the best [13]. The level of problem reported on each of the EQ-5D dimensions determines a unique health state. Health states were converted into a weighted health state index by applying scores from the EQ-5D preference weights elicited from general population samples using the Crosswalk Index calculator [14]. These weights lie on a scale on which full health has a value of 1 and dead a value of 0. For this study, Thailand population weights were used to convert to an EQ-5D index score.

Secondary: Measuring the cost of care

Cost Data

The cost related to TMEAD devices was obtained from the implementing partner. The cost was calculated under the three costing heads – manufacturing cost, variable costs and Human Resource cost. Assumption (based on the field practical experiences), each device can be reused twice.

The cost related to the standard of care was obtained from the secondary literature by taking the mean of the costs by adjusting it with GDP deflater rate [15-17]. All future costs and consequences were discounted at 3% as per WHO guidelines.

Conceptual framework for Decision tree model

A decision tree was parameterized on MS Excel spreadsheet to estimate the change in QALYs and cost from a societal perspective. In the decision tree model, the intervention (TMEAD) was compared to the Control arm (Standard of care). The Adherence was categorised into full adherence (patient's achieving above 90% of adherence), partial adherence (between 80-90%) and non-adherence (below 80% adherence). Treatment outcomes like treatment completed, Treatment extended, death and defaulter were modelled to estimate QALY gained. For modelling purpose, we have excluded patients who were on treatment.

Transition Probability were derived from primary as well as secondary literature. The transition probability of the TMEAD and Standard of care was calculated based on the proportion distribution of the patients under each adherence category. The probability of the TMEAD device for full adherence for the treatment completed group, for treatment extended group, death and defaulter were calculated from the proportional distribution of the patients under each outcome. Likewise, the probability of the TMEAD device for partial adherence and non-adherence were calculated from the proportional distribution of the patients with respect to each treatment outcome. The transition probability of QALYs were calculated using EQ-5D utility value (Thailand index) for the full adherence, partial adherence and non-adherence group. The cost of the treatment by TMEAD device were calculated from the per-beneficiary cost of the TMEAD device. Further, the cost of treatment by TMEAD device was apportioned to adherence category i.e full adherence, partial adherence and non-adherence. The cost of full adherence was apportioned to treatment completed, treatment extended, death and defaulter Similarly, the cost of partial adherence and non-adherence were calculated with each treatment outcome. The cost of death and defaulter under full adherence and partial adherence was zero as there were no deaths and defaulter in that group. The average age of the cohort was reported from the primary data. The same calculations were applied for the control arm. The transition probability table is an appendix as supplementary table 2. Decision tree model was developed and prepared by using TreeAge Pro Software Healthcare Version 2022 R.1 as shown in Figure 3.

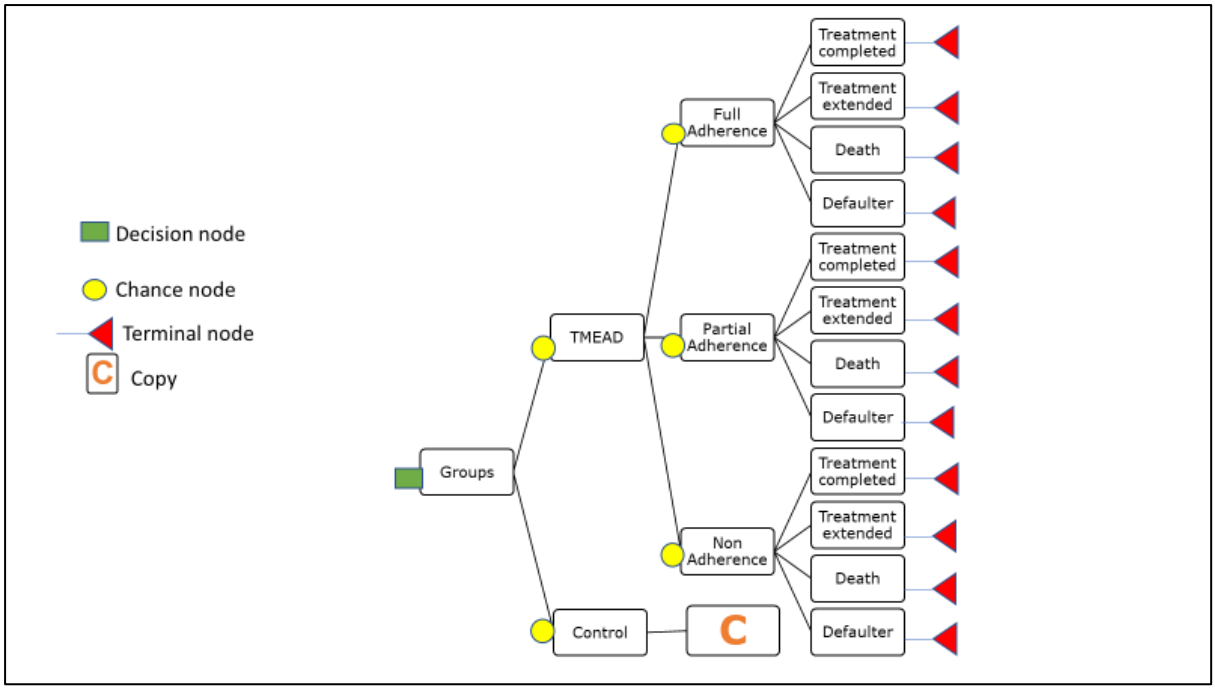

Figure 3:Decision tree model

Measuring the cost-effectiveness

The total cost and total QALYs gained for the interventions and control were calculated from the decision tree model. Incremental cost/QALY was the difference in the total cost/QALY between the intervention and control. ICER was obtained by taking the ratio of incremental cost and incremental QALY. The CEA results was expressed in cost per QALY gained. Time horizon of the study was one year and 3% discounting was applied. We applied Gross Domestic Product (GDP) per capita based on WHO guideline for willingness to pay threshold, and considered ICER of less than GDP per capita as highly cost-effective. In our study, India's 2020 GDP per capita of INR 1,45,679 has been considered the cost-effectiveness threshold value per QALY gained. One-way sensitivity analysis was carried out by varying model parameters to estimate uncertainty in all parameters. A tornado chart is presented using ICER values to depict changes in selected variables that influence the results.

Results

Quantitative findings

The present study was conducted in the urban area of the city Nasik where a total of 400 patients were enrolled. The patients were allocated in two arms, intervention and control arm. As per the NTEP and based on administrative feasibility, Nasik is divided into 5 TUs. Efforts were made done to include TUs in the respective arm which were non-contaminating. Table 1 presents TU-wise patient enrolments in the intervention and control arm.

Table 1:TU Wise Distribution Patients enrolled in the Study

TB Unit	Intervention (%)	Control (%)	Total (%)
Central TU	0(0)	59(30)	59(15)
CIDCO TU	86(43)	0(0)	86(22)
Nasik road TU	114(57)	0(0)	114(29)
Panchavati TU	0(0)	70(35)	70(18)
Satpur TU	0(0)	71(36)	71(18)
Total	**200 (50)**	**200 (50)**	**400 (100)**

Sociodemographic Profile

Sociodemographic characteristics of the patients in the intervention and control arm are presented in Table 2. The study had 43.8% male participants and 56.3% Female participants. The mean age of the patients was 37 (SD±14) years ranging from (18-92) years. It was observed that around one-third of the participants were from the open category, 34.5% and 33.5% in intervention and control arm respectively.

The majority of the patients (89.3%) were Hindu, 91% and 87.5% in intervention and control arm respectively. Overall, the literacy level was low (37.5%), about 70% in the intervention arm and 55% in the control arm were illiterate. It was observed that 47.3% of the patients were unemployed, which was 40.5% and 54% in the intervention and control arm respectively. One-third of the population was BPL which included 36% and 32.5% in intervention and control arm respectively. The average family size was 4 and the average monthly expenditure in the household was INR 2,414, INR 2,010 and INR 2,628 in the intervention and control arm respectively.

***Table 2:*Baseline sociodemographic characteristics of the study participants**

Variables	Intervention (%)	Control (%)	Total (%)
Gender			
Male	88(44)	87(43.5)	175(43.8)
Female	112(56)	113(56.5)	225(56.3)
Age group (in years)			
18 to 20 Years	15(7.5)	21(10.5)	36(9)
21 to 30 Years	66(33)	70(35)	136(34)
31 to 40 Years	45(22.5)	44(22)	89(22.3)
41 to 50 Years	38(19)	33(16.5)	71(17.8)
51 to 60 Years	25(12.5)	19(9.5)	44(11)

61 Years & Above	11(5.5)	13(6.5)	24(6)
Age in Mean Years	37	37	37 (18-92)
Caste			
General/Open	69(34.5)	67(33.5)	136(34)
S.C/S. T	79(39.5)	57(28.5)	136(34)
O.B.C	52(26)	76(38)	128(32)
Religion			
Hindu	182(91)	175(87.5)	357(89.3)
Muslim	15(7.5)	25(12.5)	40(10)
Others	3(1.5)	0(0)	3(0.8)
Education			
Literate	60(30)	90(45)	150(37.5)
Illiterate	140(70)	110(55)	250(62.5)
Marital status			
Unmarried	49(24.5)	51(25.5)	100(25)
Married	135(67.5)	142(71)	277(69.3)
Divorced/Widowed/Separated	16(8)	7(3.5)	23(5.8)
Occupation			
Unemployed	81(40.5)	108(54)	189(47.3)
Private employee	49(24.5)	55(27.5)	104(26)
Govt employee	8(4)	2(1)	10(2.5)
Laborer	59(29.5)	33(16.5)	92(23)
Self employed	3(1.5)	2(1)	5(1.3)
General Profile			
BPL Population	72(36)	65(32.5)	137(34.3)
Average Family Size of HH	5(1-18)	4(1-13)	4(1-18)
Monthly Expenditures in HH	2010(500-8000)	2628(0-25000)	2414(0-25000)

Treatment history

Among the patients included in the present study, in the intervention arm 41.5% were detected TB in 2020 and the rest in 2021. Overall, 61% of the patients in intervention arm were detected TB in government hospital, whereas only 49% among control arm were detected TB in the government setup. The median delay of 23 days in onset of the symptoms to diagnosis more in intervention arm (28 days) when compared to the control arm (20 days). However, there was no difference in duration between diagnosis and initiation of TB treatment between the intervention (3 days) and control (4 days). About 47% of the study population was having delay between diagnosis and treatment the reason might be due to Migration, Lack of acceptance, Lack of awareness/no answer, Lockdown and COVID-19 challenges and Poor health-seeking

behaviour. Majority (89.3%) of the study patients had chosen government facilities because of the free treatment which was affordable and convenient. Table 3 describes the treatment history of the study population.

Table 3:Treatment history

Variables	Intervention (%)	Control (%)	Total (%)
Year of TB Detection			
2020	83(41.5)	87(43.5)	170(42.5)
2021	117(58.5)	113(56.5)	230(57.5)
First Place of Diagnosis			
Government (Public)	122(61)	98(49)	220(55)
Private	78(39)	102(51)	180(45)
Delay in the onset of the symptoms to diagnosis (in days)	28	20	23
Delay in treatment initiation for TB (in days)	3	4	3
Reasons for the delay between diagnosis and treatment			
No Delay	124(62)	87(43.5)	211(52.8)
Provider asked me to wait until drugs become available	0(0)	1(0.5)	1(0.3)
Did not have time to go to Providers	9(4.5)	5(2.5)	14(3.5)
Others (specify) Migration Lack of acceptance Lack of awareness/no answer Lockdown and covid challenges Poor health seeking behaviour	67(33.5)	107(53.5)	174(43.5)
Reason for choosing Government facility			
Free Treatment/ Affordable and Convenient	166(83)	191(95.5)	357(89.3)
Easy to Access	6(3)	9(4.5)	15(3.8)
Trustworthy facilities	28(14)	0(0.0)	28(7)
Travel			
Mean Distance (KMs)	**5 (0-99)**	**5(2-25)**	**6km (0-99)**
Mean Time (Min)	**16(0-99)**	**25(5-60)**	**21 min (0-99)**

Clinical Outcomes and follow-up

As per the objective of the study, three longitudinal follow ups were done. All patients could be tracked in 1st follow-up. However, a total of 380 (95%) patients could be followed during the 2nd visit and 261 (71%) during the 3rd visit. Out of the remaining patients 108 were on treatment, 15 died and 16 patients were defaulters (Table 4). The most common reasons for attrition were migration and Covid-19 lockdown restrictions.

Table 4:Study Follow-up

Variables	Follow-up 1(N: 400)			Follow-up 2 (N:380)			Follow-up 3 (N:261)		
	Intervention (N: 200)	Control (N:200)	Total	Intervention (N:190)	Control (N:190)	Total	Intervention (N:122)	Control (N:139)	Total
Missed Any Doses									
Yes	39(19.5)	42(21)	81(20.25)	19(10)	151(79.5)	170(44.7)	9(7.3)	128(92.1)	137(52.5)
Missed Dose Duration (in hr									
Denominators			81			170			137
More than 24 Hr.	5(6.2)	13(16)	18(22.2)	0	0	0	0	0	0
Within 24 Hr.	34(41.9)	29(35.8)	63(77.7)	19(11.2)	151(88.8)	170(100)	9(6.6)	128(93.4)	137(100)
Reasons for it									
Due to Personal Negligence	28(34.6)	25(30.7)	53(65.4)	9(5.3)	73(43)	82(48.2)	9(6.6)	62(45.3)	71(51.8)
Due to Medicine _Side-effects	6(7.4)	0	6(7.4)	2(1.2)	17(10)	19(11.2)	0	0	0
Due to social Reason	0	5(6.2)	5(6.2)	2(1.2)	22(12.9)	24(14.1)	0	3(2.2)	03(2.2)
Due to travelling	5(6.2)	12(14.9)	17(21)	3(1.8)	23(13.5)	26(15.3)	0	43(31.4)	43(31.4)
No Answer	0	0	0	3(1.8)	16(9.4)	19(11.2)	0	20(14.6)	20(14.6)
Experienced any side-effects of your TB drugs									
Yes	87(65.9)	45(34.1)	**132(33)**	36(55.4)	29(44.6)	65(17.1)	0	0	0
Management of Side-effects									
Denominators			132			65			0
Self-Medication	06(4.5)	01(0.7)	07(5.3)	01(1.5)	01(1.5)	02(03)	0	0	0
Contacted HCP	26(19.7)	32(24.2)	58(43.9)	09(13.8)	16(24.6)	25(38.4)	0	0	0
No action taken	54(40.9)	11(8.3)	65(49.2)	25(38.4)	11(16.9)	36(55.3)	0	0	0
Stop TB medication without consultation temporary	01(0.8)	0	01(0.8)	01(1.5)	01(1.5)	02(03)	0	0	0
Stop TB medication without consultation permanent	0	0	0	0	0	0	0	0	0
Started alternate medication to manage side effects	01(0.8)	0	01(0.8)	0	0	0	0	0	0

Adherence

Adherence to treatment was calculated after the third follow-up. Overall adherence was 94% among those who completed treatment (Table 5). Adherence in the intervention arm was 99% compared to 90% in the control arm. The average adherence reported by TMEAD devices was 88.2% in intervention group. Point adherence among those who are on treatment was 97.4% with higher adherence reported in the intervention arm (98.7%) compared to 95.24% in control arm.

***Table 5:*Adherence (%) among DS-TB patients**

Treatment outcomes	Intervention (%)	Control (%)	Overall (%)
Treatment completed_ Adherence	122(99)	139(90)	261(94)
On Treatment _Point Adherence	66(98.7)	42(95.24)	108(97.4)
Technology_ Adherence	188(88.2)	-	188(88.2)

Urine rifampicin analysis

A 24 hours recall of drug consumption was elicited and those who had consumed the tablets were requested to give the urine sample. A total of 104 samples in the intervention arm were collected which included 40, 38 and 26 over 3 cycles respectively. However, in the control arm 108 samples were collected which included 40, 38 and 30 over 3 cycles respectively. The number of samples collected were more or less similar. However, the number of samples processed in intervention arm were 36, 32 and 22 respectively. Whereas in the control arm the number of samples processed were 37, 31 and 22 respectively. Hence, the number of samples processed in each cycle and overall were almost similar in both arms (Table 6).

It was observed that in the intervention arm out of the total samples processed in the 1st cycle, 90.6% had urine rifampicin traces. At the end of third cycles for urine sample collection in the intervention arm, 86.3% of samples were positive for urine rifampicin. Whereas, in the control arm 77.2% of the samples were rifampicin positive (Table 7).

Table 6: **Adherence as per Urine Analysis**

Treatment adherence	Urine samples			
	Proposed over 3 cycles	**Collected**	**Analyzed**	**Rifampicin trace above 100 mcg**
Intervention	120	104	90	76(84.44)
Control	120	108	90	72(80.00)
Total	240	212	180	148(82.22)

Table 7: **Urine Analysis across all rounds**

Group	Collection process	1st sample		2nd sample		3rd sample		Total
		N	%	N	%	N	%	
Intervention arm	Collected samples	**40**		**38**		**26**		104
	Processed	**36**		**32**		**22**		90
	Urine rifampicin present	**29**	**90.62**	**28**	**87.50**	**19**	**86.36**	
Control arm	Collected samples	40		38		30		108
	Processed	37		31		22		90
	Urine rifampicin present	30	81.08	25	80.64	17	77.27	

Health related Quality of Life (HQoL)

Health Related Quality of Life of patients were assessed using EQ5D5Ltool. We used EuroQol's Crosswalk value sets of Thailand using EQ5D5L profile. EQ5D5L utility index value was slightly higher in the control group as compared to intervention (Table 8).

Table 8: **EQ5D5L Index Values of study participants**

	Intervention	**Control**
EQ5D5L profile	12212	21113
Index score	0.626	0.666

Incremental Cost of TMEAD

Total Annualized cost of the program implementation for the intervention was INR 13,55,324. Table 9 shows summary of key cost and per beneficiary cost. Detail cost data for TMEAD is provided in the supplementary annexure. The intervention is INR 6,573. The per beneficiary cost for the standard of care was INR 4,764.

Table 9:Per beneficiary cost of the intervention (TMEAD Device)

Sr. No	**Particulars**	**Total Program Cost (INR)**	**Remarks**
1	Manufacturing Cost	2,03,486.17	Total 200 devices deployed.
2	Implementation Cost	1,73,424.10	Server support, SIM cost, SMS service, training, transportation & AMC/repairs
3	HR Costs	9,78,413.50	Cost of human resource included service engineer, app developer, web developer, electronics hardware engineer, program manager, helper, operation manager
Total Annualized cost		13,55,323.77	
Per Beneficiary Cost		6,573	Applying 3% discount

Cost-effectiveness Analysis

The total cost and total QALYs gained for the interventions and control were calculated from the decision tree model. Incremental cost/QALY was the difference in the total cost/QALY between the intervention and control. ICER was obtained by taking the ratio of incremental cost and incremental QALY. We applied Gross Domestic Product (GDP) per capita based on WHO guideline for willingness to pay threshold, and considered ICER of less than one GDP per capita as highly cost-effective. In our study, India's 2020 GDP per capita of INR 1,45,679 has been considered the cost-effectiveness threshold value per QALY gained. TMEAD incurs an incremental cost of INR 11,599.46 per QALY gained which is 0.07% of the per capita GDP of India. This suggests our intervention is highly cost-effective as compared to the control. Table 10 shows the results of cost-effectiveness analysis between Intervention and Control.

Table 10:Results of cost-effectiveness analysis between Intervention and Control

Outcomes	Intervention	Control
Cost (in INR) per patient treated as per modelling	6573	4764
Difference in Cost (in INR)	2042.17	
Difference in QALYs	0.176	
ICER	11,599.46	

Cost-effectiveness Plane

Figure 4 illustrates cost-effectiveness plane. Orange dot indicates ICER value which falls above the reference line and in first quadrant. It shows that our intervention is highly cost-effective as compared to the control.

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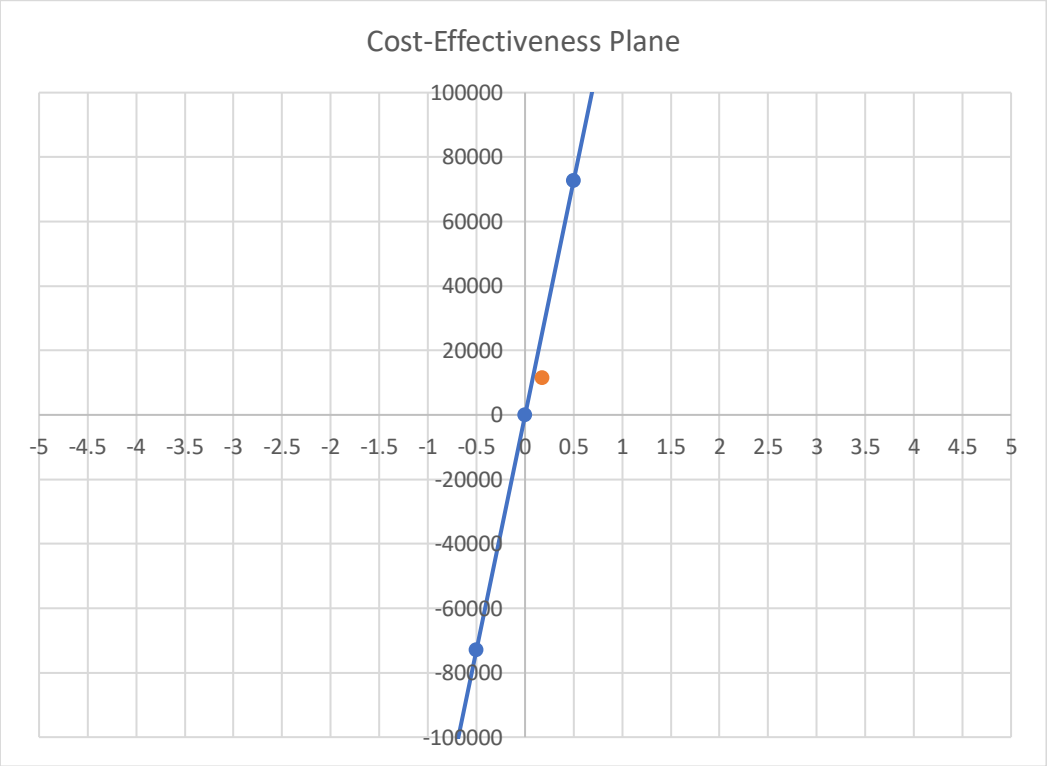

Figure 4: Cost-effectiveness plane of the study

One Way Sensitivity Analysis (OWSA)

In one-way sensitivity analysis, 95% CI values for utility values for the model input parameters were used and reported as tornado diagrams. Figure 5 presents results from simulations done as part of one-way sensitivity analysis. The tornado diagram of one-way sensitivity analysis shows that ICER value is slightly changed when the input parameters is changed in multiple indicators. The cost of control arm, the cost for full adherence in the treatment completed group, QALYs among the full adherent patients in both intervention and control arm, the cost for defaulters among partial adherent to control arm are key parameters that influence the model.

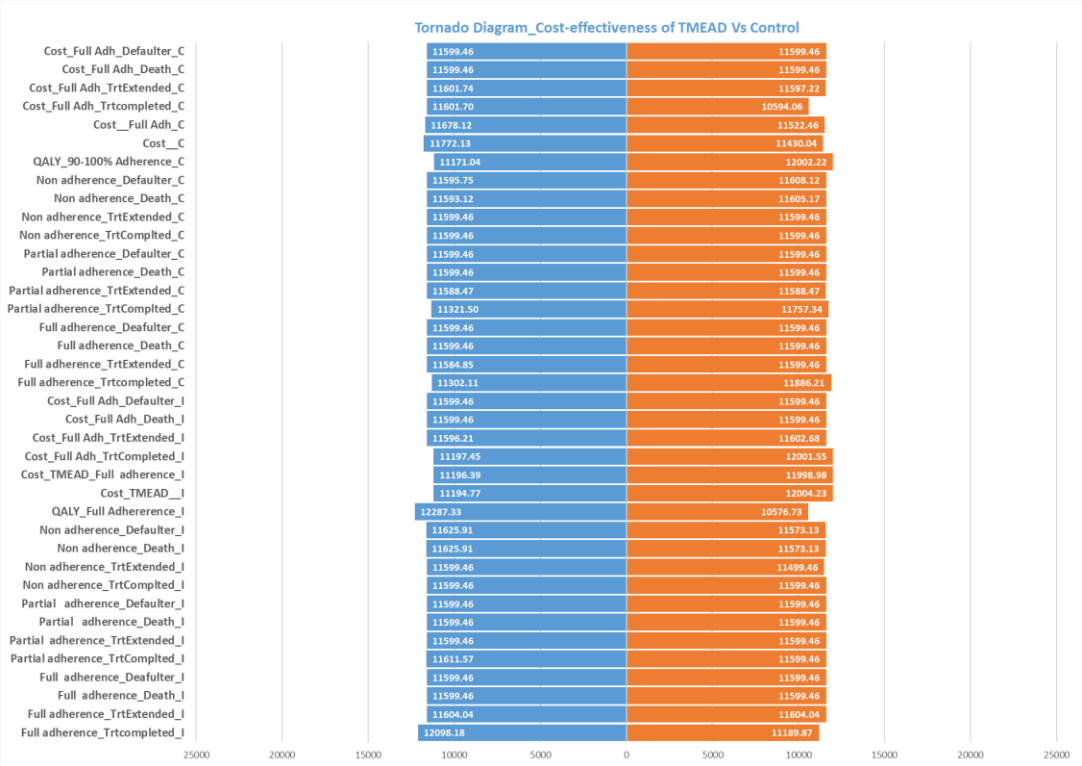

Figure 5:Tornado diagram of cost-effectiveness of intervention and control

Budget Impact Analysis

Budget Impact Analysis (BIA) has been performed to estimate the cost for the roll-out of TMEAD intervention at the State level (Maharashtra). The BIA has been performed at 2021 Prices. The BIA model was based on the above cost-effectiveness model for the intervention (TMEAD) and the Standard of care among DSTB patients. Only health- system costs were considered in the BIA.

The following assumptions were made in the BIA.

i) The annual economic model holds true for 5 years.

ii) The annual budget is based on unit cost of manufacturing, capital cost and HR cost assumed in the Health System Perspective CEA model for DSTB patients.

iii) The uptake of rolling out the device was taken between 30-65% for 5 years.

The Budget Impact Analysis depicts budget allocation for the five years. Using top down approach, we have calculated eligible population and supply side costing was used to assess incremental costs of intervention to be delivered in horizontal platform (Table 11).

Table 11: Estimation of eligible population for TMEAD roll-out using top-down approach

S.no	Steps for Top-down approach	Source
1	Maharashtra's Total TB notified cases (Year 2021)	Taken from India TB report 2022
2	DSTB Patients	Taken from India TB report 2022
3	Coverage between 30-65%	30% coverage in year 2022 extending to 65% in the year 2026

We have considered 30% coverage of DSTB patient for the Maharashtra state taken from the India TB report 2022 for the first year, 40%, 50%, 60% and 65% in subsequent years. Table 12 shows budget impact analysis and assumptions used. The state-wide scale-up for the state would cost INR 26,11,73,788 for the first year, with above costs in subsequent years. All other budget subheads are calculated based on the primary study data as the reference. For calculations, we have not discounted the cost but we have calculated the average inflation rate (3%) and added the cost for the second year onwards.

Budget impact analysis shows that in-order to scale up the TMEAD intervention for DSTB to the entire state of Maharashtra, the burden on the exchequer will be to the tune of 55 crores. This is just 0.02% of Maharashtra’s annual health budget of 3232 crores. Further, it is important to remember that the intervention was found to be cost-effective from a health system perspective.

Table 12: Budget Impact Analysis

					Annualized cost (INR)				
Sr. No.	**Budget Head**	**Budget sub-heads**	**Base year 2021**		**Year 1 2021-22**	**Year 2 2022-23**	**Year 3 2023-24**	**Year 4 2024-25**	**Year 5 2025-26**
			Units	**Unit Price**					
A	Capital cost	Manufacturing cost	1,70,295	2,872	14,67,43,685	19,56,58,247	24,45,72,809	29,34,87,370	31,79,44,651
Total (A)					**14,67,43,685**	19,56,58,247	**24,45,72,809**	**29,34,87,370**	**31,79,44,651**
B	Variable cost	Server for Support - Backend	1,70,295	86	5,29,45,383.06	7,05,93,844	8,82,42,305	10,58,90,766	11,47,14,997
		SIM per device	1,70,295	32	16,34,117	21,78,822	27,23,528	32,68,234	35,40,586
		SMS service - Server to Patient	1,70,295	60	3,67,83,720	4,90,44,960	6,13,06,200	7,35,67,440	7,96,98,060
		Trainings	635	66	83,541	83,541	83,541	83,541	83,541

		Transportation	1,70,295	17	8,70,012	11,60,015	14,50,019	17,40,023	18,85,025
		AMC / Repairs	17,030	150	7,66,328	10,21,770	12,77,213	15,32,655	16,60,376
Total (B)					**9,30,83,100**	12,40,82,953	**15,50,82,805**	**18,60,82,658**	**20,15,82,585**
C	HR Cost	Service Engineer	10,000	36	43,20,000	43,20,000	43,20,000	43,20,000	43,20,000
		App Developer	12,000	1	1,44,000	1,44,000	1,44,000	1,44,000	1,44,000
		Web Developer	25,000	1	3,00,000	3,00,000	3,00,000	3,00,000	3,00,000
		Electronics Hardware Engineer	10,000	5	6,00,000	6,00,000	6,00,000	6,00,000	6,00,000
		Program Manager	25,000	2	6,00,000	6,00,000	6,00,000	6,00,000	6,00,000
		Helper	8,000	36	34,56,000	34,56,000	34,56,000	34,56,000	34,56,000
		Operation Manager	10,000	36	43,20,000	43,20,000	43,20,000	43,20,000	43,20,000
Total (C)					**1,37,40,000**	1,37,40,000	**1,37,40,000**	**1,37,40,000**	**1,37,40,000**
Grand Total (without inflation rate)					**25,35,66,785**	**33,34,81,199**	**41,33,95,614**	**49,33,10,029**	**53,32,67,236**
Grand Total (with inflation rate 3%)					**26,11,73,788**	**34,34,85,635**	**42,57,97,482**	**50,81,09,330**	**54,92,65,253**

Qualitative findings

KII and in-depth interviews were done from patients, house hold members and dots supporters in the intervention arm. All interviews were conducted as open-ended free themes. The interviews were done for

a) Patients: 10 (Five Male and Five Female)
b) DOTS / Supporter / House hold members: 6 (Three HH from Male patient and Three HH members from Female patients).
c) Patients who dropped out from intervention and returned the device back: 3 patients

The interviews were transcribed from Marathi into English and then qualitative data was synthesized using thematic analysis. Major themes emerged from that data were (1) acceptability of the device, (2) perceived benefit of the device, (3) saving time and money and (4) availability of medicines.

Acceptability of the device

Most of the Patients who used device for 3-5 months have accepted the device and were quite satisfied with it. They considered the device helpful in treatment compliance. Following excerpts of patients' feedback (translated from *Marathi*) echo the acceptability of the device.

> *"The concept of delivering medicine through this device is good, this system helps me to manage the consumption of medicine on time due to its Alarm mechanism. With this system the medicine consumption can be monitored well. This system also helps to carry medicine when I am outdoor, the daily reminder /alarm facility not only help me but with this device my family member can also keep a close watch on my medicine intake."* ***A male patient from TU-1***

> *This device is good in making reminder. I too was a patient of TB few years ago and a nurse use to monitor my drug and give me drugs. In my previous experience, monitoring my medicine consumption schedule was quite hectic job. Sometimes I used to forget to take medicine. But with this there is no need for any nurse but even I can hear the alarm and can remind my son to take drug.*

A female Dots supporter from TU 1
"The concept of reminder machine Is good. I am satisfied with its use. I used this machine during my treatment due to which there is no breaks in my treatment. ***A patient from TU-2***

My entire family was excited because of this box machine and treatment system. Not only me, [but] all my family members keep close eye on the system and its alarm, eventually kept the index case reminded to take medicine on time." ***A male DOTS supporter from TU 2***

Initially I had some issues with charging and net work but the XXX was very helpful in responding to our calls and assisted us to put things in place. But yes sometimes visitor do ask about the Box and hence we need to keep it in cup board hidden so that visitors do not know that there is a TB patient in house. ***A female patient from TU 2***

Perceived benefit of TMEAD in medication adherence

Many patients perceived device to be beneficial in adhering to medication. Sometimes the alarm also sets in pace for other medication too ……A patient shared

I am diabetic patient and in my previous experience of taking anti diabetic drugs, many times, I forgot to take pills, sometime for 1 to 3 days, which caused irregularity and sometimes emergency. This device and its regular alarm system proven to the most useful during my treatment and I have also tuned myself to take other drugs too." ***A patient from TU-4***

One of the patients shared that device has alleviated the stress of her household regarding continuity of treatment one patient shared

"My parents felt, that as treatment is long I will over a period of time become careless and will often forget to take medicine on time and my family members will have to take extra mile. But this system and its alarm facility are very useful to me as it reduced my dependency on others." ***A patient fromTU-2***

One of the Dots supporter shared that the curiosity and use of technology might itself have increased compliance.

> *The patients seem to be exited and through Device and the family members were more exited, Sometimes I feel the device was instrumental in generating a better rapport with the patient also.*
> ***A NTEP staff***

One the NTEP staff also shared that the amount of time that is invested in refilling should be accounted: -

> *All about device may be good but in present format the system or the person appointed by you are cutting the strips and re filling it. there must be a mechanism to get it refilled not sure how, buy unless this is done, long term sustainability / roll out can be a challenge.*
> ***One NTEP Staff***

Time and money

One of the important objectives of the present intervention was also to document the costing and how has the users found this device to be time and money saving.

Different responses were gathered, Following are few of the reflection on same .

> *…the concept of machine reminding medication is interesting. Surely it saves time as you are not occupied only with thinking about the medication but you are relaxed and can use quality time in other work:* ***A patient from TU-1***

> *During initial month of my treatment, I had to travel to hospital to get my monthly quota of medicine which was time and money consuming. And many a time, medicines were not available at the DOTs centre which was so disappointing. With this system this problem of getting medicine and traveling is solved."* ***A patient from TU-3***

…the system is good, I assume that, due to this system, I might not have to visit hospital again as I am taking all doses and I will be sure else I will have to again get treatment and spend my time and money. I am happy to use the system." ***A patient from TU-3***

Overall, in the KII and IDI the respondents were of opinion that the system has a definite value over the conventional no device type of medication and in longer run due to better adherence there will be lesser expense on treatment and frequently visiting to hospital.

Availability of medicines

Patients reported improvement in the availability of medicines after introduction of this device as the team itself delivers essential medicines and hence frequent visits are avoided.

A patient stated, "*… the regular follow-up taken by you [TMEAD team member] ensure the continuous supply of medicine in hospital. Previously the timely availability of medicine in hospital was rare. That problem is not faced anymore."*
A patient from TU-3

One of the staff did mention that the availability of medicine has also improved as the team with device gives us list of patients prior and hence it assists in better management.

The team with device is keeping a close watch and informs us about the need of medicine well in advance and hence it assists us in better logistic management, earlier there was very frequent gaps between patients coming to hospital couple of weeks after exhausting all drugs: ***A staff of NTEP.***

Problems reported with the device

It was documented that there were issues / challenges with use of device, this was more during the early installation but over period of time the issues were sorted out.

Most common issues documented across various qualitative interviews as well as informal feedbacks were

a) Problem with device like no alarms/reminder.
b) Problem with charging (both over charging and need for repeated charging).
c) Difficult to remove the drugs box due to damaged device/ jammed boxes.
d) Few of the participants also shared that only telephonic assistance by technical team was given and they had to make 3-4 calls to get this sorted out, in person assistance was not given.
e) On asking the suggestion to improve this, a leaflet with DO's and Don'ts was requested to be pasted along with the device itself. There was also a suggestion for trouble shooting videos to be shared with participants in vernacular language.

Feedbacks from Patients who returned the device/Refused to Use the Device

Few patients returned the device or refused to use the device after agreeing to be part of same. It was important to document the reasons why the intervention was not completed. IDI of three such participants was done to document the reasons for same.

The primary reasons were stigma associated with TB, and issues of charging the device and taking device at workplace. Following verbatim reflect these reasons.

> *"I have recently got engaged and planning to get married soon. My fiancée and in-laws are not aware that I am having TB and I am under treatment. Presence of this device at home and scheduled alarms in between can expose my secrets and ultimately my marriage may be ruined. So, I wish not to use it."* ***A female patient from intervention arm who returned the device after 4 weeks***

> *"We have a very small house and alarm of this device rings through the close neighboring houses just a wall apart. This device threatens our family as tool for discrimination and stigma by neighbors and visitors coming to our home.* ***"A male patient from intervention arm who returned the device after 2 weeks and was residing in one room rented house.***

"Most of the time, I am outdoors for daily labour for earning my livelihood, in shifts. My shift changes as and when needed, Keeping this device charged and carrying it to workplace is hectic and not feasible for me. Also alarms in between at workplace makes my co-fellows conscious/doubtful about me. Hence, I decided to carry on with strips only." ***A male patient from intervention arm who returned the device after 2 weeks and was working in one of the factories.***

"My father-in-law tells me that the electricity consumption will go up due to use of device and hence I discontinued: ***A 30-year female from intervention arm who returned the device after 4 weeks and was residing in a joint family with in laws.***

"Sometimes the device becomes very hot during charging and I have read that due to overcharging electronic instruments can burst, hence I returned back: ***A 25-year-old college going male student who returned the device after complains of device getting hot during charging.***

To summarise there were few concerns about the device its electricity consumption and also size. A big device that needs to be kept in open for signals can be a surrogate for TB patient and can create stigma as perceived by the patients. There is also need for clarifying the requirements for charging and cost incurred.

Discussion

This study assessed the adherence (clinical and digital) and cost-effectiveness of TMEAD as a tool for measuring and promoting medication adherence among DSTB patients. The participants' demographic characteristics, such as age, the ratio of males to females and their treatment outcomes, were comparable to the pilot study done by Cross A et al. in the Mumbai region [18]. This suggests that we studied a regionally representative patient sample. However, the adherence rates of our patients could have been biased by their participation in the study.

Digital health interventions are increasingly used to support TB treatment in diverse settings globally. Our study found that the use of TMEAD Device to remind TB patients to take their drugs has medication adherence of 99% compared to 90% in the standard of care scenario. This increase was seen for all TB treatment adherence measures in this study. The results demonstrate convincingly that the intervention strategy works, and the more of the intervention received by the patients, the better the response.

Stagg and colleagues cited prior validation of electronic monitoring with urine rifampicin levels, the pharmacokinetics of that drug limit interpretability [19]. In line with the other digital adherence technologies, TMEAD also report adherence which is confirmed in this study by the urine analysis. Our findings further support the adherence results as per urine analysis, for those patients' samples processed in the 1st cycle, 90.6% had urine rifampicin traces. At the end of the third cycles for urine sample collection in the intervention arm, 86.3% of samples were positive for urine rifampicin. Whereas, in the control arm, 77.2% of the samples were rifampicin positive.

Even though many types of DATs exist and have been used for different disease conditions, a systematic review done by Ngwatu et al (2018) suggest that some digital interventions can potentially improve medication adherence and patient outcomes [20]. While evidence remains incomplete, and generalisability limited, the studies reviewed suggest these technologies may be at least as effective as the standard of care [21].

Cost-effectiveness analysis (CEA) has been used as a tool for addressing efficiency issues in the allocation of scarce health resources, providing as it does a method for comparing the relative costs and health gains of different (and often competing) health interventions. In our study an incremental cost-effectiveness ratio (ICER) was INR 11,599 per quality-adjusted life-year (QALY) which is 0.07% of the per capita GDP of the country. Our results show improvement in health conditions is very cost-ineffective according to willingness-to-pay for health i.e low-value care. Further sensitivity analysis found our result to be robust.

Strengths and limitations

A major strength of this study is that it comprises a real-world evaluation of the impact of TMEAD on TB treatment outcomes. We used routinely collected programmatic data for the quantitative component and thus the difference in the treatment outcomes reflects the realities in the field.

One of the limitations of the present study is non-random selection/ allocation of the study participants hence, the study subjects were not representative of all patients taking treatment for TB in Nasik. The COVID-19 induced prolonged lockdown has resulted in migration and patient attrition. Moreover, deployment of the device was delayed due to interruptions in the manufacturing of devices. Second, migrant workers returned to their native villages which impacted enrolment. Third, most of the NTEP staff were not available due to COVID-19 duties. Fourth, movement restrictions in Containment zones resulted in delays in contacting patients and collection of follow-up data. There were various implementation challenges like actual consumption could not be monitored. There is a need to create a patient facing application where patients can update their status. This can serve as an additional point of confirmation of medicine consumption. Problems with the mobile network resulted in contacting patients and device alerts and refilling devices.

Conclusion

This study has several important public health implications for the use of a TMEAD device in resource-limited settings. Evaluation of patient and health worker behaviours and beliefs following implementation of this technology in a new setting will be essential in optimising its acceptability and clinical impact. Secondly, the introduction of new technologies alone is just one part of a broader approach to adherence support. Technological innovations must be accompanied by sustainable health system strategies to address and overcome diverse barriers to treatment completion.

This study revealed that patient-reported treatment adherence was high in TMEAD as compared to standard therapy of care for the DSTB patients and the intervention is cost-effective. This study shows innovative approaches to adherence, promotion by creating interventions to enhance treatment adherence can improve treatment outcomes. TMEAD can complement the national strategy of TB elimination by improving adherence to the treatment regimen.

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Annexure 1: TMEAD costing

SN	Particulars	Unit Cost	FY 1 (8 months)	FY 2* (12 months)	Annualized cost	Remark
1.	**Manufacturing cost**	5,388.00	4,04,100.00	7,18,085.70	2,03,486.17	Number of total 200 devices (for year 1-75 and year 2-125) Device used twice
2. Implementation cost						
2.1	Server for Support - Backend	81.00	9,112.50	1,29,543.30	69,327.90	INR 81 per device per month - Support cost for running the TMEAD intervention
2.2	SIM per device	30.00	3,375.00	47,979.00	25,677.00	Rs. 30/- per month per SIM card
2.3	SMS service - Server to Patient	72.00	8,100.00	1,15,149.60	61,624.80	[INR 0.50 Per SMS, sent maximum 4 times a day, to 200 patients (75 in first year, 125 in second year]
2.4	Trainings	2,500.00	2,500.00	-	2,500.00	one Session conducted with 35 HV's, STS, CTO, DTO in Nashik at the cost of Rs. 2500.
2.5	Transportation	500.00	750.00	6,397.20	3,573.60	Rs. 10,000/- budgeted and spent in transportation of devices to and for
2.6	AMC / Repairs	150.00	2,250.00	19,191.60	10,720.80	Rs. 150/- budgeted for repairs and AMC per device (10 devices repair in year 1 and 10 in year2)
3 HR Cost						
3.1	Service Engineer	10,000.00	80,000.00	1,27,944.00	1,03,972.00	Cost Apportioned for 8 Months in Year One and 12months in Year 2
3.2	App Developer	12,000.00	96,000.00	1,53,532.80	1,24,766.40	Cost Apportioned for 8 Months in Year One and 12months in Year 2
3.3	Web Developer	25,000.00	2,00,000.00	3,19,860.00	2,59,930.00	Cost Apportioned for 8 Months in Year One and 12months in Year 2
3.4	Electronics Hardware Engineer	10,000.00	80,000.00	85,296.00	82,648.00	Cost Apportioned for 8 Months in Year One and 8 months in Year 2 as requirement was over
3.5	Program Manager	25,000.00	2,00,000.00	2,39,895.00	2,19,947.50	Cost Apportioned for 8 Months in Year One and 9 months in Year

						2 as requirement was over
3.6	Helper	8,000.00	64,000.00	1,02,355.20	83,177.60	Cost Apportioned for 8 Months in Year One and 12months in Year 2
3.7	Operation Manager	10,000.00	80,000.00	1,27,944.00	1,03,972.00	Cost Apportioned for 8 Months in Year One and 12months in Year 2
	Total		**12,30,187.50**	**21,93,173.40**	**13,55,323.77**	

*****_2021-inflation rate 6.62% https://www.worlddata.info/asia/india/inflation-rates.php_

Annexure 2: Transition Probability of intervention and control arm

Transition from and to	Transition Probability	
	Intervention	Control
Probability of Full adherence	0.896	0.422
Probability of Partial adherence	0.015	0.460
Probability of Non adherence	0.089	0.118
Probability of Full adherence from Treatment completed	0.992	0.971
Probability of Full adherence from Treatment Extended	0.008	0.029
Probability of Full adherence from Death	0.000	0.000
Probability of Full adherence from Defaulter	0.000	0.000
Probability of Partial adherence from Treatment completed	1.000	0.986
Probability of Partial adherence from Treatment extended	0.000	0.014
Probability of Partial adherence from Death	0.000	0.000
Probability of Partial adherence from Defaulter	0.000	0.000
Probability of Non adherence from Treatment completed	0.000	0.000
Probability of Non adherence from Treatment extended	0.000	0.000
Probability of Non adherence from Death	0.500	0.474
Probability of Non adherence from Defaulter	0.500	0.526
Probability of QALY from full adherence	0.007	0.007
Probability of QALY from partial adherence	0.006	0.005
Probability of QALY from non-adherence	0.005	0.001
Probability of overall QALY	0.006	0.007
Cost of Treatment completed	44.370	38.352
Cost oF FULL ADHERENCE	39.769	16.198
Cost Of Full Adherence_Treatment completed	39.440	15.722
Cost Of Fulladherence_Treatment extended	39.769	16.198
Cost Of Fulladherence_Death	0.000	0.000
Cost Of Fulladherence_Defaulter	0.000	0.000
Cost Of Partial Adherence	0.657	17.628
Cost Of Partial Adherence_Treatment Completed	0.657	17.390
Cost Of Partialadherence_Treatment Extended	0.000	17.628
Cost Of Partialadherence_Death	0.000	0.000
Cost Of Partialadherence_Defaulter	0.000	0.000
Cost Of Nonadherence	3.944	4.526
Cost_Non Adherence_Treatment Completed	0.000	0.000
Cost Of Non Adherence_Treatment Extended	0.000	0.000

Cost Of Non Adherence_Death	1.972	2.144
Cost Of Nonadherence Defaulter	1.972	2.382
Cost Of Per Beneficiary	65.733	47.643
Average Age OF Cohort	37	37

SenseDose Technologies

KNOWLEDGE TO ACTION phfi INDIAN INSTITUTE OF PUBLIC HEALTH GANDHINAGAR

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