

Evaluation of the Acceptability of the Medication Event Reminder Monitor for Promoting Adherence to Multidrug-Resistant Tuberculosis Therapy in India: Qualitative Study of Patients and Healthcare Providers

Beena E Thomas, J. Vignesh Kumar, Murugesan Periyasamy, Amit Subhash Khandewale, J. Hephzibah Mercy, E. Michael Raj, S. Kokila, Apurva Shashikant Walgude, Gunjan Rahul Gaurkhede, Jagannath Dattraja Kumbar, Senthano Ovung, Mariyamman Paul, B. Sathyan Rajkumar, Ramnath Subbaraman

Submitted to: Journal of Medical Internet Research
on: August 06, 2020

Disclaimer: © The authors. All rights reserved. This is a privileged document currently under peer-review/community review. Authors have provided JMIR Publications with an exclusive license to publish this preprint on its website for review purposes only. While the final peer-reviewed paper may be licensed under a CC BY license on publication, at this stage authors and publisher expressly prohibit redistribution of this draft paper other than for review purposes.

Table of Contents

Original Manuscript.....	5
Supplementary Files.....	45
Figures	46
Multimedia Appendixes	47
Multimedia Appendix 1.....	48



Evaluation of the Acceptability of the Medication Event Reminder Monitor for Promoting Adherence to Multidrug-Resistant Tuberculosis Therapy in India: Qualitative Study of Patients and Healthcare Providers

Beena E Thomas PhD, MSW, J. Vignesh Kumar PhD, Murugesan Periyasamy MSW, Amit Subhash Khandewale MSW, J. Hephzibah Mercy, E. Michael Raj, S. Kokila, Apurva Shashikant Walgude, Gunjan Rahul Gaurkhede, Jagannath Dattraja Kumbar, Senthandro Ovung, Mariyamman Paul, B. Sathyan Rajkumar, Ramnath Subbaraman MD, MSc, FACP

Corresponding Author:

Ramnath Subbaraman MD, MSc, FACP

Department of Public Health and Community Medicine

Tufts University School of Medicine

136 Harrison Ave

MV237

Boston

US

Phone: +16176360985

Email: ramnath.subbaraman@tufts.edu

Abstract

Background: Multidrug-resistant TB (MDR TB) patients face challenges adhering to medications, given that treatment is prolonged and has a high rate of adverse effects. The Medication Event Reminder Monitor (MERM) is a digital pillbox that provides daily pill-taking reminders and facilitates remote monitoring of medication adherence.

Objective: We assessed the MERM's acceptability to patients and healthcare providers (HCPs) during pilot implementation in India's public sector MDR TB program.

Methods: From October 2017 to September 2018, we conducted qualitative interviews with patients taking MDR TB therapy, who were being monitored with the MERM, and HCPs in the government program in Chennai and Mumbai. Interviews transcripts were independently coded by two researchers and analyzed to identify emergent themes. We organized findings using the unified theory of acceptance and use of technology (UTAUT), which outlines four constructs that predict technology acceptance: performance expectancy, effort expectancy, social influences, and facilitating conditions.

Results: We interviewed 65 MDR TB patients and 10 HCPs. In patient interviews, greater acceptance of the MERM was related to perceptions that the audible and visual reminders improved medication adherence and that remote monitoring reduced the frequency of clinic visits (performance expectancy); that the device's organization and labeling made it easier to take medications correctly (effort expectancy); that the device facilitated positive family involvement in the patient's care (social influences); and that remote monitoring made patients feel more "cared for" by the health system (facilitating conditions). Lower patient acceptance was related to problems with the durability of the MERM's cardboard construction and difficulties with portability and storage due to its large size (effort expectancy); concerns regarding stigma and disclosure of patients' MDR TB diagnoses (social influences); and incorrect understanding of the MERM due to suboptimal counseling (facilitating conditions). In their interviews, HCPs reported that MERM implementation resulted in reduced in-person interactions with patients, allowing HCPs to dedicate more time to other tasks, which improved job satisfaction.

Conclusions: Several features of the MERM support its acceptability among MDR TB patients and HCPs, and some barriers to patient use could be addressed with improved design of the device. However, some barriers to patient use—such as disease-related stigma—are more difficult to modify and may limit its use by some MDR TB patients. Further research is needed to assess the MERM's accuracy for measuring adherence, its effectiveness for improving treatment outcomes, and patients' sustained use of the device in larger-scale implementation.

(JMIR Preprints 06/08/2020:23294)

DOI: <https://doi.org/10.2196/preprints.23294>

Preprint Settings

1) Would you like to publish your submitted manuscript as preprint?

✓ **Please make my preprint PDF available to anyone at any time (recommended).**

Please make my preprint PDF available only to logged-in users; I understand that my title and abstract will remain visible to all users.

Only make the preprint title and abstract visible.

No, I do not wish to publish my submitted manuscript as a preprint.

2) If accepted for publication in a JMIR journal, would you like the PDF to be visible to the public?

✓ **Yes, please make my accepted manuscript PDF available to anyone at any time (Recommended).**

Yes, but please make my accepted manuscript PDF available only to logged-in users; I understand that the title and abstract will remain visible to all users.

Yes, but only make the title and abstract visible (see Important note, above). I understand that if I later pay to participate in [JMIR Publications](#)

Original Manuscript



Title: Evaluation of the Acceptability of the Medication Event Reminder Monitor for Promoting Adherence to Multidrug-Resistant Tuberculosis Therapy in India: Qualitative Study of Patients and Healthcare Providers

Authors: Beena E. Thomas^{1¶}, J. Vignesh Kumar¹, P. Murugesan¹, Amit Khandewale¹, J. Hephzibah Mercy¹, E. Michael Raj¹, S. Kokila¹, Apurva Shashikant Walgude¹, Gunjan Rahul Gaurkhede¹, Jagannath Dattraja Kumbar¹, Senthanro Ovung,¹ Mariyamman Paul¹, B. Sathyan Rajkumar¹, Ramnath Subbaraman^{2,3¶*}

Affiliations

¹Department of Social and Behavioural Research, National Institute for Research in Tuberculosis, Chennai, India

²Department of Public Health and Community Medicine and Center for Global Public Health, Tufts University School of Medicine, Boston, MA

[¶]These authors contributed equally to this work

*Corresponding author

Corresponding author address and email information:

Ramnath Subbaraman, MD, MSc, FACP

136 Harrison Ave, MV237

Boston, MA 02111

Abstract

Background. Multidrug-resistant TB (MDR TB) patients face challenges adhering to medications, given that treatment is prolonged and has a high rate of adverse effects. The Medication Event Reminder Monitor (MERM) is a digital pillbox that provides daily pill-taking reminders and facilitates remote monitoring of medication adherence.

Objective. We assessed the MERM's acceptability to patients and healthcare providers (HCPs) during pilot implementation in India's public sector MDR TB program.

Methods. From October 2017 to September 2018, we conducted qualitative interviews with patients taking MDR TB therapy, who were being monitored with the MERM, and HCPs in the government program in Chennai and Mumbai. Interviews transcripts were independently coded by two researchers and analyzed to identify emergent themes. We organized findings using the unified theory of acceptance and use of technology (UTAUT), which outlines four constructs that predict technology acceptance: performance expectancy, effort expectancy, social influences, and facilitating conditions.

Results. We interviewed 65 MDR TB patients and 10 HCPs. In patient interviews, greater acceptance of the MERM was related to perceptions that the audible and visual reminders improved medication adherence and that remote monitoring reduced the frequency of clinic visits (performance expectancy); that the device's organization and labeling made it easier to take medications correctly (effort expectancy); that the device facilitated positive family involvement in the patient's care (social influences); and that remote monitoring made patients feel more "cared for" by the health system (facilitating conditions). Lower patient acceptance was related to problems with the durability of the MERM's cardboard construction and difficulties with portability and storage due to its large size (effort expectancy); concerns regarding stigma and disclosure of patients' MDR TB diagnoses (social influences); and incorrect understanding of the MERM due to suboptimal counseling (facilitating conditions). In their interviews, HCPs reported that MERM implementation resulted in reduced in-person interactions with patients, allowing HCPs to dedicate more time to other tasks, which improved job satisfaction.

Conclusion. Several features of the MERM support its acceptability among MDR TB patients and HCPs, and

some barriers to patient use could be addressed with improved design of the device. However, some barriers to patient use—such as disease-related stigma—are more difficult to modify and may limit its use by some MDR TB patients. Further research is needed to assess the MERM's accuracy for measuring adherence, its effectiveness for improving treatment outcomes, and patients' sustained use of the device in larger-scale implementation.

Key words: tuberculosis; drug-resistant; medication adherence; mHealth; digital adherence technologies; India

Introduction

Background

Multidrug-resistant tuberculosis (MDR TB) is a major challenge to TB control globally. In 2018, about 484,000 people worldwide were estimated to have developed MDR TB, including about 130,000 people in India [1]. Despite considerable advances in therapy in the last decade, treatment outcomes remain poor for individuals with MDR TB, with treatment success rates of 56% worldwide and 48% in India for the 2017 patient cohort [1]. While some of the variability in treatment outcomes may be attributable to the composition of the patient's drug regimen [2], suboptimal adherence to medications may be another critical problem contributing to poor MDR TB treatment outcomes.

Successful adherence to medications for diseases with a prolonged treatment course, such as MDR TB, requires a high level of dosing implementation (ie, taking a medication dose on a given day) and persistence (ie, taking medications for the entire duration of therapy [3]). Underlying factors contributing to non-adherence are complex and include therapy-related (eg, toxicities [4]), psychosocial (eg, alcohol use [5], depression [6], and stigma [7]), structural (eg, distance from clinics, medication costs [8,9]), and health system-related challenges (eg, poor user-experience with the health system). Many of these challenges are particularly severe for patients with MDR TB. For example, recent systematic reviews have shown that MDR TB patients face particularly high levels of drug toxicities [4] and psychosocial barriers, including depression, substance use disorders, stigma, and discrimination [10]. These challenges may, in turn, increase non-adherence to medications, thereby leading to poor treatment outcomes and increased transmission of drug-resistant strains.

As such, there is an urgent need for new strategies to improve adherence to medications for people living with MDR TB. Many TB programs have historically used directly observed therapy (DOT) to monitor

adherence; however, recent studies have questioned the efficacy of this strategy for improving clinical outcomes [11–13] and raised concerns that DOT adversely impacts patient autonomy [14,15]. Concerns about limited patient autonomy with DOT may be greater for patients taking MDR TB treatment, given the prolonged course of therapy required. In addition, recent recommendations favoring use of regimens containing only oral medications may decrease the required frequency of clinic visits for MDR TB patients [16].

In recent years, driven by the global expansion in the reach of cellular networks, there has been growing use of digital adherence technologies (DATs) as an alternative approach for monitoring and improving adherence to TB medications [3]. These technologies, which include cellphones, digital pillboxes, and ingestion sensors, have the potential to improve clinical outcomes via multiple pathways [3]. While there are numerous DATs aimed at addressing non-adherence in patients with drug-susceptible TB [3], few have attempted to address the more complex medication regimens taken by MDR TB patients [17].

The Medication Event Reminder Monitor (MERM) is a digital pillbox that has been designed to monitor MDR TB treatment in resource-constrained settings, using relatively affordable evriMED technology produced by Wisepill Technologies. This system is specifically designed to be used with multiple blister-packaged TB medications in MDR TB regimens, incorporates visual and audible reminders for both daily dosing and refills, compiles detailed dosing histories by capturing data on pillbox opening as a proxy for dose ingestion, and transmits these data to a server so that healthcare providers (HCPs) can remotely visualize patients' dosing histories to support enhanced adherence counseling. By providing near real-time adherence data, the MERM may facilitate identification of high-risk patients and prompt early intervention by HCPs to reduce non-adherence. When compared to facility-based DOT—in which patients travel to clinics to be observed taking their medications—monitoring using the MERM may also reduce the required frequency of patient visits to TB clinics.

Earlier pilot studies of similar digital pillboxes conducted in Uganda and China with drug-susceptible TB patients and in South Africa with MDR TB patients have shown these devices to have relatively high acceptability [17–19]. A cluster-randomized trial conducted in China with drug-susceptible TB patients found digital pillboxes to be effective in reducing the percentage of patient-months with high non-adherence [20]. However, subsequent studies of the large-scale implementation of these digital pillboxes in China have revealed challenges in uptake. For example, after accounting for patients who were not eligible to use these pillboxes, refused to use them, withdrew from using them early in treatment, or got shifted to monitoring with DOT, only about 49% and 39% of TB patients used digital pillboxes in a sustained manner in a single province [21] and 30 counties [22] in China, respectively. In addition, a study of the MERM conducted in Vietnam with drug-susceptible TB patients found that only about half of patients used the device as intended, with many separating the time when the pillbox was opened from the time that doses were ingested, due to concerns about the device's portability [23]. These existing studies evaluating use of digital pillboxes reveal variability in patient acceptance and use in different contexts and highlight a relative paucity of data on use of these devices for MDR TB patients.

Objectives

In this study, based on qualitative interviews with both patients and HCPs, we evaluate the acceptability of the MERM for monitoring adherence to MDR TB therapy during a pilot rollout in two major Indian cities in the government's National TB Elimination Program (NTEP). While this novel monitoring strategy has potential advantages, prior research has not been conducted in India to evaluate whether patients will accept and use the MERM, to identify potential modifiable and non-modifiable barriers to its acceptability, and to understand how implementation of this technology might impact HCP work efficiency and quality of care. Understanding the acceptability of the MERM during pilot implementation is also important because recent studies of other DATs in India suggest that suboptimal acceptability and use by patients could reduce the

accuracy of these technologies for measuring adherence [24], which might in turn greatly reduce the value of real-time adherence data for guiding interventions by HCPs. We analyze our findings using the unified theory of acceptance and use of technology (UTAUT), a framework which synthesizes a variety of constructs that predict engagement with novel technologies [25,26].

Methods

Ethics Approvals

This research protocol received approval from the Indian Council of Medical Research (ICMR)-National Institute for Research in TB (NIRT) Institutional Ethics Committee (FWA00005104) and its Scientific Advisory Committee. It also received approval from the Brigham and Women's Hospital Institutional Review Board (FWA00000484) and the Tufts Health Sciences Institutional Review Board (FWA00004517). We obtained written informed consent from all study participants.

Study Setting

This study was conducted in two major Indian cities with a high TB burden in the general population [27,28]: Chennai (estimated population of 7.1 million in metropolitan area) and Mumbai (estimated population of 18.4 million in the metropolitan area). Mumbai in particular has one of the world's most severe urban epidemics of drug-resistant TB [29-31].

MERM Implementation

With the MERM, medications are dispensed in blister packs and each drug is placed in a different partitioned compartment within the pillbox, which facilitates storage and organization of the multiple medications that comprise most MDR TB regimens (Figure 1). In India's initial pilot implementation, the container and internal partitions were made of cardboard. The device was provided to patients at different time points in the

continuation phase of MDR TB therapy, when injectable agents had generally been discontinued and patients were only taking oral medications. More specifically, at the time of our study, most MDR TB patients in India's NTEP were placed on a standardized drug regimen for a treatment course lasting 24 to 27 months, with the continuation phase consisting of levofloxacin, ethionamide, cycloserine, and ethambutol taken once daily [32].



Figure 1. The Medication Event and Reminder Monitor, in a cardboard version used for the initial rollout among multidrug-resistant tuberculosis (MDR TB) patients in India. The device includes partitions for

organizing medications, labeling of medications inside the box lid, and a digital module that provides reminders and captures adherence data. Courtesy: Wisepill Technologies.



The MERM was programmed to provide both audible and visual reminders to take medications at a specific time of the day, per patient and HCP preference. The visual reminder consisted of a blinking green light corresponding to a label encouraging the patient to take a dose; separate yellow and red lights blink to alert patients about the need to refill medications and replace the MERM's battery, respectively. The audio reminder consisted of a ringing sound that would occur at the same time as the visual dose-taking reminder.

The device contained a removable electronic battery-powered module. Triggered by a magnetic sensor, this module captures and stores data on each time the container is opened, as a proxy for medication ingestion.

These data on patient engagement with the MERM were transmitted every 72 hours using cellular networks and recorded on a computer server. HCPs could log into an application on a mobile device (most often a smartphone) or a website on a computer, where they could view each patient's adherence history. In the application, each patient's adherence history was presented as a color-coded calendar in which green suggested that the MERM was opened on a given day (suggesting probable dose ingestion) while red suggested that the device was not opened (suggesting that a dose was probably not ingested).

These dosing histories were meant to help HCPs have individualized discussions with patients regarding their adherence. In addition, a series of possible missed doses (ie, red-colored calendar days) would result in SMS notifications that were automated, to prompt HCPs to intervene upon patients potentially at higher risk for unfavorable outcomes.

Recruitment of Study Participants and Collection of Qualitative Data

Screening and interviews were conducted by field researchers with a master's degree in social work or another social science field who underwent a two-day uniform training in qualitative interviewing at the National Institute for Research in TB in Chennai. Study participants included both MDR TB patients and healthcare providers. Note that we use the term "MDR TB" to describe patients with confirmed resistance to isoniazid and rifampin, as well as individuals who were diagnosed as having rifampin-resistant TB using Xpert MTB/RIF, because patients with rifampin-resistant TB in India are treated as having likely MDR TB. Data collection was conducted a few months after the MERM was introduced in Mumbai and Chennai for monitoring MDR TB patients, from October 2017 to September 2018. Prior to rollout of the MERM, HCPs were given extensive training on the appropriate use of the MERM before they started issuing it to patients. HCPs in the NTEP dispensed medication refills in the MERM for MDR TB patients in the continuation phase of therapy, after any injectable agents (eg, kanamycin) had been discontinued.

NIRT field researchers met patients who had been given the MERM at MDR TB clinics, where patients were screened for inclusion in the study. At these same clinics, HCPs were recruited for the study, including health visitors (individuals with at least a high school level of education who monitor TB therapy), senior treatment supervisors (individuals with at least a high school level of education who supervise health visitors), medical officers (doctors with a MBBS or higher degree), and district TB officers (doctors who supervise TB care across a district).

For MDR TB patients, an unannounced home visit was made at least three weeks after enrollment into the study to conduct the qualitative in-depth interviews (IDIs) regarding the MERM, which lasted about 45 minutes. A pill count was also conducted to better understand their adherence to their TB medications. We ensured a minimum of three weeks lapsed between when a patient was consented for the study and when the unannounced home visit was conducted. This time gap helped to minimize the impact of any temporary change in medication adherence that may result from the patient knowing that he or she will be visited as part of the study (ie, the “Hawthorne effect”). For HCPs, interviews lasted about 30 to 45 minutes and were conducted in a private space in the TB clinic.

To ensure uniformity in data collection, separate patient and HCP interview guides, each consisting of open-ended and semi-structured question with follow-up probes, were used to conduct the qualitative in-depth interviews. Examples of questions from the patient interview guide are provided in Multimedia Appendix 1. Interview questions had the goal of assessing key constructs in the UTAUT framework as discussed further below. Interviews were conducted in Tamil, Hindi, Marathi, or English with audio recording, and they were later transcribed and translated to produce de-identified English-language transcripts. To maintain confidentiality of participant data, any physical records (eg, informed consent forms) were stored in a locked cabinet at the NIRT and interview recordings and transcripts were stored on an encrypted password-protected computer server. To ensure translation accuracy, one-quarter of English language transcripts were

randomly selected and evaluated against the original audio recordings for correctness and completeness.

Analytical Framework: UTAUT

The UTAUT integrates multiple constructs from previous literature on technology acceptance into a single framework [25,26]. Three of these constructs—performance expectancy, effort expectancy, and social influences—help to predict the behavioral intention of individuals to use a technology, which is necessary, but not sufficient, to result in actual use. Performance expectancy refers to the perceived usefulness of a technology to users. For example, for MDR TB patients this may refer to the extent to which the MERM is perceived to improve their medical care, whereas for HCPs it may refer to the extent to which it is perceived to improve the quality or efficiency of their work. Effort expectancy refers to the ease of using a technology. For patients, this may refer to the effort required to correctly use and understand different functions of the digital pillbox (eg, storage function, audible and visual reminders, etc), whereas for HCPs this may refer to the effort required to use and understand the online adherence dashboard and SMS text messaging reminders for notifying HCPs about patients who are non-adherent. Social influences refer to how other individuals may influence a person's acceptance and use of a technology. For patients, this may include community residents or family members, whereas for HCPs this may include other HCPs in their work environment. Of these three constructs, evidence from a variety of contexts suggests that performance expectancy often has the strongest influence on behavioral intention to use a technology [25].

In contrast to these other three constructs, facilitating conditions, the fourth construct in the UTAUT, is thought to directly affect actual use of a new technology by individuals. Facilitating conditions comprise the underlying infrastructure in place to facilitate use of a new technology. For MDR TB patients, we interpret this broadly to include factors in the TB program such as the quality of counselling provided to patients in use of the MERM and any outreach by HCPs to patients that might have been prompted by adherence data from the MERM. For HCPs, we interpret this to include factors such as the quality of training they received prior to

rollout of the MERM and any higher-level support related to the MERM that they received during the rollout process.

Analysis of Qualitative Data

Transcribed interviews were coded using a thematic approach and analyzed using Dedoose software (version 8.0.35, Los Angeles, CA: SocioCultural Research Consultants, LLC; www.dedoose.com). Before the coding process started, the study team met to identify possible codes (ie, themes) related to the central research question from the data collected, using the qualitative interview guides as a foundation and the UTAUT as an organizing framework. The transcripts were then independently coded by two researchers for relevant themes using descriptive content analysis. In parallel, the researchers kept track of any new codes that were added to the coding scheme to describe unexpected themes that emerged in the transcripts. Coded transcripts were continually reviewed by the two researchers, who met frequently to reconcile any inconsistencies in application of codes and to ensure emergent codes were added to the coding scheme.

We then analyzed the data to identify emergent themes that could influence the acceptability and use of the MERM. Emergent themes were organized within the four constructs of the UTAUT, and we selected illustrative quotations for each theme. In reporting our findings, we follow important principles of qualitative research by avoiding quantification of codes (or themes) from our data [33]. Quantification of themes may imply that the same questions were systematically administered to study participants, as is the case with structured questionnaires. While our field researchers did follow a uniform interview guide, they were encouraged to elicit further information using follow-up probe questions that could vary depending on prior responses from the study participant. The ability to elicit unique information from each participant is a strength of the qualitative research approach. Another reason we avoided quantification of themes is that quantification often implies that study findings are representative of a larger population; however, we used purposeful sampling, so our sample is not necessarily representative of the larger MDR TB patient population. Finally, we report common themes (ie, those that emerged most frequently in the data) but also

salient themes (ie, themes reported by a minority but are still important).

We also specifically did not classify each patient who was interviewed based on whether they reported “high” or “low” acceptance or use of the MERM. In contrast, we focus on reporting specific features of the MERM or the implementation process that were associated with higher or lower acceptance of the device, because individual patients might find some components of the device to be acceptable while simultaneously finding other components to be unacceptable. For example, a patient might appreciate the way the MERM facilitates organization of medications but, at the same time, have concerns about the audible reminder because of fear that it could lead to disclosure of her or his MDR TB diagnosis. In addition, there is often considerable individual variation in whether patients accept a particular technology [34]. As such, we focus on understanding factors that might increase or decrease the MERM’s acceptability and use, rather than aiming to make a blanket declaration that the device is either “acceptable” or “unacceptable” to the MDR TB patient population in India.

Results

Characteristics of Study Participants

We interviewed 65 MDR TB patients, for whom the median age was 33 years (range 18 to 75 years). The majority were men, had some primary or secondary school education, and lived in the Chennai metropolitan area (Table 1). Only one-fifth lived within walking distance of their clinic.

Table 1. Descriptive statistics for multidrug-resistant tuberculosis (MDR TB) patients being monitored with the MERM

Characteristic	N (%)
Location	
Chennai	40 (62)
Mumbai	25 (38)
Gender	
Male	42 (65)

Female	23 (35)
Educational attainment	
No formal education / low literacy	13 (20)
Some primary or secondary education	44 (68)
Some college education, including degree or diploma holders	8 (12)
Occupation	
Unemployed	16 (25)
Student	7 (11)
Homemaker	7 (11)
Formal government or private sector job	6 (9)
Self-employed	29 (45)
Mode of transport to MDR TB clinic	
Walking or bicycle	14 (22)
Bus or other public transportation	11 (17)
Auto-rickshaw	11 (17)
Taxi	9 (14)
Motorcycle	20 (31)

We interviewed 10 HCPs, with a median age of 35 years (range 29 to 54 years). They had a median of 5.5 years of work experience in the government TB program (range 2 to 15 years). The majority were men, had an undergraduate education, and had jobs as health visitors (Table 2).

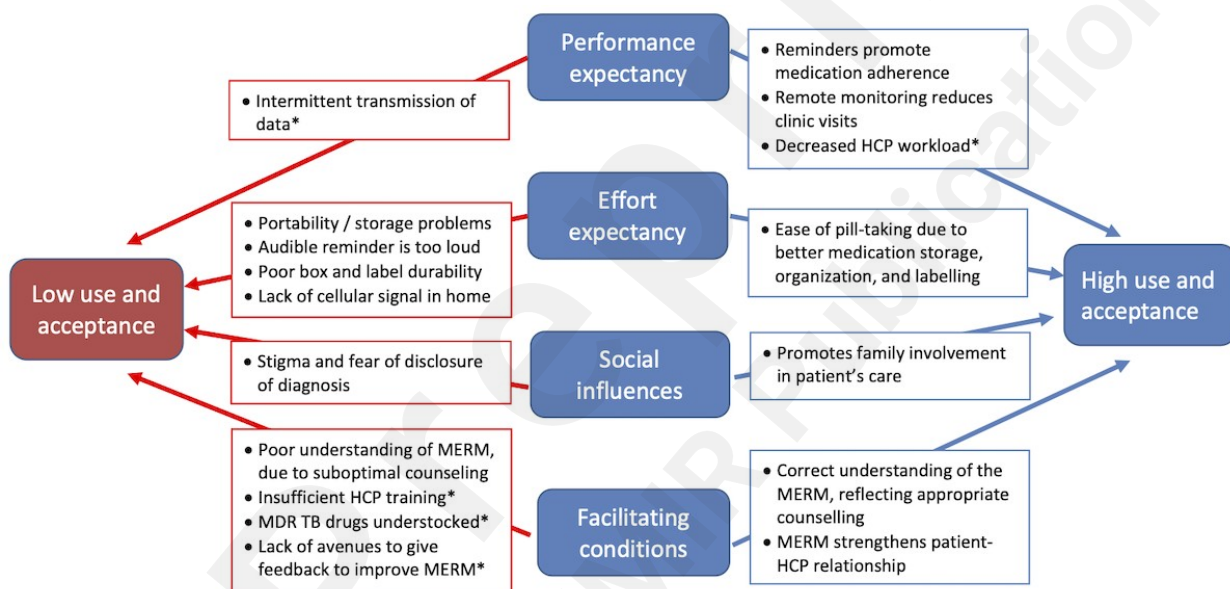
Table 2. Descriptive statistics for HCPs interviewed to understand their acceptance of the MERM

Characteristic	N (%)
Location	
Chennai	5 (50)
Mumbai	5 (50)
Gender	
Male	6 (60)
Female	4 (40)
Educational attainment	
Undergraduate college education only	8 (80)
Post-graduate education	2 (20)
Designated position	
TB health visitor	5 (50)
Senior treatment supervisor	2 (20)
Treatment coordinator	1 (10)
Deputy director of TB programs	1 (10)
District TB officer	1 (10)

Findings From MDR TB Patients

Interview findings revealed both facilitators and barriers to patient acceptance of the MERM (Figure 2).

Figure 2. Key findings regarding the determinants of high and low acceptance and use of the MERM by patients with MDR TB and HCPs, based on the framework of the UTAUT. *Indicates findings from HCP interviews; all other findings are primarily from patient interviews. HCP: healthcare provider; MERM: Medication Event Reminder Monitor.



Facilitators of Patient Acceptance and Use of the MERM

Several factors were associated with higher acceptance of the MERM (Table 3). With regard to performance expectancy (perceived usefulness), many patients felt that the reminders prevented them from forgetting to take their medications and helped them take it at the same time every day, with most preferring audible (Table 3, Q1) and a few preferring visual (Q2) reminders. For example, one patient described the following benefits of the audible reminders:

I had told [the HCPs] to set the alarm for 10 O' clock . . . I finish my breakfast before 10 O' clock and wait for the alarm to ring. The alarm is useful because even when I forget it reminds me to take the tablets. (49-year-old male patient)

Some patients also appreciated the yellow light, which served as a reminder to return to the clinic for medication refills.

Prior to being given their medications in the MERM, MDR TB patients usually visited clinics on a more frequent basis (eg, daily or weekly) for closer monitoring by HCPs. Some patients appreciated that remote monitoring of medication adherence resulted in reduced time and money spent on clinic visits (Q3), as described by the following patient:

I previously had to visit the hospital three or four times in a month, but now I am going there once a month, so it is very good that you have provided this box. It is like a blessing for me. (39-year-old male patient)

Several patients also appreciated the manner in which the MERM stores, organizes, and provides helpful internal labeling of medications. Patients previously stored the multiple medication blister packs in the MDR TB regimen in plastic bags or a cardboard box provided by the TB program that did not have internal partitions to organize medications (Q4, Q5). These findings speak both to favorable perceived usefulness (ie, performance expectancy) of the MERM for storing and organization medications and favorable ease of use (ie, effort expectancy), because most patients found it easy to follow and understand the MERM's internal labels that guide pill-taking, as noted by the following patient:

There are different compartments for each tablet, so they don't get mixed with each other... It is helpful. I like the arrows with the dots which explain how many of each medication I need to take. (38-year-old male patient)

With regard to social influences, several patients reported that the audible reminder function promoted increased involvement of family members in their TB care (Q6—Q8), although occasionally such involvement was due to annoyance from the audible reminder (Q7) or perceptions that the MERM facilitates government surveillance (Q8). In some cases, however, this family involvement was prompted by a more positive perception that the MERM represents an extension of the care provided by HCPs:

As soon as the alarm rings, my son immediately runs to me and says ‘Your doctor is calling you. Go and take your medicine and then do your work.’ (49-year-old male patient)

Counseling of patients by HCPs in appropriate use of the MERM is an important facilitating condition. Quality of counseling was assessed indirectly based on whether patients had appropriate or inappropriate knowledge of the MERM’s functions and components. As described further below, there was variability in patient understanding of the MERM; however, most patients expressed correct understanding of its medication labelling (Q9) and other basic functions. For example, the following patient correctly interpreted the different lights on the MERM, reflecting appropriate counseling in the device’s use:

If red color [light] blinks there is no charge; if the green color blinks, it signals that the tablets have to be taken at 10 O’ clock; and if the yellow color blinks, it means that the tablets are going to run out. (22-year-old male patient)

Some patients reported perceptions that HCPs deployed the MERM in a manner that provided encouragement to patients and strengthened the patient-HCP relationship (Q10). These findings highlight aspects of the MERM’s perceived usefulness (performance expectancy) for MDR TB care, as well as favorable facilitating conditions in the health system’s implementation of this technology. For example, patients appreciated the fact that HCPs within the health system seemed to be using the adherence data generated

by the MERM in positive manner that resulted in a feeling of being “cared” for remotely:

If I don't open the [pill]box, somebody from the health center calls me to find out whether I have taken the tablets or not. They care for me. (61-year-old male patient)

Table 3. Representative quotations on factors facilitating acceptance of the MERM by patients based on constructs in the UTAUT

Performance Expectancy
Reminders promote medication adherence
Q1. <i>The sound of the alarm forces me to take the medicine on time. (42-year-old female patient)</i>
Q2. <i>Even when the alarm is not audible, the light is useful, especially when I am not near the box. (25-year-old male patient)</i>
Remote monitoring reduces clinic visits
Q3. <i>I can do work at home properly now and do not have to worry about going to the health center. (27-year-old female patient)</i>
Effort expectancy
Ease of pill-taking due to better medication storage, organization, and labelling
Q4. <i>Previously, I kept the tablets in a plastic cover, but now they are safer in the box. I used to be so confused, as there were so many medicines to take. Now it is easier as I feel the medications are safe and the reminders are so helpful. (21-year-old female patients)</i>
Q5. <i>The pills were previously given in an ordinary cardboard tablet box, which does not have an alarm, but this box has an alarm to remind me. (61-year-old male patient)</i>
Social Influences
Promotes family involvement in patient's care
Q6. <i>When the alarm rings and I am outside my house, they send a person to inform me to take my pills. (49-year-old male patient)</i>
Q7. <i>My mother complains when I delay taking the medicines. She would say, 'The box has been making noise constantly' and makes sure I take the medicines so the noise will stop. (44-year-old male patient)</i>
Q8. <i>There is a camera in the box, so if you don't take the pills, people in Delhi will come to know. So take your pills. (Mother of a 25-year-old male patient)</i>
Facilitating conditions
Correct understanding of the MERM, reflecting appropriate counselling
Q9. <i>I take the tablets according to the dots shaded in each column above the compartment. (28-year-old female patient)</i>
MERM strengthens patient-HCP relationship

Q10. *At the time of discharge... [a] health worker explained the MERM box and told me about the need to take my medicines regularly and that the box would help remind me. Those words motivated and encouraged me. My anxiety was reduced, and I was filled with happiness. (53-year-old male patient)*

Barriers to Patient Acceptance and Use of the MERM

Patients also experienced a variety of barriers to acceptance and use of the MERM (Table 4). A few patients did admit to lack of understanding regarding the purpose of the MERM, which suggests potential limitations to performance expectancy (perceived usefulness) for this minority of individuals:

I did not know that when I don't take pills, it will be shown [to HCPs] by a computer. (45-year-old female patient)

More commonly, patients described limitations in effort expectancy (ease of use) as barriers to acceptance and use of the MERM. In particular, the relatively large size of the MERM, as designed to facilitate storage of the multiple medications in the MDR TB regimen, limited its portability and posed problems for storage of the device. For example, one patient described how these barriers led him to remove his medication blister packs from the device, which would result in the MERM recording inaccurate adherence information:

I take out my pills out of the box when I leave for work and put them in my pocket. I cannot carry such a big box to work that makes so much noise when I open it. I take the medicines [at work] when I am free. I do not benefit from the alarm or the light [audible and visual reminders] because I leave the box at home. (21-year-old male patient)

Other patients similarly described how the large size of the device served as a barrier to taking it to work (Table 4, Q11) or storing it inside the house (Q12). In addition, some patients' concerns with the device's large size and audible reminder stemmed from worries related to stigma and privacy. Patients were concerned that the device's size and the loud sound of the audible reminder would draw attention,

potentially raising questions from others about the patient's underlying medication condition (Q13, Q14). Some patients found the audible reminder to be a major annoyance (Q15). For example, one patient propped the box open to prevent the alarm from going off:

The alarm is too loud. So to avoid it [from going off], I put a paper in between the box and the lid and take the medicine. (18-year-old female patient)

Notably, this action would break the magnetic seal on the MERM's lid, interfering with appropriate recording of daily dose-taking and thereby resulting in an inaccurate adherence record.

Some patients also found the body of the MERM, which is made of commercial grade cardboard, to poorly withstand the humidity and monsoon weather conditions in India. Humidity resulted in peeling of medication labeling information from the box (Q16) and in distortion of the box's integrity and shape:

My box bulged after it had rained continuously, and the inside of the house became damp, so it would be better if the box was made out of plastic. (48-year-old male patient)

Another barrier to ease of use, is that a few patients found following of the medication labeling on the MERM to be challenging; however, some of these difficulties may have reflected poor organization of medications in the MERM box by healthcare workers, such that medications were not in the correct partitions corresponding to the appropriate medication labels:

This box is useful as there are instructions in the box about its use, but sometimes the arrows [labeling each medication] don't match with the [correct] medicines. I get confused. (40-year-old male patient)

Patients also reported a variety of other technical problems that limited the ease of using the MERM,

including weak cellular signal in the patient's home resulting in non-reporting of doses taken (Q17), failure of the device's battery (Q18), and malfunction of the reminder lights (Q19, Q20).

With regard to social influences, several patients reported concerns regarding violations of the privacy and confidentiality of their MDR TB diagnosis, which reflects the high level of stigma surrounding this disease. As described above, some patients were particularly concerned about stigma when traveling with the MERM (Q13, Q14), but many patients were equally concerned about stigma when taking the device with them to visits with their TB HCPs (Q21, Q22), when friends or relatives visited the home (Q23), or when family members heard the audible reminder, even if the device was hidden (Q24). One patient was even concerned that the audible reminder was loud enough that it could draw the attention of her neighbors:

When the alarm rings my neighbors can hear it. I am scared that they will come to know about my disease.

(21-year-old female patient)

With regard to facilitating conditions, some patients conveyed an incorrect understanding of key functions of the MERM (Q25). For example, when asked about the lights on the MERM, the following patient provided this description which reflects an incorrect understanding of what each light is meant to convey:

I have to close the box when the yellow color light blinks and I understand that if the red color light blinks the tablets are going to be over. (75-year-old female patient)

Table 4. Representative quotations on barriers to acceptance and use of the MERM by patients based on constructs in the UTAUT

Effort expectancy
Size, portability, and storage problems
Q11. <i>Sometimes I have to go for work for 2 or 3 days, and during that time I can't carry this big box to the workplace. A smaller box with an alarm would be useful when I go for work.</i> (41-year-old male patient)

Q12. I keep my box in a hen cage [outside of the house], because my children used to play with it. I don't have a place in my home to keep the box where my children won't reach it. (33-year-old male patient)
Q13. The box looks big in size [ie, easily seen by others], and I feel scared while travelling on the bus that the alarm might ring. (34-year-old female patient)
Q14. How can I carry this big box when I have to attend a marriage function in my village? I am sure my relatives will ask me questions when I take the medicines out of the box and when they hear the alarm sound. I usually take the medicines out of the box when I travel and leave the box at home. (45-year-old female patient)
Audible reminder is too loud
Q15. The sound is so loud, even the neighbors can hear it... Maybe it [the audible reminder] is useful for elders but not for youngsters like me because I feel irritated when it alerts me. (18-year-old female patient).
Limited durability of the box and labels
Q16. The label in the box is not properly fixed and it has started peeling off. (18-year-old female patient)
Other technical problems with the MERM
Q17. Sometimes due to [cellular] signal problems, although I was opening the box, these doses were not reported. I received calls from the health center [in which HCPs told me] to keep the box [at locations in the house] where the network might be better. (38-year-old male patient)
Q18. The alarm did not ring once and when I took it to the centre, they told that the box has ran out of charge and needs to be replaced or recharged. (44-year-old male patient)
Q19. I am confused because all the three lights were glowing every day. (37-year-old female patient)
Q20. I could not see the yellow light blink to get the signal as to when my tablets are over. (27-year-old male patient)
Social Influences
Problems related to privacy and stigma
Q21. When I carry the box when leaving the health center, people know that I have TB. This is embarrassing, so I try to hide it, but it is too big. (39-year-old male patient)
Q22. I do not want my name on the box because it is obvious that anyone who has such a box is a TB patient. It would be better if the box did not have my name on it. (42-year-old male patient)
Q23. Suppose that my relatives visit my home. The box's alarm could ring in front of everybody... They may come to know that I have this disease. I would be so embarrassed in front of them. So, I don't like this box. (18-year-old female patient)
Q24. I keep the MERM inside the cupboard in my bedroom. I go inside my bedroom and take the medicine [privately]. If the alarm goes off and there is somebody at home, they sometimes ask me where that sound came from. I tell them that I received a message on my phone, because the alarm's sound is similar to my phone's text message ring tone. (49-year-old male patient)
Facilitating conditions
Incorrect understanding of the MERM, reflecting suboptimal counseling

Q25. *The green color light helps me as a reminder but the red color means danger, which indicates that I have to go for the refill.* (18-year-old female patient) [Description reflects incorrect understanding of the meaning of each light]

Findings from HCPs

Interview findings revealed both facilitators and barriers to HCP acceptance of the MERM (Figure 2).

Facilitators of HCP Acceptance and Use of the MERM

For HCPs, the strongest facilitators of their acceptance and use of the MERM were perceptions of positive performance expectancy (ie, perceived usefulness). In particular, most HCPs felt that remote monitoring of medication adherence had benefits for both patients and HCPs. During pilot implementation of the MERM, MDR TB patients were generally dispensed one month of medications in the device. Patient visits to the clinic to pick up medications, which were previously required on a weekly or biweekly basis, were reduced substantially, under the assumption that remote monitoring of adherence minimized the need for more frequent in-person monitoring. Most HCPs felt that patients benefited considerably from this reduction in required clinic visits, as described in the following quotation:

Patients now do not have to travel long distances spending their money to collect their drugs every week or sometimes twice a week. Most of our MDR TB patients come from distant villages and transportation is very difficult. We feel comfortable giving them a month's supply in the box [MERM] as it is easier for them to take and the light and alarm [reminders] help them to take their drugs on time. (Senior Treatment Supervisor)

Reduced frequency of patient visits also decreased workload for many HCPs, resulting in decreased stress:

Previously we had to supervise therapy on a daily basis [ie, DOT]. But now the patients come [to the clinic] only once a month, so our work pressure has reduced. (Senior Treatment Supervisor)

Some HCPs reported that the decreased workload allowed them to focus more on each patient interaction, as well as other tasks, which increased job satisfaction:

I have more time now to check whether patients have taken their tablets or not. I am also able to concentrate on other tasks as well, which gives me more satisfaction in my work. (Health Visitor)

Finally, with regard to social influences, some HCPs perceived that providing medications in the MERM, as compared to the prior cardboard box used to dispense MDR TB medications, was potentially less stigmatizing for patients, because some of the previously used cardboard boxes contained messages regarding TB:

The good thing about the MERM box is that it does not carry any messages on TB [on the outside of the box], so there is no stigma attached to it. Patients can carry it freely. (Medical Officer)

Barriers to HCP Acceptance and Use of the MERM

HCPs also reported barriers to acceptance of the MERM for both patients and HCPs. With regard to performance expectancy, HCPs found that intermittent (every 72 hours) updating of patients' adherence records to be the most significant limitation to the perceived usefulness of the MERM, as described by the following HCP:

It takes 72 hours for the [MERM] dashboard to show that the patient has taken the medication. This makes it difficult for us to monitor the patient's drug intake on a daily basis. We cannot take action as promptly and lose time. (Pharmacist)

With regard to effort expectancy (ease of use), many HCPs felt that the size of the MERM made transporting the device to and from clinic visits prohibitive:

It is good [for patients] to have a device like the MERM but it is too big for them to carry. How do they carry it? It is difficult to carry it as it is as they need to go by bus and train. We need to provide them with a big bag for [the device]. (Health visitor)

The MERM's size also resulted in challenges for HCPs themselves:

Even for us [HCPs] at the health centers, it is difficult to find space to store these MERM boxes. (Senior treatment supervisor)

Consistent with findings from the patient interviews, HCPs described lack of cellular signal in patients' homes as being a barrier to MERM use for rural patients in particular. HCPs also noted that this resulted in difficulties in their own ability to get adherence data from, and communicate with, patients:

Some of the patients are not willing to use the box [MERM], as people living in the villages are not always getting [adequate cellular] signal, so the device is not working. They are unable to even contact the senior treatment supervisor. (Senior treatment supervisor)

During pilot implementation of the MERM, HCPs found that some facilitating conditions on the part of the health system were suboptimal. For example, some HCPs felt that the single-day training provided would be insufficient for new personnel:

One day of training will be difficult if we have newly recruited staff, because they have to understand the [MDR TB] program, and then undergo training [in use of the MERM]. (Senior treatment supervisor)

Some barriers to MERM implementation arose from other, more fundamental, challenges in the MDR TB

program. For example, MDR TB medications were supposed to be dispensed in the MERM on a monthly basis; however, specific medications were sometimes understocked at clinics. This problem of understocked medications was easier to manage when patients were refilling medications on a weekly or more frequent basis, because fewer medications had to be dispensed at any given visit. Dispensing more medications at once with the MERM accentuated this problem of understocking of drugs:

Sometimes MDR drugs are not available, and so we are not able to give all the medicines required when patients come for their medicines. How do we leave that compartment [in the MERM for a specific medication] empty, and what can we tell the patient? (Pharmacist)

Finally, some personnel felt that, when problems were identified with implementation of the MERM, they did not have clear channels to communicate these challenges so they could be addressed:

When we started using the MERM, we were excited about the device. When patients came back for their medication refills, they raised concerns with regard to technical problems with the box—the alarm, light, texture and size of the box, for example. I was not sure who to notify about these problems. Maybe we could have had those who made the device discuss our feedback so it could be improved? (Senior treatment officer)

Discussion

Implications of Findings From Patients with TB

This study describes evaluation of a low-cost digital pillbox as a tool for measuring and promoting medication adherence among MDR TB patients during pilot implementation in India's NTEP. Although multiple previous studies have evaluated use of similar digital pillboxes as part of TB care [3,18–20,22,23], to our knowledge, only one prior study conducted in South Africa [17] has evaluated use of these technologies for MDR TB patients, who face unique challenges in care, including the complexity of their medication regimens, prolonged duration of therapy, increased risk of drug toxicities, and greater disease-related stigma. In

addition, our study is unique in assessing the perspectives of both patients and HCPs. Notably, implementation of the MERM took place in the context of a broader initiative rolling out DATs in the NTEP to promote adherence among drug-susceptible TB patients [35].

Patients reported multiple factors that increased acceptability and use of the MERM. Most patients felt that the audible and visual signals served as helpful reminders to take their medications. Forgetfulness is a common barrier to medication adherence [36]. While often thought of as a cognitive barrier, forgetfulness may also reflect other psychosocial or life challenges faced by patients, such as depression or spending long hours at work. In a recent qualitative study in India assessing patient acceptance of 99DOTS, a cellphone-based DAT used to monitor drug-susceptible TB patients, most patients reported that SMS text messages did not serve as useful reminders to take their daily doses, because these messages often got lost amid a high volume of “spam” SMS text messages [34]. In contrast, in the current study, an advantage of the MERM was that the reminders drew patients to the site where medications were stored. This increased the likelihood that patients immediately took their doses, which may promote better habit formation in pill-taking behavior [37,38]. In addition, for some patients, the MERM’s reminders transformed social dynamics in the home by drawing family members into their TB care, a finding also reported in studies of other DATs, such as 99DOTS [34].

Patients also appreciated several aspects of the MERM’s design—in particular, the secure storage provided by the box, the labels to help patient take the appropriate number of tablets of each medication, and the organization and separation of different medications, facilitated by the box’s internal partitions. These features were particularly valued in light of the complexity of MDR TB treatment regimens, which generally include at least four or five different medications, as well as the fact that MDR TB medications had previously been dispensed in a cardboard box without internal partitions to separate medications or labels to guide appropriate pill-taking.

For some patients, the MERM enhanced their relationship with the health system. On the one hand, most patients reported that they appreciated saving time and money by not having to visit the clinic as often, because the frequency of routine clinic visits for MDR TB patients was reduced during pilot implementation of the MERM. Although this reduction in clinic visits resulted in decreased face-to-face interactions with HCPs, some patients actually described feeling more “cared” for. This feeling derived from the perception that HCPs were remotely watching over their clinical progress, as well as from positive responses to actual phone or in-person outreach to patients by HCPs, guided by patients’ adherence data. Previous studies evaluating the use of DATs to support HIV and TB adherence in Uganda, India, and South Africa similarly found that remote monitoring enhanced some patients’ perceptions of the care provided by the health system[17,34], and this may be one of the behavioral pathways by which DATs may motivate patients to adhere to treatment.

Patients also reported barriers to acceptance and use of the MERM. Some of these barriers may be modifiable by altering the MERM’s design or its implementation within the health system (Table 5). For example, the loud volume of the audible reminder—a common complaint from patients also reported in a prior study of the MERM from China [18]—could potentially be modified or the audible reminder disabled completely, ideally by patients themselves based on personal preference. As another example of a modifiable barrier, during this pilot implementation, the MERM was made of commercial-grade cardboard, which did not wear well in India’s monsoon weather conditions. Redesigning the MERM for MDR TB patients using plastic would be feasible and likely minimize weather-related damage, although it would likely increase the cost of the device. Similarly, other technical problems with the MERM’s design, such as battery failure or inappropriate blinking of the reminder lights, could likely be addressed with product improvements in future iterations of the device.

Table 5. Recommendations for improving the MERM device and its implementation, based on

findings from MDR TB patient and HCP interviews

Feature that could be redesigned	Recommendations
Design of the device	<ul style="list-style-type: none"> • Data transmission from the device on a daily basis may facilitate better near real-time monitoring • Redesign using plastic (rather than cardboard) may reduce wear due to weather conditions • Strengthening internal partitions may help avoid accidental mixing of different medications • Reuse of the device should be limited, given considerable wear and tear even after single patient use
Reminder functions	<ul style="list-style-type: none"> • Allowing patients to reduce the volume of the audible reminder or to deactivate audible or visual reminders may address patient concerns about privacy and stigma • Malfunction of visual reminders (eg, all lights blinking at once) should be fixed
Counseling and monitoring of patients	<ul style="list-style-type: none"> • HCPs should be trained to provide standardized counseling to ensure patient understanding of all key MERM functions • HCPs should use pill counts and administer adherence questions to patients at clinic and home visits to cross-check adherence data reported by the MERM
Screening out patients for whom MERM may not be appropriate	<ul style="list-style-type: none"> • Systematic screening should be performed up front to identify patients for whom the MERM may not be appropriate—including those with concerns about stigma, fear of disclosure of diagnosis, difficulties with portability, and lack of cellular signal in the home
Training of HCPs	<ul style="list-style-type: none"> • Mechanisms should be created for training of newly hired NTEP personnel and provision of periodic refresher training in the MERM for existing personnel • Mechanisms should be created for NTEP personnel to provide ongoing feedback to facilitate device improvements

While some barriers may be addressable, others may present more fundamental challenges that could limit the MERM's use by some patients. For example, the MERM's relatively large size was a major barrier to use for patients who were traveling or preferred to take their medications at work. On the one hand, the MERM's size is necessary to hold a one-month supply of MDR TB medications, and patients benefit from having their medications dispensed in an organized manner with appropriate labeling. On the other hand, because of the

prohibitive size of the MERM, patients who need to take doses when traveling or at work tended to remove doses from the device, rather than carry the device with them. Lack of cellular signal in the home is another non-modifiable barrier that would limit the benefits of remote monitoring, because adherence data could not be transmitted from the device on a regular basis.

Disease-related stigma—from family and community members—is a common challenge faced by MDR TB patients [10]. Due to stigma, MDR TB patients often do not disclose their diagnosis to family members, friends, and coworkers; as a result, patients often fear situations that could result in disclosure of their diagnosis to others. Not surprisingly, stigma and fear of disclosure were barriers to MERM use for some patients. In particular, the MERM's large size, which increases its visibility to others, and the audible and visual reminders raised concerns about disclosure and could potentially contribute to non-use of the device.

All of these problems—removal of doses from the device due to its lack of portability, non-reporting of box openings due to lack of cellular signal, and non-use of the device due to disease-related stigma—could result in under-reporting of medication doses, resulting in inaccuracies in some patients' adherence records. Recent studies of 99DOTS in India found that these same barriers contribute to relatively high rates of patient non-engagement with that technology [34], especially in the continuation phase of therapy, which contributed to 99DOTS' suboptimal accuracy for measuring adherence to TB medications [24]. A small qualitative study of drug-susceptible TB patients monitored using the MERM in Vietnam found that only about half of patients used the device as intended, largely due to difficulties with the device's portability, with the result that the device's data often did not reflect actual medication adherence [23]. A high rate of device non-use was also found in a study that used the Wisepill device (a similar digital pillbox) to monitor adherence to HIV preexposure prophylaxis in young men who have sex with men in the U.S. [39].

These barriers to use suggest that, if use of the MERM is expanded among MDR TB patients in India, there could be some limits to the device's reach, or overall coverage, in this patient population. Wide-scale

implementation of a similar digital pillbox among drug-susceptible TB patients in China has revealed meaningful limitations in the device's reach in that patient population [21,22]. For example, in one study of the implementation of a digital pillbox in 30 counties in China, even after excluding 41% of the patient cohort who were either not eligible to use the device or who did not receive the device for unclear reasons, only about two-thirds of the remaining 1,314 patients who received the pillbox exhibited sustained use for the remainder of treatment [22]. The other one-third of patients who received the digital pillbox either stopped using the device or met criteria to be shifted back to monitoring with DOT due to a high proportion of missed doses, as reported by the device. These missed doses could have represented either true non-adherence to medications or inappropriate use of the device.

In light of such findings from other contexts, it would be reasonable to assume that some proportion of MDR TB patients in India might not use the MERM in wide-scale implementation. As such, based on our findings, the NTEP could consider screening MDR TB patients up front to identify individuals who might be unlikely to use the device—for example, because of patient concerns about stigma and portability or lack of cellular signal in the home (Table 5). Also, HCPs should use other strategies to verify medication adherence, including pill counts and administering adherence-related questions to patients at every in-person clinic and home visit—which will help HCPs to crosscheck the adherence data being received from the MERM.

Implications of Findings From HCPs

In the HCP interviews, NTEP personnel affirmed some of the patient-oriented benefits of the MERM, in particular the time and money saved by patients from the reduced frequency of clinic visits; however, HCPs' perceptions that the MERM was associated with fewer patient concerns about stigma were not shared by some patients. HCPs in the current study also reported that implementation of the MERM reduced their workload, owing to the reduced frequency of clinic visits by patients and the ability to monitor patient adherence from the clinic rather than through visits to patients' homes. As a result, HCPs dedicated greater time to other tasks and reported improved job satisfaction, similar to findings of a previous study of the

MERM conducted in China [18]. HCPs did find some aspects of the health system's pilot implementation to be suboptimal; however, most of these concerns were potentially addressable. In particular, they reported a need for more training in appropriate use of the MERM, especially in light of high turnover of staff, and the need for a platform to communicate any implementation challenges they faced (Table 5).

Directions for Future Research

This initial evaluation has identified several features that may facilitate high acceptability of the MERM for many MDR TB patients, especially if modifications are made to improve the device. However, further research is needed to understand the MERM's accuracy for measuring adherence to MDR TB medications, its effectiveness for improving MDR TB treatment outcomes, and its actual reach—ie, coverage or uptake by patients—in large-scale implementation [3].

Even for patients who agree to use the MERM, the adherence record could be inaccurate either due to under-reporting (eg, if patients take medications out of the device, resulting in device non-use) or over-reporting (eg, if patients open and close the device without actually taking medications). Indeed, a recent study of 99DOTS, in which its adherence record was compared to urine isoniazid test results from TB patients collected during unannounced home visits, found that both under- and over-reporting of adherence contributed to that technology's suboptimal accuracy [24]. A similar research approach, involving unannounced home visits with measurement of urine biomarkers for MDR TB medications, could be used to evaluate the MERM's accuracy, although pill counts should probably also be conducted to provide insights into whether patients have differential adherence to different medications in the MDR TB regimen.

Existing studies of the use of DATs to promote adherence to TB medications have found both positive [20,40] and negative or equivocal [41–43] impacts on adherence and TB treatment outcomes. As such, studies of effectiveness, especially high-quality randomized trials, are needed to assess whether MERM use translates

into improvements in treatment outcomes and post-treatment recurrence-free survival for MDR TB patients. Even when DATs have been shown to be effective, as with digital pillboxes in China [20], subsequent studies in large-scale implementation have shown suboptimal reach, or coverage of patients, by these DATs [21,22]. As such, studies of the MERM's coverage of MDR TB patients in large-scale implementation will be critical to ensure it achieves population-level impact. Finally, in light of the diverse psychosocial barriers to adherence faced by MDR TB patients [10], the benefits of monitoring with the MERM or other DATs in this population will depend on the development of social and behavioral interventions to address problems such as medication toxicities, depression, stigma, and substance use disorder that are often the underlying causes of non-adherence in these patients [44].

Study Limitations

Our study was limited to assessing patient and HCP perceptions of the MERM—rather than more objective findings, such as the technology's accuracy of impact on clinical outcomes. As such, we may have overestimated the acceptability and benefits of this technology due to socially desirable responses from interviewees, which is a common bias in qualitative research. In addition, patients attributed the reduced frequency of their clinic visits to the MERM, as a longer supply of medications was dispensed in the device. The reduced frequency of clinic visits may have therefore biased patients in favor of higher acceptance of the device; however, provision of a longer supply of medications could have just as easily been implemented without the MERM.

Our deductive approach to analysis allowed us to organize and report our findings using the UTAUT, which is a robust and evidence-based framework for understanding technology acceptance and use; however, a limitation of this approach to analysis is that we could have overlooked some findings that did not fit into this predetermined framework.

Another limitation of our study is that we assessed patient's perceptions of the MERM within a few weeks of their initial use of the device. In light of the prolonged duration of MDR TB treatment, it is possible that patients' acceptance and use of the device could change over time. In addition, our study was limited to two major urban centers and therefore may not be representative of barriers to use of the MERM in rural parts of India. Future studies could consider including more diverse geographic settings and conducting multiple interviews to understand the acceptability of the MERM throughout the treatment course.

Conclusions

In this study of the pilot implementation of a low-cost digital pillbox to promote adherence to MDR TB medications, we identified several features that facilitate high acceptability of the device among many patients. These included helpful organization and labeling of medications, feeling more "cared for" by the health system due to remote monitoring, and appreciation of the audible and visual reminders, which often drew family members into patients' care.

At the same time, we also identified barriers that could limit acceptance and use of the MERM by some MDR TB patients. Although some of these barriers could be addressed relatively easily with modification to the device, other barriers—such as difficulties with the portability of the device, lack of cellular signal in the home, and fears about disclosure of diagnosis due to disease-related stigma—are more difficult to modify and may partly limit the reach, or population coverage, of this technology. Future research is needed to assess the MERM's accuracy for measuring adherence, its effectiveness for improving treatment outcomes, and patients' sustained use of the device in larger-scale implementation in India's MDR TB treatment program.

Acknowledgments

Maya Lubeck-Schricker assisted with referencing and editing the manuscript.

Abbreviations

HCP - Healthcare provider

MDR TB - Multidrug resistant Tuberculosis

MERM - Medication Event Reminder Monitor

NIRT - National Institute for Research in TB

NTEP - National Tuberculosis Elimination Program

UTAUT - Unified theory of acceptance and use of technology

References

1. Global Tuberculosis Report 2019. Geneva: World Health Organization; 2019 p. 264–265. URL: <https://apps.who.int/iris/bitstream/handle/10665/329368/9789241565714-eng.pdf?ua=1> [accessed August 4, 2020]
2. Ahmad N, Ahuja SD, Akkerman OW, Alffenaar J-WC, Anderson LF, Baghaei P, et al. Treatment correlates of successful outcomes in pulmonary multidrug-resistant tuberculosis: an individual patient data meta-analysis. *The Lancet* 2018 Sep 8;392(10150):821–834 [PMID:30215381] [doi:10.1016/S0140-6736(18)31644-1]
3. Subbaraman R, de Mondesert L, Musiimenta A, Pai M, Mayer KH, Thomas BE, et al. Digital adherence technologies for the management of tuberculosis therapy: mapping the landscape and research priorities. *BMJ Glob Health* 2018;3(5):e001018 [PMID:30364330] [doi:10.1136/bmjgh-2018-001018]
4. Lan Z, Ahmad N, Baghaei P, Barkane L, Benedetti A, Brode SK, et al. Drug-associated adverse events in the treatment of multidrug-resistant tuberculosis: an individual patient data meta-analysis. *The Lancet Respiratory Medicine* 2020 Apr 1;8(4):383–394 [PMID:32192585] [doi:10.1016/S2213-2600(20)30047-3]
5. Thomas B, Watson B, Senthil EK, Deepalakshmi A, Balaji G, Chandra S, et al. Alcohol intervention strategy among tuberculosis patients: a pilot study from South India. *Int J Tuberc Lung Dis* 2017 01;21(8):947–952 [PMID:28786805] [doi:10.5588/ijtld.16.0693]
6. Janse Van Rensburg A, Dube A, Curran R, Ambaw F, Murdoch J, Bachmann M, et al. Comorbidities between tuberculosis and common mental disorders: a scoping review of epidemiological patterns and person-centred care interventions from low-to-middle income and BRICS countries. *Infect Dis Poverty* 2020 Jan 15;9(1):4 [PMID:31941551] [doi:10.1186/s40249-019-0619-4]
7. Craig GM, Daftary A, Engel N, O'Driscoll S, Ioannaki A. Tuberculosis stigma as a social determinant of health: a systematic mapping review of research in low incidence countries. *Int J Infect Dis* 2017 Mar;56:90–100

[PMID:27810521] [doi:10.1016/j.ijid.2016.10.011]

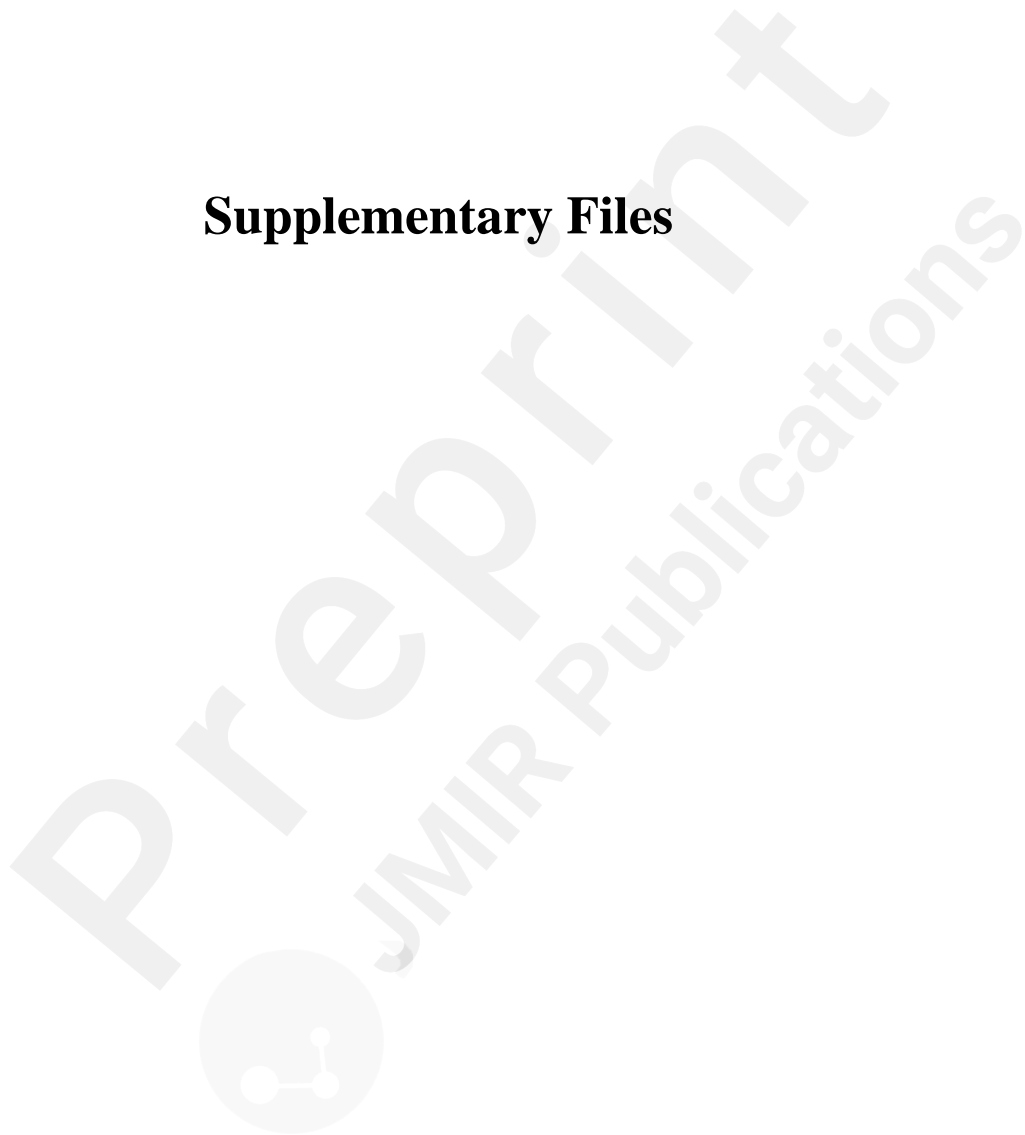
8. Cazabon D, Pande T, Sen P, Daftary A, Arsenault C, Bhatnagar H, et al. User experience and patient satisfaction with tuberculosis care in low- and middle-income countries: A systematic review. *J Clin Tuberc Other Mycobact Dis* 2020 May;19:100154 [PMID:32140571] [doi:10.1016/j.jctube.2020.100154]
9. Bhatnagar H. User-experience and patient satisfaction with quality of tuberculosis care in India: A mixed-methods literature review. *J Clin Tuberc Other Mycobact Dis* 2019 Dec;17:100127 [PMID:31788569] [doi:10.1016/j.jctube.2019.100127]
10. Thomas BE, Shanmugam P, Malaisamy M, Ovung S, Suresh C, Subbaraman R, et al. Psycho-Socio-Economic Issues Challenging Multidrug Resistant Tuberculosis Patients: A Systematic Review. *PLoS One* 2016 Jan 25;11(1):e0147397 [PMID:26807933] [doi:10.1371/journal.pone.0147397]
11. Karumbi J, Garner P. Directly observed therapy for treating tuberculosis. *Cochrane Database Syst Rev* 2015 May 29;(5):CD003343 [PMID:26022367] [doi:10.1002/14651858.CD003343.pub4]
12. Tian J-H, Lu Z-X, Bachmann MO, Song F-J. Effectiveness of directly observed treatment of tuberculosis: a systematic review of controlled studies. *Int J Tuberc Lung Dis* 2014 Sep;18(9):1092-1098 [PMID:25189558] [doi:10.5588/ijtld.13.0867]
13. Pasipanodya JG, Gumbo T. A Meta-Analysis of Self-Administered vs Directly Observed Therapy Effect on Microbiologic Failure, Relapse, and Acquired Drug Resistance in Tuberculosis Patients. *Clin Infect Dis* 2013 Jul 1;57(1):21-31 [PMID:23487389] [doi:10.1093/cid/cit167]
14. Sagbakken M, Frich JC, Bjune GA, Porter JDH. Ethical aspects of directly observed treatment for tuberculosis: a cross-cultural comparison. *BMC Med Ethics* 2013 Jul 2;14:25 [PMID:23819555] [doi:10.1186/1472-6939-14-25]
15. Yellappa V, Lefèvre P, Battaglioli T, Narayanan D, Van der Stuyft P. Coping with tuberculosis and directly observed treatment: a qualitative study among patients from South India. *BMC Health Serv Res* 2016 19;16:283 [PMID:27430557] [doi:10.1186/s12913-016-1545-9]
16. WHO consolidated guidelines on drug-resistant tuberculosis treatment. World Health Organization; 2019. URL: <http://www.who.int/tb/publications/2019/consolidated-guidelines-drug-resistant-TB-treatment/en/> [accessed August 4, 2020]
17. Bionghi N, Daftary A, Maharaj B, Msibi Z, Amico KR, Friedland G, et al. Pilot evaluation of a second-generation electronic pill box for adherence to Bedaquiline and antiretroviral therapy in drug-resistant TB/HIV co-infected patients in KwaZulu-Natal, South Africa. *BMC Infect Dis* 2018 11;18(1):171 [PMID:29642874] [doi:10.1186/s12879-018-3080-2]
18. Liu X, Blaschke T, Thomas B, De Geest S, Jiang S, Gao Y, et al. Usability of a Medication Event Reminder Monitor System (MERM) by Providers and Patients to Improve Adherence in the Management of Tuberculosis. *Int J Environ Res Public Health* 2017 25;14(10):1115 [PMID:28946683] [doi:10.3390/ijerph14101115]
19. Musiimenta A, Tumuhimbise W, Mugaba AT, Muzoora C, Armstrong-Hough M, Bangsberg D, et al. Digital monitoring technologies could enhance tuberculosis medication adherence in Uganda: Mixed methods study. *J Clin Tuberc Other Mycobact Dis* 2019 Dec;17:100119 [PMID:31788561] [doi:10.1016/j.jctube.2019.100119]
20. Liu X, Lewis JJ, Zhang H, Lu W, Zhang S, Zheng G, et al. Effectiveness of Electronic Reminders to Improve Medication Adherence in Tuberculosis Patients: A Cluster-Randomised Trial. *PLoS Med* 2015 Sep;12(9):e1001876 [PMID:26372470] [doi:10.1371/journal.pmed.1001876]
21. Wang N, Zhang H, Zhou Y, Jiang H, Dai B, Sun M, et al. Using electronic medication monitoring to guide differential management of tuberculosis patients at the community level in China. *BMC Infect Dis* 2019 Oct 15;19(1):844 [PMID:31615433] [doi:10.1186/s12879-019-4521-2]

22. Wang N, Shewade HD, Thekkur P, Huang F, Yuan Y, Wang X, et al. Electronic medication monitor for people with tuberculosis: Implementation experience from thirty counties in China. *PLoS ONE* 2020;15(4):e0232337 [PMID:32348351] [doi:10.1371/journal.pone.0232337]
23. Drabarek D, Anh NT, Nhung NV, Hoa NB, Fox GJ, Bernays S. Implementation of Medication Event Reminder Monitors among patients diagnosed with drug susceptible tuberculosis in rural Vietnam: A qualitative study. *PLoS ONE* 2019;14(7):e0219891 [PMID:31329610] [doi:10.1371/journal.pone.0219891]
24. Thomas BE, Kumar JV, Chiranjeevi M, Shah D, Khandewale A, Thiruvengadam K, et al. Evaluation of the accuracy of 99DOTS, a novel cellphone-based strategy for monitoring adherence to tuberculosis medications: Comparison of digital adherence data with urine isoniazid testing. *Clin Infect Dis* 2020 Mar 28 [PMID:32221550] [doi:10.1093/cid/ciaa333]
25. Venkatesh V, Morris MG, Davis GB, Davis FD. User Acceptance of Information Technology: Toward a Unified View. *MIS Quarterly* 2003;27(3):425–478 [doi: 10.2307/30036540]
26. Venkatesh V, Thong JYL, Xu X. Unified Theory of Acceptance and Use of Technology: A Synthesis and the Road Ahead. *Journal of the Association for Information Systems* 2016 May;17(5):328–376 [URL:http://www.vvenkatesh.com/wp-content/uploads/dlm_uploads/2016/01/2016_JAIS_Venkatesh-et-al.-UTAUT.pdf]
27. Dhanaraj B, Papanna MK, Adinarayanan S, Vedachalam C, Sundaram V, Shanmugam S, et al. Prevalence and risk factors for adult pulmonary tuberculosis in a metropolitan city of South India. *PLoS ONE* 2015;10(4):e0124260 [PMID:25905900] [doi:10.1371/journal.pone.0124260]
28. India TB Report 2019: Revised National TB Control Programme Annual Report. New Delhi: Central TB Division, Ministry of Health and Family Welfare; 2019. URL: <https://tbcindia.gov.in/WriteReadData/India%20TB%20Report%202019.pdf> [accessed August 4, 2020]
29. D'souza DTB, Mistry NF, Vira TS, Dholakia Y, Hoffner S, Pasvol G, et al. High levels of multidrug resistant tuberculosis in new and treatment-failure patients from the Revised National Tuberculosis Control Programme in an urban metropolis (Mumbai) in Western India. *BMC Public Health* 2009 Jun 29;9:21 [PMID:19563647] [doi:10.1186/1471-2458-9-211]
30. Isaakidis P, Das M, Kumar AMV, Peskett C, Khetarpal M, Bamne A, et al. Alarming levels of drug-resistant tuberculosis in HIV-infected patients in metropolitan Mumbai, India. *PLoS ONE* 2014;9(10):e110461 [PMID:25333696] [doi:10.1371/journal.pone.0110461]
31. Dalal A, Pawaskar A, Das M, Desai R, Prabhudesai P, Chhajed P, et al. Resistance patterns among multidrug-resistant tuberculosis patients in greater metropolitan Mumbai: trends over time. *PLoS ONE* 2015;10(1):e0116798 [PMID:25606853] [doi:10.1371/journal.pone.0116798]
32. Revised National TB Control Programme: Technical and Operational Guidelines for Tuberculosis Control. New Delhi: Central TB Division, Ministry of Health and Family Welfare; 2016. URL: <http://health.bih.nic.in/Docs/Guidelines/Guidelines-TB-Control.pdf> [accessed August 4, 2020]
33. Patton M. *Qualitative Research & Evaluation Methods*. 3rd ed. Thousand Oaks, CA: Sage Publications; 2002. URL: <https://us.sagepub.com/en-us/nam/qualitative-research-evaluation-methods/book232962> [accessed August 4, 2020]
34. Thomas BE, Kumar JV, Onongaya C, Bhatt SN, Galivanche A, Periyasamy M, et al. Explaining Differences in the Acceptability of 99DOTS, a Cell Phone-Based Strategy for Monitoring Adherence to Tuberculosis Medications: Qualitative Study of Patients and Health Care Providers. *JMIR mHealth and uHealth* 2020;8(7):e16634 [doi: 10.2196/16634]
35. Cross A, Gupta N, Liu B, Nair V, Kumar A, Kuttan R, et al. 99DOTS: A Low-Cost Approach to Monitoring and Improving Medication Adherence. *International Conference on Information and Communication Technologies and*

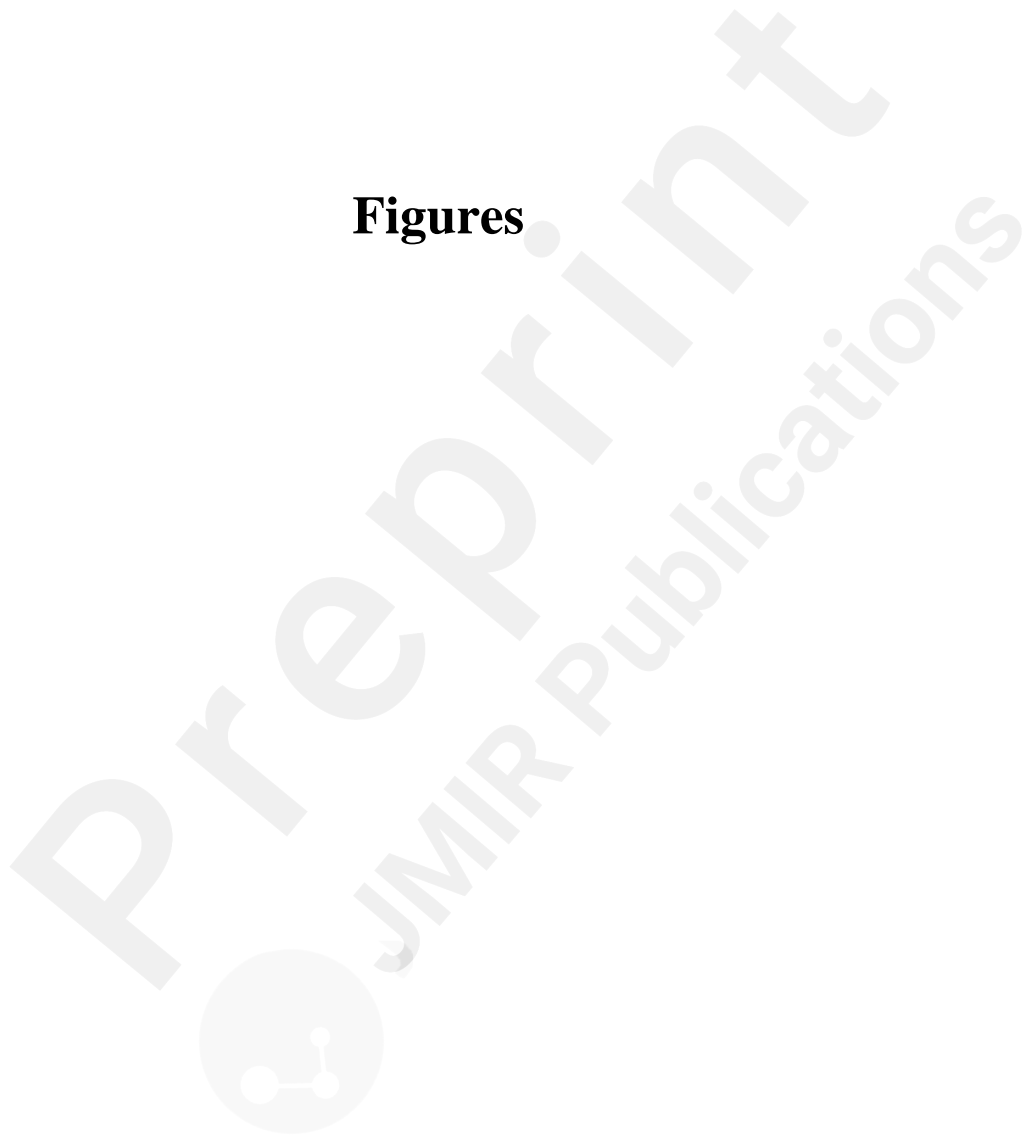
Development 2019 Jan [doi: <https://doi.org/10.1145/3287098.3287102>]

36. Shubber Z, Mills EJ, Nachega JB, Vreeman R, Freitas M, Bock P, et al. Patient-Reported Barriers to Adherence to Antiretroviral Therapy: A Systematic Review and Meta-Analysis. *PLoS medicine* 2016 Nov 29;13(11) [PMID:27898679] [doi:10.1371/journal.pmed.1002183]
37. Ware NC, Pisarski EE, Tam M, Wyatt MA, Atukunda E, Musiimenta A, et al. The Meanings in the messages: how SMS reminders and real-time adherence monitoring improve antiretroviral therapy adherence in rural Uganda. *AIDS* 2016 May 15;30(8):1287–1293 [PMID:26807967] [doi:10.1097/QAD.0000000000001035]
38. Haberer JE, Musiimenta A, Atukunda EC, Musinguzi N, Wyatt MA, Ware NC, et al. Short message service (SMS) reminders and real-time adherence monitoring improve antiretroviral therapy adherence in rural Uganda. *AIDS* 2016 May 15;30(8):1295–1299 [PMID:26760452] [doi:10.1097/QAD.0000000000001021]
39. Koss CA, Hosek SG, Bacchetti P, Anderson PL, Liu AY, Horng H, et al. Comparison of Measures of Adherence to Human Immunodeficiency Virus Preexposure Prophylaxis Among Adolescent and Young Men Who Have Sex With Men in the United States. *Clinical Infectious Diseases* 2018 Jan 6;66(2) [PMID:29020194] [doi:10.1093/cid/cix755]
40. Yoeli E, Rathauer J, Bhanot SP, Kimenyi MK, Mailu E, Masini E, et al. Digital Health Support in Treatment for Tuberculosis. *New England Journal of Medicine* 2019 September 5;381:986-987 [PMID:31483974][doi:10.1056/NEJMc1806550]
41. Thekkur P, Kumar AN, Chinnakali P, Selvaraju S, Bairy R, Singh AR, et al. Outcomes and implementation challenges of using daily treatment regimens with an innovative adherence support tool among HIV-infected tuberculosis patients in Karnataka, India: a mixed-methods study. *Global Health Action* 2019;12(1):1568826 [PMID:30712507] [doi:10.1080/16549716.2019.1568826]
42. Iribarren S, Beck S, Pearce PF, Chirico C, Etchevarria M, Cardinale D, et al. TextTB: A Mixed Method Pilot Study Evaluating Acceptance, Feasibility, and Exploring Initial Efficacy of a Text Messaging Intervention to Support TB Treatment Adherence. *Tuberculosis Research and Treatment* 2013 Dec 12;2013:349394 [PMID:24455238] [doi:<https://doi.org/10.1155/2013/349394>]
43. Mohammed S, Glennerster R, Khan AJ. Impact of a Daily SMS Medication Reminder System on Tuberculosis Treatment Outcomes: A Randomized Controlled Trial. *PloS One* 2016 Nov 1;11(11):e0162944 [PMID:27802283] [doi:10.1371/journal.pone.0162944]
44. Haberer JE, Subbaraman R. Digital Technology for Tuberculosis Medication Adherence: Promise and Peril. *Annals of the American Thoracic Society* 2020 Apr;14(4):4221–423 [PMID:32233860] [doi:10.1513/AnnalsATS.202001-027ED]

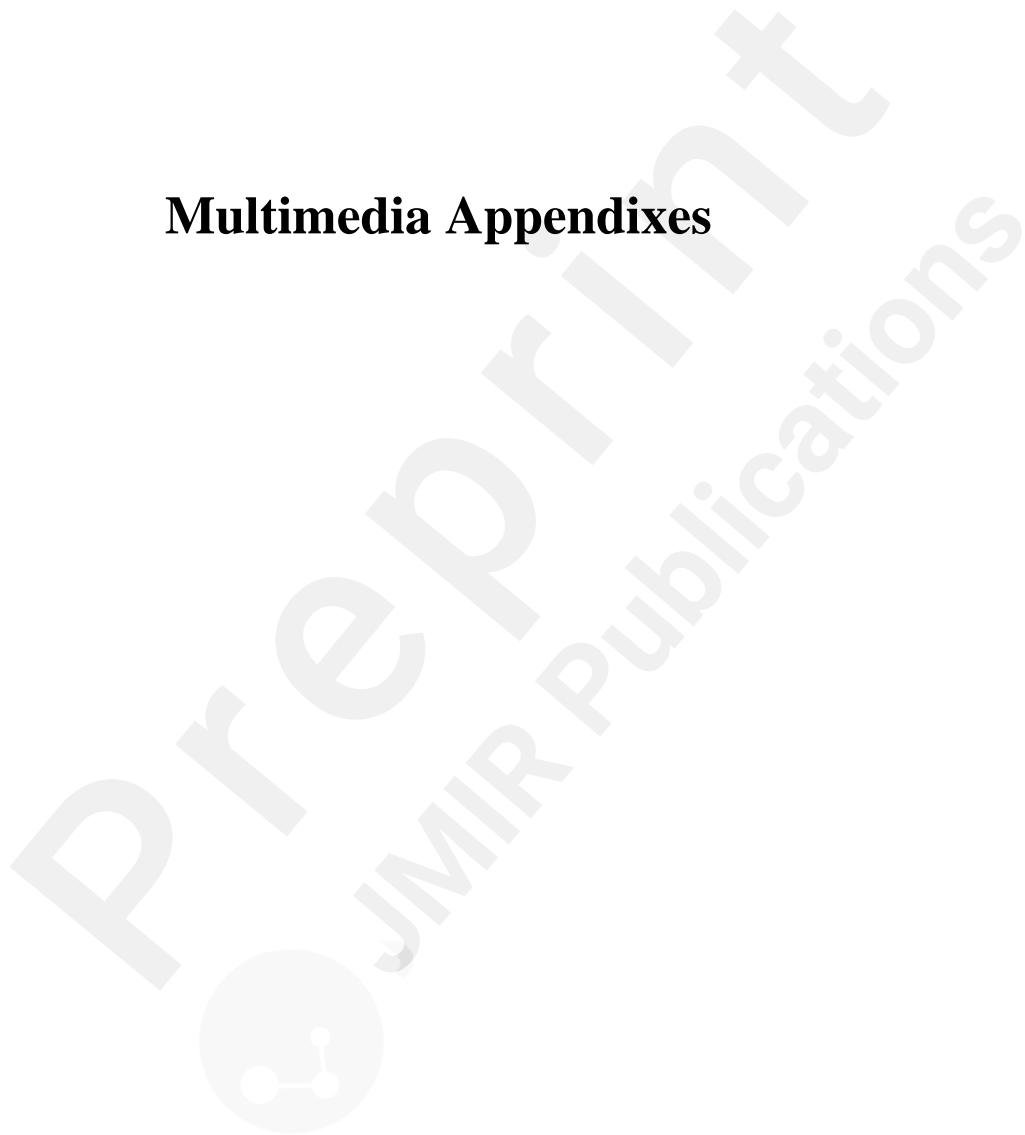
Supplementary Files



Figures



Multimedia Appendixes



Examples of questions included in the in-depth interview guide for MDR TB patients in relation to constructs in UTAUT.
URL: <https://asset.jmir.pub/assets/1eee2e27aef9283370e47e5722ee3cbb.doc>

