Choice-based Reminder Cues:

Findings from an mHealth study to improve Tuberculosis (TB) treatment adherence among the urban poor in India

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Abstract

Poor treatment outcomes due to nonadherence and consequent high levels of drug resistance continue to challenge efforts to combat Tuberculosis (TB) in India. Mobile health- or mHealth-based reminder cues have been considered in multiple health behavior modification interventions, including TB treatment nonadherence. We conducted a quasi-experimental study in Ahmedabad, India, to examine the effectiveness of mHealth-based reminder cues customized to meet diverse patient needs. Results from this experiment indicate that the potential of customized mHealth reminder cues may remain unrealized unless addressed in conjunction with multifaceted drivers of TB treatment nonadherence. The perspective we present here has broad relevance for future mHealth studies, especially in interpreting challenges that arise within resource-scarce settings of the urban poor and prevent them from adhering to recommended TB treatment regimens.

Keywords

Cues to action, reminders, mHealth, Tuberculosis, nonadherence, slums, India

1. Introduction

The Health Belief Model (HBM) is one of the oldest and most widely applied health behavior theories in public health (Glanz & Bishop 2010; Glanz, Rimer, & Lewis 2002; National Cancer Institute 2003). The HBM identifies six determinants of health behavior: i) perceived susceptibility to a disease, ii) perceived risk of a disease, iii) perceived benefits of taking action, iv) perceived barriers to taking action, v) cues to action, and vi) self-efficacy (Jones et al., 2015; Rosenstock, 1974). While cues to action have received wide recognition as a determinant motivating health behaviors, it is the least understood and the most underdeveloped among the six HBM constructs (Champion & Skinner 2008; Jones et al. 2015; Orji, Vassileva, & Mandryk 2012).

Cues to action can either be external cues (for example, mass media campaigns or influence via social networks) or internal cues (such as adverse bodily symptoms or individual perceptions about these symptoms) (Rosenstock 1974). In recent times, mobile health (mHealth), or cellular phone and other mobile-device based health interventions that focus on messaging, has increasingly been recognized for its potential to serve as an external cue to health action (Burner et al. 2014; Melznera, Heinzea, & Fritscha 2014). Given this promise of mHealth and the general lack of evidence on the role that cues to action play in health behavior motivation, we conducted a quasi-experimental study to examine a customized mobile-phone based reminder cue mechanism targeting Tuberculosis (TB) treatment adherence.

Available evidence suggests that mHealth applications could enhance Directly Observed Treatment-Short Course (DOTS) programs in resource-scarce urban slums in developing countries (Denkinger et al. 2013; WHO 2014). The DOTS program is the international standard of TB care endorsed by the World Health Organization (WHO). Under the DOTS model, designated individuals, such as healthcare workers, family, or community members, observe patients taking TB treatment drugs, thereby serving as a prompt to motivate action (Cox, Morrow, & Deutschmann 2008; Frieden & Sharbaro 2007). During our study period, India's Tuberculosis Program followed the international DOTS standard and allowed only healthcare workers but not family or community members to observe patients. Since our study, this latter exception has been discarded. Irrespective, the combination of unstable housing and poverty commonly found in slums, and a shortage of healthcare workers often overwhelms DOTS-TB care delivery in low- and middle-income countries (Denkinger et al. 2013; Frieden & Sharbaro 2007; Harvard Business Publishing 2011; WHO 2006).

As the usage of mobile phones in the global South continues to grow, mHealth applications offer the potential to counter such limitations under DOTS (Elangovan, & Arulchelvan 2013; Wigginton 2017) by providing TB-treatment-related external cues to action (Choun et al. 2017; Elangovan, & Arulchelvan 2013). Nevertheless, several barriers to implementing mHealth in low-income settings are highlighted in the literature, including low-literacy levels and limited language skills, lack of access to phones due to sharing between family members, restrictions on message length and content, reminder fatigue among message recipients, poor phone service and capacity, inability to pay for service, and high incidence of phone theft (Ahmed et al. 2012; Davey et al. 2014; DeKoekkoek et al. 2015; Nglazi et al. 2013; Thirumurthy & Lester 2012). In light of these barriers, one promising approach that thus far remains unexplored is the "customization" of mHealth-based cues to action reminders to meet the specific needs of a target population such as the urban poor (Esther 1993; Munro et al. 2007; WHO 2003).

The urban poor are distinctly unique in their mobile technology ownership, access, and usage, which are characterized by such features as household-based ownership of mobile phones and limited or interrupted access to phones due to sharing or work schedules, among others (GSMA 2015; Marcolino et al. 2018; Ministry of Health and Family Welfare 2016). An approach that takes these characteristics into account and caters to the urban poor's preferences for receiving cues-to-action messages would determine whether this population responds to mHealth. Emerging evidence from recent qualitative studies highlights the need for mHealth applications to be responsive to patient preferences (Burner et al. 2014; Park et al. 2019).

However, previous mHealth studies have not focused on cues to action modifications that may be required to serve low-income urban communities (Hall et al. 2014; Narasimhan et al. 2014). To address this gap we explicitly considered TB patients' individual preferences in our study. More specifically, we attempted to address TB treatment nonadherence in India's impoverished slums by employing a system of "choice-based" reminder cues delivered through mobile phones. We hypothesized that providing TB patients with a choice of treatment reminder cues would lead to higher treatment completion rates, as this system would be responsive to individual, heterogeneous preferences for mobile technology use and message delivery schedules. In fact, this study was one of several concurrent innovations focusing on developing mHealth solutions for TB care in India at the time.

To test our study hypothesis, we used the existing TB program infrastructure in Ahmedabad, India, and conducted a quasi-experimental study with a sample of 330 low-income TB patients in the "continuation phase" of their treatment. Under India's Revised National Tuberculosis Program (RNTCP), the first two months of the six-month TB treatment are directly observed by DOTS providers, with the remaining four months, the continuation phase, monitored through monthly patient visits to a DOTS center. We obtained approvals from both the Institutional Review Board (IRB) at George Mason University and the Ethics Committee at the Indian Institute of Public Health, Gandhinagar, India, for our study.

The results of our mHealth choice-based cues to action study indicated no statistically significant difference in the rates of adherence between our experimental and control groups. This finding complements several prior studies that report evidence of mHealth having limited to no effects in increasing TB treatment adherence (Hunchangsith et al. 2012; Nglazi et al. 2013). The findings of our quasi-experimental intervention together with the insights we derived from them confirm that nonadherence among the urban poor is a complex health behavior that is shaped by a multitude of influences. Hence, any approach aiming to promote adherence to TB treatment needs to address these factors affecting nonadherence prior to the introduction of mHealth cues to action customized specifically for the urban poor.

2. Study Context and Background

2.1 The Emergence of Multi-drug Resistant TB in India

Tuberculosis (TB), a curable but virulent airborne bacterial infection, is a significant public health concern in India (WHO 2018, 2019a). India has the highest TB burden in the world. More than a quarter of all new TB cases in the world occur in India, where the disease has killed more than 449,700 people in 2018 alone (WHO 2019). India's large population base and endemic urban poverty undoubtedly contribute to its high TB disease burden. The prevalence of TB is highest among the poor and in the urban slums of India (Kanabus 2017; WHO 2015). This trend is compatible with evidence that suggests that more than 90% of TB deaths occur in low- and middle-income countries, with high concentrations of poverty alongside rapid urbanization (Benatur & Upshur 2010; Kamineni et al. 2012).

In recent years, India has been facing an even more urgent public health crisis with the emergence and spread of drug-resistant TB (GOI 2017). Multi-drug resistant (MDR) TB began to be reported in the country in the early 1990s, followed by extremely drug resistant (XDR) TB in 2006 and totally drug resistant (TDR) TB in 2012 (Rowland 2012). India continues to be a high-burden country for these drug-resistant strains, with conservative estimates reporting that almost 3% of new cases and around 12-17% of retreatment cases in India are MDR-TB (Chatterjee, Poonawala, & Jain 2018; Kanabus 2017; Ramachandran et al. 2009; WHO 2019). In 2018, the country also recorded some of the highest numbers of XDR-TB cases in the world (WHO 2019).

Nonadherence to TB treatment is one of the leading factors fueling the emergence of drug-resistant TB (Haasnoot et al. 2010; Lipsitch & Levin 1998; Shargie & Lindtjørn 2007; WHO 2003, 2013). Nonadherence arises when a TB patient does not follow the TB treatment regimen recommended by a health care provider (WHO 2003a). Studies estimate that the TB treatment default rate, or nonadherence, in India is higher than the international rate (WHO 2012; Vijay et al. 2010; Jaggarajamma et al. 2007). Once drug resistance develops in a nonadherent TB patient, it poses a significant threat of this deadly infection to others, especially among India's urban poor, who are susceptible due to malnutrition and living in overcrowded slums (Mistry, Tolani, & Osrin 2012; Unger & Riley 2007). In other words, adherence to TB treatment is critical to not only avoid drug resistance developing in an infected individual but also to prevent a healthy person from becoming infected with drug-resistant strains. Compared to drug-susceptible TB, treatment of drug-resistant TB is more expensive, lengthy, and toxic, and the concomitant impacts on public health and national economies are staggering (Lutge et al. 2015;

Vassall et al. 2011; WHO 2010). Consequently, health interventions that promote treatment adherence among TB patients are of critical importance (Tang et al. 2015; WHO 2014).

2.2 The DOTS Program and Implementation Challenges

The DOTS strategy is followed by India under its RNTCP (GOI 2018; WHO 2002, 2019b). India launched the RNTCP, the largest TB control program in the world, in 1997. Essential to this program is the DOTS component in which an assigned motivator—a trained health worker or volunteer—provides real-time cues to action and watches the patient ingest his or her medication to ensure adherence to treatment (Cox et al. 2008; Frieden & Sharbaro 2007). Prior to recent changes in India's RNTCP, DOTS motivators also conducted follow-up home visits after patients had failed to report to DOTS centers for one week (GOI 2017).

In Rosenstock's (1974) HBM formulation, external cues to actions are stimuli arising from people, events, or things that trigger a health behavior modification. Despite the motivation and cues to action provided under DOTS by health workers and volunteers, nonadherence to TB treatment nevertheless persists (Jaggarajamma et al. 2007; Vijay et al. 2010; WHO 2012). The DOTS strategy has been especially difficult to execute in resource-scarce settings with high TB burdens and a shortage of health workers (Ahmed et al. 2012; Jaggarajamma et al. 2007; Vijay 2010). A 2015 Cochrane systematic review concluded that "DOTS did not provide a solution to poor adherence in TB treatment" when compared to self-administration of treatment across a variety of country settings, and other adherence interventions should be considered (Karumbi & Garner 2015, p.2). In addition, the WHO's *End TB Strategy* encourages and supports innovative development and integration of digital health applications into TB prevention and care programs (WHO 2015a).

2.3 Recent Rise of mHealth Applications for Reducing TB Treatment Nonadherence

As mobile phones are penetrating deeper into developing countries than any other Information and Communications Technology (ICT), mobile health technology or mHealth strategies are providing innovative opportunities for communication with patients, thereby improving the efficiency of health systems (Aranda-Jan et al. 2014; DeKoekkoek et al. 2015; Denkinger et al. 2013; Horvath et al. 2012; WHO 2015). As a component of digital health, mHealth provides health services via cellular phones or other mobile devices (WHO 2015). To address the persistence of TB treatment default or nonadherence, innovative interventions that could complement DOTS are being tested across low- and middle-income countries, including India (WHO 2003). These strategies include reminder mechanisms; material incentives; patient-provider education, counseling, and communication; provider training and management; and social and peer assistance (Ahmed et al. 2012; Liu et al. 2014; Nglazi et al. 2013). For example, 99DOTS, a recent initiative launched in India to complement traditional DOTS, requires patients to make a free call each time they take their medications so providers can monitor adherence records (99DOTS, n.d.). Similarly, Operation ASHA (OpASHA) uses technology, instead of female health workers who are accredited social health activists (ASHA), to scan patients' fingerprints and record attendance and monitor treatment adherence. In conjunction with these new efforts, mHealth-based remote delivery of health services are being developed to facilitate the implementation of the new adherence strategies (Hall et al 2014; Jongh et al. 2012; Park 2019).

Prior experimental studies have identified mobile phones as a low-cost and effective tool for both health systems and TB programs. mHealth interventions to improve and support TB treatment adherence include i) *Short Message Service (SMS) reminders* for patients to take medication or attend clinic appointments (e.g., Ahmed et al. 2012; Cole-Lewis & Kershaw 2010;

DeKoekkoek et al. 2015; Elangovan and Arulchelvan, 2013; Horvath et al. 2012; Iribarren et al. 2015; Nglazi et al. 2013); ii) *phone call reminders* for patients to take medication or attend clinic appointments (Ahmed et al. 2012; Aranda-Jan et al. 2014; Liu et al. 2014); iii) *health education or support services* for patients experiencing adverse drug effects (Ahmed et al. 2012; Liu et al. 2014); and, iv) *Virtually Observable Treatment (VOT)* that allows health workers to observe patients taking medication remotely through mobile phone cameras, saving time and travel costs for both caregivers and patients (Aranda-Jan et al. 2014; WHO 2015). Currently, a growing body of research, much of it focusing on SMS, provides evidence on the role of mHealth interventions in improving medication adherence across various diseases, including TB (Jongh et al. 2012; Narasimhan et al. 2014; Park et al. 2019).

The literature on the use of mobile phone interventions to improve TB care and anti-TB medication adherence, however, is less than conclusive. For example, Ahmed et al. (2012) identified a number of best practices for mHealth and SMS interventions in TB care that have demonstrated success in improving TB treatment adherence, including OnCue Reminders in South Africa, interactive reminders in Pakistan, SIMmed and SIMpill in South Africa, and Operation ASHA's biometric treatment compliance tracking system in India, among others. In addition, a 2014 Cochrane review found that pre-appointment reminder phone calls led to higher clinic attendance and TB treatment completion rates for people with active TB. Conversely, Nglazi et al. (2013) reviewed four studies employing SMS interventions for TB treatment adherence and reported a lack of quality evidence supporting the efficacy of the interventions, concluding that available research is inconclusive.

Nevertheless, results from OpASHA and 99DOTS are reestablishing the importance of mHealth-based reminders for TB care and treatment adherence. However, similar to previous mHealth interventions, neither OpASHA nor 99DOTS consider patient preferences, instead delivering predetermined cues to action reminders via SMS and/or automated calls (CHMI 2018; Cross et al. n.d.; WHO 2017; 99DOTS n.d.). In our study, we therefore investigate the role of mHealth-based reminder cues that are customized according to individual patient preferences together with treatment-completion reward options. In so doing, our specific objective is to determine whether providing patients with the opportunity to select their own reminder cues is more effective in reducing TB treatment nonadherence when compared to using predetermined reminder cues. However, we did not aim to compare the effectiveness of individual reminder cues. Such a comparative study would require a randomized clinical trial with a robust sample size to ensure adequate power in the analysis, which we could not consider due to resource constraints.

3. Materials & Methods

3.1 Study Site and Sample Selection: For this study, we recruited a sample of 330 TB patients from three (out of six) Tuberculosis Units (TU) in Ahmedabad, India, with a high concentration of slum areas. We determined sample size with power calculations conducted on OpenEPI (Dean et al. 2012), an open source sample size calculator. In Ahmedabad, the known annual case notification rate at the time of the study was 110 cases per 100,000 population. We also used a nonadherence rate of 7%, as reported by RNTCP Gujarat in 2013. We used a 95% confidence interval that resulted in a sample size of 101 patients per TU. Considering a 10% attrition rate and loss to follow-up due to other reasons, such as death or out-migration, we determined our final sample size to be 111. We recruited 111 patients from each TU with two TUs serving as the treatment arms (Groups A and B) and the third as the control arm (Group C). We should note that because of limited time and financial resources, we were unable to pursue a larger sample size to achieve a narrower confidence interval.

We identified the three TUs based on the feedback we received from the Government of Gujarat, Ahmedabad Municipal Corporation (AMC) and the WHO-India representative through a series of meetings between these stakeholders and the research team in January 2015. To avoid contamination between our treatment and control groups, we selected TUs from geographically distinct areas that had comparable population compositions and key sociodemographic variables. All patients within each TU belonged to the same group (A, B, or C).

The inclusion criteria for subjects within each TU were Category-I (new) adult (>18) TB patients with access to mobile phones and who were enrolled in the Government of India RNTCP from January 1, 2015 until the intended sample size of 111 patients was reached in each TU (the last patient was recruited on March 10, 2015). Category 1 TB patients are new TB cases who undergo a six-month-long treatment that consists of two phases – a 2-month-long intensive phase followed by a 4-month-long continuation phase. During the intensive phase, each TB patient has to go to a DOTS provider and take prescribed TB medication in the presence of the provider to ensure compliance. The duration of reminder intervention for Group A and Group B patients (experimental groups) coincided with the 4-month-long continuation phase of their treatment, as nonadherence is considered high during this period (Bagchi, Ambe, & Sathiakumar 2010; Tola et al. 2015).

3.2 Study Design: Of the two intervention groups, Group A patients received reminder cues and rewards of their choice, whereas Group B patients received predetermined reminder cues and rewards. The control Group C patients received neither reminder cues nor reward, instead receiving the standard DOTS under RNTCP. We obtained feedback on reminder cues and treatment-completion reward choices as well as preferences for frequency of reminder cues through a focus group discussion (FGD) with Group A patients at the beginning of the study period.

Based on our findings from the FGD, Group A patients were given the opportunity to choose from four reminder cue options: i) SMS, ii) live calls, iii) prerecorded calls, and iv) a combination of SMS and live and prerecorded calls. In addition, Group A's treatment-completion rewards, also identified through the FGD, were vouchers redeemable for payment toward one of the five options: i) mobile talk time, ii) free health check-ups from selected general physicians, iii) medical tests at a National Accreditation Board for Testing and Calibration Laboratories (NABL)-accredited laboratory, iv) purchase of drugs from selected pharmacies, and v) insurance premium for coverage against accidents for a one-year period. The monetary value of the five types of redeemable vouchers was set at INR 200 (4 USD), and vouchers were awarded at the successful completion of the four-month continuation phase treatment. Based on the FGD results and further deliberation between the research team, TB control program managers, and community participants, we concluded that an amount equal to 4 USD would serve to encourage treatment adherence while also being programmatically sustainable, given the resources of our project. However, we did not aim to explicitly examine the effect of these reward choices on TB treatment nonadherence. Instead, dictated by program logistics, we disbursed the rewards at the completion of treatment.

Live call (reminder cues) and mobile talk time (treatment-completion reward), which patients identified as the preferred choices during the FGD, constituted the predetermined reminder cues and rewards provided to Group B patients. Two on-site Research Assistants (RAs) made live calls to patients in both treatment groups until the completion of the prescribed TB treatment regimen. The RAs also documented patient responses to live phone calls. In addition, the RAs monitored Group A patients for treatment adherence via periodic mobile phone calls made to patients' DOTS providers and/or family members and by monitoring drug taking by counting empty blister packs.

3.3 Data Collection: Between January 2015 and May 2015, we conducted a primary survey to collect baseline data on socioeconomic, demographic, and health status for all three groups as well as profiles on adherence-to-treatment for the intervention groups. Prior to baseline data collection, we explained the objective of the study to patients and obtained written consent. To collect follow-up data, we tracked patients in the two treatment groups and documented treatment outcomes that were recorded as i) failure, ii) default, iii) lost to follow up, iv) completion, or v) death. We collected treatment adherence data for Group C from administrative information generated by the RNTCP. For both baseline and follow-up data collection, we conducted patient interviews in the local language (Gujarati).

We validated our baseline survey instrument by piloting it in two iterative rounds over a 4-week duration and with a sample of 11 TB patients. Based on observations made during the two rounds of pilot surveys, we made several refinements to questions in the survey instrument as well as in the process of administering the surveys. First, we added several questions to our survey instrument related to knowledge about mobile phone use, such as awareness about interactive voice response systems, which helped us to provide appropriate reminder cues. Next, we learned that several TB disease-related questions are not suitable for discussion at patients' slum residences due to lack of privacy. Our visits to the slum communities inadvertently attracted attention, with slum residents following us to patients' homes, which rendered privacy and the discreet administration of the pilot difficult. Furthermore, anonymity of disease status was particularly important for patients, who indicated a strong preference to keep their condition private from either their neighbors or family members. This preference is compatible with social stigma and taboo entrenched around the disease of TB in India (Mukerji & Turan 2018). We therefore opted to conduct the patient interviews and administer our survey at the DOTS center at times convenient for our study participants.

3.4Key Informant Interviews

We also conducted Key Informant Interviews (KII) with six DOTS providers and sixteen treatment-group patients (8 each from Groups A and B). We planned to apply the information generated through these interviews toward interpreting TB treatment nonadherence.

4. Results

4.1 Quasi-experiment

In Table 1, we provide the key sociodemographic characteristics of our study participants. Given that we selected study participants using the convenience sampling methodology – recruiting all patients within the selected TUs in a given timeframe that met our study criteria – we did not aim to match participant characteristics across the three groups. Nevertheless, the numbers included in Table 1 indicate that the three groups were more or less comparable on key sociodemographic characteristics.

<TABLE 1 & 2 ABOUT HERE>

We measured the effectiveness of our interventions on two levels: 1) the effectiveness of providing choices for reminder cues and rewards (Group A against B) and 2) the effectiveness of predetermined (no-choice) reminder cues and rewards (Group B against C). We consider an intervention effective if we observed lower nonadherence or "default" rate at the group level. We followed the RNTCP guidelines, which define a "default" case as any patient treatment interrupted for more than 2 consecutive months after initiation.

As indicated in Table 2, the treatment adherence rate for the choice intervention group (Group A) were comparable to that of the predetermined no-choice intervention group (Group B). We did not find any statistically significant difference in nonadherence rates between Groups A and B (RR = 2.37, $p > 0.05$). Surprisingly, our results also did not indicate any evidence in support of higher rates of adherence in either Group A (nonadherence RR: 5.33, $p < 0.01$) or B (nonadherence RR: 2.24, $p < 0.01$) when compared to control Group C. These results indicate that mHealth interventions may not always be effective in achieving better health outcomes. We investigated this finding further with the help of KII which we discuss next.

4.2 Key Informant Interviews: According to the DOTS providers we interviewed, the main reasons for nonadherence were related either to patient characteristics such as alcohol addiction or to TB treatment side effects, none of them ripe for tackling with mHealth. Another set of reasons for nonadherence were related to the providers' own work situation, such as high workload, and low motivation due to lack of commensurate salaries and benefits. Once again, these issues are unlikely to be remedied with mHealth solutions. There is one exception though: DOTS providers find their workloads to be a major barrier to providing adequate counseling services that could increase patients' adherence. We believe that it is possible to design mHealth solutions that provide counseling services through call centers, removing some of the existing burdens of field staff.

Finally, the DOTS providers cited migration within- or out-of-state as a key reason that nonadherent patients are difficult to track once they migrate to a location outside their own service area, which agrees with our findings from one of our TB patient case studies. This is one of the barriers that could be addressed with mHealth solutions. It is possible to trace patients with mobile phones and connect them with health services at their new locations.

DOTS providers we interviewed also noted that patients' self-motivation, rather than cue-to-action reminders, is the key reason for adherence to TB treatment. However, when we interviewed patients following the completion of our experiment, they pointed out that our reminder cues served their purpose, especially since many were at work and would have missed taking their medication in the absence of such external reminder cues. According to these patients, our reminder cues indeed contributed to an increase in their self-motivation to take their anti-TB drugs regularly. Moreover, the interviewed patients also indicated feeling that they had received personal care, with someone always there to remind them to take their medicine on a regular basis.

5. Discussion

As discussed in the Results section, we did not find any statistically significant evidence in favor of either customized or predetermined mHealth reminder cues to action in our experimental study. Nevertheless, this result provides a nuanced perspective on the role of mHealth reminder cues targeting complex health behaviors, such as TB treatment, that require prolonged adherence to prescribed medications. In the rest of this section, we contextualize our findings for the purpose of identifying conceptual areas to enhance the effectiveness of mHealth, discuss some limitations of our study, and suggest implications for future research. We believe that such a discussion, missing but long overdue in the literature, will be helpful in enriching future mHealth study protocols aiming to modify health behaviors using cues to action reminder mechanisms.

A finding of no statistically significant difference in nonadherence rates between Groups A and B may indicate that customized mHealth cues have no benefits. However, this result may be due to our relatively small sample size. It is also possible that providing Group B patients with the most popular reminder-reward choice—a choice that these patients may well have made themselves had they been asked—may have been a mistake. In hindsight, we realize a better approach would have been to remind Group B patients using the standard SMS reminder cues. SMS reminders are easy to provide but, as revealed by our Group A FGD results, were the least preferred by patients. Only 6.3% of Group A patients opted to receive SMS reminders, but they eventually switched to receiving reminders via live calls. We accommodated such a switch because we found it to be consistent with our research design, which offered reminder choices to this group.

Our results also did not provide evidence in support of higher rates of adherence in intervention Groups A or B when compared to control Group C. This finding agrees with prior studies that report inconclusive to no effects of mHealth TB care interventions including cues to action reminders (Hunchangsith et al. 2012; Nglazi et al. 2013). Such a finding could potentially indicate no benefit of either customized or predetermined standard mHealth cues to action reminder mechanisms, particularly for health behaviors requiring adherence to long-term treatment or chronic management of disease conditions. However, we have a more cautious interpretation of this finding for multiple reasons, which we discuss next.

We did not collect adherence-to-treatment data for the control group ourselves. Instead, we obtained this data from the RNTCP surveillance and monitoring system. However, patient data under RNTCP is updated only at quarterly intervals and therefore lacks periodicity and real-time information on patient treatment adherence. Data from RNTCP also lacks the inbuilt validity required for a regular cross-check of patient treatment status. We therefore suspect that nonadherence cases were not captured rigorously by the RNTCP surveillance and monitoring system (Paresh et al. 2013; Parmar et al. 2018). As listed in Table 1 under the Results section, underreporting of treatment outcomes from the RNTCP system can be detected—all five treatment outcome categories of switch to category 2, treatment failure, default, death, and loss to follow-up had fewer incidences in RNTCP Group C data compared to the study Group A and B data that we collected.

Second, in the course of our study, we encountered a number of practical field challenges during both the patient recruitment and implementation phases that limited our ability to sustain contact with patients via mHealth. First, our project had a high participant attrition rate, with about 8 and 10% of the study participants in Groups A and B, respectively, lost to follow-up over time. A reason for the sample attrition was the difficulty of obtaining complete patient addresses from the DOTS centers, as our study participants often had informal housing arrangements commonly found in slums. As a result, we often could not undertake home visits to follow-up with patients. This difficulty was exacerbated by study participants frequently changing their mobile phone numbers when they changed their service providers (number portability did not exist in India at the time), leaving us with no possibility of finding them over mobile phone either. Consequently, patients without complete home addresses could not be reminded and/or followed-up. We now realize that switching subscriptions from one mobile service provider to another will remain a standard practice among our study population that it should be a factor of consideration in future study designs.

In addition, more than half (about 55%) of our study participants were seasonal and/or migrant workers. Depending on the work cycle, these seasonal and migrant workers frequently relocate either locally within Gujarat or to nearby states. Link-up of all study participants via the recently launched AADHAR cards could be one option to circumvent these problems in future studies. Similar to Social Security numbers in the United States, AADHAR cards can uniquely identify individuals in India.

Third, about a third of our Group A patients (34%) could not read SMS in English. To cater to patients' preference for receiving reminders in their native language, we attempted to send SMS using vernacular texts. However, we quickly realized that mobile phones are generally not compatible with vernacular fonts. This technological challenge together with patients' lower mobile phone familiarity as well as low literacy need to be better managed in future mHealth cues to action studies. To accurately capture and evaluate the role of ICT-based reminder mechanisms, developing graphics-based mobile reminder apps may become essential for future projects to minimize the impacts of technological, linguistic, and literacy challenges.

Fourth, our study revealed the effectiveness of live calls in providing a human touch to study participants. However, our RAs were neither equipped nor allowed to counsel patients about their concerns regarding drug-related side effects of TB treatment, an issue that often came up during the calls. Along the same lines, during our study we found that health workers, including DOTS providers, lack proper training and competency to counsel patients on TB-treatment-related side effects. This factor was further highlighted in our follow-up patient interviews, which revealed that TB-drug-induced side effects, and the lack of information thereof, directly impacted patients' motivations to continue with the prescribed six-month-long treatment regimen. Developing online and mobile app-based educational and training videos on the side-effects of TB treatment aimed at both TB patients and DOTS providers should, therefore, be considered together with any reminder mechanisms.

Finally, in the FGD conducted prior to the initiation of our experimental study, we omitted the choice of nutrition supplements as a reward option. Follow-up patient interviews as well as subsequent interactions with TB health workers and government officials identified nutrition supplementation as both a necessity among the urban poor and a possible counter to the side effects of TB drugs. In future mHealth studies, utilization of the AADHAR card mechanism to channel nutrition supplementation to patients should be considered.

Conclusion

Nonadherence is a complex health behavior, and the factors influencing it are multifaceted in the case of TB and other diseases that require long-term treatment (Munro et al. 2007). In addition to simple forgetfulness, nonadherence in resource-poor settings is rooted within the prevailing broader sociobehavioral and economic environment as well as in personal health experiences during TB treatment (DeKoekkoek et al. 2015; Lutge et al. 2015). The social determinants of nonadherence are in fact diverse. They include variable related to: i) sociobehavior (misplaced beliefs and lack of knowledge about disease, medication, and treatment; social stigma and lack of social support; and substance abuse), ii) socioeconomics (the inability to travel to a health center due to travel time and cost and the opportunity cost of missing work) and iii) treatment and health-systems experiences (the adverse effects of medication and dissatisfaction with providers and available health services) (Deshmukh et al. 2015; Tola et al. 2015).

Furthermore, research also identifies that such demographic and personal characteristics as age, race, sex, and depression level impact adherence to TB treatment (DeKoekkoek et al. 2015). Despite our finding of no statistically significant difference between our experimental and control groups, we believe that there is room for customized mHealth to further improve TB treatment adherence, especially if and when the broader environment of nonadherence is taken into account.

Since the completion of our data collection in 2015, several policy changes have been implemented in India's tuberculosis program, including those that increased the use of mHealth. Our study was one of many innovations that was being tried out in the country at the time. The most notable of these new mHealth approaches, 99 DOTS and OpASHA, are currently in place alongside the introduction and creation of such countrywide changes as unique identities for residents of India through a biometric AADHAR card.

Moreover, the current TB program of India, at the time of this writing in 2020, has already incorporated innovations to address barriers that we discuss in this study. For example, the current program replaces volunteer DOTS providers with family members, who serve as direct observers providing cues to action (Kanabus 2018). Given this shift, providing treatment reminder cues via mHealth may be that much more important to remind both patients and their family members. Establishing a network of call centers for this purpose may be a necessity and could be supported by the vastly expanded budget for TB treatment (GOI 2017). This budget allocation, in addition to providing cash incentive to patients, providers, and DOTS supporters, is also being used to give nutritional support to TB patients (Kanabus 2018).

Another major change in the current TB program of India is the introduction of e-Nikshay, a national electronic database of TB patients, to facilitate both mHealth interventions and a seamless transfer of TB cases between care providers (GOI, n.d.). Along the same lines, 99DOTS, which was being tested on an experimental basis in 2015, is now fully integrated into the e-Nikshay program. Given this broader environment of policies and strategies for TB care in India, we foresee the customization of mHealth to address diverse needs of the urban poor, as well as various factors driving nonadherence among this population, to be a fertile area for future TB care research. Examining innovations like ours is especially warranted given that TB is a disease that has been placed under active surveillance, with the Government of India committed to eliminating it by the year 2025 (GOI 2017).

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Tables

Table 1: Key socio-demographic characteristics of study participants

Characteristics	N (%)	Group A (%)	Group B (%)	Group C (%)	p-value
All	333 (100.0)	111 (33.3)	111 (33.3)	111 (33.3)	-
Sex					0.242†
Female	126 (37.8)	49 (44.1)	39 (35.1)	38 (34.2)	
Male	207 (62.2)	62 (55.9)	72 (64.9)	73 (65.8)	
Age (Mean)	36.1	36.1	36.7	35.7	0.889††
Education					0.081†
Illiterate	62 (18.6)	27 (24.3)	21 (18.9)	14 (12.6)	
Literate	271 (81.4)	84 (75.7)	90 (81.1)	97 (87.4)	
Migrants					0.866†
Yes	162 (48.6)	54 (48.6)	52 (46.8)	56 (50.5)	
No	171 (51.4)	57 (51.4)	59 (53.2)	55 (49.5)	
Below Poverty Line (BPL)					0.584†
Yes	74 (22.2)	21 (18.9)	26 (23.4)	27 (24.3)	
No	259 (77.8)	90 (81.1)	85 (76.6)	84 (75.7)	

NOTE: † p values refer to $\chi 2$ results; †† p-value refers to Anova F-test

Table 2: Comparison of treatment categories across study groups

Treatment outcome	Study Groups			Total
	A Intervention 1: Choice-based reminder cues (Study Data)	B Intervention 2: Predetermined Reminder Cues (Study Data)	C Control (RNTCP Data)	
Treatment completed	93(83.8%)	91(82.0%)	104 (93.7%)	288 (86.5%)
Switched to Category 2	1(0.9%)	3 (2.7%)	3(2.7%)	7 (2.1%)
Treatment failure	1(0.9%)	0 (0.0%)	1(0.9%)	2(0.6%)
Default Cases	5 (4.5%)	2 (1.8%)	1 (0.9%)	8 (2.4%)
Death	3 (2.7%)	3 (2.7%)	0 (0.0%)	6 (1.8%)
Loss to follow up	8 (7.2%)	12 (10.8%)	2 (1.8%)	22 (6.6%)
Total	111 (100.0%)	111 (100.0%)	111 (100.0%)	333 (100.0%)