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Improving Compliance to Tuberculosis Treatment: Supporting Patients through Mobile Graphic-based Reminders

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ABSTRACT

Background: Tuberculosis (TB) treatment is a complex task and requires medical supervision and support. The objective of this study was to assess the utility of a mobile graphic-based reminder (GBR) in improving compliance of patients with TB treatment. Compared to text and speech-based reminder systems, the visual or graphic application is suggested to be more effective in supporting treatment particularly in semi-literate and illiterate patients.

Methods: The study was conducted in Zanzibar, Tanzania and included patients with active TB and already taking anti-TB drugs. The study was conducted over five weeks from July to August 2015. Participants were randomly assigned into three groups: control (n=10), speech-based reminder (n=10), and GBR (n=10) groups. Participants in the intervention groups (speech-based and GBR) received daily mobile reminder messages. Quantitative application responses and qualitative data resulting from semi-structured interviews from the patients were collected. Comparative analyses were undertaken between GBR and traditional care, and between GBR and speech-based reminders.

Results: The findings indicated that the GBR system led to increase in treatment adherence (90%) compared with speech-based reminder (70%) and traditional care (60%). Findings also show that there were high efficacy and acceptability of mobile reminders in the GBR group with the average response rate of 60.1 compared with 50.6 in the speech-based reminder group ($p<0.01$).

Conclusions: The GBR was more beneficial and accepted for use by the majority of the patients including those with limited education. This study suggests that mobile GBR system can be used to support compliance with the treatment regimen in both literate and illiterate TB patients.

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INTRODUCTION

Pulmonary Tuberculosis (TB) is a global health problem [1]. It is spread from one person to another through coughing, sneezing, or spiting. In 2012, there were almost nine million new cases of TB in the world with more than a million die each year due to this disease [2]. According to the World Health Organization (WHO), all countries are affected by TB, but about 85% of all cases occur in Africa and Asia [2,3]. Sub-Saharan Africa has the largest number of TB cases with a prevalence of 30%. It is estimated that there are over 260 TB cases per 100,000 people in sub-Saharan Africa [2].

The standard approach to treating TB is by Directly Observed Therapy Short-course (DOTS). DOTS is an intervention by which the patient is observed taking his/her drugs [1]. The drugs are taken once a day and the treatment continues for at least six months [1,2]. DOTS requires time, human labour and economic resources that are very challenging in developing countries [2], as the treatment necessitates face-to-face contact between a patient and health worker. This makes it a difficult task for most patients as it requires daily supervision and support [4]. The literature shows that patients self-administrating TB therapy have shown improvement in treatment outcomes in comparison to DOTS (observation) [5]. Nevertheless, it appears that patients fail to remember the time of medication due to forgetfulness. This leads to prolonged treatment, medication being no longer effective, and possibility of further complications such as the Multi-Drug Resistant (MDR)-TB. This also results in making this a critical issue in human health, both from the viewpoint of health economics and patient survival. To overcome this problem, technology-assisted DOTS seek to reach more patients at a lower cost through automated reminders via mobile phones.

The rate of use of mobile phones in developing regions has increased rapidly in the past decade [6]. In 2014, seven billion mobile phones were available throughout the world. The developing countries are home to more than three quarters of all mobile phone subscriptions. According to International Telecommunication Union (ITU), in 2014, 40% of the world's population is using the Internet and two-thirds of the world's Internet users are from the developing nations [6]. Further, at the end of 2015, there were 1.91 billion smartphone users worldwide and more than 78% of them were using Android smartphones [7]. The rapid increase in the use of mobile technology in healthcare has shown to improve adherence to treatment particularly for HIV [8-14]. However, current mobile interventions, such as text messages and speech reminder systems have limited use for people with low literacy levels. In comparison, the graphic or visual applications are more relevant, easier to use and provide ease of understanding the contents of the messages regardless of the literacy level of the user. The potential of graphic applications in supporting patients' treatment has been emphasized by various studies.

Ngoh and Shepherd [15] explored visual objects' ability to help illiterate women in following drug dosage instructions, while Seth and Sorathia [16] proposed 'Parichaya' as a system designed to educate TB patients using the medical kit so as to increase medication adherence. A study from South Africa by Dowse and Ehlers [17] evaluated the use of pharmaceutical pictograms for conveying medication instructions in the Xhosa community. Medhi [18] and Thies [19] investigated the relevance of ICT user interface (UI) for novice and illiterate users. They found that, compared with text- and speech-based, a graphic-based UI appeared to be preferred by people of all literacy levels. Furthermore, literature shows that visual communication is the best method to support semi-literate or illiterate people to understand content [20,21]. Visual communication also empowers people to facilitate cross-language engagement in order to understand one another. It also enables people to receive information quickly and can affect people emotionally in ways that other methods of communication, such as oral or written communication, cannot [20].

The aim of this study was to measure the effectiveness of a mobile graphic-based reminder (GBR) system to support TB patients in improving compliance with treatment regimen, especially for the semi-literate and illiterate patients.

MATERIALS AND METHODS

Graphic-based Reminder System

The study was based on a participatory design approach and was influenced by User Centred Design (UCD). End users were involved in the design decisions of a mobile GBR system that was developed based on their needs and requirements, as reported elsewhere [22,23]. The prototype application was developed using the Java programming language for the Android platform. Android platform was selected due to two main reasons. First, Android is an open source [24] and, second, it is the most popular operating system that runs on smartphones [25]. Figure 1 shows the iteration of the components of the GBR applications.

As we aimed to assess a mobile reminder system in the context of developing countries, the application was designed to work offline in order to limit engagement with mobile service providers. Once the user has successfully downloaded and logged in to the system, the rest of the application works offline. The offline system enables users to work locally on the mobile device at anytime and anywhere regardless of mobile network availability. When needed, the data synchronize with the backend systems [26]. The system contained the graphic messages that were triggered based on the TB treatment schedule predefined by the health care professionals. The system contained eight reminder messages which were categorized into four groups: (1) medication reminders such as taking pills, refilling drugs and submitting smear sputum; (2) clinic follow-up reminders regarding clinic appointment or consultation; (3) education reminders for behaviour improvement such as avoiding pain or spreading the disease to others; and (4) health reminders to improve eating habits. The reminders were set to automatically activate on different days and times, which included daily, after every two days, and on weekly basis.

The GBR system is a two-way communication system that provides communication between the user and the server. The user side is the mobile phone that contains a GBR application. The phone communicates with the server only when downloading the reminder system and forwarding the feedback responses. A patient is asked to respond by pressing a 'feedback button', as shown in Figure 1 (5) to indicate that (s)he has received the reminder and the medication has been taken. The response is then sent to the local hospital database, Structured Query Language (MySQL). When disconnected, a SQLite database stores the feedback offline for automatic forwarding as soon as the Internet connection is available, as shown in Figure 1 (7). The medication response reports can then be viewed by a healthcare worker for further treatment processes. This also helps the healthcare worker to follow the routine of a patient's treatment regimen.

Study Design

The study made use of a parallel group design to assess the effectiveness of GBRs in supporting TB patients to adhere to treatment. The study measured two types of trials: (1) between mobile GBR and traditional (usual) care, and (2) between GBRs and speech-based reminders. As the study subjects were already under supervision of healthcare workers, cluster sampling was used to randomly select the participants. Participants were then randomly assigned into three groups: control (n=10), speech-based reminder (n=10), and GBR (n=10). Participants in the intervention groups (speech-based and GBR) received daily mobile reminder messages. These participants first, received same audio-notification message (without content of the reminder message), telling them that they have received an important reminder message, for example: "Hi! This is reminder system, you have received the important picture message, please check your phone" (English translation). After this, the users of the GBR system were directed to view graphic messages, and those receiving the speech-based reminder were directed to press a button to listen to speech messages. The notification messages did not contain the words such as TB, medications or pills, clinic, and sputum. These words directly represent a sign of a patient which may lead to stigma as reported in previous studies [27-29]. Participants in the control group received routine medical procedure but did not receive any mobile reminders. All participants were assessed every week either at the clinic during their appointment times or at their homes.

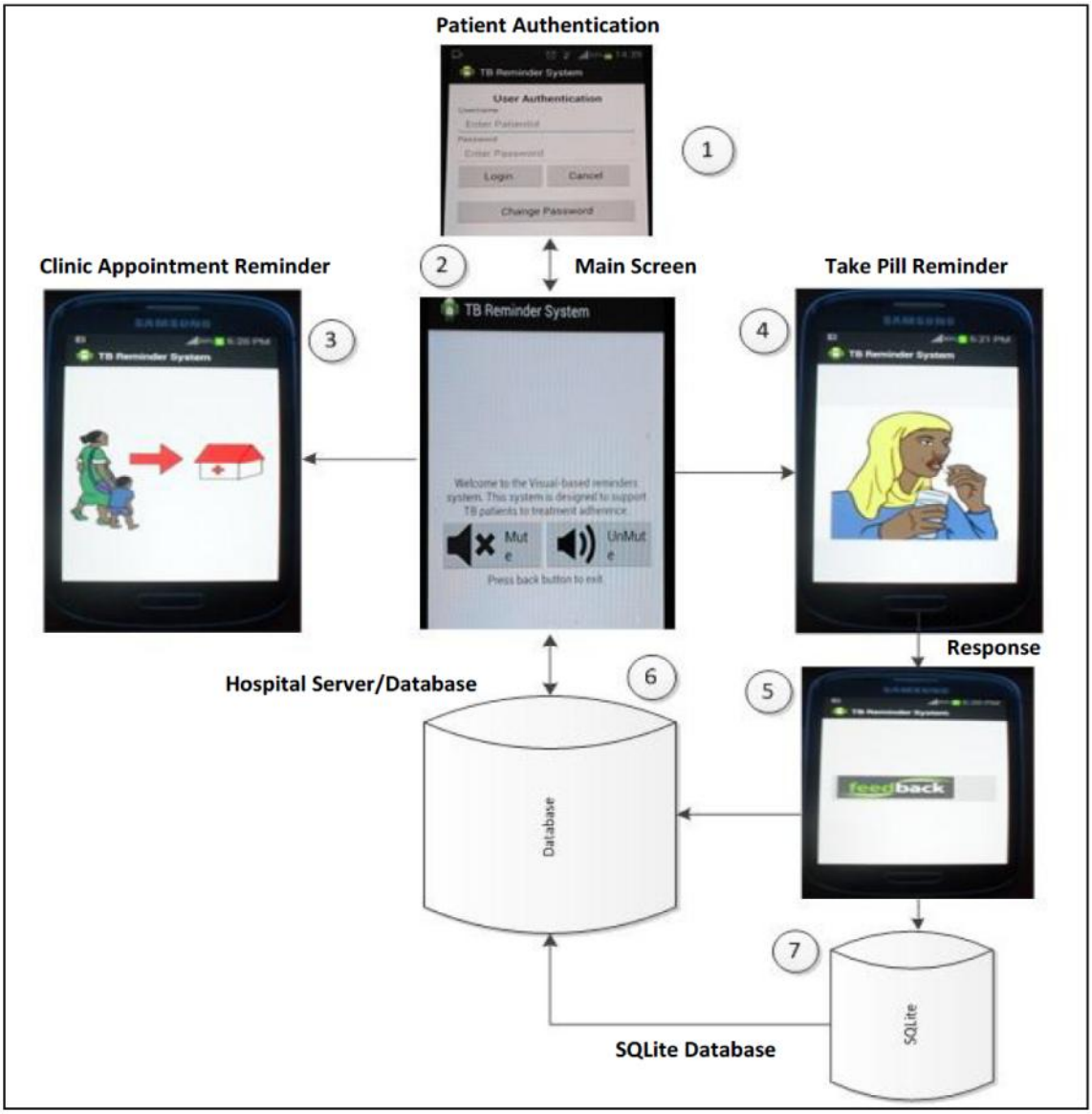

Figure 1: The Iteration of the GBR Application Components

(1) Patient presents his/her authentication, (2) The main interface after a user logs in to the system, (3) Example of the reminder message (clinic appointment reminder), (4) Example of the reminder message (take pill reminder reminds patients to take medication), (5) Feedback button screen, (6) Hospital server/database in which mobile application and users' responses are stored, (7) SQLite database, which stores responses offline.

Study Setting

The study was conducted in Zanzibar, Tanzania with TB patients under the supervision of the TB department at the MnaziMmoja Hospital. The experiment was implemented for the duration of five weeks from July to August 2015. Kiswahili was used as a medium for instructions.

Study Participants

The study included subjects who had active TB and were already taking anti-TB drugs. The participants were all aged 18 and above and were undergoing home-based care as out-patients. In order to measure the acceptance of the technology, all groups included participants with different levels of education and literacy, both men and women, and those who owned and did not own their mobile phones. The study excluded patients under 18 years of age, who were severely ill, and all in-patients. All intervention participants were given mobile phones, which were collected after the experiments.

Participants Training

The participants were given an overview on the functionality of the system and were assigned tasks to do such as pressing a feedback button once a reminder had been triggered. The training sessions were conducted both individually and in groups. Each session lasted between 45-90 minutes. Those participants who had no experience on the mobile phone use before were given additional training on the use of the phones. After the participants were comfortable in using the phone and following the instructions, they were then included in the study.

Feedback Loop

A feedback button was created that appeared once a reminder message was triggered (Figure 1 (5)). This button was used in order to measure the usage of mobile reminder systems between GBR and speech-based reminders. Once a reminder was triggered, users were instructed to press this button in order to send a feedback message to database server. The database registers the user ID, date and time of every reminder message. Phones were connected to the Internet (using hospital WiFi or mobile data) every time the participants visited the clinic. Once the phone was connected to the Internet, it automatically synchronized the data with the database.

Study Outcome Measures

To evaluate the effectiveness of GBRs, the study measured the TB treatment adherence rates in:

(1) the mobile GBR group versus the control group, and

(2) the mobile GBR group versus the speech-based reminder group.

The reason to use a speech-based reminder system alongside the GBRs instead of other reminder methods that are text-based was that some participants were illiterate and, therefore, could not read the texts but could understood verbal communications. The measured variables included adherence rates, efficacy and acceptability of the technology. The adherence rates were measured by comparing the patients' health records before and after the trial. There are various methods that are used to measure or evaluate adherence to TB treatment. For this study, we used the Self-Reported (SR), and Pharmacy Refill Data (PRD) or Pill Count (PC) [8] to evaluate adherence. SR was used as the primary method that measured treatment adherence through self-evaluation [8,30]. During follow-up times, a patient reported on his/her adherence. The following equation was used to determine the SR adherence rate for TB treatment:

$$\%\ SR\ adherence = \frac{x1}{xn}\ x\ 100$$

x1=number of patients with improved adherence

xn=total number of patients in a group

The PRD was used to measure pill success rates. Every time the patient attended the clinic for medication refills, the visit was registered and the remaining pills were counted. The efficacy and acceptance of the technology were assessed by application responses (event logs) and the user feedback collected through face-to-face interviews. The following equation was used to determine the PC adherence rate for TB treatment:

$$\%\ PC\ adherence = \frac{pn - pt}{pd\ x\ td\ x\ xn} x\ 100$$

pn = quantity of pills dispensed

pt = quantity of pills not taken

pd = number of pills per day

td = trial days

xn = number of patients

Interviews

Interviews were conducted at the end of the experiment. Only the patients in the intervention group were interviewed regarding the reminder systems. Patients were asked which mobile reminder system they found useful for supporting their treatment regimen. Patients were also asked about their perceptions and the challenges that they faced while using the applications. Each interview session lasted between 30 and 45 minutes, and was recorded by a voice recorder and notes were taken in a notebook.

Ethical Considerations

This study was approved by the University of Cape Town and the Ministry of Health and Social Welfare in Zanzibar. Written informed consent was obtained from all participants. Before the experiment began, participants were briefed on the purpose of the research and the interviews were recorded after their permission.

Statistical Analyses

Two types of data--quantitative application responses and qualitative data resulting from semi-structured interviews from patients--were generated in this study. The quantitative data were obtained from the application responses and converted into numerical form. The numerical data was then entered in and analysed with SPSS version 21 (IBM, NY, USA). A Mann-Whitney U test was conducted to compare the adherence rates between the study groups, number and time of responses in the GBR and speech-based reminder groups. A p-value of <0.05 was used to detect a significant difference for all analyses. For the qualitative data obtained from interview, the transcripts were read individually by the researchers and every interesting idea or concept was written using analytic memo. Audio recording data were first transcribed into written form so that they can be considered in detail. This was carefully done by the research team. The data were then discussed in detail among the research team members including healthcare workers to obtain meaningful and reliable concepts.

RESULTS

Demographic Characteristics of the Participants

The overall distribution of the study participants is shown in Table 1. All participants (30) were included in the analyses. Their average age was 40 years (ranging from 18 to 72 years), and 57% were women. Twenty-three (37%) participants were either illiterate or semi-literate, 40% resided in rural areas, 60% were receiving treatment in the continuation phase, and the majority of participants were self-employed (37%).

Table 1. Socio-demographic Characteristics of Participants (n=30)

Characteristics	Frequency	Percentage
Gender		
Male	13	43.3
Female	17	56.7
Age groups (years)		
18-27	6	20.0
28-37	8	26.7
38-47	6	20.0
≥48	10	33.3
Educational level		
Can read and write	19	63.3
Cannot read and write	11	36.7
Residence status		
Urban	18	60.0
Rural	12	40.0
Occupation		
Employed	9	30.0
Unemployed	7	23.3
Self-employed	11	36.7
Student	3	10.0
TB treatment type		
Intensive	12	40.0
Continuation	18	60.0

Treatment Adherence Rates

Figure 2 shows the treatment adherence rates for the control, speech-based reminder, and the GBR groups. The patients' SR adherence rates were 60% in the control group, 70% in the speech-based reminder group, and 90% in the GBR group. The PC adherence rate for the control was 70.3%, 89.4% in the speech-based reminder, and 89.9% for the GBR group. A Mann-Whitney U test indicated that the treatment adherence rate was significantly higher for the GBR group (mean ranks=17.45)

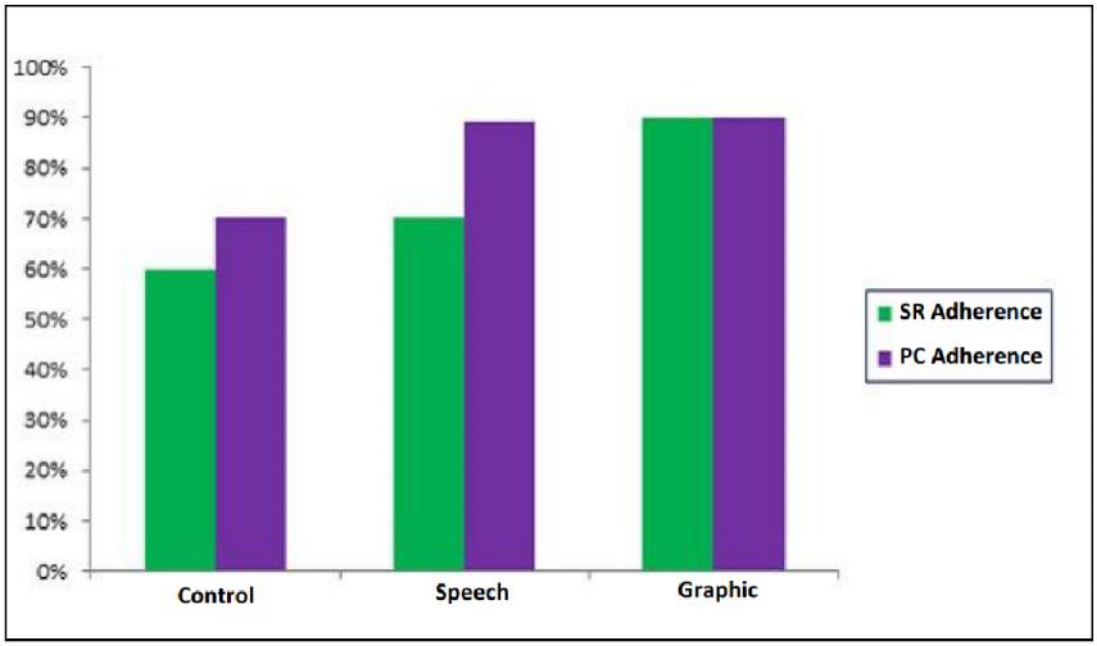

Figure 2: Treatment Adherence Rates for the Control, Speech-based Reminder and Graphic-based Reminder Groups (SR - Self-Reported, PC - Pill Count)

than for the control group (mean ranks=11.60), (U=61.0, Z=-2.130, r=-0.389, p=0.033). Similarly, the adherence rate in the GBR group was higher than in the speech-based reminder group. However the difference was not statistically significant. A Mann-Whitney U test indicated that the mean ranks for GBR group was 23.10, and 17.90 for the speech-based reminder group (U=148.0, Z=-1.747, r=-0.276, p=0.081).

Effect of Reminders on the Number of Responses

Figure 3 shows the mean number of reminder responses for the speech-based and the GBR groups. The mean number of reminder responses to the system was 60.1 in the GBR group and 50.6 in the speech-based group. A Mann-Whitney U test indicated that the number of responses to the system was significantly higher for the GBR group (mean ranks=25.58, median=60.5) than for speech-based group (mean ranks=15.43, median=51), with U=98.5, Z=-2.75, r=-0.435, p=0.006. The findings indicate that the patients sent more feedback in the GBR system than from the speech-based system.

Effect of Reminders on Response Time

Figure 4 shows the mean time taken by the patients to respond to the system for the speech-based reminder and the GBR groups. The mean response time to the system was 24.4 in the GBR group and 32.1 in the speech-based reminder group. A Mann-Whitney U test indicated that the response time to the system was significantly lower for the GBR than the speech-based reminder (the mean ranks of the GBR was 4.29 and speech reminder, 10.71; U=2.0, Z=-2.88, r=-0.769, p=0.004). This finding indicates that the patients in the GBR group responded significantly faster than the speech-based reminder group. This was the case for all reminder times. For example, the mean response time for “taking pill” and “clinic appointment” reminders was 24 and 28 in the GBR, and 30 and 33 in the speech-based reminder groups, respectively. However there was no significant difference between these reminder notifications (U=135.5, Z=-1.747, r=-0.276, p=0.081) for the taking pill reminder and (U=149.5, Z=-1.3.69, r=-0.216, p=0.171) for the clinic appointment reminder. Overall findings show that there was a significant difference in the response time to the system between the speech-based and the GBR groups, with p-value <0.01.

Acceptability and Preferences of GBR to Supplement TB Treatment

The qualitative findings indicated that all patients found the mobile GBR system more useful than the speech-based reminder in supporting them

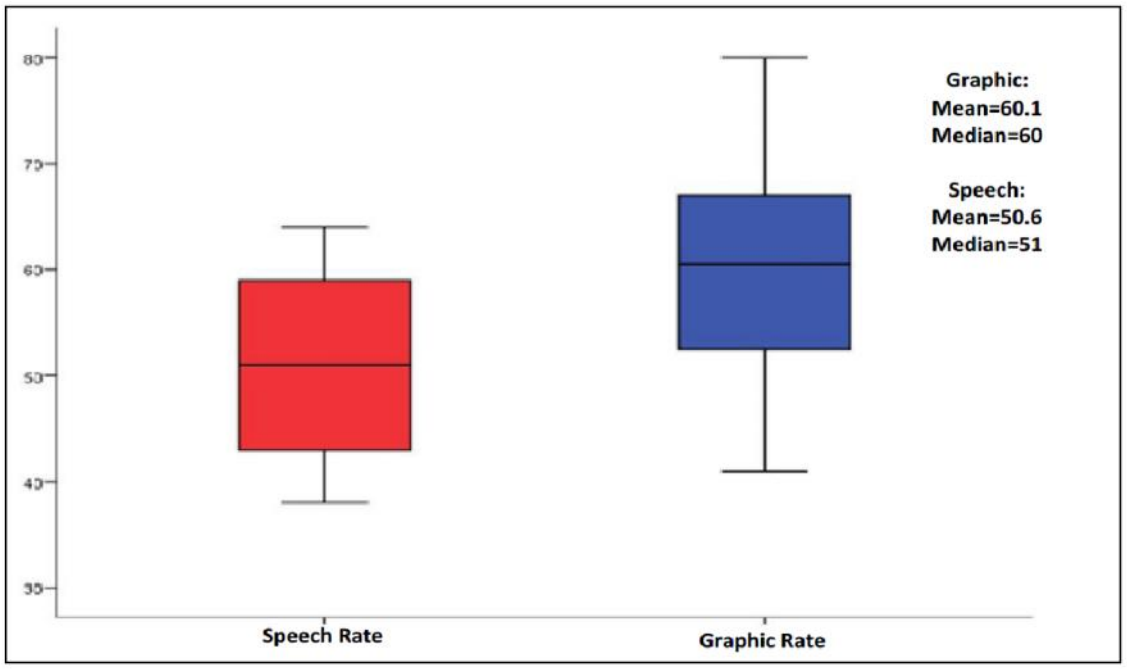

Figure 3: Number of Responses to the System for Speech-based and Graphic-based Reminder Groups

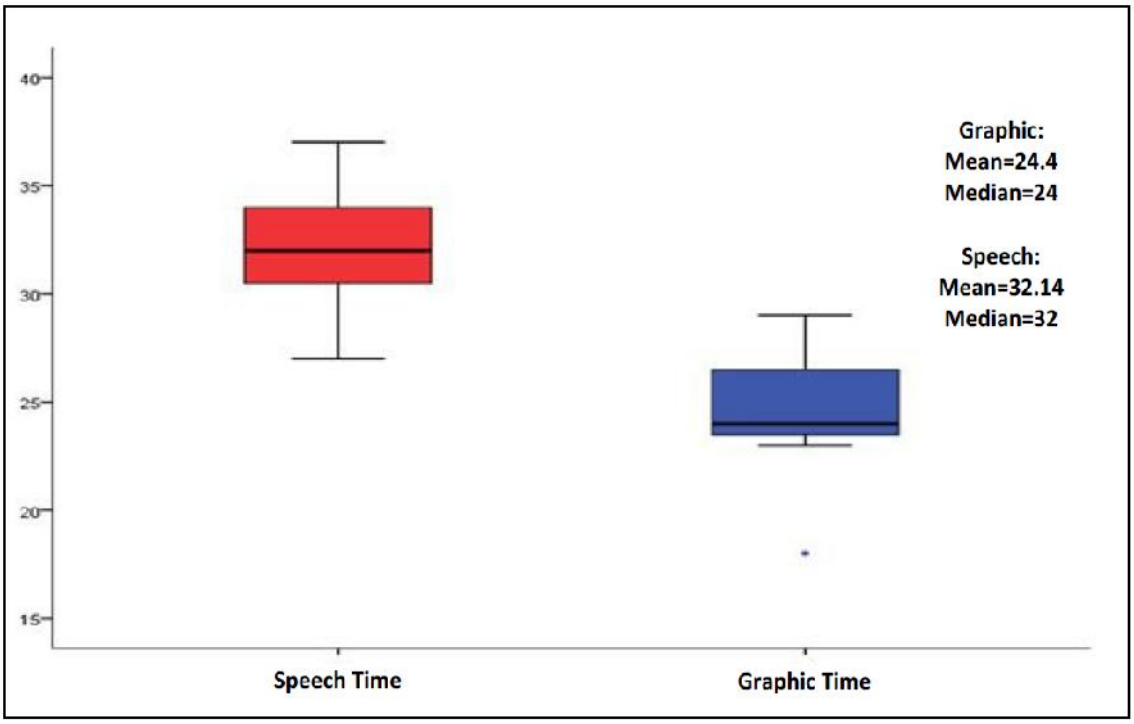

Figure 4: Effect of Reminders on Response Time – Time Taken by the Patients to Respond to the System in Speech-based and Graphic-based Reminder Groups

to adhere to their treatment. The following is some of the verbatim feedback from the respondents:

> "The GBR system was helpful in supporting me to comply with my treatment. It was very interesting, I liked it very much. This system can be also used even for people who speak different languages. The problem of the speech reminder was that, however, the voice reminded me what to do, but sometimes it was difficult to retrieve the content of message due to the background noises." -Respondent 1

> "This system was very interesting. I was reminded of every medication time. I did not miss taking my tablets during the system period. I will [be] very happy if this system continued to operate." -Respondent 2

> "Compared to speech system, the graphic was very good, I liked it … (during the interview, she received an image message, then she said) … look …! This picture is clearly interpreted that I remembered to eat vegetarian" (she was pointing at the GBRs – it was of a healthy meal). –Respondent 3

The findings further suggest that a GBR system could be used, even for patients who have problems with hearing. One of the respondents said:

> "I have a hearing problem, I cannot hear well. I always set my phone to vibrate mode, if I do not hear a phone alert I feel the vibration. During the speech system, I missed the content of several reminders, but in GBR system, I understood the content of every image." -Respondent 4

The qualitative feedback also conveyed the patients' experiences with the mobile reminder systems. For example, one patient indicated that during the system he experienced 7AM as the time to take the medication. This was different a time to the traditional care, with which he was taking his tablets irregularly. The target of the system is not only to remind patients to take their tablets and attend clinic appointments, but also to help them change their behaviour. For instance, one patient reported that, although he did remember to take his tablets, the reminder system supported him in complying with other treatment behaviours. He further added that the system could be beneficial to others, especially those who have a habit of forgetting their medications and clinic appointments. Other participants indicated that the system encouraged them to eat vegetables. The participants suggested that the GBR system was more effective and easier to understand than the speech-based reminder system.

DISCUSSION

The study findings indicate that the adherence rates in the GBR group were higher than the control and speech-based reminder groups. This mostly resulted in pills being taken by the patients and improved adherence to the prescribed doses. It is important to note that the PC adherence was assessed based on the pill refill behaviours, such as calculating the number of pills that were not taken compared to those that were collected. Pill-taking behaviour was not directly measured. The pill-taking behaviour can only be measured by observing while a patient swallows the tablets. The qualitative findings indicate that the main reasons for patients missing some pills were: forgetting to take the pills, being away from home, and a few cases of patients running out of tablets. Those patients who reported running out of tablets explained this as a loss of pills or missed appointment, particularly for the patients in the control group. Nackers et al. [31] also found these challenges causing non-adherence to TB treatment.

These findings that the mobile reminder system helps to improve the patients' adherence rates have been reported by various studies. For instance, Iribarren et al. [12] assessed adherence to TB treatment and Hardy et al. [32] assessed adherence to ARV treatment, using a SR patient survey. The results of these studies show that mobile reminder systems were more effective for improving the patients' adherence rate than traditional care. Our findings are in line with the above studies as we also found that, compared with traditional care and speech-based reminders, GBR system effectively improved treatment adherence among TB patients. It was also found that the clinic attendance rates among patients in mobile reminder groups were higher when compared to

those in the control group. Previous studies have also reported similar results. For example, Chen et al. [33] found that the clinic attendance rate amongst outpatients was significantly higher in the mobile groups than in the controls. Prasad and Anand [9] found similar results: that mobile SMSs reminder increased the rate of clinic attendance of patients in their treatment when compared to traditional care.

The findings of the effect of reminders on the number of responses indicated that the GBP system played an important role in supporting the treatment than speech-based reminders (p-value <0.01). A number of studies have also assessed the effectiveness of the mobile reminder between SMS text messages and speech systems. For example, Chen et al. [33] investigated the effectiveness of a mobile reminder, between SMS and phone call reminders, for improving patients' clinic attendance. Their study found SMS more effective than a phone call to support patients in clinic attendance. Sidney et al. [10] investigated usefulness between SMS text messages and voice reminders in supporting HIV patients, where patients preferred the speech-based system over SMS text messages. In the same way, this current study found that GBR system was more useful to support TB treatment than the speech-based reminder system.

Another important finding was from the participants who also participated in the 'wired mothers' project. They found the GBRs useful when compared with text and speech reminders in supporting them with their compliance to treatment. This project was designed to provide health education and appointment reminders to encourage pregnant mothers to attend the routine antenatal care and delivery attendance using SMS text message reminders in Zanzibar, Tanzania [34]. The findings of the efficiency of reminders on response time indicated that the time taken by patients to respond to the system between the speech-based reminder group and the GBR group were significantly different (p-value <0.01). The patients using GBRs replied faster to the system (replied sooner after having received reminders) than that with the speech-based reminders. It is worthwhile to note that with the patients receiving GBRs were taking their medication sooner of receiving the reminder messages than with the speech-based reminders.

Furthermore, the qualitative findings indicate that the patients found the GBR system to be useful in supporting them to remember the days and times of taking medication and clinic appointments. The participants' feedback showed a preference for the GBRs over speech-based and traditional care. All patients preferred receiving GBRs, compared with speech-based reminders. Finkelstein et al. [35] indicates that if the participants show preferences for a technology, they will be more likely to use and respond to the system. Finkelstein et al. [35] further mentions that when the patients are using a method they prefer, they will be more likely to comply with the treatment regimen. This study further found that the participants showed high enthusiasm for how the system had motivated them to adherence to treatment. This was evidenced as it was found that the majority of them were able and willing to spend their money on using mobile data for feedback delivery. It was found that some participants were found to frequently use the Internet and responded that they were specifically connected their phones to the Internet for sending feedback.

Comparison with Other TB Treatment Adherence Studies

To our knowledge, this is the first effective experimental study assessing the ability of a mobile GBR system to support TB treatment in a resource-limited setting. However, SMS text messages and speech-based systems, such as phone calls, have previously been studied. Three studies have provided much information for assessing SMS text reminders in promoting TB treatment adherence. The assessment of these studies yielded new insights into the technology used, number of participants, and the analysis methods made possible by reporting inequality.

The first study, conducted in Argentina by Iribarren et al. [12], assessed the effect of text messages in supporting TB patients who owned or had access to mobile phones and who were text literate. The adherence rate of patients assessed by SR was higher in the SMS texting group (77%), compared with 53% in control group. The study only involved specific patients.

Involving particular participants suggest that the technology was developed for a specific group of people. This was different from our study as it included participants from different groups, including: literate and illiterate or semi-literate; those who owned or not owned/had no access to mobile phone; and urban or rural patients. A second study from Pakistan presented by Mohammed et al. [36] measured user acceptance, perceptions and engagement with an SMS text message reminder system designed for supporting TB treatment. The SMS reminders were found to be helpful and encouraged TB patients to take their medicines. The response rates to the system were higher with participants who had some schooling and amongst women. Furthermore, the mean response to the system decreased over the study period, from 57% during the first ten days to 49% during the last ten. This shows that if the trial was deployed within a long period, it is possible that the mean response rate may be further diminished.

A third study by Husler [37] investigated the effects of SMS text reminders on TB treatment completion and cure rates. The study was conducted in Cape Town, South Africa. Though the results of the study showed higher rate of completion of TB treatment in the intervention group (10.6% compared with the controls at 3%), the rates of TB cures were similar between the two groups. Nevertheless, the study did not report the number of participants in the controls. This may bar the calculation of a risk ratio and, as a result, the findings may report inequality. Furthermore, languages used for the SMS reminders were barriers to some participants.

Other studies from the developing world have also suggested that mobile reminder approaches using a telephone call can improve compliance to treatment for TB patients [13,28]. The participants in these studies were given a daily phone call reminder to take their tablets. Kunawararak's study [13] assessed the effects of telephone reminders for promoting TB treatment. While Tanke and Leirer study [28] investigated the use of phone calls in supporting TB patients to treatment adherence. Noteworthy advantages of the current study compared with these studies include the assessment of the effects of a reminder system by capturing the patients' response rate, and the use of more personal measures such as weekly reports, and objective measurement of SR and PC to assess patients' adherence. More importantly, this study involved patients with different literacy levels.

In addition, loss to follow-ups and missing data were low in this study, and participants' involvement was constant over the duration of the study. However, the study population was only from one country, Zanzibar, Tanzania. It is interesting to note that these findings may have credential toward GBR systems in supporting TB treatment, particularly in a resource-limited setting and with mixed literacy levels in developing worlds. The study had some limitations. Firstly, the duration of the implementation of the trial was short, considering the timeline of a six months TB treatment. The second limitation was that the size of the research population was small, compared to the entire TB population. Further research will include deploying the system over a longer period and involving larger numbers of patients in order to further evaluate the effectiveness of GBR systems.

CONCLUSIONS

The aim of this study was to evaluate the effectiveness of GBR system and its impact on TB patients and adherence to the treatment. The results indicated that there was a high degree of GBR system acceptance among the patients. Overall, the findings indicated that the mobile GBR application has a potential as a reminder system that would be appropriate to support TB treatment in Zanzibar, Tanzania and beyond. The graphic applications can be applied to support the management of various other diseases including HIV and diabetes. It is hoped that the results of this study will place graphics and other forms of visual communication into the broader picture of TB treatment programs to support the most vulnerable in our societies.

AUTHORS' CONTRIBUTIONS

HAH and HS are responsible for concept development and design of the study. HAH undertook literature review, data collection,

analysis and interpretation. UR and HS critically reviewed the manuscript. All authors have read and approved the final manuscript.

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CONFLICT OF INTEREST

Authors have declared that no competing interests exist.

REFERENCES

1. WHO. Global tuberculosis report 2015. World Health Organization.
2. WHO. Global tuberculosis report 2013. World Health Organization.
3. Stop TB Partnership, (2010), 'The Global Plan to Stop TB: 2011-2015'. *World Health Organization, Geneva, Switzerland*.
4. Adane A, Alene K, Koye D, Zeleke B. Non-adherence to anti-tuberculosis treatment and determinant factors among patients with tuberculosis in Northwest Ethiopia. *PLOS ONE*. 2013; 8: e78791.
5. Walley J, Khan M, Newell J, Khan M. Effectiveness of the direct observation component of DOTS for tuberculosis: a randomised controlled trial in Pakistan. *Lancet.* 2011; 357: 664-9.
6. International Telecommunication Union, The world in 2014: ICT facts and figures. Geneva, Switzerland, 2014.
7. Oleaga M. iOS vs. Android vs. Windows Phone Market Share 2013: Google Smartphones OS Hits 78 Percent Globally As Apple Inc. Drops Despite Strong iPhone Sales, 2014 (Accessed 23 March 2015, at http://www.latinpost.com /articles/7356/20140215/ios-vs-android-windows-phone-market-share-2013-google-smartphones.htm).
8. Mbuagbaw L, Thabane L, Ongolo-Zogo P, Lester R, Mills E, Volmink J, *et al*. The Cameroon mobile phone SMS (CAMPS) trial: a protocol for a randomized controlled trial of mobile phone text messaging versus usual care for improving adherence to highly active anti-retroviral therapy. *Trials*. 2011; 12: 5.
9. Prasad S, Anand R. Use of mobile telephone short message service as a reminder: the effect on patient attendance. *International Dental J*. 2012; 62: 21-6.
10. Sidney K, Antony J, Rodrigues R, Arumugam K, Krishnamurthy S, D'souza G, *et al*. Supporting patient adherence to antiretrovirals using mobile phone reminders: patient responses from South India. *AIDS Care*. 2012; 24: 612-7.
11. Lester R, Ritvo P, Mills E, Kariri A, Karanja S, Chung M, *et al*. Effects of a mobile phone short message service on antiretroviral treatment adherence in Kenya (WelTel Kenya): a randomised trial. *The Lancet*. 2010; 376: 1838-45.
12. Iribarren S, Beck S, Pearce P, Chirico C, Etchevarria M, Cardinale D, *et al*. TB: 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.
13. Kunawararak P, Pongpanich S, Chantawong S, Pokaew P, Traisathit P, Srithanaviboonchai K, *et al*. Tuberculosis treatment with mobile-phone medication reminders in northern Thailand. *Southeast Asian J Trop Med Public Health*. 2011; 42: 1444.
14. Bediang G, Stoll B, Elia N, Abena J, Nolna D, Chastonay P, *et al*. SMS reminders to improve the tuberculosis cure rate in developing countries (TB-SMS Cameroon): a protocol of a randomised control study. *Trials*. 2014; 15: 35.
15. Ngoh N, Shepherd D. Design, development, and evaluation of visual aids for communicating prescription drug instructions to nonliterate patients in rural Cameroon. *Patient Educ Couns*. 1997; 31: 245-61.
16. Seth H, Sorathia K. Parichaya - a low-cost device to increase adherence among Tuberculosis patients in rural Assam. In *Proceedings of the 11th Asia Pacific Conference on Computer Human Interaction*. 2013; pp. 55-62. ACM.
17. Dowse R, Ehlers M. The evaluation of pharmaceutical pictograms in a low-literate South African population. *Patient Educ Couns.* 2001; 45: 87-99.
18. Medhi I, Sagar A, Toyama K. Text-free user interfaces for illiterate and semi-literate users. In *Information and Communication*

Technologies and Development, 2006. ICTD'06. International Conference on 2006: pp. 72-82. IEEE.
19. Thies I. User interface design for low-literate and novice users: Past, present and future. *Interaction*. 2014; 8: 1-72.
20. Gupta I. Public signage system to combat problems of illiteracy and multilingualism. *J Int Soc Res.* 2008; 1: 4.
21. Wileman R. Visual communicating. Educational Technology, 1993.
22. Haji A, Suleman H, Rivett U. Developing Mobile Graphic Reminders for Reinforcing Compliance in Tuberculosis Treatment in Africa. Proceedings of 1st International Conference on the Use of Mobile ICT in Africa 2014, Stellenbosch, South Africa. ISBN: 978-0-7972-1533-7, 2014a: pp. 11-15, 2014.
23. Haji A, Suleman H, Rivett U. Mobile Graphic-based Communication: Investigating Reminder Notifications to Support Tuberculosis Treatment in Africa: HIS 2014, LNCS 8423, 2014b: pp. 204-211.
24. Rogers R, Lombardo J, Mednieks Z. Android application development: Programming with the Google SDK. O'Reilly Media, Inc, 2009.
25. Michael O. iOS vs. Android vs.Windows Phone Market Share 2013: Google Smartphones OS Hits 78 Percent Globally As Apple Inc. Drops Despite Strong iPhone Sales, 2014.
26. Wu H, Hamdi L, Mahe N. Tango: a flexible mobility-enabled architecture for online and offline mobile enterprise applications. In *Mobile Data Management (MDM), 2010 Eleventh International Conference on* 2010: pp. 230-238. IEEE.
27. Rana Y, Haberer J, Huang H, Kambugu A, Mukasa B, Thirumurthy H, Linnemayr S. Short message service (SMS)-based intervention to improve treatment adherence among HIV-positive youth in Uganda: Focus Group Findings, 2015.
28. Tanke E, Leirer V. Automated telephone reminders in tuberculosis care. *Med Care*. 1994; 32: 380-9.
29. Albino S, Tabb K, Requena D, Egoavil M, Pineros-Leano M, Zunt J, *et al*. Perceptions and acceptability of short message services technology to improve treatment adherence amongst tuberculosis patients in Peru: a Focus Group Study. *PLOS ONE*. 2014; 9: e95770.
30. Arnsten H, Demas A, Farzadegan H, Grant W, Gourevitch N, Chang J, *et al*. Antiretroviral therapy adherence and viral suppression in HIV-infected drug users: comparison of self-report and electronic monitoring. *Clin Infect Dis*. 2001; 33: 1417-23.
31. Nackers F, Huerga H, Espié E, Aloo A, Bastard M, Etard J, *et al*. Adherence to self-administered tuberculosis treatment in a high HIV-prevalence setting: a cross-sectional survey in Homa Bay, Kenya. *PLOS ONE*. 2012; *7:* e32140.
32. Hardy H, Kumar V, Doros G. Randomized controlled trial of a personalized cellular phone reminder system to enhance adherence to antiretroviral therapy. *AIDS Patient Care STDS*. 2011; 25: 153-161.
33. Chen Z, Fang L, Chen Y, Dai H. Comparison of an SMS text messaging and phone reminder to improve attendance at a health promotion center: a randomized controlled trial. *J Zhejiang Univ Sci B*. 2008; 9: 34-8.
34. Lund S, Hemed M, Nielsen B, Said A, Said K, Makungu M, *et al*. Mobile phones as a health communication tool to improve skilled attendance at delivery in Zanzibar: a cluster-randomised controlled trial. *BJOG*. 2012*;* 119: 1256–64.
35. Finkelstein S, Liu N, Jani B. Appointment reminder systems and patient preferences: Patient technology usage and familiarity with other service providers as predictive variables. *Health informatics J*. 2013; 19: 79-90.
36. Mohammed S, Siddiqi O, Ali O, Habib A, Haqqi F, Kausar M, *et al*. User engagement with and attitudes towards an interactive SMS reminder system for patients with tuberculosis. *J Telemed Telecare*. 2012; 18: 404-8.
37. Husler J. Evaluation of the on Cue compliance service pilot: Testing the use of SMS reminders in the treatment of tuberculosis in Cape Town, South Africa. Bridges. Org, 2005.