THE ROLE OF MOBILE SMS-REMINDERS IN IMPROVING DRUGS COMPLIANCE IN PATIENTS RECEIVING ANTI-TB TREATMENT FROM DOTS PROGRAM

Rukhsana Javed Farooqi[1], Sadia Ashraf[2], Mukhtiar Zaman[3]

[1-3] Department of Pulmonology, Khyber Teaching Hospital, Peshawar - Pakistan.
Address for Correspondence:
Dr. Rukhsana Javed Farooqi
Department of Pulmonology, Khyber Teaching Hospital, Peshawar - Pakistan.
Email: dr_farooqi@hotmail.com
Date Received:
September 07 , 2016
Date Revised:
February 28, 2017
Date Accepted:
March 09, 2017

ABSTRACT

Objective: To find out the role of mobile SMS-reminders in improving drugs compliance in patients receiving anti-TB treatment from DOTS program.

Methodology: This randomized controlled trial was conducted from June 2014 to June 2015, in two centres: Khyber Teaching Hospital Peshawar and Emergency Satellite Hospital Nahaqi. Patients enrolled for anti-TB drugs were distributed in intervention and control groups; daily mobile SMS reminders were sent to patients of intervention group on top of usual DOTS. Patients were followed on monthly basis. Primary outcome measure was default, defined as not taking medicine for two consecutive months.

Results: Total of 148 patients were enrolled, 74 in each group. Baseline characteristics of both groups were comparable. Mean age was 29.4 ±17.6 years, with 63 (42.6%) males, 65 (43.9%) smear-positive TB, 24 (16.2%) smear-negative TB, and 59 (39.9%) extra-pulmonary TB. Treatment-default was found in 7 (4.7%) patients, out of these 3 patients (4.1%) were in "intervention group" and 4 patients (5.4%) were in "control group", both groups were comparable with no significant statistical difference (p = 0.983).

Conclusion: Number of treatment-default cases was lower in "intervention group" than "control group", but this numerical difference was not significant statistically.

Key Words: Tuberculosis, Tuberculosis treatment, Compliance, Default rate, Mobile phone, SMS, Text messages

This article may be cited as: **Farooq RJ, Ashraf S, Zaman M. The role of mobile SMS-reminders in improving drugs compliance in patients receiving anti-TB treatment from DOTS program. J Postgrad Med Inst 2017; 31(2): 156-62.**

INTRODUCTION

Tuberculosis (TB) is amongst the major health problems worldwide. In 2014, about 9.6 million new cases were reported from across the world and about 1.5 million patients died because of this infection. Pakistan ranks at 5th position according to the burden of this disease[1].

Drugs adherence may be defined as "taking of drug(s) in prescribed dosage and for prescribed time duration. It has a fundamental role for the success of any treatment". Like any chronic infection, drugs adherence has a pivotal role in tuberculosis[2]. It improves cure rate and avoid drugs resistance. Drugs adherence greater than 90% ensures cure and sure avoidance of drugs resistance[2,3]. Highly effective anti-TB drugs are available to treat tuberculosis but because of poor adherence we haven't been able to achieve global control of this disease.

According to World Health Organization (WHO), patients suffering from TB need rifampicin-based combination therapy for six months (new cases) and eight months (retreatment cases). All anti-TB drugs are associated with many side effects. Therefore, these three factors, namely i) combination of drugs, ii) prolonged duration, and iii) drugs-associated side effects, result in poor drugs' adherence which results in many worse consequences. These include: prolonged time duration of infectious stage of TB[4] ,high relapse rate after treatment[5], resistance to anti-TB drugs[6,7], expensive treatment regimens for prolonged duration with less reported efficacy[8] and finally, increased morbidity and mortality[4]. Therefore, after starting a patient on anti-TB treatment, regular drugs taking must be ensured by uninterrupted provision of drugs, managing for side-effects of these drugs and even psychological and social support. To ensure all this, WHO recommends directly observed treatment short course (DOTS) strategy to achieve desirable results of TB treatment worldwide[8,9].

Mobile phone is the most commonly used technology of communication worldwide. It provides video, audio and text messaging facilities to communicate with one another. It is the most cost-effective way to communicate with people residing in difficult to reach areas. The communication can be made in any language and at any time. Mobile text message, known as SMS (Short Messaging Service) is being used in healthcare systems. This is called mobile health (mHealth).[10,11] It provides excellent and most cost-effective means of communication to healthcare system to be used among healthcare workers themselves as well as healthcare workers and patients. Barriers of long distances are successfully eliminated by mHealth.[12] It has been successfully used for improving drugs compliance with anti-HIV drugs.[13] Similarly it may be used to improve drugs compliance with anti-TB drugs.

Only couple of studies have studied mHealth technology in patients taking anti-TB drugs;[11,14,15] all these evaluating adherence to anti-TB drugs, but none has reported impact of SMS-reminders on cure rate. We conducted this study to find out the role of SMS-reminder strategy on drugs compliance, treatment outcome specially cure and default rate.

METHODOLOGY

This was interventional, double blind, randomized controlled study approved by ethics committees of Khyber Medical University Peshawar. The study was conducted to find out the role of mobile SMS-reminders in improving drugs compliance in patients receiving anti-TB treatment. It was conducted from June 2014 to June 2015 on TB patients registered in TB Clinics of Khyber Teaching Hospital (KTH) and Emergency Satellite Hospital (ESH) Nahaqi. There were two groups in this study: interventional and control. Patients in both groups were given anti-TB drugs on monthly basis for 6 months. As an intervention, mobile SMS-reminders were sent daily to patients during intensive phase (initial 2 months) of anti-TB treatment in the intervention group but not in the control group (Figure1).

Following was the inclusion and exclusion criteria of this study: Inclusion criteria consisted of i) all new cases of pulmonary and extra pulmonary tuberculosis registered in TB control program, ii) having personal mobile phone or an access to mobile phone of his/her relative, and iii) able to read and/or understand SMS-reminder (himself/herself or via his/her relative). Exclusion criteria included those i) having no access to mobile phone, ii) those with visual problems, iii) those physically unable to handle mobile phone, iv) those unable to read and/or understand SMS-reminder (himself/herself or via his/her relative), v) those with category-II treatment (relapse and treatment failure cases), and vi) those with meningeal, miliary and abdominal TB.

The sample size was calculated by using WHO sample size calculator for random control study. Studies have reported 19% default rate in patients taking anti-TB drugs, but we could not find any study suggesting improved default rate by SMS-reminder strategy; therefore we took 10% expected default rate after SMS-reminder intervention in our study. Therefore, taking p as 0.20 and 0.10 with 95% confidence level and margin of error (0.05), the sample size was calculated to be 148. Each group comprised 74 patients.

The data was planned to be collected through interview technique using pretested structured questionnaire. Special mobile phone SMS package was taken to deliver the reminder message. Research assistants were identified to collect data. They were medical technologists working in the two above-mentioned TB clinics. Training sessions were arranged for these research assistants in which they were educated on study aims and objectives, questionnaire was discussed with them, and they were practically trained how to collect and enter data in the given questionnaire. Questionnaire was pretested on patients in TB Clinic of KTH and necessary changes were made as required. The required sample of 148 was divided into two (intervention and control) groups, 74 patients in each group, by random assignment using the computer-generated numbers.

Study was conducted among new TB patients, who were registered in TB control program for anti-TB drugs. Patients fulfilling the inclusion criteria were identified and study was introduced to them. In case of willing patients and absence of exclusion criteria, informed consent (verbal/written) was obtained and they were enrolled in the study. If the patient was allocated to intervention group, he/she was asked to come to TB clinic every month to collect anti-TB drugs as per TB control programme protocol; in addition, reminder was given by SMS on daily basis to take drugs during intensive phase (initial 2 months) of anti-TB treatment. If the patient was allocated to control group, he/she was asked to come to TB clinic every month to collect anti-TB drugs as per TB control programme protocol; but no reminder was given by SMS. Participants in the intervention group were educated for understanding SMS text message. The SMS comprised two components: a) message in Urdu language saying "You are suffering from tuberculosis, please take your anti TB drugs daily on empty stomach", and b) an illustrated figure showing "hand carrying tablets" for illiterate patients.

On first visit, the basic demographic data was recorded in the questionnaire. It included age, gender, education in years, weight of the participants, disease status, sputum smear result, contact person and understanding of mobile phone message. Patients of both groups were followed up on monthly basis for six months. Standard TB program parameters were recorded in all patients.

Following parameters were recorded after the end of anti-TB treatment: a) total number of visits of patient in TB clinic, b) weight of patient in kg, and c) category of treatment outcome (i.e. cure, treatment complete, treatment default, and treatment failure) defined as follows:

Cure: "when smear (culture) became negative during treatment and remained negative after the end of treatment in a patient with positive smear (culture) before treatment."

Treatment success: "a sum of patients with cure and treatment complete (for smear or culture positive patients only)."

Treatment failure: " a) patient whose sputum smear (culture) remained positive at 5 months or later during treatment, and b) a patient found to harbor a multi-drug-resistant (MDR) strain at any point of time during the treatment, irrespective of smear-negative or -positive."

Default: "a patient whose treatment was interrupted for 2 consecutive months or more." It was the primary outcome measure of the study.

Study data was analysed by SPSS 19 version. Descriptive statistics like percentage and mean were calculated for variables like sex, age and education status. Comparative analysis between two study groups was done by Chi-square test. At 95% confidence limit, p value <0.05 was considered as significant.

RESULTS

One hundred and forty-eight (148) patients were enrolled: 88 patients (59.5%) were enrolled in KTH and 60 (40.5%0 in ESH. Mean age was 29.4 $\pm$17.6 years. Male patients were 63 (43%) and female patients were 85 (57%). Majority of patients was uneducated (n =105, 71%). Pulmonary TB was the most common type of disease (n =89, 60%), out of which 73% cases were sputum smear-positive. There were 74 patients in each group; the demographics of both groups were comparable (Table1). There were no dropouts; all patients completed the study.

After completing anti-TB treatment of six months duration; one patient had treatment failure in each group (both groups were comparable). Forty-nine patients had treatment complete in each group (both groups were comparable). Twenty-one patients had cured in intervention group as compared to 20 patients in control group. Three patients had treatment default in intervention group as compared to 4 patients in control group (Figure 2).

DISCUSSION

Mobile phone technology is being used across the world and almost 6.8 billion people are using it to communicate with one another[16]. It is quick, reliable and most cost-effective tool of communication, and therefore increasingly used in healthcare systems now a days[17]. It offers many ways of communication like phone video calls, audio calls, MMS and SMS. Many online apps can be also used like WhatsApp and others. Its being used: 1) among healthcare workers for shift reminders, for sharing medical updates, seeking opinion of one another, etc. 2) among healthcare workers and patients for disease management and research, and 3) among patients themselves to share experiences and support one another in patients groups.

Chronic diseases like diabetes, hypertension, epilepsy, asthma, chronic renal failure, cirrhosis and arthritis,

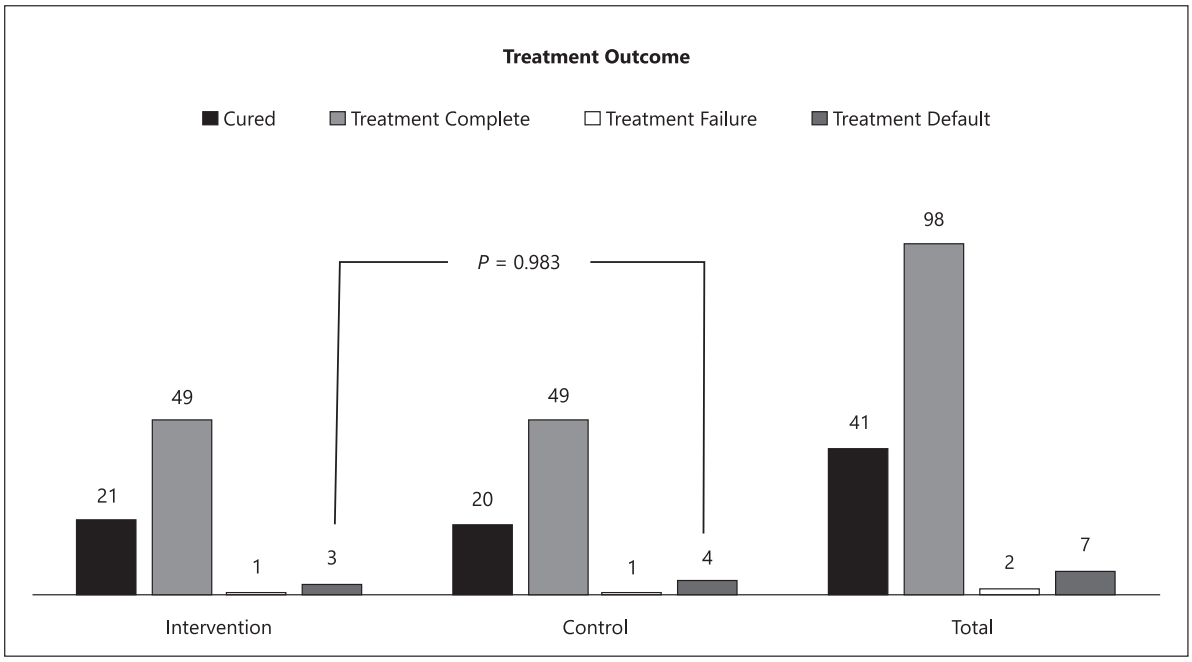
Table 1: Comparison baseline characteristics of two groups

Baseline Characteristics	Intervention (n=74)	Control (n=74)	Total (n=148)
Gender			
Male	32 (43.2%)	31 (41.9%	63 (42.6%)
Female	42 (56.8%)	43 (58.1%)	85 (57.4%)
Education Status			
Yes	22 (29.7%)	21 (28.4%)	43 (29.1%)
No	52 (70.3%)	53 (71.6%)	105 (70.9%)
TB Status			
Smear Positive	31 (41.9%)	34 (45.9%)	65 (43.9%)
Smear Negative	14 (18.9%)	10 (13.5%)	24 (16.2%)
Extra-Pulmonary	29 (39.2%)	30 (40.6%)	59 (39.9%)
Mean Body Weight			
Before Treatment	49.3 Kg	48.8 Kg	
After Treatment	50.8 Kg	50.2 Kg	

Figure 1: Study protocol

Recruitment	1st Month	2nd Month	3rd Month	4th Month	5th Month	6th Month	Outcome
Monthly Visits							
Intervention Group	Mobile SMS sent daily		Drugs	Drugs	Drugs	Drugs	
	Drugs	Drugs					
Control Group	Drugs	Drugs	Drugs	Drugs	Drugs	Drugs	

Figure 2: Comparison of results in two groups after 6 months treatment



HIV, etc. need life-long management. All these diseases are progressive in nature and are associated with many complications. Patients of all such chronic diseases need to take drugs regularly, most of the times two or more in number, and at least once everyday. All these drugs are having side effects and may interact with one another. Therefore its vital to take drugs regularly to control these diseases so the associated complications can be avoided or their onset can be delayed. In addition it's equally important to evaluate these patients for the efficacy of their drugs as well as to monitor for their side effects. Because of possible side effects of drugs and even believing drugs that drugs are not needed after disease control is achieved, drugs' adherence is compromised not uncommonly. Therefore SMS-reminders are being used in many centres in an attempt to improve drugs' compliance and disease monitoring. Patients have accepted this intervention across the world in many studies[18,19].

In Pakistan, till 2014, total mobile phone subscriptions had reached almost 140 million (76.2% of total population) [20]. Evidently, mobile phone technology provides unique opportunity to target difficult-to reach people in our country. Tuberculosis is also chronic infection and needs regular drugs' taking for at least 6 months. In the national TB control, under DOTS strategy, patients are given free anti-TB drugs on monthly basis from TB centres across Pakistan. Poor drugs' adherence is also not uncommon in our patients because of many known factors mentioned in chapter-2 (Literature Review). To improve drugs' adherence, SMS text message can be sent daily, early in the morning, to remind patients to take their drugs[21,22]. Even patients can confirm drugs' taking by reply-SMS text message[23-27]. We have provided new evidence that SMS-reminders are effective in improving drugs' adherence in our TB patients and may improve cure rate in our national TB program.

We found that SMS-reminders decreased default rate and consequently improved cured rate. Number of "default" cases was low in intervention group as compared

to control group, but this difference was statistically not significant (P =0.983). This may be due to low default rate in the control group than the presumed rate of 10% used for sample size calculations. We found four studies on literature review: Bridges.org[28] and Broomhead S, et al[29] from South Africa, and Owiti et al[30] from Kenya reported the same findings with SMS-reminders, whereas Iribarren et al[31] from Argentina found no improvement with SMS-reminders. Recently, Mohammed et al[32] reported no significant difference between SMS intervention or control groups for treatment success in Karachi.

We conducted parallel-randomized control study. Iribarren et al[31] had adopted the same design in their pilot study in 2012. Recently published study by Mohammed et al[32] from Karachi had also the same design. The other three studies had adopted different designs. Bridges.Org[28] conducted questionnaire based interviews among patients & staff as well as collected data from patients' files. Broomhead et al[29] conducted a retrospective analysis of patients' files. Owiti et al[30] conducted feasibility pilot study.

We enrolled 148 patients, 74 in each group. Bridges.Org[28] analysed data of 221 patients. Broomhead et al[29] compared 24 files of intervention with 96 files of control. Owiti et al[30] analysed files of 187 patients. Iribarren et al[31] compared 18 patients of intervention group with 19 patients in control group.

We used SMS-text messages to remind our patients to take their drugs. Broomhead et al[29] used SIMpill® (wireless pill bottle) connected with a central server. SMS used to be sent automatically this server to notify that patient had taken drug. The other studies[28, 30-32] sent SMS-reminders like in our study.

Technically this study is superior to above-mentioned four studies[28-31] as regards to research bias parameters: performance bias, detection bias, attrition bias and reporting bias. Study from Karachi[32] is comparable with this study.

LIMITATIONS

Rich data was obtained through both qualitative and quantitative methods. Nonetheless, this study has some important limitations:

This study lacked an objective adherence measure. Self-reporting method was used to assess drugs adherence. It has been found that patients reports higher adherence than actual by recall method[33]. This bias could have been limited by daily assessment of drug adherence. Because of this potential bias, we assessed sputum or culture conversion and treatment outcomes for objective measures to support evidence of actual treatment adherence.

Final treatment success rates were high in both groups which may indicate that it is possible that those who agreed to participate were more likely to be adherent with treatment.

We did not assess background knowledge of participants about the nature of TB, which determines motivation level and drug adherence. We could have analyzed the impact of background knowledge and level of motivation on treatment outcome in both groups.

SMS reminder was "one-way" process; there was no system like patients telephonic confirmation of drug taking as result of text message.

CONCLUSIONS

Number of treatment-default cases was lower in "intervention group" than "control group", but this numerical difference was not significant statistically. We can improve drugs' adherence in our TB patients by sending them regular mobile phone SMS-reminder.

RECOMMENDATIONS

Mobile phone SMS-reminder is a cost-effective, feasible and widely acceptable tool in our everyday clinical practice. It's easy to adopt and bring it in practice. Concerned healthcare workers and patients can be easily trained on it. By decreasing default rate, it may potentially improve cure rates of our TB control program.

ACKNOWLEDGEMENTS

We acknowledge the followings for helping us in different phases of our study, like patients' data collection and analysis: Mr. Nazir and Mr. Ashfaq medical technologist at TB clinic at KTH and ESH Nahaqi respectively. Dr. Aysha for helping me in formatting this article. Prof. Javed Iqbal Farooqi helped me to bring out the final manuscript.

REFERENCES

1. Global Tuberculosis Report 2016. Available at: www.who.int/tb/publications/global_report/en
2. Awofeso N. Antituberculous medication side-effects constitute major factor for poor adherence to tuberculosis treatment. Bull World Health Organ 2008; 86:B-D.
3. Harries A, Maher D, Graham S. TB/HIV: A CLINICAL MANUAL. World Health Organization Geneva 2004; 2:1-210p
4. M'Imunya JM, Kredo T, Volmink J. Patient education and counselling for promoting adherence to treatment for tuberculosis (review). Cochrane database Syst Rev 2012; 16:CD006591.
5. Ormerod LP, Prescott RJ. Inter-relations between relapses, drug regimens and compliance with treatment in tuberculosis. Respir Med 1991; 85:239–42.
6. Weis SE, Slocum PC, Blais FX, King B, Nunn M, Matney GB

et al. The effect of directly observed therapy on the rates of drug resistance and relapse in tuberculosis. N Engl J Med 1994; 330:1179–84.

7. Mitchison DA. How drug resistance emerges as a result of poor compliance during short course chemotherapy for tuberculosis. Int J Tuberc Lung Dis 1998; 2:10–5.
8. World Health Organization: Global Tuberculosis Report. Geneva: WHO 2012; 2012:1-89. http://apps.who.int/iris/bitstream/10665/75938/1/9789241564502_eng.pdf
9. Frieden TR, Sbarbaro JA. Promoting adherence to treatment for tuberculosis: the importance of direct observation. Bull World Health Organ 2007; 85:407–9.
10. Kay M. World Health Organization: mHealth: new horizons for health through mobile technologies. 2nd Glob Surv Health 2011; 3:1–103.
11. Person AK, Blain ML, Jiang H, Rasmussen PW, Stout JE. Text messaging for enhancement for testing and treatment for tuberculosis, human immunodeficiency virus, and syphilis: a survey of attitudes toward cellular phones and healthcare. Telemed J E Health 2011; 17:189–95.
12. Mahmud N, Rodriguez J, Nesbit J. A text message-based intervention to bridge the healthcare communication gap in the rural developing world. Technol Health Care 2010; 18:137–44.
13. Finitsis DJ, Pellowski JA, Johnson BT. Text message intervention designs to promote adherence to antiretroviral therapy (ART): a meta-analysis of randomized controlled trials. PLoS One 2014; 9:e88166.
14. Albino S, Tabb KM, Requena D, Egoavil M, Pineros-Leano MF, Zunt JR et al. Perceptions and accept- ability of short message services technology to improve treatment adherence amongst tuberculosis patients in Peru: a focus group study. PLoS ONE 2014; 9:e95770.
15. Hüsler J: Evaluation of the On Cue Compliance Service Pilot. In: Testing the Use of SMS Reminders in the Treatment of Tuberculosis in Cape Town, South Africa: Technology Associate, bridges.org. Health Direct Int Develop Res Coun (IDRC); 2005.
16. International Telecommunication Union. ICT Facts and Figures. The World in 2013. Int Telecom Un; 2013. Available at: http://www.itu.int/en/ITU-D/Statistics/Documents/facts/ICTFactsFigures2013-e.pdf.
17. Atun RF, Sittampalam SR. The role of mobile phones in increasing accessibility and efficiency in healthcare. A Review of the Characteristics and Benefits of SMS in Delivering Healthcare. Vodafone Policy Paper Seri 2006; 4:1-48. Available at: webcitehttp://www.enlightenmenteconomics.com/assets/vodafone_policy_paper_4_march06.pdf.
18. da Costa TM, Barbosa BJ, Gomes e Costa DA, Sigulem D, de Fátima Marin H, Filho AC et al. Results of a randomized controlled trial to assess the effects of a mobile SMS-based intervention on treatment adherence in HIV/AIDS-infected Brazilian women and impressions and satisfaction with respect to incoming messages. Int J Med Inform 2012; 81:257–69.
19. Guy R, Hocking J, Wand H, Stott S, Ali H, Kaldor J. How effective are short message service reminders at increasing clinic attendance? A meta-analysis and systematic review. Health Serv Res 2012; 47:614–32. http://europepmc.org/abstract/MED/22091980.
20. http://tribune.com.pk/story/733830/record-high-mobile-phone-subscriptions-spike-up-to-140m/
21. Horvath T, Azman H, Kennedy GE, Rutherford GW. Mobile phone text messaging for promoting adherence to antiretroviral therapy in patients with HIV infection. Cochrane Database Syst Rev 2012; 3:CD009756.
22. Ahmed J, Skarbek S, Codlin A, Khan A, Mohaupt DK. mHealth to improve TB care. Interac Res Develop Karachi; 2012.
23. Thirumurthy H, Lester RT. M-health for health behaviour change in resource-limited settings: applications to HIV care and beyond. Bull World Health Organ 2012; 90:390-2.
24. Lester RT, Ritvo P, Mills EJ, Kariri A, Karanja S, Chung MH et al. Effects of a mobile phone short message service on antiretroviral treatment adherence in Kenya (Wel Tel Kenya1): a randomised trial. Lancet 2010; 376:1838–45.
25. Pop-Eleches C, Thirumurthy H, Habyarimana JP, Zivin JG, Goldstein MP, de Walque D et al. Mobile phone technologies improve adherence to antiretroviral treatment in a resource-limited setting: a randomized controlled trial of text message reminders. AIDS 2011; 25:825–34.
26. Metzger P, Clerizier S, McCue D, Murphy K. Texts for Tuberculosis: Enabling Patient Advocacy; 2011. http://triplehelixblog.com/2011/02/texts-for-tuberculosis-enabling-patient-advocacy/print/.
27. Barclay E. Text messages could hasten tuberculosis drug compliance. Lancet 2009; 373:15–6.
28. Bridges.org. Evaluation of the On Cue Compliance Service pilot: Testing the Use of SMS Reminders in the Treatment of Tuberculosis in Cape Town, South Africa Cape Town. Bridges.org; 2005. Available at: http://healthmarketinnovations.org/sites/ default/files/Evaluation%20of%20the%20On%20Cue%20Compliance%20Service %20Pilot.pdf.
29. Broomhead S, Mars M. Retrospective return on investment analysis of an electronic treatment adherence device piloted in the Northern Cape Province. Telemed J E Health 2012; 18:24–31.
30. Owiti P, Gardner A, Szkwarko D, Diero L, Carter EJ. Mobile phone text messaging reminders to aid adherence to tuberculosis care in Eldoret, Kenya. 43rd World Conference

on Lung Health of The Union, Kuala Lumpur, Malaysia 2012. Int J Tuberc Lung Dis 2012; 16:S200.

31. Iribarren S, Chirico C, Echevarrria M, Cardinali D. Text TB: a parallel design randomized control pilot study to evaluate acceptance and feasibility of a patient-driven mobile phone based intervention to support adherence to TB treatment. J Mob Technol Med 2012; 1:23–4.

32. 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; 11:1-13. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27802283

33. Balshem H, Helfand M, Schunemann HJ, Oxman AD, Kunz R, Brozek J et al. Grade guidelines: 3. Rating the quality of evidence. J Clin Epidemiol 2011; 64:401–6.

CONTRIBUTORS

RJF Conceived, designed, and collected data, statistical analysis, prepared manuscript. SA and MZ Collected data, conducted data analysis, edited manuscript. All authors contributed significantly to the submitted manuscript.