Use of interactive messaging to reduce pre-diagnosis loss to follow-up for TB care

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OBJECTIVE: To investigate the uptake and usage of a WhatsApp-based interactive communication strategy to avert pre-diagnosis loss to follow-up (LTFU) from TB care in a high-incidence setting.

METHODS: We enrolled adults (≥18 years) who underwent routine sputum TB testing in two primary healthcare clinics in Khayelitsha, Cape Town, South Africa. The intervention consisted of structured WhatsApp-based reminders (prompts) sent prior to a routine clinic appointment scheduled 2–3 days after the diagnostic visit. Pre-diagnosis LTFU was defined as failure to return for the scheduled appointment and within 10 days.

RESULTS: We approached 332 adults with presumptive TB, of whom 103 (31%) were successfully enrolled; 213 (64%) did not own a WhatsApp-compatible phone. Of 103 participants, 74 (72%) actively responded to WhatsApp prompts; 69 (67%) opted to include a close contact in group communication to co-receive reminders. Pre-diagnosis LTFU was low overall (n = 7, 6.8%) and was not associated with failure to respond to WhatsApp prompts.

CONCLUSION: In this high-incidence setting, enrolment in a WhatsApp-based communication intervention among adults with presumptive TB was low, mainly due to low availability of WhatsApp-compatible phones. Among participants, we observed high message response rates and low LTFU, suggesting potential for interactive messaging services to support pre-diagnosis TB care.

KEY WORDS: tuberculosis; digital health tools; loss to follow-up; WhatsApp; South Africa

Strengthening the TB care cascade, particularly in countries and settings with a high burden of disease, remains crucial to ensure progress towards the milestones and targets of the WHO's Global End TB Strategy.[1] Reviews of the TB care cascade in India[2] and South Africa[3] have highlighted considerable losses from TB care in adults who had accessed TB diagnostic testing but had not yet started anti-TB treatment. Loss to follow-up (LTFU) during pre-treatment TB care has been attributed to health system barriers and patient-related challenges to engaging in care; improving the quality of healthcare provider and patient interaction may therefore be important to prevent these losses.[4]

Novel digital health information and communication tools provide exciting opportunities to overcome health system barriers and strengthen communication between healthcare providers and persons with TB.[5] Digital health tools investigated for TB care have focused on the support of adherence to TB treatment, including those enabling short message services (SMS) as reminders,[6] video-observed therapy[7] and medication monitors.[8,9] Evidence for such tools to improve individual patient outcomes remains limited.[9,10] Interactive (two-way) communication strategies that allow patients to respond to reminders and prompts appear to be superior to one-way messaging in improving medication adherence, but have rarely been considered for TB care.[11] A recent trial of an interactive digital health platform for TB patients showed significant improvement in treatment outcomes compared to standard of care, suggesting potential for such interactive strategies to support TB care.[12]

To date, most studies of digital health technologies have focused on interventions during treatment; few have investigated the effect of using such technologies to reduce delays in treatment initiation and pre-treatment LTFU. A recent study in Cape Town, South Africa, yielded promising results for one-way SMS reminders to reduce pre-treatment LTFU among individuals with presumptive TB.[13] Similar studies are currently under way.[14,15] It is currently not known whether two-way (interactive) communication interventions are feasible and effective in reducing pre-treatment LTFU from TB care.

In this study, we made use of WhatsApp (WhatsApp Ireland Ltd, Dublin, Ireland), an interactive messaging platform that is considered a simple, inexpensive and effective tool for communication in the health sector.[16] It has previously been used in various contexts, for example, as a telemedicine tool for medical imaging,[17] to improve medication adherence,[18] to support long-distance learning,[19] and patient consultation and support.[19,20]

We piloted a WhatsApp-based interactive communication strategy among individuals with presumptive TB attending two primary healthcare clinics in a high-incidence setting situated in Cape Town, South Africa. We aimed to investigate the uptake and usage of this intervention as a means to avert LTFU during the TB diagnostic period. We also aimed to investigate whether failure to respond to WhatsApp prompts was associated with pre-diagnosis LTFU.

METHODS

Study context and setting

This study was embedded in the LinkedIn study, a large intervention study currently being conducted in three South African provinces. The LinkedIn study aims at investigating the effect of a hospital-based TB notification system and a community-level patient management system as a means to improve linkage to care among individuals diagnosed with TB.

We conducted the present study in two primary health care facilities in Khayelitsha, Cape Town, a community with a high burden of TB and HIV. Individuals evaluated for TB are routinely scheduled to return to the clinic 2 days after their initial diagnostic visit, to receive test results and to initiate TB treatment if diagnosed with TB. Preliminary review of routine programme data in this setting indicated considerable delays and LTFU during diagnostic evaluation for TB.

Study design

We prospectively enrolled adults who underwent routine sputum testing for TB between September and December 2019. Individuals were eligible if they were aged ≥18 years, literate (i.e., able to read and respond to text messages), in possession of a WhatsApp-compatible phone, and either already had the application installed and in use or were willing to install and use WhatsApp for the purpose of this study. Individuals were enrolled after providing written informed consent. Participants were offered technical assistance to download and install WhatsApp on their personal phone using the Wi-Fi network provided at the clinic (as needed) and underwent training about the components and procedures of and participation in the intervention. We conducted a baseline survey which included collection of sociodemographic and socio-economic data, TB treatment history, healthcare seeking and mobile phone use. Participants were invited to a WhatsApp chat used for two-way communication between patients and a study team dedicated to support retention in TB care.

The intervention consisted of three components: we sent three structured WhatsApp-based prompts on the day of the initial (diagnostic) visit, the day prior to and the day of the routine follow-up appointment, scheduled 2–3 days after the diagnostic visit (Component 1). WhatsApp prompts included reminders of the appointment data and time at the clinic; participants were requested to respond to either confirm or reschedule their appointment. Those deciding to reschedule were provided further additional information how to contact the clinic to reschedule. At recruitment, participants were invited to appoint a close contact (e.g., a family member or a close friend) to be included in the WhatsApp chat for three-way communication (Component 2). Contacts of participants received information about the study and were invited to use the chat to send additional reminders. Participants who were missing a scheduled clinic appointment were alerted and advised to receive a phone call for re-scheduling and to provide location information (Component 3). Messages were sent in the participants' language of choice which included Xhosa, Afrikaans and English. Message history, including time stamps, were recorded for analysis. Attendance at the scheduled follow-up appointment was verified through in-person daily monitoring by the study team.

Data analysis

We described characteristics of study participants, as well as the uptake and use of the intervention by participants and designated close contacts. We documented the extent to which participants responded to WhatsApp prompts received. In addition, we conducted a cross-sectional analysis to investigate whether failure to respond to WhatsApp prompts was associated with pre-diagnosis LTFU. We distinguished individuals who responded at least once to WhatsApp prompts and those who did not respond at all. The main outcome for this study, pre-diagnosis LTFU, was dedicated to individuals who failed to attend their scheduled appointment and who did not return to the clinic within the following 10 days to collect their TB test results. We used non-parametric test statistics (Wilcoxon rank sum test at alpha = 0.05 significance level) to assess the association between message response and LTFU.

Ethics

The study was approved by the Health Research Ethics Committee of Stellenbosch University, Cape Town (N18/07/069), as part of the LinkedIn study and by the City of Cape Town Health Directorate,
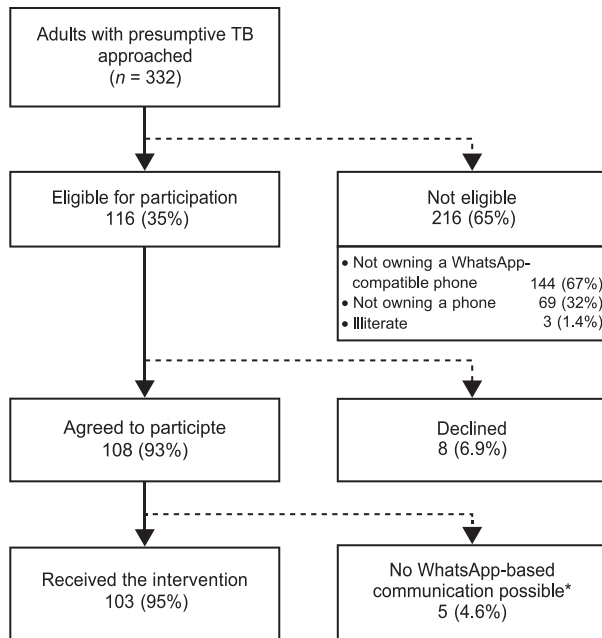
Figure 1 Overview of the study sample. * Individuals provided phone numbers that were not recognised by WhatsApp.

Cape Town, South Africa (study ID number 8053). All participants provided written informed consent for participation in the study.

RESULTS

Overview and characteristics of the study population

We approached a total of 332 adults with presumptive TB, of whom 116 (35%) were eligible for participation, and 103 (31%) were successfully enrolled. Of the 216 adults not eligible, 144 (67%) reported that they did not own a WhatsApp-compatible phone, 69 (32%) reported that they did

not own a phone at all, and 3 (1.4%) were illiterate. Of the 13 adults eligible but not enrolled, 8 declined participation and for 5 WhatsApp communication failed. A full breakdown of individuals included in the study is shown in Figure 1. Participation decreased with age (Figure 2); it was the highest among individuals less than 30 years of age (33/56, 59%).

Participants were younger (median age: 36 vs. 47 years) and more often female (58% vs. 38%) than individuals who were not eligible or who declined to participate. The majority of participants had completed secondary education (83/103, 81%); 42 (41%) were unemployed or informally employed. Forty-one (40%) reported to be living with HIV; 33 (32%) had a history of previous TB treatment. The majority had felt unwell when presenting to the clinic ($n = 76$, 74%). Additional characteristics of the participants recorded at the baseline survey are shown in Tables 1 and 2.

Use of the intervention

WhatsApp chat histories for six of the 103 participants were lost due to a technical issue. While all participants received WhatsApp reminders, 74/97 (76%) actively responded to prompts at least once. Nine (9.3%) stated that they would like to reschedule their appointment. Two-third of participants (69/103, 67%) appointed a close contact for three-way communication, of whom 18 (26%) actively engaged in conversation; the most common contacts were spouses and siblings (Table 2). No responses to alert messages were recorded among individuals who had missed their appointment. Timelines of WhatsApp messages in relation to the appointment date are shown in Figure 3.
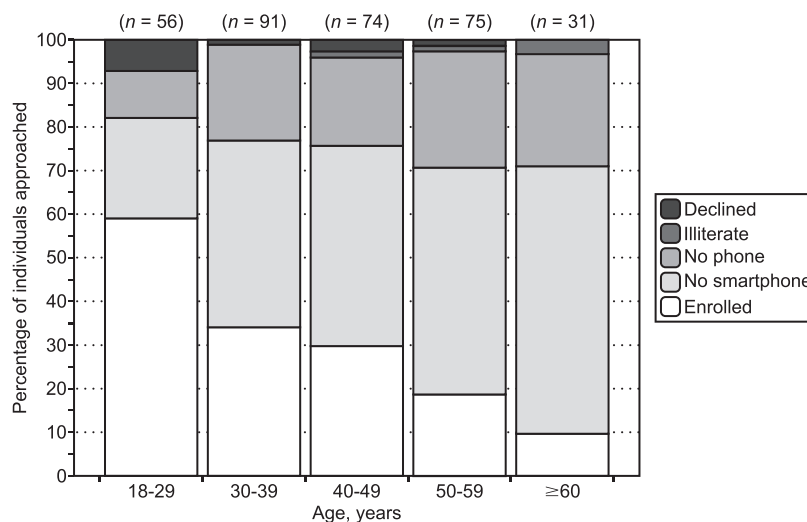

Figure 2 Participation rates and reasons for non-enrolment by age group. Five individuals who consented to participate but provided phone numbers not recognised by WhatsApp were excluded.

Table 1 General characteristics of participants (self-reported; $n = 103$)

Variable	Categories	n	%
Total		103	100.0
Sex	Female	59	57.3
	Male	44	42.7
Age, years	18–29	33	32.0
	30–39	31	30.1
	40–49	22	21.4
	50–59	14	13.6
	≥60	3	2.9
Education	Primary	4	3.9
	Secondary	83	80.6
	College/university	15	14.6
	Not stated	1	1.0
Employment	Unemployed	28	27.2
	Informal	14	13.6
	Formal	52	50.5
	Student	6	5.8
	Not stated	3	2.9
HIV status	Negative	59	57.3
	Positive	41	39.8
	Unknown/not stated	3	2.9
History of previous TB treatment	No	70	68.0
	Yes	33	32.0
Anyone with TB in the household?	No	92	89.3
	Yes	7	6.8
	Unknown/not stated	4	3.9
TB symptoms: cough	No	16	15.5
	Yes, <2 weeks	31	30.1
	Yes, ≥2 weeks	56	54.4
TB symptoms: any one of fever, night sweats, weight loss	No	17	16.5
	Yes	86	83.5
TB symptoms: any one of cough (any duration) fever, night sweats, weight loss	No	3	2.9
	Yes	100	97.1
Reason for presentation at the clinic	Felt unwell	76	73.8
	Accompanied someone else who felt unwell	2	1.9
	Referred from another facility	3	2.9
	Planned/scheduled visit	20	19.4
	Other/not stated	2	1.9

Table 2 Mobile phone intervention-related characteristics in participants ($n = 103$)

Variable	Categories	n	%
How interested are you in knowing your TB test result?	Very interested	88	85.4
	Rather interested	11	10.7
	Ambivalent	1	1.0
	Not stated	3	2.9
How likely do you think you have TB?	Very likely	6	5.8
	Likely	68	66.0
	Somewhat likely	13	12.6
	Unlikely	15	14.6
	Very unlikely	1	1.0
Phone ownership	Own	92	89.3
	Shared	11	10.7
How much airtime data do you spend per month?	<ZAR10	2	1.9
	ZAR10–ZAR49	32	31.1
	ZAR50–ZAR99	36	35.0
	≥ZAR100	27	26.2
	Not disclosed	6	5.8
Willing to receive diagnostic test results via WhatsApp	No	9	8.7
	Yes	94	91.3
How likely will you respond to WhatsApp reminders sent by the research team?	Very likely	16	15.5
	Likely	87	84.5
	Somewhat likely	0	0.0
	Unlikely	0	0.0
	Very unlikely	0	0.0
Close contact appointed to join WhatsApp group to receive reminders	None	34	33.0
	Spouse	22	21.4
	Parent	4	3.9
	Daughter or son	13	12.6
	Sibling	20	19.4
	Other relative	4	3.9
	Friend	6	5.8

ZAR = South African rand.

Pre-diagnosis loss to follow-up

Of the 103 participants, 73 (70.9%) returned on (or before) the day of the scheduled appointment; 23 (22.3%) returned within 10 days and seven (6.8%) were lost to follow-up (Figure 4). We did not find any association between failure to respond to WhatsApp prompts and LTFU (Table 3). One (4.4%) of 23 individuals who did not respond was lost to follow-up vs. five (6.8%) of 74 who responded at least once
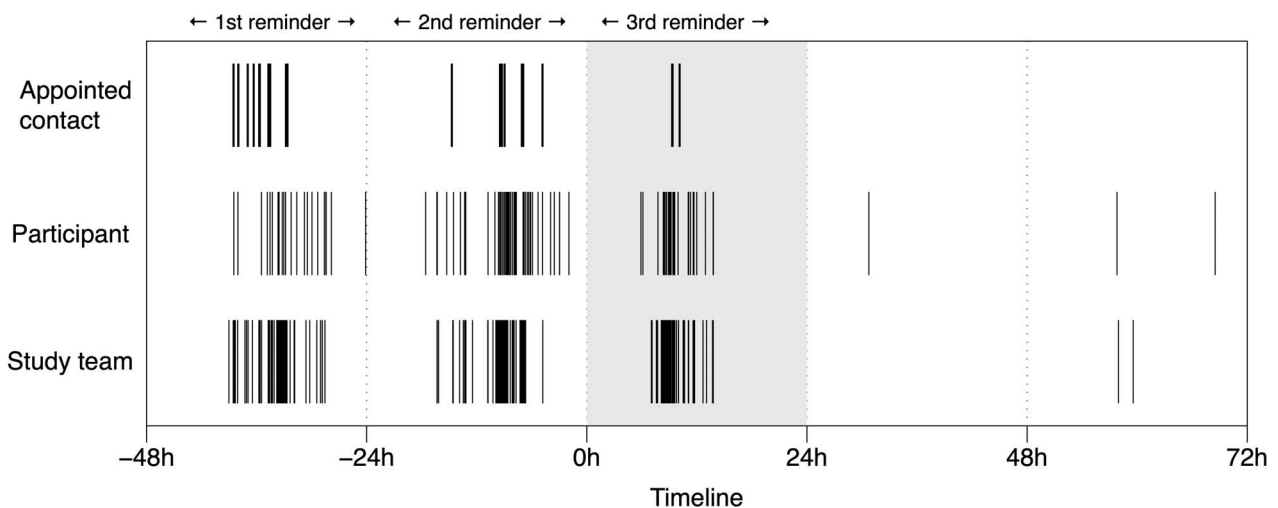

Figure 3 Timeline of interactive study messages sent via WhatsApp by the study team, participants and appointed contacts. The day of the scheduled clinic appointment is shaded in grey.
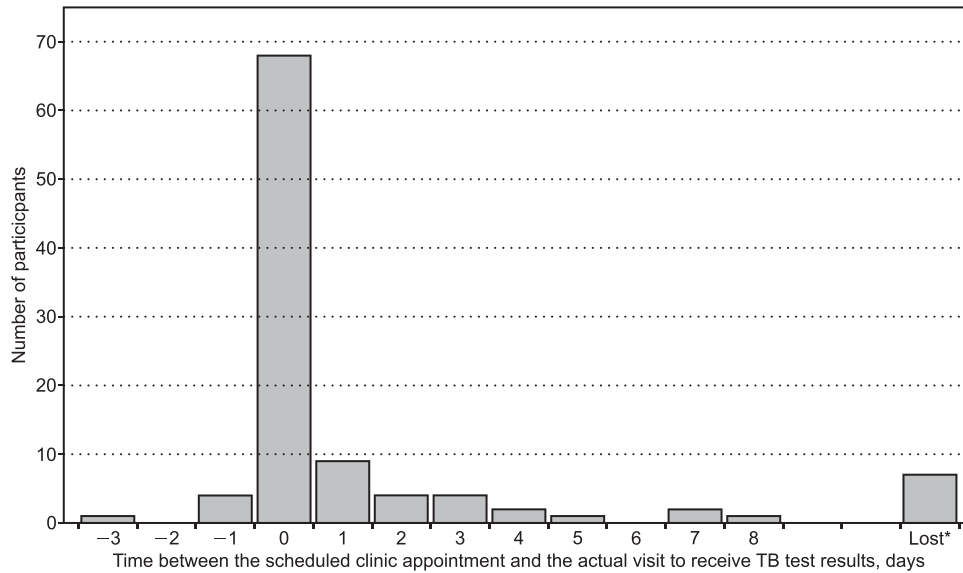
Figure 4 Timeliness to return for scheduled clinic appointments among 103 adults with presumptive TB who participated in the study; negative days refer to individuals who returned to the clinic earlier/prior to their scheduled appointment. * Includes individuals with a delay of more than 10 days or no attendance at all.

($P = 0.68$). Four of the seven individuals who were lost to follow-up responded that they were planning to reschedule, three had left the WhatsApp group early.

DISCUSSION

In this study, we piloted a WhatsApp-based interactive communication intervention among adults with presumptive TB awaiting their sputum test results in a high-incidence setting.

We found that only about one-third of adults with presumptive TB attending primary healthcare participated in the study. Uptake was low, particularly among older adults, because many did not own a WhatsApp-compatible phone. Our findings are consistent with a recent study of mobile phone use among patients receiving TB and HIV care in Pune, India, and Matlosana, South Africa, which showed that, although most patients had access to a phone, the majority owned conventional phones without smartphone capabilities.[21] Limited availability of suitable phones, inability to afford airtime,[21,22] and limited internet coverage[23] therefore temper enthusiasm about more wide-scale use of WhatsApp or other web-based phone applications, including for TB prevention and care.

Among the mostly younger study participants, we found that the intervention was well-received and well-utilised, with 80% responding to reminders and prompts, two-third involving family members or friends in three-way communication, about one-fourth of whom actively participated in communication. At the baseline survey and during WhatsApp communication, a large majority expressed an interest in receiving diagnostic results on their phone, suggesting that instant, interactive messaging tools could deliver health-related (diagnostic) information and thereby, further reduce delays in treatment initiation. However, a lack of standards about the safe use of instant messaging services for healthcare delivery[24] and data protection concerns, particularly for WhatsApp,[25] represent potential barriers at present.

We observed low pre-diagnosis LTFU, with 93% of participants either attending their scheduled clinic appointment (71%) or returning shortly after to receive their test results. Clinic attendance was higher than in a recent pragmatic trial of SMS-based reminders and prompts conducted in a similar setting,

Table 3 Response to WhatsApp prompts and appointment attendance

| Response to WhatsApp prompts | Attendance of follow-up appointment | | | |
	As scheduled n (%)	Delayed (1–10 days) n (%)	Lost to follow-up n (%)	Total n (%)
No response	16 (69.6)	6 (26.1)	1 (4.4)	23 (100)
At least 1 response	52 (70.3)	17 (23.0)	5 (6.8)	74 (100)
Missing*	5 (83.3)	0 (0)	1 (16.7)	6 (100)
Total	73 (70.9)	23 (22.3)	7 (6.8)	103 (100)

* WhatsApp chat histories for 6 participants were lost due to a technical problem.

which found that 62% of SMS recipients returned to the clinic to receive TB test results.[13] Although we did not formally assess the effect of the intervention, the high retention observed and the positive feedback received from several participants suggest that WhatsApp-based interactive messaging could effectively be used to support retention in pre-treatment TB care. We did not find evidence that LTFU was associated with failure to respond to WhatsApp messages; retention was high, regardless of whether or not participants responded. Four of the seven individuals lost to follow-up had messaged that they were intending to re-schedule their follow-up appointment, suggesting that more rigorous follow-up with those intending to reschedule might help prevent losses.

To our knowledge, our study is the first to pilot a WhatsApp-based interactive communication strategy to support retention in pre-treatment TB care. We conducted this study to generate preliminary data and knowledge about the delivery of a mobile communication intervention dedicated to support the retention in pre-treatment TB care – information that can be useful for the design of future interventions to strengthen TB services. We note the following limitations.

The design of our study did not enable us to determine the effect of the intervention, i.e., to what extent high retention rates observed were attributable to the intervention itself. Selection bias at recruitment could have contributed to higher retention if individuals participating in the study represented those more likely to attend their follow-up appointments. In addition, awareness among clinic staff and patients of being involved in the study might have led to more rigorous follow up and higher retention rates (Hawthorne effect).

Our study was limited to the diagnostic period; we were unable to determine whether participants further remained in TB care if diagnosed with TB. Ideally, interactive communication between care providers and patients could extend to the post-diagnosis/pre-treatment and treatment period, to support those suffering from TB throughout the care cascade.

Logistical constraints precluded systematic follow-up with participants after the intervention to obtain detailed and representative feedback. A post-intervention survey shared with a subset of participants suggested that the intervention was perceived positively, but numbers were insufficient to conduct formal analysis.

Involving contacts into WhatsApp reminders and prompts was commonly utilised among participants, suggesting a role for three-way communication to support retention in care. However, we were unable to determine the incremental benefit of involving contacts as opposed to sending reminders and prompts to the participants alone.

In conclusion, we show that in this high-incidence setting, uptake of a WhatsApp-based communication intervention among individuals with presumptive TB was low, mainly due to the lack of WhatsApp-compatible phones. However, among participants, we observed high uptake and utilisation of the intervention, and high retention in TB care. Higher participation rates among younger adults (Figure 2; 59% among participants aged <30 years) suggest that this intervention could support efforts to strengthen linkage to TB care particularly among youth and young adults. Additional research is needed to understand whether mobile interactive messaging services, including WhatsApp, could be leveraged to strengthen the TB care cascade in high-incidence settings. Formal evaluation of interventions to determine the effectiveness of this approach are warranted. Rather than isolated interventions, a platform that integrates interactive reminders, one-way text messages, phone calls, social and clinic-based support and more rigorous follow-up of individuals throughout the care cascade could help to strengthen provider-patient interaction, linkage to and the completion of TB care.

References

1 Uplekar M, et al. WHO's new end TB strategy. Lancet 2015; 385(9979): 1799–1801.

2 Subbaraman R, et al. The tuberculosis cascade of care in India's public sector: a systematic review and meta-analysis. PLoS Med 2016; 13(10): e1002149.

3 Naidoo P, et al. The South African tuberculosis care cascade: estimated losses and methodological challenges. J Infect Dis 2017; 216(suppl_7): S702–S713.

4 Thomas BE, et al. Understanding pretreatment loss to follow-up of tuberculosis patients: an explanatory qualitative study in Chennai, India. BMJ Global Health 2020; 5(2): e001974.

5 Falzon D, et al. Digital health for the End TB Strategy: developing priority products and making them work. Eur Respir J 2016; 48(1): 29–45.

6 Musiimenta A, et al. Digital monitoring technologies could enhance tuberculosis medication adherence in Uganda: mixed methods study. J Clin Tuberc Other Mycobact Dis 2019; 17: 100119.

7 Ravenscroft L, et al. Video-observed therapy and medication adherence for tuberculosis patients: randomised controlled trial in Moldova. Eur Respir J 2020; 56(2): 2000493.

8 Lee Y, Raviglione MC, Flahault A. Use of digital technology to enhance tuberculosis control: scoping review. J Med Internet Res 2020; 22(2): e15727.

9 Ngwatu BK, et al. The impact of digital health technologies on tuberculosis treatment: a systematic review. Eur Respir J 2018; 51(1): 1701596.

10 Nsengiyumva NP, et al. Evaluating the potential costs and impact of digital health technologies for tuberculosis treatment support. Eur Respir J 2018; 52(5): 1801363.

11 Wald DS, Butt S, Bestwick JP. One-way versus two-way text messaging on improving medication adherence: meta-analysis of randomized trials. Am J Med 2015; 128(10): 1139 e1-5.

12 Yoeli E, et al. Digital Health Support in Treatment for Tuberculosis. N Engl J Med 2019; 381(10): 986–987.

13 Wagstaff A, van Doorslaer E, Burger R. SMS nudges as a tool to reduce tuberculosis treatment delay and pretreatment loss to follow-up. A randomized controlled trial. PLoS One 2019; 14(6): e0218527.

14 Mwansa-Kambafwile JRM, et al. Initial loss to follow up among tuberculosis patients: the role of ward-based outreach teams and short message service (SMS) technology (research proposal). BMC Res Notes 2019; 12(1): 737.

15 Maraba N, et al. Using mHealth to improve tuberculosis case identification and treatment initiation in South Africa: Results from a pilot study. PLoS One 2018; 13(7): e0199687.

16 Mars M, Scott RE. WhatsApp in clinical practice: a literature review. Stud Health Technol Inform 2016; 231: 82–90.

17 Giansanti D. WhatsApp in mHealth: an overview on the potentialities and the opportunities in medical imaging. Mhealth 2020; 6: 19.

18 Sartori AC, et al. Educational intervention using WhatsApp on medication adherence in hypertension and diabetes patients: a randomized clinical trial. Telemed J E Health 2020; 26(12): 1526–1532.

19 Woods J, Moorhouse M, Knight L. A descriptive analysis of the role of a WhatsApp clinical discussion group as a forum for continuing medical education in the management of complicated HIV and TB clinical cases in a group of doctors in the Eastern Cape, South Africa. South Afr J HIV Med 2019; 20(1): 982.

20 Rozenberg G, et al. Standard pre-travel consultation versus shorter consultation combined with smartphone support: a randomized controlled trial. J Travel Med 2019; 26(3): taz025.

21 Cox SN, et al. Mobile phone access and comfort: implications for HIV and tuberculosis care in India and South Africa. Int J Tuberc Lung Dis 2019; 23(7): 865–872.

22 Anstey Watkins JOT, et al. Mobile phone use among patients and health workers to enhance primary healthcare: a qualitative study in rural South Africa. Soc Sci Med 2018; 198: 139–147.

23 Kubheka BZ, Carter V, Mwaura J. Social media health promotion in South Africa: Opportunities and challenges. Afr J Prim Health Care Family Med 2020; 12(1): e1–e7.

24 Mars M, Morris C, Scott RE. WhatsApp guidelines - what guidelines? A literature review. J Telemed Telecare 2019; 25(9): 524–529.

25 Masoni M, Guelfi MR. WhatsApp and other messaging apps in medicine: opportunities and risks. Intern Emerg Med 2020; 15(2): 171–173.

RÉSUMÉ

OBJECTIF : Évaluer la mise en place et l'utilisation d'une stratégie de communication interactive par WhatsApp pour prévenir la perte de vue des patients (LTFU) avant diagnostic en centres de prise en charge de la TB dans un pays à forte incidence.

MÉTHODES : Nous avons sélectionné des adultes (≥18 ans) ayant subi un test de dépistage de routine de la TB par examen des expectorations dans deux cliniques de soins primaires de Khayelitsha, Le Cap, Afrique du Sud. L'intervention consistait en des rappels WhatsApp structurés (relances) envoyés avant une consultation de routine à la clinique prévue 2 à 3 jours après la consultation ayant établi le diagnostic. La LTFU pré-diagnostic a été définie comme la non-présentation à la consultation programmée ainsi que dans les 10 jours suivant.

RÉSULTATS : Nous avons contacté 332 adultes suspects de TB, dont 103 (31%) ont été inclus dans l'étude et 213 (64%) ne possédaient pas de téléphone compatible avec l'utilisation de WhatsApp. Sur 103 participants, 74 (72%) ont activement répondu aux relances WhatsApp et 69 (67%) ont choisi d'inclure un contact étroit dans les communications du groupe afin de co-recevoir les rappels. La LTFU pré-diagnostic était globalement faible ($n = 7$; 6,8%) et n'a pas été associée à l'échec de réponse aux relances WhatsApp.

CONCLUSION : Dans ce pays à forte incidence, l'inclusion d'adultes suspects de TB dans une intervention sous forme de communications par WhatsApp était faible, principalement due à la faible disponibilité de téléphones compatibles avec l'utilisation de WhatsApp. Parmi les participants, nous avons observé un taux élevé de réponse aux messages et une faible LTFU. Cela suggère qu'il serait possible de mettre en place des services de messagerie interactive pour consolider la prise en charge de la TB avant diagnostic.