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ORIGINAL ARTICLE
TUBERCULOSIS

The impact of digital health technologies on tuberculosis treatment: a systematic review

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Digital technologies are being used to support TB treatment adherence, but evidence for their impact needs to improve http://ow.ly/1riC30h6hu3

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ABSTRACT Digital technologies are increasingly harnessed to support treatment of persons with tuberculosis (TB). Since in-person directly observed treatment (DOT) can be resource intensive and challenging to implement, these technologies may have the potential to improve adherence and clinical outcomes. We reviewed the effect of these technologies on TB treatment adherence and patient outcomes.

We searched several bibliographical databases for studies reporting the effect of digital interventions, including short message service (SMS), video-observed therapy (VOT) and medication monitors (MMs), to support treatment for active TB. Only studies with a control group and which reported effect estimates were included.

Four trials showed no statistically significant effect on treatment completion when SMS was added to standard care. Two observational studies of VOT reported comparable treatment completion rates when compared with in-person DOT. MMs increased the probability of cure (RR 2.3, 95% CI 1.6–3.4) in one observational study, and one trial reported a statistically significant reduction in missed treatment doses relative to standard care (adjusted means ratio 0.58, 95% CI 0.42–0.79).

Evidence of the effect of digital technologies to improve TB care remains limited. More studies of better quality are needed to determine how such technologies can enhance programme performance.

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Introduction

Digital technologies are changing healthcare delivery globally, as witnessed by the dramatic growth in such areas as electronic health records, telehealth for "virtual" patient encounters, and teleradiology for remote interpretation of imaging studies [1]. There is also increasing recognition that digital technologies can support medication adherence. Examples include the use of video phone calls for observation of medication ingestion, and for live discussion of any problems or concerns; the use of short message service ((SMS), *i.e.* text messaging) for ongoing communication between patients and providers; and the use of SMS or electronic medication monitors (MMs) for automatic reminders, and/or for real-time monitoring of medication self-administration which is then fed back to providers. MMs most commonly take the form of "smart" pill bottles, which can keep track of pill counts and bottle openings, and transmit adherence reports to treating health professionals [2–4].

Digital treatment support can lead to better treatment results in patients with chronic diseases, such as diabetes [5–7]. As with tuberculosis (TB), these chronic conditions require long-term commitment to treatment by patients and caregivers. Several systematic reviews aimed at measuring the effectiveness of mobile communication technologies, such as SMS, have also documented improved adherence to antiretroviral treatment [8], and higher rates of smoking cessation [9]. Other studies evaluating SMS-based interventions in maternal–child health services [10, 11] found improved contraceptive pill adherence [12] and higher proportions of deliveries by trained personnel [13].

Suboptimal adherence to TB treatment is common, with a global treatment success rate of 75% for new and relapse TB cases in 2014 [14], despite long-standing support for strategies such as direct observation to help patients complete their treatment[15]. While barriers to adherence have been much researched, there has been little progress in lessening treatment burden by mitigating frequent adverse reactions, or substantially shortening the duration of current regimens; minimum 6 months for drug-susceptible TB (DS-TB) and typically 18 months or more for rifampicin-resistant TB (RR-TB). Globally, the treatment success rate for RR-TB is approximately 50%; about one in seven RR-TB patients is lost to follow-up during treatment [14]. It is highly relevant to identify which programmatic solutions could contribute to improved TB treatment adherence, and ultimately lead to better patient outcomes.

For example, enhanced communication *via* SMS or video calls could strengthen relationships between patients, families and healthcare providers, and promote retention in care as well as treatment adherence. Early detection of missed treatment doses (*e.g.* by electronic MMs) could allow healthcare workers to address any patient concerns or barriers, to suggest specific steps to improve adherence, and to mitigate potential loss to follow-up. Similarly, early signalling to healthcare providers of potential drug side-effects could allow for treatment changes and/or effective symptomatic management.

The use of digital health applications to improve treatment support for active TB patients also appeals to TB programme managers, because of affordable mobile electronic devices in many settings. The potential of these technologies to support patient-centred interventions, a key element of the End TB Strategy, has been recognised in recent years by the World Health Organization (WHO) [16–18].

Digital interventions are gradually being integrated into practice, and are tested and evaluated in field trials focused specifically on TB prevention and care [19]. SMS and other technologies which can communicate *via* cellular or internet networks, such as video-observed therapy (VOT) and the Medication Event Monitoring System and other electronic medication monitors (MMs), are being employed. For example, VOT was first used for TB in 2007 in several clinical programmes in London, UK, as an alternative to in-person treatment observation [20]; it has also been evaluated in studies in Australia, the USA and Mexico [21–23].

Although several evaluations involving TB patients have now been completed, a comprehensive review of the role of digital technologies in improving TB care has not been performed. We reviewed the published literature to determine whether digital technologies were effective at improving TB treatment adherence, and treatment outcomes (*e.g.* completion, cure, loss to follow-up) as defined by the WHO [24].

Methods

Cochrane guidelines for systematic reviews of interventions were followed [25].

Search strategy

In July 2016, using search terms to denote TB disease, digital technologies and TB treatment outcomes, we searched for relevant studies from the following bibliographical databases: MEDLINE/PubMed, EMBASE, Cochrane Library of Trials, and Web of Science, as well as clinicaltrials.gov and *Journal of Global Health*, *Journal of Telemedicine and Telecare* and the *Journal of Telemedicine and e-Health*. WHO databases and reports were also searched. Given the dearth of published studies, we included unpublished literature when

full results had been provided to the WHO and were available from its databases. The complete list of search terms is provided in supplementary table S1. We set no restrictions in terms of language or publication dates.

Study selection; inclusion and exclusion criteria

After the preliminary search, two authors (B.K. Ngwatu and N.P. Nsengiyumva) independently screened all titles and abstracts for eligibility. Upon initial review, any studies not related to digital health interventions for TB treatment support were excluded.

We then conducted a detailed review of the remaining abstracts and full text articles. Specifically, we included studies that reported on digital health technology interventions supporting active TB treatment, such as SMS reminders, VOT and MMs, and compared them to the local standard of care as defined by the authors, with no additional specific intervention.

We included randomised controlled trials (RCTs) and observational studies, if they had a control group and reported the effect of digital technologies on adherence to treatment or appointments, and/or any of the following standard TB treatment outcomes: cure, treatment success (cure or treatment completed) [24], loss to follow-up from treatment, or a combination of unfavourable outcomes, including death, failure and/or loss to follow-up.

We excluded studies that did not report an estimate of effect related to the intervention, and those that did not report a study end-point of relevance to our review's objective (*i.e.* those that only reported TB incidence, number of secondary TB cases, costs for patients and services, patient acceptability and feasibility). We excluded reports that only described study protocols, those where only an abstract was available, letters, editorials and position papers. If the same study was reported in different publications, we considered only the most recent publication.

Data extraction

Two reviewers (B.K. Ngwatu and N.P. Nsengiyumva) extracted data from relevant articles into a standardised template, with the following information: authors, study design, method/description (title, aim, primary and secondary outcomes and duration of study), publication year, country, target population characteristics (numbers, age and sex distribution, smear status), type of digital health intervention, comparator (DOT, or no specific intervention) and measures of effect (means ratios, risk ratios, or odds ratios with respective confidence intervals). Data were then reviewed and discussed with additional reviewers (O. Oxlade, K. Schwartzman, D. Falzon and B. Mappin-Kasirer).

Quality assessment of studies

We assessed the risk of bias in the RCTs using the Cochrane risk-of-bias 2.0 (RoB 2.0) tool [26] and reported on selection bias, performance bias, detection bias, attrition bias and reporting bias. For each feature of interest, three scores were used: low risk, high risk and unclear risk.

Selection bias in RCTs was assessed by examining whether proper sequence generation and concealment of allocation sequence were carried out. Performance bias was evaluated by reviewing the blinding of participants and/or investigators administering the interventions. Detection/outcome measurement bias was assessed by reviewing who was aware of the intervention received by study participants. Bias due to attrition or incomplete or missing outcome data was evaluated by looking at whether outcome data was available for all, or nearly all, participants. Reporting bias was assessed by the extent to which the authors appeared to report their results in the way they had originally proposed in their protocols.

For observational studies, we adapted the ROBINS-I (risk of bias in non-randomised studies of interventions) tool [27] to assess selection bias, bias due to confounding, bias due to missing data, and bias in measurement of outcomes. We used the same scoring system as for RCTs.

Results

Study selection

Our search initially identified 342 studies (figure 1). Screening of titles yielded 57 (17%) relevant studies after eliminating 24 duplicates, 33 studies were retained.

Excluded studies

After screening the 33 abstracts, nine studies (27%) were excluded: two study protocols, two systematic reviews, three ongoing studies, and two feasibility studies (a microchip system with an ingestible sensor, and a voice call based reminder system for adherence).

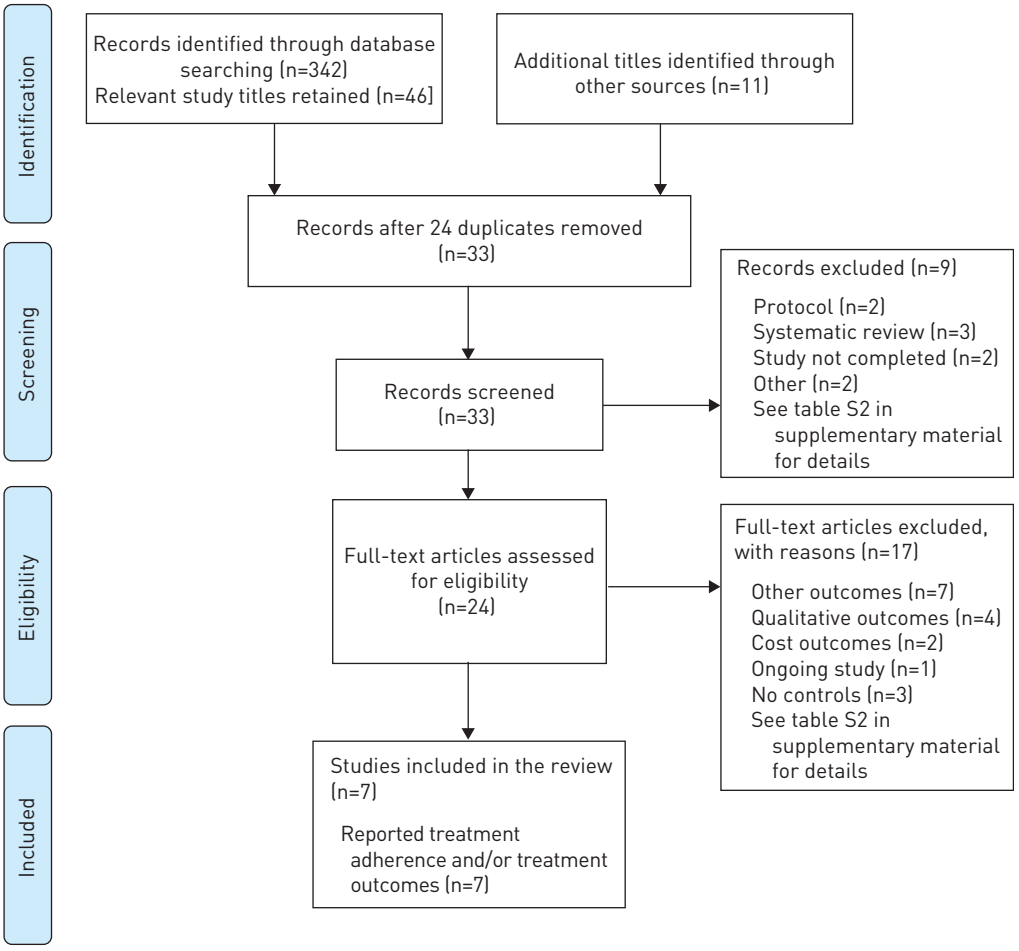

FIGURE 1 PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram for selection of studies.

After full-text review of the 24 articles, 17 (71%) were excluded: seven used end-points that differed from our primary end-points of interest, three had no control group, four reported only qualitative outcomes, two focused only on costs, and one was an ongoing study.

Details of the excluded studies are provided in supplementary table S2.

Included studies

Ultimately, seven studies were retained: three observational studies and four RCTs. All seven had a control group and provided estimates of effect: one evaluated MMs [28], three evaluated SMS reminders [29–31], two examined VOT [22, 23] and one examined the combination of SMS and MM [32]. The studies were carried out in seven geographically diverse settings: Argentina, Australia, Cameroon, China, Pakistan, South Africa and the USA [22, 23, 28–32]. Details of these seven studies, including details of the intervention evaluated, are listed in table 1.

Findings

Detailed results for each intervention studied are shown in table 2. Treatment adherence is reported as described in the articles. Most often it was based on the number of expected doses actually taken, but sometimes on the retention of patients during the study period.

MM

A South African pilot study reported a risk ratio of 2.3 (95% CI 1.6–3.4) [28] for improvement in cure rates, but the comparison group was a historical, non-concurrent control group. This study also suggested significant improvement in smear conversion at 2 months, with risk ratio 1.62 (95% CI 1.09–2.42), although again the control group was historical (non-concurrent). A larger RCT in China reported a statistically

TABLE 1 Details of studies included in this systematic literature review

Digital intervention	Objective	Method/ study design/ location	Subjects n	Intervention	Standard of care in control arm
Electronic medication monitors					
Broomhead [28]	To evaluate cost implications and health outcomes of the implementation of SIMPill, in new smear-positive TB patients receiving TB medication	A single-arm trial, with retrospective analysis of data from TB patients (historic controls) at a clinic in Northern Cape Province, South Africa	120 participants (24 intervention, 96 in historic control arm), new smear-positive TB	SIMPill a pillbox which, when opened, sends an SMS to a server, indicating that the patient has taken their medication	DOT#
SMS reminders					
Bediang [31]	To evaluate the effectiveness of SMS reminders as an adjunct to DOT in improving TB treatment adherence and success.	Randomised, concealed, single-blinded controlled trial conducted at 12 TB treatment centres in Yaoundé, Cameroon	279 patients with active TB (137 in intervention group, 142 in control group)	One-way SMS; daily reminders for TB medication as adjunct to DOT	DOT#
Iribarren [29]	To evaluate the acceptance and feasibility of a patient-based text intervention to promote their adherence to TB treatment	Randomised, concealed non-blinded controlled trial, conducted within a specialised hospital in Buenos Aires, Argentina	37 newly diagnosed TB patients (18 in intervention group, 19 in control group)	Two-way SMS; patients were instructed to SMS the clinic after self-administration of medication as a proxy of adherence (they received reminders if they did not send a message)	SAT
Mohammed [30]	To measure the impact of a two-way SMS reminder system on TB treatment outcomes	Randomised, non-blinded controlled trial at TB treatment facilities in Karachi, Pakistan	2207 newly diagnosed TB patients (1110 in intervention arm, 1097 in control arm)	Two-way SMS; daily automated SMS reminders sent at prescheduled time Patient responds back *via* SMS or phone call	DOT#
Video-observed therapy					
Chuck [22]	To determine whether video technology for remote observation of patients on anti-TB treatment (VOT) is as effective as in-person DOT	Prospective cohort study 390 patients using DOT for TB treatment support, New York, USA	61 patients (16%) were assigned to VOT and 329 (84%) to in person DOT	VOT worker and patient pre-arranged a schedule for the VOT calls	DOT#
Wade [23]	To assess the effectiveness related to patient compliance, cost effectiveness, acceptability and sustainability of video-based DOT	A retrospective cohort design was used, recipients of VOT were compared to in-person-DOT recipients using data at a facility in Adelaide, South Australia	128 patients with active TB at the community nursing service (58 in intervention group, 70 in control group)	VOT; patients received daily video calls from the facility	DOT*

Continued

TABLE 1 Continued

Digital intervention	Objective	Method/ study design/ location	Subjects n	Intervention	Standard of care in control arm
SMS reminders, medication/ electronic monitors (evaluated alone or in combination)					
Liu [32]	To evaluate the effectiveness of text messaging and medication monitors in improving TB medication adherence	Cluster randomised trial (using stratification and restriction) conducted in four provinces in China	4173 TB patients (1104 control, 1008 SMS arm, 997 MM arm, 1064 combined SMS and MM)	Two-way SMS, MM or combination of two-way SMS and MM reminders on dose days to take medicine and to attend follow-up visits Physicians were advised to provide more active follow-up to patients with adherence issues	DOT[#] and MM without reminders

TB: tuberculosis; MM: medication monitor; SMS: short message service; DOT: directly observed treatment; SAT: self-administered treatment. [#]: patients on in-person DOT were defined as those who had doses of medication observed at a health department or hospital clinic or in the community, and did not receive the intervention being evaluated in the study. Depending on the study, some treatment doses in the "DOT" arm were, in fact, self-administered.

significant effect on adherence with a MM relative to standard care, with an adjusted means ratio of 0.58 for percentage of patient-months where at least 20% of doses were missed (95% CI 0.42–0.79) [32].

SMS

Four RCTs [29–32] evaluating SMS as medication reminders showed no statistically significant effect on treatment completion, when compared with the local standard of TB care. In three of these [23, 24, 26], the risk ratios for completion, success or cure ranged from 1.0–1.45, and the 95% CI fell within these values in all three trials. In the SMS arm of the fourth trial [25], compared to standard care the adjusted risk ratio for failure, death, and loss to follow-up combined was 0.44 (95% CI 0.17–1.13). In the same four studies, SMS reminders were found to have very little to no, impact on TB medication doses taken, with risk or means ratios approaching 1. Three of the four studies [23–25] employed two-way text messaging between patients and providers, while one study used one-way text reminders to patients [26].

VOT

One study in New York City (NY, USA) reported a risk ratio of 0.99 (95% CI 0.93–1.05) for treatment completion with VOT compared with in-person DOT, although it also reported a positive effect on appointment attendance (95% adherence to scheduled VOT sessions compared to 91% of scheduled DOT visits) [22]. Another study in Australia reported a higher proportion of observed treatment doses with VOT compared to in-person DOT, but the effect on treatment completion rates was not statistically significant [23]. In both studies, VOT substantially reduced the personnel time needed for treatment supervision. These studies used synchronous (videoconferencing) technology, which might have a different effect on adherence compared with asynchronous (recorded) VOT [21].

SMS and MM

The RCT in China [25] included an additional arm that combined both two-way SMS and MM used as medication dose reminders; there was potential synergy in that the adjusted means ratio for percentage of patient-months where at least 20% of doses were missed was 0.49 (95% CI 0.27–0.88). In that study, 14% of participants in the combined intervention arm missed 20% or more doses, compared to 30% in the control arm [32].

Assessment of methodological quality

Quality assessment and risk of bias in the randomised trials reviewed are shown in table 3. We found low selection bias, as all publications of randomised trials provided information about the processes of random sequence generation and/or allocation concealment in the studies. Overall, there was high bias of performance across the trials. Detection/outcome measurement bias was high for one trial since the

TABLE 2 Impact of digital health interventions on study outcomes: intervention *versus* control groups

First author [ref.]	Intervention	Subjects n control: intervention	Study outcome (definition)	Findings in control group/ standard care %	Findings in intervention group%	Measure of effect (95% CI)
Broomhead [28]	MM[#]	96:24	Smear conversion rate at 2nd month	38	63	RR: 1.62 (1.09–2.42)
			Cure rate: negative sputum smear in last month of treatment	32	75	RR: 2.32 (1.60–3.36)
Bediang [31]	SMS	142:137	Treatment success rate (assessed at 5th month)	75	81	RR: 1.45 (0.81–2.56)
			Cure rate	62	64	RR: 1.06 (0.65–1.73)
			Drop-out proportion, 6th month	32	34	RR: 1.08 (0.77–1.51)
Iribarren [29]	SMS	19:18	Adherence: self-reported adherence (booklets/ calendars *versus* SMS)[¶]	53	77	Not calculated[¶]
			Treatment success: cured or completed treatment	90	94	RR: 1.06 (0.87–1.28)
Mohammed [30]	SMS	1097:1110	Treatment success: cured or completed treatment	83	83	RR: 1 (0.96–1.04)
			Completed: completed treatment but does not have a negative smear	30	30	RR: 1 (0.79–1.26)
			Cure: sputum smear or culture-negative in the last month	53	53	RR: 1 (0.90–1.12)
Chuck [22]	VOT	329:61	Treatment completion	97	96	RR: 0.99 (0.93–1.05)
			Adherence: appointment compliance (visits attended)[+]	91	95	RR: 1.05 (1.04–1.06)
Wade [23]	VOT	70:58	Treatment completion	33	48	RR: 1.47 (0.96–2.25)
			Adherence: observed doses[§]	69	88	Not calculated[##]
Liu [32]	MM	1091:992	Non-adherence: months with at least 20% of doses missed[*f*]	30	17	aMR: 0.58 (0.42–0.79)
	SMS	1091:996	Non-adherence: months with at least 20% of doses missed[*f*]	30	27	aMR: 0.94 (0.71–1.24)
	MM and SMS	1091:1059	Non-adherence: months with at least 20% of doses missed[*f*]	30	14	aMR: 0.49 (0.27–0.88)
	MM	1066:955	Poor treatment outcome: failure, death and LTFU	9	6	aRR: 0.71 (0.33–1.51)
	SMS	1066:966	Poor treatment outcome: failure, death and LTFU	9	4	aRR: 0.44 (0.17–1.13)
	MM and SMS	1066:992	Poor treatment outcome: failure, death and LTFU	9	9	aRR: 1.00 (0.45–2.20)

MM: medication monitor; RR: risk ratio; SMS: short message service; VOT: video-observed therapy; aMR: adjusted means ratio; LTFU: loss to follow-up; aRR: adjusted risk ratio. [#]: historical control; [¶]: adherence comparison between the intervention and control groups is hampered by the fact that 47% of the calendars were not returned for analysis; [+]: 3292 (95%) out of 3455 sessions scheduled for patients on VOT were successfully attended, compared to 32 204 (91%) out of 35 442 among patients on in-person DOT; [§]: calculated using data provided in original text articles; [*f*]: mean of the percentage of patient-months on TB treatment where at least 20% of doses were missed; [##]: could not be calculated, as no risk ratios were reported in the article and absolute numbers were not provided.

assessors were aware of the intervention received by study participants, while in the remaining three trials it was unclear. Studies varied with respect to attrition bias. We found low reporting bias in three of the trials; we could not evaluate one of the trials as the trial protocol was not available. Further details of the quality assessment for the randomised trials are in supplementary table S3 and supplementary figures S1 and S2.

TABLE 3 Quality assessment/risk of bias of randomised trials included in the review

First author [ref.]	Selection bias	Performance bias	Detection bias	Attrition bias	Reporting bias
Bediang [31]	Low	High	High	Low	Low
Iribarren [29]	Low	High	Unclear	High	Unclear
Mohammed [30]	Low	High	Unclear	Low	Low
Liu [32]	Low	High	Unclear	Low	Low

Quality assessment and risk of bias in the observational studies is shown in table 4. Selection bias could not be assessed, but there was high risk of bias due to confounding in most studies as demographic characteristics, disease severity, socioeconomic status and other confounding factors were not evaluated or accounted for. Outcome measurement bias was also high since the assessors were aware of interventions received by study participants. Bias due to missing data varied. We could not evaluate reporting bias as the study protocols were not available.

Discussion

Digital health interventions are increasingly used to support TB treatment in diverse settings globally. Studies in this review suggest that some digital interventions can potentially improve medication adherence and patient outcomes. While evidence remains incomplete, and generalisability limited, the studies reviewed suggest these technologies may be at least as effective as the standard of care. Compared with direct in-person treatment observation, VOT and MM technologies may improve efficiency, save money and reduce burden on patients and healthcare workers. VOT used for treatment observation in London, UK, led to improved communication between patients and providers [20, 33]. Pilot single-arm VOT studies in the USA, Mexico and Belarus suggested that treatment outcomes were comparable to those with in-person DOT, with markedly reduced health system costs [21, 34]. These studies compared VOT to high-functioning DOT programmes; there was no difference in adherence, which suggests that comparably high adherence can be obtained using digital technologies for treatment support. In settings where digital solutions cost less and/or are easier to implement and use than the standard of care, VOT may be a beneficial alternative. Along similar lines, a pilot study of MM use in South Africa [28] suggested substantial return on investment through improved treatment outcomes and cost savings.

SMS studies in this review showed no significant effect on clinical treatment outcomes and adherence, though there was weak evidence of an impact on loss to follow-up during treatment. Results from three large RCTs of one- or two-way SMS during TB treatment [30–32] contrast with evidence from meta-analyses of RCTs in other disease settings. For example, studies have shown a positive effect of two-way SMS on HIV treatment adherence and treatment outcomes [35–37]. One potential explanation for this difference is that SMS communication and support add more to self-administered treatment (as is the case for HIV) than to direct observation and in-person treatment support, as is done in well-functioning TB programmes.

More generally, where DOT is systematically well delivered, digital technologies such as VOT and MMs are unlikely to improve adherence or clinical outcomes, but can substantially bolster efficiency and convenience for patients and providers. In TB treatment contexts where DOT is not effectively delivered, digital technologies offer the possibility of improving adherence and clinical outcomes, though suitable evidence is needed. An important example is latent TB infection, where most treatment is currently self-administered.

The application of mobile phone interventions to help TB efforts continues to generate interest. After we completed this systematic review, two RCTs were completed. A study of SMS reminders used among TB

TABLE 4 Quality assessment/risk of bias of observational studies included in the review

First author [ref.]	Selection bias	Confounding	Measurement of outcome	Missing data	Reporting bias
Broomhead [28]	Unclear	High	High	Low	Unclear
Chuck [22]	Unclear	High	High	Low	Unclear
Wade [23]	Unclear	High	High	Unclear	Unclear

patients in China described improved treatment completion and fewer missed doses with daily one-way SMS reminders [38]. The results of another RCT, in Kenya, investigating treatment support and supervision built around daily two-way SMS communication, are not yet published, but the protocol is available online [39].

Until recently, the evidence base underpinning the use of digital interventions to support TB care has relied largely on experience in other disease contexts. Although a systematic review of studies examining the effect of SMS technology on TB treatment adherence was published in 2013 [40], our systematic review, to our knowledge, is the first to consider studies evaluating the effect of several digital health technologies on TB treatment adherence and treatment outcomes. Since 2015, the World Health Organization (WHO), the European Respiratory Society, and other leading technical and funding partners have developed target product profiles for digital health interventions to help steward the implementation and evolution of these potentially useful tools [19]. The latest WHO TB treatment guidelines highlight the potential contributions of SMS, VOT and MMs in supporting adherence and treatment delivery for patients and programmes [18]. This policy now needs to be complemented by additional evidence as well as by pragmatic implementation guidance, to enable users to translate research findings into local practice.

Our review has several limitations. We focused on quantitative comparisons of adherence and clinical outcomes, as these are fundamental to the evidence base. For this reason, we have not provided a detailed review of studies which focused exclusively on cost, feasibility, acceptability and/or qualitative assessments. However, these are also essential in considering introduction and scale-up of such technologies, and in supplementary table S2, we provide suitable references to such studies.

Despite an extensive search, we only found seven relevant reports. Given the marked heterogeneity of study designs, end-points and settings, we were unable to pool the estimates of effect, and could only summarise findings as reported from each of the seven studies. It was difficult to fully characterise the methodological quality of some studies, as the necessary information was often incompletely reported. This should be kept in mind when interpreting study results. Finally, a recurrent limitation of the existing literature is the emphasis on short-term measures of medication adherence, *e.g.* missed doses. The relationship of such measures to relevant clinical outcomes for patients and providers is not always certain.

With the growing interest in mobile technologies and the increasing affordability and global expansion of broadband internet and mobile phones [11], further evaluation of digital health interventions is urgently needed – ideally in adequately powered RCTs, or at a minimum, in observational studies with adequate sample size, suitable controls, and appropriate TB treatment outcomes as study end-points. Practices such as registering and publishing study protocols *a priori*, and using reporting guidelines such as CONSORT (consolidated standards for reporting trials) for RCTs, can improve the quality of the evidence. Currently there are several ongoing or unpublished RCTs evaluating clinical outcomes of TB treatment which apply these technologies in diverse settings; their protocols are available online [31, 33, 39, 41–43]. Beyond RCTs, further research on implementation is needed to evaluate and understand the feasibility, acceptability and cost of the various digital health interventions in diverse communities and locations. It will be relevant to explore the possible influence of digital technologies on behaviour change at other points on the patient pathway – for example, in preventing initial loss-to-follow-up before TB treatment initiation, or in detecting and managing adverse events during treatment [44].

In conclusion, the evidence base from studies on digital technologies targeting TB is slowly growing. Despite interest in the use of digital technologies to improve the care of persons with TB, their reported impact has been variable and evidence from implementation studies remains sparse. Our findings suggest that certain digital technologies can support TB treatment efforts while reducing both patient and provider costs, as well as patient inconvenience. Worldwide, patients and providers are increasingly using mobile devices to communicate. It is thus important to understand how technologies could best be used to provide better patient-centred treatment support and to allocate resources more judiciously. Data from ongoing and future research, including non-inferiority studies, pragmatic trials and cost-effectiveness analyses, will aid in the optimisation of practical approaches. These could include targeting different entry points on the behaviour change pathway which have not yet been explored, and combining several technologies – either sequentially or simultaneously – to better leverage their effects on TB treatment adherence, and ultimately, clinical outcomes.

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