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by Somchit Han

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Patient-Centered Digital Interventions for Self-Care Ability Among People with Pulmonary Tuberculosis: A Systematic Review

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Abstract

Tuberculosis remains a global health challenge, with treatment adherence crucial for successful outcomes. This systematic review assessed the effectiveness of patient-centered digital interventions (e.g., mobile health apps, SMS reminders, video-observed therapy) in promoting self-care behaviors among people with pulmonary tuberculosis and identified implementation challenges. A review of studies published between 2019 and 2024 was conducted across six databases, guided by the PRISMA framework. Eligible studies included adults with pulmonary tuberculosis, utilized digital interventions, and reported outcomes on treatment adherence, completion rates, patient knowledge, quality of life, cost-effectiveness, and satisfaction. Study designs included randomized controlled trials, quasi-experimental, and observational studies with control groups. Data were synthesized narratively due to heterogeneity in interventions and outcomes.

Twenty studies from 12 countries, involving over 9,000 participants, were included. Digital interventions showed significant improvements in treatment adherence in six out of ten studies, but evidence for improved completion rates was less conclusive. Patients generally found digital interventions acceptable and satisfactory. Implementation challenges included technological barriers, connectivity issues, and privacy concerns. Facilitators included user-friendly design, contextual customization, and adequate support. Patient-centered digital interventions show promise in enhancing treatment adherence for pulmonary tuberculosis but have fewer clear effects on completion rates. Future research should address identified challenges and explore long-term impacts on patient knowledge and quality of life.

Keywords: Medication Adherence, Patient-Centered Care, Self-Care, Telemedicine, Tuberculosis, Pulmonary

Introduction

Tuberculosis (TB) remains a global health challenge, particularly in low- and middle-income countries. In 2019, an estimated 10 million people worldwide contracted TB, making it one of the top 10 causes of death globally.[1] Pulmonary TB, the most common form, is preventable and curable but continues to impose substantial health and economic burdens (2). Effective self-care, especially medication adherence, is crucial for successful TB treatment and preventing drug resistance (3). However, the lengthy treatment and side effects often lead to poor adherence and treatment discontinuation (4). Traditional support methods like directly observed therapy (DOT) are effective but resource-intensive and may not always align with patient preferences (5).

Digital health interventions, including mobile health (mHealth) applications, SMS reminders, and telemedicine, show promise in supporting self-care and improving treatment adherence in TB management (6). The effectiveness of these interventions varies depending on the technology used and the target population. For instance, smartphone-based video observed therapy (VOT) improved treatment adherence in urban settings, while text message reminders were more effective in rural areas with limited smartphone access (7). There is a need to explore these interventions across diverse socioeconomic contexts, considering factors like technology access, literacy, and cultural attitudes toward digital health (7). From a nursing perspective, these interventions could significantly impact patient care and the role of nurses in TB management. However, there are gaps in understanding the full range of digital interventions for TB self-care, their effectiveness across contexts, and their implications for nursing practice.

While digital interventions show promise in improving TB care, particularly in treatment adherence and patient engagement, significant gaps persist. The evidence on patient-centered digital interventions for pulmonary TB across various socioeconomic contexts is incomplete,

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and their implications for nursing practice are underexplored. Additionally, how these interventions integrate with existing TB care models, such as the Chronic Care Model, is not well understood. The long-term impact and cost-effectiveness of these interventions, especially in resource-limited settings, also remain unclear. This review aims to address these gaps by synthesizing current evidence on their effectiveness, implementation challenges, and nursing implications.

Aim

This review aims to synthesize evidence on patient-centered digital interventions for self-care in pulmonary TB, focusing on their effectiveness, implementation challenges, and implications for nursing practice. We hypothesize that these interventions will enhance treatment adherence and completion rates compared to standard care, though effectiveness may vary by socioeconomic context.

Literature review

Standard care for tuberculosis

The World Health Organization (WHO) recommends a patient-centered approach for treating drug-susceptible TB, emphasizing daily drug regimens and fixed-dose combination tablets to enhance adherence. Directly Observed Treatment, Short-course (DOTS), integrated with education and counseling, has improved outcomes (3). New drugs like bedaquiline and delamanid offer hope for multidrug-resistant TB (MDR-TB) (8).

Adherence to Treatment

Improving TB treatment adherence requires a multifaceted approach. Combined interventions like case management with DOTS are more effective than DOTS alone (9). Personalized interventions, such as community-supervised DOTS and SMS reminders, have varied effectiveness (10). There is a need for further research on SMS reminders to improve adherence (11).

Challenges in standard TB care

Challenges in TB care include treatment fatigue, socioeconomic barriers, stigma, and comorbidities (12). Low-resource settings face additional challenges, such as drug stock-outs and a lack of trained healthcare workers (13). Nurses, particularly in resource-limited settings, face high workloads and the need for continuous training to keep up with evolving treatment protocols (14)

Self-care approaches in TB management

Self-care in TB involves promoting health and managing illness with or without healthcare provider support. Self-management interventions have improved treatment adherence and quality of life (15). Patient-centered care models, including self-administered treatment, can be as effective as DOTS in specific contexts (16).

Digital interventions in TB care

Digital health interventions are increasingly effective in TB care. Low-cost SMS interventions have significantly improved TB treatment completion rates (17). Video observed therapy (VOT) is more cost-effective than in-person DOT in the UK (18). However, more robust evidence is needed on the impact of digital technologies in high-burden TB settings (19). Scaling up digital interventions faces challenges, including data privacy and health equity issues (20).

Chronic Care Model

The Chronic Care Model (CCM) improves chronic illness management in primary care settings, comprising six key elements: health system, delivery system design, decision support, clinical information systems, self-management support, and community resources (21). In TB care, aligning with CCM principles leads to improved outcomes (22). Digital interventions can support CCM components, from self-management to system responsiveness (23).

Nursing perspective on TB care and digital interventions

Nurses are vital in TB care, especially in resource-limited settings, where they often lead integrated TB-HIV care models (24). Digital health tools can enhance patient monitoring but may increase nurses' workloads (25). Mobile health applications support more efficient and personalized TB care, particularly in community settings (26).

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METHODS

Protocol and Registration

This systematic review protocol was registered with PROSPERO (International Prospective Register of Systematic Reviews) under registration number CRD42024563077. The review conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.

Eligibility Criteria

We included studies based on the following criteria: adults (≥18 years) with pulmonary tuberculosis diagnosed in any setting (outpatient, inpatient, community). The interventions were patient-centered digital tools aimed at promoting self-care behaviors, such as mHealth apps, SMS reminders, telemedicine, and wearables. Comparators included standard care, non-digital interventions, or no intervention. Primary outcomes were treatment adherence and completion rates, while secondary outcomes included patient knowledge, quality of life, cost-effectiveness, patient satisfaction, and implementation challenges. We considered RCTs, cluster-RCTs, quasi-experimental studies, and observational studies with control groups, excluding case reports, case series, and studies without a control group. These inclusion criteria were applied consistently throughout the study selection process, and all reasons for exclusion were documented at the full-text screening stage.

Information Sources

We conducted a comprehensive search of electronic databases from 2019 to August 2024, including PubMed, Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science, ProQuest, ScienceDirect, and Scopus. The search was restricted to studies published in English.

Search Strategy

The search strategy was developed by the research team and used a combination of Medical Subject Headings (MeSH) terms and free-text terms related to tuberculosis, digital interventions, and self-care. A sample search strategy for PubMed is provided in **Appendix, Table 1** with adaptations for other databases. The search strategy was limited to electronic database searches. No grey literature or hand-searches were conducted, which may have affected the comprehensiveness of the review. Publication bias was assessed by examining the likelihood of publication bias across included studies and considering its potential impact on the review findings.

Study Selection

Three reviewers independently screened titles and abstracts of all retrieved records for potential eligibility. Full texts of potentially eligible studies were then obtained and screened independently by the same two reviewers. Any disagreements were resolved through discussion or, if necessary, consultation with a third and fourth reviewer. We used Mendeley software to manage the screening process and document reasons for exclusion at the full-text stage.

Data Extraction

A standardized, pre-piloted form was used to extract data from the included studies. Two reviewers independently extracted data, with discrepancies resolved through discussion or arbitration by a third reviewer. We extracted the following information into Study

characteristics, Participant characteristics, Intervention details, Outcome measures and time points, Results for primary and secondary outcomes, and Information on implementation challenges and facilitators.

Risk of Bias Assessment

Two reviewers independently assessed the risk of bias for each included study. For randomized controlled trials, we used the revised Cochrane Risk of Bias tool (RoB 2). For non-randomized studies, we used the Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) tool. Disagreements were resolved through discussion or arbitration by a third and fourth reviewer. Publication bias was assessed by evaluating the risk of bias in included studies and considering the potential impact of unpublished studies on the review results.

Data Synthesis

We provide a narrative synthesis of the findings from the included studies, structured around the types of interventions, target population characteristics, and outcome measures. We also summarize implementation challenges and facilitators identified in the studies. Due to the expected heterogeneity in interventions and outcome measures, we did not conduct meta-analyses.

Certainty of Evidence

We used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach to assess the certainty of evidence for each outcome.

Results

Study Selection

The search yielded 523 records from PubMed (44), Cochrane CENTRAL (19), Web of Science (7), ProQuest (29), ScienceDirect (348), and Scopus (76). After removing 45 duplicates, 478 records remained. Of these, 293 were excluded for irrelevant titles and 149 for irrelevant abstracts. Thirty-six reports were sought for retrieval, with 5 unobtainable. The

remaining 31 reports were assessed, leading to the exclusion of 11 due to incorrect study design (5), population (2), or intervention (4). Consequently, 20 studies were included in the review **(Figure 1).**

Study Characteristics

This systematic review included 20 studies published between 2019 and 2024, evaluating digital interventions for tuberculosis (TB) treatment adherence. The studies were conducted across 12 countries, with 9 studies from low- and middle-income countries and 3 from high-income countries. In low- and middle-income countries, the research was conducted in Uganda (27–30), South Africa (31), Ethiopia (32), China (33,34), Thailand (35), Argentina (36), India (37–40), Tibet (41), and Morocco (42). In high-income countries, the studies were conducted in the USA (43,44), the UK (18), and New York City, USA (45).

Eight studies employed randomized controlled trial designs(18,31–33,35,41,43,46), while others used quasi-experimental (39), observational (38,42,44,47), and mixed-methods approaches (27,28). Additional study designs included a feasibility study (40), a comparison study (48), a pre-post study (38), a usability study (47), and economic evaluations (29,45). Sample sizes ranged from 25 to 3074 participants, with a total of at least 9,254 participants across all studies.

The digital interventions evaluated included mobile applications (n=5) (27,30,44,46,47), SMS reminders (n=4) (28,39,49,50), video-observed therapy (VOT) (n=6) (18,35,40,43,45,47), electronic monitors/99DOTS (n=5) (29,32,38,48,51), and other digital adherence technologies (n=3) (28,41,42). Intervention durations varied from 8 weeks to 78 weeks, with most studies focusing on the intensive phase of TB treatment. **Appendix Table A2** presents the key characteristics of the included studies.

Quality Assessment of Included Studies

We assessed the methodological quality of the included studies using the Cochrane Risk of Bias tool for randomized controlled trials and the ROBINS-I tool for non-randomized studies. Of the 8 RCTs, 5 were assessed as having low risk of bias and 3 as having some concerns. For the 12 non-randomized studies, 4 were assessed as having low risk of bias, 6 as moderate risk, and 2 as serious risk of bias. The primary issues were confounding and selection bias.

Effects of Interventions

Primary Outcomes:

Treatment Adherence: Ten studies reported on treatment adherence. Six studies found significant improvements in adherence with digital interventions compared to standard care, while four studies found no significant difference or mixed results. Studies showing significant improvements include Kumwichar et al. (2024), who reported a mean difference of 15.2 days in compliance during the intensive phase (95% CI 4.8-25.6; P=.005) using smartphone-based Video-Observed Therapy (VOT). Burzynski et al. (2022) demonstrated that electronic DOT was non-inferior to in-person DOT, achieving high completion rates for doses administered. Manyazewal et al. (2022) showed non-inferiority of mobile electronic medication adherence technology (MERM) to in-person DOT. Story et al. (2019) found that Video-Observed Therapy (VOT) was significantly more effective than DOT in achieving treatment outcomes, with higher adherence rates. Santra et al. (2021) reported that mHealth intervention significantly improved medication adherence among people with pulmonary tuberculosis on DOTS therapy. Guo et al. (2020) demonstrated significantly higher observed doses with VOT compared to routine DOT.

Studies showing no significant difference or mixed results include Liu et al. (2023), who found that digital adherence technologies did not significantly affect primary outcomes compared to standard care. Thomas et al. (2020) reported that 99DOTS exhibited suboptimal

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accuracy in measuring adherence. Chen et al. (2023) observed that despite widespread adoption, 99DOTS did not significantly improve TB treatment outcomes. Musiimenta et al. (2019) found mixed results, with some people with pulmonary tuberculosis reporting improved adherence while others faced challenges.

Treatment Completion Rates: 8 studies reported on treatment completion or success rates. The findings were mixed, with some studies showing improvements and others finding no significant difference. Three studies found significant improvements in treatment success with digital interventions. Story et al. (2019) reported that Video-Observed Therapy (VOT) was significantly more effective than Directly Observed Treatment (DOT) in achieving treatment outcomes. Iribarren et al. (2022) demonstrated higher treatment success rates with the TB Treatment Support Tools (TB-TSTs) intervention compared to usual care. Park et al. (2021) found that integrated patient management using a "smart pillbox" effectively improved TB treatment outcomes in Morocco. Conversely, five studies found no significant difference in treatment completion rates compared to standard care. Louwagie et al. (2022) observed no significant differences in treatment success rates between the ProLife intervention and usual care in South Africa. Manyazewal et al. (2022) found no significant impact on treatment outcomes despite the non-inferiority of mobile electronic medication adherence technology (MERM) to in-person DOT in Ethiopia. Liu et al. (2023) reported that digital adherence technologies did not significantly affect primary outcomes, including treatment completion, in their large-scale study in China. Chen et al. (2023) noted that 99DOTS did not significantly improve TB treatment outcomes despite widespread adoption in India. Kumwichar et al. (2024) found no statistically significant difference in sputum conversion rates between VOT (73%) and DOT (61.5%) groups (P=.17) in Thailand, although they did observe improvements in compliance days.

Secondary Outcomes:

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It's noteworthy that none of the included studies explicitly reported on patient knowledge or quality of life outcomes. This gap in reporting highlights a need for future research to address these important patient-centered outcomes in the context of digital interventions for TB care

a. Patient Knowledge: No studies explicitly reported on changes in patient knowledge.
b. Quality of Life: No studies explicitly reported on quality of life outcomes.
c. Cost-effectiveness: 2 studies reported on cost-effectiveness. The study by Thompson et al. (2022) found varying costs per treatment success for 99DOTS implementation, suggesting potential cost savings in certain scenarios. Lam et al. (2019) demonstrated cost-effectiveness of Video Directly Observed Therapy (VDOT) technologies in TB treatment.
d. Patient Satisfaction: 5 studies reported on patient satisfaction or acceptability. Generally, people with pulmonary tuberculosis found digital interventions acceptable and satisfactory. For example, Musiimenta et al. (2024) reported high acceptability of SMS reminders and incentives, while Do et al. (2019) found that VDOT enhanced people with pulmonary tuberculosis' comfort in using mobile phone features for medication adherence.

GRADE assessments showed moderate certainty for treatment adherence, low certainty for treatment completion rates, and low to moderate certainty for cost-effectiveness and patient satisfaction due to inconsistencies and limited study numbers. Summary in **Table 1.**

Implementation Challenges and Facilitators

Seven studies examined implementation challenges and facilitators (28,30,37,38,44,47,49). Key challenges included technological barriers, such as difficulties using smartphones and unreliable connectivity in rural areas (28,37,38), privacy concerns about

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health information (28), and maintaining long-term patient engagement (37,38). Logistical issues with integrating new technologies into existing practices were also noted (30).

Facilitators for successful implementation included user-friendly design, customization to local contexts, and adequate training and support for healthcare workers and patients (30,44,47). Integration with existing healthcare systems, incentives like mobile money, and using human-centered design principles also enhanced adoption (27,28,30,47). Interventions showing cost savings or efficiency improvements were more likely to be sustained (29,45). These findings highlight the need to address both technical and human factors in digital TB interventions.

Dicussion

This systematic review is grounded in the Chronic Care Model (CCM) adapted for tuberculosis (TB) care (52–54). The CCM emphasizes patient-centered care, self-management support, and the integration of health information technology to improve outcomes for chronic conditions. In the context of TB, digital interventions align with this model by empowering people with pulmonary tuberculosis, enhancing communication with healthcare providers, and supporting adherence to long-term treatment regimens (55). This review adhered to the PRISMA guidelines for systematic reviews. We conducted a comprehensive search of multiple databases, focusing on studies published between 2019 and 2024. The included studies were assessed for risk of bias using standardized tools, and the certainty of evidence was evaluated using the GRADE approach. This rigorous methodology enhances the reliability and transparency of our findings.

The quality of the included studies varied, which influenced the certainty of the evidence across different outcomes. For treatment adherence, six out of ten studies reported significant improvements with digital interventions compared to standard care, particularly with smartphone-based Video-Observed Therapy (VOT) and mobile electronic medication

adherence technology (MERM). The certainty of evidence for this outcome was rated as moderate, reflecting confidence in the findings but acknowledging some limitations, such as study design heterogeneity and potential bias. These results align with previous research by Story et al. (2019), who demonstrated the superiority of smartphone-enabled VOT over directly observed treatment in a randomized controlled trial (18).

However, the mixed results across studies suggest that the effectiveness of digital interventions may be context-dependent. This variability echoes the findings of Ngwatu et al. (2018), who also reported heterogeneous outcomes in their review of digital health technologies for TB treatment (19). The inconsistency in results underscores the need for careful consideration of local factors when implementing digital interventions, highlighting the moderate certainty of evidence due to the influence of these variables.

The evidence for improved treatment completion rates was less conclusive, with only three out of eight studies reporting significant improvements. The certainty of evidence for this outcome was rated as low to moderate, reflecting concerns about study quality, small sample sizes, and variability in outcome measures. This discrepancy between adherence and completion rates suggests that while digital interventions may enhance day-to-day medication adherence, other factors likely influence overall treatment success. These could include socioeconomic determinants, comorbidities, or healthcare system capacity, as highlighted by the Stop TB Partnership (2020) in their analysis of TB care challenges (56).

The role of nurses in implementing digital interventions for TB care emerged as a crucial theme in our review. Nurses, as frontline healthcare providers, play a pivotal role in the successful integration of digital tools into TB management. Several studies highlighted the potential of digital interventions to support and enhance nursing practice in TB care. For instance, mobile health applications were found to assist nurses in delivering more efficient and personalized care, particularly in community settings (26). These tools enabled nurses to

remotely monitor patient adherence, manage side effects, and provide timely support, aligning with the CCM's emphasis on proactive care and self-management support.

However, the implementation of digital interventions also presented challenges for nursing practice. Some studies reported increased workload for nurses, particularly during the initial implementation phase, as they had to learn new technologies and integrate them into their existing workflows (25) This finding underscores the need for adequate training and support for nurses when introducing digital interventions. Additionally, the review highlighted the importance of involving nurses in the design and implementation of digital interventions to ensure their feasibility and acceptability in clinical practice.

The review results indicate potential benefits of digital interventions in TB care, but their generalizability is limited by context variability. Effectiveness varied across settings, with smartphone-based interventions performing well in urban areas with good internet but potentially less applicable in rural or low-resource settings. Patient satisfaction with digital interventions was high in all five studies, though evidence certainty was moderate due to potential self-report bias. This positive feedback supports the use of digital tools to enhance patient engagement in TB care, aligning with CCM principles. Cost-effectiveness, reported in two studies, also showed potential economic benefits, but evidence was moderate and limited. Further robust economic evaluations are needed to confirm these findings and guide policy decisions, especially in resource-constrained settings (17).

Our findings suggest that integrating digital interventions into TB care aligns with the Chronic Care Model (CCM) and supports treatment adherence. However, effectiveness varies by context, requiring adaptable policies tailored to local needs. Healthcare systems should evaluate their technology, workforce, and patient preferences, ensuring adequate training for effective use. The high patient acceptability highlights the potential for enhancing engagement

and empowerment, but policies must also address barriers to access to avoid worsening health inequities.

This review identified several implementation challenges, including technological barriers and privacy concerns. These issues highlight the need for careful consideration of local contexts and infrastructure when deploying digital interventions. Future research should focus on strategies to overcome these barriers and ensure equitable access to digital health solutions, as suggested by Falzon et al. (2016) in their review of digital technologies for TB care (57).

In terms of nursing practice, the applicability of our findings may vary depending on the specific roles and responsibilities of nurses in different healthcare systems. In some settings, nurses may have greater autonomy in managing TB care and implementing digital interventions, while in others, their role may be more limited. This variability underscores the importance of considering local nursing practices and healthcare system structures when applying our findings to specific contexts.

The intervention and outcome measure diversity prevented meta-analysis, limiting quantitative conclusions. The absence of data on patient knowledge and quality of life highlights significant gaps. Recommendations include: 1) Long-term studies on treatment completion and relapse rates, 2) Research on impacts on patient knowledge, empowerment, and quality of life, 3) Studies on effectiveness factors in various contexts, 4) Robust cost-effectiveness analyses, and 5) Qualitative research on patient and provider experiences for user-centered design.

Conclusions

Patient-centered digital interventions show promise in improving treatment adherence for pulmonary tuberculosis, with high patient acceptability. However, their impact on treatment

completion rates is less clear. The effectiveness of these interventions appears to be context-dependent, highlighting the need for tailored implementation strategies. While digital interventions represent a valuable tool in TB care, they should be seen as part of a comprehensive approach that addresses the multiple factors influencing TB treatment outcomes.

The role of nurses in implementing and optimizing these digital interventions is crucial. As frontline providers, nurses are uniquely positioned to bridge the gap between technology and patient care, ensuring that digital tools enhance rather than replace the human elements of TB management. Future research and policy initiatives should focus on supporting nurses in this evolving role, recognizing their potential to drive innovation and improve outcomes in TB care through the effective use of digital health technologies.

Acknowledgement

We would like to express our sincere gratitude to Universitas Airlangga for providing access to the databases essential for conducting the literature search for this systematic review.

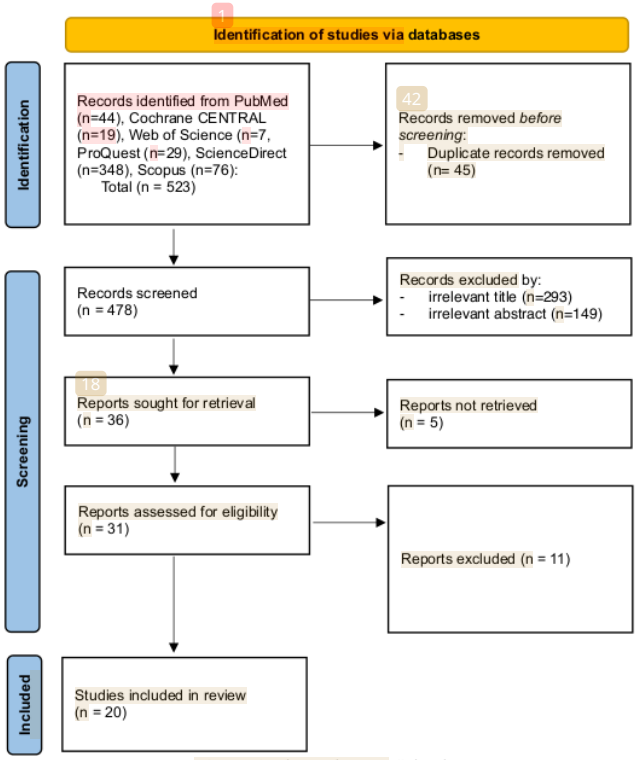

Figure 1. Flow Diagram Selection Process

Appendix

Table A2. Key Characteristics of the Included Studies

No.	Author (Year), Country	Study Design	Sample Size & Population Characteristics	Intervention Type, Duration, and Comparator	Primary Outcome Measured	Key Findings
1.	Musiimenta A, Tumuhimbise W, Mugaba AT, et al. (2024), Uganda	Mixed Methods Feasibility and Acceptability Study	39 people with tuberculosis, aged ≥18, who either started TB treatment at enrollment or within the past 4 weeks, owned a mobile phone, were able to use SMS text messaging, and lived in Mbarara district.	Digital Adherence Technologies (My Mobile Wallet) including real-time adherence monitoring, SMS text message reminders, and mobile money incentives, over 6 months	Feasibility and acceptability of My Mobile Wallet intervention	SMS reminders and incentives were highly feasible and acceptable, with high transmission success rates for adherence data, fostering participant support and medication adherence.
2.	Louwagie G, Kanaan M, Morojele NK, et al. (2022), South Africa	Multicentre, Randomised Controlled Trial	574 adults starting treatment for drug-sensitive pulmonary TB who smoked tobacco or reported harmful/hazardous alcohol use	ProLife intervention (3 brief motivational interviewing sessions and SMS messages) vs. usual care, over 6-9 months	TB treatment success rate at 6-9 months	No significant differences in treatment success rates or secondary outcomes between intervention and control groups were observed, suggesting limited impact of the intervention on TB treatment outcomes.
3.	Burzynski J, Schluger NW, Gaeddert M, et al. (2022), USA	Randomized Noninferiority Trial	216 participants with physician-suspected or bacteriologically confirmed TB	Electronic DOT vs. in-person DOT, crossover design with each method used for 20 doses	Percentage of medication doses observed to be completely ingested	Electronic DOT demonstrated noninferiority to in-person DOT in terms of medication adherence, achieving high completion rates for doses administered.
4.	Manyazewal T, Woldeamanuel Y, Holland DP, et al. (2022), Ethiopia	Multicenter Randomized Controlled Trial	114 adults with new or previously treated, bacteriologically confirmed, drug-sensitive pulmonary TB	Digital medication event reminder and monitor (MERM) device-observed self-administered therapy vs. in-person DOT, over 2-month intensive treatment phase	Individual-level percentage adherence and sputum smear conversion after 2 months	Mobile electronic medication adherence technology (MERM) showed non-inferiority to in-person DOT, with potential superiority in managing non-ingested doses, but no significant impact on treatment outcomes was observed.
5.	Liu X, Lewis JJ, Zhang H, et al. (2023), China	Cluster-Randomised Superiority Trial	3074 patients across 24 counties/districts in China	Daily reminder medication monitor, monthly review of adherence data, and differentiated care vs.	Composite of death, loss to follow-up, treatment failure, switch to MDR-TB treatment, or	Digital adherence technologies did not significantly affect primary outcomes compared to standard care, indicating limited effectiveness in improving

No.	Author (Year), Country	Study Design	Sample Size & Population Characteristics	Intervention Type, Duration, and Comparator	Primary Outcome Measured	Key Findings
				routine care, over 18 months	tuberculosis recurrence by 18 months	treatment outcomes despite technology use.
6.	Story A, Aldridge RW, Smith CM, et al. (2019), UK	Multicentre, Randomised Controlled Superiority Trial	226 patients with active pulmonary or non-pulmonary TB, eligible for DOT	Video-observed therapy (VOT) using a smartphone app vs. Directly observed treatment (DOT) 3-5 times per week, over 2 months	Completion of ≥80% scheduled treatment observations over first 2 months	Video-Observed Therapy (VOT) was significantly more effective than DOT in achieving treatment outcomes, with higher adherence rates and fewer adverse events reported.
7.	Kumwichar P, Prappre T, Chongsuvivatwong V. (2024), Thailand	Cluster Randomized Controlled Trial	Pulmonary TB patients in Hat Yai and Meuang Songkhla districts, Southern Thailand	Video-Observed Therapy (VOT) vs. Community-Based Directly Observed Therapy (DOT)	Mean cumulative compliance days during intensive phase of TB treatment	Smartphone-based Video-Observed Therapy (VOT) significantly improved average compliance days for both patients (mean difference 15.2 days, 95% CI 4.8-25.6; P=.005) and observers (mean difference 21.2 days, 95% CI 13.5-28.9; P<.001) compared to Community-Based Directly Observed Therapy (DOT). However, no statistically significant difference in sputum conversion rates was observed between the VOT (73%) and DOT (61.5%) groups (P=.17).
8.	Iribarren SJ, Schnall R, Stone PW, et al. (2022), Argentina	Parallel-designed Randomized Controlled Trial	Newly diagnosed TB patients from Buenos Aires province	TB Treatment Support Tools (TB-TSTs) intervention (mobile app, urine test, treatment supporter interaction) vs. usual care	Feasibility, acceptability, treatment outcomes	TB-TSTs demonstrated higher treatment success rates compared to usual care, with high participant engagement and satisfaction with the intervention's usability.
9.	Thomas BE, Kumar JV, Chiranjeevi M, et al. (2020), India	Comparison study	597 Indian patients with tuberculosis	Evaluation of 99DOTS (cellphone-based strategy) vs. urine isoniazid testing	Adherence to TB medications	99DOTS exhibited suboptimal accuracy in measuring adherence, particularly in TB, highlighting challenges in engagement and reliability of digital adherence technologies.
10.	Musiimenta A, Tumuhimbise W,	Mixed methods study	35 TB patients from Mbarara Regional Referral Hospital	Digital adherence intervention with a	Patients' perceptions of	Participants found that the digital adherence intervention, including a digital monitor and SMS reminders,

No.	Author (Year), Country	Study Design	Sample Size & Population Characteristics	Intervention Type, Duration, and Comparator	Primary Outcome Measured	Key Findings
	Mugaba AT, et al. (2019), Uganda			monitor and SMS reminders	digital adherence intervention	improved medication adherence by providing timely reminders and managing complex medication schedules, demonstrating their commitment to adherence.
11.	Thompson RR, Jiang S, Sekaggya-Wiltshire C, et al. (2022), Uganda	Pragmatic, stepped-wedge randomized trial	Implemented at 18 clinics in Uganda	99DOTS digital adherence technology	Cost and cost-effectiveness of 99DOTS for TB treatment support	Cost-effectiveness analysis of 99DOTS implementation showed varying costs per treatment success, suggesting potential cost savings with extended activities and marginal clinic scenarios.
12.	Wei X, Hicks JP, Pasang P, et al. (2019), Tibet	Multicentre, parallel-group, individually randomised controlled trial	New pulmonary TB outpatients from Shigatse, Tibet	Electronic monitors (e-monitors) with smartphone app vs usual care	Rate of poor adherence (missing ≥ 20% of doses in a month)	E-monitors with voice reminders and app connectivity aimed to improve treatment adherence among TB patients, with ongoing evaluation of feasibility, effectiveness, and cost-effectiveness.
13.	Chen AZ, Kilaru A, Subbaraman R, et al. (2023), India	Pre-Post Study	Adults with drug-sensitive TB in Himachal Pradesh, India	Implementation of 99DOTS digital adherence technology	Favorable treatment outcomes (cured or treatment complete)	Despite widespread adoption, 99DOTS did not significantly improve TB treatment outcomes, indicating variability in its effectiveness across different settings and populations.
14.	Santra S, Basu S, Jana S, Mandal A, Mandal S. (2021), India	Quasi-experimental study	220 newly diagnosed TB patients in Delhi, India	mHealth intervention package for 90 days vs. standard DOTS therapy	Medication adherence measured using Morisky, Green, and Levine Adherence Scale	mHealth intervention significantly improved medication adherence among TB patients on DOTS therapy, suggesting potential for enhancing treatment adherence in similar settings.
15.	Guo XJ, Min HJ, Pang MC, et al. (2020), China	Usability study	158 patients in DOT group (retrospective data) and 235 patients in VOT group	Video-Observed Therapy (VOT) app installed on smartphones vs. routine Directly Observed Therapy (DOT)	Treatment adherence, treatment discontinuations, patient preferences, healthcare worker attitudes	VOT demonstrated significantly higher observed doses and lower treatment discontinuations compared to DOT, indicating its feasibility and acceptance among patients and healthcare workers.

No.	Author (Year), Country	Study Design	Sample Size & Population Characteristics	Intervention Type, Duration, and Comparator	Primary Outcome Measured	Key Findings
16.	Holzman SB, Zenilman A, Shah M (2019), India	Single-arm, prospective feasibility study	25 patients in Pune, India	Video Directly Observed Therapy (vDOT) using smartphones	Adherence (proportion of prescribed doses observed by video), verifiable fraction (proportion of doses observed by video or verbally confirmed)	Video Directly Observed Therapy (vDOT) showed feasibility and acceptability in resource-limited settings, supporting its potential as an alternative to traditional DOT.
17.	Do D, Garfein RS, Cuevas-Mota J, Collins K, Liu L (2019), USA	Longitudinal study	120 participants receiving antituberculosis treatment	Video Directly Observed Therapy (VDOT) app	Change in comfort level using mobile phones (making calls, taking pictures, recording videos, text messaging, internet and email use)	VDOT app enhanced patients' comfort in using mobile phone features for medication adherence, suggesting broader applicability of mHealth apps in healthcare settings.
18.	Patel D, Srinivasan K, Hasselberg M, et al. (2020), Uganda	Qualitative study using human-centered design	Health workers (n=52), patients (n=7)	Adaptation of 99DOTS digital adherence technology	Iterative adaptation of 99DOTS based on human-centered design principles	Optimization of 99DOTS in Uganda through human-centered design highlighted improvements in usability and patient engagement, potentially enhancing treatment outcomes.
19.	Lam CK, Fluegge KR, Macaraig M, Burzynski J. (2019), New York City	Retrospective economic evaluation using program data	Not applicable	Cost analysis of various types of directly observed therapy (DOT) for tuberculosis	Cost savings associated with Video Directly Observed Therapy (VDOT)	Micro-costing evaluation demonstrated cost-effectiveness of VDOT technologies in TB treatment, emphasizing potential economic benefits in program implementation
20.	Park, S., Moon, N., Oh, B., Park, M., Kang, K., Sentissi, I., & Bae, S.-H. (2021), Morocco	Observational study	3605 TB patients in Morocco's five prefectures	Integrated patient management using a patient-centered and community-based approach with mobile health technology	Treatment adherence, successful treatment rate, lost to follow-up rate	Integrated patient management with a "smart pillbox" effectively improved TB treatment adherence and outcomes, suggesting a viable approach for resource-constrained settings.

Table 1 Summary of the Main Outcomes Across Studies.

Outcome	Number of Studies	Summary of Findings	Certainty of Evidence (GRADE)
Treatment Adherence	10	6 studies found significant improvements with digital interventions; 4 studies found no significant difference or mixed results	Moderate
Treatment Completion Rates	8	3 studies found significant improvements; 5 studies found no significant difference	Low to moderate
Patient Knowledge about TB and Self-care	0	No studies explicitly reported on this outcome	Very low
Quality of Life	0	No studies explicitly reported on this outcome	Very low
Cost-effectiveness of Interventions	2	Both studies suggested potential cost-effectiveness of digital interventions	Moderate
Patient Satisfaction with Care	5	All studies reported high patient satisfaction or acceptability of digital interventions	Moderate

Appendix Table A1 SYNTAXIS PubMed

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#1 AND #2 AND #3 AND ((y_5[Filter]) AND (ffrft[Filter]) AND (english[Filter]))	9
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