Digital Health Interventions to Improve Adherence in Patients with Latent Tuberculosis: a Systematic Review and Meta-Analysis

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Abstract

Background: The poor adherence has been one of the barriers to the success of prophylactic treatment in latent tuberculosis (LTBI) patients, as well as an obstacle to tuberculosis prevention and elimination. Digital health interventions have offered a promising solution to low and nonadherence of LTBI treatment.

Objective: This systematic review and meta-analysis aims to evaluate the effect of digital health interventions on treatment adherence of latent tuberculosis treatment. We focus on the effects of different digital health interventions on LTBI treatment completion and clinic outcomes compared with traditional supervision.

Methods: A literature search in seven databases and gray database was conducted. Both randomized controlled trails (RCTs) and observational studies that evaluating treatment completion or adherence of digital interventions for latent tuberculosis treatment were included. Outcomes were measured as odd ratio (OR) with 95% confidence intervals. RoB1 approach was used for quality assessment of RCTs and ROBINS-I approach was used for quality assessment of observational studies.

Results: Overall, 3 RCTs,18 observational studies and 10 clinic trails meet the inclusion criteria were analyzed. Among the included studies, 6 studies are for remote supervision (message or telephone reminders), 8 studies are for direct supervision (directly observed therapy and video observed therapy), and 18 studies are for online supervision (electronic medicine box, telephone application and WeChat supervision). In general, digital health interventions can improve treatment completion (OR:1.36, 95%CI 1.18-1.57) and regular medicine-taking (OR:5.39, 95%CI 2.28-10.10) when compared with standard supervision, but the effect varies according to the intervention (online supervision: OR:1.67, 95%CI 1.46-1.92, remote and/or direct supervision: OR:2.06, 95%CI 1.74-2.42) Remote supervision is associated with better completion compared with standard supervision (OR:1.37, 95%CI 2.28-1.57). Direct supervision has positive effect on adherence when compared with standard supervision (OR:8.66, 95%CI 2.77-27.05). Among all online intervention, Telephone application and WeChat supervision have shown evidence of improving adherence (OR:1.37, 95%CI 1.15-1.63) when compared with electronic medicine box.

Conclusions: It was found that digital health interventions can improve treatment adherence of LTBI treatment. However, the effect of improving adherence and clinic outcomes varies in the type of interventions. When choosing proper interventions, factors like type of intervention, time of the regime, cost and efficiency, facilities and patients satisfaction should also be considered. Clinical Trial: This study is prospectively registered in PROSPERO (ID: CRD420251007138)

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Digital Health Interventions to Improve Adherence in Patients with Latent Tuberculosis: a Systematic Review and Meta-Analysis

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Abstract

Background: The poor adherence has been one of the barriers to the success of prophylactic treatment in latent tuberculosis (LTBI) patients, as well as an obstacle to tuberculosis prevention and elimination. Digital health interventions have offered a promising solution to low and nonadherence of LTBI treatment.

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Conclusion: It was found that digital health interventions can improve treatment adherence of LTBI treatment. However, the effect of improving adherence and clinic outcomes varies in the type of interventions. When choosing proper interventions, factors like type of intervention, time of the regime, cost and efficiency, facilities and patients satisfaction should also be considered.

Key words: Digital health, intervention, latent tuberculosis, adherence, systematic review and meta-analysis

Introduction

Tuberculosis (TB), caused by *Mycobacterium tuberculosis* (*Mtb*), remains one of the deadliest infectious diseases worldwide, and spread through airborne transmission from individuals with pulmonary TB to healthy individuals. According to the World Health Organization (WHO), TB surpassed COVID-19 in 2023 as the top cause of death from a single pathogen, with annual cases exceeding 10 million in 2023[1]. A critical challenge in TB control lies in latent tuberculosis infection (LTBI), affecting nearly 25 of the global population[2,3]. While LTBI patients lack clinical symptoms, they face a 5-10% lifetime risk of progressing to active TB (ATB) and may contribute to transmission through asymptomatic bacterial shedding[4]. Effective LTBI treatment is therefore essential not only for individual health but also for interrupting community transmission. Adherence to treatment is a key determinant of LTBI treatment success. However, achieving this goal hinges critically on treatment adherence—a factor shown to reduce future TB cases by 60% when fully implemented[5]. Despite its significance, suboptimal adherence persists across both high- and low- TB-burden countries, leading to severe consequences such as treatment failure and disease relapse[5-7]. Studies attribute poor adherence to multifactorial causes including objective factors (e.g., adverse drug reactions and treatment duration) and subjective factors (e.g., perceived stigma and discrimination)[8-11].

To enhance treatment adherence, WHO has recommended directly observed therapy (DOT), which has demonstrated effectiveness over the past decades[4]. However, several limitations of DOT have become increasingly apparent. For instance, during the COVID-19 pandemic, lockdown measures rendered DOT unfeasible. Although a decline in ATB and LTBI cases was observed during this period, no evidence linked this reduction to DOT; instead, it was primarily attributed to decreased interpersonal contact and widespread mask usage[12]. Another major drawback of DOT is its high cost and low efficiency. It requires substantial medical resources and increases the workload of healthcare workers. Additionally, some patients have negative perceptions of DOT[13]. On one hand, they fear that physician visits may compromise their privacy, leading to stigma and discrimination. On the other hand, some patients perceive supervised medication intake as unnecessary and disruptive to their daily lives and work schedules. The logistical challenges of DOT are further exacerbated when patients reside far from healthcare facilities or have scheduling conflicts with home visits. Moreover, the large number of patients and limited medical resources make it impractical to implement DOT universally, particularly in high TB burden countries.

To address these gaps, digital health interventions (DHIs)—such as electronic medication boxes (EMBs) and mobile app-based supervision (e.g., WeChat)—have emerged as promising alternatives. EMBs are devices that track medication intake and provide reminders to patients, making them useful for early drug monitoring, which is critical for maintaining adherence [14]. However, some researchers question the accuracy of EMB-generated data, as removing a pill from the device does not necessarily indicate that the patients have ingested it. Telephone- and WeChat-based supervision utilizes dedicated applications or social media platforms (such as WeChat) to facilitate remote patient monitoring. These applications provide a platform for patients to record their medicine intake and communicate with their doctors online. Additionally, WeChat supervision promotes peer support and interaction among patients, leveraging its widespread use in China. Several studies have indicated that these digital interventions hold promise in enhancing treatment adherence while optimizing limited medical resources. However, the evidence remains inconclusive, as these online supervision tools have only been implemented in a limited number of trails in recent years. Further research and larger-scale studies are needed to establish their long-term effectiveness and feasibility.

Although DHIs have been in use for a relatively short period, they show promise in improving adherence in LTBI management due to their ease of use and efficiency. While some studies suggest that DHIs significantly enhance adherence, others argue that their effects may be overestimated. For example, a case-control conducted by Li et al.[6] in Jilin China, reported a notable increase in adherence with DHIs compared to the control group (98% VS 86%). However, a subsequent study by Li et al[15] found no significant difference in treatment success rates between DHI and traditional interventions (both reaching 90%), although DHIs were associated with shorter treatment duration. Similarly, several other studies have concluded that while the difference in adherence between digital health and control groups is not statistically significant, DHIs tend to yield higher patient satisfaction and acceptance[16-19]. Hence, to provide a comprehensive assessment of the impact of DHIs on adherence and clinic outcomes, we conducted this systematic review and meta-analysis, synthesizing evidence from recent studies on their effectiveness in LTBI management.

Method

Search Strategies

This systematic review and meta-analysis followed PRISMA 2020 guidelines and was prospectively registered in PROSPERO (ID: CRD420251007138). Seven databases (PubMed, EMBASE, OVID, Web of Science, CNKI, Wanfang, and VIPC) and gray literature sources (WHO reports, CDC

repositories from UN/USA/China) were systematically queried from the establishment of the database to April 14, 2024. The search syntax combined MeSH terms and free-text keywords across two conceptual clusters: 1) LTBI Epidemiology (Latent tuberculosis infection OR LTBI OR latent tuberculosis); 2) Digital Health Technology (Digital health OR digital health technology OR digital health intervention OR adherence intervention OR telemedicine OR e-health OR mobile health OR m-health OR health information technology OR e-learning video OR educational video OR artificial intelligence OR mobile phone application OR smart pillbox OR electronic medicine monitor OR remote patient monitoring OR mobile healthcare).

Selection Criteria

Regarding to the selection process, the inclusion criteria are as follows: 1) digital health interventions are used in the study 2) participants of the study should be LTBI patients or at least including LTBI patients 3) have primary data. We excluded publications that 1) did not measure the adherence or outcome of digital intervention 2) have incomplete data or without primary data. Titles, abstracts and full texts were reviewed independently by two reviewers (AS and XW). Any disagreement between two reviewers were discussed and then consulted the third reviewer (QC) if necessary.

Data Extraction and Synthesis

AS and XW conducted the data extraction independently from included studies using a standard data extraction form. The extracted data were checked by the two reviewers and any disagreement were solved by QC and Y. Zhou. The quality assessment was conducted by AS and Y. Zhu. Extracted data were as following: publication information (study title, author(s), publication year, time and location of the trail), study design, characteristic of participants (number, age, gender and comparison), interventions, outcomes.

All dichotomous outcomes were estimated as odd ratio (OR) with 95% confidence intervals. Fixed-effects model was used when more than one studies evaluating the same outcome. I^2 test and heterogeneity were calculated and presented in forest plots. Publication bias was showed in funnel plots if more than 10 studies were in a particular comparison. Both the forest plots and funnel plots were created by RevMan5.0 software.

Quality Assessment

The quality assessment for RCTs was done with Cochrane collection's tool for assessing risk of bias in randomized trail (RoB1) and each RCT was evaluated in random sequence, allocation concealment, blinding of participants, incomplete outcome, selective reporting, and other bias[20]. The quality of non-randomized controlled trail (NRCT) was evaluated using ROBINS-I (Risk of bias In Non-randomized Studies-of Intervention)[21,22]. ROBINS-I approach is suitable for the quality assessment of different kinds of NRCTs, including cohort study, case-control study, clinic trail and so on. Each NRCTs was evaluated in six aspects (bias due to confounding, bias in selection of participants into the study, bias in classification of interventions, bias due to missing data, bias in measurement of outcomes and bias in selective of reported results) in order to get an overall risk of bias of the study. They quality of each aspect was marked as low, moderate, high and very high according to the answers to the corresponding signaling questions of each aspect. The overall risk of bias depended on the quality of each aspect.

Result

Study Selection

A total of 3,791 articles were identified from different databases and 1,157 articles were identified from gray database through initial search. After the removal of duplicates, 3839 articles were screen for title and abstract. 3,724 articles were excluded in this process and 115 articles were left for full-text screening. Thirty-one articles were finally included. The process of study selection is shown in .

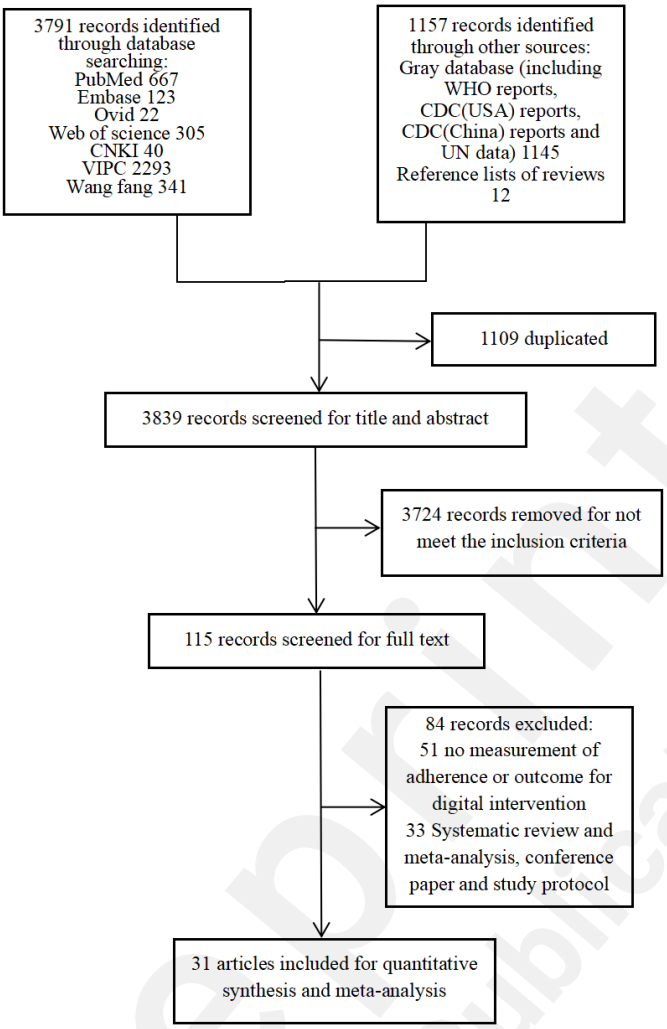

Figure 1. Summary of study selection

Study Characteristics

Among the 31 articles, 18 are observational studies, 3 are randomized controlled trails and 10 are clinic trails. Other characteristics of included studied are shown in **Table 1**. We regrouped the interventions applied in these articles into three categories: (1) remote supervision (RS): message or telephone reminder; (2) direct supervision (DS): DOT (directly observed therapy), VOT (video observe therapy) or VDOT (video directly observed therapy); (3) online supervision (OS): electric medicine box (EMB), WeChat supervision or telephone application (TA). According to WHO operation handbook on tuberculosis as well as completion is assessed by most studies and has a strong connection with adherence of LTBI treatment[23],we choose completion as primary outcome in our article. Treatment adherence (regular medicine-taking and good adherence rate) is the second outcome. We also estimate clinic outcomes like re-examination, visits and treatment success.

Table 1. Characteristics of included studies

No	Authors, publication year	Country	Study period	Population and Gender: (% of male)	Average age (year) (control/ intervention)	Number of partici-pants	Study design	Interven-tion(s)	Control	Outcome(s)
1	Holzschuh et al., 2017[24]	USA	2015.3-2017.3	Not clear	Not clear	50	Cohort study	DS[d]	DOT	Treatment completion (sum of completed treatment)
2	Laza et al., 2023[25]	France	2003-2022	53.6	32.3	2962	Cohort study	RS[a]	Standard supervision[*]	Treatment completion (sum of participants finished 80% prescribed does)
3	Lam et al., 2018[26]	USA	2015.2-2015.10	25.0	33/33.5	352	Clinic trail	DS[d]	DOT	Treatment completion (sum of participants finishing 11 or more does within 16 months)
4	Light et al., 2019[27]	USA	2017.9-2018.1	50.0	Not clear	50	Cohort study	DS[d]	None	Treatment completion (sum of completed treatment)
5	Belknap et al., 2017[28]	USA	2012.9-2014.4	40.3	36	1002	RCT	RS[c]	DOT	Treatment completion (sum of participants finishing 11 or more does within 16 months)
6	Soler et al., 2017[29]	USA	2016.6-2017.7	Not clear	Not clear	17	Cohort study	DS[d]	None	Treatment completion (sum of completed treatment)
7	Comellas et al., 2018[30]	Spain	2011.1-2016.6	44.9	6.3	98	Cohort study	RS[b]	None	Treatment completion (sum of completed treatment)
8	Johnston et al., 2017[19]	Canada	2012.6-2015.9	Not clear	42/45	358	RCT	RS[c]	Standard supervision	Treatment completion (sum of participants finishing 80% prescribed does)
9	Garfein et al., 2018[31]	USA	2014.10-2015.10	44.0	44	433	Cohort study	DS[d]	DOT	Treatment completion (sum of completed treatment)
10	Scott et al., 2023[32]	USA etc	Not clear	Not clear	Not clear	1002	Cohort study	OS[f]	Standard supervision	Treatment completion (sum of participants finishing 11 or more does within 16 months)
11	Chunk et al., 2016[33]	USA	2013.9-2014.9	60.0	48/36	390	Cohort study	DS[d]	DOT	Treatment completion (sum of completed treatment)
12	Rukhsana et al., 2017[34]	Pakistan	2014.6-2015.6	43.2	29.4	148	PCT	RS[c]	DOT	Cure (a negative sputum smear at the end of treatment) and treatment success (sum of cure and completed treatment)
13	Dai et al., 2020[35]	China	2017.10-2017.12	70.9	57.26	206	Cohort study	OS[f]	None	Adherence (sum of participants regularly taking medicine)
14	Deng et al., 2019[36]	China	2018.3-2018.6	46.1	Not clear	85	Cohort study	OS[f]	Telephone application	Adherence (sum of participants regularly taking medicine)
15	Jing et al.,	China	2017.9-2018.3	Not clear	Not clear	60	Cohort	OS[f]	WeChat	Adherence (sum of participants regularly

* Standard supervision refers to a self-administrated intervention with regular health education and follow-ups, which is defined according to WHO guidelines and accepted by most countries.

a: telephone follow-up by a nurse case manager

b: telephone-call reminders

c: text messages or short message reminders (SMS)

d: VOT (video observed therapy) or VDOT (video directly observed therapy)

e: VOT with family member supervision

f: EMB (electronic medicine box)

g: WeChat supervision

h: telephone application

i: EMB or WeChat supervision

j: EMB with telephone application

Study Outcome

In total, 124,629 participants were included in the analysis, ranging from 10 to 14,659. Also, the age of participants ranges from 6 to 89 and the gender of all the including participants was shown in **Table 1**. Overall, digital health interventions can improve treatment completion (OR:1.36, 95%CI 1.18-1.57) and regular medicine-taking (OR:5.39, 95%CI 2.28-10.10) when compared with standard supervision. High heterogeneity was found in the comparison of treatment completion (I^2: 92%) and low heterogeneity was found in the comparison of regular medicine-taking (I^2: 0%) The analysis results of the forest plot are shown in **Figure 2** and **Figure 3**.

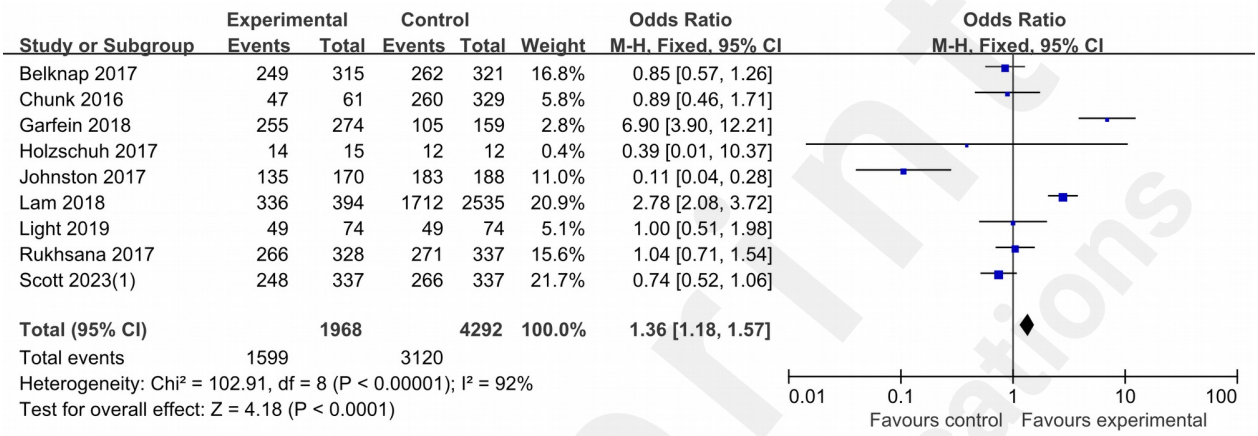

Figure 2. Meta- analysis of treatment completion in DHIs (RS&DS&OS) compared with standard supervision.

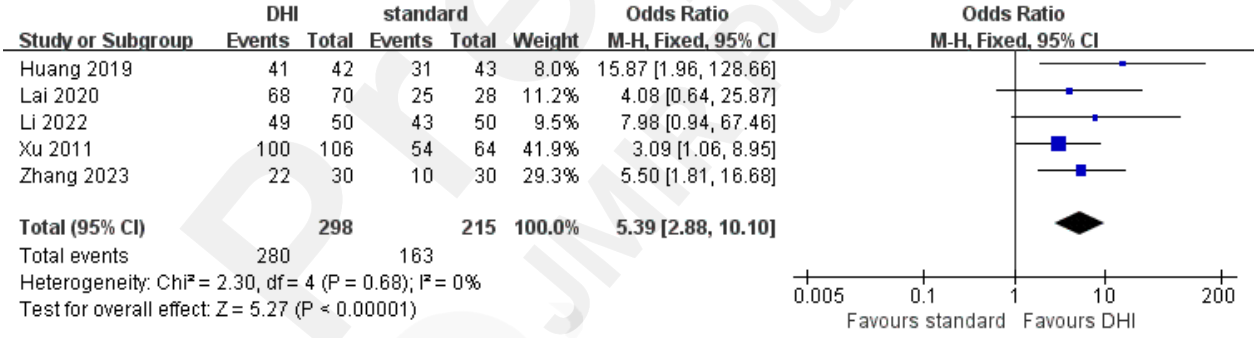

Figure 3. Meta-analysis of adherence (regular medicine-taking) in DHIs (RS&DS&OS) compared with standard supervision.

Remote supervision: 3 RCTs and 2 cohort studies assessed the outcome treatment completion and it was the only outcome mentioned in these studies. Remote supervision is associated with better completion when compared with standard supervision (OR 1.37 95%CI 1.15-1.63). High heterogeneity was found in this result (I^2: 93%). The analysis result of the forest plot is shown in **Figure 4**.

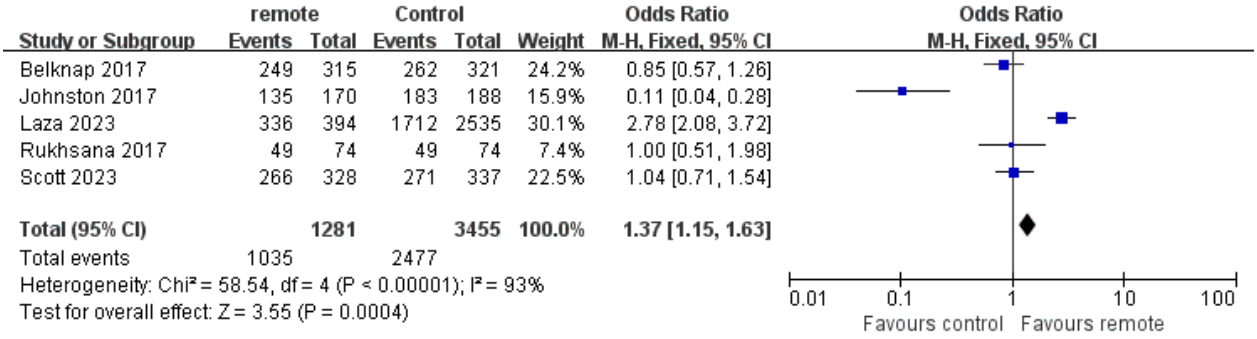

Figure 4. Meta-analysis of completion in remote supervision compared with standard supervision

Direct supervision: 4 observational studies (3cohort study and 1 case-control study) and 4 clinic trail studies compared the outcome of VOT and DOT. VOT was associated with higher rate of adherence (regular medicine-taking and good adherence) (OR:8.66, 95%CI 2.77-27.05) compared with DOT. Relatively high heterogeneity was found in this result (I^2: 74%). The analysis result of the forest plot is shown in **Figure 5**.

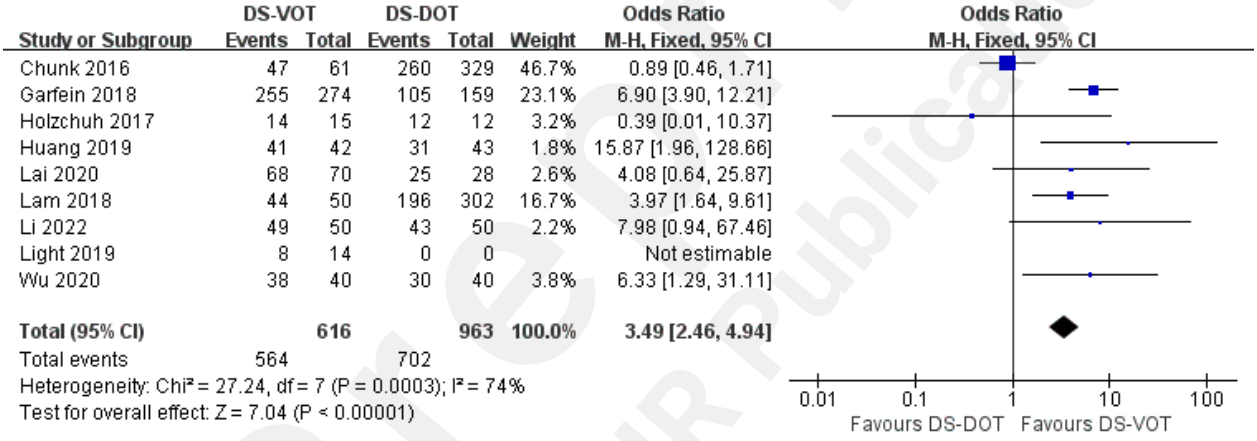

Figure 5. Meta-analysis of adherence (including completion) in direct supervision compared with standard supervision

Online supervision: 5 clinic trails and 10 observational studies (7 cohort study and 3 case-control study) evaluated the outcomes of online supervision. All the three main outcomes were estimated in these studies. However, most studies vary in outcome indicators and comparisons, which made it difficult to do the mate-analysis or caused high heterogeneity in the results. When it comes to detailed intervention in online supervision, WeChat supervision and telephone application have a positive effect on adherence compared with electronic pillbox (OR:1.37, 95%CI 1.15-1.63). WeChat supervision and telephone application are also associated with positive clinic outcomes such as treatment success (OR 0.14, 95%CI 0.04-0.47). Relatively high heterogeneity was found in this result (I^2: 84%). The analysis result of the forest plot is shown in **Figure 6**.

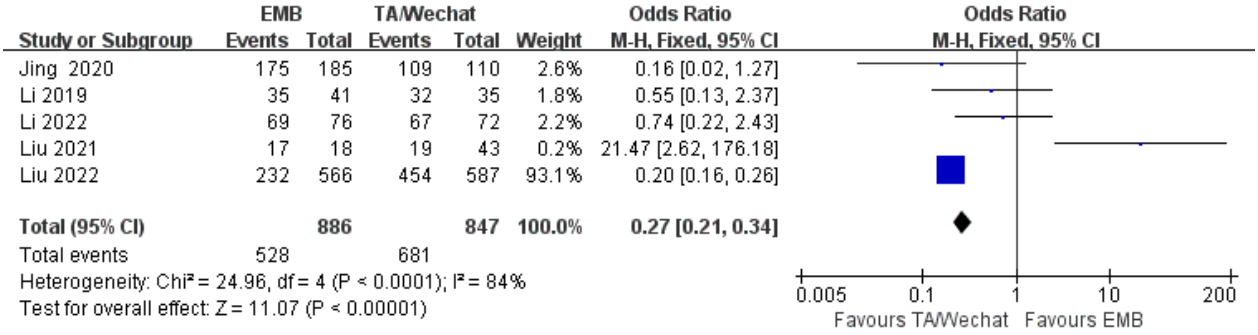

Figure 6. Meta-analysis of adherence (regular medicine-taking and good adherence) in EMB compared with TA/WeChat supervision

OS (online supervision) versus R/DS (remote and/or direction supervision): both OS and R/DS are associated with better completion situation in comparison with standard supervision (OS: OR 1.67,95%CI 1.46-1.92, RS&DS: OR 2.06, 95%CI 1.74-2.42) High heterogeneity was found in this result (I^2: 95.7%). The analysis result of the forest plot is shown in **Figure 7**.

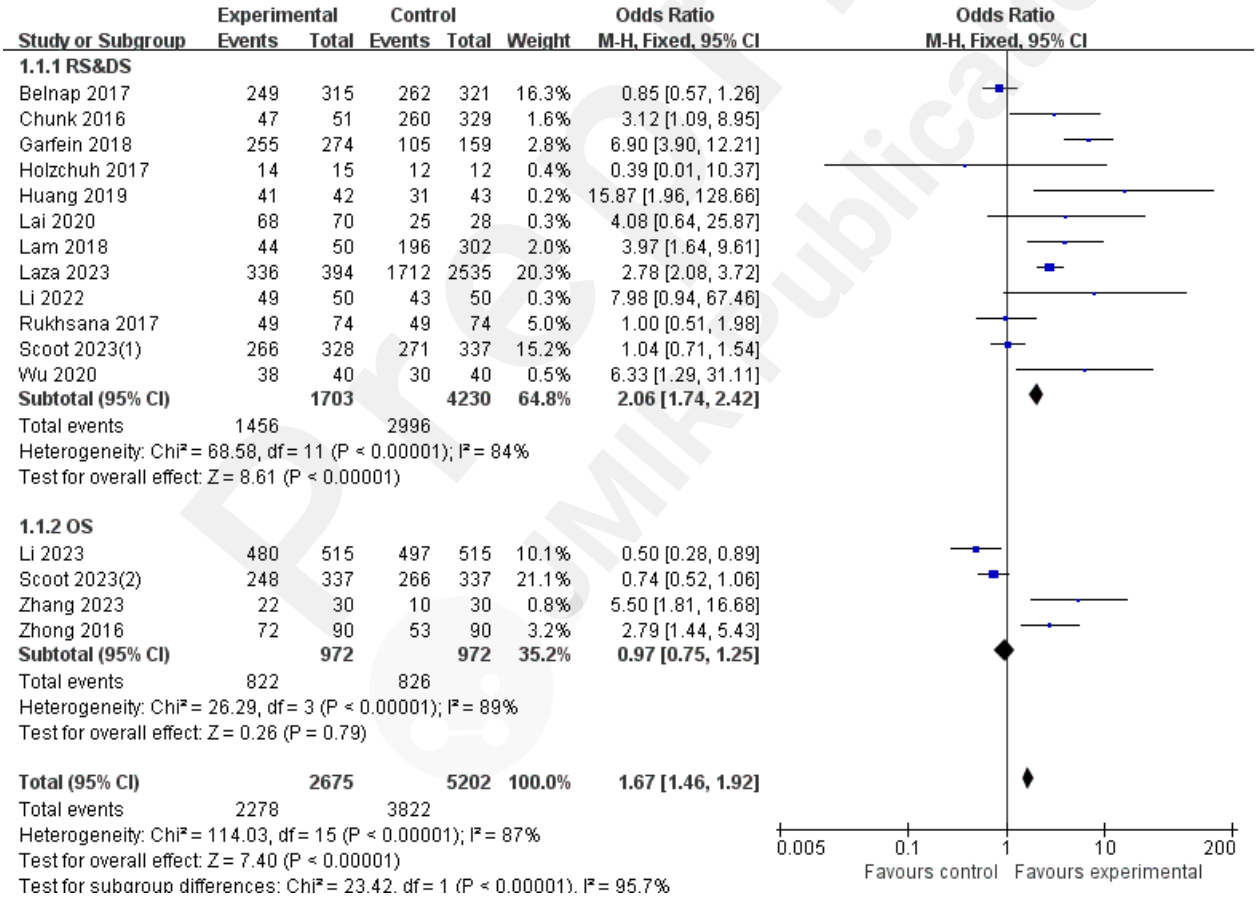

Figure 7. Meta-analysis of completion in OS compared with R/DS. Scott 2023(1): intervention was RS, Scott 2023(2): intervention was online supervision.

Quality Assessment

Three RCTs were assessed with RoB1 and 28 NRCTs were assessed with RBOINS-I. Among RCTs, most result for risk of bias measurement is low. For overall 28 non-randomized controlled studies, 1

study (3.6%) was assessed with high risk of bias, 8 studies (28.6%) were assessed with moderate risk of bias and 19 studies (67.9%) were assessed with low risk of bias. The entire result can be seen in Supplementary information 2.

The assessment of publication bias did not show asymmetry in funnel plot for treatment completion between OS and RS&DS, which suggest the existence of significant heterogeneity and possible publication bias. No other funnel plots were created because less than 10 studies are in the comparisons. The evaluation of heterogeneity was also presented in I^2 test. Significant heterogeneity (I^2 over 90%) were observed in treatment completion between digital health intervention and standard supervision, treatment completion between remote supervision and standard supervision, treatment completion between OS and R/DS. Additional I^2 values can be found in the corresponding forest plots.

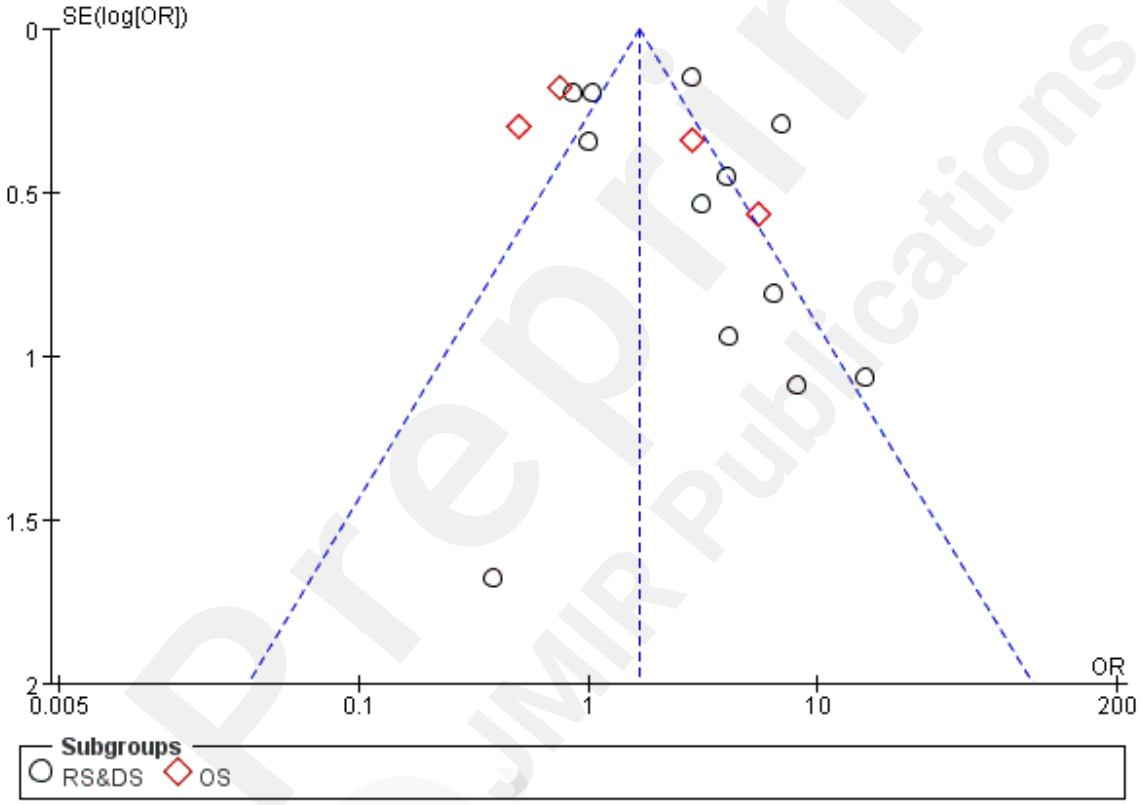

Figure 8. Funnel plot for completion in OS compared with R/DS.

Discussion

Principal Results

Tuberculosis, which became world's leading cause of death from a single infection agent again in 2023, remains a serious unfinished public health issue[1,48]. While causing almost twice as many deaths as HIV/AIDS, tuberculosis is still showing a incredibly high incidence rate with more than 10 million people infected with TB every year[1]. The increasing number of people getting tuberculosis also indicates the high prevalence of latent tuberculosis infection. To advance TB/LTBI programs and move closer to the objective of eliminating tuberculosis, it is imperative to enhance

treatment adherence and improve outcomes. A pivotal aspect of achieving better treatment completion and adherence in LIBI programs involves selecting appropriate interventions to manage and supervise the patients, particularly those with poor adherence, in a manner that is both highly efficient and cost-effective.

After analyzing 31 included studies, we have consistently observed that digital health interventions are associated with improved treatment adherence and higher completion rates compared to standard supervision, particularly in supervising regular medicine adherence. We have recategorized the interventions from these included studies into three categories (remote supervision, direct supervision and online supervision), all of which demonstrate positive impacts on treatment adherence or outcomes. Remote supervision includes telephone or message reminders, though it is replaced by more advanced intervention tools with the development of technology, but its great potential has been confirmed in years of practice and it is still used in many locations. In this review, remote supervision is associated with better treatment completion compared with standard supervision. A Canadian study also reported that message reminders are more cost-effective than standard care and less sensitive to intervention cost[5].

Direct supervision includes DOT and V(D)OT, both of which significantly improved adherence and clinic outcomes. Notably, V(D)OT is associated with superior adherence and clinic outcomes. The WHO recommends DOT as a standard intervention for monitoring adherence in LTBI patients due to its accuracy and reliability. However, its strict requirements and high demand for medical resources limit its global implementation. With advancements in technology, V(D)OT has increasingly replaced DOT. This method enables patients upload videos of themselves taking their medicine, which healthcare workers can review to ensure adherence and send reminders when necessary. V(DOT) offers greater flexibility by eliminating the need for travel, benefiting both patients and health care providers[33]. Additionally, it is more efficient and cost-effective, allowing a single healthcare worker to supervise a larger number of patients compared to DOT. There are generally two primary types of V(D)OT: synchronous and asynchronous. Asynchronous V(D)OT, in particular, offers greater flexibility and patient acceptability[31]. However, V(D)OT may pose challenges for older patients or those unfamiliar with smartphones. Potential barriers include software malfunctions, limited access to digital platforms, and concerns over patient privacy, which may reduce its effectiveness[31,49]. Therefore, a comprehensive evaluation of both the benefits and limitations of these interventions is essential, along with tailored approaches that accommodate individual patient needs.

Online supervision, including EMB and telephone or WeChat-based monitoring, has demonstrated potential in improving adherence and clinic outcomes in LTBI treatment. Studies conducted in China have report relatively high feasibility and acceptability of these interventions[13], aligning with our meta-analysis (OR 1.67, 95%CI 1.46-1.92). Among these methods, telephone and WeChat supervision show a slight advantage over EMBs. However, EMBs are preferred by elderly patients, while younger and middle-aged individuals, who are more familiar with smartphone applications, tend to choose telephone or WeChat monitoring[39]. Telephone and WeChat supervision, which rely on mobile application or software, facilitate daily medication recording and immediate communication with healthcare providers or other patients. In contrast, EMBs automatically log medication intake and issue reminders when doses are missed, ensuring treatment consistency and reducing medication mismanagement or overdosing[50]. Despite these advantages, technical issues

such as connectivity problems, device damage, and long charging times have been reported[15,50]. Moreover, combing telephone or WeChat supervision with EMBs has shown positive effects on treatment completion, suggesting the feasibility of integrated interventions. However, some studies in China have indicated that online supervision may impose an additional burden on patients by complicating the medication-taking process[40]. Furthermore, the long-term impact of these interventions on adherence and clinical outcomes remains uncertain, as their implementation has been relatively recent and most supporting studies have been conducted in China—particularly regarding WeChat supervision. Additional research across diverse settings is necessary to gain a comprehensive understanding of their long-term effectiveness and to inform decision-making. Overall, online supervisions ensures the timeliness, completeness, and accuracy of data recording[16], making it an almost ideal intervention for patients who face difficulties. Although most studies on online supervision have been conducted in China, they encompass diverse settings, including economically developed cities (e.g. Shanghai), economically underdeveloped regions (e.g. Guizhou), high TB burden areas (e.g. Xinjiang), and low TB burden cities (e.g. Beijing). The majority of these studies have reported positive outcomes regarding the impact of online supervision on treatment adherence. The implementation of EMBs in China has also been recognized by the WHO and recommended as a digital heath intervention for monitoring TB treatment[51]. Given these findings, the successful experience of online supervision in China may offer valuable insights for its adoption in other countries.

Heterogeneity Analysis

In this review, substantial heterogeneity was observed both in meta-analysis and sub-group analysis. Several factors may contribute to this variability. First, outcomes are assessed differently across studies: for treatment completion, which is assessed both in European/American studies and Chinese studies, is defined as completing 80% or 90% of the entire treatment; while for treatment adherence, it is mostly measured in Chinese studies by good adherence rate or regular medicine-taking frequency. The slight difference in definition of outcome indicators may introduce heterogeneity. Secondly, high heterogeneity may suggest that intervention is not the solo determination of treatment adherence. According to previous studies, adherence can be influenced by multiple factors, including patient characteristics such as age and gender, the duration and efficiency of the treatment regime, and the level of healthcare or community support available[8]. We included studies with diverse participants characteristics (age and gender), country, as well as treatment regimens and this may contribute to the high heterogeneity. Although high heterogeneity inevitably affects the quality of analysis, we can still conclude that DHIs are promising in improving treatment adherence for the meta-analysis and sub-group analysis both show improved adherence with DHIs compared with traditional supervision. Beyond the effects on adherence, DHIs also have great advantages over traditional supervision in real-world practice for its easy-operation and high efficiency.

Comparison With Prior Work

Our findings align with previous systematic reviews. Pradipta and colleagues reported that message and telephone reminders effectively improve LTBI treatment completion[52], consistent with our conclusions. Additionally, both our review and Pradipta et al.'s study identified direct supervision—through DOT and VOT— as being associated with improved treatment adherence and completion. However, Ridho et al.[53] reported mixed results, with both positive and negative findings, whereas our review predominantly found positive outcomes. This discrepancy may be attributed to

differences in study design and participant characteristics. Pradipta et al.'s review included only RCTs and considered various forms of TB, whereas our analysis focused specifically on LTBI. Similarly, Alipanah et al.[49] found no significant difference in treatment completion between VOT and DOT, differing from our findings. However, their review included both ATB and LTBI patients and was published in 2018, whereas our review focuses exclusively on LTBI, incorporating more recent studies on VOT published after 2018. Jiang et al.[13] also highlighted the effectiveness of EMBs and telephone reminders in enhancing treatment completion and adherence, consistent with our review. They noted that online supervision methods were generally more acceptable to both patients and healthcare workers compared to remote and/or direct supervision. Furthermore, their review emphasized that the widespread adoption of smartphones in China has facilitated the expansion of online supervision. In our review, WeChat— the most widely used social media platform in China— was identified as a key factor in the effectiveness of WeChat-based supervision within online monitoring interventions.

Strengths and Limitations

Although LTBI is less severe than other life-threatening diseases, it carries a risk of progressing to ATB, posing significant health and societal challenges. LTBI treatment typically requires at least six months, and in some cases, up to one or two years to complete. Adherence to medication throughout the entire course is essential for successful treatment outcomes. To our knowledge, this is the first comprehensive systematic review and mate-analysis evaluating the effectiveness of digital adherence interventions compared to standard supervision in LTBI treatment. Our findings indicate that digital health interventions are associated with improved treatment adherence and outcomes, with effectiveness varying across different intervention types. These results suggest that selecting appropriate digital health interventions can enhance the monitoring and management of LTBI programs, leading to greater efficacy and effectiveness. However, this review has certain limitations. Substantial heterogeneity exists in the mate-analysis, no detailed subgroup analysis of the interventions was conducted and potential publication bias is detected. These limitations stem from the predominance of non-randomized studies, inconsistencies in outcome measurement, and presence of confounding factors influencing adherence. Future high-quality research, particularly randomized controlled trials with standardized outcome assessments, is needed to provide more precise insights into the impact of digital health interventions on treatment adherence in LTBI programs.

Our review examined various digital health interventions for improving treatment completion and adherence in LTBI management, including message and telephone reminders, DOT&VOT, electronic pillbox, mobile applications, and WeChat supervision. We provided a detailed, up-to-date, and comprehensive analysis of their effects, highlighting the growing impact and acceptance of online supervision, particularly the success of WeChat-based monitoring in China. However, several limitations should be acknowledged. Firstly, most included studies were observational, with a limited number of RCTs — known as the gold standard in analyzing the effects of interventions, will definitely decrease the overall quality of the results in meta-analysis. Additionally, the lack of standardized outcome measurements introduces a potential risk of bias. Secondly, some studies included both active and latent tuberculosis patients, and in cases where TB type was not specified, those studies were still included. To mitigate this limitation, we extracted only data related to LTBI patients. Furthermore, our analysis focused exclusively on adult LTBI patients without HIV or other underlying conditions, excluding high-risk populations such as children and healthcare workers.

Future research should explore the effectiveness of DHIs in these groups. Lastly, our mate-analysis included comparisons between DOT and non-DOT standard supervision, combining these studies to provide a broader assessment. However, similar methodological challenges are common in reviews evaluating interventions for improving treatment adherence. A more refined approach in future studies could enhance the accuracy and applicability of findings.

Conclusion

This review demonstrates that DHIs can enhance adherence and clinical outcomes in LTBI treatment and management. Both remote supervision (e.g., message and telephone reminders) and direct supervision (DOT&V(D)OT) are associated with improved treatment completion and adherence compared to standard supervision. Similarly, online supervision methods, including electronic medicine box, telephone application and WeChat supervision, also show a positive impact. Among these, mobile applications and WeChat-based supervision are linked to higher treatment completion rates compared to electronic medicine box. However, several challenges exist in implementing DHIs, such as technology errors and limited internet access. Additionally, adherence is influenced by factors such as treatment duration and patient characteristics. Therefore, further research is required to improve treatment adherence through DHIs. Existing evidence highlights the need for a transdisciplinary investigation into the complex factors influencing adherence, including technological feasibility, patient behavioral economics, and healthcare system readiness. This approach will facilitate the development of adaptive, context-sensitive implementation frameworks that optimize adherence to LTBI treatment.

Multimedia Appendix 1

PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) checklist

Multimedia Appendix 2

search strategies and results

Multimedia Appendix 3

quality assessment of each study

Conflicts of interest

None declared

Abbreviations

LTBI latent tuberculosis
ATB active tuberculosis
DHI digital health intervention
RCT randomized controlled trails
NRCT non-randomized controlled trails
OR odd ratio
RS remote supervision
DS direct supervision
OS online supervision
DOT direct observed therapy
V(D)OT video (directly) observed therapy

EMB electric medicine box
TA telephone application

Data availability
All data analyzed in this review are included in this article and its supplementary files.

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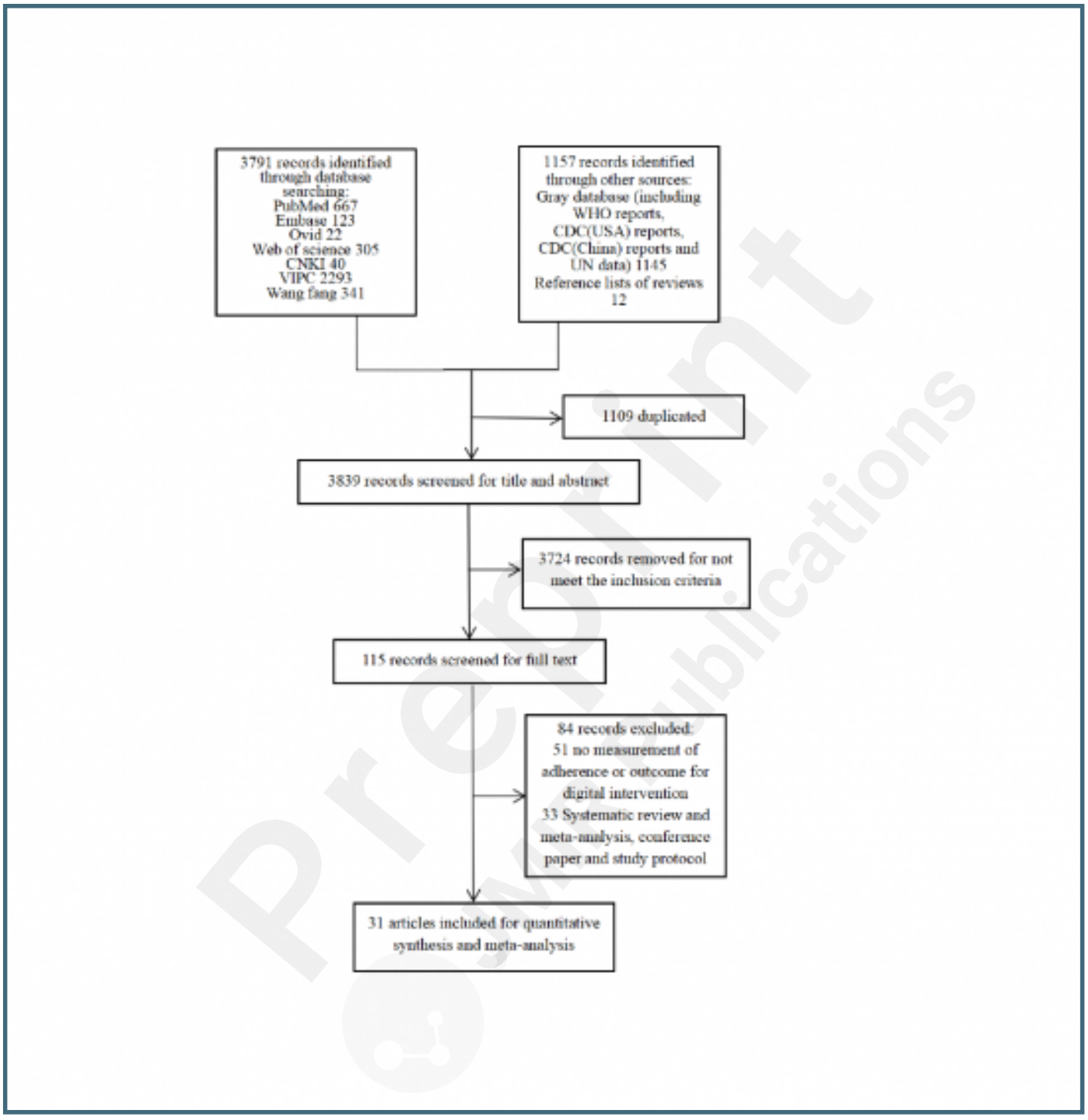
Supplementary Files

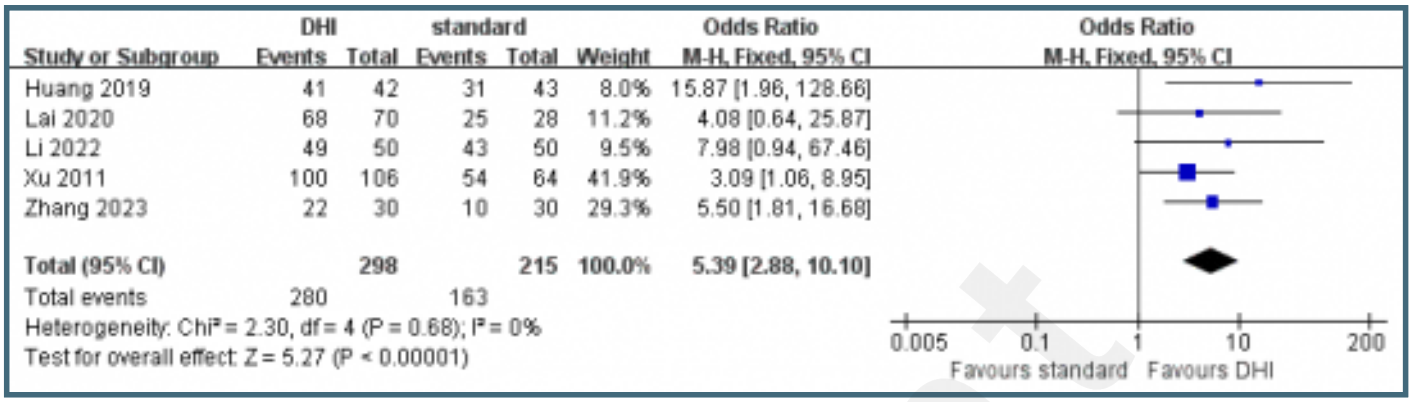
Figures

This figure shows the summary of study selection.

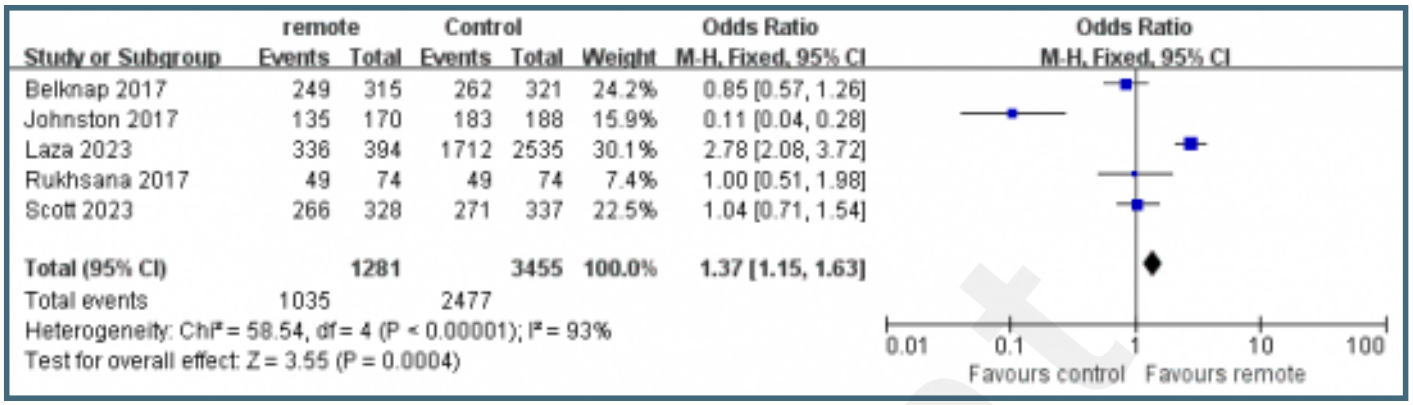


This figure shows Meta- analysis of treatment completion in DHIs (RS&DS&OS) compared with standard supervision.

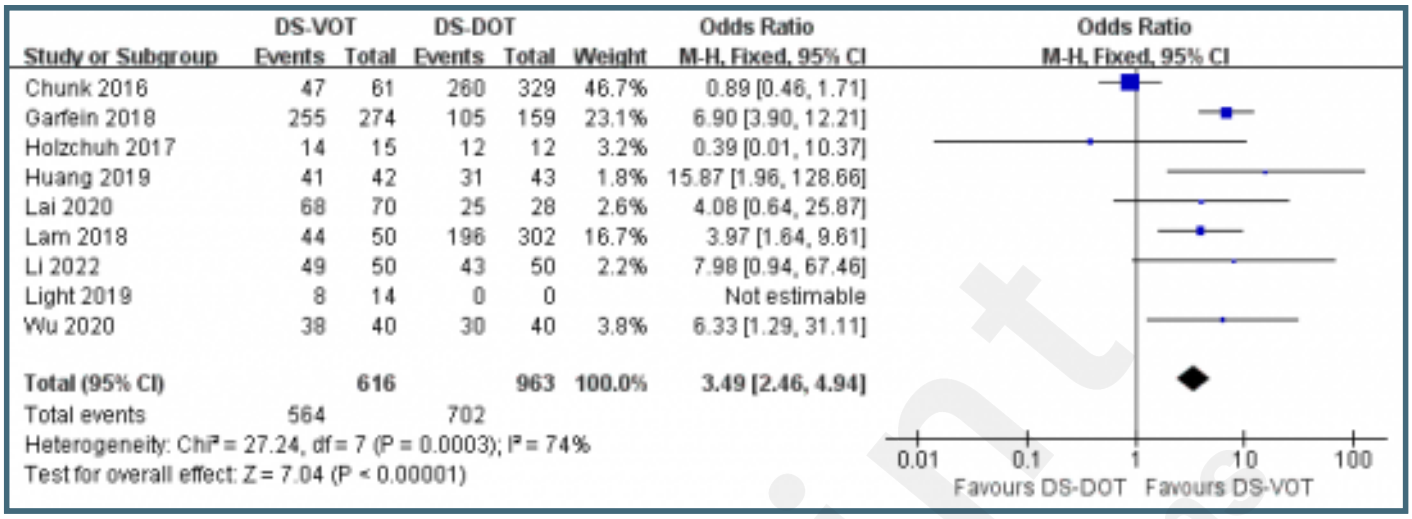
This figure shows meta-analysis of adherence (regular medicine-taking) in DHIs (RS&DS&OS) compared with standard supervision.



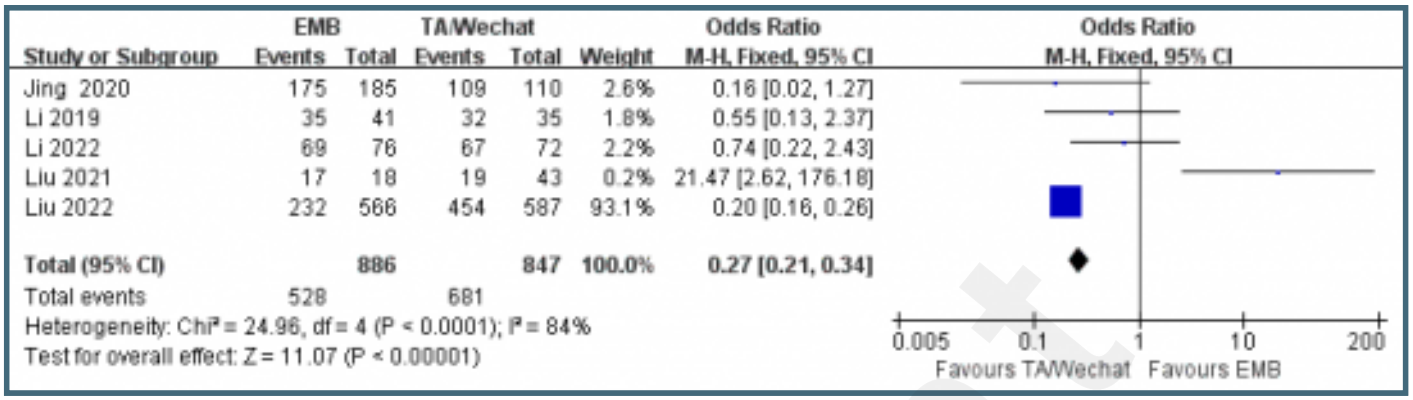
This figure shows meta-analysis of completion in remote supervision compared with standard supervision.



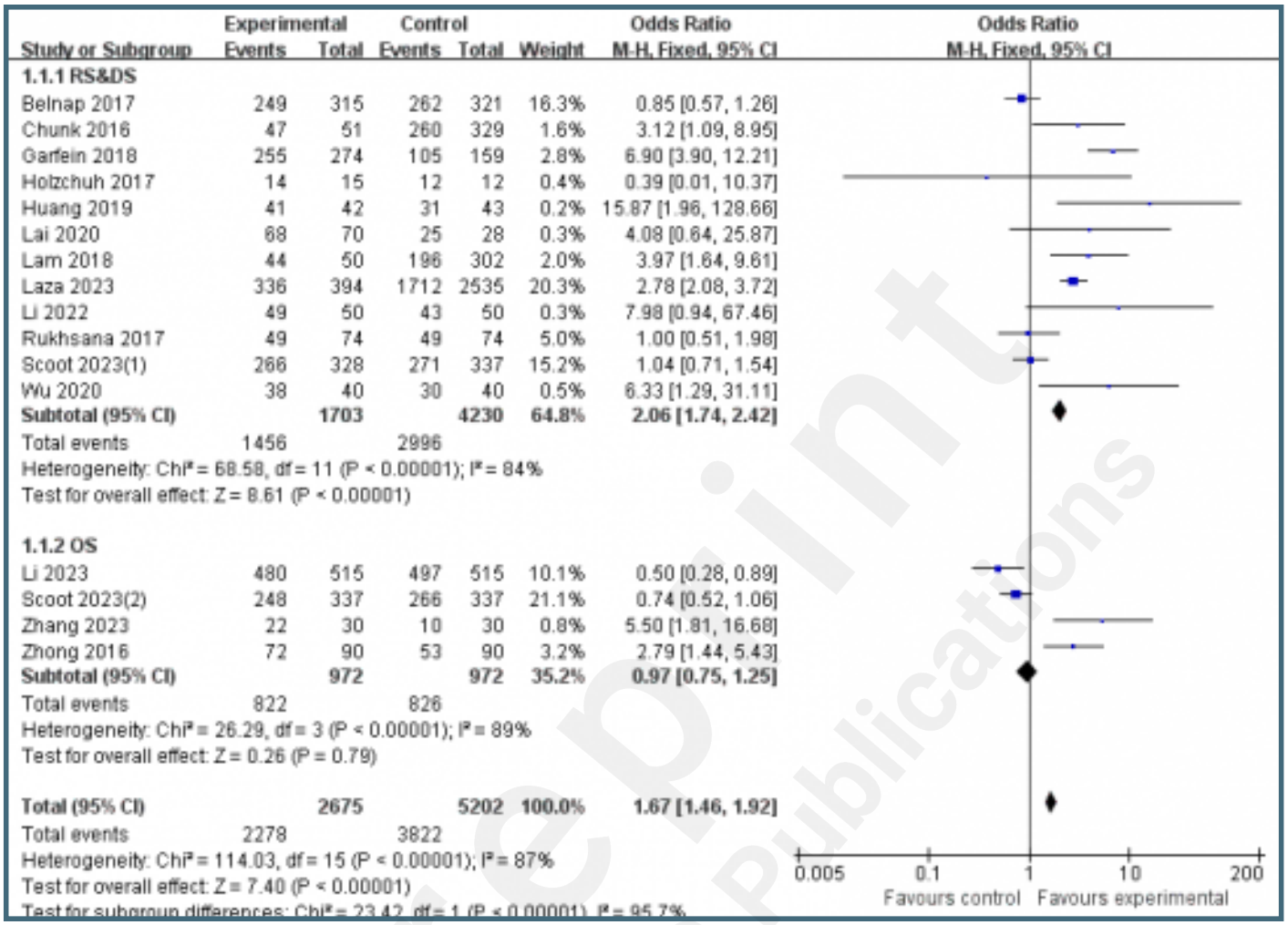
This figure shows meta-analysis of adherence (including completion) in direct supervision compared with standard supervision.



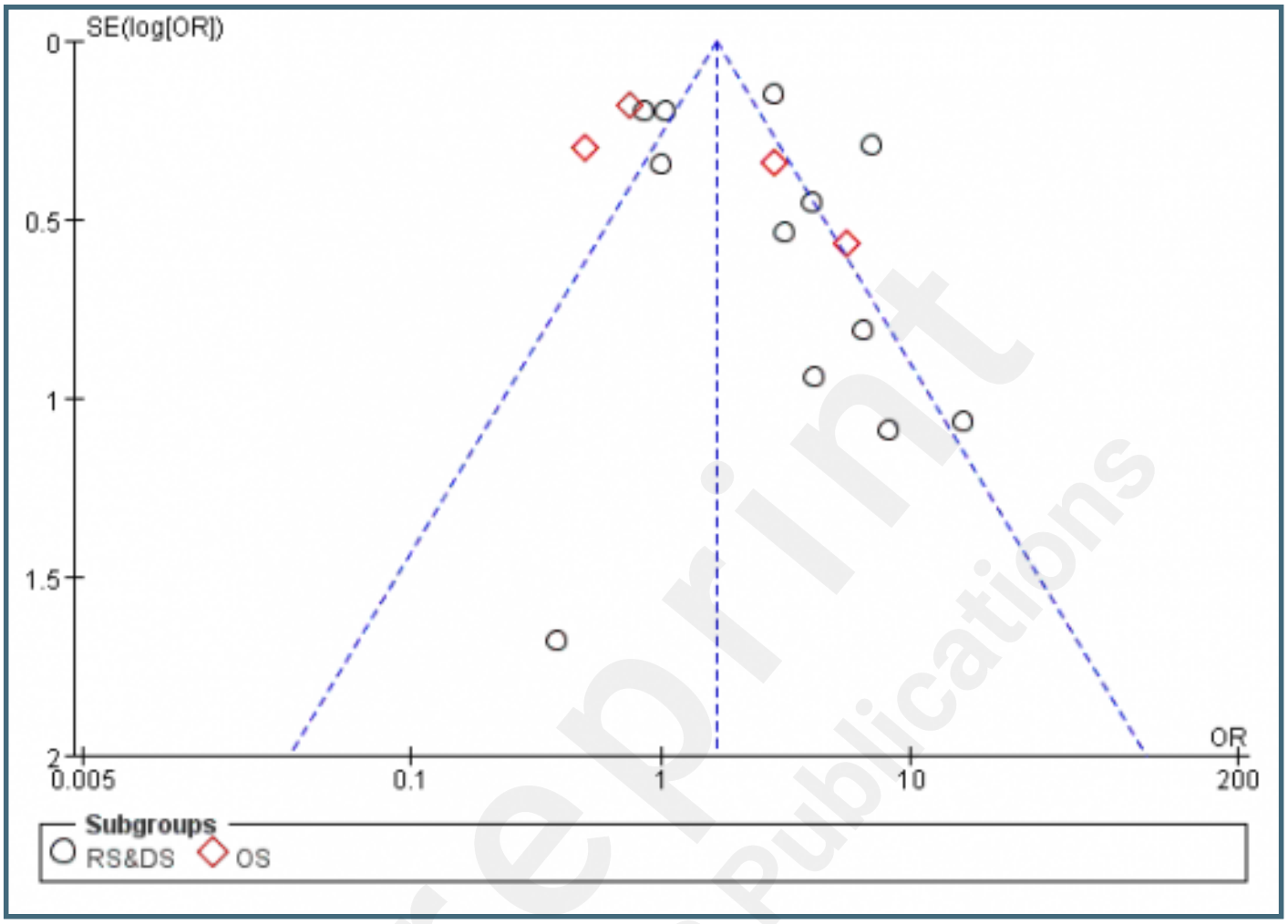
This figure shows meta-analysis of adherence (regular medicine-taking and good adherence) in EMB compared with TA/WeChat supervision.



This figure shows meta-analysis of completion in OS compared with R/DS.



This figure shows Funnel plot for completion in OS compared with R/DS.



Multimedia Appendixes

PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) checklist.
URL: http://asset.jmir.pub/assets/ef49251ec2b009f55df6d87b221f8e23.docx

Search strategies and results.
URL: http://asset.jmir.pub/assets/a56bbac9d4107361705e183618b893a9.docx

The result of quality assessment of each study.
URL: http://asset.jmir.pub/assets/c2cf7cbe49b6632c5f8c3e9f46efb1ad.docx