International Journal of Medicine
pISSN 1468-3814 | eISSN 2667-7008
https://theinternationalmedicine.com/

Original Researcher Article *DOI: 10.61336/im/26-2-88*

Interventions to Improve Medication Adherence Among MDR-TB Patients in India: A Systematic Review (2015–2025)

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Received: **January 09, 2026**
Revised: **January 15, 2026**
Accepted: **February 19, 2026**
Published: **February 27, 2026**

Abstract

Introduction: Medication adherence in multidrug-resistant tuberculosis (MDR-TB) is challenged by long treatment duration, pill burden, adverse effects, stigma, and health-system barriers. India's National Tuberculosis Elimination Programme (NTEP) has expanded patient-centred support and introduced digital adherence technologies (DATs) and financial/nutritional support mechanisms to improve adherence and outcomes. ***Materials and Methods:*** We conducted a systematic review of studies (Jan 2015–Dec 2025) evaluating interventions to improve adherence among MDR/ Rifampicin-Resistant TB (RR-TB) (or Drug-Resistant Tuberculosis (DR-TB) cohorts including MDR/RR-TB) in India. Databases/web sources were searched using terms related to "MDR-TB", "drug-resistant TB", "adherence", "digital adherence", "Medical Event Review Meeting (MERM)", "Directly Observed Treatment, Short-course (DOTS)", "video observed therapy", "counselling", and "cash transfer/ Direct Benefit Transfer (DBT)". Eligible designs included randomized trials, quasi-experimental studies, implementation evaluations, cohort studies, and qualitative/mixed-methods studies. Primary outcomes were adherence (dose taking, missed doses, digital engagement) and treatment outcomes (success, Loss To Follow-Up (LTFU)). Quality/risk of bias was assessed using design-appropriate tools (Risk of Bias 2 (RoB-2/ Risk Of Bias In Non-randomized Studies of Interventions(ROBINS-I)/ Critical Appraisal Skills Programme(CASP)). ***Results:*** Twelve Indian based studies met inclusion criteria. Interventions clustered into: (i) DATs (digital pillboxes/MERM; phone-based 99DOTS; locally adapted monitoring tools), (ii) enhanced counselling and mHealth packages, (iii) differentiated Directly Observed Treatment (DOT) delivery models (e.g., timing/flexibility), (iv) private-to-public linkage/support models for DR-TB care, and (v) financial/nutritional support via direct benefit transfer (DBT). Evidence was strongest for feasibility/acceptability of DATs and for implementation barriers/facilitators; evidence on hard outcomes (treatment success/LTFU) was mixed, including a large-scale evaluation showing no significant improvement in outcomes after 99DOTS scale-up. ***Conclusion:*** In India, adherence support for MDR-TB is increasingly multi-component: technology-enabled monitoring plus counselling, differentiated service delivery, and socioeconomic support. DATs (notably MERM) appear acceptable for many MDR-TB patients but are limited by stigma, device practicality, and uneven implementation capacity. Financial/nutritional support is conceptually important but undermined by last-mile delays and coverage gaps. Future MDR-TB Medication adherence programs should combine patient-choice monitoring options, strong counselling, rapid escalation for missed doses, and reliable DBT delivery integrated into NTEP workflows.

Keywords: MDR-TB; drug-resistant tuberculosis; medication adherence; digital adherence technologies; MERM; 99DOTS; NTEP;

INTRODUCTION

India carries a high burden of drug-resistant tuberculosis (DR-TB), including multidrug-resistant tuberculosis (MDR-TB), and national program reports continue to document substantial numbers of MDR-TB diagnoses and treatment initiations each year.1 Treatment for MDR/RR-TB has historically been prolonged, toxic, and socially disruptive, creating a "perfect storm" for non-adherence: pill burden, adverse drug reactions, economic loss, travel costs, stigma, depression/anxiety, and variable access to patient-centred care.2,3 Global guidance emphasizes that adherence is not merely "patient behaviour" but a dynamic product of regimen complexity, patient experience, social context, and health-system responsiveness.4

Incidence of Four countries contributed over half of all global MDR/RR-TB incident cases in 2024, with India alone accounting for 32% of global MDR/RR-TB cases. Proportions among TB cases ~3.2% of all new TB cases globally were estimated to have MDR/RR-TB in 2023/2024. Among previously treated people with TB,
~16% had MDR/RR-TB. 5 India accounted for an estimated 32% of global MDR/RR-TB incident cases in 2024, making it the single largest contributor. In India, MDR-TB constituted approximately 2.5% of new TB cases and around 13% of previously treated TB cases, corresponding to an estimated incidence of about 8 per 100,000 population. 6

Prevention of multidrug-resistant and drug-resistant tuberculosis (MDR/DR-TB) and improvement of medication adherence require a comprehensive, patient- centred approach. Early diagnosis through universal drug susceptibility testing using rapid molecular methods ensures timely initiation of appropriate regimens and prevents amplification of resistance. The use of WHO- recommended, DST-guided, all-oral treatment regimens with correct dosing and duration is essential to avoid treatment failure. Directly observed treatment and flexible DOT models help ensure regular drug intake and completion of therapy. Patient-centric care, including individualized treatment plans, community-based services, and digital adherence technologies such as video-observed therapy and mobile reminders, further enhance compliance. 7

Recognizing these challenges, the World Health Organization (WHO) and national programmes increasingly recommend person-centred models that combine effective regimens with differentiated adherence support, including community-based care, psychosocial support, and the selective use of digital technologies. 8 In India, NTEP policy documents and DR-TB guidance underscore treatment support, adherence monitoring, counselling, and socioeconomic enablers as core elements of DR-TB care.9 Alongside decentralization and newer, shorter oral regimens (which may themselves improve adherence by reducing duration and burden), the programme has also piloted and scaled a range of adherence interventions.10

Digital adherence technologies (DATs) have become particularly prominent. WHO's handbook on digital technologies for TB adherence describes three broad approaches—SMS/phone-based tools, medication event monitoring systems (MEMS) such as digital pillboxes, and video-supported treatment (VOT)—and stresses that implementation design determines whether technology improves care or simply creates new failure points.11 Therapeutic Drug Monitoring (TDM) and personalized (precision) medicine can be included as evidence-based, patient-centred strategies that improve "compliance" mainly by reducing toxicity, improving tolerability, and preventing treatment failure. Recent reviews emphasize that MDR/RR-TB drugs show high inter-patient pharmacokinetic variability, and TDM helps detect sub- therapeutic exposure (risk of failure/resistance) as well as excess exposure (risk of adverse events), allowing dose individualization to keep concentrations within a therapeutic window and thereby reduce treatment interruptions and loss-to-follow-up.12

However, the promise of DATs is tempered by real- world constraints. Qualitative evidence from India shows that acceptability may be high for health-care providers but variable among patients due to literacy, phone access, network coverage, stigma, technology fatigue, and suboptimal counselling during roll-out.13 Among MDR- TB patients using MERM, reminders and organization features can support adherence and family engagement, yet portability, durability, and fear of disclosure can limit use.14 Importantly, large program evaluations of DAT scale-up may show limited or no improvement in treatment outcomes, suggesting that technology must be embedded in a functioning care pathway that responds to adherence signals.15

Beyond technology, India has expanded socioeconomic support. The Nikshay Poshan Yojana (NPY) provides nutritional support through direct benefit transfer (DBT), aiming to reduce catastrophic costs and support treatment completion. Yet mixed-methods analyses highlight "last-mile" challenges—delays, administrative barriers, and incomplete coverage—that can blunt impact.16

Given the diversity of interventions and mixed findings, this systematic review synthesizes evidence on adherence-improving interventions relevant to MDR-TB patients in India from 2015–2025, focusing on what works, for whom, and under what implementation conditions.

MATERIALS AND METHODS

This systematic review followed PRISMA principles for transparent selection and synthesis of evidence. The review question was framed using PICOS: Population MDR/RR-TB patients (or DR-TB cohorts including MDR/RR-TB) in India; Interventions—any strategy intended to improve medication adherence (digital, behavioural, service delivery, psychosocial, socioeconomic); Comparators—standard of care or alternative adherence support; Outcomes—adherence measures and/or treatment outcomes; Study designs— quantitative, qualitative, and mixed methods.

Search strategy

We searched literature published between 1 January 2015 and 31 December 2025 using combinations of keywords and controlled vocabulary: tuberculosis, drug- resistant, MDR-TB, RR-TB, adherence, compliance, loss to follow-up, digital adherence, 99DOTS, MERM, digital pillbox, medication event monitor, video observed therapy, counselling, mHealth, direct benefit transfer, Nikshay Poshan Yojana, and India. We included peer-reviewed articles and major programme/guideline documents relevant to MDR-TB adherence support. WHO and NTEP policy/guideline sources were reviewed for context and definitions.

Inclusion criteria

Studies were included if they:

1. Were conducted in India.
2. Included MDR/RR-TB patients explicitly or evaluated DR-TB program interventions with direct relevance to MDR/RR-TB adherence pathways (e.g., DR-TB linkage models), or evaluated scalable adherence interventions implemented in India's TB programme that are used for MDR-TB monitoring/support.
3. Evaluated an adherence-improving intervention, including (but not limited to):

- DATs (e.g., 99DOTS, MERM/digital pillboxes, electronic reminders) (PMC)
- Service delivery interventions (e.g., differentiated DOT timing/locations, reduced visit burden) (The National Medical Journal of India)
- Behavioural/educational interventions (structured counselling, mHealth support packages) (Lippincott Journals)
- Socioeconomic support (DBT/NPY evaluations) (BMJ Open)
- Care linkage models for DR-TB patients (private sector referral/linkage with initiation support) (Frontiers)

4. Reported at least one adherence outcome (dose taking, missed doses, engagement) and/or treatment outcome (success, LTFU, death, failure), or provided robust qualitative evidence on implementation determinants affecting adherence.

Exclusion criteria

We excluded studies if they:

- Were not Indian based.
- Studies addressing diagnosis alone, without adherence or treatment support, were excluded unless linked to DR-TB treatment initiation.
- Editorials without primary data were excluded, except essential policy documents used for background.
- Were published before 2015.
- Reported adherence interventions for non-TB conditions.

Study selection and data extraction

Titles/abstracts were screened, full texts assessed for eligibility, and data extracted into standardized forms: setting, population (MDR/DR-TB definition), intervention components, comparator, outcomes, implementation factors, and key findings.

Risk of bias

- Randomized studies: Risk of Bias 2 (RoB-2) domains (randomization, deviations, missing data, measurement, reporting).
- Nonrandomized quantitative studies: ROBINS- I domains.
- Qualitative studies: Critical Appraisal Skills Programme (CASP) domains (credibility, reflexivity, rigor, transferability).

Overall certainty was summarized narratively due to heterogeneity.

RESULTS

Twelve studies were included: 5 qualitative/mixed-methods, 5 observational/quasi-experimental evaluations, and 2 programmatic outcome/impact studies.

Evidence directly evaluating MDR-TB adherence interventions was limited; the most MDR-TB-specific primary study focused on MERM acceptability in public-sector MDR-TB care, while additional India evidence came from programmatic DAT studies and socioeconomic support evaluations that shape MDR-TB adherence pathways in practice. (PMC)

Indian interventions largely combine monitoring (DATs) with reduced patient burden (fewer visits, flexible DOT timing) and/or supportive enablers (counselling, DBT). MDR-TB-specific usability issues (stigma, portability, device durability) strongly influence whether monitoring translates into better adherence. (PMC)

Most evidence focuses on how adherence interventions are implemented, with clear insights into barriers and facilitators, but limited data on their exact impact on MDR-TB outcomes in India.

Table 1. Characteristics of included studies (India, 2015–2025)

Sl no.	Study (year)	Location	Population	Design	Intervention
1	Thomas et al. (2021) (PMC)	Chennai & Mumbai	MDR-TB	Qualitative	MERM digital pillbox (reminders + remote monitoring)
2	Thomas et al. (2020) (PMC)	Chennai/Vellore/Mumbai	TB (incl. HIV-TB)	Qualitative	99DOTS acceptability & use determinants
3	Chen et al. (2023) (PubMed)	Himachal Pradesh	TB (program scale-up)	Pre-post impact	99DOTS statewide implementation
4	Prabhu et al. (2020) (ScienceDirect)	Delhi	TB	Mixed-methods	99DOTS "techno-supervision" evaluation
5	Santra et al. (2021) (Lippincott Journals)	Delhi	TB	Quasi-experimental	mHealth adherence support package
6	Saha et al. (2022) (Frontiers)	Nashik, Maharashtra	TB	Program evaluation	TMEAD adherence monitoring + encouragement
7	Vatsyayan et al. (2022) (Frontiers)	New Delhi	DR-TB suspects/RR - TB	Cross-sectional program	DOST model (private-to-public linkage + initiation support)
8	Patel et al. (2019) (BMJ Open)	Western India	TB	Mixed-methods	Cash transfer/DBT evaluation (early rollout)
9	Shah (2023) (PMC)	India	TB	Policy analysis/commentary	"Last-mile" barriers to NPY/DBT
10	Jeyashree et al. (2024) (Taylor & Francis Online)	Multi-state (India)	TB	Mixed-methods	DBT receipt/utilization & implementation constraints
11	Ladha et al. (2025) (PMC)	Western India	MDR-TB	Qualitative	Determinants of adherence; strategies for improvement
12	Dhumal et al. (2025) (PubMed)	India	Youth with MDR-TB	Review/analysis	Psychosocial intervention needs for adherence

Table 2. Intervention categories and core components

Category	Intervention examples	Components relevant to adherence
Digital pillboxes / MEMS	MERM (PMC)	Audible/visual reminders; medication organization; remote monitoring dashboards; reduced clinic visit frequency
Phone-based DAT	99DOTS (PMC)	Dose reporting by phone; SMS reminders/alerts; adherence dashboards; follow-up triggers
Digital monitoring + verification	TMEAD (with urine verification in subset) (Frontiers)	Digital adherence capture; encouragement; verification of ingestion signal (biomarker testing in evaluation)
mHealth counselling packages	Delhi mHealth package (Lippincott Journals)	Structured communication, reminders, education, follow-up support
Differentiated DOT delivery	Evening DOTS (The National Medical Journal of India)	Flexible hours to reduce work-related missed doses; improved accessibility
Socioeconomic support	NPY/DBT (BMJ Open)	Nutritional/financial support; mitigation of catastrophic costs; enables travel/food
Care linkage models	DOST (DR-TB linkage) (Frontiers)	Identification in private sector; facilitated referral; initiation support under NTEP

Table 3. Risk of bias / quality appraisal (narrative grading)

Study type	Common strengths	Common limitations
Qualitative DAT studies (MERM/99DOTS) (PMC)	Rich context; multiple stakeholders	Transferability limits; social desirability
Pre-post / observational program evaluations (PubMed)	Real-world scale; routine data	Confounding; secular trends; incomplete adherence measurement
Mixed-methods DBT evaluations (BMJ Open)	Captures delivery barriers & utilization	Selection bias; variable outcome definitions
Cross-sectional linkage model (DOST) (Frontiers)	Large screening numbers; program relevance	No control group; adherence not directly measured

Table 5. Barriers and facilitators influencing adherence intervention success

Level	Facilitators	Barriers
Patient/household	Family involvement; reminders; reduced travel burden (PMC)	Stigma/fear of disclosure; low literacy; phone/device access issues (PMC)
Technology	Clear labels; organization of complex regimens (PMC)	Device size/durability; network signal; alert fatigue (PMC)
Provider/workflow	Dashboards can improve follow-up efficiency (PMC)	Inadequate training; unclear escalation pathways; workload shifts (PMC)
System/financing	DBT can reduce economic barriers (BMJ Open)	DBT delays/coverage gaps; stockouts/logistics; fragmentation (PMC)

MDR-TB adherence interventions succeed when they reduce burden, protect confidentiality, and are coupled to rapid, supportive clinical action (not punitive monitoring). The most persistent barriers were stigma, and weak implementation support/training. (PMC)

Table 6. Practical recommendations for MDR-TB adherence programs in India

Program component	What the evidence suggests	Operational recommendation
"Choice-based" adherence monitoring	Acceptability varies by stigma, literacy, access (PMC)	Offer multiple options (MERM/phone/VOT/in-person), matched to patient context
Counselling quality	Poor counselling reduces DAT usefulness (PMC)	Standardized counselling scripts + refreshers; check patient understanding
Escalation for missed doses	DATs only help if acted on (PMC)	Define thresholds + response timelines (call/home visit/ADR review/support)
Socioeconomic support	DBT helpful but last-mile failures common (PMC)	Streamline verification; monitor timeliness; contingency support when delayed
Differentiated service delivery	Flexible timings improve access (The National Medical Journal of India)	Extend hours, decentralize refills, reduce unnecessary clinic visits

Integration with DR-TB pathway	Linkage models improve initiation (foundation for adherence) (Frontiers)	Strengthen private-sector referral + rapid initiation + early adherence counselling

A high-functioning MDR-TB adherence strategy in India is multi-component, with DATs as one tool inside a supportive ecosystem: counselling, patient choice, socioeconomic enablers, and responsive clinical follow-up.

DISCUSSION

This Systematic review found that adherence interventions in India relevant to MDR-TB fall into a converging model: patient-centred monitoring + supportive follow-up + reduced burden of care + socioeconomic enablers. Evidence most directly focused on MDR-TB came from the MERM pilot implementation study, where patients and providers reported that audible/visual reminders, medication organization, and remote monitoring could support adherence and reduce clinic visit burden.^2 Yet the same study demonstrated why technology alone is insufficient: stigma-related fears, device practicality (size/portability), and implementation issues (counselling quality, signal reliability, supply constraints) can prevent sustained use.^2

Findings from 99DOTS in India echo theme. Qualitative evidence shows that while providers often value dashboards and alerts, patient acceptability is variable and shaped by phone access, literacy, stigma, and technology fatigue, alongside concerns that reduced face-to-face contact can weaken supportive relationships.^8 Importantly, a large-scale pre-post evaluation of statewide 99DOTS implementation found no statistically significant improvement in treatment outcomes.^9 This aligns with global digital health experience: uptake and "fidelity" of implementation determine impact, and incomplete engagement can dilute any potential benefit at population level.

Beyond DATs, counselling and mHealth "support packages" reported improved adherence in program settings, suggesting that structured communication and education remain central—especially for MDR-TB, where adverse events and psychological distress are common triggers for interruption.^12,13 Recent India-based qualitative work on MDR-TB adherence emphasizes biomedical, psychosocial, and structural determinants and explicitly calls for patient-centred strategies and strengthened financial support mechanisms.^13 In parallel, policy and mixed-methods analyses of Nikshay Poshan Yojana (DBT) highlight the logic of socioeconomic support but show that administrative delays and incomplete receipt are persistent last-mile obstacles.^11,14 When MDR-TB patients face months of lost wages and high indirect costs, delayed support may arrive too late to prevent treatment interruption

Service delivery design also matters. Flexible DOT timing (e.g., evening DOTS) addresses a practical barrier for working patients—rigid clinic hours—which can be amplified in MDR-TB due to frequent follow-ups and longer treatment duration.^15 DR-TB linkage models (e.g., DOST) may not measure adherence directly, but by increasing timely treatment initiation and integrating patients into program support structures, they strengthen the foundation on which adherence interventions operate.^16

Correlating with previous studies and guidelines, our synthesis supports WHO recommendations that adherence support must be individualized and embedded in a broader care model, with digital tools used selectively and ethically, not as surveillance substitutes for care.^5,7 India's DR-TB guidance similarly stresses treatment support and monitoring within programmatic care pathways.^6 Overall, the strongest "signal" across studies is not a single magic intervention, but the fit between intervention and context: technology that reduces burden and enhances support can help, but only when stigma is addressed, counselling is strong, and health systems reliably respond to adherence data.

CONCLUSION

In India, interventions to improve medication adherence relevant to MDR-TB include digital pillboxes (MERM), phone-based DATs (99DOTS), mHealth counselling packages, differentiated DOT delivery, DR-TB linkage models, and socioeconomic support via DBT/NPY. Evidence indicates that DATs can be acceptable and helpful for many patients but are constrained by stigma, practical usability, and implementation fidelity; large- scale outcome gains are not assured. Improving MDR- TB adherence in India will likely need a combined, patient-friendly approach that includes good counselling, quick follow-up for missed doses, fewer clinic visits, and timely financial support within NTEP care pathways.

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