Section: Community Medicine

Systematic Review & Meta-analysis

ADHERENCE TO ANTIRETROVIRAL THERAPY AND ASSOCIATED BARRIERS AMONG PEOPLE LIVING WITH HIV (PLHIV) IN INDIA: A SYSTEMATIC REVIEW AND META-ANALYSIS

P.M. Siva[1], Sunitha Kandasamy[2], K. Christa[3], M. Kavisri[4], R. Deepa[5], R. Kavipriya[6], D. Daniela[7]

[1,3] *Associate Professor, Department of Community Medicine, Tirunelveli Medical College, India.*
[2] *Professor and Head, Department of Community Medicine, Tirunelveli Medical College, India.*
[4-7] *CRMI, Department of Community Medicine, Tirunelveli Medical College, India.*

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Corresponding Author:
Dr. P.M. Siva,
Associate Professor, Department of Community Medicine, Tirunelveli Medical College, Tirunelveli, Tamil Nadu, India.
Email: bonitospm@gmail.com

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ABSTRACT

Background: Human immunodeficiency virus (HIV) continues to pose a major global public health challenge.[1] Effective antiretroviral therapy (ART) depends on high adherence.[2,3] Poor adherence leads to treatment failure, drug resistance, disease progression, and increased transmission.[4,5] Identifying barriers to ART adherence in India is essential for improving outcomes among people living with HIV (PLHIV).[6,7] **Objective:** To systematically review and meta-analyze quantitative evidence on ART adherence and its barriers among people living with HIV in India.

Materials and Methods: We searched PubMed and the Cochrane Library for studies published from January 2016 to February 2026 that assessed ART adherence and reported barriers to ART adherence among PLHIV in India. Qualitative studies and those without adherence rates were excluded. Data extracted included study characteristics, adherence definitions, measurement methods, adherence estimates, and reported barriers. We calculated the pooled proportion of adherence using a random-effects meta-analysis.

Results: Sixteen studies involving 5,090 participants were included: 13 cross-sectional, 2 longitudinal, and 1 case series. Reported adherence ranged from 16.6% to 97.5%, with a pooled adherence of 74% (95% CI: 63–84%) and high heterogeneity (I^2 = 98.7%). Subgroup analysis revealed that measurement tools significantly influenced adherence estimates, with MAS/MAQ scales reporting the highest (94%) and visual analogue scales (VAS) the lowest (64%). Common barriers included forgetfulness, alcohol use, HIV-related stigma, depression or emotional stress, long travel distances to ART centers (>50 km), and financial constraints.

Conclusion: ART adherence among PLHIV in India remains suboptimal and is influenced by patient, therapy, socioeconomic, and health system factors. Enhancing adherence counseling, integrating mental health and alcohol use support, improving access to ART services, and implementing flexible, patient-centered refill systems are essential to improve long-term outcomes.

Keywords: HIV, antiretroviral therapy, adherence, barriers, PLHIV, India, systematic review, meta-analysis.

INTRODUCTION

HIV infection remains a major global public health issue, particularly in low- and middle-income countries.[1] Antiretroviral therapy (ART) has significantly reduced HIV-related morbidity and mortality, making HIV a chronic, manageable condition.[8] However, ART effectiveness depends on optimal adherence, with about 95% adherence needed for sustained viral suppression and reduced drug resistance.[9,10] Poor adherence can cause virological failure, disease progression, increased

transmission, and the emergence of resistant viral strains.[11,12] Although free ART is available through national programs such as the National AIDS Control Organization (NACO) in India, adherence remains inadequate in many areas.[10,13] Socioeconomic, psychological, health-system, and treatment-related factors all contribute to poor adherence in Indian populations.[10,13,14] This systematic review aims to synthesize the magnitude of adherence to ART and its barriers among people living with HIV (PLHIV) in India.

Objectives

Primary objective

To synthesize the magnitude of adherence to anti-retroviral therapy (ART) among people living with HIV (PLHIV) in India.

Secondary objectives

To identify barriers affecting ART adherence.

MATERIALS AND METHODS

Literature search

This systematic review and meta-analysis were conducted in accordance with the MOOSE (Meta-analyses Of Observational Studies in Epidemiology) guidelines[15]. We conducted a systematic literature search in MEDLINE (PubMed) and the Cochrane Library for studies published from January 2016 to February 2026. The search strategy used text words and MeSH terms related to HIV and adherence, including "antiretroviral therapy," "medication adherence," "barriers to adherence," "patient compliance," "treatment failure," "HIV," "PLHIV," "AIDS," and "India." Reference lists of included articles and relevant reviews were also hand-searched for additional studies.

Eligibility criteria

We included observational studies from India (January 2016 to February 2026) that reported quantitative estimates of ART adherence and assessed barriers to ART adherence among PLHIV. Studies conducted outside India, qualitative studies, reviews, case reports, and those lacking adherence data or barrier assessment were excluded.

Study selection and data extraction

Five reviewers (investigators) independently screened titles and abstracts, then assessed full texts using predefined criteria. Disagreements were resolved by discussion and consensus. For each study, we extracted data on adherence definitions, adherence estimates, study design, setting, sample size, population characteristics, recall period, study time frame, and adherence assessment method (such as pill count, self-report, visual analogue scale, or adherence scale). We also collected information on reported barriers and methodological quality indicators.

Identification of included studies

Figure 1 shows the study identification and selection process. The initial search identified 22 citations; 6 were excluded as detailed in Figure 1. The remaining 16 studies, with 5,090 participants, met the inclusion criteria and were included in the systematic review and meta-analysis.

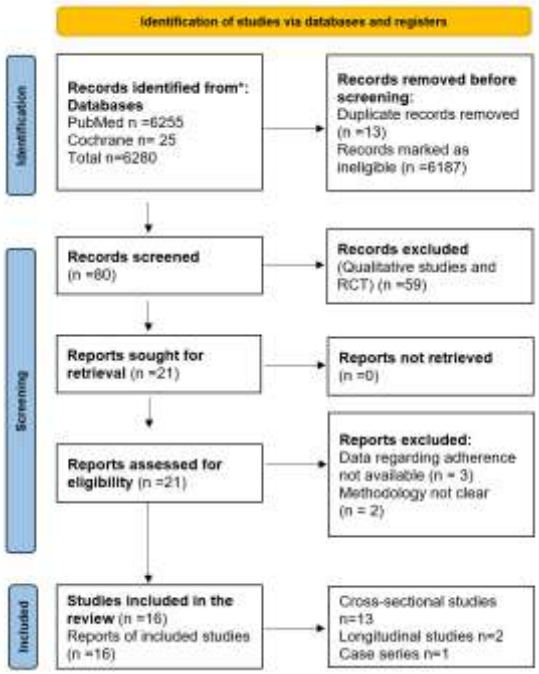

Figure 1: PRISMA flow chart of selection of articles for systematic review and meta-analysis[16]

Characteristics of included studies

The 16 studies included 5,090 PLHIV on ART. Most studies included both men and women; 11 participants were transgender women, and one study from Ranchi did not report gender for 60 participants. Study designs were 13 cross-sectional,[14,17-28] 2 longitudinal,[29,30] and 1 case series.[31] Geographically, 7 studies were from southern India, 4 from northern India, 2 from eastern India, and 1 each from western, central, and north-eastern India.

Definitions and cut-offs for adherence

As per the National AIDS Control Organization, we used a threshold of ≥95% of prescribed doses taken,[32] which was applied in 11 of 16 studies (pill count, recall, and MAS/MAQ groups). In these studies, adherence was typically calculated as, and participants with adherence ≥95% were classified as adherent. Raju BN et al,[21] categorized adherence as >95% if fewer than 3 pills were missed per month, 80–95% if 3–12 pills were missed, and <80% if more than 12 pills were missed per month. Kujur et al,[27] defined adherence as consumption of ≥95% of prescribed doses over a 4-week period within the previous 6 months.

Balaji et al,[30] assessed adherence using the Medication Adherence Questionnaire (MAQ), classifying a score of 0 as high adherence, 1–2 as medium adherence, and higher scores as low adherence. Singh et al,[24] (Haryana) used a multi-item medication adherence scale, with higher scores indicating better adherence.

Two studies defined adherence as 100%. Biswas and Mandal,[17] classified 100% intake as perfect adherence, 95–100% as adequate, and <95% as inadequate, whereas Pina et al,[20] considered each missed dose over the recall period (<100%) as non-adherence. Bandyopadhyay et al,[29] defined non-adherence as missing at least one dose in the past week, and Heylen et al,[14] measured adherence on a visual analogue scale (0–100%) over the past 30 days, reporting adherence as a continuous percentage without imposing a ≥95% cut-off.

Recalling periods and adherence assessment methods

Recall periods for adherence assessment ranged from 7 days to 12 months, depending on whether pill count or ART card data were used.

Based on the primary adherence measure used, studies were grouped into four subgroups in the meta-analysis: pill count (6 studies),[17,18,21,25,26,31] recall/self-report (6 studies),[19,20,22,23,27,29] MAS/MAQ scales (2 studies),[24,30] and VAS (2 studies).[14,28] Self-reported adherence using structured or semi-structured questionnaires (including recall-based estimates and MAQ-type scales) was the most common method, used in 12 of 16 studies, often in combination with pill count or treatment card verification. Pill count alone contributed to a distinct subgroup of 6 studies in the pooled analysis, and one study (Kujur et al,[27]) additionally used pharmacy refill data. Two studies (Heylen et al,[14] and Irene Lalhruaimawii et al,[28]) used a VAS to estimate the percentage of pills taken in the previous month.

ART duration, regimens, and counselling

Duration on ART was inconsistently reported; a few studies categorized it in broad groups (e.g., <6 vs ≥6 months or <12 vs ≥12 months), while others reported mean duration in years. Treatment regimens were specified in 7 of 16 studies, all of which used combinations of nucleoside reverse transcriptase inhibitors (NRTIs) and non-nucleoside reverse transcriptase inhibitors (NNRTIs); Balaji et al,[30] and Irene Lalhruaimawii et al,[28] also reported protease inhibitor–based regimens among patients with first-line failure. None of the studies reported detailed ART dosages.

Several studies reported better adherence among participants who received structured or repeated counseling, though counseling protocols varied.[13,33,34]

Methodological quality assessment:

The quality of the 16 included studies was assessed using the JBI Critical Appraisal Tools.[35] Given the diversity in study designs, three specific checklists were employed: the Analytical Cross-Sectional Studies Checklist (13 studies), the Cohort Studies Checklist (2 studies), and the Case Series Checklist (1 study).

Fourteen,[14,17-20,22-24,26-31] of the 16 studies (87.5%) demonstrated high methodological quality, achieving over 80% compliance with JBI criteria and indicating low risk of bias. The remaining two studies,[21,25] (12.5%) were rated as moderate quality due to unclear reporting of confounding variables or loss to follow-up. No studies were rated low quality or excluded for this reason.

All 16 studies clearly described their samples and settings, including who was included or excluded and the clinical context. They all used validated or objective tools to measure ART adherence, like pill counts, self-reported recall (MMAS-8 or MAQ), and visual analogue scales (VAS), which helped ensure reliable results for the main outcome.

Variability was observed in the management of confounding factors. Most studies (n=14) identified key confounders such as age, income, and stigma, but about 25% of cross-sectional studies did not detail countermeasures such as matching or multivariate adjustments. Follow-up reporting was generally adequate in the two longitudinal studies. Bandyopadhyay et al,[29] explained participant dropouts, while Balaji et al,[30] did not clarify how incomplete follow-up was handled, which may introduce attrition bias.

Statistical Analysis

The extracted articles were analysed using Medcalc 23.0.2-64-bit,[36] and MetaAnalysisOnline.com, a web-based tool.[37] A random-effects statistical model was used to measure the pooled proportion of ART adherence. To measure heterogeneity, the Cochrane Q test is used, with the I2 statistic quantifying it. To investigate potential sources of this variance, subgroup analyses were conducted, categorized by the adherence measurement methodology (Pill Count, Recall, MAS/MAQ, and VAS). The Chi-square test for subgroup differences was used to assess whether the measurement tool significantly influenced the adherence estimates. The potential for publication bias and small-study effects was assessed visually via Funnel Plots. For statistical verification, Egger's and Begg's tests were performed using Medcalc. A two-tailed p-value of <0.05 was considered statistically significant for the presence of bias.

RESULTS

Adherence Rates (Table 1)

Adherence rates ranged from 16.6% to 97.5%. Two studies (Biswas et al,[17] Balaji RA et al.[30]) reported high adherence (≥90%). Six studies reported suboptimal adherence (70%–89%), and eight studies (50% of the total) reported low adherence (<70%), below the recommended 95% threshold. Khede MK et al,[25] reported the lowest rate at 16.6%, and Raju BN et al,[21] reported 50.1%.

Table 1: Summary of studies selected for review

SNO	Author	Year	Method used	Study design	Study population	Sample size	Adherence rate	Adherence rate
1	Biswas A et al[17]	2016	Pill count	Cross-sectional	PLHIV ≥15 years on ART for ≥1 year	279	262	93.9%
2	Shukla M et al[18]	2016	Pill count	Cross-sectional	Adult PLHIV (≧18 y) on ART for ≥6 months	322	287	89.1%
3	Banagi Yathiraj A et al[19]	2016	Recall	Cross-sectional	Adult PLHIV ≥18 y on ART	409	288	70.4%
4	Pina C et al[20]	2018	Recall	Cross-sectional	MSM and transgender women living with HIV, ≥18 y, on ART	65	44	67.7%
5	Hiregoudar V et al[31]	2019	Pill count	Case series	PLHIV ≥15 years on ART for ≥6 months	536	359	67.0%
6	Raju BN et al[21]	2019	Pill count	Cross-sectional	Adult PLHIV (>18 y) on ART for ≥2 years	1000	501	50.1%
7	Bandyopadhyay A et al[29]	2019	Recall	Longitudinal study	Adult PLHIV ≥18 y on ART	152	103	67.8%
8	Meena KS et al[22]	2019	Recall	Cross-sectional	Adult PLHIV (≥18 y)on ART for ≥3 months	160	139	86.9%
9	Sameeksha MD et al[23]	2020	Recall	Cross-sectional	Adult PLHIV (≥18 y)on ART for ≥6 months	110	93	84.5%
10	Singh A et al[24]	2021	MAS/MAQ	Cross-sectional	Adult PLHIV (≥18 y)on ART for ≥6 months	257	227	88.3%
11	Heylen E et al[14]	2021	VAS	Baseline cross-sectional	Adult PLHIV ≥18 y on ART	527	359	68.1%
12	Khede MK et al[25]	2022	Pill count	Cross-sectional	Adult PLHIV (≥18 y)on ART for ≥3 months	415	69	16.6%
13	Surendereddy S et al[26]	2024	Pill count	Cross-sectional	Adult PLHIV (≥18 y)on ART for ≥6 months	300	205	68.3%
14	Kujur A et al[27]	2024	Recall	Cross-sectional	Adult PLHIV (>18 y) on ART	60	47	78.3%
15	Balaji RA et al[30]	2024	MAS/MAQ	Longitudinal study	Adult PLHIV (>18 y) on ART	198	193	97.5%
16	Lalhruaimawii I et al[28]	2026	VAS	Cross-sectional	Adult PLHIV (≥18 y)on ART for ≥1 month	300	208	69.3%

Identified Barriers to Adherence (Table 2)

Individual and psychosocial factors: Forgetfulness was the most cited reason for missed doses. Other significant factors included depression or emotional stress, alcohol use, and negative beliefs about ART efficacy.

Socio-structural factors: HIV-related stigma and discrimination were pervasive barriers. Financial constraints, low literacy, and unemployment were also significantly associated with poor adherence.

Logistical and systemic factors: Long travel distances to ART centers (often ≥50 km) and work commitments were frequently reported. Structural issues such as drug stock-outs and dissatisfaction with healthcare facilities also affected adherence.

Clinical factors: Adverse drug reactions (ADRs) or fear of side effects often led to treatment interruptions. Some patients also skip doses when "feeling better," indicating a lack of understanding about the need for lifelong therapy.

Table 2: Barriers to drug adherence among the studies reviewed

S.no.	Author	Barriers to adherence
1	Biswas A et al[17]	*NA*
2	Shukla M et al[18]	Non-beneficial perceptions toward ART, long gap since last counselling (>3 months), depression, dissatisfaction with healthcare facilities; patient-reported reasons: being busy, feeling sick, lack of money, being away from home, fear of side-effects, feeling drugs are toxic.
3	Banagi Yathiraj A et al[19]	Forgetfulness, being away from home, financial problems, depression, alcohol use, longer distance, side-effects, stigma, and low family support
4	Pina C et al[20]	Younger age, negative beliefs about ART, alcohol use (avoiding doses when drinking), forgetfulness, running out of medicines, feeling healthy, and financial constraints.
5	Hiregoudar V et al[31]	Financial constraints, long distance, side-effects, forgetfulness, busy schedule, stigma and non-disclosure, alcohol use.
6	Raju BN et al[21]	Lower literacy, smoking, alcohol use, longer travel distance ≥50 km, and unemployment
7	Bandyopadhyay A et al[29]	Non-disclosure and stigma, financial constraints, distance to ART centre, alcohol use, forgetfulness, side-effects, co-morbid illnesses.
8	Meena KS et al[22]	Forgetfulness, drug side-effects, drug unavailability/stock-outs, feeling better and therefore skipping medicines; adherence is lower in higher socio-economic classes and with longer duration since diagnosis.
9	Sameeksha MD et al[23]	Greater distance travelled to ART centre; forgetting doses, inability to collect tablets, and emotional stress.
10	Singh A et al[24]	*NA*
11	Heylen E et al[14]	forgetfulness, being busy, being away from home, social-structural barriers (stigma, poverty), clinic/regimen barriers (side-effects, stock-outs, clinic wait time), family-level financial difficulties; fear of stigma from friends and workplace
12	Khede MK et al[25]	Illiteracy, alcohol use, side-effects, lack of social support, longer distance to ART centre, stigma, forgetfulness
13	Surendereddy S et al[26]	Lower education, irregular clinic follow-up, late pharmacy refill, history of missed doses (past month/6 months); self-reported reasons: feeling depressed, too busy, forgetfulness, occasional drug allergy, some giving no reason.
14	Kujur A et al[27]	Forgetfulness, travelling, busy schedule, financial problems, alcohol use, depression, low education and unemployment.
15	Balaji RA et al[30]	Forgetfulness, being busy, running out of pills, travelling, depression and anxiety, alcohol use, stigma, and poor social support.
16	Lalhruaimawii I et al[28]	Stigma and Descrimination

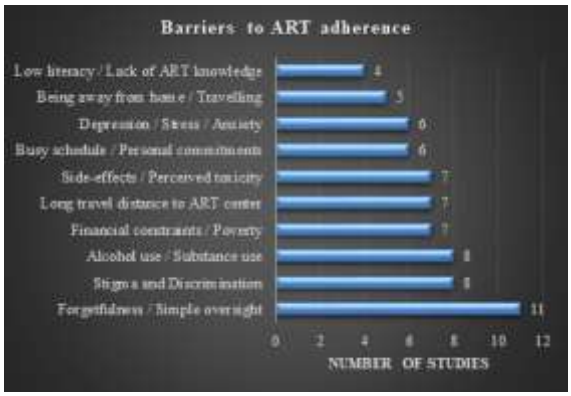

Figure 2: Barriers to ART adherence

Results of Meta-analysis

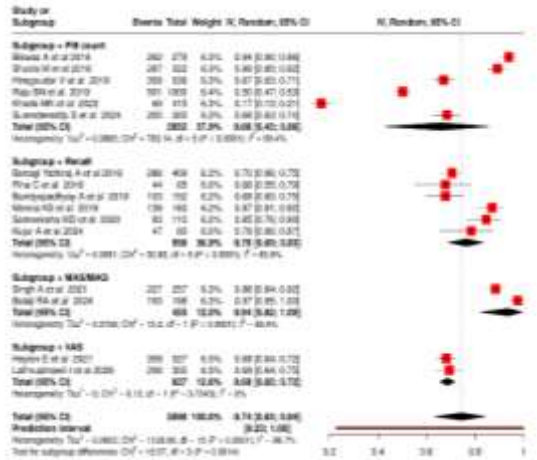

Figure 3: Forest plot comparing 16 studies

A random-effects meta-analysis of 16 studies (N=5,090) showed that the measurement method significantly influenced reported adherence. The pooled adherence rate was 74% (95% CI: 63–84%), with extremely high heterogeneity (I^2 = 98.7%, Tau^2 = 0.0603, $p < 0.0001$), indicating substantial variability between studies (Figure 3).

Subgroup Analysis

MAS/MAQ questionnaires produced the highest pooled adherence (94%, 95% CI: 82–100; I^2 = 93.4%), while pill count yielded a moderate estimate (74%, 95% CI: 63–86; I^2 = 99.4%) with wide variation. Recall-based measures showed lower adherence (65%, 95% CI: 52–76; I^2 = 83.8%), and VAS scores were consistent (64%, 95% CI: 61–67; I^2 = 0%) but tended to underestimate adherence compared to questionnaires. The test for subgroup differences was statistically significant (Chi^2 = 15.57, df = 3, p = 0.0014), confirming that adherence estimates vary by measurement method. These findings highlight the need for caution when interpreting adherence rates and suggest that combining objective and subjective measures may provide a more accurate understanding of patient behavior.

Publication Bias Assessment using funnel plot

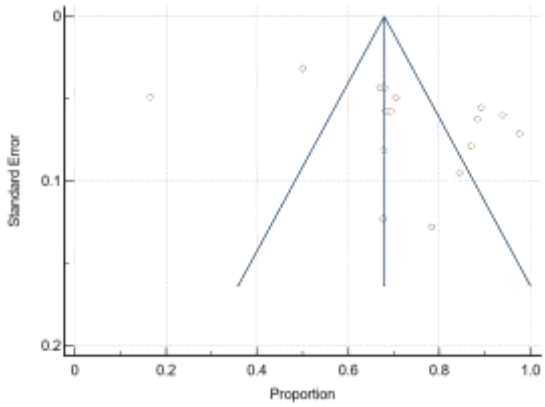

Figure 4: Funnel plot

The meta-analysis revealed significant heterogeneity across studies ($Q = 1128.06$, $df = 15$, $P < 0.001$; $I^2 = 98.7\%$), indicating that ART adherence rates in India are strongly influenced by study-specific factors. Asymmetry in the funnel plot and high heterogeneity suggest that measurement tools and potential publication bias in smaller studies affect reported adherence. However, Egger's test ($P = 0.0758$) and Begg's test (Kendall's Tau = 0.2594) did not show significant evidence of bias, indicating that observed variations likely reflect genuine clinical and methodological differences rather than selective reporting.

DISCUSSION

This systematic review and meta-analysis synthesize evidence from 16 studies involving 5,090 PLHIV in India. The pooled adherence rate of 74% highlights a persistent gap in meeting the "95-95-95" UNAIDS targets. Compared with historical data, these results provide important insights into the progress of India's HIV care program.

Comparative Trends in Adherence (2009–2026) (Table 3)

Comparison with previous meta-analyses shows a plateau in adherence levels. Mhaskar et al[13]. (2013) reported a pooled adherence rate of 70% (studies up to 2009), and Chakraborty et al[38]. (2020) found 77% (2007–2017). Our estimate of 74% indicates that, despite expanded free ART under NACP-IV and NACP-V, optimal adherence rates have not significantly improved. This stagnation suggests that initial interventions have reached their limits, and new strategies targeting behavioral and structural factors are needed. Our findings are higher than the 54.1% reported by Basu et al. (2019)[39], likely due to the inclusion of recent studies (2024–2026) reflecting the adoption of Tenofovir/Lamivudine/Dolutegravir (TLD) regimens[40], which have a lower pill burden and better tolerability than older regimens.

Table 3: Comparison of the previous three meta-analyses' results with the present study

Study	Period Covered	Pooled Adherence	Primary Barrier Identified
Mhaskar et al. (2013)[13]	Up to 2009	70%	Financial cost, Access
Chakraborty et al. (2020)[38]	2007–2017	77%	Depression, Anxiety
Basu et al. (2019)[39]	2012–2018	54.1%	Forgetfulness, Alcohol
Present Study (2026)	**2016–2026**	**74%**	**Forgetfulness, Travel/Distance**

The Measurement Sensitivity and Methodological Bias

Subgroup analysis in this study highlights the "Methodological Paradox" in adherence research. Consistent with Chakraborty et al,[38] self-reported scales (MAS/MAQ) yielded higher adherence rates (94%) than recall-based methods or VAS (64–65%). This suggests a persistent social desirability bias, with patients potentially over-reporting adherence to satisfy healthcare providers.

Pill counts (74%) closely matched the overall mean but were lower than MAS/MAQ results, highlighting the need for objective verification. As Basu et al.[39] noted, facility-based reporting often yields higher rates than community-based assessments, suggesting that clinical monitoring may improve adherence or introduce reporting bias.

The Evolving Landscape of Barriers

Transition from economic to psychosocial barriers: While Mhaskar et al,[13] identified "medication cost" as a primary barrier before free ART, our review and those by Basu et al,[39] and Chakraborty et al,[38] find that forgetfulness and alcohol use are now the main impediments. This shift indicates that challenges have moved from drug access to daily integration.

Mental health crisis: Our review identifies depression and emotional stress as pervasive factors, consistent with Chakraborty et al.'s finding that mental health issues are significant risk factors for non-adherence. All four meta-analyses indicate that Indian ART centers are not adequately equipped to address psychological comorbidities.

Persistence of structural stigma: Despite ongoing advocacy, HIV-related stigma remains a universal barrier from 2009 to 2026. Patients continue to miss doses or skip clinic visits to avoid disclosure, a challenge that medication-focused policies alone cannot address.

Logistical hardships: Our study and Basu et al. both highlight long travel distances as a major barrier, emphasizing the need for Differentiated Service Delivery (DSD) models to bring medications closer to patients' homes, and for a paradigm shift in National AIDS Control Organization (NACO) strategies.[41]

Decentralization: To address distance barriers, multi-month dispensing and community-based refills should be expanded.

Integrated care: Mental health and substance use screening should be implemented at every ART visit.

Technological integration: Digital health tools (mHealth) can help address forgetfulness, a leading cause of non-adherence identified in recent meta-analyses.

Strengths and Limitations

This review is the first to include data up to 2026, capturing the post-pandemic recovery of the Indian health system. However, as in previous meta-analyses, we observed extreme heterogeneity ($I^2 > 90\%$), likely due to varying adherence definitions and diverse socio-cultural contexts. The geographic focus on southern India remains a limitation, potentially under-representing challenges in north-eastern states.

CONCLUSION

In conclusion, this meta-analysis shows that while India has made significant progress toward universal ART access, patient adherence remains a challenge, with a pooled rate of 74%. The gap between current adherence and the 95% clinical ideal suggests that behavioral and structural vulnerabilities are limiting the impact of the "Test and Treat" policy.[42] The shift from economic to psychosocial barriers marks a new phase in the epidemic. Future clinical success will depend more on sustaining patient commitment to lifelong therapy than on the availability of drugs.

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