ISSN 2394-7446
INTERNATIONAL JOURNAL OF APPLIED PHARMACEUTICAL SCIENCES

MEDICATION ADHERENCE IN CHRONIC DISEASE: DETERMINANTS, MEASUREMENT, CONSEQUENCES AND EVIDENCE-BASED INTERVENTIONS

T. Sai Siva Kumar[1,*], M. Meghana Venkata Sai Sri[1], M. Prabhu Krupa[1], K. Mythili[1], K. Jessy Krupa[1]

[1]Department of Pharmacy Practice, Sir C. R. Reddy College of Pharmaceutical Sciences, Shanthi Nagar, Eluru - 534007, Andhra Pradesh, India.

ABSTRACT

OBJECTIVE: To synthesize evidence on the terminology, epidemiology, conceptual models, measurement, disease-specific patterns, clinical and economic results, determinants, and evidence-based interventions relevant to medication adherence in persistent disease, incorporating India and other low- and middle-income settings.

METHODS: A narrative review was conducted following SANRA principles [1]. PubMed, Scopus, supplemented by hand-searching reference lists of fundamental evaluations and by consulting WHO and Global Initiative for Asthma plan documents. Search conditions combined “medication adherence,” “adherence,” “concordance,” and “persistence” with disease- and intervention-specific conditions; methodical and organized evaluations, meta-analyses, and landmark primary studies were prioritized for inclusion.

OUTCOMES: Long-term adherence to prescribed therapy in developed countries remains adjacent to 50%, and are frequently reduced in resource-limited settings. The World Health Organization (WHO) five-dimension model; patient-related, condition-related, therapy-related, health-system-related, and socioeconomic aspects; remains the predominant and prevailing organising framework. No single measurement procedure is a gold standard; impartial and unbiased and self-reported methods each include distinct trade-offs between accuracy and practicality. Multi-component interventions unifying education, behavioural support, regimen simplification, and digital condition instruments generate the most steady and regular, if modest, improvements. Indian evidence shows adherence for hypertension and type 2 diabetes frequently below worldwide averages, driven significantly by out-of-pocket medication costs.

CONCLUSION: Non-adherence is best approached as a flexible, multifactorial clinical problem instead than a corrected patient trait. Individualised, technology-enabled, team-based care, combined with structural interventions tackling cost and entry, provides the most encouraging path to closing the adherence gap, especially in India.

Keywords: Medication adherence; Chronic disease; Persistence; Patient adherence; Behavioural intervention; Digital condition; Pharmaceutical care; Patient-centred care

ABBREVIATIONS

ART, antiretroviral therapy; COPD, persistent obstructive pulmonary disease; DOT, directly recorded therapy; ED, emergency department; GINA, Global Initiative for Asthma; HbA1c, glycated haemoglobin; HIV/AIDS, human immunodeficiency virus/obtained immunodeficiency syndrome; MEMS, Medication Event Monitoring System; mHealth, mobile condition; MMAS-8, 8-item Morisky Medication Adherence Scale; MPR, Medication Possession Ratio; PDC, Proportion of Days Covered; SMS, short message service; WHO, World Health Organization.

Address for Correspondence:

*Corresponding author: T. Sai Siva Kumar - Department of Pharmacy Practice, Sir C. R. Reddy College of Pharmaceutical Sciences, Shanthi Nagar, Eluru - 534007, Andhra Pradesh, India. Telephone: +91-9177781954 E-mail: [saisivakumarskrv@gmail.com]

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1. INTRODUCTION

Chronic diseases; incorporating hypertension, type 2 diabetes mellitus, cardiovascular disease, persistent respiratory disorders, and mental sickness; now account for the majority of morbidity, mortality, and medical care expenditure internationally. Effective pharmacological management is available for most of these conditions, yet the clinical advantage of any medication depends on it actually being taken as prescribed. The gap between what is prescribed and what is consumed is described by the idea of medication adherence, and this gap has proven remarkably resistant to more than fifty years of clinical and behavioural study.

The World Health Organization‘s landmark 2003 document, Adherence to Long-Term Therapies: Evidence for Action, was among the first to frame poor adherence not as a peripheral behavioural nuisance but as a health-systems failure of striking worldwide magnitude, estimating that around half of patients with persistent disease in developed countries take their medication as prescribed, with even reduced rates anticipated in advancing regions [2]. More than two decades later, new and fresh evaluations verify that this figure has changed exclusively slightly, despite the proliferation of new drug classes, digital reminder instruments, and adherence-focused clinical guidelines [3,4].

Because persistent disease therapy is, by definition, long-term and often lifelong, adherence is not a single occurrence but a dynamic behaviour that fluctuates across the course of treatment; from the decision to begin a new prescription, through first implementation, to long-term persistence or discontinuation. Each of these stages is impacted by distinct clinical, mental, social, and system-level aspects, meaning that a single intervention delivered at a single time point is improbable and doubtful to sustain adherence indefinitely.

This review aims to provide clinicians, pharmacists, nurses, public condition practitioners, and health-services researchers with an organised, evidence-based synthesis of the contemporary and ongoing understanding of medication adherence in persistent disease. It addresses the terminology and conceptual models used to describe adherence, the epidemiological scale of the problem, methods used to measure it, disease-specific adherence patterns, the clinical and economic effects of non-adherence, the multi-level determinants that drive it, the interventions with the strongest evidence for enhancing it (comprising the growing role of digital condition technologies), and the precise and particular evidence foundation in India and other low- and middle-income countries.

2. CONCEPTS AND DEFINITIONS: COMPLIANCE, ADHERENCE, CONCORDANCE, PERSISTENCE

Terminology in this domain has evolved significantly, and the option of term reflects an essential and primary philosophy of the patient-provider relationship.

2.1 Compliance

The earliest term used was adherence, specified as the extent to which a patient‘s behaviour corresponds to the prescriber’s recommendations. This term has been increasingly criticised for suggesting a paternalistic, one-directional relationship in which the patient is a passive recipient of instructions [5,6].

2.2 Adherence

Adherence is now the favored term in most clinical and inquiry literature. It is specified as “the extent to which a person‘s behaviour; obtaining medication, following a diet, and/or executing lifestyle changes; corresponds with agreed recommendations from a condition care provider” [2]. Critically, the term “agreed” implies that the patient has participated in setting the treatment plan, differentiating adherence from straightforward obedience to instruction.

2.3 Concordance

Concordance goes further still, describing a consultation process in which the patient and prescriber negotiate an agreement that respects the patient‘s principles and wishes, and in which the treatment plan is a joint decision alternatively than an instruction to be followed [7].

2.4 Persistence

Persistence refers to the length of time from initiation to discontinuation of therapy, and is distinct from adherence, which describes the quality of medication-taking while therapy proceeds. A patient may be extremely adherent for a period of months and then discontinue therapy completely (poor persistence), or may persist with therapy for years while often missing individual doses (poor adherence within good persistence) [6,7].

2.5 The ABC Taxonomy

Vrijens and colleagues proposed a broadly accepted taxonomy that splits adherence into three sequential stages: (A) Initiation, the point at which the patient takes the first dose; (B) Implementation, the extent to which the patient‘s factual and concrete dosing corresponds to the prescribed regimen over time; and (C) Discontinuation, the point at which the patient stops acquiring the medication entirely, marking the end of persistence [7]. This taxonomy is now recommended as a standard framework for adherence study because it enables each phase to be measured and aimed individually.

Table 1: Key terminology in medication-taking behaviour research [6,7].

Term	Definition
Compliance	Degree to which a patient's behaviour matches a prescriber's instructions; implies a passive, one-directional relationship.
Adherence	Extent to which a patient's medication-taking corresponds with mutually agreed recommendations; implies patient participation.
Concordance	A negotiated, shared-decision consultation process between prescriber and patient regarding treatment.
Persistence	Duration of time from treatment initiation to discontinuation.
Initiation (A)	The act of taking the first dose of a newly prescribed medication.
Implementation (B)	The extent to which actual dosing matches the prescribed dosing regimen during the course of therapy.
Discontinuation (C)	The point at which the patient stops taking the medication, ending the period of persistence.

3. SEARCH STRATEGY

This review follows a narrative instead than structured and orderly design, uniform and unchanging with its goal of offering a broad, integrative synthesis across terminology, epidemiology, measurement, and intervention study instead than answering a single quantitative query; the SANRA (Scale for the Assessment of Narrative Review Articles) criteria were used to direct reporting [1]. The electronic databases PubMed, Scopus, and the Cochrane Library were searched for English-language articles issued between January 2000 and August 2026. The search identified approximately 50 records, with prior landmark sources (incorporating the initial WHO 2003 document) retained where they persist the primary reference for an idea. Search conditions combined "medication adherence," "adherence," "concordance," and "persistence" with disease-specific conditions (hypertension, diabetes, dyslipidaemia, asthma, COPD, HIV, depression, heart failure, tuberculosis) and with method- and intervention-related conditions (measurement, Morisky, pharmacy refill, electronic tracking, behavioural intervention, digital condition, mHealth). Reference lists of important and significant methodical assessments and Cochrane assessments were hand-searched for extra sources, and the WHO and GINA approach documents were consulted directly for definitional and epidemiological statements. Priority was given to structured and orderly evaluations, meta-analyses, and big and substantial primary studies; single small studies were generally used solely where no bigger synthesis was available. As a narrative instead than methodical review, no protocol was recorded, and official risk-of-bias assessment and duplicate independent

screening was not performed (see Limitations, Section 14).

4. EPIDEMIOLOGY AND GLOBAL MAGNITUDE OF THE PROBLEM

Non-adherence to prescribed medication is not a minor phenomenon limited to a tough and arduous subgroup of patients; it is the norm instead than the anomaly across virtually every persistent disease category studied. The WHO calculated in 2003 that approximately 50% of patients with persistent disease in developed countries do not take their medications as prescribed [2], a figure that has been repeatedly reproduced in following decades of study across varied populations and medical care systems [3,4,8,9].

Landmark assessments have quantified this problem across disease states. Osterberg and Blaschke‘s broadly cited 2005 New England Journal of Medicine review reported that usual and customary adherence rates recorded in clinical trials; commonly greater than in routine practice because of adjacent observation; commonly range between approximately 43% and 78% [5]. DiMatteo’s meta-analysis of fifty years of adherence studies across more than 500 studies similarly found substantial non-adherence across all important and significant disease sorts, with the utmost and preeminent rates of non-adherence noted in conditions requiring sophisticated and multifaceted, asymptomatic, preventative therapy such as hypertension and hyperlipidaemia [10].

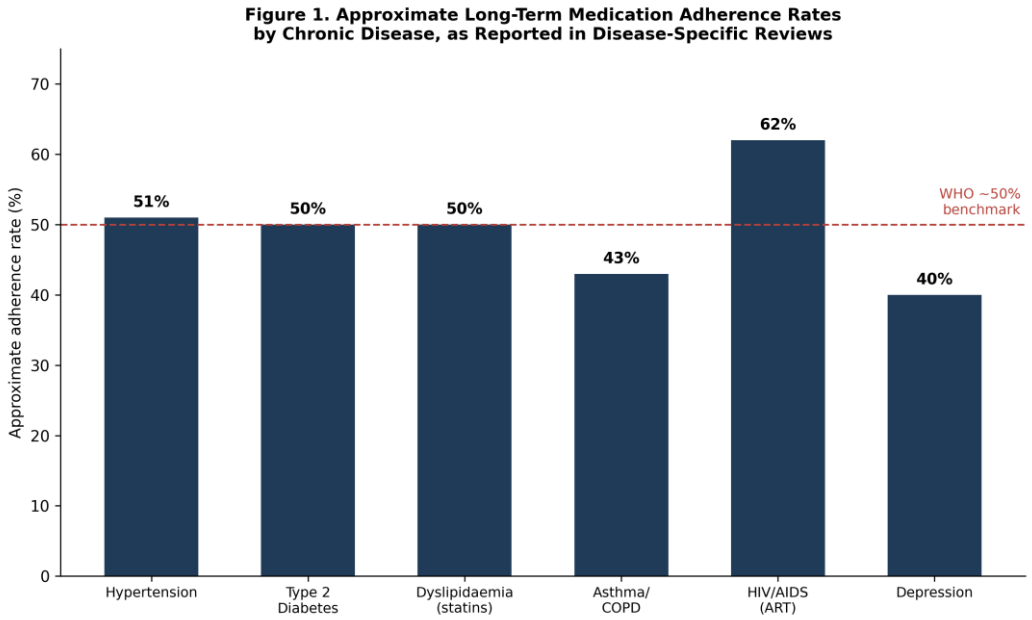

Fig. 1: Approximate long-term adherence rates for six chronic diseases, each drawn from a single disease-specific review cited in Table 1a [11,12,26,13,27,28,14]

A steady and regular observation across studies is that adherence declines increasingly over the course of treatment, particularly during the first weeks to months

after a new prescription is distributed. UK primary-care data suggest that as numerous as one in three patients starting a new medication for a persistent state are already non-adherent within ten days of the first prescription [29].

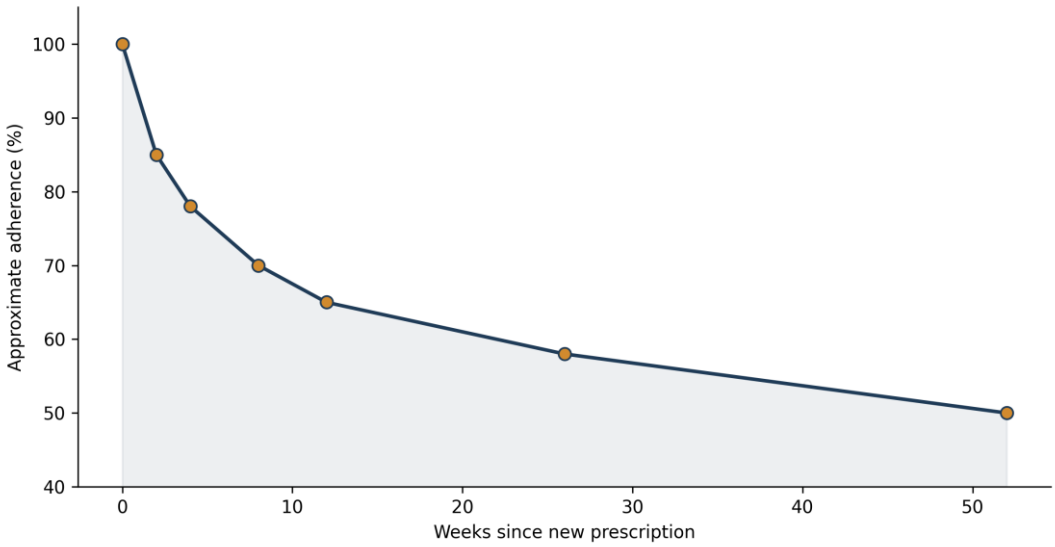

Fig. 2: Illustrative trajectory of adherence decline following initiation of chronic-disease pharmacotherapy (conceptual illustration, not measured data), based on patterns reported in longitudinal adherence studies [5,18,30]

The scale of the problem is magnified by the sheer number of patients influenced: non-communicable diseases, most of which need long-term pharmacotherapy, are projected to account for the majority of the worldwide strain of disease, meaning that even modest improvements in adherence rates could translate into substantial population-level condition gains [9].

5. CONCEPTUAL MODEL: THE WHO FIVE INTERACTING DIMENSIONS

To move the area beyond watching non-adherence entirely as a matter of individual patient duty, the WHO proposed a multidimensional model describing five interacting groups of aspects that jointly ascertain adherence behaviour [2]. This framework remains the most broadly cited conceptual model in the adherence literature and underlies most present and existing intervention design.

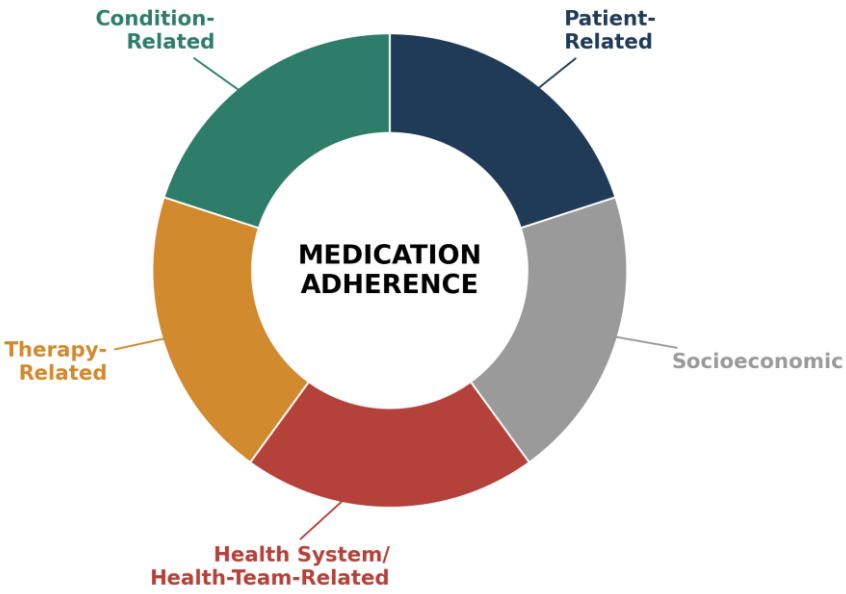

Fig. 3: The WHO five interacting dimensions of medication adherence [2]

5.1 Patient-Related Factors

These contain the patient's knowledge and principles about their sickness and treatment, motivation, self-efficacy, cognitive impairment, physical limitations such as impaired vision or dexterity, forgetfulness, and mental condition comorbidities incorporating depression and anxiety [16,17].

5.2 Condition-Related Factors

The nature of the disease itself influences adherence. Asymptomatic conditions such as hypertension and dyslipidaemia are particularly prone to non-adherence because patients receive no immediate symptomatic feedback confirming the medication's advantage, whereas conditions with serious, concrete symptoms often show comparatively greater short-term adherence [10,15].

5.3 Therapy-Related Factors

Regimen intricacy, incorporating tablet strain, dosing frequency, length of treatment, and the presence of side effects, is among the most consistently identified predictors of non-adherence. Meta-analytic evidence shows an inverse relationship between the number of daily doses required and adherence rates, with once-daily regimens generally outperforming multiple-daily-dose regimens [20,18].

5.4 Health-System and Health-Team-Related Factors

These contain the quality of the patient-provider relationship, continuity of care, consultation time, entry to pharmacists and follow-up services, health-insurance coverage and medication cost-sharing structures, and the overall accessibility of the medical care system [9,12].

5.5 Socioeconomic Factors

Poverty, low condition literacy, unsteady and volatile housing, lack of social support, unemployment, and high out-of-pocket medication costs are strongly associated with poorer adherence, notably in low- and middle-income settings and among socioeconomically disadvantaged populations in high-income countries [2,19]. A significant implication of this model is that no single intervention targeting solely one dimension, such as patient education, is probable and expected to achieve big and substantial or durable improvements in adherence, because determinants act simultaneously across all five domains [20,21].

6. CLINICAL AND ECONOMIC CONSEQUENCES OF NON-ADHERENCE

6.1 Clinical Consequences

Non-adherence is strongly and consistently associated with inferior clinical results across virtually every persistent disease studied, comprising greater rates of uncontrolled blood pressure, poor glycaemic control, increased risk of myocardial infarction and stroke, graft rejection following transplantation, virological failure in HIV infection, and increased overall and cardiovascular mortality [12,14,17,22]. A huge and massive meta-analysis of over 376,000 patients found that good adherence to cardiovascular preventative medication was associated with substantially reduced mortality compared with poor adherence, independent of the explicit and defined drug class studied [14].

6.2 Healthcare Utilisation

Poor adherence is a crucial and vital driver of avoidable medical care utilisation. A methodical review of prospective empirical studies found a median of 4.3% of hospital admissions associated with medication non-adherence, with commonness estimates extending from under 1% to almost 11% depending on setting and definition, and identified cardiovascular medicines as the class most frequently implicated [22]. Non-adherence has moreover been linked to a substantial proportion of emergency unit presentations among patients with persistent disease [23].

6.3 Economic Burden

The economic cost of medication non-adherence is approximated in the tens to hundreds of billions of dollars annually in the United States solely. A broadly cited sector analysis calculated that avoidable costs associated with medication non-adherence and related suboptimal application could reach approximately $200 billion annually in the U.S. medical care system [24]. A methodical review across disease groups similarly found that non-adherence were consistently associated with greater total

medical care costs, driven primarily by increased hospitalisation instead than by pharmacy costs exclusively [3,8].

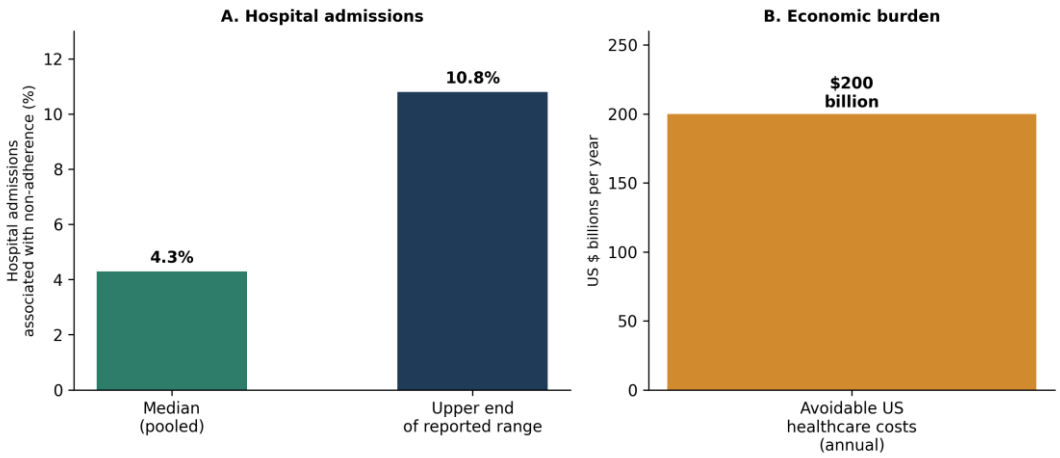

Fig. 4: Selected clinical and economic consequences of medication non-adherence, compiled from published U.S.-focused estimates [3,5,8,28,29]

Table 2: Downstream clinical, health-system, and economic consequences of medication non-adherence across chronic disease domains.

Domain	Representative Consequence
Cardiovascular	Increased risk of myocardial infarction, stroke, heart-failure hospitalisation, and cardiovascular death [12,14,25].
Metabolic	Poor glycaemic control, higher HbA1c, increased risk of microvascular and macrovascular diabetic complications [13].
Respiratory	Increased exacerbations, emergency visits, and hospitalisations in asthma and COPD [15,31].
Infectious disease	Virological failure and drug resistance in HIV/AIDS due to suboptimal antiretroviral adherence [16].
Mental health	Symptom relapse and higher psychiatric hospitalisation rates in depression and other disorders [17].
Health-system	Increased hospital admissions, ED visits, and overall healthcare resource utilisation [3,27,28].
Economic	Estimated $200 billion in avoidable U.S. healthcare costs annually [29].

7. MEASUREMENT OF MEDICATION ADHERENCE

There is no universally accepted "gold standard" approach for measuring medication adherence; each available procedure carries distinct strengths, limitations, and trade-offs between objectivity, cost, and practicality in routine clinical settings [4]. Measurement methods are broadly grouped into direct and indirect techniques.

7.1 Direct Methods

Direct strategies contain directly recorded therapy, measurement of drug or metabolite concentration in blood or urine, and detection of biological markers added to a formulation. These procedures provide impartial confirmation that a dose was ingested but is invasive, expensive, and unrealistic and unworkable for routine long-term monitoring outside of specialised settings such as tuberculosis or HIV treatment programmes [2,4].

7.2 Indirect Methods

Indirect procedures are more broadly used in both clinical practice and study. These contain:

Self-report questionnaires, such as the 8-item Morisky Medication Adherence Scale (MMAS-8), a broadly confirmed and thoroughly used instrument across hypertension, diabetes, asthma, and persistent pain populations [11,14,22,24,32,33].

Pill counts, comparing the number of dosage units remaining against the number expected to have been consumed since the final count.

Electronic monitoring, employing devices such as Medication Event Monitoring Systems (MEMS) that record the time and date each time a tablet container is opened, which is one of the more neutral and detached indirect techniques [4].

Pharmacy refill data, comprising the Medication Possession Ratio (MPR) and Proportion of Days Covered (PDC), calculated from prescription assertions or dispensing records and broadly used in large-scale health-services inquiry [19,34].

Clinical outcome surrogates, such as blood pressure control or HbA1c, which are impacted by adherence but are moreover confounded by multiple other aspects, restricting their specificity as adherence measures.

7.3 The Morisky Medication Adherence Scale (MMAS-8)

The MMAS-8 is among the most thoroughly confirmed and broadly deployed self-report instruments in adherence study. It comprises seven dichotomous items and one five-point Likert item, producing a total score from 0 to 8, with greater scores indicating better adherence; scores are typically categorised as low (< 6), medium (6 to < 8), and high (= 8) adherence [11]. A structured and orderly review and meta-analysis of 28 validation studies found pooled sensitivity of approximately 68–93% and more variable specificity across populations, and generally acceptable and adequate internal consistency, though psychometric performance changes by disease state, language version, and cultural setting [32]. Validated translations exist for hypertension, type 2 diabetes, asthma, and persistent pain populations

across various languages, comprising a Persian version confirmed in Iranian hypertensive patients, though internal consistency has occasionally been reported as low in precise validation samples, highlighting the need for context-specific psychometric evaluation before adopting the instrument in a new population [13,15,22,24,33,35]. The MMAS-8 is a proprietary, copyrighted instrument; its application in study or clinical practice necessitates a licence from the copyright owner, and prospective users should contact the licence owner before adopting the scale [11].

Because the MMAS-8 is not the sole confirmed self-report choice, multiple options are now in broad application. The Adherence to Refills and Medications Scale (ARMS) was developed for application in populations with limited condition literacy and has been confirmed across various persistent conditions. The Medication Adherence Report Scale (MARS-5) is a five-item scale that has been used thoroughly in respiratory and psychiatric populations. The ASK-12 evaluates both adherence behaviour and its underlying obstacles in a single instrument. A systematic debate has surrounded the Morisky instruments, centred on licensing costs and on discrepancies in how the scale has been scored and confirmed across studies; researchers selecting a self-report instrument should weigh these factors alongside psychometric performance and licensing necessities.

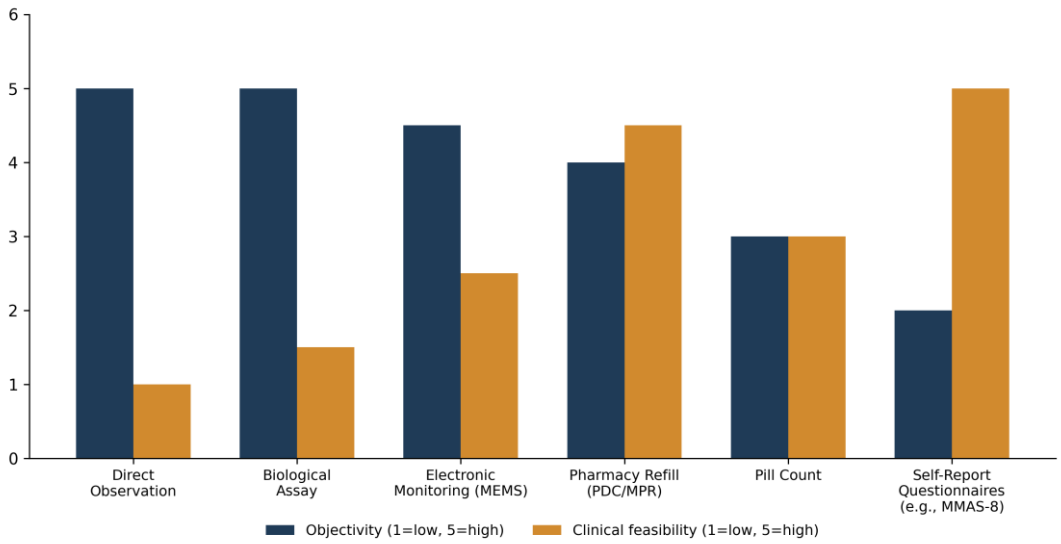

Fig. 5: Trade-off between objectivity and clinical feasibility across commonly used adherence measurement methods (conceptual illustration, not measured data), synthesised from methodological reviews [2,4,34]

Table 3: Comparison of common medication adherence measurement methods [2,4,11,32,34].

Method	Advantages	Limitations
Directly observed therapy	Highly objective; confirms ingestion	Resource-intensive; impractical long-term; not feasible outside specialised programmes
Biological assay	Objective; measurable drug/metabolite levels	Costly; invasive; reflects only recent dosing; requires laboratory infrastructure
Electronic monitoring (MEMS)	Captures timing and pattern of dosing; considered relatively objective	Expensive; device may be opened without ingestion; requires patient cooperation
Pharmacy refill / PDC / MPR	Scalable; uses existing administrative data; low patient burden	Assumes possession equals consumption; misses free samples/hospital-supplied doses
Pill counts	Simple; inexpensive	Easily manipulated ("pill dumping"); burdensome for staff
Self-report (e.g., MMAS-8, ARMS, MARS-5)	Low-cost; quick; captures patient perspective and barriers	Subject to recall bias and social-desirability bias; may overestimate adherence

8. DISEASE-SPECIFIC PATTERNS OF ADHERENCE

8.1 Hypertension

Hypertension is among the most studied persistent conditions in adherence study, in part because it is pervasive and far-reaching, largely asymptomatic, and necessitates indefinite pharmacotherapy. Reported adherence rates cluster around 50%, and non-adherence is strongly associated with poor blood-pressure control and increased cardiovascular occurrence rates [11,12,22]. Regimen simplification through fixed-dose combination antihypertensive products has been associated with meaningfully enhanced adherence relative to equivalent free-drug combinations [12].

8.2 Type 2 Diabetes Mellitus

Adherence to oral hypoglycaemic agents and insulin is approximately 50%. Non-adherence in diabetes is strongly linked to elevated HbA1c and increased risk of both microvascular and macrovascular problems [13].

8.3 Dyslipidaemia and Cardiovascular Prevention

Statin adherence tends to decline substantially within the first year of therapy, in part because dyslipidaemia produces no symptoms and patients may not perceive concrete advantage from continued treatment. Meta-analytic evidence across more than 376,000 patients found that good adherence to cardiovascular preventative medications, incorporating statins, was

associated with substantially reduced all-cause mortality than poor adherence [14].

8.4 Asthma and Chronic Obstructive Pulmonary Disease (COPD)

Adherence to inhaled upkeep therapy in asthma and COPD is frequently reported below 50%, complicated by inhaler-technique errors, which can create the appearance of non-adherence even when doses are technically administered [3,15,31]. The Global Initiative for Asthma identifies both intentional and unplanned non-adherence as significant and essential hurdles to achieving disease control [31].

8.5 HIV/AIDS (Antiretroviral Therapy)

Because partial adherence to antiretroviral therapy risks the emergence of resistant viral strains, HIV adherence study has historically demanded a greater functional adherence threshold than most other persistent diseases, historically cited as approximately 90–95% for durable virological suppression with older, unboosted regimens. A meta-analysis synthesising 43 studies across more than 26 countries found that this threshold is broader and more extensive than commonly presumed with newer, better-tolerated regimens, with high adherenceis required for virological suppression on non-nucleoside- and integrase-inhibitor-based therapy [16]. Self-report remains a regular and recurring but imperfect measurement approach in this population [16].

8.6 Depression and Mental Health Conditions

Adherence to antidepressant and other psychotropic medication are often complicated by stigma, side effects that appear before therapeutic advantage is felt, and the cognitive and motivational symptoms of the underlying sickness itself, contributing to adherence rates frequently below 50% [17].

8.7 Heart Failure

Adherence to guideline-directed medical therapy in heart failure has been directly linked to reduced mortality and hospital readmission; a meta-analysis of adherence-focused interventions found quantifiable reductions in both readmission and mortality among patients obtaining ordered and methodical adherence support [30].

8.8 Tuberculosis

Tuberculosis occupies a distinctive place in the adherence literature because directly noted therapy (DOT) was, for decades, the WHO-endorsed standard of care specifically to counter the risk of poor adherence, treatment failure, and the emergence of drug opposition. DOT is resource-intensive for both patients and condition systems, and in India; which carries the world‘s biggest tuberculosis strain; it has increasingly been supplemented or substituted by digital adherence technologies. 99DOTS, a low-cost, cellphone-based technology in which

patients call a toll-free number revealed on specifically designed medication packaging, has been deployed to more than 500,000 people with TB across India [36]. A huge and massive pre-post evaluation of a statewide 99DOTS rollout in Himachal Pradesh found no statistically notable difference in favourable treatment results compared with traditional DOT, although engagement with the technology was itself associated with better results, a discovery probably confounded by non-random absorption [36]. Video-observed therapy, in which patients record or livestream themselves obtaining medication for remote review, has displayed comparable pledge and equivalent implementation obstacles, incorporating reliance on phone possession, network linkage, and digital literacy. These results echo the broader pattern described in Section 11: digital adherence instruments extend the reach of oversight but do not, on their own, resolve the underlying obstacles to adherence.

Table 4: Approximate adherence rates and contributing factors by chronic disease.

Disease	Approx. Adherence	Key Contributing Factors
Hypertension	~50% (global); as low as ~16-20% in Indian cohorts	Asymptomatic disease; regimen complexity; side effects; cost [11,12,22,42]
Type 2 diabetes	~50% (global); ~48-61% non-adherence pooled in Indian studies	Injection burden (insulin); hypoglycaemia fear; polypharmacy [13,33,43]
Dyslipidaemia (statins)	~50% (declining over time)	Lack of symptomatic feedback; perceived low necessity [14]
Asthma / COPD	~30-50%	Inhaler technique errors; symptom fluctuation; steroid concerns [15,31]
HIV/AIDS (ART)	Varies; threshold now regimen-dependent	Stigma, regimen complexity, side effects; resistance risk [16]
Depression	~40-50%	Stigma; delayed therapeutic onset; early side effects [17]
Heart failure	~50-60%	Polypharmacy; cognitive impairment; frequent hospitalisation [30]
Tuberculosis	Varies by supervision model	Treatment duration; stigma; DOT burden; connectivity for digital tools [36]

The estimated rates summarised in Figure 1 and this table are compiled from the six sources cited above; because study populations, adherence definitions, and measurement windows differ significantly between the initial reports, these figures should be read as broad, order-of-magnitude indications alternatively than precise, directly comparable estimates.

9. DETERMINANTS AND obstacles TO ADHERENCE

Systematic assessments of structured assessments have tried to unify the highly huge and massive number of individual determinants identified across the adherence literature [37]. Commonly and consistently reported determinants contain:

Regimen intricacy and capsule strain, incorporating dosing frequency and number of concurrent medications [20,23].

Side effects and the patient‘s perception of medication need relative to recognised concerns [21,38].

Health literacy and patient understanding of their state and treatment justification [20,21].

Quality of the patient-provider relationship, incorporating communication style and shared decision-making [9,22].

Cost and coverage, incorporating out-of-pocket expenditure and cost-related medication underuse [2,24].

Cognitive and physical impairment, notably in older adults with memory or dexterity limitations [24].

Psychological aspects, comprising depression, anxiety, and low self-efficacy [17,21].

Social support and family participation in medication management [2,24].

A new methodical review proposed an integrative framework grouping these determinants into patient, medication, medical care team/system, and socioeconomic/environmental domains, closely mirroring the initial WHO model but including more new evidence on digital literacy and telehealth admittance as emerging aspects [40]. Notably, the relative weight of each determinant changes by disease, population, and medical care setting, reinforcing the conclusion that adherence interventions should be separately customized instead than applied as one-size-fits-all solutions [20,25,26].

10. EVIDENCE-BASED INTERVENTIONS TO IMPROVE ADHERENCE

A 2014 Cochrane methodical and organized review of interventions for enhancing medication adherence concluded that, even among the most effective, well-conducted studies, improvements in adherence and clinical results were often modest, and that no single type of intervention was dependably effective across all diseases and settings, reinforcing the need for interventions customized to individual patient hurdles [25]. Broad intervention categories with supporting evidence contain the following.

10.1 Educational Interventions

Patient education about disease procedures, treatment reasoning, and expected advantages improves adherence knowledge but, delivered solely, produces exclusively modest and frequently short-lived

improvements in real and genuine medication-taking behaviour [26,39].

10.2 Behavioural and Motivational Interventions

Approaches such as motivational interviewing, cognitive-behavioural procedures, self-monitoring, goal-setting, and habit-formation techniques (for illustration, linking dosing to an existing daily routine) have displayed more uniform and unchanging effects than education exclusively, notably when combined with other intervention components [26,41,40].

10.3 Regimen Simplification

Reducing tablet strain and dosing frequency, for illustration through once-daily dosing or fixed-dose combination products, are one of the most consistently effective single approaches for enhancing adherence across various persistent disease states [12,20,23].

10.4 Reminder Systems and Packaging Aids

Pill organisers, blister packaging, and reminder devices can meaningfully improve adherence, particularly for patients whose primary obstacle is forgetfulness alternatively than intentional non-adherence [41,42].

10.5 Pharmacist-Led and Team-Based Care

Structured pharmacist-led medication therapy management, joint care models, and multidisciplinary follow-up have displayed some of the strongest and most durable effects on both adherence and downstream clinical results, notably in heart failure, hypertension, and diabetes [12,30,42].

10.6 Financial and Policy Interventions

Reducing patient out-of-pocket costs through value-based coverage design, reduced co-payments for necessary and fundamental chronic-disease medications, and simplified prescription-refill operations has been associated with better and refined adherence, particularly among lower-income populations [2,24,29].

10.7 Meta-Analytic Evidence on Effect Sizes

A big and substantial meta-analysis of 771 adherence intervention trials found generally small-to-moderate typical effect sizes, with the most effective interventions normally integrating various techniques (for case, education plus behavioural support plus efficient and optimized dosing) instead than depending on any single component [26]. This discovery is echoed across other structured evaluations, which consistently conclude that multi-component, separately customized interventions outperform single-strategy methods [25,41,42].

Table 5: Summary of intervention categories for improving medication adherence.

Intervention Type	Mechanism	Typical Evidence Strength
Education alone	Improves knowledge of disease/treatment rationale	Modest; often short-lived [26,41]
Behavioural/motivational support	Builds self-efficacy, habit formation, addresses ambivalence	Moderate, more durable when combined [26,41,42]
Regimen simplification	Reduces pill burden and dosing frequency	Consistently among the strongest single strategies [12,20,23]
Reminder tools/packaging	Reduces unintentional (forgetfulness-related) non-adherence	Moderate for forgetfulness-driven non-adherence [41,42]
Pharmacist-led/team-based care	Ongoing monitoring, counselling, and follow-up	Among the most robust, particularly multi-component [12,30,42]
Financial/policy interventions	Reduces cost-related barriers to obtaining medication	Effective, especially in low-income populations [2,24,29]
Digital health/mHealth tools	Automated reminders, tracking, remote monitoring, telehealth	Promising but heterogeneous evidence [41]

11. THE ROLE OF DIGITAL HEALTH AND EMERGING TECHNOLOGIES

The past decade has seen a swift and speedy increase in digital instruments intended to support medication adherence, incorporating SMS text-message reminders, smartphone applications, smart capsule bottles and blister packs that record opening events, wearable sensors, and remote patient-monitoring platforms linked to clinical teams.

Systematic evaluations of mobile-health (mHealth) interventions for persistent disease management have found generally favourable but variable effects on adherence and condition behaviours, with substantial variability in study quality, intervention design, and length of follow-up, and with most evidence describing improvements in short-to-medium-term results instead than verified long-term persistence [41,43]. Text-message-based reminder interventions in specific and precise have displayed uniform and unchanging, if modest, benefit for enhancing adherence and meeting attendance across a range of persistent conditions [43].

Electronic monitoring devices, originally developed as adherence measurement instruments, are increasingly being modified into intervention platforms themselves; for illustration, smart tablet bottles that trigger an automated reminder if a scheduled dose is not recorded as taken, occasionally combined with warnings to caregivers or care teams [4]. Telehealth and remote tracking have moreover expanded the practicality of regular, low-burden check-ins between patients and pharmacists or nurses, potentially extending the reach of team-based

adherence support beyond the conventional clinic visit [41].

Nonetheless, digital interventions are not a universal solution: their effectiveness depends heavily on patient digital literacy, entry to dependable technology and linkage, and thoughtful integration into existing care pathways alternatively than deployment as a stand-alone replacement for clinical contact and behavioural support [40,43]. As Section 8.8 illustrates in the precise case of tuberculosis, digital adherence instruments can extend the reach of oversight without necessarily enhancing clinical results on their own. Emerging evidence increasingly frames digital instruments as one component within a broader, multi-level adherence plan instead than as a solution in themselves.

12. MEDICATION ADHERENCE IN INDIA AND OTHER LOW- AND MIDDLE-INCOME SETTINGS

Most of the evidence summarised in the preceding sections originates from high-income, mainly North American and European settings, and the WHO's broad and inclusive observation that adherence is "even reduced" in evolving regions has, until recently, remained largely unquantified for India specifically [2]. This is a substantial gap for a journal serving Indian pharmacy practice, and latest and current Indian and local evidence signifies that the adherence problem in India is, if anything, more serious than the worldwide averages presented above.

A methodical and organized review and meta-analysis of antihypertensive adherence in India, covering twelve studies and more than 3,000 participants, found a pooled adherence rate of exclusively 15.8%, significantly reduced than worldwide benchmarks; individual Indian studies included in the review reported adherence as low as 10–20% [37].

A separate methodical review and meta-analysis of adherence to anti-diabetic medication in India found that pooled non-adherence utilizing MMAS-8-based studies was approximately 48%, with individual study estimates extending from 11% to 68% non-adherent, in a population of almost 90 million Indians living with type 2 diabetes [38]. Out-of-pocket expenditure accounts for a highly big and substantial portion of total condition spending in India, and cost-related non-adherence are correspondingly notable and distinguished among the determinants identified in Indian adherence studies, uniform and unchanging with the socioeconomic dimension of the WHO model described in Section 5.5 [37,38].

Several India-specific policy and health-system initiatives are directly relevant to adherence, although they have received little attention in the global adherence literature. The Pradhan Mantri Bhartiya Janaushadhi

Pariyojana, India‘s generic-medicine retail scheme, aims to reduce out-of-pocket medication costs by making common and nonspecific options available at Janaushadhi Kendra outlets; by enhancing affordability, such schemes address one of the most consistently identified socioeconomic hurdles to adherence. Community pharmacists, whose extent of practice is specified under the Pharmacy Practice Regulations 2015, are well positioned to support adherence counselling, medication reconciliation, and refill tracking at the point of dispensing, extending the reach of the pharmacist-led interventions described in Section 10.5 into the community setting. At the health-system level, India‘s National Programme for Prevention and Control of Non-Communicable Diseases (NPCDCS) and the Ayushman Bharat Health and Wellness Centres provide structural platforms through which adherence support could, in rule, be integrated into routine primary care for hypertension and diabetes, though the extent to which adherence-specific support has been officially built into these platforms is not well recorded in the released literature. Validated adherence instruments are increasingly available in Indian languages, incorporating Hindi, Telugu, and Tamil translations of self-report scales used in the studies cited above, which supports more correct future measurement of the problem across the country’s linguistically varied and distinct population.

Tuberculosis adherence, discussed in Section 8.8, is a further area of substantia l Indian relevance: India carries the world‘s biggest tuberculosis strain, and adherence support for TB; incorporating the shift from facility-based directly recorded therapy toward digital adherence technologies such as 99DOTS; denotes the single biggest adherence-focused programme functioning in the country [36]. Taken together, the Indian and local evidence examined here indicates that the determinants, measurement obstacles, and intervention priorities described elsewhere in this review apply in India, but with amplified socioeconomic and health-system obstacles that warrant dedicated attention in future Indian pharmacy practice study.

13. ROLE OF HEALTHCARE PROFESSIONALS AND HEALTH SYSTEMS

Clinicians is frequently poor at identifying which of their patients are non-adherent; various studies have found that physician estimates of individual patient adherence correlate weakly with objectively measured adherence, meaning that non-adherence frequently goes unrecognised and therefore unaddressed [5]. This has led some authors to contend that medication non-adherence should be actively screened for and treated as

a diagnosable, changeable clinical problem in its own right, instead than presumed or overlooked [44].

Recommended pragmatic steps for clinicians and condition systems contain routinely asking non-judgemental, open-ended queries about medication-taking challenges alternatively thanpresuming adherence; employing confirmed concise screening instruments such as the MMAS-8 where fitting and right (subject to the licensing points noted in Section 7.3); simplifying regimens wherever clinically viable; involving pharmacists in medication reconciliation and counselling; tackling cost obstacles proactively; and guaranteeing continuity of care through uniform and unchanging follow-up [5,11,12,42,44].

At the systems level, integrating adherence support into chronic-disease management programmes, reimbursement models that incentivise medication therapy management, and electronic condition records capable of flagging refill gaps all represent structural opportunities to make adherence support a routine, instead than remarkable and excellent, part of persistent disease care [9,42].

14. LIMITATIONS

This review has various limitations inherent to its narrative design. No protocol was recorded in advance, and study identification, though led by explicit search conditions and databases (Section 3), was not accompanied by identical independent screening or official inter-rater agreement inspections. No official risk-of-bias or quality assessment instrument was applied to the individual studies and methodical and organized evaluations synthesised here, and the review thus relies significantly on the quality evaluations already performed within the cited methodical assessments and meta-analyses alternatively than on independent re-appraisal. The evidence foundation remains mainly drawn from high-income, English-language sources; although Section 12 tries to partly address this by including latest and current Indian and local data, the fundamental primary literature on adherence in numerous low- and middle-income settings,and in languages other than English, remains comparatively scant and was not comprehensively searched. Finally, because adherence is measured inconsistently across the underlying studies; utilizing self-report, pharmacy refill data, and electronic observation interchangeably; the estimated adherence rates presented in Table 4 and Figure 1 should be understood as broad indications alternatively than precise, directly comparable estimates, as noted in Section 8.

15. CONCLUSIONS

Medication adherence remains one of the most notable, and most persistently

underestimated, determinants of results in persistent disease management. Despite more than half a century ofstudy, standard and normal adherence rates across important and significant persistent conditions persist near to the identical 50% figure highlighted by the WHO in 2003, imposing a substantial and largely preventable strain of morbidity, mortality, and medical care cost [2,3,4,8].

The evidence examined here supports multiple converging conclusions. First, non-adherence is multifactorial and is best understood through frameworks such as the WHO‘s five interacting dimensions, alternatively than being linked completely to patient carelessness or non-compliance [2]. Second, no single measurement approach is definitively superior; merging impartial and unbiased data sources, such as pharmacy refill records,with patient-reported instruments, such as the MMAS-8, offers a more full and comprehensive picture than either approach solely [4,11,19]. Third, the most effective interventions are multi-component, separately customized, and delivered through sustained, team-based connections alternatively than a single instructional encounter [4,22,42]. Fourth, digital condition technologies offer a truly auspicious and favourable, swiftly evolving avenue for scalable adherence support, but as the tuberculosis and broad digital-health evidence examined in Sections 8.8 and 11 both show, they should complement instead than supplant clinical connections and structural interventions that address cost and admittance [41,43].Fifth, the Indian and low- and middle-income-country evidence examined in Section 12 signifies that these broad and inclusive conclusions hold, but with adherence rates frequently lower and cost-related obstacles more obvious than in the high-income settings that dominate the broader literature [37,38].

Future study priorities contain the development of more standardised, comparable adherence measurement techniques; longer-term evaluation of digital and artificial-intelligence-enabled adherence instruments beyond first pilot periods; greater attention to adherence inequalities linked to socioeconomic limitation and condition literacy,comprising within India; and the design of health-system reimbursement structures that explicitly reward sustained adherence support alternatively than isolated clinical encounters. Ultimately, closing the adherence gap will need reframing non-adherence not as a patient failing, but as a solvable, shared obligation of patients, clinicians, pharmacists, condition systems, and policymakers working in concert.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest relevant to the material of this review.

ACKNOWLEDGEMENTS

The authors thank the Department of Pharmacy Practice, Sir C. R. Reddy College of Pharmaceutical Sciences, for organizational support during the preparation of this review. No particular individual, beyond the listed authors, contributed materially to the manuscript.

FUNDING

This review received no precise grant from any funding agency in the public, commercial, or not-for-profit sectors.

AUTHOR CONTRIBUTIONS

T.S.S.K.: conceptualisation, literature search, drafting of the manuscript. M.M.: literature search, data/figure collection, drafting. P.K.M.: literature search, table collection, drafting. K.M.: literature search, manuscript review and editing. J.K.K.: literature search, manuscript review and editing. All authors read and approved the conclusive and definitive manuscript.

ETHICS STATEMENT

Not applicable; this review did not include human participants or animals.

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