

One Adherence Intervention Cannot Address Every Form of Nonadherence: Matching Initiation, Implementation, Persistence, Treatment Burden, and Patient Capability to Pharmacy Practice Interventions

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ABSTRACT

Medication nonadherence is commonly managed as if one problem could be corrected by one broadly applicable adherence intervention. This paper develops a methodological approach for matching pharmacy-practice interventions to the medication-taking process that has failed, while separately considering treatment burden, patient capability, access constraints, and implementation feasibility. An evidence-bounded conceptual development process was used. Established distinctions among initiation, implementation, and persistence were combined with evidence on adherence measurement, patient-reported assessment, intervention content, treatment burden, medication-management capacity, affordability, and implementation. Evidence-supported distinctions were separated from new synthesis. The resulting method was constructed as a proposed decision approach rather than a validated clinical algorithm. The analysis indicates that an identical observed adherence deficit may arise from different temporal processes and mechanisms. A patient who never initiates treatment, a patient who intermittently implements a regimen, and a patient who discontinues treatment require different diagnostic questions before intervention selection. Treatment burden and patient capability further modify whether an otherwise plausible intervention is feasible. The proposed method therefore sequences phase identification, barrier assessment, burden–capability appraisal, intervention-mechanism selection, and reassessment. It also identifies predictable mismatch conditions, including access barriers treated with reminders, adverse-effect-related discontinuation treated as forgetfulness, and digitally delivered support that adds workload. Pharmacy adherence support should be conceptualized as a matching problem rather than intervention escalation. The approach remains unvalidated, context dependent, and subject to measurement uncertainty; prospective and pragmatic testing is required before claims of clinical effectiveness or implementation readiness.

Keywords: Medication adherence, Initiation, Implementation, Persistence, Treatment burden, Patient capability

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Introduction

Medication adherence is often compressed into a single label, yet medication-taking behavior unfolds through distinguishable phases. Initiation concerns whether treatment is started, implementation concerns how actual dosing corresponds with the prescribed regimen while treatment is ongoing, and persistence concerns how long treatment continues before discontinuation. These distinctions matter because the observable problem, the information needed to understand it, and the plausible corrective action can differ across phases [1]. Treating all three as one deficit risks selecting an intervention because it is available or familiar rather than because its mechanism addresses the process that has failed.

The timing of intervention is similarly important. Early engagement with treatment may be influenced by expectations, beliefs, anticipated burden, and willingness to begin therapy, whereas later implementation or persistence problems may emerge after experience with dosing demands, adverse effects, costs, competing priorities, or changing circumstances [2]. An intervention intended to support initiation therefore should not be assumed to remediate a persistence problem that develops months later. Conversely, waiting for refill gaps may miss an opportunity to address uncertainty or reluctance before treatment starts.

Intervention evidence also argues against a universal adherence solution. Education, reminders, behavioral strategies, regimen changes, financial approaches, pharmacist-led services, and multicomponent interventions differ in content, intensity, and mechanism, while their effects are heterogeneous across conditions and outcomes [3]. This heterogeneity does not prove that formal matching will improve outcomes, but it weakens the assumption that any single intervention category is intrinsically suitable for all nonadherence.

Practice adds another layer of variability. A missed dose, unfilled prescription, or discontinuation can reflect patient-level beliefs or capability, regimen-level burden, clinician-directed change, or health-system access; the same visible signal therefore should not be assigned automatically to a patient-level cause. Healthcare professionals differ in how they assess and manage medication adherence, meaning that similar adherence signals may generate different responses across settings [4]. The methodological problem addressed here is therefore not simply how to intensify adherence support, but how to decide what kind of support is logically aligned with the identified failure. This paper proposes an evidence-bounded adherence–intervention matching method for pharmacy practice. It separates medication-taking phase from plausible mechanism, then considers treatment burden, patient capability, access, delivery feasibility, and reassessment. The method is explicitly proposed: it organizes existing distinctions and evidence into a decision approach but does not claim prospective predictive validity, universal applicability, or clinical effectiveness.

Materials and Methods

This article used a conceptual-development procedure rather than an empirical study or systematic review. The purpose was to construct a transparent matching method from established adherence terminology, measurement evidence, intervention research, patient-workload concepts, and implementation scholarship. The process began by treating initiation, implementation, and persistence as separate medication-taking constructs and by preserving explicit definitions in accordance with adherence-reporting guidance [5]. These constructs were used as temporal descriptors, not as diagnoses of patient motivation or causal mechanism.

A second step examined what common adherence information can and cannot establish. Electronic health records and pharmacy dispensing records can identify patterns compatible with non-initiation, gaps in medication availability, or discontinuation, but estimates depend on data provenance, definitions, observation windows, and computation rules [6]. Accordingly, a recorded fill pattern was not treated as direct evidence of ingestion, intention, beliefs, or the reason for a gap. Structured patient report was considered an additional information source because pharmacy-based screening can elicit adherence behaviors or barriers that are not visible in dispensing histories [7]. However, screening results were not treated as definitive causal classifications.

Third, measurement uncertainty was made an explicit design condition. Patient-reported adherence measures differ in construct coverage and measurement properties [8]. The method therefore permits triangulation among dispensing information, patient report, clinical context, regimen characteristics, and professional assessment, while retaining an indeterminate classification when available information does not justify a stronger inference. No single instrument is designated a universal gold standard.

Evidence status was recorded separately from the new synthesis. Established phase definitions, observed measurement limitations, and reported intervention or implementation findings were treated as evidence-supported premises. The ordering of these premises into a matching sequence, including any decision gate or reassessment rule, was treated as proposed unless directly established by the selected literature.

Finally, intervention evidence was organized by the process or barrier an intervention could plausibly modify rather than by intervention name alone. Treatment burden, medication-management capability, affordability or access, delivery requirements, and implementation feasibility were treated as separate matching dimensions. The conceptual output was then challenged against anticipated mismatch conditions: wrong adherence phase, wrong barrier mechanism, excessive intervention workload, capability mismatch, system-level constraints outside the

intervention's reach, and failure of delivery in routine practice. These steps generated a proposed decision sequence and failure-mode logic. They did not generate effect estimates, diagnostic thresholds, or validated predictions, and no inference was made that conceptual fit guarantees adherence improvement or downstream clinical benefit.

Results and Discussion

The conceptual analysis produced four linked outputs. First, adherence was separated into temporal failure processes before any intervention category was considered. This prevents a broad label such as “nonadherent” from functioning as the intervention diagnosis. Second, intervention descriptions were decomposed conceptually into mechanisms and delivery requirements. This is important because adherence interventions carrying similar labels can contain different behavior-change techniques and therefore cannot be assumed to act through the same pathway [9].

Third, intervention outcome and intervention fit were kept distinct. Pharmacist-led care has been evaluated prospectively for medication adherence, including in chronic heart failure, but an observed adherence effect is not interchangeable with a clinical outcome and does not validate a general matching rule [10]. The proposed method therefore asks whether an intervention mechanism is aligned with a plausible adherence barrier before asking whether the intervention category has evidence in another population. It also preserves therapeutic appropriateness: increasing medication use is not an appropriate objective when discontinuation reflects a clinically warranted treatment change.

Fourth, delivery modality was treated as a conditional property rather than an intervention mechanism in itself. A digital tool may facilitate patient–pharmacist interaction, but pilot evidence does not establish that digital delivery is suitable for every patient or barrier [11]. Access, literacy, preference, sensory or cognitive demands, and the additional work created by the tool may alter practical fit.

Across these outputs, the principal methodological result is underdetermination rather than a single hierarchy of interventions. Classification must remain revisable when new patient, dispensing, clinical, or system information changes the interpretation: similar observed adherence patterns can arise from different causes, and different measures can characterize the same patient differently. Contemporary adherence scholarship continues to distinguish definitions, measurement approaches, and multiple causes of nonadherence [12]. The proposed approach therefore does not force every case into a unique mechanism. It uses the medication-taking phase as an initial discriminator, seeks the most plausible modifiable barrier at the appropriate patient, regimen, clinician, or system level, and retains uncertainty when evidence is discordant. The following sections develop these outputs as intervention targets, matching variables, and decision rules rather than as empirically validated findings.

Forms of nonadherence as distinct intervention targets

The first matching decision is temporal: what part of medication taking has failed? Primary adherence or initiation concerns whether a newly prescribed medicine is obtained and treatment begins. Real-world data on medications for major depressive disorder demonstrate that initial filling can be studied as an adherence event distinct from subsequent medication use [13]. A nonfilled prescription, however, does not by itself reveal refusal, forgetfulness, affordability, prescribing change, or another reason. The appropriate target is therefore initiation only after clinical and contextual information supports that interpretation.

Implementation begins after treatment has been initiated. Its failures include irregular dosing, gaps in medicine availability, incorrect timing, or other departures from the prescribed regimen while the patient remains in treatment. Persistence concerns continuation over time. Real-world lipid-lowering evidence illustrates that adherence during treatment and persistence can be measured separately and may not move identically [14]. This distinction matters operationally: reminders or dose-organization support may be relevant to an implementation problem, whereas repeated short-term reminder escalation may be poorly aligned with a patient who has discontinued because treatment has become unacceptable, inaccessible, or clinically changed.

Phase classification is necessary but not sufficient. Adherence and persistence with obesity medication, for example, are influenced by multiple patient, treatment, and contextual determinants rather than one uniform mechanism [15]. The proposed method therefore uses phase as a first discriminator and barrier assessment as a

second. It also permits mixed or uncertain classifications when a patient has several medicines, discordant information sources, or a transition in which the reason for discontinuation cannot yet be established.

A further safeguard is medicine specificity. The same patient may initiate one medicine promptly, implement another inconsistently, and discontinue a third. A person-level label can therefore erase regimen-level distinctions that are directly relevant to pharmacy action. Classification should be attached to a particular medicine or regimen and observation period whenever feasible.

Table 1 translates these distinctions into an adherence-process failure discriminator for use before intervention selection.

Table 1. Discriminating initiation, implementation, and persistence failure before adherence support is selected

Failure pattern	Temporal signature	Plausible mechanism	Information needed	Inappropriate generic response	Matching target
Non-initiation	Prescribed therapy not started	Beliefs, uncertainty, cost, access, treatment change	Prescription status, patient intention, affordability, access	Refill reminder	Resolve the barrier to starting treatment
Poor implementation	Treatment started but dosing or supply is inconsistent	Forgetting, regimen complexity, capability limits, access interruptions	Dose pattern, refill history, routine, regimen demands	Assuming discontinuation	Support correct ongoing implementation
Non-persistence	Treatment started then stopped	Burden, adverse effects, acceptability, access, clinical change	Stop timing, reason, clinical appropriateness	Repeated reminder escalation	Clarify continuation barrier or need for clinical review
Mixed or indeterminate*	Signals conflict or vary by medicine/time	Multiple or unresolved mechanisms	Triangulated patient, dispensing, regimen, and clinical information	Forced single label	Clarify before matching an intervention

*Proposed decision state used when available information does not justify a unique phase-mechanism interpretation.

Treatment burden and patient capability as matching variables

Identifying the adherence phase and a plausible barrier does not establish that an intervention is workable. Treatment burden concerns the workload and impact created by treatment and healthcare demands. In multimorbidity this burden can include complex medication routines, monitoring, appointments, coordination, administrative tasks, and the cumulative effort required to manage several conditions [16]. An adherence intervention can reduce that workload, leave it unchanged, or add another task. The proposed method therefore treats net workload as part of intervention fit rather than assuming that additional support is automatically beneficial.

Some adherence barriers are also located partly outside the patient. Cost-related nonadherence is a clear example: changes in affordability and policy context can alter whether medicines are practically obtainable [17]. When cost or access is the dominant constraint, education about importance or increasingly frequent reminders may be mechanistically weak because they do not alter the feasibility of obtaining treatment. Pharmacy action may instead require benefits navigation, lower-cost alternatives, prescriber coordination, or referral within the limits of local services. These are level-of-analysis decisions: a system constraint should not be misclassified as deficient patient motivation.

Capability is related to burden but analytically separate. A scoping review of tools for older adults identified cognitive, physical, sensory, motivational, and environmental barriers to medication-management capacity, while no single identified tool covered every relevant domain [18]. Thus, an identical medication workload may be manageable for one patient and unmanageable for another, and effective capability may change with illness, caregiver support, environment, or technology.

The matching implication is a burden-capability fit test. Before adding reminders, education, monitoring, packaging, digital tasks, or follow-up contacts, the pharmacist should ask whether the intervention removes the identified barrier without imposing demands the patient cannot reasonably meet. This is a proposed decision principle, not a validated threshold. Burden and capability should be reassessed when treatment, health status, support, access, or adherence behavior changes.

The proposed adherence-intervention matching method

The proposed method begins only after the medicine-specific adherence process has been characterized. Its first decision is whether the dominant problem concerns initiation, implementation, persistence, or remains indeterminate. The second is mechanistic: what modifiable barrier most plausibly explains the observed pattern? Evidence that targeted and tailored pharmacist-led intervention can improve adherence in a defined population supports the plausibility of barrier-responsive pharmacy care, but does not validate the broader matching method proposed here [19]. The method therefore requires pharmacists to distinguish evidence-supported patient information from inference and to revise the working explanation when subsequent information conflicts with it. The third decision is a burden–capability–access test. An intervention should not be selected only because its nominal mechanism appears relevant. Digital interventions, for example, may reduce some aspects of treatment work while adding new technological, monitoring, communication, or self-management demands [20]. A reminder application may therefore fit forgetfulness yet remain poorly matched to a patient with low digital capability, sensory limitations, unstable connectivity, or already excessive treatment workload. Similarly, counseling cannot by itself remove a cost barrier, and simplification cannot correct a medicine that the patient never obtained.

The fourth decision concerns delivery feasibility. Evidence from implementation science shows that trial-level adherence interventions do not automatically transfer into routine practice: reach, adoption, workflow fit, fidelity, resources, and sustainability can alter what patients actually receive [21]. Consequently, the proposed method treats feasibility as part of matching rather than as a downstream administrative consideration.

The final decision is reassessment. The initial classification is a working state, not a permanent patient characteristic. A barrier can resolve, emerge, migrate between levels, or be superseded by a new clinical issue. The method therefore proposes a recursive sequence: identify the medication-taking process, identify the plausible barrier, assess burden/capability/access, select the least-burdensome feasible mechanism that can act on that barrier, and reassess both adherence and the interpretation behind the intervention.

Table 2 converts this logic into a decision register that preserves the distinction between the adherence process being targeted and the demands created by the intervention itself.

Table 2. Choosing pharmacy adherence support by process, burden, capability, and reassessment trigger

Targeted adherence process	Dominant burden driver	Capability requirement	Intervention mechanism	Expected mismatch risk	Reassessment criterion
Initiation	Cost, uncertainty, access, anticipated treatment work	Ability to obtain and begin therapy	Barrier resolution, shared clarification, access support	Education without resolving access or acceptability	Medicine started, barrier persists, or reason for non-start changes
Implementation	Complex routine, forgetfulness, supply interruptions	Ability to organize, remember, obtain, and administer doses	Simplification, cueing, packaging, refill or pharmacist support	Added tasks exceed capability or wrong mechanism selected	Pattern improves, remains inconsistent, or new barrier appears
Persistence	Ongoing burden, adverse effects, reduced acceptability, access loss	Capacity and willingness to continue safely	Clinical review, burden reduction, coordinated continuation support	Reminder escalation when stopping reflects tolerability or clinical change	Continuation restored, treatment changed, or discontinuation judged appropriate
Indeterminate or mixed*	Multiple interacting demands	Capability cannot yet be confidently characterized	Clarification, triangulation, staged support	Premature intervention locks in the wrong explanation	Sufficient new information permits reclassification

*Proposed decision state. The register does not establish intervention effectiveness or prescribe a universal intervention sequence.

Figure 1 shows why the same broad label of nonadherence should lead to different pharmacy decisions depending on the failed medication-taking process and the cross-cutting burden and capability conditions.

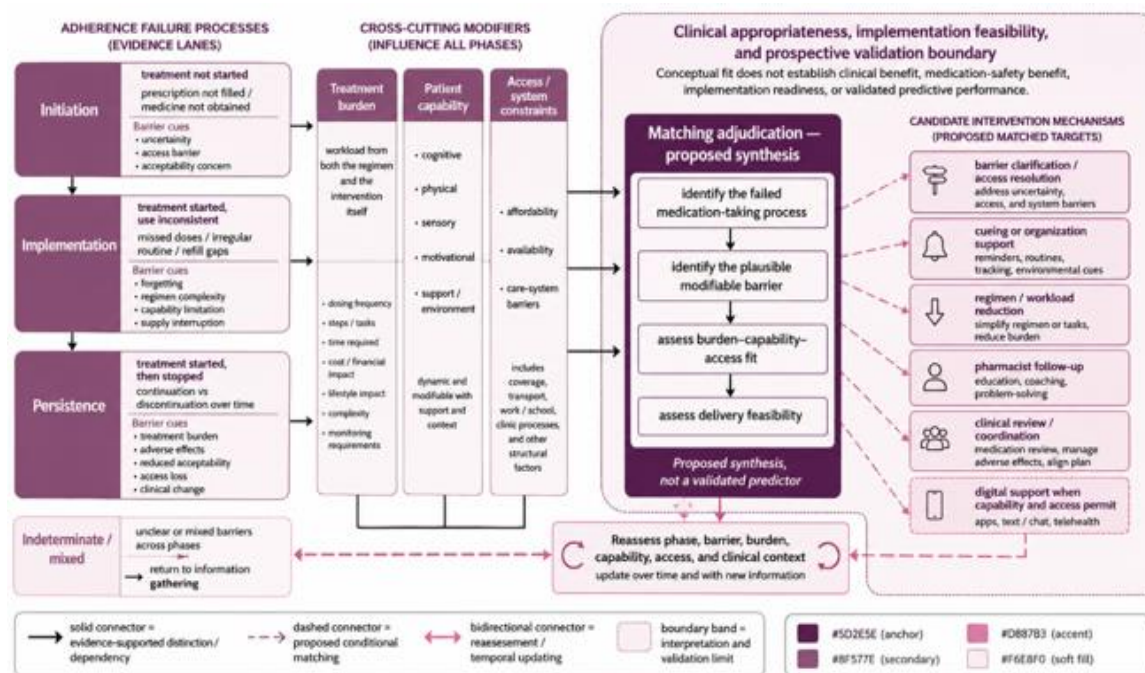


Figure 1. Failure process, treatment burden, and patient capability jointly determine whether adherence support fits the problem

Mismatch patterns and expected failure modes

The usefulness of matching becomes clearest when plausible failure mechanisms are considered. One failure type occurs after apparently appropriate tailoring: the planned intervention may not reach the intended patients or may be delivered inconsistently because workflow, resources, adoption, or fidelity differ from the conditions assumed during intervention design. Process evaluation of pharmacist-led adherence care demonstrates that implementation itself can become a source of variation [22]. A mechanistically plausible intervention can therefore fail without proving that the initial barrier assessment was wrong.

A second mismatch occurs when a patient-level response is applied to a problem produced at a care-transition or system level. Medication discontinuation after hospital discharge has been documented in population-based COPD care, but administrative observations cannot determine that every discontinuation represents intentional or inappropriate patient nonadherence [23]. The methodological consequence is important: repeated education or reminders may be poorly matched when the operative problem is prescribing discontinuity, medication-list change, access after discharge, or uncertainty about therapeutic intent.

A third mismatch arises when implementation or persistence is interpreted without considering tolerability and clinical appropriateness. Side effects have been associated with adherence and persistence to hormone therapy in breast cancer survivors [24]. When adverse effects plausibly govern discontinuation, a reminder mechanism cannot resolve the underlying problem and may be inappropriate if it delays necessary clinical reassessment. The matching output may therefore be pharmacist–prescriber coordination or treatment review rather than stronger adherence prompting.

These examples support a proposed failure taxonomy rather than an exhaustive causal classification. Mismatch may occur between the observed adherence process and the assigned process, between the barrier and intervention mechanism, between intervention workload and patient capability, or between an intended service and real-world implementation. Null outcomes may also result from inadequate measurement, insufficient intervention intensity, inappropriate outcome choice, spontaneous behavioral change, or factors outside the framework. Failure should therefore trigger reassessment rather than retrospective certainty about why an intervention did not work.

Figure 2 represents these mismatch pathways as recursive branches in which an intervention is retained, redirected, or clinically escalated according to the barrier it can actually modify.

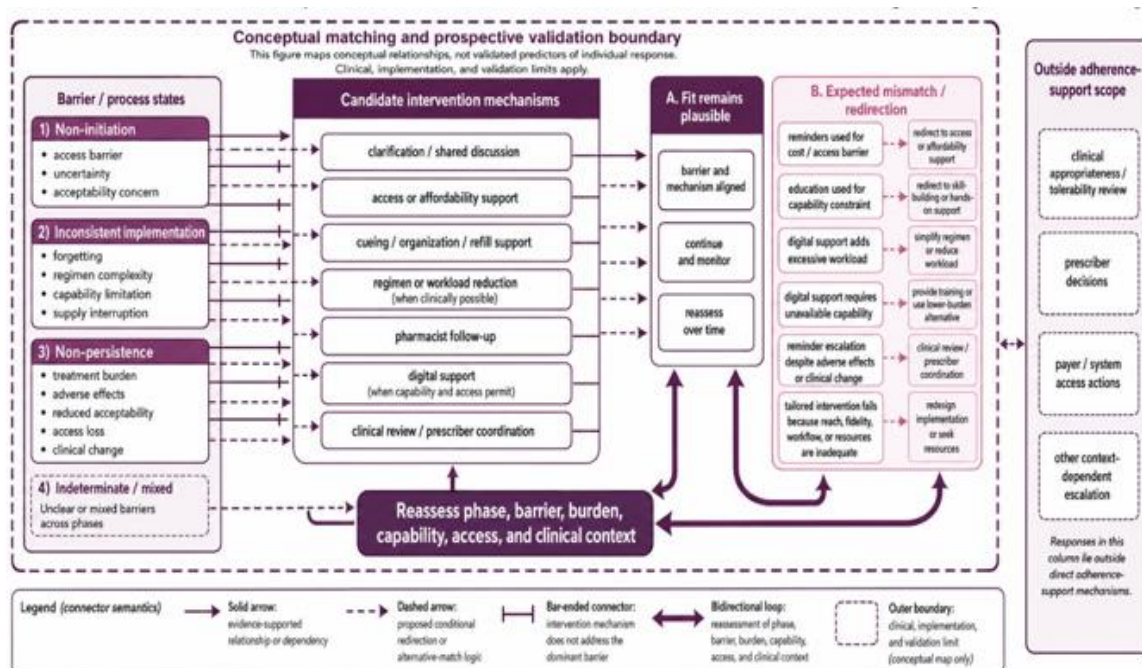


Figure 2. Intervention failure becomes predictable when the intervention mechanism misses the barrier governing medication taking

The central argument is that medication nonadherence is not a sufficiently specific intervention diagnosis. Phase-based definitions, contemporary work on the causes of nonadherence, and therapy-specific determinant evidence are inconsistent with treating nonadherence as one stable phenotype [1, 12, 15]. A patient who does not start a medicine, one who misses doses after starting, and one who intentionally or unintentionally stops after months of treatment may all appear “nonadherent,” yet the information needed to understand those states differs. The proposed method converts that distinction into a pharmacy-practice question: which medication-taking process has failed, what barrier most plausibly governs that failure, and what intervention mechanism can alter the barrier without creating unacceptable additional work?

This logic also changes the role of adherence measurement. A refill gap, self-report score, or digital record becomes evidence contributing to classification rather than a complete diagnosis. Discordant information should therefore produce uncertainty or renewed assessment, not automatic escalation. The same principle applies to multimедication regimens: adherence should be characterized at the medicine or regimen level where possible because one patient may simultaneously show different adherence processes across therapies.

Treatment burden and patient capability add a further safeguard. An intervention can be conceptually relevant but practically unsuitable if it adds monitoring, communication, technology, travel, cognitive work, or organizational demands that exceed available capacity. Conversely, a seemingly patient-level deficit may actually be driven by affordability, fragmented care, or a clinically appropriate treatment change. Matching therefore requires explicit movement between patient, regimen, pharmacist, prescriber, organization, and health-system levels rather than locating all responsibility within the patient.

The framework is deliberately recursive. An apparent fit should be reassessed when behavior does not change, when adverse effects or clinical priorities emerge, or when the delivery context changes. This avoids interpreting every null response as insufficient motivation or insufficient intervention intensity. It also preserves an important outcome distinction: greater medication taking is not itself evidence of therapeutic appropriateness, clinical benefit, safety, or successful implementation.

The contribution is thus methodological rather than predictive. The framework offers a structured way to expose assumptions that are often hidden when interventions are selected from a generic adherence label. Its value will depend on whether those assumptions can be classified reliably, whether matching improves decisions without increasing burden or inequity, and whether the additional assessment work is feasible in routine pharmacy practice.

Implications for pharmacy practice and research

For pharmacy practice, the immediate implication is to diagnose before intensifying. Community and clinical pharmacy services should preferentially select feasible interventions that address a plausible barrier and can be delivered within local scope, workflow, and health-system constraints. Evidence on patient-directed interventions that could be implemented in routine care remains heterogeneous, reinforcing the need to avoid a universal ranking of adherence strategies [25]. The least-burdensome intervention capable of modifying the identified barrier is therefore a defensible starting principle, but it remains a proposed principle rather than a proven optimum.

Documentation should distinguish the observed medication-taking pattern from the inferred explanation. Recording “persistent refill gap; affordability suspected and being assessed” is methodologically stronger than converting an incomplete signal into a definitive label such as “unmotivated.” Referral should also be treated as a legitimate matching outcome. Cost barriers, adverse effects, therapeutic uncertainty, regimen redesign, and care-transition discontinuity may require payer navigation, prescriber communication, or multidisciplinary action rather than another patient-facing adherence message.

Research should now test matching rather than assuming it. Reviews of adherence interventions in comorbid hypertension show the prevalence of multimodal approaches and the difficulty of attributing benefit to particular components [26]. Future pragmatic studies should therefore specify the targeted phase and barrier, record why each intervention component was selected, and compare matched with usual or nonmatched adherence support where ethically and operationally feasible. Outcomes should separately include adherence behavior, clinical and medication-safety outcomes, patient burden, acceptability, equity, reach, adoption, fidelity, time, cost, and sustainability.

Pharmacists are plausible implementers because pharmacist-led care has been associated with improved adherence in real-world older-adult populations, although observational association does not establish causal effectiveness [27]. Validation should therefore span community, ambulatory, hospital-transition, and managed-care settings and test whether the method remains useful when pharmacist scope, staffing, reimbursement, digital access, and available referral pathways differ.

Limitations

This paper is a methodological synthesis, not a systematic review, diagnostic study, or prospective intervention trial. Its evidence base was selected to support specific conceptual distinctions and therefore should not be interpreted as exhaustive. Restricting evidence to high-ranked peer-reviewed journals also excludes potentially informative work from other sources and settings.

The proposed classifications remain vulnerable to measurement error. Dispensing records do not establish ingestion or intention; self-report can be affected by recall and social desirability; and available medication-management-capacity instruments do not cover every relevant capability domain. Triangulation can reduce but not eliminate uncertainty. Some cases will remain indeterminate, and forcing them into a single barrier category would create false precision.

The framework may also oversimplify coexisting mechanisms. Cost, beliefs, adverse effects, regimen complexity, cognitive limitations, caregiver availability, and implementation failures can operate simultaneously or change over time. The relative importance of these mechanisms may differ by medicine, disease, patient, healthcare professional, organization, and health system.

Most importantly, the proposed matching sequence has not been prospectively validated. Its classification reliability, feasibility, incremental workload, equity consequences, cost, effect on adherence, and downstream clinical or safety outcomes are unknown. A more complex matching service could perform no better than simpler pharmacy support or could reduce reach if assessment demands are excessive. External pragmatic evaluation is therefore required before the method is used as a prescriptive algorithm, performance standard, or basis for policy.

Conclusion

Medication nonadherence should not automatically trigger a generic adherence intervention. Initiation, implementation, and persistence describe different points at which medication taking can fail, while treatment burden, patient capability, affordability, tolerability, clinical appropriateness, and health-system conditions can change what an observed failure means and what a pharmacy intervention can realistically modify.

This paper proposes a methodological response to that heterogeneity. The approach first identifies the medicine-specific adherence process, then seeks the most plausible modifiable barrier, evaluates treatment burden and capability, considers access and implementation feasibility, selects an intervention mechanism that can plausibly act on the barrier, and reassesses the classification when behavior or context changes. It also treats referral, clinical review, or system-level action as legitimate outcomes when the dominant problem lies outside the mechanism or scope of patient-facing adherence support.

The framework is intentionally evidence-bounded. It does not establish that matched interventions improve adherence, clinical outcomes, medication safety, equity, or implementation performance, nor does it imply that every patient can be assigned a single stable cause of nonadherence. Its contribution is to make intervention assumptions explicit and testable.

The next step is empirical: determine whether phase- and mechanism-sensitive matching can be applied reliably, with acceptable workload and patient burden, across medicines, populations, pharmacy settings, and health systems. Until such validation exists, the method should be used as a conceptual aid for disciplined reasoning rather than as a validated clinical decision rule.

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