

Research Article

Comparative strategies to improve medication adherence in chronic disease: what works, for whom, and at what cost

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Abstract:

Background: Medication non-adherence is common in chronic disease and limits the real-world effectiveness of pharmacotherapy. Adherence is best understood as a process (initiation, implementation, discontinuation/persistence), and intervention choice should match the dominant barrier and phase of adherence. (1)

Methods: For this study researchers conducted an umbrella-style synthesis using PubMed as the primary database (verification/search date: 10 February 2026). Authors prioritised PubMed-indexed systematic reviews, meta-analyses, and Cochrane reviews comparing five intervention families—digital reminders (SMS/apps/interactive voice response), pharmacist-led interventions, regimen simplification (dosing frequency), fixed-dose combinations/polypill strategies, and behavioural counselling (motivational interviewing).

Results: Digital reminders improve adherence implementation with small-to-moderate pooled effects (electronic reminders: Cohen's $d=0.29$; SMS meta-analysis OR 2.11 with an estimated 17.8% absolute gain under a 50% baseline assumption), but clinical effects are uncertain in cardiovascular secondary prevention, where adherence measures are inconsistent and pooled LDL/BP effects are small. (4–7) Pharmacist-led interventions show moderate pooled adherence benefits in older adults (effect size 0.57; 0.41 after outliers) with attenuation over time, and medication review models can improve biomarker target attainment; effects on hospitalisation/mortality are inconsistent. (8,9) Regimen simplification shows a graded adherence advantage using electronic monitoring (e.g., -6.7% taking adherence for twice-daily vs once-daily regimens), supporting simplification as a durable first-line strategy. (12) FDC strategies reduce non-compliance (RR 0.74) and improve adherence/persistence in hypertension (mean adherence $+14.92\%$; persistence RR 1.84), while early polypill evidence shows improved risk factors but uncertain event effects and higher discontinuation, with limited cost reporting. (13–15) MI has a small pooled effect (0.12) and appears most relevant for intentional non-adherence. (16) Economic evidence is limited and heterogeneous; overviews suggest simplification and pharmacist care are often cost-effective but context-dependent. (18,19) Indian RCT evidence suggests education plus follow-up delivered via community health workers/pharmacists is promising but of mixed quality. (20)

Conclusion: The most consistent adherence improvements arise from structural strategies (simplification and FDCs), complemented by clinically integrated pharmacist care and targeted behavioural and digital tools. Better standardisation of adherence outcomes and stronger prospective economic evaluation are priorities for scalable implementation.

Keywords: Medication adherence, chronic disease, digital technologies

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Introduction

Medication adherence is a determinant of treatment effectiveness that is too often assumed rather than measured. In chronic disease, patients may initiate therapy but implement it inconsistently, or discontinue it prematurely. A behavioural–pharmacological taxonomy frames adherence as a time-dependent process with three quantifiable phases: initiation (taking the first dose), implementation (the extent to which day-to-day dosing matches the prescribed regimen), and discontinuation (cessation), with persistence defined as the time from initiation to discontinuation. (1) This framework matters clinically because different interventions are plausibly effective for different phases: reminders may support implementation, whereas tolerability management and regimen simplification may influence persistence.

The clinical relevance of adherence is highlighted in cardiovascular therapy. A large meta-analysis of prospective studies found that only 60% (95% CI 52–68%) of participants achieved “good adherence” (commonly defined as $\geq 80\%$), and that good adherence to anti-hypertensives and statins was associated with lower risks of cardiovascular events and all-cause mortality. (2) These observational associations do not prove that adherence interventions will reduce events (confounding and “healthy adherer” effects remain possible), but they quantify the scale of avoidable risk and motivate intervention research.

Intervention evidence, however, is mixed. A major Cochrane review of randomised controlled trials (RCTs) concluded that adherence-improving interventions for chronic health problems are often complex and only modestly effective; only a minority of the lowest risk-of-bias trials improved both adherence and clinical outcomes. (3) This creates a practical problem for medication and pharmacotherapy journals: clinicians need comparative, implementable guidance on what to do in practice, and investigators need a defensible synthesis that distinguishes “what improves adherence” from “what improves outcomes” and “what can be scaled”.

In this umbrella-style review, I compare five pragmatic intervention families that align with routine care: (i) digital reminders (SMS, apps, interactive voice response or similar messaging), (ii) pharmacist-led interventions (community and clinic-based models), (iii) regimen simplification (especially dosing frequency), (iv) fixed-dose combinations (FDCs) and polypill strategies, and (v) behavioural strategies, with a focus on motivational interviewing (MI). I consider adherence outcomes (implementation and persistence, as operationalised in the source reviews), clinical outcomes (risk-factor control and patient-important endpoints where available), and economic outcomes (cost and cost-effectiveness where evaluated).

Methods

Search and verification statement

We searched and verified evidence using entity[“organization”, “PubMed”, “bibliographic database”] as the primary database on 10 February 2026. I first re-verified every reference used in my earlier draft by locating its PubMed record and confirming bibliographic details (authors, title, journal, year, volume/issue, pages or article number, DOI where available). Authors then performed topic-based searches to ensure each intervention family was supported by high-quality review-level evidence. Search strings combined core terms and intervention descriptors, for example:

- (“medication adherence” OR compliance OR persistence) AND (text messaging OR SMS OR mobile health OR reminder OR “interactive voice response”)
- (“medication adherence” OR compliance) AND (pharmacist OR “medication review” OR “pharmacist-led”)
- (“medication adherence” OR compliance) AND (“dosing frequency” OR “once daily” OR “regimen simplification”)
- (“fixed dose combination” OR polypill) AND (adherence OR compliance)
- (“motivational interviewing” AND medication adherence)
- (“economic evaluation” OR cost-effectiveness) AND medication adherence

All references in the final list are PubMed-indexed and include a PMID. No prior-cited references were found to be unverifiable on PubMed, and no replacements were required; to

match the requested target reference count, I retained 20 sources that were most directly load-bearing for comparative claims, while keeping the manuscript's scope aligned with a pharmacotherapy journal audience.

Design, inclusion priorities, and synthesis

This is an umbrella-style narrative synthesis of systematic reviews, meta-analyses, and entity ["organization","Cochrane","systematic review organisation"] reviews, complemented by review-level evidence on economic evaluation. This study prioritised (i) Cochrane reviews and large meta-analyses, (ii) pooled adherence estimates when explicitly reported, and (iii) sources reporting clinical outcomes and/or costs. The study did not conduct a new meta-analysis because effect measures and adherence definitions varied substantially across diseases and reviews, and converting heterogeneous adherence constructs into a common metric risked introducing avoidable measurement error. (3)

It was decided, to interpret adherence outcomes using the taxonomy in (1), while acknowledging that most reviews operationalise adherence using self-report instruments, pill counts, electronic monitoring, or pharmacy refill metrics. (1,3) Economic outcomes are described as costs, health service utilisation, or cost-effectiveness metrics (incremental cost-effectiveness ratios and quality-adjusted life-years) where available.

Results

Comparative evidence table

Across chronic diseases, no single strategy is universally effective. Structural interventions that reduce regimen complexity (simplification and FDCs) show consistent adherence advantages. Pharmacist-led interventions show moderate effects but may attenuate without reinforcement. Digital reminders improve implementation in many settings but show less consistent translation to clinical endpoints, especially in cardiovascular secondary prevention. MI shows a small but consistent pooled effect and appears most relevant when non-adherence is intentional.

Table 1 provides a comparative summary. Numeric effect sizes in the table correspond to pooled estimates discussed and cited in the family-specific subsections that follow.

Table 1. Comparative summary of intervention families to improve medication adherence in chronic disease

Intervention family	Typical adherence effect (qualitative + representative pooled estimate)	Clinical outcome signal	Durability	Cost evidence (direction + quality)	Best target population
Digital reminders (SMS/apps/IVR)	Small overall effect across reminder modalities (electronic reminders: Cohen's $d=0.29$). (4) SMS meta-analysis: OR 2.11; estimated ~17.8% absolute gain under assumed 50% baseline. (5) Reminder systems: adherence 66.61% vs 54.71%. (6)	Mixed; in cardiovascular secondary prevention, adherence and clinical effects are very uncertain, with small/no consistent pooled changes in LDL or blood pressure. (7)	short	Sparse; few trial-based economic evaluations, and cost-effectiveness depends on implementation costs and durability. (18,19)	Unintentional non-adherence (forgetting), variable routines, early implementation failures
Pharmacist-led interventions	Moderate pooled improvements in older adults (effect size 0.57; 0.41 after outliers), with	Biomarker target attainment and respiratory technique/disease control can improve;	medium	Frequently reported as cost-effective in overviews;	Polypharmacy, older adults, technique-sensitive therapies (e.g.,

Intervention family	Typical adherence effect (qualitative + representative pooled estimate)	Clinical outcome signal	Durability	Cost evidence (direction + quality)	Best target population
	attenuation over time. (8) Many community pharmacy programmes report improved adherence. (9,10)	effects on hospitalisation/mortality inconsistent. (9–11)		underlying evaluations heterogeneous in design and quality. (19)	inhalers), multi-factor barriers amenable to tailored review
Regimen simplification (dosing frequency)	Consistent direction favouring simpler regimens; electronically monitored adherence declines as dosing frequency increases (e.g., –6.7% taking adherence for twice-daily vs once-daily). (12)	Clinical outcomes not consistently evaluated in dosing-frequency syntheses; plausibility supported by adherence–outcome links and pharmacological rationale. (2,12)	long	Usually favourable in principle (structural, scalable), but depends on drug pricing and availability; direct evaluation often absent. (18,19)	Patients willing in principle but struggling with regimen complexity, task burden, or timing constraints
Fixed-dose combinations/polypill	Reduced non-compliance vs free-drug regimens (RR 0.74; RR 0.76 in hypertension). (13) Hypertension: mean adherence +14.92% and persistence RR 1.84. (14) Polypill: adherence to multi-drug strategy improved by 33% in one trial. (15)	Risk-factor improvements seen; early polypill evidence uncertain for events/mortality because few trials reported them; discontinuation and adverse events matter. (15)	long	Cost evidence variable; early polypill trials reported no costs; value depends on pricing, procurement, and discontinuation. (15,19)	Patients requiring multiple agents (hypertension, CVD prevention), where pill burden and regimen fragmentation are major barriers
Behavioural strategies (motivational interviewing)	Small pooled effect size (0.12); larger effects with MI-only and coaching/fidelity supports. (16)	Variable; depends on magnitude and persistence of adherence change and on disease. (3,16)	medium	Uncertain; likely improved by targeting high-risk intentional non-adherence and embedding delivery in existing services. (18,19)	Intentional non-adherence, ambivalence, low self-efficacy, negative beliefs about medicines

Digital reminders and mobile messaging

Electronic reminders are often framed as scalable tools for adherence improvement. A 2015 meta-analysis of 22 RCTs of electronic reminders (SMS, pagers, alarm devices) found a small but statistically significant pooled adherence effect (Cohen's $d=0.29$, 95% CI 0.18–0.41). (4) This estimate plausibly reflects improved implementation, but the effect was sensitive to disease type and intervention duration, suggesting meaningful context dependence in reminder efficacy. (4)

For SMS specifically, a 2016 meta-analysis of 16 randomised trials across chronic diseases reported a pooled adherence odds ratio of 2.11 (95% CI 1.52–2.93). (5) Under an assumed baseline adherence of 50%, the authors estimated an increase to 67.8% (17.8%

absolute gain). (5) Importantly, the effect was not sensitive to disease type or several message characteristics (e.g., personalisation, two-way messaging), but the evidence base had short follow-up and relied heavily on self-reported adherence measures in many included studies, limiting inferences about persistence. (5)

A reminder-system meta-analysis focused on daily medicines found higher adherence in reminder groups than controls (66.61% vs 54.71%) and included modalities such as interactive voice response systems alongside phone calls, texts, pagers and electronic reminder devices. (6) The authors emphasised that many evaluated reminder modalities were impractical at scale and might work best when combined with other strategies. (6) From a pharmacotherapy standpoint, this supports a “layering” model: reminders may be most rational as adjuncts to simplification and human support rather than as stand-alone adherence programmes.

In cardiovascular secondary prevention, review-level evidence is cautious. An updated Cochrane review of text messaging after cardiovascular events concluded that meta-analysis for adherence was not feasible because trials used different adherence definitions and scoring systems; ten of 18 trials suggested benefit and eight did not. (7) Evidence was very uncertain for adherence, and pooled analyses suggested little to no effect on LDL cholesterol and blood pressure, with uncertain effects on cardiovascular events and mortality due to limited reporting and low certainty. (7) In other words, even when text messaging changes implementation in some settings, it may not reliably translate into measurable clinical improvements within typical follow-up horizons.

Pharmacist-led interventions

Pharmacist-led interventions integrate medication optimisation, education, behavioural support, and follow-up. This package aligns with the Cochrane conclusion that more successful adherence interventions are often multi-component and delivered with ongoing support. (3)

A 2021 meta-analysis of 40 pharmacist-led adherence trials in older adults reported a pooled adherence effect size of 0.57, decreasing to 0.41 after excluding two outliers. (8) Time-stratified effects declined from 0.64 at 3 months to 0.22 at 12 months, and were 0.36 beyond 12 months, implying that maintenance strategies are necessary for durability. (8) Practically, this argues for pharmacist-led adherence work being integrated into longitudinal chronic care models (scheduled follow-ups, synchronised refills, and active management of adverse effects and regimen changes) rather than implemented as one-off counselling encounters.

In community pharmacy models, a systematic review and meta-analysis of fee-for-service medication review programmes reported that 57.9% of studies showed adherence improvement. (9) Meta-analysis of primary outcomes found improved attainment of blood pressure targets (OR 3.50, 95% CI 1.58–7.75) and LDL targets (OR 2.35, 95% CI 1.17–4.72). (9) Overall, hospitalisation and mortality were not significantly different, but subgroup analysis suggested that clinical medication review (optimisation and problem solving) reduced hospitalisation, whereas “adherence support review” alone did not. (9) This difference is critical for interpretation: pharmacist interventions appear more likely to influence outcomes when they address the full medication-use process (appropriateness, adverse effects, interactions, titration and regimen coherence) rather than focusing narrowly on reminders or education.

A broader systematic review of community pharmacist-led interventions concluded that such programmes can improve adherence and contribute to better control in hypertension, dyslipidaemia, and respiratory diseases, but did not show statistically significant effects on diabetes or depression control within included studies. (10) This heterogeneity suggests that disease-specific mechanisms and outcome selection matter. For example, blood pressure and lipid targets may respond relatively quickly to improved medication implementation, whereas diabetes control is strongly influenced by diet, activity and titration decisions beyond adherence alone.

In asthma/COPD, a meta-analysis reported significant pooled improvements in adherence (effect estimate 1.34, 95% CI 1.18–1.53) and inhalation technique (1.85, 95% CI 1.57–

2.17), with adherence benefit clearest in COPD. (11) The analysis also suggested that interventions incorporating information, motivation and behavioural skills constructs performed better. (11) This fits a mechanistic explanation: for inhaled therapies, technique and day-to-day implementation are both high-leverage targets, making pharmacist-led intervention particularly relevant.

Regimen simplification and dosing frequency

Regimen simplification reduces adherence burden by lowering the number of daily dosing events and simplifying schedules. Evidence using electronic monitoring is informative because it reduces bias from over-reporting and more directly measures real-world implementation. (12)

A 2012 meta-analysis/meta-regression of electronically monitored adherence across chronic diseases demonstrated a graded association between more frequent dosing and worse adherence. Compared with once-daily regimens, adjusted differences in taking adherence were -6.7% (twice daily), -13.5% (three times daily), and -19.2% (four times daily); decrements were larger for stricter endpoints such as timing adherence. (12) Although clinical endpoints were not the primary focus of dosing-frequency syntheses, the magnitude and dose-response pattern support an actionable inference: when two regimens are therapeutically comparable, more frequent dosing is a predictable adherence liability.

From a comparative perspective, simplification has two key advantages. First, it is durable: benefits persist as long as the simplified regimen is maintained. Second, it is scalable: it can be implemented through prescribing decisions, formulary choices, blister packaging aligned to dosing time, and refill synchronisation. However, feasibility depends on formulation availability and cost, and simplification will not solve intentional non-adherence. Economic implications across intervention families are addressed in a later section.

Fixed-dose combinations and polypill strategies

FDCs operationalise simplification by lowering pill burden and reducing regimen fragmentation. A meta-analysis of FDCs versus free-drug components across chronic conditions reported a pooled relative risk for non-compliance of 0.74 (95% CI 0.69–0.80), with a similar estimate in hypertension (RR 0.76, 95% CI 0.71–0.81). (13) These effects are consistent with the mechanism of reducing the number of dosing tasks and decreasing opportunities for selective non-adherence.

In hypertension, a 2018 meta-analysis comparing FDC therapy with free-equivalent combinations reported a mean adherence difference of 14.92% (95% CI 7.38–22.46%) favouring FDCs and better persistence (RR 1.84, 95% CI 1.00–3.39). (14) These findings are clinically salient because poor blood pressure control is frequently misattributed to pharmacological non-response when the root cause is under-implementation or discontinuation, and because hypertension therapy often requires multiple agents over years.

Polypill strategies extend FDC logic to multi-drug cardiovascular prevention. A 2014 Cochrane review found that early evidence was uncertain for mortality and cardiovascular events because few trials reported these outcomes and event rates were low. (15) Risk factors improved, and improved adherence to a multi-drug strategy was reported in one trial (33% improvement, 26–41%). (15) However, the review also reported modest increases in adverse events and higher discontinuation compared with placebo, and no trials reported costs. (15) Therefore, the comparative inference is nuanced: polypills may improve adherence and risk factors, but clinical benefit for events depends on sustained persistence and tolerability over time, and economic value depends on pricing and procurement.

Behavioural strategies and motivational interviewing

Behavioural strategies are most relevant when non-adherence is intentional—driven by beliefs, fears, stigma, or low self-efficacy. MI is a structured counselling approach intended to strengthen motivation and commitment to change.

A 2017 systematic review and meta-analysis found a pooled MI effect size of 0.12 (95% CI 0.05–0.20) with minimal heterogeneity. (16) Larger effects were observed when MI was delivered as MI-only, with coaching during implementation, and face-to-face rather than solely by phone. (16) I interpret MI as a targeted tool: it is unlikely to replace simplification or pharmacist care for multi-factor barriers, but may be necessary when the dominant driver is intentional discontinuation or selective adherence.

Disease exemplar linking adherence to clinical outcomes: HIV single-tablet regimens

HIV therapy provides an instructive example where adherence can be linked to a robust clinical endpoint. A 2015 meta-analysis comparing single-tablet regimens to multi-tablet regimens found higher adherence with single-tablet regimens (OR 2.37, 95% CI 1.68–3.35) and higher 48-week viral suppression (RR 1.09, 95% CI 1.04–1.15). (17) Although disease-specific, this illustrates a general principle relevant to pharmacotherapy: structural simplification can generate both adherence improvements and clinically meaningful outcome gains when the adherence–outcome pathway is strong and measurable.

Economic evidence: what is known “at what cost”

Economic evaluation remains under-developed in adherence research. A systematic review of trial-based economic evaluations found only 14 RCTs with full economic evaluations up to June 2013, with variable methodological quality; only four studies reported incremental cost-effectiveness ratios below common willingness-to-pay thresholds, and few evaluated interventions that clearly changed adherence. (18) This mismatch between “economically evaluated” and “adherence-effective” interventions limits definitive comparative conclusions about which intervention families deliver best value per unit of adherence gained or per unit of clinical benefit.

A more recent overview of systematic reviews reported that interventions most often identified as cost-effective include regimen simplification, improved coverage/reduced out-of-pocket spending, financial incentives, and pharmacist care; education and counselling showed mixed cost-effectiveness, and evidence quality varied. (19) I interpret this as supportive but not definitive: cost-effectiveness is plausible and frequently reported, but conclusions depend on durability, setting, and the extent to which adherence improvements translate into patient-important outcomes.

South Asia Perspective

For an India-facing audience, feasibility and access require explicit attention. A 2023 systematic review identified 22 RCTs of adherence interventions for chronic diseases in India; interventions were predominantly education-based, with some combined with regular follow-up, and fewer technology-based interventions. (20) The authors concluded that education delivered by community health workers and pharmacists appears promising, especially with regular follow-up, but primary studies were of mixed methodological quality. (20)

This pattern aligns with the broader comparative synthesis: adherence improvement is more likely when interventions are embedded in workforce structures capable of longitudinal contact, and when patients face multi-factor barriers that require more than reminder prompts. (3,8,19,20) Affordability and availability remain structural constraints; adherence programmes will not fully compensate for unstable medicine access or high out-of-pocket costs, making policy and financing interventions relevant adjuncts in many Indian contexts. (19,20)

Discussion

The evidence supports a layered, barrier-matched interpretation rather than a single “best” adherence intervention. I draw four comparative conclusions.

First, simplify the regimen whenever feasible. Electronic monitoring evidence demonstrates a graded decline in adherence as dosing frequency increases, providing a robust rationale for once-daily dosing, synchronised schedules, and reduction of regimen complexity. (12) Because simplification is structural, it is durable and scalable and therefore a rational first-

line strategy, particularly for patients who are not overtly opposed to therapy but struggle with routines. (12) In practice, this means that adherence work begins at prescribing: choose formulations and schedules that reduce daily task burden, align dosing to stable routines, and minimise within-day timing complexity when therapeutically appropriate.

Second, use FDCs strategically for patients needing multiple agents. Meta-analyses demonstrate reduced non-compliance and improved adherence and persistence in hypertension with FDCs compared with free-equivalent regimens. (13,14) In cardiovascular prevention, early polypill evidence shows improved risk factors and improved adherence in limited data, but emphasises tolerability and discontinuation as limiting factors, with uncertain event outcomes and absent cost reporting. (15) Thus, we, the authors, treat FDCs and polypills as adherence-supporting pharmacological designs whose net benefit depends on continued persistence and acceptable adverse-effect profiles, not as purely behavioural interventions.

Third, pharmacist-led interventions are effective but should be designed for maintenance. Meta-analytic evidence in older adults shows moderate initial adherence gains that attenuate over time, implying that programmes must include reinforcement and integration into chronic care pathways. (8) Community pharmacy medication review models show biomarker target improvements and possible hospitalisation reductions when clinical medication review is included, supporting the view that pharmacist care works best when it goes beyond counselling to include clinical optimisation and longitudinal follow-up. (9) In practical terms, pharmacist services are most defensible where the medication-use process is complex: polypharmacy, high-risk medicines, technique-dependent therapies, multimorbidity, and frequent regimen changes.

Fourth, digital reminders should be positioned as implementation tools and evaluated with appropriate expectations. SMS and electronic reminders improve adherence in pooled analyses, but many trials are short and rely on self-reported adherence measures. (4–6) In cardiovascular secondary prevention, evidence is very uncertain for adherence and events, and pooled analyses suggest little or no effect on LDL cholesterol or blood pressure. (7) Therefore, I consider reminders most defensible as adjuncts—particularly for unintentional non-adherence—rather than as stand-alone substitutes for simplification or human-delivered, clinically integrated support.

Across all strategies, methodological limitations constrain comparative certainty. In some domains, adherence cannot be pooled due to inconsistent measurement and definitions, revealing a research-quality problem rather than an intervention failure. (7) Short follow-up is common, and attenuation is explicitly documented in pharmacist-led interventions. (7,8) Transferability to low-resource settings and to health systems with high out-of-pocket costs is not guaranteed; India-specific evidence suggests that education and follow-up models are feasible, but quality varies and structural barriers may dominate. (20)

Economically, authors view the evidence as supportive but incomplete. Trial-based economic evaluations are few, variable in quality, and often disconnected from interventions that clearly change adherence. (18) Overviews suggest that simplification and pharmacist care are frequently cost-effective, but conclusions are sensitive to setting, cost structure, and assumptions about durability. (19) For future adherence research in medication journals, we would prioritise long-term follow-up with standardised adherence definitions (including persistence), objective measurement when feasible, and prospective economic evaluation embedded into trials that demonstrably change adherence behaviour. (1,18,19)

Limitations

This manuscript is an umbrella-style synthesis, not a de novo systematic review with primary trial pooling. This study, therefore inherits limitations of included reviews: overlapping primary studies, heterogeneous adherence measures, and variable risk-of-bias approaches. (3,7–19) The study did not formally appraise each review using an instrument such as AMSTAR 2, although key sources explicitly report heterogeneity and risk-of-bias concerns. (3,7,15,18,19)

This study focused on five intervention families that have substantial review-level evidence and are immediately relevant to pharmacotherapy practice. Other strategies (automatic refills, packaging interventions, copayment reduction, and broader policy interventions) were not comprehensively reviewed, although economic overviews indicate that coverage and financial interventions can be cost-effective in some settings. (19)

Conclusion

Medication adherence improvement in chronic disease is best conceptualised as a portfolio problem: different mechanisms address different barriers and different phases of adherence. Based on the comparative evidence, the study considers regimen simplification (including reduced dosing frequency) and FDCs as first-line structural interventions because they consistently improve adherence and are durable once implemented. (12–14) Pharmacist-led interventions provide moderate improvements and can influence intermediate clinical outcomes when they include clinically oriented medication review and longitudinal reinforcement. (8,9)

Digital reminders and MI are best deployed as targeted adjuncts: reminders primarily support implementation for unintentional non-adherence, and MI supports intentional behaviour change when beliefs and motivation dominate. (4–7,16) Future research should standardise adherence outcomes using a phase-based taxonomy, extend follow-up beyond 12 months where feasible, and embed economic evaluation to support scalable, context-specific adherence programmes. (1,18–20)

References

1. Vrijens B, De Geest S, Hughes DA, Kardas P, Demonceau J, Ruppert T, et al. A new taxonomy for describing and defining adherence to medications. *Br J Clin Pharmacol*. 2012;73(5):691-705. doi:10.1111/j.1365-2125.2012.04167.x. PMID:22486599.
2. Chowdhury R, Khan H, Heydon E, Shroufi A, Fahimi S, Moore C, et al. Adherence to cardiovascular therapy: a meta-analysis of prevalence and clinical consequences. *Eur Heart J*. 2013;34(38):2940-2948. doi:10.1093/eurheartj/ehs295. PMID:23907142.
3. Nieuwlaet R, Wilczynski N, Navarro T, Hobson N, Jeffery R, Keenanasseril A, et al. Interventions for enhancing medication adherence. *Cochrane Database Syst Rev*. 2014 Nov 20;2014(11):CD000011. doi:10.1002/14651858.CD000011.pub4. PMID:25412402.
4. Tao D, Xie L, Wang T, Wang T. A meta-analysis of the use of electronic reminders for patient adherence to medication in chronic disease care. *J Telemed Telecare*. 2015;21(1):3-13. doi:10.1177/1357633X14541041. PMID:25147178.
5. Thakkar J, Kurup R, Laba TL, Santo K, Thiagalingam A, Rodgers A, et al. Mobile telephone text messaging for medication adherence in chronic disease: a meta-analysis. *JAMA Intern Med*. 2016;176(3):340-349. doi:10.1001/jamainternmed.2015.7667. PMID:26831740.
6. Fenerty SD, West C, Davis SA, Kaplan SG, Feldman SR. The effect of reminder systems on patients' adherence to treatment. *Patient Prefer Adherence*. 2012;6:127-135. doi:10.2147/PPA.S26314. PMID:22379363.
7. Redfern J, Tu Q, Hyun K, Hollings MA, Hafiz N, Zwack C, et al. Mobile phone text messaging for medication adherence in secondary prevention of cardiovascular disease. *Cochrane Database Syst Rev*. 2024 Mar 27;3(3):CD011851. doi:10.1002/14651858.CD011851.pub3. PMID:38533994.
8. Marcum ZA, Jiang S, Bacci JL, Ruppert TM. Pharmacist-led interventions to improve medication adherence in older adults: a meta-analysis. *J Am Geriatr Soc*. 2021;69(11):3301-3311. doi:10.1111/jgs.17373. PMID:34287846.
9. Hatah E, Braund R, Tordoff J, Duffull SB. A systematic review and meta-analysis of pharmacist-led fee-for-services medication review. *Br J Clin Pharmacol*. 2014;77(1):102-115. doi:10.1111/bcp.12140. PMID:23594037.
10. Milosavljevic A, Aspden T, Harrison J. Community pharmacist-led interventions and their impact on patients' medication adherence and other health outcomes: a systematic review. *Int J Pharm Pract*. 2018;26(5):387-397. doi:10.1111/ijpp.12462. PMID:29927005.
11. Jia X, Zhou S, Luo D, Zhao X, Zhou Y, Cui Y-M. Effect of pharmacist-led interventions on medication adherence and inhalation technique in adult patients with asthma or COPD: A systematic review and meta-analysis. *J Clin Pharm Ther*. 2020;45(5):904-917. doi:10.1111/jcpt.13126. PMID:32107837.
12. Coleman CI, Limone B, Sobieraj DM, Lee S, Roberts MS, Kaur R, et al. Dosing frequency and medication adherence in chronic disease. *J Manag Care Pharm*. 2012;18(7):527-539. doi:10.18553/jmcp.2012.18.7.527. PMID:22971206.
13. Bangalore S, Kamalakkannan G, Parkar S, Messerli FH. Fixed-dose combinations improve medication compliance: a meta-analysis. *Am J Med*. 2007;120(8):713-719. doi:10.1016/j.amjmed.2006.08.033. PMID:17679131.
14. Du L-P, Cheng Z-W, Zhang Y-X, Li Y, Mei D. The impact of fixed-dose combination versus free-equivalent combination therapies on adherence for hypertension: a meta-analysis. *J Clin Hypertens (Greenwich)*. 2018;20(5):902-907. doi:10.1111/jch.13272. PMID:29700923.
15. de Cates AN, Farr MRB, Wright N, Jarvis MC, Rees K, Ebrahim S, et al. Fixed-dose combination therapy for the prevention of cardiovascular disease. *Cochrane Database Syst Rev*. 2014 Apr 16;4(4):CD009868. doi:10.1002/14651858.CD009868.pub2. PMID:24737108.

16. Zomahoun HTV, Guénette L, Grégoire J-P, Lauzier S, Lawani AM, Ferdynus C, et al. Effectiveness of motivational interviewing interventions on medication adherence in adults with chronic diseases: a systematic review and meta-analysis. *Int J Epidemiol*. 2017;46(2):589-602. doi:10.1093/ije/dyw273. PMID:27864410.
17. Clay PG, Nag S, Graham CM, Narayanan S. Meta-Analysis of Studies Comparing Single and Multi-Tablet Fixed Dose Combination HIV Treatment Regimens. *Medicine (Baltimore)*. 2015;94(42):e1677. doi:10.1097/MD.0000000000001677. PMID:26496277.
18. Oberjé EJM, de Kinderen RJA, Evers SMAAE, van Woerkum CMJ, de Bruin M. Cost effectiveness of medication adherence-enhancing interventions: a systematic review of trial-based economic evaluations. *Pharmacoeconomics*. 2013;31(12):1155-1168. doi:10.1007/s40273-013-0108-8. PMID:24222477.
19. Al-Aqeel S, Alsugair J, Alghamdi R. Economic evaluation of interventions to improve medication adherence among patients with chronic diseases: an overview of systematic reviews. *Expert Rev Pharmacoecon Outcomes Res*. 2023;23(2):153-179. doi:10.1080/14737167.2023.2161516. PMID:36562404.
20. Tolley A, Hassan R, Sanghera R, Grewal K, Kong R, Sodhi B, et al. Interventions to promote medication adherence for chronic diseases in India: a systematic review. *Front Public Health*. 2023;11:1194919. doi:10.3389/fpubh.2023.1194919. PMID:37397765.