IJEBM International Journal of Evidence-Based Medicine

International Journal of Evidence-Based Medicine
(eISSN 3083-1776)

Australasia Publishing Group

Review Article

Rational Use of Antidiabetics and Antihypertensives Among Adults with Coexisting Diabetes and Hypertension: A Systematic Review and a Proposed ADHERE-Prescription Medication Optimisation Framework

Leo Tata[1], Anyebe Daniel Ameh[2], Adesina Saheed Musa[3], Adetayo Olufunlayo Adewale[4]

[1]*Department of Human Development and Family Studies, College of Health and Human Sciences, Lowa State University, Ames, IA, USA*
[2]*Department of Professional Studies, University of Denver, Denver, CO, USA*
[3]*Department of Medical Laboratory Science, Lagos State University, Lagos, Nigeria*
[4]*Department of Pharmacology, Microbiology & Immunology, School of Medicine, St. George's University, St George, Grenada*

Received: Sep 15, 2026
Accepted: Nov 12, 2026

Corresponding author's email:
leotata@iastate.edu

Citation: Tata L, Ameh AD, Musa AS, Adewale AO. Rational Use of Antidiabetics and Antihypertensives Among Adults with Coexisting Diabetes and Hypertension: A Systematic Review and a Proposed ADHERE-Prescription Medication Optimisation Framework. International Journal of Evidence-Based Medicine. 2026;1(4):jebm018.
https://doi.org/10.63946/jebm/19983

Copyright: By the author(s).

License: A non-exclusive license by the publisher. Published by Australasia Publishing Group LLP.

Open Access: This article is an open access article distributed under the terms and conditions of the CC-BY Creative Commons Attribution license
https://creativecommons.org/licenses/by/4.0

ABSTRACT

Background: Diabetes mellitus and hypertension frequently coexist, and adults with both conditions often require multiple medicines, increasing the risk of medication burden, poor adherence, and suboptimal disease control.

Objective: To synthesise evidence on the patterns, determinants, and interventions associated with rational antidiabetic and antihypertensive medication use among adults with coexisting diabetes and hypertension, and to propose a conceptual framework.

Methods: Following PRISMA 2020, PubMed, ScienceDirect, and Google Scholar (first 300 records) were searched for English-language studies published from January 2015 to July 2026. Quality was assessed using the Kmet criteria, and findings were synthesised narratively.

Results: Thirteen studies were included (five intervention, six cross-sectional, two qualitative), with quality scores of 85.7–100%; 11 were from low- and middle-income countries, and six enrolled mixed populations without separate results for the comorbid subgroup. All five interventions were pharmacist-led, and all four with extractable results improved at least one adherence measure, whereas effects on blood pressure and glycaemic control were inconsistent. Medication burden, limited knowledge, beliefs about medicines, affordability, and inadequate follow-up were recurring barriers. No study evaluated deprescribing or provider-focused interventions. Findings were organised into a six-component conceptual framework (ADHERE), in which deprescribing and provider support remain untested hypotheses.

Conclusion: Pharmacist-led education and follow-up were associated with improved adherence, but evidence on clinical outcomes and prescribing quality is limited. ADHERE is unvalidated and requires consensus and feasibility testing before implementation.

Keywords: Rational Medication Use; Diabetes Mellitus; Hypertension; Medication Adherence; Polypharmacy; Medication Optimisation; Health Literacy; Conceptual Framework

Introduction

Diabetes mellitus and hypertension have become defining challenges of contemporary non-communicable disease management because they frequently occur together and substantially increase the burden of cardiovascular, renal, and cerebrovascular complications. Diabetes affects hundreds of millions of adults globally, while hypertension remains the leading modifiable risk factor for cardiovascular morbidity and mortality worldwide [1, 2]. The coexistence of these two conditions is increasingly common because they share several biological pathways, including insulin resistance, chronic inflammation, endothelial dysfunction, oxidative stress, and vascular injury. Adults living with both diabetes and hypertension experience a greater risk of coronary heart disease, stroke, heart failure, and chronic kidney disease compared with individuals affected by either condition alone [3, 4]. Thus, diabetes-hypertension comorbidity represents a distinct clinical challenge that requires medication management approaches beyond traditional single-disease care.

The management of adults with diabetes and hypertension commonly requires long-term use of multiple medications aimed at controlling blood glucose, blood pressure, cardiovascular risk, and associated complications. These regimens may include glucose-lowering medicines, renin-angiotensin system inhibitors, calcium channel blockers, diuretics, lipid-lowering therapy, and other preventive treatments when clinically indicated. Although the use of several medicines may represent appropriate polypharmacy when each medicine has a clear indication and contributes to improved outcomes, it may become problematic when medication burden exceeds clinical benefit. Problematic polypharmacy increases the likelihood of adverse drug reactions, drug-drug interactions, medication errors, financial burden, and difficulties with adherence [5, 6]. For patients managing several chronic conditions simultaneously, the challenge is therefore not simply obtaining more medicines but ensuring that every medicine prescribed remains necessary, effective, safe, and understood.

The concept of rational drug use provides an important foundation for addressing these challenges. The World Health Organization defines rational medicine use as the process whereby patients receive appropriate medicines according to their clinical needs, in suitable doses, for an adequate duration, and at the lowest possible cost to them and the healthcare system [7, 8]. Rational medicine use is therefore broader than medication adherence: it spans prescribing (choice of medicine, dose, combination, and duration), access and affordability, and patient use. Medication adherence, defined as the extent to which a person's medicine-taking corresponds with agreed recommendations from a healthcare provider [9], is the patient-use component of this pathway, whereas medicines optimisation describes a person-centred approach to ensuring that the overall regimen achieves the best possible outcomes [10]. This distinction is maintained throughout this review. However, adults with diabetes and hypertension frequently experience irrational medication use arising from several interconnected problems. Medication duplication may occur when patients receive overlapping therapies from different healthcare providers. Inappropriate combinations may expose patients to avoidable drug interactions or adverse effects. Poor adherence may result from complex treatment schedules, medication costs, inadequate understanding, or treatment fatigue. Self-medication can introduce additional risks when patients use non-prescribed medicines without informing healthcare professionals. In contrast, clinical inertia represents the opposite challenge, where treatment intensification is delayed despite persistent uncontrolled blood glucose or blood pressure levels. These problems are particularly concerning in low- and middle-income countries where healthcare access, continuity of care, medication affordability, and monitoring systems may remain limited [11, 12].

Although clinical guidelines for diabetes and hypertension have improved substantially, many recommendations continue to address these diseases separately. Guidelines from organisations such as the American Diabetes Association and international hypertension societies provide evidence-based recommendations for individual disease management, but adults with multimorbidity often require decisions that consider the interaction between multiple therapies, competing treatment priorities, renal function, medication burden, and individual preferences [13, 14]. The gap between guideline recommendations and real-world medication management is further influenced by health system limitations, including fragmented care between healthcare providers, inadequate medication reconciliation, insufficient follow-up, limited access to pharmacists, medicine shortages, and high out-of-pocket expenditure. Consequently, many patients navigate complex medication regimens without receiving the coordinated support required for safe and effective use.

The consequences of poor medication optimisation extend beyond individual prescribing decisions and directly affect patient outcomes and healthcare systems. Inadequate medication adherence

and inappropriate prescribing contribute to uncontrolled hypertension, poor glycaemic management, avoidable complications, hospital admissions, and increased healthcare expenditure [15, 16]. For patients, the burden may involve uncertainty about why medicines are needed, difficulty remembering multiple doses, fear of adverse effects, and frustration associated with lifelong treatment. For healthcare professionals, these challenges create the need for structured approaches that support medication review, shared decision-making, monitoring, and continuous adjustment of treatment plans. Effective management of diabetes and hypertension therefore requires attention not only to what medicines are prescribed but also to how medicines are selected, explained, monitored, and adapted over time.

Existing research has evaluated several strategies aimed at improving medication use, including pharmacist-led medication reviews, patient education, digital reminders, telemonitoring, and provider-focused interventions. However, much of the available evidence remains fragmented, with many studies examining isolated interventions instead of addressing the complete medication-use pathway among adults living with diabetes and hypertension together. A recent systematic review by Maniki et al. synthesised seven intervention studies in patients with coexisting diabetes and hypertension and found that multifaceted, education-based interventions improved adherence [17]. That review, however, was restricted to interventions and adherence outcomes; it did not synthesise observational and qualitative evidence on the determinants of medication use, did not examine the prescribing dimension of rational medicine use, and did not translate its findings into a framework for practice. There remains a need to synthesise evidence on prescribing patterns, medication-related problems, adherence barriers, and interventions that improve rational medicine use across different healthcare settings. An integrated framework that connects medication assessment, optimisation, patient education, healthcare professional support, digital reinforcement, and follow-up may provide a more practical approach for managing this growing population.

Therefore, this systematic review aimed to synthesise evidence on the patterns, determinants, barriers, enablers, and interventions associated with rational antidiabetic and antihypertensive medication use among adults with coexisting diabetes and hypertension. Specifically, the review examined medication utilisation patterns, polypharmacy, prescribing challenges, adherence-related factors, and the reported effects of strategies designed to improve medication optimisation. A secondary aim was to use the synthesised findings to propose a conceptual framework, the ADHERE-Prescription Medication Optimisation Framework, intended to guide future validation and implementation research rather than to serve as a validated clinical model.

Methods

Review Design and Reporting Framework

This study employed a systematic review design to synthesise evidence on rational antidiabetic and antihypertensive medication use among adults with coexisting diabetes mellitus and hypertension. Systematic reviews provide a structured approach for identifying, evaluating, and integrating existing evidence to answer focused research questions while reducing selection bias through transparent and reproducible methods [18]. The review was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement, which provides evidence-based guidance for reporting systematic reviews, including search methods, study selection, data synthesis, and transparent presentation of findings [19]. Because no meta-analysis was performed, the synthesis was also reported with reference to the Synthesis Without Meta-analysis (SWiM) guideline [20].

Protocol Registration

The review protocol was not prospectively registered in PROSPERO or any other systematic review registry. However, the review process followed the methodological principles recommended by PRISMA 2020, including predefined eligibility criteria, systematic searching, structured study selection, data extraction, and quality assessment procedures [19]. A clarification of the eligibility criteria made during peer review is described in Section 2.3 and acknowledged as a limitation.

Eligibility Criteria

Studies were eligible if they included adults aged ≥18 years with coexisting diabetes mellitus (type 1 or type 2) and hypertension. Because many primary studies recruit from combined diabetes and hypertension clinics, studies with mixed samples (participants with diabetes only, hypertension only, or both) were eligible when participants with both conditions formed an identifiable part of the sample. On re-examination of the full texts during peer review, we found that six included studies enrolled such mixed samples and did not report results separately for the comorbid subgroup [21, 22, 23, 24, 25, 26]. Because this criterion had not been stated explicitly in the original

review plan, its application is reported transparently here: these studies were retained but classified as indirect evidence, were used only to describe barriers and enablers shared across diabetes and hypertension care, and were not used to support statements about intervention effects (Table 1). Findings from these studies should therefore be interpreted with caution. Eligible studies examined medication utilisation patterns, prescribing practices, polypharmacy, medication adherence, drug-related problems, or interventions aimed at improving rational medication use. Studies reporting outcomes related to medication safety, adherence, blood pressure control, glycaemic control, barriers, enablers, or optimisation strategies were included. Randomised controlled trials, quasi-experimental studies, observational studies, qualitative studies, and mixed-method studies published in English between January 2015 and July 2026 were considered. Studies involving children, gestational diabetes or hypertension alone, single-drug efficacy trials without medication-use outcomes, case reports, editorials, conference abstracts without full data, and studies without accessible full texts were excluded.

Operational definitions. Rational medication use was operationalised using the World Health Organization definition [7] and was considered to comprise three domains: (i) prescribing (appropriateness of medicine choice, dose, combination, duration, and regimen complexity); (ii) access and affordability; and (iii) patient use, including medication adherence, knowledge, and beliefs. Medication adherence was treated as one component of the patient-use domain [9], not as a synonym for rational medication use. Studies addressing any of these domains were eligible, and each study was classified according to the domain(s) it informed (Table 1).

Information Sources and Search Strategy

A comprehensive literature search was conducted in PubMed, Google Scholar, and ScienceDirect. PubMed searching incorporated Medical Subject Headings (MeSH), a controlled vocabulary system developed by the National Library of Medicine to improve retrieval accuracy by identifying articles indexed under standardised biomedical concepts [27]. Boolean operators were applied to combine related concepts and improve search precision. The use of "OR" expanded retrieval by combining synonymous terms, while "AND" narrowed retrieval by linking essential concepts within the research question [28].

The search strategy combined five concept blocks: diabetes; hypertension; medication use and rational medication optimisation; medication adherence; and polypharmacy, drug-related problems, or medication safety. MeSH terms and free-text synonyms were combined with Boolean operators in PubMed, and an equivalent keyword string was used in Google Scholar and ScienceDirect. The searches covered publications from 1 January 2015 to July 2026, and the final searches were run in July 2026. Database limits corresponding to the eligibility criteria (publication years 2015–2026 and English language, with human and adult limits where available) were then applied; records removed by these filters (n = 482) are shown in Figure 1 as records removed before screening. Because Google Scholar returns very large, relevance-ranked result sets that cannot be exported in full, the first 300 records ranked by relevance were screened, consistent with evidence that relevant records are concentrated in the first 200–300 Google Scholar results [29]. Other bibliographic databases (e.g., Embase, CINAHL, Scopus, Web of Science, and the Cochrane Library) were not searched, grey literature beyond Google Scholar was not systematically sought, and non-English publications were excluded; the potential for missed studies arising from these restrictions is acknowledged in Section 4.6. Reference lists of included studies and relevant reviews were hand-searched, yielding 16 additional records. The exact database-specific search strings, limits, and numbers of records retrieved from each source are provided in Supplementary File S1 (Table S1).

Study Selection Process

Retrieved records were imported into a reference management system, where duplicates were identified automatically and checked manually (n = 8 removed). Two reviewers independently screened titles and abstracts against the eligibility criteria, followed by independent full-text assessment of potentially eligible reports. Disagreements were resolved through discussion and consensus. Of the 515 records screened, 487 were excluded at the title and abstract stage. Twenty-eight reports were sought for retrieval, of which six could not be obtained in full text. Twenty-two full-text reports were assessed for eligibility, and nine were excluded because the study population did not include adults with coexisting diabetes and hypertension (diabetes-only or hypertension-only samples). Thirteen studies were included. The selection process is summarised in the PRISMA 2020 flow diagram (Figure 1).

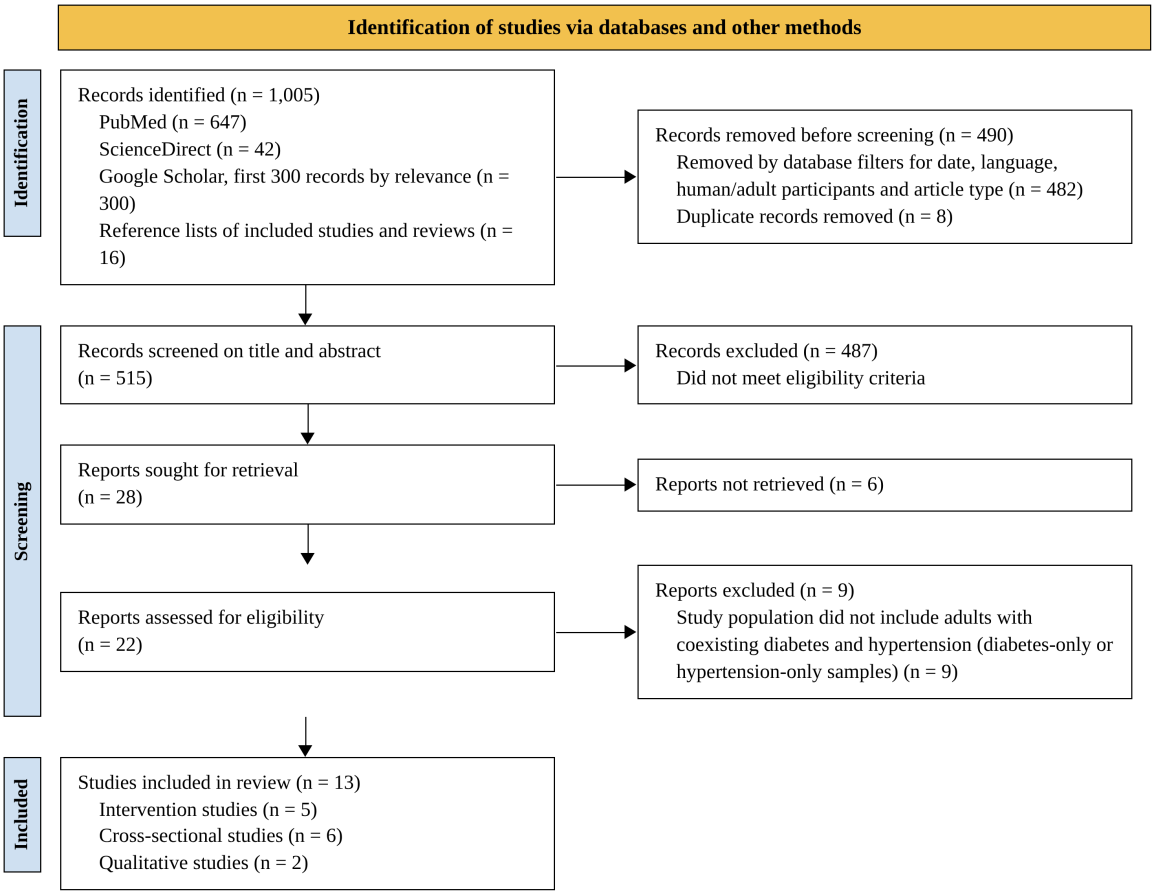


Figure 1: PRISMA 2020 flow diagram of study identification, screening, and inclusion

Data Extraction

A standardised extraction form was developed to capture author, year, country, setting, study design, sample size (and, for mixed samples, the number of participants with both conditions), follow-up duration, intervention and comparator, adherence measure, baseline and follow-up values for adherence, blood pressure, glycaemic control, and other clinical outcomes, effect estimates with 95% confidence intervals (CIs) and p-values where available, non-significant findings, and reported barriers and facilitators. Adherence outcomes and clinical outcomes were extracted separately. Data extraction was independently performed and verified to minimise errors; where effect estimates or CIs were not reported, this is stated rather than estimated.

Quality Assessment

The methodological quality of the included studies was assessed using the Standard Quality Assessment Criteria for Evaluating Primary Research Papers developed by Kmet et al. (2004) [30]. This tool was selected because it provides separate criteria for evaluating quantitative and qualitative primary research papers, allowing methodological appraisal to be conducted according to the design characteristics of each included study. Quantitative studies were assessed using the 14-item checklist, while qualitative studies were evaluated using the 10-item checklist.

Each criterion was scored according to the Kmet et al. framework as follows: Yes = 2 points, Partial = 1 point, No = 0 points, and Not Applicable (NA) = excluded from the denominator. The overall quality score for each study was calculated using the formula:

$$\text{Quality Score (\%)} = \frac{Total\ obtained\ score}{Maximum\ applicable\ score} \times 100$$

The assessment considered methodological domains including clarity of research objectives, appropriateness of study design, participant selection, description of study characteristics, validity and reliability of outcome measures, analytical procedures, control of confounding factors, reporting of findings, and whether conclusions were supported by the study results. For qualitative studies, additional criteria relating to the suitability of the qualitative approach, sampling strategy, data collection methods, data analysis procedures, credibility procedures, and reflexivity were assessed.

The quality appraisal was conducted independently by two reviewers, and discrepancies were resolved through discussion. Kmet et al. suggest a summary score of 55% as a liberal and 75% as a conservative threshold for inclusion [30]; in this review, scores above 80% were described as high quality. No

study was excluded on the basis of quality. Individual study scores are reported in Table 1, and criterion-by-criterion scores are provided in Supplementary File S1 (Table S2).

Data Synthesis

Findings from the included studies were synthesised using a narrative thematic synthesis approach [31, 32]. Due to the heterogeneity of the included studies in terms of study designs, settings, populations, interventions, and outcome measures, statistical pooling was considered inappropriate. Instead, extracted data were systematically reviewed and grouped according to recurring themes identified across the included studies.

The synthesis process involved identifying common patterns related to medication use challenges, determinants of rational medication use, and strategies that improved medication optimization among adults with co-existing diabetes and hypertension. Findings were organised into major themes and subthemes, including medication burden and polypharmacy, medication adherence patterns, patient-level factors, healthcare professional factors, medication-related factors, health-system influences, and effectiveness of medication optimisation interventions.

Quantitative and qualitative findings were integrated to provide a comprehensive understanding of the factors influencing rational medication use. Quantitative studies contributed evidence on medication adherence, treatment outcomes, and intervention effectiveness, while qualitative studies provided contextual explanations regarding patient experiences, beliefs, barriers, and healthcare interactions.

Study quality and population directness were considered during synthesis. Statements about intervention effects were based only on the five intervention studies, all of which enrolled adults with both conditions; within these, greater weight was given to randomised designs [33, 34, 35, 36] than to the non-randomised comparison [37]. Findings from mixed-population studies were used only to describe barriers and enablers and are identified as such in the text. Because meta-analysis was not possible, intervention effects were summarised by the direction of effect, adherence and clinical outcomes were summarised separately, and non-significant findings were reported alongside significant ones [20]. The procedure used to derive the proposed ADHERE framework from the synthesised themes is described in Section 3.6.

Results

Overview of Included Studies

Thirteen studies met the eligibility criteria (Figure 1). They were published between 2016 and 2023 and were conducted in 11 countries; 11 of the 13 studies were from low- and middle-income countries (Ghana, Nigeria, Ethiopia, Mexico, Colombia, Brazil, Indonesia, Pakistan, and India), and two were from high-income countries (Saudi Arabia and the United States). The evidence comprised five intervention studies (one randomised controlled trial [33], one cluster randomised controlled trial [34], one controlled pre–post study in which pharmacies were randomised [36], one randomised controlled intervention study [35], and one non-randomised pharmacist telephone intervention study with a comparison group [37]), six cross-sectional studies [21, 23, 25, 26, 38, 39], and two qualitative studies [22, 24]. Sample sizes ranged from 45 to 500 participants (Table 1).

Seven studies enrolled only adults with both diabetes and hypertension [33, 34, 35, 36, 37, 38, 39]. Six enrolled mixed samples: 146 of 300 participants (48.7%) had both conditions in Khayyat et al. [25], 21 of 45 (46.7%) in Sharma et al. [24], and approximately 28.6% of patient participants in Atinga et al. [22], while 35.0% of participants in Shimels et al. had hypertension alone [26]; Adisa et al. and Parra et al. enrolled patients with hypertension, type 2 diabetes, or both without reporting the comorbid proportion separately [21, 23]. None of these six studies reported results separately for participants with both conditions, so their findings were treated as indirect evidence and should be interpreted with caution when applied to adults with both conditions.

All 13 studies examined medication adherence or adherence-related behaviour, which belongs to the patient-use domain of rational medication use. Access and affordability were examined in four studies [21, 22, 26, 38] and medication burden or regimen complexity in two [22, 38]. No study assessed prescribing appropriateness against explicit criteria, deprescribing, or interventions directed at prescribers. The evidence base therefore informs medication adherence and patient support more directly than prescribing quality. Study characteristics are shown in Table 1, intervention details and outcomes in Table 2, and the key findings of the observational and qualitative studies in Table 3.

Table 1: Characteristics, population directness, and quality scores of the included studies (n = 13)

Study	Country; setting	Design; follow-up	Participants (n); population directness	Focus / exposure	Domain(s) of rational use addressed	Kmet score (%)
Contreras-Vergara et al., 2022 [33]	Mexico; internal medicine outpatient clinic, teaching hospital	RCT; 6 months	103 (52 I, 51 C); all with DM + HTN	Pharmacist education, brochure and medication wallet card vs physician education	Patient use (adherence); clinical outcomes	89.3
Adisa et al., 2017 [21]	Nigeria; two hospitals, Ibadan	Cross-sectional	Ambulatory patients with HTN only, T2DM only, or both (mixed); comorbid results not reported separately	Social support, affordability and adherence	Patient use; access and affordability	86.4
Alfian et al., 2021 [34]	Indonesia; 10 community health centres	Cluster RCT; 3 months	113 enrolled, 89 completed; T2DM using antihypertensives (all DM + HTN)	Barrier-targeted, tailored pharmacist intervention vs usual care	Patient use (adherence); clinical outcomes	92.9
Atinga et al., 2018 [22]	Ghana; Korle Bu Teaching Hospital	Qualitative (in-depth interviews)	49 (32 patients, 17 caregivers); mixed (≈28.6% of patients had both)	Reasons for long-term non-adherence	Patient use; medication burden; access	85
Parra et al., 2019 [23]	Colombia; two primary care institutions	Analytical cross-sectional	500; HTN and/or T2DM (mixed/unclear; proportion with both not reported)	Factors influencing adherence	Patient use; access	100
Baah-Nyarkoh et al., 2023 [38]	Ghana; primary healthcare facility	Cross-sectional	329; all with DM + HTN	Medication-related burden and adherence	Prescribing (regimen burden); patient use	100
Mazzuchello et al., 2016 [39]	Brazil; HIPERDIA programme	Cross-sectional, descriptive	102; HTN and T2DM	Knowledge, attitudes and adherence	Patient use	86.4
Kwakye et al., 2021 [35]	Ghana; municipal hospital outpatient department	Controlled intervention study with random allocation; 6 months	338 (144 I, 194 C; 141 and 187 followed up); all with DM + HTN	Clinical pharmacist education and counselling vs usual care	Patient use (adherence); clinical outcomes	89.3
Malik et al., 2022 [36]	Pakistan; 8 community pharmacies (4 I, 4 C)	Pharmacy-randomised controlled pre–post study; 6 months	80 planned (40 per arm); DM + HTN	Community pharmacist counselling vs usual pharmacy services	Patient use (adherence, knowledge); clinical outcomes	85.7

Study	Country; setting	Design; follow-up	Participants (n); population directness	Focus / exposure	Domain(s) of rational use addressed	Kmet score (%)
Sharma et al., 2023 [24]	India; government dispensary, low-income urban colony, Delhi	Qualitative (in-depth interviews)	45; mixed (21 both, 9 DM only, 15 HTN only)	Care pathways and adherence	Patient use; access	85
Khayyat et al., 2019 [25]	Saudi Arabia; 5 primary care clinics	Cross-sectional	300; mixed (146 both, 96 DM only, 58 HTN only)	Adherence (MMAS-8) and quality of life	Patient use	100
Abughosh et al., 2016 [37]	United States; Medicare Advantage plan	Non-randomised pharmacist telephone intervention with comparison group	Non-adherent ACEI/ARB users with DM + HTN	Telephone identification of adherence barriers and pharmacist support	Patient use (adherence, discontinuation)	100
Shimels et al., 2021 [26]	Ethiopia; public health facilities	Multisite cross-sectional	409; mixed (35.0% HTN only; comorbid results not reported separately)	Factors associated with poor adherence	Patient use; access and affordability	100

ACEI/ARB, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; C, control; DM, diabetes mellitus; HTN, hypertension; I, intervention; MMAS-8, 8-item Morisky Medication Adherence Scale; RCT, randomised controlled trial; T2DM, type 2 diabetes mellitus. "Mixed" denotes studies that also enrolled participants with only one condition and did not report results separately for those with both (indirect evidence; see Section 2.3).

Table 2: Interventions and outcomes in the five intervention studies

Study	Intervention (I) vs comparator (C); duration	Adherence measure	Adherence outcomes	Blood pressure and glycaemic outcomes	Non-significant or unreported findings
Contreras-Vergara et al. [33]	I: pharmacist sessions (20–25 min) at 0, 3 and 6 months, brochure, medication wallet card; C: standard physician education; 6 months	MMAS-8	High adherence 8.7% → 43.5% in I; mean MMAS-8 7.04 ± 1.4 at 6 months (within-group P < 0.001); no significant change in C	Significant within-group reductions in glucose, HbA1c, SBP and DBP in I only	Glucose change in C not significant (P = 0.194); lipids changed in both groups; between-group estimates and 95% CIs not reported
Alfian et al. [34]	I: pharmacist intervention tailored to each patient's adherence barriers; C: usual care; 3 months	MARS-5	Between-group difference 4.62 points (95% CI 0.93–8.34; P = 0.008)	No significant change in blood pressure	Blood pressure and beliefs about medicines not significant; 79% completed follow-up

Study	Intervention (I) vs comparator (C); duration	Adherence measure	Adherence outcomes	Blood pressure and glycaemic outcomes	Non-significant or unreported findings
Kwakye et al. [35]	I: clinical pharmacist education and counselling; C: usual care; 6 months	MARS-10 (adherent vs non-adherent)	Adherent: 30.47% vs 19.23% at 3 months and 39.64% vs 22.19% at 6 months (I vs C; P < 0.0001)	Median SBP 130 → 120 mmHg (I) vs 140 → 130 mmHg (C); median FPG 8.1 → 6.2 (I) vs 7.5 → 8.8 mmol/L (C); P < 0.0001 for SBP, DBP and FPG; BMI P = 0.005	SBP also fell in C; randomisation procedure incompletely described; effect sizes and 95% CIs not reported
Malik et al. [36]	I: structured pharmacist counselling (≥20 min) with patient kits; C: usual dispensing services; 6 months	Brief Medication Questionnaire	Regimen screen improved for antidiabetic and antihypertensive medicines (P = 0.001); belief and recall screens improved for antidiabetic medicines (P = 0.001)	I vs C, baseline → 6 months: FBG 11.92 → 8.25 vs 11.60 → 11.54 mmol/L; SBP 145.85 → 130.10 vs 142.15 → 145.48 mmHg; DBP 95.08 → 88.83 vs 95.00 → 97.00 mmHg	Antihypertensive belief (P = 0.152) and recall (P = 0.051) screens and access screen (P = 0.568) not significant; HbA1c, dropouts, test statistics and 95% CIs not reported
Abughosh et al. [37]	I: pharmacist telephone calls to identify adherence barriers and provide support; C: non-randomised comparison group	ACEI/ARB adherence and discontinuation	Reported as the primary outcomes; quantitative estimates not extracted	Not reported	Effect estimates not extracted (see Section 3.5.1)

BMI, body mass index; CI, confidence interval; DBP, diastolic blood pressure; FBG, fasting blood glucose; MARS-5, 5-item Medication Adherence Report Scale; PDC, proportion of days covered; SBP, systolic blood pressure. All five studies enrolled only adults with both conditions.

Table 3: Key findings of the observational and qualitative studies

Study	Population directness	Measures	Key findings
Baah-Nyarkoh et al. [38]	DM + HTN only	Living with Medicines Questionnaire; Medication Adherence Report Scale	30.7% moderate-to-high medication burden; 36.8% adherent. Burden associated with uncontrolled DBP (AOR 2.46, 95% CI 1.20–5.05) and high glucose (AOR 4.24, 2.13–8.46). Lower odds of adherence with uncontrolled DBP (AOR 0.48, 0.25–0.94), hypertension ≥5 years (AOR 0.55, 0.30–0.99) and moderate-to-high burden (AOR 0.33, 0.16–0.69)
Mazzuchello et al. [39]	DM + HTN	DKN-A, ATT-19, Martín-Bayarre-Grau questionnaire	Unsatisfactory knowledge, negative attitudes towards treatment and partial adherence; median age 68.5 years
Adisa et al. [21]	Mixed	Questionnaire-guided interview	Social support and medicine affordability associated with adherence and treatment outcomes

Study	Population directness	Measures	Key findings
Parra et al. [23]	Mixed/unclear	Factors influencing adherence instrument; NOC treatment behaviour	Subsidised health regime, never being able to read written information about the disease and never receiving information on medicine benefits negatively associated with adherence
Khayyat et al. [25]	Mixed (146/300 with both)	MMAS-8; WHOQOL-BREF	Adherence was an independent predictor of all quality-of-life domains: adherent patients scored +14.6 (overall QoL perception) and +17.2 (health score) points higher (both P = 0.001); comorbid subgroup not reported separately
Shimels et al. [26]	Mixed (35.0% HTN only)	MMAS-8	Poor adherence 72%. AOR (95% CI) for poor adherence: health centre vs hospital 1.71 (1.02–2.85); comorbidity 2.05 (1.13–3.71); substance use 11.57 (1.52–88.05); extreme poverty 0.59 (0.36–0.97). 57% reported COVID-19 disruption of follow-up, medicine availability or affordability
Atinga et al. [22]	Mixed (≈28.6% of patients with both)	In-depth interviews, thematic network analysis	Doubts about effectiveness, herbal medicine use, spiritual healing, polypharmacy (including OTC and herbal products), work schedules, social norms, unclear prescriber instructions and fear of side effects drove non-adherence
Sharma et al. [24]	Mixed (21/45 with both)	In-depth interviews, thematic analysis	≈27% reported non-adherence, mainly forgetfulness; limited knowledge of complications; pills recognised by appearance; delayed or omitted monitoring tests; free medicines at government facilities and family reminders acted as enablers

AOR, adjusted odds ratio; ATT-19, Diabetes Attitude Questionnaire; DKN-A, Diabetes Knowledge Questionnaire; NOC, Nursing Outcomes Classification; OTC, over the counter; QoL, quality of life; WHOQOL-BREF, World Health Organization Quality of Life brief version.

Quality Appraisal of the Included Studies

Thirteen studies were appraised: 11 quantitative and 2 qualitative. Quality scores for the quantitative studies ranged from 85.7% to 100%, and both qualitative studies scored 85% (Table 1 and Table 4). All studies therefore exceeded the conservative 75% threshold suggested by Kmet et al. [30]. Among the quantitative studies, partial scores were given for blinding of investigators and participants in all four randomised intervention studies, which is difficult to achieve in behavioural and pharmacist-led interventions; for control of confounding in five studies [21, 33, 35, 36, 39]; for sample size in three studies [21, 36, 39]; and for reporting of variance estimates in two studies [21, 39]. The qualitative studies received partial scores for linkage to a theoretical framework, verification procedures, and reflexivity.

Summary scores did not capture all limitations relevant to this review. Contreras-Vergara et al. reported mainly within-group comparisons without between-group effect estimates [33]; Malik et al. did not report dropouts, confidence intervals, or test statistics for between-group differences in blood pressure and glucose [36]; and the published report of Kwakye et al. gave p-values without effect sizes or confidence intervals [35]. Only the cluster randomised trial by Alfian et al. reported an adjusted between-group effect with a 95% CI [34]. The evidence was therefore judged sufficient to indicate the direction of effect on adherence but not the magnitude of effects on clinical outcomes, and the conclusions of this review are worded accordingly. The criterion-by-criterion assessment is provided in Supplementary File S1 (Table S2).

Table 4: Summary of quality appraisal (Kmet et al. criteria)

Study design	Number of studies assessed	Quality range	Overall classification
Quantitative studies	11	85.7%–100%	High quality
Qualitative studies	2	85%	High quality

Study design	Number of studies assessed	Quality range	Overall classification
Total	13	85.7%–100%	High quality

Patterns of Medication Use and Medication-Related Challenges Among Adults with Diabetes and Hypertension

The included studies demonstrated that medication management among adults with diabetes and hypertension extends beyond the selection of appropriate medicines. The coexistence of these chronic conditions requires prolonged treatment with multiple therapeutic agents, creating challenges related to medication burden, adherence, affordability, and continuity of care. Across the reviewed studies, medication use patterns reflected the difficulties patients and healthcare systems encounter when managing long-term multidrug therapies.

Medication Burden and Polypharmacy

Medication burden was measured directly in only one study. Among 329 adults with type 2 diabetes and hypertension in Ghana, Baah-Nyarkoh et al. found that approximately 31% reported moderate-to-high medication-related burden; higher burden was associated with uncontrolled diastolic blood pressure and elevated blood glucose, and with lower adherence [38]. Participants in the qualitative study by Atinga et al. described polypharmacy, including concurrent over-the-counter and herbal products, as a cause of adverse effects and missed doses [22]. Mazzuchello et al. reported that all 102 participants in a Brazilian HIPERDIA programme used medicines but that knowledge was unsatisfactory, attitudes towards treatment were negative, and adherence was only partial [39].

Polypharmacy in adults with diabetes and hypertension requires careful interpretation because the presence of multiple medicines does not always represent inappropriate treatment. Appropriate polypharmacy occurs when several medicines are clinically justified to manage different disease processes, prevent complications, and improve long-term outcomes. For example, patients with diabetes and hypertension may require glucose-lowering therapy alongside antihypertensive agents and cardiovascular risk-reduction medicines. However, problematic polypharmacy occurs when medication burden exceeds expected clinical benefit due to unnecessary medicines, complex regimens, avoidable treatment costs, or increased risk of medication-related difficulties.

No included study assessed the number or combination of medicines against explicit appropriateness criteria, so it was not possible to determine how much of the observed burden reflected problematic rather than appropriate polypharmacy. Regimen burden is therefore a plausible target for optimisation, but this review identified no evidence that reducing burden improves outcomes in this population.

Medication Adherence Patterns and Medication-Related Problems

Suboptimal adherence was common wherever it was quantified. Only 37% of participants with both conditions in the study by Baah-Nyarkoh et al. had good adherence [38], and 72% of 409 participants with diabetes and/or hypertension in Ethiopia had poor adherence on the MMAS-8 [26]. Forgetfulness (42%) and lack of knowledge (18%) were the most frequent baseline barriers among non-adherent patients in the trial by Alfian et al. [34], and forgetfulness was also the main reason given by the approximately one quarter of participants who reported non-adherence in Sharma et al. [24].

Several cross-sectional studies identified factors associated with adherence (Table 3). Adisa et al. reported that social support and medicine affordability influenced adherence and treatment outcomes in Nigeria [21]. Among 500 primary care patients in Colombia, belonging to the subsidised health regime, never being able to read written information about the disease, and never receiving information about the benefits of prescribed medicines were negatively associated with adherence [23]. In Ethiopia, attending a health centre rather than a hospital (adjusted odds ratio [AOR] 1.71, 95% CI 1.02–2.85), comorbidity (AOR 2.05, 95% CI 1.13–3.71), and current substance use (AOR 11.57, 95% CI 1.52–88.05) were associated with poor adherence, whereas extreme poverty was associated with lower odds of poor adherence (AOR 0.59, 95% CI 0.36–0.97) [26]. Khayyat et al. found that adherent patients had higher adjusted quality-of-life scores (+14.6 points for overall quality-of-life perception and +17.2 points for health score; both P = 0.001) [25]. These four studies enrolled mixed populations, so their findings are indirect evidence for adults with both conditions.

The qualitative studies helped explain these patterns, although both also included participants with only one condition. Among 49 patients and caregivers in Ghana, Atinga et al. identified doubts about the effectiveness of medicines, use of herbal medicines, reliance on spiritual healing, polypharmacy, busy work schedules, unfavourable social norms, unclear prescriber instructions, and fear of side effects as

drivers of non-adherence [22]. In a low-income urban community in Delhi, Sharma et al. described limited knowledge of disease complications, recognition of pills by appearance rather than name, and delayed or omitted monitoring tests, while free medicines at government facilities and family reminders supported adherence [24].

Taken together, adherence problems were frequent and multifactorial. Because most determinants were identified in cross-sectional or qualitative studies, the associations described cannot be interpreted as causal.

Multilevel Determinants Influencing Rational Medication Use

The determinants identified above were grouped into patient, healthcare professional, medication, and health-system levels. These levels correspond closely to the five dimensions of adherence described by the World Health Organization (patient-related, condition-related, therapy-related, health care team and system-related, and socioeconomic factors) [9]. To avoid repeating Section 3.3, this section summarises the evidence at each level and indicates its strength.

Patient-Level Factors

Patient-level barriers were the most frequently reported and included limited knowledge of disease and medicines [22, 24, 39], doubts about the effectiveness or safety of medicines [22], forgetfulness [24, 34], and the use of herbal or spiritual alternatives [22]. Socioeconomic factors such as affordability and insurance status were reported in four studies [21, 23, 26, 38]. Social and family support was the most consistently reported enabler [21, 24]. Evidence at this level comes largely from cross-sectional and qualitative studies and from mixed populations.

Healthcare Professional Factors

At the professional level, insufficient explanation of treatment and unclear prescriber instructions [22], and never having received information about the benefits of prescribed medicines [23], were associated with poorer adherence. All five intervention studies relied on pharmacists to deliver education, counselling, or follow-up [33, 34, 35, 36, 37], indicating that an expanded pharmacist role was feasible in the settings studied. No study evaluated interventions directed at prescribers, such as training or decision support.

Medication-Level Factors

Medication-level determinants were medication burden and regimen complexity [22, 38] and adverse effects or fear of them [22]. Multiple medicines are often clinically justified in this population, and no study assessed whether regimens could be appropriately simplified.

Health System-Level Factors

System-level determinants included the type of facility attended [26], insurance regime [23], disruption of follow-up and medicine supply during the COVID-19 pandemic, reported by 57% of participants in Ethiopia [26], and delayed laboratory monitoring [24]. Free medicines at government facilities were an enabler in the study by Sharma et al. [24].

Reported Effects of Interventions on Medication Use and Clinical Outcomes

Five intervention studies, all conducted in adults with both conditions and all pharmacist-led, evaluated strategies to improve medication use (Table 2). Each combined patient education or counselling with follow-up, and two also included structured identification of individual adherence barriers [34, 37]. Because components overlapped and comparators, durations (3 to 6 months where reported), and outcome measures differed, the contribution of individual components could not be separated. Results are therefore summarised by outcome rather than by intervention type, with adherence outcomes reported separately from blood pressure and glycaemic outcomes.

Effects on Medication Adherence

All four studies with extractable quantitative results reported improvement in at least one adherence measure. In the cluster randomised trial by Alfian et al. (113 patients enrolled in 10 community health centres, 89 completing follow-up), the tailored pharmacist-led intervention increased MARS-5 adherence scores by 4.62 points (95% CI 0.93–8.34; P = 0.008) at 3 months compared with usual care [34]. In the randomised trial by Contreras-Vergara et al. (n = 103), the proportion of intervention participants with high MMAS-8 adherence rose from 8.7% to 43.5% over 6 months, whereas adherence did not change significantly in the control group; between-group effect estimates were not reported [33]. In Kwakye et al. (n = 338; 144 intervention, 194 control), 39.64% of the intervention group versus 22.19% of the control group were adherent on the MARS-10 at 6 months (P < 0.0001) [35]. In Malik et al. (eight randomised pharmacies; 80 participants planned), the regimen screen of the Brief Medication Questionnaire improved for both antidiabetic and antihypertensive medicines (P = 0.001), but improvements in the belief and recall screens were significant only for antidiabetic medicines, and the access screen did not change (P = 0.568) [36]. Abughosh et al. evaluated pharmacist telephone outreach to non-adherent ACEI/ARB users against a non-randomised comparison group, with adherence and discontinuation

as outcomes; quantitative estimates could not be extracted for this review [37].

Effects on Blood Pressure and Glycaemic Control

Effects on clinical outcomes were less consistent. Kwakye et al. reported larger improvements in the intervention group for systolic and diastolic blood pressure and fasting plasma glucose (all $P < 0.0001$); median fasting plasma glucose fell from 8.1 to 6.2 mmol/L in the intervention group and rose from 7.5 to 8.8 mmol/L in the control group, although median systolic blood pressure fell by 10 mmHg in both groups [35]. In Malik et al., mean fasting blood glucose fell from 11.92 to 8.25 mmol/L and systolic blood pressure from 145.85 to 130.10 mmHg in the intervention arm, whereas values in the control arm were unchanged or rose (11.60 to 11.54 mmol/L; 142.15 to 145.48 mmHg); HbA1c was not reported, and between-group test statistics and CIs were not provided [36]. Contreras-Vergara et al. reported significant within-group reductions in glucose, HbA1c, and blood pressure in the intervention group only, while lipid parameters changed in both groups [33]. In contrast, the trial by Alfian et al., which had the most rigorous design and reporting, found no significant change in blood pressure or in beliefs about medicines [34]. Abughosh et al. did not report clinical outcomes [37]. Follow-up was 3 to 6 months in all intervention studies where reported, and none assessed longer-term clinical outcomes such as cardiovascular events, renal complications, hospital admissions, or mortality. Improvements in knowledge were reported in the intervention groups of Malik et al. (diabetes knowledge score 16.02 to 19.97; hypertension knowledge score 15.60 to 18.35) and Kwakye et al. ($P < 0.0001$) [35, 36].

Evidence Gaps

No included study evaluated deprescribing, dose optimisation, prescriber education or decision support, or SMS- or app-based digital interventions. The only remote intervention was pharmacist telephone outreach in a US Medicare Advantage plan [37], which may not transfer to primary health centres in low-resource settings. Because every intervention combined several components and none was compared with a single-component alternative, the present evidence cannot show that multicomponent interventions are more effective than simpler ones; it shows only that the pharmacist-led, education-based packages evaluated were associated with improved adherence over 3 to 6 months.

Development of the Proposed ADHERE-Prescription Medication Optimisation Framework

The ADHERE framework (Figure 2) is a proposed conceptual framework that emerged from the narrative synthesis. It has not been validated with stakeholders or tested empirically, and it is presented to organise the evidence and guide future research rather than as a ready-to-implement clinical model.

The framework was developed by two authors (LT and ADA) and refined iteratively with all authors in four steps. First, findings extracted from the 13 studies were coded and grouped into descriptive themes (Sections 3.3–3.5). Second, each theme was classified either as a problem (a barrier or medication-related problem) or as a response (an intervention element evaluated in, or recommended by, the included studies). Third, problems and responses were arranged along the medication-use process (assess the regimen, modify it, support the patient, support the professional, reinforce between visits, and evaluate) and cross-checked against the WHO dimensions of adherence [9], the Chronic Care Model [40], and the COM-B model of behaviour [41] to identify gaps and avoid duplication. Fourth, overlapping candidate components were merged or separated using two rules: who performs the action (prescriber, pharmacist or nurse, patient, or health system) and whether the action changes the regimen. For example, Assessment and Deprescribing were initially combined as "medication review" but were separated because assessment identifies and documents problems without changing the regimen, whereas deprescribing and dose optimisation are prescriber decisions that act on that assessment. Disagreements were resolved through discussion. The resulting operational definitions and boundaries are given in Table 5.

Table 6 shows, for each component, the themes and included studies from which it was derived, the external frameworks that informed it, and the strength of supporting evidence from this review. Three components (Assessment and reconciliation, Health literacy and patient engagement, and Evaluation and follow-up) are supported directly by intervention studies in adults with both conditions, and Reminders and digital reinforcement by a single telephone-based study. Deprescribing and dose optimisation, and Education and decision support for providers, were not evaluated in any included study. They were added because the synthesis identified the corresponding problems (medication burden, unclear prescriber instructions, and lack of information on medicine benefits) and because existing guidance addresses them [8, 10]. These two components are therefore hypotheses for testing rather than evidence-based recommendations. Neither these two components nor the framework as a whole are presented as established evidence-based strategies.

Many elements of ADHERE are shared with generic adherence and chronic care frameworks. The contribution specific to diabetes–hypertension comorbidity lies in three emphases derived from the synthesis: (i) a single combined review of antidiabetic and antihypertensive regimens rather than separate disease-specific reviews, because burden arises from the combined regimen [38]; (ii) explicit attention to cost, access, and herbal or over-the-counter co-medication, which were prominent in the studies from low- and middle-income countries [21, 22, 26]; and (iii) a cyclical structure that links evaluation of both blood pressure and glycaemic targets back to reassessment, reflecting reports of delayed monitoring [24].

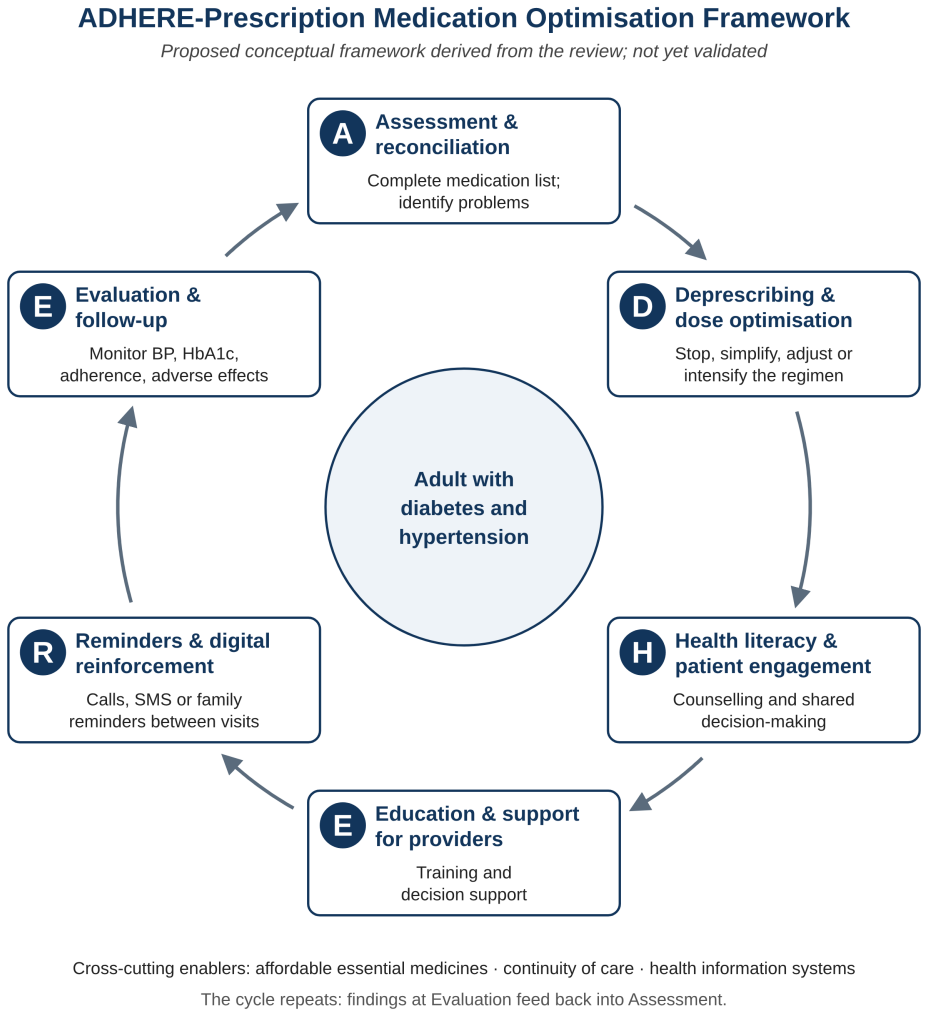


Figure 2: The proposed ADHERE-Prescription Medication Optimisation Framework (conceptual; not yet validated)

Table 5: Operational definitions and boundaries of the components of the proposed ADHERE framework

Component	Operational definition	Boundary with other components	Main actions	Responsible personnel	Intended outcomes (to be tested)
A – Assessment and reconciliation of the medication regimen	A structured review that compiles a complete, verified list of all medicines (prescribed, over the counter and herbal) and identifies medication-related problems: indication, effectiveness, safety,	Identifies and documents problems only; does not change the regimen	Medication reconciliation; indication and dose check; interaction screening; assessment of adherence barriers and affordability	Pharmacists, nurses, physicians	Accurate medication list and documented problem list

	interactions, burden, cost and adherence barriers				
D – Deprescribing and dose optimisation	Prescriber decisions that act on the assessment to stop, reduce, switch, simplify (e.g., fixed-dose combinations, once-daily dosing) or intensify therapy to reach targets	The only component that changes the regimen; includes intensification to address clinical inertia	Discontinue unnecessary medicines; simplify regimens; adjust doses; intensify when targets are not met	Prescribers, with pharmacist input	Lower regimen burden; appropriate treatment intensity
H – Health literacy and patient engagement	Patient-directed education, counselling and shared decision-making that build understanding of each medicine's purpose, benefits and risks, and address beliefs	Directed at patients and families; no regimen change	Tailored counselling; written medication lists; culturally appropriate communication; involving family members	Pharmacists, nurses, community health workers	Improved knowledge and adherence
E – Education and decision support for healthcare providers	Training, guideline tools and prompts that help professionals prescribe, communicate and coordinate care for both conditions together	Directed at professionals, not patients	Training on combined diabetes–hypertension management; prescribing checklists; clear written instructions; referral pathways	Health facilities, training institutions	Improved prescribing and communication
R – Reminders and digital reinforcement	Low-intensity contact between visits to sustain medicine-taking and detect problems early, using the simplest technology available	Reinforces the existing plan; does not deliver new education or change the regimen	Telephone calls; SMS or voice reminders; refill reminders; family reminders where phones are unavailable	Pharmacists, nurses, community health workers	Fewer missed doses and refill gaps
E – Evaluation and continuous follow-up	Scheduled measurement of blood pressure, glycaemic control (HbA1c or fasting glucose), adherence and adverse effects, with results fed back into reassessment	Measures and feeds back; treatment decisions are taken within A and D	Scheduled reviews; BP and glucose/HbA1c monitoring; adherence and adverse-effect checks	Primary healthcare teams	Timely detection of uncontrolled disease or new problems

Table 6: Linkage between ADHERE components, review findings, and supporting evidence

Component	**Themes from the synthesis**	**Direct evidence (intervention studies, DM + HTN)**	**Indirect evidence (observational / qualitative)**	**External frameworks or guidance**	**Strength of support from this review**
A – Assessment and	Polypharmacy including herbal/OTC products; unclear	Barrier identification [34, 37]; updated	[22, 38]	WHO medication safety in polypharmacy [8]; Chronic Care	Limited to moderate (always part of

reconciliation	instructions; individual adherence barriers	medication lists [33]		Model – delivery system design [40]	multicomponent packages)
D – Deprescribing and dose optimisation	Medication burden; regimen complexity	None	Burden linked to uncontrolled DBP and lower adherence [38]; polypharmacy [22]	WHO polypharmacy report [8]; NICE medicines optimisation [10]	Not directly evaluated (hypothesis)
H – Health literacy and patient engagement	Limited knowledge; beliefs about medicines; lack of information on benefits	[33, 34, 35, 36]	[22, 23, 24, 39]	COM-B – capability and reflective motivation [41]; Chronic Care Model – self-management support [40]	Moderate for adherence; inconsistent for clinical outcomes
E – Education and decision support for providers	Unclear prescriber instructions; no information on medicine benefits; communication gaps	None	[22, 23]	Chronic Care Model – decision support [40]; COM-B – provider capability [41]	Not directly evaluated (hypothesis)
R – Reminders and digital reinforcement	Forgetfulness; continuity between visits	Pharmacist telephone outreach [37]	Forgetfulness as main barrier [24, 34]; family reminders [24]	COM-B – physical opportunity and automatic motivation [41]	Limited (one high-income, telephone-based study)
E – Evaluation and continuous follow-up	Inadequate follow-up; delayed monitoring; service disruption	Scheduled follow-up embedded in [33, 35, 36]	[24, 26]	Chronic Care Model – clinical information systems [40]	Limited to moderate (embedded in interventions)

COM-B, Capability–Opportunity–Motivation–Behaviour model; DBP, diastolic blood pressure; OTC, over the counter.

Discussion

Main Findings

This review synthesised 13 studies on medication use among adults with coexisting diabetes and hypertension, and three main findings emerged. First, suboptimal adherence was common and was associated with patient, medication, and health-system factors, particularly limited knowledge, beliefs about medicines, cost and access, and medication burden. Several of these associations came from studies with mixed populations that did not report results separately for adults with both conditions, and they should be interpreted with caution. Second, pharmacist-led education and follow-up were associated with improved adherence in all four intervention studies with extractable results, but effects on blood pressure and glycaemic control were inconsistent and often incompletely reported. Because the included evidence relates mainly to medication adherence over 3 to 6 months, any improvement in blood pressure, glycaemic control, or longer-term clinical outcomes that may follow improved adherence is a conceptual implication of this review rather than a demonstrated finding, and it is presented as such throughout. Third, evidence on the prescribing domain of rational medication use, including appropriateness, deprescribing, and clinical inertia, was almost entirely absent.

On the basis of these findings, we proposed the ADHERE framework. Its value lies in organising the

available evidence along the medication-use pathway and in making explicit which components are supported by evidence and which remain untested (Table 6); it is not a validated intervention model.

Comparison with Existing Literature

Kini and Ho (2018) concluded that adherence interventions that combine behavioural support, education, and engagement with healthcare providers tend to perform better than reminders alone [42]. This is consistent with the present review, although none of the intervention studies included here directly compared multicomponent with single-component approaches.

The findings are closest to those of Maniki et al., who reviewed seven intervention studies in patients with coexisting diabetes and hypertension and found that five improved adherence, four of them multifaceted and education-based [17]. The present review differs in four respects. It searched different sources (PubMed, ScienceDirect, and Google Scholar rather than CINAHL, Embase, and Medline) over a different period (2015–2026 rather than 2012–2023); it included observational and qualitative studies of the determinants of medication use in addition to interventions; it examined rational medication use more broadly than adherence and identified the absence of evidence on prescribing and deprescribing; and it translated the findings into a conceptual framework with explicit links to the supporting evidence. The two reviews are therefore complementary, and their consistent conclusions about education-based pharmacist interventions strengthen confidence in that finding.

Recent systematic reviews have also demonstrated the value of pharmacist involvement in chronic disease management. Reeves et al. (2021) [43], through a systematic review of pharmacist interventions for hypertension management, reported that pharmacist-led care improved blood pressure control and medication adherence. Their findings reinforce the evidence from this review that pharmacists can provide important contributions through medication review, counselling, and follow-up support.

Similarly, Bingham et al. (2021) [44] examined telehealth interventions for medication adherence among patients with chronic conditions, including diabetes and hypertension, and found that technology-supported approaches improved adherence when combined with personalised communication. This is consistent with the inclusion of digital reinforcement within the ADHERE framework, while also emphasising that technology functions most effectively when incorporated into broader patient support systems.

The importance of integrated approaches has also been demonstrated by recent systematic reviews examining digital and multidisciplinary interventions. Yap et al. (2024) [45] reported that digital health interventions improved hypertension-related outcomes, particularly when interventions included monitoring and communication components. These findings align with the present review by showing that digital strategies should support continuous engagement between patients and healthcare providers rather than operate as independent solutions.

Furthermore, evidence from medication review research supports the need for structured optimisation processes among patients with multiple chronic conditions. A meta-analysis of randomised controlled trials outside the scope of this review found that medication review reduced the number of drug-related problems, although its effect on clinical outcomes was minimal [46]. This evidence provides a rationale for including medication assessment and reconciliation as the first stage of the ADHERE framework.

The ADHERE Framework: Theoretical Positioning and Feasibility in Low-Resource Settings

ADHERE is intended to be consistent with established frameworks rather than an alternative to them. Its patient-facing components map onto the COM-B model: health literacy addresses psychological capability and reflective motivation, reminders address physical opportunity and automatic motivation, and evaluation provides feedback [41]. Its system-facing components correspond to elements of the Chronic Care Model: decision support (provider education), delivery system design (assessment and deprescribing), self-management support (health literacy), and clinical information systems (evaluation) [40]. These links provide a basis for selecting behaviour change techniques and implementation strategies in future work, and an implementation framework such as the Consolidated Framework for Implementation Research (CFIR) could be used to examine contextual barriers during feasibility testing [47].

Feasibility in low-resource settings requires particular caution. The telephone intervention was delivered in a US Medicare Advantage plan [37], and the other four interventions relied on pharmacists working in hospitals, health centres, or community pharmacies [33, 34, 35, 36]. In many primary health centres in low- and middle-income countries, including in Nigeria and Ghana, pharmacists, reliable medicine supplies, and laboratory monitoring are limited, as reflected in the included studies from Ethiopia and India [24, 26]. Implementation of ADHERE in such

settings would therefore depend on adaptations such as task-sharing of assessment and counselling with trained nurses or community health workers [24]; paper-based medication lists or wallet cards, as used by Contreras-Vergara et al. [33]; SMS or voice reminders that work on basic mobile phones, or family reminders where phones are unavailable [24]; and regimen simplification using fixed-dose combinations available on national essential medicines lists [2]. These adaptations were not evaluated in the included studies and require testing.

Implications for Practice and Research

For practice, the most consistent finding supports incorporating structured medication counselling and follow-up, delivered by pharmacists or other trained staff, into routine care for adults with both conditions. This recommendation rests on improvements in adherence; any resulting benefits for blood pressure, glycaemic control, and long-term outcomes are anticipated rather than established and require confirmation in trials with longer follow-up. The other components of ADHERE should be regarded as promising rather than established.

For research, we propose a staged validation pathway consistent with the Medical Research Council framework for complex interventions [48]: (1) a modified Delphi study with clinicians, pharmacists, nurses, community health workers, policymakers, and patients from low-, middle-, and high-income settings to refine component definitions and reach consensus on content and feasibility [49]; (2) development of a core version of ADHERE for low-resource settings and an enhanced version for better-resourced settings; (3) feasibility and acceptability testing in primary health centres, including in Nigeria and Ghana, using mixed methods and a CFIR-guided process evaluation [47]; and (4) a pragmatic cluster randomised trial measuring adherence, blood pressure, HbA1c, medication burden, prescribing appropriateness, and cost. Future primary studies should also report results separately for adults with both conditions, use validated adherence measures, and report between-group effect estimates with confidence intervals.

Strengths

This review integrates quantitative and qualitative evidence, distinguishes medication adherence from the broader concept of rational medication use, reports effect estimates and non-significant findings alongside positive ones, and makes the evidence base for each component of the proposed framework explicit.

Limitations

This review has several limitations. First, the ADHERE framework is conceptual and has not been validated through stakeholder consultation, expert consensus, or empirical testing; its components, particularly deprescribing and provider education, which were not evaluated in any included study, should be regarded as hypotheses. Second, six of the 13 studies enrolled mixed populations and did not report results for participants with both conditions; the criterion for including such studies was made explicit only after study selection, and their findings may not apply fully to adults with both conditions. Although these studies were used only to describe barriers and enablers, and not to support statements about intervention effects, the nature or magnitude of those barriers and enablers may differ among adults with both conditions, so these findings should be interpreted with caution. Third, the protocol was not prospectively registered. Fourth, the search strategy was restricted. Only three sources (PubMed, ScienceDirect, and Google Scholar) were searched, and other major databases such as Embase, CINAHL, Scopus, Web of Science, and the Cochrane Library were not; Google Scholar screening was limited to the first 300 relevance-ranked records; grey literature was not systematically searched; only English-language publications were included; and six potentially eligible reports could not be retrieved in full text. Because most included studies were conducted in low- and middle-income countries, where relevant research is often published in regional or non-English-language journals, these restrictions may have resulted in relevant studies being missed, and the findings should be interpreted with this in mind. Fifth, the included studies were heterogeneous in design, interventions, comparators, follow-up (3 to 6 months where reported), and outcome measures, and several did not report effect estimates or confidence intervals; this precluded meta-analysis and limits conclusions to the direction of effects. Sixth, most evidence on determinants came from cross-sectional and qualitative studies, which cannot establish causality. Finally, all intervention studies were pharmacist-led and of short duration, so long-term effects, cost-effectiveness, and transferability to settings with few pharmacists are unknown.

Conclusion

This systematic review found that suboptimal adherence is common among adults with coexisting diabetes and hypertension and is associated with limited knowledge, beliefs about medicines, medication burden, cost, and gaps in follow-up. In the included studies, pharmacist-led education and follow-up

interventions were associated with improvements in medication adherence, whereas their effects on blood pressure and glycaemic control were inconsistent. Evidence on prescribing quality and deprescribing in this population is lacking.

The proposed ADHERE-Prescription Medication Optimisation Framework organises these findings into six components spanning regimen assessment, optimisation, patient engagement, provider support, reinforcement, and follow-up. It is a conceptual framework that has not been validated and should not yet be used as a clinical protocol. In particular, its deprescribing and provider-education components were not evaluated in any included study and are proposed for future testing rather than as established evidence-based strategies.

Future work should validate the framework through expert and patient consensus, adapt it for settings with limited pharmacist and digital infrastructure, and test its feasibility and effectiveness, particularly in low- and middle-income countries. Primary studies should report outcomes separately for adults with both conditions and include prescribing-related outcomes.

Acknowledgements

Competing Interests: All the authors declare that they have no conflict of interest.

Ethics approval and consent to participate: Not applicable

Consent for publication: Not applicable

Availability of data and material: All the resources consulted in the review were provided in the reference section. The full search strategies and criterion-by-criterion quality appraisal scores are provided in Supplementary File S1.

Funding: No funding of any kind was received from an individual/organization.

Authors' Contributions: Conceptualization (LT and ADA), Methodology (LT and ADA), Data curation (LT, ADA and ASM), Writing – Original Draft (LT, ADA, ASM and AOA); Review & Editing (AOA). All authors read and approved the final manuscript.

Disclosure of AI Use: ChatGPT (OpenAI) was used to assist with language editing, grammatical refinement, and improvement of manuscript readability. The authors critically reviewed and edited all AI-assisted suggestions and take full responsibility for the accuracy, originality, and integrity of the manuscript.

References

1. International Diabetes Federation. IDF Diabetes Atlas 2025 [Internet]. 2025 [cited 2026 Jul 12]. Available from: https://diabetesatlas.org/resources/idf-diabetes-atlas-2025/
2. World Health Organization. Global report on hypertension: the race against a silent killer [Internet]. 2023 [cited 2026 Sep 12]. Available from: https://www.who.int/publications/i/item/9789240081062
3. Einarson TR, Acs A, Ludwig C, Panton UH. Prevalence of cardiovascular disease in type 2 diabetes: a systematic literature review of scientific evidence from across the world in 2007–2017. Cardiovasc Diabetol. 2018 Jun 8;17(1):83. doi:10.1186/s12933-018-0728-6
4. Petrie JR, Guzik TJ, Touyz RM. Diabetes, hypertension, and cardiovascular disease: clinical insights and vascular mechanisms. Can J Cardiol. 2018 May 1;34(5):575–84. doi:10.1016/j.cjca.2017.12.005
5. Masnoon N, Shakib S, Kalisch-Ellett L, Caughey GE. What is polypharmacy? A systematic review of definitions. BMC Geriatr. 2017 Oct 10;17(1):230. doi:10.1186/s12877-017-0621-2
6. Varghese D, Patel P. Polypharmacy. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2026 [cited 2026 Jul 12]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK532953/
7. World Health Organization. The rational use of drugs: report of the Conference of Experts, Nairobi, 25–29 November 1985. Geneva: World Health Organization; 1987.
8. World Health Organization. Medication safety in polypharmacy: technical report [Internet]. 2019 [cited 2026 Jul 12]. Available from: https://www.who.int/publications/i/item/WHO-UHC-SDS-2019.11
9. Sabaté E, editor. Adherence to long-term therapies: evidence for action. Geneva: World Health Organization; 2003.
10. National Institute for Health and Care Excellence. Medicines optimisation: the safe

and effective use of medicines to enable the best possible outcomes. NICE guideline NG5. London: NICE; 2015.

11. Wang J, Tan F, Wang Z, Yu Y, Yang J, Wang Y, et al. Understanding gaps in the hypertension and diabetes care cascade: systematic scoping review. JMIR Public Health Surveill. 2024 Feb 16;10:e51802. doi:10.2196/51802
12. Zaman Huri H, Fun Wee H. Drug related problems in type 2 diabetes patients with hypertension: a cross-sectional retrospective study. BMC Endocr Disord. 2013 Jan 7;13:2. doi:10.1186/1472-6823-13-2
13. American Diabetes Association Professional Practice Committee. 2. Diagnosis and classification of diabetes: Standards of Care in Diabetes—2025. Diabetes Care. 2025 Jan 1;48(1 Suppl 1):S27–49. doi:10.2337/dc25-S002
14. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension: The Task Force for the management of arterial hypertension of the European Society of Cardiology (ESC) and the European Society of Hypertension (ESH). Eur Heart J. 2018 Sep 1;39(33):3021–104. doi:10.1093/eurheartj/ehy339
15. Polonsky WH, Henry RR. Poor medication adherence in type 2 diabetes: recognizing the scope of the problem and its key contributors. Patient Prefer Adherence. 2016 Jul 22;10:1299–307. doi:10.2147/PPA.S106821
16. Khunti S, Khunti K, Seidu S. Therapeutic inertia in type 2 diabetes: prevalence, causes, consequences and methods to overcome inertia. Ther Adv Endocrinol Metab. 2019 May 3;10:2042018819844694. doi:10.1177/2042018819844694
17. Maniki PT, Chaar BB, Aslani P. Impact of interventions on medication adherence in patients with coexisting diabetes and hypertension. Health Expect. 2024;27(5):e70010. doi:10.1111/hex.70010
18. Siddaway AP, Wood AM, Hedges LV. How to do a systematic review: a best practice guide for conducting and reporting narrative reviews, meta-analyses, and meta-syntheses. Annu Rev Psychol. 2019;70:747–70. doi:10.1146/annurev-psych-010418-102803
19. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021 Mar 29;372:n71. doi:10.1136/bmj.n71
20. Campbell M, McKenzie JE, Sowden A, Katikireddi SV, Brennan SE, Ellis S, et al. Synthesis without meta-analysis (SWiM) in systematic reviews: reporting guideline. BMJ. 2020;368:l6890. doi:10.1136/bmj.l6890
21. Adisa R, Olajide OO, Fakeye TO. Social support, treatment adherence and outcome among hypertensive and type 2 diabetes patients in ambulatory care settings in southwestern Nigeria. Ghana Med J. 2017 Jun;51(2):64–77.
22. Atinga RA, Yarney L, Gavu NM. Factors influencing long-term medication non-adherence among diabetes and hypertensive patients in Ghana: a qualitative investigation. PLoS One. 2018 Mar 28;13(3):e0193995. doi:10.1371/journal.pone.0193995
23. Parra DI, Guevara SLR, Rojas LZ. Influential factors in adherence to the therapeutic regime in hypertension and diabetes. Invest Educ Enferm. 2019 Oct 23;37(3). doi:10.17533/udea.iee.v37n3e02
24. Sharma N, Mariam W, Basu S, Shrivastava R, Rao S, Sharma P, et al. Determinants of treatment adherence and health outcomes in patients with type 2 diabetes and hypertension in a low-income urban agglomerate in Delhi, India: a qualitative study. Cureus. 2023 Feb 9;15. doi:10.7759/cureus.34826
25. Khayyat SM, Mohamed MMA, Khayyat SMS, Hyat Alhazmi RS, Korani MF, Allugmani EB, et al. Association between medication adherence and quality of life of patients with diabetes and hypertension attending primary care clinics: a cross-sectional survey. Qual Life Res. 2019 Apr 1;28(4):1053–61. doi:10.1007/s11136-018-2060-8
26. Shimels T, Kassu RA, Bogale G, Bekele M, Getnet M, Getachew A, et al. Magnitude and associated factors of poor medication adherence among diabetic and hypertensive

patients visiting public health facilities in Ethiopia during the COVID-19 pandemic. PLoS One. 2021 Apr 6;16(4):e0249222. doi:10.1371/journal.pone.0249222

27. National Library of Medicine. Medical Subject Headings – Home Page [Internet]. U.S. National Library of Medicine; [cited 2026 Jul 12]. Available from: https://www.nlm.nih.gov/mesh/meshhome.html
28. Bramer WM, de Jonge GB, Rethlefsen ML, Mast F, Kleijnen J. A systematic approach to searching: an efficient and complete method to develop literature searches. J Med Libr Assoc. 2018 Oct 4;106(4):531–41. doi:10.5195/jmla.2018.283
29. Haddaway NR, Collins AM, Coughlin D, Kirk S. The role of Google Scholar in evidence reviews and its applicability to grey literature searching. PLoS One. 2015;10(9):e0138237. doi:10.1371/journal.pone.0138237
30. Kmet LM, Cook LS, Lee RC. Standard quality assessment criteria for evaluating primary research papers from a variety of fields [Internet]. 2004 Feb 1. doi:10.7939/R37M04F16
31. Popay J, Roberts H, Sowden A, Petticrew M, Arai L, Rodgers M, et al. Guidance on the conduct of narrative synthesis in systematic reviews: a product from the ESRC Methods Programme. Lancaster: Lancaster University; 2006.
32. Thomas J, Harden A. Methods for the thematic synthesis of qualitative research in systematic reviews. BMC Med Res Methodol. 2008;8:45. doi:10.1186/1471-2288-8-45
33. Contreras-Vergara A, Sifuentes-Franco S, Haack S, Graciano-Machuca O, Rodriguez-Carrizalez AD, López-Contreras AK, et al. Impact of pharmaceutical education on medication adherence and its clinical efficacy in patients with type 2 diabetes and systemic arterial hypertension. Patient Prefer Adherence. 2022 Aug 5;16:1999–2007. doi:10.2147/PPA.S370323
34. Alfian SD, van Boven JFM, Abdulah R, Sukandar H, Denig P, Hak E. Effectiveness of a targeted and tailored pharmacist-led intervention to improve adherence to antihypertensive drugs among patients with type 2 diabetes in Indonesia: a cluster randomised controlled trial. Br J Clin Pharmacol. 2021;87(4):2032–42. doi:10.1111/bcp.14610
35. Kwakye AO, O BK, M OANA, E OD. Clinical pharmacists education and counselling in patients with co-morbid hypertension and diabetes in a municipal hospital in Ghana. Afr J Pharm Pharmacol. 2021 Oct 31;15(10):183–90. doi:10.5897/AJPP2021.5267
36. Malik M, Hussain A, Aslam U, Hashmi A, Vaismoradi M, Hayat K, et al. Effectiveness of community pharmacy diabetes and hypertension care program: an unexplored opportunity for community pharmacists in Pakistan. Front Pharmacol. 2022 May 17;13. doi:10.3389/fphar.2022.710617
37. Abughosh SM, Wang X, Serna O, Henges C, Masilamani S, James Essien E, et al. A pharmacist telephone intervention to identify adherence barriers and improve adherence among nonadherent patients with comorbid hypertension and diabetes in a Medicare Advantage plan. J Manag Care Spec Pharm. 2016 Jan;22(1):63–73. doi:10.18553/jmcp.2016.22.1.63
38. Baah-Nyarkoh E, Alhassan Y, Dwomoh AK, Kretchy IA. Medication-related burden and adherence in patients with co-morbid type 2 diabetes mellitus and hypertension. Heliyon. 2023 Apr 1;9(4). doi:10.1016/j.heliyon.2023.e15448
39. Mazzuchello FR, Tuon L, Simões PW, Mazon J, Dagostin VS, Tomasi CD, et al. Knowledge, attitudes and adherence to treatment in individuals with hypertension and diabetes mellitus. Mundo Saúde. 2016 Oct 1;40(4):418–32. doi:10.15343/0104-7809.20164004418432
40. Wagner EH. Chronic disease management: what will it take to improve care for chronic illness? Eff Clin Pract. 1998;1(1):2–4.
41. Michie S, van Stralen MM, West R. The behaviour change wheel: a new method for characterising and designing behaviour change

interventions. Implement Sci. 2011;6:42. doi:10.1186/1748-5908-6-42

42. Kini V, Ho PM. Interventions to improve medication adherence: a review. JAMA. 2018 Dec 18;320(23):2461–73. doi:10.1001/jama.2018.19271
43. Reeves L, Robinson K, McClelland T, Adedoyin CA, Broeseker A, Adunlin G. Pharmacist interventions in the management of blood pressure control and adherence to antihypertensive medications: a systematic review of randomized controlled trials. J Pharm Pract. 2021 Jun;34(3):480–92. doi:10.1177/0897190020903573
44. Bingham JM, Black M, Anderson EJ, Li Y, Toselli N, Fox S, et al. Impact of telehealth interventions on medication adherence for patients with type 2 diabetes, hypertension, and/or dyslipidemia: a systematic review. Ann Pharmacother. 2021 May;55(5):637–49. doi:10.1177/1060028020950726
45. Yap HJ, Lim JJJ, Tan SYD, Ang CS. Effectiveness of digital health interventions on adherence and control of hypertension: a systematic review and meta-analysis. J Hypertens. 2024 Sep 1;42(9):1490–504. doi:10.1097/HJH.0000000000003793
46. Huiskes VJB, Burger DM, van den Ende CHM, van den Bemt BJF. Effectiveness of medication review: a systematic review and meta-analysis of randomized controlled trials. BMC Fam Pract. 2017 Jan 17;18:5. doi:10.1186/s12875-016-0577-x
47. Damschroder LJ, Aron DC, Keith RE, Kirsh SR, Alexander JA, Lowery JC. Fostering implementation of health services research findings into practice: a consolidated framework for advancing implementation science. Implement Sci. 2009;4:50. doi:10.1186/1748-5908-4-50
48. Skivington K, Matthews L, Simpson SA, Craig P, Baird J, Blazeby JM, et al. A new framework for developing and evaluating complex interventions: update of Medical Research Council guidance. BMJ. 2021;374:n2061. doi:10.1136/bmj.n2061
49. Jünger S, Payne SA, Brine J, Radbruch L, Brearley SG. Guidance on conducting and reporting Delphi studies (CREDES) in palliative care: recommendations based on a methodological systematic review. Palliat Med. 2017;31(8):684–706. doi:10.1177/0269216317690685