Current Pharmaceutical Research (CPR)
Vol 2, Issue 2, April-June 2026
Journal Homepage: https://cpr.org.in/

A Systematic Review on Medication Adherence in Hypertensive Patients: Determinants, Assessment Methods, and Clinical Outcomes

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Keywords

Hypertension, adherence to therapy, antihypertensive drugs, medication adherence.

Abstract

The global epidemic of hypertension is still mostly unchecked, and it continues to be the primary cause of mortality from non-communicable diseases. In order to provide a comprehensive perspective, the current study set out to conduct a scoping review of medication adherence treatments in hypertension patients. Additionally, an evidence-based classification system for interventions was created. By offering an overview of the study area and developing a new, evidence-based intervention classification tool, this work is a significant step toward promoting more informed and effective future research endeavors. Additionally, it gives medical professionals important information on antihypertensive drug adherence. The process by which patients take their prescriptions as directed is known as adherence to medication, and it may be divided into three phases: initiation, implementation, and perseverance. In comparison to free-equivalent combination (FEC) medication, this systematic review evaluated whether single-pill combination (SPC) therapy improved adherence, persistence, and blood pressure management in hypertension patients. The goal of this review is to provide an overview of the latest research on resistant hypertension. These investigations also found patient subgroups with much greater risks of morbidity and death, which likely call for more intensive medical care. A patient-centered approach, nonjudgmental communication techniques, and cooperative multidisciplinary management-including patient participation in their treatment through self-blood pressure monitoring-can greatly increase medication adherence.

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Article Info
Received: 02 June 2026, Received in revised form: 28 July 2026, Accepted: 28 July 2026, Available online: 30 July 2026; Volume: 2; Issue: 2; Pages: 150–165.

ISSN: 3049-2955/The authors © 2026, under exclusive license to the Sprout Publication.
DOI: https://doi.org/10.63785/2026.2.2.150165

1. Introduction

1.1. Definition of Hypertension

The most significant modifiable risk factor for cardiovascular (CV) disease, stroke, disability, and mortality worldwide is hypertension [1]. Many people may not reach their blood pressure (BP) target despite advancements in the diagnosis and treatment of hypertension. When three anti-hypertensives (including a diuretic) are used at optimum or maximum tolerated dosages, blood pressure that stays over guideline-directed objectives is commonly referred to as resistant hypertension (RHT). The primary avoidable risk factor for cardiovascular disease (CVD) and all-cause death globally is hypertension [2]. Hypertension, which is defined as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg, affected 31.1% of the world's adult population (1.39 billion people) in 2010. Due to population aging and increased exposure to lifestyle risk factors, such as poor diets (high salt and low potassium consumption) and inactivity, the incidence of hypertension is growing internationally [3]. However, variations in the prevalence of hypertension are not consistent across the globe. We address global estimates and trends in mean blood pressure levels as well as the prevalence, awareness, management, and control of hypertension in this review [4].

We also look at evidence of the financial impact of hypertension, techniques for controlling hypertension, and risk factors for hypertension. We wrap up by talking about the implications of current hypertension trends and areas that require further investigation. Hypertension is a worldwide public health issue that affects both sexes and is becoming more common and burdensome worldwide [5]. This is crucial since managing hypertension significantly lowers the chance of developing cardiovascular disease later on. Studies indicate that many people are still not under optimal control, despite compelling evidence supporting such therapy. Unusual sleep length has been shown to alter blood pressure response and raise the risk of hypertension. The assessed incidence of hypertension, which is more prevalent in those who sleep for fewer than 6 hours per night, has been linked to habitual sleep duration less than 7–8 hours, according to several research. "The extent to which a person's behavior - taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a healthcare provider" is the World Health Organization's definition of adherence to long-term therapy [6]. Depending on the group under study, the length of the follow-up period, the techniques used to assess adherence, and the various medication classes involved, reported rates of pharmacotherapy adherence range from 50 to 70%. This study aims to provide an overview, via a systematic approach, of the current status and recent developments regarding the determinants of patient adherence to treatment in the adult population by evaluating and comparing various predictors of adherence to both pharmacological and non-pharmacological treatment for hypertension, given the significance of medication adherence (MA) in the control of blood pressure and the critical role of various factors in patient adherence [7].

Unquestionably, hypertension has epidemiological effects that call for more debate in the context of healthcare. According to recent data, people with hypertension have a lower health-related quality of life (HRQoL) than those with normotension. The very existence of the illness and its chronic-degenerative nature, the diagnosis of the condition, the detrimental effects on social, emotional, and physical aspects, as well as those associated with medication lowers mortality and disability from a variety of illnesses, such as cardiovascular, renal, and cerebrovascular disease. Antihypertensive medication therapy has been shown to lower the risk of cardiovascular disease and mortality. However, with certain regional variations and variations related to socioeconomic position within a nation or geographic region, less than half of the treated therapy, all have an impact on the quality of life of individuals with hypertension [8]. Given the topic's still limited inclusion in international literature, our study will provide a deeper understanding of the relationship between quality of life and medication adherence in individuals with hypertension while also elucidating the impact of treatment adherence on patients. Blood pressure-lowering medications are the most often recommended medications by doctors, and medication is a typical and modern strategy to controlling hypertension [9].

The reported rates of blood pressure control are quite unsatisfactory, even though there are over a hundred different medications that have been shown to be successful in treating hypertension. Non-adherence to antihypertensive medications is the root cause of uncontrolled hypertension. Patients who are aware of their medication regimens are better able to adhere to them, which helps prevent the debilitating complications of hypertension and, if left unchecked, can increase the burden of a disease that is already on the rise [10]. Improving quality of life is hampered by poor treatment compliance. The attitudes and obstacles to the adherence to hypertension treatment in rural populations, however, are poorly understood. Therefore, the purpose of this study was to identify the characteristics that affect hypertension medication adherence based on HBM. Despite the fact that over one-third of individuals may have hypertension, patients are rarely aware of this illness, and blood pressure regulation is often subpar in both rural and urban areas [11].

Additionally, the health care system and poor socioeconomic level may be a barrier to blood pressure control since the low socioeconomic group may not be able to effectively control their hypertension due to the high expenses of screening and treatment. Major hypertension guidelines employ a mix of blood pressure level and patient risk factors, such as atherosclerotic cardiovascular disease (ASCVD) risk, for their recommendations on blood pressure management, even if they use various blood pressure thresholds to define hypertension and its phases [12]. According to the most recent research (2010), HT contributes to the Global Burden of Disease second only to smoking. For the majority of people, it is readily managed, and its management patients reach a blood pressure target below 140/90 mmHg. Globally, cardiovascular diseases (CVD) are regarded as one of the main causes of mortality. Nearly 23.6 million individuals are predicted to die from CVD in 2030. CVD risk factors can be further divided into two categories: modifiable and non-modifiable [13], [14].

Tobacco use, elevated blood cholesterol, hypertension, inactivity, poor nutrition, and obesity are a few examples of modifiable risk factors. Age, gender, socioeconomic level, and a family history of CVD are all regarded as non-modifiable risk factors. Adjunctive lifestyle change is as significant in lowering the risk of recurrent cardiovascular events, even while data suggests guidelines-based pharmacotherapies for lowering the risk of CVD. A major worldwide health problem, hypertension is a major risk factor for death and disability, especially from cardiovascular illnesses [15]. Nonetheless, hypertension may be prevented and controlled, and treating it mostly depends on precise and current clinical practice recommendations. HTN need lifetime care, but in LMICs, where health systems are frequently created to offer curative treatment for acute disorders above everything else, issue recognition, access to treatment and successful control are impaired. Only 10% of persons with chronic illnesses receive proper treatment worldwide. With rare exceptions, care for non-communicable illnesses is frequently limited to the delayed treatment of complications or exacerbations in specialized settings [16].

Figure 1 illustrates a comprehensive framework for medication adherence in hypertension management. It highlights the determinants influencing adherence, the three phases of the adherence process (initiation, implementation, and persistence), assessment methods, evidence-based interventions to improve adherence, and their impact on clinical outcomes. The continuous feedback loop emphasizes ongoing monitoring and patient provider communication to sustain long-term adherence and optimize blood pressure control [17].

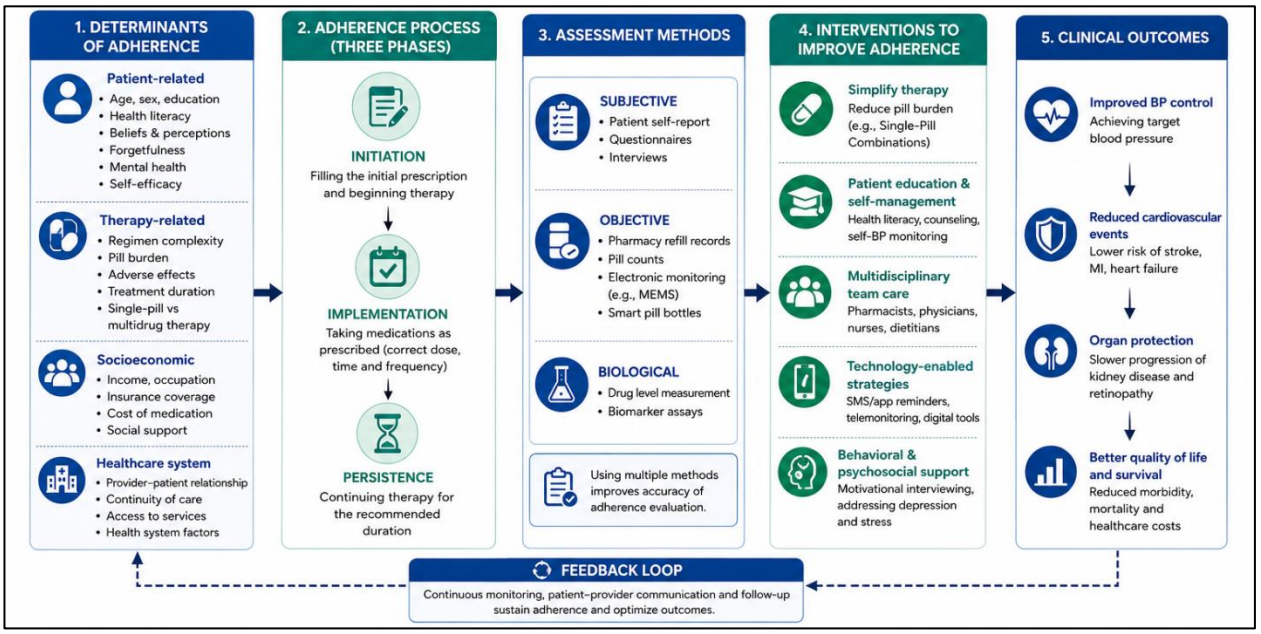

Figure 1: Framework of medication adherence in hypertension: determinants, assessment methods, interventions, and clinical outcomes.

1.2. Epidemiology (Global Burden)

We calculated that the global age-standardized prevalence of hypertension (defined as systolic blood pressure ≥140 mm Hg, diastolic blood pressure ≥90 mm Hg, and/or current use of antihypertensive medication) was 31.1% (95% CI 30.0–32.2%) in 2010 based on an analysis of data from 135 population-based studies that included 968,419 adults from 90 countries. Eastern Europe and Central Asia had the nutrition, and inactivity [18].

Under treatment or therapeutic inertia, which occurs when a healthcare provider does not modify a patient's antihypertensive regimen despite a clear indication, and non-adherence to antihypertensive therapy are well-known but underappreciated major greatest prevalence of hypertension in men (39.0%), whereas South Asia had the lowest incidence (26.4%). The prevalence of hypertension in women was highest in Sub-Saharan Africa (36.3%) and lowest in HICs (25.3%). Although the exact causes of these regional variations in the incidence of hypertension are unknown, they are probably impacted by variations in the prevalence of risk factors for the condition, such as obesity, poor barriers to blood pressure control to manage hypertension and aTRH. As a result, it's critical to include medication adherence evaluation in routine evaluations of individuals with uncontrolled hypertension or aTRH. Accordingly, understanding medication non-adherence is essential for improving hypertension management and patient outcomes.

This includes defining what medication non-adherence is, identifying the patient-, therapy-, socioeconomic-, and healthcare system-related factors that contribute to poor adherence, and recognizing effective methods for its identification and screening. It is equally important to evaluate the clinical and economic consequences of inadequate adherence, including uncontrolled blood pressure, increased cardiovascular risk, greater healthcare utilization, and higher medical costs. Furthermore, implementing practical, evidence-based strategies such as patient education, treatment simplification, multidisciplinary care, and digital health interventions is crucial for enhancing medication adherence and achieving optimal therapeutic outcomes. The conceptual relationship between the determinants of medication adherence, assessment methods, adherence-enhancing interventions, and their impact on clinical outcomes in hypertension is illustrated in Figure 1. Medication adherence involves three measurable stages, although it begins when the patient receives a prescription. When the patient takes the first tablet, the first phase, known as initiation, begins. Information on the actual dosage is provided in the second step, implementation, which may be less than ideal because of carelessness or forgetfulness. Treatment interruptions may be deliberate or unintentional. The patient may exhibit either timing or taking non-adherence. The patient quits taking the drug even when their prescription is refilled during the third and final phase, known as discontinuation. Together, these three stages are referred to as persistence [19].

1.3. Consequences of Non-Adherence

One of the most important issues in the treatment of hypertension is medication non-adherence. The disease's chronic asymptomatic state and the sporadic or even frequent failure to take the prescribed dosage seem to have no immediate repercussions. With the course of therapy, medication adherence varies greatly and typically decreases with time. Medication non-adherence is a multifaceted, intricate variable with several interrelated components that need to be addressed concurrently [20].

2. Methodology

2.1. Study Design

The improved Overview Quality evaluation versus non-adherence; (O) changes in adherence to the therapeutic plan; and (S) any study design (apart from review articles) written in English, French, Spanish, or Portuguese. The reviewing committee decided to include adherence to both pharmaceutical and non-pharmacological therapy since prior research has often focused on factors influencing Questionnaire (OQAQ), a checklist developed by Sacks, and three extra questions recently deemed methodologically significant were combined to produce a 37-item evaluation instrument. This method was used on 52 electronic and 99 paper-based systematic reviews. The underlying components were found via exploratory factor analysis. Methodological specialists used a nominal group strategy to evaluate the outcomes in order to reduce the number of items and create an evaluation instrument with face and content validity.

2.2. Data Sources

To find systematic reviews on the relationship between sleep duration and hypertension, we examined the literature from inception to December 31st, 2022 in three major databases: PubMed, Web of Science, and Embase. We also reviewed the references of all included studies and relevant citations in PubMed to find new publications in order to reduce the possibility of overlooking the eloigible article. The PROSPERO registration number for this study is CRD42023459901, and it is accessible at http://www.crd.york.ac.uk/prospero.

2.3. Search Strategy

Electronic databases including Medline (via PubMed), Web of Science, Scientific Electronic Library Online (SciELO), and other national/regional databases (Index - Revistas Españicas Portuguesas) were searched for pertinent articles published between January 1, 2017, and December 31, 2021. The following general search terms were used on Pubmed: ("Patient Compliance"[Title/Abstract] OR "Medication Adherence"[Title/Abstract]) OR ("Patient Compliance"[Majr] OR "Medication Adherence"[Majr])) AND ((high blood pressure [Title/Abstract] OR hypertension [Title/Abstract]) OR ("Hypertension"[Majr]) AND ("Antihypertensive Agents"[Majr]). The search was limited to adult population-focused papers authored in English, French, Spanish, and Portuguese with online abstracts. Other databases employed a similar search method, but the text words and MeSH keywords were changed to meet the unique needs of each database. The PICOS model was used to develop the research question: (P) Adult patients diagnosed with primary hypertension who use at least one antihypertensive medication; (I) all pharmacological and non-pharmacological interventions; (C) patient adherence both forms of treatment. Because treatment adherence combines these two factors together, the findings would be more trustworthy.

2.4. Inclusion Criteria and Exclusion Criteria

Table 1 summarizes the predefined eligibility criteria used for study selection. It outlines the inclusion and

exclusion criteria across study aim, population, interventions, comparators, outcomes, settings, study design, country, language, and quality. These criteria ensured the inclusion of high-quality, clinically relevant evidence applicable to hypertension screening in primary care settings.

Table 1: Inclusion and Exclusion Criteria.

S. No.	Category	Included	Excluded
1.	Aim	Primary care hypertension screening/diagnosis	Non-screening BP measurements
2.	Population	Adults ≥18 years	Pregnant women, children, treated HTN, secondary HTN, CKD/transplant, institutionalized/inpatients
3.	Intervention	Clinic/home brachial BP measurement, ABPM	Wrist/finger/ankle devices, invasive/central BP, Osler's maneuver
4.	Comparator	No screening or ABPM	Device validation/comparison studies
5.	Outcomes	Mortality, CVD, ESRD, QoL, diagnostic accuracy, screening harms	Surrogate outcomes or insufficient diagnostic data
6.	Timing	No restriction	—
7.	Setting	Primary care, home/pharmacy	Inpatient/non-primary care
8.	Study Design	RCT, CCT, diagnostic accuracy, cohort	Case reports/series, case-control, cross-sectional, simulation, before–after; KQ3 n<100
9.	Country	Very high HDI	Other countries
10.	Language	English	Non-English
11.	Quality	Fair/Good	Poor

Abbreviations: ABPM = ambulatory blood pressure measurement; CCT = controlled clinical trial; RCT = randomized controlled trial.

2.5. Data Extraction & Analysis

Three of the thirty studies that made up this review reported changes in the prevalence of hypertension, two of which reported blood pressure control in hypertensive patients and one of which reported preventing hypertension in the general population; twenty-five of the studies reported changes in mean blood pressure; and two of the studies reported both outcome measures (mean blood pressure changes and changes in hypertension prevalence). Education and counseling intervention techniques were used in thirteen research; management intervention strategies were used in four studies; education, counseling, and management intervention strategies were combined in seven studies; and screening and referral for management intervention strategies were used in six studies. Fourteen studies tracked participants for less than a year. Twelve studies were carried out in the US, and the majority of them covered all racial and ethnic groups as well as both genders.

3. Assessment Methods of Medication Adherence

3.1. Subjective Methods and Objective Methods

Many additional research classified adherence measures as direct and indirect in addition to subjective and objective. Measurement of the drug or its metabolite concentration in bodily fluids, such as blood or urine, assessment of the presence of a biological marker administered with the medicine, and direct observation of the patient's medication-taking behavior are examples of direct measurements. These measurements may be taken at predetermined intervals or at random [21]. There are several disadvantages to using direct measurements, despite the fact that they are thought to be the most precise and can serve as tangible proof that the patient has taken the drug. They only produce a Yes/No answer without disclosing any trends or reasons for nonadherence [22].

Additionally, tests themselves can be quite invasive, which can put patients under stress and worry. Additionally, because several specialists and experts are needed to oversee the procedure and conduct the tests, direct measures are very costly and challenging to execute. Using direct observation as an example, patients can conceal their medications beneath their tongues and then throw them away, making routine scrutiny unfeasible. As a result, these measurements are mostly used to hospitalize patients receiving single-dose treatment or intermittent delivery [23].

This implies that there might be a false adherence, which should be taken into account while implementing these measures. In order to reduce this obstacle, healthcare providers should ideally not let patients know when they will be seen, yet doing so violates their right to manage their own care [24].

3.2. Pill Count

The quantity of dose units taken in between two planned appointments or clinic visits is counted in this indirect, objective metric. The adherence ratio would then be determined by comparing this figure with the total number of units the patient received [25]. This approach is popular since it is inexpensive and easy to use. Nonetheless, a number of restrictions have been noted. Pill count does not produce a medicine-taking pattern like MEMS does, even though it is predicated on the same premise that removing the dosage unit is comparable to taking the drug. The patient may not always adhere to the dose schedule even if the right amount of dosage units are taken out of the container [26]. In addition to failing to describe the adherence pattern, pill count also fails to pinpoint the reasons behind it. In the 1990s, MEMS took the role of pill count as a reference standard for validating other adherence metrics, despite pill count's superior accuracy when compared to other subjective approaches [27].

3.3. Pharmacy Refill Records

Sequences and patterns from carefully selected primary data in systems like pharmacy insurance claims or electronic prescription services are included in secondary database data [28]. Medication adherence to different refill adherence metrics may be quantified using such data. Refill adherence is predicated on the idea that a patient's medication-taking behavior and prescription-refilling routines match. This assumption has been regarded as a reasonable approximation [29]. Additionally, these measurements are predicated on the prescription being taken precisely as directed.

Therefore, these metrics cannot identify incomplete adherence, in which patients merely take a portion of the drug within that time. According to Farmer, there are three types of refill adherence: continuous variables, like the Medication Possession Ratio (MPR), which are evaluated "from the first to the last prescription record"; dichotomous variables, which classify patients as either compliant or noncompliant based on criteria like a specified treatment gap; and examining "the time between prescription refills from the perspective of time gaps (periods of nonadherence) or consumption (medication availability, the days' supply/days between refills)," such as Continuous Measure of Medication Acquisition (CMA), Continuous, Single Interval Measure of Medication Acquisition (CSA), and Continuous, Single Interval Measure of Medication Gaps (CSG) [30].

A centralized computerized system and uniformity across prescribers and dispensers are necessary for reviewing prescription refill records in order to gather a comprehensive dataset during the specified time frame. This makes it possible to analyze a sizable population, which contributes to the method's appeal in research. Additionally, this approach can identify patients who are at risk of therapy failure and evaluate multidrug adherence [31]. Although obstacles like demographic characteristics may be compared and identified as nonadherence variables, this approach does not provide the researcher or medical professionals with many hints on the barriers associated with the observed nonadherence in terms of specific patients [32].

3.4. Electronic Monitoring Devices

The term "adherence-monitoring devices incorporated into the packaging of a prescription medication" refers to EMP devices [33]. They have a number of options, but they all have several things in common: (i) recorded dosing events and saved adherence data; (ii) audiovisual reminders to indicate when the next dosage is due; (iii) digital displays; (iv) real-time monitoring; and (v) feedback on adherence performance [34]. The aforementioned gadget characteristics are ordered in decreasing order of popularity. Recording adherence performance is crucial for analysis and to customize appropriate treatments, even if not all devices have these characteristics [35].

The most used EMP tool in medication adherence research is the Medication Events Monitoring System (MEMS). It may provide the number of daily doses in any partial adherence scenario and assist in determining if the nonadherence is irregular, regular, or any other atypical medication-taking pattern. MEMS are more beneficial than biochemical and self-report tests because of these characteristics [36]. Despite MEMS's unquestionable accuracy, its exorbitant price and the quantity of support needed make it unsuitable for normal usage or large-population research like clinical trials [37].

The cost of the equipment alone is high. MEMS studies cost a lot of money to finish because of the potential for patient equipment loss, the need to rent gear and software for data retrieval, staff time, bed days, and the expense of encouraging patients to return the cap. In a 2001 trial that assessed drug adherence in individuals with schizophrenia or

schizoaffective disorder, a 6-month study cost USD $274 per patient [36].

4. Determinants of Medication Adherence

4.1. Patient-Related Factors

Our hospital's Institutional Review Board authorized this study, and each participant provided written consent. In order to control their hypertension, 556 hypertensive individuals were interviewed between January 2010 and May 2012 [38]. Following a radio and television campaign, these patients were chosen from among those who visited our hospital's free health check clinics. Every patient had spent more than five years residing in Liaocheng City, a regional city in China's southwest Shandong Province [39].

Following the collection of medical histories, each patient underwent a thorough physical examination that included taking their blood pressure. Additionally, blood biochemistry tests and an ECG were carried out. Data was gathered on the patient's antihypertensive therapy, namely the usage of antihypertensive drugs. A mercury sphygmomanometer was used to take the patient's blood pressure when they were seated and had rested for ten minutes [40]. The diastolic blood pressure was measured using phase V Korotkoff sounds. Systolic blood pressure of 140 mm Hg or diastolic blood pressure of 90 mm Hg was considered hypertension [41].

4.1.1. Health literacy Beliefs & attitudes

Five professionals in the field of health education in an expert panel validated the face validity of the health belief model questionnaire, which was created based on a survey of the literature. The content validity index and ratio were used to approve the content validity [42]. The researcher used ten hypertension patients to pilot test the questionnaire in order to identify any confusing or ambiguous questions [43]. Questions that were unclear were changed or eliminated. The questionnaire's pilot testing assisted in estimating the average response time of 15 minutes. Alpha Cronbakh was computed for the revised questionnaire in 30 additional hypertensive patients; the reliability for perceived susceptibility, severity, benefit, barriers, and self-efficacy sections was 0.89, 0.82, 0.88, 0.91, and 0.92, respectively [44]. The pilot participants were not included in the main study. SPSS version 18.0 for Windows (SPSS Inc., Chicago, IL, USA) was used to analyze the data. Descriptive statistics (means, proportions, and frequencies) were used to report the participants' demographics [45]. To ascertain if noncompliant patients varied substantially from compliant patients, the Chi-square test was employed. Odds ratios reflecting the relationship between certain factors and compliance were estimated using logistic regression. $P < 0.05$ was regarded as statistically significant [46].

Table 2 summarizes the major determinants of medication adherence, methods for adherence assessment, common barriers, evidence-based interventions, and associated clinical outcomes in hypertension management. It highlights that identifying adherence barriers, applying reliable assessment methods, and implementing multifaceted interventions are essential for improving blood pressure control, reducing cardiovascular risk, and achieving long-term therapeutic success [47], [48].

Table 2: Summary of the key determinants, assessment methods, adherence-enhancing interventions, and clinical outcomes in the management of hypertension.

S. No.	Domain	Key Highlights	Clinical Importance	References
1.	Determinants of Adherence	Adherence is influenced by patient characteristics, treatment complexity, socioeconomic status, and healthcare system factors.	Identification of modifiable barriers enables individualized adherence strategies.	[49], [50]
2.	Assessment of Adherence	Medication adherence can be evaluated using subjective (self-report), objective (pill count, pharmacy refill, electronic monitoring), and direct biological methods.	Combining multiple assessment tools improves the reliability of adherence evaluation.	[51]
3.	Barriers to Adherence	Poor health literacy, polypharmacy, complex dosing regimens, treatment costs,	Early recognition of barriers supports timely	[52], [53]

		inadequate patient–provider communication, and limited healthcare access are common barriers.	intervention and sustained treatment adherence.	
4.	Evidence-Based Interventions	Patient education, simplified treatment regimens, pharmacist-led services, multidisciplinary care, behavioral counseling, and digital health technologies effectively improve adherence.	Multifaceted interventions consistently produce greater improvements in adherence than single-component approaches.	[54], [55]
5.	Clinical Outcomes	Improved adherence enhances blood pressure control, reduces cardiovascular events and hospitalizations, improves quality of life, and decreases healthcare expenditure.	Sustained adherence is a key determinant of long-term hypertension control and cardiovascular risk reduction.	[56]

4.2. Therapy-Related Factors

4.2.1. Polypharmacy

In 2012, 42% of older persons were taking five or more drugs, up from five at age 65 to seven at age 85, according to data from the Intercontinental Marketing Services (IMS) health prescription database [57]. Additionally, in 2012, 13% of all older persons were taking ten or more prescriptions, and the degree of polypharmacy was directly correlated with adverse drug events in older adults, which in turn led to higher healthcare costs [58]. Another major factor contributing to drug nonadherence, which carries a heavy financial and medical cost, is polypharmacy [59].

Additionally, increasing polypharmacy may help elderly people manage their hypertension. According to a new review of data from the National Health and Nutrition Examination Surveys (NHANES) 13 1988–1994, 1999–2004, and 2005–2010, older Americans are using more hypertensive drugs [60]. The percentage of people 60 years of age and older who use three or more blood pressure medications has gradually increased from 9%±1% to 17%±1% to 26%±1% with each survey, which is linked to ongoing improved blood pressure control in older US individuals [61]. Recent research has demonstrated that high adherence to CV drugs considerably improves healthcare outcomes and lowers annual expenses for secondary prevention of CAD [62].

In the US, polypharmacy mismanagement among older individuals costs over $1.3 billion that might be prevented. Due to problems and adverse medication events, the majority of the costs are incurred through hospital stays, ER visits, and inpatient treatment. As a result, polypharmacy is becoming a more pressing social issue due to the rising percentage of older persons in the US who have hypertension [63]. There are several factors contributing to the higher incidence of adverse medication events in older persons. Polypharmacy nonadherence is greater in older persons because they are more likely to be weak, have much comorbidity, and make mistakes when self-administering their drugs. Adverse events, inadequate medication management and tracking, at-risk body composition, and age-related changes in metabolism and absorption are all factors linked to polypharmacy [60], [64].

4.3. Healthcare System Factors

The World Health Organization defines health systems as "all the organizations, institutions, and resources that are devoted to producing health actions." Weaknesses can be found at the national, regional, district, community, and household levels [65]. The effects of health systems interventions provided at the community or health facility level on HT care have been the subject of earlier systematic reviews [66]. Examples of these interventions include provider-focused education, organizational interventions that enhance physician-pharmacist collaboration, and the use of electronic records to improve management. Nevertheless, we are not aware of any prior systematic evaluation examining the impact on HT outcomes of activities originating at the national or regional health systems level, such as health policies, programs, and interventions. Strategies for obtaining necessary drugs, the presence of straightforward national guidelines for HT

management, the introduction of financial incentives for medical professionals to diagnose or treat HT, and improved health insurance coverage are some of the actions that have been proposed to impact HT care [67].

In order to close this gap, we conducted a thorough evaluation of the literature on the impact of regional or national health system structures on HT care and control and offered suggestions for further study and legislation. To depict the health system and its components and to direct our systematic evaluation, we employed a well-established framework [67]. The framework seeks to capture the intricate relationships and interactions that exist between the components of a health system, recognizing that successful health systems require effective integration and alignment of these inputs rather than just a "laundry list" of building blocks (as the WHO's 2007 framework is frequently perceived) [68]. The paradigm also emphasizes how context shapes the link between inputs and outcomes in health systems, acknowledging that health systems are complexly adaptable and that modifications may have different effects in different contexts [69].

Research on the effects of national or regional HT care policies or interventions that are relevant to other disease programs or to the overall design of the health system, such as those that necessitate or result in modifications to primary care delivery or other general aspects of the health system [70], [71].

4.4. Socioeconomic Factors

A significant predictor of hypertension, knowledge of the condition, and compliance with management procedures is socioeconomic level (SES) [72]. People with lesser incomes and levels of education have been linked to a higher incidence of hypertension in high-income countries. This relationship is complicated in LMIC, though. For example, high SES groups in South Asian nations have a higher prevalence of hypertension than low SES groups in Brazil and Peru. Research from Nepal has also shown that wealthy people have higher blood pressure, while highly educated people and males who work hard have normal blood pressure [73]. Higher SES groups in LMICs may have a reduced prevalence of hypertension because of improved access to and adherence to medical care, less psychological stresses, and growing health consciousness. However, sedentary lifestyle choices, which are increasing as a result of urbanization and globalization in LMICs like Nepal, may be the cause of the increased incidence observed among low SES groups. With certain geographical variations and variations related to socioeconomic position within a nation or geographic region, less than half of the treated patients reach a blood pressure target below 140/90 mmHg. Low socioeconomic level has been identified as a risk factor for uncontrolled blood pressure, suggesting a goal for better antihypertensive therapy [74], [75].

However, research on potential correlations between achieved blood pressure and socioeconomic status variables has been conflicting and varies among individuals and geographical areas [76]. The current study is to shed light on the relationship between socioeconomic status and achieving blood pressure targets in a hypertensive population in a Swedish primary care environment. More precisely, the study evaluated the relationship between attained blood pressure and sex as well as indicators of socioeconomic position (such as country of birth, income, and educational attainment) [76].

5. Clinical Outcomes of Medication Adherence

It is crucial to distinguish between compliance and adherence, as the latter is often associated with negativity [77]. When a patient is obedient to the prescriber and passively follows the advice of the healthcare professional, this is known as compliance. On the other hand, the World Health Organization (WHO) defines adherence as the degree to which a person's behavior—taking medicine, adhering to a diet, and making lifestyle modifications—corresponds with established guidelines from a healthcare professional [78]. Medication adherence involves three measurable stages, although it begins when the patient receives a prescription. When the patient takes the first tablet, the first phase, known as initiation, begins. Information on the actual dosage is provided in the second step, implementation, which may be less than ideal because of carelessness or forgetfulness [79].

Treatment interruptions may be deliberate or unintentional. The patient may exhibit either timing or taking non-adherence [80]. The patient quits taking the drug even when their prescription is refilled during the third and final phase, known as discontinuation. Together, these three stages are referred to as persistence. Patients' understanding and proper appraisal of the illness, as well as their happiness with clinic visits, are highly correlated with better drug adherence. Therefore, the key elements of managing hypertension are patient-centered care and nonjudgmental physician communication skills. Healthcare professionals should be educated on these elements, the value of patient education and counseling, and the need to clear up any misconceptions or false ideas about long-term therapy [81].

A multidisciplinary, patient-centered strategy can be used to maximize adherence to hypertension medication by enlisting the help of other medical professionals, including as pharmacists, to offer extra education and behavior therapy. Better patient outcomes and health benefits are linked to drug adherence [82]. According to a meta-analysis, adhering to recommended beneficial medication including a placebo is linked to a much lower death rate than inadequate adherence. Depending on the technique employed to evaluate adherence, adherence can be qualitatively assessed as either adherent or nonadherent. The percentage of patients who take their medications as prescribed is a frequently used quantitative metric. It is described as the proportion of pills consumed over a specific time period compared to the quantity of tablets a doctor prescribes during that same time period. Another crucial measure of how well patients accept a medication is adherence [83].

Only 33-46% of published randomized controlled trials (RCTs) provide adherence rates, despite the significance of adherence in clinical studies. However, these RCTs frequently have extremely high reported rates of adherence, which might lead to an overestimation of adherence because of underreporting. This might have to do with patient selection, the observer effect changing patient behavior, and the additional attention research participants receive. There are several ways to evaluate how patients take their medications, and they may be roughly divided into direct and indirect techniques. Direct methods include the patient's direct observation of the medication being consumed, the detection of a drug or its metabolite in the blood or urine, the detection of a biological marker present in the drug formulation, and, more recently, the automatic electronic monitoring of drug ingestion through the incorporation of a specially designed microchip into each dose of a drug. Direct approaches are the most accurate way to monitor adherence since they offer evidence that the patient has taken their medicine [84], [85].

The most popular approaches in research have been indirect measures of adherence. These consist of physiological marker assessment, medication event monitoring system (MEMS), patient interview, pill count, patient diary, and patient questionnaire. Adherence is used interchangeably with compliance; however, the motivational level seems to be varied between them, where adherence denotes better patients' engagement with the instructions of healthcare providers [84], [86]. The major determinants, assessment methods, barriers, evidence-based interventions, and clinical outcomes related to medication adherence in hypertension. An overview of the present body of research supporting digital interventions to enhance adherence will be given first in this narrative review. This will be followed by a summary of problems in the area and elements linked to the effectiveness of digital health adherence tools [87].

6. Role of Clinical Pharmacist

Among healthcare professions, pharmacists are thought to be the most approachable. Pharmacists now provide patient counseling on lifestyle changes, drug therapy management, disease state management, and maintaining optimal medication adherence in addition to their traditional job of dispensing prescriptions [88]. The International Pharmaceutical Federation's 2019 policy statement on pharmacists' roles in non-communicable diseases states that by offering pharmaceutical care, reviewing medications, and encouraging medication adherence, pharmacists successfully contribute to the proper management of CVD. The kind and efficacy of pharmacists' interventions in enhancing medication adherence by patients with hypertension and hyperlipidemia, however, are little understood [89].

Therefore, this study was carried out to describe the various pharmacist interventions according to their degree of influence on patients' medication adherence. It also sought to provide light on the relationship between pharmacist interventions, adherence rates, and the attainment of the intended therapeutic objectives. To the best of the authors' knowledge, this is the first research to describe the various pharmacist treatments according to how much of an influence they have on clinical outcomes and medication adherence. The reasonable use of hyperlipidemia drugs was found to improve with pharmacist-led treatments, according to prior study [90], [91].

A substantial influence of pharmacist interventions on patient medication adherence was documented in almost 65% of the studies that were included of this analysis. Medication adherence was evaluated as a secondary outcome measure in three trials. Two of these trials found no discernible improvement in adherence after the pharmacists' involvement [92]. According to reports, the total success percentage of pharmacists' efforts to improve medication adherence was 75% for multifaceted treatments, 62.5% for in-person counseling, and 60% for telephone-based interventions. These results imply that the greatest potential to increase medication adherence was demonstrated by the pharmacists' direct participation in multifaceted care models with a multidisciplinary collaboration component.

Although they were less likely to be consistently linked to the achievement of clinical objectives, pharmacist-led interventions were linked to better patient adherence to their prescriptions. Variations in the kind and design of the intervention, controlgroup, choice of primary and secondary objectives, and adherence assessment instruments appear to have an impact on the study's findings [93].

Following the evaluation of medication adherence as primary outcomes, the majority of the studies examined clinical outcomes as secondary results. Some studies lacked clinical outcome measurement, which made it difficult to examine the relationship between adherence and clinical results [94].

7. Discussion

Lifestyle modification was taken into consideration as the intervention in the PICO question about the first-line treatment for individuals with pre-hypertension and hypertension [95]. Despite the fact that lifestyle modification is a successful non-pharmacological treatment for hypertension, the results of the systematic review showed that either there were not enough research in this field or that the evidence ranking was poor [96]. A significant information vacuum and a lack of high-quality cost-effectiveness studies were also shown by the findings of a systematic review conducted in the Asia-Pacific region on primary prevention by lifestyle change. Our research exposed important gaps in the literature, especially with regard to certain populations and outcomes [97]. It is also crucial to follow up with people who have hypertension on a regular basis. Shorter follow-up intervals enhance adherence to medication and blood pressure management and make monitoring adverse effects more practicable, but they can have negative consequences, such as an increased treatment burden for patients and the national health system. Nevertheless, neither the cost, resources, nor the cost-effectiveness of shortening or lengthening follow-up intervals were supported by any data with a high degree of assurance of impact. Nonetheless, it seems more economical to decrease the number of visits for senior citizens [98].

8. Conclusion

Although they differ in maturity, digital health and artificial intelligence are starting to change how hypertension is managed. AI-guided titration systems that follow ESC/ESH standards and new digital twin models that directly address therapy inertia and promote individualized treatment are the most promising uses. Cuffless blood pressure monitoring, on the other hand, is still the least developed field because to ongoing issues with validity and accuracy. Practical multicenter randomized trials with cost-effectiveness and equity outcomes across a variety of groups are needed for future advancements. Crucially, in order to guarantee that these technologies provide safe, fair, and long-lasting advances in the treatment of hypertension, development and implementation must be accompanied by measures addressing algorithmic bias, accountability, and privacy. One viable solution to the major worldwide problem of pharmaceutical non-adherence is the use of digital technology. However, there is conflicting data about the efficacy of these digital therapies, with several research demonstrating inconsistent or transient increases in adherence. The variety of designs, content, and distribution strategies employed in digital tools many of which lack a solid evidence foundation or user-centered design is primarily to blame for this heterogeneity. Digital treatments may save healthcare costs and increase drug adherence, but caution must be taken to prevent new technologies from unintentionally escalating already-existing health disparities.

Acknowledgements

The authors sincerely acknowledge the Faculty of Pharmacy, Swami Vivekanand Subharti University, Meerut, for providing the necessary academic support and facilities to complete this review. The authors also thank all researchers whose published work contributed to this systematic review.

Author Contributions

SAA: Conceptualization, methodology, writing–original draft; **LS:** Literature review, data curation, writing–review & editing.

Declaration of Interest statement

The authors declare no financial or non-financial conflict of interests.

Funding

Not applicable

Ethics approval and consent to participate

Not applicable

AI Declaration

The author declares that no artificial intelligence (AI) tool was used to generate or draft the scientific content of this manuscript. Paperpal AI was used solely to improve the language, grammar, readability, and overall clarity of the manuscript. The author carefully reviewed and edited all suggested changes and takes full responsibility for the accuracy, originality, and integrity of the final content.

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