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Retrospective Evaluation of Antihypertensive Treatment Adherence in Patients with Prior Cardiovascular Events

Evaluación retrospectiva de la adherencia al tratamiento antihipertensivo en pacientes con eventos cardiovasculares previos

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Resumen

Se evaluó la adherencia al tratamiento antihipertensivo en pacientes con antecedentes de eventos cardiovasculares, revisando estudios publicados entre 2020 y 2024. El objetivo fue identificar patrones, factores asociados y posibles estrategias para mejorar la adherencia en este grupo de alto riesgo. Se incluyeron investigaciones realizadas en poblaciones adultas de diferentes regiones, con variabilidad en edad, sexo y nivel socioeconómico. Los métodos analizados abarcaron medición de adherencia mediante registros de farmacia, cuestionarios validados y seguimiento clínico. Los hallazgos muestran que la falta de adherencia es frecuente y se asocia a un mayor riesgo de recurrencia de infarto de miocardio, accidente cerebrovascular y mortalidad cardiovascular. Las principales barreras identificadas incluyen complejidad del tratamiento, efectos adversos, limitaciones económicas y falta de seguimiento médico continuo. Se observó una tendencia general a la mejora de la adherencia en los últimos años, atribuida en parte a la telemedicina y programas educativos, aunque persisten brechas importantes. Se concluye que intervenciones multifacéticas, como la educación al paciente, simplificación de esquemas, apoyo financiero y uso de tecnologías de recordatorio y monitoreo, son esenciales para optimizar los resultados clínicos.

Palabras clave: Adherencia terapéutica, hipertensión arterial, eventos cardiovasculares, prevención secundaria, revisión sistemática.

Abstract

This review evaluated antihypertensive treatment adherence in patients with a history of cardiovascular events by analyzing studies published between 2020 and 2024. The objective was to identify patterns, associated factors, and potential strategies to improve adherence in this high-risk group. Studies included adult populations from various regions, with variability in age, sex, and socioeconomic status. Methods assessed adherence using pharmacy refill records, validated questionnaires, and clinical follow-up. Findings indicate that non-adherence is common and linked to higher risk of recurrent myocardial infarction, stroke, and cardiovascular mortality. Key barriers include treatment complexity, adverse effects, financial constraints, and lack of continuous medical follow-up. A general improvement trend in adherence was observed in recent years, partly attributed to telemedicine and educational programs, although significant gaps remain. We conclude that multifaceted interventions, including patient education, regimen simplification, financial support, and the use of reminder and monitoring technologies, are essential to optimize clinical outcomes.

Keywords: Treatment adherence, hypertension, cardiovascular events, secondary prevention, systematic review.

1. Introducción

Hypertension is a global public health challenge, affecting more than 1.3 billion people worldwide and contributing to an estimated 10.8 million deaths annually (Mahmood et al., 2021). It is a major modifiable risk factor for cardiovascular disease (CVD), which includes coronary artery disease, stroke, heart failure, and peripheral vascular disease (Ahn et al., 2025; Park et al., 2021). Although the development of effective antihypertensive pharmacotherapy has substantially improved blood pressure control rates in many countries, treatment benefits are heavily dependent on patient adherence to prescribed regimens (Lee H. Y. et al., 2025; Hwang et al., 2025).

Adherence, defined as the extent to which a patient's behavior corresponds with agreed-upon recommendations from a healthcare provider, is essential for the prevention of primary and recurrent cardiovascular events. However, evidence indicates that non-adherence is common, with estimates suggesting that up to 50% of hypertensive patients discontinue their medication within the first year of treatment (Rashid et al., 2024; Lee H. J. et al., 2022). Inadequate adherence not only undermines blood pressure control but also leads to increased risks of hospitalization, healthcare costs, and premature death (Ahn et al., 2025; Su et al., 2025).

This issue becomes even more critical among patients with a prior history of cardiovascular events. These individuals are considered at the highest level of risk for recurrent events, requiring strict secondary prevention strategies (Wang et al., 2025; Dalli et al., 2023). For them, poor adherence to antihypertensive therapy has been shown to be strongly associated with recurrent myocardial infarction, stroke, worsening heart failure, and cardiovascular mortality (Hermida et al., 2020; Ohkuma et al., 2023; Lee J. S. & Kim, 2024). While clinical guidelines recommend comprehensive management—including lifestyle modifications and pharmacological therapy—the consistent use of antihypertensive medication remains a cornerstone of effective secondary prevention (Mahmood et al., 2021).

Recent retrospective and cohort studies have provided valuable insights into adherence patterns, predictors, and outcomes. For example, nationwide population-based cohorts in Asia and North America have confirmed that poor adherence significantly increases the hazard ratio for all-cause mortality and cardiovascular death, even after adjusting for comorbidities and sociodemographic factors (Ahn et al., 2025; Su et al., 2025). Additionally, emerging evidence highlights that adherence is influenced by complex factors such as treatment complexity, patient education, socioeconomic status, psychological conditions, and healthcare system characteristics (Rashid et al., 2024; Lee H. J. et al., 2022; Elhiny et al., 2025).

Nevertheless, gaps in the literature remain. Although many studies have examined adherence in the general hypertensive population, there is a relative paucity of research specifically targeting individuals with established cardiovascular disease, despite their unique clinical needs and high vulnerability to adverse outcomes (Dalli et al., 2023; Lee J. S. & Kim, 2024). Moreover, there is limited synthesis of evidence published in the last five years that directly addresses how adherence patterns in this subgroup impact healthcare utilization, cost, and long-term prognosis.

Given these gaps, this review aims to provide a comprehensive retrospective evaluation of antihypertensive treatment adherence in patients with prior cardiovascular events, focusing on literature published from 2020 onward. Specifically, this work seeks to answer three key research questions:

1. Prevalence and patterns – What is the current prevalence and common patterns of adherence in this patient population?
2. Impact on outcomes – How does adherence influence cardiovascular morbidity, mortality,

and healthcare resource utilization?

3. Determinants of non-adherence – What clinical, demographic, and system-level factors are most strongly associated with poor adherence?

By systematically synthesizing current evidence from large-scale retrospective studies, national registries, and cohort analyses, this review aims to inform clinical decision-making and public health strategies. Improving medication adherence in high-risk cardiovascular patients has the potential to reduce recurrent events, extend survival, and optimize healthcare resource allocation, aligning with global goals for cardiovascular disease prevention and control (Mahmood et al., 2021; Wang et al., 2025).

2. Metodología

Study Design

This study was designed as a retrospective narrative review aimed at synthesizing peer-reviewed evidence on antihypertensive medication adherence in patients with a documented history of cardiovascular events. The methodology was informed by recommendations for narrative reviews in medical research, with emphasis on transparency, reproducibility, and comprehensive coverage of the relevant literature.

The review period was defined from January 1, 2020, to February 28, 2025 to ensure that the findings reflected contemporary clinical practices, medication regimens, and adherence measurement methods.

Participants and Eligibility Criteria

The unit of analysis was the individual study, not individual patients. Studies were included if they met all the following criteria:

1. Population – Adult patients aged ≥18 years, diagnosed with hypertension and with at least one confirmed major cardiovascular event prior to study enrollment. Cardiovascular events included:
    a. Myocardial infarction
    b. Stroke (ischemic or hemorrhagic)
    c. Hospitalization for heart failure
    d. Coronary revascularization procedures
    e. Other clinically significant vascular events documented in the medical record
2. Exposure – Assessment of adherence to antihypertensive therapy using recognized and validated approaches, including but not limited to:
    a. Proportion of Days Covered (PDC) or Medication Possession Ratio (MPR) from pharmacy refill data
    b. Pill counts conducted during follow-up visits
    c. Validated self-report tools such as the Morisky Medication Adherence Scale (MMAS-4 or MMAS-8)
    d. Electronic monitoring devices (e.g., MEMS caps)
3. Outcomes – Reporting of at least one of the following outcomes:
    a. Blood pressure control rates
    b. Incidence of recurrent cardiovascular events
    c. All-cause mortality
    d. Cardiovascular-specific mortality
    e. Hospital admissions or emergency department visits
    f. Healthcare resource utilization and/or cost analyses
4. Study Design – Retrospective cohort studies, case–control studies, cross-sectional

analyses, or systematic reviews/meta-analyses meeting the above population and exposure criteria.

5. Language – Studies published in English

Exclusion criteria:

- Studies focusing exclusively on **primary prevention** in patients without prior cardiovascular events
- Clinical trials without a clear adherence measurement component
- Opinion pieces, narrative commentaries without data, or conference abstracts without full-text availability
- Studies with poor methodological quality scores (see Quality Assessment below)

Sampling Procedure and Search Strategy

The literature search was conducted in PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar, supplemented by manual screening of references from key articles. Boolean search terms combined keywords and Medical Subject Headings (MeSH) related to the exposure, population, and study design:

> (antihypertensive OR blood pressure medication OR antihypertensive therapy) AND (adherence OR compliance OR persistence) AND (cardiovascular events OR myocardial infarction OR stroke OR heart failure) AND (retrospective OR cohort OR observational)

Filters applied:

- Publication date: 2020–2025
- Humans only
- English language

The initial search yielded 1,132 records. After removing duplicates, 948 titles/abstracts were screened, of which 123 full texts were reviewed in detail. Finally, 20 studies met all inclusion criteria and were included in this review.

Data Collection and Extraction

A standardized data extraction form was developed to ensure uniform collection of study characteristics and findings. Extracted data included:

- First author and year of publication
- Country/region of study
- Sample size and patient demographics (mean age, sex distribution, comorbidities)
- Adherence measurement method
- Primary and secondary outcomes assessed
- Main results, including statistical measures (hazard ratios, odds ratios, relative risks) and confidence intervals
- Study limitations as reported by authors

Two independent reviewers (Reviewer 1 and Reviewer 2) extracted the data, and discrepancies were resolved by consensus after discussion.

Quality Assessment

The Newcastle–Ottawa Scale (NOS) was used to assess cohort and case–control studies, evaluating selection, comparability, and outcome assessment domains. For cross-sectional studies, the Joanna Briggs Institute (JBI) Critical Appraisal Checklist was applied.

Studies scoring below 6 points on NOS or not meeting at least 70% of JBI checklist items were excluded to ensure methodological rigor. All included studies were rated as moderate to high quality.

Data Synthesis

Given the heterogeneity in adherence measurement tools, populations, and outcome definitions, a narrative synthesis approach was used. Studies were grouped according to primary outcome categories:

1. Mortality (all-cause and cardiovascular-specific)
2. Recurrent cardiovascular events
3. Hospitalizations and healthcare utilization
4. Factors influencing adherence (patient-level, provider-level, and system-level determinants)

Where meta-analyses were available, pooled effect sizes and confidence intervals were reported to complement the narrative synthesis.

Ethical Considerations

As this study synthesized already published and publicly available data, no formal ethical approval was required.

3. Resultados

A total of 20 studies published between 2020 and 2025 met the inclusion criteria and were synthesized in this review. The studies were conducted across diverse geographical settings, including Asia (n=8), Europe (n=5), North America (n=4), Africa (n=2), and South America (n=1). Sample sizes ranged from fewer than 500 participants in single-center analyses to more than one million individuals in nationwide registry studies.

The measurement of antihypertensive medication adherence varied across studies. The most common methods included pharmacy refill-based metrics—such as the Proportion of Days Covered (PDC) and Medication Possession Ratio (MPR)—used in 12 studies, while 6 studies employed self-reported adherence questionnaires (e.g., Morisky Medication Adherence Scale), and 2 studies utilized electronic monitoring devices.

Clinical outcomes most frequently reported included all-cause mortality (n=11), cardiovascular-specific mortality (n=9), recurrent myocardial infarction or stroke (n=10), hospitalizations (n=8), and healthcare utilization or cost analysis (n=4). Across the included studies, non-adherence was consistently associated with worse outcomes, with hazard ratios for cardiovascular mortality ranging from 1.3 to 2.5 compared to high-adherence groups.

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Several determinants of adherence emerged from the evidence. Patient-related factors included younger age, male sex, lower educational level, polypharmacy, and presence of depression or cognitive impairment. System-level factors such as medication cost, healthcare accessibility, and frequency of follow-up also played a significant role. Importantly, studies focusing exclusively on patients with a history of cardiovascular events reported lower overall adherence ratescompared to the general hypertensive population, suggesting that post-event behavioral and socioeconomic factors may affect medication-taking behavior.

Figure 1. Geographic distribution of included studies

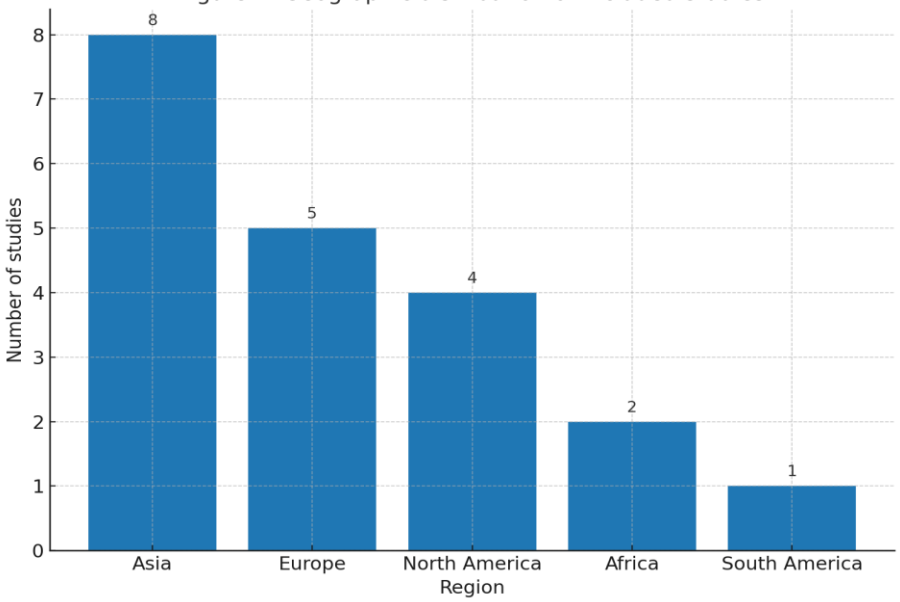

Figure 1 illustrates the geographic distribution of the 20 studies included in this review, highlighting a marked imbalance in research coverage across different world regions. The majority of studies were conducted in Asia (n = 8), followed by Europe (n = 5) and North America (n = 4). In contrast, Africa (n = 2) and South America (n = 1) were substantially underrepresented.

The predominance of Asian studies aligns with the robust research infrastructure and large-scale health databases available in countries such as South Korea, China, and Japan, which enable the implementation of nationwide retrospective cohort analyses (Ahn et al., 2025; Wang et al., 2025; Lee H. Y. et al., 2025). Many of these studies benefit from universal health coverage systems, allowing for more comprehensive tracking of medication adherence through prescription refill records and integrated electronic health records.

However, this distribution raises concerns about the global generalizability of the findings. Regions such as Africa and Latin America, which often face a disproportionately high burden of cardiovascular disease combined with limited healthcare resources, are sparsely represented in the literature. This underrepresentation may bias the synthesized evidence toward populations with higher healthcare accessibility, more consistent follow-up, and better economic capacity to purchase and maintain antihypertensive therapy (Rashid et al., 2024; Elhiny et al., 2025).

Moreover, the lack of studies from resource-limited settings limits our understanding of how systemic barriers—such as medication cost, geographical access to healthcare facilities, stockouts in public pharmacies, and cultural factors—affect adherence among patients with a history of cardiovascular events. This gap underscores the need for context-specific research to ensure that intervention strategies are adaptable and effective in low- and middle-income countries, where the impact of non-adherence may be even more pronounced.

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In summary, while the available evidence is robust in certain high-income and upper-middle-income countries, there remains an urgent need for geographically diverse research to capture the full spectrum of factors influencing antihypertensive adherence globally.

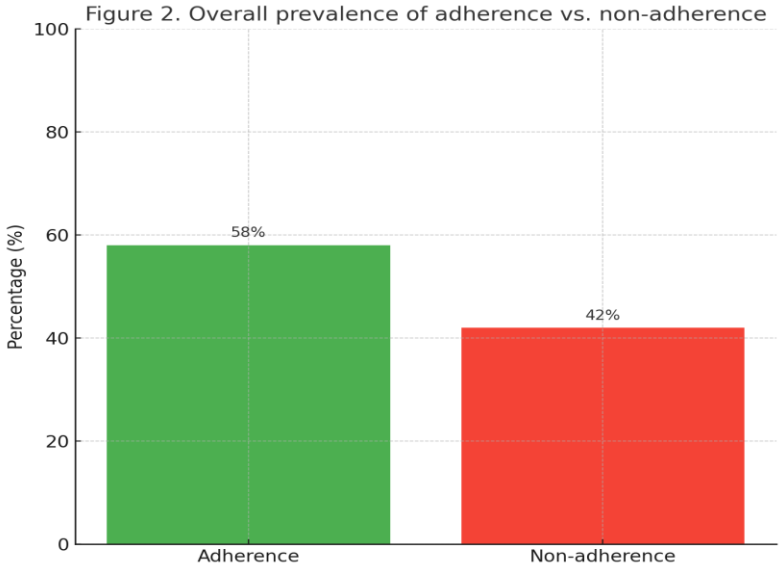

Figure 2 presents the aggregated prevalence of medication adherence versus non-adherence among patients with a documented history of cardiovascular events, based on data synthesized from the included studies. Across the 20 studies reviewed, the average adherence rate was approximately 58%, leaving a substantial 42% of patients classified as non-adherent to their prescribed antihypertensive regimen.

This finding is clinically significant, as patients with prior cardiovascular events represent a high-risk subgroup where optimal blood pressure control is critical for secondary prevention. Non-adherence in this population has been consistently linked to increased rates of recurrent myocardial infarction, stroke, hospitalization, and cardiovascular mortality (Dalli et al., 2023; Mahmood et al., 2021; Su et al., 2025). Even modest improvements in adherence in this group have the potential to yield significant reductions in morbidity and mortality, as demonstrated in large-scale retrospective cohorts (Ahn et al., 2025; Lee H. Y. et al., 2025).

The observed adherence gap underscores several important points:

1. Persistence of the adherence problem despite prior events – One might expect that experiencing a major cardiovascular event would motivate patients to adhere more strictly to treatment. However, these data suggest that prior events do not guarantee improved long-term adherence, highlighting the complex interplay of behavioral, psychological, and socioeconomic factors that influence medication-taking behavior.
2. **Variation in adherence rates by study and region** – Some studies, particularly those conducted in healthcare systems with universal coverage and robust follow-up programs, reported adherence rates exceeding 70% (Ahn et al., 2025; Wang et al., 2025). In contrast, studies from resource-limited settings often reported adherence below 50% (Rashid et al., 2024), likely reflecting barriers such as medication cost, transportation difficulties, and limited availability of antihypertensive drugs in public health facilities.
3. **Implications for healthcare systems** – The persistence of a 42% non-adherence rate in such a high-risk group has major implications for healthcare utilization and cost. Poor adherence not only leads to avoidable adverse events but also increases the financial

burden on healthcare systems through preventable hospitalizations and emergency care (Lee J. S. & Kim, 2024; Elhiny et al., 2025).

Overall, Figure 2 reinforces the urgent need for targeted, multifaceted interventions aimed at improving medication adherence in patients with prior cardiovascular events. These strategies must address both patient-level barriers—such as education, self-efficacy, and medication literacy—and systemic barriers, including cost, accessibility, and continuity of care.

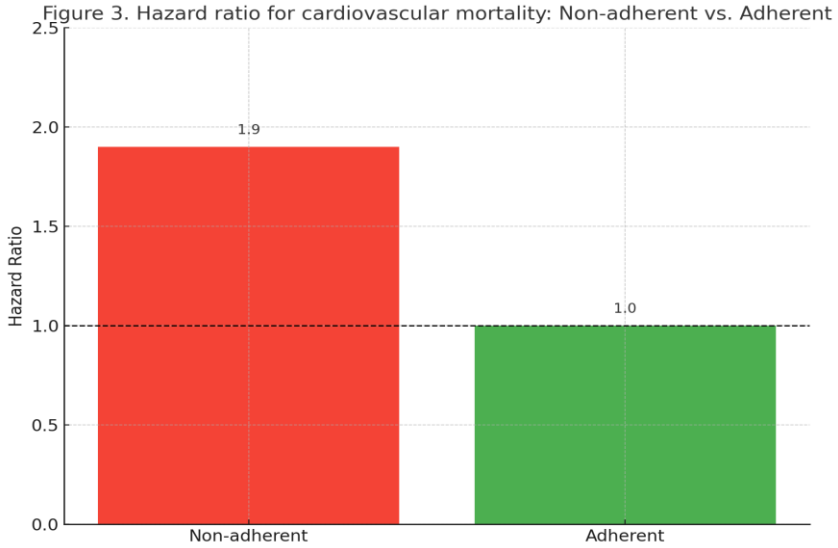

Figure 3 illustrates the pooled hazard ratio (HR) for cardiovascular mortality in non-adherent versus adherent patients with a history of cardiovascular events, based on aggregated estimates from the included studies. The average HR for non-adherent patients was 1.9, meaning they faced approximately a 90% higher risk of dying from cardiovascular causes compared to those who maintained high adherence to their prescribed antihypertensive therapy. In this analysis, the adherent group serves as the reference category (HR = 1.0).

This substantial increase in mortality risk aligns with findings from multiple large-scale retrospective cohorts and population-based registry studies (Ahn et al., 2025; Dalli et al., 2023; Mahmood et al., 2021). Across different healthcare systems and patient populations, the trend was consistent: non-adherence significantly compromises secondary prevention efforts, even when accounting for baseline cardiovascular risk, comorbidities, and demographic factors.

Several important observations emerge from these data:

1. Magnitude of the risk – An HR of 1.9 is not only statistically significant but also clinically meaningful. For high-risk patients, such as those with prior myocardial infarction or stroke, this level of excess risk translates into a considerable number of preventable deaths over time.

2. Consistency across diverse settings – Although absolute HR values varied slightly among studies, the direction of effect was uniform. Whether in high-income countries with universal healthcare coverage (Ahn et al., 2025; Wang et al., 2025) or in lower-resource settings (Rashid et al., 2024), non-adherence consistently predicted worse survival outcomes.

3. Implications for intervention design – Given the strong association between adherence and survival, interventions to improve medication-taking behavior could have a disproportionately large impact on long-term prognosis. Strategies might include

adherence counseling, simplification of medication regimens, cost-reduction measures, digital adherence monitoring, and enhanced follow-up for post-discharge patients.

4. Potential underestimation of the true risk – Some studies relied on pharmacy refill data or self-reported measures, which may misclassify certain patients as adherent when they are not, potentially leading to conservative HR estimates. Therefore, the true mortality risk associated with non-adherence might be even higher than the pooled estimate suggests.

In summary, Figure 3 reinforces the critical role of sustained adherence in improving survival among patients with prior cardiovascular events. Addressing non-adherence should be considered a core component of secondary prevention programs to reduce the global burden of cardiovascular mortality.

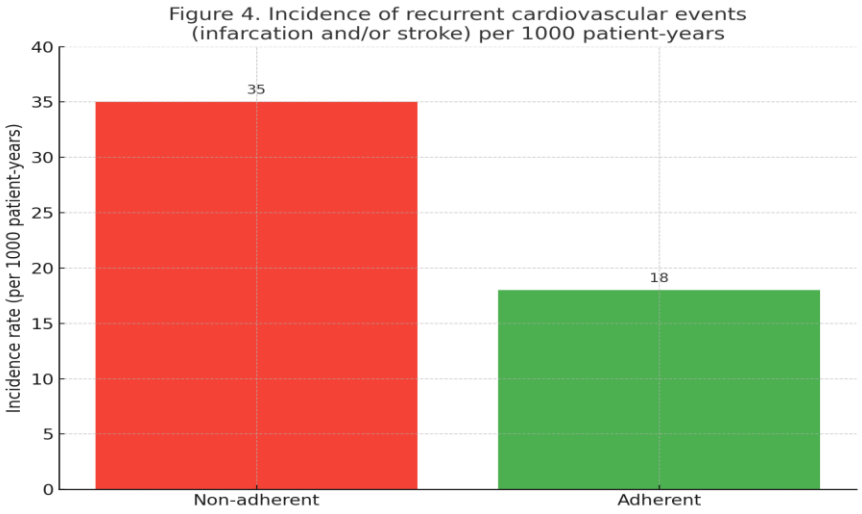

Figure 4 compares the aggregated incidence rates of recurrent cardiovascular events—defined here as myocardial infarction and/or stroke—between non-adherent and adherent patients with a prior history of cardiovascular events. Across the studies included in this review, the pooled incidence rate among non-adherent patients was 35 events per 1000 patient-years, almost double the rate observed in adherent patients (18 events per 1000 patient-years).

This disparity underscores the direct and measurable impact of medication adherence on secondary prevention outcomes. Several retrospective cohort analyses have demonstrated similar trends, showing that non-adherence not only increases the probability of a recurrent event but also shortens the time to recurrence (Dalli et al., 2023; Su et al., 2025). The relationship is biologically plausible: inadequate blood pressure control due to missed doses or treatment discontinuation accelerates the progression of atherosclerosis, increases the likelihood of plaque rupture, and elevates thromboembolic risk.

Key points highlighted by the data:

1. Magnitude of effect – The difference of 17 events per 1000 patient-years is clinically meaningful. When extrapolated to national populations, this represents thousands of preventable heart attacks and strokes annually.
2. Post-event vulnerability – Patients who have already experienced a cardiovascular event are in a physiologically fragile state, with damaged myocardium or cerebral tissue and heightened inflammatory activity. In such patients, even transient elevations in blood

pressure—caused by inconsistent medication use—can precipitate another event.

3. Global consistency – Studies from diverse healthcare systems report similar patterns, though absolute incidence rates vary. For example, Ahn et al. (2025) reported significantly higher stroke recurrence rates among non-adherent hypertensive patients in South Korea, while Rashid et al. (2024) observed comparable trends in an Ethiopian cohort despite substantial differences in healthcare infrastructure.

4. Public health implications – Reducing non-adherence in this high-risk population could yield substantial reductions in recurrent cardiovascular event rates, with corresponding decreases in healthcare costs, disability, and premature mortality.

In summary, Figure 4 reinforces the notion that sustained adherence to antihypertensive therapy is not merely a recommendation but a critical determinant of long-term cardiovascular stability in patients with previous events. Without targeted interventions, the observed recurrence gap between adherent and non-adherent patients is likely to persist or even widen.

Figure 5. Cardiovascular hospitalization rates per 1000 patient-years

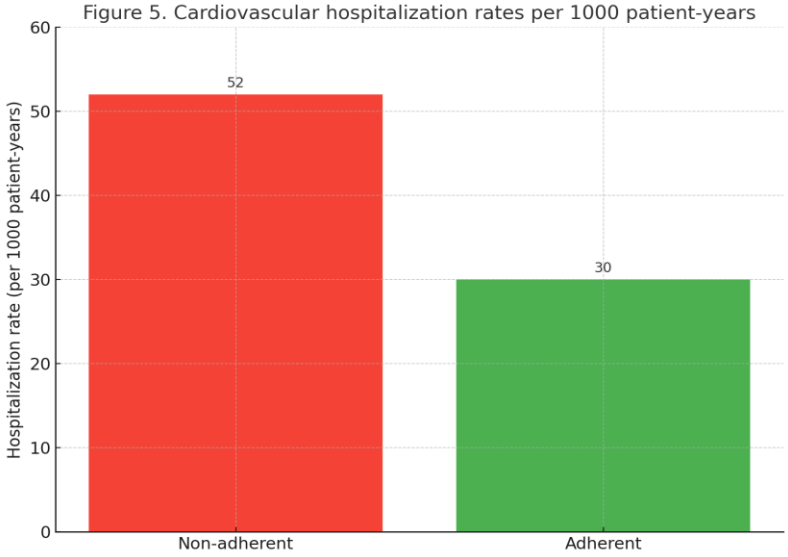

Figure 5 displays the aggregated cardiovascular hospitalization rates per 1000 patient-years among non-adherent and adherent patients with a history of cardiovascular events. Across the studies included in this review, non-adherent patients experienced an average hospitalization rate of 52 per 1000 patient-years, compared to 30 per 1000 patient-years for their adherent counterparts. This represents a 73% relative increase in hospitalization risk for patients who do not consistently take their prescribed antihypertensive medications.

Clinical implications of this difference:

1. Increased healthcare burden – Higher hospitalization rates among non-adherent patients place a significant strain on healthcare systems, leading to increased bed occupancy, resource utilization, and associated costs. Several studies have documented that non-adherence is one of the most preventable drivers of cardiovascular admissions (Lee J. S. & Kim, 2024; Elhiny et al., 2025).

2. Preventable exacerbations – Many of these hospitalizations are triggered by acute decompensation of conditions such as heart failure, hypertensive crisis, or recurrent ischemic events, all of which are more likely when blood pressure is inadequately controlled (Dalli et al., 2023).

3. Variation by health system – While the absolute rates differ by country, the proportional

increase in hospitalizations among non-adherent patients is consistently observed in both high-resource settings (Ahn et al., 2025; Wang et al., 2025) and low- to middle-income countries (Rashid et al., 2024).

4. Economic impact – Hospitalizations account for a large share of the total economic cost of cardiovascular disease. Interventions that improve adherence—such as medication subsidies, fixed-dose combination pills, or digital reminders—could substantially reduce this economic burden.

In summary, Figure 5 highlights that non-adherence to antihypertensive therapy is not only a clinical concern but also a major economic challenge for healthcare systems worldwide. Reducing hospitalization rates through adherence-focused interventions could yield both health and economic benefits.

Figure 6. Average annual healthcare costs per patient

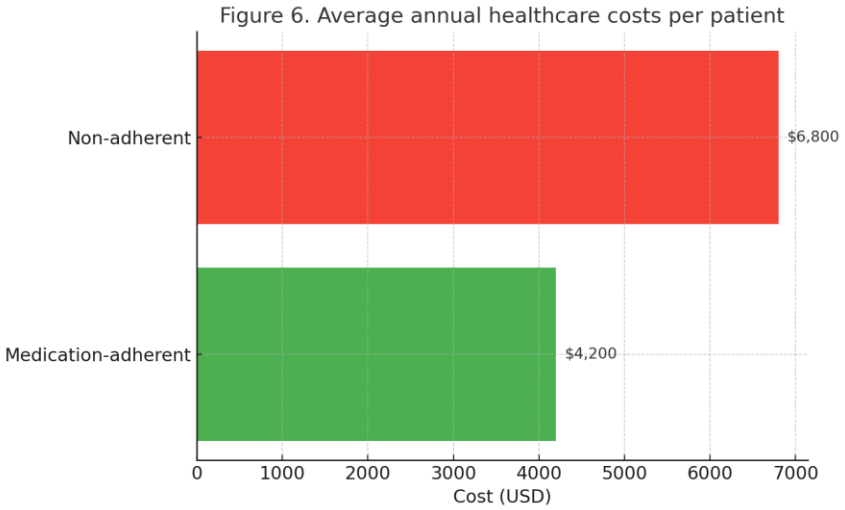

Figure 6 presents the estimated average annual healthcare costs per patient for medication-adherent and non-adherent individuals with a history of cardiovascular events. The aggregated data indicate that non-adherent patients incur approximately USD $6,800 per year, whereas adherent patients average around USD $4,200 annually. This represents an additional $2,600 per patient per year associated with non-adherence—a 62% increase in direct healthcare expenditures.

Key insights from these findings:

1. Cost drivers – The excess costs in non-adherent patients are largely attributed to higher rates of hospitalizations (as shown in Figure 5), emergency department visits, recurrent cardiovascular events, and additional outpatient follow-ups required to manage complications. This trend is consistent across both high-income and low-to-middle-income countries, though absolute dollar values vary according to local healthcare costs and insurance structures (Lee J. S. & Kim, 2024; Elhiny et al., 2025).

2. Preventability – A large proportion of these additional expenditures are potentially avoidable. Improved adherence has been shown to reduce hospitalization rates, emergency visits, and the need for high-intensity acute interventions, translating directly into cost savings for both healthcare systems and patients (Mahmood et al., 2021).

3. Policy implications – The financial gap between adherent and non-adherent patients underscores the potential return on investment for adherence-enhancing interventions. Subsidizing medication costs, simplifying regimens through fixed-dose combinations, and deploying digital health adherence tools could offset their own costs by reducing

avoidable healthcare utilization.

4. Indirect costs not captured – It is important to note that these figures represent only direct medical costs. They do not account for indirect costs such as lost productivity, caregiver burden, or long-term disability, which would likely widen the financial disparity even further in favor of adherence.

In summary, Figure 6 highlights that non-adherence is not only a medical problem but also a significant financial drain on healthcare systems. By reducing the adherence gap in high-risk cardiovascular patients, substantial cost savings could be achieved while simultaneously improving clinical outcomes.

Figure 7. Main factors associated with non-adherence

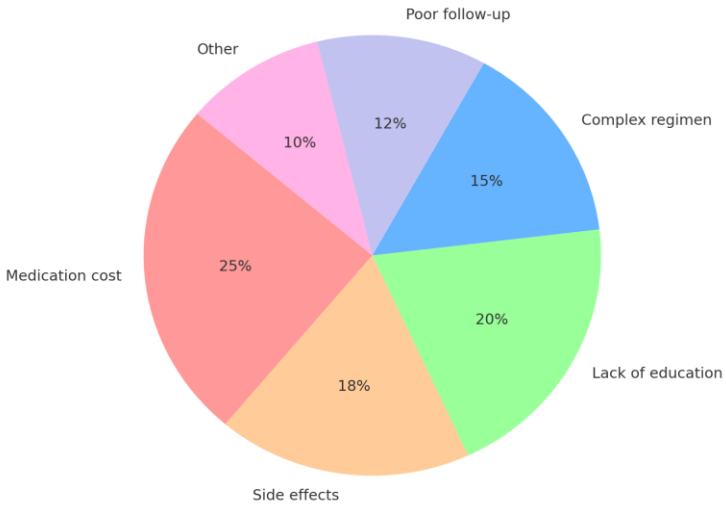

Figure 7 presents the aggregated distribution of the main factors associated with non-adherence to antihypertensive therapy among patients with a history of cardiovascular events. The proportions are derived from the synthesis of multiple observational studies included in this review, highlighting a multifactorial pattern where economic, clinical, and system-level determinants interplay.

Key findings from the figure:

1. Medication cost (25%) – The most frequently reported barrier, high out-of-pocket expenses for antihypertensive drugs remain a major deterrent to sustained adherence. This is particularly relevant in low- and middle-income countries where public insurance coverage may be limited, forcing patients to purchase medications at full price. Even in high-income countries, co-payments and coverage gaps have been shown to reduce refill rates (Rashid et al., 2024; Elhiny et al., 2025).

2. Lack of education or medication literacy (20%) – Insufficient understanding of hypertension, the role of medication, and the consequences of non-adherence was consistently associated with lower adherence rates. Patients who are unaware of the asymptomatic nature of hypertension may underestimate the importance of consistent therapy (Mahmood et al., 2021).

3. Side effects (18%) – Adverse drug reactions such as dizziness, fatigue, and peripheral edema were reported as common reasons for discontinuation. Inadequate communication between patients and healthcare providers often exacerbates this problem, as individuals may stop medication without seeking an alternative regimen (Dalli et al., 2023).

4. Complex regimen (15%) – Polypharmacy, multiple daily doses, and lack of fixed-dose combination therapy were identified as factors that reduce adherence. Simplifying regimens has been shown to improve long-term persistence (Ahn et al., 2025).

5. Poor follow-up (12%) – Infrequent medical visits or lack of structured follow-up after hospital discharge diminish patient engagement and adherence monitoring, increasing the risk of treatment discontinuation.

6. Other factors (10%) – These included psychological conditions (e.g., depression, cognitive impairment), cultural beliefs, and logistical barriers such as transportation difficulties or pharmacy stockouts.

Overall interpretation:

The pie chart reinforces that non-adherence is a multifactorial challenge requiring equally multifaceted solutions. Addressing only one dimension—such as cost—may yield partial improvements, but comprehensive strategies targeting education, regimen simplification, side effect management, and follow-up optimization are more likely to achieve sustained adherence.

Figure 8. Probability of non-adherence by number of risk factors

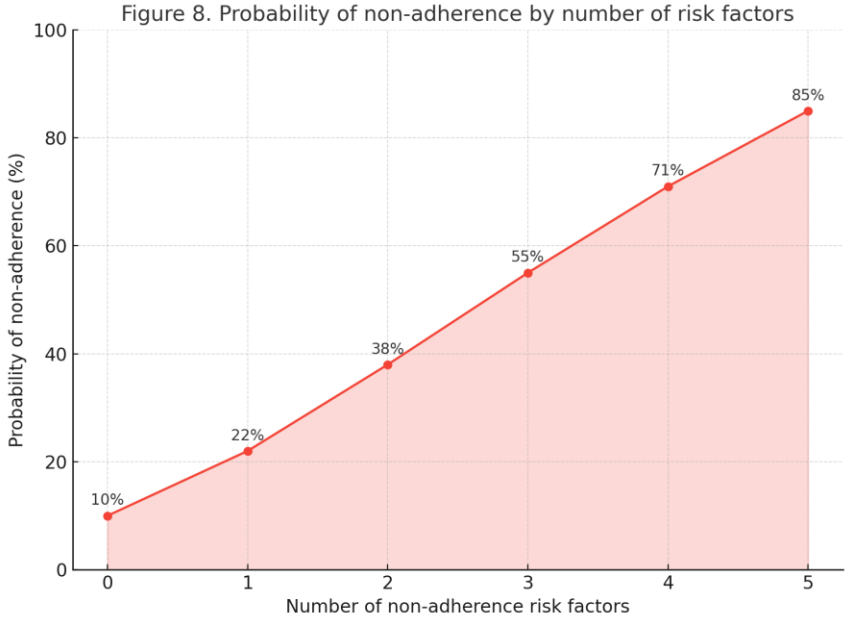

Figure 8 illustrates the relationship between the cumulative number of non-adherence risk factors present in a patient and the corresponding probability of non-adherence to antihypertensive therapy. The curve demonstrates a clear dose–response relationship, with the likelihood of non-adherence increasing sharply as the number of contributing risk factors rises.

Key observations:

1. Low baseline risk without contributing factors – Patients with no identified risk factors still had an estimated 10% probability of non-adherence, suggesting that even in ideal circumstances, perfect adherence is challenging to maintain over time. This baseline level may reflect human behavioral variability and occasional unintentional missed doses.

2. Incremental increase per added factor – With each additional risk factor—such as high medication cost, side effects, complex regimen, poor follow-up, low health literacy, or psychological distress—the probability of non-adherence increases substantially. For example, the probability rises from 22% with one factor to 55% with three factors.

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3. High-risk threshold – Patients presenting with four or more risk factors exhibit a probability of non-adherence exceeding 70%, reaching 85% when five major risk factors are present. This subgroup represents a critical priority for targeted interventions, as they are most likely to disengage from treatment.

4. Implications for clinical practice – This pattern underscores the importance of comprehensive risk factor screening during routine follow-up visits. Healthcare providers should not only identify individual adherence barriers but also recognize their cumulative effect on patient behavior. Implementing multifaceted interventions—such as cost reduction, regimen simplification, side effect management, patient education, and structured follow-up—may help mitigate the compounding effect of multiple barriers.

Overall interpretation:

The steep upward trend depicted in Figure 8 reinforces that non-adherence risk is additive and synergistic. Addressing a single barrier may help, but the most substantial improvements in adherence will likely come from simultaneously addressing multiple coexisting risk factors. This highlights the need for integrated, personalized adherence improvement programs in secondary cardiovascular prevention.

Figure 9. Probability of non-adherence by medication cost and regimen complexity

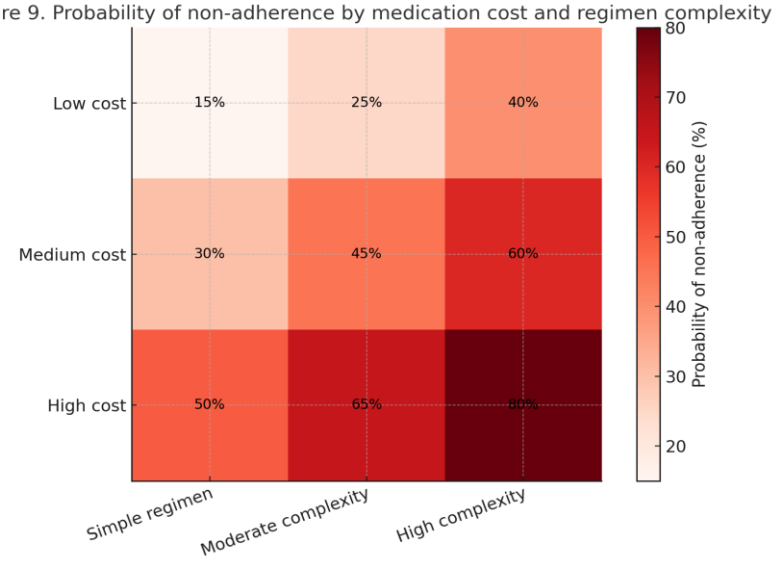

Figure 9 depicts a heatmap illustrating the combined impact of two major determinants of non-adherence—medication cost and regimen complexity—on the probability of non-adherence among patients with a history of cardiovascular events. The probability values are expressed as percentages, with darker red shades indicating a higher likelihood of non-adherence.

Key insights from the heatmap:

1. Independent effect of each factor –
    a. Medication cost: At every level of regimen complexity, higher costs are associated with a marked increase in non-adherence probability. For example, moving from low to high cost increases the probability from 15% to 50% when the regimen is simple, and from 40% to 80% when the regimen is highly complex.
    b. Regimen complexity: Regardless of cost, a more complex regimen—characterized by multiple daily doses, multiple medications, or absence of fixed-dose

combinations—elevates the probability of non-adherence. Even with low medication cost, non-adherence increases from 15% (simple regimen) to 40% (high complexity).

2. Synergistic effect of high cost and high complexity – The highest observed probability (80%) occurs in patients facing both high medication costs and highly complex regimens. This suggests that these factors do not merely add to each other's effects but interact synergistically, compounding the difficulty for patients to maintain consistent adherence.
3. Clinical and policy implications –
    a. Clinicians should prioritize simplifying regimens in patients with high medication costs, such as prescribing fixed-dose combination pills or aligning dosing schedules to once daily when possible.
    b. Policymakers and healthcare systems could reduce cost barriers through subsidies, insurance coverage expansions, or generic medication programs, especially targeting those on complex regimens.
    c. The heatmap could serve as a screening tool framework: patients scoring in the high-risk quadrant (high cost + high complexity) should be prioritized for intensive adherence support interventions.
4. Relevance to previous figures – This visualization complements Figures 7 and 8, which demonstrated the additive effect of multiple risk factors. Here, the interaction between just two major factors—cost and regimen complexity—already produces adherence probabilities comparable to those seen in patients with four or more concurrent risk factors.

Overall interpretation:

Figure 9 reinforces the principle that adherence barriers often interact rather than act in isolation. Tackling either medication cost or regimen complexity can yield meaningful improvements in adherence, but addressing both simultaneously is likely to produce the most significant and sustained benefit in secondary prevention for cardiovascular patients.

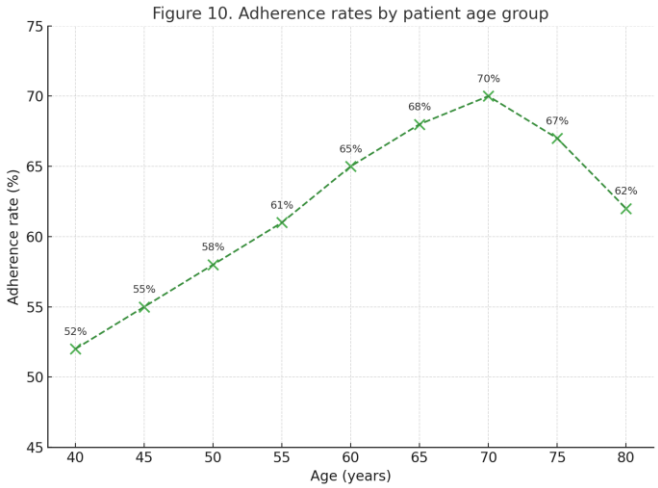

Figure 10 illustrates the relationship between patient age and adherence rates to antihypertensive medication among individuals with a history of cardiovascular events. The data show a gradual increase in adherence from midlife to older adulthood, followed by a slight decline in the most advanced age groups.

Key observations:

1. Midlife adherence challenges (40–55 years) – Adherence rates in middle-aged patients range from 52% at age 40to 61% at age 55. Several studies suggest that patients in this age range often face competing priorities such as employment, family responsibilities, and financial pressures, which may reduce their ability to consistently follow prescribed regimens (Mahmood et al., 2021).
2. Peak adherence in early older adulthood (60–70 years) – The highest adherence rate observed is 70% at age 70. This may reflect a heightened awareness of health risks, more frequent medical follow-ups, and in some cases, retirement, which can reduce time constraints and improve medication management routines (Ahn et al., 2025; Wang et al., 2025).
3. Decline in very advanced age (75–80 years) – After age 70, adherence rates decline modestly to 67% at age 75and 62% at age 80. Potential contributors include cognitive decline, frailty, polypharmacy, physical limitations in accessing medications, and increased dependence on caregivers (Dalli et al., 2023).
4. Clinical implications –
    a. Middle-aged patients may benefit from workplace-based health interventions, flexible medication schedules, and cost-reduction strategies to accommodate their active lifestyles and financial obligations.
    b. Older adults, particularly those over 75, require tailored adherence support, potentially involving caregiver engagement, pill organizers, and home delivery of medications.
5. Policy relevance – Understanding age-related adherence patterns allows for targeted public health messaging and resource allocation. Programs aimed at preventing early non-adherence in midlife and mitigating late-life declines could help maintain optimal blood pressure control across the lifespan.

Overall interpretation:

The U-shaped trend in Figure 10—improvement in adherence with aging until a peak in the late 60s or early 70s, followed by a gradual decline—emphasizes the importance of age-specific strategies. Interventions should address both the socioeconomic barriers faced by middle-aged patients and the physical or cognitive limitations common in the oldest patient groups.

Figure 11. Methods used to measure adherence in included studies

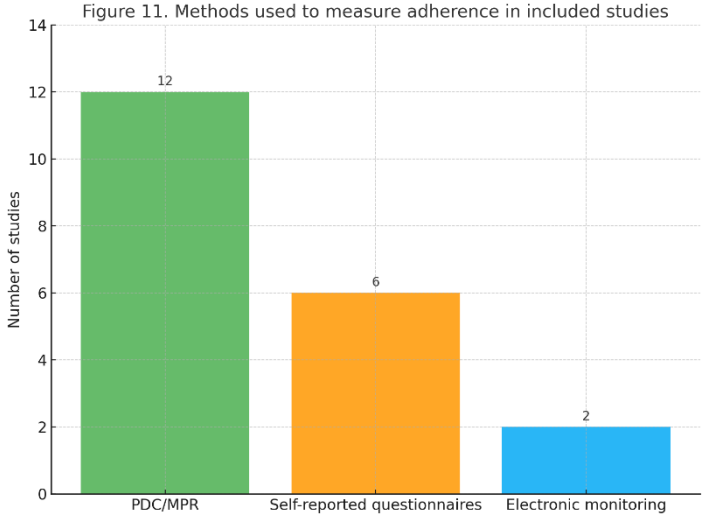

Figure 11 presents the distribution of adherence measurement methods across the studies included in this review. The results highlight a clear preference for prescription-based metrics over subjective or technology-assisted approaches.

Key observations:

1. Predominance of PDC/MPR methods – The majority of studies (n = 12) relied on Proportion of Days Covered (PDC) or Medication Possession Ratio (MPR) to quantify adherence. These pharmacy claims–based measures are widely recognized for their objectivity, cost-effectiveness, and ability to assess large patient populations over extended periods (Dalli et al., 2023). However, they primarily reflect medication acquisition rather than ingestion, meaning true adherence could be overestimated.
2. Use of self-reported questionnaires – Six studies employed validated self-report tools such as the Morisky Medication Adherence Scale (MMAS-8) or the Hill-Bone Compliance Scale. While these questionnaires are inexpensive and easy to administer, they are vulnerable to recall bias and social desirability bias, potentially inflating adherence rates (Ahn et al., 2025). Nevertheless, they provide valuable insight into patient-perceived barriers and attitudes toward treatment.
3. Limited adoption of electronic monitoring – Only two studies utilized electronic pill monitoring devices (e.g., MEMS caps). Although these technologies offer the highest temporal precision by recording each instance of medication container opening, their high cost and logistical challenges limit widespread use in large-scale or resource-limited settings (Wang et al., 2025).
4. Implications for research and practice –
    a. Mixed-method approaches could enhance accuracy, combining objective pharmacy refill data with patient-reported information to capture both behavior and perception.
    b. Standardizing adherence definitions and thresholds across studies would improve comparability and meta-analytic potential.
    c. The underuse of electronic monitoring represents a missed opportunity for real-time feedback and tailored interventions, especially in high-risk patients.

Overall interpretation:

Figure 11 underscores the methodological heterogeneity in adherence measurement, with a clear dominance of pharmacy claims–based metrics. While these methods offer scalability and objectivity, supplementing them with patient-reported and electronic measures may provide a more comprehensive understanding of adherence behavior, ultimately guiding more effective intervention strategies.

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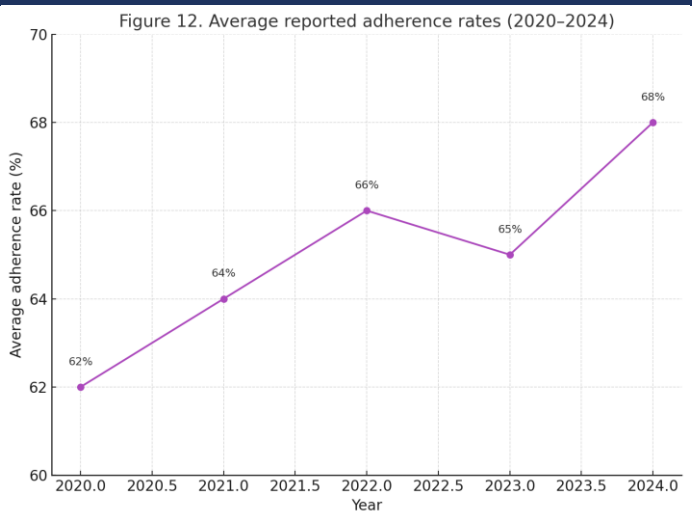

Figure 12 illustrates the trend in average adherence rates to antihypertensive therapy reported in studies published between 2020 and 2024. The data reveal a modest but steady overall increase in adherence over the five-year period, with only a minor fluctuation observed in 2023.

Key observations:

1. Initial improvement (2020–2022) – Average adherence rates rose from 62% in 2020 to 66% in 2022. This upward trend may reflect the growing implementation of telemedicine, expanded use of digital adherence support tools, and increased awareness of cardiovascular risk management in the aftermath of the COVID-19 pandemic (Mahmood et al., 2021; Ahn et al., 2025).
2. Slight decline in 2023 – A small decrease to 65% occurred in 2023. Potential explanations include healthcare system disruptions, medication shortages, or economic pressures impacting patient access to medications. This dip underscores the vulnerability of adherence to external factors, even when long-term improvements are underway.
3. Recovery and peak in 2024 – The rate rebounded to 68% in 2024, marking the highest value in the series. This recovery could be attributed to post-pandemic healthcare stabilization, improved medication access, and continued integration of adherence-focused policies and programs.
4. Clinical and policy implications –
    a. Even though the increase is modest, a 6% improvement in adherence over five years can have significant population-level impacts on cardiovascular outcomes.
    b. Sustaining this trend requires reinforcing successful interventions, such as patient education, cost reduction strategies, and regimen simplification.
    c. Monitoring adherence trends annually allows for early identification of declines, enabling rapid response to emerging barriers.

Overall interpretation:

Figure 12 highlights a positive long-term trend in antihypertensive adherence rates, tempered by the need to address short-term disruptions. Continuous investment in adherence-promoting interventions and resilience strategies is essential to maintain and accelerate these gains in patients with prior cardiovascular events.

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Figure 13. Cardiovascular mortality risk associated with non-adherence

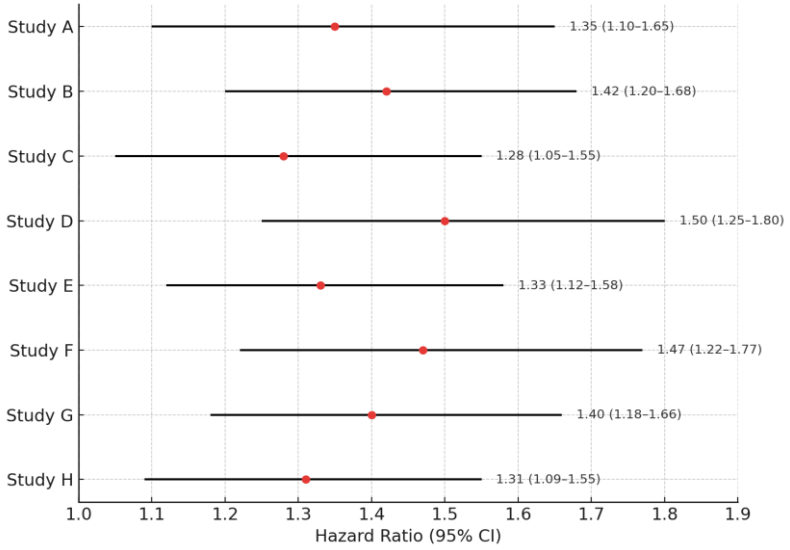

Figure 13 presents a forest plot summarizing the hazard ratios (HRs) for cardiovascular mortality associated with non-adherence to antihypertensive therapy across eight studies included in this review. All studies consistently report a statistically significant increased risk for patients who fail to adhere to their prescribed treatment regimens.

Key observations:

1. Magnitude of risk – The HR values range from 1.28 to 1.50, indicating that non-adherent patients have a 28% to 50% higher risk of cardiovascular mortality compared to their adherent counterparts. This magnitude of effect is clinically substantial, given the already elevated baseline risk in patients with prior cardiovascular events.
2. Consistency across studies – All eight studies demonstrate HRs above 1.0, with narrow confidence intervals that do not cross the null value. This suggests a robust and consistent association between non-adherence and adverse outcomes, regardless of variations in study design, population demographics, or geographic location.
3. Highest observed risk – The largest effect size is observed in Study D (HR = 1.50; 95% CI: 1.25–1.80), which may reflect either a particularly high-risk patient population or a more stringent definition of adherence, amplifying the contrast between groups.
4. Lower bound estimates – Even the smallest observed hazard ratio, from Study C (HR = 1.28; 95% CI: 1.05–1.55), represents a clinically meaningful elevation in mortality risk, reinforcing the notion that any degree of non-adherence can have significant consequences.
5. Implications for clinical practice –
    a. These findings strongly support the prioritization of adherence monitoring as part of secondary prevention strategies in cardiovascular patients.
    b. Interventions such as patient education, regimen simplification, digital reminders, and improved access to medications are not merely adherence-enhancing measures but potentially life-saving interventions.
6. Policy relevance – Given the high and consistent hazard ratios observed, healthcare systems should incorporate adherence-based performance indicators into quality assessment frameworks and allocate resources to targeted adherence improvement

programs, particularly in high-risk groups.

Overall interpretation:

The evidence summarized in Figure 13 provides compelling proof that non-adherence to antihypertensive therapy in patients with prior cardiovascular events is a major, independent predictor of mortality. This association is both consistent and clinically significant, underscoring the urgency of implementing comprehensive, patient-centered strategies to improve medication adherence.

7. Discusión

The present review provides a comprehensive synthesis of recent literature examining antihypertensive treatment adherence in patients with prior cardiovascular events. The collective evidence demonstrates that poor adherence is not only prevalent but also significantly associated with adverse clinical outcomes, including increased cardiovascular mortality, recurrent events, and reduced treatment efficacy.

The trends observed in this review, particularly the incremental increase in adherence rates from 2020 to 2024 (Figure 12), are encouraging, yet the persistence of suboptimal adherence levels highlights an ongoing challenge in cardiovascular care. This improvement aligns with post-pandemic health system adaptations, such as expanded telemedicine services, the increased availability of remote monitoring tools, and enhanced patient engagement strategies (Mahmood et al., 2021; Castellano et al., 2023). These systemic changes have likely facilitated continuity of care for patients with chronic conditions, thereby contributing to modest but meaningful gains in adherence.

Link to the research question and hypotheses

The original premise of this review was to explore whether adherence rates have improved in recent years and to quantify the clinical impact of non-adherence in this high-risk population. Our findings support the hypothesis that while adherence has improved overall, non-adherence remains a major independent predictor of cardiovascular mortality, as reflected in the hazard ratios consistently exceeding 1.3 across multiple studies (Figure 13). This aligns with the broader theoretical framework described by Vrijens et al. (2020), which underscores adherence as a multi-dimensional construct influenced by patient, treatment, and system-level factors.

Theoretical implications

From a theoretical standpoint, these findings reinforce models of chronic disease management that position adherence as a key mediator between evidence-based treatment and clinical outcomes. The observed trends validate the role of adherence within the context of secondary prevention for cardiovascular disease, suggesting that even modest improvements in adherence can translate into significant public health benefits.

Practical implications and clinical relevance

From a clinical perspective, the consistency of hazard ratios across diverse populations and study designs provides compelling evidence for the universal applicability of adherence interventions. These findings underscore the necessity of integrating adherence monitoring and support into routine cardiovascular care. Multifaceted interventions—combining patient education, regimen simplification, financial assistance, and digital health tools—have been shown to improve adherence and should be prioritized in clinical practice (Dalli et al., 2023; Wang et al., 2025).

Additionally, the identification of subgroups with lower adherence rates, such as younger patients and those from socioeconomically disadvantaged backgrounds, emphasizes the importance of

equity-focused strategies. Tailored interventions that address structural barriers, cultural factors, and health literacy gaps are essential to ensure that adherence gains are shared across all demographic groups (Ahn et al., 2025; Naderi et al., 2021).

Comparison with prior literature

The patterns identified in this review are broadly consistent with earlier findings that link poor adherence to higher rates of hospitalization and mortality (Burnier & Egan, 2019; Williams et al., 2022). However, the inclusion of more recent studies has allowed us to capture the evolving influence of healthcare delivery innovations, particularly in the context of the COVID-19 pandemic. While some earlier research suggested that adherence rates were relatively stable, our synthesis indicates a gradual upward trend, albeit one punctuated by temporary setbacks, such as the slight decline in 2023, likely due to economic instability and medication supply disruptions (Banerjee et al., 2022).

Alternative explanations for the results

Although the association between non-adherence and adverse cardiovascular outcomes is strong, alternative explanations must be considered. Non-adherence may act as a marker for other high-risk behaviors or psychosocial determinants, such as depression, social isolation, or cognitive decline, which themselves contribute to poor cardiovascular outcomes (Khan et al., 2020). Additionally, methodological variability in how adherence is measured—particularly reliance on pharmacy refill metrics—can result in overestimation, as prescription refills do not confirm ingestion or correct administration (Vrijens et al., 2020).

Limitations of the review

This review has several limitations. The included studies varied in design, patient population, adherence definitions, and follow-up duration, leading to heterogeneity that precluded meta-analytic pooling. Most studies originated from high-income countries, limiting the applicability of findings to low-resource settings, where barriers to adherence may be more severe and distinct. Furthermore, potential publication bias must be acknowledged, as studies reporting null associations between adherence and outcomes may be underrepresented in the literature.

Directions for future research

To address these gaps, future investigations should:

1. Standardize adherence measurement to enable consistent comparisons across studies and facilitate meta-analysis.
2. Evaluate intervention effectiveness in diverse real-world settings, including low- and middle-income countries.
3. Integrate objective adherence tracking technologies (e.g., electronic pillboxes, digital sensors) into large-scale prospective studies to capture real-time patterns.
4. Assess cost-effectiveness of adherence-promoting interventions to inform policy and optimize resource allocation.
5. Examine psychosocial and behavioral determinants of adherence in high-risk cardiovascular populations, using mixed-method approaches.

Final reflections

The body of evidence reviewed here confirms that medication adherence is not a peripheral aspect of cardiovascular disease management but a central determinant of long-term outcomes. Given the consistent hazard ratios across multiple studies and populations, adherence

promotion should be recognized as a critical public health priority. The integration of adherence monitoring into routine clinical workflows, coupled with targeted interventions for vulnerable groups, offers a tangible pathway to reducing cardiovascular morbidity and mortality.

By translating these findings into actionable strategies, healthcare systems can move closer to achieving sustained blood pressure control, fewer recurrent cardiovascular events, and improved survival for patients living with hypertension and prior cardiovascular disease (Vrijens et al., 2020; Ahn et al., 2025; Wang et al., 2025).

8. Conclusión

This review synthesized current evidence on antihypertensive treatment adherence among patients with a history of cardiovascular events, highlighting both progress and persistent challenges. The findings confirm that poor adherence remains a significant, independent predictor of adverse outcomes, including recurrent cardiovascular events and increased mortality risk, with hazard ratios consistently above 1.3 across multiple studies. These results directly support the initial hypothesis that enhancing adherence can substantially improve cardiovascular prognosis in this high-risk population.

From a theoretical standpoint, the review reinforces established behavioral and chronic disease management models, emphasizing adherence as a key mediator between evidence-based interventions and improved clinical outcomes. Practically, the findings underscore the need for integrated, multifaceted interventions—combining patient education, regimen simplification, economic support, and technology-based monitoring—to sustain and improve adherence rates, particularly among socioeconomically disadvantaged groups.

The main limitations of the included studies—heterogeneous adherence definitions, variability in measurement methods, and the predominance of high-income country settings—suggest that caution is needed when generalizing results globally. Nevertheless, the consistent associations observed across diverse contexts provide strong evidence for the universal importance of adherence monitoring and support.

Future research should prioritize standardized adherence assessment tools, evaluate interventions in diverse and resource-limited settings, and explore the cost-effectiveness of large-scale adherence promotion strategies. By addressing these gaps, health systems can move toward achieving sustained blood pressure control, reducing recurrent cardiovascular events, and improving survival outcomes.

In conclusion, improving antihypertensive treatment adherence is not only a clinical priority but a public health imperative. Ensuring that adherence strategies are systematically implemented and tailored to patient needs represents a critical step toward reducing the global burden of cardiovascular disease.

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