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The link between adherence to antihypertensive medications and mortality rates in patients with hypertension: a systematic review and meta-analysis of cohort studies

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Abstract

Background Hypertension (HTN) significantly contributes to cardiovascular disease (CVD) and mortality. This systematic review and meta-analysis specifically investigates how different levels of adherence to antihypertensive therapy (AHT) affect mortality rates in HTN patients. By synthesizing cohort studies, it aims to enhance understanding and inform clinical practices to improve outcomes in hypertensive populations.

Methods Our meta-analysis employed a comprehensive search strategy using keywords related to hypertension, medical adherence, and mortality across PubMed, Scopus, and Web of Science, up to July 2024. The eligibility criteria focused on cohort studies linking AHT adherence to mortality. The Newcastle–Ottawa Scale (NOS) was used to assess the risk of bias (ROB). Quantitative analyses involved hazard ratios (HR) and confidence intervals (CI), with an 80% adherence threshold. Subgroup and meta-regression analyses were also conducted using STATA-17 to explore various outcome factors.

Results From initial 1,999 studies 12 cohort studies included in our analysis. All included studies had low ROB score. A meta-analysis of 12 studies involving 2,198,311 patient with HTN revealed that poor adherence to treatment significantly increased all-cause mortality (HR: 1.32 [1.14, 1.51], $p < 0.001$) with high heterogeneity (I^2: 98.73%). Additionally, an analysis of four studies with 1,695,872 patients indicated that low adherence was linked to elevated cardiovascular mortality (HR: 1.61 [1.43, 1.78], $p < 0.001$), showing moderate heterogeneity (I^2: 49.51%).

Conclusions The study found that poor adherence to AHT significantly increases overall and cardiovascular mortality risk, underscoring the need for improved compliance strategies. Limitations like inconsistent definitions, observational biases, and varying follow-up durations necessitate further research to validate these findings.

Clinical trial number Not applicable.

Keywords Antihypertensive medications, Adherence, Mortality rates, Hypertension, Cohort

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Introduction

Hypertension (HTN) remains a leading global health issue, contributing significantly to morbidity and mortality rates worldwide. In 2019 it is estimated that high blood pressure accounts for over 0.85 million deaths and 14.56 million disability-adjusted life-years annually [1]. Medication adherence is defined as the degree to which patients follow their prescribed medication regimens [2]. Despite hypertension being one of the most prevalent chronic conditions and a significant global health threat, medication nonadherence among patient with HTN remains alarmingly high [3]. Research indicates that nearly 50% of patients discontinue antihypertensive medications within the first year, complicating global blood pressure management. Less than one-third of patients in high-income countries and only one-tenth in low- and middle-income nations achieve optimal blood pressure, contributing to rising cardiovascular diseases and mortality worldwide [4–6].

Clinical trials have shown that consistent use of antihypertensive medications (AHM) successfully lowers blood pressure in many patients, resulting in substantial reductions in cardiovascular-related morbidity and mortality [7]. Cardiovascular diseases (CVDs) represent a significant global health challenge, with the Global Burden of Disease Study indicating that over 485.6 million individuals were affected by these conditions in 2017. CVDs are also the leading cause of death worldwide, responsible for more than 17.79 million fatalities, which accounts for 31.8% of all deaths globally. This alarming prevalence underscores the urgent need for effective strategies to mitigate the incidence of CVD events [8–10].

In contrast, nonadherence to medication, which refers to the extent that patients do not follow their healthcare provider's recommendations regarding medication use, hinders the effectiveness of treatments aimed at managing cardiovascular risks [11, 12]. The World Health Organization (WHO) identifies various factors contributing to nonadherence, including socioeconomic aspects like age, gender, and education; patient-specific traits such as willingness to change and self-confidence; treatment complexities; coexisting health conditions; and healthcare system challenges like doctor-patient relationships and physician burnout [13, 14].

AHT markedly decreases the morbidity and mortality associated with cardiovascular disease, as evidenced by various randomized controlled trials (RCTs) [15–17]. Following AHT guidelines significantly lowers the risk of mortality; in contrast, nonadherence increases all-cause mortality by 1.57 times and the likelihood of cardiovascular hospitalization by 1.25 times [18]. Furthermore, a recent investigation revealed that each percentage point rise in adherence is linked to a decrease of approximately 7.13 cardiovascular deaths per 100,000 individuals [19]. Many studies have found that adherence to AHT reduces both all-cause mortality and CVD mortality among patient with HTN [20, 21]. However, the relationship between adherence to AHT and mortality is complex; some research presents neutral findings, suggesting a need for further investigation [22, 23]. High adherence to AHT leads to better health outcomes, significantly reducing complications like stroke and heart failure, with intervention adherence rates reaching 98.63% versus 49.14% in controls [24].

This systematic review and meta-analysis is the first to explore how sticking to AHT affects mortality rates in patients with HTN. By looking at various cohort studies, the research aims to fill important knowledge gaps and provide valuable insights for better managing HTN. A more specific focus on how AHT adherence influences overall and CVD mortality could clarify these relationships. Ultimately, this work seeks to enhance patient outcomes by improving adherence strategies in clinical practice.

Methods

This systematic review and meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines 2020 [25] (its checklist in Supplementary Material 1). The registration number in PROSPERO is CRD42024592893.

Search strategy

The final search keywords comprised three primary terms: Hypertension, Medical Adherence, and Mortality (Search using AND for every three main terms, and use OR for synonyms within each main term). All relevant synonyms and MESH terms were utilized to develop the most effective search strategy. Three databases—PubMed, Scopus, and Web of Science— were searched for English-language records until July 2024 without any restrictions based on time or age. Additionally, grey literature was explored through manual searches on Google Scholar and by reviewing the references of all included studies (detailed search information for the databases can be found in Supplementary Material 1).

Eligibility criteria

We conducted a systematic review and meta-analysis of cohort studies that investigated the relationship between adherence to antihypertensive therapy (AHT) and mortality rates among individuals diagnosed with hypertension. The primary exposure of interest was the consumption of antihypertensive medications, while the outcomes were all-cause mortality and cardiovascular (CV) mortality. Studies were excluded from the analysis if they lacked sufficient data (absence of the report detailing the effect size in a format suitable for analysis

extraction) for statistical evaluation or employed study designs other than cohort studies.

Study selection and data extraction

Two researchers independently reviewed the titles and abstracts of potentially relevant studies to determine eligibility. For the studies that passed this initial screening, different researchers separately assessed the full texts. Any disagreements about study design, methodology, or the final decision to include a study were resolved through a consensus meeting involving all the review authors. The same two original researchers then independently extracted data from the selected articles. They collected the following general characteristics for each study: Author, Country, Number of Participants, Percentage of Male, Medical Adherence Tool Used, Condition (Hypertension), Follow-up Duration (in years), and NOS Score (presented in Table 1).

Risk of bias (ROB) assessment

Two investigators independently conducted a quality assessment using the Newcastle–Ottawa Quality Scale (NOS) to evaluate the risk of bias (ROB) in the included cohort studies [26], which were classified as having a low (≥7 stars), moderate (5–6 stars), or high ROB score (≤4 stars), with an overall quality score of 9 stars; any discrepancies were resolved through discussion and consensus, including a third investigator if needed.

Quantitative analysis

To determine the final effect size, we utilized hazard ratio (HR) and standard error (SE) statistics. To standardize the HR reported in the studies, we classified medical adherence as good if it was over 80% and poor if it was below that threshold; in some studies, the groups with poor adherence were combined. A random effects model, specifically the restricted maximum likelihood model, was employed to aggregate the extracted HR values. We assessed heterogeneity among the studies using the chi-square test and the I-squared statistic. Publication bias was evaluated through Begg and Egger tests, along with a funnel plot. Additionally, a sensitivity analysis was conducted to examine the reliability of the pooled effect size. A subgroup analysis was carried out to estimate the pooled effect based on factors such as nationality, total population, mean age, percentage of males, assessment tool, diagnosis, and follow-up duration. Meta-regression was performed considering the publication year, mean age, percentage of males, and follow-up duration. All analyses were conducted using Stata-17 software, with p-values below 0.05 deemed statistically significant.

Results

Study selection

From an initial set of 1,999 records retrieved from databases, 793 duplicate records were removed. Of the remaining 1,206 records, 1,133 were excluded based on title and abstract screening. After full-text review of 73 articles, 12 studies [7, 12, 18, 20, 21, 23, 27–31] were ultimately included in the analysis (Fig. 1).

Characteristics of studies

In total thirteen cohort studies with total 2,198,311 HTN patients included in our studies. The studies involved a wide range of participants, from as few as 2,199 in Canada to over 1.6 million in South Korea. The percentage of male participants varied significantly, with the highest at 91.4% in a US study by Gosmanova et al. and the lowest at 45.1% in a study from Hong Kong by Wong et al. Different tools were employed to assess adherence, including the Proportion of Days Covered (PDC), Medication Possession Ratio (MPR), and Visual Analog Scale (VAS). The most commonly used tool across studies was PDC, utilized in six out of the ten studies. The studies differentiated between newly treated and older patients. Most studies focused on newly treated patients, with only three studies examining old HTN patients. Follow-up periods

Table 1 Overall characteristics of all included studies

Author	Country	Participants (*N*)	Male (%)	Medical adherence tool	Condition (cvd)	Follow up (year)	NOS
Esposti et al. 2011 [7]	Italy	31,306	48	PDC	Newly treated	1.9	8/Low
Gosmanova et al. 2014 [27]	US	18,822	91.4	PDC	Newly treated	3.8	8/Low
Ibrahim et al. 2023 [12]	US	9,278	64.4	VAS	Old	3.8	7/Low
Jung et al. 2023 a [20]	South Korea	19,246	62.4	MPR	Old	8.4	8/Low
Jung et al. 2023 b [21]	South Korea	4,226	52.6	PDC	Old	8.2	8/Low
Kim et al. 2016 [28]	South Korea	33,728	46.6	CMA	Newly treated	5	8/Low
Kim et al. 2021 [29]	South Korea	20,836	47.4	PDC	Newly treated	9.6	8/Low
Lee et al. 2019 [30]	South Korea	1,651,564	52.5	MPR	Newly treated	10	8/Low
Liu et al. 2014 [22]	China	148,651	46	PDC	Newly treated	6.18	7/Low
Shin et al. 2013 [18]	South Korea	40,408	50.3	MPR	Newly treated	1	8/Low
Tang et al. 2017 [23]	Canada	2,199	45.4	PDC	Newly treated	4	7/Low
Wong et al. 2013 [31]	Hong Kong	218,047	45.1	PDC	Newly treated	5	7/Low

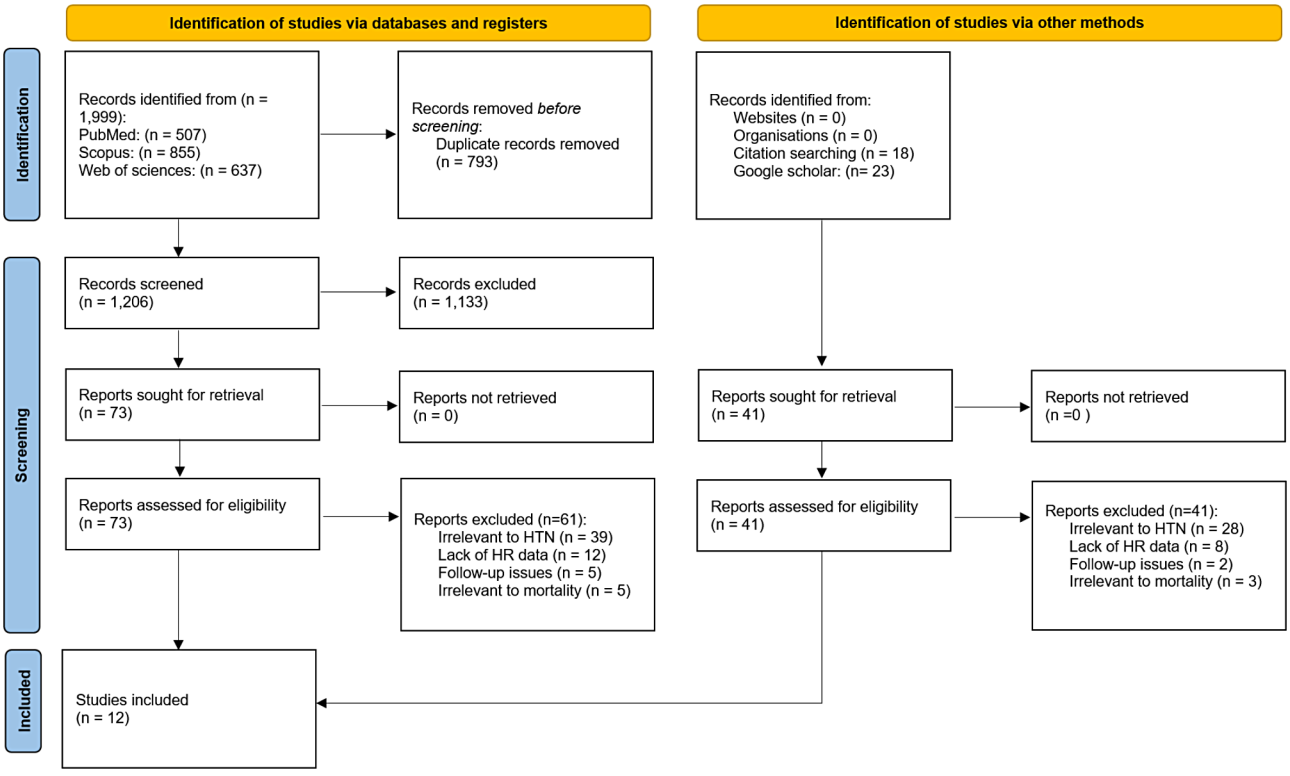

Fig. 1 PRISMA flow diagram of all included studies

varied, ranging from 1 year (Shin et al. 2013) to 10 years (Lee et al. 2019) (Table 1).

ROB

All studies were assessed as having low ROB. Ten of the studies achieved a NOS score of eight, indicating a low risk of bias. Additionally, two other studies also received the same NOS score of seven (Table 1).

Synthesis of results

All-cause mortality

In a meta-analysis of all-cause mortality related to adherence, 12 studies encompassing 15 effect sizes and a total of 2,198,311 patients with hypertension were examined. The findings indicated that poor adherence was linked to an increased mortality rate (HR: 1.32 [1.14, 1.51], $p < 0.001$), exhibiting considerable heterogeneity (I^2: 98.73%) (Fig. 2). A sensitivity analysis revealed that excluding any individual study did not significantly alter the overall effect size. Additionally, funnel plots and the Egger ($p = 0.95$) and Begg ($p = 0.10$) tests indicated no evidence of publication bias (Fig. 3).

A subgroup meta-analysis was conducted based on various factors including nationality, total population, mean age, percentage of males, assessment tools, diagnosis, and follow-up duration. Most subgroups showed non-significant results, with the exception of the diagnosis category. The analysis indicated that newly treated patients had a lower hazard ratio (HR: 1.22 [1.07, 1.37]) compared to those who had been on antihypertensive medication for a longer time (HR: 1.75 [1.33, 2.18]) ($p = 0.02$), as detailed in Fig. 4. Furthermore, a meta-regression analysis was performed considering publication year, mean age, percentage of males, and follow-up duration. All factors were found to be non-significant, except for the publication year, which positively influenced the hazard ratio (0.049) with statistical significance ($p = 0.012$) and a 95% confidence interval of (0.011, 0.088) (see Table 2; Fig. 5).

CV mortality

In a thorough examination of CV mortality associated with adherence, four studies were analyzed, which included four effect sizes and a total of 1,695,872 patients with hypertension. The results showed that low adherence was associated with a higher rate of CV mortality (HR: 1.61 [1.43, 1.78], $p < 0.001$), with moderate heterogeneity observed (I^2: 49.51%) (Fig. 6). A sensitivity analysis demonstrated that removing any single study did not significantly impact the overall effect size. Furthermore, funnel plots along with the Egger ($p = 0.44$) and Begg ($p = 0.73$) tests indicated no signs of publication bias (Fig. 7).

A subgroup meta-analysis was conducted based on various factors including total population, mean age,

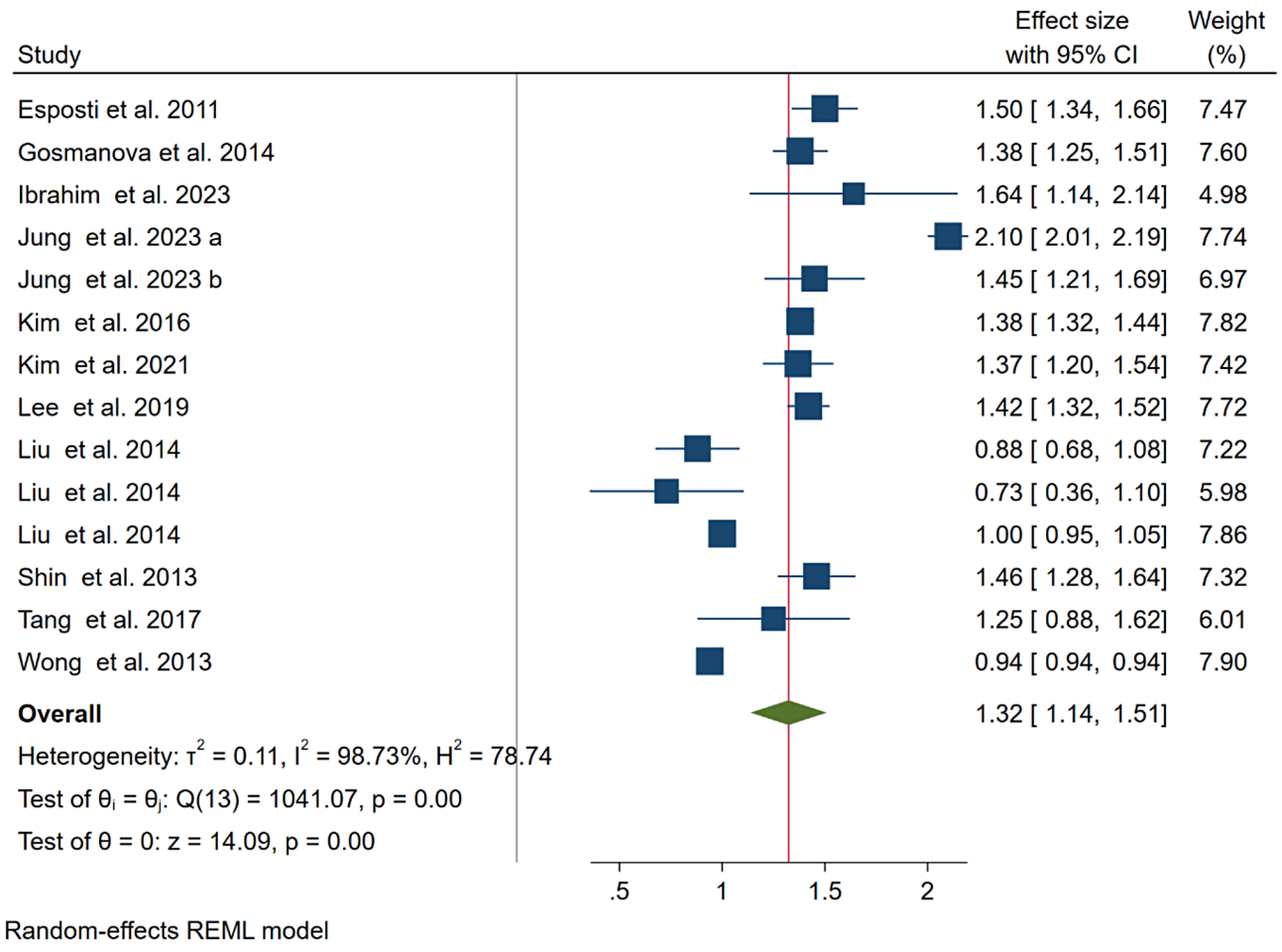

Fig. 2 Meta-analysis of the all-cause mortality related to adherence to antihypertensive medication in patient with HTN

percentage of males, assessment tools, and diagnosis. Most subgroups showed non-significant results, with the exception of the diagnosis category. The analysis indicated that newly treated patients had a lower hazard ratio (HR: 1.53 [1.49, 1.57]) compared to those who had been on antihypertensive medication for a longer time (HR: 1.80 [1.57, 2.03]) ($p = 0.02$), as detailed in Fig. 8.

Discussion

This systematic review and meta-analysis provide strong evidence linking AHT with mortality rates in patients with HTN. Analysing 12 studies involving over 2 million patients, the results indicated that poor adherence is significantly associated with an higher risk of all-cause mortality, reflected by a HR of 1.32. This discovery highlights the essential importance of AHT in successfully managing hypertension, as nonadherence not only jeopardizes blood pressure regulation but is also linked to a higher risk of CV complications and increased mortality. The considerable heterogeneity observed across studies suggests variability in patient populations, adherence measurement methods, and follow-up durations, warranting further investigation into these factors. The subgroup analysis showed that patients on long-term AHT had a higher mortality risk (HR: 1.75) compared to newly treated patients (HR: 1.22), likely due to the cumulative effects of poor adherence and worsening complications over time. Newly treated patients may have better adherence initially due to closer follow-up or motivation. The meta-regression further indicated that the adverse effects of poor adherence have intensified in more recent years.

In terms of CV mortality, the analysis of four studies [20, 21, 29, 30] with nearly 1.7 million patients revealed that low adherence correlates with a significantly higher rate of CV mortality (HR: 1.61). The subgroup analysis for CV mortality mirrored the results seen in all-cause mortality, with newly treated patients having a lower hazard ratio (HR: 1.53) compared to those on longer-term treatment (HR: 1.80). This finding underscores the urgency of addressing non-adherence early in the treatment course to prevent the compounding risks associated with chronic hypertension and its complications.

Overall, this study underscores the necessity of enhancing medication adherence to improve health outcomes

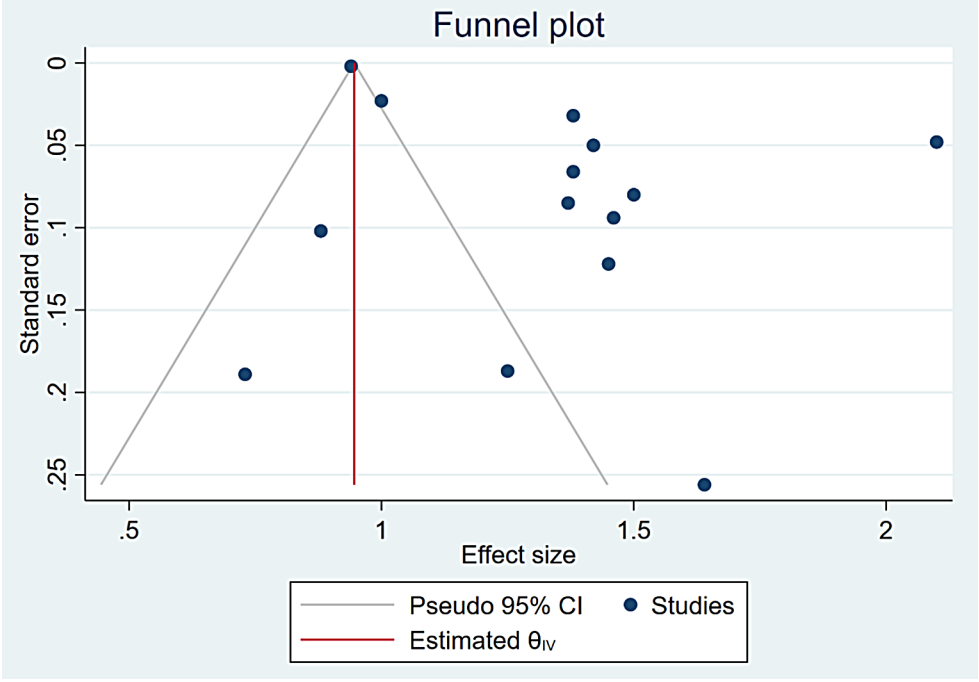

Fig. 3 Funnel plot of the all-cause mortality related to adherence to antihypertensive medication in patient with HTN

and reduce mortality rates among patient with HTN. Our meta-regression analysis revealed that while several factors such as total population size and mean age were non-significant, the year of publication positively influenced the hazard ratio ($p = 0.012$). This suggests that recent advancements in hypertension management and increased awareness of the importance of medication adherence may have contributed to improved outcomes over time.

Following antihypertensive therapy can look very different depending on cultural backgrounds and healthcare systems. Factors like cultural beliefs, understanding of health, and communication between patients and providers greatly affect how well people stick to their medication. In diverse places like Singapore, language barriers and cultural views on medicine can create challenges [32]. Additionally, research shows that ethnic minorities, especially Black patients, tend to struggle with sticking to their treatment plans. This often stems from limited understanding of their condition and poor communication with healthcare providers [33]. Effective antihypertensive therapy is essential for managing hypertension and preventing cardiovascular diseases, making cultural competence in healthcare delivery vital for improving patient outcomes [34, 35].

Current guidelines recommend a target office blood pressure of less than 140/90 mm Hg for treatment, irrespective of cardiovascular risk or comorbidities. Recent meta-analyses indicate that a 10 mm Hg reduction in systolic blood pressure significantly lowers the risk of major cardiovascular events [16, 36]. However, studies by Benegas JR et al. and Chow CK et al. reveal that fewer than 50% of patients reach the target systolic blood pressure of < 140 mm Hg [37, 38].

Non-adherence to medication is a significant factor in the failure to manage hypertension effectively within the general population. Identifying and assessing non-adherence in clinical settings poses challenges [39]. Methods used to address this issue typically rely on indirect indicators, such as pill counts, pharmacy records, or blood pressure measurements, rather than concrete outcomes like major adverse cardiovascular events. However, pill counts can be unreliable, and patients frequently forget to bring their medication containers to appointments [40]. While pharmacy records demonstrate good validity, they are infrequently utilized due to various professional, acceptability, and organizational challenges [41]. Despite the well-documented importance of blood pressure management in preventing CVD and mortality, as shown in earlier studies [42–45], there remains limited evidence at the clinical level linking adherence to antihypertensive medication with clinical outcomes.

In contrast, studies included in our analysis have found a positive relationship between medication adherence and clinical outcomes, such as the risk of all-cause mortality and cardiovascular events [7, 22, 42], underscoring the significance of sustaining optimal medication adherence. Research indicates a significant link between low adherence to antihypertensive medications and insufficient blood pressure control, resulting in an increased

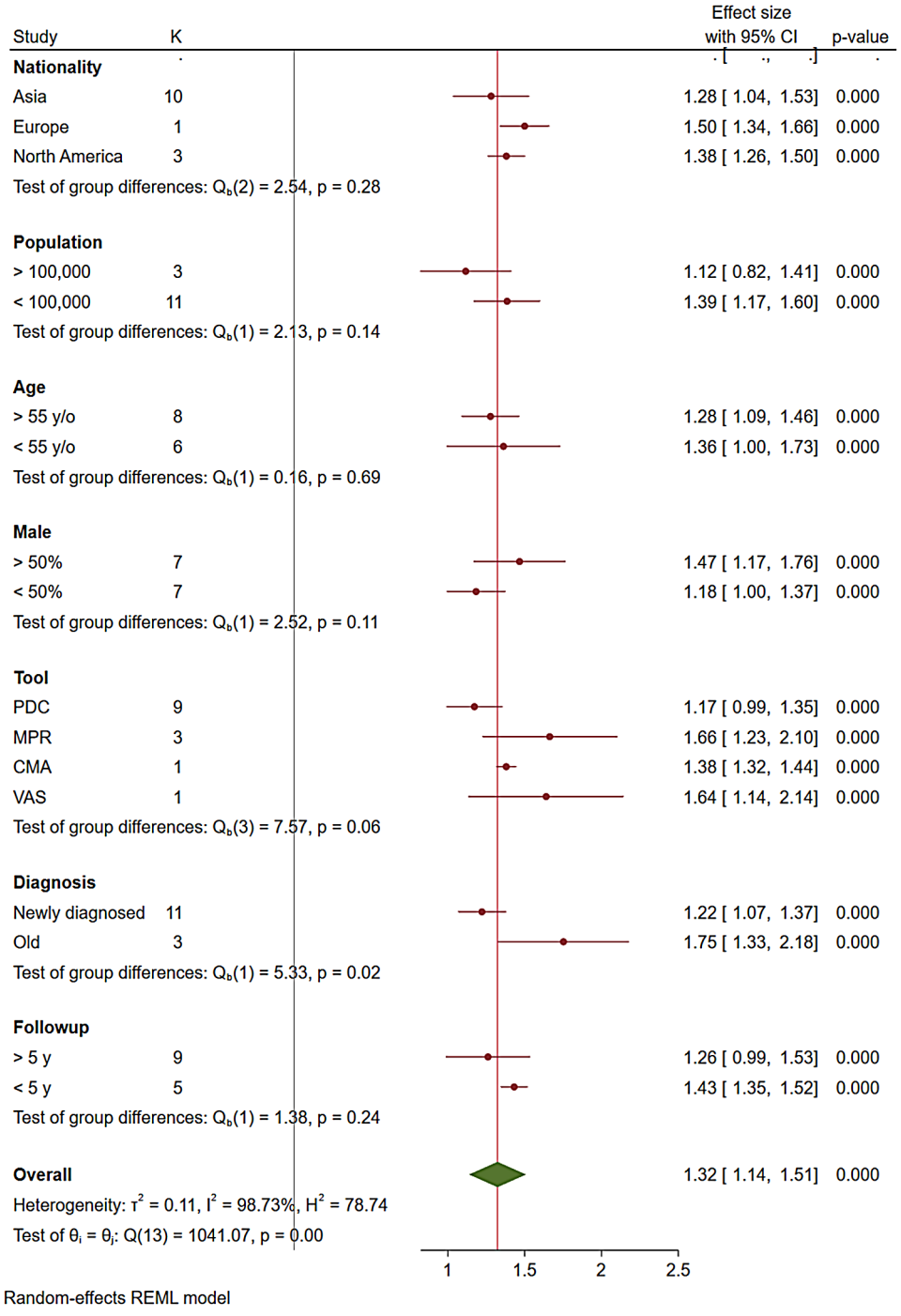

Fig. 4 Subgroup meta-analysis of the all-cause mortality related to adherence to antihypertensive medication in patient with HTN

Table 2 Meta regression of the studies based on variables

Variables	Coefficient	Standard error	95% Confidence interval	*P*-value
Publish year	0.049	0.020	0.011, 0.088	**0.012**
Mean age	0.004	0.016	-0.026, 0.034	0.798
Male (%)	0.010	0.008	-0.005, 0.025	0.189
Follow-up (year)	0.011	0.037	-0.062, 0.083	0.773

risk of cardiovascular events [46–49]. Research by Bramley TJ et al. found that high adherence (medication possession ratio of 80–100%) was associated with better odds of achieving blood pressure control compared to lower adherence levels [50]. Another study showed that strong adherence to antihypertensive medication significantly reduced cardiovascular events in primary prevention [51].

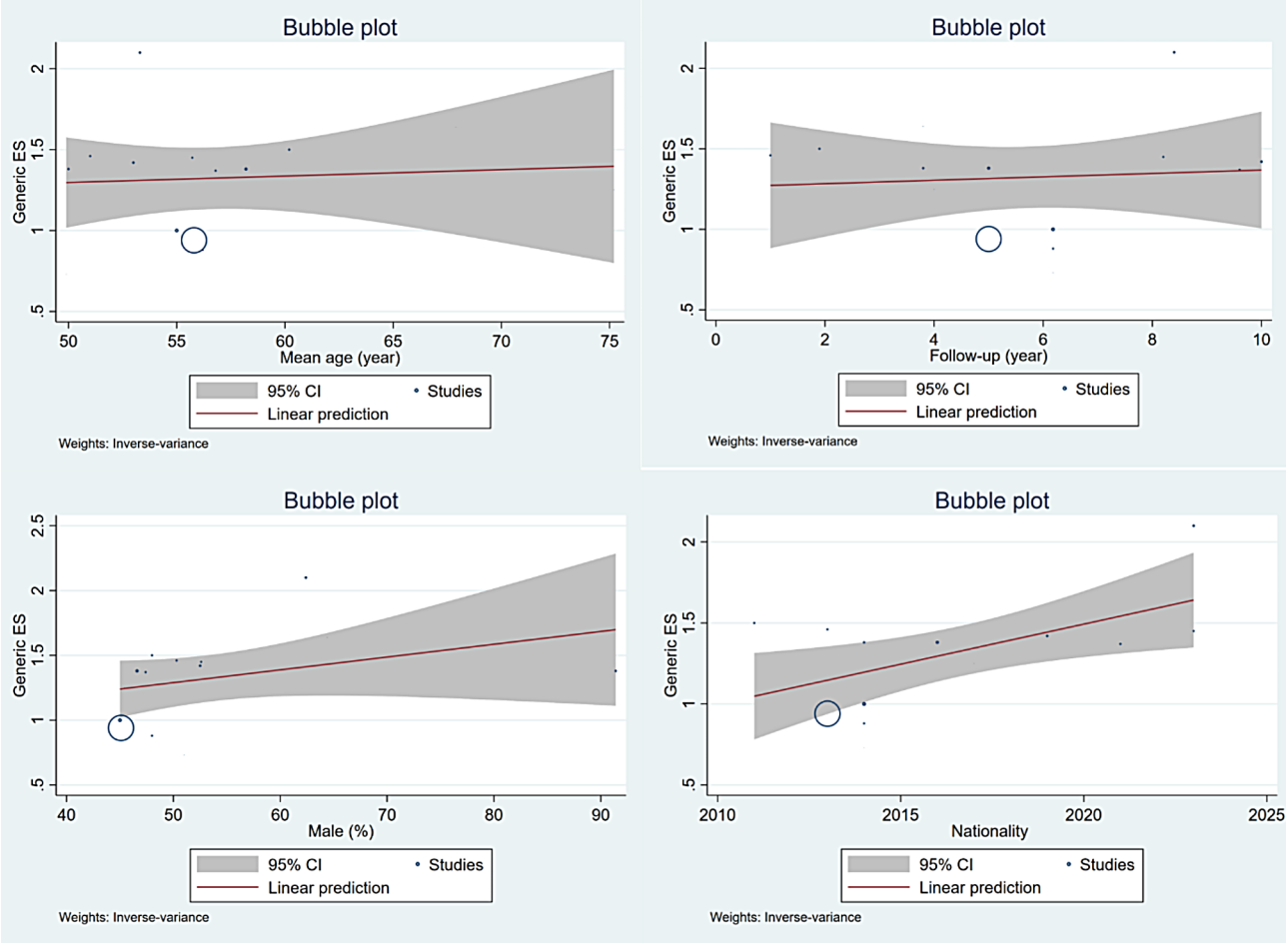

Fig. 5 Bubble Plot for Meta-Regression of Desired Variables

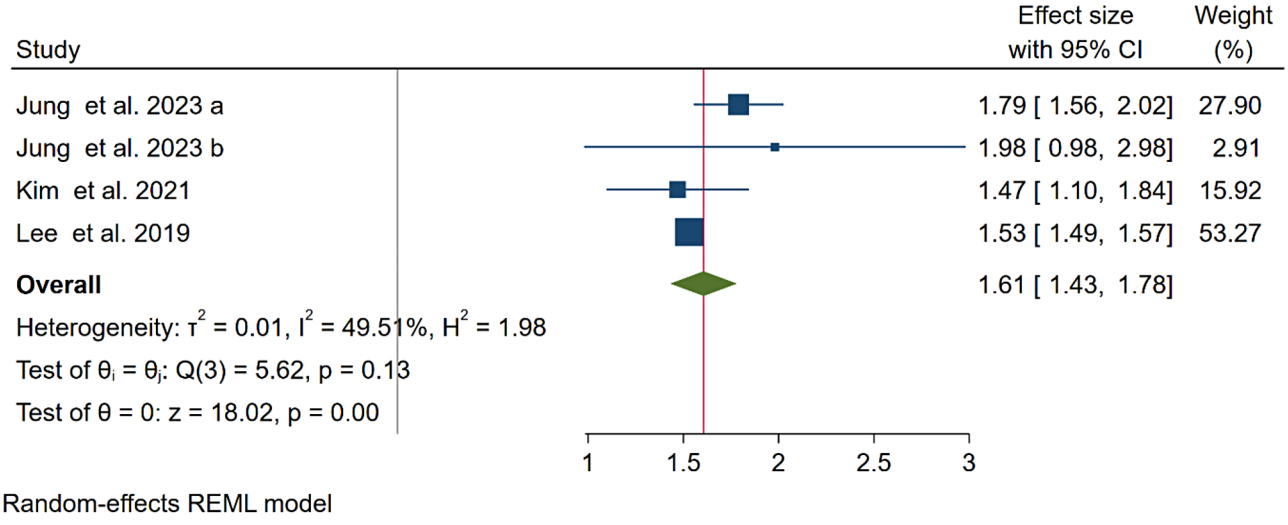

Fig. 6 Meta-analysis of the cardiovascular mortality related to adherence to antihypertensive medication in patient with HTN

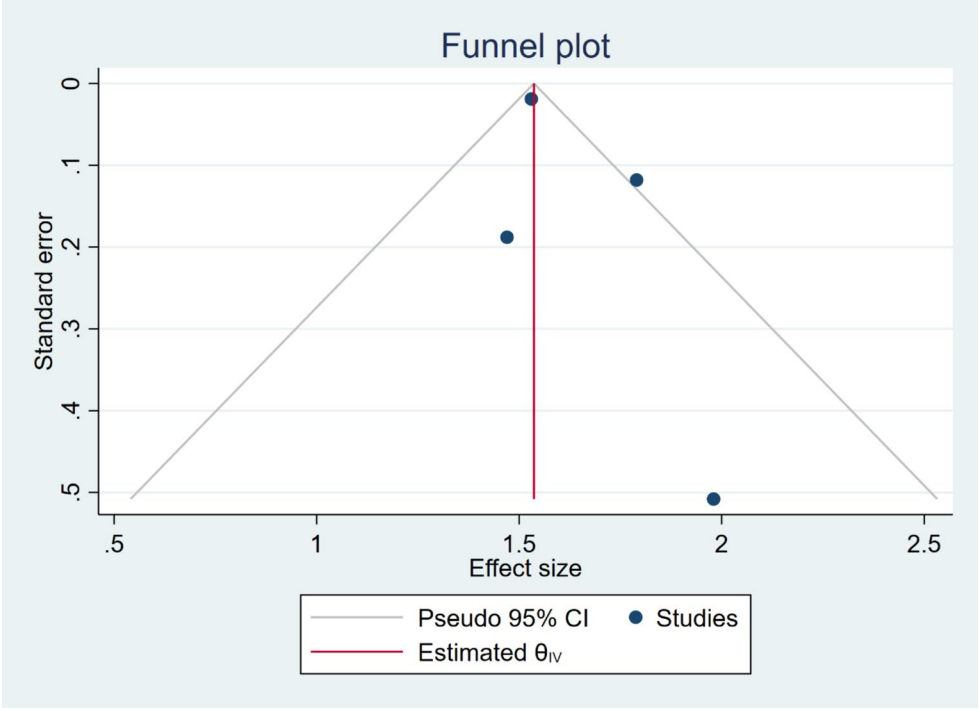

Fig. 7 Funnel plot of the cardiovascular mortality related to adherence to antihypertensive medication in patient with HTN

A recent meta-analysis confirmed that good adherence lowers the risk of stroke [52], and another indicated that high adherence is linked to lower mortality risk [53]. Ho et al. [54] explored the link between CVD mortality and adherence in coronary artery disease patients, revealing that nonadherence increased both CVD and all-cause mortality risks. Interestingly, the increase in all-cause mortality risk (e.g., HR = 1.50 for beta-blockers, HR = 1.74 for ACE inhibitors) was greater than the rise in CVD hospitalization risk (HR = 1.10 for beta-blockers, HR = 1.40 for ACE inhibitors). Other studies supported these findings, showing that low adherence results in a higher risk of all-cause mortality compared to CVD-related hospitalization [55, 56]. In comparison, the adherence to medications in other diseases has also been investigated. For example, in a meta-analysis of 39 studies involving 2,117,789 participants found that medication non-adherence in patients with atrial fibrillation, hyperlipidaemia, hypertension, and type 2 diabetes mellitus, all without prior stroke, significantly increased the risk of stroke and stroke-related mortality, emphasizing the need for improved adherence in primary stroke prevention [57].

In addition, a prospective cohort study of 785 patients with diabetes and peripheral arterial disease found that non-adherence to both medications and lifestyle recommendations significantly increased the risk of one-year all-cause mortality and major adverse cardiovascular events, highlighting the importance of adherence in secondary prevention efforts [58].

Limitation and strength

The study boasts several strengths. It is the first meta-analysis to systematically evaluate this relationship, providing a comprehensive overview of existing literature. By employing a consistent cutoff for adherence scores, it enhances comparability across studies, allowing for more robust conclusions. The inclusion of subgroup analyses and meta-regression facilitates the exploration of heterogeneity among studies, revealing patterns that might otherwise remain obscured. Furthermore, the analysis is supported by a large sample size, increasing statistical power and the reliability of findings, thereby contributing valuable insights into the impact of medication adherence on mortality rates in patient with HTN.

The study has several limitations. Firstly, it primarily draws data from a limited number of countries, which may impact the generalizability of the findings across diverse populations. Additionally, the variability in definitions of medication adherence among included studies complicates comparisons and synthesis of results. The observational design of these studies introduces potential biases, such as confounding variables that could influence both adherence and mortality outcomes; We also included the cohort studies that introduce certain biases which may influence the study's results. Moreover, differences in follow-up durations and methodologies across studies may lead to inconsistent data regarding the long-term effects of adherence on mortality rates. Another limitation regarding cardiovascular mortality is

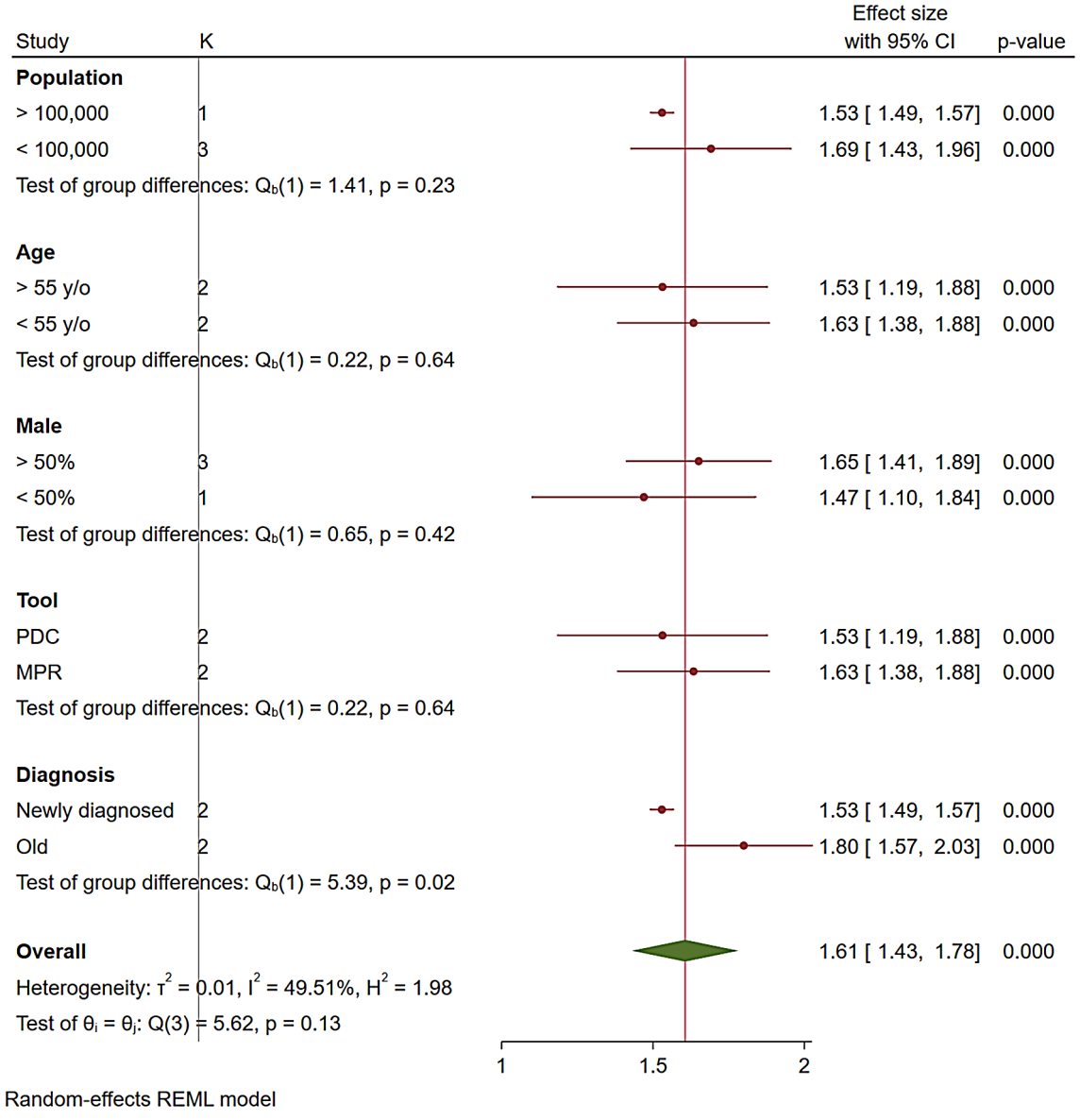

Fig. 8 Subgroup meta-analysis of the cardiovascular mortality related to adherence to antihypertensive medication in patient with HTN

the small number of included studies (four), which may elevate the risk of Type II errors, resulting in false negatives and missed significant effects. However, due to the strong significance of the results, a larger analysis might confirm these findings, as indicated by the primary study. Finally, the results show a high degree of heterogeneity, likely influenced by numerous confounding variables such as sociodemographic and cultural factors. Controlling for these variables is challenging and requires extensive research in each specific context.

Future research should assess this correlation in various settings with diverse socioeconomic and cultural contexts that may affect outcomes, incorporating additional factors influencing mortality beyond AHT. Moreover, interventions to enhance adherence should be tailored to the specific context of the study. For instance, effective strategies include patient education [59], simplifying medication regimens with single-pill combinations [60], involving pharmacists for support, and utilizing digital tools like smartphone apps [61] for reminders and adherence tracking, all of which promote understanding and motivation.

Conclusions

In conclusion, this systematic review highlights a clear link between adherence to antihypertensive medications and mortality rates among patients with hypertension. Given the substantial burden of cardiovascular disease related to poor medication adherence, healthcare providers must prioritize strategies aimed at improving patient

adherence to treatment regimens. Future research should focus on identifying effective interventions tailored to enhance adherence, particularly in populations at higher risk for nonadherence, such as those newly initiated on antihypertensive therapy. By addressing these challenges, we can improve health outcomes and reduce mortality rates in patient with HTN globally.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12872-025-04538-6.

Supplementary Material 1

Author contributions

XP and LW were involved in developing the hypothesis, gathering and analyzing data, writing the manuscript, and creating tables and figures. JZ contributed to the hypothesis, engineered and edited the collected data, handled correspondence, and revised the manuscript prior to submission.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethical approval

Not applicable.

Consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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References

1. Yang R, Zhang X, Bai J, Wang L, Wang W, Cai J. Global, regional, and national burden of hypertensive heart disease among older adults in 204 countries and territories between 1990 and 2019: a trend analysis. Chin Med J (Engl). 2023;136(20):2421–30.
2. Hamdidouche I, Jullien V, Boutouyrie P, Billaud E, Azizi M, Laurent S. Drug adherence in hypertension: from methodological issues to cardiovascular outcomes. J Hypertens. 2017;35(6).
3. Burnier M, Egan BM. Adherence in hypertension. Circul Res. 2019;124(7):1124–40.
4. Mills KT, Bundy JD, Kelly TN, Reed JE, Kearney PM, Reynolds K, et al. Global Disparities Hypertens Preval Control Circulation. 2016;134(6):441–50.
5. Vrijens B, Vincze G, Kristanto P, Urquhart J, Burnier M. Adherence to prescribed antihypertensive drug treatments: longitudinal study of electronically compiled dosing histories. BMJ. 2008;336(7653):1114.
6. Lee EKP, Poon P, Yip BHK, Bo Y, Zhu MT, Yu CP, et al. Global Burden, Regional differences, trends, and Health Consequences of Medication Nonadherence for Hypertension during 2010 to 2020: a Meta-analysis Involving 27 million patients. J Am Heart Assoc. 2022;11(17):e026582.
7. Esposti LD, Saragoni S, Benemei S, Batacchi P, Geppetti P, Di Bari M et al. Adherence to antihypertensive medications and health outcomes among newly treated hypertensive patients. ClinicoEconomics Outcomes Res. 2011:47–54.
8. Global regional. National incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: a systematic analysis for the global burden of Disease Study 2017. Lancet. 2018;392(10159):1789–858.
9. Becerra-Tomás N, Paz-Graniel I, C WCK, Kahleova H, Rahelić D, Sievenpiper JL, et al. Nut consumption and incidence of cardiovascular diseases and cardiovascular disease mortality: a meta-analysis of prospective cohort studies. Nutr Rev. 2019;77(10):691–709.
10. Feng Y, Zhao Y, Yang X, Li Y, Han M, Qie R, et al. Adherence to antihypertensive medication and cardiovascular disease events in hypertensive patients: a dose-response meta-analysis of 2 769 700 participants in cohort study. QJM. 2022;115(5):279–86.
11. Valgimigli M, Garcia-Garcia HM, Vrijens B, Vranckx P, McFadden EP, Costa F, et al. Standardized classification and framework for reporting, interpreting, and analysing medication non-adherence in cardiovascular clinical trials: a consensus report from the non-adherence Academic Research Consortium (NARC). Eur Heart J. 2019;40(25):2070–85.
12. Ibrahim S, Nurmohamed NS, Collard D, de Weger A, Hovingh GK, van den Born BJH, et al. Association between Self-Rated Medication Adherence and adverse Cardiovascular outcomes in patients with hypertension. J Am Heart Association. 2023;12(22):e031418.
13. Brown MT, Bussell JK, Medication Adherence. WHO Cares? Mayo Clinic Proceedings. 2011;86(4):304– 14.
14. Nielsen JØ, Shrestha AD, Neupane D, Kallestrup P. Non-adherence to anti-hypertensive medication in low- and middle-income countries: a systematic review and meta-analysis of 92443 subjects. J Hum Hypertens. 2017;31(1):14–21.
15. James PA, Oparil S, Carter BL, Cushman WC, Dennison-Himmelfarb C, Handler J, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). JAMA. 2014;311(5):507–20.
16. Ettehad D, Emdin CA, Kiran A, Anderson SG, Callender T, Emberson J, et al. Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis. Lancet. 2016;387(10022):957–67.
17. Nissen SE, Tuzcu EM, Libby P, Thompson PD, Ghali M, Garza D, et al. Effect of antihypertensive agents on cardiovascular events in patients with coronary disease and normal blood pressure: the CAMELOT study: a randomized controlled trial. JAMA. 2004;292(18):2217–25.
18. Shin S, Song H, Oh S-K, Choi KE, Kim H, Jang S. Effect of antihypertensive medication adherence on hospitalization for cardiovascular disease and mortality in hypertensive patients. Hypertens Res. 2013;36(11):1000–5.
19. Gardezi SKM, Aitken WW, Jilani MH. The impact of non-adherence to Antihypertensive Drug Therapy. Healthcare. 2023;11(22):2979.
20. Jung MH, Lee SY, Youn JC, Chung WB, Ihm SH, Kang D, et al. Antihypertensive Medication Adherence and Cardiovascular outcomes in patients with Cancer: a Nationwide Population-based Cohort Study. J Am Heart Association. 2023;12(14):e029362.
21. Jung M, Choo E, Lee S. A comparison of methods for the measurement of adherence to antihypertensive multidrug therapy and the clinical consequences: a retrospective cohort study using the Korean nationwide claims database. Epidemiol Health. 2023;45.
22. Liu Q, Quan H, Chen G, Qian H, Khan N. Antihypertensive medication adherence and mortality according to ethnicity: a cohort study. Can J Cardiol. 2014;30(8):925–31.
23. Tang KL, Quan H, Rabi DM. Measuring medication adherence in patients with incident hypertension: a retrospective cohort study. BMC Health Serv Res. 2017;17:1–16.
24. Marin GH, Marín L, Errecalde JO. Impact in the reduction of complications through a personalized follow-up strategy to ensure adherence to antihypertensive therapy. Int J Adv Sci Eng Technol. 2019;7.
25. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71.
26. Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. Eur J Epidemiol. 2010;25:603–5.

27. Gosmanova EO, Lu JL, Streja E, Cushman WC, Kalantar-Zadeh K, Kovesdy CP. Association of medical treatment nonadherence with all-cause mortality in newly treated hypertensive US veterans. Hypertension. 2014;64(5):951–7.
28. Kim S, Shin DW, Yun JM, Hwang Y, Park SK, Ko Y-J, et al. Medication adherence and the risk of cardiovascular mortality and hospitalization among patients with newly prescribed antihypertensive medications. Hypertension. 2016;67(3):506–12.
29. Kim CL, Do YS, Kim BJ, Lee KS, Nah MA, Kim U, et al. Clinical impact of medication adherence on 10-year cardio-cerebrovascular mortality in newly diagnosed hypertensive patients. J Clin Hypertens. 2021;23(9):1695–702.
30. Lee H, Park JH, Floyd JS, Park S, Kim HC. Combined effect of income and medication adherence on mortality in newly treated hypertension: nationwide study of 16 million person-years. J Am Heart Association. 2019;8(16):e013148.
31. Wong MC, Tam WW, Cheung CS, Wang HH, Tong EL, Sek AC, et al. Drug adherence and the incidence of coronary heart disease-and stroke-specific mortality among 218,047 patients newly prescribed an antihypertensive medication: a five-year cohort study. Int J Cardiol. 2013;168(2):928–33.
32. Yoon S, Kwan YH, Yap WL, Lim ZY, Phang JK, Loo YX, et al. Factors influencing medication adherence in multi-ethnic Asian patients with chronic diseases in Singapore: a qualitative study. Front Pharmacol. 2023;14:1124297.
33. Adebayo OO. The moderating effect of ethnicity on the relationship between type of Healthcare Professional and Antihypertensive. Medication Adherence: Walden University; 2024.
34. Schoenthaler A, Knafl GJ, Fiscella K, Ogedegbe G. Addressing the social needs of hypertensive patients: the role of patient–provider communication as a predictor of medication adherence. Circulation: Cardiovasc Qual Outcomes. 2017;10(9):e003659.
35. Singh H, Fulton Jt, Mirzazada S, Saragosa M, Uleryk EM, Nelson MLA. Community-Based Culturally Tailored Education Programs for Black Communities with Cardiovascular Disease, Diabetes, Hypertension, and stroke: systematic review findings. J Racial Ethn Health Disparities. 2023;10(6):2986–3006.
36. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, et al. 2018 ESC/ESH guidelines for the management of arterial hypertension: the Task Force for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension: the Task Force for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension. J Hypertens. 2018;36(10):1953–2041.
37. Banegas JR, López-García E, Dallongeville J, Guallar E, Halcox JP, Borghi C, et al. Achievement of treatment goals for primary prevention of cardiovascular disease in clinical practice across Europe: the EURIKA study. Eur Heart J. 2011;32(17):2143–52.
38. Chow CK, Teo KK, Rangarajan S, Islam S, Gupta R, Avezum A, et al. Prevalence, awareness, treatment, and control of hypertension in rural and urban communities in high-, middle-, and low-income countries. JAMA. 2013;310(9):959–68.
39. Pokharel P, Jha SK, Adhikari A, Katwal S, Ghimire S, Shrestha AB, et al. Non-adherence to anti-hypertensive medications in a low-resource country Nepal: a systematic review and meta-analysis. Ann Med Surg (Lond). 2023;85(9):4520–30.
40. Anghel LA, Farcas AM, Oprean RN. An overview of the common methods used to measure treatment adherence. Med Pharm Rep. 2019;92(2):117–22.
41. Lima-Dellamora EC, Osorio-de-Castro CGS, Madruga LGSL, Azeredo TB. Use of pharmacy records to measure treatment adherence: a critical review of the literature. Cadernos De saúde pública. 2017;33:e00136216.
42. Law MR, Morris JK, Wald NJ. Use of blood pressure lowering drugs in the prevention of cardiovascular disease: meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies. BMJ. 2009;338:b1665.
43. Law M, Wald N, Morris J. Lowering blood pressure to prevent myocardial infarction and stroke: a new preventive strategy. Health Technol Assess. 2003;7(31):1–94.
44. Wang JG, Li Y. Primary and secondary prevention of stroke by antihypertensive drug treatment. Expert Rev Neurother. 2004;4(6):1023–31.
45. Staessen JA, Li Y, Thijs L, Wang JG. Blood pressure reduction and cardiovascular prevention: an update including the 2003–2004 secondary prevention trials. Hypertens Res. 2005;28(5):385–407.
46. Thomopoulos C, Parati G, Zanchetti A. Effects of blood-pressure-lowering treatment in hypertension: 9. Discontinuations for adverse events attributed to different classes of antihypertensive drugs: meta-analyses of randomized trials. J Hypertens. 2016;34(10):1921–32.
47. Krousel-Wood M, Joyce C, Holt E, Muntner P, Webber LS, Morisky DE, et al. Predictors of decline in medication adherence: results from the cohort study of medication adherence among older adults. Hypertension. 2011;58(5):804–10.
48. Corrao G, Parodi A, Nicotra F, Zambon A, Merlino L, Cesana G, et al. Better compliance to antihypertensive medications reduces cardiovascular risk. J Hypertens. 2011;29(3):610–8.
49. Burnier M, Wuerzner G, Struijker-Boudier H, Urquhart J. Measuring, analyzing, and managing drug adherence in resistant hypertension. Hypertension. 2013;62(2):218–25.
50. Bramley TJ, Nightengale BS, Frech-Tamas F, Gerbino PP. Relationship of blood pressure control to Adherence with Antihypertensive Monotherapy in 13 Managed Care Organizations. J Managed Care Pharm. 2006;12(3):239–45.
51. Li X, Bijlsma MJ, De Vos S, Bos JH, Mubarik S, Schuiling-Veninga CC, et al. Comparative effectiveness of antihypertensive monotherapies in primary prevention of cardiovascular events—a real-world longitudinal inception cohort study. Front Pharmacol. 2024;15:1357567.
52. Xu T, Yu X, Ou S, Liu X, Yuan J, Tan X et al. Adherence to Antihypertensive Medications and stroke risk: a dose-response Meta-analysis. J Am Heart Assoc. 2017;6(7).
53. Simpson SH, Eurich DT, Majumdar SR, Padwal RS, Tsuyuki RT, Varney J, et al. A meta-analysis of the association between adherence to drug therapy and mortality. BMJ. 2006;333(7557):15.
54. Ho PM, Magid DJ, Shetterly SM, Olson KL, Maddox TM, Peterson PN, et al. Medication nonadherence is associated with a broad range of adverse outcomes in patients with coronary artery disease. Am Heart J. 2008;155(4):772–9.
55. Hong JS, Kang HC. Relationship between oral antihyperglycemic medication adherence and hospitalization, mortality, and healthcare costs in adult ambulatory care patients with type 2 diabetes in South Korea. Med Care. 2011;49(4):378–84.
56. Degli Esposti L, Saragoni S, Batacchi P, Benemei S, Geppetti P, Sturani A, et al. Adherence to statin treatment and health outcomes in an Italian cohort of newly treated patients: results from an administrative database analysis. Clin Ther. 2012;34(1):190–9.
57. Mafruhah OR, Huang Y-M, Lin H-W. Impacts of medication non-adherence to major modifiable stroke-related diseases on stroke prevention and mortality: a meta-analysis. J Neurol. 2023;270(5):2504–16.
58. Shalaeva EV, Bano A, Kasimov U, Janabaev B, Laimer M, Saner H. Impact of persistent medication adherence and compliance with lifestyle recommendations on Major Cardiovascular events and one-year mortality in patients with type 2 diabetes and Advanced stages of atherosclerosis: results from a prospective cohort study. Glob Heart. 2023;18(1):61.
59. Ghembaza M, Senoussaoui Y, Kendouci Tani M, Meguenni K. Impact of patient knowledge of hypertension complications on adherence to antihypertensive therapy. Curr Hypertens Reviews. 2014;10(1):41–8.
60. Parati G, Kjeldsen S, Coca A, Cushman WC, Wang J. Adherence to single-pill versus free-equivalent combination therapy in hypertension: a systematic review and meta-analysis. Hypertension. 2021;77(2):692–705.
61. Morrissey EC, Casey M, Glynn LG, Walsh JC, Molloy GJ. Smartphone apps for improving medication adherence in hypertension: patients' perspectives. Patient preference and adherence. 2018:813– 22.

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