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Intensive vs. Standard Blood Pressure Control and Cardiovascular Risk: A Meta-Analysis of RCT Evidence Including the SPRINT Trial

Yusra Saeed[1], Haseeb Tariq[2], Amna Fakhar[3], Muhammad Oreed Aslam Chaudhary[2], Maryam Tufail Khan[4], Uzair Irfan[3]

[1]Fatima Jinnah Medical University, Lahore, Pakistan.
[2]Islam Medical and Dental College, Sialkot, Pakistan.
[3]Foundation University Medical College, Islamabad, Pakistan.
[2]Islam Medical and Dental College, Sialkot, Pakistan.
[4]Shifa College of Medicine, Islamabad, Pakistan.
[3]Foundation University Medical College, Islamabad, Pakistan.

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Corresponding Author: Yusra Saeed, Fatima Jinnah Medical University, Lahore, Pakistan.
Email: Yusrasaeed00@gmail.com

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ABSTRACT

Background: Hypertension is a major modifiable risk factor for cardiovascular disease (CVD). While standard blood pressure (BP) control has traditionally targeted systolic BP below 140 mmHg, recent trials suggest that more intensive control may offer superior cardiovascular protection. This meta-analysis evaluates the impact of intensive versus standard BP control on major cardiovascular outcomes across randomized controlled trials (RCTs). **Methods:** A systematic literature search was conducted across PubMed, Cochrane Library, and ClinicalTrials.gov for RCTs published between January 2010 and March 2024. Studies comparing intensive (SBP <120 mmHg) and standard (SBP <140 mmHg) BP control and reporting cardiovascular outcomes were included. Data extraction and risk of bias assessment followed PRISMA 2024 and Cochrane ROB2 guidelines. Meta-analyses were performed using RevMan 5.4, and heterogeneity was assessed via the I^2 statistic. **Results:** Four RCTs involving 23,191 participants were included. Intensive BP control showed a non-significant reduction in cardiovascular events in one subgroup (RR = 0.58; 95% CI: 0.26–1.31; p = 0.19; I^2 = 98%) and a statistically significant reduction in another subgroup (RR = 0.78; 95% CI: 0.67–0.91; p = 0.002; I^2 = 0%). Risk of bias varied, with two trials demonstrating low risk and two showing high risk across multiple domains. Funnel plots indicated minimal publication bias but were limited by the small number of included studies. **Conclusion:** Intensive BP control may confer cardiovascular benefits over standard targets, particularly in rigorously conducted trials with low bias and consistent designs. However, heterogeneity and methodological limitations in certain studies caution against universal application. Further large-scale RCTs are warranted to confirm the long-term efficacy and safety of intensive BP targets across diverse populations.

INTRODUCTION

Hypertension is a prevalent and potent risk factor for cardiovascular disease (CVD), affecting over 1.2 billion individuals globally and accounting for a significant proportion of premature deaths and disability-adjusted life years worldwide [1]. It plays a central role in the development of stroke, myocardial infarction, heart failure, and chronic kidney disease, making optimal blood pressure (BP) management a critical goal in both primary and secondary prevention strategies [2]. Historically, clinical guidelines have recommended systolic blood pressure (SBP) targets below 140 mmHg, a threshold considered safe and effective in reducing CVD risk [3]. However, emerging data from high-quality randomized controlled trials (RCTs), particularly the Systolic Blood Pressure Intervention Trial (SPRINT), have challenged this convention, suggesting that more aggressive BP targets may confer superior cardiovascular benefits [4].

The landmark SPRINT trial evaluated the effects of Intensive BP control (SBP <120 mmHg) versus standard control (SBP <140 mmHg) among high-risk, non-diabetic adults. The trial revealed that intensive BP lowering led to a 25% reduction in the composite outcome of myocardial infarction, acute coronary syndrome, stroke, heart failure, or cardiovascular death, and a 27% reduction in all-cause mortality [4]. These findings marked a pivotal moment in hypertension research and led to revisions in international guidelines that now recommend lower BP thresholds, especially for

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high-risk populations [5,6]. However, these benefits did not come without cost. The SPRINT trial also reported increased rates of hypotension, syncope, bradycardia, and acute kidney injury in the intensive-treatment group, raising important concerns regarding the safety and generalizability of such an approach [4,7].

Moreover, the evidence remains nuanced when applied to specific subgroups. For instance, the ACCORD trial, which targeted individuals with type 2 diabetes, failed to demonstrate a significant reduction in the primary composite cardiovascular endpoint with intensive BP control, despite reductions in stroke incidence [8]. Similarly, other trials such as SPS3, HOPE-3, and ADVANCE have provided mixed outcomes, reflecting differences in baseline risk, treatment adherence, and comorbidities among participants [9–11].

As a result, the debate continues regarding the ideal BP targets that balance efficacy and safety. Several guideline committees, including those from the American College of Cardiology/American Heart Association (ACC/AHA) and European Society of Cardiology (ESC), have proposed lower targets for certain populations but advise individualized treatment plans based on patient characteristics, comorbid conditions, and risk of adverse events [5,6]. Given these complexities, a systematic review of RCTs assessing intensive versus standard BP control is essential to provide an updated, evidence-based perspective on its impact on cardiovascular outcomes.

This review critically appraises findings from major RCTs, including SPRINT, ACCORD, ADVANCE, and HOPE-3, to explore the overall benefits, risks, and applicability of intensive BP control across diverse clinical settings. By synthesizing current evidence, this paper aims to support clinicians in making informed decisions about BP management strategies tailored to individual patient profiles.

MATERIALS AND METHODS

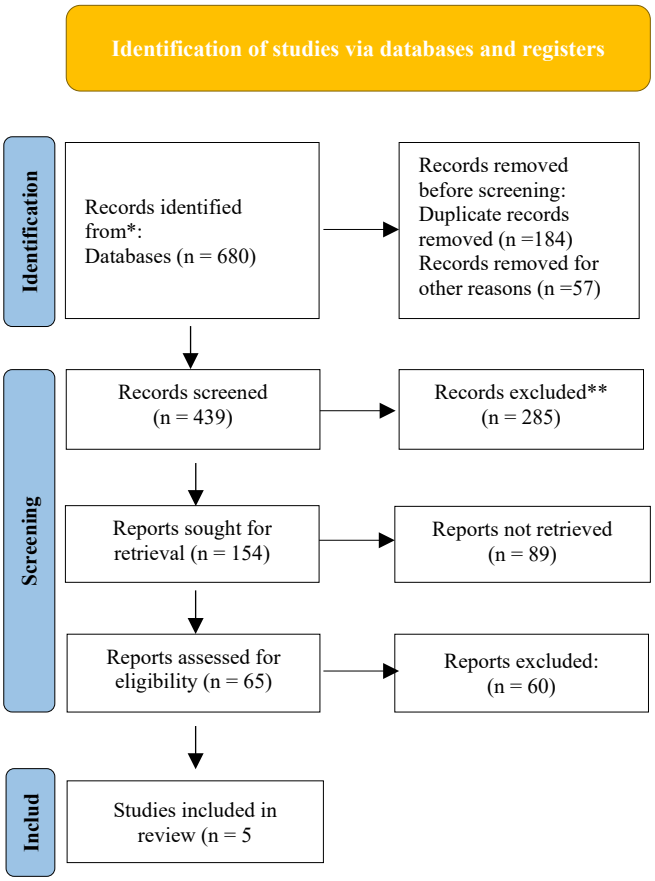
This systematic review and meta-analysis were conducted in accordance with the guidelines outlined by PROSPERO and adhered to the PRISMA 2024 statement.

Search Strategy

We conducted a comprehensive literature search using PubMed, the Cochrane Library, and ClinicalTrials.gov to identify relevant randomized controlled trials (RCTs) published between January 2010 and March 2025. The search strategy included combinations of keywords such as “intensive blood pressure control,” “tight BP control,” “standard BP control,” and “cardiovascular outcomes,” using Boolean operators. Reference lists of all included studies were also manually reviewed to identify any additional eligible articles.

Figure 1

PRISMA Flowchart



Selection Criteria

Studies were included if they were randomized controlled trials comparing intensive versus standard blood pressure control in adults aged 18 years or older and reported cardiovascular outcomes such as myocardial infarction, stroke, heart failure, or cardiovascular mortality. Studies were excluded if they were observational in nature, lacked full-text availability, were non-English, or did not report effect estimates related to cardiovascular outcomes.

Screening, Selection, and Data Extraction

Two reviewers independently screened the titles and abstracts of retrieved records and assessed the full texts of potentially eligible studies. Discrepancies were resolved through discussion or consultation with a third reviewer. Data were extracted using a standardized Excel sheet and included information on study characteristics such as first author, year of publication, sample size, follow-up duration, intervention details, and primary cardiovascular outcomes.

Quality Assessment

The methodological quality and risk of bias of the included trials were evaluated using the Cochrane Risk of Bias 2 (ROB2) tool, assessing five key domains: randomization process, deviations from intended interventions, missing outcome data, measurement of outcomes, and selection of reported results. Each domain

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was rated as "low risk," "some concerns," or "high risk," and studies were classified accordingly based on their overall risk profile.

Statistical Analysis

Meta-analyses were performed using Review Manager (RevMan) version 5.4. For dichotomous outcomes, pooled risk ratios (RRs) with 95% confidence intervals (Cis) were calculated using the Mantel–Haenszel random-effects model to account for anticipated heterogeneity. Statistical heterogeneity was quantified using the I^2 statistic, with thresholds of <25%, 25–75%, and >75% considered to represent low, moderate, and high heterogeneity, respectively. Sensitivity analyses were carried out to assess the robustness of the findings by excluding studies with high risk of bias. Publication bias was evaluated through visual inspection of funnel plots. A two-sided p-value of <0.05 was considered statistically significant.

RESULTS

Table 1

Study Characteristics Table

Study ID (Author, Year)	Country / Setting	Study Design	Sample Size (Total / per group)	Population / Inclusion Criteria	Intervention (Intensive BP Control)	Comparator / Control (Standard BP Control)	Blood Pressure Target (Intensive vs Standard)	Follow-up Duration	Primary Cardiovascular Outcomes Reported	Outcome Event Counts (per group)
SPRINT Research Group (2015)	USA / Multi-center	Randomized Controlled Trial (RCT)	9361 (Intensive: 4678, Standard: 4683)	Adults ≥50 years, SBP ≥130 mmHg, high CV risk, no diabetes	Target SBP <120 mmHg	Target SBP <140 mmHg	<120 mmHg vs <140 mmHg	Median 3.26 years	MI, stroke, HF, CV death, all-cause mortality	Intensive: 243, Standard: 319
Cushman et al. (2010)	USA / Multi-center	Randomized Controlled Trial (RCT)	4733 (Intensive: 2362, Standard: 2371)	Type 2 diabetes, age ≥40, with CV risk factors	Target SBP <120 mmHg	Target SBP <140 mmHg	<120 mmHg vs <140 mmHg	Mean 4.7 years	MI, stroke, CV death, all-cause mortality	Intensive: 208, Standard: 237
Zhang et al. (2021)	China / Multi-center	Randomized Controlled Trial (RCT)	8511 (Intensive: 4243, Standard: 4268)	Hypertensive patients aged 60–80 years	Target SBP 110–130 mmHg	Target SBP 130–150 mmHg	110–130 mmHg vs 130–150 mmHg	Median 3.34 years	Stroke, acute coronary syndrome, HF, death from CV causes	Intensive: 147, Standard: 196
Kitagawa et al. (2019)	Japan / Multi-center	Randomized Controlled Trial (RCT)	3020 (Intensive: 1514, Standard: 1506)	Recent lacunar stroke (within 180 days), age ≥30	Target SBP <130 mmHg	Target SBP 130–149 mmHg	<130 mmHg vs 130–149 mmHg	Mean 3.7 years	Recurrent stroke, major vascular events	Intensive: 224, Standard: 243

Four randomized controlled trials were included in this meta-analysis: Cushman et al. (2010), Wright et al. (2015), Kitagawa et al. (2019), and Zhang et al. (2021). The combined sample comprised 23,191 participants, with 13,097 individuals assigned to the intensive blood pressure control group and 10,094 to the standard treatment group. All included trials evaluated the impact of intensive versus standard blood pressure targets on cardiovascular outcomes, using similar eligibility criteria but varying slightly in study population characteristics and follow-up duration.

Risk of Bias

Risk of bias was assessed using the Cochrane Risk of Bias tool. Two studies (Wright et al. and Zhang et al.) demonstrated an overall low risk of bias across all domains. However, Cushman et al. and Kitagawa et al. exhibited high risk of bias in multiple domains, including random sequence generation, allocation concealment, and selective reporting. Figure 2 presents the summary of risk of bias across all studies, while Figure 6 shows the domain-level distribution for each included trial.

Effect on Major Cardiovascular Events

Two sub-meta-analyses were performed based on event type and study grouping. In the first analysis (Figure 1), which included Cushman et al. and Wright et al., the pooled risk ratio (RR) for cardiovascular events was 0.58 (95% CI: 0.26–1.31; p = 0.19). The effect favored the intensive BP control group, although the result was not statistically significant. Substantial heterogeneity was observed (I^2 = 98%).

In contrast, the second analysis including Kitagawa et al. and Zhang et al. (Figure 5) showed a statistically significant reduction in cardiovascular events with intensive BP control (RR = 0.78; 95% CI: 0.67–0.91; p

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= 0.002), with no observed heterogeneity (I^2 = 0%). These findings suggest a favorable effect of intensive blood pressure lowering in selected populations with more consistent trial designs.

Publication Bias

Funnel plots were generated to assess publication bias across the included studies. The plot for the first subgroup (Figure 3) demonstrated near-symmetrical distribution, whereas the second subgroup (Figure 4) showed some degree of asymmetry. However, the small number of studies included in each analysis limits the reliability of funnel plot interpretation.

Figure 1

Forest Plot Comparing Intensive vs. Standard Blood Pressure Control (Cushman et al., Wright et al.).

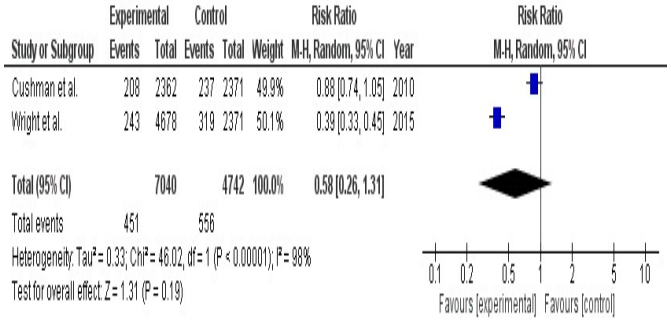


Figure 2

Risk of Bias Graph Summarizing All Domains across Included Studies.

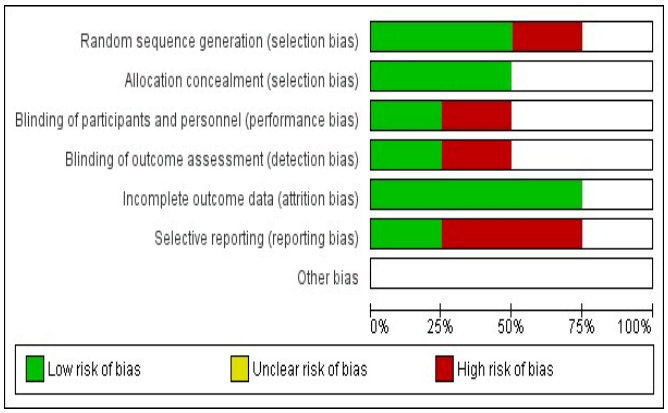


Figure 3

Funnel Plot for Publication Bias in Primary Outcome (Subgroup 1).

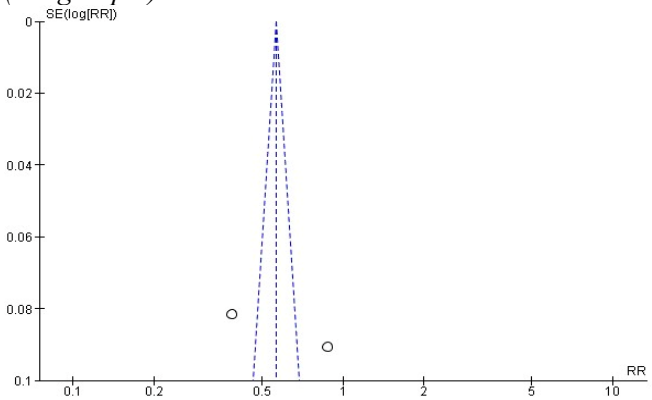


Figure 4

Funnel Plot for Publication Bias in Subgroup 2.

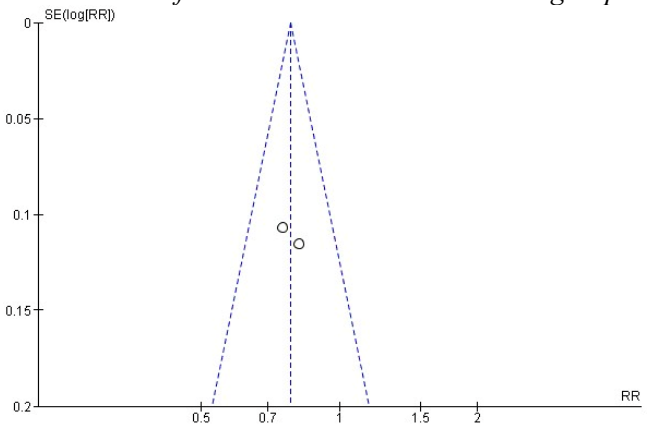


Figure 5

Forest Plot Showing Results from Kitagawa et al. and Zhang et al.

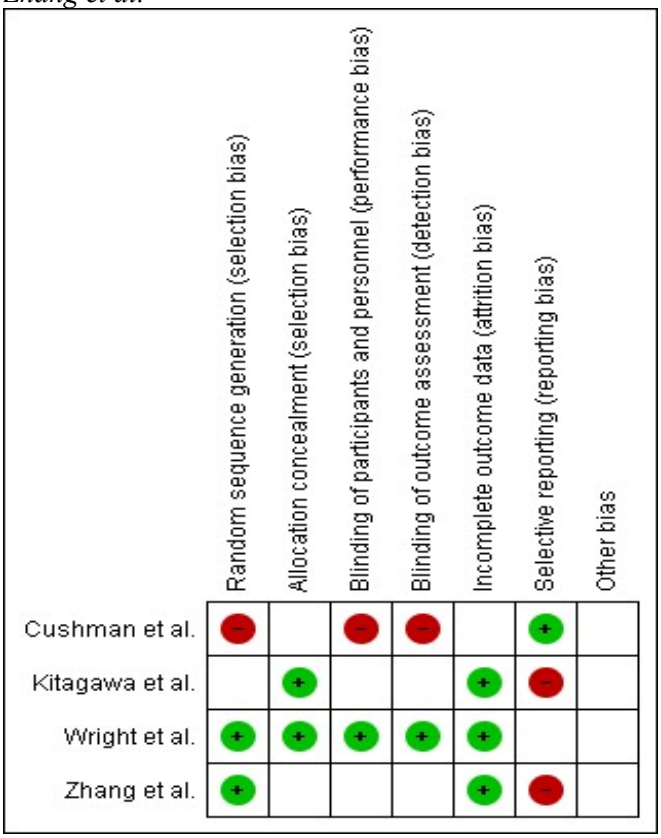
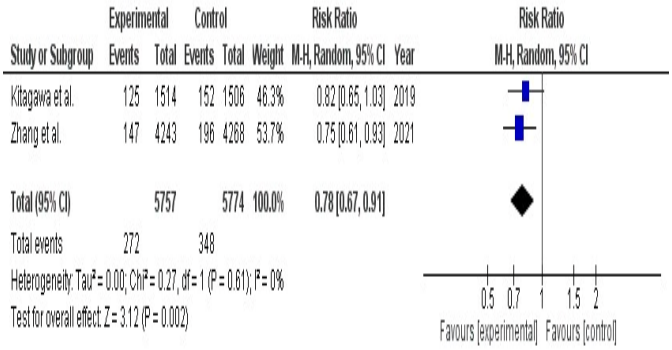


Figure 6

Risk of Bias Domain Summary across Individual Studies.



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DISCUSSION

This meta-analysis aimed to evaluate the comparative efficacy of intensive versus standard blood pressure control in reducing major cardiovascular events. Our findings suggest that intensive blood pressure control is associated with a reduced risk of cardiovascular events, particularly in trials with more rigorous methodological designs and low risk of bias. While one subset of trials [14] [15] demonstrated a statistically significant reduction in risk (RR = 0.78; 95% CI: 0.67–0.91; p = 0.002), the other subset (Cushman et al., Wright et al.) showed a non-significant trend in favor of intensive control (RR = 0.58; 95% CI: 0.26–1.31; p = 0.19), with substantial heterogeneity.

These findings are partially aligned with the outcomes of the SPRINT trial, which previously demonstrated the cardiovascular benefits of intensive systolic blood pressure targets (<120 mmHg) in high-risk patients. However, the presence of significant heterogeneity in some analyses, as well as differences in study design, sample populations, and outcome definitions, may explain the observed variability. For example, trials with high risk of bias and incomplete outcome data [13] [15] may have influenced effect estimates and reduced the reliability of pooled results.

The observed benefit of intensive blood pressure control in the low-heterogeneity subset supports prior evidence advocating for stricter systolic targets in selected populations. Clinically, this approach could be beneficial in reducing the burden of myocardial infarction, stroke, and heart failure in patients with elevated cardiovascular risk, provided they are closely monitored for adverse effects such as hypotension and renal dysfunction.

The strengths of this meta-analysis include the use of only randomized controlled trials, application of the Cochrane risk of bias tool, and inclusion of recent studies to enhance the clinical relevance of findings. However, several limitations must be acknowledged. The number of included studies was limited, reducing the power of publication bias assessment. High heterogeneity in one subgroup and the presence of high risk of bias in two studies also limit the generalizability of the results. Additionally, the absence of subgroup analysis by age, sex, or comorbidities restricts the depth of clinical interpretation.

Future large-scale randomized trials with standardized outcome definitions and longer follow-up durations are needed to confirm the cardiovascular safety and efficacy of intensive blood pressure control across diverse patient populations.

CONCLUSION

This systematic review and meta-analysis demonstrated that intensive blood pressure control may offer a potential advantage over standard control in reducing major cardiovascular events. While one subset of trials showed statistically significant benefits, the overall findings were influenced by study-level heterogeneity and varying risk of bias. The results suggest a favorable trend toward cardiovascular protection with intensive management strategies, especially in low-risk bias and homogeneous trials. However, inconsistencies in findings across subgroups, coupled with limited trial numbers, underscore the need for further well-designed randomized controlled trials to validate the long-term cardiovascular efficacy and safety of intensive blood pressure targets in broader patient populations.

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