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Intensive vs Standard Blood Pressure Lowering in People With and Without Chronic Kidney Disease
A Systematic Review and Meta-Analysis

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IMPORTANCE There is uncertainty about the effects of intensive blood pressure (BP) lowering on risks of cardiovascular disease and kidney failure in patients with chronic kidney disease (CKD).

OBJECTIVE To assess the standardized effects of intensive BP lowering on cardiovascular and kidney outcomes overall, and then to assess for effect modification by CKD status.

DATA SOURCES MEDLINE and Embase databases were searched from inception to January 16, 2026.

STUDY SELECTION Randomized clinical trials comparing intensive vs standard BP lowering in adults with and without CKD, with at least 1 year of follow-up, were eligible for inclusion.

DATA EXTRACTION AND SYNTHESIS Meta-analyses were performed using inverse variance weighting after standardizing trial results according to the between-group difference in achieved systolic BP (SBP). Differences in relative effects between CKD and non-CKD populations were assessed using χ^2 tests for heterogeneity.

MAIN OUTCOMES AND MEASURES The primary outcome was major cardiovascular events; secondary outcomes included kidney failure and estimated glomerular filtration rate (eGFR)–based surrogate outcomes for kidney failure.

RESULTS We identified 27 studies including 88 830 participants. Intensive BP lowering reduced the risk of cardiovascular events by 15% per 10-mm Hg lower SBP (relative risk [RR], 0.85; 95% CI, 0.81-0.89), without heterogeneity by CKD status. This corresponded to an estimated (SE) absolute reduction of 4.3 (1.2) cardiovascular events per 1000 person-years in individuals with CKD and 2.7 (0.4) events per 1000 person-years in those without CKD. Intensive BP lowering did not affect risk of kidney failure (RR per 10-mm Hg reduction, 0.97; 95% CI, 0.84-1.11) nor risk of 57% or 50% sustained eGFR declines (RR, 0.97; 95% CI, 0.83-1.14; and RR, 1.29; 95% CI, 0.94-1.76, respectively), without heterogeneity by CKD subgroup. Intensive BP lowering increased risk of 30% or greater and 40% or greater declines by 42% (RR, 1.42; 95% CI, 1.28-1.58) and 47% (RR, 1.47; 95% CI, 1.30-1.66).

CONCLUSIONS AND RELEVANCE Results of this systematic review and meta-analysis indicate that in adults with or without CKD, intensive BP lowering reduced the risk of cardiovascular events by 15% per 10-mm Hg lower SBP and increased the risk of sustained declines in eGFR, without an increase in risk of kidney failure. However, since baseline cardiovascular risk is higher in CKD, the absolute reduction in cardiovascular events was at least as large in this population; therefore, intensive BP lowering should be recommended in people with and without CKD.

Supplemental content

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In apparently healthy adults, observational analyses show each 20-mm Hg higher usual systolic blood pressure (SBP) is associated with an approximate doubling of the risk of cardiovascular death.[1] Meta-analyses of BP-lowering trials in the general population demonstrate that lowering BP reduces cardiovascular mortality risk by a corresponding magnitude,[2,3] supporting a causal relationship. The log-linear nature of these associations suggests that larger BP reductions should result in larger relative reductions in cardiovascular risk.[4] In addition, evidence from genetic epidemiological studies implicates elevated BP, even within the high-normal range, in the development of chronic kidney disease (CKD).[5]

Although a target BP of less than 120 mm Hg has been recommended for people with CKD by the Kidney Disease Improving Global Outcomes (KDIGO) guidelines since 2021,[6] the effects of more intensive BP lowering in patients with established CKD remain uncertain,[4,7-9] particularly among those with an estimated glomerular filtration rate (eGFR) below 30 mL/min/1.73 m^2,[10] leading to inconsistent recommendations for BP targets between guidelines.[7-9,11] This uncertainty is partly driven by J- or U-shaped associations between BP and cardiovascular risk observed in observational studies of populations with established cardiovascular disease,[12-14] older individuals,[15-17] and individuals with moderate to severe CKD,[17-23] in whom comorbid conditions, such as structural heart disease or heart failure, may confound the relationship between BP and cardiovascular outcomes.[24] Concerns that the cardiovascular benefits of intensive BP lowering may be smaller among individuals with CKD have been reinforced by a previous meta-analysis reporting an interaction between CKD and non-CKD subgroups[3] and by a recent Cochrane meta-analysis restricted to CKD populations that found no additional benefit of more intensive compared with standard BP targets for cardiovascular or CKD progression outcomes.[25]

Since the development of 2 key recent CKD-focused BP meta-analyses,[25,26] 3 large intensive BP-lowering trials have been reported: the ESPRIT (n = 11 255),[27] BPROAD (n = 12 821),[28] and STEP (n = 8511) randomized clinical trials.[29] Together, they contribute an additional 32 587 participants, including 1843 with CKD. To ensure inclusion of all contemporary data and address residual uncertainty in the efficacy of intensive BP lowering on cardiorenal outcomes, we conducted an updated systematic review and meta-analysis of randomized clinical trials comparing intensive vs standard BP lowering to assess the effects on (1) major cardiovascular events, (2) kidney failure, and (3) eGFR-based surrogate outcomes for kidney failure. We standardized treatment effects per 10-mm Hg reduction in achieved SBP and then assessed for heterogeneity between populations with and without CKD.

Key Points

Question What are the effects of intensive blood pressure (BP) lowering on cardiovascular and kidney outcomes among adults with and without chronic kidney disease (CKD)?

Findings This systematic review and meta-analysis indicates that in people with and without CKD, intensive BP lowering reduced risk of cardiovascular events by 15% per 10-mm Hg lower systolic BP. Intensive BP lowering did not affect risk of kidney failure but increased risk of sustained declines in kidney function.

Meaning Intensive BP lowering should be recommended in people with and without CKD to reduce cardiovascular risk; clinicians should implement BP-lowering strategies with careful monitoring of kidney function, despite no increased risk of kidney failure.

Methods

Search Strategy and Study Selection

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) reporting guideline in the reporting of this study. MEDLINE and Embase were searched from inception to January 16, 2026 for relevant randomized clinical trials using standardized search filters.[30] The full search strategy is provided in eTable 1 in Supplement 1. Titles and abstracts for studies identified in the initial database search were screened for relevance by 3 authors (F.I., A.J.R., A.A.-M.), and full texts were reviewed independently and in duplicate. Parallel-group trials were eligible for inclusion if they (1) randomized adults (aged >18 years) to specified intensive vs standard BP targets; (2) reported achieved BP in each study arm or BP differences between them; (3) reported effects on specific cardiovascular or kidney progression outcomes; and (4) had at least 1 year of intervention and follow-up. We also included studies reporting kidney outcome data from posttrial follow-up periods of up to 10 years (data beyond 10 years were not included, as confounding factors may accumulate with longer follow-up). Trials assessing interventions other than intensive vs standard BP lowering (unless in a factorial design) were excluded. Trials that randomly allocated participants to different BP-lowering treatments but not specific BP targets were also excluded to minimize the impact of effects of study treatments other than BP lowering. Crossover or cluster randomized trials; trials in hospitalized or pregnant patients or those undergoing dialysis; and trials in acute settings were also excluded. Reference lists of eligible studies and previous meta-analyses were reviewed for further relevant studies and data.

Data Extraction and Quality Assessment

Study-level data from each eligible trial were extracted independently by 3 authors and in duplicate (F.I., R.A., P.K.J.), including information on study population (including trial-defined CKD or non-CKD populations), number of participants, mean or median baseline eGFR, mean baseline BP, BP comparison targets, median follow-up duration, achieved BP difference at 1 year or closest available time point (overall and by trial-defined CKD status, wherever possible), and each trial's definitions of cardiovascular, kidney failure, and kidney disease progression outcomes (eTable 2 in Supplement 1). Where achieved SBP was not reported specifically in CKD or non-CKD subgroups, achieved SBP in each arm of the

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whole cohort was used. For all outcomes, the number of outcomes in each arm and reported relative effect estimates with 95% confidence intervals for the intensive vs standard BP target comparisons in the within-trial period were also extracted. Posttrial follow-up results for kidney outcomes (limited to a maximum of 10 years of posttrial follow-up) from available trials were also extracted to provide maximum information on the definitive outcome of kidney failure (often a late-accruing outcome). Where patients with CKD might constitute a large proportion of a trial population and such results were not publicly available, analyses or data were requested from trial investigators; additional data were provided by the MDRD,[31] AASK,[32] and ESPRIT investigators.[27]

Risk of bias assessment of each eligible study was performed using the Cochrane Risk of Bias tool 2 independently by 2 authors (F.I. and R.A.), with conflicts resolved by a third author (A.J.R.). Publication bias was assessed by visual inspection and by estimating asymmetry of funnel plots (the Egger test).

Outcomes

The primary outcome of this study was major cardiovascular events as reported by each individual included trial (eTable 2 in Supplement 1), as previous comprehensive analyses[3] suggest similar effects of BP lowering on each of the individual components of these composite events. The key secondary outcome was kidney failure (in general, initiation of dialysis or kidney transplant). Additional categorical CKD outcomes were collected without restricting to a specific definition. These included a doubling of serum creatinine (ie, ≥57% declines in eGFR from randomization) to 30% or more sustained declines in eGFR (eTable 2 in Supplement 1). All-cause mortality was included as an exploratory analysis.

BP Standardization

As with other recent meta-analyses,[4] to facilitate between-population comparisons, we selected a priori to standardize trial results by their achieved SBP differences, as these differences vary widely by trial (ranging from 1.3 to 15.4 mm Hg). This approach, which assumes that the effects of BP-lowering medication on cardiovascular and kidney outcomes are mediated through their BP-lowering effect alone, accounts for between-trial heterogeneity in achieved BP differences. This technique has not been implemented in previous meta-analyses focusing on CKD.[25,33,34] The method assumes an underlying log-linear association between BP and outcomes. Previous work has suggested this a reasonable assumption, as U-shaped associations in CKD appear to result from distorting effects from confounding.[24] Nevertheless, sensitivity analyses using nonstandardized trial results are presented for the key kidney and cardiovascular outcomes for comparison (and avoid any log-linear assumptions).

Statistical Analysis

Relative risks (RRs) per 10-mm Hg lower SBP were estimated using established methodology.[35] Specifically, we standardized the analyses by multiplying the log RR for each trial (and its standard error) by 10/d, where d was the between-group difference in SBP in that trial. Such standardization used the reported average achieved SBP levels in each arm or SBP difference (or, for some trials, the difference in change in BP from baseline) at about 1 year after randomization. This standardization approach does not change the significance of the standardized result for any given trial. Where not reported in individual trial publications, RRs and 95% confidence intervals were estimated using 2 × 2 contingency tables and used for standardization and subsequent meta-analysis.

Following standardization, trial results were meta-analyzed using weights proportional to the amount of statistical information (ie, inverse variance weighting). Specifically, the weight of the ith trial, w_i, was given by the inverse of the variance for the log-RR in trial i. Average BP differences were also obtained using inverse variance weighting with w_i as trial-specific weights. CKD vs non-CKD trial results were compared by standard χ^2 heterogeneity tests, and differences between trials ordered by achieved SBP difference were assessed by χ^2 tests for trend. Two-tailed P values were calculated for tests for trend, and 1-tailed P values for heterogeneity. No formal threshold for significance was defined. Main analyses included effects of intensive BP lowering on kidney disease progression outcomes using within-trial data from participants with and without CKD. An additional analysis was conducted combining within-trial and posttrial follow-up data. Absolute effects on rate of outcomes were estimated for the included populations by applying the overall estimated RR to the event rate in the control arm and are expressed in terms of outcomes avoided or caused (with intensive BP lowering) per 1000 person-years of treatment.

To mitigate against overemphasis on small studies, we implemented analyses without standardization as described, plus an additional sensitivity analysis limiting analyses to trials randomizing more than 500 participants. Data were presented as forest plots where applicable. All analyses were performed using R version 4.4.3 (R Foundation).

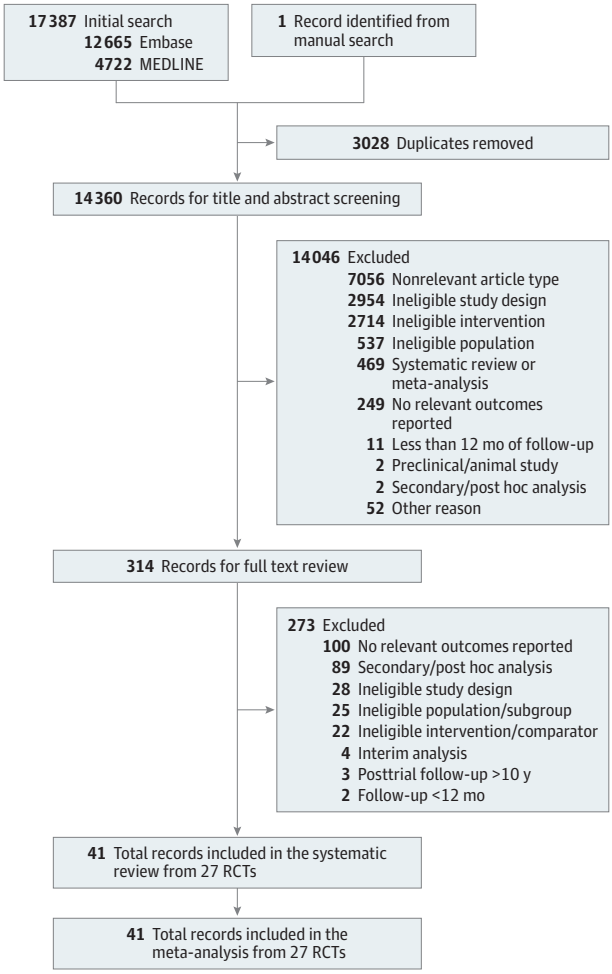
Results

The systematic search was conducted from inception up to January 16, 2026, and identified a total of 17 387 publications, including 1 study identified by manual search. After duplicates were removed, 14 360 were screened by title and abstract and 314 were selected for full-text review. Among them, 27 trials comprising a total of 41 reports[27-29,31,32,36-71] were included in this meta-analysis (**Figure 1**). Bias assessment resulted in 16 studies deemed at low risk of bias and 11 rated with some concerns (eTable 3 in Supplement 1).

The 27 trials included 88 830 participants, with average within-trial follow-up periods ranging from 1 to 8.4 years (**Table**). Fourteen trials provided information on patients with CKD.[27,28,31,32,36,42-44,57-62] These included a total of 1142 car-

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Figure 1. Flowchart of Study Selection



RCT indicates randomized clinical trial.

diovascular events among 11 103 patients and 422 kidney failure outcomes among 5855 patients during the within-trial period (Table). Among the 19 trials reporting data for participants without CKD,[27-29,37-41,47-58,64-67] 4498 cardiovascular events were reported among 76 785 participants, and 158 kidney failure events were reported among 31 647 participants. An additional 751 kidney failure outcomes were reported in 5 trials with available posttrial follow-up[45,46,69-71] (average within- and posttrial follow-up ranging from 5.6 to 10.6 years) (Table). JATOS included 2499 patients with eGFR less than 60 mL/min/1.73 m^2, but subgroup-specific event rates or RRs between intensive and standard arms were not reported.[47,50]

Intensive SBP targets varied across studies, but SBP targets less than 120 mm Hg[27,28,44,51,54,61,66] or less than 130 mm Hg[29,42,49,55,56,60,65] were most commonly used (in 7 of 27 [26%] and 7 of 27 studies [26%], respectively). Four trials used diastolic BP[36,38,40,41] and 2 used mean arterial pressure[31,32] targets. Trial-level achieved between-group SBP differences at about 1 year across all trials ranged from 1.3 to 15.4 mm Hg (Table). The overall achieved SBP reduction was similar in CKD and non-CKD populations (11.1 vs 11.2 mm Hg, respectively). Antihypertensive regimens used to achieve BP lowering by trial are presented in eTable 4 in Supplement 1.

A total of 5640 cardiovascular events were reported in 24 trials.[24-26,30,36-40,46-59,63-66] Overall, intensive BP lowering reduced the risk of cardiovascular events by 15% per 10-mm Hg reduction in SBP (RR per 10-mm Hg lower SBP, 0.85; 95% CI, 0.81-0.89) (**Figure 2**). Of these 24 trials, 11 reported effects of more intensive BP lowering among people with CKD; from a total 1142 cardiovascular events, 819 (72%) were reported in 4 large trials: 254 (22%) from the SPRINT-CKD subgroup,[62] 240 (21%) from the ACCORD-CKD subgroup,[57] 176 (15%) from the HOT-CKD subgroup,[43] and 149 (13%) from AASK.[32] Among participants with CKD, intensive BP lowering reduced cardiovascular events by 11% per 10-mm Hg lower SBP (RR per 10-mm Hg lower SBP, 0.89; 95% CI, 0.81-0.99), which was comparable to the reduction observed in the remaining 19 non-CKD populations of 16% (RR per 10-mm Hg lower SBP, 0.84; 95% CI, 0.80-0.88; CKD vs non-CKD population heterogeneity: $P = .26$) (Figure 2; eFigure 1 in Supplement 1). Overall, the estimated (SE) absolute reduction in cardiovascular events was 3.0 (0.4) outcomes avoided per 1000 person-years of treatment. Because cardiovascular events occurred more frequently among people with CKD than those without, the estimated (SE) absolute reduction in cardiovascular events with intensive BP lowering was at least as large among those with CKD than without (4.2 [1.2] vs 2.7 [0.4] outcomes avoided per 1000 person-years of treatment, respectively; $P = .24$).

Among the 11 trials[27,29,31,32,36,39,42,44-46,51,54,61,68] (37 502 participants) reporting 580 kidney failure outcomes, 4 trials contributed 487 outcomes (84%): 171 (29%) from AASK,[32] 127 (22%) from MDRD,[31] 117 (20%) from ACCORD,[51] and 72 (12%) from the REIN-2 trial.[42] Overall, there was no effect of intensive BP lowering on risk of kidney failure (RR per 10-mm Hg lower SBP, 0.97; 95% CI, 0.84-1.11), with similar results when CKD and non-CKD populations were compared (CKD vs non-CKD population heterogeneity: $P = .77$) (**Figure 3**; eFigure 2 in Supplement 1). Effects on kidney failure were similar to the main analyses when considering nonstandardized effect estimates (eFigure 2 in Supplement 1). There was no effect on kidney failure risk when within- and posttrial periods were combined (RR, 0.93; 95% CI, 0.84-1.02; 1331 outcomes) (eFigures 3 and 5 in Supplement 1). As there was no significant relative effect on intensive BP lowering on kidney failure outcomes, there was no absolute reduction in kidney failure overall or in either CKD or non-CKD populations.

Kidney disease progression outcomes using various thresholds of proportional changes in eGFR or serum creatinine were reported in 9 trials with CKD populations[27-29,32,36,38,46,47,50,54,60,62,68] (including 10 279 participants) and 6 trials with non-CKD populations[27-29,47,50,54,55,63,64,68] (including 41 832 participants). Intensive BP lowering was associated with increased risk of 30% or greater and 40% or greater eGFR declines (RR per 10-mm Hg lower SBP, 1.42; 95% CI, 1.28-1.58; and 1.47;

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Table. Characteristics of Included Trials and Achieved Blood Pressure (BP) Differences

Study	Study population	BP comparison, mm Hg	eGFR or Cr, mean (SD)	Proportion with diabetes, %	Baseline BP, mean (SD), mm Hg	BP difference, mm Hg	Achieved BP, mm Hg	Average (or total) within-trial follow-up, y	Average (or total) within- and posttrial follow-up, y
CKD									
AASK[32,46]	1094 African American participants with hypertensive kidney disease	MAP ≤92 vs 102-107	eGFR, 47 (13) mL/min/1.73 m^2	0	151 (24)/97 (14)	−13/−7	128/78 vs 141/85	4	8.8-12.2
ACCORD (CKD)[51,57,69]	1726 Individuals with type 2 diabetes and cardiovascular disease or risk factors with CKD (eGFR <60 mL/min/1.73 m^2) and/or albuminuria (UACR ≥30 µg/mg)	SBP <120 vs <140	Cr, 1.0 (0.3) mg/dL	100	143 (17)/76 (11)	−12.8/NR	123/NR vs 136/NR	4.7	5.6[a]
BPROAD (CKD)[28]	970 Participants with hypertension, type 2 diabetes, and CKD (eGFR <60 mL/min/1.73 m^2)	SBP <120 vs <140	NR	100	NR	−11.6/NR[a]	122/NR vs 133/NR[a]	4.2	NA
ESPRIT (CKD)[27]	677 Individuals with SBP ≥130 mm Hg, high cardiovascular risk, and CKD (eGFR <60 mL/min/1.73 m^2)	SBP <120 vs <140	eGFR, 53 (7) mL/min/1.73 m^2	39[a]	146 (10)/80 (11)	−13.3/−5.9	122/68 vs 135/74	3.4	NA
FANTASTIC[60]	341 Participants with SBP ≥130 mm Hg, type 2 diabetes, and CKD (UACR ≥30 µg/mg and eGFR ≥30 mL/min/1.73 m^2)	SBP <130 vs <140	Median (IQR) eGFR, 56.0 (42-75) mL/min/1.73 m^2	100	155 (10)/84 (10)	−4.8/NR	134/NR vs 139/NR	2.8	NA
HALT-PKD[59,70]	558 Participants with ADPKD (eGFR >60 mL/min/1.73 m^2) and hypertension	95-110/70-75 vs 120-130/70-80	eGFR, 92 (18) mL/min/1.73 m^2	0	127 (14)/80 (11)	−10/−7	108/71 vs 118/78	5.7	10.6
HOT (CKD)[25,43]	2821 Participants with DBP 100-115 mm Hg and CKD (Cr clearance <60 mL/min)[b]	DBP ≤80 vs ≤85 or ≤90	Cr, 1.24 (0.5) mg/dL	7	171 (15)/105 (6)	−3.4/−3.4	140/81 vs 143/84	3.8	NA
PERFORMANCE[61]	108 Participants with advanced CKD (eGFR ≤30 mL/min/1.73 m^2) and hypertension	SBP <120 vs less intensive (130-140)	Median (IQR) eGFR, 24 (18-27) mL/min/1.73 m^2	31	134 (20)/79 (11)[c]	−13.5/−6.8	125/73 vs 138/82	1.6	NA
MDRD[31,45]	840 Participants with eGFR 13-55 mL/min/1.73 m^2 and MAP <125 mm Hg	Low MAP (<92 mm Hg) vs usual MAP (<107 mm Hg)	eGFR, 33 (12) mL/min/1.73 m^2	5	130 (17)/80 (10)	−7.6/−3.8	126/77 vs 134/81	2.2	5.9
REIN-2[42]	338 Participants with nondiabetic proteinuric nephropathy	<130/80 vs DBP <90	eGFR, 35 (18) mL/min/1.73 m^2	0	137 (17)/84 (10)	−4.1/−2.8	130/80 vs 134/82	1.6	NA

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Table. Characteristics of Included Trials and Achieved Blood Pressure (BP) Differences (continued)

Study	Study population	BP comparison, mm Hg	eGFR or Cr, mean (SD)	Proportion with diabetes, %	Baseline BP, mean (SD), mm Hg	BP difference, mm Hg	Achieved BP, mm Hg	Average (or total) within-trial follow-up, y	Average (or total) within- and posttrial follow-up, y
SPRINT (CKD)[54,62,68,71]	2646 Participants with SBP ≥130 mm Hg and CKD (eGFR <60 mL/min/1.73 m^2) at baseline (excluding PKD)	SBP <120 vs <140	eGFR, 48 (10) mL/min/1.73 m^2	0	139 (16)/75 (12)	−13.6/−6.9	123/67 vs 137/74	3.3	8.6[a]
Schrier et al,[44] 2002	75 Participants with ADPKD and left ventricular hypertrophy	<120/80 vs 135-140/85-90	eGFR, 83 (29) mL/min/1.73 m^2	NR	143 (16)/95 (11)	−11/−8	116/77 vs 127/85	7	NA
SPS3 (CKD)[55,58]	474 Participants with recent MRI-defined lacunar infarction and eGFR <60 mL/min/1.73 m^2	SBP <130 vs 130-149	eGFR, 51 (7) mL/min/1.73 m^2	35	147 (21)/77 (11)	−10.5/−6.1	130/68 vs 141/74	3.7	NA
Toto et al,[36] 1995	77 Participants with DBP ≥95 mm Hg and CKD (GFR ≤70 mL/min/1.73 m^2) without diabetes	DBP 65-80 vs DBP 85-95	eGFR, 38 (2) mL/min/1.73 m^2	0	123 (18)/76 (9)[d]	−5/−5.7	133/81 vs 138/87	3.4	NA
Non-CKD									
ABCD (H)[37,40]	470 Participants with DBP ≥90 mm Hg and type 2 diabetes	DBP 75 vs 80-89	eGFR, 86 (36) mL/min/1.73 m^2	100	156 (18)/98 (7)	−6/−8	132/78 vs 138/86	5	NA
ABCD (N)[41]	480 Participants with DBP 80-89 mm Hg and type 2 diabetes	DBP −10 from baseline vs 80-89	eGFR, 84 (22) mL/min/1.73 m^2	100	136 (13)/84 (3)	−9/−6	128/75 vs 137/81[c]	5.3	NA
ACCORD (non-CKD)[51,57,69]	2952 Participants with type 2 diabetes and cardiovascular disease or risk factors without CKD	SBP <120 vs <140	Cr, 0.8 (0.2) mg/dL	100	137 (15)/76 (10)	−14/NR	120/NR vs 134/NR	4.7	5.6[a]
BPROAD (non-CKD)[28]	11 851 Participants with hypertension, type 2 diabetes, and increased risk of cardiovascular disease without CKD	SBP <120 vs <140	NR	100	NR	−11.6/NR[a]	122/NR vs 133/NR[a]	4.2	NA
Cardio-Sis[49]	1111 Participants with SBP ≥150 mm Hg and ≥1 cardiovascular risk factor (no diabetes)	SBP <130 vs <140	Cr, 1.10 (0.25) mg/dL	0	163 (11)/90 (9)	−3.8/−1.5	133/78 vs 138/80	2	NA
ESPRIT (non-CKD)[27]	10 578 Participants with SBP ≥130 mm Hg and high cardiovascular risk with eGFR >60 mL/min/1.73 m^2	SBP <120 vs <140	eGFR, 85 (12) mL/min/1.73 m^2	39[a]	147 (11)/83 (10)	−15.4/−6.9	120/70 vs 136/77	3.4	NA
HOMED-BP[53]	3518 Japanese participants with home readings of SBP 135-179 mm Hg or DBP 85-119 mm Hg	<125/<80 vs 125-134/80-84	NR	15	154 (17)/90 (12)	−1.3/−0.8	134/80 vs 135/81	5.3	NA
HOT (non-CKD)[38,43]	15 770 Participants with DBP 100-115 mm Hg with eGFR >60 mL/min/1.73 m^2[e]	DBP ≤80 vs ≤85 or ≤90	Cr, 0.96 (0.19) mg/dL	8	169 (14)/106 (3)[a]	−2.8/−3.1[a]	140/81 vs 143/84[a]	3.8	NA
INFINITY[65]	199 Participants aged ≥75 y with systolic hypertension and MRI evidence of white matter hyperintensity lesions	24-h SBP <130 vs <145	Cr, 1.09 (0.32) mg/dL	16	151 (16)/76 (10)	−15.2/NR	130/NR vs 146/NR	3	NA
JATOS[47,50]	4418 Older Japanese patients with SBP ≥160 mm Hg	SBP <140 vs ≥140 to <160	eGFR, 59 (10) mL/min/1.73 m^2	12	172 (10)/89 (9)	−9.7/−3.3	136/75 vs 146/78	2	NA
PAST-BP[56]	529 Patients with a past history of stroke or TIA with SBP ≥125 mm Hg	SBP <130 (or −10 if already <140) vs <140	NR	10	143 (14)/80 (10)	−2/−2.4	127/72 vs 129/74	1	NA
PODCAST[67]	83 Patients with recent stroke, SBP 125-170 mm Hg, and eGFR >45 mL/min/1.73 m^2	SBP <125 vs <140	NR	21	147 (19)/82 (11)	−10.6/−5.5	130/73 vs 141/77	2	NA
RESPECT[66]	1263 Participants aged 50-85 y with SBP 130-180 mm Hg or DBP 80-110 mm Hg with history of stroke within the previous 3 y	<120/80 vs <140/90 or <130/80 with risk factors	Cr, 0.82 (0.2) mg/dL	23	145 (13)/84 (10)	−8.3/−4.7	124/73 vs 132/76	3.9	NA
SPS3 (non-CKD)[55,58,63]	2543 Participants with recent MRI-defined lacunar infarction with eGFR ≥60 mL/min/1.73 m^2	SBP <130 vs 130-149	eGFR, 86 (15) mL/min/1.73 m^2	33	142 (18)/79 (10)	−11/−6.1	127/76 vs 138/70	3.7	NA

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Table. Characteristics of Included Trials and Achieved Blood Pressure (BP) Differences (continued) (continued)

Study	Study population	BP comparison, mm Hg	eGFR or Cr, mean (SD)	Proportion with diabetes, %	Baseline BP, mean (SD), mm Hg	BP difference, mm Hg	Achieved BP, mm Hg	Average (or total) within-trial follow-up, y	Average (or total) within- and posttrial follow-up, y
SPRINT (non-CKD)[54,64,68,71]	6677 Participants with SBP ≥130 mm Hg and 1 cardiovascular risk factor (without diabetes) with eGFR ≥60 mL/min/1.73 m^2	SBP <120 vs <140	eGFR, 81 (16) mL/min/1.73 m^2	0	140 (15)/79 (12)	−15/NR	121/NR vs 136/NR	3.3	8.6[a]
STEP[29]	8511 Patients aged 60-80 y with SBP 140-190 mm Hg or taking antihypertensive medication	SBP 110-<130 vs 130-<150	NR	19	146 (17)/83 (11)	−7.8/−2.8	128/76 vs 135/79	3.3	NA
UKPDS-HDS[39]	1148 Participants with BP ≥160/90 mm Hg not receiving treatment or ≥150/85 receiving treatment and type 2 diabetes	<150/85 vs <180/105	NR	100	160 (19)/94 (10)	−10/−5	144/82 vs 154/87	8.4	NA
VALISH[48]	3260 Older Japanese patients with SBP >160 mm Hg and DBP <90 mm Hg	SBP <140 vs ≥140 to <150	NR	12	170 (8)/81 (7)	−5.6/−1.7	137/75 vs 142/77	3.1	NA
Wei et al,[52] 2013	724 Chinese participants aged >70 y with SBP ≥150 mm Hg and/or DBP ≥90 mm Hg	≤140/90 vs ≤150/90	Cr, 1.15 (0.35) mg/dL	23	159 (16)/84 (10)	−14/−6	136/76 vs 150/82	4	NA

Abbreviations: AASK, African American Study of Kidney Disease and Hypertension; ABCD, Appropriate Blood Pressure Control in Diabetes (-H = hypertensive; -N = normotensive); ACCORD, Action to Control Cardiovascular Risk in Diabetes; ADPKD, autosomal-dominant polycystic kidney disease; BPROAD, Blood Pressure Control Target in Diabetes; Cardio-Sis, Usual vs tight control of systolic blood pressure in non-diabetic patients with hypertension; CKD, chronic kidney disease; Cr, creatinine; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; ESPRIT, Effects of Intensive Systolic Blood Pressure Lowering Treatment in Reducing Risk of Vascular Events Study; FANTASTIC, Fimasartan Proteinuria Sustained Reduction in Comparison With Losartan in Diabetic Chronic Kidney Disease; HALT-PKD, Halt Progression of Polycystic Kidney Disease; HOMED-BP, Hypertension Objective Treatment Based on Measurement by Electrical Devices of Blood Pressure; HOT, Hypertension Optimal Treatment; INFINITY, Intensive vs Standard Ambulatory Blood Pressure Lowering to Prevent Functional Decline in the Elderly; JATOS, Japanese Trial to Assess Optimal Systolic Blood Pressure in Elderly Hypertensive Patients; MAP, mean arterial pressure; MDRD, Modification of Diet in Renal Disease; MRI, magnetic resonance imaging; NA, not applicable; NR, not reported; PAST-BP, Prevention After Stroke-Blood Pressure; PERFORMANCE, Pilot to Examine Risk and Feasibility of Remote Management of BP From CKD Through ESRD; PKD, polycystic kidney disease; PODCAST, Prevention of Decline in Cognition After Stroke Trial; REIN-2, Ramipril Efficacy In Nephropathy-2; RESPECT, Recurrent Stroke Prevention Clinical Outcome Study; SBP, systolic blood pressure; SPRINT, Systolic Blood Pressure Intervention Trial; SPS3, Secondary Prevention of Small Subcortical Strokes; STEP, Strategy of Blood Pressure Intervention in the Elderly Hypertensive Patients; TIA, transient ischemic attack; UACR, urinary albumin to creatinine ratio; UKPDS-HDS, The UK Prospective Diabetes Study, Hypertension in Diabetes Study; VALISH, Valsartan in Elderly Isolated Systolic Hypertension Study.

SI conversion factor: To convert creatinine from mg/dL to µmol/L, multiply by 76.25.

[a] Reported for overall cohort only; not reported by CKD subgroup.

[b] Number of patients with CKD included in analysis (n = 2175) was reported in published data.[25]

[c] Mean (SD) estimated from median and IQR.

[d] SD estimated from standard error of the mean (SEM) or confidence interval.

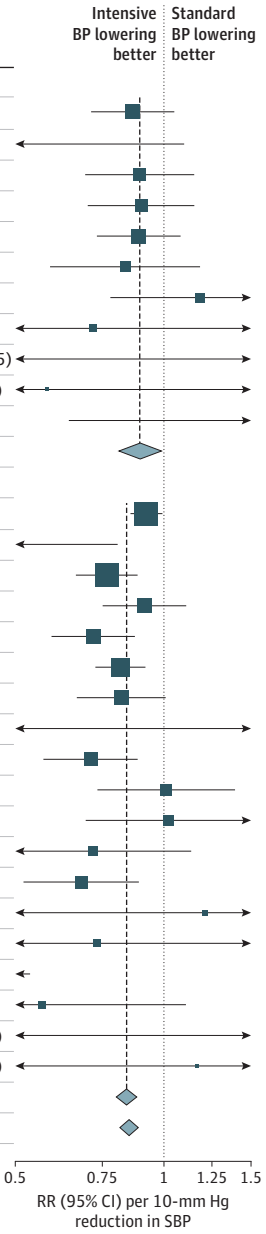
[e] Number of patients without CKD included in analysis (n = 16 615) was calculated by subtracting the number of patients with CKD reported in published data[25] from the total cohort (n = 18 790). These numbers differ slightly from those reported in the primary HOT publication.

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Figure 2. Forest Plot Showing Effects of Intensive vs Standard Blood Pressure (BP) Lowering on Major Cardiovascular Outcomes[a]

Study	Difference in SBP	Event, No./total No. (%)		Participant, No./total No. (%)		Rate per 1000 patient-years		RR (95% CI) per 10-mm Hg reduction in SBP
		Intensive BP lowering		Standard BP lowering		Intensive BP lowering	Standard BP lowering	
CKD								
SPRINT (CKD)[54,62,68,71]	13.6	118/1329 (8.9)		136/1316 (10.3)		27	31	0.86 (0.71-1.05)
PERFORMANCE[61]	13.5	0/66 (0.0)		5/42 (11.9)		0	74	0.13 (0.02-1.10)
ESPRIT (CKD)[27]	13.3	52/337 (15.4)		61/340 (17.9)		45	53	0.89 (0.69-1.15)
AASK[32,46]	13	71/540 (13.1)		78/554 (14.1)		33	35	0.90 (0.70-1.15)
ACCORD (CKD)[51,57,69]	12.8							0.89 (0.73-1.08)
BPROAD (CKD)[28]	11.6	44/501 (8.8)		55/469 (11.7)		21	28	0.83 (0.59-1.18)
SPS3 (CKD)[55,58]	10.5	39/247 (15.8)		30/227 (13.2)		43	36	1.18 (0.78-1.80)
HALT-PKD[59,70]	10	9/274 (3.3)		13/284 (4.6)		6	8	0.72 (0.31-1.65)
FANTASTIC[60]	4.8	4/169 (2.4)		2/172 (1.2)		8	4	4.60 (0.13-158.75)
REIN-2[42]	4.1	4/167 (2.4)		5/168 (3.0)		15	19	0.58 (0.02-13.52)
HOT (CKD)[25,43]	3.4	66/744 (8.9)		110/1431 (7.7)		23	20	1.51 (0.64-3.55)
Overall CKD	11.1	407/4374 (9.3)[b]		495/5003 (9.9)[b]		26	28	0.89 (0.81-0.99)
Non-CKD								
ESPRIT (non-CKD)[27]	15.4	495/5287 (9.4)		562/5291 (10.6)		28	31	0.92 (0.86-0.99)
INFINITY[65]	15.2	4/99 (4.0)		17/100 (17.0)		14	57	0.39 (0.19-0.81)
SPRINT (non-CKD)[54,64,68,71]	15	146/3349 (4.4)		218/3367 (6.5)		13	20	0.77 (0.66-0.88)
ACCORD (non-CKD)[51,57,69]	14							0.91 (0.75-1.11)
Wei et al,[52] 2013	14	40/363 (11.0)		67/361 (18.6)		28	46	0.72 (0.59-0.87)
BPROAD (non-CKD)[28]	11.6	349/5913 (5.9)		437/5938 (7.4)		14	18	0.82 (0.73-0.92)
SPS3 (non-CKD)[55,58,63]	11.1	116/1253 (9.3)		149/1290 (11.6)		25	31	0.82 (0.67-1.01)
PODCAST[67]	10.6	1/41 (2.4)		4/42 (9.5)				0.28 (0.04-2.10)
UKPDS-HDS[39]	10	153/758 (20.2)		111/390 (28.5)		24	34	0.71 (0.57-0.88)
JATOS[47,50]	9.7	78/2212 (3.5)		77/2206 (3.5)		18	17	1.01 (0.73-1.39)
ABCD (N)[41]	9	48/237 (20.3)		48/243 (19.8)		38	37	1.02 (0.69-1.51)
RESPECT[66]	8.3	46/633 (7.3)		59/630 (9.4)		19	24	0.72 (0.45-1.13)
STEP[29]	7.8	147/4243 (3.5)		196/4268 (4.6)		10	14	0.68 (0.52-0.89)
ABCD (H)[37,40]	6	16/237 (6.8)		14/231 (6.1)		14	12	1.21 (0.38-3.83)
VALISH[48]	5.6	32/1545 (2.1)		37/1534 (2.4)		7	8	0.73 (0.32-1.67)
Cardio-Sis[49]	3.8	23/557 (4.1)		47/553 (8.5)		21	42	0.15 (0.04-0.54)
HOT (non-CKD)[38,43]	2.8	151/5518 (2.7)		356/11 097 (3.2)		7	8	0.57 (0.29-1.11)
PAST-BP[56]	2	1/266 (0.4)		5/263 (1.9)		4	19	0.00 (0.00-19.16)
HOMED-BP[53]	1.3	26/1759 (1.5)		25/1759 (1.4)		3	3	1.16 (0.02-78.52)
Overall non-CKD	11.2	1872/34 270 (5.5)[b]		2429/39 563 (6.1)[b]		14	18	0.84 (0.80-0.88)
Overall	11.2	2279/38 644 (5.9)[b]		2924/44 566 (6.6)[b]		16	19	0.85 (0.81-0.89)

CKD vs non-CKD het test: $P = .26$



Relative risks (RRs) presented per 10-mm Hg lower systolic BP (SBP). See eFigure 1 in Supplement 1 for analysis before and after standardization to a 10-mm Hg lower SBP. Heterogeneity within chronic kidney disease (CKD) and non-CKD subgroups was assessed using the Cochran Q test (CKD: $P = .65$; non-CKD: $P = .01$). Het indicates heterogeneity.

[a]See eTable 2 in Supplement 1 for detailed outcome definitions.

[b]Does not include numbers of events or participants from ACCORD, as these were not reported by CKD status.

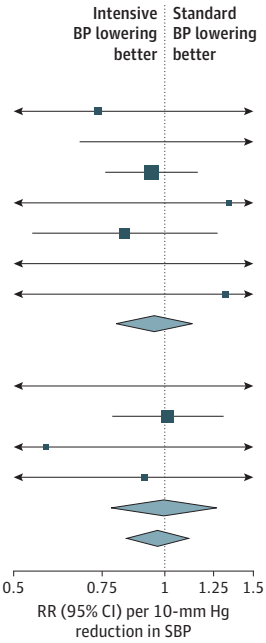
95% CI, 1.30-1.66, respectively) (**Figure 4**; eFigures 3 and 4 in Supplement 1). Intensive BP lowering did not significantly increase the risk of sustained decline of 50% or greater in eGFR (RR per 10-mm Hg lower SBP, 1.29; 95% CI, 0.94-1.76) or a composite of doubling of serum creatinine or kidney failure (RR per 10-mm Hg lower SBP, 0.97; 95% CI, 0.83-1.14). Findings were similar when CKD vs non-CKD results were compared (Figure 4; eFigure 3 in Supplement 1) and when additional information using posttrial follow-up data from AASK,[46] ACCORD,[69] HALT-PKD,[70] MDRD,[45] and SPRINT[68,71] trials were included in analyses (eFigures 3 and 5 in Supplement 1). When considering posttrial follow-up data, intensive BP lowering appeared to increase doubling of serum creatinine (RR, 1.15; 95% CI, 1.04-1.27; 4 trials) without an increase in kidney failure (RR, 0.93; 95% CI, 0.84-1.02; 12 trials) (eFigures 3 and 5 in Supplement 1).

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Figure 3. Forest Plot Showing Effects of Intensive vs Standard Blood Pressure (BP) Lowering on Kidney Failure Outcomes[a]

Study	Difference in SBP	Event, No./total No. (%) Intensive BP lowering	Participant, No./total No. (%) Standard BP lowering	Rate per 1000 patient-years Intensive BP lowering	Standard BP lowering	RR (95% CI) per 10-mm Hg reduction in SBP
CKD						
SPRINT (CKD)[54,62,68,71]	13.6	7/1330 (0.5)	10/1316 (0.8)	2	2	0.74 (0.35-1.55)
PERFORMANCE[61]	13.5	14/66 (21.2)	4/42 (9.5)	133	60	1.55 (0.68-3.56)
AASK[32,46]	13	81/540 (15.0)	90/554 (16.2)	38	41	0.94 (0.76-1.16)
Schrier et al,[44] 2002	11	5/41 (12.2)	3/34 (8.8)	17	13	1.34 (0.39-4.61)
MDRD[31,45]	7.6	61/432 (14.1)	66/408 (16.2)	64	74	0.83 (0.54-1.27)
Toto et al,[36] 1995	5	7/42 (16.7)	2/35 (5.7)	49	17	8.53 (0.42-172.07)
REIN-2[42]	4.1	38/169 (22.5)	34/169 (20.1)	141	126	1.32 (0.48-3.62)
Overall CKD	9.6	213/2620 (8.1)	209/2558 (8.2)	32	32	0.95 (0.80-1.13)
Non-CKD						
ESPRIT (non-CKD)[27]	15.4	1/5287 (0.0)	0/5291 (0.0)	0	0	1.58 (0.18-14.01)
ACCORD (non-CKD)[51,57,69]	14.2	59/2362 (2.5)	58/2371 (2.4)	5	5	1.01 (0.79-1.31)
UKPDS-HDS[39]	10	8/758 (1.1)	7/390 (1.8)	1	2	0.58 (0.15-2.24)
STEP[29]	7.8	12/4243 (0.3)	13/4268 (0.3)	1	1	0.91 (0.33-2.52)
Overall non-CKD	12.9	80/12 650 (0.6)	78/12 320 (0.6)	1	1	1.00 (0.78-1.27)
Overall	10.4	293/15 270 (1.9)	287/14 878 (1.9)	7	7	0.97 (0.84-1.11)

CKD vs non-CKD het test: $P = .77$



Relative risks (RRs) presented per 10-mm Hg lower systolic BP (SBP). Studies with 0 vs 0 number of events not shown. See eFigure 2 in Supplement 1 for analysis before and after standardization to a 10-mm Hg lower SBP. Heterogeneity within chronic kidney disease (CKD) and non-CKD subgroups was assessed using the Cochran *Q* test (CKD: $P = .67$; non-CKD: $P = .84$). Het indicates heterogeneity.

[a]See eTable 2 in Supplement 1 for detailed outcome definitions.

A total of 2737 deaths were reported in 24 trials.[27-29,32,36,38,39,41,42,44,48-60,65-68] Overall, intensive BP lowering reduced overall mortality by 11% per 10-mm Hg reduction in SBP (RR per 10-mm Hg lower SBP, 0.89; 95% CI, 0.83-0.95) (Figure 4), with no evidence of heterogeneity by CKD status (eFigure 6 in Supplement 1). Analyses without standardization for achieved SBP differences and excluding trials with fewer than 500 participants showed similar results to the main analyses (eTable 5, eFigures 1 and 2 in Supplement 1). Funnel plots suggested some asymmetry for cardiovascular events, although not for kidney failure (in both cases, the test for asymmetry was nonsignificant) (eFigure 7 in Supplement 1).

Discussion

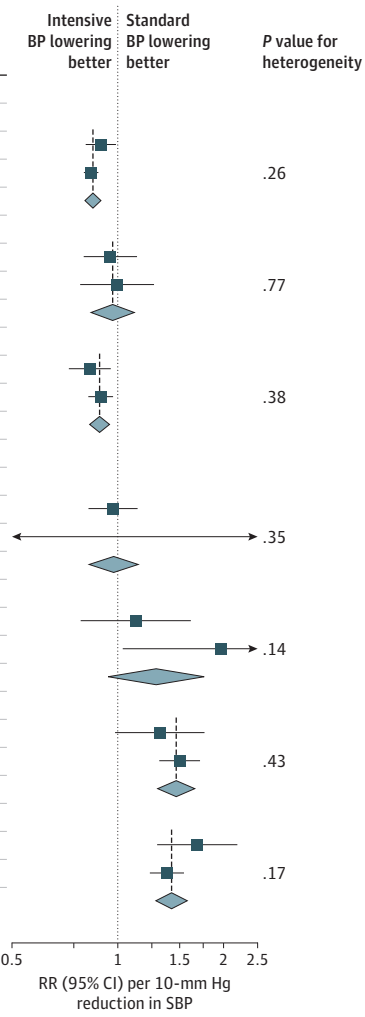
This new meta-analysis incorporates 3 new major intensive BP-lowering trials to consider cardiovascular and kidney effects of intensive BP lowering in patients with and without CKD. Data were aggregated from 27 trials, including almost 90 000 participants with about 5500 cardiovascular events and 1300 kidney failure events. Overall, there was a 15% reduction in risk of cardiovascular events for each 10-mm Hg lower SBP, irrespective of CKD status. Because cardiovascular events were more frequent among the studied CKD populations, the estimated absolute benefits from intensive BP lowering appeared at least as large among adults with CKD than those without CKD. In contrast, there was no evidence that intensive BP lowering affected the risk of kidney failure when within-trial and long-term posttrial follow-up data were analyzed, despite increased risk for declines in eGFR.

A recent Cochrane meta-analysis focusing solely on data from patients with CKD reported that intensive BP lowering had no significant effect on risk of cardiovascular events compared to standard BP lowering (hazard ratio [HR], 1.00, 95% CI, 0.87-1.15).[25] Compared to that systematic review, the present analysis considers the totality of trial evidence in both CKD and non-CKD participants before then considering effects by CKD status. New data from 6 additional trials include more than a 30% increase in the number of available cardiovascular events to analyze among patients with CKD (693 vs 1142 cardiovascular events in the 2 reports, respectively). The findings of homogenous relative effects of BP lowering on cardiovascular risk in patients with and without CKD are consistent with the recent Blood Pressure Lowering Treatment Trialists' Collaboration (BPLTTC) cardiovascular outcomes meta-analysis combining placebo-controlled, head-to-head antihypertensive and intensive vs standard BP-lowering trials.[26] Our findings on cardiovascular disease are an important update, as we focused solely on intensive vs standard BP-lowering trials and incorporated additional trial data from 15 trials including approximately 60 000 participants and 3500 cardiovascular events.

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Figure 4. Forest Plot Showing Effects of Intensive vs Standard Blood Pressure (BP) Lowering on Different Disease Progression Outcomes by Chronic Kidney Disease (CKD) Status

Disease progression definition	Difference in SBP, mm Hg	Studies, No.	Event, No./total No. (%)		RR (95% CI) per 10-mm Hg reduction in SBP	*P* value for heterogeneity
			Intensive BP lowering	Standard BP lowering		
Clinical outcomes						
Major cardiovascular events						
CKD	11.1	11	407/4374 (9.3)	495/5003 (9.9)	0.89 (0.81-0.99)	
Non-CKD	11.2	19	1872/34 270 (5.5)	2429/39 563 (6.1)	0.84 (0.80-0.88)	.26
Overall	11.2	24	2279/38 644 (5.9)	2924/44 566 (6.6)	0.85 (0.81-0.89)	
Kidney failure alone						
CKD	9.6	7	213/2620 (8.1)	209/2558 (8.2)	0.95 (0.80-1.13)	
Non-CKD	12.9	4	80/12 650 (0.6)	78/12 320 (0.6)	1.00 (0.78-1.27)	.77
Overall	10.4	11	293/15 270 (1.9)	287/14 878 (1.9)	0.97 (0.84-1.11)	
All-cause mortality[a]						
CKD	11.1	10	198/3721 (5.3)	272/4389 (6.2)	0.83 (0.73-0.96)	
Non-CKD	9.6	17	862/28 120 (3.1)	1057/33 394 (3.2)	0.89 (0.82-0.97)	.38
Overall	10	22	1229/38 255 (3.2)	1508/44 190 (3.4)	0.89 (0.83-0.95)	
Biochemical outcomes						
Doubling of serum creatinine or kidney failure						
CKD	12.6	3	137/1812 (7.6)	148/1858 (8.0)	0.97 (0.83-1.14)	
Non-CKD	7.6	1	3/982 (0.3)	1/936 (0.1)	3.98 (0.20-78.10)	.35
Overall	12.5	3	140/2794 (5.0)	149/2794 (5.3)	0.97 (0.83-1.14)	
≥50% Decline in eGFR						
CKD	9.3	5	60/2711 (2.2)	61/3221 (1.9)	1.12 (0.78-1.61)	
Non-CKD	15	1	14/3332 (0.4)	5/3345 (0.1)	1.96 (1.03-3.73)	.14
Overall	10.1	5	74/6043 (1.2)	66/6566 (1.0)	1.29 (0.94-1.76)	
≥40% Decline in eGFR						
CKD	13.4	2	59/1667 (3.5)	40/1656 (2.4)	1.32 (0.98-1.77)	
Non-CKD	12.8	3	197/8619 (2.3)	97/8636 (1.1)	1.50 (1.31-1.71)	.43
Overall	12.9	3	256/10 286 (2.5)	137/10 292 (1.3)	1.47 (1.30-1.66)	
≥30% Decline in eGFR						
CKD	13.6	1	92/1330 (6.9)	44/1316 (3.3)	1.68 (1.29-2.19)	
Non-CKD	11.2	4	748/14 627 (5.1)	563/14 709 (3.8)	1.38 (1.23-1.54)	.17
Overall	11.4	4	840/15 957 (5.3)	607/16 025 (3.8)	1.42 (1.28-1.58)	



Relative risks (RRs) presented per 10-mm Hg lower systolic BP (SBP). eGFR indicates estimated glomerular filtration rate.

[a]All-cause mortality was conducted as an exploratory analysis. See eTable 2 in Supplement 1 for detailed outcome definitions.

We found intensive BP lowering increased the risk of a range of kidney progression outcomes based on 40% or greater or 30% or greater sustained declines in eGFR. In the SPRINT trial, the intensive SBP target of less than 120 mm Hg—implemented using largely unattended standardized measurements[72]—led to increased risks of 40% or greater and 30% or greater declines in eGFR. In SPRINT, a hazard of acute kidney injury (AKI) adverse events was also evident (204 of 4678 [4.4%] vs 120 of 4683 [2.6%]; HR, 1.71; *P* < .001).[54] Similarly, in the recent ESPRIT trial, an intensive SBP target of less than 120 mm Hg—measured using clinician-attended standardized office-based BP—increased the risk of 40% or greater decline in eGFR.[27] However, despite these potential kidney safety concerns, our meta-analysis included 1331 kidney failure outcomes recorded during within- and posttrial periods and did not demonstrate any hazard of kidney failure.

Intensive BP lowering in the recent large trials was achieved with greater use of diuretics and calcium-channel blockers compared with the standard BP arm but only modest differences in use of renin-angiotensin system inhibitors between study arms.[27,54] For example, use of diuretics at study end in the intensive vs standard arms was 43% vs 15% in ESPRIT,[27] 67% vs 43% in SPRINT,[54] and 26% vs 10% in BPROAD (eTable 4 in Supplement 1).[28] Kidney disease outcomes based on smaller sustained percentage eGFR declines, and particularly 30% or greater declines, are less sensitive surrogates of kidney failure when assessing treatment, which causes an acute eGFR dip.[73] It is therefore plausible that the reported pattern of increased risk of declines in eGFR observed with more intensive BP-lowering treatment may reflect hemodynamic responses to the additional treatment with diuretics required to achieve lower BP targets.[74] Although this is supported by the absence of a sig-

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nal for kidney failure, a small harm is not excluded, and it is prudent to monitor BP, eGFR, and electrolytes carefully when implementing an intensive strategy.

In addition to adverse effects on AKI, other meta-analyses have highlighted that intensive BP lowering can increase risk of adverse events attributed to hypotension, including syncope and falls.[75] All-cause mortality is a composite outcome of many different underlying causes of death, rendering it particularly insensitive to benefits and harms of interventions in patients with CKD, who have a wide range of causes of death.[76] Nevertheless, exploration of the effects of intensive BP lowering on mortality were reassuring and even suggested net mortality benefits in the studied patients with and without CKD. Among the studies included in the analysis, there was also evidence of a reduction in albuminuria among intensively treated participants, with incident albuminuria reduced by 13% and 29% in people without CKD in BPROAD and SPRINT, respectively.[28,68]

Limitations

Despite its size, this study has some limitations. First, we relied mainly on tabular data from the reported randomized clinical trials to generate treatment effect estimates. Individual participant-level data would allow for some investigation of individual components of composite outcomes and clinically relevant subgroup analyses by diabetes status, eGFR, and albuminuria categories. However, more intensive vs standard trials are needed to definitively confirm benefits on different types of cardiovascular outcomes in patients with an eGFR less than 30 mL/min/1.73 m^2, where some uncertainty remains, even in BPLTTC analyses.[11,26] Second, some participants included in non-CKD analyses may have occult or overt CKD; these participants are likely to disproportionately contribute to kidney-related outcomes among non-CKD trials. While this may reduce power to detect differences between CKD and non-CKD populations and may affect estimates of absolute benefits by subgroup, it will not affect the overall point estimates. Finally, different trials used differing methods of measuring BP and different target parameters (eg, targeting systolic or diastolic BP), contributing to some between-trial heterogeneity.

Conclusions

In summary, per the results of this systematic review and meta-analysis, more intensive BP lowering reduced risk of cardiovascular events by 15% for each 10-mm Hg lower SBP, irrespective of CKD status. In the analyzed populations, absolute cardiovascular benefits of intensive BP lowering in CKD are at least as large as benefits in people without CKD. While more intensive BP lowering increased the risk of sustained declines in kidney function, these did not translate into an increased risk of kidney failure, with a suggestion there are net benefits on mortality. These data should encourage clinical guidelines to recommend intensive BP lowering in patients with and without CKD to reduce cardiovascular risk and encourage clinicians to implement such regimens with careful kidney function monitoring.

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