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Outcomes of Intensive Blood Pressure Lowering in Older Hypertensive Patients

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ABSTRACT

BACKGROUND The 2014 Eighth Joint National Committee panel recommended a therapeutic target of systolic blood pressure (BP) <150 mm Hg in patients ≥60 years of age, a departure from prior recommendation of <140 mm Hg.

OBJECTIVES This study assessed the efficacy and safety of intensive BP-lowering strategies in older (age ≥65 years) hypertensive patients.

METHODS The MEDLINE, Scopus, EMBASE, and Cochrane databases were searched for all relevant randomized controlled trials from 1965 through July 1, 2016. Cardiovascular (major adverse cardiovascular events [MACE], cardiovascular mortality, stroke, myocardial infarction, and heart failure), and safety (serious adverse events and renal failure) were evaluated. Random and fixed effects analysis were used to calculate pooled relative risks (RRs) and 95% confidence intervals (CIs).

RESULTS We identified 4 high-quality trials involving 10,857 older hypertensive patients with a mean follow-up of 3.1 years. Intensive BP lowering was associated with a 29% reduction in MACE (RR: 0.71; 95% CI: 0.60 to 0.84), 33% in cardiovascular mortality (RR: 0.67; 95% CI: 0.45 to 0.98), and 37% in heart failure (RR: 0.63; 95% CI: 0.43 to 0.99) compared with standard BP lowering. Rates of myocardial infarction and stroke did not differ between the 2 groups. There was no significant difference in the incidence of serious adverse events (RR: 1.02; 95% CI: 0.94 to 1.09) or renal failure (RR: 1.81; 95% CI: 0.86 to 3.80) between the 2 groups. The fixed effects model yielded largely similar results, except for an increase in the risk of renal failure (RR: 2.03; 95% CI: 1.30 to 3.18) with intensive BP-lowering therapy.

CONCLUSIONS In older hypertensive patients, intensive BP control (systolic BP <140 mm Hg) decreased MACE, including cardiovascular mortality and heart failure. Data on adverse events were limited, but suggested an increased risk of renal failure. When considering intensive BP control, clinicians should carefully weigh benefits against potential risks. (J Am Coll Cardiol 2017;69:486–93) © 2017 by the American College of Cardiology Foundation.

In the United States, the number of individuals age ≥65 years is projected to nearly double to 84 million by 2050 (1). The prevalence of hypertension is also expected to increase in parallel in this rapidly aging population, for whom cardiovascular disease remains the major cause of mortality and morbidity (2). The 2014 Eighth Joint National Committee (JNC 8) panel recommended a therapeutic target of systolic blood pressure (BP) <150 mm Hg in patients ≥60 years of age, a departure from prior recommendations of <140 mm Hg (3). However, many experts (4) and subsequent analyses (5) have argued against lowering the BP cut-off and continue to recommend a systolic BP treatment goal of <140 mm Hg. The recent publication of the pre-specified subgroup analysis of SPRINT-SENIOR (Systolic Blood Pressure Intervention Trial in older adults) in patients age ≥75 years has re-ignited the controversy of the optimal BP target in older hypertensive patients (6). The SPRINT-SENIOR trial evaluated a more aggressive

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strategy of a systolic BP target of <120 mm Hg versus a target of <140 mm Hg and showed a significant reduction of fatal and nonfatal major cardiovascular events and all-cause mortality, with no increase in serious adverse events with intensive treatment in patients age ≥75 years [6]. We aimed to assess the efficacy and safety of intensive BP-lowering strategies in older (age ≥65 years) hypertensive patients on the basis of the available evidence from all randomized controlled trials (RCTs).

METHODS

DATA SOURCES AND SEARCHES. We performed a systematic search, without language restriction, using the MEDLINE, Scopus, EMBASE, and Cochrane databases from 1965 to July 1, 2016, for RCTs comparing intensive BP lowering versus standard/liberal BP lowering in older hypertensive patients. Furthermore, we performed manual searches through the reference lists of studies, reviews, and pertinent meta-analyses. The search key words included the following MeSH terms: randomized controlled trial, target blood pressure, goal blood pressure, intensive blood pressure, tight blood pressure, elderly, and older patients (Online Table 1).

STUDY SELECTION. Studies were included if they met the following criteria: 1) RCTs comparing intensive versus standard or less intensive BP control; 2) including only older patients (≥65 years) with hypertension; and 3) providing long-term data on cardiovascular and safety outcomes. Two physician reviewers (C.B. and S.B.) independently performed the data search, reviewed the originally identified titles and abstracts, and selected studies for pooled analysis on the basis of the inclusion criteria. Any divergence was resolved by consensus.

DATA EXTRACTION AND QUALITY ASSESSMENT. We extracted the following data from individual studies: first author, year of publication, individual study inclusion and exclusion criteria, study and patient's characteristics, follow-up duration, and clinical outcomes in intensive and standard groups. Two investigators (C.B. and S.B.) independently assessed the study quality using Jadad criteria [7] as well as by the Cochrane collaboration's tool for assessing the bias in randomized trials [8], focusing on the following domains: sequence generation, allocation concealment, blinding, outcomes assessment, and selective reporting.

STUDY OUTCOMES. We evaluated the following cardiovascular outcomes: 1) major adverse cardiovascular events (MACE); 2) cardiovascular mortality; 3) stroke; 4) myocardial infarction (MI); and 5) heart failure (HF). Safety outcomes of serious adverse events and renal failure were evaluated. The definition of MACE differed across studies, and the trial-specific definitions for each outcome were used.

DATA SYNTHESIS AND ANALYSIS. Statistical analysis was performed per recommendations from the Cochrane Collaboration and the Preferred Reporting Items for Systematic reviews and Meta-analyses guidelines [9,10] (Online Table 2). The analysis was performed on an intention-to-treat basis. Considering that the heterogeneity of the included trials might influence the treatment effect, we used a random-effects model as the primary analysis to examine relative risks (RRs) and 95% confidence intervals (CIs) [11]. The results were confirmed by a fixed effects model to avoid small studies being overly weighted. Heterogeneity was assessed using Higgins and Thompson's I^2 statistic. I^2 is the proportion of total variation observed between the trials attributable to differences between trials rather than sampling error (chance), with I^2 values of <25%, 50 to 75%, and >75% corresponding to low, moderate, and high levels of heterogeneity, respectively [12]. Publication bias was not evaluated due to the small number of trials limiting the ability of funnel plots or regression analysis to test for bias [10]. A meta-regression analysis was performed to explore the relationship between achieved mean systolic BP difference in the intensive and standard BP groups and outcomes. We used residual maximum likelihood to estimate the additive (between-study) component of variance Tau^2 for the meta-regression analysis. A 2-tailed $p < 0.05$ was considered statistically significant for all analyses. Statistical analysis was performed using Stata 11 (Stata Corp., College Station, Texas) and RevMan version 5.02 (Nordic Cochrane Center, Copenhagen, the Netherlands).

RESULTS

Our search identified 22 potential RCTs, but the majority of trials did not provide separate results for adults 65 years or older. Four trials [6,13–15] met our eligibility criteria (Online Figure 1). A total of 10,857 older hypertensive patients from 4 RCTs were included in the analysis. Of these, 5,437 patients were randomized to intensive BP control, whereas 5,420 patients were randomized to standard BP control strategy. The mean follow-up duration across the trials was 3.1 years (2 to 4 years). JATOS (Japanese Trial to

TABLE 1 Characteristics of Trials

	JATOS (13)	SPRINT-SENIOR (6)	VALISH (14)	Wei et al. (15)
Yr	2008	2016	2010	2013
Participants	4,418	2,636	3,079	724
Inclusion criteria	Essential hypertension, age 65–85 yrs	Hypertension, age ≥75 yrs at increased risk for CVD (history of clinical or subclinical CVD, chronic kidney disease, a 10-yr Framingham general CVD risk ≥15%)	Isolated systolic hypertension, age 70-85 yrs	Essential hypertension, age ≥70 yrs
Trial location	Japan	North America	Japan	China
Comparison	Intensive (<140 mm Hg) vs. standard (140-159 mm Hg) lowering	Intensive (<120 mm Hg) vs. standard (<140 mm Hg) lowering	Intensive (<140 mm Hg) vs. standard (140-149 mm Hg) lowering	Intensive (<140 mm Hg) vs. standard (140-149 mm Hg) lowering
Drug strategy	Efonidipine with add-on other antihypertensive agents if needed.	Protocol based	Valsartan with add-on other antihypertensive agents if needed.	Protocol based
Median follow-up, yrs	2	3.1	3.1	4*
MACE definition	MI, angina pectoris requiring hospitalization, heart failure, sudden death, dissecting aneurysms of the aorta, and occlusive arterial disease	Nonfatal MI, acute coronary syndrome not resulting in a MI, nonfatal stroke, nonfatal acute decompensated heart failure, and death from cardiovascular causes	Cardiovascular death, nonfatal stroke, and nonfatal myocardial infarction	Fatal/nonfatal stroke, acute MI, and other cardiovascular deaths (sudden death and heart failure death)
Mean in-treatment difference, mm Hg	9.7/3.3	11.4/5.2	5.4/1.7	14/6

*Mean follow-up, yrs.

CVD = cardiovascular diseases; JATOS = Japanese Trial to Assess Optimal Systolic Blood Pressure in Elderly Hypertensive Patients; MACE = major adverse cardiovascular event(s); MI = myocardial infarction; SPRINT-SENIOR = Systolic Blood Pressure Intervention Trial in older adults; VALISH = Valsartan in Elderly Isolated Systolic Hypertension.

Assess Optimal Systolic Blood Pressure in Elderly Hypertensive Patients) (13), VALISH (Valsartan in Elderly Isolated Systolic Hypertension) (14), and a trial by Wei et al. (15) tested an intensive strategy of target systolic BP <140 mm Hg versus a standard BP-lowering strategy of systolic BP >140 mm Hg. The SPRINT-SENIOR trial evaluated intensive (<120 mm Hg) versus standard (<140 mm Hg) systolic BP targets (6). The characteristics of the included trials are shown in Table 1. The exclusion criteria used in each trial is presented in Online Table 3. The JATOS trial included patients age ≥65 years, VALISH and Wei et al. (15) included patients age ≥70 years, and the SPRINT-SENIOR trial included patients age ≥75 years. The characteristics of patients in the included trials are shown in Table 2. The SPRINT-SENIOR trial excluded patients with diabetes, and the proportion of patients with diabetes in the rest of the trials was low. Assessment of reporting quality and risk of bias is presented in Online Table 4. All studies were rated as high quality on the basis of the Jadad scale, and no evidence of high risk of bias was noted using the Cochrane tool.

An intensive BP control strategy significantly decreased MACE by 29% when compared with a standard strategy (3.7% vs. 5.2%; RR: 0.71; 95% CI: 0.60 to 0.84; p = 0.0001) (Figure 1A, Table 3). Similarly, intensive BP control resulted in a 33% reduction in cardiovascular mortality (1.1% vs. 1.7%; RR: 0.67; 95% CI: 0.45 to 0.98; p = 0.04) when compared with standard BP control (Figure 1B). Rates for MI (1.0% vs. 1.3%; RR: 0.79; 95% CI: 0.56 to 1.12; p = 0.18) and stroke (2.1% vs. 2.6%; RR: 0.80; 95% CI: 0.61 to 1.05; p = 0.11) were numerically lower with intensive BP control; this was not statistically significant (Figures 1C and 1D). The risk for HF was significantly decreased in the intensive BP group (1.3% vs. 2.0%; RR: 0.63; 95% CI: 0.40 to 0.99; p = 0.04) (Figure 1E). For safety outcomes, we extracted data on serious adverse events and renal failure from the included studies. There was no significant difference in incidence of serious adverse events (25.1% vs. 24.7%; RR: 1.02; 95% CI: 0.94 to 1.09; p = 0.69) and renal failure (1.1% vs. 0.6%; RR: 1.81; 95% CI: 0.86 to 3.80; p = 0.12) between intensive and standard BP lowering groups (Figure 2, Table 3).

No heterogeneity was found in analysis for MACE and MI outcomes; low heterogeneity was observed for cardiovascular mortality (I^2 = 25%), stroke (I^2 = 19%), HF (I^2 = 21%), and serious adverse events (I^2 = 19%) outcomes; and moderate heterogeneity was found for renal failure (I^2 = 46%). Analysis by a fixed effects model yielded largely similar results, except that intensive BP lowering was associated with an increased risk of renal failure (RR: 2.03; 95% CI: 1.30 to 3.18) (Online Table 5).

TABLE 2 Characteristics of Patients in the Included Trials

	JATOS (13)		SPRINT-SENIOR (6)		VALISH (14)		Wei et al. (15)	
	Intensive	Standard	Intensive	Standard	Intensive	Standard	Intensive	Standard
Age, yrs	NR	NR	80 ± 4	80 ± 4	76 ± 4	76 ± 4	77 ± 5	77 ± 5
Male	40	38	62.1	62	37.7	37.5	66.9	65.7
Diabetes	11.9	11.7	0	0	13.7	12.3	22.0	24.7
History of CVD	7.6	7.2	25.7	23.4	13.3	13.2	6.9	6.4
Baseline SBP, mm Hg	171.6 ± 9.7	171.5 ± 9.8	141.6 ± 15.7	141.6 ± 15.8	169.5 ± 7.9	169.6 ± 7.9	158.8 ± 16.0	160.3 ± 16.9
Baseline DBP, mm Hg	89.1 ± 9.5	89.10 ± 9.54	71.5 ± 11	70.9 ± 11	81.7 ± 6.6	81.2 ± 6.8	83.7 ± 9.6	84.8 ± 9.5
Final systolic BP, mm Hg	135.9 ± 11.7	145.6 ± 11.1	123.4 ± 8.3	134.8 ± 8.3	136.6 ± 13.3	142.0 ± 12.5	135.7 ± 9.0	149.7 ± 11.0
Final diastolic BP, mm Hg	74.8 ± 9.1	78.1 ± 8.9	62 ± 5.6	67.2 ± 6.5	74.8 ± 8.8	76.5 ± 8.9	76.2 ± 6.1	82.1 ± 7.5
Antihypertensive use on follow-up								
ACEIs/ARBs	40.7	30.9	70.6	52.2	58.3	60.1	31.5	29.6
BBs	NR	NR	43.2	33.5	6.0	5.0	21.2	19.4
CCBs	49.9	59.8	56	34.8	37.1	36.4	27.2	29.8
Diuretic agents	15.3	8.9	61.7	42.3	13.0	11.9	21.2	19.4
Others	0.8	0.7	22.7	10.5	5.8	5.5	NR	NR

Values are % or mean ± SD.

ACEIs/ARBs = angiotensin-converting enzyme inhibitors and angiotensin receptor blockers; BB = beta-blockers; BP = blood pressure; CCB = calcium-channel blockers; DBP = diastolic blood pressure; SBP = systolic blood pressure; other abbreviations as in Table 1.

META-REGRESSION ANALYSIS. The relationship between the efficacy and safety of intensive BP treatment and achieved mean systolic BP difference (in the intensive and standard BP control groups) is shown in Online Figures 2A to 2E. Meta-regression analyses showed a 3-percentage point (95% CI: 1- to 6-percentage point) decrease in the risk of MACE for each 1-mm Hg difference in mean achieved systolic BP between the 2 groups (p = 0.027). A similar association was found for cardiovascular mortality (p = 0.05). The risk of serious adverse events and renal failure was not associated with mean achieved systolic BP difference between the 2 groups (Online Figures 3A and 3B).

DISCUSSION

Our systematic review and meta-analysis confirms that intensive BP-lowering treatment is associated with lower cardiovascular outcomes in older hypertensive patients. However, we also observed an increased risk of renal failure with intensive BP lowering (Central Illustration). The cardiovascular protection conferred by intensive BP control was related to the magnitude of the reduction in systolic BP. In all trials, the achieved systolic BP in intensive group was <140 mm Hg; the lowest was 123 mm Hg in the SPRINT-SENIOR trial.

Optimal target BP has been a topic of intense debate in recent years. The JNC 8 panel recommendation of a more liberal systolic BP threshold for initiation of treatment and a target of <150 mm Hg in

patients age ≥60 years was received with a lot of criticism. The reason for proposing these guidelines was that "setting a goal SBP of lower than 140 mm Hg in this age group provides no additional benefit compared with a higher goal SBP of 140 to 160 mm Hg or 140 to 149 mm Hg" (3). However, the evidence supporting this statement was acknowledged as being of "low-quality" (3). Of the included trials in our meta-analysis, SPRINT-SENIOR (6) and Wei et al. (15) showed a reduction in cardiovascular events, whereas in JATOS (13) and VALISH (14), there was no difference in cardiovascular events between the intensive and standard treatment groups. In our pooled analysis, we demonstrated that intensive BP control was indeed associated with a significant reduction in MACE as well as cardiovascular mortality. Although MI and stroke reduction was not significant, point estimate favored the intensive treatment group. Meta-regression analysis revealed that the difference in the magnitude of cardiovascular protection among trials was proportional to the difference in achieved systolic BP reduction between the 2 strategies. This seems to indicate that higher magnitude of reduction in systolic BP may translate into better outcomes.

More intensive antihypertensive therapy in older patients is not without drawbacks. In our analysis, the difference in serious adverse events and renal failure between the 2 strategies did not reach significance in random effect analysis, but in the fixed effect analysis, intensive BP lowering was associated with a 2-fold increase in risk for renal failure, largely driven by the SPRINT trial. In the SPRINT trial (16)

FIGURE 1 Forest Plot of Pooled Relative Risks for Intensive BP Control Compared With Standard BP Control
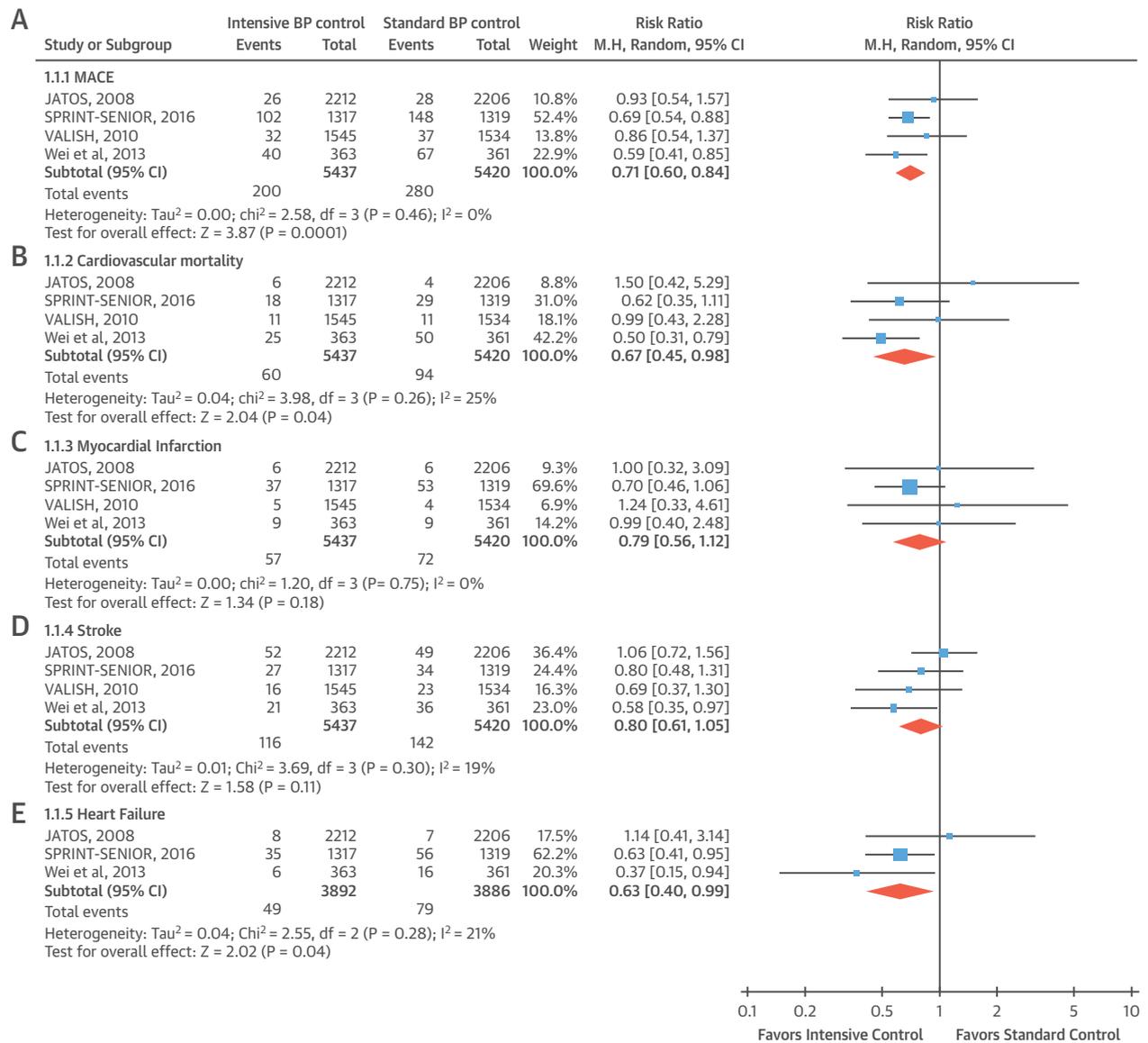
(A) Major adverse cardiovascular event(s) (MACE), **(B)** cardiovascular mortality, **(C)** myocardial infarction, **(D)** stroke, and **(E)** heart failure. **Squares** represent the risk ratio of the individual studies. **Horizontal lines** represent the 95% confidence intervals (CIs) of the risk ratios. The **size of the square** reflects the weight that the corresponding study contributes in the meta-analysis. The **diamond** represents the pooled risk ratio or the overall effect. BP = blood pressure; JATOS = Japanese Trial to Assess Optimal Systolic Blood Pressure in Elderly Hypertensive Patients; M-H = Mantel-Haenszel; SPRINT-SENIOR = Systolic Blood Pressure Intervention Trial in older adults; VALISH = Valsartan in Elderly Isolated Systolic Hypertension.

including the SPRINT-SENIOR subgroup (6), there was no significant difference for composite renal outcome (reduction in estimated glomerular filtration rate, dialysis, or renal transplant) between the intensive and standard treatment groups in participants with chronic kidney disease (CKD) at baseline.

However, in participants without CKD at baseline, there was a higher incidence of composite renal outcome in the intensive compared with the standard treatment groups. Importantly, there was no significant difference in incident albuminuria among participants with or without CKD at baseline.

TABLE 3 Pooled Relative Risk of Efficacy and Safety Outcomes With Intensive Versus Standard BP Lowering in Elderly Patients

| Clinical Outcomes	Intensive BP Lowering	Standard BP lowering	Pooled RR (95% CI)	p Value	I^2
Efficacy					
MACE	200/5,437 (3.7)	280/5,420 (5.2)	0.71 (0.60-0.84)	0.0001	0
Cardiovascular mortality	60/5,437 (1.1)	94/5,420 (1.7)	0.67 (0.45-0.98)	0.04	25%
Myocardial infarction	57/5,437 (1.0)	72/5,420 (1.3)	0.79 (0.56-1.12)	0.18	0
Stroke	116/5,437 (2.1)	142/5,420 (2.6)	0.80 (0.61-1.05)	0.11	19%
Heart failure	49/3,892 (1.3)	79/3,886 (2.0)	0.63 (0.40-0.99)	0.04	21%
Safety					
Serious adverse events	1,274/5,074 (25.1)	1,252/5,059 (24.7)	1.02 (0.94-1.09)	0.69	19%
Renal failure	57/5,067 (1.1%)	28/5,049 (0.6)	1.81 (0.86-3.80)	0.12	46%

Values are n/N (%) unless otherwise indicated.

BP = blood pressure; CI = confidence interval; MACE = major adverse cardiovascular event(s); RR = relative risk.

The greater use of diuretic agents in combination with angiotensin-converting enzyme inhibitors and angiotensin-receptor blockers in the intensive (vs. standard treatment) group of the SPRINT study, as compared to the other 3 studies, may have resulted in more pronounced alterations in intrarenal hemodynamics, leading to a rise in serum creatinine. This phenomenon is largely considered functional and reversible rather than a structural and irreversible rise in serum creatinine, in general, and is thought to be self-limited and nonprogressive (17-19). However, in the SPRINT trial, the renal events were lower than expected, and the trial was terminated early. Certainly, lo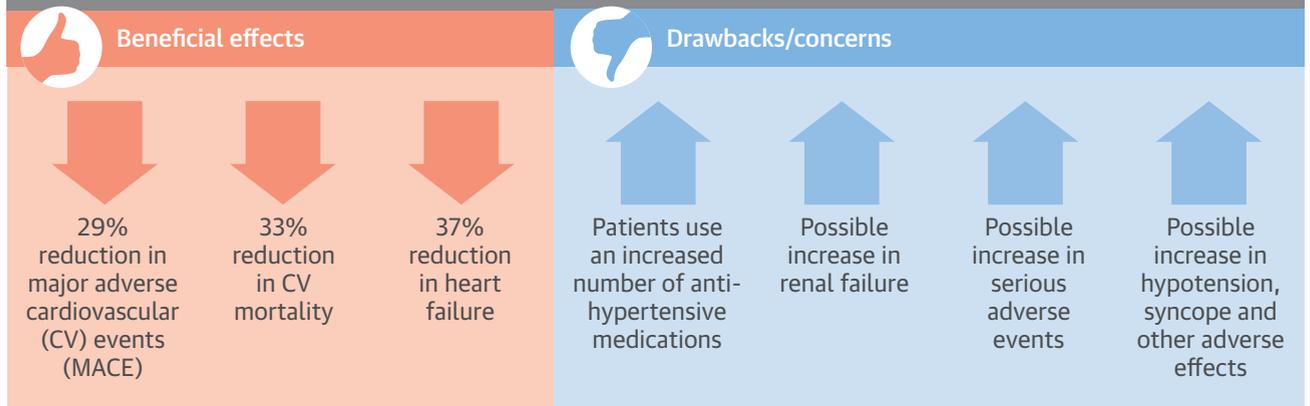ng-term follow-up is needed to evaluate the effect on worsening of renal function with intensive BP reduction. It should be noted that reporting of adverse events was not uniform, and event definitions vary across the trials. We were able to analyze only serious adverse events and renal failure, as they were most commonly reported across the trials. Except for SPRINT (6,16), none of the trials evaluated for frailty status, symptomatic hypotension, and syncope. Additional trials are needed to thoroughly investigate the effect of intensive BP control on renal function and serious adverse events.

When interpreting the risks and benefits of intensive therapy, some numbers should be taken into

FIGURE 2 Forest Plot of Pooled Relative Risks for Intensive BP Control Compared With Standard BP Control
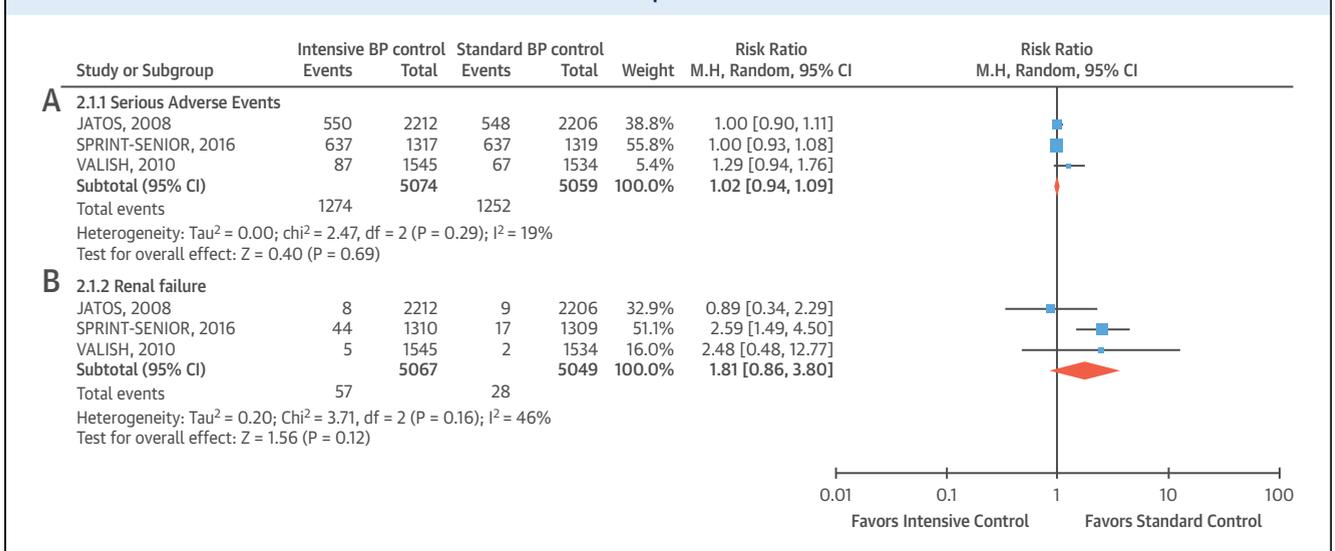
(A) Serious adverse events and (B) renal failure. **Squares** represent the risk ratio of the individual studies. **Horizontal lines** represent the 95% CIs of the risk ratios. The **size of the square** reflects the weight that the corresponding study contributes in the meta-analysis. The **diamond** represents the pooled risk ratio or the overall effect. Abbreviations as in Figure 1.

CENTRAL ILLUSTRATION Intensive BP Lowering and Cardiovascular and Safety Outcomes in Older Hypertensive Patients

Effects of Intensive BP-lowering in Older (≥ 65 Years) Hypertensive Patients

Beneficial effects

Drawbacks/concerns

| 29% reduction in major adverse cardiovascular (CV) events (MACE) | 33% reduction in CV mortality | 37% reduction in heart failure | Patients use an increased number of anti-hypertensive medications | Possible increase in renal failure | Possible increase in serious adverse events | Possible increase in hypotension, syncope and other adverse effects |

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BP = blood pressure; CV = cardiovascular; MACE = major adverse cardiovascular event(s).

perspective. Intensive therapy was associated with a 29% reduction in MACE corresponding to a decrease in event rate from 5.2% to 3.7% over a mean follow-up of 3.1 years, or an absolute risk reduction of 1.5%. Conversely, renal failure increased from 0.6% to 1.1%, or an absolute risk of 0.5% over the same time period. Although one can argue that cardiovascular events and renal failure cannot be considered equivalent, clinicians and patients should be aware of the trade-off involved with intensive therapy. Nevertheless in older patients, the cardiovascular benefit of intensive therapy may come at the expense of increase in adverse events. As shown in Table 2, patients in the intensive treatment group used a higher number of antihypertensive medications, which was evident in all trials. The SPRINT-SENIOR (6) participants, on average, were taking more than 3 drugs every day in the intensive group. Also, the intensity of treatment may vary, and high medication dosages to achieve desired BP levels could substantially increase adverse effects. More importantly, older patients a have higher burden of comorbidities and are often exposed to polypharmacy (20), which may further potentiate the risk of adverse events.

STUDY LIMITATIONS. First, the meta-analysis included 4 trials, and similar to other trial-level meta-analyses, there is variability in the inclusion/exclusion criteria, choice of antihypertensive therapies, and definitions of outcomes. Second, the criteria

for target systolic BP in the intensive group was <140 mm Hg in 3 trials (13-15), whereas it was <120 mm Hg in SPRINT-SENIOR (6). Although the achieved systolic BP in the intensive treatment arm of SPRINT-SENIOR was slightly higher (123 mm Hg) than its target goal of <120 mm Hg, it was lower than the achieved systolic BP in the intensive treatment arms of the other 3 trials (136 to 137 mm Hg). However, it should be noted that BP measurements in SPRINT were taken in patients sitting in a quiet room without a nurse or physician present. Accordingly, the intensive BP arm in SPRINT may translate into a systolic BP <136 mm Hg, which is not very different from systolic BP <140 mm Hg in other trials (21). Third, in the absence of patient-level data, we were unable to test for other cut-offs for optimal target systolic BP other than that set forth by the individual trials. The ongoing ESH-CHL-SHOT (Optimal Blood Pressure and Cholesterol Targets for Preventing Recurrent Stroke in Hypertensives) trial (22) in Europe should provide further data on optimal BP targets. Fourth, the trials included a minimal number of patients with diabetes and cardiovascular disease; hence, the findings of this analysis may not be applicable to these high-risk populations.

CONCLUSIONS

In elderly hypertensive patients, intensive BP control (systolic BP <140 mm Hg) decreased MACE, including cardiovascular mortality and HF. Data on adverse

events were limited, but suggested an increased risk of renal failure. When considering more intensive BP control in the elderly, clinicians should carefully balance benefits against potential risks.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: In older hypertensive patients, intensive BP control (systolic BP <140 mm Hg) reduces MACE, cardiovascular mortality, and HF, but may increase the risk of renal failure.

TRANSLATIONAL OUTLOOK: Future randomized trials should investigate the safety of intensive BP control in older patients.

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KEY WORDS blood pressure, hypertension, older adults, prognosis

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APPENDIX For supplemental tables and figures, please see the online version of this article.