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Ohio Cardiovascular Health Collaborative

School of Medicine
Case Western Reserve University

In partnership with:

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College of Medicine and Life Sciences, The University of Toledo

Ohio University Heritage College of Osteopathic Medicine

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Blood Pressure Targets: Talking with Your Team

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Talking With Your Team

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- Feel free to adapt these slides to review with your providers
- The presentation typically takes 20 minutes to discuss the data and answer questions or concerns about the blood pressure (BP) targets and timely follow-up
- The slide set includes common questions & answers at the end of the slides

Hazard Ratios (95% CI) for Major Cardiovascular Disease at Different Levels of Achieved Systolic BP

- Meta-analyses of hypertension treatment trials showing the lower the Systolic Blood Pressure (SBP) achieved in the trials, the lower the risk for stroke, coronary heart disease (CHD), and death from any cause
- Progressive reduction in risk of cardiovascular disease (CVD) at lower levels of achieved SBP down to levels below current European & US recommendations
- Similar findings for stroke, CHD and all-cause mortality
- Similar pattern in a sensitivity analyses where:
  - SPRINT results excluded
  - Results from four trials with risk or lack of clarity for bias
- No inconsistency between direct or network (indirect) comparisons
- No inconsistency for CVD benefit in several other meta-analyses (including Xie et al., Verdecchia et al., and Bangalore et al.)

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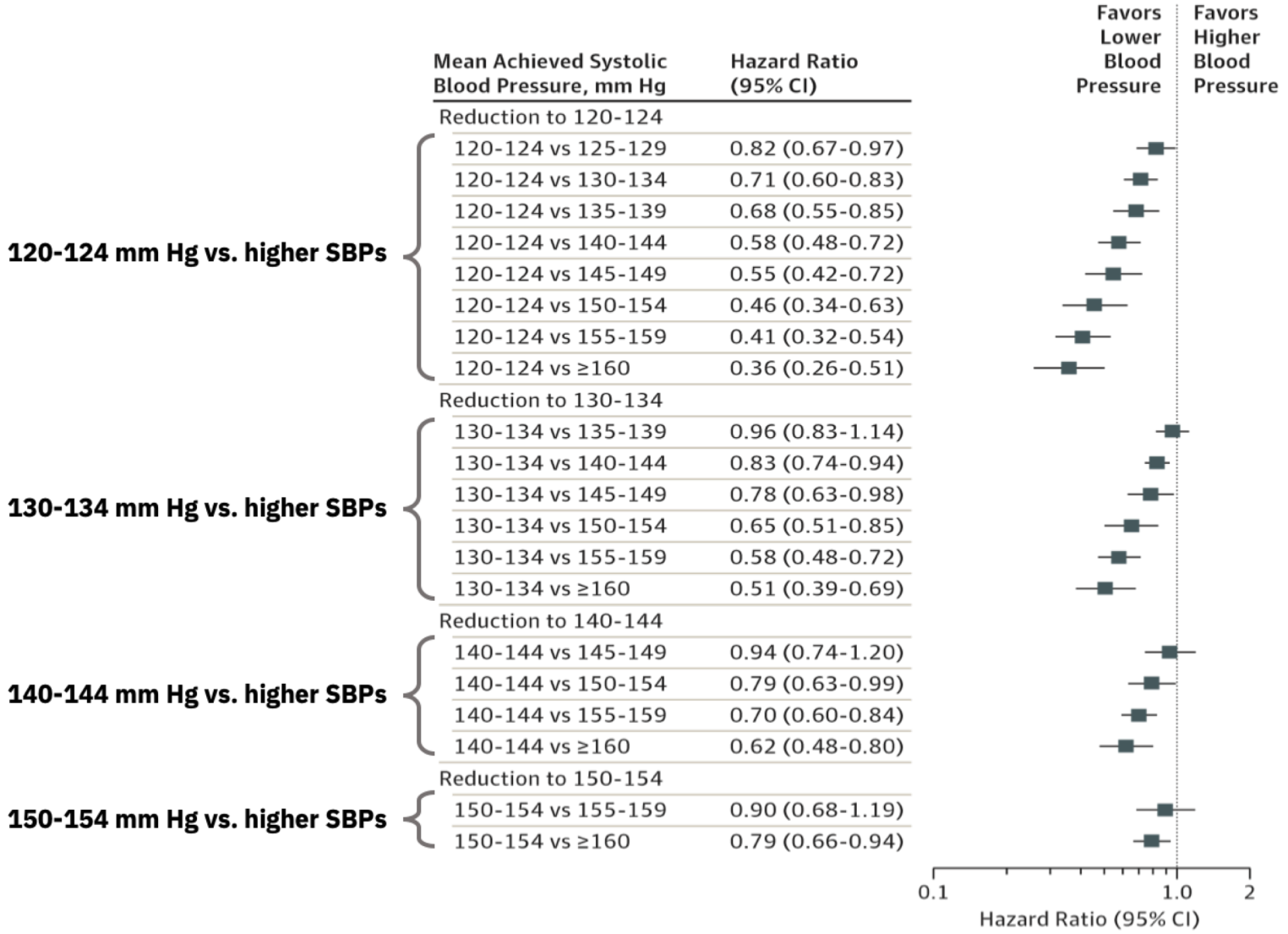
Network Meta-analysis (42 RCTs: N = 144,220)

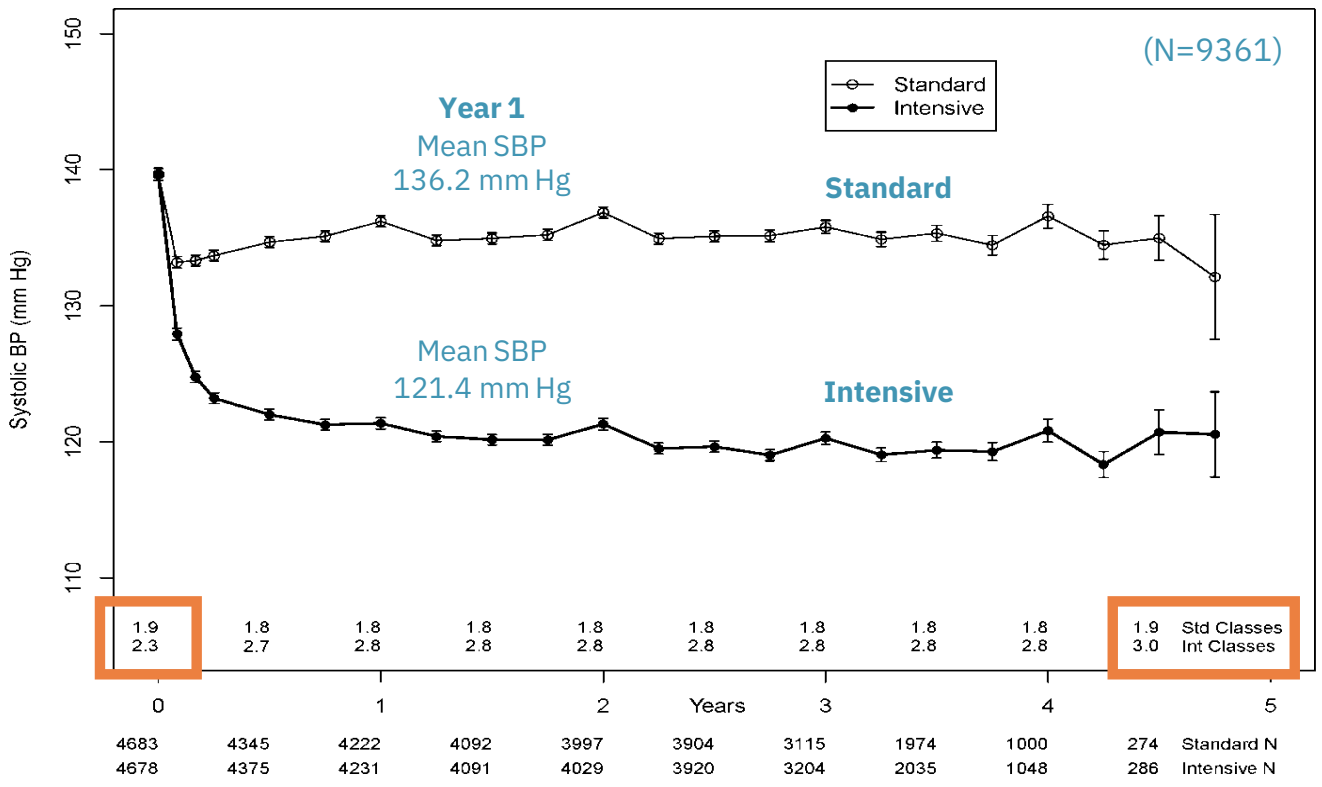


Bundy JD et al. JAMA Cardiol 2017; 2:775-781

SPRINT Trial

- Good BP separation achieved, with those randomized to <120 mmHg requiring on average one more BP medication than those randomized to the <140 mmHg target
- BP separation continued throughout trial follow-up

Mean Systolic BP (95% CI)



Average SBP
During Follow-up

Standard
134.6 mm Hg

Intensive
121.5 mm Hg

Average number of antihypertensive medications

Number of participants

SPRINT Research Group. NEJM 2015; 373:2103-2116

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SPRINT Primary Outcome* Cumulative Hazard

- *Results:*
  - Separation beginning at ~ 1 year of follow-up
  - 25% reduction in primary outcome (mostly heart failure, stroke, heart attacks, and cardiovascular death)*
  - 27% reduction in death from any cause (NNT=90)

* myocardial infarction (MI), acute coronary syndrome (ACS) other than MI, stroke, heart failure (HF)**, death from cardiovascular causes**

** primary endpoints and mortality significantly reduced

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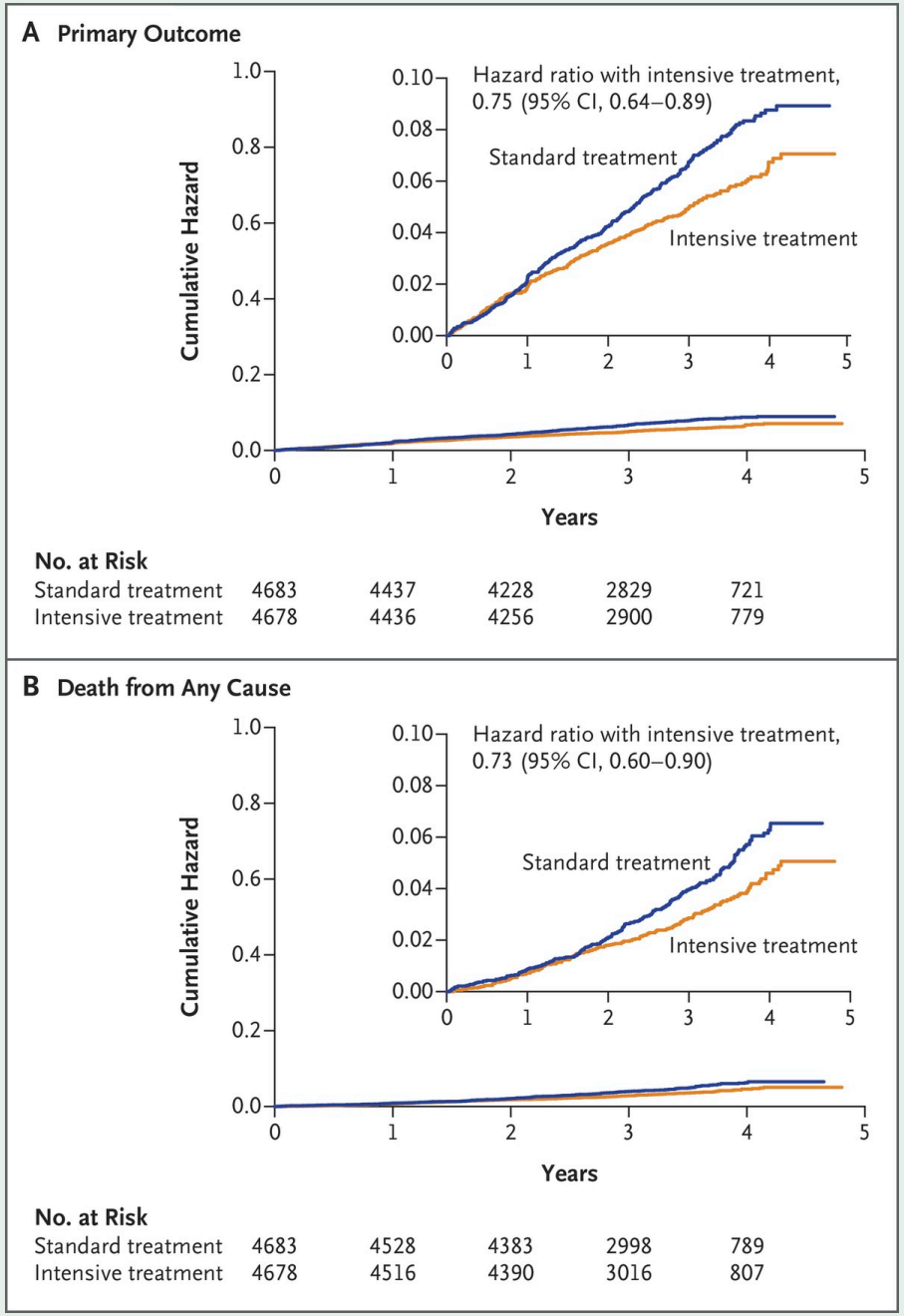
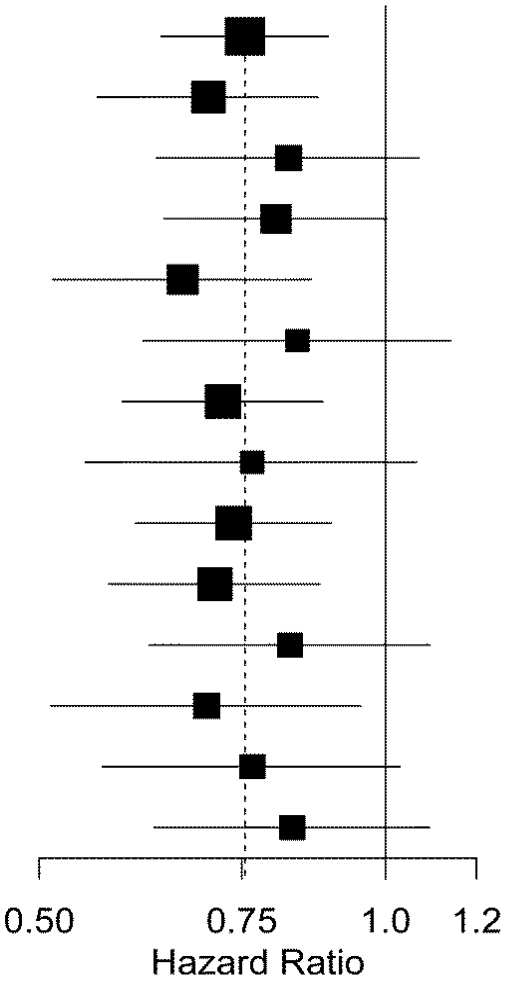


SPRINT Research Group. NEJM 2015; 373:2103-2116

SPRINT Primary Outcome Experience in the 6 Pre-Specified Subgroups of Interest

- Benefit of lower SBP target seen in all pre-specified subgroups
- Benefit also seen in Hispanic patients

Subgroup	HR	P*
Overall	0.75 (0.64,0.89)	
No Prior CKD	0.70 (0.56,0.87)	0.36
Prior CKD	0.82 (0.63,1.07)	
Age < 75	0.80 (0.64,1.00)	0.32
Age ≥ 75	0.67 (0.51,0.86)	
Female	0.84 (0.62,1.14)	0.45
Male	0.72 (0.59,0.88)	
African−American	0.77 (0.55,1.06)	0.83
Non African−American	0.74 (0.61,0.90)	
No Prior CVD	0.71 (0.57,0.88)	0.39
Prior CVD	0.83 (0.62,1.09)	
SBP ≤ 132	0.70 (0.51,0.95)	0.77
132 < SBP < 145	0.77 (0.57,1.03)	
SBP ≥ 145	0.83 (0.63,1.09)	



* Treatment by subgroup interaction.
* Unadjusted for multiplicity.

SPRINT Research Group. NEJM 2015; 373:2103-2116

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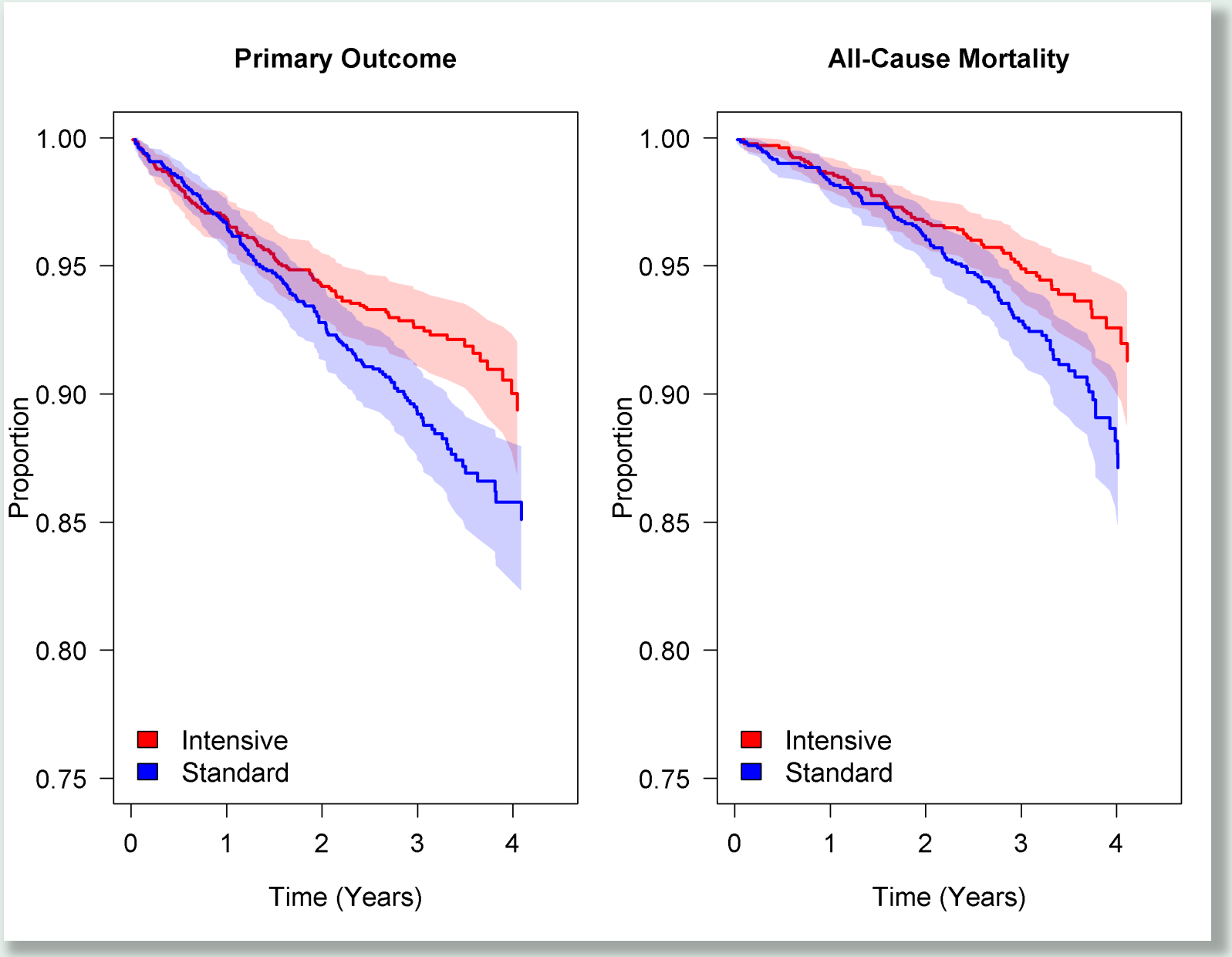
SPRINT Kaplan-Meier Survival Curves for Primary Outcome and All-Cause Mortality in Participants 75 and Older

- Mean and median age in SPRINT was 68 years-old
- 28% of participants were > age 75 years
- The number needed to treat to prevent a primary outcome was somewhat lower in those over age 75 years (28 vs. 61) and (41 vs. 90) for all-cause mortality



Willamson JD et al for the SPRINT Research Group; JAMA 2016; 315:2673-82

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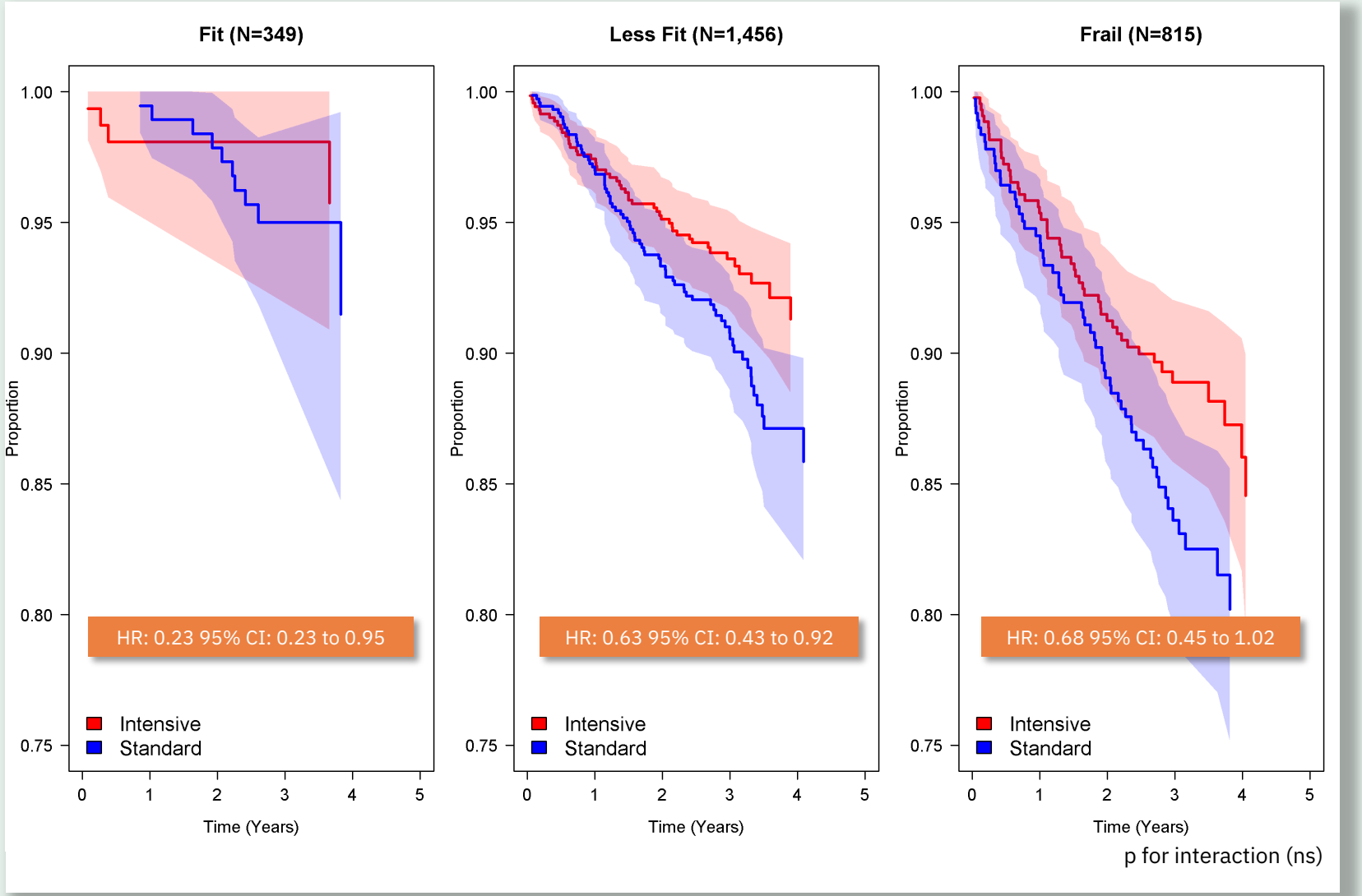
SPRINT Kaplan-Meier Survival Curves for Primary Outcome by Frailty Status

- Survey questionnaire and timed 4-meter walk used to assess frailty in those over age 75 years
- No significant difference and benefit of <120 mmHg target seen in fit, less fit, and frail
- Nursing home residents, those with < 3 year expected survival, and those with dementia at baseline were excluded



Willamson JD et al for the SPRINT Research Group; JAMA 2016; 315:2673-82

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SPRINT MIND

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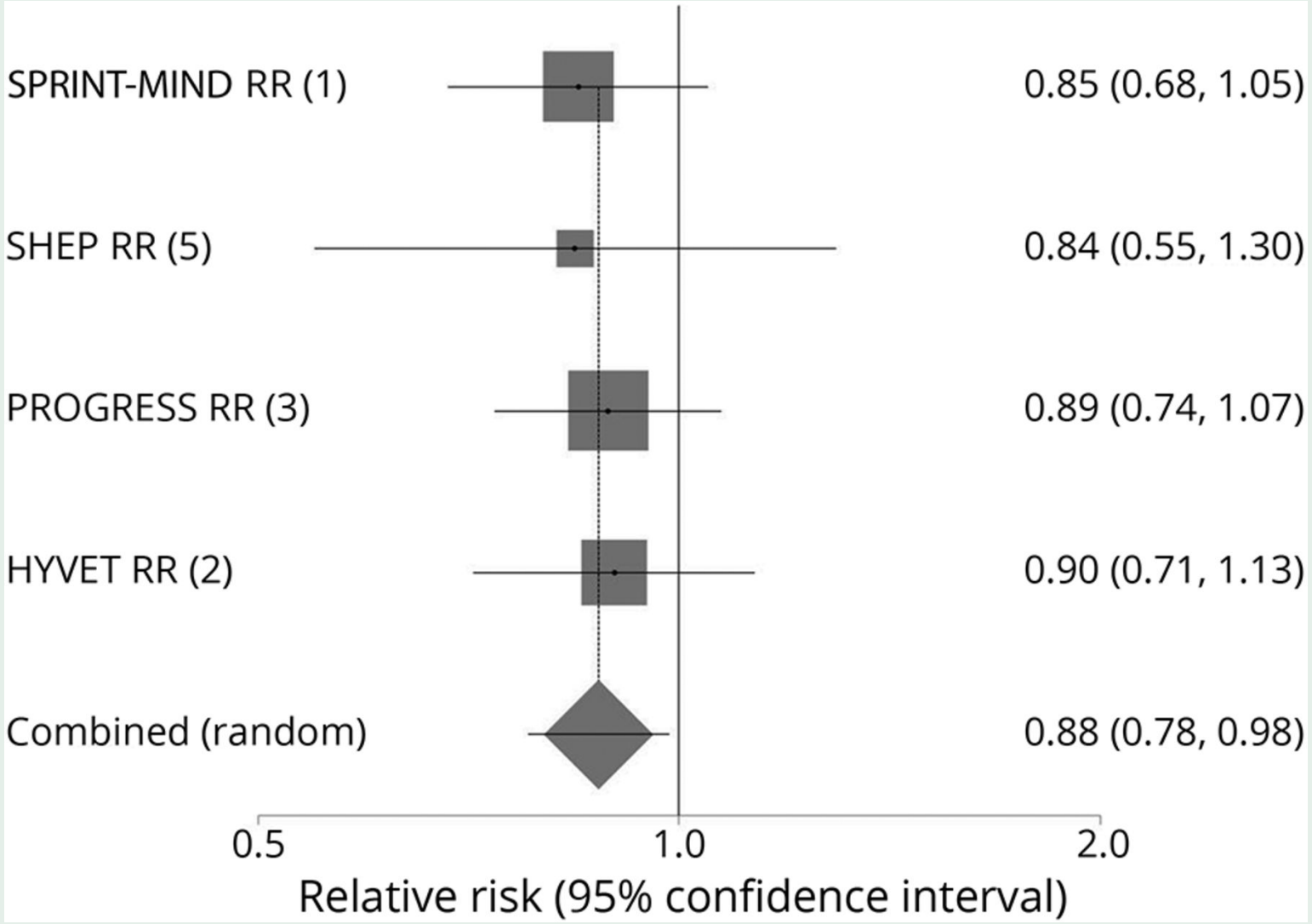
- Data from the SPRINT MIND (Systolic Blood Pressure Intervention trial - Memory and Cognition in Decreased Hypertension) component of SPRINT showing that compared to a systolic blood pressure (SBP) target of <140 mmHg, the <120 mmHg target resulted in significantly lower rates of:
  - Mild cognitive decline (MCI),
  - Composite of MCI and probable dementia (PD), as well as
  - Characteristic white matter lesions on MRI
  - Reduction in PD alone was not significant
- Aggressive BP treatment is currently the only treatment shown to prevent/slow progression of dementia

Williamson JD et al JAMA 2019; 321:1-9
Nasrallah IM et al JAMA 2019; 322:524-534

Meta-Analysis of Trials of Blood Pressure-Lowering on Dementia Outcomes

- According to having ≥10 mm Hg systolic BP difference between randomized groups
- Trials include:
  - HYVET = Hypertension in the Very Elderly Trial
  - PROGRESS = Perindopril Protection Against Recurrent Stroke Study
  - SHEP = Systolic Hypertension in the Elderly Program
  - SPRINT MIND = Systolic Blood Pressure Intervention trial - Memory and Cognition in Decreased Hypertension
- Similar significant reduction of dementia incidence provides additional evidence of dementia finding in SPRINT-MIND



Peters R et al Neurology 2019; 92:1017-1018

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SPRINT Serious Adverse Events (SAE) During Follow-Up

- SAE = fatal or life threatening event, resulting in significant or persistent disability, requiring or prolonging hospitalization, or judged an important medical event
- Large number of overall serious adverse events (SAE) in both treatment groups in this high risk population
- However, no significant difference in SAEs by treatment group, even in those over age 75 years of age

	Number (%) of Participants		
	Intensive	Standard	HR (P Value)
All SAE reports (Overall cohort)	1793 (38.3)	1736 (37.1)	1.04 (0.25)
All SAE reports (age > 75 years)	640 (48.6)	638 (48.4)	1.00 (0.93)

SPRINT Research Group

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SPRINT Serious Adverse Events (SAE) During Follow-Up (Cont.)

- Though incidence of SAEs due to hypotension, syncope, and acute kidney injury (AKI) were increased, injurious fall was not different between treatment groups. Results are similar in participants ≥75 years old
- > 3/4 of AKI events involved a < 2 fold increase in pre-AKI baseline creatinine (stage 1 or 2 AKI)
- 90% of AKI events resolved (creatinine within 20% of baseline creatinine) by end of trial follow-up, and another 5% had partial resolution (creatinine within 30% of baseline)
- SAEs, unlike study outcomes, were not adjudicated and, though serious, were mostly reversible compared to study outcomes

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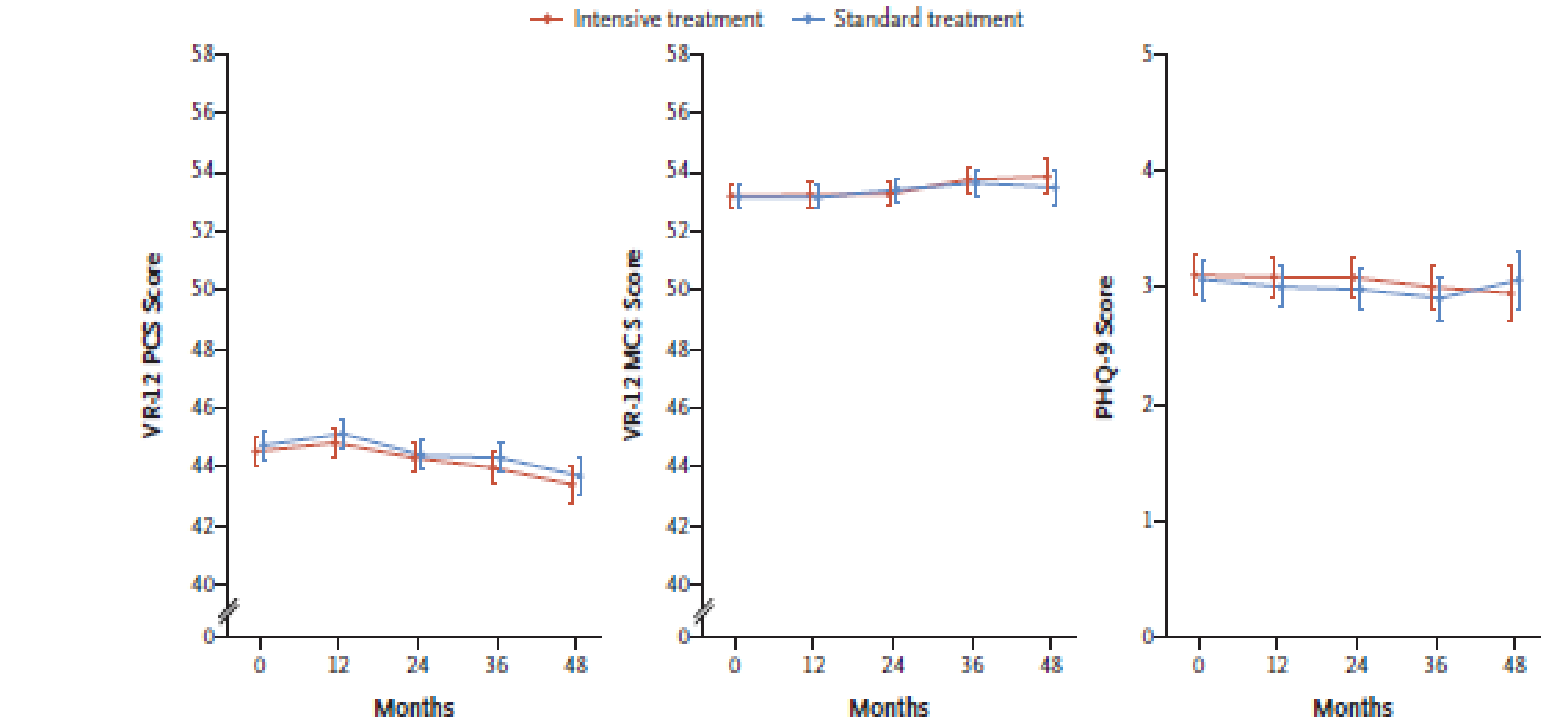
	Number (%) of Participants		
	Intensive	Standard	HR (P Value)
All SAE reports (Overall Cohort)	**1793 (38.3)**	**1736 (37.1)**	**1.04 (0.25)**
Selected SAEs (Overall Cohort)	**Intensive**	**Standard**	**HR (P Value)**
Hypotension	110 (2.4)	66 (1.4)	1.67 (0.001)
Syncope	107 (2.3)	80 (1.7)	1.33 (0.05)
Injurious Fall	105 (2.2)	110 (2.3)	0.95 (0.71)
Bradycardia	87 (1.9)	73 (1.6)	1.19 (0.28)
Electrolyte Abnormality	144 (3.1)	107 (2.3)	1.35 (0.02)
Acute Kidney Injury or Renal Failure	193 (4.1)	117 (2.5)	1.66 (<0.001)

SPRINT Research Group

SPRINT Tolerability of the <120 mmHg Systolic Blood Pressure Target

- Health-related quality of life measuring physical and mental components of VR-12 and depressive symptoms using PHQ-9 showed no difference in patient-reported quality of life overall, including no significant difference in those over age 75

Patient-Reported Outcomes in the Two Treatment Groups, Over Time



Berlowitz DR et al. NEJM 2017; 377:733-44.

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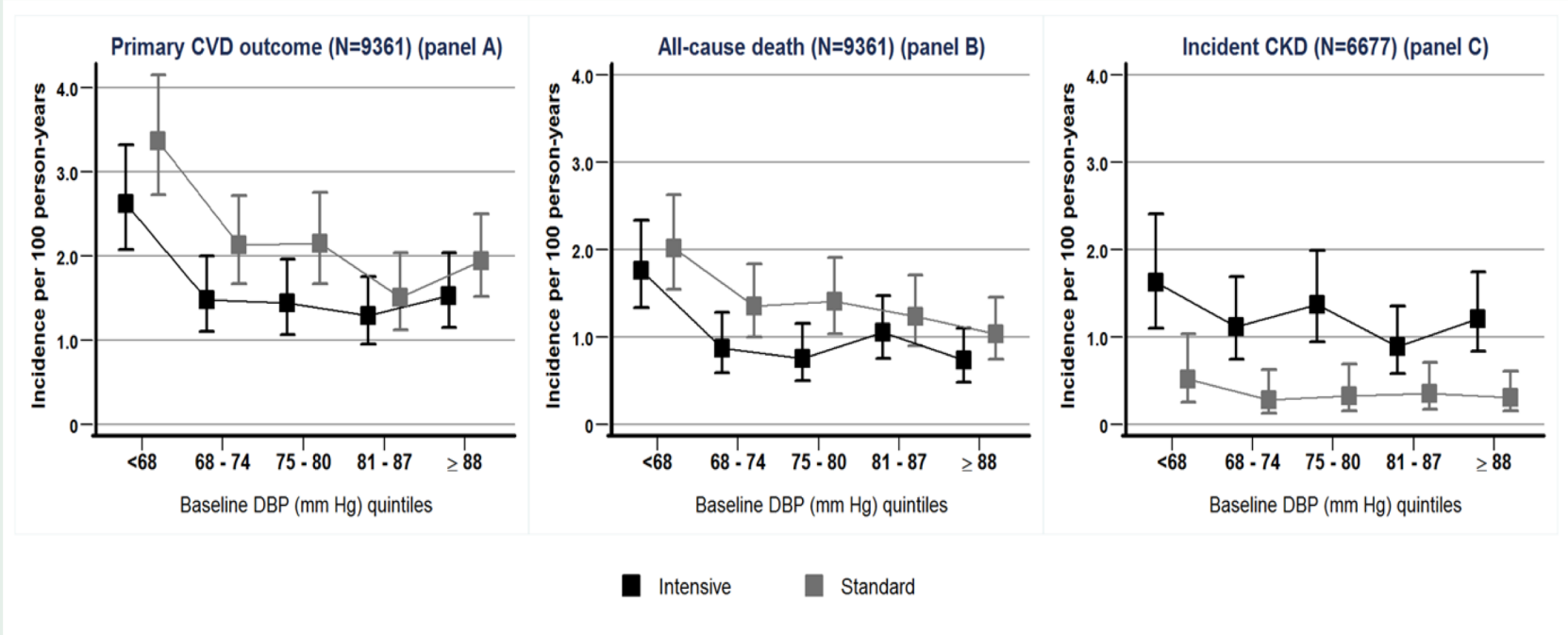
Incidence Rates of Events by Baseline Diastolic Blood Pressure and Randomized Groups in SPRINT

- Data showing risk of CVD outcomes (MI, Stroke, HF, CHD death, ACS), all cause mortality and incident CKD by baseline DBP and by randomized groups
- Lower baseline DBP is associated with increased risk, but **no** evidence of increased risk in patients randomized to intensive SBP lowering compared to standard SBP lowering



Beddhu S et al. Circ 2018; 137:134-43

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Recent Hypertension Guideline Recommendations

- Since the publication of SPRINT and consistent with the ACC/AHA guideline, most other international guidelines have lowered their BP targets
- Prior to 2014, nearly all guidelines recommended a target of <140/90 for everyone up to age 80
- The risk/benefit of more aggressive BP control in those above age 80 was not known (of course, the risk benefit of treating SBP in those < age 60 was also not known)
- In 2014, the "JNC-8" recommended backing off on BP control in those > age 60 due to lack of risk/benefit data
- Dr. Wright was an author on that document but led the group that issued a minority report denouncing that recommendation
- A year later, the independent data safety monitoring board for SPRINT recommended stopping the trial intervention because even control to <140 mmHg was shown no longer justifiable compared to the lower SBP goal

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GUIDELINE	EVIDENCE REVIEW METHODOLOGY	BP TARGET IN GENERAL ADULT POPULATION	BP TARGET IN HIGH CARDIOVASCULAR DISEASE RISK GROUPS	BP TARGET IN CHRONIC KIDNEY DIEASE AND DIABETES MELLITUS
NICE (2011, amended 2019)[1]	Systematic Review	**Age < 80:** < 140/90 **Age ≥ 80:** < 150/90	**Age < 80:** < 140/90 **Age ≥ 80:** < 150/90	< 140/90
JAMA HTN Guideline (2014)[2]	Systematic Review	**Age < 60:** < 140/90 **Age ≥ 60:** < 150/90	**Age < 60:** < 140/90 **Age ≥ 60:** < 150/90	< 140/90
CHEP (2016)[3]	Consensus (Graded)	**Age < 80:** SBP < 120 **Age ≥ 80:** SBP < 150 (if < 120 target inappropriate)	**Age < 80:** SBP < 120 **Age ≥ 80:** SBP < 150 (if < 120 target inappropriate)	< 130/80
Australian (2016)[4]	Consensus (Graded)	< 140/90	< 120/80 if thought safe	N/A
ACC/AHA (2017)[5]	Consensus (Graded)	< 130/80	<130/80	< 130/80
AAFP/ACP (2017)[6]	Consensus	**Age < 60:** < 140/90 **Age ≥ 60:** < 150/90	**Age < 60:** < 140/90 **Age ≥ 60:** < 150/90	< 140/90
ESC/ESH (2018)[7]	Consensus (Graded)	< 140/90 <130/80 if tolerated **Age ≥ 65:** SBP < 130-140	**Age < 65:** < 130/80 **Age ≥ 65:** SBP 130-140	**CKD:** SBP 130-140 **DM:** <130/80
ADA BP Targets (2018)[8] (diabetic patients)	Consensus	< 140/90	< 130/80	< 130/80
KDIGO (2019)[9]	Consensus	< 130/80	< 130/80	< 130/80

Summary

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- Data support the use of a lower BP target <130/80 mm Hg in all ages and subgroups for most individuals.
- Nearly all national and international guidelines now recommend BP targets in this range (some recommend even lower). There is ample evidence to support it.
- A minority of individuals will not tolerate or benefit from the lower BP target and the current US guideline allows for clinical judgement, especially in patients over age 65 with a high burden of co-morbidities and limited life expectancy.
- The latest HEDIS measure uses BP <140/90 mm Hg as the performance metric. However, a performance metric for a practice differs from a clinical practice guideline for individual patients.
- Monthly follow-up in patients above the BP target of 130/80 promotes the ability of clinicians to assist patients in obtaining target BPs more quickly.
- Home BP monitoring is recommended to assist with determining accurate BP control.

Common Concerns with Lower Targets

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1. I am concerned about lowering BP too much in my elderly patients due to fall risks.

   Answer: Higher risk of injurious falls was not seen in the SPRINT trial (even in those over age 75 years), and better BP control helps prevent dementia.

2. The absolute benefits are small when lowering SBP from 140 to 120 and absolute risks occur at similar rates to absolute benefits.

   Answer: Absolute benefits of reduced death generally outweigh the adverse events. For instance, acute renal insufficiency and electrolyte imbalance were reversible, and syncope did not result in greater fracture risk in SPRINT.

Common Concerns with Lower Targets

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3. What about the ACCORD trial for adults with diabetes showing no benefit in tighter targets?

Answer: The ACCORD results are the outlier in hypertension outcome trials. Although those results should not be dismissed out of hand, in nearly all other trials containing patients with and without diabetes (SHEP, HOT, Sys-Eur) the patients with diabetes derived the greatest benefit. In the SPRINT trial, patients with prediabetes and the metabolic syndrome showed similar benefits of intensive BP lowering. Current ADA guidelines recommend <140/90 in all patients with diabetes and <130/80 in high risk patients with diabetes.

Additional Questions/Concerns Which May Arise During the Lower BP Target Conversation

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1. Does monthly follow-up result in improved BP control?

   Answer: Several studies have shown more frequent follow-up does improve BP control, including the Kaiser model on which this best practice is based.

2. Patients do not want to have to come back every month.

   Answer: Consider motivational interviewing to understand and address individual barriers or consider alternate approaches such as phone follow-up with home BP monitoring.

3. We do not have access for monthly visits.

   Answer: Consider ways to enhance access (additional hours, use of team members such as medical assistants, dietitians, pharmacists, nurses, etc.)