BP CONTROL IN THE POST SPRINT ERA

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Disclosures

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OBJECTIVES

- Briefly summarize SPRINT findings with a focus on next steps to achieve the benefits in clinical practice similar to those seen in SPRINT
- Compare BP control in SPRINT with that currently seen in clinical practice
- Examine efforts and treatment algorithms used in clinical practice quality improvement programs to improve BP control and equity
- Review our current efforts working with practices in Cleveland and statewide to improve BP control and address racial disparities in BP control

SPRINT
Systolic Blood Pressure Intervention Trial

FINAL SPRINT RESULTS IN OVERALL COHORT

Lewis CE et al. NEJM 2021; 384: 1921-1930

Table 1. Outcomes during the Intervention Period (through August 20, 2015).*

Outcome	Intensive Treatment		Standard Treatment		Hazard Ratio (95% CI)	P Value†
	no. of participants	*% per year*	*no. of participants*	*% per year*		
All participants	**(N = 4678)**		**(N = 4683)**			
Primary outcome‡	264	1.77	354	2.40	0.73 (0.63–0.86)	<0.001
Primary outcome without nonfatal heart failure	222	1.48	293	1.97	0.75 (0.63–0.89)	0.001
Secondary outcomes‡						
Myocardial infarction	102	0.68	140	0.93	0.72 (0.56–0.93)	0.01
Acute coronary syndrome	42	0.28	41	0.27	1.02 (0.66–1.57)	0.93
Stroke	69	0.45	78	0.52	0.89 (0.64–1.23)	0.48
Heart failure	68	0.45	105	0.70	0.63 (0.46–0.86)	0.003
Nonfatal heart failure	66	0.43	101	0.67	0.64 (0.47–0.87)	0.004
Death from cardiovascular causes	41	0.27	71	0.47	0.58 (0.39–0.84)	0.004
Death from any cause	163	1.06	215	1.41	0.75 (0.61–0.92)	0.006
Primary outcome or death from any cause	370	2.47	474	3.20	0.77 (0.67–0.88)	<0.001
Participants with CKD at baseline	**(N = 1330)**		**(N = 1316)**			
Composite renal outcome§	17	0.39	16	0.37	1.03 (0.52–2.06)	0.93
≥50% Reduction in eGFR¶	12	0.28	12	0.28	0.98 (0.43–2.22)	0.97
Long-term dialysis	7	0.16	10	0.23	0.66 (0.24–1.72)	0.39
Kidney transplantation	0		0		—	—
Incident albuminuria‖	64	3.93	85	5.61	0.71 (0.50–1.00)	0.05
Participants without CKD at baseline	**(N = 3332)**		**(N = 3345)**			
≥30% Reduction in eGFR¶	148	1.39	41	0.38	3.67 (2.62–5.26)	<0.001
Long-term dialysis	0		0		—	—
Kidney transplantation	0		0		—	—
Incident albuminuria‖	142	2.54	184	3.25	0.77 (0.62–0.96)	0.02

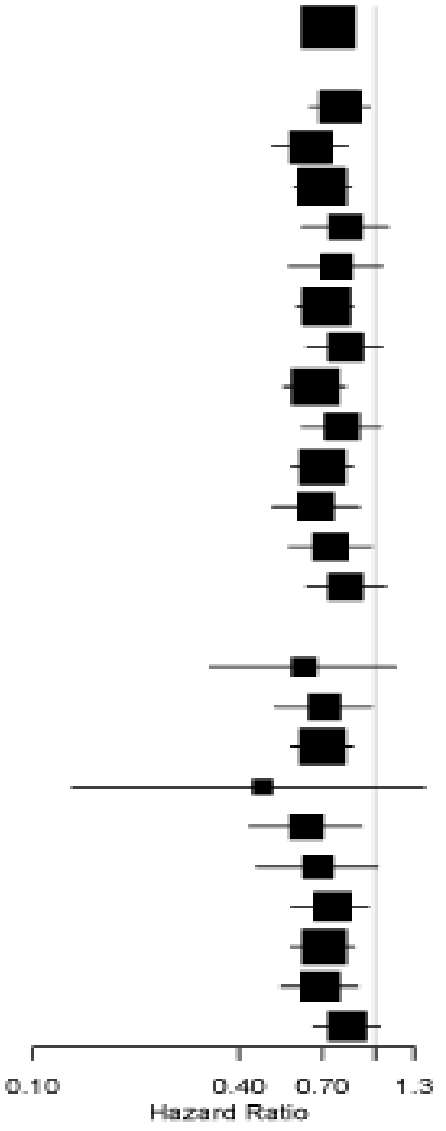
Forest Plots Primary Outcome overall and in Subgroups

Wright JT Jr et al. Hypertens 2021; 78:1701–1710. DOI: 10.1161

- Similar results in comparison of intensive vs. standard SBP treatment on primary outcome overall and in major subgroups
- Subgroups examined include those pre-specified and others of interest examined post-hoc

Forest Plots for Primary Outcome

Subgroup	Intensive	Standard	Hazard Ratio 95% CI	P value for Interaction
Overall	264/4678 (5.64)	354/4683 (7.56)	0.73 (0.63,0.86)	
Pre-Specified				
Age<75	156/3361 (4.64)	196/3364 (5.83)	0.79 (0.64,0.97)	0.24
Age≥75	108/1317 (8.20)	158/1319 (11.98)	0.65 (0.50,0.83)	
Male	179/2994 (5.98)	253/3035 (8.34)	0.70 (0.58,0.85)	0.42
Female	85/1684 (5.05)	101/1648 (6.13)	0.82 (0.61,1.09)	
Black	70/1454 (4.81)	96/1493 (6.43)	0.77 (0.56,1.05)	0.72
Nonblack	194/3224 (6.02)	258/3190 (8.09)	0.72 (0.59,0.86)	
Prior CKD	118/1330 (8.87)	136/1316 (10.33)	0.82 (0.63,1.05)	0.24
No Prior CKD	146/3348 (4.36)	218/3367 (6.47)	0.67 (0.54,0.82)	
Prior CVD	103/940 (10.96)	125/937 (13.34)	0.80 (0.61,1.04)	0.46
No prior CVD	161/3738 (4.31)	229/3746 (6.11)	0.70 (0.57,0.86)	
SBP≤132	77/1583 (4.86)	109/1553 (7.02)	0.67 (0.50,0.90)	0.64
132<SBP<145	85/1489 (5.71)	120/1549 (7.75)	0.74 (0.56,0.98)	
SBP≥145	102/1606 (6.35)	125/1581 (7.91)	0.82 (0.63,1.07)	
Not Pre-Specified				
Hispanic	20/503 (3.98)	26/481 (5.41)	0.62 (0.33,1.15)	0.85
Non-Hispanic Black	64/1379 (4.64)	93/1423 (6.54)	0.71 (0.51,0.98)	
Non-Hispanic White	167/2698 (6.19)	229/2701 (8.48)	0.70 (0.57,0.86)	
Fit	4/159 (2.52)	10/190 (5.26)	0.47 (0.13,1.39)	0.84
Less Fit	48/711 (6.75)	77/745 (10.34)	0.63 (0.43,0.91)	
Frail	50/440 (11.40)	61/375 (16.27)	0.68 (0.45,1.01)	0.30
Prior MetS	105/1737 (6.04)	141/1784 (7.90)	0.75 (0.57,0.96)	0.76
No Prior MetS	146/2807 (5.20)	205/2769 7.40)	0.71 (0.57,0.87)	
Pre-DM	101/1941 (5.20)	144/1957 (7.36)	0.69 (0.53,0.89)	0.30
Normal	142/2721 (5.22)	174/2704 (6.43)	0.83 (0.66,1.03)	



Strategy of Blood Pressure Intervention in the Elderly Hypertensive Patients (STEP) Trial

NEJM 2021; 385:1268-1279

- The SPRINT trial results in more than 9200 participants were confirmed in a trial of more than 8500 participants in the STEP Trial in China
- While SPRINT compared SBP targets of < 120 mmHg vs. < 140 mmHg in patients aged ≥50 yrs, the STEP trial compared treated to a SBP target of 110- 130 mmHg compared to one 130-150 mmHg between the ages of 60-80 yrs of age

Table 2. Hazard Ratios for the Primary and Secondary Outcomes.*

Outcome	Intensive Treatment (N=4243)		Standard Treatment (N=4268)		Hazard Ratio (95% CI)	P Value
	no. of patients (%)	*% with event per year*	*no. of patients (%)*	*% with event per year*		
Primary outcome†	147 (3.5)	1.0	196 (4.6)	1.4	0.74 (0.60–0.92)	0.007
Secondary outcomes						
Components of primary outcome						
Stroke	48 (1.1)	0.3	71 (1.7)	0.5	0.67 (0.47–0.97)	—
Acute coronary syndrome	55 (1.3)	0.4	82 (1.9)	0.6	0.67 (0.47–0.94)	—
Acute decompensated heart failure	3 (0.1)	0.03	11 (0.3)	0.09	0.27 (0.08–0.98)	—
Coronary revascularization	22 (0.5)	0.1	32 (0.7)	0.2	0.69 (0.40–1.18)	—
Atrial fibrillation	24 (0.6)	0.2	25 (0.6)	0.2	0.96 (0.55–1.68)	—
Death from cardiovascular causes	18 (0.4)	0.1	25 (0.6)	0.2	0.72 (0.39–1.32)	—
Death from any cause	67 (1.6)	0.5	64 (1.5)	0.5	1.11 (0.78–1.56)	—
Major adverse cardiac events‡	100 (2.4)	0.7	138 (3.2)	1.0	0.72 (0.56–0.93)	—

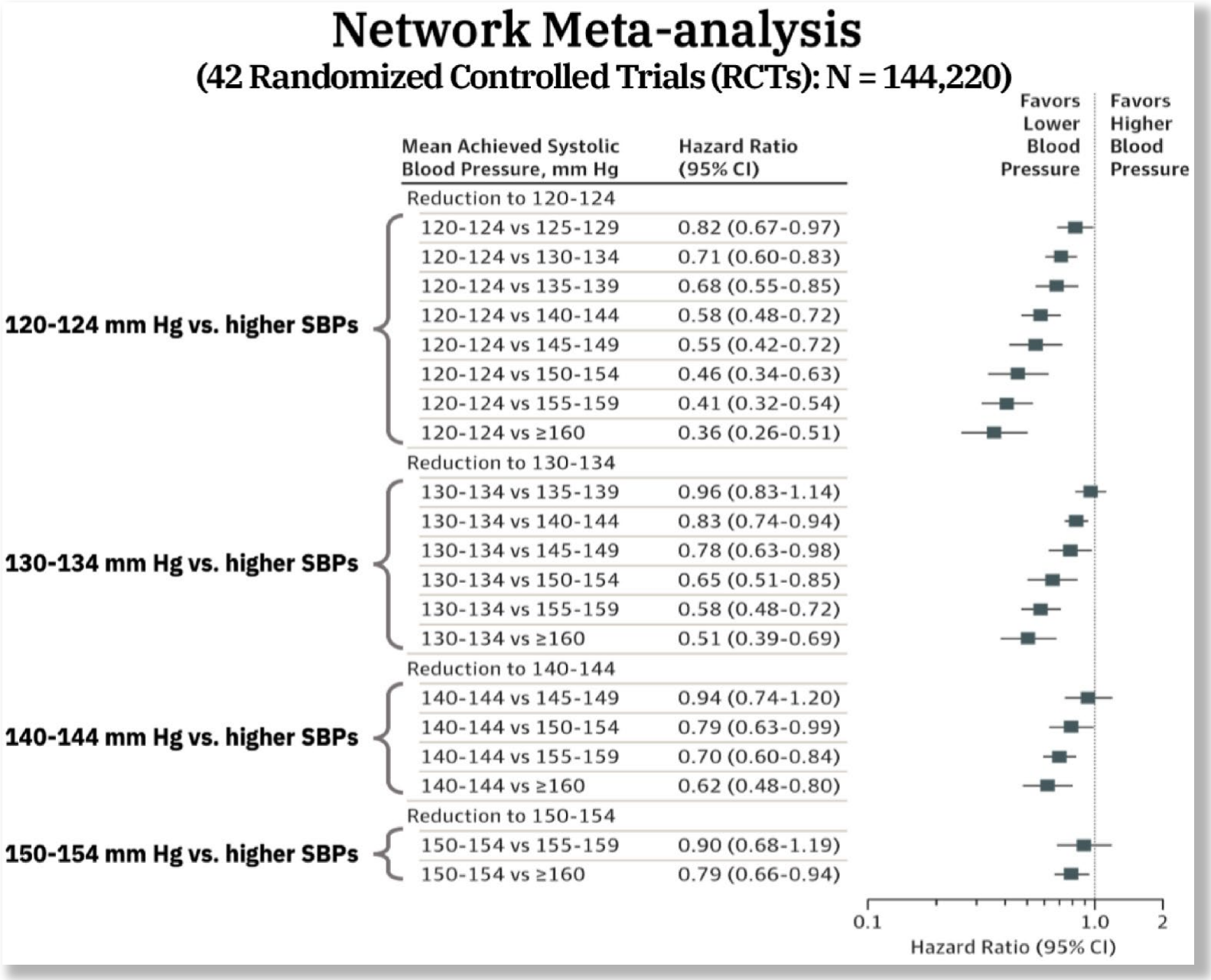
* For the primary outcome and secondary outcomes except for death from any cause, the hazard ratios, 95% confidence intervals, and P value were calculated with the use of the Fine–Gray subdistribution hazard model for the competing risk of death. For death from any cause, the Cox regression model was used. All models were adjusted for clinical center.

† The primary outcome was a composite of stroke, acute coronary syndrome, acute decompensated heart failure, coronary revascularization, atrial fibrillation, or death from cardiovascular causes.

‡ The secondary outcome of major adverse cardiac events was a composite of the individual components of the primary outcome except for stroke.

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

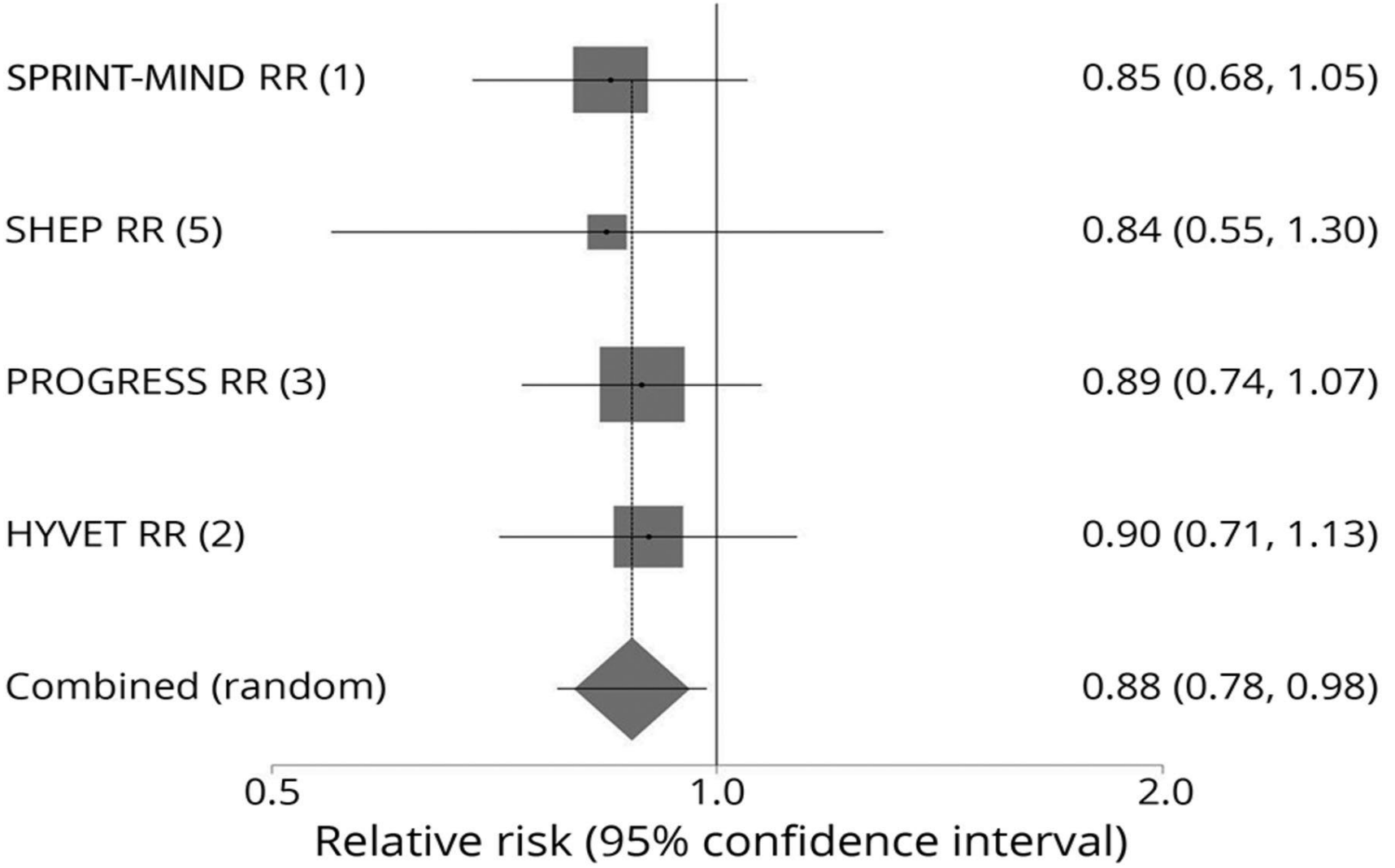
- Meta-analyses of hypertension treatment trials showing the lower the SBP achieved in the trials, the lower the risk for stroke, coronary heart disease (CHD), and death from any cause
- Progressive reduction in risk of CVD at lower levels of achieved SBP down to levels below current European & US recommendations
- Similar findings for stroke, CHD and all-cause mortality
- Similar pattern in a sensitivity analyses where:
  - SPRINT and STEP trial results excluded
  - Results from four trials with risk or lack of clarity for bias excluded
- 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.)



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

- The SPRINT-MIND Substudy showed a significant decrease in:
  - rate of cognitive decline
  - the composite of cognitive decline and dementia
  - as well as white matter lesions on MRI characteristic for dementia
- Rate of definite dementia was not significantly reduced likely b/o low statistical power
- The point estimate was favorable and when the SPRINT-MIND data were added to a meta-analysis including other trials of SBP lowering on dementia, the overall results was significant

Figure. Meta-analysis of trials of blood pressure (BP)–lowering on dementia outcomes, according to having ≥10 mm Hg systolic BP difference between randomized groups



Ruth Peters et al. Neurology 2019; 92: 1017-1018

AMERICAN ACADEMY OF NEUROLOGY

SPRINT Serious Adverse Events 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

	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

STEP Trial
Adverse Events Related to BP Intervention

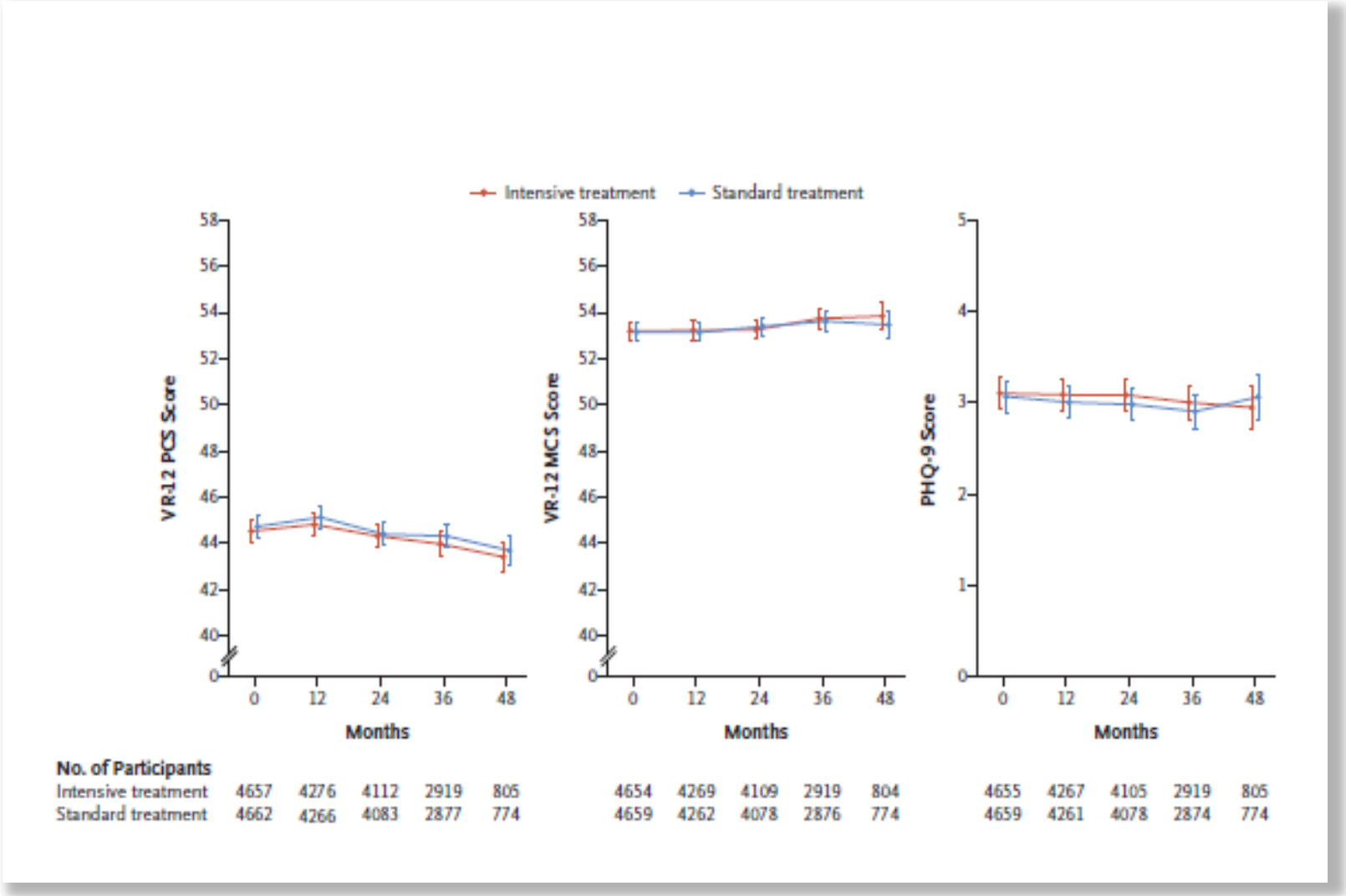
NEJM 2021; 385:1268-1279

Adverse Events	Intensive treatment (n=4243) no. of participants	Standard treatment (n=4268) no. of participants	Relative risks (95% CI)	*P* Value*
Angioedema	44 (1.0%)	50 (1.2%)	0.88 (0.59-1.33)	0.55
Headache	38 (0.9%)	40 (0.9%)	0.96 (0.61-1.49)	0.84
Cough	9 (0.2%)	14 (0.3%)	0.65 (0.28-1.49)	0.31
Hives	11 (0.3%)	13 (0.3%)	0.85 (0.38-1.90)	0.69

SPRINT
Tolerability of the
< 120 mm Hg SBP
Target

- Health-related quality of life measured using physical and mental components of VR-12 and depressive sxs using PHQ-9 shows 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.

BASELINE DBP AND SPRINT OUTCOMES
J-CURVE EFFECT IN SPRINT
Beddhu S et al. Circ 2018;137:134–143

- Analysis from SPRINT on clinical outcomes based on baseline DBP in patients randomized to the Intensive vs. Standard SBP targets
- Higher rates of clinical outcomes was associated with lower DBP in both treatment groups
- However, there was no evidence that Intensive SBP lowering was associated with higher rates of the primary CVD outcome or all cause mortality in those with lower DBP
- Higher rate of incident CKD in Intensive group explained by reversible hemodynamic effect of SBP reduction on eGFR

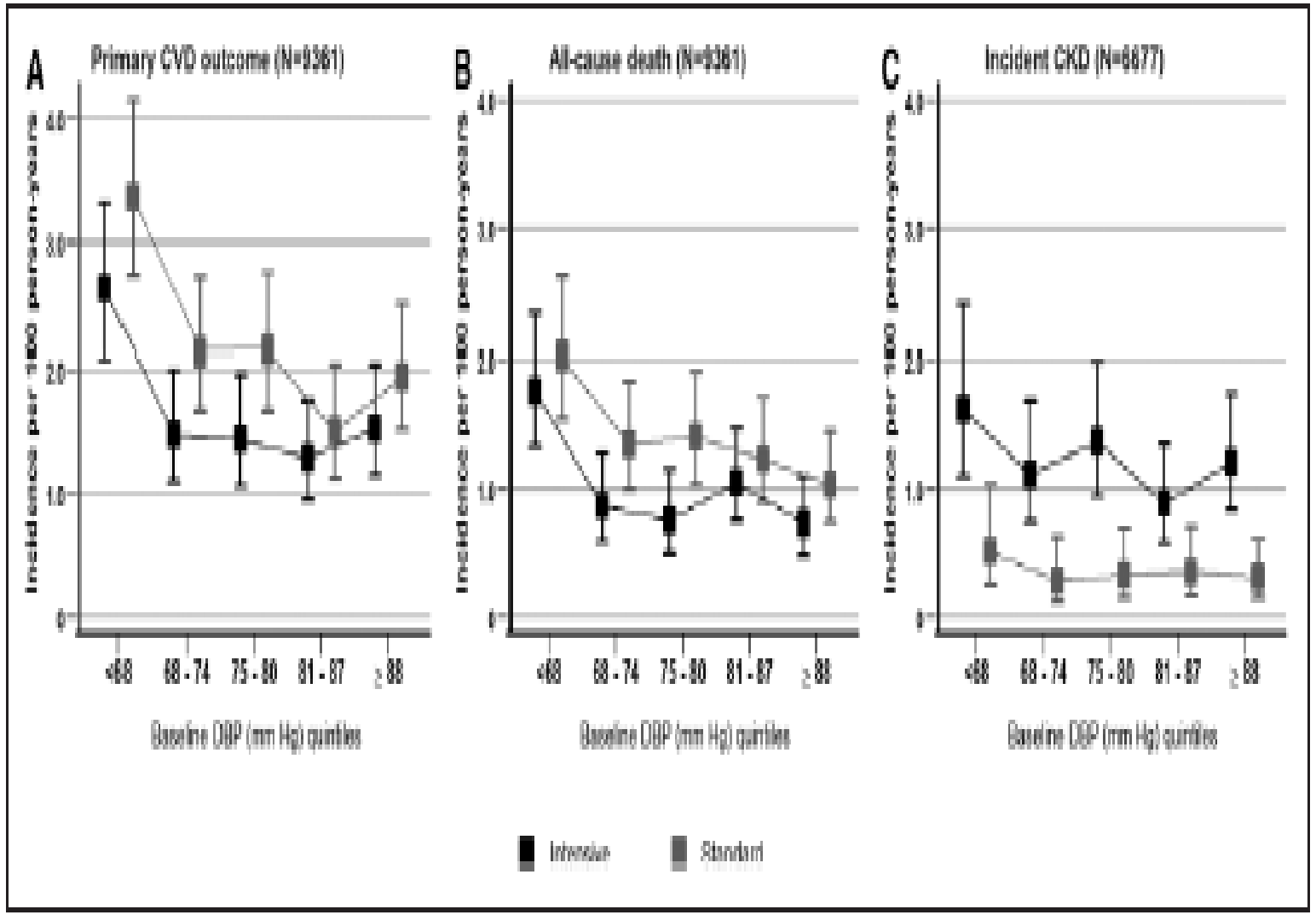


Figure 2. Incidence rates of events of interest by randomized SBP intervention and quintile of baseline DBP.

Blood Pressure Intervention and Control in SPRINT

Cushman WC, et al. DOI: 10.1161/HYPERTENSIONAHA.121.17233

Table 3. SBP Control at Last Visit on or Before August 20, 2015 by Randomized Group and Various Cut Points

	Intensive group		Standard group	
SBP, mm Hg Cut point*	*N*	%	*N*	%
<90	28	0.6	5	0.1
<100	200	4.3	46	1.0
<110	892	19.1	166	3.5
<120	2880	61.6	636	13.6
<130	3741	80.0	1564	33.4
<140	4223	90.3	3331	71.1
<150	4478	95.7	4201	89.7
<160	4602	98.4	4518	96.5
≥160	76	1.6	165	3.5

*Individual participants may be included in > 1 category.

RECENT HYPERTENSION GUIDELINE RECOMMENDATIONS

Guideline	Evidence Review Methodology	BP Target in General Adult Population	BP Target in High CVD Risk Grps	BP Target in CKD and DM
NICE (2011, amended 2022)	Systematic Review	Age < 80: <140/90 Age ≥ 80: <150/90	Age < 80: <140/90 Age ≥ 80: <150/90	<140/90
CHEP (2016)	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)	Consensus (Graded)	<140/90	<120/80 if thought safe	N/A
AHA/ACC (2017)	Consensus (Graded)	< 130/80	< 130/80	< 130/80
AAFP/ACP (2017)	Consensus	Age <60: <140/90 Age ≥60: <150/90	Age < 60: <140/90 Age ≥ 60: <150/90	<140/90
AAFP (2023)	Consensus	< 140/90 Consider <135/85 (though no evidence of added benefit)	< 140/90 Consider <135/85 (weak recommendation)	< 140/90
ESH/ESC (2018)	Consensus (Graded)	Age < 65: <140/90 But < 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
ESH (2023)	Consensus (Graded)	Age 18-64: <130/80 Age 64-80 < 130/80 if tolerated Age ≥ 80 SBP 130-140	Age < 80: <130/80 Age ≥ 80: SBP 130-140	CKD: SBP 130-140 DM: <130/80
ADA BP Targets (2023)	Consensus	<130/80	<130/80	<130/80
KDIGO (2021)	Consensus			<120/80 (CKD ± DM)
WHO (2021)	Consensus	<140/90	<130/80	<130/80

Treatment intensification over time based on guideline recommendations

- Data from a representative sample of 7404 practices/293 million visits from the National Ambulatory Medical Care Survey of US ambulatory medical care services from 2008-2018 (mean age 72.3 yrs)
- Assessed % of time antihypertensive medications added to treatment when BP in range where intensification recommended by various guidelines
- Appropriate increase in treatment intensity IAW AAFP/ACP guideline decreased from 24.7% in 2008-09 to 14.9% in 2015-2018
- Per the ACC/AHA guideline, increased treatment intensity decreased from 13.6 to 10.4%
- Thus, population at highest risk from HTN and that shows greatest benefit less likely to be treated to goal

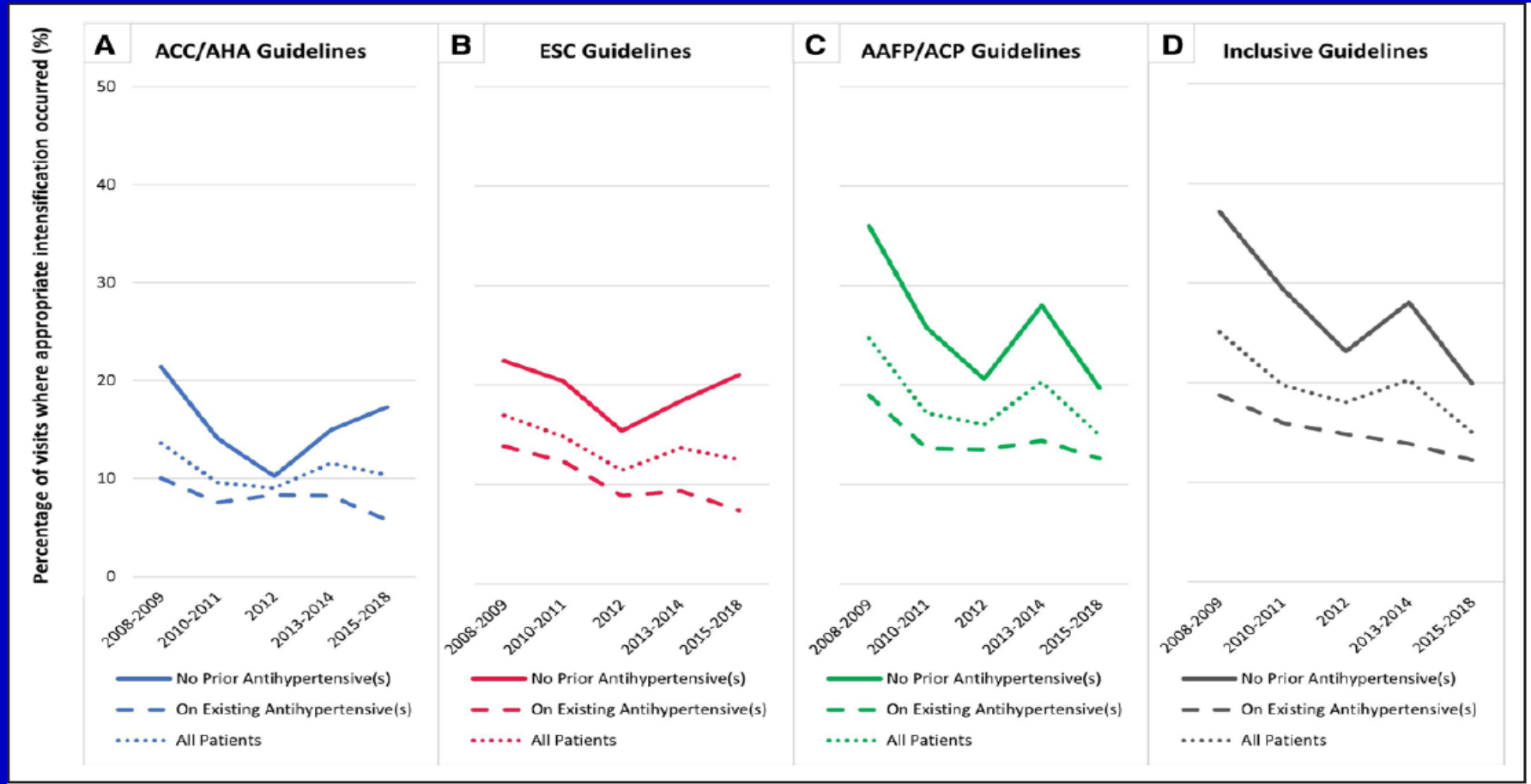


Figure 2. Proportion of visits where appropriate intensification occurred in older adults by guideline recommendations, 2008 to 2018.

A, Appropriate intensification by American College of Cardiology (ACC)/American Heart Association (AHA) guidelines; (**B**) shows appropriate intensification by European Society of Cardiology (ESC) guidelines; (**C**) appropriate intensification by American Academy of Family Physicians (AAFP)/American College of Physicians (ACP) guidelines; (**D**) appropriate intensification indicated by all three guideline criteria.

Kaiser Improvement

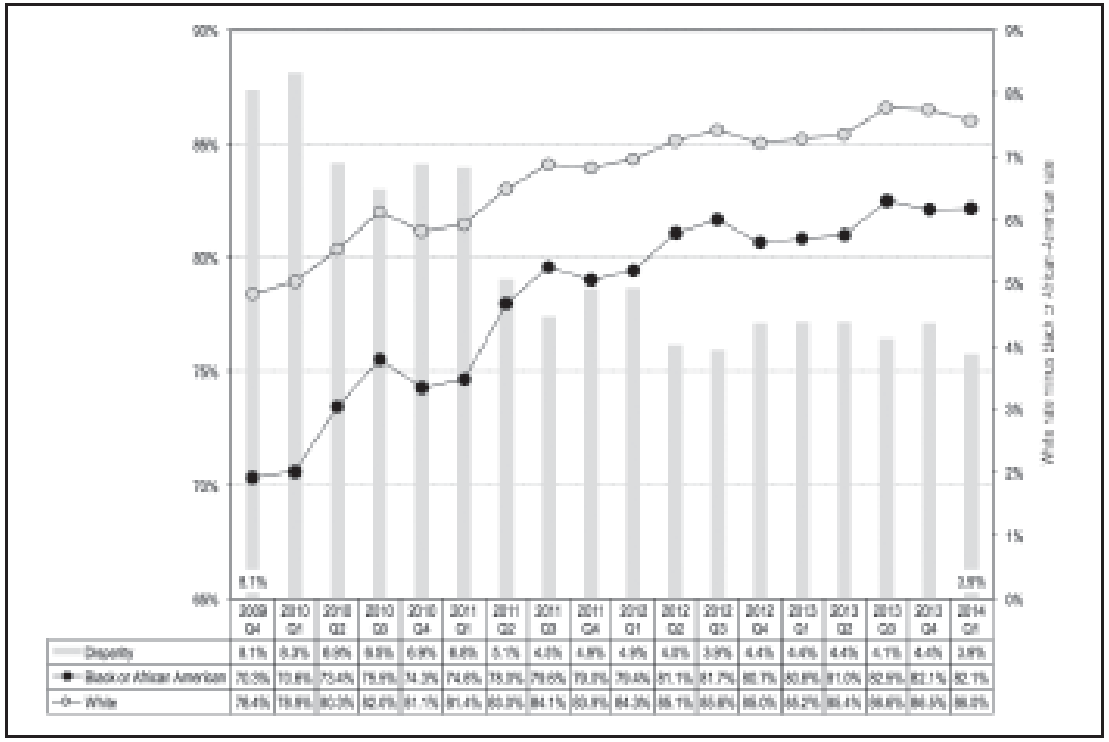


Figure 3. Hypertension control for Kaiser Permanente programwide.[1]

Percentage of members in hypertension registry with blood pressure below 140/90 mmHg (left x-axis) and disparity between control rates for white and black members (bars), 2009 Quarter (Q) 4 through 2014 Q1.

1. Platt ST. Kaiser Permanente Programwide Quarterly ECHO (Equitable Care Health Outcomes) Report (unpublished). Oakland, CA: Center for Healthcare Analytics, Hospitals, Quality and Care Delivery Excellence; 2014.

Table 2. BP Values and Hypertension Control Rates at the Past Visit of the Baseline and After Months 1 to 6 and 7 to 12 of MAP

Variables	Baseline	6 Months	12 Months	12 Months LOCF
n	16 787	16 787	11 863	16 787
Blood pressure values at baseline, 6 and 12 mo				
SBP, mm Hg	132.6±0.13	130.7±0.12	130.3±0.14	130.5±0.12
DBP, mm Hg	78.7±0.08	77.2±0.08	77.0±0.10	77.1±0.08
Change in BP from baseline to 6 and 12 mo				
Δ SBP from baseline, mm Hg		−1.9±0.14*	−2.1±0.17*	−2.0±0.14*
Δ DBP from baseline, mm Hg		−1.5±0.08*	−1.6±0.10*	−1.6±0.08*
Blood pressure categories				
BP <140/<90 mm Hg (controlled), n (%)	10 816 (64.4)	12 475 (74.3)	8797 (74.2)	12 346 (73.6)
BP 140–159/90–99 mm Hg, n (%)	4722 (28.1)	3359 (20.0)	2482 (20.9)	3557 (21.2)
BP ≥160/≥100 mm Hg, n (%)	1249 (7.4)	953 (5.7)	584 (4.9)	884 (5.3)
Hypertension control in black and white hypertensive adults				
BP <140/ <90 mm Hg whites, n (%)	7472 (67.3)	8524 (76.8)	6406 (76.1)	8442 (76.0)
BP <140/<90 mm Hg blacks, n (%)	1076 (56.8)	1352 (71.4)	1056 (69.7)	1318 (69.6)
White:black comparison	*P*<0.0001	*P*<0.0001	*P*<0.0001	*P*<0.0001

All data shown as mean±SE or n (number) and percent (%). BP indicates blood pressure; DBP, diastolic BP; LOCF, last observation carried forward; MAP, Measure accurately, Act rapidly, and Partner with patients; and SBP, systolic BP.

*$P<0.001$.

Egan BR, et al. HTN 2018; 72:1320-1327

SPRINT
Systolic Blood Pressure Intervention Trial

Median achieved SBPs overall and after 6 months medication titration period

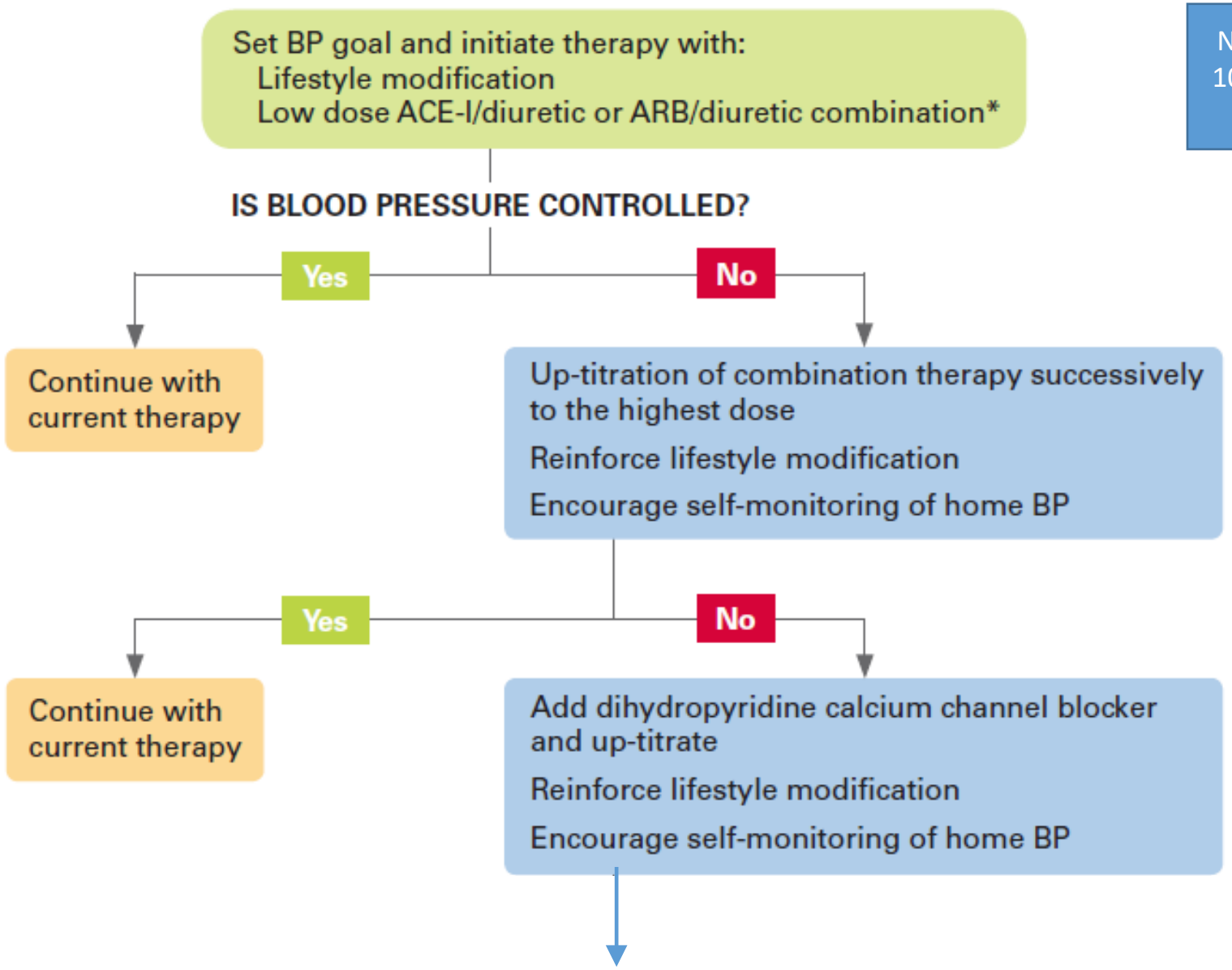
Wright JT Jr et al. Hypertens 2021; 78:1701–1710. DOI: 10.1161

Subgroup	Intensive	Standard	Baseline SBP	Median F/U SBPs		Median F/U intensive vs standard SBP	Median F/U SBP after 6 Months		Median F/U intensive vs standard SBP after 6 Months
				Intensive	standard		Intensive	standard	
Overall	4678	4683	138.0	120.5	135.1	-14.6	119.2	135.8	-16.6
Pre-Specified									
age<75	3361	3364	138.0	120.0	135.0	-15.0	118.5	135.6	-17.1
age>=75	1317	1319	140.0	122.4	135.5	-13.1	121.2	136.2	-15.0
Male	2994	3035	138.0	120.5	135.0	-14.5	119.0	135.6	-16.6
Female	1684	1648	140.0	120.6	135.4	-14.8	119.3	136.0	-16.7
Black	1454	1493	138.5	120.8	135.6	-14.7	119.4	136.2	-16.9
Nonblack	3224	3190	138.0	120.4	135.0	-14.6	119.1	135.5	-16.4
Prior CKD	1329	1316	138.0	121.7	135.4	-13.7	120.7	136.2	-15.5
No Prior CKD	3349	3367	139.0	120.1	135.1	-15.0	118.6	135.6	-17.0
Prior CVD	940	937	138.0	120.7	134.7	-14.1	119.4	135.5	-16.1
No Prior CVD	3738	3746	139.0	120.5	135.2	-14.7	119.1	135.8	-16.7
Not Pre-Specified									
Fit	178	196	138.0	119.9	135.7	-15.8	118.9	136.3	-17.4
Less Fit	659	680	140.0	122.5	135.2	-12.7	121.4	136.0	-14.6
Frail	474	434	143.0	123.4	135.9	-12.5	121.8	136.4	-14.6
Non-Hispanic White	2698	2701	138.0	120.6	134.9	-14.2	119.3	135.4	-16.2
Non-Hispanic Black	1379	1423	138.0	121.0	135.5	-14.5	119.5	136.2	-16.7
Hispanic	503	481	139.0	118.8	135.3	-16.5	117.7	135.9	-18.2
Prior Metabolic Syndrome	1825	1870	137.0	119.7	134.8	-15.1	118.4	135.2	-16.8
No Prior Metabolic Syndrome	2812	2755	139.0	121.1	135.4	-14.4	119.7	136.1	-16.5
Pre-diabetes	1941	1957	138.0	120.3	135.2	-14.9	119.0	135.7	-16.7
Normal	2721	2704	139.0	120.7	135.1	-14.4	119.2	135.8	-16.5

FEATURES OF MOST HTN QUALITY IMPROVEMENT PROGRAMS

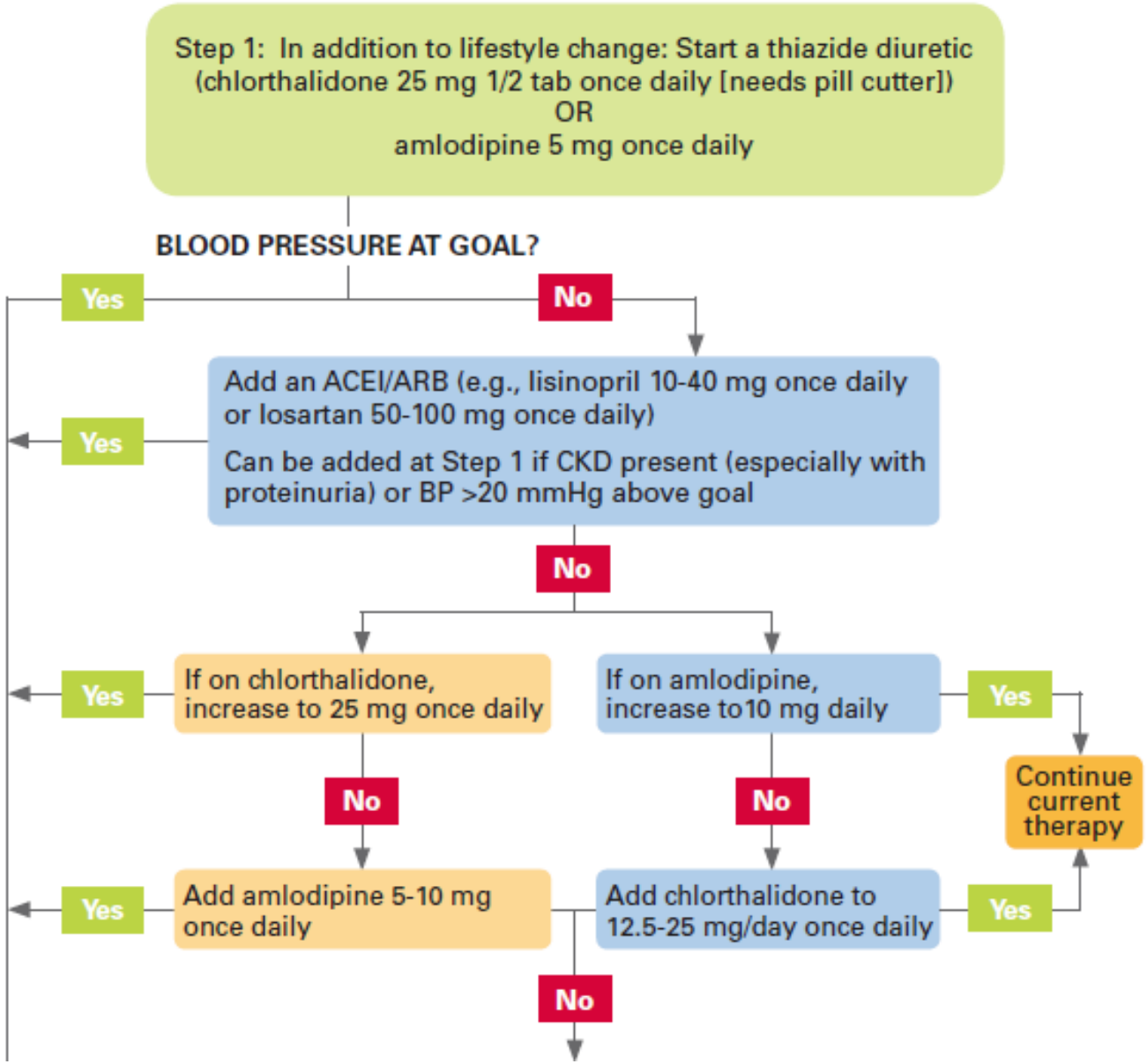
- Accurate BP measurement
- Repeat BP in patients with elevated BP (only) Improved communication with patients
- Use of fixed-dose combinations usually starting with low dose THZD/RASI combinations
- Increase treatment intensity and address clinical inertia in patients with elevated BP
- Target control based on < 140/90 goal

Classic HTN Treatment Algorithm

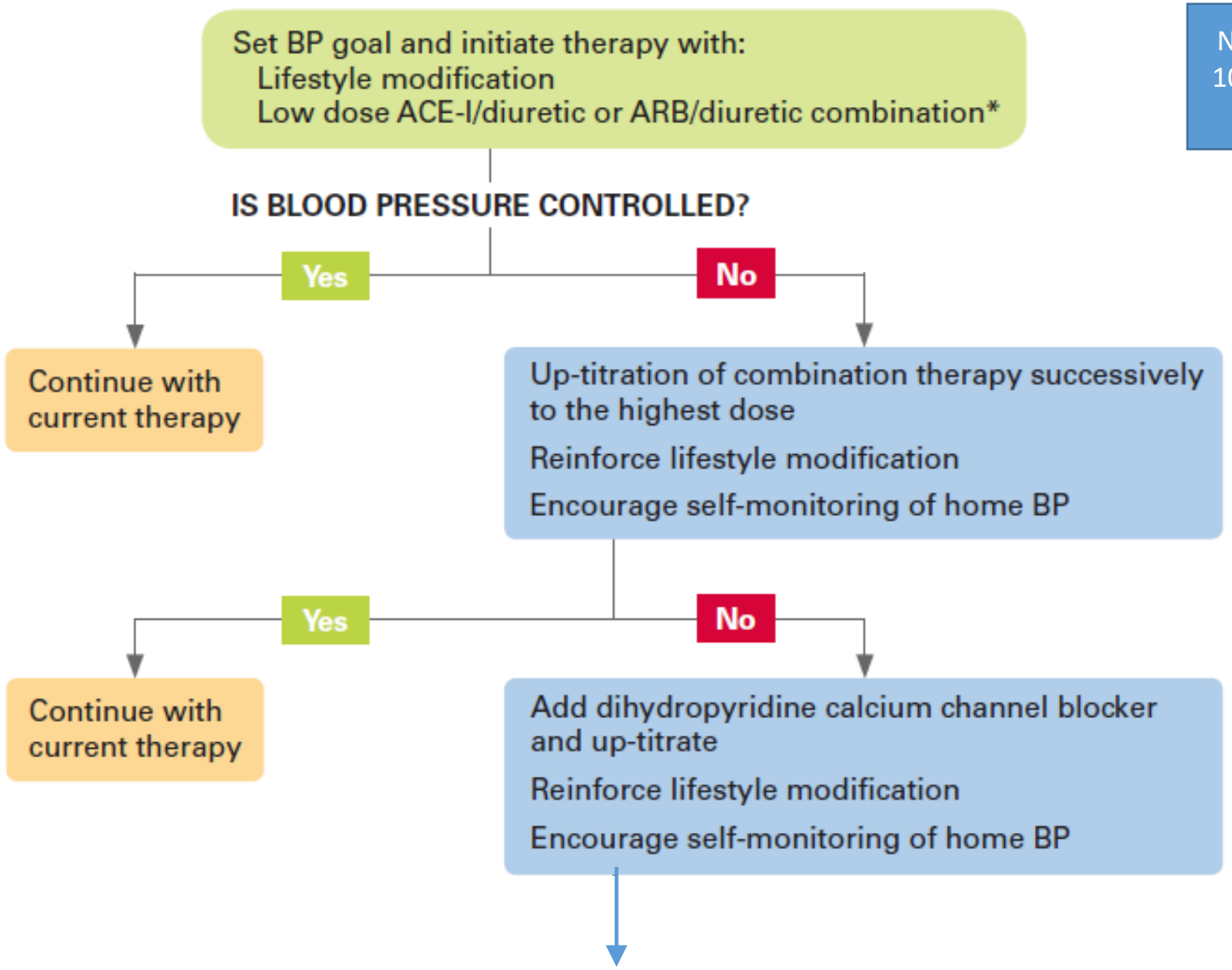


Note: In pts with SBP≥20 mmHg or DBP ≥ 10 mmHg above goal use full starting dose of 2 agents (since JNC-VII in 2003)

Updated HTN Drug Treatment Algorithm



Recommended Revision of Classic HTN Treatment Algorithm



Note: In pts with SBP≥20 mmHg or DBP ≥ 10 mmHg above goal use full starting dose of 2 agents (since JNC-VII in 2003)

About Cardi-OH

CARDI·OH

Ohio Cardiovascular and Diabetes Health Collaborative

Founded in 2017, the mission of Cardi-OH is to improve cardiovascular and diabetes health outcomes and eliminate disparities in Ohio's Medicaid population.

WHO WE ARE: Brings together all 7 Schools of Medicine across the state of Ohio

- Funded by the Ohio Department of Medicaid
- Focused on hypertension, diabetes, and social determinants of health

WHAT WE DO: Identify, produce and disseminate evidence-based cardiovascular and diabetes best practices to primary care teams.

- Provider education and quality improvement within primary care
- It included a separately funded quality improvement project paired with the Medicaid Managed Care Plans

HOW WE DO IT: Utilize monthly newsletters and an online repository of resources at Cardi-OH.org, podcasts available on Cardi-OH Radio, and the Project ECHO® virtual training model. Informed by an annual needs assessment.

Learn more at Cardi-OH.org

School of Medicine Case Western Reserve University

In partnership with:

The Ohio State University College of Medicine

College of Medicine and Life Sciences The University of Toledo

Ohio University Heritage College of Osteopathic Medicine

Northeast Ohio Medical University

University of Cincinnati Family and Community Medicine

Boonshoft School of Medicine Wright State University

Ohio Colleges of Medicine Government Resource Center

Ohio Department of Medicaid

medtapp

Executive PIs

CARDI·OH
Ohio Cardiovascular and Diabetes Health Collaborative

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The Ohio State University

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Saundra Regan, PhD

University of Toledo

Lance Dworkin, MD
Juan Jaume, MD

Northeast Ohio Medical University

Kris Baughman, PhD

Six Amazing Teams

CARDI·OH
Ohio Cardiovascular and Diabetes Health Collaborative

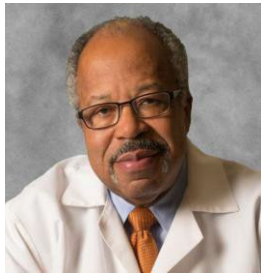
Data & Evaluation


Sarah Koopman Gonzalez, PhD
Elizabeth Beverly, PhD

Cardi-OH ECHO


Goutham Rao, MD
Claire Rollins, MBA

Best Practices

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HEART HEALTHY OHIO (HHOI)

Funded by AHRQ

Achieving Outstanding Cardiovascular Health Outcomes for All Ohioans: a Statewide Cardiovascular Health Collaborative (Cardio-OH)

SPECIFIC AIMS:

1. Expand a nascent statewide cardiovascular health collaborative and establish a sustainable external QI support infrastructure.
2. Co-design, implement and evaluate the effectiveness, adoption, implementation, and maintenance of the heart healthy QI intervention overall and by subgroup (e.g., geography, insurance, race/ethnicity) using a group randomized stepped wedge design.
3. Determine patient, provider, clinic, and other contextual factors associated with greater improvements in cardiovascular care at the heart healthy QIP clinics.

Note: 1) ***Prescibing patterns were derived from Ohio Department of Medicaid using pharmacy fill data***
2) HHOI prescribing pattern derived by EHR data download

Overview of ACHIEVE GREATER Project

ACHIEVE GreatER Center: **A**ddressing **C**ardiometabolic **H**ealth **I**nequities by **E**arly Pre**V**Ention in the Great Lak**E**s Region

- Aim: To reduce disparities in cardiovascular and metabolic (diabetes) risk factor control at an early stage for Black Participants in **Detroit, MI** and **Cleveland, OH**
- Center consists of 3 Cores (**Administrative, Community Engagement**, and **Investigator Development**) and 3 research studies focused on:
  - **Low risk, stage I hypertension** (PI: Robert Brook, Wayne State Univ.)
  - **Early-stage heart failure** (PI: David Lanfear, Henry Ford Health System)
  - **Subclinical coronary heart disease** (PI: Sanjay Rajagopalan, Chief, Division of Cardiovascular Medicine, CWRU/UH)
- In addition to the above studies, 6 pilot studies ~$40K awarded each year of grant

Funded by NIMHD as a P-50 in the Health Equity Action Network (HEAN)

Cleveland ACHIEVE Greater Project Design

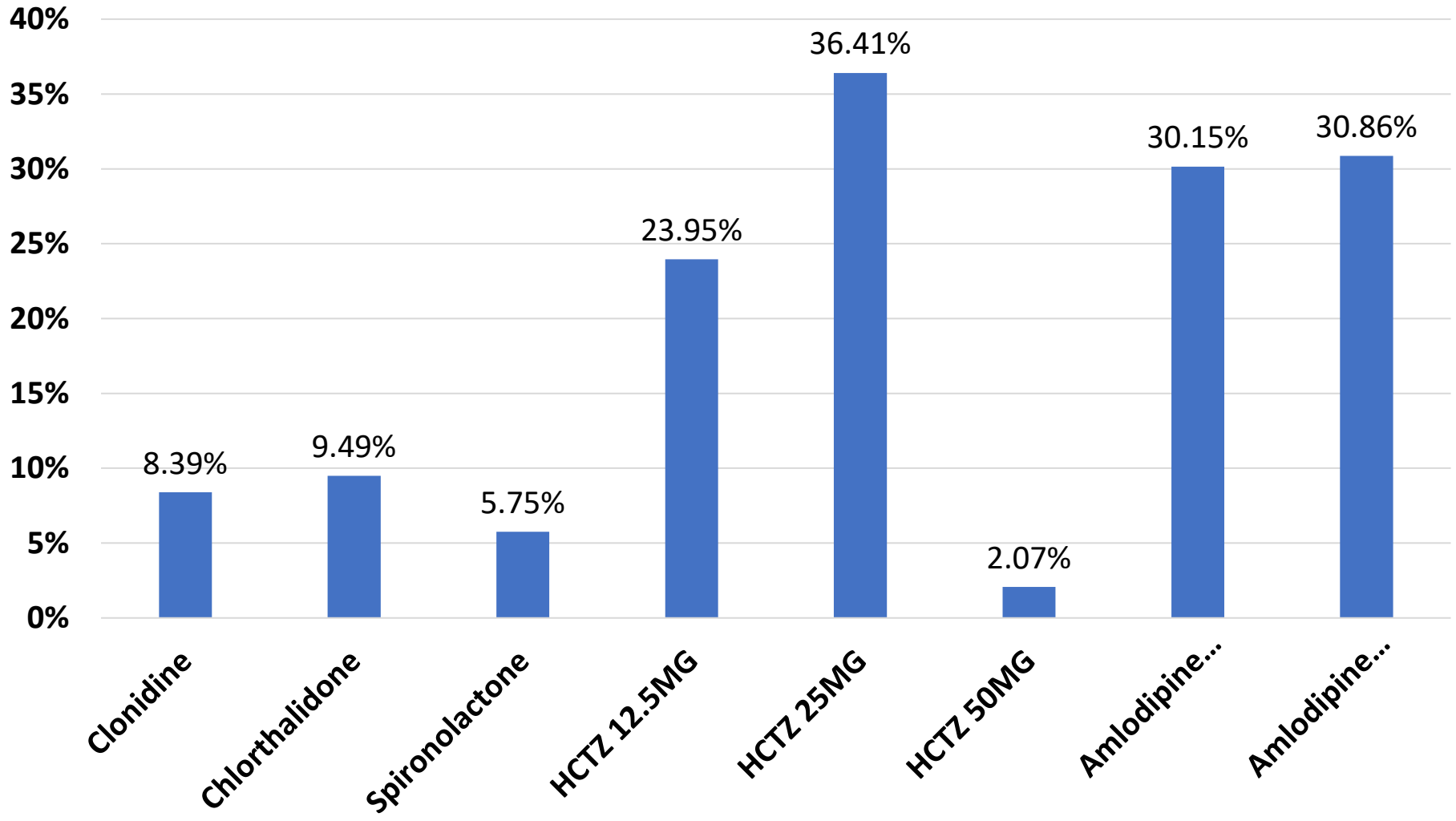
Objective: Risk factor control of hypertension, obesity, hyperlipidemia, and tobacco in Black patients age 40- with 2 of the following: a) BMI≥30 mg/dL; b) History of smoking; c) Elevated blood pressure defined as SBP>140 or DBP>80 mmHg; d) HbA1c≥5.7%; e) LDL≥130

- On the basis Ca scoring, participants divided into high (CAC score > 100) and low risk (CAC score < 100)
- Both groups will receive initial training of the clinical CHW-facilitated called PAL2 [personalized, adaptable lifestyle and life circumstance intervention]
- High risk participants with seen in Cardiology specialty clinic
- Lower risk participants with continue follow-up by their PCP with care augmented by CHWs to address SDOH and continued training in the PAL2 lifestyle intervention
- Plan is to recruit 500 participants and assess for following endpoints:
  - Primary outcome: % with triple goal of BP <130/80 mm Hg, HbA1c<5.7% and LDL-C <130 mg/dl (<100 if high-risk) at 12 months
  - Secondary outcome: % 1-year change in HbA1c, LDL-C, BP, weight vs baseline.
  - Tertiary outcome: 1-year rate of new medical/mental health visit, smoking cessation, diet and activity changes and durability of intervention 12 months after cessation of intervention or 24 months after enrollment.

KEY LESSONS LEARNED
Factors Associated With Inadequate Control at Practice Level

- Level of treatment intensity
  - Many patients with elevated BP were only taking 2 or fewer meds
  - Subtherapeutic levels of HCTZ and inadequate doses of amlodipine were prescribed
- Use of lower than recommended doses of HCTZ rather than recommended or low dose chlorthalidone in pts prescribed a THZD
- Many patients were prescribed 30 rather than 90 day prescriptions that were not synchronized for refills
- Resources for team-based care are markedly inadequate for risk factor control
  - *(estimated that in order to fullfil and document recommended elements of care by PCPs would require 27hr/day)*

Selected BP Medications Filled in Adults on Medicaid with uncontrolled BP *Calendar Years* 2017-2018 (N=1549)



Ohio Department of Medicaid's (ODM's) Chronic Conditions Quality Collaborative Ohio MEDTAPP funded ODM Hypertension Quality Improvement Project, 2019. https://grc.osu.edu/Projects/MEDTAPP/HypertensionQIP

Health Center #146 Dashboard Summary 2/1/2023

(n = 298 visits with BP data)

BP Control	≤ 140/90 mmHg (Financial Benefit)	≤ 130/80 mmHg (Patient Benefit)
ALL	70.1%	31.5%
NHB	63.0%	25.3%
NHW	76.8%	37.6%

Health Center #146 Dashboard Summary 2/1/2023

(n = 298 visits with BP data)

Patients With Elevated BP (>130/80) At Last Visit

HTN Treatment Intensity	
O meds	7.9%
1 med	25.8%
2 meds	24.7%
Total on < 3 meds	58.4%
HCTZ dosing	
12.5 mg/day	10.7%
25 mg/day	10.7%
50 mg/day	0%
Chlorthalidone Use	13.1%
Amlodipine Use	½ patients on AML on only 2.5 or 5 mg/day

Cross-Sectional Estimate BP Control Rate at UH 2021

	N	(%) controlled ≤ 140/90 mmHg	(%) controlled ≤ 130/80 mmHg
System-Wide Patients	302,588	66.8	33.4
Black Race	51,027	58.0	26.1
Patients with Diabetes	100,361	68.7	37.5
Patients with CKD	52,658	68.9	41.4

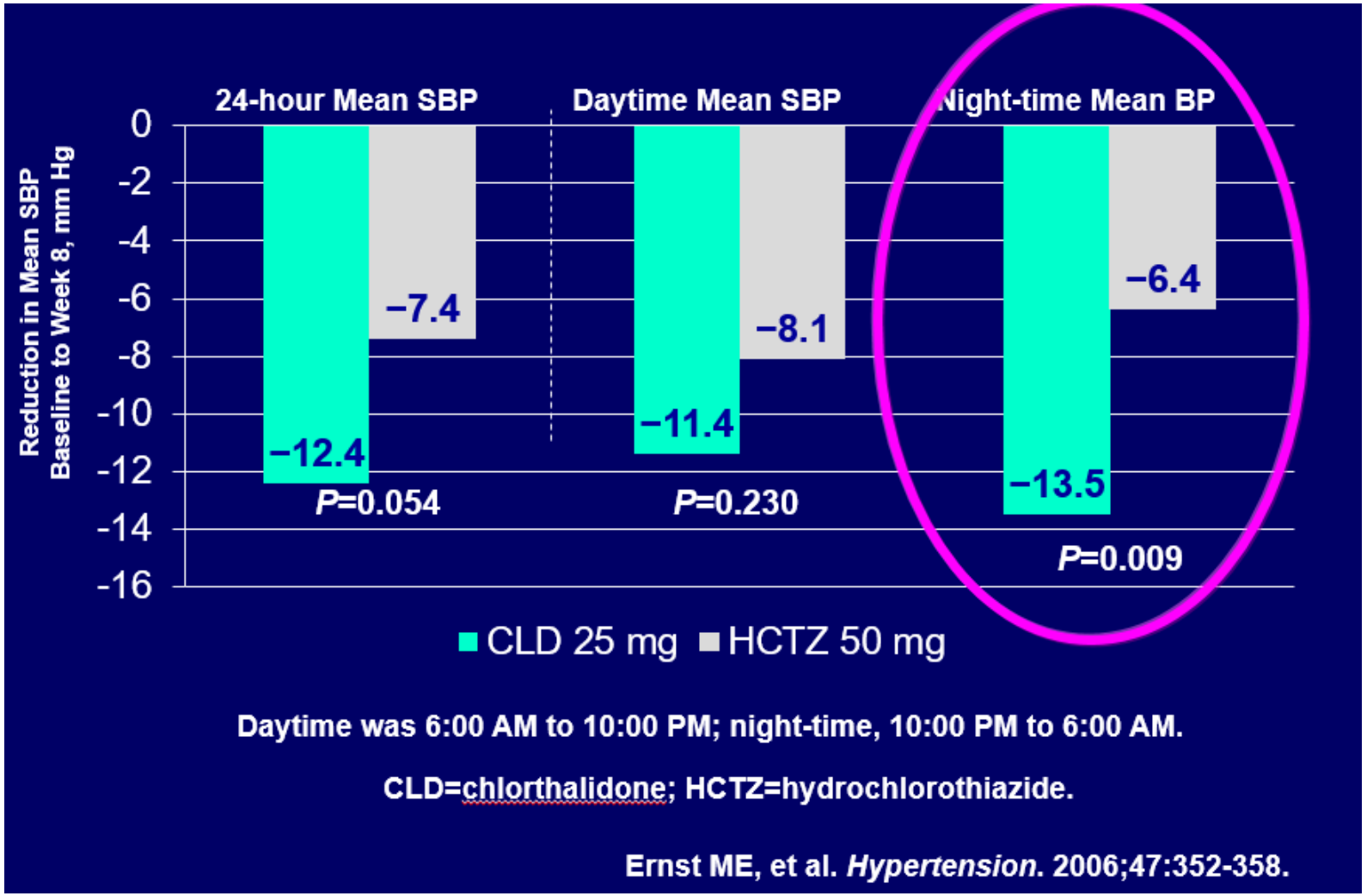
Potential Opportunities to Increase BP Control Rates
UH 2021

	(%) with BP ≥ 130/80 and < 90 day refills	(%) with BP ≥ 130/80 on ≥ 3 BP meds	(%) not on spironolactone or eplerenone)	(%) receiving either chlorthalidone 25 mg/day or HCTZ 50 mg/day
System-Wide Patients	46.9	1.5	82.8	3.2
Black Race	47.5	2.7	78.1	6.8
Patients with Diabetes	44.0	2.4	82.3	3.3
Patients with CKD	47.5	2.9	81.1	3.2

Thiazide-type Diuretic Doses in Hypertension Outcome Trials

Trial	Drug	Dose of Thiazide (mg/d)
VA CSP M&M	HCTZ	100
HDFP	chlorthalidone	25-100
MRC I	bendroflumethiazide	10
HAPPHY	bendroflumethiazide	5-10
	HCTZ	50-100
EWPHE	HCTZ/triamterine	25-50
MRC Elderly	HCTZ/amiloride	25-50
ACCOMPLISH	HCTZ/ACEI vs CCB/ACEI	12.5-25
SHEP	chlorthalidone	12.5-25
ALLHAT	chlorthalidone	12.5-25
SPRINT	chlorthalidone	12.5-25
PATS	indapamide	2.5
PROGRESS	indapamide (+ACEI)	2.5
HYVET	indapamide	1.5

Chlorthalidone Has Greater BP-Lowering Efficacy vs. HCTZ, Especially at Night



Diuretic Duration of Action and Pharmacokinetics							
Drug	Vol of Distribution	BP↓/mg	Oral Bioavail	Onset of Effect	Peak Effect	Half-life (chronic dosing)	Duration (chronic dosing)
HCTZ	**3-4 L/kg 40% protein bound**	**ref**	**~70%**	**2 hr**	**4-6 hr**	**8-15 hr**	**16-24 hr**
Chlorthalidone	**3-13/kg 75% protein bound (*98% RBC distribution*)**	**2**	**~65%**	**2-3 hr**	**2-6 hr**	**40-60 hr**	**48-72 hr**
Indapamide		**20**	**~93%**	**1-2 hr**	**< 2 hr**	**14 hr**	**~36 hr**
Amlodipine				**4-6 hr**		**40-60**	**24-72 hr**
Verapamil (SR)				**1-2 hr**		**4.5-12 hr**	**~24 hr**

Note: Compared to HCTZ, chlorthalidone ~ twice as potent in BP lowering, more gradual onset of diuretic action, longer duration of action of BP lowering, and has larger evidence base documenting CVD reduction

Carter BL, Ernst ME, Cohen JD. Hypertension 2004;43:4-9.
Abernathy DR, Cardiol 1992; 80:31-36

SUMMARY

- Evidence from the SPRINT trial now confirmed by the STEP trial and multiple meta-analyses supports use of a lower BP target (<130/80 mmHg) in nearly all ages and subgroups.
- All showed substantial reduction in cardiovascular events including CV, all cause mortality, and some evidence for slowing cognitive decline, and excellent safety profile *even in older age groups* with intensive BP lowering
- Nearly all national and international guidelines now recommend BP targets in this range (some recommend lower)
- Only a minority of individuals may not tolerate or benefit from the lower BP target may as risks may outweigh the benefits (e.g., dementia, orthostatic hypotension)
- Note: More aggressive BP control also decreases rather than increases incidence of orthostatic hypotension (see refs below)

Townsend RR et al. J Am Soc Hypertens. 2016 10:847-856. doi: 10.1016/j.jash.2016.08.005..
Juraschek SP, et al. Ann Intern Med 2020 ;174: 58-68.doi:10.7326/M20-4298)

SUMMARY (Con't)

- Chlorthalidone is more potent than HCTZ at similar dose levels and along with amlodipine has a very long half life (40-60 hrs) and thus more tolerant of missed doses.
- THZDs are effective regardless of age or race, and chlorthalidone use in SPRINT achieved similar levels of BP control in the < 120 mmHg arm by race and Hispanic ethnicity.
- The medical community should no longer accept as ethical 70% control to < 140/90 mmHg and disparate BP control as acceptable care
- The tracking of prescription patterns for evidence of clinical inertia and encouraging the use of long acting/more potent antihypertensive agents in HTN QI programs are needed to achieve the recommended lower BP targets.
- The management of chronic diseases like hypertension will require additional support to PCPs to address SDOH to achieve achieve equity

Questions and Discussion

BACKUP SLIDES

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Career Phases

- Throughout my career, I have been fortunate to work with talented and dedicated investigators to:
  - Determine the best target BP and drug regimen to slow the progression of kidney decline in Black patients with hypertension-related CKD in the AASK
  - Along with Bill Cushman determine whether newer more costly BP lowering agents were more effective in preventing cardiovascular and kidney disease outcomes than tried and true much less expensive thiazide type diuretics in the ALLHAT in a multi-racial and ethnic high risk hypertensive population
  - Again with Bill and Karen Johnson, determine the optimal SBP target to prevent CVD outcomes and slow the progression of cognitive
- After accomplishing those challenges, I decided to relax in retirement and only take on easy projects

DIURETIC COMPARISON PROJECT (NCT:02185417)

Ishani I., Cushman W.C., et al. *NEJM.* 2022; 387:2401-2410

- **Question:** Does treatment with chlorthalidone reduce major adverse cardiovascular events (MACE) compared with hydrochlorothiazide (HCTZ) in older veterans with hypertension?
- **Method:**
  - Comparison of HCTZ 25-50 mg/day vs chlorthalidone 12.5-25 mg/day, N=13,500
  - Primary outcome: Stroke, MI, hospitalized HF, urgent coronary revascularization for unstable angina, non-cancer death
- **Results:**
  - No difference in either BP control or CVD outcomes
- **However:**
  - Only 5% of participants in each arm were titrated above the starting dose (25 mg/day HCTZ, 12.5 mg chlorthalidone)
  - Thus, only the effect of starting doses of each arm were evaluated

Systolic Blood Pressure Intervention Trial (SPRINT)

SPRINT compared the effect of treating to a SBP target of < 120 mm Hg vs treatment to < 140 mm Hg

Sprint recruited a diverse population of 9,361 patients with elevated CVD risk:

- 28% over age 75
- ~30% African American
- ~11% Hispanic

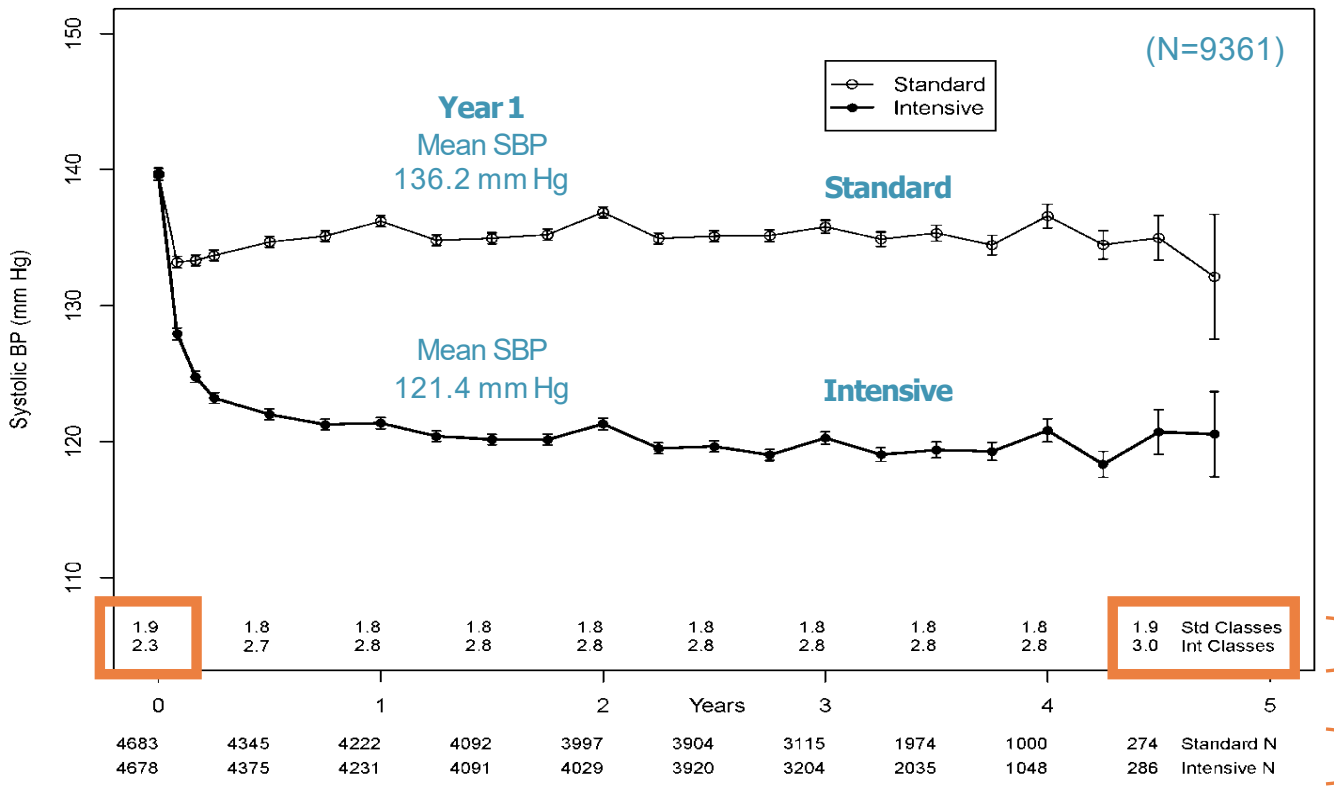
Demographic and Baseline Characteristics			
Trial	*Total N=9361*	*Intensive N=4678*	*Standard N=4683*
Mean (SD) age, years	67.9 (9.4)	67.9 (9.4)	67.9 (9.5)
% ≥75 years	28.2%	28.2%	28.2%
Female, %	35.6%	36.0%	35.2%
White, %	57.7%	57.7%	57.7%
African American, %	29.9%	29.5%	30.4%
Hispanic, %	10.5%	10.8%	10.3%
Prior CVD, %	20.1%	20.1%	20.0%
Mean 10-year Framingham CVD risk, %	24.8%	24.8%	24.8%
Taking antihypertensive meds, %	90.6%	90.8%	90.4%
Mean (SD) number of antihypertensive meds	1.8 (1.0)	1.8 (1.0)	1.8 (1.0)
Mean (SD) Baseline BP, mm Hg			
Systolic	139.7 (15.6)	139.7 (15.8)	139.7 (15.4)
Diastolic	78.1 (11.9)	78.2 (11.9)	78.0 (12.0)

SPRINT BP Findings

Good BP separation achieved, with those randomized to < 120 mm Hg requiring on average one more BP medication than those randomized to the <140 mm Hg target

BP separation continued throughout trial follow-up

Mean Systolic Blood Pressure (95% CI)



Average SBP
During Follow-up

Standard
134.6 mm Hg

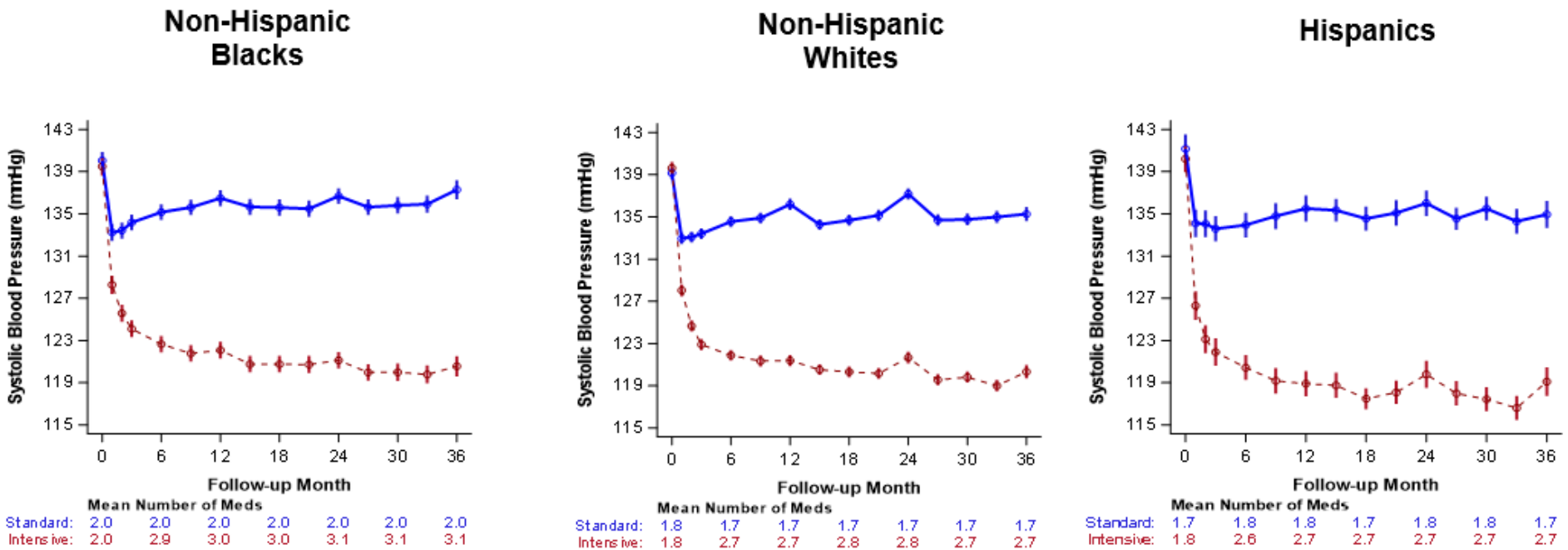
Intensive
121.5 mm Hg

Average number of antihypertensive medications

Number of participants

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

Systolic BP During Follow-Up



Average post-baseline follow-up SBP mean±SE for standard (vs intensive) group: NHW=134.7±0.1 (vs 119.9±0.4) mmHg; NHB = 135.5±0.2 (vs of 121.8±0.2) mmHg; Hispanic= 134.8±0.3 (vs 122.6±0.2) mmHg.

Still CH et al. Am J Hypertens 2017, https://doi.org/10.1093/ajh/hpx138

SPRINT
Systolic Blood Pressure Intervention Trial

ALLHAT

Angioedema

	Total	Blacks	Non-blacks
Chlorthalidone	8 / 15,255 0.1%	2 / 5,369 <0.1%	6 / 9,886 0.1%
Lisinopril	38 / 9,054 0.4%	23 / 3,210 0.7%	15 / 5,844 0.3%
	p<.001	p<.001	p=.002

There were 3 cases (<0.1%) of angioedema in the amlodipine group (comparison to chlorthalidone not significant).

Wright JT Jr, for the ALLHAT Collaborative Research Group. JAMA 2005; 6: 293:1595-608

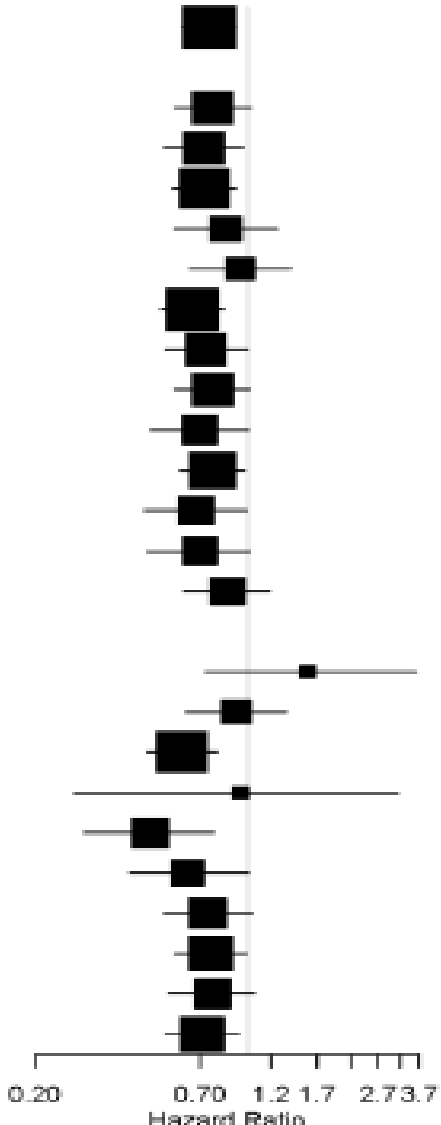
Forest Plots All Cause Mortality overall and in Subgroups.

Wright JT Jr et al. Hypertens 2021; 78:1701–1710. DOI: 10.1161

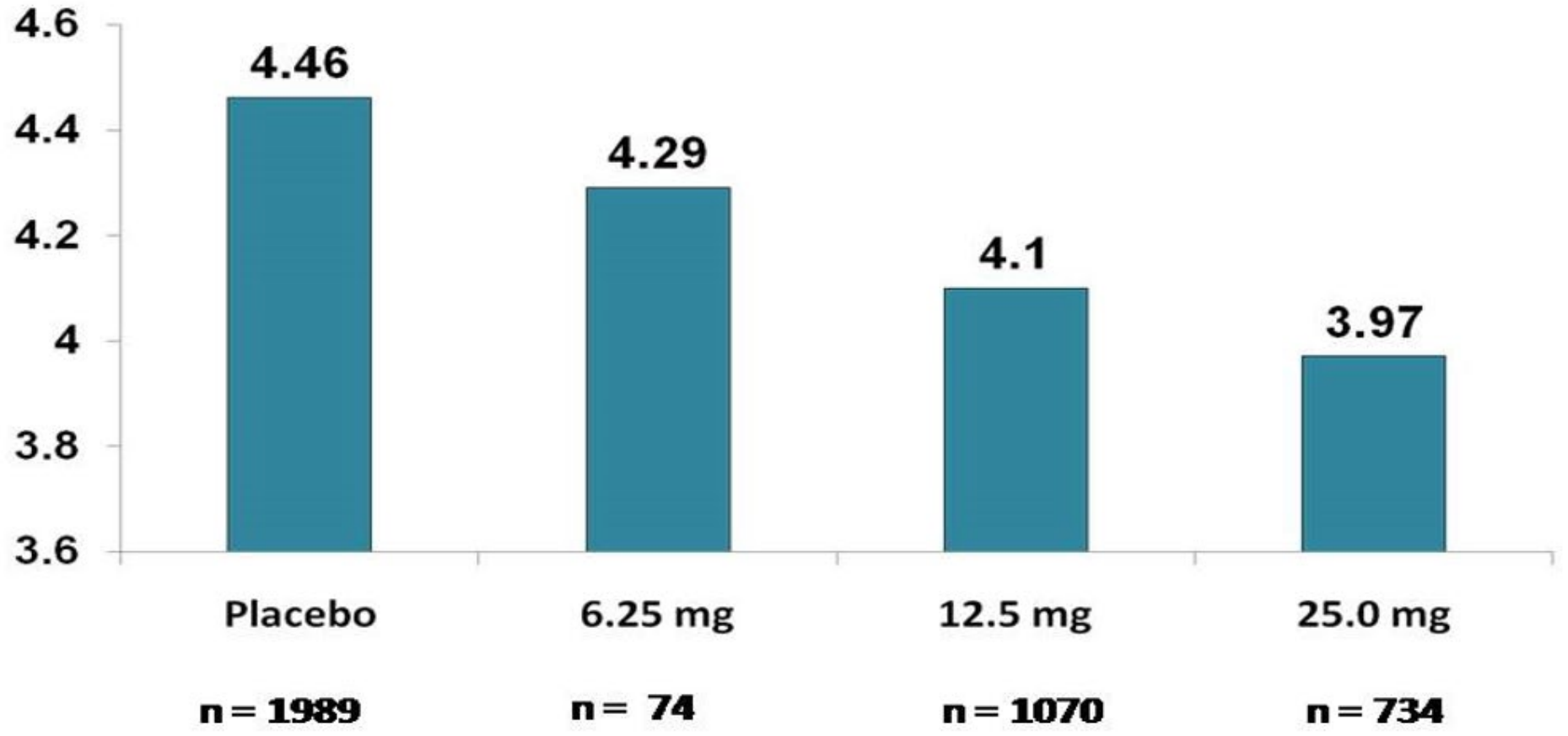
- Similar findings seen with all-cause mortality outcome
- Note: all-cause mortality result in Hispanic subgroup due to increase in non-CV outcome
- Hazard ratio (95% CI) for CV outcome in Hispanics was 0.17 (0.01 1.08)

Forest Plots for All-Cause Mortality

Subgroup	Intensive	Standard	Hazard Ratio 95% CI	P Value for Interaction
Overall	163/4678 (3.48)	215/4683 (4.59)	0.75 (0.61,0.92)	
Pre-Specified				
Age<75	84/3361 (2.50)	107/3364 (3.18)	0.77 (0.58,1.03)	0.77
Age≥75	79/1317 (6.00)	108/1319 (8.19)	0.72 (0.53,0.97)	
Male	114/2994 (3.81)	159/3035 (5.24)	0.72 (0.57,0.92)	0.49
Female	49/1684 (2.91)	56/1648 (3.40)	0.85 (0.58,1.25)	
Black	54/1454 (3.71)	57/1493 (3.82)	0.95 (0.65,1.39)	0.09
Nonblack	109/3224 (3.38)	158/3190 (4.95)	0.66 (0.52,0.84)	
Prior CKD	75/1330 (5.64)	99/1316 (7.52)	0.73 (0.54,1.00)	0.76
No Prior CKD	88/3348 (2.63)	116/3367 (3.45)	0.77 (0.58,1.02)	
Prior CVD	52/940 (5.53)	72/937 (7.68)	0.70 (0.48,1.01)	0.74
No prior CVD	111/3738 (2.97)	143/3746 (3.82)	0.77 (0.60,0.98)	
SBP≤132	48/1583 (3.03)	85/1553 (4.19)	0.68 (0.46,0.99)	0.33
132<SBP<145	44/1489 (2.96)	65/1549 (4.20)	0.70 (0.47,1.02)	
SBP≥145	71/1606 (4.42)	85/1581 (5.38)	0.86 (0.62,1.19)	
Not Pre-Specified				
Hispanic	19/503 (3.78)	12/481 (2.49)	1.58 (0.73,3.62)	0.01
Non-Hispanic Black	51/1379 (3.70)	56/1423 (3.94)	0.92 (0.63,1.35)	
Non-Hispanic White	89/2698 (3.30)	144/2701 (5.33)	0.61 (0.47,0.80)	
Fit	5/159 (3.14)	6/190 (3.16)	0.95 (0.27,3.15)	0.52
Less Fit	26/711 (3.66)	52/745 (6.98)	0.48 (0.29,0.78)	
Frail	40/440 (9.09)	49/375 (13.07)	0.64 (0.41,1.01)	
Prior MetS	60/1737 (3.45)	80/1784 (4.48)	0.74 (0.53,1.04)	0.91
No Prior MetS	98/2807 (3.49)	129/2769 (4.66)	0.76 (0.58,0.99)	
Pre-DM	65/1941 (3.35)	84/1957 (4.29)	0.77 (0.55,1.06)	0.74
Normal	89/2721 (3.27)	125/2704 (4.62)	0.71 (0.54,0.94)	



SHEP-ROLE of Low K+



Franse et al Hyper. 35:1025, 2000

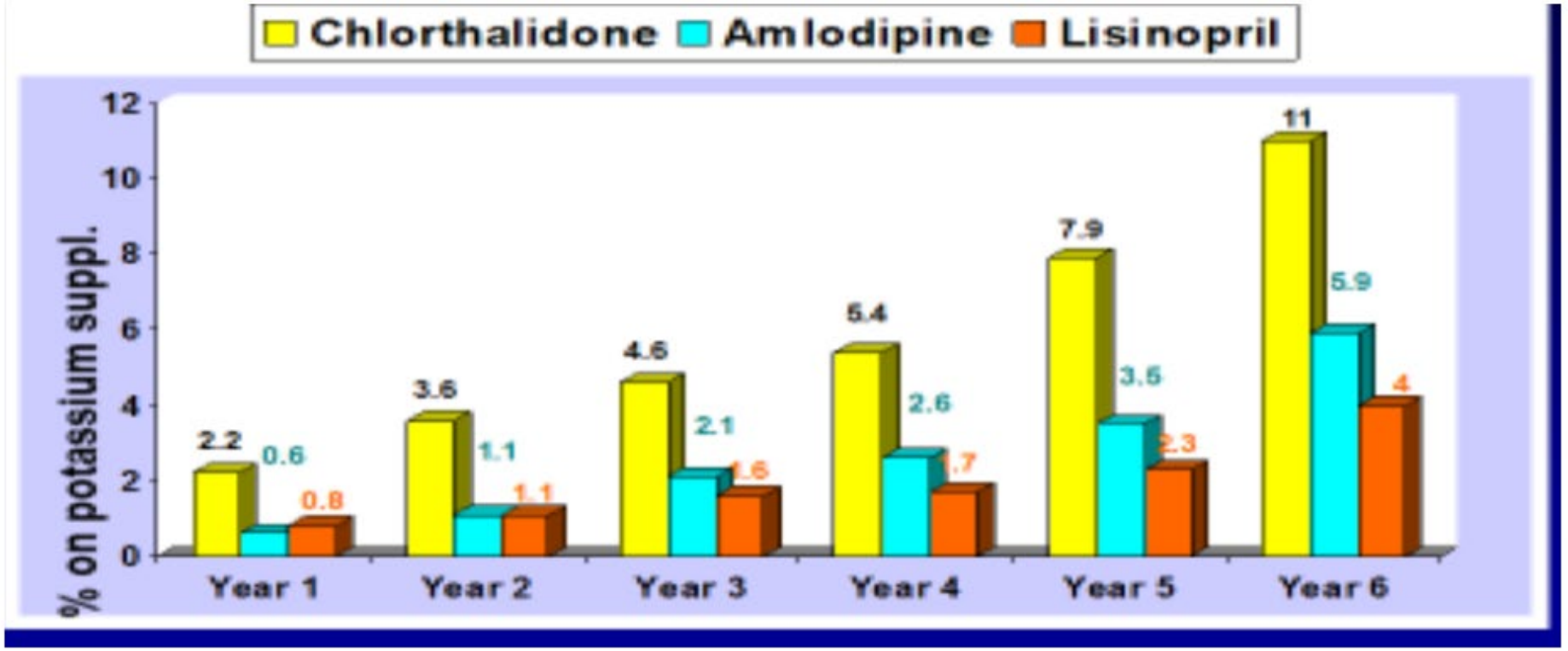
Blood Pressure at 5 Years by Race

		Chlorthalidone	Amlodipine	Lisinopril
SBP – mean (sd)	Black	135.0 (15.8)	136.1 (15.3)	139.1 (19.7)
	Non-Black	133.3 (14.8)	133.8 (14.6)	134.2 (16.7)
DBP – mean (sd)	Black	77.4 (10.0)	76.3 (10.1)	78.0 (11.4)
	Non-Black	74.4 (9.5)	73.6 (9.6)	74.1 (10.1)
Δ BP compared with chlorthalidone	Black	---	+1.1 / -1.1*	+4.1* / +0.6
	Non-Black	---	+0.5 / -0.8*	+0.9 / -0.3

*$P<0.005$

Wright JT et al. JAMA 2005; 293:1593

Use of Potassium Supplementation in ALLHAT



JAMA 2002;288:2981-2991

Hyponatremia with Chlorthalidone

Hwang KS, Kim GH. *Electrolyte Blood Press*. 2010;8(1):51–57

- **4.1% of pts receiving chlorthalidone vs 1.3% of control patients among the > 4,700 pts in SHEP trial developed hyponatremia.**
- **Mean age 72 yrs**
- **60% of patients were on chlorthalidone > 25 mg/day**