



CARDI•OH

Ohio Cardiovascular Health Collaborative



In partnership with:



Cardi-OH ECHO - Hypertension

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The following planners, speakers, moderators, and/or panelists of the CME activity have financial relationships with commercial interests to disclose:

- Adam T. Perzynski, PhD reports being co-founder of Global Health Metrics LLC, a Cleveland-based software company and royalty agreements for forthcoming books with Springer publishing and Taylor Francis publishing.
- Siran M. Koroukian, PhD reports ownership interests in American Renal Associates, and Research Investigator subcontract support from Celgene Corporation.
- George L. Bakris, MD reports partial salary from Bayer as FIDELIO PI, partial salary from Janssen as CREDENCE Steering Committee, partial salary from Vascular Dynamics as Calm-2 Steering Committee, and receiving honorarium as a consultant to Merck, NovoNordisk.
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Treatment of Hypertension in Special Populations



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Hypertension in the Elderly

Larry Lawhorne, MD

Objectives



- Review the definition of elderly.
- Consider how management of hypertension in the elderly has evolved up to and including the publication of the 2017 ACC/AHA guidelines.
- Discuss current knowledge gaps and recommendations based on a report from an ACC/AGS/NIA workshop.

Who's elderly?



- Working definition: The age at which pensions, social security or medical benefits usually become available...65 years of age in U.S.
- Operationally: Age + Life Expectancy!

Factors Influencing Life Expectancy



- Current age
- Gender
- Social support
- Current living situation
 - Community
 - Assisted Living Facility
 - Nursing Facility
- Frailty
- Neurocognitive function
- ADL dependencies
- Multimorbidity
- Polypharmacy
- Fall history

Life Expectancy in Older Men (Years Still to Live)



Age	70	75	80	85	90	95
Fit	18	14.2	10.8	7.9	5.8	4.3
Less Fit	12.4	9.3	6.7	4.7	3.2	2.3
Frail	6.7	4.9	3.3	2.2	1.5	1.0

Life Expectancy in Older Women (Years Still to Live)



Age	70	75	80	85	90	95
Fit	21.3	17.0	13.0	9.6	6.8	4.8
Less Fit	15.7	11.9	8.6	5.9	3.9	2.7
Frail	9.5	6.8	4.6	2.9	1.8	1.7

Is Hypertension in Old Folks...

An Essential Malady?
or
A Treatable Condition?

Roosevelt at Yalta

- Elevated BP first noted 1937. BP as high as 220/120 thereafter.
- Fatal stroke in 1945 at age 63 (two months after this photograph).



From Essential Malady...



To Treatable Condition

Evidence for Treatment

- Multicenter VA Co-operative study (1964-71) demonstrated the benefit of treating elevated DBP.
- Systolic Hypertension in the Elderly (SHEP) demonstrated the benefit of treating elevated SBP (1991).
- In addition, the benefits of antihypertensive drugs in older people demonstrated in a succession of RCTs over the past 3 to 4 decades.

Benefits:

- Decreased strokes
- Decreased myocardial infarctions
- Increased survival

Brief Summary of Trials

Trial	Subjects	Intervention	Outcome
SHEP	4376 patients (72 yo; mean BP 170/77)	chlorthalidone (+ atenolol or reserpine if needed) vs placebo	143/68 with active therapy vs 155/72 with placebo
Syst-Eur trial	4695 patients (70 yo; mean BP 174/86)	nitrendipine + enalapril and HCTZ if needed vs placebo	BP reduction greater with active therapy: (151/79 vs 161/84)
MRC	3496 patients (65 to 74; mean BP 185/91)	HCTZ + amiloride vs atenolol vs placebo	Both treatment groups with similar decrease in DBP compared to placebo

Trial	Subjects	Intervention	Outcome
HYVET	3845 patients (84 years; mean BP 173/91)	indapamide vs placebo; perindopril or matching placebo added in individuals not reaching target BP of 150/80	mean BP lower with active therapy: 143/78 vs 158/84
ALLHAT	41,000 patients mild HTN + ≥ 1 other RF for CHD; 57% of the patients ≥ 65	chlorthalidone, 12.5 to 25 mg/d vs amlodipine vs lisinopril.	low-to-moderate-dose chlorthalidone fewer CV complications than amlodipine and lisinopril. (Doxepin arm discontinued.)
SPRINT (subgroup)	2600 ≥ 75 ; 142/71 (349 fit, 1456 less fit, 815 frail)	intensive (goal of <120) vs less intensive (<140) SBP lowering	primary CV endpoint, all-cause mortality better in intensive treatment group

Comments on SHEP



- Almost 50 % at goal BP on low-dose chlorthalidone alone.
- Potential risk of low DBP, but incidence of stroke at 4-5 years significantly lower in treated patients (5.5 vs 8.2 % with placebo).
- 25% to 33% reduction in cardiac events, but not quite statistically significant.
- Benefits in both men and women and in all age groups, including patients ≥ 80 years old.
- Caveat: reduction in CV events not seen in the 7.2 % who developed hypokalemia (serum potassium less than 3.5 mEq/L).

Comments on Syst-Eur trial

- Treat 1000 patients for 5 years to prevent 53 cardiovascular endpoints and 29 strokes
- Subgroup analysis: mortality benefit increased with a higher SBP at entry and was more pronounced in patients with diabetes mellitus, but decreased with increasing age.
- Subset of Syst-Eur (Vascular Dementia Project, over 2400 patients): Antihypertensive therapy significantly lowered incidence of dementia compared to placebo (3.8 versus 7.7 cases per 1000 patient-years)...estimated that treatment of 1000 patients for 5 years would prevent 19 cases of dementia.

Update on Hypertension and Dementia



SPRINT MIND Investigators for the Sprint Research Group:

- Among ambulatory adults with hypertension, treating to SBP goal of less than 120 (n = 4678) compared to goal less than 140 (n = 4683) did not result in a significant reduction in the risk of probable dementia.
- Authors caution that study may have been underpowered for this endpoint (fewer than expected cases of dementia).

JAMA.2019; 321(6): 553-561.

Comments on MRC

- HCTZ + amiloride significantly reduced the incidence of stroke, coronary events, and all cardiovascular events by 31, 44, and 35 %, respectively.
- Atenolol did not produce significant reductions in these endpoints.*

*Similar findings seen in other trials in which beta blockers were associated with worse cardiovascular outcomes than other antihypertensive drugs, an effect that was primarily limited to patients over age 60 years.

Comments on HYVET

- Primary endpoint: fatal or nonfatal stroke.
- At 2 years, active therapy associated with
 - A significant reduction in fatal stroke (6.5 versus 10.7 percent)
 - An almost significant reduction in all strokes (12.4 versus 17.7 percent, $p < 0.06$).
- Death from all causes was reduced from 59.6 per 1000 persons / year (placebo) to 47.2 per 1000 persons / year in the active treatment group.
- The authors suggested that the results of HYVET support a target blood pressure of less than 150/80 mmHg in treated patients over age 80 years and that the efficacy of further reductions in blood pressure need to be established.

Comments on ALLHAT

For patients over 65:

- Incidence of fatal coronary heart disease, nonfatal myocardial infarction, and all-cause mortality was the same for all 3 drugs (chlorthalidone, amlodipine, lisinopril).
- Higher rate of CHF with amlodipine vs chlorthalidone.
- Compared with chlorthalidone, lisinopril had higher rates of combined cardiovascular disease outcomes, combined coronary heart disease, and CHF.
- There was also a nonsignificant trend for a higher rate of stroke with lisinopril.

Concerns about the RCTs

Older participants in most of the trials, including SPRINT and HYVET, had less multimorbidity, frailty, and polypharmacy than we see in many primary care settings.

Stott DJ, Applegate WM. Perspectives on hypertensive treatment in older adults. *Journal of the American Geriatrics Society* 2018; 66: 1060-1061.

More Concerns

- SPRINT subgroup participants
 - Good baseline renal function
 - Little cardiovascular disease
 - No heart failure, diabetes or dementia
- Hypertension in the Very Elderly trial (HYVET) participants
 - All over 80
 - But much lower levels of diabetes and cardiovascular disease than in most geriatric medicine practices

Conroy S, Westendorp R. Hypertension treatment for older people. *Age Aging* 2018; May 21. doi: 10.1093/ageing/afy053. [Epub ahead of print]

AGS on ACC/AHA Recommendations



- Initial pharmacotherapy with one of the classes with best CVD outcomes in RCTs:
 - Thiazide diuretic
 - CCB
 - ACEI or ARB (but not together)
- African Americans:
 - Thiazide diuretic or CCB preferred over ACEI or ARB
- Old, old
 - Chlorthalidone may be particularly effective in preventing CHF
- Cautionary note
 - Alpha₁ and Central Alpha₂ Blockers have many side effects

Cushman WC, Johnson KC. The 2017 U.S. Hypertension Guidelines: What is Important for Older Adults? *Journal of the American Geriatrics Society* 2018; 66: 1062-1067.

Target BP in the Elderly

- $\leq 130 / 80$ in the U.S. based on ACC/AHA 2017 guidelines and SPRINT (Cushman WC, Johnson KC. The 2017 U.S. Hypertension Guidelines: What is Important for Older Adults? Journal of the American Geriatrics Society 2018; 66: 1062-1067.)
- $\leq 150 / 90$ in Europe (Conroy S, Westendorp R. Hypertension treatment for older people. Age Aging 2018; May 21. doi: 10.1093/ageing/afy053. [Epub ahead of print])
- Caveat for both suggested targets:
 - For some older patients, lowering BP to prevent vascular complications will be a high priority with the potential for substantial benefits.
 - For others, antihypertensive treatment may be irrelevant or even harmful (ADEs, postural hypotension, the U-shaped curve)

Unanswered Questions



- Are the needs of the elderly with CVD different from the needs of people the current health care system has been designed to meet?
- Should detection, evaluation, treatment, and monitoring be different?



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Knowledge And Implementation Gaps for Newer Approaches to Care in Older Adults with CVD

Schwartz JB, et al. Pharmacotherapy in Older Adults with CVD: Report from an ACC/AGS/NIA Workshop. *Journal of the American Geriatrics Society* 2019; 67: 371-380.

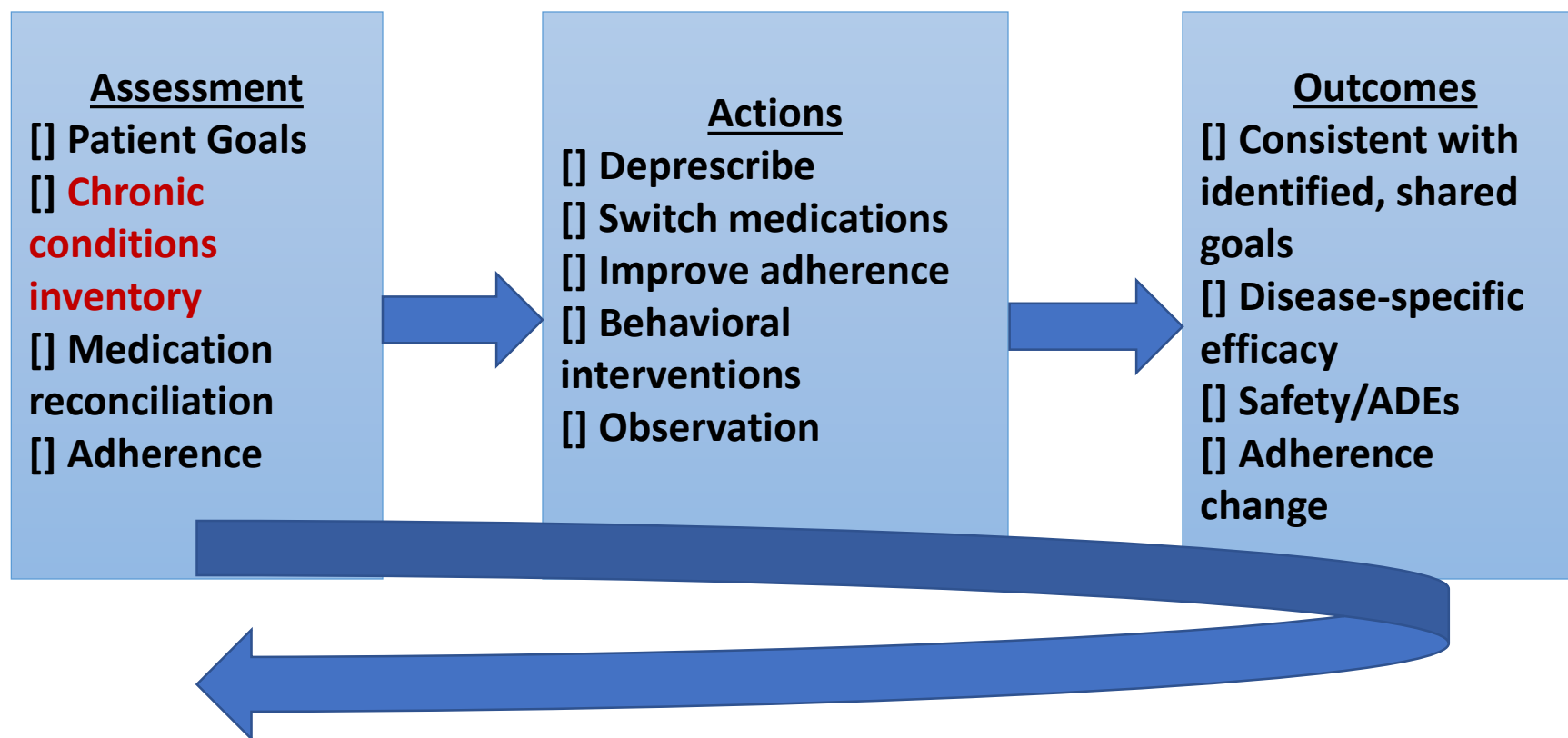
Suggested Approaches from the Workshop



- Dosing models that include a broad range of personalization factors.
- Cognitive and interventional studies to learn how best to incorporate elements of precision medicine in clinical practice.
- Ongoing evaluation of telemedicine and wearable sensors.
- Integration and cost effectiveness of multidimensional/multidisciplinary care models.
- Practical methods to integrate services, provide access to information, and optimize care coordination.

Steps in Management

Recommendations from the ACC, AGS, NIA workshop:





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Minority Health

Lance D. Dworkin, MD
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Hypertension: Selected Epidemiologic Data



- In 2010, high BP was the leading cause of death and disability worldwide.
- In the USA, hypertension accounts for more CVD deaths than any other modifiable risk factor
- Hypertension is second only to Diabetes as a cause of ESRD in the US (34% of incident ESRD)
- 25% of all adverse cardiovascular events are attributable to hypertension
- Adverse cardiovascular events attributable to hypertension are higher in Women than Men (32% vs. 19%) and in Blacks than in Whites (36% vs. 21%)

Adapted from 2017 ACC/AHA Guideline. 2018. Hypertension
71:1269/

Topics for Discussion

- Relative efficacy of different classes of medications in Blacks vs. Whites
- Picking a Target Blood Pressure, does race affect the recommendation for a low target
- How many drugs are needed to achieve target BPs in Black vs. White people



It may very well bring about immortality, but it's going to take forever to test it.



Selected Clinical Trial Data

Pitfalls of Clinical Trials

Racial and Ethnic Differences in Treatment



COR	LOE	Recommendations for Race and Ethnicity
I	B-R	In black adults with hypertension but without HF or CKD, including those with DM, initial antihypertensive treatment should include a thiazide-type diuretic or CCB.
I	C-LD	Two or more antihypertensive medications are recommended to achieve a BP target of less than 130/80 mm Hg in most adults with hypertension, especially in black adults with hypertension.

Adapted from the 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/ NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults

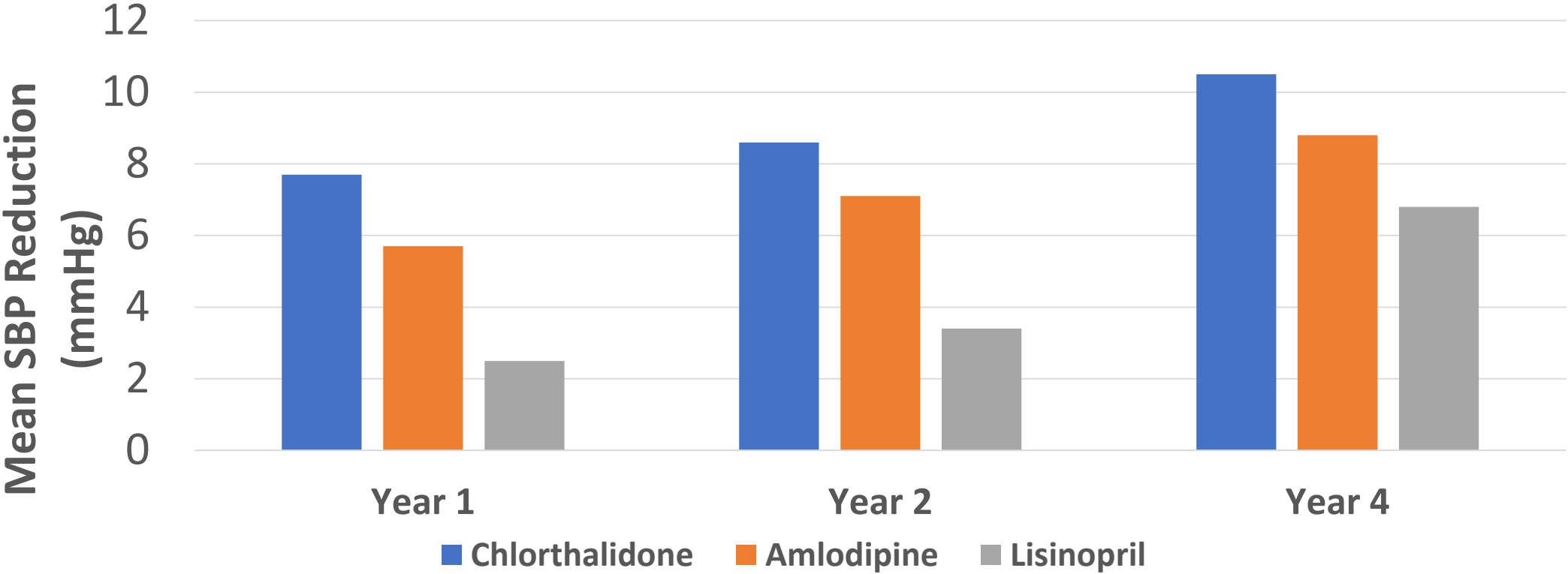
Published November 13, 2017, available at: *Hypertension* and *Journal of the American College of Cardiology*.

ALLHAT (Antihypertensive & Lipid-Lowering treatment to prevent Heart Attack Trial)



- High risk Hypertensives
- 42,418 participants
- ~Equal # Men & Women
- Age >55
- 35% Blacks
- Randomized to Amlodipine, Lisinopril, Chlorthalidone, Doxazosin (stopped early due to worse outcomes)
- Follow-up = 5 years

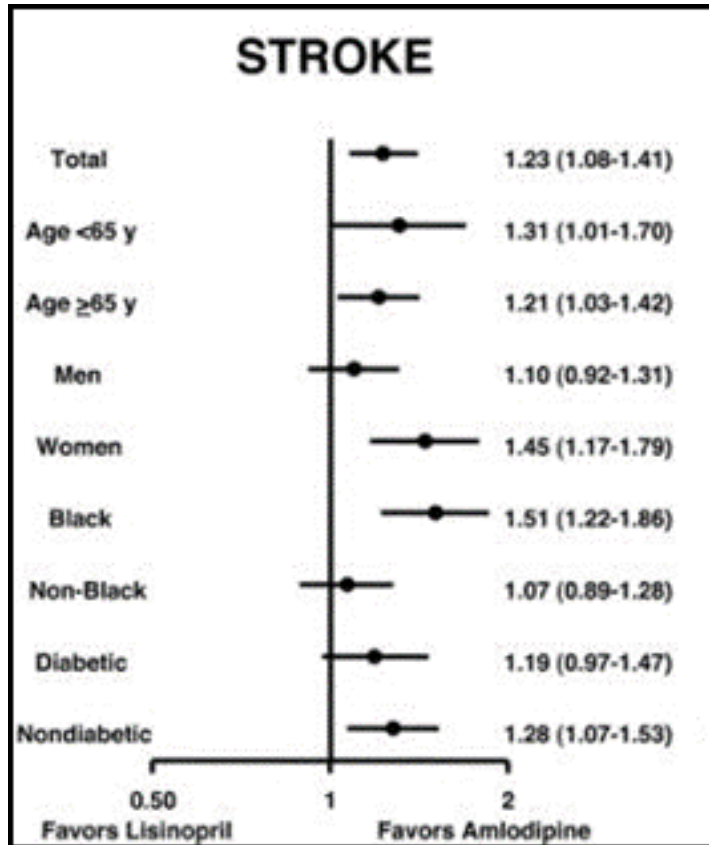
ALLHAT: Effect in Blacks* of First Line Medication on Magnitude of SBP Reduction from Baseline



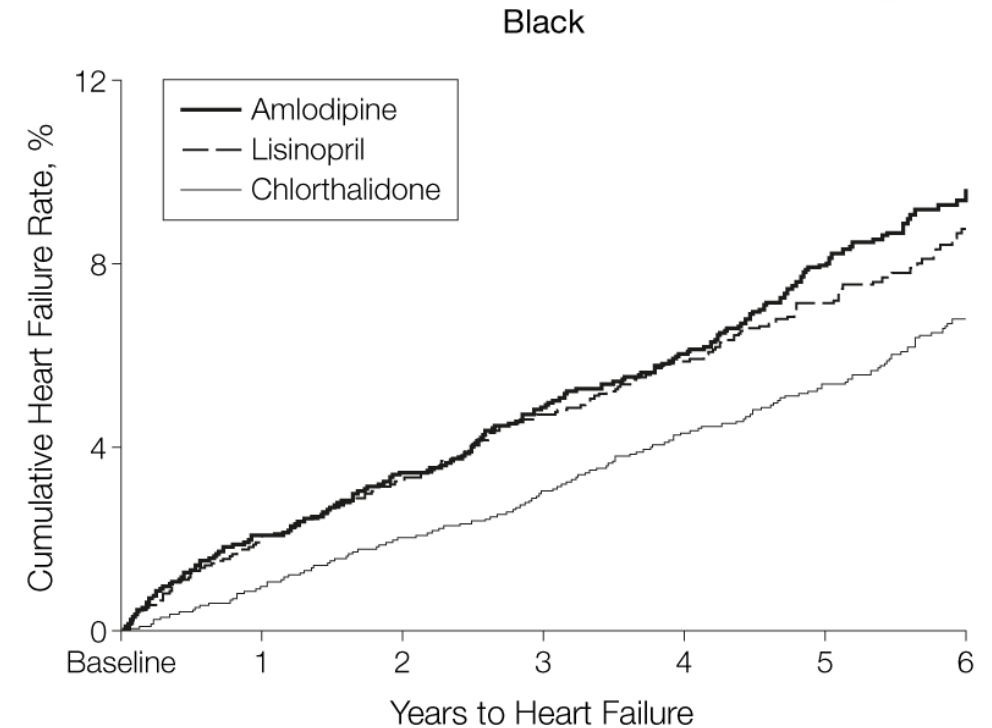
*SBP reductions were similar with all 3 drugs in Whites

Wright. 2005. JAMA 293;1595

ALLHAT: Variable Clinical Outcomes Based on Race



Leenen. Hypertension. 48(3):374-384, September 2006.

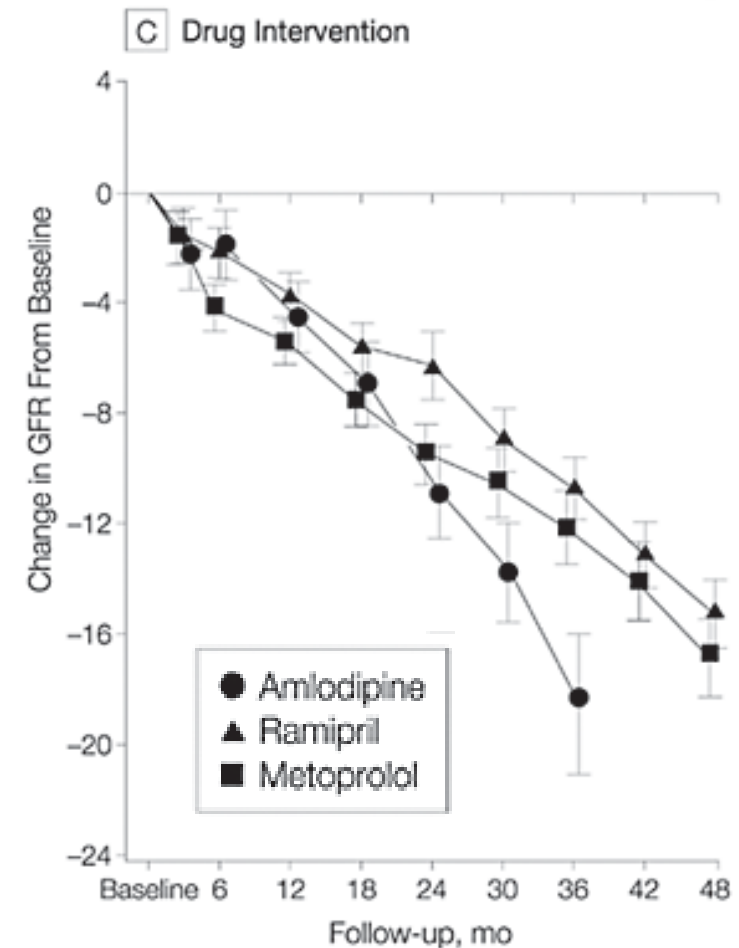


No. at Risk	Baseline	1	2	3	4	5	6
Amlodipine	3213	2879	2423	2043	1643	1243	720
Lisinopril	3210	2837	2361	1961	1561	1161	711
Chlorthalidone	5369	4838	4041	3241	2441	1641	1175

Wright. 2005. JAMA 293;1595

ASSK Study

- 1094 African American hypertensives with renal disease (GFR 25-60 ml/min)
- Randomized to amlodipine, ramipril or atenolol
- Randomized to usual or low BP
- Other agents used to control BP – average 4 per patient
- Amlodipine arm stopped prematurely



Change in GFR by Drug Class

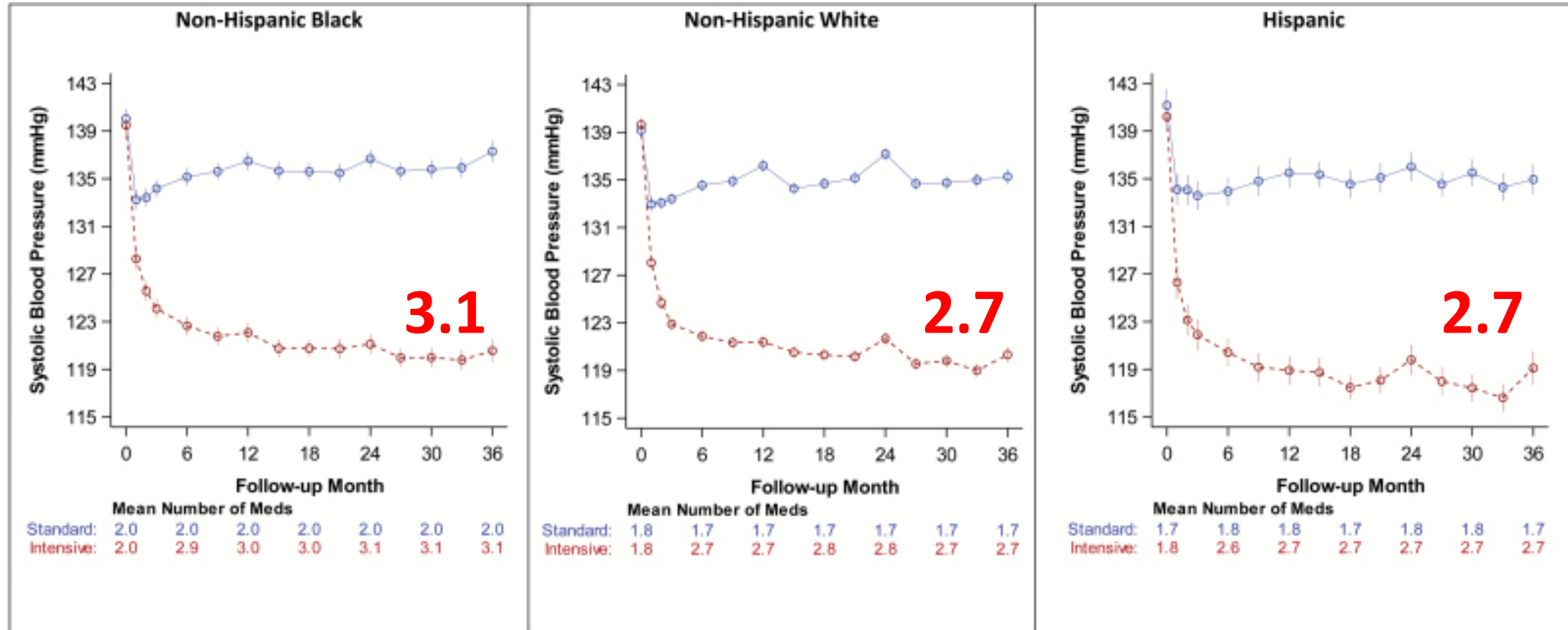
SPRINT: Systolic Blood Pressure Intervention Trial Clinical Outcomes by Race and Ethnicity



- 9,361 High CVD risk patients randomized
 - Age > 50
 - SBP > 130 on 0 to 4 meds
 - Self Reported as non-Hispanic Black (2802), non-Hispanic White (5399), or Hispanic (984)
- Intensive (SBP < 120) vs. Standard (SBP < 140) BP control
- Diabetics Excluded
- Outcome = MI, Coronary Syndrome, Stroke, CHF, CV Death

SPRINT Research Group. NEJM 2015; 373:2103

SBP and Mean No. of BP Meds by Treatment Arm and Race/Ethnicity in SPRINT



* ~30% Risk Reduction for Primary Endpoint with Low BP Target **not affected by race or ethnicity.**

Still. 2018. Am J Hypertension 31;97

Average Number of Meds Needed to Achieve BP Goal

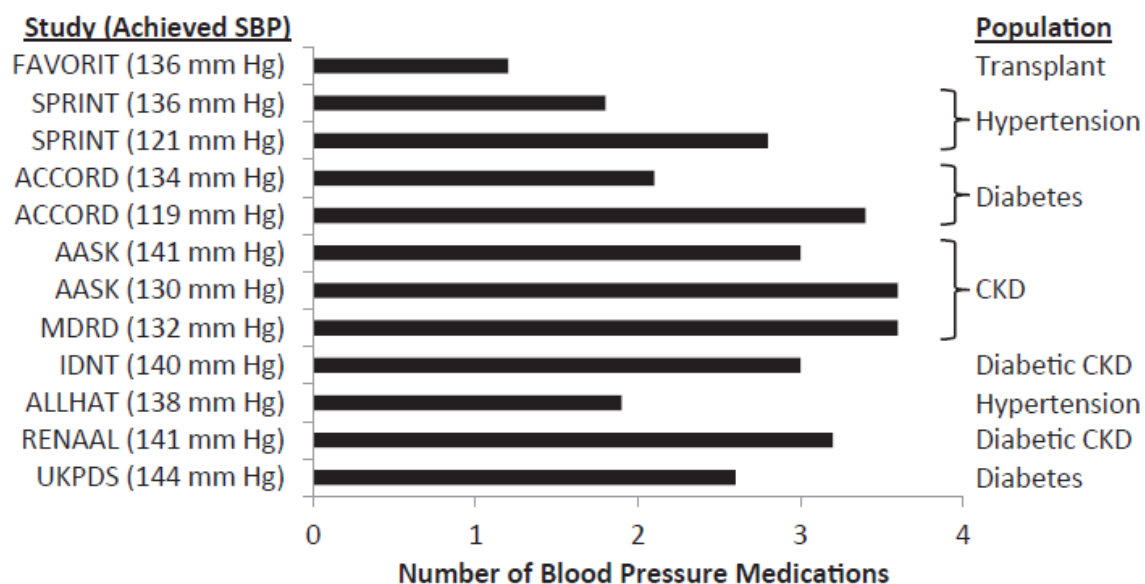


Figure 2. Average number of blood pressure (BP) medications needed to achieve a BP goal in clinical trials. Abbreviations: AASK, African American Study of Kidney Disease and Hypertension⁹³; ACCORD, Action to Control Cardiovascular Disease in Diabetes⁷⁷; ALLHAT, Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial; CKD, chronic kidney disease; IDNT, Irbesartan Diabetic Nephropathy Trial¹³²; MDRD, Modification of Diet in Renal Disease⁹⁴; RENAAL, Reduction of Endpoints in NIDDM With the Angiotensin II Antagonist Losartan^{133,134} SBP, systolic blood pressure; SPRINT, Systolic Blood Pressure Intervention Trial³; UKPKDS, United Kingdom Prospective Kidney Disease Study.¹³⁴

Summary & Conclusions



- Many factors, including patient preference, age, co-morbidities, racial/ethnic background, and lifestyle should be considered when selecting a BP medication regimen for an individual patient
- Thiazide diuretics or CCBs are reasonable first line agents for black adults with uncomplicated hypertension
- For patients with Diabetes, CKD and proteinuria, and/or CHF an ACEI or ARB should be a first line therapy
- Depending on co-morbidities, 2 to 4 medications will likely be needed to achieve the recommended target BP < 130/80 mmHg in minority patients.
- The risk of angioedema associated with the use of ACE inhibitors & ARBs is greater in women and in Black Americans than in others; patients should be monitored for this side effect.

Thank you!

Questions/Discussion