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Update on the Pharmacologic Management of Hypertension in the Older Patient

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Learning Objectives

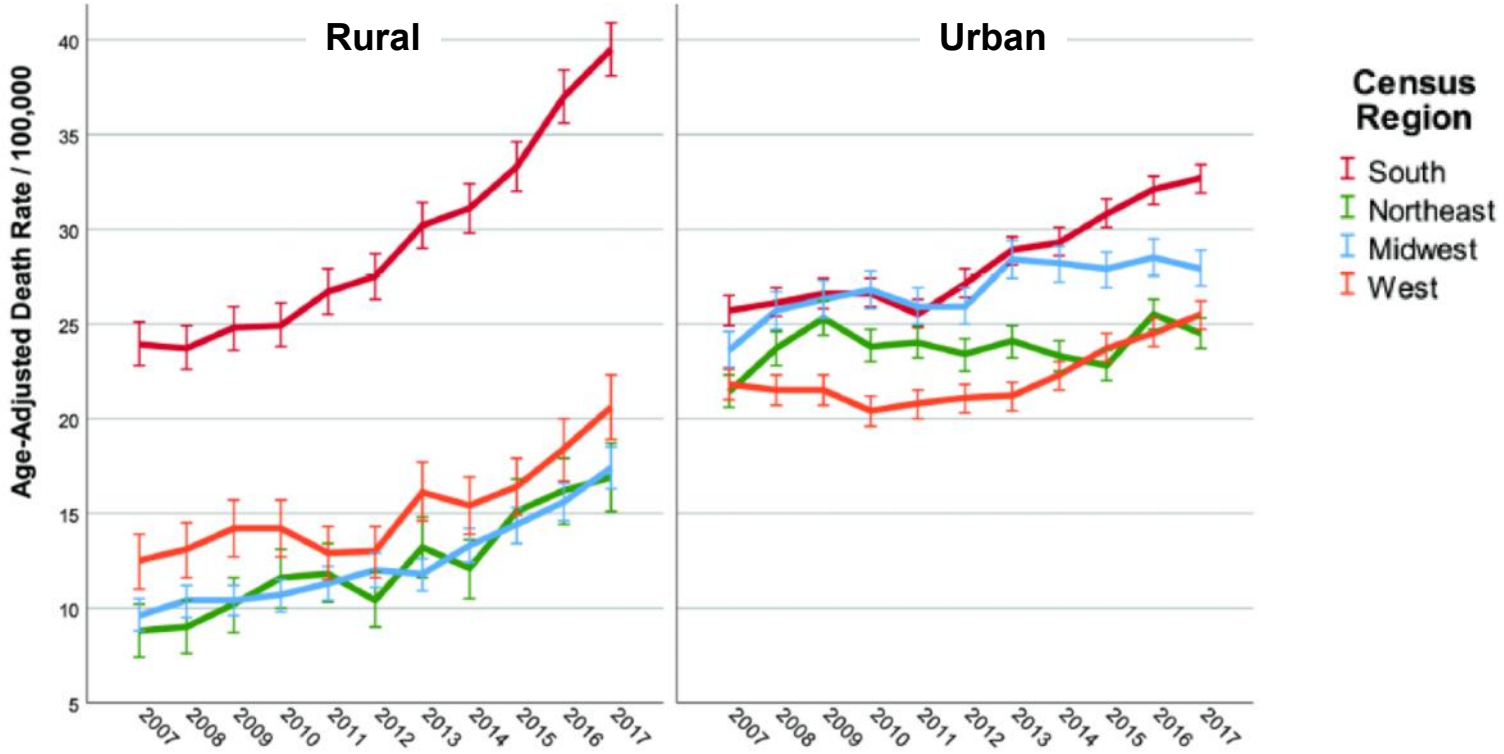
- Explain 2017 ACC/AHA hypertension guideline recommendations for management of hypertension
- Describe the evidence supporting lower BP goals for the treatment of older patients with hypertension
- Identify challenges when treating older patients with hypertension
- Discuss recommendations for managing resistant hypertension vs routine hypertension care
- Outline appropriate treatment plans for older patients with hypertension

Polling Question…

Which of the following describes the changes in hypertension-related mortality in the United States over the past decade?

a) No changes
b) Decreasing in urban and rural areas
c) Decreasing in urban and increasing in rural areas
d) Increasing in urban and rural areas

Hypertension-Related Mortality is Rising



Nambiar L, et al. *J Am Coll Cardiol*. 2020;75(11)

2017 ACC/AHA Hypertension Guideline

Class of Recommendation (COR) - Strength

Class I (Strong) — **Benefit >>> Risk**
- Is recommended, is indicated, should be performed

Class IIa (Moderate) — **Benefit >> Risk**
- Is reasonable, can be useful

Class IIb (Weak) — **Benefit ≥ Risk**
- May/might be reasonable/considered, effectiveness unknown

Class III: No Benefit (Moderate) — **Benefit = Risk**
- Is not recommended, is not useful

Class III: Harm (Strong) — **Benefit < Risk**
- Potentially harmful, causes harm

Level of Evidence (LOE) - Quality

Level A
- High-quality evidence from > one randomized clinical trial (RCT)
- Meta-analyses of high-quality RCTs

Level B-R (Randomized)
- Moderate-quality evidence from > one RCT
- Meta-analyses of moderate-quality RCTs

Level B-NR (Nonrandomized)
- Moderate-quality from nonrandomized studies, observational, registry

Level C-D (Limited Data)

Level C-EO (Expert Opinion)

Whelton PK, et al. *J Am Coll Cardiol*. 2018;71:e127-e248

2017 ACC/AHA: BP Categories

BP Category	Systolic BP (mm Hg)		Diastolic BP (mm Hg)
Normal	<120	and	<80
Elevated	120–129	and	<80
Hypertension Stage 1	130–139	or	80–89
Hypertension Stage 2	≥140	or	≥90

DBP, diastolic blood pressure; and SBP systolic blood pressure.

Whelton PK, et al. *J Am Coll Cardiol*. 2018;71:e127-e248

2017 ACC/AHA Hypertension Guideline

Goal BP of <130/80 mm Hg for most

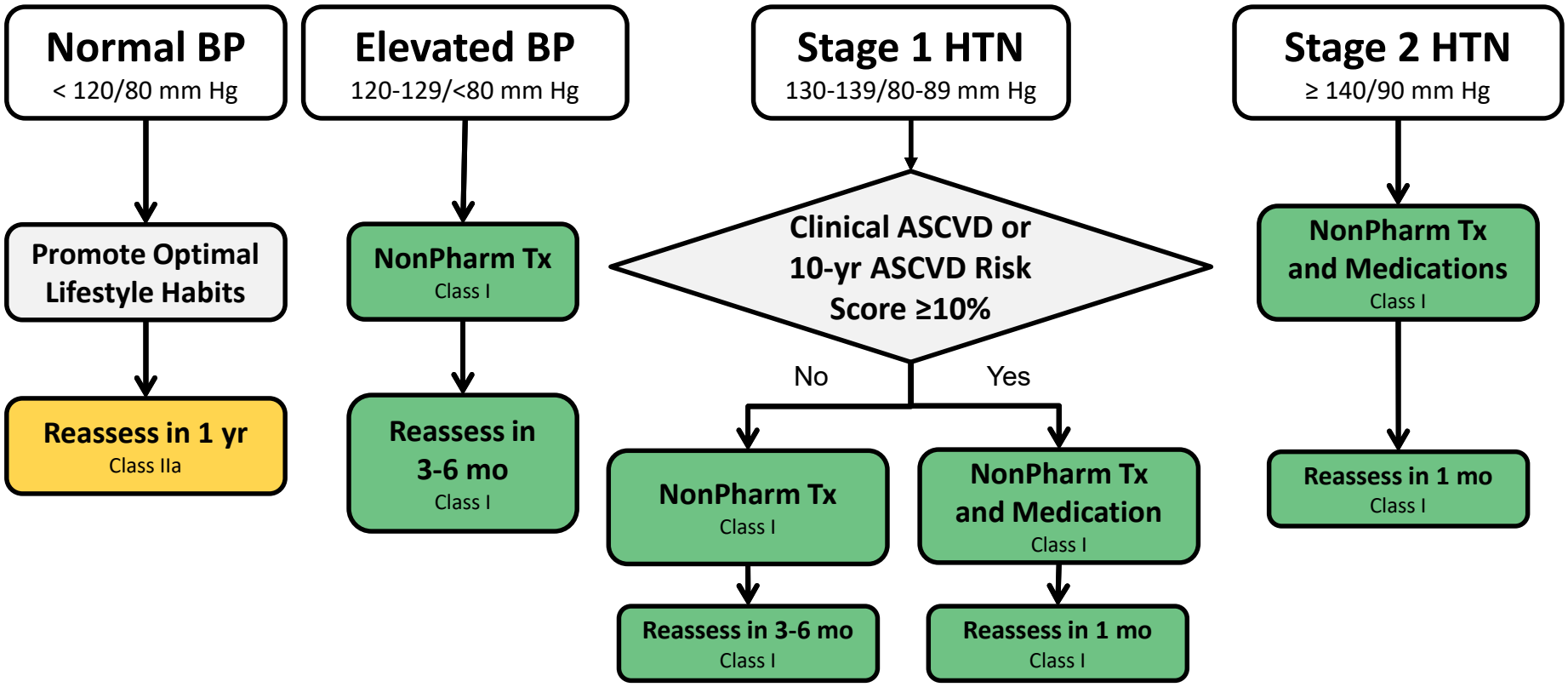
COR	LOE	Patients With Hypertension
I	SBP: B-R	Known CVD, diabetes, CKD, or 10-year ASCVD event risk of ≥10% a BP target <130/80 mm Hg
	DBP: C-EO	
IIb	SBP: B-NR	Without additional markers of increased CVD risk, a BP target <130/80 mm Hg
	DBP: C-EO	

COR	LOE	BP Goals: Older
I	A	SBP goal <130 mm Hg for non-institutionalized ambulatory community-dwelling adults ≥65 yr

Whelton PK, et al. *J Am Coll Cardiol*. 2018;71:e127-e248

CVD = cardiovascular disease
CKD = chronic kidney disease

2017 ACC/AHA: Treatment Algorithm



Whelton PK, et al. *J Am Coll Cardiol*. 2018;71:e127-e248

2017 ACC-AHA: Lifestyle Changes

COR	LOE	Nonpharmacological Interventions
I	A	Weight loss in adults who are overweight or obese
		Healthy diet (e.g., DASH) that facilitates achieving desirable weight
		Sodium reduction
		Potassium supplementation (preferably diet) unless contraindicated
		Increased physical activity with a structured exercise program
		Drink no more than 2 (men) or 1 (women) standard drinks/day

DASH = Dietary Approaches to Stop Hypertension

Whelton PK, et al. *J Am Coll Cardiol*. 2018;71:e127-e248

2017 ACC/AHA: Medication Selection

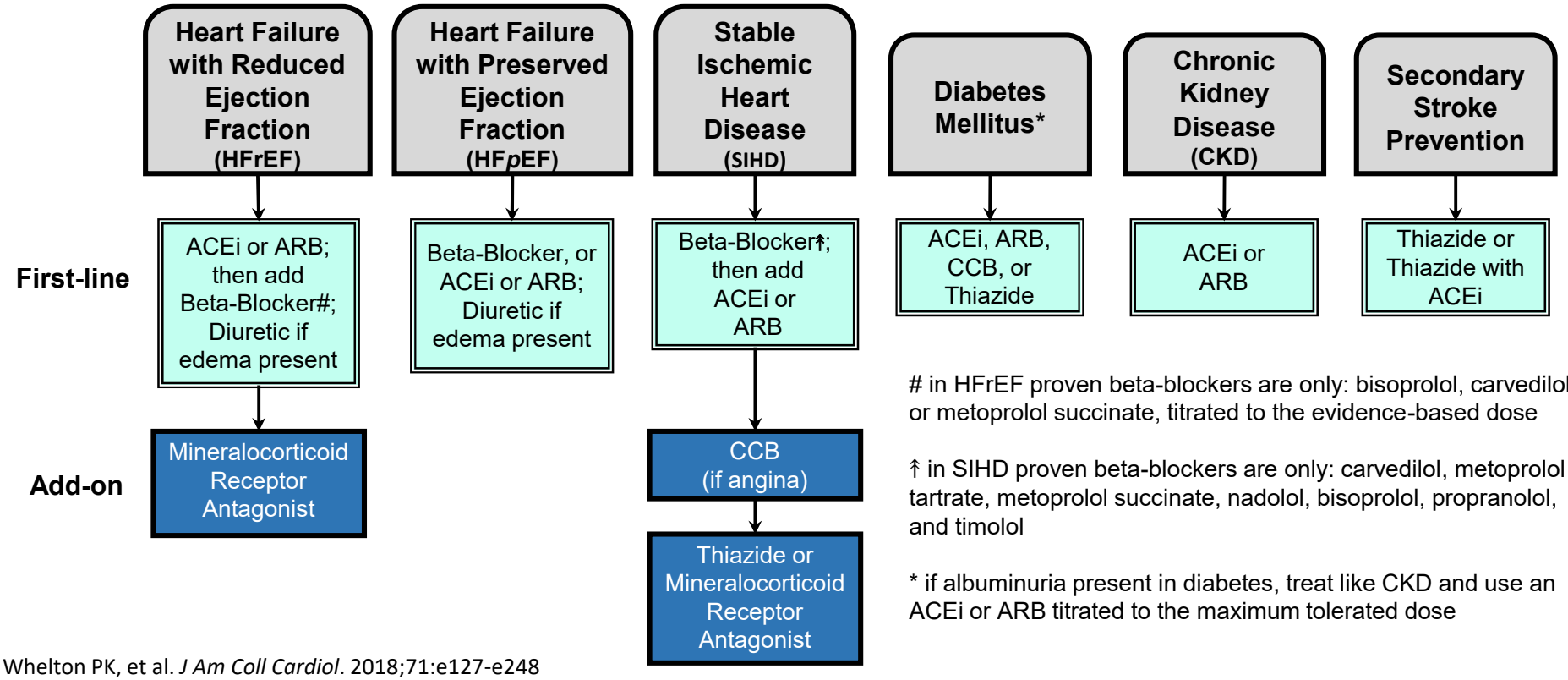
COR	LOE	Initial Medication
I	A^{SR}	First-line: thiazide diuretics, CCBs, and ACE inhibitors or ARBs

COR	LOE	Initial Monotherapy Versus Combination Therapy
I	C-EO	2 first-line agents of different classes in stage 2 hypertension and BP > 20/10 mm Hg above goal

COR	LOE	Race and Ethnicity
I	B-R	Black patients without HF or CKD (with or without diabetes), initial treatment should include a thiazide diuretic or CCB
I	C-LD	2+ medications are recommended to achieve a BP <130/80 mm Hg in most adults, especially in black patients

Whelton PK, et al. *J Am Coll Cardiol*. 2018;71:e127-e248

2017 ACC/AHA: Compelling Indications



in HFrEF proven beta-blockers are only: bisoprolol, carvedilol, or metoprolol succinate, titrated to the evidence-based dose

↟ in SIHD proven beta-blockers are only: carvedilol, metoprolol tartrate, metoprolol succinate, nadolol, bisoprolol, propranolol, and timolol

* if albuminuria present in diabetes, treat like CKD and use an ACEi or ARB titrated to the maximum tolerated dose

Whelton PK, et al. *J Am Coll Cardiol*. 2018;71:e127-e248

Follow-Up and Monitoring

COR	LOE	Follow-Up After Initiating Drug Therapy
I	B-R	Evaluation of adherence and response to treatment at monthly intervals until control is achieved

COR	LOE	Monitoring Strategies to Improve Control of BP
I	A	Follow-up and monitoring should include systematic strategies including home BP monitoring, team-based care, and telehealth strategies

Whelton PK, et al. *J Am Coll Cardiol*. 2018;71:e127-e248

AHA Policy Statement:
Self-Measured Blood Pressure Monitoring at Home

Indication	• Identification of white coat effect and masked uncontrolled hypertension
Evidence	• Self-measured BP monitoring is associated with a reduction in BP and improved BP control
Cost-Effective	• Addition of self-measured BP monitoring to office-based monitoring versus office-based alone

Shimbo D, et al. *Circulation*. 2020;142:e42–e63.

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Systolic Blood Pressure Intervention Trial (SPRINT)

- Multicenter, randomized, controlled trial
- 9,361 patients with hypertension randomized open-label to:
  - Intensive treatment: SBP <120 mm Hg
  - Standard treatment: SBP <140 mm Hg
- Primary outcome: first the occurrence of a MI, acute coronary syndrome, stroke, heart failure, or CV disease death

Ambrosius WT, et al. Clin Trials. 2014;11(5):532–546.

SPRINT: Study Criteria

Inclusion

- ≥ 50 years old
- SBP 130–180 mm Hg
- Increased risk for ASCVD based on additional criteria

Exclusion

- Secondary hypertension
- Diabetes, previous stroke, or CV event within 3 months
- Symptomatic heart failure within 6 months or EF < 35%
- Proteinuria (> 1 g/day), polycystic kidney disease, glomerulonephritis, eGFR< 20 mL/min/1.73m^2

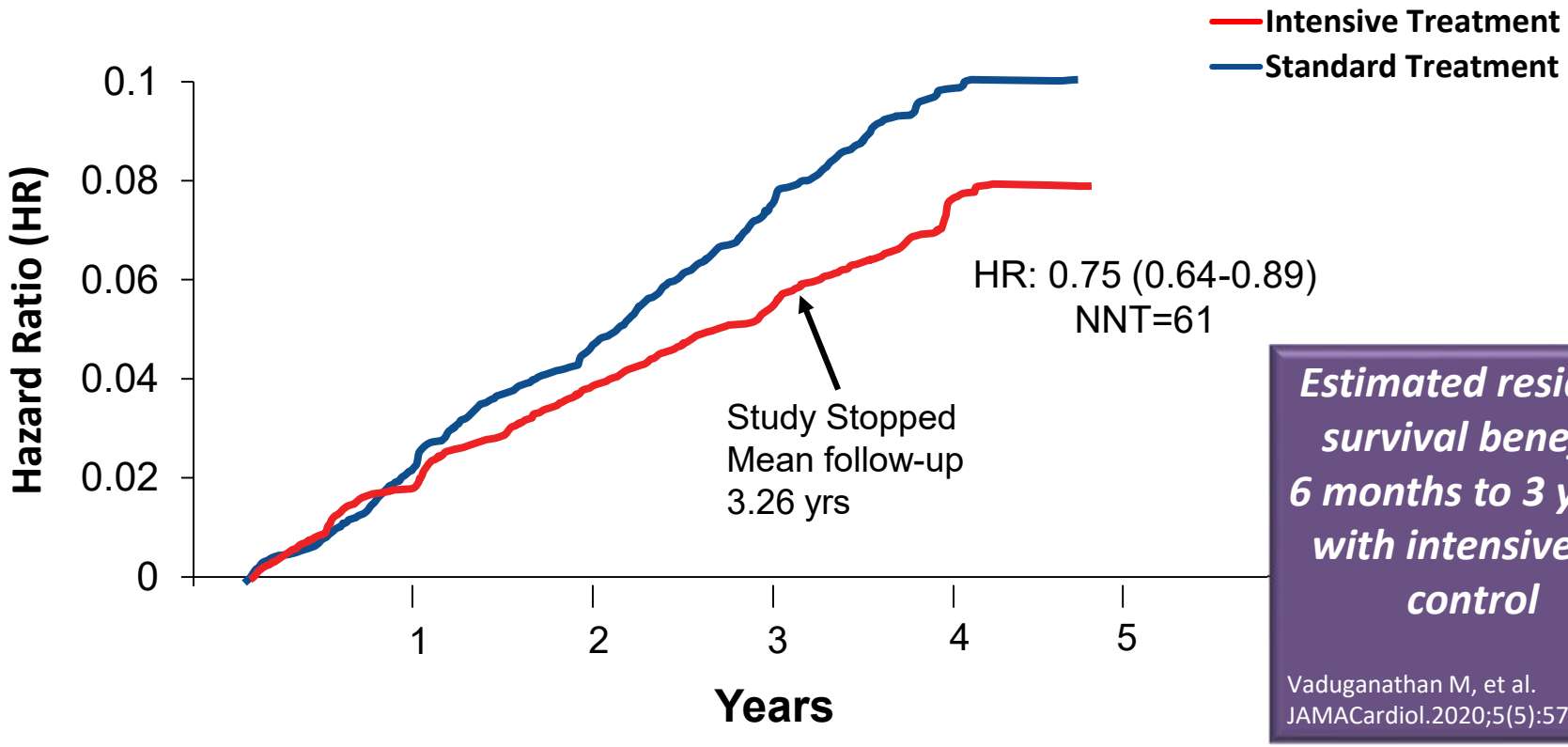
Ambrosius WT, et al. *Clin Trials*. 2014;11(5):532–546.

SPRINT: Protocol Procedures

- Medication choice:
  - ACEi, ARB, CCB, thiazide first-line; beta-blocker in coronary disease
  - Chlorthalidone encouraged as the primary thiazide
  - Amlodipine as the preferred CCB
- Titration of medications was based on:
  - Mean of three office BP measurements, seated with automated device
- Frequent routine measurement of BP and screening for hypotension

Ambrosius WT, et al. Clin Trials. 2014;11(5):532–546.

SPRINT: Primary Endpoint Result



Estimated residual survival benefit: 6 months to 3 years with intensive BP control

Vaduganathan M, et al. JAMACardiol.2020;5(5):576-581.

The SPRINT Research Group. *N Engl J Med*. 2015;373(22):2103-2106.

SPRINT-Senior

- 2636 patients from the SPRINT trial
  - Specifically funded to enhance recruitment of adults aged ≥75 yr, included measures of functional status and frailty
- Exclusion criteria:
  - Diagnosis of or treatment of dementia
  - Expected survival <3 years
  - Unintentional weight loss >10% during preceding 6 mos.
  - SBP <110 mm Hg after 1 min of standing
  - Nursing home resident
- Median follow up: 3.14 yr

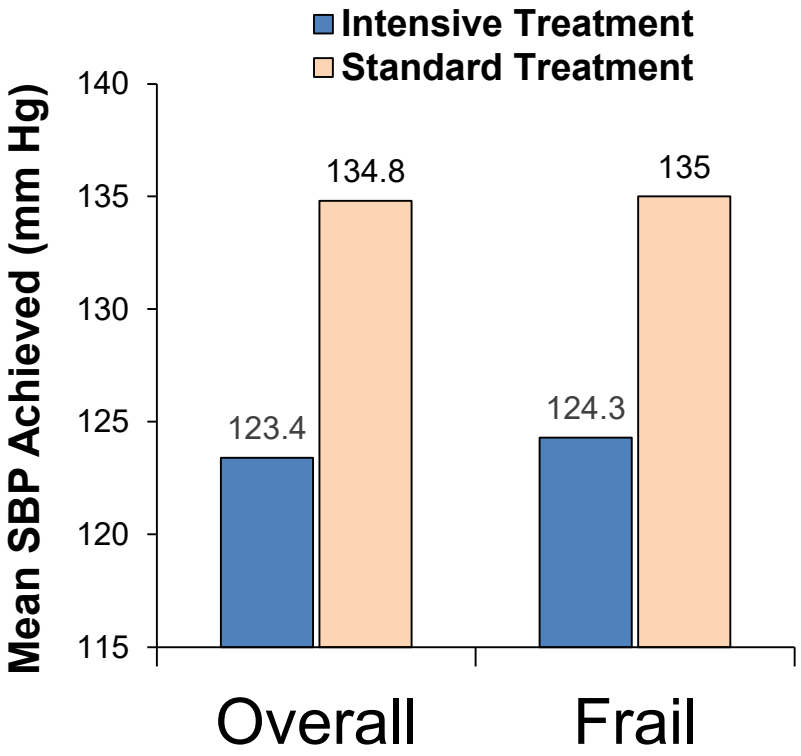
Williamson JD, et al. *JAMA* 2016;315(24):2673-82.

SPRINT-Senior: Demographics

Characteristic	Intensive Treatment (n=1317)	Standard Treatment (n=1310)
Age(yr)	79.8	79.9
Female sex	37.9%	38%
Seated SBP (mm Hg)	141.6	141.6
Orthostatic hypotension	9.6%	9.4%
History of CVD	25.7%	23.4%
No. BP meds at baseline	1.9	1.9
Frailty (using a 37-item frailty index) • Fit (FI ≤ 0.10) • Less fit (FI >0.10 to ≤0.21) • Frail (FI >0.21)	 12.1% 54.0% 33.4%	 14.4% 56.5% 28.4%

Williamson JD, et al. *JAMA* 2016;315(24):2673-82.

SPRINT-Senior: Results



Outcome	Intensive Treatment N=1317 no. (%)	Standard Treatment N=1319 no. (%)	Hazard Ratio (95% CI)
CVD Primary Outcome	102 (7.7)	148 (11.2)	**0.66 (0.51-0.85)**
All-Cause Mortality	73 (5.5)	107 (8.1)	**0.67 (0.49-0.91)**
Primary Outcome or Death	144 (10.9)	205 (15.5)	**0.68 (0.54-0.84)**

Williamson JD, et al. *JAMA* 2016;315(24):2673-82.

Polling Question…

Which adverse effect was higher in the SPRINT-seniors study in the intensive treatment arm compared with the standard treatment arm?

a) Hyponatremia
b) Hypotension
c) Injurious falls
d) Syncope

SPRINT-Senior: Safety

Outcome	Intensive N=1317; no.(%)	Standard N=1319; no.(%)	Hazard Ratio (P-Value)
Serious Adverse Event ‡	640 (48.6)	638 (48.4)	1.00 (0.93)
Individual Serious Adverse Event			
• Hypotension	36 (2.7)	24 (1.8)	1.49 (0.13)
• Syncope	46 (3.5)	37 (2.8)	1.24 (0.33)
• Electrolyte abnormality	58 (4.4)	107 (2.3)	1.40 (0.10)
• Injurious fall	70 (5.3)	79 (6.0)	0.88 (0.42)
• Acute kidney injury/acute renal failure	75 (5.7)	54 (4.1)	1.38 (0.07)
Emergency department visit or SAE			
• Electrolyte abnormality	66 (5.0)	48 (3.6)	**1.37 (0.01)**
• Injurious fall	158 (12.0)	193 (14.6)	**0.79 (0.03)**
• Acute kidney injury/acute renal failure	78 (5.9)	55 (4.2)	1.42 (0.05)
Sodium <130 mmol/L	66 (5.0)	44 (3.3)	**1.50 (0.04)**
‡ Serious adverse event defined as fatal or life-threatening or that resulted in clinically significant or persistent disability			

Williamson JD, et al. *JAMA* 2016;315(24):2673-82.

2017 ACC/AHA: Older Patients

COR	LOE	BP Goals: Older
I	A	SBP treatment goal <130 mm Hg for non-institutionalized ambulatory community-dwelling adults ≥65 yr
IIa	C-EO	≥65 yr with high burden of comorbidity and limited life expectancy, clinical judgment, patient preference, and a team-based approach to assess risk/benefit for decisions regarding intensity of treatment

COR	LOE	Prevention of Cognitive Decline and Dementia
IIa	B-R	In adults with hypertension, BP lowering is reasonable to prevent cognitive decline and dementia.

Whelton PK, et al. *J Am Coll Cardiol*. 2018;71:e127-e248

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Concerns with Older Adults

- Physiologic age is different than chronological age
- Outcome trials from decades ago did include older patients, but:
  - Not many were very elderly
  - Frailty among patients decades ago is different than now
- Increased risk for medication related adverse effects:
  - Isolated systolic hypertension with wide pulse pressure
  - Decline in organ function and altered body composition
  - Increased risk of drug-drug interactions

Drug Therapy Monitoring

- Increased propensity for adverse effects results in an increased need for monitoring

Class	Parameters
Diuretic	BUN/SCr; serum electrolytes (potassium, magnesium, sodium); uric acid
Mineralocorticoid Receptor Antagonist	BUN/SCr; serum potassium
Beta-Blocker	Heart rate
ACEI	BUN/SCr; serum potassium
ARB	BUN/SCr; serum potassium
CCB	Heart rate

Common Prescribing Cascade:
Diuretic Use after CCB Initiation for Hypertension

- Cohort study; 1,206,093 patients, age <65 years who started dihydropyridine CCB therapy:
  - Excess loop diuretics use in lieu of dose reductions or CCB discontinuation
  - More pronounced with high dose CCBs
- Cohort study; 41,086 community dwelling patients, age >65 years (mean 74.5) who started CCB therapy:
  - Increased subsequent loop diuretic use (~2-fold)
  - Persistent up to 360 days
  - Lower with amlodipine vs other CCBs

Savage RD, et al. *JAMA Intern Med.* 2020;180(5):643-651.
Vouri SM, et al. *JAMA Network Open*. 2019;2(12):e1918425.

Polling Question…

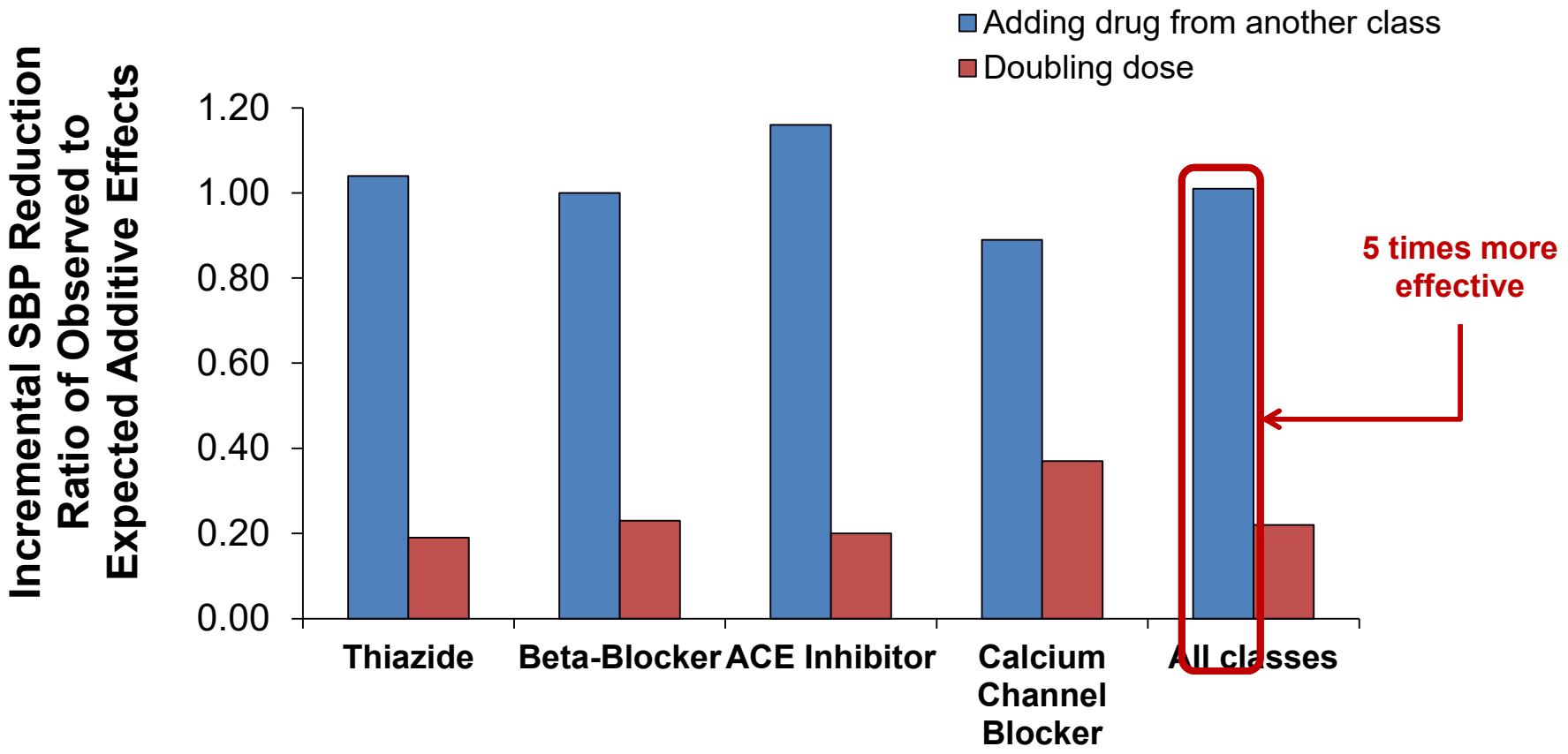
A patient is treated with one antihypertensive drug at the starting dose. However, after 4 weeks they still are not at their BP goal. Which of the following strategies is most likely to lower BP the most?

a) Wait another 4 weeks

b) Add a second antihypertensive drug

c) Double the dose of the antihypertensive drug

d) Replace the antihypertensive drug with another one



Wald DS, et al. *AM J Med* 2009;122:290-300.

Optimizing Treatment for Mild Systolic Hypertension in the Elderly (OPTIMISE) study

- Randomized, unblinded, noninferiority trial conducted in 69 primary care sites in England
  - 534 patients, age ≥80 years, SBP<150 mm Hg, and receiving ≥2 antihypertensive medications

Results at 12-weeks	Removal of 1 Drug (n=265)	Usual Care (n=269)
SBP <150 mm Hg (primary endpoint)	229 (86.4%)	236 (87.7%)
Mean SBP (mm Hg)*	133.7	130.8
		*P=0.005

Sheppard JP, et al. *JAMA*. 2020;323(20):2039-2051.

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AHA Scientific Statement: Resistant Hypertension (rHTN)

- Definition:
  - Patients not at their goal BP despite concurrent use of 3 antihypertensive drug classes commonly including a long-acting CCB, ACEi or ARB, and a diuretic
    - At maximum or maximally tolerated daily doses
  - Patient at BP target on 4 or more antihypertensive medications

Carey RM, et al. *Hypertension*. 2018;72:e53-e90.

rHTN Secondary Causes

Common Medications	Others	Diseases
• NSAIDs • Oral contraceptives • Sympathomimetics • Amphetamines • Antidepressants • Glucocorticoids, mineralocorticoids	• Alcohol • Cocaine • Cyclosporine, tacrolimus • Erythropoietin • Vascular endothelial growth factor inhibitors	• Primary Aldosteronism • Renal Parenchymal Disease • Renal Artery Stenosis • Pheochromocytoma/ Paraganglioma • Cushing Syndrome • Coarctation of the Aorta • Others

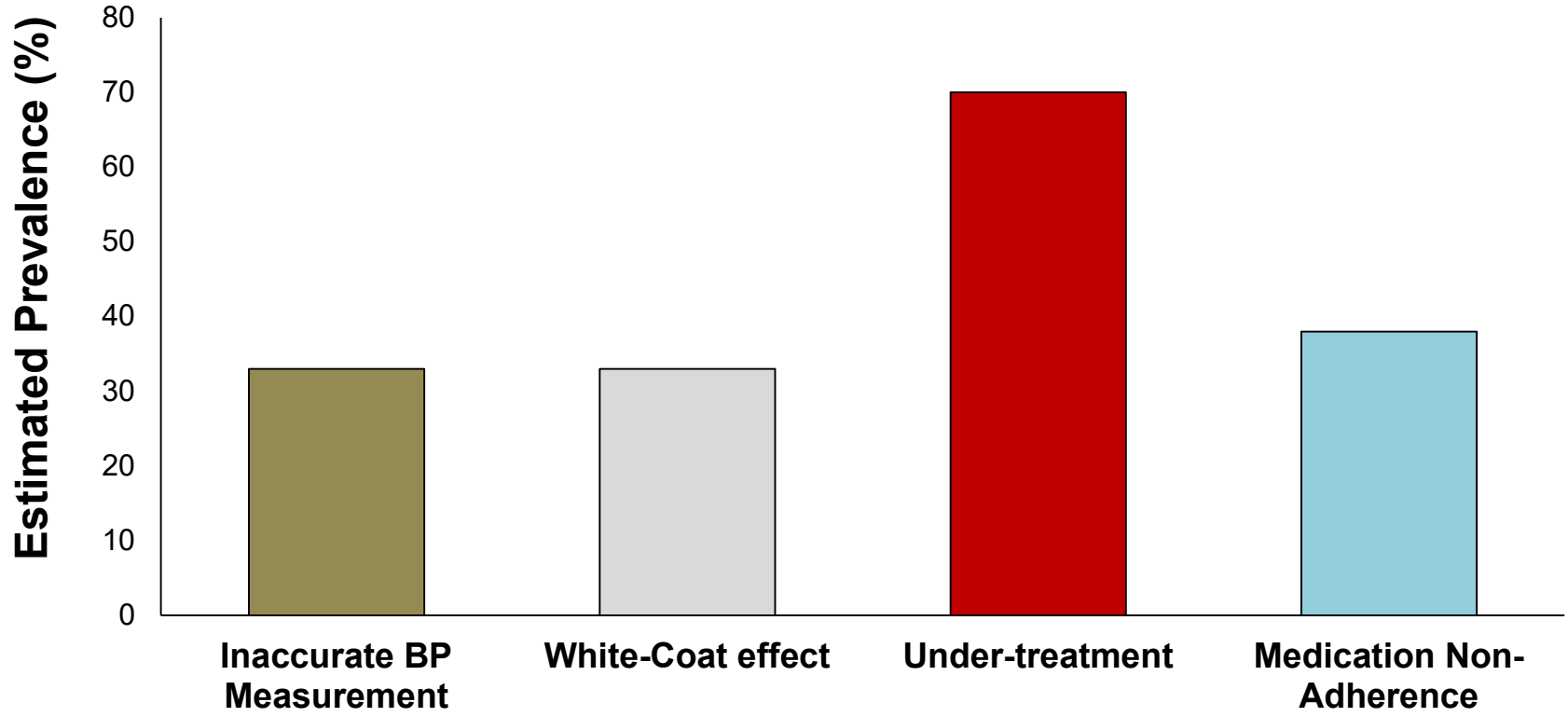
Carey RM, et al. *Hypertension*. 2018;72:e53-e90.

Polling Question…

Which of the following is the common cause of pseudoresistant hypertension?

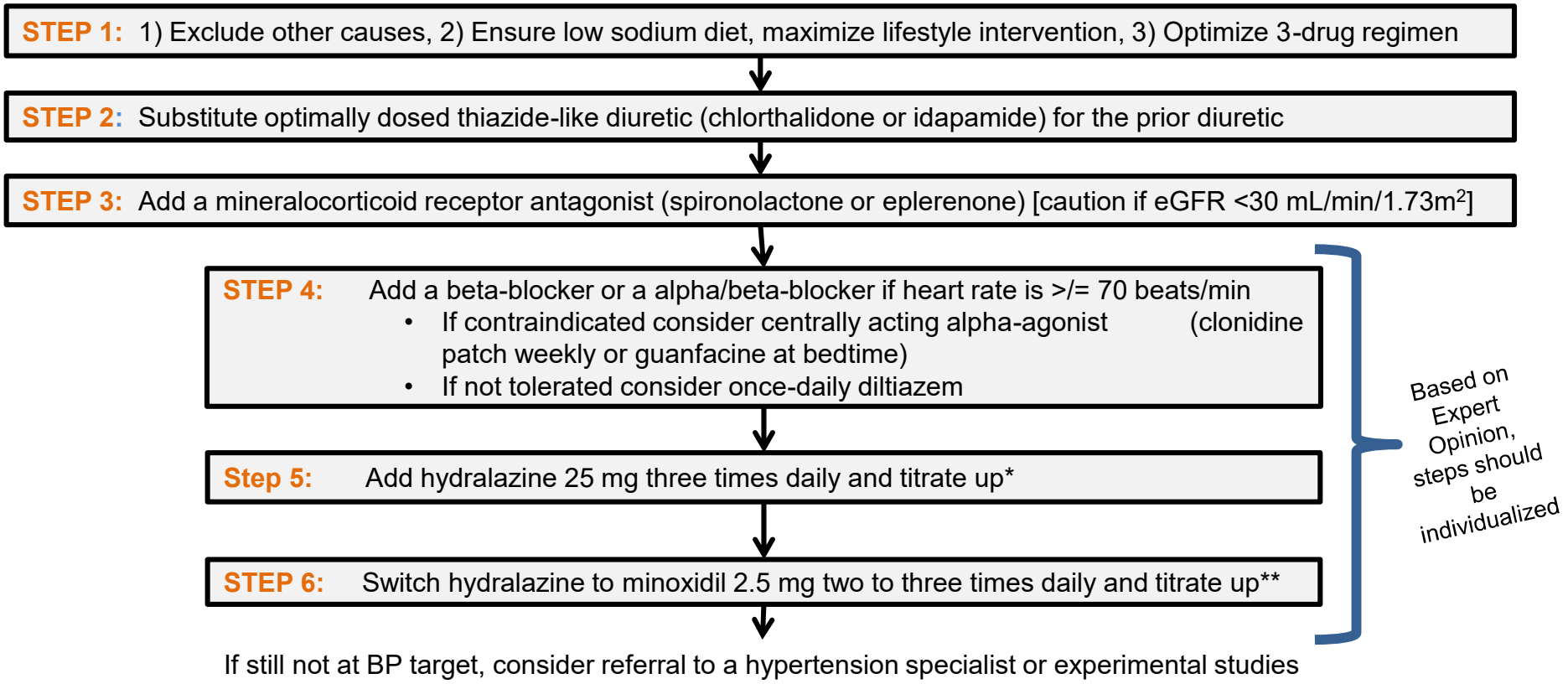
a) Inaccurate BP measurement
b) White-coat hypertension
c) Undertreatment
d) Medication non-adherence

Causes of Pseudoresistant Hypertension



Carey RM, et al. *Hypertension*. 2018;72:e53-e90.

rHTN Management



Carey RM, et al. *Hypertension*. 2018;72:e53-e90.

*Requires concomitant use of a β-blocker and diuretic
**Requires concomitant use of a β-blocker and loop diuretic

A Tale of Two Thiazides

	Hydrochlorothiazide (HCTZ)	Chlorthalidone (CTD)
Category	Thiazide-type	Thiazide-like
Half-life	9-10 hours	50-60 hours
Equivalent doses	25 mg	12.5-18.75 mg
Utilization	Frequently prescribed, many fixed-dose combinations	Preferred in resistant hypertension
Landmark Trials	Rarely used	Extensively used

- Cohort trial in 730,225 patients prescribed HCTZ or CTD:
  - No difference MI, hospitalized heart failure, or stroke
    - HR 1.00 (95% CI, 0.85-1.17)
  - CTD associated with higher risks of hypokalemia, hyponatremia, acute renal failure, CKD, and new onset type 2 diabetes
  - CTD associated with a lower risk of abnormal weight gain

Hripcsak G, et al. *JAMA Intern Med*. 2020;180(4):542-551.

PATHWAY-2 Trial

- Double-blind, randomized, crossover trial (n=335) in patients with rHTN for 12 wk

	SBP Decrease from Baseline in mm Hg (95% CI)
Spironolactone (25-50 mg)	12.8
Doxazosin (4-8 mg)	8.7
Bisoprolol (5-10 mg)	8.3
Placebo	4.1

- Hyperkalemia occurred in 6 of 285 patients receiving spironolactone (serum potassium > 6.0 mmol/L)

Williams B, et al *Lancet* 2015;386:2059–2068.

Alternative Antihypertensive Agents

Class (drugs)	Comments
Alpha-1 Blockers (Doxazosin, Prazosin, Terazosin)	• Potential orthostatic hypotension; • Additional benefits in benign prostatic hyperplasia
Central Alpha-2 Agonists (Clonidine [transdermal], Methyldopa)	• Rebound hypertension with abrupt discontinuation • Anticholinergic side effects • Use with a diuretic to diminish fluid retention; • Per AHA Scientific Statement" ***"Clonidine tablets should be avoided because of the need for frequent administration and the risk of rebound hypertension during periods of non-adherence and after discontinuation."***
Arterial Vasodilators (Hydralazine, Minoxidil)	• Use with diuretic to diminish fluid retention • Use with beta-blocker to diminish tachycardia; • Especially effective in kidney failure

Carey RM, et al. *Hypertension*. 2018;72:e53-e90.

Challenges

"Drugs don't work in patients who don't take them."

- Former U.S. surgeon general C. Everett Koop

http://usatoday30.usatoday.com/news/health/2007-03-28-taking-medicine_N.htm

Predictors of Poor Adherence

- Low patient centeredness
- Less discussion about sociodemographic circumstance (living situation, relationship status)
  - Greater negative impact among black patients
- Less discussion about medications

Schoenthaler A, et al. *Circ Cardiovasc Qual Outcomes*. 2017;10:e003659

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Case MA

- 87-year-old black woman with hypertension, osteoporosis, dementia, COPD, anxiety, depression
- Current medications:
  - Amlodipine 5 mg daily, denosumab, memantine, escitalopram, alprazolam prn, tiotropium, albuterol prn, salmeterol/fluticasone
  - Experienced edema with amlodipine 10 mg daily
- Many medication intolerances
- Hospitalized 2 times over the past year for COPD; history of falls (once this year)
- Former smoker; no exercise
- Resides in assisted living
  - Husband died last year
- Vitals/other parameters:
  - BP 158/74, 160/72 mm Hg
  - BMI 18.9 kg/m^2
- Laboratory values (fasting)
  - eGFR 37 mL/min/1.73m^2
  - All other labs are normal

Polling Question…

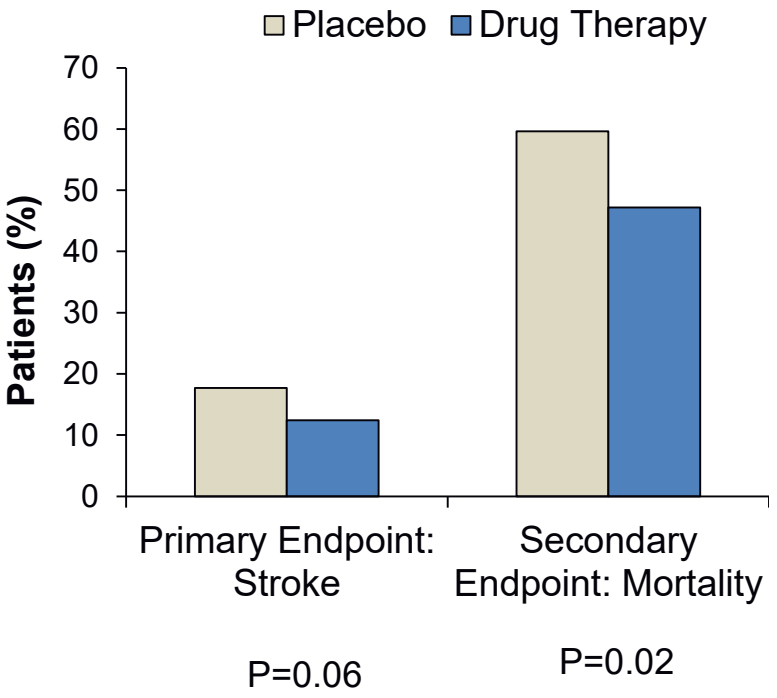
Which of the following systolic BP goals would you recommend for this patient?

a) <130 mm Hg
b) <140 mm Hg
c) <150 mm Hg
d) No goal at all

Hypertension in the Very Elderly Trial (HYVET)

- 3845 patients ≥80 yrs with hypertension
- Randomized, double-blind, to:
  - Placebo or
  - Perindopril +/- Indapamide
- Stopped early after 1.8 years

Target BP = 150/80 mm Hg



Beckett NS, et al. *N Engl J Med* 2008;358:1887-98.

ACCF-AHA 2011: Hypertension in the Elderly

Target SBP values

- Age 55-79: ≤140 mm Hg
- Aged ≥80+: ≤140 mm Hg
  - Achieved values <140 mm Hg are appropriate;
  - 140 to 145 mm Hg, if tolerated, can be acceptable

Pharmacotherapy

- Appropriate doses, titrate carefully with monitoring to mitigate orthostatic hypotension and fall risk
  - Start at the lowest dose and gradually increase
- Monitoring is crucial

2019 AGS Beers Criteria®

Potentially Inappropriate Medication Use in Older Adults

Therapeutic Category	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation
Peripheral α_1-blockers	Orthostatic hypotension	Avoid for hypertension	Moderate	Strong
Central α-agonists	CNS effects, bradycardia	Avoid	Low	Strong
Nifedipine (immediate-release)	Hypotension, risk of precipitating CV event	Avoid	High	Strong

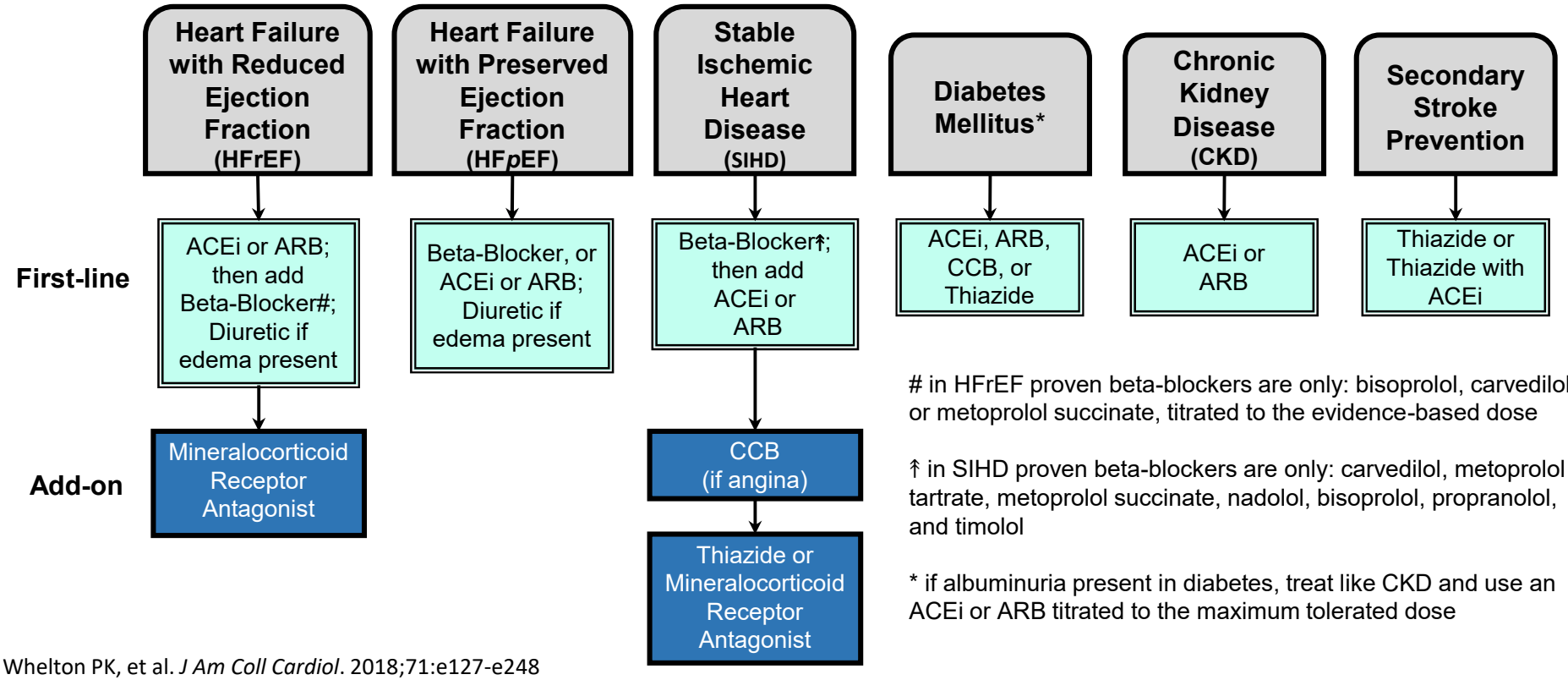
2019 American Geriatrics Society Beers Criteria® Update Expert Panel. *J Am Geriatr Soc*. 2019;67(4):674-694.

Polling Question…

Which of the following medications would you add to this patient's regimen?

a) Add chlorthalidone
b) Add lisinopril
c) Increase amlodipine to 7.5 mg and add a diuretic
d) Replace amlodipine with metoprolol succinate

2017 ACC/AHA: Compelling Indications



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* if albuminuria present in diabetes, treat like CKD and use an ACEi or ARB titrated to the maximum tolerated dose

Whelton PK, et al. *J Am Coll Cardiol*. 2018;71:e127-e248

Case MA: Creating a plan

- Patient is frail and at risk for adverse effects:
  - Lifestyle modifications are always helpful
  - Treatment to a SBP goal <150 mm Hg provides benefit
  - Low-dose combination therapy may be the best strategy to mitigate risk of hypotension/falls
- Add a low-dose ACEi or ARB
  - Should benefit CKD
  - Careful monitoring for adverse effects (e.g., orthostatic hypotension, electrolyte abnormalities)

Summary

- Titrate therapy to achieve BP goal using first-line medications (ACEi, ARB, CCB, thiazide) and combination therapy as necessary
- SBP goal <130 mm Hg is evidence-based; higher goals may be needed for some older patients
- Older patients have several challenges related to adverse effects related to medication use
- Treat resistant hypertension with combination therapy and assess to rule out secondary causes