Management of Hypertension: Update 2023

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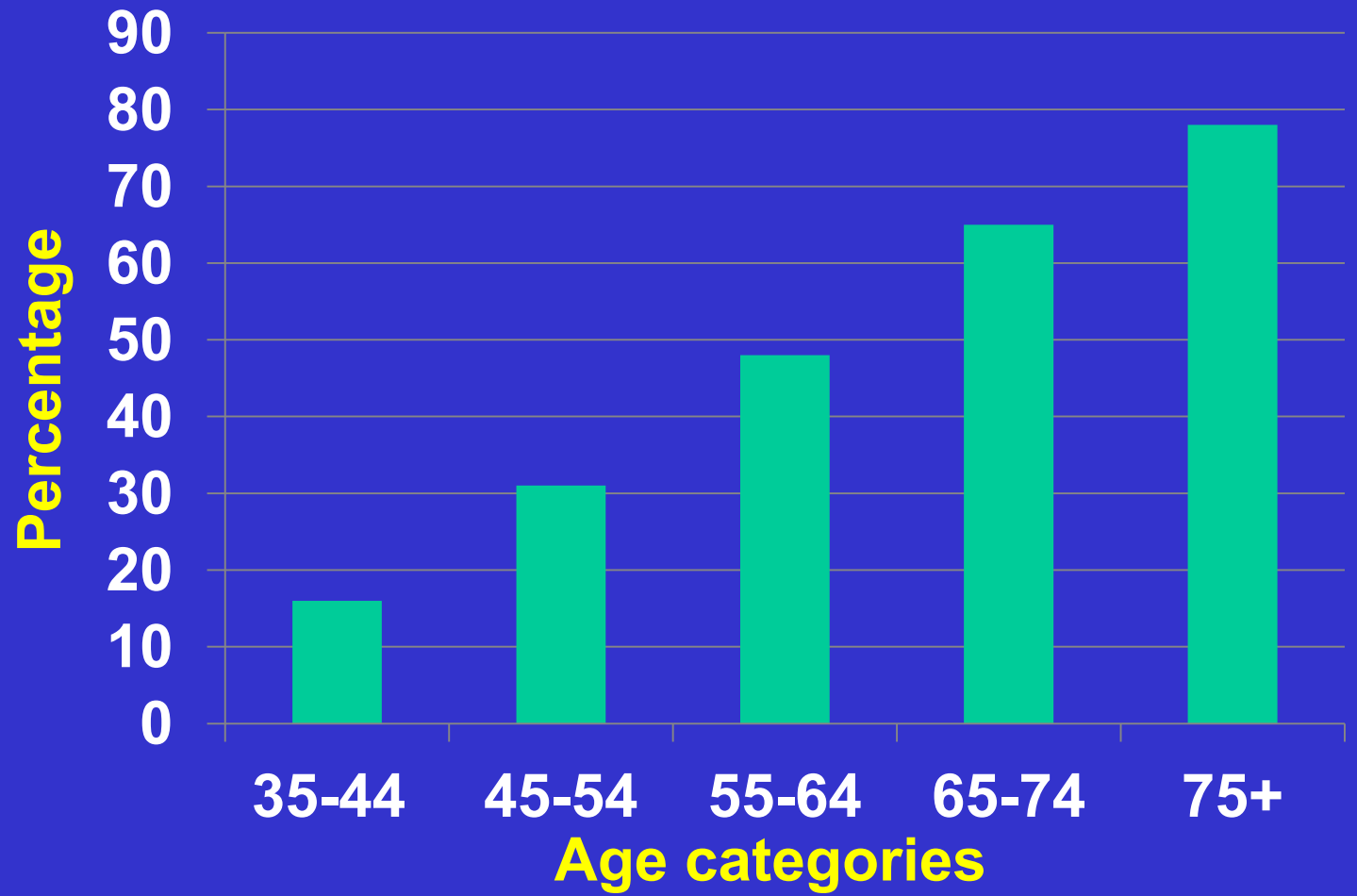
…and I have no disclosures

Key topics in hypertension: 2023

1. Who should be screened?
2. How do I know if a patient has HTN?
3. What is the role of 24-hour BP devices?
4. What should our targets be for BP control?
5. What about non-pharmacologic options?
6. What are the preferred medications?
7. Should BP medications be given before bed?
8. What are our “talking points?”

Most of us are headed toward hypertension

The prevalence of HTN (>140/90) in US:

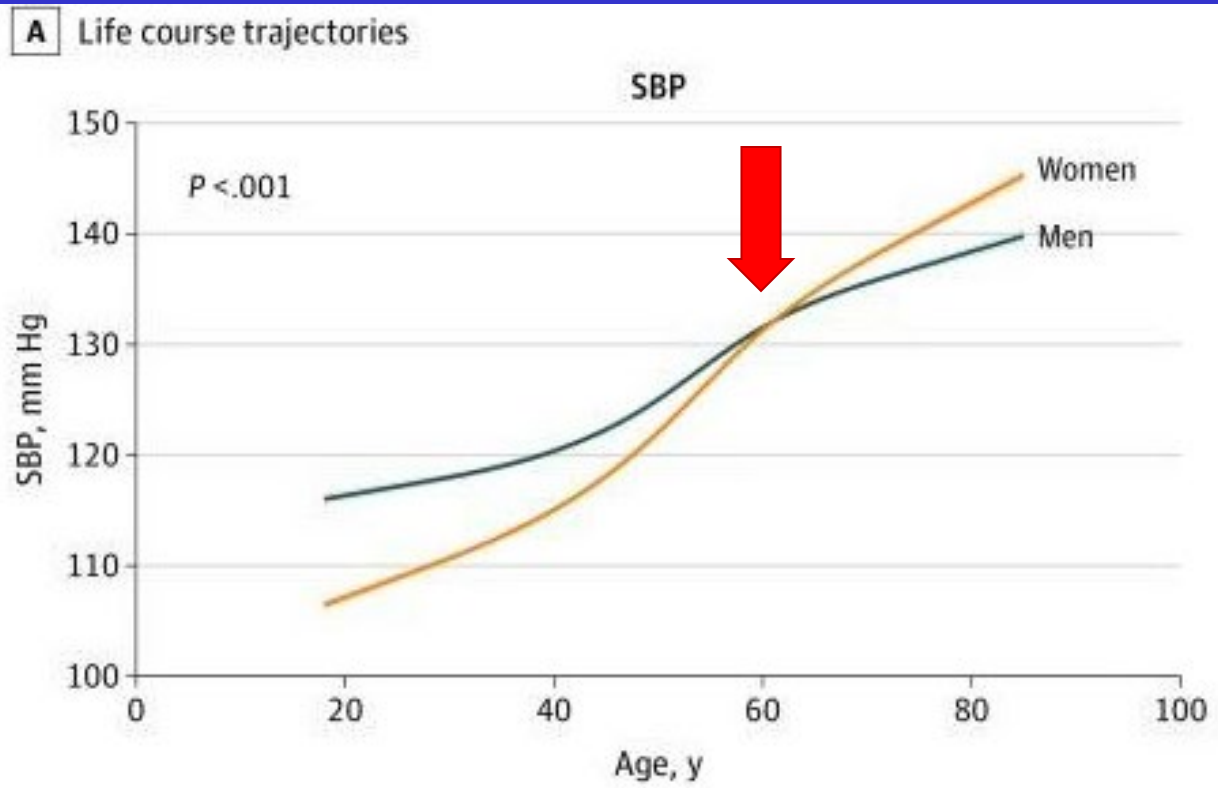


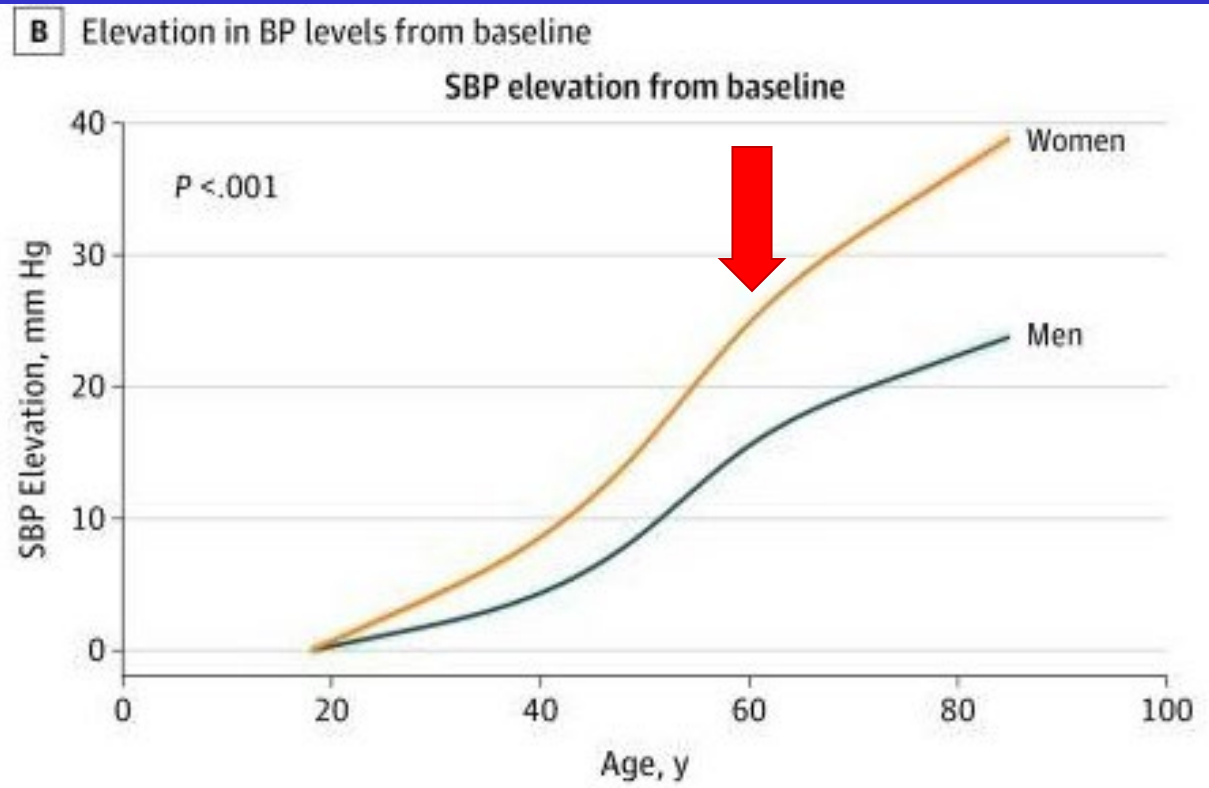
Over 80% by age 80

BP "creep:" More in women than men

(Framingham data, N=17733, 54% women, 43 yrs. FU)

At age 60, BP increase accelerates in women





JAMA Cardiology 2021;5:255

The benefit from treatments are substantial!

2021 Meta-analysis, 48 RCTs, N = 344,716. 4.15 yrs. FU.

For each 5 mmHg drop of SBP, 11 % drop in risk for major CV events at all SPB levels for patients without risk factors.

	Intervention		Comparator		HR (95% CI)
	Events	Total	Events	Total	
Major cardiovascular events					
<120	268	2193	395	2581	0·83 (0·71–0·97)
120–129	542	4542	788	5552	0·94 (0·84–1·06)
130–139	981	8538	1438	10313	0·89 (0·81–0·97)
140–149	1571	14249	2175	16947	0·95 (0·88–1·03)
150–159	1524	14737	2173	16948	0·87 (0·80–0·95)
160–169	1571	18773	2049	19811	0·89 (0·83–0·95)
≥170	2470	23933	3295	26614	–0·95)
Adjusted $p_{interaction}$ 1·00					
Unadjusted $p_{interaction}$ 0·66					

HR for each 5 mm drop of SBP

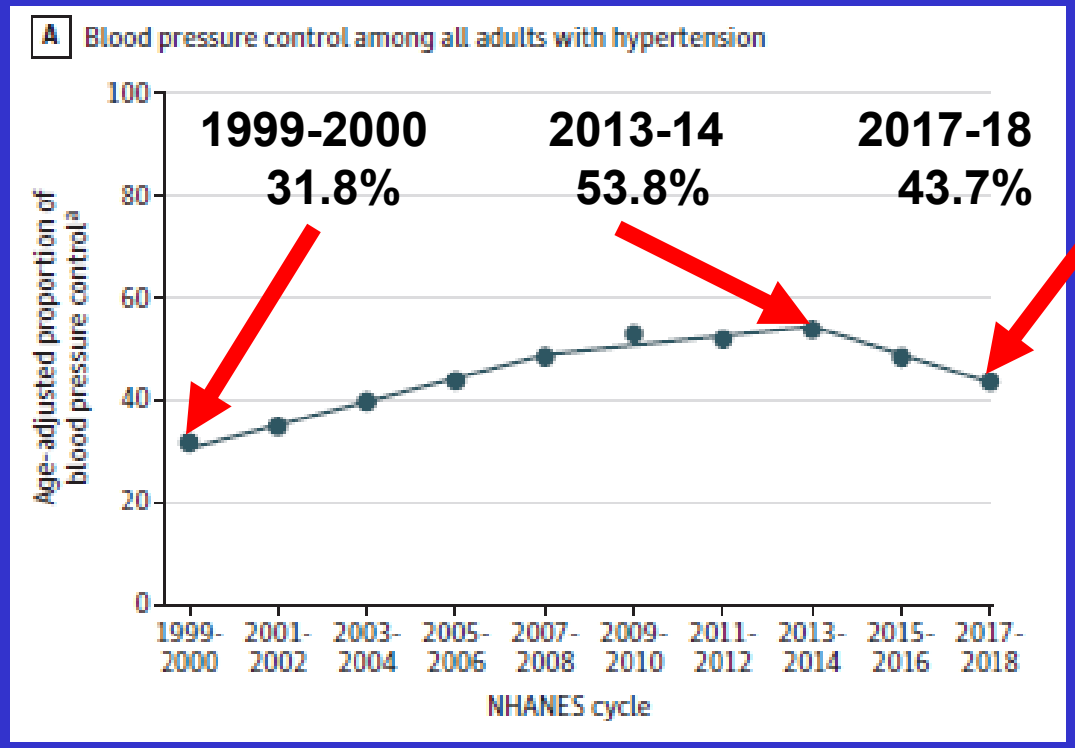
Drop from SBP 140 to 120 = 44% RR

Lancet 2021;397:1625

Our latest report:
We are not doing as well as we were!

(National Health and Nutrition Study, NANES, N=18262, 1999-2018, 10 cross-sectional cohorts, ≥18 yrs.)

Proportion "ever told" had HTN with home BP<140/90



Only 44% of those told they had HTN were < 140/90 at home in 2017-18

Down from 54% in 2013-14

JAMA 2020: Online 9-9-2020

USPSTF: April 2021

Screen all ≥18 - 40 years in office every 3-5 yrs., annually > 40. Readings recommended "outside of clinical setting for confirmation."

Threshold defined as either >130/80 and >140/90

JAMA 2021 326;1650

Will 24-hour BP devices become the new normal?

Why did USPFTF recommend outside of office confirmation?

- **Ambulatory BP Monitoring (ABPM): Gold standard.** 12-24 hours, brachial. Readings every 20-30 minutes vs.
- **Office:** Traditional or Oscillometric
- **Home BP Monitoring (HBPM):** Brachial, "multiple times over several days"

Table 5. Sensitivity, Specificity, and Likelihood Ratios of Office Oscillometric and Home Blood Pressure Monitoring Compared With Ambulatory Blood Pressure Monitoring[a]

Screening test	No. of studies	Sensitivity (95% CI), %	Specificity (95% CI), %	Likelihood ratio (95% CI)	
				Positive	Negative
Office	12[13-24]	51 (36-67)	88 (80-96)	4.2 (2.5-6.0)	0.56 (0.42-0.69)
Home	6[13,14,21-23]	75 (65-86)	76 (65-86)	3.1 (2.2-4.0)	0.33 (0.20-0.47)

JAMA 2021 326;339

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  several days"

Office only weakly predictive of ABPM HTN: 51% sensitivity

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JAMA 2021 326;339

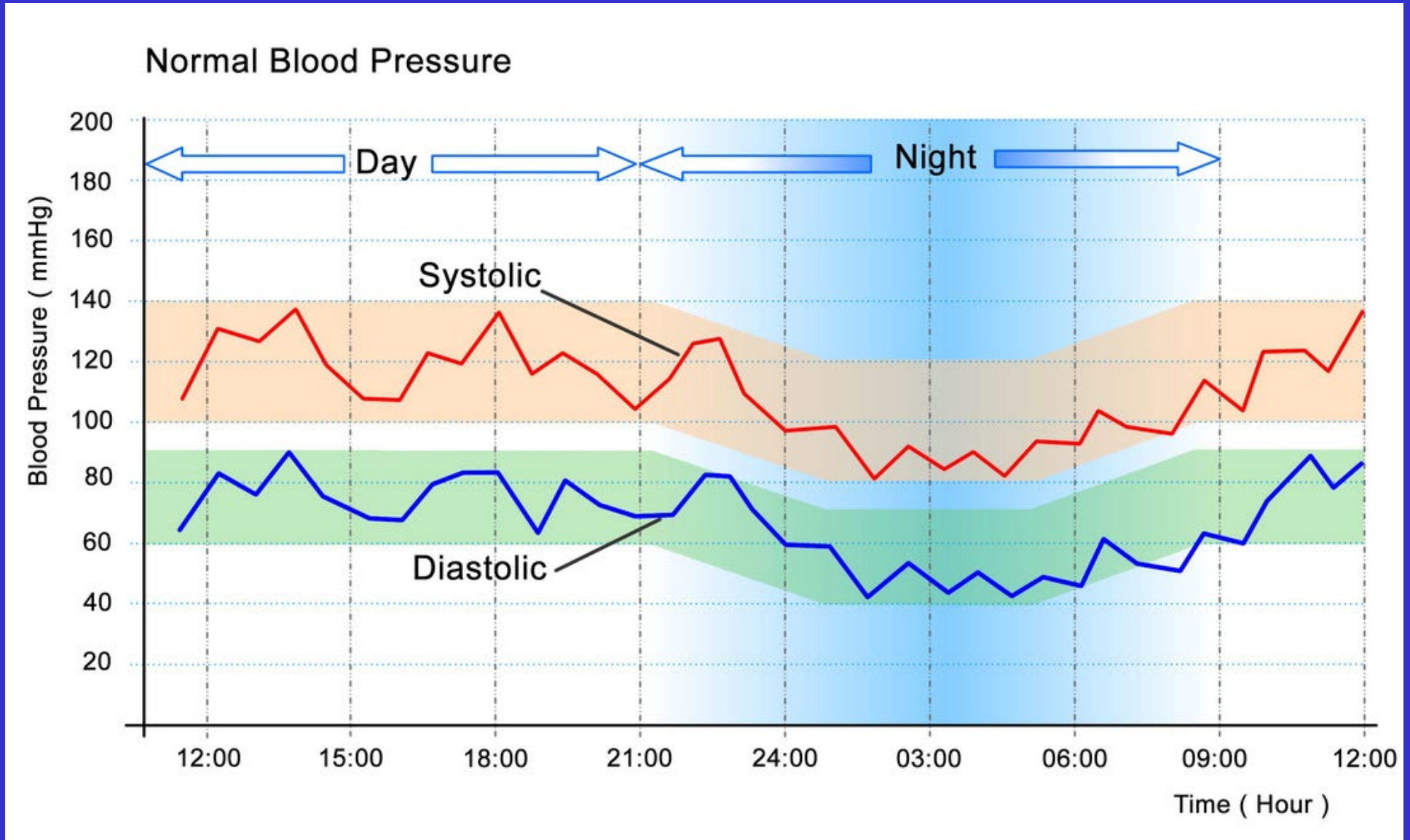
Will ambulatory BP monitoring become the gold standard?

(N= 63910 Spanish adults, average of 4.7 years follow-up, 3808 deaths)

	Hazard ratio
HR for each adjusted daytime average SD BP increase vs. normal	1.55
HR for each adjusted nighttime average SD BP increase vs. normal	1.54
Masked HTN vs. normal	2.83
White coat HTN vs. normal	1.79
Controlled HTN vs. normal	0.81 (NS)

NEJM 2018;378:1509

The BP normally drops during sleep



Ambulatory BP definitions

24-hour average BP

- Stage 1 HTN ≥ 125/75 mmHg
- Stage 2 HTN ≥ 130/80 mmHg

Daytime (awake) BP

- Stage 1 HTN ≥ 130/80 mmHg
- Stage 2 HTN ≥ 135/85 mmHg

Nighttime (asleep) BP

- Stage 1 HTN ≥ 110/65 mmHg
- Stage 2 HTN ≥ 130/80 mmHg

Nocturnal dipping

JAMA 2021 326;339

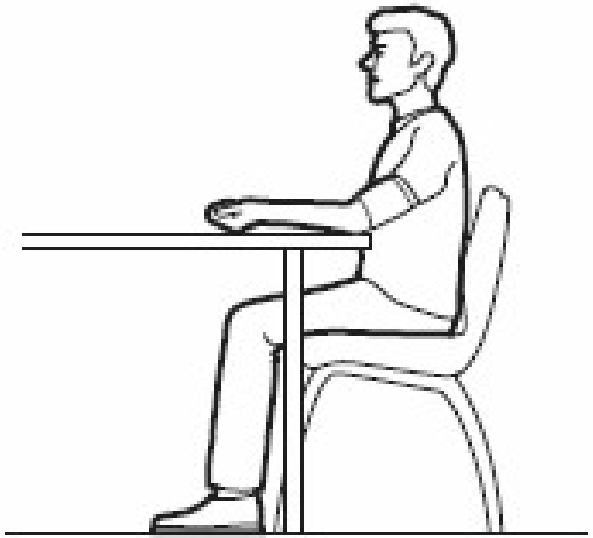
Are your BP readings accurate?

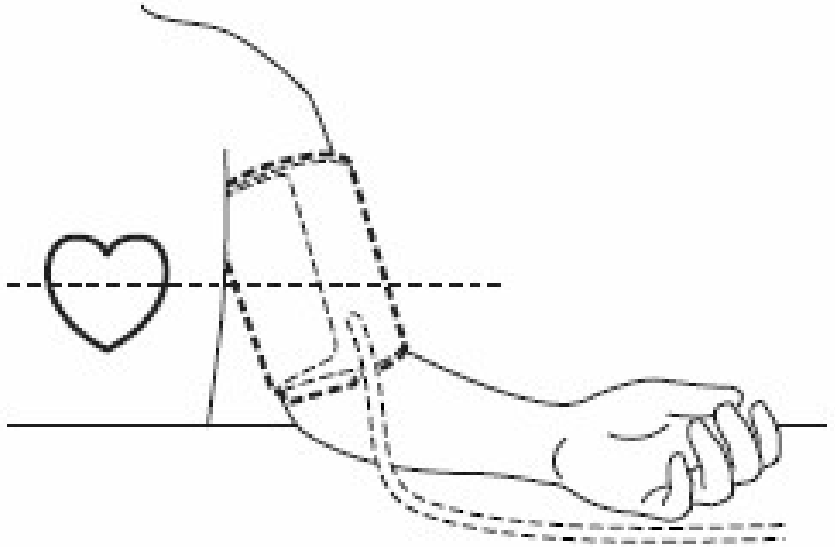
ACC/AHA BP checklist for your office

Step 1: Proper position	-No caffeine, exercise, smoking for > 30 minutes -Bladder empty -Seated, relaxed, arm supported for > 5 minutes. No talking. -No clothing under the cuff
Step 2: Proper technique	-Cuff 80% -Cuff at mid sternum
Step 3: Proper measurements	-Check both arms, follow higher arm -Initially palpate systolic, inflate 20–30 mm Hg above, deflate 2 mm Hg per second
Step 4: Documentation	-Auscultatory: First and last Korotkoff sounds
Step 5: Averaging	-Average ≥ 2 readings obtained on ≥ 2 occasions -Note times
Step 6: Patient education	-Provide patient with readings

ACC/AHA BP checklist for your office

Step 1: Proper position	-No caffeine, exercise, smoking for > 30 minutes -Bladder empty
Step 2: Proper	
Step 3: Proper measurements	mm Hg
Step 4: Docum	
Step 5: Averaging	-Average ≥ 2 readings obtained on ≥ 2 occasions -Note times
Step 6: Patient education	-Provide patient with readings





Optimized* office BPs vs. 24 hr. Ambulatory BPs vs. Office BPs

(Meta-analysis N = 9279, 31 studies)

***5 minutes rest, quiet room, automated at 1-2 min intervals**

Optimized office vs. 24-hour ambulatory BPs	**No difference**	**Equal**
Optimized office vs. Research BPs	**7 mm Hg.**	**Optimal office higher than structured research level BPs.**
Optimized office vs. Routine office	**14.5 mm Hg.**	**Routine office much higher than optimized office**

"Automated office BP should now be the preferred method for recording BP in routine clinical practice…"

JAMA Intern Med 2019;179:351-362

Key Points: High Blood Pressure

- There remains considerable controversy in how we define hypertension since BPs are continuously variable and responsive to emotional and physiologic factors.
- The higher the cutoffs, the more accurate office BPs become but accumulating data supports earlier treatment and lower BP goals.
- USPSTF advocates out of office confirmation…which may or may not be feasible.
- You make the call. If systolic BPs 125-140 mmHg: Does this patient have hypertension? Then what?

What should our targets be for blood pressure control?

In 2017, the ACC and AHA changed our world

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THE AMERICAN HEART ASSOCIATION, INC.

VOL. 71, NO. 19, 2018

CLINICAL PRACTICE GUIDELINE

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

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

ACC/AHA < 130/80

ACC/AHA: 2018 guidelines

Table 23. BP Thresholds for and Goals of Pharmacological Therapy in Patients With Hypertension According to Clinical Conditions

Clinical Condition(s)	BP Threshold, mm Hg	BP Goal, mm Hg
General		
Clinical CVD or 10-year ASCVD risk ≥10%	≥130/80	<130/80
No clinical	≥140/90	<130/80
Older per ambulato	≥130 (SBP)	<130 (SBP)
Specific com		
Diabetes	≥130/80	<130/80
Chronic k	≥130/80	<130/80
Chronic k	≥130/80	<130/80
Heart failure	≥130/80	<130/80
Stable ischemic heart disease	≥130/80	<130/80
Secondary stroke prevention	≥140/90	<130/80
Secondary stroke prevention (lacunar)	≥130/80	<130/80
Peripheral arterial disease	≥130/80	<130/80

ASCVD indicates atherosclerotic cardiovascular disease; BP, blood pressure; CVD, cardiovascular disease; and SBP, systolic blood pressure.

Target < 130/80 except for low ASCVD risk

JACC 2018;71:2176

The competing guidelines: JNC 7/8, ACC/AHA, ESC/ESH

Systolic		Diastolic	JNC 7	ACC/AHA	ESC/ESH
<120	and	< 80	Normal	Normal	Optimal
120-129	and	<80	Pre HTN	Elevated	Normal
	and/or	80-84			
		85-89			
130-139	and/or	85-89		Stage 1 HTN	High Normal
140-159	and/or	90-99	Stage 1 HTN	Stage 2 HTN	Grade 1 HTN
≥ 160-179	and/or	≥ 100-109	Stage 2 HTN		Grade 2 HTN
≥ 180	and/or	≥ 110			Grade 3 HTN

JAMA 2018 320;1760

SPRINT (Systolic Blood Pressure Intervention Trial), 2015

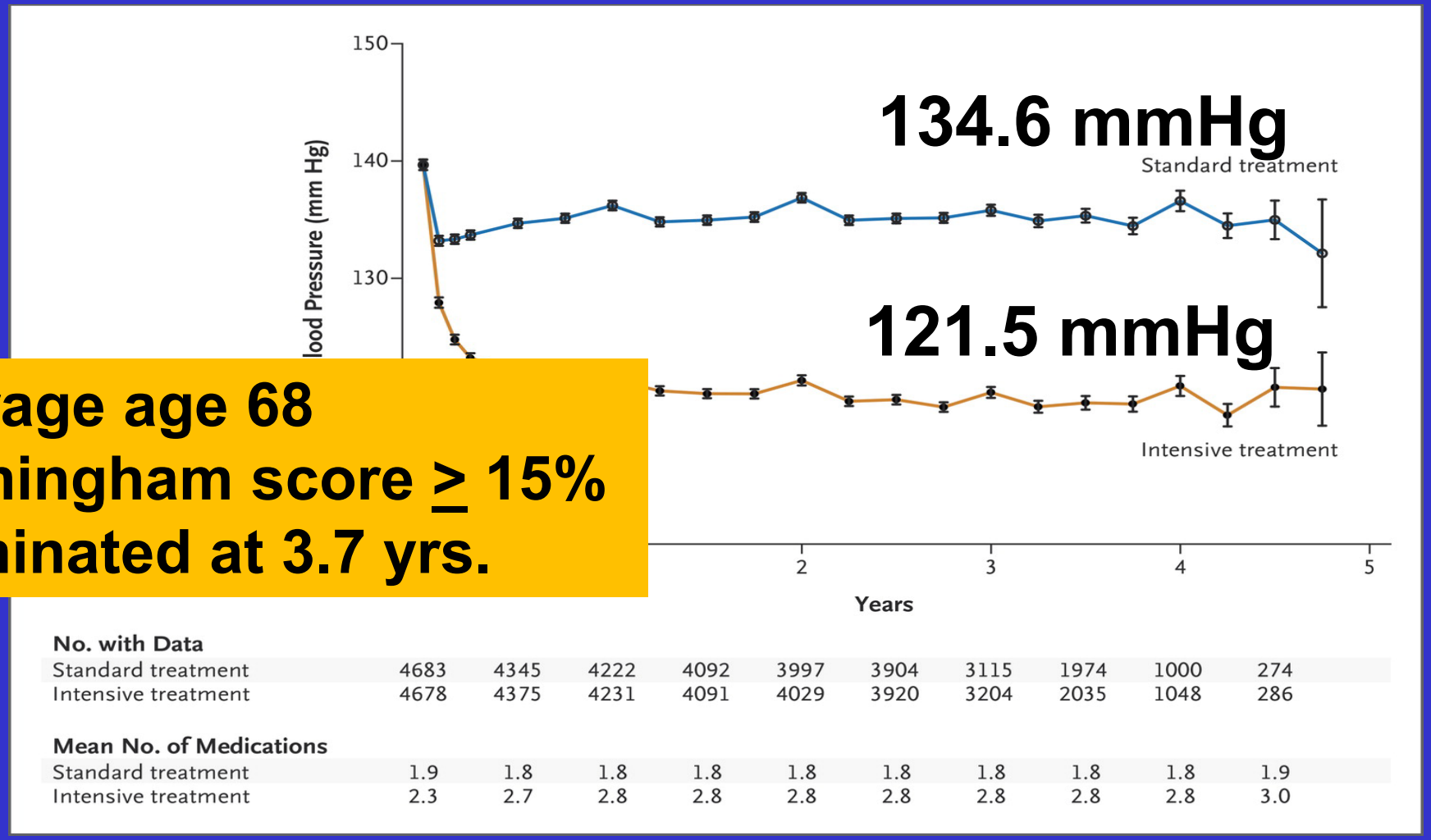
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 NOVEMBER 26, 2015 VOL. 373 NO. 22

A Randomized Trial of Intensive versus Standard Blood-Pressure Control

The SPRINT Research Group*

Systolic Blood Pressure in the two treatment groups over the course of the SPRINT trial

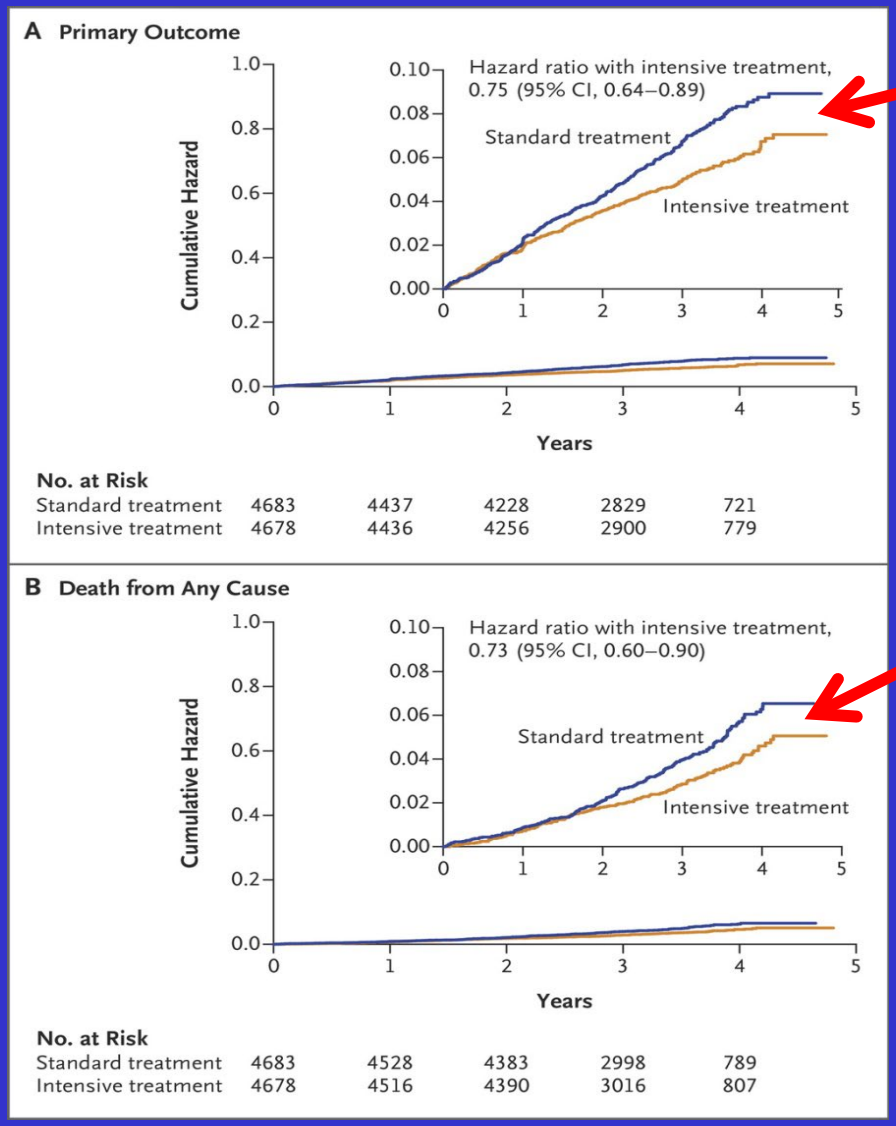


No. with Data										
Standard treatment	4683	4345	4222	4092	3997	3904	3115	1974	1000	274
Intensive treatment	4678	4375	4231	4091	4029	3920	3204	2035	1048	286
Mean No. of Medications										
Standard treatment	1.9	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.9
Intensive treatment	2.3	2.7	2.8	2.8	2.8	2.8	2.8	2.8	2.8	3.0

Average age 68
Framingham score ≥ 15%
Terminated at 3.7 yrs.

NEJM 2015;373:2103-2116

Primary Outcome from SPRINT Trial

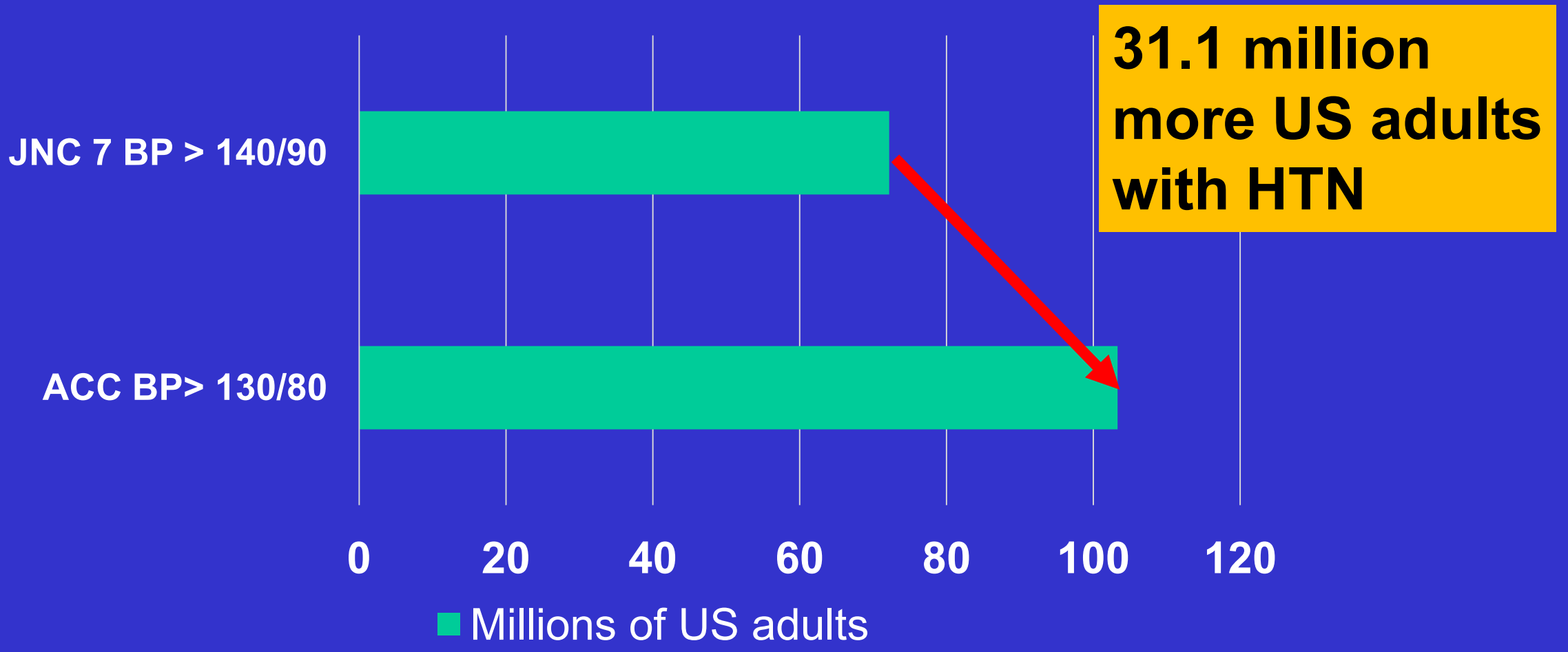


25% reduction in composite outcome, MI, ACS, CVA, HF, mortality

27 % reduction in all cause mortality

NEJM 2015;373:2103-2116

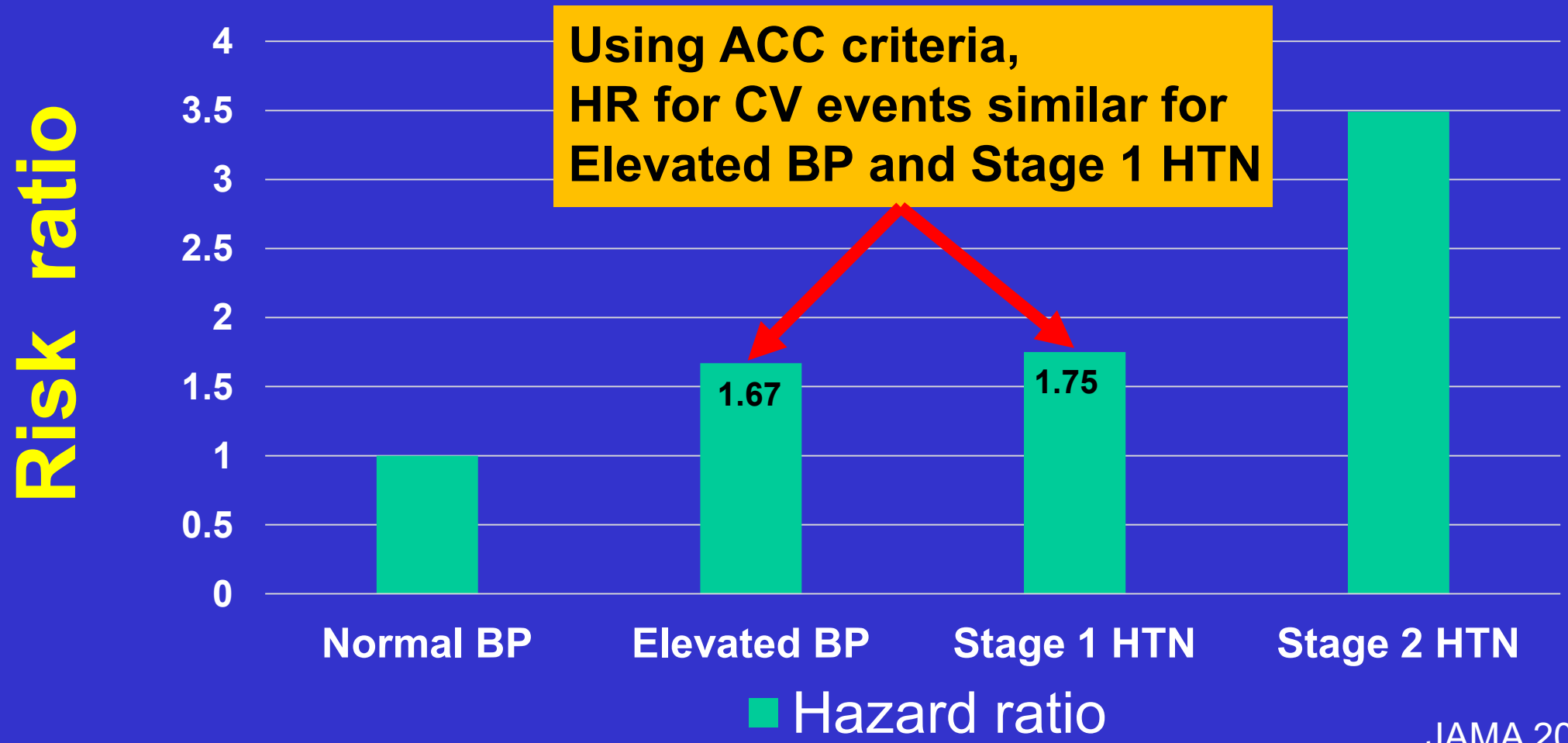
What happens to the prevalence of HTN with the ACC definition?



NEJM 2018; 378:497

What about early life elevated BPs?

(CARDIA N = 4851, age 35.7, followed 18.8 years)



JAMA 2018;320:1774

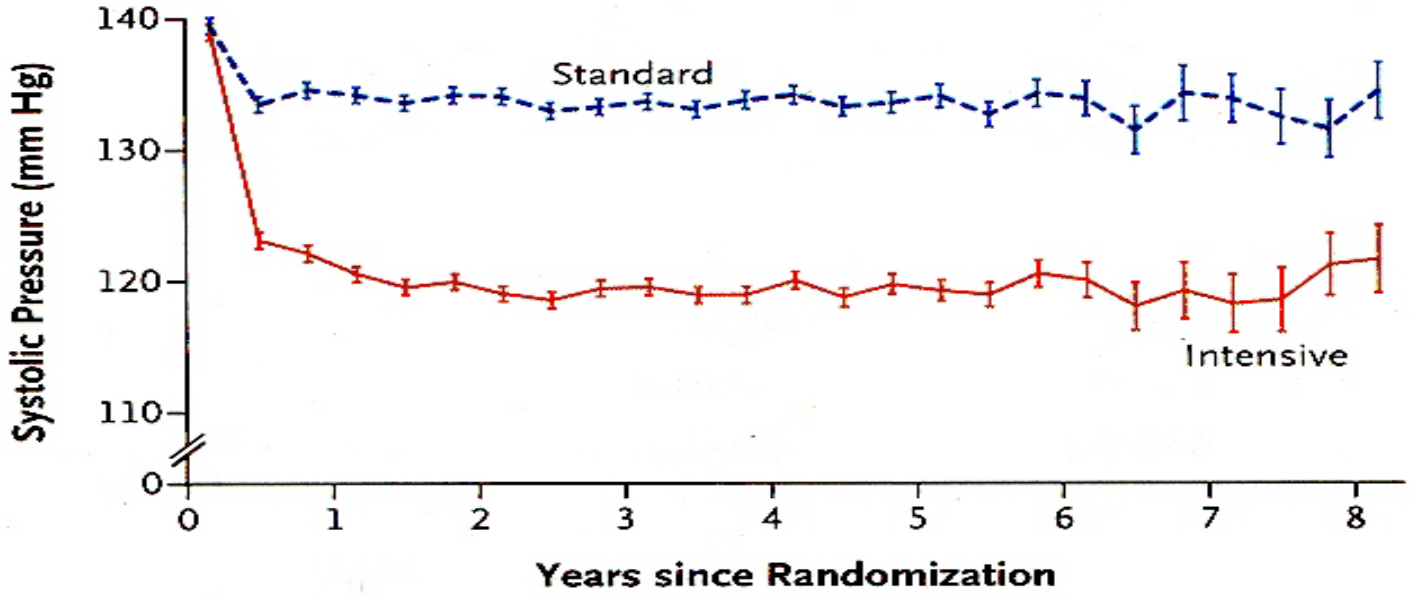
Should BP targets be higher for patients with Type 2 DM?

Study design (ACCORD, 2010):

- US and Canada, 77 sites
- RCT
- 4733 patients
- Randomized to
  - **Intensive control, SBP < 120 mm Hg**
  - **Standard control, SBP < 140 mm Hg**
- 4.7 year follow up

BP targets for Type 2 DM

ACCORD outcomes, SBPs

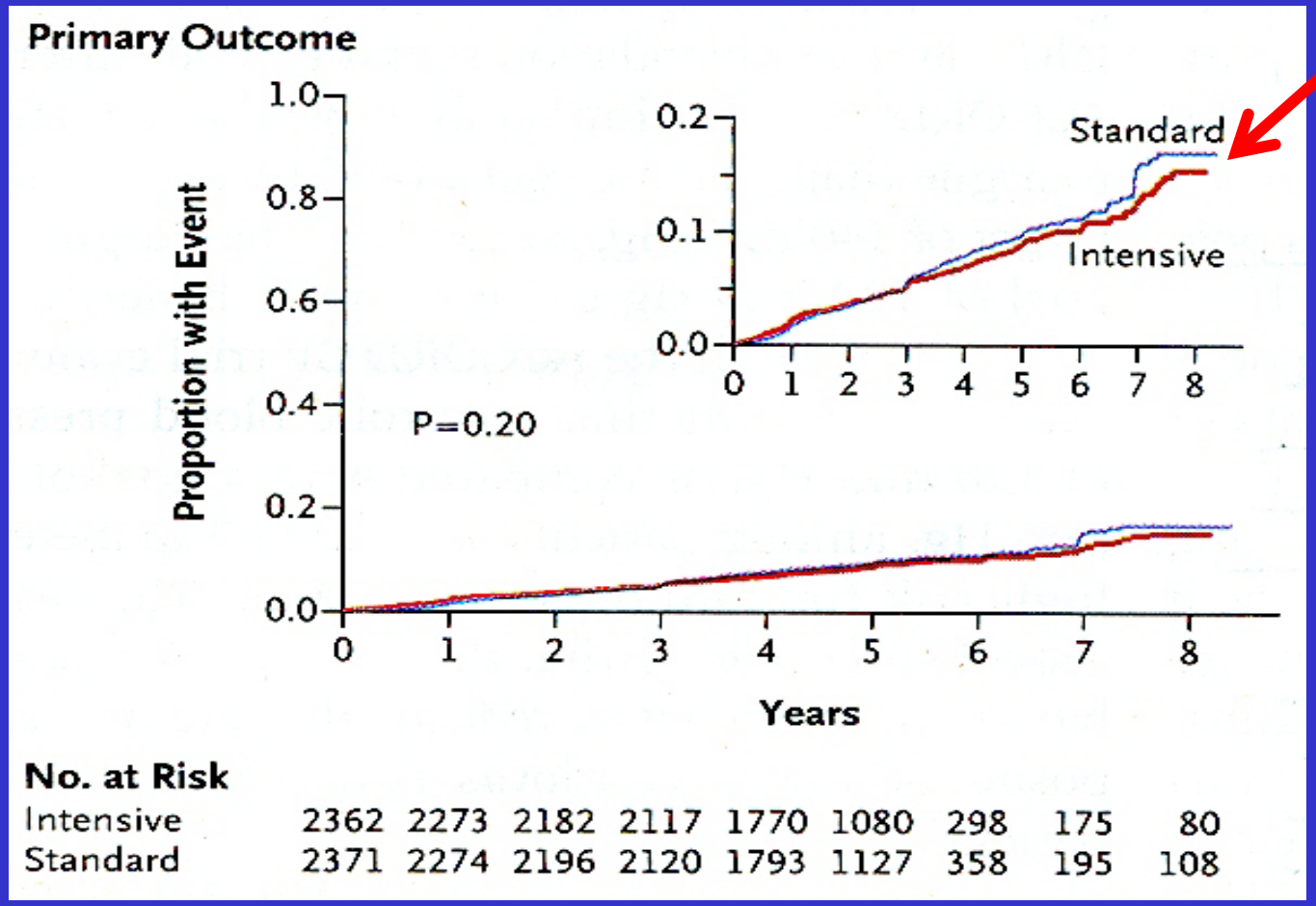


Mean No. of Medications Prescribed								
Intensive	3.2	3.4	3.4	3.5	3.5	3.5	3.4	3.4
Standard	1.9	2.1	2.1	2.2	2.2	2.3	2.3	2.3
No. of Patients								
Intensive	2174	2071	1973	1792	1150	445	156	156
Standard	2208	2136	2077	1860	1241	504	203	201

N Engl J Med 2010;362:17:1580

BP targets for Type 2 DM

ACCORD primary outcomes



No benefit from intensive therapy

N Engl J Med 2010;362:17:1583

BP targets for Type 2 DM

ACCORD patient outcomes, % per year

	Intensive	Standard	P value
Primary*	1.87	2.09	NS
Adverse events			
Attributable to tx**	**3.3**	**1.27**	**<0.001**

*Non-fatal MI, non-fatal CVA, CV death

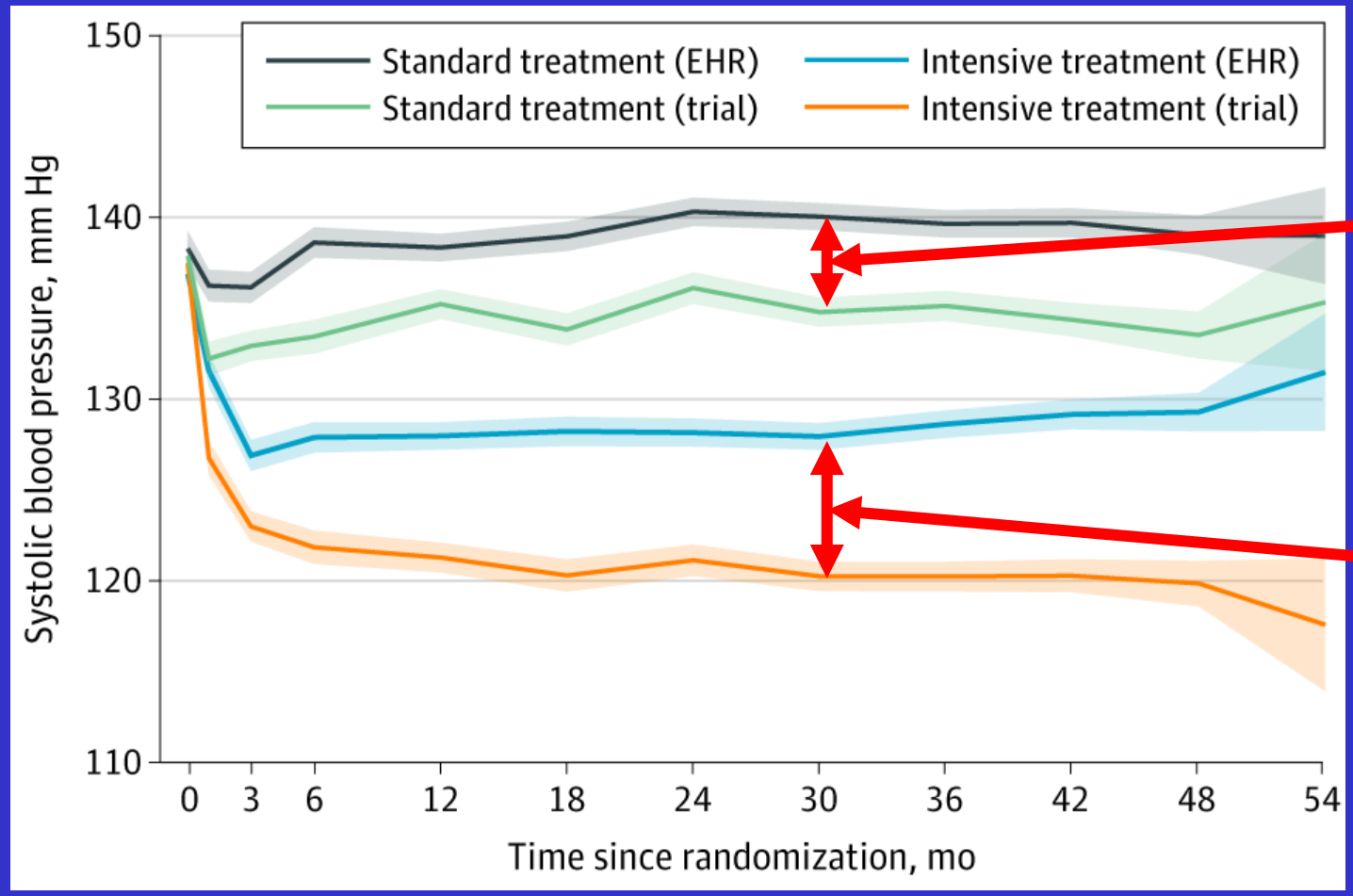
**Hypotension, syncope, bradycardia, hyperkalemia, angioedema, CKD

Setting goals for BP control: A work in progress

- For most adults, focus on office BP goal of ≤130/85 BUT…
  - If possible, work this down to low 120s/80
    - May need more medication…
    - Slightly higher may be ideal for DM
- Consider a target of <<130/80
  - Younger
    - May mean medications…

How well did "official" SPRINT SBPs compare to EHR recorded BPs?

(FU 49/102 SPRINT sites, N = 3074. EHR SBPs vs. trial recorded SBPs)



EHR SBPs vs. Trial

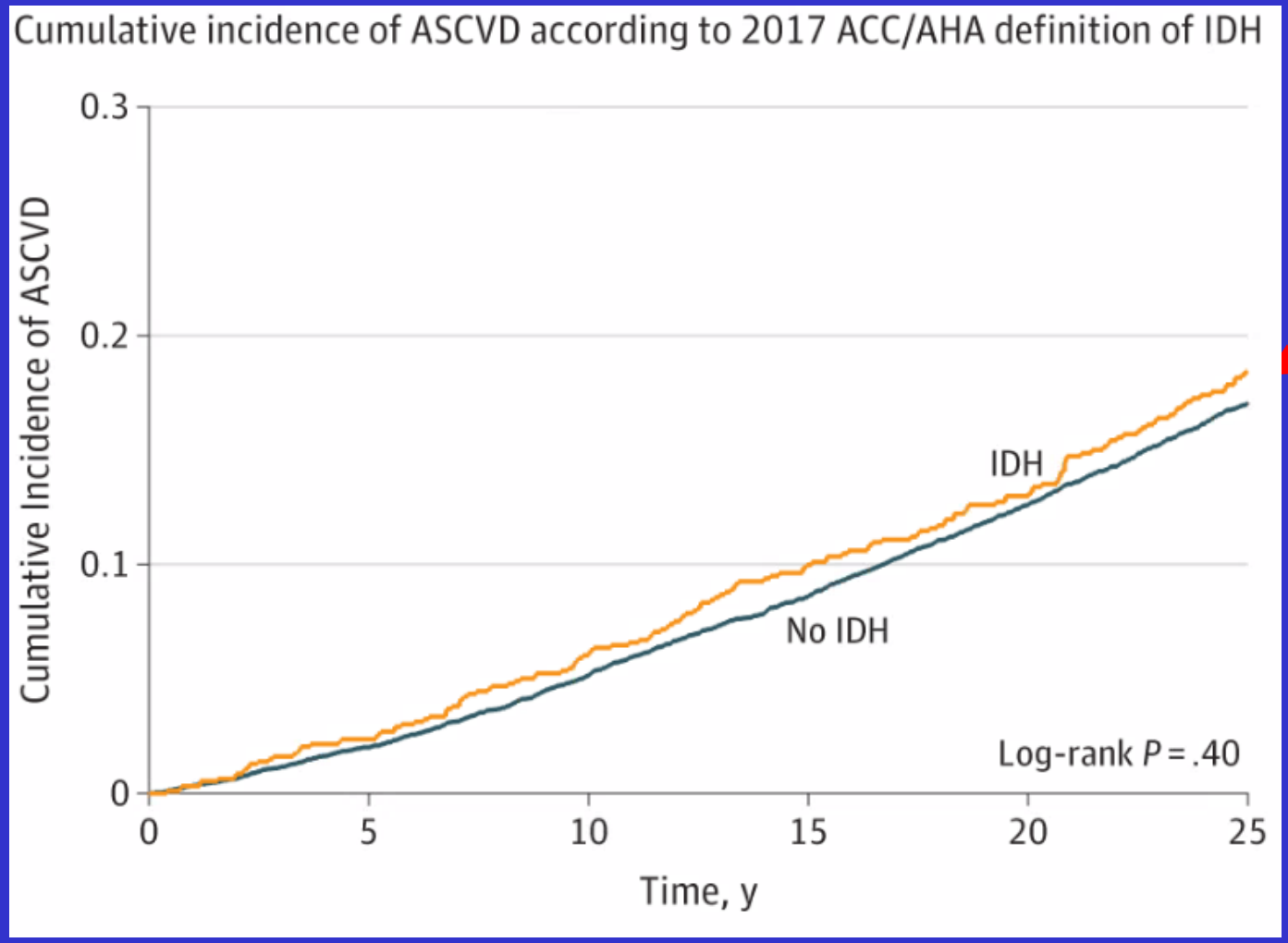
Standard therapy
4.6 mm Hg higher:
139.3 vs. 134.6

Intensive therapy
7.3 mm Hg higher:
128.2 vs. 120.9

JAMA Intern Med 2020;180:1655-1663

Is there risk from isolated diastolic HTN?

(NHANES and ARIC Cohorts, N=15792, 25 yrs. Follow-up)



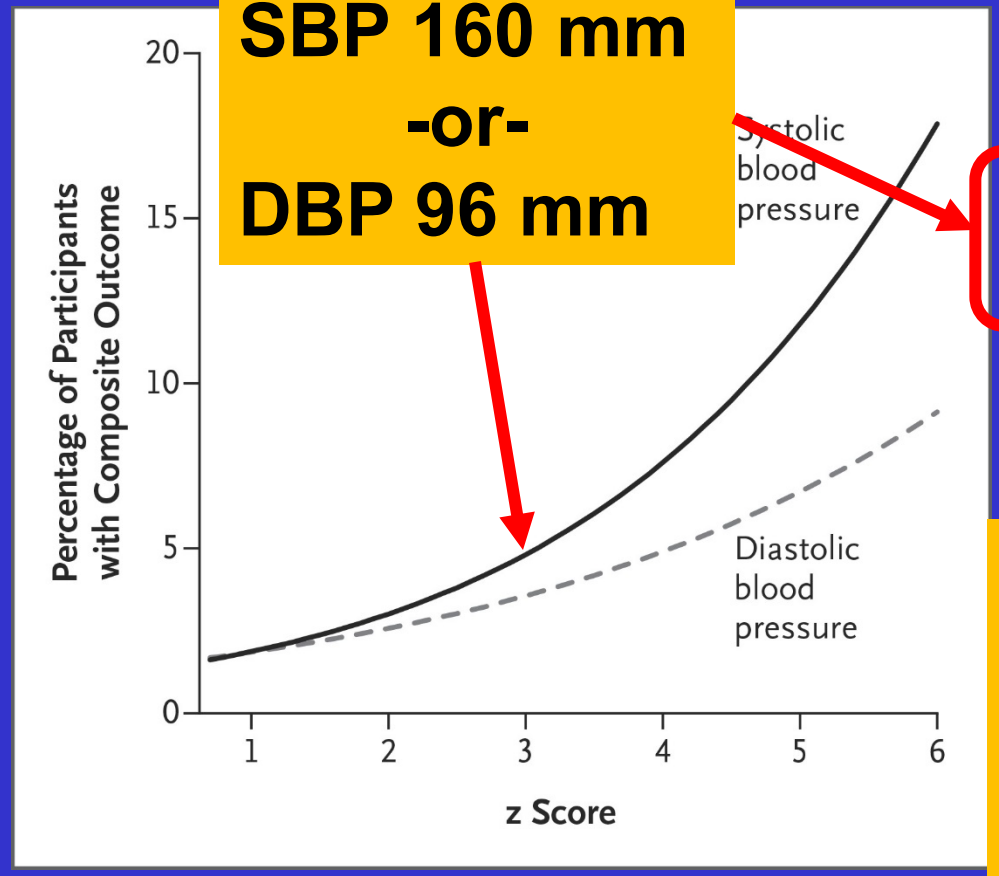
No increase in CV risk for DBP ≥ 80 if SBP <130 mm Hg over 25 yrs.

JAMA. 2020;323(4):329-338

It there diastolic BP that is too high?

(Kaiser cohort, N=1.3 million, 8 yrs. follow-up)

SBP 160 mm
-or-
DBP 96 mm



	Risk of CV event over 8 yrs.
Ave SBP 160 mm Hg	4.8 %
Ave DPB 96 mm Hg	3.6 %
Ave SPB 136 mm Hg	1.9 %
Ave DBP 81 mm Hg	1.9 %

The DBP where risk started to increase was 96 mmHg… Consensus to act if > 90 mm Hg but benefit not clear from the data

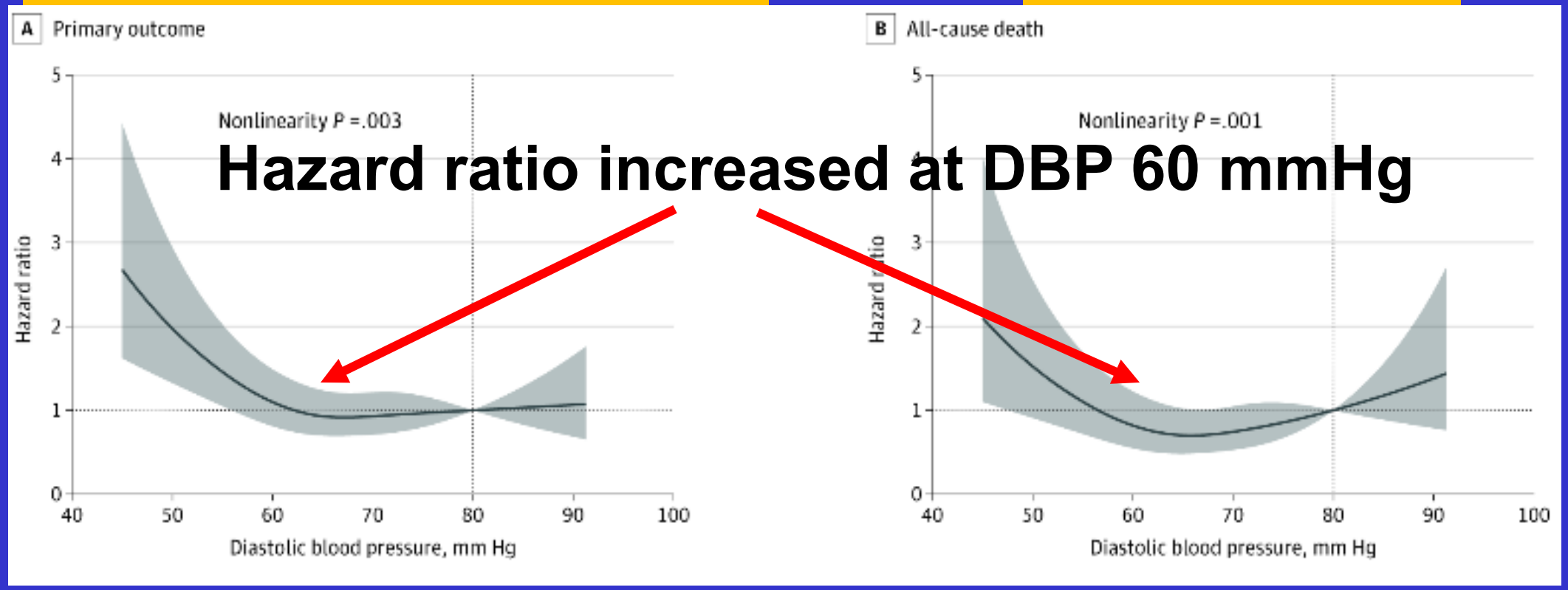
NEJM 2019;381:243-251

What diastolic BPs is too low?

(Combined SPRINT and ACCORD Data, N = 7515 with high CV risk and Sys BP <130 mm Hg)

All cause death, MI, or CVA

All cause death



JAMA Open Network. 2021;4(2):e2037554

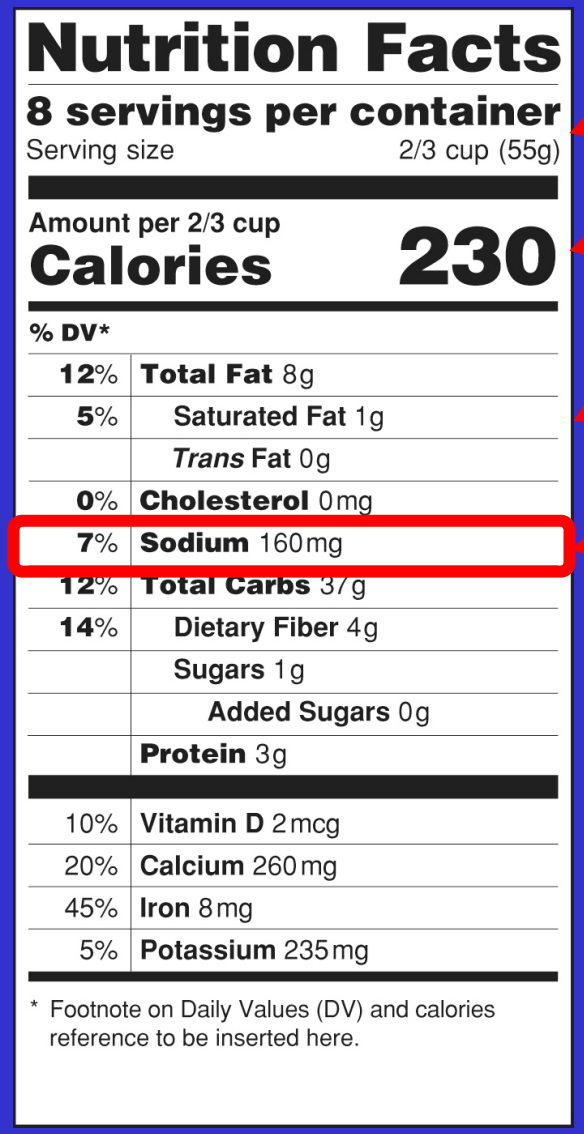
- Go with the systolic in most cases.
- Be sure you know which arm is higher and follow this arm.
- Think about the bladder (SBP: 4 mm Hg +/- 10)
- Upper arm cuff only, no wrist or finger cuffs.
- Reduce meds when standing BP < 110 after one minute.

What are our core “lifestyle” messages?

ACC/AHA nonpharmacologic recommendations

Intervention	Goal	Expected benefit
Weight loss	1-5 kg	1 mm Hg/1 Kg
DASH diet	Fruits, vegetables, whole gr, low-fat dairy	11 mm Hg
Sodium restriction	Less than 1500 mg per day, minimum 1000 mg per day reduction	5–6 mm Hg
High potassium diet	3500–5000 milligrams per day	4 –5 mm Hg
Exercise	90–150 minutes per week	4–5 mm Hg
Moderate alcohol	Men: ≤ 2 drinks daily Women: ≤ 1 drink daily	4 mm Hg

Know where you want your patients to find the information they need



Nutrition Facts

8 servings per container

Serving size 2/3 cup (55g)

Amount per 2/3 cup
Calories **230**

% DV*	
12%	**Total Fat** 8g
5%	**Saturated Fat** 1g
	***Trans* Fat** 0g
0%	**Cholesterol** 0mg
7%	**Sodium** 160mg
12%	**Total Carbs** 37g
14%	**Dietary Fiber** 4g
	Sugars 1g
	Added Sugars 0g
	Protein 3g
10%	**Vitamin D** 2mcg
20%	**Calcium** 260mg
45%	**Iron** 8mg
5%	**Potassium** 235mg

* Footnote on Daily Values (DV) and calories reference to be inserted here.

Serving

Calories

Fat

Sodium, AKA “salt”

DASH: Dietary content, servings per day

	Control Diet	Fruit/Vegetable Diet	Combination Diet
Fruits/juices	1.6	5.2	5.2
Vegetables	2	3.3	4.4
Grains	8.2	6.9	7.5
Low-fat dairy	0.1	0.0	2.0
Reg-fat dairy	0.4	0.3	0.7
Nuts/seeds/legumes	0.0	0.6	0.7
Beef/pork/ham	1.5	1.8	0.5
Poultry	0.8	0.4	0.6
Fish	0.2	0.3	0.5
Fats/oils/salad dress.	5.8	5.3	2.5
Snacks/sweets	4.1	1.4	0.7

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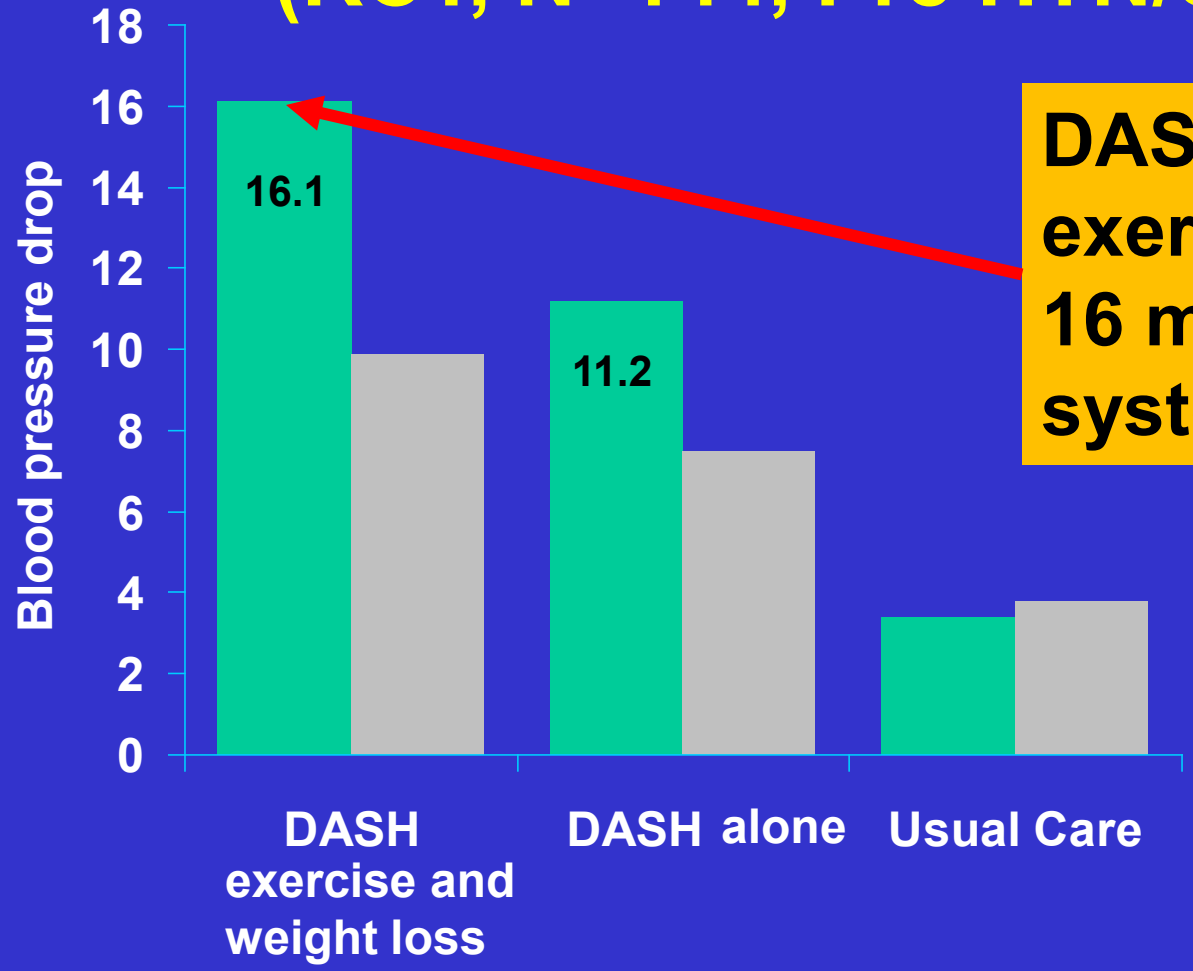
Poultry	0.8		0.6
Fish	0.2		0.5
Fats/oils/salad dress.	5.8		2.5
Snacks/sweets	4.1	1.4	0.7

Cut snacks, oils, fats sweets! Replace with fruits and veggies!

DASH works, DASH + weight Management (20 lb loss) works better

(RCT, N=144, Pre HTN/Stage 1, 5 years)



DASH+ weight loss+ exercise => 16 mm Hg systolic BP drop

Arch Intern Med 2010;170:126-135

Sodium content of common foods:

Classic potato chips (sm bag)	180 mg
White bread (one slice)	147 mg
Bagel	561 mg
Cheerios	280 mg
One pickle spear	380 mg
Tomato soup	450 mg
Nine pretzels	560 mg
1 Tbs. Soy sauce	870 mg
Big Mac	1100 mg
Ham Sandwich with mustard	2340 mg
Lo mein	3460 mg

Let's talk about alcohol

(Cochrane meta-analysis, 32 RCTs N=767, mean age 33 yrs., 83% male)

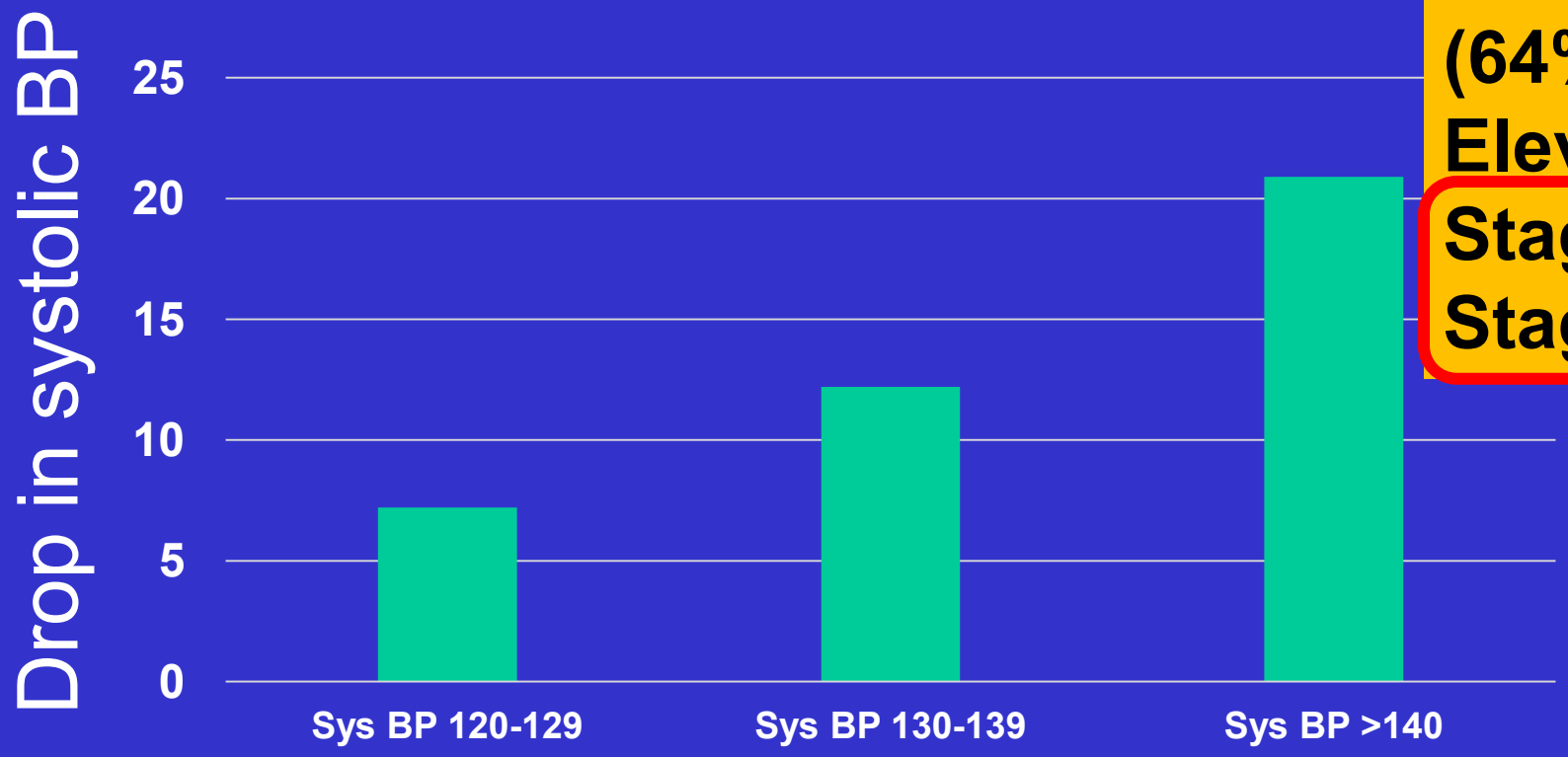
"Drinks"		6 hours	7-12 hours	>13 hours
1	HR	+ 5 BPM	No change	No change
	Systolic BP	No change	No change	No change
> 1-2	HR	+ 4.6 BPM	No change	No change
	Systolic BP	- 5.6 mm Hg	No change	No change
> 3	HR	+ 5.8 BPM	+ 6.2 BPM	+ 2.7 BPM
	Systolic BP	- 3.5 mm Hg	- 3.7 mm Hg	+ 3.7 mm Hg

Cochrane July 1, 2020

Is home monitoring a therapeutic option?

Home monitoring, medication reminders, and lifestyle tracking via an app for Stage 1 and 2 Hypertension

(Cohort N=28189, employer sponsored (21), 3 yr. follow-up)



For "engaged patients" (64% of men, 36% of women):
Elevated BP - 7.2 mm Hg
Stage 1 = - 12.2 mm Hg
Stage 2 = - 20.9 mm Hg

JAMA NO2021;4(10):e2127008

One drug, two drugs…what drugs are best?

ACC/AHA treatment recommendations

8.1.6. Choice of Initial Medication

Recommendation for Choice of Initial Medication

References that support the recommendation are summarized in Online Data Supplement 27 and Systematic Review Report.

COR	LOE	Recommendation
I	A^{SR}	1. For initiation of antihypertensive drug therapy, first-line agents include thiazide diuretics, CCBs, and ACE inhibitors or ARBs. (1, 2)

SR indicates systematic review.

Thiazides
CCBs
ACEIs
ARBs

Combination Therapy if Stage 2 and > 20/10 over target

8.1.6.1. Choice of Initial Monotherapy Versus Initial Combination Drug Therapy

Recommendations for Choice of Initial Monotherapy Versus Initial Combination Drug Therapy*

COR	LOE	Recommendation
I	C-EO	1. Initiation of antihypertensive drug therapy with 2 first-line agents of different classes, either as separate agents or in a fixed-dose combination, is recommended in adults with stage 2 hypertension and an average BP more than 20/10 mm Hg above their BP target.
IIa	C-EO	2. Initiation of antihypertensive drug therapy with a single antihypertensive drug is reasonable in adults with stage 1 hypertension and BP goal <130/80 mm Hg with dosage titration and sequential addition of other agents to achieve the BP target.

*Fixed-dose combination antihypertensive medications are listed in Online Data Supplement D.

ACC comparison review: All agents had higher risk ratios vs. thiazides, esp. BBs

	All cause death	CV death	Heart Failure	Stroke	Major CV event
ACEIs	1.0	1.1	1.2	1.1	1.1
ARBs	0.99	1.1	1.1	1.1	1.0
Beta Blockers	1.1	1.2	1.3	1.3	1.2**
Ca Channel Blockers	0.97	1.0	1.3	0.96	1.1

** statistically significant

JACC 2018;71:2176

ASCOT: Initial HTN treatment with B-blocker increased risk in comparison to calcium channel blocker

Outcomes	Hazard risk: Amlodipine vs atenolol
Stroke	0.77 (0.66 – 0.89)
CV events	0.84 (0.78 – 0.90)
Mortality	0.89 (0.81 – 0.99)
Diabetes	0.70 (0.63 – 0.78)

ACC comparison review: Thiazides vs. other agents for Black Americans

	All cause death	Heart Failure
ACEIs	1.1	1.4
Beta Blockers	1.3	1.2
Ca Channel Blockers	0.98	1.4

No agent superior to thiazides

JACC 2018;71:2176, supplement

Is there a preferred thiazide?

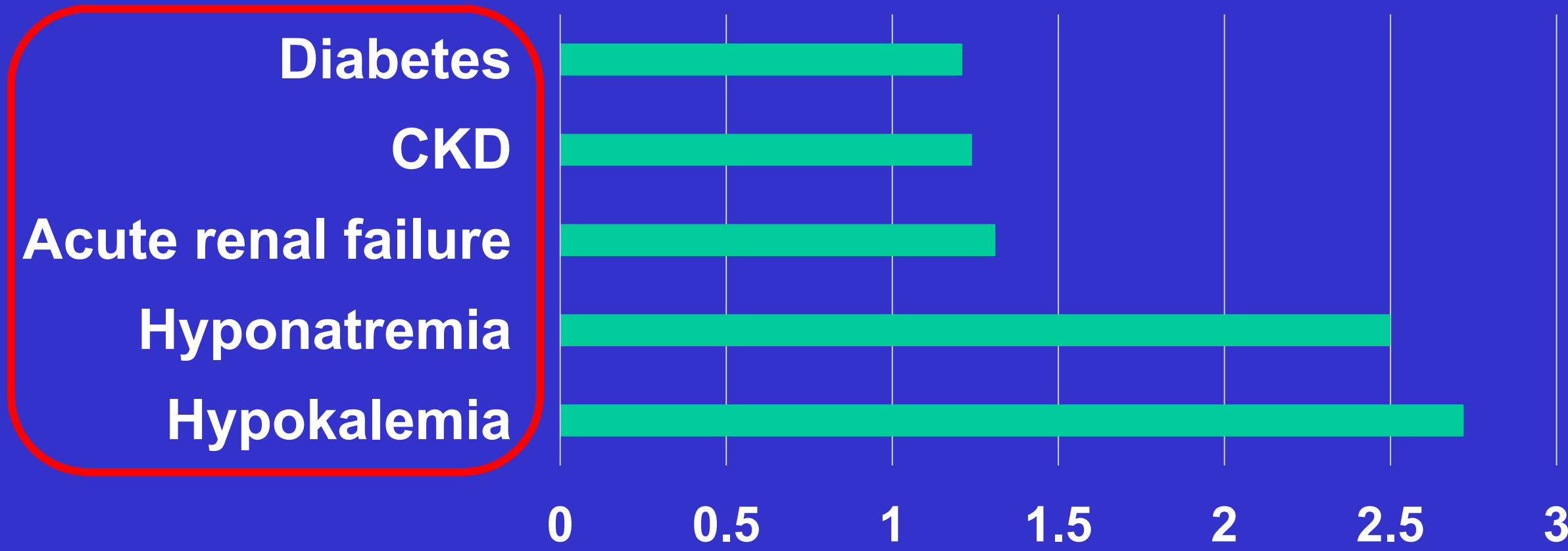
	Protein binding	Half life, hours
HCTZ	40%	9-10
Chlorthalidone	99%	50-60
Metolazone	95%	8-14

No appreciable difference in cost but chlorthalidone can be tough to find and is rarely combined with other medications such as ACEIs or ARBs

Chlorthalidone vs. HCTZ

(N=730,225, US Meta-analysis, first time users, 2001-2018, 61.6% women)

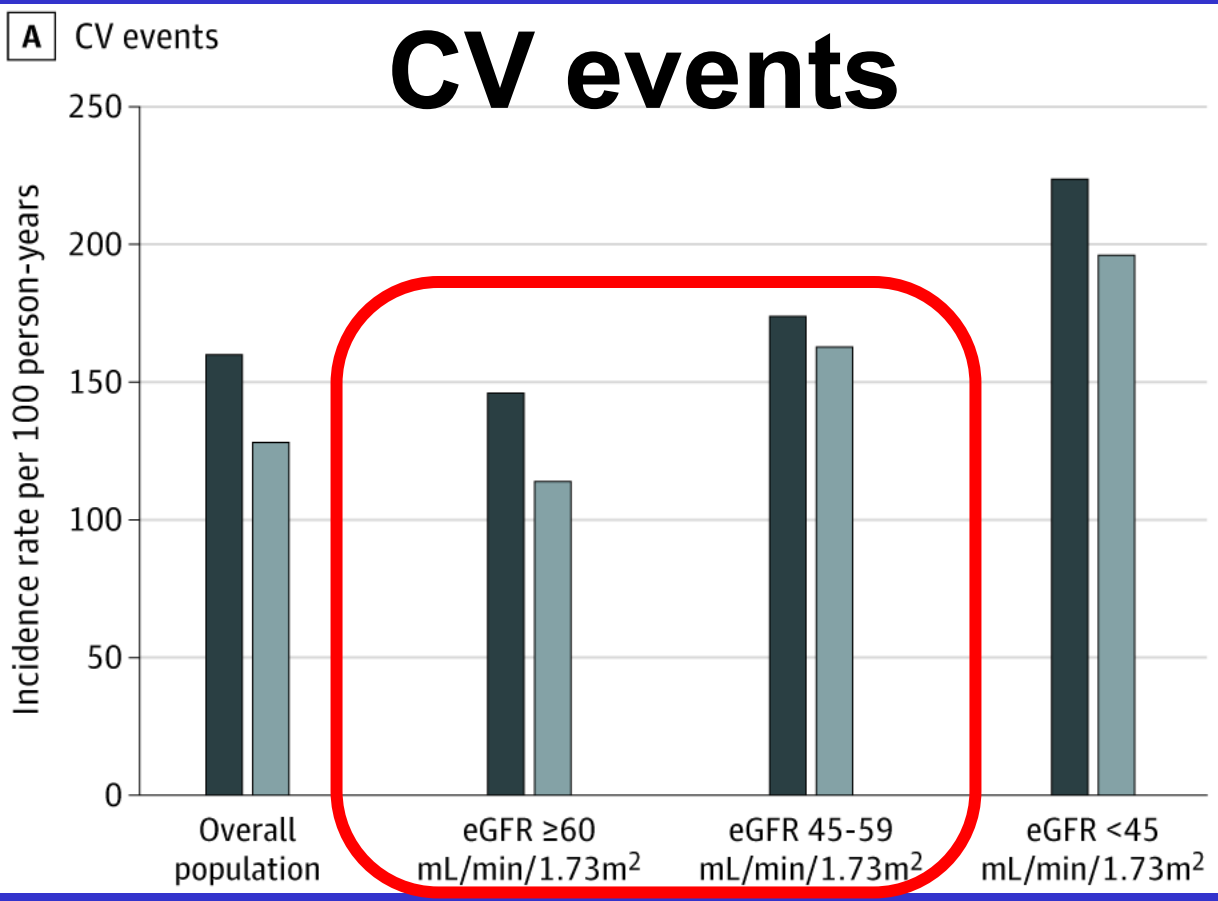
Hazard Ratios

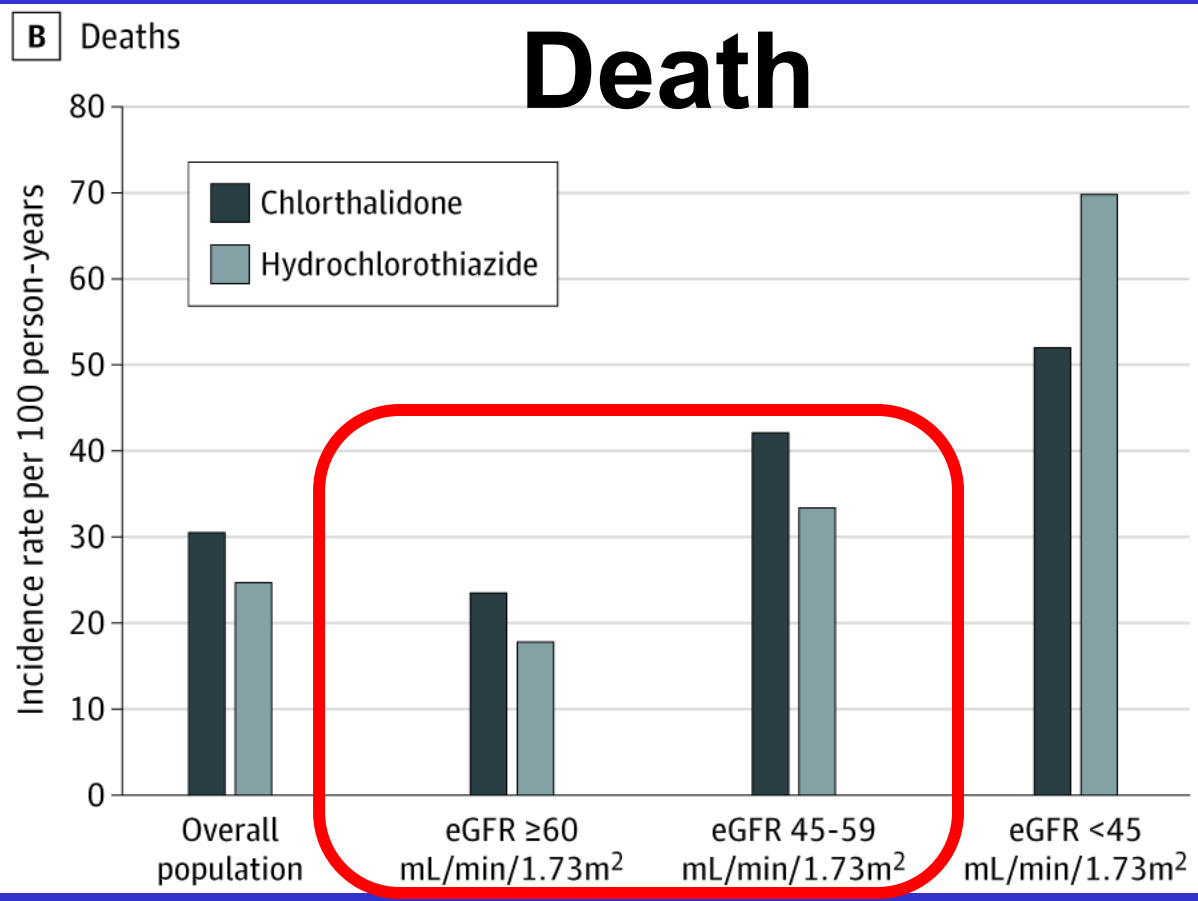


JAMA IM 2020;180:542-551

Chlorthalidone had higher rates of CV events mortality and than HCTZ at all GFRs

(Canadian cohort, N = 12777. Age ≥ 66 yrs. 5-13 yr. FU)

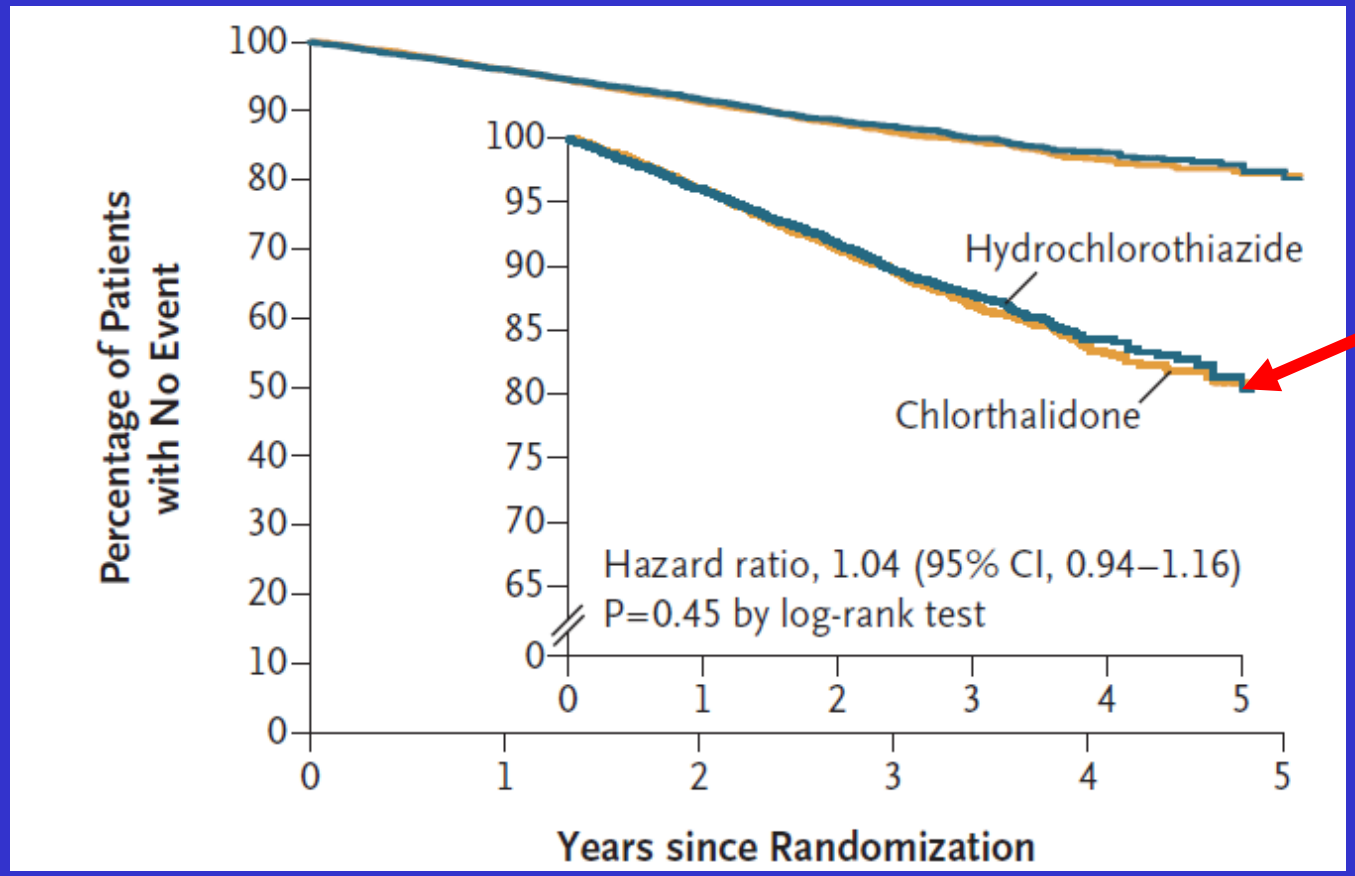




JAMA Open Network 2021;4:e2123365

HCTZ vs. Chlorthalidone

(VA RCT, N = 13523, HCTZ 25-50 mg vs. chlorthalidone 12.5-25 mg/d, 2.5 yr. FU)



No difference in BPs (SBPs 139 mm HG)

No difference in CV outcomes

Higher hypokalemia with chlorthalidone vs. HCTZ, 6.0% vs. 4.4%

Note: HCTZ dose high

NEJM Dec 2022

What about the side effects with thiazides?

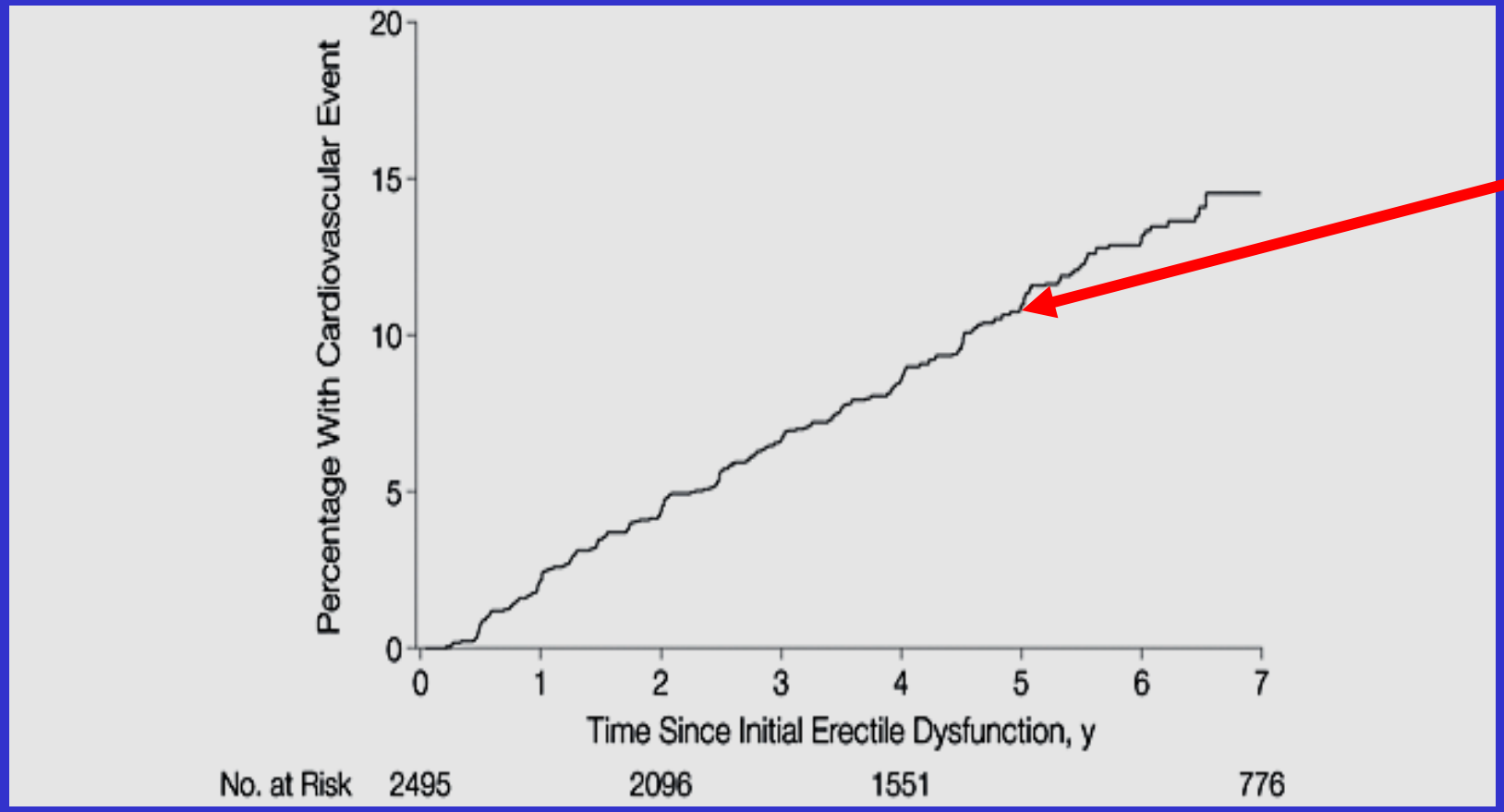
- Erectile dysfunction
- Hypokalemia
- Hyponatremia

TOMHS: Incidence of erectile dysfunction equal to placebo with thiazides

	ACB		AML		CTH		DOXA		ENAL		PLBO	
	N	%	N	%	N	%	N	%	N	%	N	%
48 Months												
Problems obtaining erection	8	10.5	8	13.3	12	10.9	6	8.3	7	10.9	15	11.9
Problems maintaining erection	6	7.9	9	15.0	13	18.3	8	11.1	8	12.5	19	15.1

Erectile dysfunction is a predictor of CV disease

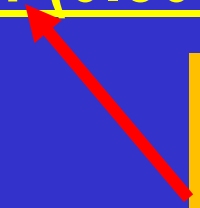
PCPT placebo cohort: Time to CV event among patients who developed ED, finasteride control group



Five-year risk of CV events in men with ED = 11%

SHEP: Benefit of HTN control attenuated by hypokalemia

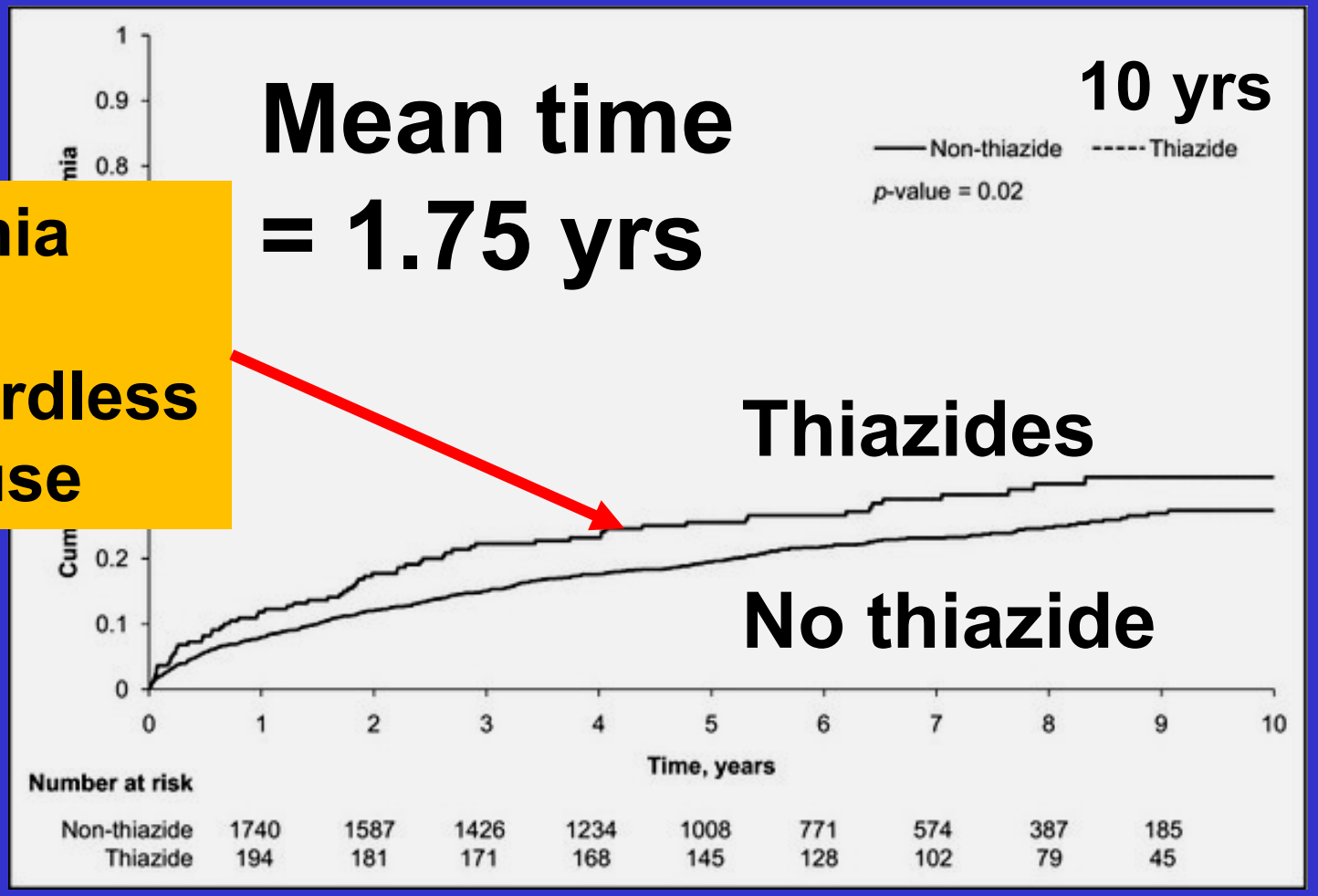
	CV Event	CHD	CVA
Placebo, K > 3.5	1.00	1.00	1.00
Active tx, K < 3.5	1.18 (NS)	1.46 (NS)	1.43 (NS)
Active tx, K > 3.5	0.61 (0.50-0.75)	0.75 (0.50-1.01)	0.51 (0.36-0.71)



-39% lower CV event rate for HTN patients when K kept > 3.5
-No benefit if K < 3.5

Risk of hyponatremia (Na <130) continues over time but no mortality effect

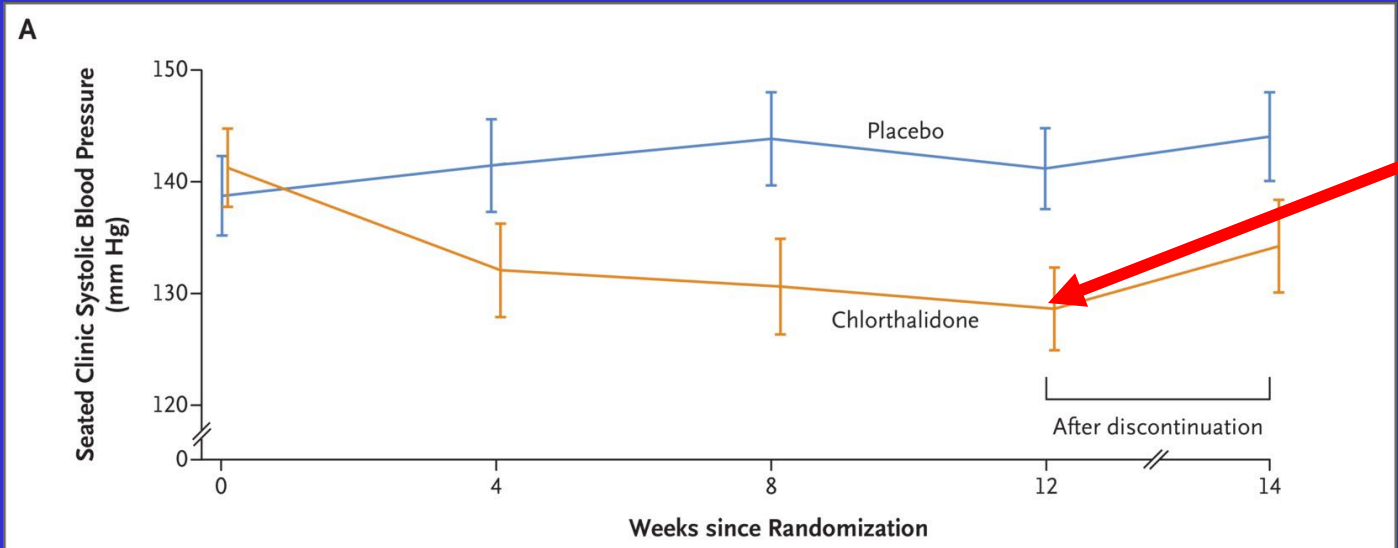
Hyponatremia incidence similar regardless of diuretic use



Am J Med 2011; 124:1064-1072

What about thiazides with CKD 4?

(RCT N = 160, chlortalidone vs. placebo, 12 week follow-up)



Mean Change from Baseline (95% CI) — mm Hg				
Placebo	2.7 (–0.9 to 6.3)	5.1 (1.4 to 8.8)	2.4 (–0.6 to 5.5)	5.3 (1.8 to 8.8)
Chlorthalidone	–9.2 (–12.9 to –5.5)	–10.6 (–14.5 to –6.8)	–12.6 (–15.8 to –9.5)	–7.0 (–10.7 to –3.3)
Difference	–11.9 (–17.1 to –6.7)	–15.7 (–21.0 to –10.5)	–15.1 (–19.4 to –10.7)	–12.3 (–17.5 to –7.2)

10.5 mm Hg greater improvement of SBP, average dose 23.1 mg

But…short study, GFR went down (possibly due to reduced glomerular pressure), micro albumen dropped.

Bottom line: Not unreasonable to use thiazides

NEJM 385;385:2507-2519

Why not start with ACEIs?

ACEIs themselves have a high incidence of cough.

Thiazides combine well with ACEIs, ARBs, BB, CCBs.

But the debate continues…

Are ACEIs and ARBs equally effective?

2011 meta-analysis of 97 published studies comparing ACEIs and ARBs showed no difference
(JGIM 2011; 27: 716-729)

Cough with ACEIs = 9%
Cough with ARBs = 2%

ACEIs remain the drugs of first choice…for now because there is more data

But…ARBs are not all equal: Losartan underperforms

BP reductions (mm Hg) at different levels of dosage maximums

	25%	50%	100%
All ARBs SBP	**10.3**	**11.7**	**13.0**
DBP	**6.7**	**7.7**	**8.3**

ARB response flattens with dosage increases

All other ARBs vs. Losartan

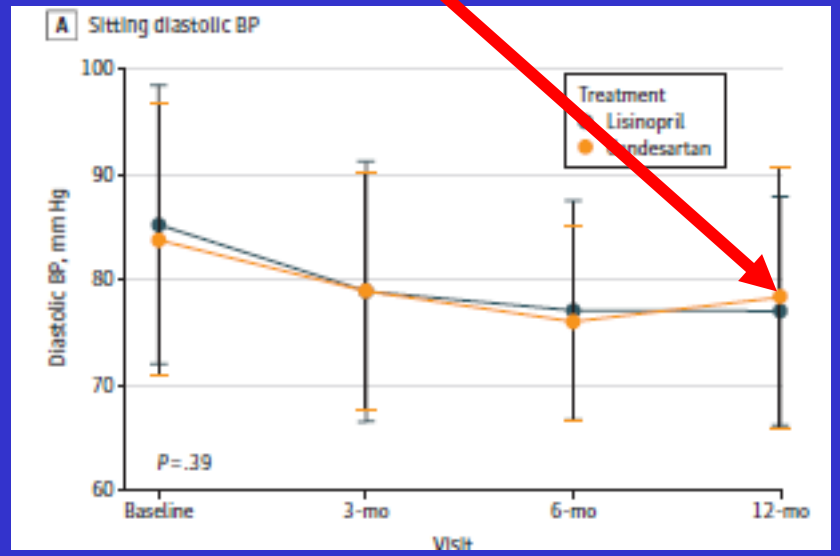
SBP drop	- 2.5	- 3.9
DBP drop	- 1.8	- 2.2

Other ARBs outperform losartan

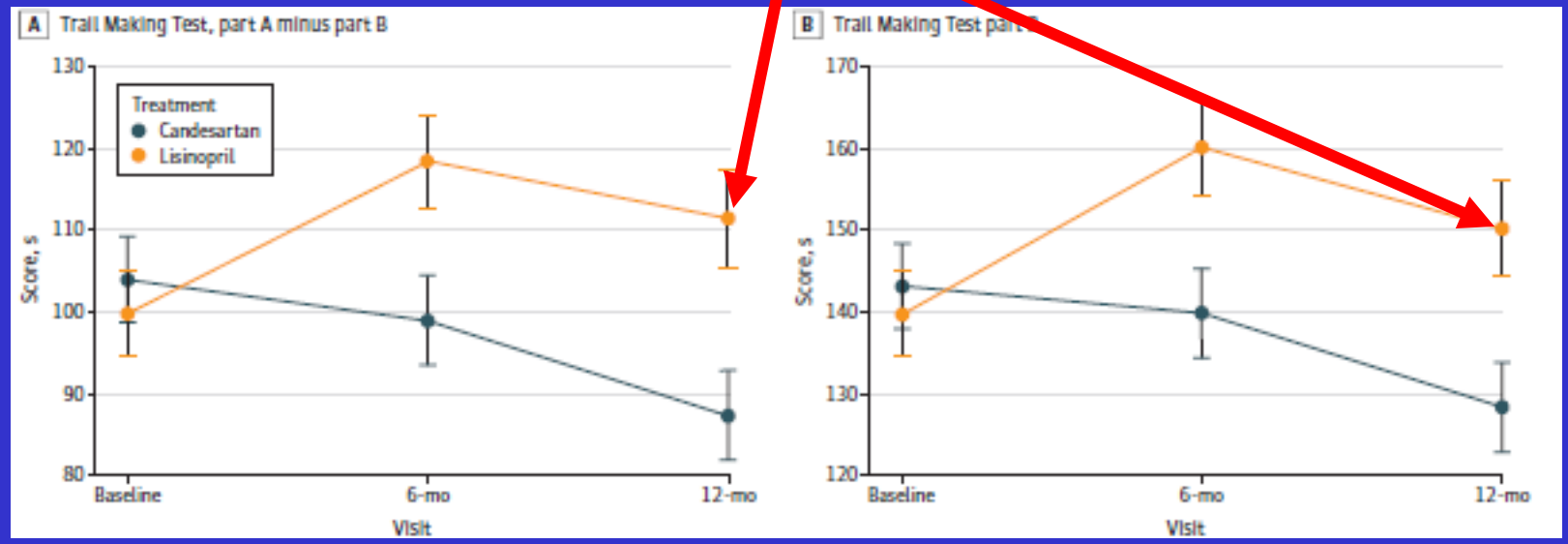
ARB vs. ACEIs: Is there a cognitive benefit with ARBs ?

(RCT, N = 176 with MCI, Atlanta, GA, history of BP ≥140/90, age 66, 57.4% women, 12-month follow-up)

No difference in Sys BPs

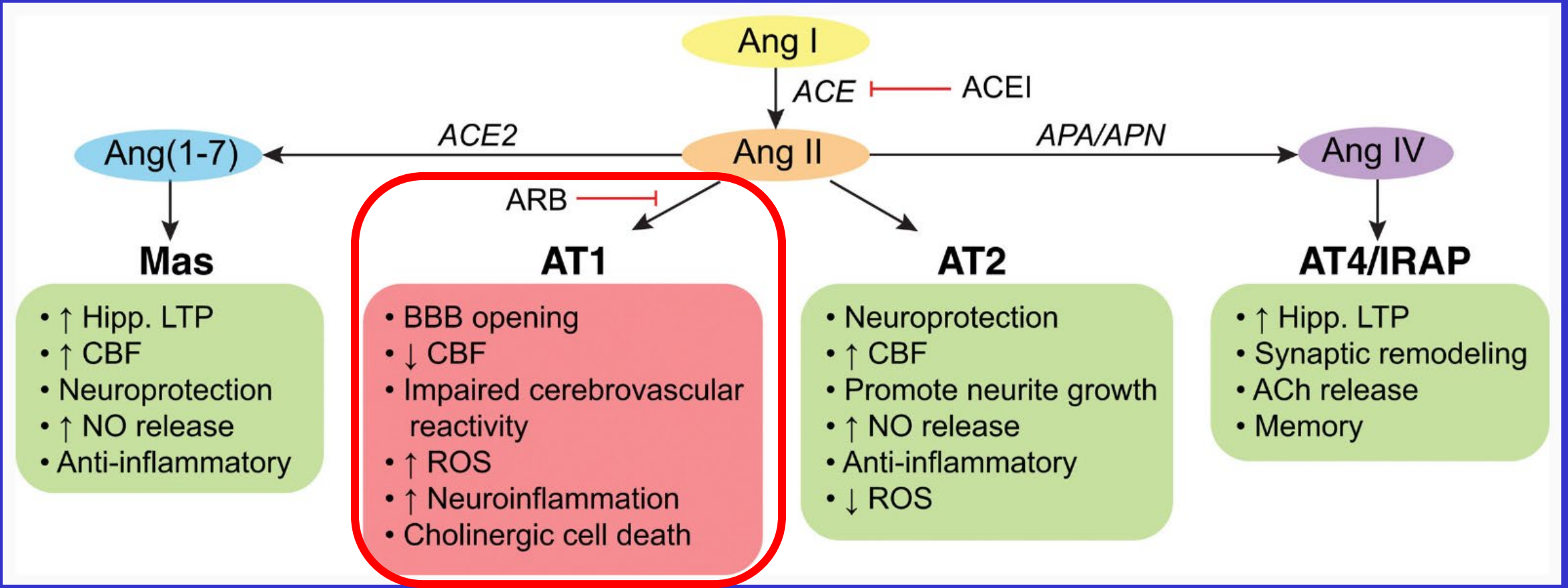


Less decline in executive function and episodic memory



JAMA Open Network August 6, 2020

ARB* stimulation of neuroprotective angiotensin 2 and 4 receptors

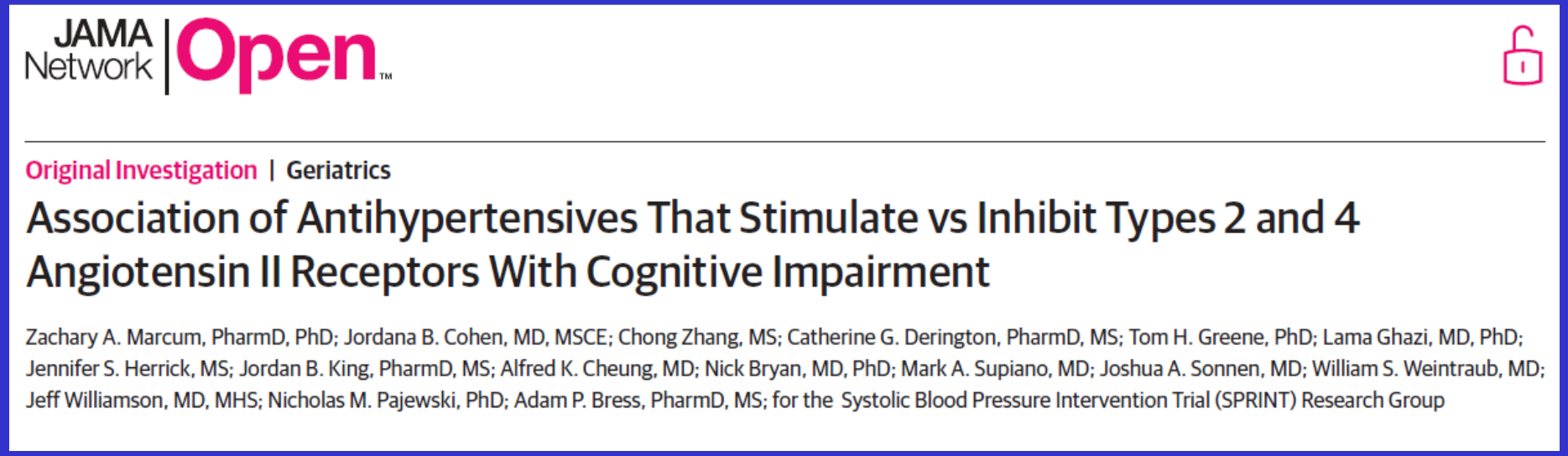


*candesartan and telmisartan cross BB barrier

Hypertension 2021; 78: 644-646

There's more: SPRINT secondary analysis

(SPRINT N = 2644/8685 patients on Angiotensin II stimulation vs. blocking)



JAMA Network Open

Original Investigation | Geriatrics

Association of Antihypertensives That Stimulate vs Inhibit Types 2 and 4 Angiotensin II Receptors With Cognitive Impairment

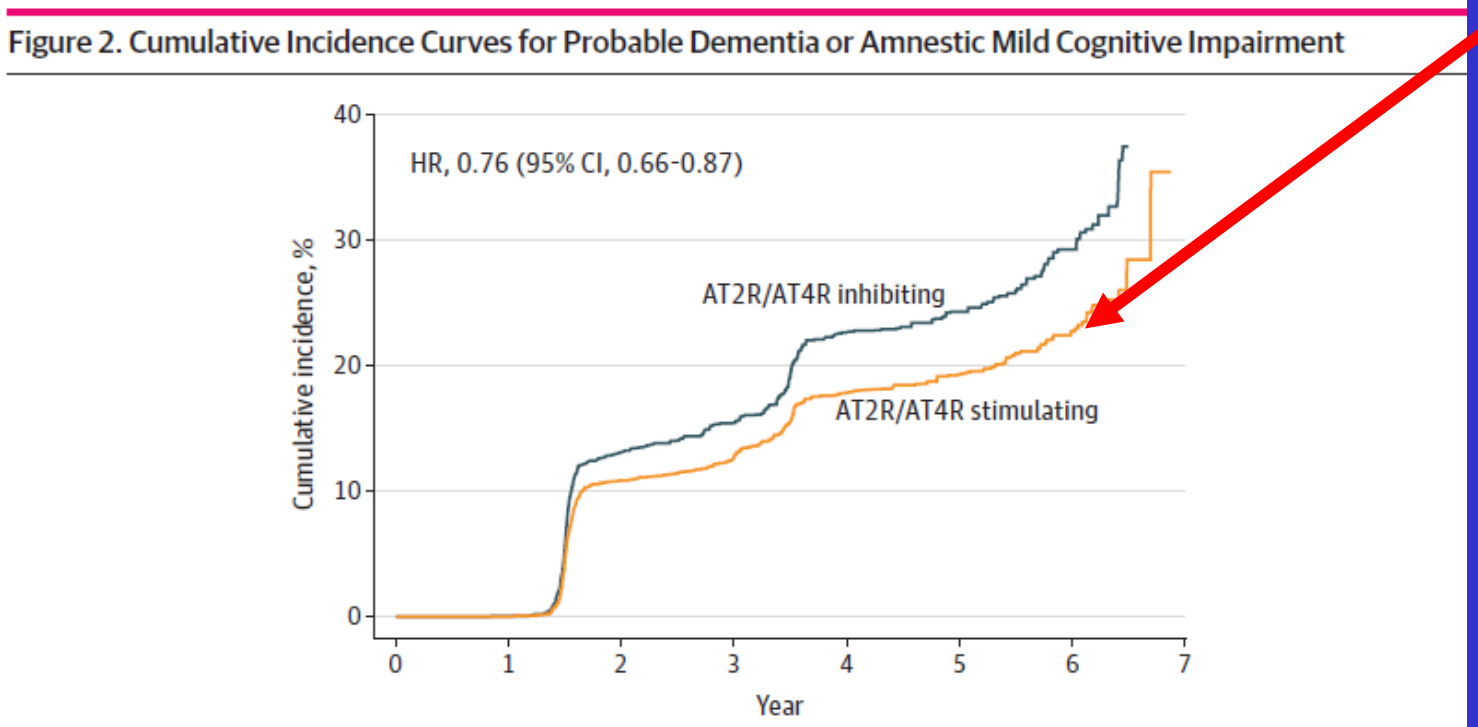
Zachary A. Marcum, PharmD, PhD; Jordana B. Cohen, MD, MSCE; Chong Zhang, MS; Catherine G. Derington, PharmD, MS; Tom H. Greene, PhD; Lama Ghazi, MD, PhD; Jennifer S. Herrick, MS; Jordan B. King, PharmD, MS; Alfred K. Cheung, MD; Nick Bryan, MD, PhD; Mark A. Supiano, MD; Joshua A. Sonnen, MD; William S. Weintraub, MD; Jeff Williamson, MD, MHS; Nicholas M. Pajewski, PhD; Adam P. Bress, PharmD, MS; for the Systolic Blood Pressure Intervention Trial (SPRINT) Research Group

Hypertension treated with use of only angiotensin II receptor type 2 and 4–stimulating antihypertensives (angiotensin II receptor type 1 blockers, dihydropyridine calcium channel blockers, and thiazides).

Hypertension treated with only angiotensin II receptor–inhibiting antihypertensives (ACE inhibitors, β-blockers, and nondihydropyridine calcium channel blockers).

JAMA Network Open. 2022;5(1):e2145319

SPRINT: Angiotensin II 2 and 4 stimulating therapies reduced Amnestic MCI and Dementia

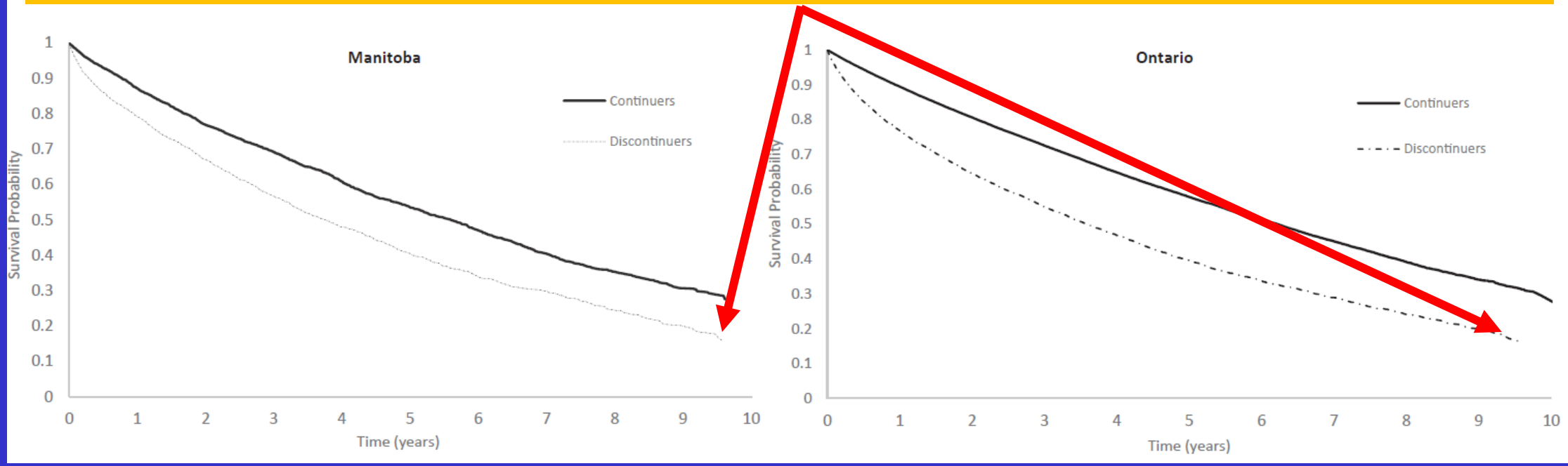


24% lower rates of MCI and Dementia: ARBs, thiazides, nifedipine, amlodipine vs. ACEIs, BBs, diltiazem, verapamil over 4.7 yrs.

What about hyperkalemia with ACEs and ARBs? Carry on and adjust!

(Manitoba, N=7200, and Ontario, N=71290, cohorts; GFRs = 41; Age ≥ 66 yrs. K ≥ 5.5 mmol/L. Maintained therapy vs. stopped before 90 days 10 yrs. follow-up)

RAAS discontinuation associated with higher mortality, 32% higher in Manitoba, 47% Ontario



Am J Kidney Dis 2022;80:164

Increased risk for fetal abnormalities from ACEI exposure in the first trimester (95% C.I.)

Overall increased risk	2.71 (1.72-4.27)
CV malformation risk	3.72 (1.89-7.30)
CNS malformation risk	4.39 (1.37-14.02)

Be mindful of the diabetic with potential pregnancy

The currently acceptable agents for use in pregnancy or considering pregnancy

BB blockers (labetalol)*, nifedipine, methyldopa

Possibly, if used prior to pregnancy: HCTZ, chlorthalidone, chlorothiazide

<u>Drugs that must not be used</u>: ACEIs, ARBs, and direct renin inhibitors

*Ann Intern Med 2019;169:665-673

In summary, the first choice is either a thiazide, an ACEI/ARB or a CCB

Thiazides (HCTZ)

- Less variance of treated BP readings
- Easily combined

ACEIs vs. ARBs

- ACEIs for patients with diabetes
- ARBs for patients with asthma*

CCBs

- Patients with asthma*
- Nifedipine in pregnancy

Labetalol

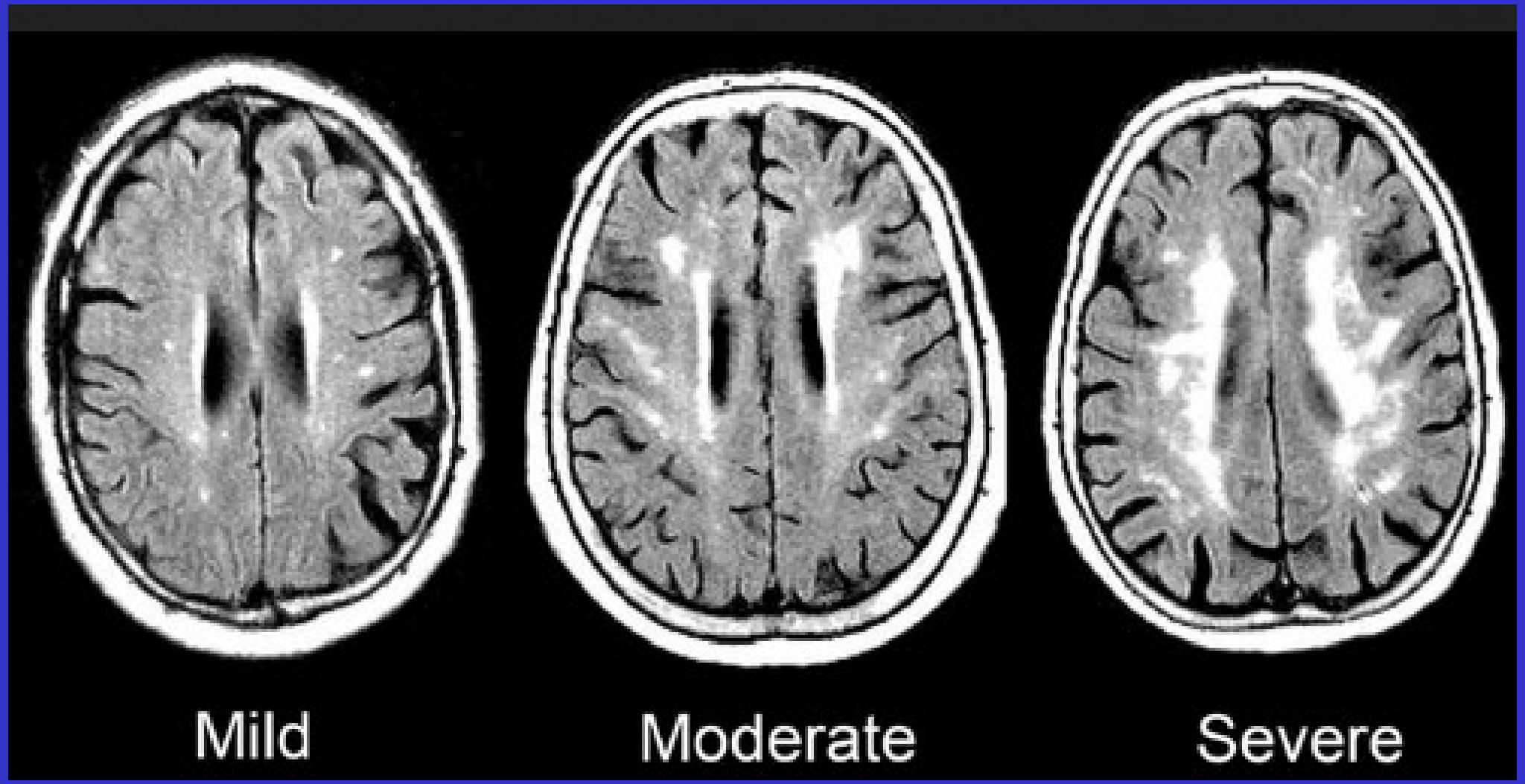
- Pregnancy

* NEJM 2019; 381:1046-1057

- Avoid alpha blockers as single agents
  - -ALLHAT stopped alpha blocker treatment due to higher rates of HF
- Avoid ACEIs and ARBs if pregnancy possible
- *Beta blocker indications*
  - *-Recent ACS (acute coronary syndrome)*
  - *-Risk for an alcohol withdrawal syndrome*
  - *-Associated arrhythmias*

Why wait to get BPs lower for older patients?

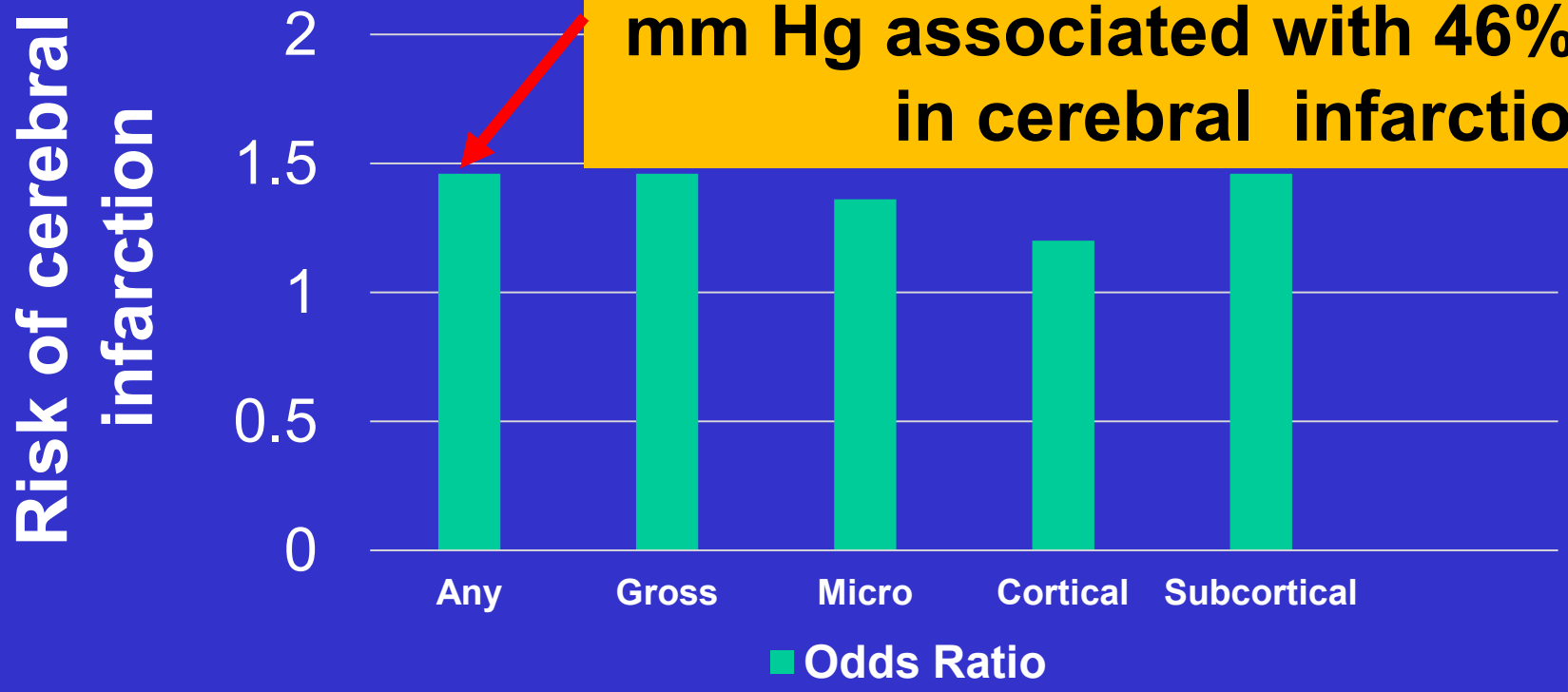
Microvascular disease is our enemy:



The brains of hypertensive octogenarians show more microinfarction

N = 2188 community dwelling, followed for an average of 8 years prior to death. Average age at death, 88.6 yrs. 65% women

Each 13 mg Hg SBP elevation > 134 mm Hg associated with 46% increase in cerebral infarction



Neurology 2018;91:e517

Research

Original Investigation

Intensive vs Standard Blood Pressure Control and Cardiovascular Disease Outcomes in Adults Aged ≥75 Years
A Randomized Clinical Trial

Jeff D. Williamson, MD, MHS; Mark A. Supiano, MD; William B. Applegate, MD, MPH; Dan R. Berlowitz, MD; Ruth C. Campbell, MD, MSPH; Glenn M. Chertow, MD; Larry J. Fine, MD; William E. Haley, MD; Amret T. Hawfield, MD; Joachim H. Ix, MD, MAS; Dalane W. Kitzman, MD; John B. Kostis, MD; Marie A. Krousel-Wood, MD; Lenore J. Launer, PhD; Suzanne Oparil, MD; Carlos J. Rodriguez, MD, MPH; Christianne L. Roumie, MD, MPH; Ronald I. Shorr, MD, MS; Kaycee M. Sink, MD, MAS; Virginia G. Wadley, PhD; Paul K. Whelton, MD; Jeffrey Whittle, MD; Nancy F. Woolard; Jackson T. Wright Jr, MD, PhD; Nicholas M. Pajewski, PhD; for the SPRINT Research Group

JAMA 2016; 315:2673-2682

EDITORIAL

SPRINT Results in Older Patients
How Low to Go?

Aram V. Chobanian, MD

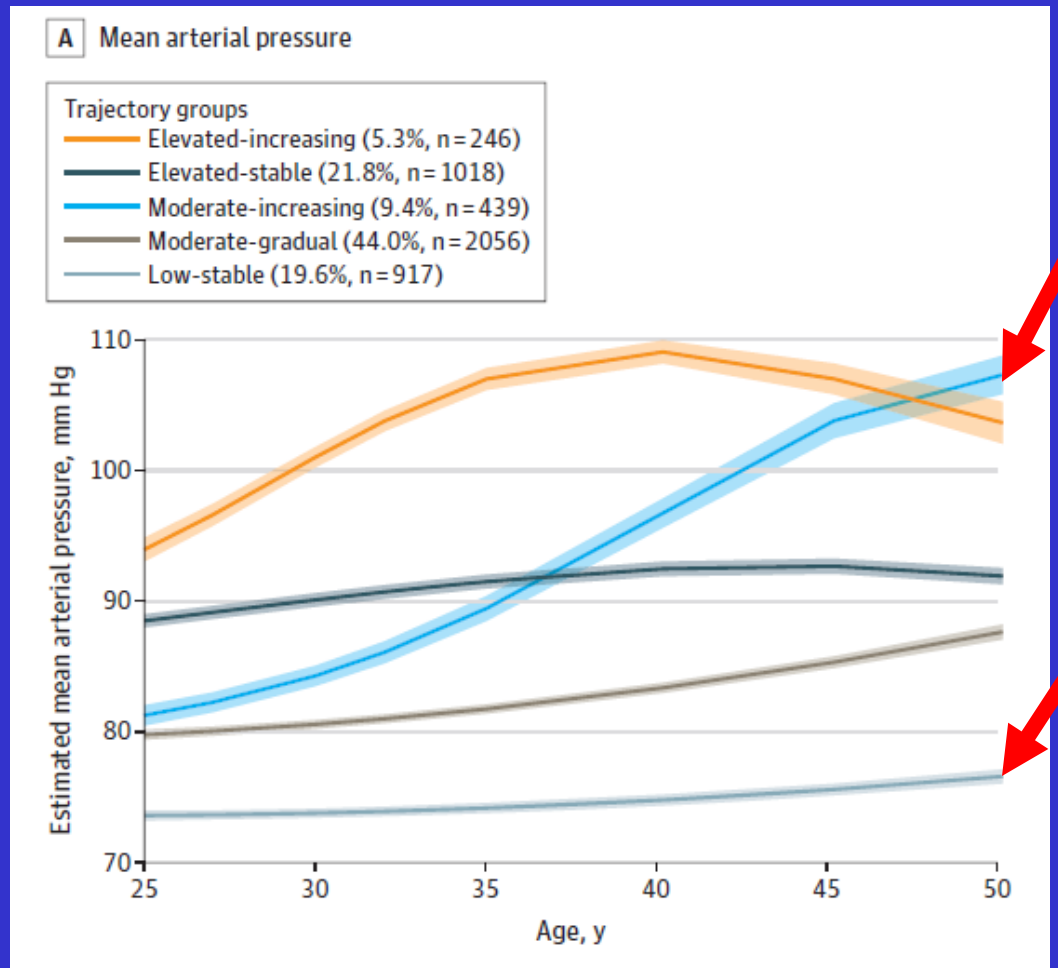
SPRINT data: Patients ≥ 75 yrs. Fit, less fit and frail all did better!

	Intensive N= 1317	Standard N =1319
Sys BP, mm Hg	123.4	134.8
Dias BP, mm Hg	62.0	67.2
MI	2.8	4.0
Heart failure,%	2.6	4.2
All cause mortality, %	5.5	8.1
Fit	3.1	3.6 (NS)
Less Fit	3.7	7.0
Frail	9.1	13.1
Secondary CKD outcome**	5.1	1.8

**30% reduction in GFR to GFR under 60, dialysis or transplant

Early life BP elevations associated with later life changes in white and gray matter

(CARDIA N = 853 MRIs, age 35.7; followed from 1985 to 2016)



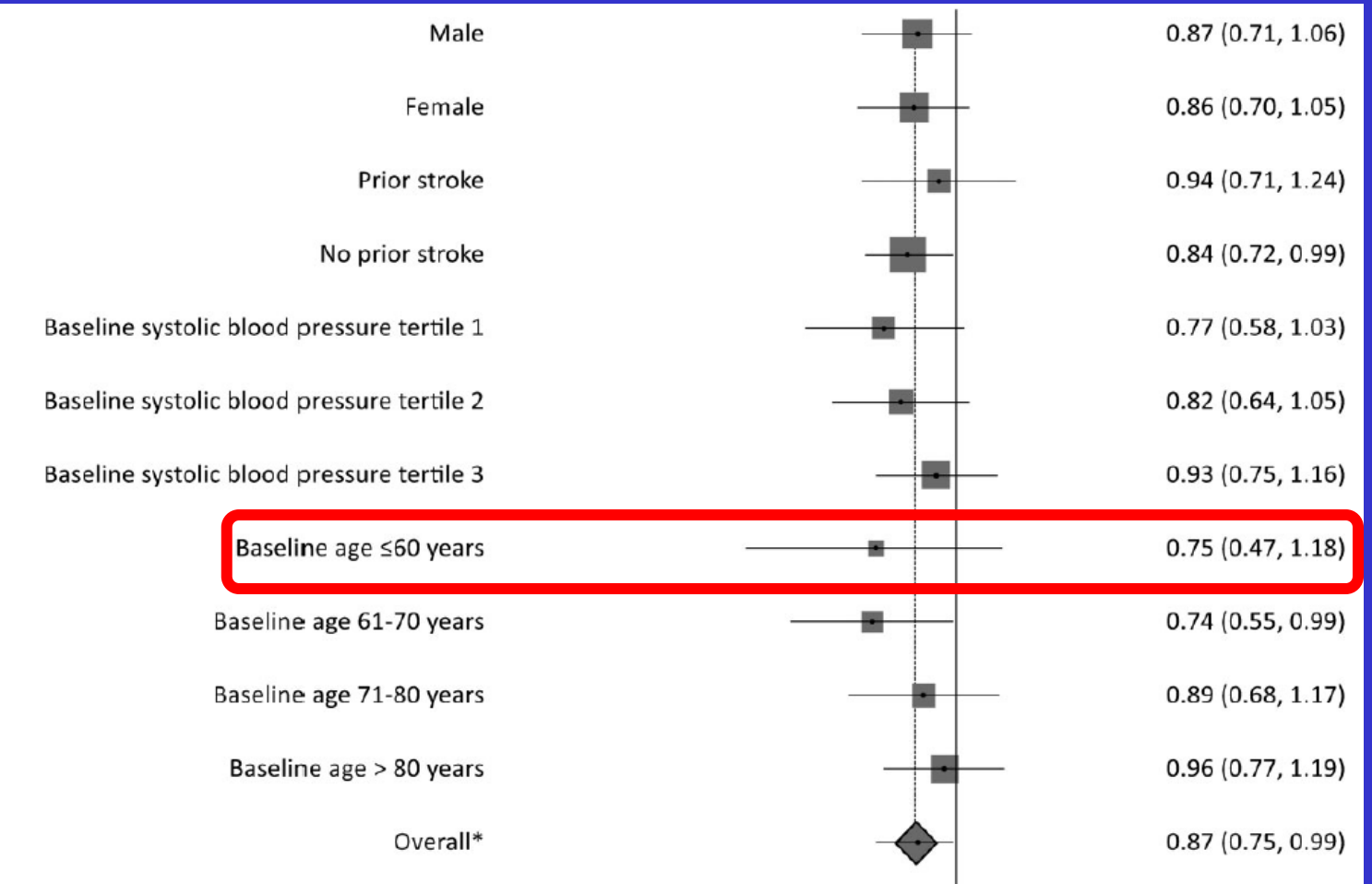
-"Moderate increasing" and "elevated increasing" associated with abnormal white matter volume.

vs. low stable

JAMA Network Open. 2022;5(3):e221175.

BP control reduces risk dementia

(multilevel regression analysis, 5 RCTs, N=28008 individual patients, 20 countries, 4.3 yrs. follow up)



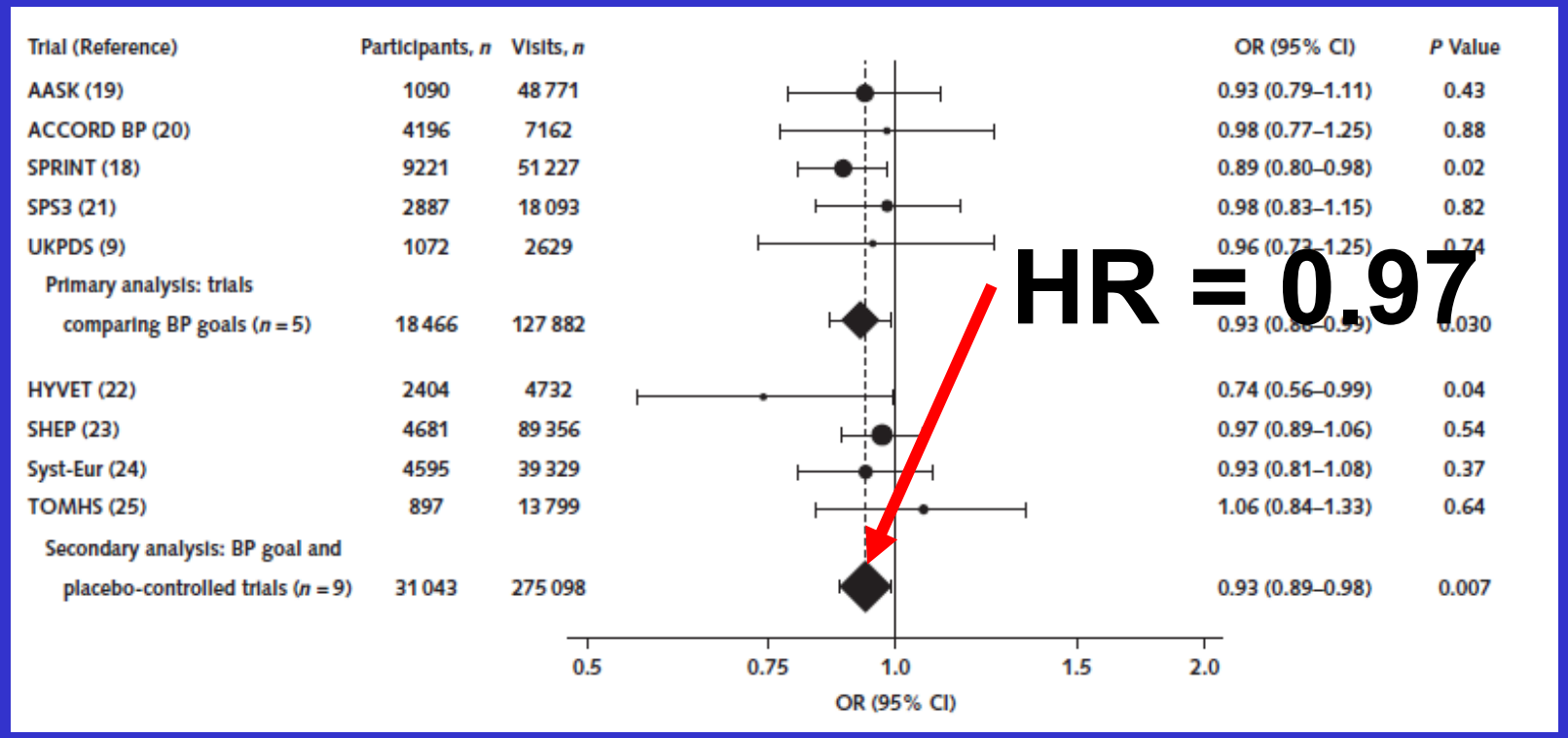
13% lower risk of dementia for BP drop of 10/4 mmHg

25% lower for those 60 and lower

European Heart Journal (2022) 00, 1–11
https://doi.org/10.1093/eurheartj/ehac584

The risks of orthostatic hypotension (>20 mm Hg SBP drop sitting to standing) decreased with more intense treatment

(Meta-analysis, N=18466)



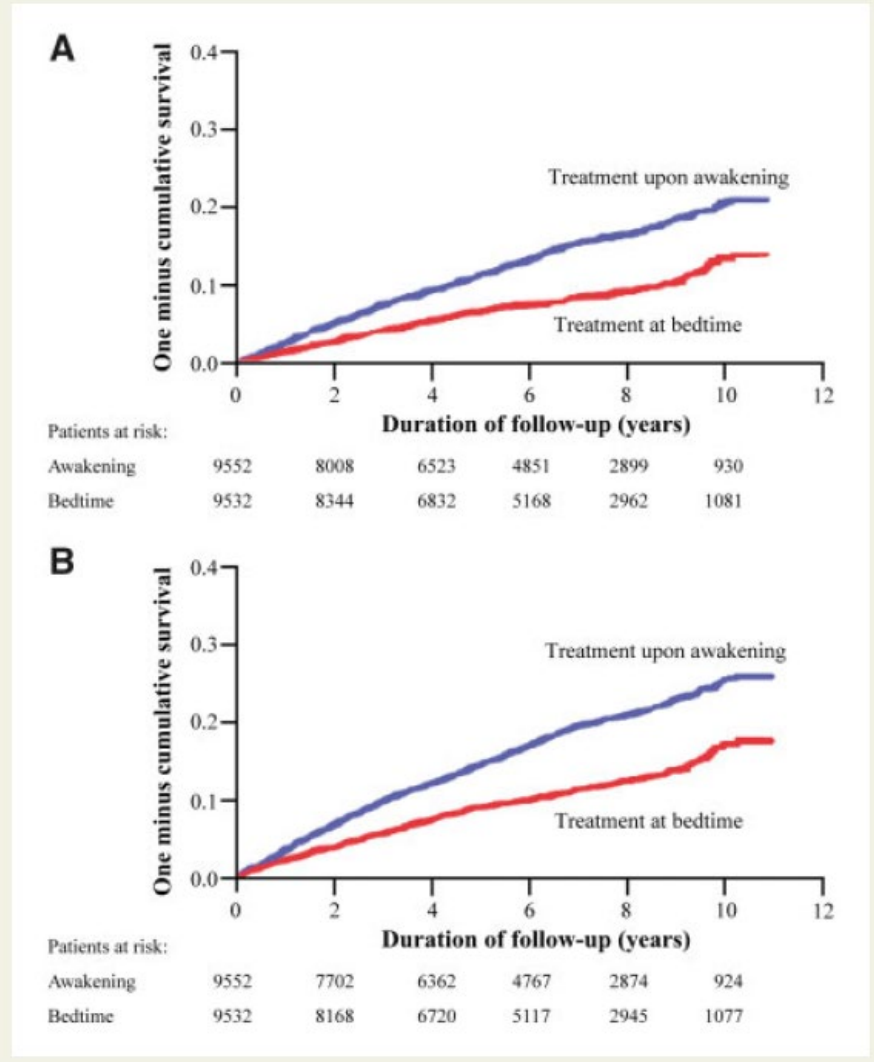
Risk of systolic orthostatic drop was lower with more intense treatment

Ann Intern Med 2021;174:58-68

Should BP medications be taken before bed?

Hygia study

(RCT, 40 Spanish PC Centers; N = 19,084; age 60.5 yrs. +/- 13.7 yrs.; meds AM vs. PM; 6.3 yr. follow-up)



Bedtime HTN medications had risk reductions of

- 43% lower CVD events
- 42% lower HF
- 42% fewer events
- 49% fewer strokes
- 45% lower death rate

Was this too good to be true?

Eur Heart J 2020;41:4565

Hygia study

BLOOD PRESSURE
2020, VOL. 29, NO. 3, 135-136
https://doi.org/10.1080/08037051.2020.1747696

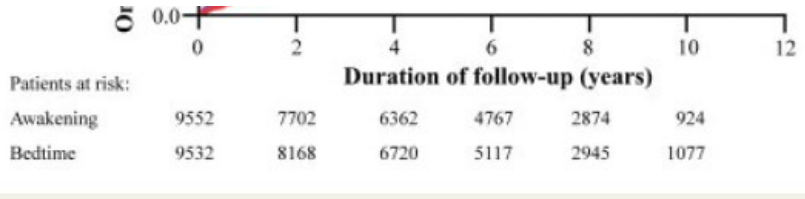
Taylor & Francis
Taylor & Francis Group

A

Blood pressure medication should not be routinely dosed at bedtime. We must disregard the data from the HYGIA project

Reinhold Kreutz[a], Sverre E. Kjeldsen[b], Michel Burnier[c], Krzysztof Narkiewicz[d], Suzanne Oparil[e], and Giuseppe Mancia[f]

B [a] Department of Clinical Pharmacology and Toxicology, Charité University Medicine, Berlin, Germany; [b] Department of Cardiology, University of Oslo, Ullevaal Hospital, Oslo Norway; [c] Service of Nephrology and Hypertension, Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland; [d] Department of Hypertension and Diabetology, Medical University of Gdansk, Poland; [e] Vascular Biology and Hypertension Program, Department of Medicine, University of Alabama at Birmingham, AL, USA; [f] University of Milano-Bicocca, Milan, Italy



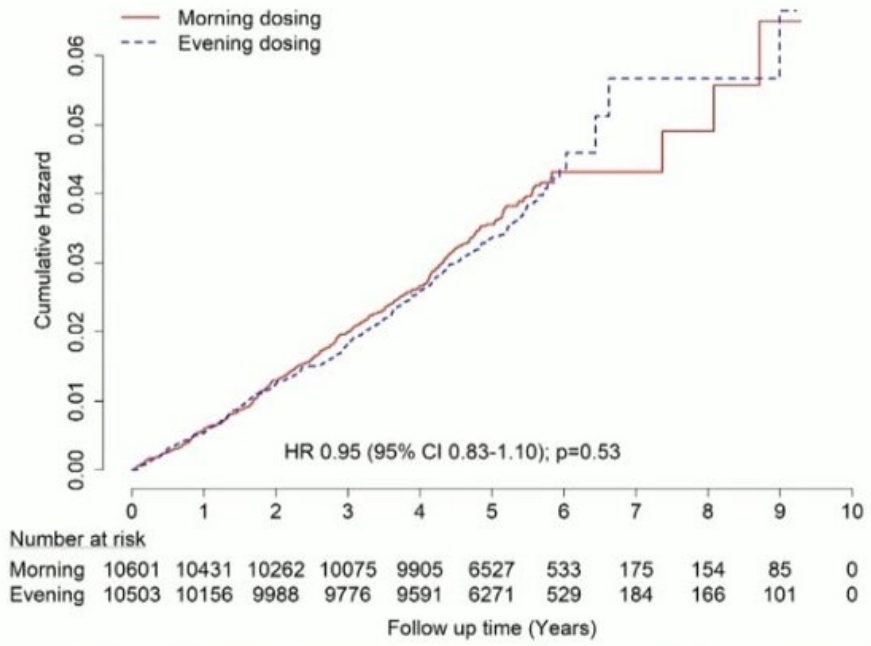
Eur Heart J 2020;41:4565

Treatment in Morning vs. Evening (TIME):
(RCT N=21104, 5.2 yrs. follow-up): No benefit to PM dosing

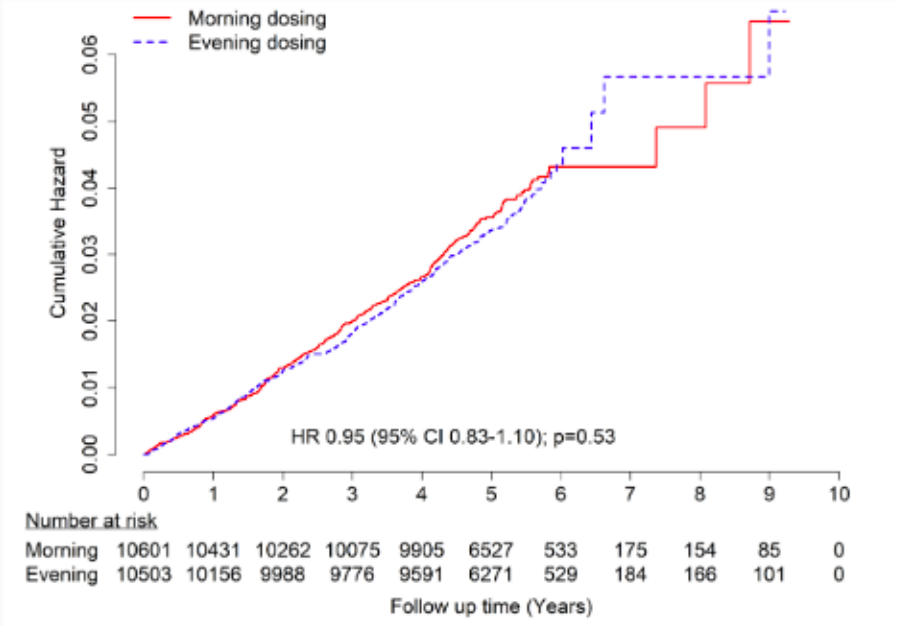
No benefit, no harm from evening dosing

• TIME - The Treatment in Morning versus Evening study.

Primary Endpoint



Results –MI, stroke or vascular death



ESC CONGRESS 2022
Barcelona & Online

What if the BP is not responding?

Return to basics

- Sodium
- Alcohol
- NSAIDS

Improve diuretic therapy

- Add thiazide
- Change HCTZ to chlorthalidone 12.5-25 mg QD
- Change to furosemide if CKD Stage 3b-4

Add aldosterone antagonist

- Spironolactone 25-50 mg QD
- Eplerenone 25 mg QD- 50 mg BID

Add a central alpha agonist

- Clonidine (Catapres)
  - Oral 0.1-0.3 mg; QD-BID
  - Patch 0.1-0.3 mg/wk

Add a peripheral alpha blocker

- Doxazosin (Cardura) 1-4 mg; QD-BID
- Terazosin (Hytrin) 1-5 mg; QD-BID

Switch to a mixed alpha/beta blocker

- Labetalol 100-600 mg BID

Direct renin inhibitor (DRIs)

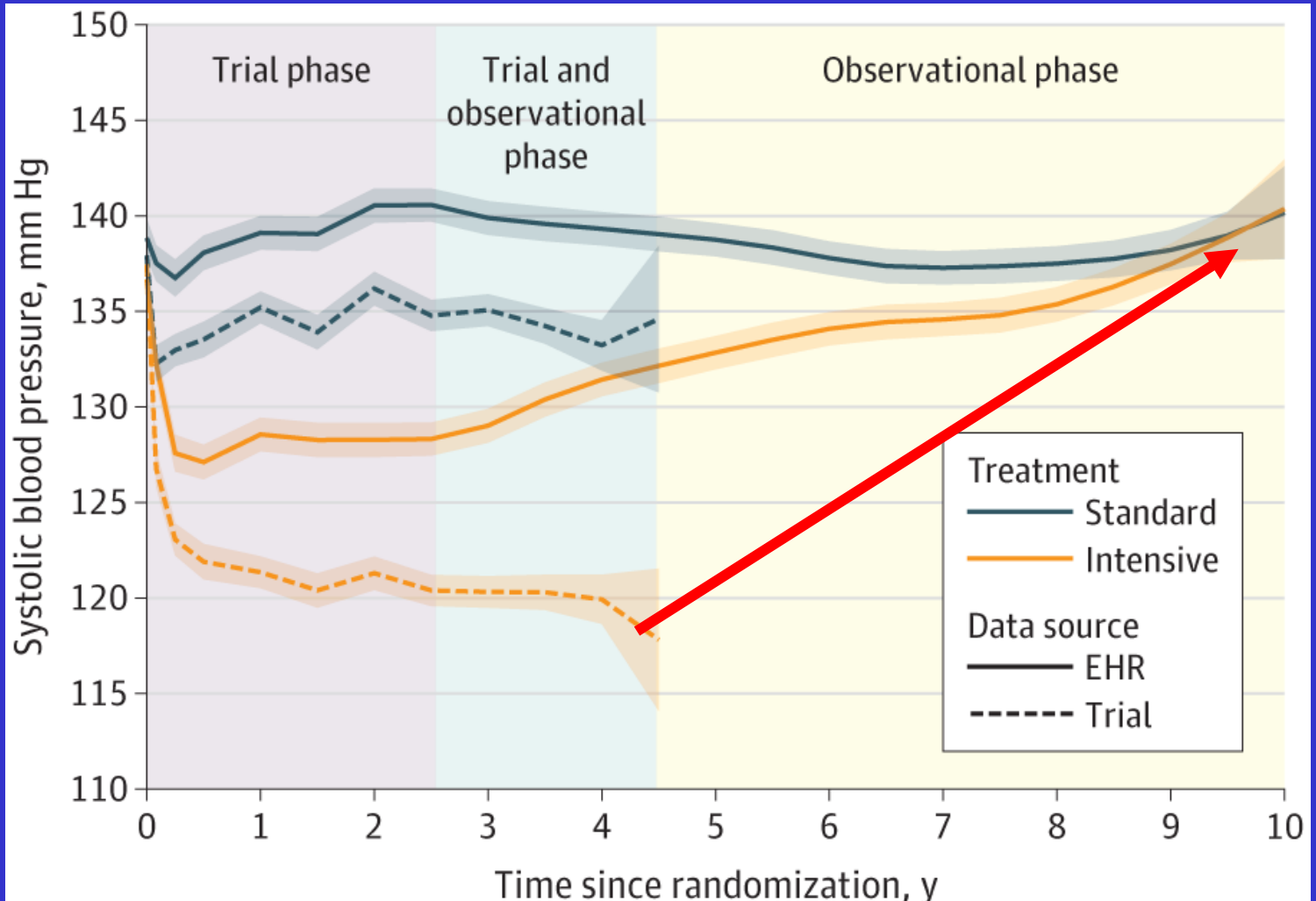
- Aliskirin (Tekturna) 150-300 mg QD

Select uncommon causes of hypertension

Cause	Prevalence	Screening test	Confirmatory test
Pheochromocytoma	0.1%–0.6%	24-hour fractionated metanephrine or plasma metanephrine	Abdominal CT/MR
Cushing's syndrome	<0.1%	Overnight 1 mg dexamethasone suppression	24-hour urine free cortisol
Renal artery stenosis	5–34 %	Ultrasound/MRA/CTA	Renal arteriogram
Primary aldosteronism	8–20%	Plasma aldosterone/renin ratio	Adrenal CT Sodium loading test

JACC Online, October 2017

What happened after SPRINT? (N=9361, 8.8 yrs. Follow up)



At 3.3 years:

- **44% reduction of CV mortality**
- **17% reduction of all cause mortality**

At 8.8 years:

- **Intensive control drifted from 133 to 140mmHg**
- **No improved outcomes!**

JAMA Cardiol.
Published doi:10.1001/jamacardio.2022.3345

Current topics in hypertension: 2023

1. **Who should be screened?**
   Over 18
2. **How do I know if a patient has HTN?**
   Office values may not be sufficiently sensitive, consider home or ambulatory monitoring. Ultimately, your call.
3. **What is the role of 24-hour BP devices?**
   These may become gold standard for clinical categorization but use in day-to-day practice may or may not be become standard of care.

4. **What should our targets be for BP control?**

   SBPs of under 130 mmHg. DBP < 85 mm Hg,

5. **What about non-pharmacologic options?**

   Exercise (150 min per week), Na < 1500 mg, DASH (no condiments, dressings, etc.). Be careful about alcohol.

6. **What are the preferred medications?**

   Start with a thiazide and then add an ACE/ARB and/or a CCB.

   However, emerging evidence suggests that ARBs may be preferable for cognitive preservation

8. **Should BP medications be given before bed?**
   Consider for all patients for convenience.
9. **What are our "talking points?"**
   Reduced heart attack, heart failure, stroke: 44% reduction in major cardiovascular going from systolic 150 to systolic 130
   Reduced microvascular burden: Cognitive and renal

Take home points:

1. SBP >120 is a call to action
2. Thiazides remain the cornerstone HTN therapy
3. Consider more home BP monitoring
4. Consider 24-hour BP monitoring
5. Consider spironolactone/eplerenone

Next steps:

1. Consider increasing therapies if SBP $\geq$ 130-135, DBP >95
2. Consider active therapy in younger patients (< 40 years) with SBP $\geq$ 130

Thank you!

Questions?