Blood Pressure Targets in Older Adults

Geriatrics Fellow Talk
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The little I thought I knew about treating geriatric patients.

- Geriatricians focus on achieving the patient's highest priorities in the context of multiple chronic conditions, and on preserving function.
  - Extended length of life may not always be highest priority.
- “Start low and go slow.”
- “Do no harm.”
- Polypharmacy is real, and can lead to adverse drug events, pill burden, and diminished quality of life. In general, patients don’t like taking them.
- Almost all elderly patients have hypertension, defined by > 140/90mmHg.
- Blood pressure guidelines have varied dramatically over the past decade. Its confusing. Easier and perhaps better (patient preference, less side effects) to treat less aggressively.

Confusing Guidelines for BP Management

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- 2003, JNC-7, SBP < 140 mmHg.
- 2014, JNC-8, SBP < 150 mmHg if aged > 60 years.
- 2015, Release of Primary Results of the SPRINT Trial
- 2017, AHA-ACC Guidelines, SBP < 130 mmHg (if 10 year CVD risk > 10%, or **CKD**, DM, or age > 65).
- 2021, KDIGO Guidelines, SBP < 120 mmHg in CKD patients.

Outline

- Two cases
- Why do we care about BP?
- Epidemiology of blood pressure by age and over calendar years in the US.
- Observational vs. trial data on BP targets.
- Summary of the SPRINT trial overall, and in the oldest and frailest.
- Recognizing systematic bias in the “do no harm” approach to clinical care.
- A few words about standardized BP measurements.
- Outcomes of our two cases.

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Case 1

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- 75 yo female, generally healthy, hx of benign ovarian cyst removed 2 years ago. Physically active (walks daily, hikes up to 10 miles on weekends). Meds include only vitamin D supplements. Last 3 PCP visits. Generally does not want pills, but willing to take if necessary. Biggest fears, dying in pain or having a stroke:

Date	BP	Plan
Sept. 2013	157/70	Diet and Exercise
October 2014	148/65	New guidelines say you're at target for your age.
May 2015	180/70	Diet, exercise, come back in 6 months instead of a year
November 2015	178/68	Cut salt, come back in 3 months
January 2016	188/70	Start Amlo 2.5mg

Case 2

Kidney Research Innovation Hub of San Diego

- 78 year old man with Crohn's disease, hypertension, and CKD (Cr 1.6, no protein). Participant in the SPRINT trial in 2013. BP guidelines at that time recommended SBP < 150 mm Hg. He was randomized to the intensive arm (goal SBP < 120 mm Hg).
- BP titrated up on losartan 100mg, chlorthalidone 25m, and amlodipine 5mg daily. Last clinic BP 124/60.
- 5 days diarrhea/fever. Presents to ED with SBP 90/40, K 6.0, CO2 12, BUN 111, Cr 5.7.
- Smart UCSD resident, "How could you ethically treat him to an SBP < 120 when guidelines recommend SBP < 150? Look what happened here."

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Hypertension is the quintessential disease for prevention

- Extremely common.
- Strongly linked with CVD, particularly stroke.
- Stroke is devastating.
- BP is very treatable.
- Drugs are readily available, cheap, and very effective.
- Its undeniable that treatment prevents CVD, stroke, and death.
- Hypertension is often forgotten, but it is central to preventive medicine.
- The question is not whether to treat, but how aggressively, and among whom?

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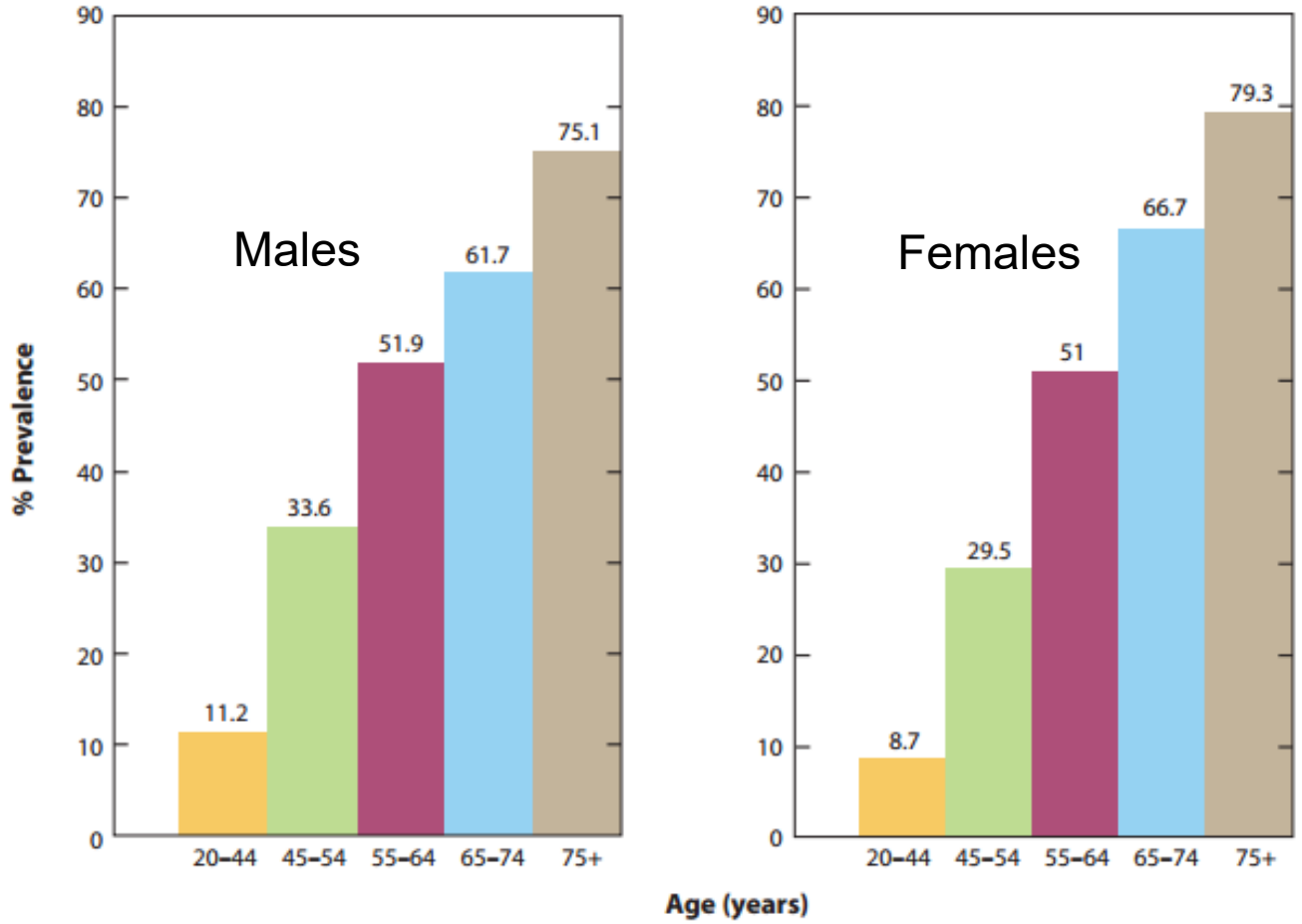
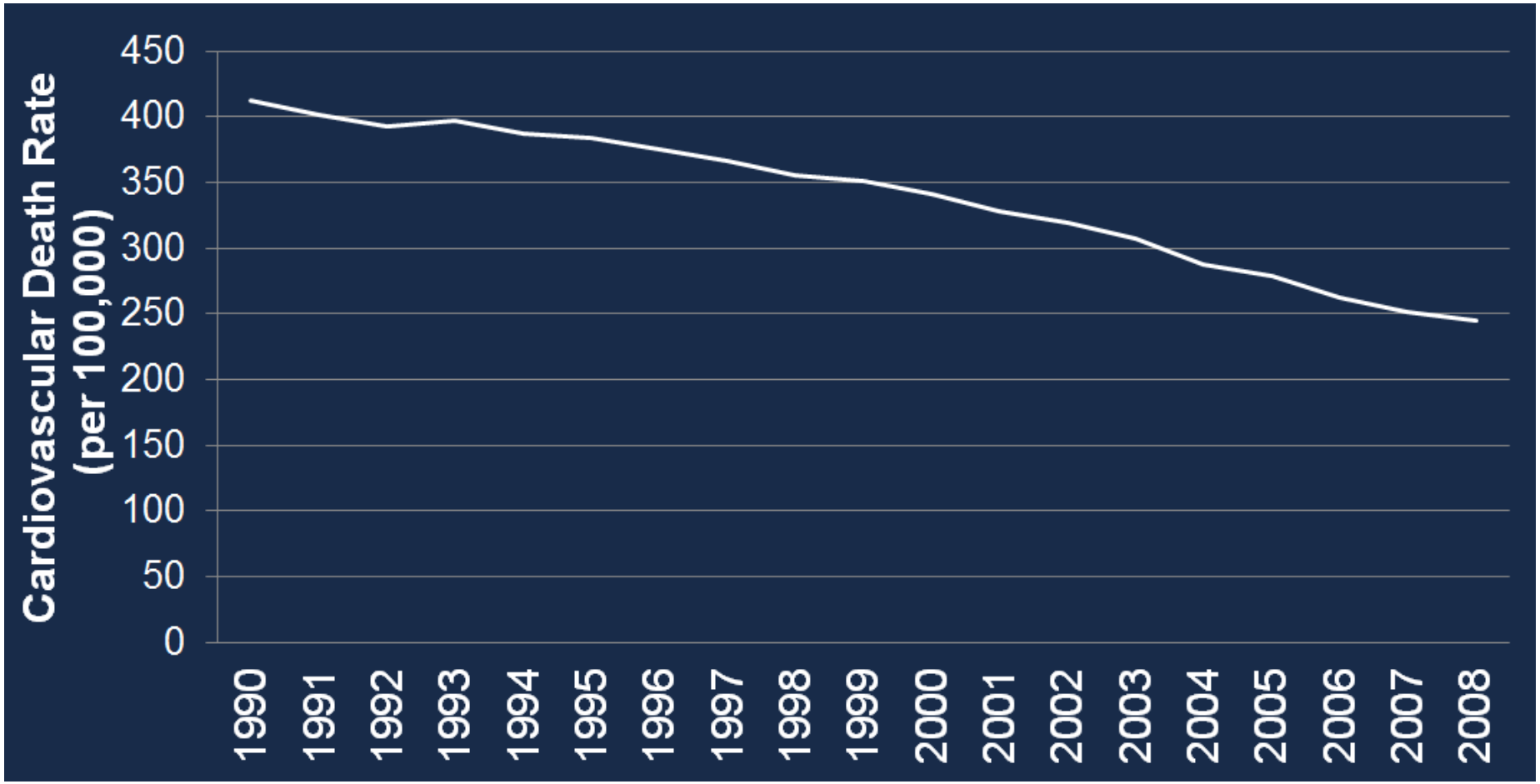
Prevalence of Hypertension is Extremely High, Approximately Equal to Age



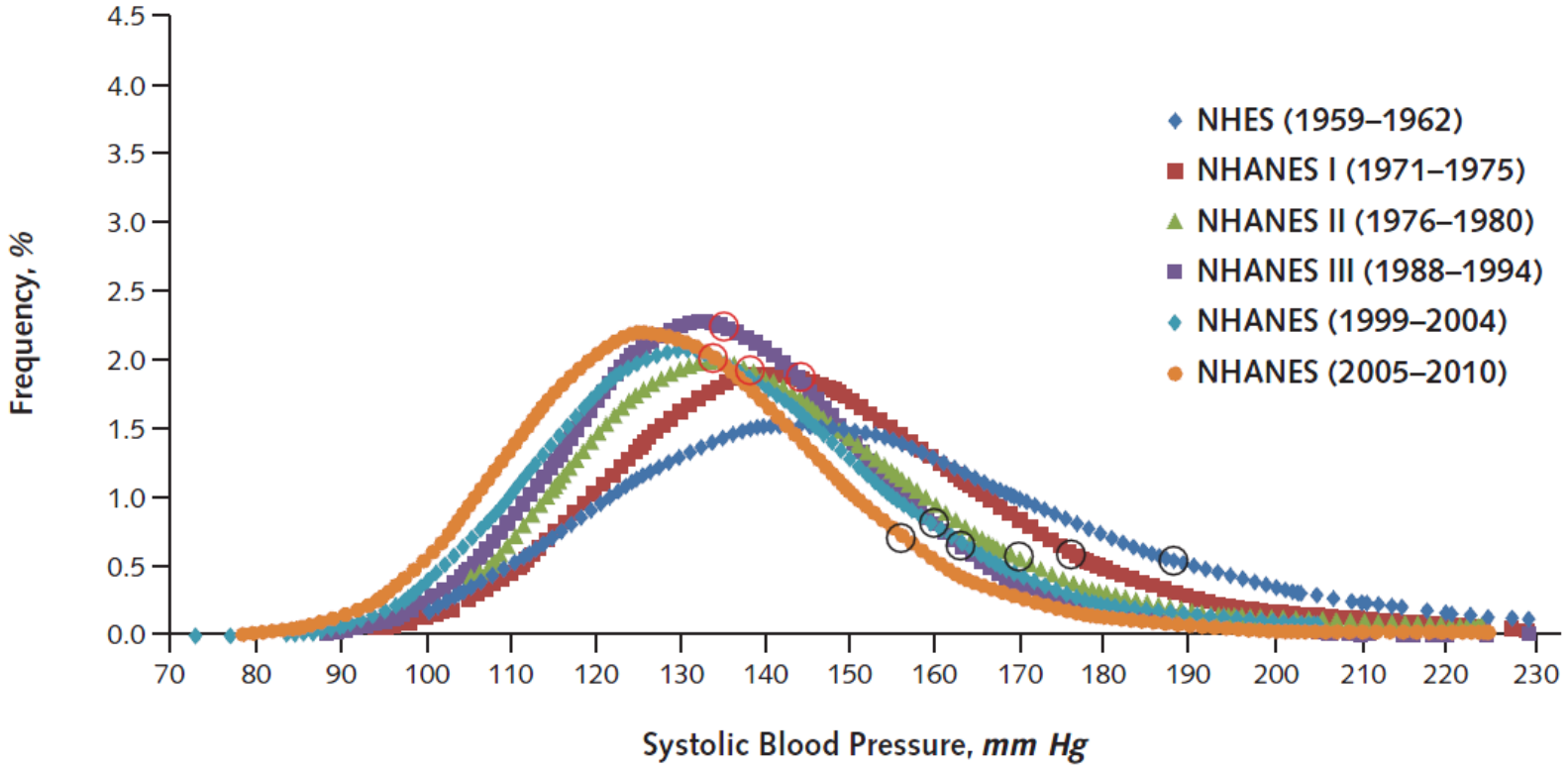
Whelton P, *Ann. Rev. Public Health* 2015. 36:109–30.

Age-Adjusted Death Rates from Cardiovascular Disease in the US 1990 - 2008



http://www.cdc.gov/nchs/datawh/statab/unpubd/mortabs.htm.

Trend in Mean SBP in the US Population Over Past Half Century



Adapted from Wright JA, *JAMA* 2014; 160: 499-503.

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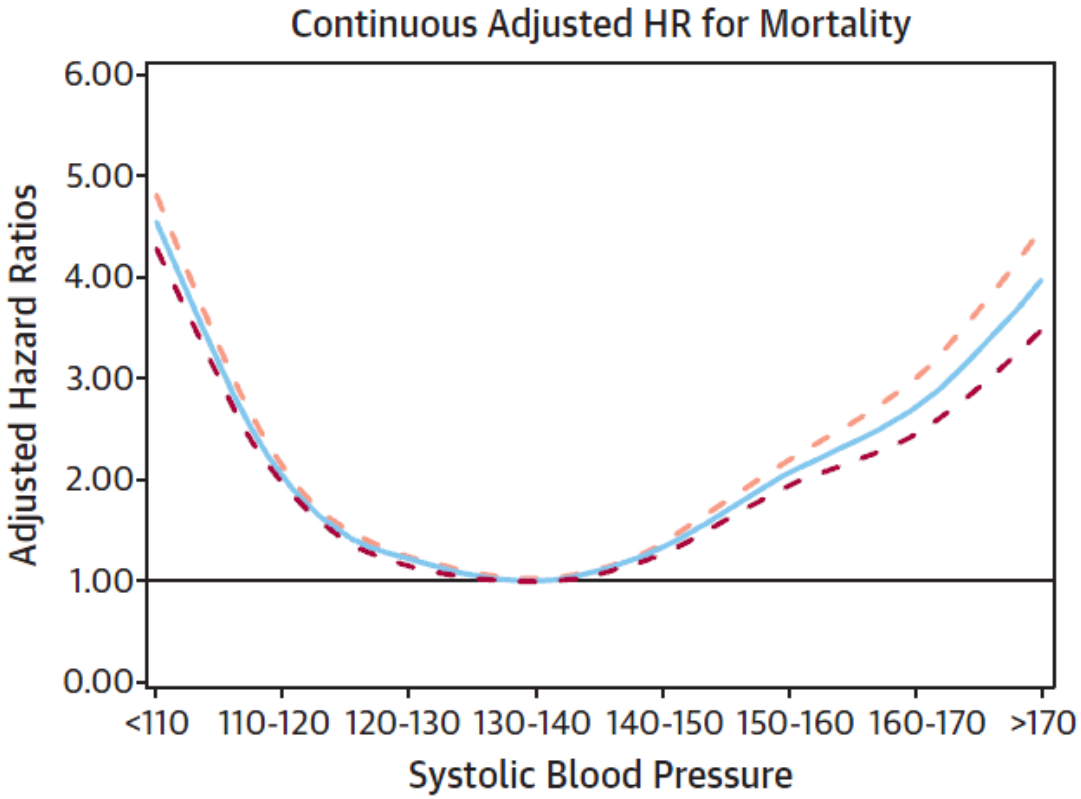
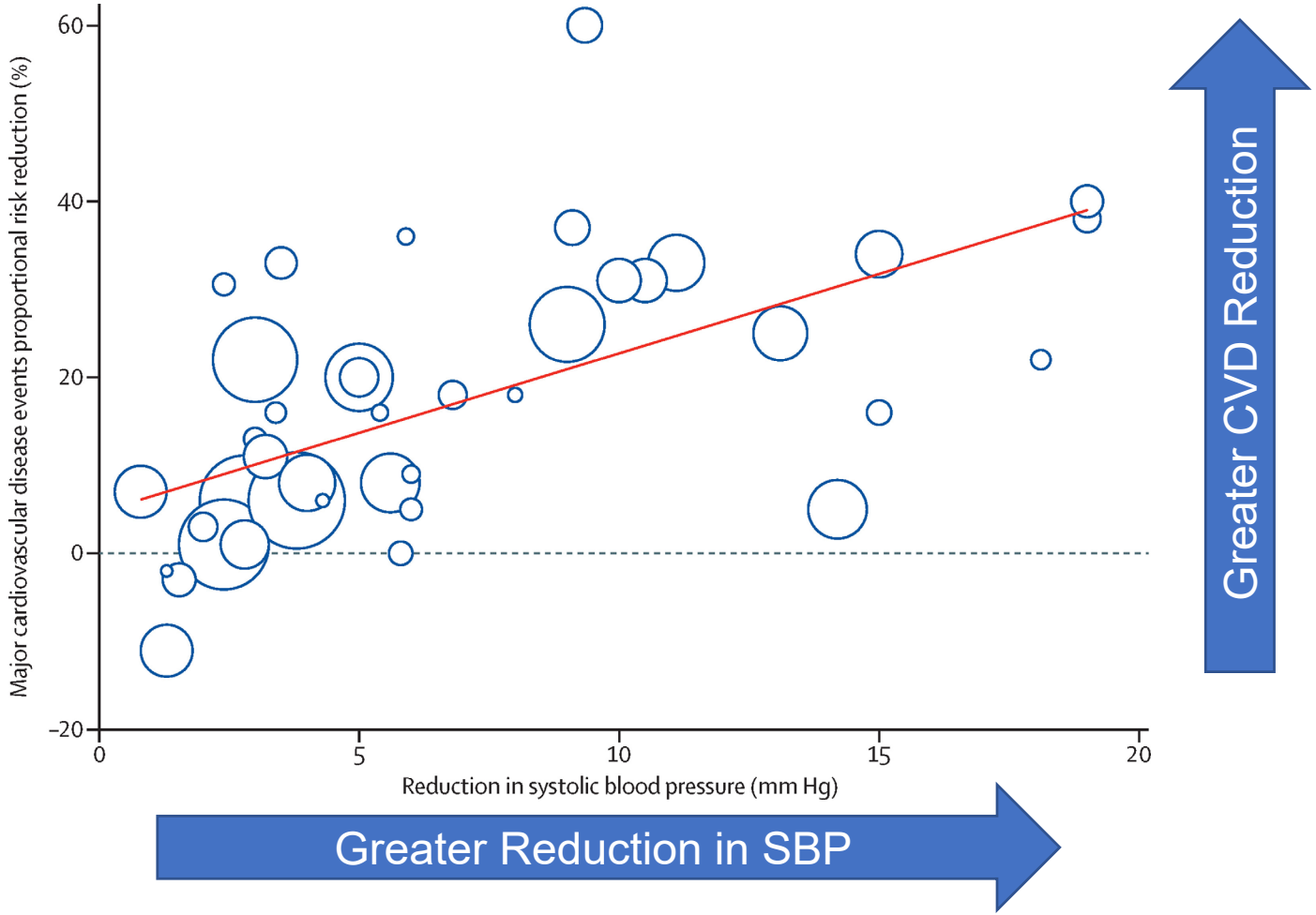
Observational Data – Hazard Ratio* for Mortality by SBP Level in 398,419 Kaiser So. California Patients



* Adjusted for age, sex, race, BMI, CKD, DM, CVD, CVA.

Sim JJ, *J Am Coll. Cardiol.,* 2014; 65: 588-97.

Meta Regression Showing CVD Benefits by Difference in BP Across Arms in Randomized Trials



Ettehad D, *Lancet* 2016; 387: 957-67.

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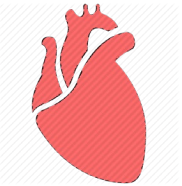
SPRINT TRIAL

Excluded individuals with:
- diabetes,
- proteinuria > 1g/d,
- ADPKD

N=9361

Mean age 68

All hypertensive



All with 1+ CVD risk factor
17% CVD

28% eGFR <60 ml/min/1.73m²

RANDOMIZED

Intensive SBP
<120 mm Hg

Standard SBP
<140 mm Hg

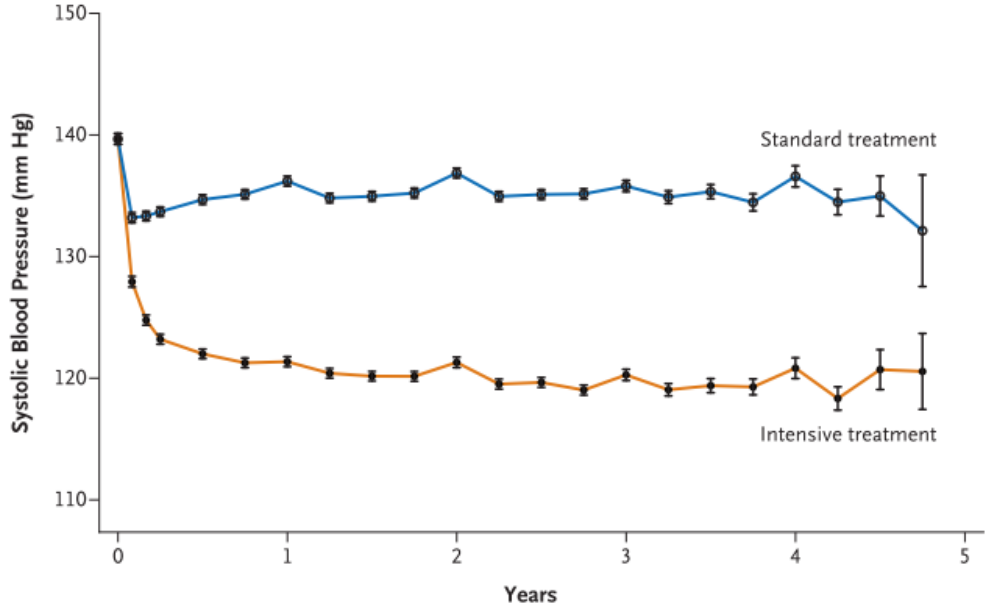
Median follow-up=3.3 y

SPRINT Research Group. N Engl J Med 2015.

SPRINT Trial Outcomes

- **Primary Outcome:** Composite CVD
  - Nonfatal MI, ACS, nonfatal stroke, nonfatal acute decompensated heart failure, CVD death
- **Secondary Outcomes:**
  - **Mortality**
  - **Kidney outcomes:**
    - Kidney failure (50% eGFR decline, ESRD, or transplant)
    - Incident CKD (sustained [> 3 months] 30% reduction in eGFR and eGFR < 60)
    - Acute kidney injury (emergency room visits and hospitalizations)
  - **Brain outcomes:** dementia and mild cognitive impairment (MCI)

Achieved large separation in systolic blood pressure



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

Figure 2. Systolic Blood Pressure in the Two Treatment Groups over the Course of the Trial.

The systolic blood-pressure target in the intensive-treatment group was less than 120 mm Hg, and the target in the standard-treatment group was less than 140 mm Hg. The mean number of medications is the number of blood-pressure medications administered at the exit of each visit. I bars represent 95% confidence intervals.

NEJM, 2015

Reduction of Cardiovascular Events

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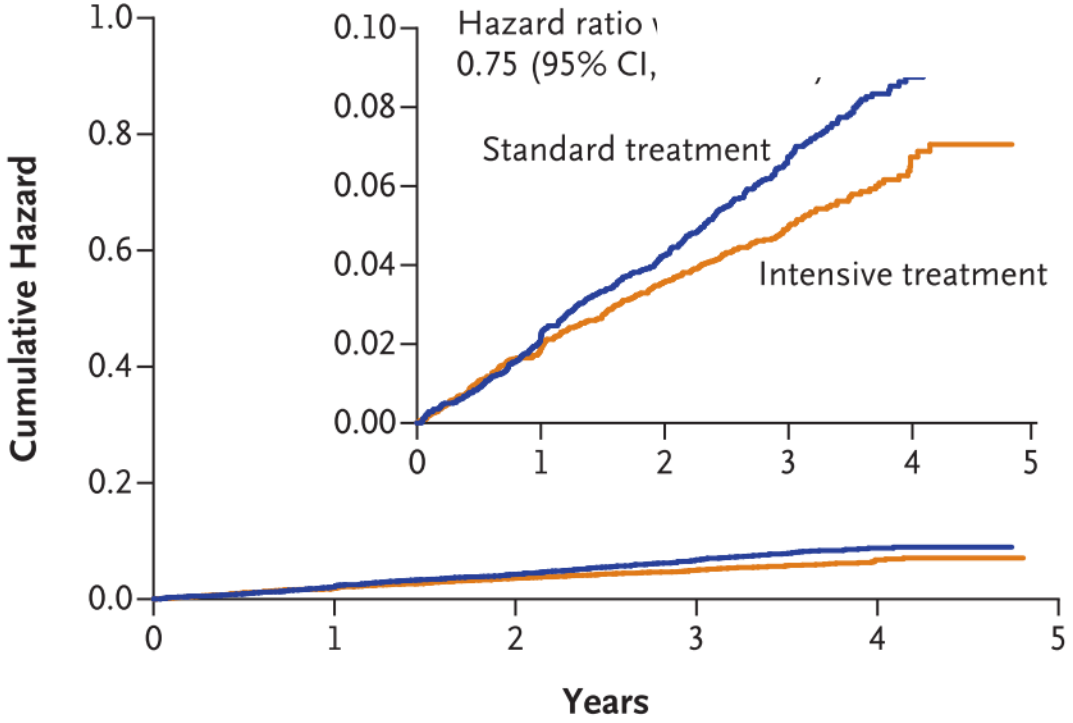
A Primary Outcome



No. at Risk

Standard treatment	4683	4437	4228	2829	721
Intensive treatment	4678	4436	4256	2900	779

Hazard Ratio: 0.75 (0.64-0.89)

Number Needed to Treat for 3.26 Years

61

NEJM, 2015

Effects of Intensive (<120 mmHg) Compared with Standard SBP Lowering (<140) in SPRINT

Kidney Research Innovation Hub of San Diego

	Hazard Ratio	95% Confidence Interval
CVD	0.75	0.64-0.84
Mortality	0.73	0.60-0.90
Mild Cognitive Impairment	0.85	0.74-0.97

Effects of Intensive (<120 mmHg) Compared with Standard SBP Lowering (<140) in SPRINT

	Hazard Ratio	95% Confidence Interval
CVD	0.75	0.64-0.84
Mortality	0.73	0.60-0.90
Mild Cognitive Impairment	0.85	0.74-0.97
Incident CKD	*3.49*	*2.44-5.10*
Acute Kidney Injury (Hosp.)	*1.66*	*1.32-2.08*
Hypotension	*1.67*	*1.30-2.11*
Syncope	*1.33*	*1.00-1.89*
Injurious Falls	*0.95*	*0.78-1.32*

SPRINT Outcomes in Participants Aged ≥ 75

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Event	Intensive (1317)	Standard (1319)	HR (95% CI)	P-value
Achieved SBP	123.4	134.8		< 0.001
CVD (Primary) End			.85)	0.001
Death (Secondary) Endpoint			.91)	0.009
All SAEs				0.93
Injurious Falls	71	80	0.92	0.63
Hypotension	36	24	1.49	0.13
Syncope	46	37	1.24	0.33

Number Needed to Treat

To Prevent 1 CVD Event:

Overall = 61, Age > 75 = 27

To Prevent 1 Death:

Overall = 90, Age > 75 = 41

Williamson,… Ix,… Pajewski. *JAMA* 2016; 315: 2673-2682

SPRINT Outcomes in Participants Aged ≥ 75 by Frailty Status

Kidney Research Innovation Hub of San Diego

Event	Intensive (1317)	Standard (1319)	HR (95% CI)	P-value Interaction
CVD				
Fit (N=349)	4	10	0.47 (0.13, 1.39)	0.84
Less Fit (N=1456)	48	77	0.63 (0.43, 0.91)	
Frail (N=815)	50	61	0.68 (0.45,1.01)	
Death				
Fit (N=349)	5	6	0.95 (0.27, 3.15)	0.52
Less Fit (N=1456)	26	52	0.48 (0.29, 0.78)	
Frail (N=815)	40	49	0.64 (0.41, 1.01)	

Williamson,… Ix,… Pajewski. *JAMA* 2016; 315: 2673-2682

Similar results in HYVET, Trial of Persons > 80 years with HTN (SBP ≥ 160 mm Hg) randomized to indapamide and perindopril vs. Placebo.

Variables included in the model	Stroke (95 events)	Cardiovascular events (231 events)	Total mortality (294 events)
Treatment group	0.65 (0.43–0.98)	0.59 (0.45–0.77)	0.83 (0.66–1.05)
Treatment group, sex, and age	0.65 (0.43–0.98)	0.59 (0.45–0.77)	0.83 (0.66–1.05)
Treatment group, sex, age, and FI at entry to the study	0.64 (0.42–0.96)	0.59 (0.45–0.77)	0.83 (0.66–1.04)

Warwick, *BMC Medicine*, 2015

Results Stratified by Frailty in HYVET

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	Stroke		Cardiovascular events		Total mortality	
Frailty index	HR	95% CI	HR	95% CI	HR	95% CI
0.1	0.75	0.40–1.38	0.62	0.42–0.92	0.89	0.63–1.25
0.2	0.66	0.43–1.01	0.60	0.45–0.78	0.84	0.66–1.07
0.3	0.59	0.36–0.96	0.57	0.42–0.79	0.80	0.61–1.04
0.4	0.52	0.25–1.09	0.55	0.34–0.89	0.76	0.50–1.14
0.5	0.47	0.16–1.33	0.53	0.26–1.06	0.72	0.40–1.29
0.6	0.41	0.10–1.65	0.50	0.20–1.27	0.68	0.32–1.48

Warwick, *BMC Medicine*, 2015

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Systematic bias in our clinical experience that may push us to be less aggressive

- Consider how you feel as the treating physician in these scenarios:
  - 79 yo female, hypertensive but otherwise healthy. BP 146/70 on amlodipine 5mg. Based on recent recommendations, over a series of visits, you increase amlodipine to 10mg, add chlorthalidone 12.5mg daily, and losartan 50mg daily. BP at last visit was 123/62, she was feeling well. Presents with hip fracture. BP on presentation to ED ranged 90-105/50, which improved with fluids.

  - *Did you cause her hip fracture?*

Systematic bias in our clinical experience that may push us to be less aggressive

- Consider how you feel as the treating physician in these scenarios:
  - Lovely 82 year old patient in your care for the past 5 years. Recently admitted with stroke, new aphasia and difficulty walking. BP at your visit 6 months ago was 143/80, and 3 months ago 148/70. Treated with amlodipine, pravastatin, aspirin, tolerating all well. You had encouraged diet and exercise.

  - *Did you cause his stroke?*

SPRINT Outcomes in Participants Aged ≥ 75

Kidney Research Innovation Hub of San Diego

Event	Intensive (1317)	Standard (1319)	HR (95% CI)	P-value
Achieved SBP	123.4	134.8		< 0.001
CVD (Primary) Endpoint	102	148	0.66 (0.51, 0.85)	0.001
Death (Secondary) Endpoint	73	107	0.67 (0.49, 0.91)	0.009
All SAEs	640	638	1.00	0.93
Injurious Falls	71	80	0.92	0.63
Hypotension	36	24	1.49	0.13
Syncope	46	37	1.24	0.33

Williamson,… Ix,… Pajewski. *JAMA* 2016; 315: 2673-2682

Systematic bias in our clinical experience that may push us to be less aggressive – What I learned from SPRINT

- When we provide an intervention, and it contributes to a physical sign or symptom, or may lead to an adverse outcome, we naturally feel badly, maybe shameful, maybe embarrassed that we caused harm.

- When we provide a preventive therapy, and the event we are trying to prevent never happens, we don't ever know if we helped that patient, the next patient, or none at all.

- We need clinical trials that randomize two groups, and carefully count both benefits and harms.

- These clinical experience naturally bias us towards wanting to be less aggressive. And yet, are we doing the best thing for our patients?

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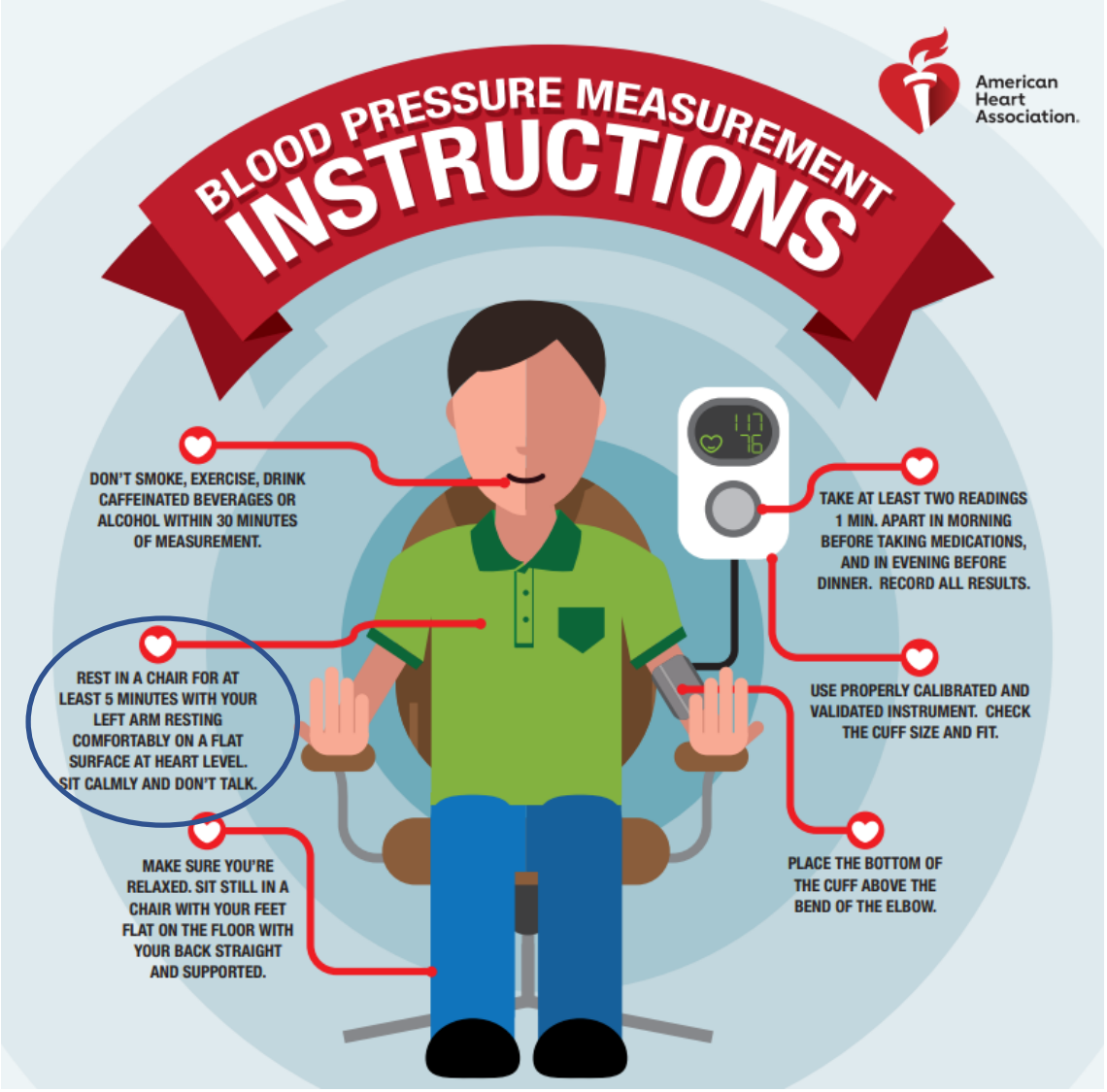
Its critical to take BP measurements by the AHA protocol

Kidney Research Innovation Hub of San Diego

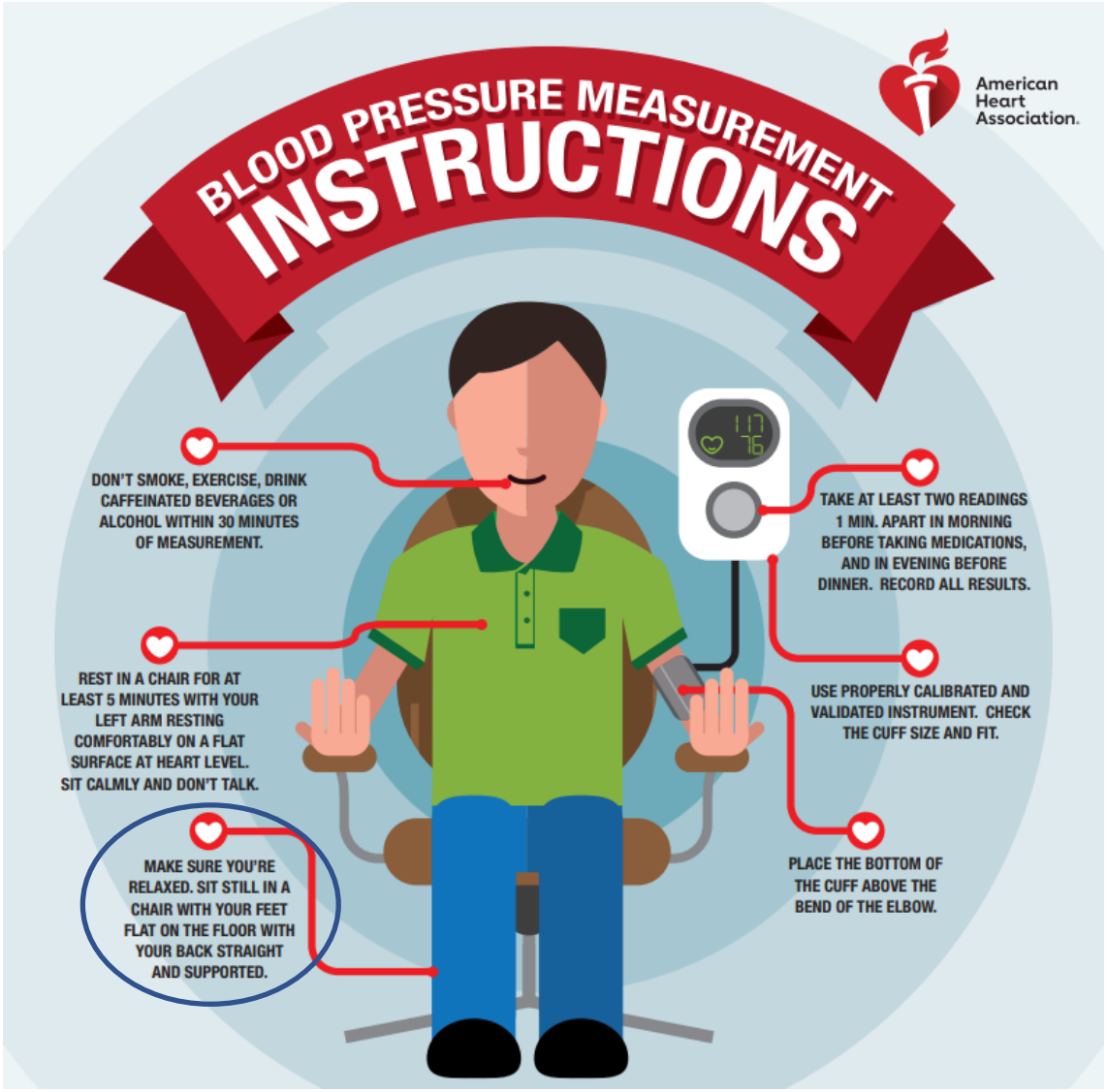


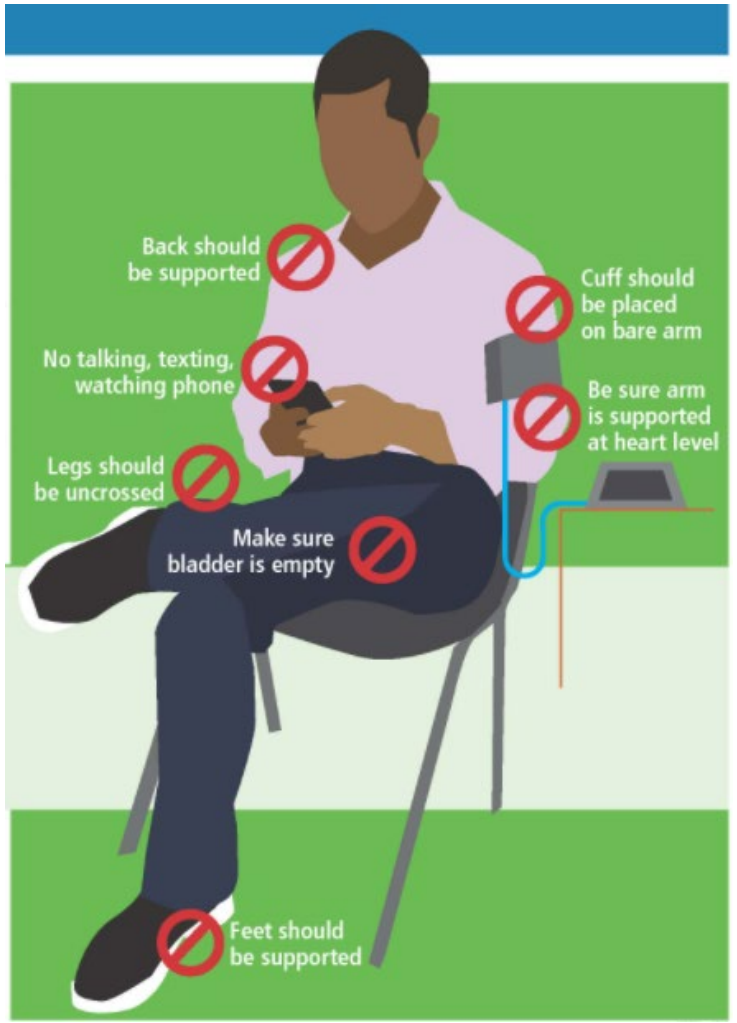
Whelton P, *JACC*, 2018

Before	After
164/94	148/87
129/87	146/84
154/91	149/90

Its critical to take BP measurements by the AHA protocol

Kidney Research Innovation Hub of San Diego





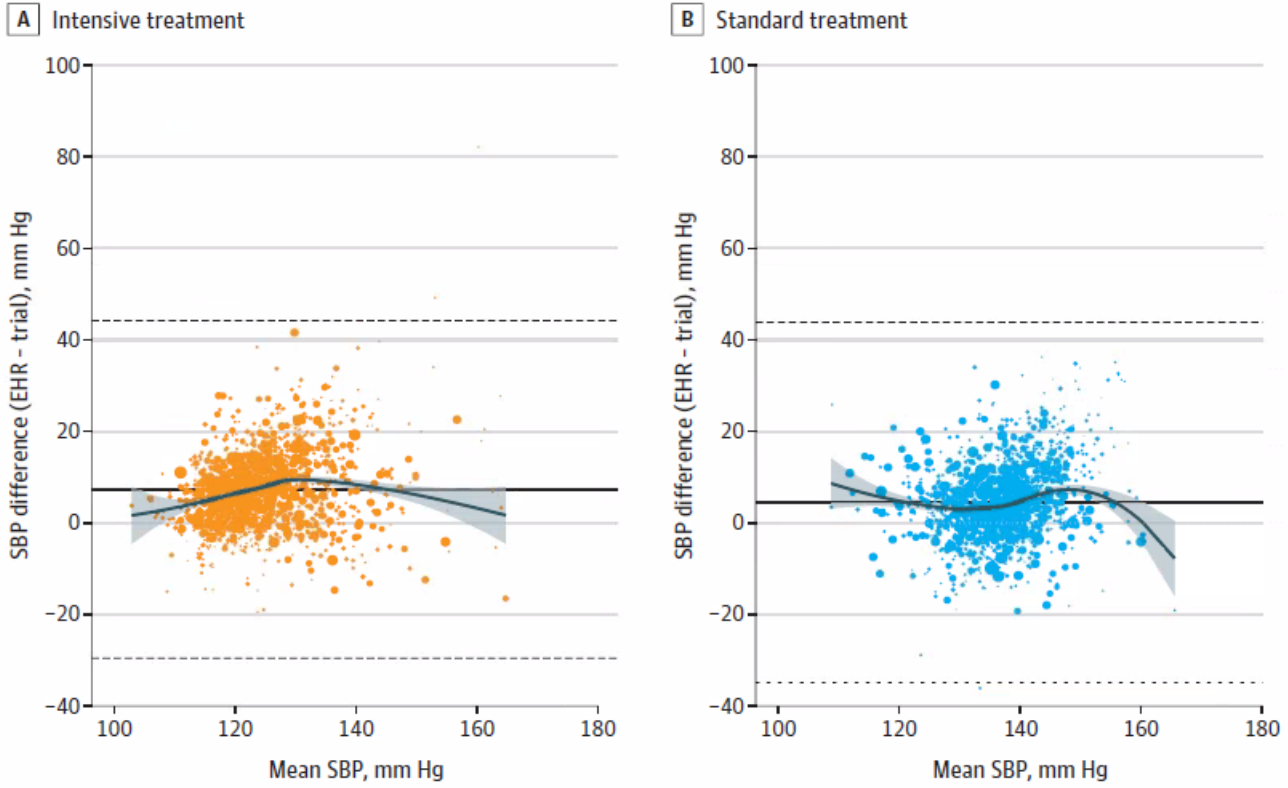
Whelton P, *JACC*, 2018

JAMA Internal Medicine | Original Investigation

Concordance Between Blood Pressure in the Systolic Blood Pressure Intervention Trial and in Routine Clinical Practice

Paul E. Drawz, MD, MHS, MS; Anil Agarwal, MD; Jamie P. Dwyer, MD; Edward Horwitz, MD; James Lash, MD; Kristin Lenoir, MPH; Andrew McWilliams, MD, MPH; Suzanne Oparil, MD; Frederic Rahbari-Oskoui, MD; Mahboob Rahman, MD, MS; Mark A. Parkulo, MD; Priscilla Pemu, MBBS; Dominic S. Raj, MD; Michael Rocco, MD; Sandeep Soman, MD; George Thomas, MD; Delphine S. Tuot, MDCM, MAS; Paul K. Whelton, MD, MSc; Nicholas M. Pajewski, PhD

Figure 3. Bland-Altman Plot Comparing Outpatient Systolic Blood Pressure (SBP) Readings From the Electronic Health Record (EHR) With Trial Measurements



Kidney Research Innovation Hub of San Diego

· On average, casual clinic SBPs were about 10mmHg higher than SPRINT trial (AHA protocol) BPs in SPRINT participants going to regular care appointments

· However, the 95% Limits of Agreement were ± 35mmHg.

· *Casual BPs are highly variable.*
· *You can't simply subtract off 10 from a casual BP.*

Drawz P, *JAMA Int Med*, 2020

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Case 1

Kidney Research Innovation Hub of San Diego

- 75 yo female, generally healthy, hx of benign ovarian cyst removed 2 years ago. Physically active (walks daily, hikes up to 10 miles on weekends). Meds include only vitamin D

- **SBP is now 120-130 at home and in clinic on Amlodipine 10mg and Chlorthalidone 25mg daily.**
- **She feels well, no falls, orthostasis or pre-syncope.**
- **She has strict instructions to avoid NSAIDs, and hold BP meds if unable to eat or drink normally, has fever, or diarrhea.**

October 2014	148/65	New guidelines say you're at target for your age.
May 2015	180/70	Diet, exercise, come back in 6 months instead of a year
November 2015	178/68	Cut salt, come back in 3 months
January 2016	188/70	Start Amlo 2.5mg

Case 2

- 78 year old man with Crohn's disease, hypertension, and CKD (Cr 1.6, no protein). Participant in the SPRINT trial in 2013. BP

- **Diagnosed with c. difficile colitis and pre-renal azotemia.**
- **BP meds held, fluids given, Cr returned to 1.6 within 3 days.**
- **I restarted BP meds with goal SBP < 120 about 2 months later.**
- **Died of malignant pleural effusion about 2 years later. Never had cognitive impairment, CVD, or stroke prior to death.**

- **I'll never know if I helped him individually or hurt him.**

SBP < 120 when guidelines recommend SBP < 150? Look what happened here."

My take home points

- Guidelines are guidelines. *Of course*, you should individualize, and weigh patient's preferences.
- Observational data are really not practical for this question.
- BP meds work well, and are generally well tolerated. Many patients don't want cognitive impairment or stroke, much less mortality.
- Remember that we never see the events we prevent, and the bias that engenders in our clinical care. Don't be afraid to be a bit more aggressive, even those that are older and/or are a bit more frail. On average, you're more likely to give benefit than do harm.
- Start low, go slow.
- Ask your patients how they're feeling.
- Get high quality BP measurements.
- Remember to give sick day management advice.