

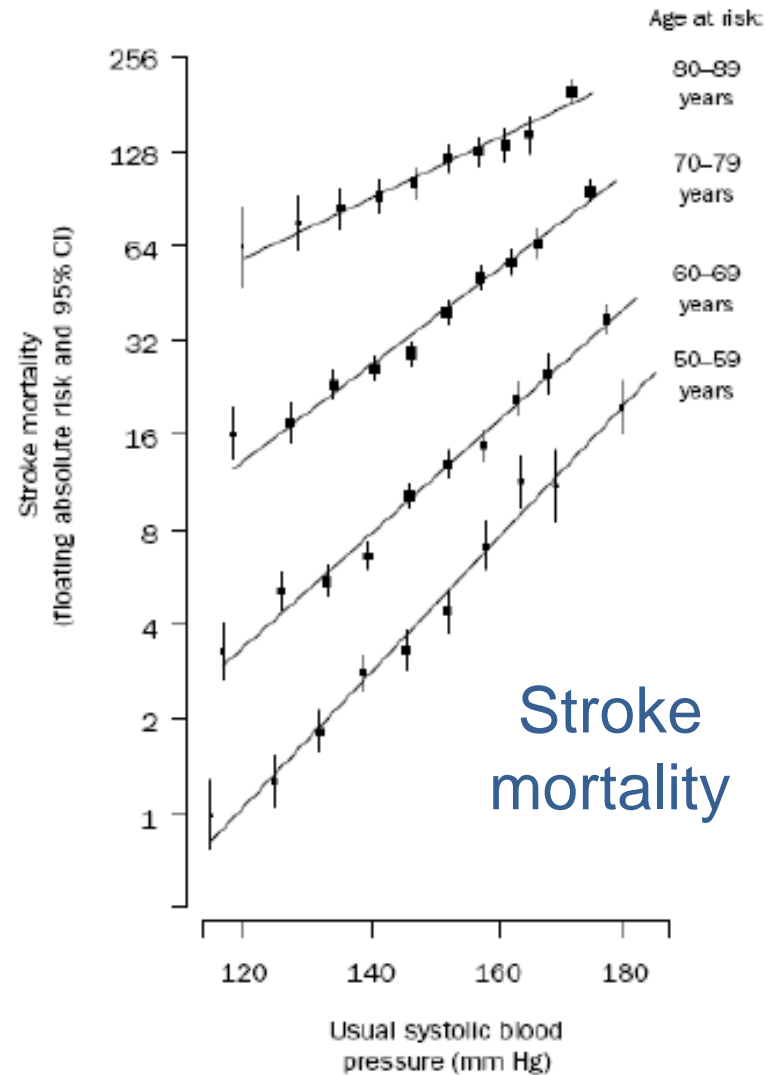
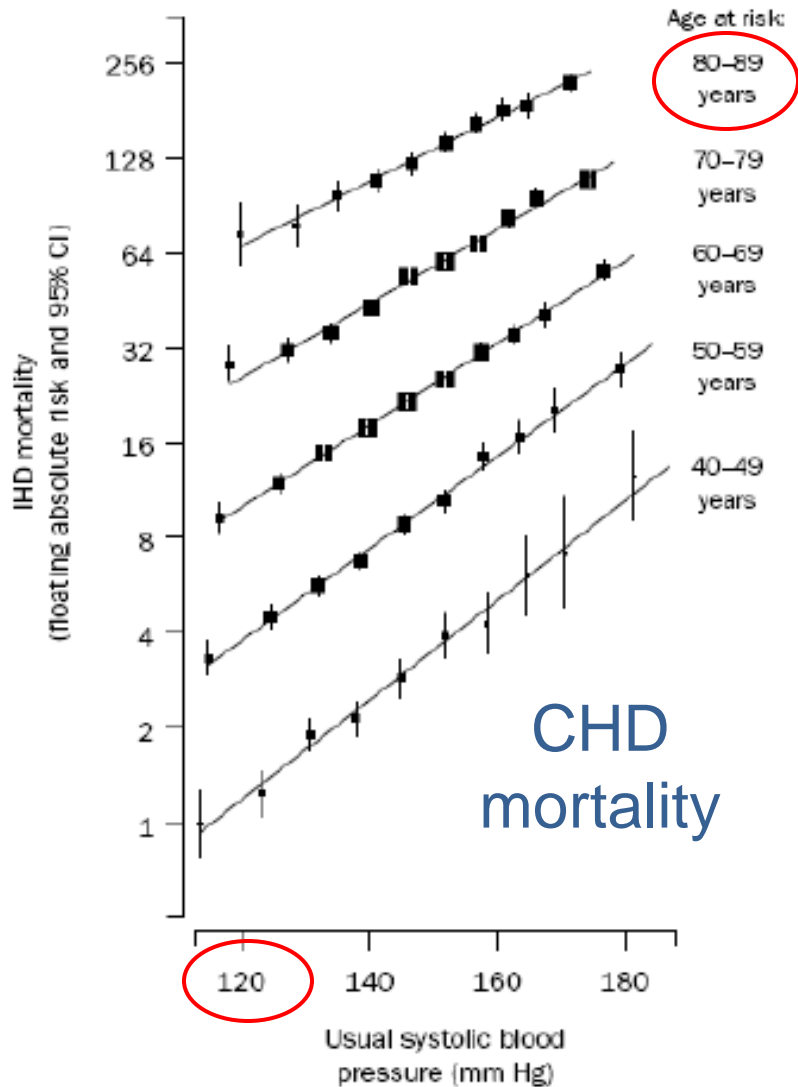
Blood pressure target: A critical review

1st International Congress of Chinese
Nephrologists (ICCN 2015)
Hong Kong, December 13, 2015

Alfred K. Cheung, M.D.
University of Utah

Association between SBP and CVD mortality

12.7x10⁶ pt-yr in 61 prospective observational studies



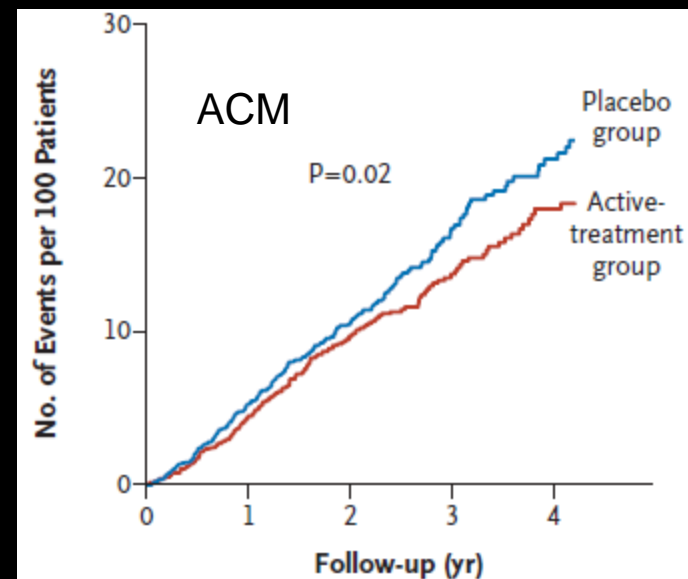
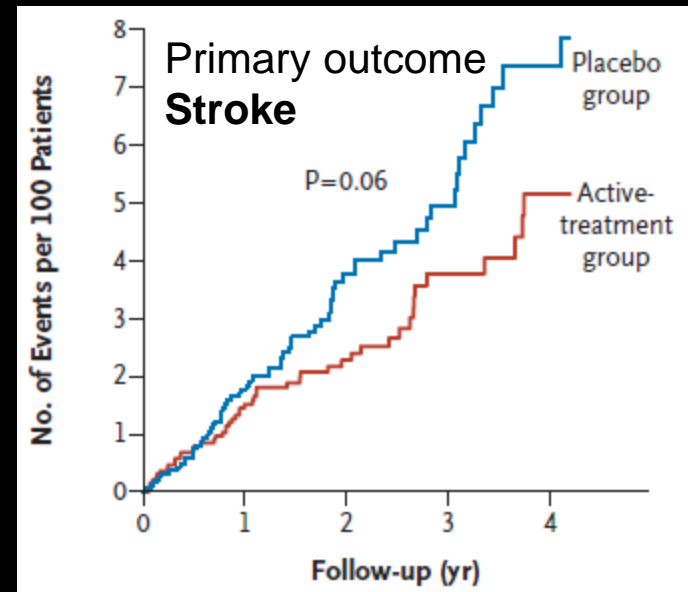
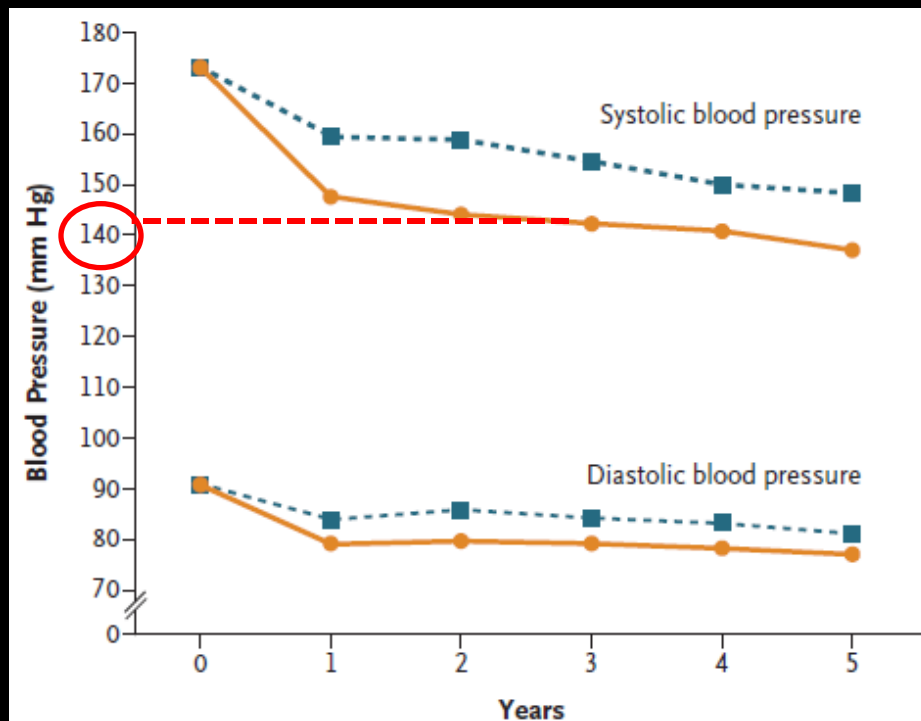
Randomized trials of SBP Treatment on CVD Outcomes in General Population

Trial	N	Low BP Goal	Comparison Arms	Primary Results
SHEP* (1991)	4,736	143/68	Diuretic-based regimen vs. placebo	RR=0.36 for stroke

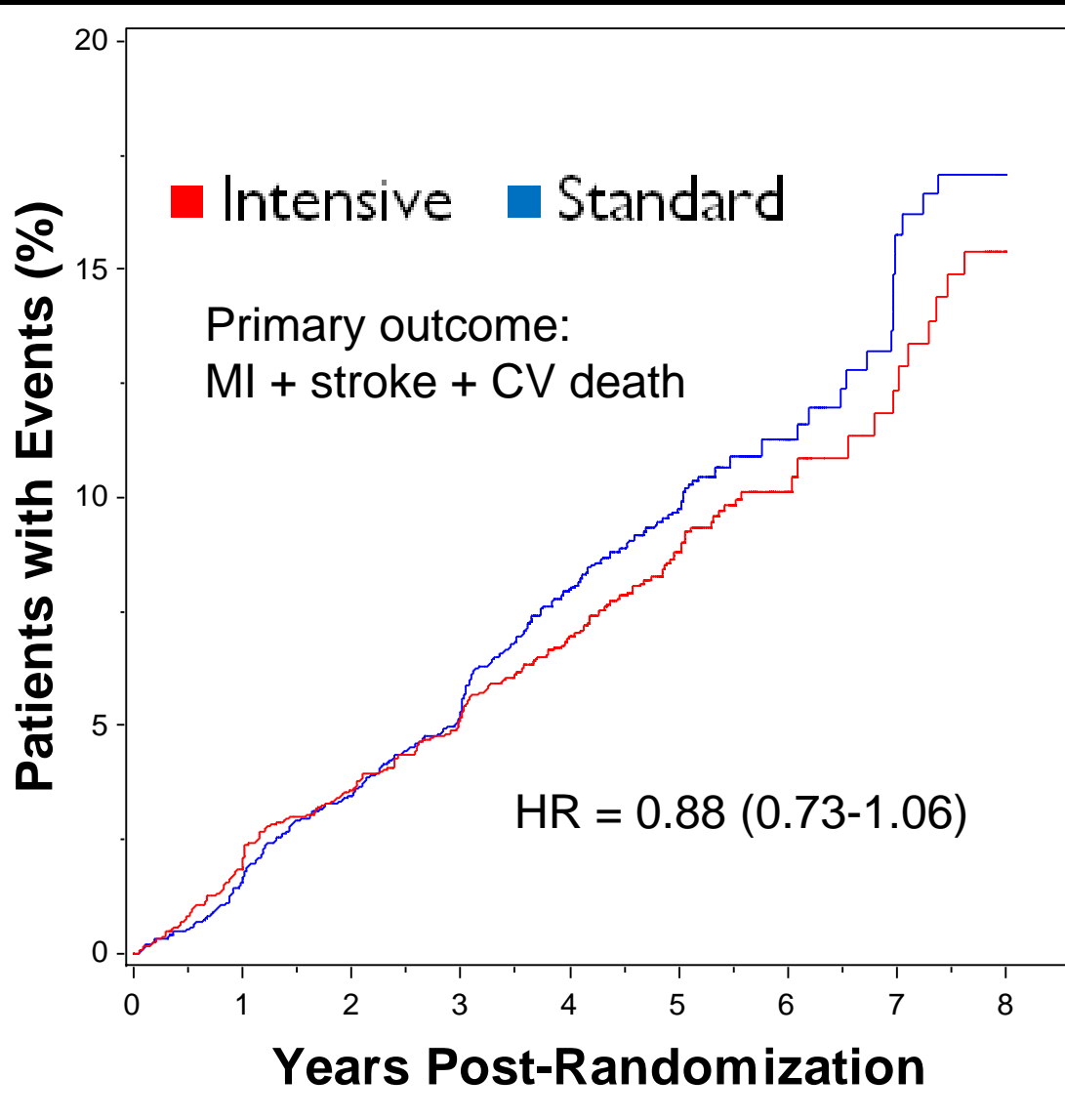
* Systolic Hypertension in the Elderly Program, *JAMA*, 1991

HYVET (Hypertension in Very Elderly) RCT in General Population

- N = 3,845
- Age = 83.6 yrs
- BP 173/91
- Add diuretics + ACEI to BP 150/80
- Exclude SCr >1.7 mg/dL



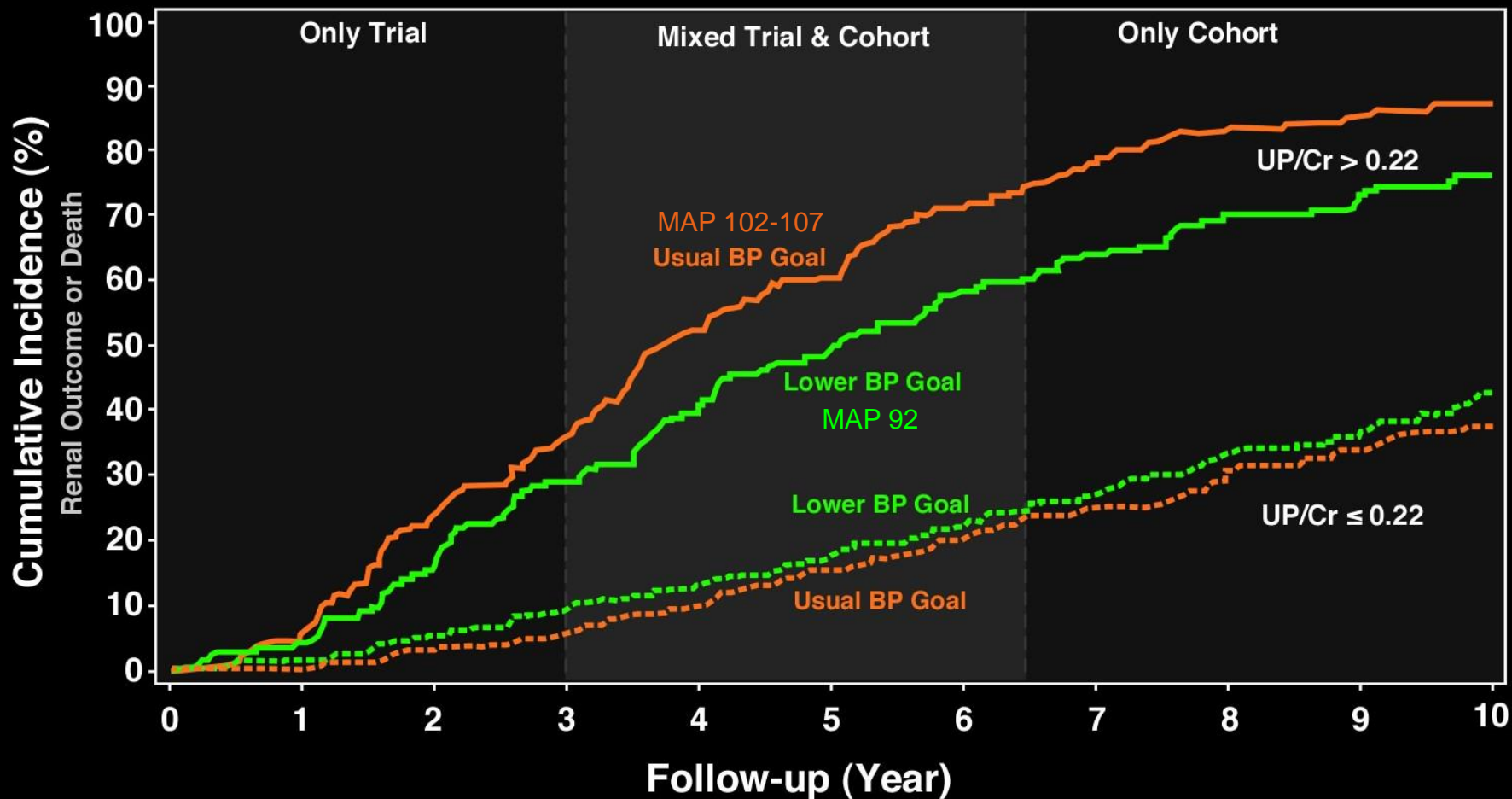
ACCORD (Action to Control Cardiovascular Risk in Diabetes)



- Target SBP <140 mm Hg (N=2,371) vs. SBP <120 mm Hg (N=2,362)
- Achieved SBP 133.5 mm Hg vs. 119.3 mm Hg ($\Delta=14.2$ mm Hg)
- Exclude SCr >1.5 mg/dL (mean eGFR = 92 mL/min/1.73m²)
- **RR for stroke = 0.59 (0.39-0.89)**

Legacy Benefit on Renal Outcome or Death Associated with Lower BP in AASK

(African-American Study of Kidney Disease & HTN)



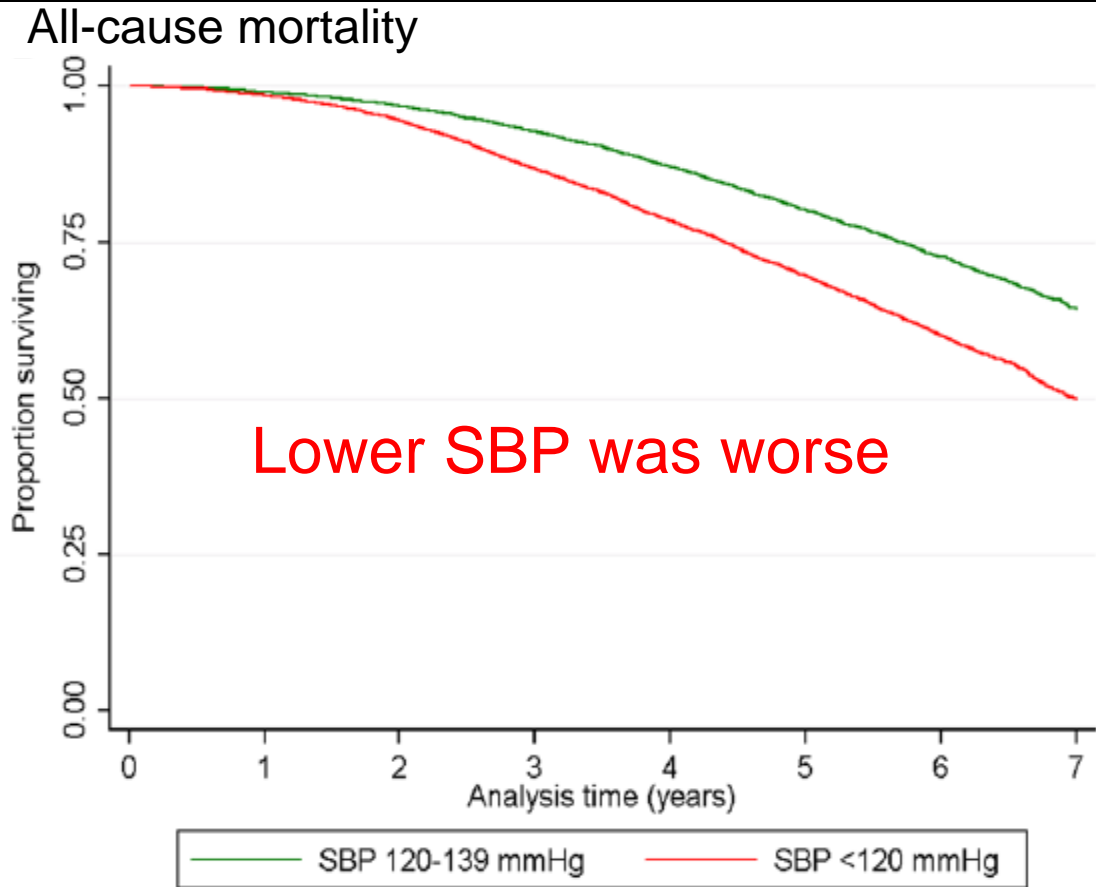
N=1,094

Appel, NEJM, 2010

Practice Guidelines

Guideline	Year	Recommended BP target for CKD
JNC7	2003	130/80
K/DOQI	2007	130/80
ASH	2008	130/80
ADA	2010	130/80

Association Between SBP <120 mm Hg (vs. 120-<140 mm Hg) and Mortality

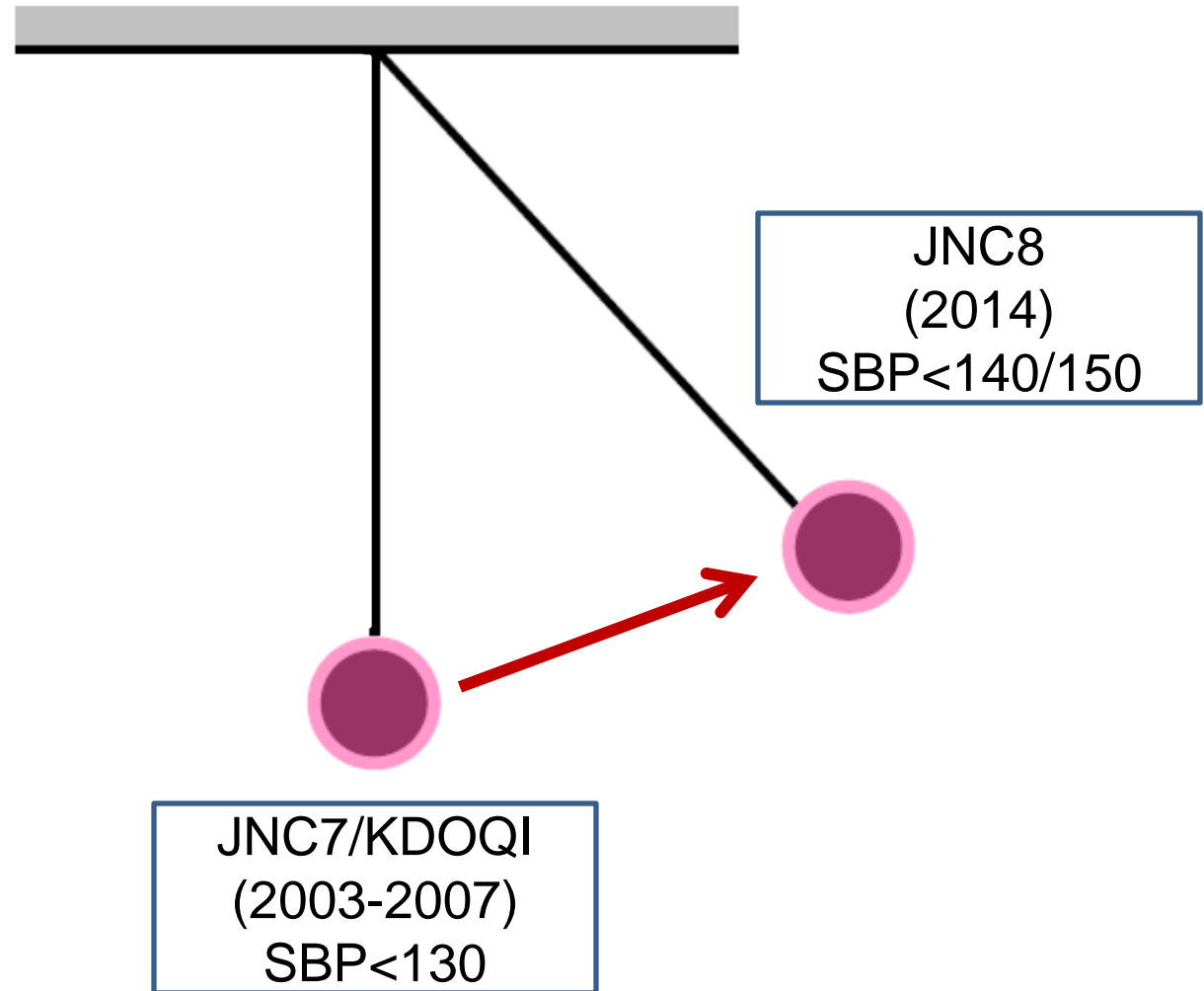


- N=11,520 U.S. veterans
- eGFR <60 (actual 48)
- Propensity matching

2014 “JNC 8”

- Age >60 yrs: Target BP <150/90 mm Hg (Grade A)
(concern about safety and dementia)
- CKD
 - = eGFR <60 mL/min/1.73m² in age <70 yrs or
ACR >30 mg/g:
 - Target <140/90 mm Hg (Grade E)

BP Target Pendulum Swing in CKD





SPRINT
Systolic Blood Pressure Intervention Trial

Sponsored by NHLBI/NIDDK/NINDS/NIA

www.SPRINTTrial.org

SPRINT Design

RCT of 9,361 people in U.S.
Target SBP

Intensive Goal
SBP < 120 mm Hg

Standard Goal
SBP < 140 mm Hg

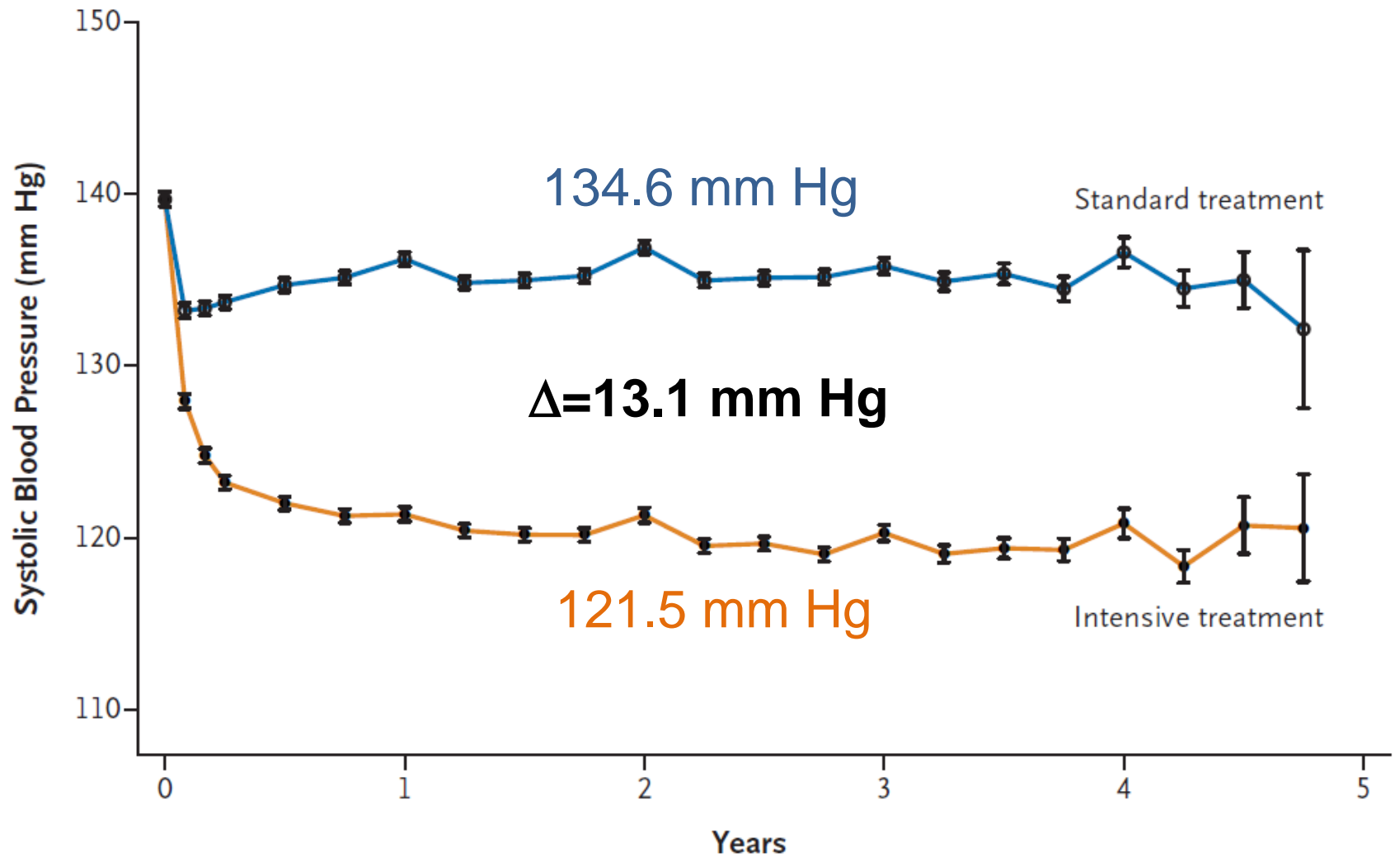
Major Inclusion Criteria

- ≥ 50 years old
- At least one additional cardiovascular risk
 - Clinical or subclinical CVD
 - CKD (eGFR 20 – <60 ml/min/1.73m²)
 - Framingham Risk Score for 10-year CVD risk $\geq 15\%$
 - Age ≥ 75 years

Major Exclusion Criteria

- Diabetes mellitus
- Stroke
- Proteinuria >1 g/d

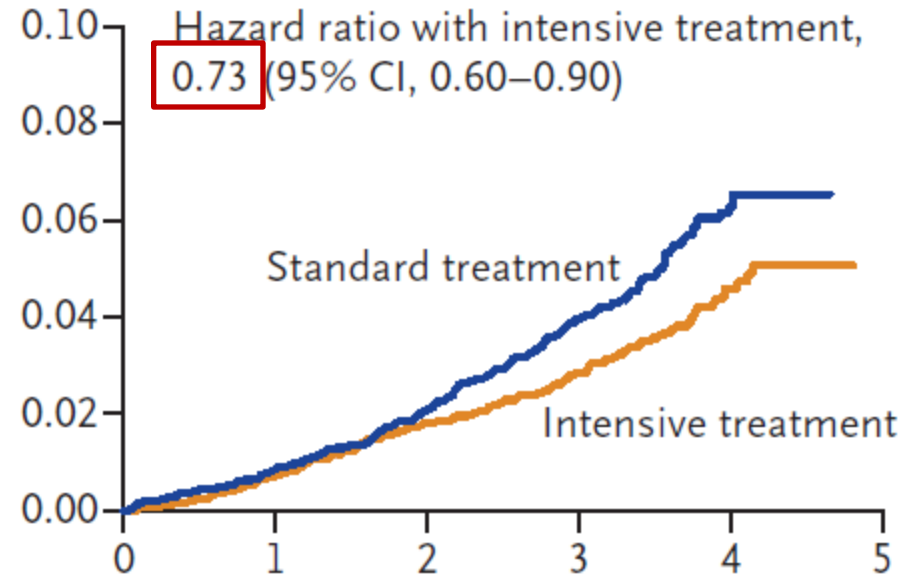
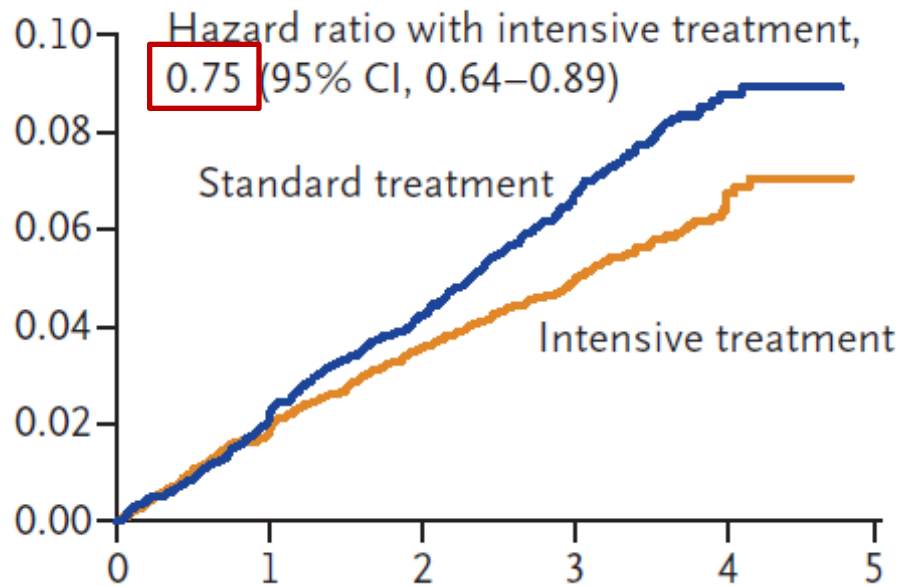
Average SBP Over Time in SPRINT



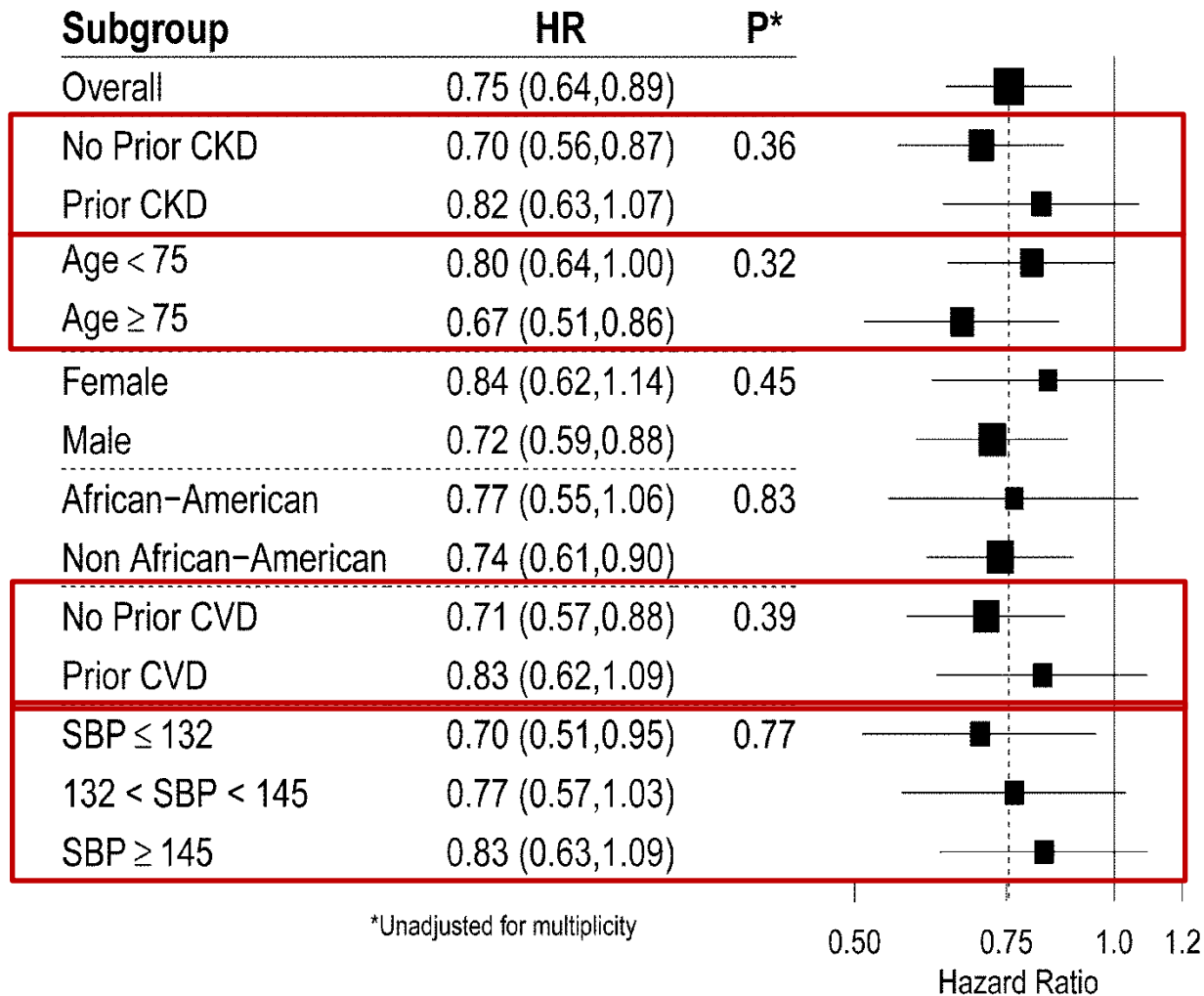
Outcomes in SPRINT

Primary Outcome
(Cardiovascular events =
MI, ACS, stroke, CHF, CV death)

All-Cause Mortality



Primary Outcomes in Pre-specified Subgroups



Kidney Outcomes in SPRINT

	% of Participants with Events			
	Intensive BP (n=1330)	Standard BP (n=1316)	HR	P
CKD				
Composite	1.1	1.1	0.89	0.76
50% Δ GFR	0.8	0.8	0.87	0.75
ESRD	0.5	0.8	0.57	0.27

Kidney Outcomes in SPRINT

	% of Participants with Events			
	Intensive BP	Standard BP	HR	P
CKD	(n=1330)	(n=1316)		
Composite	1.1	1.1	0.89	0.76
50% Δ GFR	0.8	0.8	0.87	0.75
ESRD	0.5	0.8	0.57	0.27
Non-CKD	(n=3332)	(n=3345)	0.87	0.75
30% Δ GFR	3.8	1.1	3.49	<0.001

Serious Adverse Events in SPRINT

	% of Participants with SAE		HR	P
	Intensive BP	Standard BP		
Hypotension	2.4	1.4	1.67	0.001
Syncope	2.3	1.7	1.33	0.05
Injurious fall	2.2	2.3	0.95	0.71
Bradycardia	1.9	1.6	1.19	0.28
Electrolyte abnormalities	3.1	2.3	1.35	0.02
AKI/ARF	4.1	2.5	1.66	<0.001

Serious Adverse Events in SPRINT

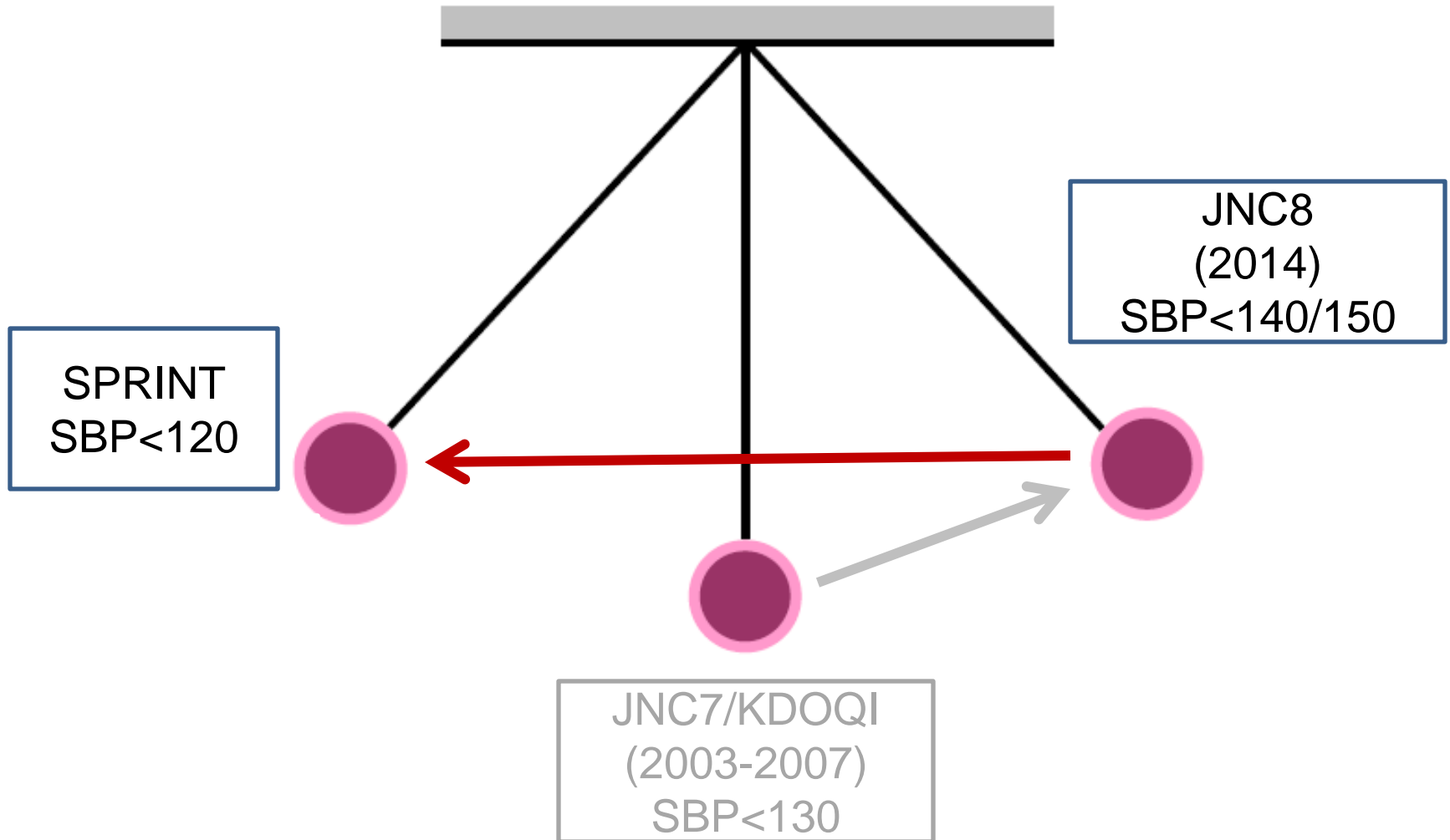
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AKI/ARF	4.1	2.5	1.66	<0.001
TOTAL	38.3	37.1	1.04	0.25

Conclusions

(Personal and not official SPRINT opinion)

- For *cardiovascular* health of most people age >50 yrs, SBP target should probably be <120 mm Hg.
- Expect some side-effects to be more frequent at this SBP level; tolerability needs to be taken into consideration.
- Overall, benefits exceed potential harm.
- Effects on brain and long-term effects on kidney are currently uncertain.
- Global health implications are substantial; overall effects on healthcare costs require detailed analysis.

BP Target Pendulum Swing in CKD





SPRINT Primary Outcome and its Components

Event Rates and Hazard Ratios

	Intensive		Standard			
	<i>No. of Events</i>	<i>Rate, %/year</i>	<i>No. of Events</i>	<i>Rate, %/year</i>	<i>HR (95% CI)</i>	<i>P value</i>
Primary Outcome	243	1.65	319	2.19	0.75 (0.64, 0.89)	<0.001
All MI	97	0.65	116	0.78	0.83 (0.64, 1.09)	0.19
Non-MI ACS	40	0.27	40	0.27	1.00 (0.64, 1.55)	0.99
All Stroke	62	0.41	70	0.47	0.89 (0.63, 1.25)	0.50
All HF	62	0.41	100	0.67	0.62 (0.45, 0.85)	0.00

Adverse Events in ACCORD by BP Groups

	Intensive N (%)	Standard N (%)	P
Overall SAE	77 (3.3)	30 (1.27)	<0.001
Syncope	12 (0.5)	5 (0.2)	0.10
Urinary Alb/Cr (mg/g) at last visit	12.6	14.9	<0.0001
Serum creatinine (mg/dL) at last visit	1.1 ± 0.4	1.0 ± 0.5	<0.0001
eGFR ever <30 mL/min/1.73m ²	99 (4.2)	52 (2.2)	<0.001
Any dialysis or ESRD	59 (2.5)	58 (2.4)	0.93

Demographic and Baseline Characteristics

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

Selected Baseline Laboratory Characteristics

	Total N=9361	Intensive N=4678	Standard N=4683
Mean (SD) eGFR, mL/min/1.73 m²	71.7 (20.6)	71.8 (20.7)	71.7 (20.5)
% with eGFR<60 mL/min/1.73m²	28.3	28.4	28.1
Mean (SD) Urine albumin/creatinine, mg/g	42.6 (166.3)	44.1 (178.7)	41.1 (152.9)
Mean (SD) Total cholesterol, mg/dL	190.1 (41.2)	190.2 (41.4)	190.0 (40.9)
Mean (SD) Fasting plasma glucose, mg/dL	98.8 (13.5)	98.8 (13.7)	98.8 (13.4)