#### NEW HYPERTENSION GUIDELINES: WHY THE CHANGE?

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#### DISCLOSURES

• None

# OBJECTIVES

- Understand trend in blood pressure clinical practice guidelines
- Understand new guideline recommendations
- Critically review SPRINT to determine what benefit our patients receive from targeting lower blood pressures (Is it worth it?)

# HISTORY OF BP TRIALS 1

- VA 1967 Is severe hypertension (diastolic) 115–129 treatable - Yes, less stroke/CHF
- VA 1970 Same question for moderate BP (90–115) -Treated group less stroke/CHF
- HDFP 1979 Goal-oriented BP therapy better than usual therapy? - Yes. Targeting BP goal of diastolic 90 reduced CVA by 36% more
- EWHPE 1986 Hypertension treatment in older people (60) beneficial? - Yes. Mortality reduction 26%, decrease in CV mortality 43%

# HISTORY OF BP TRIALS 1

- SHEP 1991 Is treatment of systolic hypertension beneficial? – Treating systolic hypertension over 160 prevented stroke (ARR 3%), MI, and all CVD
- HOT 1998 Lowering Diastolic BP to 85 or 80 beneficial compared to standard 90 goal - No significant benefit in whole study but small benefit in diabetic

### HISTORY OF BP TRIALS 1

- HYVET 2008 Should we treat elderly (>80) hypertensive (sys > 160) - Yes. Treated group had 30% less stroke and 64% less CHF, 21% less death
- ACCRD 2010 In diabetics goal BP sys < 120 better than 140? - No significant difference in mortality, total CV events, or renal protection
- SPRINT 2015 Same as ACCORD but in non-diabetic
   27% improved all-cause mortality and 25% improvement in primary CV outcomes

#### HISTORY OF HYPERTENSION GUIDELINES 2

• 1977 First Guidelines released by JNC



#### MEDICATIONS 2



#### JNC 7 <sub>3</sub>

• Released in 2003

Table 1. Classification and Management of Blood Pressure for Adults Aged 18 Years or Older

				Management*			
55					Initial Drug Therapy		
BP Classification	Systolic BP, mm Hg*		Diastolic BP, mm Hg*	Lifestyle Modification	Without Compelling Indication	With Compelling Indications†	
Normal	<120	and	<80	Encourage			
Prehypertension	120-139	or	80-89	Yes	No antihypertensive drug indicated	Drug(s) for the compelling indications‡	
Stage 1 hypertension	140-159	Or	90-99	Yes	Thiazide-type diuretics for most; may consider ACE inhibitor, ARB, β-blocker, CCB, or combination	Drug(s) for the compelling indications Other antihypertensive drugs (diuretics, ACE inhibitor, ARB, β-blocker, CCB) as needed	
Stage 2 hypertension	≥160	or	≥100	Yes	2-Drug combination for most (usually thiazide-type diuretic and ACE inhibitor or ARB or β-blocker or CCB)§	Drug(s) for the compelling indications Other antihypertensive drugs (diuretics, ACE inhibitor, ARB, β-blocker, CCB) as needed	
Abbreviations: ACE, angiote	ensin-converting en	zyme; A	RB, angiotensin-re	ceptor blocker; BP,	blood pressure; CCB, calcium channel bl	ocker.	

\*Treatment determined by highest BP category.

†See Table 6.

‡Treat patients with chronic kidney disease or diabetes to BP goal of less than 130/80 mm Hg. Sinitial combined therapy should be used cautiously in those at risk for orthostatic hypotension.

# JNC 7 KEY MESSAGES 3

- 1. Age > 50, SBP >140 is much more important CVD risk factor than DBP
- 2. Risk of CVD beginning at 115/75 doubles with each 20/10 mmHg
- 3. SBP 120-139 or DBP 80-89 should be considered pre-hypertensive and require lifestyle modification
- 4. Thiazide diuretics should be used for most with uncomplicated hypertension
- 5. Most patients with hypertension will require 2 or more meds to achieve goal (140/90 or <130/80 with diabetes or CKD)
- 6. If BP more than 20/10 mmHg above goal, initiate 2 meds, 1 of which should be thiazide
- 7. Motivated patients will do better with BP control

#### JNC 8 4





# JNC 8 4

#### Table 1. Comparison of Current Recommendations With JNC 7 Guidelines

Торіс	JNC 7	2014 Hypertension Guideline
Methodology	Nonsystematic literature review by expert committee including a range of study designs Recommendations based on consensus	Critical questions and review criteria defined by expert panel with input from methodology team Initial systematic review by methodologists restricted to RCT evidence Subsequent review of RCT evidence and recommendations by the panel according to a standardized protocol
Definitions	Defined hypertension and prehypertension	Definitions of hypertension and prehypertension not addressed, but thresholds for pharmacologic treatment were defined
Treatment goals	Separate treatment goals defined for "uncomplicated" hypertension and for subsets with various comorbid conditions (diabetes and CKD)	Similar treatment goals defined for all hypertensive populations except when evidence review supports different goals for a particu- lar subpopulation
Lifestyle recommendations	Recommended lifestyle modifications based on literature review and expert opinion	Lifestyle modifications recommended by endorsing the evidence- based Recommendations of the Lifestyle Work Group
Drug therapy	Recommended 5 classes to be considered as initial therapy but rec- ommended thiazide-type diuretics as initial therapy for most pa- tients without compelling indication for another class Specified particular antihypertensive medication classes for patients with compelling indications, ie, diabetes, CKD, heart failure, myocar- dial infarction, stroke, and high CVD risk Included a comprehensive table of oral antihypertensive drugs in- cluding names and usual dose ranges	Recommended selection among 4 specific medication classes (ACEI or ARB, CCB or diuretics) and doses based on RCT evidence Recommended specific medication classes based on evidence review for racial, CKD, and diabetic subgroups Panel created a table of drugs and doses used in the outcome trials
Scope of topics	Addressed multiple issues (blood pressure measurement methods, patient evaluation components, secondary hypertension, adherence to regimens, resistant hypertension, and hypertension in special populations) based on literature review and expert opinion	Evidence review of RCTs addressed a limited number of questions, those judged by the panel to be of highest priority.
Review process prior to publication	Reviewed by the National High Blood Pressure Education Program Coordinating Committee, a coalition of 39 major professional, pub- lic, and voluntary organizations and 7 federal agencies	Reviewed by experts including those affiliated with professional and public organizations and federal agencies; no official sponsorship by any organization should be inferred

#### NEW GUIDELINES 5

- Published November 13<sup>th</sup>, 2017
- 2017

ACC/AHA/AAPA/ABC/ACPM/AGS/AphA/ASH/ASPC/N MA/PCNA Guidelines for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults

- 481 pages in length
- Sought to determine the optimal targets for BP lowering during antihypertensive therapy in adults
- In prior guidelines, there was insufficient evidence to demonstrate benefit of BP goal <140/90
- Newly completed trials allowed to determine whether lower BP goal conferred additional benefit either in general population or specific subpopulation

#### BLOOD PRESSURE GOALS 5

	SBP	DBP
Normal	<120	<80
Elevated	120–129	<80
Hypertension		
• Stage 1	130–139	80–89
• Stage 2	≥140	≥90

# PREVALENCE OF HYPERTENSION 5

	≥130/80 or reported BP Med		≥140/90 or reported BP Med	
Overall, Crude	46%		32%	
	Men	Women	Men	Women
Overall, Age/Sex adjusted	48%	43%	31%	32%

# LABS IN NEW HYPERTENSION 5

- Fasting Glucose, CBC, Lipids, BMP, TSH, UA, ECG
- Optional Testing: Echocardiogram, Uric Acid, Urinary albumin to creatinine ratio

# RECOMMENDATIONS FOR TREATMENT 5

#### Normal BP (<120/80)

Promote optimal lifestyle habits

#### Reassess in 1 year

Elevated BP (120-129/<80)

Nonpharmacologic therapies

Reassess in 3-6 months

# RECOMMENDATIONS FOR TREATMENT 5



First line initial antihypertensive drugs include ACE, ARB, CCB, or thiazide diuretic

#### ASCVD CALCULATOR

#### 10.5%

10-year risk of heart disease or stroke

On the basis of your age and calculated risk for heart disease or stroke over 10%, the USPSTF guidelines suggest you start taking aspirin 81mg every day if you are not at increased risk for bleeding and are willing to take it every day for at least 10 years. On the basis of your age and calculated risk for heart disease or stroke over 7.5%, the ACC/AHA guidelines suggest you should be on a moderate to high intensity statin. Based on your age, your blood pressure is well-controlled.

Demography	Cholesterol	Blood pressure	Risk factors
Age: 50	Total: 200	Systolic: 135	Diabetes: no
Gender: male	HDL: 40	Diastolic: 85	Smoking: yes
Race: not African-American		On medication: no	

Would/Should you convince a patient with these characteristics that they need blood pressure medication?

#### SYSTEMATIC REVIEW 6

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#### ACCEPTED MANUSCRIPT

#### Hydrochlorothiazide use and risk of non-melanoma skin cancer: A nationwide case-control study from Denmark

#### Results

High use of hydrochlorothiazide ( $\geq$ 50,000 mg) was associated with ORs of 1.29 (95% confidence interval [CI] 1.23-1.35) for BCC and 3.98 (95% CI 3.68-4.31) for SCC. We found clear dose-response relationships between hydrochlorothiazide use and both BCC and SCC; the highest cumulative dose category ( $\geq$ 200,000 mg HCTZ) had ORs of 1.54 (95% CI 1.38-1.71) and 7.38 (95% CI 6.32-8.60) for BCC and SCC, respectively. Use of other diuretics and antihypertensives was not associated with NMSC.

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outcomes compared to other anti-hypertensives

#### ELIGIBILITY CRITERIA 6

- Randomized control trials
- Adults (≥18 years of age) with primary HTN or due to CKD
- Intervention included target BP that was more intensive or lower than standard target BP
- Outcome included all-cause mortality, CV mortality, major CV events, MI, stroke, heart failure, or renal outcomes

#### STUDY SELECTION 6

- Total of 33 publications from 15 studies considered
- 14 publications excluded because outcomes reported in another publication, outcome presented by subgroup, no outcome of interest, no in-trial results presented, intent to treat analysis not presented or event counts unavailable

# STUDY CHARACTERISTICS 6

- 19 publications from 1998-2015
- 9 had SBP target <130 for the lower therapy group
- Many included patients with comorbid conditions
- Most excluded prior or recent MI or stroke, secondary hypertension, CHF, or other serious illnessess
- Mean follow-up 1.6 to 8.4 years
- Mean age at baseline 36.3 years to 76.6 years with 8 studies mean age of ≥60 years at baseline

# ANALYSIS OF RESULTS 6

- Any lower BP target vs. standard or higher BP target found that greater BP lowering significantly reduced the risks of:
  - 1. Major CV event (RR: 0.81)
  - 2. MI (RR: 0.86)
  - 3. Stroke (RR: 0.77)
  - 4. Heart Failure (RR:0.75)

Major CV event: composite outcome of CV death, stroke, MI, and heart failure

### ANALYSIS OF RESULTS 6

- Limit to SBP <130 in the lower BP target group vs. higher BP target:
- 1. Major CV events (RR: 0.84)
- 2. Stroke (RR: 0.82)
- Lost Heart failure and MI for statistical significance
- Little impact on findings if included only participants with DM, CKD, or age ≥60

# LIMITATIONS OF GUIDELINES 6

- Differences in time periods and study designs
- Protocol differences
- Unable to pool subgroup findings secondary to variable reporting in trials
- Outcome definitions varied

# SUMMARY OF GUIDELINES 5

	SBP	DBP
Normal	<120	<80
Elevated	120–129	<80
Hypertension		
Stage 1	130–139	80–89
• Stage 2	≥140	≥90

• Give Meds if ASCVD risk greater than 10 % for stage 1 and all people in stage 2

# WHY DIFFERENT FROM JNC 8? 5,6

- JNC 8 only used systematic review of original studies
- Systematic reviews and meta-analyses were not included in the formal evidence review
- Evidence by the different groups identified different target BP levels and subsequent confusion in clinical recommendations
- The new recommendations included new evidence from clinical studies and presented in a rigorous metaanalysis

# SPRINT TRIAL 7

- Published in 2015
- Randomly assigned 9361 people with BP >130 but <180 and an increased cardiovascular risk to target less than 120 or less than 140
- Age greater than 50
- Increased CV risk defined as one or more of the following:
  - Clinical or subclinical CV disease other than stroke
  - CKD with eGFR of 20 to less than 60 ml/min
  - 15% or greater Framingham score
  - Age 75 or greater
- Diabetics and previous stroke excluded

#### PRIMARY OUTCOME 7

- MI
- Stroke
- Other Acute Coronary Syndrome
- Heart Failure
- Death from Cardiovascular cause

Median follow-up 3.26 years

#### ELIGIBILITY 7



#### BASELINE CHARACTERISTICS 7

Characteristic	Intensive Treatment (N=4678)	Standard Treatment (N = 4683)
Criterion for increased cardiovascular risk — no. (%)†		
Age ≥75 yr	1317 (28.2)	1319 (28.2)
Chronic kidney disease‡	1330 (28.4)	1316 (28.1)
Cardiovascular disease	940 (20.1)	937 (20.0)
Clinical	779 (16.7)	783 (16.7)
Subclinical	247 (5.3)	246 (5.3)
Framingham 10-yr cardiovascular disease risk score ≥15%	3556 (76.0)	3547 (75.7)
Female sex — no. (%)	1684 (36.0)	1648 (35.2)
Age — yr		
Overall	67.9±9.4	67.9±9.5
Among those ≥75 yr of age	79.8±3.9	79.9±4.1
Race or ethnic group — no. (%)∬		
Non-Hispanic black	1379 (29.5)	1423 (30.4)
Hispanic	503 (10.8)	481 (10.3)
Non-Hispanic white	2698 (57.7)	2701 (57.7)
Other	98 (2.1)	78 (1.7)
Black race§¶	1454 (31.1)	1493 (31.9)
Baseline blood pressure — mm Hg		
Systolic	139.7±15.8	139.7±15.4
Diastolic	78.2±11.9	78.0±12.0

#### RESULTS 7

Table 2. Primary and Secondary Outcomes and Renal Outcomes.*								
Outcome	Intensive Treatment		Standard Treatment		Hazard Ratio (95% CI)	P Value		
	no. of patients (%)	% per year	no. of patients (%)	% per year				
All participants	(N = 4678)		(N=4683)					
Primary outcome†	243 (5.2)	1.65	319 (6.8)	2.19	0.75 (0.64–0.89)	<0.001		
Secondary outcomes								
Myocardial infarction	97 (2.1)	0.65	116 (2.5)	0.78	0.83 (0.64–1.09)	0.19		
Acute coronary syndrome	40 (0.9)	0.27	40 (0.9)	0.27	1.00 (0.64–1.55)	0.99		
Stroke	62 (1.3)	0.41	70 (1.5)	0.47	0.89 (0.63-1.25)	0.50		
Heart failure	62 (1.3)	0.41	100 (2.1)	0.67	0.62 (0.45-0.84)	0.002		
Death from cardiovascular causes	37 (0.8)	0.25	65 (1.4)	0.43	0.57 (0.38–0.85)	0.005		
Death from any cause	155 (3.3)	1.03	210 (4.5)	1.40	0.73 (0.60-0.90)	0.003		
Primary outcome or death	332 (7.1)	2.25	423 (9.0)	2.90	0.78 (0.67-0.90)	< 0.001		

#### ADVERSE EVENTS 7

Variable	Intensive Treatment (N = 4678)	Standard Treatment (N = 4683)	Hazard Ratio	P Value
	no. of po			
Serious adverse event*	1793 (38.3)	1736 (37.1)	1.04	0.25
Conditions of interest				
Serious adverse event only				
Hypotension	110 (2.4)	66 (1.4)	1.67	0.001
Syncope	107 (2.3)	80 (1.7)	1.33	0.05
Bradycardia	87 (1.9)	73 (1.6)	1.19	0.28
Electrolyte abnormality	144 (3.1)	107 (2.3)	1.35	0.02
Injurious fall†	105 (2.2)	110 (2.3)	0.95	0.71
Acute kidney injury or acute renal failure‡	193 (4.1)	117 (2.5)	1.66	< 0.001
Emergency department visit or serious adverse event				
Hypotension	158 (3.4)	93 (2.0)	1.70	< 0.001
Syncope	163 (3.5)	113 (2.4)	1.44	0.003
Bradycardia	104 (2.2)	83 (1.8)	1.25	0.13
Electrolyte abnormality	177 (3.8)	129 (2.8)	1.38	0.006
Injurious fall†	334 (7.1)	332 (7.1)	1.00	0.97
Acute kidney injury or acute renal failure:	204 (4.4)	120 (2.6)	1.71	< 0.001

\* A serious adverse event was defined as an event that was fatal or life-threatening, that resulted in clinically significant or persistent disability, that required or prolonged a hospitalization, or that was judged by the investigator to represent a clinically significant hazard or harm to the participant that might require medical or surgical intervention to prevent one of the other events listed above.

# TRIALS CONCLUSIONS 7

- 1. Intense treatment group had 25% lower relative risk of primary outcome, 38% lower relative risk for heart failure, 43% lower relative risk for death from CV cause, 27% lower relative risk for death from any cause
- 2. NNT was 61 for primary outcome and number needed to prevent one death from any cause was 90
- 3. Benefits with respect to primary outcome and death were across all ages and subgroups

#### DISCUSSION 7

- ACCORD vs. SPRINT
  - Diabetics vs. Diabetics excluded
- Same BP goals but ACCORD results not statistically significant
- Twice as many patients enrolled in SPRINT
- SPRINT participants older (68 vs 62)

#### CRITICAL REVIEW

- Only 2 subgroups that were statistically significant
  - Heart failure with ARR 0.84%
  - Death from CV cause with ARR 0.63%
- Once pooled, primary outcome becomes significant
  - ARR 1.6%

# RESULTS 7

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#### CRITICAL REVIEW

- Only 2 subgroups that were statistically significant
  - Heart failure with ARR 0.84%
  - Death from CV cause with ARR 0.63%
- Once pooled, primary outcome becomes significant
  ARR 1.6%
- Cannot conclude death from any cause a result of BP lowering (Remember older population, mean age 68)
- Few patients were untreated at baseline, about 9%, so SPRINT provides little if any insight regarding BP lowering medication initiation for untreated people with SBP 130-139

#### PRACTICAL CONCERN

- At 1 year, mean blood pressure 121.4 in intense group vs. 136.2 in standard group
- More than half of the people in intensive treatment group could not reach goal and required on average 1 more medication to achieve lower average
- Achieving results will be more demanding and time consuming, raising costs for medications and increased clinic visits each year

# PRACTICAL QUESTIONS

- Can we obtain these ideal results within our practices?
- Should SPRINT's blood pressure threshold recommendations be given to a general population given how high risk they were to start with? Remember ACCORD used diabetics and results weren't significant.
- Will the small statistically significant results be negated in routine clinical practice?
- Will our patients be willing to take another pill to try to achieve these results? Especially when their main concern when it relates to hypertension is risk of stroke and heart attack and these don't show statistical improvement in an ideal world trial

### MIPS HYPERTENSION MEASURE 8

 Percentage of patients 18-85 years of age who had a diagnosis of hypertension and whose blood pressure was adequately controlled (<140/90) during the measurement period

#### QUESTIONS?



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