Hypertension Guidelines Have Your Blood Pressure Up?

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Conflicts of Interest

- Diana Isaacs, PharmD, BCPS, BC-ADM, has no actual or potential conflicts of interest in relation to this program.

Learning Objectives-Pharmacist

- Discuss the most recent hypertension guidelines including JNC8 and the American Society of Hypertension/International Society of Hypertension.
- Describe how the current guidelines differ between previous guidelines and other organization guidelines and what evidence exists for these changes.
- Identify blood pressure goals and recommended drug therapy for special populations including the elderly, African Americans, patients with diabetes, and patients with chronic kidney disease.

Learning Objectives-Technician

- Define hypertension (HTN).
- Identify drug classes used to treat hypertension.
- Define blood pressure goals for specified patient populations.

Patient Case

AL is a 65 year old African American male. AL's in-office BP today is 148/88mmHg and same on repeat. One month ago, AL's BP was 146/88mmHg.

- PMH: Sleep apnea, allergic rhinitis
- Meds: Loratadine 10mg po daily
- No known drug allergies/ADR's
- Height: 5'11" 225lbs, BMI=31.4
- Family history: mother with type 2 diabetes
- Social history: non-smoker, frequently eats out at restaurants, adds salt to food

Questions to Think About

- How would you classify AL's blood pressure?
  - Normal, Pre-hypertension, Stage 1 HTN, Stage 2 HTN
- What is AL's blood pressure goal?
- How would you treat AL's blood pressure?
- How would your treatment plan differ if AL had diabetes? CKD?

Definition/Epidemiology

- HTN defined: BP≥140/90mm Hg on repeated examination
- About 1/3 of adults have HTN
  - Most common condition seen in primary care
- Close relationship with high BP and risk of MI, stroke, renal failure and death
- Events lowest at BP=115/75 mmHg
  - CV and stroke events double for each increase of 20/10mmHg in SBP/DBP

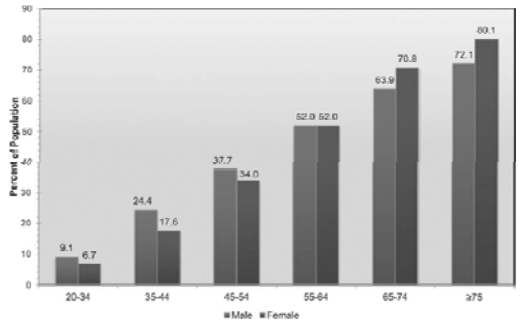
Weber MA, et al. J Clin Hypertens. 2014 Jan;16(1):14-26.
James PA, et al. *JAMA*. 2014;311(5):507-520.

Trends in Awareness, Treatment, and Control of HTN

	National Health & Nutrition Examination Survey, %				
	1976-80	1988-91	1991-94	1999-2000	2007-10
Awareness	51	73	68	70	81.5
Treatment	31	55	54	59	74.9
Control	10	29	27	34	52.5

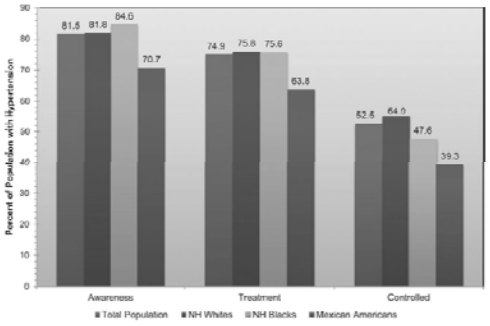
Chobanian AV et al. *JAMA*. 2003;289:2560-2572.
Go A S et al. Circulation. 2014;129:e28-e292

Prevalence of high blood pressure in adults ≥20 years of age by age and sex (National Health and Nutrition Examination Survey: 2007–2010).



Go A S et al. Circulation. 2014;129:e28-e292

Extent of awareness, treatment, and control of high blood pressure by race/ethnicity (National Health and Nutrition Examination Survey: 2007–2010).



Go A S et al. Circulation. 2014;129:e28-e292

HTN in Black Patients

- Higher prevalence in black patients
- High BP develops earlier in life and average BP is higher
- Higher risk compared to whites
  - 1.3-times more nonfatal strokes
  - 1.8-times more fatal strokes
  - 1.5-times more deaths attributed to HTN
  - 4.2-times more end stage kidney disease
- The odds of reaching BP goal is 27% lower in blacks than whites

Go A S et al. Circulation. 2014;129:e28-e292

Joint National Committee (JNC7) Guidelines -Published in 2003

We anxiously waited for JNC8, but the years kept passing…

Critics dub JNC-8 as 'JNC-Late'

And then all of a sudden!

A Flood of HTN Guidelines

- UK: National Institute for Health and Clinical Excellence (NICE)-2011
- Kidney Disease: Improving Global Outcomes (KDIGO)-2012
- European Society of Cardiology/European Society of Hypertension-2013
- American College of Cardiology/American Heart Association/Centers for Disease Control (ACC/AHA/CDC) Scientific Advisory-2013
- 2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults-2013 ("JNC8")
- American Society of Hypertension/International Society of Hypertension (ASH/ISH)-2013
- Canadian Hypertension Educational Program (CHEP)-2014
- American Diabetes Association (ADA) Standards of Care-2014

A Look Into JNC

- The Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood pressure (JNC)
- JNC1 through 7 were consensus guidelines produced by the National Heart, Lung, and Blood Institute (NHLBI)
  - JNC 1: published 1976
  - JNC 2: published 1980
  - JNC 3: published 1984
  - JNC 4: published 1988
  - JNC 5: published 1992
  - JNC 6 published 1997
  - JNC 7 published 2003
  - JNC8 panel assembled in 2008
- New guideline development process in 2011
  - The IOM Report "Clinical Practice Guidelines We Can Trust"
- NHLBI pulled out from all guidelines in June, 2013
- The 2014 HTN guideline released in Dec, 2013 by the JNC8 appointed committee is not endorsed by any organization

Refocusing the Agenda on Cardiovascular Guidelines: An Announcement from the National Heart, Lung, and Blood Institute. Available at: http://circ.ahajournals.org/content/early/2013/06/18/CIRCULATIONAHA.113.004587 Accessed: July 30, 2014
National Heart, Lung, and Blood Institute. Available at: http://www.nhlbi.nih.gov/health-pro/guidelines/current/hypertension-pro/7/index.htm. Accessed July 30, 2014

JNC8 Headlines

theheart.org on Medscape > Private practice with Dr Seth Bilazarian

Hypertension Guidelines: Clear as Mud

Hypertension Guidelines in Need of Guidance

HEART DISEASE

Why Doctors Are Fighting Over Blood Pressure Guidelines

Hypertension Guide May Affect 7.4 Million

By GINA KOLATA
Published: December 18, 2013

Heartwire

ASH/ISH Issue Separate Hypertension Guidelines From JNC 8, Hinting at Discord

How is JNC8 Different From JNC7?

Topic	JNC7	JNC8
Methodology	Nonsystematic literature review including a range of study designs	Systematic review restricted to randomized controlled trials and focused on 3 critical questions
Definitions	Defines pre-HTN and HTN	Defines thresholds for pharmacologic treatment
Treatment goals	Separate treatment goals for comorbid conditions (CKD, DM)	Separate treatment goals for patients ≥60 years
Lifestyle recommendations	Recommendations provided	Endorsed Lifestyle Work Group recommendations
Drug therapy	• 5 classes as initial treatment (BB, ACEI or ARB, diuretic, CCB) • Thiazide diuretics as initial therapy for most • Specified meds for compelling indications	• 4 classes recommended (ACEI or ARB, CCB, diuretics) and doses based on RCT evidence • Specified meds for race, CKD, DM

James PA, et al. *JAMA.* 2014;311(5):507-520.

JNC8: Evidence Review

- Only included randomized, controlled trials (RCT's)
  - No observational studies or meta-analyses
- Inclusion: Must measure at least 1 major health outcomes
  - Ex: mortality, myocardial infarction, heart failure, stroke, coronary revascularization, peripheral revascularization, end stage renal disease
- Exclusion:
  - Follow-up<1 year
  - Participants<18years
  - Sample size<100
  - Participants with normal BP or pre-hypertension

James PA, et al. *JAMA.* 2014;311(5):507-520

JNC8 : 3 Critical Questions

1. Threshold to initiate BP lowering treatment?
2. What BP goals lead to improved outcomes?
3. What drug classes are best?

James PA, et al. *JAMA.* 2014;311(5):507-520.

Strength of Recommendation

Strength of Recommendation	Grade
Strong: High certainty based on evidence that net benefit is substantial.	**A**
Moderate: Moderate certainty that net benefit is moderate to substantial or high certainty the net benefit is moderate.	**B**
Weak: At least moderate certainty based on evidence that there is a small net benefit.	**C**
Against: At least moderate certainty based on evidence that it has no net benefit or risks/harms outweigh benefits.	**D**
Expert Opinion: Insufficient evidence or evidence is unclear or conflicting but the committee thought it was important to provide clinical guidance. Further research in this area needed.	**E**
No Recommendation for or Against: Insufficient evidence of evidence is unclear or conflicting. Further research is recommended in this area.	**N**

James PA, et al. *JAMA.* 2014;311(5):507-520

JNC8 Recommendations

#	Recommendation	Grade
1	Patients≥60 years, initiate pharmacologic treatment at SBP≥150 or DBP≥90. Goal<150/90. Corollary: If SBP<140 and treatment is well tolerated, treatment does not need to be adjusted	A E
2	Patients<60 years, initiate pharmacologic treatment at DBP≥90. Goal DBP<90.	A: Ages 30-59 E: Ages 18-29
3	Patients<60 years, initiate pharmacologic treatment at SBP≥140. Goal SBP<140.	E
4	Patients≥18 years with CKD, initiate pharmacologic treatment at SBP≥140 or DBP≥90. Goal<140/90.	E
5	Patients≥18 with diabetes, initiate pharmacologic treatment at SBP≥140 or DBP≥90. Goal<140/90.	E

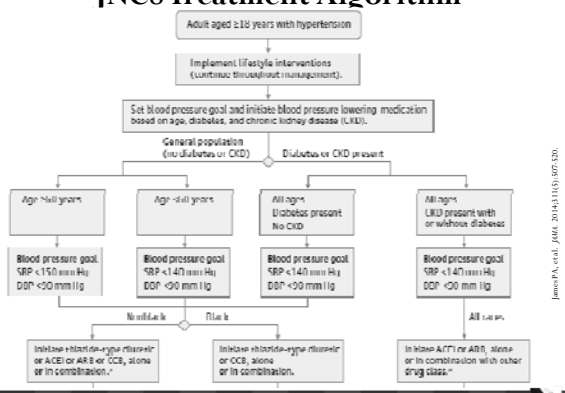
James PA, et al. *JAMA.* 2014;311(5):507-520.

JNC8 Recommendations

#	Recommendation	Grade
6	Initial antihypertensive treatment for nonblacks (includes DM): Thiazides, CCB, ACEI, ARB	B
7	Initial antihypertensive treatment for blacks: Thiazides or CCB	B C (with DM)
8	Initial antihypertensive treatment for patients≥18 years with CKD: ACEI or ARB to improve kidney outcomes	B
9	Strategies for Dosing Antihypertensives: ❑ Start 1 drug, titrate to maximum dose, then add 2nd drug • Thiazide, CCB, ACEI or ARB • If still above goal, select a 3rd agent from above list • Avoid ACEI + ARB combo ❑ Start 1 drug, add 2nd before achieving maximum dose and titrate both to goal • If still above goal, titrate to max doses of 1st 2 drugs and then add a 3rd ❑ Begin with 2 drugs at the same time (separate or combo form) • Consider if BP≥160/100 or if BP≥20/10 above goal	E

James PA, et al. *JAMA.* 2014;311(5):507-520.

JNC8 Treatment Algorithm



James PA, et al. *JAMA.* 2014;311(5):507-520.

Evidence-Based Antihypertensive Dosing

Antihypertensive Medication	Initial Daily Dose, mg	Target Dose in RCTs Reviewed, mg	No. of Doses per Day
ACE Inhibitors			
Captopril	50	150-200	2
Enalapril	5	20	1-2
Lisinopril	10	40	1
Angiotensin receptor blockers			
Eprosartan	400	600-800	1-2
Candesartan	4	12-32	1
Losartan	50	100	1-2
Valsartan	40-80	160-320	1
Irbesartan	75	300	1
β-Blockers			
Atenolol	25-50	100	1
Metoprolol	50	100-200	1-2
Calcium Channel blockers			
Amlodipine	2.5	10	1
Diltiazem extended release	120-180	360	1
Nitrendipine	10	20	1-2
Thiazide-type diuretics			
Bendroflumethiazide	5	10	1
Chlorthalidone	12.5	12.5-25	1
Hydrochlorothiazide	12.5-25	25-100*	1-2
Indapamide	1.25	1.25-2.5	1

James PA, et al. *JAMA.* 2014;311(5):507-520.

The Evidence Behind the JNC8 Recommendations

Trials in Elderly to Support BP Goal<150/90

Grade A Recommendation

Trial	Inclusion	Treatment (tx)	Outcomes
HYVET (HTN in the Very Elderly) N=3845 2008	Age≥80 with SBP≥160mmHg Mean baseline SBP=173mmHg Mean follow-up: 2.1 yrs	BP goal<150/80mmHg Mean SBP: 144 (tx) vs 150 (placebo) mmHg Perindopril +/- indapamide	↓ **fatal or non-fatal stroke (primary):** HR 0.7, CI: 0.49-1.01, P=0.06 ↓**morality**: HR=0.79, CI:0.65-0.95, P=0.02 ↓**death from stroke:** HR=0.661, CI: 0.38-0.99, P=0.046 ↓ **fatal or non-fatal HF:** HR=0.36, CI: 0.22-0.58, P<0.001
SYST-EUR (Systolic HTN in Europe) N=4695 1997	Age≥60 with SBP 160-219 and DBP<95mmHg Mean baseline SBP=173.8mmHg Median follow-up: 2 yrs	SBP goal<150 and ↓ SBP by ≥20mmHg Mean ↓ in BP: 23/7(tx) vs 13/2 (placebo)mmHg Nitrendipine +/- enalapril +/- HCTZ	↓ **fatal and non-fatal stroke (primary):** HR: 0.59, CI: 0.38-0.79, P<0.01 ↓ **fatal and non-fatal cardiac endpoints:** HR: 0.71, CI: 0.54-0.94, P<0.05 44% ↓ **non-fatal stroke ,** p=0.007 56% ↓ **fatal MI,** p=0.08 36% ↓ **non-fatal HF**, p=0.06

Beckett NS et al. N Engl J Med 2008;358:1887-98, Lancet. 1997;350(9080):757-764, James PA, et al. JAMA. 2014;311(5):507-520.

Trials in Elderly to Support BP Goal<150/90

Trial	Inclusion	Treatment(tx)	Outcomes
SHEP (Systolic HTN in the Elderly Program) N=4736 1991	Age≥60 , SBP 160-219, DBP<90mmHg Mean follow-up: 4.5yrs	SBP<160 or ↓ SBP by ≥20mmHg Mean SBP: 144 (tx) vs 155.1 (placebo) mmHg Chlorthalidone +/- atenolol +/-reserpine	↓**Non-fatal plus fatal stroke (primary):** RR: 0.64, CI:0.50-0.82, p=0.0003 ↓ **Non-fatal MI:** RR: 0.67,CI:0.47-0.96 ↓ **Symptomatic MI events:** 63 (tx) vs 98 (placebo), p=0 .005 ↓ **CHD:** RR:0.75,CI:0.60-0.94 ↓ **Non-fatal MI or CHD deaths:** RR: 0.73,CI:0.57-0.94 **Fatal and non-fatal HF:** RR: 0.51, CI:0.37-0.71, p<0.001
EWPHE (European Working Party on High Blood Pressure in the Elderly) N=840 1985	Age≥60, SBP 160-239 and DBP 90-119 mmHg Mean follow-up: 4.6yrs	SBP<160 mmHg Mean difference in BP: 19/5mmHg HCTZ/ triamterene +/- methyldopa	**Non-fatal cerebrovascular events (primary)**: 11% ↓per 1000 py, p<0.05 **Cerebrovascular deaths (primary)** 32% ↓in tx, CI (-61-19),p=0.16 **Cardiac mortality:** 38% ↓per 1000 py, p=0.036 **Severe CHF:** 8% ↓per 1000 py, p < 0.05

JAMA. 1991;265(24):3255-3264. / *Hypertens Suppl.* 1986;4(6):S642-647., James PA, et al. *JAMA.* 2014;311(5):507-520.

No benefit of SBP<140 in age≥60

Trial	Inclusion	Treatment (tx)	Outcomes (Placebo vs. tx)
JATOS (Japanese Trial to Assess Optimal systolic BP in Elderly Hypertensive Patients) N=4418 2008	Age 65-85, SBP≥160 and DBP<120mmHg Mean follow-up: 2 yrs	SBP<140 vs SBP 140-160 Mean 135.9 (tx) vs. 145.6 (placebo) Efonidipine +/- others	**Primary endpoint:** Events: 86 vs 86, p=0.99 **Death from any cause:** Events: 54 vs 42, p=0.22 **Cerebrovascular disease:** Events: 52 vs 49, p=0.77 **Cardiac and vascular disease:** Events: 26 vs 28, p=0.78
VALISH (Valsartan in Elderly Isolated Systolic HTN) N=3260 2010	Age 70-85 SBP≥160 and DBP<90mmHg Mean follow-up: 2.85 yrs	SBP<140 vs. SBP140-149mmHg Mean 136.6 (tx) vs. 142 (placebo)mmHg Valsartan +/- others	**Composite of CV events (primary)** Events: 52 vs. 47, p=0.564 **All cause death:** Events: 30 vs 24, p=0.362 **Fatal and non-fatal MI:** Events:4 vs. 5, p=0.761 **Fatal and non-fatal stroke:** Events: 23 vs. 16, p=0.237

Hypertens Res.2008;31:2115-27.
Hypertension. 2010;56:196-202.

The Controversy:

In the absence of definitive evidence, is increasing the SBP goal the right approach?

Annals of Internal Medicine | SPECIAL ARTICLE

Evidence Supporting a Systolic Blood Pressure Goal of Less Than 150 mm Hg in Patients Aged 60 Years or Older: The Minority View

Jackson T. Wright Jr., MD, PhD; Lawrence J. Fine, MD, DrPH; Daniel T. Lackland, DrPH; Gbenga Ogedegbe, MD, MPH, MS; and Cheryl R. Dennison Himmelfarb, PhD, RN, ANP

The Minority View

- Report from 5 members of the JNC8 panel detailing why they disagree with the SBP goal <150/90 in patients≥60
  - More than half of persons with HTN in the US are over 60
  - Age increases risk for CV events
    - Higher BP goals in elderly will lead to more CV risk
  - Observational studies and RCT data that the panel did not systematically review more strongly support the SBP goal<140
    - Especially in high risk individuals

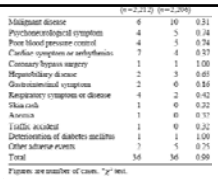
Wright, JT et al. *Ann Intern Med.* 2014;160(7):499-503

Trials not Included by JNC8

- SPS3 (Secondary Prevention of Small Subcortical Strokes)
  - SBP target <130 versus 144 in 3020 patients (mean age, 63 years) reduced subsequent strokes by 19% (*P* =0.08) and hemorrhagic strokes by nearly 50% (*P*=0.01)
- FEVER (Felodipine Event Reduction Trial)
  - Reported a 44% (*P*=0.001) reduction in all strokes in a subgroup analysis of patients>65
- 2 Meta-analyses showed benefit with BP goal<140

Wright, JT et al. *Ann Intern Med.* 2014;160(7):499-503

Minority View Conclusions



	(n=2,212)	(n=2,206)	
Malignant disease	6	10	0.31
Psychoneurological symptom	4	5	0.38
Poor blood pressure control	4	5	0.74
Cardiac symptom or arrhythmias	7	4	0.37
Coronary bypass surgery	1	1	1.00
Hepatobiliary disease	2	3	0.65
Gastrointestinal symptom	2	0	0.16
Respiratory symptom or disease	4	2	0.42
Skin rash	1	0	0.32
Anemia	1	0	0.32
Traffic accident	1	0	0.32
Deterioration of diabetes mellitus	1	1	1.00
Other adverse events	3	5	0.75
Total	36	36	0.99

Figures are number of cases. "p" test.

- JATOS &VALISH were underpowered
  - Lower goal was still safe
- HYVET and SHEP trials provide evidence that reducing SBP to ~140 has substantial benefit without major harm
- BP goal should be <140/90 in patients <80 and **<150/90 in patients ≥80**
- Other guidelines support this goal
  - Canada, Europe, UK, ASH/ISH, ACCF/AHA

Hypertens Res.2008;31:2115-27
Wright, JT et al. *Ann Intern Med.* 2014;160(7):499-503

Evidence in Diabetes: BP Goal<140/90

Grade E Recommendation

Trial	Inclusion	Treatment (tx)	Outcomes
ACCORD-BP (Action to Control Cardiovascular Risk in Diabetes) N=4733 2010	T2DM, A1c≥7.5%, Age≥40 SBP: 130-180mmHg Mean follow-up: 4.7 yrs	SBP goal<140 vs <120mmHg Mean SBP=119.3 vs. 133.1mmHg ACEI or ARB or BB or CCB or diuretic or combo	**↓Non-fatal stroke:** HR: 0.63, CI:0.41-0.96, p=0.03 **↓Any stroke:** HR: 0.59, CI:0.39- 0.89, p = 0.01 **↑syncope and hyperkalemia in<120 group:** (3.3% vs 1.3%, p=0.001) No statistical difference in composite of first occurrence of major CV event (**primary**), death, non-fatal MI, major coronary disease event, fatal or non-fatal HF, renal failure, ESRD
UKPDS (UK Prospective Diabetes Study Group) N=1148 1998	T2DM Age 25-65 BP≥150/85 mmHg Mean follow-up: 8.4 yrs	SBP goal<150/85 vs. <185/105mmHg Mean BP change: 15/12 vs. 12/7mmHg Captopril or atenolol	**Any DM related endpoint (primary):** RR:0.76, CI:0.62-0.92,p=0.0046 **Stroke:** RR:0.56,CI:0.35-0.89,p=0.013 **HF:**RR: 0.44,CI:0.20,-0.94, p=0.0043 **Death related to DM:** RR:0.68,CI:0.49-0.94,p=0.019 No statistical different in all cause mortality, MI, sudden death, death from renal failure

BMJ. 1998;317(7160):703-713.
N Engl J Med. 2010;362(17):1575-1585

Evidence in Diabetes: BP Goal<140/90

Trial	Inclusion	Treatment	Outcomes
HOT (Hypertension Optimal Treatment) N=18790 (1501 with DM) 1998	T2DM, age 50-80 with DBP 100-115mmHg Mean follow-up: 3.8 yrs	Compared DBP≤80 vs ≤85 vs ≤90mmHg Mean BP not reported for DM subpopulation Felopidpine +/-ACE +/-BB +/- diuretic	**Major CV Events (Primary):** 45(≤90) vs. 22(≤80), HR:2.06, CI: 1.24-3.44 **Total mortality: ≤ 90 vs ≤ 80:** RR: 1.77, CI:0.98-3.21 No statistical difference in MI, stroke for ≤90 vs. ≤ 80. No statistical difference in any outcomes for ≤ 90 or ≤ 80 vs. ≤ 85

Lancet. 1998;351(9118):1755-1762,.

Rationale for Diabetes Recommendations

- ACCORD-BP had similar outcomes for SBP=140 vs SBP=120
- HOT Trial supports DBP<80 over DBP<90, but was considered low quality evidence
  - ❖ Post hoc analysis of a small subgroup (8% of study population)
- UKPDS: BP=150/85 had better outcomes than 180/105
  - ❖ However, unable to determine if positive outcomes from SBP or DBP
- Lack of evidence comparing BP<150/90 vs. <140/90
  - ❖ Expert opinion to make BP goal<140/90
- Large HTN trials including patients with diabetes had similar outcomes comparing ACEI, ARB, thiazide, CCB
  - ❖ Grade B recommendation to initiate treatment with any of these agents

James PA, et al. *JAMA.* 2014;311(5):507-520.

Thiazides & CCB in Black Patients:

Grade B

Trial	Inclusion	Treatment (tx)	Outcomes
ALLHAT (The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial) N=33,357 total Black=35% CCB vs. ACEI N=18,102 ACEI vs. Thiazide N=24,309 2002	Age≥55 with HTN and at least 1 additional risk factor for CHD Mean baseline BP=146/84mmHg Mean follow-up=4.9yrs	BP goal<140/90mmHg Amlodipine vs. lisinopril +/- atenolol, clonidine, reserpine Chlorthalidone vs. lisinopril +/- atenolol, clonidine, reserpine	CHD (Primary): no difference ↑ Stroke with lisinopril vs. amlodipine RR:1.51, CI:1.22-1.86 ↑ Stroke with lisinopril vs. chlorthalidone, RR:1.40 CI: 1.17-1.68

JAMA. 2002;288(23):2981-2997.
Leenan et al. *Hypertension.* 2006;48:374-384

Black Population Concerns

- International Society on Hypertension in Blacks Consensus Statement-2010
  - Support CCB and diuretic as 1st line
  - BP goal<135/85 or <130/80 with target organ damage
- Association of Black Cardiologists Position
  - African Americans are at higher risk for CV events
  - Increasing the BP goal for patients ≥60 may worsen health disparities and have detrimental effects for black patients
  - Wait for further guidance from other organizations before changing treatment goals

Flack JM, et al. Hypertension. 2010;56L780-800.
Krakoff, LR. Et al. Journal of the American College of Cardiology. 2014. Vol.64, no.4, 394-402.

JNC8 Strengths

- Rigorous process of evidence review
- Simplifies BP management, 1 BP goal for most
- Algorithm provided along with evidence based antihypertensive dosing
- Guideline is concise and straight to the point (14 pages)
- Online supplement provides in depth information on evidence review (316 pages)

James PA, et al. *JAMA*. 2014;311(5):507-520.

JNC8 Limitations

- Limited in scope, only focused on 3 critical questions
- Often not enough RCT evidence to make strong recommendations
- Guideline was not endorsed by any federal agency or professional society prior to publication
- No public comment period
- 5/10 recommendations (including corollary) are based on expert opinion

James PA, et al. *JAMA*. 2014;311(5):507-520.

The American Society of Hypertension/International Society of Hypertension Guideline

(ASH/ISH Guideline)

"These guidelines should be considered more as 'an expert opinion piece,' given that they are not systematically evidence-based and were not developed using guideline development protocol stipulated by the Institute of Medicine (IOM)."

http://www.ash-us.org/About-Hypertension/Hypertension-Guidelines.aspx. Accessed July 30, 2014

ASH/ISH HTN Guidelines

- Written to provide a straight-forward approach to manage HTN in the community
- More comprehensive than JNC8
  - Includes HTN definition, classification, measurement, diagnosis, physical exam, tests, causes, nonpharm treatment, drug class monitoring, resistant HTN
- Many recommendations based on expert opinion and experience
  - No rating of evidence or grades for recommendations
  - No online supplement
- 3 authors were the same as JNC8

Weber MA et al. J Clin Hypertens. 2014 Jan;16(1):14-26

ASH/ISH Summary

- Hypertension defined:
  - BP≥140/90 or SBP≥150 if age ≥80 on repeat exam
  - BP≥180, consider diagnosis/treatment after 1 exam
- For all patients 18-79, BP goal<140/90
  - Includes CKD, Diabetes
- For all **patients≥80**, BP goal<150/90
- HTN Classification

Classification	SBP (mm Hg)	DBP (mm Hg)
Normal	< 120	< 80
Prehypertension	120-139	80-89
Stage 1 HTN	140-159	90-99
Stage 2 HTN	≥160	≥100

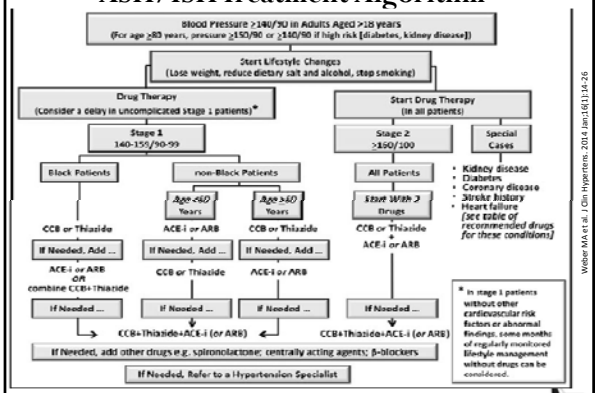
Weber MA et al. J Clin Hypertens. 2014 Jan;16(1):14-26

Treatment Differences from JNC8

- Stage 1 HTN
  - If no other CV risk factors, may start with lifestyle modifications for 6-12 months
- Non black <60→start with ACEI or ARB
- Non black≥60→start with CCB or thiazide
- Diabetes→use ACEI
- More suggestive of starting 2-drug treatment in patients with stage 2 HTN

Weber MA et al. J Clin Hypertens. 2014 Jan;16(1):14-26

ASH/ISH Treatment Algorithm



Weber MA et al. J Clin Hypertens. 2014 Jan;16(1):14-26

Drugs for Specific Comorbidities

Condition	First Drug(s)	If Additional Drugs Needed to Achieve BP Goal<140/90
Diabetes	ARB or ACEI Black patients: may start with CCB or thiazide	CCB or thiazide Black patients: add on ARB or ACEI
CKD	ARB or ACEI	CCB or thiazide
Clinical CAD	Beta blocker + ARB or ACEI	CCB or thiazide
Stroke	ACEI or ARB	CCB or thiazide
Heart Failure	ARB or ACEI + beta blocker + diuretic + spironolactone	Dihydropyridine CCB

Weber MA et al. J Clin Hypertens. 2014 Jan;16(1):14-26

Resistant HTN

- 2 drugs combinations (ex. ACEI/CCB or ACEI/thiazide) control BP in ~80% patients
- Confirm BP is uncontrolled
  - Check home BP or ambulatory BP
  - Adherence
- Identify any secondary causes
  - Ex. Salt intake, sleep apnea, drug-induced, aldosterone excess
- If not controlled on 3 drugs (thiazide + ACEI/ARB + CCB)
  - Add mineralcorticoid antagonist, beta blocker, centrally acting agent, alpha blocker or direct vasodilator

Weber MA et al. J Clin Hypertens. 2014 Jan;16(1):14-26

Brief Comments on Drug Classes

ACEI /ARB's
- Side effects include hyperkalemia, cough (ACEI)
- Increase Scr up to 30%, which is reversible
- Avoid in pregnancy
- Less effective as monotherapy in black patients
- Do not combine ACEI and ARB

CCB's
- Equally effective in all racial/ethnic groups
- More evidence with dihydropyridines vs. non-dihydropyridines
- Dihydropyridines can cause peripheral edema
- Nondihydropyridines slow heart rate
- Avoid nondihydropyridines in heart failure

Thiazide Diuretics
- Side effects include hypokalemia, hyperglycemia, hyperuricemia
- Very effective in combo with ACEI or CCB
- Chlorthalidone more potent than HCTZ

Beta Blockers
- Less effective in black patients
- Side effects include reduced sexual function, fatigue, reduced exercise tolerance

Mineralcarticoid Antagonists
- Side effects include gynecomastria (spironolactone), sexual dysfunction, hyperkalemia
- Caution with eGFR<50ml/min

Direct Vasodilators
- Cause fluid retention and tachycardia
- Combine with a diuretic and beta blocker

Centrally Acting Agents
- Side effects include drowsiness, dry mouth
- Methyldopa is safe in pregnancy

Alpha Blockers
- Use for resistant HTN and/or BPH

Weber MA et al. J Clin Hypertens. 2014 Jan;16(1):14-26

ACC/AHA/CDC Scientific Advisory

- Call to action for broad-based efforts to improve HTN awareness and treatment
- Advise using treatment algorithms for HTN
- Endorse specific meds for certain populations
  - Similar to JNC7 & ASH/ISH
- AHA does not support JNC8
  - Endorses JNC7 until new guidelines come out

Go AS et al. High Blood Pressure Control. J Am coll Cardiol. 2013;00
http://www.heart.org/HEARTORG/Conditions/HighBloodPressure/PreventionTreatmentofHighBloodPressure/American-Heart-Association-backs-current-BP-treatments_UCM_459129_Article.jsp. Accessed Aug. 3rd, 2014

AHA/ACC/CDC Treatment Summary

- BP goal<140/90 for most
  - Lower targets may be appropriate for some populations
- Stage 1 HTN
  - Consider 3 month trial of lifestyle +/- thiazide
  - Add on ACEI, ARB, or CCB
- Stage 2 HTN
  - Thiazide + ACEI, ARB or CCB
  - Or ACEI + CCB
- Recheck BP at 2-4 week intervals, titrate meds to reach goals

Go AS et al. High Blood Pressure Control. J Am coll Cardiol. 2013;00

ACC/AHA Science Advisory

Modification	Recommendation	SBP Reduction (mm HG)
Reduce weight	Maintain normal body weight, BMI 18.5-24.9kg/m^2	5-20 per 10kg
Adopt DASH eating plan	Consume a diet rich in fruits, vegetables, and low-fat dairy products with a reduced content of saturated and total fats	8-14
Lower salt intake	1. Consume no more than 2400mg/day 2. Further reduce to 1500mg/day is associated with greater BP reduction 3. Reduce intake by at least 1000mg/day even if desired daily sodium intake is not achieved	2-8
Physical activity	Engage in regular aerobic physical activity such as brisk walker at least 30 min/day most days of the week	4-9
Moderation of alcohol	Limit to 2 drinks/day in men and 1 drink/day in women 1 drink=12oz beer, 1.5oz 80 proof whiskey, 5 oz wine	2-4

Go AS et al. High Blood Pressure Control. J Am coll Cardiol. 2013;00

BP Goals: Guideline Comparison

	JNC7 2003	NICE 2011	ASH/ISH 2013	ESH/ESC 2013	JNC8 2014	CHEP 2014	Disease Specific
General HTN	<140/90	<140/90	<140/90	<140/90	<140/90	<140/90	NA
Diabetes	<130/80	NA	<140/90	<140/85	<140/90	<130/80	ADA: <140/80
CKD	<130/80	NA	<140/90 Proteinurea: consider <130/80	<140/90 Proteinurea: <130/80	<140/90	<140/90	KDIGO: <140/90 Proteinurea: <130/80
Elderly	Same as general	Age≥80 <150/90	Age≥80 <150/90	Age≥80 <150/90	Age≥60 <150/90	Age≥80 <150/90	NA

JNC: Joint National Committee
NICE: National Institute for Health and Clinical Excellence
ASH/ISH: American Society of Hypertension/International Society of Hypertension
ESH/ESC: European Society of Cardiology/European Society of Hypertension
CHEP: Canadian Hypertension Education Program
ADA: American Diabetes Association
KDIGO: Kidney Disease: Improving Global Outcomes

Chobanioan AV et al. *JAMA*. 2003;289(19):2560-2572
NICE. Hypertension (CG127). http://www.nice.org.uk/Guidance/CG127 Accessed Aug 3rd, 2014
Weber MA et al. J Clin Hypertens. 2014 Jan;16(1):14-26.
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Dasgupta K et al. Canadian Journal of Cardiology 30 (2014) 485-501.
Diabetes Care 2014. (Suppl 1).Vol 37. S14-S80.
Kidney Intl Suppl 2012;2:337-414.

1st Line Agent: Guideline Comparison

	JNC7 2003	NICE 2011	ASH/ISH 2013	ESH/ESC 2013	JNC8 2014	CHEP 2014
General HTN	Thiazide	<55, ACEI or ARB	<60, ACEI or ARB	Diuretic, BB, CCB, ACEI or ARB	Thiazide, ACEI, ARB, or CCB	Thiazide, CCB, BB ACEI, or ARB
Diabetes	ACEI or ARB	NA	ACEI or ARB	ACEI or ARB	Same as general	ACE or ARB (preferred with CV risk) CCB, Thiazide
CKD	ACEI or ARB	NA	ACEI or ARB	ACEI or ARB	ACEI or ARB	ACEI or ARB
Black	Same as general	CCB	Thiazide or CCB	Diuretic or CCB	Thiazide or CCB	Same as general except avoid ACEI
Elderly	Same as general	Age≥55, CCB	Age≥60, Thiazide or CCB	Same as general	Same as general	Age≥60, Same as general except avoid BB

Chobanioan AV et al. Hypertension 2003;42:1206-52.
James PA et al. *JAMA*. 2014;311(5):507-520.
Mancia G et al. J. Hypertension 2013;31:1281-357
NICE. Hypertension (CG127). http://www.nice.org.uk/Guidance/CG127 . Accessed Aug 3, 2014
Weber MA et al. J Clin Hypertens. 2014 Jan;16(1):14-26.
Dasgupta K et al. Canadian Journal of Cardiology 30 (2014) 485-501

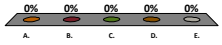
Patient Case

AL is a 65 year old African American male. AL's in-office BP today is 148/88mmHg and same on repeat. One month ago, AL's BP was 146/88mmHg.

- PMH: Sleep apnea, allergic rhinitis
- Meds: Loratadine 10mg po daily
- No known drug allergies/ADR's
- Height: 5'11", 225lbs, BMI=31.4
- Family history: mother with type 2 diabetes
- Social history: non-smoker, frequently eats out at restaurants, adds salt to food

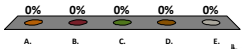
According to the in-office BP readings, what is the correct classification of AL's BP?

A. Normal blood pressure
B. Pre-hypertension
C. Stage 1 hypertension
D. Stage 2 hypertension
E. Stage 3 hypertension



What is AL's blood pressure goal according to the JNC8 panel and ASH/ISH?

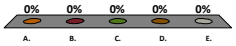
A. JNC8 and ASH/ISH<140/90
B. JNC8 and ASH/ISH<150/90
C. JNC8<140/90 and ASH/ISH<150/90
D. JNC8<150/90 and ASH/ISH<140/90
E. JNC8<160/90 and ASH/ISH<150/90



JNC: Joint National Committee
ASH/ISH: American Society of Hypertension/International Society of Hypertension

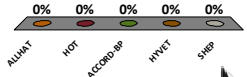
What is the most appropriate treatment at this time?

A. Lifestyle modifications only
B. Lifestyle modifications + ACEI or ARB
C. Lifestyle modifications + Thiazide or CCB
D. Lifestyle modifications + Beta blocker
E. Lifestyle modifications + Loop diuretic



Which clinical trial provides evidence for using thiazides and CCB's as preferred initial agents in black patients?

A. ALLHAT
B. HOT
C. ACCORD-BP
D. HYVET
E. SHEP



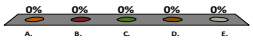
Fast forward 2 years later

AL's BP was well-controlled on chlorthalidone 12.5mg po qam and a reduced salt diet. Unfortunately, AL is diagnosed with type 2 diabetes today with an A1c=8%. AL will be starting metformin 500mg po bid, atorvastatin 10mg po daily, and aspirin 81mg po daily.

- In clinic BP=136/78, P: 72
- Home BP readings:
  - Range: 128-138/74-80, P: 70-80
- Urine alb/creat ratio =24mg/g
- Chem7, CBC, Lipid panel, LFT's are wnl except glucose=134mg/dL

What changes are most appropriate to make to AL's HTN regimen today?

A. Add an ACEI or ARB
B. Add a CCB
C. Replace chlorthalidone with an ACEI or ARB
D. Replace chlorthalidone with a CCB
E. Continue present management



Would your plan change if AL was also diagnosed with CKD?

In Summary

- New guidelines have simplified BP goals
  - <140/90 works well for most
- All patients with elevated BP should be treated with lifestyle modifications
- Thiazides, CCB, ACE-inhibitors, ARB's are 1st line agents
- Specific choice of agent/treatment depends on race, age, comorbidities, and cardiovascular risk
- New guidelines provide a general framework, but always consider the individual patient

Questions

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