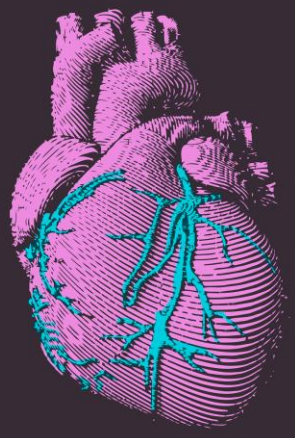


HYPERTENSION IN WOMEN: WHAT ARE THE IMPLICATIONS OF THE NEW HYPERTENSION GUIDELINES?

ANGELA L. BROWN, MD

Associate Professor of Medicine // Cardiovascular Division
Washington University School of Medicine in St. Louis, MO

Disclosure of Relationships past 12 months

- Research Support: Medtronic
- Speaker's Bureau: Arbor
- Consultant: Lundbeck

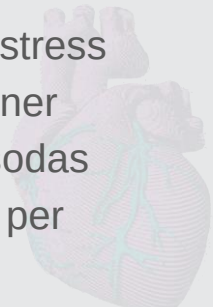
I do not plan to discuss off-label content

Learning Objectives

- Understand the unique issues related to hypertension diagnosis and management that effect women throughout the lifespan
- Understand how the new hypertension guidelines effect the diagnosis and management of hypertension in women

Case Presentation

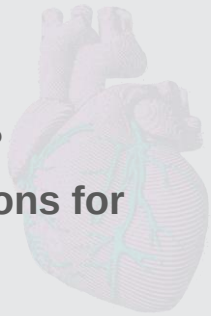
- 52 yo woman with no known history of HTN presents for yearly gynecologic follow-up
- No significant PMH; G2P2; LMP ~ 1 yr ago
- Meds: MVI, Tylenol prn
- Works as an accountant – moderate stress
- No tobacco; occasional wine with dinner
- 1 cup of caffeinated coffee daily, no sodas
- aerobic exercise 30 minutes 3 times per week



Case Presentation

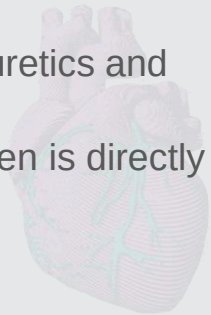
- BP 152/96 RUE, 150/92 LUE; repeat 144/88 RUE
  - (last year 132/76)
- Exam unremarkable
- Labs unremarkable

- **Does this lady have hypertension?**
- **If so, are there special considerations for diagnosis and therapy?**

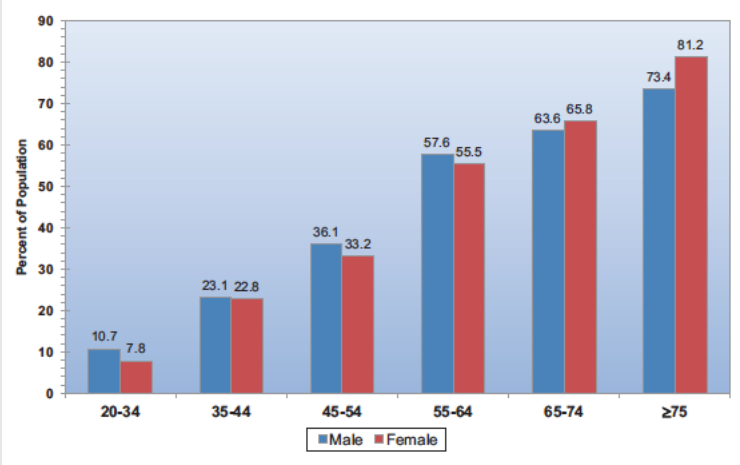


Hypertension

- Estimated 103 million US adults with HTN
- Prevalence of HTN increases with age in both sexes
- Women - more likely to be aware of their diagnosis, to be treated with medications, and to have controlled BP
- Women - more commonly prescribed diuretics and less frequently ACEIs
- Diagnosis and treatment of HTN in women is directly related to stage of reproductive health

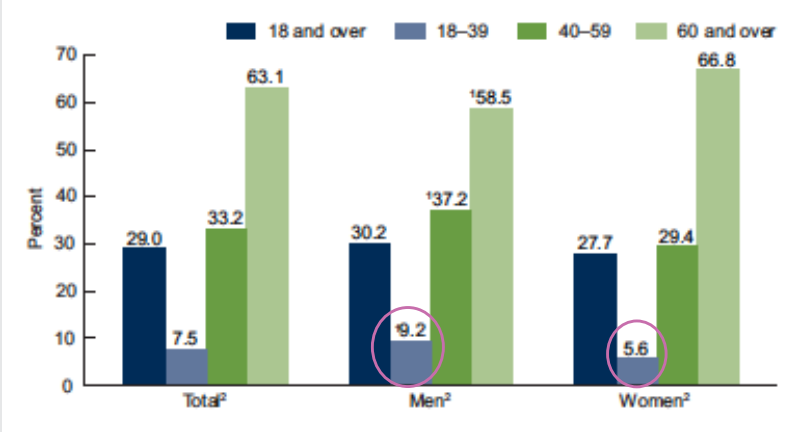


Prevalence of HTN Among US Adults NHANES 2011-2014



Benjamin, Circ 2017;135-146

Prevalence of HTN Among US Adults NHANES 2015-2016

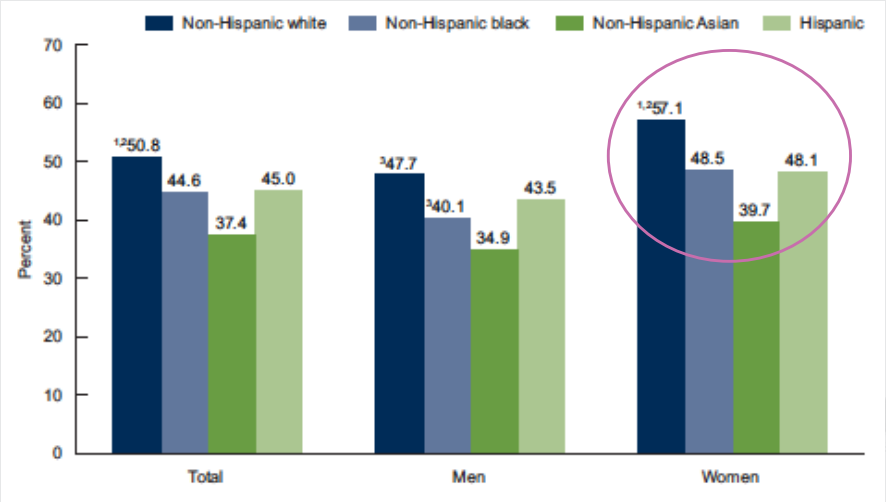


https://www.cdc.gov/nchs/data/databriefs/db289

Prevalence of Controlled HTN by Sex and Age, 2015-2016

https://www.cdc.gov/nchs/data/databriefs/db289

Prevalence of Controlled HTN by Sex, Race and Hispanic Origin, 2015-2016



https://www.cdc.gov/nchs/data/databriefs/db289

Women Through the Lifespan

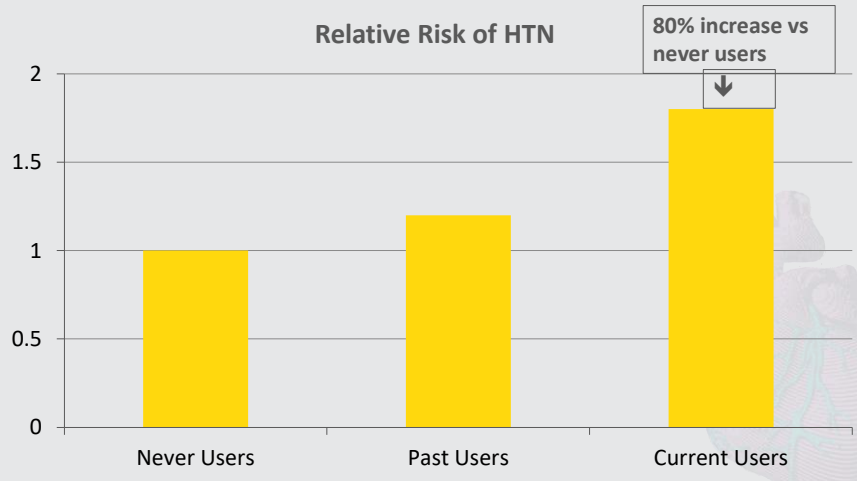
- Childbearing
- Pregnancy
- Menopause
- Postmenopause

Oral Contraceptives and HTN

- OCPs associated with increase in BP and risk of CV events
  - 2x risk of CHD, CVA, and VTE
  - absolute risk is low in those without risk factors
- Risk increases with:
  - increasing age
  - tobacco use
  - duration of OCP use
  - obesity
- Generally reversible with discontinuation of OCP

Ahmed, Oparil. *Hypertension*. 2017;70:19-26.

Relative Risk for Development of HTN by OC Use in Nurses Health Study



Adapted from Chasan-Taber et al. Circ 1996;94:483-489

Arq Bras Cardiol 2007;88(6):604-613

Oral Contraceptives and HTN

- Associated with concentration of ethinyl estradiol
- Less effect on BP with newer 3rd generation combination OCP (Estrogen 20 - 35 mcg and progesterone)
- Drospirenone (progestin) has antimineralocorticoid/diuretic effects that minimize BP effects of estrogen when used in combination
- ACOG recommends:
  - low-dose combination OCP use in women with well-controlled HTN
  - progestin only or levonorgestrel IUD in women with uncontrolled HTN
  - monitor closely

Ahmed, Oparil. *Hypertension*. 2017;70:19-26.

Pregnancy and HTN
ACOG Categories

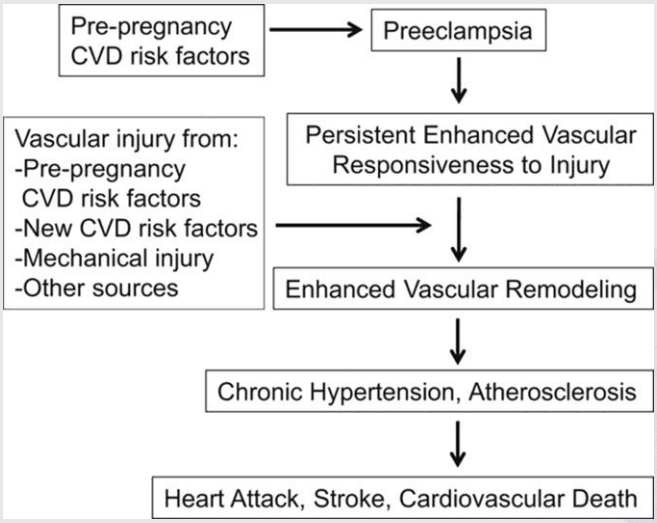
- Preeclampsia/eclampsia
  - New onset HTN and proteinuria or HTN associated with TOD (in absence of proteinuria)
- Chronic HTN of any cause
  - BP >140/90 before pregnancy, before the 20th week of pregnancy, or lasting > 12 weeks postpartum
- Chronic HTN with superimposed preeclampsia
  - Development preeclampsia/eclampsia in women with chronic hypertension
- Gestational HTN
  - Elevated BP after 20 weeks without preeclampsia

Pregnancy and HTN
Risk Factor for CVD Postpartum

- Early-onset preeclampsia associated with HTN (38% vs 14%) and metabolic syndrome (18% vs 2%) compared with normotensive pregnant women
- More frequent development of cardiomyopathy
- Offspring of women with HTN during pregnancy develop higher BP in adolescence (long-term CVD risk unclear)

Ahmed, Oparil. *Hypertension*. 2017;70:19-26.

New paradigm for enhanced cardiovascular risk in women exposed to preeclampsia



Dafina Pruthi et al. Hypertension. 2015;65:863-870

Pregnancy and HTN Treatment

- All antihypertensive medications cross the placenta
- Methyldopa – long-term safety profile
- Labetalol, nifedipine, hydralazine considered safe

- **AVOID:**
  - **ACEIs, ARBs, DRI, nitroprusside**

Estrogens and CVD

Pre-menopause

- Estrogen receptor-mediated phenotype is CVD protective
- Decreases AT_1 receptor expression
- Decreases ACE expression and activity
- Inhibits endothelin synthesis
- Antimitogenic; protecting against neointimal proliferation
- Antioxidant; protects against oxidative stress

Post-menopause

- Estrogen receptor-mediated phenotype changes to promote CVD
- Reduced inhibitory effects of estrogens on vasoconstriction of vascular smooth muscle
- [Androgens] relative increase and [estrogens] decrease may:
  - Promote renal Na^+ retention
  - Increase Angiotensin II and endothelin production
  - Increase oxidative stress

Relative balance of sex steroids may be critical in post-menopausal HTN development?

Adapted from: Reckelhoff JF. *Hypertension*. 2005;45:170–4.

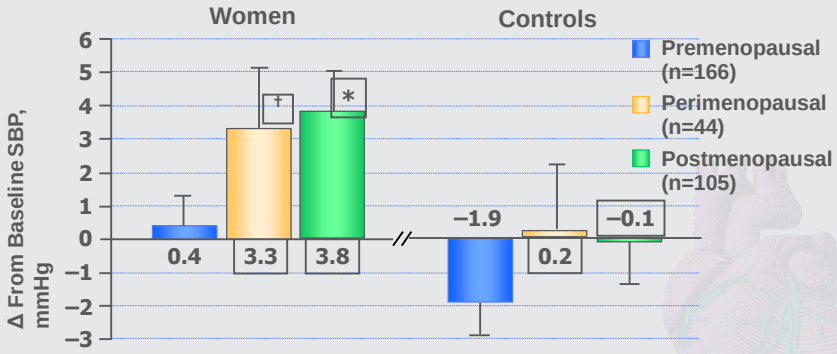
Menopause and Hypertension

- Postmenopausal women have increased incidence of HTN and CVD
- Increase in SBP
  - withdrawal of vasodilator effects of endogenous estrogen
  - increased arterial stiffness
  - increased salt sensitivity
  - diminished endothelial nitric oxide production
  - upregulation of AT_1 receptor expression
  - obesity – 40% postmenopausal women
  - higher rates of depression and anxiety

Nickenig G et al. *Circulation*. 1998;97:2197–2201. Oparil S, Miller AP. *J Clin Hypertens* (Greenwich). 2005;7:300–309.
Harrison-Bernard LM et al. *Hypertension*. 2003;42:1157–1163. Ahmed, Oparil. *Hypertension*. 2017;70:19-26.

BP Rises After Menopause—Risk of Hypertension Triples

Changes in SBP From Baseline to Follow-up (Mean 5.2 Years)

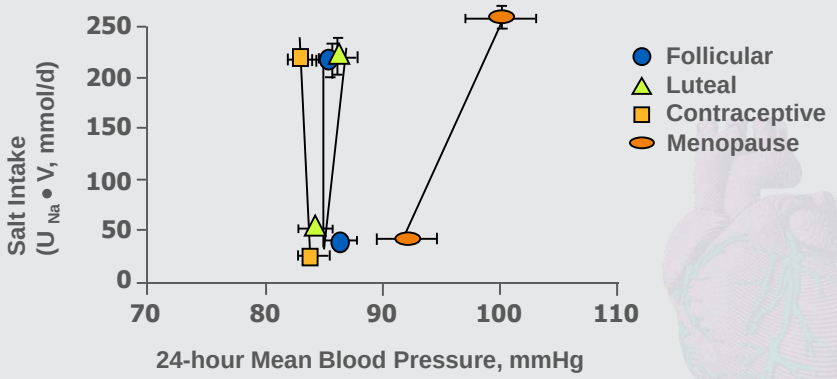


*$P \leq 0.05$.
†$P = 0.07$.
Baseline SBP: Pre=121.4 ± 1.3 mmHg; Peri=122.0 ± 1.8 mmHg; Post=126.5 ± 1.7 mmHg;
Controls: men matched by age and BMI.

Staessen JA et al. *J Hum Hypertens*. 1997;11:507–514.

Menopause Increases Salt-sensitivity

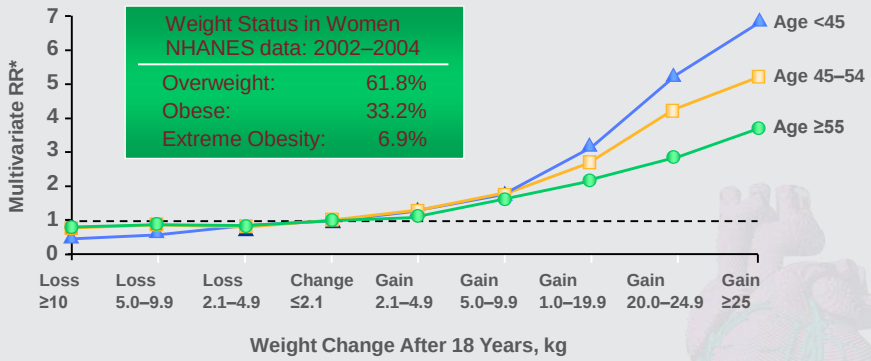
Increases in Salt Intake Lead to Increases in Blood Pressure in Postmenopausal Women



Oparil S, Miller AP. *J Clin Hypertens* (Greenwich). 2005;7:300–309.

Hypertension Increases With Weight Gain in Women

Nurses' Health Study: Hypertension† According to Weight Change



Overweight=BMI ≥25 kg/m^2; obese=BMI ≥30 kg/m^2; extreme obesity=BMI ≥40 kg/m^2
*Adjusted for age, BMI at age 18 years, height, family history of myocardial infarction, parity, oral contraceptive use, menopausal status, postmenopausal use of hormones, and smoking.
†>140/90 mmHg.

Huang Z et al. *Ann Intern Med.* 1998;128:81–88.
Ogden C et al. *JAMA.* 2006;295(13):1549-55.

Ambulatory Blood Pressure Monitoring Important for Diagnosis

- Superior to in-office measurements in diagnosis HTN and predicting CV outcomes
- ABPM in Women
  - lower day-time and night-time BPs
  - higher control rates
  - higher rates of hypotension in older women
- White-coat HTN
  - More prevalent in older or pregnant women
- USPSTF and AHA/ACC guidelines recommend ABPM in all patients before initiating treatment
  - Grade A (USPSTF)

Ahmed, Oparil. *Hypertension*. 2017;70:19-26.

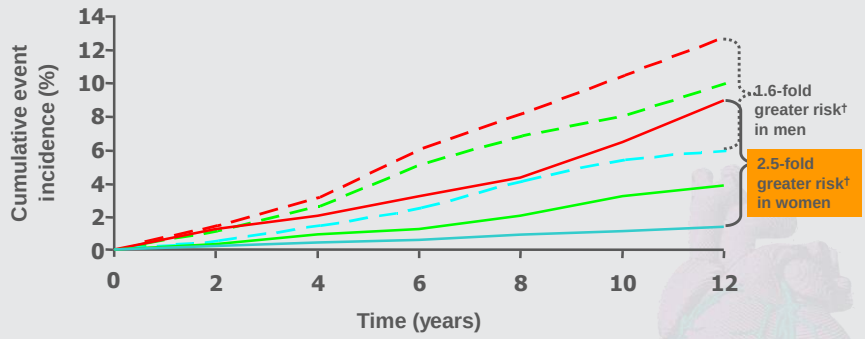
ABPM
Important for CV risk stratification

- White-coat HTN
  - More prevalent in older or pregnant women
  - Increased anxiety and metabolic syndrome
  - Small studies suggest 2x increased CVD outcomes in those with >3 CVD risk factors
- Elevated Nocturnal BP – Nondippers
  - Greater prevalence CVD events and mortality
  - Increases with age in both men and women
- Masked HTN
  - CVD risk factor
  - More prevalent in men
  - Increases in women with increases in BMI and alcohol intake

Ahmed, Oparil. *Hypertension*. 2017;70:19-26.

CV Event Incidence and Risk in Individuals Without HTN

CV death, MI, Stroke, and HF Incidence in the Framingham Cohort



†Adjusted for concomitant CV risk factors
Optimal = <120/<80 mmHg
Normal = 120–129/80–84 mmHg
High normal = 130–139/84–89 mmHg

Adapted from: Vasan RS et al. *NEJM*. 2001;345:1291–1297.

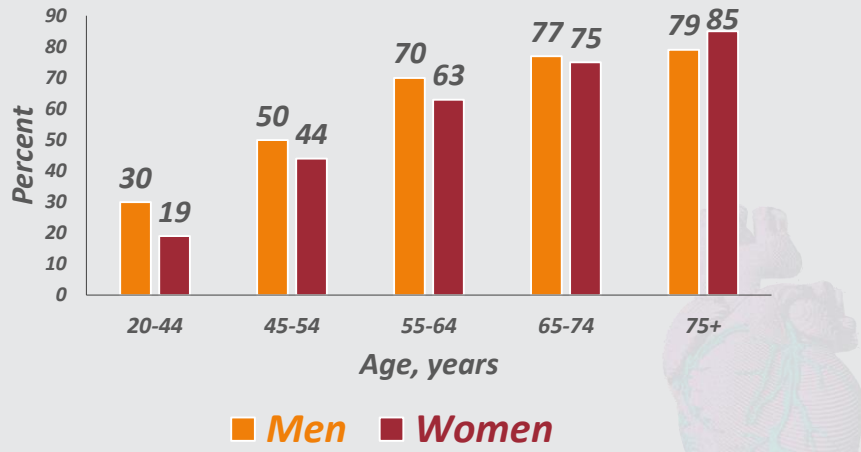
2017 Guideline for the Prevention, Detection, Evaluation and Management of High Blood Pressure in Adults

BP Classification (JNC 7 and ACC/AHA Guidelines)

SBP		DBP	JNC 7	2017 ACC/AHA
<120	and	<80	Normal BP	Normal BP
120–129	and	<80	Prehypertension	Elevated BP
130–139	or	80–89	Prehypertension	Stage 1 hypertension
140–159	or	90-99	Stage 1 hypertension	Stage 2 hypertension
≥160	or	≥100	Stage 2 hypertension	Stage 2 hypertension

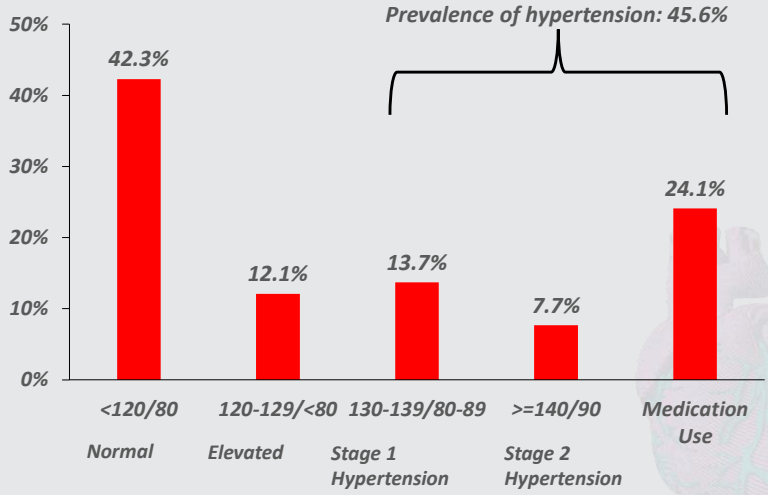
- *Blood Pressure should be based on an average of ≥2 careful readings on ≥2 occasions*
- *Adults being treated with antihypertensive medication designated as having hypertension*

Prevalence of Hypertension, by Age and Sex



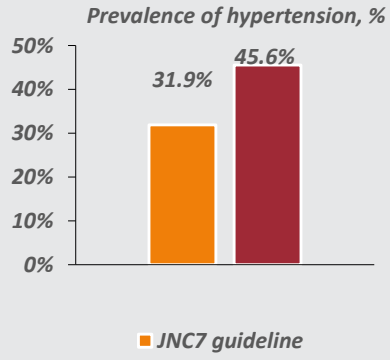
Whelton PK et al. Hypertension. 2017
Whelton PK et al. JACC. 2017

Distribution of US adults into BP Categories NHANES 2011-2014

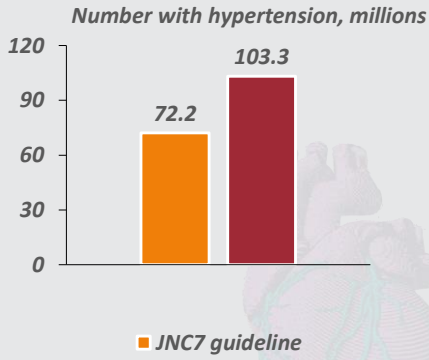


Muntner et. al., JACC. 2017
Muntner, et. al., Circulation. 2017

Prevalence of Hypertension 2017 ACC/AHA and JN7 Guidelines

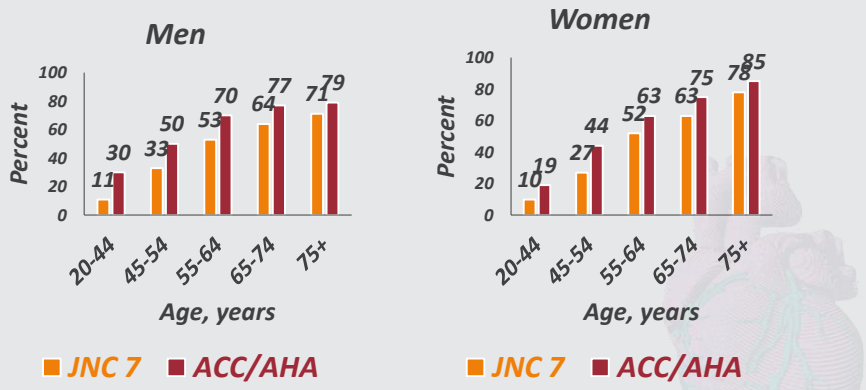


Whelton PK et al. Hypertension. 2017
Whelton PK et al. JACC. 2017



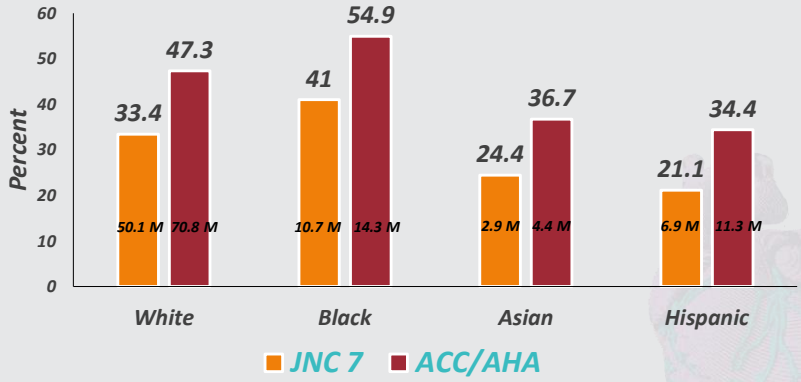
Muntner et. al. JACC. 2017
Muntner, et. al. Circulation 2017

Comparison of Prevalence using the 2003 JNC 7 and 2017 BP Guideline Definitions of Hypertension, by Age and Sex



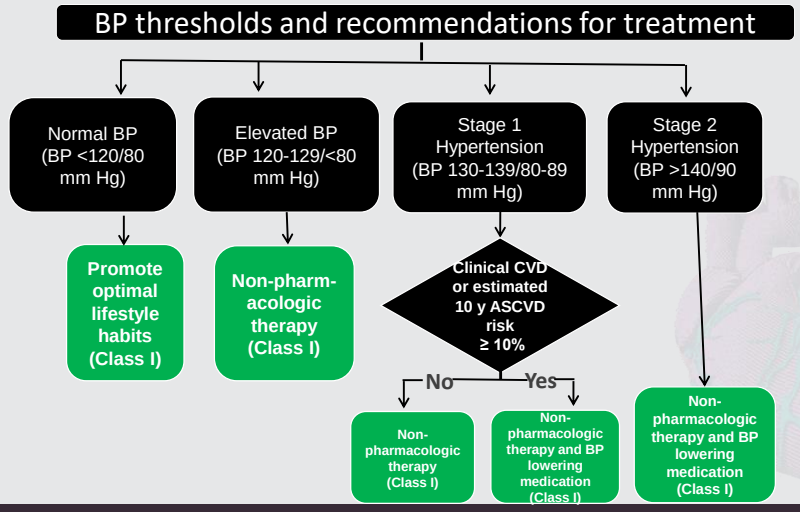
Whelton PK et al. Hypertension. 2017
Whelton PK et al. JACC. 2017

Comparison of Prevalence using the 2003 JNC 7 and 2017 BP Guideline Definitions of Hypertension, by Race-Ethnicity



Whelton PK et al. Hypertension. 2017
Whelton PK et al. JACC 2017

BP THRESHOLDS and RECOMMENDATIONS for TREATMENT



NONPHARMACOLOGIC (LIFESTYLE) INTERVENTIONS FOR PREVENTION AND TREATMENT OF HYPERTENSION

	Nonpharmacologic Intervention	Dose
Weight loss	Weight/body fat	Ideal body weight best goal, but at least 1 kg reduction in body weight for most adults
Healthy diet	DASH dietary pattern	Diet rich in fruits, vegetables, whole grains, and low-fat dairy products with low saturated and total fat
Reduce sodium intake	Dietary sodium	<1,500 mg/day optimal, but at least 1,000 mg reduction in most adults
Enhance potassium intake	Dietary potassium	3,500 mg/day, preferably by consumption of a diet rich in potassium
Physical activity	Aerobic, dynamic resistance, isometric resistance	90-150 min/week
Moderate alcohol intake	Alcohol consumption	Men: limit to 2 drinks daily Women: limit to 1 drink daily

BP Treatment Threshold and the use of ASCVD Risk Estimation to Guide Drug Treatment of Hypertension

Recommendations for BP Treatment Threshold and Use of ASCVD Risk Estimation* to Guide Drug Treatment of Hypertension

COR	LOE	Recommendations
I	SBP: A DBP: C-EO	1. Use of BP-lowering medications is recommended for secondary prevention of recurrent CVD events in patients with clinical CVD and an average SBP of 130 mm Hg or higher or an average DBP of 80 mm Hg or higher, and for primary prevention in adults with an estimated 10-year atherosclerotic cardiovascular disease (ASCVD) risk of 10% or higher and an average SBP 130 mm Hg or higher or an average DBP 80 mm Hg or higher.
I	C-LD	2. Use of BP-lowering medication is recommended for primary prevention of CVD in adults with no history of CVD and with an estimated 10-year ASCVD risk <10% and an SBP of 140 mm Hg or higher or a DBP of 90 mm Hg or higher

* ACC/AHA Pooled Cohort Equations to estimate 10-y risk of ASCVD. ASCVD was defined as a first nonfatal MI or CHD death, or fatal or nonfatal stroke among adults free of CVD.

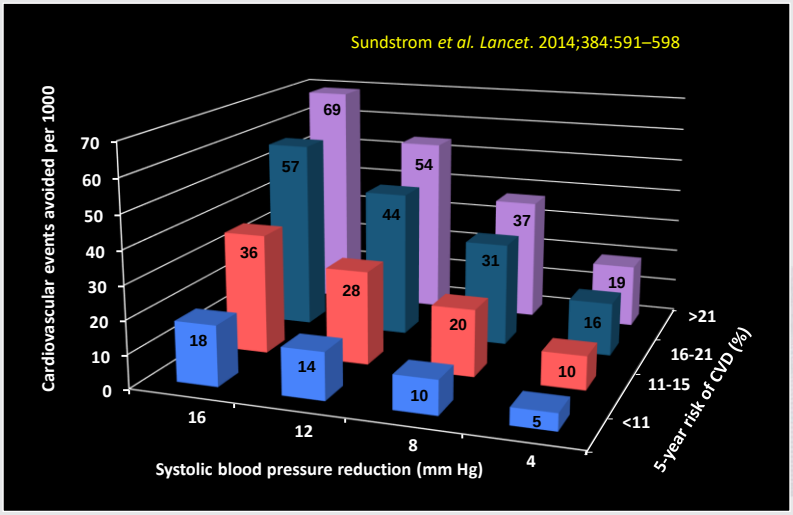
ACC/AHA Pooled Cohort Equations

To estimate the 10-year risk of atherosclerotic CVD

Based on age, race sex, total cholesterol, LDL cholesterol, HDL cholesterol, treatment with a statin, systolic BP, treatment for hypertension, history of diabetes, current smoker, aspirin therapy

http://tools.acc.org/ASCVD-Risk-Estimator/

CVD EVENTS AVOIDED BY BASELINE RISK AND MAGNITUDE OF SBP LOWERING



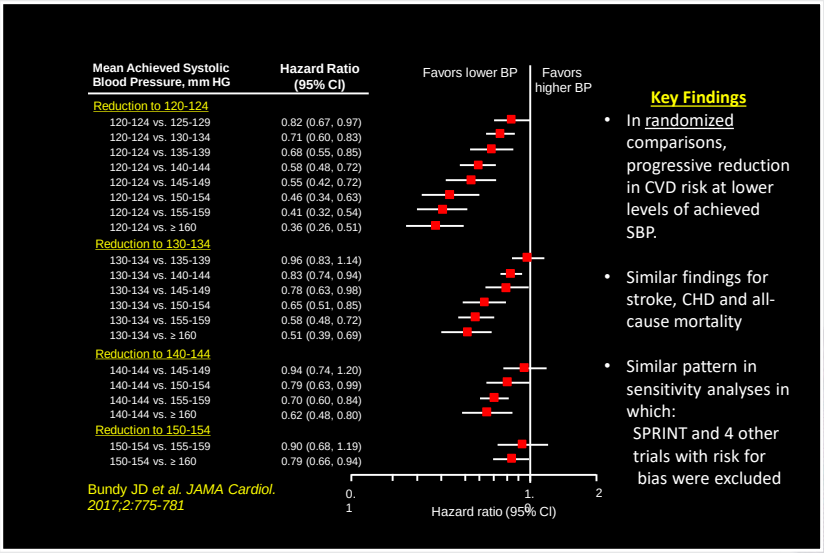
Benefits of using both BP and ASCVD risk assessment in determining BP thresholds for antihypertensive drug therapy

- Treatment is focused on patients most likely to have events
- More CVD events are prevented
- Larger absolute CVD risk reduction with treatment
- Lower number needed-to-treat to prevent one CVD event
- More quality-adjusted life years are saved
- Lower cost of care

BP GOAL FOR PATIENTS WITH HYPERTENSION

COR	LOE	Recommendations
I	SBP: B-R[SR] DBP: C-EO	1. For adults with confirmed hypertension and known CVD or 10-year ASCVD event risk of 10% or higher, a BP target of less than 130/80 mm Hg is recommended.
IIb	SBP: B-NR	2. For adults with confirmed hypertension, without additional markers of increased CVD risk, a BP target of less than 130/80 mm Hg may be reasonable .

MAJOR CV EVENTS



SUMMARY: TREATMENT RECOMMENDATIONS

- ***Lifestyle modification is the <u>cornerstone</u> of the treatment of hypertension.***
- ***New thresholds for initiation of antihypertensive drug therapy in stage1 hypertension, use of ASCVD risk estimation to determine whether to treat with***
  - ***Nonpharmacological therapy alone ("low" risk patients)***
  - ***Antihypertensive drug therapy, in addition to***
  - ***nonpharmacological therapy ("high" risk patients)***
- ***New target for BP reduction during treatment of hypertension***

Recommendations for Older Persons

Recommendations for Treatment of Hypertension in Older Persons References that support recommendations are summarized in Online Data Supplement 54.		
COR	**LOE**	**Recommendations**
I	A	3. Treatment of hypertension with a SBP treatment goal of less than 130 mm Hg is recommended for noninstitutionalized ambulatory community-dwelling adults (≥65 years of age) with an average SBP of 130 mm Hg or higher).
IIa	C-EO	4. For older adults (≥65 years of age) with hypertension and a high burden of comorbidity and limited life expectancy, clinical judgment, patient preference, and a team-based approach to assess risk/benefit is reasonable for decisions regarding intensity of BP lowering and choice of antihypertensive drugs.

Rationale for Blood Pressure Goal of <130 mmHg in Older Adults

- **Large number of older adults have been enrolled in BP lowering treatment trials**
- **BP lowering trials have shown:**
  - **Decreased CVD morbidity and mortality**
    - **SPRINT Research Group. JAMA.2016;315:2673-2682.**
  - **No increased risk for falls or orthostatic hypotension**
    - **SPRINT Research Group. JAMA.2016;315:2673-2682.**
    - **ACCORD: Margolis KL et al. JGIM. 2014; 29:1599-606.**

Recommendations for Women

- Clinical trials are without significant difference in blood pressure lowering or outcomes by sex
  - ALLHAT – no difference primary outcome; post hoc analysis showed higher stroke rate in women on Lisinopril
  - SPRINT – statistically nonsignificant benefit in the intensive treatment group for women; enrollment of fewer women than expected
- Guidelines have some variation by age and comorbidities, but not by sex: target ≤ 130/80
- CVD risk-based strategy accounts for sex

Ahmed, Oparil. *Hypertension*. 2017;70:19-26.
Whelton, *Hypertension.* 2017.

Antihypertensive Agents – Special Considerations

- ACEIs, ARBs, and DRIs should not be prescribed for women who are or intend to become pregnant
- Mineralocorticoid antagonists – ambiguous genitalia
- Women 3x more likely to develop ACE-related cough
- Women more likely to complain of CCB-related edema and minoxidil-induced hirsutism
- Diuretics useful in some elderly at-risk patients due to decreased risk of hip fracture
- Women more likely to develop diuretic-induced hyponatremia and hypokalemia
- Men more frequently develop gout from thiazides and sexual dysfunction from thiazides and beta blockers

Chobanian AV et al. *Hypertension*. 2003;42:1206–1252. Ahmed, Oparil. *Hypertension*. 2017;70:19-26.

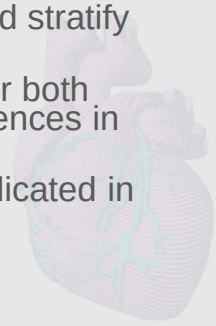
Case Presentation

- 52 yo woman with no known history of HTN presents for yearly gynecologic follow-up
- BP 152/96 RUE, 150/92 LUE; repeat 144/88 RUE - (last year 132/76)

- **Does this lady have hypertension?**
  - ***Confirm with 24 hour ABPM***
- **ASCVD risk = 2.2% white; 5% AA previous yr**
- **Are there special considerations for therapy?**
  - ***Initiate therapy if 24 hr average greater than 135/85 or office BP greater than 140/90 (stage 2)***
  - ***Thiazide diuretic, CCB, RAS blocker***

Summary

- Women have special issues related to BP and HTN throughout their reproductive cycle
- Endogenous estrogen appears to be protective in younger women
- HTN prevalence increases with age as does the risk for CV events
- ABPM is a useful tool to diagnose HTN and stratify CVD risk
- Treatment recommendations are similar for both sexes; however, individualize due to differences in adverse events
- RAS blockers are ABSOLUTELY contraindicated in pregnancy



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