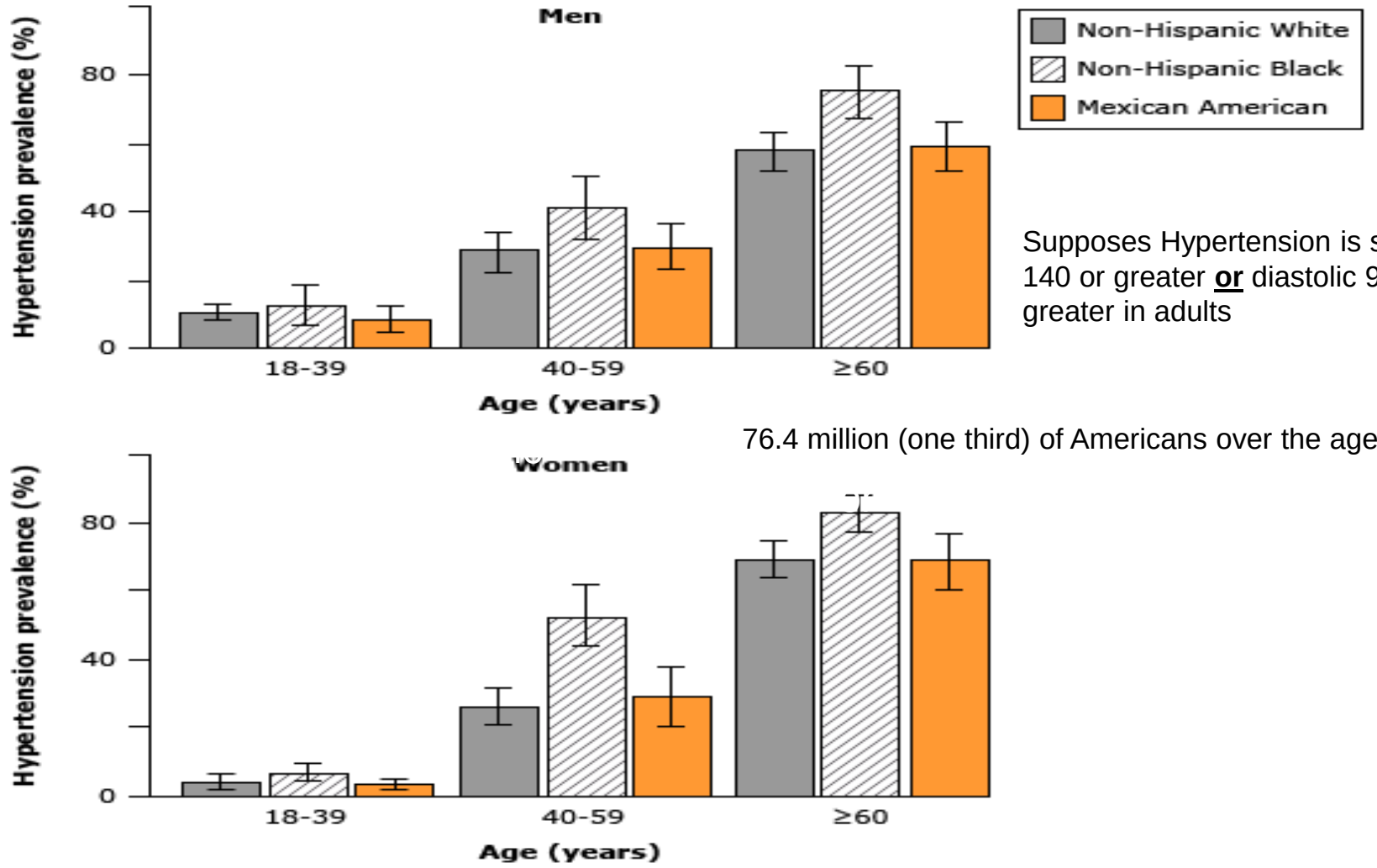
# The Practical Treatment of Hypertension

2019

## Prevalence of hypertension in the United States




Supposes Hypertension is systolic 140 or greater **or** diastolic 90 or greater in adults

76.4 million (one third) of Americans over the age of 20

Prevalence of hypertension in men (upper graph) and women (lower graph) according to age and race/ethnicity in the United States from the NHANES survey. Hypertension occurs earlier and more frequently in non-Hispanic blacks.

*Data from: Egan BM, Zhao Y, Axon RN. JAMA 2010; 303:2043.*

# Overall Benefits of BP Control
## (Based on Large-Scale Randomized Trials)

- 50% relative risk reduction in the incidence of heart failure
- 30-40% relative risk reduction in the incidence of stroke
- 20-25% relative risk reduction in the incidence of myocardial infarction
- Prevents or prolongs time to ESRD
- Hypertension is the # 1 risk factor for:
  - Heart failure
  - Stroke
  - Myocardial infarction (arguably)
- Hypertension is the #2 risk factor for ESRD

# JNC 8 Blood Pressure Goals (2014)

- BP Goal 60 years old and greater*- systolic <150 and diastolic <90. (Grade A)***
  If CKD** present at any age – systolic < 140 and diastolic <90. (Grade E)***
- BP Goal 18-59 years old* – diastolic <90. Ages 30–59 (Grade A)** Ages 18-29 (Grade E)***
- BP Goal 18 - 59 years old* – systolic < 140 (Grade E)***
- BP Goal 18 - ***69*** years old with **CKD** (without albuminuria) – systolic < 140 and diastolic < 90 (Grade E)*** > 18 years and albuminuria** > 30 mg/day, alone – systolic < 140 and diastolic < 90 (Grade E)***
- BP Goal ≥ 18 years with diabetes - systolic < 140 and diastolic < 90 (Grade E)***

***Note:*** The only comorbid conditions specifically addressed are CKD (GFR < 60 or albuminuria > 30mg per g of creatinine) and diabetes mellitus.

*Without comorbid conditions

**Albuminuria with GFR > 90 is considered to be CKD Stage I.

**Grade A – Strong recommendation. Grade B – Moderate rec. Grade C – Weak rec. Grade D – Against. Grade E – Expert opinion.

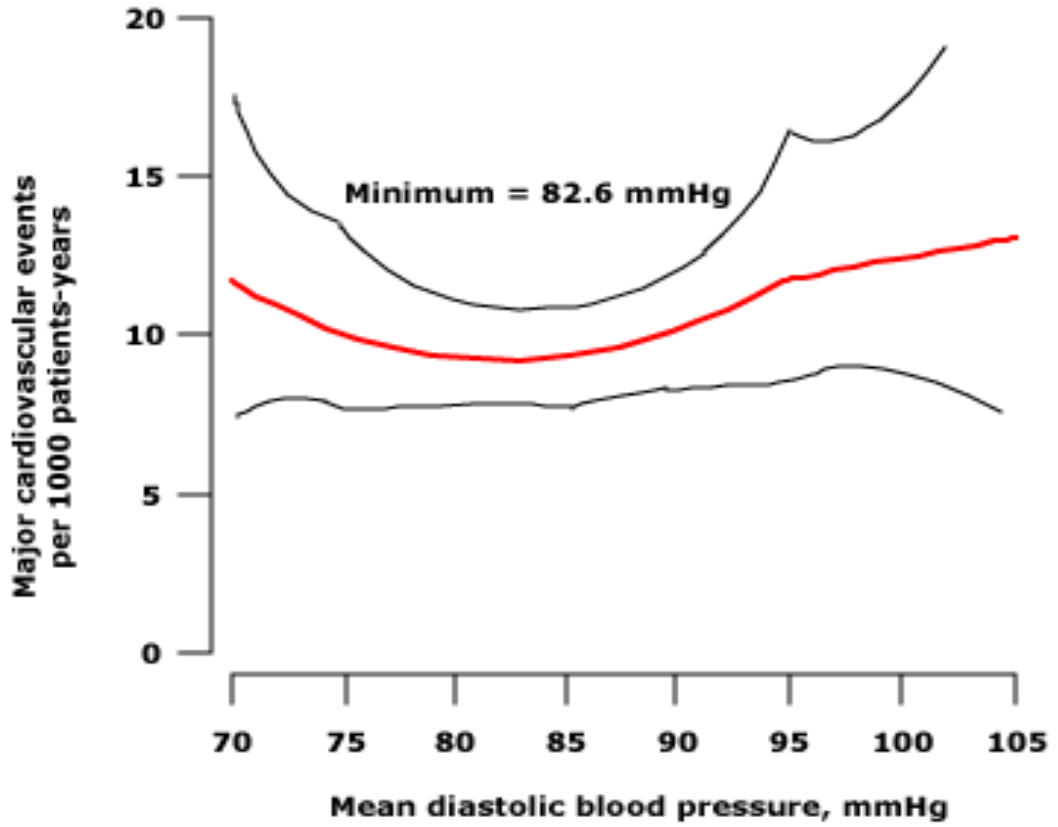
# BP Goal for patients 70 and Older and with CKD (but no Albuminuria or Diabetes)

- Specific recommendation not made
- No outcomes trial included large number of patients 70 and older
- Individualize treatment
  - Frailty
  - Comorbidities (especially CHF, albuminuria and CKD)
  - Rising creatinine
  - Orthostatic symptoms
- Inference is that BP goal may be higher than 140 systolic unless albuminuria or diabetes are present

# Inferences Based on Recommendations

- The older the patient, the less aggressive BP control
- BP goal may be > 140/90 in CKD patients without albuminuria if ≥ 70 years old
- BP goal in patients with urine albumin ≥ 30 mg/g creatinine who are 60 and older is the same as under 60
- BP goal in diabetics 60 and older is the same as under 60
- BP goal in patients with atherosclerotic cardiovascular disease is the same as for the general population
- The only recommendations made with high probability:
  - BP goal for age 60 and older and no comorbid conditions is systolic < 150 and diastolic < 90
  - Diastolic BP goal for ages 30 – 59 is < 90
- All other recommendations are expert opinion.

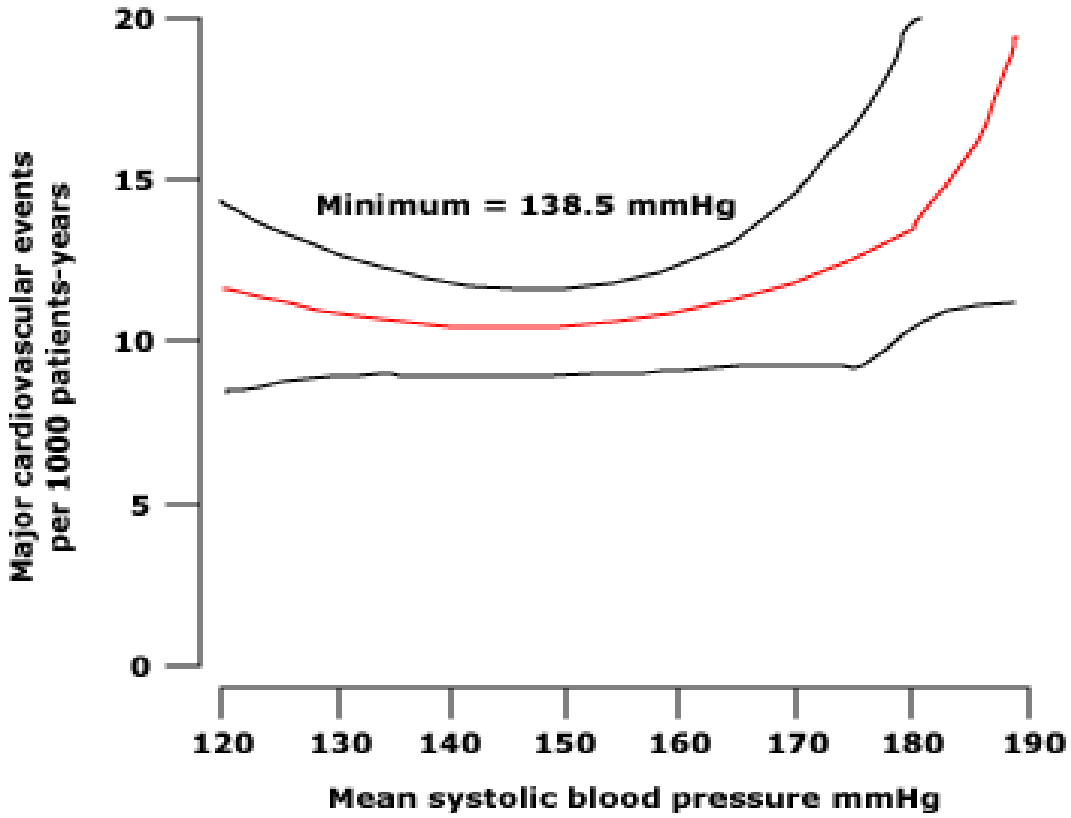
## Diastolic pressure and cardiovascular events in HOT trial




Estimated incidence (95 percent CI) of major cardiovascular events in relation to achieved mean diastolic blood pressure in the HOT trial. The diastolic pressure at the lowest point of the curve is indicated (minimum).

*Adapted from Hansson, L, Zanchetti, A, Carruthers, SG, et al, Lancet 1998; 351:1755.*

## Systolic pressure and cardiovascular events in HOT trial




Estimated incidence (95 percent CI) of major cardiovascular events in relation to achieved mean systolic blood pressure in the HOT trial. The systolic pressure at the lowest point of the curve is indicated (minimum).

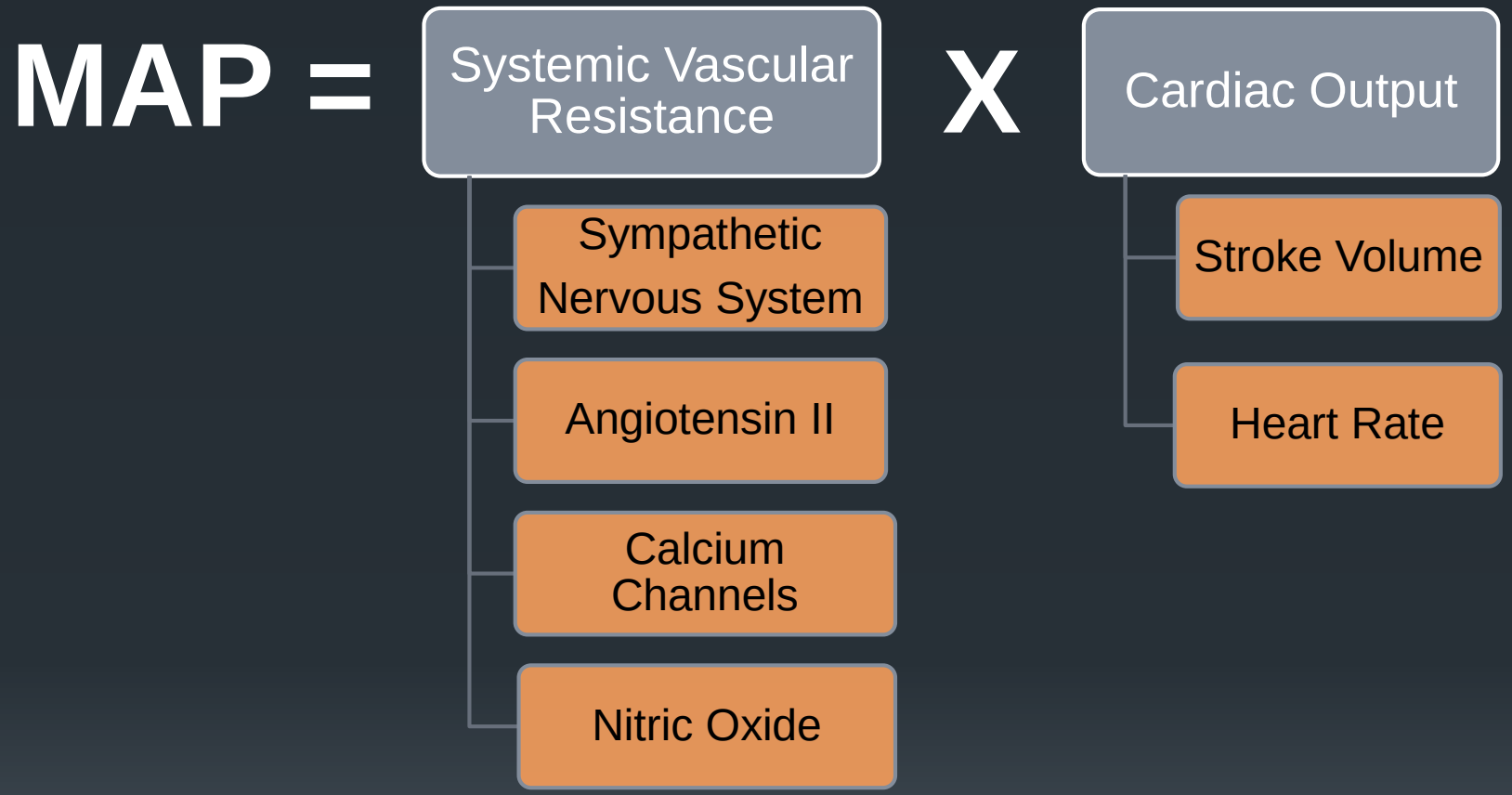
*Adapted from Hansson, L, Zanchetti, A, Carruthers, SG, et al, Lancet 1998; 351:1755.*

# When to Allow BP to increase

- Diastolic BP < 70 (unless systolic BP>160) or systolic BP <120 and age 60 or older with one of the following:
  - Chest pain
  - Rising creatinine
  - Orthostatic symptoms
  - Easy fatigability
  - TIA like symptoms
  - Or patient states, “I just don’t feel good.”
- 60 years or older and diastolic BP < 60 or systolic BP < 110 even without symptoms
- Allow permissive hypertension (systolic up to 160) if 70 years or older (even if diabetic or albuminuria is present) with one of the following :
  - Rising creatinine in CKD 3b or higher (GFR 44 or lower)
  - Carotid artery disease with symptoms
  - Diastolic BP < 70 and chest pain
- If findings of CHF maintain BP <120/80

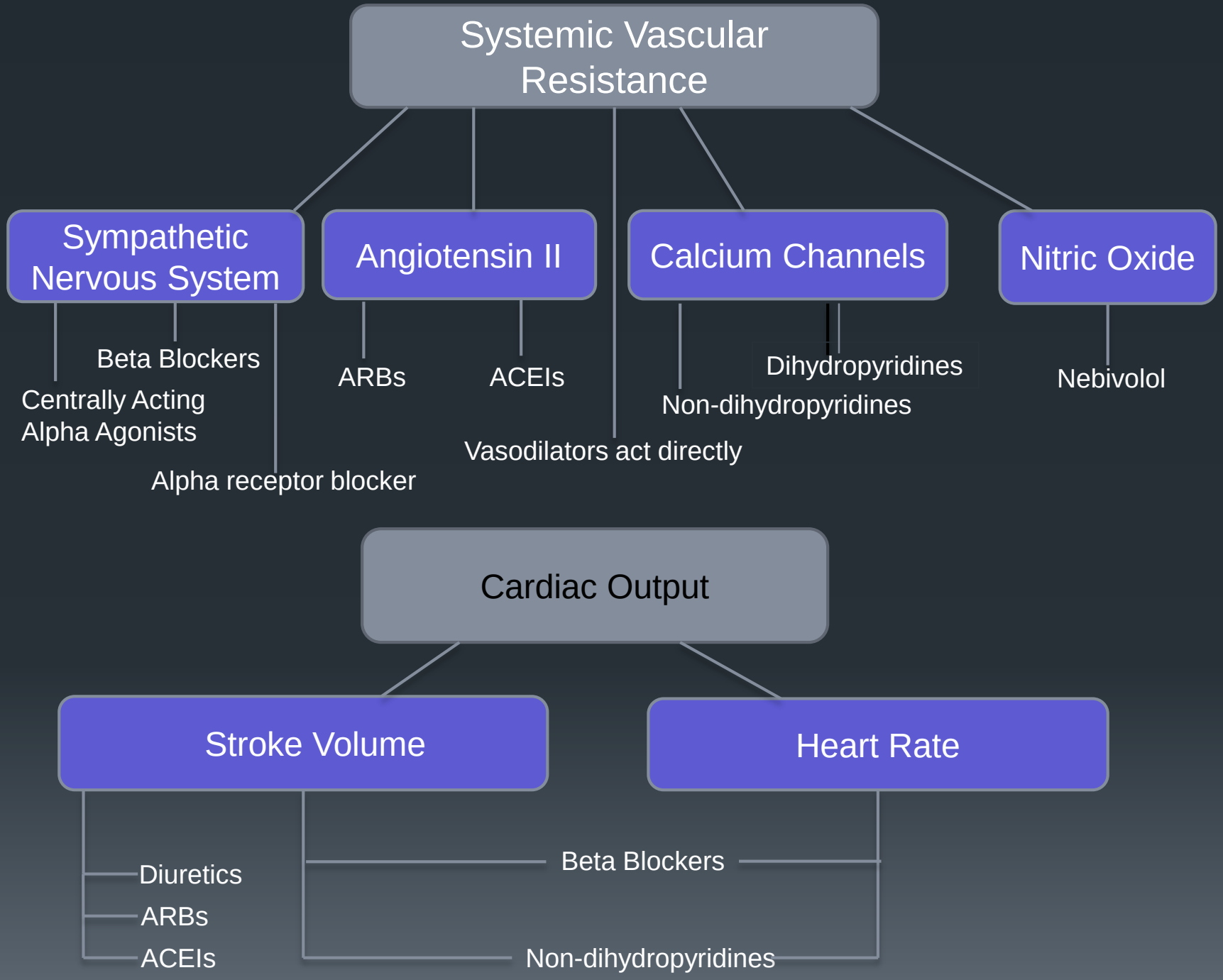
“Expert” opinion - Mine

# Derivation of Blood Pressure



# Classes of Antihypertensives

- Diuretics
  - Thiazide and thiazide-like
  - Loops
  - Potassium retaining
- Adrenergic blockers
  - Alpha receptor blockers
  - Beta receptor blockers
  - Centrally acting alpha agonists
- Vasodilators
- Angiotensin converting enzyme inhibitors
- Calcium channel blockers
  - Non-dihydropyridines
  - Dihydropyridines
- Angiotensin II receptor blockers


Systemic Vascular Resistance
Sympathetic Nervous System
Angiotensin II
Calcium Channels
Nitric Oxide
Beta Blockers
Centrally Acting Alpha Agonists
Alpha receptor blocker
ARBs
ACEIs
Vasodilators act directly
Dihydropyridines
Non-dihydropyridines
Nebivolol
Cardiac Output
Stroke Volume
Heart Rate
Diuretics
ARBs
ACEIs
Beta Blockers
Non-dihydropyridines

## Lifestyle modifications in the management of hypertension

| Modification | Recommendation | Approximate systolic BP reduction, range* |
|---|---|---|
| Weight reduction | Maintain normal body weight (BMI, 18.5 to 24.9 kg/m$^2$) | 5 to 20 mmHg per 10 kg weight loss |
| Adopt DASH eating plan | Consume a diet rich in fruits, vegetables, and low-fat dairy products with a reduced content of saturated and total fat | 8 to 14 mmHg |
| Dietary sodium reduction | Reduce dietary sodium intake to no more than 100 meq/day (2.4 g sodium or 6 g sodium chloride) | 2 to 8 mmHg |
| Physical activity | Engage in regular aerobic physical activity such as brisk walking (at least 30 minutes per day, most days of the week) | 4 to 9 mmHg |
| Moderation of alcohol consumption | Limit consumption to no more than 2 drinks per day in most men and no more than 1 drink per day in women and lighter-weight persons | 2 to 4 mmHg |

For overall cardiovascular risk reduction, stop smoking. The effects of implementing these modifications are dose and time dependent and could be higher for some individuals; they are not all additive.

BMI: body mass index; BP: blood pressure; DASH: Dietary Approaches to Stop Hypertension.

*Reproduced from: The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Available at http://www.nhlbi.nih.gov/guidelines/hypertension/jnc7full.pdf.*

# JNC 8 Medication Treatment recommendations

- General nonblack population, including diabetes – thiazides, CCB, ACEI or ARB initially (Grade B)
- General black population - thiazides or CCB initially (Grade B if not diabetic, but Grade C if diabetic)
- CKD - treatment should include ACEI or ARB, all races (Grade B)
- Attaining and maintaining goal blood pressure
  - Increase or add a drug after 1 month if BP goal not met
  - Add third drug if not controlled with 2 drugs
  - Don't use ACEI and ARB together
  - If greater than 3 drugs needed, refer

(Grade E)

CCB – calcium channel blocker, ACEI – angiotensin converting enzyme inhibitor
ARB – angiotensin receptor blocker

# Inferences from JNC 8 Treatment Recommendations

- Do not initiate treatment with alpha blocker, alpha agonist, beta blocker, or vasodilator
- Do not initiate treatment in the black population with ACEI or ARB unless CKD present
- Increase dose or add a drug if BP not controlled. The added drug is not defined.
- Life style modification should always be part of the treatment and, in some cases, may be the only treatment

# SPRINT Trial (November 2015)

- 9361 persons with systolic BP 130 mm Hg or higher
- All were 50 years old or greater
- All had increased cardiovascular risk, but no diabetes
- Group 1 target systolic BP <120 – intensive treatment group
- Group 2 target systolic BP <140 – standard treatment group
- Primary composite outcome – MI, other coronary syndrome, stroke, CHF, or death from CV cause
- Lower rate of primary composite outcome in Group 1 – $p<0.001$
- Lower all-cause mortality in Group 1 – $p<0.003$
- Lower rate of serious side effects in Group 2

# BP Characteristics of Participants

- Average starting systolic BP 139.7 mm Hg
- One third had systolic BP less than or equal to of 132 mm Hg
- One third had systolic BP 133 – 144 mm Hg
- One third  had systolic BP greater than or equal to 145 mm Hg
- Average drop in systolic BP of standard treatment group 5 mm Hg
- Average end systolic BP of standard treatment group 136.2 mm Hg
- Average drop in systolic BP intensive treatment group 18 mm Hg
- Average end systolic BP of intensive treatment group 121.4 mm Hg

# Secondary Outcome Differences

- Myocardial infarction – p 0.19
- Other acute coronary syndrome - p 0.95
- Stroke - p 0.50
- Heart failure - p 0.002 in favor of intensive treatment group
- Albuminuria - p 0.11 in favor of intensive treatment group
- >30% reduction of GFR - p<0.001 in favor of standard treatment group

# Serious Adverse Events

## Significantly Higher in Intensive Treatment Group

- Hypotension – p 0.001
- Syncope – p 0.05
- Bradycardia – p 0.28
- Electrolyte abnormality – p 0.02
  - Sodium <130 – p<0.001
  - Potassium <3 – p 0.006
- Injurious fall – p 0.71 (not significant)
- Acute kidney injury – p<0.001

# Concerns with SPRINT Trial

- In conflict with ACCORD Trial (opposite findings)
- No diabetics in SPRINT, all diabetics in ACCORD
- Renal function made worse in both trials
- Stroke,* MI, other coronary events were not significantly decreased in both trials
- Only heart failure was significantly decreased in SPRINT
- Average starting BP was only 139.7
- Higher incidence of adverse events in intensive treatment groups in both trials
- If starting systolic much higher, adverse events likely even worse

*Stroke approaching significance in both trials

# Accord Trial (2010)

- Total patients about 10,000
- All diabetic and with CVD
- All patients randomized to intensive glycemic control (A1C <6 or standard therapy (A1C 7– 8)
- About 5000 patients randomized to lipid lowering arm (statin alone or statin with fenofibrate)
- 4,700 patients randomized to the hypertension arm
  - Treat to <120 vs <140 systolic
  - No benefit in intensive treatment group except tendency toward decrease in strokes
  - Significantly more adverse events with intensive treatment

# So What Do You Do?

- In general, keep BP below 140/90 (all ages, DM and CKD without albuminuria)
- If history of CHF or EF <45%, keep BP <120/80
- If albuminuria >30 mg/day, keep BP <130/80
- Circumstances when BP may be higher or decreased more slowly in each instance
  - Dizziness when standing
  - TIA-like symptoms
  - Fatigued most of time
  - Diastolic BP <65
  - Rapidly rising creatinine
  - In general be less aggressive age 60 and older

# Common, Difficult Cases

## Case # 1

85 year old white female with BP of 210/70 HR 65, and no complaints when originally seen. Normal renal function for age and no history of cardiac problems.  Denies HA, dizziness or visual problems.  Has no peripheral edema.

# How do you Treat Her?

- Low sodium diet only
- Hydrochlorothiazide daily and diet
- Clonidine bid and diet
- ACE inhibitor daily and diet
- Beta blocker daily and diet

# BP decreased to 160/56
# Now what?

- No additional medication
- Add a second drug that has not been used
- Add 2 additional drugs, one of which should be minoxidil
- Add furosemide to the HCTZ
- Double the dose of HCTZ

# Case # 2

26 year old, male, type I diabetic has no cardiac disease, but GFR of 42 cc/min (S. creatinine 2.1) and 4.5 grams of protein in 24 hour urine specimen.  Has 1+ PTE and lungs are clear.  Presently taking furosemide 40 mg bid and  amlodipine 10 mg daily.  BP is 138/88.

# How do you treat him?

- Place on low sodium diet.
- Increase furosemide dose and diet.
- Add an ACE and diet.
- Add metolazone and diet.
- Increase furosemide, add an ACE, diet and DC Norvasc
- DC Norvasc, add and ACE, diet

# Case # 3

65 year old white male with BP 132/78. GFR is 52 cc/min (serum creatinine 1.4) and history of MI at age 62. Has no edema but has difficulty starting urinary stream. Presently on HCTZ 25 mg daily, lisinopril 20 mg daily, and amlodipine 10 mg daily. US of kidneys reveals mild hydronephrosis.

# How do you treat him?

- Low sodium diet only.
- Increase lisinopril and diet.
- Increase amlodipine and diet
- Add beta blocker and diet, and DC amlodipine
- Add beta blocker, alpha 1 blocker, diet and DC amlodipine

# Case # 4

72 year old diabetic female with previous history of MI and has 2 coronary artery stents.  3 grams protein in 24 hour urine.  Recent episode of CHF and C/O orthopnea.  GFR 34 cc/min (S. creatinine 1.8) and has 2+ PTE.  BP 176/98 and taking Lasix 40 mg bid, ramipril 20 mg daily, and carvedilol 25 mg bid.

# How do you treat her?

1. Low sodium diet only
2. Increase furosemide and diet
3. Increase ramipril and diet
4. Increase furosemide, ramipril and diet
5. Add calcium channel blocker and diet

# Case # 5

42 year old female with BP 160/90 and already on HCTZ 50 mg  daily, lisinopril 20 mg bid, labetalol 300 mg bid, and amlodipine 10 mg daily.  Normal renal function and no history of CAD.  Has 600 mg protein in 24 hour urine. No peripheral edema.

# How do you treat her?

- Add furosemide 40 mg bid and low sodium diet
- Increase amlodipine to 20 mg qd and diet
- Increase lisinopril to 40 mg bid and diet
- Add minoxidil 10 mg daily and diet
- Add doxazosin 4 mg at hs and diet
- Add valsartan 160 mg daily and diet

# Case # 6

68 year old male with history of recurrent CHF presents with SOB. EF is 20% but no history of MI. BP is 118/64, HR 52/min and he has 3+ PTE. Rales in both bases. GFR is 28 cc/min (S. creatinine 2.4) and he has 850 mg protein in 24 hour urine. Taking Lasix 80 mg bid, enalapril 20 mg bid and Coreg 25 mg bid.

# How do you treat him?

- Increase furosemide to 160 mg bid and place on low sodium diet
- DC Coreg and start diet
- Diet, decrease carvedilol to 12.5 mg bid and lisinopril to 20 mg daily
- Add metolazone 5 mg daily and diet
- Diet, increase furosemide to 160 mg bid, decrease carvedilol to 12.5 mg bid and lisinopril to 20 mg qd.