Hypertension and Its Treatment

A blend of European and United States guidelines

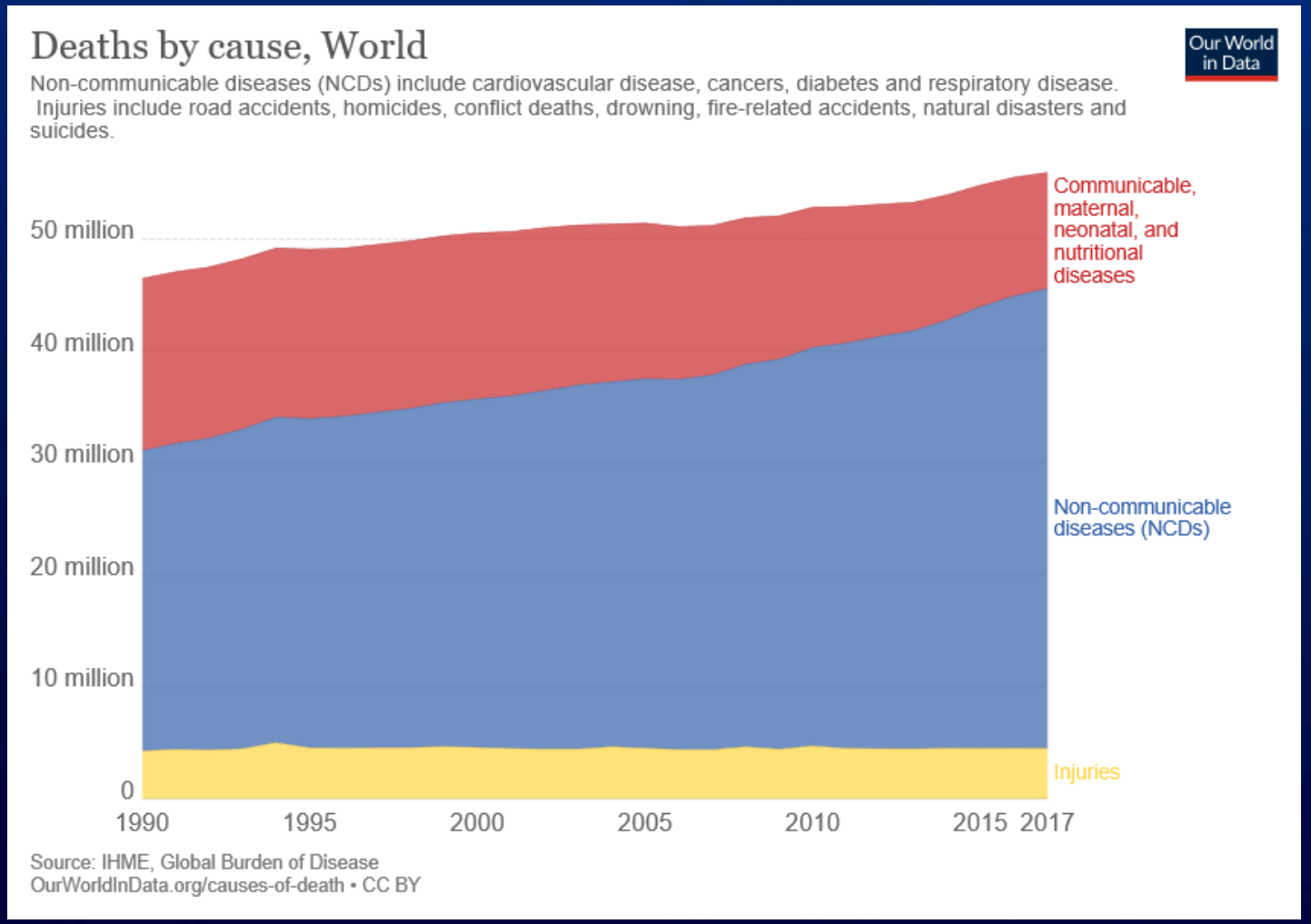
Preston Seaberg, M.D.

Learning Objectives

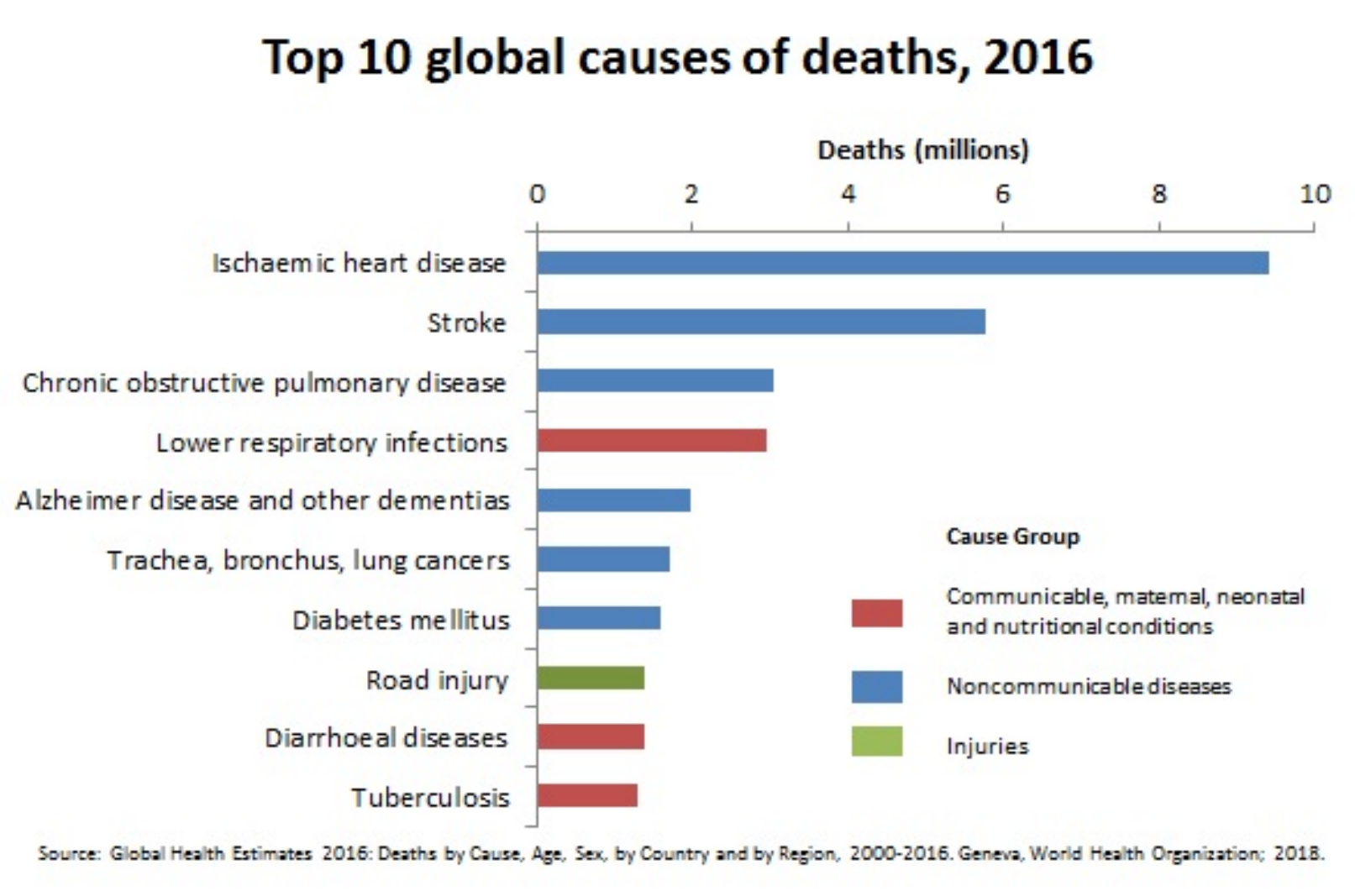
- Diagnose hypertension and evaluate a person who has it
- Treat a person with hypertension
- Prevent complications of hypertension and its treatment

Why discuss hypertension?

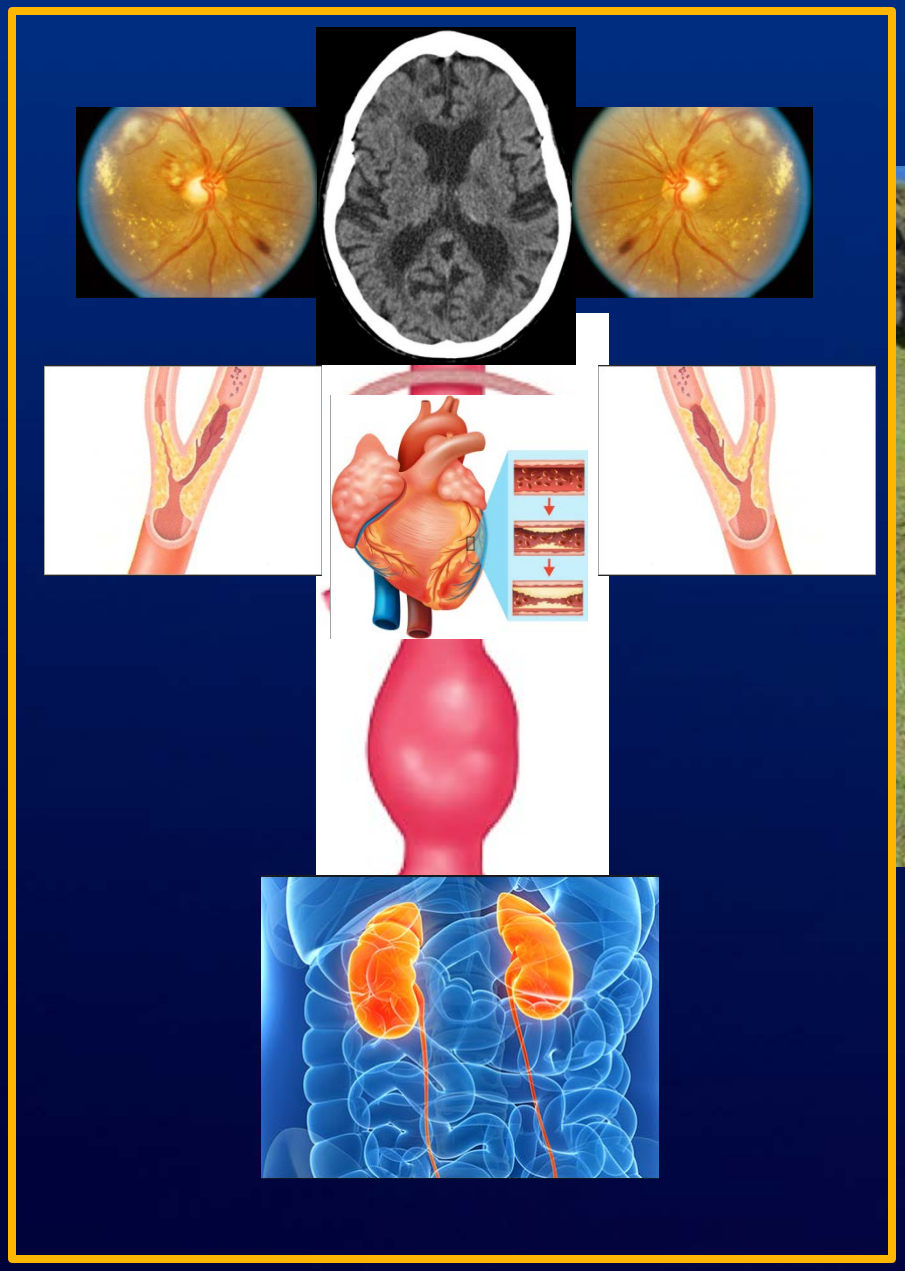
- Rising burden of noncommunicable Disease



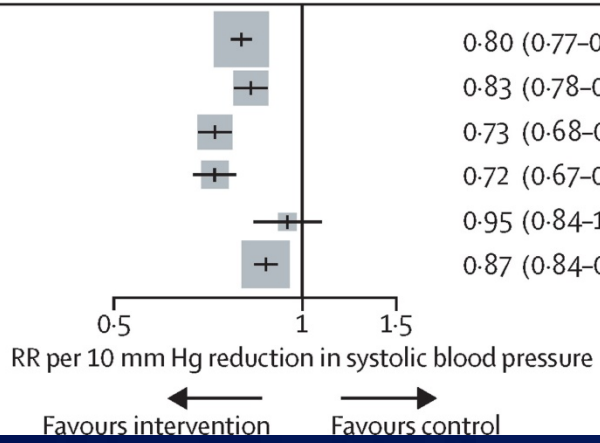
Why discuss hypertension?



Hypertension: Consequences

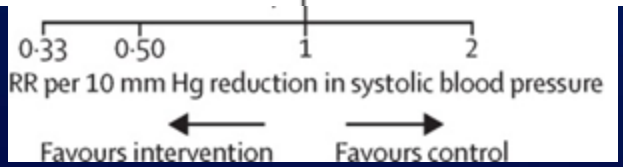


	Studies	Intervention		Control		RR (95% CI) per 10 mm Hg reduction in systolic blood pressure
		Events	Participants	Events	Participants	
Major cardiovascular events	55	13209	137319	14068	128259	0·80 (0·77–0·83)
Coronary heart disease	56	4862	136986	5301	128548	0·83 (0·78–0·88)
Stroke	54	4635	136682	5378	128641	0·73 (0·68–0·77)
Heart failure	43	3284	115411	3760	107440	0·72 (0·67–0·78)
Renal failure	16	890	39888	834	39043	0·95 (0·84–1·07)
All-cause mortality	57	9775	138298	9998	129700	0·87 (0·84–0·91)



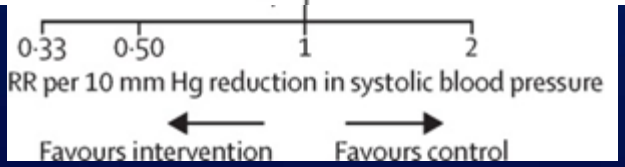
The Lancet 2016 387957-967DOI: (10.1016/S0140-6736(15)01225-8)

	Studies	Intervention		Control		RR (95% CI) per 10 mm Hg reduction in systolic blood pressure	p_{trend}
		Events	Participants	Events	Participants		
Major cardiovascular events							0·22
<130	4	542	4547	530	3881	0·63 (0·50–0·80)	
130–139	17	5375	47103	5856	47167	0·87 (0·82–0·92)	
140–149	7	4365	33333	4694	33062	0·79 (0·72–0·87)	
150–159	13	1289	21290	1257	20088	0·80 (0·71–0·91)	
≥160	14	1638	31045	1731	24060	0·74 (0·69–0·79)	
Total						**0·80 (0·77–0·83)**	



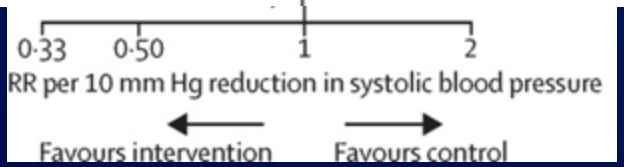
The Lancet 2016 387957-967DOI: (10.1016/S0140-6736(15)01225-8)

	Studies	Intervention		Control		RR (95% CI) per 10 mm Hg reduction in systolic blood pressure	p_{trend}
		Events	Participants	Events	Participants		
Coronary heart disease							0·93
<130	5	489	6071	620	5395	0·55 (0·42–0·72)	
130–139	18	2258	47608	2461	47670	0·88 (0·80–0·96)	
140–149	8	1225	34834	1307	34581	0·80 (0·69–0·94)	
150–159	12	409	20386	442	19788	0·84 (0·68–1·05)	
≥160	13	481	28086	471	21113	0·82 (0·73–0·92)	
Total						**0·83 (0·78–0·88)**	



The Lancet 2016 387957-967DOI: (10.1016/S0140-6736(15)01225-8)

	Studies	Intervention		Control		RR (95% CI) per 10 mm Hg reduction in systolic blood pressure	p_{trend}
		Events	Participants	Events	Participants		
Stroke							0·38
<130	3	48	3669	47	2984	0·65 (0·27–1·57)	
130–139	18	1191	47608	1403	47670	0·73 (0·62–0·85)	
140–149	7	2130	34166	2381	34347	0·78 (0·70–0·87)	
150–159	11	538	19636	702	19026	0·65 (0·54–0·78)	
≥160	15	728	31603	845	24613	0·70 (0·64–0·78)	
Total						**0·73 (0·68–0·77)**	



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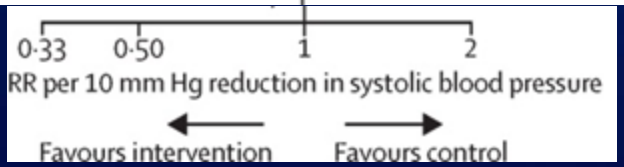
	Studies	Intervention		Control		RR (95% CI) per 10 mm Hg reduction in systolic blood pressure	p_{trend}
		Events	Participants	Events	Participants		
Heart failure							0·27
<130	3	137	3669	138	2984	0·83 (0·41–1·70)	
130–139	15	1493	44029	1778	44104	0·75 (0·66–0·85)	
140–149	6	1121	32665	1207	32828	0·83 (0·70–1·00)	
150–159	7	304	8507	271	7945	0·96 (0·71–1·30)	
≥160	12	229	26541	366	19579	0·61 (0·54–0·70)	
Total						**0·72 (0·67–0·78)**	



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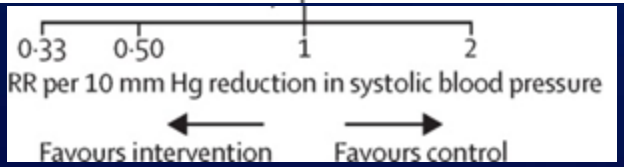
	Studies	Intervention		Control		RR (95% CI) per 10 mm Hg reduction in systolic blood pressure	p_{trend}
		Events	Participants	Events	Participants		
All-cause mortality							0·79
<130	7	320	7733	410	7059	0·53 (0·37–0·76)	
130–139	18	3596	47608	3782	47670	0·89 (0·82–0·98)	
140–149	7	3338	34166	3318	34347	0·99 (0·89–1·09)	
150–159	12	1127	20705	1197	19511	0·78 (0·69–0·90)	
≥160	13	1394	28086	1291	21113	0·86 (0·80–0·92)	
Total						**0·87 (0·84–0·91)**	



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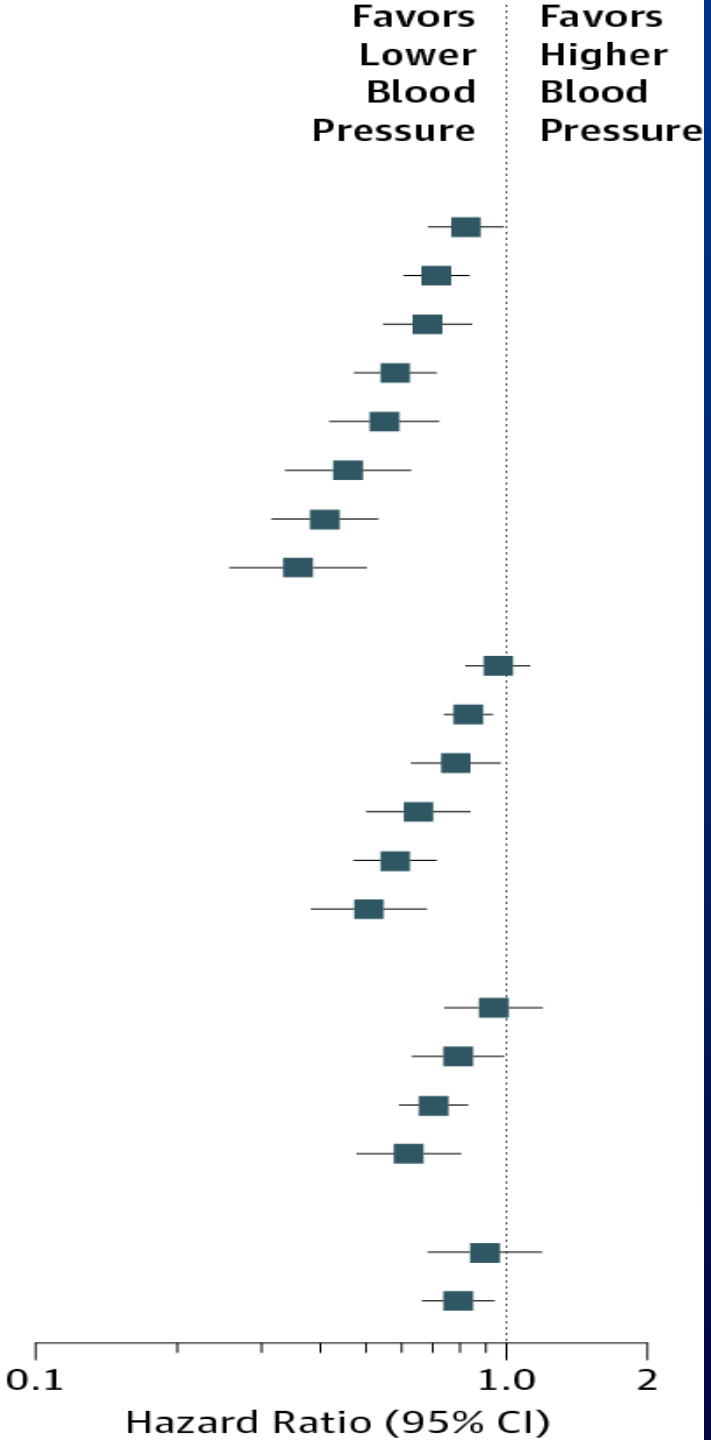
Mean Achieved Systolic Blood Pressure, mm Hg	Hazard Ratio (95% CI)
Reduction to 120-124	
120-124 vs 125-129	0.82 (0.67-0.97)
120-124 vs 130-134	0.71 (0.60-0.83)
120-124 vs 135-139	0.68 (0.55-0.85)
120-124 vs 140-144	0.58 (0.48-0.72)
120-124 vs 145-149	0.55 (0.42-0.72)
120-124 vs 150-154	0.46 (0.34-0.63)
120-124 vs 155-159	0.41 (0.32-0.54)
120-124 vs ≥160	0.36 (0.26-0.51)
Reduction to 130-134	
130-134 vs 135-139	0.96 (0.83-1.14)
130-134 vs 140-144	0.83 (0.74-0.94)
130-134 vs 145-149	0.78 (0.63-0.98)
130-134 vs 150-154	0.65 (0.51-0.85)
130-134 vs 155-159	0.58 (0.48-0.72)
130-134 vs ≥160	0.51 (0.39-0.69)
Reduction to 140-144	
140-144 vs 145-149	0.94 (0.74-1.20)
140-144 vs 150-154	0.79 (0.63-0.99)
140-144 vs 155-159	0.70 (0.60-0.84)
140-144 vs ≥160	0.62 (0.48-0.80)
Reduction to 150-154	
150-154 vs 155-159	0.90 (0.68-1.19)
150-154 vs ≥160	0.79 (0.66-0.94)



Bundy JD et al (2017)

Diagnose and evaluate hypertension

Define hypertension

Evaluate newly diagnosed hypertension

On differences between US and European hypertension guidelines

They really have more similarities than differences

Treat differently those with increased risk of morbidity/mortality

Treat intensively, but balance with treatment tolerability

Hypertension (HTN): Definition

- Ideal: BP <120/<80
- Risks rise after BP ≥130/ ≥80
- ≥2 readings, separated in time

HTN: Definitions (European Guidelines)

Classification of office blood pressure[a] and definitions of hypertension grade[b]

Category	Systolic (mmHg)		Diastolic (mmHg)
Optimal	<120	and	<80
Normal	120–129	and/or	80–84
High normal	130–139	and/or	85–89
Grade 1 hypertension	140–159	and/or	90–99
Grade 2 hypertension	160–179	and/or	100–109
Grade 3 hypertension	≥180	and/or	≥110
Isolated systolic hypertension[b]	≥140	and	<90

HTN: More Definitions, Fine Tuning

- 24-hour ambulatory blood pressure (ABPM)
  - Risk rises after BP ≥125/≥75
- "White coat" hypertension
  - BP elevated in office, normal at home
  - Natural history closer to normotension
- "Masked" hypertension
  - BP normal in office, elevated at home
  - Natural history closer to hypertension

HTN: More Definitions

- Pregnancy: same definitions
  - Pre-existing: onset prior to 20 wk gestation
  - Gestational: onset ≥20 wk gestation
  - Pre-existing + gestational
  - Pre-eclampsia: gestational hypertension with proteinuria > 300 mg/24 h
  - Antenatally unclassifiable hypertension

Hypertension: Screening and Diagnosis

- Screen all adults
  - Young+low risk: every 3-5 years
  - ≥40 years or high risk: yearly
  - Pregnancy: each visit
- ≥ 2 readings, ≥ 2 occasions
  - Or HTN + target organ damage (Europe)
  - Out-of-office/self-test to confirm
- White coat/masked HTN: 24-hour ABPM
- 90-95% of cases are primary HTN

HTN: Evaluation

- Identify cardiovascular risk factors
- Briefly screen for secondary causes
- Assess for target-organ damage

HTN: Formal Risk Assessment

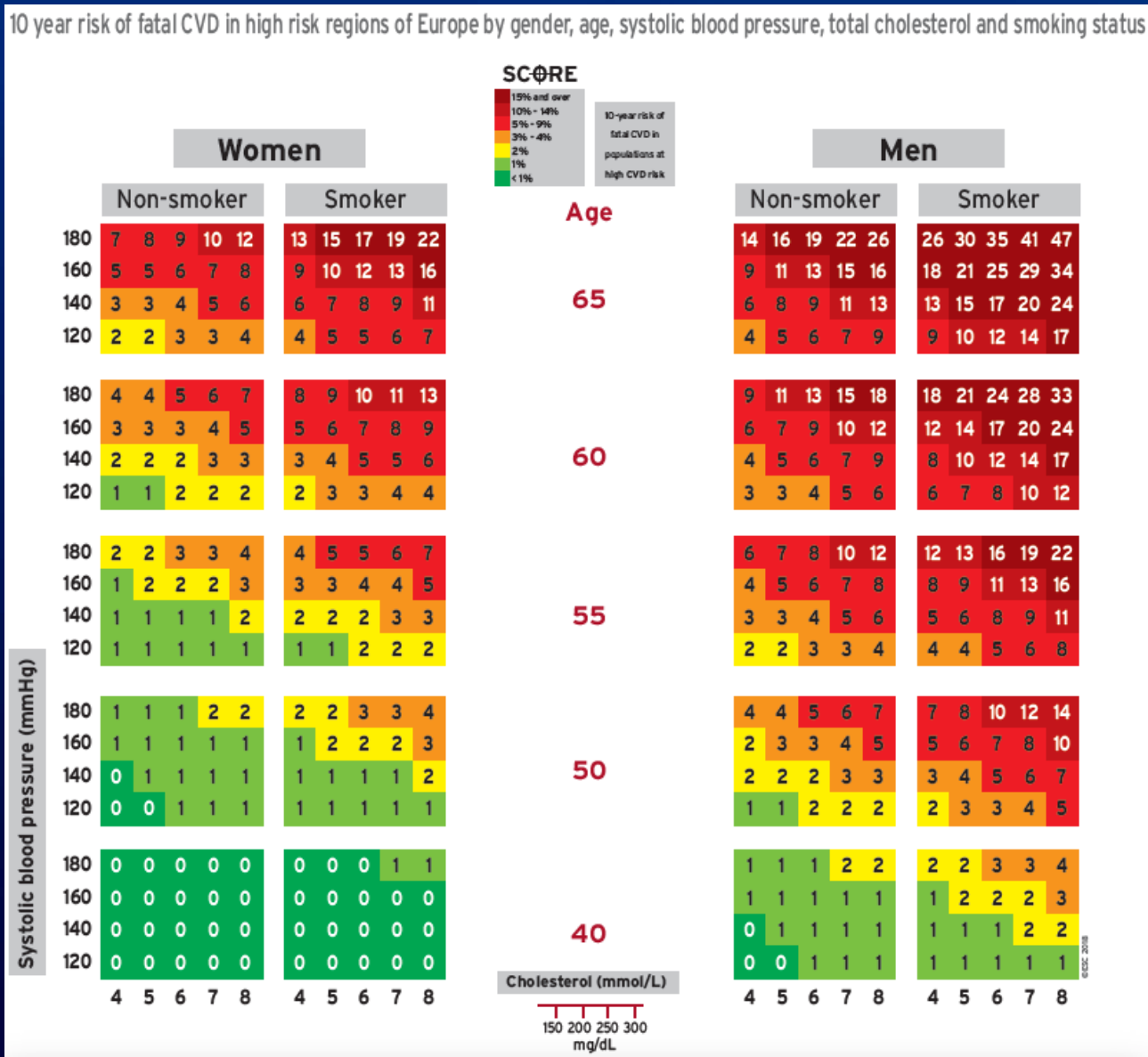
- Systemic Coronary Risk Evaluation (SCORE), in European Guidelines
- Pooled Cohort Equation, in United States Guidelines

- Overlap: automatically high risk if known ASCVD
- Differences: risk estimates in younger persons

- Recommendation: pick one, use it consistently

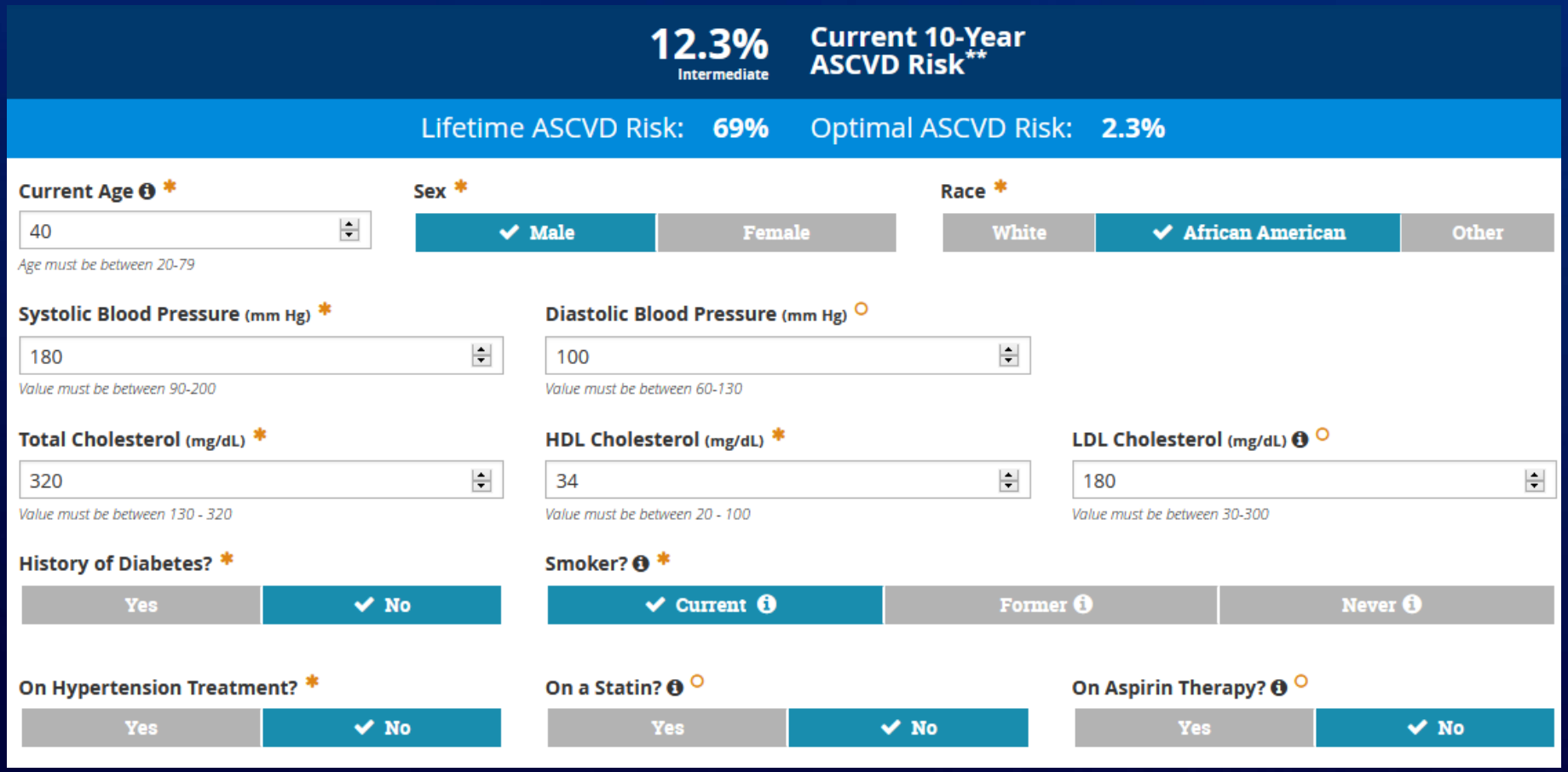
Systematic Coronary Risk Evaluation (SCORE)

- http://www.escardio.org/Guidelines-&-Education/Practice-tools/%20CVD-prevention-toolbox/SCORE-Risk-Charts



Pooled Cohort Equation for 10-Year Risk of Atherosclerotic Cardiovascular Disease

- http://tools.acc.org/ASCVD-Risk-Estimator-Plus/#!/calculate/estimate/

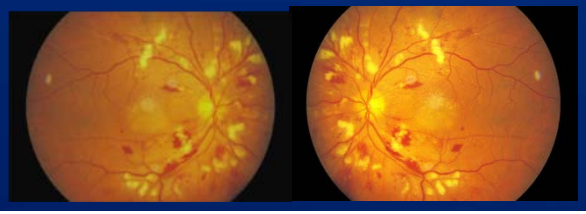


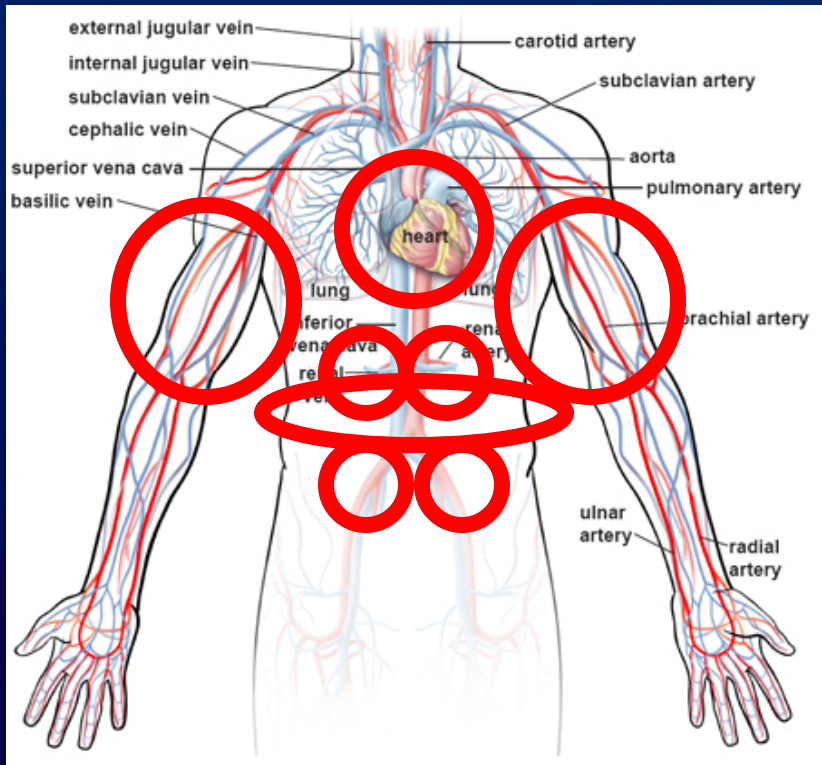
HTN: Informal Risk Adjustments

- Coronary artery disease
- Peripheral arterial disease
- Cerebrovascular disease
- Chronic kidney disease
- Diabetes mellitus
- Obstructive sleep apnea
- Preeclampsia
- Sedentary lifestyle
- Family history

HTN Evaluation: Physical Exam

- Check BP in both arms
- Funduscopic exam
- BMI and waist circumference
- Heart
- Vessels





HTN Evaluation: Testing

- Urea, creatinine and electrolytes
- Urinalysis
  - With urine albumin, urine creatinine for some
- Fasting glucose
- Glycohemoglobin
- Fasting cholesterol profile
- Hematocrit (full blood count)
- Electrocardiogram
- Thyroid stimulating hormone
- Medication review

Routine annual follow-up tests in yellow

Hypertension: Why Those Tests?

- ECG: LVH? Previous MI?
- CBC: polycythemia?
- BMP (U&E): CKD? HypoK^{+}? HyperCa^{2+}?)
- TSH (hypothyroid: diastolic HTN, classically)
- Cholesterol profile (risk adjustment)
- UA (hematuria, “active” urine sediment,
- Urine albumin:creatinine (risk for progressive kidney disease, inform use of certain medications)

Treat hypertension

Choose whom and when to treat

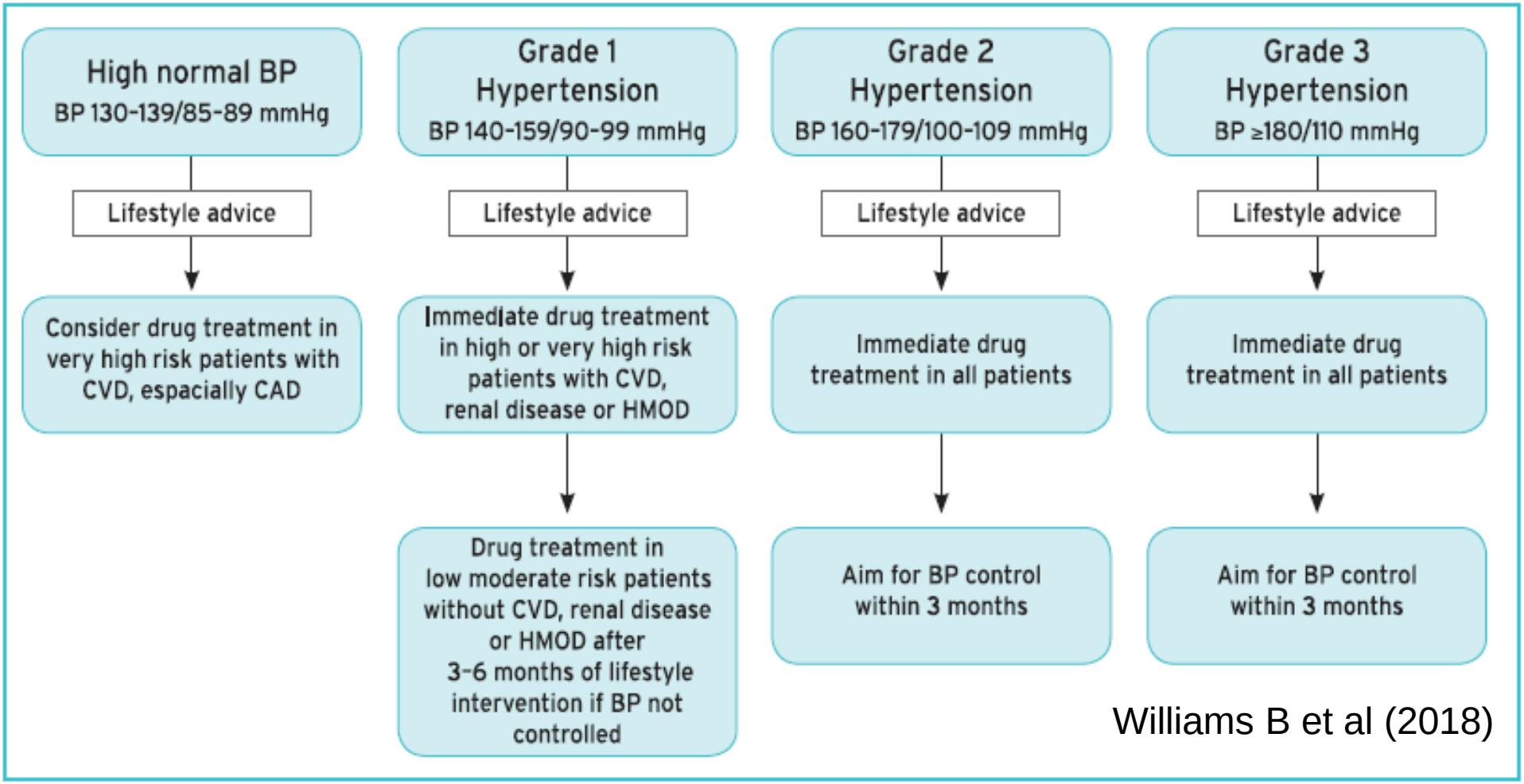
Counsel on effective lifestyle modification

Select medication(s) based on comorbidities

Set treatment target

Troubleshoot suboptimal treatment response

HTN Treatment: Who, When and How?



Williams B et al (2018)

- **BP 120-129/<80: lifestyle advice**

HTN: Treatment Targets

- First objective: <140/90 mm Hg
- Once there: try even harder, if tolerated!
- Optimal goal: SBP < 130 mm Hg and DBP < 80 mm Hg
  - If BP medications start to cause activity-limiting orthostatic symptoms, reaching optimal goal may not be possible

HTN Treatment: How About Pregnancy?

- All women w/ BP ≥150/95mmHg;
- Gestational hypertension BP > 140/90
- Pre-existing HTN + gestational HTN > 140/90
- Note: essentially based on opinion

Williams B et al (2018)

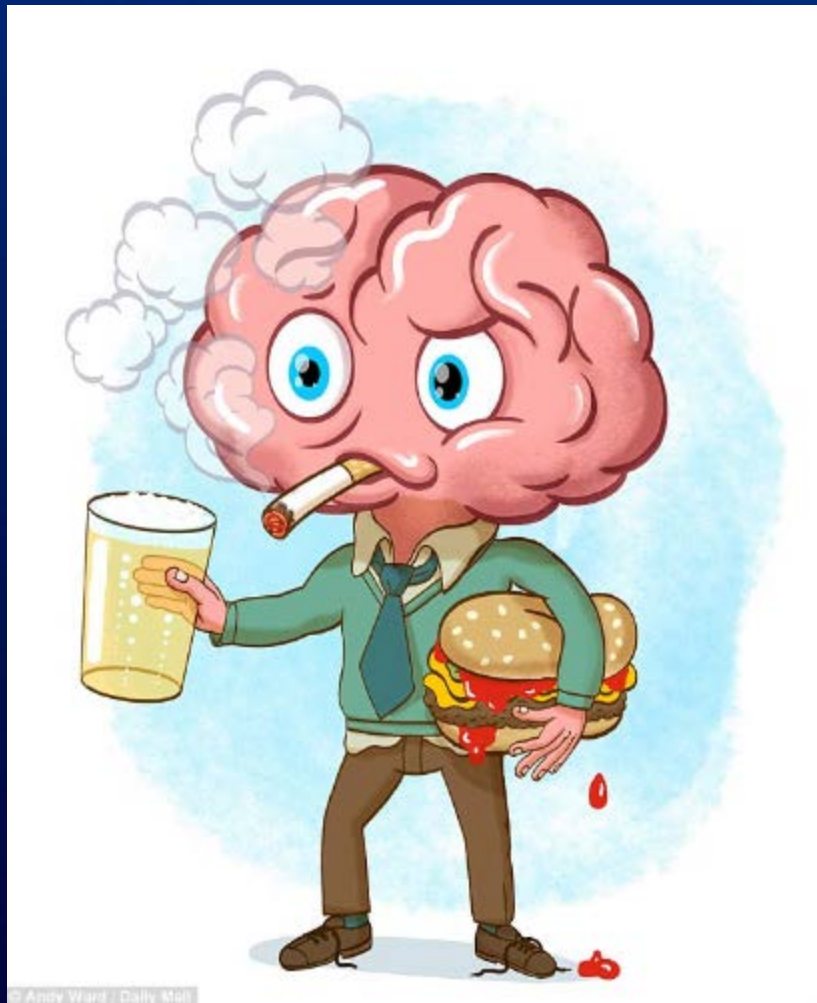
- Probably safe: labetalol, methyldopa, hydralazine, nifedipine
- Avoid: ACE inhibitors (e.g. lisinopril), ARBs (e.g. losartan), mineralocorticoid receptor antagonists (e.g. spironolactone)

HTN Treatment: First Consider Problem Meds

- Nonsteroidal anti-inflammatory medications
- Combined oral contraceptive pills
  - If HTN troublesome and after weighing risks/benefits to discontinuing COC
- Menopausal hormone therapy

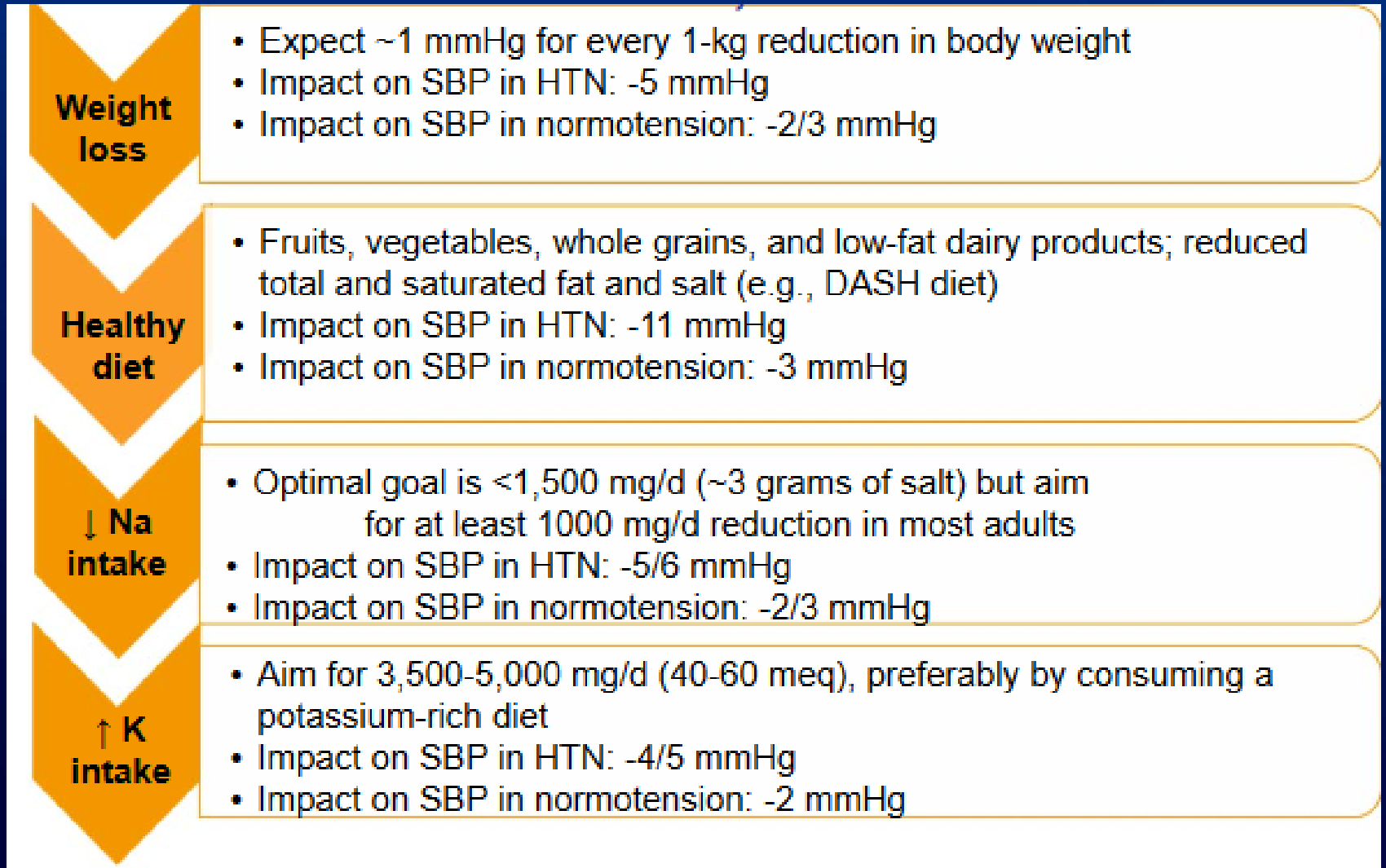
HTN: Then, Lifestyle Modifications

- Alcohol moderation
- Smoking cessation
- Salt restriction
- DASH diet
- Get to ideal body weight
- Regular physical activity



HTN: Lifestyle Modifications

- **Stop smoking!**

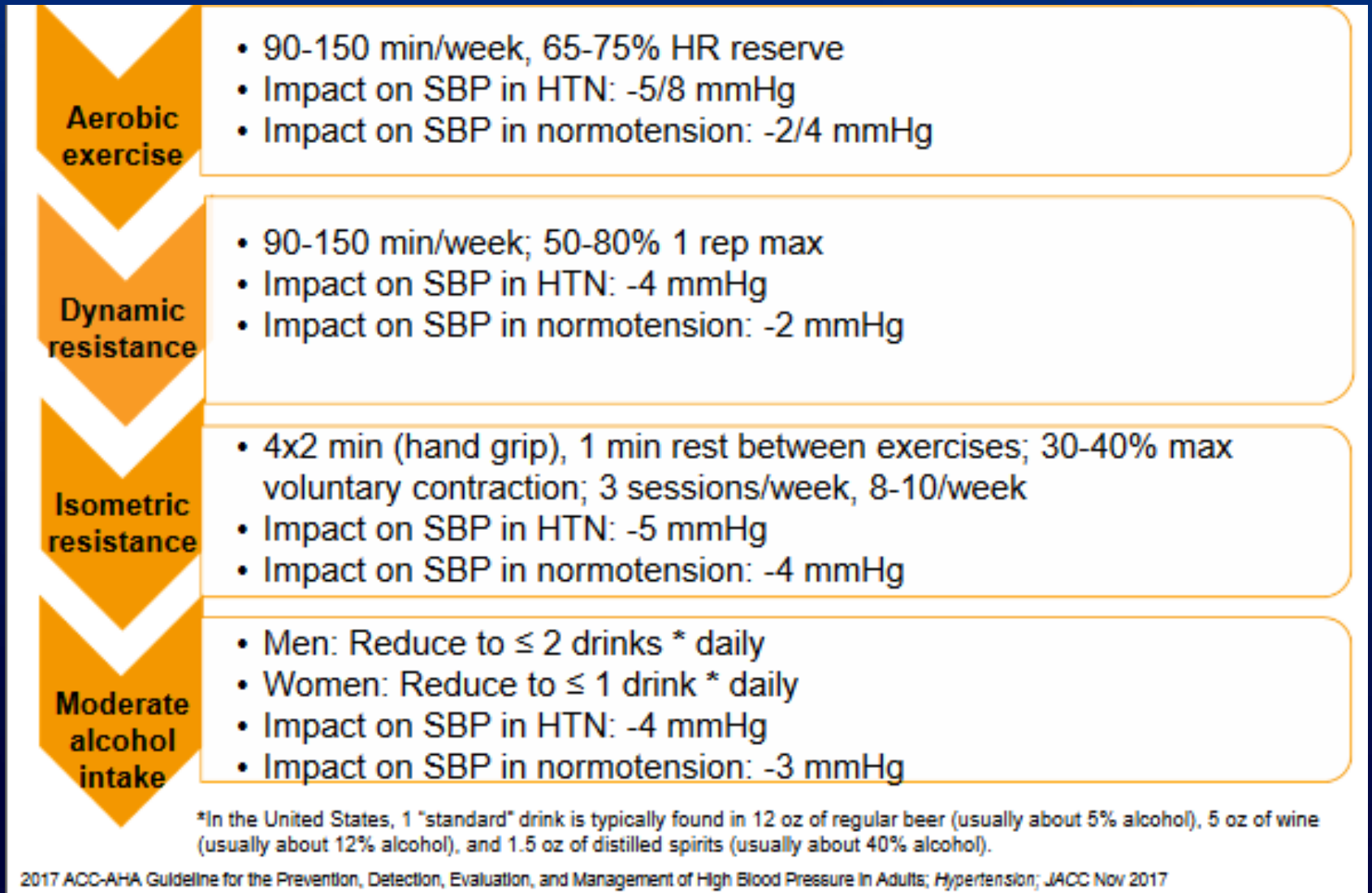


2017 ACC-AHA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults; *Hypertension*; JACC Nov 2017

HTN: DASH Diet

HTN: Lifestyle Modifications

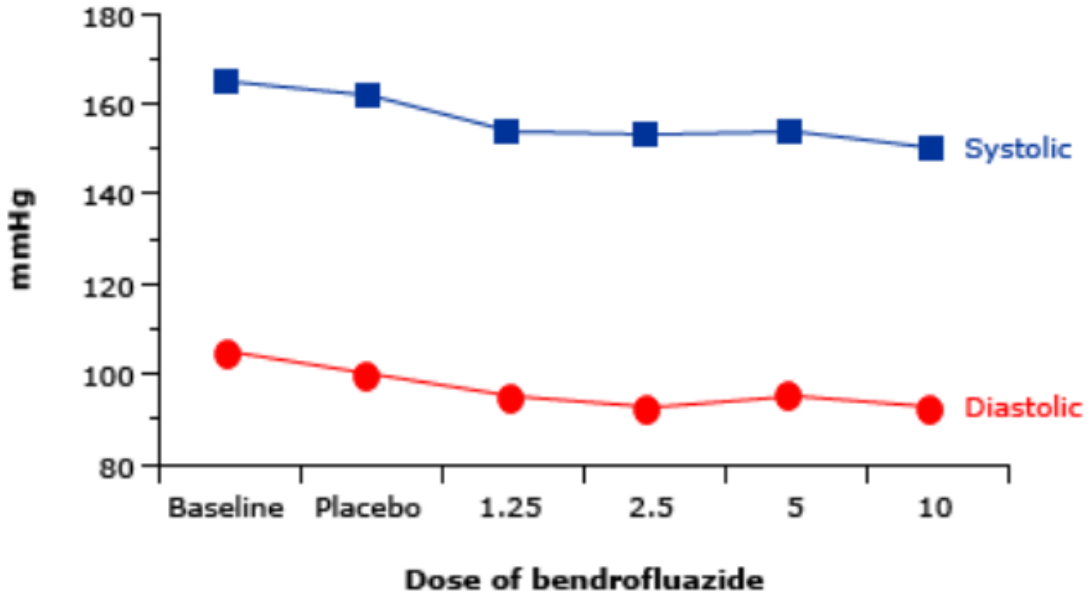
- **Stop smoking!**



HTN: Combination Therapy Early

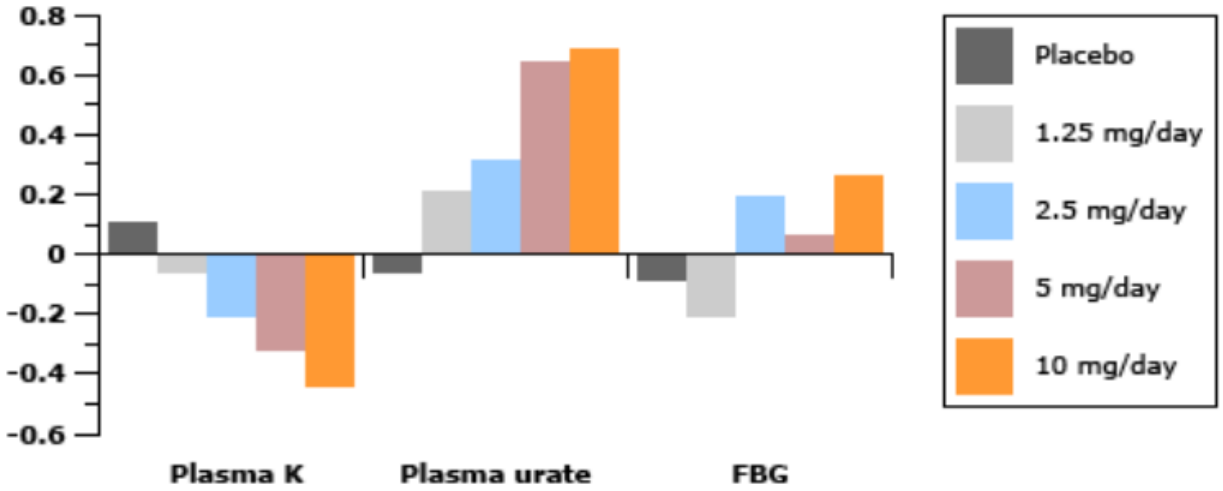
- Early combination therapy makes sense
  - May mitigate side effects
  - Preempts provider or patient inertia
  - Faster HTN control
  - SPCs can be used for convenience
  - ESC/ESH recommend early
  - Just don’t combine the wrong things (e.g. ACE+ARB)
  - Caution in frail persons

Antihypertensive dose response to thiazide therapy



Treatment effects reach plateau early…

Dose dependence of thiazide-induced side effects



…but side effects increase with each incremental dose increase

Mann JFE. "Choice of drug therapy in primary (essential) hypertension." In: UpToDate, Bakris GL and White WB, Waltham, MA, 2020.

HTN: Effective Pharmacotherapy Options

- Dihydropiridine calcium channel blocker (CCB)
  - e.g. amlodipine, nifedipine
- Diuretic
  - e.g. chlorthalidone, indapamide, hydrochlorothiazide
- Angiotensin converting enzyme (ACE) inhibitor
  - e.g. lisinopril, perindopril, enalapril
- Angiotensin receptor blocker (ARB)
  - e.g. losartan, valsartan

HTN: a Word on β-blockers

- Not particularly effective for hypertension
- Use as part of combination when indicated:
  - Ischemic heart disease
  - Heart failure with reduced ejection fraction
    - Carvedilol, metoprolol succinate, bisoprolol
  - Atrial fibrillation

HTN: Wise Prescribing

- Chronic kidney disease, albuminuria (even moderately increased at > 30 mg/day)
  - Consider ACE-inhibitor or ARB
- Patient is black
  - Diuretic or CCB better than ACE-inhibitor or ARB
- Patient has angina despite β-blocker: CCB
- Stroke reduction: ACE+CCB > ACE+diuretic
- α-blockers linked to higher risk of heart failure
- Do not combine ACE and ARB!

HTN: Lack of Treatment Response

- Physician inertia
- Insufficient combo therapy
- Treatment complexity
- Patient adherence
- Secondary causes

- 90-95% of patients can achieve target

HTN: Resistant Hypertension

- BP > goal on ≥3 drugs (including diuretic)
- 1. Exclude nonadherence, iatrogenesis
- 2. Consider secondary causes (5-10% of HTN)
- 3. Add spironolactone 25-50 mg OD

  or

- Add bisoprolol or nitrate/hydralazine
- 4. Refer to internist or specialist
  - Advanced Rx strategies: change diuretics

Hypertension: Secondary HTN

- Suspect if
  - Age < 30 years at onset
  - Diastolic HTN after age 65
  - Abrupt onset, or abrupt worsening of previously controlled HTN
  - Drug resistance
  - Suggestive clinical features
  - Disproportionate target organ damage
  - Hypokalemia

Hypertension: Renovascular HTN

- For most, medical therapy equals benefit of invasive procedures
  - Hence, for most, no eval needed
- For young persons with suspected FMD, may consider renal artery imaging

Hypertension: Aldosteronism

- First step: plasma aldosterone:plasma renin activity ratio
  - Very high ratio = suggestive
- Second step: saline suppression test
- Third step: imaging + adrenal venous sampling
  - Unilateral: adrenalectomy?
  - Bilateral (hyperplasia): medical therapy

Prevent complications

Prevent and treat complications and comorbidities

Mitigate adverse effects of medications

HTN: Prevention of Complications

- Yearly Screening
  - Urea, creatinine and electrolytes
  - Urinalysis (urine protein:creatinine for some)
  - Glycohemoglobin
  - Fasting cholesterol profile
  - Hematocrit (full blood count)
- Statin
  - Diabetes
  - ASCVD or high risk of it
- Aspirin
  - Coronary or cerebrovascular disease

Table 20 Compelling and possible contraindications to the use of specific antihypertensive drugs

Drug	Contraindications	
	Compelling	Possible
Diuretics (thiazides/thiazide-like, e.g. chlorthalidone and indapamide)	• Gout	• Metabolic syndrome • Glucose intolerance • Pregnancy • Hypercalcaemia • Hypokalaemia
Beta-blockers	• Asthma • Any high-grade sinoatrial or atrioventricular block • Bradycardia (heart rate <60 beats per min)	• Metabolic syndrome • Glucose intolerance • Athletes and physically active patients
Calcium antagonists (dihydropyridines)		• Tachyarrhythmia • Heart failure (HFrEF, class III or IV) • Pre-existing severe leg oedema
Calcium antagonists (verapamil, diltiazem)	• Any high-grade sinoatrial or atrioventricular block • Severe LV dysfunction (LV ejection fraction <40%) • Bradycardia (heart rate <60 beats per min)	• Constipation
ACE inhibitors	• Pregnancy • Previous angioneurotic oedema • Hyperkalaemia (potassium >5.5 mmol/L) • Bilateral renal artery stenosis	• Women of child-bearing potential without reliable contraception
ARBs	• Pregnancy • Hyperkalaemia (potassium >5.5 mmol/L) • Bilateral renal artery stenosis	• Women of child-bearing potential without reliable contraception

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; HFrEF = heart failure with reduced ejection fraction; LV = left ventricular.

Summary

Summary: HTN Evaluation

- Urea, creatinine and electrolytes
- Urinalysis (urine albumin:creatinine for some)
- Fasting glucose
- Glycohemoglobin
- Fasting cholesterol profile
- Hematocrit (full blood count)
- Electrocardiogram
- Thyroid stimulating hormone
- Medication review

Routine annual follow-up tests in yellow

Summary: HTN Treatment, Goal < 130/80

Initial therapy
Dual combination

Two of these: diuretic, CCB, ACE-inhibitor/ARB

Consider monotherapy in low risk grade 1 hypertension (systolic BP <150mmHg), or in very old (≥80 years) or frailer patients

2-4 weeks ↓ **Max or add**

Step 2
Triple combination

All of these*: diuretic, CCB, ACE-inhibitor/ARB

Consider initiating therapy when systolic BP is ≥130 mmHg in very high risk patients with established CVD

↓

Step 3
Triple combination + spironolactone or other drug

Resistant hypertension
Add spironolactone (25–50 mg o.d.) or other diuretic, alpha-blocker or beta-blocker

Consider referral to a specialist centre for further investigation

Lifestyle modifications for all with BP > 120/80: smoking cessation, weight loss if overweight, healthy diet such as DASH diet, sodium restriction, aerobic exercise, reduce alcohol consumption if more than moderate

Beta-blockers

Consider beta-blockers at any treatment step, when there is a specific indication for their use, e.g. heart failure, angina, post-MI, atrial fibrillation, or younger women with, or planning, pregnancy

A reduction in eGFR and rise in serum creatinine is expected in patients with CKD[a] who receive BP-lowering therapy, especially in those treated with an ACEi or ARB but a rise in serum creatinine of >30% should prompt evaluation of the patient for possible renovascular disease.

Table 20 Compelling and possible contraindications to the use of specific antihypertensive drugs

Drug	Contraindications	
	Compelling	Possible
Diuretics (thiazides/thiazide-like, e.g. chlorthalidone and indapamide)	• Gout	• Metabolic syndrome • Glucose intolerance • Pregnancy • Hypercalcaemia • Hypokalaemia
Beta-blockers	• Asthma • Any high-grade sinoatrial or atrioventricular block • Bradycardia (heart rate <60 beats per min)	• Metabolic syndrome • Glucose intolerance • Athletes and physically active patients
Calcium antagonists (dihydropyridines)		• Tachyarrhythmia • Heart failure (HFrEF, class III or IV) • Pre-existing severe leg oedema
Calcium antagonists (verapamil, diltiazem)	• Any high-grade sinoatrial or atrioventricular block • Severe LV dysfunction (LV ejection fraction <40%) • Bradycardia (heart rate <60 beats per min)	• Constipation
ACE inhibitors	• Pregnancy • Previous angioneurotic oedema • Hyperkalaemia (potassium >5.5 mmol/L) • Bilateral renal artery stenosis	• Women of child-bearing potential without reliable contraception
ARBs	• Pregnancy • Hyperkalaemia (potassium >5.5 mmol/L) • Bilateral renal artery stenosis	• Women of child-bearing potential without reliable contraception

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; HFrEF = heart failure with reduced ejection fraction; LV = left ventricular.

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