

HYPERTENSION: 2015 UPDATE

Learning Objectives:

- Recognize that HTN is the leading contributor to global mortality and disability and is increasing in prevalence in the U.S. due to the obesity epidemic and population aging.
- Understand that while HTN control rates have improved in the past 30 years, these rates remain unacceptable.
 - Be able to look at your individual, group, and system practices to find both previously undetected as well as uncontrolled hypertensive patients.
- Be aware of key differences/controversies among the multitude of new HTN practice guidelines in 2013-2015.
 - Understand the different rationales for variable BP goals.
- Be able to make a more accurate diagnosis of HTN in view of new recommendations – including 2015 recommendations from the U.S. Preventive Services Task Force and the Canadian Hypertension Education Program – to routinely incorporate out-of-office BP measurement in all patients to confirm the diagnosis of hypertension.
- Be able to effectively use home BP monitoring (HBPM) for your patients.
- Be able to provide effective lifestyle modification – recognizing the controversies surrounding sodium restriction – to reduce BP.
- Be able to select optimal 1-4 drug regimens to improve HTN control rates.
- Be able to select the few patients who may benefit from evaluation and treatment of renal artery stenosis.

The Bottom Line:

HTN continues to be the leading risk factor for global mortality and disability at a cost of \$94 billion/y in the U.S. One third of all adult Americans and two thirds of Americans age ≥ 60 y have hypertension with prevalence likely to increase to 41% by 2030 due to the increasing obesity and aging of the population. Only 54% of hypertensive Americans have their BP controlled below 140/90 mm Hg, with lower control rates in blacks and Hispanics. Recent EHR studies indicate substantial numbers of undetected/untreated hypertensive persons in U.S. medical practices.

The accurate diagnosis of HTN requires correct BP measurement preparation and technique - infrequently accomplished in busy primary care practices – and detection of the 15-30% of patients with elevated office BP who have white-coat or isolated office HTN. Otherwise, many patients will be over-diagnosed and overtreated, an important patient safety issue. While office BP measurement (OBPM) has historically been the gold standard for HTN diagnosis, new 2015 recommendations from the U.S. Preventive Services Task Force, the Canadian Hypertension Education Program, and the French, UK, and Taiwan HTN guidelines now propose out-of-office BP measurement (24-hour ambulatory BP studies, or if not available, standardized home BP measurement) to confirm all office diagnoses of HTN prior to treatment.

There is no consensus among new HTN practice guidelines as to target treatment BP among various subpopulations of patients. While most guidelines have a target BP < 140/90 mm Hg for the general population, the JNC-8 task force – but only a majority of this group – favors a target BP < 150/90 mm Hg for persons age ≥ 60y. Their rationales include the absence of a definitive RCT that treated patients with BP = 140-149, a 2012 Cochrane Review that found no decrease in CVD events in such patients, and the presence of potential treatment side effects. However, many other groups favor the < 140/90 target, citing the considerable epidemiologic CVD risk of BP= 140-149 and other meta-analyses suggesting reduction of CVD events with BP = 140-149. Most guidelines now target a BP < 150/90 for persons age ≥ 80y. Most guidelines now target a BP < 140/90 for patients with diabetes or CKD, while a few others target a BP < 130/80 if diabetes, albuminuria, or high stroke risk is present.

With respect to treatment, controversy continues to surround the benefits, or lack of benefit, or even toxicity of very low sodium diets < 1500-2300 mg/d. Algorithms have been published in the new guidelines recommending optimal one, two, three, and four drug regimens to more effectively treat HTN; most guidelines have relegated beta-blockers to step 3 or step 4 therapy unless there are compelling indications for their use. Finally, recent studies suggest that evaluation and treatment of renal artery stenosis should be limited to a very small subgroup of patients with very high BP and/or declining eGFR and/or flash pulmonary edema.

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- **Home BP Monitoring:**
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 2. Japanese Society of Hypertension. Guidelines for self-monitoring of blood pressure at home. Hypertension Research 2012; 35:777-795.

- **How Low Should We Go?**
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 2. Gradman AH. Optimal BP targets in older adults: how low is low enough? J Am Coll Card 2014; 64:794-796.

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 3. JNC-8 Panel. 2014 evidence-based guideline for the management of hypertension in adults. JAMA 2014; 311:507-520.
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HYPERTENSION 2015 UPDATE

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HYPERTENSION: MORBID, LETHAL!

TOP RF FOR GLOBAL MORTALITY/DISABILITY

Increases RR by 2.0-4.0 fold for:

- CAD, stroke, HF, PAD, AF, CKD
- Dementia: vascular, Alzheimers
- Mild cognitive deficits

Attributable risk for HTN:

- Stroke → 62%
- CKD → 56%
- HF → 49%
- MI → 25%
- Premature death → 24%

Aftermath:

- Shortens lifespan 5y – 16% of deaths
- \$46.4 billion/y in U.S. (\$94 billion/y, total)

HYPERTENSION: UNBELIEVABLY COMMON!

- **Prevalence:**

- 33% of adult Americans
- 45% of adult black Americans – highest in world
- 65% of Americans age ≥ 60 y
- 90% of Americans age ≥ 85 y
- CKD:
 - eGFR ≤ 60 : 67% < 30: 92%
 - Hemodialysis: 60% Peritoneal: 30%



80 million Americans with HTN!
Projected prevalence in 2030: 41% of adults

HYPERTENSION: VERY TREATABLE

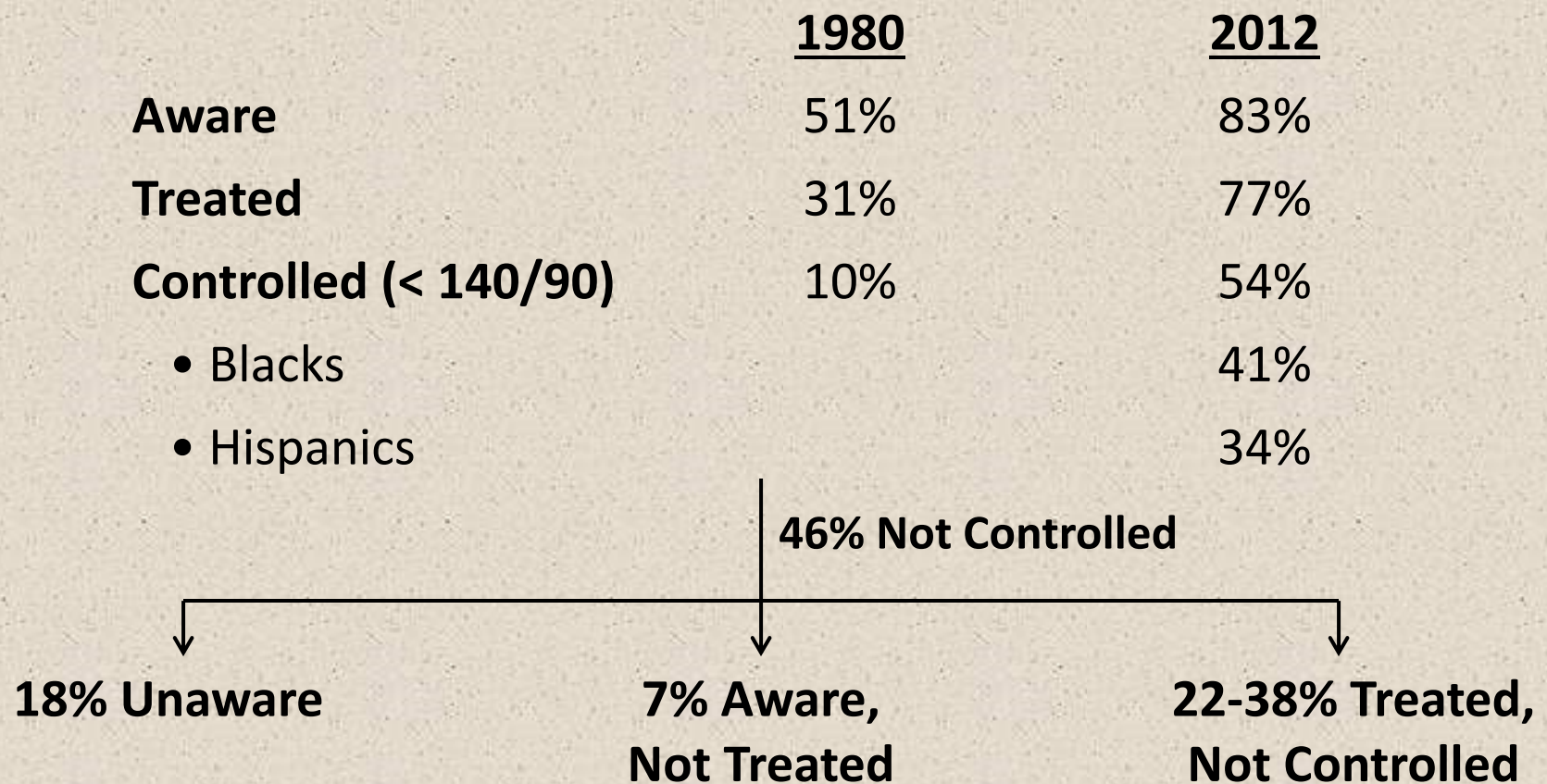
Meta-analysis: 68 RCTs; 245,885 pts; 4.3y FU

- ↓ SBP/DBP by 10/5 mm Hg for 5y:

<u>Complication</u>	<u>% Risk Reduction</u>	<u>NNT x 5y</u>
CVD events	25%	36
Heart failure	43%	73
Stroke	36%	58
MI	16%	160
Mortality	11%	125
Dementia	?	?

HTN CONTROL: IMPROVING, BUT STILL UNACCEPTABLE

NHANES:



UNDIAGNOSED HYPERTENSION: HIDING IN PLAIN SIGHT IN OUR OFFICES?

- **Geisinger Health System:**

- EHR search of 400,000 pts with ≥ 3 visits over 4y
 - 29,000 pts had ≥ 2 BP readings $\geq 140/90$ but no evaluation

- **Palo Alto Medical Foundation:**

- EHR search of 250,000 pts over 2y
 - 37% with ≥ 2 BP readings $\geq 140/90$ had no evaluation

- **North Shore University Health System:**

- 47% of recalled pts from EHR search had HTN previously undiagnosed

NEW HYPERTENSION GUIDELINES, 2015

- JNC-8 Panel: JAMA 2014; 311:507
- JNC-8 Minority Panelists: Ann Int Med 2014; 160:449
- AHA/ACC/CDC Advisory: J Am Coll Card 2014; 63:1230
- Am Society of Hypertension: J Clin Hypertens 2014; 16:14
- Canadian Hypertension Education Program: Can J Card 2014; 30:485
- Joint British Societies 3: Heart 2014; 100 (Suppl 2):1
- ESH/ESC: J Hypertens 2013; 31:1281
- Japanese Society of Hypertension: Hypertension Res 2014; 37:253
- KDIGO Blood Pressure Work Group: Kid Int 2012; Suppl 2
- American Diabetes Association: Diabetes Care 2015; 38 (Suppl 1):S49
- Taiwan Hypertension Society: J Clin Med Assoc; on-line 12/26/2014

HYPERTENSION GUIDELINES 2015: NOT SO MUCH CLARITY

“Hypertension guidelines – clear as mud.”

TheHeart.org

“Why doctors are fighting over blood pressure guidelines.”

Time, 2014

“The multitude of guidelines from respected professional bodies and individuals have caused needless confusion bordering on chaos.”

Editorial, J Clin Hypertens 2014; 16:251

HOW TO DIAGNOSE HYPERTENSION IN 2015?

- **Essential to measure office BP accurately!**

“Blood pressure reading does not seem to be done correctly in any clinic...It appears to be so simple that anyone can do it, but they can’t...”

JAMA 2008; 299:2842

- 9 studies with 9000 patients, 1995-2011:

**Routine clinical practice
BP measurement**

vs

**Guideline-based
BP measurement**

– **Accurate BP measurement ↓ BP ≈ 10/7 mm Hg
and doubled HTN control rates!**

BP MEASUREMENT: KEY TECHNIQUES

	<u>△ BP (mm Hg) if not done</u>
Rest ≥ 5 min, quiet	↑ 12/6
Seated, back supported	↑ 6/8
Cuff at midsternal level	↑ ↓ 2/inch
Correct cuff size	↑ 6-18/4-13 if too small
	↓ 7/5 if too large
Bladder center over artery	↑ 3-5/2-3
Deflate 2 mm Hg/sec	↓ SBP/↑ DBP
No talking during measurement	↑ 17/13
If initial BP > goal BP:	1st reading higher
3 readings, 1 min apart	• “Alerting response”
Discard 1st, average last 2	• Reclassify 18-34% as normotensive
	• Requires 8-11 minutes!

OFFICE BP MEASUREMENT: HOW TO DO IT?

- **Can we teach/implement accurate manual BP measurement?**
 - Doubtful: repetitive training/monitoring/time too difficult
- **Automated electronic BP measurement favored by ASH, 2014 and by CHEP 2015**
 - Only accurate devices validated by AAMI/BHS/IP protocols
 - www.bhsoc.org/bp-monitors/bp-monitors/
 - www.dableducational.org
 - Consider unattended AOBP devices taking 3-6 measurements automatically
 - ↑ accuracy and reproducibility, and ↓ white-coat effect
 - BpTRU(6), Omron HEM-907 (3), MicroLife Watch BP Office (3)

OUT-OF-OFFICE BP MEASUREMENT: ESSENTIAL TO DX HTN?

- **White-coat (isolated office) HTN very common!**

WCH Prevalence

General population	10-15%
Office BP \geq 140/90	20-30%
• Office BP = 140-159	55%
• Office BP \geq 180	10%

OUT-OF-OFFICE BP MEASUREMENT: ESSENTIAL TO DX HTN?

AHRQ 2014 Systematic Review:

- Predicts CVD events superior to OBPM:

	<u>HR for CVD vs OBPM</u>
ABPM (11 studies)	1.28-1.40
HBPM (4 studies)	1.17-1.39

- Diagnoses HTN more accurately than OBPM:

Measurement error of OBPM ————
Regression to mean —————→ not confirmed by
White-coat HTN in 15-30% ———— ABPM in 27 studies

5-65% of office HTN

OUT-OF-OFFICE BP MEASUREMENT: ESSENTIAL TO DX HTN?

USPSTF Draft Statement, January, 2015:

“The USPSTF recommends screening for HTN in adults ≥ 18 y old. Ambulatory BP monitoring is recommended to confirm high BP before the diagnosis of HTN, except in cases for which immediate initiation of therapy is necessary...Good quality evidence suggest that confirmation of hypertension using home BP monitoring may be acceptable...More research is needed on the best home BP monitoring protocols for followup of elevated office BP measurements...”

HOW TO DIAGNOSE HYPERTENSION IN 2015?

Guideline

ASH/ISH 2014;

ESH 2013

CHEP 2015

Taiwan 2015; FSH 2013

NICE (UK) 2011; USPSTF 2015

Gold Standard to Dx HTN

OBPM \geq 2 visits

- ABPM/HBPM if suspect WCH, “borderline” BP, variable BP
- OBPM x 2 visits if TOD, CKD, DM, or BP \geq 180/110
- Confirm with ABPM > HBPM
- OBPM x 2 visits if TOD
- Confirm Dx in all others with ABPM or HBPM

Confirm with ABPM > HBPM

CAN SEQUENTIAL AUTOMATED OBP ON ISOLATED PTS DETECT WCH?

	<u>Routine Office BP</u>	<u>BpTRU AOBP</u>	<u>Daytime ABPM</u>
Beckett, 2005 • 481 pts	151/83	140/80	142/80
Myers, 2009 • 309 pts	152/87	132/75	134/77
Myers, 2010 • 254 pts	150/89	133/80	135/81
*Godwin, 2011 • 654 pts	149/83	138/80	141/80
*Myers, 2011 • 303 pts	150/81	136/78	133/74

AOBP, isolated pt, is within 1-2 mm Hg of daytime ABPM: reduces WCH
AOBP superior to Office BP to predict target organ damage

* 1° care

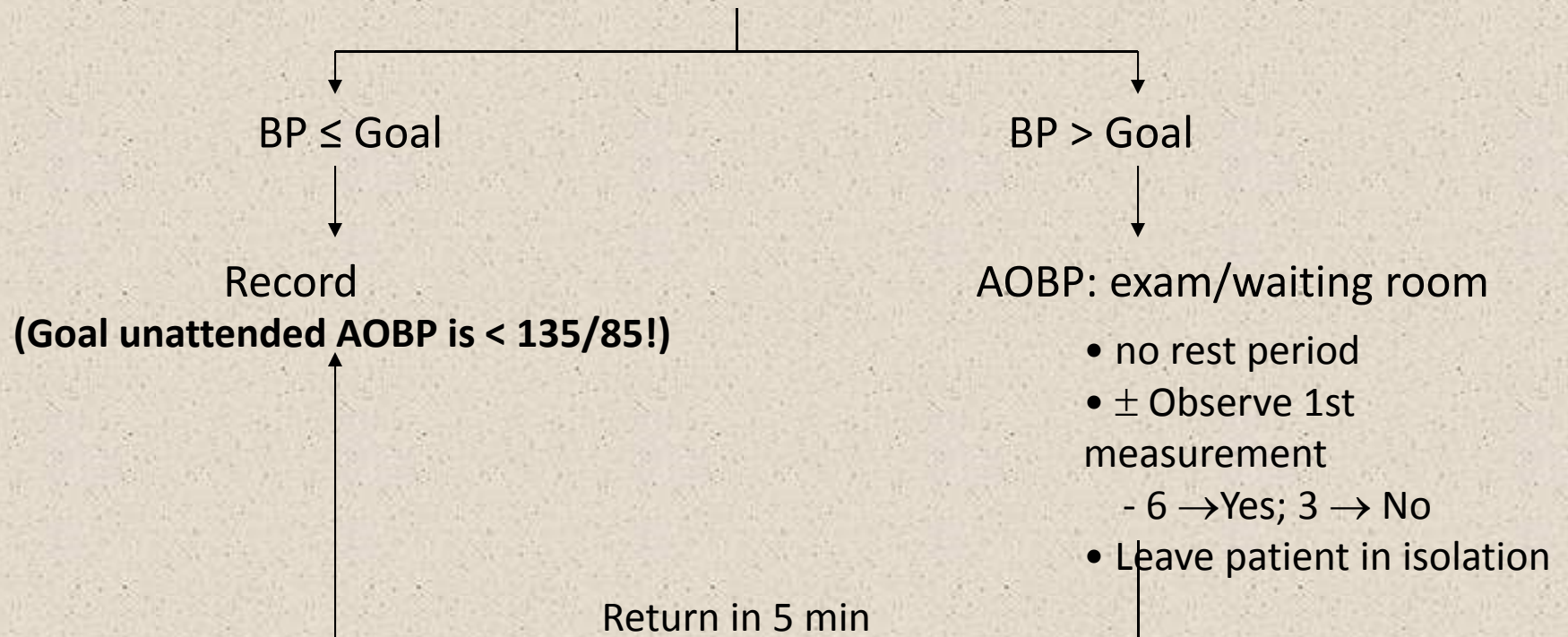
AOBP ON ISOLATED PATIENT IS LOWER THAN
MANUAL ACCURATE BP ON OBSERVED PATIENT

<u>Equivalent BPs to Dx HTN:</u>	<u>BP (mm/Hg)</u>
Research quality manual office BP	140/90
AOBP on isolated patient	135/85
Home BP, mean of 3-7 days	135/85
24 hour ABPM study:	
- Mean daytime awake	135/85
- Full 24 hour mean	130/80

AOBP IN OFFICE PRACTICE: ALGORITHM

High quality manual or electronic 1st BP measurement

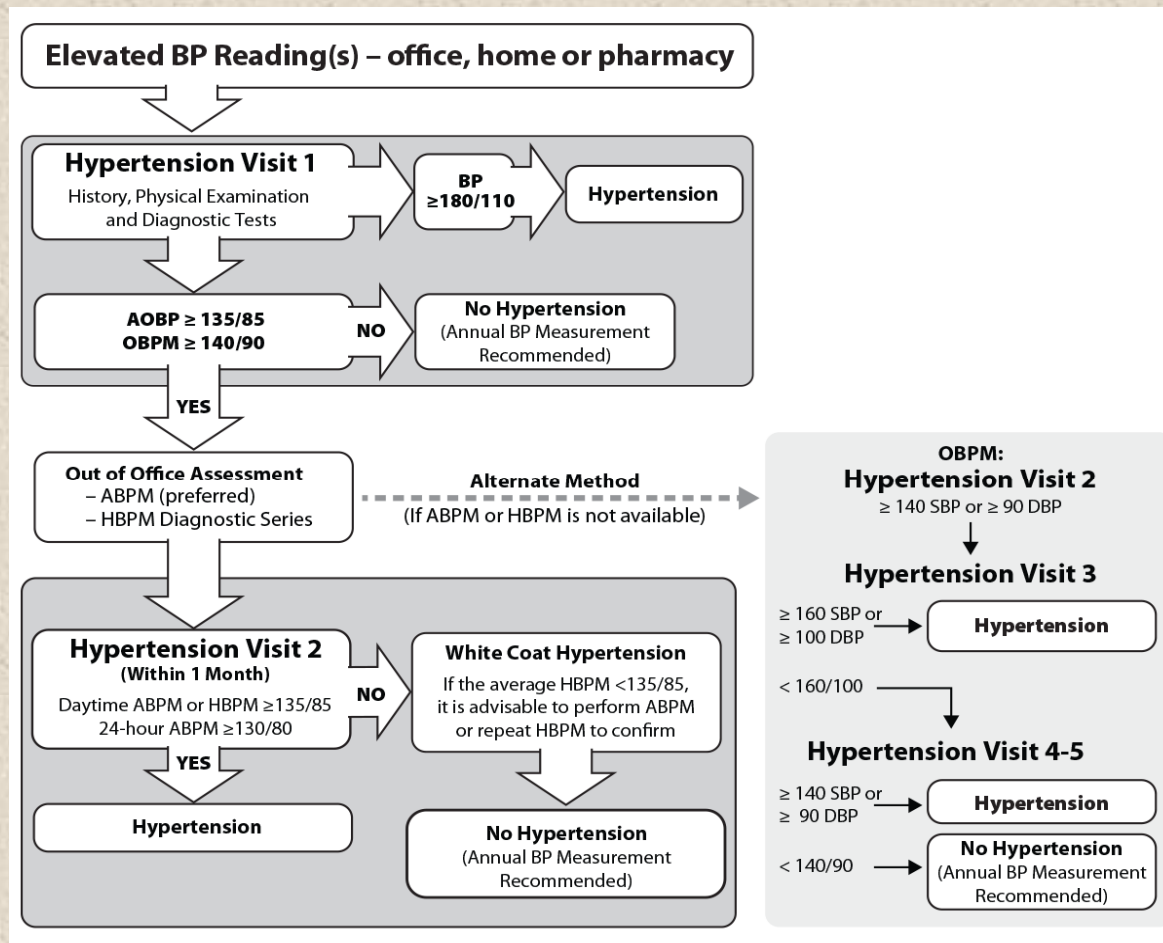
- Rest 5 min
- Correct cuff size
- Etc.



SEQUENTIAL BpTRU READINGS IN 284 HTN PATIENTS IN PRIMARY CARE

<u>Reading No.</u>	<u>AOBP</u>
1 (observer present)	147/82
2 (observer absent)	140/79
3 “	136/78
4 “	134/77
5 “	132/76
6 “	133/77
<hr/> Mean 2-6	<hr/> 136/78

Criteria for the diagnosis of hypertension and recommendations for follow-up: overview



Measurement using electronic (oscillometric) upper arm devices is preferred over auscultation
 ABPM: Ambulatory Blood Pressure Measurement
 AOBP: Automated Office Blood Pressure
 HBPM: Home Blood Pressure measurement
 OBPM: Office Blood Pressure measurement

HBPM MONITORS

- **Must be validated: AAMI, BHS, and/or IP protocols**
 - Omron (www.omronhealthcare.com)
 - A&D – Lifesource (www.andmedical.com)
 - MicroLife (www.microlife.com)
 - www.hypertension.ca/devices-endorsed-by-hypertension-canada
 - www.bhsoc.org/bp-monitors/bp-monitors/
- **Arm cuffs only (unless massive obesity)**
- **Correct cuff size for mid-arm circumference**
 - < 33 cm —————> regular cuff
 - 33-43 cm —————> large adult or self-adjusting
 - > 43 cm —————> wrist cuff (if wrist < 22 cm)

HBPM: PRECISE PREPARATION/MEASUREMENT TECHNIQUE

Same careful preparation/technique as required in office:

- **Home BP technique video from CHEP**
 - www.youtube.com/watch?v=eqajdX5XU9Y&feature=plcp
- **Home BP technique written instructions:**
 - UUMC/VAMC Home BP Measurement handouts
- **Check patient technique, cuff accuracy in office**
 - Pt R arm/Office L arm → Office R arm/Pt L arm
 - < 5 mm hg difference between averages

HBPM: RECOMMENDED MONITORING PROTOCOL

Morning

≤ 1h post-awaken

Post-micturition

Pre-breakfast

Pre-BP med

Rest quietly 3-5 min

Measure X 2, 1 min apart

Work

?

Evening

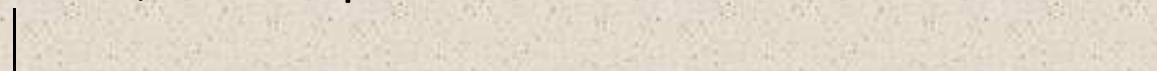
6-9 PM

Pre-supper (or pre-bed?)

Pre-BP med

Rest quietly 3-5 min

Measure X 2, 1 min apart



Dx/FU Rx Δ

FU controlled BP

BID x 3-7d:

12-28 readings

BID x 3-7d:

q 3 mo

Goal BP < 135/85

TREATMENT OF HYPERTENSION

TARGET BP 2014: STILL NO CONSENSUS!

<u>Guideline</u>	<u>General Population</u>	<u>Age ≥ 80y</u>	<u>CKD</u>	<u>DM</u>
ASH 2014	< 140/90	< 150/90	< 140/90	< 140/90
ACC/AHA 2014	< 140/90	< 150/90	< 140/90	< 140/90
CHEP 2015, JBS3 2014	< 140/90*	< 150/90 (Rx if ≥ 160**)	< 140/90	< 130/80
JNC-8 2014				
• Majority:				
- Age < 60	< 140/90	---	< 140/90	< 140/90
- Age ≥ 60	< 150/90***	< 150/90		
• Minority:	< 140/90	< 150/90		
ADA 2015	---	---	---	< 140/90****
NKF/KDIGO 2012	---	< 150/90?	< 140/90	< 140/90
• ACR ≥ 30	---	?	< 130/80	< 130/80

* < 160/100 if no TOD or CVD risk factors

**** < 130 if ↑ stroke risk

** If no TOD or DM; otherwise Rx if ≥ 140/90

*** No down-titration needed if tolerate < 140/90

WHEN TO INITIATE HTN TREATMENT?

Support for $\geq 150/90$ For Age ≥ 60 y, No CKD/DM

No definitive RCT for 140-149
Cochrane 2012 meta-analysis:
- No \downarrow CVD events for 140-149
Marginal benefits/side effects

Support for $\geq 140/90$ For Age ≥ 60 y, No CKD/DM

One RCT, CARDIO-SIS
2014 meta-analysis:
– \downarrow Stroke, CHD for 140-149
Epidemiologic data:
 \uparrow CVD begins at SBP=90

JAMA 2014; 311:507
J Hypertens 2014; 32:2296

JACC 2014; 64:394

Heart 2014; 100:317

Cochrane Syst Rev 2012; 8:CD006742

STAGE 1 HTN: SUBSTANTIAL CVD RISK!

- **1.3 million 1^o care pts, 1997 → 2010:**

Hazard Ratios For SBP = 140-159 mm Hg

	<u>Age 30-59</u>	<u>Age 60-79</u>	<u>Age ≥ 80</u>
MI	1.89	1.69	1.44 (NS)
Heart Failure	2.57	1.38	1.14 (NS)
Stroke, ischemic	2.05	1.23	1.04(NS)
Stroke, hemorrhagic	2.49	1.34 (NS)	1.19 (NS)

Lifetime CVD risk at age 30:

- BP ≥ 140/90 → 63%
 - CVD occurs 5y earlier
- BP < 140/90 → 46%

HOW LOW TO GO?

2014 Meta-analysis of RCTs of Achieved SBP:

	<u>RRR</u>	<u>NNT/5y</u>
Stroke		
140-149 <u>vs</u> 150-159*	↓ 35%	52
130-139 <u>vs</u> 140-149**	↓ 27%	90
120-129 <u>vs</u> 130-139***	↓ 31%	106
Coronary Heart Disease:		
140-149 <u>vs</u> 150-159*	↓ 21%	169
130-139 <u>vs</u> 140-149**	↓ 23%	122
120-129 <u>vs</u> 130-139***	↓ 12% (NS)	---

*5RCTs; 12,406 pts **13 RCTs; 79,736 pts ***4 RCTs; 24,404 pts

Groups without Prior Cardiovascular Disease	<div style="display: flex; justify-content: space-around; font-size: small;"> ■ Cost-saving ■ Cost-effective (ICER <\$50,000) ■ Intermediate value (ICER ≥\$50,000 and <\$150,000) ■ Low value (ICER ≥\$150,000) </div>					
	Men			Women		
	Stage 2 hypertension	Stage 1 hypertension, diabetes or CKD	Stage 1 hypertension, no diabetes or CKD	Stage 2 hypertension	Stage 1 hypertension, diabetes or CKD	Stage 1 hypertension, no diabetes or CKD
33–44 Yr	Cost-saving	\$13,000	\$40,000	\$26,000	\$125,000	\$181,000
45–59 Yr	Cost-saving	Cost-saving	Cost-saving	Cost-saving	\$16,000	\$22,000
60–74 Yr	Cost-saving	Cost-saving	Cost-saving	Cost-saving	\$3,000	\$7,000

Projected Average Cost-Effectiveness of Full Implementation of the 2014 Guidelines for Hypertension Treatment in Patients without Cardiovascular Disease, According to Sex, Age, Hypertension Stage, and Status with Respect to Diabetes and Chronic Kidney Disease.

CAN WE GO TOO LOW? J-CURVE FOR DBP?

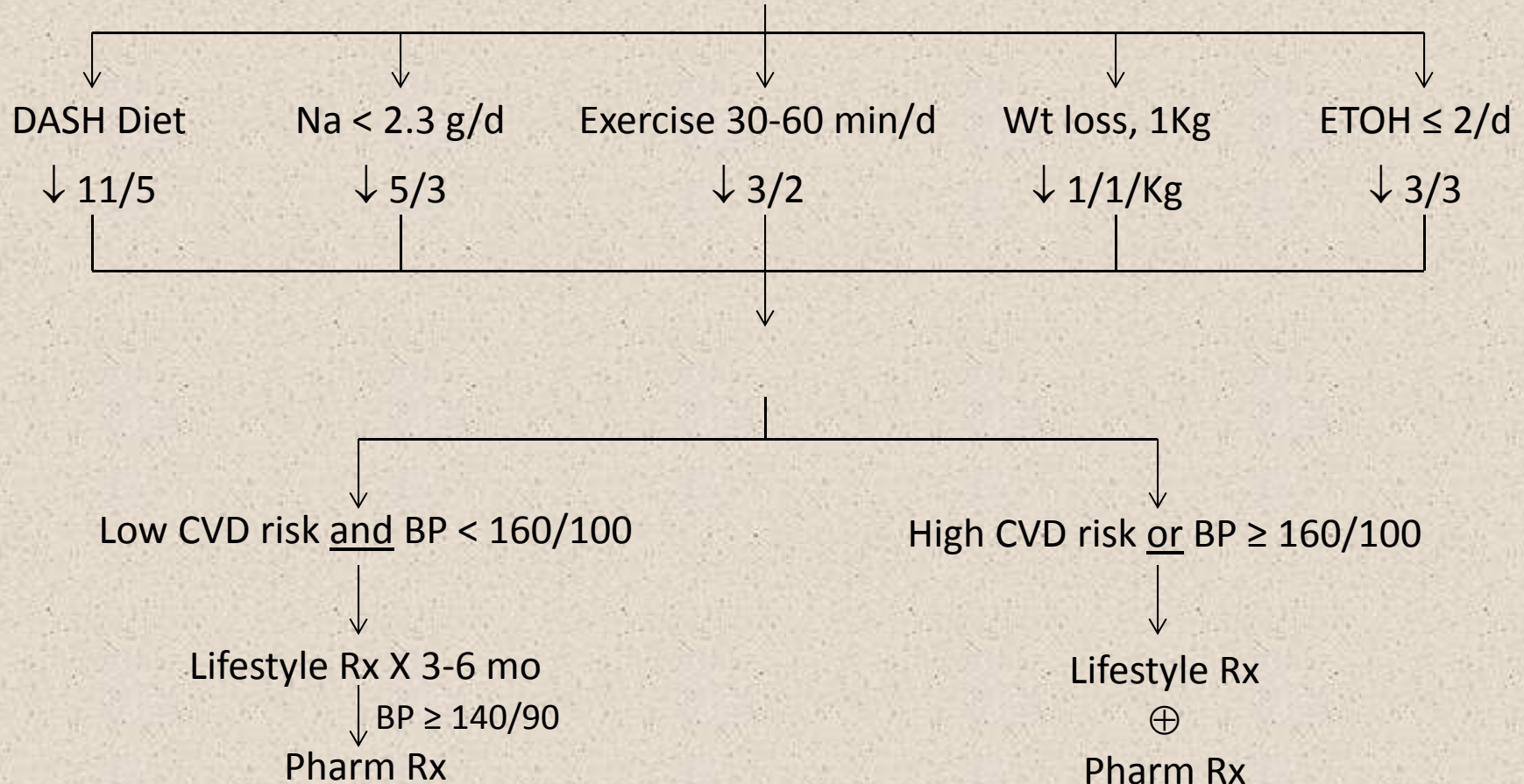
Framingham HS: recurrent CVD events in 791 survivors

	<u>DBP < 70 mm Hg</u>	<u>DBP 70-89 mm Hg</u>	<u>p value</u>
Recurrent CVD events	68%	48%	< 0.0001
Hazard ratio <u>vs</u> DBP = 70-89 mm Hg:			
Treated	5.1	---	< 0.0001
Untreated	11.7	---	< 0.0001

- **↑ CVD events with DBP < 70 only if PP ≥ 68 mm Hg regardless of Rx – ie, reflects ↑ SBP**
 - Antihypertensive Rx may not increase CVD events
 - Arterial stiffness → low DBP as cause of CVD events
- **Caution ↓ DBP < 60 if CAD?**

LIFESTYLE MODIFICATION FOR HYPERTENSION

Select ≥ 1 Intervention \propto Motivation



AHA 2013: RECOMMENDED ALTERNATIVE APPROACHES TO LOWER BP IN CLINICAL PRACTICE

<u>Approach</u>	<u>Δ BP (mm Hg)</u>	<u>Class of Recommendation</u>
Transcendental meditation	↓ 5/3	IIB
Device-guided breathing	↓ 4/3	IIA

Candidates: Low CVD risk and BP < 160/100, for 6-12 mo
Multiple drug side effect pts
Desire to ↓ drug doses
Refractory HTN

Not useful:

- Other meditation/relaxation techniques
- Yoga; biofeedback; acupuncture

Hypertension 2013; 61:1360
JAMA Int Med 2014; 174:1815

Am J Hypertens 2008; 21:310
J Hypertens 2012; 30:852

DOES ↓ DIETARY Na REDUCE CVD?
(IT CLEARLY LOWERS BP!)



Minimal RCT data:

- Require 30,000 pts x 5y



Cohort data: 31 analyses of 285,530 pts

- Substantial methodologic deficiencies in most

13 studies —————> ↓ CVD

8 studies —————> ↑ CVD

2 studies —————> J-curve

8 studies —————> No effect

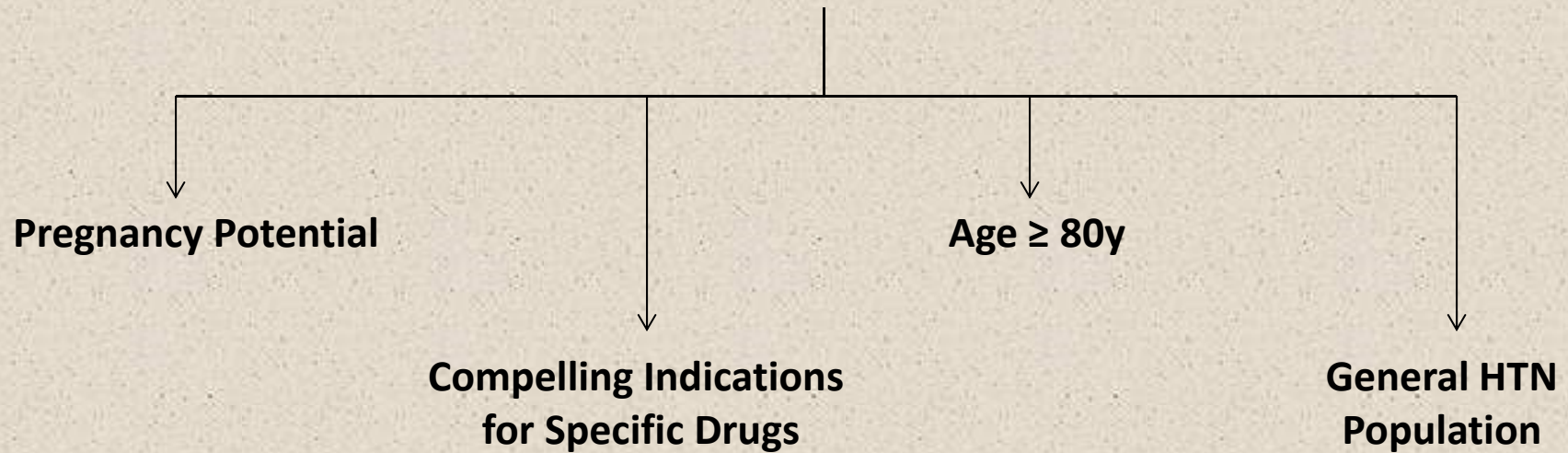
Post-hoc 15y FU of TOHP: 2275 pts

> 3600 vs < 2300 mg/d —————> low Na ↓ CVD by 32%

Na RESTRICTION: CURRENT GUIDELINES

	<u>Na (mg/d)</u>
AHA, 2012/2014	< 1500
WHO, 2012	< 2000
CHEP, 2015	< 2000
DHSS, 2010	< 2300
IOM, 2013	2300
Graudal, et al 2014	2600-4900

SELECTING INITIAL PHARMACOLOGIC THERAPY



J Clin Hypertens 2013; 15:874

J Hypertens 2013; 31:1925

JAMA 2013; 310:1274

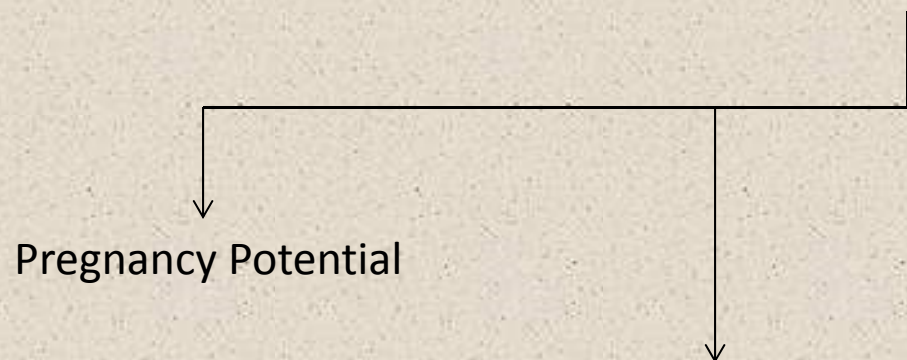
SELECTING INITIAL PHARMACOLOGIC THERAPY



Pregnancy Potential

- No ACE-I or ARB
- OK:
 - Thiazides
 - CCBs
 - BBs

SELECTING INITIAL PHARMACOLOGIC THERAPY



Pregnancy Potential

Compelling Indications for Specific Drugs

- **DM or CKD:**

- Albuminuria → ACE-I or ARB

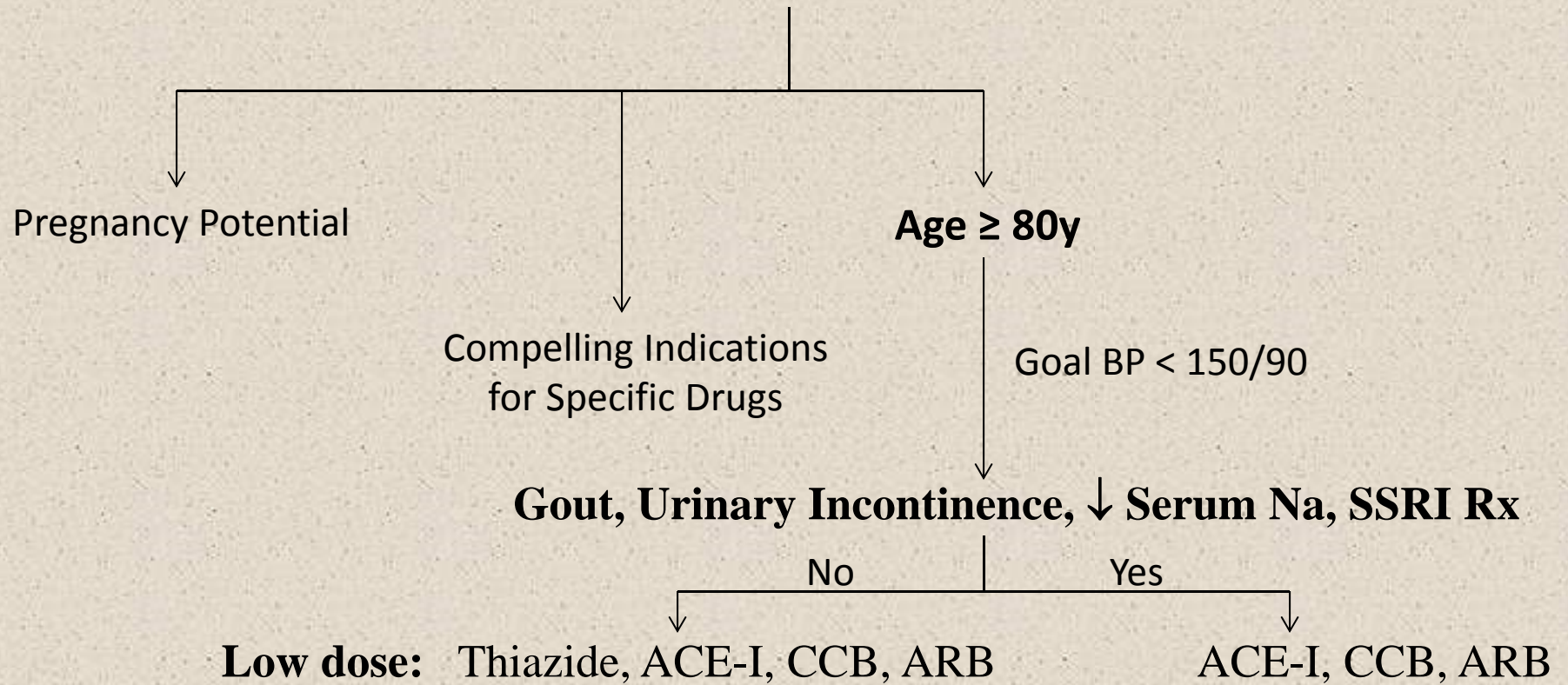
- No albuminuria → ACE-I, ARB, CCB, Thiazide*

- **Recent MI or Systolic HF** → ACE-I (ARB) ⊕ BB

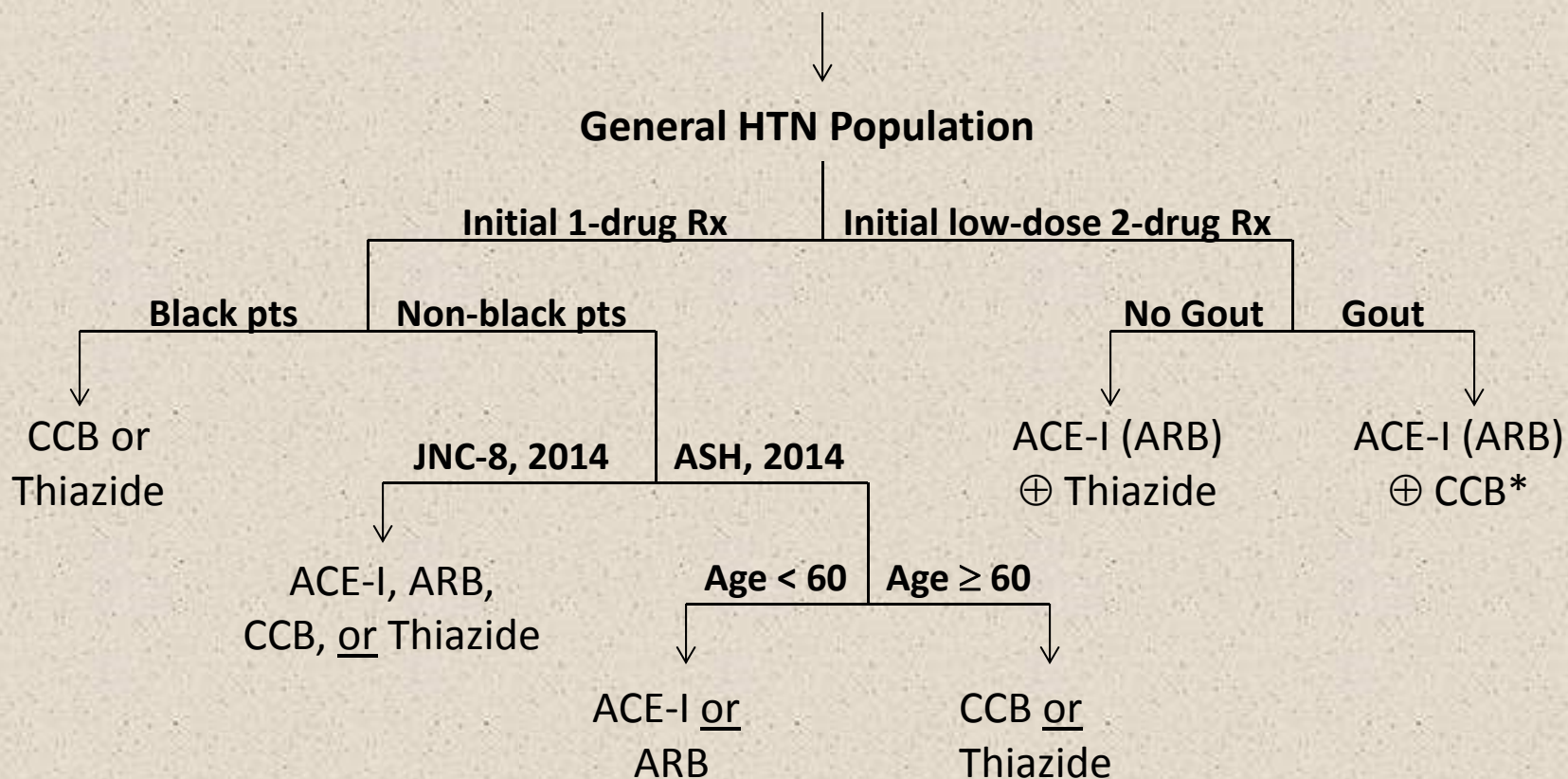
- **Stable CAD** → ACE-I (BB/CCB if angina)

*JNC-8: ACE-I/ARB for all CKD

SELECTING INITIAL PHARMACOLOGIC THERAPY



SELECTING INITIAL PHARMACOLOGIC THERAPY



*Consider this Rx if high CVD risk (ACCOMPLISH RCT, 2008)

GUIDELINE COMPARISONS: BBs AND DRUGS FOR BLACKS

	<u>BB Use*</u>	<u>1st Drug in Blacks</u>
ESH/ESC 2013	Step 1 Alt. (carvedilol, nebivolol)	Thiazide/CCB
CCS 2015	<ul style="list-style-type: none">• Step 1 Alt <u>if</u> age < 60y• Step 4 Age ≥ 60y	Thiazide/CCB
JNC-8, 2014	Step 4	Thiazide/CCB
ACC/AHA 2013	Step 3, 4	---
ASH/ISH 2014	Step 4	Thiazide/CCB
JSH 2014	Step 4	---

- **BBs provide less stroke protection over age 60**

*Unless special indication

“OPTIMAL” 2-DRUG RX: GENERAL HTN POPULATION

↓ ASH, 2014

- Effectively ↓ BP, ↓ CVD events, ↓ side effects

ACE-I (ARB) ⊕ Thiazide

- ↓ BP additively, many studies
- ↓ CVD in RCTs: HYVET, PROGRESS, ADVANCE
- ↓ hypokalemia

ACE-I (ARB) ⊕ CCB (amlodipine)

- ↓ BP additively, many studies
- ↓ CVD in RCTs: ASCOT, ACCOMPLISH
- ↓ CCB-induced edema

ACCOMPLISH RCT, 2008: 11,056 high CVD risk pts x 36 mo

ACE-I ⊕ Thiazide vs ACE-I ⊕ Amlodipine

- **ACE-I ⊕ amlodipine ↓ CVD events 20%, CKD by 48%**

“OPTIMAL” 3-DRUG RX: GENERAL HTN POPULATION



- Effectively ↓ BP, ↓ CVD events, ↓ side effects



Less evidence

- **ACE-I (ARB) ⊕ CCB ⊕ Thiazide diuretic**

- ↓ BP additively in several studies
- ↓ side effects of Δ potassium, CCB-induced edema
- ? ↓ CVD events: post-hoc analysis of ADVANCE

Hypertension 2009; 54:19; 32 Hypertension 2014; 63:220; 259

↓ Hypertens 2014; 32:3

Diabetes Care 2013; 36:S4

General HTN Population: Control BP in < 8-12 wks

Older, no gout, not high CVD risk or DM-prone

Lisinopril 20 mg/HCTZ 25 mg tabs:

$\frac{1}{2} \xrightarrow{2-4 \text{ wk}} 1 \xrightarrow{2-4 \text{ wk}} 2 \text{ tabs, } \underline{\text{prn}}$
↓ Not controlled, 2-4 wk

Add Amlodipine 5 mg tabs:

$\frac{1}{2} \xrightarrow{2-4 \text{ wk}} 1 \text{ tab, } \underline{\text{prn}}$
↓ Not controlled, 2-4 wk

Increase amlodipine to 10 mg tab qd

Younger, gout, high CVD risk, or DM-prone

Lisinopril 20 mg tabs ⊕ Amlodipine 5 mg tabs:

$\frac{1}{2} \text{ tab each} \xrightarrow{2-4 \text{ wk}} 1 \text{ tab each, } \underline{\text{prn}}$
↓ Not controlled, 2-4 wk

2 tab Lisinopril ⊕ 10 mg amlodipine tab

↓ Not controlled, 2-4 wk

1 tab Lisinopril 20 mg/HCTZ 25 mg

⊕ Amlodipine 10 mg

↓ Not controlled, 2-4 wk

2 tab Lisinopril 20 mg/HCTZ 25 mg

⊕ Amlodipine 10 mg

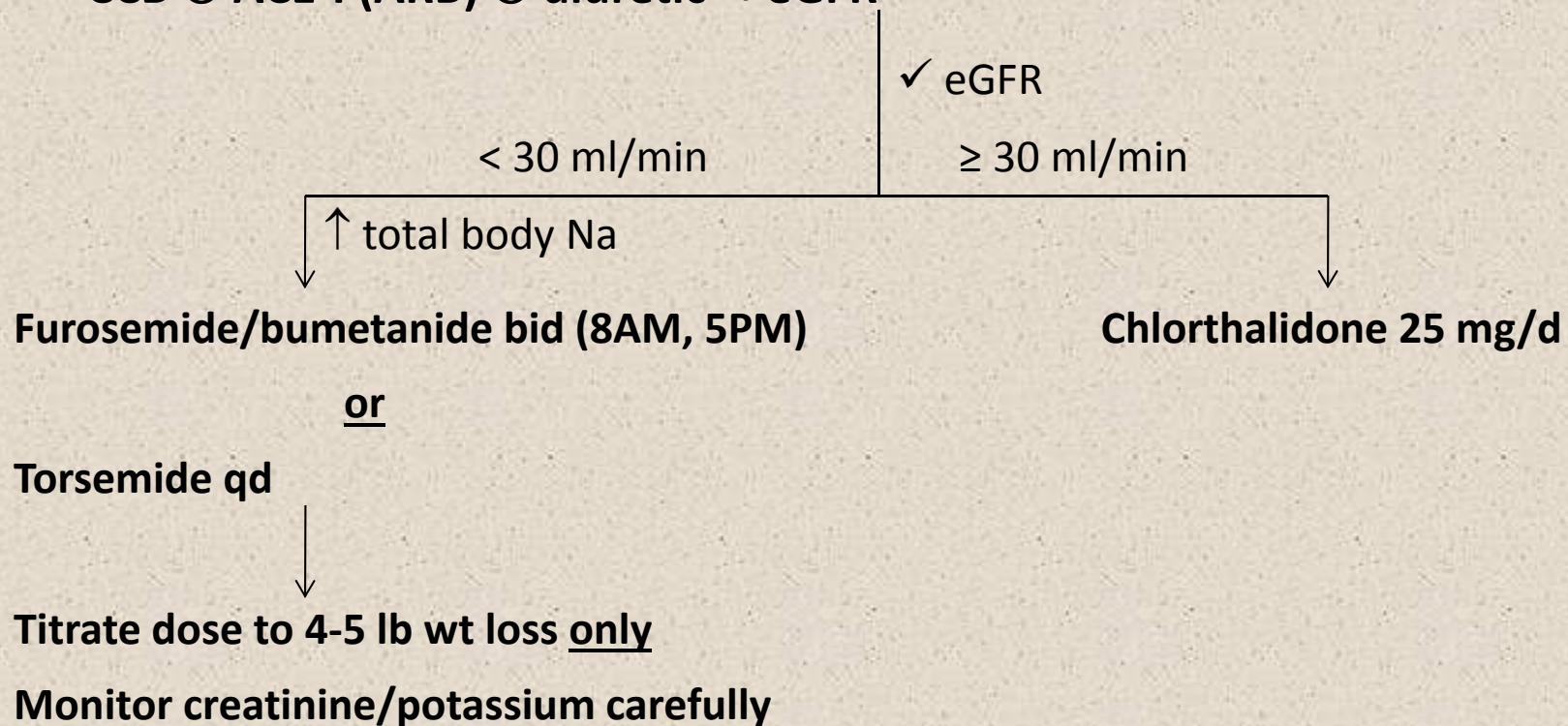
***Monitor potassium/sodium/creatinine with dose changes**

- Delays > 6 weeks to intensify Rx increase CVD risk

SELECT DIURETIC \propto eGFR

✓ for optimal 3-drug Rx – maximal tolerated doses of:

- CCB \oplus ACE-I (ARB) \oplus diuretic \propto eGFR



APPROACH TO UNCONTROLLED HTN ON 3 DRUGS: “RESISTANT HYPERTENSION”

- ✓ for suboptimal Rx regimen
- ✓ for white-coat resistant HTN: present in $\geq 30\%$
 - Home BP monitoring bid x 3-7d
 - 24h ambulatory BP monitor study
- ✓ for medication non-adherence: present in $\geq 30\%$
 - Ask, Morisky questionnaire, ✓ refill use
- ✓ for drugs that \uparrow BP: NSAIDS, estrogen, \uparrow ETOH, epogens
- Review (\pm testing) for 2^o causes of HTN
- Δ HCTZ \rightarrow chlorthalidone 25 mg/d: \downarrow SBP 5-6 mm Hg
- Consider consultation

ALDOSTERONE ANTAGONISTS ↓ BP IN RESISTANT HTN

Meta-analysis: 13 studies; 2505 patients

Mean BP Reduction, mm Hg

3 RCTs:

17/4

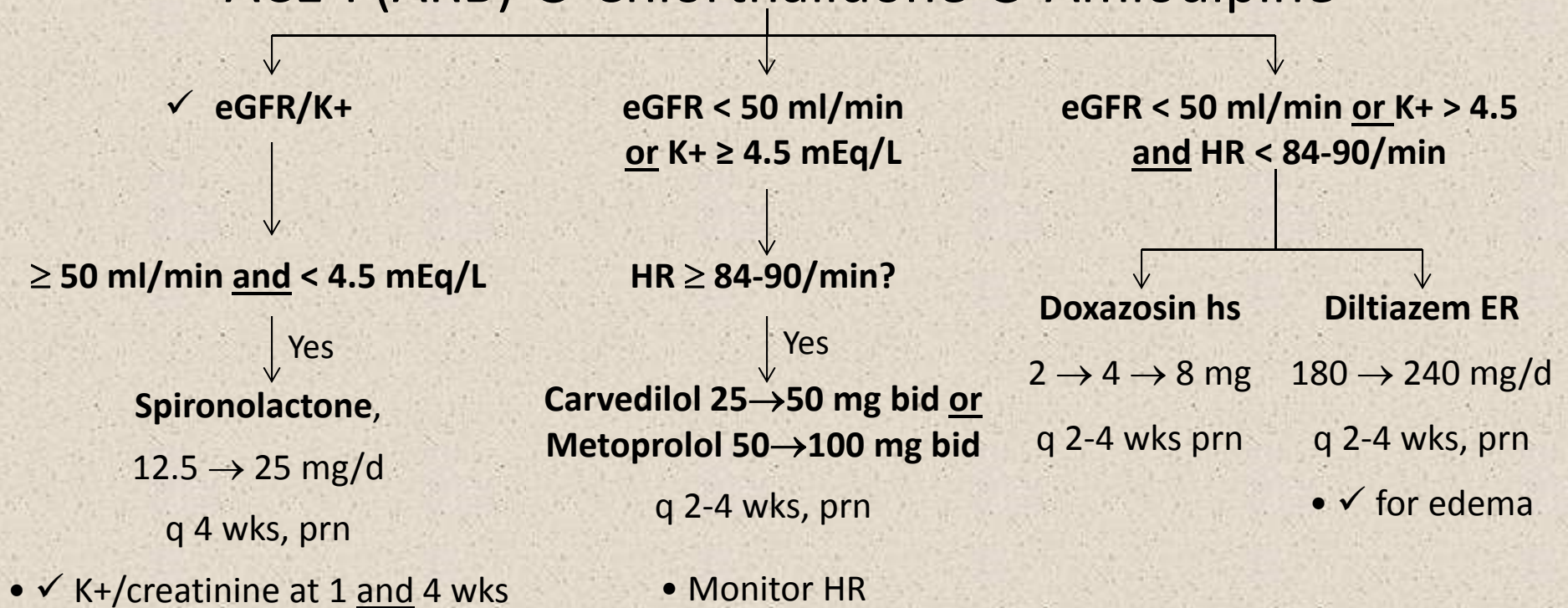
135 pts

10 Observational studies:

20/9

2208 pts

Resistant Hypertension On ACE-I (ARB) ⊕ Chlorthalidone ⊕ Amlodipine



RENAL ARTERY STENOSIS $\geq 60\%$

Epidemiology

- Gen. pop. $\geq 65y$: 7%
- CAD at cath: 9%
- HTN \oplus CKD: 20%
- HF-ASCVD: 50%

Clinical Syndromes

Incidental:

- $< 80\%$ stenosis and < 20 mm Hg gradient

Flash

Pulm. Edema

- Acute HF, EF $> 40\%$, $\uparrow\uparrow$ BP

Resistant

HTN

$\uparrow\uparrow$ ASCVD

Ischemic CKD

Theory: Restore Renal Q

- \downarrow HF
- \downarrow BP
- \downarrow CVD events
- Preserve GFR

RA STENTING ⊕ MEDICAL RX vs MEDICAL RX

Meta-analysis: 8 RCTs; 2223 pts; 34 mo follow-up

<u>Outcome</u>	<u>Relative Risk (95% CI)</u>	<u>p value</u>
△ BP	0.99 (0.97-1.21)	0.83
Mortality	0.91 (0.75-1.11)	0.98
Heart failure	0.89 (0.68-1.17)	0.80
Stroke	0.80 (0.54-1.21)	0.85
↓ GFR	0.96 (0.79-1.16)	0.71

- Only CORAL (2014) with all pts > 60-80% stenosis
- Few pts with bilateral stenoses, stenosis to solitary kidney
- Mild HTN and Stage 3 CKD in most pts
- Highest risk pts excluded: ↑↑↑ BP, progressively ↓ eGFR, recurrent flash pulm. edema

RA STENTING ⊕ MEDICAL RX vs MEDICAL RX

Observational data: 234 “high risk” pts; 50% stented; 3.8y FU

- **Recurrent flash pulmonary edema subset:**

- Mortality HR = 0.4 favoring stenting

- Class I AHA recommendation, 2013

- **Resistant HTN ⊕ ↓ eGFR over 6 mo.**

- Mortality HR = 0.15 favoring stenting

- CVD HR = 0.23 favoring stenting

- **Bilateral severe RAS??**

Severe RAS to solitary functioning kidney??