

HYPERTENSION UPDATE, 2010

Learning Objectives:

- Recognize the epidemic of hypertension and its consequences in the U.S.
- Recognize the multiple contributors to inadequate hypertension control in the U.S.
- Understand the necessity of a public health approach to hypertension control in the U.S. to prevent hypertension and identify patients at highest risk to develop hypertension to facilitate focused management.
- Be able to recognize and begin to address the major barriers to hypertension control among treated patients.
- Recognize the inadequacy of usual manual office BP measurement to diagnose and monitor hypertension and be able to implement accurate manual BP office measurement, automated office BP measurement on isolated patients in the exam room, and out-of-office BP measurement with home BP or 24-hour ambulatory BP studies to make a more accurate assessment of a patient's "true" or usual BP.
- Understand the increasing controversy over goal BP.
- Recognize the need for multiple BP medications in 70% of hypertension patients and be able to select optimal agents and combinations of agents to control hypertension.

Selected References:

1. Egan BM, et al. U.S. trends in prevalence, awareness, treatment, and control of hypertension, 1988-2008. JAMA 2010; 303: 2043-2050.
2. Vasan RS. A risk score for risk factors: rationale and roadmap for preventing hypertension. Hypertension 2009; 54: 454-456.
3. Kotchen TA. The search for strategies to control hypertension. Circulation 2010; 122: 1141-1143.
4. Myers MG, et al. Measurement of blood pressure in the office: recognizing the problem and proposing the solution. Hypertension 2010; 55: 195-200.
5. Bibbins-Domingo K, et al. Projected effect of dietary salt reductions on future cardiovascular disease. NEJM 2010; 362: 590-599.
6. Sacks FM and Campos H. Dietary therapy in hypertension. NEJM 2010; 362: 2102-2012
7. American Society of Hypertension. Position paper: dietary approaches to lower BP, 2009. Available at: http://www.ash-us.org/pub/position_papers.htm
8. American Society of Hypertension. Position paper: adherence and persistence with taking medication to control high blood pressure. J Clin Hypertension 2010; 12: 757-764.
9. Czernichow S, et al. The effects of blood pressure reduction and of different BP-lowering regimens on major cardiovascular events according to baseline BP: meta-analysis of randomized trials. J Hypertension 2010; Vol 28: In Press, available on-line.
10. American Society of Hypertension. Position paper: combination therapy in hypertension, 2010. Available at: http://www.ash-us.org/pub/position_papers.htm
11. Canadian Hypertension Education Program. The 2010 CHEP recommendations for the management of hypertension: Part I – Blood pressure measurement, diagnosis, and assessment of risk. Part II – therapy. Canadian Journal of Cardiology 2010; 26: 241-258.

HYPERTENSION UPDATE, 2010

“Hypertension: Uncontrolled and Conquering the World”

Lancet Editorial, August 18, 2007

“Hypertension is the most important health problem that clinicians don’t manage well.”

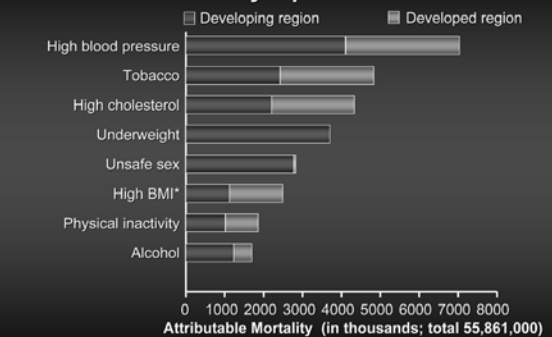
Annals of Internal Medicine Editorial, May 20, 2008

“Hypertension – the neglected disease”

Institute of Medicine, 2010

Barry Stults, M.D.
Division of General Internal Medicine
University of Utah Medical Center

Global Mortality 2000: Impact of Hypertension and Dyslipidemia



*BMI=body mass index.
Ezzati et al. *Lancet*. 2002;360:1347-1360.

4

PREVENTABLE MORTALITY: U.S., 2010

	Total deaths/y	Male	Female
Tobacco smoking	467,000	248,000	219,000
Hypertension	395,000	164,000	231,000
Overweight/obesity	216,000	114,000	102,000
Physical inactivity	191,000	88,000	103,000
Diabetes	190,000	102,000	89,000
High LDL-Cholesterol	113,000	60,000	53,000

PLoS Med 2009; 6:e1000058

HTN AS A RISK FACTOR

Increases RR by 2.0-4.0 fold for:

- CAD, stroke, HF, PAD
- Renal failure, AF, dementia, ↓ cognition

Attributable risk for HTN:

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

Aftermath:

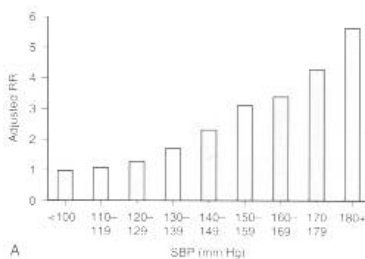
- Shortens lifespan 5y
- \$77 billion/y in U.S. in 2010

Circulation 2010; 121:e70

J Hum Hypertension 2008; 22:63

Hypertension 2007; 50:1006

RELATIVE RISK OF CARDIOVASCULAR EVENTS INCREASES WITH SYSTOLIC BP > 110 mm Hg



From SBP ≥ 110 mm Hg (125 million Americans):

20 mm Hg ↑ SBP → 2X ↑ CVD

2 mm Hg SBP → 10% ↑ Stroke, 7% ↑ MI *Lloyd-Jones and Levy, Hypertension, 2007*

BENEFITS OF LOWERING BP

• ↓ 10/5 mm Hg at age 65 for 10y:

Complication	Average % Reduction
MI	25%
Stroke	40%
CHF	50%
Death	15%

BMJ 2009; 338:b1665

Health Affairs 2007; 26:97

JAMA 2003; 289: 2560

HYPERTENSION: AN EPIDEMIC

	1988-1994	1999-2000	2007-2008
Total in millions	50	65	75
% BP ≥ 140/90 or Rx	24%	28%	29%
- Age ≥ 60y	---	---	66%
- Age ≥ 60y, AA	---	---	81%
- Age ≥ 90y	---	---	> 90%
- Age ≤ 17y	---	---	≥ 6%

Utah: 20% → Tennessee: 34%

Hypertension 2009; 54:502 J Am Ger Soc 2007; 55: 1056 Hypertension 2004; 44:398
 JAMA 2010; 303:2043 Circulation 2010; 121:e70 Hypertension 2007; 49:69

HTN CONTROL RATES: IMPROVING BUT DISMAL!

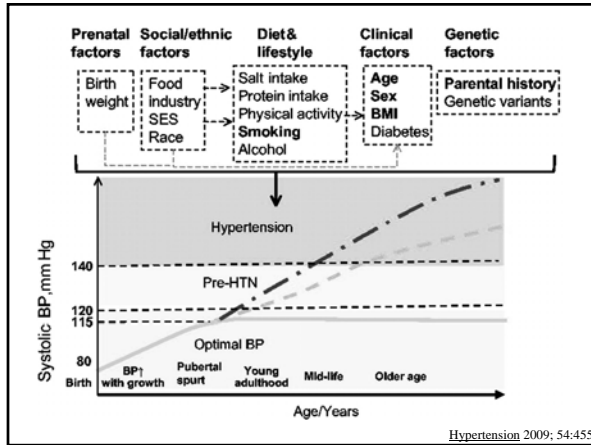
	1990	2000	2008
% Aware	69	69	81*
% Treated	52	58	73*
% Controlled:			
All pts.	25	31	50**
Rx'd pts.	47	53	69***

*Blacks > Whites > Hispanics

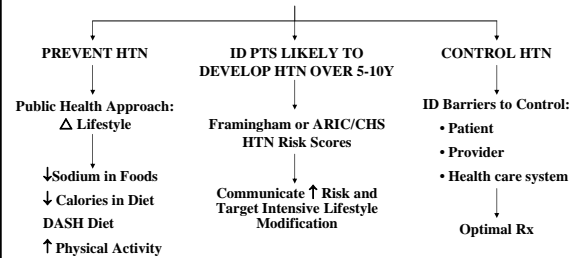
**Blacks = Whites > Hispanics

*** Whites > Blacks = Hispanics

Circulation 2010; 122:1141 JAMA 2010; 303:2043 JAMA 2003; 290:199



ATTACK THE HYPERTENSION EPIDEMIC!



J Clin Hypertens 2010; 12:800

Hypertension 2009; 54:454

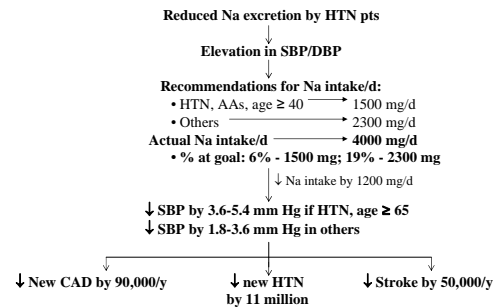
ASSIST PATIENTS TO Δ LIFESTYLE!

“The adoption of healthy lifestyles by all persons is critical for the prevention of high blood pressure and is indispensable for the management of those with hypertension.”

JNC-7, 2003

JAMA 2003; 289:2560

SODIUM RESTRICTION: A NATIONAL NECESSITY!



Am J Health Promot 2009; 24:49

MMWR 2010; 59:746

NEJM 2010; 362:590

SOURCES OF DIETARY Na

	<u>% of Intake</u>
Added Na (table, cooking)	10%
Foods:	90%
• Grains (bread, cookies)	37%
• Meats (lunch meats, etc)	28%
• Vegetables (canned, sauces)	12%
• Top 5: breads, frozen dinners, pizza, pasta dishes, coldcuts - Restaurant foods a real killer!	
Essential to read labels.	
More essential to ↓ Na content of prepared foods	

MMWR 2010; 59:746

WHAT ARE WE DOING AS A SOCIETY TO REDUCE Na INTAKE?

Institute of Medicine, April, 2010:

- Mandatory national standards to ↓ Na intake
 - Interim strategy of voluntary action

NYC/nationwide coalition, April, 2010:

- 16 companies committed to ↓ Na in ≥ 1 target food

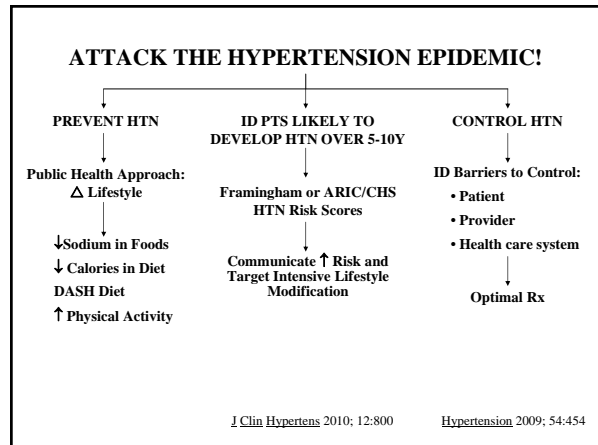
MMWR 2010; 59:746

WHAT DO HTN PATIENTS KNOW AND DO?

	<u>% With Appropriate Behavior</u>
Reduced Na intake (2008)	56%
Read food labels for Na content	53%
Follow DASH diet	24%
• ≥ 5 servings/d fruit/veg	
Physical activity, moderate	40%
• ≥ 30 min/d, 5d/wk	
Received diet/activity advice from clinician	21-24%

Clinician advice improves lifestyle adherence!

Am J Hypertens 2010; 23:762 J Clin Hypertens 2010; 12:784 J Clin Hypertens 2010; 12:793



RISK CALCULATORS TO PREDICT HTN

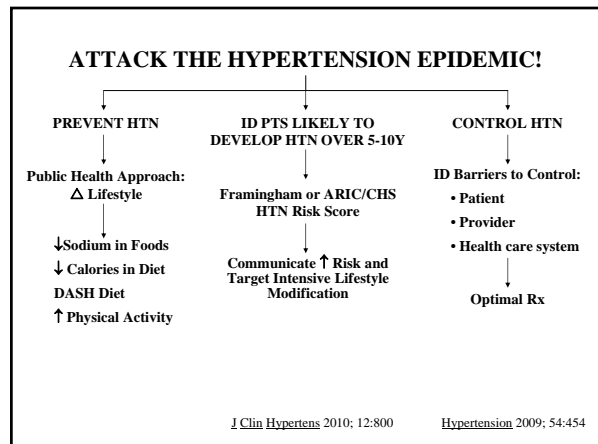
Potential utility:

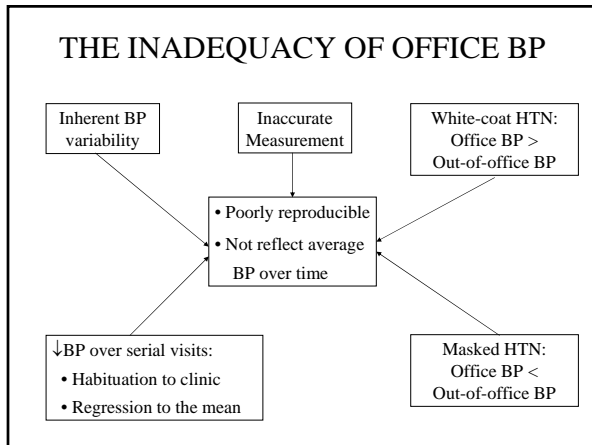
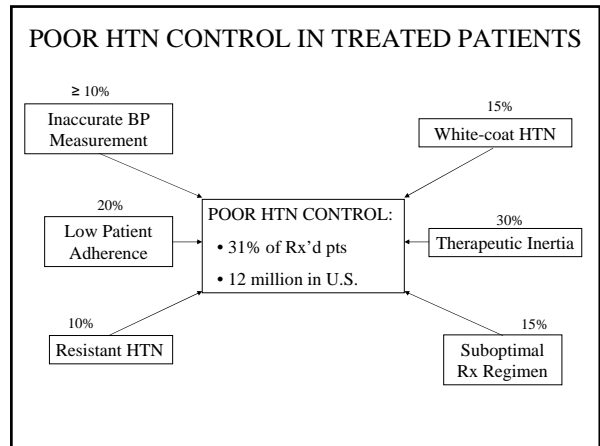
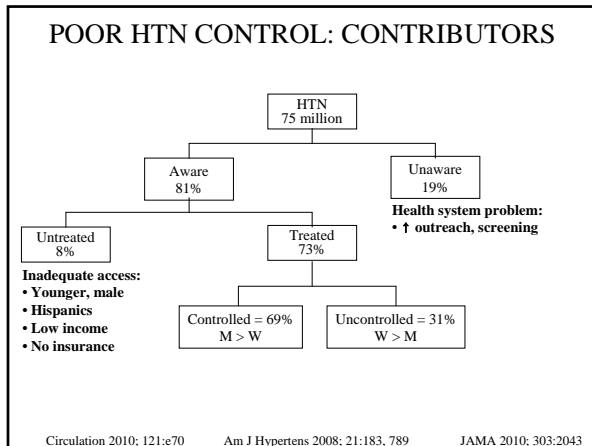
- ID/Communicate high risk to individuals → motivation?
- Target intensive lifestyle Δ to highest risk
- Public websites to ↑ health referrals, HTN awareness

Tools:

- Age, BMI, sex, SBP/DBP, parental HTN, smoking, ± DM, ± exercise
- Framingham: based on white pop.; 1, 2, 4y risk
 - Compares to optimal risk
 - www.annals.org/content/suppl/2008/01/09/148.2DC1/Vasan_RC_148-2-102-DC1-1.xls
 - ARIC/CHS: mixed racial; 3, 6, 9y risk
 - Paper tables in journal article

Ann Int Med 2008; 148:102 J Clin Hypertens 2010; 12:800





DO WE ACCURATELY MEASURE OFFICE BP?

“Blood pressure reading does not seem to be done correctly in any clinic...physicians and their staff are not trained to do it the right way. It appears to be so simple that anyone can do it, but they can't...”

Grim and Izzo, *JAMA* 2008; 299:2842

BP MEASUREMENT: KEY TECHNIQUES

	<u>Δ BP (mm Hg) if not done</u>
Rest ≥ 5 min, quiet	↑ 12/6
Seated, back supported	↑ 6/8
Cuff at midsternal level	↑ ↓ 2/inch
Large enough cuff	↑ 6-18/4-13
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	

Hypertension 2005; 45:142 J Hypertens 2005; 23:697 Can J Card 2008; 24:455

RESEARCH QUALITY vs ROUTINE OFFICE BP

Study	# of pts	Routine Clinical	Research Quality	Difference
		Practice BP	Office BP	
Myers, 1995	147	146/87	140/83	- 6/4
Brown, 2001	611	161/95	152/85	-9/10
Myers, 2009	309	152/87	140/80	-12/5
Graves, 2003	104	152/84	138/74	-14/8
Gustavsen, 2003	420	165/104	156/100	-9/4
Campbell, 2005	107	150/91	139/86	-11/5

Accurate measurement ↓ BP by ≈ 10/5 mm Hg

- Lower BP if ✓'d by non-MD

Am J Hypertens 2005; 18:1522 Hypertension 2010; 55:195

ELEVATED BP ↓ OVER MULTIPLE VISITS

- **2-5 office visits over 2-12 weeks ∝ level of BP**
 - Habituation ⊕ regression to mean → ↓ BP over time
 - New pts with ↑ BP: ↓ 15/7 after 3 visits
 - # of visits to confirm HTN Dx:
 - BP ≥ 180/110 → 2 visits (mean of all)
 - BP 160-179/100-109 → 3 visits (mean of all)
 - BP 140-159/90-99 → 5 visits (mean of all)

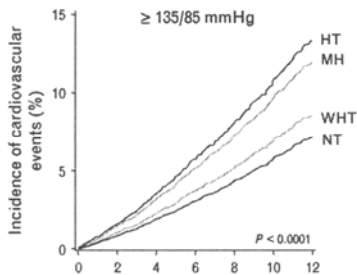
Labor intense!

J Hypertens 1987; 5:207 *BMJ* 2001; 322:977 *Can J Cardiol* 2010; 26:249

OFFICE BP MAY NOT REFLECT USUAL OUT-OF-OFFICE BP!

DAYTIME OUT-OF- OFFICE BP	MASKED HTN: 10%	SUSTAINED HTN: 25%
	<ul style="list-style-type: none"> • Office BP < 140/90 • Day ABPM ≥ 135/85 • Home BP ≥ 135/85 	<ul style="list-style-type: none"> • Office BP ≥ 140/90 • Day ABPM ≥ 135/85 • Home BP ≥ 135/85
135/85	NORMOTENSION: 50%	WHITE-COAT HTN: 15%
	<ul style="list-style-type: none"> • Office BP < 140/90 • Day ABPM < 135/85 • Home BP < 135/85 	<ul style="list-style-type: none"> • Office BP ≥ 140/90 • Day ABPM < 135/85 • Home BP < 135/85
	140/90	
	OFFICE BP	

DAYTIME ABPM: PROGNOSIS IN 7030 PTS



- Masked HTN similar to sustained HTN for prognosis
- White-coat HTN similar to normotension for prognosis

J Hypertens 2007; 25:1554

OUT-OF-OFFICE BP TO DETECT WHITE COAT HTN

24-h Ambulatory BP Monitoring

- Best predictor of CVD outcome (13 studies)
- Best detector of “white coat” HTN
- Covered by most insurance (eg., Medicare)
- Variable availability

Home BP Monitoring

- Better CVD and CKD predictor than office BP (7 studies)
- May improve adherence and BP control
- Misclassify 10-20% of true HTN as normal
- **Often performed inaccurately – pt education!**

J Hypertens 2006; 24:437, 2327 *J Am Coll Cardiol* 2005; 46:743
Hypertension 2008; 52:10 *J Hypertens* 2007; 25:1554

HOME BP MONITORING FOR MOST!

AHA, 2008:

“Home BP monitoring should become a routine component of BP measurement in the majority of patients with known or suspected hypertension.”

Detailed recommendations for use in 2008:

- AHA: *Hypertension* 2008; 52:10
- Am Soc HTN: *J Clin Hypertens* 2008; 10:850
- Eur Soc HTN: *J Hypertens* 2008; 26:1505

HOME BP MEASUREMENT

- **Avoid pharmacy, grocery store – inaccurate**
- **Fully automatic, upper arm cuffs only**
 - Wrist cuffs may underestimate SBP
- **AAMI/BHS or IP validated equipment only**
 - Omron (www.Omronhealthcare.com)
 - A&D-LifeSource (www.andmedical.com)
- **Large adult cuff or self-adjusting if mid-arm > 33cm**
- **Memory ± printer ± computer interface**
 - Inaccurate reporting, underreporting of highs

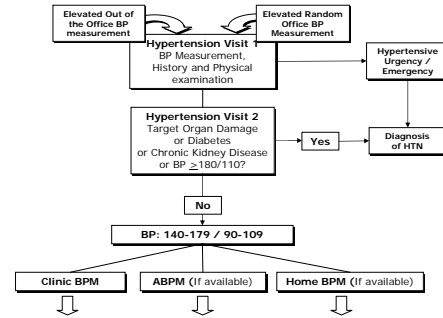
Hypertension 2008; 52:10

HOME BP MEASUREMENT

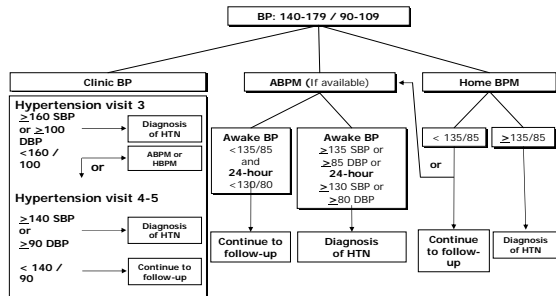
- Careful patient education
 - See handout
 - Preparation and technique
 - Monitoring protocol to correlate with 24h ABPM
 - 3 Measurements AM, PM bid X 7d
 - o Up 30 min AM, pre-meds and breakfast
 - o Pre-meds in evening
 - o Drop 1st measurement, average last 2
 - o Drop 1st day, average last 6, ie, ≥ 12 measurements
 - Collect data for 7d pre-clinic visit for Dx, FU, Rx Δ

J Hypertens 2008; 26:1505 J Hypertens 2007; 25:1992 Hypertension 2008; 52:10

II. Criteria for the diagnosis of hypertension and recommendations for follow-up



II. Criteria for the diagnosis of hypertension and recommendations for follow-up



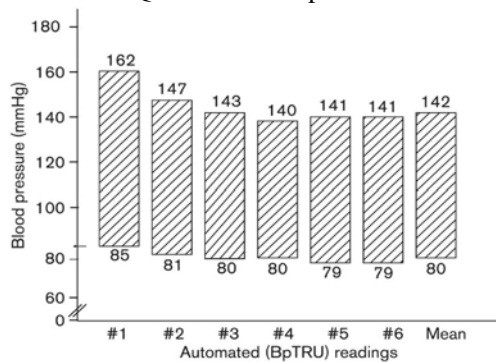
Patients with high normal blood pressure (clinic SBP 130-139 and/or DBP 85-89) should be followed annually.

A NEW APPROACH TO OFFICE BP MEASUREMENT: SERIAL AUTOMATED MEASUREMENTS ON ISOLATED PATIENTS

- **Equipment:** BpTRU, Omron HEM-907, Microlife WATCH-BP
 - 3-6 automatic measurements at 1 min intervals
- **Clinical use:**
 - Patient to exam room
 - Health personnel/others leave room after 1st measurement
 - Next 2-5 measurements done in isolation
- **Clinical utility:**
 - Eliminates most technical errors
 - Reduces/eliminates white coat HTN?

J Hypertension 2010; 28:703 Hypertension 2010; 55:195

TYPICAL SEQUENCE OF Bp-TRU READINGS



Blood Press Monit 2006; 11:60

RECENT STUDIES OF AUTOMATED OFFICE BP

Study	Routine Clinical Practice	Research Quality Office	Automated Office	Mean Awake 24-h ABPM
Myers, 2009	152/87	140/80	132/75	134/77
• 309 pts				
Myers, 2010	150/89	---	133/80	135/81
• 254 pts				
Graves, 2003	152/84	138/74	136/79	---
• 104 pts				
Becket, 2005	151/83	---	140/80	142/80
• 481 pts				

From Hypertension 2010; 55:195 and Myers MG, J Hypertension 2010; 28: 28:703

BP GOALS AND MEASUREMENT TECHNIQUE

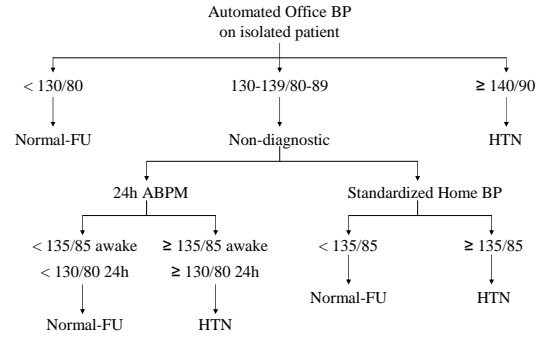
AOBP, Isolated Patient = Mean awake BP, 24h ABPM = Mean Home BP

• All are 5/5 mm Hg < Research quality manual BP

Goal BP:	Research Quality Office	AOBP	Home BP	Mean Awake BP 24h ABPM
Uncomplicated HTN	< 140/90	< 135/85	< 135/85	< 135/85
DM, CKD, CVD	< 130/80	< 125/75 (?)	< 125/75 (?)	< 125/75 (?)

Hypertension 2010; 55:195

AUTOMATED OFFICE BP: ALGORITHM TO DX HTN



J Hypertension 2010; 28:703

MORE ACCURATE DX/MONITORING OF HTN

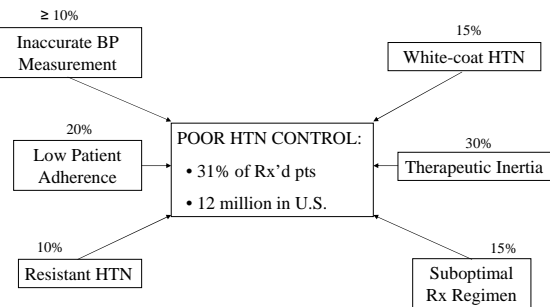
Inherent BP variability → ↑ measurements over time

Inaccurate measurement → Train/Audit/Re-train Automated BP (AOBP)

↓ BP over serial visits → Mean BP over 2-5 visits:
 • ≥ 180/110 → 2 visits
 • 160-179/100-109 → 3 visits
 • 140-159/90-99 → 5 visits

White-coat/Masked HTN → Out-of-office BP measurement
 • Home and/or 24h ABPM
 • ? AOBP to ↓ white-coat HTN

POOR HTN CONTROL IN TREATED PATIENTS



LOW ADHERENCE/PERSISTENCE TO RX

20-30% of poor HTN control – 15-40% do not admit!

- Poorly understood – best practices to improve it not developed
- Complex, multifactorial strategies appear most effective
 - Methods to measure/monitor adherence needed
 - Detect barriers/feedback to patient
 - Cultural/social competence
 - Provider communication skills – interactive, motivational
 - Regimen simplification/medication intake strategies
 - Cost monitoring/minimization
 - Address voiced/unvoiced side effect concerns
 - Facilitate self-management – home BP with feedback

J Clin Hypertens 2010; 12:757

Cochrane Reviews 2010; 3:CD005182

WHAT DO HTN PATIENTS KNOW AND DO?

% With Appropriate Knowledge, 2008

Know HTN is threat to health	85%
Know consequences of HTN	63%
Know last BP	80%
Know BP goal	30%
Educated about possible medication side effects	44%
Interested in learning more	50%

• Better education needed!

J Clin Hypertens 2010; 12:328

J Clin Hypertens 2010; 12:784

CLINICIAN THERAPEUTIC INERTIA

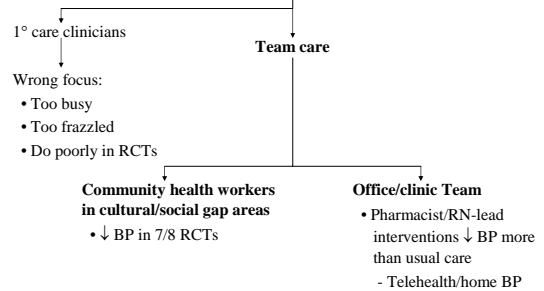
≥ 30% of poor HTN control!

- **Ineffective provider response to BP > goal**
 - Fail to ↑ Rx despite BP > goal for ≥ 6 mo
 - Occur on 30-60% of visits with BP > goal
- **Multifactorial causation:**
 - Competing demands/limited time
 - Uncertainty about “true” BP
 - “Soft clinical reasoning”
 - “Just white-coat effect” but never proven
 - “Let’s work on wt loss/Na restriction, again”

NEED NEW APPROACH TO HTN CONTROL!

Restructuring of health care system:

- Bridge adherence gap
- Reduce clinician inertia



Circulation 2010; 122:1141
Am J Hypertens 2010; 23:949 BMJ 2010; 341:c3995
J Gen Intern med 2010; 25:1090

GOAL BP IN HTN: HOW LOW TO GO?

BP and CVD risk: continuous, log-linear, no plateau

- Lower should be better, so...
- Guideline goal BP, internationally ∝ absolute CVD risk

CVD Risk	Goal BP
Low/moderate ≤ 20%/10y	<140/90
High > 20%/10y	< 130/80

 - DM, CKD, CVD

BUT IS LOWER REALLY BETTER?

GOAL BP IN HTN: HOW LOW TO GO?

Contrasting meta-analyses:

- Cochrane: 7 RCTs; 22,009 pts
 - No RRR in CVD/ESRD with BP target ≤ 135/85
- BPLTT Collaboration: 32 RCTs; 201,566 pts
 - Same RRR in CVD if SBP baseline < 140 vs ≥ 140

Cochrane Database 2009; (3):CD004349 J Hypertens. Czernichow, 2010, in press

GOAL BP IN HTN: HOW LOW TO GO?

Contrasting RCTs:

- **ACCORD: 4733 T2DM pts – SBP < 120 vs < 140**
 - No RRR in MI/CVD death
 - 40% RRR in stroke
- **CARDIO-SIS: 1111 HTN pts – SBP < 130 vs < 140**
 - 35% RRR in new LVH
- **AASK Cohort FU: 1094 AA CKD pts – SBP < 130 vs < 140**
 - 27% RRR in CKD progression if proteinuria (> 300 mg/d)

NEJM 2010; 362:1575 Lancet 2009; 374:525 NEJM 2010; 363:918

GOAL BP IN HTN: HOW LOW TO GO?

Await SPRINT (NIH) 2010 → 2019

- 10,000 pts: < 120/80 vs < 140/90 in 3 groups:
 - Moderate CVD risk, CKD, age ≥ 75y

In the meantime...

- Target < 130/80, at least if:
 - CKD ⊕ significant proteinuria (ACR > 300, TP/Cr > 0.20)
 - T2DM and ↑ stroke risk:
 - Prior stroke, Fam Hx of stroke
 - Smoker, poor glycemic control, or no statin Rx
 - Caution in elderly

J Clin Hypertens 2010; 12:472 Curr Hypertens Rep 2010; 12:313 NEJM 2010; 363:974

GOAL BP IN HTN: HOW TO GET THERE?

Lifestyle modification:

	↓ BP mm Hg
Weight loss/Kg	1/1
Low Na < 2.4 g/d	5/3
DASH Diet	11/5
ETOH ≤ 2 drinks/d	4/2
Brisk walking, 150 min/wk	5/4
Dark chocolate, 500 cal/d	5/3

www.nhlbi.nih.gov/health/public/heart/hbp/hbp_low/hbp_low.pdf

J Hypertens 2006; 24:269 Hypertension 2006; 47:296 Can J Cardiol 2010; 26:249

GOAL BP IN HTN: HOW TO GET THERE?

Pharmacologic Rx:

Focus 1990-2007:

- Best drug to ↓ BP
- Best drug to ↓ CVD, CKD

Current focus:

- Best combos to ↓ BP
- Best combos to ↓ CVD, CKD

Most HTN pts need > 1 drug for control:

1 drug	→ 30%
2 drugs	→ 40%
≥ 3 drugs	→ 30%

J Am Soc Hypertens 2010; 4:42

BEST DRUGS TO LOWER BP AS MONO-RX

Age and race affect BP-lowering of some drugs:

- **Whites < 60y:**
ACE-I/ARB/BB > Diuretic/?CCB
- **Whites ≥ 60y:**
ACE-I/ARB = BB = Diuretic = CCB
- **Blacks of any age:**
Diuretic/CCB > ACE-I/ARB/BB

Am J Hypertens 2007; 20:311 Am J Hypertens 2007; 20:923 Hypertension 2007; 49:272

BEST HTN DRUGS TO ↓ CVD/↓ CKD

BP-lowering most important, but...

- **ACE-Is/ARBs preferred IF:**
 - CKD ⊕ proteinuria (> 200 mg TP/g creatinine)
 - Systolic HF
 - Post-MI?
- **BBs preferred IF:**
 - Post-MI, first two years
 - Systolic HF

Ann Int Med 2006; 144:213 Can J Cardiol 2010; 26:249 BMJ 2009; 338:b1665

LESS EFFECTIVE HTN DRUGS TO ↓ CVD/↓ CKD

BP-lowering most important, but...

- **BBs less effective IF:**
 - Age ≥ 60y – 15 to 18% less stroke reduction
- **αBs less effective:**
 - 26% less stroke reduction
 - 66% less HF reduction

J Int Med 2009; 266:232 BMJ 2009; 338:b1665 Hypertension 2003; 42:239

COMBO-RX FOR HTN: ASH, 2010

<u>Preferred</u>	<u>Acceptable</u>	<u>Less Effective</u>
ACE-I/D*	BB/D*	ACE-I/BB
ARB/D*	DHP CCB/BB	ARB/BB
ACE-I/CCB*	CCB/D	ACE-I/ARB
ARB/CCB*	DRI/D*	Non-DHP CCB/BB
	DRI/ARB*	Clonidine/BB

*Available as single pill combination in U.S.

J Am Soc Hypertens 2010; 4:42

ACE-I/CCB vs ACE-I/DIURETIC?

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

Benazepril/Amlodipine vs Benazepril/HCTZ
 ⊕ Others ⊕ Others

	<u>ACE-I</u>	<u>ACE-I/D</u>	<u>HR</u>	<u>CI</u>
CVD events	9.6%	11.8%	0.80	0.72-0.90
CKD events	2.0%	3.7%	0.52	0.41-0.65

- 2X ↑ Cr
- Dialysis

• Multiple controversies about study conclusions

NEJM 2008; 359:2417 Lancet 2010; 375:1173

INITIAL LOW-DOSE 2-DRUG RX FOR HTN?

Yes: most pts with BP ≥ 20/10 mm Hg above goal

- Greater BP reduction
- Faster BP reduction
- Improved adherence
- ↑ HTN control at 6 mo: STITCH 2009, Weir meta-analysis 2007
 - ↓ CVD events 25% in high risk pts (VALUE, 2004)

Consider: many Stage 1 HTN pts with BP < 20/10 above goal

- ↑ HTN control rates in STITCH, Weir meta-analysis

Caution/avoid:

- Frail elderly, postural hypotension, volume depletion

J Am Soc Hypertens 2010; 4:42 Hypertension 2009; 53:598, 646
 Am J Hypertens 2007; 20:807 Corrao, J Hypertension 2010; IN PRESS

“OPTIMAL” 3-DRUG REGIMENS

Expert consensus, not evidence-based:

	<u>Regimen 1*</u>	<u>Regimen 2*</u>
Control volume	Diuretic appropriate to eGFR	Diuretic appropriate to eGFR
Control heart rate	Non-DHP CCB: verapamil or diltiazem	BB**
Control vasoconstriction	ACE-I or ARB	DHP-CCB amlodipine, nifedipine, etc.

*Presumes optimal dosing of each agent

**Adding BB to ACE-I or ARB provides minimal BP reduction unless HR > 84/min

Am J Kid Dis 2000; 36:646 J Am Coll Cardiol 2008; 52:1749

ALDOSTERONE BLOCKADE AS STEP 4 RX

Spirolactone, 12.5-50 mg/d:

<u>Study</u>	<u># Patients</u>	<u>Δ BP</u>
ASCOT, 2007	1411	-22/10
DeSouza, 2010	175	-16/9
Lane, 2007	119	-22/9
Rodilla, 2009	88	-28/12
Nishizaka, 2003	76	-25/12
Mahmud, 2005	69	-28/13
Sharabi, 2005	48	-23/13
Ouzan, 2002	23	-24/10

Eplerenone, 50-100 mg/d

Calhoun, 2008	52	-18/8
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ALDOSTERONE BLOCKADE AS STEP 4 RX

Clinical use:

- **Contraindicated if eGFR < 30 or K⁺ ≥ 5.0**
- **Minimize hyperkalemia risk:**
 - Low K⁺ diet; off K⁺, salt substitute, triamterene
- **Dosing:**

	<u>Initial</u>	<u>Final</u>
Spirolactone	12.5-25 mg/d	≥ 50 mg/d (if PA)
Eplerenone	50 mg/d	100 mg/d
Amiloride	2.5-5.0 mg/d	10-20 mg/d

• **Adjust dose q 4 wk**

- ✓ K⁺ at 1 and 4 wks
 - DC if K⁺ > 5.5; ↓ dose 50% if K = 5.0-5.5

J Am Soc Hypertens 2008; 2:462 Curr Hypertens Rep 2008; 10:496

ALGORITHM FOR HTN RX

