RESISTANT HYPERTENSION
AND SELECTED HYPERTENSION UPDATES

CARL J. PEPINE, MD, MACC, FESC
PROFESSOR OF MEDICINE
DIVISION OF CARDIOVASCULAR MEDICINE
UNIVERSITY OF FLORIDA

TAKE-HOME POINTS

1. Causes of treatment resistant hypertension (TRH).
2. Role of clinic, home, and ambulatory BP in TRH.
   - Selecting validated automated BP devices.
   - Use of automated BP devices.
3. Clinical evidence regarding efficacy/safety of treatment options .
4. Assess appropriate treatment strategies for TRH
5. Emerging Interventional Approaches to TRH
6. HTN Updates

LEARNING OBJECTIVES

Upon completion of this activity, participants should be able to:

- Recognize TRH and adjust antiHTN therapy in pts not achieving BP control with life-style and initial pharmacologic management.
- Develop strategies to overcome pt-related adherence barriers to use of antiHTN drugs.
- Summarize current evidence-based practice guidelines for BP control.
- Describe benefits and risks of currently approved antiHTN therapies.
- Better understand novel therapies for TRH.

SOME TERMINOLOGY

"**Resistant Hypertension**" (RH) or

"**Treatment-resistant hypertension**" (TRH)
(HTN requiring ≥**4** antihypertensive drugs to achieve BP control)

- Taking 3 antihypertensive agents with uncontrolled BP
- Taking ≥4 antihypertensive agents, regardless of BP

ADDITIONAL CAVEATS SOMETIMES APPLIED:

- Inclusion of a diuretic
- "Optimal" or "maximally tolerated" doses
- Drugs of different pharmacological classes
- Exclusion of pseudoresistance

TERMINOLOGY CONTINUED

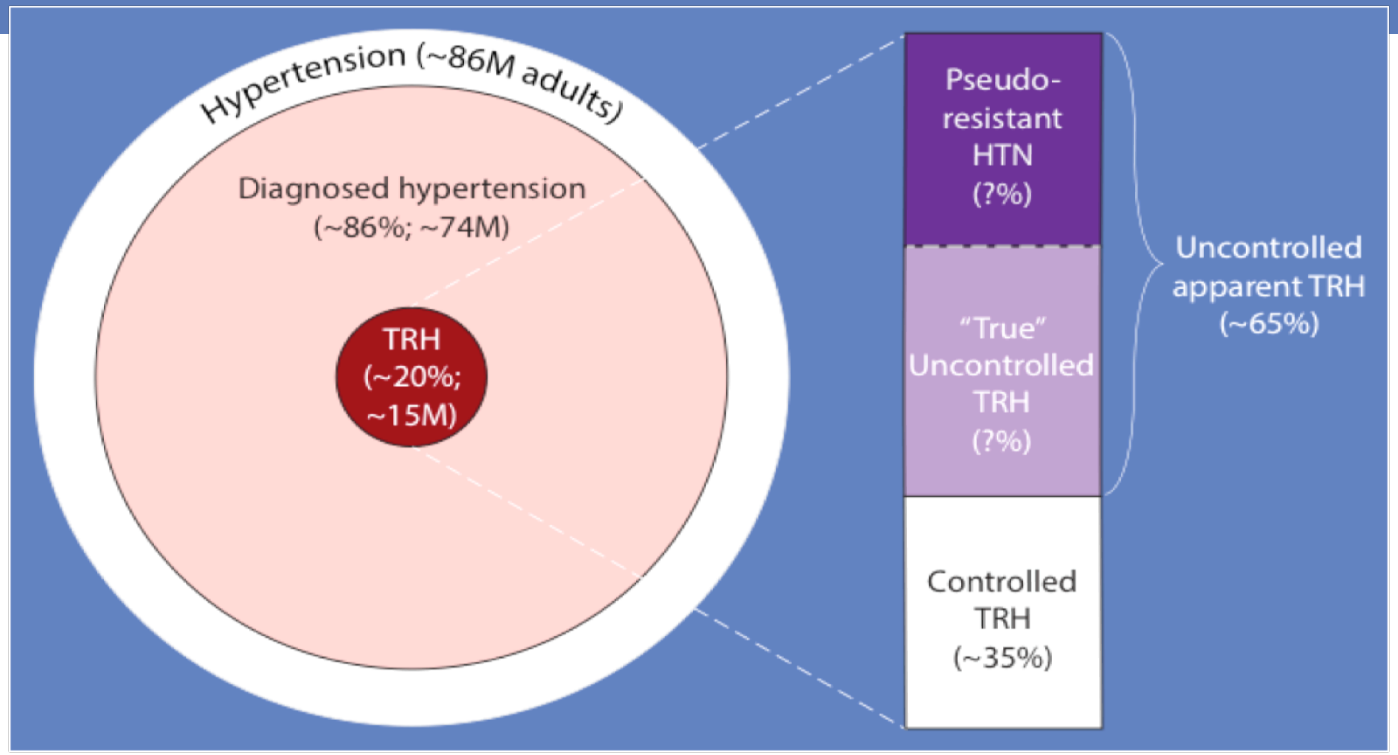
- "**Pseudoresistant hypertension**" (or *pseudoresistance*) – meeting RTH definition, but actually caused by factors unrelated to pathophysiologic mechanisms causing HTN
  - Nonadherence
  - Improper BP measurement
  - Use of interacting medications
  - 'White coat' effect
- **"Apparent resistant hypertension"** – meeting RTH definition, but pseudoresistance not excluded

TERMINOLOGY CONTINUED

- "**Refractory hypertension**" – uncontrolled BP despite ≥5 antihypertensive drugs, including an aldosterone antagonist, all at maximally-tolerated doses

- **Secondary hypertension** – hypertension due to an identifiable cause. Generally not considered TRH since most causes have curative or highly effective therapy

TREATMENT RESISTANT HTN PREVALENCE



FROM SMITH SM, ET AL. TREATMENT-RESISTANT HYPERTENSION. ACSAP 2018 F

TRH PORTENDS WORSE OUTCOMES

- **TRH associated with 30-90% excess risk, versus non-TRH, for**:
  - Stroke
  - Myocardial infarction
  - Heart failure
  - Progression of CKD
  - Cardiovascular death
  - All-cause death
- **Increased risk of DM, OSA, etc.**
- **And poorer health-related quality of life**

CONTRIBUTORS TO TRH

Patient Behaviors

- **Poor dietary habits**
- **Inadequate exercise/activity**
- **Poor adherence to antihypertensive therapy**
- Inadequate follow-up
- Use of OTC interacting meds
- Illicit drug use

CONTRIBUTORS TO TRH

Patient Comorbidities

- Older Age
- African ancestry
- Non-Hispanic ethnicity
- Female sex
- Geographic location
- Diet (high Na, excess EtOH)
- Sedentary lifestyle
- Smoking
- LVH
- Heart failure
- CKD
- Dyslipidemia
- Overwt/Obesity
- Diabetes
- Sleep apnea
- CAD/PAD
- Prior stroke/TIA

CONTRIBUTORS TO TRH

Provider/System Behaviors

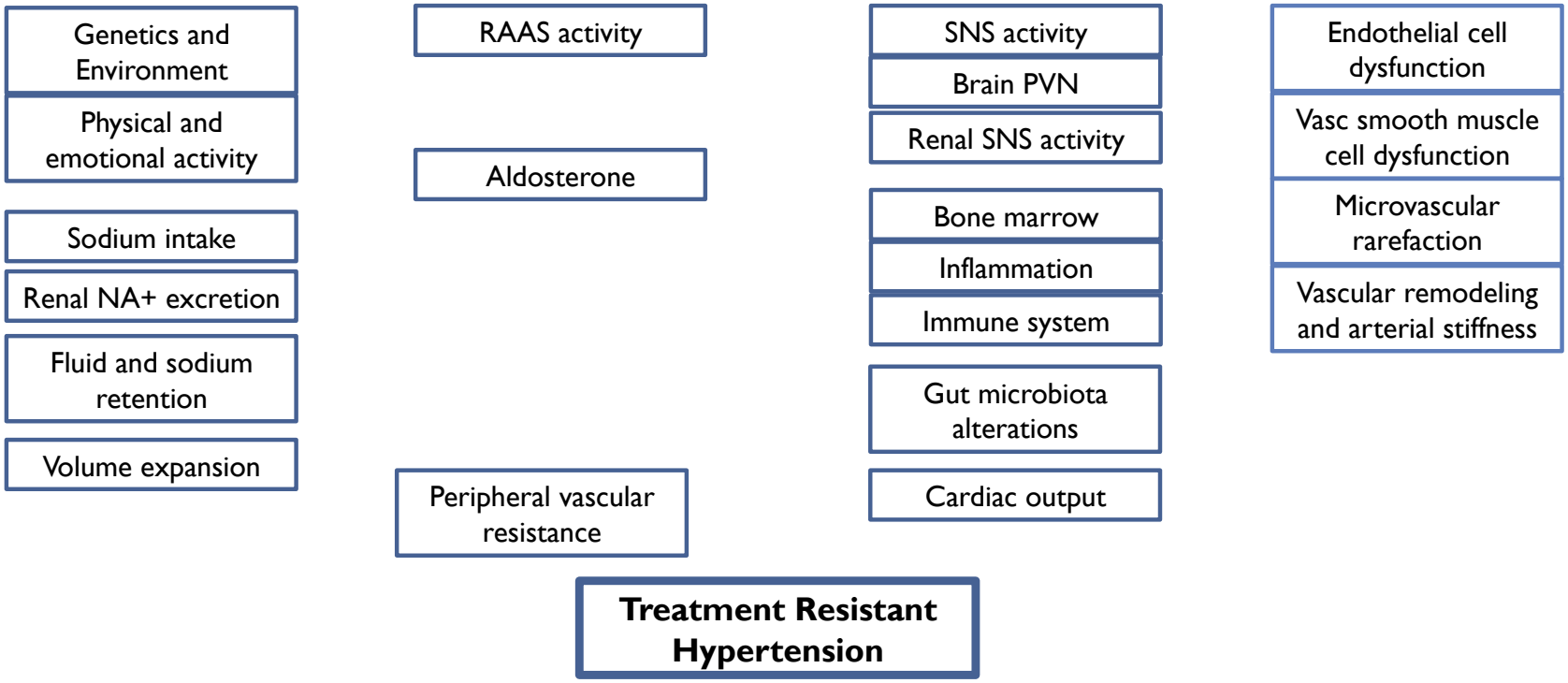
- Improper BP measurement
- Treatment inertia
- Suboptimal antihypertensive combinations
- Prescribing interacting meds
- Unrecognized/untreated secondary causes

CONTRIBUTORS TO MECHANISMS FOR TRH

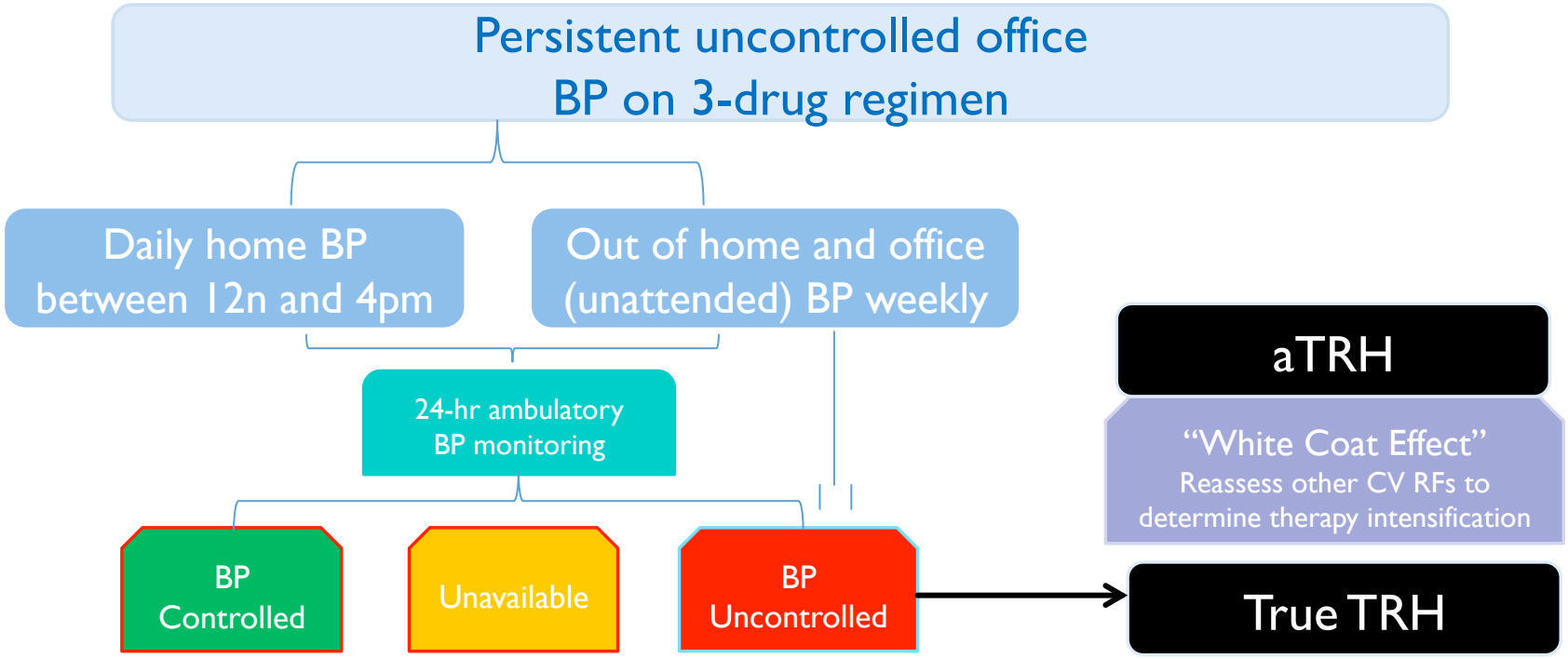
Blood Vessels (Conduit and Microvessels)
- **Endothelial Cells**
- **Vascular Smooth Muscle Cells**
- **Adventitia**

Heart
Kidney
Brain
Sympathetic Nervous System
Bone Marrow
Immune System
Gut (Epithelial Cells, Microbiota, Metabolome)

MECHANISMS CONRTIBUTING TO TRH DEVELOPMENT



BP MONITORING FOR TRH



RELATIONSHIP BETWEEN BP MEASUREMENTS: 2017 HTN GUIDELINE VALUES FOR DIAGNOSIS OF HTN

Office BP	Home BP	Daytime ABPM	Nighttime ABPM	24-hr ABPM
120/80	120/80	120/80	100/65	115/75
130/80	**130/80**	**130/80**	**110/65**	**125/75**
140/90	135/85	135/85	120/70	130/80
160/100	145/90	145/90	140/85	145/90

*note that divergence in office vs HBP and ABP increases at higher BPs

Whelton, et al. *J Am Coll Cardiol* 2018;71:e127-248

CHOOSING A HOME BP MONITOR

	Wide array of options/features
Ideal	Measurement/rest/measurement automation with averaging of BP
Ideal	Electronic storage of BP log
Useful for some patients	BP log transmission through media (eg, USB), Bluetooth, (eg, smartphone) or internet
Ideal for select patients	Button/digit size/display type [*visually-impaired or low dexterity*]
Ideal for select patients	Auditory cues/"talking" monitors [*blind/non-deaf*]
Usually unnecessary	BP interpretation
Usually unnecessary	Arrhythmia detection
Patient preference	Battery –powered vs. cord-powered (or both)
Patient preference	Weight/size of monitor

HOME BP MONITORING

- **Advantages**
  - Identify/minimize white coat & masked effect
  - Better prediction of CV risk than usual office BP
  - Captures day-to-day BP variability
  - Relatively inexpensive (most <$100)
  - Many devices log BP electronically; some transmit data online for telemonitoring

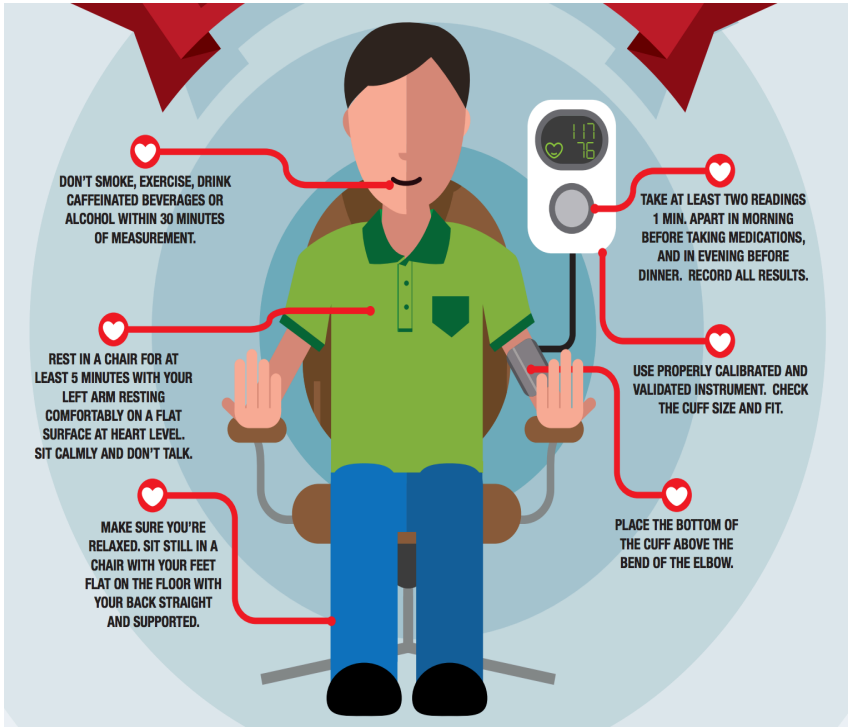
- **Disadvantages**
  - Requires additional pt work at home
  - Values reflect "relaxed environment"
  - High values may prompt anxiety/ calls to office, etc.
  - Provides no data on nighttime BP, dipping status, early AM surge, etc.
  - BP log can be gamed
  - No reimbursement for provider; rarely reimbursement for pt

HOME BP MONITORING (CONTINUED)

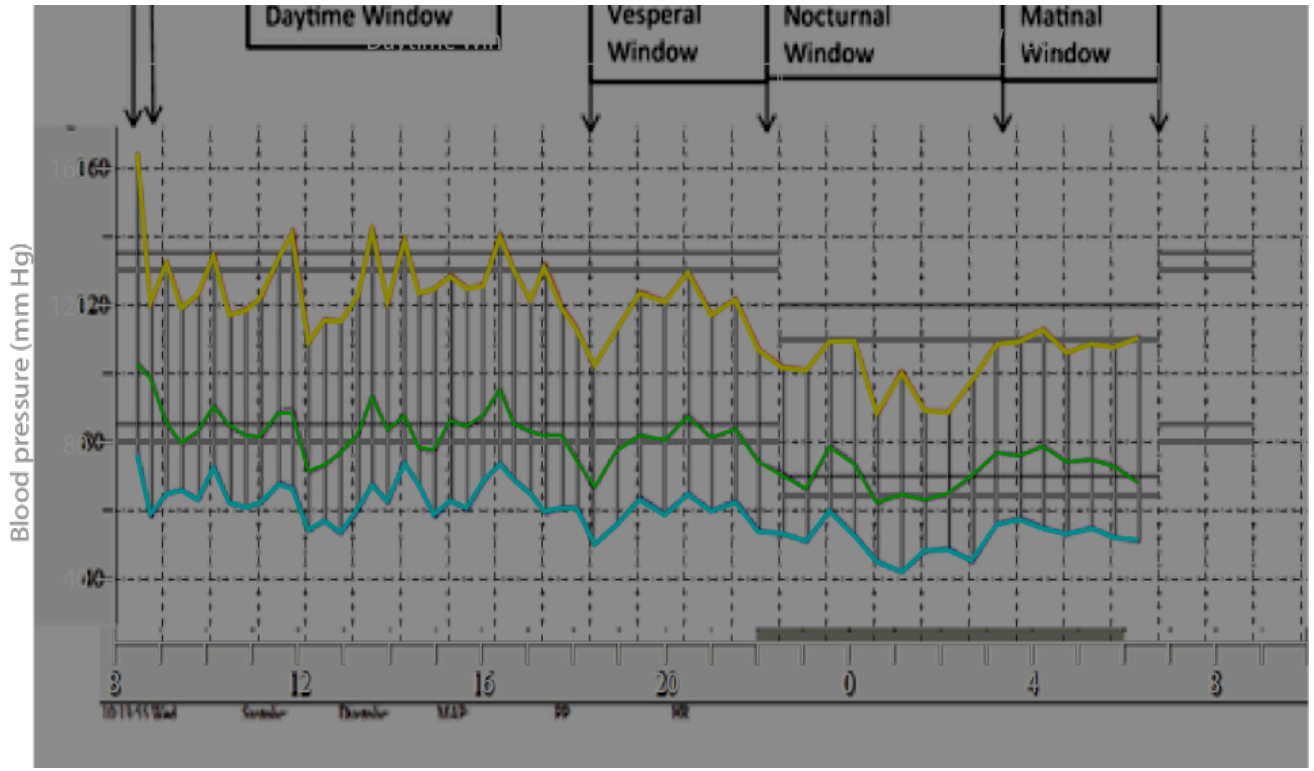
- Recommend a ***validated upper arm*** monitor from reputable company
  - Note that monitors may be validated for general adult population, but not all special populations (pregnancy, arrhythmias, children, etc.)
  - Avoid wrist/finger monitors, phone apps, etc.
- Choose monitor with oscillometric or auscultatory design (former subject to motion artifact)
  - Instruct patient on proper measurement technique
  - Establish protocol for periodically validating measurement accuracy against manual sphygmomanometry

HOME BP MONITORING (CONTINUED)

- **Instruct patient on proper BP measurement technique** (online resources: AHA, ACC, VA, NIH, etc)
- Ensure proper cuff size!
- Ensure patients understand/follow manufacturer-specified maintenance
- Give patient a log or encourage online tracking systems (e.g., AHA Check. Change Control tracker)
- Encourage twice-daily (AM/PM) monitoring, with 3 measurements at each time.



AMBULATORY BP MONITORING (ABPM)



Blood Pressure, mm Hg	
Office	158/86
ABPM	
24-hr mean	117/59
Daytime	125/63
Nighttime	104/52

AMBULATORY BP MONITORING (ABPM)

- Advantages:
  - Completely automated (from pt perspective)
  - Identify/exclude white coat effect
  - Best BP predictor of CV risk
  - Measurement of diurnal BP patterns and variability
  - Most devices incl. software that provides summary statistics ± interpretation for abnormal readings
- Disadvantages:
  - Cumbersome for patients
  - Limited reimbursement (U.S.)
    - Medicare median for full procedure ≅ $58 (IQR, $38-$72)[1]
    - ABPM components: ~$15-40 apiece
    - Commercial: variable, if covered, often follows Medicare criteria
  - Initial costs (hundreds to >$2.5k) plus ongoing maintenance

[1]Kent ST, et al. J Am Soc Hypertens 2014;8:898-908.

AMBULATORY BP MONITORING (ABPM) CONTINUED

- Use a validated monitor from reputable company
  - Same caveats as HBPM re: validation in special populations
  - Choose oscillometric or auscultatory (former subject to motion artifact)
  - Instruct proper attire (short sleeves; loose fitting shirt; sturdy belt), minimize arm movement during measurement
  - Protocol for periodic validation against manual sphygmomanometer
  - Establish protocol for device retrieval – avoid mail back!
  - Launder cuffs/holster regularly; replace batteries proactively
- Inquire on typical wake/sleep timing to program device accordingly (prior to visit if possible)
- Instruct on what to expect & how to reapply cuff if needed
- Have patient keep activity log with accurate time during monitoring day
- Consider repeat monitoring if <80% of readings successful

ERNST M. PHARMACOTHERAPY 2013;33:69-83.

AMBULATORY BP MONITORING (ABPM) CONTINUED

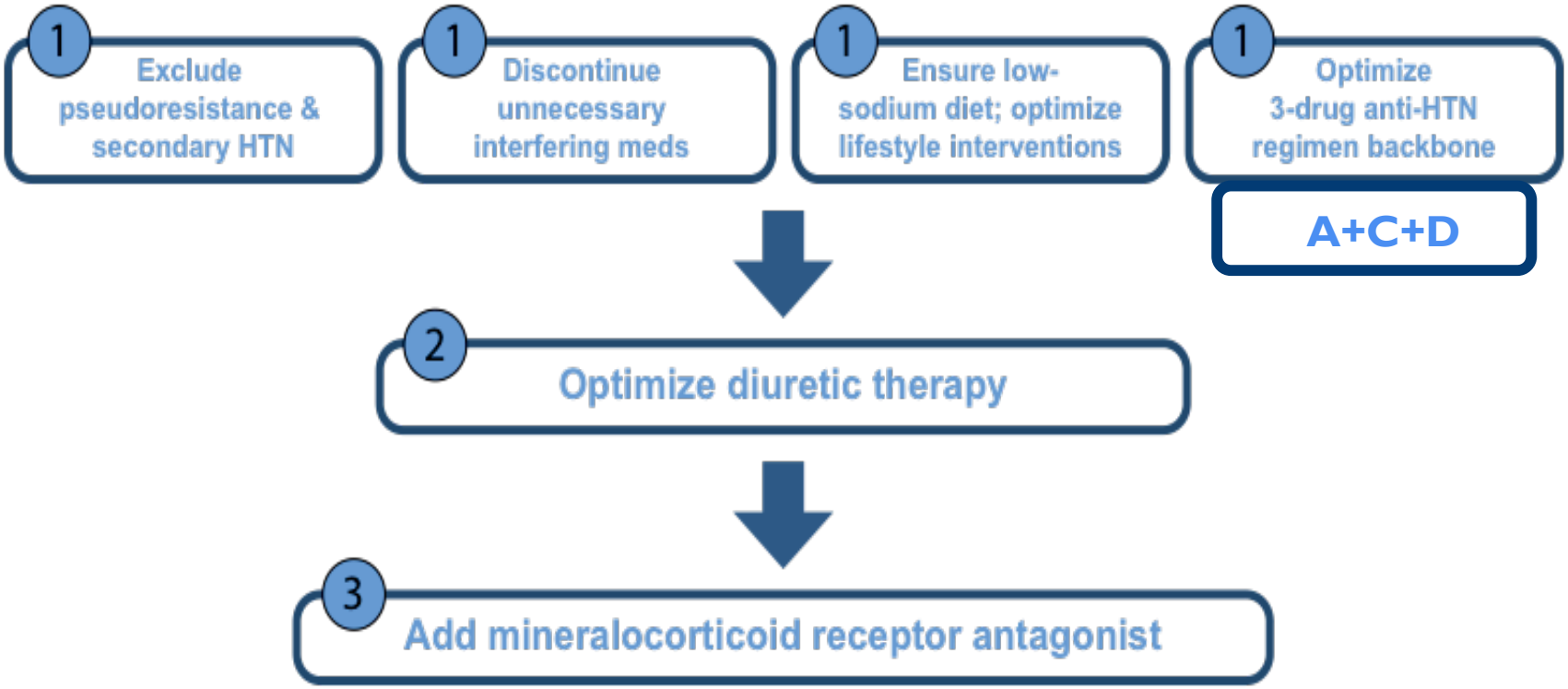
Billing:

- For **Medicare** (some private insurance): bill w/ **ICD10 R03.0** ("Elevated BP, w/o dx of HTN") and **CPT 93784** (other codes if doing only partial components)
- Should have documentation of:
  - elevated office BPs on ≥3 separate occasions
  - controlled out-of-office BP on ≥2 separate occasions
  - no evidence for HTN-mediated organ damage
  - insurance coverage, and that patient is aware of charges, if insurance rejects

MANAGEMENT OF TRH

- Data regarding optimal BP target in TRH are sparse and inconsistent.
- Current recommendations extrapolated from general HTN population.
- But most TRH pts that we see have CVD and/or diabetes.
- Among 14,094 SPRINT and ACCORD-BP participants, **~20% had aTRH** by 2017 ACC/AHA hypertension guidelines.
- **SBP target <120 mm Hg vs <140 mmHg reduced risk of most major CV outcomes and death.**

MANAGEMENT OF TRH: (AHA RECOMMENDATIONS, CARY 2018)



MANAGEMENT OF TRH

- RCTs of best drug to add to an ACE-I (or ARB or DRI), CCB, and thiazide-like diuretic (**A+C+D**) regimen
  - PATHWAY-2
  - REHOT
- Interventional therapy
  - Renal denervation
  - Carotid baroreceptor activation
- Renin-guided therapy
- Collaborative Care

Selecting Validated Monitors

- British and Irish Hypertension Society (https://bihsoc.org/bp-monitors/)
- dabl Educational Trust (http://www.dableducational.org)
- Hypertension Canada (https://hypertension.ca/hypertension-and-you/managing-hypertension/measuring-blood-pressure/devices/)
- AMA Validated Device List (Q1 '19)
- New universal standard forthcoming from AAMI/ESH/ISO[1]

Device	Mode	AAMI	BHS	ESH 2002	ESH 2010	Circumstance	Recommendation Ref
A&D UA-631 (UA-779 Life Source)	Osc			Pass		At rest, Recruitment violations	Recommended 4
A&D UA-651	Osc				Pass	Study (96) extended to ESH-IP 2010 requirements	Recommended 97
					Pass	With a wide range cuff study extended to ESH-IP 2010 requirements	Recommended 106
A&D UA-704	Osc		A/A			Study details omitted	Questionable 8
A&D UA-705	Osc		A/A			At rest	Recommended 18
A&D UA-767	Osc	Pass	A/A			At rest; not high BP	Recommended 3
A&D UA-767F	Osc				Pass	UA-651 Equivalence	Recommended E119
A&D UA-767S	Osc				Pass	UA-651 Equivalence	Recommended E120
A&D UA-774 (UA-767 Plus)	Osc		A/A			At rest; tables incomplete	Recommended 11
			A/A			At rest; Recruitment violations; Simultaneous readings	Questionable 2
A&D UA-778	Osc	Pass	B/A			Children Only, Ad hoc protocol adaptation. (No general validation)	Recommended 53

1. Stergiou GS. Hypertension 2018;71(3):368-374

UFHealth

TREATMENT OF TRH

- **Ensure low-sodium diet**
  - 24-hr urine sample
  - Intake: ideally <1500 mg/d; alternatively ≤2300 mg, or 1000 mg/d reduction
  - <1% of U.S. adults ingest <1500 mg/d[1]
  - Single center experience in US: TRH patients ingest, on avg, **10 g/d**[2]
  - 1 wk of 1150 mg Na^+/d vs 5750 mg Na^+/d reduced office BP by ~23/9 mmHg in a small RCT[3]
- **Optimize healthy lifestyle**
  - Sleep ≥6 hrs/d
  - Improve overall dietary pattern
  - Regular exercise 3-4x/wk
  - Weight loss
  - Multiple healthy lifestyle factors have been associated with improved prognosis in RH[4]

[1]Benjamin, *Circulation* 2017;135(10):e146-60. [2]Nishizaka, *Am Hypertens* 2005;18:805-12.
[3]Pimenta, *Hypertension.* 2009;54:475-81.

OPTIMIZE DIURETIC-TREATMENT OF TRH

Thiazide	Equiv. dose	Elim. $t_{1/2}$	Outcome Data
HCTZ	25 mg	9-10 h	~0
CLD	6.25-12.5 mg	50-60 h	+++
Indap	1.25-2.5 mg	14 h	+

- Ideally, switch to CLD (indapamide as alternative)
- Example: ↑ BP on 25 mg HCTZ ⇨ CLD 25 mg/d or indap 2.5-5 mg/d
- If must continue HCTZ: dose BID

TREATMENT OF TRH

- **RCTs** for **best 4th-drug** added to an ACE-I (or ARB or DRI), CCB, and thiazide-like diuretic **(A +C+D) regimen**
  - **PATHWAY-2**[1,2]
  - **REHOT**[3]
  - Both trials **Spironolactone better than Clonidine** (and Doxazosin or Bisoprolol in PATHWAY-2).

[1]Williams B, et al. *Lancet Diabetes Endocrinol* 2018;6:464-75; [2]Williams B, et al. *Lancet* 2015;386:2059-68; [3]Krieger EM, et al. *Clin Cardiol* 2014; 37:1-6

- Interventional therapy
  - Renal denervation
  - Carotid baroreceptor activation
- Renin-guided therapy
- Collaborative Care

TREATMENT OF TRH

Add aldosterone antagonist

- >70% of TRH pts candidates based on eGFR / serum K^+
- Usual start doses:
  - Spironolactone: 25 mg/d
  - Eplerenone: 25-50 mg/d (divided BID)
  - Amiloride (alt): 10-20 mg/d
- Monitor: SCr/eGFR, serum K^+
- eGFR <30: avoid spiro, caution w/ eplerenone (↑ risk of hyperkalemia)

Hwang, et al. *Hypertension* 2016;68:1349-54.

TREATMENT OF TRH

Other drugs 5th line- all debatable:

- **β-blockers: metoprolol**, **bisoprolol-** ***Avoid*** carvedilol, labetalol
- **Non-DHP CCB**: diltiazem ER (3A4 inhibition boosts effects of DHP-CCB)
- α_2-agonists: clonidine patch (weekly), guanfacine (HS)-***Avoid all***
- α_1-blockers: doxazosin-***Avoid all***

Experimental Approaches

- Minocycline
- Consider Interventional Approach

SUMMARY-TREATMENT OF TRH

- When available, out-of-office monitoring preferred for suspected TRH
  - Diagnosis: ABPM > HBPM
  - Ongoing monitoring: HBPM > ABPM
- HBPM: minimally, ~2-4 wks after tx adjustment, and again just prior to office visit; ≥3 consecutive days of twice-daily measurement, ideal
- Regular, continuing monitoring preferred, once daily, 2-3x/wk
- White coat effect may warrant less aggressive therapy / high-risk ABPM profiles may warrant more aggressive therapy

INTERVENTIONAL TREATMENT OF TRH

- Catheter-based renal sympathetic denervation (RDN) emerged as alternative/adjunct.
- Following neutral results of first sham-controlled RDN study, SYMPLICITY-HTN3, benefit doubted?
- Subsequently, 3-proof-of-principle studies[1-3] ***confirmed RDN efficacy*** and revealed ***substantial variability of BP lowering***:
  - Pt characteristics,
  - Co-medications and adherence,
  - Technical aspects of RDN procedure.
  - Uncertainties about completeness of denervation within SYMPLICITY-HTN3, especially in larger renal arteries (e.g. sympathetic nerves too far from main renal artery lumen) but closer to lumen within branch arteries and therefore more amenable to RDN.

[1]SPYRAL HTN-OFF MED. *Lancet*. 2017;390:2160-70. [2]RADIANCE-HTN SOLO. *Lancet*. 2018;391:2335-45. [3]SPYRAL HTN-ON MED. *Lancet*. 2018;391:2346-55

INTERVENTIONAL TREATMENT OF TRH

THREE-ARM RANDOMIZED TRIAL OF DIFFERENT RENAL DENERVATION (RDN) DEVICES AND TECHNIQUES IN TRH (RADIOSOUND-HTN) *CIRCULATION* 2018; 10.1161/CIRCULATIONAHA.118.037654

- TRH pts randomized 1:1:1 to 1) RF-RDN-main renal arteries, 2) combined RF-RDN of main renal arteries, side-branches and accessories, or 3) endovascular US-based RDN of main renal artery.
- 120 pts (mean age 64 yrs, mean daytime BP 153/86±12/13 mmHg.
- At 3-mos, systolic daytime ABPM decreased 9.5±12.3 mmHg, $p<0.001$ in all cohorts, >BP reduction in US ablation vs RF ablation of main renal artery -13±14 vs. -6.5±10 mmHg, mean difference -6.7 mmHg, $p=0.038$ but p ns between US and side branch ablation groups.
- Endovascular US-based RDN ***superio***r to RF ablation of ***main renal arteries*** only; combined RF ablation of main arteries, accessories and side branches was not.

TREATMENT RESISTANT HYPERTENSION

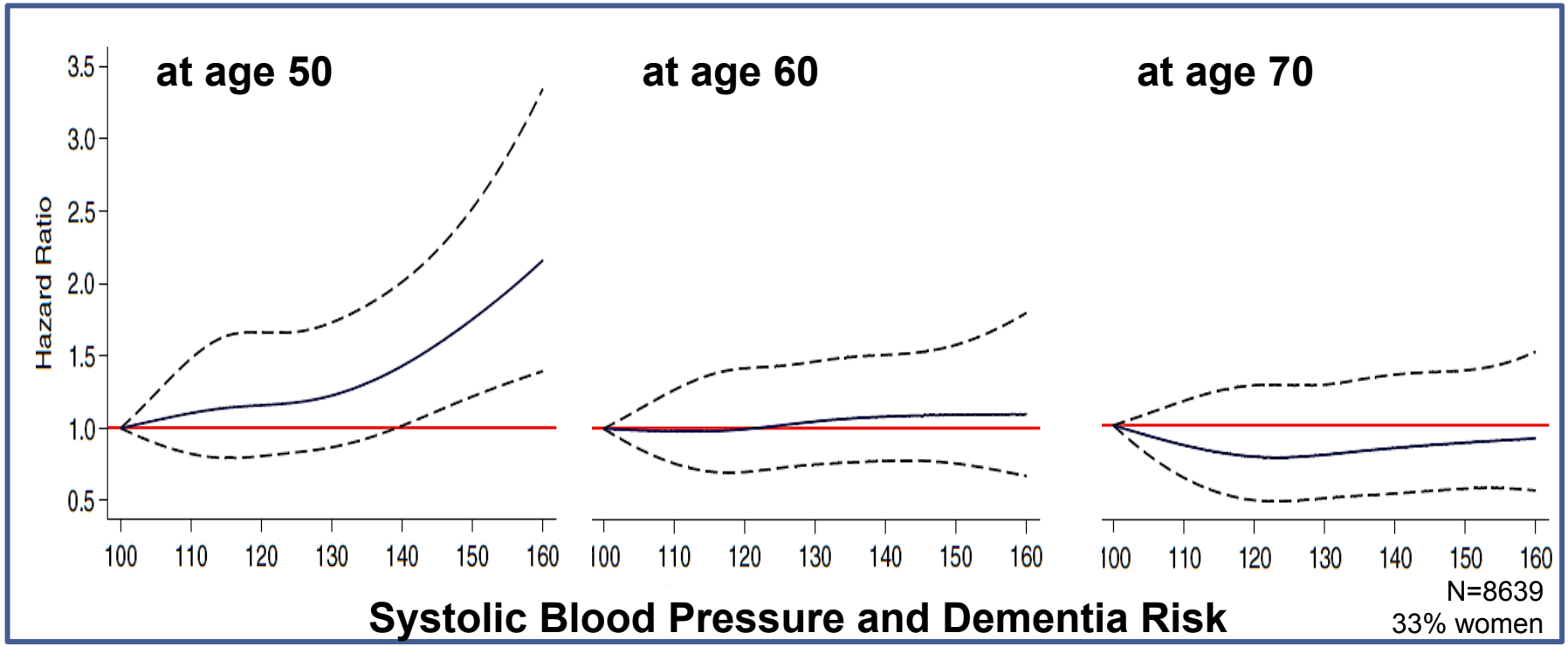
SUMMARY AND CONCLUSIONS

- TRH increasingly common and associated with worse prognosis
- Out-of-office BP measurements important: diagnosis/monitoring
- Optimizing baseline therapy important, but many pts require 'second-line'
- Adherence to medications, lifestyle interventions, esp. sodium reduction, are crucial
- Interventional approaches promising

- ***Most importantly, engage the patient in their own care!***

LOWER MIDLIFE BP LINKED WITH REDUCED COGNATIVE IMPAIRMENT

ABELL, *EUROPEAN HEART JOURNAL* 2018; 39:3119-25



Systolic Blood Pressure and Dementia Risk

LOWER BP REDUCES COGNATIVE IMPAIRMENT

SPRINT (Memory and Cognition IN Decreased Hypertension) MINDS:

Intensive BP control in older people significantly reduced risk of developing mild cognitive impairment (MCI), a precursor of early dementia

POPULATION

6029 Men
3332 Women

Adults aged ≥50 years with hypertension and without diabetes or stroke

Mean age: **68** years

LOCATIONS

102 US sites (including Puerto Rico)

INTERVENTIONS

9361 Patients randomized
8563 Patients analyzed (≥1 cognitive assessment)

4278	4285
Intensive control (Target SBP <120 mm Hg)	**Standard control** (Target SBP <140 mm Hg)

Median treatment period, 3.3 years

PRIMARY OUTCOME

Occurrence of adjudicated probable dementia

SECONDARY OUTCOMES

Adjudicated mild cognitive impairment (MCI)

Composite outcome of MCI or probable dementia

FINDINGS

PRIMARY OUTCOME: Adjudicated probable dementia

Intensive control	Standard control
149 patients (7.2 cases/1000 person-years)	**176** patients (8.6 cases/1000 person-years)

Hazard ratio: **0.83** (95% CI, 0.67-1.04)

SECONDARY OUTCOME: Adjudicated MCI

Intensive control	Standard control
287 patients (14.6 cases/1000 person-years)	**353** patients (18.3 cases/1000 person-years)

Hazard ratio: **0.81** (95% CI, 0.69-0.95)

SECONDARY OUTCOME: Composite outcome

Intensive control	Standard control
402 patients (20.2 cases/1000 person-years)	**469** patients (24.1 cases/1000 person-years)

Hazard ratio: **0.85** (95% CI, 0.74-0.97)

The SPRINT MIND Investigators for the SPRINT Research Group. Effect of intensive vs standard blood pressure control on probable dementia: a randomized clinical trial [published January 28, 2019]. *JAMA*. doi:10.1001/jama.2018.21442

LIKELY MECHANISMS CONRTIBUTING TO PREVENTION OF DEMENTIA DEVELOPMENT

- **SPRINT Brain MRI Sub-study** evaluated change in total ***white matter lesion*** (WML) ***volume*** and ***total brain volume*** (TBV) over time during active treatment and passive follow-up phases. (*Blood Pressure* 2018;27:247-48)

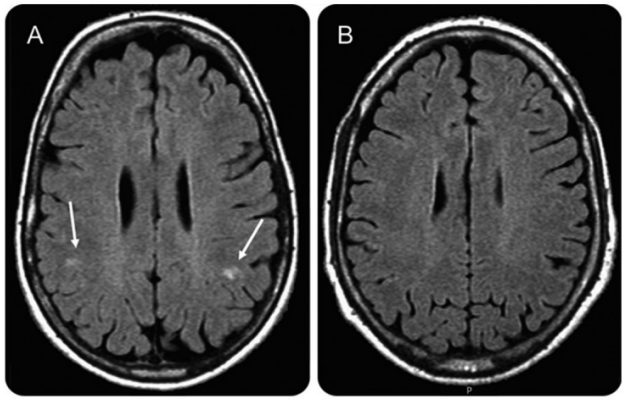
- Brain ***WML volume*** increases at 4-yrs F/U were significantly less in the intensive treatment group (0.28 cm3 compared to 0.92 cm3, in the standard treatment group, mean difference 0.64 cm3, p=0.004).

- TBV decreased similarly in both treatment groups.

HIGH BP & MICROVASCULAR MECHANISMS CONRTIBUTE TO COGNATIVE INSUFFIENCY & DEMENTIA DEVELOPMENT

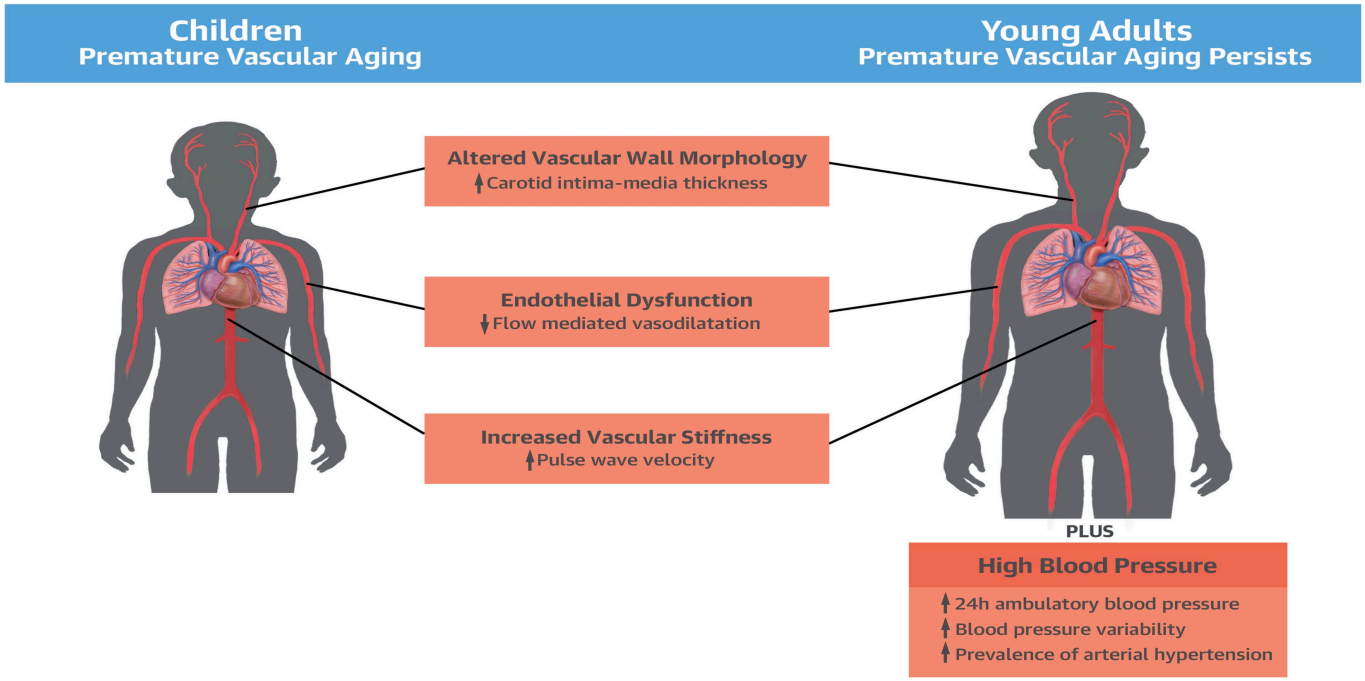
- ***White matter lesions*** indicate ***impaired microcirculation*** and predict ***stroke, dementia*** (both vascular dementia and Alzheimer's disease) and increased ***mortality.***
- Finding that ***intensive BP lowering prevents reduction in WML volume*** is consistent with finding of ***reductions*** in ***MCI*** and in the combined outcome of ***MCI and probable all-cause dementia*** in the intensive treatment group of SPRINT MIND.
- Despite a ***low incidence of probable dementia related to exclusion of diabetes and prior stroke*** and ***limited follow-up time*** due to early discontinuation of SPRINT because of CVD benefit, reducing the time required for development of probable dementia.
- **These observations provide the first randomized trial evidence for the argument that high BP should be normalized by treatment to prevent development of cognitive decline.**

WHITE MATTER HYPERINTENSITIES ASSOCIATED WITH MILD COGNITIVE IMPAIRMENT LIKELY RELATED TO HTN



Panel A Brain scan 45-yo woman with white matter hyperintensities (arrows).
Panel B Normal brain scan 47-yo woman. *Neurology* 2013;80:1958-65.

CENTRAL ILLUSTRATION: Assisted Reproductive Technologies-Induced Alterations of the Cardiovascular Phenotype



Meister, T.A. et al. J Am Coll Cardiol. 2018;72(11):1267-74.

CLINICAL PRACTICE GUIDELINE FOR SCREENING AND MANAGEMENT OF HIGH BP IN CHILDREN AND ADOLESCENTS

Significant changes in these guidelines:

- (1) replacement of "prehypertension" with "elevated BP",
- (2) new normative pediatric BP tables based on normal-weight children,
- (3) simplified screening table for identifying BPs needing further evaluation,
- (4) simplified BP classification in adolescents ≥13 yo aligns with 2017 ACC/ AHA adult BP guidelines,
- (5) recommendations for screening BP measurements at preventive care visits,
- (6) streamlined recommendations on initial evaluation and management of abnormal BPs,
- (7) role for ABPM in diagnosis/ management of pediatric HTN, and
- (8) revised recommendations for echocardiography in newly diagnosed HTN in pediatric pts and revised definition of LVH.

PEDIATRICS Volume 140, number 3, September 2017:e20171904

CLINICAL PRACTICE GUIDELINE FOR SCREENING AND MANAGEMENT OF HIGH BP IN CHILDREN AND ADOLESCENTS

pdated Definitions of BP Categories and Stages

For Children Aged 1–13 y	For Children Aged ≥13 y
Normal BP: <90th percentile	Normal BP: <120/<80 mm Hg
Elevated BP: ≥90th percentile to <95th percentile or 120/80 mm Hg to <95th percentile (whichever is lower)	Elevated BP: 120/<80 to 129/<80 mm Hg
Stage 1 HTN: ≥95th percentile to <95th percentile + 12 mmHg, or 130/80 to 139/89 mm Hg (whichever is lower)	Stage 1 HTN: 130/80 to 139/89 mm Hg
Stage 2 HTN: ≥95th percentile + 12 mm Hg, or ≥140/90 mm Hg (whichever is lower)	Stage 2 HTN: ≥140/90 mm Hg

PEDIATRICS Volume 140, number 3, September 2017:e20171904

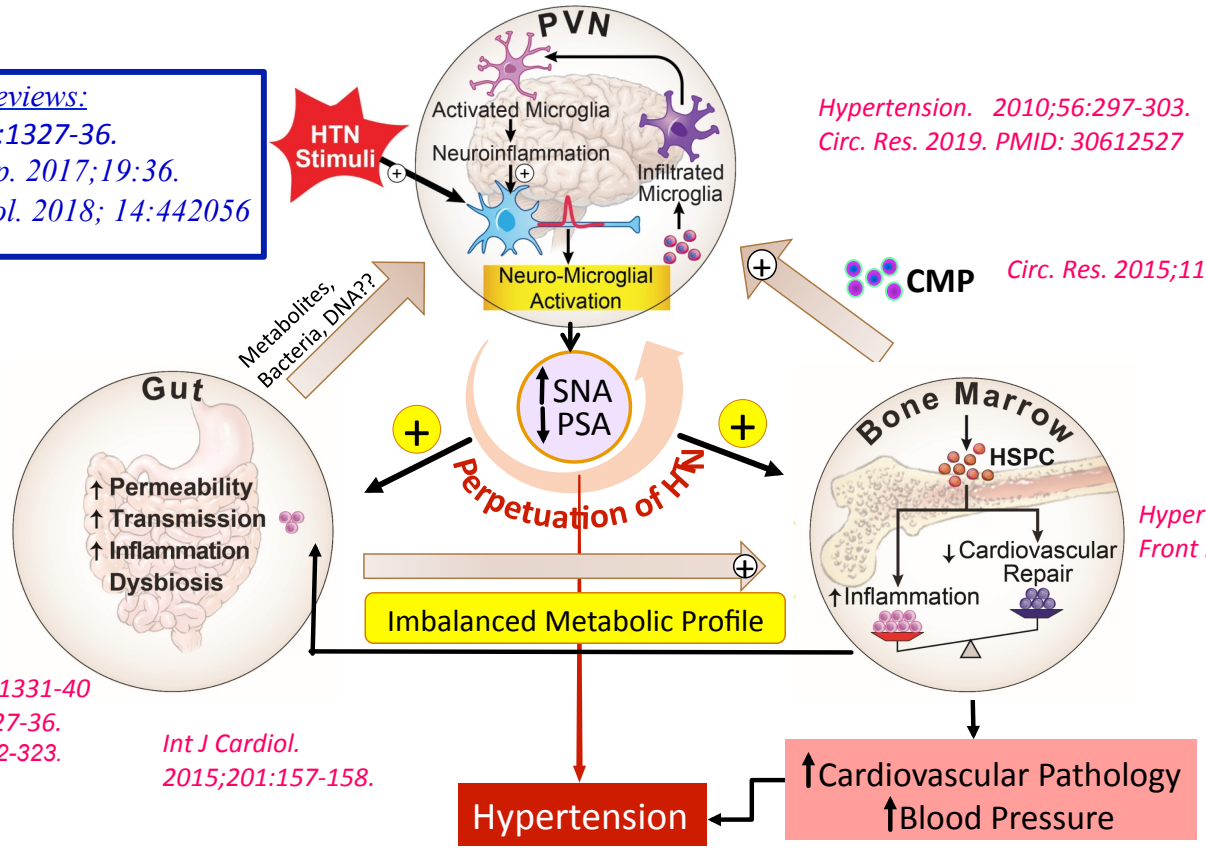
- QUESTIONS

LIKELY MECHANISMS CONRTIBUTING TO TRH DEVELOPMENT

Brain-Gut- Bone Marrow Interactions:

Triangular Hypothesis for Hypertension

Reviews:
Circ. Res.2016; 118:1327-36.
Curr Hypertens Rep. 2017;19:36.
Nature Rev. Nephrol. 2018; 14:442056



Hypertension. 2010;56:297-303.
Circ. Res. 2019. PMID: 30612527

Circ. Res. 2015;117:178-91.

Hypertension. 2014;63:542-50
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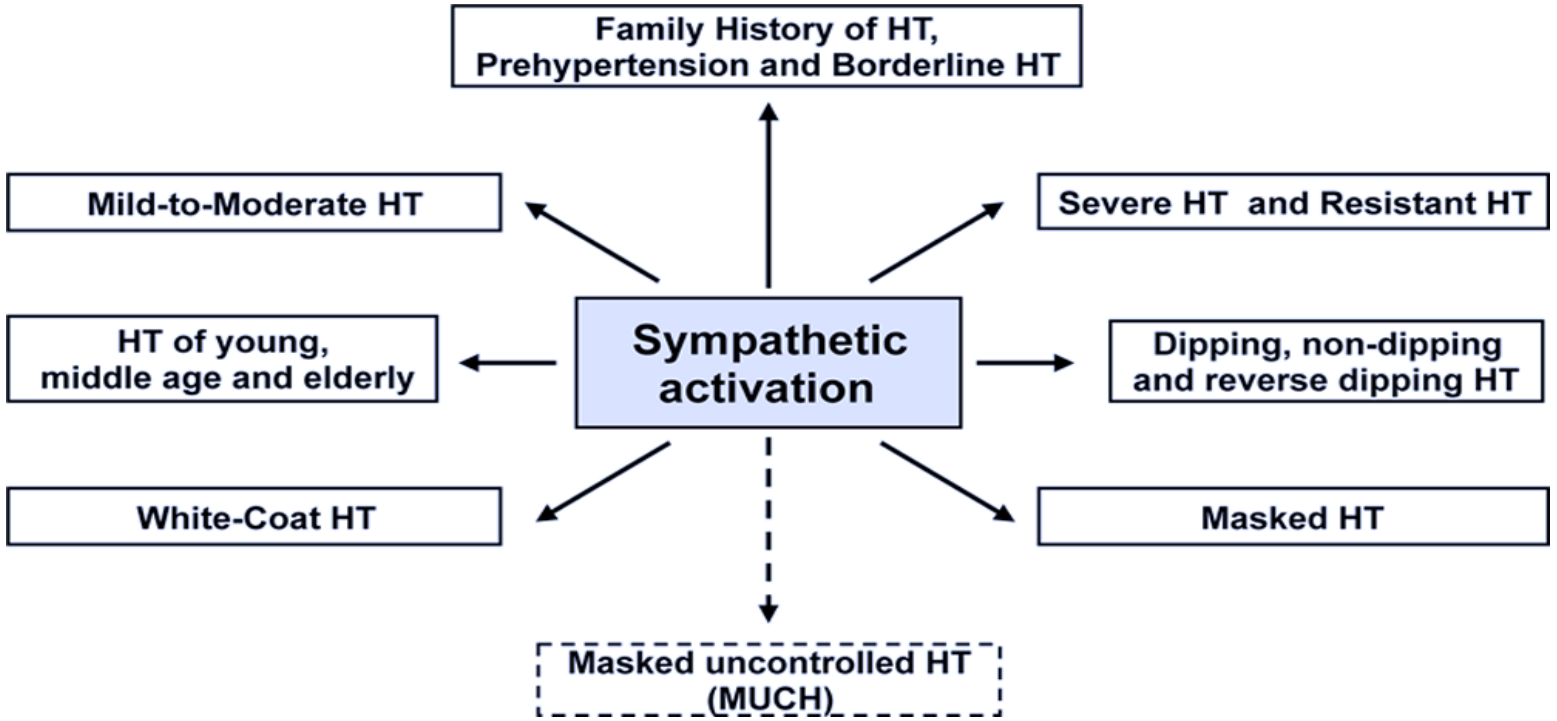
Out-of-Clinic Sympathetic Activity Is Increased in Patients With Masked Uncontrolled Hypertension *Hypertension* 2019;73:132-41

- Masked uncontrolled hypertension (MUCH)= *controlled* automated office BP (AOBP <135/85 mmHg in pts receiving antiHTN meds but *uncontrolled* BP out-of clinic by ABPM (awake ≥135/85 mmHg).
- Among 72 true controlled HTN and 80 MUCH pts, MUCH ps had ***higher out-of-clinic BP variability and lower HR variability*** vs. true controlled hypertensives, as well as higher levels of out-of-clinic urinary catecholamines and metanephrines levels consistent with ***higher out of clinic sympathetic activity***.
- In contrast, no difference in in-clinic plasma catecholamines and spot-urine/plasma levels of metanephrines between the groups, consistent with ***similar levels of sympathetic activity while in clinic.***
- ***MUCH patients have heightened out of-clinic sympathetic activity compared with true controlled HTN, which may contribute to development of MUCH.***

Masked Uncontrolled Hypertension (MUCH):

Too Much Daily Life Sympathetic Overdrive

***Hypertension* 2019;73:39-41**



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Observational Data Link Hypertension and Dementia

- Having uncontrolled high BP during midlife (age 45-65 yrs) is associated with increased risk for dementia later in life[1-4].
- Vascular dementia, one of the most common types of dementia, is usually caused by multiple “mini-strokes” over time, including small “silent” strokes that occur unnoticed.
- Hypertension is main cause of these strokes[1-4].

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