TAKE-HOME POINTS

2. Role of clinic, home, and ambulatory BP in TRH.
   - Selecting validated automated BP devices.
   - Use of automated BP devices.
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.
“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

SOME TERMINOLOGY
ADDITIONAL CAVEATS SOMETIMES APPLIED:

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

- Older Age
- African ancestry
- Non-Hispanic ethnicity
- Female sex
- Geographic location
- Diet (high Na, excess EtOH)
- Sedentary lifestyle
- Smoking

Patient Comorbidities

- LVH
- Heart failure
- CKD
- Dyslipidemia
- Overwt/Obesity
- Diabetes
- Sleep apnea
- CAD/PAD
- Prior stroke/TIA
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 CONTRIBUTING TO TRH DEVELOPMENT

- Genetics and Environment
  - Physical and emotional activity
- Sodium intake
- Renal NA+ excretion
- Fluid and sodium retention
- Volume expansion
- RAAS activity
- Aldosterone
- SNS activity
- Brain PVN
- Renal SNS activity
- Bone marrow
- Inflammation
- Immune system
- Gut microbiota alterations
- Cardiac output
- Peripheral vascular resistance
- Endothelial cell dysfunction
- Vasc smooth muscle cell dysfunction
- Microvascular rarefaction
- Vascular remodeling and arterial stiffness

Treatment Resistant Hypertension
BP MONITORING FOR TRH

Persistent uncontrolled office BP on 3-drug regimen

- Daily home BP between 12n and 4pm
- Out of home and office (unattended) BP weekly
- 24-hr ambulatory BP monitoring

- BP Controlled
- Unavailable
- BP Uncontrolled

aTRH

“White Coat Effect”
Reassess other CV RFs to determine therapy intensification

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

<table>
<thead>
<tr>
<th>Office BP</th>
<th>Home BP</th>
<th>Daytime ABPM</th>
<th>Nighttime ABPM</th>
<th>24-hr ABPM</th>
</tr>
</thead>
<tbody>
<tr>
<td>120/80</td>
<td>120/80</td>
<td>120/80</td>
<td>100/65</td>
<td>115/75</td>
</tr>
<tr>
<td>130/80</td>
<td>130/80</td>
<td>130/80</td>
<td>110/65</td>
<td>125/75</td>
</tr>
<tr>
<td>140/90</td>
<td>135/85</td>
<td>135/85</td>
<td>120/70</td>
<td>130/80</td>
</tr>
<tr>
<td>160/100</td>
<td>145/90</td>
<td>145/90</td>
<td>140/85</td>
<td>145/90</td>
</tr>
</tbody>
</table>

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

## Choosing a Home BP Monitor

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

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Office</td>
<td>158/86</td>
</tr>
<tr>
<td>ABPM</td>
<td></td>
</tr>
<tr>
<td>24-hr mean</td>
<td>117/59</td>
</tr>
<tr>
<td>Daytime</td>
<td>125/63</td>
</tr>
<tr>
<td>Nighttime</td>
<td>104/52</td>
</tr>
</tbody>
</table>
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)
    - ABPM components: ~$15-40 apiece
    - Commercial: variable, if covered, often follows Medicare criteria
  - Initial costs (hundreds to >$2.5k) plus ongoing maintenance

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

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)

1. Exclude pseudoresistance & secondary HTN
2. Discontinue unnecessary interfering meds
3. Ensure low-sodium diet; optimize lifestyle interventions
4. Optimize 3-drug anti-HTN regimen backbone

A+C+D

Optimize diuretic therapy

Add mineralocorticoid receptor antagonist
- 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
- Interventionsal 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. Stergiou GS. Hypertension 2018;71(3):368-374
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.  
OPTIMIZE DIURETIC-TREATMENT OF TRH

- 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

<table>
<thead>
<tr>
<th>Thiazide</th>
<th>Equiv. dose</th>
<th>Elim. $t_{1/2}$</th>
<th>Outcome Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCTZ</td>
<td>25 mg</td>
<td>9-10 h</td>
<td>~0</td>
</tr>
<tr>
<td>CLD</td>
<td>6.25-12.5 mg</td>
<td>50-60 h</td>
<td>+++</td>
</tr>
<tr>
<td>Indap</td>
<td>1.25-2.5 mg</td>
<td>14 h</td>
<td>+</td>
</tr>
</tbody>
</table>
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**
  - **REHOT**
    - Both trials *Spironolactone better than Clonidine* (and Doxazosin or Bisoprolol in PATHWAY-2).


- **Interventional therapy**
  - Renal denervation
  - Carotid baroreceptor activation

- **Renin-guided therapy**

- **Collaborative Care**
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)

TREATMENT OF TRH

Other drugs 5\textsuperscript{th} line- all debatable:

- **β-blockers**: metoprolol, bisoprolol- \textit{Avoid} carvedilol, labetalol
- **Non-DHP CCB**: diltiazem ER (3A4 inhibition boosts effects of DHP-CCB)
- **α\textsubscript{2}-agonists**: clonidine patch (weekly), guanfacine (HS)-\textit{Avoid all}
- **α\textsubscript{1}-blockers**: doxazosin- \textit{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
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.

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 superior 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 COGNITIVE IMPAIRMENT
ABELL, EUROPEAN HEART JOURNAL 2018; 39:3119-25

Systolic Blood Pressure and Dementia Risk

- at age 50
- at age 60
- at age 70

N=8639
33% women
LOWER BP REDUCES COGNITIVE 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

<table>
<thead>
<tr>
<th>POPULATION</th>
<th>6029 Men</th>
<th>3332 Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults aged ≥50 years with hypertension and without diabetes or stroke</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean age: 68 years</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>INTERVENTIONS</th>
<th>9361 Patients randomized</th>
<th>8563 Patients analyzed</th>
</tr>
</thead>
<tbody>
<tr>
<td>4278 Intensive control</td>
<td></td>
<td>(≥1 cognitive assessment)</td>
</tr>
<tr>
<td>4285 Standard control</td>
<td></td>
<td>(Target SBP &lt;120 mm Hg)</td>
</tr>
<tr>
<td>Median treatment period, 3.3 years</td>
<td></td>
<td>(Target SBP &lt;140 mm Hg)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PRIMARY OUTCOME</th>
<th>Occurrence of adjudicated probable dementia</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>SECONDARY OUTCOMES</th>
<th>Adjudicated mild cognitive impairment (MCI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite outcome of MCI or probable dementia</td>
<td></td>
</tr>
</tbody>
</table>
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 Contribute to Cognitive Insufficiency & 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).
**CENTRAL ILLUSTRATION:** Assisted Reproductive Technologies-Induced Alterations of the Cardiovascular Phenotype

<table>
<thead>
<tr>
<th>Children</th>
<th>Young Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premature Vascular Aging</td>
<td>Premature Vascular Aging Persists</td>
</tr>
</tbody>
</table>

- **Altered Vascular Wall Morphology**
  - Carotid intima-media thickness

- **Endothelial Dysfunction**
  - Flow mediated vasodilatation

- **Increased Vascular Stiffness**
  - Pulse wave velocity

**PLUS**

- **High Blood Pressure**
  - 24h ambulatory blood pressure
  - Blood pressure variability
  - Prevalence of arterial hypertension

---

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
### Updated Definitions of BP Categories and Stages

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

_PEDIATRICS_ Volume 140, number 3, September 2017:e20171904
QUESTIONS
LIKELY MECHANISMS CONTRIBUTING TO TRH DEVELOPMENT
Brain-Gut-Bone Marrow Interactions:

Triangular Hypothesis for Hypertension

**Reviews:**
- Nature Rev. Nephrol. 2018; 14:442056

- Circ. Res. 2019. PMID: 30612527

- Hypertension. 2014;63:542-50
- Front Physiol. 2017, Apr 12;8:220

- Int J Cardiol. 2015;201:157-158.
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
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\(^1\text{-}^4\).

• 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\(^1\text{-}^4\).

\(^1\)National Institute of Neurological Disorders and Stroke; 2016. https://mindyourrisks.nih.gov/research.html  
\(^4\)Abell, European Heart Journal 2018; 39:3119-25