Hypertension Management

From Guidelines to Practice

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Disclosures

I have no relevant financial relationships

Objectives

- Incidence and Impact of Hypertension: Analyze the global prevalence of hypertension and its significant impact on public health.
- Workup of Hypertension: Evaluate the comprehensive diagnostic approach for hypertension, including assessment of underlying causes and comorbidities.
- Current Pharmacotherapies and Invasive Therapies: Critically review contemporary pharmacologic treatments and invasive interventions for hypertension management.
- Barriers to Clinical Practice: Identify and assess the key barriers to effective hypertension management in clinical practice and explore potential solutions.

Blood Pressure Categories

American Heart Association.

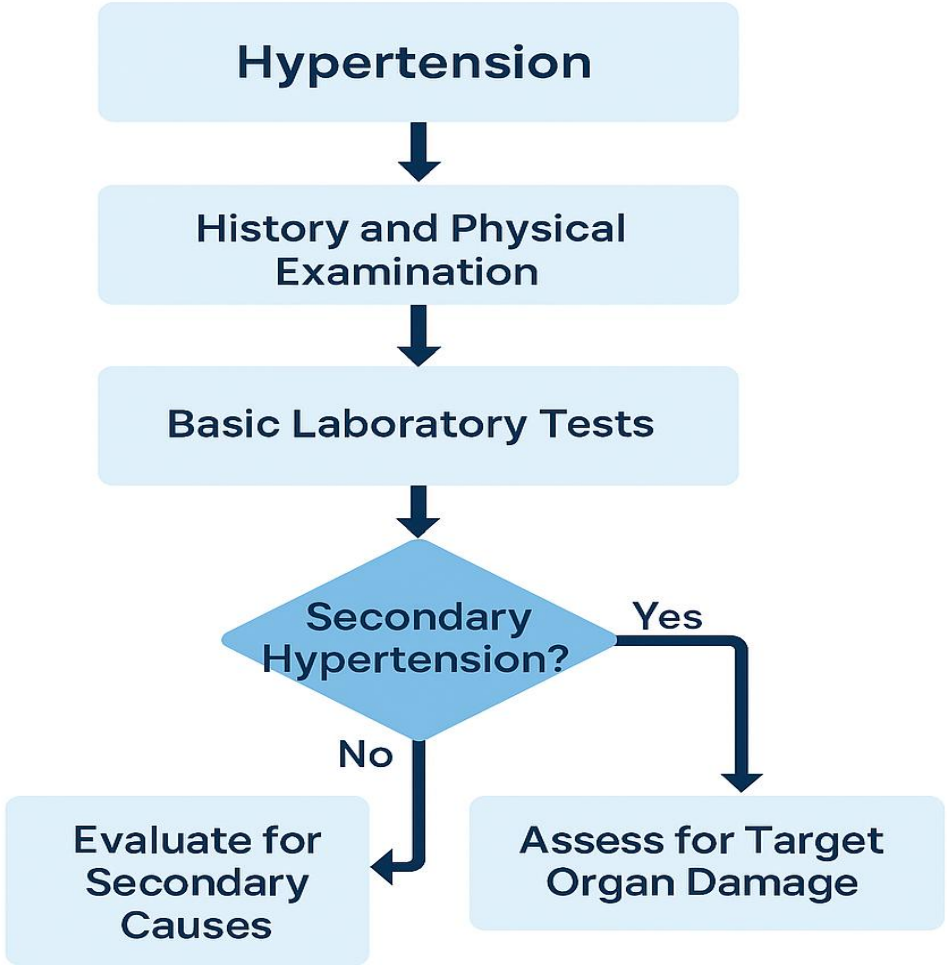
BLOOD PRESSURE CATEGORY	SYSTOLIC mm Hg (upper number)		DIASTOLIC mm Hg (lower number)
NORMAL	LESS THAN 120	and	LESS THAN 80
ELEVATED	120 – 129	and	LESS THAN 80
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 1	130 – 139	or	80 – 89
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 2	140 OR HIGHER	or	90 OR HIGHER
HYPERTENSIVE CRISIS (consult your doctor immediately)	HIGHER THAN 180	and/or	HIGHER THAN 120

Silent Epidemic

- **59%** of people with hypertension are aware they have it.
- **80%** of those aware receive treatment, but only **52%** have controlled BP.
- **1.28 billion** adults worldwide have hypertension.
- Only **42%** are diagnosed and treated.
- Major risk factor for **heart disease, stroke, and kidney failure**.
- Causes **10.8 million deaths** annually.
- **$131 billion/year** in U.S. healthcare costs (CDC, 2022).
- **Indirect costs**: Lost productivity, absenteeism, and disability.
- Economic burden will rise with aging populations.

CDC Hypertension Surveillance Report, 2023; NHANES 2017–2020, American Heart Association (AHA), (WHO), 2023

Modifiable Risk Factors	Non-Modifiable Risk Factors
High sodium (salt) intake	Family history of hypertension
Low potassium intake	Advancing age
Physical inactivity	Male sex
Unhealthy diet	Genetic predisposition
Excessive alcohol consumption	Chronic kidney disease
Tobacco use	Obstructive sleep apnea
Overweight and obesity	Socioeconomic/educational status
Diabetes mellitus	
Dyslipidemia (high cholesterol)	
Chronic stress	



Patient with Elevated BP
(≥130/80 mmHg on ≥2 occasions)

Confirm Diagnosis
- Measure BP in both arms
- Use ambulatory or home BP monitoring (ABPM/HBPM) if needed

Initial Evaluation
- History: lifestyle, family history, medication use, symptoms of secondary
- Physical Exam: BMI, pulses, signs of end-organ damage

Basic Laboratory Workup
- CBC, BMP iNa, K, Cr, glucose)
- Lipid profile
- Urinalysis
- TSH
- ECG

Assess for Cardiovasular Risk
- ASCVD risk calculator
- Other comorbidities (diabetes, CKD, etc.)

Management Plan
- Lifestyle modifications
- Initiate pharmacologic therapy if indicated

EXCUSE EXCUSES FOR MY DOCTOR

Medication is not something I'm open to

I'm worried about the side effects.

I'm interested in holistic or alternative theranpies.

I don't thint the medication is needed for my condition.

I've had bad experiences with medication before.

I don't want to take something long term.

I prefer to take a more proactive approach with my health

Lifestyle modification

Plant based/Vegetarian diet

Obesity management

OSA treatment

Exercise

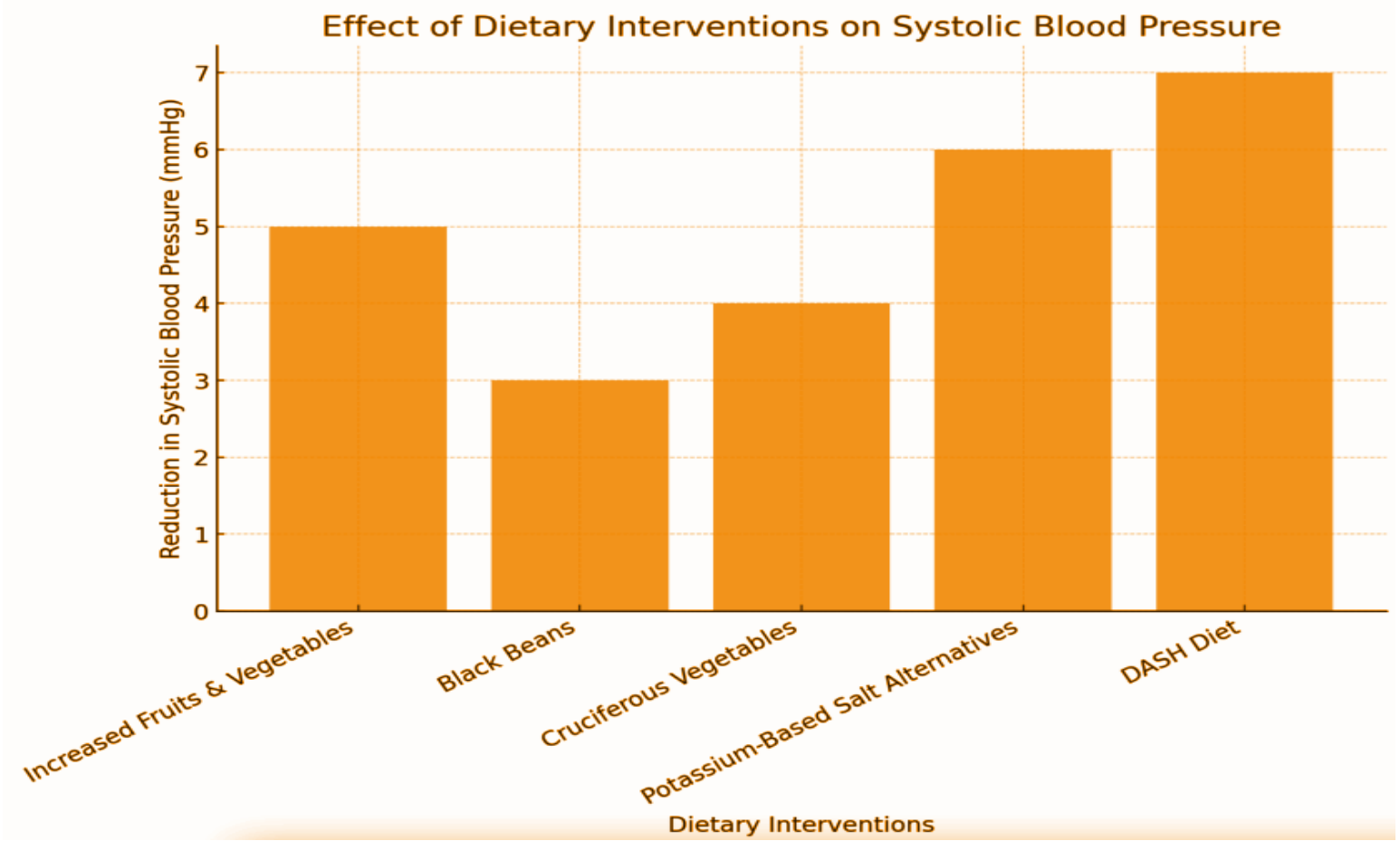
ACC/AHA 2017: Nonpharmacological Interventions

COR	LOE	Recommendations for Nonpharmacological Interventions
I	A	Weight loss is recommended to reduce BP in adults with elevated BP or hypertension who are overweight or obese.
I	A	A heart-healthy diet, such as the DASH (Dietary Approaches to Stop Hypertension) diet, that facilitates achieving a desirable weight is recommended for adults with elevated BP or hypertension.
I	A	Sodium reduction is recommended for adults with elevated BP or hypertension.
I	A	Potassium supplementation, preferably in dietary modification, is recommended for adults with elevated BP or hypertension, unless contraindicated by the presence of CKD or use of drugs that reduce potassium excretion.

ACC/AHA 2017: Nonpharmacological Interventions

COR	LOE	Recommendations for Nonpharmacological Interventions
I	A	Increased physical activity with a structured exercise program is recommended for adults with elevated BP or hypertension.
I	A	~~Adult men and women with elevated BP or hypertension who currently consume alcohol should be advised to drink no more than 2 and 1 standard drinks* per day, respectively.~~

*In the United States, 1 "standard" drink contains roughly 14 g of pure alcohol, which is typically found in 12 oz of regular beer (usually about 5% alcohol), 5 oz of wine (usually about 12% alcohol), and 1.5 oz of distilled spirits (usually about 40% alcohol).



Increased Fruits & Vegetables Intake
Wesson DE et al. Am J Physiol Renal Physiol. 2024;326(4):F551–F559.

Black Beans
Bazzano LA et al. Arch Intern Med. 2001;161(21):2573–2578.

Cruciferous Vegetables
Liu X et al. J Acad Nutr Diet. 2014;114(5):700–708.

Potassium-Based Salt Alternatives
He FJ, MacGregor GA. J Hum Hypertens. 2002;16(11):761–770.
Source: en.wikipedia.org

DASH Diet
Sacks FM et al. N Engl J Med. 2001;344(1):3–18.

Original Investigation

Vegetarian Diets and Blood Pressure
A Meta-analysis

Yoko Yokoyama, PhD, MPH; Kunihiro Nishimura, MD, PhD, MPH; Neal D. Barnard, MD; Misa Takegami, RN, PhD, MPH; Makoto Watanabe, MD, PhD; Akira Sekikawa, MD, PhD; Tomonori Okamura, MD, PhD; Yoshihiro Miyamoto, MD, PhD

Meta-analysis of **39 studies** (7 clinical trials, 32 observational)

Over **21,000 participants** included

Vegetarian diets significantly lowered blood pressure

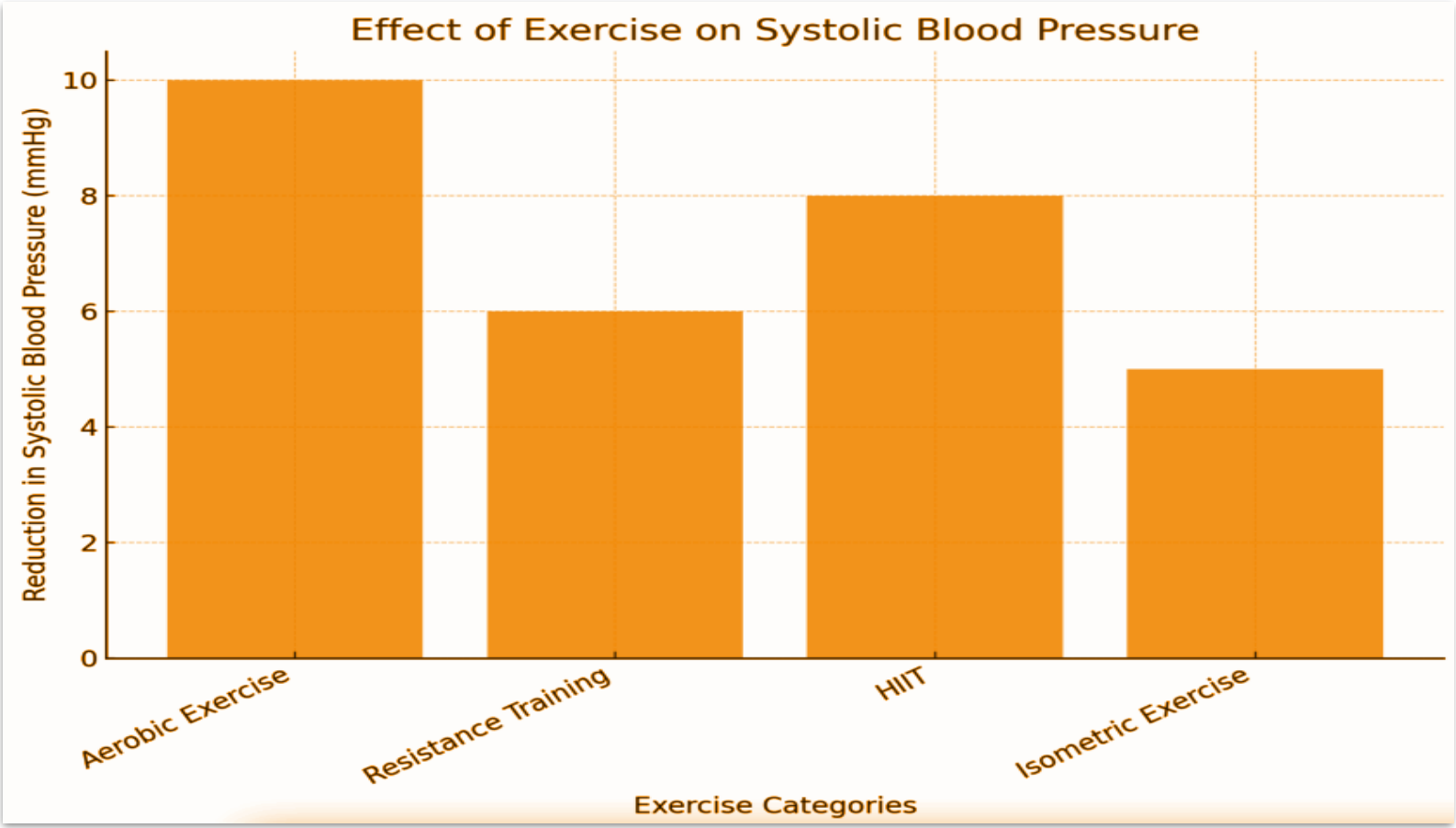
- **Systolic BP** ↓ 4.8–6.9 mmHg
- **Diastolic BP** ↓ 2.2–4.7 mmHg

Shows strong potential as a **non-drug strategy** for hypertension

Microbiome in Hypertension

- **Reduced microbial diversity** (“alpha diversity”) seen in hypertensive patients
- **Increased gram-negative bacteria** associated with higher BP:
    - *Klebsiella*, *Parabacteroides*, *Desulfovibrio*, *Lactobacillus*, *Akkermansia*, *Prevotella*
- **Decreased levels of beneficial, butyrate-producing bacteria**:
    - *Roseburia*, *Faecalibacterium*, *Lachnospiraceae*, *Ruminococcaceae*

X, Zhou X,Adv Nutr. 2020 Jan 1;11(1):66-76.



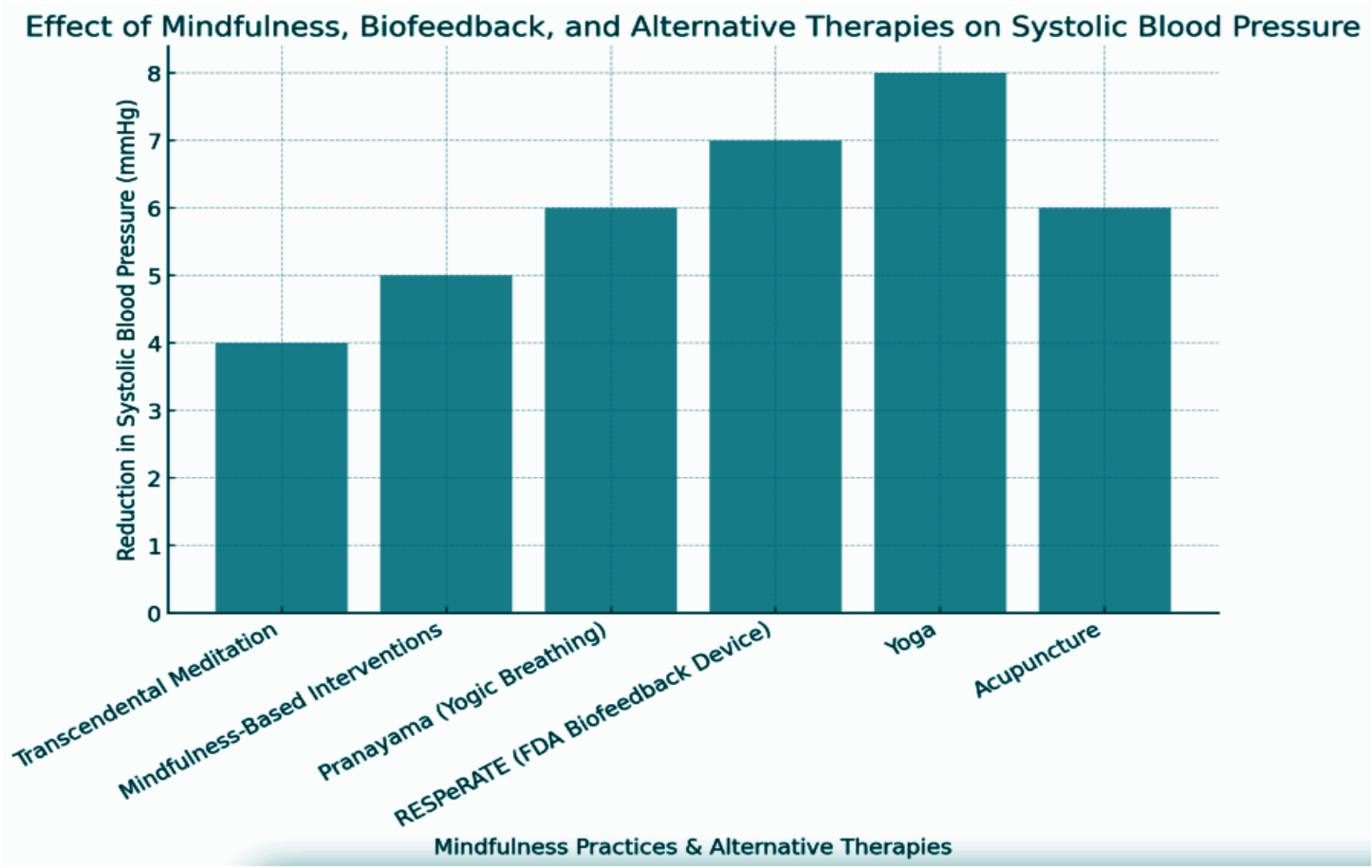
1. **Aerobic Exercise**
Cornelissen VA, Smart NA. J Am Heart Assoc. 2013;2(1):e004473.

2. ***Muscle-Strengthening Activities***
Momma H et al. Br J Sports Med. 2022;56(13):755–763.

3. ***Nonpharmacologic Interventions***
Fu J et al. J Am Heart Assoc. 2020;9(19):e016804.

4. ***Exercise as Therapy***
Kokkinos PF et al. Cardiol Clin. 2001;19(3):507–516.

5. ***Step Count & Health Outcomes***
Sheng M et al. J Sport Health Sci. 2021;10(6):620–628.



- ***Transcendental Meditation (TM) - 2015 Meta-Analysis***
  TM significantly lowers blood pressure, with effects comparable to other lifestyle interventions.
  Source: Journal of Hypertension, 2015.

- ***Mindfulness-Based Interventions (MBIs) - 2020 Meta-Analysis***
  MBIs show modest BP reductions in adults with cardiovascular disease.
  Source: American Journal of Hypertension, 2020.

- ***Pranayama (Yogic Breathing)***
  Linked to BP reduction through parasympathetic activation and relaxation.
  Source: Journal of Alternative and Complementary Medicine, 2019.

- ***RESPeRATE Device***
  FDA-approved device using slow breathing to lower BP through guided musical tones.

OMM Therapy modulating autonomic tone

Technique	Region	Purpose
Rib Raising	T1–T6 (sympathetic chain)	↓ Sympathetic tone to heart, kidneys, and vessels
Suboccipital Decompression	OA Junction (C0–C1)	↑ Parasympathetic tone via vagus nerve (CN X)
Thoracic Inlet Release	Cervicothoracic fascia	Enhance lymphatic drainage & autonomic balance
Chapman's Reflexes	Kidneys, adrenals	Treat viscerosomatic reflexes impacting BP regulation
Soft Tissue Techniques	Cervical & thoracic spine	↓ Paraspinal muscle tension and sympathetic drive
Lymphatic Pump Techniques	Thoracic/pedal regions	Improve venous return, reduce fluid overload
HVLA (T-Spine)	T1–T4	Reset somatic dysfunction influencing autonomics

Dalton et al. (2013) – *JAOA* – doi.org/10.7556/jaoa.2013.006

Cerritelli et al. (2015) – *BMC CAM* – doi.org/10.1186/s12906-015-0733-7

Licciardone et al. (2010) – *JAOA* – jaoa.org

OSA and Obesity

Obstructive Sleep Apnea

- **Prevalence:** 20-30% of adults have OSA.
- **Obesity & OSA:** 70-80% of people with OSA are overweight/obese.
- **OSA & Blood Pressure:** OSA increases the risk of high blood pressure by 2-3 times.
- **Treatment Impact:** CPAP therapy can lower blood pressure by 3-5 mmHg.

Obesity Treatment

- **Obesity Prevalence:** 42% of adults in the U.S. are obese.
- **Weight Loss & BP:** Losing 5-10% of body weight can lower blood pressure by 5-10 mmHg.
- **Lifestyle Changes:** Diet and exercise can help reduce weight by 5-10%, improving BP.

NIH Obesity Statistics
NIH - Obesity

AHA - Weight Loss and Heart Disease
AHA - Lose Weight

Sleep Foundation - OSA
Sleep Foundation - OSA

Hypertension Canada
Hypertension Canada

Pharmacotherapy

Optimal Combination

- **ACE-I** or **ARB** + **CCB** + **HCTZ** or **CT**

Ideal Combination Medication

- One med + **HCTZ** or **CCB** + **ACE-I**/**ARB**
- **Combination meds** linked to lower **BP**.
- **Triple combos** are commercially available.

Meta-Analysis on Combination Therapy: PubMed, 2023

Efficacy of ARB/HCTZ: PubMed, 2021

Triple Combination Therapy: PMC, 2021

Pharmacotherapy

Combination Pill Options

- Add **Aldosterone Blocker** (e.g., **Spironolactone** or **Eplerenone**)
- Consider **Finerenone** (non-mineralocorticoid Aldo blocker)
  Fewer side effects

Other Medications for Additional Benefits

- **SGLT-2 Inhibitor** for **CHF**, **proteinuric CKD**, or **Type 2 DM**
- Modest drop in **BP**

- **Spironolactone and Eplerenone for Hypertension**: PubMed, 2022
- **Finerenone for Hypertension**: The Lancet, 2021
- **SGLT-2 Inhibitors in Heart Failure and CKD**: NEJM, 2023
- **Study: Many People with Hypertension Unintentionally Take Medications that Worsen It**: NHLBI, 2021
- **Combination Therapy in Hypertension**: JAMA, 2022

Pharmacotherapy

Medication Class	Blood Pressure Reduction	Key Findings
SGLT-2 Inhibitors	~3.5-4 mmHg systolic BP reduction	- Consistent BP reduction in patients with type 2 diabetes and kidney disease. - Benefits seen regardless of kidney function. - BP reduction observed in heart failure.
GLP-1 Receptor Agonists	~3.4 mmHg systolic BP reduction (average)	- Modest reductions in BP across different formulations. - Stronger BP-lowering effects observed with certain agents. - BP reduction linked with weight loss and better glycemic control.

SGLT-2 Inhibitors and BP Reduction: *American Heart Association (AHA), 2024*

GLP-1 Agonists and BP Reduction: *PubMed, 2023*

Pharmacotherapy- Next Step

- **Alpha-Beta Blockers**
  - *Labetalol*: Allows for significant dose escalation
  - *Carvedilol*: Preferred if cardiac comorbidities present
- **Clonidine Patch**
  - Not a pill; applied weekly
  - Useful for patients with adherence issues; can be applied by caregivers
- **Hydralazine or Minoxidil**
  - Consider if other antihypertensives are contraindicated or poorly tolerated
  - Use cautiously due to potential side effects (e.g., fluid retention, tachycardia)
- **Future Therapies**
  - Emerging agents under study (e.g., endothelin receptor antagonists, new aldosterone antagonists)

Whelton PK et al. **2017 ACC/AHA Hypertension Guidelines.** *Hypertension*, 2018.

Bakris GL, Sica D. **Combination and Rescue Therapy in Hypertension.** *J Clin Hypertens*, 2019.

NHLBI. Managing Resistant Hypertension.

CDC. *High Blood Pressure Facts*, 2023.

NEJM Journal Watch

GENERAL MEDICINE SPECIALTIES TOPICS VOICES CME GUIDELINE WATCH

DRUG WATCH | GENERAL MEDICINE, AMBULATORY MEDICINE, HOSPITAL MEDICINE, CARDIOLOGY, NEUROLOGY

DRUG/DEVICE INFORMATION

April 11, 2024

Aprocitentan, a Newly Approved Drug for Resistant Hypertension

- Approved as **add-on** for adults with uncontrolled hypertension
- **Black-box warning** for fetal harm — requires prescriber certification (REMS program)
- Lowers **systolic BP by ~4 mmHg** vs. placebo
- **Placebo response** was high (11 mmHg)
- 24-hour BP: ~**138/83 mmHg** after treatment
- May be **less effective** than older add-ons like spironolactone
- **Cost**: $700–$1100/month

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Zilebesiran, an RNA Interference Therapeutic Agent for Hypertension

Authors: Akshay S. Desai, M.D., M.P.H., David J. Webb, M.D., D.Sc., Jorg Taubel, M.D., Sarah Casey, M.B., Ch.B., Yansong Cheng, Ph.D., Gabriel J. Robbie, Ph.D., Don Foster, M.S., Stephen A. Huang, M.D., Sean Rhyee, M.D., M.P.H., Marianne T. Sweetser, M.D., Ph.D., and George L. Bakris, M.D. Author Info & Affiliations

Published July 19, 2023 | N Engl J Med 2023;389:228-238 | DOI: 10.1056/NEJMoa2208391 | VOL. 389 NO. 3

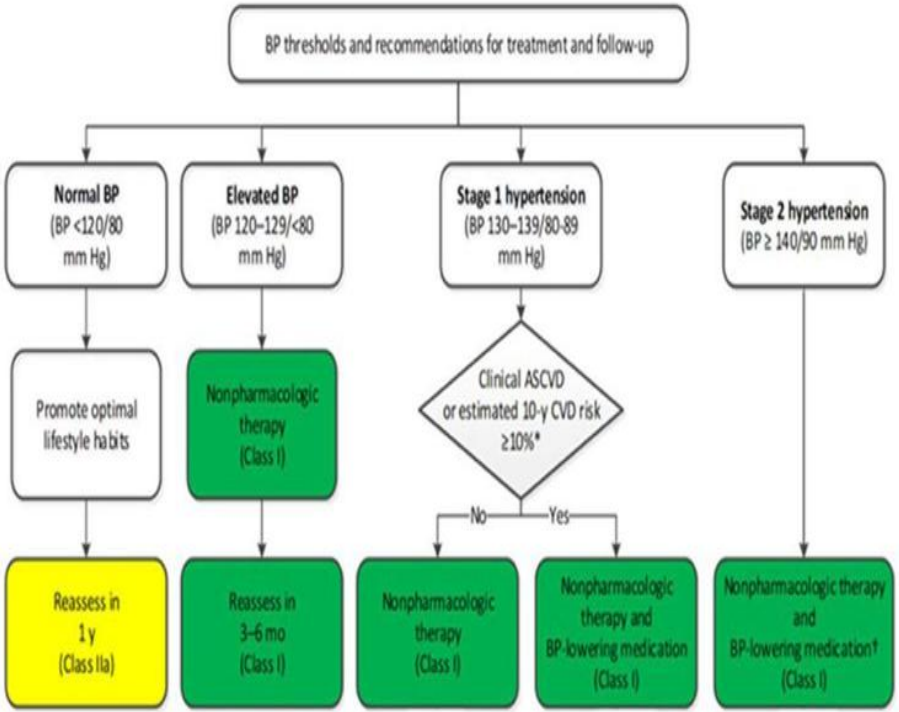
- **Not FDA approved**
- **RNA interference agent** that blocks liver production of angiotensinogen
- **Long-acting**, given as a **subcutaneous injection biannual sustaining 10-20 mmHg reduction over 6 months**
- **Part A**:
    - Doses from **10–800 mg** tested
    - Patients followed for **24 weeks**
- **Part B**:
    - 800 mg studied under **low- and high-salt diets**
- **Part E**:
    - 800 mg combined with **irbesartan** to assess additive effect

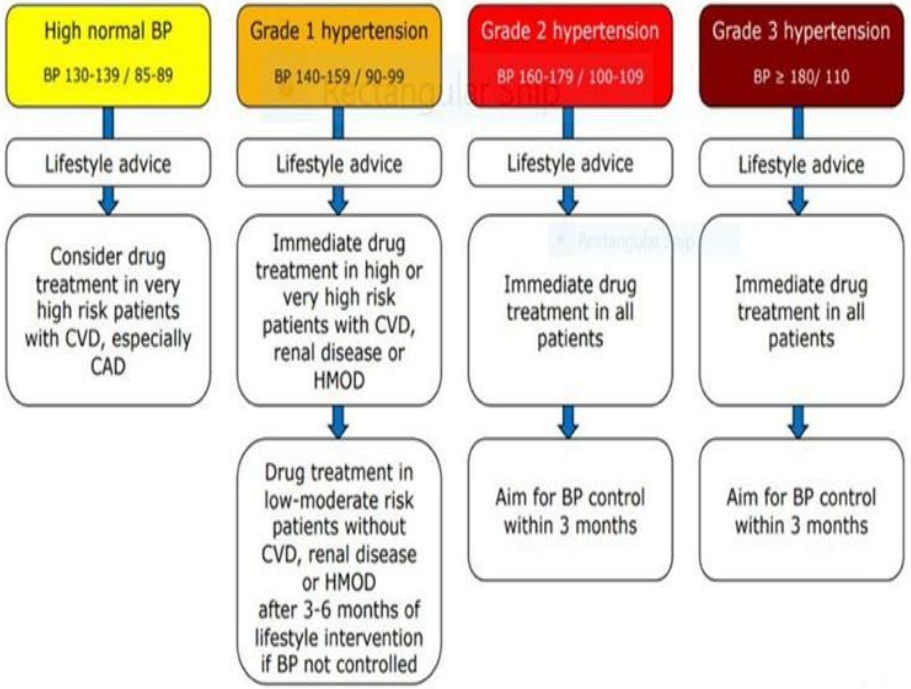
VERONICA Trial – Triple Combination Polypill vs. Standard Care

- Telmisartan (ARB)
- Amlodipine (CCB)
- Indapamide (Diuretic)
- **BP Control at 1 Month**:
    - GMRx2: 81%
    - Standard Care: 55%
- **BP Control at 6 Months**:
    - GMRx2: 82%
    - Standard Care: 72%
- **Home Systolic BP Reduction**:
    - GMRx2: ↓31 mmHg
    - Standard Care: ↓26 mmHg
    - **Difference**: 5.8 mmHg ($p<0.001$)
- **Well-tolerated**, high adherence
- **Simplifies treatment** and improves access
- Promising for **high-risk population**

Trial	Primary Outcome	Key Results / Stats
SPRINT (2015)	CV events & mortality	↓ 25% relative risk of CV events; ↓ 27% all-cause mortality (SBP target <120 mmHg)
SPRINT-MIND (2019)	Cognitive decline	↓ 19% risk of mild cognitive impairment (not statistically significant for dementia)
Salt Substitute Trial (2021, China)	Systolic BP reduction, stroke risk	↓ Stroke risk by 14%, ↓ all-cause mortality by 12%
GMRx2 Triple-Pill Trial (2021)	BP control rate	70% BP control in 4 weeks vs 55% in usual care
Lorundrostat (Target-HTN) (2023)	Change in systolic AOBP	↓ ~9.6 mmHg (50 mg dose) vs placebo
Baxdrostat (HALO) (2023)	Seated systolic BP change	↓ ~11 mmHg vs placebo, but not statistically significant
Zilebesiran (2023)	Change in systolic BP	↓ 10–20 mmHg sustained over 6 months with biannual injection
ONTARGET (2008; ongoing implications)	CV death, MI, stroke, HF hospitalization	No added benefit of telmisartan + ramipril combo vs either alone
ALLHAT (2002; still widely referenced)	Fatal/nonfatal CHD	Thiazide-like diuretic (chlorthalidone) as effective as newer agents

Pharmacotherapy guidelines





https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.121.054602

BP Category	Recommended First-Line Agents	When to Start Medication
Stage 1 HTN (130–139 / 80–89 mmHg)	- Thiazide diuretic - ACE inhibitor/ARB - CCB	If ASCVD risk ≥10% or with comorbidities (e.g., diabetes)
Stage 2 HTN (≥140 / ≥90 mmHg)	**2 first-line agents** from different classes	Start immediately
CKD (any stage)	ACE inhibitor or ARB (for kidney protection)	Start at diagnosis of CKD with HTN
Diabetes (with albuminuria)	ACE inhibitor or ARB	Start at BP ≥130/80 mmHg
Heart Failure (HFrEF)	ACE inhibitor or ARB + Beta-blocker + Diuretic + MRA (as needed)	Use guideline-directed therapy
Black patients (without CKD)	Thiazide-type diuretic or CCB preferred	Due to better BP response
Elderly (≥65 years)	Start low-dose; focus on safety and frailty	Individualized based on comorbidities and fall risk

Invasive Therapies: Back to the Future of Hypertension Treatment

Invasive therapy trials

Trial	Year	Design	Key Findings
SYMPLICITY HTN-1	2009	Open-label, non-randomized	Significant BP reduction sustained over 36 months. No control group.
SYMPLICITY HTN-2	2010	Randomized controlled trial (RCT)	RDN group had 32 mmHg systolic BP drop at 6 months.
SYMPLICITY HTN-3	2014	Sham-controlled RCT (US)	No significant BP difference vs sham. Raised concerns on technique/selection.
SPYRAL HTN-OFF MED	2017	Sham-controlled RCT (off meds)	Modest but significant BP drop (~5 mmHg systolic). Proof of concept.
SPYRAL HTN-ON MED	2018	Sham-controlled RCT (on meds)	Additional BP reduction (~7.4 mmHg) on top of meds.
RADIANCE-HTN SOLO	2018	Ultrasound-based RDN, sham-controlled	6.3 mmHg systolic BP reduction (daytime ABPM) at 2 months.
RADIANCE-HTN TRIO	2021	Resistant HTN, ultrasound RDN	4.5 mmHg greater systolic BP reduction at 2 months vs sham.
SYMPLICITY HTN-ON MED	2023	Global sham-controlled RCT	Met primary endpoint; significant drop in 24h systolic BP.

Consensus statements support the use of RDN

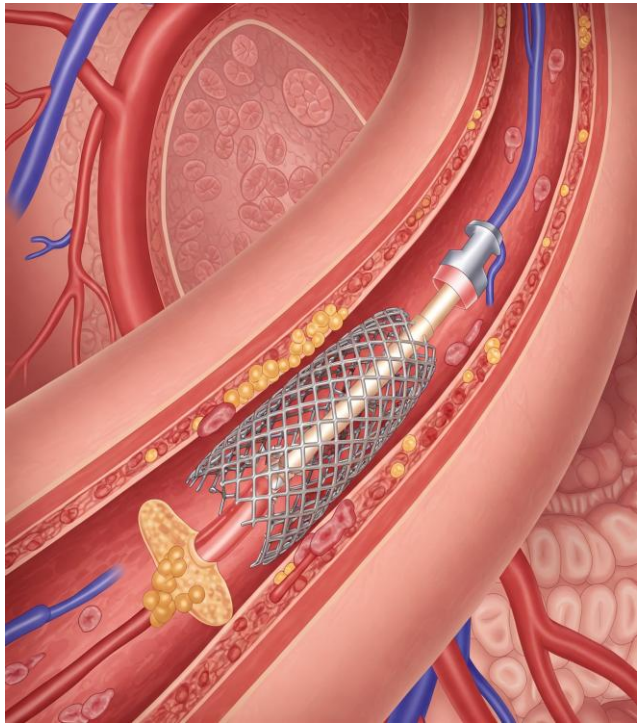
1. **ESC 2023**: Barbato E, et al. *Renal Denervation in Hypertension*. Eur Heart J. 2023;44:1313–1330.

2. **AHA 2024**: Cluett JL, et al. *Renal Denervation for Hypertension: A Scientific Statement*. Hypertension. 2024;81:e135–e148.

3. **SCAI 2023**: Swaminathan RV, et al. *SCAI Position Statement on Renal Denervation*. J Soc Cardiovasc Angiogr Interv. 2023.

4. **ESH 2023**: Mancia G, et al. *ESH Guidelines for the Management of Hypertension*. J Hypertens.

Renal Artery Stenosis



Prevalence & Relevance:

- Affects ~6.8% of adults >65, higher in those with CV risk factors.
- Common secondary cause of HTN, affecting 5–34% of patients with resistant HTN.

Evidence from CORAL Trial:

- The CORAL trial showed renal stenting didn't significantly reduce major CV or renal events compared to medical therapy, except in select subgroups.

Guideline-Recommended Screening:

- ACC/AHA guidelines recommend RAS screening in cases of:
    - Onset of HTN before age 30 or severe HTN after age 55
    - Resistant or malignant HTN
    - Sudden renal function decline with ACEi/ARB
    - Flash pulmonary edema
    - Asymmetric kidneys (>1.5 cm difference)

Cooper CJ et al., *NEJM 2014*

Tullius K et al., *Lancet 2008*

CORAL Trial, *NEJM 2014*

Renal Artery Stenosis

Diagnostic Modalities:

- Imaging recommendations include duplex ultrasound, CT angiography, MRA, and renal angiography (gold standard).
- CT and MRA may underperform in diagnosing fibromuscular dysplasia

Indications for Revascularization:

- **Class I**: RAS with recurrent unexplained pulmonary edema or heart failure
- **Class IIa**: Hemodynamically significant RAS with unstable angina, resistant hypertension, intolerance to meds, or progressive CKD with bilateral RAS or solitary kidney

Patient Selection & Hemodynamic Criteria:

- Significant RAS: >70% stenosis or 50–70% with pressure gradient >20 mmHg or Pd/Pa ≤0.90.
- Poor outcomes associated with nonviable kidneys (length <10 cm, RRI >0.8, or proteinuria >1 g/day).

ACC/AHA 2017 BP Guideline – Whelton PK et al., *JACC 2018*

Lawton JS et al., *JACC 2022*

ACC/AHA/SCAI 2021 Revascularization Guideline – Lawton JS et al., *JACC 2022*

Barriers

- **People don’t know they have high BP**
- **Patients don’t take meds regularly**
- **Hard to see doctors or get follow-up**
- **Doctors delay changing treatment**
- **Poor communication between providers**
- **Unhealthy lifestyle is hard to change**
- **Low understanding of BP risks**

Conclusion

Acknowledge the Patient: Address concerns and encourage involvement.

Aggressive Treatment: Target optimal BP, start early.

Be Honest: Discuss lifestyle risks and BP importance.

Identify Barriers: Overcome obstacles to treatment.

Follow-Up: Regular check-ins and home BP monitoring.

Escalate Treatment: Adjust meds and combine with lifestyle changes.

Consider Invasive Options: Use when traditional methods fail.

Questions