Hypertension in 2021

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Outline

- Why treat high blood pressure
- Prevalence
- Forces driving practice
- Evolution of guidelines
- Current status of guidelines
- Problems of implementation
- What issues affect your ability to treat your patients?

Heart Foundation

Guideline for the diagnosis and management of hypertension in adults

2016

Clinical Practice Guidelines

2020 International Society of Hypertension Global Hypertension Practice Guidelines

Thomas Unger, Claudio Borghi, Fadi Charchar, Nadia A. Khan, Neil R. Poulter, Dorairaj Prabhakaran, Agustin Ramirez, Markus Schlaich, George S. Stergiou, Maciej Tomaszewski, Richard D. Wainford, Bryan Williams, Aletta E. Schutte

(*Hypertension*. 2020;75:1334-1357. DOI: 10.1161/HYPERTENSIONAHA.120.15026.)

Hypertension is available at https://www.ahajournals.org/journal/hyp DOI: 10.1161/HYPERTENSIONAHA.120.15026

Why treat high blood pressure

Association with

- Stroke
- Heart Failure
- Kidney disease
- Aortic Syndromes and aneurysms
- Atherosclerosis
- Dementia

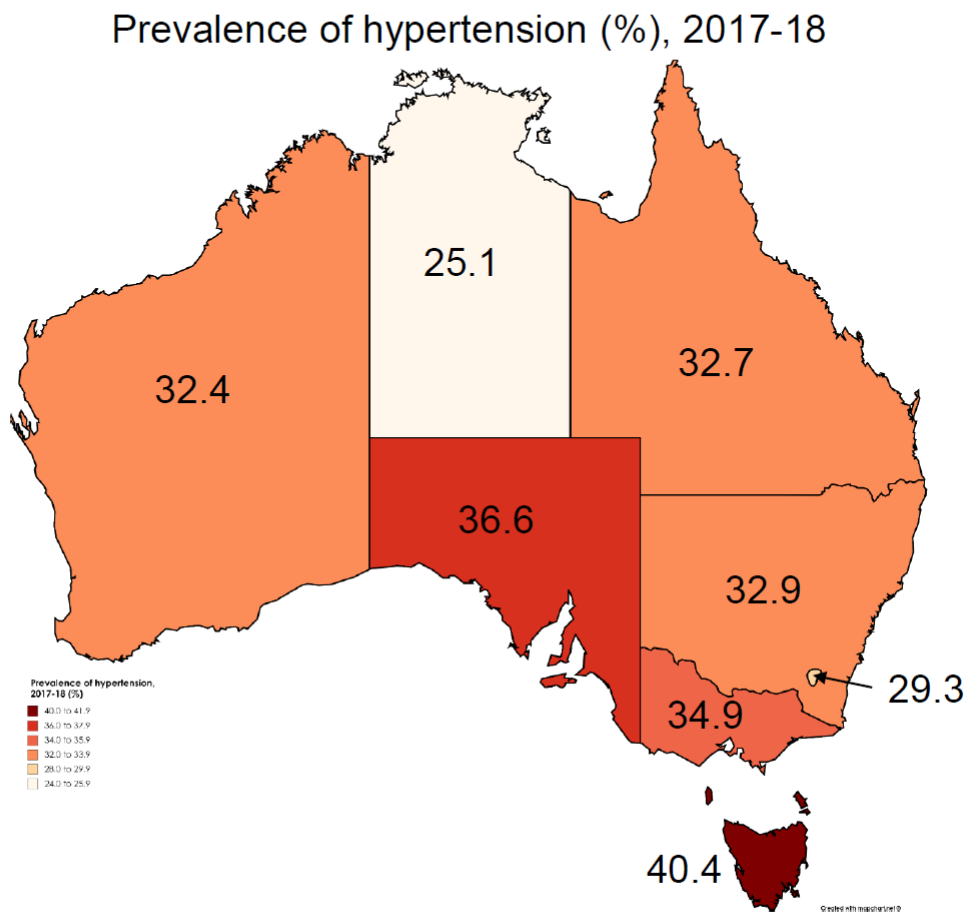
Prevalence of hypertension

- Definition dependent
- Adult Australians (>18y) 34% (2017-18)
  - 11% controlled on medication
  - 23% not controlled or untreated
  - 25% men
  - 20% women
  - Higher prevalence in lower SES areas

Hypertension

Prevalence rate,[a] 2017-18

Australian Bureau of Statistics 2018, National Health Survey: First results, 2017-18, *data customised using TableBuilder.*



- Overall, the prevalence of hypertension in Australia was 33.7 percent in 2017-18.
- NT has the **lowest** prevalence with 25.1 percent of people living with hypertension.
- Tasmania has the **highest** prevalence with 40.4 percent of people living with hypertension.
- Tasmania has more than 60 percent **more** people living with hypertension than NT, and 20 percent **more** than the national average.

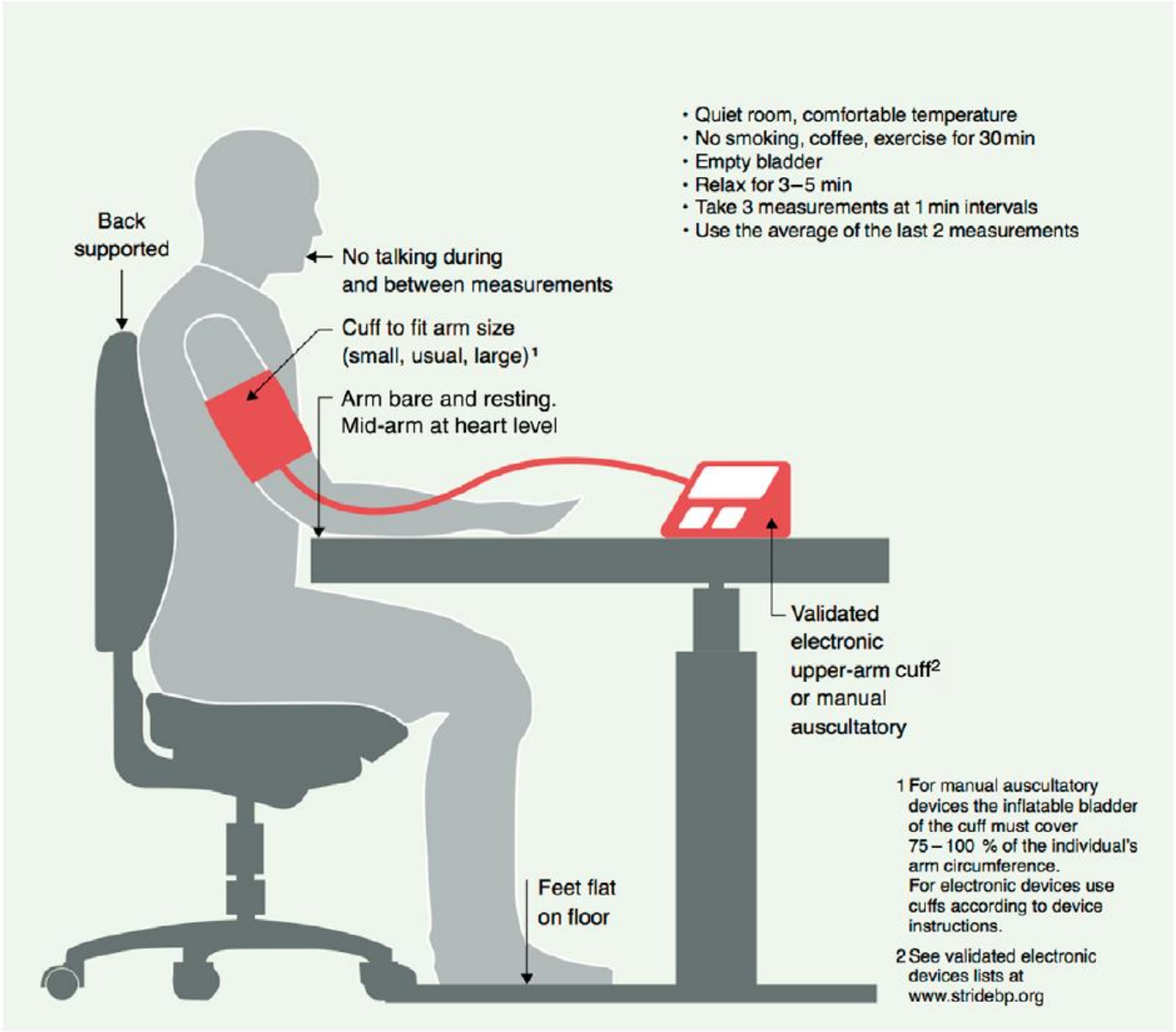
Note: a. Prevalence of hypertension is defined as all Australian adults that had high measured blood pressure (>140/90), and/or self-reported as having hypertension, and/or are taking blood pressure lowering medication.

Return to contents

Forces Driving Practice

- Ability and ease of measuring BP
- Treatments that are safe and effective
- Evidence of utility in different clinical scenarios
- Consumer attitude and engagement
- Commercial influences – time efficiency, reimbursement, advertising

How to measure BP



Evolution of guidelines

- Expert opinion based on knowledge base with extrapolation and interpolation where there are gaps.

BP goals for hypertension control JNC1 – JNC7

Report number (year of publication)	Committee chair	BP Goal (mm Hg)	Examples of seminal studies/influential reports
1 (1977)	Marvin Moser	DBP <90	8
2 (1980)	Iqbal Krishan	a. DBP <90 b. DBP 90–100 for individuals with moderate or severe hypertension	9
3 (1984)	Harriet Dustan	DBP <90	10–14
4 (1988)	Aram Chobanian	BP <140/90	15–17
5 (1993)	Ray Gifford	BP <140/90	18,19
6 (1997)	Sheldon Sheps	BP <140/90 and "lower if tolerated"	20–24
7 (2003)	Aram Chobanian	a. BP <140/90 b. <130/80 in patients with diabetes or renal disease	25,26

Abbreviations: BP, blood pressure; DBP, diastolic blood pressure; JNC, Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure.

Current status of guidelines

- Divergences of opinion
- The problem of short and medium term studies and legacy effects
- The area under the curve issue
- The distraction of absolute risk calculators

2020 ISH Global Hypertension Practice Guidelines

Table 1. Classification of Hypertension Based on Office Blood Pressure (BP) Measurement

Category	Systolic (mm Hg)		Diastolic (mm Hg)
Normal BP	<130	and	<85
High-normal BP	130–139	and/or	85–89
Grade 1 hypertension	140–159	and/or	90–99
Grade 2 hypertension	≥160	and/or	≥100

2020 ISH Global Hypertension Practice Guidelines

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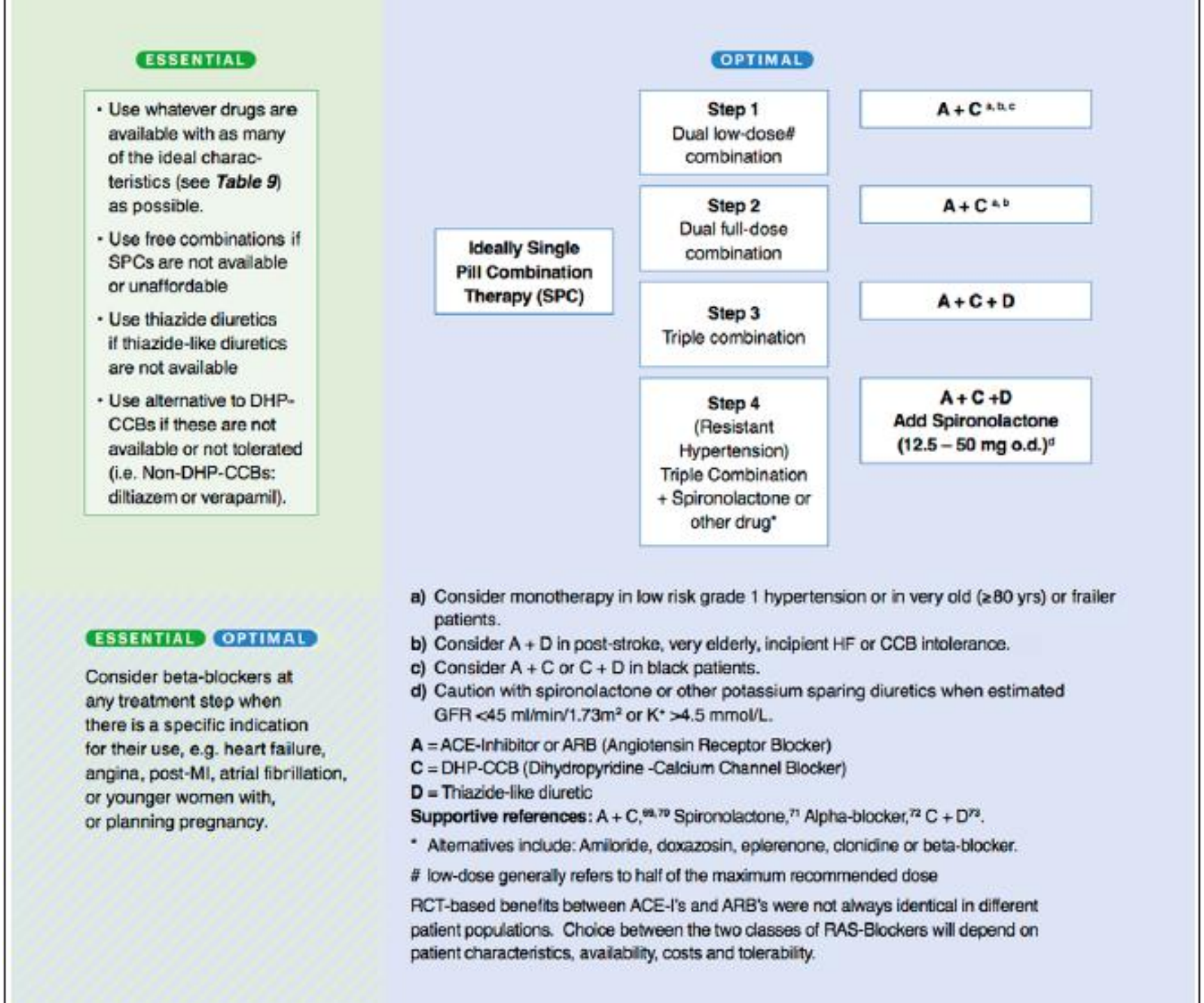
Table 2. Criteria for Hypertension Based on Office-, Ambulatory (ABPM)-, and Home Blood Pressure (HBPM) Measurement

	SBP/DBP, mm Hg
Office BP	≥140 and/or ≥90
ABPM	
24-h average	≥130 and/or ≥80
Day time (or awake) average	≥135 and/or ≥85
Night time (or asleep) average	≥120 and/or ≥70
HBPM	≥135 and/or ≥85

ISH Core Drug Treatment Strategy



ESSENTIAL

- Use whatever drugs are available with as many of the ideal characteristics (see ***Table 9***) as possible.
- Use free combinations if SPCs are not available or unaffordable
- Use thiazide diuretics if thiazide-like diuretics are not available
- Use alternative to DHP-CCBs if these are not available or not tolerated (i.e. Non-DHP-CCBs: diltiazem or verapamil).

OPTIMAL

Ideally Single Pill Combination Therapy (SPC)

Step 1 Dual low-dose# combination	**A + C** [a,b,c]
Step 2 Dual full-dose combination	**A + C** [a,b]
Step 3 Triple combination	**A + C + D**
Step 4 (Resistant Hypertension) Triple Combination + Spironolactone or other drug*	**A + C + D Add Spironolactone (12.5 – 50 mg o.d.)**[d]

ESSENTIAL OPTIMAL

Consider beta-blockers at any treatment step when there is a specific indication for their use, e.g. heart failure, angina, post-MI, atrial fibrillation, or younger women with, or planning pregnancy.

a) Consider monotherapy in low risk grade 1 hypertension or in very old (≥80 yrs) or frailer patients.
b) Consider A + D in post-stroke, very elderly, incipient HF or CCB intolerance.
c) Consider A + C or C + D in black patients.
d) Caution with spironolactone or other potassium sparing diuretics when estimated GFR <45 ml/min/1.73m² or K⁺ >4.5 mmol/L.

A = ACE-Inhibitor or ARB (Angiotensin Receptor Blocker)
C = DHP-CCB (Dihydropyridine -Calcium Channel Blocker)
D = Thiazide-like diuretic
Supportive references: A + C,[69,70] Spironolactone,[71] Alpha-blocker,[72] C + D[73].

* Alternatives include: Amiloride, doxazosin, eplerenone, clonidine or beta-blocker.

low-dose generally refers to half of the maximum recommended dose

RCT-based benefits between ACE-I's and ARB's were not always identical in different patient populations. Choice between the two classes of RAS-Blockers will depend on patient characteristics, availability, costs and tolerability.

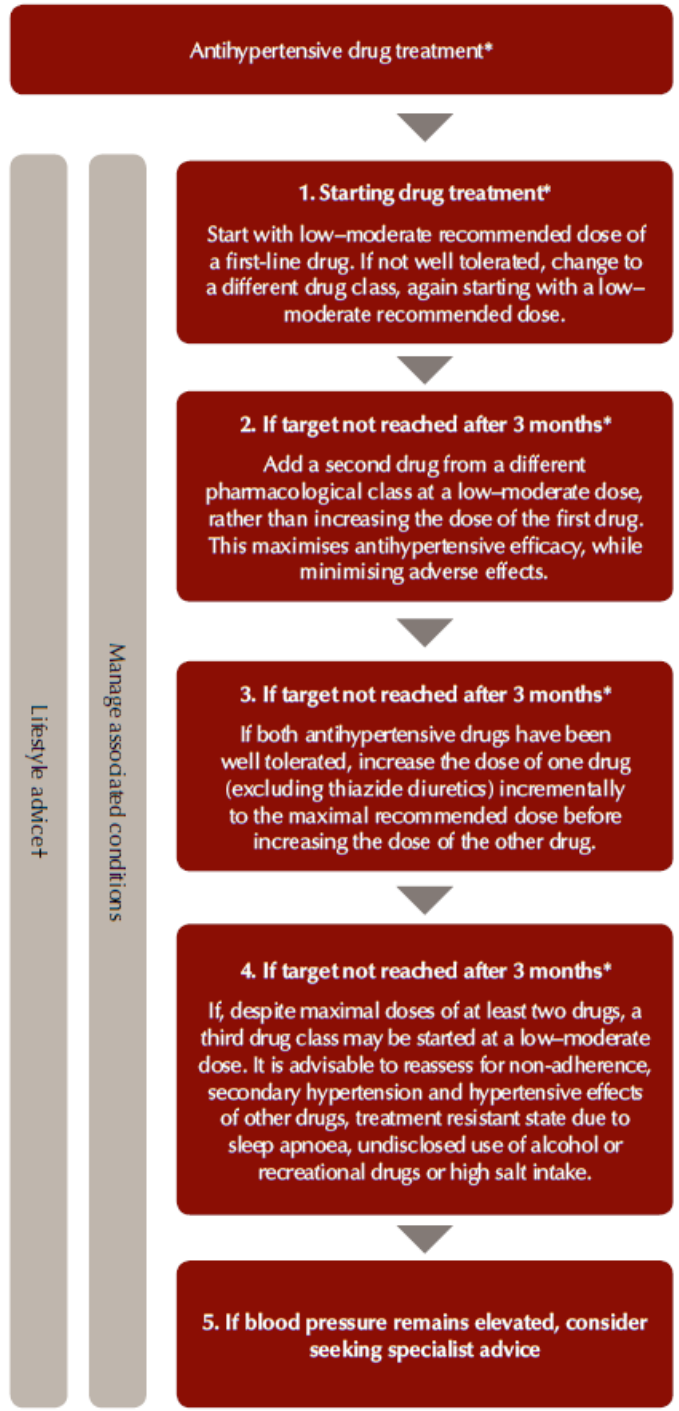

Antihypertensive drug treatment*
1. Starting drug treatment*
Start with low–moderate recommended dose of a first-line drug. If not well tolerated, change to a different drug class, again starting with a low–moderate recommended dose.
2. If target not reached after 3 months*
Add a second drug from a different pharmacological class at a low–moderate dose, rather than increasing the dose of the first drug. This maximises antihypertensive efficacy, while minimising adverse effects.
3. If target not reached after 3 months*
If both antihypertensive drugs have been well tolerated, increase the dose of one drug (excluding thiazide diuretics) incrementally to the maximal recommended dose before increasing the dose of the other drug.
4. If target not reached after 3 months*
If, despite maximal doses of at least two drugs, a third drug class may be started at a low–moderate dose. It is advisable to reassess for non-adherence, secondary hypertension and hypertensive effects of other drugs, treatment resistant state due to sleep apnoea, undisclosed use of alcohol or recreational drugs or high salt intake.
5. If blood pressure remains elevated, consider seeking specialist advice
Lifestyle advice†
Manage associated conditions

Table 6.2 Effective drug combinations

First drug		Second drug	Comment
Effective combination			
ACE inhibitor or ARB*	plus	Calcium channel blocker	Particularly useful in presence of diabetes and/or lipid abnormalities[124]
ACE inhibitor or ARB*	plus	Thiazide diuretic	Useful in presence of heart failure or post stroke
ACE inhibitor or ARB*	plus	Beta-blocker	Recommended post myocardial infarction or in patients with heart failure†
Beta-blocker	plus	Dihydropyridine calcium channel blocker	Useful in presence of symptomatic coronary heart disease
Thiazide diuretic	plus	Calcium channel blocker	
Thiazide diuretic	plus	Beta-blocker	Not recommended in presence of glucose intolerance, metabolic syndrome or established diabetes
Combinations to use with care			
Diltiazem	plus	Beta-blocker	Due to risk of heart block, but risk is less than with verapamil
ACE inhibitor or ARB	plus	Potassium-sparing diuretic	Due to risk of hyperkalaemia
Combinations to avoid			
ACE inhibitor	plus	ARB	Increased risk of renal dysfunction[120]
Verapamil	plus	Beta-blocker	Due to risk of heart block

ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker

*In head-to-head trials ACE inhibitors and ARB's are equally effective in blood pressure reduction and prevention of cardiovascular events overall, however may have important differences in their efficacy, so that they are not interchangeable, in some clinical conditions.

†Carvedilol; bisoprolol (beta-1 selective antagonist); metoprolol extended release (beta-1 selective antagonist); nebivolol.[125]

Problems of implementation

- Patient attendance, engagement, compliance
- How to best measure
- Lifestyle intervention
- Orthostatic intolerance and other comorbidity
- Resistant Hypertension
- Medication intolerance
- Other non-pharmacological interventions

Lifestyle Modification

Table 8. Lifestyle Modifications

Salt reduction	There is strong evidence for a relationship between high salt intake and increased blood pressure.[47] Reduce salt added when preparing foods, and at the table. Avoid or limit consumption of high salt foods such as soy sauce, fast foods and processed food including breads and cereals high in salt.
Healthy diet	Eating a diet that is rich in whole grains, fruits, vegetables, polyunsaturated fats and dairy products and reducing food high in sugar, saturated fat and trans fats, such as the DASH diet (http://www.dashforhealth.com).[48] Increase intake of vegetables high in nitrates known to reduce BP, such as leafy vegetables and beetroot. Other beneficial foods and nutrients include those high in magnesium, calcium and potassium such as avocados, nuts, seeds, legumes and tofu.[49]
Healthy drinks	Moderate consumption of coffee, green and black tea.[50] Other beverages that can be beneficial include karkadé (hibiscus) tea, pomegranate juice, beetroot juice and cocoa.[49]
Moderation of alcohol consumption	Positive linear association exists between alcohol consumption, blood pressure, the prevalence of hypertension, and CVD risk.[51] The recommended daily limit for alcohol consumptions is 2 standard drinks for men and 1.5 for women (10 g alcohol/standard drink). Avoid binge drinking.
Weight reduction	Body weight control is indicated to avoid obesity. Particularly abdominal obesity should be managed. Ethnic-specific cut-offs for BMI and waist circumference should be used.[52] Alternatively, a waist-to-height ratio <0.5 is recommended for all populations.[53,54]
Smoking cessation	Smoking is a major risk factor for CVD, COPD and cancer. Smoking cessation and referral to smoking cessation programs are advised.[55]
Regular physical activity	Studies suggest that regular aerobic and resistance exercise may be beneficial for both the prevention and treatment of hypertension.[56–58] Moderate intensity aerobic exercise (walking, jogging, cycling, yoga, or swimming) for 30 minutes on 5–7 days per week or HIIT (high intensity interval training) which involves alternating short bursts of intense activity with subsequent recovery periods of lighter activity. Strength training also can help reduce blood pressure. Performance of resistance/strength exercises on 2–3 days per week.
Reduce stress and induce mindfulness	Chronic stress has been associated to high blood pressure later in life.[59] Although more research is needed to determine the effects of chronic stress on blood pressure, randomized clinical trials examining the effects of transcendental meditation/mindfulness on blood pressure suggest that this practice lowers blood pressure.[60] Stress should be reduced and mindfulness or meditation introduced into the daily routine.
Complementary, alternative or traditional medicines	Large proportions of hypertensive patients use complementary, alternative or traditional medicines (in regions such as Africa and China)[61,62] yet large-scale and appropriate clinical trials are required to evaluate the efficacy and safety of these medicines. Thus, use of such treatment is not yet supported.
Reduce exposure to air pollution and cold temperature	Evidence from studies support a negative effect of air pollution on blood pressure in the long-term.[63,64]

What issues affect your ability to treat your patients?

- Should targets be relaxed for older patients? JNC8
- Does BP variability matter?
- When to start treatment?

When to start treatment

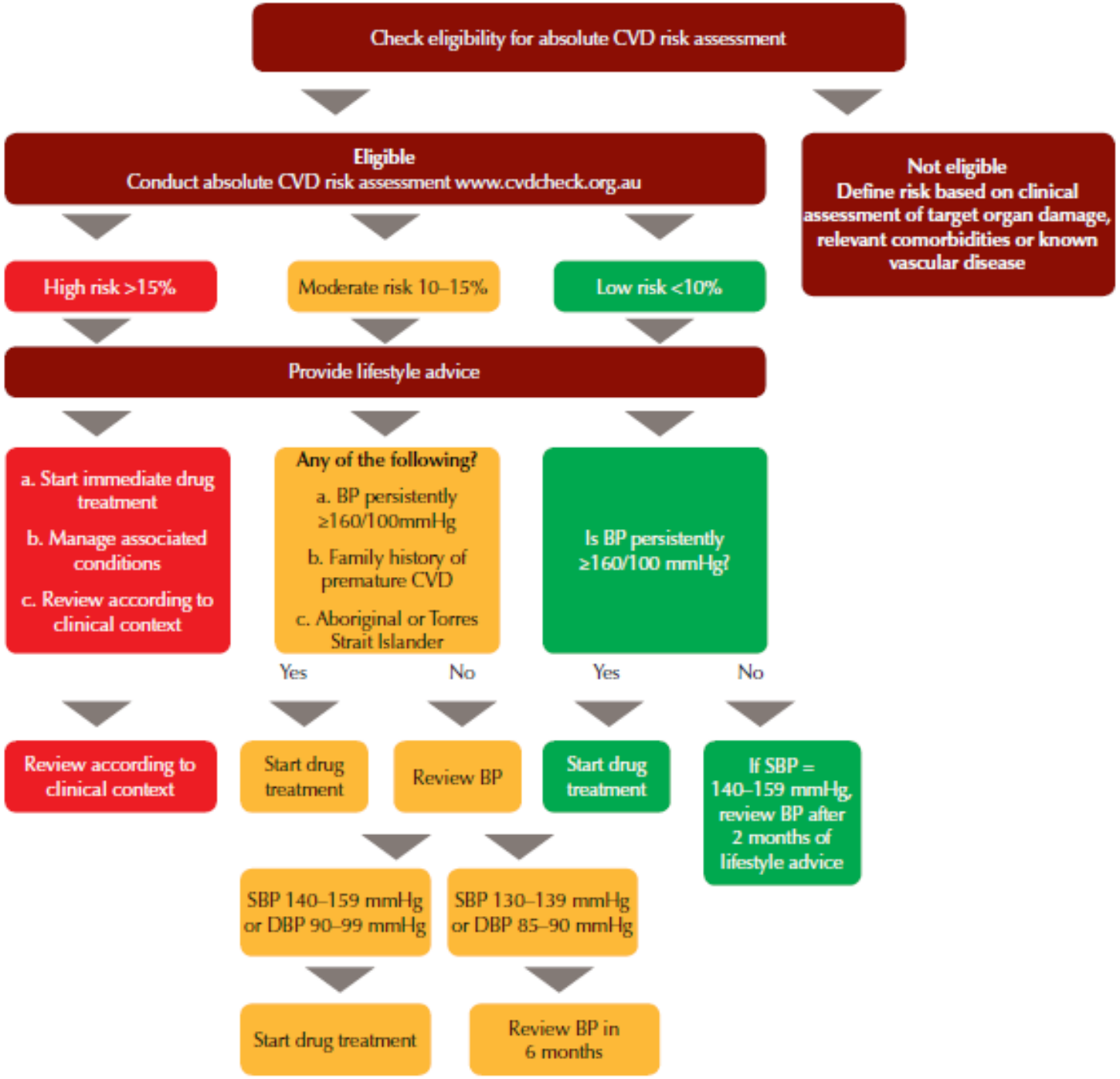
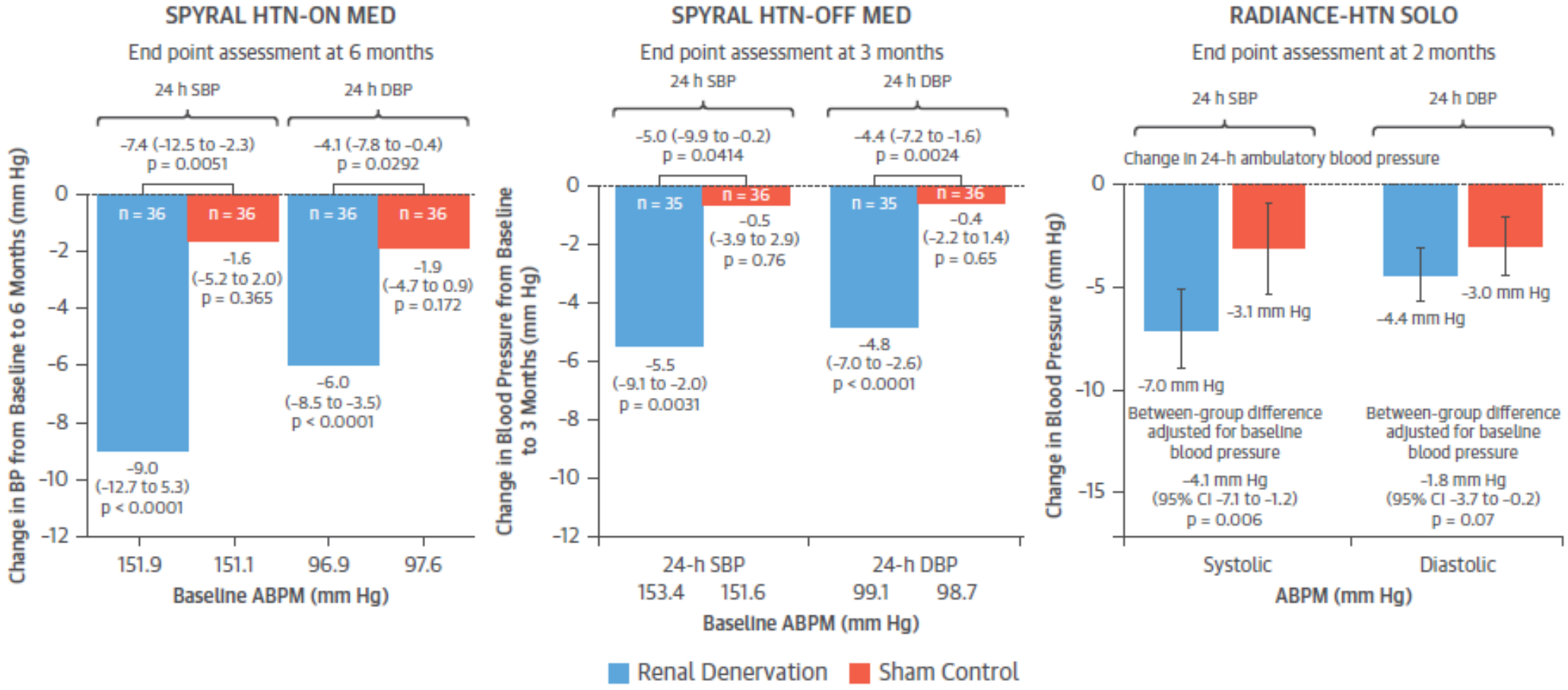


FIGURE 1 **Results From Recent Renal Denervation Randomized, Sham-Controlled Clinical Trials**



Comparison of changes in 24-h systolic blood pressure (SBP) and diastolic blood pressure (DBP) in renal denervation versus sham-control groups in 3 recent randomized, sham-controlled clinical trials. Reprinted with permission from Kandzari et al. (13), Townsend et al. (15), and Azizi et al (16). ABPM = ambulatory blood pressure monitoring; BP = blood pressure; CI = confidence interval; SPYRAL HTN-ON MED = Effect of renal denervation on blood pressure in the presence of antihypertensive drugs: 6-month efficacy and safety results from the SPYRAL HTN-ON MED proof-of-concept randomized trial; SPYRAL HTN-OFF MED = Catheter-based renal denervation in patients with uncontrolled hypertension in the absence of antihypertensive medications (SPYRAL HTN-OFF MED): a randomized, sham-controlled, proof-of-concept trial; RADIANCE-HTN SOLO = Endovascular ultrasound renal denervation to treat hypertension (RADIANCE-HTN SOLO): a multicenter, international, single-blind, randomized, sham-controlled trial.

CENTRAL ILLUSTRATION Areas of Ongoing Research in the Field of Renal Denervation

PATHOPHYSIOLOGY

Mechanisms of Renal Denervation-Induced BP Lowering

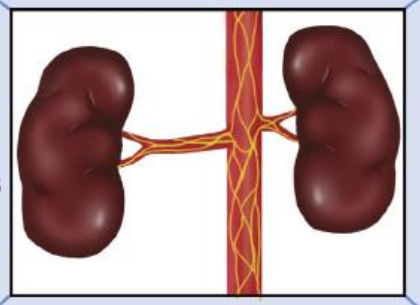
- Renal Efferent Neural Signaling
- Renal Afferent Signaling
- Potential Role of Inflammatory Pathways
- Drug Interactions

CV OUTCOMES

Expected Prospective Outcomes From Renal Denervation Trials

Age Population ~ 65 Years Old

- ↓ Systolic Blood Pressure-10 mm Hg
- ↓ ~25% in Overall Cardiovascular Events
- ↓ ~20% in Coronary Artery Disease
- ↓ ~25% in Stroke
- ↓ ~30% in Heart Failure



EFFICACY

Results From New Renal Denervation Trials
(systolic/diastolic blood pressure-lowering effect)

- **SPYRAL HTN-OFF MED**
  (-5.3/-4.8 mm Hg)
- **SPYRAL HTN-ON MED**
  (-7.0/-4.3 mm Hg)
- **RADIANCE-HTN SOLO**
  (-7.0/-4.4 mm Hg)

MONITORING

Methods to Assess the Efficacy of Renal Denervation

- **Direct Neural Stimulation of Afferent Renal Nerves**
  ("pressor" vs. "depressor" nerves)
- **Indirect Testing via Reflex Responses**
  (mental stress, head-up tilt, lower body negative pressure, and isometric handgrip)
- **Passive Monitoring**
  (renal NE spillover, spontaneous renal sympathetic nerve traffic detection, and pressure-flow monitoring)

Kiuchi, M.G. et al. J Am Coll Cardiol. 2019;73(23):3006-17.

BP = blood pressure; NE = norepinephrine; RADIANCE-HTN SOLO = Endovascular ultrasound renal denervation to treat hypertension (RADIANCE-HTN SOLO): a multicenter, international, single-blind, randomized, sham-controlled trial; SPYRAL HTN-ON MED = Effect of renal denervation on blood pressure in the presence of antihypertensive drugs: 6-month efficacy and safety results from the SPYRAL HTN-ON MED proof-of-concept randomized trial; SPYRAL HTN-OFF MED = Catheter-based renal denervation in patients with uncontrolled hypertension in the absence of antihypertensive medications (SPYRAL HTN-OFF MED): a randomized, sham-controlled, proof-of-concept trial.