RESISTANT HYPERTENSION

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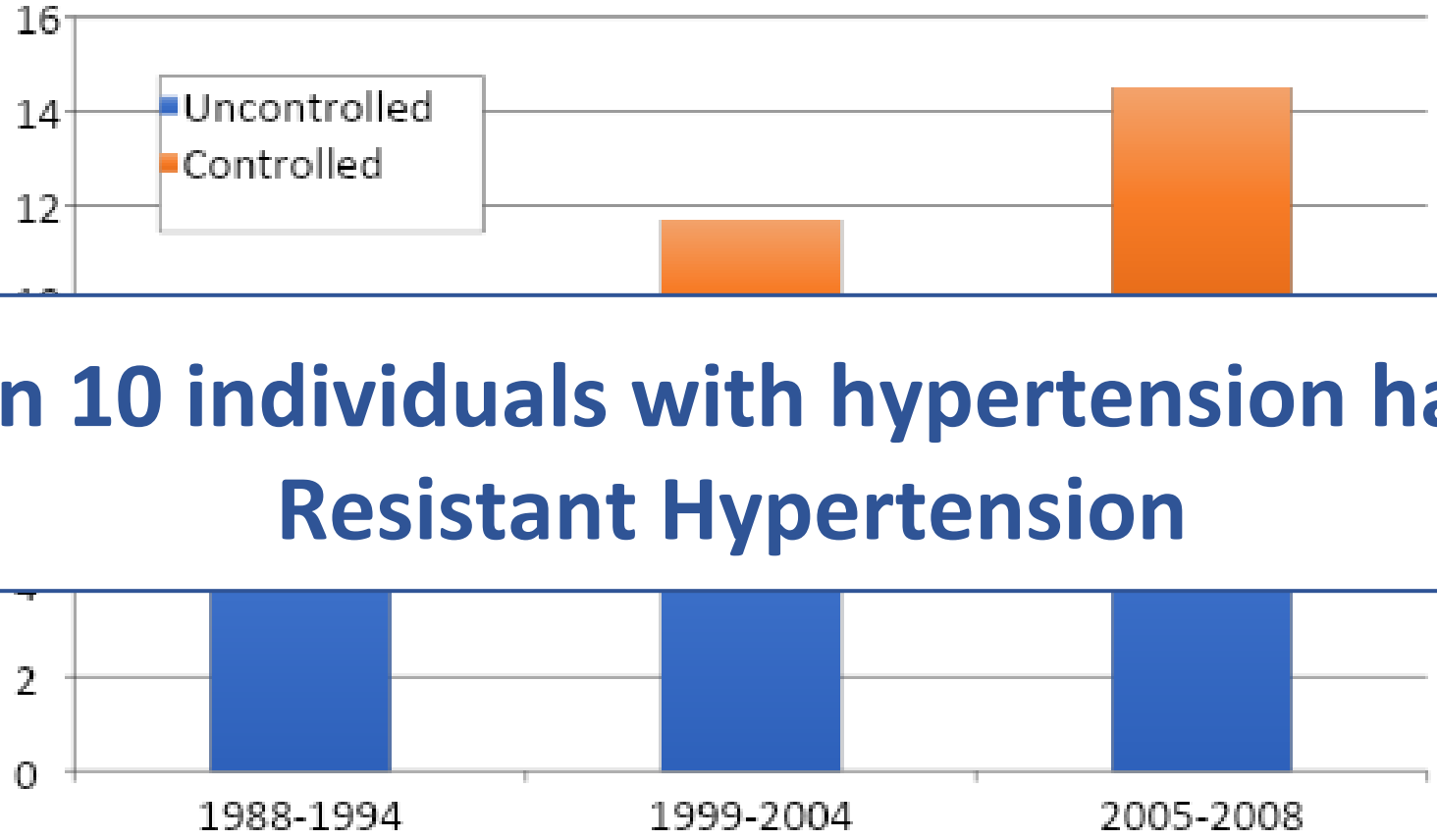
Hypertension CANADA

UBC

Objectives

1. To understand the definition of resistant hypertension
2. To understand the epidemiology and clinical implications of resistant hypertension
3. To assess work-up of resistant hypertension and interpretation of investigations
4. To learn pharmacological management of resistant hypertension
5. Review resistant hypertension cases

Emerging Global Clinical & Public Health Issue: Unmet Need in Hypertension Control



1 in 10 individuals with hypertension have Resistant Hypertension

US NHANES data, AHA Hypertension 2018, Noubiap J et al. BMJ 2018

Canadian Journal of Cardiology 36 (2020) 625–634

Guidelines

Hypertension Canada's 2020 Evidence Review and Guidelines for the Management of Resistant Hypertension

Swapnil Hiremath, MD, MPH,[a] Ruth Sapir-Pichhadze, MD, MSc, PhD,[b] Meranda Nakhla, MD, MSc,[c] Jonathan Y. Gabor, MD, MSc,[d] Nadia A. Khan, MD, MSc,[e] Laura M. Kuyper, MD,[e] Marcel Ruzicka, MD, PhD,[a] Sheldon W. Tobe, MD, MScH,[f] Karen Tran, MD,[e] Doreen M. Rabi, MD, MSc,[g,‡] and Stella S. Daskalopoulou, MD, MSc, DIC, PhD[h,‡]

Resistant Hypertension Definition

- Inadequately controlled blood pressure ***above target***, despite receiving ***three or more*** antihypertensive medications at ***optimal doses***, preferably including a ***diuretic***

- Controlled blood pressure to treatment target, requiring ***four or more*** antihypertensive agents

Carey R et al. AHA Scientific Statement 2018
Calhoun DA, et al. Hypertension. 2008; 51(6):1403–19.

Resistant Hypertension has a Poor Prognosis

Up to 50% increase risk of cardiovascular events

46% increased risk of heart failure

24% increased risk of an ischemic cardiac event

32% increased risk of end-stage renal disease

14% increased risk of stroke

6% increased risk of premature death

Daugherty SL et al. Circ 2012
Rimoldi SF et al. Eur Heart J 2015
Sim JJ et al. Kidney Int 2015

Multifactorial Mechanisms of Resistant Hypertension

- **Fluid retention:** increased sodium sensitivity, excessive salt intake, and renal dysfunction
- **Aldosterone excess**
- **Low renin states** – 2/3rd of patients with RHTN had suppressed plasma renin activity despite use of ACEI/ARB and diuretics
- **RAAS activation**

- **Sympathetic nervous hyperactivity**: elevated 24-h urinary metanephrines, higher heart rate
- Increased **arterial stiffness**

Pimenta E. Hypertens 2009
Elrin A. Trends Cardiovasc Med 2016
Gaddam KK Arch Int Med 2008
Eide K et al. J of Hypertens 2004
Pimenta E. Curr Hypertens Rep 2007
Tsioufis C. Int J Hypertens 2011

Management of Resistant Hypertension

1

Confirm the Diagnosis

- Medication adherence
- AOBP
- 24h ABPM/HBPM
- Secondary hypertension work-up

2

Health Behaviour Modifications

- Exercise
- DASH diet
- Low sodium, high potassium
- Non-smoking
- Moderate EtOH

3

Pharmacological

- Review current antihypertensive regimen before adding new agents

Most Uncontrolled Hypertension is NOT truly Resistant

- **Non-Adherence**
- **Improper BP Measurement**
- **White Coat Hypertension**
- **Treatment Inertia**
- **Aggravating Medications**
- **Excessive Salt**

Review Medication Aggravators

- NSAIDS
- Corticosteroids
- OCPs
- Vasoconstricting/Sympathomimetic decongestants
- Calcineurin inhibitors (tacrolimus, cyclosporine)
- Erythropoietin
- Midodrine
- Anti-depressants (MAOIs, SSRIs, SNRIs)
- Licorice root

Secondary Causes of Hypertension

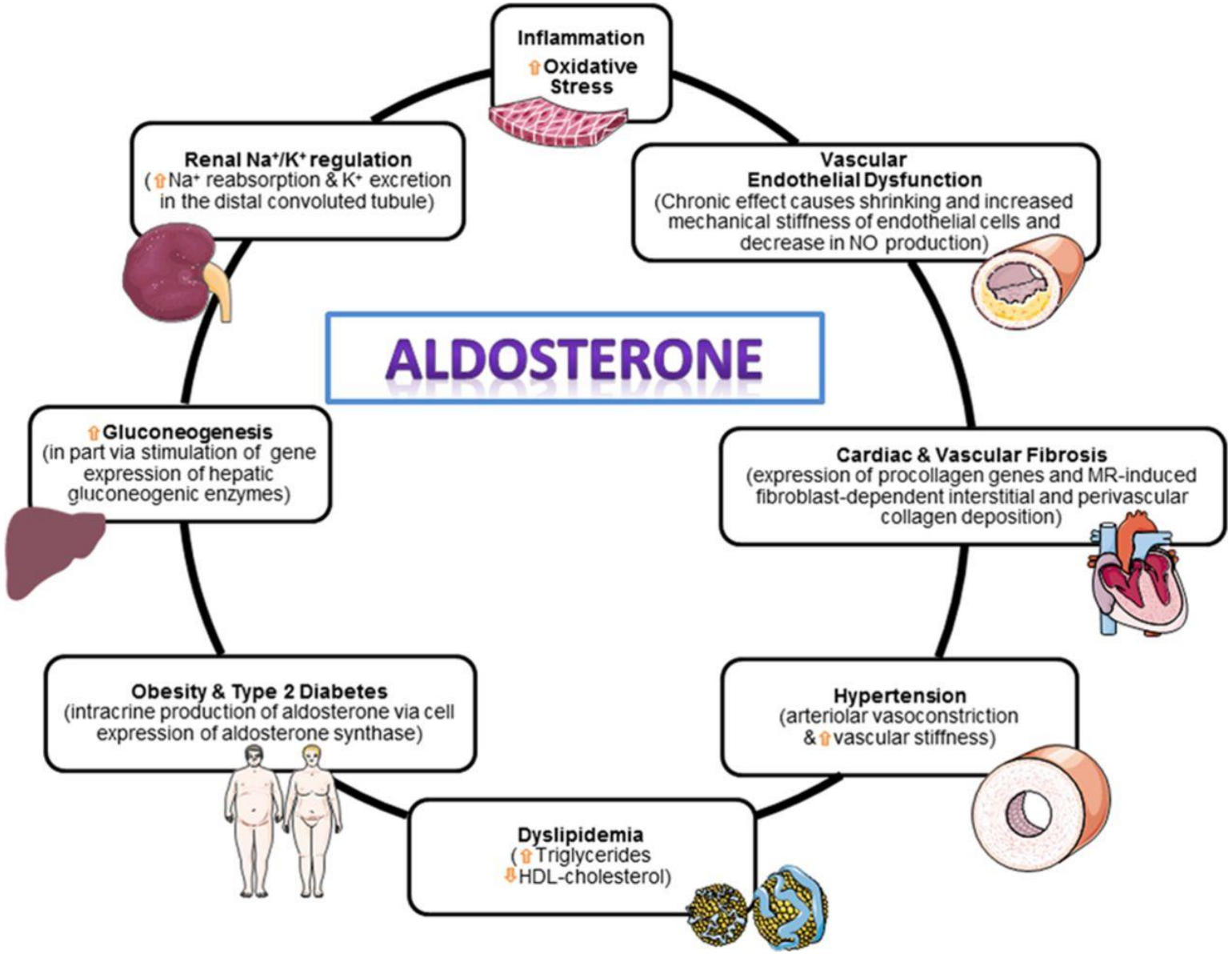
Endocrine	**Primary Aldosteronism,** Pheochromocytoma, Cushing's Syndrome, Thyroid Disease, Parathyroid Disease
Renal	**Chronic Kidney Disease,** Renal artery stenosis, Fibromuscular Dysplasia
Other	**Obstructive Sleep Apnea**

Primary Aldosteronism

Importance of Detecting PA

- Prognosis: worse for PA patients than patients with primary HTN at same blood pressure
  - Aldosterone excess has toxic effects on heart and vasculature
  - Higher prevalence of stroke, MI, A Fib, LVH in PA patients
  - Increased vascular stiffness/remodeling
- Treatment: possible to cure or at least dramatically improve HTN via mineralocorticoid receptor antagonist therapy or adrenalectomy

Actions of Aldosterone on the Cardiovascular Disease



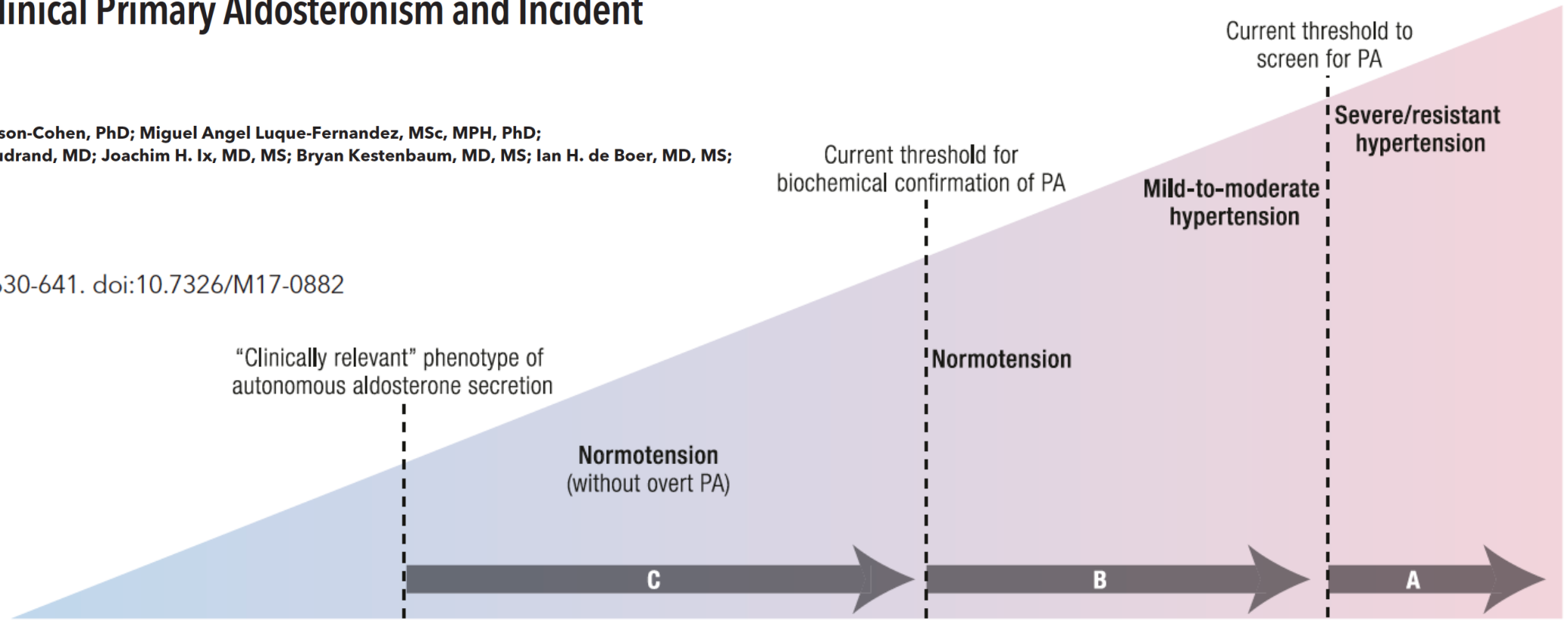
Carlos M. Ferrario. Circulation Research. Role of Mineralocorticoid Receptor Antagonists in Cardiovascular Disease, Volume: 116, Issue: 1, Pages: 206-213, DOI: (10.1161/CIRCRESAHA.116.302706)

The Spectrum of Subclinical Primary Aldosteronism and Incident Hypertension

A Cohort Study

Jenifer M. Brown, MD; Cassianne Robinson-Cohen, PhD; Miguel Angel Luque-Fernandez, MSc, MPH, PhD; Matthew A. Allison, MD, MPH; Rene Baudrand, MD; Joachim H. Ix, MD, MS; Bryan Kestenbaum, MD, MS; Ian H. de Boer, MD, MS; and Anand Vaidya, MD, MMSc

Ann Intern Med. 2017;167:630-641. doi:10.7326/M17-0882



Cardiovascular risk	*Lower* → *Higher*		
Disease	"Subclinical" or "non-classical" primary aldosteronism	"Unrecognized yet biochemically overt PA"	"Overt PA"
Obvious clinical syndrome of excessive MR activation?	No	No	Yes
Biochemical confirmation of PA using classical criteria?	No	Yes	Yes
Hypothesized pathologic corollaries	Non-neoplasia: APCCs → (?) → Neoplasia: APA/BAH Neoplasia: Nonfunctional adenoma/hyperplasia → (?) → Secretory somatic alteration: APA/BAH		

Indications for PA Screening

- Hypertension Canada Guidelines

  - Resistant HTN
  - Unexplained hypoK <3.5
  - HypoK <3.0 with diuretics
  - Adrenal adenoma >1cm

- Endocrine Society Guidelines

  - Sustained BP > 150/100
  - Resistant HTN
  - HTN & spontaneous/ diuretic induced hypoK
  - HTN and adrenal incidentaloma
  - HTN and sleep apnea
  - HTN & FHX of early onset HTN/stroke < 40 years old
  - First degree relatives of PA

< 3% of patients for whom screening is recommended are screened

How to screen for Hyperaldosteronism

- Upright serum aldosterone level and plasma renin activity
- Aldo: Renin Ratio
- Measured before 10AM, Upright/standing measures
- Perform in hospital lab
- Must be measured without any mineralacorticoid receptor blockers 4-6 wks
- Ideally, without RAAS inhibitors, beta blockers or diuretics but may not be feasible

- Diagnostic feature: Suppressed renin

How to screen for Hyperaldosteronism

- Beta blockers, clonidine, methlydopa → false +ve (if low aldosterone cut off used)
- RAS blockers, diuretics, DHP-CCB → false –ve

- Antihypertensives that affect ARR least → hydralazine, alpha blockers, non-DHP-CCBs (verapamil/diltazem)

Optimal use and interpretation of the aldosterone renin ratio to detect aldosterone excess in hypertension

S A R Doi ✉, S Abalkhail, M M Al-Qudhaiby, K Al-Humood, M F Hafez & K A S Al-Shoumer

Journal of Human Hypertension **20**, 482–489(2006) | Cite this article

Drug	***Renin***	***Aldosterone***	***Effect***
No-effect			
Non-Dihydropyridine calcium channel blocker – Nifedipine/Verapamil[17, 40, 57, 58]	Minimal	Minimal	No effect
Dihydropyridine calcium channel blocker- Amlodipine[8, 59]	Minimal	Decreased-minimal	Nil – False negative
α-blockers[8, 17, 40, 60]	Nil	Nil	No effect
Hydralazine[17]	Minimal	Minimal	No effect
False-negative effect			
ACE inhibitors[8, 40, 61, 62]	Increased	Decreased	False negative
Diuretics[40]	Increased markedly	Increased	False negative
Minoxidil[17]	Increased	Minimal	False negative
Angiotensin receptor blockers[8, 40, 63]	Increased	Decreased	False negative probably similar to ACEI
False-positive effect			
β-blockers[8, 40, 61, 64]	Decreased	Minimal	False positive
α-methyl dopa[17]	Decreased	Minimal	False positive

Confirmatory Testing for Hyperaldosteronism

- **Saline Suppression Test**
  - Infusion 2 L IVNS over 4 hours, check ARR
- **Oral Salt loading Test (5g Sodium for 3 days)**
  - Measure 24h urine aldosterone levels
- **Fludrocortisone Suppression Test**
  - Fludrocortisone 0.1 mg po q6h x 4days with K+ supplements, check ARR
- **Captopril challenge Test**
  - Captopril 25-50 mg po x1, check Aldo, renin, and cortisol at 0, 1, 2 hours post

- No Gold Standard Confirmatory Test

- Adrenal vein Sampling: gold standard test for diagnosing PA

Saline Suppression Test Instructions

SALINE SUPPRESSION TEST ORDERS

(Items with check boxes must be selected to be ordered)

INDICATION: To confirm a diagnosis of primary aldosteronism following a positive screening test

DO NOT perform this test on patients with severe uncontrolled hypertension, renal insufficiency, cardiac arrhythmia or severe hypokalemia.

PATIENT PREPARATION:

Confirm blood pressure medications such as beta-blockers, ACE inhibitors/ARBs and thiazides were discontinued minimum one week prior to testing

If needed, the following medications can be taken to control blood pressure in the days leading up to the test: verapamil
hydrALAZINE
prazosin, doxazosin, or terazosin

Patient is NPO during the test

Review preparation instructions with patient and document any deviation from the ideal preparation

Inform Lab of testing and coordinate timed bloodwork

Patients should remain sitting down throughout the test

PROCEDURE: Begin test before 0900 Start time: _____

Monitoring: Monitor blood pressure and heart rate Q1H throughout test

Bloodwork: Baseline blood sample for aldosterone and renin prior to IV infusion

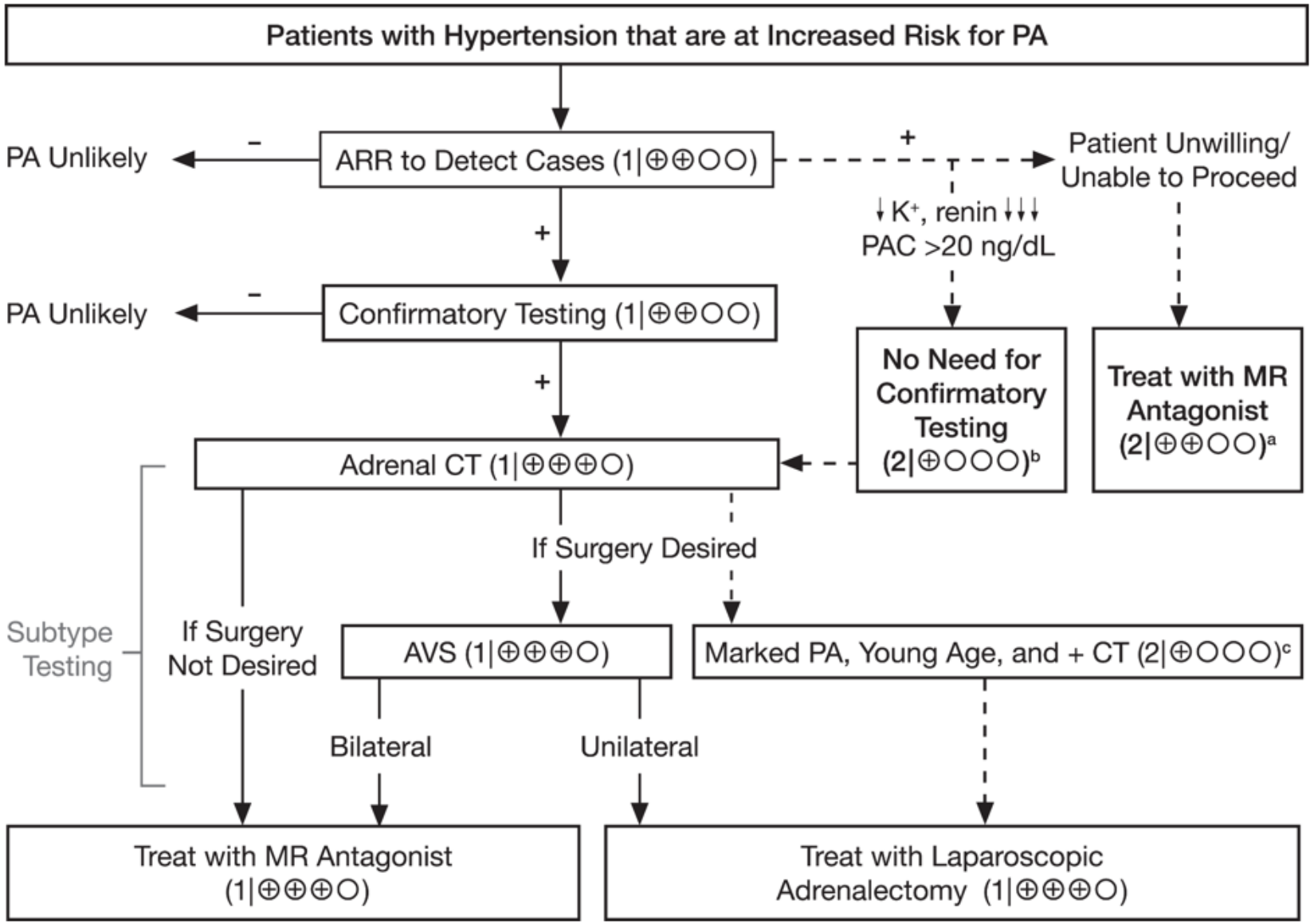
Infusion: Establish IV access and infuse sodium chloride 0.9% at 500 mL/hour for 4 hours

Timed bloodwork: after 4 hours of infusion, draw sample for aldosterone and renin

DISCHARGE: Discontinue IV and discharge

Figure 1. Algorithm for the detection, confirmation, subtype testing, and treatment of PA.

[a] We recommend ...



Adrenal Vein Sampling Results

Acc	Time	Loc	ACTH stim	Aldo (pmol/L)	Cort (nmol/L)	SI	Cath	A/C	LI
F1727830	10:14:00 AM	PRE IVC	N	562	339	1.0	NA	1.7	
F1727813	10:14:00 AM	PRE RIGHT ADRENAL	N	1090	652	1.9	Y	1.7	
F1727806	09:57:00 AM	PRE LEFT ADRENAL	N	3320	697	2.1	Y	4.8	2.8
F1727851	10:28:00 AM	POST IVC	Y	927	475	1.0	NA	2.0	
F1727839	10:27:00 AM	POST RIGHT ADRENAL	Y	6180	30500	64.2	Y	0.2	
F1727863	10:29:00 AM	POST LEFT ADRENAL	Y	170000	9930	20.9	Y	17.1	84.5

SI = Selectivity Index LI = Lateralization Index

Lateralization Index > 4 suggests biochemical evidence of lateralization

Diagnosis of PA in the Young

- Normally CT is only accurate ~50% of the time in detecting the adenoma and therefore AVS is needed

- In individuals < 35 years, CT adrenals have a good correlation with AVS and therefore AVS may not be needed in this population

Risk for Incident Composite Cardiovascular Events

HR= 1.91 (1.63, 2.25) for PA MRA Therapy vs Essential HTN

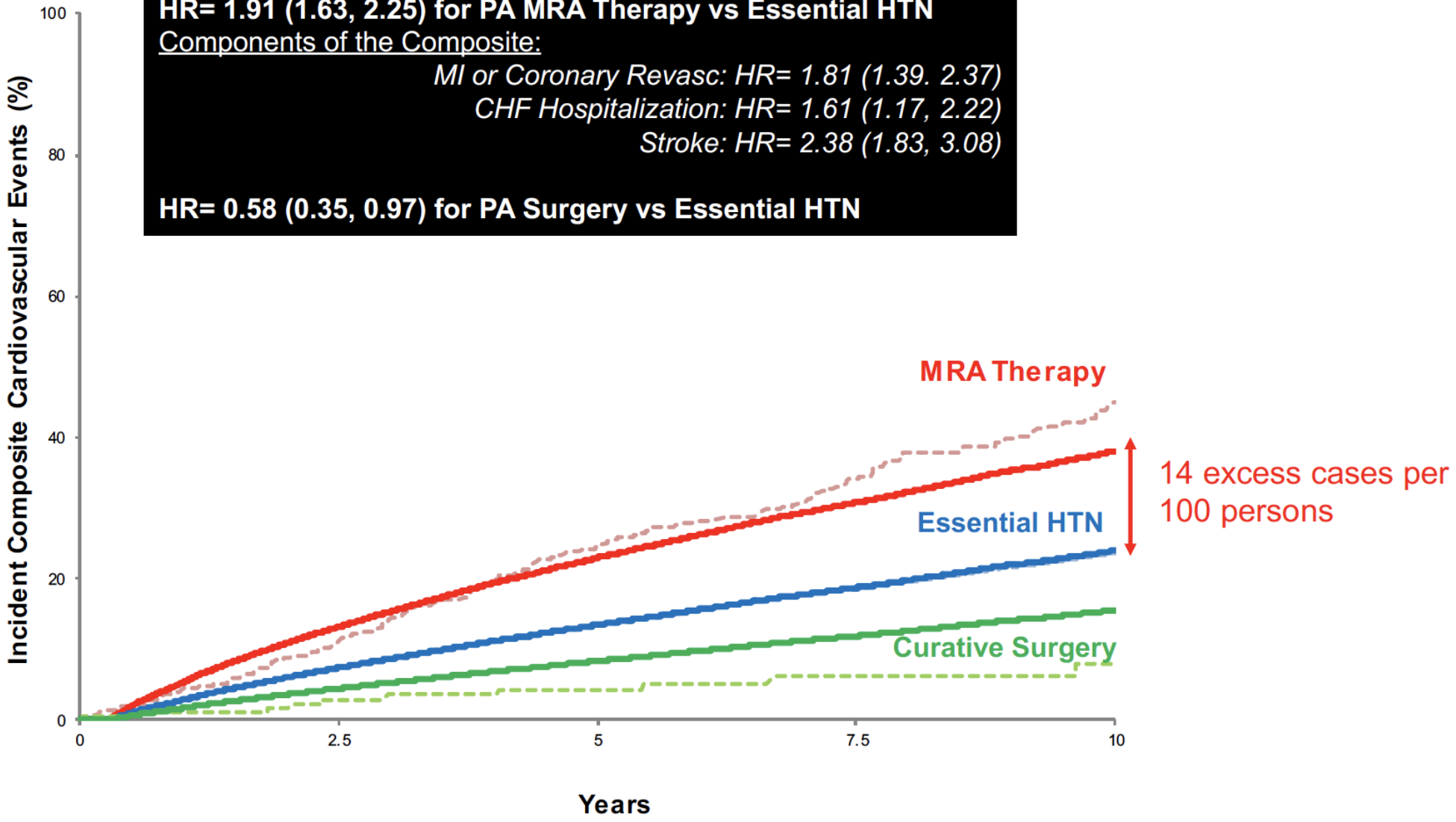
Components of the Composite:

MI or Coronary Revasc: HR= 1.81 (1.39. 2.37)

CHF Hospitalization: HR= 1.61 (1.17, 2.22)

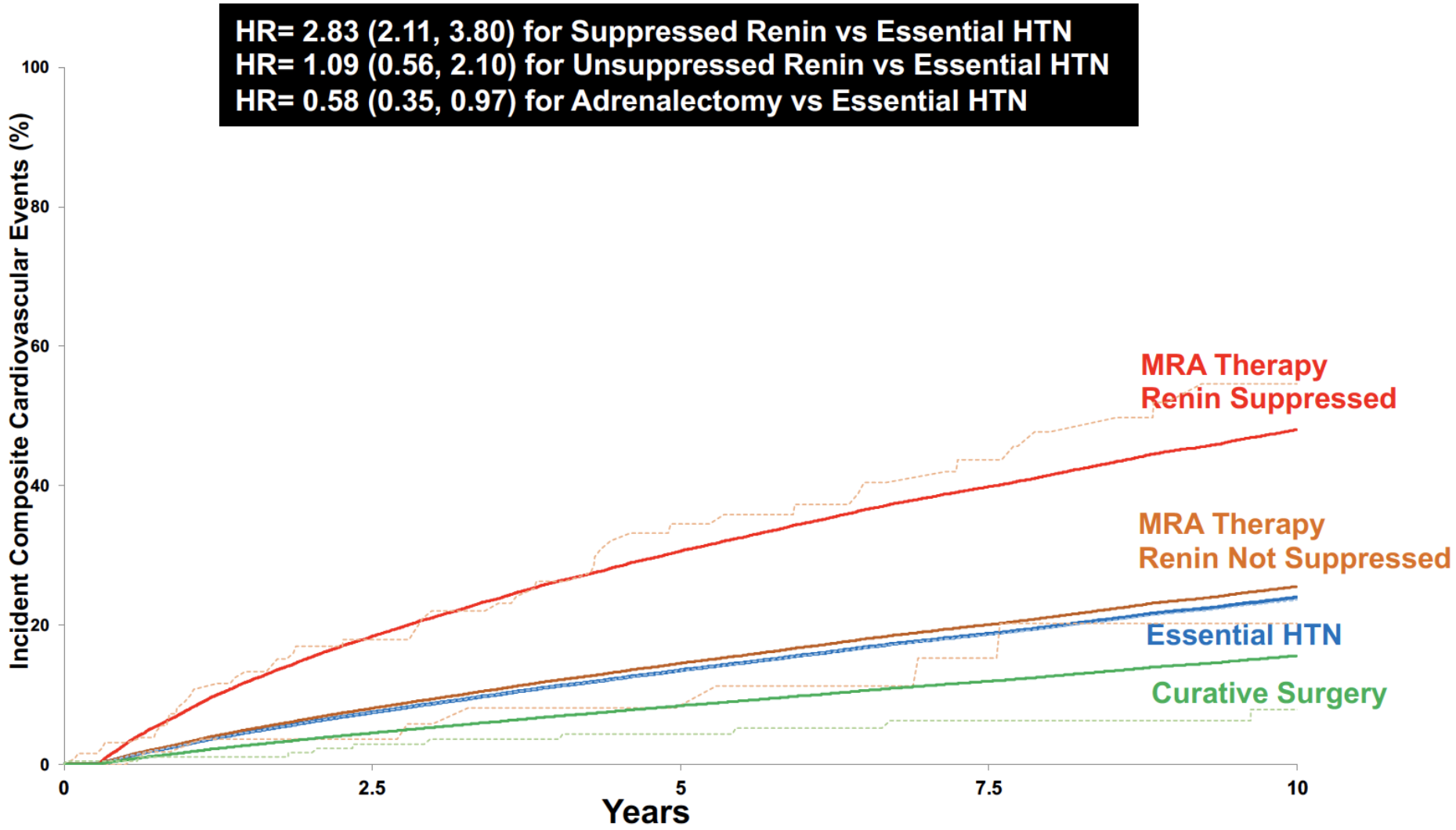
Stroke: HR= 2.38 (1.83, 3.08)

HR= 0.58 (0.35, 0.97) for PA Surgery vs Essential HTN



Hundemer et al, The Lancet D&E 2018

Risk for Incident Composite Cardiovascular Events



Hundemer et al, The Lancet D&E 2017; Hundemer et al, *JAMA Cardiology* 2018

Asses only based on Signs and Symptoms

- Renovascular Disease
  - CTA or MRA
- Cushing Syndrome
  - 24h urine cortisol, 1 mg Dexamethasone suppression test, 11 pm salivary cortisol
- Pheochromocytoma
  - 24h urine catecholamines and fractionated catecholamines
  - Chronic HTN can have up to 2x ULN
- Coarctation of the Aorta
  - Echo or CTA

Pheo

- < 0.1-0.5% of all causes of HTN
  - Only 1/300 turn out to be Pheo that are investigated
- > 50 X if adrenal incidentaloma
- When to suspect?
  - Classic triad/spells
  - Episodic
  - Extremes of age
  - Severe
  - Refractory to > 3 drugs
  - Other clues clinical & biochemical
  - Family Hx
  - During anesthesia/OR/certain drugs/foods
  - 1º dilated cardiomyopathy

The seven P's:

•**P** ressure (HTN)	90%
•**P** ain (Headache)	80%
•**P** erspiration	71%
•**P** alpitation	64%
•**P** allor	42%
•**P** ostural Hypotension	10-50%
•**P** aroxysms	

Complications

- Cardiomyopathy/CHF
- End organ damage due to HTN
- Arrhythmias
- Death

Pheo Detection

Localization Studies

STUDY	SN	SP
CT	89-100	29-70
MRI	93-100	70-100
I-123 MIBG	90	95-100
Ga-68 Dotatate PET-CT	88-100	
I-131 MIBG	77-100	88-100
Octreotide Scan	87	
Ultrasound	83	
Angiography	67	

Always confirm biochemically first!

Basic Resistant Hypertension Work-up

- 24h ABPM or Home BP series
- Calcium and TSH
- Upright plasma aldosterone and renin ratio
- Level 3 Sleep study

- Cushing’s and Pheo work up only if there are signs or symptoms

Management of Resistant Hypertension

1

Confirm the Diagnosis

- Medication adherence
- AOBP
- 24h ABPM/HBPM
- Secondary hypertension work-up

2

Health Behaviour Modifications

- Exercise
- DASH diet
- Low sodium, high potassium
- Non-smoking
- Moderate EtOH

3

Pharmacological

- Review current antihypertensive regimen before adding new agents

Healthy Lifestyle Really Makes a Difference

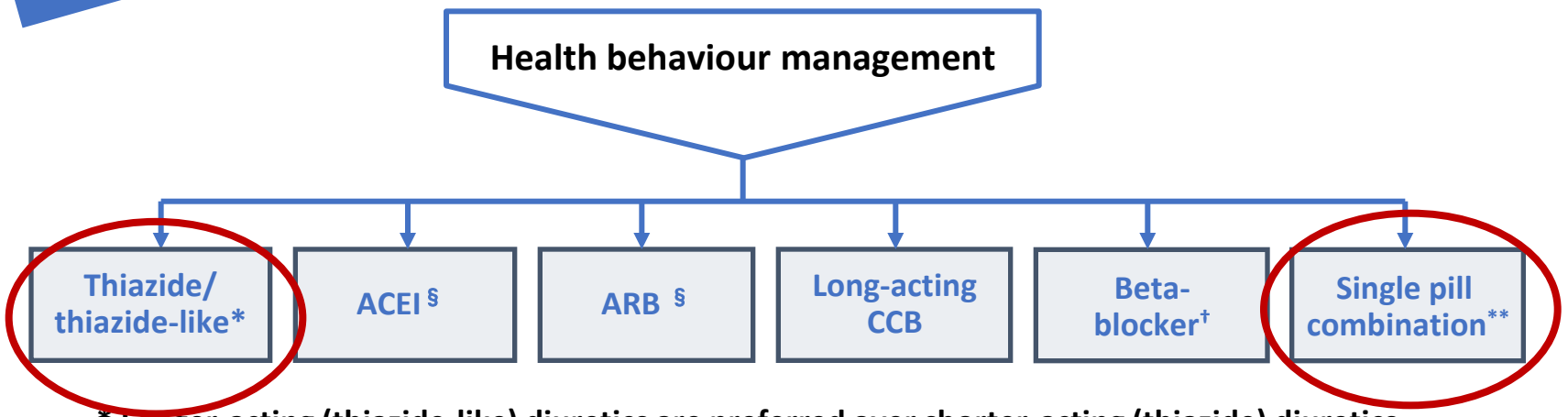
Intervention	Systolic BP (mmHg)	Diastolic BP (mmHg)
Diet and weight control	-6.0	-4.8
Reduced salt/sodium intake	- 5.4	- 2.8
High potassium diet	- 3.5	- 2.0
Reduced alcohol intake (heavy drinkers)	-3.4	- 3.4
DASH diet	-11.4	- 5.5
Physical activity	- 3.1	- 1.8
Relaxation therapies	- 5.5	- 3.5

First Line Treatment of Adults with HTN without other compelling Indications

TARGET <135/85 mmHg (automated measurement method)

New 2017

INITIAL TREATMENT



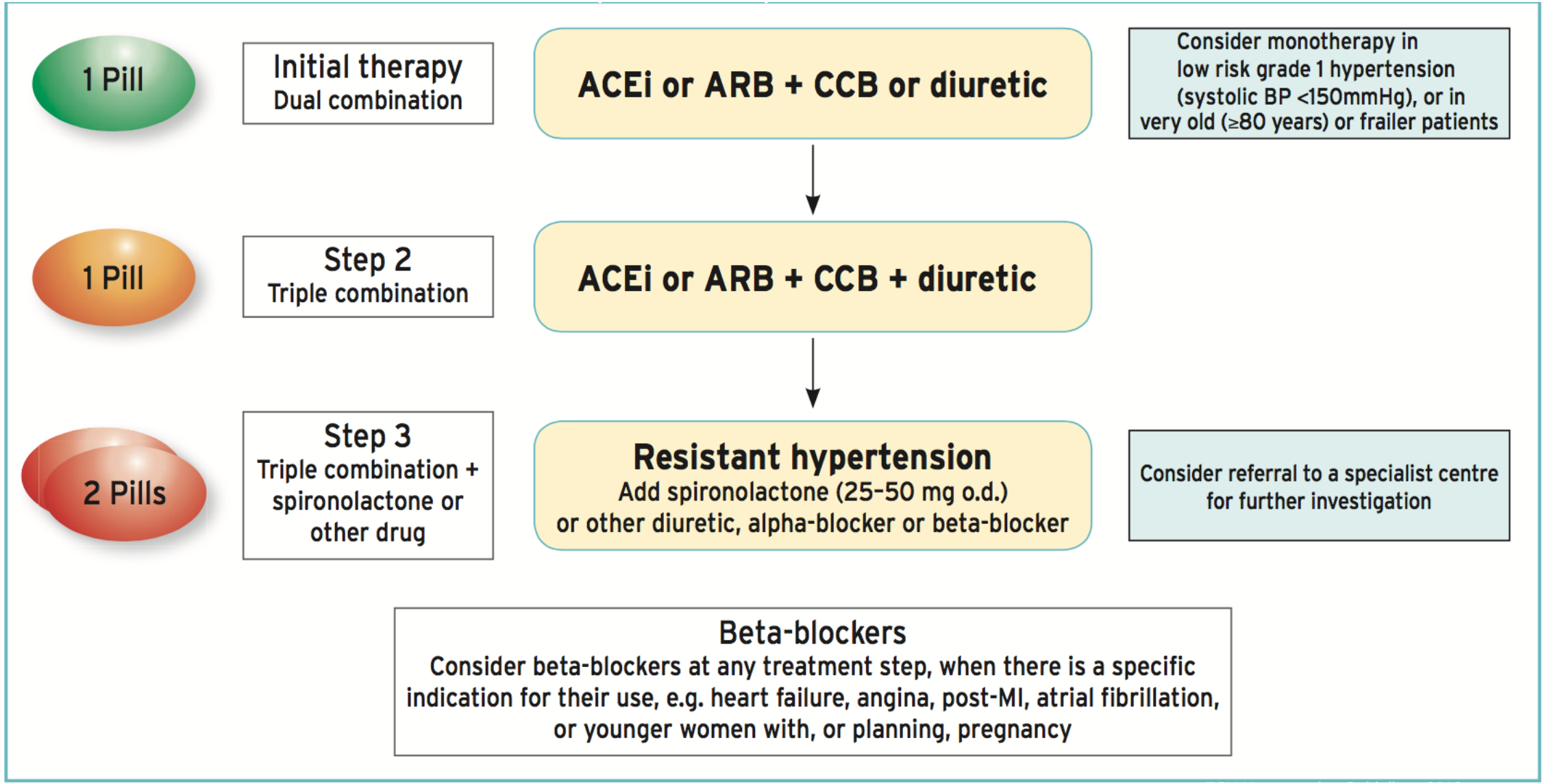
*** Longer-acting (thiazide-like) diuretics are preferred over shorter-acting (thiazide) diuretics**

† BBs are not indicated as first line therapy for age 60 and above

§ Renin angiotensin system (RAS) inhibitors are contraindicated in pregnancy and caution is required in prescribing to women of child bearing potential

****Recommended SPC choices are those in which an ACE-I is combined with a CCB, an ARB with a CCB, or an ACE-I or ARB with a diuretic**

Anti-hypertensive Therapy-Practical Suggestions



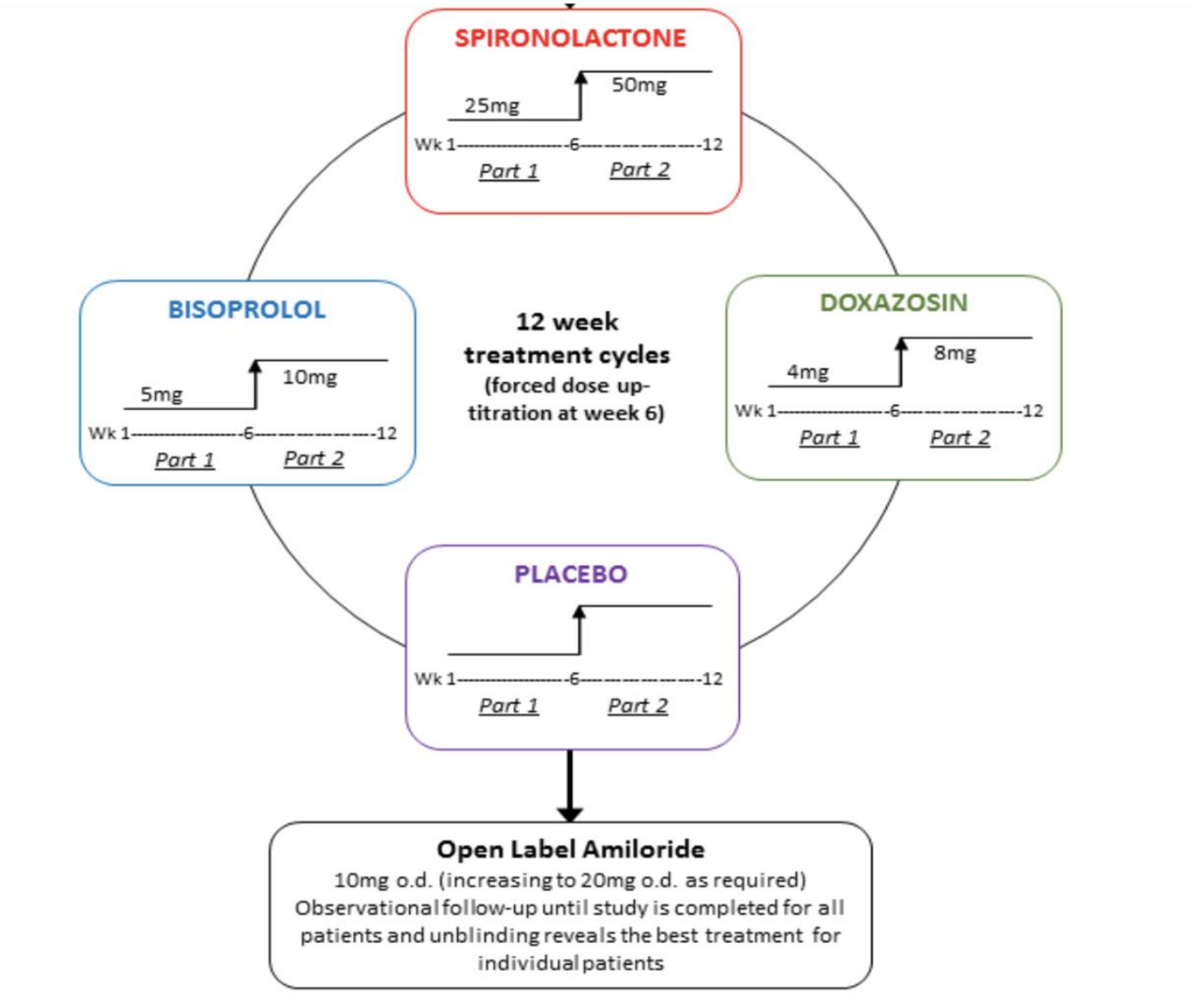
Spironolactone versus placebo, bisoprolol, and doxazosin to determine the optimal treatment for drug-resistant hypertension (PATHWAY-2): a randomised, double-blind, crossover trial

*Bryan Williams, Thomas M MacDonald, Steve Morant, David J Webb, Peter Sever, Gordon McInnes, Ian Ford, J Kennedy Cruickshank, Mark J Caulfield, Jackie Salsbury, Isla Mackenzie, Sandosh Padmanabhan, Morris J Brown, for The British Hypertension Society's PATHWAY Studies Group**

- Double-blind, placebo-controlled, crossover trial
  335 patients aged 18-79 with elevated office and home BP, on at least 3 drugs for at least 3 months
- Exclusion: Non-compliance, secondary hypertension, eGFR<45 ml/min or abnormal K^+
- **Primary endpoint**: change in home SBP

Williams B, The Lancet 2015

Crossover Medication

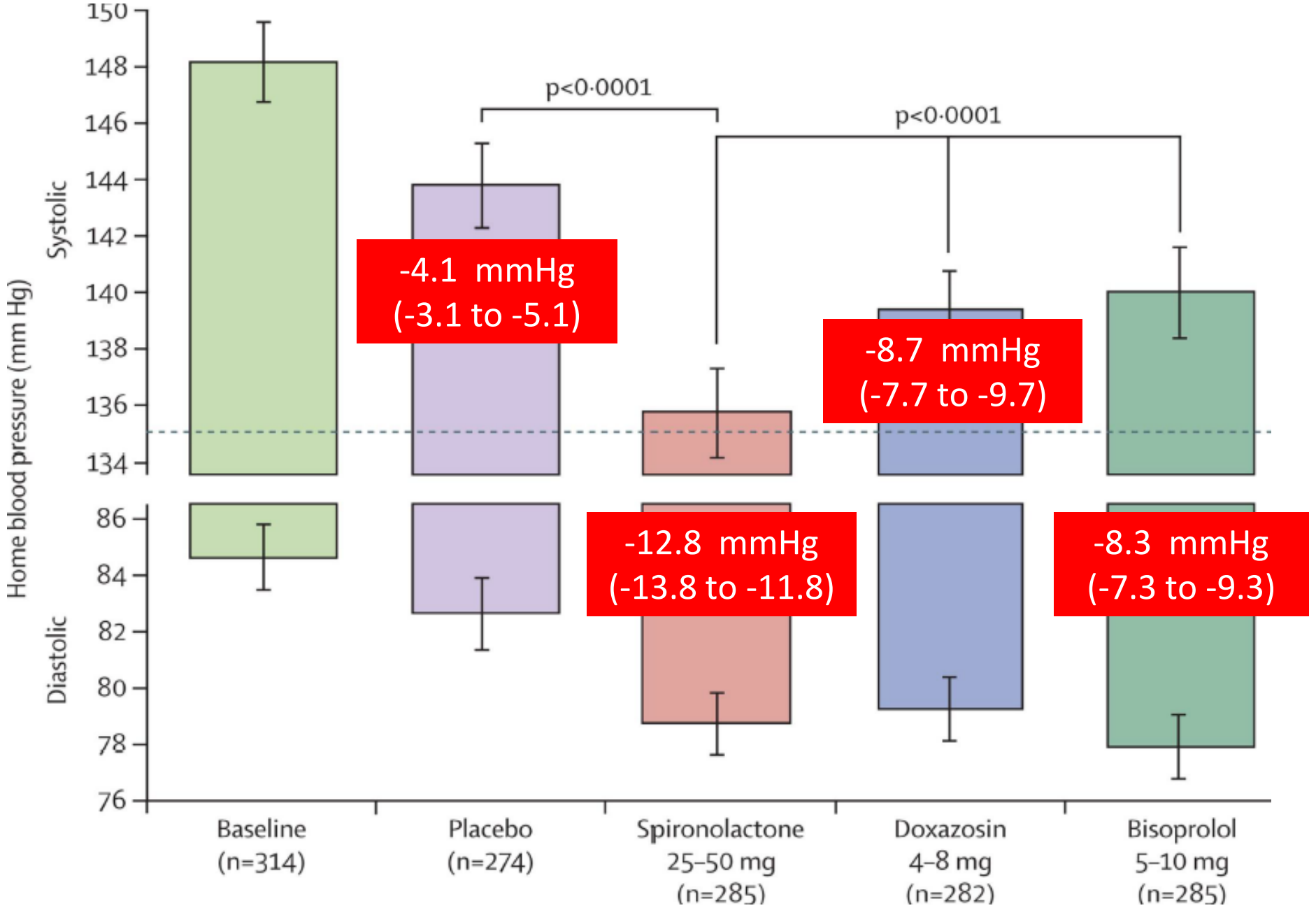


Williams B, The Lancet 2015

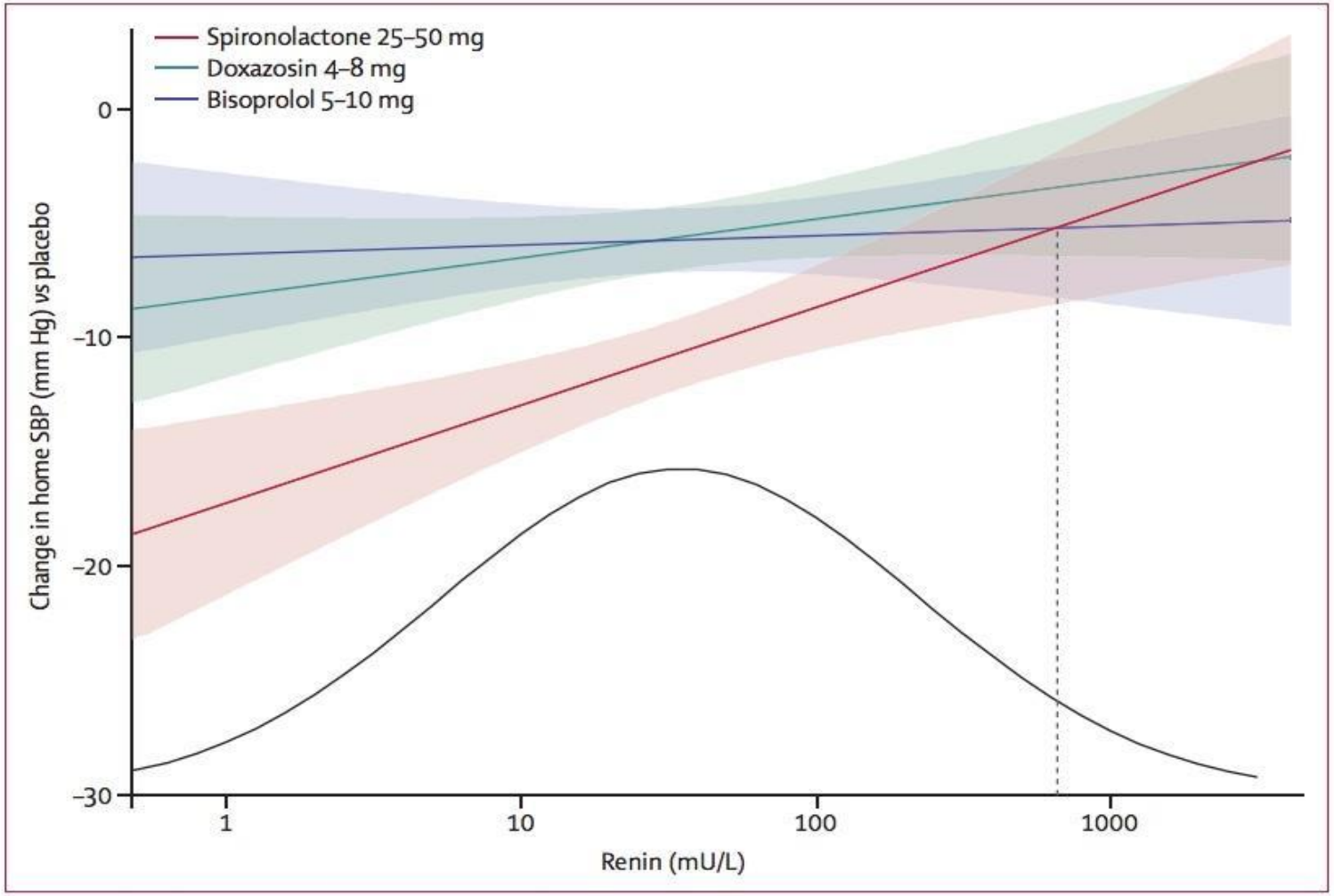
Baseline Characteristics

Characteristic	PATHWAY-2
Age (mean)	61 years
Women	31%
Diabetes	14%
Home BP	147.6/84.2 mmHg

Williams B, The Lancet 2015


Home blood pressure (mm Hg)
Systolic
Diastolic
150
148
146
144
142
140
138
136
134
86
84
82
80
78
76
p<0·0001
p<0·0001
-4.1 mmHg
(-3.1 to -5.1)
-8.7 mmHg
(-7.7 to -9.7)
-12.8 mmHg
(-13.8 to -11.8)
-8.3 mmHg
(-7.3 to -9.3)
Baseline
(n=314)
Placebo
(n=274)
Spironolactone
25–50 mg
(n=285)
Doxazosin
4–8 mg
(n=282)
Bisoprolol
5–10 mg
(n=285)

Greatest BP reductions with Spironolactone were associated with low renin levels



Williams B, The Lancet 2015

Spironolactone was well tolerated

	Spironolactone	Doxazosin	Bisoprolol	Placebo	p value*
Serious adverse events	7 (2%)	5 (2%)	8 (3%)	5 (2%)	0·82
Any adverse event	58 (19%)	67 (23%)	68 (23%)	42 (15%)	0·036
Withdrawals for adverse events	4 (1%)	9 (3%)	4 (1%)	3 (1%)	0·28

- No difference in serious adverse events
- Hyperkalemia >6.0 mmol/L occurred in 2% of patients exposed to spironolactone

Williams B, The Lancet 2015

Spironolactone vs. Eplerenone

- No direct comparison study
- Spironolactone greater BP lowering than eplerenone in mild–moderate hypertension (spironolactone 25–50 mg daily and 50–100 mg daily for eplerenone)
- Eplerenone alternative to spironolactone if anti-androgen side effects

Manolis et al. Curr Hypertens Rep. 2019

Cases

Case HS

- ID: 38 M
- HPI: History of HTN for 2 years
- Tried on HCTZ, bisoprolol, ramipril without improvement
- Home BP 140-160/100
- No exacerbating medications/dietary noncompliance
- No history of TOD
- ROS: Snores, but no choking spells. C/o of hyperhydrosis/palpitations. No symptoms of Cushings, thyroid disease
- PMHx: HTN
- Meds: Bisoprolol 10, ramipril 10, amlodipine 10, fluoxetine 80
- Intolerant HCTZ due to hypoK
- FHx: Father DM2, mother dyslipidemia. No HTN

Case HS

- O/E: L arm 141-156/89-101
- R. arm 133-140/84-93
- Fundoscopy: Normal
- Cardiac: N S1, S2, no S3, S4 or murmurs. No sustained apex
- Abdo: No Renal bruits
- Ext: PPPB x4

- **Labs**
- CBC Normal
- Na 140, K 3.9, Cr 75, eGFR 99
- ECG normal

- **What would you want to do now?**

Case HS

- Work up for secondary causes of HTN
- Calcium normal
- TSH normal
- 24 hour urine norepinephrines 480 (normal 470)
- 24 hour urine metanephrines normal
- Upright Aldosterone 700 (normal for upright <300), renin <0.05, ARR > 14,000 (normal < 1500)

Case HS

- CT adrenals: Small 7 mm tissue nodule on most inferior L. adrenal gland, likely small adenoma

Case HS

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- Adrenal vein sampling:
  - Lateralization to the R. adrenal gland

Case HS

- CT adrenals: Small 7 mm tissue nodule on most inferior L. adrenal gland, likely small adenoma
- Adrenal vein sampling:
  - Lateralization to the R. adrenal gland
- Refer for surgical resection of R. adrenal gland
  - 50-90% show resolution of hypertension
  - If NOT surgical candidate or no lateralization, treat with MRA (spironolactone, eplereone)

Case RM

- ID: 33M
- HPI: HTN dx 1 yr ago.
- BP still not controlled despite up-titration of medications
- Presented to RCH with headache, tinnitus and severe HTN
- 1 month history of diaphoresis, night sweats, severe frontal headache
- PMHx: HTN
- Meds:
  - Amlodipine 10 mg, Ramipril 10 mg
- FHx: Father HTN

Case RM

- O/E: R. arm 185/113,
- L. arm 176/106
- Fundoscopy normal
- Chest clear
- Cardiac exam: N S1, S2 no S3, S4, EHS. JVP 1 cm
- Abdo: No renal bruits

- Labs: Normal CBC, lytes, Cr

ECG: LVH

- **What do you want to do next?**

Case RM

METANEPHRINE EXCRETION	0.26-1.73 umol/d	0.69	6 Aug 18		<0.15 l
NORMETANEPH EXCRETION	0.48-2.42 umol/d	17.01 h @b4	6 Aug 18		85.22 h @
VMA EXCRETION	10-35 umol/d	118 h @b4	16 May 20		201 h @b4
NOREPINEPH EXCRETION	89-470 nmol/d	6612 h	16 May 20		19921 h @d0
EPINEPHRINE EXCRETION	<160 nmol/d	<101	16 May 20		<29
DOPAMINE EXCRETION	0.4-3.3 umol/d	1.4	16 May 20		2.5
CATECHOLAMINES COMMENT		See Detail @b4	16 May 20		See Detail @b4
URINE VOLUME	0.600-2.400 L	5.047 h	16 May 20		1.468
NUMBER OF HOURS	hrs	24	16 May 20		24

Normetanephrine 35 x ULN
VMA 5.7x ULN
Norepinephrine: 42 x ULN

CT head: highly vascular aggressive mass in the right spenoid bone and right spenopalantine foramen. Destruction of the bone and extracranial intracranial invasion of the right middle fossa. Encasement of cavernous sinus right ICA and multiple cranial nerves

Case RM: How to titrate anti-hypertensive medications prior to surgery?

- Goals: controlling HTN and tachycardia and volume expansion
- Alpha blockade prior to OR (at least 7 days prior to OR)
  - Short acting: Doxazosin, prazosin, terazosin
  - Long acting: Phenoxybenzamine
- Aim for seated BP < 120/80 and standing SBP > 110 in a standing position
- High sodium diet (> 5 g per day) and hydration to limit the affects of catecholamine-induced volume contraction and orthostasis
- Beta-blockers (after adequate alpha-blockade)
- CCB (amlodipine)

Post-op

- Most cases can stop all BP meds postop
  - Postop hypotension: IV crystalloid
  - HTN free
    - 5 years 74%
    - 10 years 45%
- 24h urine or plasma MN few wks post-op
- Surveillance:
  - 24h urine collections q1yr for at least 10yrs
  - Lifelong follow-up for high risk
    - Young, large tumour, genetic +, extra-adrenal PPGL
  - Imaging/scope if silent depending on site

Case SB

- ID: 65F
- HPI: HTN dx 8 yrs ago.
- Increased anti-HTN meds
- BP at home 130-150/68-72
- Remote history of irregular renal arteries seen 25 years ago
- ROS: No symptoms of OSA, pheochromocytoma, Cushings, Thyroid disease
- Ppt meds: HRT, no NSAIDS
- PMHx: HTN, Asthma, GERD
- Meds:
  - Irbesartan 300 mg daily, HCTZ 25 mg daily, Amlodipine 10 mg daily, Premarin 0.25 daily, Progesterone 2.5 mg daily, Tecta 40 mg daily
- FHx: Brother kidney transplant. Mother has HTN/CVA

Case SB

- O/E: R. arm 140-160/80
- L. arm 164/80
- Fundoscopy normal
- Chest clear
- Cardiac exam: N S1, S2 no S3, S4, EHS. JVP 1 cm
- Abdo: No renal bruits

- Labs: Normal CBC, lytes, Cr
- CT scan: calcification of the ostium with mild to moderate focal narrowing of the R. renal artery (approx. 50%)

- **What do you want to do next?**
- **Would you recommend stenting to help with renovascular HTN?**

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Stenting and Medical Therapy for Atherosclerotic Renal-Artery Stenosis

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NEJM 2014; 370; 13-22.

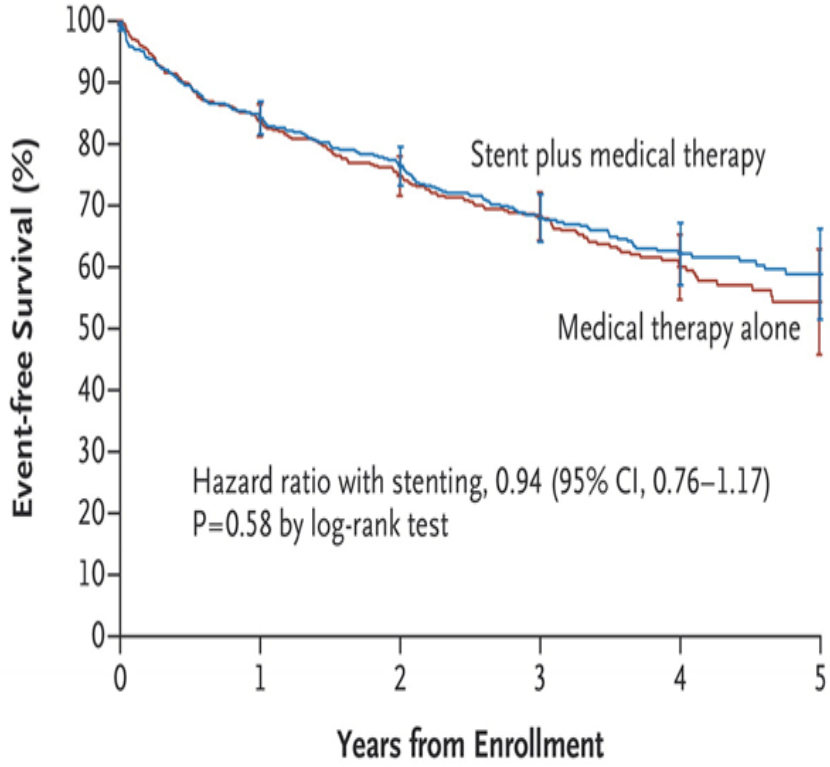
CORAL

947 Patients:
-HT with SBP≥155 while on ≥2 drugs; **OR**
-CKD: GFR <60 mL/min/1.73 m^2 **AND**
-RAS ≥80% or ≥60% with SBP gradient ≥20 mmHg

Intervention (1:1):
-Palmaz Genesis stent (Cordis)

Concurrent Medical Rx:
-antiplatelet;
-Anti-HT to <140/90 (DM: 130/80) with candesartan, HCTZ, amlodipine;
-lipid Rx (atorvastatin); glucose

Primary Outcome:
-Composite: Death (CV/renal), stroke, MI, stroke, HF hosp, prog renal insuff, perm RRT



No. at Risk						
Medical therapy alone	472	371	314	214	115	40
Stent plus medical therapy	459	362	318	224	131	59

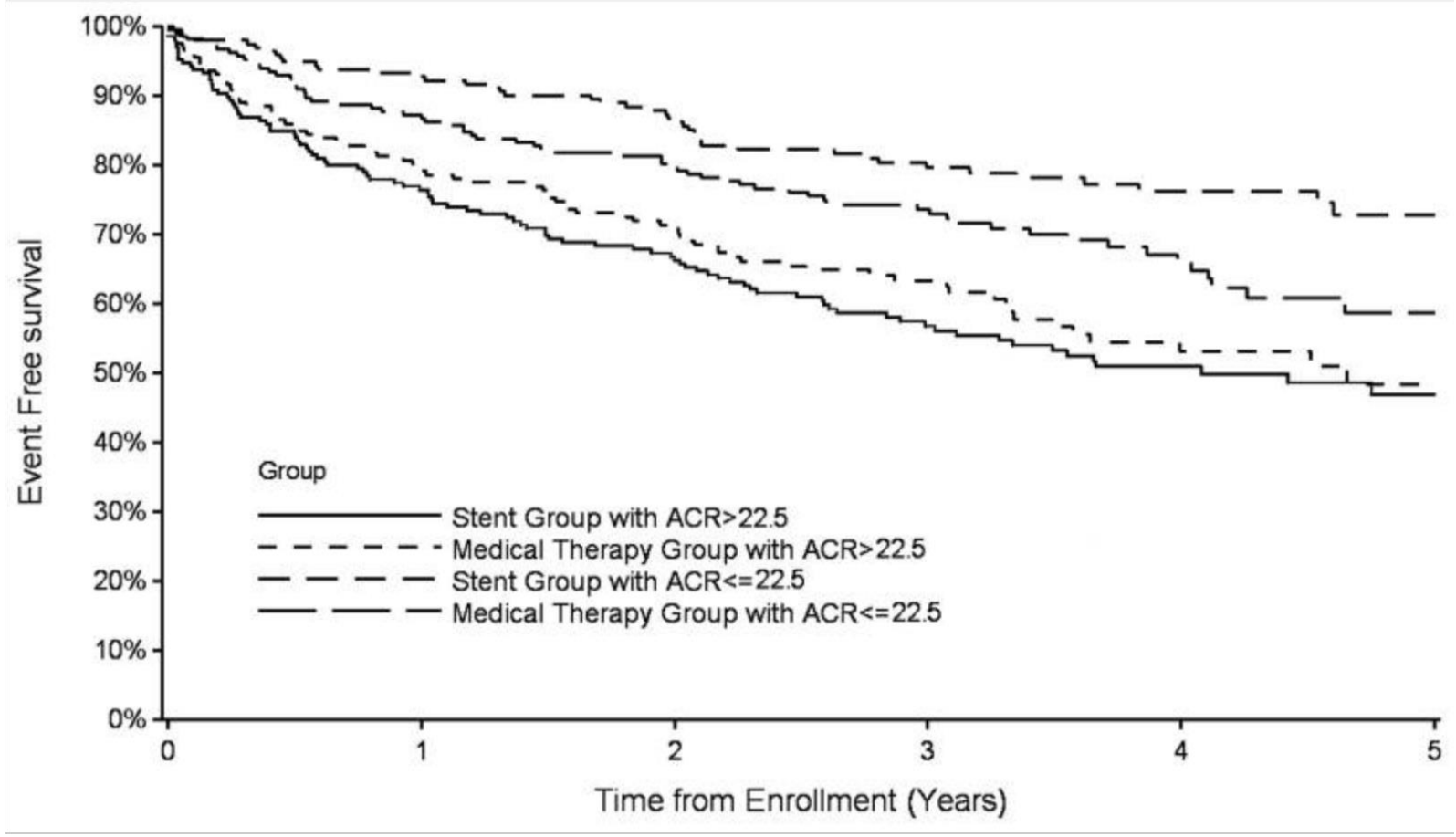
NEJM 2014; 370; 13-22.

CORAL

- **Conclusion:**
  - Renal-artery stenting did not confer a significant benefit with respect to the prevention of clinical events when added to comprehensive, multifactorial medical therapy in people with atherosclerotic RAS and HTN or CKD.

NEJM 2014; 370; 13-22.

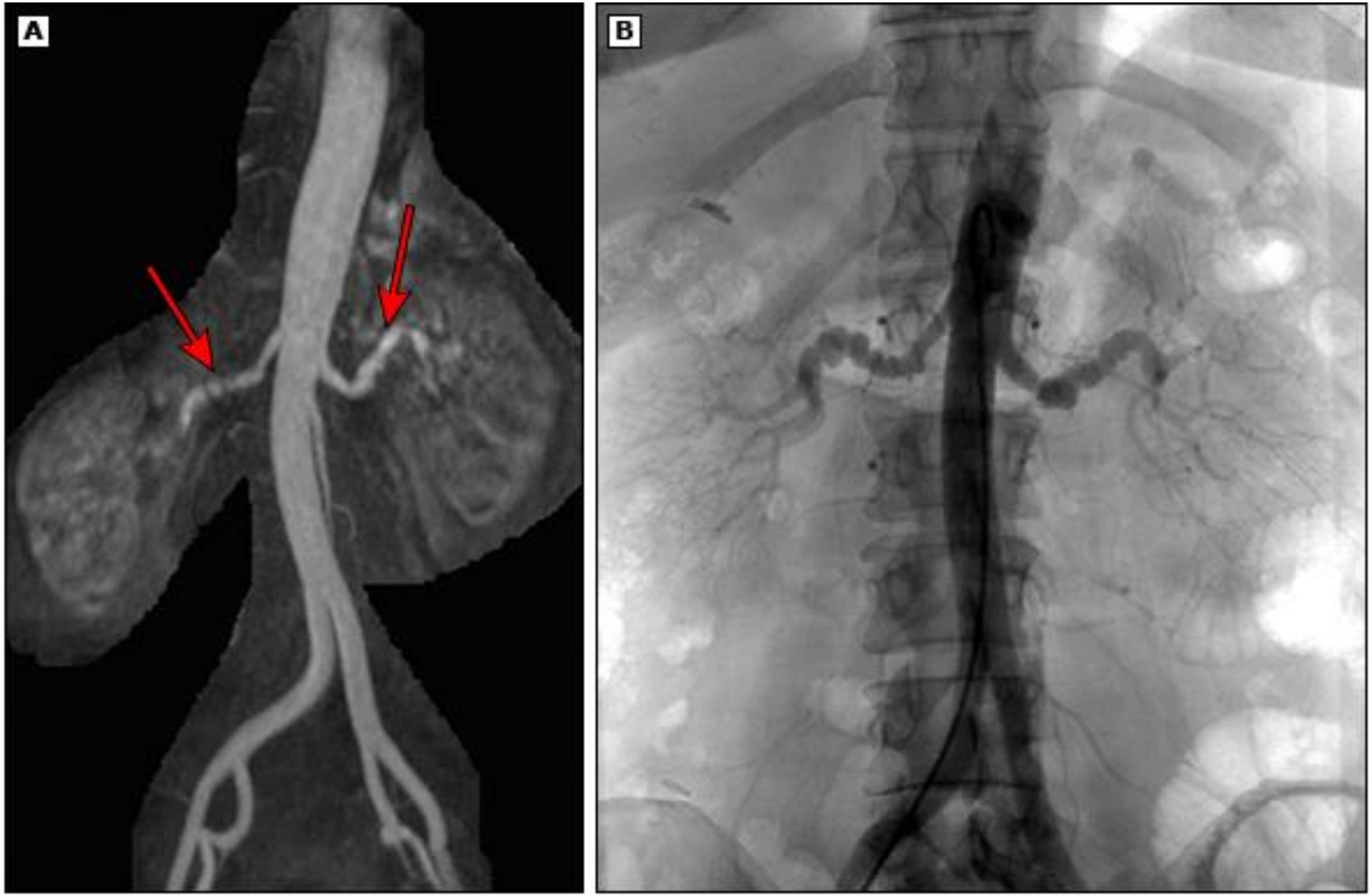
CORAL: Impact of Albuminuria



Murphy et al. Hypertens 2016; 68(5):1145-1152.

Case SB

- 24 hour ambulatory BP monitoring: daytime BP 129/63 with nocturnal dipping
- TSH, Calcium normal
- Aldosterone 137, Renin 0.82
- CT imaging reviewed by Vascular Radiologists/Vascular Surgeons
  - Irregularities on the R. renal artery consistent with fibromuscular dysplasia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Case SB

- 24 hour ambulatory BP monitoring: daytime BP 129/63 with nocturnal dipping
- TSH, Calcium normal
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- CT imaging reviewed by Vascular Radiologists/Vascular Surgeons
  - Irregularities on the R. renal artery consistent with fibromuscular dysplasia
  - Given BP controlled on 3 agents, and that segment of irregularity long, there is a high risk of complications
  - Recommend medical treatment of BP, no angioplasty

Summary Implications

- Resistant Hypertension represents a population at high risk of morbidity and mortality
- Requires careful identification with a focus on measurement, adherence and exclusion of secondary causes
- Majority of RCTs and physiologic data support use of Spironolactone as 4th line agent
- Use of an agent from different class to lower BP may be an alternative

THANK YOU

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