Mass General Brigham

Primary Aldosteronism

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Disclosures

Consulting: HRA Pharma, Mineralys, Corcept, AstraZeneca, Moderna, Vertex

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Training

Harvard Medical School

Internal Medicine Residency @BWH

Clinical Endocrinology Fellowship @BWH

Cardiovascular Endocrinology Research Post-Doc @BWH

Positions

Chief, Division of Endocrinology, Diabetes, and Metabolism

Director, Center for Adrenal Disorders

Associate Professor of Medicine

Director, e-Learning Initiative BWH/NEJM

Key Learning Points

1955

Primary aldosteronism is a rare, hormonal cause of essential hypertension

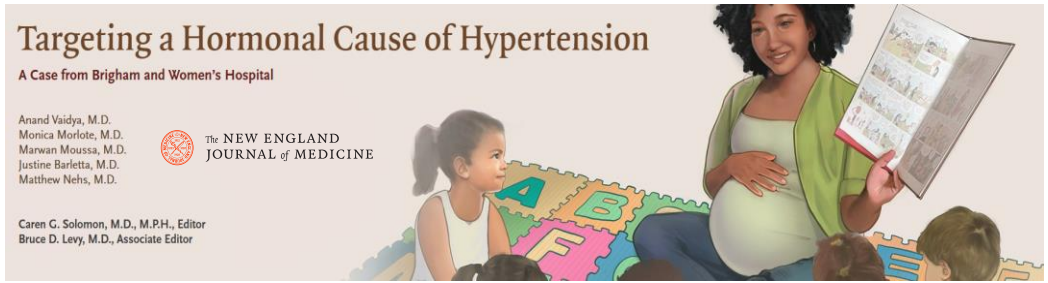
2026

“Essential hypertension” is *primarily* aldosteronism

Resources

Primary Aldosteronism: An Endocrine Society Clinical Practice Guideline

Gail K. Adler,[1] Michael Stowasser,[2] Ricardo R. Correa,[3] Nadia Khan,[4] Gregory Kline,[5] Michael J. McGowan,[6] Paolo Mulatero,[7] M. Hassan Murad,[8] Rhian M. Touyz,[9] Anand Vaidya,[1] Tracy A. Williams,[10] Jun Yang,[11,12] William F. Young,[8] Maria-Christina Zennaro,[13,14] and Juan P. Brito[8,15]



The Curbsiders Podcast

Primary Aldosteronism

Ubiquitous, Yet Unrecognized

Jenifer M. Brown, MD,[a,b] Anand Vaidya, MD, MMSc[a]

Redefining Primary Aldosteronism

Anand Vaidya, MD, MMSc,[a] Jenifer M. Brown, MD[b]

Vaidya et al. NEJM 2025
Brown & Vaidya. JACC 2025
Adler, al. JCEM 2025
Vaidya et al. JACC 2026

What is Primary Aldosteronism?

PATHOPHYSIOLOGIC SYNDROME:

- Inappropriate aldosterone production: **renin-independent aldosterone production, relatively non-suppressible**
- Excessive activation of the MR, vicious cycle of volume expansion, hypertension, **CV and Kidney disease *independent of BP***

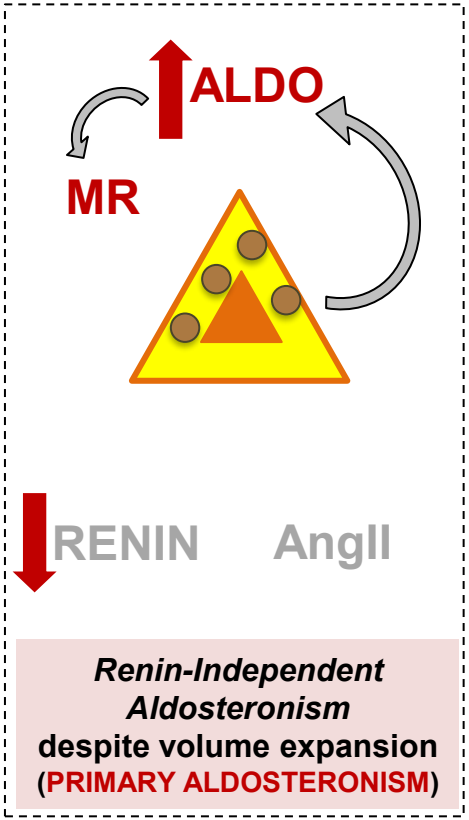
Clinical Manifestations:

Most patients **do not have** hypokalemia or Resistant HTN

Hallmark Biochemical Diagnostics:

Low or Suppressed Renin

Inappropriate/Dysregulated Production of Aldosterone



Vaidya et al. Endocrine Reviews 2018

Case

36-year old woman presents for hypertension management

Age 27: 1st pregnancy, preeclampsia => Persistent HTN => nifedipine

Age 28 (CCB)	Age 32 (no meds)	Age 33 (CCB, **ACEi**)	Age 36 (CCB, **ACEi**)
PAC (LC-MS/MS): 8.3 ng/dL (230 pmol/L)	PAC (LC-MS/MS): 6.6 ng/dL (183 pmol/L)	K 3.3 mEq/L	PAC (LC-MS/MS): 8.1 ng/dL (225 pmol/L)
PRA <0.6 ng/mL/h	PRA <0.6 ng/mL/h		PRA <0.6 ng/mL/h
ARR >14	ARR >11		ARR >14
K 4.1 mEq/L	K 4.4 mEq/L		K 4.3 mEq/L

Vaidya et al. NEJM 2025

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ARR >14	ARR >11		ARR >14
K 4.1 mEq/L	K 4.4 mEq/L		K 4.3 mEq/L

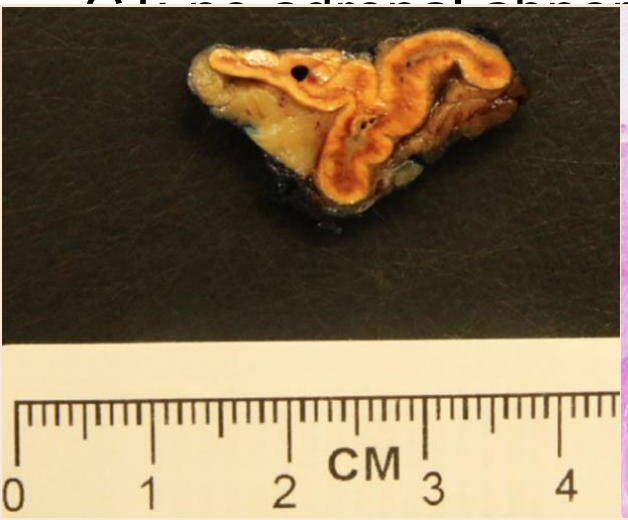
Does she have primary aldosteronism?

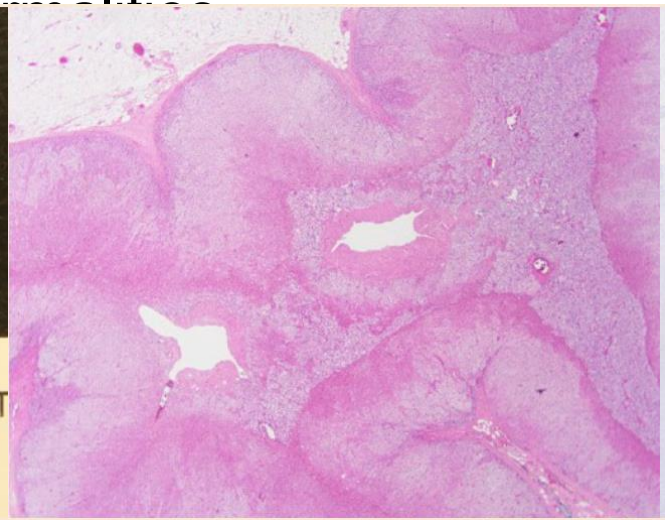
A. Yes, obvi
B. Maybe, depends on aldosterone suppression testing results
C. Maybe, repeat testing after washing out medications
D. No

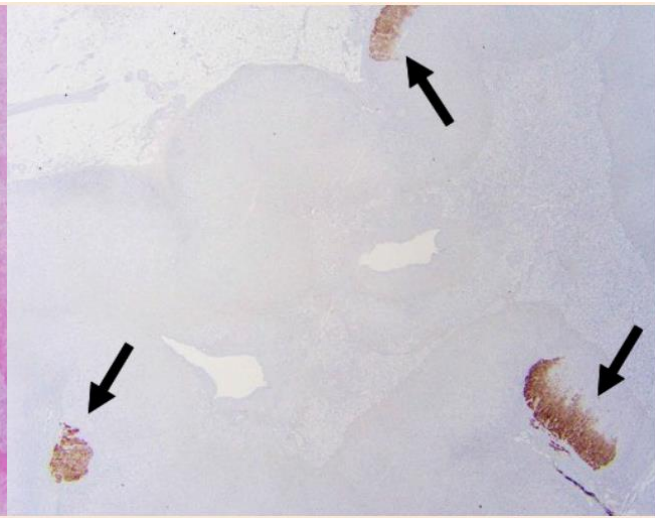
Vaidya et al. NEJM 2025

Case

CT: no adrenal abnormalities







OUTCOME: Normotensive, normokalemic, without medications

Vaidya et al. NEJM 2025

Pathogenesis of PA

Key Point: The vast majority of primary aldosteronism is attributable to *diffuse and bilateral* foci of autonomous aldosterone production

Pathogenesis & Morphologies of PA

Early Life

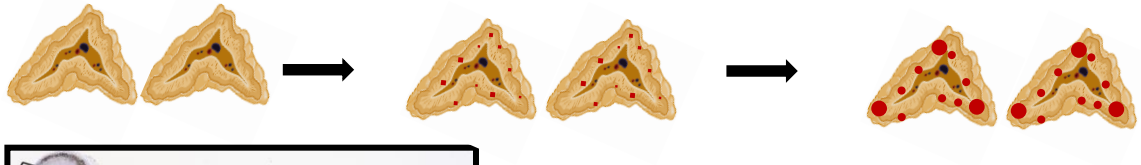
Normal Physiology & Structure

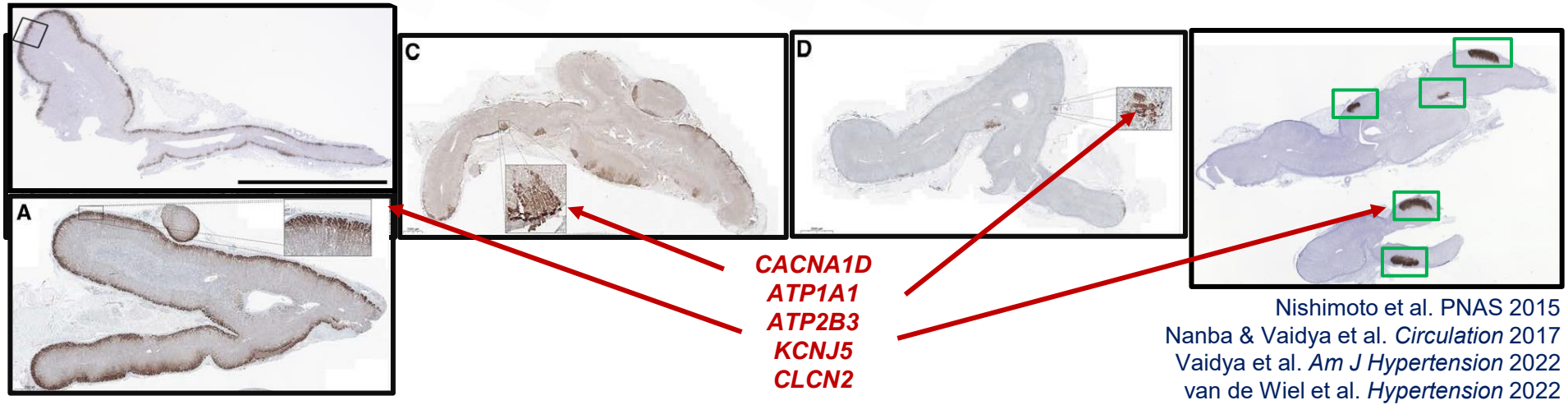
- Continuous CYP11B2 in ZG
- No neoplasia

Progressive Aging

Primary Aldosteronism with Morphologically Normal Adrenal Glands

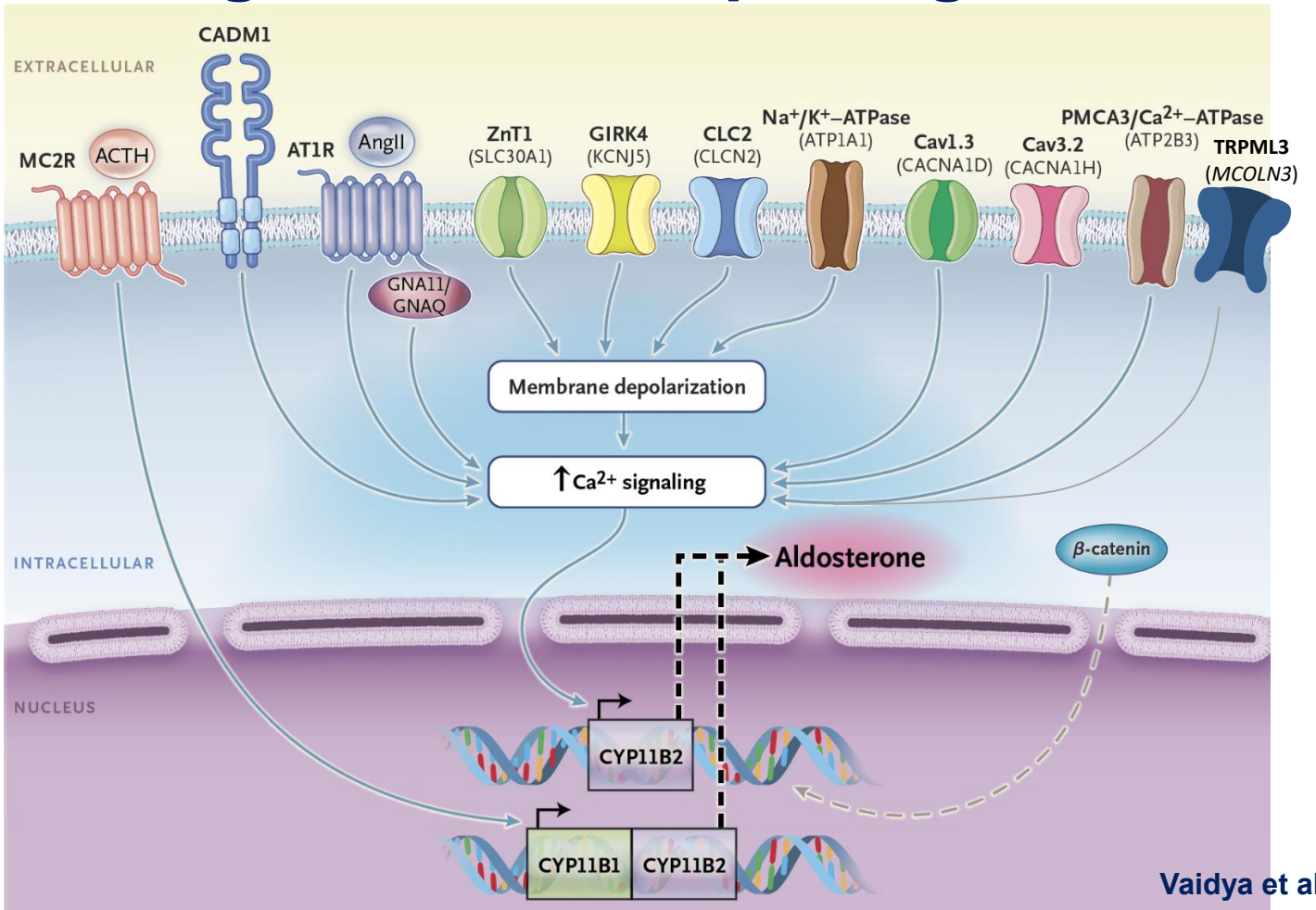
- Progressive loss of continuous ZG
- Emergence of Aldosterone Producing Cell Clusters
- Aldo-Driver somatic mutations within APCCs





Nishimoto et al. PNAS 2015
Nanba & Vaidya et al. *Circulation* 2017
Vaidya et al. *Am J Hypertension* 2022
van de Wiel et al. *Hypertension* 2022

Pathogenesis & Morphologies of PA



Vaidya et al. *NEJM* 2025

Genetic Mutations Affecting *Zona Glomerulosa* Cells to Cause Primary Aldosteronism

Mutation		Inheritance		Consequences
Gene	Protein	Germline	Somatic	
CYP11B1/CYP11B2 hybrid	CYP11B1/CYP11B2 fusion	X		Fusion of *CYP11B1* promoter to the 5'-end of *CYP11B2* such that CYP11B2 expression is regulated by adrenocorticotropic hormone (ACTH). Cause of familial hyperaldosteronism type I.
CLCN2	CLC2	X	X	Increases chloride ion efflux, which results in a lower membrane depolarization threshold. Cause of familial hyperaldosteronism type II when germline variant.
KCNJ5	GIRK4	X	X	Permits sodium ion influx, which results in a lower membrane depolarization threshold. Cause of familial hyperaldosteronism type III when germline variant.
CACNA1D	Cav1.3	X	X	Increases calcium ion influx, which causes membrane depolarization. Cause of familial hyperaldosteronism type IV when germline variant.
ATP1A1	Na^+/K^+–ATPase		X	Increases influx of sodium and hydrogen ions, which results in a lower membrane depolarization threshold.
ATP2B3	PMCA3/Ca^{2+}–ATPase		X	Increases influx of sodium and calcium ions, which results in a lower membrane depolarization threshold.
CACNA1H	Cav3.2		X	Increases calcium ion influx, which causes membrane depolarization.
CTNNB1	β–catenin		X	Increases β–catenin signaling, which in concert with other genomic and nongenomic factors can synergize primary aldosteronism pathophysiology.
GNA11/GNAQ	GNA11/GNAQ		X	Increases G-protein signaling, which in turn increases intracellular calcium signaling.
CADM1	CADM1		X	Inhibits gap-junction permeability.
SLC30A1	ZnT1		X	Increases sodium ion influx, which results in a lower membrane depolarization threshold.
MCOLN3	TRPML3		X	Increases sodium and calcium ion influex, which results in lower membrane depolarization threshold

<<1% of all PA is due to inheritable/germline mutations

>95% of all unilateral APA surgical specimens harbor ***pathogenic somatic mutations***

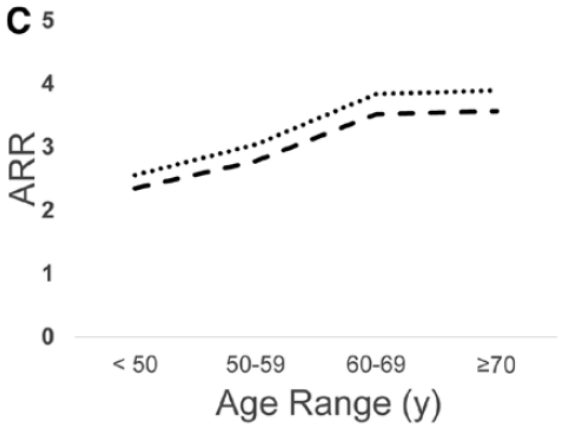
>60% of all bilateral PA surgical specimens harbor ***pathogenic somatic mutation***

PA is largely a genetic disorder driven by somatic mutagenesis in the adrenal cortex

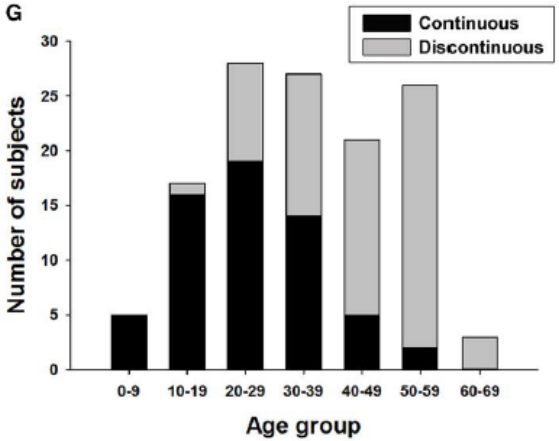
Vaidya et al. NEJM 2025

Morphologically normal adrenals/no neoplasia

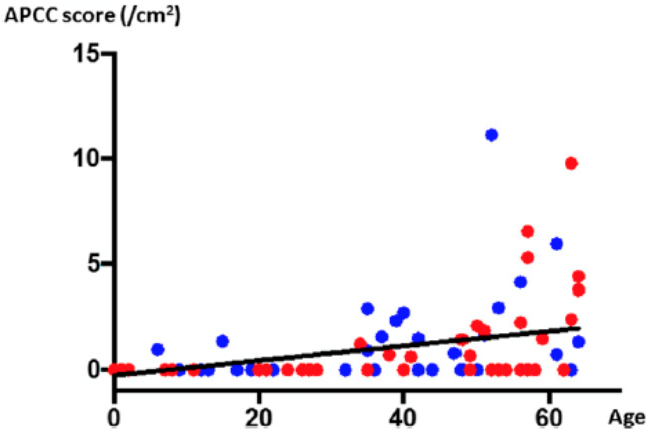
- Time/Age-dependent dysregulation CYP11B2 expression
  (loss of continuous ZG and emergence of APCCs)
- Enriched with Pathogenic Somatic Mutations in Aldosterone Driver Genes
- Bilateral process



Newman et al. *Hypertension* 2026



Nanba & Vaidya et al. *Circulation* 2017



Omata et al. *JES* 2017

Pathogenesis & Morphologies of PA

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Progressive Aging

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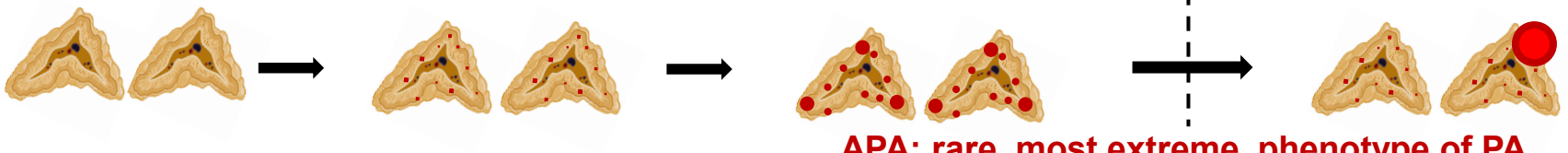
Stochastic Collision/Co-Occurrence

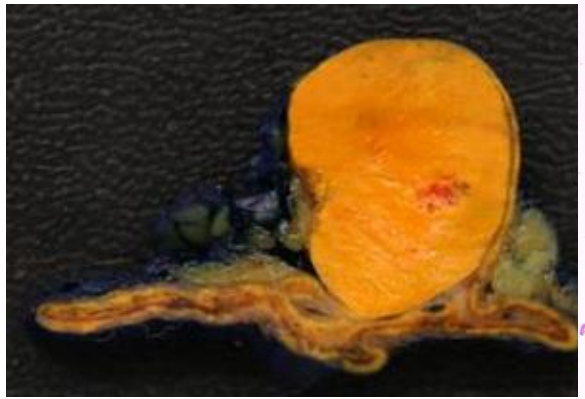
Neoplastic PA

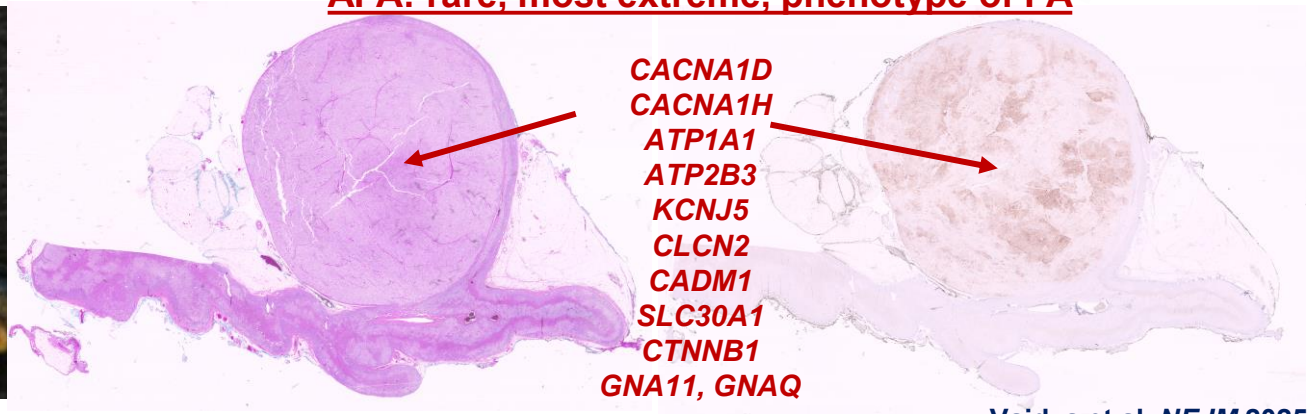
Overt Primary Aldosteronism with Aldosterone Producing Adenoma

- Aldo-Driver somatic mutations *within* adrenocortical neoplasia



APA: rare, most extreme, phenotype of PA



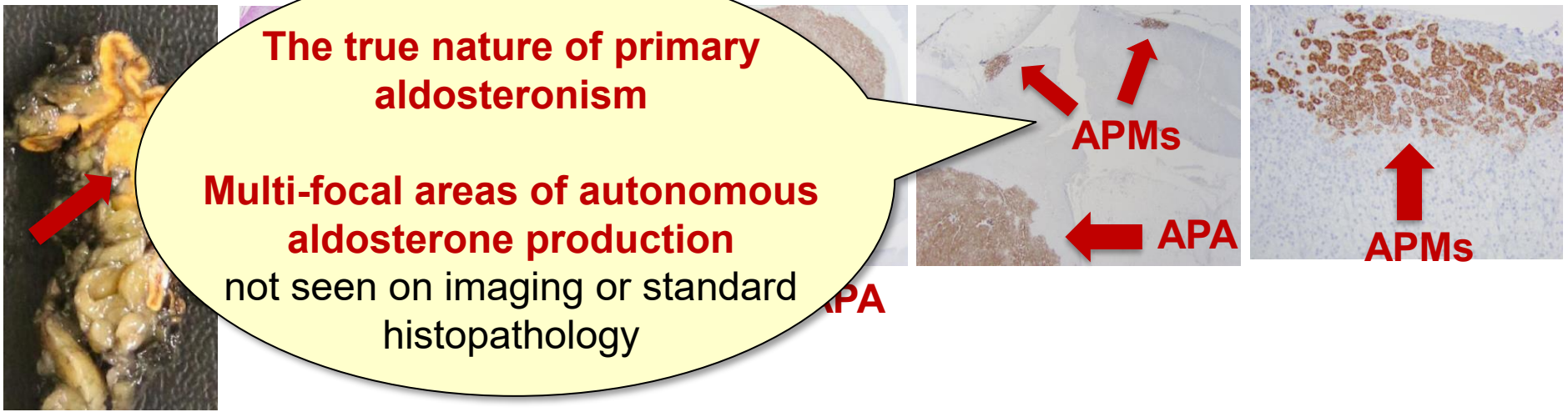


Vaidya et al. *NEJM* 2025

Vaidya et al. *Am J Hypertension* 2022

The True Nature of Primary Aldosteronism

38yoM with severe, classic PA: rHTN (5 meds)+ hypokalemia
K 3.1 mEq/L; PRA 0.33 ng/mL/h, PAC 40 ng/dL
Preferred medical therapy: Eplerenone 75mg BID + HCTZ 25mg QD (2 meds)
(BP 120/70 mmHg, K 4.3 mEq/L)
Medical therapy (MRAs) can be very effective!



Vaidya et al. *NEJM* 2025
Parisien-La Salle et al. *Hypertension* 2026

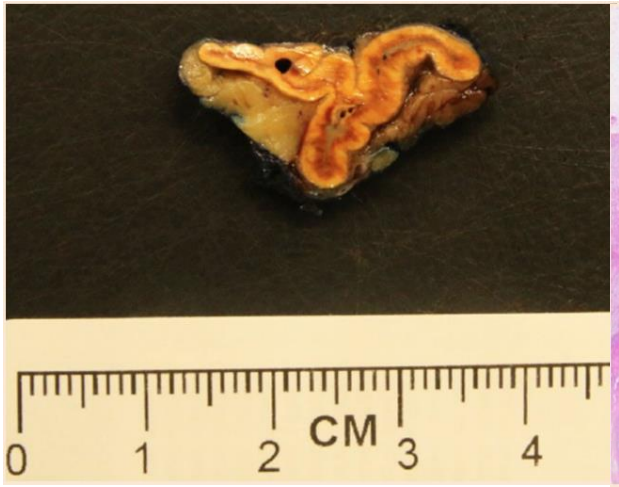
The True Nature of Primary Aldosteronism

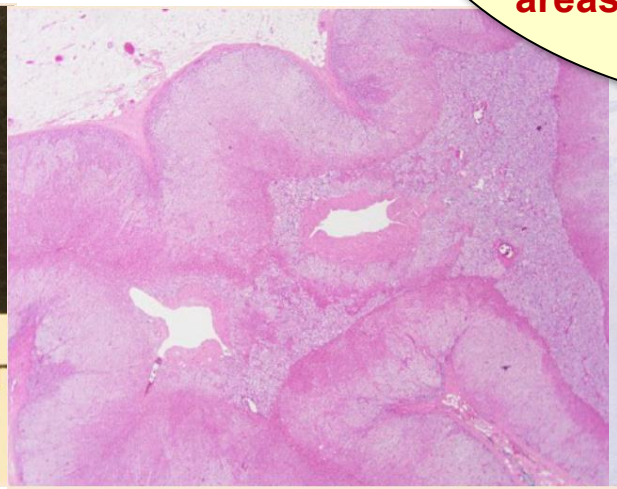
36yoF with HTN
No hypokalemia
No adrenal abnormalities on CT
PRA<0.6 ng/mL/h; Aldosterone 6.6-8.3 ng/dL
AVS lateralized to the right
Right adrenalectomy
Post-op remission

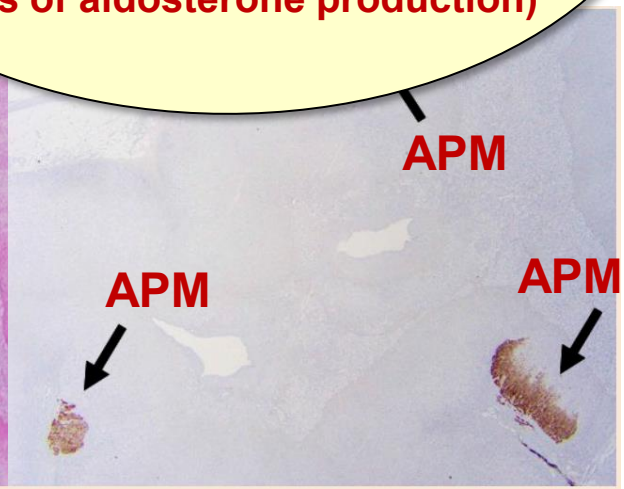
No hypokalemia?
No adrenal mass?
Aldosterone levels in single digits?

Is this Primary "Hyper"aldosteronism?

YES – this is the true nature of primary aldosteronism (renin-independent aldosterone production due to multi-focal areas of aldosterone production)







Vaidya et al. *NEJM* 2025
Parisien-La Salle et al. *Hypertension* 2026

Prevalence

Severity of Primary Aldosteronism

Early Life

Normal Physiology & Structure

- Continuous CYP11B2 in ZG
- No neoplasia

Progressive Aging

Primary Aldosteronism with Morphologically Normal Adrenal Glands

- Progressive loss of continuous ZG
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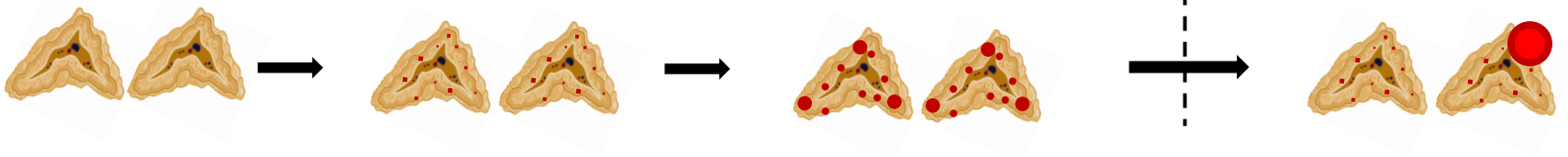
Stochastic Collision/Co-Occurrence

Neoplastic PA

Overt Primary Aldosteronism with Aldosterone Producing Adenoma

- Aldo-Driver somatic mutations *within* adrenocortical neoplasia



Almost universally unrecognized

Vaidya et al. *NEJM* 2025

Vaidya et al. *Am J Hypertension* 2022

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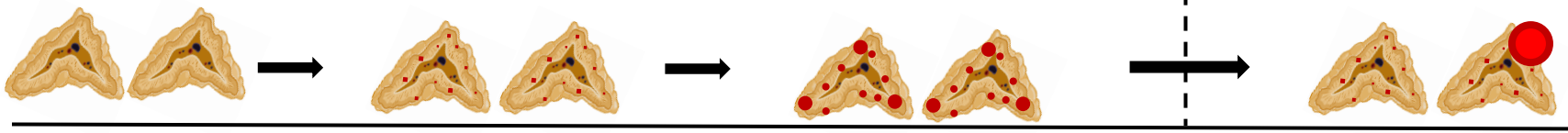
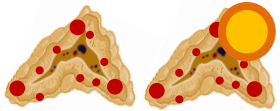


Other Stochastic Collisions/Co-Occurrence

Primary Aldosteronism with Incidental Non-functional Adenoma

- APCCs with somatic mutations
- Incidental non-functional adrenocortical tumor



Vaidya et al. *NEJM* 2025
Vaidya et al. *Am J Hypertension* 2022

The True Nature of Primary Aldosteronism

56yoF wit
CT wit
AVS
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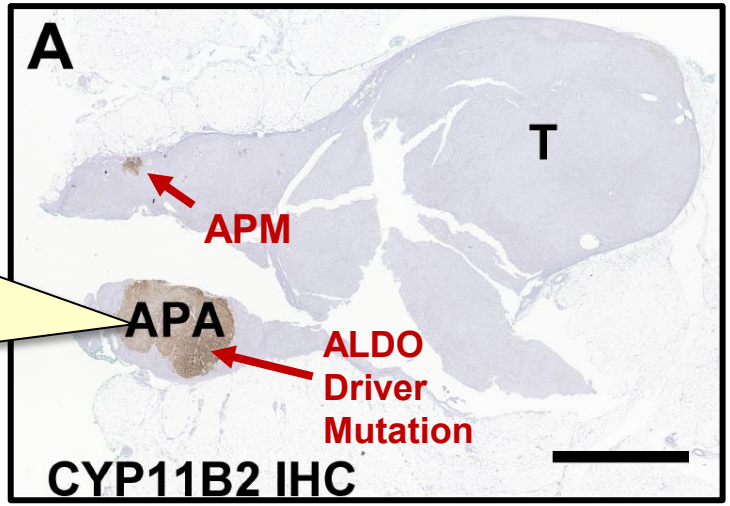
The true nature of primary aldosteronism

Multi-focal areas of autonomous aldosterone production
not seen on imaging or standard histopathology



Nanba et al. JCEM 2018

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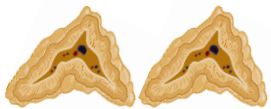

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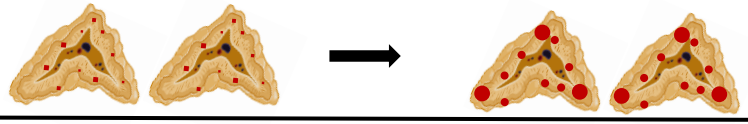

Stochastic Collision/Co-Occurrence

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Overt Primary Aldosteronism with Aldosterone Producing Adenoma

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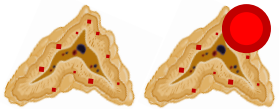

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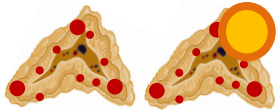
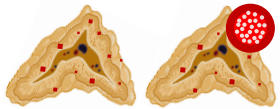
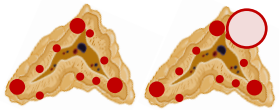


Overt Primary Aldosteronism *with* Mild or Overt Hypercortisolism

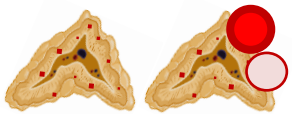
Scenario 1:
Somatic mutations that induce heterogeneous aldosterone *and* cortisol production *within* adrenocortical neoplasia



Scenario 2:
- ↑Aldo-Driver somatic mutations/APCCs
- *Only* cortisol-driver somatic mutations *within* adrenocortical neoplasia



Scenario 3:
Independent adrenocortical neoplasia containing Aldo- and Cortisol-driver somatic mutations



Vaidya et al. *NEJM* 2025
Vaidya et al. *Am J Hypertension* 2022

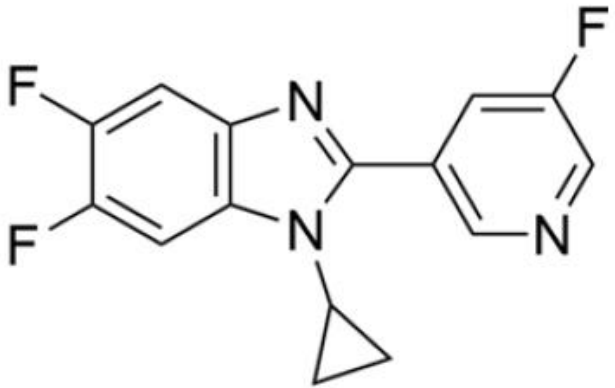
Pathogenesis & Morphology of PA

Nearly all PA is caused by *pathogenic somatic mutations* resulting in microscopic foci of autonomous aldosterone production

These foci of aldosterone production generally arise *diffusely and bilaterally*, accumulate with age

The absence of an adrenal mass or hypokalemia does not exclude the possibility of PA; the presence of an adrenal mass(es) does not imply that it is the source of PA

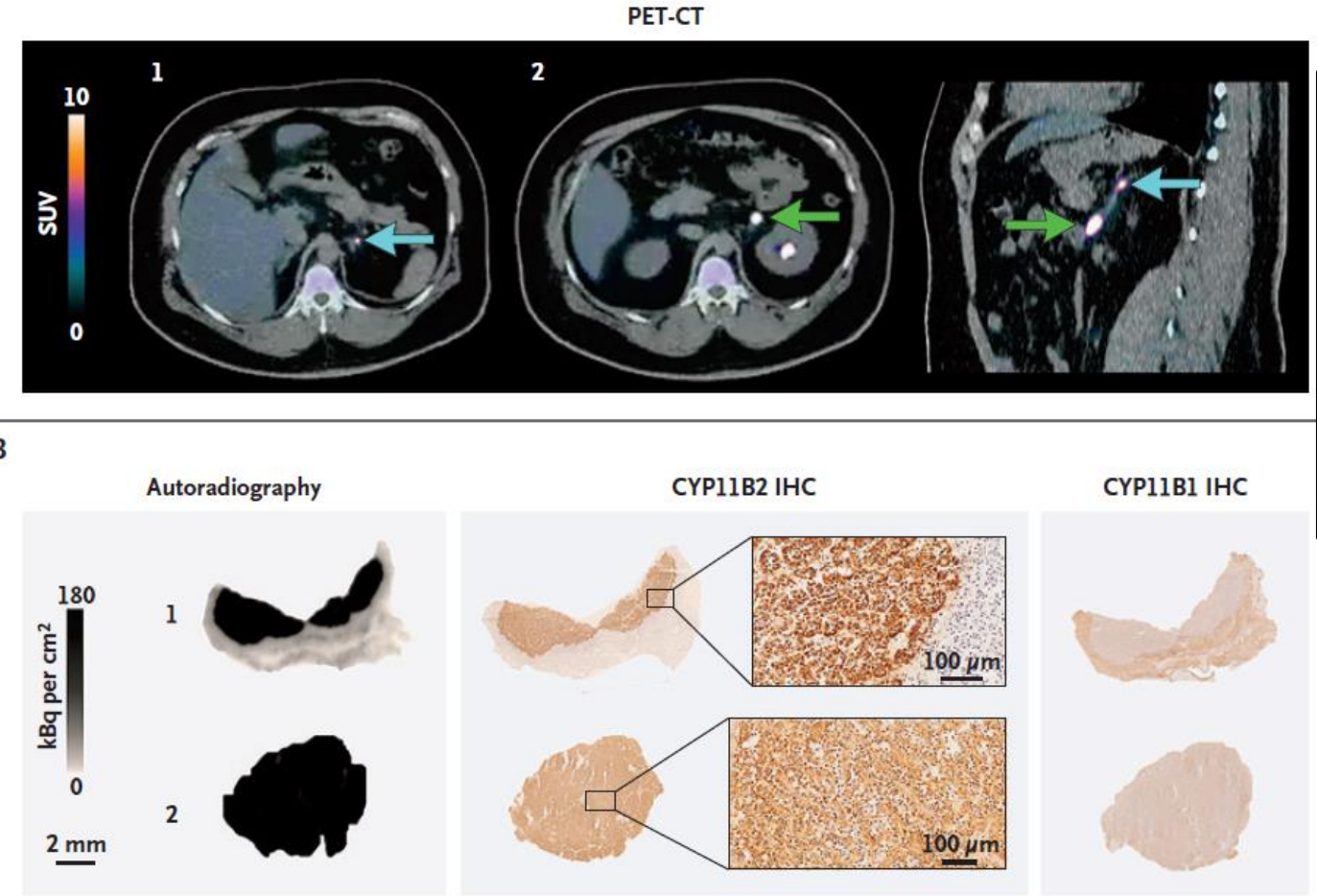
CYP11B2-Specific Radioligand



^{18}F-labeled CYP11B2-specific ligand
“ALDOVIEW”

Arstad et al. NEJM 2025

CYP11B2-Specific Radioligand



CT: no nodules

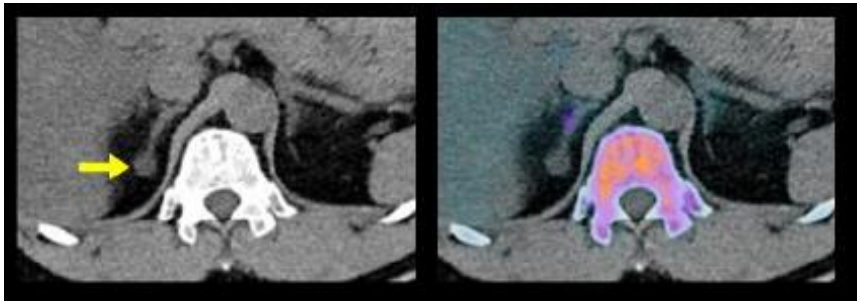
AVS: L lateralization

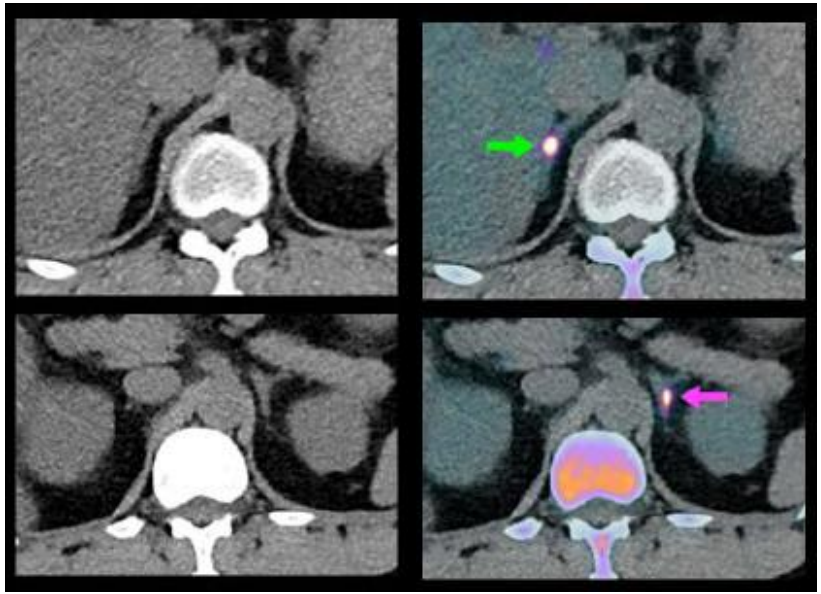
PET: 2 CYP11B2+ lesions

Dx: Unilateral, multi-focal, PA

Arstad et al. NEJM 2025

CYP11B2-Specific Radioligand





CT: R adrenal nodule

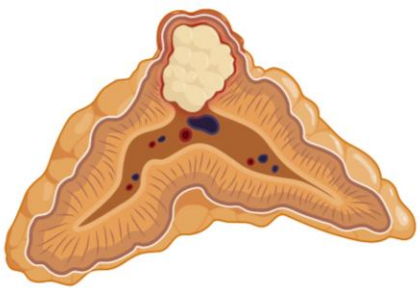
AVS: R lateralization

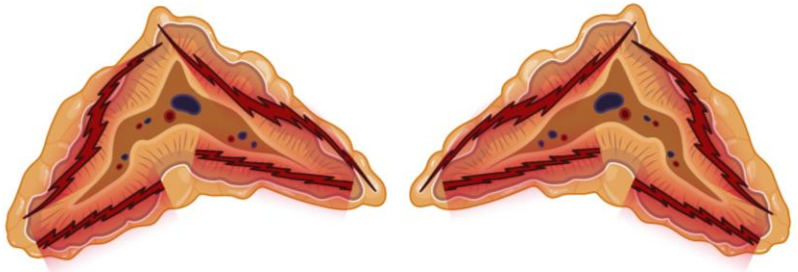
PET: Nodule is NOT CYP11B2+, 2 bilateral microscopic CYP11B2+ lesions

Dx: Bilateral, multi-focal, non-adenomatous, PA + an incidental adrenal adenoma

Arstad et al. NEJM 2025

Seeing is Believing





~~"Unilateral"~~
~~"Aldosterone-producing adenoma"~~

vs.

~~"Bilateral"~~
~~"Adrenal Hyperplasia"~~

The majority of primary aldosteronism is attributable to diffuse, bilateral, microscopic foci of aldosterone production

Testing for PA

Key Points: The traditional landscape of PA testing was dominated by *relatively arbitrary* and *unnecessarily complex* practices that relied on *unvalidated* diagnostic thresholds…

A plasma aldosterone and renin, without stopping medications, is a simple method to effectively test for PA…

***Any* renin-independent aldosterone production is indicative of PA Pathophysiology amenable to targeted therapy**

Continuum of Primary Aldosteronism

Arbitrary/conventional diagnostic thresholds aside

How common is "*inappropriate, non-suppressible, renin-independent aldosterone production*"
(aka *Primary Aldosteronism Pathophysiology*)?

Aldosterone Suppression Test → **Visualize the spectrum of PA**
(agnostic of conventional thresholds)

Continuum of Primary Aldosteronism

Oral Sodium Suppression Test

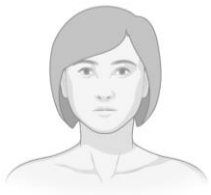
Brown et al. *Annals of Int Med* 2020

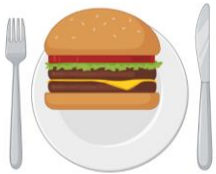
Continuum of Primary Aldosteronism

Oral Sodium Suppression Test

Supplemental Na^+ Intake

~2-4 g/d x 3-4 days





+

Mean U.S. Dietary Na^+ Intake

~3.5 g/d

Net Summary

~4-6 g/d Na^+ x 3-4d
~1.5 L/d H_2O/NS x 3-4d

Physiologic Expectations

ECV/IVV Expansion
↓Renin
↓AngII
↓**Aldosterone**

Brown et al. *Annals of Int Med* 2020

Continuum of Primary Aldosteronism

CONTINUUM: severity spectrum of non-suppressible, renin/AngII-independent aldosterone production

This is physiologic

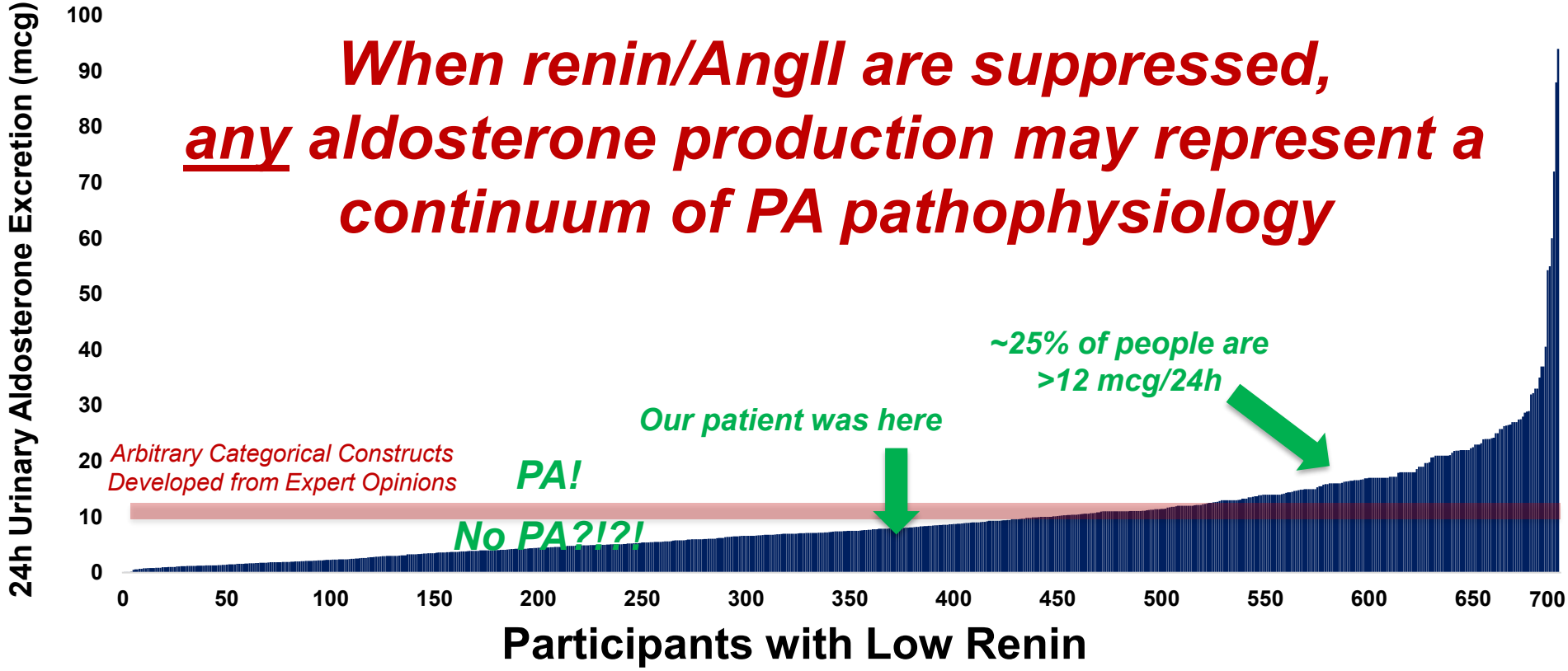
When does physiology end?
When does pathophysiology begin?

This is pathophysiologic (aka overt PA)

Participants with Low Renin

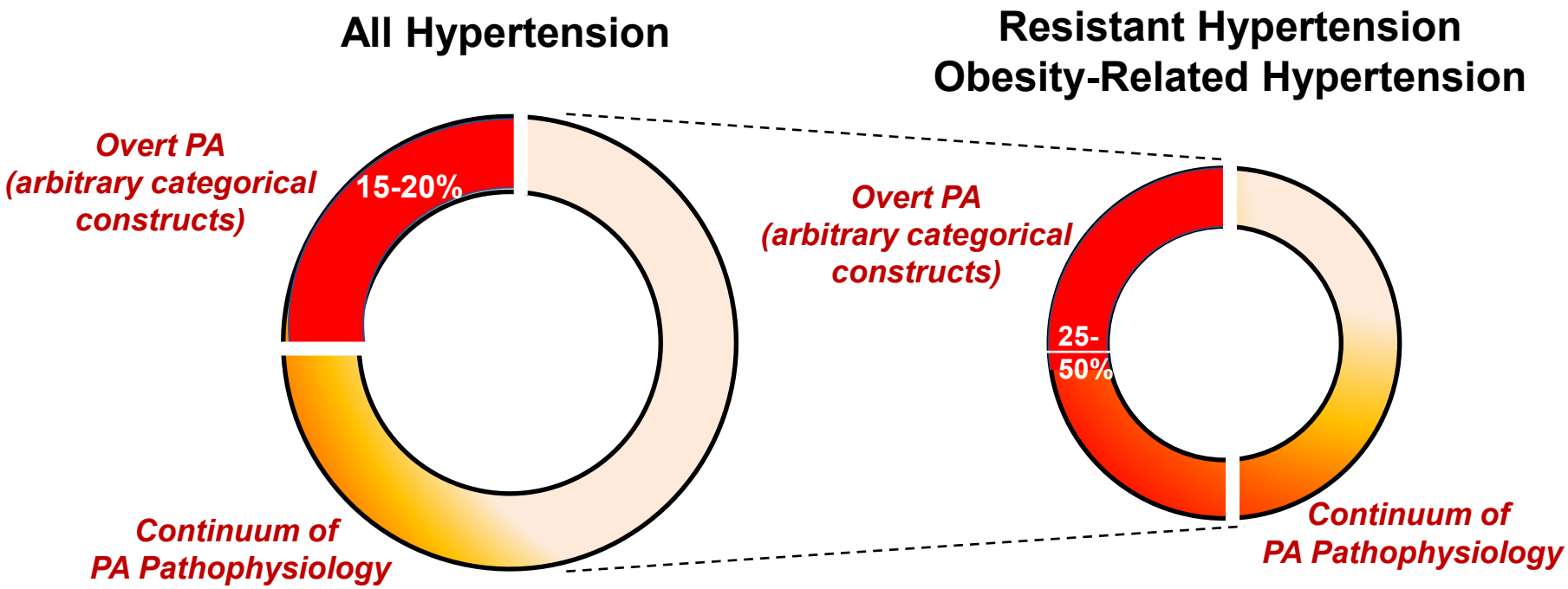
Brown et al. *Annals of Int Med* 2020

Continuum of Primary Aldosteronism



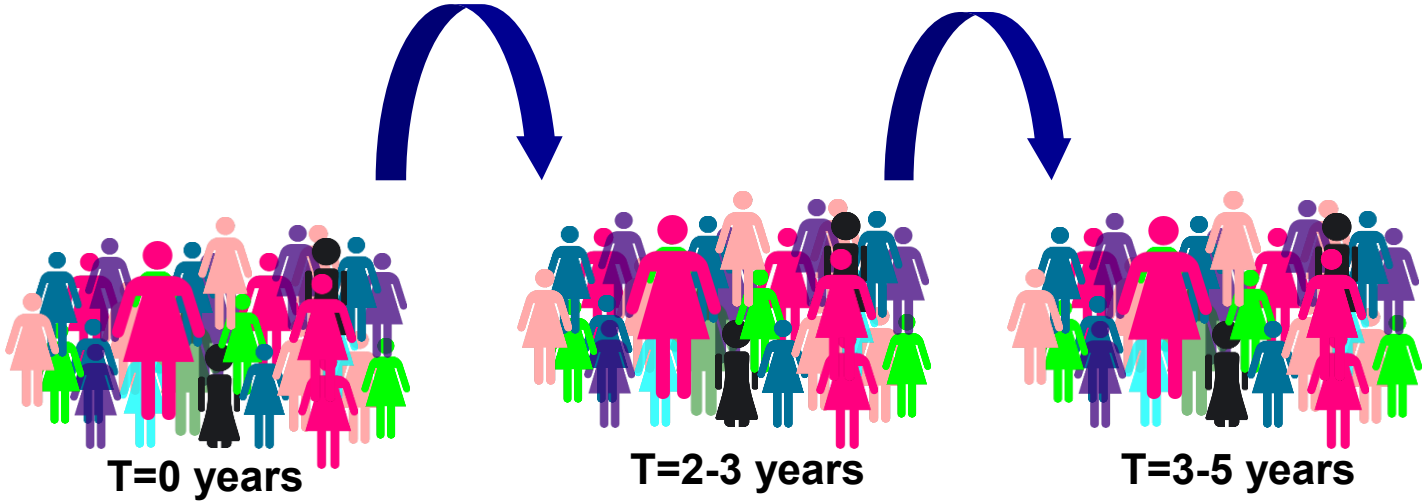
Brown et al. *Annals of Int Med* 2020

The Prevalence of Primary Aldosteronism

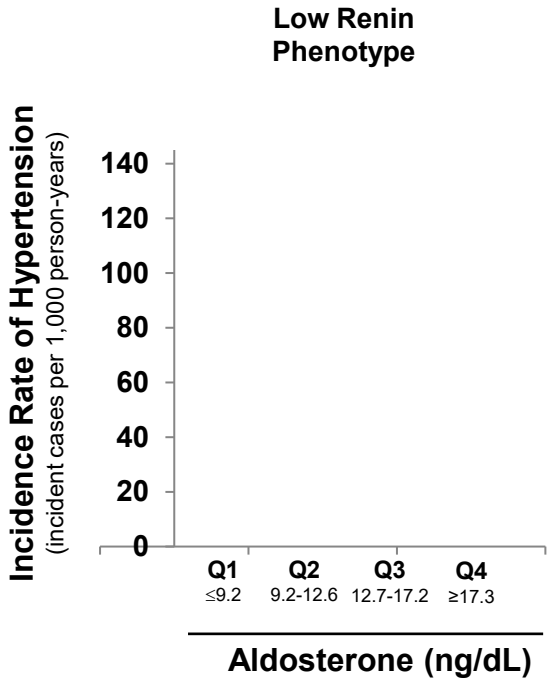


Vaidya et al. *Am J Hypertension* 2022
Tsai et al. *Circulation* 2026
Parisien-La Salle et al. *JACC BTS* 2026

Prospective Cohort Studies

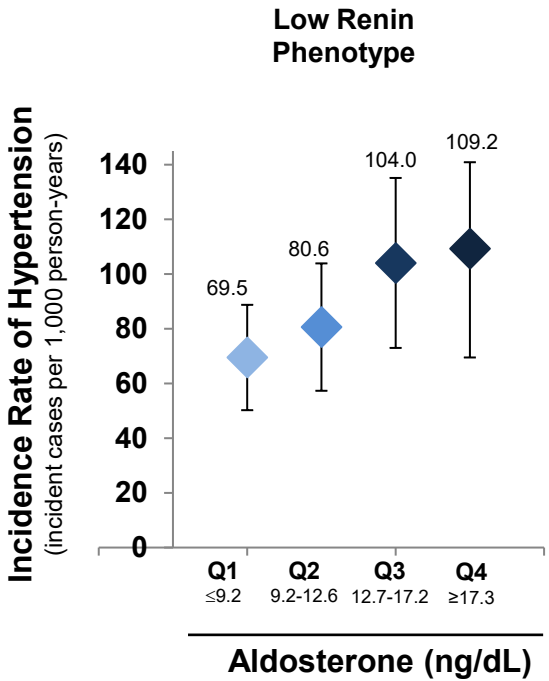


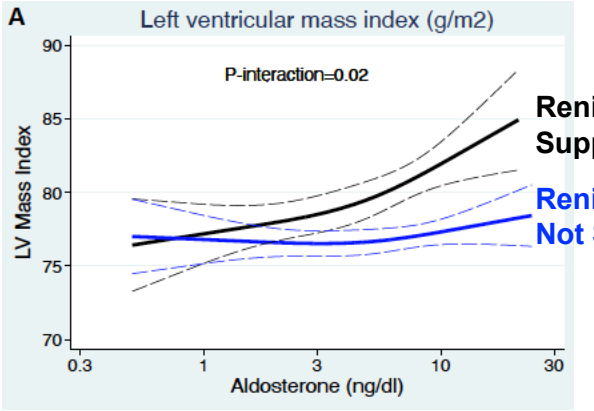
Normotensive Cohort Studies

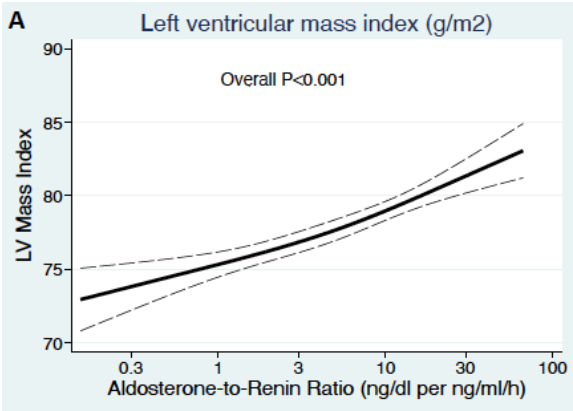


Brown et al. *Annals of Internal Medicine* 2017; Brown et al. *Hypertension* 2022

Normotensive Cohort Studies





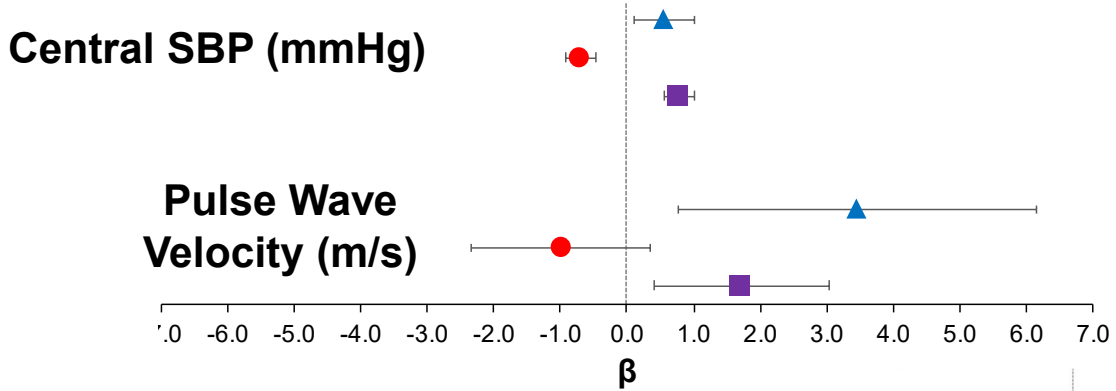


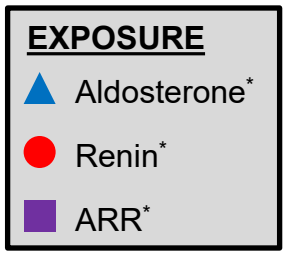
LVMI
AFib

Brown et al. *Annals of Internal Medicine* 2017; Brown et al. *Hypertension* 2022

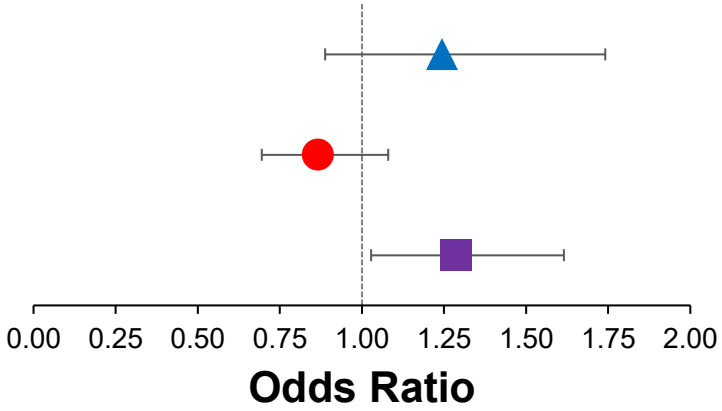
Normotensive Cohort Studies

ARTERIAL STIFFNESS

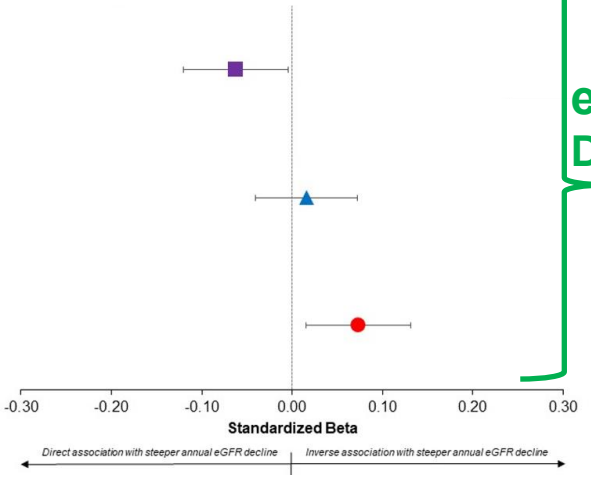




INCIDENT HYPERTENSION



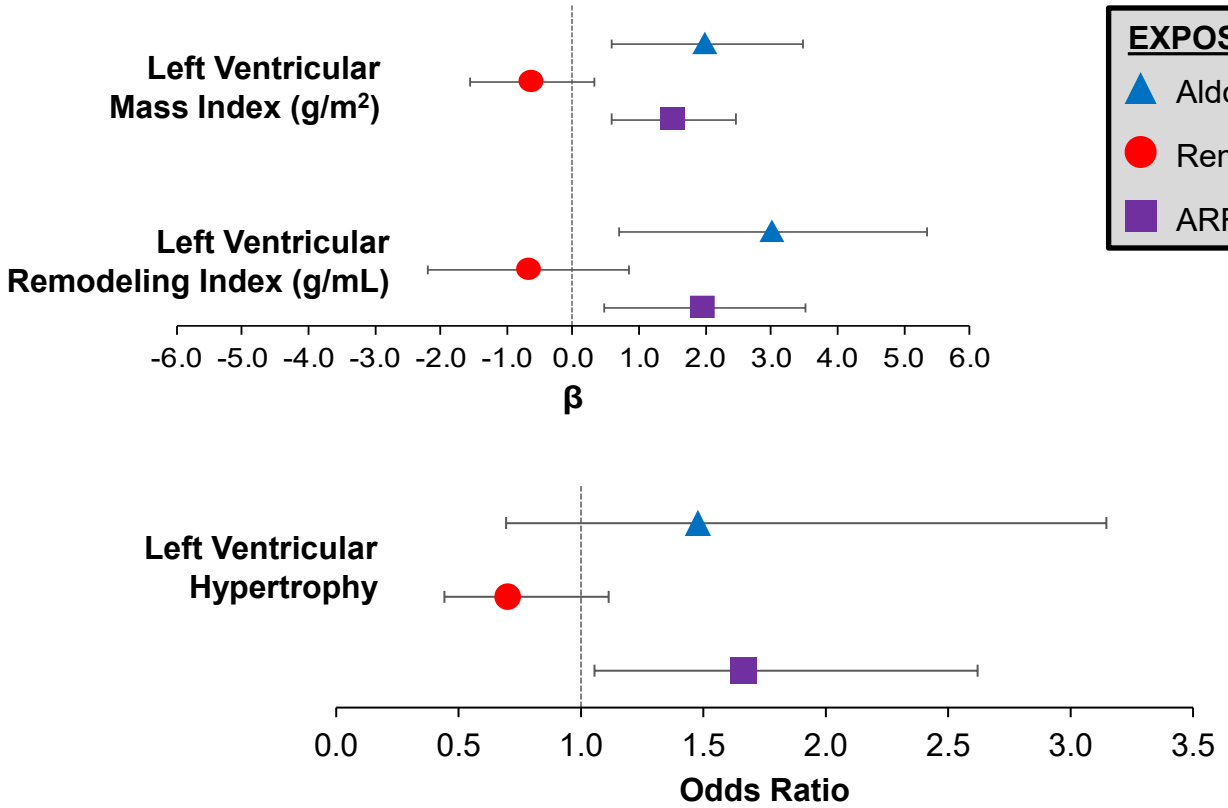
eGFR Decline



Hundemer et al. Circulation 2023
Hundemer et al. *JASN* 2026

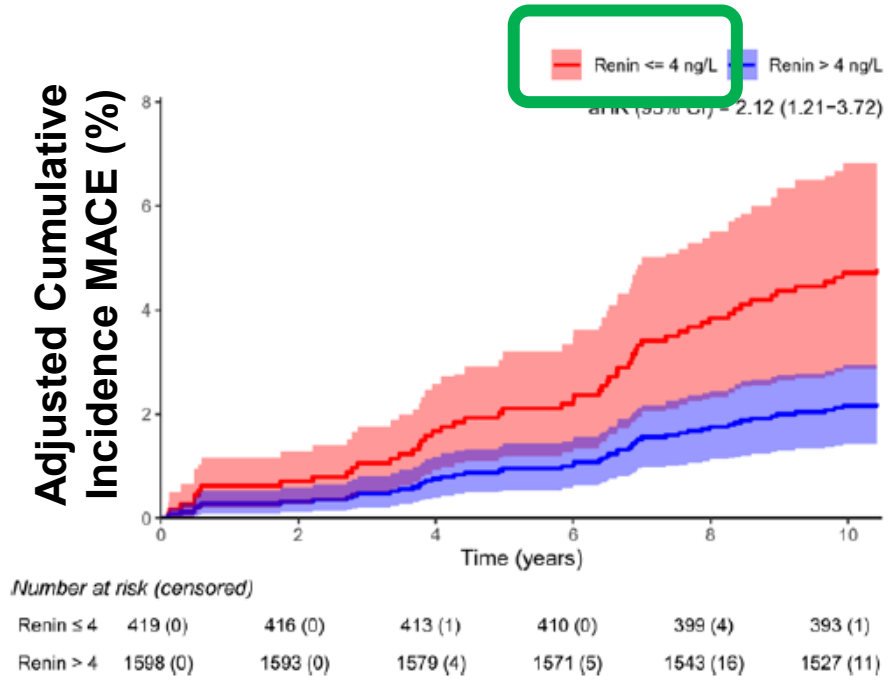
Normotensive Cohort Studies

CARDIAC MRI PARAMETERS



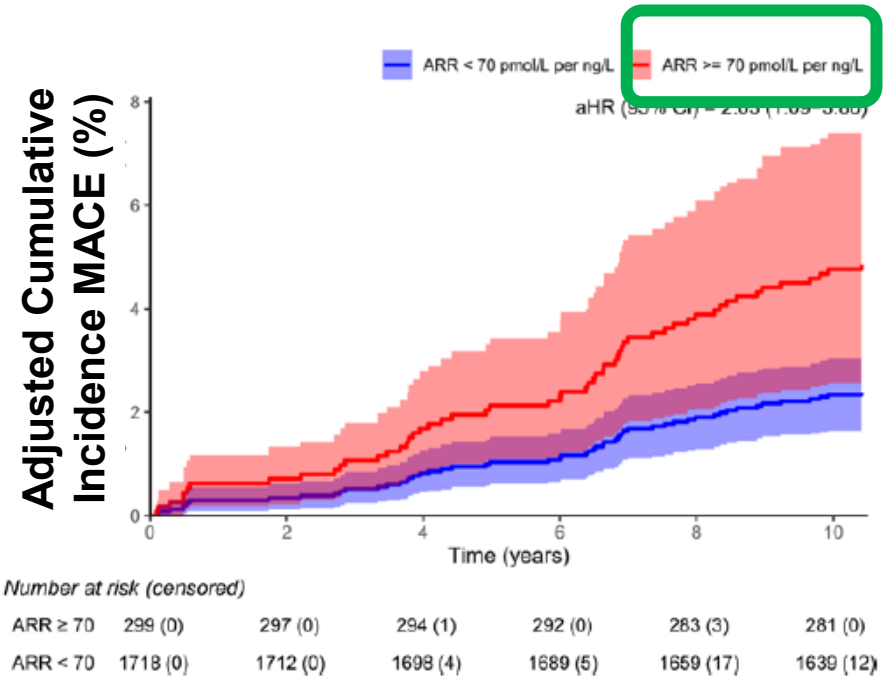
Hundemer et al. Circulation 2023

Normotensive Cohort Studies



Number at risk (censored)

Renin ≤ 4	419 (0)	416 (0)	413 (1)	410 (0)	399 (4)	393 (1)
Renin > 4	1598 (0)	1593 (0)	1579 (4)	1571 (5)	1543 (16)	1527 (11)



Number at risk (censored)

ARR ≥ 70	299 (0)	297 (0)	294 (1)	292 (0)	283 (3)	281 (0)
ARR < 70	1718 (0)	1712 (0)	1698 (4)	1689 (5)	1659 (17)	1639 (12)

Goupil et al. *Circulation* 2025

Normotensive Cohort Studies

Normotensive

Magnitude of Renin-Independent Aldosteronism

→

Arterial Stiffness
Incident Hypertension
Subclinical Structural CVD
Atrial Fibrillation
MACE

RAINE	MESA	FHS	JHS	ARIC	CARTaGENE
Young	*Multi-ethnic*	*White (mostly)*	*Black*	*Nationwide*	*Quebec*
Perth, Australia	*Nationwide*	*Framingham, MA*	*Jackson, MS*	*USA*	*Canada*

Brown et al. *Annals of Internal Medicine* 2017
Brown et al. *Hypertension* 2022

Vasan et al. *NEJM* 2004
Newton-Cheh et al. *Hypertension* 2007

Joseph et al. *Circulation* 2021
Hundemer et al. *Circulation* 2023
Goupil et al. *Circulation* 2025

Hypertensive Cohort Studies

Magnitude of Renin-Independent Aldosteronism

→

Worsening BP
CKD/ESKD
MACE
All-Cause Mortality

FHS
White (mostly)
Framingham, MA

MESA
Multi-ethnic
USA

JHS
Black
Jackson, MS

CONPASS
Chinese
Chongqing, China

EIMDS
Chinese
Chongqing, China

UK BIOBANK
Nationwide
UK

ARIC
Nationwide
USA

CRIC
Nationwide
USA

Danish Registry
Nationwide Denmark

TriNetX
Nationwide USA

CARTaGENE
Quebec
Canada

Brown et al. *Annals Int Med* 2017; Inoue et al. *Hypertension* 2020; Joseph et al. *Circulation* 2021; Hu et al. *JAHA* 2021; Brown et al. *Hypertension* 2022; Verma et al *Eur Heart J* 2022; Hu et al Metabolism 2023; Hundemer et al. 2023, Goupil et al. *Circulation* 2025; Townsend et al. AJH 2025; Lassen et al. JAMA Cardiology 2026; Ljundberg et al. JACC 2026

Primary Aldosteronism is not a Rare, Categorical Disease… it is a Common Syndrome that Manifests on a Severity Spectrum… Contributing to Risk for developing HTN and CV/Kidney Disease

KEY CONCEPT

Primary Aldosteronism is *any* aldosterone production when renin is low; there is no lower limit of aldosterone that confidently excludes PA or risk amenable to aldosterone-directed therapy

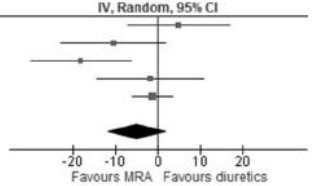
Brown et al. *Annals of Internal Medicine* 2017, Vaidya et al. *Endocrine Reviews* 2018

Meta-Analysis of RCTs in LRH

MRA vs Thiazides (- 4.8 mmHg)

Study or Subgroup	MRA Mean [mmHg]	MRA SD [mmHg]	MRA Total	Diuretic Mean [mmHg]	Diuretic SD [mmHg]	Diuretic Total	Weight	Mean Difference IV, Random, 95% CI	Year
Adlin	-24	15.8	18	-29	15.1	10	17.8%	5.00 [-6.87, 16.87]	1972
Vaughan	-28.3	17.8	21	-17.9	19.7	16	17.2%	-10.40 [-22.69, 1.89]	1973
Spark	-32	11.4	10	-13.9	15.3	10	17.9%	-18.10 [-29.93, -6.27]	1974
Ferguson	-13.1	15.1	11	-11.4	15.1	11	16.8%	-1.70 [-14.32, 10.92]	1977
Hood (bendroflumethiazide)	-11.6	13.8	51	-10.5	10.4	51	30.3%	-1.10 [-5.84, 3.64]	2007
Total (95% CI)			111			98	100.0%	-4.75 [-11.91, 2.40]	

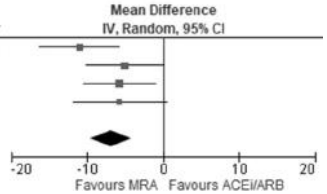
Heterogeneity: Tau² = 38.05; Chi² = 10.05, df = 4 (P = 0.04); I² = 60%
Test for overall effect: Z = 1.30 (P = 0.19)



MRA vs ACEi/ARB (- 6.8 mmHg)

Study or Subgroup	MRA Mean [mmHg]	MRA SD [mmHg]	MRA Total	ACEi/ARB Mean [mmHg]	ACEi/ARB SD [mmHg]	ACEi/ARB Total	Weight	Mean Difference IV, Random, 95% CI	Year
Flack 2003	-16	15.5	60	-5	14.2	62	24.7%	-11.00 [-16.28, -5.72]	2003
Williams 2004	-15.3	15.7	67	-10.3	16	82	26.3%	-5.00 [-10.11, 0.11]	2004
Weinberger 2005	-15.8	15.8	86	-10.1	15.4	82	30.4%	-5.70 [-10.42, -0.98]	2005
Hood 2007 (losartan)	-11.6	13.8	51	-5.9	17.7	51	18.5%	-5.70 [-11.86, 0.46]	2007
Total (95% CI)			264			277	100.0%	-6.83 [-9.56, -4.10]	

Heterogeneity: Tau² = 0.58; Chi² = 3.24, df = 3 (P = 0.36); I² = 7%
Test for overall effect: Z = 4.90 (P < 0.00001)



MRA vs β-blocker (- 4.5 mmHg)
MRA vs α-blocker (- 4.0 mmHg)

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


ESC European Heart Journal - Cardiovascular Pharmacotherapy ORIGINAL ARTICLE

Spironolactone effect on the blood pressure of patients at risk of developing heart failure: an analysis from the HOMAGE trial

João Pedro Ferreira, Timothy Collier, Andrew L. Clark, Mamas A. Mamas, Hans-Peter Brunner-La Rocca, Stephane Heymans, Arantxa González, Fozia Z. Ahmed, Johannes Petutschnigg, Blerim Mujaj, Joe Cuthbert, Philippe Rouet, Pierpaolo Pellicori, Beatrice Mariottoni, Franco Cosmi, Frank Edelmann, Lutgarde Thijs, Jan A. Staessen, Mark Hazebroek, Job Verdonschot, Patrick Rossignol, Nicolas Girerd, John G. Cleland, and Faiez Zannad

Williams et al. Lancet 2015; Shah et al. JHH 2024

Aldosterone Synthase Inhibitors

The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 FEBRUARY 2, 2023 VOL. 388 NO. 5

Phase 2 Trial of Baxdrostat for Treatment-Resistant Hypertension

Mason W. Freeman, M.D., Yuan-Di Halvorsen, Ph.D., William Marshall, M.D., Mackenzie Pater, Ph.D., Jon Isaacsohn, M.D., Catherine Pearce, D.H.Sc., Brian Murphy, M.D., M.P.H., Nicholas Alp, M.D., Ajay Srivastava, M.D., Deepak L. Bhatt, M.D., M.P.H., and Morris J. Brown, M.D., for the BrigHTN Investigators*

ORIGINAL ARTICLE

Lorundrostat Efficacy and Safety in Patients with Uncontrolled Hypertension

L.J. Laffin,[1,2] B. Kopjar,[3] C. Melgaard,[2] K. Wolski,[2] J. Ibbitson,[4] S. Bhikam,[4] M.R. Weir,[5] E.O. Ofili,[6] R. Mehra,[7] J.M. Luther,[8] D.L. Cohen,[9] A. Sarraju,[1,2] M.J. Wilkinson,[10] J.M. Flack,[11] D. Rodman,[4] and S.E. Nissen,[1,2] for the Advance-HTN Investigators*

JAMA | Original Investigation

Aldosterone Synthase Inhibition With Lorundrostat for Uncontrolled Hypertension
The Target-HTN Randomized Clinical Trial

Luke J. Laffin, MD; David Rodman, MD; James M. Luther, MD; Anand Vaidya, MD; Matthew R. Weir, MD; Natasa Rajicic, ScD; B. T. Slingsby, MD, PhD; Steven E. Nissen, MD; for the Target-HTN Investigators

Safety and efficacy of once-daily dexfadrostat phosphate in patients with primary aldosteronism: a randomised, parallel group, multicentre, phase 2 trial

Paolo Mulatero,[a,*] Gregoire Wuerzner,[b] Michael Groessl,[c] Elisa Sconfienza,[a] Aikaterini Damianaki,[b] Vittorio Forestiera,[a] Bruno Vogt,[c] Hans Brunner,[d] Teresa Gerlock,[e] Ronald Steele,[e] and Christoph Schumacher[e]

CORRESPONDENCE

Phase 2a Study of Baxdrostat in Primary Aldosteronism

JAMA | Original Investigation

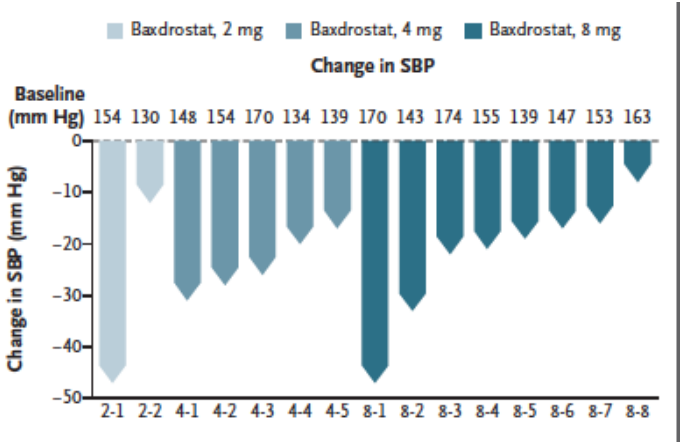
Lorundrostat in Participants With Uncontrolled Hypertension and Treatment-Resistant Hypertension
The Launch-HTN Randomized Clinical Trial

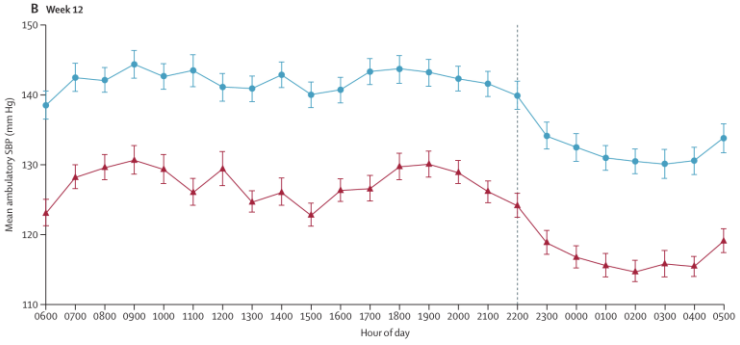
Manish Saxena, MBBS; Luke Laffin, MD; Claudio Borghi, MD; Beatriz Fernandez Fernandez, MD, PhD; Jalal K. Ghali, MD; Branko Kopjar, MD, PhD; Krishna Polu, MD; Simon D. Roger, MD; B. T. Slingsby, MD, PhD; Frank Strutz, MD; Liffert Vogt, MD, PhD; Matthew R. Weir, MD; David Rodman, MD; for the Launch-HTN Investigators

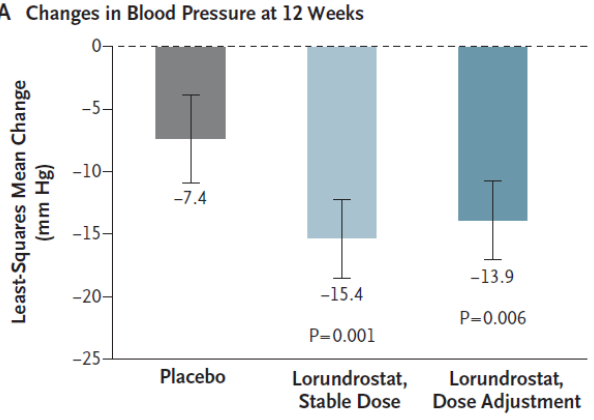
ORIGINAL ARTICLE

Efficacy and Safety of Baxdrostat in Uncontrolled and Resistant Hypertension

John M. Flack, M.D.,[1] Michel Azizi, M.D.,[2,3] Jenifer M. Brown, M.D.,[4] Jamie P. Dwyer, M.D.,[5] Jakub Fronczek, M.D.,[6] Erika S.W. Jones, M.D.,[7] Daniel S. Olsson, M.D.,[8] Shira Perl, M.D.,[9] Hirotaka Shibata, M.D., Ph.D.,[10] Ji-Guang Wang, M.D.,[11] Ulrica Wilderäng, Ph.D.,[8] Janet Wittes, Ph.D.,[12] and Bryan Williams, M.D.,[13] for the BaxHTN Investigators*







Aldosterone Synthase Inhibitors appear to be a new anti-HTN class, highly effective at lowering aldosterone, and BP in R-HTN, uncontrolled HTN, and PA

They affirm that a large proportion of essential/idiopathic HTN is aldosterone-mediated; in fact, many have unrecognized PRIMARY Aldosteronism

"Medical Aldosterone-ectomy" may be the treatment of the future

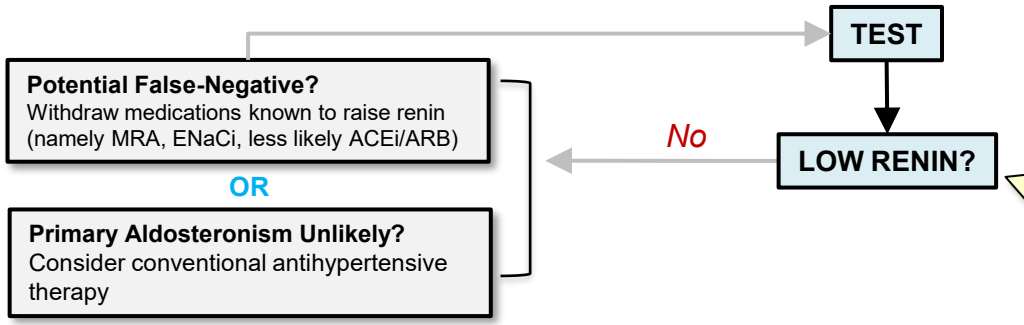
A Practical & Re-Calibrated Approach

Adopting a new mindset…

"It's Primary Aldosteronism Until Proven Otherwise"

"It is never wrong to start an MRA when you suspect PA or low-renin HTN"

Diagnostic
Pre-Test Probability



WHO AND HOW TEST

WHO:

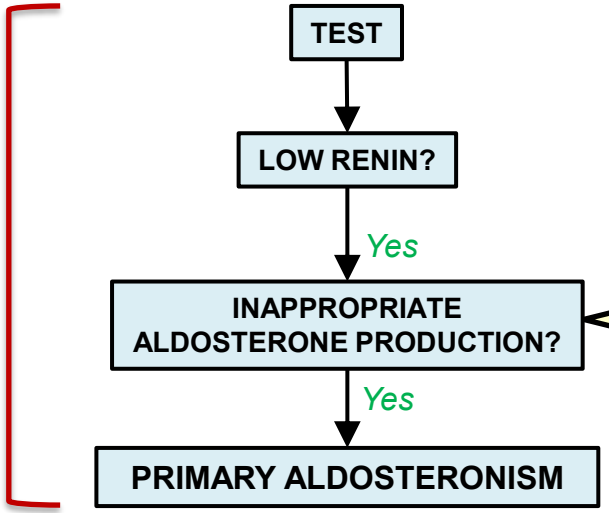
Majority PA pts have low renin
PRA < 1.0 ng/mL/h
PRC < 10 mU/L

If low renin despite
MRA or ENaCi or RAASi or Diuretic
(>80% of HTNive pts):
"PA until proven otherwise"

Adapted from:
Vaidya et al. NEJM 2025
Brown & Vaidya. JACC 2025
Adler…Vaidya…et al. JCEM 2025

Diagnostic
Pre-Test Probability
>25%

CENTRAL DOGMA



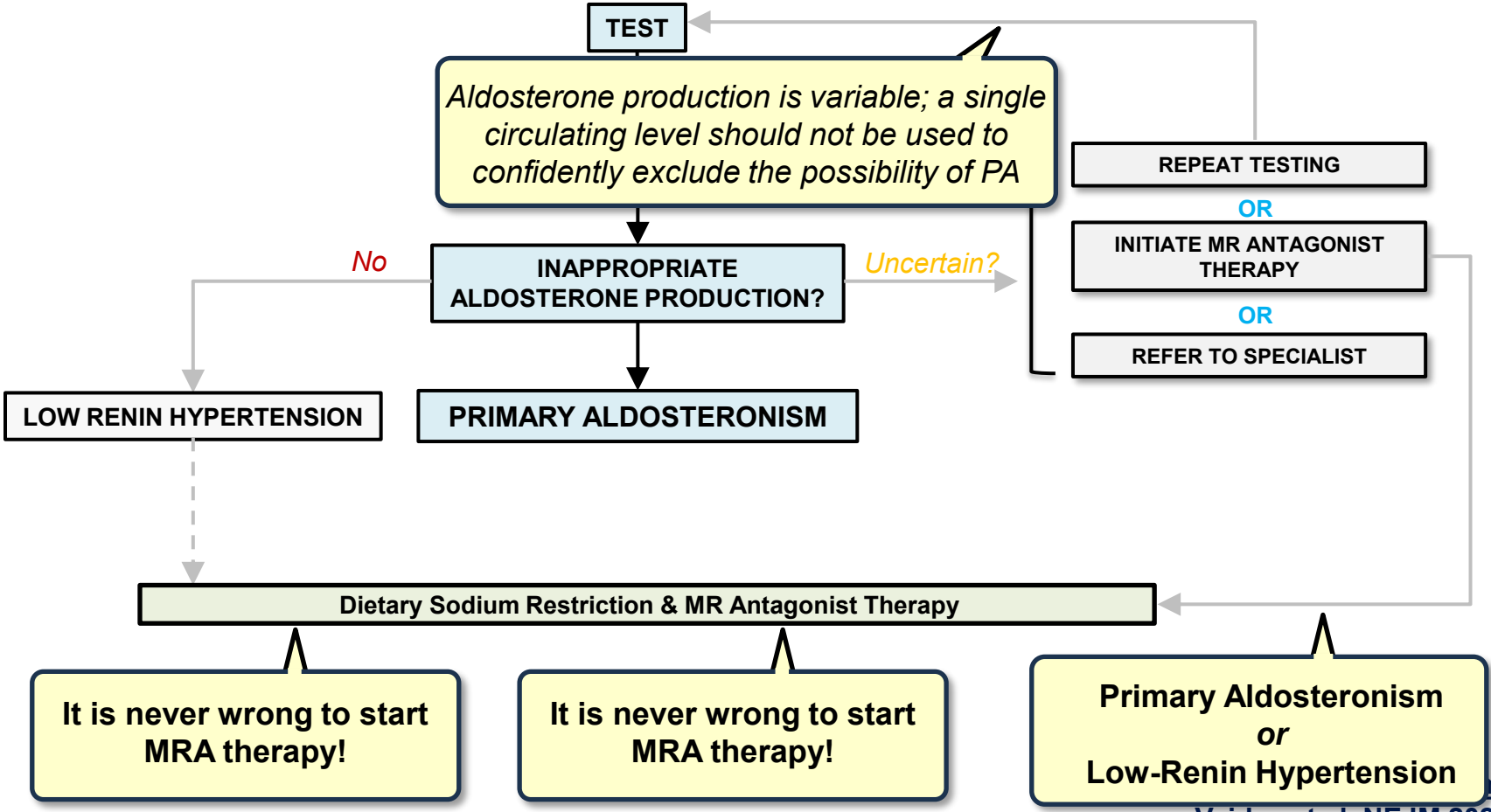
Continuum: *any aldosterone production when renin is low represents PA Pathophysiology amenable to targeted therapy*

Categorical: > 7.5 ng/dL (LC-MS/MS)
> 10 ng/dL (IA)

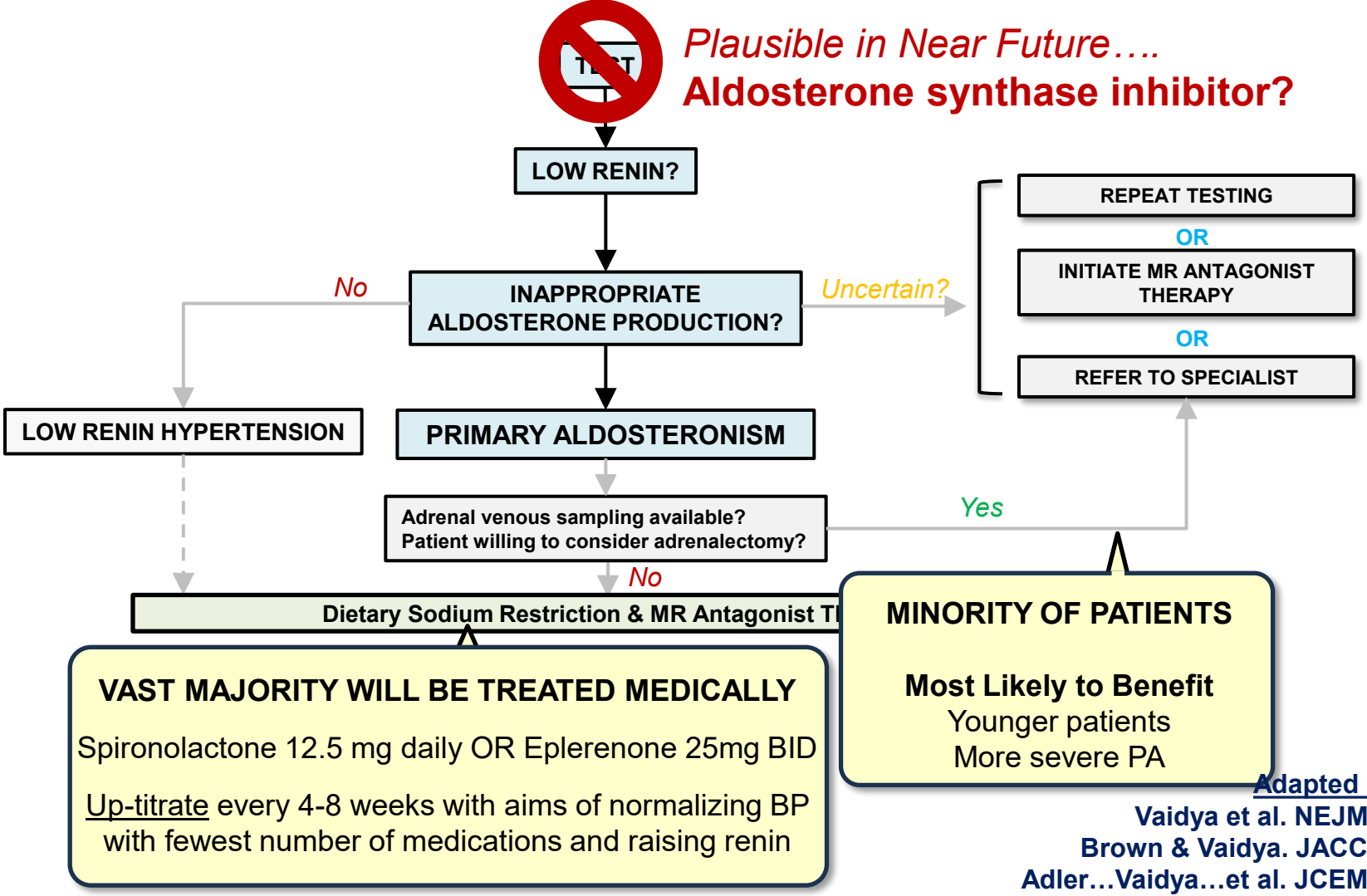
****If on ACEi/ARB (75-80%):*
"PA until proven otherwise"

1. **Liberally test people with hypertension**
2. **Low or persistently suppressed renin is highly indicative**
3. **Any inappropriate aldosterone production when renin is low**

Adapted from:
Vaidya et al. NEJM 2025
Brown & Vaidya. JACC 2025
Adler…Vaidya…et al. JCEM 2025



n:
Vaidya et al. NEJM 2025
Brown & Vaidya. JACC 2025
Adler…Vaidya…et al. JCEM 2025



Adapted from:
Vaidya et al. NEJM 2025
Brown & Vaidya. JACC 2025
Adler…Vaidya…et al. JCEM 2025

Take Home Objectives

Primary aldosteronism is common

essential hypertension is primarily aldosteronism

Primary aldosteronism causes hypertension and cardiorenal disease that can be mitigated with widely available targeted therapies

A simplified approach to diagnosis and treatment involves simplified testing and liberalized use of MR antagonsits