

# Rethinking Primary Aldosteronism

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## Disclosure

I have no financial interests or relationships to disclose.



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## OBJECTIVES

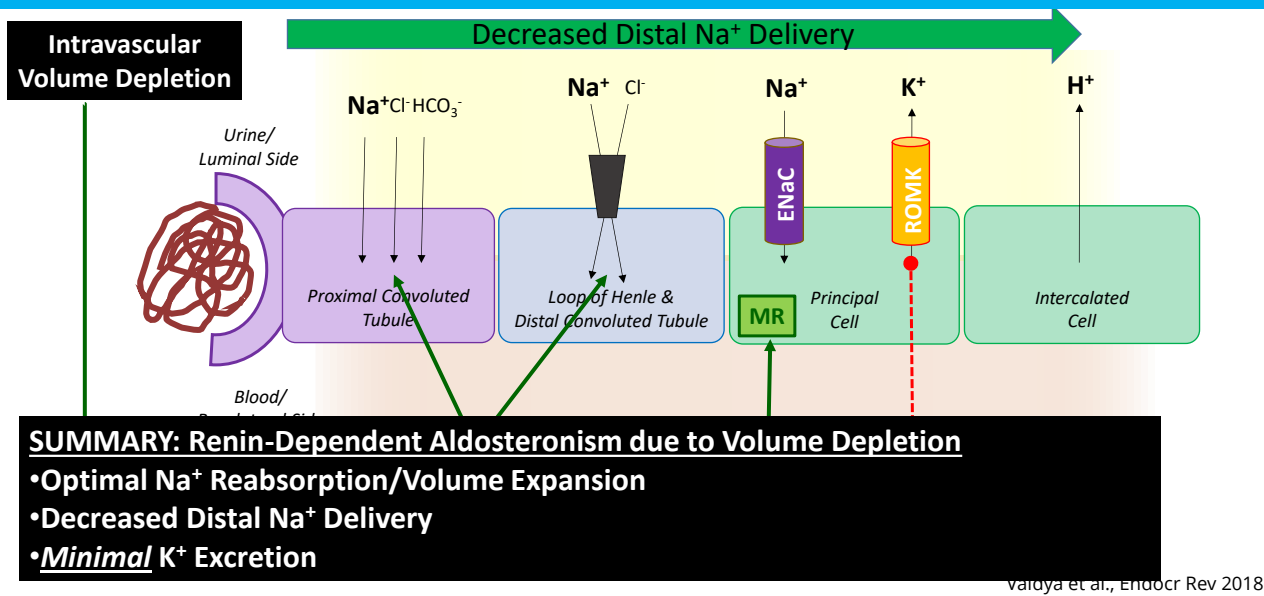
1. To provide an overview of primary aldosteronism (PA).
2. To describe the under-recognized continuum of PA.
3. To discuss the pitfalls of traditional diagnostic pathways in PA.
4. To detail novel treatment approaches in PA.

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## BACKGROUND

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# SECONDARY (RENIN-DEPENDENT) ALDOSTERONISM



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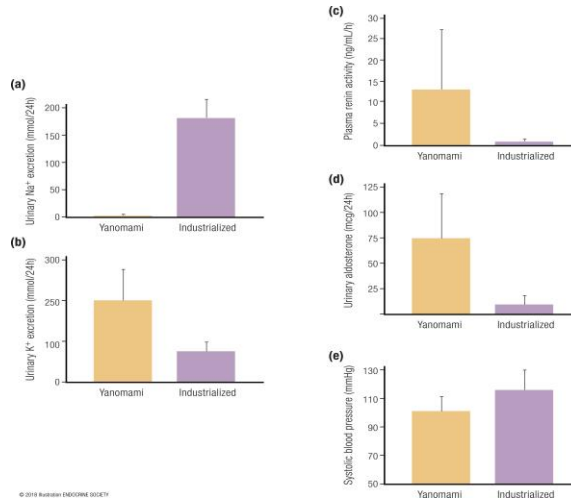
# YANOMAMI



<https://www.telegraphindia.com/health/keep-away-blood-pressure-diabetes-the-yanomami-way/cid/1679249>

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# YANOMAMI



Vaidya et al., Endocr Rev 2018

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# ENEMY TO THE YANOMAMI

## Brazilian Pit Viper (*Bothrops jararaca*)



**ACE Inhibitor**

*“Over thousands of years, the same environmental pressures that forced Yanomami and other terrestrial animals to evolve a hyperactive RAAS, also led *Bothrops jararaca* to conserve an efficient killing mechanism that targeted its enemies’ haemodynamic vulnerabilities. The bradykinin-potentiating peptides that would become the first ACEi’s were, in essence, the viper’s weapon of choice in a predator-prey arms race.”*

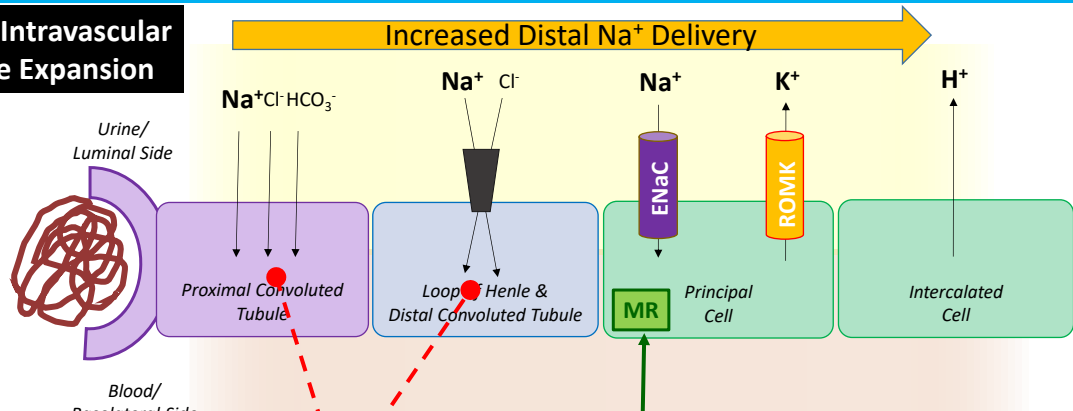
Ciolek et al., PNAS 2017

[https://en.wikipedia.org/wiki/Bothrops\\_jararaca](https://en.wikipedia.org/wiki/Bothrops_jararaca)

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# PRIMARY (RENIN-INDEPENDENT) ALDOSTERONISM

**Chronic Intravascular Volume Expansion**



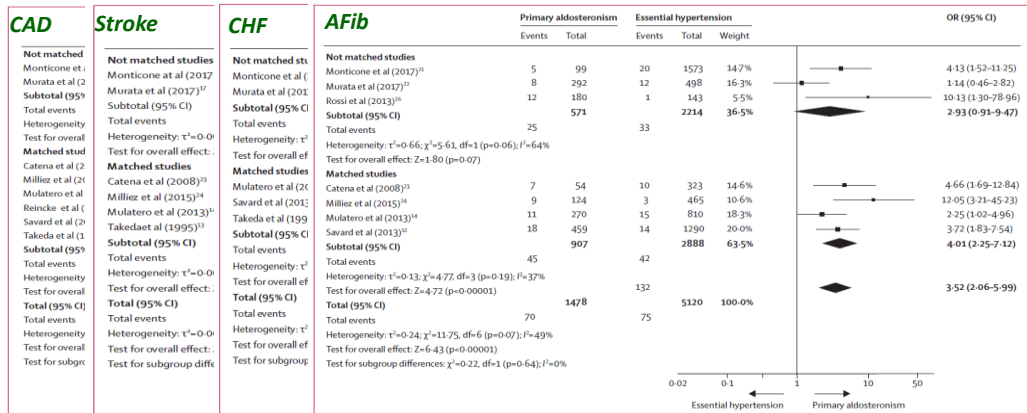
**SUMMARY: Vicious Cycle that Leads to Adverse Heart and Kidney Outcomes**

- ↑↑↑ Distal Na<sup>+</sup> Delivery
- ↑↑↑ Na<sup>+</sup> Reabsorption/Volume Expansion/Blood Pressure
- ↑↑↑ K<sup>+</sup>/H<sup>+</sup> Excretion (Hypokalemia/Metabolic Alkalosis)

Varuya et al., Endocr Rev 2018

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# ADVERSE OUTCOMES IN UNTREATED PA



**Therefore, early diagnosis and targeted therapy (MRA/adrenalectomy) are essential.**

Monticone et al., Lancet D&E 2018

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## ADVERSE OUTCOMES IN UNTREATED PA

### Long-term health impact of primary aldosteronism

#### Cardiovascular disease risk

Coronary artery disease

Congestive heart failure

Left ventricular hypertrophy

Atrial fibrillation

Stroke

Cardiovascular mortality

#### Kidney disease risk

Glomerular hyperfiltration

Accelerated decline in glomerular filtration rate

End-stage kidney disease

Proteinuria

#### Metabolic disease risk

Type 2 diabetes mellitus

Metabolic syndrome/obesity

Obstructive sleep apnea

Osteoporosis/fractures

Vaidya et al., Am J Hypertens 2022

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## HOW COMMON IS PA?

Complicated question that depends on:

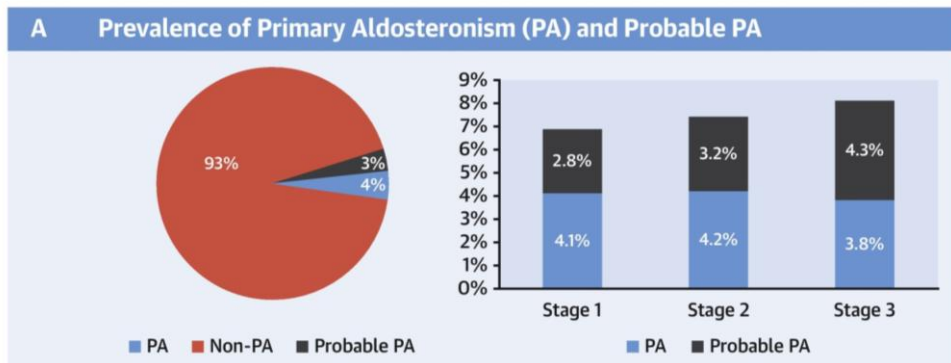
1. Population studied
2. Study setting
3. PA disease definitions

Vaidya et al., Am J Hypertens 2022

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# HOW COMMON IS PA?

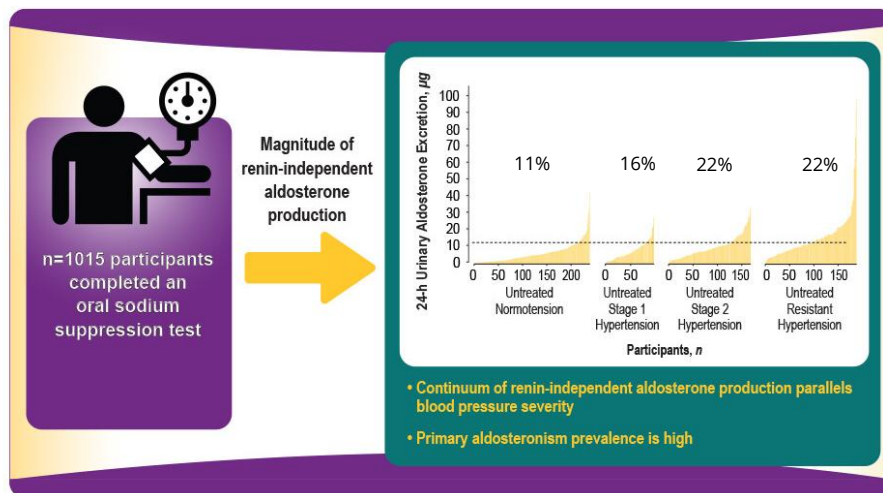
**CENTRAL ILLUSTRATION: Prevalence and Clinical Outcomes of PA in Patients With Newly Diagnosed Hypertension**



Xu et al., J Am Coll Cardiol 2020

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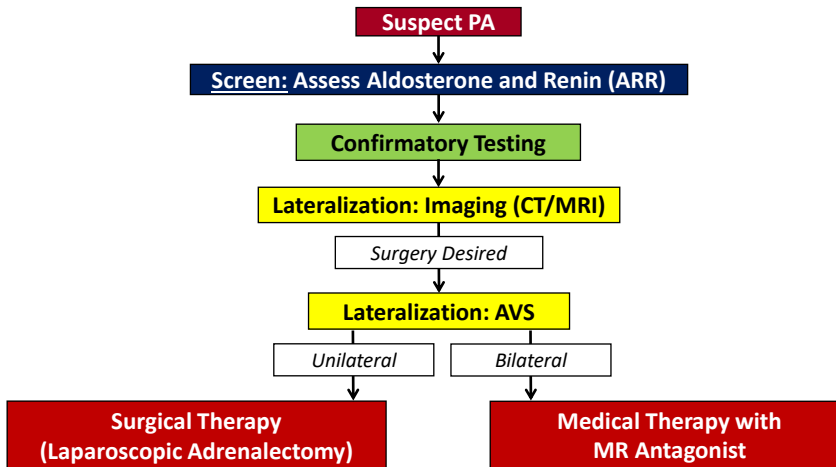
# HOW COMMON IS PA?



Brown et al., Ann Int Med 2020

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# TRADITIONAL PA ALGORITHM



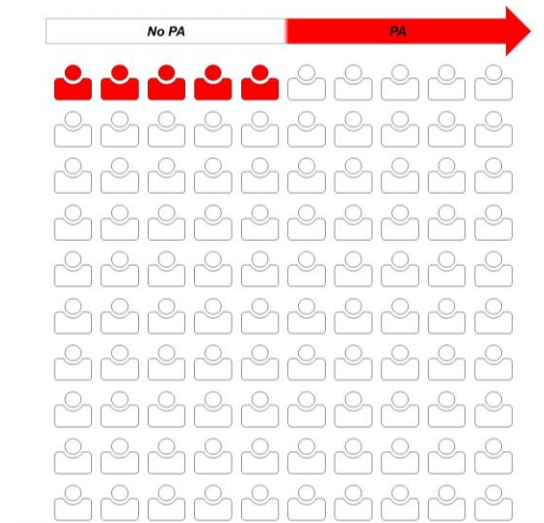
Vaidya et al., Endocr Rev 2018

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# CONTINUUM OF PA

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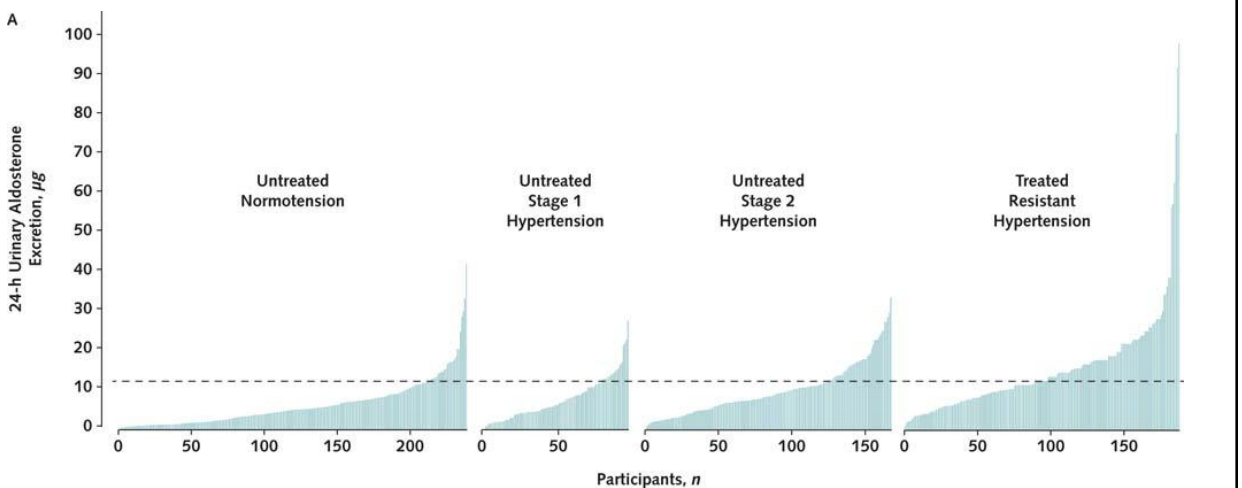
# TRADITIONAL VIEW OF PA IN HTN



Hundemer et al., Am J Hypertens 2025

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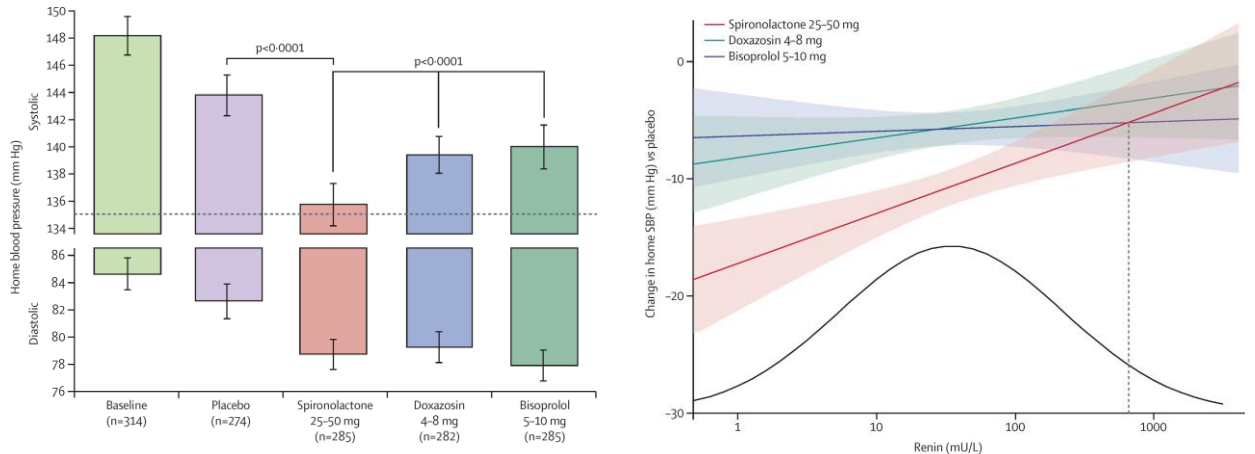
# IS PA REALLY A DICHOTOMOUS DISEASE?



Brown et al., Ann Int Med 2020

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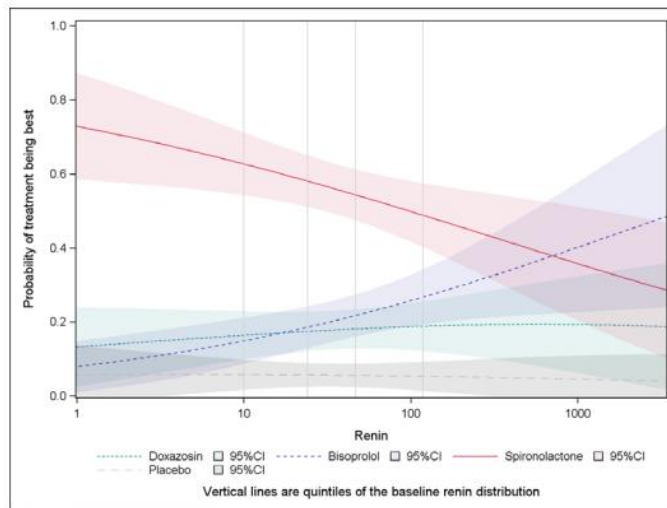
# PATHWAY-2



Williams et al., Lancet 2015

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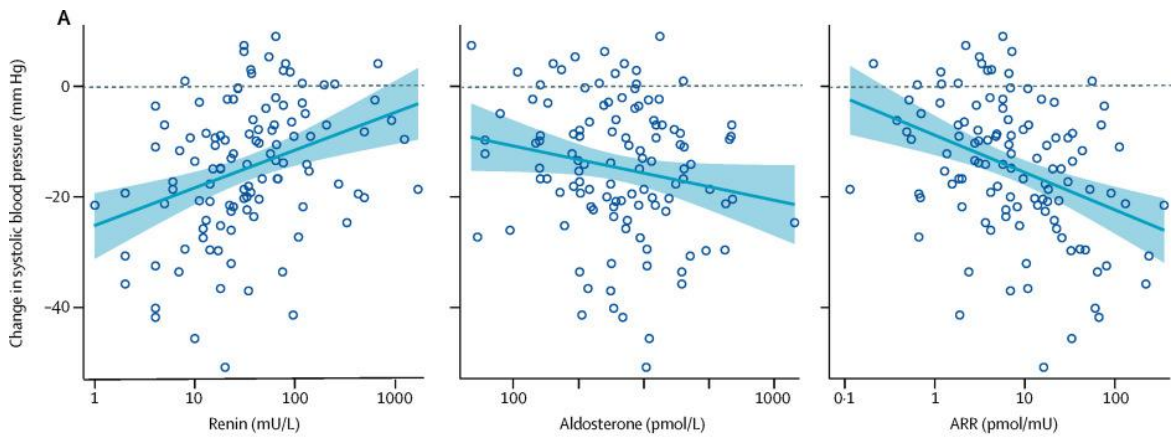
# PATHWAY-2



Williams et al., Lancet 2015

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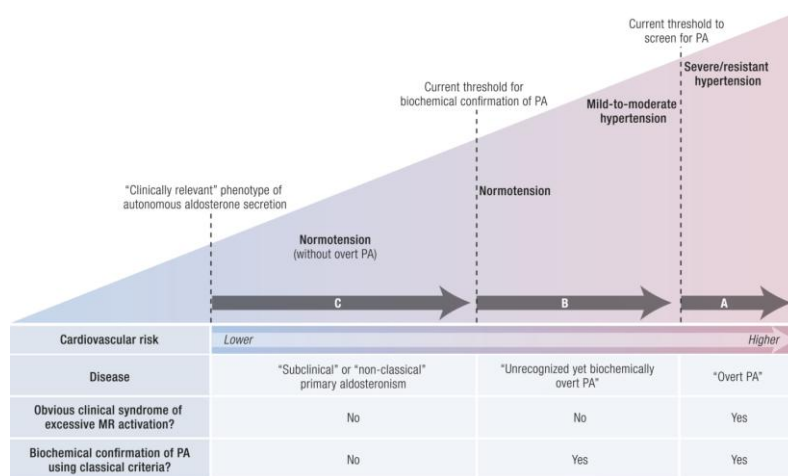
# PATHWAY-2



Williams et al., Lancet D&E 2018

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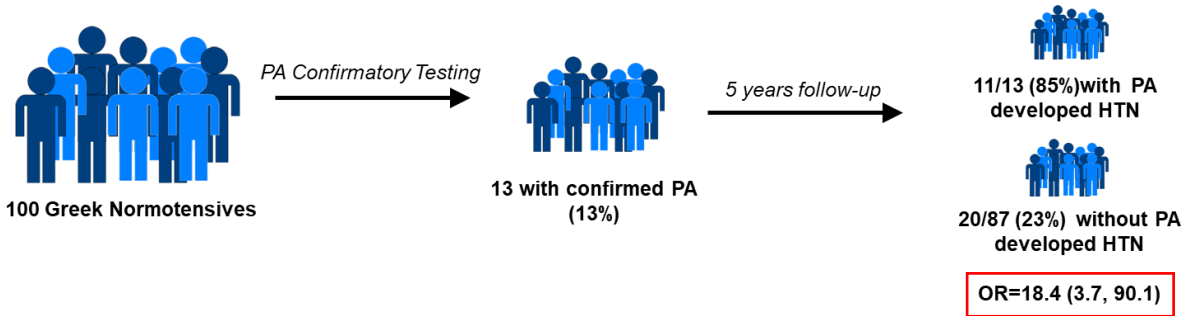
# CONTINUUM OF PA PATHOPHYSIOLOGY



Vaidya et al., Endocr Rev 2018

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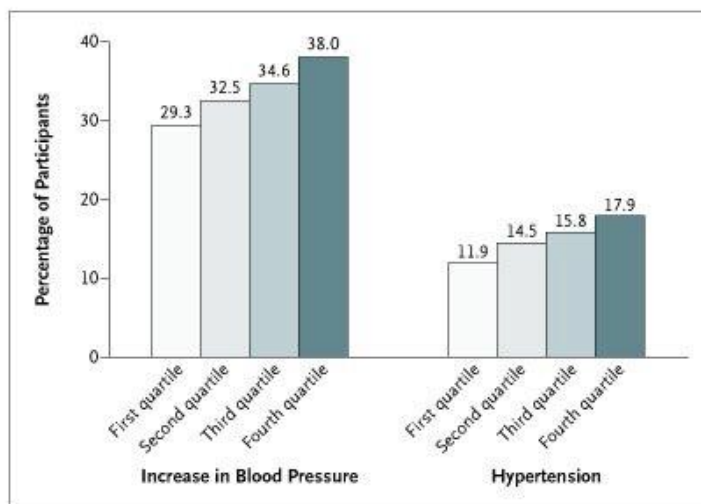
# UNRECOGNIZED YET BIOCHEMICALLY OVERT PA



Markou et al., JCEM 2013

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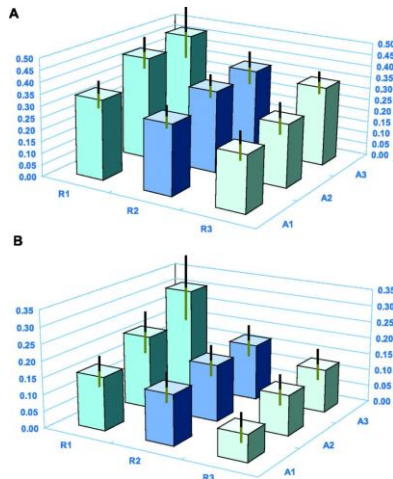
# SUBCLINICAL PRIMARY ALDOSTERONISM



Vasan et al., NEJM 2004

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## SUBCLINICAL PRIMARY ALDOSTERONISM



BP Progression

Incident HTN

Newton-Cheh et al., Hypertension 2004

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## SUBCLINICAL PRIMARY ALDOSTERONISM

Renin-independent aldosterone production present in:

- ~1/3 of individuals with HTN
- ~1/5 of individuals with normal BP

Leads to:

- ↑ MR activation
- ↑ Kaliuresis
- ↑ BP/HTN

*Does it lead to worse cardiovascular and kidney outcomes in a BP-independent fashion like overt PA?*

Parisien-La Salle et al., Arch Endocrinol Metab 2025

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# CARTAGENE

Population-based cohort from Quebec, Canada

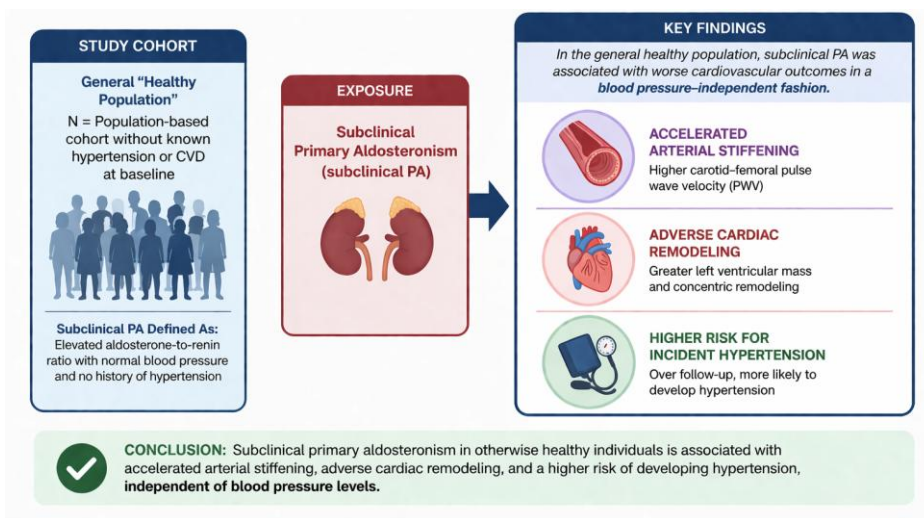
- ~20,000 residents enrolled between 2009-10
- Ages 40-69 years
- Representative of the general adult population of Quebec
- Cohort generally healthy with few comorbidities and most had normal BP or mild HTN



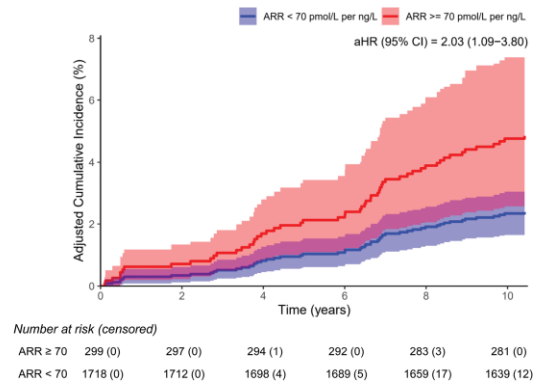
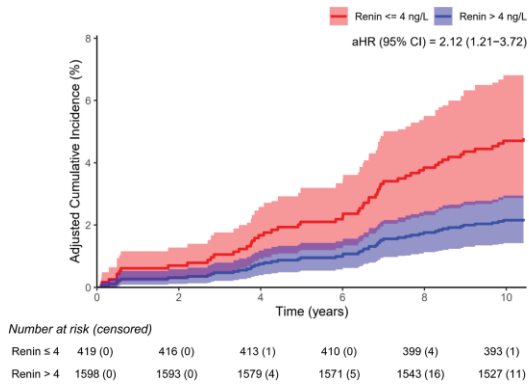
Awadalla et al., Int J Epidemiol 2013

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# SUBCLINICAL PA AND CV HEALTH



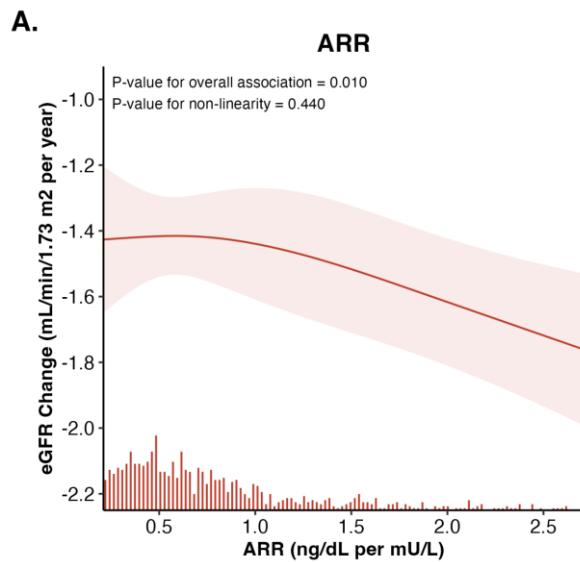
# SUBCLINICAL PA AND MACE



Goupil et al., Circulation 2025

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# SUBCLINICAL PA AND KIDNEY OUTCOMES



Hundemer et al., JASN 2026

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## SUBCLINICAL PA – POPULATION HEALTH SIGNIFICANCE

Highly prevalent in the general population but largely unrecognized

Leads to a higher risk of:

- HTN
- Arterial stiffness, adverse cardiac remodeling
- MACE – MI, CHF, stroke
- Kidney disease

We have cheap and widely available medical therapies that are effective in targeting renin-independent aldosterone production

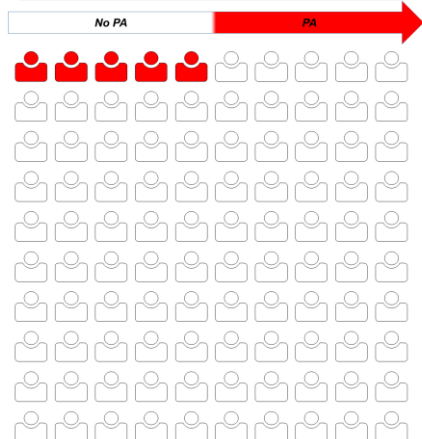
*Will early identification and targeted therapy for Subclinical PA effectively mitigate this increased CV and kidney disease risk?*

Parisien-La Salle et al., Arch Endocrinol Metab 2025

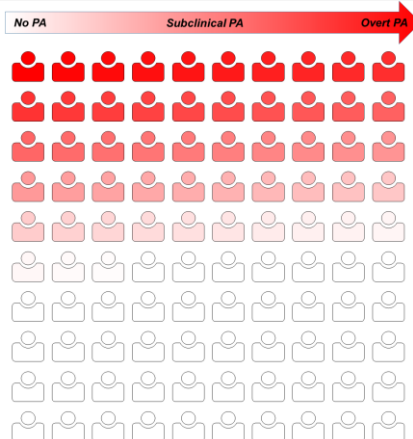
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## SUBCLINICAL PA – POPULATION HEALTH SIGNIFICANCE

Traditional View of PA in Hypertension: Dichotomous Disease



Modern View of PA in Hypertension: Continuum of PA Pathophysiology



Hundemer et al., Am J Hypertens 2025

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# PITFALLS OF TRADITIONAL DIAGNOSTIC PATHWAYS IN PA

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## PITFALLS OF PA DIAGNOSTIC PATHWAYS

As a medical community, we struggle to diagnose (and treat) many cases of overt and classically defined PA

There are pitfalls across all steps along traditional PA diagnostic pathways that contribute:

- Screening
- Confirmatory testing
- Localization testing

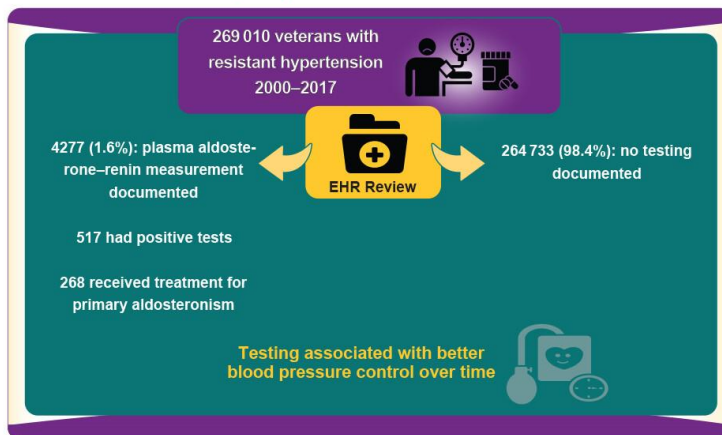
*It is estimated that <1% of patients with PA are ever diagnosed.*

Hundemer et al., Am J Hypertens 2025

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## SCREENING – POOR UPTAKE

Are patients with resistant hypertension receiving appropriate testing to determine if primary aldosteronism is the cause?

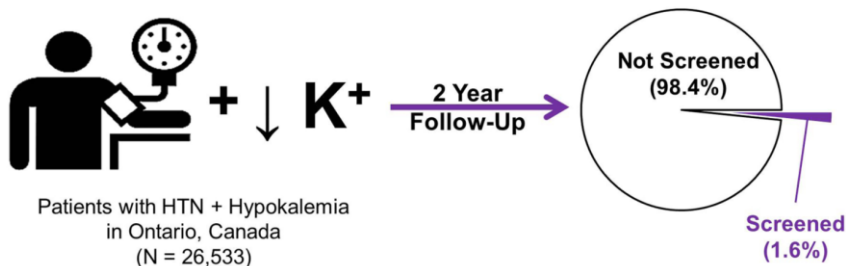


Cohen et al., Ann Int Med 2020

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## SCREENING – POOR UPTAKE

How often are patients with hypertension plus hypokalemia being screened for primary aldosteronism at the population level?

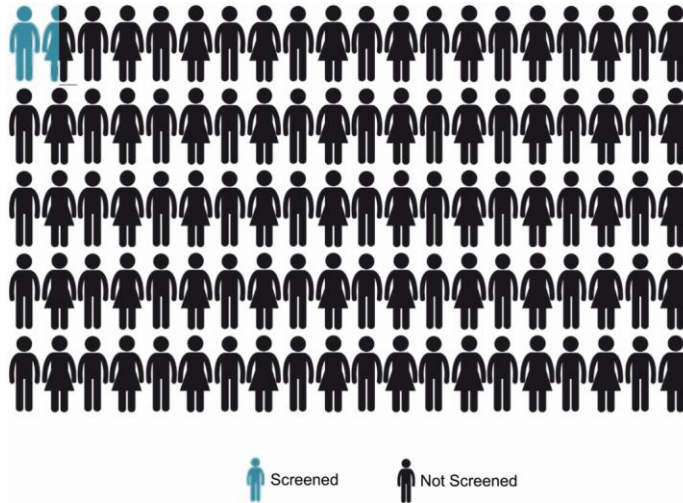


**Conclusion:** Population-level uptake of guideline-recommended screening for primary aldosteronism is exceedingly low. This underscores a lack of awareness and testing as the primary reason for why primary aldosteronism is severely unrecognized.

Hundemer et al., Hypertension 2022

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# SCREENING – POOR UPTAKE



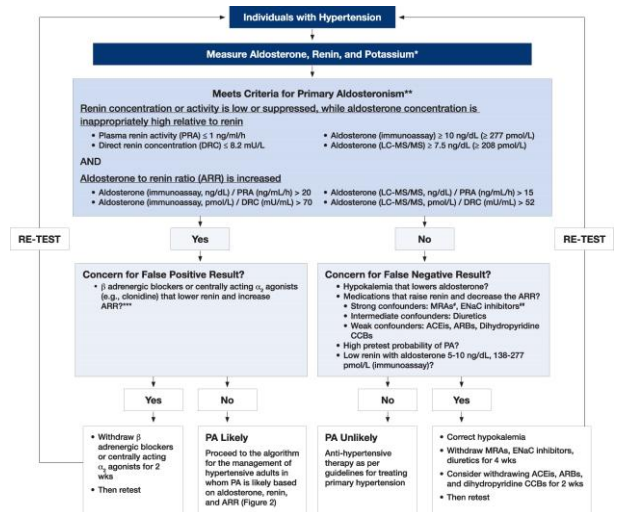
Vaidya et al., Am J Hypertens 2022

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# WHY THE CLINICAL INERTIA WITH PA SCREENING?

May relate to testing procedures being perceived as overly complex and cumbersome.

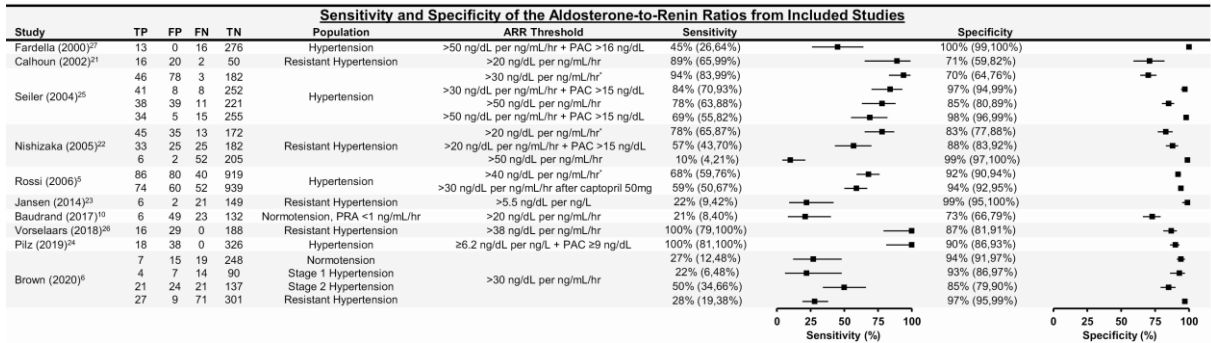
- Prior recommendations advised switching many BP medications to alternative agents that have less effect on ARR (e.g.,  $\alpha$ -blockers, hydralazine, and non-dihydropyridine CCBs)
- Inconvenient, time consuming, and places the patient at unnecessary risk
- Addressed with new 2025 PA guidelines



Adler et al., JCEM 2025

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# ARR LIMITATIONS



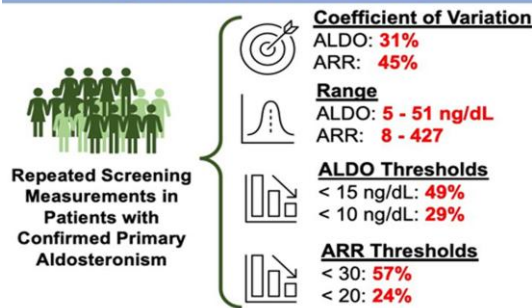
**ARR performance varies widely based on patient populations and diagnostic thresholds; therefore no single ARR threshold can be recommended. Many studies report ARR sensitivity <50% at standard thresholds.**

Hung et al., JCEM 2021

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# ARR LIMITATIONS

## Intra-Individual Variability of Aldosterone Concentrations in Primary Aldosteronism: Implications for Case Detection



**SUMMARY:** Screening aldosterone and ARR are highly variable in primary aldosteronism, with many values falling below conventionally accepted diagnostic thresholds. Re-calibrating the definition of a 'positive screen' to include more liberal thresholds may increase the diagnostic yield.

Yozamp et al., Hypertension 2020

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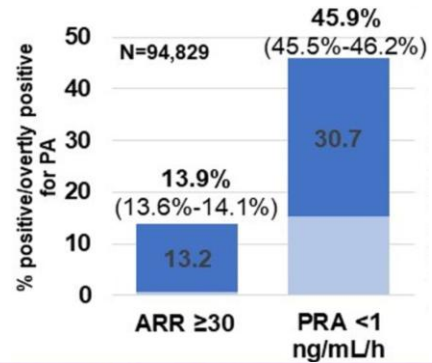
# POTENTIAL ALTERNATIVES FOR PA SCREENING

## 1. Interpreting aldosterone and renin levels on their own without the ARR

A positive screen meets both of the following conditions in most circumstances:

1. Renin is low/suppressed (hallmark of diagnosis) and aldosterone is inappropriately high relative to renin: indicative of PA if plasma renin activity (PRA) is  $\leq 1$  ng/mL/h or direct renin concentration (DRC) is  $\leq 8.2$  mU/L AND serum/plasma aldosterone concentration is  $\geq 10$  ng/dL ( $\geq 277$  pmol/L) when measured by immunoassay or  $\geq 7.5$  ng/dL ( $\geq 208$  pmol/L) when measured by liquid chromatography–tandem mass spectrometry (LC-MS/MS)
2. Elevated aldosterone to renin ratio (ARR): indicative of PA if the aldosterone [ng/dL] to PRA [ng/mL/h] ratio is  $>20$  or aldosterone [pmol/L] to DRC [mU/L] ratio is  $>70$  when aldosterone is measured by immunoassay; the ARR indicative of PA is about 25% lower when aldosterone is measured by LC-MS/MS). (Fig. 1 and Table 5 for ARR cut points for differing assays and units).





## 2. Renin suppression alone



**Conclusion:** In this retrospective analysis, PRA  $< 1$  ng/mL/h appears to be a better screening test to identify PA in patients with hypertension vs. ARR  $\geq 30$ .

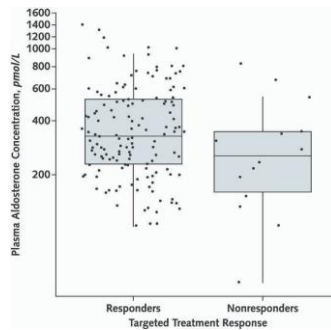
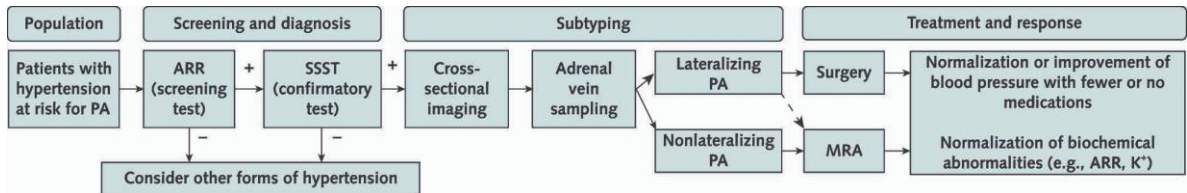
Adler et al., JCEM 2025  
Marcelli et al., Hypertension 2024

# "CONFIRMATORY" TESTING PITFALLS

<p><b>What is the supporting evidence for confirmatory tests for primary aldosteronism?</b></p>  <p>Systematic review and meta-analysis of 55 studies</p>	<p><b>Large variations in how tests conducted, interpreted, and verified</b></p>  <p>Risk of bias and concerns of applicability high in most primary studies</p>	<p><b>Spectrum bias and verification bias resulting in overestimation of accuracy by 5- to 7-fold</b></p>  <p>Use of confirmatory tests based on very low-quality evidence</p>
<p><b>Under most clinical scenarios, use of confirmatory tests led to an excess of missed cases</b></p>		
<p><b>Patients with primary aldosteronism but normal results (overlooked for treatment)</b></p> 		<p><b>People without primary but abnormal results (receiving unnecessary investigation)</b></p>

Leung et al., Hypertension 2022

# "CONFIRMATORY" TESTING PITFALLS



Leung et al., Ann Intern Med 2025

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# "CONFIRMATORY" TESTING PITFALLS

Table 2. Diagnostic Performance of the SSST According to Varying Cutoffs for Plasma Aldosterone Concentration Measured Using Immunoassay for All Patients

PAC Cutoff, pmol/L	TP, n	FP, n	FN, n	TN, n	Sensitivity (95% CI), %	Specificity (95% CI), %	PPV (95% CI), %	NPV (95% CI), %	FNR (95% CI), %	PLR (95% CI)	NLR (95% CI)
140	132	11	10	3	93.0 (87.4-96.6)	21.4 (4.7-50.8)	92.3 (86.7-96.1)	23.1 (5.0-53.8)	76.9 (46.2-95.0)	1.2 (0.9-1.6)	0.3 (0.1-1.1)
150	130	11	12	3	91.5 (85.7-95.6)	21.4 (4.7-50.8)	92.2 (86.5-96.0)	20.0 (4.3-48.1)	80.0 (51.9-95.7)	1.2 (0.9-1.5)	0.4 (0.1-1.2)
160	129	10	13	4	90.8 (84.9-95.0)	28.6 (8.4-58.1)	92.8 (87.2-96.5)	23.5 (6.8-49.9)	76.5 (50.1-93.2)	1.3 (0.9-1.8)	0.3 (0.1-0.9)
170	124	10	18	4	87.3 (80.7-92.3)	28.6 (8.4-58.1)	92.5 (86.7-96.4)	18.2 (5.2-40.3)	81.8 (59.7-94.8)	1.2 (0.9-1.7)	0.4 (0.2-1.1)
180	121	10	21	4	85.2 (78.3-90.6)	28.6 (8.4-58.1)	92.4 (86.4-96.3)	16.0 (4.5-36.1)	84.0 (63.9-95.5)	1.2 (0.9-1.7)	0.5 (0.2-1.3)
190	119	10	23	4	83.8 (76.7-89.4)	28.6 (8.4-58.1)	92.2 (86.2-96.2)	14.8 (4.2-33.7)	85.2 (66.3-95.8)	1.2 (0.8-1.6)	0.6 (0.2-1.4)
200	113	9	29	5	79.6 (72.0-85.9)	35.7 (12.8-64.9)	92.6 (86.5-96.6)	14.7 (5.0-31.1)	85.3 (68.9-95.0)	1.2 (0.8-1.8)	0.6 (0.3-1.2)
210	111	9	31	5	78.2 (70.5-84.7)	35.7 (12.8-64.9)	92.5 (86.2-96.5)	13.9 (4.7-29.5)	86.1 (70.5-95.3)	1.2 (0.8-1.8)	0.6 (0.3-1.1)
220	107	8	35	6	75.4 (67.4-82.2)	42.9 (17.7-71.1)	93.0 (86.8-96.9)	14.6 (5.6-29.2)	85.4 (70.8-94.4)	1.3 (0.8-2.1)	0.6 (0.3-1.1)
230	103	8	39	6	72.5 (64.4-79.7)	42.9 (17.7-71.1)	92.8 (86.3-96.8)	13.3 (5.1-26.8)	86.7 (73.2-94.9)	1.3 (0.8-2.0)	0.6 (0.3-1.2)
240	101	7	41	7	71.1 (62.9-78.4)	50.0 (23.0-77.0)	93.5 (87.1-97.4)	14.6 (6.1-27.8)	85.4 (72.2-93.9)	1.4 (0.8-2.4)	0.6 (0.3-1.0)
250	97	7	45	7	68.3 (60.0-75.9)	50.0 (23.0-77.0)	93.3 (86.6-97.3)	13.5 (5.6-25.8)	86.5 (74.2-94.4)	1.4 (0.8-2.3)	0.6 (0.4-1.1)
260	90	7	52	7	63.4 (54.9-71.3)	50.0 (23.0-77.0)	92.8 (85.7-97.0)	11.9 (4.9-22.9)	88.1 (77.1-95.1)	1.3 (0.7-2.2)	0.7 (0.4-1.3)
270	87	7	55	7	61.3 (52.7-69.3)	50.0 (23.0-77.0)	92.6 (85.3-97.0)	11.3 (4.7-21.9)	88.7 (78.1-95.3)	1.2 (0.7-2.1)	0.8 (0.4-1.4)
280	85	6	57	8	59.9 (51.3-68.0)	57.1 (28.9-82.3)	93.4 (86.2-97.5)	12.3 (5.5-22.8)	87.7 (77.2-94.5)	1.4 (0.8-2.6)	0.7 (0.4-1.2)
290	79	6	63	8	55.6 (47.1-64.0)	57.1 (28.9-82.3)	92.9 (85.3-97.4)	11.3 (5.0-21.0)	88.7 (79.0-95.0)	1.3 (0.7-2.4)	0.8 (0.5-1.3)
300	77	6	65	8	54.2 (45.7-62.6)	57.1 (28.9-82.3)	92.8 (84.9-97.3)	11.0 (4.9-20.5)	89.0 (79.5-95.1)	1.3 (0.7-2.4)	0.8 (0.5-1.3)

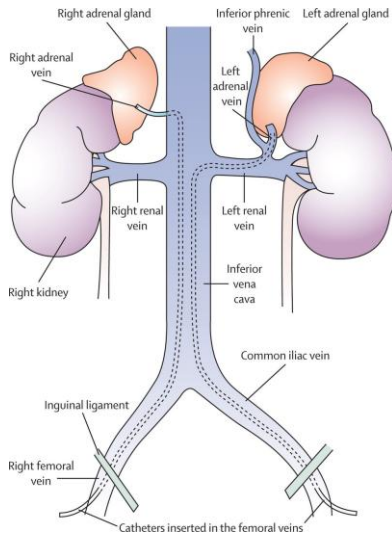
FN = false negative; FNR = FN rate (i.e., miss rate); FP = false positive; NLR = negative likelihood ratio; NPV = negative predictive value; PAC = plasma aldosterone concentration; PLR = positive likelihood ratio; PPV = positive predictive value; SSST = seated saline suppression test; TN = true negative; TP = true positive.

**NOTE: The updated 2025 Endocrine Society PA guidelines have majorly de-emphasized confirmatory testing for PA diagnosis.**

Leung et al., Ann Intern Med 2025

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# AVS PITFALLS



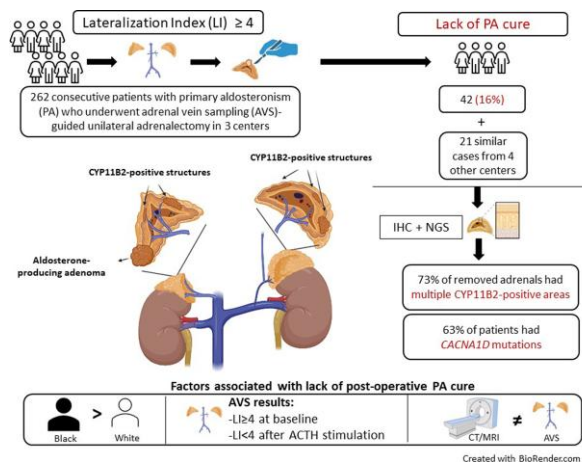
## Limitations of AVS:

- Invasive
- Center-to-center variability in procedures and interpretation thresholds
- Limited resource at specialized centers only
- Technically challenging
- Requires an experienced interventional radiologist

Rossi et al., Hypertension 2014

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# AVS PITFALLS

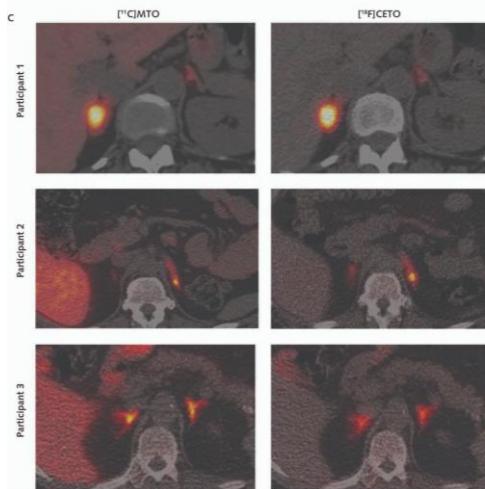


**Argues against the commonly held belief that AVS lateralization is synonymous with unilateral PA (e.g., APA); rather, AVS lateralization also commonly includes asymmetric bilateral PA.**

Turcu et al., Hypertension 2024

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## NUCLEAR IMAGING: ALTERNATIVE FOR LOCALIZATION?



- Potential benefits over AVS:
- Non-invasive
  - Not technically challenging
  - Not operator-dependent
  - Not limited to specialized centers
  - Highly scalable
  - May detect asymmetric bilateral PA cases that AVS fails to capture

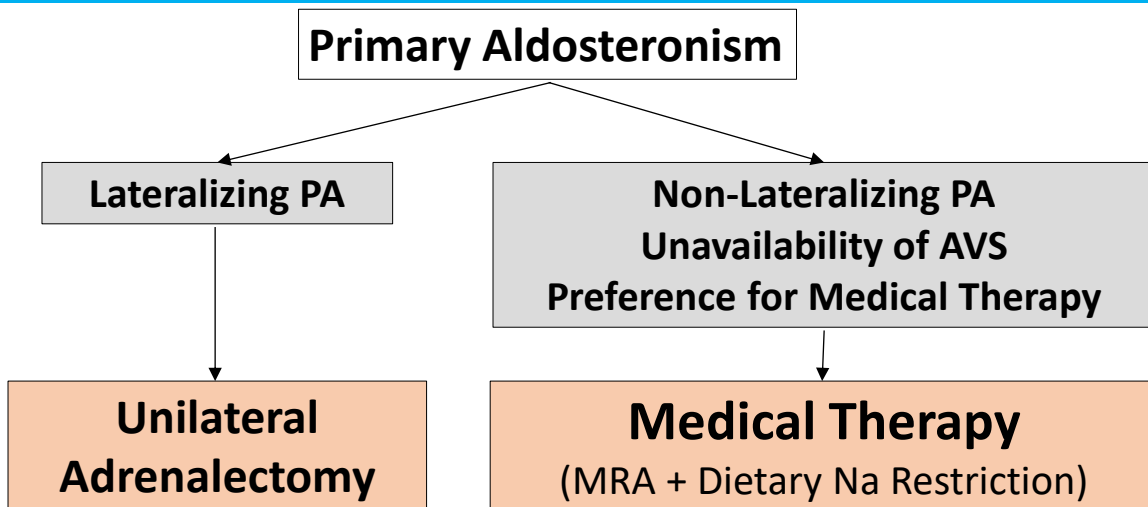
Goodchild et al., Ann Intern Med 2025

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## NOVEL TREATMENT APPROACHES IN PA

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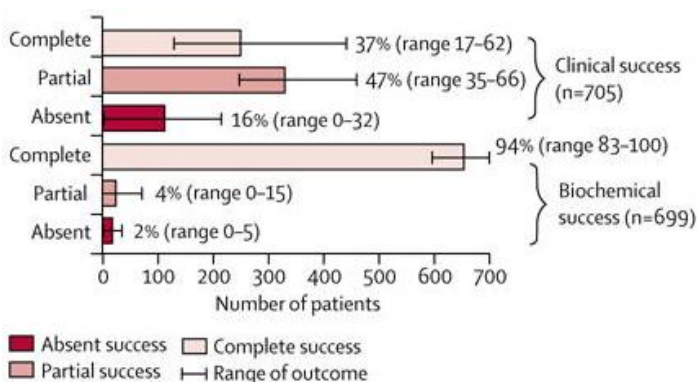
# TRADITIONAL PA TREATMENT ALGORITHM



Vaidya et al., Endocr Rev 2018

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# ADRENALECTOMY FOR LATERALIZING PA

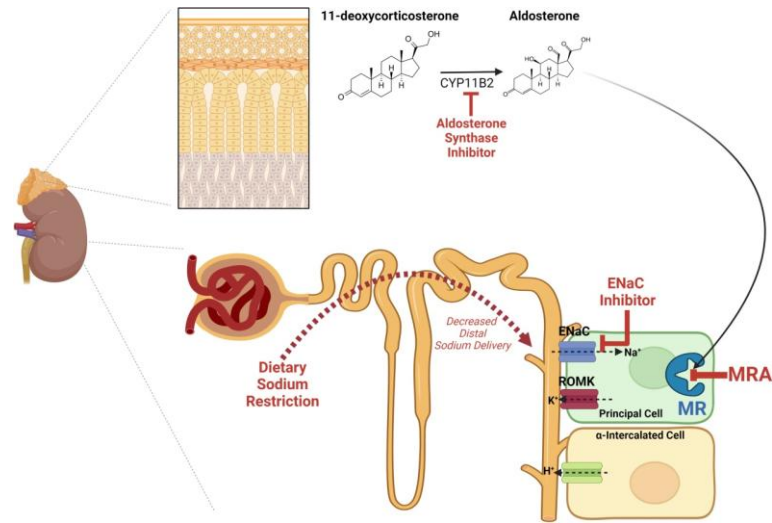


**BOTTOM LINE:** The vast majority of patients with lateralizing PA treated with adrenalectomy will achieve good clinical and biochemical outcomes.

Williams et al., Lancet D&E 2017

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# MEDICAL THERAPY IN PA



Hundemer et al., Endocr Rev 2024

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# WHAT ARE THE GOALS OF MEDICAL THERAPY IN PA?

SPECIAL FEATURE  
Clinical Practice Guideline

**The Management of Primary Aldosteronism: Case Detection, Diagnosis, and Treatment: An Endocrine Society Clinical Practice Guideline**

John W. Funder (chair), Robert M. Carey, Franco Mantero, M. Hassan Murad, Martin Reincke, Hirotsuka Shibata, Michael Stowasser, and William F. Young, Jr  
Hudson Institute of Medical Research (J.W.F.), Clayton, Australia; University of Virginia Health System (R.M.C.), Charlottesville, VA; University of Padova (F.M.), Padova, Italy; Mayo Clinic, Evidence-based Practice Center (M.H.M.), Rochester, MN; Klinikum der Ludwig-Maximilians-University of Munich (M.R.), München, Bavaria, Germany; Oita University (H.S.), Oita, Japan; University of Queensland (M.S.S.), Brisbane, Australia; and Mayo Clinic (W.F.Y.), Rochester, MN.

**Objective:** To develop clinical practice guidelines for the management of patients with primary aldosteronism

**Participants:** The Task Force included a chair, selected by the Clinical Guidelines Subcommittee of the Endocrine Society, six additional experts, a methodologist, and a medical writer. The Task Force received no corporate funding or remuneration.

**Evidence:** We searched for systematic reviews and primary studies to formulate the key treatment and prevention recommendations. We used the Grading of Recommendations, Assessment, Development, and Evaluation group criteria to describe both the quality of evidence and the strength of recommendations. We used 'recommend' for strong recommendations and 'suggest' for weak recommendations.

**Consensus Process:** We achieved consensus by collecting the best available evidence and conducting one group meeting, several conference calls, and multiple e-mail communications. With the help of a medical writer, the Endocrine Society's Clinical Guidelines Subcommittee, Clinical Affairs Core Committee, and Council successfully reviewed the drafts prepared by the Task Force. We placed the version approved by the Clinical Guidelines Subcommittee and Clinical Affairs Core Committee on the Endocrine Society's Website for comments by members. At each stage of review, the Task Force received written comments and incorporated necessary changes.

## Standard Practice

- Fixed doses of MRAs
- Titration of MRAs with the goals of:
  1. Normalizing potassium
  2. Normalizing BP

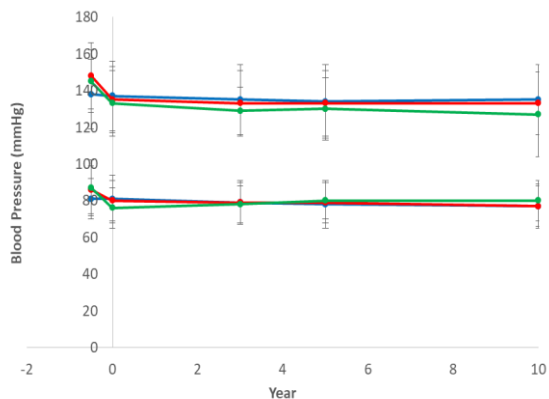
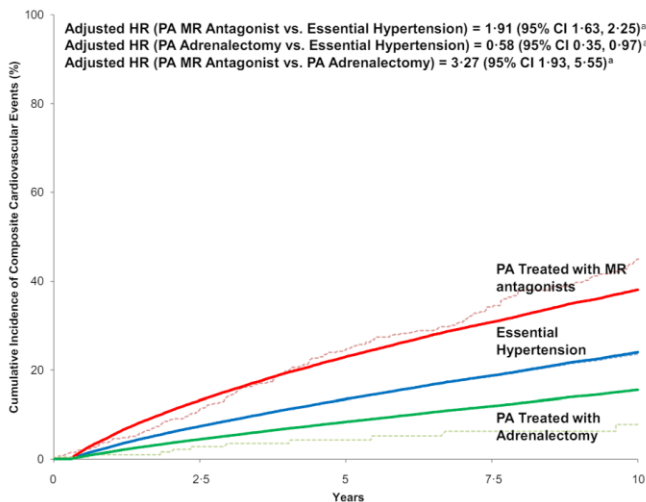
## Ultimate Goals

- Reverse pathophysiology of PA via effective MR blockade
- Mitigate the excess cardiovascular and kidney disease risk inherent to PA
  - ✓ Rise in renin

Funder et al., JCEM 2016

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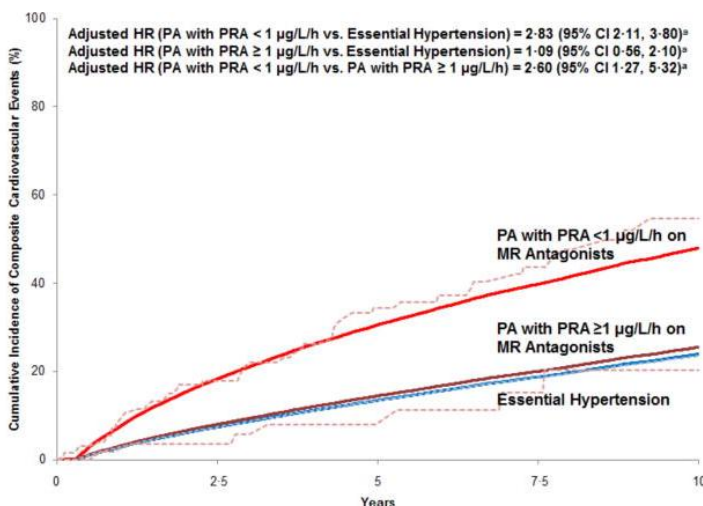
# CARDIOVASCULAR OUTCOMES WITH TARGETED THERAPY



Hundemer et al., Lancet D&E 2018

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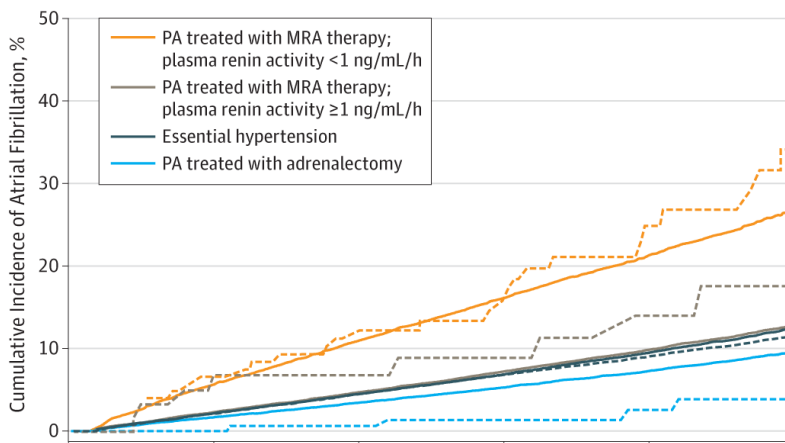
# CARDIOVASCULAR OUTCOMES WITH TARGETED THERAPY



Hundemer et al., Lancet D&E 2018

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## CARDIOVASCULAR OUTCOMES WITH TARGETED THERAPY

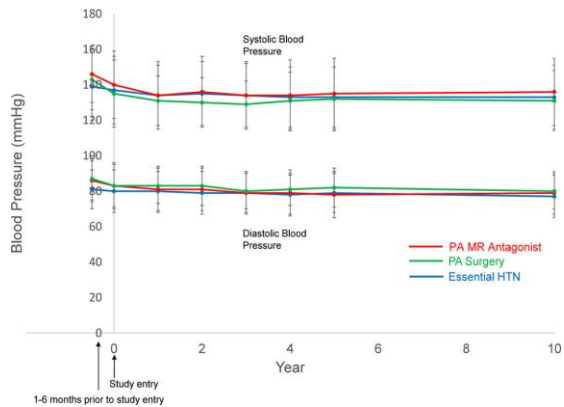
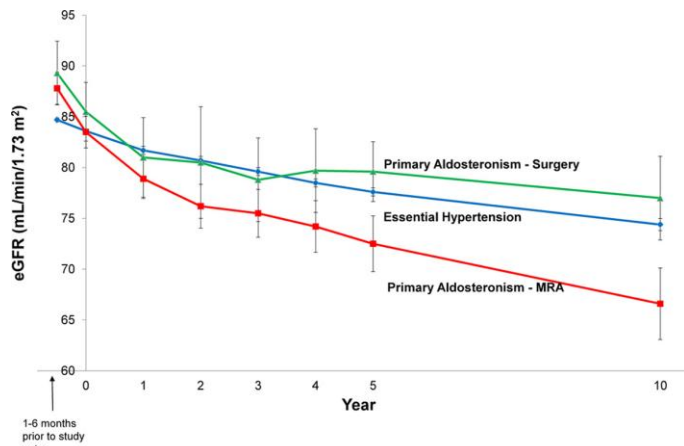


**BOTTOM LINE:** For patients with PA treated with MRAs, “unsuppression” of renin was associated with a significant reduction in cardiovascular disease risk.

Hundemer et al., JAMA Cardiology 2018

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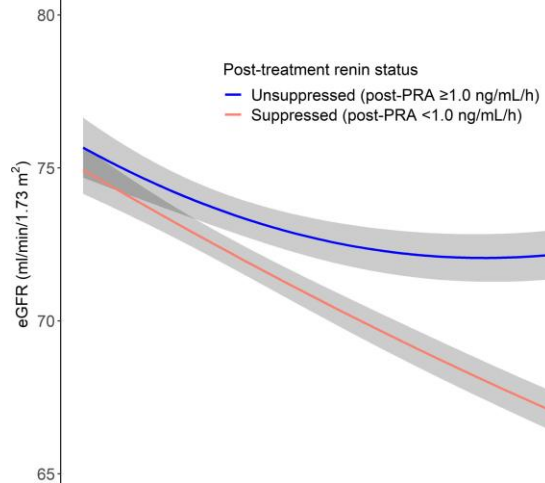
## KIDNEY OUTCOMES WITH TARGETED THERAPY



Hundemer et al., Hypertension 2018

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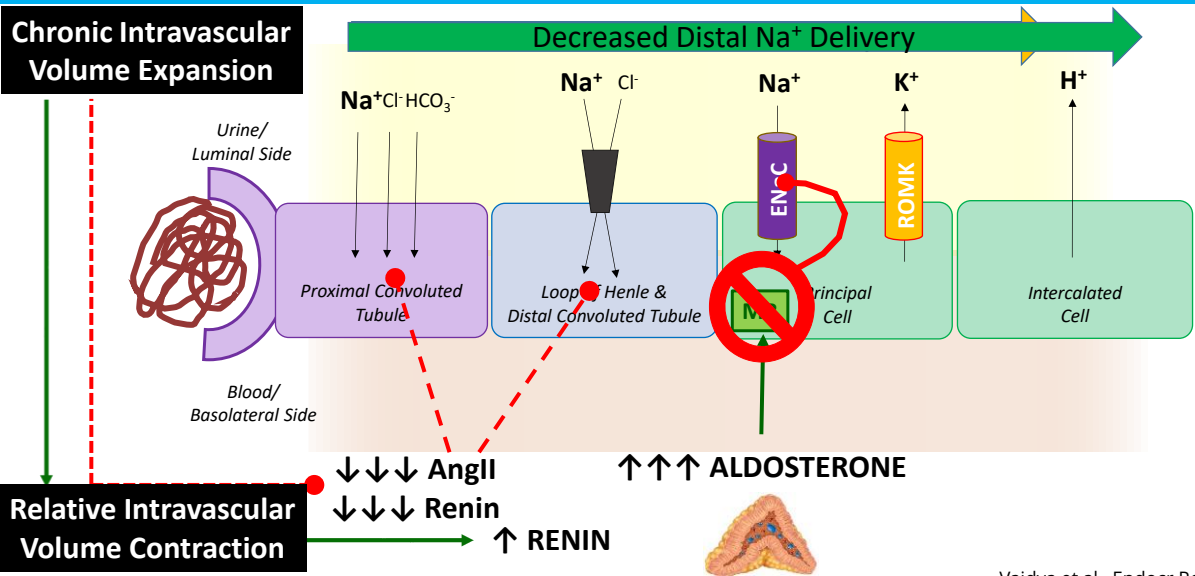
# KIDNEY OUTCOMES WITH TARGETED THERAPY



**BOTTOM LINE:** For patients with PA treated with MRAs, “unsuppression” of renin was associated with a significant reduction in kidney disease risk.

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# RENIN AS A BIOMARKER IN MEDICALLY TREATED PA



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# RENIN AS A BIOMARKER IN MEDICALLY TREATED PA

**Table 3. Prior studies that have evaluated renin as a biomarker reflecting optimized therapy in patients with primary aldosteronism treated with mineralocorticoid receptor antagonist medications**

Study	Location	Design	Populations compared	Renin target or change	Outcomes
Hundemer et al, 2018 (55)	USA	Retrospective	PA treated with MRAs PA treated with adrenalectomy Essential HTN	1.0 ng/mL/h	MACE Death
Hundemer et al, 2018 (58)	USA	Retrospective	PA treated with MRAs PA treated with adrenalectomy Essential HTN	1.0 ng/mL/h	Atrial fibrillation
Kohler et al, 2021 (242)	Germany	Retrospective	PA treated with MRAs PA treated with adrenalectomy Essential HTN	12 mU/L	Cardiac function/structure Pro-BNP levels
Wu et al, 2021 (165)	Taiwan	Retrospective	Lateralizing PA Only: • MRA • Adrenalectomy	0.6 ng/mL/h	MACE Death
Saiki et al, 2022 (222)	Japan	Prospective	PA treated with MRAs only	1.0 ng/mL/h	Blood pressure Albuminuria
Ueda et al, 2022 (243)	Japan	Retrospective	PA treated with MRAs PA treated with adrenalectomy	$\Delta$ of 0.32 ng/mL/h	Cardiac function/structure
Puar et al, 2022 (244)	Singapore	Prospective	PA treated with MRAs PA treated with adrenalectomy	1.0 ng/mL/h	Cardiac function/structure
Chen et al, 2022 (245)	Taiwan	Retrospective	PA treated with MRAs PA treated with adrenalectomy	1.5 ng/mL/h	Pulse wave velocity
Yoshida et al, 2023 (114)	Japan	Retrospective	PA treated with MRAs/dietary salt intake	5 pg/mL	Blood pressure Serum potassium Salt sensitivity
Mansur et al, 2023 (246)	USA	Prospective	PA treated with MRAs only	1.0 ng/mL/h	Blood pressure Antihypertensive medications Albuminuria
Katsuragawa et al, 2023 (247)	Japan	Retrospective	PA Treated with MRAs Only	1.0 ng/mL/h	Longitudinal changes in estimated glomerular filtration rate

Hundemer et al., Endocr Rev 2024

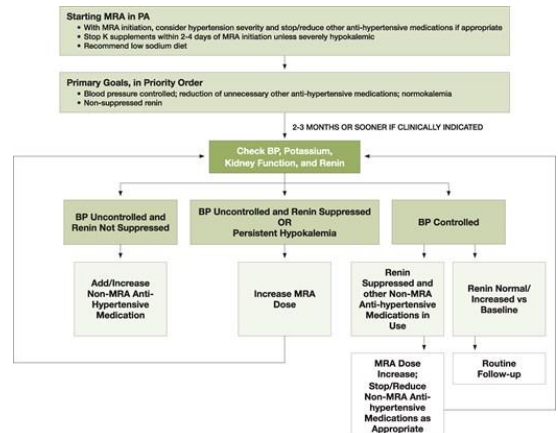
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# RENIN AS A BIOMARKER IN MEDICALLY TREATED PA

## PA Medical Outcomes (PAMO) Criteria

clinical response. “Complete biochemical response” was defined as “correction of hypokalemia without potassium supplementation, and normalization of plasma renin activity or concentration”; while “absent biochemical response” was defined as “persistent hypokalemia and/or persistently suppressed or low plasma renin activity or concentration without change from baseline”. “Complete clinical response” was de-

## 2025 Endocrine Society Guideline



Yang et al., Lancet D&E 2025  
Adler et al., JCEM 2025

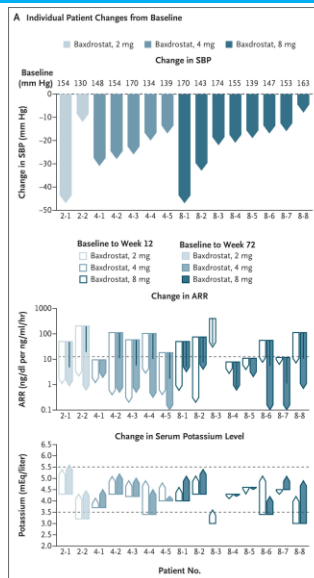
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# EMERGING TREATMENT APPROACHES IN PA

## Phase 2a Study of Baxdrostat in Primary Aldosteronism

Published July 13, 2025 | N Engl J Med 2025;393:515-518 | DOI: 10.1056/NEJM2508629 | VOL. 393 NO. 5

***Phase 3 BaxPA clinical trial currently underway.***



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## SUMMARY – KEY POINTS

1. PA pathophysiology spans a much broader continuum than previously recognized with important cardiovascular and kidney implications for the general population.
2. A number of pitfalls along traditional diagnostic pathways lead to many missed PA cases.
3. When titrating MRA therapy in the treatment of PA, targeting a rise in renin is associated with improved cardiovascular and kidney outcomes.

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**THANK YOU**

**Questions?**