CASE #1

Robert is a 19 year-old male who presents to you following a minor sporting injury. BP noted to be 180/110 HR 95. Follow up BPs remain high. There is a strong family history of high blood pressure and strokes on his father's side.

WHAT WOULD YOU DO NEXT?

WHAT MEDS WOULD YOU START?

GUIDELINES

Choose any sequence of: **ACE-** Angiotensin Converting Enzyme Inhibitor or **ARB-** Angiotensin Receptor Blocker or **D-** Diuretic or **CCB**- Calcium Channel Blocker:

a. HCTZ- ACE/ARB- CCB
b. HCTZ- CCB- ACE/ARB
c. ACE/ARB - HCTZ- CCB
d. ACE/ARB – CCB -HCTZ
e. CCB - HCTZ- ACE/ARB
f. CCB- ACE/ARB -HCTZ
g. Other therapy off guideline recommendations
h. The order doesn't matter

CASE #2

William is a 19 year-old male who presents to you following a minor sporting injury. BP noted to be 180/110 HR 95. Follow up BPs remain high. There is a strong family history of high blood pressure and strokes on his father’s side.

WHAT WOULD YOU DO NEXT?

WHAT MEDS WOULD YOU START?

GUIDELINES

Choose any sequence of: **ACE-** Angiotensin Converting Enzyme Inhibitor or **ARB-** Angiotensin Receptor Blocker or **D-** Diuretic or **CCB**- Calcium Channel Blocker:

a. HCTZ- ACE/ARB- CCB
b. HCTZ- CCB- ACE/ARB
c. ACE/ARB - HCTZ- CCB
d. ACE/ARB – CCB -HCTZ
e. CCB - HCTZ- ACE/ARB
f. CCB- ACE/ARB -HCTZ
g. Other therapy off guideline recommendations
h. The order doesn't matter

CASE #3

Nancy is a 19 year-old female who presents to you following a minor sporting injury. BP noted to be 180/110 HR 95. Follow up BPs remain high. There is a strong family history of high blood pressure and strokes on his father's side.

WHAT WOULD YOU DO NEXT?

WHAT MEDS WOULD YOU START?

GUIDELINES

Choose any sequence of: **ACE-** Angiotensin Converting Enzyme Inhibitor or **ARB-** Angiotensin Receptor Blocker or **D-** Diuretic or **CCB**- Calcium Channel Blocker:

a. HCTZ- ACE/ARB- CCB
b. HCTZ- CCB- ACE/ARB
c. ACE/ARB - HCTZ- CCB
d. ACE/ARB – CCB -HCTZ
e. CCB - HCTZ- ACE/ARB
f. CCB- ACE/ARB -HCTZ
g. Other therapy off guideline recommendations
h. The order doesn't matter

GUIDELINE MEDS

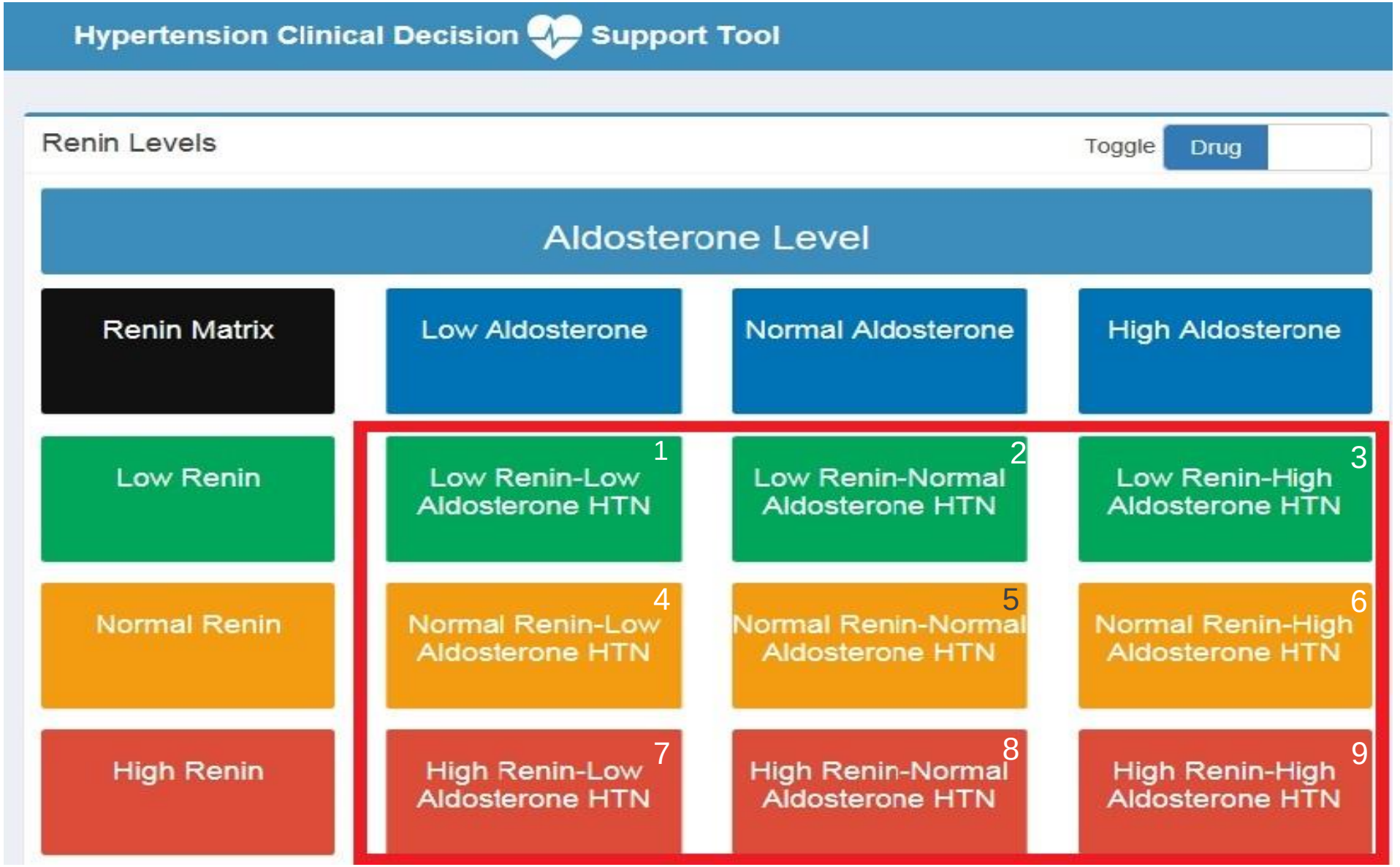
None of the guideline meds you have chosen have reached your BP goal.

What would you do next?

POINT

- Hypertension is not a singular disease. These are 3 different cases.
- Therapy must be individualized based on age, gender, ethnicity, associate disease, and renin/aldosterone levels.
- Using a renin and aldosterone classification system (RAS Class), we can sort over 50 secondary causes of HTN each with a specific therapy medical or surgical.
- Get an Aldosterone/Renin ratio (ARR) in patients with rHTN

THE RENIN-ALDOSTERONE RAS MATRIX



Laragh Classification & RAS Distribution

Renin	Low Aldosterone	Normal Aldosterone	High Aldosterone	Range
Low Renin	5-8% (1)	13-21% (2)	1-2% (3)	19-31%
Normal Renin	2-6% (4)	36-54% (5)	3-6% (6)	41-66%
High Renin	<1% (7)	8-12% (8)	6-9% (9)	15-22%
Range	8-15%	57-87%	10-17%	

RAS = Renin Aldosterone System

CASE #1 LABS

Robert is a 19 year-old male who presents to you following a minor sporting injury. BP noted to be 180/110. Follow up BPs remain high. There is a family history of high blood pressure and strokes on his father's side.

LABS: Na 144, K 3.1, Urea 5, Creatinine 80, Bicarb 31, Renin < 3mU/L (low), Aldosterone 980 ug/l (high).

Low renin-high aldosterone HTN is Box 3:

WHAT WOULD YOU DO KNOWING THIS IS LOW RENIN-HIGH ALDOSTERONE HTN?

CASE #1 LABS

Robert is a 19 year-old male who presents to you following a minor sporting injury. BP noted to be 180/110. Follow up BPs remain high. There is a family history of high blood pressure and strokes on his father's side.

LABS: Na 144, K 3.1, Urea 5, Creatinine 80, Bicarb 31, Renin < 3mU/L (low), Aldosterone 980 ug/l (high).

Low renin-high aldosterone HTN is Box 3:

WHAT WOULD YOU DO KNOWING THIS IS LOW RENIN-HIGH ALDOSTERONE HTN?

Do a Saline Suppression test

Conn's Syndrome

Primary Aldosteronism

Autonomous overproduction of aldosterone by the adrenal glands. 1-2% of mild hypertension & up to 20% in resistant hypertension. Hypokalaemia is a clinical hall mark but it is a late sign and a variable manifestation; >50% have normokalemia

DxD of low renin-high aldosterone HTN in the CDST:

- BAH- Bilateral Adrenal Hyperplasia (common)
- APA- Discrete aldosterone-producing adenoma
- Unilateral adrenal hyperplasia (rare)
- Familial hyperaldosteronism (FH1-2-3)
- Adrenocortical carcinomas
- Ectopic aldosterone secreting tumors
- Simple virilizing form of partial 21-hydroxylase enzyme deficiency congenital adrenal hyperplasia
- A list of drugs that raise aldosterone or lower renin

W/U of Primary Aldosteronism

Seated resting mid-morning plasma renin and aldosterone

↓

If suppressed renin (<10mU/l) **+** elevated aldosterone (> 400ug/l) **+** A/R ratio > 40

↓

Saline suppression test (2000 ml IV normal saline over 4 hours with pre and post aldosterone levels)

↓

If post saline-aldosterone is non-suppressible (> 200ug/l)

↓

Adrenal CT scan

↓

Unilateral adenoma > 2.0cm

↓

Laparoscopic adrenalectomy

Normal **or** unilateral adenoma < 2cm **or** bilateral hyperplasia **or** unilateral hyperplasia

↓

Genetic test for GRA (Glucocorticoid Remediable Aldosteronism)

↓

If GRA negative do adrenal vein sampling

- Bilateral Hyperplasia or FH3

+ for lateralization: APA or unilateral hyperplasia

CASE #1 LABS

Robert is a 19 year-old male who presents to you following a minor sporting injury. BP noted to be 180/110. Follow up BPs remain high. There is a family history of high blood pressure and strokes on his father's side. LABS: Na 144, K 3.1, Urea 5, Creatinine 80, Bicarb 31, Renin < 3mU/L (low), Aldosterone 980 ug/l (high). Low renin-high aldosterone HTN is Box 3

WHAT IS THE DIAGNOSIS?

Dx: Low renin-high aldosterone HTN -secondary to Conn's Syndrome- due to APA.

Rx: Surgery to remove the adenoma

CASE #2 LABS

William is a 19 year-old male who presents to you following a minor sporting injury. BP noted to be 180/110. His BP remains high over time. There is a family history of high blood pressure and strokes on his father's side.

LABS: Na 144, K 3.1, Urea 5, Creatinine 80, Bicarb 31, Renin < 3mU/L (low), Aldosterone 90 ug/l (low). Low renin-low aldosterone HTN is Box 1

WHAT WOULD YOU DO KNOWING THIS IS LOW RENIN-LOW ALDOSTERONE HTN?

CASE #2 LABS

William is a 19 year-old male who presents to you following a minor sporting injury. BP noted to be 180/110. His BP remains high over time. There is a family history of high blood pressure and strokes on his father's side.
LABS: Na 144, K 3.1, Urea 5, Creatinine 80, Bicarb 31, Renin < 3mU/L (low), Aldosterone 90 ug/l (low).
Cortisol is normal.

WHAT WOULD YOU DO KNOWING THIS IS LOW RENIN-LOW ALDOSTERONE HTN?

Low renin – low aldosterone HTN needs a serum cortisol to sort the 3 diagnostic possibilities (Low-Normal-High Cortisol). *The cortisol comes back normal.*

DxD of Low renin – low aldosterone HTN in the Matrix:

Liddle's Disease- Weinstein-Spitzer- Gordon's syndrome- Geller's syndrome- Exogenous sources (drugs, foods)- CKD

DX: Low renin- low aldosterone HTN secondary to Liddle's Syndrome

Rx: ENaC disease is diuretic sensitive and responds best to Amiloride or Triamterene not thiazides!

CASE #3 LABS

Nancy is a 19 year-old female who presents to you following a minor sporting injury. BP noted to be 180/110 HR 95. Follow up BPs remain high. There is a strong family history of high blood pressure and strokes on her father's side. Labs: Na 140, K 3.1, creatinine clearance 70, pH 7.43, HCO3 34, Renin 2mU/l (low), Aldosterone 175ug/l (low). She does not respond to Triamterene but improves with high dose spironolactone.

WHAT WOULD YOU DO KNOWING THIS IS LOW RENIN-LOW ALDOSTERONE HTN?

CASE #3 LABS

Nancy is a 19 year-old female who presents to you following a minor sporting injury. BP noted to be 180/110 HR 95. Follow up BPs remain high. There is a strong family history of high blood pressure and strokes on her father's side. Labs: Na 140, K 3.1, creatinine clearance 70, pH 7.43, HCO3 34, Renin 2mU/l (low), Aldosterone 175ug/l (low). She does not respond to Triamterene but improves with high dose spironolactone.

NEXT STEP- low renin – low aldosterone HTN (Box1) needs a serum cortisol to sort the diagnostic possibilities. The cortisol is high. The DxD is:

1. **Cushing's syndrome or Cushing's disease or Pseudo-Cushings's Syndrome**
2. **Apparent Mineralocorticoid Excess (AME) - both Congenital Apparent Mineralocorticoid Excess (CAME) & Acquired Apparent Mineralocorticoid Excess**
3. **Generalized Glucocorticoid Resistance (Chrousos Syndrome)**
4. **Ectopic production of ACTH** -small cell cancer of the lung and bronchial carcinoids can cause ectopic production of ACTH resulting in Cushing's syndrome.

Dx: Low renin-low aldosterone HTN secondary to congenital AME

Rx: Apparent Mineralocorticoid Excess has low K that suggests hyperaldosteronism (Box 3) but AME has low Aldosterone levels that responds to Aldactone/Spironolactone.

CASE # 4

Linda is a 32 YOWF referred to you with 5-year history of difficult to control hypertension on 3 drugs: HCTZ, Lisinopril, Amlodipine to max tolerated dosing.

LABS: Na 138, K 4.2, Bun 28, Cr 1.6, GFR 92 ml/min. Renin 260 ng/ml-hour(>10X normal). Aldosterone is low at 1 ng/dl i.e.

High renin-low aldosterone HTN

WHAT WOULD YOU DO NEXT FOR HIGH RENIN HTN?

WHAT IS THE LIKELY DIAGNOSIS (in a young female with normal kidney function)?

CASE # 4

32 YOWF with 5-year history of difficult to control hypertension on 3 drugs: HCTZ, Lisinopril, Amlodipine to max tolerated dosing. LABS: Na 138, K 4.2, Bun 28, Cr 1.6, GFR 92 ml/min. Renin 260 ng/ml-hour (>10X) Aldosterone low at 1 ng/dl i.e. high renin - low aldosterone HTN.

High renin HTN implies reno-vascular disease!

WHAT WOULD YOU DO NEXT? Renal duplex ultrasound-

Renal Duplex Scan shows right renal artery velocity of 380 cm/sec (normal < 200 cm/sec). The likely differential: renal artery stenosis (Rx: CORAL medications ARB, D, CCB, ASA, Statins vs stenting) or Fibromuscular Hyperplasia (Rx: CORAL meds vs. angioplasty)

Next Step- angiography


Dx: High renin-low aldosterone HTN secondary to Fibromuscular Hyperplasia
RX: Angioplasty

A4M- because in science truth is a moving target

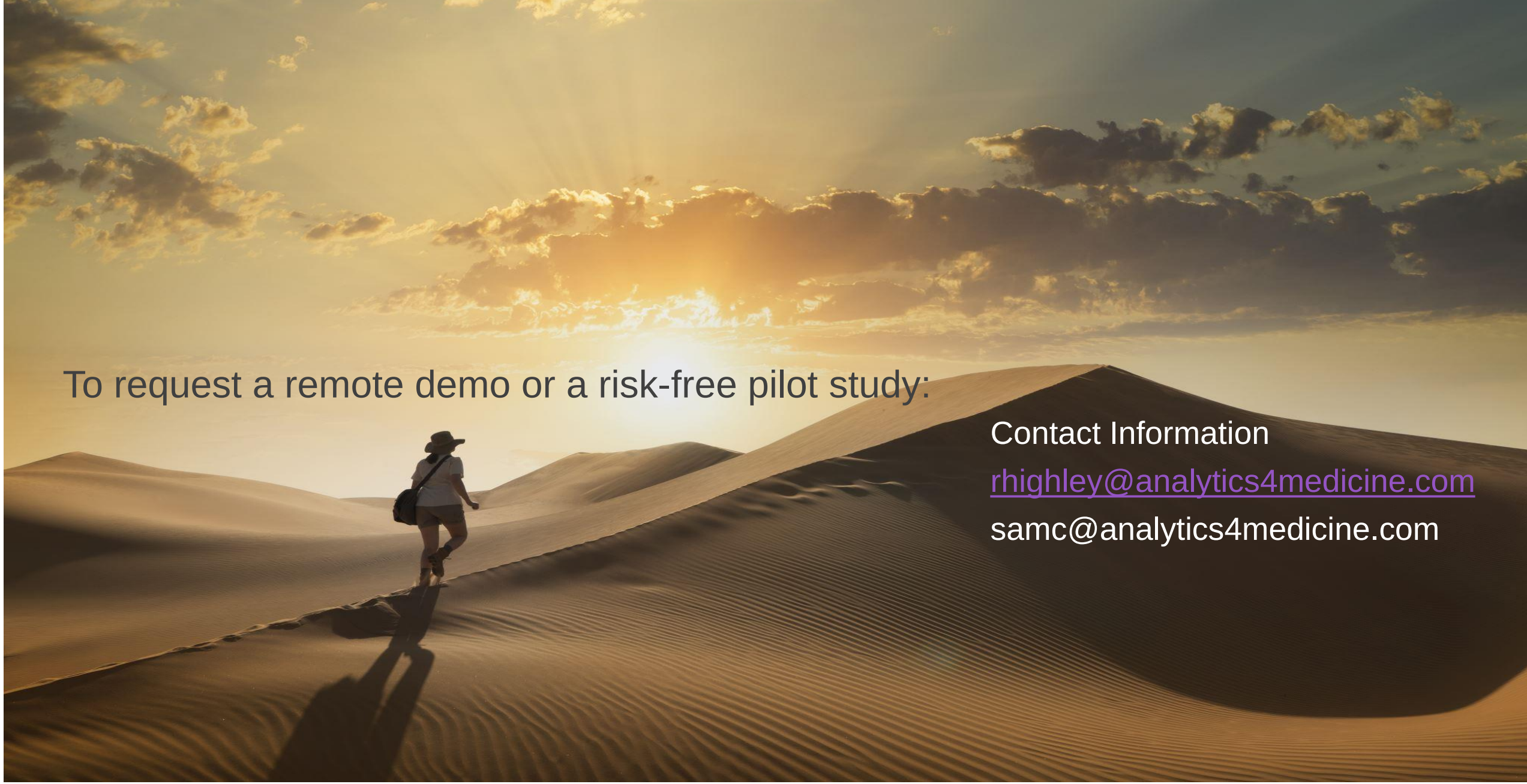
Without an ARR and a sorting mechanism, we would have failed these 4 patients. Trial and error is inefficient, time consuming, expensive and does not work in over half the cases. It needs to be replaced with personalized medicine to better serve these patients, save you time, and lower the cost of care.

A4M's CDST helps you make the diagnosis and matches the mechanism of HTN to peer reviewed therapy.

Our drug sequencing algorithm- uses age, ethnicity, associated disease and renin/aldosterone levels to enforce guidelines, select appropriate drugs and control BP better than all the docs in the USA (76% vs. 48%).

Our Diagnostic Matrix- helps sort out over 50 secondary causes of HTN and provides peer reviewed therapy for each diagnosis. The CDST can efficiently run a specialty HTN Clinic. It is a self contained clinical trial to follow patients over time and across delivery systems to track outcomes and do machine learning to constantly improve the treatment of HTN with your help.

It is worth a conversation.



To request a remote demo or a risk-free pilot study:

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