

RDN to treat Resistant Hypertension

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Disclosures

- ◆ **Medtronic - Advisory Board**
- ◆ **Recor Medical – Advisory Board**
- ◆ **Sonivie Medical – Advisory Board**

Outline

- ◆ **Basis of RDN**
- ◆ **Current data on RDN**
- ◆ **Where are we with RDN technologies?**

Global Hypertension Control Rates are Low

Less Than 25% of HTN Patients are Controlled Worldwide

Hypertension Treatment Cascade in 2019



NCD, Lancet, 2021. [https://doi.org/10.1016/S0140-6736\(21\)01330-1](https://doi.org/10.1016/S0140-6736(21)01330-1)

Slide 4

HD1

I like the flow: 1 Prevalance high. 2. Control Rates low. 3. Control rates worsening 4. Covid not helping 5. Adherence: the elephant in the living room

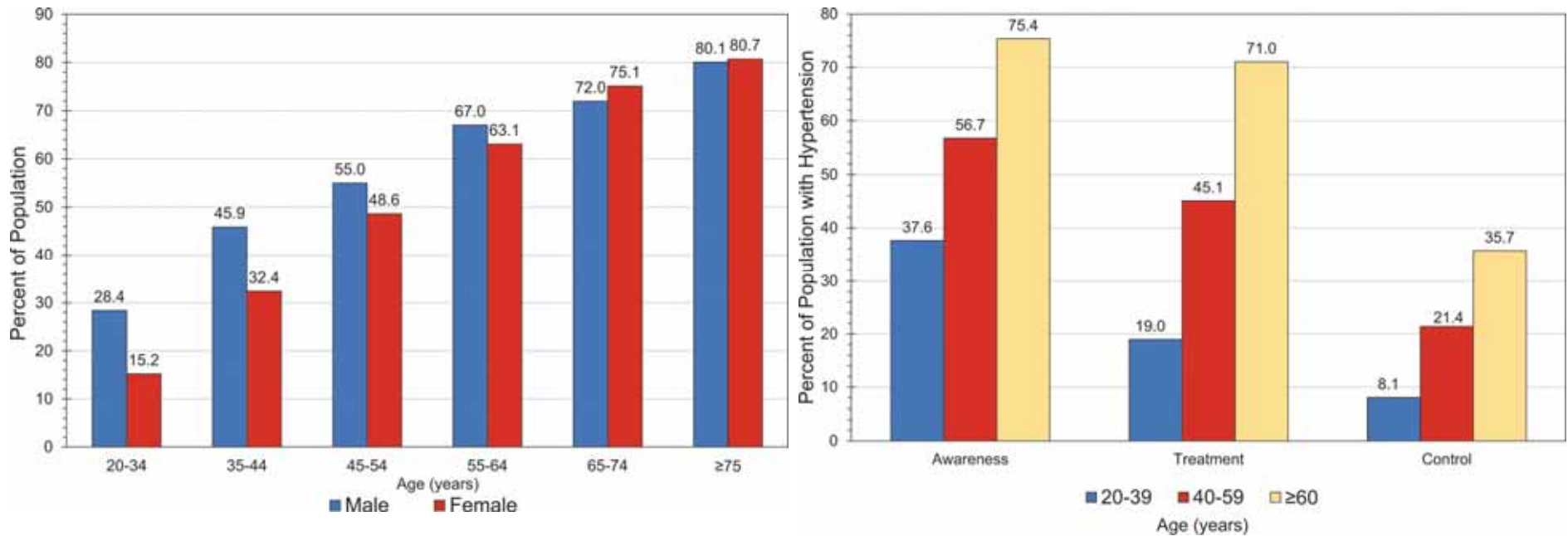
Hettrick, Doug, 2/10/2022

MC1

Great! thanks for helping shape the story even better. I wanted to try to throw in the message around, if you CAN help get BP in control- 5 to 10 mmHg reductions are clinically meaningful.

Mobley, Chris, 2/14/2022

Incidence of HTN in US population



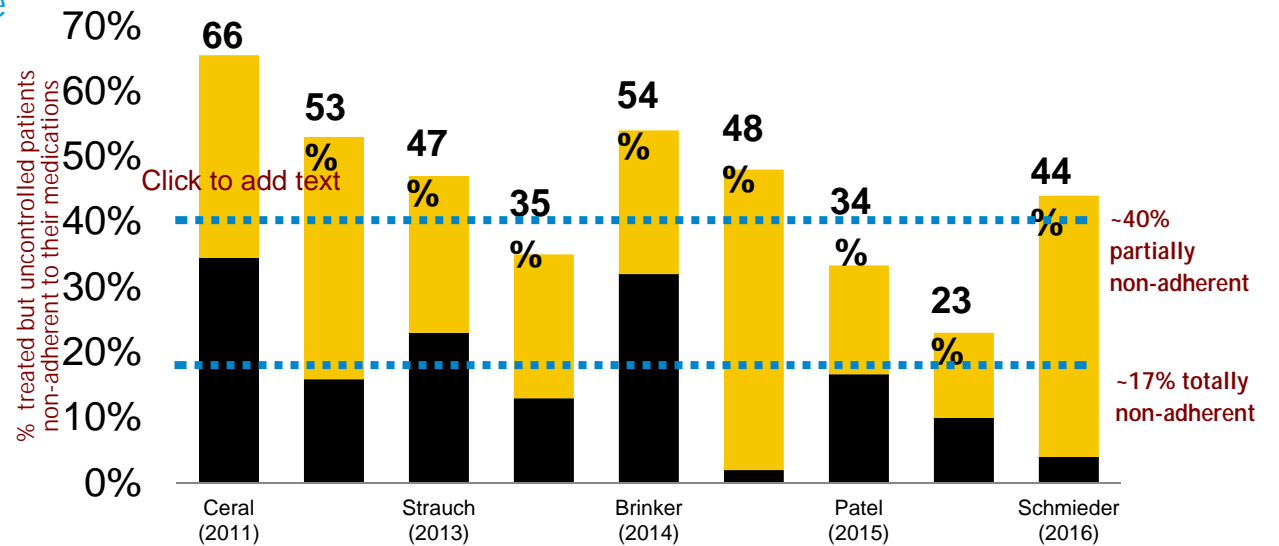
Tsao et al. Circ. 2023

ADHERENCE TO ANTIHYPERTENSIVE MEDICATIONS IS POOR

Multiple clinical trials quantified antihypertensive drug adherence using objective **blood and urine testing**

Among treated uncontrolled hypertensive patients:
 ~40% were not taking **all** antihypertensive medications
 ~17% were not taking **any** antihypertensive medications

PATIENT NON-ADHERENCE HAS REACHED EPIDEMIC PROPORTIONS¹



Many patients cannot tolerate polypharmacy and abandon it¹

Berra E, et al. Hypertension. 2016;68:297-306

Slide 6

HD2 I think a dashed line is missing for 17%

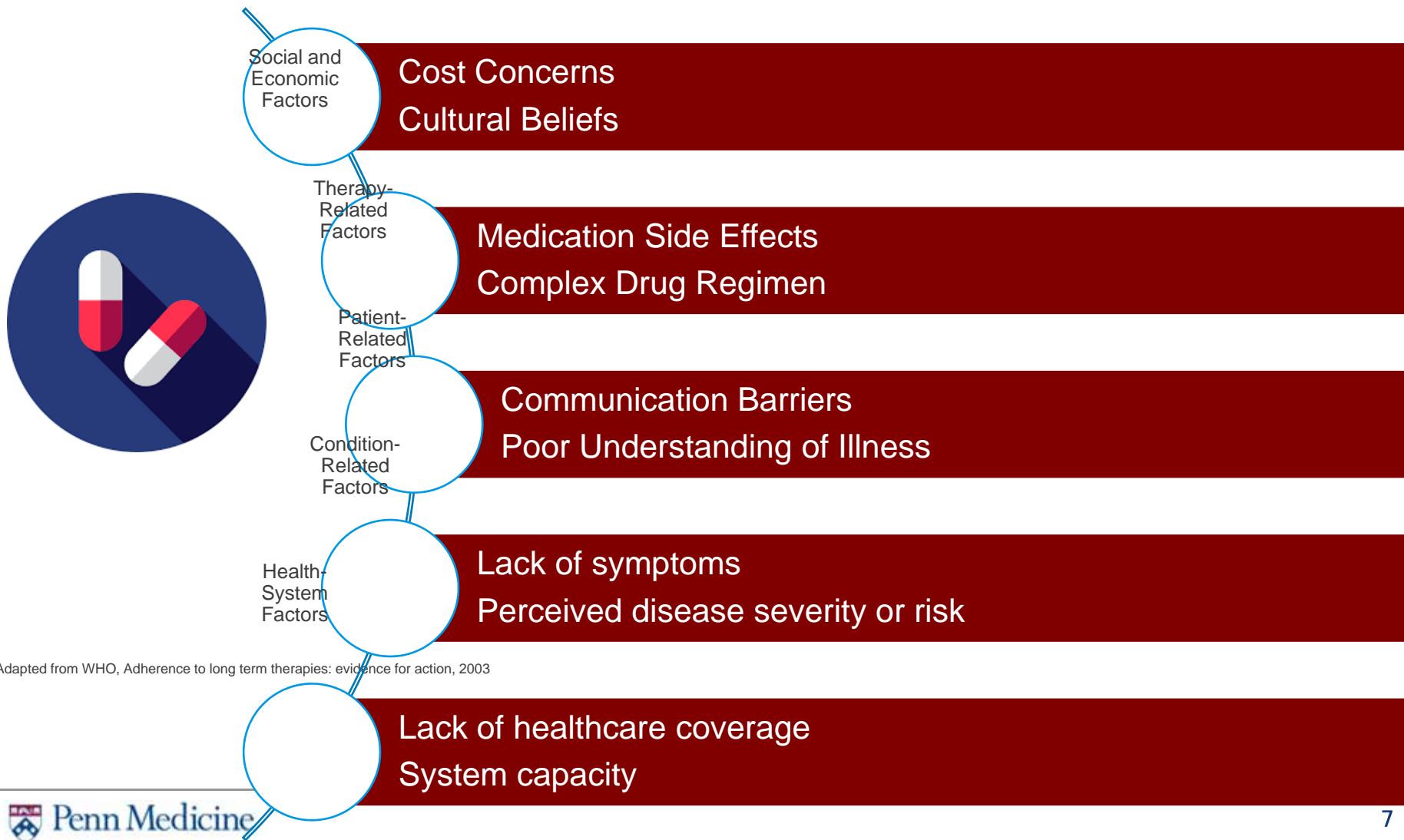
Hettrick, Doug, 8/27/2021

MC2 updated

Mobley, Chris, 8/30/2021

Barriers to Medication Adherence are Multidimensional

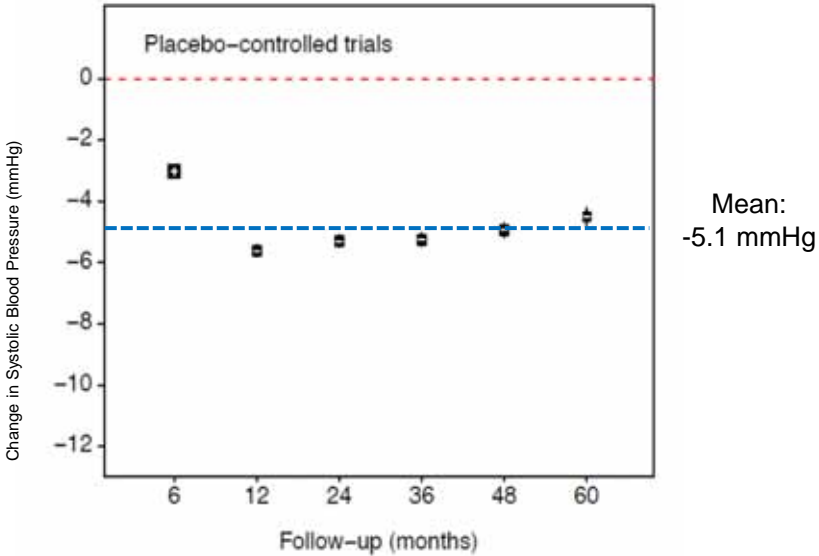
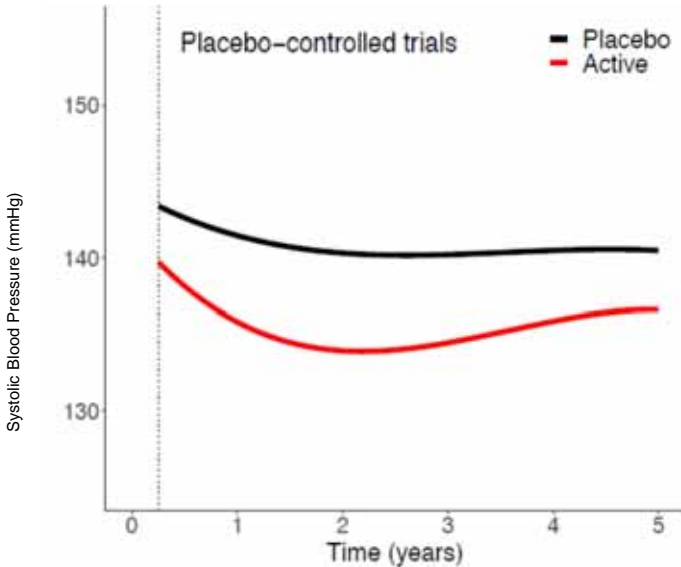
Include Economic, Psychological, and Social Influences



Adapted from WHO, Adherence to long term therapies: evidence for action, 2003

What is success?

- ◆ Individual patient-level data meta-analysis of 352,744 participants from 51 large-scale RCT's

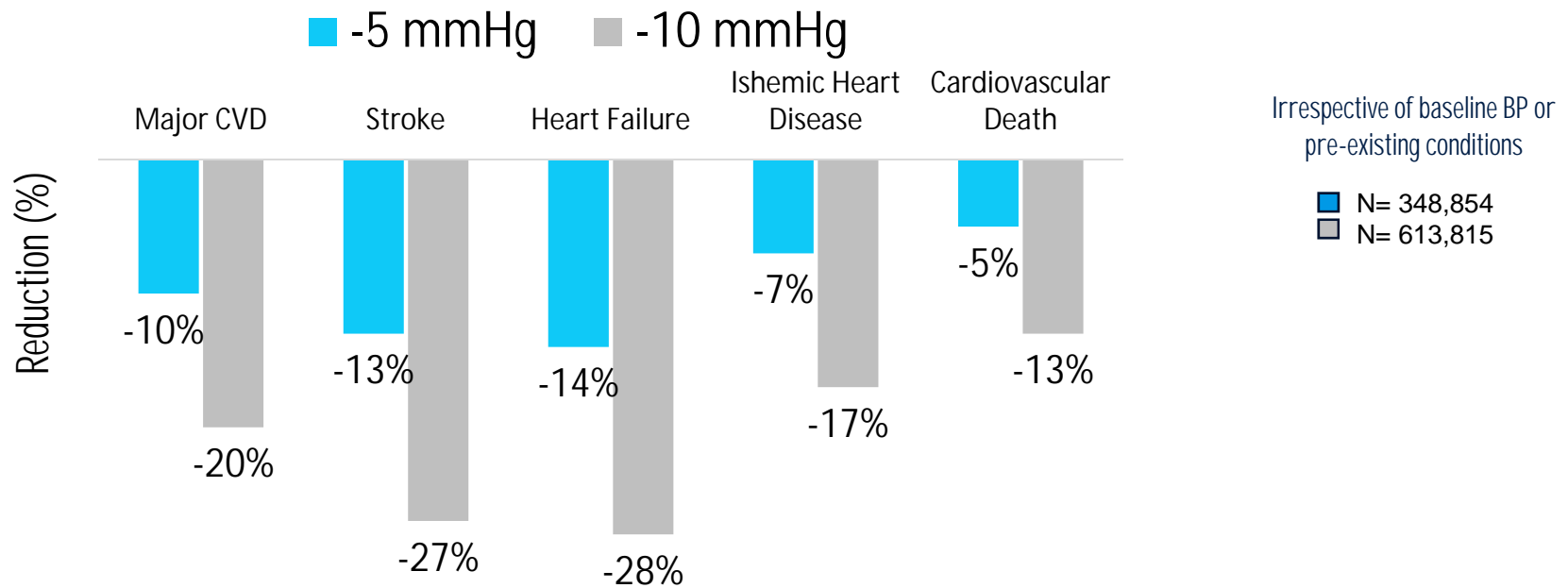


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Heart Published Online First: 20 January 2022. doi: 10.1136/heartjnl-2021-320171

BP decrease leads to clinically meaningful reduction in CV risk

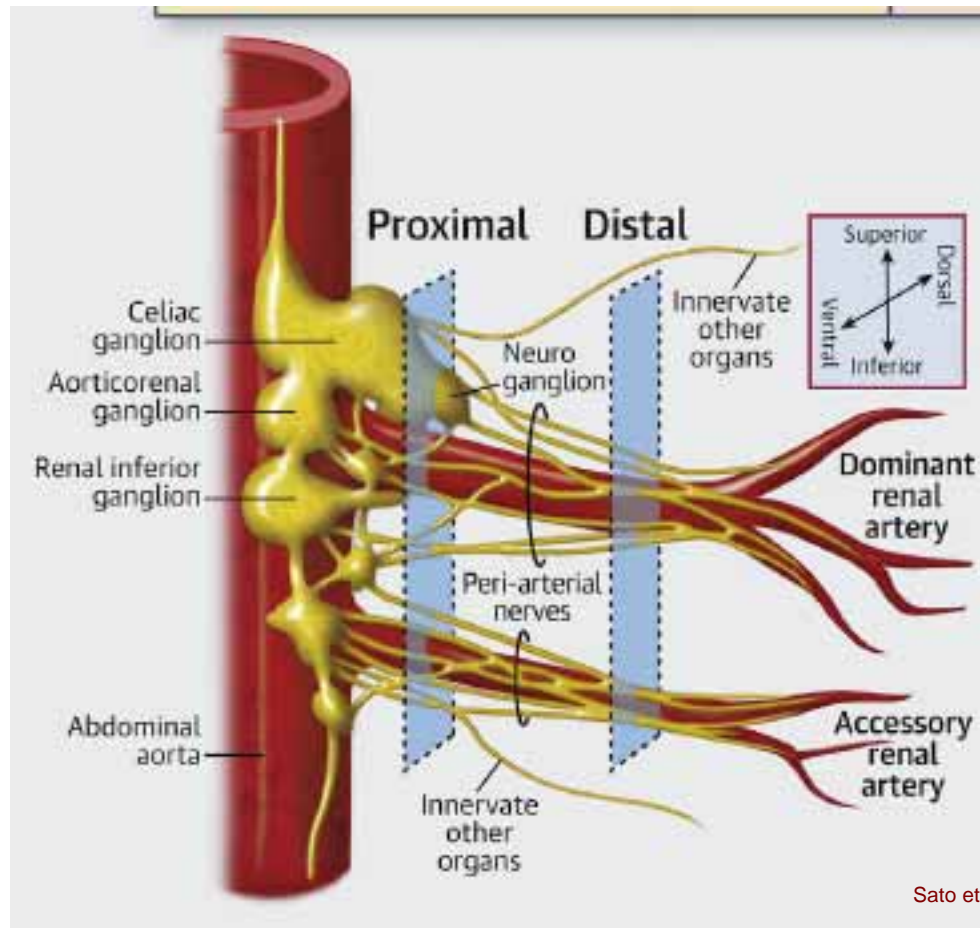
- ◆ Relative risk reduction proportional to decrease in OSBP



-5 mmHg reduction in OSBP provides a 10% relative risk reduction in major cardiovascular events.

- ◆ 1. Rahimi, LBCT; Virtual ESC, August 31, 2020 2. Ettehad D, et al. Lancet 2016; 387: 957-67

What are the targets for RDN?



Sato et al. JACC Int. 2021

Outline

- ◆ **Basis of RDN**

- ½ of the US population has HTN and upto 20% of those do not have control
- Perivascular renal sympathetic nerves run in line with renal arteries

- ◆ **Current data on RDN**

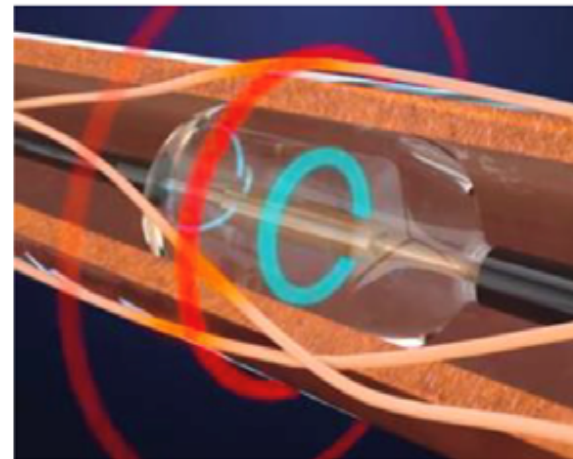
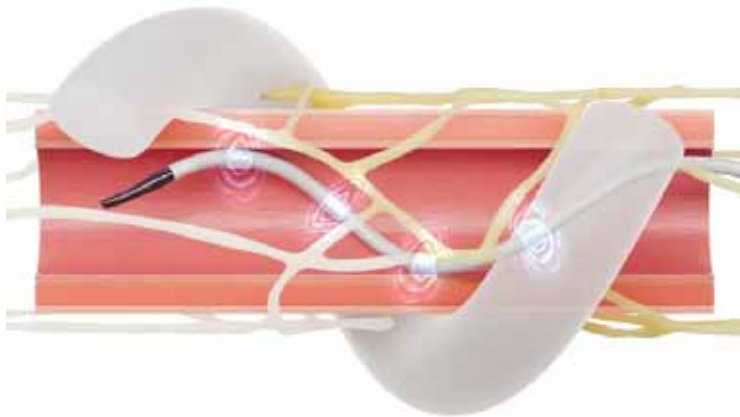
- ◆ **Where are we with RDN technologies?**

Merits of Different Contemporary Evidence Sets

OFF MED TRIALS	ON MED TRIALS	REGISTRY
<p>Scientific evidence of efficacy</p> <p>SPYRAL HTN OFF</p> <p>RADIANCE HTN SOLO</p> <p>RADIANCE II</p>	<p>Prospective evidence in context of background medication</p> <p>RADIANCE HTN TRIO CAP*</p> <p>SPYRAL HTN ON</p> <p>SPYRAL AFFIRM*</p>	<p>Large dataset with multiple subgroups</p> <p>Durability and safety</p> <p>Real-world setting</p> <p>GSR DEFINE</p> <p>GPS Registry</p>
SAFETY		
Safety evaluated across all studies and populations		

Table 1. Completed Trials of Renal Denervation^{24-27,41-44}

Study	Method	N	Active:Sham	Inclusion	Primary Outcome	Results
Trials excluding patients with reduced eGFR^a						
SPYRAL HTN-OFF MED Pivotal ²⁵	RFA	331	1:1	Office BP 150-179/ ≥90 mm Hg on no BP meds	24-h ABPM SBP at 3 mo	RDN: ↓5 mm Hg; sham: ↓1 mm Hg
RADIANCE-HTN SOLO ²⁴	US	146	1:1	Office BP 140-180/ 90-110 mm Hg on no BP meds	Daytime ABPM SBP at 2 mo	RDN: ↓7 mm Hg; sham: ↓2 mm Hg
SPYRAL HTN-ON MED Pilot ²⁷	RFA	80	1:1	Office BP 150-179/ ≥90 mm Hg on 1-3 stable BP meds	24-h ABPM SBP at 6 mo	RDN: ↓9 mm Hg; sham: ↓2 mm Hg
RADIANCE-HTN TRIO ²⁶	US	136	1:1	Office BP ≥140/ ≥90 mm Hg on 3 stable BP meds ^c	Daytime ABPM SBP at 2 mo	RDN: ↓8 mm Hg; sham: ↓3 mm Hg

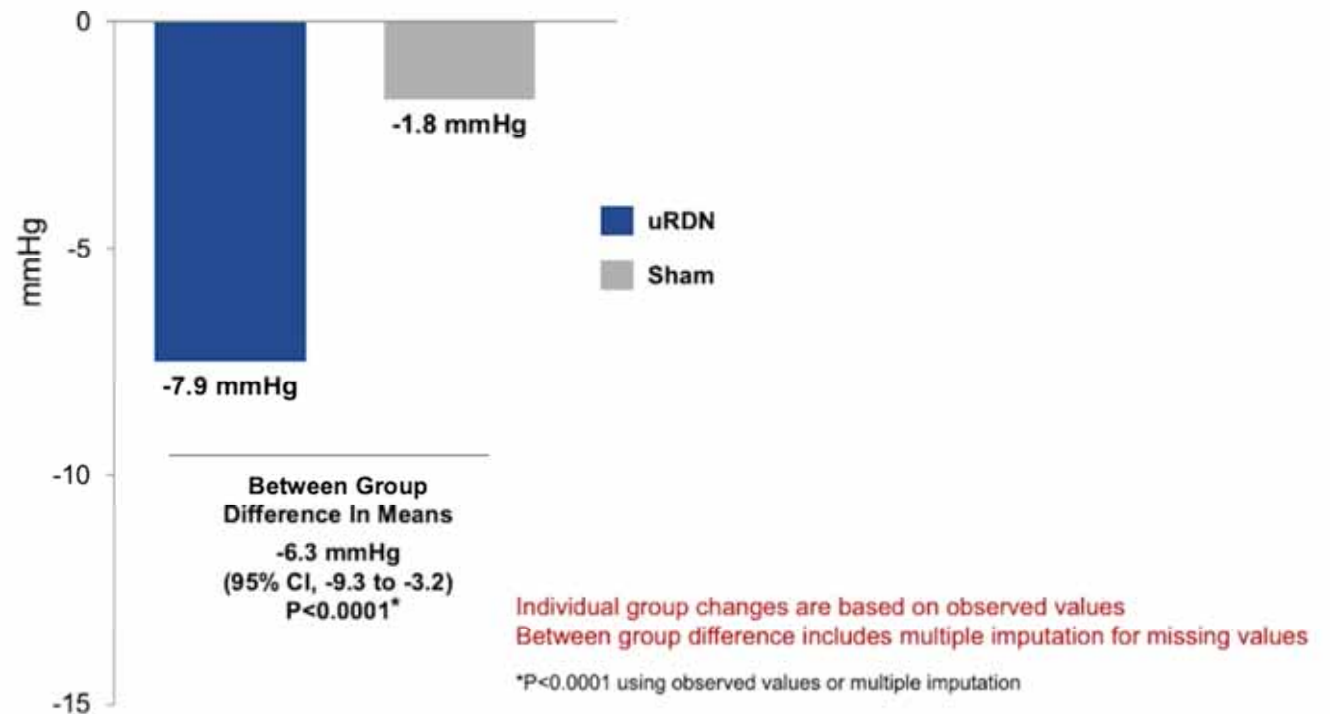


Rey-Garcia and Townsend. AJKD. 2022

RADIANCE II

Primary Efficacy Endpoint (ITT):
Change in Daytime Ambulatory SBP at 2 Months

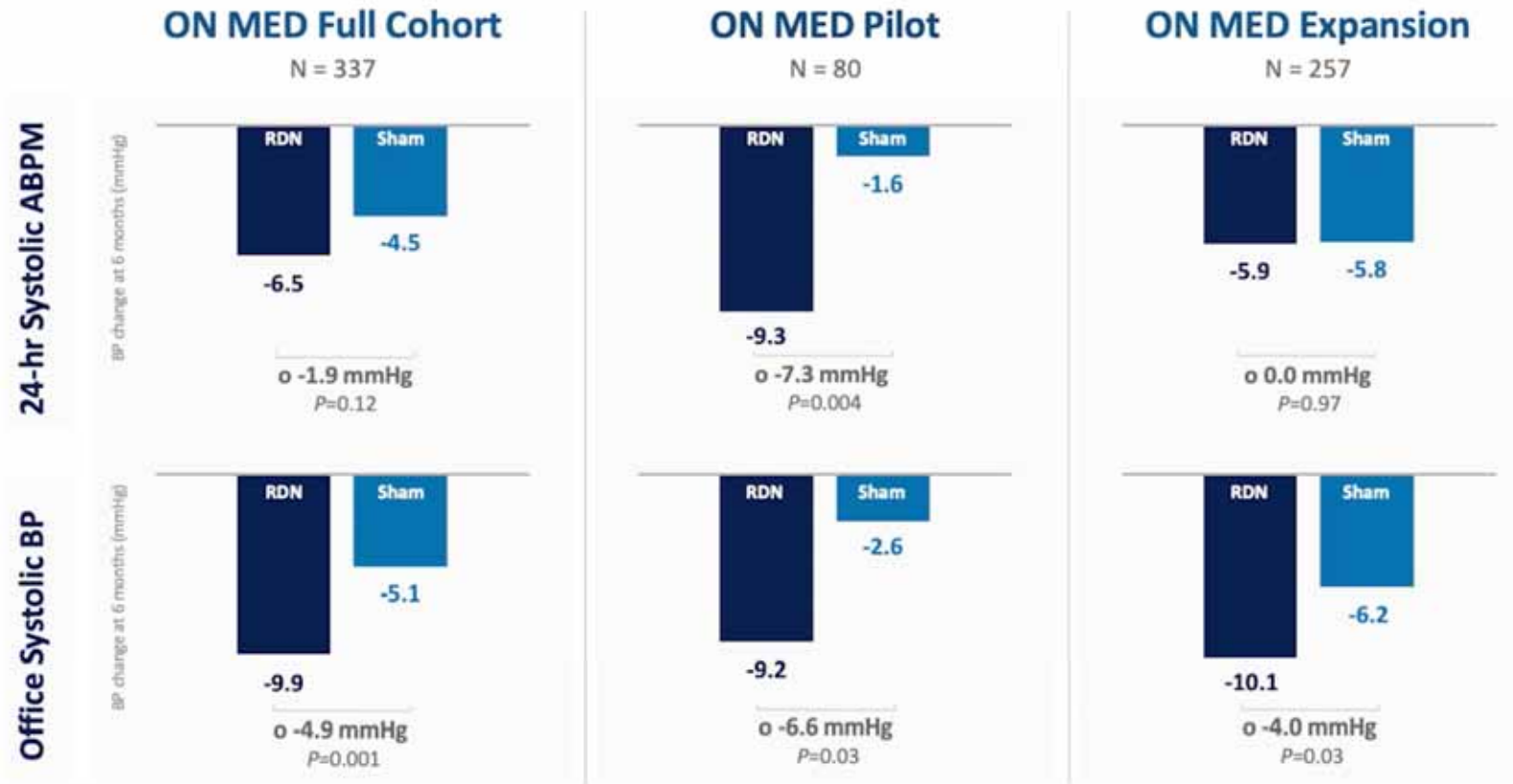
Baseline-Adjusted Change in Daytime Ambulatory SBP



Slide taken from Ajay Kirtane. TCT 2022

SPYRAL ON pilot and expansion

Blood Pressure Changes at 6 Months By Enrollment Cohort

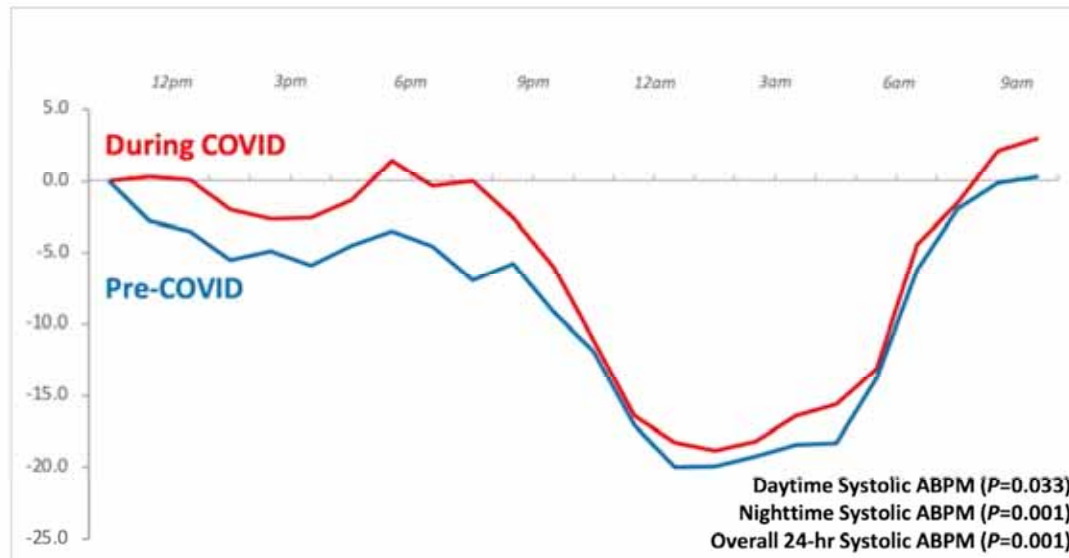


Slide taken from Kandzari. AHA 2022

COVID Impact on ABPM Assessment

Office and ABPM Variances Relative to Timing of Enrollment and Follow-Up

Baseline Systolic ABPM Change (RDN+Sham Combined) Upon Leaving Hospital (mmHg)



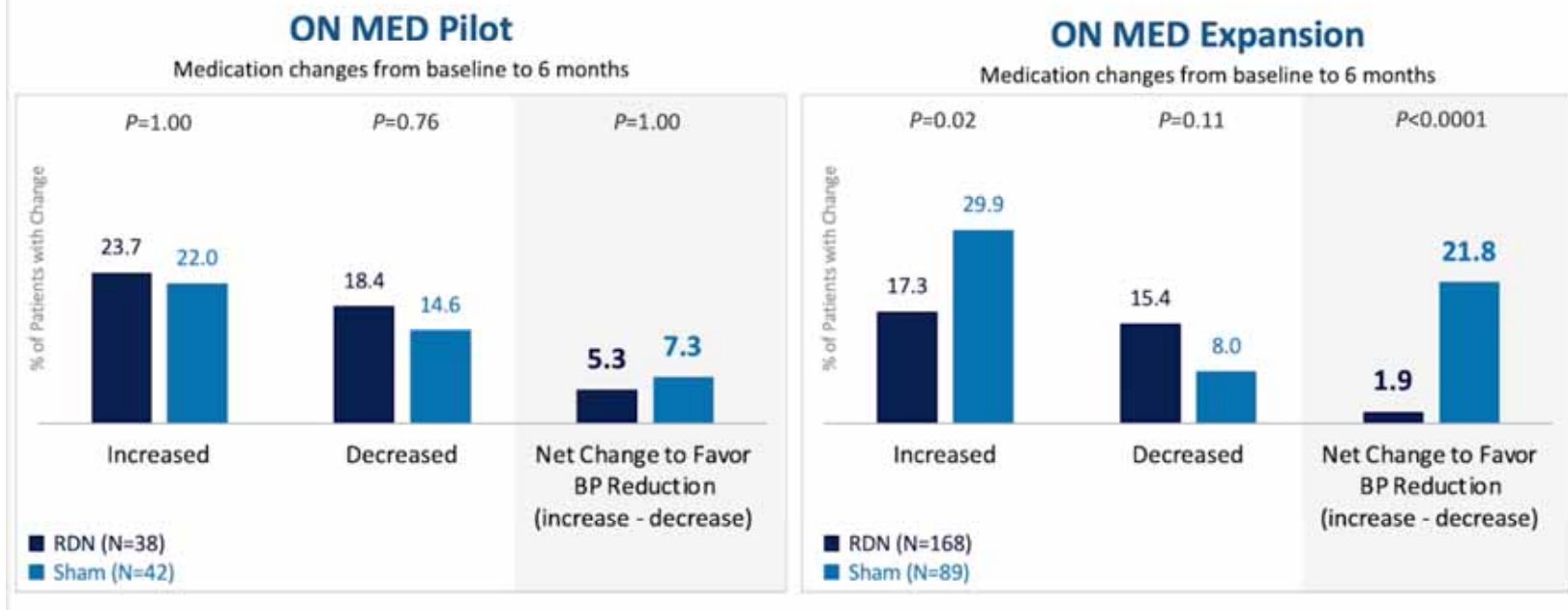
Pre- and During-COVID:

- Significant differences in baseline 24-hr SBP
- No significant differences in baseline Office SBP ($P=0.69$)

Slide taken from Kandzari. AHA 2022

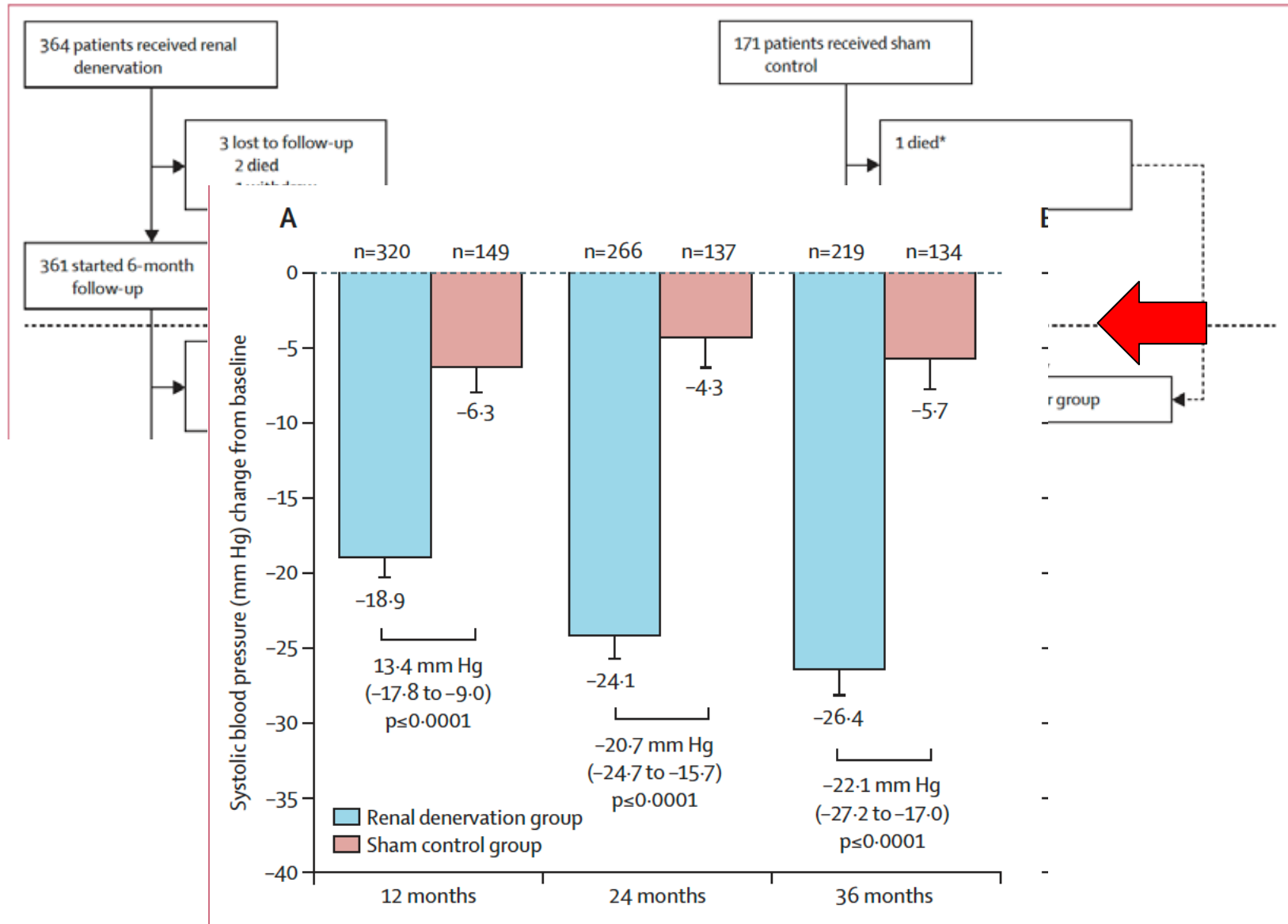
Medication Changes Confirmed by Drug Testing

Imbalanced Medication Changes Between RDN and Sham Groups in Expansion Cohort

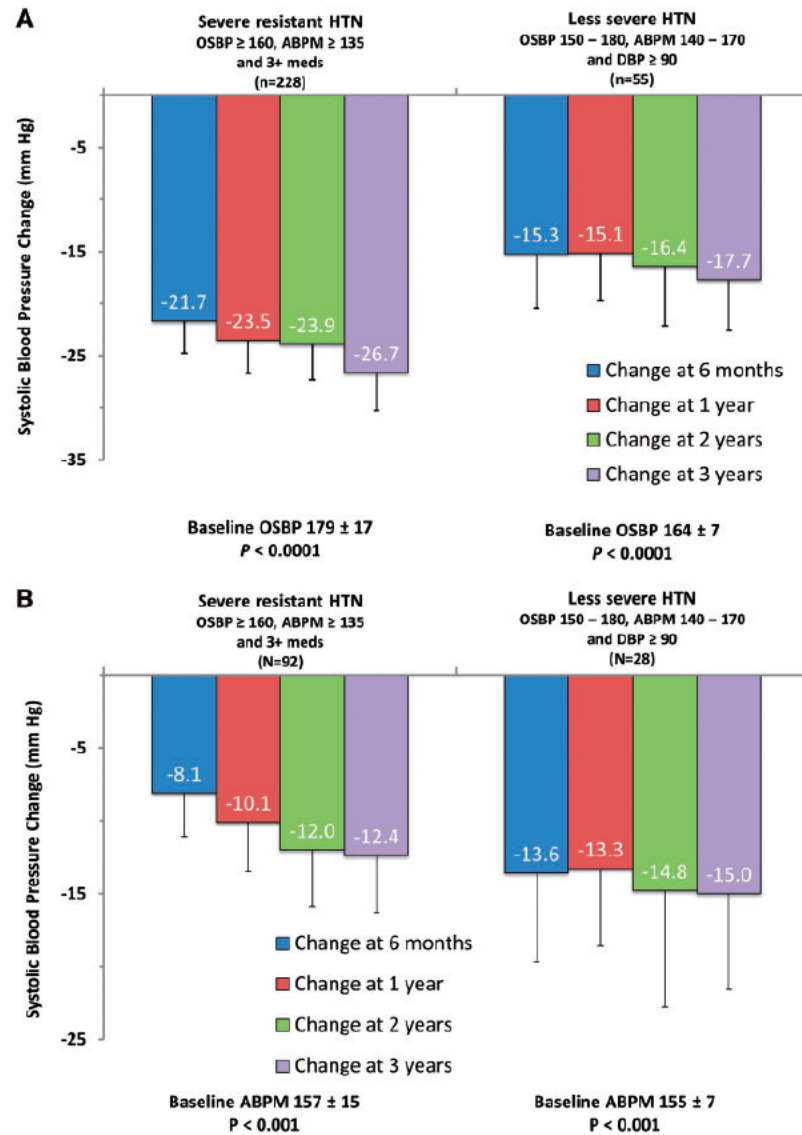


Slide taken from Kandzari. AHA 2022

What's old is new



Can this be real?



Outline

◆ **Basis of RDN**

- ½ of the US population has HTN and upto 20% of those do not have control
- Perivascular renal sympathetic nerves run in line with renal arteries

◆ **Current data on RDN**

- Both radiofrequency and ultrasound based RDN have shown efficacy and safety in multiple sham-controlled trials

◆ **Where are we with RDN technologies?**

How do we measure success?

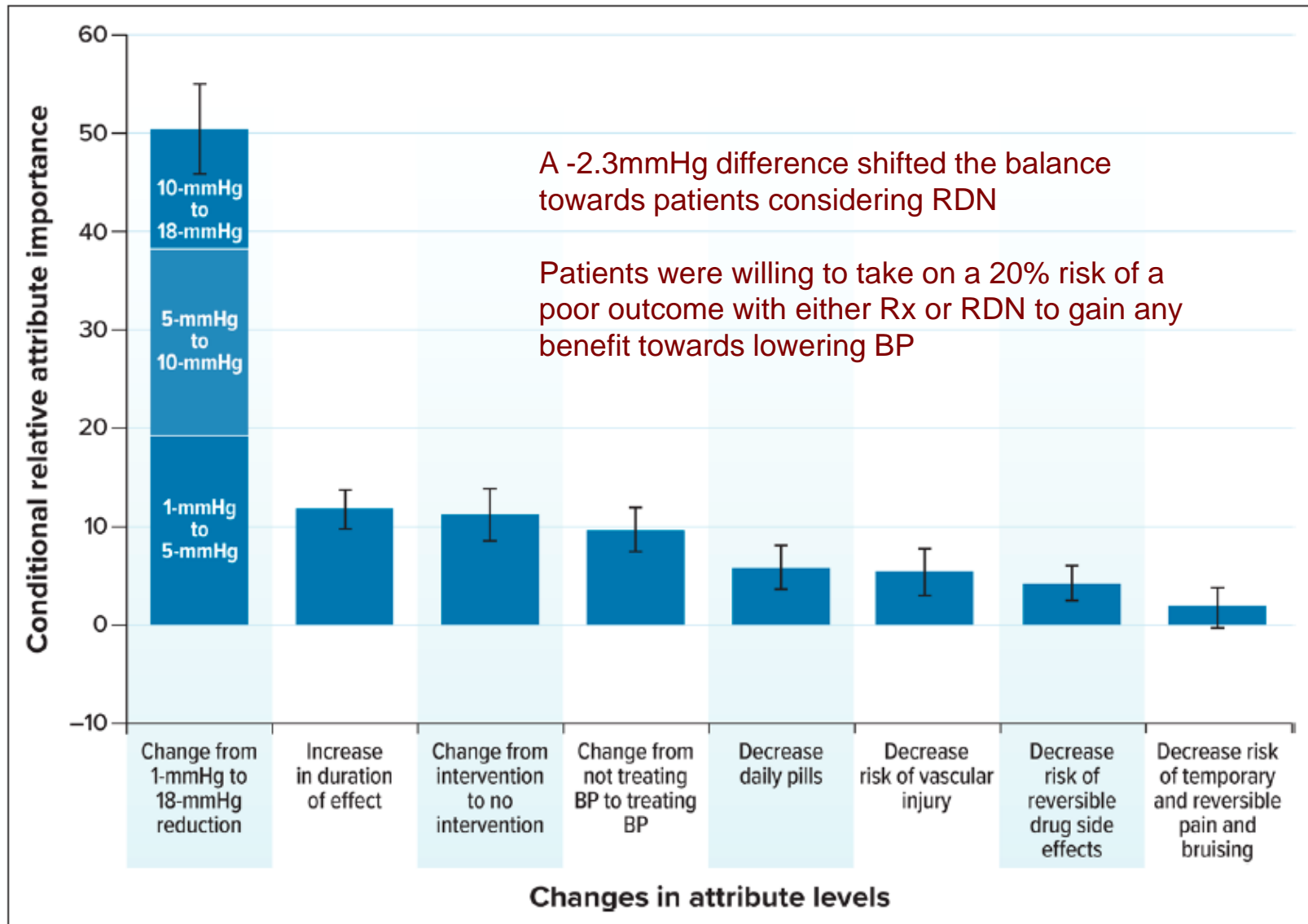
- ◆ **Drops in blood pressure?**

- Not that easy → how do we measure this? Ambulatory day time BP? 24 hour systolic blood pressures?
- When is a reasonable time to look at endpoints?
 - 2mo? 6mo? Recent pooled data for RADIANCE showed continued efficacy at 6 months

- ◆ **Do we need hard outcomes like mortality, MACE?**

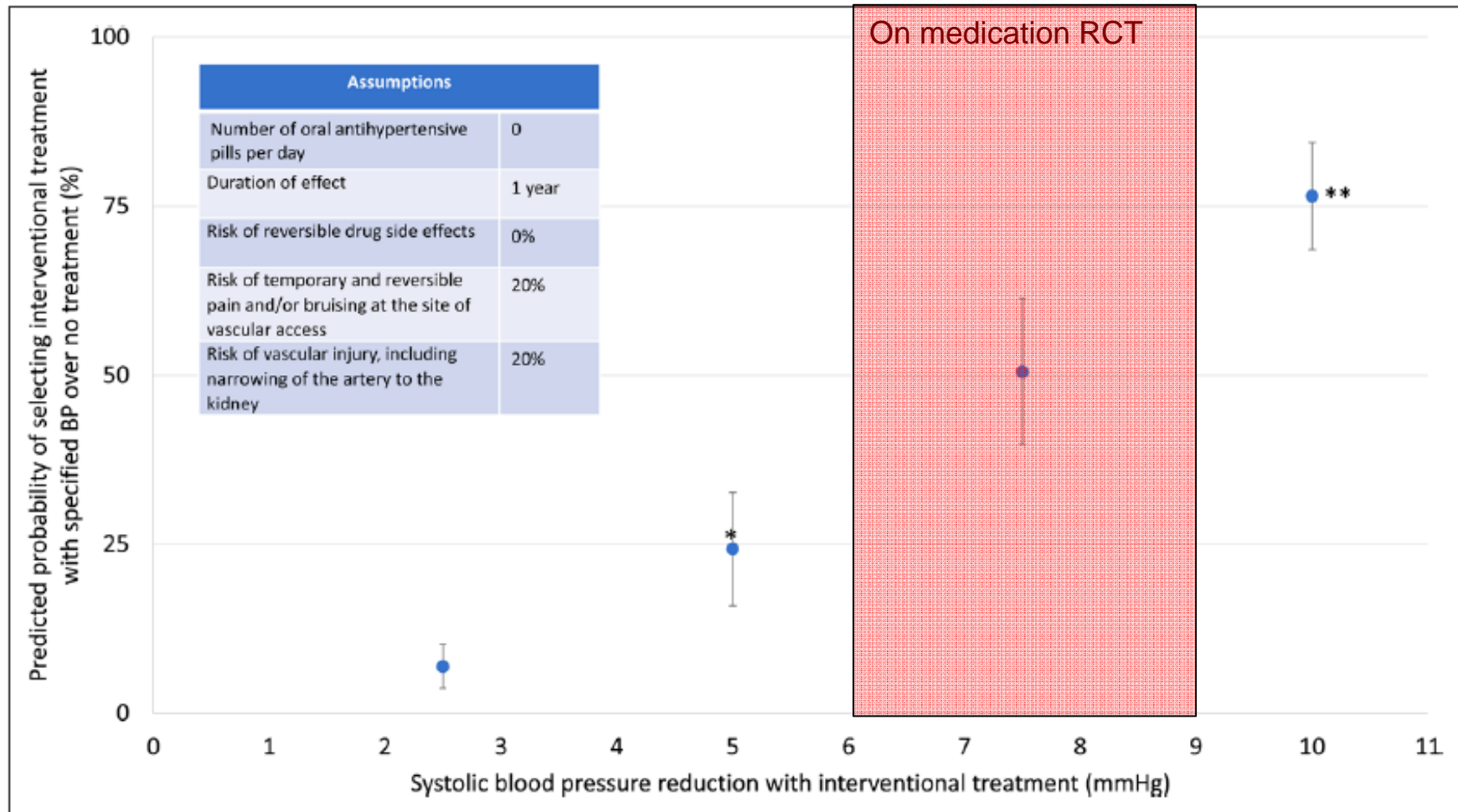
- ◆ **What matters to patients?**

Patient preference study



Kandzari et al. Circ Card Qual Outcomes. 2023

Even when presented with worst case scenario



First RDN Device to receive FDA approval

- ◆ **uRDN – Paradise system**

- “This device is indicated to reduce blood pressure as an adjunctive treatment in hypertension patients in whom lifestyle modifications and antihypertensive medications do not adequately control blood pressure.”

- ◆ **We are eagerly awaiting the FDA approval for the rRDN SPYRAL device**

- ◆ **Reimbursement information is yet to be clearly understood**

Future of RDN

- ◆ **Downstream effects of RDN is vast**

- Afib
- ICH
- CKD
- DM
- HFpEF
- MI
- Ischemic Stroke
- Systems based cost effectiveness for decrease in inpatient hypertension related emergencies

- ◆ **Intraprocedural Markers for successful RDN**

Summary

◆ **Basis of RDN**

- ½ of the US population has HTN and upto 20% of those do not have control
- Perivascular renal sympathetic nerves run in line with renal arteries

◆ **Current data on RDN**

- Both radiofrequency and ultrasound based RDN have shown efficacy and safety in multiple sham-controlled trials
- Awaiting FDA decisions on FDA approval

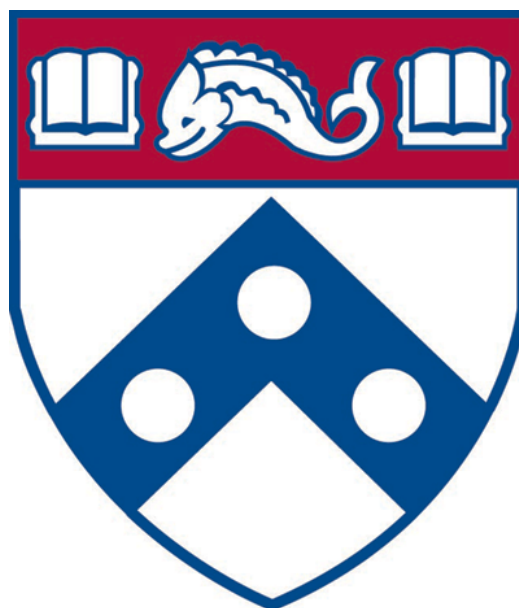
◆ **Where are we with RDN technologies?**

- How do we measure success
- Downstream effects of HTN

Thank you

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<http://upenn.cloud-cme.com/Invasivehypertension2023>.

Virtual and in-person to include the first videos of both RDN platforms shown in a symposium in the US.