ACC.24

Effect of Alcohol-mediated Renal Denervation on Blood Pressure in the Presence of Antihypertensive Drugs: 3-month Primary Results From the Target BP I Randomized Trial

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Disclosure

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below

Affiliation/Financial Relationship	Company
Grant/Research Support (Institutional)	Ablative Solutions, Biotronik, Medtronic Orbus Neich, Teleflex
Consulting Fees/Honoraria	Medtronic, HyperQure
Major Stock Shareholder/Equity	BioStar Ventures (none related to ASI)
Royalty Income	None
Ownership/Founder	None
Intellectual Property Rights	None
Other Financial Benefit	None

TARGET BP I
Background

- Globally, over 1/3 of adults have hypertension, yet many remain uncontrolled, leading to increased risk of cardiovascular events

  A 5-mmHg absolute reduction in office systolic blood pressure leads to a 10% reduction in major CV events[1]

- New blood pressure guidelines motivated by increasing awareness of benefit with more intensive blood pressure control, unacceptable levels of hypertension control[2,3], and increasing recognition of non-adherence to antihypertensive medications identify the need for alternative treatment options

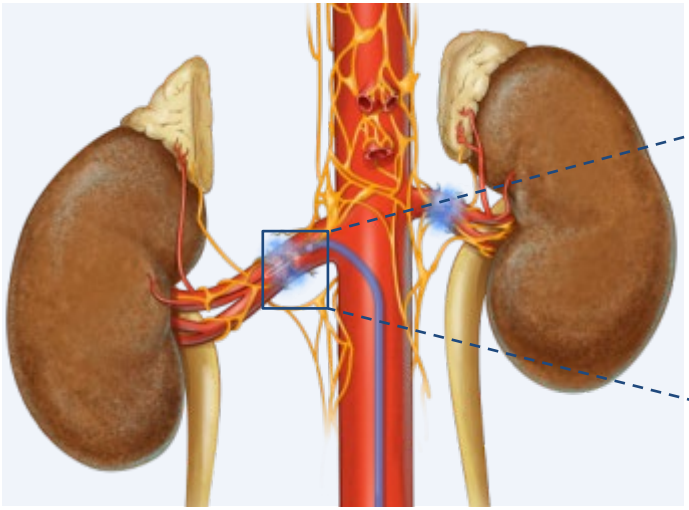
- Renal denervation (RDN) procedure targets the sympathetic nervous system to lower blood pressure

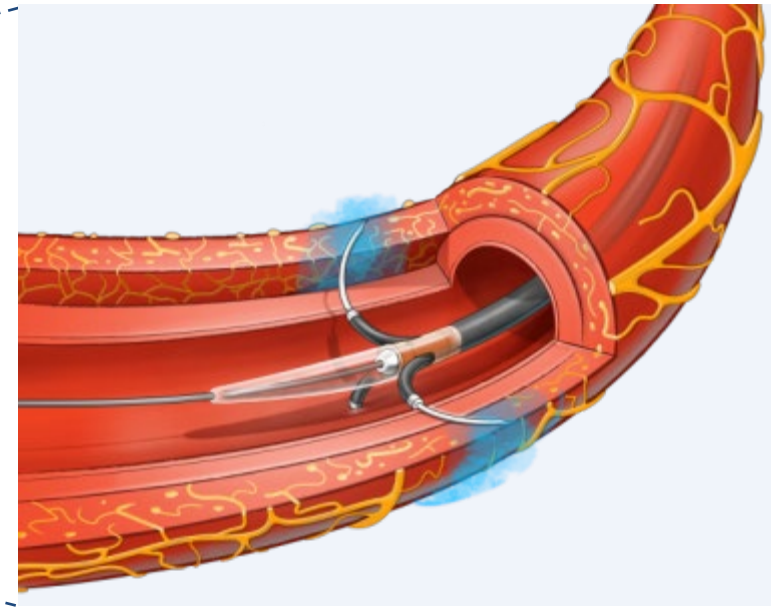
- Catheter-based perivascular delivery of dehydrated alcohol represents a novel method of neural ablation, achieving a confluent arc of ablation with single, targeted treatment within the renal artery

- To further explore outcomes with alcohol-mediated RDN in the presence of antihypertensive medications, an international sham-controlled RCT was performed

[1] Blood Pressure Lowering Treatment Trialists' Collaboration. *Lancet* 2021
[2] Muntner et al. *JAMA* 2020
[3] NHANES 2017–2020. Centers for Disease Control and Prevention. https://millionhearts.hhs.gov/data-reports/hypertension-prevalence.html. Accessed February 10, 2024.

Alcohol-Mediated Renal Denervation





Perivascular Delivery of Alcohol to Adventitial Space

Expanded View of Device Infusing Alcohol

Site-specific delivery of alcohol: Local nerve inactivation, no collateral damage

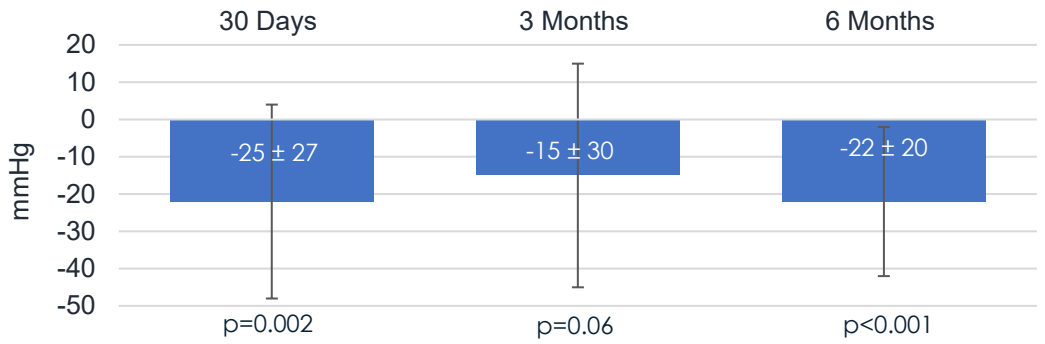
1. Micro-volume (0.6 mL) infused directly to the perivascular region
2. Extracellular fluid helps spread alcohol circumferentially in the perivascular region
3. Alcohol activity range self-limited through dilution by extracellular fluid

Fischell et al. *J Am Coll Cardiol Intv* 2016

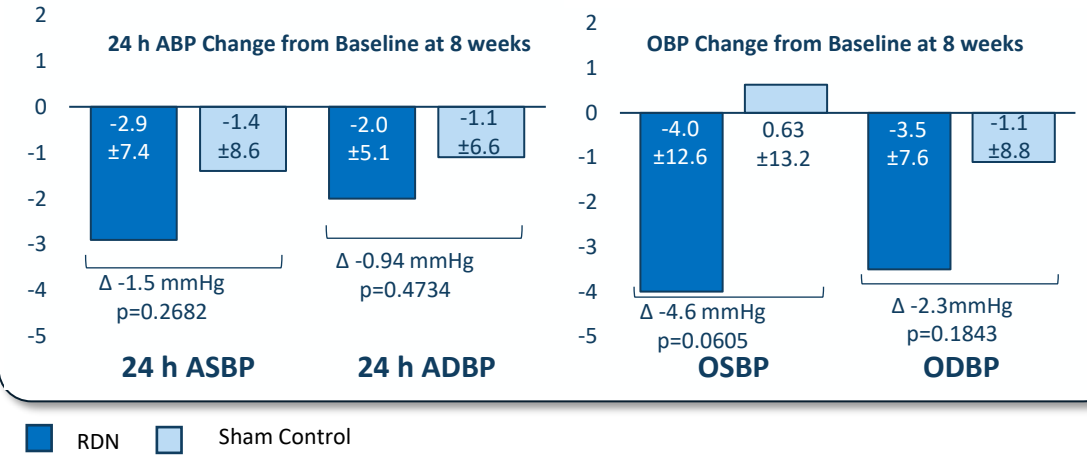
Prior Studies of Alcohol-Mediated RDN

Peregrine First In Human[1] N=17

OSBP Change From Baseline

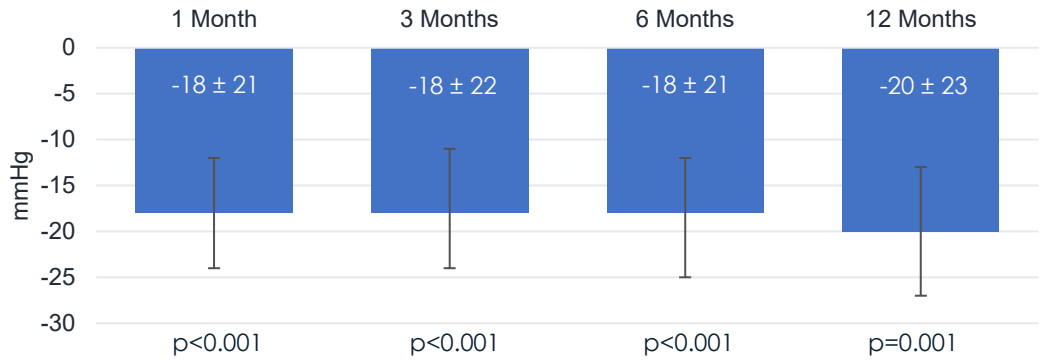


Target BP OFF MED[2] N=106

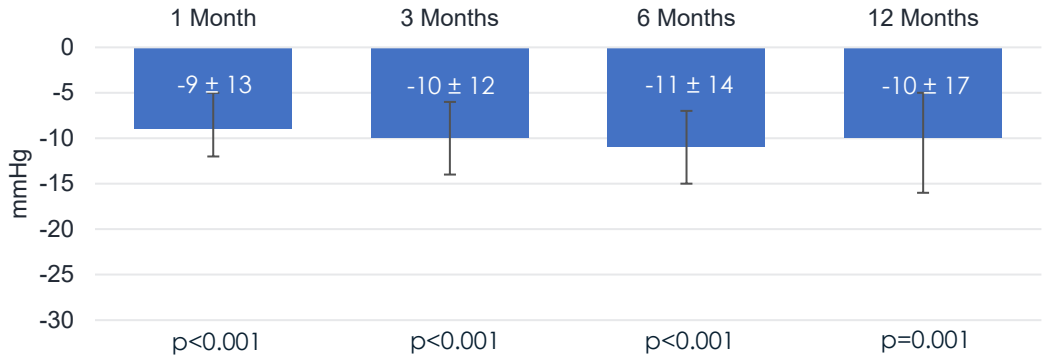


Peregrine Post-Market Study[3] N=45

OSBP Change from Baseline



ABPM Change from Baseline



1.Fischell et al. *Cardiovasc Revasc Med* 2015
2.Pathak et al. *EuroIntervention* 2023
3.Mahfoud et al. *Circ Cardiovasc Interv* 2021

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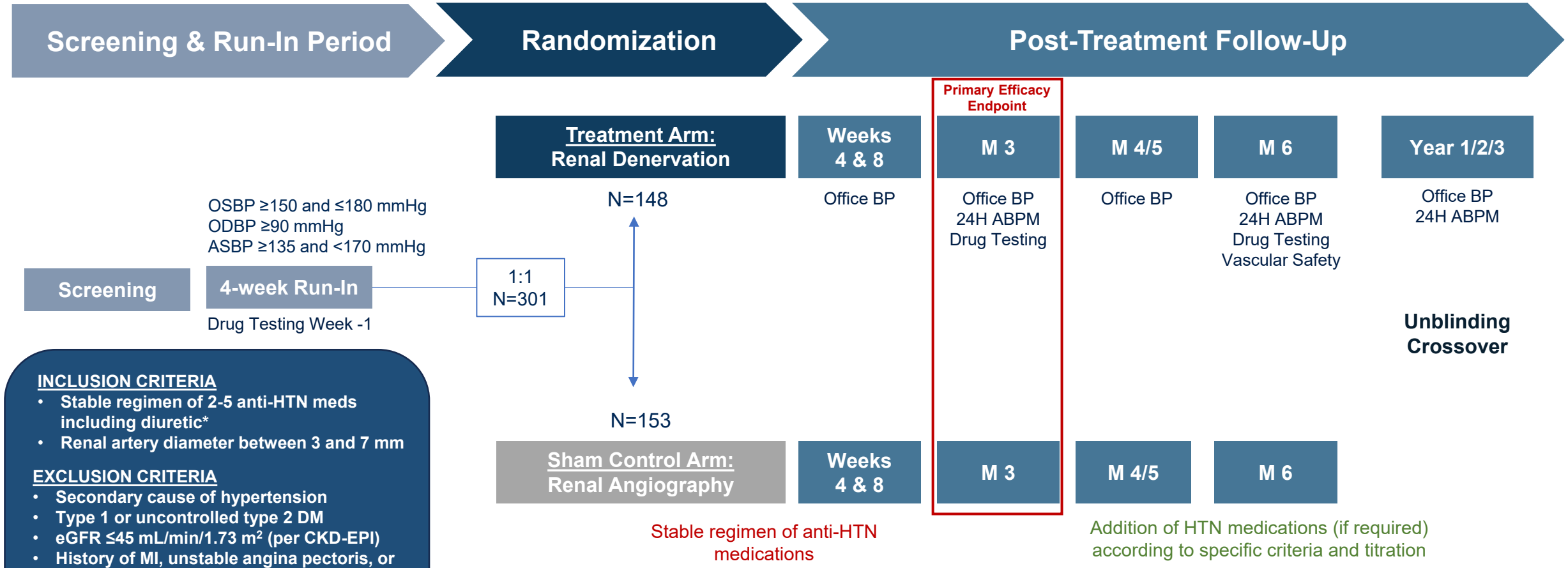
Study Design



INCLUSION CRITERIA
- Stable regimen of 2-5 anti-HTN meds including diuretic*
- Renal artery diameter between 3 and 7 mm

EXCLUSION CRITERIA
- Secondary cause of hypertension
- Type 1 or uncontrolled type 2 DM
- eGFR ≤45 mL/min/1.73 m^2 (per CKD-EPI)
- History of MI, unstable angina pectoris, or stroke/TIA in prior 6 months
- Heart failure (NYHA III or IV) or EF ≤30%
- Chronic AF

*Diuretic therapy required unless documented intolerance

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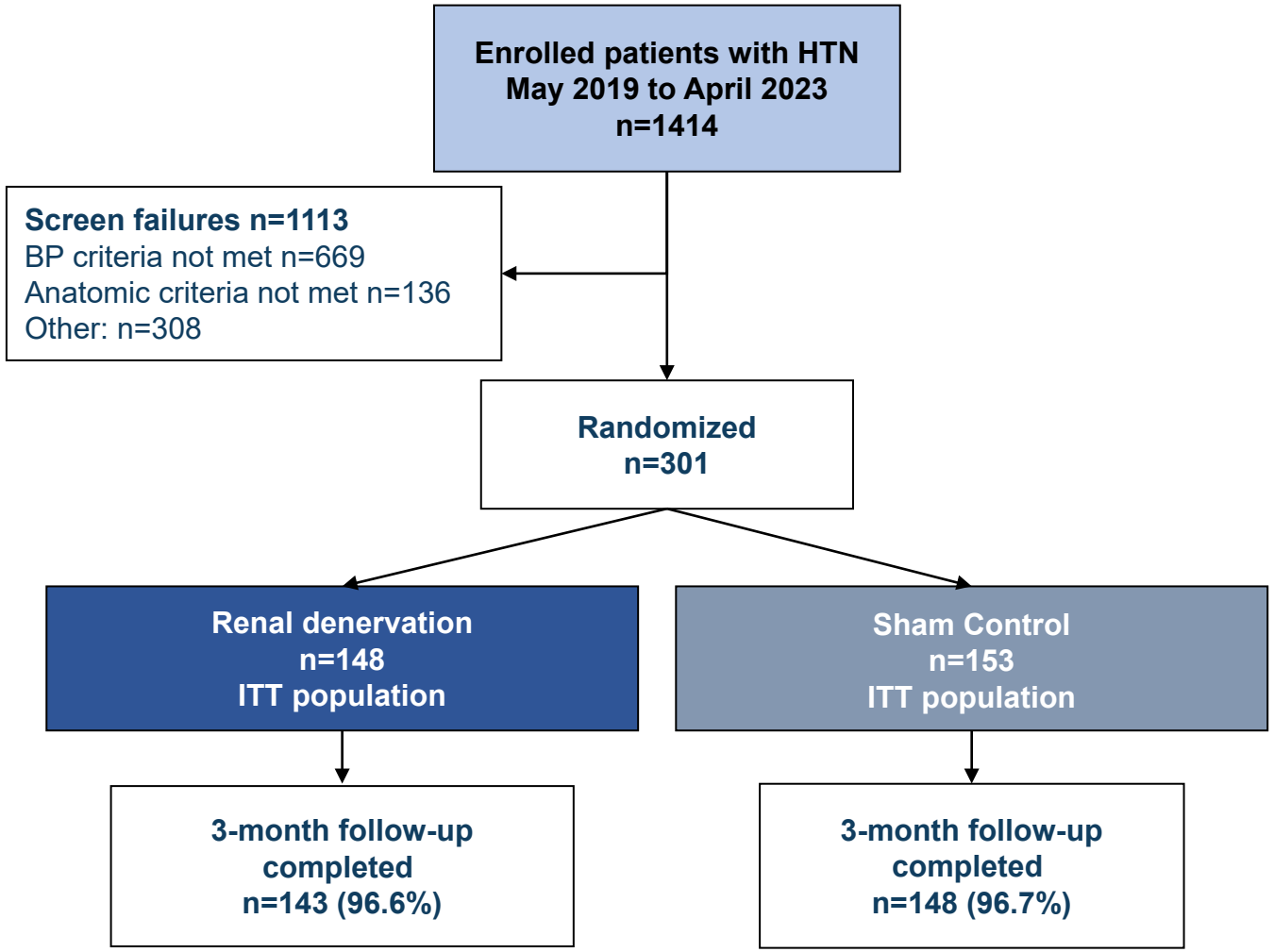
Patient Flow Chart



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Baseline Patient Characteristics

	RDN (N=148)	Sham (N=153)
Age	56.7 ± 10.0	55.6 ± 9.1
Male	113 (76.4%)	111 (72.5%)
Body-mass index (kg/m^2)	32.6 ± 5.3	32.1 ± 5.3
Chronic kidney disease (eGFR <60 mL/min per 1.73m^2)	15 (10.1%)	20 (13.1%)
Type 2 diabetes	30 (20.3%)	40 (26.1%)
History of arrhythmia	14 (9.5%)	11 (7.2%)
History of congestive heart failure	7 (4.7%)	8 (5.2%)
Smoking (current)	14 (9.5%)	20 (13.1%)
Hyperlipidemia	57 (38.5%)	74 (48.4%)

	RDN (N=148)	Sham (N=153)
Race*		
White	45 (30.4%)	42 (27.5%)
Black/African American	23 (15.5%)	30 (19.6%)
Asian	0	2 (1.3%)
Not reported	80 (55.1%)	79 (51.6%)
Number of anti-HTN medications		
2	32 (21.6%)	35 (22.9%)
3	48 (32.4%)	40 (26.1%)
4	41 (27.7%)	43 (28.1%)
≥5	27 (18.2%)	34 (22.2%)
Aldosterone antagonist use	23 (15.5%)	35 (22.9%)

ITT population; data represented as N (%) or mean ± SD

*Information on race was not allowed to be collected by law in certain countries

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Baseline Blood Pressure and Heart Rate Measures

	RDN (N=148)	Sham (N=153)
Office Measurements		
Office Systolic BP	164 ± 9	164 ± 9
Office Diastolic BP	98 ± 7	100 ± 7
24-hour Ambulatory Measurements		
Mean 24-hour Systolic BP	146 ± 9	146 ± 8
Mean 24-hour Diastolic BP	87 ± 8	88 ± 9
Heart Rate (bpm)	75 ± 12	75 + 14

Data represented as mean ± standard deviation

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Procedural Characteristics

	RDN (N=150)	Sham (N=151)
Total procedure time (min)	55.7 ± 27.0 (150)	33.7 ± 24.1 (151)
Total volume contrast (mL)	95.7 ± 47.4 (150)	40.0 ± 22.6 (151)
Total fluoroscopy time (min)	10.8 ± 7.7 (150)	3.1 ± 2.8 (151)
Device success	143 (95.3%)	—
Procedure success	139 (92.7%)	—
Number arteries treated/patient	2.2	—

Data represented as mean ± standard deviation (N) or N (%)

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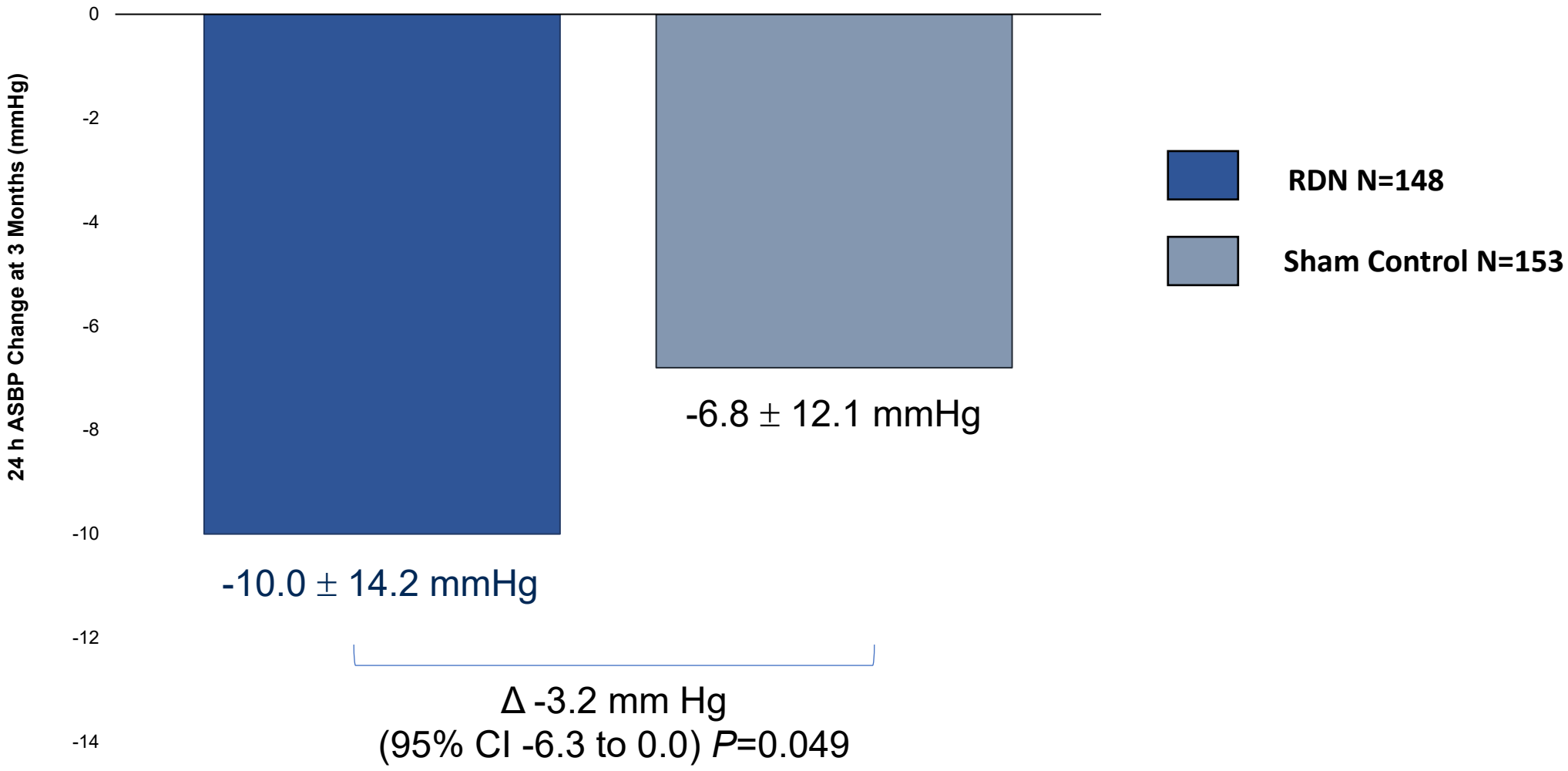
Primary Endpoint: 24-hr ASBP at 3 Months



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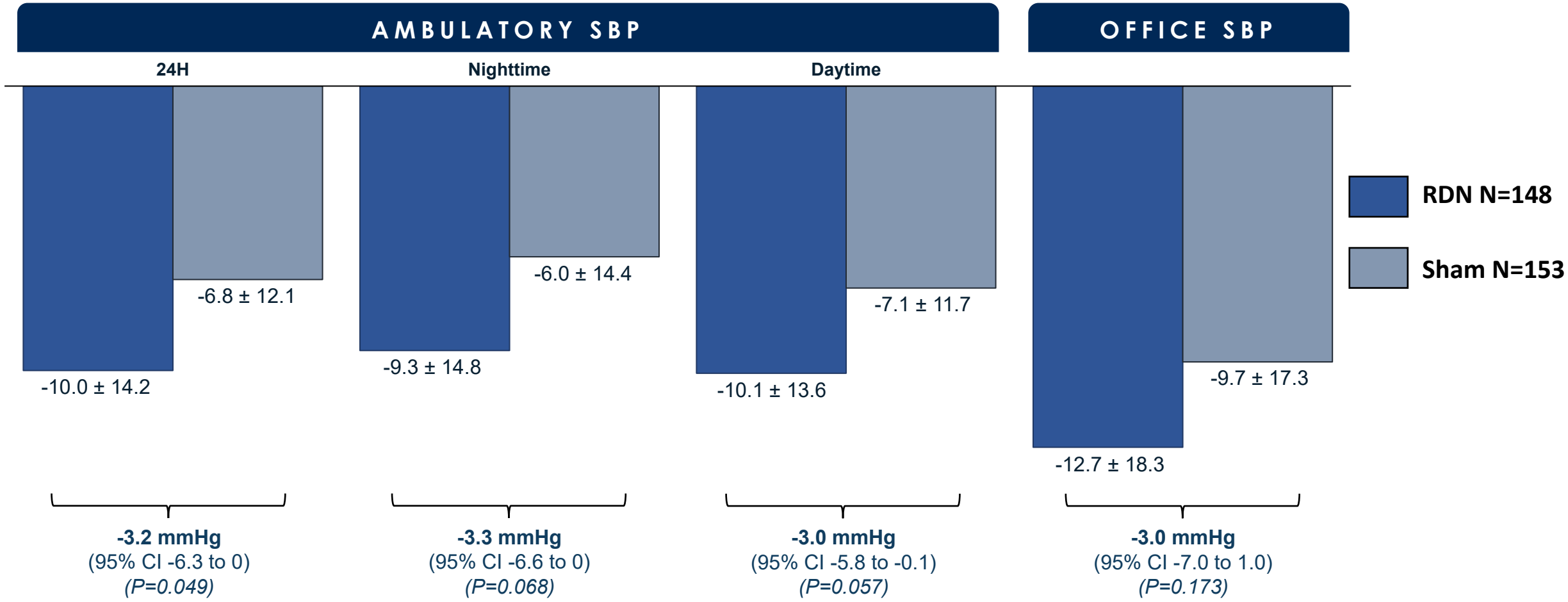
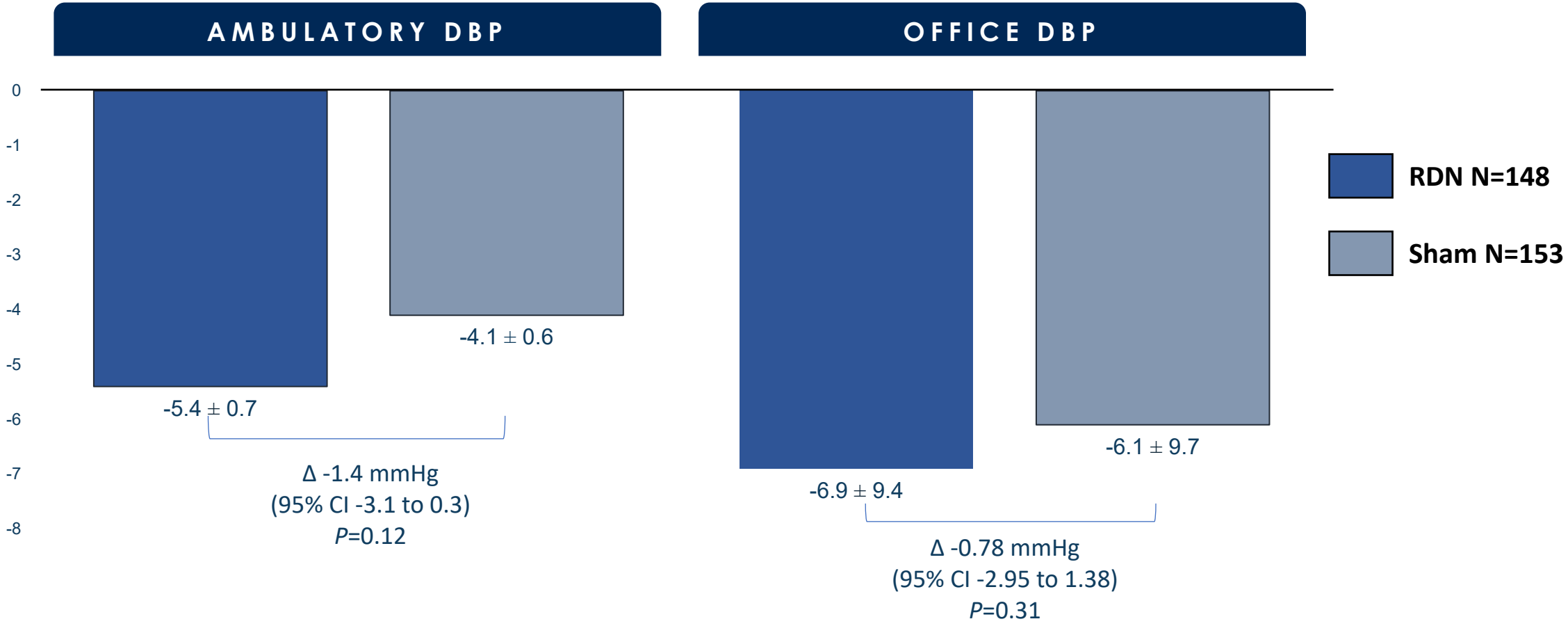
Ambulatory and Office Systolic BP at 3 Months



TARGET BP I

Ambulatory and Office Diastolic BP at 3 Months



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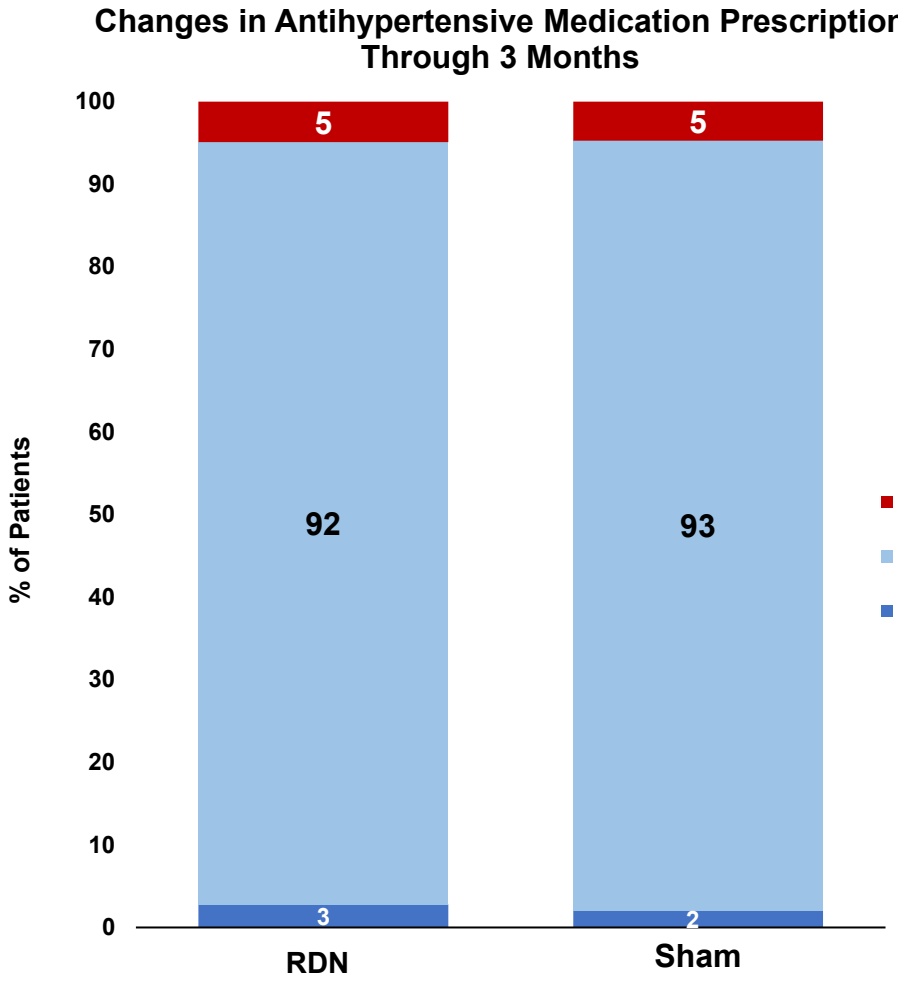
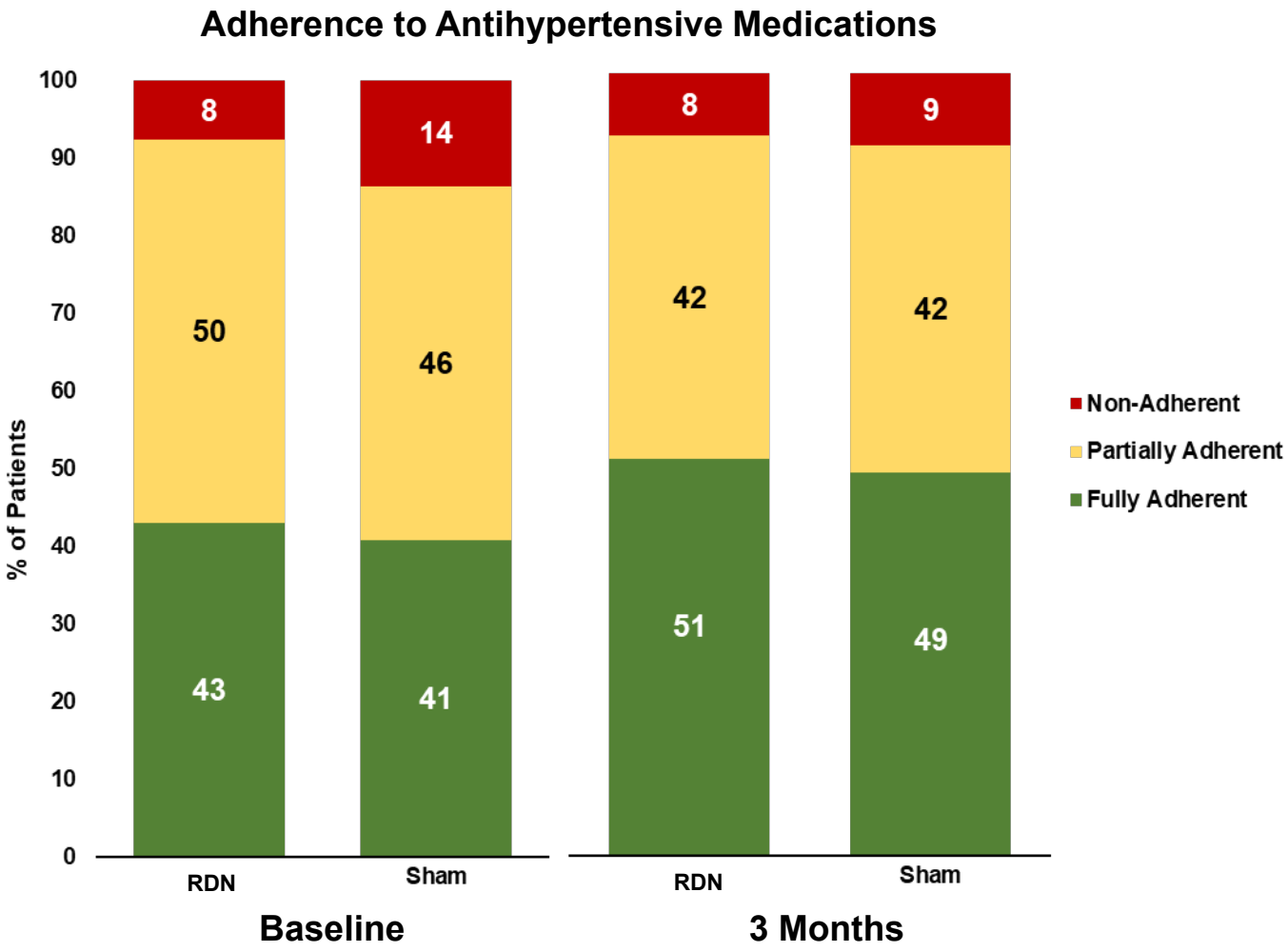
Prescription Changes and Adherence Results





Counts are by patient visit; not individual medications or dose
Excludes subject visit compliance results that are not available

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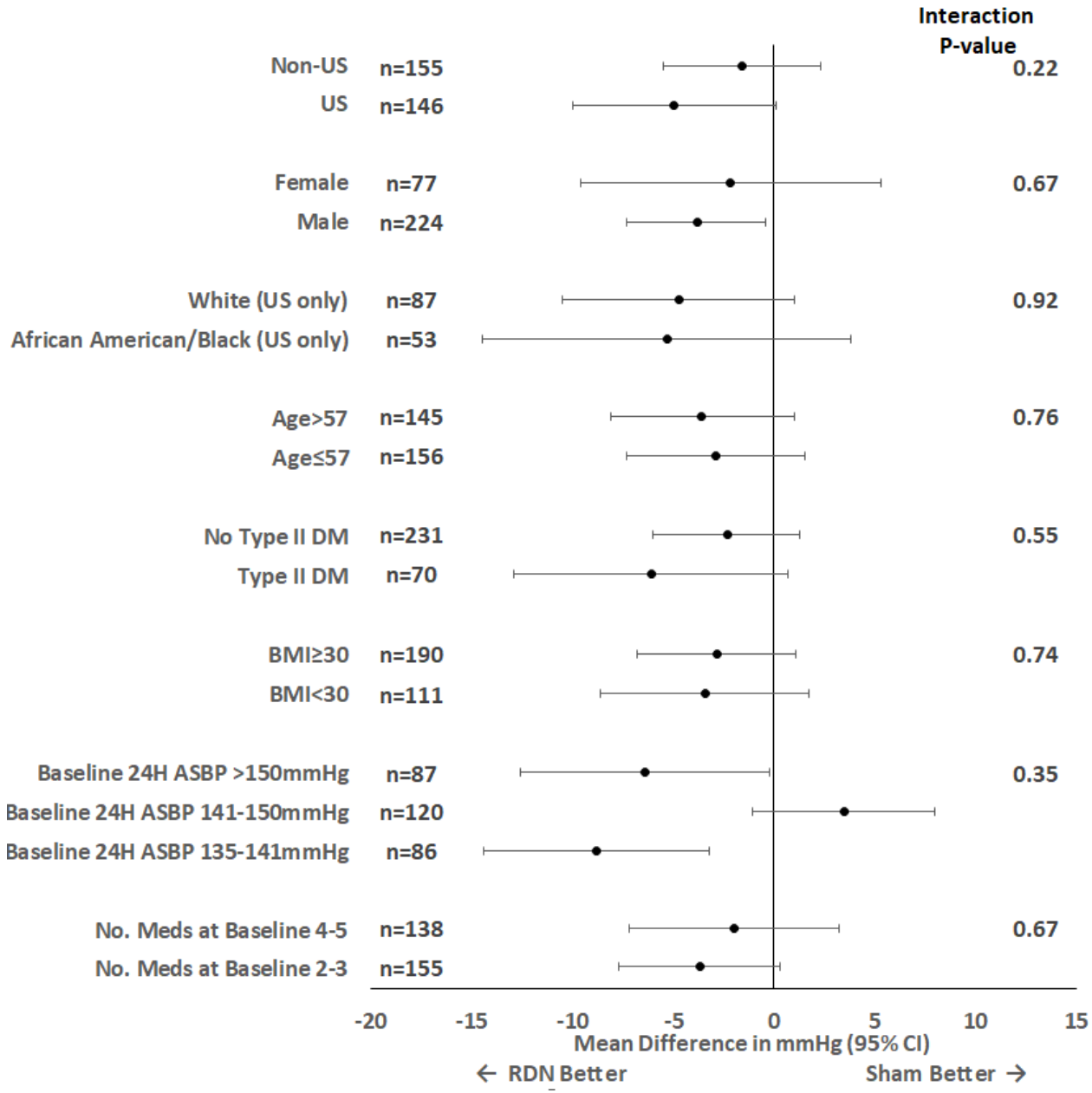
3-Month 24-hr ASBP Subgroup Analyses



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Safety Outcomes

	30 Days			6 Months		
	RDN (N=149)	**Sham (N=150)**	***P* value**	**RDN (N=145)**	**Sham (N=146)**	***P* value**
Total Major Adverse Events	7 (4.7%)	0	0.007	11 (5.3%)	6 (4.0%)	0.22
All Cause Death	0	0	—	1 (0.7%)	0	0.50
Myocardial Infarction	0	0	—	1 (0.7%)	1 (0.7%)	1.00
Major Vascular Complication	1 (0.7%)	0	0.50	1 (0.7%)	0	0.50
Hypertensive Emergency	1 (0.7%)	0	0.50	2 (1.4%)	2 (1.4%)	1.00
Hypotension*	6 (4.0%)	0	0.02	7 (4.8%)	3 (2.0%)	0.22
eGFR ($mL/min/1.73m^2$) Change ± SD (N)				-1.2 ± 9.9 (138)	-0.86 ± 9.0 (146)	0.73
Vessel Safety Patency (<60% stenosis)				99.6% (280 vessels)	—	—

*Hypotension requiring intervention or medication change

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Limitations

- High rates of medication nonadherence both at baseline and follow-up
  - No significant differences between groups relative to medication increase/decrease or general adherence
  - Inability of current methods to assess changes in medications within same class or timing of last administration
- Potential influence of home BP assessment uncertain
- Findings limited to 3 months follow-up, and whether progressive declines in BP occur over later follow-up uncertain
- No procedural assessment regarding completeness of denervation
- Results observed with this therapy and in this specific population may not be generalizable to alternative interventional therapies for hypertension and more varied clinical populations

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Conclusions

- In this sham-controlled, randomized trial inclusive of patients with both uncontrolled and treatment resistant HTN, alcohol-mediated RDN met its primary endpoint, with a modest but significant decrease in 24-hr ambulatory SBP at 3-month follow-up
  - Results consistent across both day/night ABPM and prespecified subgroups
- No significant between group differences were observed relative to office blood pressure assessments
- RDN results observed in context of large BP reductions in sham control cohort
  - Strikingly high rates of partial and complete nonadherence
- Safety of alcohol-mediated RDN associated with favorable procedural performance and intermediate-term safety
- Ongoing, dedicated late-term follow-up will be important to inform the effectiveness as a treatment for uncontrolled HTN