

2013 TCTAP

Wrap-Up Interview

Renal Denervation

Moderator

Horst Sievert

Interviewees

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Issues Briefs

Transcatheter Renal Denervation

Catheter based treatment for resistant hypertension

- Clinical studies: SYMPLICITY HTN-1 and 2
- Discussion: Interpretation, Future perspective

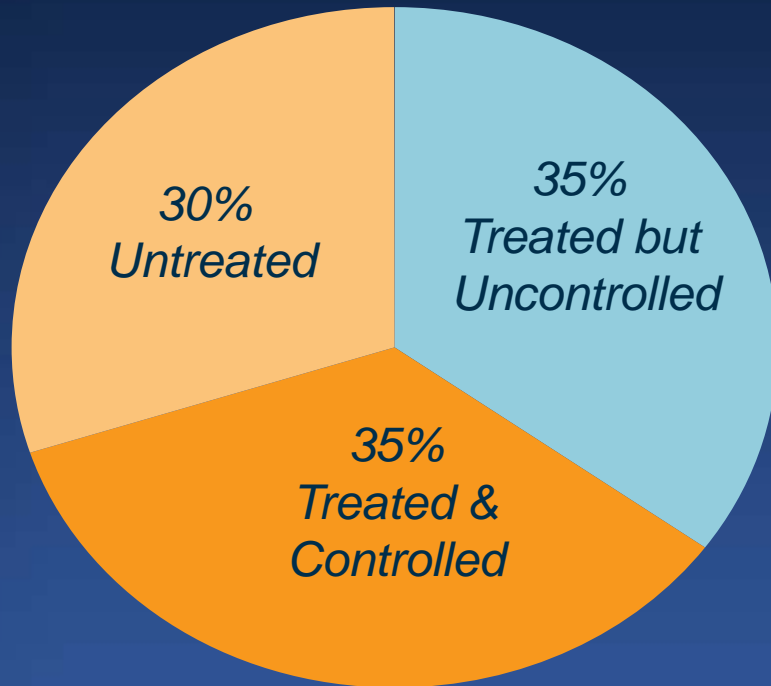
SYMPLICITY HTN 3 trial

- Debates in sham trial

Beyond Resistant Hypertension

- Sympathetic modulation therapy
- CHF, Diabetes, OSA

Hypertension Epidemiology

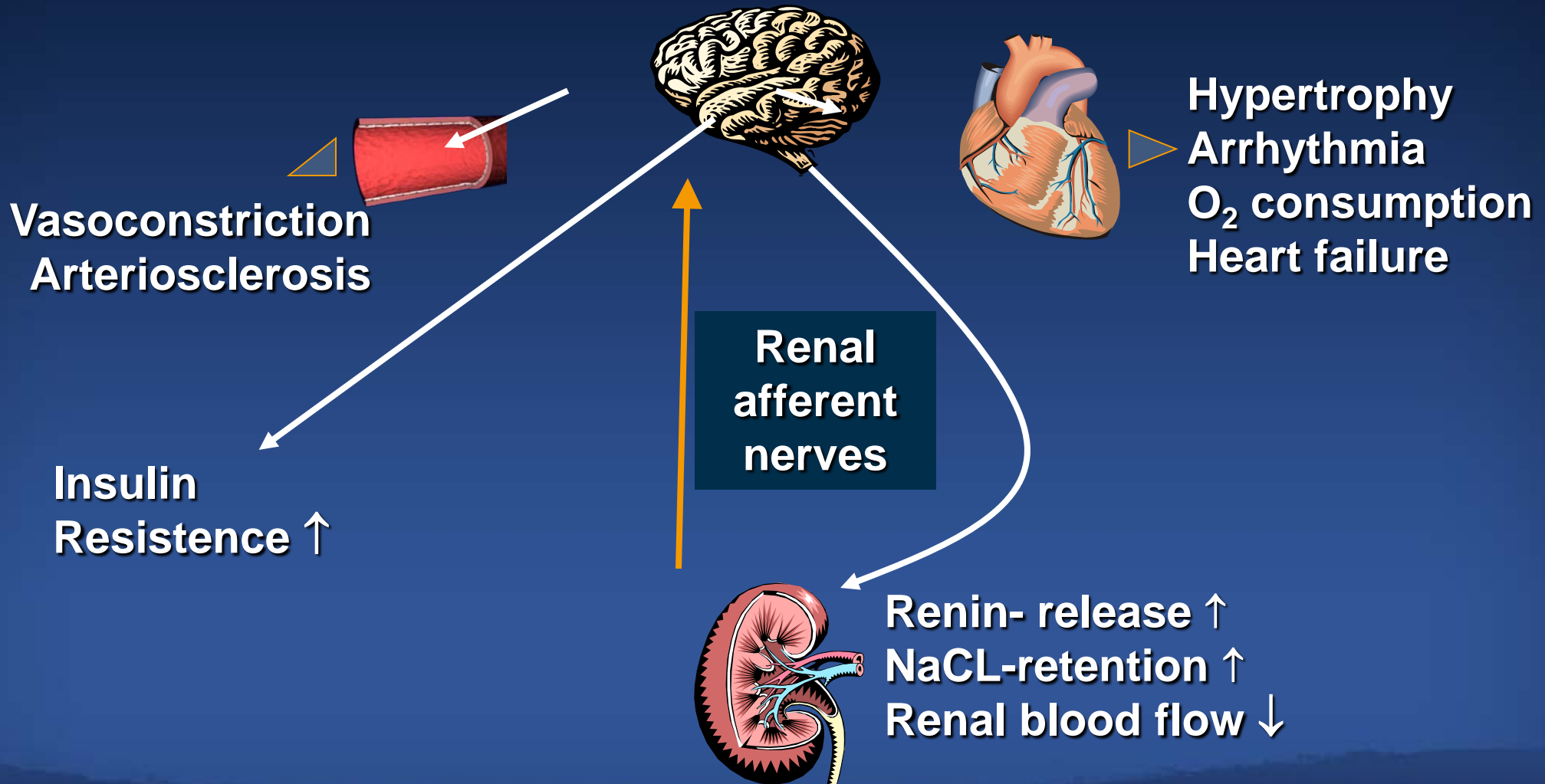


- Single largest contributor to death worldwide
- Every 20/10 mmHg increase in BP correlates with a doubling of 10-year cardiovascular mortality
- Dramatically increases risk of stroke, heart attack, heart failure, & kidney failure
- Only half of all treated hypertensive patients are controlled to established BP targets
- High prevalence:
 - Affects 1 in 3 adults
 - 1B people worldwide → 1.6 B by 2025
- Resistant HTN : 5-30%

Chobanian et al. Hypertension. 2003;42(6):1206–1252.

Renal Afferent Nerves

Kidney as the origin of central sympathetic drive



The Symplicity HTN Clinical Trial Program

Symplicity HTN-1
First-in-Man, and Expanded
Cohort (N=153)^{1,2}



Symplicity HTN-2
Randomized,
Controlled Trial
(N=106)³



Symplicity HTN-3
Randomized,
Blinded, Controlled
Trial
(N~530)⁴



= Primary endpoint
 = Planned follow up
 = Partial cohort reports

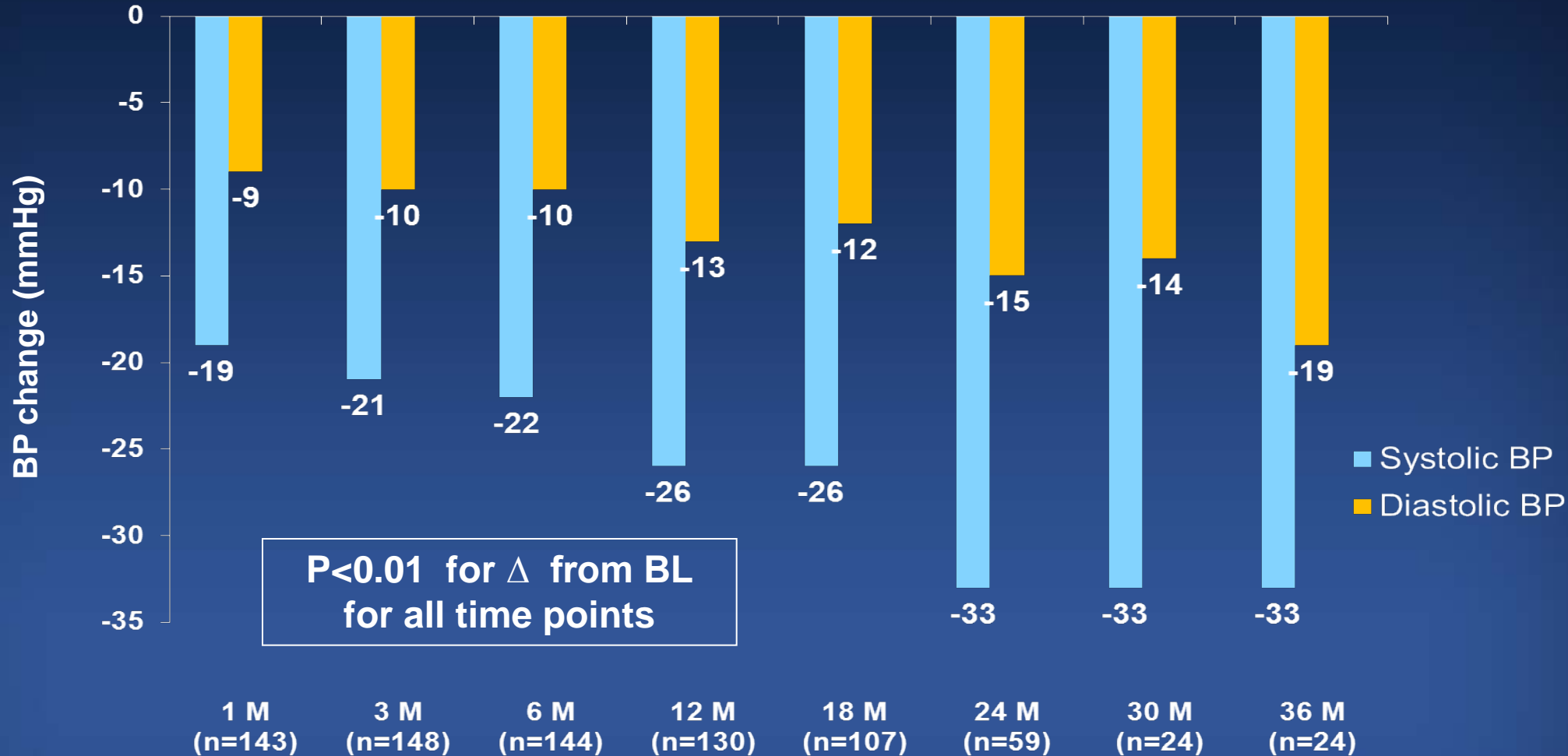


Shading on bars indicates clinical trial enrollment periods.
 Enrollment period for HTN-3 is estimated.

1. Krum H, et al. *Lancet*. 2009;373:1275-1281.
2. Symplicity HTN-1 Investigators. *Hypertension*. 2011;57:911-917.
3. Esler et al. *Lancet*. 2010;376:1903-1909.
4. Data on file, Medtronic.

SYMPPLICITY HTN 1

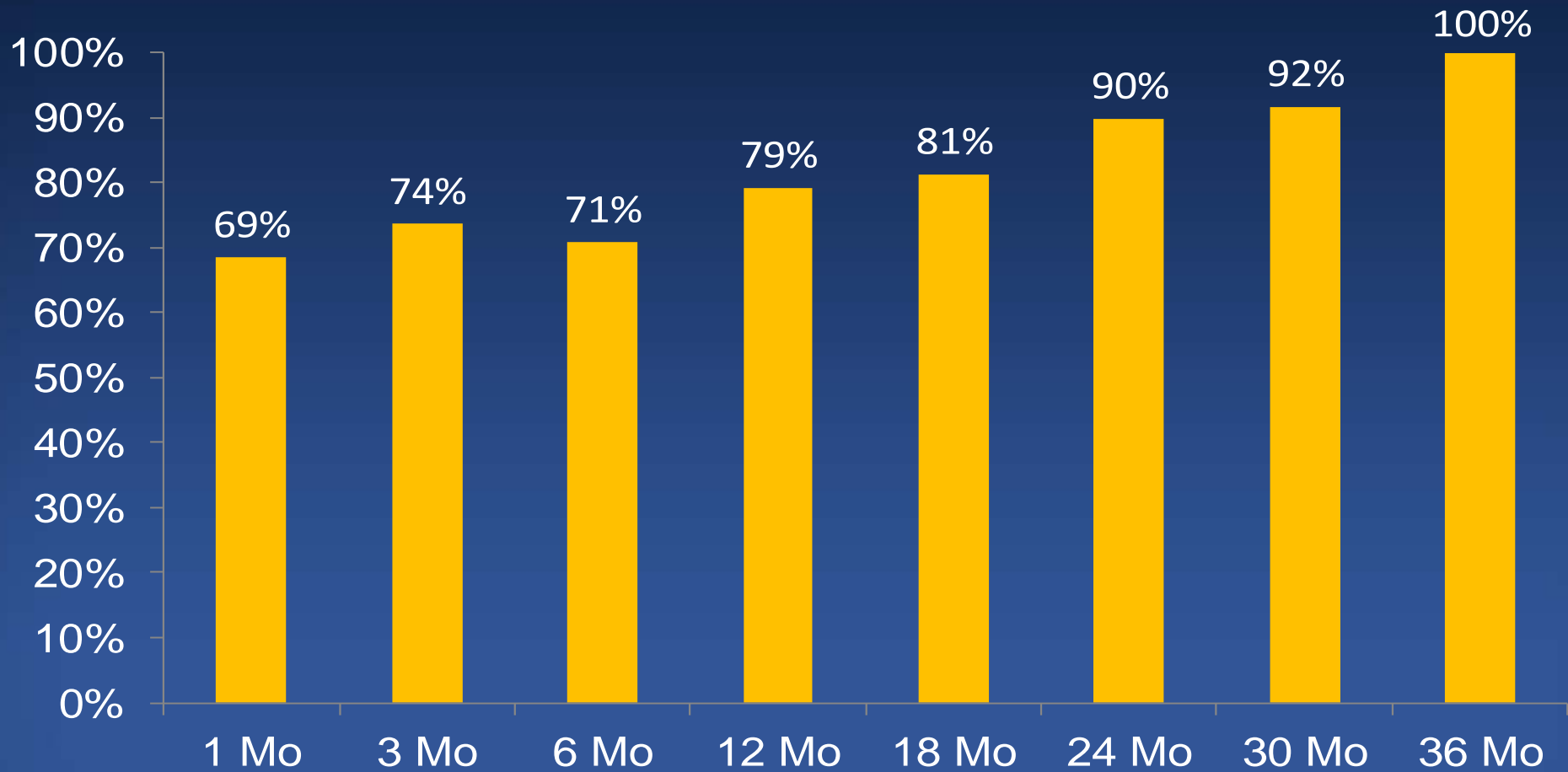
Change in Office Blood Pressure Through 3 Years



SYMPPLICITY HTN-1

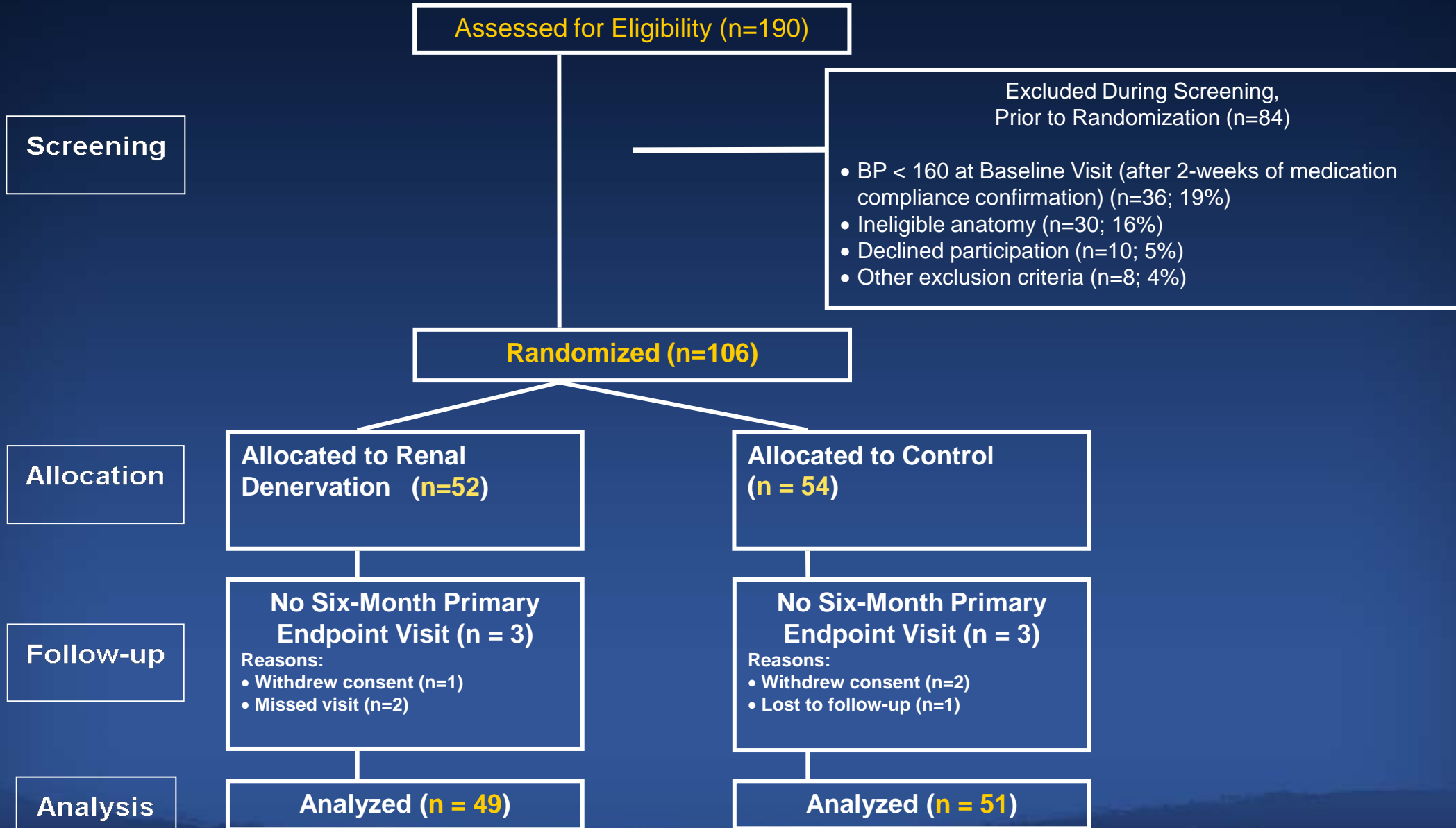
Percentage Responders Over Time

Responder was defined as an office SBP reduction ≥ 10 mm Hg



Sobotka et al. ACC 2012

SYMPPLICITY HTN 2



Screening

Allocation

Follow-up

Analysis

Assessed for Eligibility (n=190)

Excluded During Screening,
Prior to Randomization (n=84)

- BP < 160 at Baseline Visit (after 2-weeks of medication compliance confirmation) (n=36; 19%)
- Ineligible anatomy (n=30; 16%)
- Declined participation (n=10; 5%)
- Other exclusion criteria (n=8; 4%)

Randomized (n=106)

Allocated to Renal
Denervation (n=52)

Allocated to Control
(n = 54)

No Six-Month Primary
Endpoint Visit (n = 3)

- Reasons:
- Withdrew consent (n=1)
 - Missed visit (n=2)

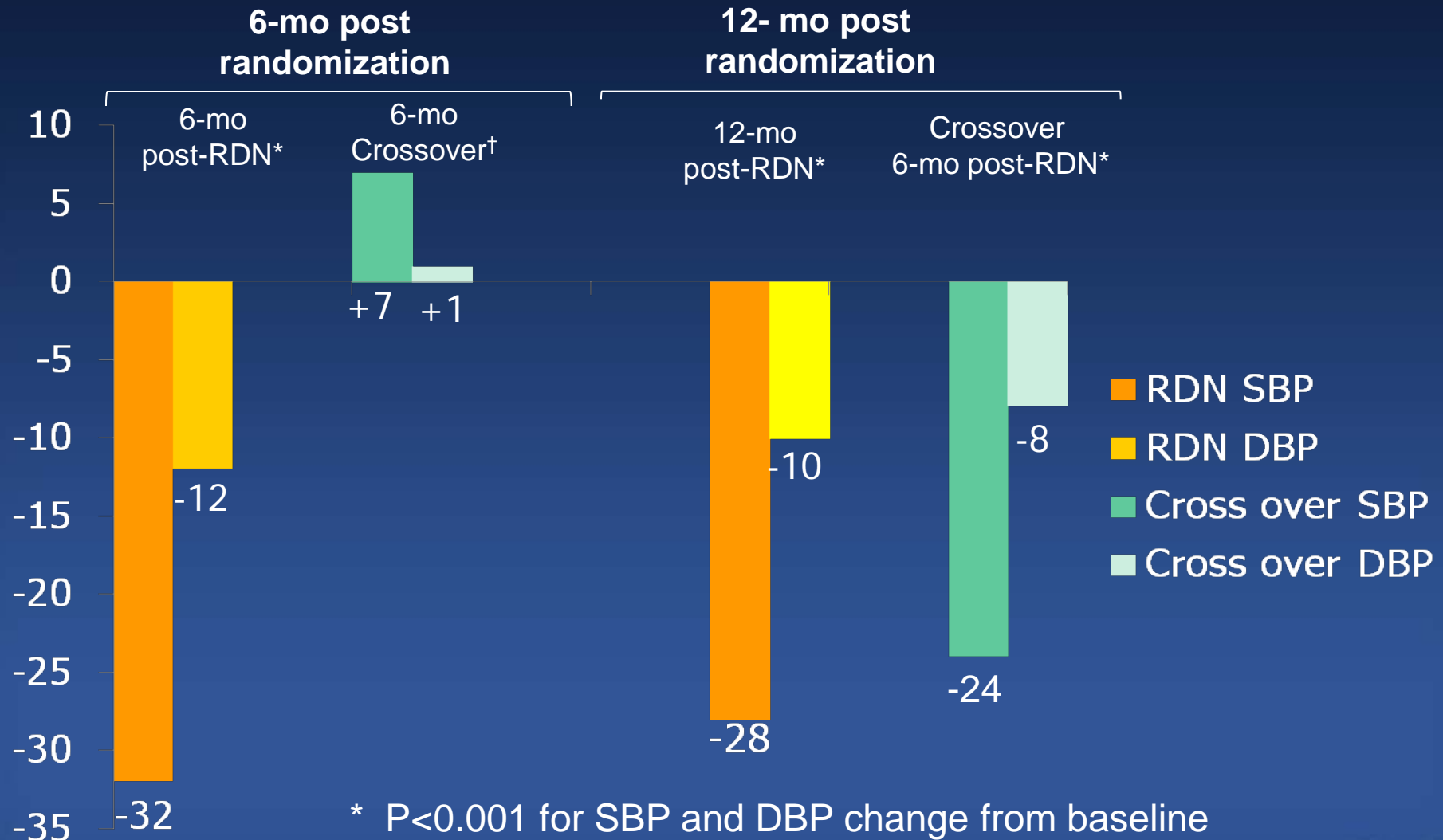
No Six-Month Primary
Endpoint Visit (n = 3)

- Reasons:
- Withdrew consent (n=2)
 - Lost to follow-up (n=1)

Analyzed (n = 49)

Analyzed (n = 51)

Change in Office BP (mm Hg)

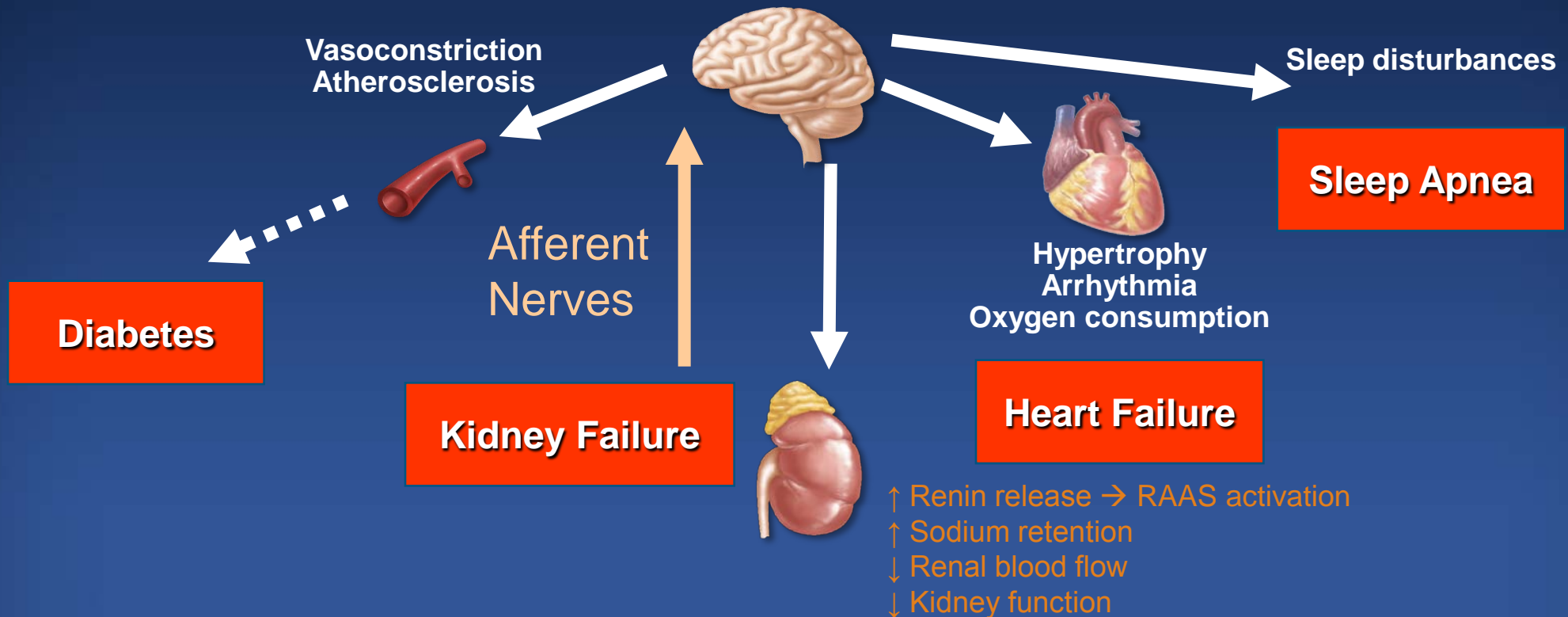


* P<0.001 for SBP and DBP change from baseline

† P=0.026 for SBP change from baseline

Future Directions for Research

- Chronic activation of renal nerves is common in multiple conditions/disease states^{1,2}
- Future research may be warranted in disease states characterized by hyperactive afferent and efferent renal nerves



RAAS = renin-angiotensin-aldosterone system.

1. Adapted from Schlaich MP, et al. *Hypertension*. 2009;54:1195-1201.

2. Blankestijn PJ, et al. *Nephrol Dial Transplant*. 2011;26:2732-2734.

Discussion

- Resistant Hypertension
 - Long-term efficacy and safety
 - New devices: Strengths and Weakness
- Sham Trials
 - SYMPLICITY HTN-1,2: Enough to prove
 - SYMPLICITY HTN-3: Must do
- Future Perspectives
 - CHF, Diabetes, Sleep Apnea