Renal Denervation Highlights: Results of Symplicity HTN-3

TCTAP 2014
Seoul, S. Korea

Krishna Rocha-Singh, MD, FACC
Prairie Heart Institute
Springfield, IL

Background

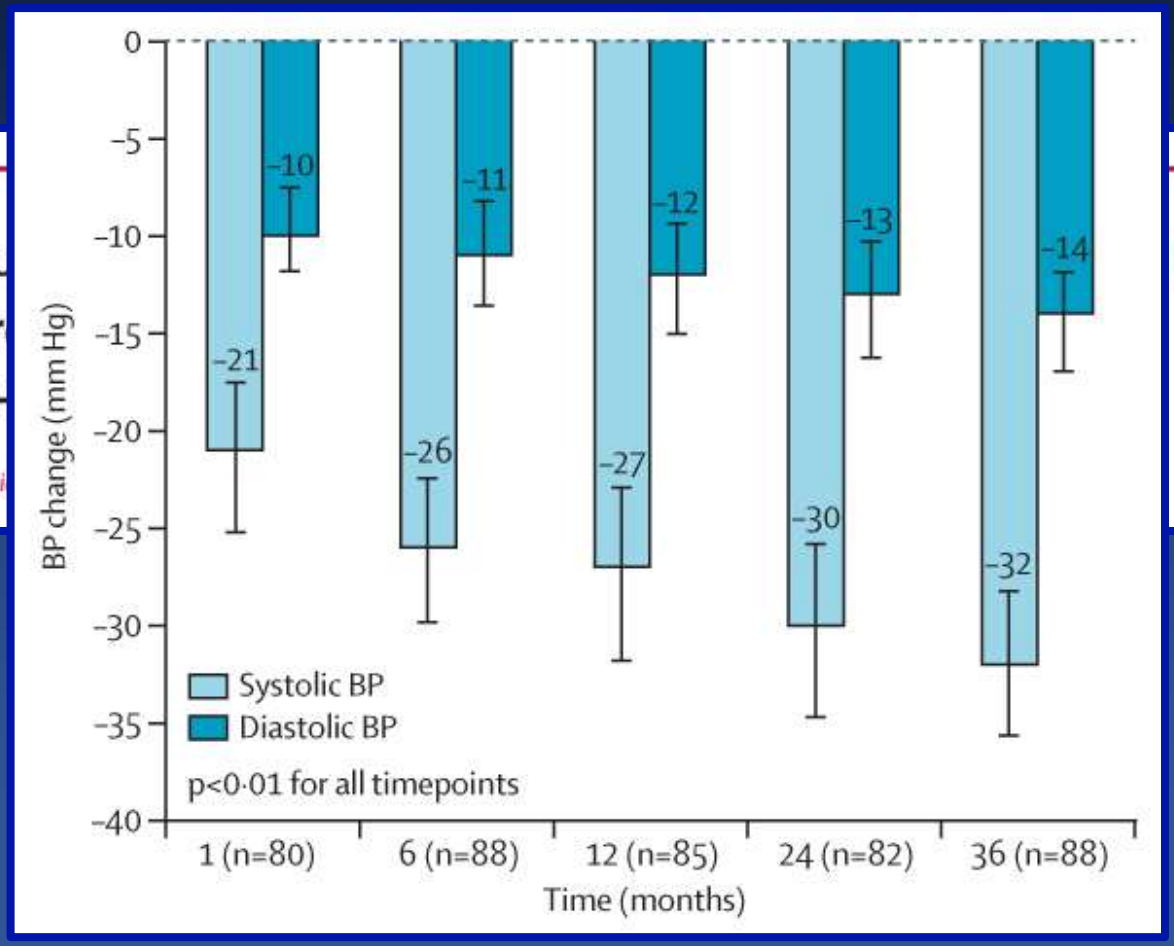
Symplicity HTN - 3 Clinical Study

- Due to aging of the population and greater trends towards obesity, hypertension is growing in prevalence worldwide.
- Approximately 10% of patients with diagnosed hypertension have “resistant” hypertension.
- The sympathetic nervous system appears to play an important role in resistant hypertension.
- Prior non-blinded studies have suggested that catheter-based renal artery denervation reduces blood pressure in resistant hypertension.

OBP Response to RDN: Symplicity HTN-1 Three-Yr Follow-up

Percutaneou
treatment-r
Symplicity H

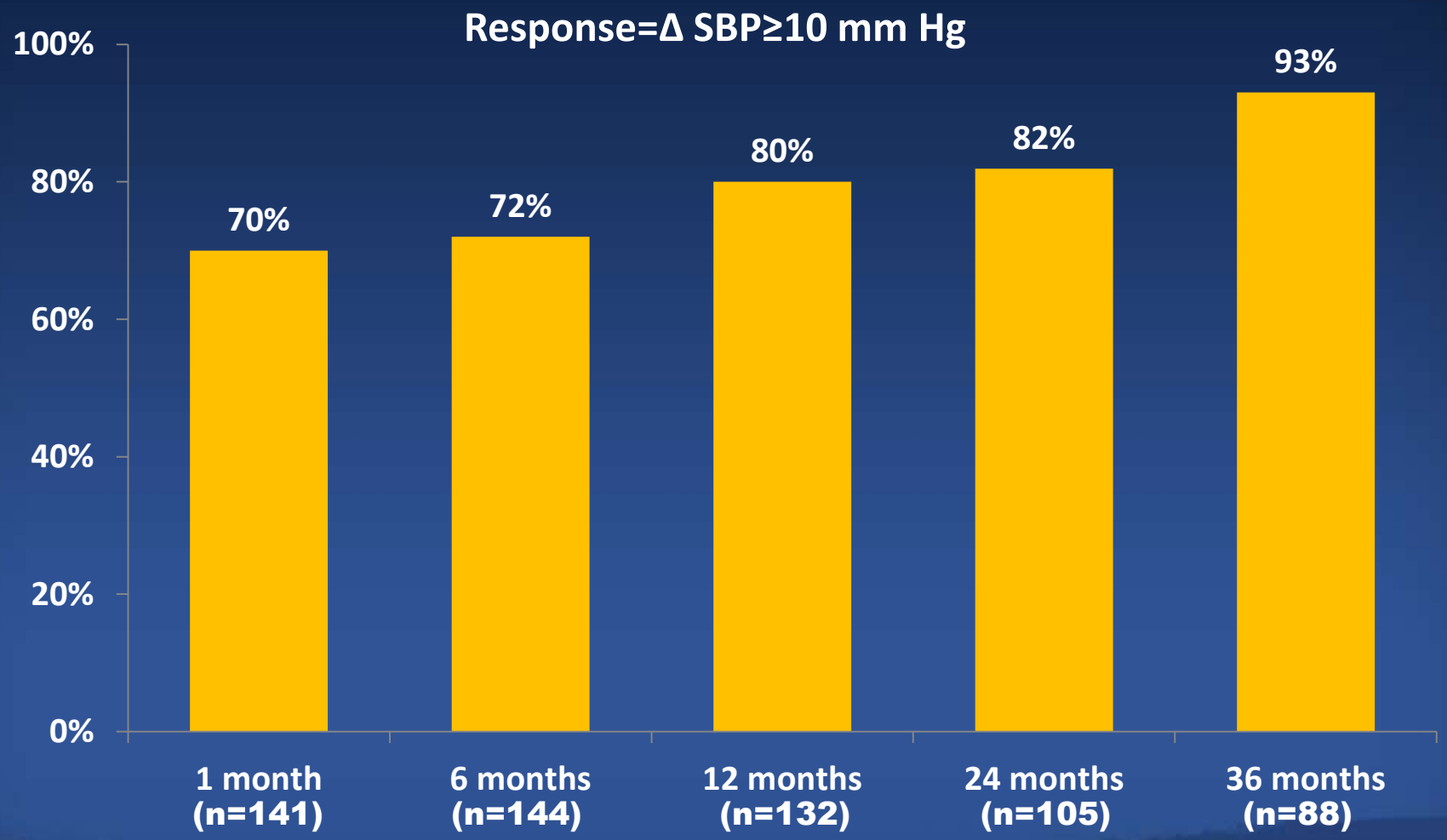
Henry Krum, Markus P Schlai



Lancet 2013

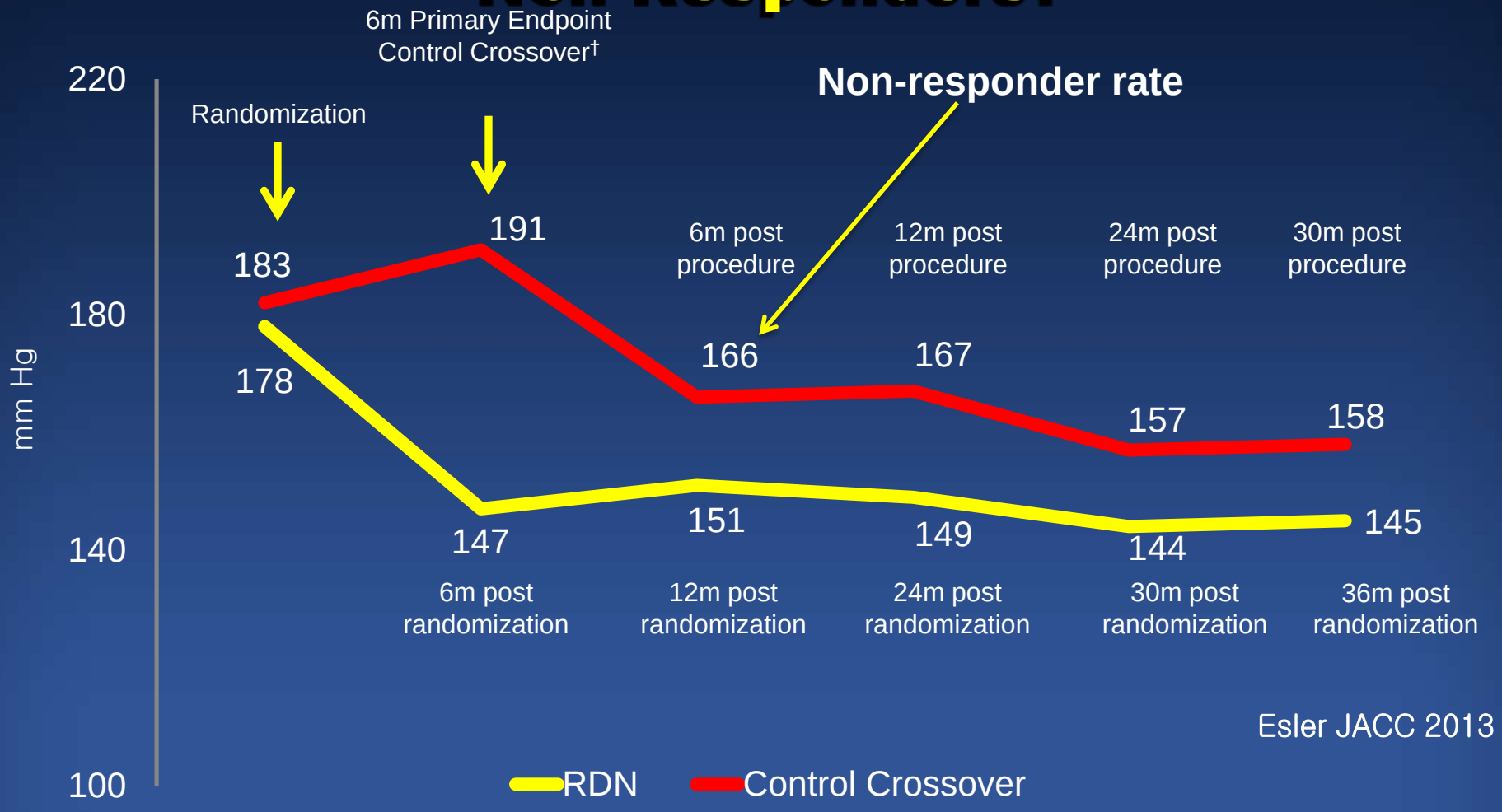
Too good to be true?

SYMPLICITY HTN-1 % Responders Over Time (All Patients)



Krum H. *Lancet 2013*

SYMPLICITY HTN-2 Office SBP through 3 6 Mos* Early Concerns About Non-Responders?



*only patients in the RDN group have reached their 36 month post procedure visit
†Patients randomized to control were offered RDN following the primary endpoint assessment.
Only patients still meeting entry criteria (SBP ≥ 160 mmHg) were included in this analysis (n=37)

Trial Objectives

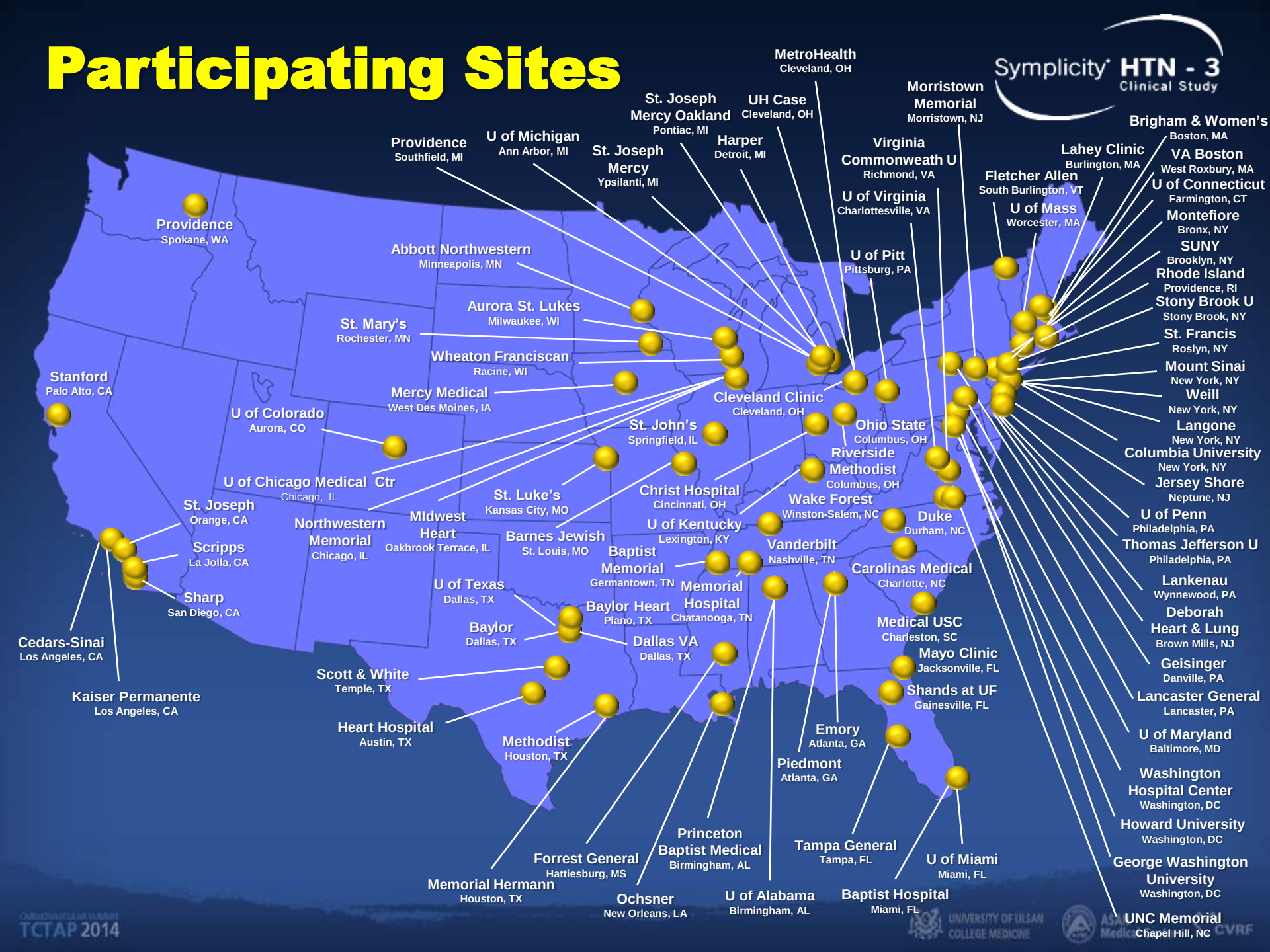
Symplicity HTN - 3 Clinical Study

- **SYMPLICITY HTN-3 is the first prospective, multi-center, randomized, blinded, sham control led study to evaluate both the safety and efficacy of percutaneous renal artery denervation in patients with severe treatment-resistant hypertension.**
- **The trial included 535 patients enrolled by 88 participating US centers.**

Bhatt DL, Kandzari DE, O'Neill WW, et al...Bakris GL. N Engl J Med 2014

Participating Sites

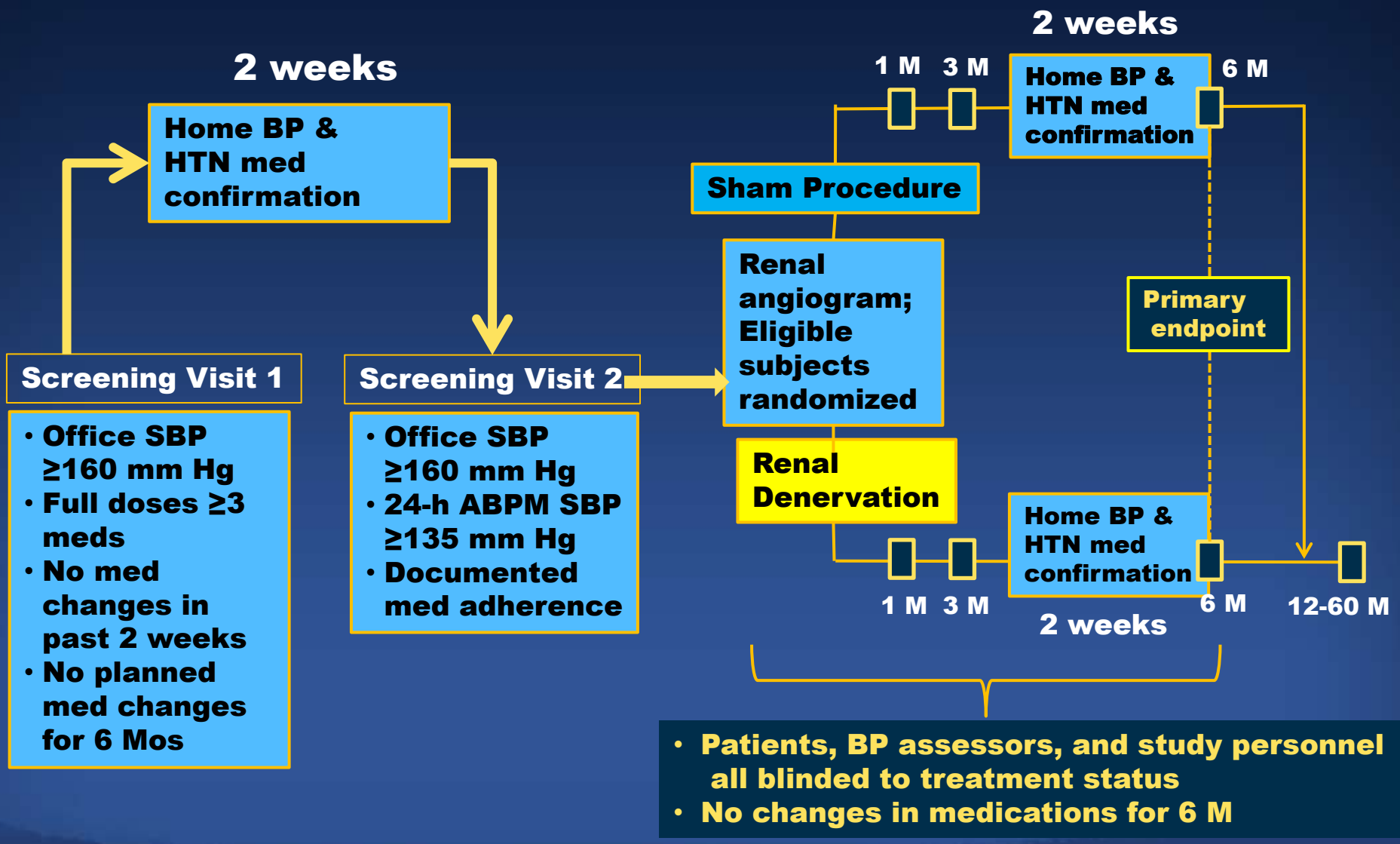
Symplicity HTN - 3 Clinical Study



TCTAP 2014

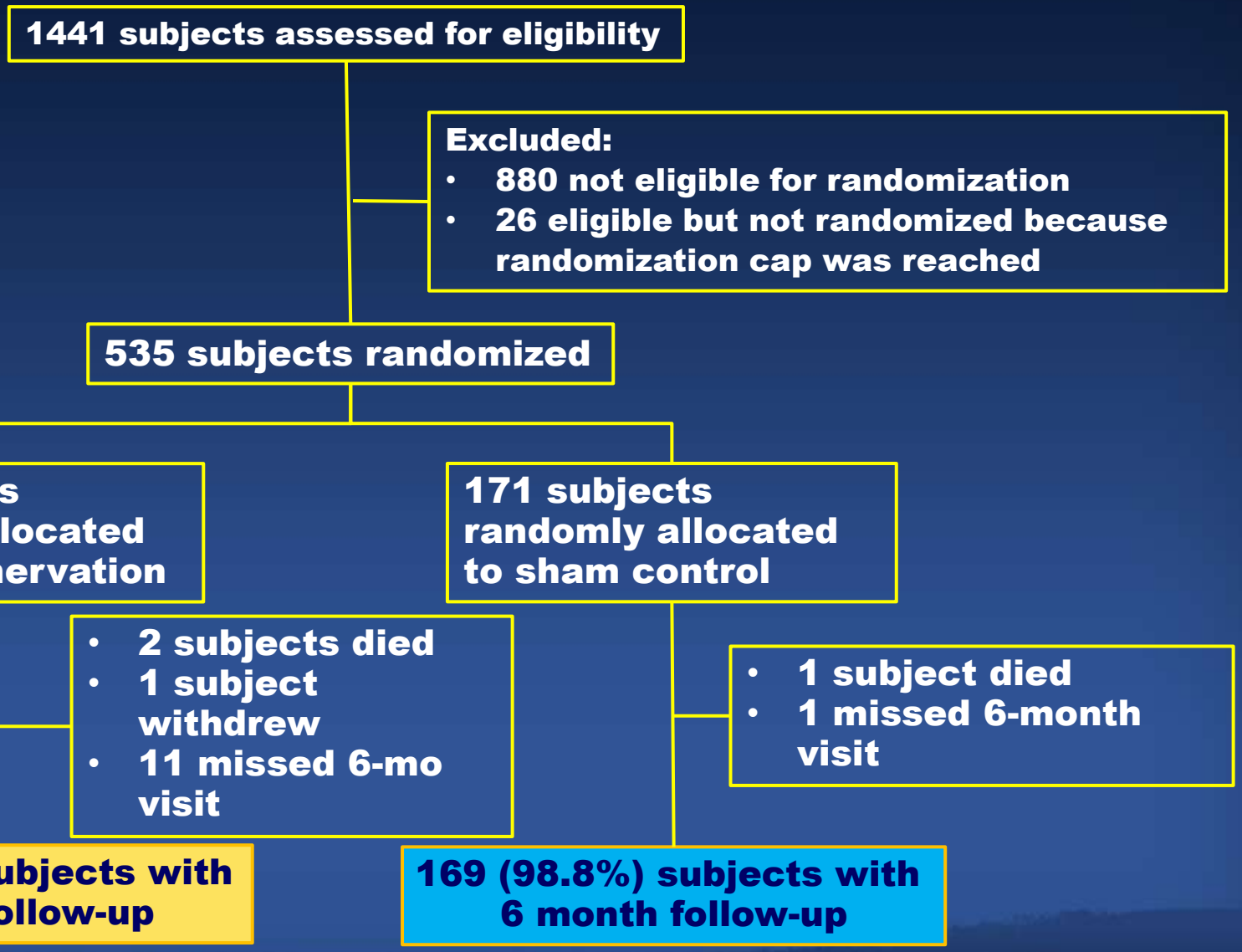
SYMPLICITY HTN-3 Trial Design

Symplicity HTN - 3 Clinical Study



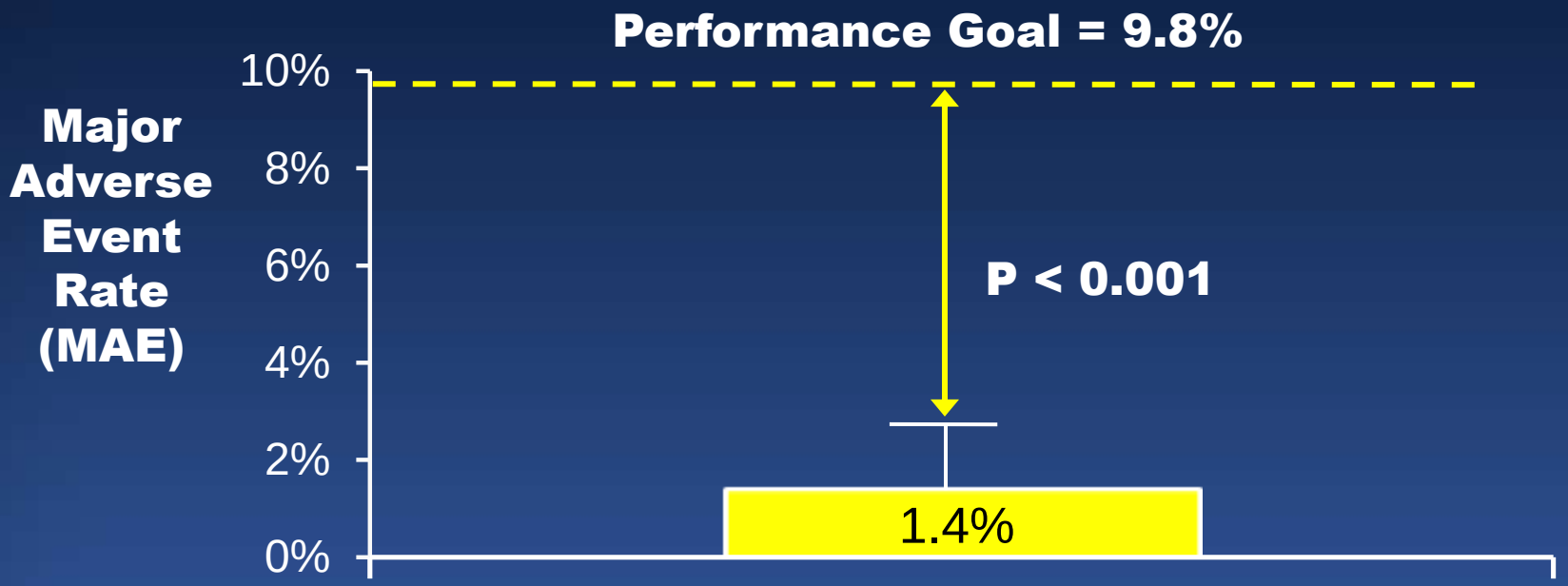
Patient Disposition

Symplicity HTN - 3 Clinical Study



Primary Safety Endpoint

Symplicity HTN - 3 Clinical Study



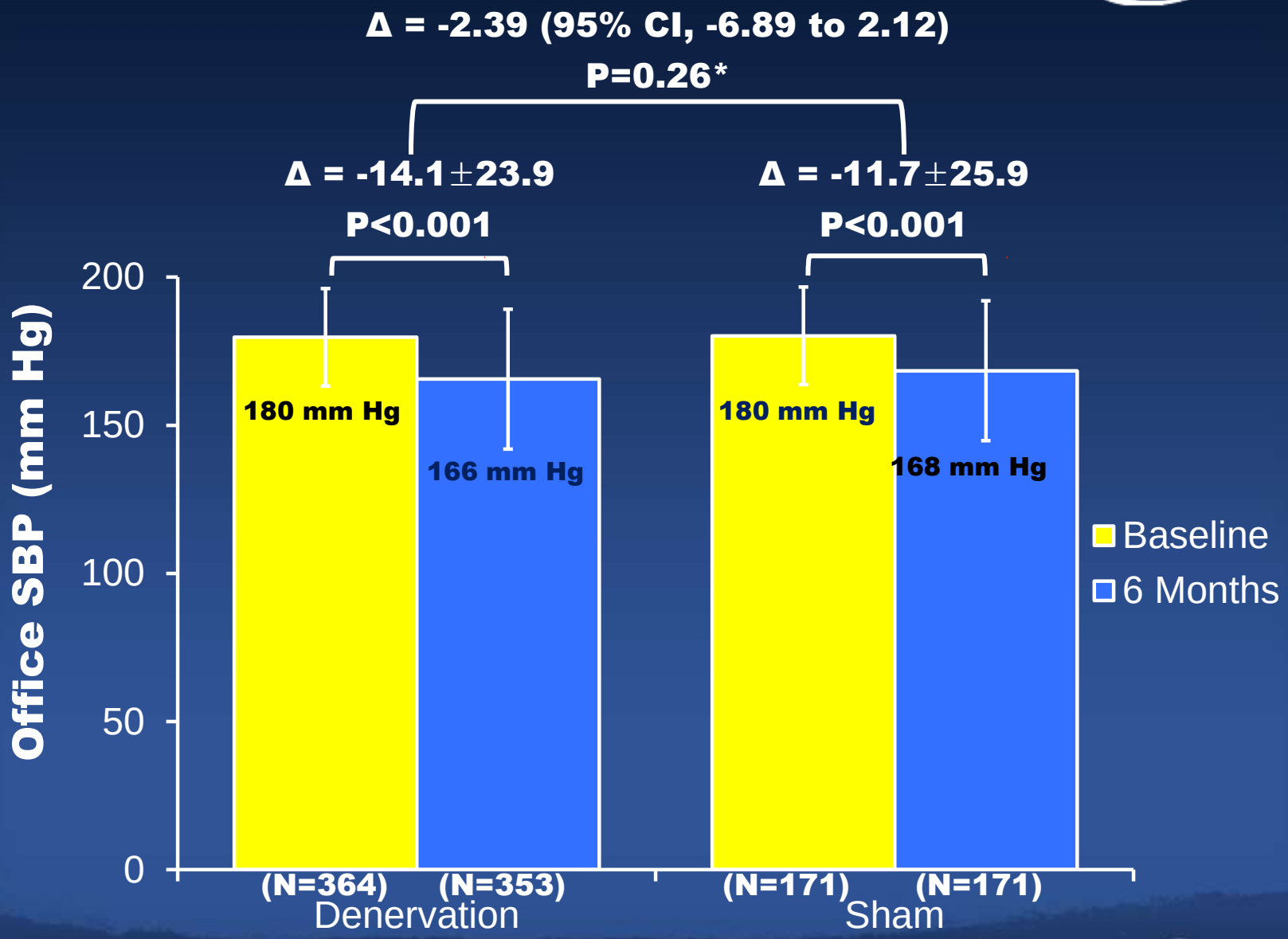
	Renal Denervation (N=364)	Sham Procedure (N=171)	Difference [95% CI]	P*
MAE	1.4% (5/361)	0.6% (1/171)	0.8% [-0.9%, 2.5 %]	0.67

*comparison of MAE to control group

Bhatt DL, Kandzari DE, O'Neill WW, et al...Bakris GL. N Engl J Med 2014

Primary Efficacy Endpoint

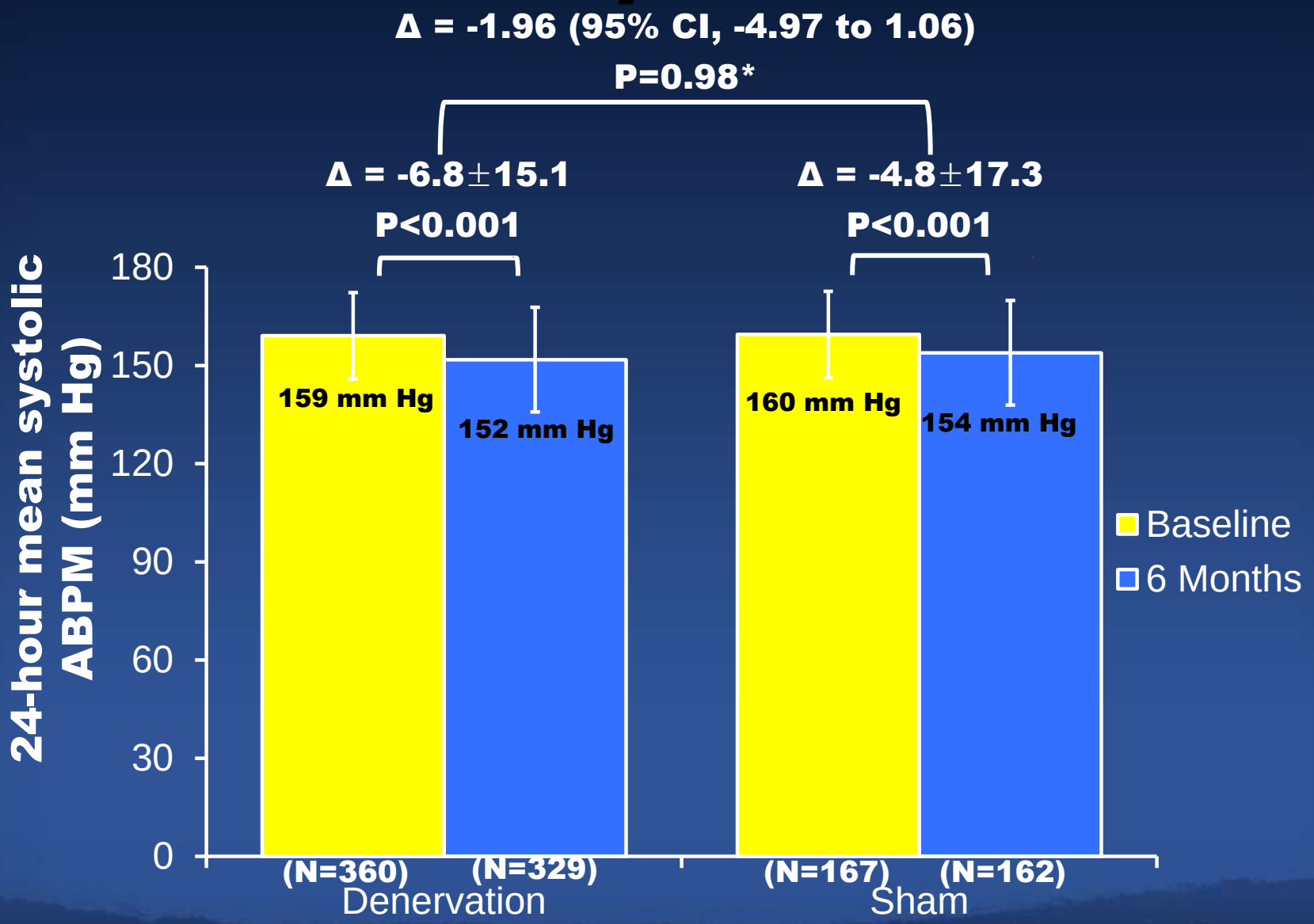
HTN - 3 Clinical Study



*P value for superiority with a 5 mm Hg margin; bars denote standard deviations

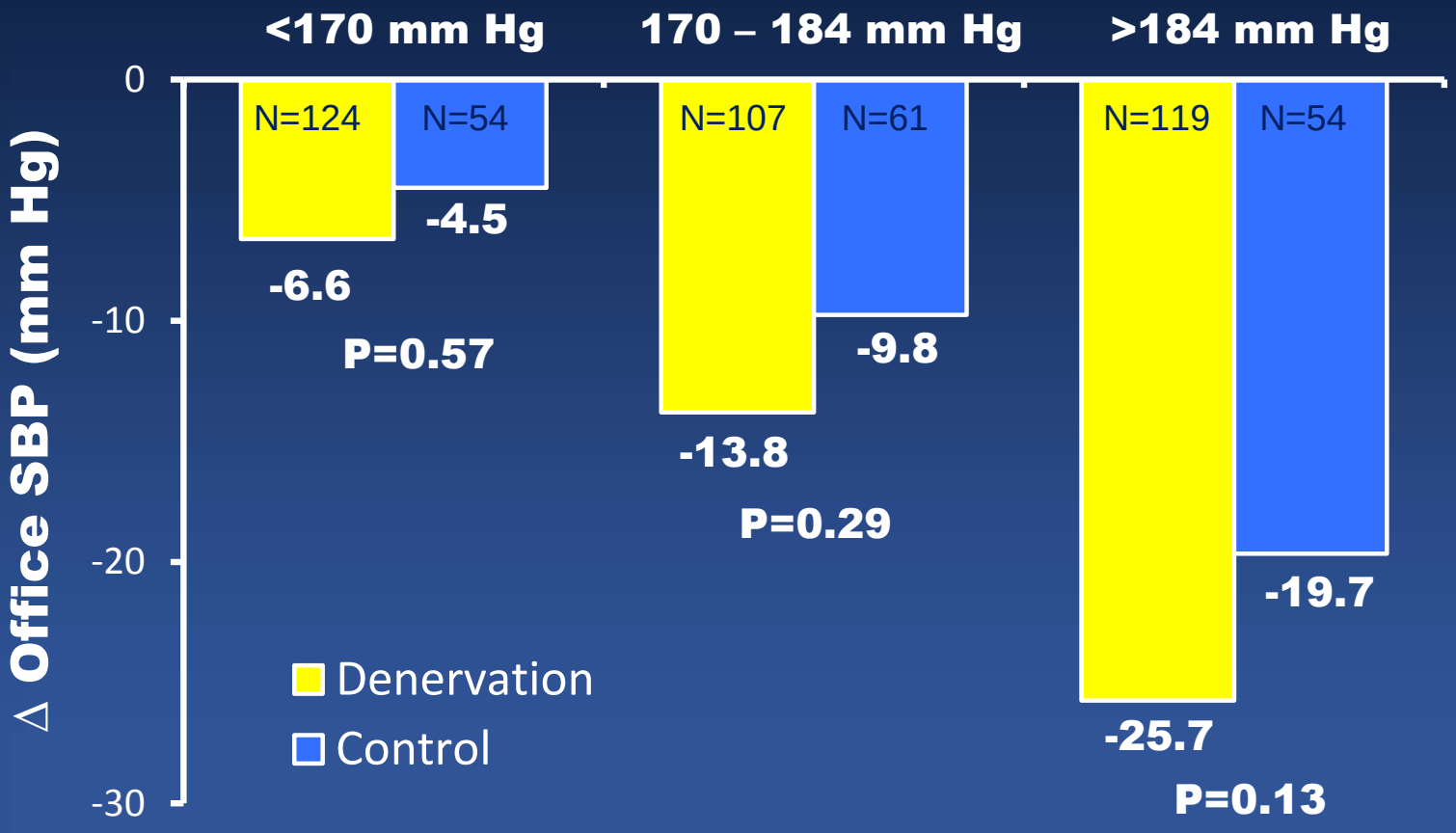
Powered Secondary Efficacy Endpoint

Symplicity HTN - 3 Clinical Study



*P value for superiority with a 2 mm Hg margin; bars denote standard deviations

Change in Office SBP by Tertiles of Baseline Office SBP

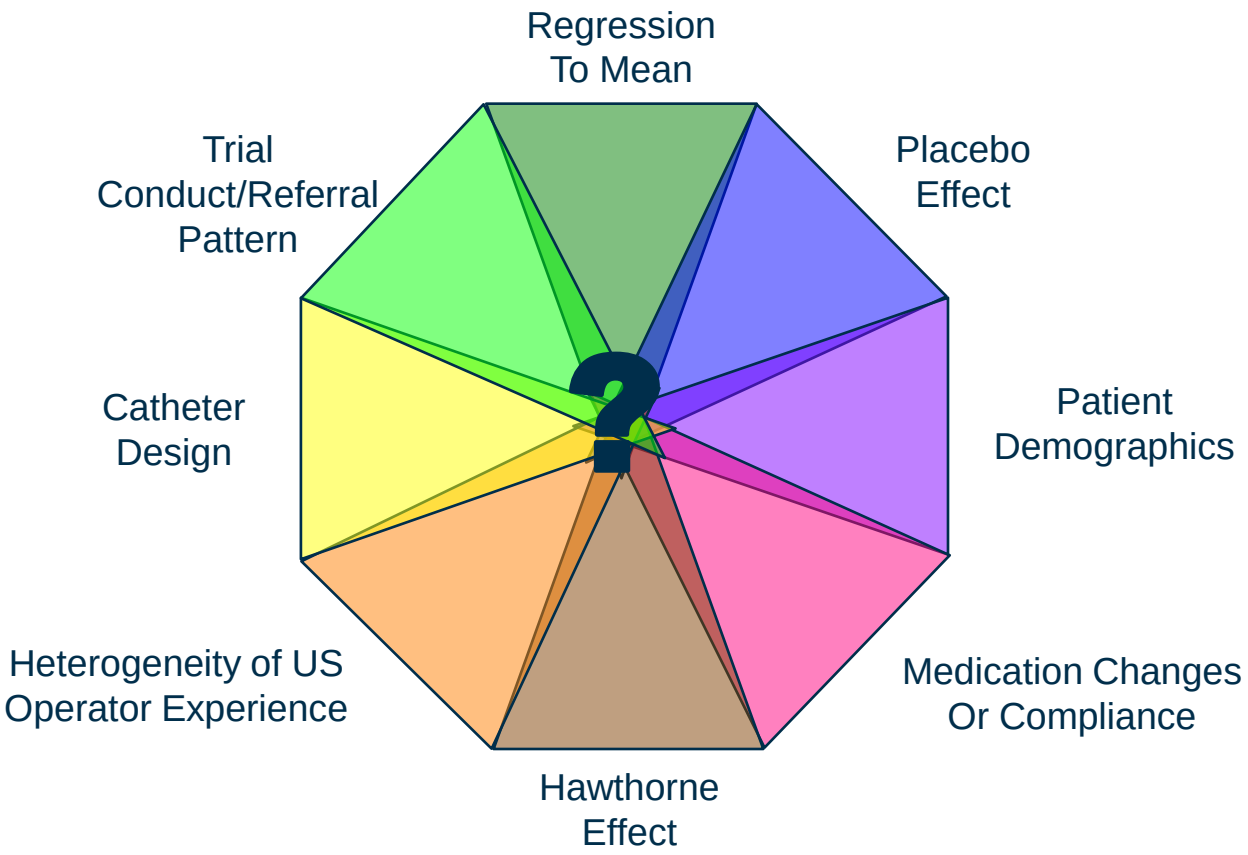


Potential Limitations

Symplicity HTN - 3 Clinical Study

- Drug adherence not measured by blood levels, but adherence was measured by patient diaries at baseline and 6 months.
- Medication changes did occur, but results unchanged even when these patients were censored.
- Duration of primary endpoint may have been too short, but prior studies had found benefit by 6 months.
- Operator learning curve is always a possibility, but we found no relationship with procedural volume in the trial.
- Biological confirmation of denervation did not occur, as there is no accepted measure, but appropriate energy delivery was confirmed.

Why Did Symplicity HTN-3 Fail?



Symplicity HTN-3 Conclusions

Symplicity HTN - 3 Clinical Study

- In a prospective, multicenter, randomized, blinded, sham controlled trial of patients with uncontrolled resistant hypertension, percutaneous renal denervation was safe but not associated with significant additional reductions in office or ambulatory blood pressure.

- These results underscore the importance of blinding and sham controls in evaluations of new devices.

- Further study in rigorously designed clinical trials will be necessary to confirm previously reported benefits of renal denervation in patients with resistant hypertension or to validate alternate methods of renal denervation.

My Personal Take-Aways

Symplicity HTN - 3 Clinical Study

- If results looks to good to be true…
- Was the translational model correct?
  -Do renal pig arteries = renal anatomy in elderly patients with possible circumferential atherosclerosis?
- Beware of the sham!
- Managing patient behavior + compliance is substantial variable and difficult to control
- We need to shine the light on the RDN procedure