

Clinician and Patient Perspective on Potential of Renal Denervation

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Disclosures

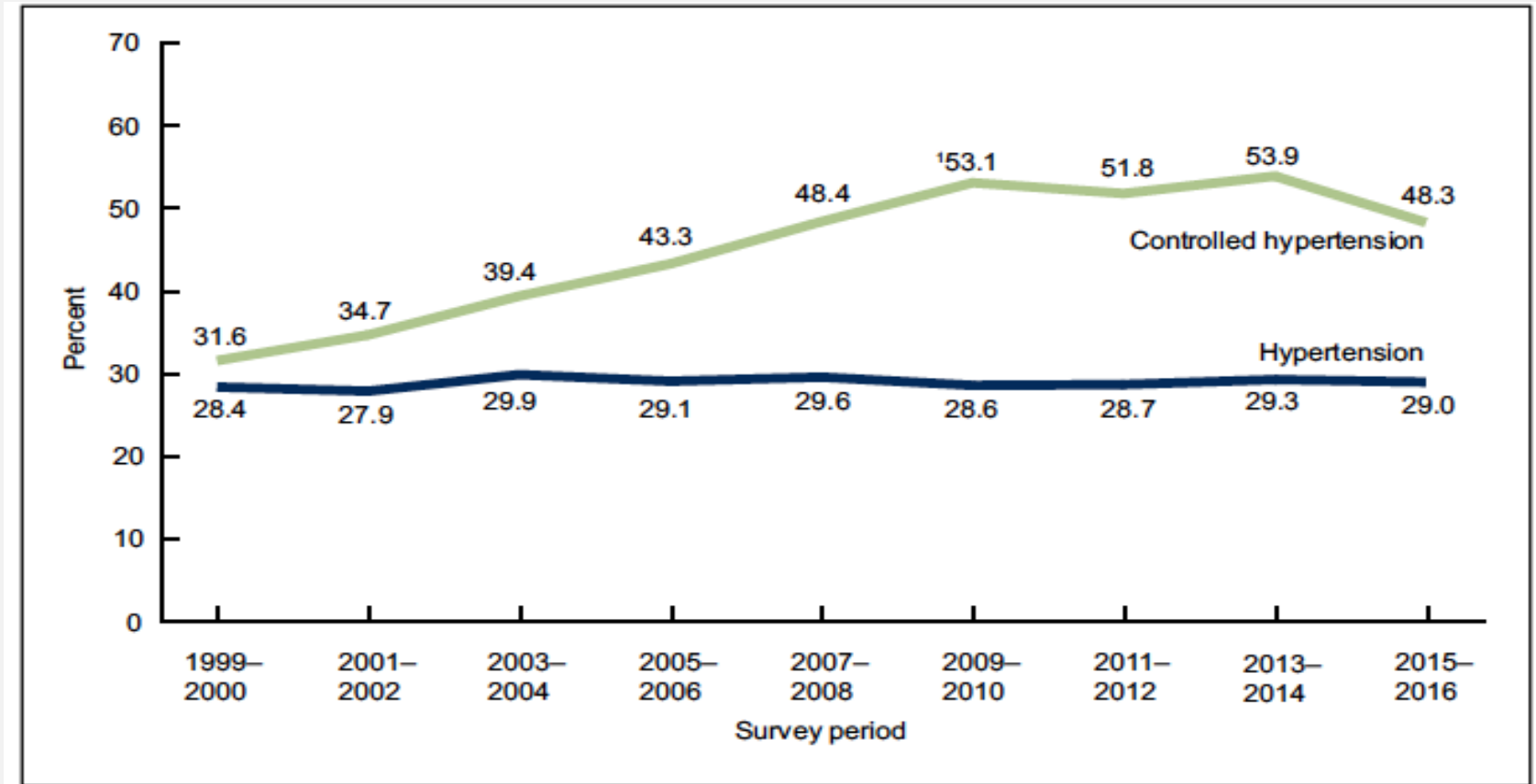
- Research Support – ReCor Medical, AstraZeneca, Vascular Dynamics
- Consultant/Honoraria – ReCor Medical, Medtronic, Amgen, Esperion, Janssen, Takeda International, Relypsa, Pfizer

Outline

- What is the unmet clinical need?
- What is a clinically meaningful reduction in blood pressure?
- What is the benefit-risk of renal denervation vs adding another anti-hypertensive medication?
- Based on available data what would be a clinically appropriate indication to consider at this time?

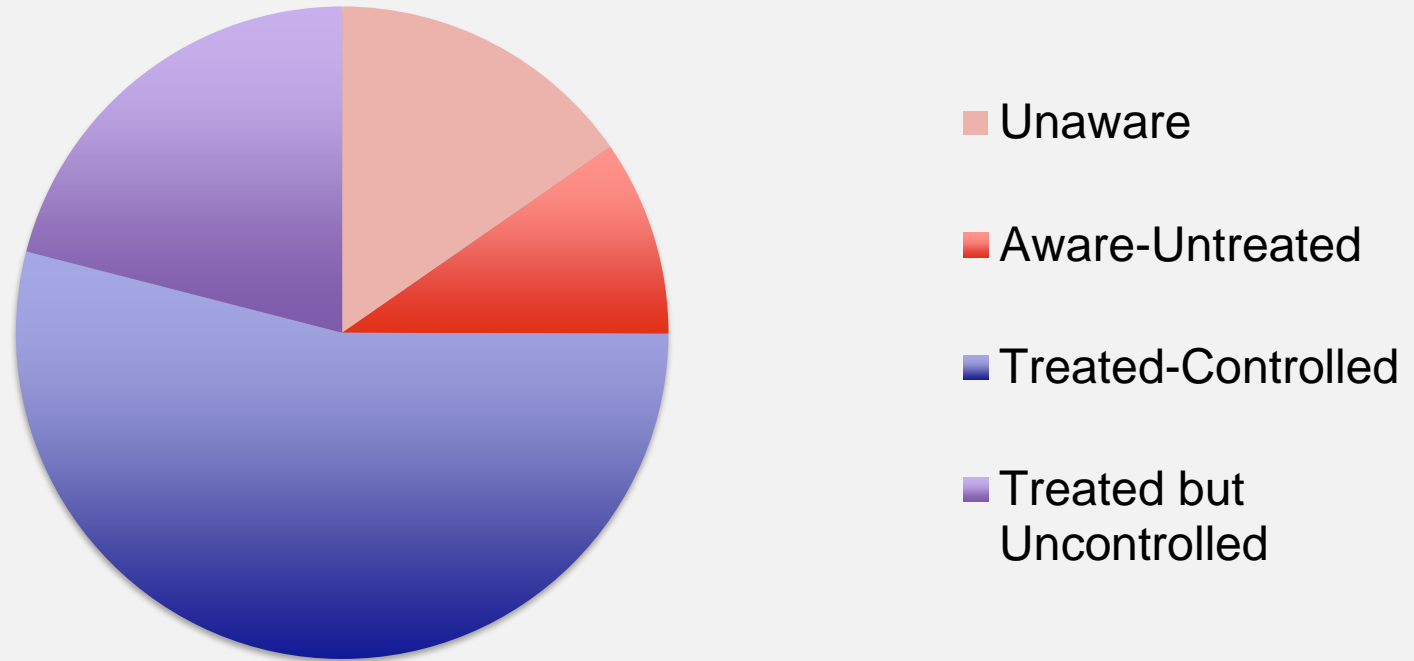
Trends in Hypertension Control

Healthy People 2020 Goal = 61.2%



BP Treated But Not Controlled

NHANES Awareness, Treatment, Control 2013-14



Uncontrolled Despite Active Treatment for Hypertension = 27%

Why Might Patients Be Treated But Not Controlled?

Multiple Reasons for Lack of Control:


- Medication non-adherence
- Medication intolerability (side effects)
- Therapeutic inertia
- Patient comorbidities & high pill burden
- Lack of access to health care

How Might RDN Potentially Address This?

- Procedure with durable effect
- Reduced dependence on medication adherence
- Reduced pill burden
- Reduced medication side effects

Only 39% of Patients are Controlled to New 2017 ACC/AHA BP Targets

What is a Meaningful Reduction in BP?

 European Heart Journal (2017) 0, 1–11
doi:10.1093/eurheartj/ehx215

CURRENT OPINION

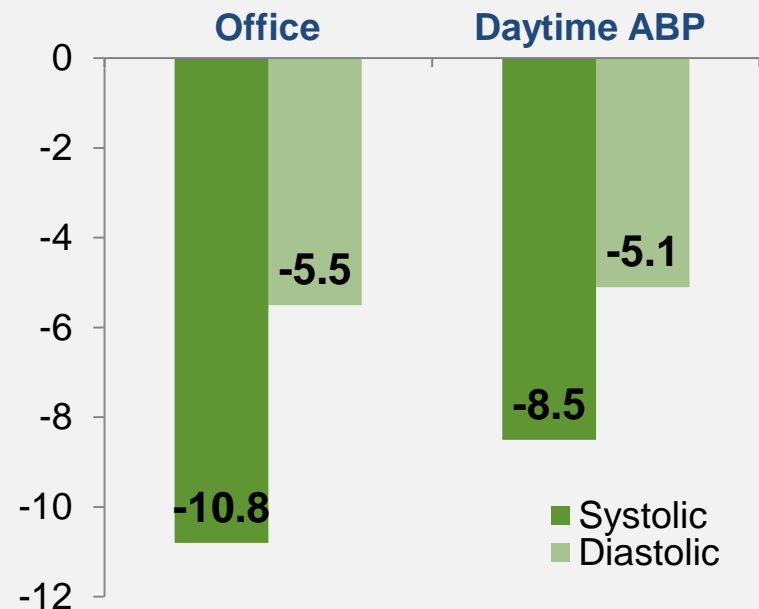
Proceedings from the 2nd European Clinical Consensus Conference for device-based therapies for hypertension: state of the art and considerations for the future

Felix Mahfoud^{1,2*}, Roland E. Schmieder³, Michel Azizi^{4,5,6}, Atul Pathak^{7,8}, Horst Sievert^{9,10}, Costas Tsioufis¹¹, Thomas Zeller¹², Stefan Bertog⁹, Peter J. Blankestijn¹³, Michael Böhm¹, Michel Burnier¹⁴, Gilles Chatellier^{15,16}, Isabelle Durand Zaleski^{17,18}, Sebastian Ewen¹, Guido Grassi^{19,20}, Michael Joner^{21,22}, Sverre E. Kjeldsen^{23,24}, Melvin D. Lobo²⁵, Chaim Lotan²⁶, Thomas Felix Lüscher²⁷, Gianfranco Parati²⁸, Patrick Rossignol²⁹, Luis Ruilope³⁰, Faisal Sharif³¹, Evert van Leeuwen³², Massimo Volpe³³, Stephan Windecker³⁴, Adam Witkowski³⁵, and William Wijns^{36,37}

The European expert group determined:

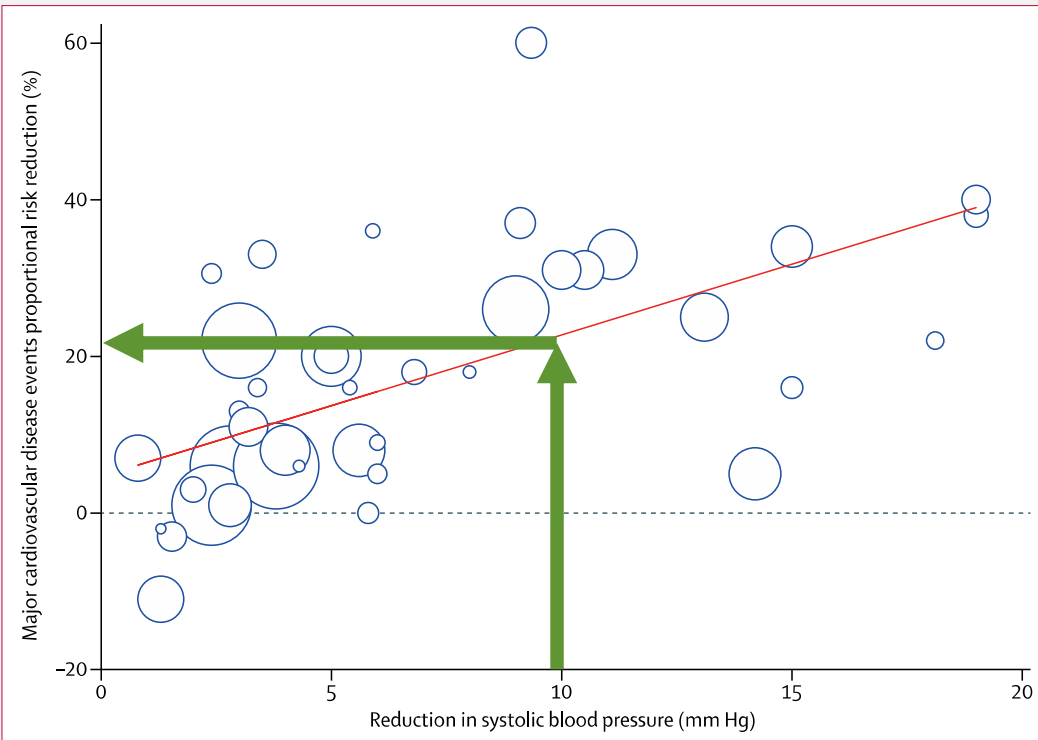
- A 10mmHg reduction in office SBP to be a clinically meaningful outcome.
- This corresponds to 6-7mmHg reduction in ABP.

BP Reductions in RDN Arm of RADIANCE-HTN SOLO at 2M



What Is Clinically Meaningful Reduction in BP?

Correlation Between BP Reduction and CV Events



Meta-regression plot shows the percentage risk reduction in major cardiovascular events regressed against the difference in achieved systolic blood pressure between study treatment groups.

**Meta-analysis of 613,815 Patients
from 123 Studies**

**Reduction of Systolic Office BP by 10
mmHg Leads to Reduction of Risk:**

<i>CV Events</i>	20%
<i>Mortality</i>	13%
<i>Coronary Disease</i>	17%
<i>Stroke</i>	27%
<i>Heart Failure</i>	28%
<i>Chronic Renal Failure</i>	5%

Who Is A Potential Candidate for RDN?

My Clinical Perspective

Treated But Uncontrolled Hypertension



What is the potential relative benefit-risk of adding another antihypertensive medication vs RDN?

- Efficacy – roughly equivalent
- Tolerability – may favor RDN
- Safety – both appear safe
- Adherence – likely favors RDN
- Durability – unclear
- Cost – likely favors medication
- Patient Preference – vary based on individual

Patient Interest in RADIANCE-HTN Trial

- Short, targeted direct-to-patient campaigns: 5 days, 20-30 miles around trial sites
- 536 campaigns run in 6 countries at 41 RADIANCE-HTN sites

Clicks: expression of interest in other options for HTN
N=1,097,171

Answer 20 question survey on eligibility
N=47,403

Pass criteria & sent for secondary screening
N=10,839

Excluded for
clinical reasons
N=33,918

Excluded out of
lack of desire for a
procedure
N=2,646

Strong Patient Interest Exhibited Across Genders, Ages,
and All Geographies
(from Charleston, SC to Los Angeles, CA to Reno, NV)

From a Clinical Perspective: Proposed Target Population for RDN

- Diagnosed with hypertension
- Have been prescribed antihypertensive medications
- Uncontrolled BP based on the following definition
 - Office BP ≥ 140 mmHg systolic and ≥ 90 diastolic, and
 - Confirmatory BP ≥ 135 mmHg systolic using one of the following:
 - Mean daytime ABPM,
 - Documented mean home, or
 - Repeated office automated (i.e. SPRINT style BP)
- Patient preference for device therapy

Conclusions

- ReCor's trial program will yield valuable data both in the absence and in the presence of medications
 - 3 independently powered RCTs: SOLO / TRIO / RADIANCE-II
- ReCor's clinical program is designed to provide information on the safety & effectiveness of ultrasound based renal denervation
 - Blood pressure change over time
 - Blood pressure control
 - Medication burden reductions
 - Vascular and renal safety
- Plan to conduct post-market registry to capture real-world, long-term safety and durability
- Plan to conduct future studies to address additional patient populations