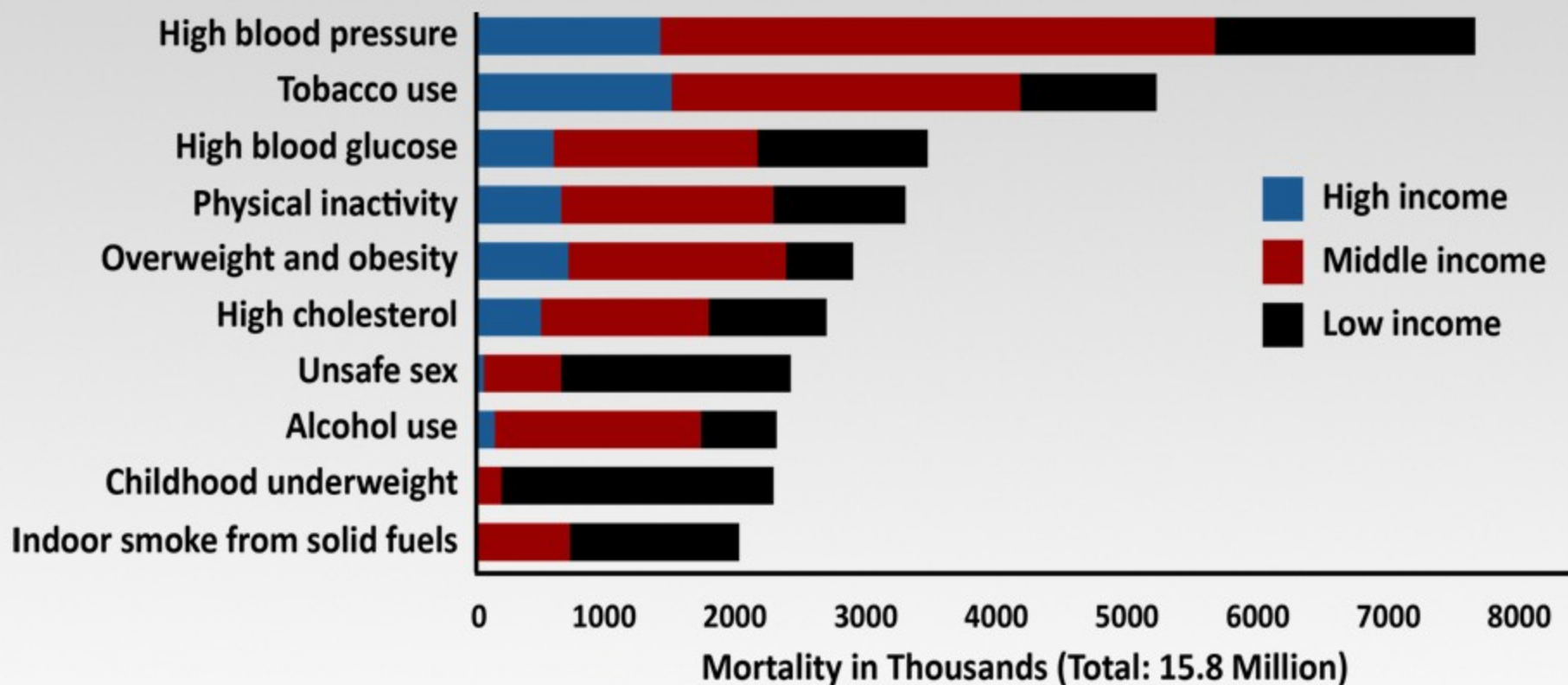
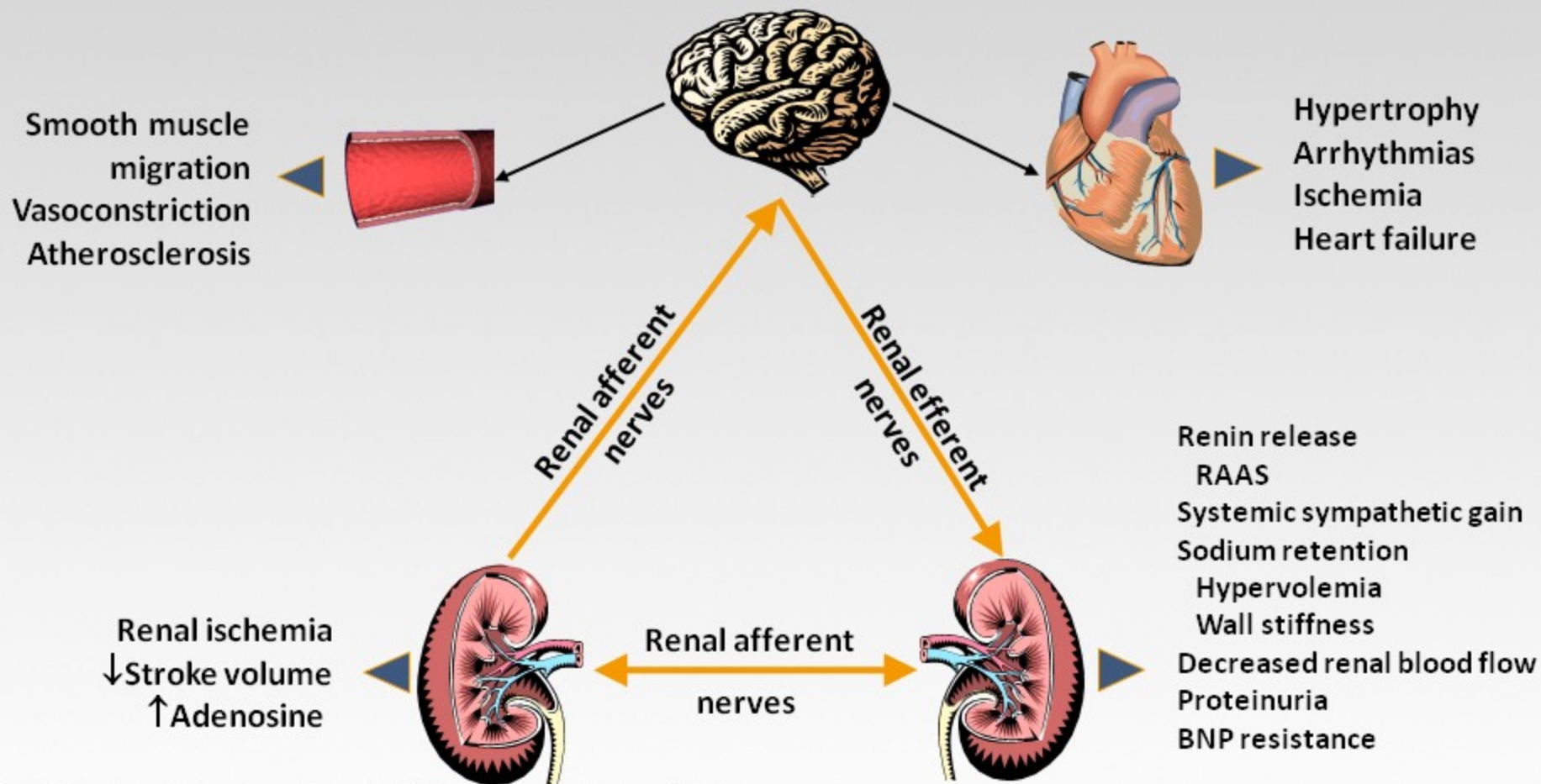


Global Health Risks



Deaths attributed to 10 leading risk factors, by country income level, 2004

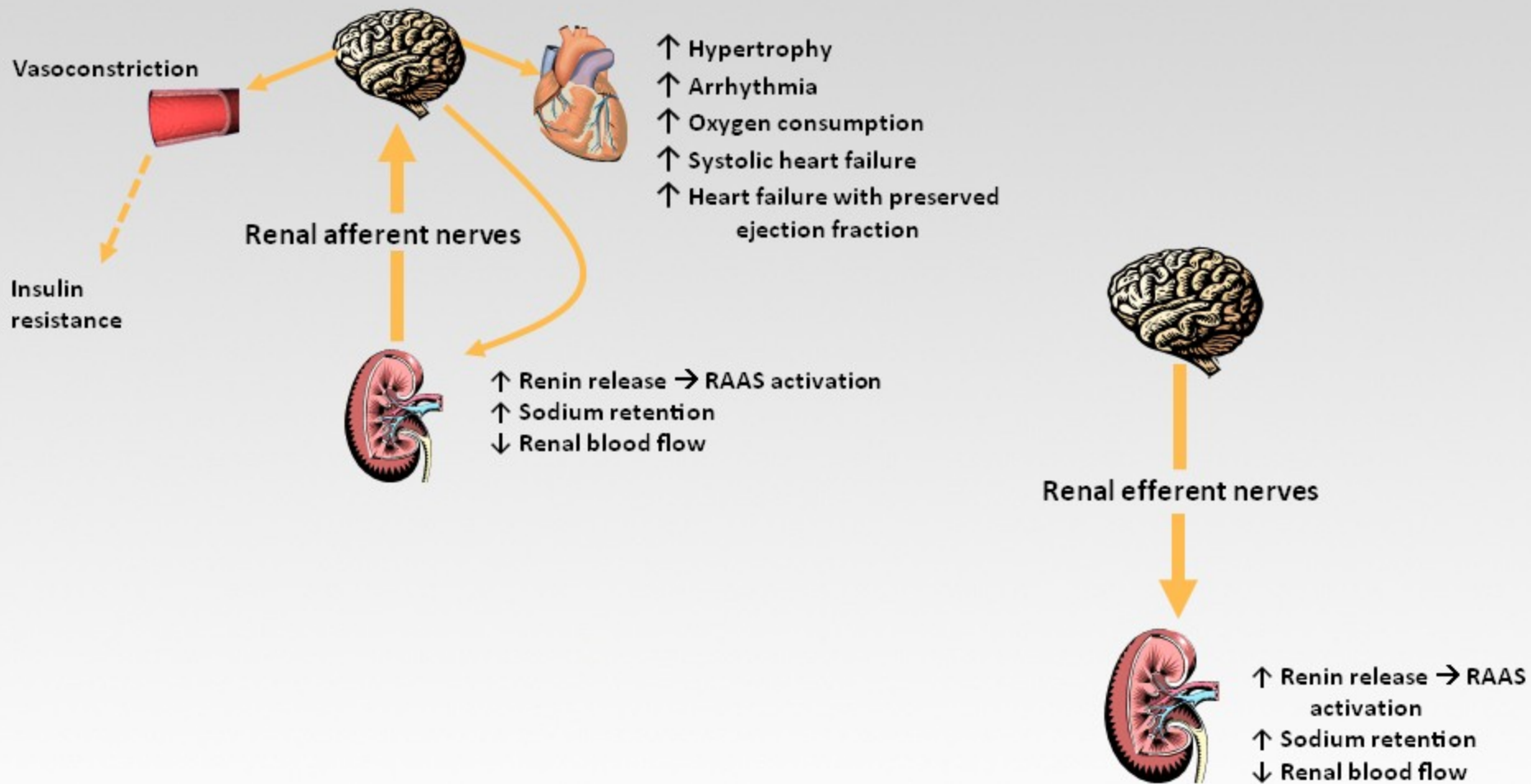
Renal Sympathetic Activation in Hypertension



BNP = brain natriuretic peptide; RAAS = renin-angiotensin-aldosterone system

From Krum H, et al. *Circulation*. 2011;123:209-215.
 Republished with permission.

Renal Sympathetic *Afferent* and *Efferent* Nerve Activity



Анатомия на бъбречните нерви

- От нивото на T10-L2
- Предимно в адвенцията



**Vessel
Lumen**

**Medi
a**

**Adventi
tia**

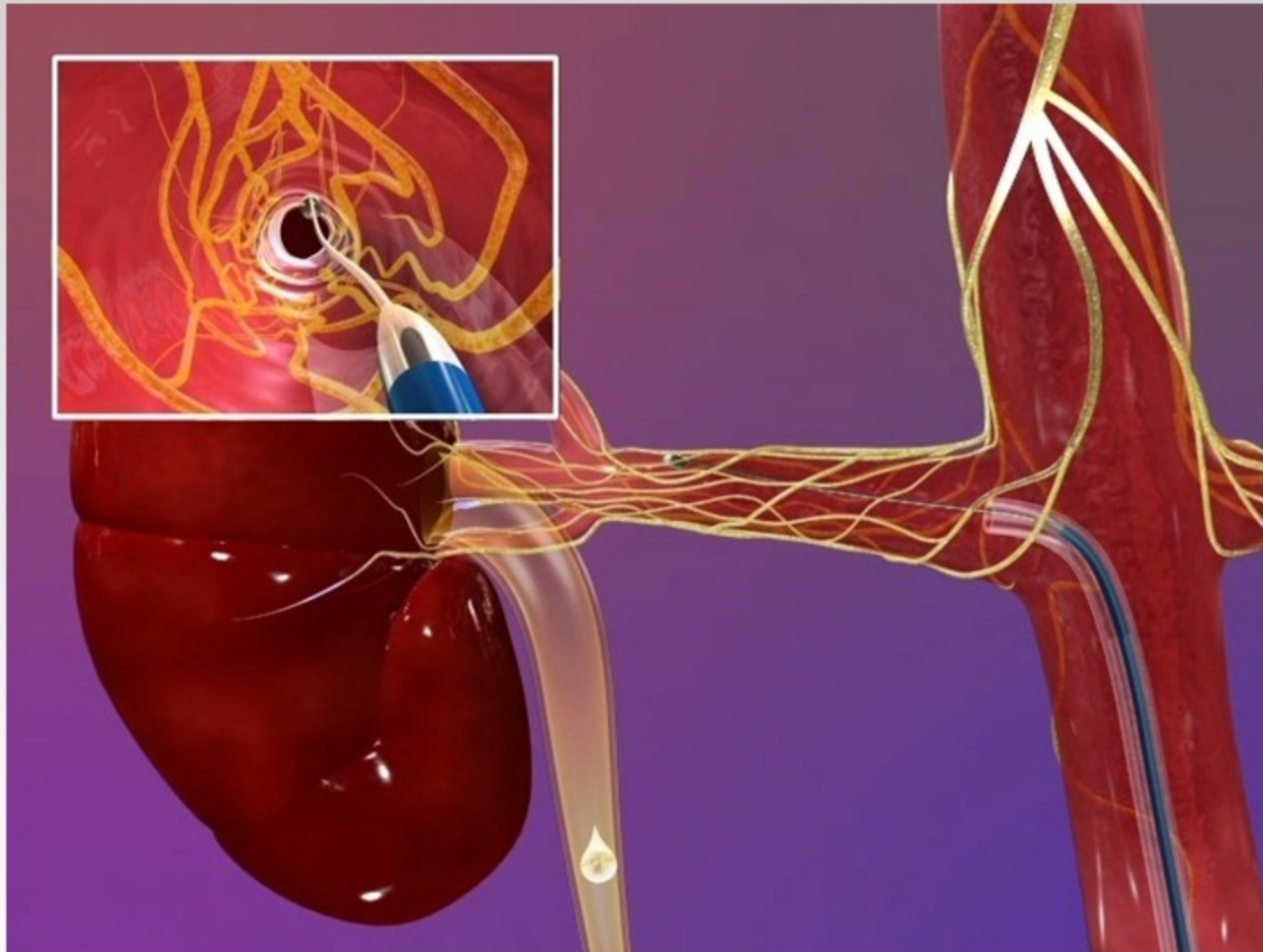
**Renal
Nerves**

1000 μ m



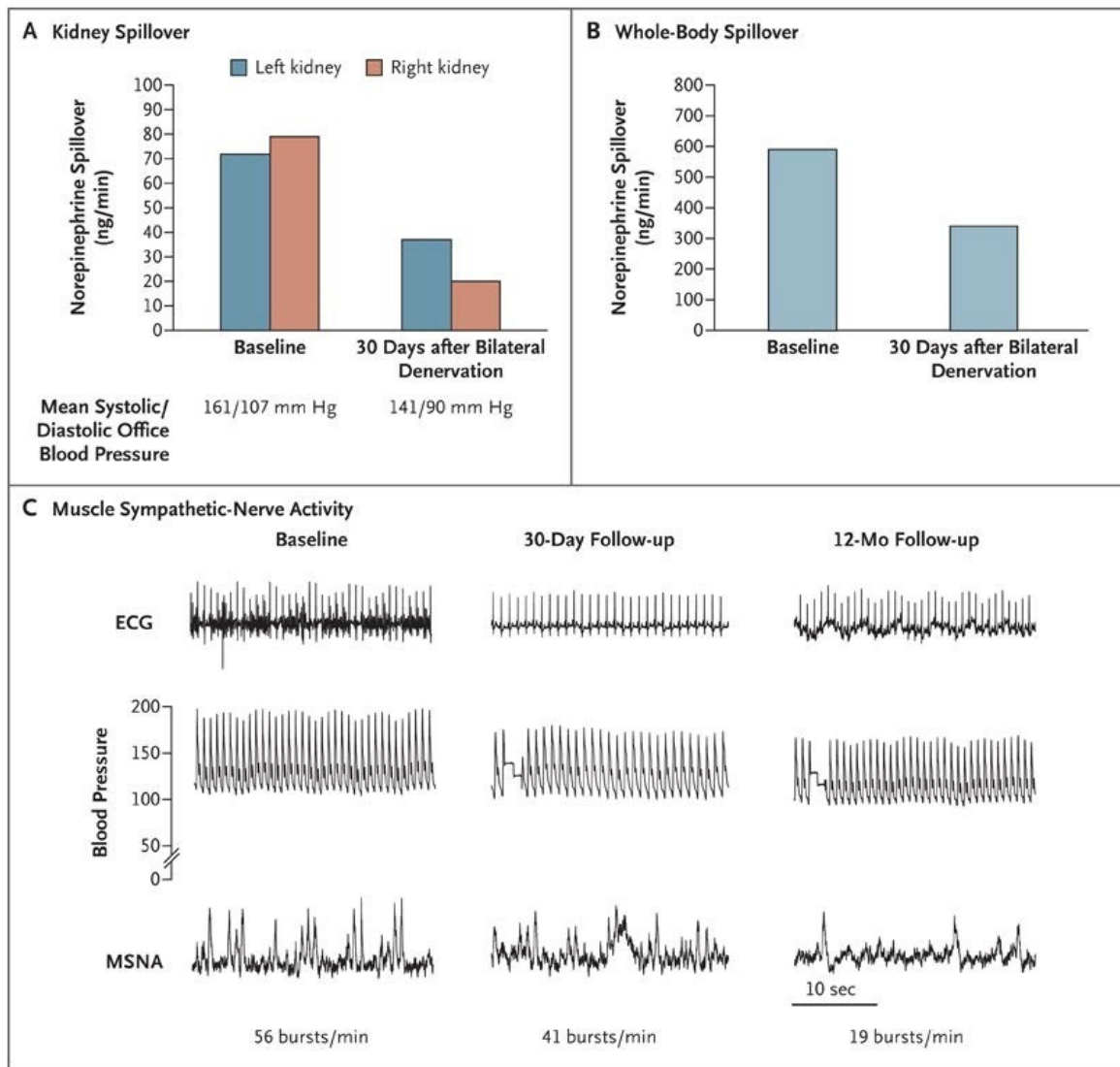
Medtronic

Placement of Renal RF Catheter



From Krum H, et al. *Circulation*. 2011;123;209-215.
Republished with permission.

Renal Sympathetic-Nerve Ablation for Uncontrolled Hypertension



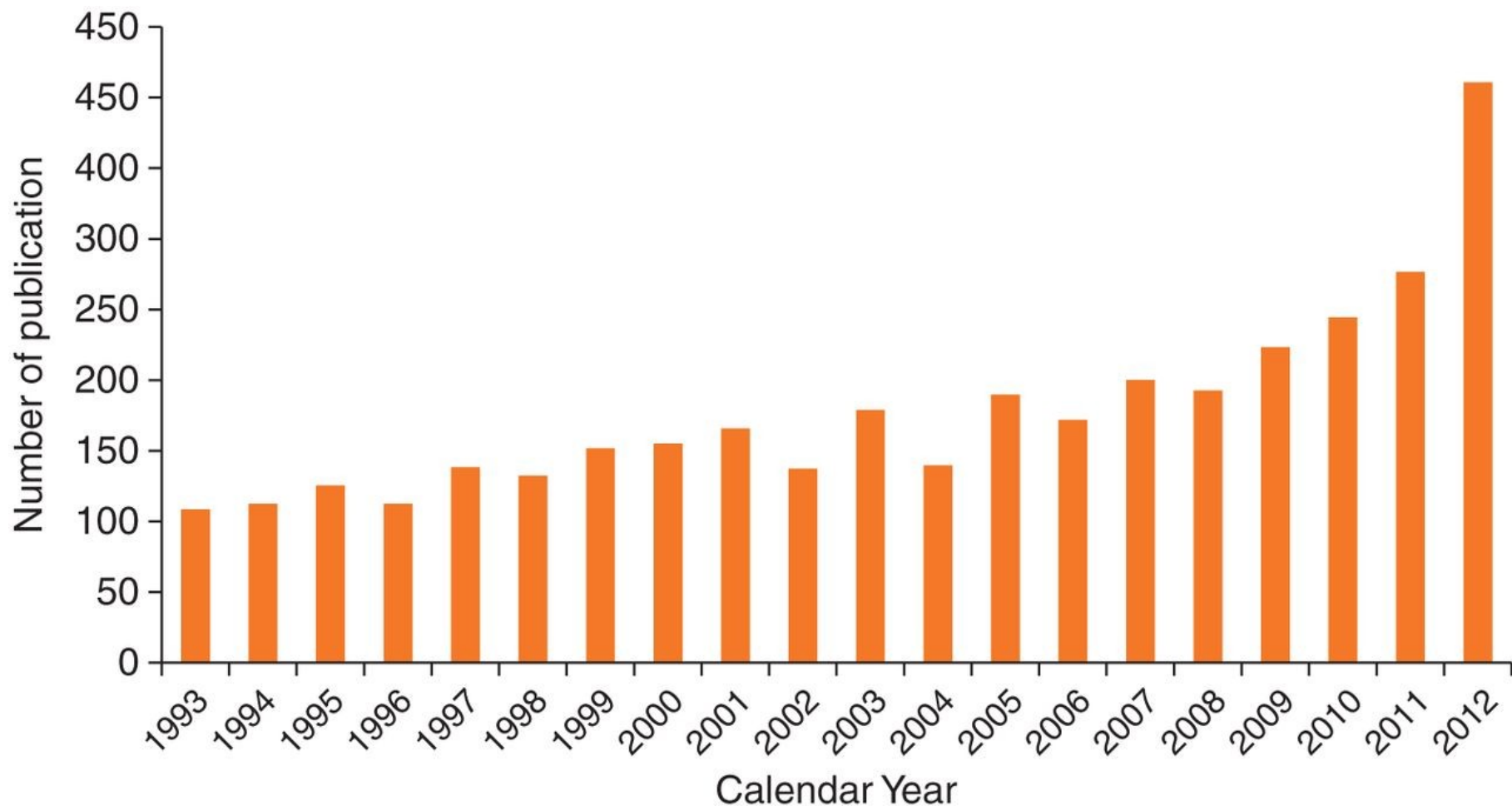
- **Първата описана ренална денервация**
- **Резистентна хипертония**
- **7 медикамента**
- **AH 161/107 -> 127/81 mm Hg**

Schlaich MP et al. *N Engl J Med* 2009; 361: 932 - 934.



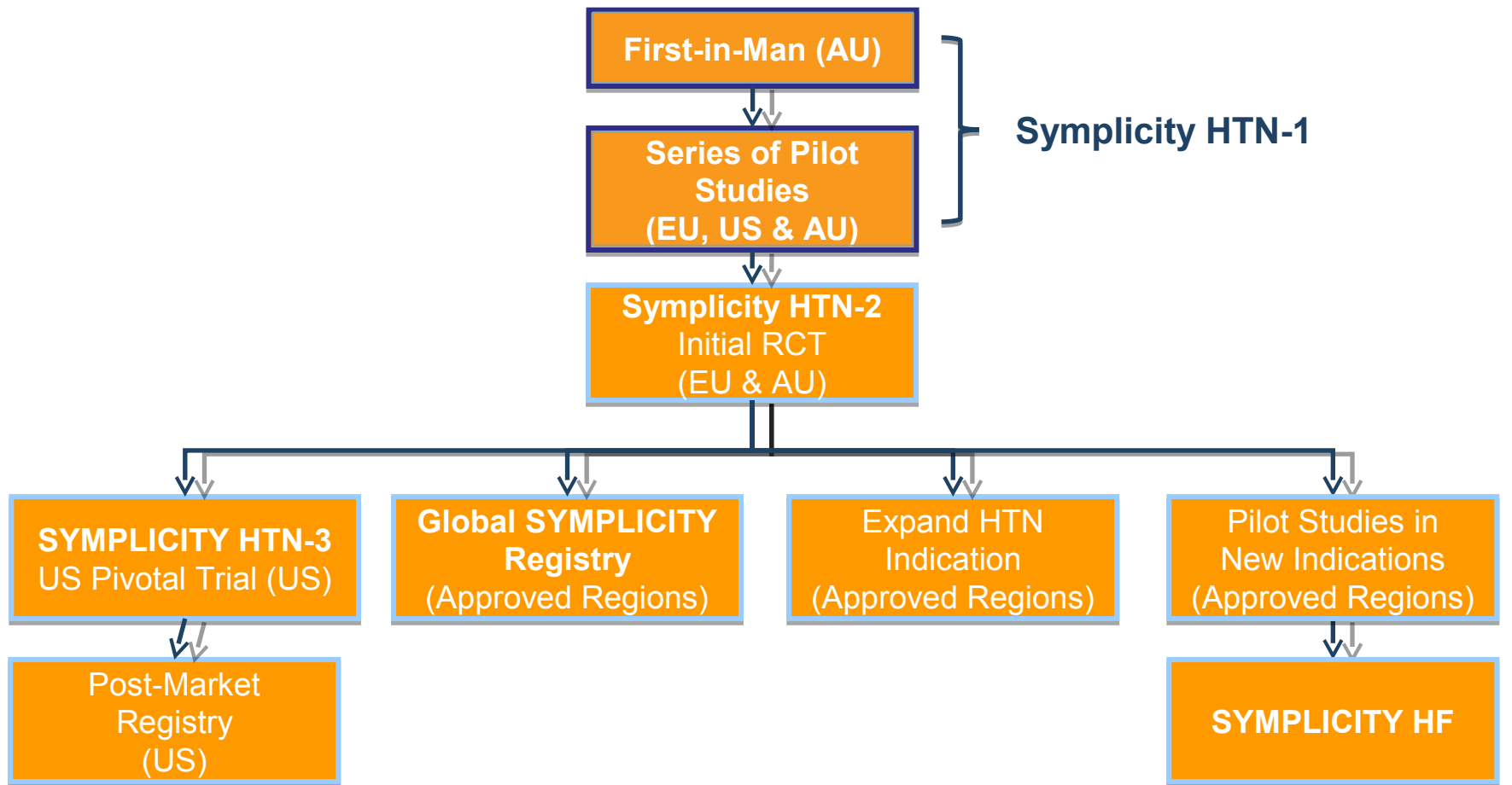
The NEW ENGLAND
JOURNAL of MEDICINE

Увеличаване съобщенията в пресата за резистентна хипертония



Messerli F H , and Bangalore S Eur Heart J 2013;
eurheartj.eht028

SYMPPLICITY – серији от КЛИНИЧНИ ИЗПИТВАНИЈА



SYMPPLICITY HTN-1

THE LANCET Hypertension

Volume 373 · Number 9671 · Pages 1223-1310 · April 11-17, 2009

www.thelancet.com

Celebrating 30 Years: 1979 to 2009

JOURNAL OF THE AMERICAN HEART ASSOCIATION

Catheter-based renal sympathetic denervation for resistant hypertension: a multicentre safety and proof-of-principle cohort study

Henry Krum, Markus Schlaich, Rob Whitbourn, Paul A Sobotka, Jerzy Sadowski, Krzysztof Bartus, Boguslaw Kapelak, Anthony Walton, Horst Sievert, Suku Thambar, William T Abraham, Murray Esler

Lancet. 2009; 373: 1275 – 1281

Catheter-Based Renal Sympathetic Denervation for Resistant Hypertension
Durability of Blood Pressure Reduction Out to 24 Months

Symplcity HTN-1 Investigators*

Hypertension. 2011; 57: 911 - 917.

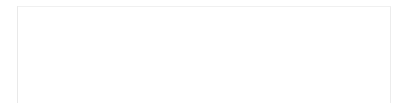
Първоначална кохорта, докладвана в *Lancet* 2009 г:

- За първи път при хора; нерандомизирано проучване
- 45 пациента с резистентна на лечение хипертония (CAH ≥ 160 mmHg на ≥ 3 антихипертензивни медикамента, включително и диуретик; eGFR ≥ 45 mL/min)
- 12 месеца

Разширена кохорта* – Symplcity HTN-1:

- 153 пациента
- 36 месечно проследяване

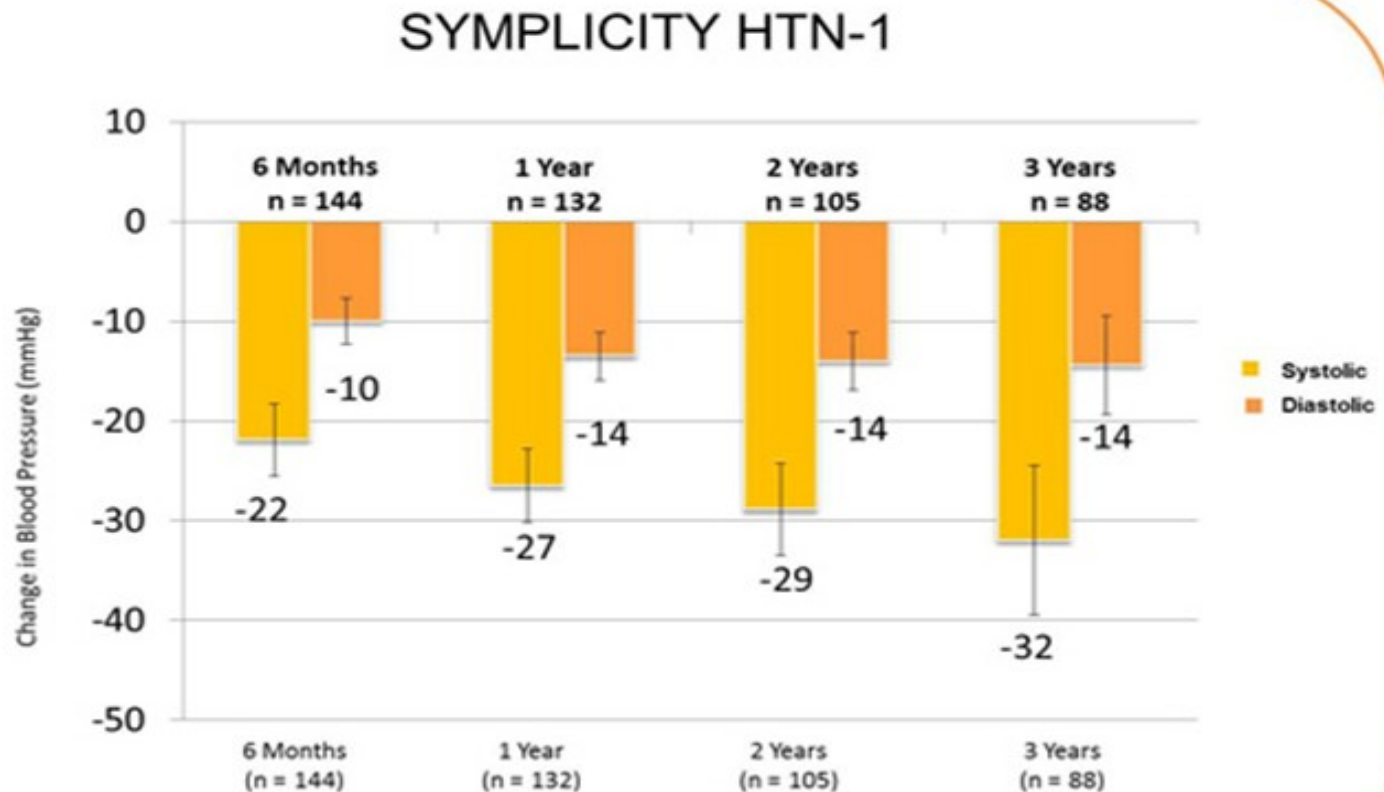
*Expanded results presented at the *American College of Cardiology Annual Meeting* 2012 (Krum, H.)



Catheter-Based Renal Sympathetic Denervation for Resistant Hypertension: Durability of Blood Pressure Reduction Out to 24 Months

Symlicity HTN-1 Investigators

Hypertension. 2011;57:911-917



$p < 0.01$ for Δ from baseline for all time points.
Data is reported only on the patients available at each time point.

SYMPPLICITY HTN-2



Renal Sympathetic Denervation for Treatment of Drug-Resistant Hypertension: One-Year Results From the Symplicity HTN-2 Randomized, Controlled Trial

Murray D. Esler, Henry Krum, Markus Schlaich, Roland E. Schmieder, Michael Böhm and Paul A. Sobotka

for the Symplicity HTN-2 Investigators

Circulation. 2012;126:2976-2982

- **Цел:** Да оцени ефективността на катетър базирана ренална денервация за редукция на артериалното налягане при пациенти с резистентна хипертония. Рандомизирано, проспективно, контролирано клинично изпитване.
- **Patients:** 106 пациенти рандомизирани 1:1 (ренална денервация / плацебо група без ренална денервация)
- **Клинични сайтове:** 24 центъра в Европа, Австралия и Нова Зеландия.

Renal Sympathetic Denervation for Treatment of Drug-Resistant Hypertension: One-Year Results From the Symplicity HTN-2 Randomized, Controlled Trial

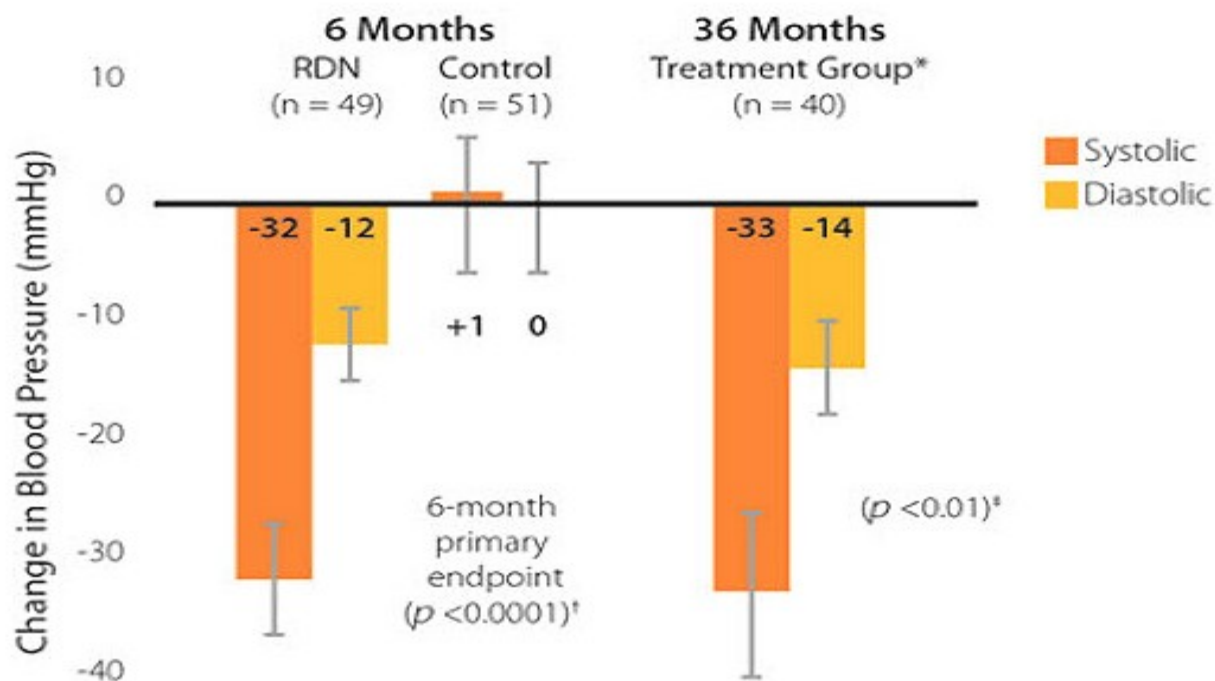
Murray D. Esler, Henry Krum, Markus Schlaich, Roland E. Schmieder, Michael Böhm and Paul A. Sobotka

for the Symplicity HTN-2 Investigators

Circulation. 2012;126:2976-2982

Symplicity HTN-2

Proven superior to medical management at 6 months



*At data lock, only RDN group was available for evaluation.

[†]Indicates between-group differences at 6 months.

[‡]Compared with baseline values.



American
Heart
Association®

Learn and Live

Radio waves to kidneys lower persistent high blood pressure

December 17, 2012

Съобщение на American Heart Association – Далас 2012 г

- *Реналната денервация е минимално инвазивна процедура, която понижава АН при пациенти без ефект от медикаментозното лечение*
- *Безопасна и ефективна една година след лечението, без да са демонстрирани увреждания на бъбречната функция*
- *Може да е алтернатива на медикаментозната терапия за артериална хипертония*

ORIGINAL ARTICLE

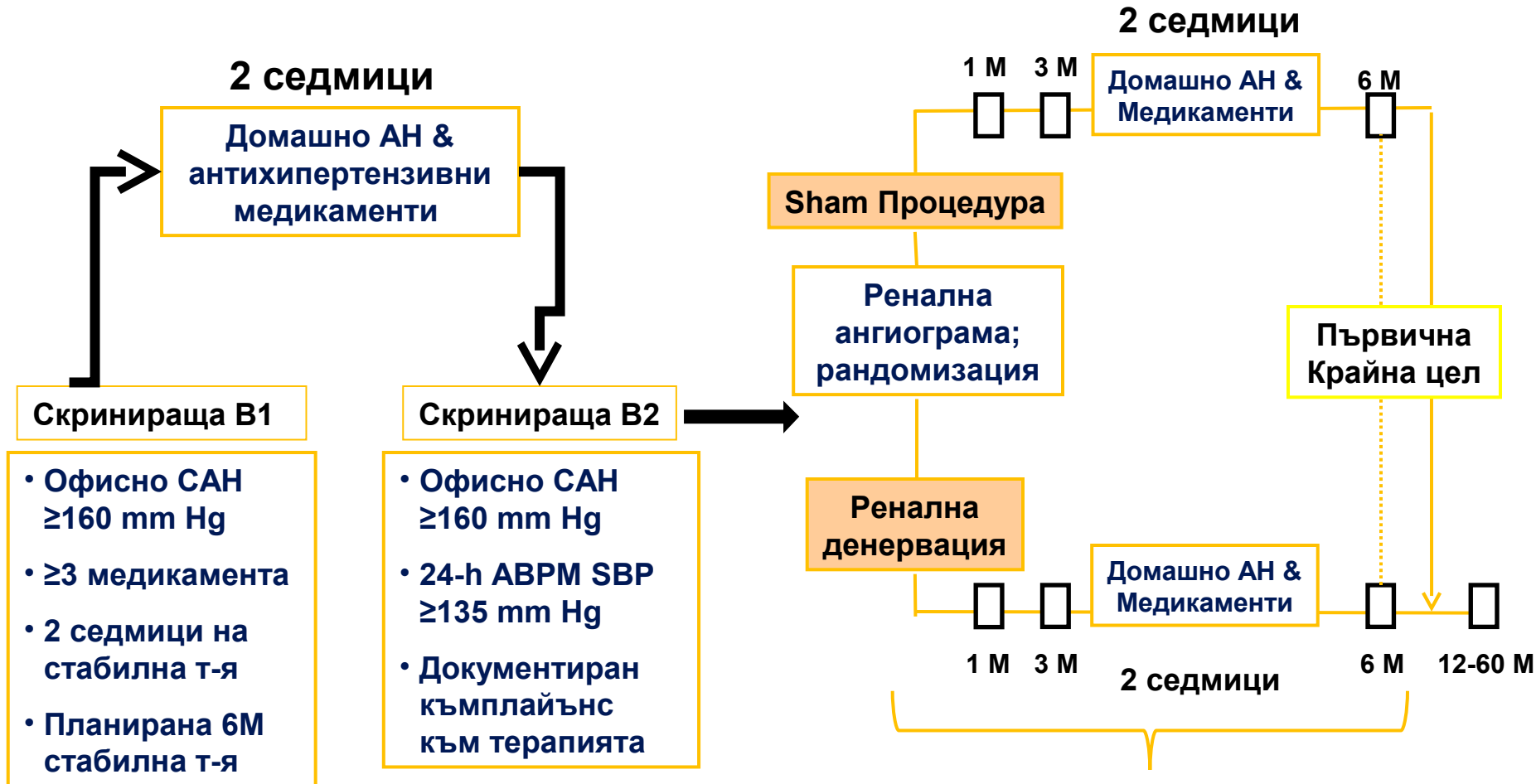
A Controlled Trial of Renal Denervation for Resistant Hypertension

Deepak L. Bhatt, M.D., M.P.H., David E. Kandzari, M.D., William W. O'Neill, M.D.,
Ralph D'Agostino, Ph.D., John M. Flack, M.D., M.P.H., Barry T. Katzen, M.D.,
Martin B. Leon, M.D., Minglei Liu, Ph.D., Laura Mauri, M.D., Manuela Negoita, M.D.,
Sidney A. Cohen, M.D., Ph.D., Suzanne Oparil, M.D., Krishna Rocha-Singh, M.D.,
Raymond R. Townsend, M.D., and George L. Bakris, M.D.,
for the SYMPPLICITY HTN-3 Investigators*

CONCLUSIONS

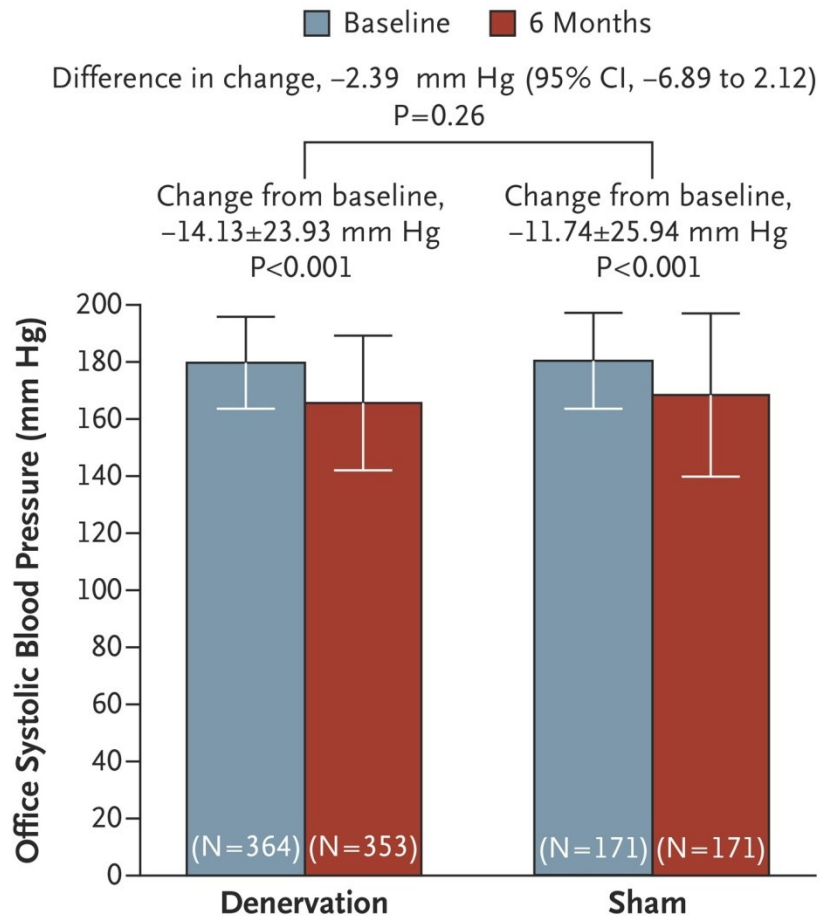
This blinded trial did not show a significant reduction of systolic blood pressure in patients with resistant hypertension 6 months after renal-artery denervation as compared with a sham control. (Funded by Medtronic; SYMPPLICITY HTN-3 ClinicalTrials.gov number, NCT01418261.)

SYMPPLICITY HTN-3

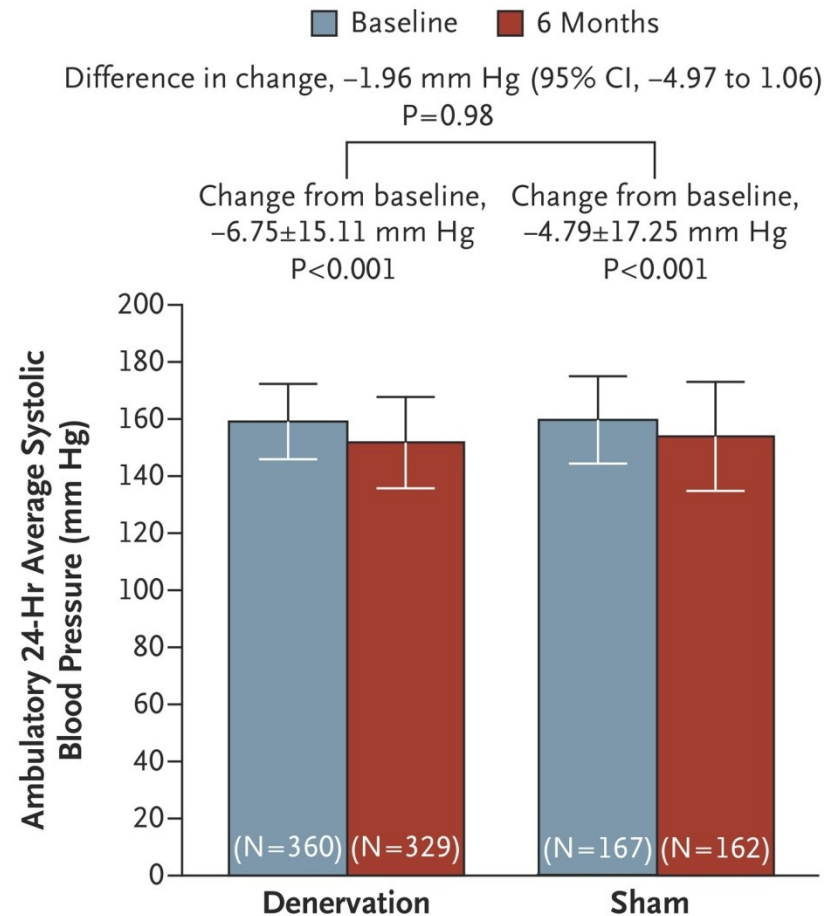


- Пациентите, персонала участващ клиничното проучване са заслепени по отношение на извършената процедура
- Стабилна антихипертензивна терапия 6 М

Primary Efficacy End Point



Secondary Efficacy End Point



Variable	SYMPPLICITY HTN-2		SYMPPLICITY HTN-3	
	Renal Denervation	No Renal Denervation	Renal Denervation	Sham Procedure
No. of patients	52	54	364	171
No. of antihypertensive medications at baseline	5.2±1.5	5.3±1.8	5.1±1.4	5.2±1.4
Aldosterone antagonist at baseline (% of patients)	17	17	22.5	28.7
Office systolic blood pressure at baseline (mm Hg)	178±18	178±16	179.7±16.1	180.2±16.8
Heart rate at baseline (beats/min)	75±15	71±15	NR	NR
Change in office systolic blood pressure at 6 mo (mm Hg)				
Absolute change	-32±23	1±21	-14.1±23.9	-11.7±25.9
Change relative to control group	-33		-2.4	
Change in home systolic blood pressure at 6 mo (mm Hg)				
Absolute change†	-20±17	2±21	-7.4	-6.0
Change relative to control group	-22		-1.3	
Change in 24-hr ambulatory systolic blood pressure at 6 mo (mm Hg)				
Absolute change‡	-11±15	-3±19	-6.8±15.1	-4.8±17.2
Change relative to control group	-8		-1.96	
Change in antihypertensive medication (% of patients)				
Decrease in dose or no. of medications	20	6	NR	NR
Increase in dose or no. of medications	8	12	NR	NR

ACC: SYMPLICITY Failure -- No Surprises

Published: Mar 29, 2014 | Updated: Mar 30, 2014

"These results underscore the importance of blinding and sham controls in evaluations of new devices and have ramifications that go beyond interventional cardiology," Bhatt said during his presentation.

Although the trial addressed some of the limitations of prior studies, it had some of its own shortcomings, according to Bhatt, including the fact that drug adherence was not confirmed through blood testing, the relatively short follow-up, the possible influence of operators who were inexperienced with renal denervation, and the lack of a direct measurement of whether the renal arteries were actually denervated.

"It may not be that the procedure doesn't work, but that the technique was not adequate," according to Michael Rinaldi, MD, medical director of research at Carolinas HealthCare System's Sanger Heart & Vascular Institute. "This could suggest that we need better devices, which are more complete in their denervation and in a more targeted way."

Other potential explanations for the failure to show a difference between the two groups included the placebo effect, the Hawthorne effect (where behavior -- adherence to treatment, in this case -- improves when someone is paying close attention), patient selection, the lack of experience for many of the operators, or some problem with the Symplicity device itself.

"A single trial showing negative results shouldn't end our efforts and we need to try harder to figure out which patients respond positively and which patients do not," Rinaldi said.

Despite having a front row seat for the trial's failure, Bhatt said he still remains "cautiously optimistic" about renal denervation's chances.

"I don't think the field should end," he said. "Future investigations should occur, but in a careful way. And the first step has got to be to make sure we are actually denervating on a biological level."

Adjusted Drug Treatment Is Superior to Renal Sympathetic Denervation in Patients With True Treatment-Resistant Hypertension

Fadi Elmula M. Fadi Elmula, Pavel Hoffmann, Anne C. Larstorp, Eigil Fossum, Magne Brekke, Sverre E. Kjeldsen, Eyvind Gjønness, Ulla Hjørnholm, Vibeke N. Kjær, Morten Rostrup, Ingrid Os, Aud Stenehjem, Aud Høieggren

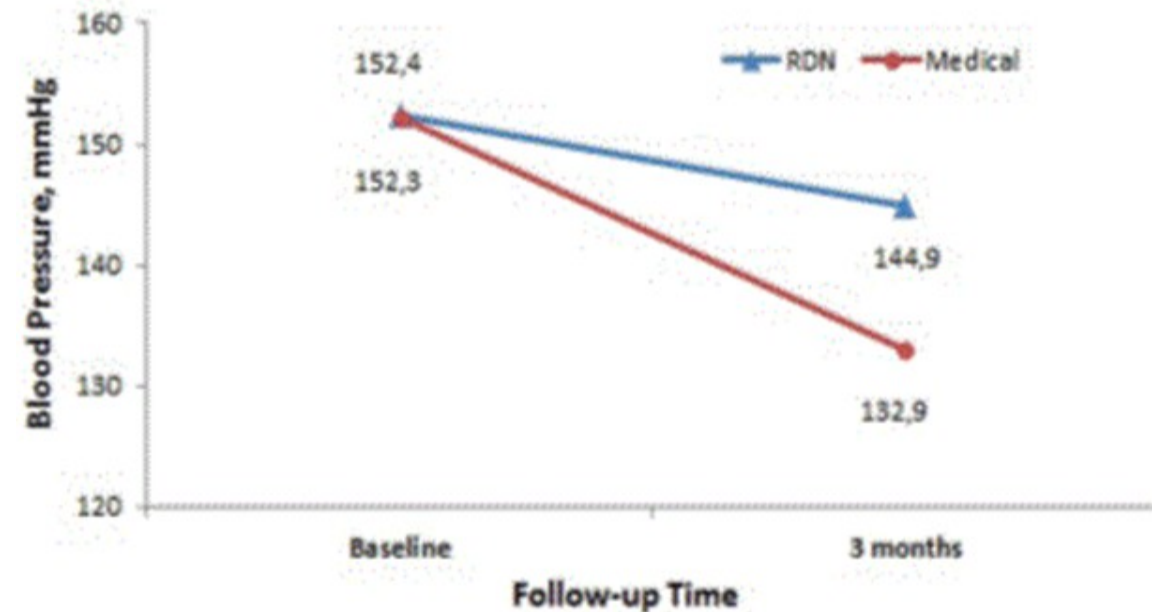
Hypertension 03 March 2014



Prevention

ADJUSTED DRUG TREATMENT IS SUPERIOR TO RENAL SYMPATHETIC DENERVATION IN PATIENTS WITH TRUE TREATMENT RESISTANT HYPERTENSION, A RANDOMIZED CLINICAL TRIAL

Mean Ambulatory Daytime Systolic Blood Pressure Changes at 3 months follow-up



Малко проучване при резистентна хипертония

- 9 пац. ренална денервация
- 10 пац. Оптимизирана т-я
- Офисно САН 160 -> 132 mm Hg ($P < 0.0005$) - медикаменти
- Офисно САН 156 -> 148 mm Hg ($P = 0.42$) - денервация

Treatment-resistant hypertension: another Cinderella story

Franz H. Messerli^{1*} and Sripal Bangalore²

If history is an indication, it appears that as long as therapies such as renal denervation prove to be efficacious and, perhaps more importantly, remain in fashion, there will be powerful motives to get Cinderella to the ball. However, the lack of a solid definition of TRH, particularly one not including a CCB, should alert us that there is blood in the slipper and serve to distinguish Cinderella from her useless and vile stepsisters.