How to manage HTA in 2014?

JM Krzesinski

ULg-CHU Liège

Topics discussed on HTA

- Recent international guidelines
- Importance of the quality of BP measurements
- Role of Salt restriction for BP and CV risk management
- Recent antihypertensive trials to test the new BP targets
- Special clinical situations:
  - BP target in CKD
  - Resistant HTA
  - Atherosclerotic RAS
  - Hemodialysis

2013 ESH/ESC Guidelines for the management of arterial hypertension

June2013

The Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC)

Journal of Hypertension 2013, 31:1281–1357

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2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults Report From the Panel Members Appointed to the Eighth Joint National Committee (JNC 8)

JAMA. doi:10.1001/jama.2013.284427
Published online December 18, 2013.

Dec 2013

Paul A. James, MD; Suzanne Oparil, MD; Barry L. Carter, PharmD; William C. Cushman, MD; Cheryl Dennison-Himmelfarb, RN, ANP, PhD; Joel Handler, MD; Daniel T. Lackland, DrPH; Michael L. LeFevre, MD, MSPH; Thomas D. MacKenzie, MD, MSPH; Olugbenga Ogedegbe, MD, MPH, MS; Sidney C. Smith Jr, MD; Laura P. Svetkey, MD, MHS; Sandra J. Taler, MD; Raymond R. Townsend, MD; Jackson T. Wright Jr, MD, PhD; Andrew S. Narva, MD; Eduardo Ortiz, MD, MPH

Clinical Practice Guidelines for the Management of Hypertension in the Community A Statement by the American Society of Hypertension and the International Society of Hypertension

Jan 2014

Journal of Hypertension 2014, 32:3–15

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Summary of 2013 ESH guidelines

- Stimulation of out of the office BP measurements
- No initiation of drug anti HTA when high normal BP
- Simplification and less strict BP targets
- Delay before starting antiHTA treatment in the very old (>80y) and higher BP target than before
- Coming back of the beta-blockers as first line treatment

2013 ESH/ESC Guidelines for the management of arterial hypertension

The Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC)

When proposing out of the office measurement?

Clinical indications for HBPM or ABPM
• Suspicion of white-coat hypertension
- Grade I hypertension in the office
- High office BP in individuals without asymptomatic organ damage and at low total CV risk
• Suspicion of masked hypertension
- High normal BP in the office
- Normal office BP in individuals with asymptomatic organ damage or at high total CV risk
• Identification of white-coat effect in hypertensive patients
• Considerable variability of office BP over the same or different visits
• Autonomic, postural, post-prandial, siesta- and drug-induced hypotension
• Elevated office BP or suspected pre-eclampsia in pregnant women
• Identification of true and false resistant hypertension
Specific indications for ABPM
• Marked discordance between office BP and home BP
• Assessment of dipping status
• Suspicion of nocturnal hypertension or absence of dipping, such as in patients with sleep apnoea, CKD, or diabetes
• Assessment of BP variability

Home BP

- WCHTA
- Masked HTA
- Pregnancy induced HTA
- Highly variable office BP
- Resistant HTA

ABPM

- Dipping
- Discordance office and home BP values
- Variability approach

Interpretation of Ambulatory Blood Pressure Profile for Risk Stratification: Keep It Simple

Gianpaolo Reboldi, Fabio Angeli and Paolo Verdecchia

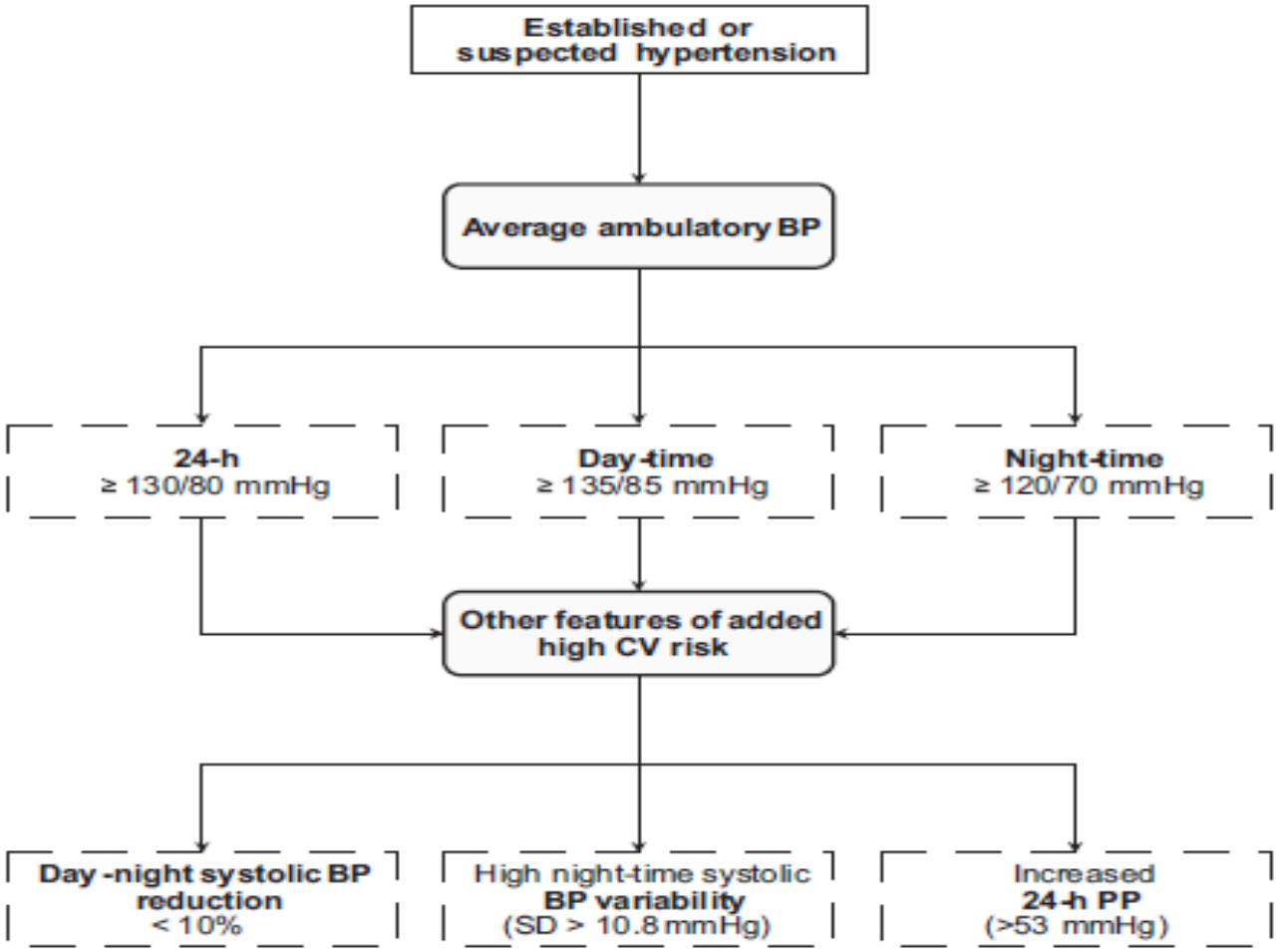

Figure. Components of ambulatory blood pressure (BP) monitoring that identify candidates for commencing antihypertensive drug treatment for increased cardiovascular (CV) risk. PP indicates pulse pressure.

2013 ESH/ESC Guidelines for the management of arterial hypertension

Other risk factors, asymptomatic organ damage or disease	Blood Pressure (mmHg)			
	High normal SBP 130–139 or DBP 85–89	Grade 1 HT SBP 140–159 or DBP 90–99	Grade 2 HT SBP 160–179 or DBP 100–109	Grade 3 HT SBP ≥180 or DBP ≥110
No other RF	• No BP intervention	• Lifestyle changes for several months • Then add BP drugs targeting <140/90	• Lifestyle changes for several weeks • Then add BP drugs targeting <140/90	• Lifestyle changes • Immediate BP drugs targeting <140/90
1–2 RF	• Lifestyle changes • No BP intervention	• Lifestyle changes for several weeks • Then add BP drugs targeting <140/90	• Lifestyle changes for several weeks • Then add BP drugs targeting <140/90	• Lifestyle changes • Immediate BP drugs targeting <140/90
≥3 RF	• Lifestyle changes • No BP intervention	• Lifestyle changes for several weeks • Then add BP drugs targeting <140/90	• Lifestyle changes • BP drugs targeting <140/90	• Lifestyle changes • Immediate BP drugs targeting <140/90
OD, CKD stage 3 or diabetes	• Lifestyle changes • No BP intervention	• Lifestyle changes • BP drugs targeting <140/90	• Lifestyle changes • BP drugs targeting <140/90	• Lifestyle changes • Immediate BP drugs targeting <140/90
Symptomatic CVD, CKD stage ≥4 or diabetes with OD/RFs	• Lifestyle changes • No BP intervention	• Lifestyle changes • BP drugs targeting <140/90	• Lifestyle changes • BP drugs targeting <140/90	• Lifestyle changes • Immediate BP drugs targeting <140/90

Diet and lifestyle in HTA

Lower Levels of Sodium Intake and Reduced Cardiovascular Risk

(*Circulation*. 2014;129:981-989.

Nancy R. Cook, ScD; Lawrence J. Appel, MD, MPH; Paul K. Whelton, MB, MD, MSc

Methods and Results—Phases 1 and 2 of the Trials of Hypertension Prevention (TOHP) collected multiple 24-hour urine specimens among prehypertensive individuals. During extended posttrial surveillance, 193 cardiovascular events or cardiovascular disease deaths occurred among 2275 participants not in a sodium reduction intervention with 10 (TOHP II) or 15 (TOHP I) years of posttrial follow-up. Median sodium excretion was 3630 mg/d, with 1.4% of the participants having intake <1500 mg/d and 10% <2300 mg/d, consistent with national levels. Compared with those with sodium excretion of 3600 to <4800 mg/d, risk for those with sodium <2300 mg/d was 32% lower after multivariable adjustment (hazard ratio, 0.68; 95% confidence interval, 0.34–1.37; *P* for trend=0.13). There was a linear 17% increase in risk per 1000 mg/d increase in sodium (*P*=0.05). Spline curves supported a linear association of sodium with cardiovascular events, which continued to decrease from 3600 to 2300 and 1500 mg/d, although the data were sparse at the lowest levels.

Lower Levels of Sodium Intake and Reduced Cardiovascular Risk

(*Circulation*. 2014;129:981-989.

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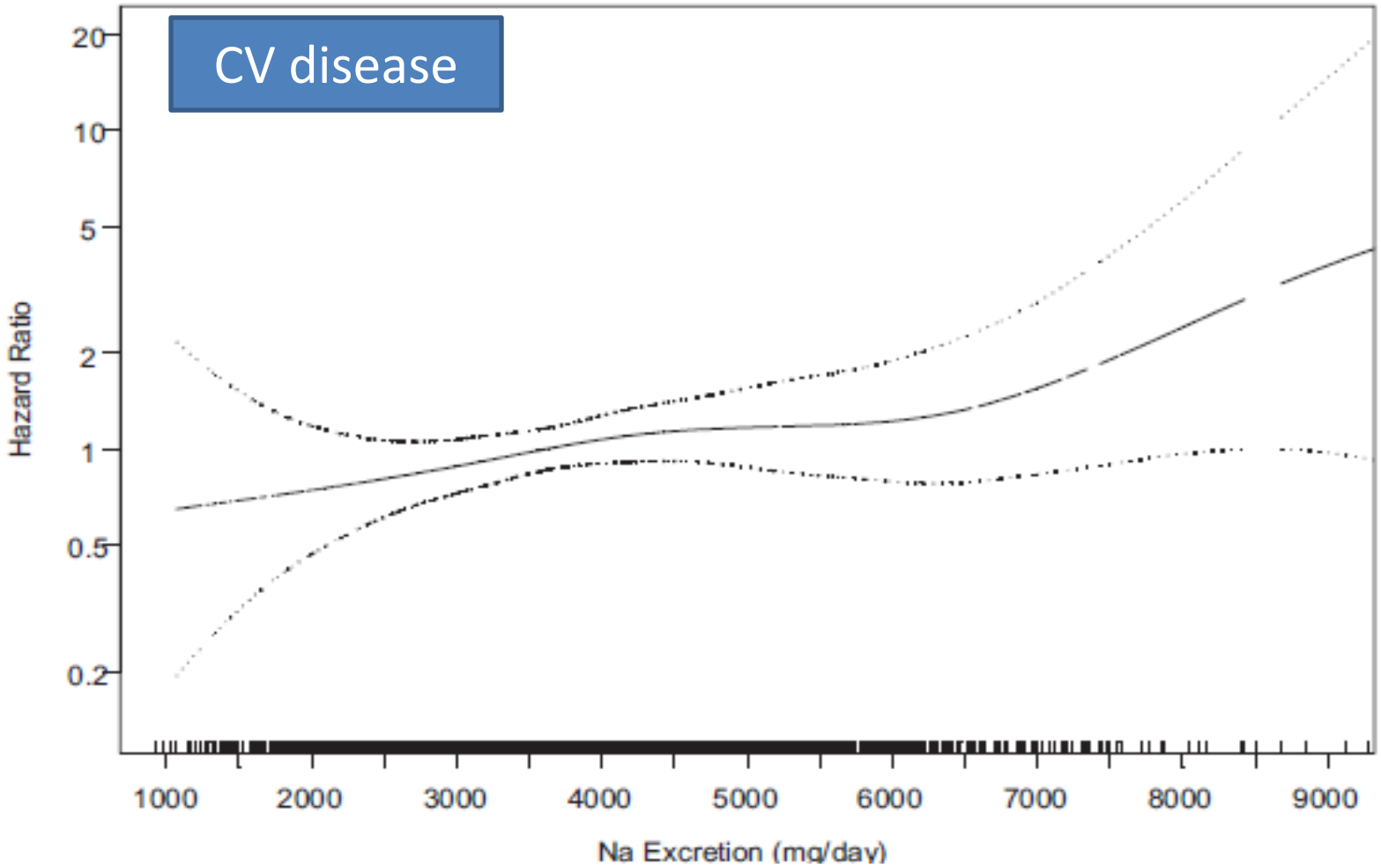


Global Sodium Consumption and Death from Cardiovascular Causes

Dariush Mozaffarian, M.D., Dr.P.H., Saman Fahimi, M.D., Gitanjali M. Singh, Ph.D., Renata Micha, R.D., Ph.D., Shahab Khatibzadeh, M.D., M.P.H., Rebecca E. Engell, B.A., Stephen Lim, Ph.D., Goodarz Danaei, Ph.D., Majid Ezzati, Ph.D., and John Powles, M.B., B.S., for the Global Burden of Diseases Nutrition and Chronic Diseases Expert Group (NUTRICODE)

N Engl J Med 2014;371:624-34

METHODS

We collected data from surveys on sodium intake as determined by urinary excretion and diet in persons from 66 countries (accounting for 74.1% of adults throughout the world), and we used these data to quantify the global consumption of sodium according to age, sex, and country. The effects of sodium on blood pressure, according to age, race, and the presence or absence of hypertension, were calculated from data in a new meta-analysis of 107 randomized interventions, and the effects of blood pressure on cardiovascular mortality, according to age, were calculated from a meta-analysis of cohorts. Cause-specific mortality was derived from the Global Burden of Disease Study 2010. Using comparative risk assessment, we estimated the cardiovascular effects of current sodium intake, as compared with a

In 2010, the estimated mean level of global sodium consumption was 3.95 g per day, and regional mean levels ranged from 2.18 to 5.51 g per day. Globally, 1.65 million annual deaths from cardiovascular causes (95% uncertainty interval [confidence interval], 1.10 million to 2.22 million) were attributed to sodium intake above the reference level; 61.9% of these deaths occurred in men and 38.1% occurred in women. These deaths accounted for nearly 1 of every 10 deaths from cardiovascular causes (9.5%). Four of every 5 deaths (84.3%) occurred in low- and middle-income countries, and 2 of every 5 deaths (40.4%) were premature (before 70 years of age). The rate of death from cardiovascular causes associated with sodium intake above the reference level was highest in the country of Georgia and lowest in Kenya.

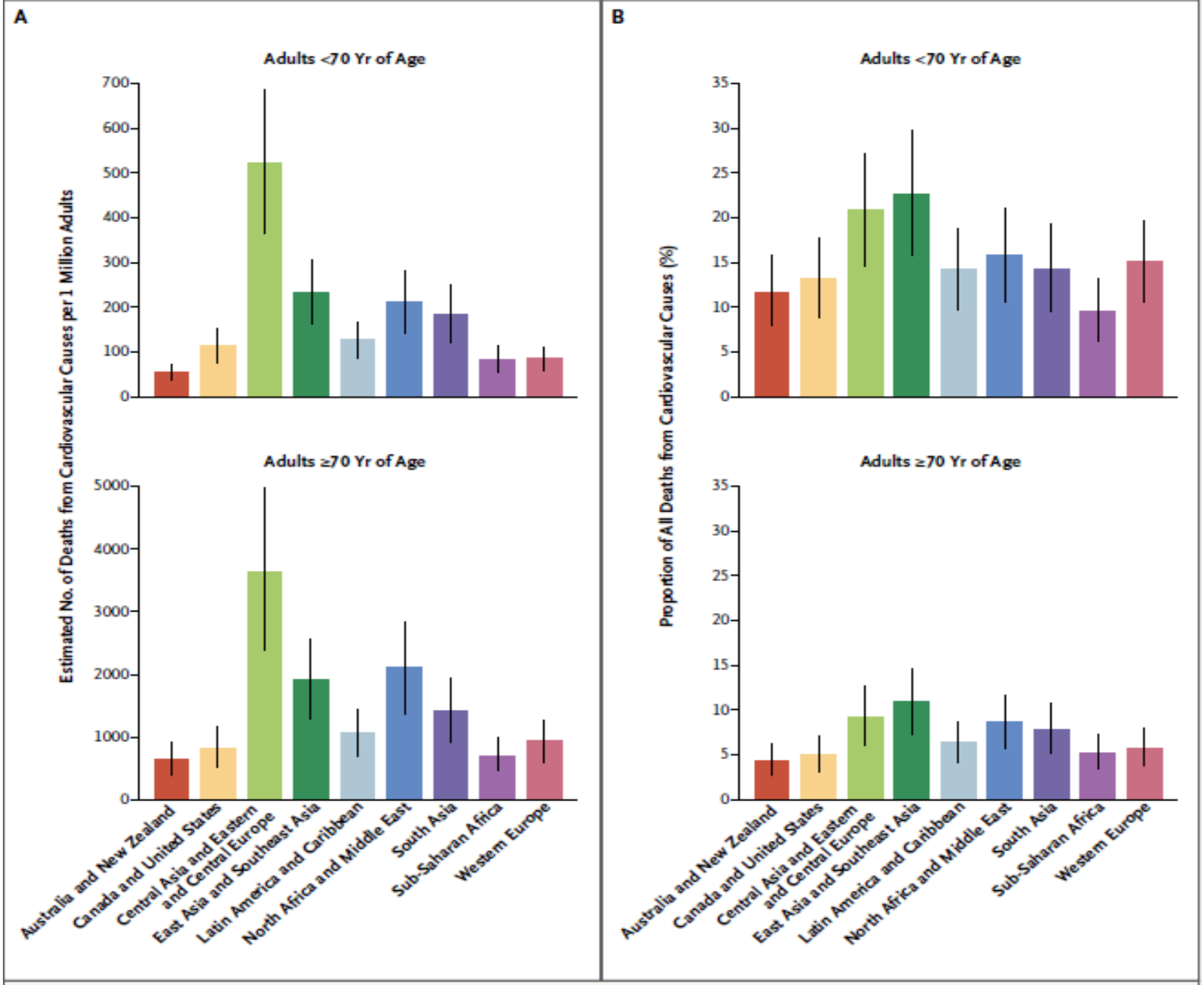
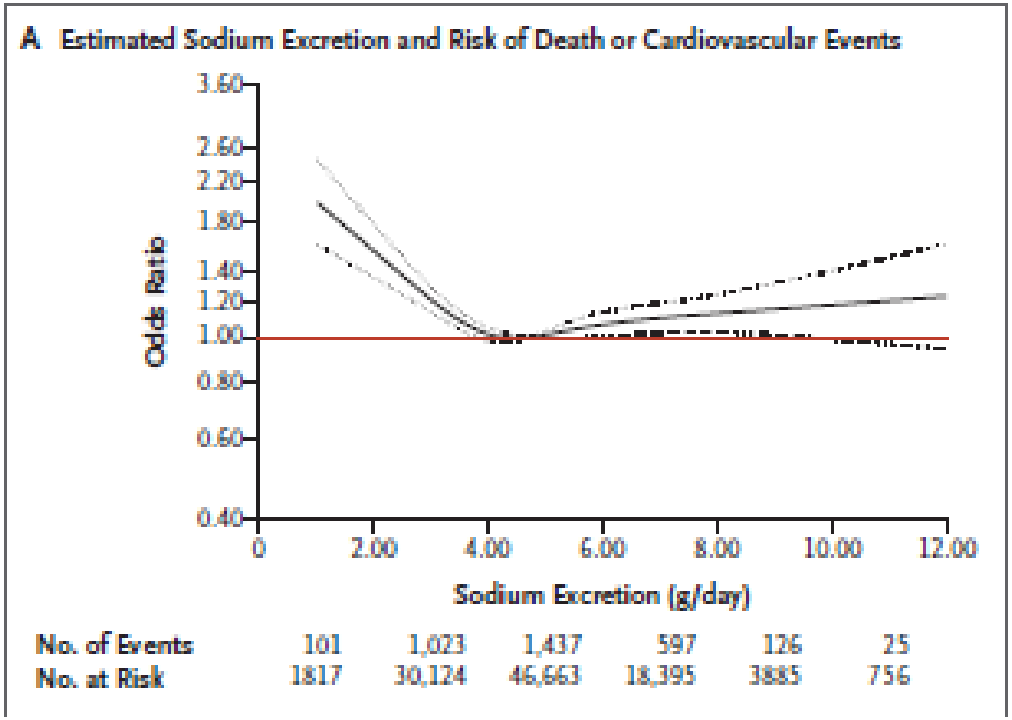


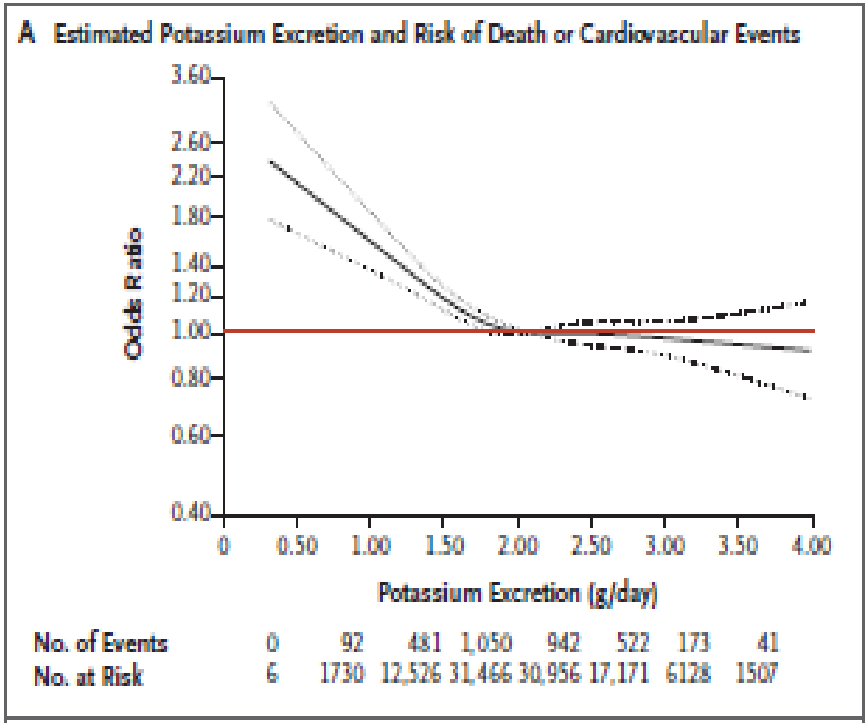
Figure 2. Cardiovascular Mortality Attributed to Sodium Consumption of More than 2.0 g per Day in 2010, According to Age and Region.

Urinary Sodium and Potassium Excretion, Mortality, and Cardiovascular Events

Martin O'Donnell, M.B., Ph.D., Andrew Mente, Ph.D., Sumathy Rangarajan, M.Sc., Matthew J. McQueen, M.B., Ph.D., Xingyu Wang, Ph.D., Lisheng Liu, M.D., Hou Yan, Ph.D., Shun Fu Lee, Ph.D., Prem Mony, M.D., Anitha Devanath, M.D., Annika Rosengren, M.D., Patricio Lopez-Jaramillo, M.D., Ph.D., Rafael Diaz, M.D., Alvaro Avezum, M.D., Ph.D., Fernando Lanas, M.D., Khalid Yusoff, M.B., B.S., Romaina Iqbal, Ph.D., Rafal Ilow, Ph.D., Noushin Mohammadifard, M.Sc., Sadi Gulec, M.D., Afzal Hussein Yusufali, M.D., Lanthe Kruger, Ph.D., Rita Yusuf, Ph.D., Jephat Chifamba, M.Phil., Conrad Kabali, Ph.D., Gilles Dagenais, M.D., Scott A. Lear, Ph.D., Koon Teo, M.B., Ph.D., and Salim Yusuf, D.Phil., for the PURE Investigators*

N Engl J Med 2014;371:612-23.





The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 AUGUST 14, 2014 VOL. 371 NO. 7

Association of Urinary Sodium and Potassium Excretion with Blood Pressure

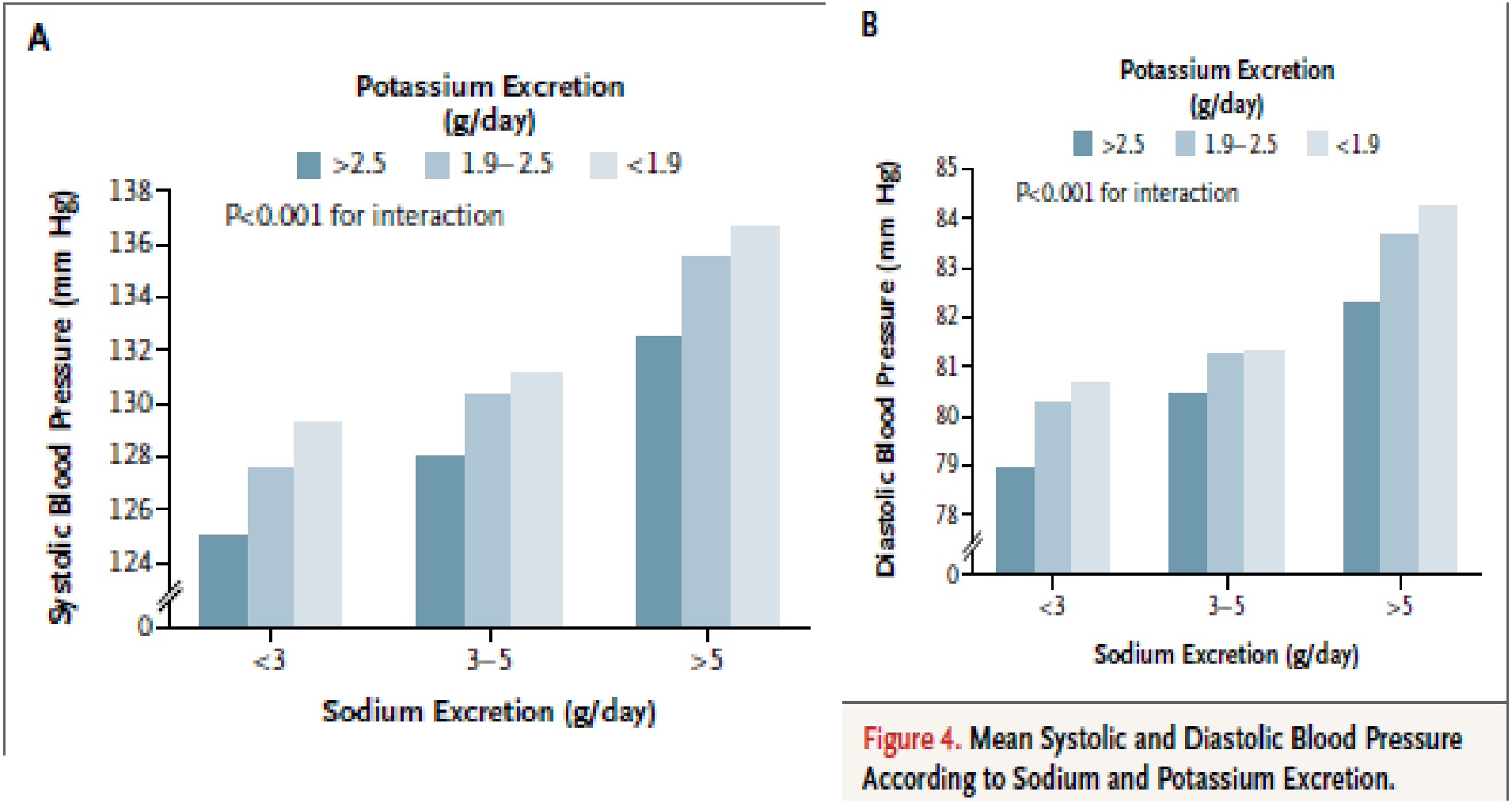


Figure 4. Mean Systolic and Diastolic Blood Pressure According to Sodium and Potassium Excretion.

When starting the treatment in HTA? ESH guidelines 2013

Recommendations	Class[a]	Level
Prompt initiation of drug treatment is recommended in individuals with grade 2 and 3 hypertension with any level of CV risk, a few weeks after or simultaneously with initiation of lifestyle changes.	I	A
Lowering BP with drugs is also recommended when total CV risk is high because of OD, diabetes, CVD or CKD, even when hypertension is in the grade 1 range.	I	B
Initiation of antihypertensive drug treatment should also be considered in grade 1 hypertensive patients at low to moderate risk, when BP is within this range at several repeated visits or elevated by ambulatory BP criteria, and remains within this range despite a reasonable period of time with lifestyle measures.	IIa	B
In elderly hypertensive patients drug treatment is recommended when SBP is ≥160 mmHg.	I	A

ESH–ESC and JNC 7 Summary: Target BP Goals (2003 and 2007)

Type of hypertension	BP goal (mmHg)
Uncomplicated	<140/90
Complicated	
Diabetes mellitus	<130/80
Kidney disease	<130/80
Other high risk (stroke, myocardial infarction)	<130/80

Task Force of ESH–ESC. J Hypertens 2007;25:1105–87
Chobanian et al. JAMA 2003;289:2560–72

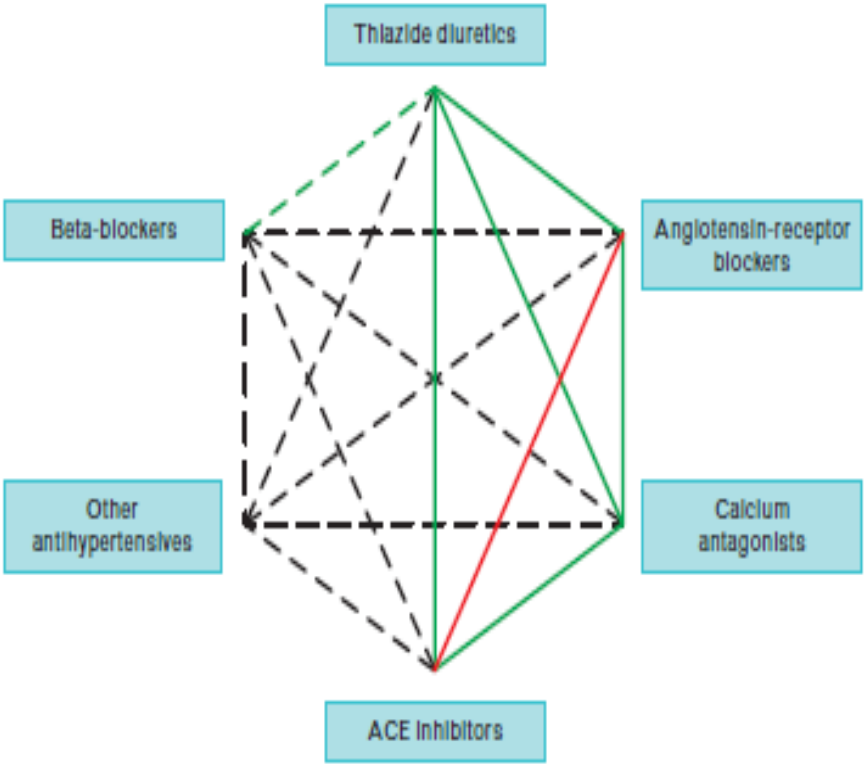
New BP targets

- **SBP < 140/90 mmHg** in all adults < 80 ans (with or without CV complications)
- In people **older than 80 ans** and in good health: start antiHTA drugs when SBP> 160 mmHg with a BP target between 140 and 150 mmHg.
- In **Diabetes**, target <140/85 mmHg
- In **CKD**, target <140/90 mmHg except when proteinuria (130/90 mmHg)

2013 ESH/ESC Guidelines for the management of arterial hypertension

Treatment strategies and choice of drugs

Recommendations	Class[a]	Level[b]
Diuretics (thiazides, chlorthalidone and indapamide), beta-blockers, calcium antagonists, ACE inhibitors, and angiotensin receptor blockers are all suitable and recommended for the initiation and maintenance of antihypertensive treatment, either as monotherapy or in some combinations with each other.	I	A



Clinical implications

- Systolic and Diastolic BP have different influences on the CV system
- HTA carries a substantial lifetime burden despite treatment, with a 5y earlier development of CV than those with normal BP
- There was no J-shaped increased risk for CV disease at lower BP.

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Impact of Achieved Blood Pressures on Mortality Risk and End-Stage Renal Disease Among a Large, Diverse Hypertension Population

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ABSTRACT

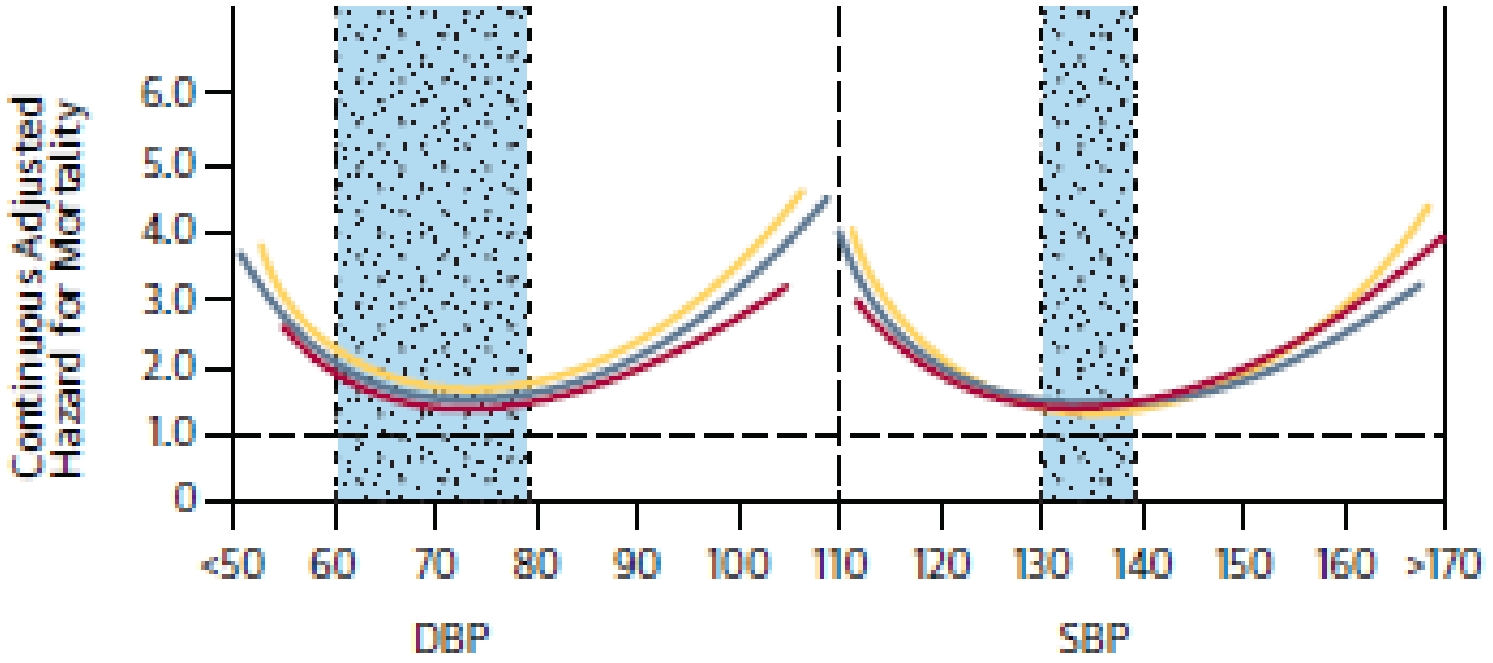
BACKGROUND Medical data or clinical guidelines have not adequately addressed the ideal blood pressure (BP) treatment targets for survival and renal outcome.

OBJECTIVES This study sought to evaluate ranges of treated BP in a large hypertension population and compare risk of mortality and end-stage renal disease (ESRD).

METHODS A retrospective cohort study within the Kaiser Permanente Southern California health system was performed from January 1, 2006, to December 31, 2010. Treated hypertensive subjects ≥18 years of age were studied. Cox proportional hazards regression models were used to evaluate the risks (hazard ratios) for mortality and/or ESRD among different BP categories with and without stratification for diabetes mellitus and older age.

RESULTS Among 398,419 treated hypertensive subjects (30% with diabetes mellitus), mortality occurred in 25,182 (6.3%) and ESRD in 4,957 (1.2%). Adjusted hazard ratios (95% confidence intervals [CI]) for composite mortality/ESRD in systolic BP <110, 110 to 119, 120 to 129, 140 to 149, 150 to 159, 160 to 169, and ≥170 compared with 130 to 139 mm Hg were 4.1 (95% CI: 3.8 to 1.3), 1.8 (95% CI: 1.7 to 1.9), 1.1 (95% CI: 1.1 to 1.1), 1.4 (95% CI: 1.4 to 1.5), 2.3 (95% CI: 2.2 to 2.5), 3.3 (95% CI: 3.0 to 3.6), and 4.9 (95% CI: 4.4 to 5.5) respectively. Diastolic BP 60 to 79 mm Hg were associated with the lowest risk. The nadir systolic and diastolic BP for the lowest risk was 137 and 71 mm Hg, respectively. Stratified analyses revealed that the diabetes mellitus population had a similar hazard ratio curve but a lower nadir at 131 and 69 mm Hg but age ≥70 had a higher nadir (140 and 70 mm Hg).

CONCLUSIONS Both higher and lower treated BP compared with 130 to 139 mm Hg systolic and 60 to 79 mm Hg diastolic ranges had worsened outcomes. Our study adds to the growing uncertainty about BP treatment targets.
(J Am Coll Cardiol 2014;64:588-97)



CENTRAL ILLUSTRATION **Where Is the Ideal BP in Those Treated for Hypertension?**

Cubic spline smoothing on the basis of multivariable Cox regression analyses demonstrating mortality/end-stage renal disease hazard ratios across ranges of blood pressure (BP). Achieved systolic blood pressure (SBP) range 130 to 139 and diastolic blood pressure (DBP) range 60 to 79 mm Hg were associated with the best outcomes.

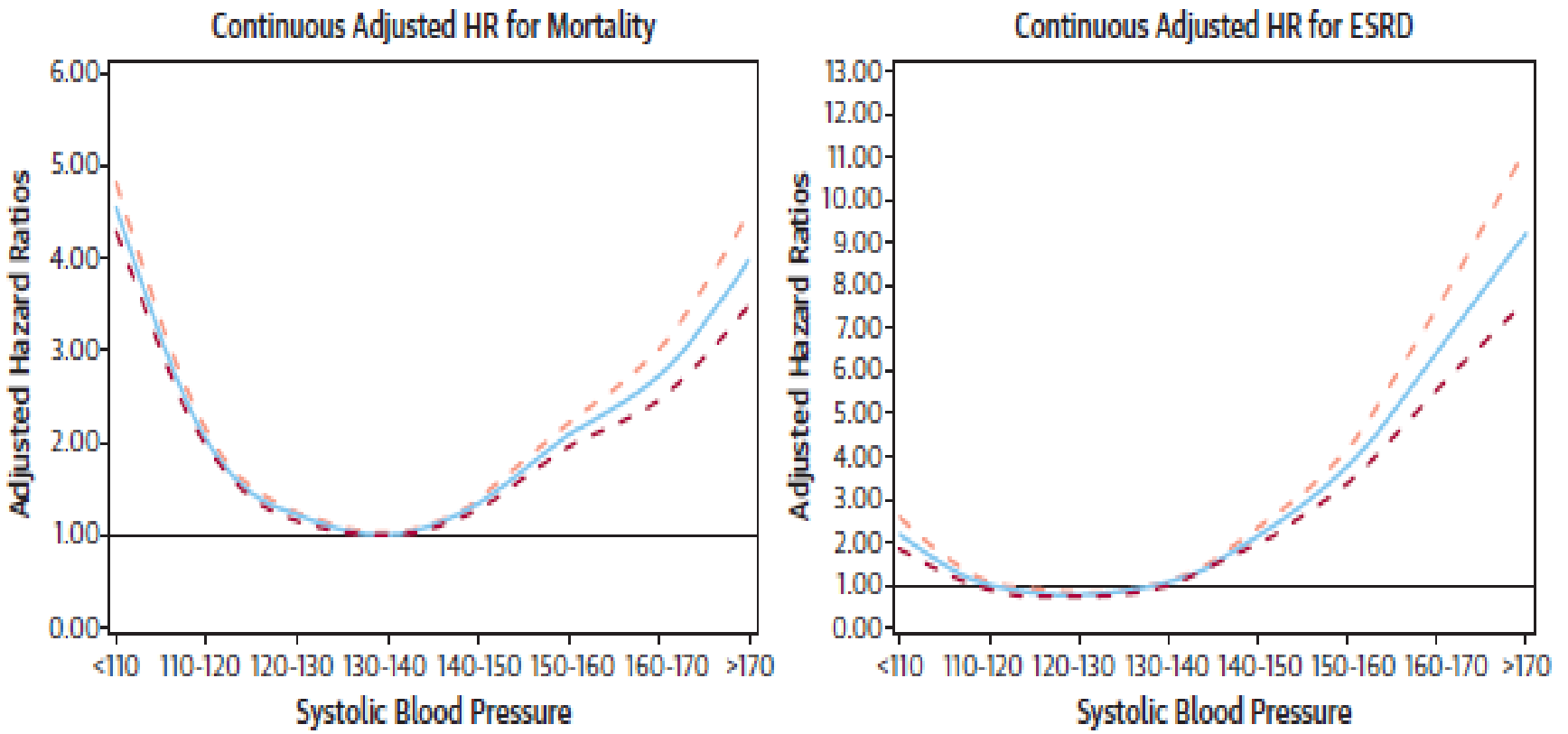


FIGURE 4 Continuous HR for Mortality and ESRD Across SBP

Blood pressure and mortality/ESRD risk

Sim et al JACC 2014

- Obervational retrospective study in treated HT
- U-shaped curve for mortality/ESRD at SBP either >139 mmHg or <130 mmHg
- Ideal BP 137/71.
- DBP <60 and >79 had similar greater risk.
- So it is recommended to adapt antiHTA drugs to reach these targets
- DM has a lower nadir for mortality/ESRD risk : 131/69 mmHg
- Age >70 had a higher nadir: 140/70 mmHg

Systolic Blood Pressure Levels Among Adults With Hypertension and Incident Cardiovascular Events

The Atherosclerosis Risk in Communities Study

OBJECTIVE To examine the risk of incident cardiovascular (CV) events among adults with HTN according to 3 SBP levels: 140 mm Hg or higher; 120 to 139 mm Hg; and a reference level of lower than 120 mm Hg.

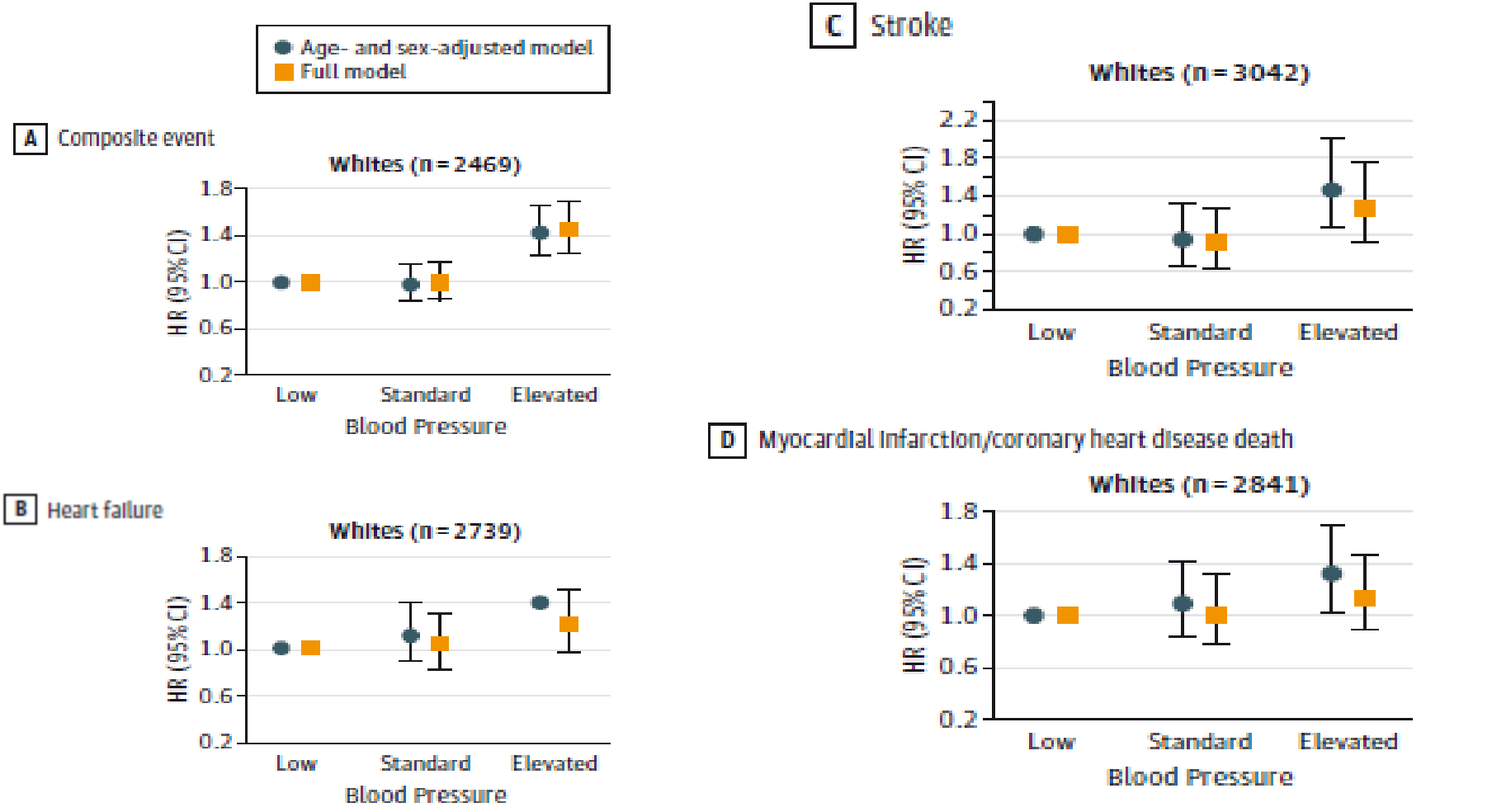
DESIGN, SETTING, AND PARTICIPANTS A total of 4480 participants with HTN but without prevalent CV disease at baseline (years 1987-1989) from the Atherosclerosis Risk in Communities Study were included. Measurements of SBP were taken at baseline and at 3 triennial visits; SBP was treated as a time-dependent variable and categorized as elevated (≥140 mm Hg), standard (120-139 mm Hg), and low (<120 mm Hg). Multivariable Cox regression models included baseline age, sex, diabetes status, BMI, high cholesterol level, smoking status, and alcohol intake.

MAIN OUTCOMES AND MEASURES Incident composite CV events (heart failure, ischemic stroke, myocardial infarction, or death related to coronary heart disease).

Characteristic	Total (n = 5466)
Sex	
Female	3054 (55.9)
Diabetes	1121 (20.8)
Cigarette use	
Current	1326 (24.3)
Former	1752 (32.1)
Alcohol use	
Current	2599 (47.9)
Former	1146 (21.1)
Antihypertensive medication use	3975 (73.0
High cholesterol	1536 (28.9)
Race	
African American	2348 (43.0)
White	3118 (57.0)
Age, mean (SD)	55.5 (5.7)
BMI, mean (SD)	29.6 (5.7)
SBP, mean (SD)	135.7 (20.7)

JAMA Intern Med. 2014;174(8):1252-1261. doi:10.1001/jamainternmed.2014.2482
Published online June 16, 2014.

The Atherosclerosis Risk in Communities Study[5] (1987-2010) stratified by composite event (heart failure, ischemic stroke, or combination measure myocardial infarction/incidence of coronary heart disease death [MI/CHD]) (A), heart failure (B), ischemic stroke (C), and MI/CHD (D). *Elevated BP* is defined as an SBP of 140 mm Hg or higher; *standard BP*, an SBP of 120 to 139 mm Hg; and *low BP*, an SBP of lower than 120 mm Hg. The vertical lines through the HRs represent 95% CIs.



JAMA Intern Med. 2014;174(8):1252-1261. doi:10.1001/jamainternmed.2014.2482
Published online June 16, 2014.

RESULTS After a median follow-up of 21.8 years, a total of 1622 incident CV events had occurred. Participants with elevated SBP developed incident CV events at a significantly higher rate than those in the low BP group (adjusted hazard ratio [HR], 1.46; 95% CI, 1.26-1.69). However, there was no difference in incident CV event-free survival among those in the standard vs low SBP group (adjusted HR, 1.00; 95% CI, 0.85-1.17). Further adjustment for BP medication use or diastolic BP did not significantly affect the results.

CONCLUSIONS AND RELEVANCE Among patients with HTN, having an elevated SBP carries the highest risk for cardiovascular events, but in this categorical analysis, once SBP was below 140 mm Hg, an SBP lower than 120 mm Hg did not appear to lessen the risk of incident CV events.

JAMA Intern Med. 2014;174(8):1252-1261. doi:10.1001/jamainternmed.2014.2482
Published online June 16, 2014.

HTA in special situations

- CKD
- Resistance
- Atherosclerotic stenosis
- Hemodialysis

Observational Modeling of Strict vs Conventional Blood Pressure Control in Patients With Chronic Kidney Disease

Csaba P. Kovesdy, MD; Jun L. Lu, MD; Miklos Z. Molnar, MD, PhD; Jennie Z. Ma, PhD; Robert B. Canada, MD; Elani Streja, PhD; Kamyar Kalantar-Zader, MD, MPH, PhD; Anthony J. Bleyer, MD, MS

JAMA Intern Med. doi:10.1001/jamainternmed.2014.3279
Published online August 4, 2014.

HTN in CKD

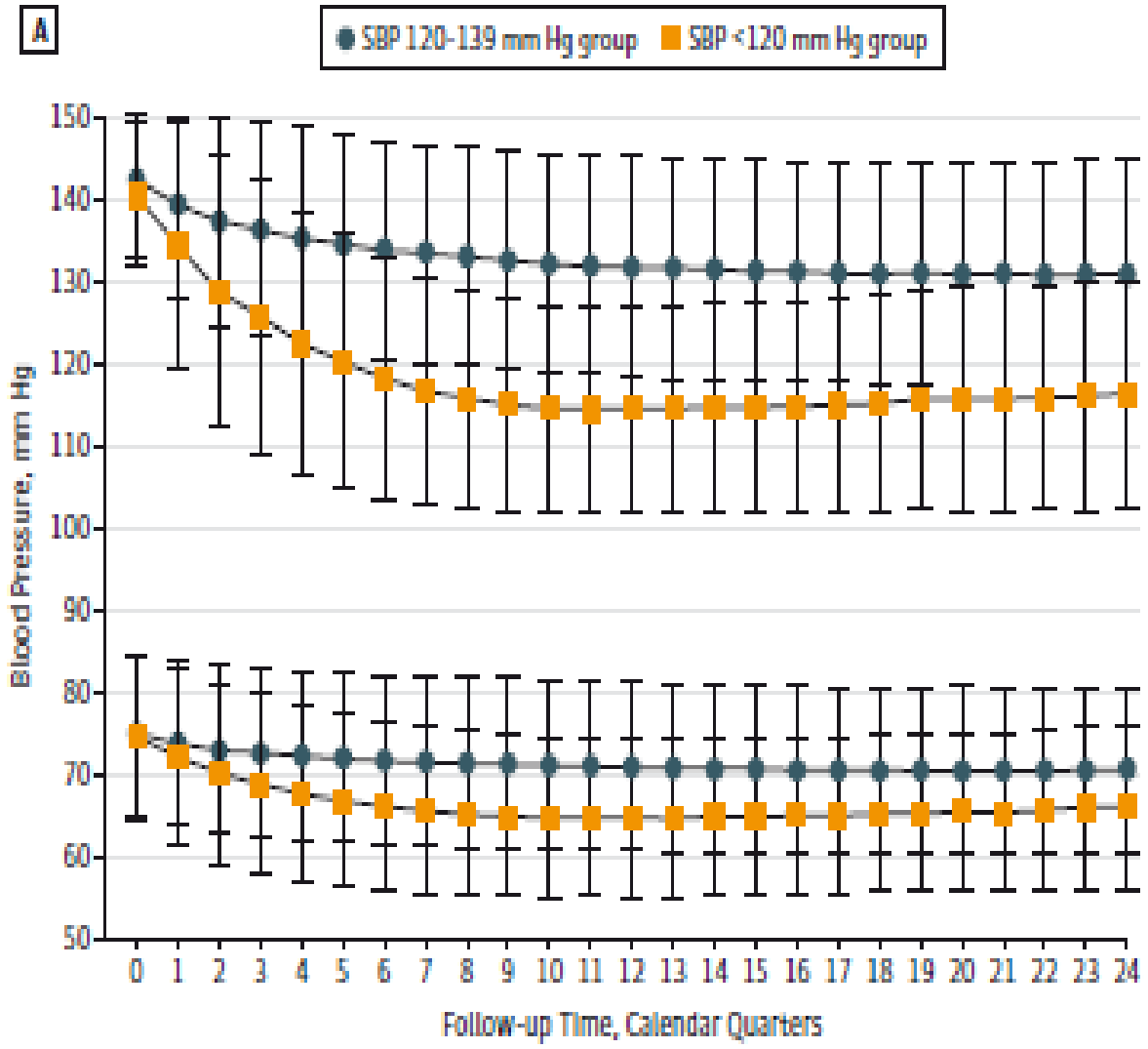
JAMA Intern Med. doi:10.1001/jamainternmed.2014.3279
Published online August 4, 2014.

. Kaplan-Meier Survival Curves of Patients With Follow-up

OBJECTIVE To compare the outcomes associated with a treated systolic blood pressure (SBP) of less than 120 mm Hg vs those associated with the currently recommended SBP of less than 140 mm Hg in a national CKD database of US veterans.

DESIGN, SETTING, AND PARTICIPANTS Historical cohort study using a nationwide cohort of US veterans with prevalent CKD, estimated glomerular filtration rate less than 60 mL/min/1.73 m^2, and uncontrolled hypertension, who then received 1 or more additional blood pressure medications with evidence of a decrease in SBP. Propensity scores were calculated to reflect each individual's probability for future SBP less than 120 vs 120 to 139 mm Hg.

Figure 2. Follow-up Systolic Blood Pressure (SBP) and Diastolic Blood Presure (DBP) in Patients With SBP Less Than 120 vs 120 to 139 mm Hg



JAMA Intern Med. doi:10.1001/jamainternmed.2014.3279
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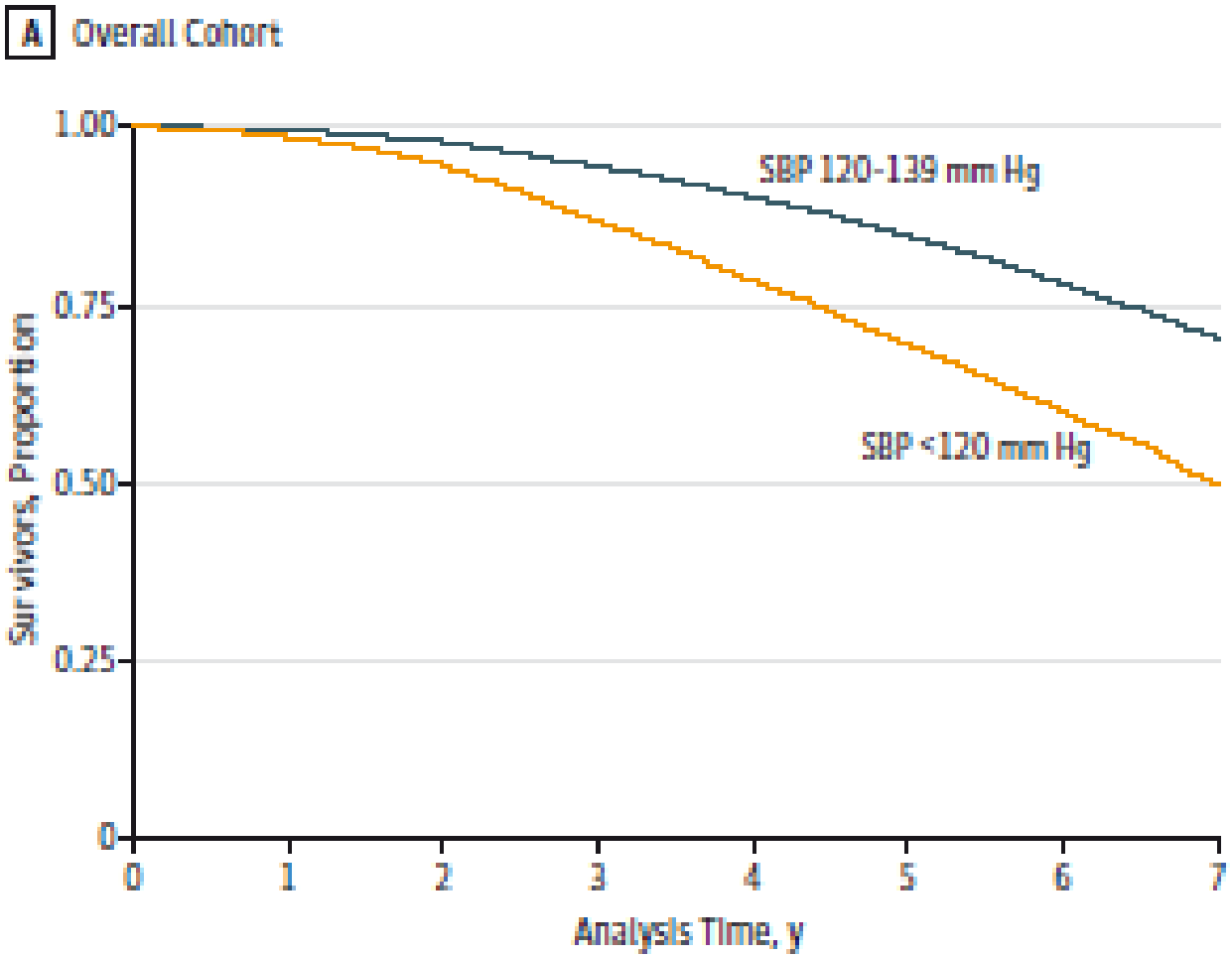
. Kaplan-Meier Survival Curves of Patients With Follow-up



JAMA Intern Med. doi:10.1001/jamainternmed.2014.3279
Published online August 4, 2014.

In summary, we have found that in a cohort of patients with CKD and uncontrolled hypertension, lowering of the SBP to less than 120 mm Hg was associated with higher all-cause mortality compared with an SBP of 120 to 139 mm Hg. Such an observational approach to estimate treatment targets for blood pressure lowering in patients with CKD could be a useful complement to clinical trials.

JAMA Intern Med. doi:10.1001/jamainternmed.2014.3279
Published online August 4, 2014.

Renal denervation in Resistant HTA ?

Refractory Hypertension

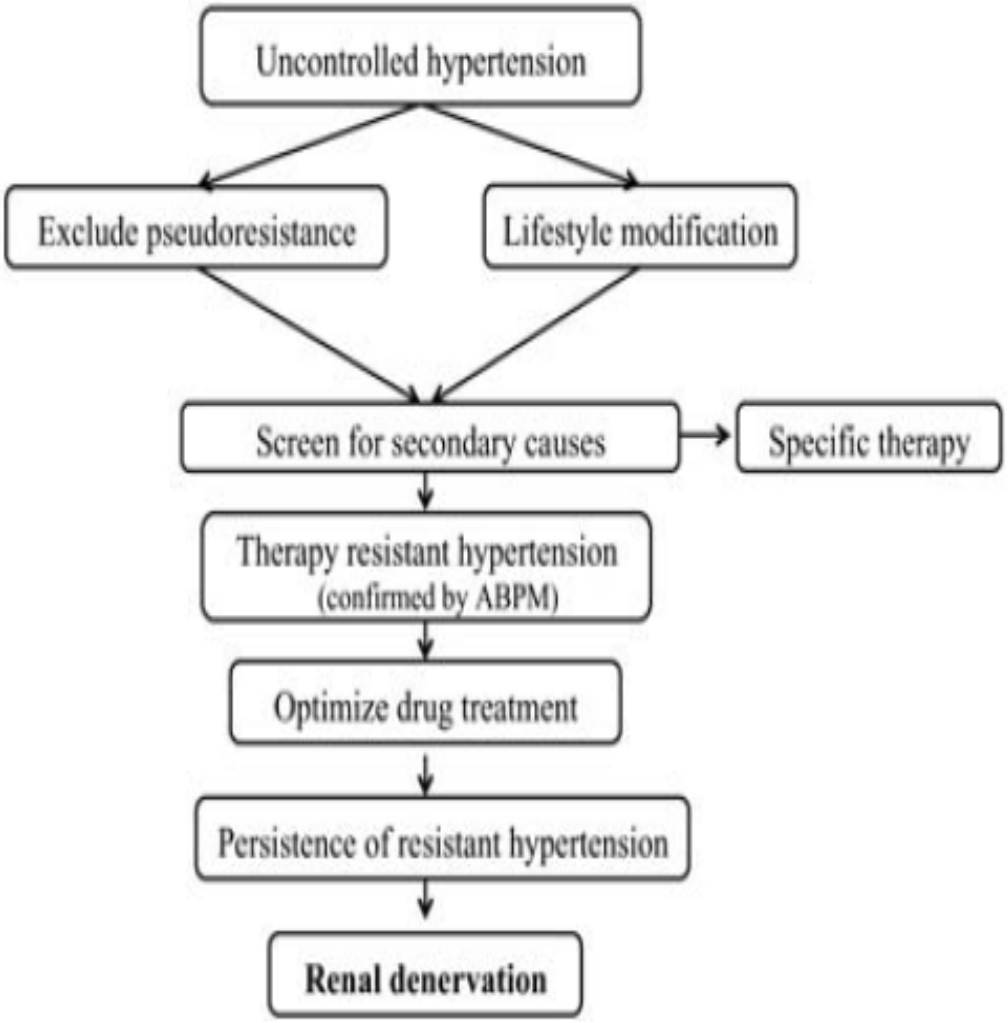
Determination of Prevalence, Risk Factors, and Comorbidities in a Large, Population-Based Cohort

David A. Calhoun, John N. Booth III, Suzanne Oparil, Marguerite R. Irvin, Daichi Shimbo, Daniel T. Lackland, George Howard, Monika M. Safford, Paul Muntner

Hypertension. 2014;63:451-458.

- Among 30000 people followed in USA, 14800 are taking antiHTA drugs
- 78 (0.5%) are refractory to 5 or more antiHTA agents
- 2066 (14%) are considered resistant (normalisation of BP with more than 3 drugs)
- Refractory people are mainly men, black, obese, diabetic, suffering from proteinuria, CKD, or having an history of CVD: so with a very high CV risk!

Treating resistant hypertension: role of renal denervation



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STATE-OF-THE-ART PAPER

International Expert Consensus Statement

Percutaneous Transluminal Renal Denervation for the Treatment of Resistant Hypertension

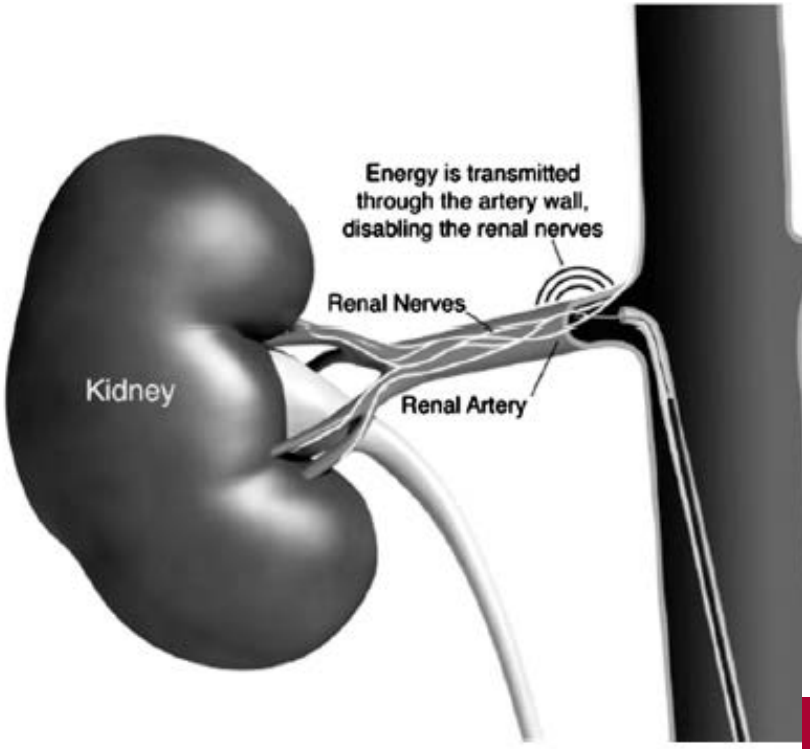


Figure 2 Schematic Illustration of the Percutaneous Catheter-Based Approach to Functionally Denervate the Human Kidney

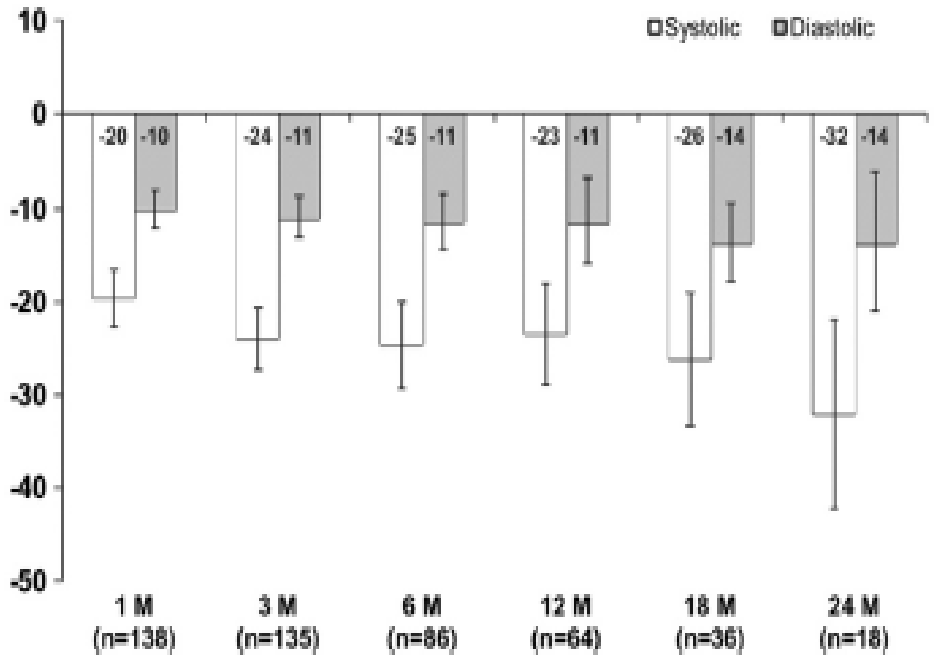
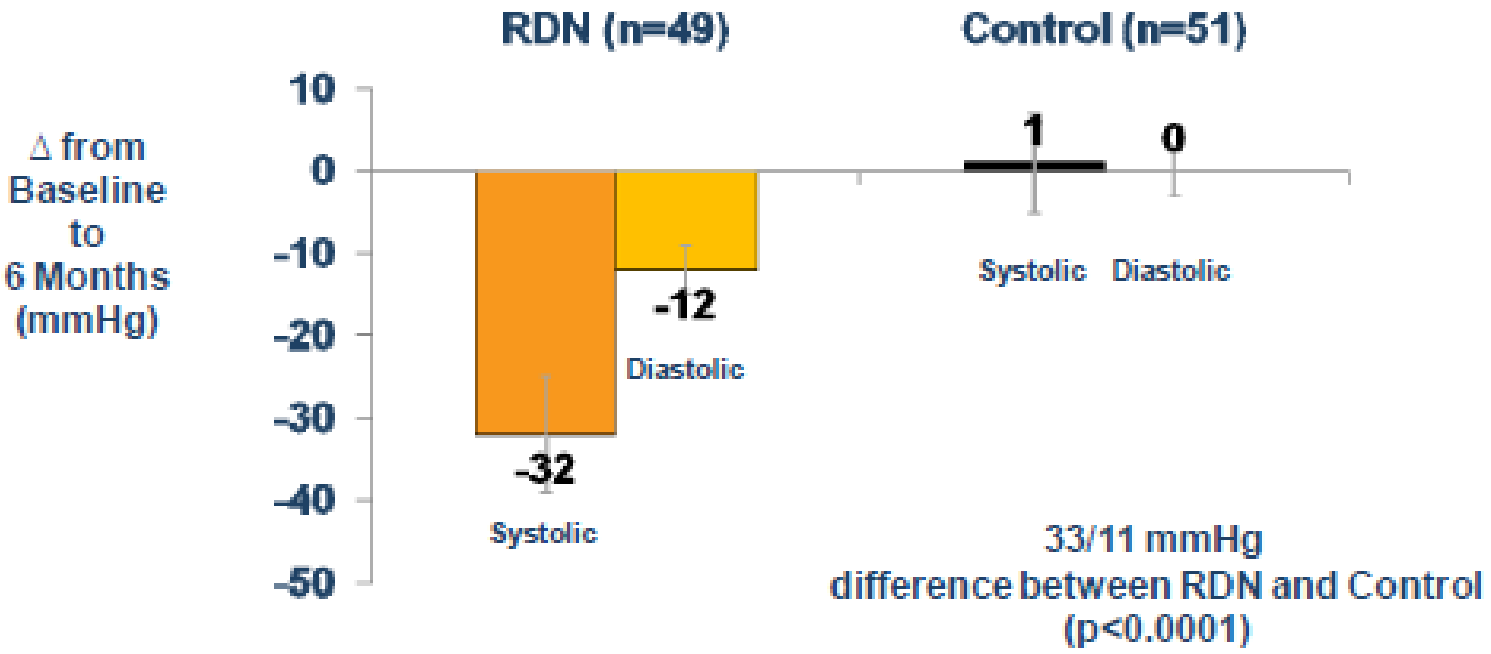


Figure 5 Mean Systolic and Diastolic BP Changes From Baseline After Renal Denervation With Up to 2 Years of Follow-Up in the Symplicity HTN-1 Trial

Hypertension. 2011;57:911-917;



- 84% of RDN patients had ≥ 10 mmHg reduction in SBP
- 10% of RDN patients had no reduction in SBP

Figure 4. Change in Office Blood Pressure from Baseline, Treatment (RDN) vs. Control

[4] Renal sympathetic denervation in patients with treatment-resistant hypertension (the Symplicity HTN-2 Trial): A randomised controlled trial. Elser, *et. al. Lancet*. 2010;376:1903-1909

A Controlled Trial of Renal Denervation for Resistant Hypertension

This article was published on March 29, 2014, at NEJM.org.

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.,

Table 1. Baseline Characteristics of the Study Population.*

Characteristic	Renal-Denervation Group (N=364)	Sham-Procedure Group (N=171)
Age — yr	57.9±10.4	56.2±11.2
Male sex — no. (%)	215 (59.1)	110 (64.3)
Body-mass index†	34.2±6.5	33.9±6.4
Race — no./total no. (%)‡		
Black	90/363 (24.8)	50/171 (29.2)
White	265/363 (73.0)	119/171 (69.6)
Asian	2/363 (0.6)	0/171
Other	6/363 (1.7)	2/171 (1.2)
Medical history — no. (%)		
Renal insufficiency§	34 (9.3)	17 (9.9)
Renal-artery stenosis	5 (1.4)	4 (2.3)
Obstructive sleep apnea	94 (25.8)	54 (31.6)
Stroke	29 (8.0)	19 (11.1)
Transient ischemic attack	28 (7.7)	13 (7.6)
Peripheral artery disease	19 (5.2)	5 (2.9)
Cardiac disease		
Coronary artery disease	101 (27.7)	43 (25.1)
Myocardial infarction	32 (8.8)	11 (6.4)
Diabetes		
Type 1	0	0
Type 2	171 (47.0)	70 (40.9)
Hyperlipidemia — no. (%)	252 (69.2)	111 (64.9)
Current smoker — no. (%)	36 (9.9)	21 (12.3)
Family history of hypertension — no./total no. (%)	305/361 (84.5)	140/170 (82.4)
Hypertension history — no. (%)		
Hospitalization for hypertensive crisis	83 (22.8)	38 (22.2)
Hospitalization for hypotension	8 (2.2)	4 (2.3)
No. of antihypertensive medications	5.1±1.4	5.2±1.4

RENAL DENERVATION FOR RESISTANT HYPERTENSION

SYMPLICITY HTN-3

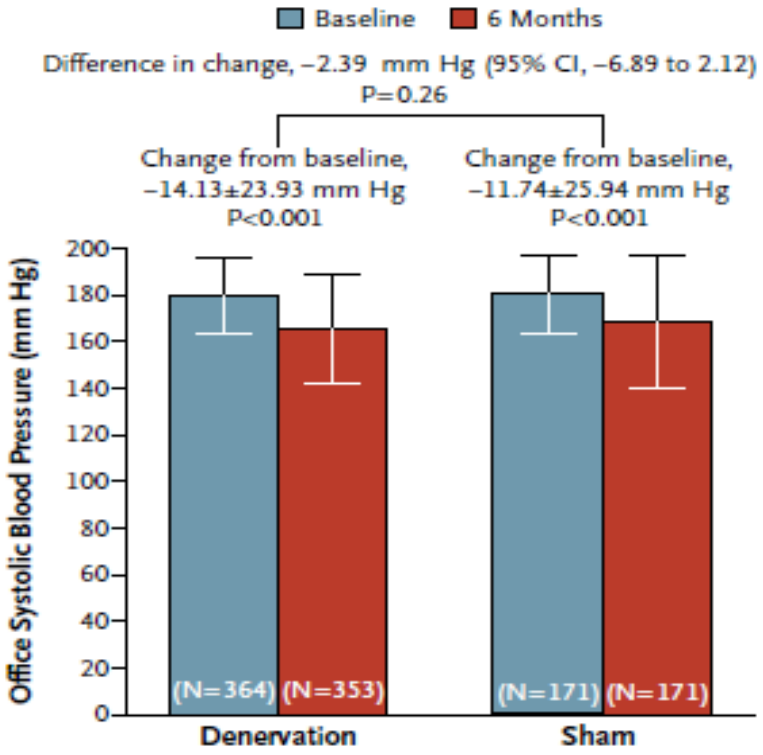


Figure 1. Primary Efficacy End Point.

A significant change from baseline to 6 months in office systolic blood pressure was observed in both study groups. The between-group difference (the primary efficacy end point) did not meet a test of superiority with a margin of 5 mm Hg. The I bars indicate standard deviations.

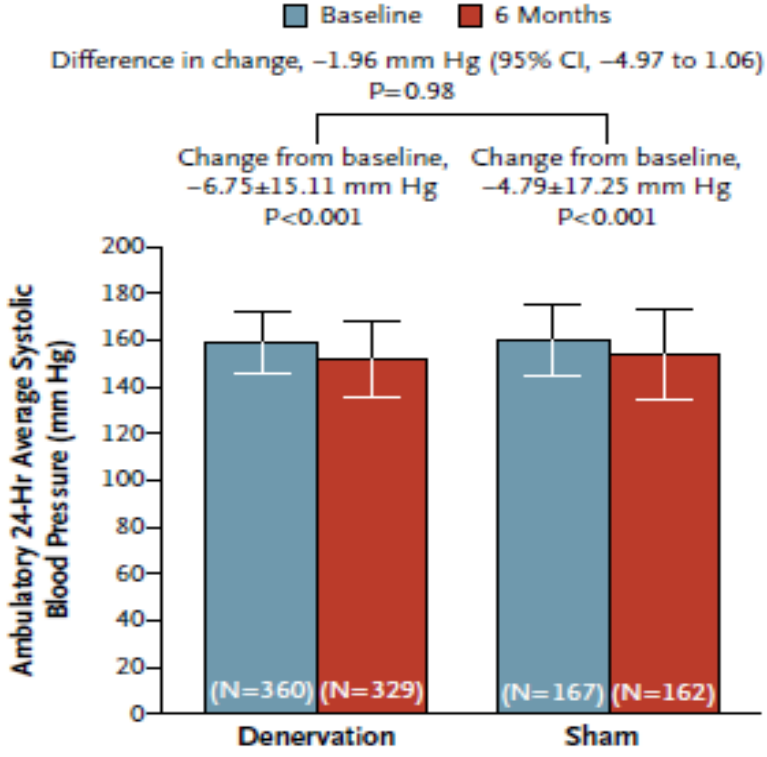


Figure 2. Secondary Efficacy End Point.

A significant change from baseline to 6 months in ambulatory 24-hour average systolic blood pressure was observed in both groups. The between-group difference (the secondary efficacy end point for which the study was powered) did not meet a test of superiority with a margin of 2 mm Hg. The I bars indicate standard deviations.

Should we still consider renal denervation for Resistant HTA?

- Interests in glucose metabolism, LVH, CHF, AF, CKD, Sleep apnea syndrome but ..

Renal denervation: still more questions than answers

Stefano Taddei[a] and Rosa Maria Bruno[a,b]

Journal of Hypertension 2014, 32:28–29

Limited destruction of renal nerves after catheter-based renal denervation: results of a human case study

Eva E. Vink[1], Roel Goldschmeding[2], Aryan Vink[2], Callista Weggemans[3], Ronald L.A.W. Bleijs[4] and Peter J. Blankestijn[1]

Nephrol Dial Transplant (2014) 29: 1608–1610
doi: 10.1093/ndt/gfu192
Advance Access publication 29 May 2014

Renal denervation (RDN) is a promising novel treatment for resistant hypertension. Effectiveness of treatment is, however, highly variable and unpredictable. Incomplete denervation of the renal nerves is a plausible explanation for the variable blood pressure lowering effect of RDN. Here, we present for the first time a histopathological evaluation of the effects of RDN on perivascular nerves of the renal arteries in a human

Nephrol Dial Transplant (2014) 29: 1608–1610
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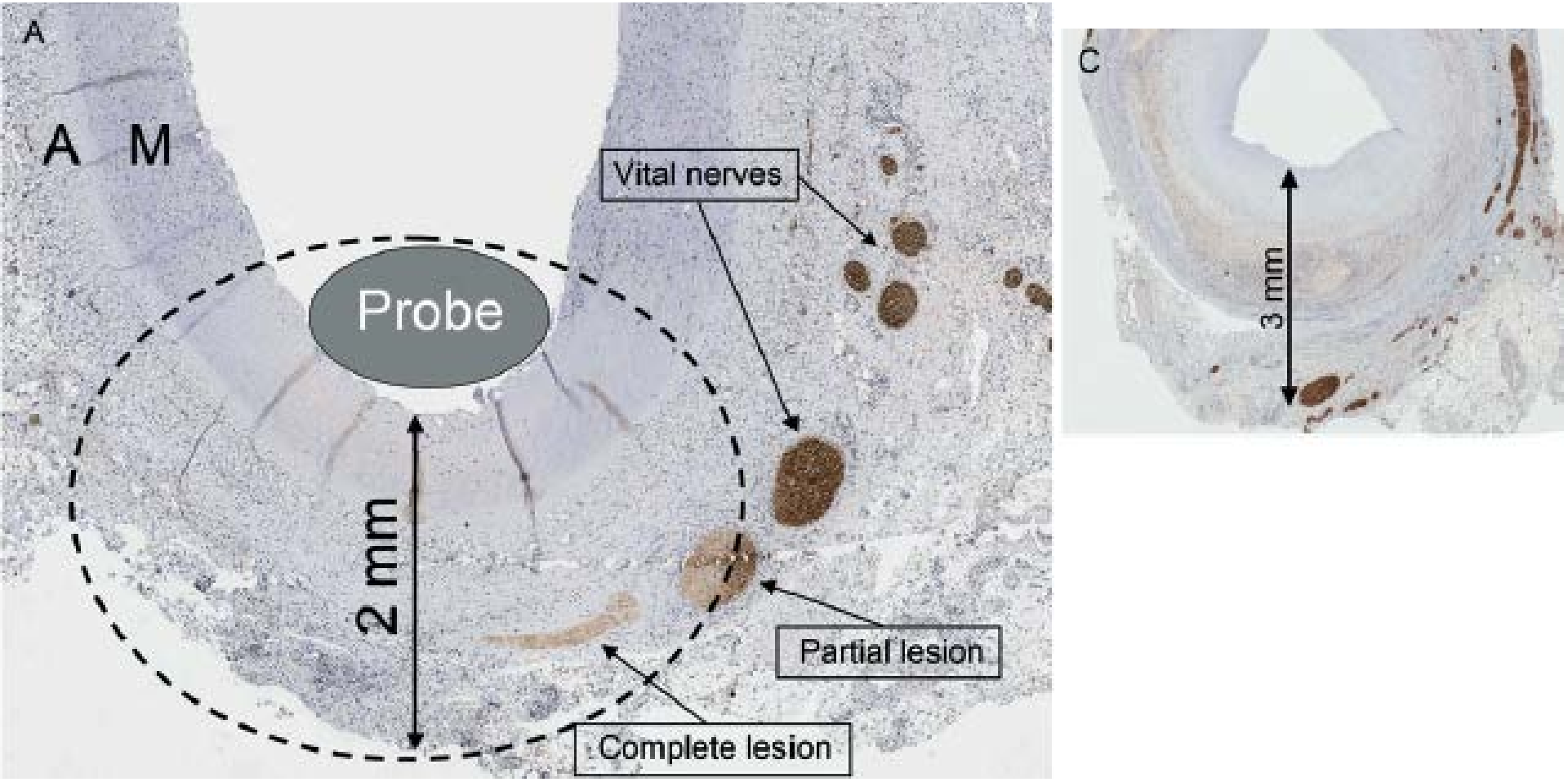
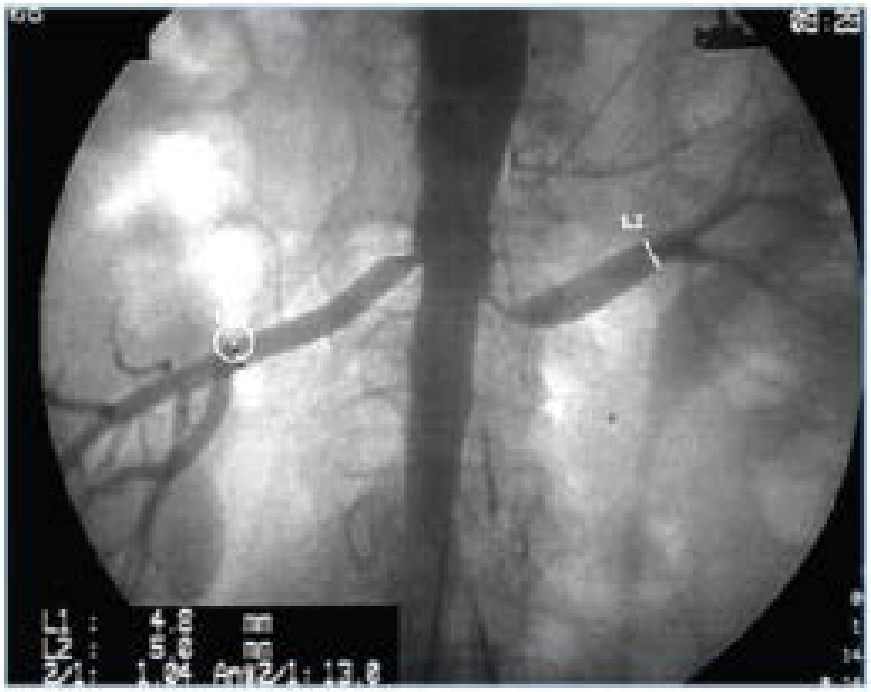
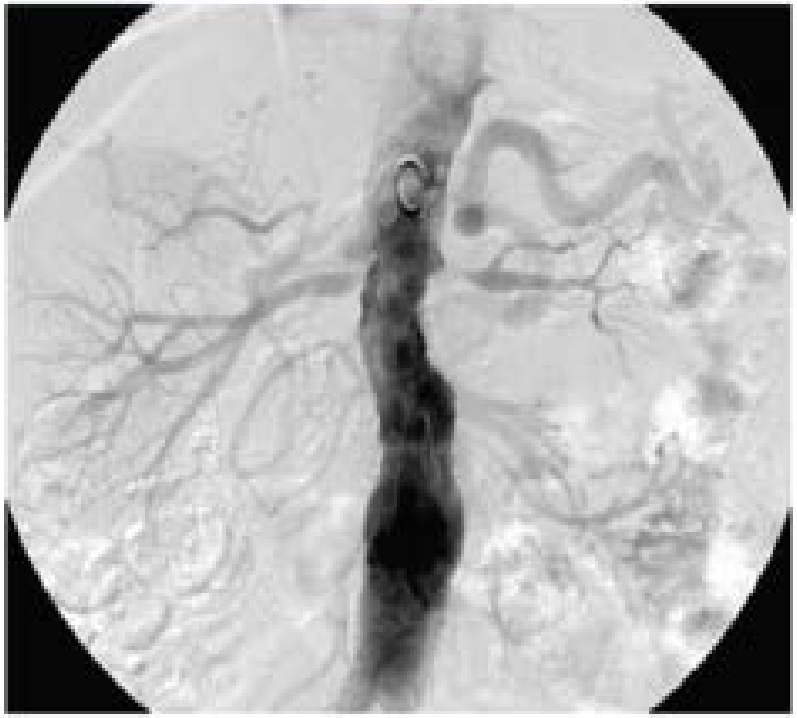


FIGURE 1: Histology of a human renal artery after renal denervation (RDN). (**A**) S-100 immunostain of RDN-treated renal artery in which the nerves are stained brown. The area that has been affected by the RND therapy is indicated by a dotted line. In this area, the nerves show almost complete absence of S-100 protein, indicating destruction of the Schwann cells of the nerves. At the border of the affected area, a partially affected nerve is present, whereas the nerves in the non-affected area are histologically vital. In the affected area, the nuclei of the smooth muscle cells in the media are almost completely absent indicating destruction of medial smooth muscle cells. A, adventitia; M, media. (**B** and **C**) Proximal part of the same renal artery near the origin from the aorta with a fibrous atherosclerotic plaque showing that, due to this plaque, the distance between the lumen and the adventitial nerves is increased. (B) Elastin van Gieson stain. P, atherosclerotic plaque; M, media and A, adventia. (C) The S-100 immunostain reveals that the distance between lumen and adventitial nerves is increased to 3 mm.

Renal Artery stenosis

Spectrum of Renovascular Disease Manifestations





Asymptomatic "Incidental RAS"

Renovascular Hypertension

Accelerated CV Disease
Congestive Heart failure
Stroke

Ischemic Nephropathy

Stenting and Medical Therapy for Atherosclerotic Renal-Artery Stenosis

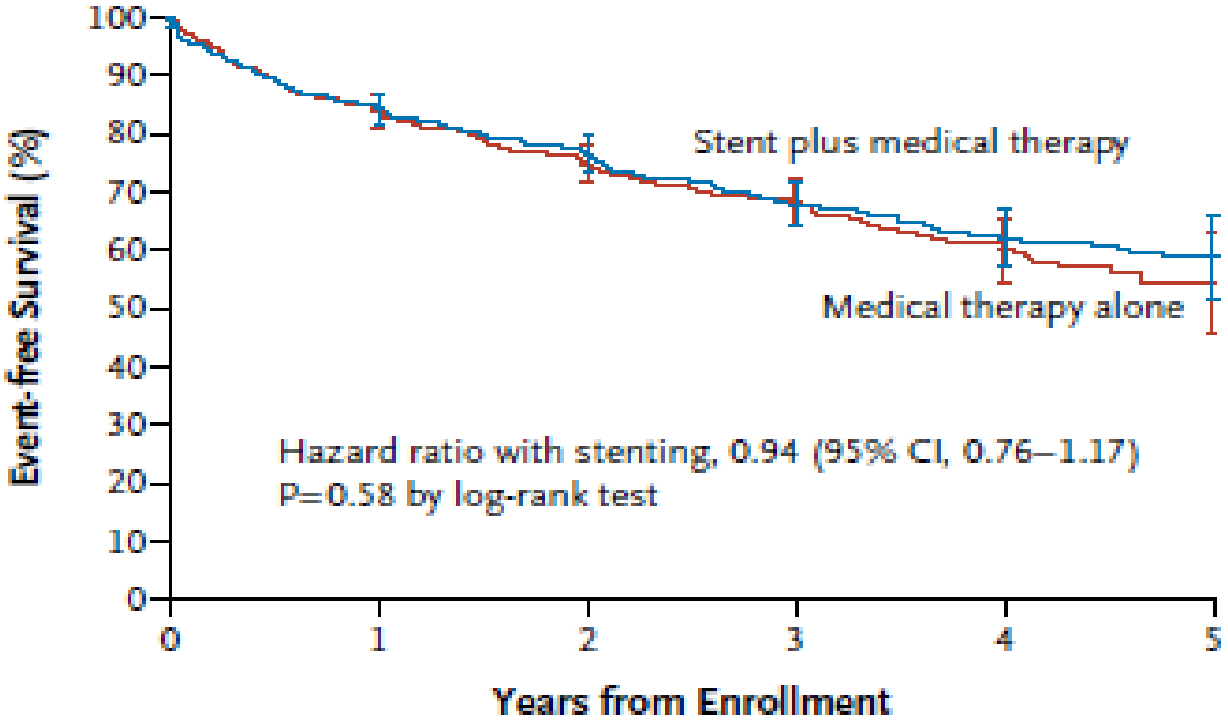
Christopher J. Cooper, M.D., Timothy P. Murphy, M.D., Donald E. Cutlip, M.D., Kenneth Jamerson, M.D., William Henrich, M.D., Diane M. Reid, M.D., David J. Cohen, M.D., Alan H. Matsumoto, M.D., Michael Steffes, M.D., Michael R. Jaff, D.O., Martin R. Prince, M.D., Ph.D., Eldrin F. Lewis, M.D., Katherine R. Tuttle, M.D., Joseph I. Shapiro, M.D., M.P.H., John H. Rundback, M.D., Joseph M. Massaro, Ph.D., Ralph B. D'Agostino, Sr., Ph.D., and Lance D. Dworkin, M.D., for the CORAL Investigators*

This article was published on November 18, 2013, at NEJM.org.

Stenting and Medical Therapy for Atherosclerotic Renal-Artery Stenosis

Table 1. Baseline Characteristics of the Study Population, According to Treatment Group.*

Characteristic	Stenting plus Medical Therapy (N=459)	Medical Therapy Only (N=472)
Age (yr)	69.3±9.4	69.0±9.0
Male sex (%)	51.0	48.9
Race (%)†		
Black	7.0	7.0
Other	93.0	93.0
Body-mass index‡	28.2±5.3	28.7±5.7
Systolic blood pressure (mm Hg)	149.9±23.2	150.4±23.0
Blood pressure at target level (%)§	29.2	25.3
Estimated GFR (ml/min/1.73 m²)¶	58.0±23.4	57.4±21.7
Stage ≥3 chronic kidney disease (%)	49.6	50.4
Method of identification of stenosis (%)		
Angiography	68.4	68.6
Duplex ultrasonography	25.5	24.2
Computed tomographic angiography	4.4	5.3
Magnetic resonance angiography	1.7	1.9
Medical history and risk factors (%)		
Diabetes	32.4	34.3
Prior myocardial infarction	26.5	30.2
History of heart failure	12.0	15.1
Smoking in past yr	28.0	32.2
Hyperlipidemia	89.4	90.0
Angiographic findings		
% Stenosis, as assessed by core laboratory	67.3±11.4	66.9±11.9
% Stenosis, as assessed by investigator	72.5±14.6	74.3±13.1
Global ischemia (%)**	20.0	16.2
Bilateral disease (%)††	22.0	18.1



No. at Risk

Medical therapy alone	472	371	314	214	115	40
Stent plus medical therapy	459	362	318	224	131	59

Figure 2. Kaplan–Meier Curves for the Primary Outcome.

Survival curves are truncated at 5 years owing to instability of the curves because few participants remained in the study after 5 years.

Stenting and Medical Therapy for Atherosclerotic Renal-Artery Stenosis

Christopher J. Cooper, M.D., Timothy P. Murphy, M.D., Donald E. Cutlip, M.D., Kenneth Jamerson, M.D., William Henrich, M.D., Diane M. Reid, M.D., David J. Cohen, M.D., Alan H. Matsumoto, M.D., Michael Steffes, M.D., Michael R. Jaff, D.O., Martin R. Prince, M.D., Ph.D., Eldrin F. Lewis, M.D., Katherine R. Tuttle, M.D., Joseph I. Shapiro, M.D., M.P.H., John H. Rundback, M.D., Joseph M. Massaro, Ph.D., Ralph B. D'Agostino, Sr., Ph.D., and Lance D. Dworkin, M.D., for the CORAL Investigators*

In summary, renal-artery stenting did not confer a significant benefit with respect to the prevention of clinical events when added to comprehensive, multifactorial medical therapy in people with atherosclerotic renal-artery stenosis and hypertension or chronic kidney disease.

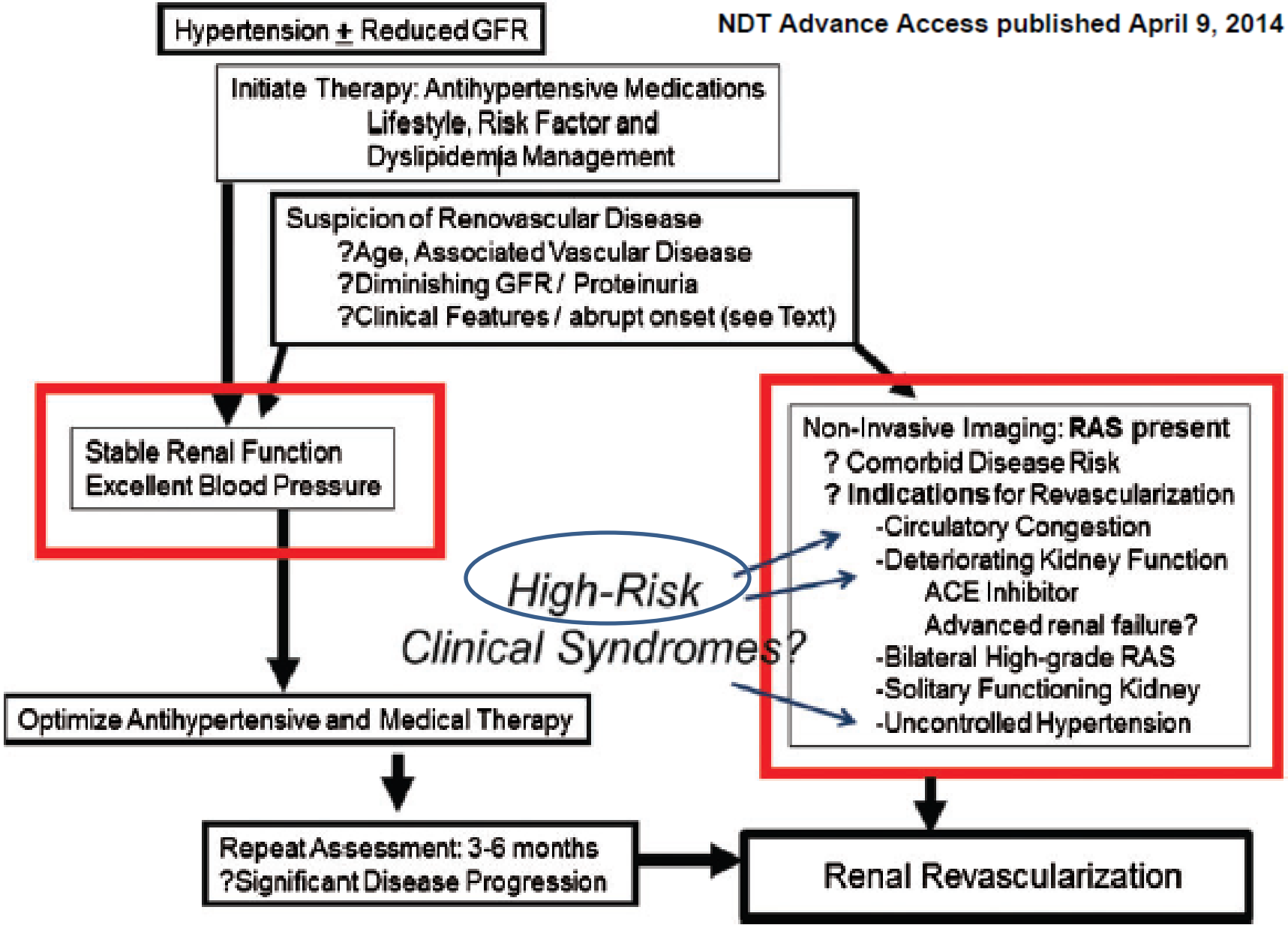
Treatment of atherosclerotic renovascular hypertension: review of observational studies and a meta-analysis of randomized clinical trials

NDT Advance Access published April 16, 2014

- Small decrease in DBP and number of antiHTA agents in the stenting group according to 7 RCT studies (2155 patients at baseline and 1741 available at FU)
- No difference in SBP, serum creatinine, incident CV event rates
- However, the patients included are those whose the baseline therapeutic decision was uncertain (low risk group)
- What about high risk patients?

Management of Renovascular Hypertension and Ischemic Nephropathy

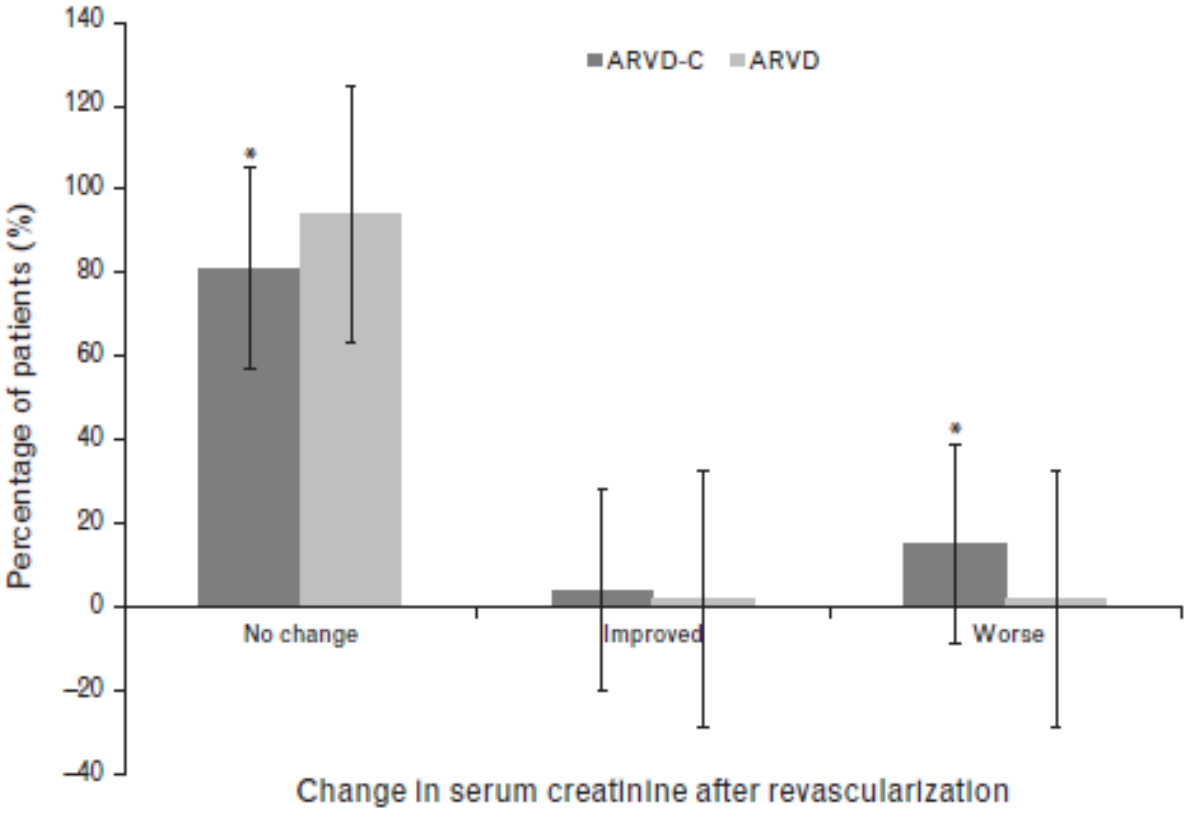
NDT Advance Access published April 9, 2014



Extrarenal atherosclerotic disease blunts renal recovery in patients with renovascular hypertension

Journal of Hypertension 2014, 32:1300–1306

Khangura *et al.*



Distribution of changes in serum creatinine after revascularization in ARVD and ARVD-C,

Extrarenal atherosclerotic disease blunts renal recovery in patients with renovascular hypertension

Journal of Hypertension 2014, 32:1300–1306

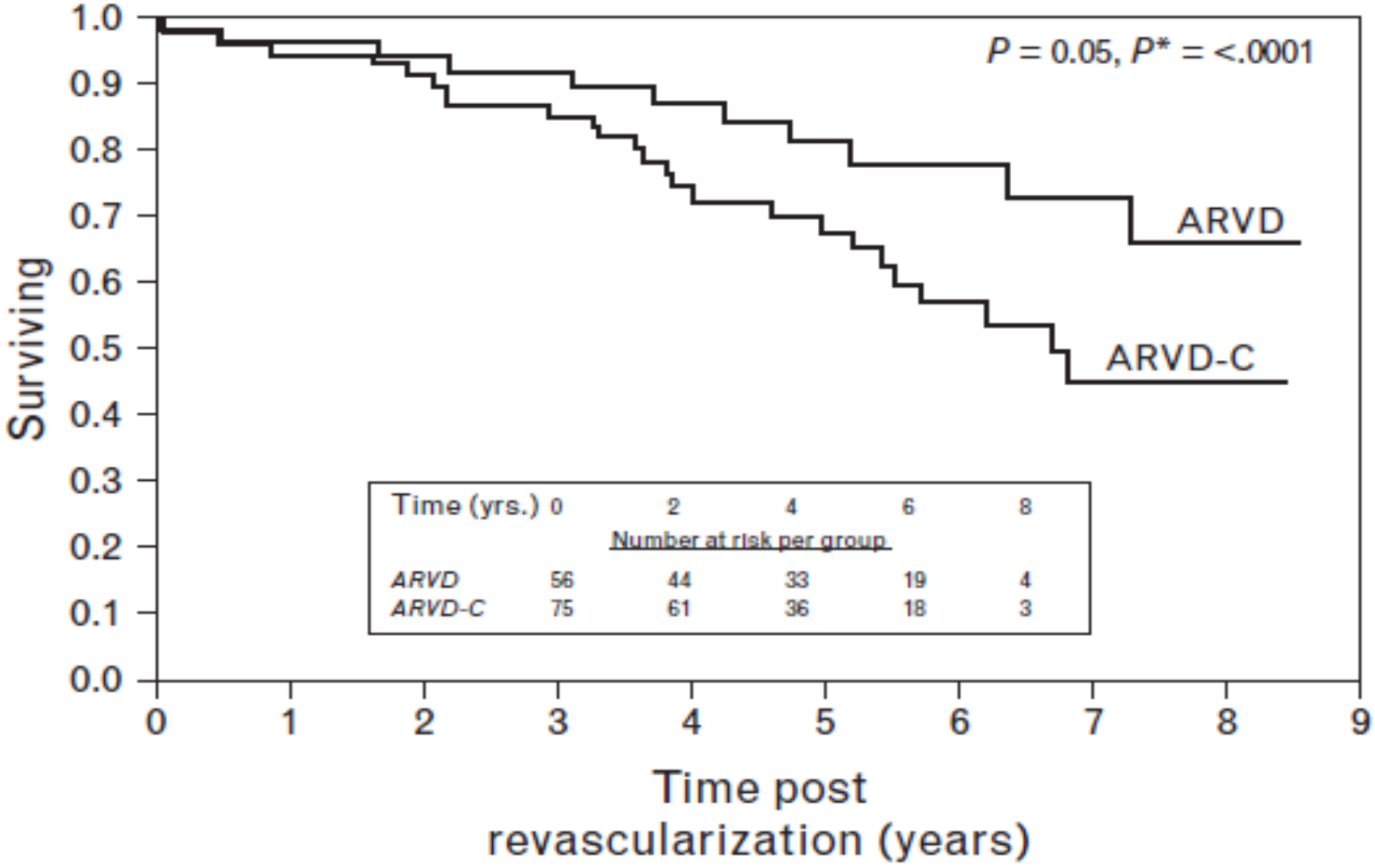


FIGURE 2 Survival plots of atherosclerotic renal artery disease patients with (ARVD-C) or without (ARVD) coronary artery disease. Events were recorded in 27 and 12 patients in the ARVD-C and ARVD groups, respectively, Log-Rank test,

Dialysis and HTA

Hypertension in hemodialysis patients treated with atenolol or lisinopril: a randomized controlled trial

Nephrol Dial Transplant (2014) 29: 672–

Rajiv Agarwal, Arjun D. Sinha, Maria K. Pappas, Terri N. Abraham and Getachew G. Tegegne

Background. The purpose of this study was to determine among maintenance hemodialysis patients with echocardiographic left ventricular hypertrophy and hypertension whether in comparison with a β-blocker-based antihypertensive therapy, an angiotensin converting enzyme-inhibitor-based antihypertensive therapy causes a greater regression of left ventricular hypertrophy.

Methods. Subjects were randomly assigned to either open-label lisinopril ($n = 100$) or atenolol ($n = 100$) each administered three times per week after dialysis. Monthly monitored home blood pressure (BP) was controlled to <140/90 mmHg with medications, dry weight adjustment and sodium restriction. The primary outcome was the change in left ventricular mass index (LVMI) from baseline to 12 months.

FIGURE 1: BP profiles at baseline and over time. BP obtained in the interdialytic period (Left panel) and self-measured by the patients at home (right panel) are shown. Ambulatory BP monitoring was performed in the interdialytic period over 44 h at baseline, 3, 6 and 12 months. Solid line shows the atenolol group and the dotted line the lisinopril group; vertical bars represent standard error of mean

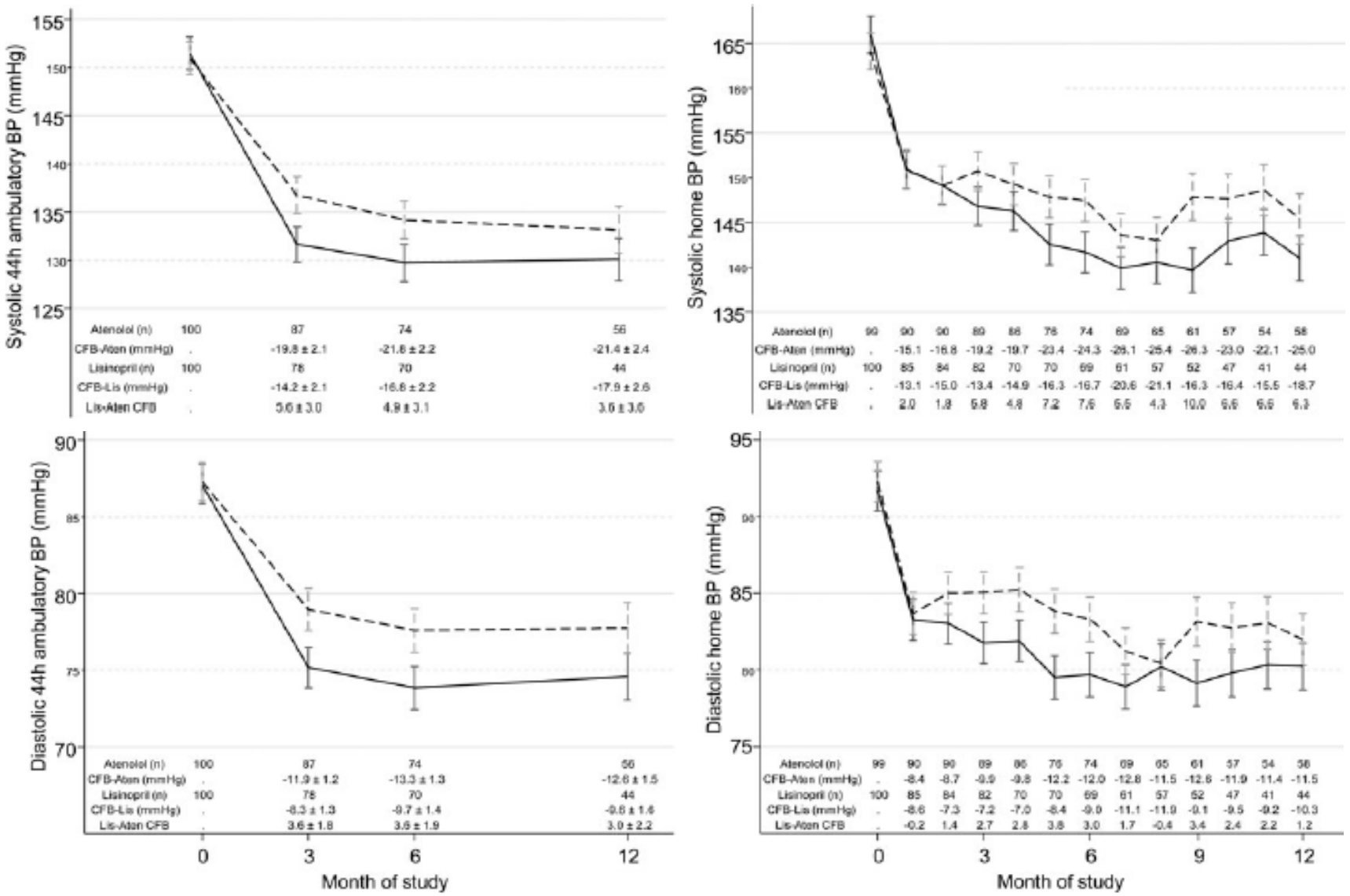


Table 3. Serious adverse events reported following randomization

Event type	Atenolol			Lisinopril				
	Subjects (*n*)	Events (*n*)	Incidence rate(events/ 100patient-years)	Subjects (*n*)	Events (*n*)	Incidence rate(events/ 100patient-years)	IRR Lisinopril/atenolol (95% CI)	P
Overall serious adverse events	58	140	172.4	70	188	253.6	1.47 (1.18–1.84)	<0.001
All-cause hospitalization rate	37	73	89.9	59	107	144.3	1.61 (1.18–2.19)	0.002
Cardiovascular events	16	20	24.6	28	43	58	2.36 (1.36–4.23)	0.001
Combined MI, Stroke, CHF;	10	11	13.5	17	23	31	2.29 (1.07–5.21)	0.02

serious adverse events of myocardial infarction, stroke and hospitalization for heart failure or cardiovascular death in the atenolol group occurred in 10 subjects, who had 11 events and in the lisinopril group in 17 subjects, who had 23 events (IRR 2.29, P = 0.021). Hospitalizations for heart failure were worse in the lisinopril group (IRR 3.13, P = 0.021). All-cause hospitalizations were higher in the lisinopril group [IRR 1.61 (95% CI 1.18–2.19, P = 0.002)]. LVMI improved with time; no difference between drugs was noted.

Hypertension in hemodialysis patients treated with atenolol or lisinopril: a randomized controlled trial

Nephrol Dial Transplant (2014) 29: 672–681

Rajiv Agarwal, Arjun D. Sinha, Maria K. Pappas, Terri N. Abraham and Getachew G. Tegegne

Conclusions. Among maintenance dialysis patients with hypertension and left ventricular hypertrophy, atenolol-based antihypertensive therapy may be superior to lisinopril-based therapy in preventing cardiovascular morbidity and all-cause hospitalizations. (Funded by the National Institute of Diabetes

Spironolactone Reduces Cardiovascular and Cerebrovascular Morbidity and Mortality in Hemodialysis Patients

Objectives This study sought to assess whether spironolactone treatment reduces the high incidence of cardiovascular and cerebrovascular (CCV) morbidity and mortality in hemodialysis (HD) patients.

Background Aldosterone receptor blockers reduce cardiac-related events, but the efficacy of the agents in HD patients is unclear.

Methods A 3-year randomized trial involving 5 clinics was performed. Of the 309 oligoanuric HD patients enrolled in the study, 157 patients were randomly assigned to receive 25 mg/day of spironolactone without any restriction on dietary potassium intake (treatment group), and 152 patients were assigned to a control group. The primary outcome was a composite of death from CCV events or hospitalization for CCV events, and the secondary outcome was death from all causes.

Results During the 3-year follow-up, the primary outcome occurred in 5.7% of patients in the treatment group and in 12.5% of patients in the control group. Hazard ratios (HRs) for the primary outcome for treatment were 0.404 (95% confidence interval [CI]: 0.202 to 0.809; $p = 0.017$) and 0.379 (95% CI: 0.173 to 0.832; $p = 0.016$) before and after adjustment, respectively. The secondary outcome was significantly reduced in the treatment group compared with the control group (6.4% vs. 19.7%; HRs: 0.355 [95% CI: 0.191 to 0.662; $p = 0.002$] and 0.335 [95% CI: 0.162 to 0.693; $p = 0.003$] before and after adjustment, respectively). Gynecomastia or breast pain was reported in 16 patients (10.2%) in the treatment group. Serious hyperkalemia led to treatment discontinuation in 3 patients (1.9%).

Conclusions Aldosterone receptor blockade using spironolactone may substantially reduce the risk of both CCV morbidity and death among HD patients; however, larger-scale studies are recommended to further confirm its efficacy. (Effects of Spironolactone on Cardio- and Cerebrovascular Morbidity and Mortality in Hemodialysis Patients; NCT01687699) (J Am Coll Cardiol 2014;63:528–36) © 2014 by the American College of Cardiology Foundation

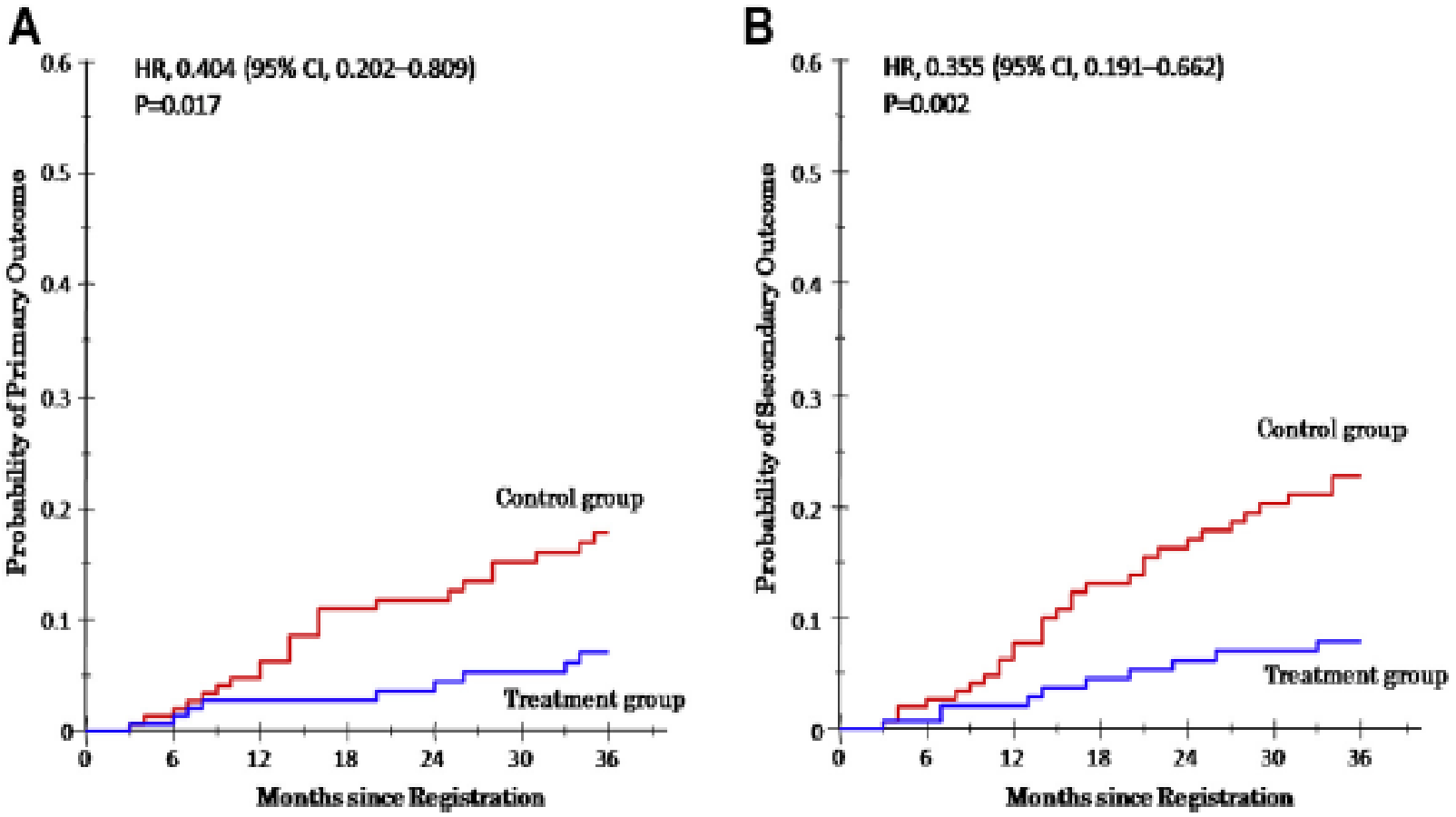


Figure 2 Cumulative Kaplan-Meier Outcomes Estimates

The Kaplan-Meier curve depicts the rates of primary (**A**) and secondary (**B**) outcomes in the control and treatment groups. HR = hazard ratio.

Take home messages (1)

- HTA is a CV risk factor which should be treated. A good definition is required (out of the office measurement). The lower the better is no more proposed.
- The ideal BP target is <140/90 mmHg for the majority < 80. Be less aggressive in people >80.
- Going lower than 120 mmHg for the SBP could be deleterious.
- Salt restriction sems useful but should not be too strict with stimulation of increasing K intake.

Take home messages (2)

- In CKD patients, the BP target is not different than in general HT population.
- In Resistant HTA, RDN is at the present time no more recommanded.
- In RAS due to atherosclerosis, encourage the medical treatment first. Angioplasty is to be reserved for a minority who must be identified.
- In HD population, interest of atenolol and spironolactone?

Thank you

Any questions?

2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults

Report From the Panel Members Appointed to the Eighth Joint National Committee (JNC 8)

Table 6. Guideline Comparisons of Goal BP and Initial Drug Therapy for Adults With Hypertension

Guideline	Population	Goal BP, mm Hg	Initial Drug Treatment Options
2014 Hypertension guideline	General ≥60 y	<150/90	Nonblack: thiazide-type diuretic, ACEI, ARB, or CCB
	General <60 y	<140/90	Black: thiazide-type diuretic or CCB
	Diabetes	<140/90	Thiazide-type diuretic, ACEI, ARB, or CCB
	CKD	<140/90	ACEI or ARB
ESH/ESC 2013[37]	General nonelderly	<140/90	β-Blocker, diuretic, CCB, ACEI, or ARB
	General elderly <80 y	<150/90	
	General ≥80 y	<150/90	
	Diabetes	<140/85	ACEI or ARB
	CKD no proteinuria	<140/90	ACEI or ARB
	CKD + proteinuria	<130/90	