Structured approach to diagnosis, investigation and treatment of hypertension including device therapy

15th March 2017

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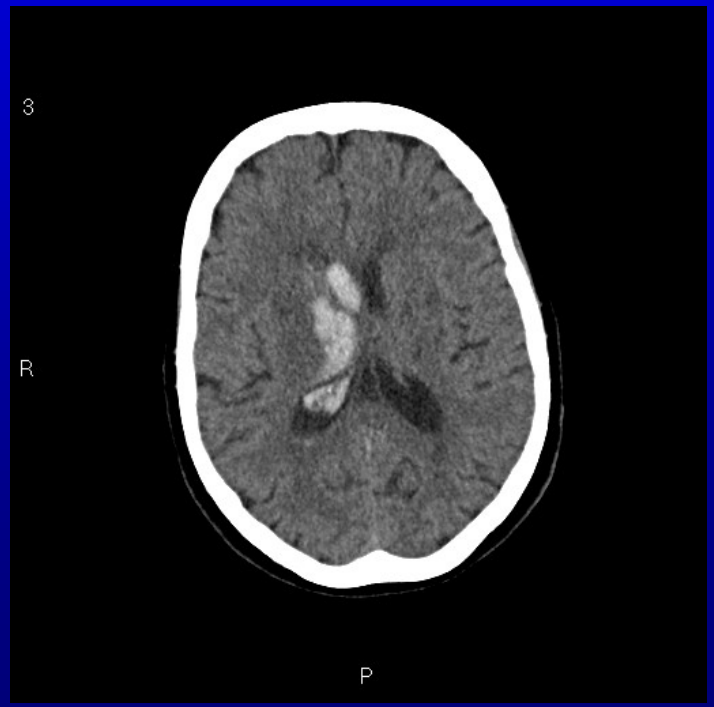
British Hypertension Society Guidelines Committee

Disclosures:
Research grants from: AstraZeneca, Bayer, Boehringer Ingelheim, Merck,, Roche, Servier

Honoraria/Consultancy:

A Cornerstone of Cardiology

- A non-fatal MI is an inconvenience.
- A non-fatal stroke is a catastrophe.



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Clinical Pharmacology – Advanced Specialist Area
Modules
Hypertension

Aims of the Hypertension/Cardiovascular Risk Module

The purpose of this module is to equip future physicians with the essential knowledge, aptitude and skill to function as independent hypertension specialists supporting other cognate specialties within the framework of the National Health Service. The training will be as an adjunct to existing specialty training and will be designed to add value to the management of hypertensive patients and cardiovascular risk.

Once training is completed the physician should:

- Be able to apply diagnostic and management knowledge and skills to the prevention of cardiovascular diseases, due to hypertension and other cardiovascular risk factors.
- Be able to formulate a differential diagnosis of potential causes for raised blood pressure and develop an appropriate treatment plan incorporating lifestyle and pharmacological therapy.
- Have the necessary understanding and appreciation of the role of multi-disciplinary working across specialties and primary care to facilitate the most cost-effective and efficient management of hypertensive patients.
- Possess the ability to advise, develop and evaluate the Clinical Effectiveness of hypertension and cardiovascular risk services in partnership with other cognate disciplines.

Question: Which risk factor accounts for the most CV disease according to the World Health Organisation?

- 1. Smoking
- 2. Dyslipidaemia
- 3. Family History of CVD
- 4. Obesity
- 5. Diabetes
- 6. Hypertension
- 7. Low birth Weight
- 8. Urban pollution

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Answer: Which risk factor accounts for the most CV disease according to the World Health Organisation?

- 1. Smoking
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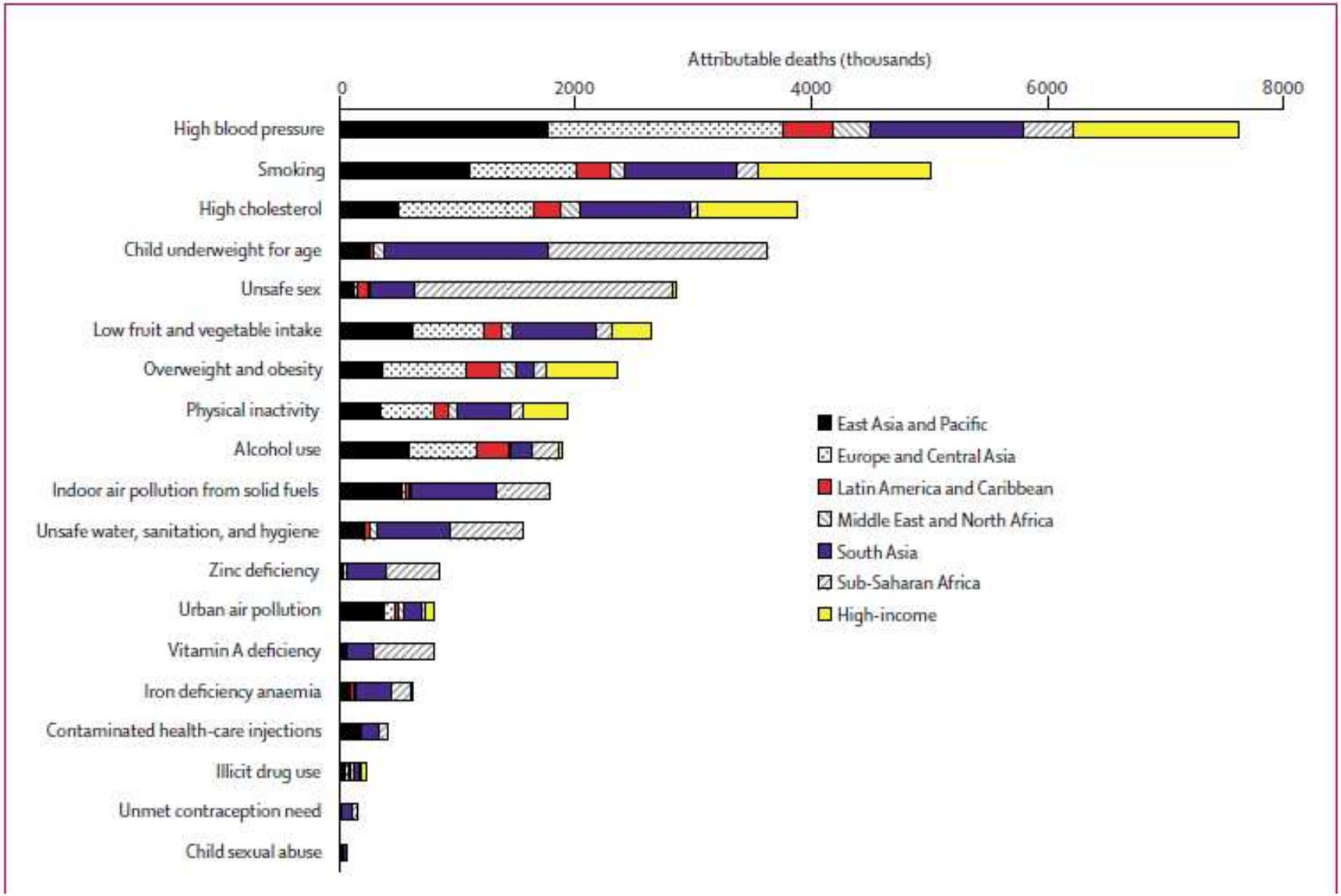
Which risk factor accounts for the most CV disease according to the World Health Organisation?



How much conference time does ESC Congress allow for Hypertension?

- **5%**
- **10%**
- **12%**
- **15%**
- **19%**

How much conference time does ESC Congress allow for Hypertension?

- **5%**
- **10%**
- **12%**
- **15%**
- **19% correct answer**

Figure 5
Prevalence of Hypertension in 5 European Countries by Gender and Age

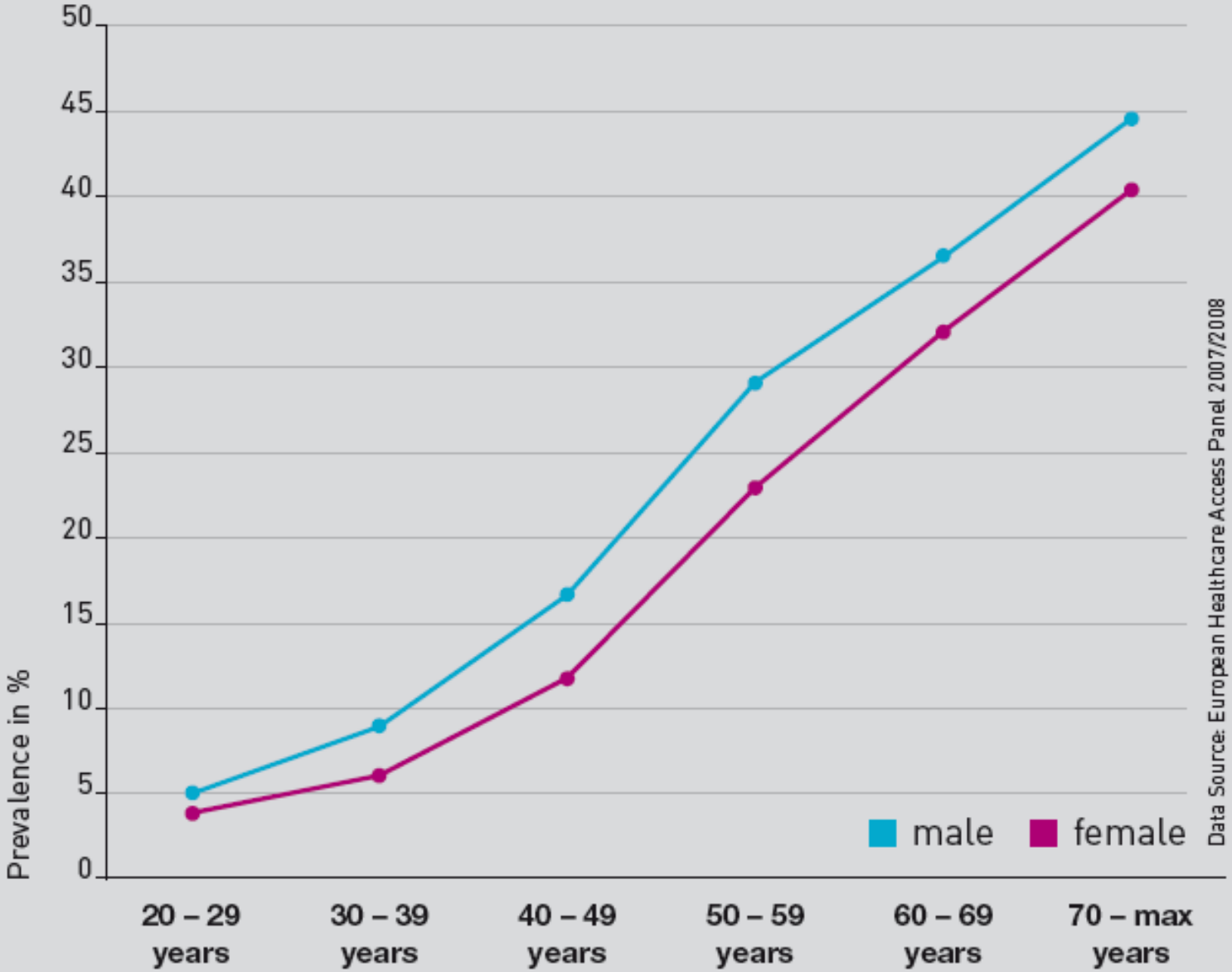
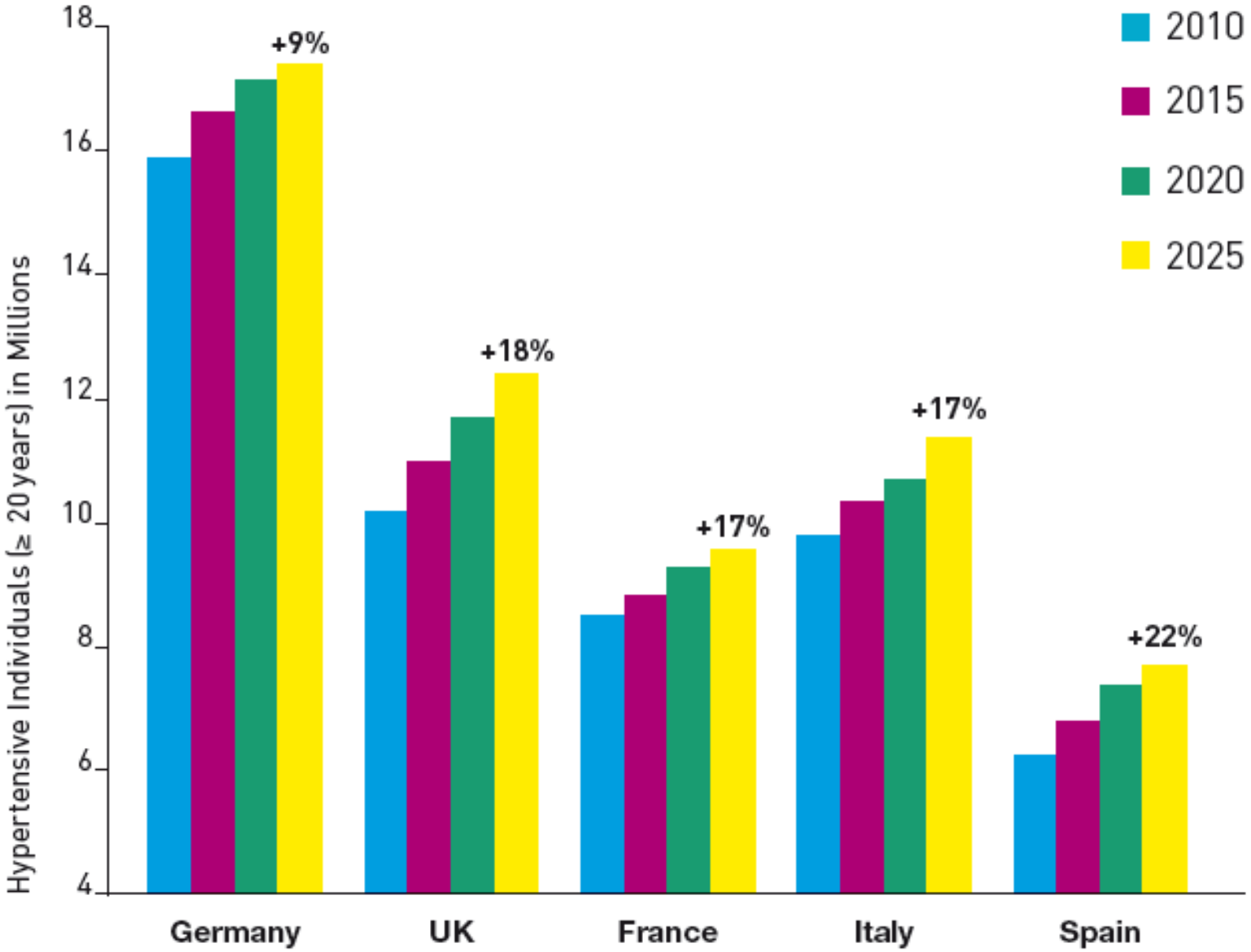
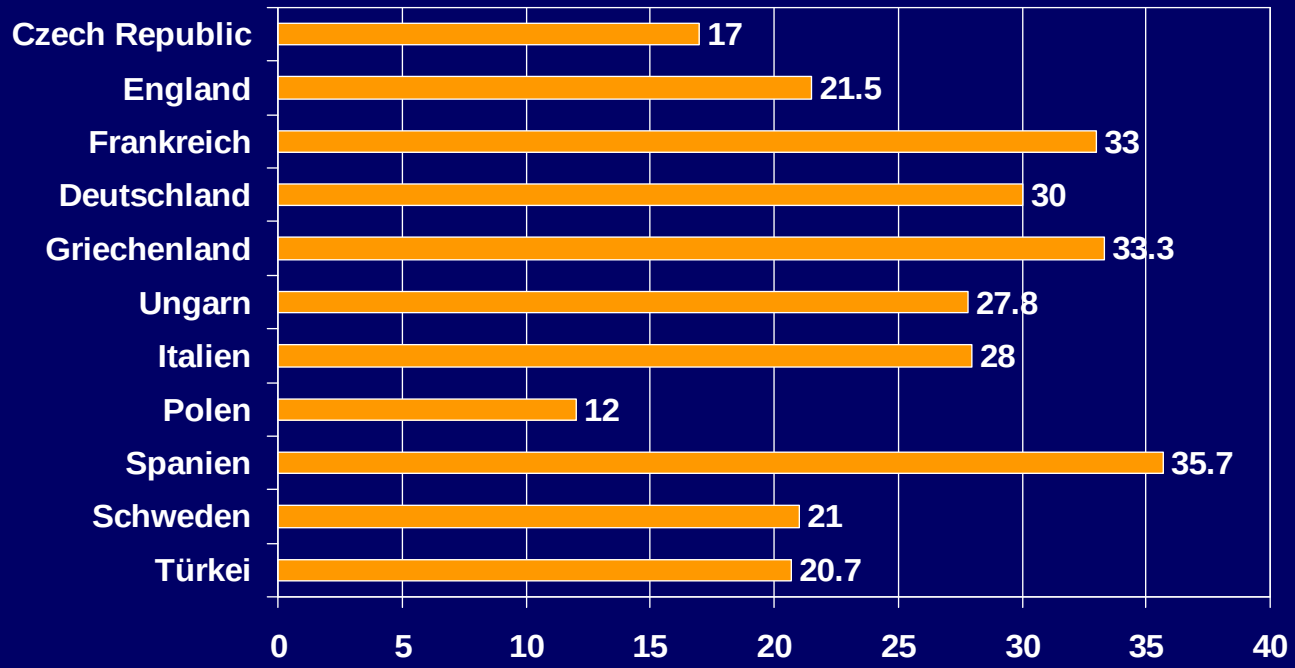


Figure 2
Projected Number of Hypertensive Individuals in 5 European Countries



Percentage of Hypertensive Patients with controlled Blood Pressure (<140/90 mmHg) in Europe



© Prof. Schmieder, FAU Erlangen

ESH Newsletter 2007;8:No 3

High blood pressure

Billion people have high blood pressure, mostly in poorer countries

Rate of hypertension doubles globally but falls in wealthy countries with health awareness, better diet and access to medicines thought to be factors

Reuters in London

Wednesday 16 November 2016
01.57 GMT

Definitions

Stage 1 hypertension:

- Clinic blood pressure (BP) is 140/90 mmHg or higher **and**
- ABPM or HBPM average is 135/85 mmHg or higher.

Stage 2 hypertension:

- Clinic BP 160/100 mmHg is or higher **and**
- ABPM or HBPM daytime average is 150/95 mmHg or higher.

Severe hypertension:

- Clinic BP is 180 mmHg or higher **or**
- Clinic diastolic BP is 110 mmHg or higher.

Key priorities for implementation

- Diagnosis.
- Initiating and monitoring antihypertensive drug treatment.
- Choosing antihypertensive drug treatment.

Diagnosis (1)

If the clinic blood pressure is 140/90 mmHg or higher, offer ambulatory blood pressure monitoring (ABPM) to confirm the diagnosis of hypertension.

Assessing cardiovascular risk and target organ damage: updated recommendations

- Use a formal estimation of cardiovascular risk to discuss prognosis and healthcare options with people with hypertension. For all people with hypertension offer to:
  - test urine for presence of protein
  - take blood to measure glucose, electrolytes, creatinine, estimated glomerular filtration rate and cholesterol
  - examine fundi for hypertensive retinopathy
  - arrange a 12-lead ECG.

Additional recommendations

Lifestyle interventions

- Offer guidance and advice about:
  - diet (including sodium and caffeine intake) and exercise
  - alcohol consumption
  - smoking.

Patient education and adherence

- Provide:
  - information about benefits of drugs and side effects
  - details of patient organisations
  - an annual review of care.

Initiating drug treatment

Offer antihypertensive drug treatment to people:

- Who have stage 1 hypertension, are aged under 80 and meet identified criteria
  - if aged under 40 also consider specialist evaluation of secondary causes of hypertension and further assessment of potential target organ damage.
- Who have stage 2 hypertension at any age.

Monitoring drug treatment (1)

Use clinic blood pressure measurements to monitor response to treatment. Aim for target blood pressure below:

- 140/90 mmHg in people aged under 80
- 150/90 mmHg in people aged 80 and over

ABPM and HBPM superior to office BP

BP Measurement Artefacts

- Cuff too small = ↑ 10–30 mm Hg
- Talking during measurement:
  ↑ 20 mm Hg

Clues to measurement artifacts:

- Less target organ damage than expected[4]
- Hypotensive symptoms with treated

[1]*JAMA* 1988;259:225–228.
[2]Am J Hypertens 2001;14:1263–1269.
[3]*Hypertension* 1983;5:122–127.
[4]*Ann Int Med* 1990;112:270-277.

Treatment Resistant Hypertension

2013 Definitions: ESC/ESH AHA BIHS

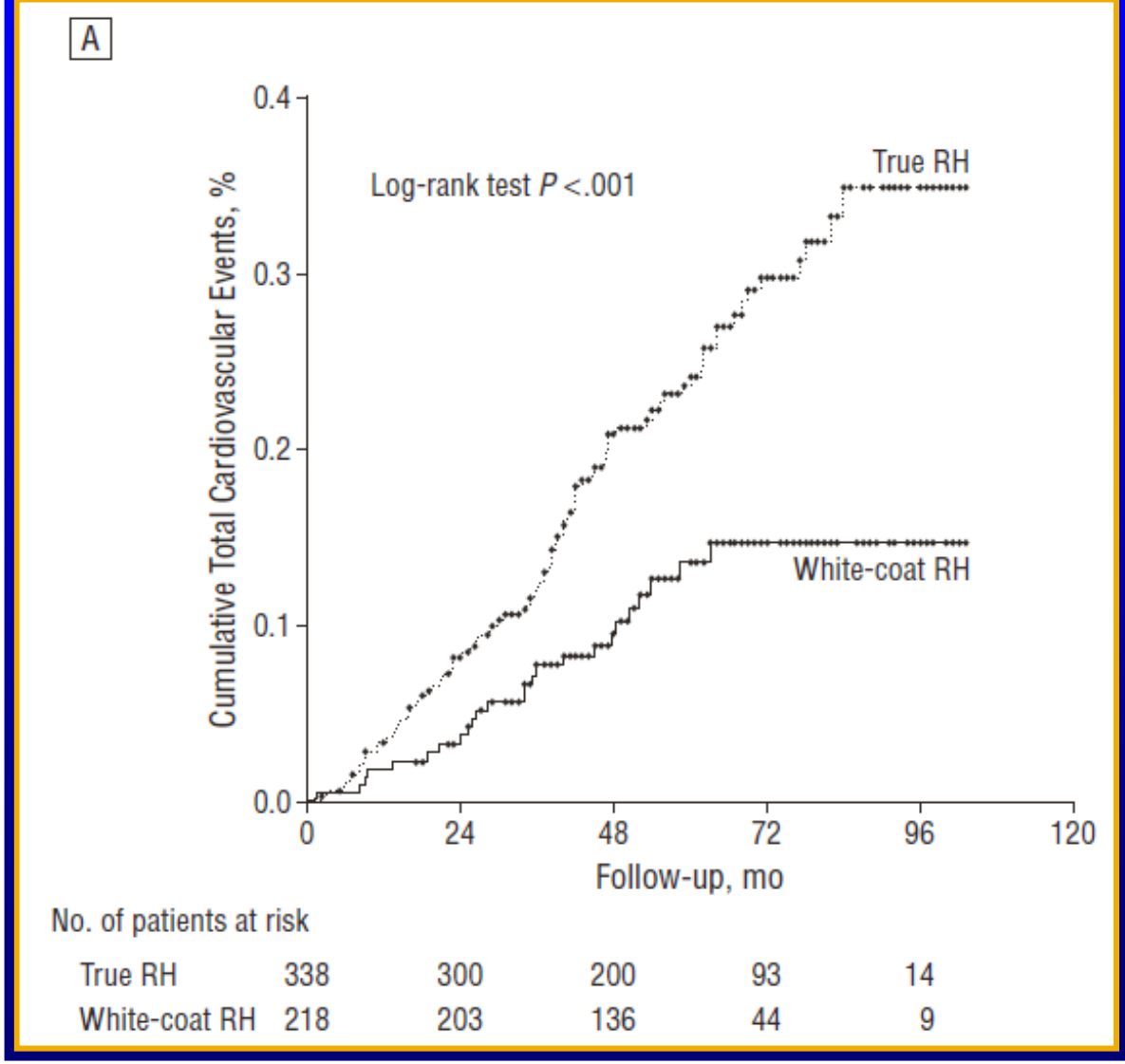
1. BP above goal on a rational ≥3 med regimen with complementary mechanisms of action at optimal doses preferably including a diuretic.

   BIHS: – A+C+D

2. Controlled Resistant Hypertension. BP controlled to goal on ≥4 BP meds (optimal doses, preferably including a diuretic).

Calhoun DA, et al. *Hypertension.* 2008;51:1403–1419.
Mancia G, et al. Eur Heart J 2013 doi:10.1093/eurheartj/eht151

Prognosis in Resistant Hypertension



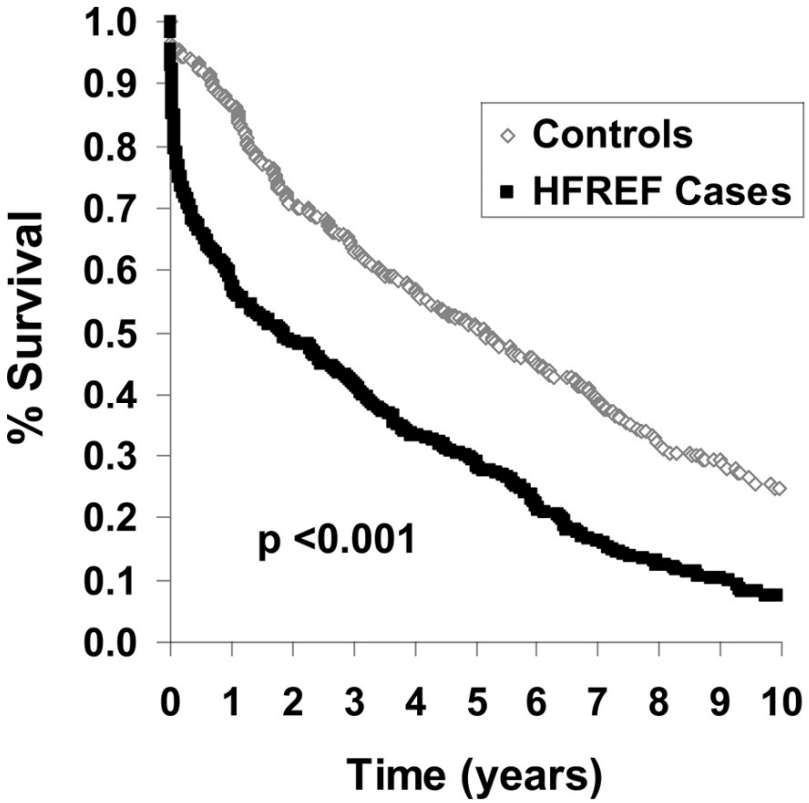
556 patients with TRH, based on office BP

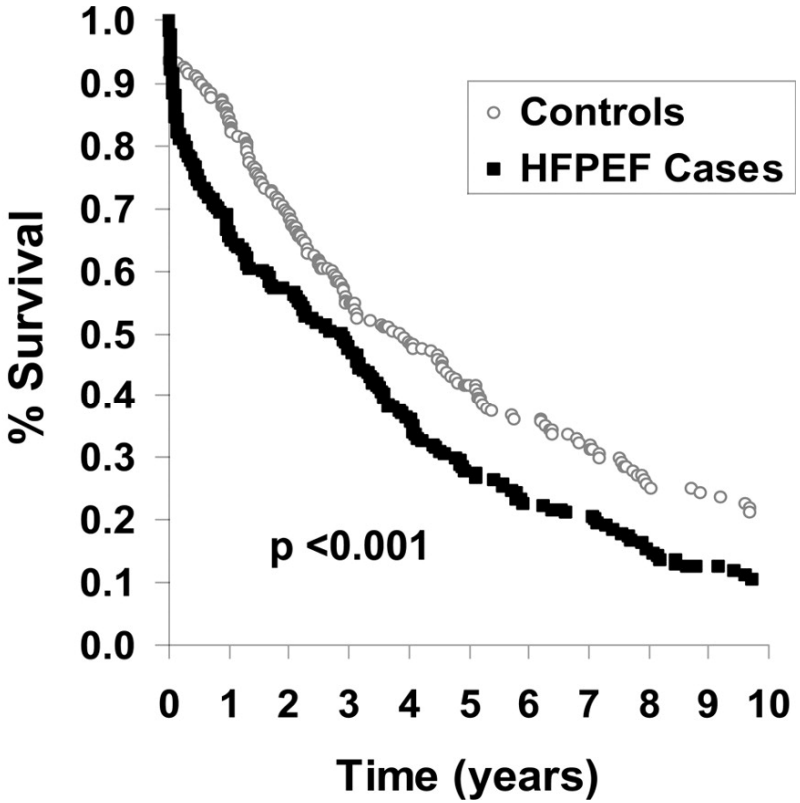
338 (61%) had confirmation of TRH on 24-hr ABPM .

Mean follow-up 4.8 years

Salles GF, et al. *Arch Int Med*. 2008;168:2840–2346. **(Brazil)**

Heart failure, hypertension, and Heart Failure with Preserved Ejection Fraction





Douglas S. Lee et al. Circulation. 2009;119:3070-3077

Bar graphs of EDVI, indexed left atrial volume (LAVI), EDP, plasma brain natriuretic peptide (BNP), and derived τ by subject group.

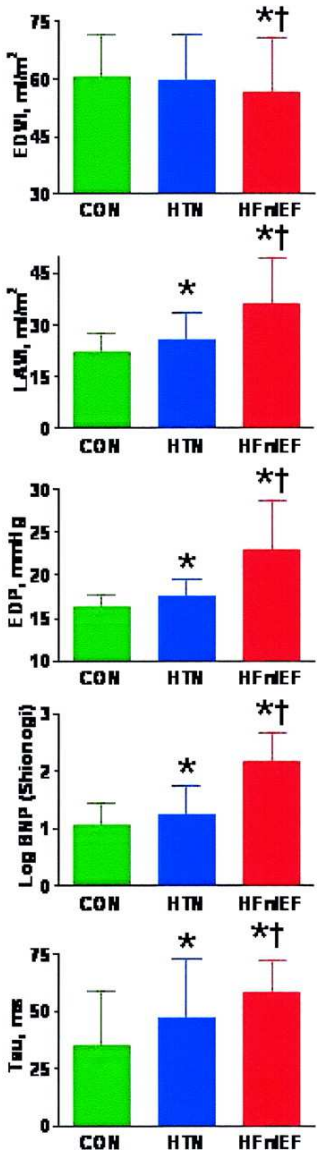
End Diastolic volume

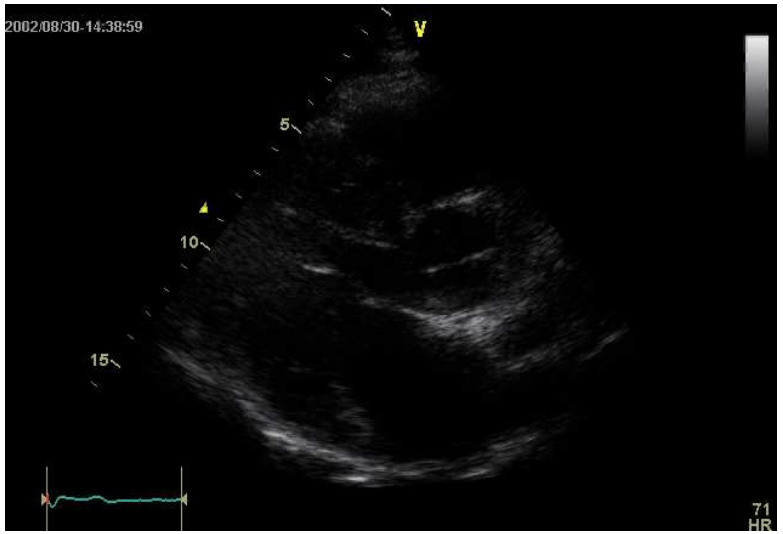
Left atrial volume

End Diastolic pressure

BNP

τ = Diastolic function time





Carolyn S.P. Lam et al. Circulation. 2007;115:1982-1990

Stratified Approach to Diagnosis and Treatment of Resistant Hypertension

1. **ABPM / HBPM**
2. Identify contributing lifestyle factors
3. Discontinue / minimize drugs that ↑ BP
4. Investigate for secondary causes of hypertension
5. Maximize and optimize pharmacotherapy
6. Consider interventional procedures

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Stratified Approach to Diagnosis and Treatment of Resistant Hypertension

1. ABPM / HBPM
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Suboptimal adherence (concordance)

- Case report: Mrs PC 76
  HT 15y
- Atenolol 100 mg, Enalapril 20 mg, Amlodipine 10 mg, Doxazosin 8 mg, Bendroflumethiazide 2.5 mg, Amiloride 5 mg.
- Referred for specialist opinion
- 177/79 mm Hg
- Heart sounds normal; heart rate 88, regular

Suboptimal adherence (concordance)

Case report: Mrs PC
76 HT 15y

- Admitted as day case – given her own medication
- Collapse in hospital shop
- BP 70/40 mm Hg

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Suboptimal Regimens

- Switching between monotherapies
- Poor combinations
- Side effects of other drugs
- Diet

Diet

- Salt restriction
- Weight loss
- Exercise

21 August 2013

Dear Dr

47

Thank you very much indeed for asking me to examine Mrs Axxx and it was a pleasure to meet Sxxx today. Mrs Axxxx has been treated for high blood pressure for about 20 years, and has been on Bendroflumethiazide 2.5 mg for a long time.

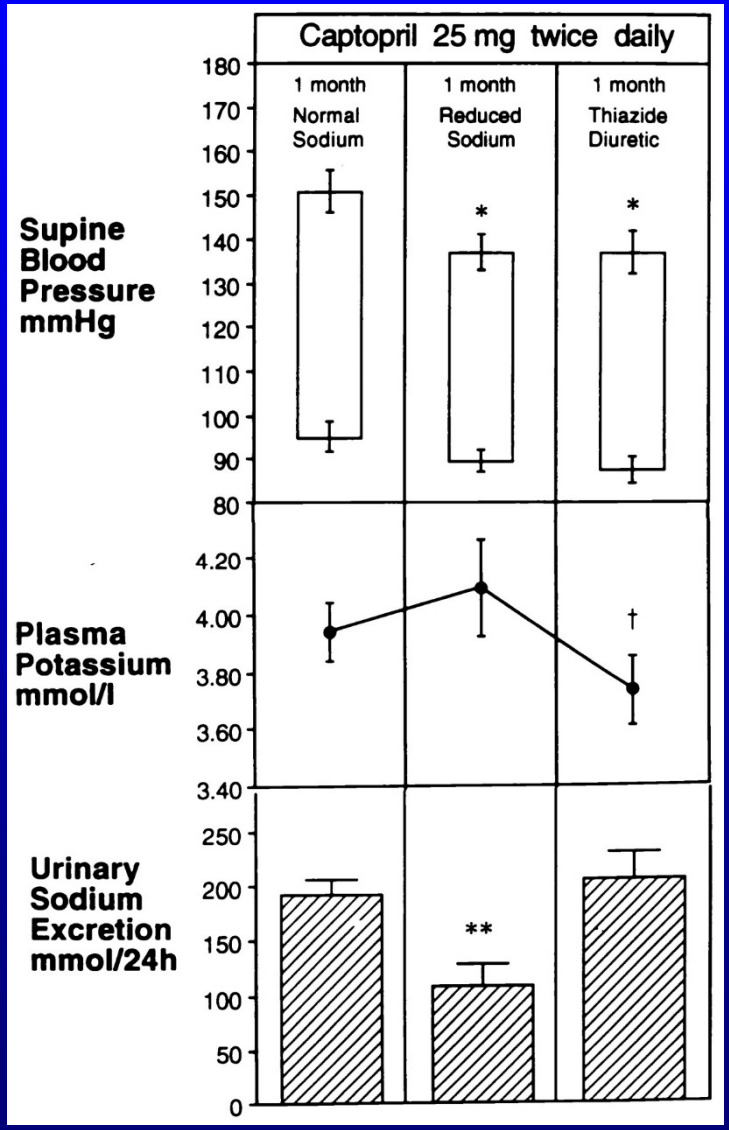
She looks after her health and measures blood pressure at home. This is variable but is often around 150/80 mmHg. This is using an Omron machine, approved by the British Hypertension Society.

You performed ambulatory blood pressure monitoring, averaging 164/94 mmHg without a nocturnal dip, although she did feel rather tense with the device insitu.

Sxxxx consumes some salt and is on no other medication.

On examination she looked well, blood pressure 165/90 mmHg, gradually falling to 151/89 mmHg.

Effects of salt restriction on blood pressure in ACEi treated patients



Singer D et al.
Hypertension
1995;25:1042-1044

Mrs S.A. Clinical Progress

- Only alteration – salt restriction and switch to LoSalt (K+ based)
- HBPM ~ 137/78 mm Hg

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NSAIDs and BP Control

Case Presentation:

AR 55 y/o man 12 year HT & arthritis.

HBPM ~156/94 mm Hg. HCTZ 25 + Losartan 100 mg daily.

Celebrex 200 mg 1–2 /d

O/E: Office BP 162/98 mm Hg & BMI 29

Rx: Switch COX 2 to paracetamol, follow the DASH Eating Plan and take more exercise.

Egan BM, unpublished

NSAIDs and BP Control (follow up)

1 month follow up visit:

Paracetamol 500 mg bd, HCTZ+ Losartan

Too busy to change eating and exercise patterns.

BP 118/72 mm Hg, BMI unchanged

Re-challenge with celocoxib X 2 raises BP 40 – 50/20 – 25 mmHg within 1–2 days with return to normal BP values within 2–3 days.

Egan BM, unpublished

Is salt bad for you?

How much should salt should we consume per day?

1-3 g

3-5g

5-7g

7-10g

European Heart Journal (2017) **0**, 1–9
doi:10.1093/eurheartj/ehw549

REVIEW

Controversies in Cardiovascular Medicine

The technical report on sodium intake and cardiovascular disease in low- and middle-income countries by the joint working group of the World Heart Federation, the European Society of Hypertension and the European Public Health Association

Giuseppe Mancia[1]*, Suzanne Oparil[2], Paul K. Whelton[3], Martin McKee[4], Anna Dominiczak[5], Friedrich C. Luft[6], Khalid AlHabib[7], Fernando Lanas[8], Albertino Damasceno[9], Dorairaj Prabhakaran[10], Giuseppe La Torre[11], Michael Weber[12], Martin O'Donnell[13], Sidney C. Smith[14], and Jagat Narula[15]

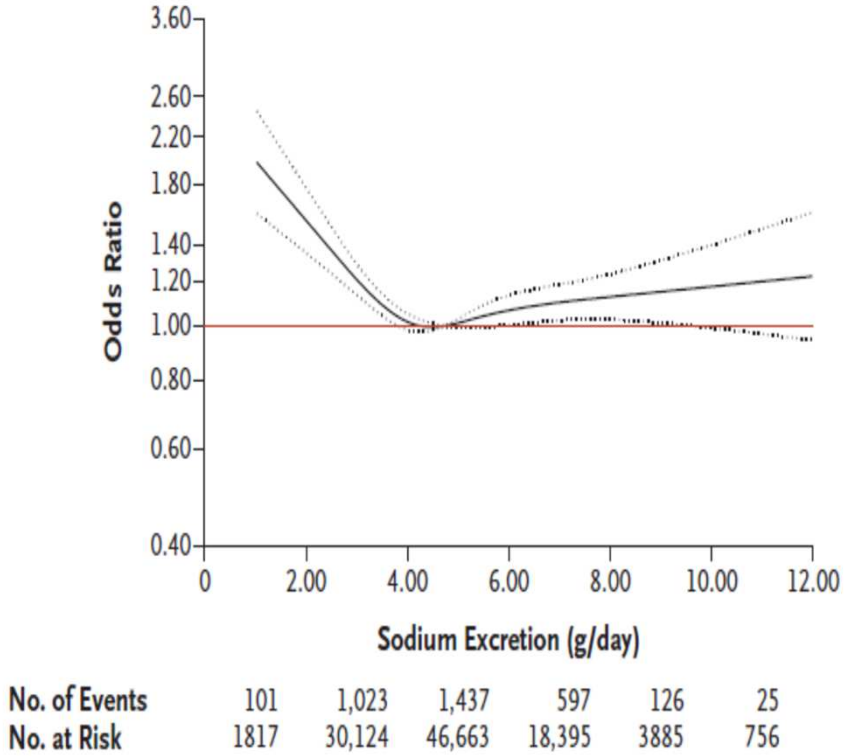
[1]University of Milano–Bicocca, Piazza dell'Ateneo Nuovo, 1, 20126 Milano, Italy; [2]University of Alabama at Birmingham, 703 19th St. South, ZRB 1034, Birmingham, Alabama 35294-0007; [3]Department of Epidemiology, Tulane University School of Public Health and Tropical Medicine, 1440 Canal Street, New Orleans, Louisiana 70112, USA;

Is salt bad for you?

- Prospective cohort studies have identified the optimal range of sodium (3–5 g/ day), where the risk of cardiovascular disease and death is lowest.
- Therefore, there is consistent evidence from clinical trials to support reducing sodium intake to <5 g/day in populations, but inconsistent evidence for further reductions below a moderate intake range (3–5 g/day).
- Unfortunately, there are no large randomized controlled trials comparing low sodium intake (< 3 g/day) to moderate sodium intake (3–5 g/day) in general populations.
- Until such trials are completed, it is likely that controversy about optimal sodium intake range will continue

Sodium Intake and Mortality + CVD (PURE)

Primary Outcome



CV Events and Death

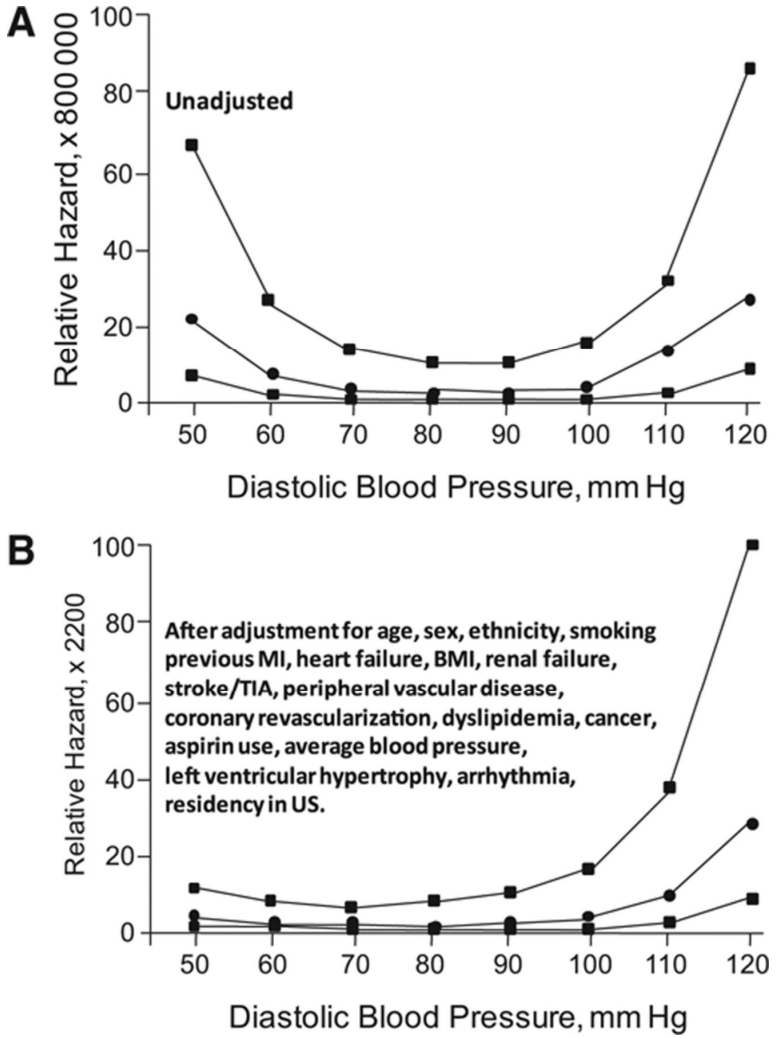
(17 Countries, N=101,945; 3,317 events)

- International Population
  - N America/Europe/Africa/Asia/S America
- Average CV Risk (General population)
  - Hx CVD (8.3%)
  - Hypertension (41.5%)
  - Diabetes (9.1%)
  - Current smoking (18.9%)
- 3.7 years Follow-up
- Morning fasting urine to estimate 24-hour intake (Kawasaki formula)
- Mean intake: 4.9g/day

PURE Investigators *NEJM* 2014

Is there a J-shaped curve for BP?

Unadjusted (A) and adjusted (B) relation between achieved (average in-treatment) diastolic blood pressure and risk of primary outcome in hypertensive patients with coronary artery disease enrolled in the International Verapamil-Trandolapril Study.



Verdecchia P et al. Hypertension. 2014;63:37-40

Causes of Secondary Hypertension

Renal artery stenosis
Sleep apnoea
Drug-induced or drug-related hypertension (e.g. NSAIDs)
Chronic renal disease
Primary aldosteronism
Renovascular disease
Chronic steroid therapy and Cushing's syndrome
Pheochromocytoma
Coarctation of the aorta
Thyroid or parathyroid disease

University of Glasgow

Brady AJB, et al. Mayo Clinic Textbook of Cardiology 2013

2013 Standard Investigations for Secondary Hypertension

U&Es, Ca^{2+}, creat, Lipids, LFTs, TFTs, glucose
urine Albumin/creatinine ratio, 24h urinary catecholamines
ECG + echo
24h ABPM + HPBM
Renin + Aldosterone + cortisol
MRI with renal angiography

University of Glasgow

Brady AJB, et al. Mayo Clinic Textbook of Cardiology 2013

Stratified Drug Therapy for Resistant Hypertension

Table 1. Dates of discovery of therapies to treat hypertension

Year	Blood pressure treatment
2000 BC–	Acupuncture, venesection, leeches, cupping
1900–	Sodium thiocyanate
1920–	Surgical sympathectomy
1930–	Reserpine
1940–	Intravenous pyrogens, ganglion blocking drugs, sulphanilamide, Kempner diet (low salt)
1950–	Thiazide-type diuretics (chlorothiazide), aldosterone-receptor antagonist (spironolactone), hydralazine, guanethidine
1960–	Methyldopa, beta blocker (propranolol), loop diuretics (furosemide)
1970–	Central alpha$_2$-agonist (clonidine), alpha$_1$-blocker (prazosin), angiotensin-converting enzyme (ACE) inhibitors (captopril), calcium channel blocker (verapamil)
1980–	Potassium-sparing diuretic (amiloride)
1990–	Angiotensin-receptor blockers (losartan)
2000–	Direct renin inhibitor (aliskiren), renal sympathetic denervation (Symplicity™)

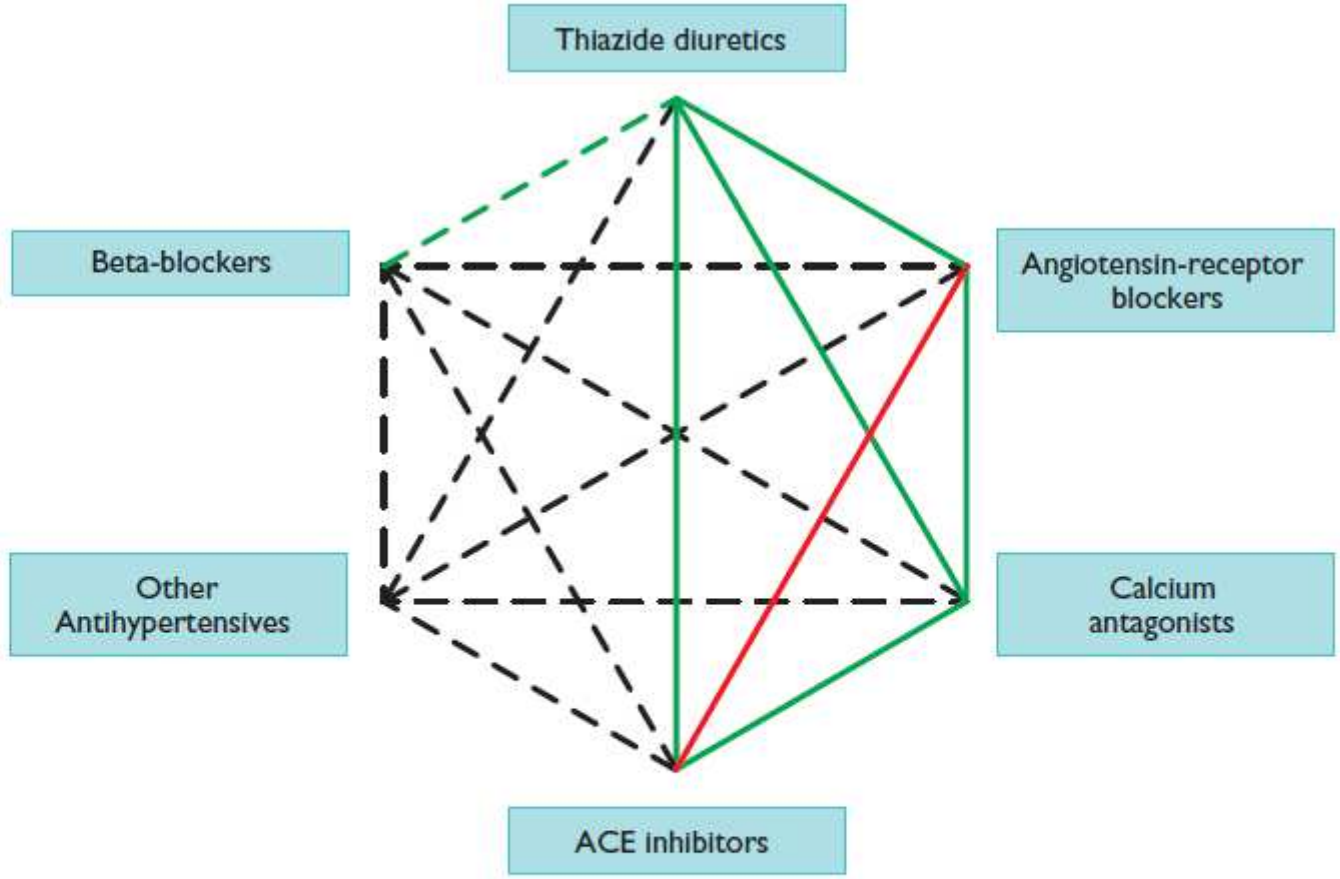
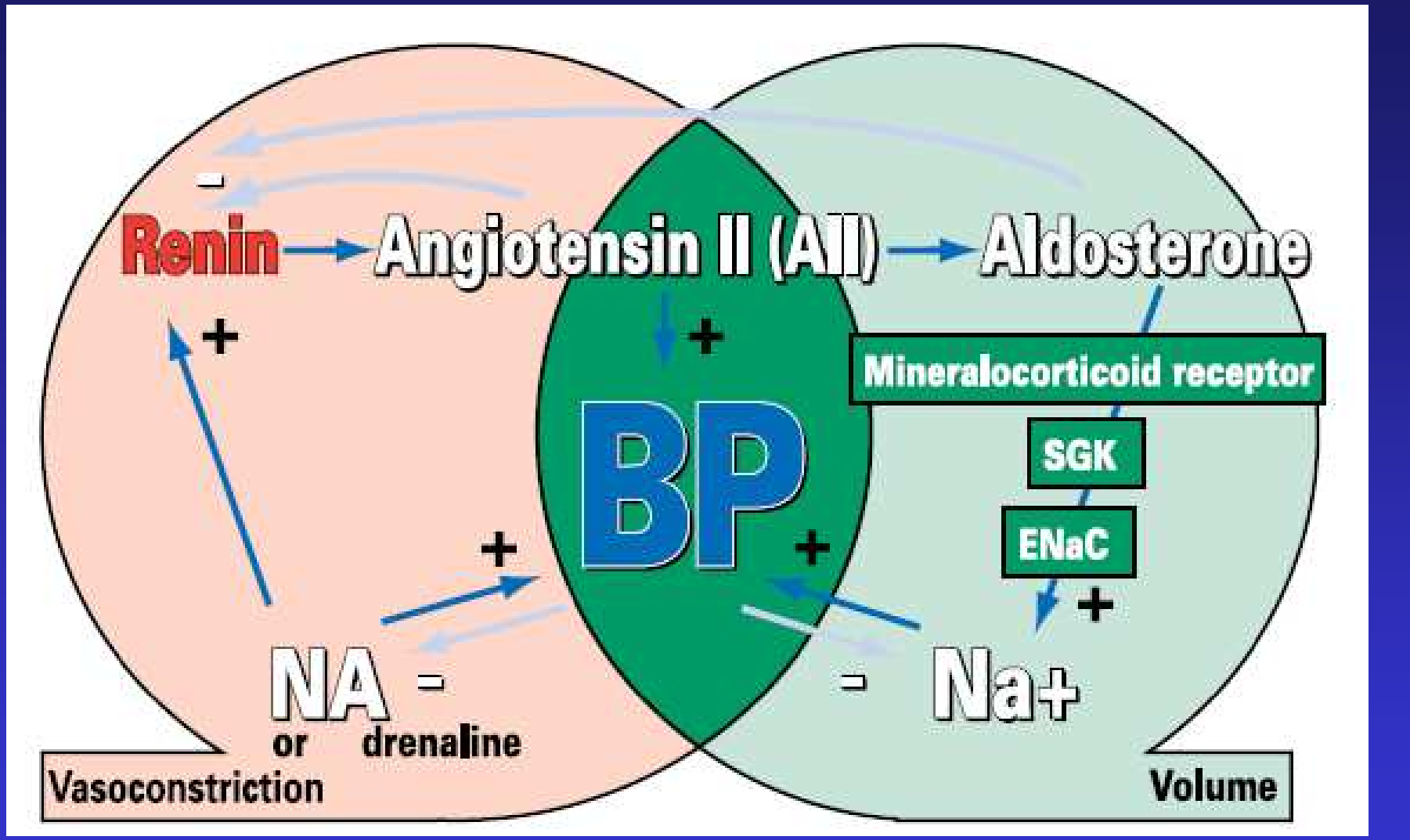
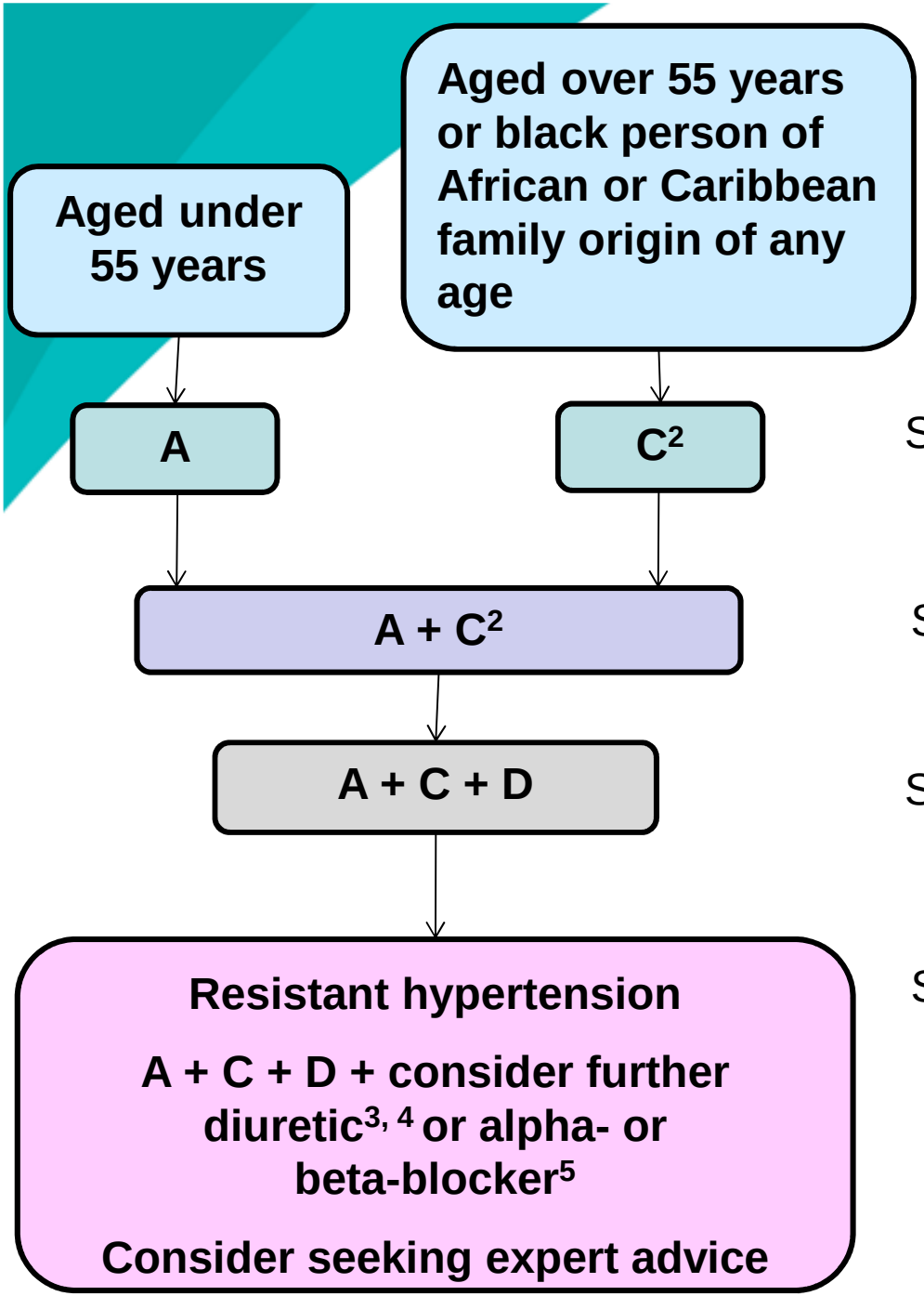


Figure 4 Possible combinations of classes of antihypertensive drugs. Green continuous lines: preferred combinations; green dashed lin combination (with some limitations); black dashed lines: possible but less well-tested combinations; red continuous line: not recommend bination. Although verapamil and diltiazem are sometimes used with a beta-blocker to improve ventricular rate control in permanent atri lation, only dihydropyridine calcium antagonists should normally be combined with beta-blockers.

ESC/ESH 2013 Guidelines. Mancia G et al. Eur Heart J

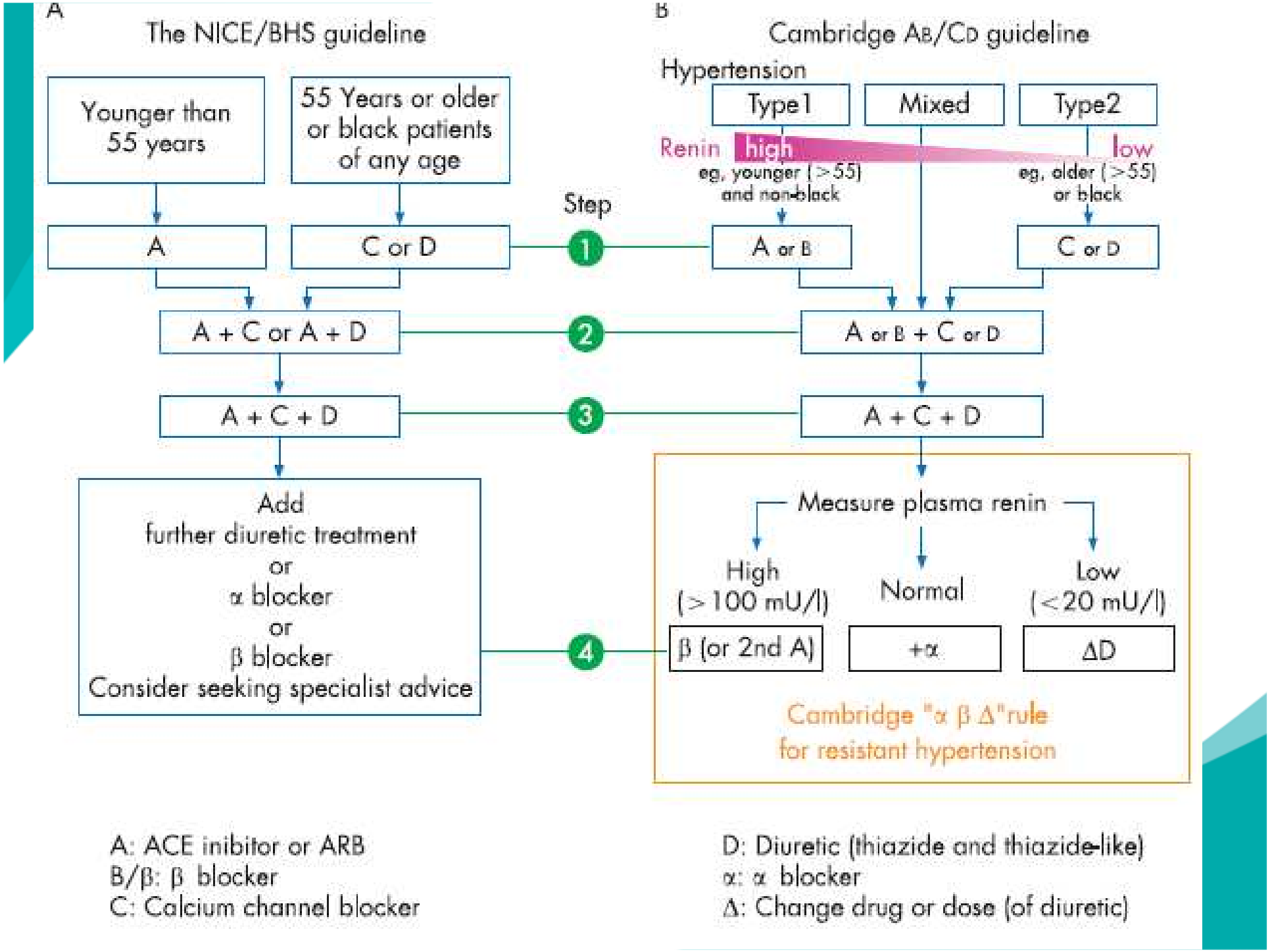

Renin
Angiotensin II (AII)
Aldosterone
BP
Mineralocorticoid receptor
SGK
ENaC
NA
or drenaline
Na+
Vasoconstriction
Volume

Drug treatment



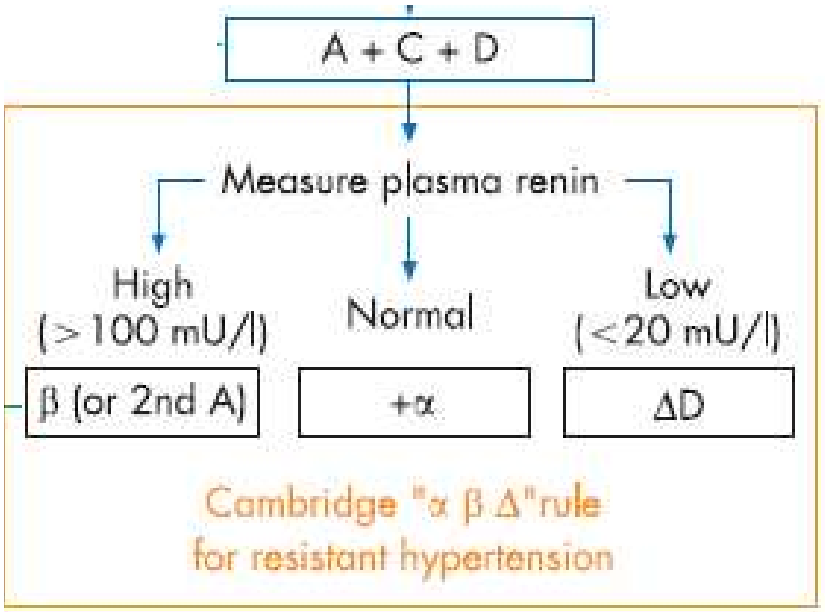
Key
A – ACE inhibitor or angiotensin II receptor blocker (ARB)[1]
C – Calcium-channel blocker (CCB)
D – Thiazide-like diuretic

2016 NICE-BIHS Guidance on Hypertension. www.bhsoc.org


A
The NICE/BHS guideline
Younger than 55 years
55 Years or older or black patients of any age
A
C or D
A + C or A + D
A + C + D
Add
further diuretic treatment
or
α blocker
or
β blocker
Consider seeking specialist advice
Step
1
2
3
4
B
Cambridge AB/CD guideline
Hypertension
Type1
Mixed
Type2
Renin high
low
eg, younger (>55) and non-black
eg, older (>55) or black
A or B
C or D
A or B + C or D
A + C + D
Measure plasma renin
High (>100 mU/l)
Normal
Low (<20 mU/l)
β (or 2nd A)
+α
ΔD
Cambridge "α β Δ" rule
for resistant hypertension
A: ACE inibitor or ARB
B/β: β blocker
C: Calcium channel blocker
D: Diuretic (thiazide and thiazide-like)
α: α blocker
Δ: Change drug or dose (of diuretic)

How to investigate and treat True Resistant Hypertension

Patient established on optimal triple therapy



D: Diuretic (thiazide and thiazide-like)
α: α blocker
Δ: Change drug or dose (of diuretic)

Other drugs for resistant hypertension

- **Doxazosin**
- **Diuretics**
- Nitrates
- Hydralazine
- Moxonidine
- Minoxidil
- Direct renin inhibitors – Aliskerin
- Methyl dopa

Optimal Treatment of Drug Resistant Hypertension
PATHWAY-2

Principal Results

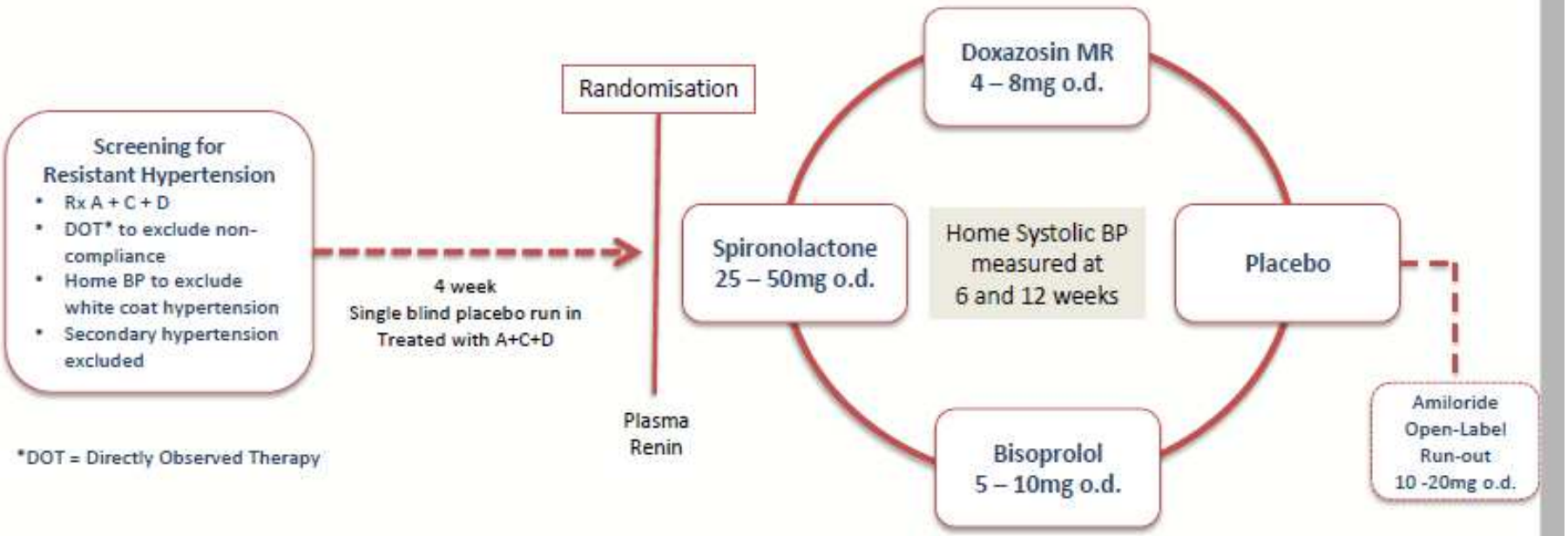
Bryan Williams, Tom MacDonald and Morris Brown
on behalf of the PATHWAY Investigators

British Heart Foundation
BHS British Hypertension Society
NHS National Institute for Health Research
ESC CONGRESS LONDON 2015
Hot Line presentation
www.escardio.org/ESC2015

PATHWAY
Clinical Trials in Hypertension

PATHWAY-2 Study Design

Double blind, Randomised, Placebo-Controlled, Cross-over Study



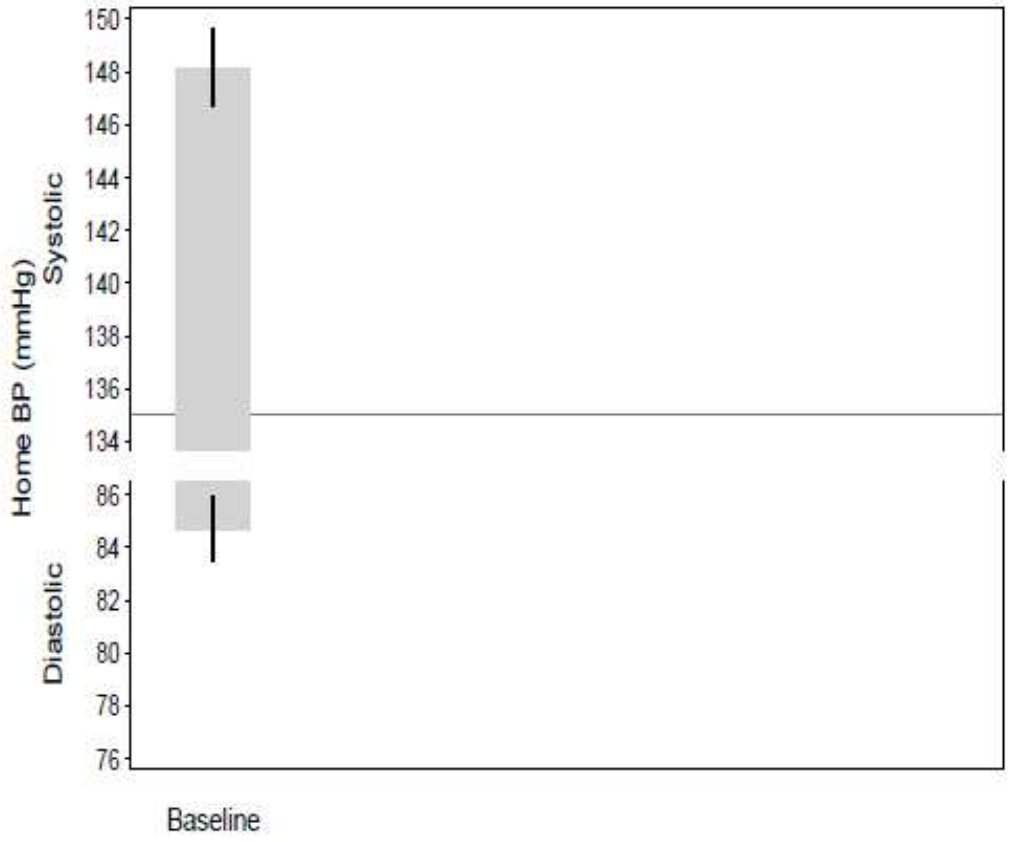
*DOT = Directly Observed Therapy

- 12 weeks per treatment cycle
- Forced titration; lower to higher dose at 6 weeks
- No washout period between cycles

Williams B, et al. BMJ Open, 2015

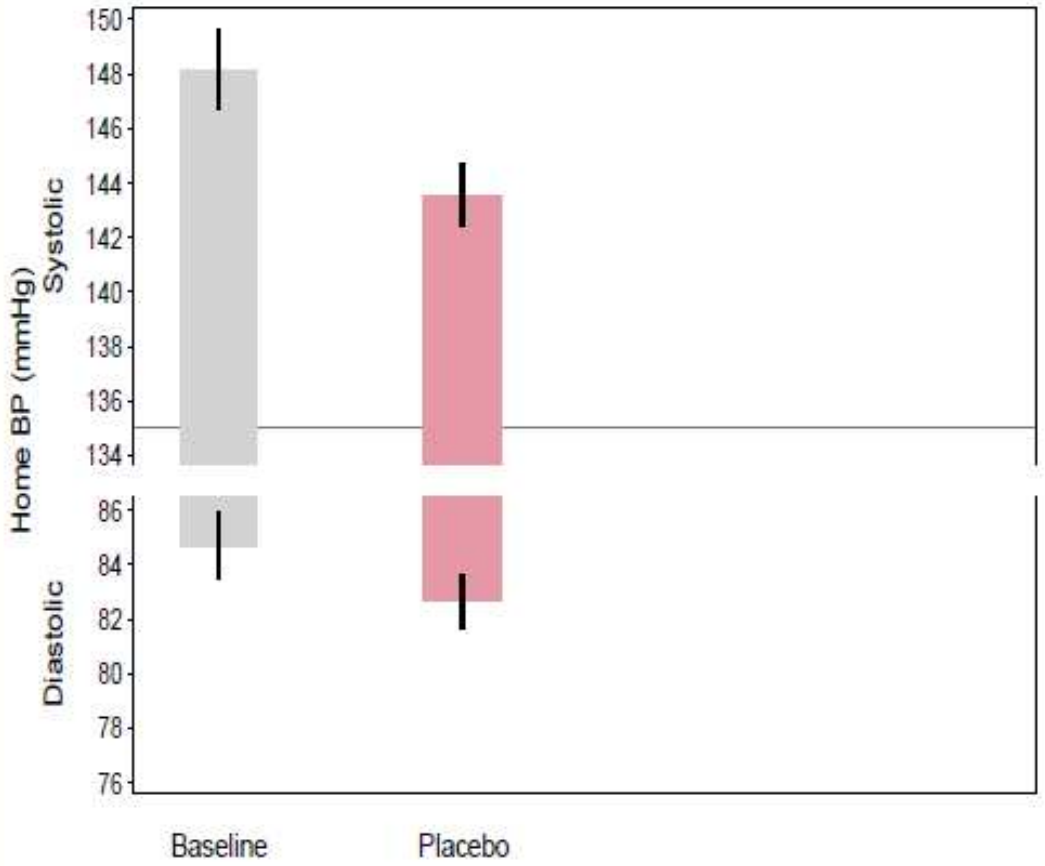
PATHWAY 2
Clinical Trials in Hypertension

Primary Outcome



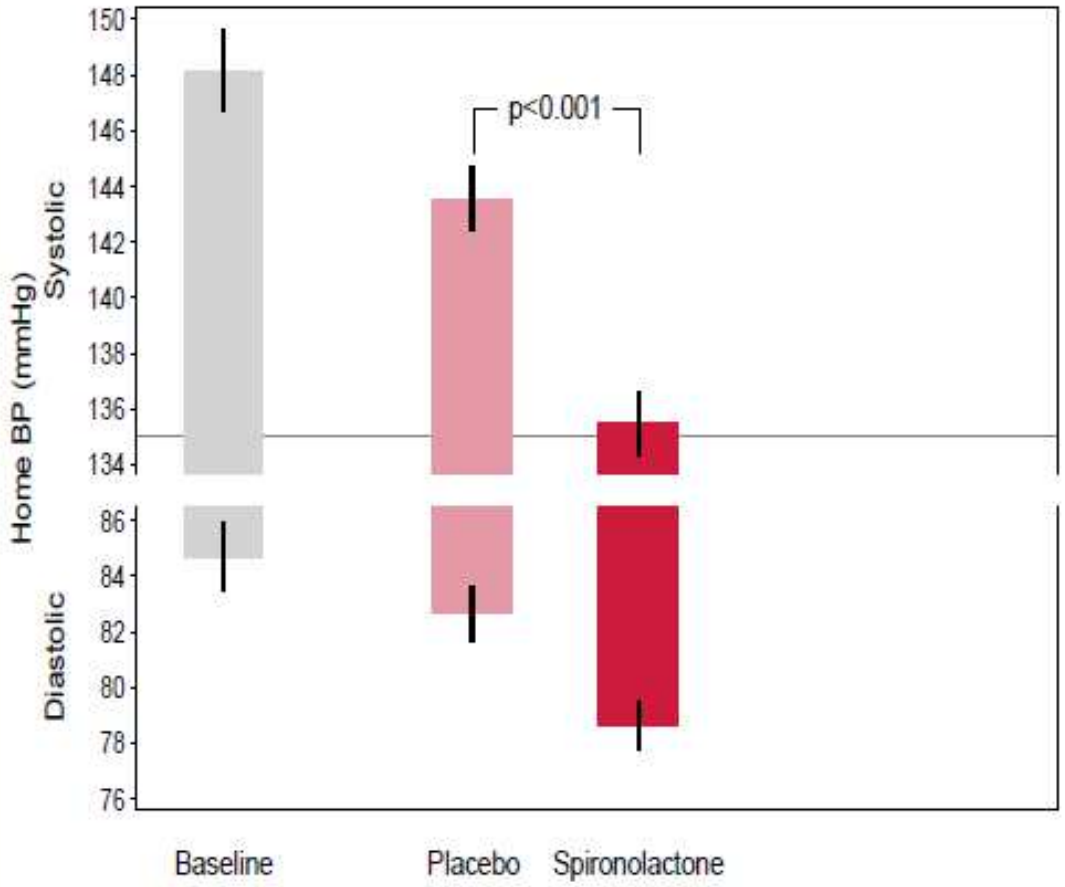
PATHWAY
Clinical Trials in Hypertension

Primary Outcome



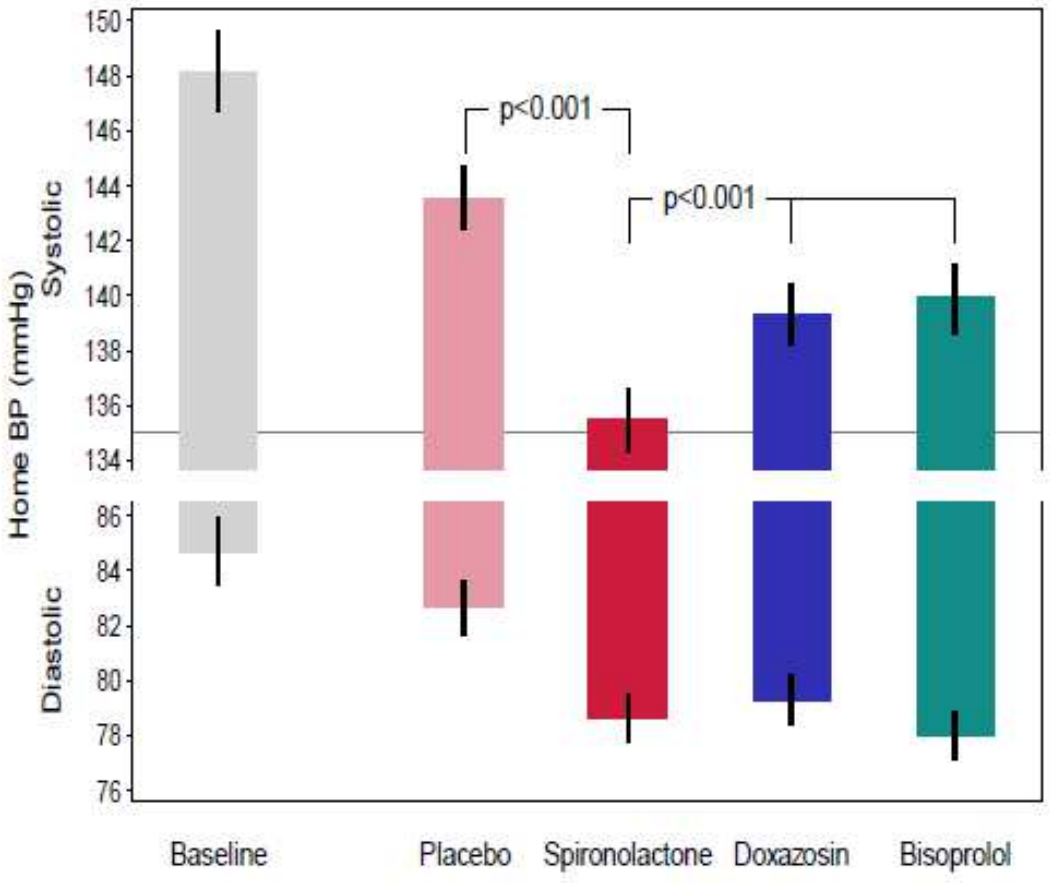
PATHWAY 2
Clinical Trials in Hypertension

Primary Outcome



PATHWAY 2
Clinical Trials in Hypertension

Primary Outcome



PATHWAY
Clinical Trials in Hypertension

Prevention And Treatment of Hypertension With Algorithm based therapY (PATHWAY)

Amiloride-hydrochlorothiazide versus individual diuretic effects on glucose tolerance and blood pressure

PATHWAY-3

Principal Results

Morris Brown, Bryan Williams, Tom Macdonald

on behalf of the British Hypertension Society's PATHWAY Investigators

British Heart Foundation

BHS
British Hypertension Society

NHS
National Institute for Health Research

Study Methods and Design

PATHWAY 3
Clinical Trials in Hypertension

Screening
Uncontrolled hypertension (SBP > 140 mmHg)
Eligible for diuretic treatment
At least 1 additional component of metabolic syndrome

Randomisation
(440 patients)

Amiloride	Amiloride + HCTZ	HCTZ
10mg to 20mg	5mg to 10mg 12·5 to 25 mg	25mg to 50mg
Force-titration at 12 weeks	*Force-titration at 12 weeks*	*Force-titration at 12 weeks*

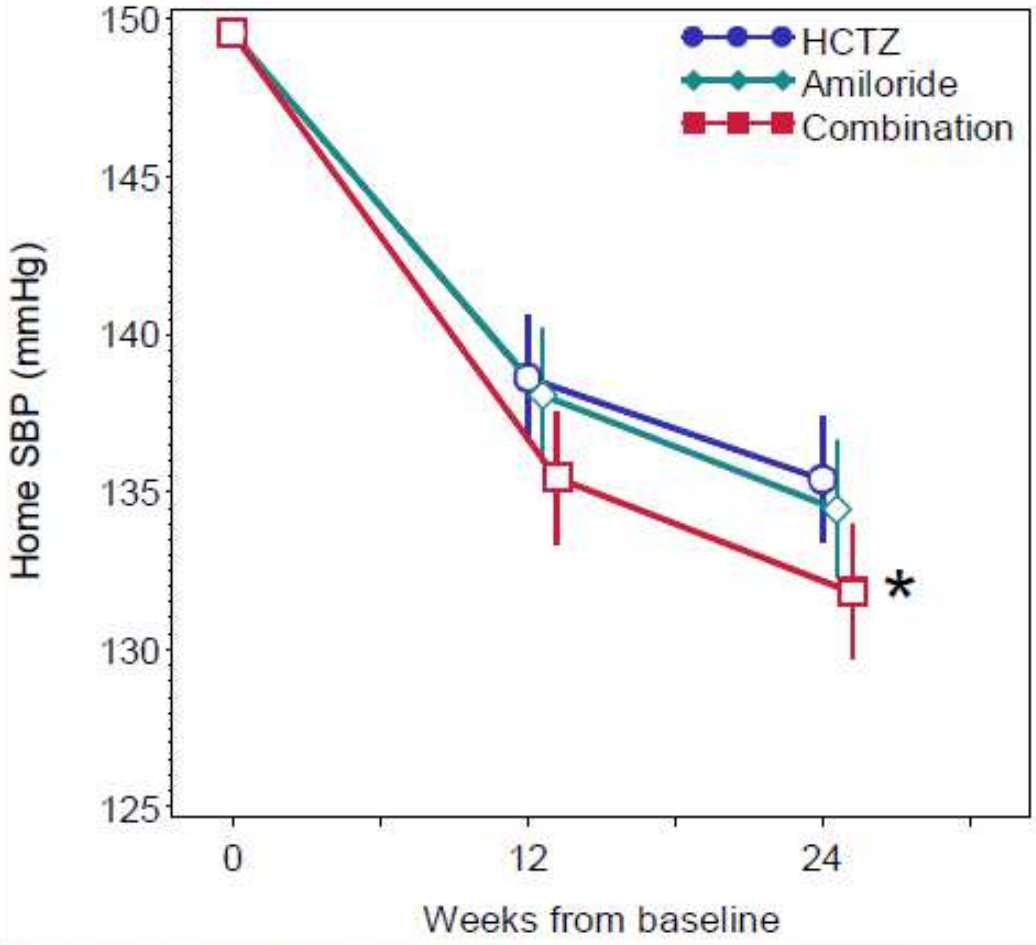
Primary Outcome
Difference from baseline in 2-hr glucose at 12 & 24 weeks, on oral glucose tolerance test (OGTT)

Principal Secondary Outcome
Difference in home SBP at 12 and 24 weeks.

PATHWAY
Clinical Trials in Hypertension

Secondary endpoints

Blood Pressure reduction



Home SBP (mean, 95% CI) adjusting for baseline covariates

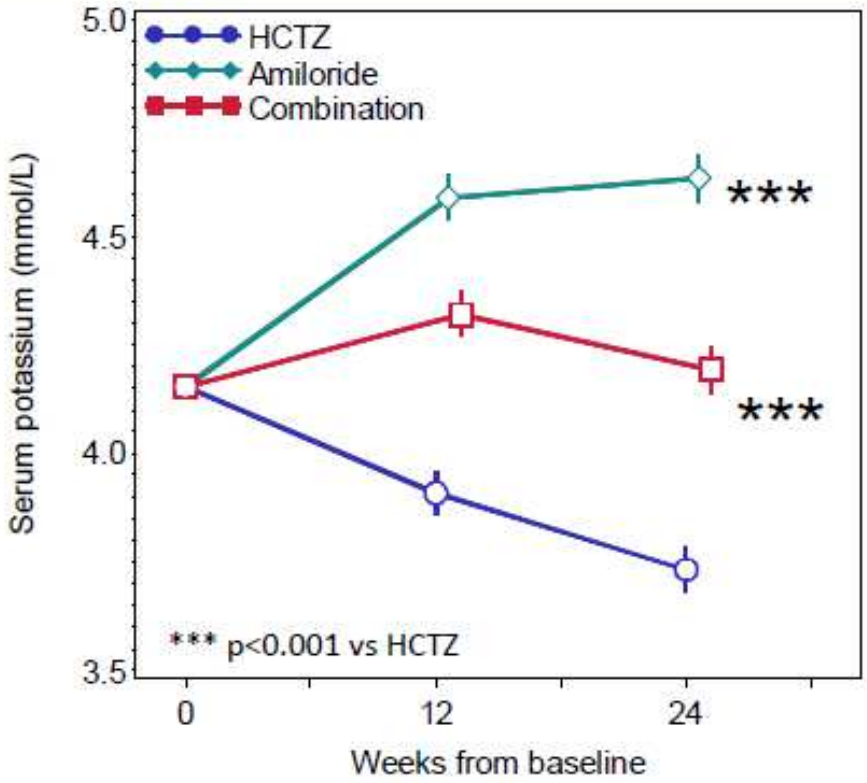
* p=0.02 for combination vs HCTZ at week 24.

Across weeks 12 (low-dose) and 24 (high-dose), BP fall on combination of amiloride and HCTZ was 3·4 (0·9, 5·8) mmHg greater than on HCTZ (p=0·007)

PATHWAY 3
Clinical Trials in Hypertension

Secondary Outcomes

Potassium

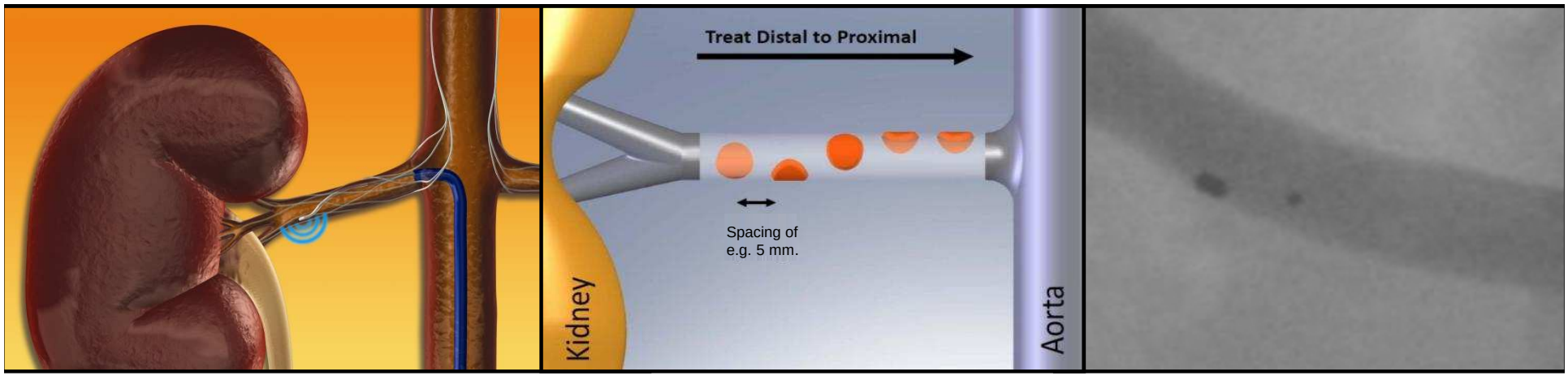


Mean (95% CI) serum potassium, on a model adjusting for baseline covariaties

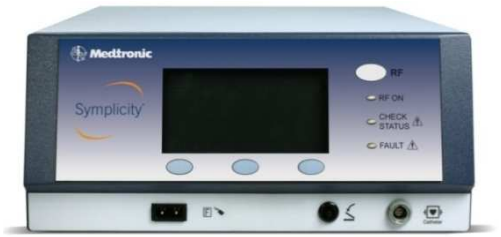
Interventional Techniques

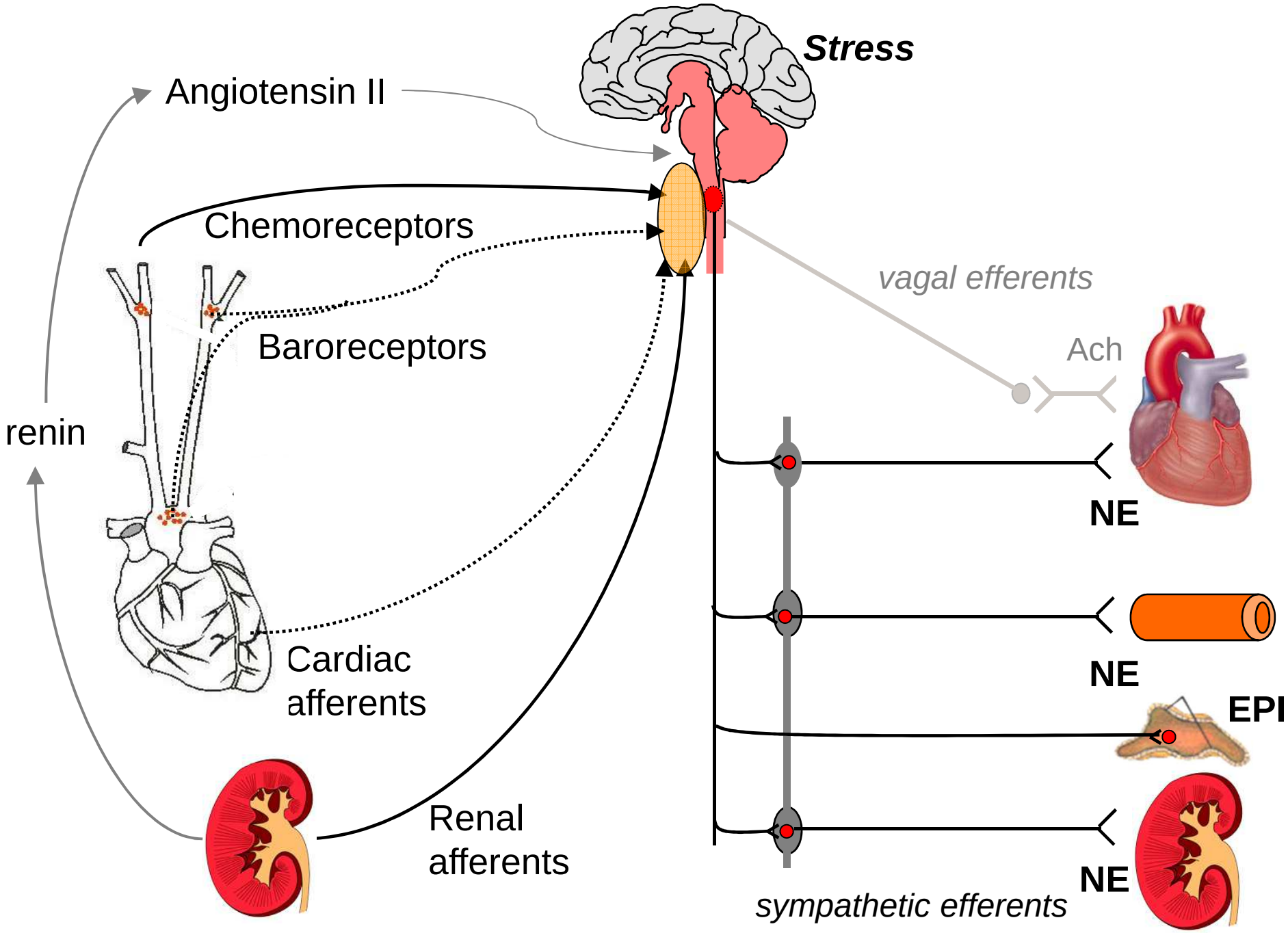
- Renal Denervation
- A-V fistula formation
- Renal Artery Stenosis
- Other techniques

Catheter-Based Approach for renal denervation



- Renal artery access via standard interventional technique
- 4-6 two-minute treatments per artery
- Proprietary RF generator
  - Automated
  - Low power
  - Built-in safety algorithms




Stress
Angiotensin II
Chemoreceptors
Baroreceptors
renin
Cardiac
afferents
Renal
afferents
vagal efferents
Ach
NE
NE
EPI
NE
sympathetic efferents

PHYSIOLOGIC EFFECTS OF EXTENSIVE SYMPATHECTOMY FOR ESSENTIAL HYPERTENSION: FURTHER OBSERVATIONS *

By Edgar V. Allen, M.D., F.A.C.P., and Alfred W. Adson, M.D.,
Rochester, Minnesota

In previous communications we have presented our experiences with extensive sympathectomy for essential hypertension.[1-5] We are now reporting our experiences with a large number of patients and with the effects of operation on patients who have been observed over longer periods of time than were those of the earlier reports. We have continued to treat patients with essential hypertension by extensive sympathectomy for we are impressed with the fact that essential hypertension is in many instances an extremely serious disease for which medical treatment is far from satisfactory. Prosecution of this work, the aim of which was remedy or cure while there yet was possibility of either, opened the opportunity to determine the effects of the operation on blood pressure, symptoms and health, and to learn whether the surgical treatment modified the eventual mortality in essential hypertension. It also became possible to investigate the question of whether good results of operation are transient or permanent and whether or not patients could be selected so that more of them would benefit from operation.

The surgical treatment of essential hypertension is relatively new and the only way one can gain information about the results of extensive sympathectomy is to survey a relatively large number of patients. Such a survey will draw more sharply the distinction between patients who are suitable, and those who are unsuitable for operation.

The Technic and Rationale of the Operation

The technic used was that which Adson devised and which has been described in detail elsewhere [3]; it consists of bilateral subdiaphragmatic extraperitoneal resection of the splanchnic nerves, celiac ganglions and the upper two lumbar sympathetic ganglions. First the operation is performed on one side and then, about ten days later, on the opposite side. In addition, in the first 25 operations one-third to two-fifths of each suprarenal gland was removed. This procedure apparently did not offer any advantage or disadvantage over removal of only the other structures named.

It is known that in essential hypertension the fundamental cause of the

Ann Intern Med. 1938;11(12):2151-2171

THE HEMODYNAMIC EFFECTS OF SYMPATHECTOMY IN ESSENTIAL HYPERTENSION *

By Robert W. Wilkins, M.D., James W. Culbertson, M.D., and Meyer H. Halperin, M.D., *Boston, Massachusetts*

Surgical sympathectomy has been employed so extensively for the treatment of essential hypertension that one might assume its hemodynamic effects to be completely understood. Quite to the contrary, however, very little is known concerning its direct vascular or indirect metabolic effects that will explain its success in some cases and its failure in others. Until these matters are fully understood the rationale for surgical treatment, and indeed for medical management, of essential hypertension must remain on an empirical basis. For this reason these problems have been and will continue to be the subject of long-term investigation in this laboratory.

Materials and Methods

Patients with essential hypertension selected for splanchnicectomy [1] have been made freely available for study through the active coöperation of Dr. Reginald H. Smithwick, under whose direction sympathectomy was performed. They were studied before and again, if possible within three weeks after bilateral operation, usually of the lumbodorsal type.[2] In addition, some patients were studied a third time four to 10 months after operation, whereas a few patients were studied only once—from one to nine years postoperatively.

Arterial pressure was measured with a Hamilton manometer [3] attached to a needle in the brachial or femoral artery. Cardiac output was determined by the Fick principle with the intravenous catheter method of Cournand.[4] Hepatic-portal (splanchnic exclusive of renal and adrenal) blood flow was estimated by the bromsulfalein method of Bradley et al.[5] Both before and after operation the patients, while under study, were given a number of vasomotor stimuli designed to produce, if possible, sympathetic nervous vasoconstriction.[6, 7] The most useful of these stimuli were (*a*) tilting the subject into the upright position and (*b*) having him perform the Valsalva maneuver.

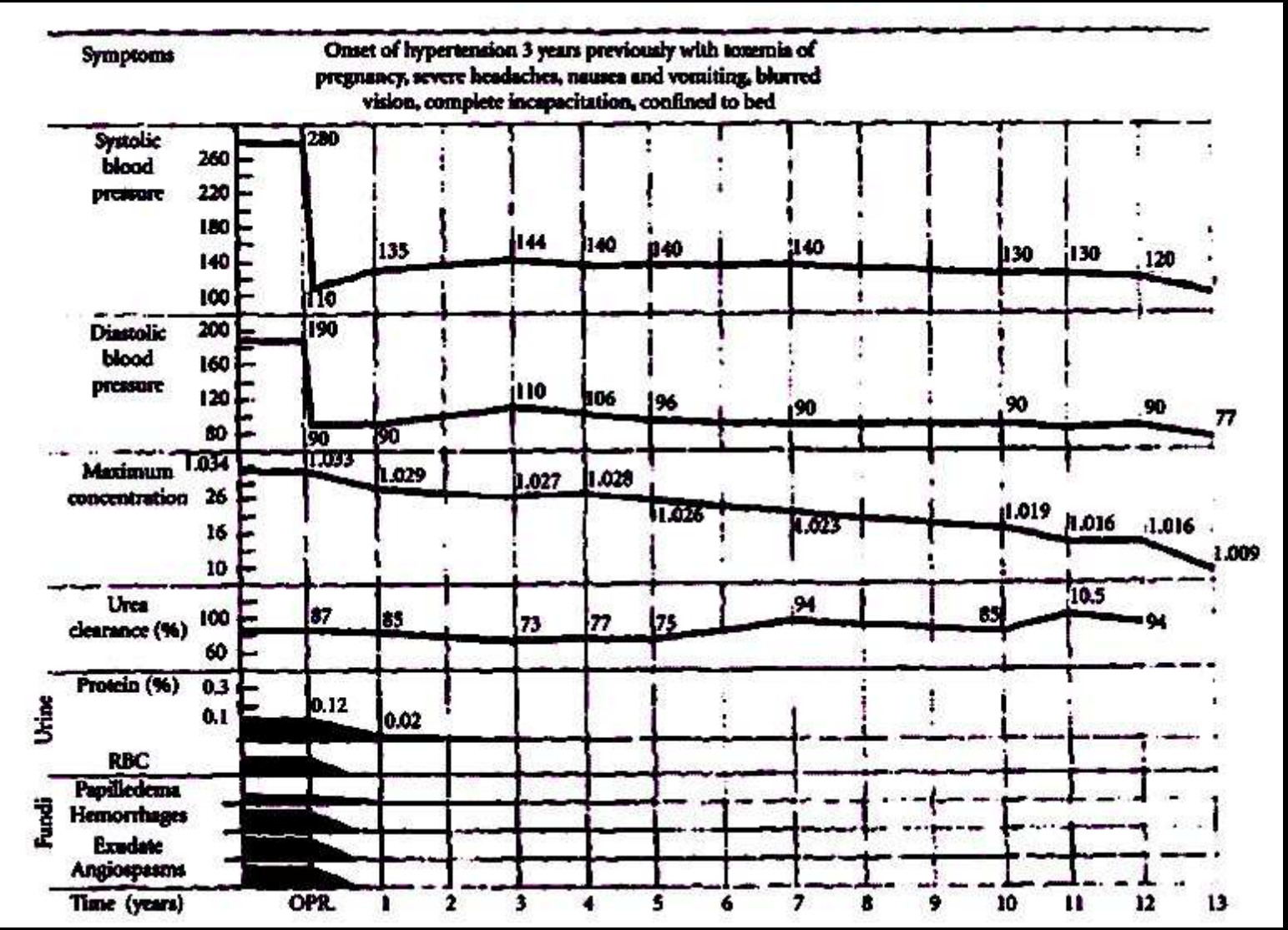
Cardiac Output. Confirming the observations of others,[8, 9] no great or consistent change was found in basal cardiac output of patients after sympathectomy as compared with before, regardless of how much the arterial

* Presented before the Fifth General Session of the Twenty-ninth Annual Session of the American College of Physicians in San Francisco, California, April 23, 1948.

From the Robert Dawson Evans Memorial, Massachusetts Memorial Hospitals, and the Department of Medicine, Boston University School of Medicine, Boston, Massachusetts.

Ann Intern Med. 1949;30(2):291-306.

Long Term Effect of Renal Denervation in Human Hypertension



Am J Surg 1948; 75: 48-68

Case Report

- 68 year old female
- First diagnosed with hypertension 1979 (age 36)

2007- 186/86 spironolactone/ramipril/atenolol/valsartan/ amlodipine/furosemide

Renin/aldo profile in normal range

MRI adrenals normal

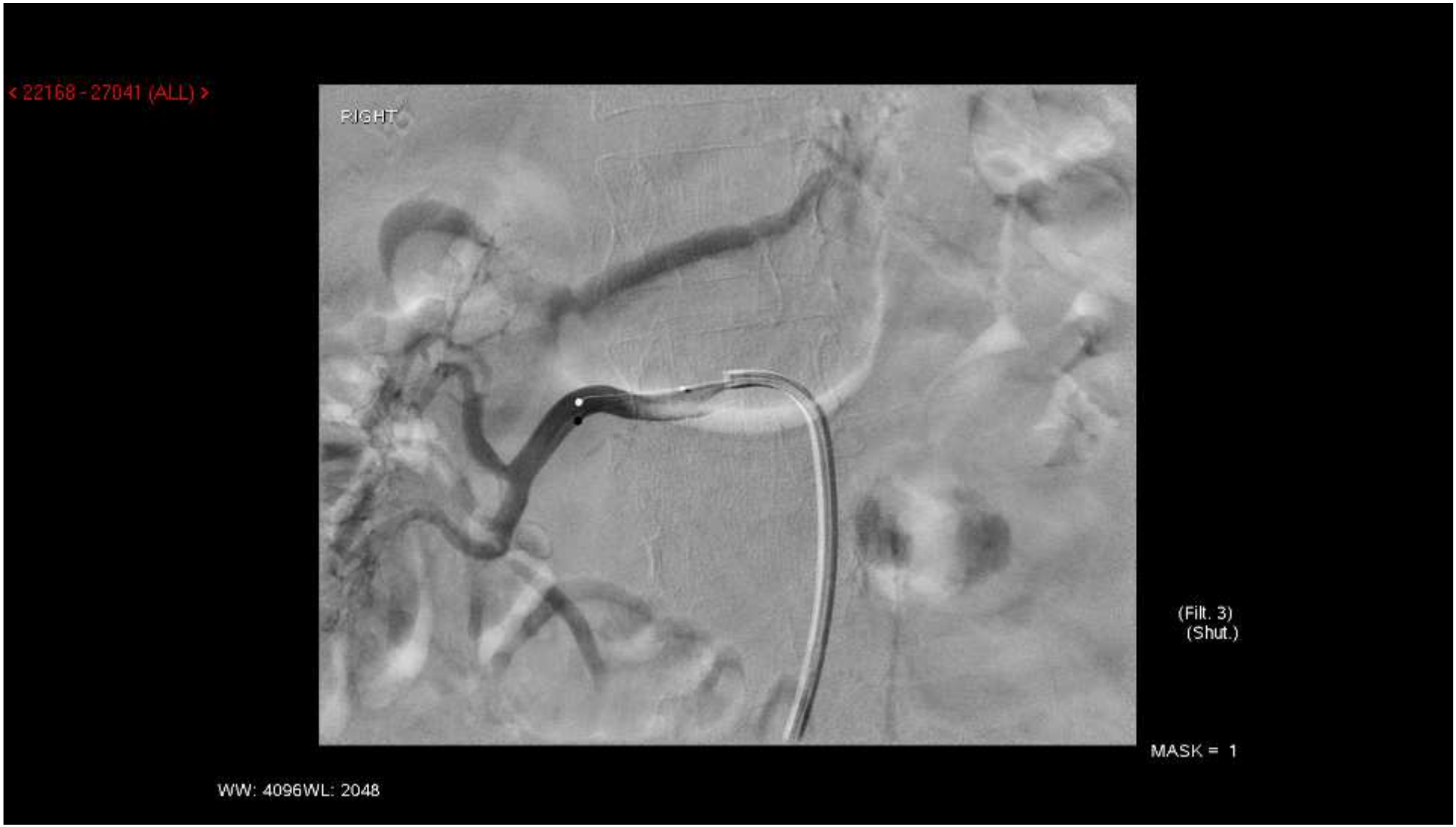
2008- 187/99 aliskerin added

- **20/09/10- admitted for renal denervation as part of SYMPLICITY-2-HTN trial**

- **Admission BP 220/120 (same therapy)**

- **Pre-procedure 190/100**

University of Glasgow



- **Post procedure BP 163/77**
- **No antihypertensives given that night**
- **Next morning 135/74 pre therapy**
- **Discharged on atenolol 25mg**
- **Stopped 1 week later**
- **1 year later BP 134/77, no antihypertensive Rx**

Creatinine 76, ACR 10.5

Glasgow Renal Artery Sympathectomy Study (GRASS) summary

Mark P, Brady AJB, et al. J Human Hypertension 2013 suppl

- Promising treatment for resistant hypertension
- In our hands approx 20-25% 'non responder'
- The rest- variable degrees of response representing 'real world experience'
- Considerable need for pre, peri, post procedural care- i.e. not a day case procedure
- Longer term studies in real world and in better defined patient groups required

Delaying Cardiac Surgery for Dental Work May Increase Risks

Study Begs FDA Rethink of CT Scan Warning on Cardiac Devices

Company Fretted Over Dabigatran Report, Documents Show

Cardiology 2014: Bob Harrington and Mike Gibson

Heartwire

Renal Denervation Fails in SYMPLICITY HTN-3

Michael O'Riordan

January 09, 2014

MINNEAPOLIS, MN — The **SYMPLICITY HTN-3** trial, a phase 3 study testing catheter-based renal denervation for the treatment of resistant hypertension, failed to achieve its primary efficacy end point, according to a statement released by Medtronic [1].

Despite no safety concerns, the study, which randomized 535 treatment-resistant hypertension patients, failed to show that treatment with the investigational procedure resulted in a

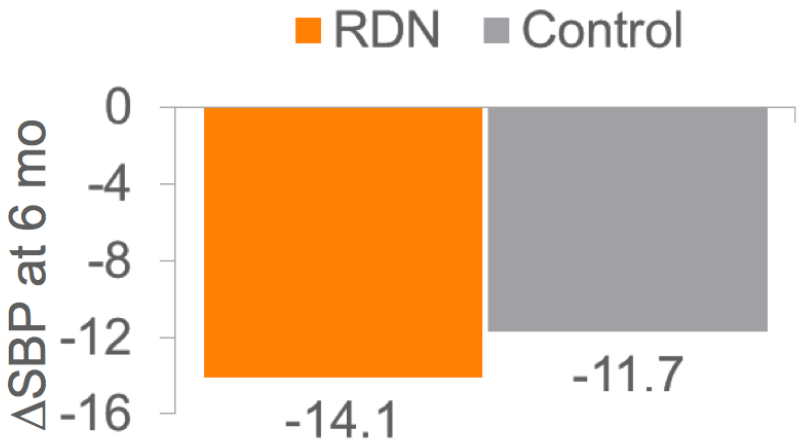
EDITORS' RECOMMENDATIONS

BP Reductions With Renal Denervation Durable to 30 Months

Hype or Hope? Renal Denervation Hits the Headlines

MOST POPULAR ARTICLES

Symplicity HTN 3-Primary efficacy endpoint



	RDN	Control	*P* value
Baseline SBP	179.7	180.2	0.765
6 mo SBP	165.6	168.4	0.260
Change	*-14.1* *P < 0.001*	*-11.7* *P < 0.001*	*0.255*[1]

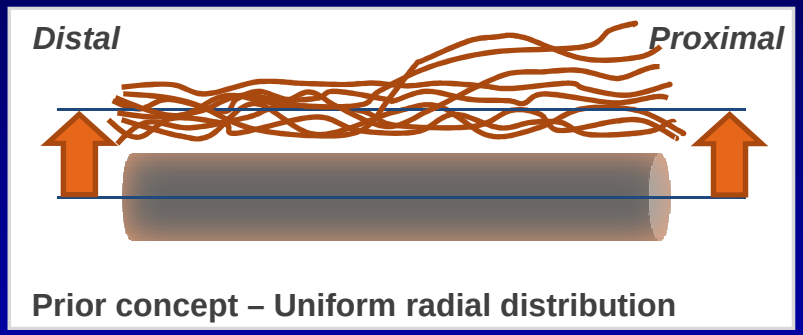
-2.39 (-6.89, 2.12), *P* = 0.255 (Primary analysis with 5 mm Hg superiority margin)

- Did not meet primary efficacy endpoint

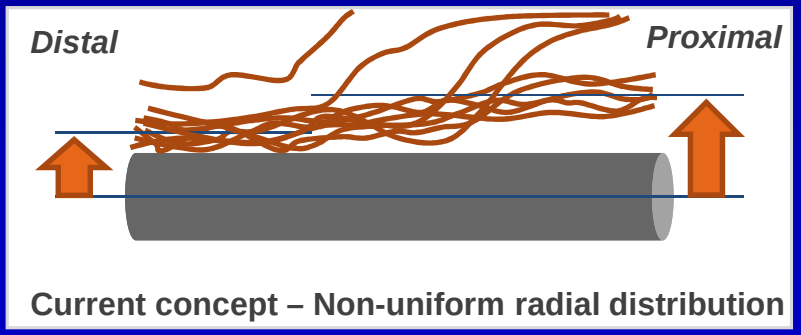
Bhatt DL, NEJM 2014

Our View of Renal Nerve Distribution Has Changed

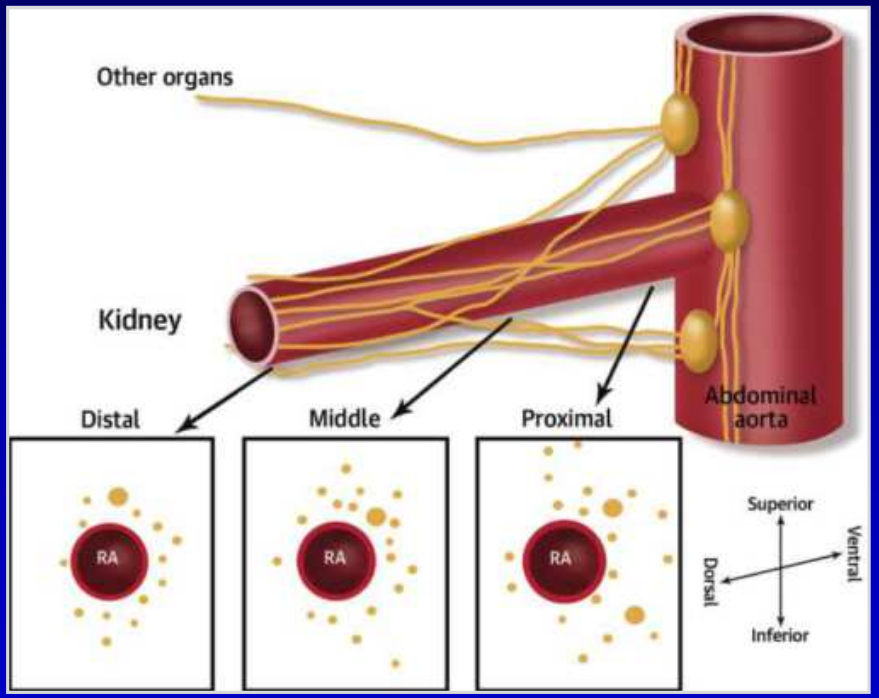
Renal nerves may have a positional bias on radial distance from arterial lumen: distal nerves are closer



Prior concept – Uniform radial distribution

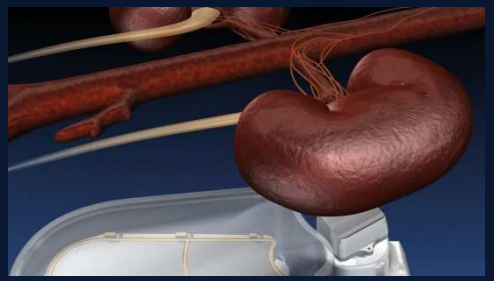


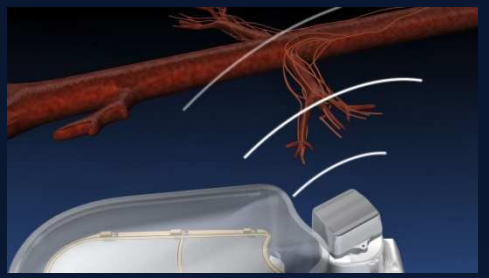
Current concept – Non-uniform radial distribution

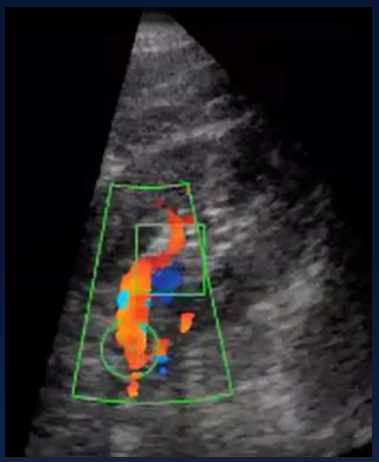


Sakakura K, et al., JACC 2014 64:634-43

Kona Medical *Surround Sound®* Hypertension Therapy
Non-Invasive Renal Denervation

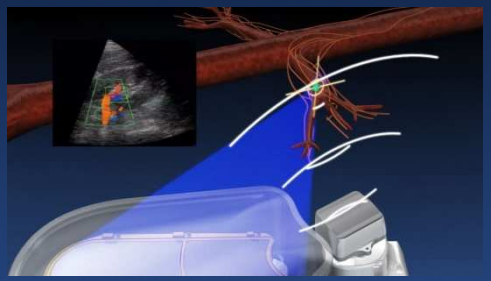


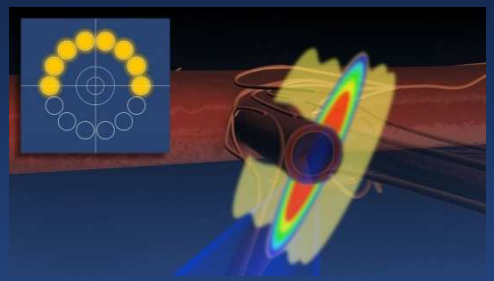


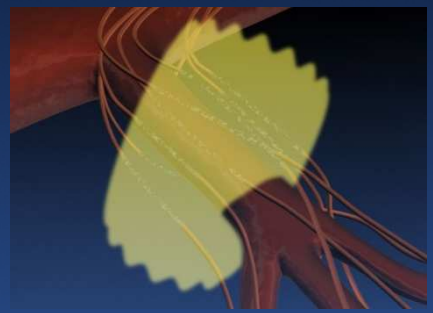


1 Imaging and therapy ultrasound positioned beneath patient

2 Ultrasound imaging used to identify renal artery







3 External ultrasound energy guided by ultrasound image and motion tracking

4 Focused ultrasound energy administered in treatment “pattern” to ablate nerves located outside of artery

5 Energy field surrounds artery, ablates renal nerves

Note: Kona Surround Sound Hypertension Therapy is investigational and not approved for sale

Case Report

- 55 year old lady; HT 10 years
- Son died 1 week previously - drugs overdose

- O/E: very anxious, tearful, tachypnoeic

Clammy, tremulous
Heart sounds I + II +IV
Chest clear
Fundi: Grade III hypertensive retinopathy
Urinalysis: proteinuria +

- Heart rate 120/min
- BP >300/150 mm Hg

University of Glasgow

Qu. Drug therapy?

- 1. i.v. sodium nitroprusside
- 2. i.v. GTN
- 3. i.v. labetalol
- 4. Oral nifedipine
- 5. Oral Bendroflumethiazide
- 6. Oral atenolol
- 7. Oral ACEi

Answer slide

Answer:

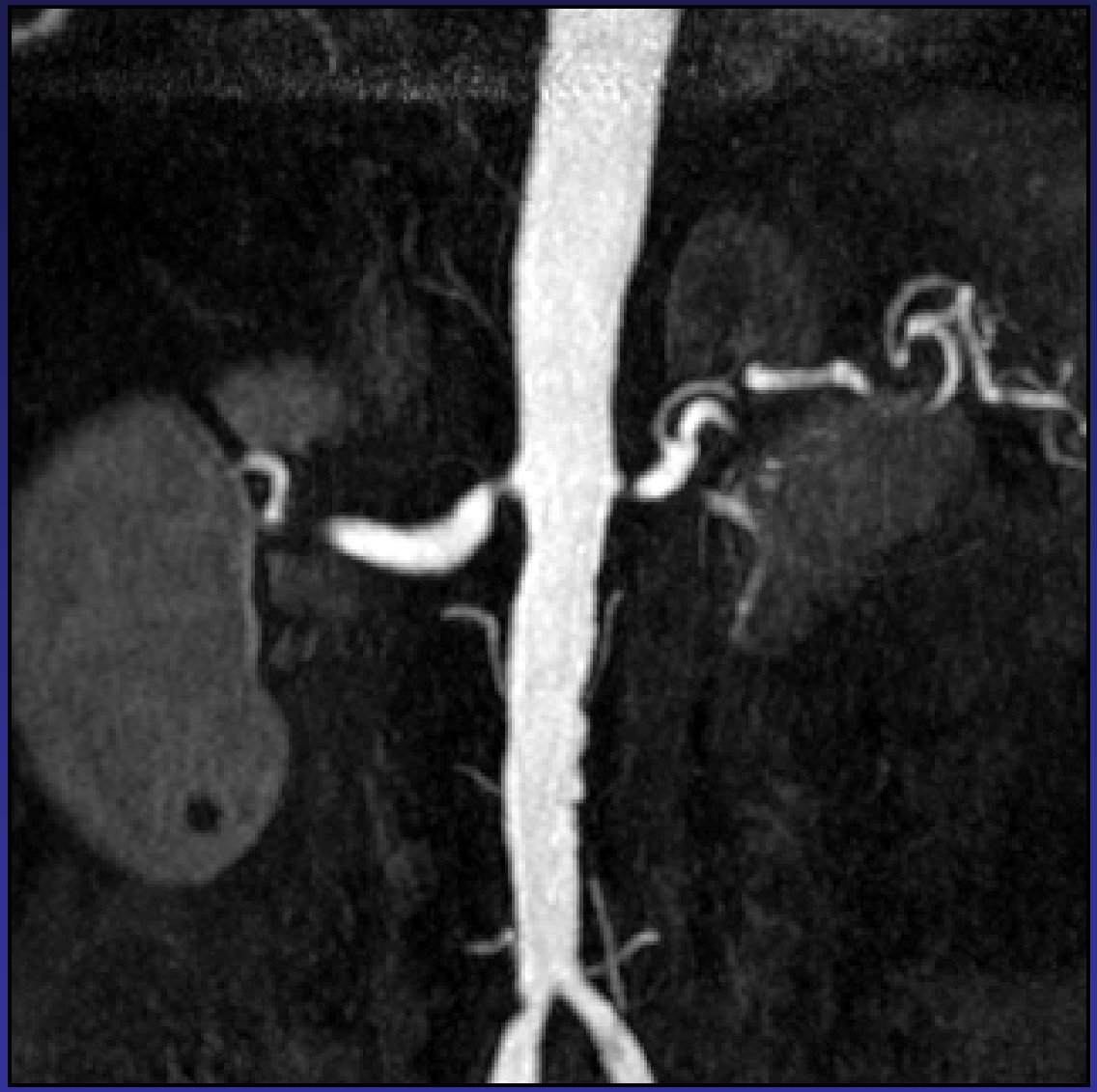
- Atenolol 25 mg p.o.

- Blood pressure fell to 205/110 mm Hg

- BFZ 2.5 mg added the next day
- BP 180/100 mm Hg

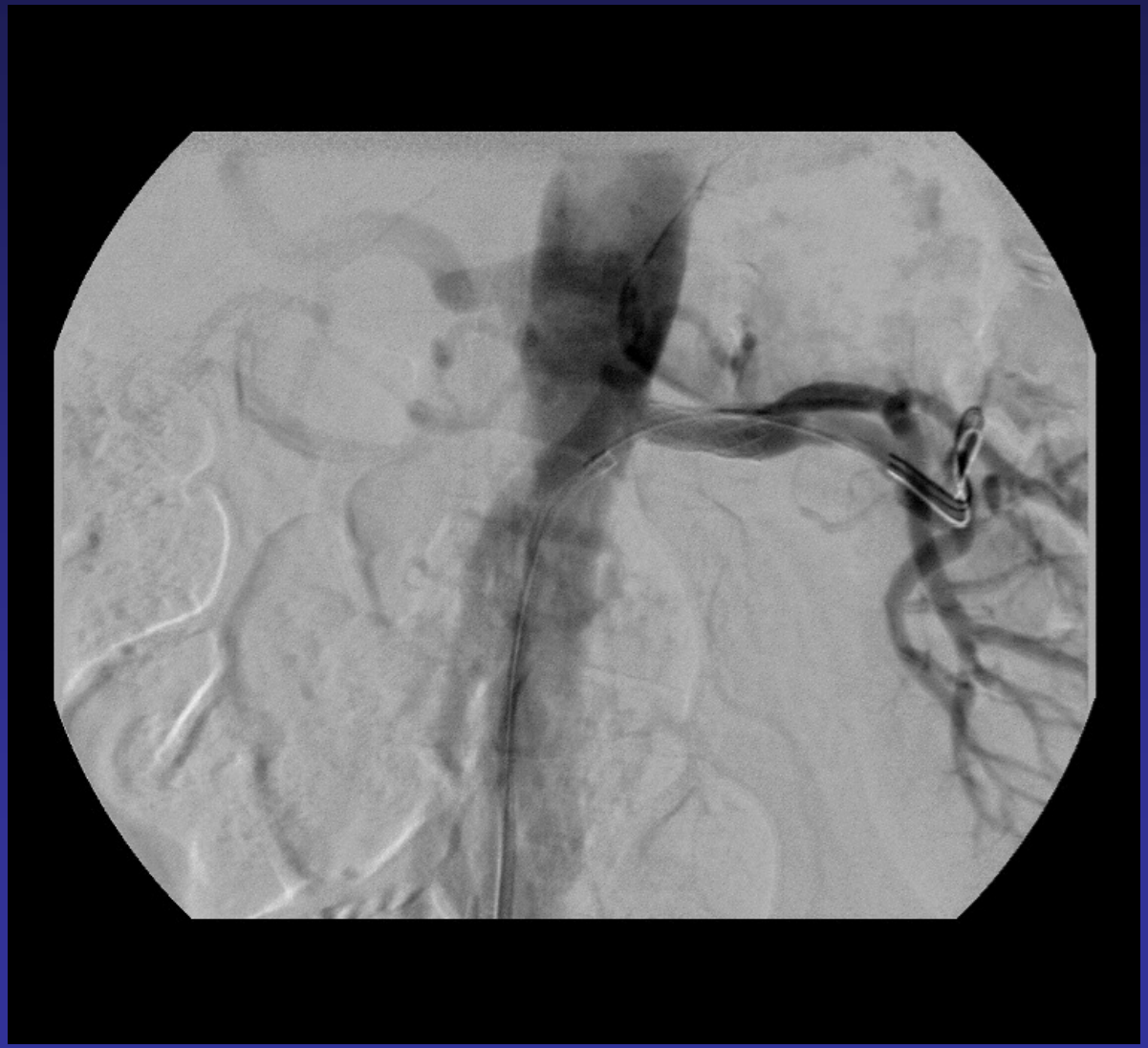
- Adalat LA 20 o.d. added
- 164/95 mm Hg

Investigations: MRI renal angiogram



University of Glasgow

Treatment: Bilateral renal artery stenting



University of Glasgow

Case Report

Discharged home:

128/66 mm Hg

Atenolol 50 mg bd; BFZ 2.5 mg

Simvastatin 40 mg; aspirin 75 mg

University of Glasgow

2013 UK Position Statement on Renal Artery Stenosis

Journal of Human Hypertension (2007) 21, 750–755

www.nature.com/jhh

GRAND ROUND

Grand Rounds at the British Hypertension Society: renal artery stenosis

AJB Brady[1], IS Mackenzie[2], S Ritchie[3] and MJ Brown[2]
[1]*Department of Medical Cardiology, Glasgow Royal Infirmary, Glasgow, UK;* [2]*Clinical Pharmacology Unit, University of Cambridge, Cambridge, UK;* [3]*Department of Medicine and Therapeutics, University of Glasgow, Glasgow, UK*

Renal artery angioplasty for renovascular hypertension is a controversial subject with considerable data but few certainties. This article is a summary of the Grand Round on Renovascular Hypertension held at the British Hypertension Society Annual Conference in September 2006.
Journal of Human Hypertension (2007) **21**, 750–755;
doi:10.1038/sj.jhh.1002260; published online 12 July 2007

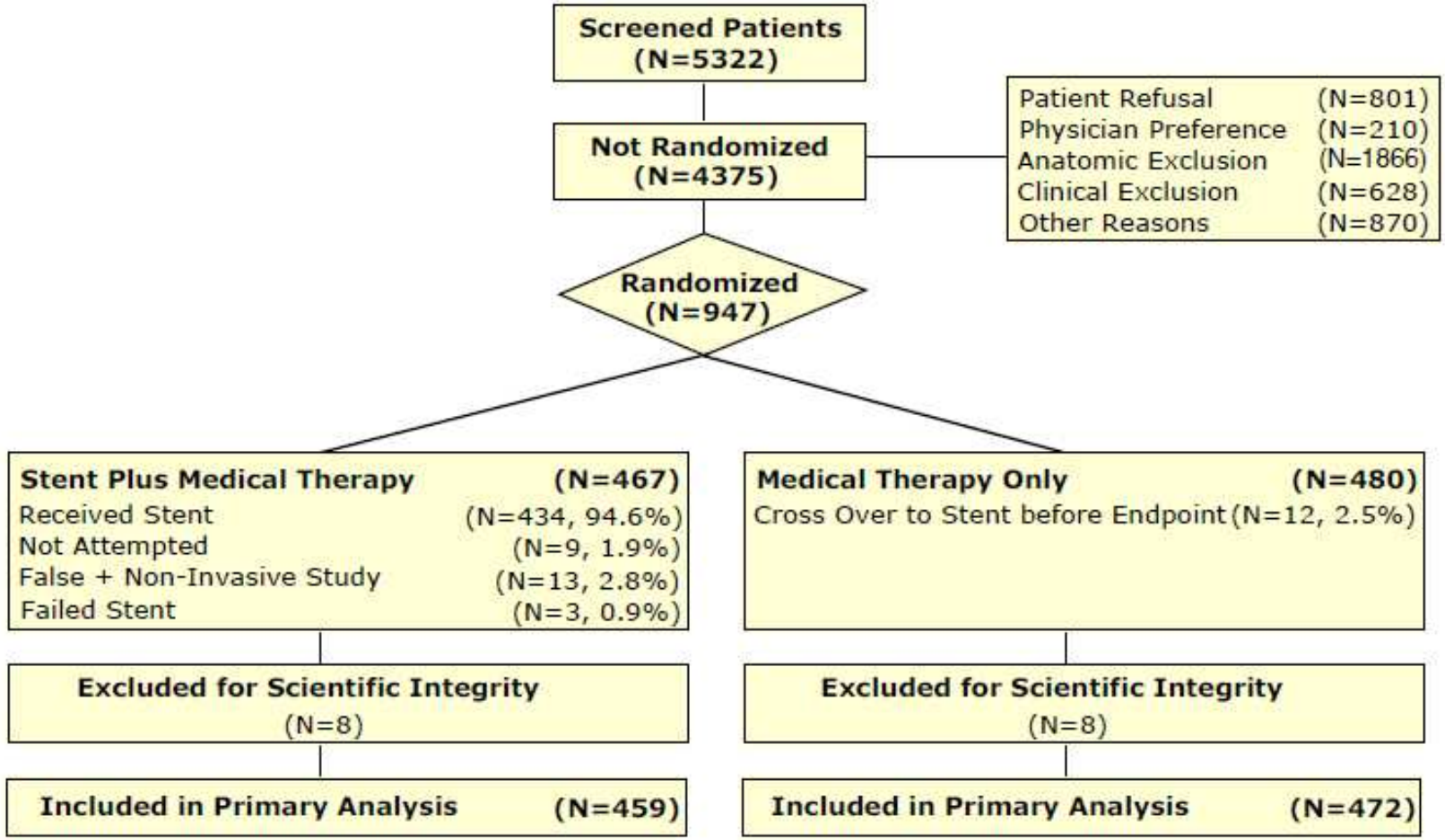
Keywords: renal artery stenosis; renovascular hypertension; renin; angioplasty; fibromuscular dysplasia; atherosclerosis

A Randomized Multicenter Clinical Trial of Renal Artery Stenting in Preventing Cardiovascular and Renal Events: Results of the CORAL Study

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., M.Sc., 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.,

on behalf of the CORAL Investigators

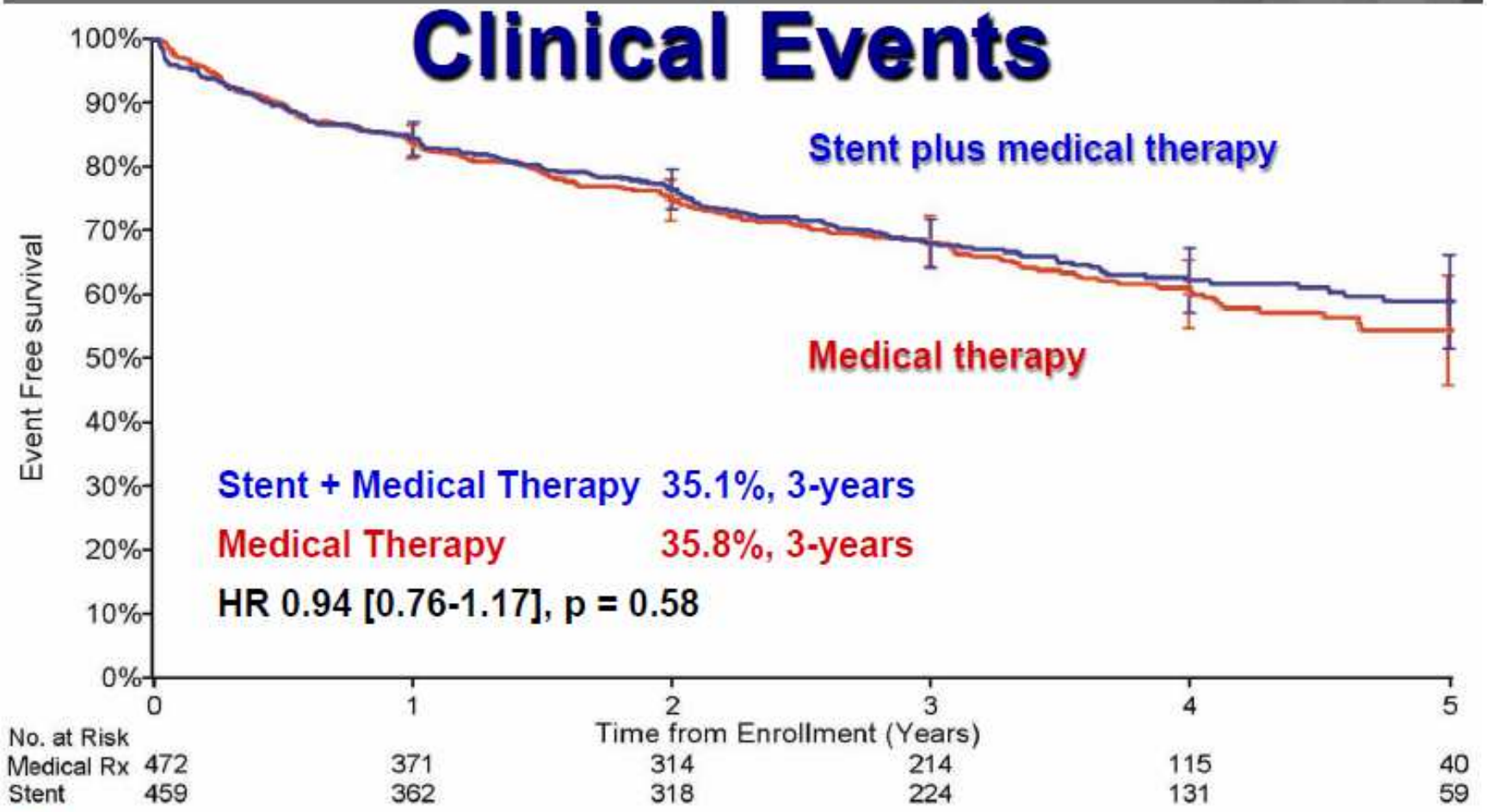
Screening and Enrollment



C. Cooper, AHA 2013

National Heart, Lung, and Blood Institute

Results: Primary Endpoint



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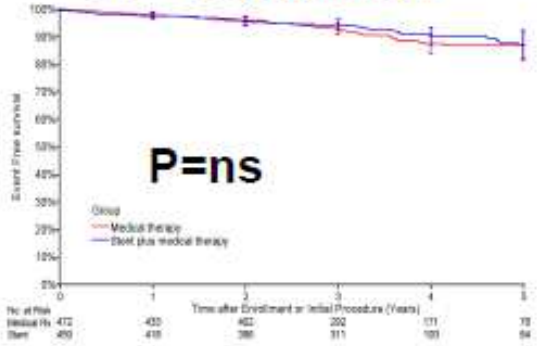
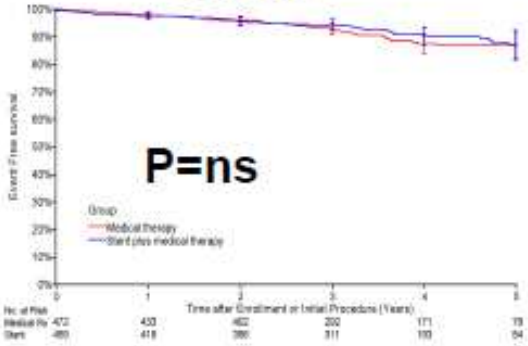
Results: Secondary Endpoints

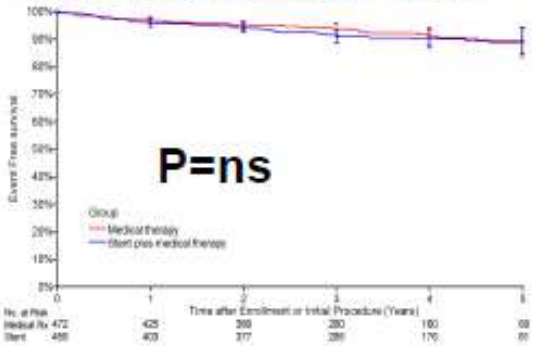
CV + Renal Death



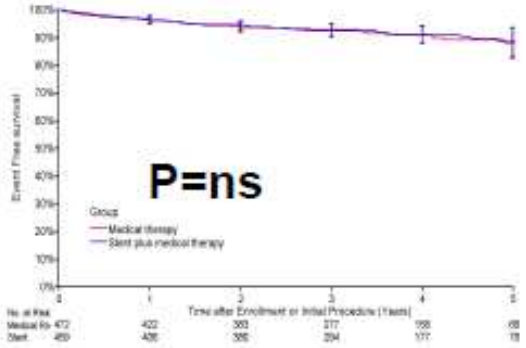
Stroke



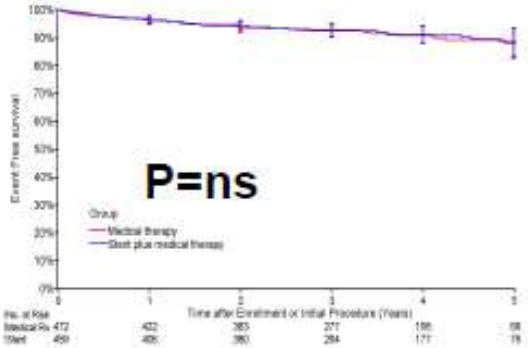
Myocardial Infarction



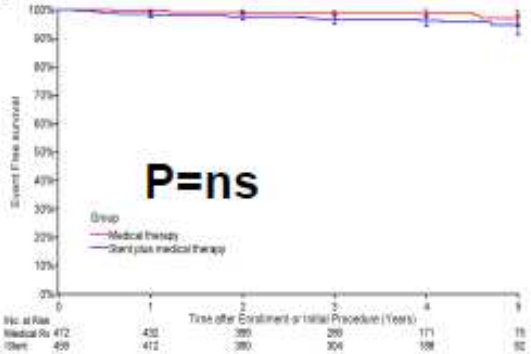
Heart Failure



Progressive Renal Insufficiency



Renal Replacement



C. Cooper, AHA 2013

National Heart, Lung, and Blood Institute

Systolic Blood Pressure Intervention Trial (SPRINT)

Principal Results

Paul K. Whelton, MB, MD, MSc

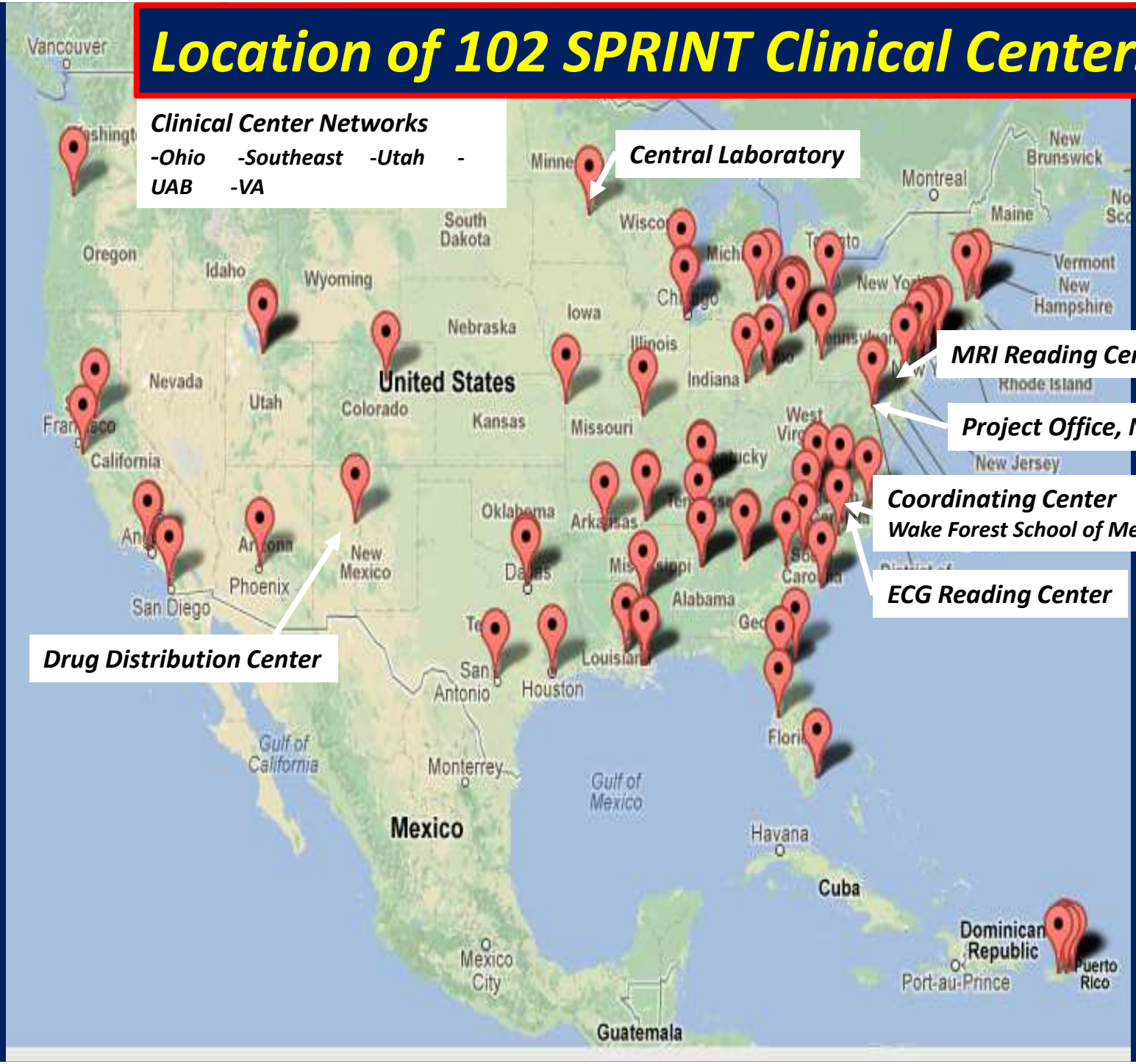
Chair, SPRINT Steering Committee

Tulane University School of Public Health and Tropical Medicine, and School of Medicine

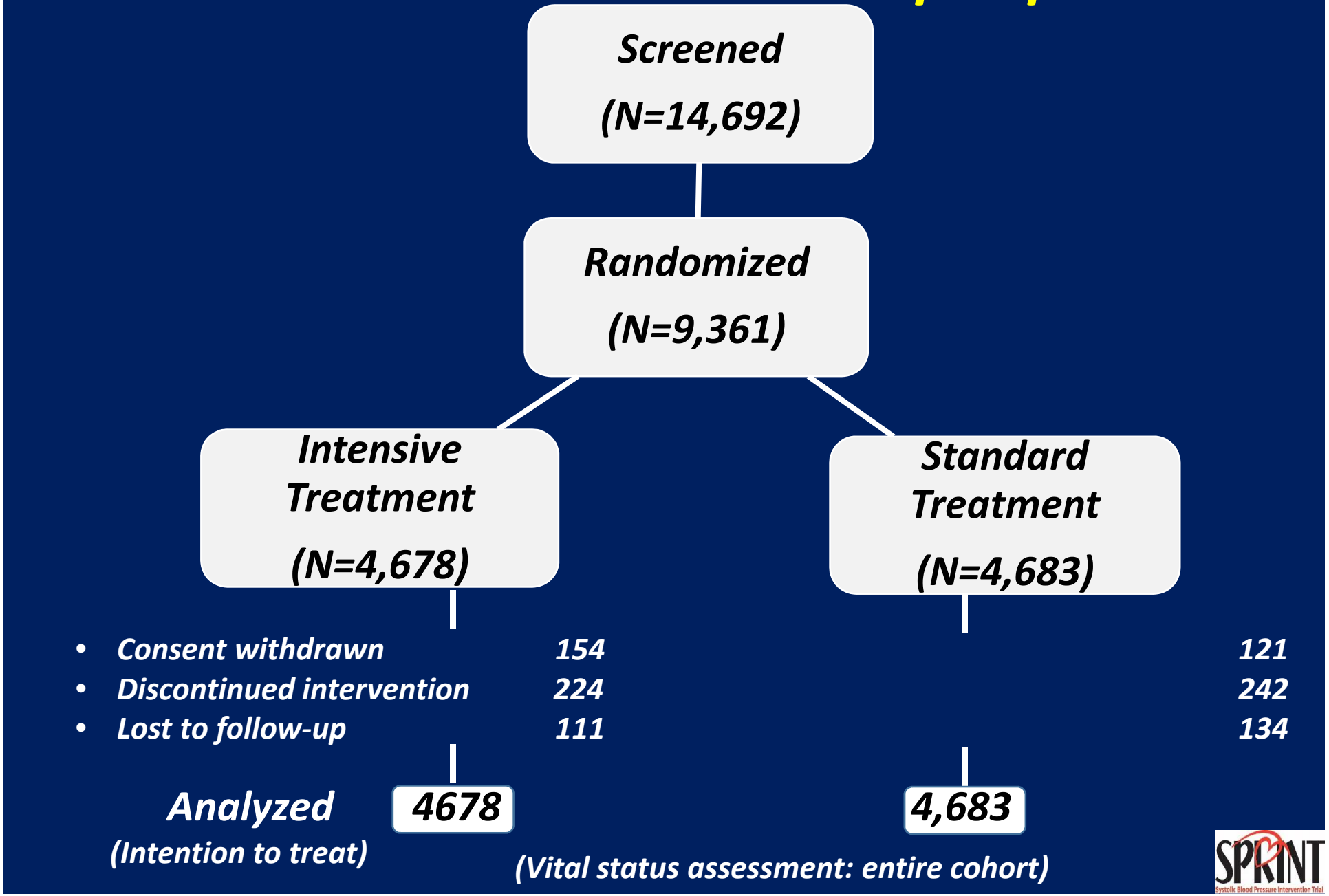
For the SPRINT Research Group

SPRINT
Systolic Blood Pressure Intervention Trial

Location of 102 SPRINT Clinical Centers



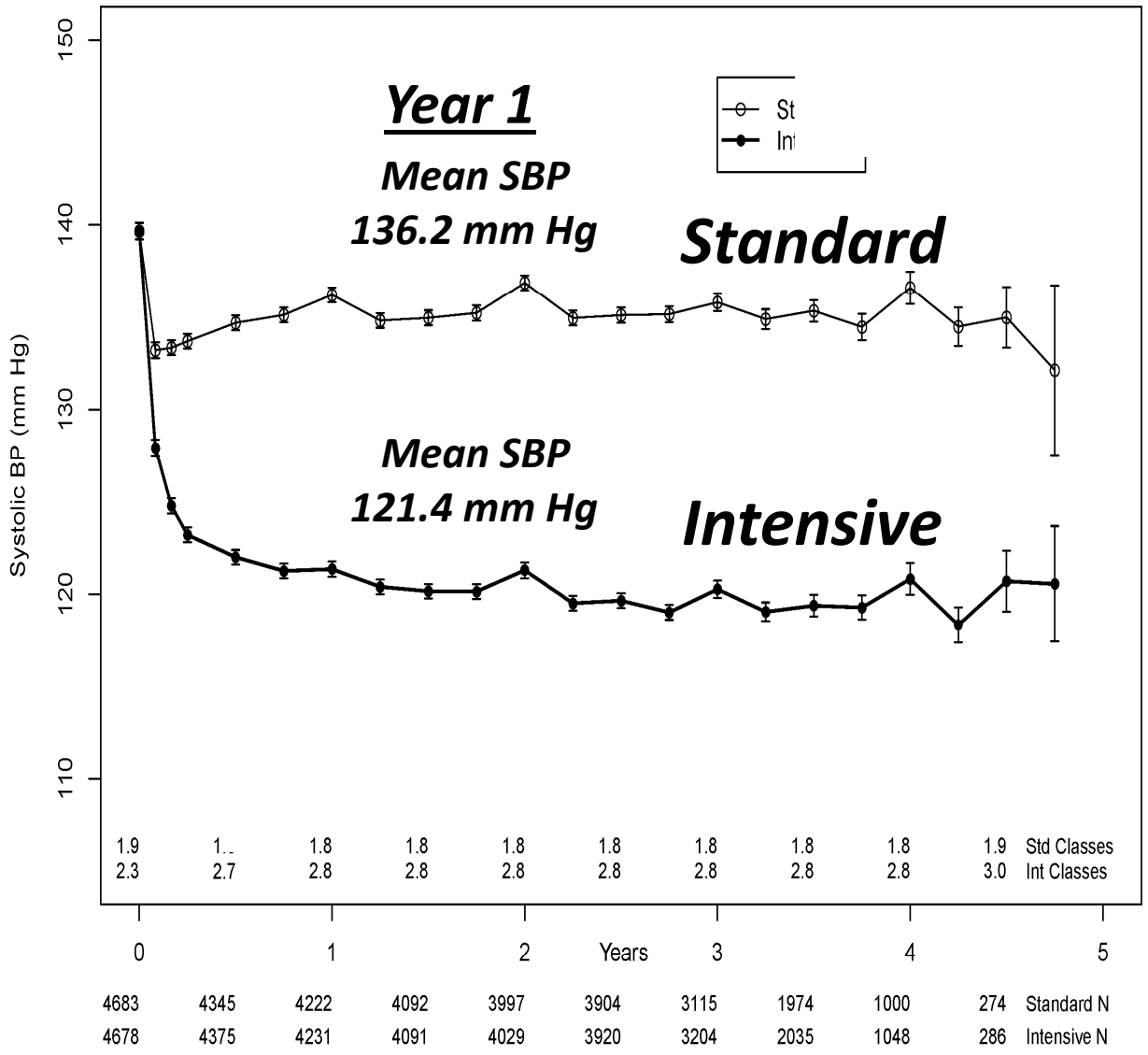
SPRINT: Enrollment and Follow-up Experience



Demographic and Baseline

	Total N=9361	Intensive N=4678	Standard N=4683
Mean (SD) age, years	67.9 (9.4)	67.9 (9.4)	67.9 (9.5)
% ≥75 years	28.2%	28.2%	28.2%
Female, %	35.6%	36.0%	35.2%
White, %	57.7%	57.7%	57.7%
African-American, %	29.9%	29.5%	30.4%
Hispanic, %	10.5%	10.8%	10.3%
Prior CVD, %	20.1%	20.1%	20.0%
Mean 10-year Framingham CVD risk, %	20.1%	20.1%	20.1%
Taking antihypertensive meds, %	90.6%	90.8%	90.4%
Mean (SD) number of antihypertensive meds	1.8 (1.0)	1.8 (1.0)	1.8 (1.0)
Mean (SD) Baseline BP, mm Hg			
Systolic	139.7 (15.6)	139.7 (15.8)	139.7 (15.4)
Diastolic	78.1 (11.9)	78.2 (11.9)	78.0 (12.0)

Systolic BP During Follow-up



Average SBP
(During Follow-up)

Standard: 134.6 mm Hg

Intensive: 121.5 mm Hg

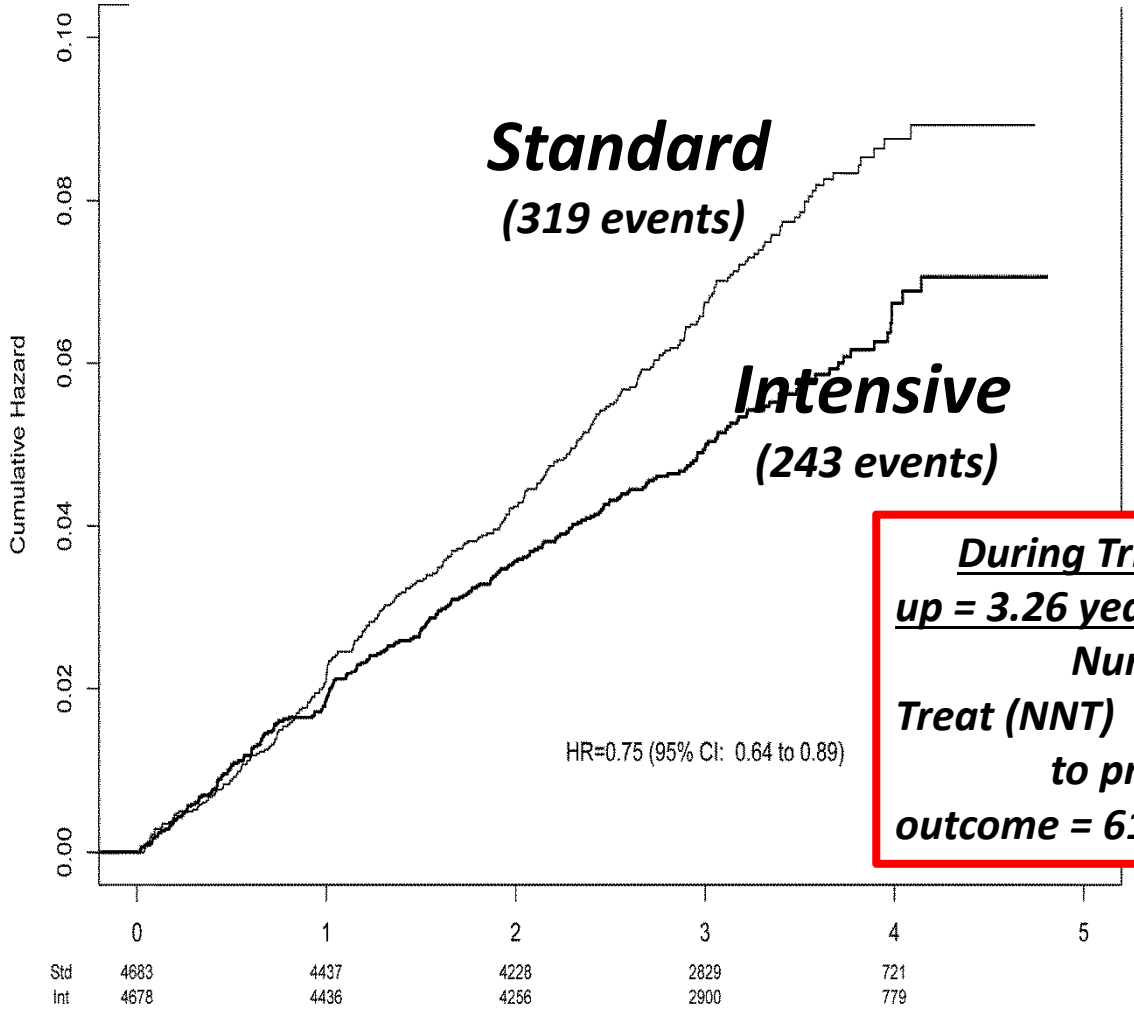
Average number of antihypertensive medications

Number of participants

SPRINT
Systolic Blood Pressure Intervention Trial

SPRINT Primary Outcome Cumulative Hazard

Hazard Ratio = 0.75 (95% CI: 0.64 to 0.89)

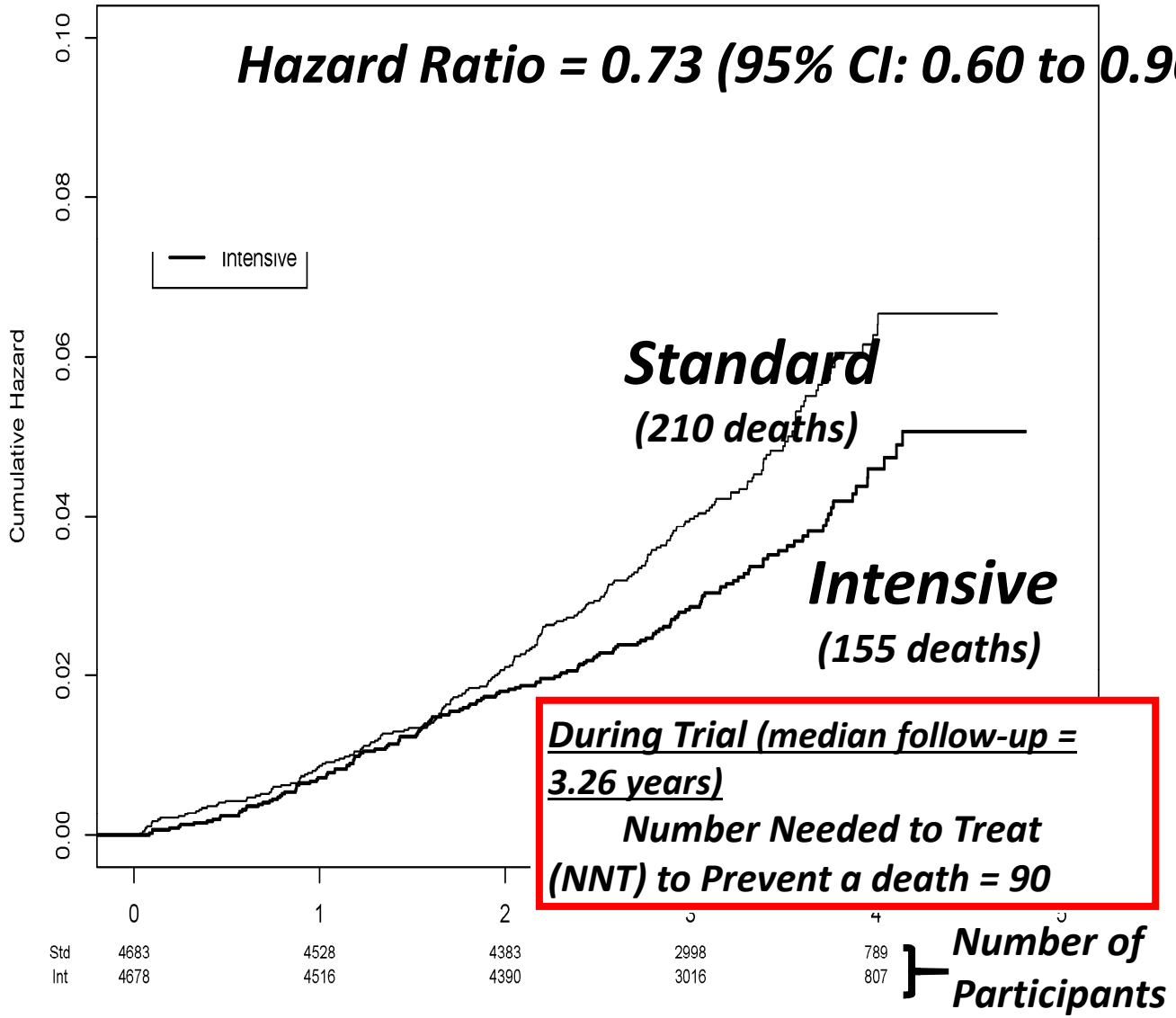


<u>During Trial (median follow-up = 3.26 years)</u>

Number Needed to Treat (NNT) to prevent a primary outcome = 61

SPRINT Systolic Blood Pressure Intervention Trial

All-cause Mortality
Cumulative Hazard



SPRINT
Systolic Blood Pressure Intervention Trial

Summary and Conclusions

- *In participants with CKD at baseline, no differences in renal outcomes*
- *In participants without CKD at baseline, incidence of eGFR reduction ≥ 30% more common in Intensive Group*
- *No overall difference in serious adverse events (SAEs) between treatment groups*
- *SAEs associated with hypotension, syncope, electrolyte abnormalities, and hospital discharge reports of acute kidney injury or acute renal failure more common in Intensive Group*
- *Overall, benefits of more intensive BP lowering exceeded the potential for harm*

SPRINT
Systolic Blood Pressure Intervention Trial

Demographic and Baseline Characteristics

	Total N=9361	Intensive N=4678	Standard N=4683
Mean (SD) number of antihypertensive meds	1.8 (1.0)	1.8 (1.0)	1.8 (1.0)
Mean (SD) Baseline BP, mm Hg			
Systolic	139.7 (15.6)	139.7 (15.8)	139.7 (15.4)
Diastolic	78.1 (11.9)	78.2 (11.9)	78.0 (12.0)

JOIN US FOR MAY MEASUREMENT MONTH 2017!

What is May Measurement Month?

May Measurement Month is a worldwide screening initiative aimed at highlighting the need for increased blood pressure awareness. This is important because many people don't know they have high blood pressure.

Who can get involved?

We're looking for adult volunteers aged 18-plus who ideally have not had their blood pressure recorded in the past year. But don't worry if you have — you can still take part. All the data we collect is anonymous. We will not record your name or anything else that could identify you as an individual on any database or anywhere else.

Where do I go to take part? [INSERT LOCAL SCREENING CENTRE DETAILS]

What happens at the screening?

You'll be asked some simple health questions then we'll measure your blood pressure. That's it. The whole process only takes around 15 to 20 minutes.

Join us now and have your blood pressure checked!

BIHS
British and Irish Hypertension Society
Committed to preventing cardiovascular disease

International Society of Hypertension

JOIN US FOR MAY MEASUREMENT MONTH 2017!

It's time to put the spotlight on raising awareness around blood pressure, and May Measurement Month is doing exactly that! During May 2017, some 25 million people will have their blood pressure measured in one of the biggest public screening exercises the world's ever seen. MMM17 is being led by the International Society of Hypertension and the World Hypertension League.

What's May Measurement Month all about?

10 million lives lost

Every year 10 million people around the world die needlessly because of high blood pressure, making it the planet's single biggest killer. They will suffer a stroke, have a heart attack, or die from another cardiovascular complication

linked to hypertension — the medical term for high blood pressure.

And the real tragedy is that only around half of those who die this way will even have known they had raised blood pressure.

We want to change this, starting now

May Measurement Month is a global initiative led by two organisations representing the world's leading cardiologists and researchers specialising in hypertension — the International Society of Hypertension and the World Hypertension League.

Our goal is to measure 25 million adults aged 18+ from 1-31 May 2017 at screening centres in 100 countries. We want each of those 25 million people to leave us knowing what their blood pressure is and what they need to do next.

Get involved!

So if you're a health professional, a medical student, or you'd like to support us as an industry partner, please join us in raising awareness and saving lives during MMM17 — just email us now at mmminfo@ish-world.com.

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Hypertension 2017: Conclusions

1. Define Hypertension with ABPM / HBPM
2. Identify contributing lifestyle factors
3. Discontinue / minimize drugs that ↑ BP
4. Investigate for secondary causes of hypertension
5. Maximize and optimize pharmacotherapy
6. Don’t overtreat older (or younger) patients
7. Avoid hypotension at all costs
8. Consider interventional procedures

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