

Traitements modernes de l'hypertension artérielle



**ALFORMEC – ECU-UCL
LUXEMBOURG 24 SEPTEMBRE 2016**

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SERVICE DE NEPHROLOGIE
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Plan de l'exposé



- Quelle mesure de la pression artérielle ?
- Quelle pression artérielle-cible ?
- Quel choix de médicament ?
- Quel bénéfice de la « technologie thérapeutique » ?

Les commandements de l'automesure



- Utiliser un appareil validé (dableducational.org)
- 2 mesures matin et soir pendant 7 jours
- Faire la moyenne des 6 derniers jours
- Mesurer tous les deux à trois mois et avant chaque consultation

Et si on définissait le seuil en fonction de la morbidité ?

Niiranen Hypertension 2013;61:27-34

	Seuil OBP	Seuil HBP
Optimale	120/80	120/75
Préhypertension	130/85	125/80
Hypertension stade 1	140/90	130/85
Hypertension stade 2	160/100	145/90

Valeur pronostique du monitoring ambulatoire

Kikuya et al *Circulation* 2007;115:2145-2152



Cabinet	ABPM 24 h	ABPM jour	ABPM nuit
120/80 mmHg Optimale	115/75 mmHg	120/80 mmHg	100/65 mmHg
130/85 mmHg Normale	125/75 mmHg	130/85 mmHg	110/70 mmHg
140/90 mmHg Hypertension	130/80 mmHg	135/85 mmHg	120/70 mmHg



Objectifs tensionnels

< 140/90 mmHg

130-139/80-85 mmHg

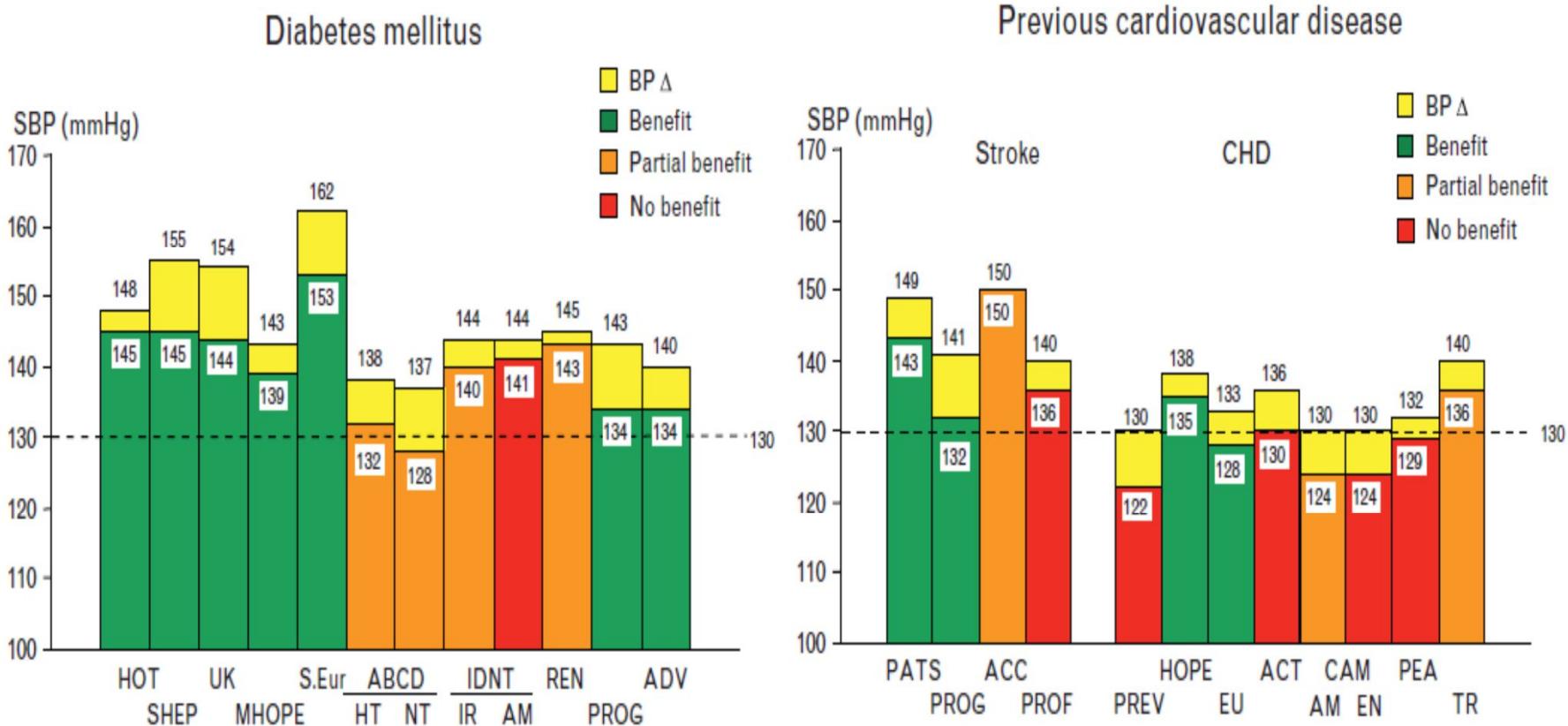
Viser une PA encore plus basse est probablement sage dans les situations suivantes:

- Néphropathie chronique
- Haut risque CV
- Diabète

When should antihypertensive drug treatment be initiated and to what levels should systolic blood pressure be lowered? A critical reappraisal

Alberto Zanchetti^{a,b}, Guido Grassi^{a,c} and Giuseppe Mancia^{a,c}

Journal of Hypertension 2009, 27:923–934



Etude MDRD: ce qu'on oublie ...

	Usual MAP	Usual BP	Low MAP	Low BP
18- 60 yrs	< 107 mmHg	< 140/90 mmHg	< 92 mmHg	125/75 mmHg
> 61 yrs	< 113 mmHg	< 160-90 mmHg	< 98 mmHg	< 135/80 mmHg

Guidelines ESH 2013



Blood pressure goals in hypertensive patients

Recommendations	Class ^a	Level ^b	Ref. ^c
A SBP goal <140 mmHg:			
a) is recommended in patients at low-moderate CV risk;	I	B	266, 269, 270
b) is recommended in patients with diabetes;	I	A	270, 275, 276
c) should be considered in patients with previous stroke or TIA;	IIa	B	296, 297
d) should be considered in patients with CHD;	IIa	B	141, 265
e) should be considered in patients with diabetic or non-diabetic CKD.	IIa	B	312, 313
In elderly hypertensives less than 80 years old with SBP ≥160 mmHg there is solid evidence to recommend reducing SBP to between 150 and 140 mmHg.	I	A	265
In fit elderly patients less than 80 years old SBP values <140 mmHg may be considered, whereas in the fragile elderly population SBP goals should be adapted to individual tolerability.	IIb	C	-
In individuals older than 80 years and with initial SBP ≥160 mmHg, it is recommended to reduce SBP to between 150 and 140 mmHg provided they are in good physical and mental conditions.	I	B	287
A DBP target of <90 mmHg is always recommended, except in patients with diabetes, in whom values <85 mmHg are recommended. It should nevertheless be considered that DBP values between 80 and 85 mmHg are safe and well tolerated.	I	A	269, 290, 293

CHD, coronary heart disease; CKD, chronic kidney disease; CV, cardiovascular; DBP, diastolic blood pressure; SBP, systolic blood pressure; TIA, transient ischaemic attack.

^aClass of recommendation.

^bLevel of evidence.

^cReference(s) supporting levels of evidence.

SPRINT (NEJM 2015)

We randomly assigned 9361 persons of **50 years or more** with a SBP of **130 mmHg or higher** and an **increased cardiovascular risk**, but **without diabetes or previous stroke**, to a SBP target of less than **120 mm Hg** or a target of less than **140 mm Hg**.

General Inclusion Criteria

1 ≥ 50 years old

2 Systolic blood pressure (SBP)

 SBP: 130 – 180 mm Hg on 0 or 1 medication

 SBP: 130 – 170 mm Hg on up to 2 medications

 SBP: 130 – 160 mm Hg on up to 3 medications

 SBP: 130 – 150 mm Hg on up to 4 medications

3 At Risk (one or more of the following):

 a. Presence of clinical or subclinical cardiovascular disease (CVD) other than stroke

 b. Chronic kidney disease, defined as estimated glomerular filtration rate $20 - 59 \text{ ml/min}/1.73\text{m}^2$

 c. Framingham Risk Score for 10-year CVD risk $\geq 15\%$ based on clinical features and laboratory results within the past 12 months for lipids

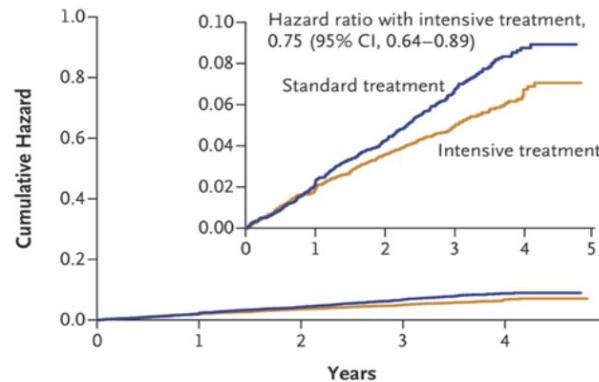
 d. Age ≥ 75 years.

Etude SPRINT

NEJM 2015;373:2103-2116



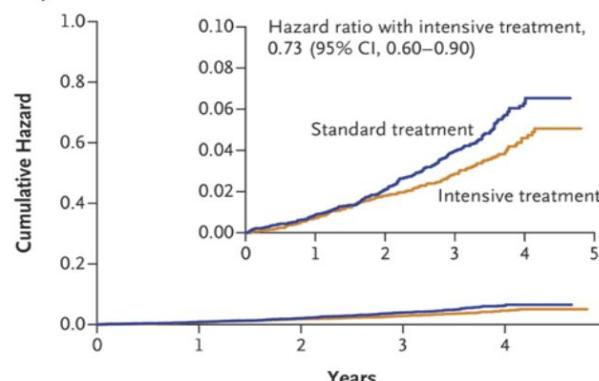
A Primary Outcome



No. at Risk

Standard treatment	4683	4437	4228	2829	721
Intensive treatment	4678	4436	4256	2900	779

B Death from Any Cause



No. at Risk

Standard treatment	4683	4528	4383	2998	789
Intensive treatment	4678	4516	4390	3016	807

Unattended Blood Pressure Measurements in the Systolic Blood Pressure Intervention Trial

Implications for Entry and Achieved Blood Pressure Values Compared With Other Trials

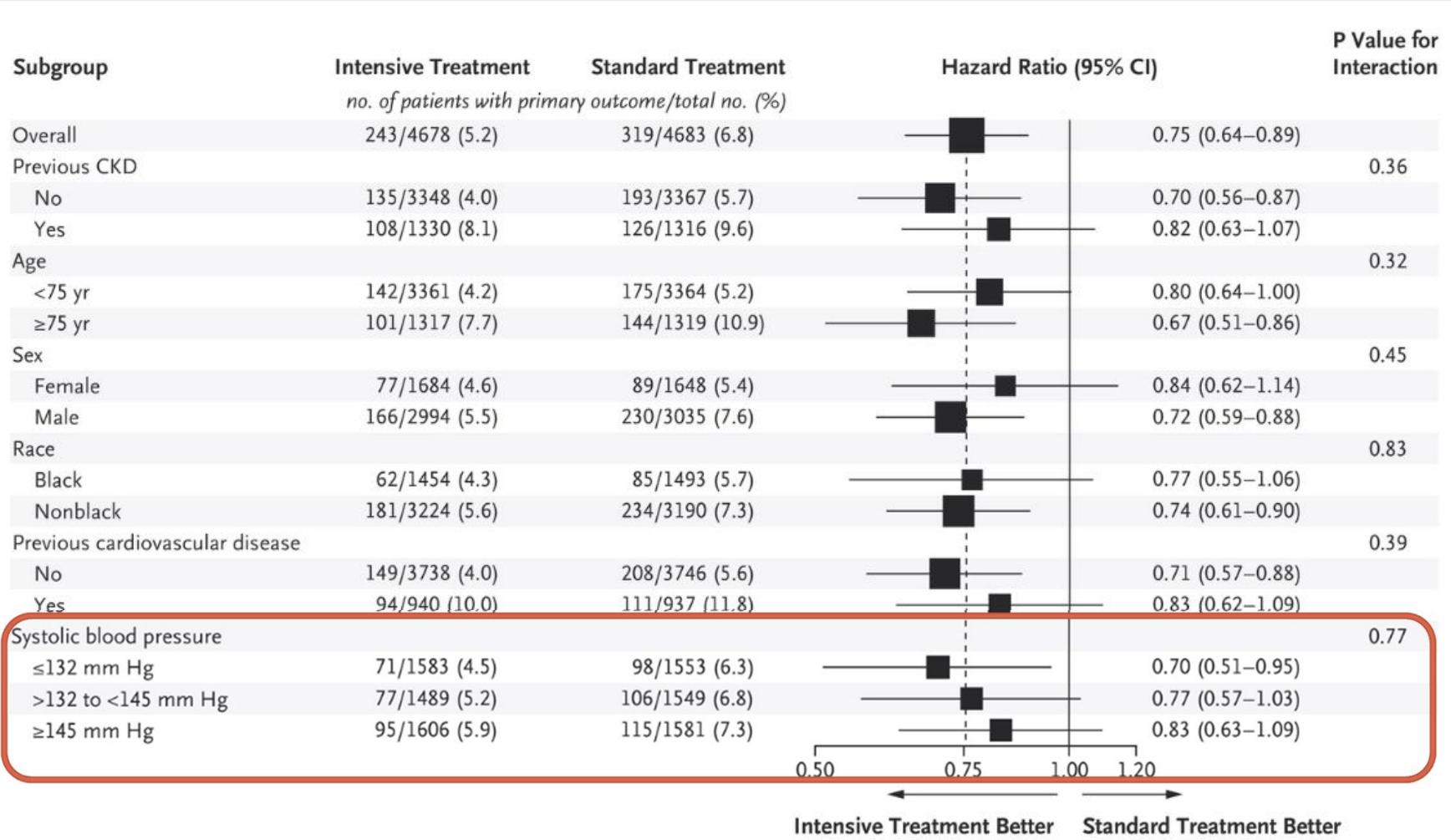
Sverre E. Kjeldsen, Per Lund-Johansen, Peter M. Nilsson, Giuseppe Mancia

Trial	Device	Status of Observation	References
ACCORD	Model 907, Omron Healthcare, Lake Forest, IL	Attended	The ACCORD Study Group ²
SPS3	Colin BP-8800C, Press Mate, Meena Medical Inc, Bedford, TX	Attended	The SPS3 Study Group ³
SPRINT	Model 907, Omron Healthcare, Lake Forest, IL	Unattended	The SPRINT Research Group ⁷
HOT	Visomat OZ, D2 International, Hestia Pharma GmbH, Germany	Attended	Hansson et al ⁹
TROPHY	HEM-705CP, Omron Healthcare, Lake Forest, IL	Attended	Julius et al ¹⁹
ONTARGET	HEM-757, Omron Corporation, Tokyo, Japan	Attended	Verdecchia et al ²⁰
TRANSCEND	HEM-757, Omron Corporation, Tokyo, Japan	Attended	Verdecchia et al ²⁰

For optimal standardization people are seated in a quiet room for 3 to 5 minutes without talking before measurements are taken as an average of 3 measurements with 1 minute apart. Measurements have been done unattended (unobserved) and fully automated in the SPRINT study (no other people in the room) while being attended (observed) in all other trials by investigator or technician who activated the device. ACCORD indicates Action to Control Cardiovascular Risk in Diabetes study; HOT, Hypertension Optimal Treatment study; ONTARGET, Ongoing Telmisartan Alone and in Combination With Ramipril Global Endpoint Trial; SPRINT, Systolic Blood Pressure Intervention Trial; SPS3, Secondary Prevention of Small Subcortical Strokes study; TRANSCEND, Telmisartan Randomized Assessment Study in ACEintolerant Subjects With Cardiovascular Disease study; and TROPHY, Trial of Preventing Hypertension study.

Etude SPRINT

NEJM 2015;373:2103-2116

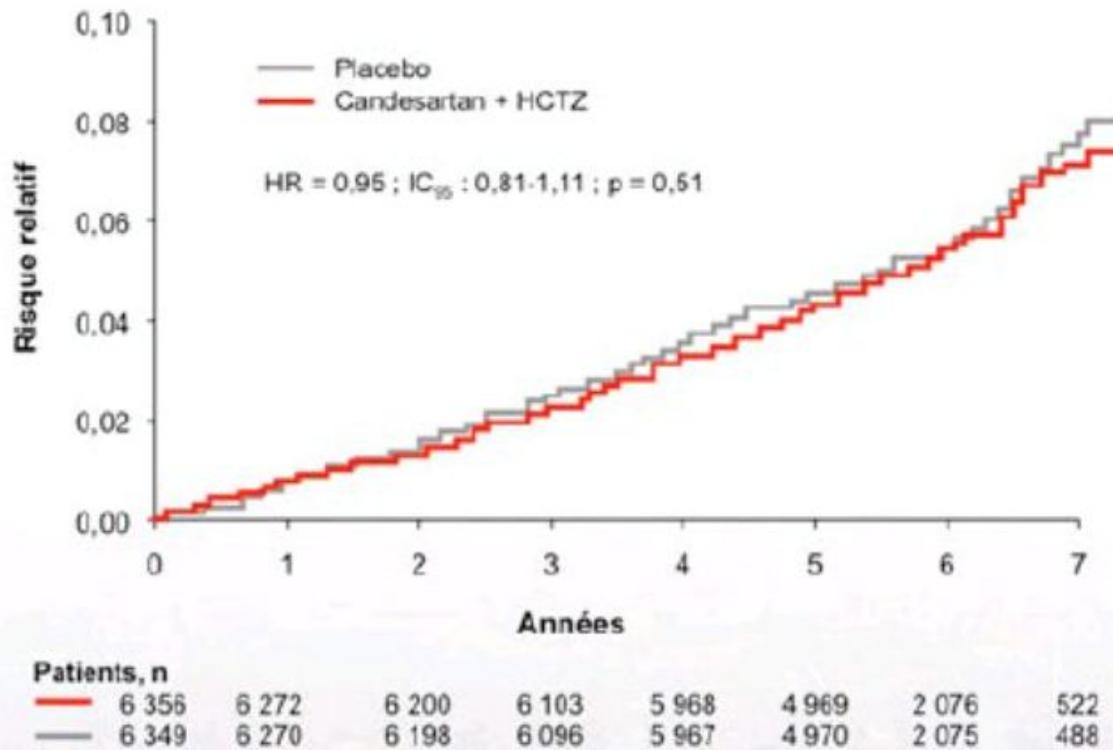


Etude HOPE-3 bras pression artérielle

NEJM 2016;374:2009-2020



Décès d'origine cardiovasculaire, infarctus, AVC, Insuffisance cardiaque, revascularisation



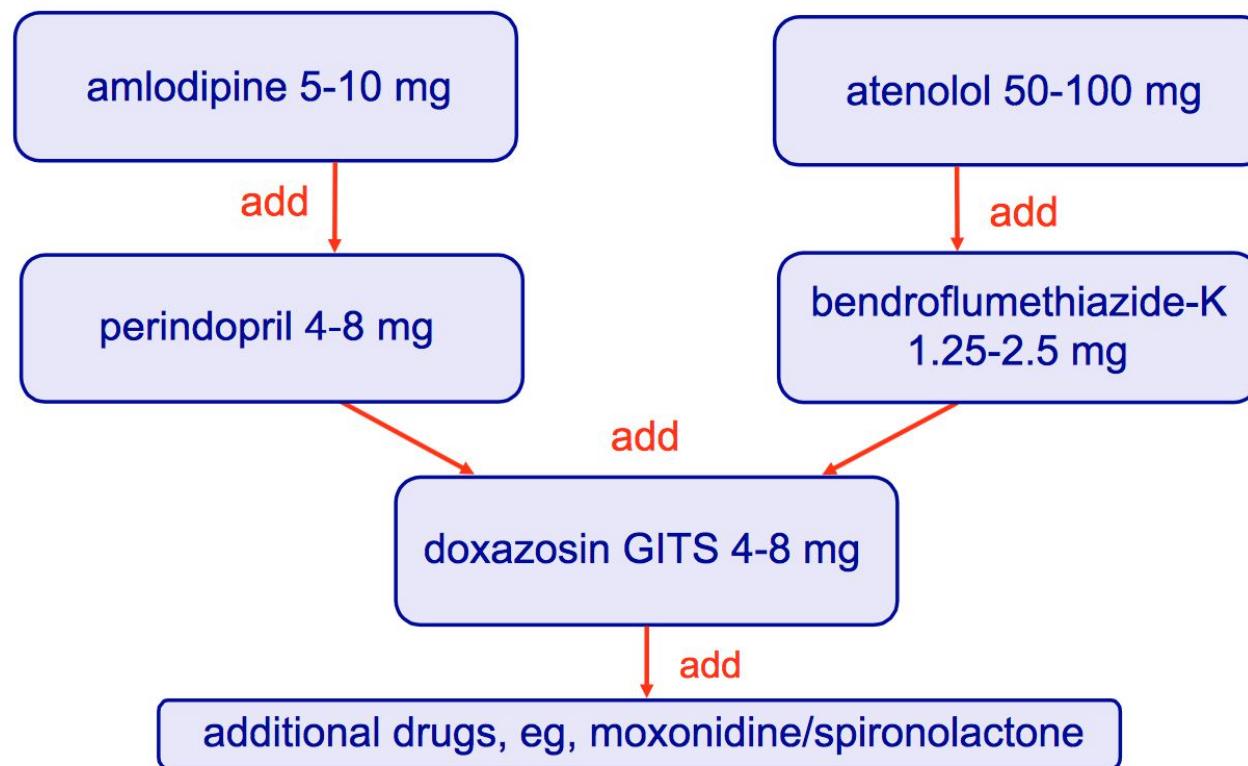
Recommandations ESH

Choix des médicaments antihypertenseurs

- Bénéfice principal dû à la diminution tensionnelle en soi (largement indépendant du médicament utilisé)
- Classes majeures de médicaments qui conviennent pour l'initiation de/ la maintenance du traitement
 - Thiazides
 - Beta-bloquants
 - Antagonistes calciques
 - IEC
 - Sartans

Etude ASCOT

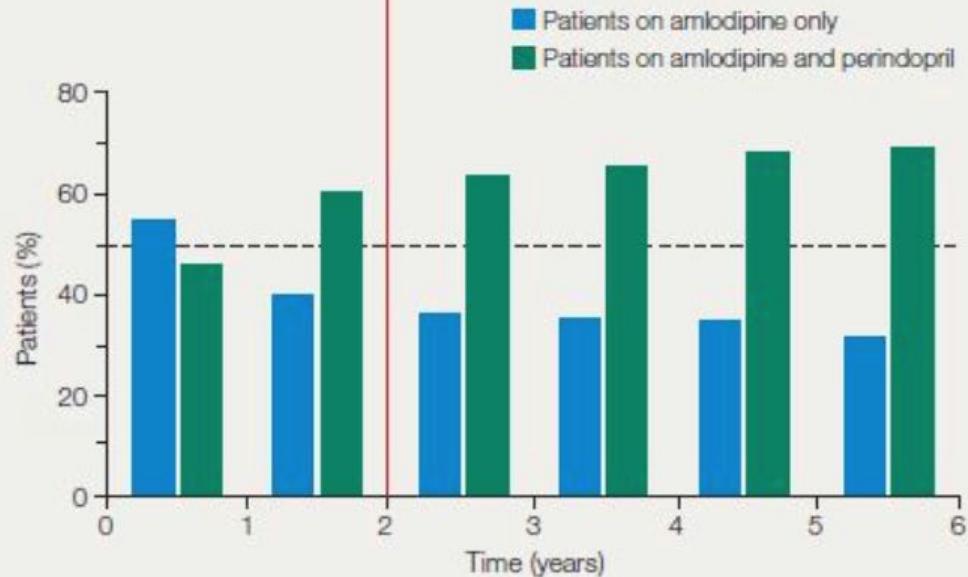
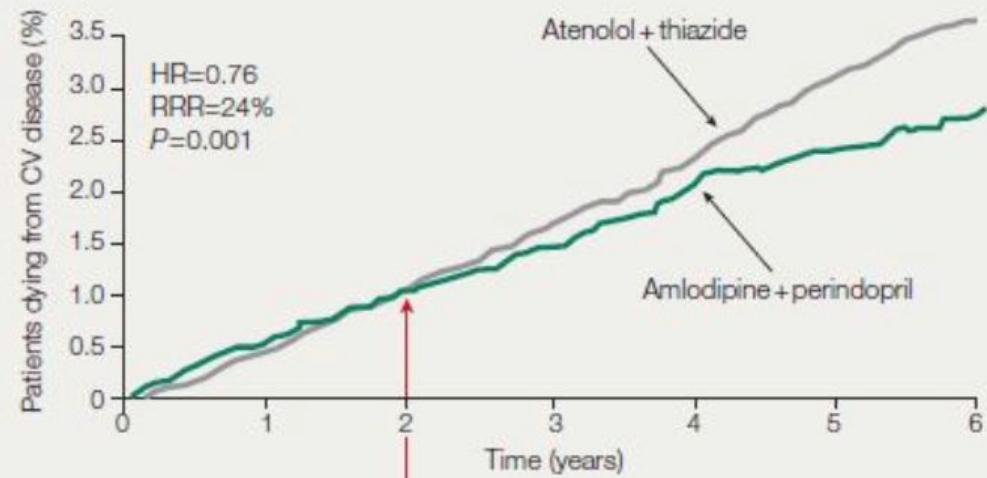
Treatment algorithm to BP targets < 140/90 mmHg or < 130/80 mmHg in patients with diabetes



Median follow up was for 5.5 years

ascot

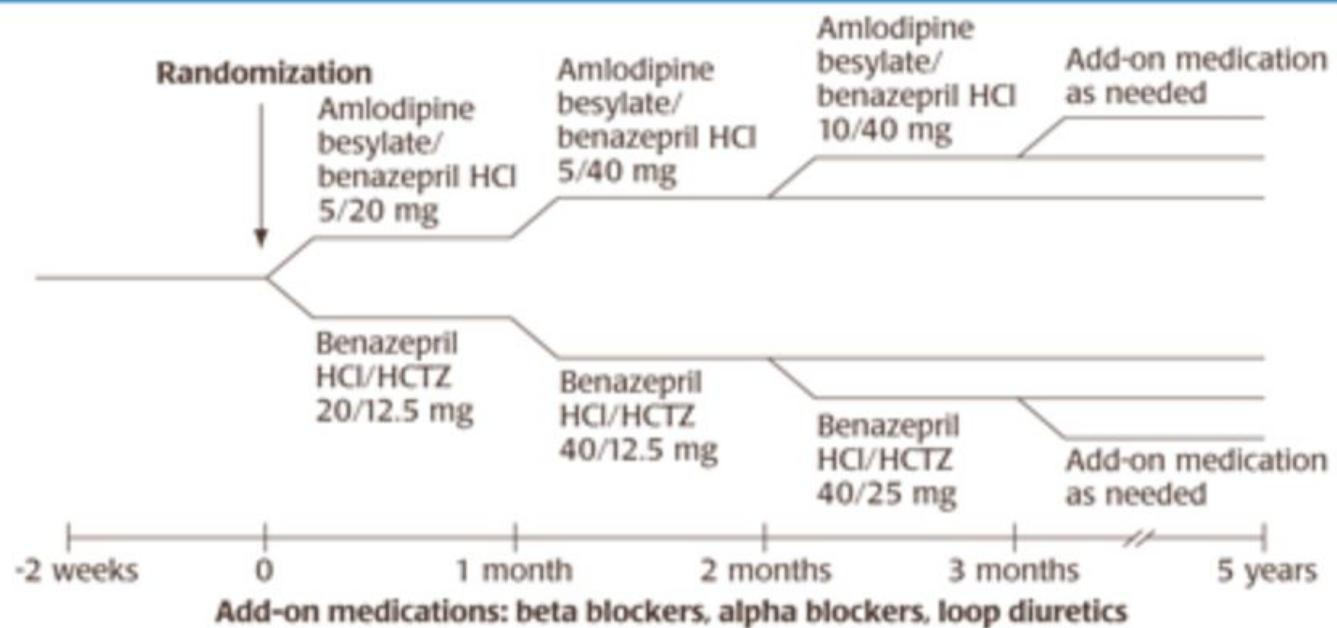
Etude ASCOT



Etude ACCOMPLISH

FIGURE 3

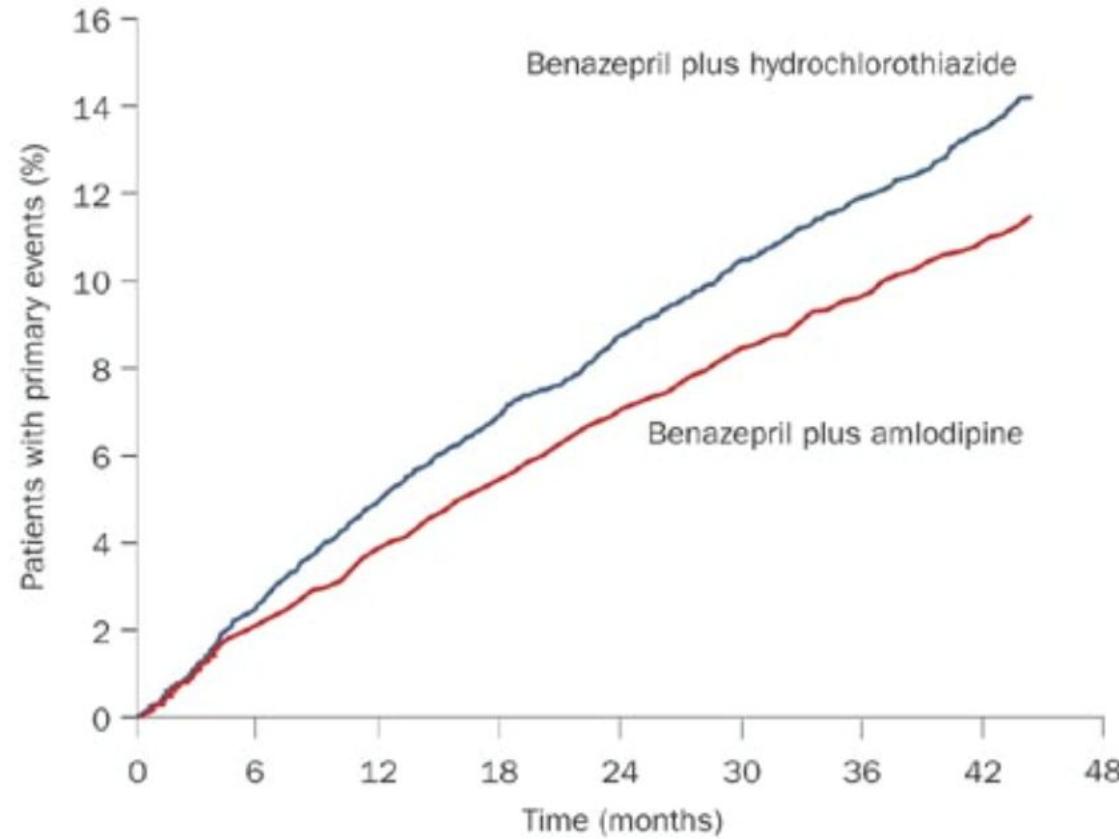
ACCOMPLISH study design



HCl = hydrochloride; HCTZ = hydrochlorothiazide; ACCOMPLISH = Avoiding Cardiovascular Events through Combination Therapy in Patients Living with Systolic Hypertension.

Source: Jamerson KA et al. *Am J Hypertens.* 2003;16(pt 2):193A.

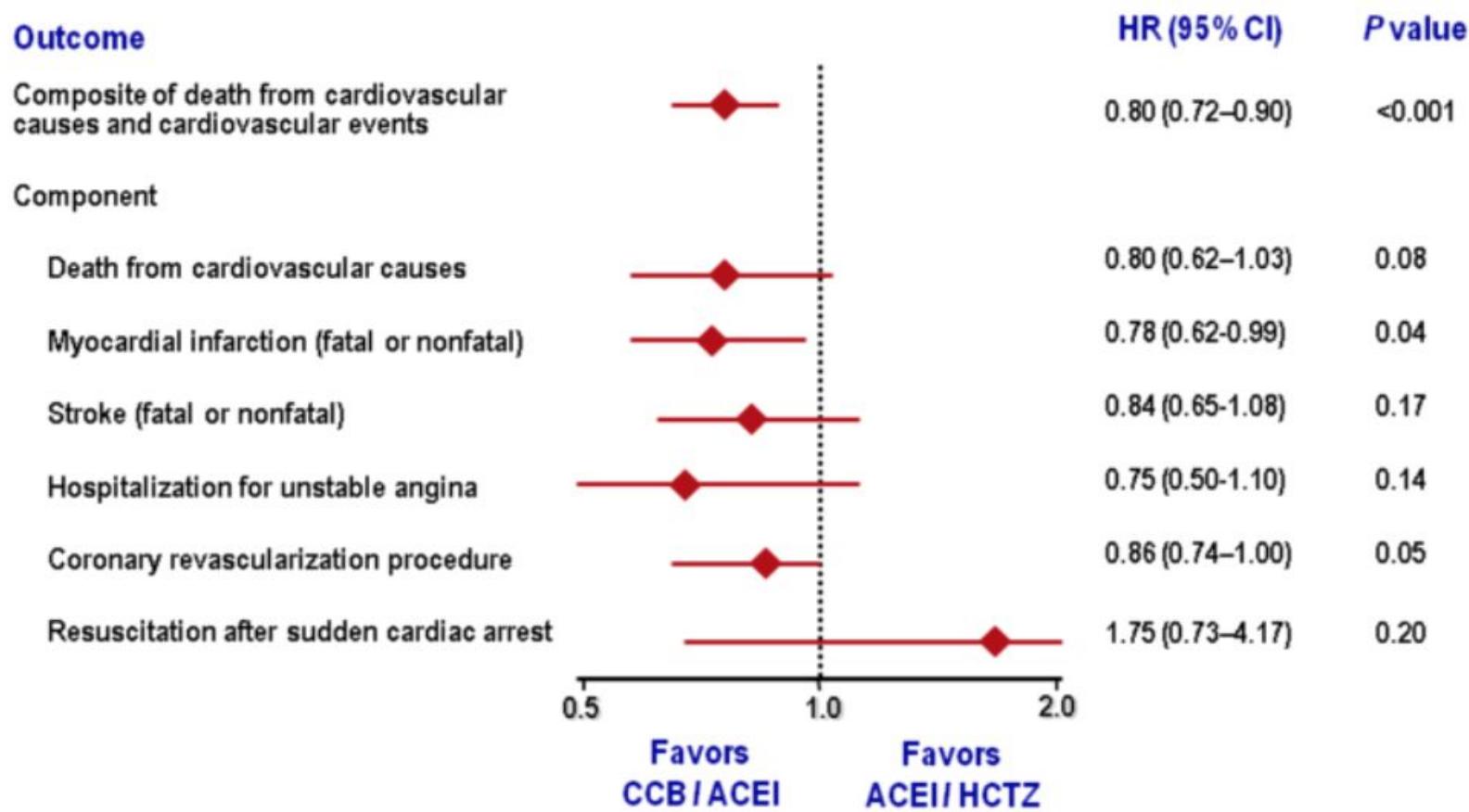
Etude ACCOMPLISH



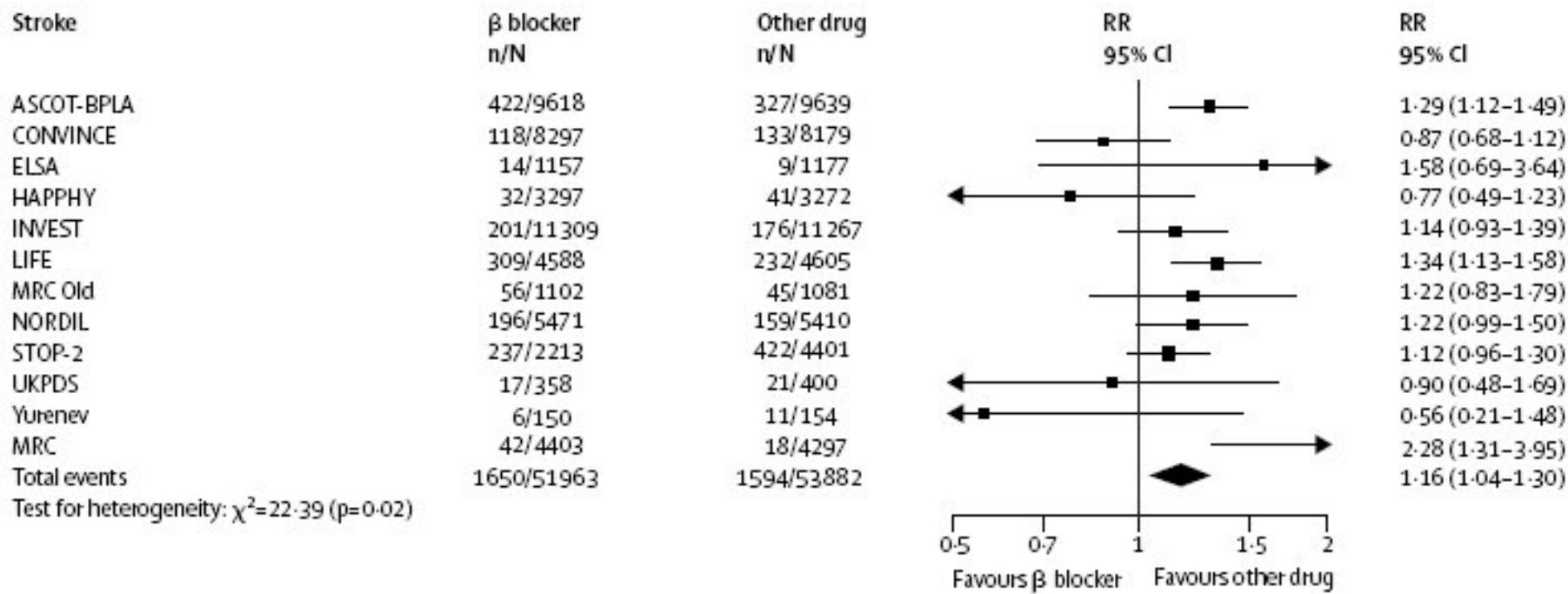
Number at risk

Benazepril plus amlodipine	5,512	5,317	5,141	4,959	4,739	2,826	1,447
Benazepril plus hydrochlorothiazide	5,483	5,274	5,082	4,892	4,655	2,749	1,390

ACCOMPLISH: Effects on Primary and Other End points



Beta-blockers versus others: stroke

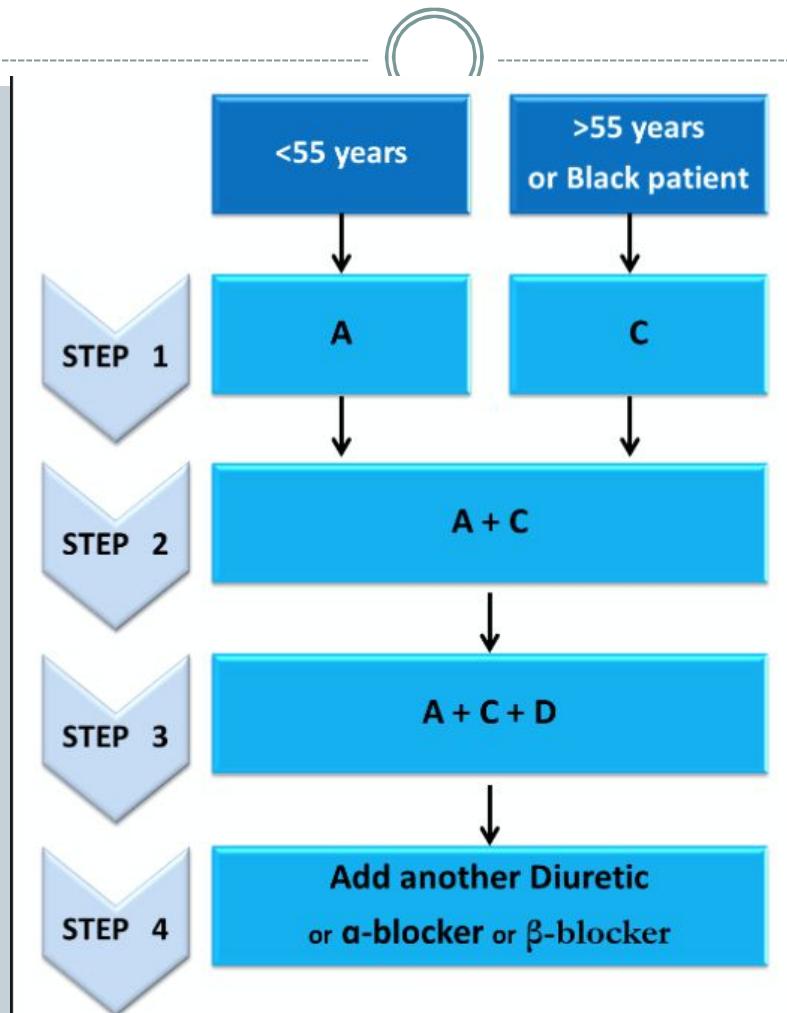


Encore une place pour les betabloquants ?



- **Angor & post-infarctus**
- **Décompensation cardiaque**
- Tachyarythmie
- Migraine
- Périopératoire
- Grossesse
- Médicaments plus récents métaboliquement plus sûrs (celiprolol, carvedilol,nébivolol)

NICE guidelines



A = ACEi or ARBs

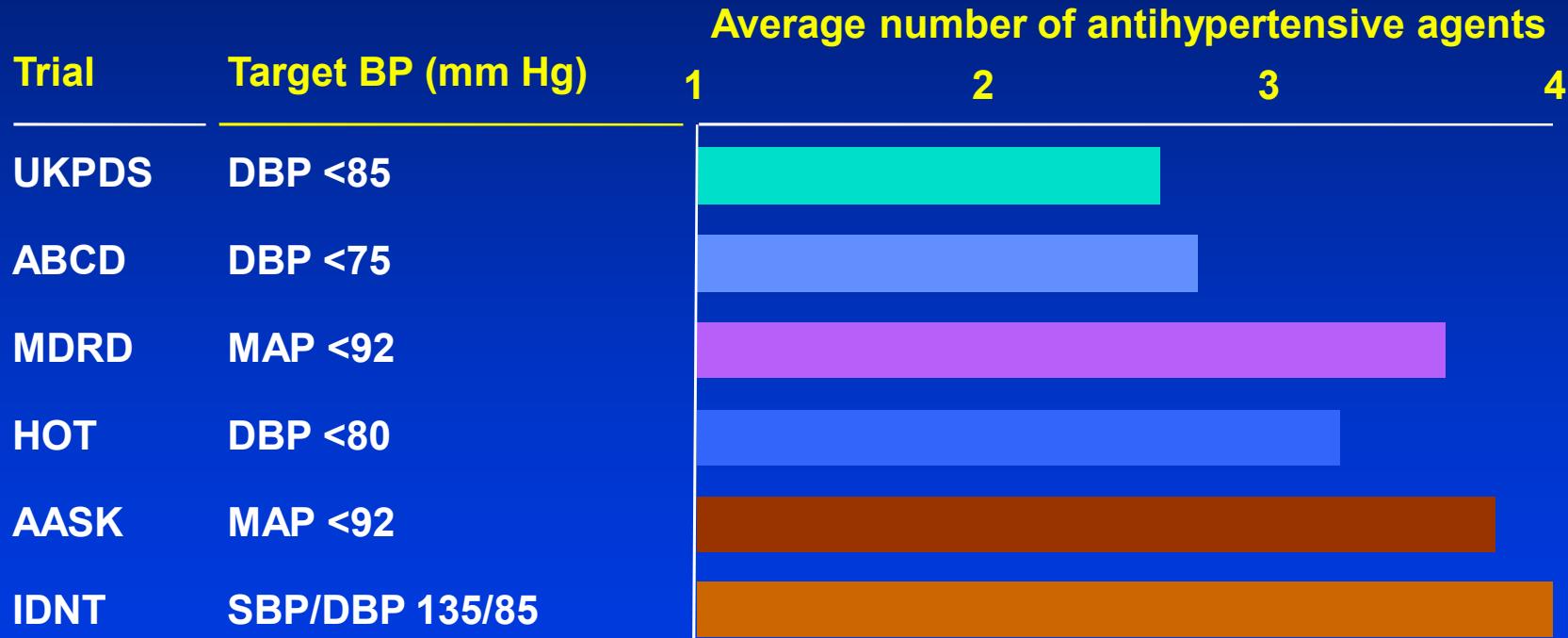
C = Calcium Channel Blockers

D = Diuretic

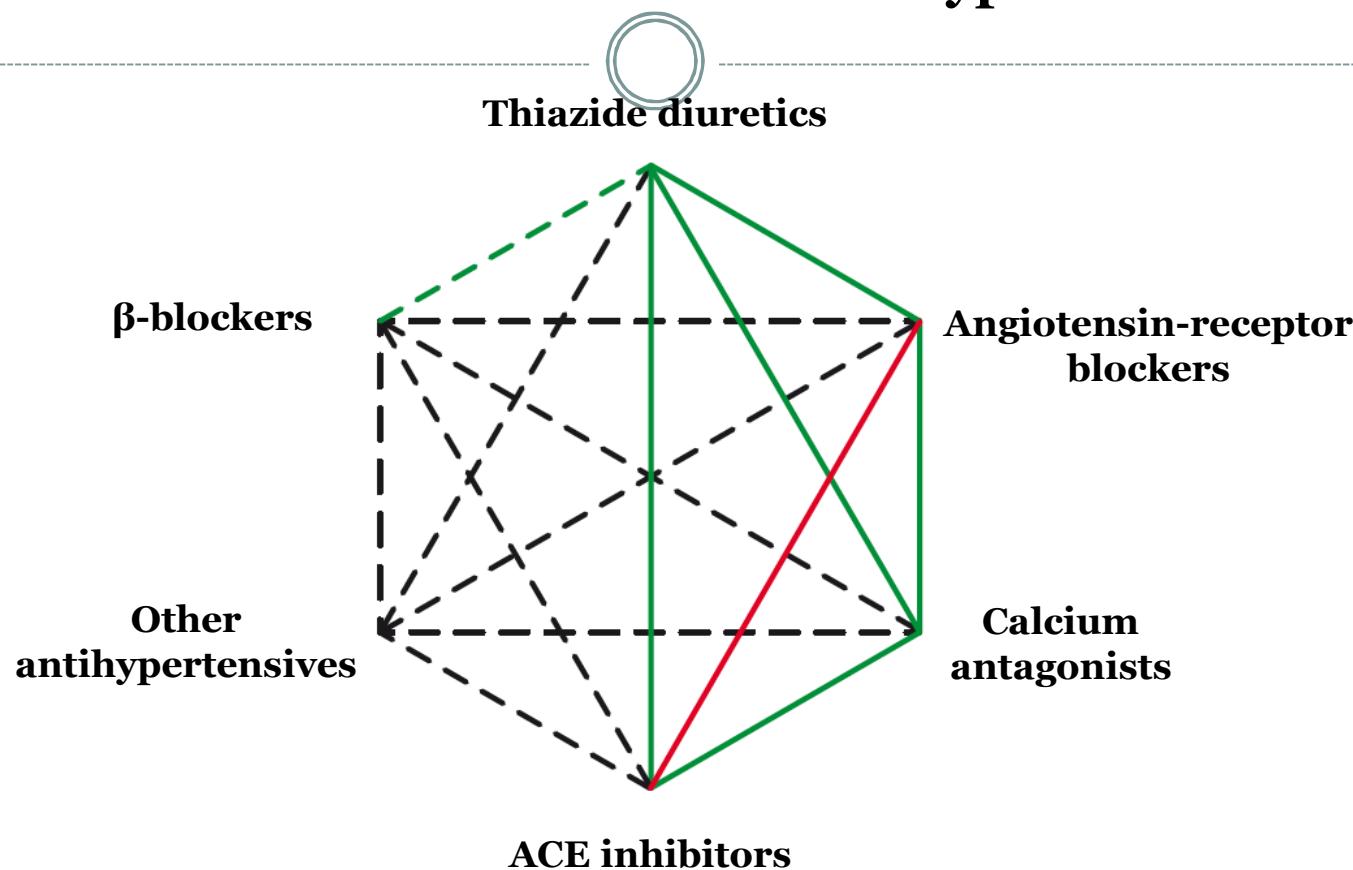
Reproduced from NICE guidelines Aug, 2011.

<http://www.nice.org.uk/nicemedia/live/13561/56015/56015.pdf>

Multiple antihypertensive agents are often needed to achieve target BP



Possible combinations of classes of antihypertensive drugs



Green continuous lines: preferred combinations; **green dashed line:** useful combination (with some limitations); **black dashed lines:** possible but less well tested combinations; **red continuous line:** not recommended combination. Although verapamil and diltiazem are sometimes used with a beta-blocker to improve ventricular rate control in permanent atrial fibrillation, only dihydropyridine calcium antagonists should normally be combined with beta-blockers.

Les thiazides sont efficaces en IRC



Table 2. Fractional excretion of sodium and chloride and renal parameters during the study

	Basal state	FUR	HCTZ	Combined regimen (FUR + HCTZ)
FENa	3.7±0.9	4.5±0.2	5.5±0.3 ^a	5.5±0.4 ^a
FECl	3.9±0.2	5.0±0.2	6.5±0.3 ^a	6.3±0.3 ^a
Mean arterial pressure (mmHg)	112±11	97±9 ^b	99±7 ^b	97±9 ^b
GFR (ml/min)	29±11	23±8 ^b	21±8 ^b	22±9 ^b
RPF (ml/min)	114±54	87±22	94±37 ^a	95±37 ^a
FF (%)	0.25±0.1	0.24±0.06	0.20±0.06	0.21±0.04

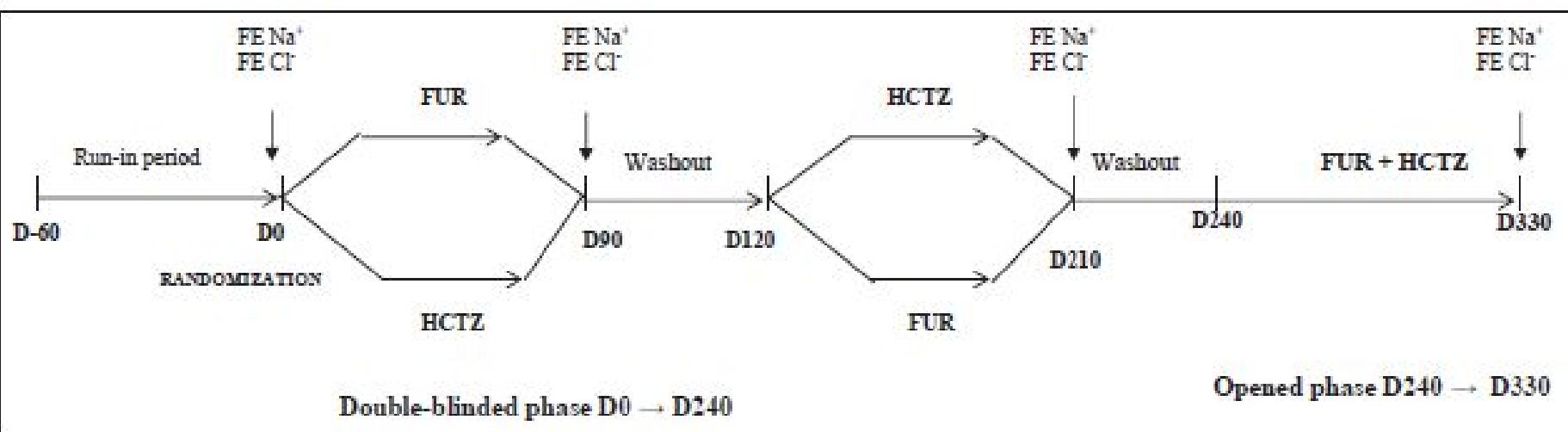
^aP<0.05 vs basal and FUR.

^bP<0.05 vs basal.

FUR = furosemide; HCTZ = hydrochlorothiazide; FENa = fractional excretion of sodium; FECl = fractional excretion of chloride; GFR = glomerular filtration rate; RPF = renal plasma flow; FF = filtration fraction.

A Pilot Study Comparing Furosemide and Hydrochlorothiazide in Patients With Hypertension and Stage 4 or 5 Chronic Kidney Disease

Bertrand Dussol, MD, PhD;^{1,2,3} Julie Moussi-Frances, MD;² Sophie Morange, MD;³ Claude Somma-Delpero, MD, PhD;^{1,4} Olivier Mundler, MD;^{1,4} Yvon Berland, MD^{1,2,3}



Pas de ≠ de tension artérielle

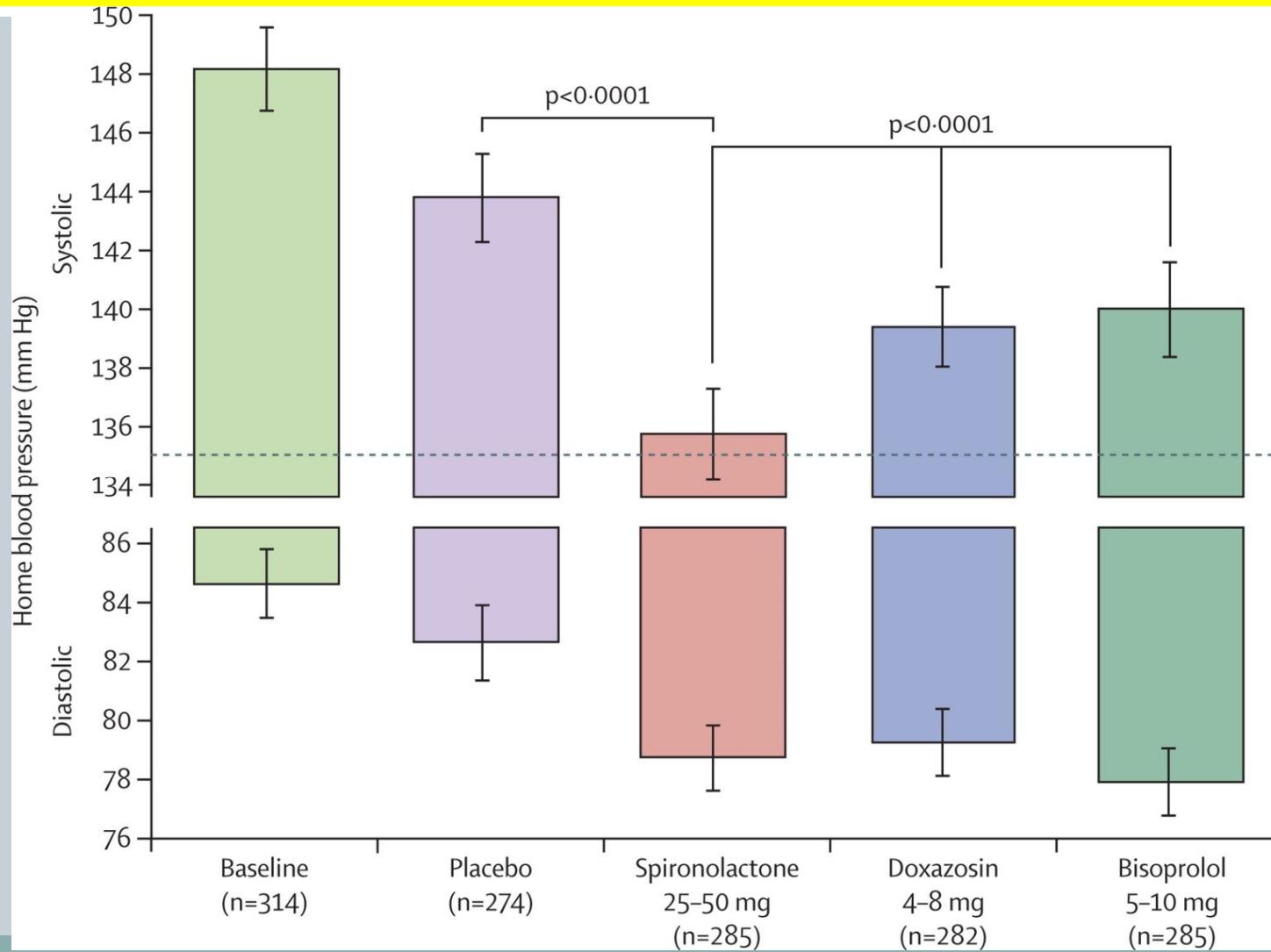
TABLE II. Fractional Excretions of Sodium and Chloride and Renal Parameters During the Study

	Basal State	FUR	HCTZ	Combined Regimen (FUR + HCTZ) ^a
FE Na ⁺	3.4±1.8	4.4±2.2	3.9±2.4	4.9±2.8 ^b
FE Cl ⁻	3.8±2.0	5.1±2.9	4.6±2.5	6.0±3.1 ^b
Mean blood pressure, mm Hg	101±13	93±9 ^b	94±7 ^b	86±13 ^c
GFR, mL/min/1.73 m ²	25±10	21±10	22±10	18±11 ^c
RPF, mL/min/1.73 m ²	95±35	96±31	94±36	85±41
RVR, mm Hg/mL/min/1.73 m ²	2.0±1.0	1.7±0.8	1.9±1.1	1.8±1.0
FF, %	27±8	22±6 ^b	23±7 ^b	20±6 ^c

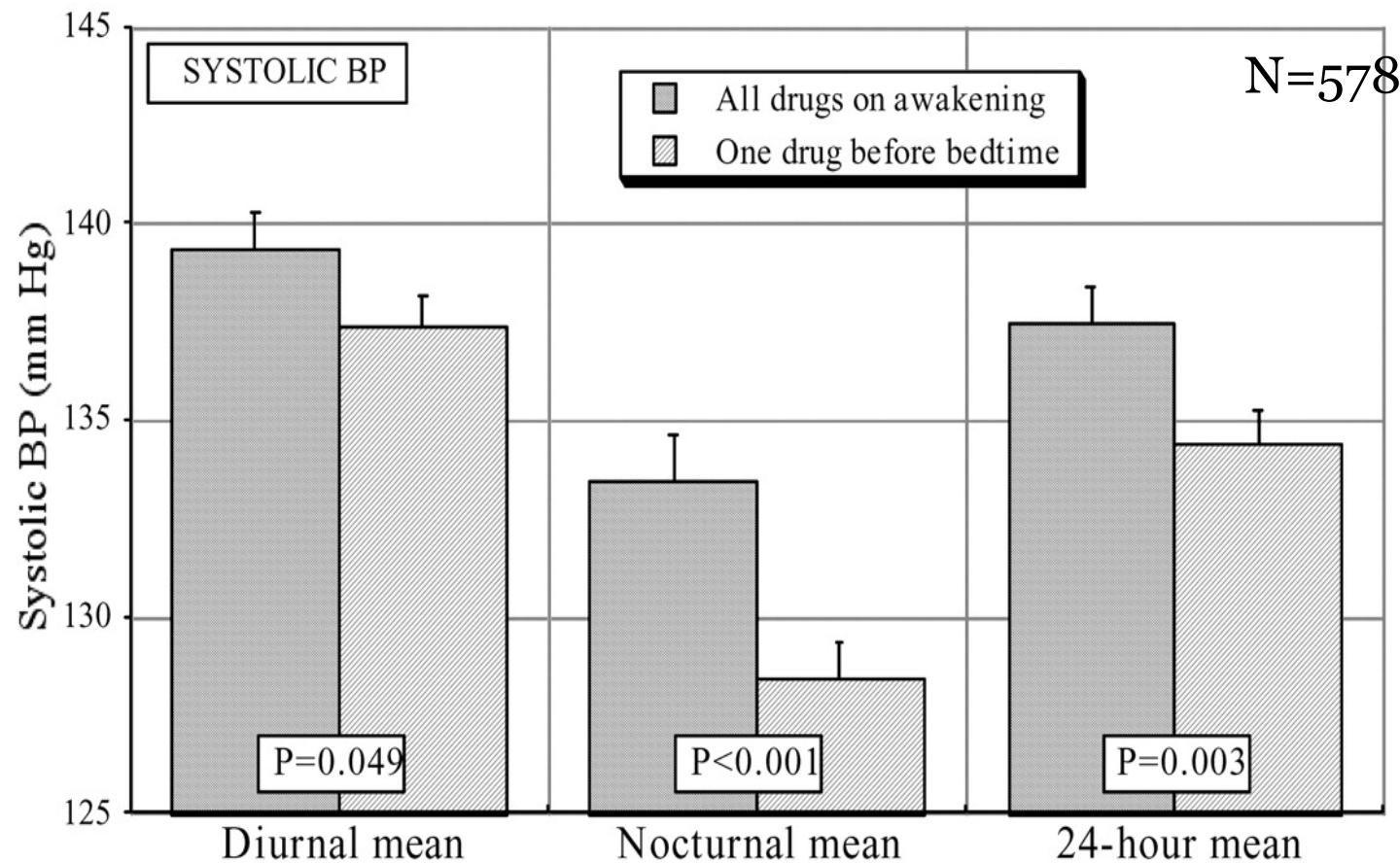
Abbreviations: FECI, fractional excretion of chloride; FE Na, fractional excretion of sodium; FF, filtration fraction; FUR, furosemide; GFR, glomerular filtration rate; HCTZ, hydrochlorothiazide; RPF, renal plasma flow; RVR, renal vascular resistance. ^aOnly 16 patients were included in the analysis.

^bP<.05 vs basal. ^cP<.01 vs basal.

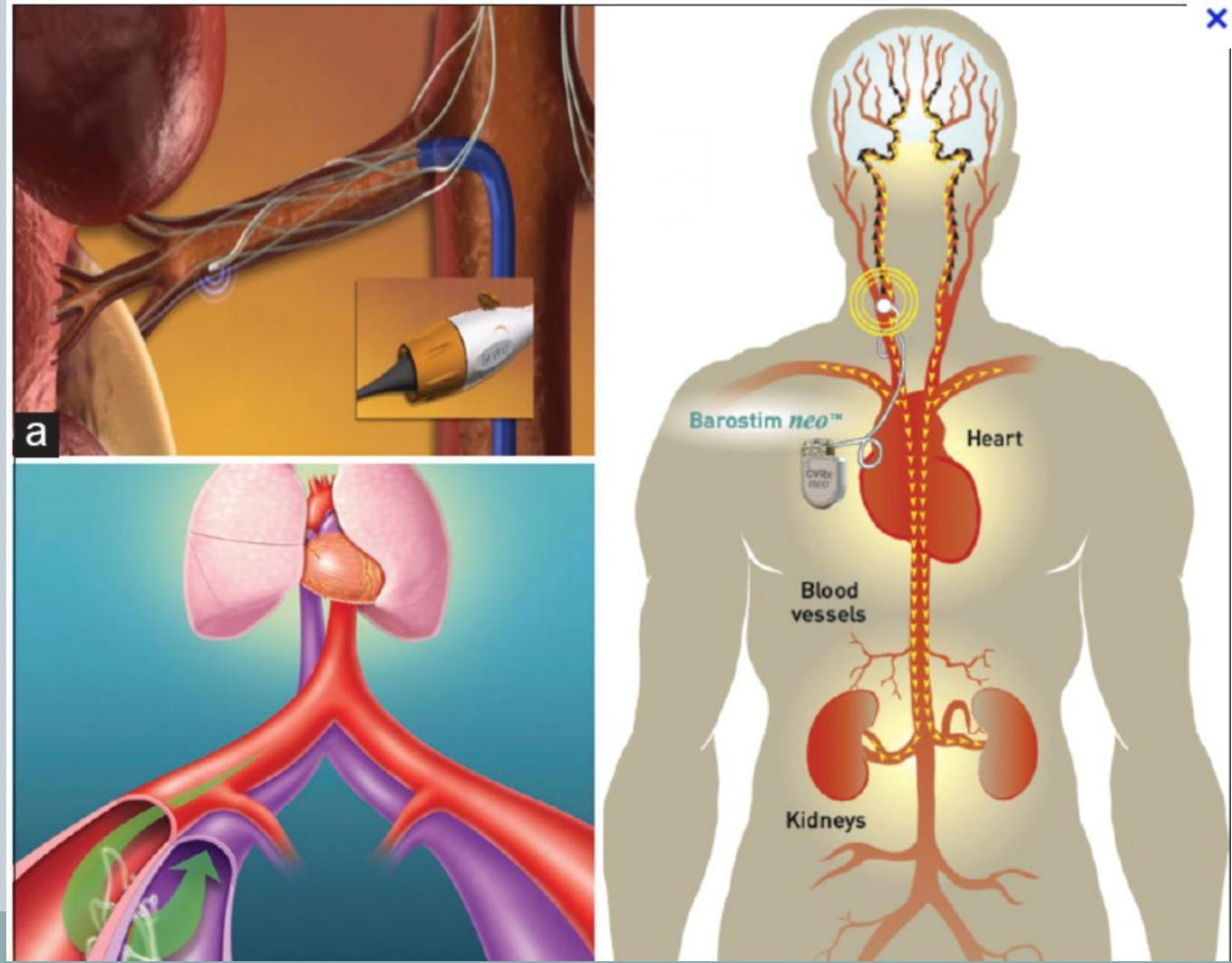
PATHWAY-2 (Lancet 2015)



Effect of time of day of treatment on ABP pattern in RH



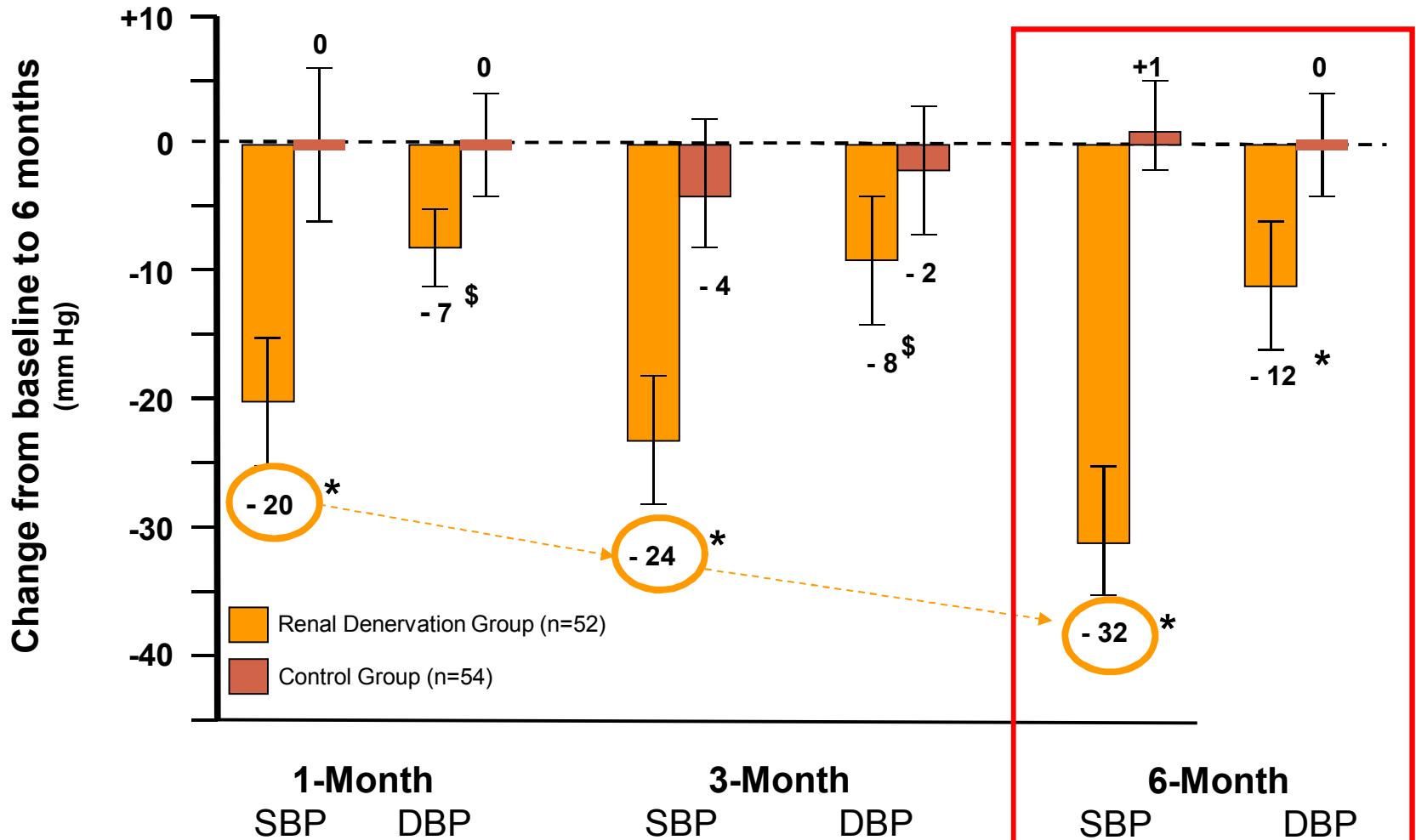
What about Star Wars ?



Symplicity HTN-2

Primary Endpoint

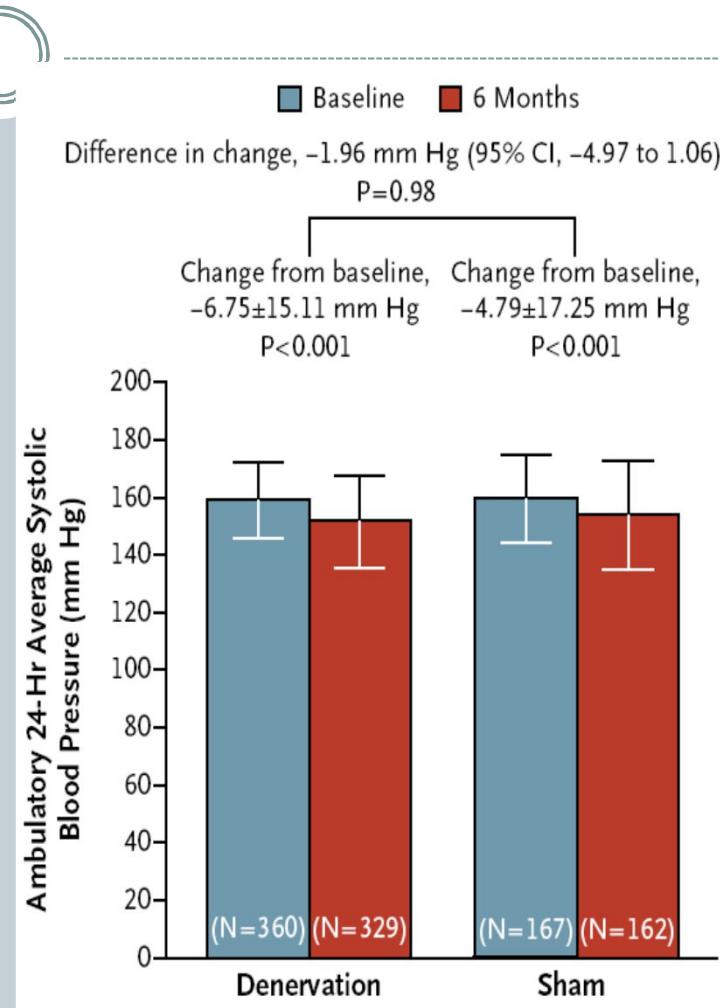
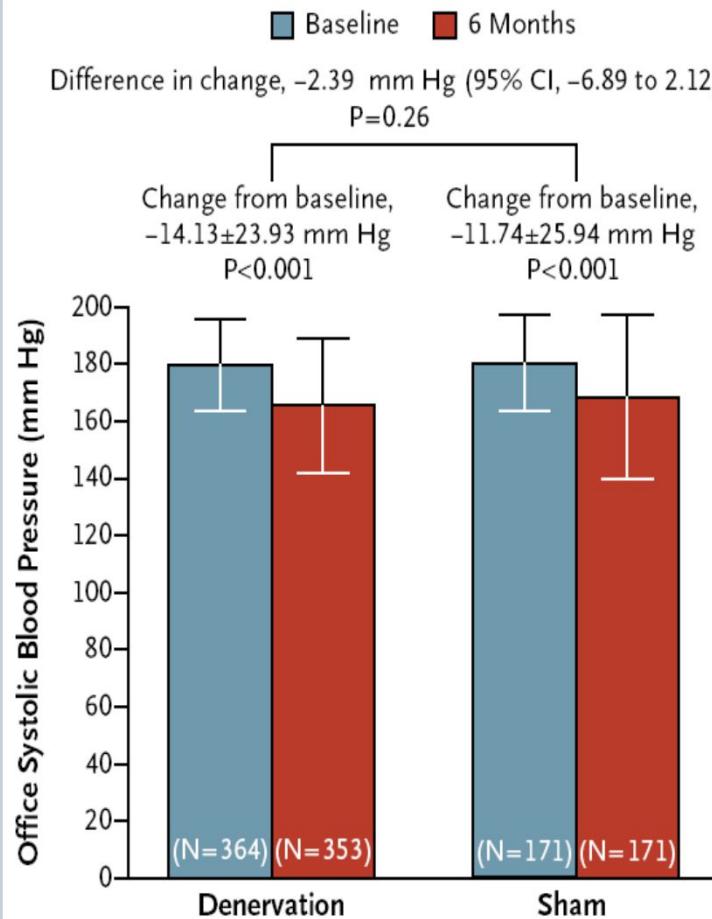
Office Blood Pressure at 6 Months



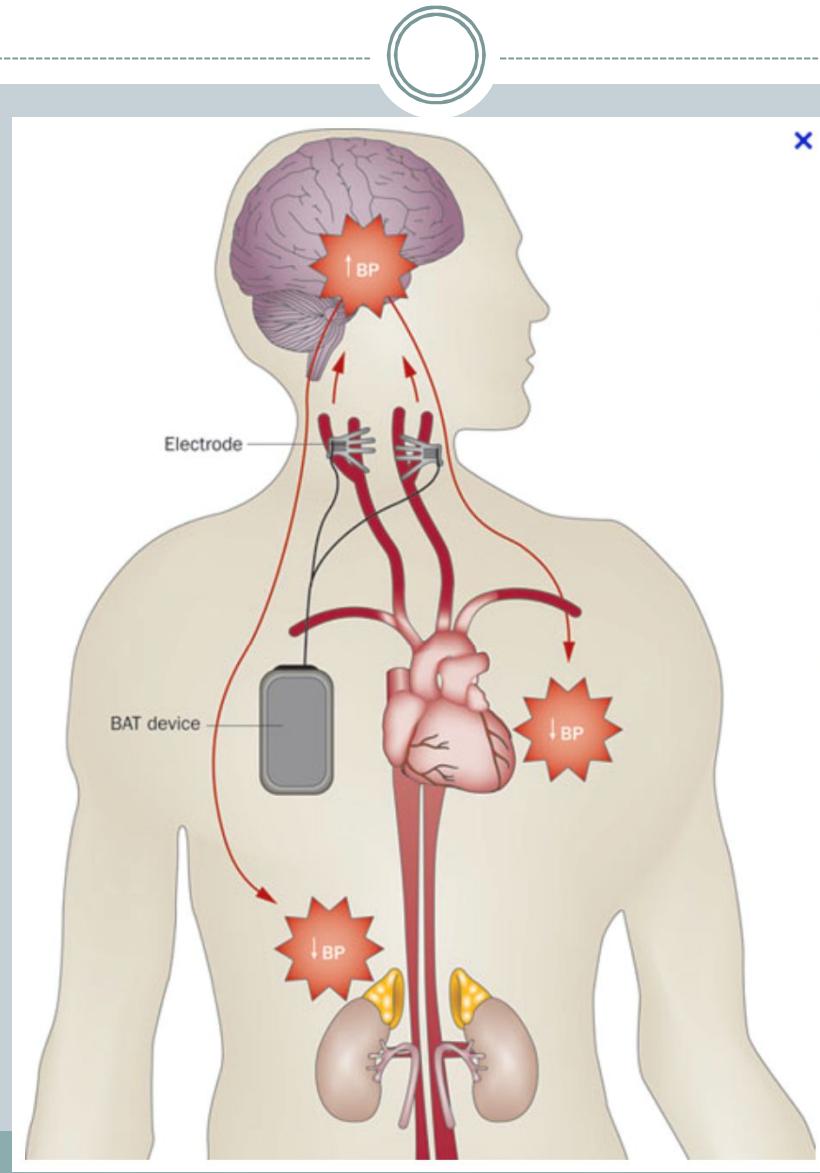
* p<0.0001 \$ p< 0.005 vs baseline

Esler M. et al. Lancet 2010

SYMPPLICITY HTN-3

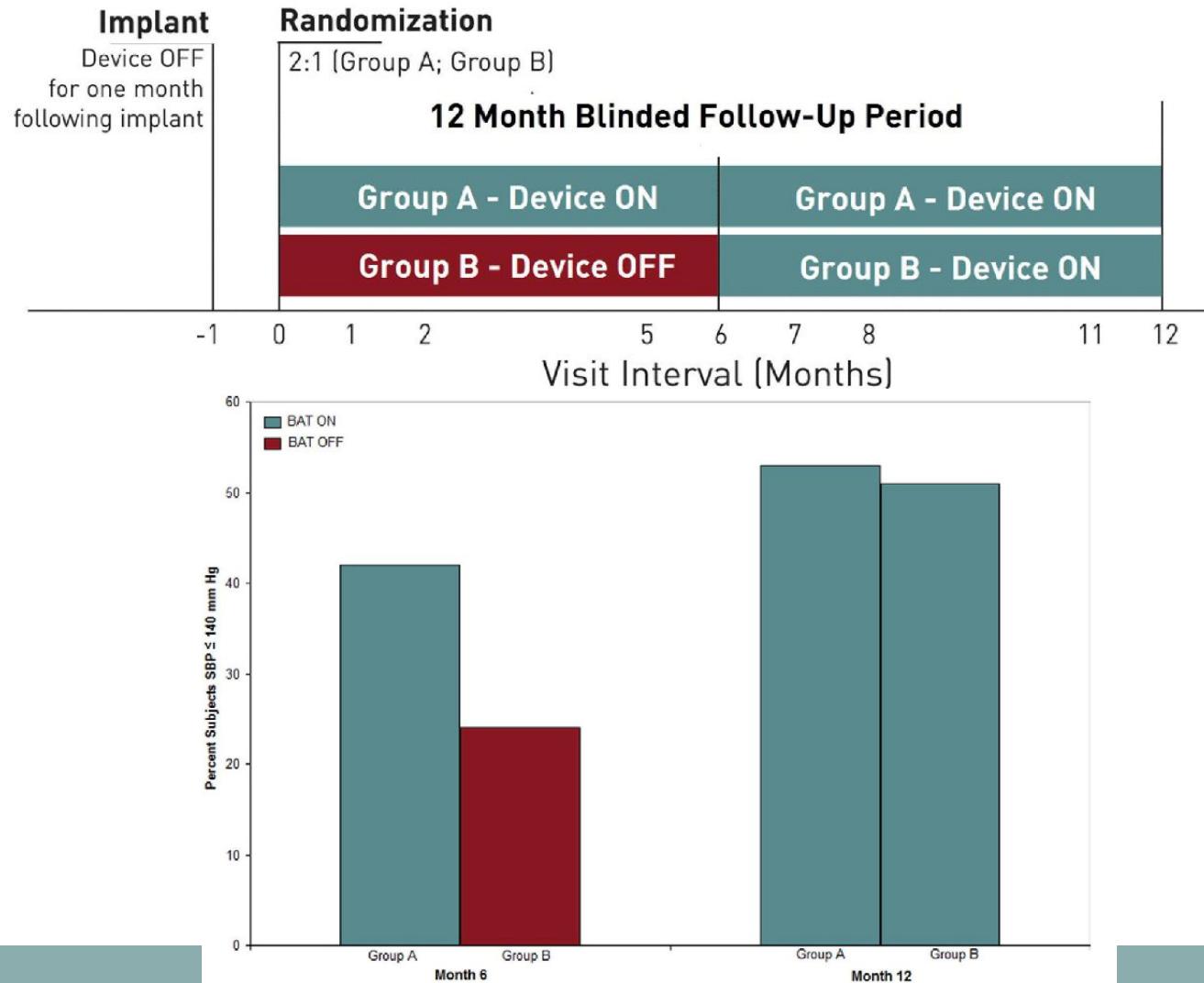


Stimulation du barorécepteur

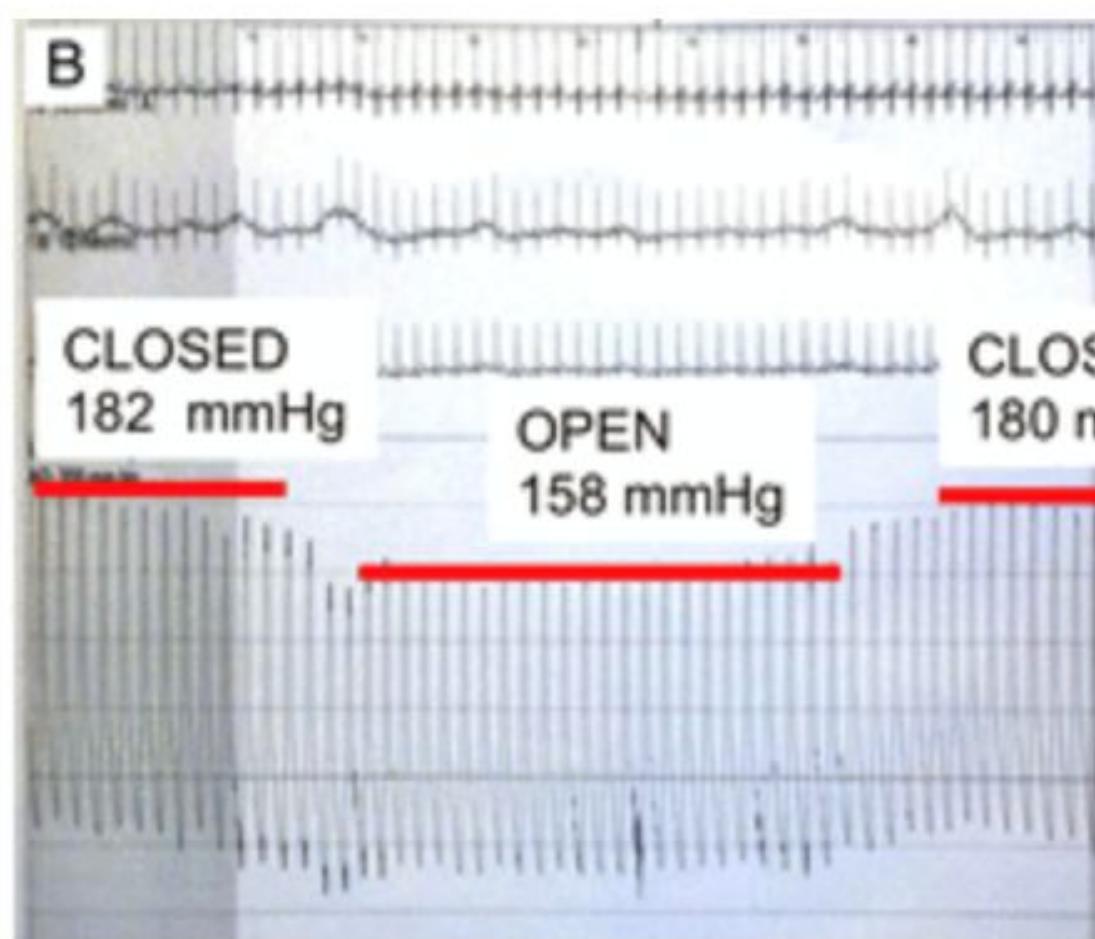
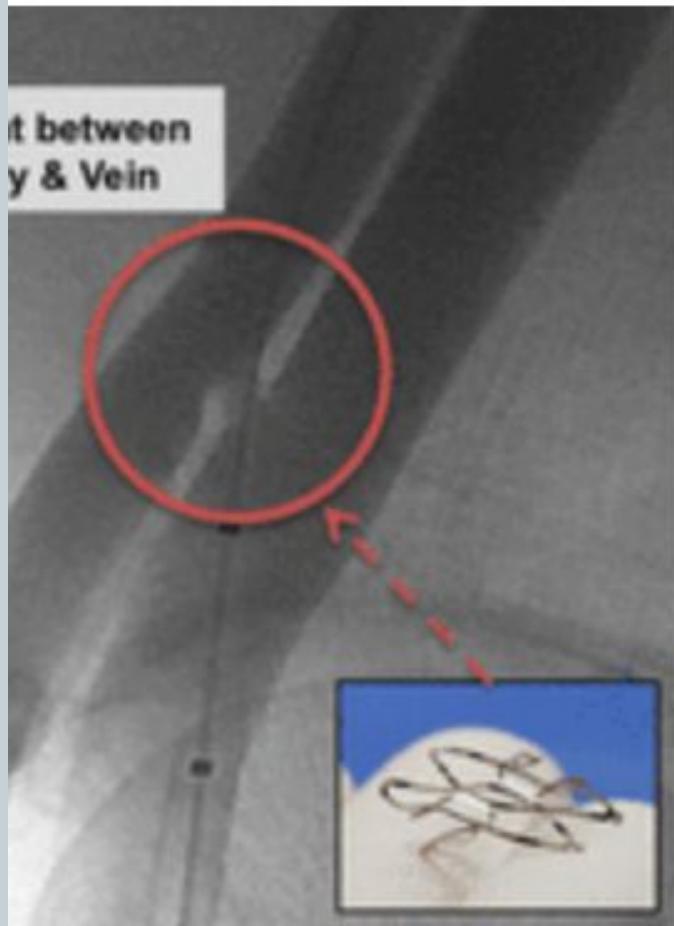


Effet de la stimulation du barorécepteur

Bisognano et al JACC 2011;58:76-83

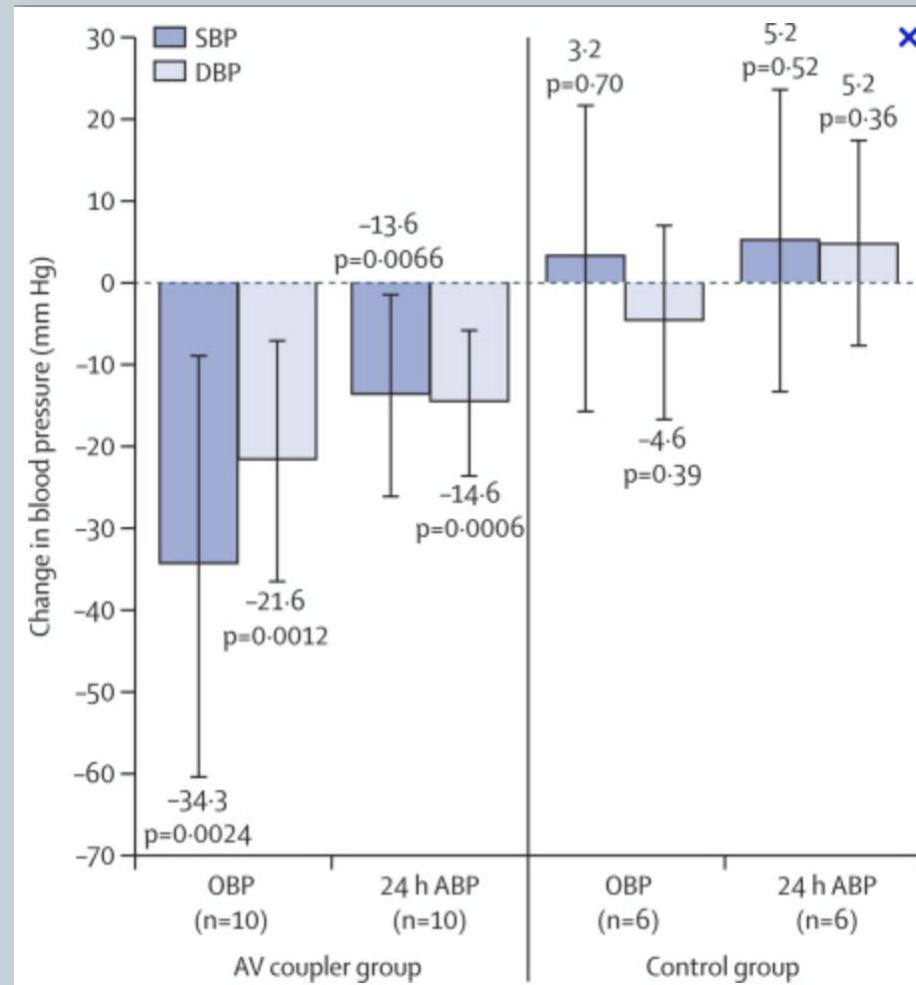


Effet d'une FAV iliaque sur la pression artérielle



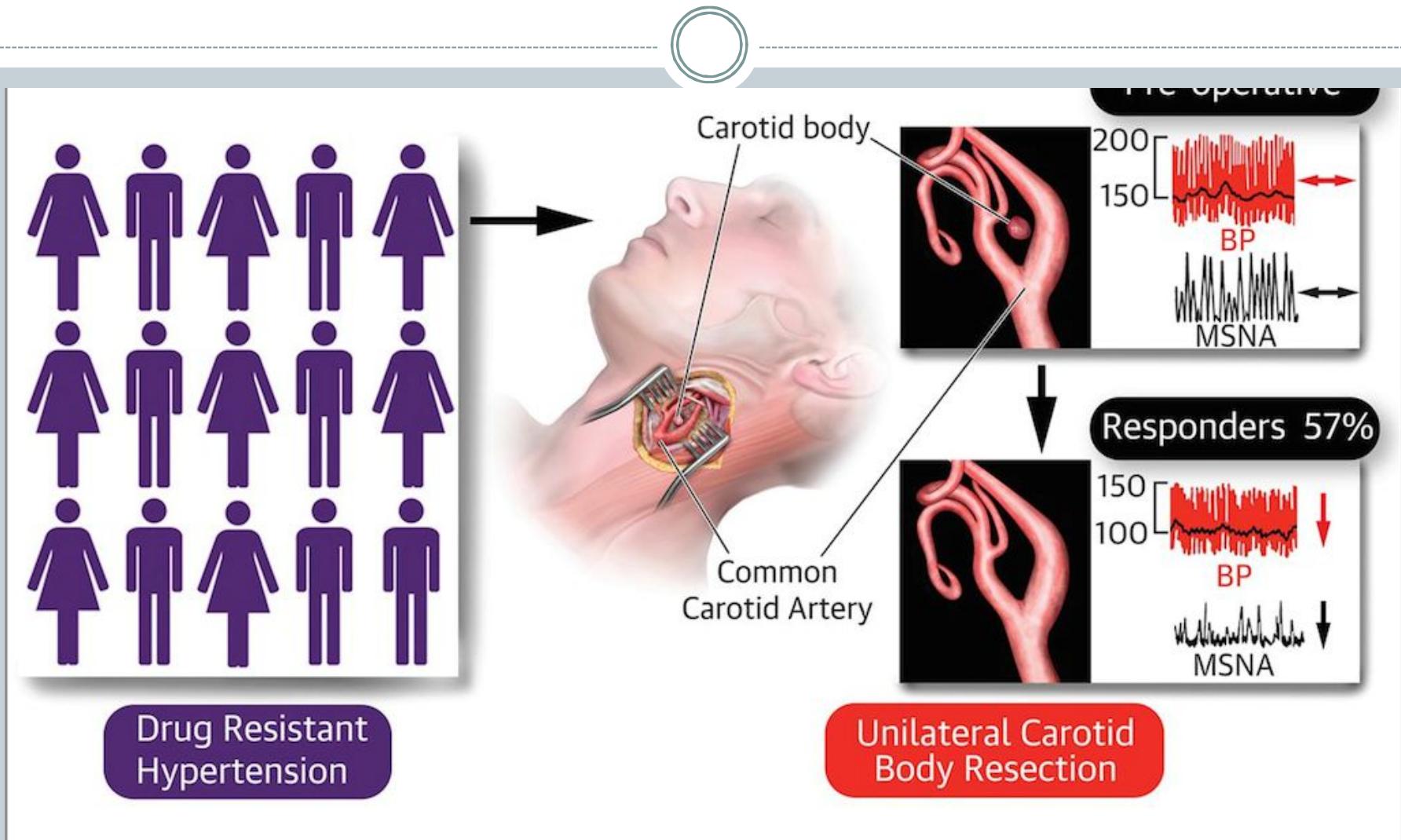
Effet tensionnel de la création d'une FAV iliaque

Lobo et al Lancet; 385:1634-1641



Résection unilatérale du corps carotidien

Narkiewicz et al JACC Basic Trans Science 2016; 1:313-324



Take home message



- Utilisons (convenablement) l'automesure
- Objectif < 140/90 mmHg et plus bas si toléré chez patients à haut risque et insuffisants rénaux
- Prudence chez le sujet âgé
- Intérêt des associations fixes
- Importance diurétiques et spironolactone
- Hypertension pas (encore) une branche de la cardiologie interventionnelle