

Conduite à tenir devant... une HTA réfractaire

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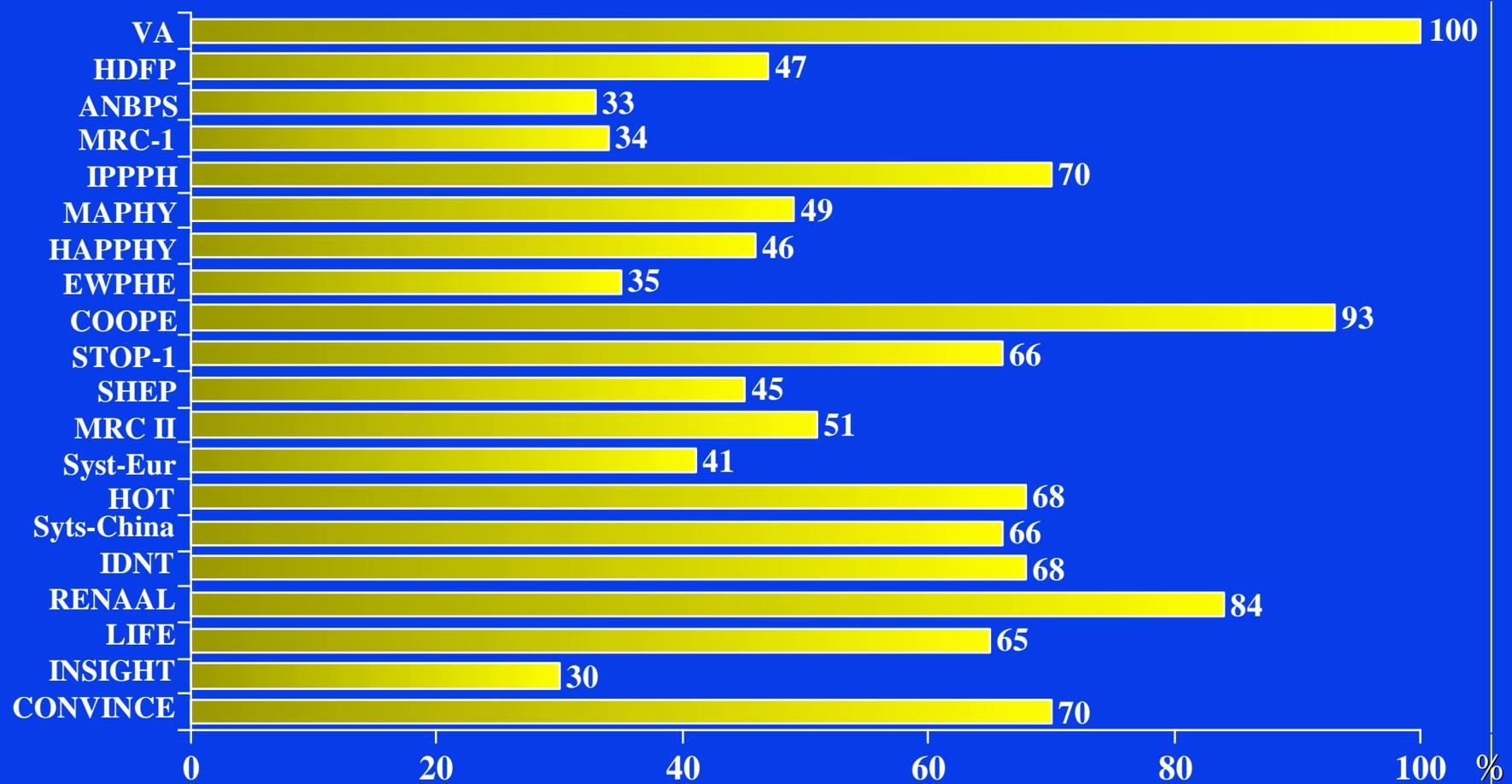


HTA réfractaire

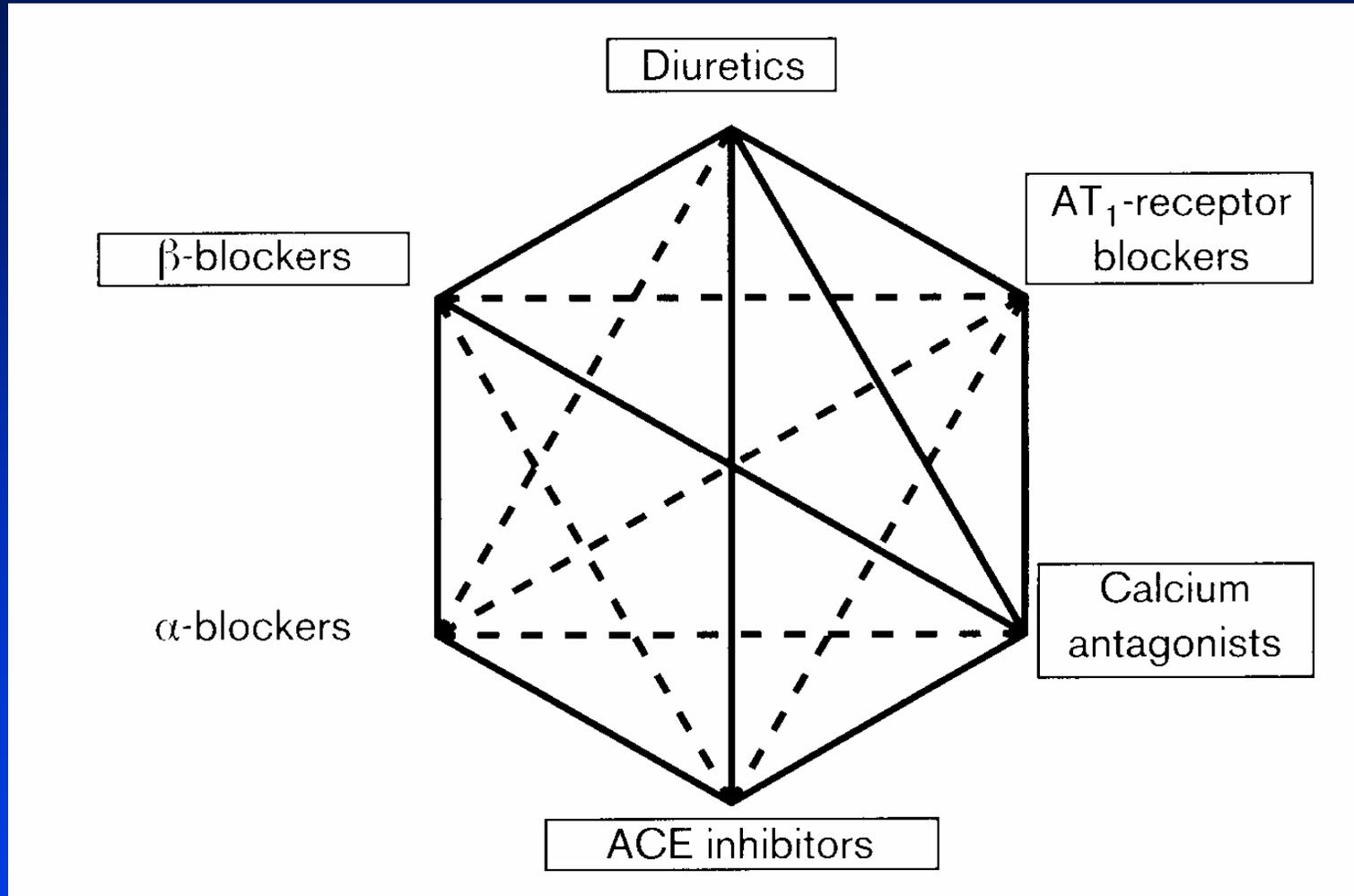
- Au moins trois médicaments
- Classes différentes
- Doses adéquates
- dont un diurétique

Chobanian AV *Am J. Hypertension*.2003;42:1206-1252

Pourcentage de patients hypertendus avec une association de traitements dans les études cliniques

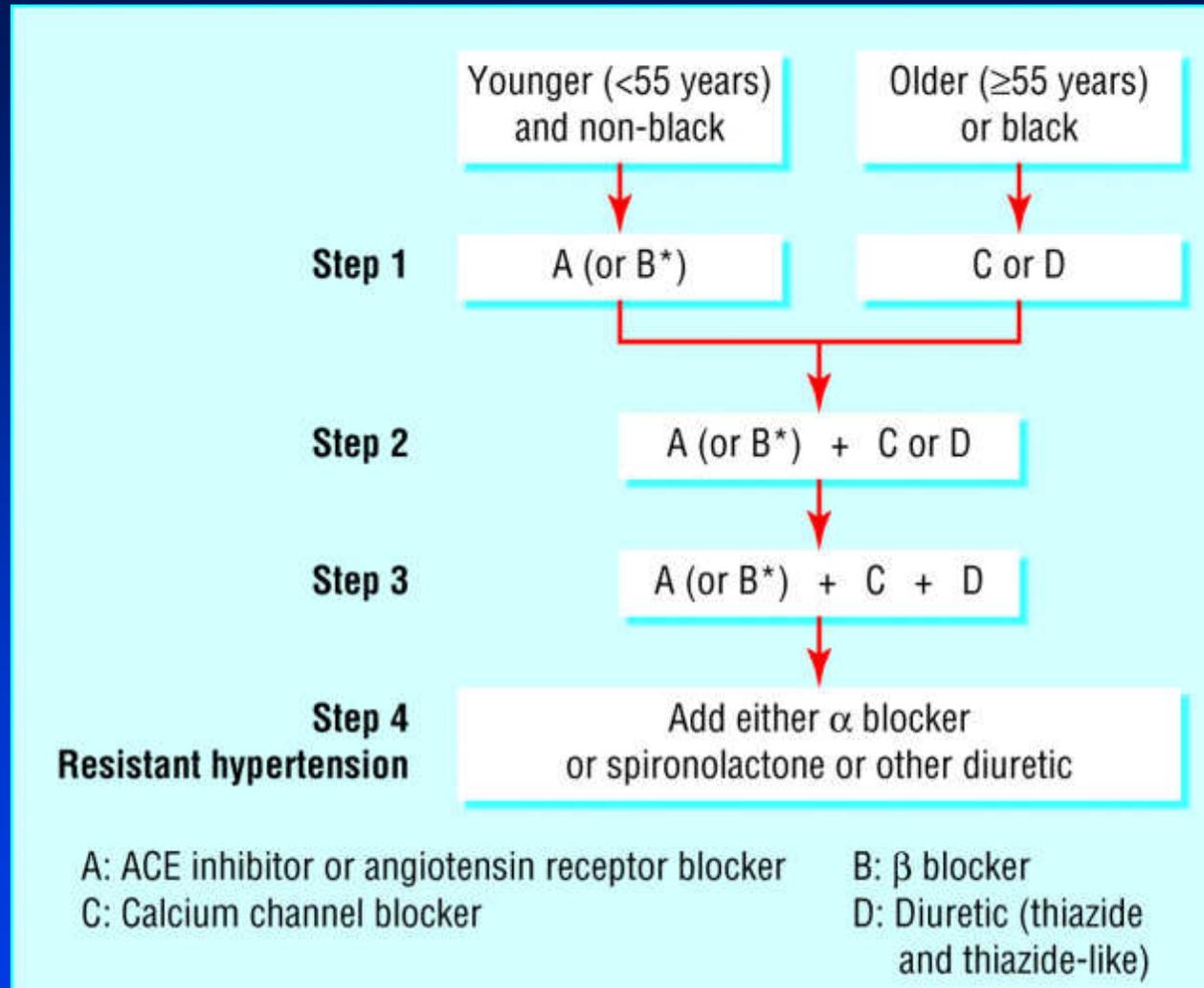


Associations recommandées



ESH recommendations for blood pressure measurement.
J Hypertens. 2003;21:821-48.

AB/CD rule



Williams B et al., *BMJ*.2004;42:328-634-640

TWO BASIC TYPES OF HYPERTENSIVE PATIENTS

“V” HYPERTENSION

PRA levels < 0.65 ng/mL/hr

Have predominately sodium-volume mediated

“R” HYPERTENSION

PRA levels > 0.65 ng/mL/hr

Have predominately renin-angiotensin mediated

TWO BASIC TYPES OF ANTIHYPERTENSIVE DRUGS

“V” DRUGS

- Reduce sodium/volume factor:

Diuretics, aldosterone receptor blockers, α -blockers, or calcium channel blockers

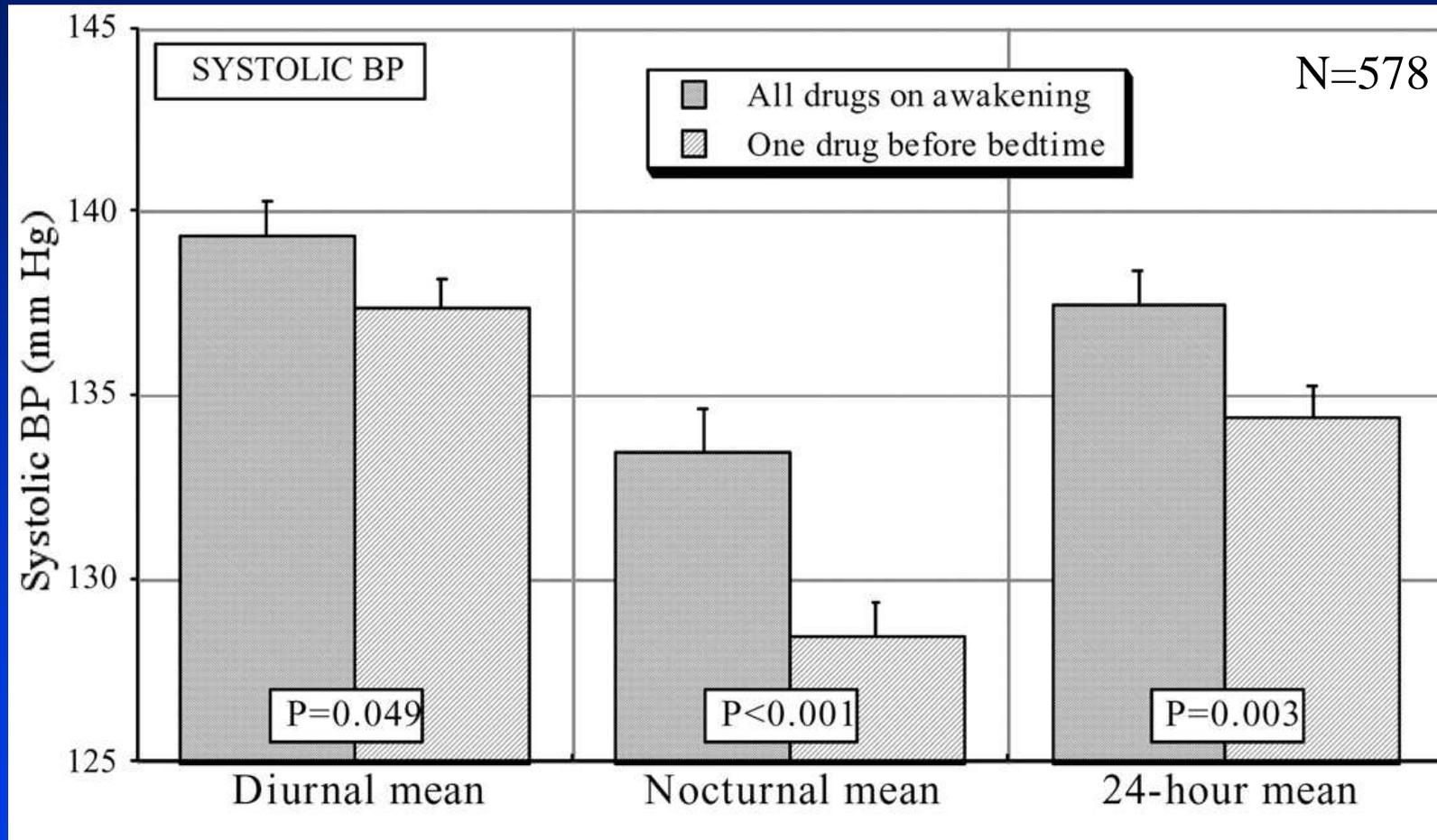
“R” DRUGS

- Block plasma renin system:

CEIs, ARBs, or β -blockers

Laragh's lessons
Am J Hypertension 2001; 14:491-503

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

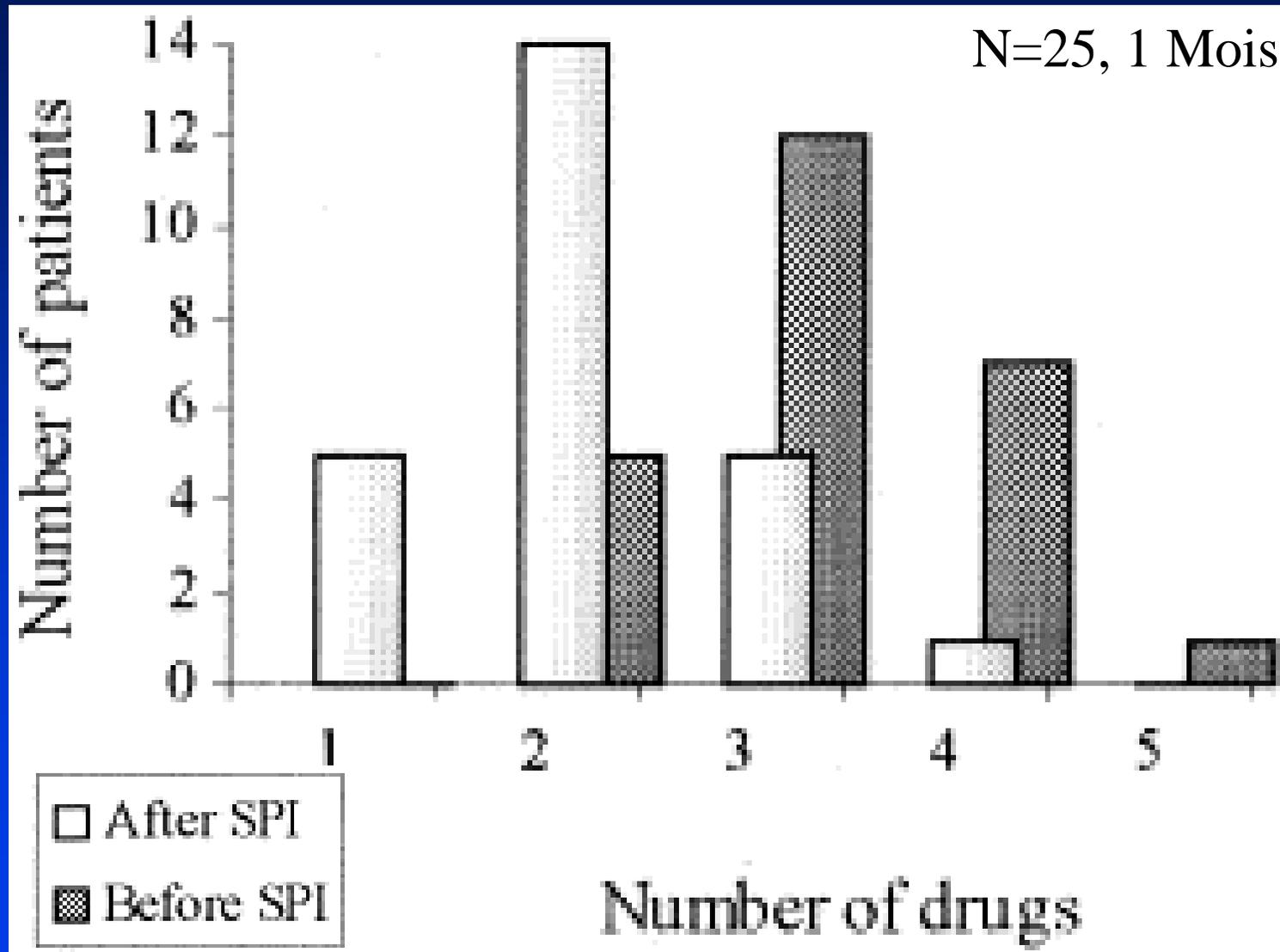


Hermida R et al., *Hypertension* .2005;46:1053-1059

Diurétiques

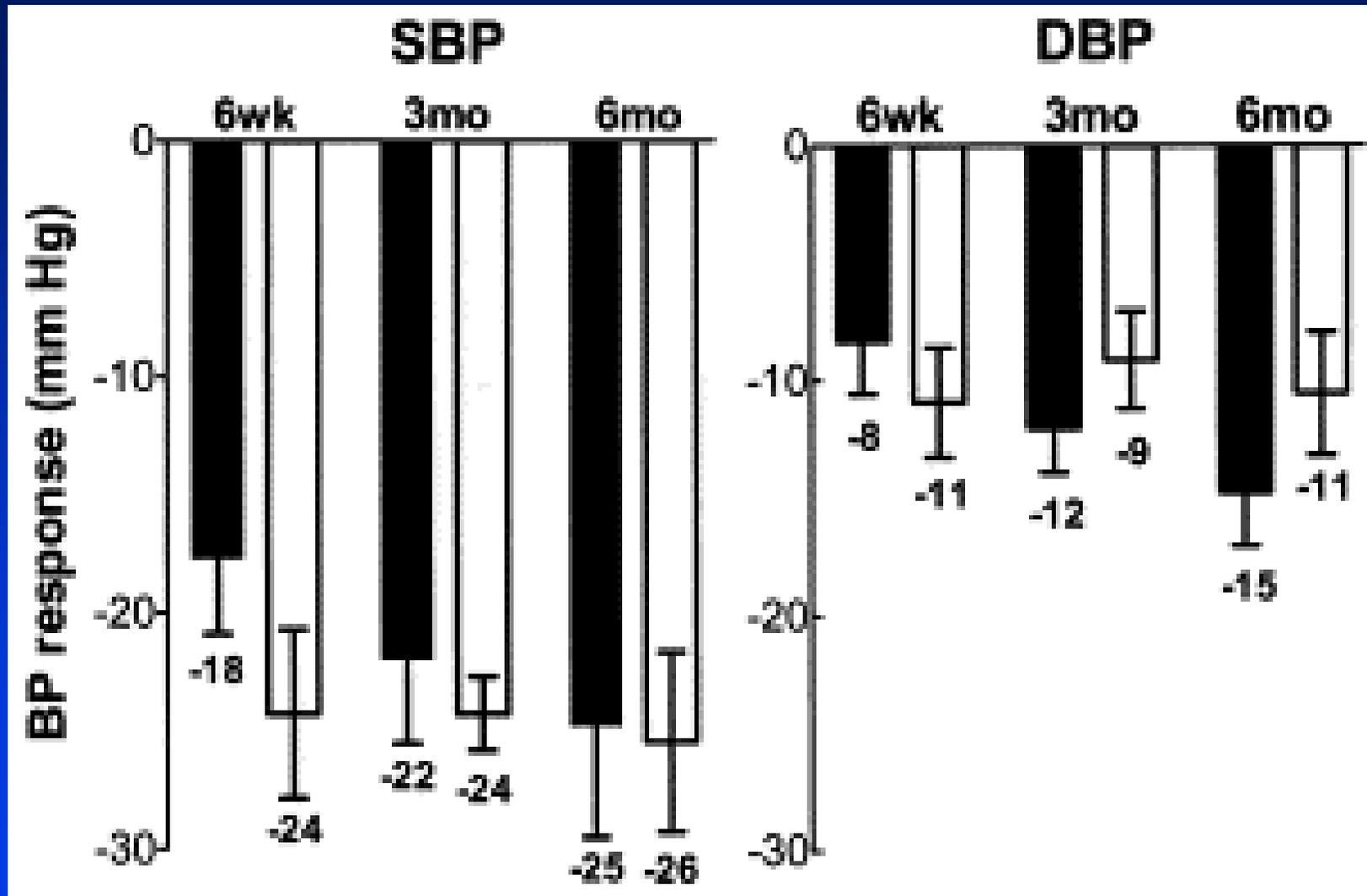
- Premier choix si origine africaine
Au moins 2^{ème} ou 3^{ème} si Caucasien
- Fonction rénale normale: thiazidé
ClCr < 30ml/min: diurétique de l'anse
- Posologie suffisante
- Place spécifique de la spironolactone

HTA réfractaire: place de la spironolactone



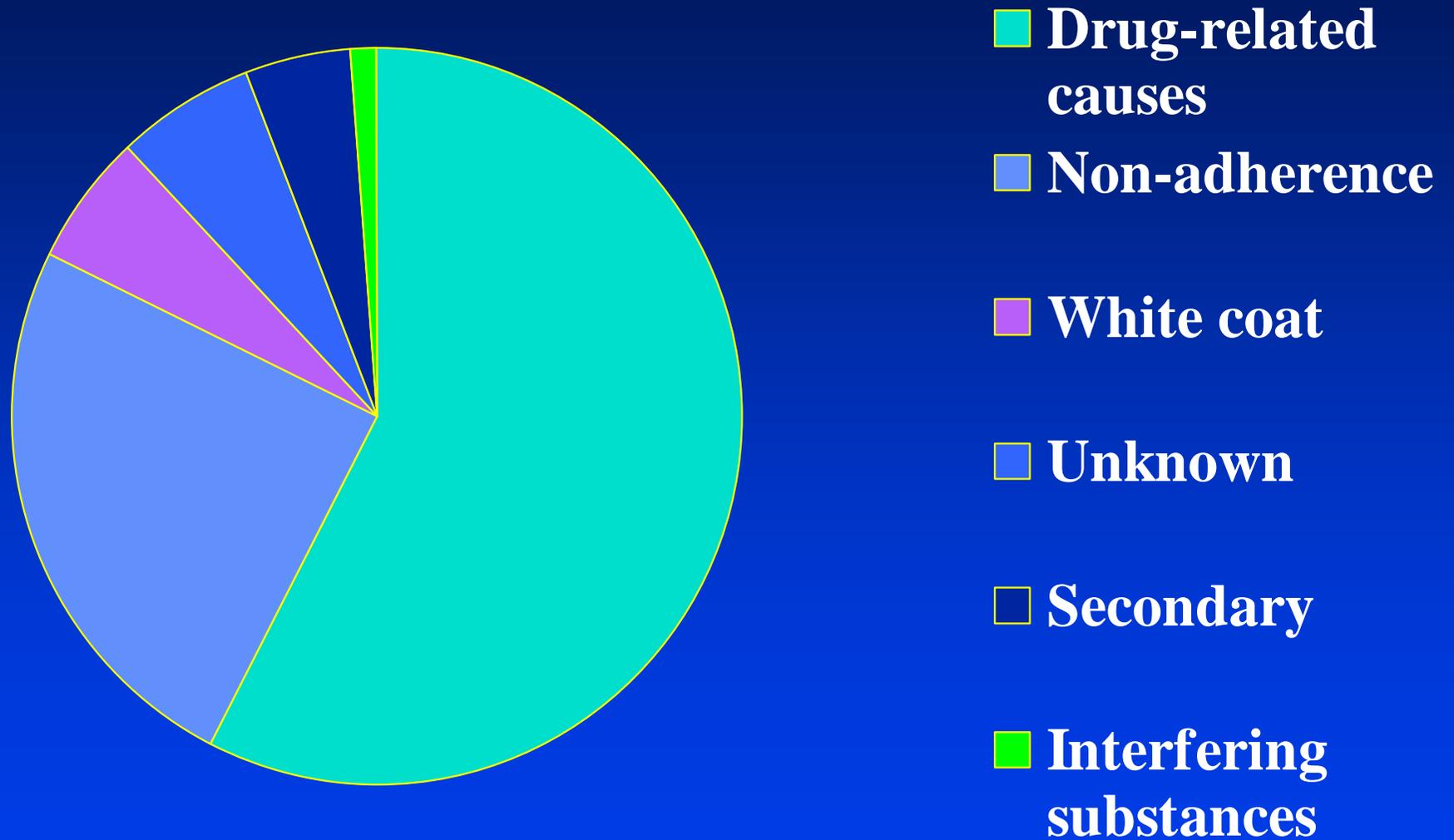
Ouzan J et al., *Am J Hypertens.* 2002;15:333-339.

Spirolactone: avec ou sans hyperaldostérionisme



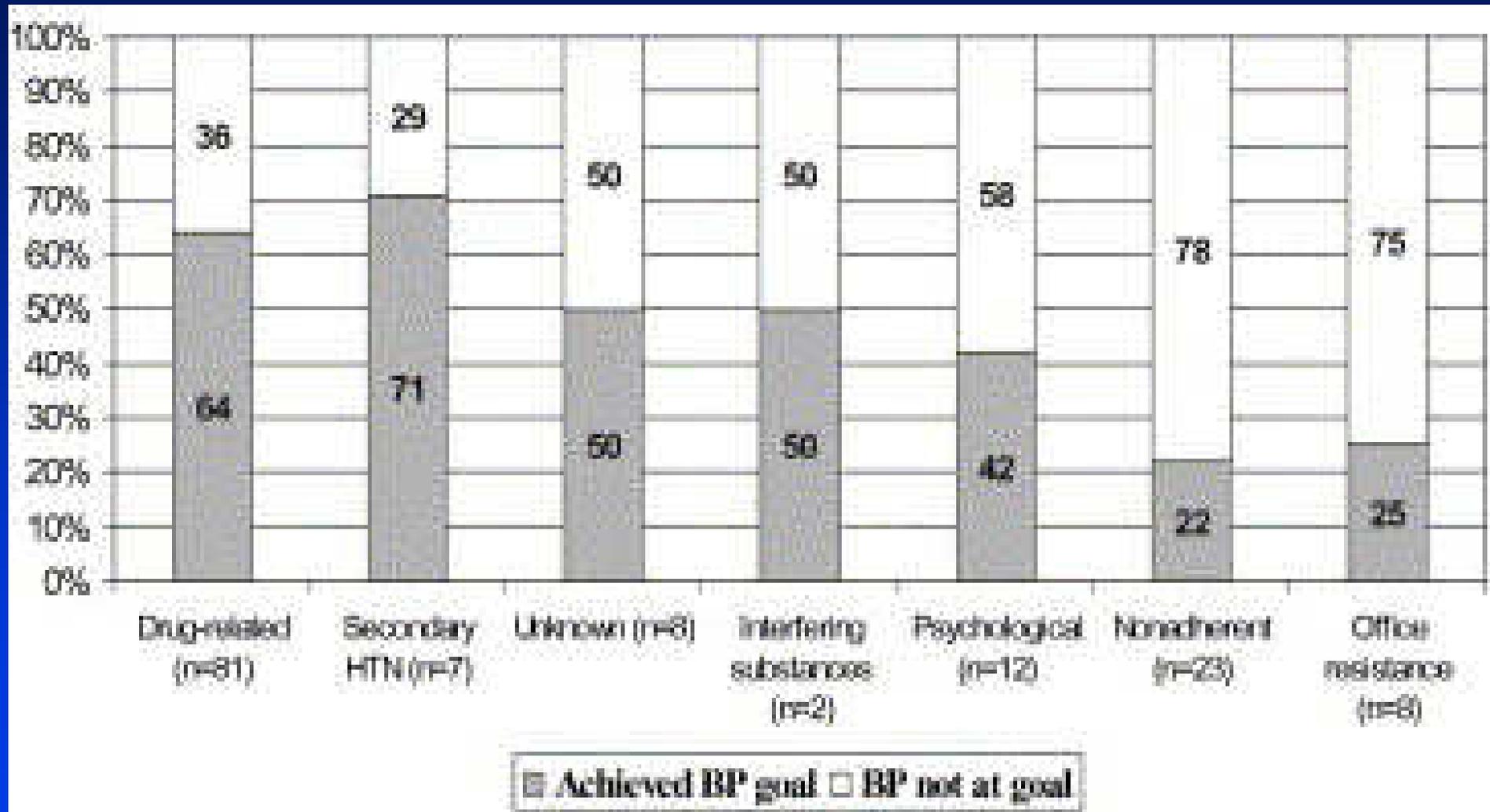
Nishizaka M et al., *Am J Hypertens.* 2003;16:925-930.

Causes of refractory HTN (n=941)



Garg JP et al., *Am J. Hypertension*.2005;18:619-626.

Causes d'HTA réfractaire et...objectif tensionnel



Garg JP et al., *Am J. Hypertension*.2005;18:619-626.

Causes d 'HTA réfractaire

- HTA pseudo-réfractaire
- Observance insuffisante
- Substances hypertensiogènes
- Conditions associées
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HTA pseudo-réfractaire

- Brassard inadapté
- HTA de la blouse blanche
- Pseudohypertension

Brassard inadapté

Mismatch	Consequence
Bladder too small (undercuffing)	Overestimation of BP Range of error 3.2/2.4 – 12/8 mmHg (as much as 30 mmHg in obesity) More common than overcuffing
Bladder too large (overcuffing)	Underestimation of BP Range of error 10 – 30 mmHg

O'Brien et al., *J Hypertens.* 2005;23:697-701

Taille du brassard

British Hypertension Society	
Standard cuff	Bladder 12 × 26 cm for the majority of adult arms
Large cuff	Bladder 12 × 40 cm for obese arms
Small cuff	Bladder 12 × 18 cm for lean adult arms and children
American Heart Association	
Small adult cuff	Bladder 10 × 24 cm for arm circumference 22–26 cm
Adult cuff	Bladder 13 × 30 cm for arm circumference 27–34 cm
Large adult cuff	Bladder 16 × 38 cm for arm circumference 35–44 cm
Adult thigh cuff	Bladder 20 × 42 cm for arm circumference 45–52 cm

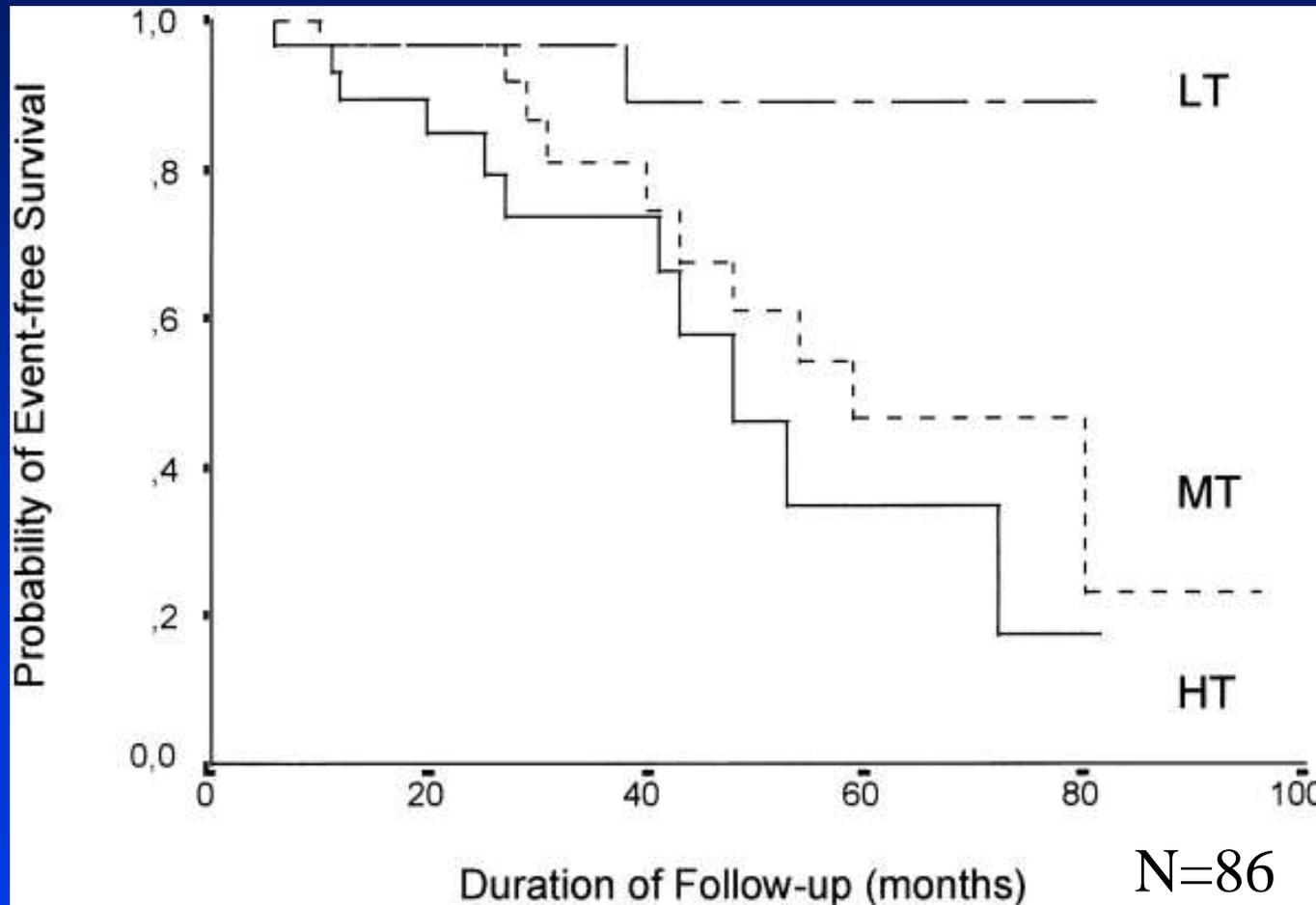
ESH recommendations for blood pressure measurement.
J Hypertens. 2003;21:821-48.

HTA de la blouse blanche

- OBP \geq 140/90 mmHg
MAPA de 24h $<$ 125/80 mmHg
- 15% de la population
- Risque léger par rapport à l 'HTA
- Etat pré-hypertensif ?

Adapted from: O 'Brien et al., *BMJ* 2001;322:531-6

Event-free survival in patients with resistant hypertension grouped by ambulatory BP



Diurnal DBP
< 88mmHg
= WHITE COAT

88-97mmHg
> 97 mmHg

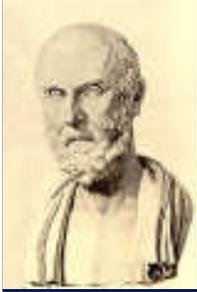
Redon J et al. *Hypertension* 1998;31:712-718

Target organ damage in true vs. white coat resistant HTN

	True RH (n=161)	White-coat RH (n=125)	P value
target organ damage			
LVH	85 (83.3%)	58 (76.3%)	0.24
LVMi (g/m ²)	152.3 ± 50.2	139.1 ± 41.3	0.03
CHD	37 (25.5%)	24 (22.6%)	0.60
Heart failure	12 (8.5%)	6 (5.7%)	0.41
Cerebrovascular diseases	31 (21.8%)	16 (15.2%)	0.19
Retinopathy	57 (58.8%)	33 (54.1%)	0.63
Nephropathy	57 (40.1%)	26 (23.9%)	0.007
PVD	8 (5.6%)	6 (5.7%)	0.98

Nocturnal dip in true vs. white coat resistant HTN

	True RH (n = 163)	White-coat RH (n = 125)	P value
Nocturnal BP reduction			
NSBP reduction (mmHg)	6.4 ± 8.8	9.8 ± 7.5	0.0004
NDBP reduction (mmHg)	10.4 ± 9.6	13.6 ± 9.2	0.001
Non-dipper	112 (68.7%)	62 (49.6%)	0.001
Pulse pressures			
24-h PP (mmHg)	65.8 ± 13.7	51.5 ± 10.0	< 0.0001
Daytime PP (mmHg)	65.7 ± 13.5	52.1 ± 9.8	< 0.0001
Night-time PP (mmHg)	65.0 ± 15.2	49.6 ± 10.9	< 0.0001



Pseudo-hypertension?

- « Fausse »HTA au brassard
- Serait liée à calcifications artérielles
- Diagnostic de certitude= mesure invasive!
- A ne pas poser trop facilement!
- Arguments pour pseudo-hypertension:
 - HTA très sévère sans atteinte d'organes-cibles
 - Manœuvre d'Osler
 - Calcifications artérielles ++ (RX)

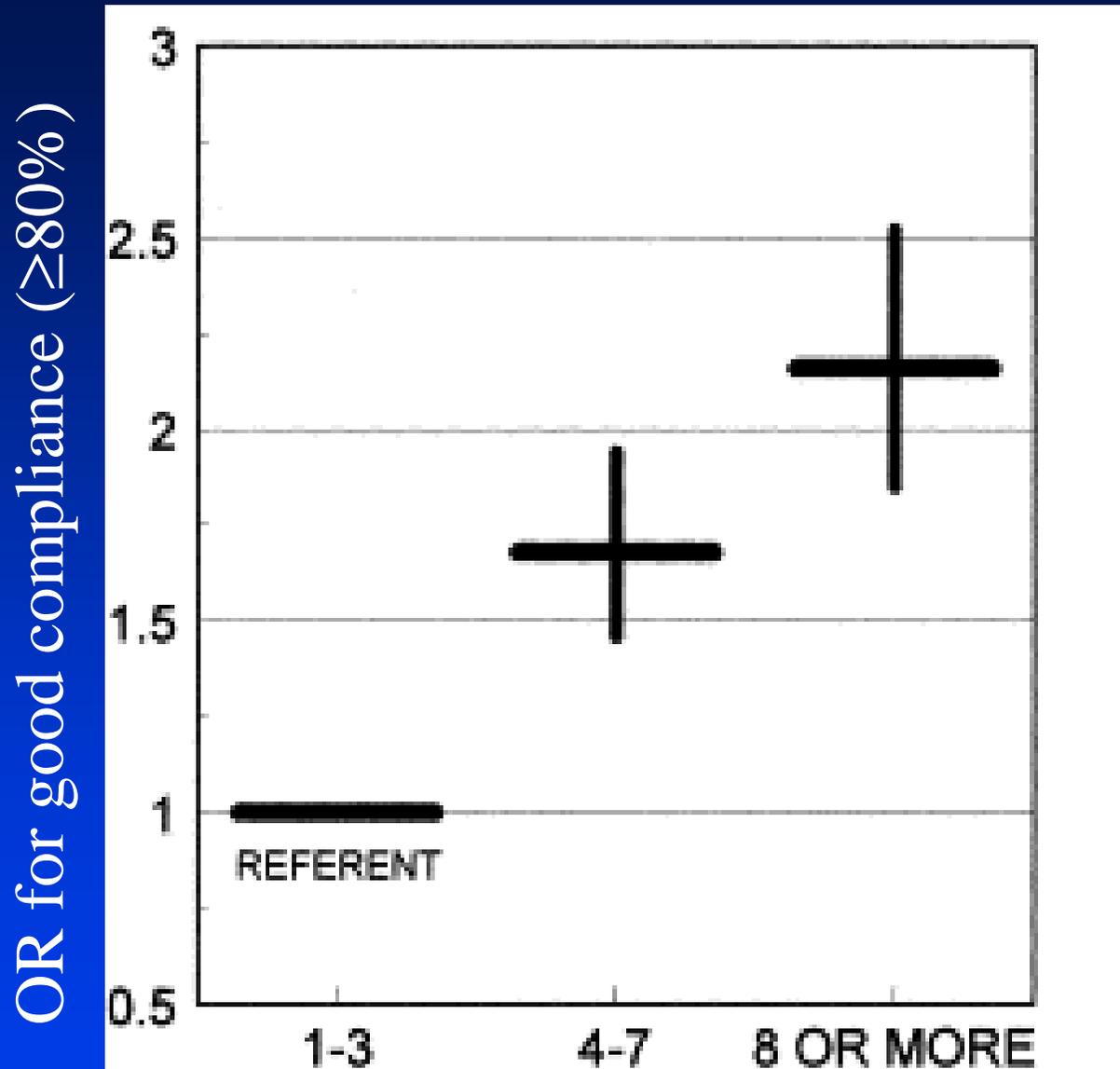
Causes d 'HTA réfractaire

- HTA pseudo-réfractaire
- **Observance insuffisante**
- Substances hypertensiogènes
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Facteurs favorisants

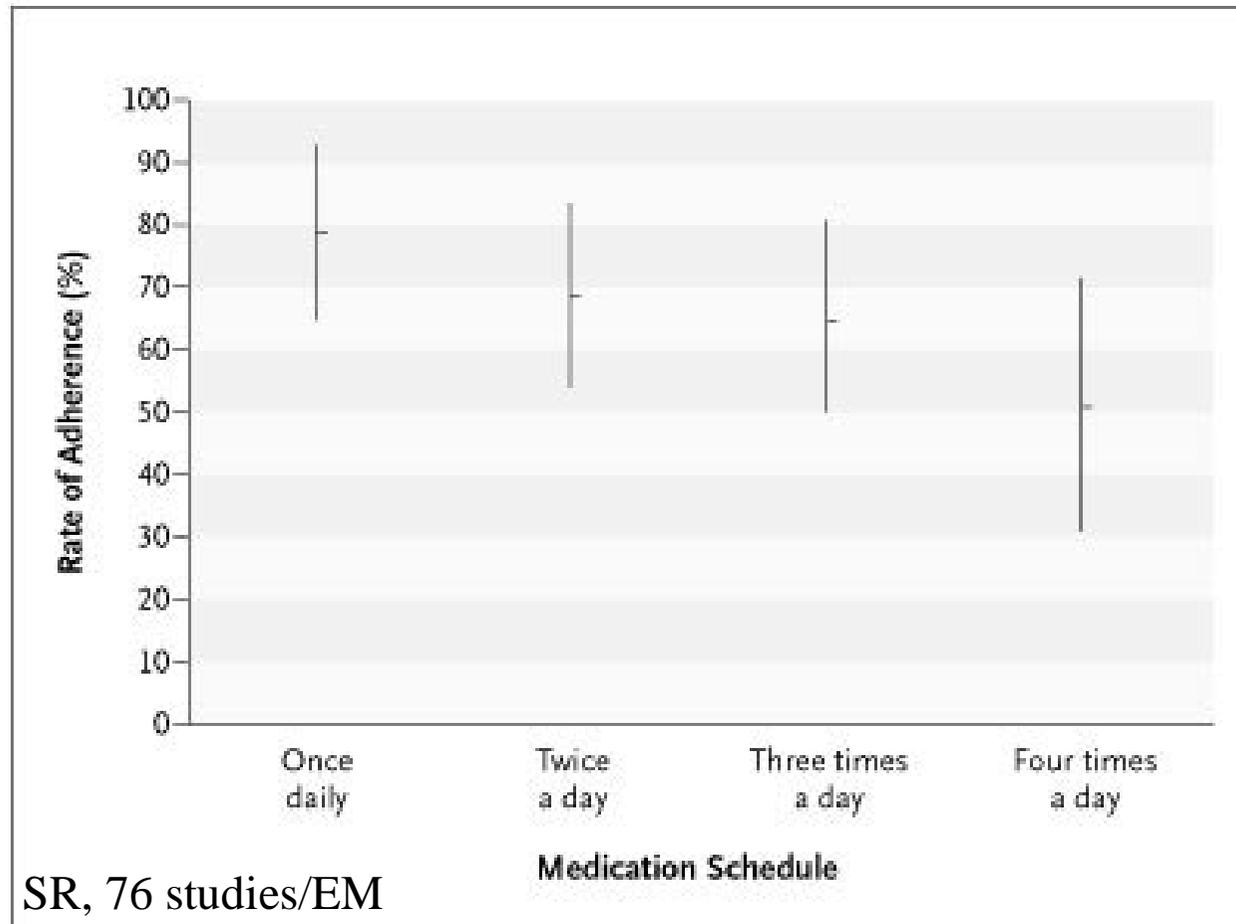
- Schéma de traitement
- Effets secondaires
- Suivi erratique
- Coût du traitement
- Instructions mal comprises
- Dépression
- Troubles mnésiques

Observance et nombre de visites (>65 ans, n=8643)



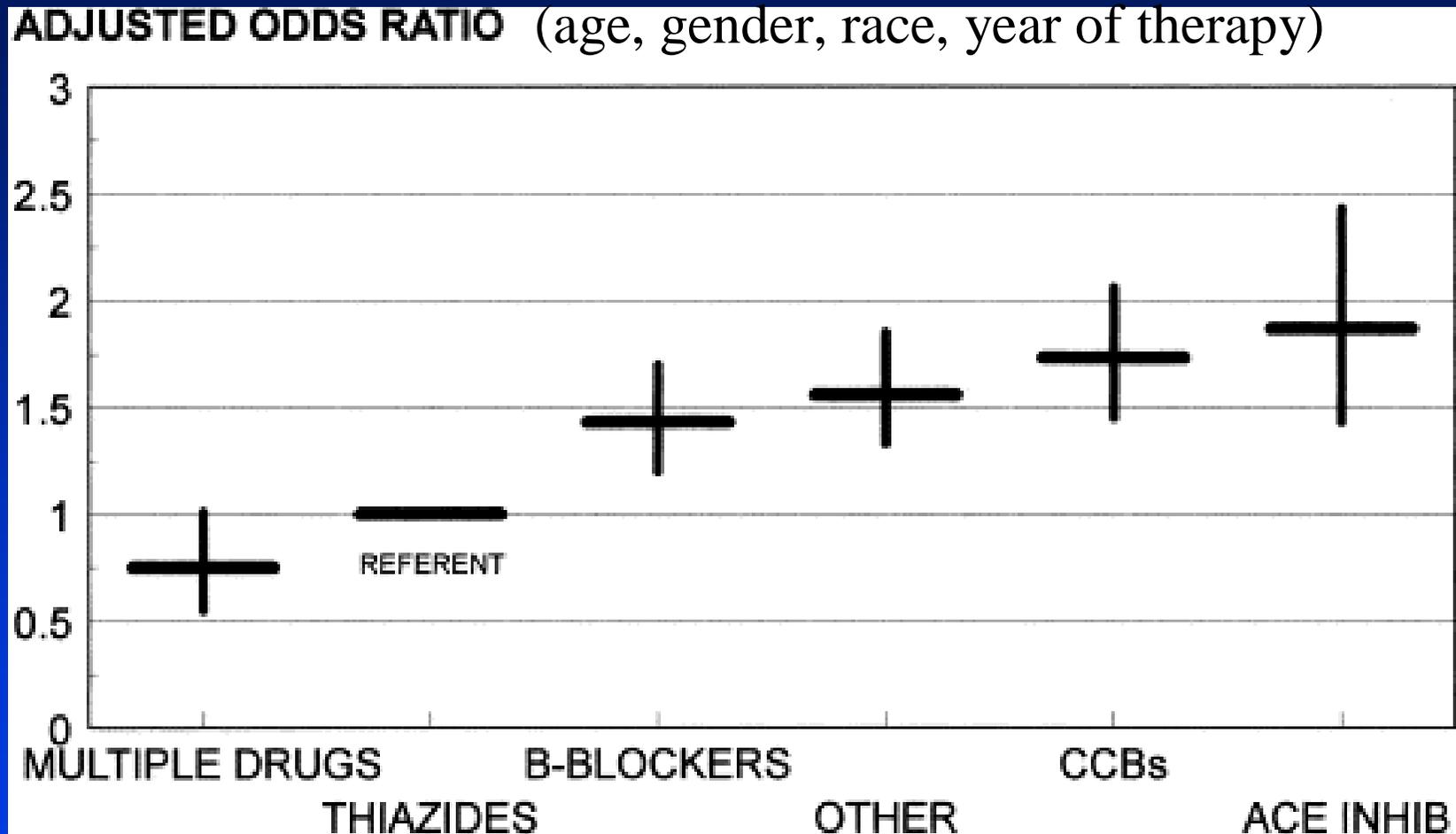
Monane M et al.,
Am J Hypertens. 1997;
10: 697-704

Observance et nombre de prises



Osterberg L, Blaschke K., *N Engl J Med.* 2005;353: 487-497.
Claxton AJ., *Clin Ther* 2001;23: 1296-1310.

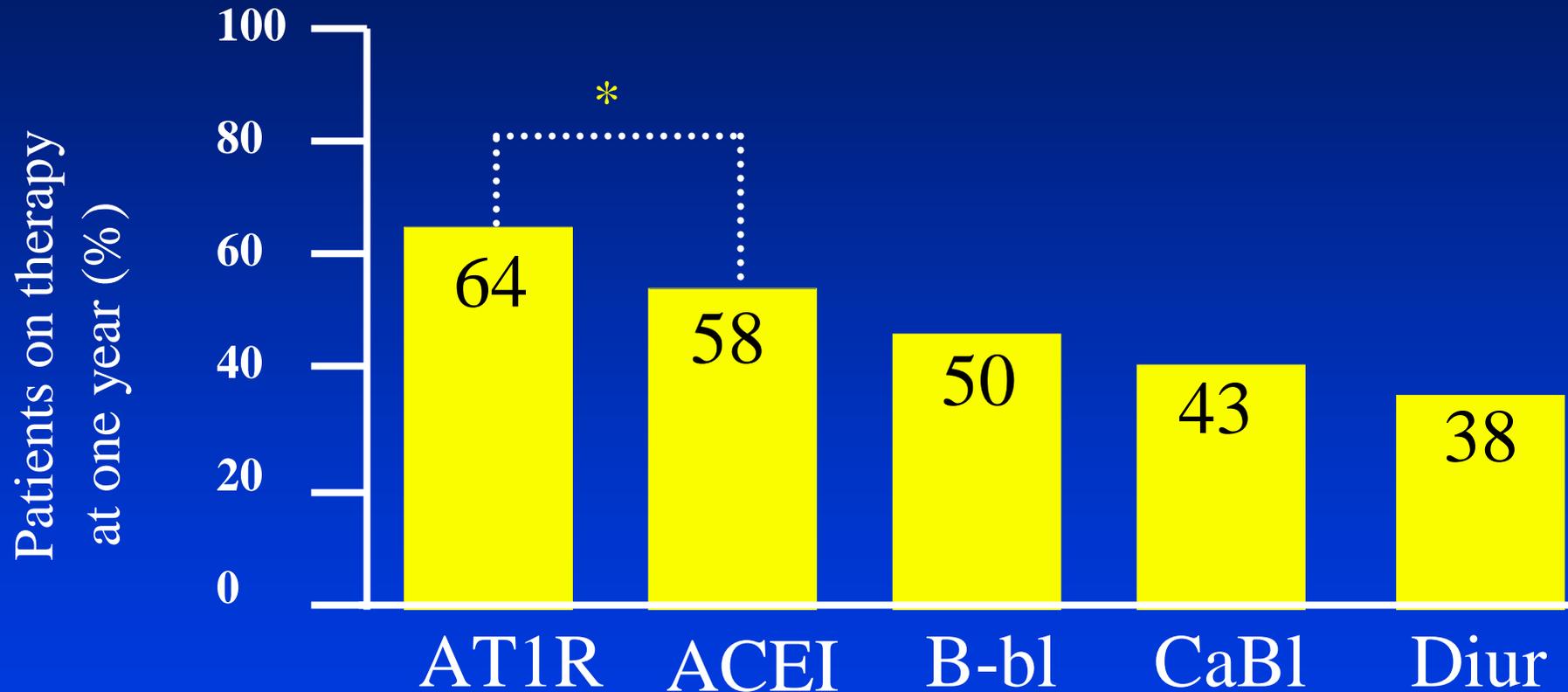
Observance et classe thérapeutique



Monane M et al., *Am J Hypertens.* 1997;10: 697-704

Observance et classe thérapeutique

N=21723



Burnier M et al., *J Hypertens.* 2003;21(2):S37-S42
Bloom.BS, *Clin Ther* 1998;20: 671-681.

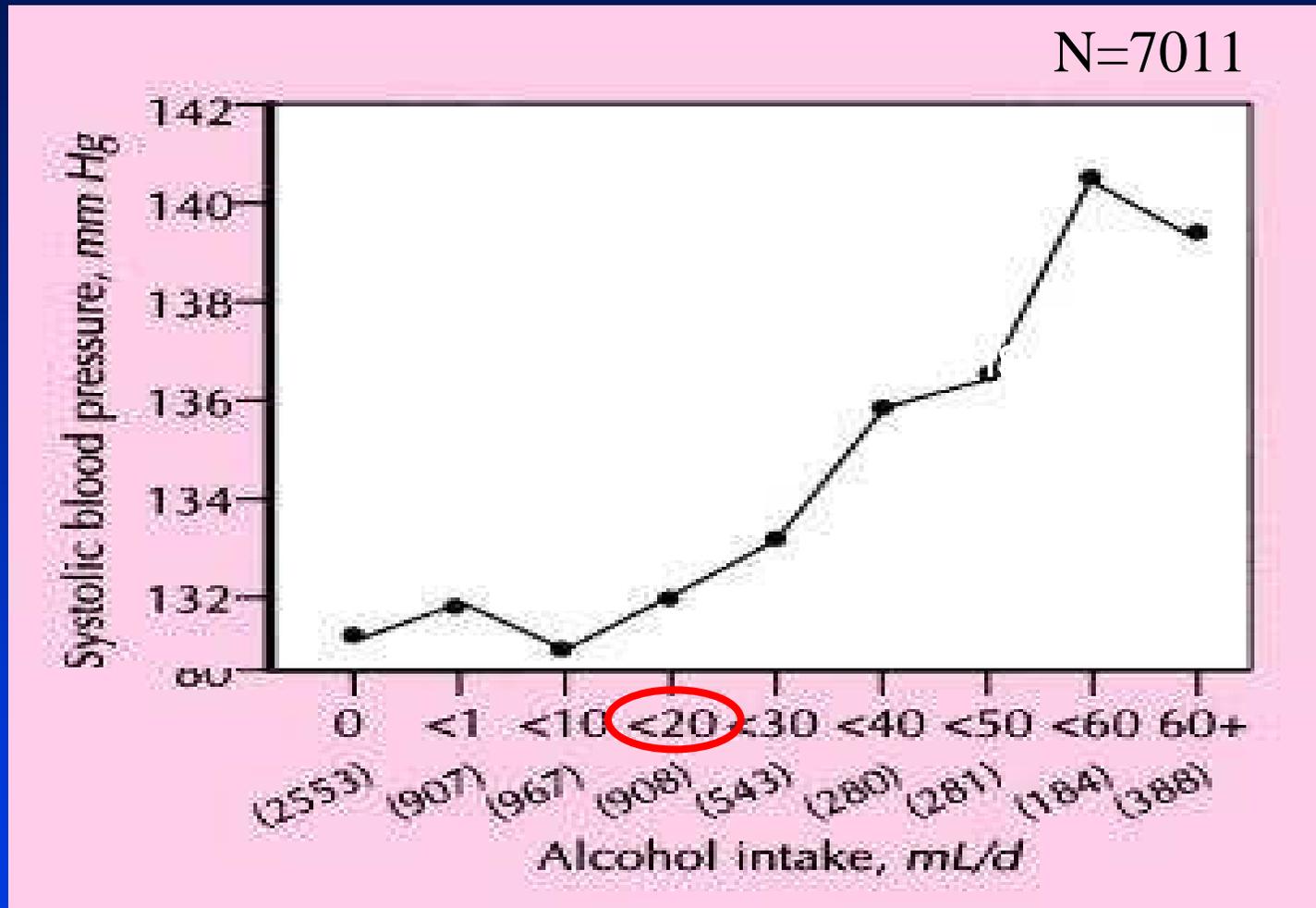
Causes d 'HTA réfractaire

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Substances hypertensiogènes

- Sel
- Alcool, (tabac)
- AINS, stéroïdes
- Gouttes nasales VC
- CO
- Antidépresseurs
- Drogues (cocaïne)
- Réglisse
- Ciclosporine
- Epo
-

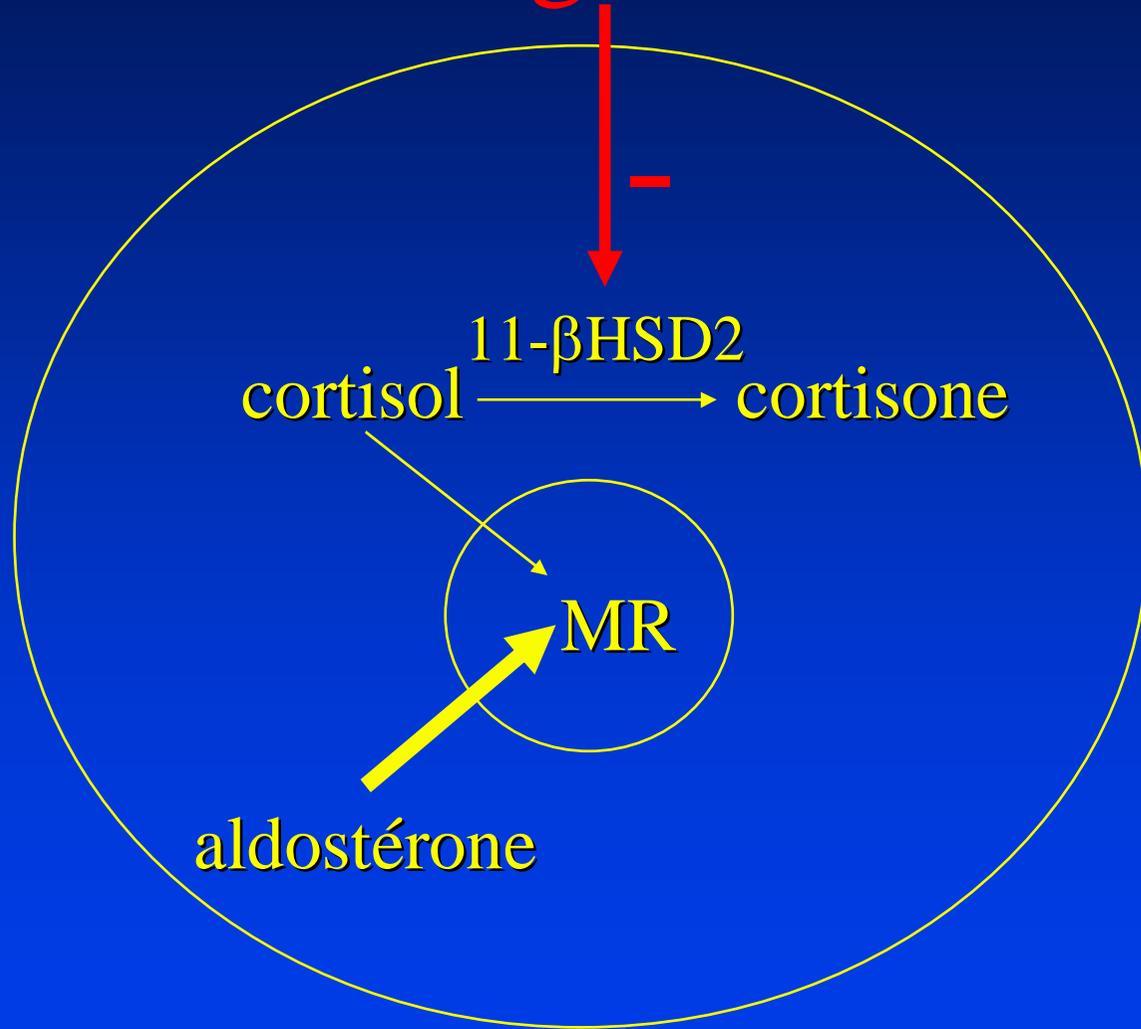
Alcohol



Criqui MH et al. *Circulation* 1989; 80: 609-614



Réglisse



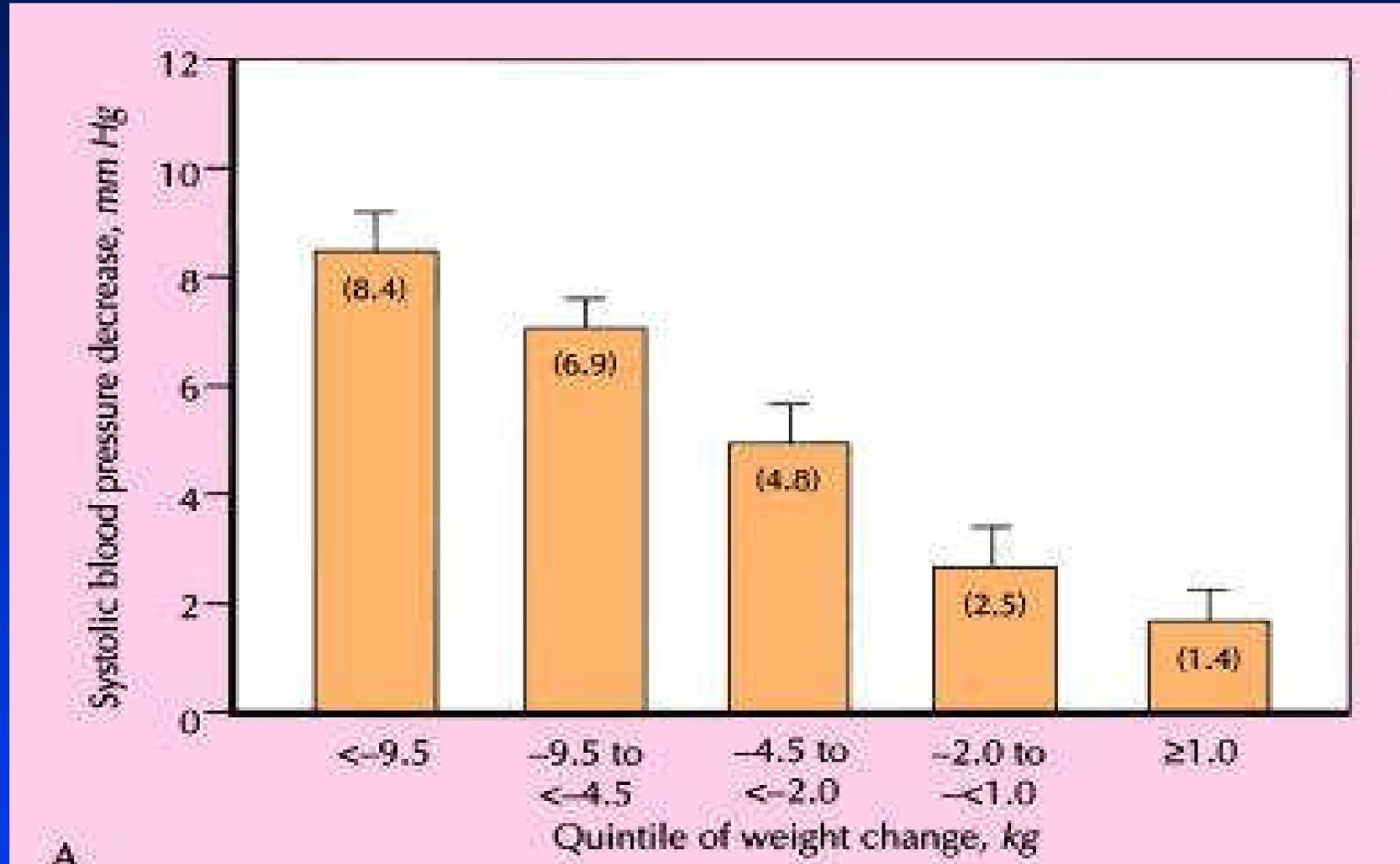
Causes d 'HTA réfractaire

- HTA pseudo-réfractaire
- Observance insuffisante
- Substances hypertensiogènes
- **Conditions associées**
- Causes secondaires

Conditions associées

- Obésité
- Apnées du sommeil
- Insulinorésistance
- Douleurs chroniques

Obésité



Stevens VJet al., *Arch Intern Med* 1993 **153** 849-858



Syndrome des apnées du sommeil



- Obésité
- Syndrome métabolique
- Ronflements avec apnées
- Somnolence diurne
- Troubles de concentration
- Irritabilité

SAS et HTA réfractaire

Table 1 Prevalence of obstructive sleep apnoea (OSA) and mean apnoea-hypopnoea index (AHI)

	Prevalence (%)	Mean AHI \pm SE (events/h)
Men	95.8*	32.2 \pm 4.5†
Women	64.7*	14.0 \pm 3.1†
All	82.9	24.7 \pm 3.2

Logan et al., *J Hypertens* 2001; 19: 2271-2277

Causes d 'HTA réfractaire

- HTA pseudo-réfractaire
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Causes secondaires = rares

- Néphropathies parenchymateuses
- HTA rénovasculaire
- Hyperaldostéronisme I
- Coarctation aortique
- Phéochromocytomes....
- Cushing

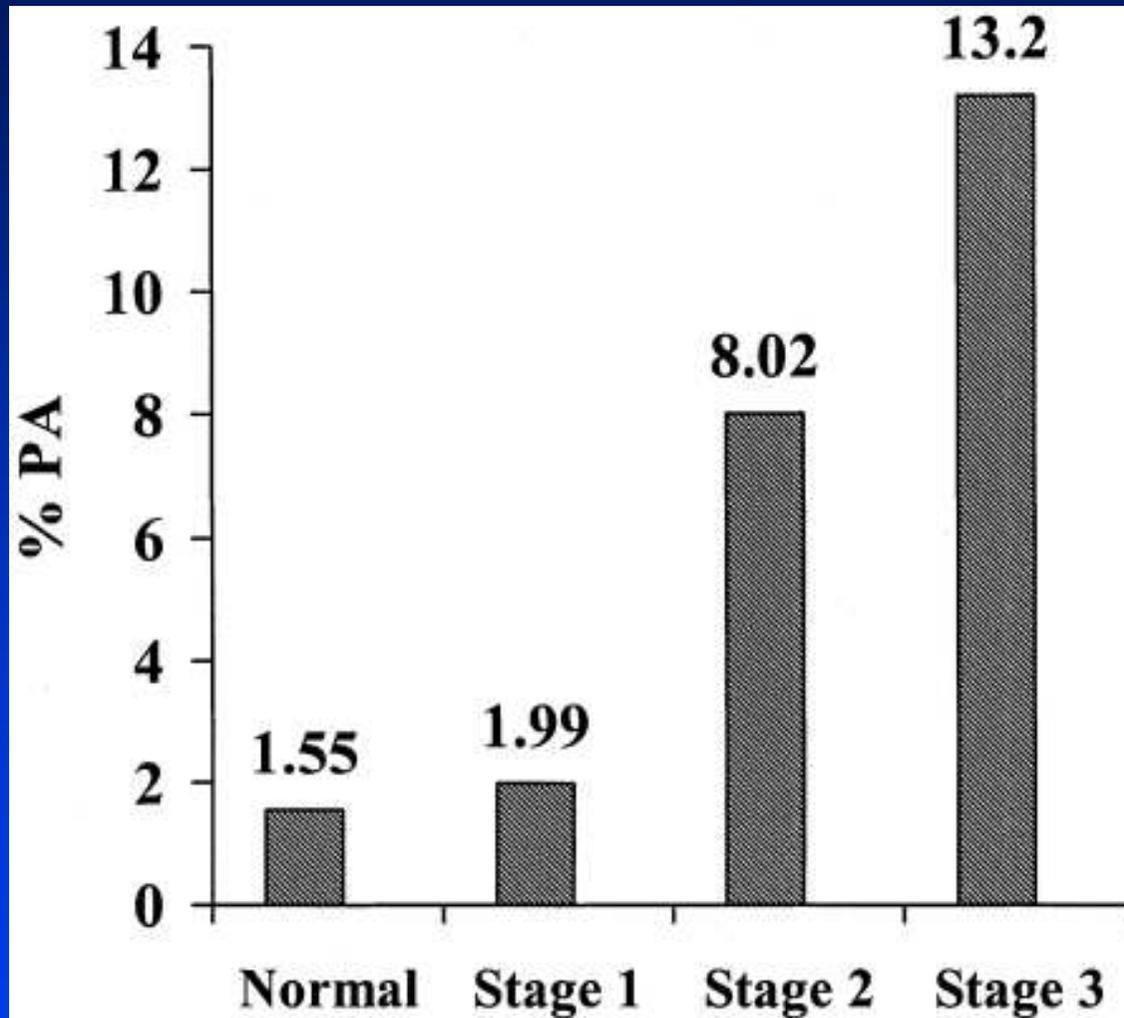
HTA réfractaire chez l'insuffisant rénal

- Manque d'observance du régime hyposodé
- Absence de diurétique
- Thiazidique et ClCr < 30ml/min
- Diurétique de l'anse à dose insuffisante
- Nombre d'antihypertenseurs insuffisant

HTA rénovasculaire: fréquente chez patient polyvasculaire

Reference	Conditions	N°	Degree Stenosis	Prev. Stenosis	Prev. HTN
Kuroda 00	Stroke (Autopsy)	346	≥ 75%	10%	NA
Uzu 97	MI (Autopsy)	297	≥ 75%	12%	NA
Harding 92	Cardiac cathe.	1235	≥ 50%	15%	53%
Appel 99	≥ 50 ans, ESRD	45	≥ 60%	22%	100%
Missouris 94	PAD	127	≥ 50%	28%	61%
MacDowall 98	Elderly, CHD	86	≥ 50%	34%	35%

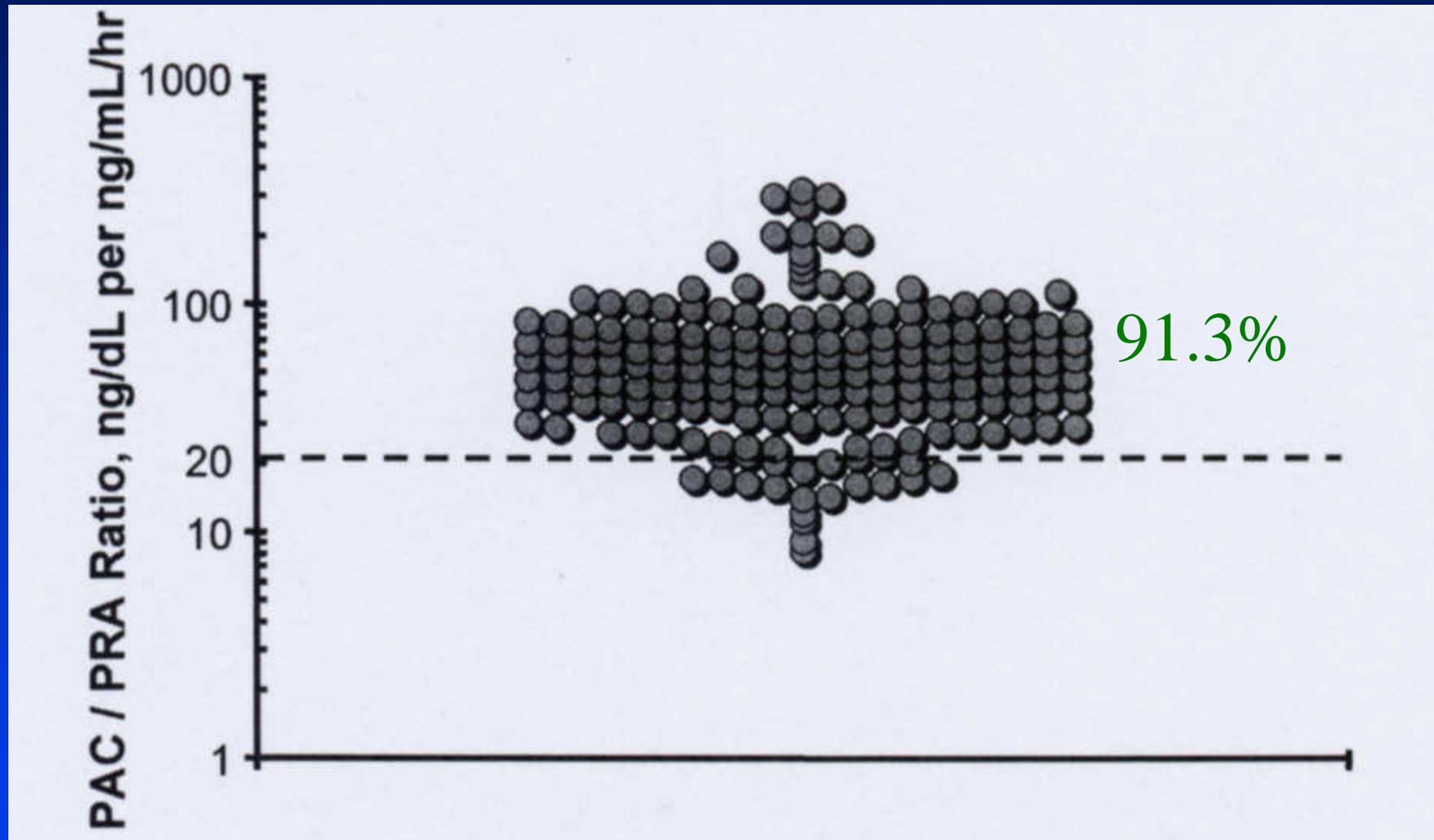
Hyperaldol : un K^+ nl. ne permet pas de l'exclure



609 HTA
37 hyperaldo I
36 K^+ normal

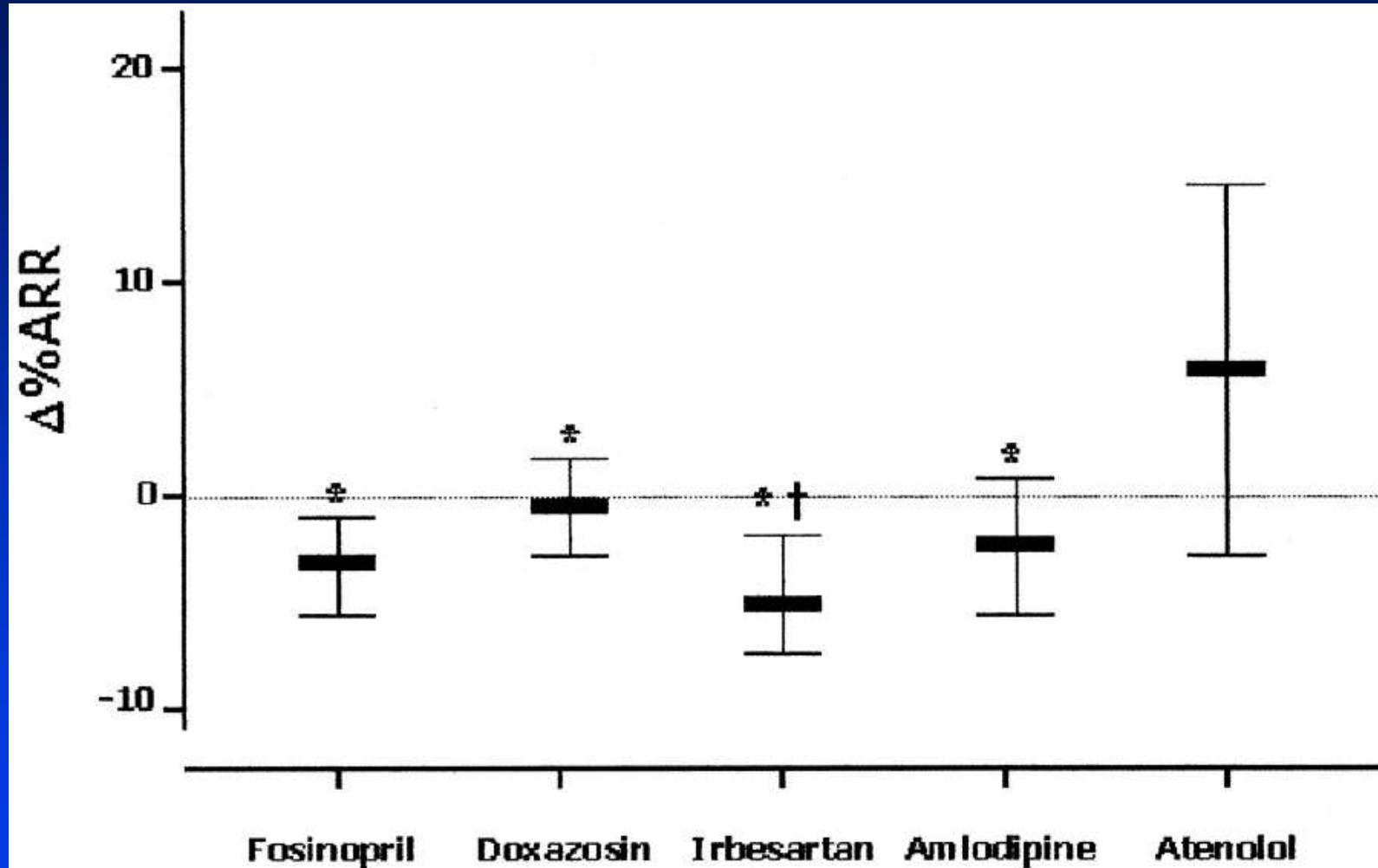
Mosso L et al. *Hypertension*. 2003;42:161-5.

Aldo/ARP chez 184 patients avec un adénome de Conn



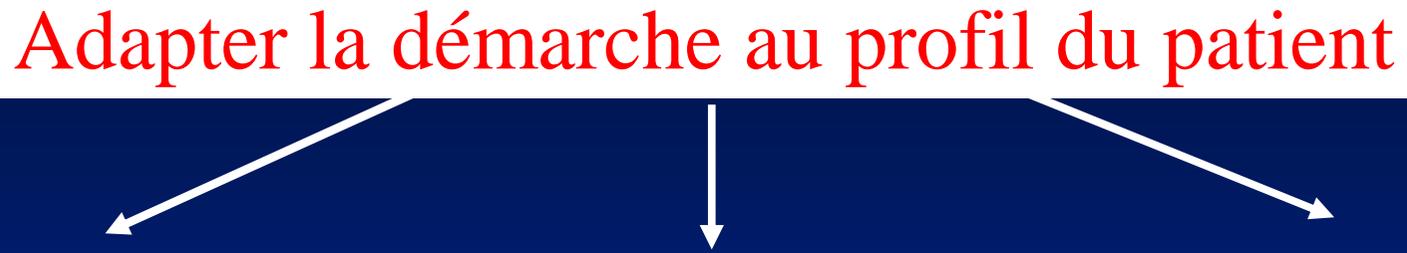
Young , Primary aldosteronism, pp. 119-137, in Mansoor ed., Humana Press 2004

Hyperaldo I: aldostérone/ARP



Mulatero P. *Hypertension*. 2002 ;;40:897-902.

Adapter la démarche au profil du patient



Diabétique obèse 45 ans

Brassard?

Incompliance

Obésité

Rétention hydrosodée

Apnées du sommeil

HTA rénovasculaire

Dame 79 ans

AINS

Oublis-erreurs

Blouse blanche

Pseudo-HTA?

Etudiante de 18 ans

CO

Goutte nasales

Réglisse

Amphétamines

Blouse blanche

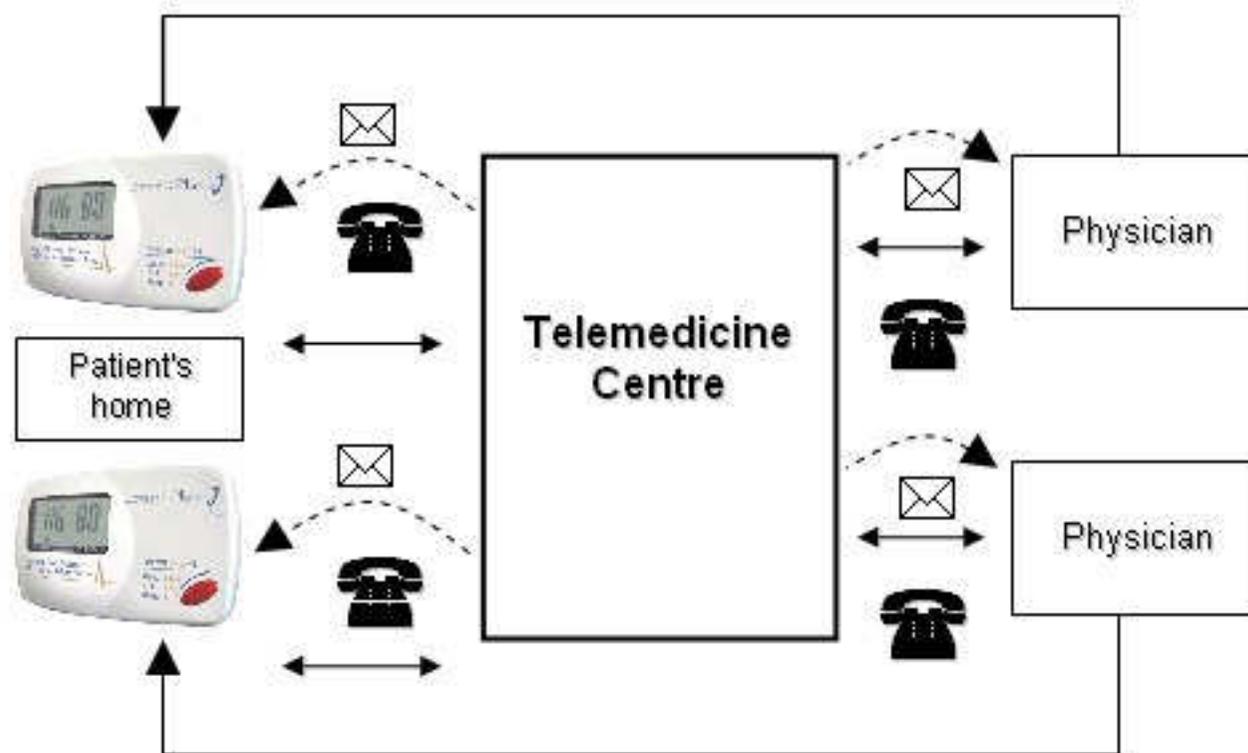
Dysplasie FM

HTA réfractaire: pistes pour l'avenir

- Telemonitoring
- Bio-impédance thoracique
- Nitrés, « cross-link breakers »?
- Pharmacogénétique...

Telemonitoring

Blood Pressure Remote Monitoring



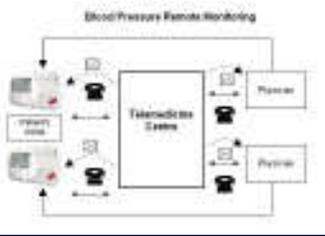
Avantages possibles du telemonitoring

- Nombreuses mesures
- Communication M-P accrue
- Intervention plus rapide et fondée (M)
- Meilleure observance (P)
- **Meilleur contrôle tensionnel**

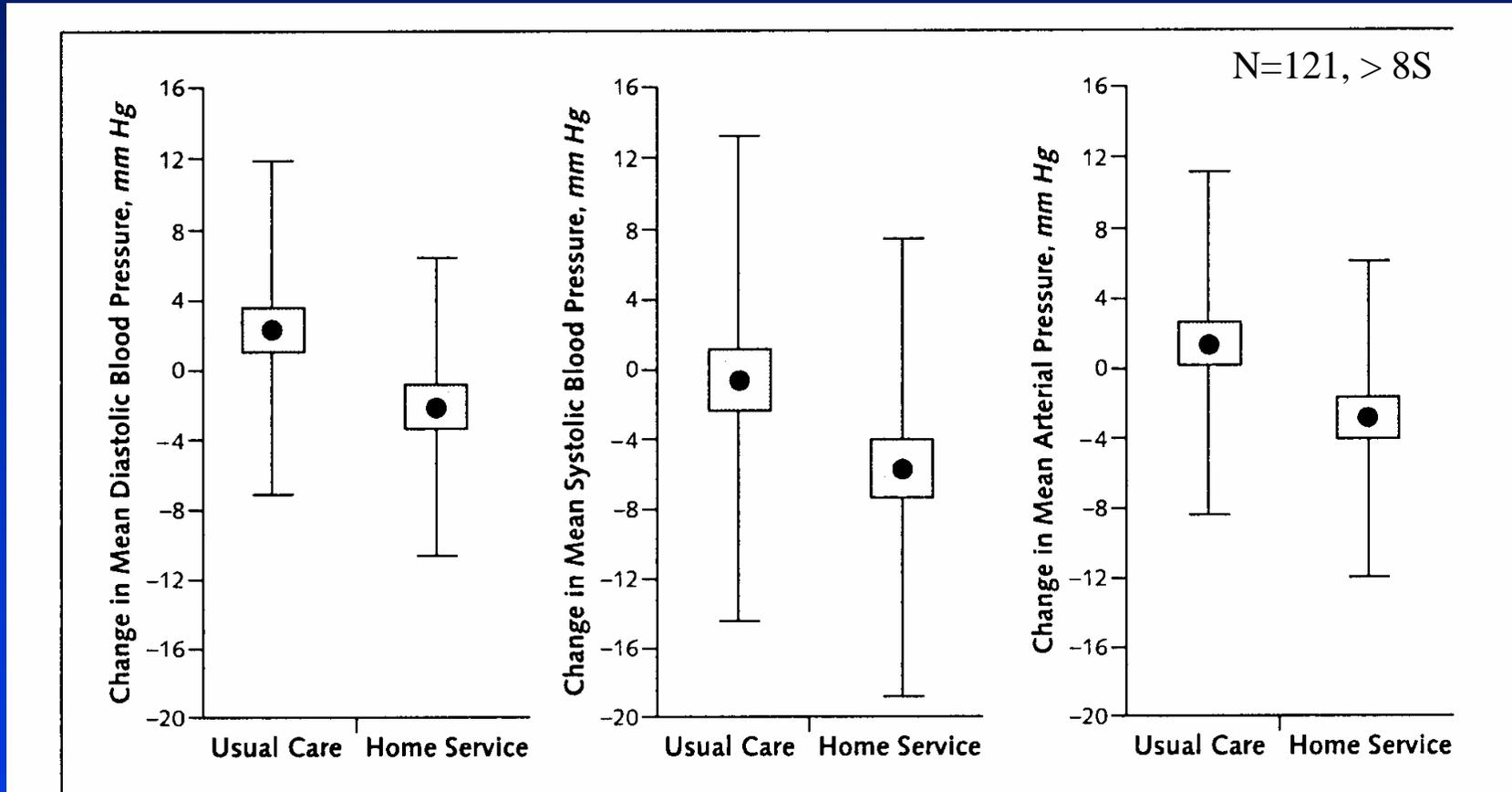
Mengden et al., *AJH* 1998;11:1413-17

Pickering et al., *Current HTN Rep* 1999; 1: 489-494

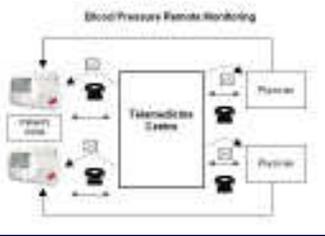
Pickering et al., *HTN* 2005;45:142-161



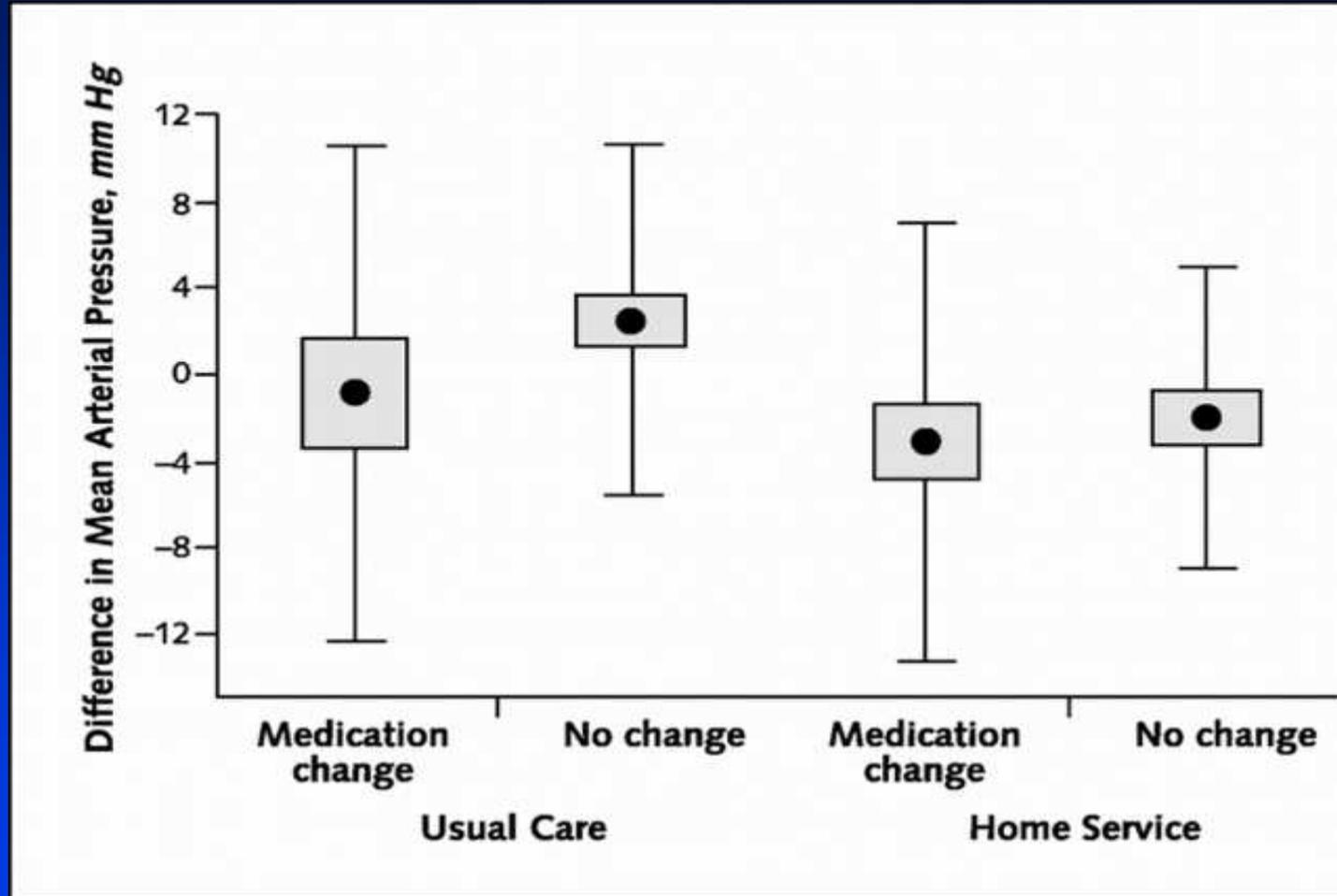
Le telemonitoring pourrait améliorer le contrôle tensionnel



Rogers et al., *AJH* 2001; 134: 1024-1032

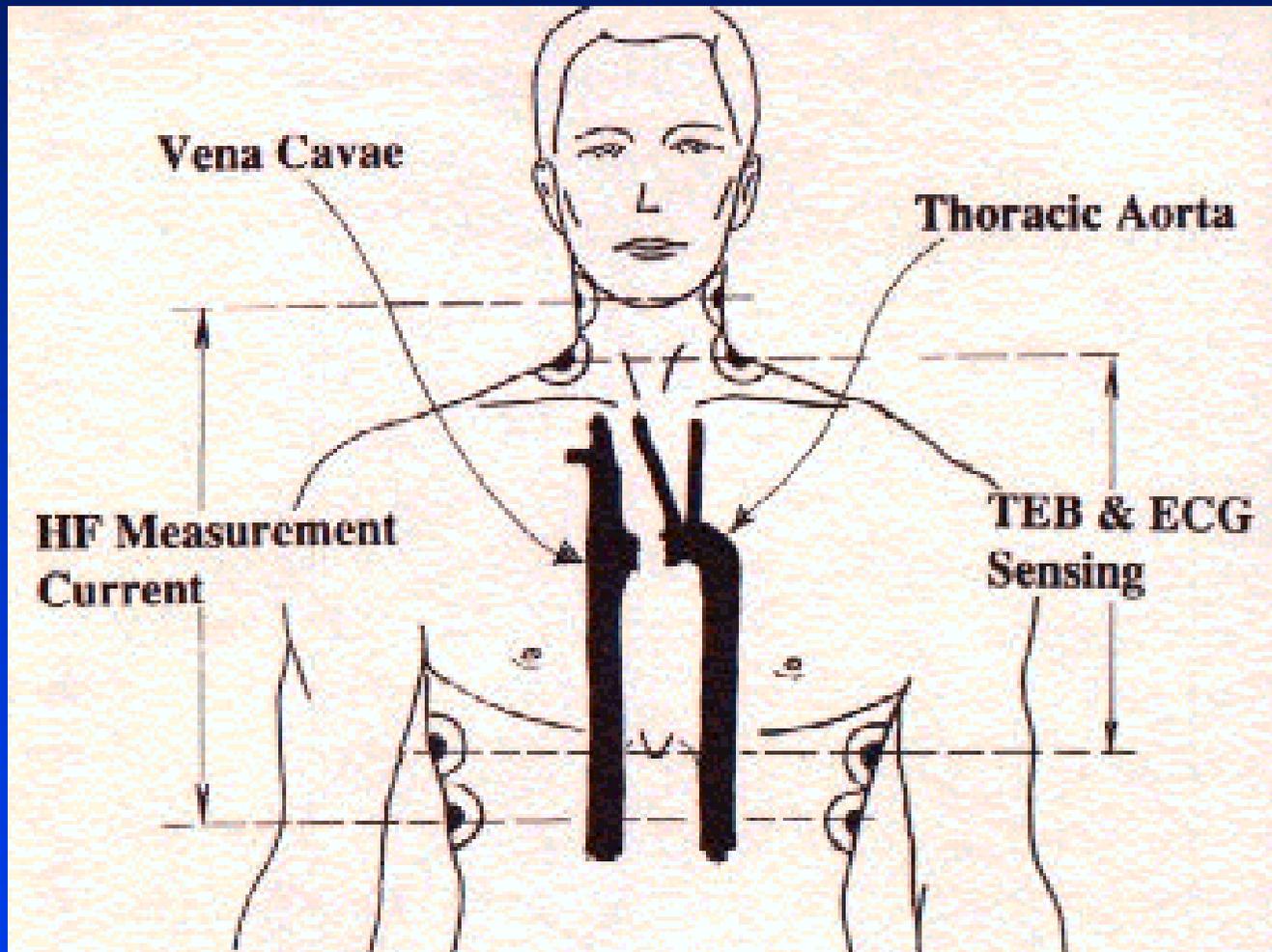


Le telemonitoring pourrait améliorer le contrôle tensionnel



Rogers et al., *AJH* 2001; 134: 1024-1032

Bio-impédance thoracique



Bio-impédance thoracique

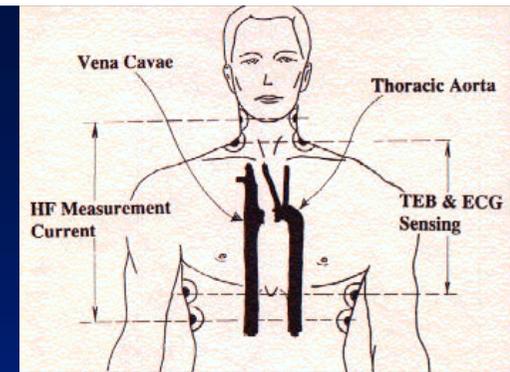


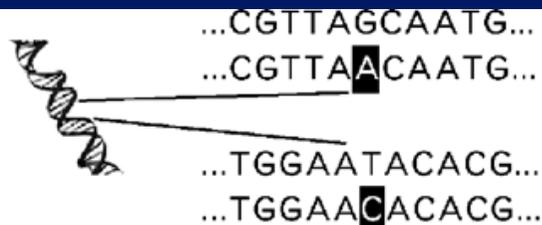
TABLE 1. Hemodynamic Care Algorithm

Cardiac Index	Systemic Vascular Resistance Index	Medication Choices
Low	High	<ol style="list-style-type: none"> 1. Add or increase dihydropyridine calcium channel blocker, ACE inhibitor, angiotensin receptor blocker, or direct vasodilator 2. Reduce β-blocker 3. Evaluate ΔTBI; if reduced, add or intensify diuretic dose
High	Low	<ol style="list-style-type: none"> 1. Add β-blocker or central agonist 2. Reduce vasodilators 3. Evaluate ΔTBI; if reduced, add or intensify diuretic dose
Normal	Normal	Evaluate Δ TBI; if reduced, add or intensify diuretic dose

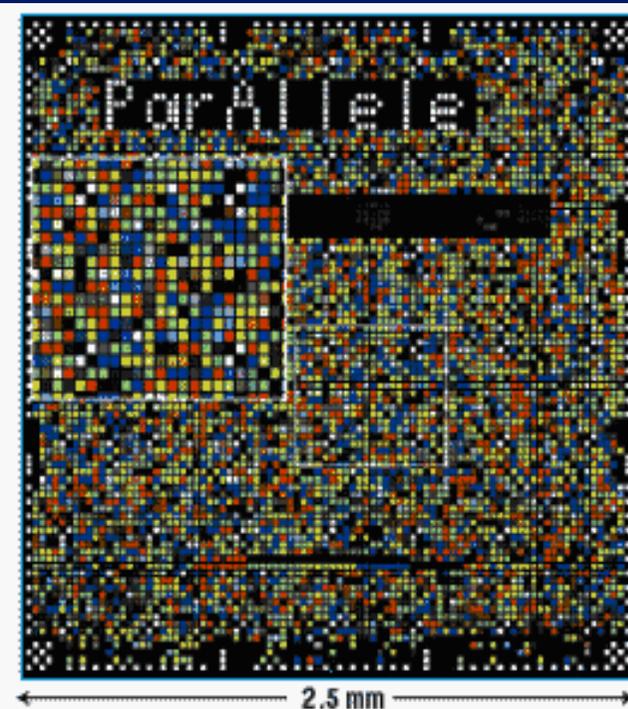
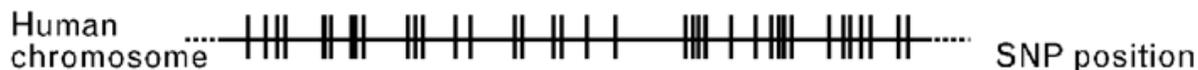
Taler SJ et al., *Hypertension* 2002; 39: 982-988

Pharmacogénétique

Single nucleotide polymorphisms (SNPs):
Across a population, different nucleotides occur at specific positions on a chromosome



A SNP map indicates the positions of SNPs along a chromosome



études d'association
à l'échelle du génome

Bain and Dominiczak., *J Hypertension* 2005;23:1327-1329.