



STCCCV

Société Tunisienne de Cardiologie
& de Chirurgie Cardio-Vasculaire



Défis dans la prise en charge de l'HTA en 2018

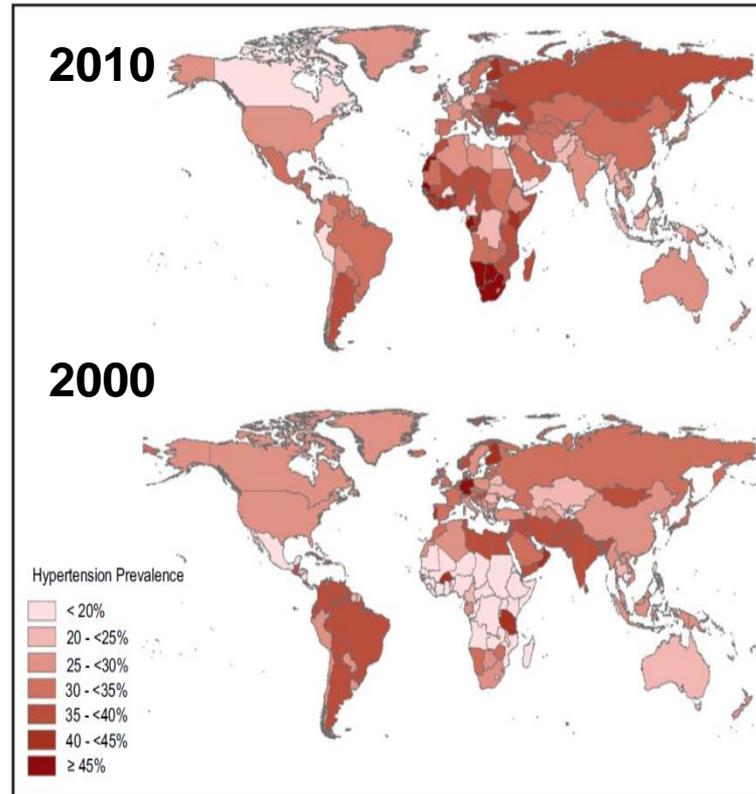


Pr Habib GAMRA
F Bourguiba University Hospital
Monastir, Tunisia

Tabarka – October 27th, 2018

What we know...

- **Growing prevalence of HTN**

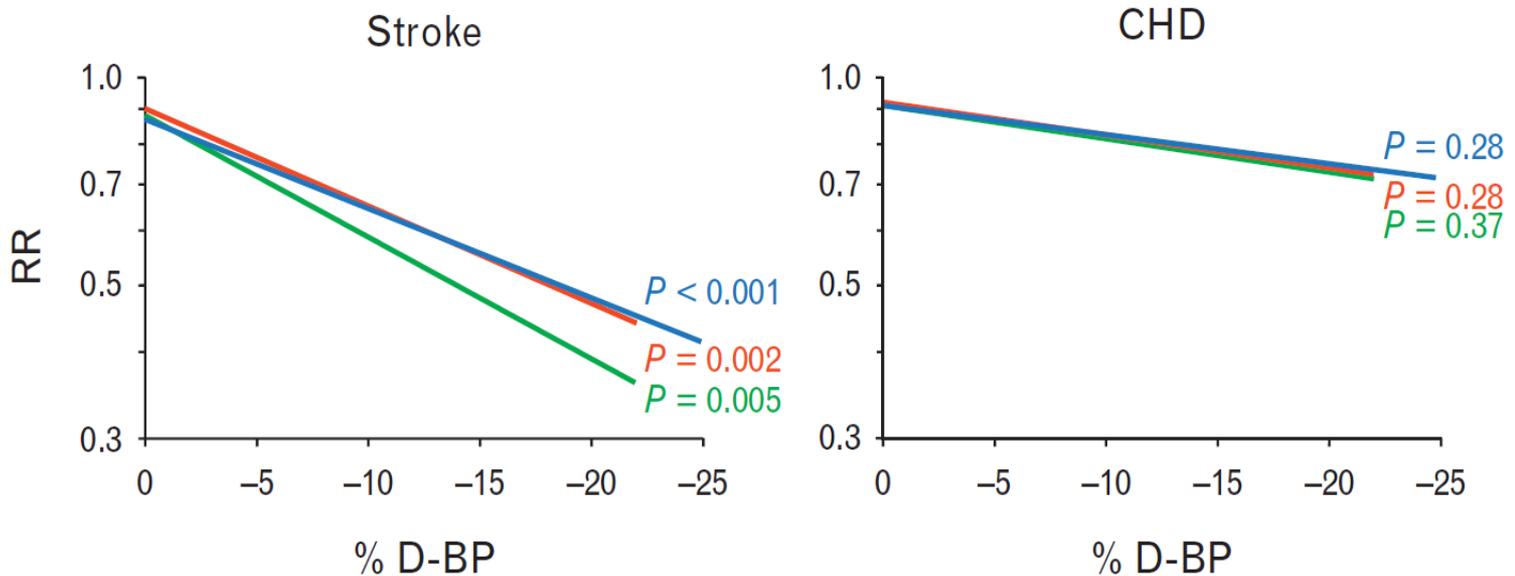


Age- and sex-standardized prevalence of hypertension in adults aged > 20 yrs

What we know...

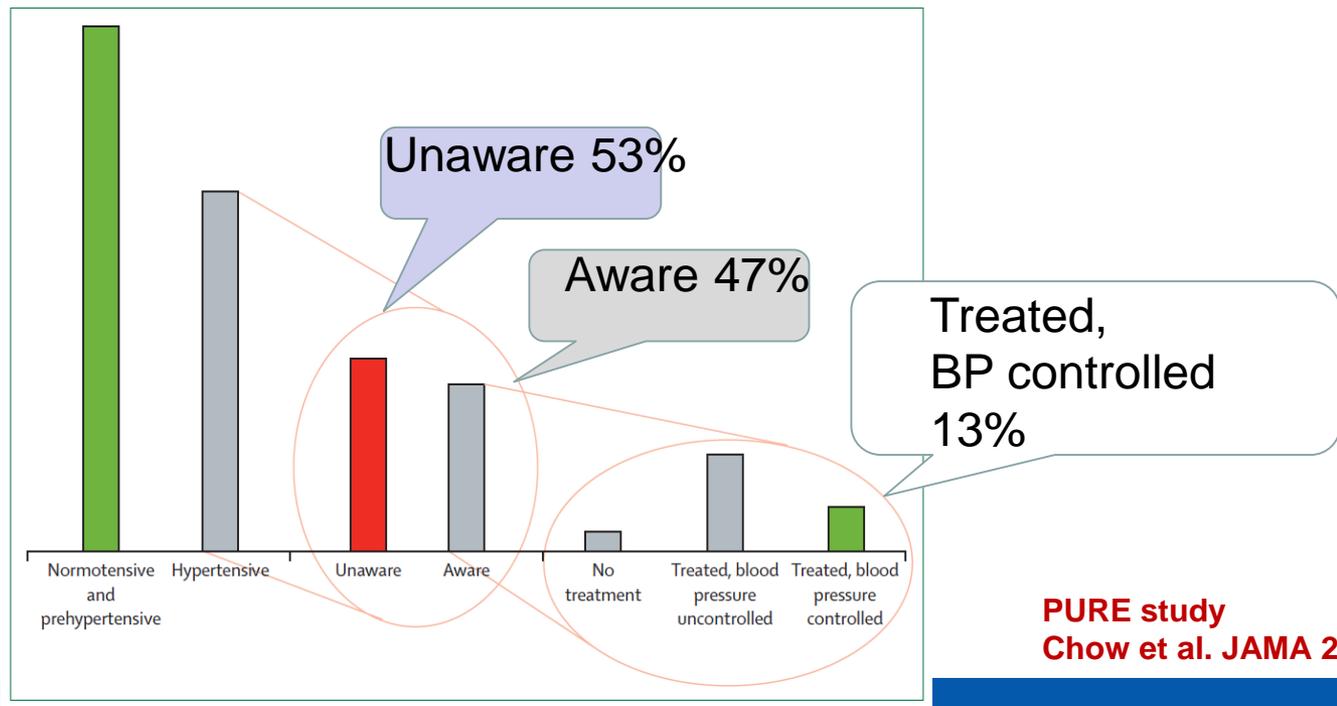
- Growing prevalence of HT **Thomopoulos C, Parati G, Zanchetti A. J Hypertens 2014**
- **The benefit of lowering BP**

43 years of RCTs: Meta-analysis of 68 RCTs (245 885 individuals)
of which 47 (153 825 individuals) were « intentional » RCTs



What we know...

- Growing prevalence of HT
- The benefit of lowering BP
- The high prevalence of uncontrolled hypertension



Prévalence de l'HTA en Tunisie 2015 (%)

	Hommes	Femmes	Total
Dist Tunis	33.8	35.0	34.4
NE	24.3	27.6	25.9

**Seulement 24 % des patients traités
sont bien équilibrés**

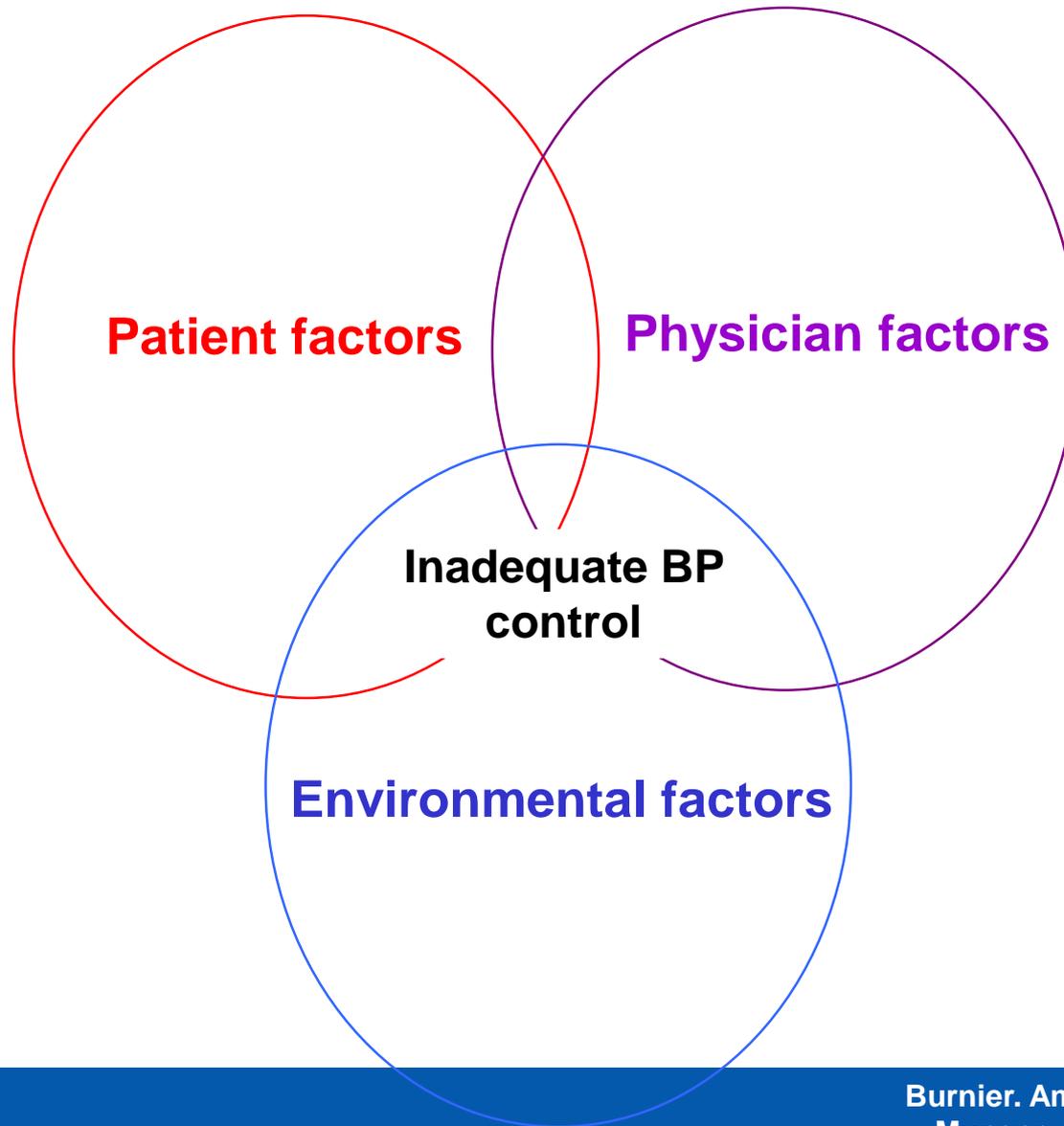
CO	25.2	28.7	27.0
SE	27.6	38.3	33.0
SO	25.9	30.9	28.5



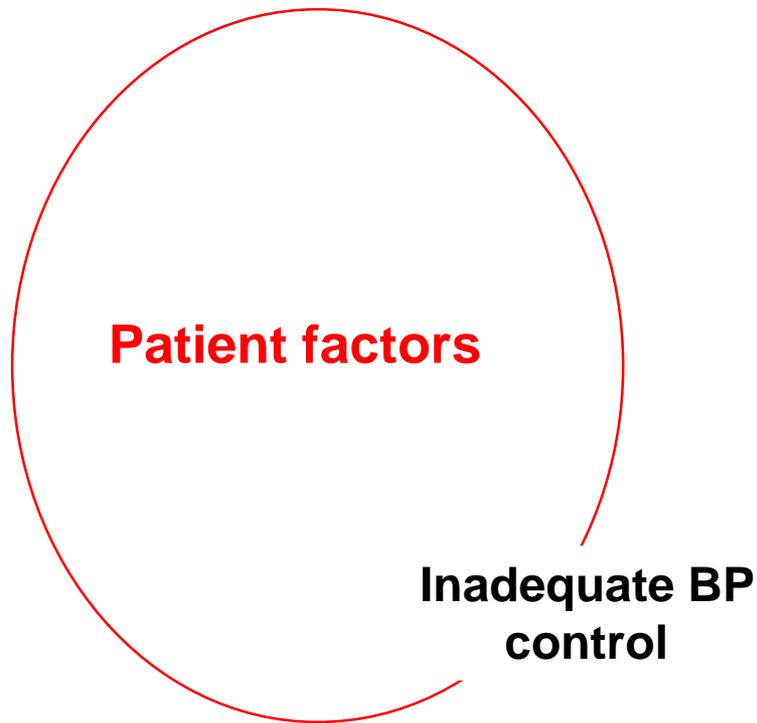
What we know...

- Growing prevalence of HT
- The benefit of lowering BP
- The high prevalence of uncontrolled hypertension
- The economic burden of inadequate BP control?
- **The reasons explaining inadequate BP control**

The key patient and physician challenges...



The key patient and physician challenges...



The key patient challenges... To view HTN as a disease

RESEARCH ARTICLE

Open Access

Perceptions of hypertension treatment among patients with and without diabetes

Heymann Anthony^{1,2*}, Liora Valinsky^{1,2}, Zucker Inbar^{1,3}, Chodick Gabriel^{1,2} and Shalev Varda^{1,2}

People with HTN

- do not see HTN as a disease (disease denial)
but as a risk factor for MI or stroke
- do not view HT as a continuous, degenerative process
of the vascular system

If there is high blood pressure, I do not want to know... thinking of that makes me anxious... I am healthy because I feel healthy

The key patient challenges... To view HTN as a disease

RESEARCH ARTICLE

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Perceptions of hypertension treatment among patients with and without diabetes

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People with HTN

- do not see HTN as a disease but as a risk factor for MI or stroke
- do not view HTN as a continuous, degenerative process of the vascular system
- consider that they know their bodies and can control their own BP
- overestimate the effects of **stress** as a causative factor

The key patient challenges... To view HT as a disease

RESEARCH ARTICLE

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Perceptions of hypertension treatment among patients with and without diabetes

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People with HTN

- do not see HTN as a disease but as a risk factor for MI or stroke
- do not view HTN as a continuous, degenerative process of the vascular system
- consider that they know their bodies and can control their own BP
- overestimate the effects of stress as a causative factor
- rather view HTN as a binary risk process: you can either be a winner or a loser
- thus, some consider that non-adherence to Rx is a gamble with positive outcome

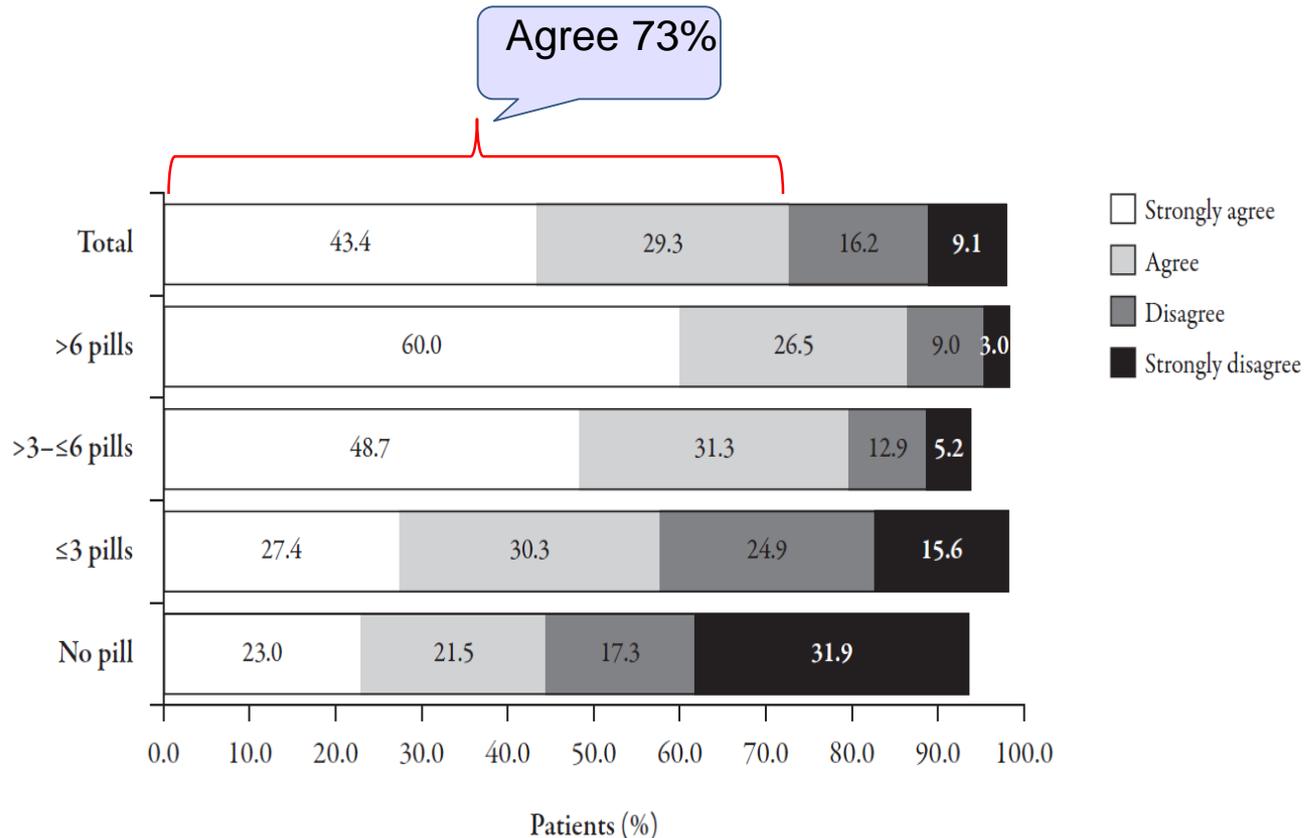
The key patient challenges... To accept the pill burden

Pill Burden in Hypertensive Patients Treated with Single-Pill Combination Therapy – An Observational Study

Andreas Hagendorff · Siegfried Freytag · Alfons Müller · Sven Klebs

Hagendorff A et al. Adv Ther 2013

« Q: Having to take several pills per day is a burden for me »



The key patient challenges...To be helped by family member

Family member-based supervision of patients with hypertension: a cluster randomized trial in rural China

Y Shen^{1,2,8}, X Peng^{2,8}, M Wang², X Zheng², G Xu², L Lü², K Xu³, B Burstrom^{4,5}, K Burstrom^{4,5,6} and J Wang^{2,3,7}

Shen Y et al. *J Human Hypertens* 2017

4 villages in Yangzhong

Patients randomized to

- **Control group** n=288, usual care
- **Intervention group** n=266

The key patient challenges...To be helped by family member

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Family member-based supervision package

- One family member = supervisor
- Regular training of patient
- Control of adherence and BP monitoring
- Accessory appliances

The key patient challenges...To be helped by family member

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4 villages in Yangzhong

Patients randomized to

- **Control group** n=288, usual care
- **Intervention group** n=266, with a

12 months FU

Face-to-face interview at 6 and 12 M

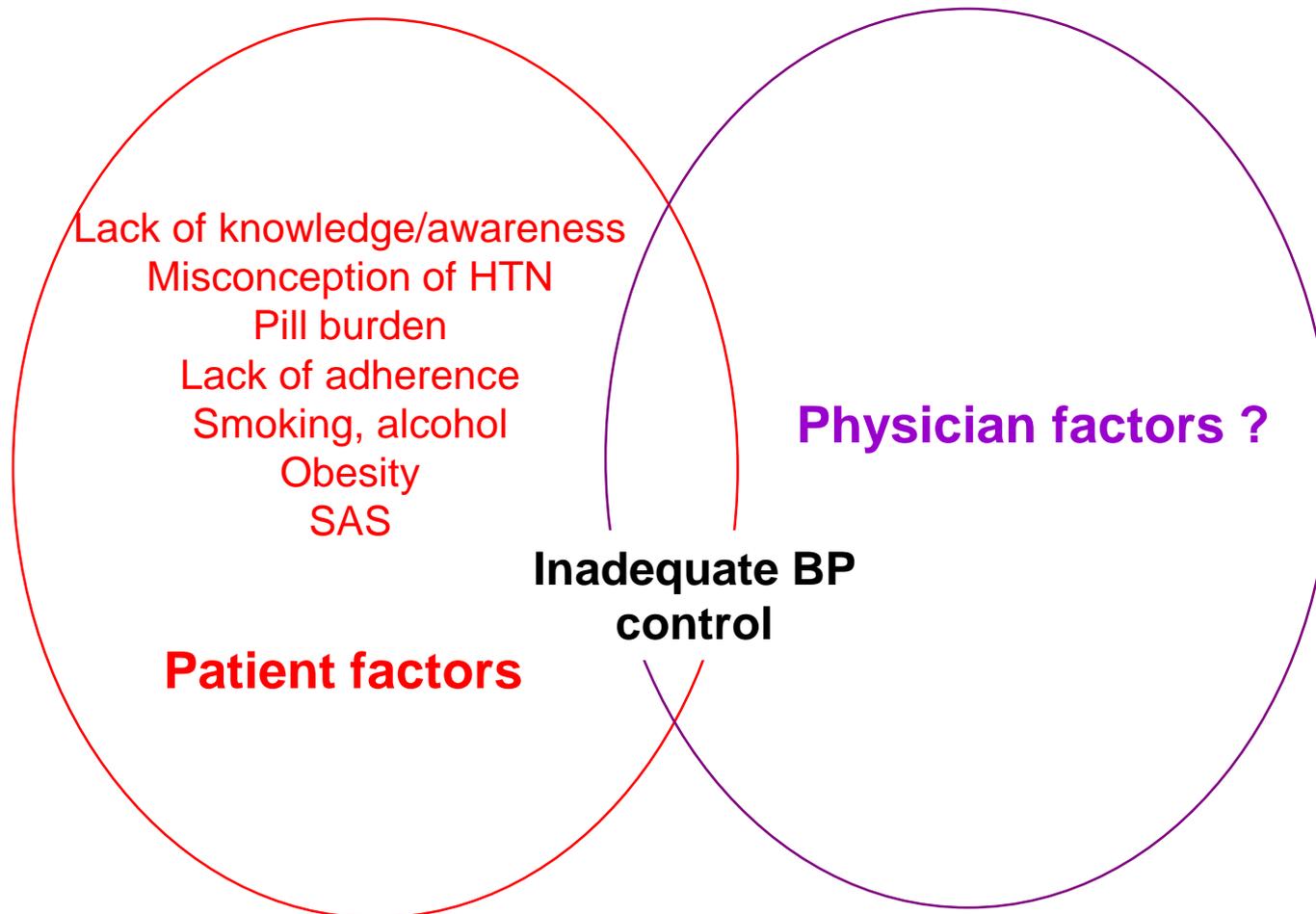
Family member-based supervision package

- One family member = supervisor
- Regular training of patient
- Control of adherence and BP monitoring
- Accessory appliances

Primary outcome: patient's medication adherence \nearrow OR 1.74 [0.91-3.32]

- Significant effect on BP control at mid-term (6M) OR 0.67 [0.40-0.93] but not at long-term (12 M)
- No significant difference in SBP/DBP at 12 M

The key patient and physician challenges...



Which measure of BP?

**Physician
Sphygmomanometer**



**Physician
Oscillometric**



**Nurse
Oscillometric**



**Patient alone
Oscillometric**



Which measure of BP?

Physician Sphygmomanometer



Physician Oscillometric



- ✓ Used in the vast majority of studies
 - Pathophysiology
 - Epidemiology
 - Pharmacology
 - Large RCTs
- ✓ Will remain the **Gold standard** for International Guidelines

2018 ESH-ESC Guidelines

Category	Systolic		Diastolic
Optimal	<120	and	<80
Normal	120–129	and/or	80–84
High normal	130–139	and/or	85–89
Grade 1 hypertension	140–159	and/or	90–99
Grade 2 hypertension	160–179	and/or	100–109
Grade 3 hypertension	≥180	and/or	≥110
Isolated systolic hypertension	≥140	and	<90

Office BP, ABPM and HBPM

Physician Sphygmomanometer



Physician Oscillometric



Ambulatory BP monitoring



Home BP measurement Oscillometric



- ✓ Used in the vast majority of studies
 - Pathophysiology
 - Epidemiology
 - Pharmacology
 - Large RCTs
- ✓ Will remain the **Gold standard** for International Guidelines

Table 9 Definitions of hypertension according to office, ambulatory, and home blood pressure levels

Category	SBP (mmHg)		DBP (mmHg)
Office BP ^a	≥140	and/or	≥90
Ambulatory BP			
Daytime (or awake) mean	≥135	and/or	≥85
Night-time (or asleep) mean	≥120	and/or	≥70
24 h mean	≥130	and/or	≥80
Home BP mean	≥135	and/or	≥85

2013 ESH-ESC Guidelines for the management of Hypertension

Evaluation of global CV risk for initiation of treatment

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		Low risk	Moderate risk	High risk
1–2 RF	Low risk	Moderate risk	Moderate to high risk	High risk
≥3 RF	Low to Moderate risk	Moderate to high risk	High Risk	High risk
OD, CKD stage 3 or diabetes	Moderate to high risk	High risk	High risk	High to very high risk
Symptomatic CVD, CKD stage ≥4 or diabetes with OD/RFs	Very high risk	Very high risk	Very high risk	Very high risk

BP = blood pressure; CKD = chronic kidney disease; CV = cardiovascular; CVD = cardiovascular disease; DBP = diastolic blood pressure; HT = hypertension; OD = organ damage; RF = risk factor; SBP = systolic blood pressure.

2013 ESH-ESC Guidelines for the management of Hypertension

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	High normal SBP 130–139 or DBP 85–89	Grade 1 HT SBP 140–159	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 • 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	• Lifestyle changes for several weeks • Then add BP drugs targeting <140/90	• Lifestyle changes • Immediate BP drugs targeting <140/90
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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

2013 ESH-ESC Guidelines for the management of Hypertension

Evaluation of global CV risk

Risk factors
Male sex
Age (men ≥ 55 years; women ≥ 65 years)
Smoking
Dyslipidaemia
Total cholesterol >4.9 mmol/L (190 mg/dL), and/or
Low-density lipoprotein cholesterol >3.0 mmol/L (115 mg/dL), and/or
High-density lipoprotein cholesterol: men <1.0 mmol/L (40 mg/dL), women <1.2 mmol/L (46 mg/dL), and/or
Triglycerides >1.7 mmol/L (150 mg/dL)
Fasting plasma glucose 5.6–6.9 mmol/L (102–125 mg/dL)
Abnormal glucose tolerance test
Obesity [BMI ≥ 30 kg/m ² (height ²)]
Abdominal obesity (waist circumference: men ≥ 102 cm; women ≥ 88 cm) (in Caucasians)
Family history of premature CVD (men aged <55 years; women aged <65 years)

2013 ESH-ESC Guidelines for the management of Hypertension

Evaluation of global CV risk

3 risk factors

Risk factors
Male sex
Age (men ≥ 55 years; women ≥ 65 years)
Smoking
Dyslipidaemia
Total cholesterol > 4.9 mmol/L (190 mg/dL), and/or
Low-density lipoprotein cholesterol > 3.0 mmol/L (115 mg/dL), and/or
High-density lipoprotein cholesterol: men < 1.0 mmol/L (40 mg/dL), women < 1.2 mmol/L (46 mg/dL), and/or
Triglycerides > 1.7 mmol/L (150 mg/dL)
Fasting plasma glucose 5.6–6.9 mmol/L (102–125 mg/dL)
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Obesity [BMI ≥ 30 kg/m ² (height ²)]
Abdominal obesity (waist circumference: men ≥ 102 cm; women ≥ 88 cm) (in Caucasians)
Family history of premature CVD (men aged < 55 years; women aged < 65 years)

2013 ESH-ESC Guidelines for the management of Hypertension

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No other RF		Low risk	Moderate risk	High risk
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Organ Damage	Moderate to high risk	High risk	High risk	High to very high risk
Symptomatic CVD, CKD stage ≥4 or diabetes with OD/RFs	Very high risk	Very high risk	Very high risk	Very high risk

BP = blood pressure; CKD = chronic kidney disease; CV = cardiovascular; CVD = cardiovascular disease; DBP = diastolic blood pressure; HT = hypertension; OD = organ damage; RF = risk factor; SBP = systolic blood pressure.

2013 ESH-ESC Guidelines: Target Organ Damage

Asymptomatic organ damage
Pulse pressure (in the elderly) ≥ 60 mmHg
Electrocardiographic LVH (Sokolow–Lyon index >3.5 mV; RaVL >1.1 mV; Cornell voltage duration product >244 mV*ms), or
Echocardiographic LVH [LVM index: men >115 g/m ² ; women >95 g/m ² (BSA)] ^a
Carotid wall thickening (IMT >0.9 mm) or plaque
Carotid–femoral PWV >10 m/s
Ankle-brachial index <0.9
CKD with eGFR 30–60 ml/min/1.73 m ² (BSA)
Microalbuminuria (30–300 mg/24 h), or albumin–creatinine ratio (30–300 mg/g; 3.4–34 mg/mmol) (preferentially on morning spot urine)

2013 ESH-ESC Guidelines for the management of Hypertension

Evaluation of global CV risk for initiating treatment

Other risk factors, asymptomatic organ damage or disease	Blood Pressure (mmHg)			
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Organ Damage	• Lifestyle changes • No BP intervention	BP drugs targeting <140/90	• Lifestyle changes • BP drugs targeting <140/90	• Lifestyle changes • Immediate BP drugs targeting <140/90
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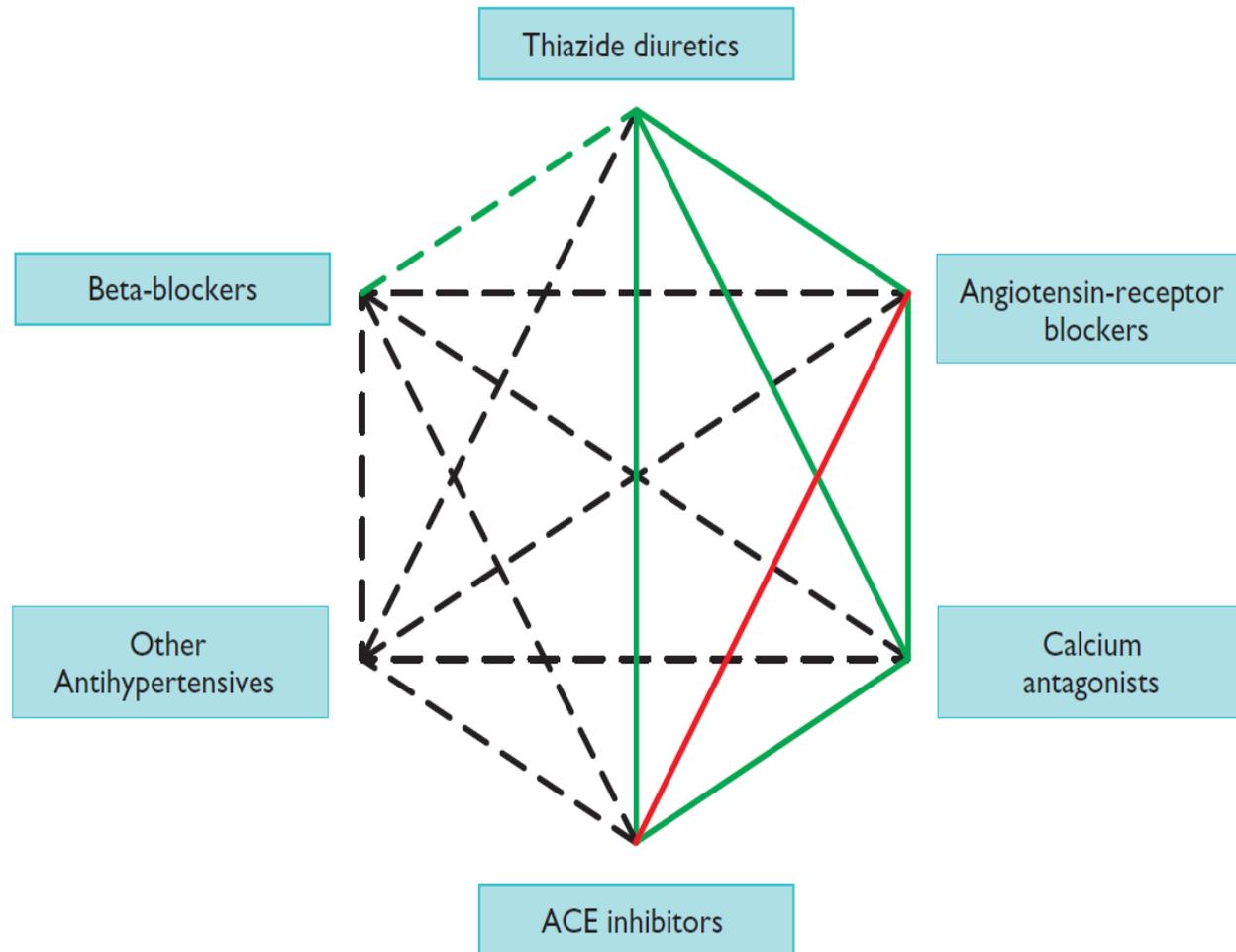
2018 ESH-ESC Guidelines: Life style

Lifestyle interventions for patients with hypertension or high-normal BP

Recommendations	Class ^a	Level ^b
Salt restriction to <5 g per day is recommended. ^{2,48,250,255,258}	I	A
It is recommended to restrict alcohol consumption to: <ul style="list-style-type: none"> • Less than 14 units per week for men. • Less than 8 units per week for women.³⁵ 	I	A
It is recommended to avoid binge drinking.	III	C
Increased consumption of vegetables, fresh fruits, fish, nuts, and unsaturated fatty acids (olive oil); low consumption of red meat; and consumption of low-fat dairy products are recommended. ^{262,265}	I	A
Body-weight control is indicated to avoid obesity (BMI >30 kg/m ² or waist circumference >102 cm in men and >88 cm in women), as is aiming at healthy BMI (about 20–25 kg/m ²) and waist circumference values (<94 cm in men and <80 cm in women) to reduce BP and CV risk. ^{262,271,273,290}	I	A
Regular aerobic exercise (e.g. at least 30 min of moderate dynamic exercise on 5–7 days per week) is recommended. ^{262,278,279}	I	A
Smoking cessation, supportive care, and referral to smoking cessation programs are recommended. ^{286,288,291}	I	B



2013 ESH-ESC Guidelines: Pharmacological treatment



2013 ESH-ESC Guidelines: Rx according to co-morbidities

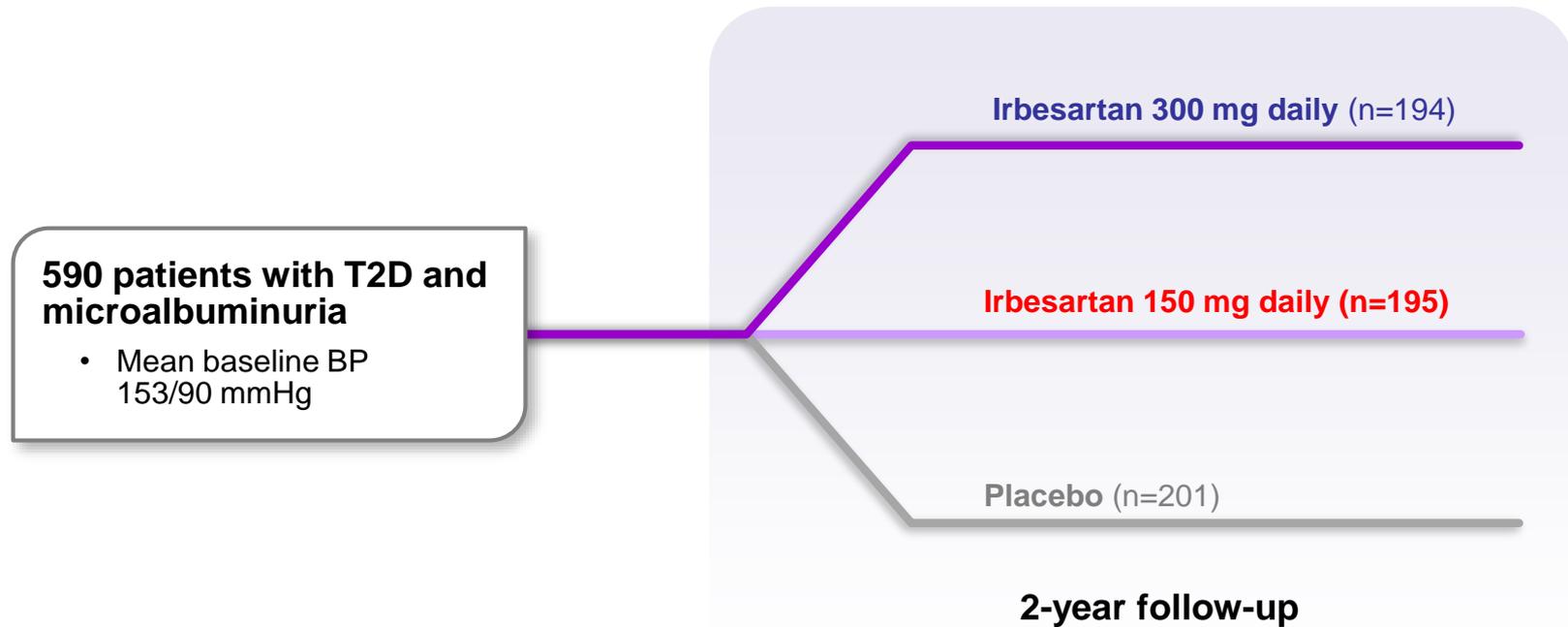
Table 15 Drugs to be preferred in specific conditions

Condition	Drug
Asymptomatic organ damage	
LVH	ACE inhibitor, calcium antagonist, ARB
Asymptomatic atherosclerosis	Calcium antagonist, ACE inhibitor
Microalbuminuria	ACE inhibitor, ARB
Renal dysfunction	ACE inhibitor, ARB
Clinical CV event	
Previous stroke	Any agent effectively lowering BP
Previous myocardial infarction	BB, ACE inhibitor, ARB
Angina pectoris	BB, calcium antagonist
Heart failure	Diuretic, BB, ACE inhibitor, ARB, mineralocorticoid receptor antagonists
Aortic aneurysm	BB
Atrial fibrillation, prevention	Consider ARB, ACE inhibitor, BB or mineralocorticoid receptor antagonist
Atrial fibrillation, ventricular rate control	BB, non-dihydropyridine calcium antagonist
ESRD/proteinuria	ACE inhibitor, ARB
Peripheral artery disease	ACE inhibitor, calcium antagonist

Renal dysfunction

Microalbuminuria +++

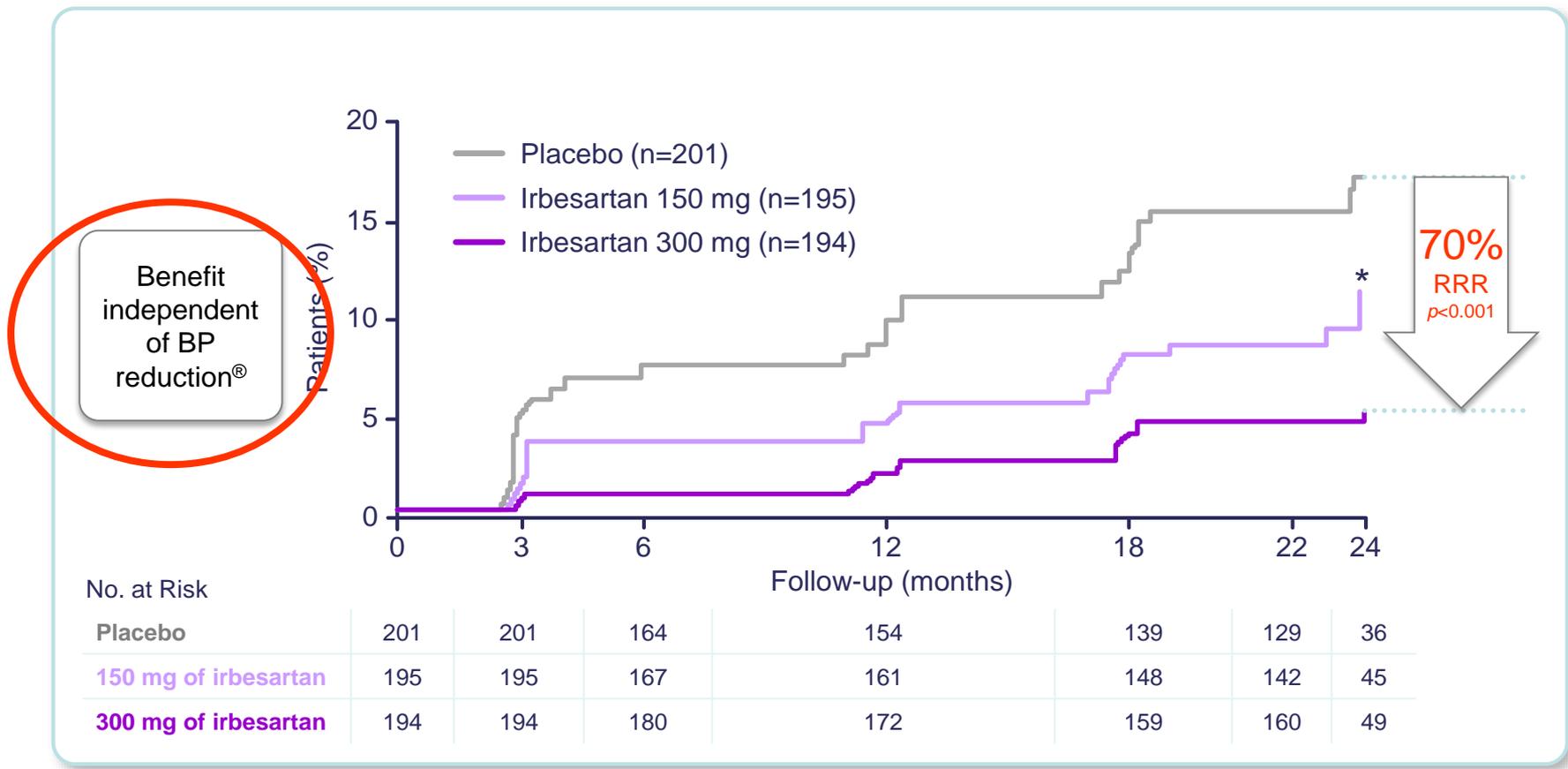
IRMA-2 examined the renoprotective effect of 2 different dosages of irbesartan



Primary endpoint: time to the onset of diabetic nephropathy

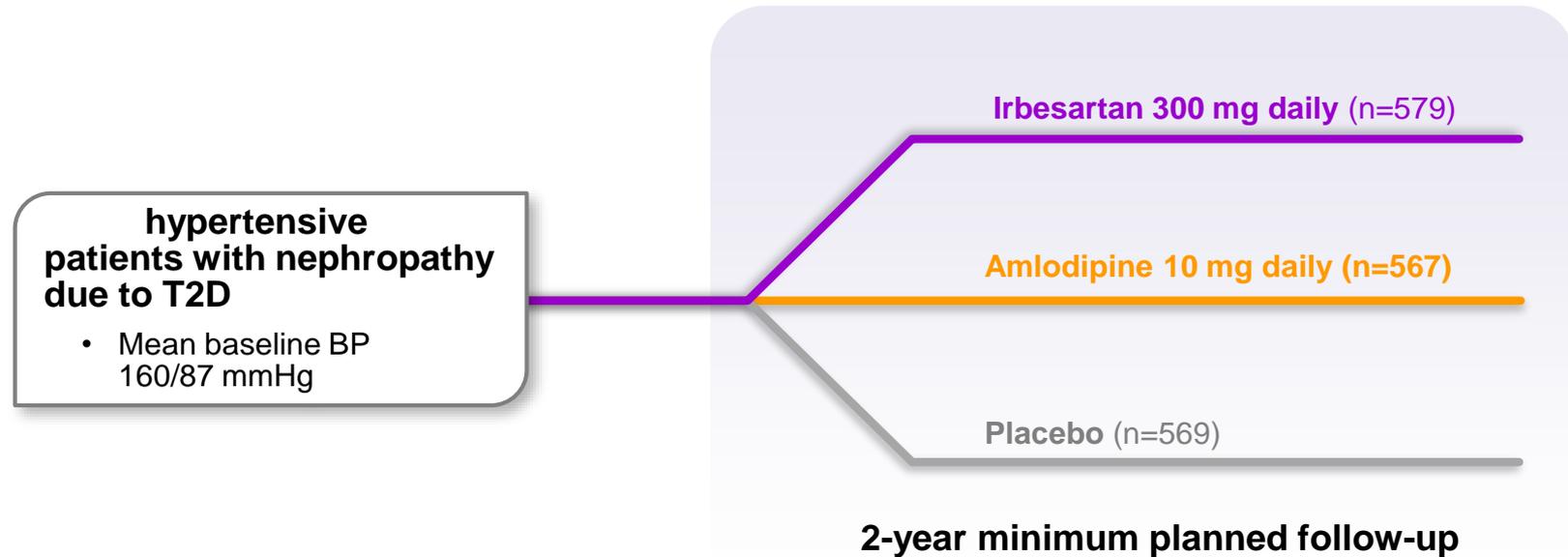
Secondary endpoints: changes in the level of albuminuria, creatinine clearance, and restoration of normoalbuminuria

Irbesartan 300 mg significantly reduced the rate of progression to diabetic nephropathy by 70%



* Relative risk reduction with irbesartan 150 mg vs. placebo: 39% ($p=0.08$)
 RRR = relative risk reduction

IDNT assessed the effect of amlodipine or irbesartan on progression of diabetic nephropathy



Primary composite endpoint: progression of diabetic nephropathy

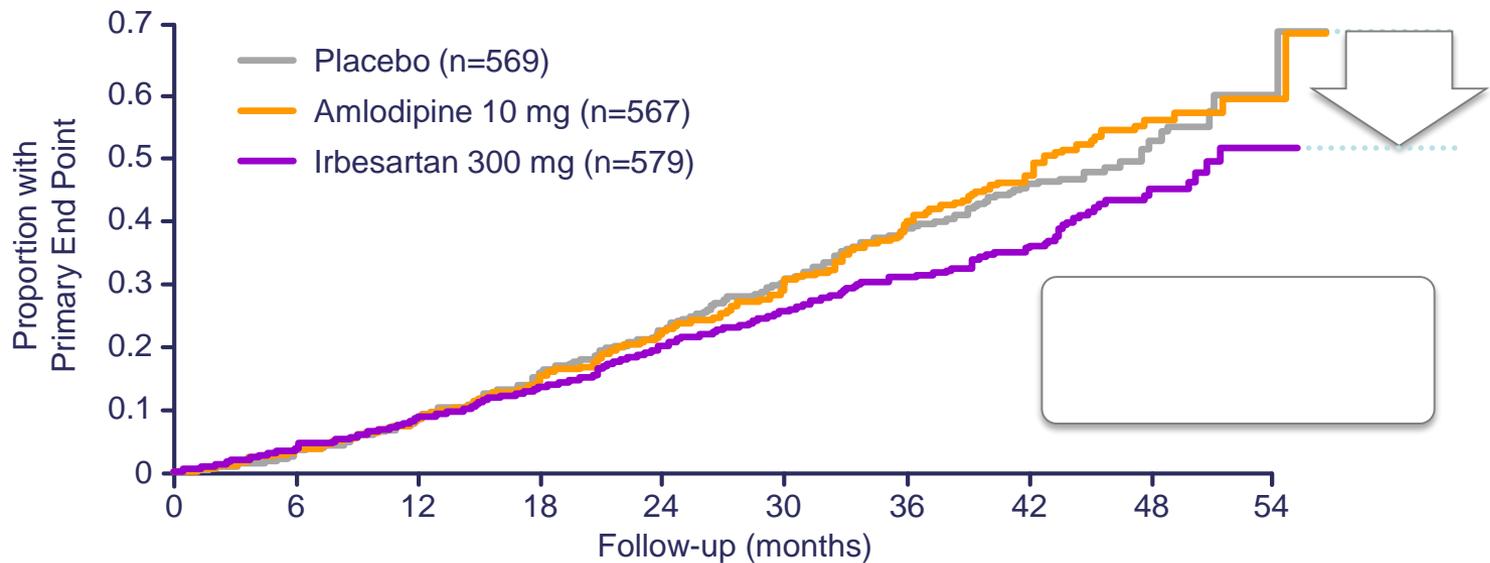
- Doubling of baseline serum creatinine concentration
- Development of end-stage renal disease
- Death from any cause

Secondary composite cardiovascular endpoint:

- Death from CV causes
- Nonfatal myocardial infarction
- Heart failure resulting in hospitalization
- Permanent neurologic deficit caused by a cerebrovascular event
- Lower limb amputation above the ankle

Irbesartan reduced the risk of diabetic nephropathy progression by 23% vs. amlodipine

Cumulative proportions of patients with progression of diabetic nephropathy



No. at Risk

Placebo	579	555	528	496	400	304	216	146	65
Amlodipine 10 mg	565	542	508	474	385	287	187	128	46
Irbesartan 300 mg	568	551	512	471	401	280	190	122	53

Treatment Initiation

Initiating Rx with combination therapy, a greater probability to reach BP targets

2018 ESH-ESC Guidelines

The advantages of initiating with combination therapy are

- 1- a more **prompt response** in a **larger number** of patients
- 2- a greater probability of **achieving the target BP** in patients with higher BP values
- 3- a **better patient adherence**



Less CV complications

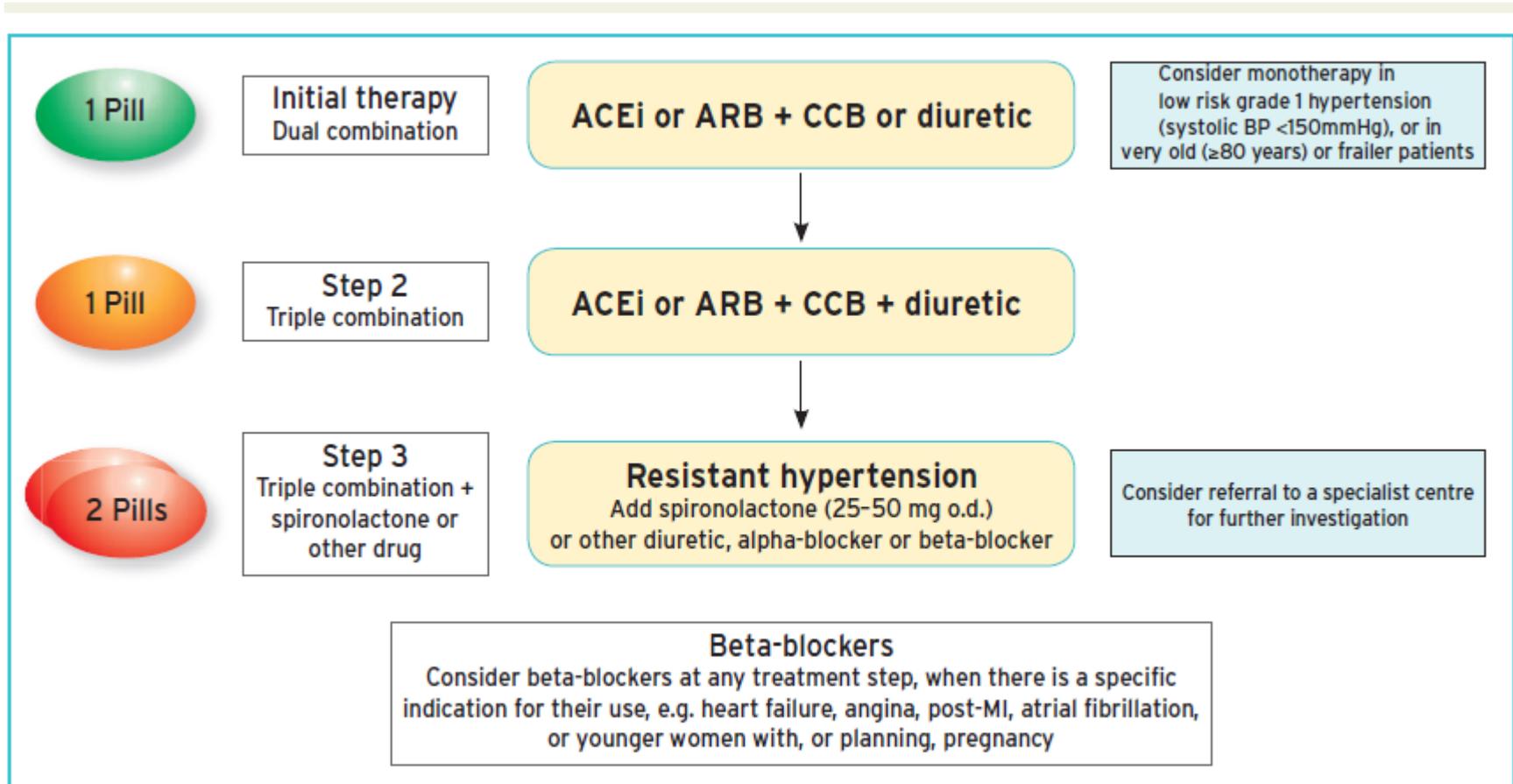
Which patients are concerned by initiation with combination therapy?

International guidelines

	SBP/DBP reduction goal or hypertension grade
AHA/ACC 2017	≥ 130 and/or ≥ 80
ASH/ISH 2014	≥ 160 and/or ≥ 100
JNC8 2014	≥ 160 and/or ≥ 100
ESH-ESC 2013	markedly elevated BP or high/very high CV risk
CHEP 2013	SBP/DBP ≥ 20 /10 mmHg above target
NICE 2011	-
China 2010	≥ 160 and/or ≥ 100 or SBP/DBP ≥ 20 /10 mmHg above target
Taiwan 2010	SBP/DBP ≥ 20 /10 mmHg above target

Initiating Rx with combination therapy, a greater probability to reach BP targets

2018 ESH-ESC Guidelines



Physician's reluctance to FDC therapy

- Side-effects are more likely to occur with 2 drugs than with one
- An earlier and greater BP lowering may be deleterious in some patients, because of the J-curve phenomenon mainly in patients with grade I hypertension
- Fixed-dose combinations (FDC) lack flexibility

Physician's reluctance to FDC therapy

- Side-effects are more likely to occur with 2 drugs than with one
- An earlier and greater BP lowering may be deleterious in some patients, because of the J-curve phenomenon mainly in patients with grade I hypertension
- Fixed-dose combinations (FDC) lack flexibility

This could be overcome

- with a better availability of different doses
- by initiating Rx with the lowest effective combined dose
- by performing a slow drug escalation



Strategy of tailored effective combined doses

From 2 drug-FDC to 3 drug-FDC

Fixed-dose triple-combinations available in Europe...

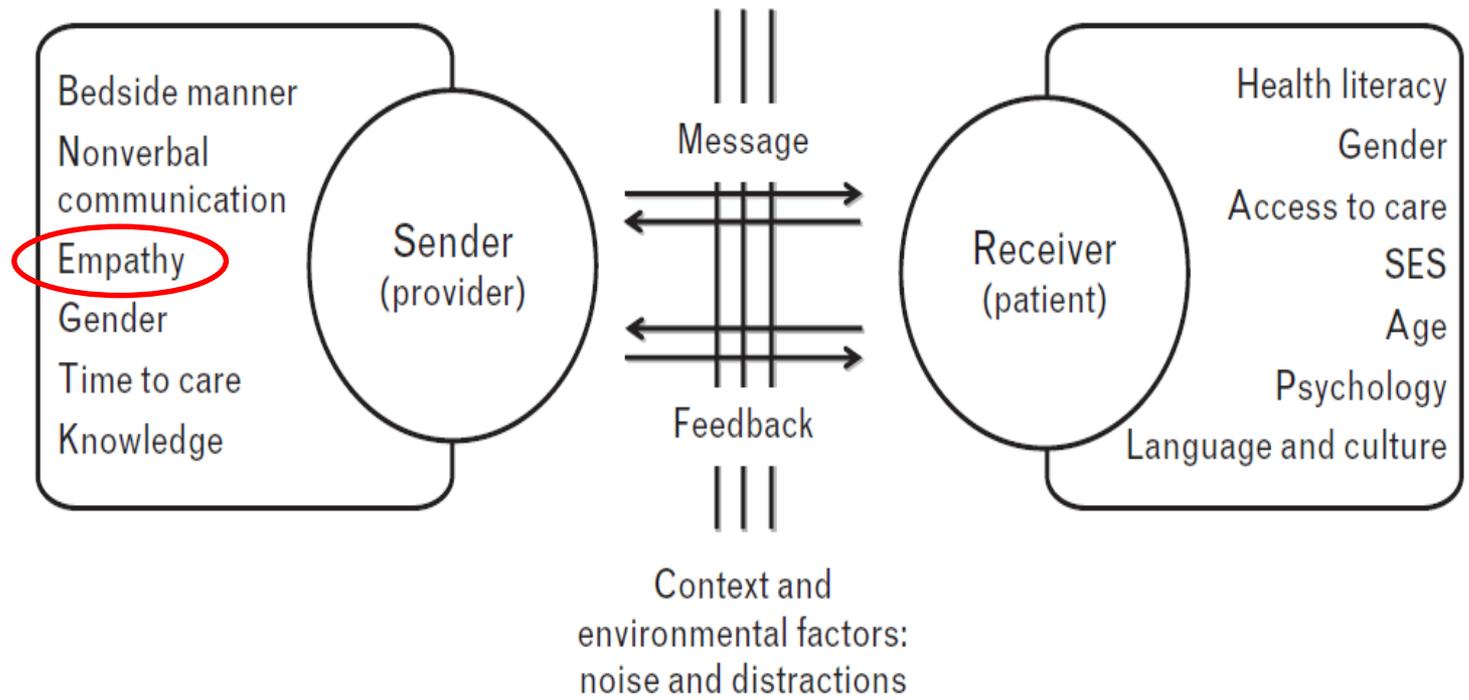
RAS blocker	CCB	Diuretic	Reimbursement (as of January 2018)
Valsartan 160 mg	Amlodipine 5, 10 mg	HCTZ 12.5, 25 mg	12 countries
Perindopril 5, 10 mg	Amlodipine 5, 10 mg	Indapamide 1.25, 2.5 mg	4 countries
Olmesartan 20, 40 mg	Amlodipine 5, 10 mg	HCTZ 12.5, 25 mg	11 countries
Aliskiren	Amlodipine	HCTZ	—

Physician's challenges: from knowledge to communication

Getting the message across: opportunities and obstacles in effective communication in hypertension care

Emily P. Jolles^a, Alexander M. Clark^b, and Branko Braam^a

Jolles EP et al. J Hypertens 2012



Physician's challenge : motivation

Physicians' degree of motivation regarding their perception of hypertension, and blood pressure control

Silla M. Consoli^{a,b}, Cédric Lemogne^{a,b,c}, Alain Levy^d, Denis Pouchain^e and Stephane Laurent^{b,f,g}

Consoli S et al. J Hypertens 2010

DUO-HTA study
346 GP, 209 cardiologists
2014 hypertensive patients

	Circle only one number per line							
1. A rewarding disease management	1	2	3	4	5	6	7	An unrewarding disease management
2. A simple disease	1	2	3	4	5	6	7	A complex disease
3. A stable course	1	2	3	4	5	6	7	A fluctuating course
4. A disease well understood by the patients	1	2	3	4	5	6	7	A disease poorly understood by the patients
5. A controllable disease if the proper means are given	1	2	3	4	5	6	7	A disease difficult to control
6. An exciting field due to its diversity	1	2	3	4	5	6	7	A repetitive and monotonous field
7. A disease trivialized by the patients	1	2	3	4	5	6	7	A disease dramatized by the patients
8. A frank disease	1	2	3	4	5	6	7	An insidious disease
9. An opportunity to improve quality of life	1	2	3	4	5	6	7	A hardship for quality of life
10. An opportunity given to the patient to find a healthier lifestyle	1	2	3	4	5	6	7	A cause of changes in patients' lifestyle, which represent a burden for them
11. An ideal training for the patient-physician relationship	1	2	3	4	5	6	7	A domain which brings little to the patient-physician relationship
12. A type of consultation in which the patients have not much to say	1	2	3	4	5	6	7	An opportunity to listen to the patient differently
13. A field in which it is preferable to trust the patients	1	2	3	4	5	6	7	A typical example in which the sincerity of a patient who says he/she is compliant is questionable

13 items questionnaire

Physician's challenge : motivation

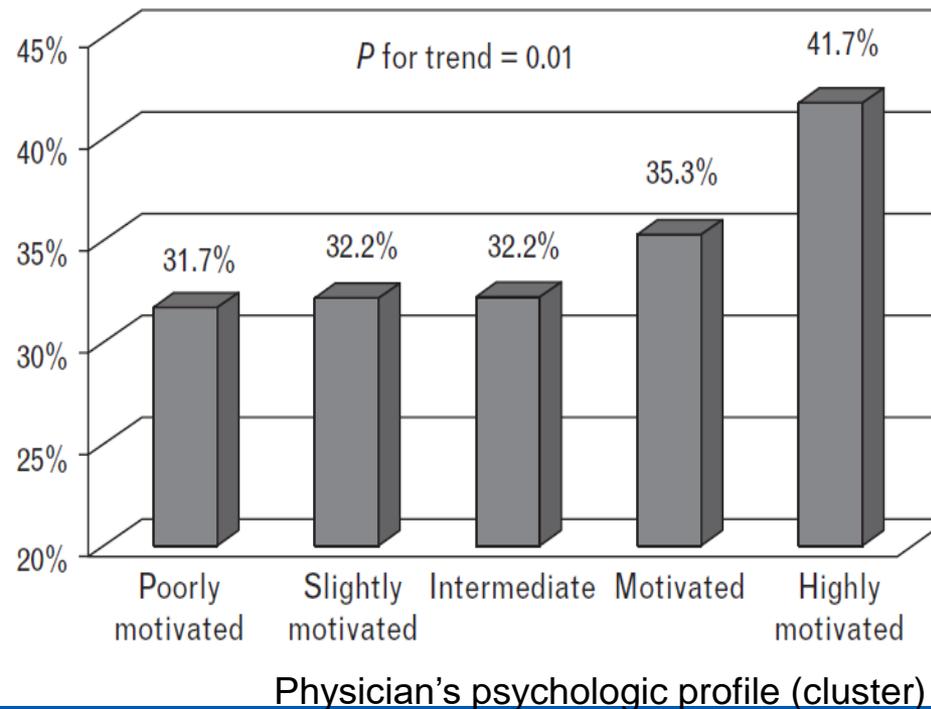
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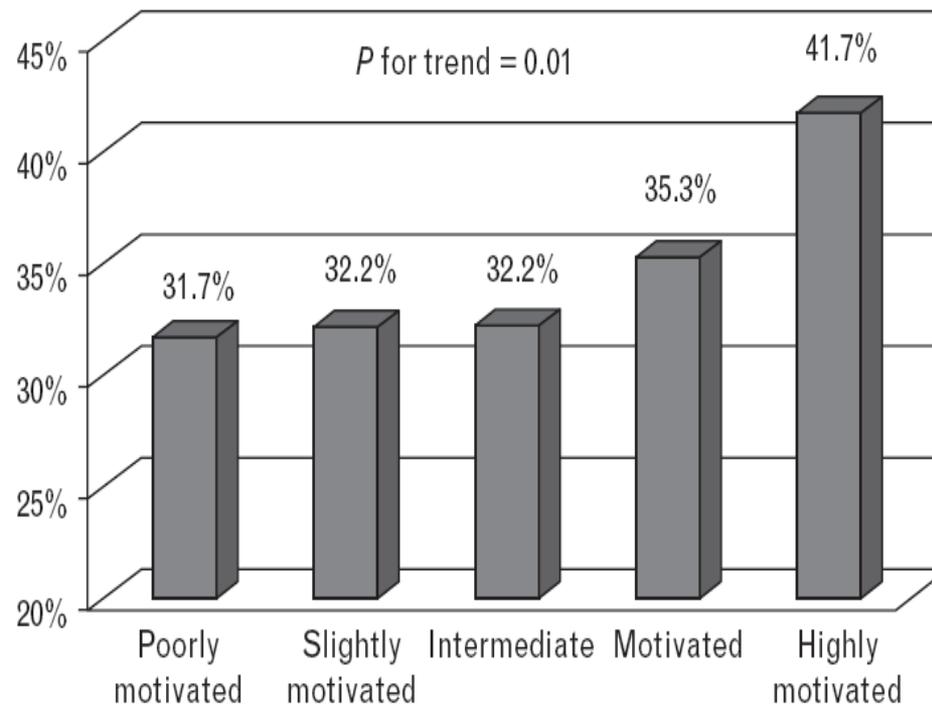
Consoli S et al. J Hypertens 2010

DUO-HTA study
346 GP, 209 cardiologists
2014 hypertensive patients

Probability, for a patient, of having a controlled BP on the day of the visit



Plus le médecin est motivé, plus son patient a une PA contrôlée



Probability, for a hypertensive patient included into the survey, of having a controlled blood pressure on the day of the visit, according to physician's cluster (unadjusted).

Simple tools for assessing drug adherence

Drug adherence in hypertension: from methodological issues to cardiovascular outcomes

Hamdidouche et al. *J Hypertens* 2017;35:1133-1144

Idir Hamdidouche^{a,c,d}, Vincent Jullien^{a,c,d}, Pierre Boutouyrie^{a,c,d}, Eliane Billaud^{a,c}, Michel Azizi^{b,c,d,e}, and Stéphane Laurent^{a,c,d}

Methods	Indirect			
	Clinician estimation	Questionnaires	Pill count	Prescription refill
Type of data	Qualitative	Qualitative	Quantitative	Quantitative
Device mostly used	Interview	MMAS-4, 8	–	MPR/PDC
Reliability	–	–	+	+
Validity	+	+	+	+
Objectivity	–	–	–	–
Simplicity	+++	+++	++	–
Cost	–	–	–	+
Availability	+++	+++	++	–
Clinical use	+++	+++	+	–

MPR, Medication Possession Ratio

PDC, Proportion of Days Covered by treatment

Simple tools for assessing drug adherence

Drug adherence in hypertension: from methodological issues to cardiovascular outcomes

Idir Hamdidouche^{a,c,d}, Vincent Jullien^{a,c,d}, Pierre Boutouyrie^{a,c,d}, Eliane Billaud^{a,c}, Michel Azizi^{b,c,d,e}, and Stéphane Laurent^{a,c,d}

Methods	Direct		
	DOT	Electronic monitoring	Drug assay
Type of data	Quantitative	Quantitative	Qualitative
Device mostly used	–	MEMS	LC–MS/MS
Reliability	+++	++	+++
Validity	+++	++	++
Objectivity	+++	+	++
Simplicity	–	+	+/-
Cost	+	+++	++
Availability	–	–	+/-
Clinical use	–	–	+

DOT Directly Observed Therapy

Simple tools for assessing drug adherence

Drug adherence in hypertension: from methodological issues to cardiovascular outcomes

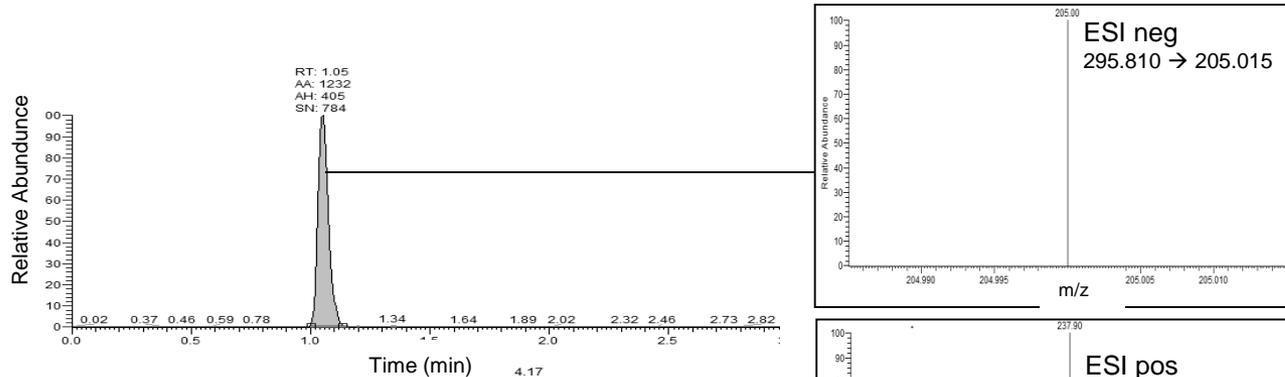
Idir Hamdidouche^{a,c,d}, Vincent Jullien^{a,c,d}, Pierre Boutouyrie^{a,c,d}, Eliane Billaud^{a,c}, Michel Azizi^{b,c,d,e}, and Stéphane Laurent^{a,c,d}

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Objectivity	+++	+	++
Simplicity	-	+	+/-
Cost	+	+++	++
Availability	-	-	+/-
Clinical use	-	-	+

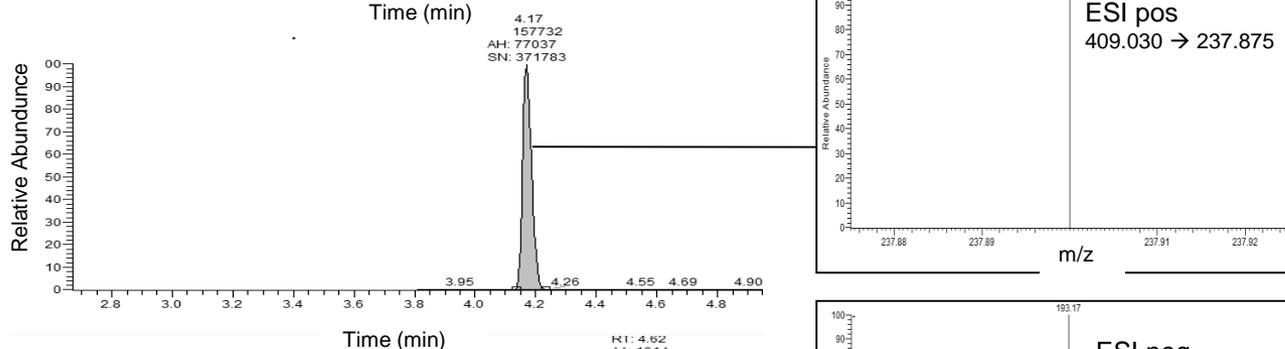
DOT Directly Observed Therapy

- Any of 24 antiHT drugs**
- Amiloride
 - Amlodipine
 - Atenolol
 - Bisoprolol
 - Candesartan
 - Carvedilol
 - Celiprolol
 - Chlortalidone
 - Clonidine
 - Furosemide
 - Hydrochlorothiazide
 - Indapamide
 - Irbesartan
 - Labetalol
 - Metoprolol
 - Moxonidine
 - Nicardipine
 - Olmesartan
 - Prazosine
 - Rilmenidine
 - Spironolactone (canrenone)
 - Urapidil
 - Valsartan
 - Verapamil

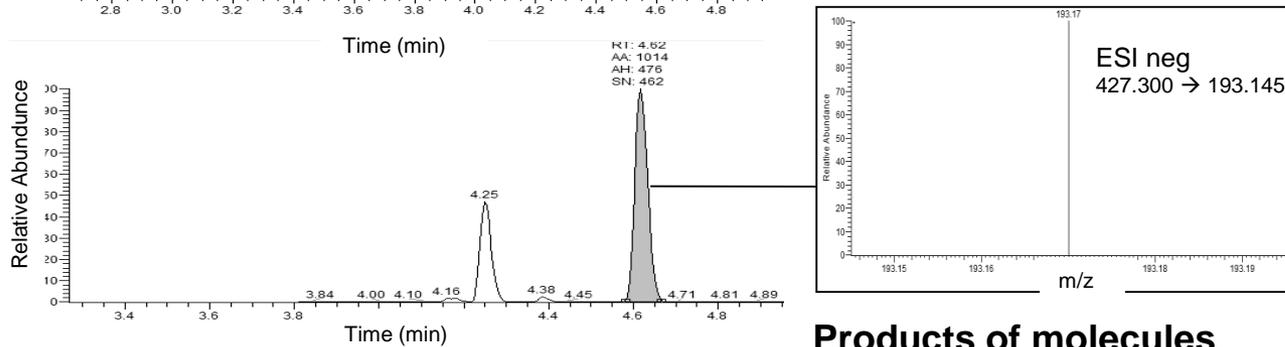
Urinary drug detection by LCMS/MS in a fully adherent patient



Hydrochlorothiazide



Amlodipine



Irbesartan

Chromatograms

Products of molecules fragmentation

Urinary drug detection by LCMS/MS in a fully NON-adherent patient

Treatment prescribed:

Irbesartan 150mg, once/day

Nebivololol, 5mg, once/day

Spirolactone 25mg,

once/day

Hydrochlorothiazide (HTCZ)

12.5mg, once/day

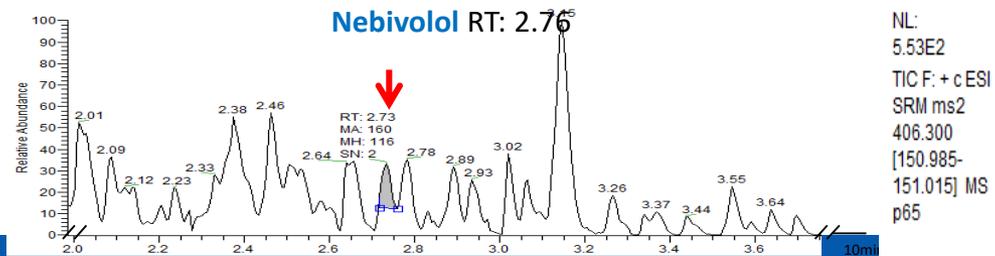
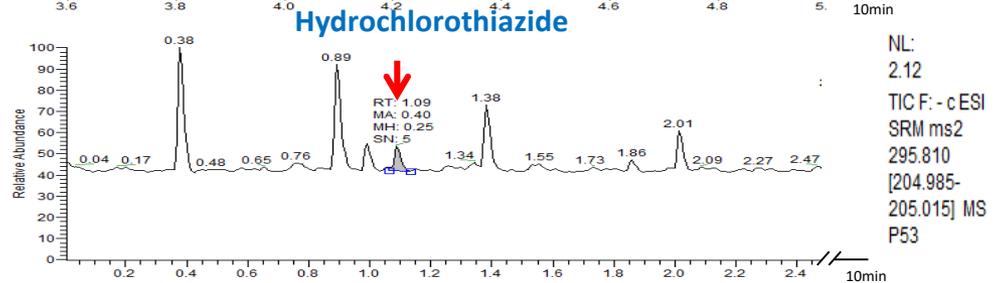
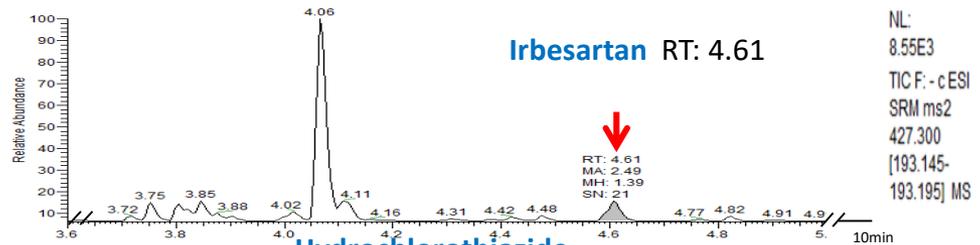
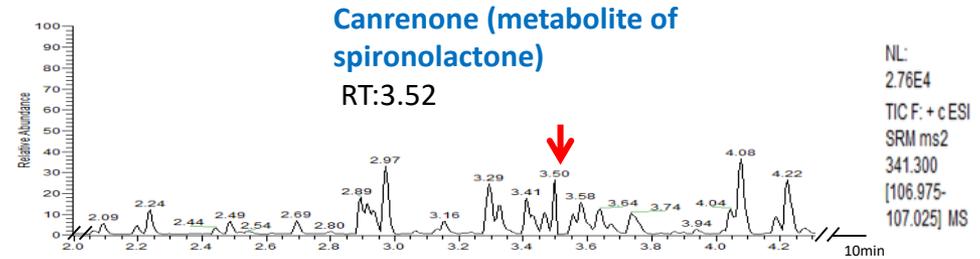
Result of LC-MS/MS analysis:

Irbesartan: not detected

Nebivololol: not detected

Spirolactone: not detected

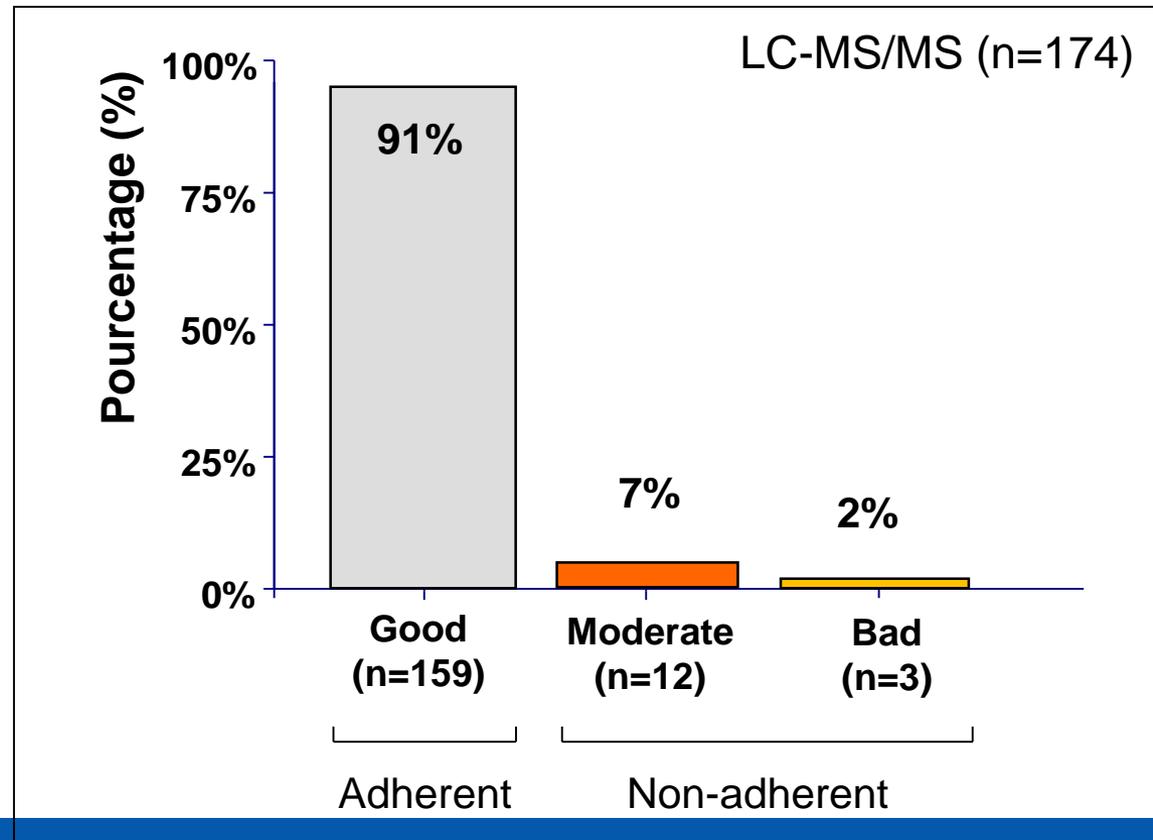
HTCZ: not detected



Urinary drug detection in well informed patients

Routine urinary detection of antihypertensive drugs for systematic evaluation of adherence to treatment in hypertensive patients

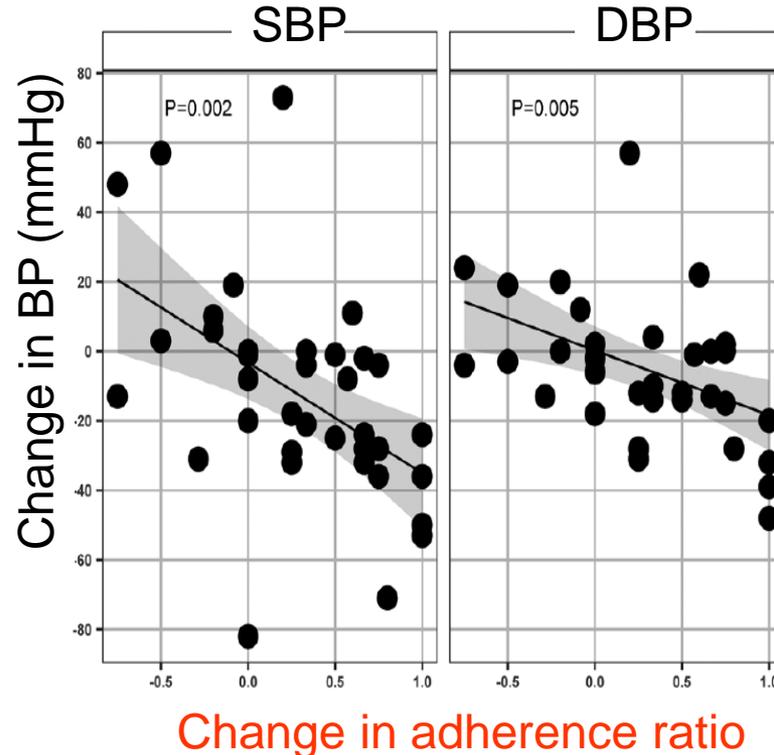
Idir Hamdidouche^{a,c,d}, Vincent Jullien^{a,c}, Pierre Boutouyrie^{a,c,d}, Eliane Billaud^{a,c}, Michel Azizi^{b,c,d,e}, and Stéphane Laurent^{a,c,d}



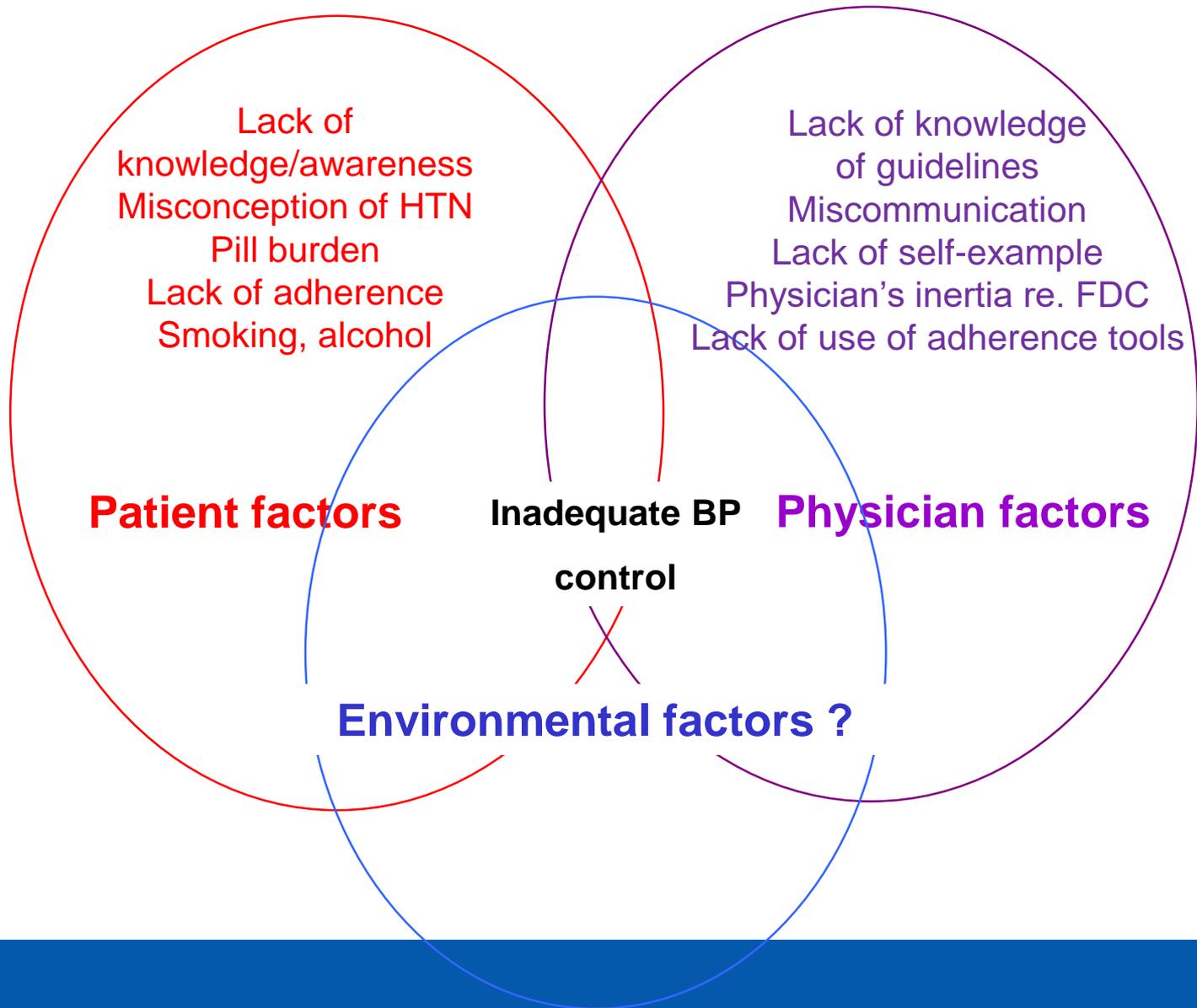
Biochemical Screening for Nonadherence Is Associated With Blood Pressure Reduction and Improvement in Adherence

Pankaj Gupta, Prashanth Patel, Branislav Štrauch, Florence Y. Lai, Artur Akbarov, Gaurav S. Gulsin, Alison Beech, Věra Marešová, Peter S. Topham, Adrian Stanley, Herbert Thurston, Paul R. Smith, Robert Horne, Jiří Widimský, Bernard Keavney, Anthony Heagerty, Nilesh J. Samani, Bryan Williams, Maciej Tomaszewski

Repeated urinary drug detection by LC-MS/MS in non adherent patients



The key patient and physician challenges...



Disentangling Complexity is Challenging – Many new guidelines?



Some confusion...which Guideline should be applied?
BP threshold for initiating Rx: AHA/ACC 2017 Guidelines

2018 ESH-ESC
2014 JNC8
2014 AHA/ACC

Table 6. Categories of BP in Adults*

BP Category	SBP		DBP
Normal	<120 mm Hg	and	<80 mm Hg
Elevated	120–129 mm Hg	and	<80 mm Hg
Hypertension			
Stage 1	130–139 mm Hg	or	80–89 mm Hg
Stage 2	≥140 mm Hg	or	≥90 mm Hg

Optimal
Normal

High normal
Grade I HT

New ACC/AHA Hypertension Guidelines Make 130 the New 140

Blood Pressure Categories



BLOOD PRESSURE CATEGORY	SYSTOLIC mm Hg (upper number)		DIASTOLIC mm Hg (lower number)
NORMAL	LESS THAN 120	and	LESS THAN 80
ELEVATED	120 – 129	and	LESS THAN 80
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 1	130 – 139	or	80 – 89
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 2	140 OR HIGHER	or	90 OR HIGHER
HYPERTENSIVE CRISIS (consult your doctor immediately)	HIGHER THAN 180	and/or	HIGHER THAN 120

Some confusion...which Guideline should be applied?

BP threshold for initiating Rx: AHA/ACC 2017 Guidelines

Table 6. Categories of BP in Adults*

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2018 ESH-ESC
2014 JNC8
2014 AHA/ACC

Optimal
Normal

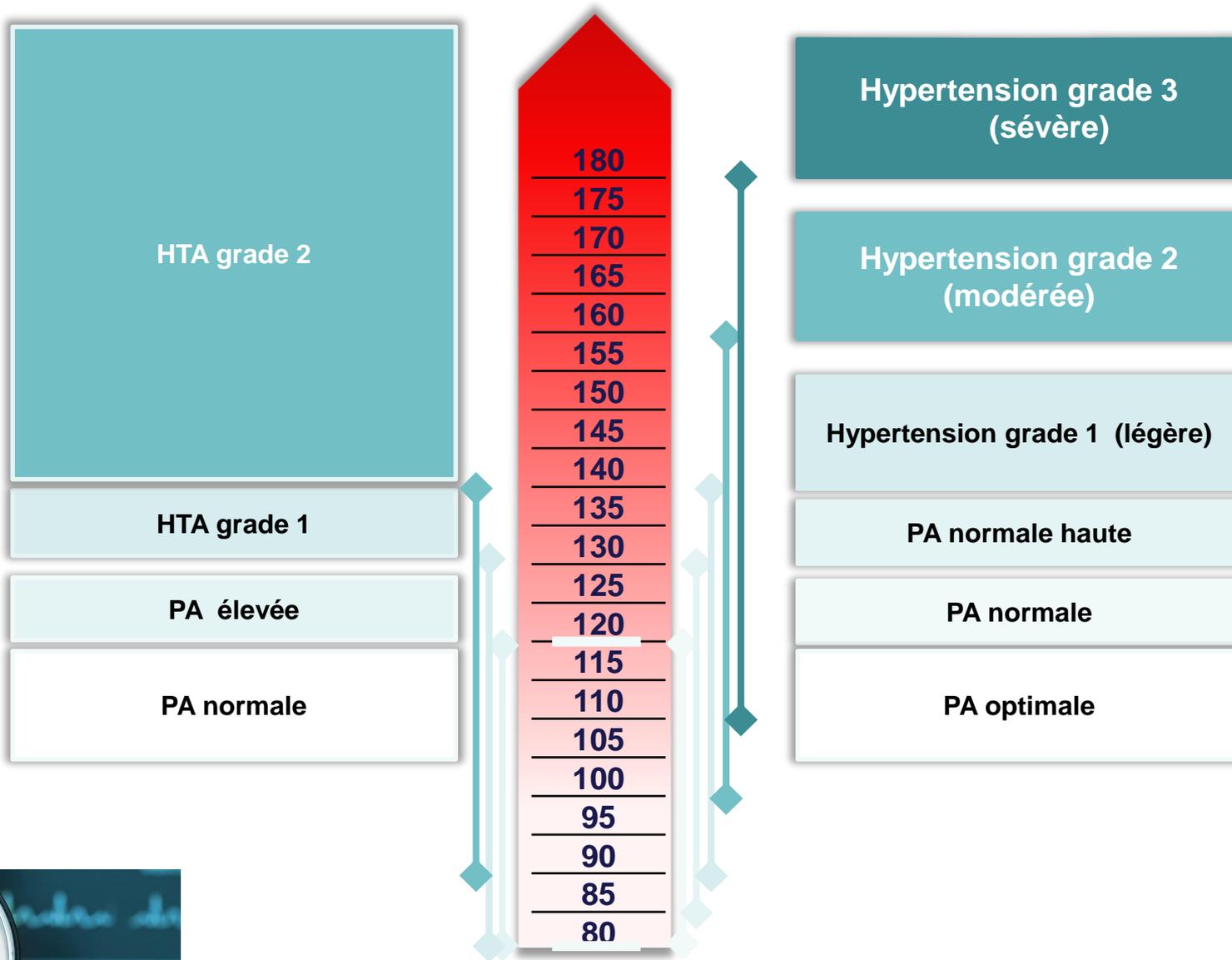
High normal
Grade I HT

Threshold
140/90 mmHg

- 130/80 mmHg = threshold for initiation of anti-HT treatment
- For secondary prevention
 - For primary prevention ONLY if 10 yrs CV risk is $\geq 10\%$

ACC/AHA 2017

ESC 2018



Drug companies inertia: a need for...

- ❑ Large RCTs in order to demonstrate that **less CV events** occur when Rx is initiated with a **FDC vs usual care**
- ❑ Large RCTs comparing benefit/risk ratios between the above 2 groups in **various populations** with various comorbidities

Drug companies inertia: a need for...

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Regulatory authorities inertia ?

CVCT – MEMA



Regulatory Summit



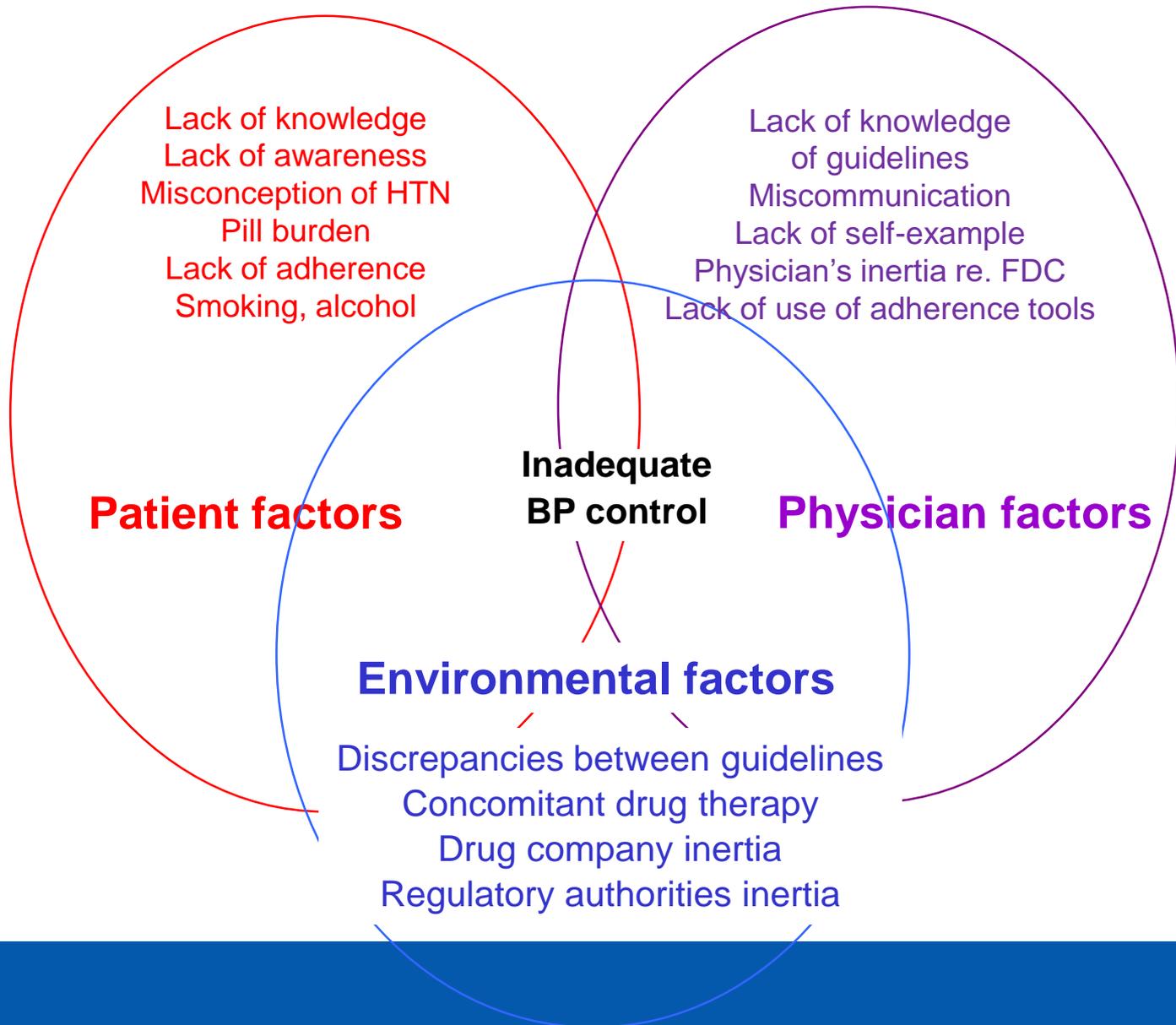
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In Summary

The key patient and physician challenges...



Merci !