



## CURRENT CHALLENGES AND FUTURE PERSPECTIVES IN HYPERTENSION MANAGEMENT

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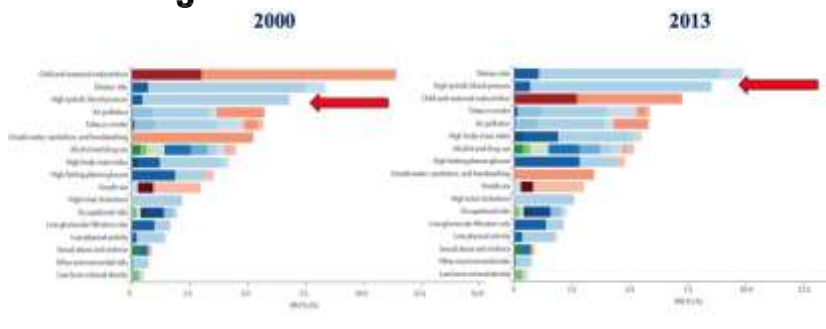
*Cairo, Feb 20-23, 2017*



## WHAT DO WE KNOW



## GLOBAL DALYS ATTRIBUTED TO LEVEL 2 RISK FACTORS IN 2000 AND IN 2013§

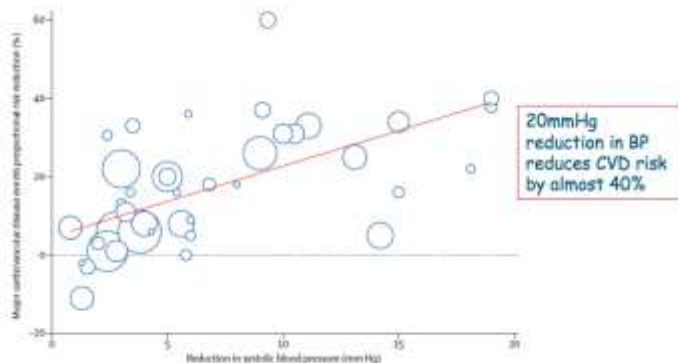


DALY, disability-adjusted life year

GBD 2013 Risk Factors Collaborators, *Lancet*, Published online September 11, 2015



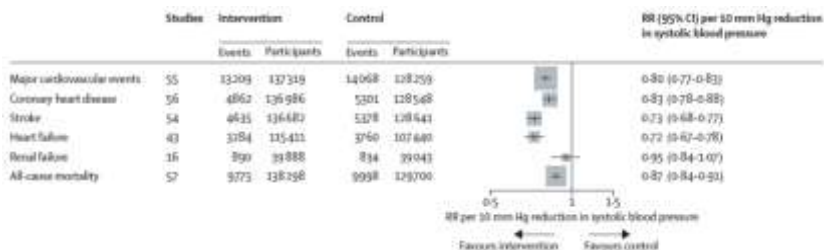
## BLOOD PRESSURE REDUCTION AND CARDIOVASCULAR DISEASE RISK REDUCTION



Ettehad D, et al. *Lancet* 2016; 387: 957-967



## STANDARDIZED EFFECT OF A 10MMHG REDUCTION IN SYSTOLIC BP ON MAJOR CLINICAL OUTCOMES

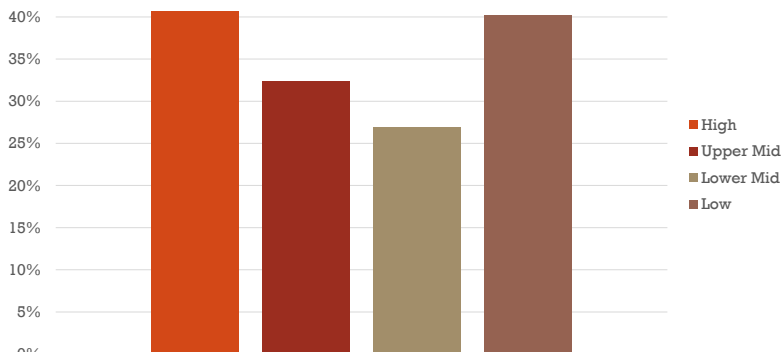


Relative risk reduction similar irrespective of baseline BP  
 Relative risk reduction similar irrespective of baseline CVD risk

Ettehad D, et al. Lancet 2016; 387: 957-967



## HYPERTENSION CONTROL IN THE PURE STUDY ACCORDING TO COUNTRY INCOME



<b>High Income Countries (HIC)</b> Canada, Sweden, UAE	<b>Upper Middle Income Countries (UMIC)</b> Argentina, Brazil, Chile, Malaysia, South Africa, Turkey	<b>Lower Middle Income Countries (LMIC)</b> China, Columbia, Iran	<b>Lower Income Countries (LIC)</b> Bangladesh, India, Pakistan, Zimbabwe
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## HOW SHOULD WE MEASURE BP?



## METHODS TO MEASURE BP

- Office BP
- Home BP
- Ambulatory BP
  - 24 hours
  - Daytime
  - Nighttime
- Central aortic pressure
- BPTtrue



## European Society of Hypertension guidelines for blood pressure monitoring at home: a summary report of the Second International Consensus Conference on Home Blood Pressure Monitoring

**HBPM should be used routinely in all treated hypertensive patients**

Gianfranco Parati<sup>a</sup>, Peter de Leeuw<sup>b</sup>, Athanasios Manolis<sup>c</sup>, Paul Padfield<sup>d</sup>, Paolo Palatini<sup>e</sup>, Thomas Pickering<sup>f</sup>, Josep Rieu<sup>g</sup>, Miriam Reverte<sup>a</sup>, Luis M. Ruilope<sup>p</sup>, Andrew Shennan<sup>q</sup>, Jan A. Staessen<sup>r</sup>, Andras Tisler<sup>s</sup>, Bernard Waeber<sup>t</sup>, Alberto Zanchetti<sup>u</sup> and Giuseppe Mancia<sup>v</sup>, on behalf of the ESH Working Group on Blood Pressure Monitoring

HBPM, home blood pressure monitoring

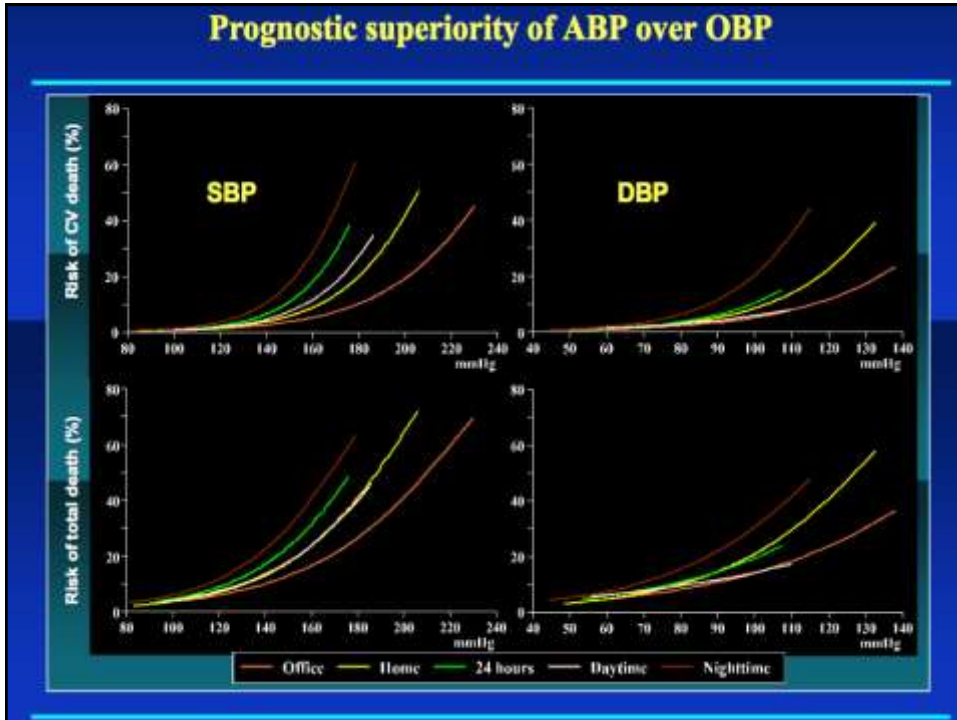
Parati G, et al. *J. Hypertens.* 2008, 26:1505–1530

## Studies Assessing HBPM and Prognosis

Study	Reference	Country	Population	N	Follow-up (years)	Outcomes
Ohsumi	Ohkubo et al. [17]	Japan	General	1,789	6.6	All-cause mortality, CV mortality
Ohsumi	Hizawa et al. [18]	Japan	General	1,913	8.6	CV mortality
Ohsumi	Ohkubo et al. [20]	Japan	General	1,491	10.6	Stroke
Ohsumi	Ohkubo et al. [21]	Japan	General	1,702	10.6	Stroke
Ohsumi	Asayama et al. [22]	Japan	General	1,702	11.0	Stroke
Ohsumi	Asayama et al. [23]	Japan	General	1,702	11.0	Stroke
Ohsumi	Izawa et al. [24]	Japan	General	2,309	11.7	Stroke
PAMELA	Segni et al. [25]	Italy	General	2,051	10.9	All-cause mortality, CV mortality
PAMELA	Mancia et al. [26]	Italy	General	2,051	12.3	All-cause mortality, CV mortality
Difema	Stegemans et al. [27]	Greece	General	665	8.2	CV events
Fin-Home	Niranen et al. [28*]	Finland	General	2,081	6.8	All-cause mortality, CV events
Flanders	Fagard et al. [29]	Belgium	Elderly	391	10.9	CV events
Nishinaga	Nishinaga et al. [30]	Japan	Elderly	465	9.0	Loss of functional independence
SHOAF	Robert et al. [31]	France	Elderly	4,939	3.2	All-cause mortality, CV mortality, CV events
Rave	Rave et al. [33]	Germany	Diabetic nephropathy	77	6.2	Decline in eGFR
Suzuki	Suzuki et al. [34]	Japan	CKD	113	3.0	Decline in eGFR
Agarwal	Agarwal and Andolen [35]	USA	CKD	217	3.5	All-cause mortality, ESRD
Agarwal	Agarwal and Andolen [37]	USA	CKD	217	3.4	All-cause mortality, CV events
Albortz	Albortz et al. [36]	USA	Hemodialysis	156	2.0	All-cause mortality, CV mortality
Agarwal	Agarwal [39*]	USA	Hemodialysis	326	2.4	All-cause mortality

CKD, chronic kidney disease; CV, cardiovascular; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; HBPM, home blood pressure monitoring

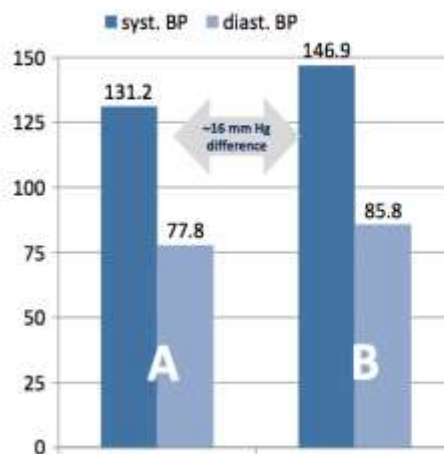
Sheikh S, et al. *Curr Hypertens Rep.* 2011; 13:192–199



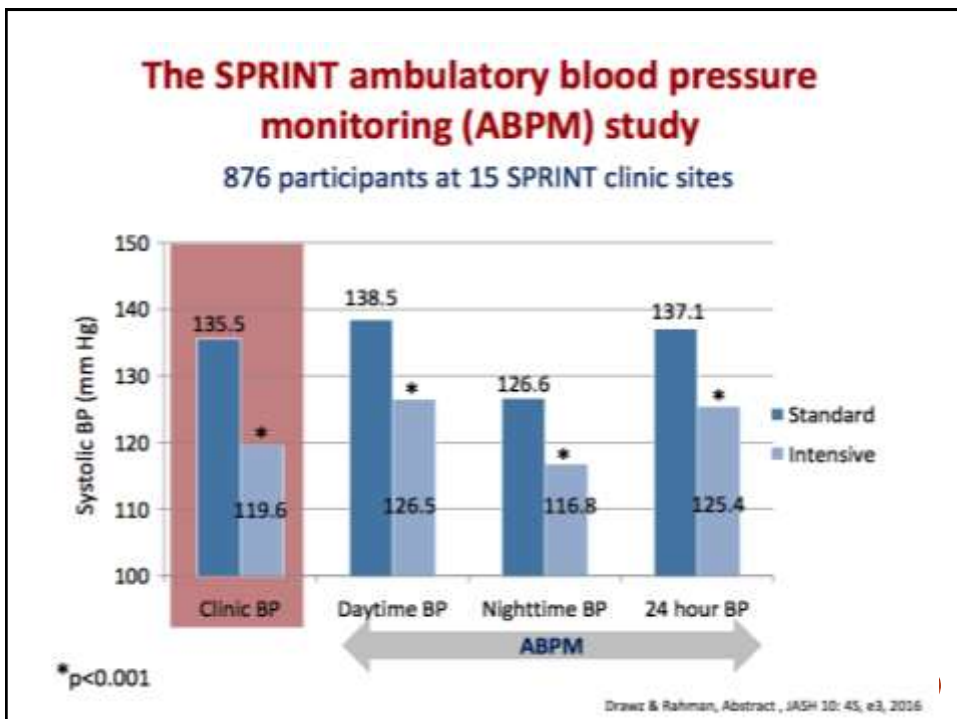
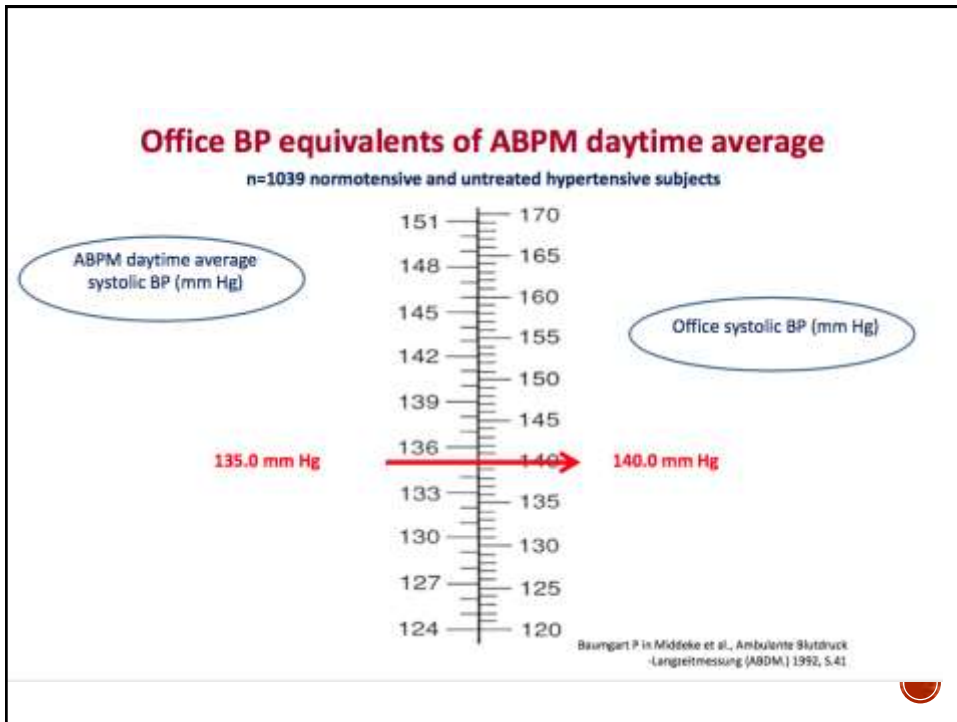
### Automated (unattended) compared to manual office blood pressure in hypertensive patients

**A** Automatic measurement using the BpTRU device with patient seated alone in a quiet room, six times (at 1 min intervals) after a 5 min rest (n=353). The first measurement is discarded and the mean of measurements 2-6 is taken as the BP value.

**B** Measurement immediately after automatic procedure using the auscultatory method (n=353)

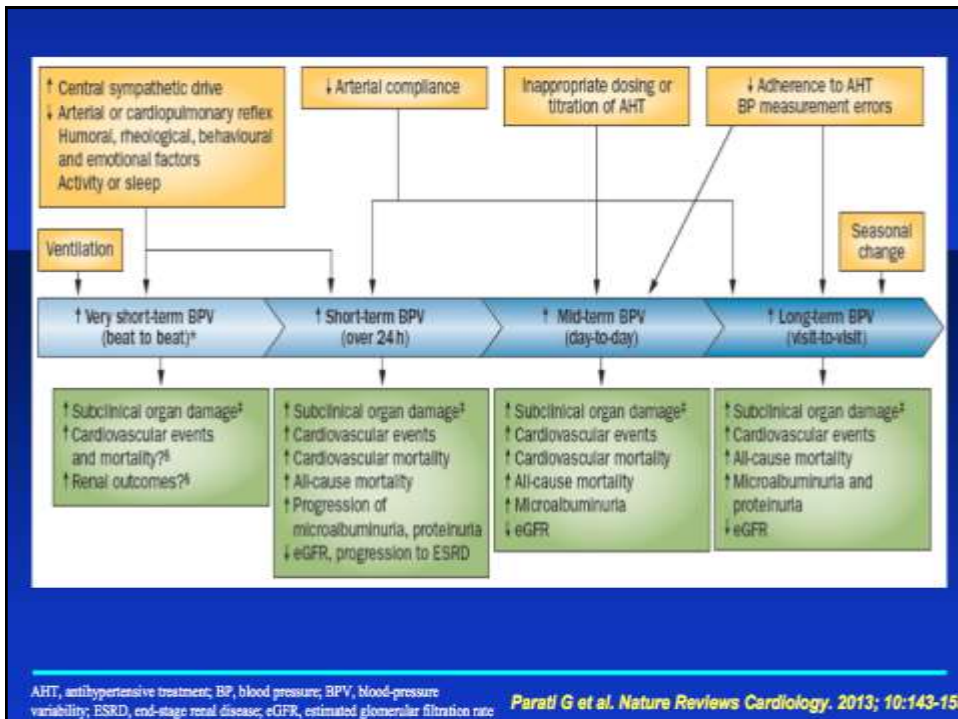


Filipovsky et al, Blood Pressure 25, 228-234, 2016





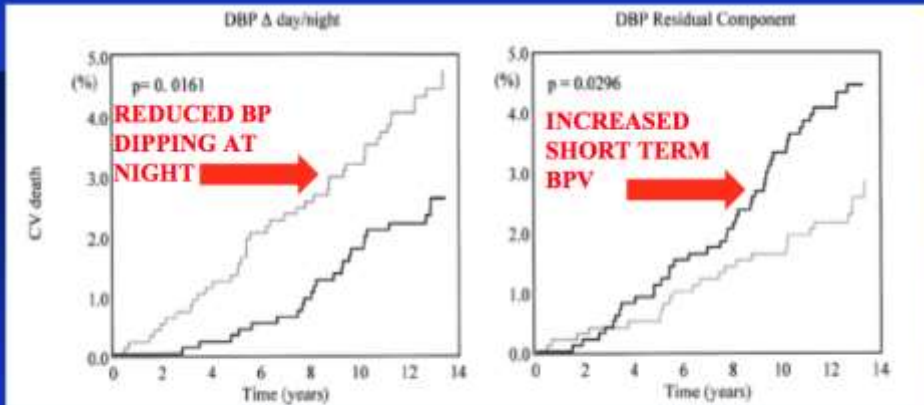
# BP VARIABILITY !! DOES IT MATTER ?





## Cardiovascular Mortality in Patients With DBP Day/Night Ratio And Residual Variability

Kaplan-Meier curves for cardiovascular mortality in patients with DBP day/night ratio and residual variability above (black line) and below (light grey line) median value



BPV, blood pressure variability; DBP, diastolic blood pressure; CV, cardiovascular

PAMELA study; Mancia et al, Hypertension. 2007; 49.6: 1265-1270.

**CENTRAL AORTIC PRESSURE !  
A HIDDEN PLAYER**



## The EXPLOR Study

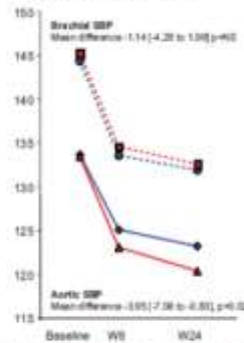
### Clinical Trials

#### Amlodipine-Valsartan Combination Decreases Central Systolic Blood Pressure More Effectively Than the Amlodipine-Atenolol Combination The EXPLOR Study

Pierre Boutouyrie, Araya Achobiti, Patrick Tross

**Abstract**—The  $\beta$ -blocker atenolol is less effective than reducing central blood pressure (CBP). The oral vasodilator amlodipine over atenolol retained significant antihypertensive. A progressive, randomized, double-blind study 500 patients with essential hypertension treated to a target systolic blood pressure (SBP) either through or adjusted or increased with application treatment (Amlodipine) or amlodipine-valsartan combination (10/50 mg and then 5/100 mg/50/50 mg). From baseline to week 24, central systolic blood pressure (CSBP) decreased by  $-13.5 \pm 1.15$  mmHg ( $P=0.0002$ ) that in the difference  $-11.0 \pm 0.8$  mmHg (95% CI:  $-11.19$  to  $-10.81$ ) difference through AAs reduction was  $-6.3\%$  (95% CI, adjusted on heart rate was significantly reduced in the  $P=0.01$ ). Heart rate decreased significantly more with AAs ( $P=0.001$ ). Pulse waves velocity (PWV) decreased by 14% in central systolic BP and through AAs treatment of amlodipine-valsartan combination decreased central to aortic combination. (Hypertension 2010;55:1314-1322)

#### Systolic pressure (mmHg)



#### Pulse pressure (mmHg)

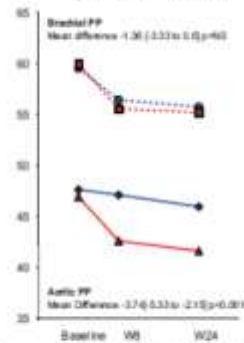


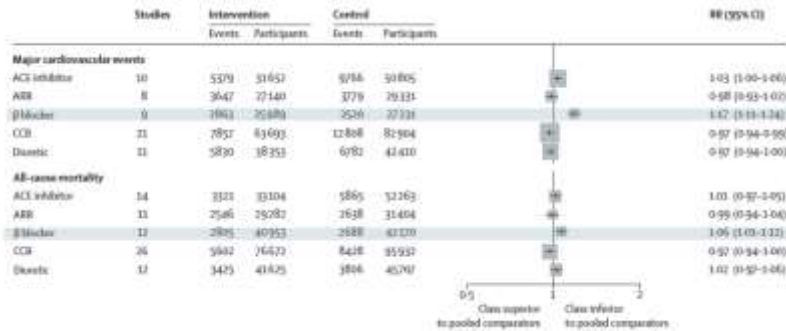
Figure 3. Brachial (dotted lines) and aortic (PPs) (continuous lines) in response to amlodipine-valsartan (red) and amlodipine-atenolol (blue). Values were obtained at a tonometry center using an Omron 705C device.

Boutouyrie, Pierre, et al. *Hypertension*. 2010; 55.6: 1314-1322.

## HOW TO TREAT?



## IMPACT OF SPECIFIC BP-LOWERING TREATMENTS VERSUS ALTERNATIVE CLASS ON MACE



Justifies the focus of treatment on ACE-I or ARB, CCB or Diuretic

Ettehad D, et al. Lancet 2016; 387: 957-967

## Consensus on drug treatment of hypertension

BHS 2006/2011, ASH/ISH 2013, ESH/ESC 2013,  
JNC 8 2013, JSH 2014

1. step

Diuretic

RAS blocker

CCB

2. step

RAS blocker  
+ diuretic

RAS blocker  
+ CCB

Diuretic  
+ CCB

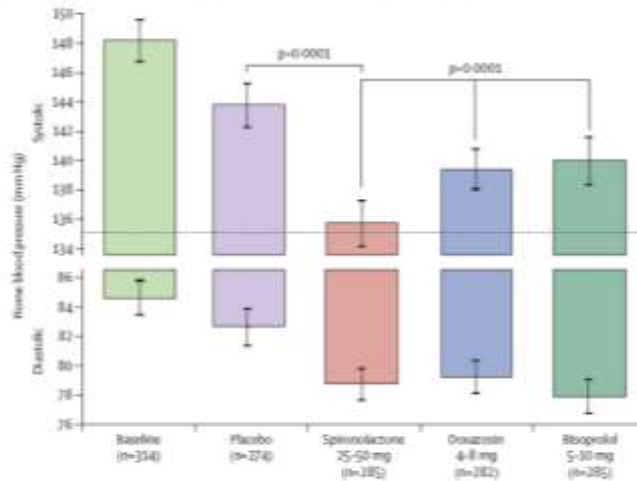
3. Step

RAS blocker  
+ CCB  
+ Diuretic

ASH, American Society of Hypertension  
BHS, British Hypertension Society  
ESC, European Society of Cardiology  
ESH, European Society of Hypertension  
ISH, International Society of Hypertension  
JNC, Joint National Committee  
JSH, Japanese Society of Hypertension

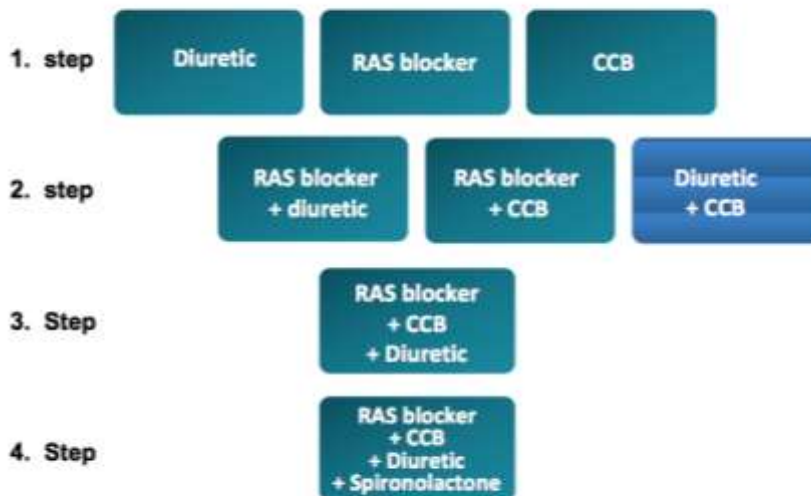
Düsing, 2016

## PATHWAY-2 study: spironolactone most effective add-on drug in resistant hypertension



Williams et al., Lancet, 2015, 386:2059-68

## Consensus on step 4 treatment?



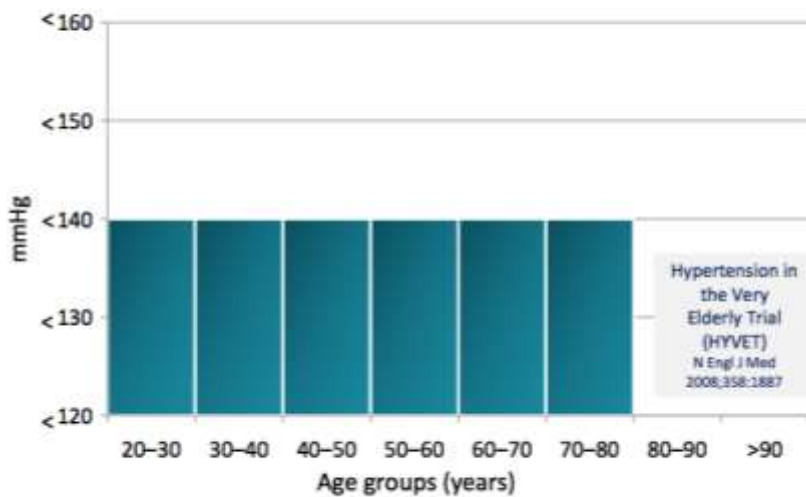
Döring, 2016



## WHAT IS THE TARGET?



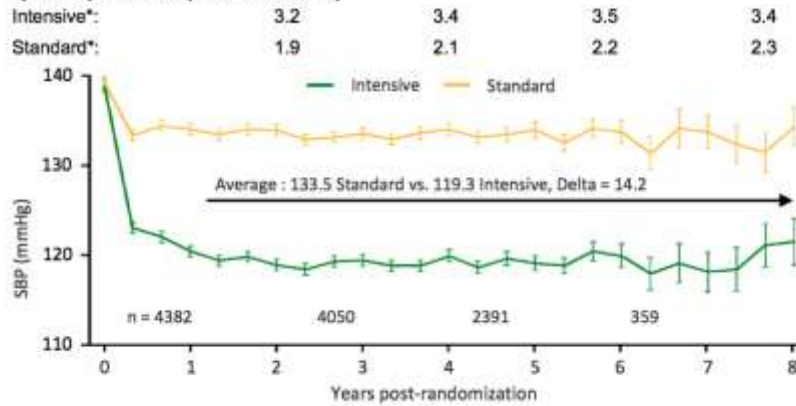
### Guidelines: target blood pressure (-2008)



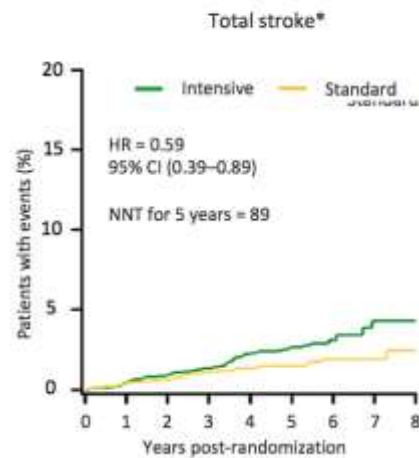
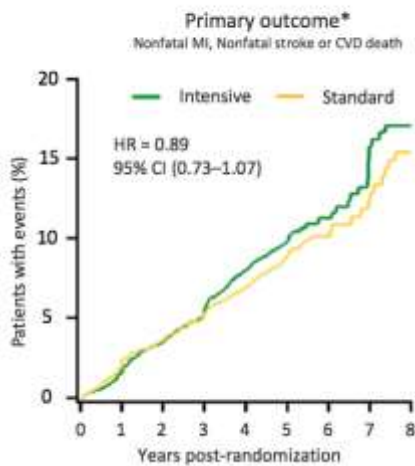
Düsing 2016  
ESH/ESC, J Hypertens 2003;21:1011-53; Mancia et al., (ESH/ESC), J Hypertens 2007;25:1751-62; Chobanian et al., (JNC 7), JAMA 2003;289:2560-72; NICE guidelines (CG127) 2011 ([www.nice.org.uk](http://www.nice.org.uk))

## ACCORD: the adequate blood pressure goal in diabetes

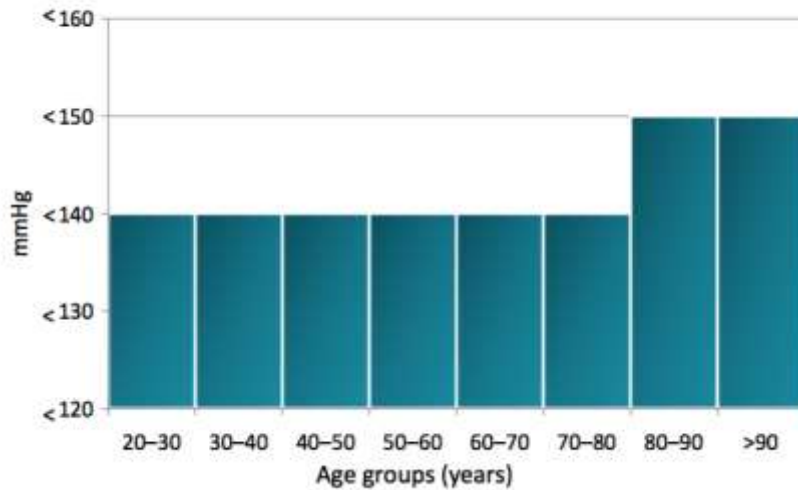
### Systolic pressures (mean $\pm$ 95% CI)



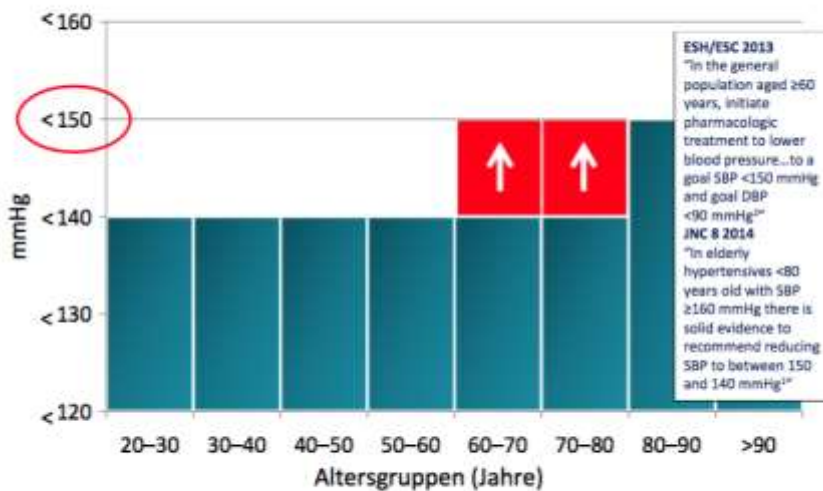
## ACCORD: primary and secondary outcomes



## Guidelines: target blood pressure (2008-2013)



## Guidelines: target blood pressure (since 2013)



<sup>1</sup>ESH-ESC, J Hypertens 2013; 31:1281-1357  
<sup>2</sup>JNC 8, JAMA 2014;311:507-20





## SPRINT Research Question

Examine the effect of more intensive high blood pressure treatment than is currently recommended

Randomized Controlled Trial  
Target Systolic BP

**Intensive Treatment**  
Goal SBP < 120 mm Hg

**Standard Treatment**  
Goal SBP < 140 mm Hg



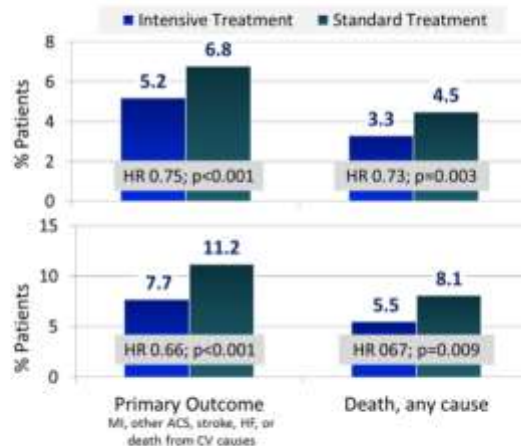
SPRINT design details available at:

- [ClinicalTrials.gov \(NCT01206062\)](https://clinicaltrials.gov/ct2/show/study/NCT01206062)
- Ambrosius WT et al. Clin Trials. 2014;11:532-546

## SPRINT results: all patients (A) and patients aged $\geq 75$ years (B)

**A**  
9361 patients  
average age:  
68 years  
follow up:  
3.26 years

**B**  
2636 patients  
average age  
80 years  
follow up  
3.14 years



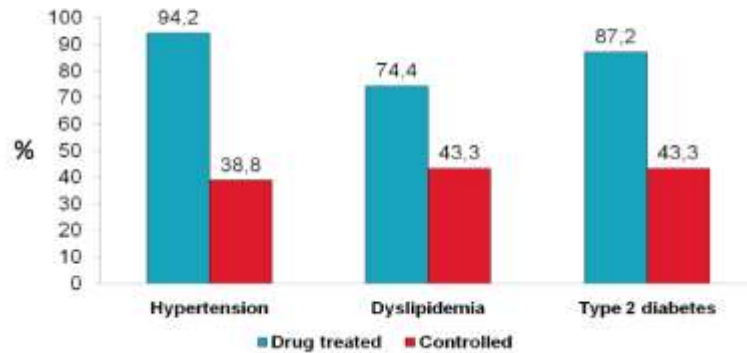
ACS, acute coronary syndrome  
CV, cardiovascular  
HF, heart failure  
MI, myocardial infarction

SPRINT Research Group, N Engl J Med 2015; 373:2103-16  
Williamson et al., JAMA 2016; 315:2673-82



## The control of BP in the real world setting

Control of main CVD risk factors among patients in the EURIKA Study –primary prev in >50 y, with >1 major CVRF

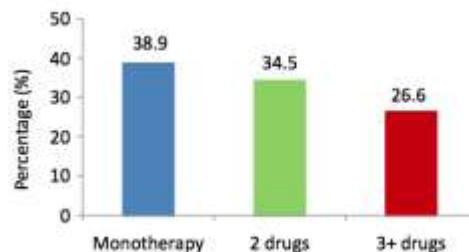


Banegas et al., EHJ, 2011

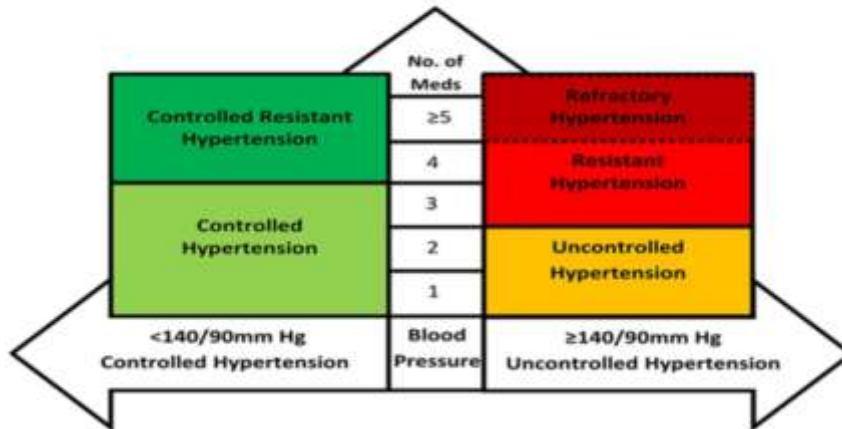
## Combinations, are they being used correctly?

Spanish ABPM Registry Data

- Among treated hypertensive patients, 48.4% had uncontrolled daytime ambulatory BP
- The percentage of uncontrolled\* patients taking 1, 2, or 3+ hypertensives:



## Hypertension classification based on blood pressure control and number of antihypertensive medications



## TAKE HOME

- MORE QUESTIONS THAN ANSWERS
- We still have a poor control rate of BP
- You need a combination to treat BP to target
- Spironolactone should be the 4<sup>th</sup> line of ttt
- Targets should be redefined
- A new consensus is needed for Methods of measuring BP
- BPV and CABP need to be taken in account
- BPV and CABP need to be studied in large prospective trials

***THANK YOU***

