



# **Simplified Hypertension Management**

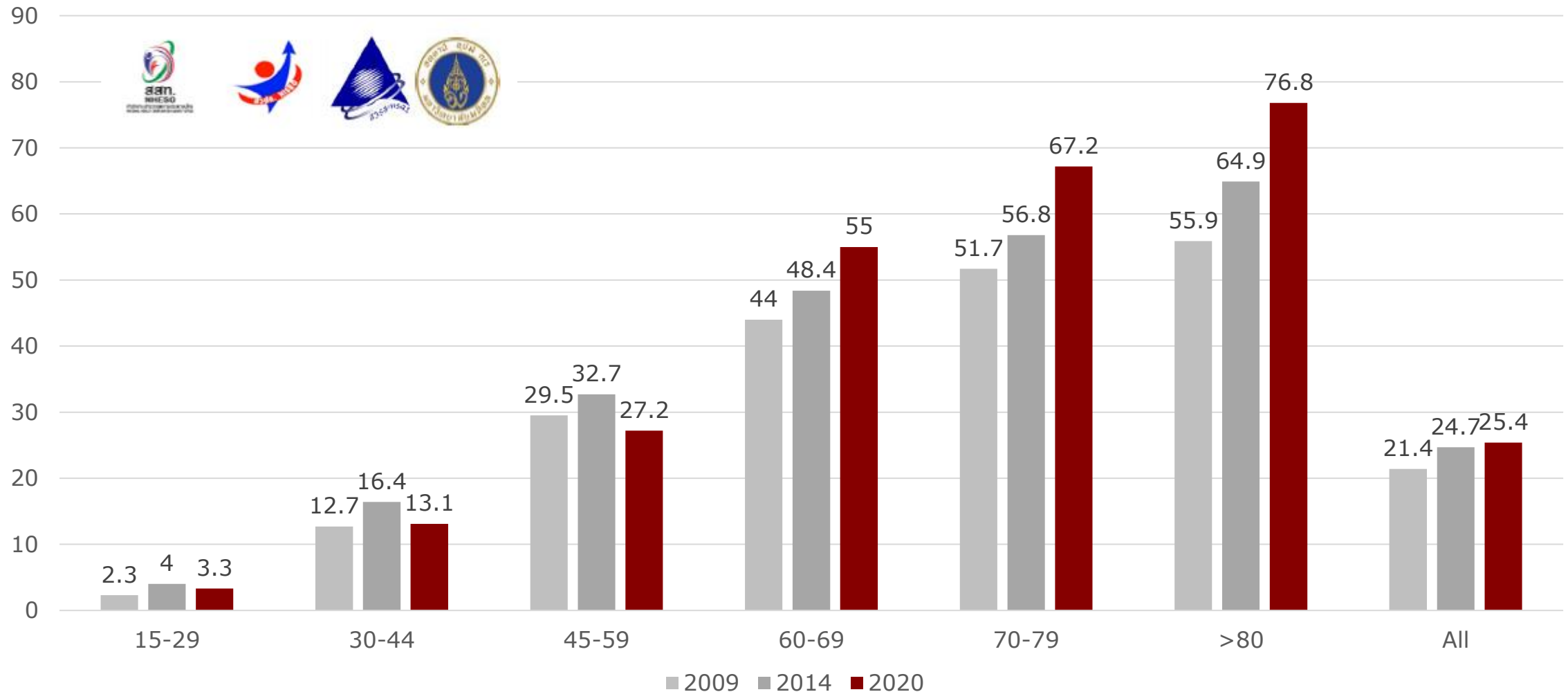
AM. Anutra Chittinandana, MD.  
Bhumibol Adulyadej Hospital

# Disclosure

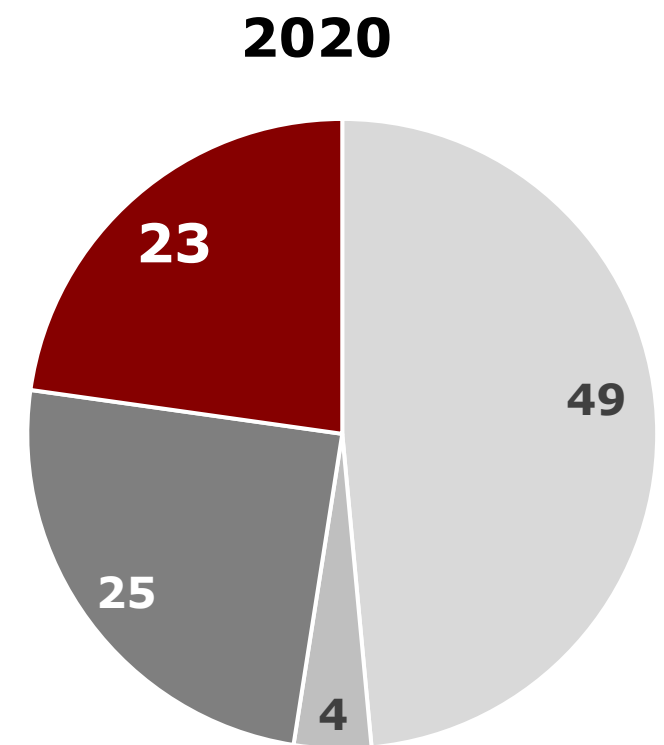
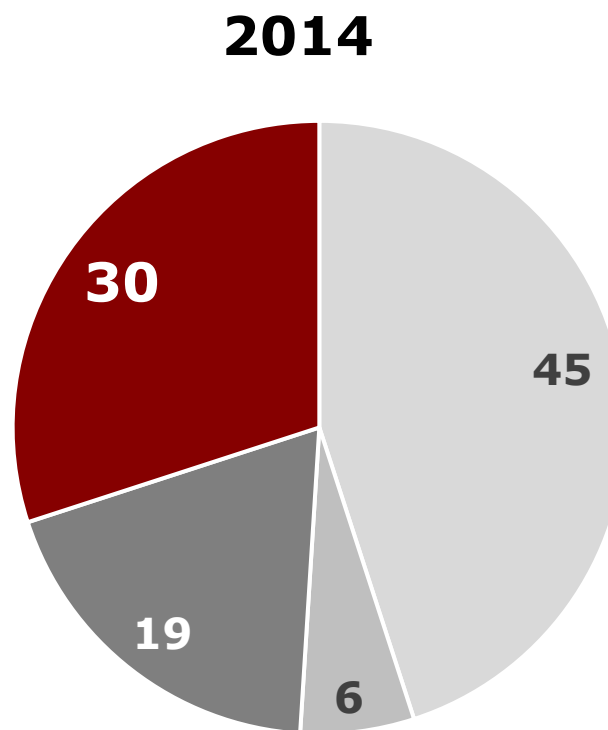
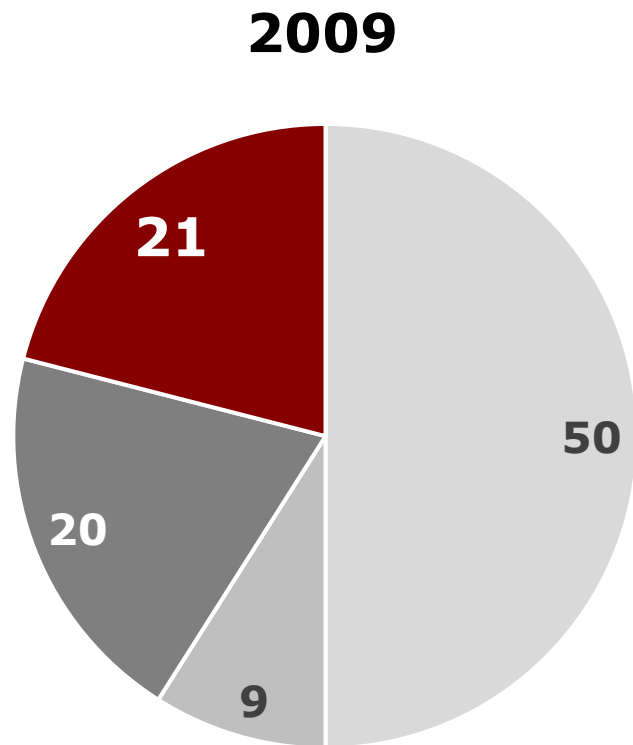
I have received honoraria and/or lecture fees from many pharmaceutical companies including Astellas, Astra Zenica, Abbott, ATB, Baxter, Berlinger Ingelheim, Biopharm, DKSH, Janssen Cilag, Masu, MSD, Novartis, Pfizer, Roche, Takeda and Sanofi but am not an employee, consultant nor stockholder for any of them.

I have **no conflicts of interest** relative to this presentation.

# Prevalence of hypertension in Thai population > 15 years old



# Trend in diagnosis and treatment of hypertension



■ Undiagnosed   ■ Dx, not treated   ■ Rx, uncontrolled   ■ Rx, controlled

# Simplified Hypertension Management



How low should we go?



What drugs should we use?



How to get there?

# Simplified Hypertension Management



**How low should we go?**



What drugs should we use?



How to get there?

## ORIGINAL ARTICLE

# ACCORD

Effects of Intensive Blood-Pressure Control  
in Type 2 Diabetes Mellitus  
2010  
The ACCORD Study Group\*

The ACCORD Study Group. *N Engl J Med* 2010;362:1575-85.

The SPRINT Research Group. *N Engl J Med* 2015;373:2103-16

the STEP Study Group. *N Engl J Med* 2021.DOI: 10.1056/NEJMoA2111437

# The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1811 NOVEMBER 26, 2015 VOL. 373 NO. 22

# SPRINT

A Randomized Trial of Intensive versus  
Standard Blood-Pressure Control

The SPRINT Research Group\*

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# STEP

Trial of Intensive Blood-Pressure Control  
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	ACCORD	SPRINT	STEP
Major inclusion	DM, BP 130-180 mmHg >40 YO with CVD or >55 YO with 2 RF	BP 130-180 mmHg >50 YO with additional RF or >75 YO	BP 140-190 mmHg 60-80 YO
Major exclusion	BMI>45, Cr >1.5	DM, Stroke, ADPKD, HF, proteinuria >1 g/d, eGFR<20	Stoke
Target SBP: standard	140 mmHg	140 mmHg	130-<150 mmHg
Target SBP: intensive	120 mmHg	120 mmHg	110-<130 mmHg
Number	4,733	9,361	8,511
Median follow up	4.7 years	3.26 years	3.34 years

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Xiaoping Chen, M.D., Yingqing Feng, M.D., Gang Tian, M.D., Xiuyin Gao, B.Sc.,

	ACCORD	SPRINT	STEP
Race or ethnic group	White : Black : Hispanic 61 : 24 : 7	White : Black : Hispanic 58 : 30 : 10	Chinese
Mean age	62.2 years	67.9 years	66.2 years
Previous CV event	33.7%	22%	6.4%
Primary Composite outcome	MI, stroke, or CV death	MI, other ACS, stroke, HF, or CV death	stroke, ACS (MI, hospital for unstable angina), acute decompensated HF, coronary revascularization , AF or CV death
Baseline SBP	139.2 ± 15.8 mmHg	139.7 ± 15.8 mmHg	146.1 ± 16.8 mmHg
Baseline DBP	76.0 ± 10.4 mmHg	78.2 ± 11.9 mmHg	82.7 ± 10.6 mmHg

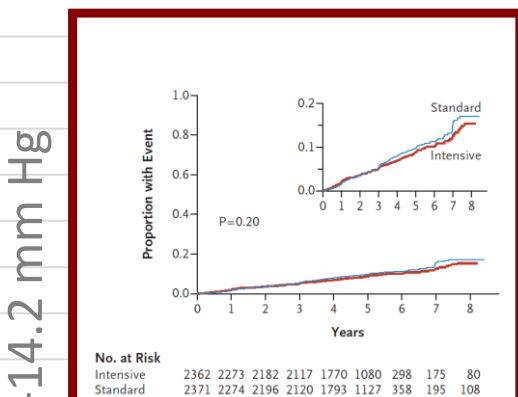


# ACCORD 2010

# SPRINT 2015

# STEP 2021

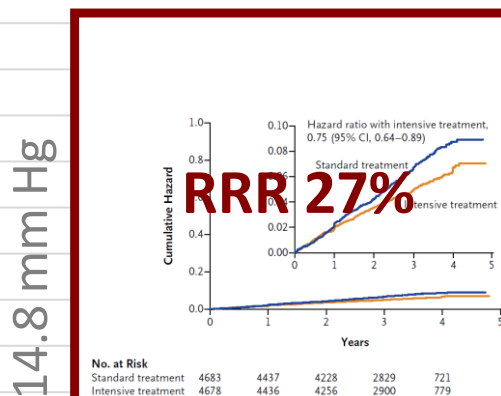
Standard **133.5** mmHg



**No Benefit**

Intensive **119.3** mmHg

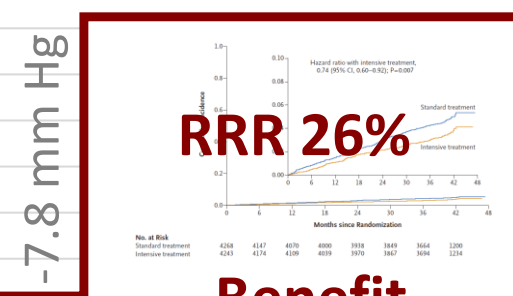
Standard **136.2** mmHg



**Benefit**

Intensive **121.4** mm Hg

Standard **135.3** mmHg



**Benefit**

Intensive **127.5** mm Hg

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	ACCORD	SPRINT	STEP
Hypotension	↑	↑	↑
Syncope	↔	↑	↔
Injurious fall	NA	↔	↔
Bradycardia	↑	↔	NA
Electrolyte abnormality	↑	↑	NA
Acute kidney injury	↔	↑	↔

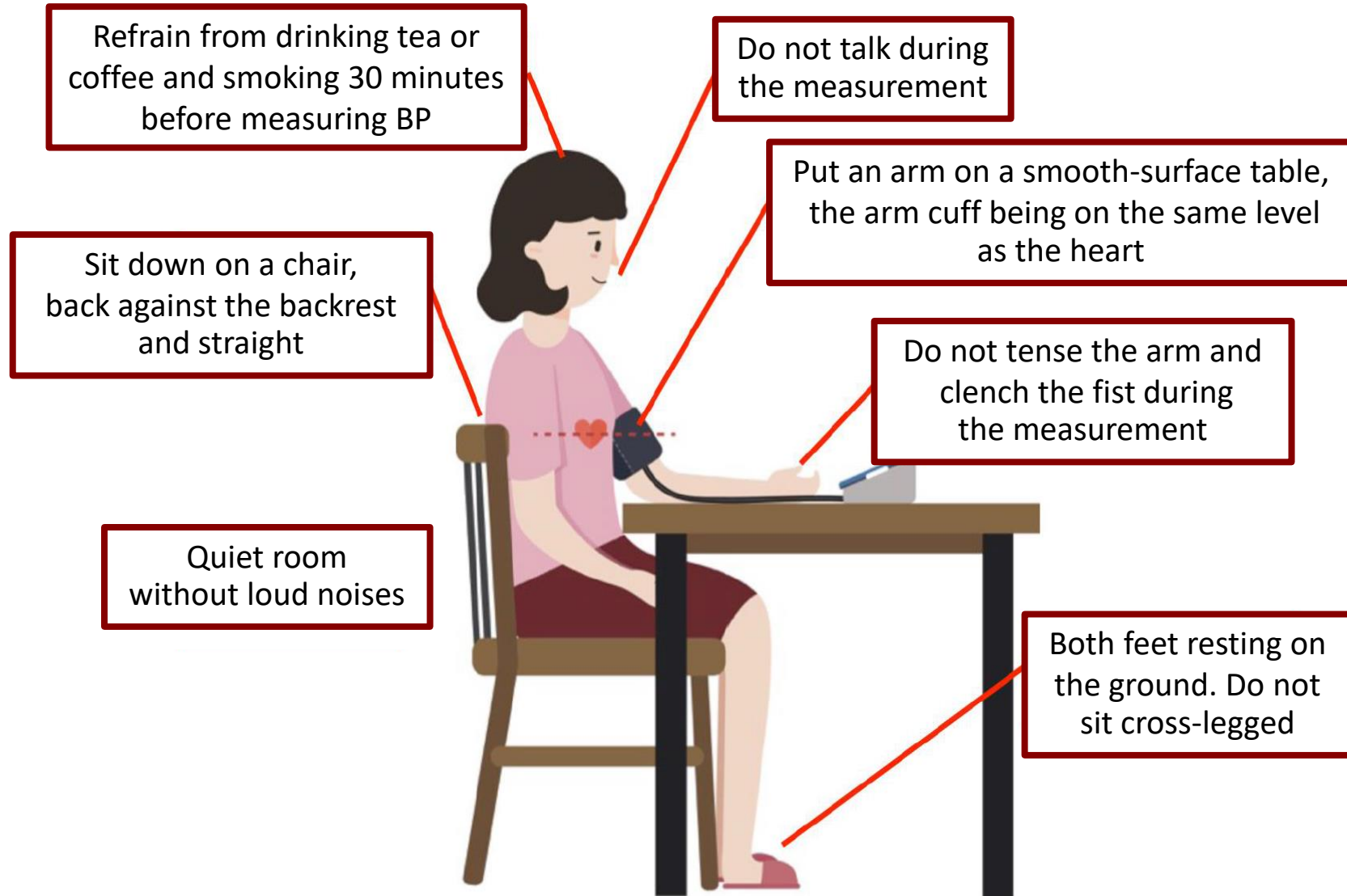
# 2017 ACC/AHA vs 2018 ESC/ESH vs 2019 Thai vs 2020ISH

## Classification of Blood pressure

Thailand  
2019

SBP (mmHg)		DBP (mmHg)	AHA/ACC 2017	ESH/ESC 2018	ISH 2020
<120	and	<80	Normal	Optimal	Normal
120-129	and/or	80-84	Elevated	Normal	
130-139	and/or	85-89	Stage 1 HT	Upper normal	High normal
140-159	and/or	90-99	Stage 2 HT	Grade 1 HT	Grade 1 HT
160-179	and/or	100-109		Grade 2 HT	Grade 2 HT
≥180	and/or	≥110		Grade 3 HT	

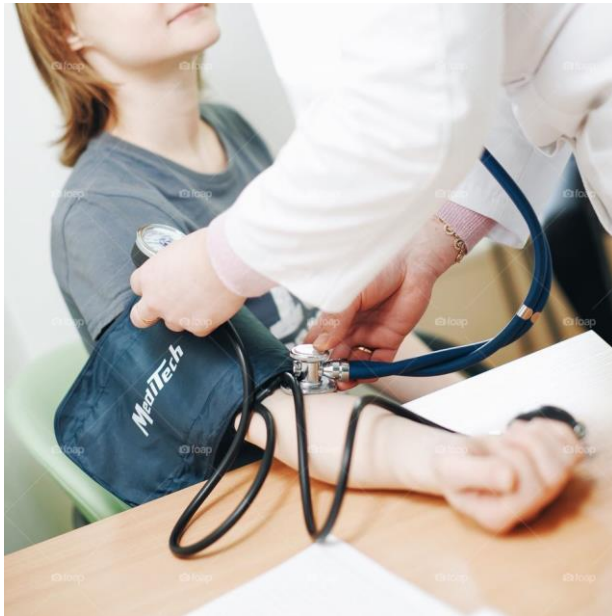
# How to prepare a patient before and during BP measurement



# Blood Pressure **Measurement**

## **Office**

### BP Measurement



#### **@ Office, clinic**

- + Convenience during visit
- + For BP classification
- + No additional cost
- White-coat effect

## **Home**

### BP Measurement



#### **@ Home**

- + Convenience
- + No white-coat effect
- + increase drug compliance
- + Good correlation with TOD
- Additional cost

## **Ambulatory**

### BP Measurement



#### **@ Home and work**

- + No white-coat effect
- + Best correlation with TOD
- Expensive
- Inconvenience

# Home BP Monitoring



1 hour after waking up & urinated

before bedtime

before breakfast & taking  
antihypertensives

BP **twice in each episode**, 1 minute apart.  
7 consecutive days or at least 3 days/wk

# Criteria of hypertension diagnosis

## in different measurement methods

Measurement method	SBP (mmHg)		DBP (mmHg)
<b>Office</b> BP measurement	<b><math>\geq 140</math></b>	and/or	<b><math>\geq 90</math></b>
<b>Home</b> BP measurement	<b><math>\geq 135</math></b>	and/or	<b><math>\geq 85</math></b>
<b>Ambulatory</b> BP measurement			
Average of daytime BP	<b><math>\geq 135</math></b>	and/or	<b><math>\geq 85</math></b>
Average of nighttime BP	<b><math>\geq 120</math></b>	and/or	<b><math>\geq 70</math></b>
Average of BP in a day	<b><math>\geq 130</math></b>	and/or	<b><math>\geq 80</math></b>



# BP patterns

informed by  
out-of-office BP  
measurements  
in addition to  
standardized  
office BP  
measurement.

Not taking antihypertensive medication	
Hypertension based on standardized office BP	Yes
	White-coat hypertension
	No
	Normotension
Hypertension based on Out-of-office BP	
Yes	
Masked hypertension	

Taking antihypertensive medication	
Hypertension based on standardized office BP	Yes
	White-coat effect
	No
	Sustained controlled hypertension
Hypertension based on Out-of-office BP	
Yes	
Masked uncontrolled hypertension	

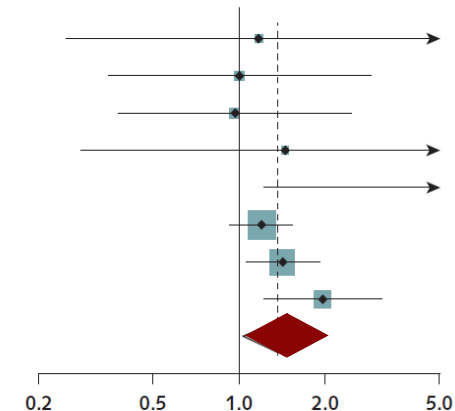


# CV event risk in White-coat hypertension and White-coat effect

27 studies 25,786 with untreated WCH or treated WCE  
38,487 with normal BP followed for a mean of 3-19 years.

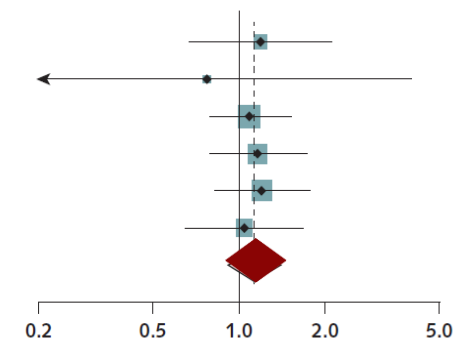
## White-coat hypertension

Study, Year (Reference)	Total Participants, <i>n</i>	HR (95% CI)
Verdecchia et al, 1994 (23)	1392	1.17 (0.25–5.33)
Fagard et al, 2005 (24)	359	1.00 (0.35–2.90)
Pierdomenico et al, 2008 (25)	2037	0.97 (0.38–2.46)
Mancia et al, 2013 (26)	1589	1.45 (0.28–7.51)
Sung et al, 2013 (27)	1257	5.59 (1.22–25.55)
Asayama et al, 2014 (28)	8237	1.20 (0.93–1.54)
Stergiou et al, 2014 (29)	6458	1.42 (1.06–1.91)
Banegas et al, 2018 (30)	63 910	1.96 (1.22–3.15)
Overall ( $I^2 = 0.0\%$ ; $P = 0.379$ )		<b>1.36 (1.03-2.00)</b>



## White-coat effect

Study, Year (Reference)	Total Participants, <i>n</i>	HR (95% CI)
Bobrie et al, 2004 (31)	4939	1.18 (0.67–2.10)
Shimada et al, 2008 (32)	2896	0.77 (0.15–3.96)
Franklin et al, 2012 (33)	7295	1.09 (0.79–1.52)
Stergiou et al, 2014 (29)	6458	1.16 (0.79–1.72)
Pierdomenico et al, 2017 (34)	1191	1.20 (0.82–1.76)
Banegas et al, 2018 (30)	63 910	1.04 (0.65–1.66)
Overall ( $I^2 = 0.0\%$ ; $P = 0.992$ )		<b>1.12 (0.91-1.39)</b>

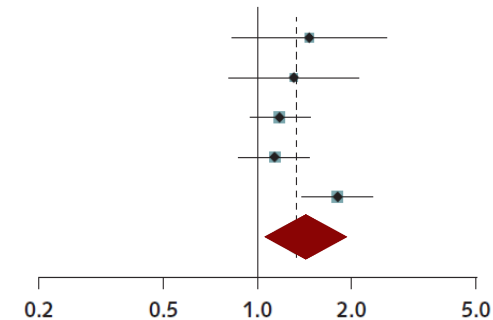


# All cause mortality in White-coat hypertension and White-coat effect

27 studies 25,786 with untreated WCH or treated WCE  
38,487 with normal BP followed for a mean of 3-19 years.

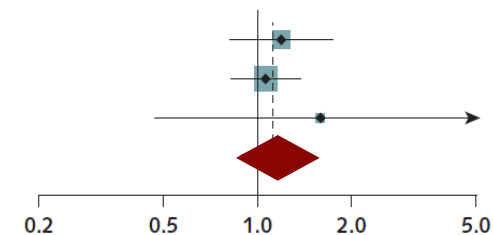
## White-coat hypertension

Study, Year (Reference)	Total Participants, <i>n</i>	HR (95% CI)
Mancia et al, 2013 (26)	1589	1.46 (0.83–2.57)
Sung et al, 2013 (27)	1257	1.30 (0.81–2.09)
Asayama et al, 2014 (28)	8237	1.17 (0.94–1.47)
Stergiou et al, 2014 (29)	6458	1.13 (0.87–1.46)
Banegas et al, 2018 (30)	63 910	1.79 (1.38–2.32)
Overall ( $I^2 = 41.1\%$ ; $P = 0.095$ )		<b>1.33 (1.07-1.67)</b>



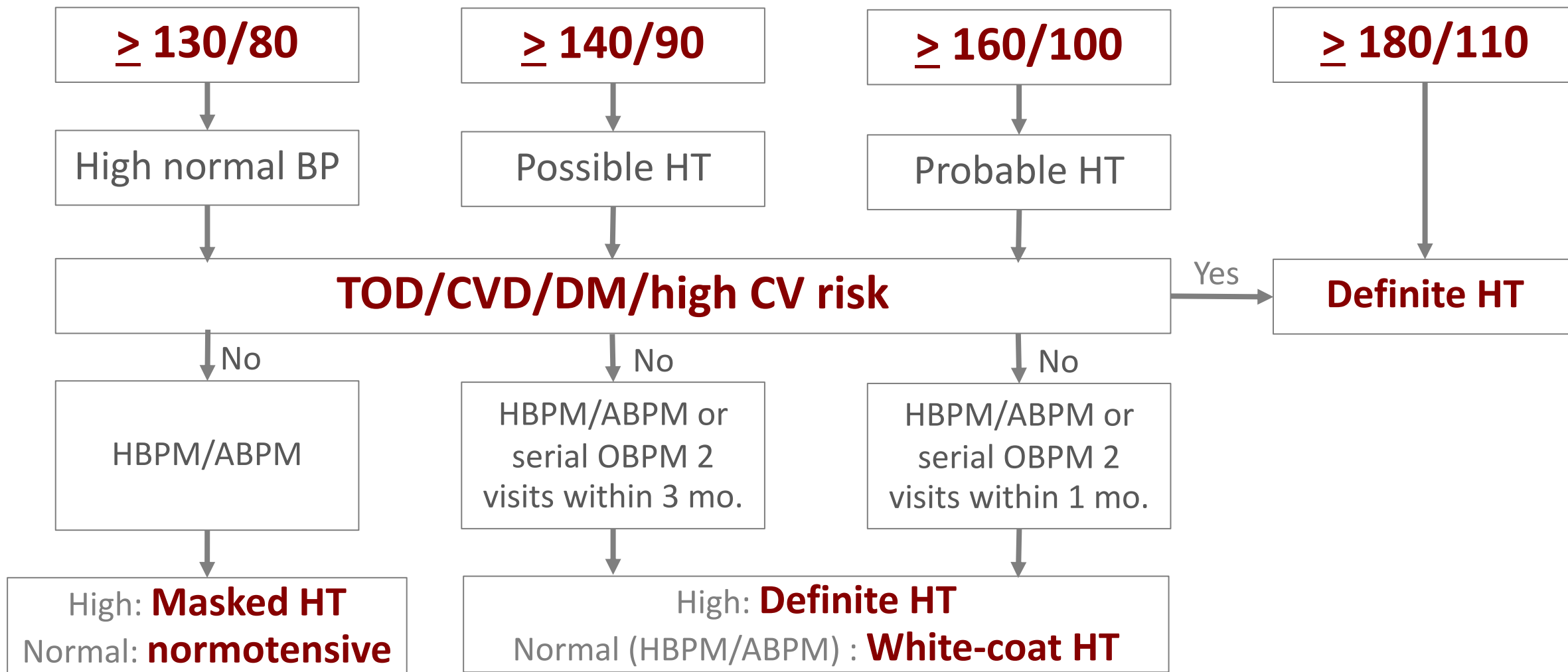
## White-coat effect

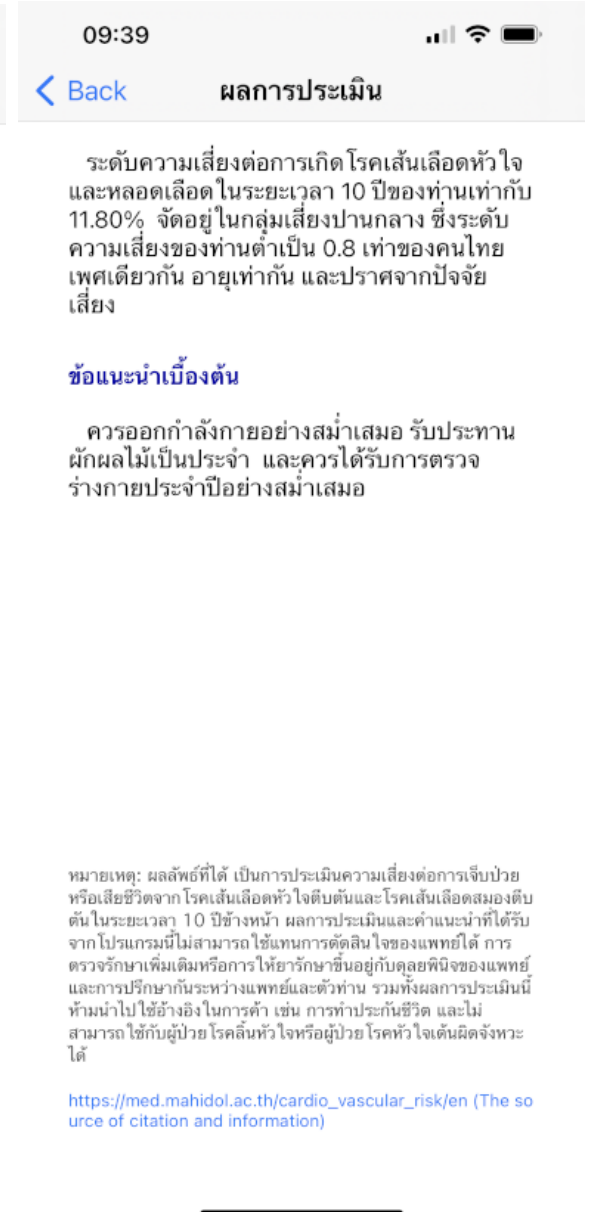
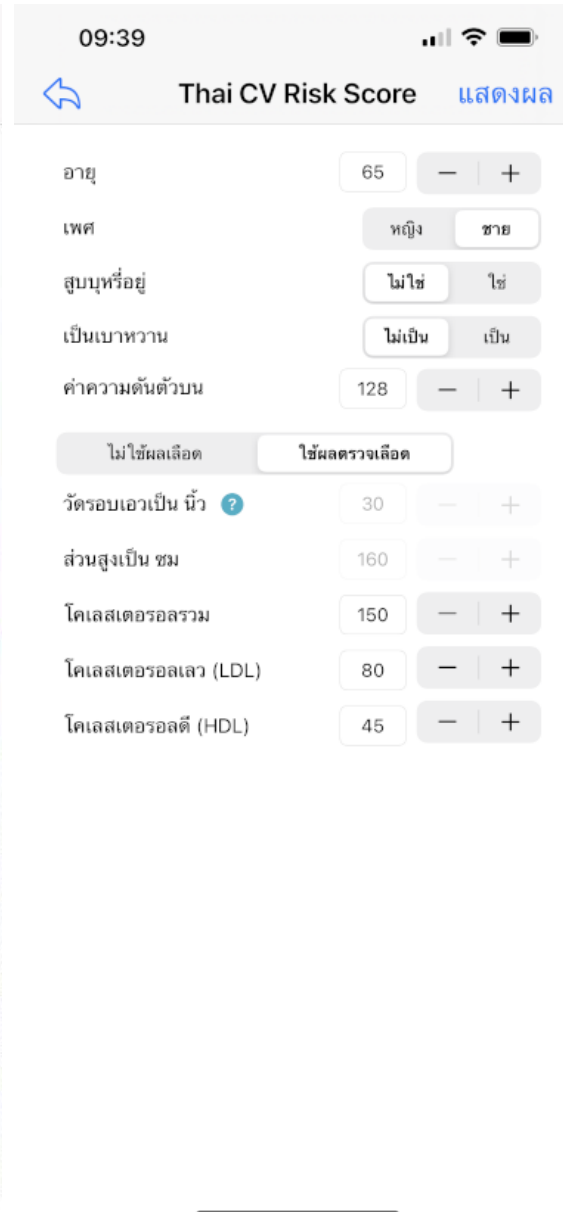
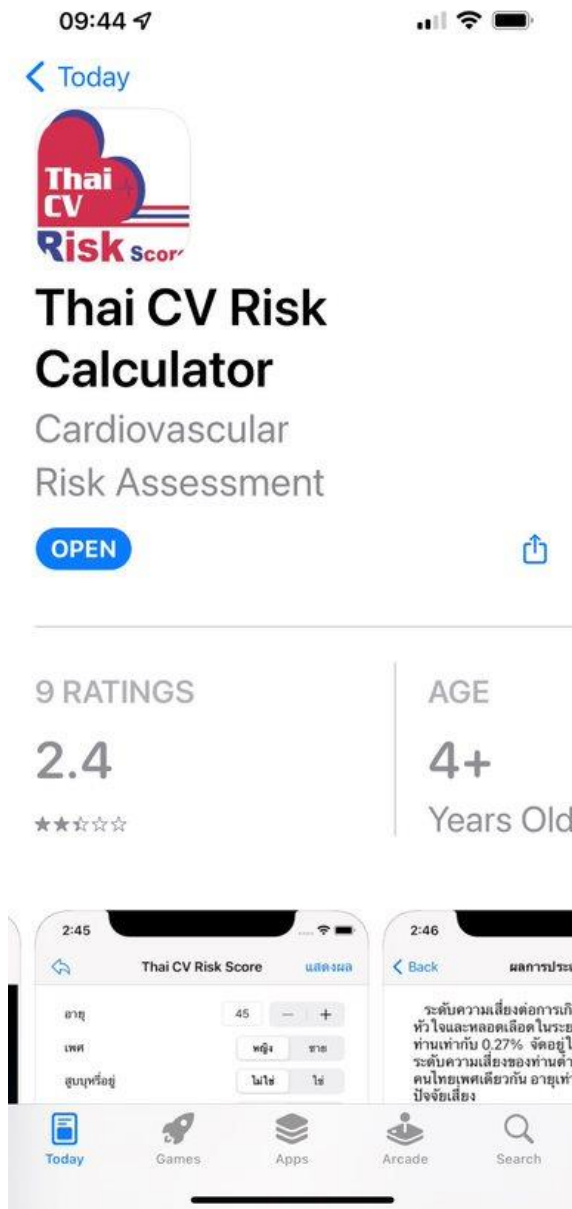
Study, Year (Reference)	Total Participants, <i>n</i>	HR (95% CI)
Stergiou et al, 2014 (29)	6458	1.19 (0.82–1.73)
Banegas et al, 2018 (30)	63 910	1.06 (0.82–1.37)
Spannella et al, 2018 (43)	120	1.58 (0.47–5.30)
Overall ( $I^2 = 0.0\%$ ; $P = 0.747$ )		<b>1.11 (0.89-1.46)</b>



# Hypertension Diagnostic Algorithm

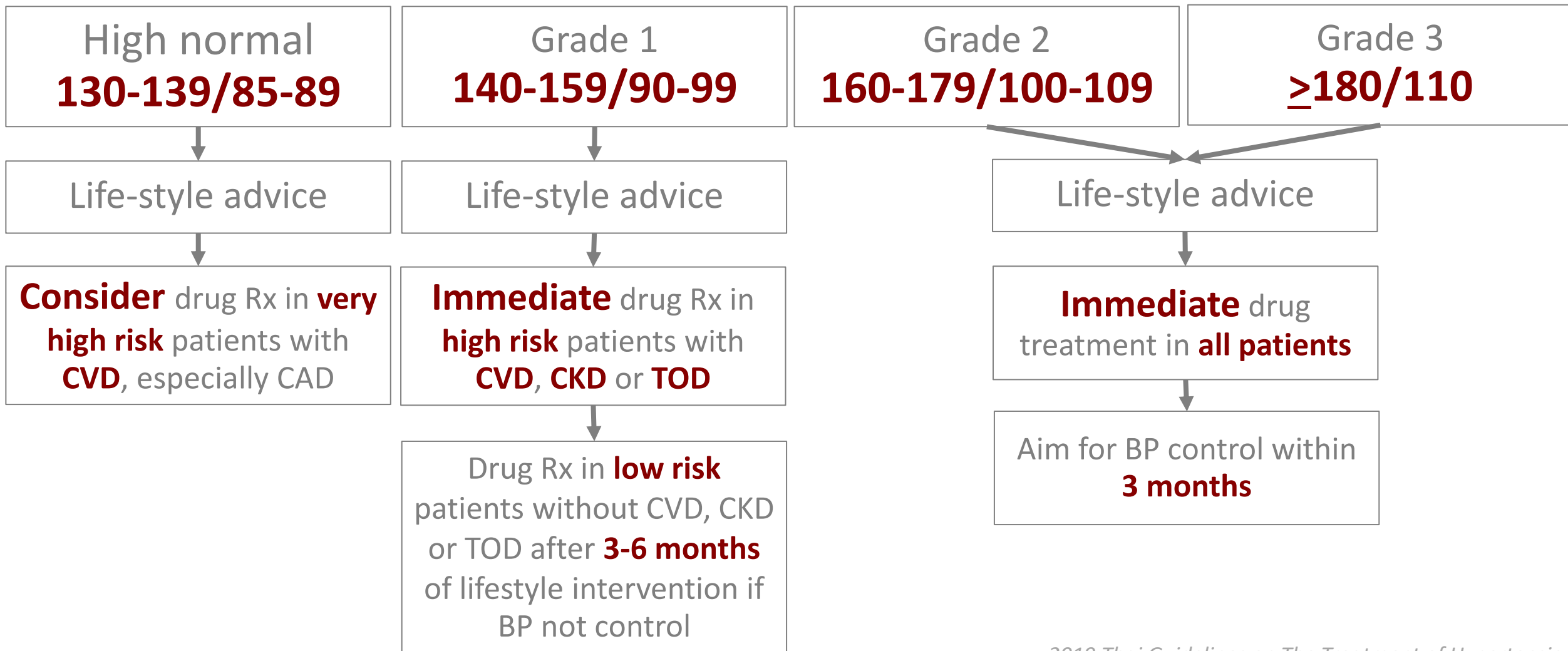
Average office BP (on the same visit)





# Hypertension treatment guideline

when considering average office BP measurement





# **Target** blood pressure levels

Age group	HT Only	with DM	with CKD	with CVD	Previous stroke/TIA
<b>18-65</b> years	<b>120-130/70-79</b>				
<b>65-79</b> years	<b>130-140/70-79</b>				
<b>≥ 80</b> years					

\* Average office BP measurement in mmHg

# Simplified Hypertension Management



How low should we go?



**What drugs should we use?**



How to get there?



# **Lifestyle modification** in controlling and preventing HT



**Exercise**



**DASH diet**



**Low salt**



**Reduce weight**



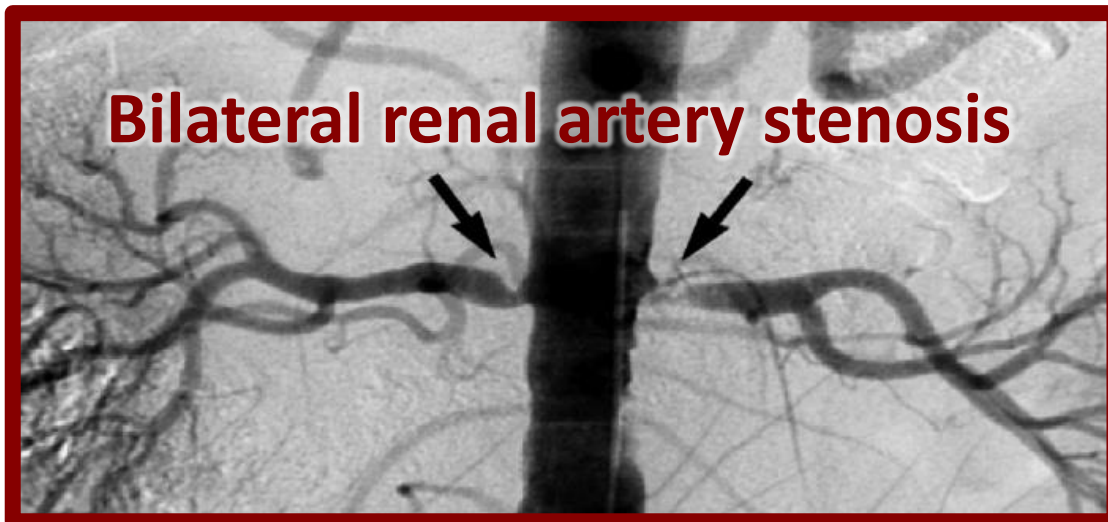
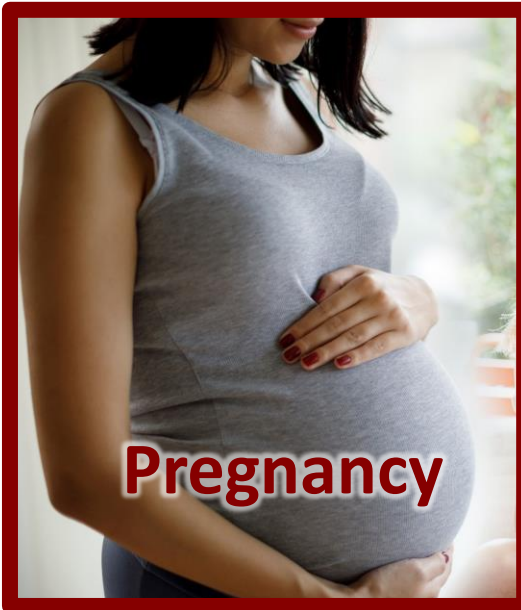
**avoidance of binge drinking**



# The First Line Antihypertensive

Drugs	HT Only	with DM	with CKD	with CVD	Previous stroke /TIA	Elderly
<b>ACEI</b>	✓	✓	✓	✓	✓	
<b>ARB</b>	✓	✓	✓	✓		
<b>CCB</b>	✓	✓				✓
<b>Diuretic</b>	✓				✓	
<b>BB</b>	✓			✓		

# ACEI/ARB Contraindication



**↑ K<sup>+</sup>**  
**>5.5**



# **KDIGO 2021:**

## CPG for the Management of **BP in CKD**



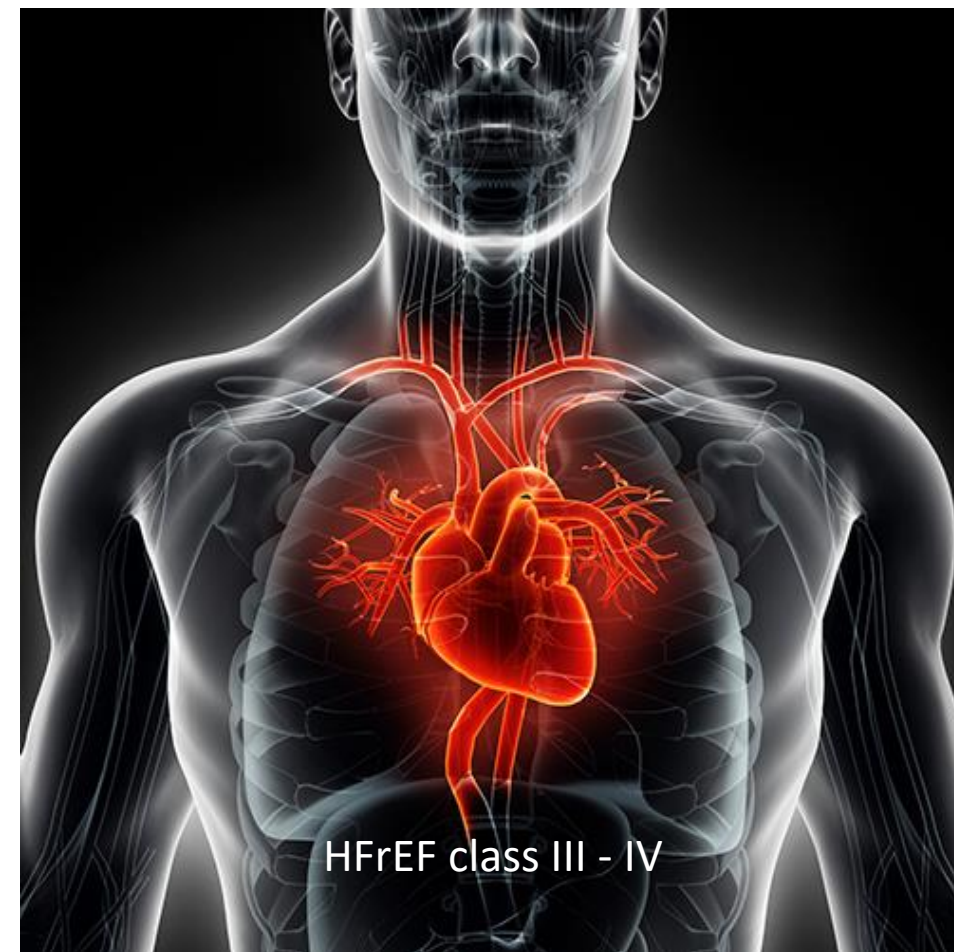
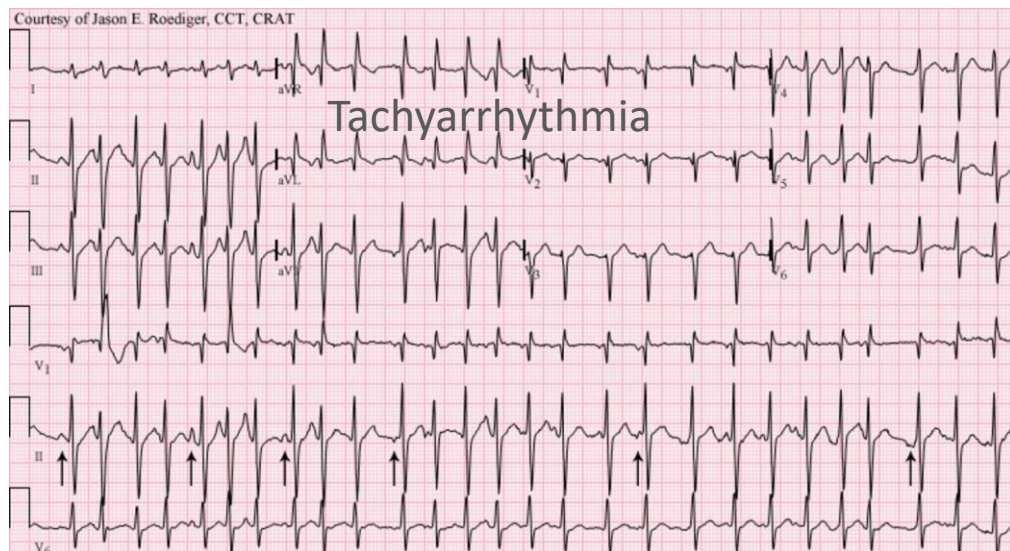
KDIGO 2021 Clinical Practice Guideline for the  
Management of Blood Pressure in Chronic Kidney Disease

Changes in BP, Cr, K<sup>+</sup> **checked 2–4 weeks** of initiation or increase in the dose of a RASi, **depending on the current GFR and K<sup>+</sup>**

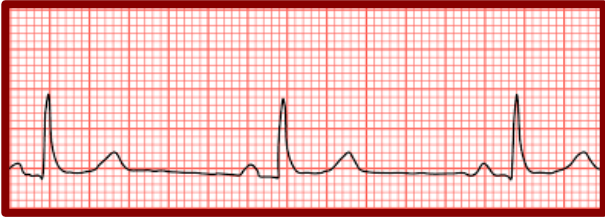
**Continue ACEi or ARB** therapy **unless** **Cr↑ >30% within 4 weeks** following initiation of treatment or an increase in dose.



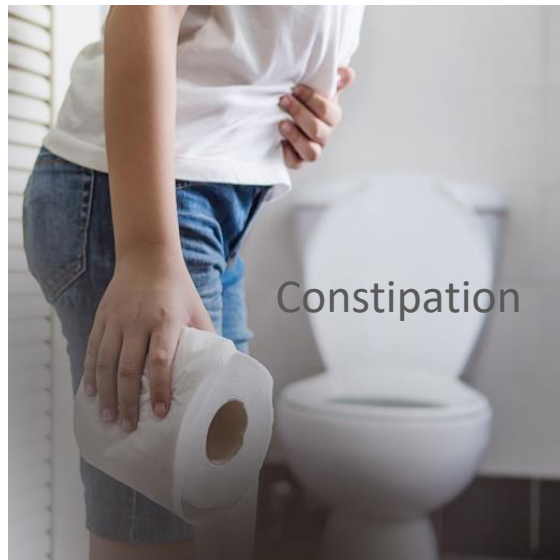
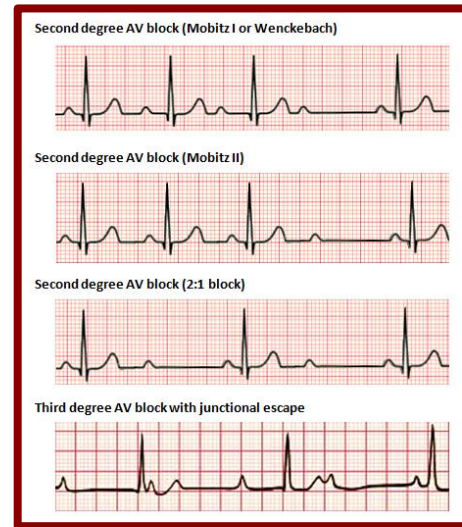
# Dihydropyridine CCB Contraindication



# Non-Dihydropyridine CCB Contraindication



**Bradycardia < 60**  
**High grade SA or**  
**AV block**





# Thiazide diuretic contraindication

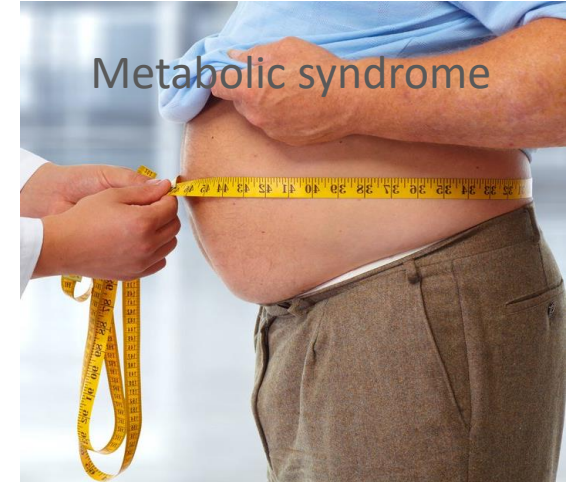
Gout



Glucose intolerance



Metabolic syndrome



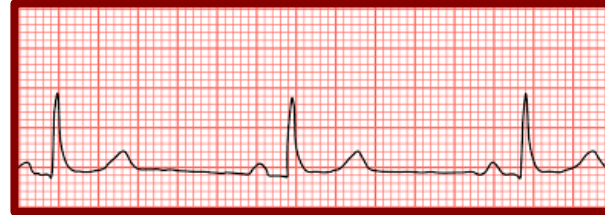
Pregnancy



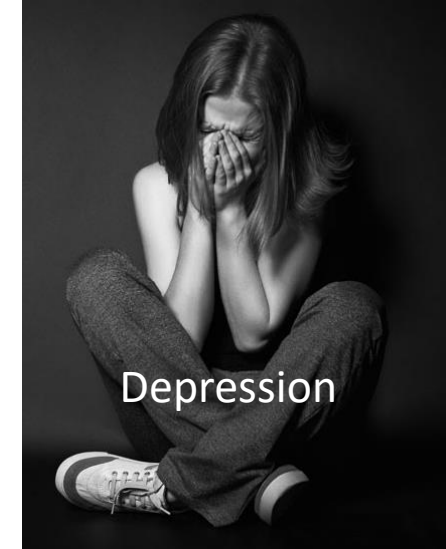
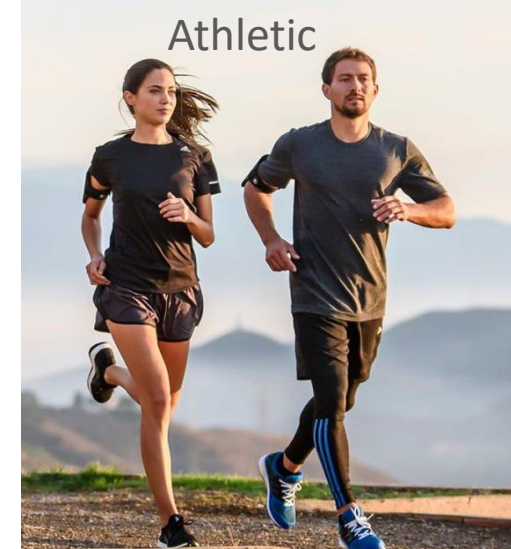
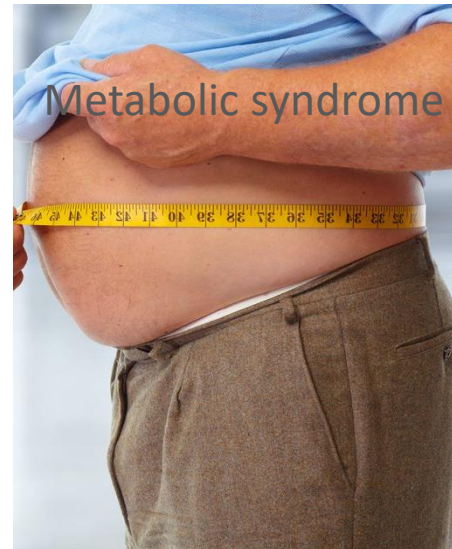
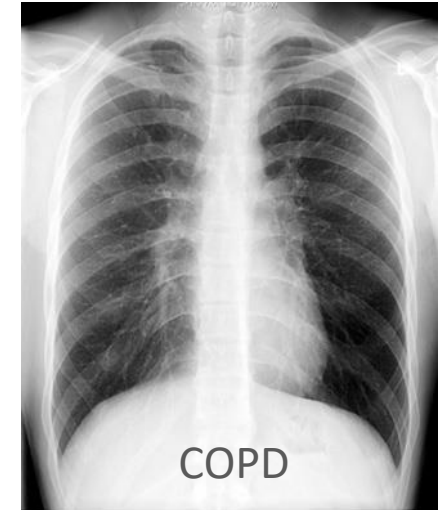
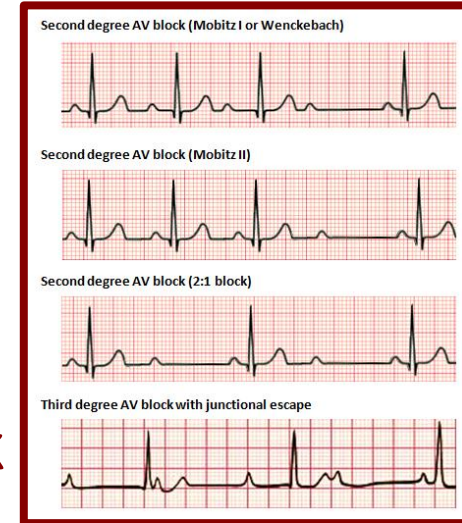
↑  $\text{Ca}^{++}$

↓  $\text{K}^{+}$

# $\beta$ -blocker Contraindication



**Bradycardia < 60**  
**High grade SA or**  
**AV block**



# Simplified Hypertension Management



How low should we go?



What drugs should we use?

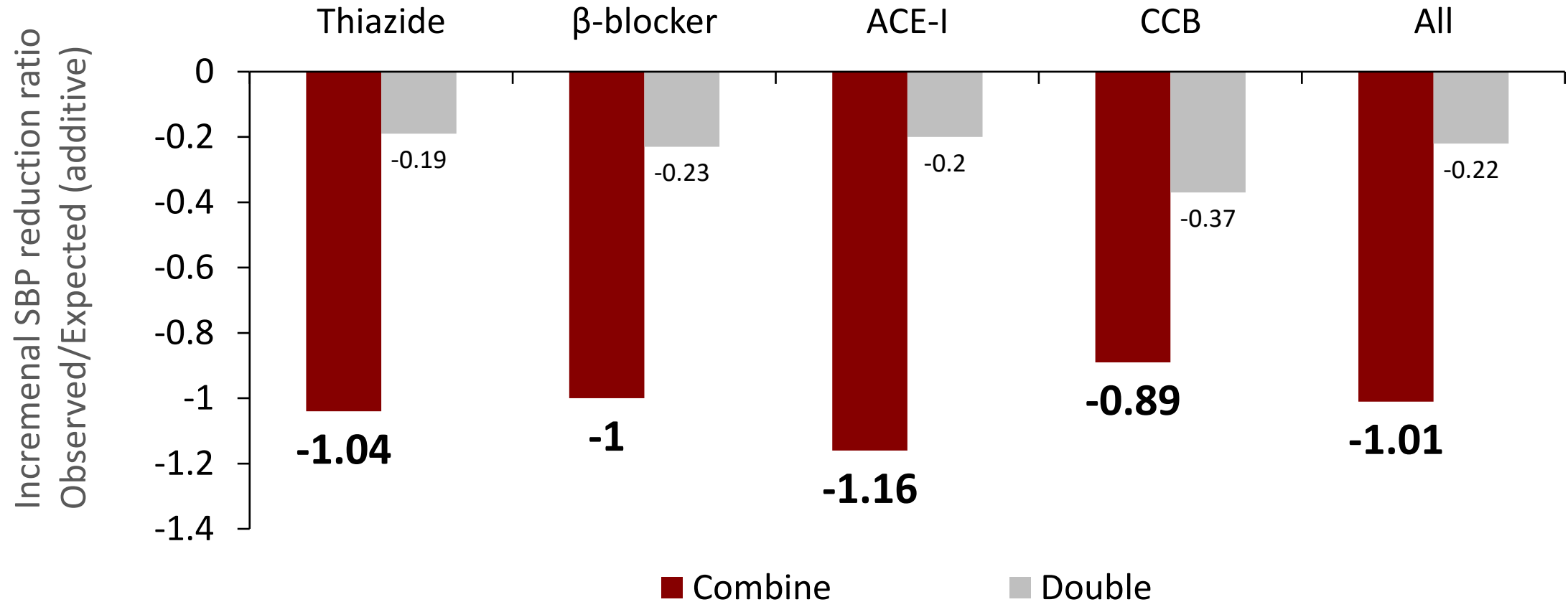


**How to get there?**

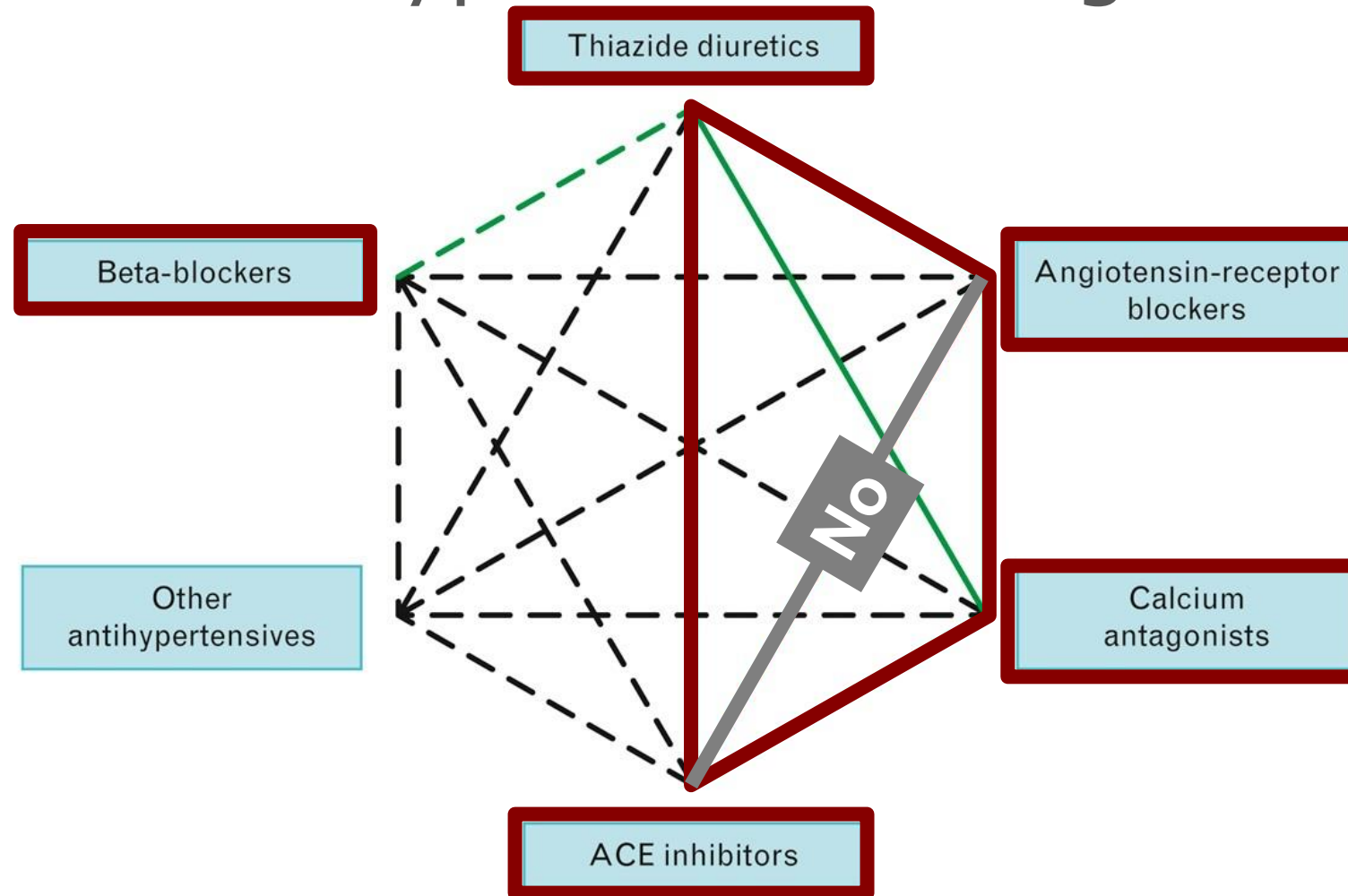


# Incremental SBP Reduction Ratio

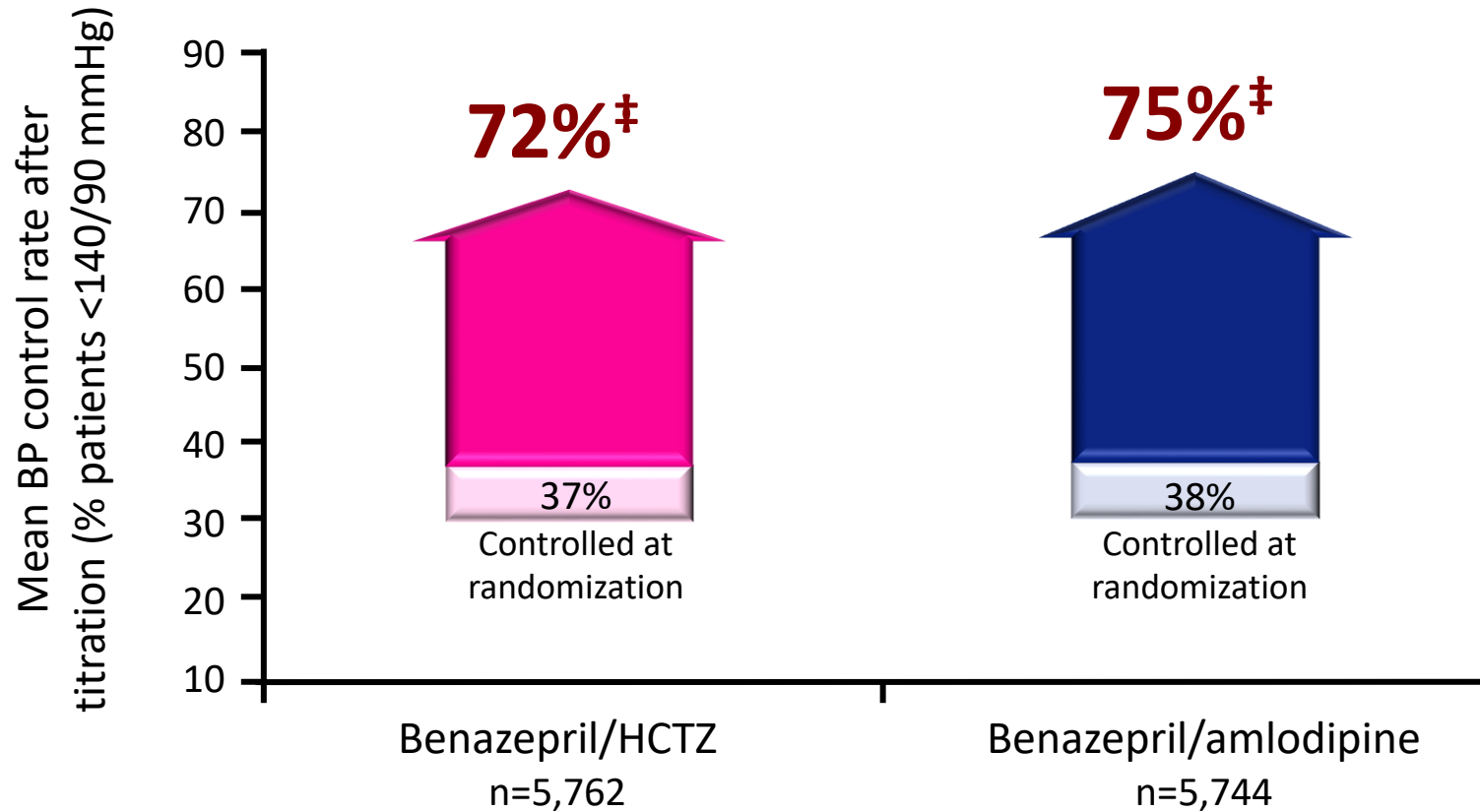
## Combine or Double?



# Possible combinations of classes of antihypertensive drugs



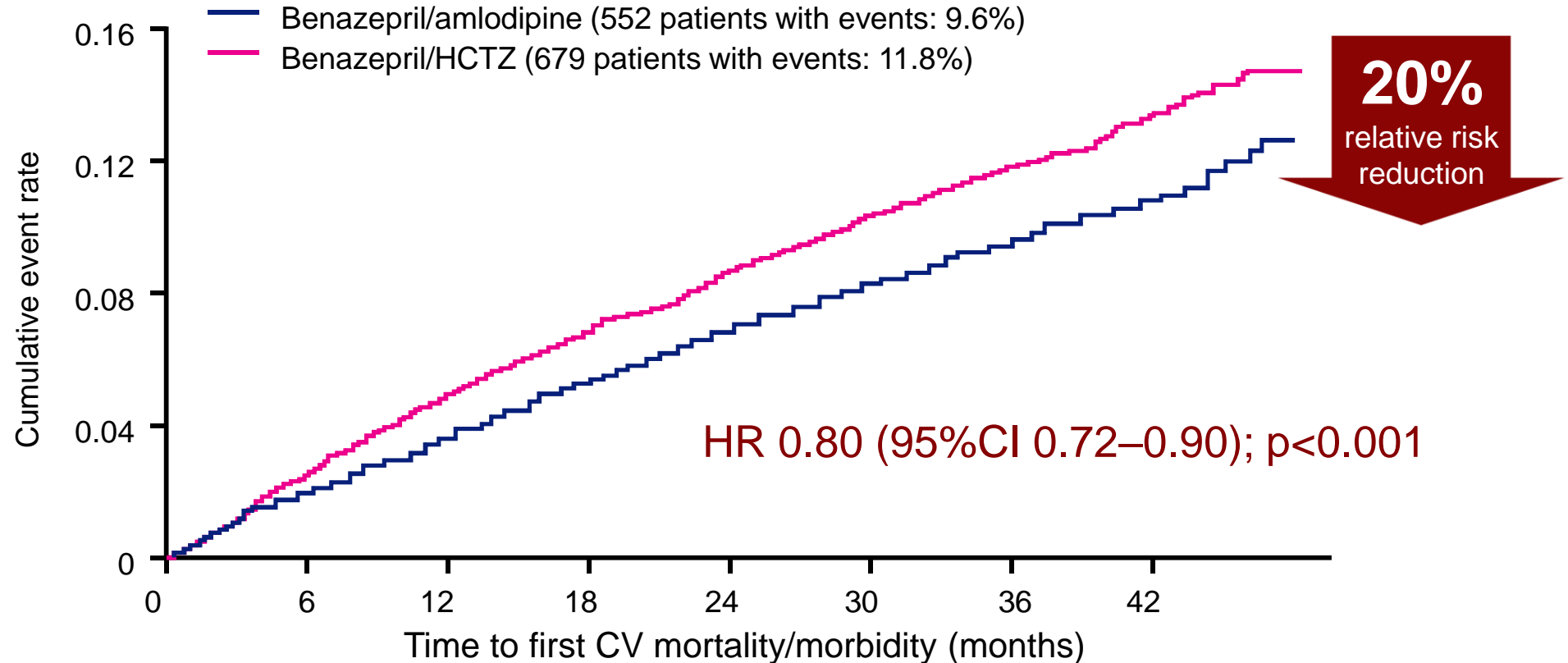
# ACCOMPLISH: BP Control with Single-pill Combinations



\*Control defined as BP <140/90 mmHg

†Values calculated from mean BP after titration and mean BP control rate over the duration of the study.

# ACCOMPLISH: **CV Outcomes**



Number at risk

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

# Drug choice & Sequencing

## Optimal

**Monotherapy** in low-risk  
Grade 1 HT in >80 yo. or frailer

Ideally Single  
Pill Combination  
Therapy (**SPC**)

**BB** in a specific indication  
eg. HF, angina, post MI, AF

### Step 1

Dual low-dose  
Combination

**A + C**

A + D in post-stroke very  
elderly, HF or CCB intolerance

### Step 2

Dual full-dose  
Combination

**A + C**

### Step 3

Triple Combination

**A + C + D**

### Step 4

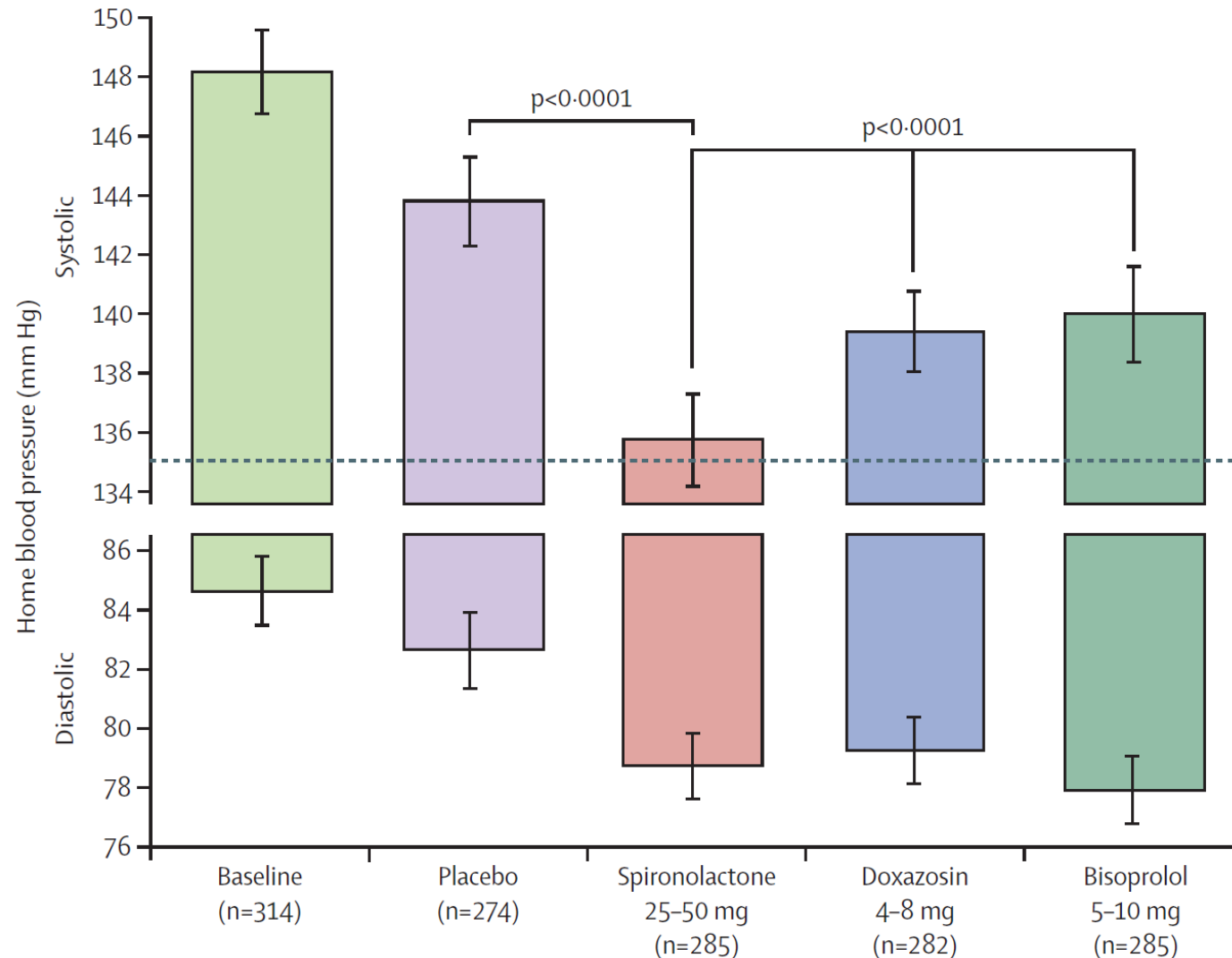
Triple Combination  
+ Spironolactone or  
other drug

**A + C + D**

+ **Spironolactone**  
(12.5-50 mg OD)

Caution when eGFR<45 or K >4.5

# Spironolactone for drug-resistant HTN



Double-blind, placebo-controlled, **crossover trial**

**335** were randomly assigned.

**spironolactone**

**doxazosin**

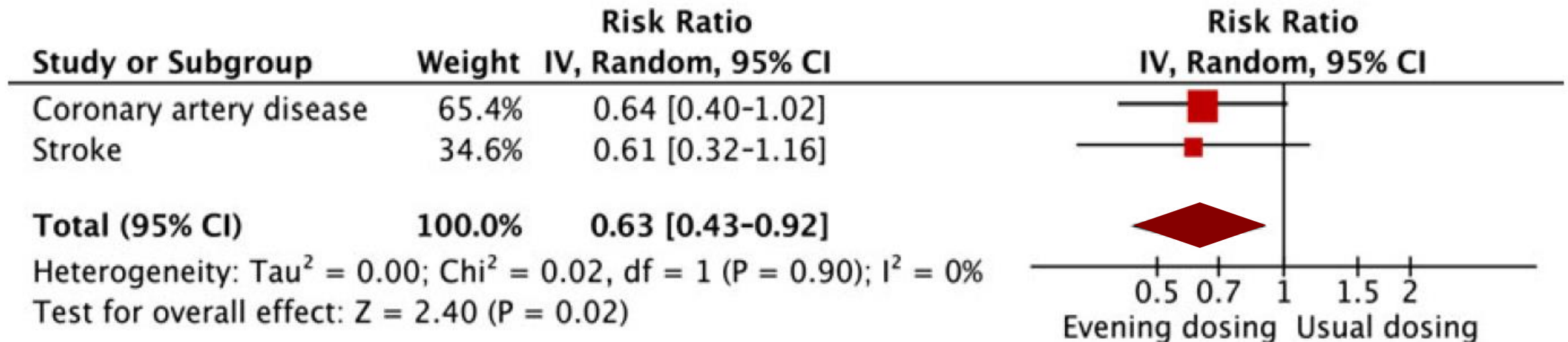
**bisoprolol**

**placebo**

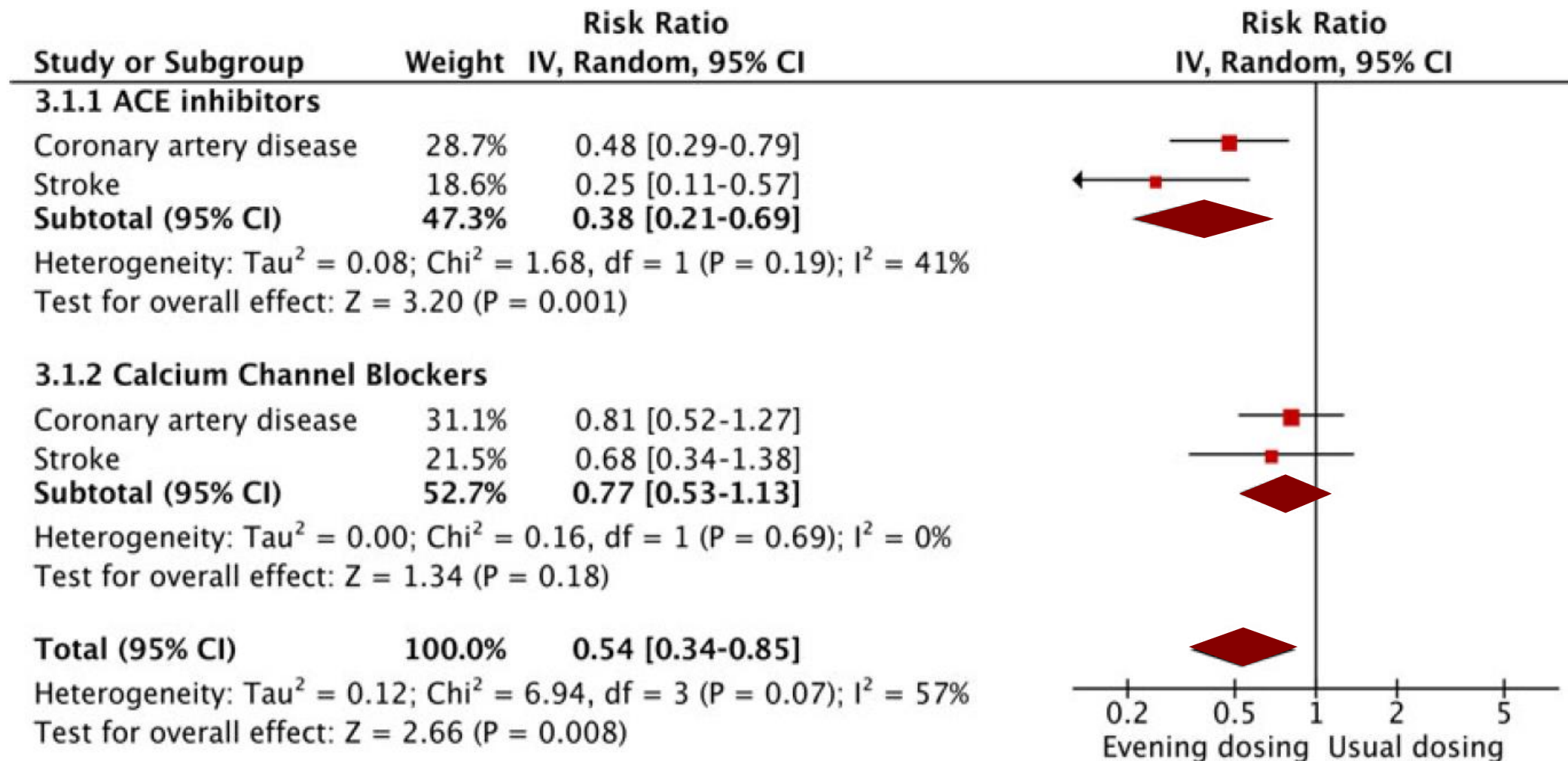
230 patients completed all treatment cycles.

# Evening Dosing of Antihypertensive Therapy

- 5 evening dose trials (EDTs) n=35,075
- HOPE study administered its entire antihypertensive dose prior to sleep and gave the greatest risk reduction.
- Head-to-head, multicenter trials are needed to test this strategy.



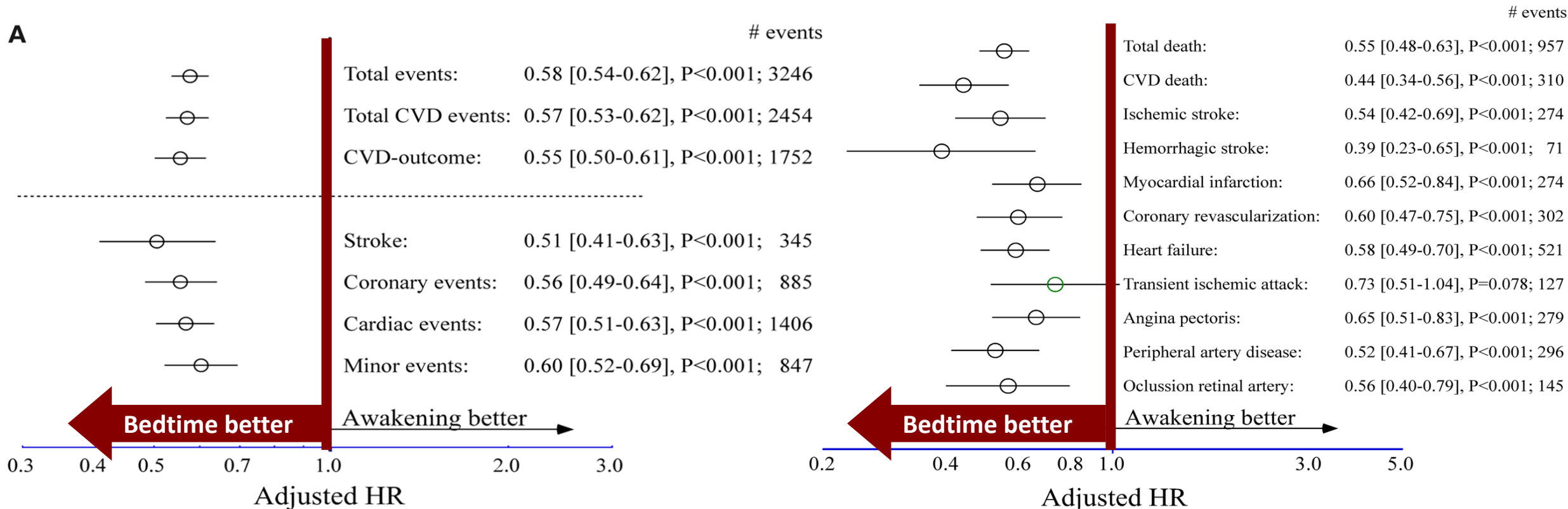
# Evening Dosing of Antihypertensive Therapy





# Bedtime hypertension treatment improves CV risk reduction: the Hygia Chronotherapy Trial

Multicentre, controlled, prospective endpoint trial, **19,084** hypertensive patients ( $60.5 \pm 13.7$  years of age) were assigned (1:1) to >1 hypertension medications at **bedtime** (n = 9552) or all of them upon **awakening** (n = 9532). **6.3-year** median patient follow-up



# Simplified Hypertension Management



How low should we go?

<65 yo: 120-130/70-79    >65 yo: 130-139/70-79



What drugs should we use?

ACEI, ARB, CCB, diuretic, BB



How to get there?

Combination, Evening dosing