

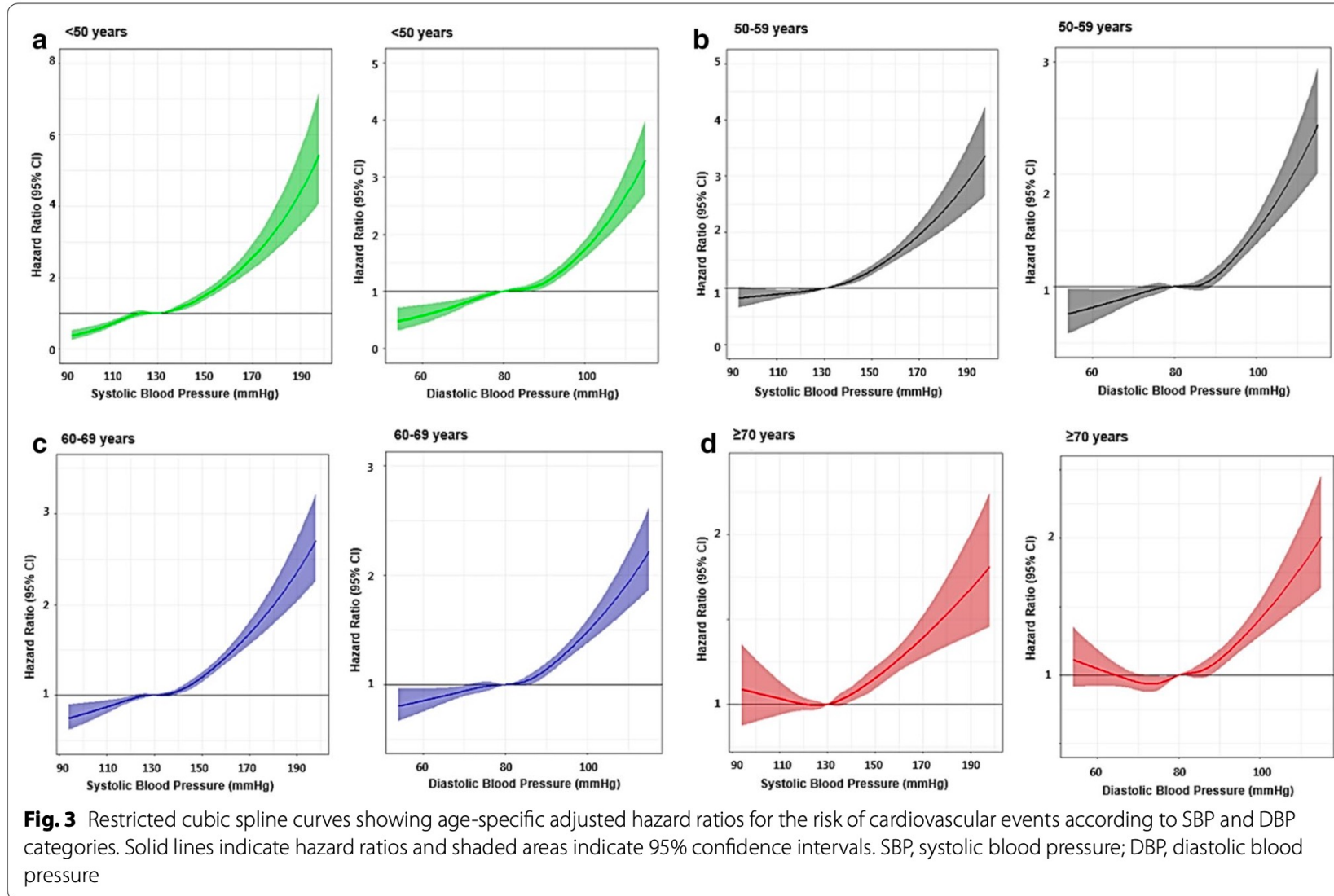
# Shifting Targets: The Latest Evidence on Hypertension Management

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# Scope

- RCTs in HT: Intensive BP control vs Standard BP control
  - ESPRIT
  - STEP
  - RESPECT
  - SPRINT
  - ACCORD
- Situation of BP control in our country

# Risk of CV Events According to SBP and DBP

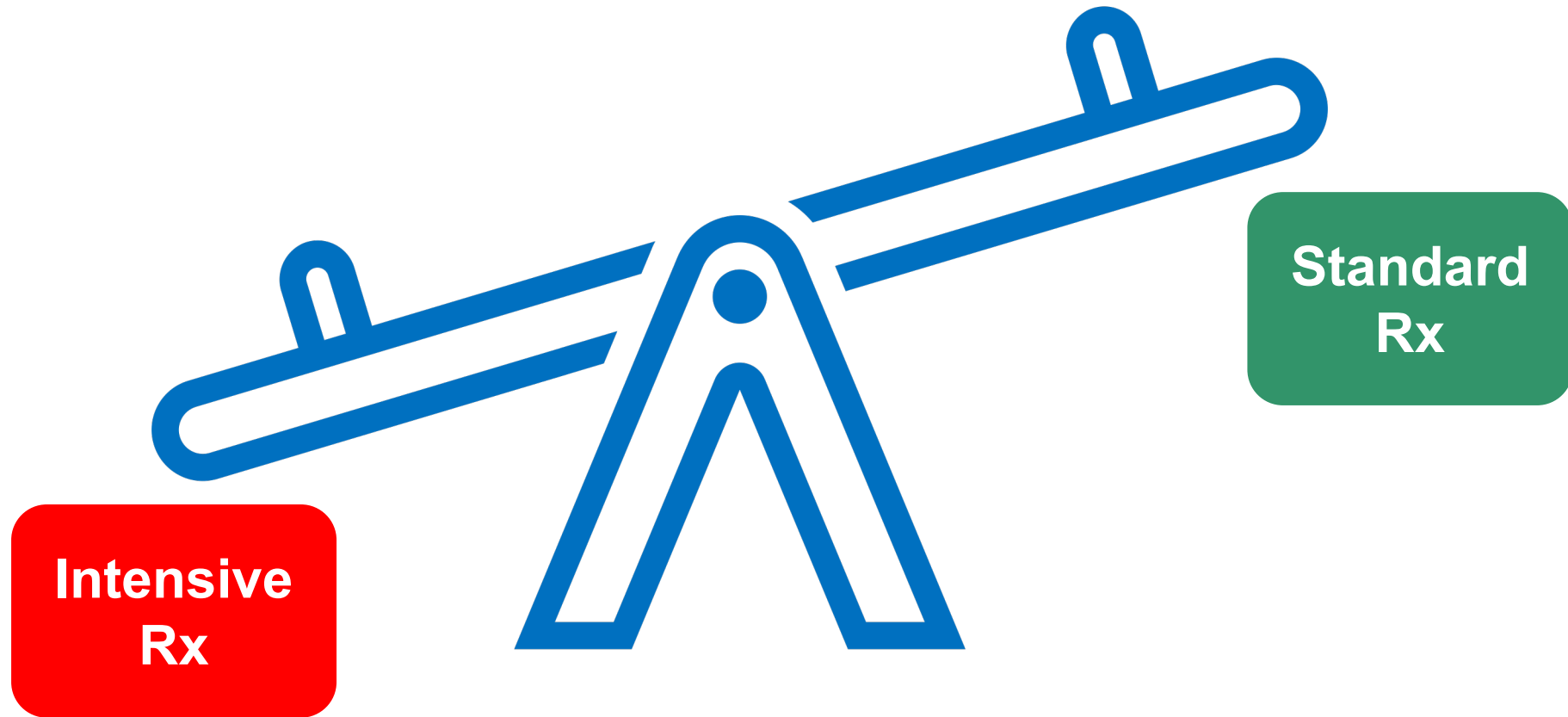


**Fig. 3** Restricted cubic spline curves showing age-specific adjusted hazard ratios for the risk of cardiovascular events according to SBP and DBP categories. Solid lines indicate hazard ratios and shaded areas indicate 95% confidence intervals. SBP, systolic blood pressure; DBP, diastolic blood pressure

# HBPM Recommendations in Major Guideline and Consensus Documents

	Diagnosis of hypertension	Diagnostic BP threshold, mm Hg	Titration and monitoring of antihypertensive therapy	Target BP threshold, mm Hg
ACC/AHA 2017 <sup>9</sup>	✓	≥130/80	✓	<130/80
ESC/ESH 2018 <sup>10</sup>	✓	≥135/85	✓	≤130/80
ISH 2020 <sup>8</sup>	✓	≥135/85	✓	<135/85
JSH 2019 <sup>7</sup>	✓	≥135/85	✓	<125/75 (age <75 y) or <135/85 (age ≥75 y)
China 2019 <sup>11</sup>	✓	≥135/85	✓	<140/90 or <130/80 if tolerated or in high-risk pts
Taiwan 2015 <sup>12</sup>	✓	≥135/85	✓	<140/90 or <130/80 if tolerated or in high-risk pts
South Korea 2018 <sup>13</sup>	✓	≥135/85	✓	<140/90 (uncomplicated/elderly) or <130/80 (high-risk pts)
HOPE Asia Network <sup>14</sup>	✓	≥135/85	✓	<135/85

# How low should we go?



# The Latest Evidence: The ESPRIT Study

**E**ffects of intensive **S**ystolic blood **P**ressure  
lowering treatment in reducing **R**isk of  
vascular even**T**s (ESPRIT) : A multicenter  
open-label randomized controlled trial

# The Latest Evidence: The ESPRIT Study

## Background

BP lowering effectively reduces the risk of CV events in high risk individuals

However, the optimal BP target among high risk individuals remains unclear

## Methods

A multi-center, open-label, randomized controlled trial to compare the efficacy and safety of intensive BP lowering strategy (SBP target <120 mmHg) vs standard BP lowering strategy (SBP target <140 mmHg)

# The Latest Evidence: The ESPRIT Study

## Inclusion Criteria

- **Chinese** adults aged  $\geq 50$  yrs old
- Baseline SBP 130-180 mm Hg at high CV risk, defined by
  - established CV diseases or
  - 2 major CV risk factors
    - $\geq 60$  yr old male or  $\geq 65$  yr old female
    - Diabetes
    - Dyslipidemia
    - Current smoker

## Exclusion Criteria

- Exclude individuals for whom the safety of intensive BP lowering Rx might be a concern
- Secondary HT
- 1-min standing SBP  $< 110$  mm Hg
- LV ejection fraction  $< 35\%$
- Estimated GRF  $< 45$  mL/min/1.73 m<sup>2</sup>
- Proteinuria  $> 2+$



# Baseline Characteristics of Participants

	ESPRIT	SPRINT
Age (yrs)	64.6 ± 7.1	67.9 ± 9.4
Age >75 yr (%)	8.4	<b><u>28.2</u></b>
Female (%)	41.3	35.6
Current smoker (%)	<b><u>31.2</u></b>	13.3
BMI (kg/m <sup>2</sup> )	26.3 ± 3.3	29.9 ± 5.8
Baseline SBP	146.9 ± 10.6	139.7 ± 15.6
Baseline DBP	82.8 ± 10.3	78.1 ± 11.9
eGFR (ml/min/1.73 m <sup>2</sup> )	88.5 ± 17.6	71.8 ± 20.6

# Baseline Characteristics of Participants

	ESPRIT	SPRINT
DM (%)	38.7	<u>0</u>
Stroke (%)	26.9	<u>0</u>
MI (%)	9.4	7.1
CV dis other than stroke (%)	29.5	16.7
Heart failure (%)	0.4	3.5
Statin (%)	46	43.3
Aspirin (%)	42.8	50.8

# The ESPRIT Study: Principal Findings

Intensive Rx

Standard Rx

P value

**1° outcome** (CV death, MI, stroke, coronary revas, noncoronary revas, or hospitalization for HF)

3.2%

3.6%

0.03

CV death

0.3%

0.5%

<0.05

Stroke

1.5%

1.7%

<0.05

Syncope

0.4%

0.1%

<0.05

# The ESPRIT Study: Interpretation

Among Asian patients with HT and a large proportion of DM & stroke, intensive BP control improves outcomes compared with standard control  
Target SBP <120 mmHg reduced major cardiac events vs <140 mm Hg  
Intensive BP control was associated with an absolute risk reduction of major adverse events of 0.4%

Intensive BP control was associated with an increased risk of syncope

The results of this trial are in line with the SPRINT trial, which enrolled <2% Asians and excluded subjects with DM or stroke.

# The ESPRIT Study: Interpretation

**Overall, intensive Rx lowered the risk of MACE by a relative 12%, with a number needed to treat of 74**

**For every 1,000 patients treated to the intensive versus conventional SBP goal for 3 yrs, 14 major vascular events & 8 deaths would be avoided at the cost of 3 additional serious adverse events involving syncope**

**This indicates the benefit & safety of Rx targeting SBP <120 mm Hg among diverse Asian population similar to individuals with other ethnic backgrounds**

# Summary of Previous Studies

## Intensive BP vs Standard BP Control

**1** The ACCORD Study (2010)

**2** The SPRINT Trial (2015)

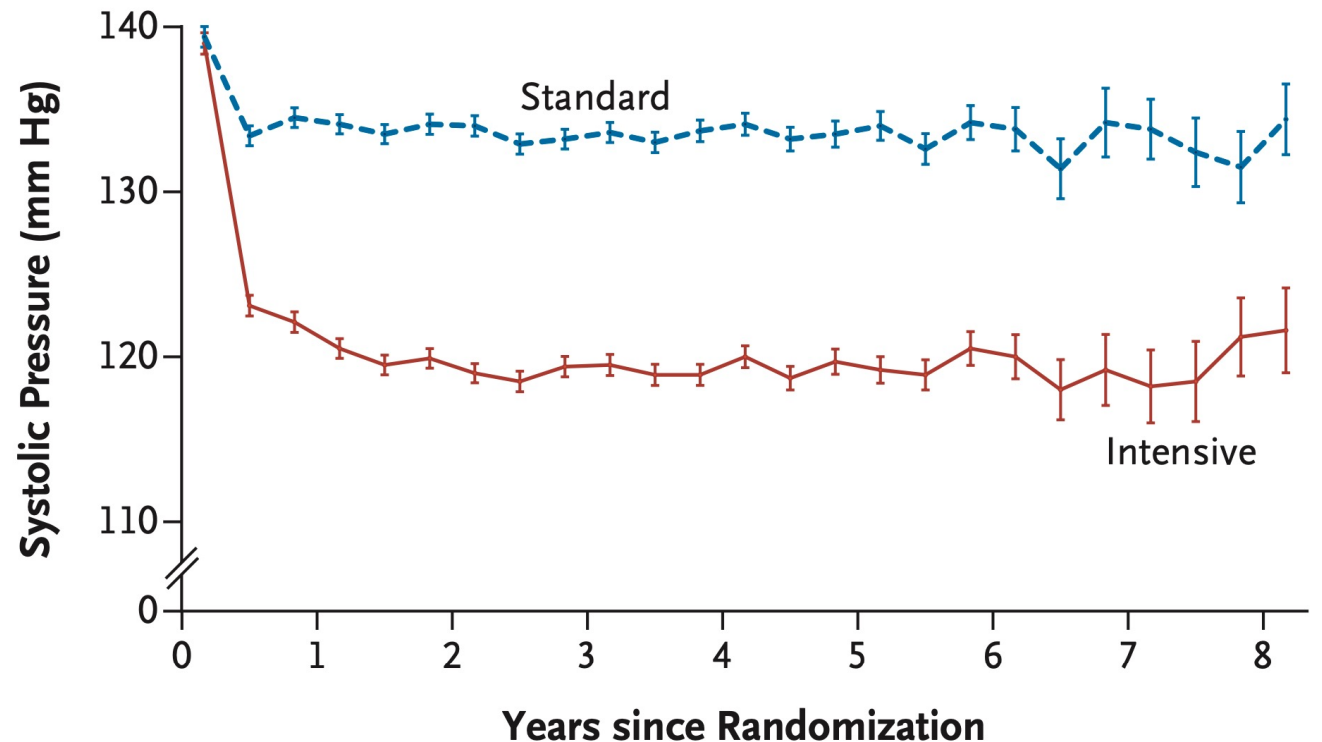
**3** The RESPECT Study (2019)

**4** The STEP Trial (2021)

# Effects of Intensive BP Control in Type 2 DM

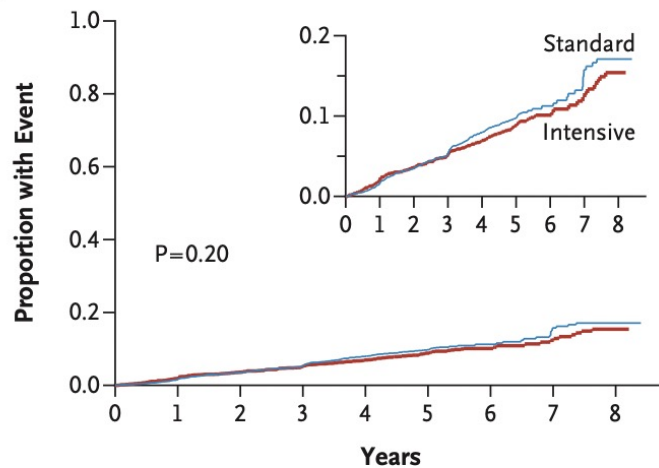
## The ACCORD Study

Parameter	Overall
N	4,733
Subjects	DM type 2, SBP 130-180 mmHg while on <3 anti-HT drugs and 24-hr UPCR <1 g
Age (yrs)	62.2
Target BP (mmHg)	SBP <120 vs <140
Achieved BP (mmHg)	At 1 yr 119.3 vs 133.5



Intensive BP control did not reduce the rate of a composite outcome of fatal & nonfatal major CV events

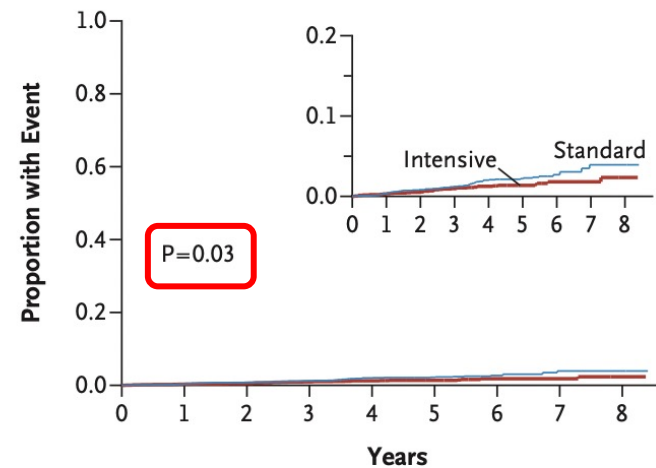
### A Primary Outcome



#### No. at Risk

Intensive	2362	2273	2182	2117	1770	1080	298	175	80
Standard	2371	2274	2196	2120	1793	1127	358	195	108

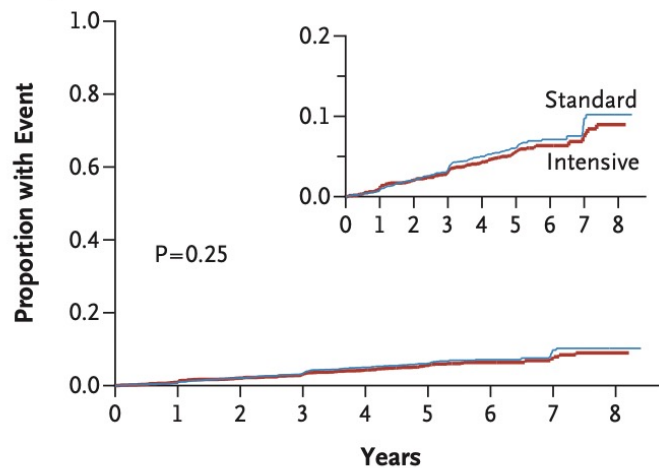
### B Nonfatal Stroke



#### No. at Risk

Intensive	2362	2291	2223	2174	1841	1128	313	186	88
Standard	2371	2287	2235	2186	1879	1196	382	215	114

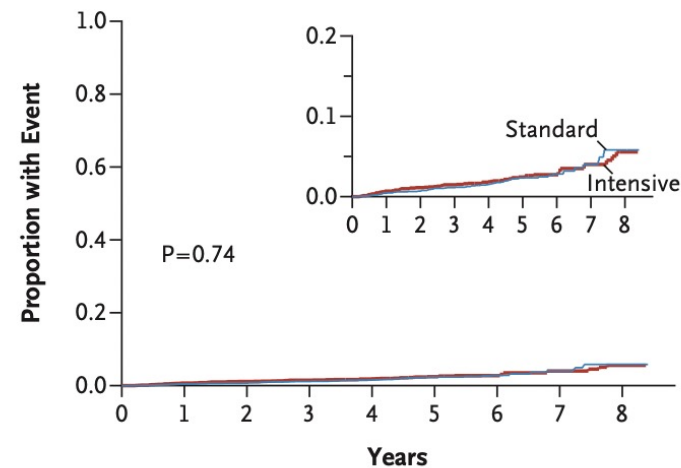
### C Nonfatal Myocardial Infarction



#### No. at Risk

Intensive	2362	2278	2190	2133	1787	1087	299	177	82
Standard	2371	2278	2208	2141	1818	1145	365	201	112

### D Death from Cardiovascular Disease



#### No. at Risk

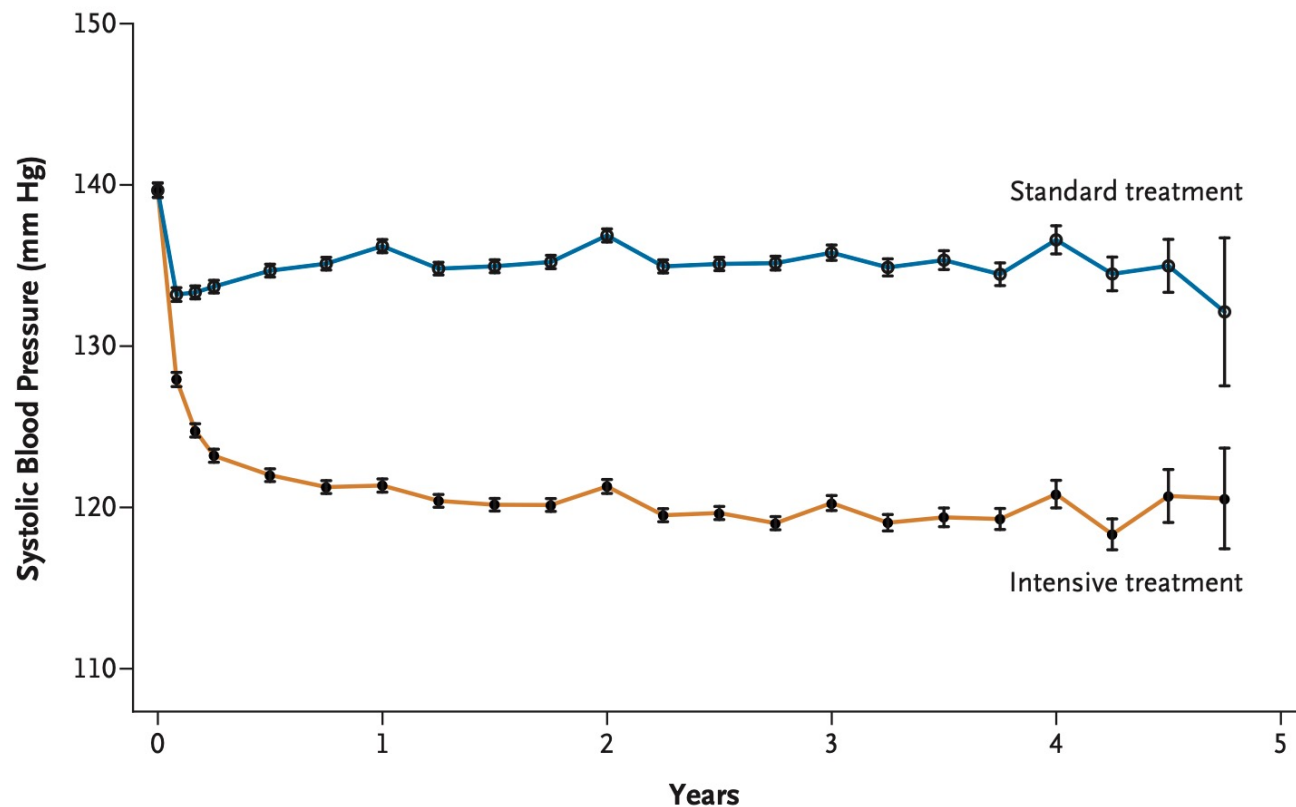
Intensive	2362	2304	2252	2201	1870	1143	317	188	91
Standard	2371	2313	2268	2218	1922	1220	393	221	118



# A Randomized Trial of Intensive versus Standard BP Control

## The SPRINT Research Group

Parameter	Overall
N	9,361
Subjects	SBP 130-180 mmHg and increased CV risk, <b>but without DM &amp; stroke</b>
Ethnicity	<b>Asian ~2%</b>
Age (yrs)	67.9 ( <b>&gt;75 yrs - 79.8%</b> )
Target BP (mmHg)	SBP <120 vs <140
Achieved BP (mmHg)	At 1 yr 121.4 vs 136.2

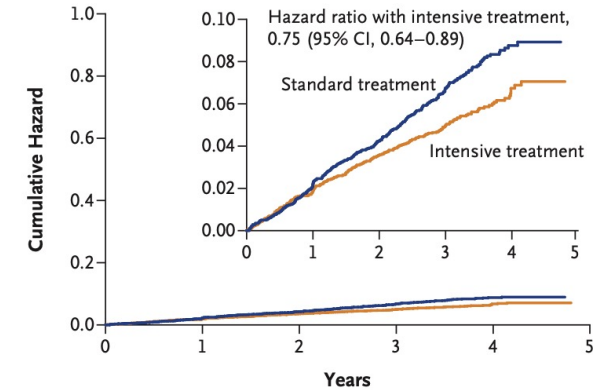


# The SPRINT Research Group: Outcomes

**Table 2. Primary and Secondary Outcomes and Renal Outcomes.\***

Outcome	Intensive Treatment		Standard Treatment		Hazard Ratio (95% CI)	P Value
	no. of patients (%)	% per year	no. of patients (%)	% per year		
<b>All participants</b>	<b>(N = 4678)</b>		<b>(N = 4683)</b>			
Primary outcome†	243 (5.2)	1.65	319 (6.8)	2.19	0.75 (0.64–0.89)	<0.001
Secondary outcomes						
Myocardial infarction	97 (2.1)	0.65	116 (2.5)	0.78	0.83 (0.64–1.09)	0.19
Acute coronary syndrome	40 (0.9)	0.27	40 (0.9)	0.27	1.00 (0.64–1.55)	0.99
Stroke	62 (1.3)	0.41	70 (1.5)	0.47	0.89 (0.63–1.25)	0.50
Heart failure	62 (1.3)	0.41	100 (2.1)	0.67	0.62 (0.45–0.84)	0.002
Death from cardiovascular causes	37 (0.8)	0.25	65 (1.4)	0.43	0.57 (0.38–0.85)	0.005
Death from any cause	155 (3.3)	1.03	210 (4.5)	1.40	0.73 (0.60–0.90)	0.003
Primary outcome or death	332 (7.1)	2.25	423 (9.0)	2.90	0.78 (0.67–0.90)	<0.001
<b>Participants with CKD at baseline</b>	<b>(N = 1330)</b>		<b>(N = 1316)</b>			
Composite renal outcome‡	14 (1.1)	0.33	15 (1.1)	0.36	0.89 (0.42–1.87)	0.76
≥50% reduction in estimated GFR§	10 (0.8)	0.23	11 (0.8)	0.26	0.87 (0.36–2.07)	0.75
Long-term dialysis	6 (0.5)	0.14	10 (0.8)	0.24	0.57 (0.19–1.54)	0.27
Kidney transplantation	0		0			
Incident albuminuria¶	49/526 (9.3)	3.02	59/500 (11.8)	3.90	0.72 (0.48–1.07)	0.11
<b>Participants without CKD at baseline  </b>	<b>(N = 3332)</b>		<b>(N = 3345)</b>			
≥30% reduction in estimated GFR to <60 ml/min/1.73 m <sup>2</sup> §	127 (3.8)	1.21	37 (1.1)	0.35	3.49 (2.44–5.10)	<0.001
Incident albuminuria¶	110/1769 (6.2)	2.00	135/1831 (7.4)	2.41	0.81 (0.63–1.04)	0.10

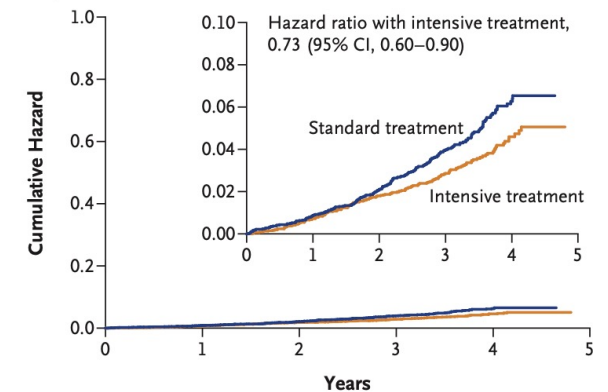
## Primary outcomes



### No. at Risk

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

## All death



### No. at Risk

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

# Effect of Standard vs Intensive BP Control on the Risk of Recurrent Stroke

## A Randomized Clinical Trial and Meta-analysis

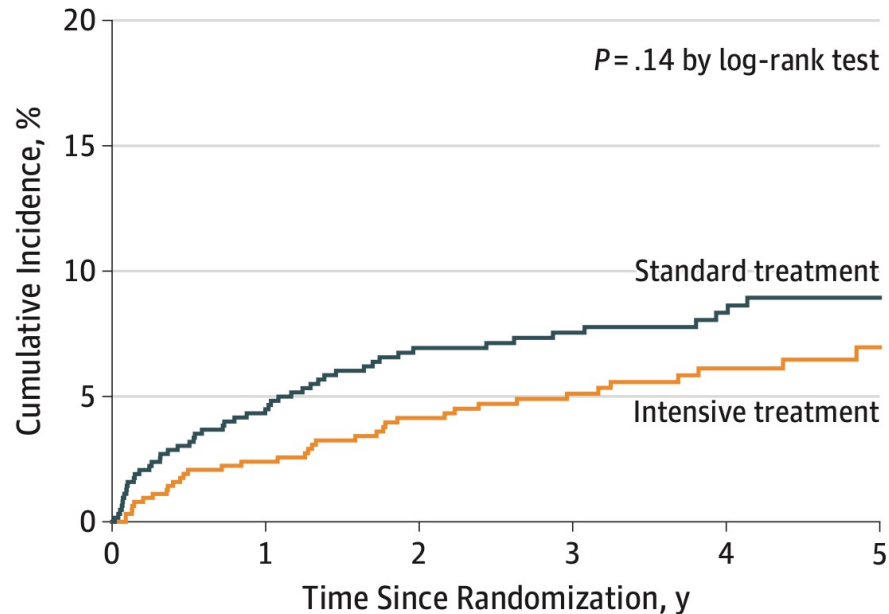
### The RESPECT Study Group

Parameter	Overall
N	1,263
Subjects	Japanese pts with previous stroke in 3 yrs
Age (yrs)	67.2
Target BP	<120/80 vs <140/90 <130/80 in DM, CKD, MI
Achieved BP	126.7/77.4 vs 133.2/77.7 throughout follow up period
Primary outcome	Recurrent stroke

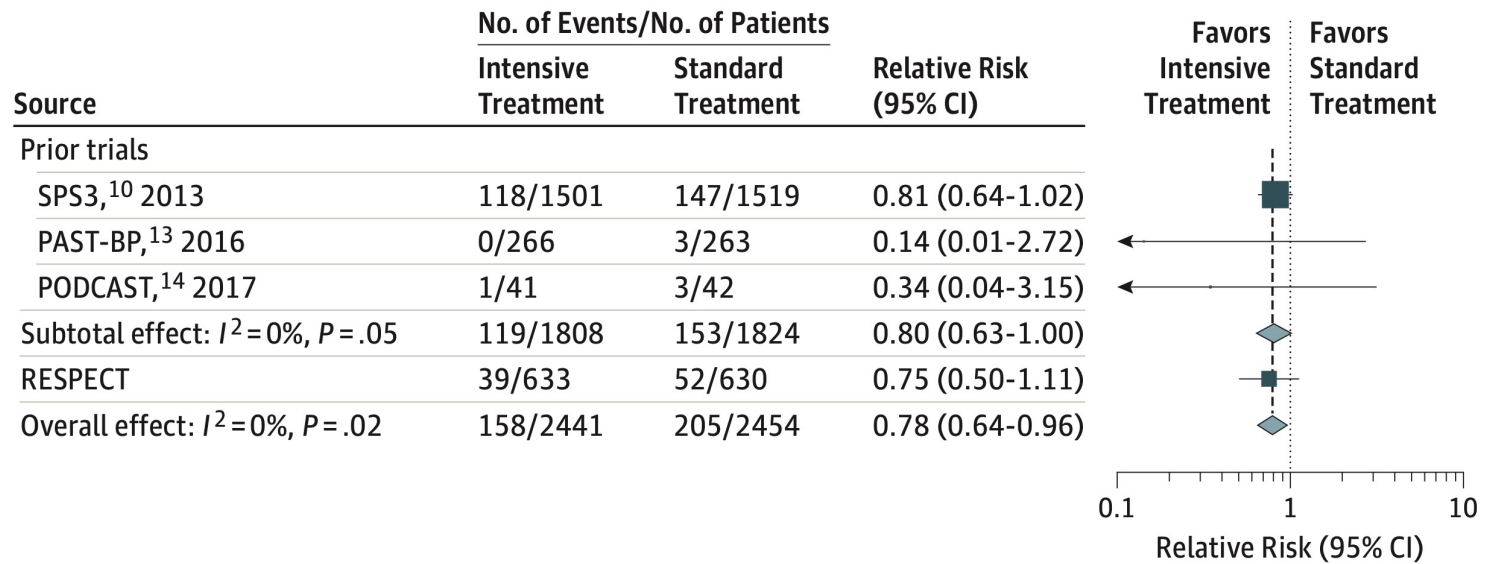
# A Randomized Clinical Trial and Meta-analysis

## The RESPECT Study Group

### Cumulative Incidence of Recurrent Stroke



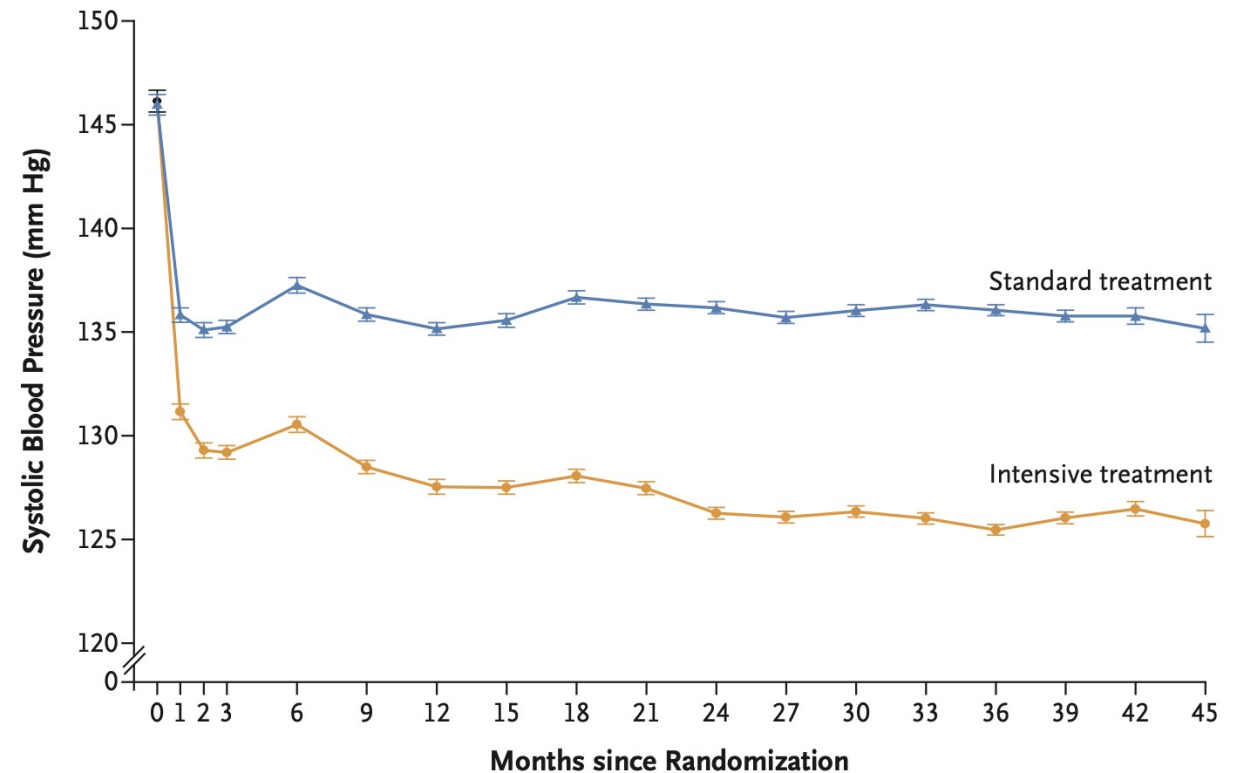
### Effects of Intensive BP Lowering on Recurrent Stroke in a Meta-analysis of Randomized Clinical Trials



# Trial of Intensive BP Control in Older Patients with HT

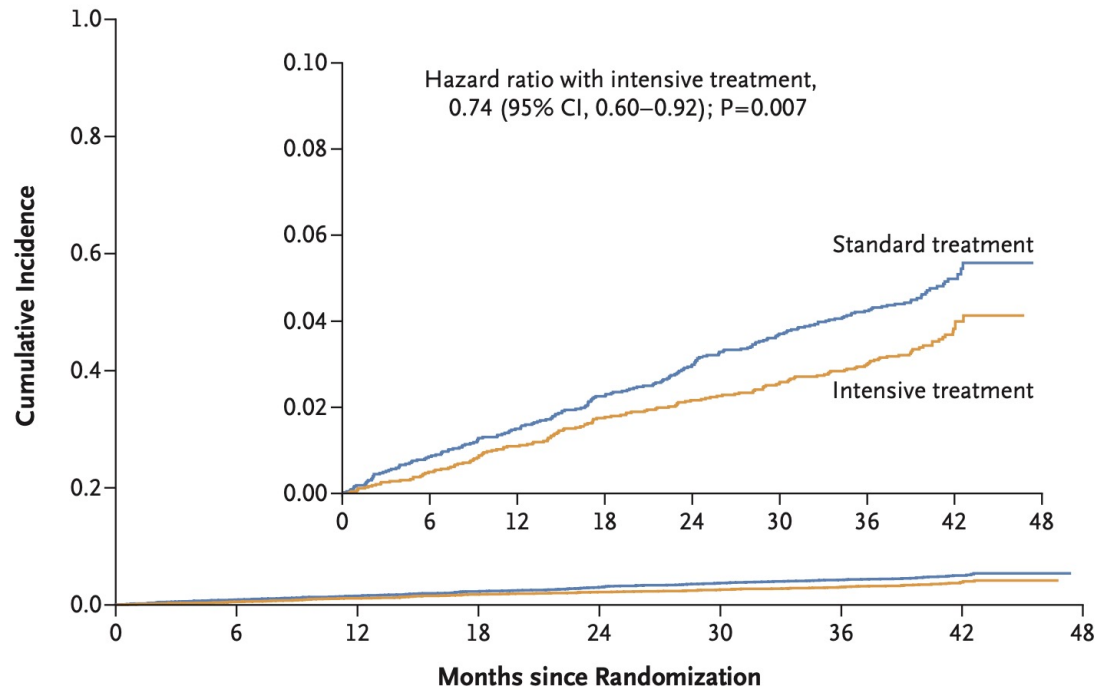
## The STEP Study

Parameter	Overall
N	8,511
Subjects	<b>Chinese</b> pts 60-80 yrs
Age	66 yrs
60-69 yrs	76%
70-80 yrs	24%
Target BP	SBP 110-130 vs 130-150
Achieved BP	At 1 yr: 127.5 vs 135.3



# The STEP Study

## Cumulative Incidence for the Primary Outcome



## Hazard Ratios for the Primary and Secondary Outcomes

Outcome	Intensive Treatment (N=4243)		Standard Treatment (N=4268)		Hazard Ratio (95% CI)	P Value
	no. of patients (%)	% with event per year	no. of patients (%)	% with event per year		
Primary outcome†	147 (3.5)	1.0	196 (4.6)	1.4	0.74 (0.60–0.92)	0.007
Secondary outcomes						
Components of primary outcome						
Stroke	48 (1.1)	0.3	71 (1.7)	0.5	0.67 (0.47–0.97)	—
Acute coronary syndrome	55 (1.3)	0.4	82 (1.9)	0.6	0.67 (0.47–0.94)	—
Acute decompensated heart failure	3 (0.1)	0.03	11 (0.3)	0.09	0.27 (0.08–0.98)	—
Coronary revascularization	22 (0.5)	0.1	32 (0.7)	0.2	0.69 (0.40–1.18)	—
Atrial fibrillation	24 (0.6)	0.2	25 (0.6)	0.2	0.96 (0.55–1.68)	—
Death from cardiovascular causes	18 (0.4)	0.1	25 (0.6)	0.2	0.72 (0.39–1.32)	—
Death from any cause	67 (1.6)	0.5	64 (1.5)	0.5	1.11 (0.78–1.56)	—
Major adverse cardiac events‡	100 (2.4)	0.7	138 (3.2)	1.0	0.72 (0.56–0.93)	—

# Summary of Achieved BP in Each Trials



# Summary of BP Reduction in Each Trials



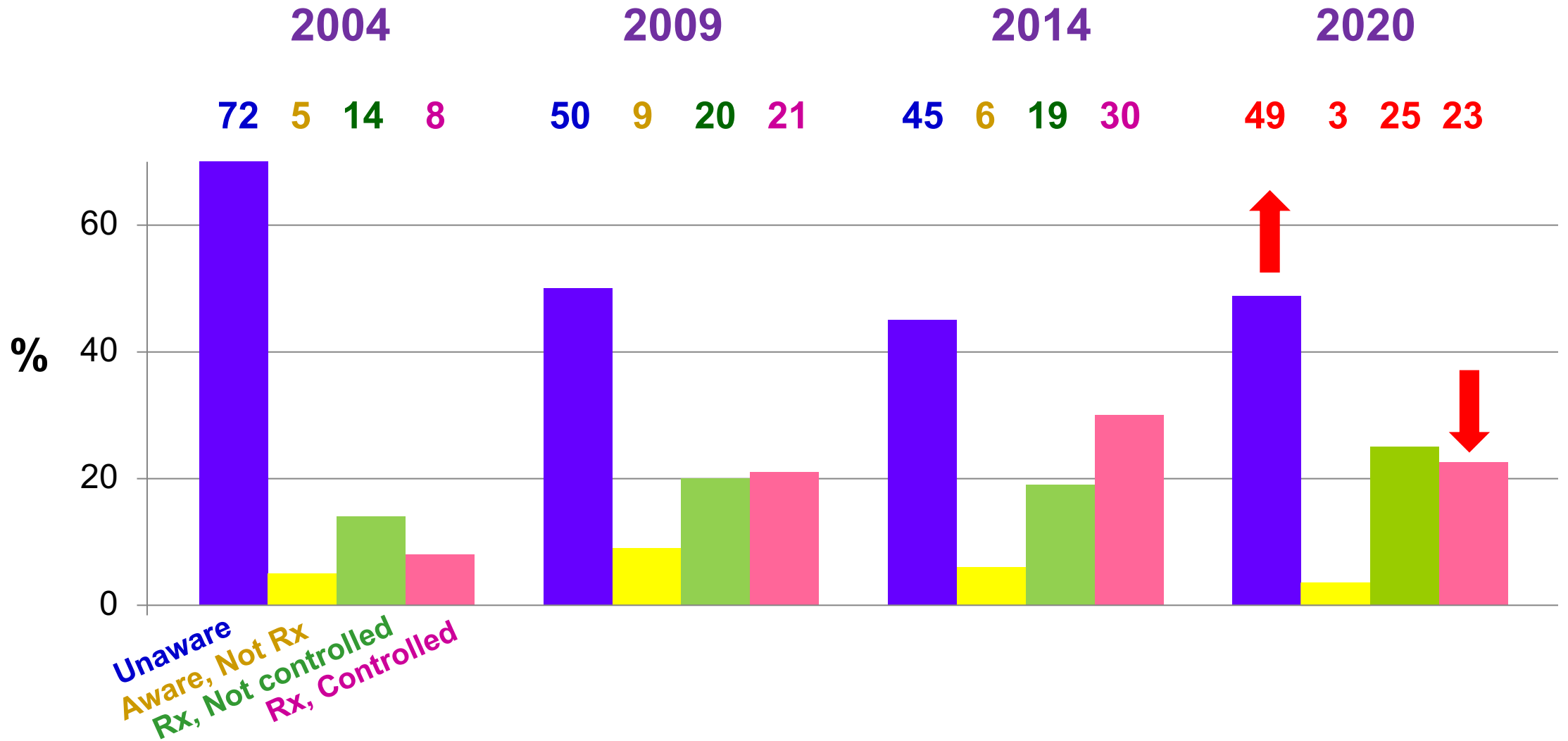


# Summary of Adverse Events in Each Trials

	ACCORD		SPRINT		RESPECT		STEP		ESPRIT	
	Inten	Std	Inten	Std	Inten	Std	Inten	Std	Inten	Std
Hypotension (%)	0.7	0.04*	3.4	2*	NA	NA	3.4	2.6*	No diff	
Syncope (%)	0.5	0.21	3.5	2.4*	0.95	0.63	0.1	<0.1	0.4	0.1
Renal failure (%)	0.2	0.04	4.4	2.6*	0.95	0.16	1	1	No diff	
SAE (%)	Higher*		38.3	37.1	No diff		No diff		42	42
Injurious fall or fracture	NA	NA	2.2	2.3	2.05	2.7	0.4	0.4	No diff	

**Better than expected**

# Unawareness, Treatment, and Control of HT: Thai NHES III (2004), IV (2009), V (2014) and VI (2020)

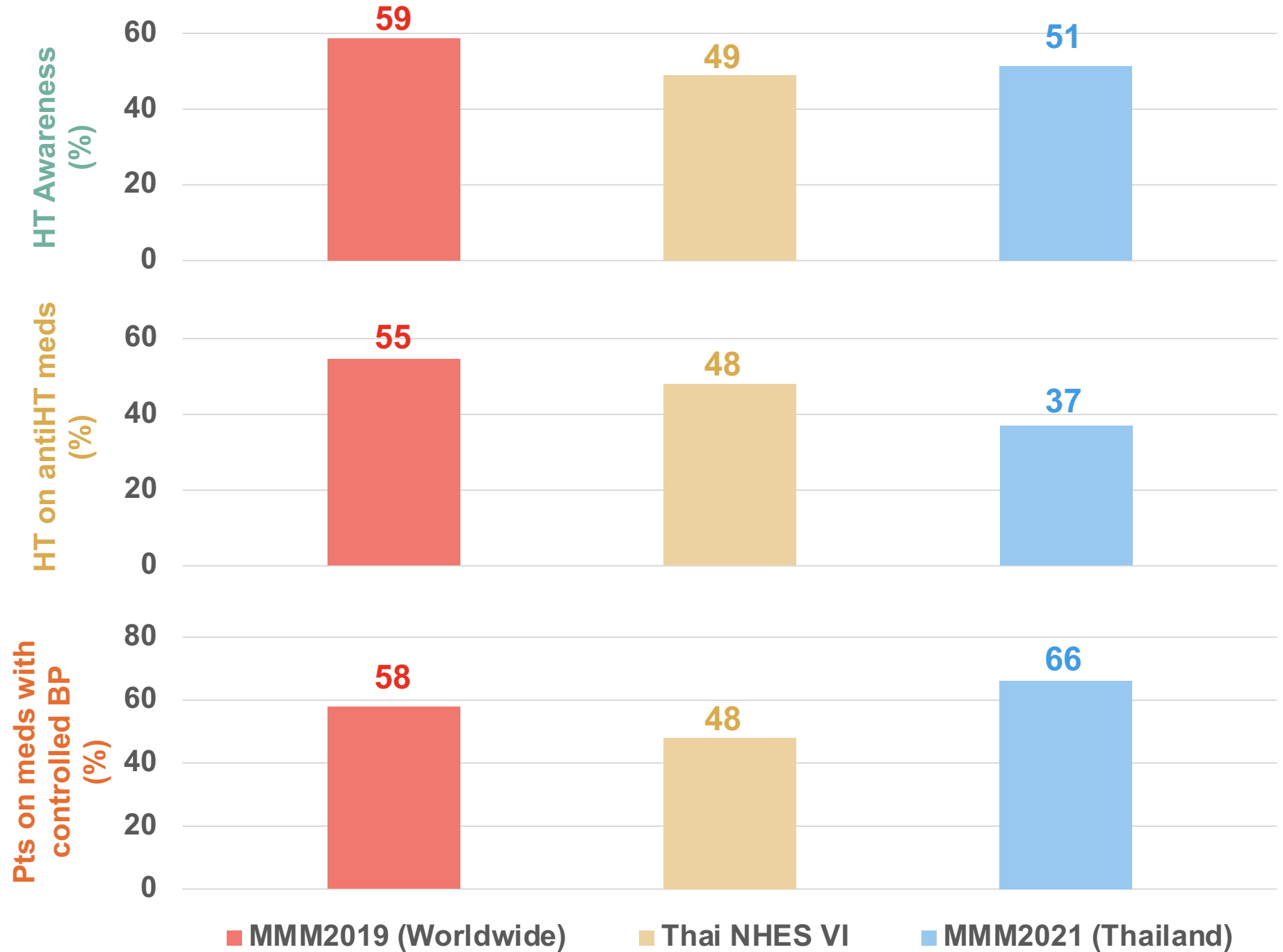




# MMM2021 THAILAND

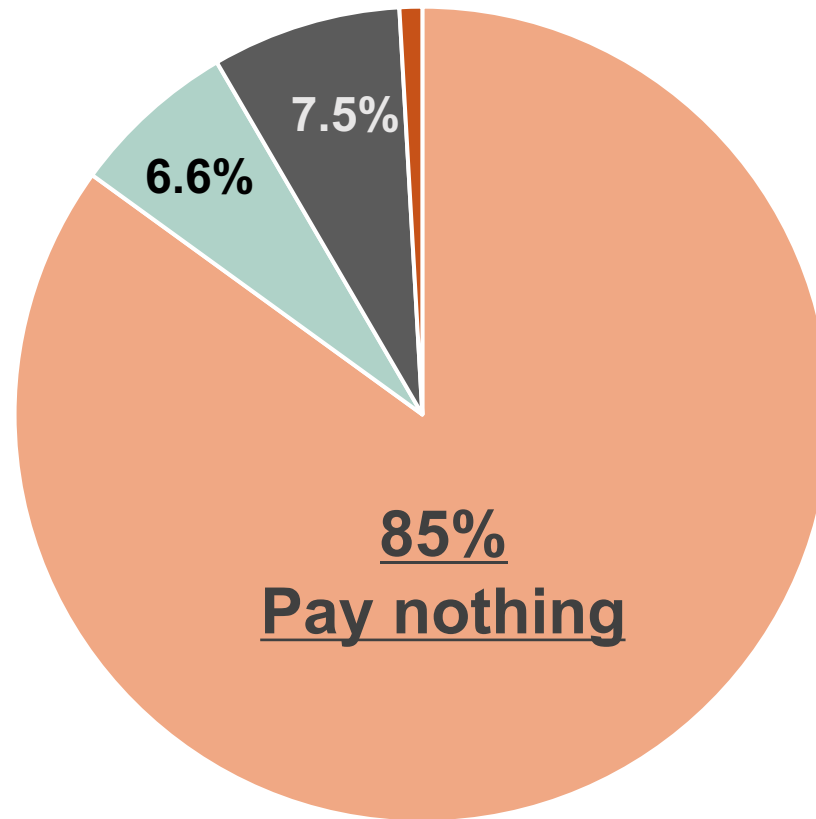
Only 6.7% never have their BP checked

10.9% were >60 yrs-of-age





# Do you usually pay fees for your consultations and/or medications when you get your BP treated?



■ Pay nothing ■ Pay partly ■ Pay fully ■ Not sure

# In Summary

- There are assuring information from many RCTs indicating the benefit of intensive BP control (achieved SBP 120-127 mmHg) over standard Rx
- However, intensive BP control may be associated with more hypotension, syncope, and AKI ----- be more careful in vulnerable subjects
- BP control rates—even using conventional goals—remain suboptimal and have worsened in recent years
- Each country should modify their healthcare strategies to better tackle BP control and also other NCD problems in their population



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Thank you for your attention