

# ***Feeling the pressure? Managing Hypertension in 2016***



ACC Latin America  
Conference 2016



**MEXICO CITY**  
OCTOBER 7 - 8, 2016

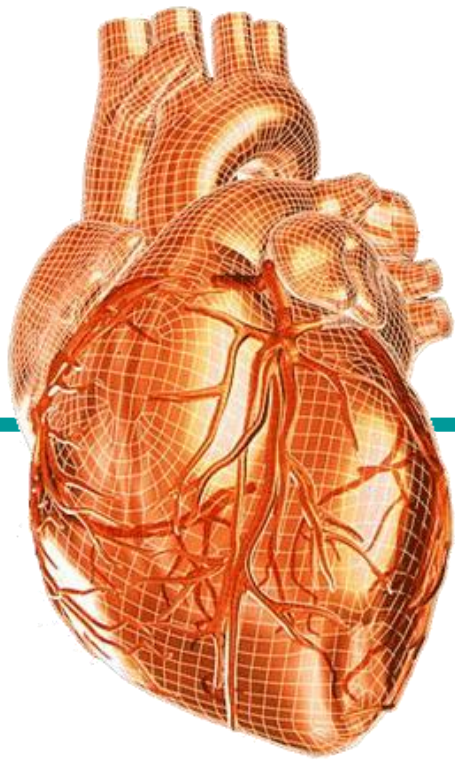


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Categories of potential conflict of interest	Company (period from 2002 to 2016)
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Sponsored in clinical trials and/or in basic research funded by pharmaceutical companies	<b>Bayer</b>
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Participate in normative committees of scientific trials sponsored by pharmaceutical companies	<b>Bayer</b>
Receive institutional support from pharmaceutical companies	<b>—</b>
Writing of educative materials sponsored by pharmaceutical companies	<b>LIBBS, NovaQuimica, Servier</b>
Hold stocks from pharmaceutical companies	<b>—</b>



Should new hypertension goals apply to all?

# Current Context of Hypertension



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# Multivariable-Adjusted Hazard Ratios for 24-Hour Systolic and Diastolic BP According to Age Groups

End Point		<50 years (n=3761)			≥50 years (n=4580)		
		n	Diastolic Pressure	Systolic Pressure	n	Diastolic Pressure	Systolic Pressure
Mortality							
Total	A	64	1.38 (1.08–1.77)†	1.20 (0.86–1.66)	863	1.17 (1.10–1.25)‡	1.21 (1.14–1.29)‡
	FA		2.05 (1.26–3.33)†	0.56 (0.30–1.05)		1.03 (0.94–1.13)	1.19 (1.08–1.30)‡
Cardiovascular	A	16	2.34 (1.61–3.39)‡	2.23 (1.32–3.78)†	340	1.31 (1.18–1.44)‡	1.47 (1.35–1.61)‡
	FA		4.07 (1.60–10.4)†	0.44 (0.13–1.56)		0.96 (0.85–1.10)	1.51 (1.34–1.70)‡
Noncardiovascular	A	46	1.13 (0.83–1.55)	0.93 (0.61–1.42)	502	1.06 (0.97–1.16)	1.03 (0.94–1.12)
	FA		1.73 (0.96–3.12)	0.53 (0.25–1.13)		1.09 (0.95–1.25)	0.96 (0.84–1.10)
Fatal plus nonfatal events							
All cardiovascular	A	47	1.65 (1.27–2.14)‡	1.68 (1.19–2.36)†	697	1.36 (1.27–1.46)‡	1.44 (1.35–1.53)‡
	FA		1.74 (1.03–2.93)*	0.92 (0.47–1.81)		1.06 (0.97–1.17)	1.39 (1.27–1.51)‡
Cardiac	A	37	1.53 (1.12–2.08)†	1.52 (1.01–2.27)*	440	1.26 (1.16–1.38)‡	1.37 (1.26–1.48)‡
	FA		1.67 (0.92–3.03)	0.88 (0.40–1.90)		1.01 (0.90–1.14)	1.36 (1.22–1.52)‡
Coronary	A	28	1.63 (1.16–2.30)†	1.67 (1.07–2.62)*	320	1.25 (1.13–1.38)‡	1.35 (1.23–1.48)‡
	FA		1.73 (0.87–3.45)	0.92 (0.37–2.24)		1.01 (0.88–1.15)	1.35 (1.18–1.53)‡
Stroke	A	7	2.31 (1.25–4.27)†	2.43 (1.12–5.26)*	249	1.61 (1.43–1.81)‡	1.65 (1.49–1.83)‡
	FA		2.24 (0.62–8.20)	1.04 (0.21–5.26)		1.14 (0.97–1.34)	1.52 (1.32–1.76)‡



# Hypertension

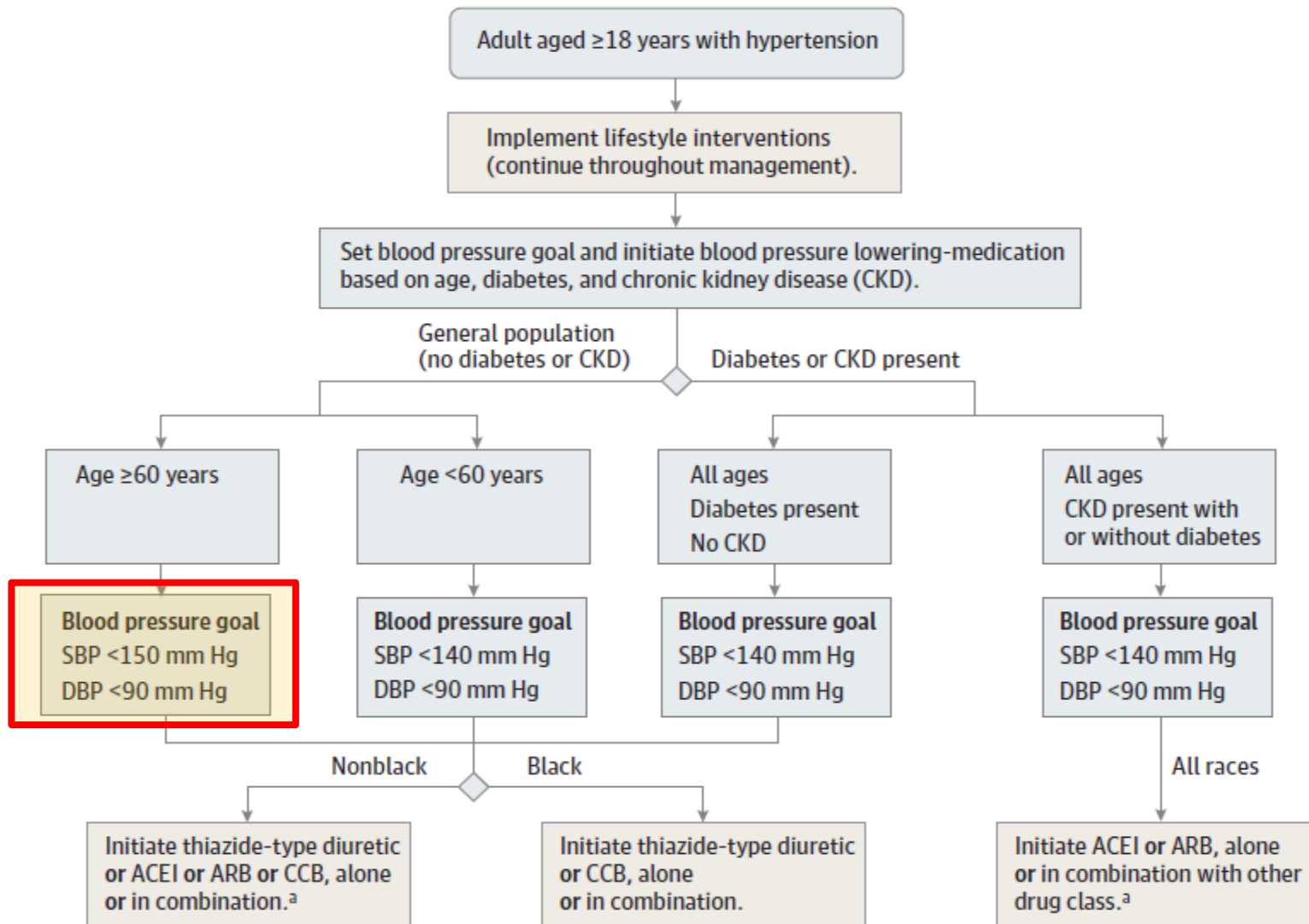
## **Ambulatory Hypertension Subtypes and 24-Hour Systolic and Diastolic Blood Pressure as Distinct Outcome Predictors in 8341 Untreated People Recruited From 12 Populations**

Yan Li, MD, PhD; Fang-Fei Wei, MD; Lutgarde Thijs, MSc; José Boggia, MD, PhD;  
Kei Asayama, MD, PhD; Tine W. Hansen, MD, PhD; Masahiro Kikuya, MD, PhD;  
Kristina Björklund-Bodegård, MD, PhD; Takayoshi Ohkubo, MD, PhD; Jørgen Jeppesen, MD;  
Yu-Mei Gu, MD; Christian Torp-Pedersen, MD, PhD; Eamon Dolan, MD, PhD;  
Yan-Ping Liu, MD; Tatiana Kuznetsova, MD, PhD; Katarzyna Stolarz-Skrzypek, MD, PhD;  
Valérie Tikhonoff, MD, PhD; Sofia Malyutina, MD, PhD; Edoardo Casiglia, MD, PhD;  
Yuri Nikitin, MD, PhD; Lars Lind, MD, PhD; Edgardo Sandoya, MD, PhD;  
Kalina Kawecka-Jaszcz, MD, PhD; Luis Mena, MD; Gladys E. Maestre, MD, PhD;  
Jan Filipovský, MD, PhD; Yutaka Imai, MD, PhD; Eoin O'Brien, MD, PhD;  
Ji-Guang Wang, MD, PhD; Jan A. Staessen, MD, PhD; on behalf of the International Database on  
Ambulatory blood pressure in relation to Cardiovascular Outcomes (IDACO) Investigators

- The risks conferred by DBP24 and SBP24 are age dependent.
- DBP24 and isolated diastolic hypertension drive coronary complications below age 50
- Above age of 50yo SBP24-h and isolated systolic, and mixed hypertension are the predominant risk factors.

# Hypertension Guidelines - JNC-8

Figure. 2014 Hypertension Guideline Management Algorithm



# 2013 ESH/ESC Hypertension Guidelines

## Blood pressure goals in hypertensive patients

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>	Ref. <sup>c</sup>
A SBP goal <140 mmHg:			
a) is recommended in patients at low-moderate CV risk;	I	B	266, 269, 270
b) is recommended in patients with diabetes;	I	A	270, 275, 276
c) should be considered in patients with previous stroke or TIA;	IIa	B	296, 297
d) should be considered in patients with CHD;	IIa	B	141, 265
e) should be considered in patients with diabetic or non-diabetic CKD.	IIa	B	312, 313
In elderly hypertensives less than 80 years old with SBP ≥160 mmHg there is solid evidence to recommend reducing SBP to between 150 and 140 mmHg.	I	A	265
In fit elderly patients less than 80 years old SBP values <140 mmHg may be considered, whereas in the fragile elderly population SBP goals should be adapted to individual tolerability.	IIb	C	-
In individuals older than 80 years and with initial SBP ≥160 mmHg, it is recommended to reduce SBP to between 150 and 140 mmHg provided they are in good physical and mental conditions.	I	B	287
A DBP target of <90 mmHg is always recommended, except in patients with diabetes, in whom values <85 mmHg are recommended. It should nevertheless be considered that DBP values between 80 and 85 mmHg are safe and well tolerated.	I	A	269, 290, 293

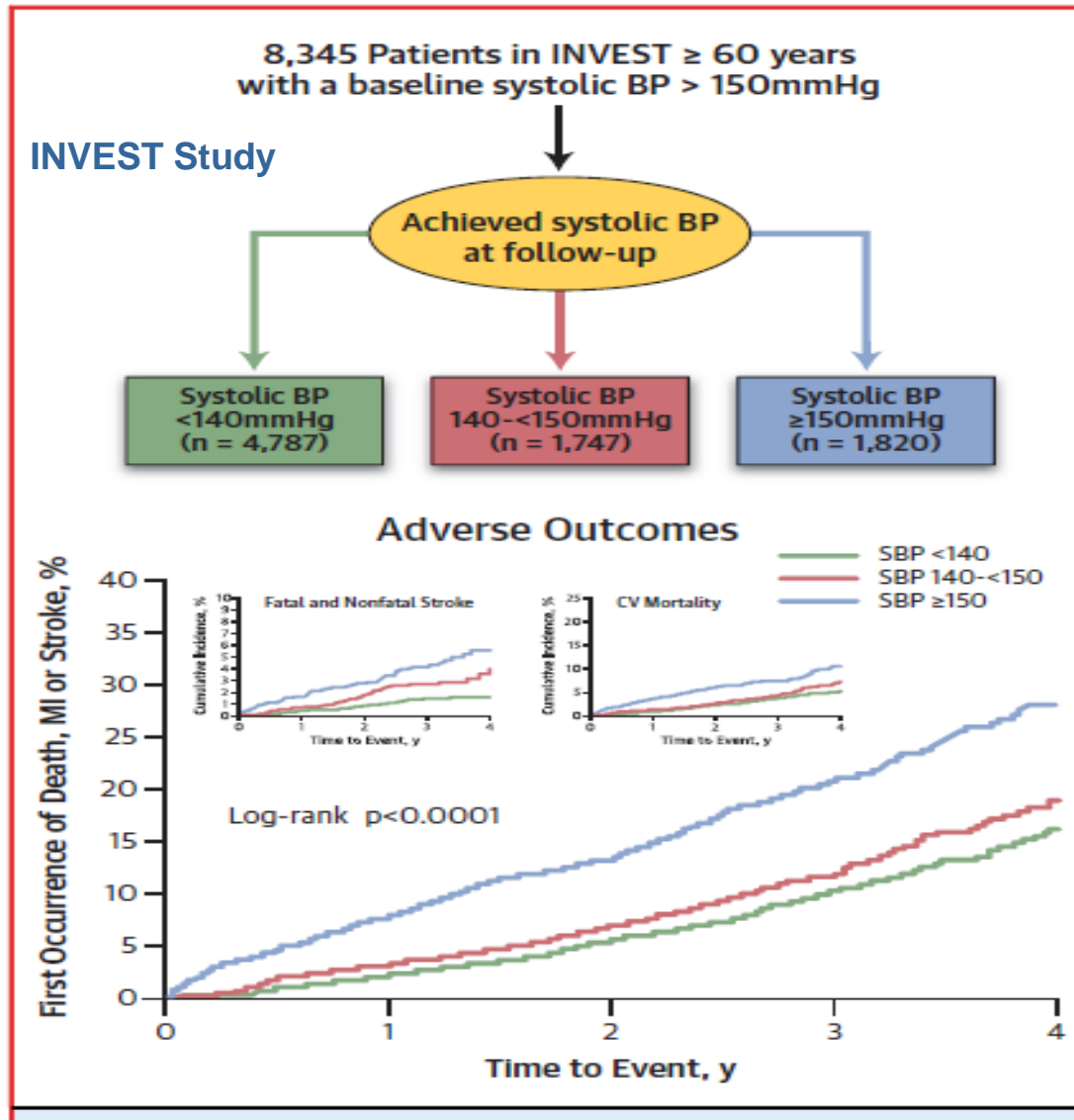
CHD = coronary heart disease; CKD = chronic kidney disease; CV = cardiovascular; DBP = diastolic blood pressure; SBP = systolic blood pressure; TIA = transient ischaemic attack.

<sup>a</sup>Class of recommendation.

<sup>b</sup>Level of evidence.

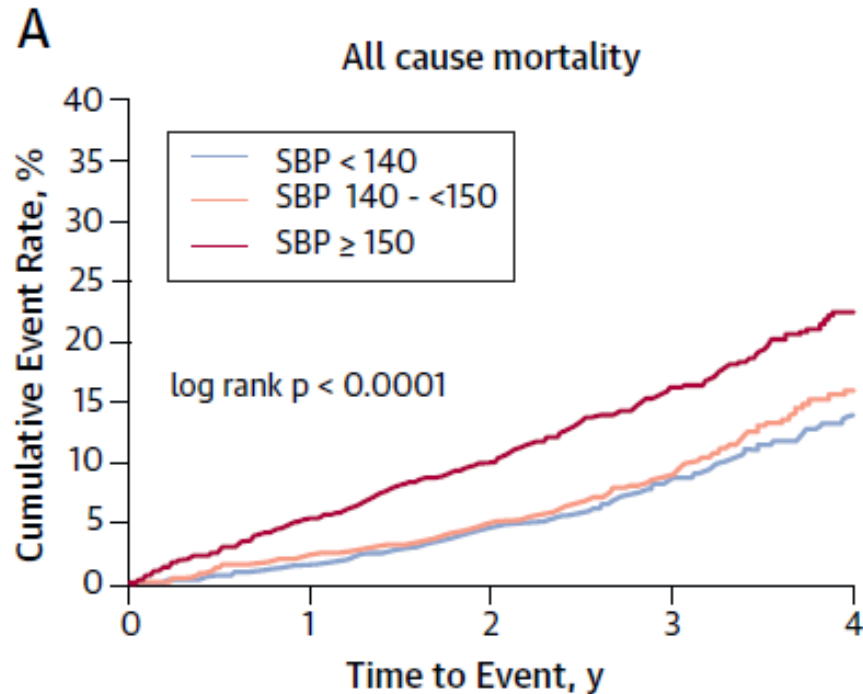
<sup>c</sup>Reference(s) supporting recommendation(s).

# Hypertension: Risk of CV Events According to Systolic BP in Patients $\geq 60$ Years

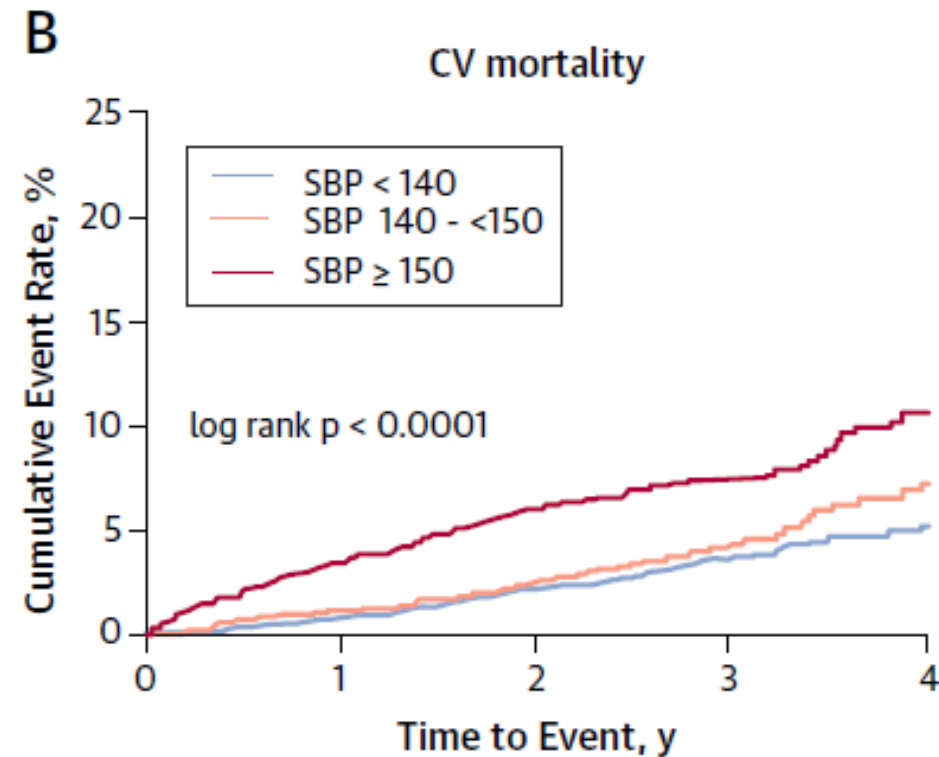




# Hypertension: Risk of CV Events According to Systolic BP in Patients $\geq 60$ Years



## INVEST Study



# INVEST Study: Risk of CV Events According to Systolic BP in Patients $\geq 60$ Years

8,345 Patients in INVEST  $\geq 60$  years  
with a baseline systolic BP  $> 150$  mmHg

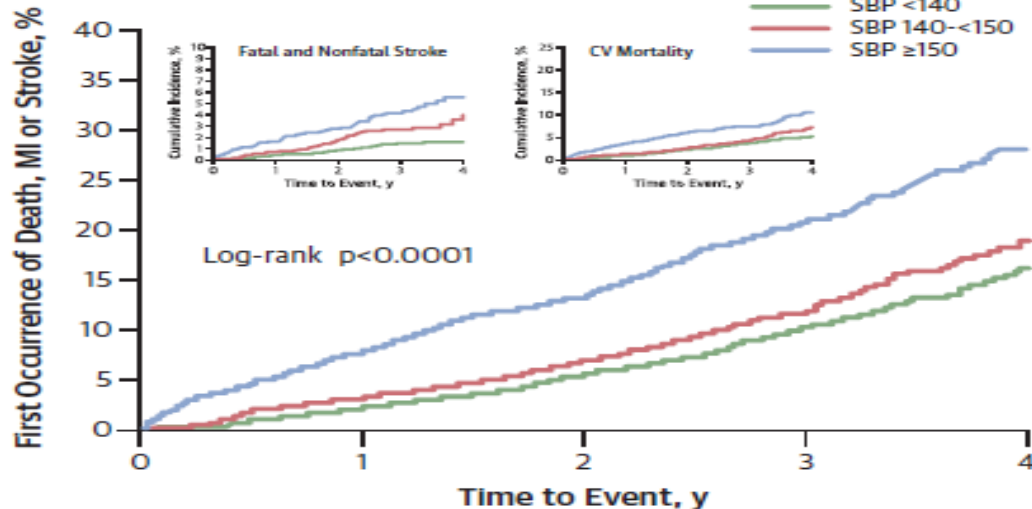
Achieved systolic BP  
at follow-up

Systolic BP  
 $< 140$  mmHg  
(n = 4,787)

Systolic BP  
140- $< 150$  mmHg  
(n = 1,747)

Systolic BP  
 $\geq 150$  mmHg  
(n = 1,820)

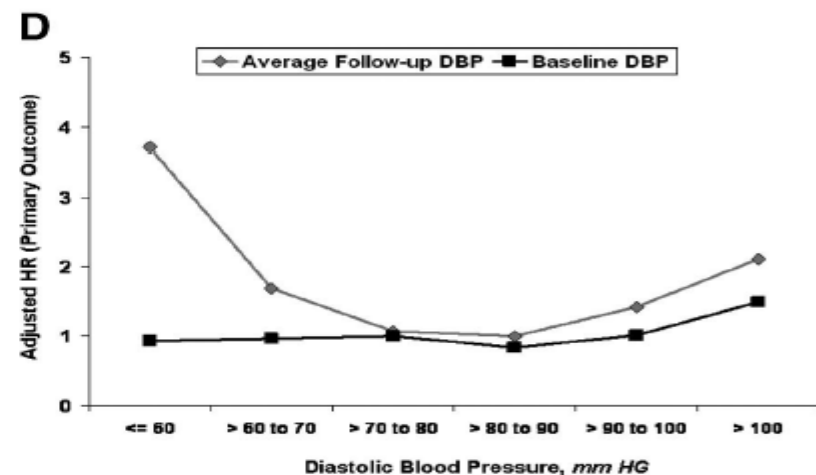
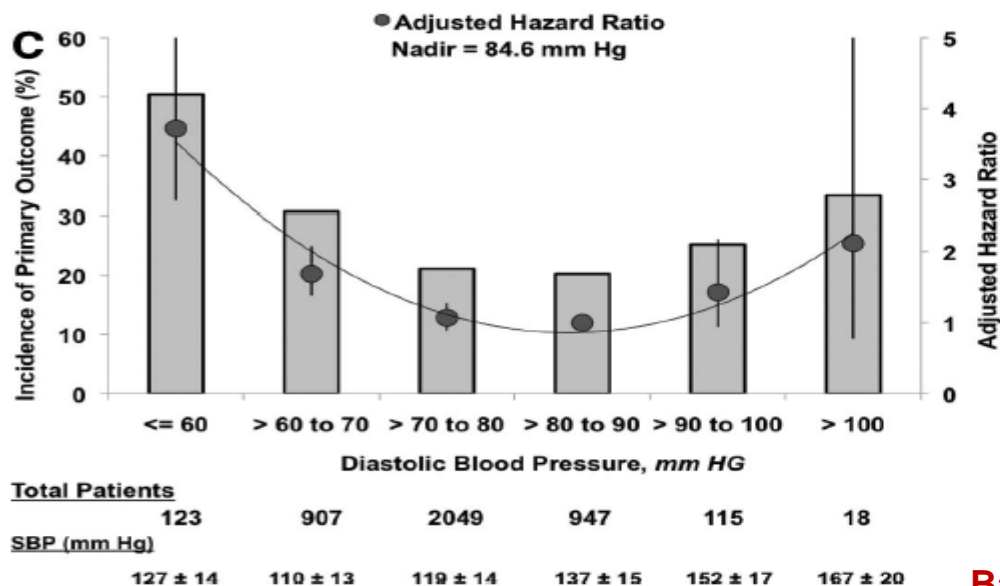
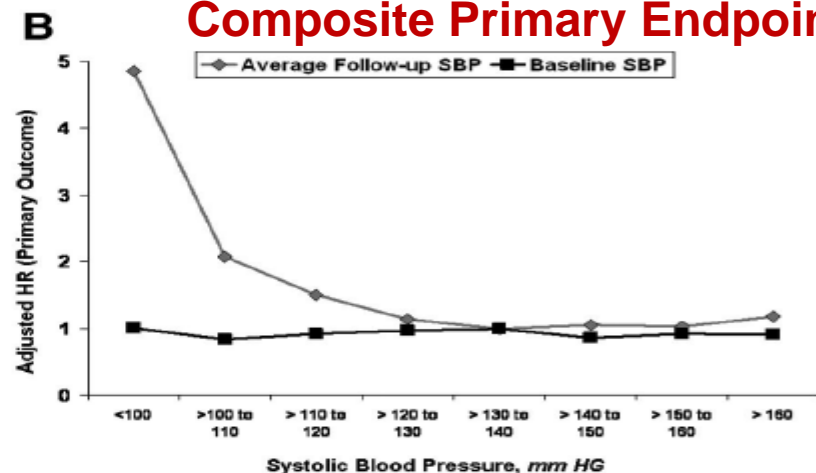
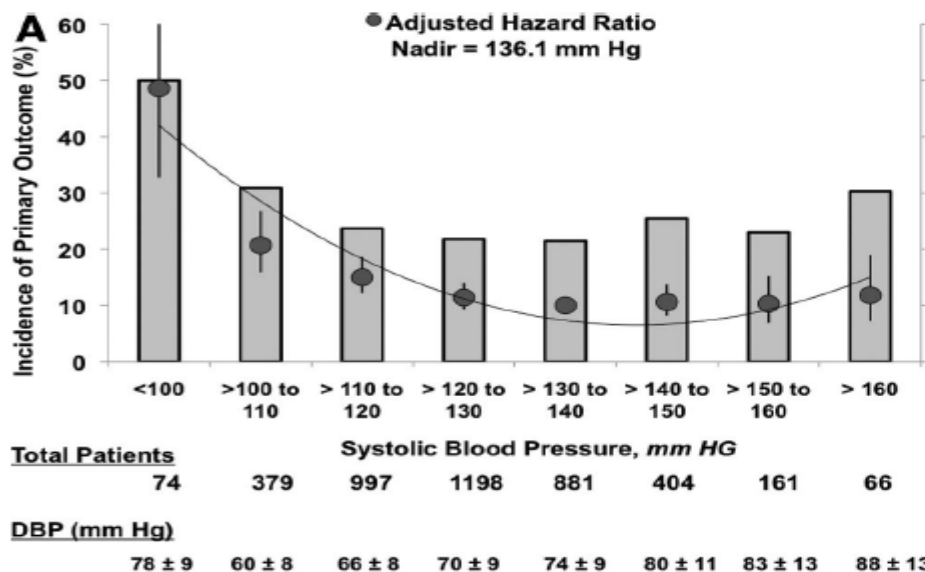
Adverse Outcomes

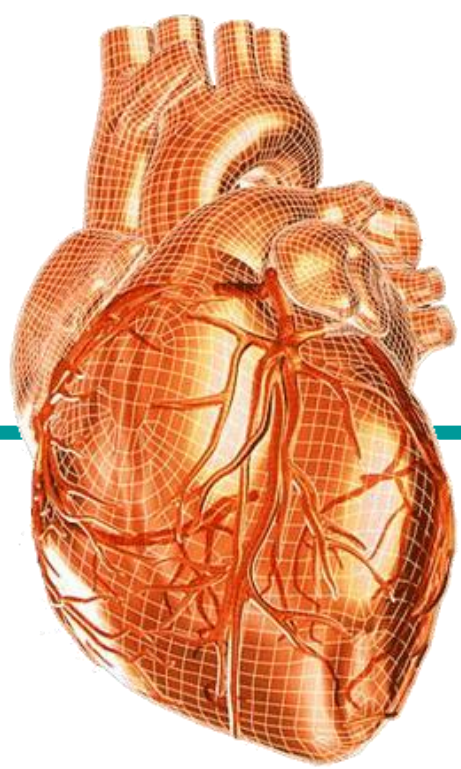


“In **hypertensive patients with CAD** who are  **$\geq 60$  years** of age, achieving a BP target of 140 to  $< 150$  mmHg as recommended by the JNC-8 panel was associated with less benefit than the previously recommended target of  $< 140$  mmHg.”

# J- or U-Shaped Curve Association Between BP and the Risk of Future CV Events After ACS

## PROVE IT-TIMI 22 Trial Composite Primary Endpoint





# ***Feeling the pressure? Managing Hypertension in 2016***

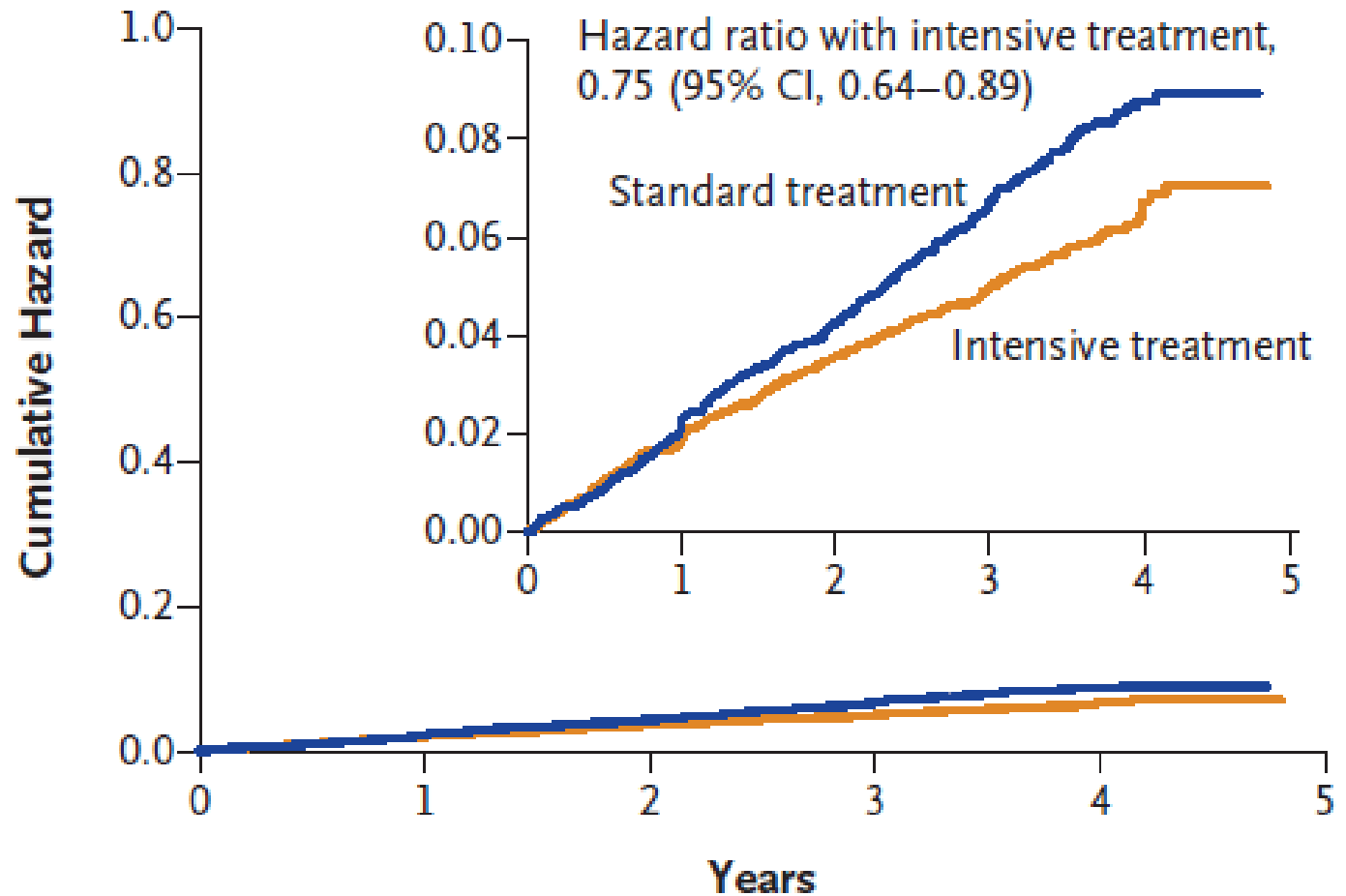
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**Should new hypertension  
goals apply to all?**

# SPRINT

A Randomized Trial of Intensive *versus* Standard Blood Pressure Control

## A Primary Outcome



### No. at Risk

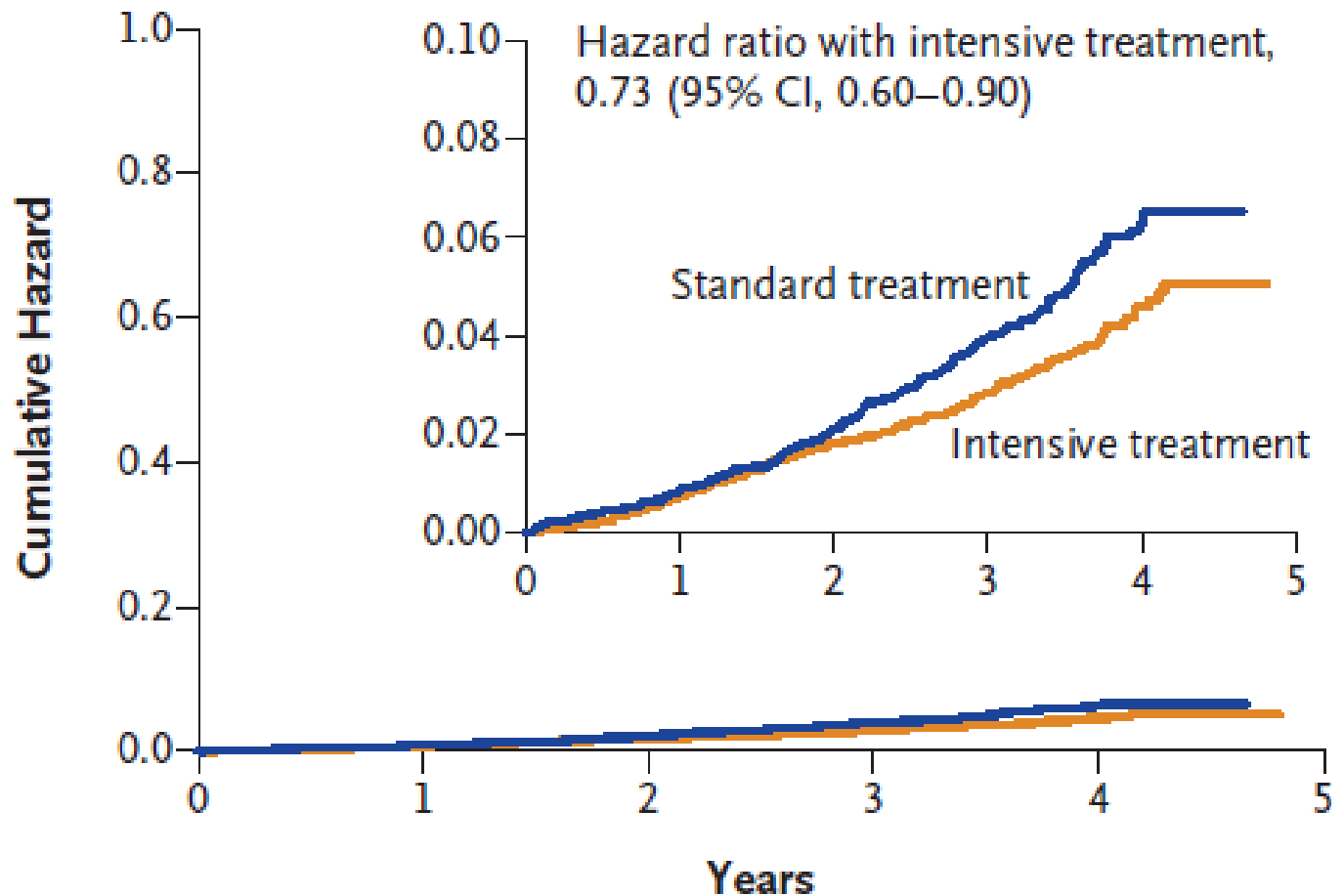
Standard treatment	4683	4437	4228	2829	721
Intensive treatment	4678	4436	4256	2900	779



# SPRINT

A Randomized Trial of Intensive *versus* Standard Blood Pressure Control

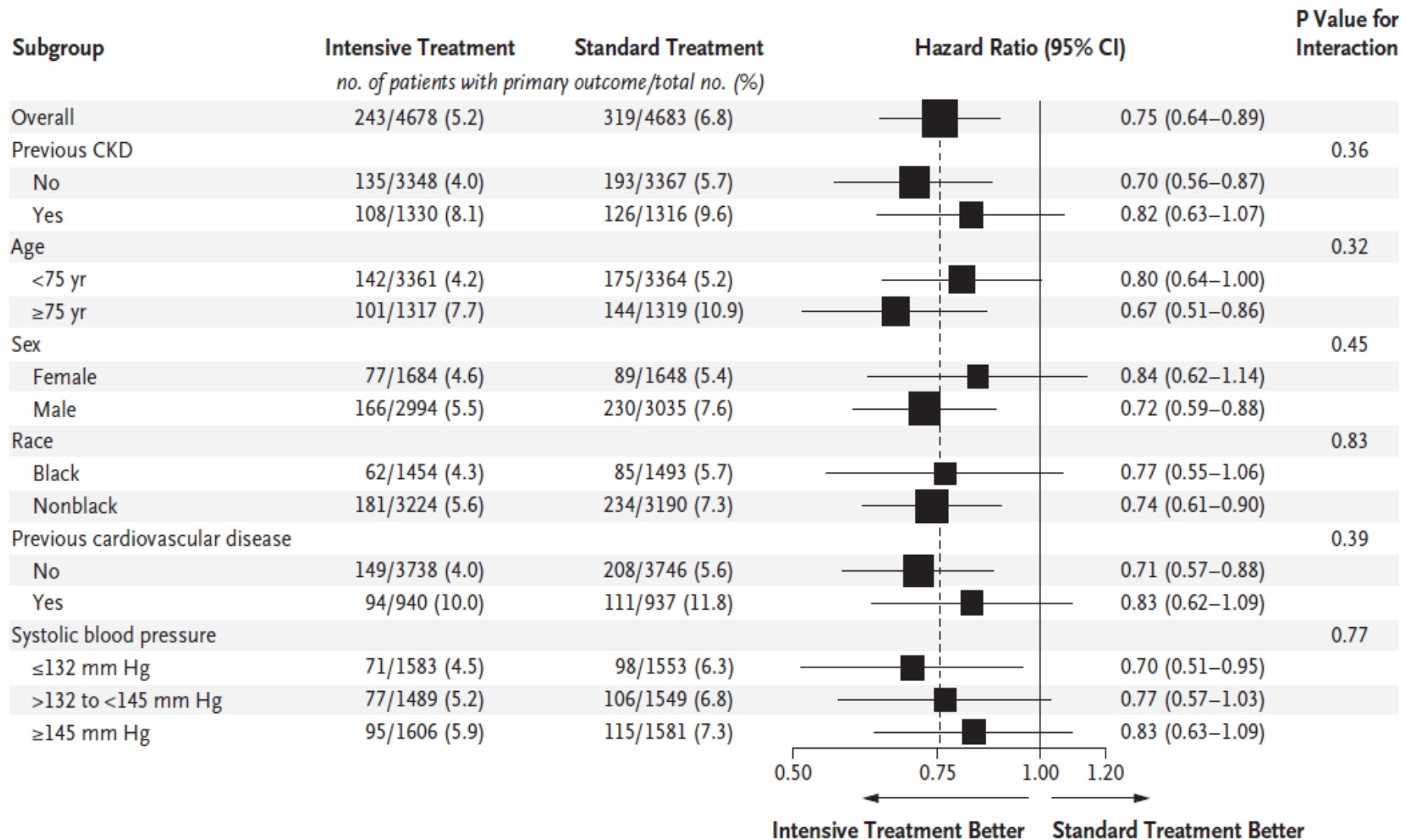
## B Death from Any Cause



### No. at Risk

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

# Forest Plot - Primary Outcome According to Subgroups



**SPRINT Research Group, Wright JT Jr, et al. *N Engl J Med* 2015;373(22):2103-16.**

# A Randomized Trial of Intensive versus Standard Blood-Pressure Control

The SPRINT Research Group\*

## Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: The SPRINT Research Group. A randomized trial of intensive versus standard blood-pressure control. *N Engl J Med* 2015;373:2103-16. DOI: 10.1056/NEJMoa1511939

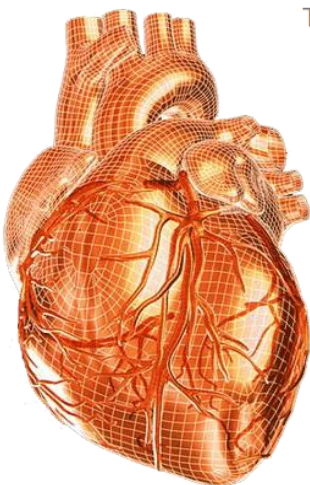
### A RANDOMIZED TRIAL OF INTENSIVE VERSUS STANDARD BLOOD PRESSURE CONTROL

#### SUPPLEMENTARY APPENDIX

**SPRINT Research Group, Wright JT Jr, et al. *N Engl J Med* 2015;373(22):2103-16. Supplementary Appendix.**

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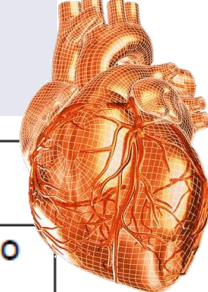
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**Table 3. Serious Adverse Events, Conditions of Interest, and Monitored Clinical Events.**

Variable	Intensive Treatment (N = 4678)	Standard Treatment (N = 4683)	Hazard Ratio	P Value
	<i>no. of patients (%)</i>			
Serious adverse event*	1793 (38.3)	1736 (37.1)	1.04	0.25
Conditions of interest	<b>SPRINT Research Group, Wright JT Jr, et al. <i>N Engl J Med</i> 2015;373(22):2103-16.</b>			
Serious adverse event only				
Hypotension	110 (2.4)	66 (1.4)	1.67	0.001
Syncope	107 (2.3)	80 (1.7)	1.33	0.05
Bradycardia	87 (1.9)	73 (1.6)	1.19	0.28
Electrolyte abnormality	144 (3.1)	107 (2.3)	1.35	0.02
Injurious fall†	105 (2.2)	110 (2.3)	0.95	0.71
Acute kidney injury or acute renal failure‡	193 (4.1)	117 (2.5)	1.66	<0.001
Emergency department visit or serious adverse event				
Hypotension	158 (3.4)	93 (2.0)	1.70	<0.001
Syncope	163 (3.5)	113 (2.4)	1.44	0.003
Bradycardia	104 (2.2)	83 (1.8)	1.25	0.13
Electrolyte abnormality	177 (3.8)	129 (2.8)	1.38	0.006
Injurious fall†	334 (7.1)	332 (7.1)	1.00	0.97
Acute kidney injury or acute renal failure‡	204 (4.4)	120 (2.6)	1.71	<0.001
Monitored clinical events				
Adverse laboratory measure§				
Serum sodium <130 mmol/liter	180 (3.8)	100 (2.1)	1.76	<0.001
Serum sodium >150 mmol/liter	6 (0.1)	0		0.02
Serum potassium <3.0 mmol/liter	114 (2.4)	74 (1.6)	1.50	0.006
Serum potassium >5.5 mmol/liter	176 (3.8)	171 (3.7)	1.00	0.97
Orthostatic hypotension¶				
Alone	777 (16.6)	857 (18.3)	0.88	0.01
With dizziness	62 (1.3)	71 (1.5)	0.85	0.35

Table S5. Serious Adverse Events and Conditions of Interest Classified as Possibly or Definitely Related to the Intervention.



	Intensive (N=4678)	Standard (N=4683)	
	no. of patients (%)	no. of patients (%)	Hazard Ratio (P Value)
Serious Adverse Events <sup>1</sup>	220 (4.7)	118 (2.5)	1.88 (<0.001)
Conditions of Interest			
SAE Only			
Hypotension	83 (1.8)	37 (0.8)	2.52 (<0.001)
Syncope	64 (1.4)	28 (0.6)	2.15 (0.006)
Bradycardia	34 (0.7)	24 (0.5)	1.28 (0.44)
Electrolyte abnormality	69 (1.5)	48 (1.0)	1.58 (0.05)
Injurious fall <sup>2</sup>	19 (0.4)	13 (0.3)	1.99 (0.21)
Acute Kidney Injury or Acute Renal Failure <sup>3</sup>	88 (1.9)	34 (0.7)	3.14 (<0.001)
ER Visit or SAE			
Hypotension	125 (2.7)	58 (1.2)	2.24 (<0.001)
Syncope	94 (2.0)	44 (0.9)	2.13 (0.005)
Bradycardia	51 (1.1)	29 (0.6)	1.68 (0.05)
Electrolyte abnormality	93 (2.0)	62 (1.3)	1.61 (0.02)
Injurious fall <sup>2</sup>	36 (0.8)	23 (0.5)	2.22 (0.05)
Acute Kidney Injury or Acute Renal Failure <sup>3</sup>	96 (2.1)	36 (0.8)	3.13 (<0.001)

1. Defined as an event that was fatal or life threatening, resulting in significant or persistent disability, requiring or prolonging a hospitalization.

2. An Injurious fall was defined as a fall that resulted in **evaluation in an emergency department** or resulted in **hospitalization**.

**SPRINT Research Group, Wright JT Jr, et al. N Engl J Med 2015;373(22):2103-16. Supplementary Appendix.**



# SPRINT

## A Randomized Trial of Intensive *versus* Standard Blood Pressure Control

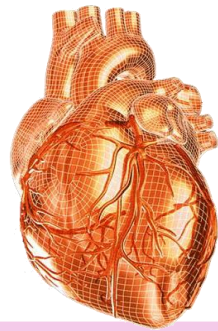


Table S2. Utilization of Antihypertensive Medication Classes at Most Recent Visit

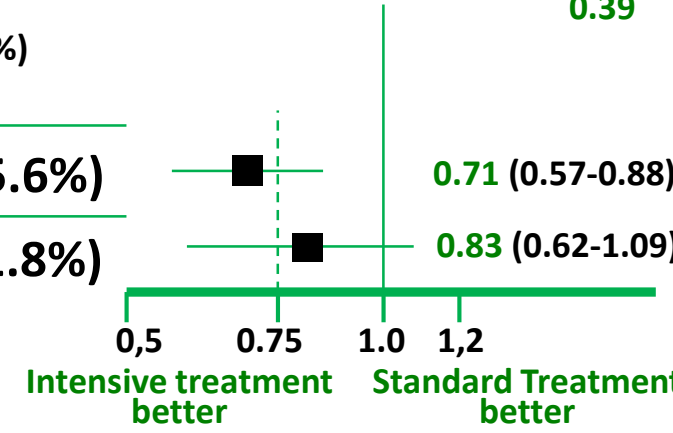
	<i>Intensive</i> (N=4678)	<i>Standard</i> (N=4683)
Number of agents		
Average	2.7 (1.2)	1.8 (1.1)
0	125 (2.7)	530 (11.3)
1	493 (10.5)	1455 (31.1)
2	1429 (30.5)	1559 (33.3)
3	1486 (31.8)	807 (17.2)
4+	1137 (24.3)	323 (6.9)

## SPRINT Study - Demographic Characteristics

	Intensive treatment (n= 4678)	Standard Treatment (n= 4683)
Presence of Cardiovascular Disease - N° (%)	940 (20.1)	937 (20.0)
Clinical	776 (16.7)	783 (16.7)
Subclinical	247 (5.3)	246 (5.3)

## SPRINT Study - Primary Endpoint in Patients with and without Previous CV Disease

	Intensive treatment	Standard Treatment	Hazard Ratio (95% CI)	p-value of interaction
Previous Cardiovascular Disease	# de patients with primary endpoint / (%)			0.39
No	149/3738 (4.0%)	208/3746 (5.6%)	0.71 (0.57-0.88)	
Yes	94/940 (10.0%)	111/937 (11.8%)	0.83 (0.62-1.09)	



0,5 0,75 1,0 1,2

Intensive treatment better Standard Treatment better

Incidence of Primary Endpoint in SPRINT Study with and without Previous CV Disease  
Based on SPRINT Research Group. [Wright et al. N Engl J Med 2015;373\(22\):2103-16.](#)

# Intensive vs Standard Blood Pressure Control and Cardiovascular Disease Outcomes in Adults Aged $\geq 75$ Years

## A Randomized Clinical Trial

Jeff D. Williamson, MD, MHS; Mark A. Supiano, MD; William B. Applegate, MD, MPH; Dan R. Berlowitz, MD; Ruth C. Campbell, MD, MSPH; Glenn M. Chertow, MD; Larry J. Fine, MD; William E. Haley, MD; Amret T. Hawfield, MD; Joachim H. Ix, MD, MAS; Dalane W. Kitzman, MD; John B. Kostis, MD; Marie A. Krousel-Wood, MD; Lenore J. Launer, PhD; Suzanne Oparil, MD; Carlos J. Rodriguez, MD, MPH; Christianne L. Rourke, MD, MPH; Ronald I. Shorr, MD, MS; Kaycee M. Sink, MD, MAS; Virginia G. Wadley, PhD; Paul K. Whelton, MD; Jeffrey Whittle, MD; Nancy F. Woolard; Jackson T. Wright Jr, MD, PhD; Nicholas M. Pajewski, PhD; for the SPRINT Research Group

### Serious Adverse Events

Detailed information regarding SAEs appears in eTable 3 and eTable 4 in [Supplement 2](#). Data on SAEs in participants older than 75 years have been previously reported (Table S6<sup>13</sup>). In the intensive treatment group, SAEs occurred in 637 participants (48.4%) compared with 637 participants (48.3%) in the standard treatment group (HR, 0.99 [95% CI, 0.89-1.11];  $P = .90$ ). The absolute rate of SAEs was higher but was not statistically significantly different in the intensive treatment group for hypotension (2.4% vs 1.4% in the standard treatment group; HR, 1.71 [95% CI, 0.97-3.09]), syncope (3.0% vs 2.4%, respectively; HR, 1.23 [95% CI, 0.76-2.00]), electrolyte abnormalities (4.0% vs 2.7%; HR, 1.51 [95% CI, 0.99-2.33]), and acute kidney injury or renal failure (5.5% vs 4.0%; HR, 1.41 [95% CI, 0.98-2.04]). However, the absolute rate of injurious falls was lower but was not statistically significantly different in the intensive treatment group (4.9% vs 5.5% in the standard treatment group; HR, 0.91 [95% CI, 0.65-1.29]).

**SPRINT Research Group**

**Williamson JD, et al. *JAMA* 2016;315(24):2673-82.**

## SPRINT - Serious adverse events, conditions of interest, and monitored clinical measures by treatment group in SPRINT participants 75 years or older

	Intensive-treatment		Standard-treatment		HR (95% CI)	p-value
	N	N with event (%)	N	N with event (%)		
<b>Serious Adverse Events<sup>1</sup></b>	1,317	637 (48.4)	1,319	637 (48.3)	0.99 (0.89, 1.11)	0.895
By Frailty Status						
Fit	159	50 (31.4)	190	66 (34.7)	0.84 (0.53, 1.31)	0.439
Less Fit	711	333 (46.8)	745	341 (45.8)	0.97 (0.83, 1.14)	0.714
Frail	440	251 (57.0)	375	227 (60.5)	1.02 (0.84, 1.24)	0.844
By Gait Speed						
≥0.8 m/s	880	419 (47.6)	893	412 (46.1)	1.03 (0.89, 1.18)	0.716
<0.8 m/s	371	187 (50.4)	369	195 (52.8)	1.00 (0.80, 1.25)	0.988
Missing	66	31 (47.0)	57	30 (52.6)	0.79 (0.42, 1.50)	0.469
<b>Individual Conditions of Interest (ER Visit or SAE)</b>						
Hypotension	1,317	44 (3.3)	1,319	27 (2.0)	1.66 (1.03, 2.73)	0.039
Syncope	1,317	57 (4.3)	1,319	43 (3.3)	1.28 (0.85, 1.92)	0.240
Bradycardia	1,317	47 (3.6)	1,319	44 (3.3)	1.01 (0.67, 1.54)	0.961
Electrolyte Abnormality	1,317	60 (4.6)	1,319	43 (3.3)	1.44 (0.97, 2.16)	0.067
Injurious Fall <sup>3</sup>	1,317	153 (11.6)	1,319	186 (14.1)	0.80 (0.64, 0.99)	0.040
Acute Kidney Injury or Acute Renal Failure <sup>4</sup>	1,317	73 (5.5)	1,319	55 (4.2)	1.39 (0.97, 1.99)	0.072
<b>Monitored Clinical Events</b>						
Laboratory Measures <sup>5</sup>						
Sodium<130 mmol/L	1,317	69 (5.2)	1,319	45 (3.4)	1.56 (1.07, 2.30)	0.02
Sodium>150 mmol/L	1,317	1 (0.1)	1,319	0 (0.0)	-	-
Potassium<3 mmol/L	1,317	17 (1.3)	1,319	11 (0.8)	1.50 (0.69, 3.37)	0.303
Potassium>5.5 mmol/L	1,317	69 (5.2)	1,319	65 (4.9)	1.01 (0.71, 1.42)	0.972
Signs and Symptoms						
Orthostatic hypotension <sup>6</sup>	1,317	277 (21.0)	1,319	288 (21.8)	0.90 (0.76, 1.07)	0.241
Orthostatic hypotension with dizziness	1,317	25 (1.9)	1,319	17 (1.3)	1.44 (0.77, 2.73)	0.252

## Let's Not SPRINT to Judgment About New Blood Pressure Goals

Eduardo Ortiz, MD, MPH, and Paul A. James, MD

Ortiz E, James PA. *Ann Intern Med* 2016 May;164(10):692-3

**S**PRINT (Systolic Blood Pressure Intervention Trial), a randomized controlled trial that compared aggressive treatment (systolic blood pressure <120 mm Hg) with standard treatment (systolic blood pressure <160 mm Hg) in patients who had not reached the primary reduction goal, found that aggressive treatment resulted in a significant reduction in cardiovascular events. However, the trial was stopped early because of a high rate of adverse events in the aggressive treatment group. The trial was stopped early because of a high rate of adverse events in the aggressive treatment group. The trial was stopped early because of a high rate of adverse events in the aggressive treatment group.

On the basis of the SPRINT trial, the goal of less than 120 mm Hg, an aggressive goal, will be the target for most patients. The benefits of aggressive treatment will be the same as the benefits of standard treatment. The benefits of aggressive treatment will be the same as the benefits of standard treatment. The benefits of aggressive treatment will be the same as the benefits of standard treatment.

SPRINT was a clinical trial with a goal of only 2.2% reduction in cardiovascular events. The trial was stopped early because of a high rate of adverse events in the aggressive treatment group. The trial was stopped early because of a high rate of adverse events in the aggressive treatment group. The trial was stopped early because of a high rate of adverse events in the aggressive treatment group.

However, the small decrease in cardiovascular events in the aggressive treatment group was not statistically significant. The trial was stopped early because of a high rate of adverse events in the aggressive treatment group. The trial was stopped early because of a high rate of adverse events in the aggressive treatment group. The trial was stopped early because of a high rate of adverse events in the aggressive treatment group.

This article was published at [www.annals.org](http://www.annals.org) on 23 Feb

cluded significant increases in hypotension, syncope, electrolyte abnormalities, and acute kidney injury.

PURLs®

Priority Updates from the Research Literature  
from the Family Physicians Inquiries Network

*J Fam Pract* 2016 May; 65(5): 342–344.

**Margaret Day, MD, MSPH; James J. Stevermer, MD, MSPH**  
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## “Go low” or say “No” to aggressive systolic BP goals?

The SPRINT trial demonstrated the benefits—and risks—of reaching a systolic target <120 mm Hg in non-diabetic patients at high risk for CV events. Here's who might benefit.

ORIGINAL RESEARCH

*J Am Heart Assoc* 2016 Jul 12;5(7). pii: e003547. doi: 10.1161/JAHA.116.003547.

## Prevalence of Eligibility Criteria for the Systolic Blood Pressure Intervention Trial in US Adults Among Excluded Groups: Age <50 Years, Diabetes Mellitus, or a History of Stroke

Adam P. Bress, PharmD, MS; Rikki M. Tanner, PhD, MPH; Rachel Hess, MD, MS; Samuel S. Gidding, MD; Lisandro D. Colantonio, MD, MS; Daichi Shimbo, MD; Paul Muntner, PhD





# Intensive vs Standard Blood Pressure Control and Cardiovascular Disease Outcomes in Adults Aged $\geq 75$ Years

## A Randomized Clinical Trial

Jeff D. Williamson, MD, MHS; Mark A. Supiano, MD; William B. Applegate, MD, MPH; Dan R. Berlowitz, MD; Ruth C. Campbell, MD, MSPH; Glenn M. Chertow, MD; Larry J. Fine, MD; William E. Haley, MD; Amret T. Hawfield, MD; Joachim H. Ix, MD, MAS; Dalane W. Kitzman, MD; John B. Kostis, MD; Marie A. Krousel-Wood, MD; Lenore J. Launer, PhD; Suzanne Oparil, MD; Carlos J. Rodriguez, MD, MPH; Christianne L. Rourke, MD, MPH; Ronald I. Shorr, MD, MS; Kaycee M. Sink, MD, MAS; Virginia G. Wadley, PhD; Paul K. Whelton, MD; Jeffrey Whittle, MD; Nancy F. Woolard; Jackson T. Wright Jr, MD, PhD; Nicholas M. Pajewski, PhD; for the SPRINT Research Group

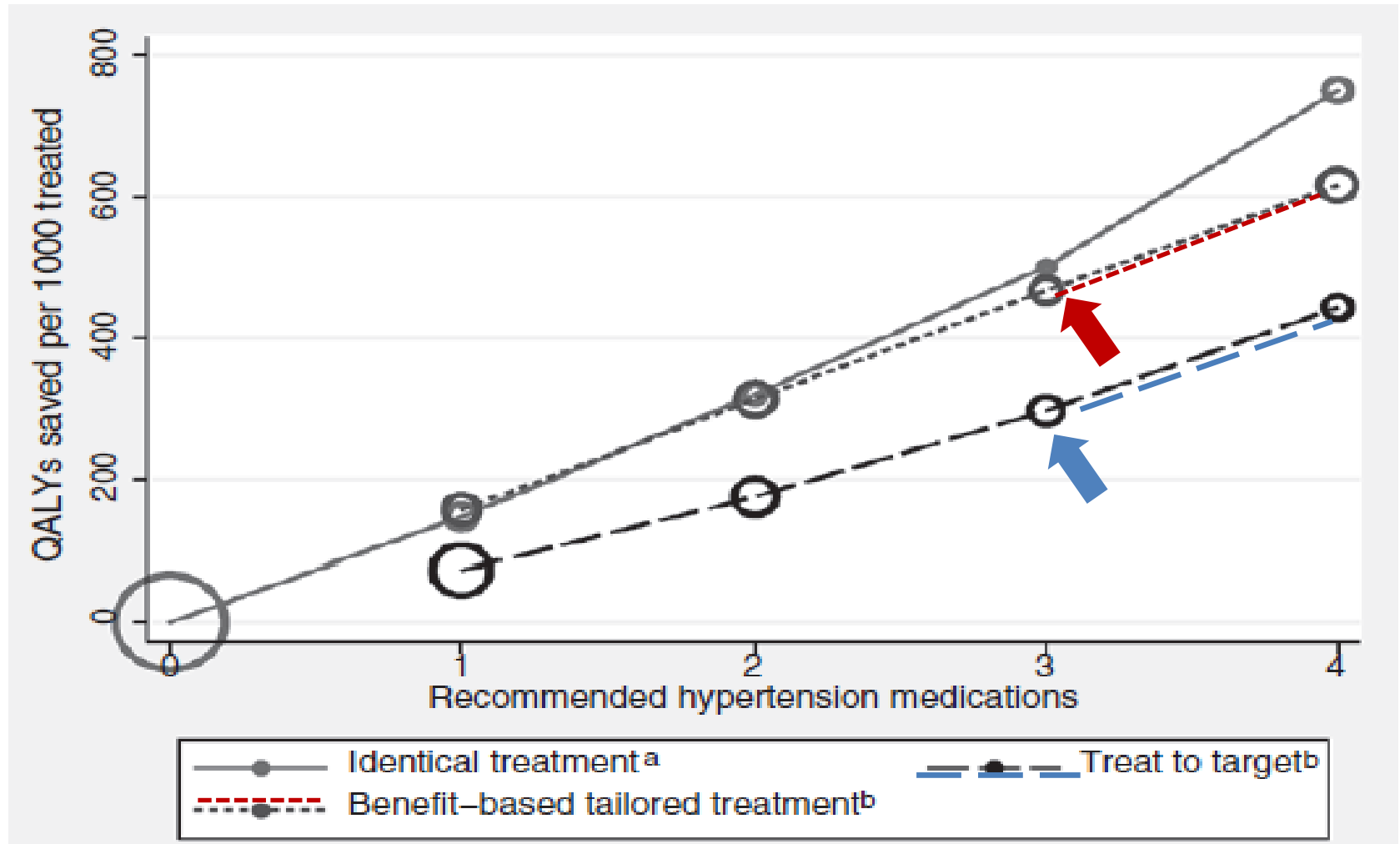
of SPRINT data may be helpful to better define the burden, costs, and benefits of intensive BP control. However, the present results have substantial implications for the future of intensive BP therapy in older adults because of this condition's high prevalence, the high absolute risk for cardiovascular disease complications from elevated BP, and the devastating consequences of such events on the independent function of older people.<sup>3,29,33,34</sup>

34. Sussman J, Vijan S, Hayward R. Using benefit-based tailored treatment to improve the use of antihypertensive medications. *Circulation*. 2013;128(21):2309-2317.

# Hypertension

## Benefit-based Tailored Treatment

Benefit-based Tailored Treatment (BTT) *versus* Treat to Target Strategy



# Hypertension

## Benefit-based Tailored Treatment

Better results

### Preventive Cardiology

## Using Benefit-Based Tailored Treatment to Improve the Use of Antihypertensive Medications

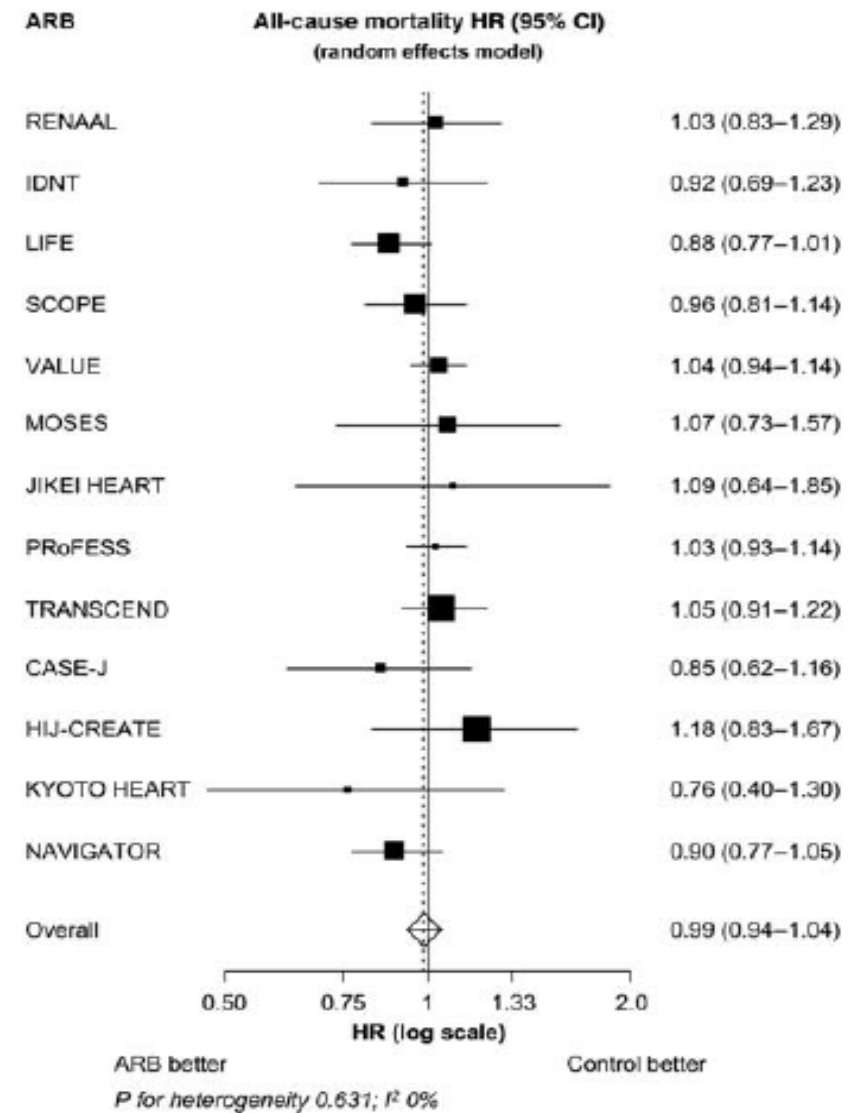
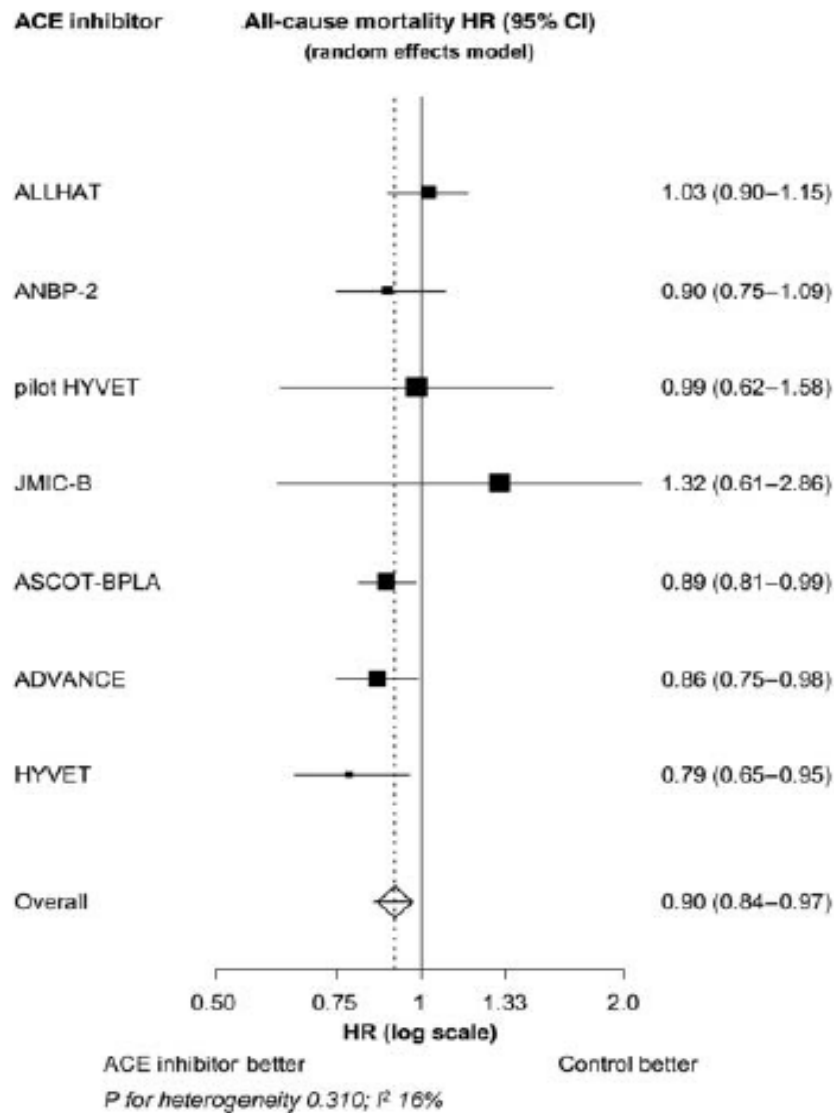
Jeremy Sussman, MD, MS; Sandeep Vijan, MD, MS; Rod Hayward, MD

In summary, the results of the present study suggest that CVD events can be prevented more effectively with a more comprehensive accounting for all available factors that contribute to net patient benefit, such as other clinical risk factors and polypharmacy, rather than by chiefly basing decisions on whether the observed BP level is above or below a prespecified BP target. The next wave of clinical treatment strategies may be more efficient, effective, and transparent, with a full assessment of risk and benefit and the use of BTT.

Sussman J, et al. *Circulation* 2014; 128: 2309-17

# Angiotensin-converting enzyme inhibitors reduce mortality in hypertension: a meta-analysis of randomized clinical trials of renin-angiotensin-aldosterone system inhibitors involving 158 998 patients

## All-Cause Mortality



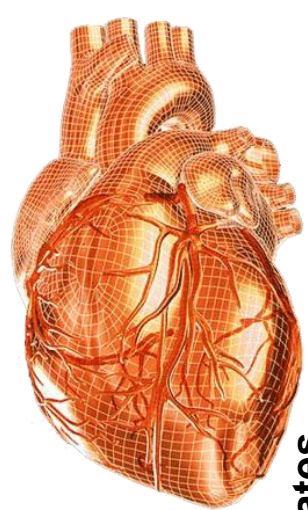
# Effects of blood pressure-lowering on outcome incidence in hypertension: 5. Head-to-head comparisons of various classes of antihypertensive drugs – overview and meta-analyses

Costas Thomopoulos<sup>a</sup>, Gianfranco Parati<sup>b</sup>, and Alberto Zanchetti<sup>c</sup>

## Head-to-Head Comparisons of Various Antihypertensive Classes

Outcome	Trials (n)	Events (n/patients)		Difference SBP/DBP (mmHg)	RR (95% CI)	RR (95% CI)	P (Heterogen)
		ACE-Inhibitors	Controls	(a) ACE-Inhibitors vs Angiotensin Receptor Blockers			
Stroke	3	413/8886	377/8842	1.01/0.61	1.09 (0.95–1.25)		0.95
CHD	3	423/8886	453/8842	1.01/0.61	0.93 (0.82–1.06)		0.72
HF	3	364/8886	406/8842	1.01/0.61	0.89 (0.78–1.02)		0.90
Stroke + CHD	3	836/8886	830/8842	1.01/0.61	1.00 (0.91–1.10)		0.70
Stroke + CHD + HF	3	1200/8886	1236/8842	1.01/0.61	0.97 (0.90–1.04)		0.60
CV Death	2	605/8706	601/8662	1.03/0.63	1.00 (0.90–1.12)		0.59
All-cause Death	2	1020/8706	995/8662	1.03/0.63	1.02 (0.94–1.11)		0.82
				(b) ACE Inhibitors vs All Other Drug Classes			
Stroke	20	1468/32381	2203/49740	1.55/0.65	1.08 (1.02–1.14)*		0.39
CHD	20	1696/32360	3325/49741	1.55/0.65	0.91 (0.83–0.99)*		0.09
HF	15	1299/31118	2522/48484	1.56/0.66	0.89 (0.80–1.01)*		< 0.01
Stroke + CHD	20	3171/32583	5538/49956	1.55/0.65	0.98 (0.91–1.04)*		0.02
Stroke + CHD + HF	14	4417/31019	7991/48397	1.57/0.67	0.95 (0.89–1.02)*		< 0.01
CV Death	21	1693/32619	2894/50190	1.50/0.63	1.01 (0.95–1.06)*		0.96
All-cause Death	21	3267/32507	5768/50078	1.54/0.65	1.01 (0.98–1.04)*		0.99
				0.5 1.0 2.0 ACE-Inhibitors better Controls better			

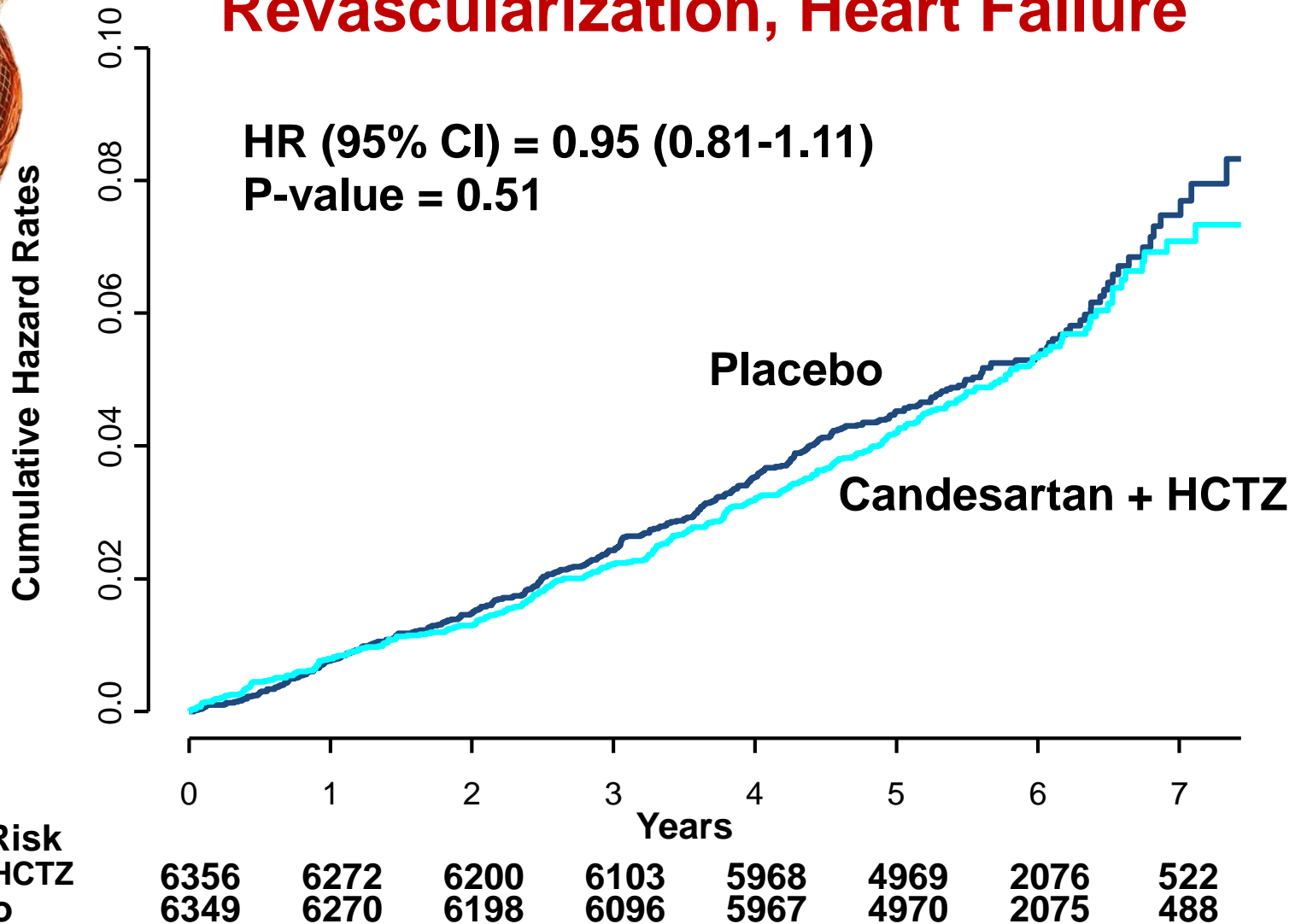


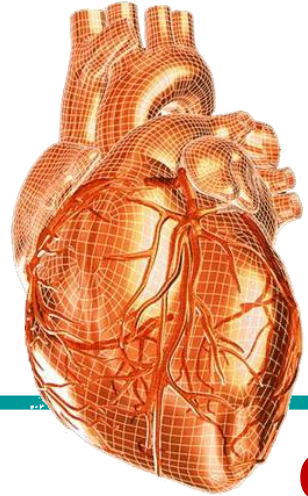


## HOPE 3

**CV Death, MI, Stroke, Cardiac Arrest,  
Revascularization, Heart Failure**

**HR (95% CI) = 0.95 (0.81-1.11)**  
**P-value = 0.51**

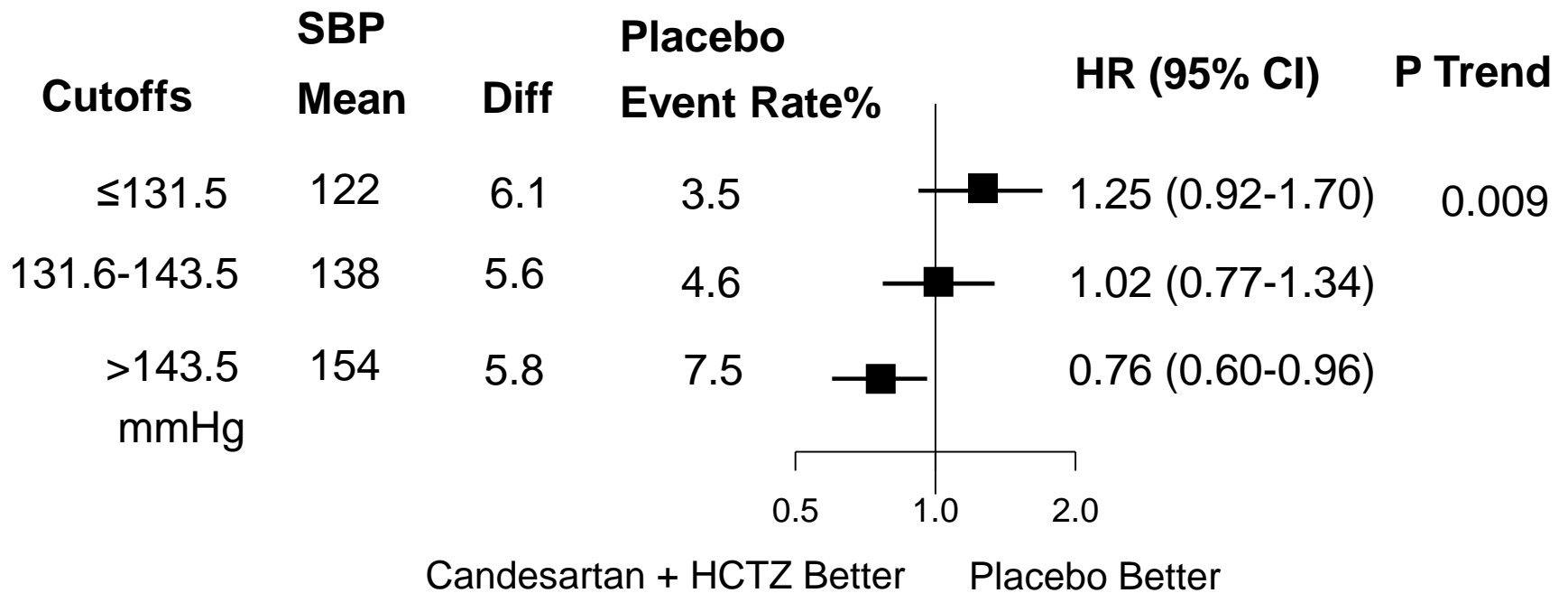




# HOPE 3

## Prespecified subgroups by tertiles of SBP

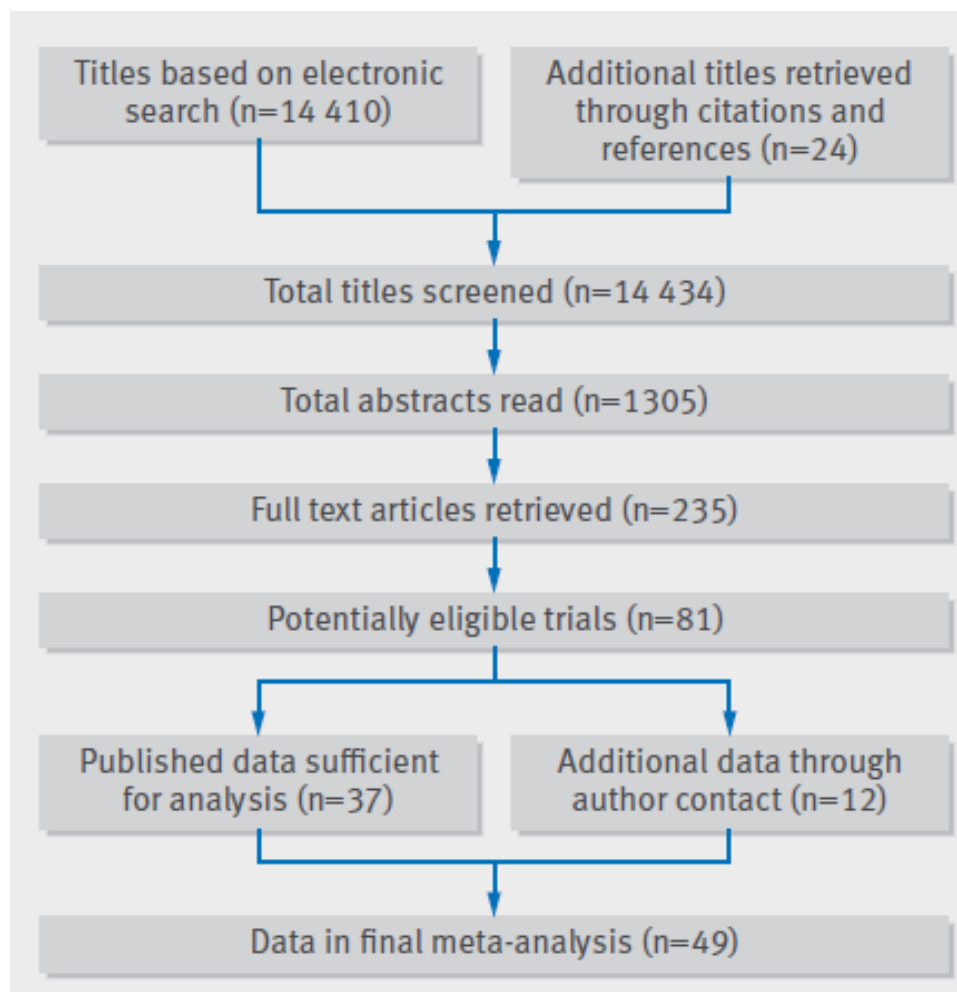
**CV Death, MI, Stroke, Cardiac Arrest, Revasc, HF**





# Effect of antihypertensive treatment at different blood pressure levels in patients with diabetes mellitus: systematic review and meta-analyses

Mattias Brunström, Bo Carlberg





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# Effect of antihypertensive treatment at different blood pressure levels in patients with diabetes mellitus: systematic review and meta-analyses

**Table 1 | Characteristics of included studies**

Study ID	No of participants	Comorbidities	Intervention group	Control group	Baseline SBP/DBP (mm Hg)	Mean in-treatment difference SBP/DBP (mm Hg)
ABCD-2V <sup>20</sup>	129	6% with previous cardiovascular disease	DBP <75 mm Hg, using valsartan	DBP 80-90 mm Hg using placebo	126/84.7	6/5
ABCD-H <sup>21</sup>	470	53% with previous cardiovascular disease, 60% with retinopathy	DBP <75 mm Hg	DBP <90 mm Hg	155/98	6/8
ABCD-N <sup>22</sup>	480	29% with previous cardiovascular disease, 50% with retinopathy	10 mmHg DBP reduction	Placebo	136.4/84.4	9/6
ACCORD <sup>23</sup>	4733	34% with previous cardiovascular disease	SBP <120 mm Hg	SBP <140 mm Hg	139.2/75.95	14.2/6.1
ACTION <sup>24, 25</sup>	1113	Stable angina in all patients, 51% with myocardial infarction	Nefedipine 60 mg	Placebo	141/80	6/3
ADVANCE <sup>26, 27</sup>	11 140	32% with previous cardiovascular disease	Perindopril 4 mg and indapamide 1.25 mg	Placebo	145/81	5.6/2.2
ALTITUDE <sup>28</sup>	8561	Chronic kidney disease in all patients, 42% with cardiovascular disease	Aliskiren 300 mg	Placebo	137.3/74.2	1.3/0.6
ATLANTIS <sup>29</sup>	140	Microalbuminuria in all patients, no data on cardiovascular disease	Ramipril 1.25 mg or 5.0 mg	Placebo	132.9/76.9	6/3.5
BENEDICT <sup>30</sup>	1204	No data on previous cardiovascular disease	Trandolapril 2 mg, verapamil 240 mg, or combination treatment 2/180 mg	Placebo	150.8/87.5	2.3/2
BENEDICT-B <sup>31</sup>	281	Microalbuminuria in all patients, no data on cardiovascular disease	Verapamil 180 mg and trandolapril 2 mg	Trandolapril 2 mg	150/86.7	0.8/0.7
CAMELOT <sup>32</sup>	364	Coronary artery disease in all patients	Amlodipine 10 mg or enalapril 20 mg	Placebo	133/77.4	4.2/1.8
DEMAND <sup>33</sup>	380	Microalbuminuria in all patients, no data on cardiovascular disease	Manidipine 10 mg+delapril 30 mg or delapril alone	Placebo	147.9/87.3	1.4/1.9
DIABHYCAR <sup>34</sup>	4912	Microalbuminuria in all patients, 24% with cardiovascular disease	Ramipril 1.25 mg	Placebo	145.4/82.3	1.3/0.7
DIRECT-P2 <sup>35</sup>	1905	Retinopathy in all patients, 6% with cardiovascular disease	Candesartan 16 mg	Placebo	132.9/78	3.3/1.3
EWPH <sup>36</sup>	111	64% with previous cardiovascular disease	Hydrochlorothiazide 25 mg and triamterene 50 mg	Placebo	186.8/101.2	16.1/5.3
FEVER <sup>37</sup>	1241	42% with previous cardiovascular disease	Felodipine 5 mg	Placebo	155.3/90.2	4.6/1.8
Fogari –02 <sup>38</sup>	309	Microalbuminuria in all patients, no cardiovascular disease	Amlodipine 5-10 mg and fosinopril 15-30 mg	Amlodipine 5-15 mg or fosinopril 10-30 mg	160.4/99.3	9.0/4.6
HDFP <sup>39</sup>	1079	8% with previous cardiovascular disease	DBP <90 mm Hg or 10 mm Hg DBP reduction by diuretic	Referred care	158.7/101.1	10/6
HOT <sup>40</sup>	1501	3% with previous cardiovascular disease	DBP <80 mm Hg	DBP <85 or DBP <90 mm Hg	174.1/105.3	3.4/2.9
HSCS <sup>41</sup>	162	Previous stroke/transient ischaemic attack in all patients	Deserpidine 0.5 mg and methyclo-thiazide 5-10 mg	Placebo	167/100	25/12.3
IDNT <sup>42</sup>	1715	Diabetic nephropathy in all patients, 29% with cardiovascular disease	Irbesartan 300 mg or amlodipine 10 mg	Placebo	159/87	3.5/3
IRMA 2 <sup>43</sup>	590	Microalbuminuria in all patients, 27% with cardiovascular disease	Irbesartan 150 mg or 300 mg	Placebo	153/90.3	2/0
JATOS <sup>44</sup>	327	7% with previous cardiovascular disease	SBP <140 mm Hg	SBP 140-160 mm Hg	172.3/87.3	5.6/0.9
Laffel –95 <sup>45</sup>	143	Microalbuminuria in all patients, no cardiovascular disease	Captopril 50 mg	Placebo	120.8/78.5	7/6
Lewis –93 <sup>46</sup>	409	Diabetic nephropathy in all patients, no cardiovascular disease	Captopril 75 mg	Placebo	138.5/85.5	1.5/2.5
MERIT-HF <sup>47</sup>	985	Heart failure NYHA II-IV in all patients	Metoprolol CR/XL 200 mg	Placebo	132/78	No data
MICRO-HOPE <sup>48</sup>	3577	69% with previous cardiovascular disease	Ramipril 10 mg	Placebo	142/79.7	3.8/0.9
ORIENT <sup>49</sup>	577	Diabetic nephropathy in all patients, 16% with cardiovascular disease	Olmesartan 10-40 mg	Placebo	138.8/76.2	3.8/1.4


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# Effect of antihypertensive treatment at different blood pressure levels in patients with diabetes mellitus: systematic review and meta-analyses

PEACE <sup>50</sup>	1386	Stable coronary artery disease in all patients	Trandolapril 4 mg	Placebo	135.3/76.6	1.5/0.9
PERSUADE <sup>51</sup>	1502	Stable coronary artery disease in all patients	Perindopril 8 mg	Placebo	140.1/81.6	4.6/1.8
PHARAO <sup>52</sup>	135	No data on previous cardiovascular disease	Ramipril 5 mg	Placebo	135.5/84.1	1.5/0
PROFESS <sup>53</sup>	5743	Previous ischaemic stroke/transient ischaemic attack in all patients	Telmisartan 80 mg	Placebo	144.2/83.8	4/2
PROGRESS <sup>54</sup>	761	Previous stroke/transient ischaemic attack in all patients	Perindopril 4 mg with or without indapamide	Placebo	149.5/84.5	9.5/4.6
RASS <sup>55</sup>	285	No previous cardiovascular disease	Losartan 100 mg or enalapril 20 mg	Placebo	120.1/70.6	3/2
RENAAL <sup>56, 57</sup>	1513	Diabetic nephropathy in all patients, 20% with cardiovascular disease	Losartan 50-100 mg	Placebo	152.5/82.0	2.3/0.7
ROADMAP <sup>58</sup>	4447	33% with previous cardiovascular disease	Olmesartan 40 mg	Placebo	136.5/80.5	3.1/1.9
Ravid –98 <sup>59</sup>	194	No previous cardiovascular disease	Enalapril 10 mg	Placebo	130/80	No data
SAVE <sup>60</sup>	496	Previous myocardial infarction and ejection fraction <40% in all patients	Captopril 75-150 mg	Placebo	117.8/70.4	No data
SCOPE <sup>61</sup>	597	8% with previous cardiovascular disease	Candesartan 8-16 mg	Placebo	166/90	5.1/1.2
SHEP <sup>62</sup>	583	No data on previous cardiovascular disease	SBP <160 mm Hg or ≥20 mm Hg SBP reduction	Placebo	170.2/75.8	10/2
SOLVD <sup>63</sup>	1310	Heart failure and ejection fraction <35% in all patients	Enalapril 20 mg	Placebo	124.9/76.8	No data
SPS3 <sup>64</sup>	1106	Previous lacunar infarction in all patients	SBP <130 mm Hg	SBP 130-149 mm Hg	143/78.5	11/5
STOP <sup>65</sup>	142	No data on previous cardiovascular disease	Atenolol 50 mg or metoprolol 100 mg or pindolol 5 mg or hydrochloro-thiazide 25 mg+amiloride 2.5 mg	Placebo	195.3/100.8	18.2/8.5
Syst-Eur <sup>66</sup>	492	30% with previous cardiovascular disease	Nitrendipine 10-40 mg with or without enalapril with or without hydrochlorothiazide	Placebo	175.3/84.5	8.6/3.9
TRACE <sup>67</sup>	237	Previous myocardial infarction and ejection fraction <35% in all patients	Trandolapril 4 mg	Placebo	126/76.5	No data
UKPDS <sup>68, 69</sup>	1148	6% with previous cardiovascular disease	Blood pressure <150/85 mm Hg	Blood pressure <180/105 (200/105) mm Hg	159.3/94	10/5
VA-NEPHRON <sup>70</sup>	1448	Diabetic nephropathy in all patients, 23% with cardiovascular disease	Losartan 100 mg+lisinopril 10-40 mg	Losartan 100 mg	137.0/72.7	1.5/1
VAL-HEFT <sup>71</sup>	1276	Heart failure NYHA II-IV in all patients	Valsartan 320 mg	Placebo	125.6/74.8	No data
VALISH <sup>72</sup>	399	No data on previous cardiovascular disease	SBP <140 mm Hg	SBP 140-150 mm Hg	168.0/80.7	3.7/0.9

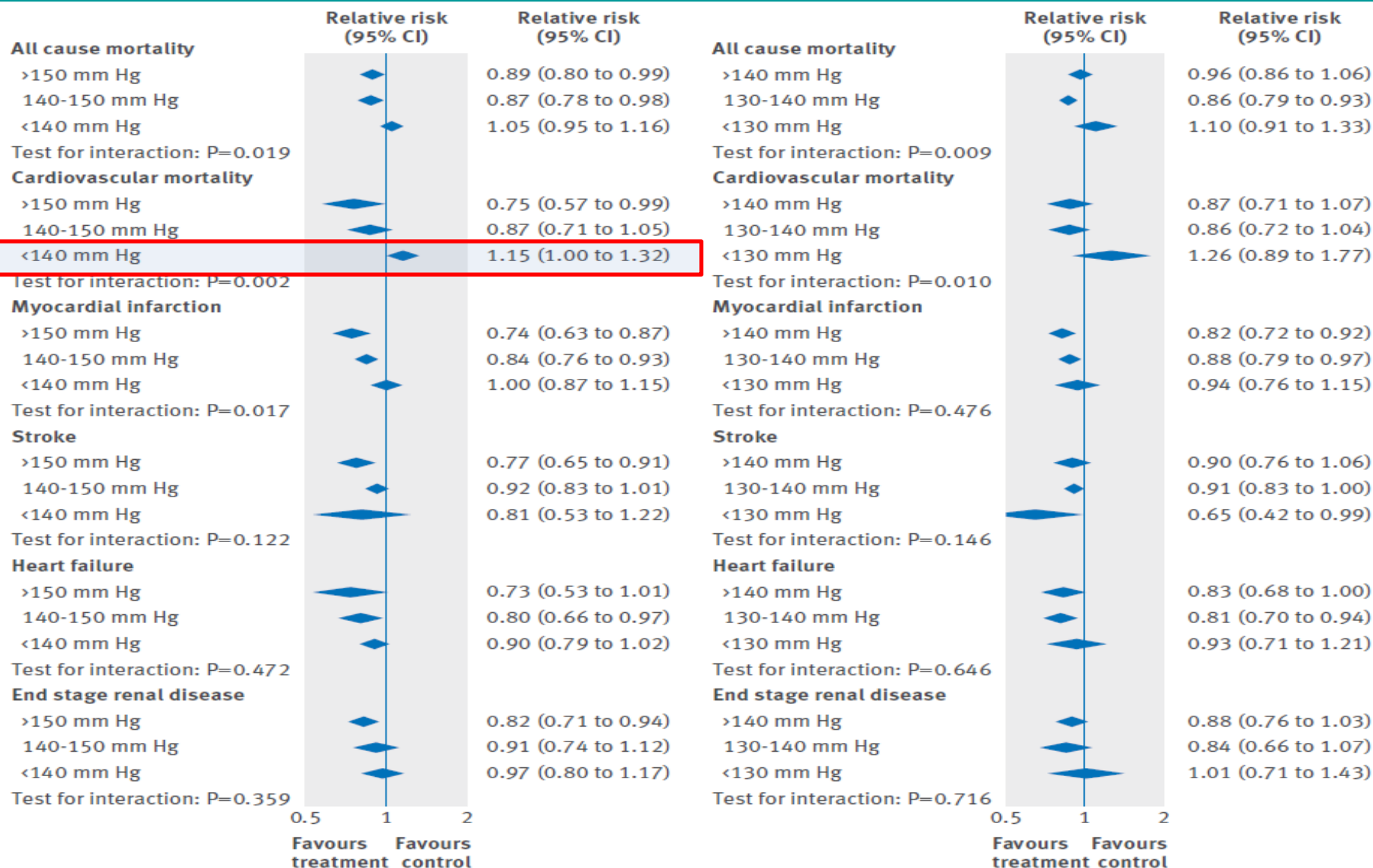
DBP=diastolic blood pressure; SBP=systolic blood pressure; NYHA=New York Heart Association function class.





# Effect of antihypertensive treatment at different blood pressure levels in patients with diabetes mellitus: systematic review and meta-analyses

Brunstrom and Carlberg. *BMJ* 2016;352:i717. doi: 10.1136/bmj.i717

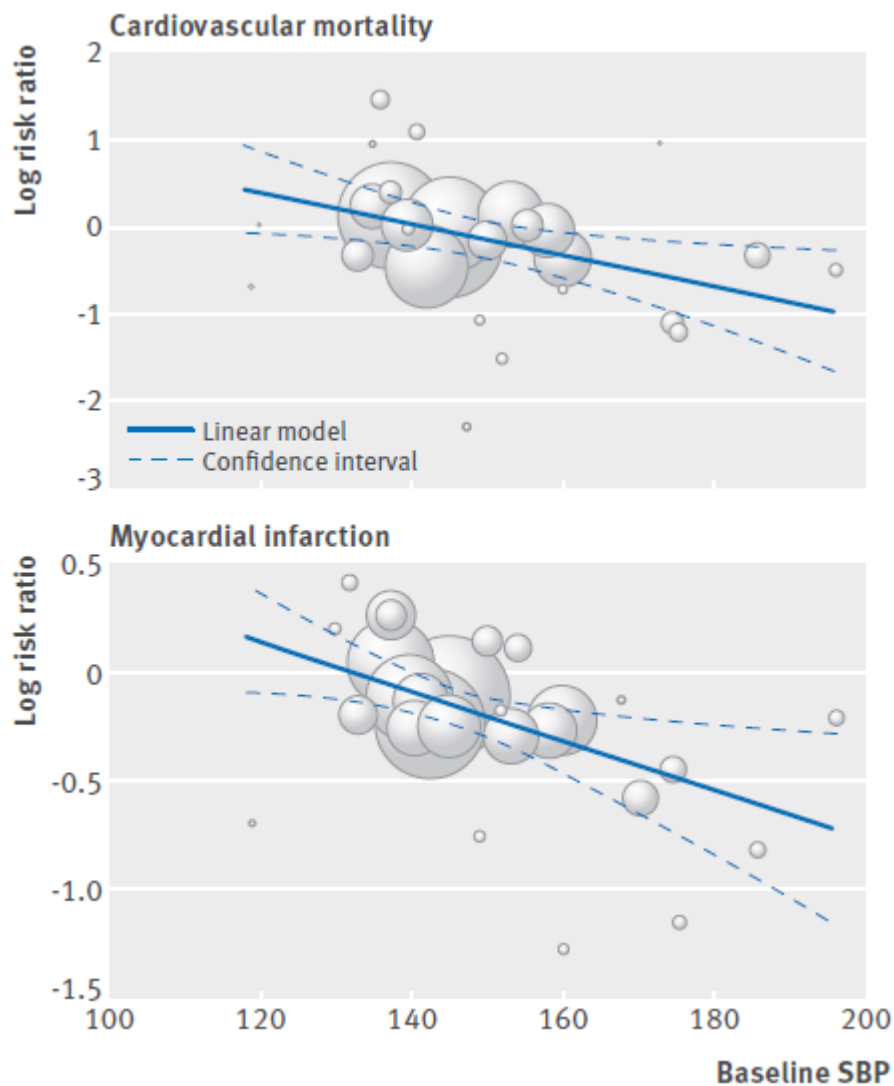






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# Effect of antihypertensive treatment at different blood pressure levels in patients with diabetes mellitus: systematic review and meta-analyses



Outcome	Relative risk (95% CI)	P value
Mortality	1.04 (0.98 to 1.10)	0.151
Cardiovascular mortality	1.15 (1.03 to 1.29)	0.015
Myocardial infarction	1.12 (1.03 to 1.22)	0.011
Stroke	1.07 (0.98 to 1.18)	0.137
Heart failure	1.05 (0.93 to 1.20)	0.401
End stage renal disease	1.05 (0.90 to 1.22)	0.496

**Fig 4 | Results from metaregression analyses of treatment effect in relation to baseline systolic blood pressure (SBP).** Relative risk is expressed as change in treatment effect for each 10 mm Hg lower baseline SBP. See table for results of all outcomes (those with significant results also presented as graphs). Each circle represents one trial and the size of each circle represents the weight given to the trial in metaregression

In patients with DM and a SBP > 140 mmHg, antihypertensive treatment is associated with a ↓ risk of mortality and CV disease.

In patients with DM and a SBP < 140mmHg, however, antihypertensive treatment is associated with an ↑ risk of cardiovascular death.

# Should We SPRINT Toward New Blood Pressure Goals or Let the Dust Settle?



Table Blood Pressure Goals Then and Now		
Blood Pressure Goals	Hypertension	Hypertension with Diabetes
Previous*	<140/90 mm Hg	<130/80 mm Hg
Now†	<120/? mm Hg	>140/90 mm Hg
*Recent (2013) on-treatment blood pressure goals of most national and international hypertension guidelines.		
†Based on treatment blood pressure goals from references 1 and 4.		

“Regardless of whether your patient has hypertension with or without diabetes, we should remember a simple but inescapable truth in medicine:

**patients are genetically, physiologically, metabolically, pathologically, psychologically, and culturally different.**

Accordingly there never will be only one way to diagnose and treat many medical disorders, including hypertension.

To lower blood pressure of **all hypertensive patients uniformly to 120 mm Hg clearly has to be considered absurd**, regardless of the SPRINT results.

**Equally absurd would it be to maintain blood pressure levels above 140/90 mm Hg in all diabetic patients.** We can only hope that despite (or even because of) SPRINT, physicians will continue to treat patients and not blood pressure numbers alone.

# Diastolic Blood Pressure, Subclinical Myocardial Damage, and Cardiac Events

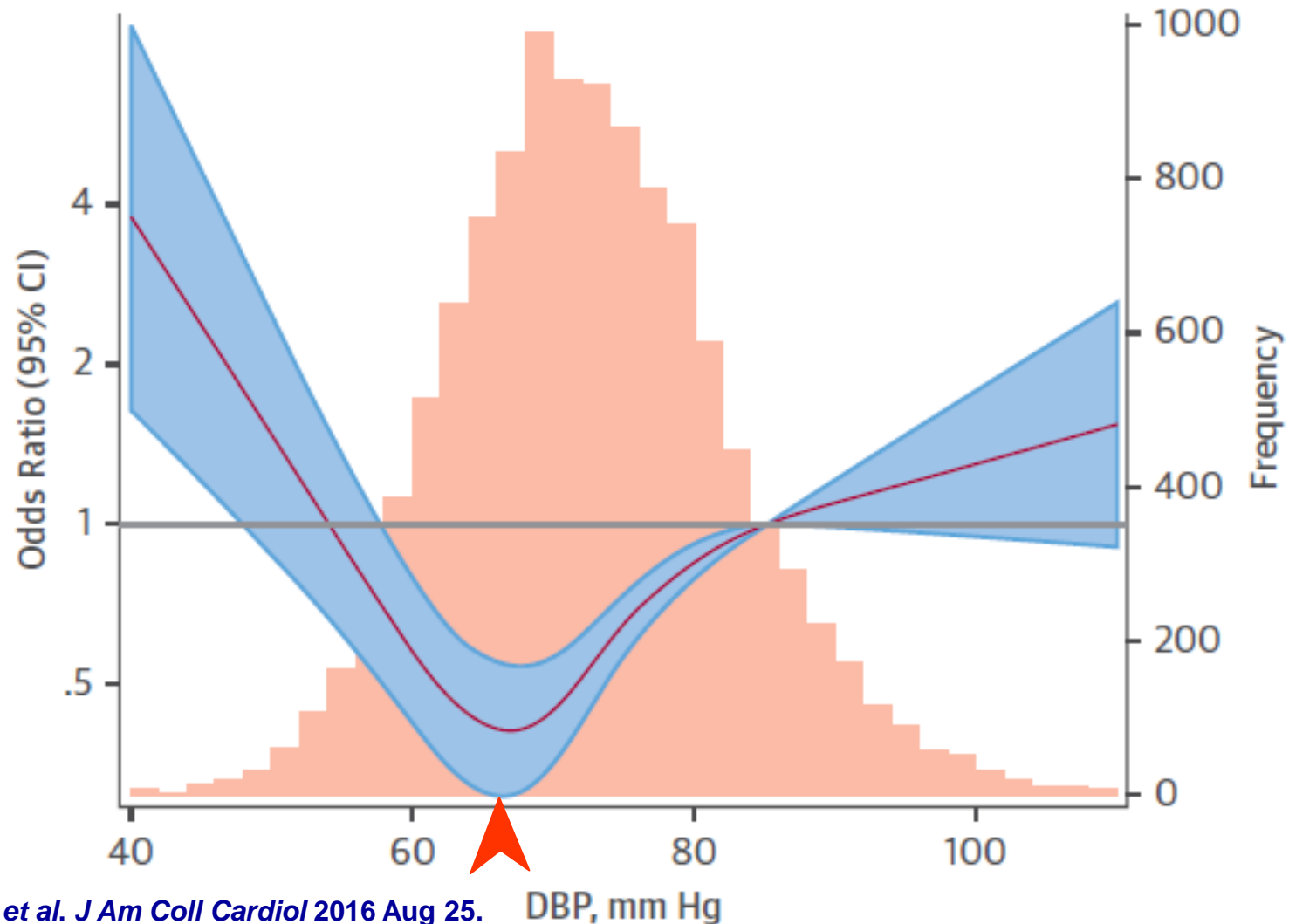
## Implications for Blood Pressure Control

John W. McEvoy, MB, BCH, BAO, MHS,<sup>a,b</sup> Yuan Chen, MS,<sup>a</sup> Andreea Rawlings, PhD,<sup>a</sup> Ron C. Hoogeveen, PhD,<sup>c</sup> Christie M. Ballantyne, MD,<sup>c</sup> Roger S. Blumenthal, MD,<sup>b</sup> Josef Coresh, MD, PhD,<sup>a</sup> Elizabeth Selvin, MPH, PhD<sup>a</sup>

- **11,565 adults from the ARIC (*Atherosclerosis Risk In Communities*) cohort**
- **Patients analyzed for:**
  - ✓ **Associations between DBP and hs-cTnT**
  - ✓ **Prospective associations between DBP and events**

# Linear Inverse Relationship Between DBP and hs-cTnT When DBP < 65 mmHg

**FIGURE 1** Relationship Between DBP and Elevated hs-cTnT

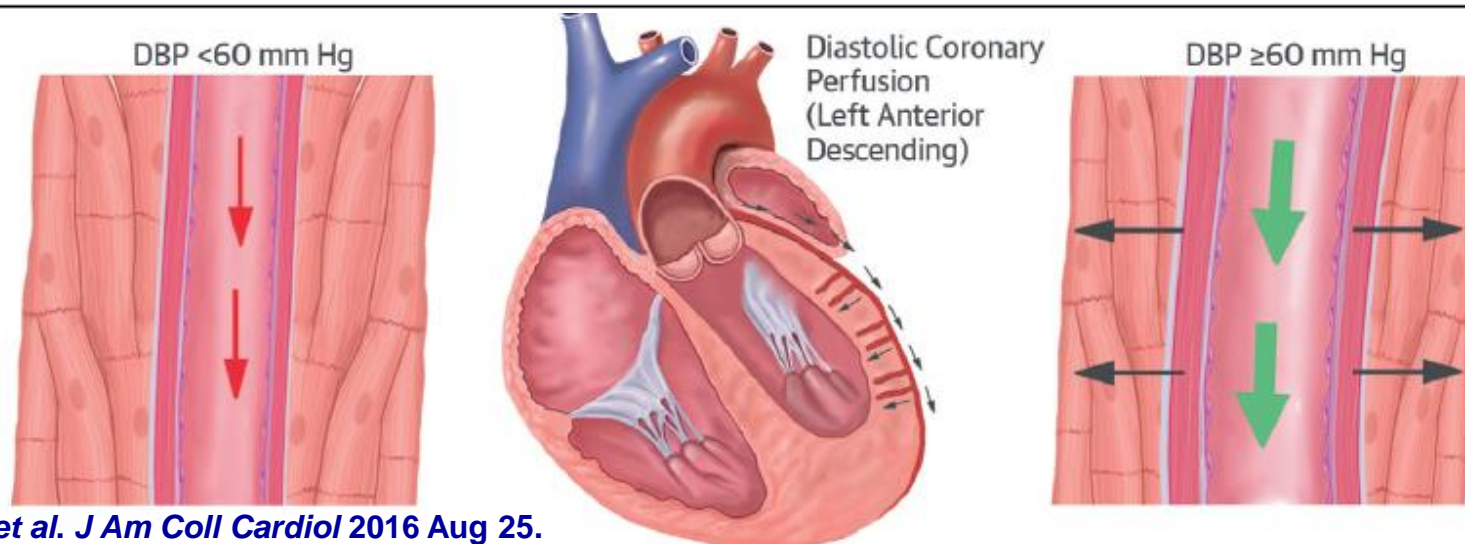


# Association Between Low DBP and CHD

**TABLE 3** CHD, Stroke, or Mortality Events

Significant values in bold  
\*Cox Model adjustment for variables

Visit 2 DBP	CHD			Stroke			Mortality		
	n/N	HR* (95% CI)	p Value	n/N	HR* (95% CI)	p Value	n/N	HR* (95% CI)	p Value
<60 mm Hg	165/1,087	<b>1.49 (1.20-1.85)</b>	<b>&lt;0.001</b>	56/1,084	1.13 (0.79-1.61)	0.52	345/1,087	<b>1.32 (1.13-1.55)</b>	<b>&lt;0.001</b>
60-69 mm Hg	547/3,728	<b>1.23 (1.05-1.44)</b>	<b>0.01</b>	197/3,722	1.03 (0.80-1.32)	0.83	1,017/3,727	1.10 (0.98-1.23)	0.12
70-79 mm Hg	752/4,247	<b>1.20 (1.05-1.37)</b>	<b>0.01</b>	271/4,234	1.07 (0.86-1.32)	0.55	1,142/4,247	0.99 (0.89-1.10)	0.89
80-89 mm Hg	350/1,902	1.00 (reference)	—	143/1,894	1.00 (reference)	—	597/1,902	1.00 (reference)	—
90-99 mm Hg	104/487	0.93 (0.74-1.16)	0.52	53/484	1.20 (0.87-1.66)	0.27	189/487	1.01 (0.85-1.19)	0.92
≥100 mm Hg	25/112	0.76 (0.50-1.17)	0.21	19/112	1.50 (0.90-2.50)	0.12	49/112	1.03 (0.76-1.40)	0.84





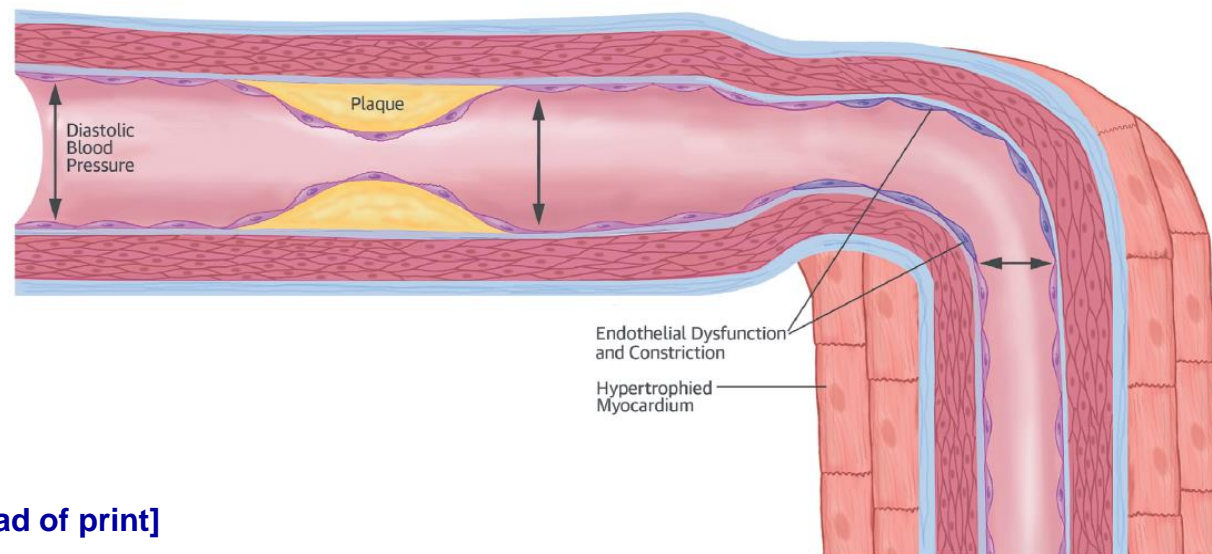
## EDITORIAL COMMENT

# Troponin and the J-Curve of Diastolic Blood Pressure

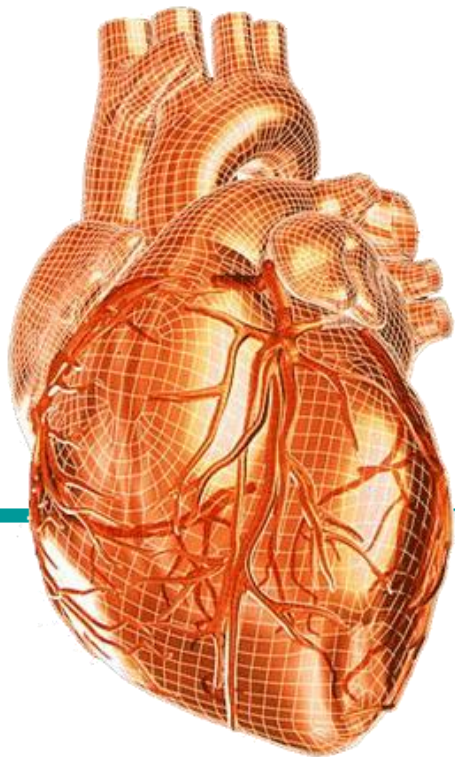
## When Lower Is Not Better\*

Deepak L. Bhatt, MD, MPH

**FIGURE 1** Factors Potentially Modulating Optimal BP Target for Pharmacotherapy







# ***Feeling the pressure? Managing Hypertension in 2016***



## **Conclusions:**

- Hypertension is a highly prevalent disease and CV risk factor
- Target systolic blood pressure still under discussion

Blood Pressure Goals	Hypertension	Hypertension with Diabetes
Previous*	<140/90 mm Hg	<130/80 mm Hg
Now†	<120/? mm Hg	>140/90 mm Hg

- Physicians should continue to treat patients and not blood pressure numbers alone (BTT)
- Individualized treatment of hypertension: should it be considered from the point of preventing CV diseases?