

중앙대학교병원 신경과 강의
Challenges in Hypertension 2017



박광열

중앙대학교 신경과

Hypertension and Stroke

J curve in Stroke?

BP Goal

SPRINT

HOPE-3

Summary

Why $p = 0.05$?

In February 2014, George Cobb, Professor Emeritus of Mathematics and Statistics at Mount Holyoke College, posed these questions to an ASA discussion forum:

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- A Because that's still what the scientific community and journal editors use.
- Q Why do so many people still use $p = 0.05$?
- A Because that's what they were taught in college or grad school.

Pre-requisite quiz

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- ▶ *If the p-value is less than the required significance level, we say the null hypothesis is rejected at the given level of significance.*
- ▶ What is the meaning of $p > 0.05$?
- ▶ *If the p-value is not less than the required significance level, the test has no result. The evidence is insufficient to support a conclusion.*

Absence of evidence is not evidence of absence.

Future life expectancy in 35 industrialised countries: projections with a Bayesian model ensemble



Vassilis Kontis*, James E Bennett*, Colin D Mather, Guangguan Li, Kyle Foreman, Majid Ezzati

Summary

Background Projections of future mortality and life expectancy are needed to plan for health and social services and

Lancet 2017; 389: 1323–35

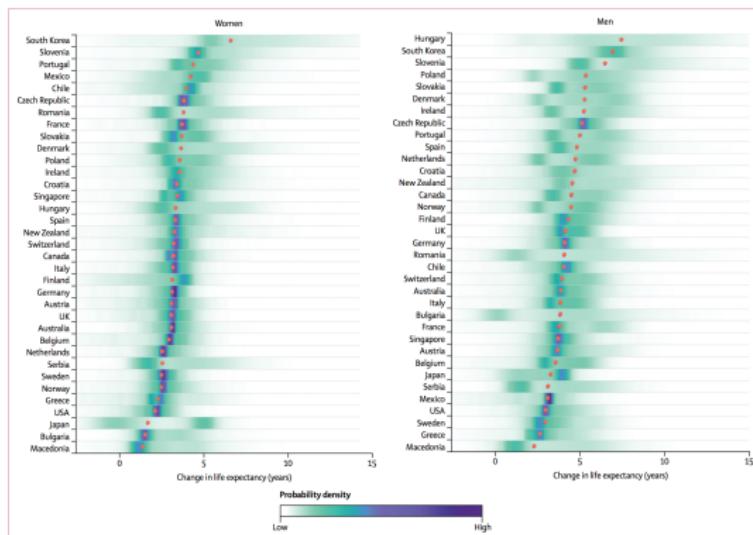
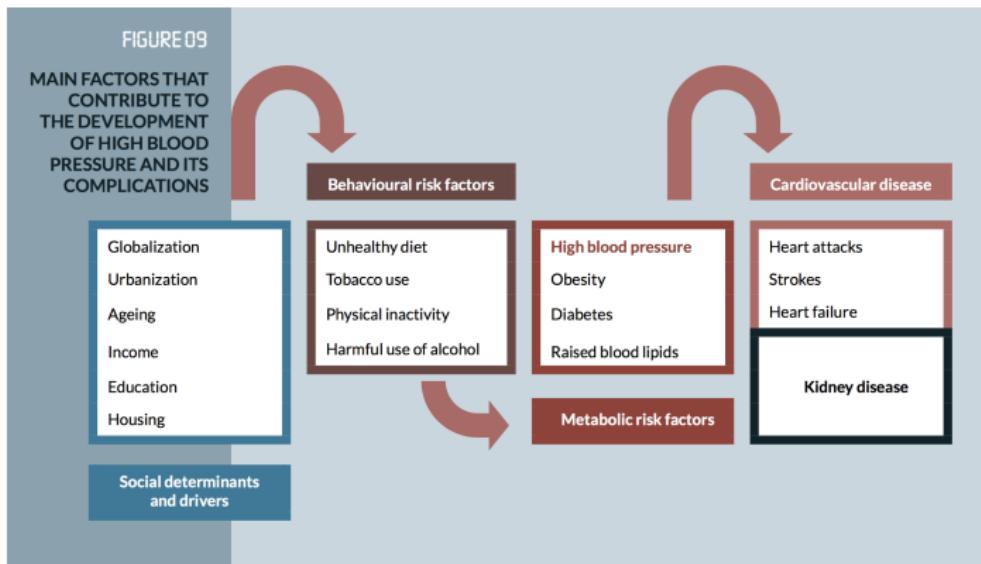


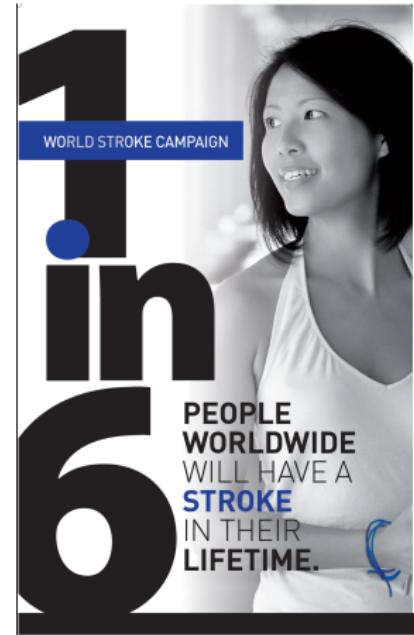
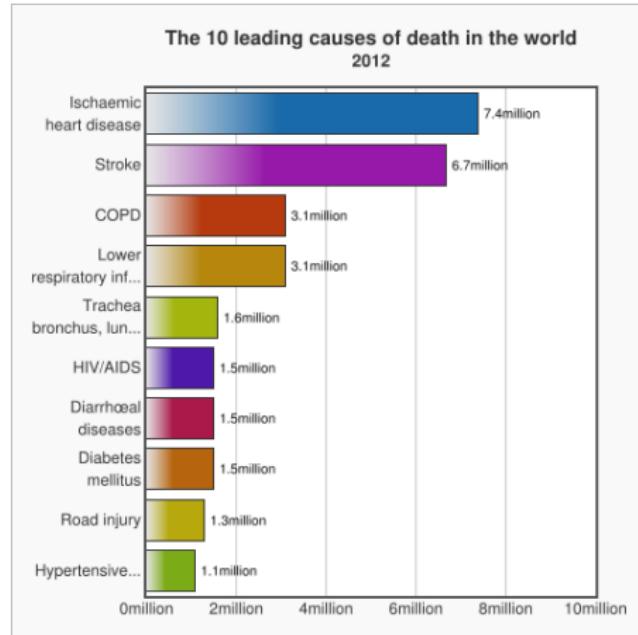
Figure 1: Posterior distribution of projected change in life expectancy at birth from 2010 to 2030
Red dots show the posterior medians. Countries are ordered vertically by median projected increase from largest (at the top) to smallest (at the bottom).

There is a **90% probability that life expectancy at birth among South Korean women in 2030 will be higher than 86 · 7 years, and a 57% probability that it will be higher than 90 years.**

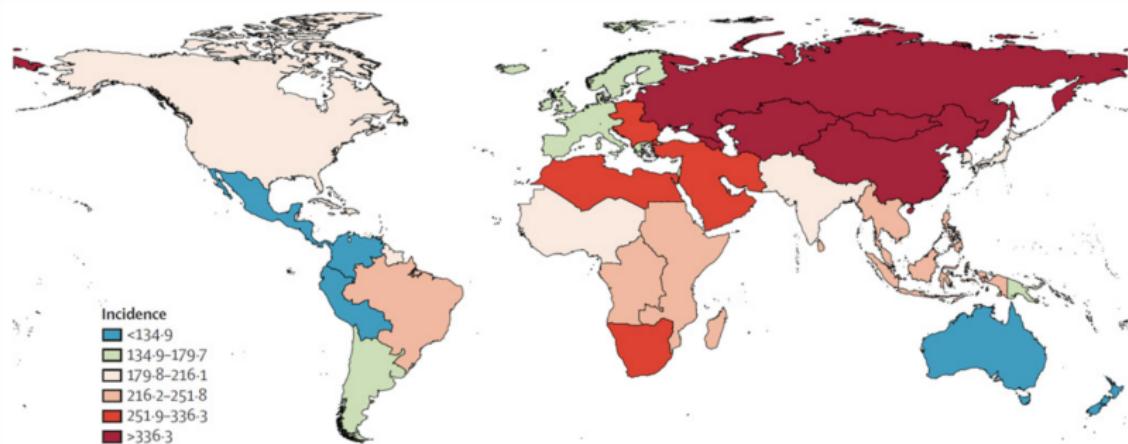
There is a **greater than 95% probability that life expectancy at birth among men in South Korea, Australia, and Switzerland will surpass 80 years in 2030, and a greater than 27% probability that it will surpass 85 years.**



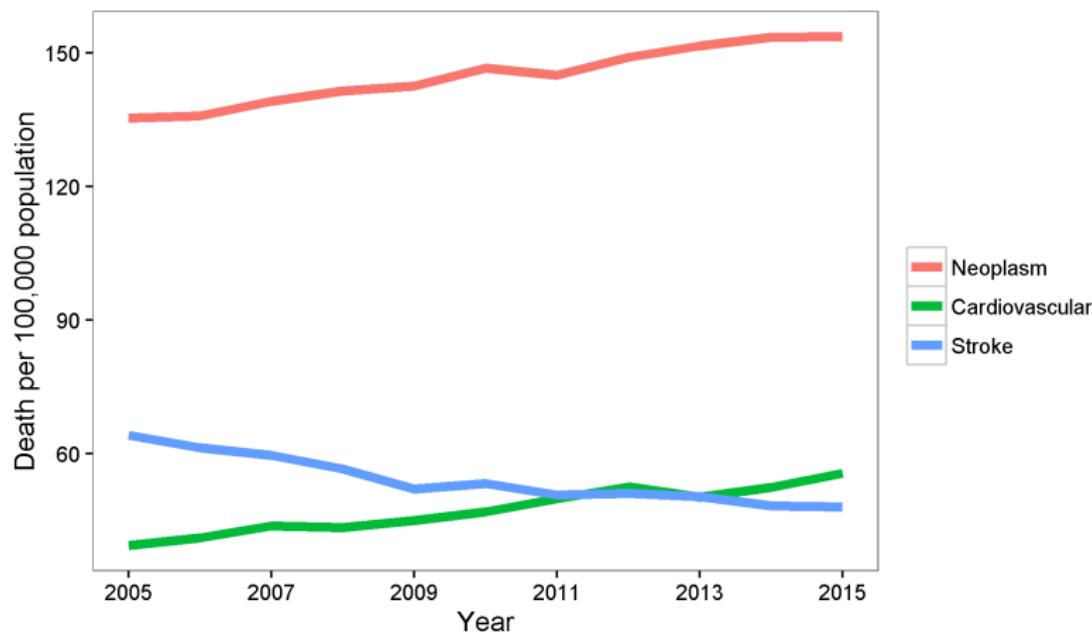
Global burden of stroke



Age-standardised stroke incidence per 100 000 person-years for 2010



Secular trend of mortality in Korea



Etiologies of stroke

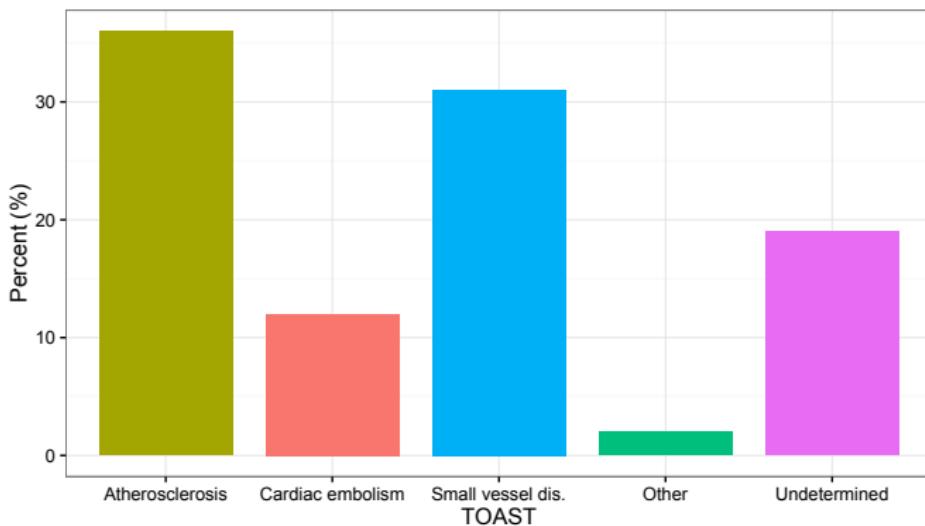
Ischemic Stroke

- ▶ Atherosclerosis
- ▶ Small artery occlusion
- ▶ Cardiac disease causing embolism
- ▶ Other causes such as moyamoya disease

Hemorrhagic Stroke

- ▶ Hypertensive hemorrhage
- ▶ Cerebral amyloid angiopathy
- ▶ Arteriovenous malformations
- ▶ Subarachnoid hemorrhage

Ischemic stroke in Korea: Analysis of 10,861 cases in Korean Stroke Registry



Risk factors for Stroke

Non-modifiable factors

1. Age
2. Sex
3. Race
4. Family history

Modifiable factors

1. **Hypertension**
2. Diabetes
3. Dyslipidemia
4. Smoking
5. Carotid disease
6. Cardiac disease such as atrial fibrillation
7. Obesity
8. Inactivity

Stroke and HT

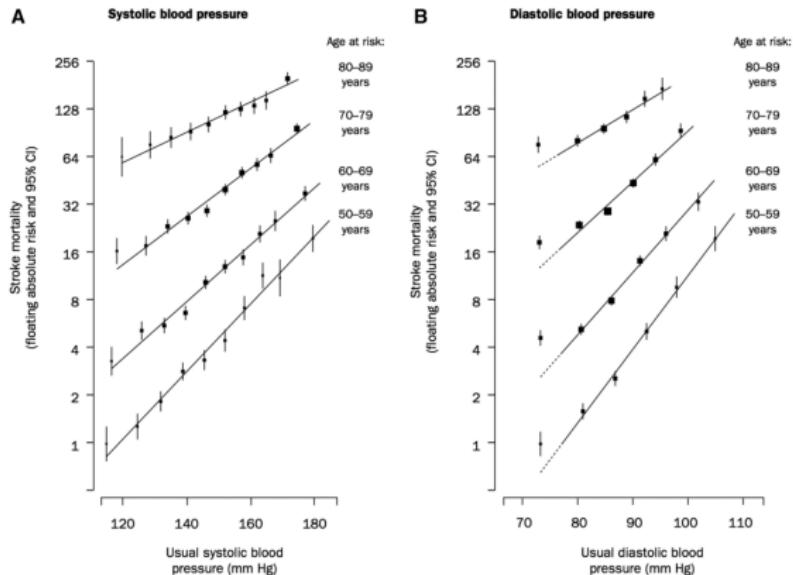


Figure 2. Stroke mortality in each decade of age vs usual blood pressure at the start of the decade. CI indicates confidence interval.
Adapted from the Prospective Studies Collaboration (Lewington et al¹²) with permission of the publisher. Copyright ©2002, Elsevier.

IHD and HT

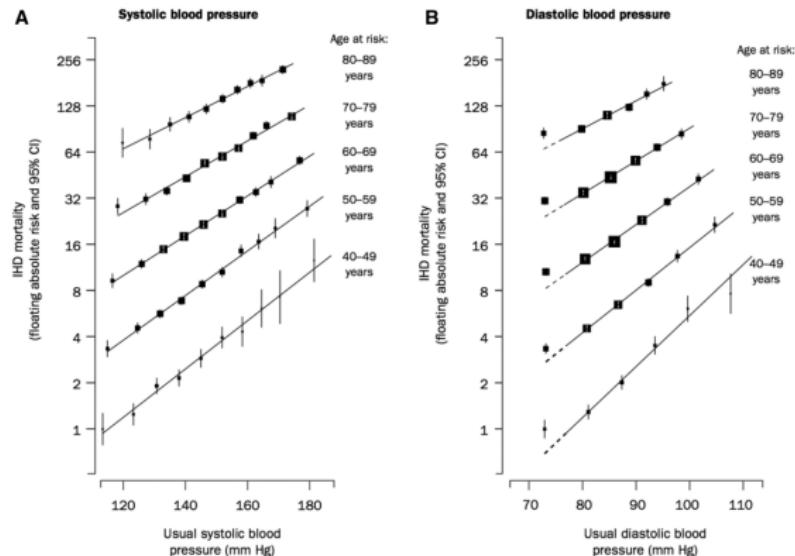


Figure 1. Ischemic heart disease (IHD) mortality in each decade of age vs usual blood pressure at the start of the decade. CI indicates confidence interval. Adapted from the Prospective Studies Collaboration (Lewington et al¹⁷) with permission of the publisher.

IHD vs Stroke and SBP

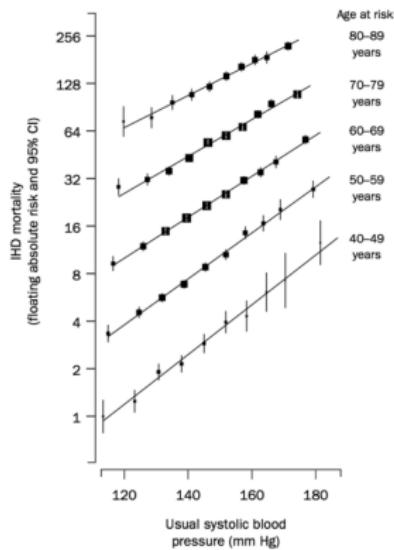


Figure 1. Ischemic heart disease (IHD) mortality

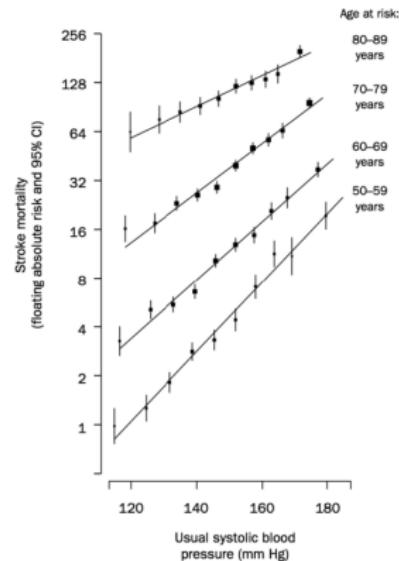
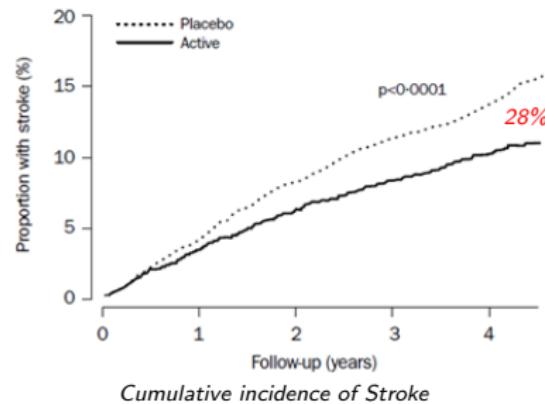
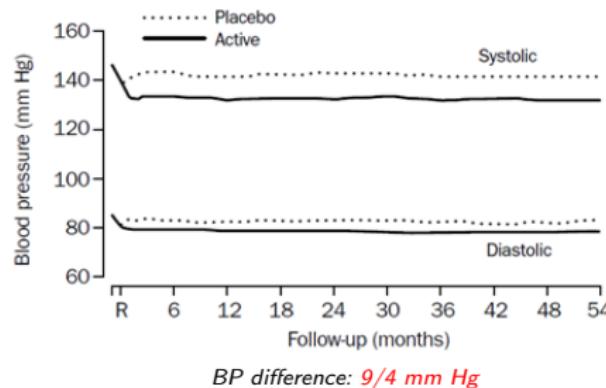


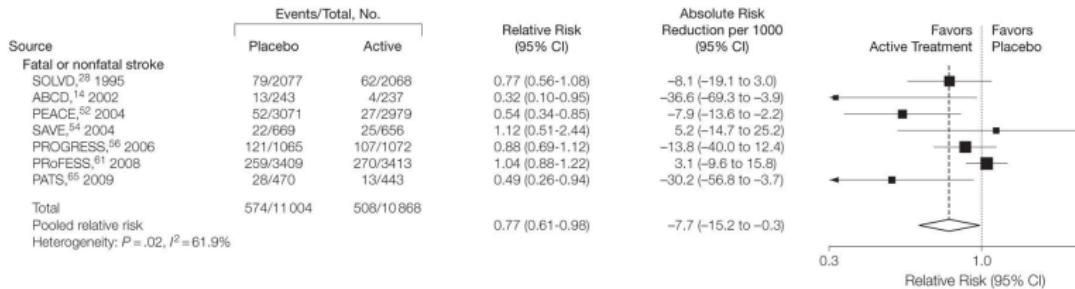
Figure 2. Stroke mortality

PROGRESS

Randomized trial enrolling 6,105 patients with a history of TIA or stroke (ischemic or hemorrhagic) to perindopril+ indapamide or placebo



Anti-HT Tx. and stroke

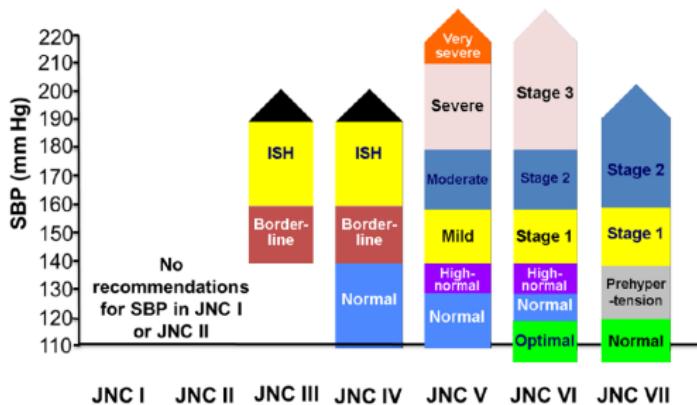


Hypertension in 2017

└ Hypertension and Stroke

WASHINGTON, D.C. April 9, 1944			
9th	202/102	P.M.	196/96
10th	196/94	"	200/104
11th	192/96	"	204/100
12th	200/102	"	204/98
13th	196/100	"	202/98
14th	206/100	"	200/96
15th	206/102	"	196/100
16th	215/102	"	206/120
17th	216/120	"	206/116 (Dr.Bruen 6th sound)
18th	220/120	(4th sound)	Unicsep 1; XI \neq x.t.i.d. ac.
19th	218/120	P.M.	204/104
20th	212/106	Noon	210/96 9:54 p.m. 190/100 (XI discontinued)
21st	9:05 a.m.	234/126; 10:15 a.m. (sitting)	210/116; 10:05 a.m. 218/120 (prone, both arms checked) 6:45 p.m. after outing 214/120; 9:50 p.m. 220/114.
22nd	9:30 a.m.	214/120; 11:30 a.m.	210/114; 6:30 p.m. (after boat trip) 206/110.
23rd	10:15 a.m.	214/118 (2 1/2 hr drive)	9:45 212/114.
24th	10:15 a.m.	222/122	10:30 p.m. 220/116
25th	10:05	224/116	10 p.m. 214/106 (after luncheon party).
26th	10. a.m.	214/112	10:30 p.m. 222/110
27th	10:15 a.m.	222/118;	9:45 p.m. 210/114
28th	224/124	P.M.	230/120 (one additional digit tablet Tuesday and Friday)
29th	9:15 a.m. (on swaying)	196/112; (sitting after breakfast)	10:10 226/120; (Prone, after E.E.) 220/118; 2:15 (after lunch) 226/112 (Thesodate discontinued); 9:30 p.m. 210/110
30th	8:45 (Prone, on swaying)	210/110; (after breakfast)	10:00 206/104; ; after lunch 206/114; 9:00 p.m. 224/120
May 1st. Prone 9:15 a.m. 220/116; Noon 210/110; 2 p.m. (after lunch 210/ 106; 10:30 p.m. 210/118.			

Franklin D. Roosevelt Library

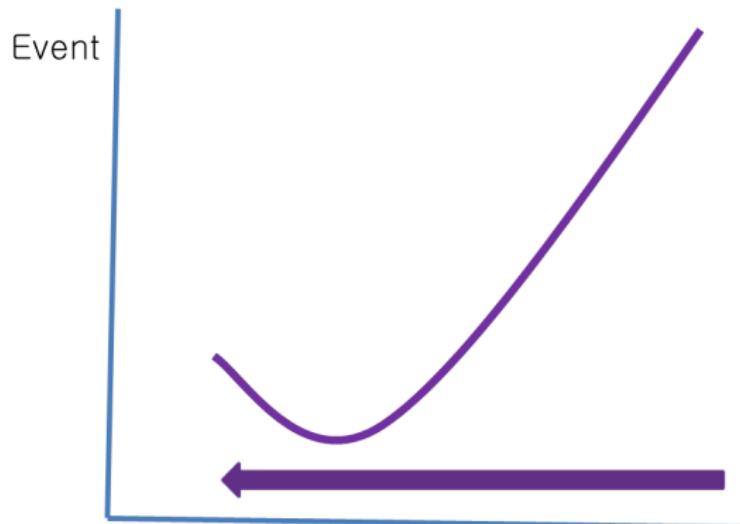


*JNC I. JAMA. 1977;JNC II. Arch Intern Med. 1980; JNC III. Arch Intern Med. 1984;
JNC IV. Arch Intern Med. 1988; JNC V. Arch Intern Med. 1993;JNC VI. Arch Intern
Med. 1997;JNC 7 Express*

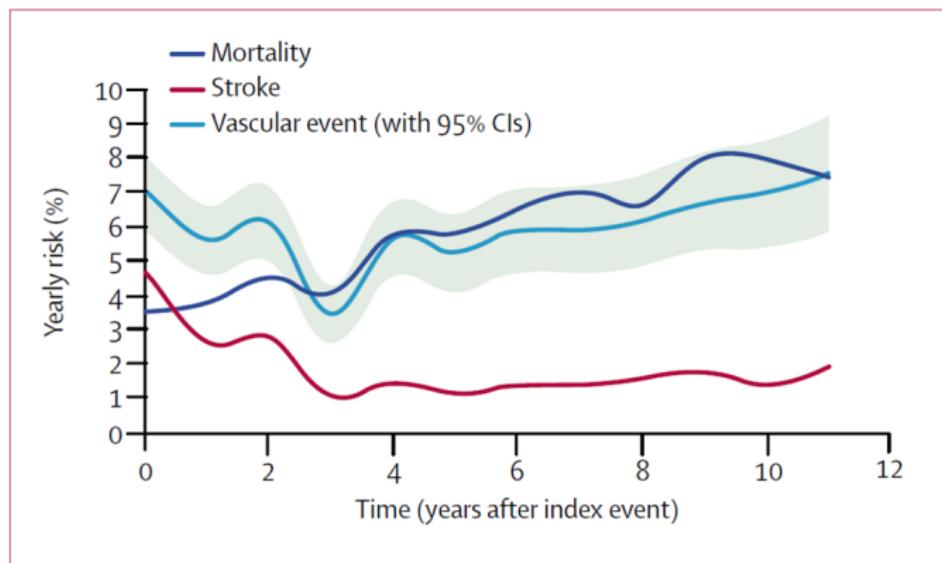
Hypertension in 2017

└ J curve in Stroke?

Hypertension: J curve ?



Yearly Risk over Time in Dutch TIA trial



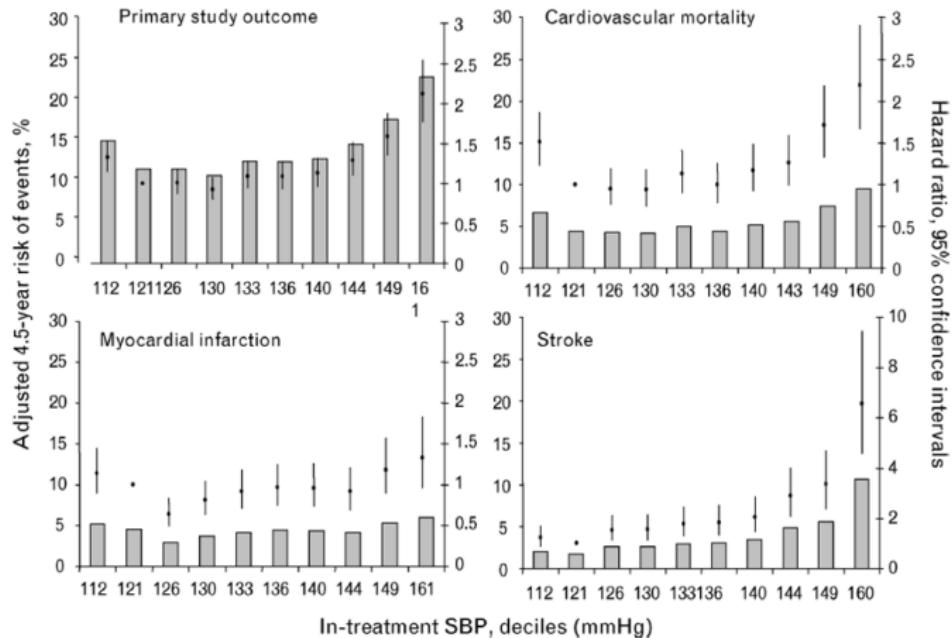
Vascular events after stroke

Risk of Myocardial Infarction and Vascular Death After Transient Ischemic Attack and Ischemic Stroke A Systematic Review and Meta-Analysis

Emmanuel Touzé, MD; Olivier Varenne, MD, PhD; Gilles Chatellier, MD, PhD;
Séverine Peyrard, MSc; Peter M. Rothwell, MD, PhD, FRCP; Jean-Louis Mas, MD

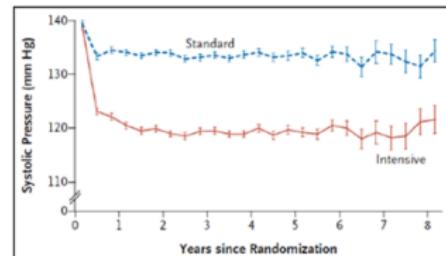
	Annual Risk
Nonstroke vascular death	2.1% (1.9 to 2.4)
Total MI	2.2% (1.7 to 2.7)
Nonfatal MI	0.9% (0.7 to 1.2)
Fatal MI	1.1% (0.8 to 1.5)

Ontarget study



The lower BP looks beneficial in stroke: ACCORD

- 4733 patients with type 2 DM
- SBP
< 140 mm Hg vs. < 120 mm Hg



Outcome	Intensive Therapy (N=2363)		Standard Therapy (N=2371)		Hazard Ratio (95% CI)	P Value
	no. of events	%/yr	no. of events	%/yr		
Primary outcome*	208	1.87	237	2.09	0.88 (0.73–1.06)	0.20
Prespecified secondary outcomes						
Nonfatal myocardial infarction	126	1.13	146	1.28	0.87 (0.68–1.10)	0.25
Stroke						
Any	36	0.32	62	0.53	0.59 (0.39–0.89)	0.01
Nonfatal	34	0.30	55	0.47	0.63 (0.41–0.96)	0.03

N Engl J Med. 2010 362(17):1575-85

ACCORD	
Population	4733 DM
Intervention	<120 vs. <140
Primary endpoint	MI, Stroke, CV death
SBP at 1yr	119 vs. 134
Outcome/yr	1.87% vs. 2.09%
All cause mortality/yr	1.28% vs. 1.19%
Stroke	0.32% vs. 0.53% *

Special Communication

2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults

Report From the Panel Members Appointed to the Eighth Joint National Committee (JNC 8)

Paul A. James, MD; Suzanne Oparil, MD; Barry L. Carter, PharmD; William C. Cushman, MD;
Cheryl Dennison-Himmelfarb, RN, ANP, PhD; Joel Handler, MD; Daniel T. Lackland, DrPH;
Michael L. LeFevre, MD, MSPH; Thomas D. MacKenzie, MD, MSPH; Olugbenga Ogedegbe, MD, MPH, MS;
Sidney C. Smith Jr, MD; Laura P. Svetkey, MD, MHS; Sandra J. Taler, MD; Raymond R. Townsend, MD;
Jackson T. Wright Jr, MD, PhD; Andrew S. Narva, MD; Eduardo Ortiz, MD, MPH

Recommendation 1

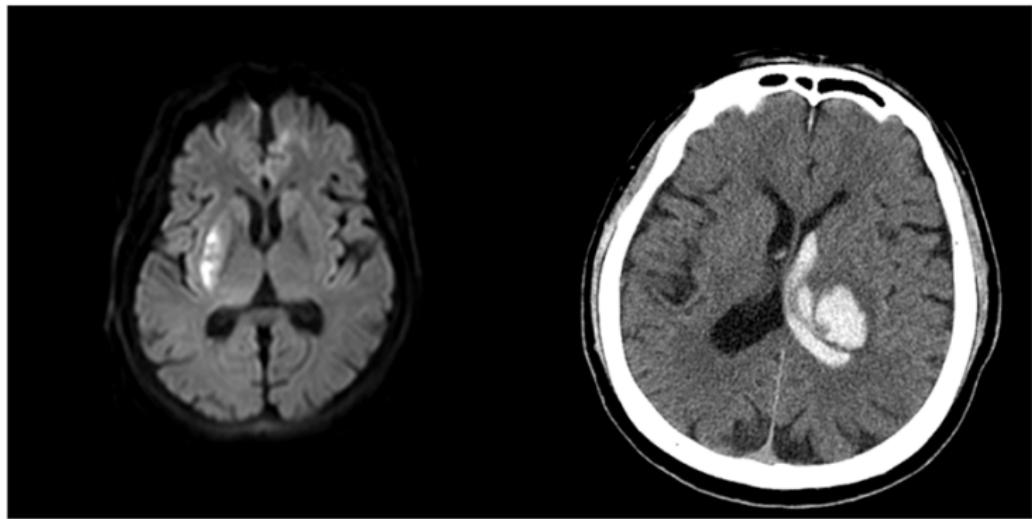
In the general population aged ≥ 60 years, initiate pharmacologic treatment to lower blood pressure (BP) at systolic blood pressure (SBP) ≥ 150 mm Hg or diastolic blood pressure (DBP) ≥ 90 mm Hg and treat to a goal SBP < 150 mm Hg and goal DBP < 90 mm Hg. (Strong Recommendation – Grade A)

Corollary Recommendation

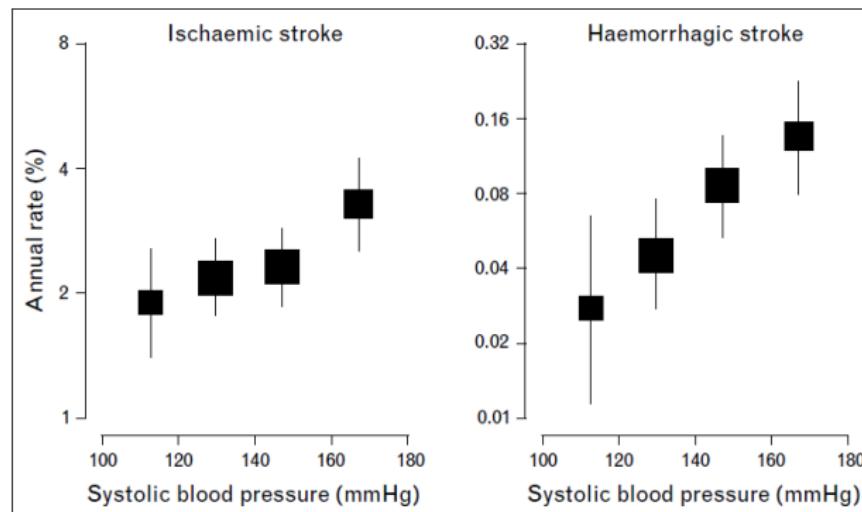
In the general population aged ≥ 60 years, if pharmacologic treatment for high BP results in lower achieved SBP (eg, < 140 mm Hg) and treatment is well tolerated and without adverse effects on health or quality of life, treatment does not need to be adjusted. (Expert Opinion – Grade E)

Hypertension in 2017

└ J curve in Stroke?

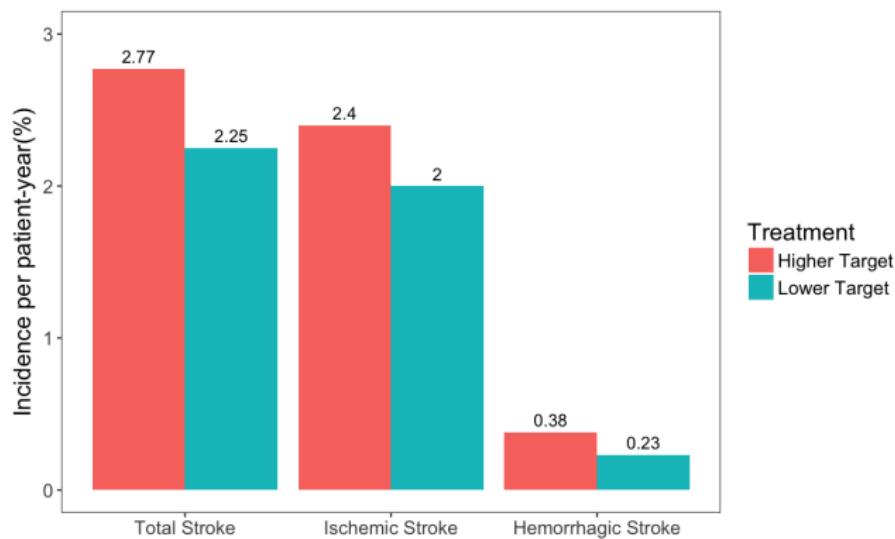


Lower target BP for stroke prevention: PROGRESS



BP targets in recent lacunar stroke: SPS3

3020 patients assigned to a SBP target of 130–149 or < 130 mm Hg.
After 1 year, mean SBP was 138 mm Hg vs. 127 mm Hg.



2014 AHA/ASA 2ndary Prevention of Stroke Guideline

For patients with a recent lacunar stroke, it might be reasonable to target an SBP of <130 mmHg (Class IIb; Level of Evidence B). (Revised recommendation)

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

NOVEMBER 26, 2015

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A Randomized Trial of Intensive versus Standard Blood-Pressure Control

The SPRINT Research Group*

ABSTRACT

BACKGROUND

The most appropriate targets for systolic blood pressure to reduce cardiovascular morbidity and mortality among persons without diabetes remain uncertain.

METHODS

We randomly assigned 9361 persons with a systolic blood pressure of 130 mm Hg or higher and an increased cardiovascular risk, but without diabetes, to a systolic blood-pressure target of less than 120 mm Hg (intensive treatment) or a target of less than 140 mm Hg (standard treatment). The primary composite outcome was myocardial infarction, other acute coronary syndromes, stroke, heart failure, or death from cardiovascular causes.

The members of the writing committee (Jackson T. Wright, Jr., M.D., Ph.D., Jeff D. Williamson, M.D., M.H.S., Paul K. Whelton, M.D., Joni K. Snyder, R.N., B.S.N., M.A., Kayce M. Sink, M.D., M.A.S., Michael V. Rocco, M.D., M.S.C.E., David M. Rebourdin, Ph.D., Mahboob Rahman, M.D., Suzanne Oparil, M.D., Cora E. Lewis, M.D., M.S.P.H., Paul L. Kimmel, M.D., Karen C. Johnson, M.D., M.P.H., David C. Goff, Jr., M.D., Ph.D., Lawrence J. Fine, M.D., Dr.P.H., Jeffrey A. Cutler, M.D., M.P.H., William C. Cush-

SPRINT: Demographics

	Intensive Tx.	Standard Tx.
Number	4678	4683
Age	67.9 ± 9.4	67.9 ± 9.5
Female	1684 (36.0%)	1648 (35.2%)
CVD	940 (20.1%)	937 (20.0%)
CKD	1330 (28.4%)	1315 (28.1%)
GFR	71.8 ± 20.7	71.7 ± 20.5
Initial BP	139.7/78.2 mm Hg	139.7/78.0 mm Hg
Mean SBP	121.5 mm Hg	134.6 mm Hg

SPRINT: Primary outcome

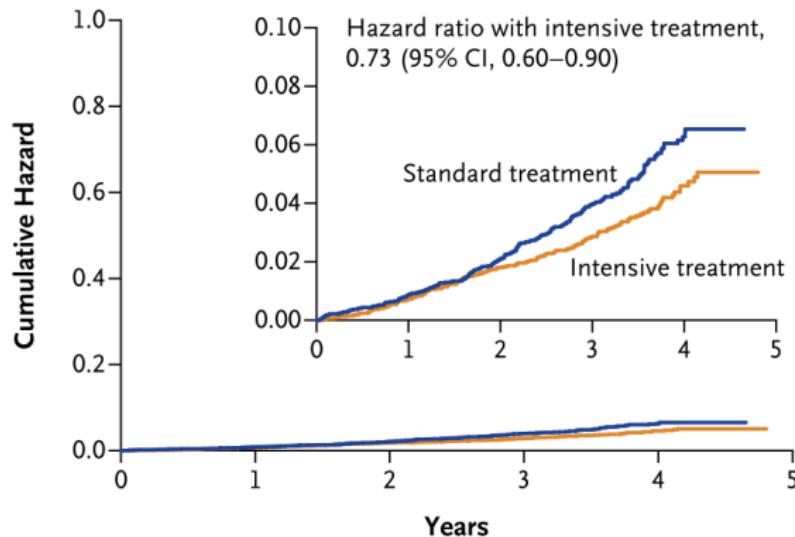
The first occurrence of myocardial infarction, acute coronary syndrome, stroke, heart failure, or death from cardiovascular causes.

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		
All participants	(N=4678)		(N=4683)			
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

SPRINT: All cause mortality

Death from Any Cause



Data sharing and SPRINT

SPRINT and ACCORD

	ACCORD	SPRINT
Population	4733 DM	9631 non-DM
Intervention	<120 vs. <140	<120 vs. <140
Primary endpoint	MI, Stroke, CV death	+ HF, other ACS
SBP at 1yr	119 vs. 134	121 vs. 136
Outcome/yr	1.87% vs. 2.09%	1.65% vs. 2.19% *
All cause mortality/yr	1.28% vs. 1.19%	1.03% vs. 1.40% *
Stroke	0.32% vs. 0.53% *	0.41% vs. 0.47%

SPRINT and ACCORD

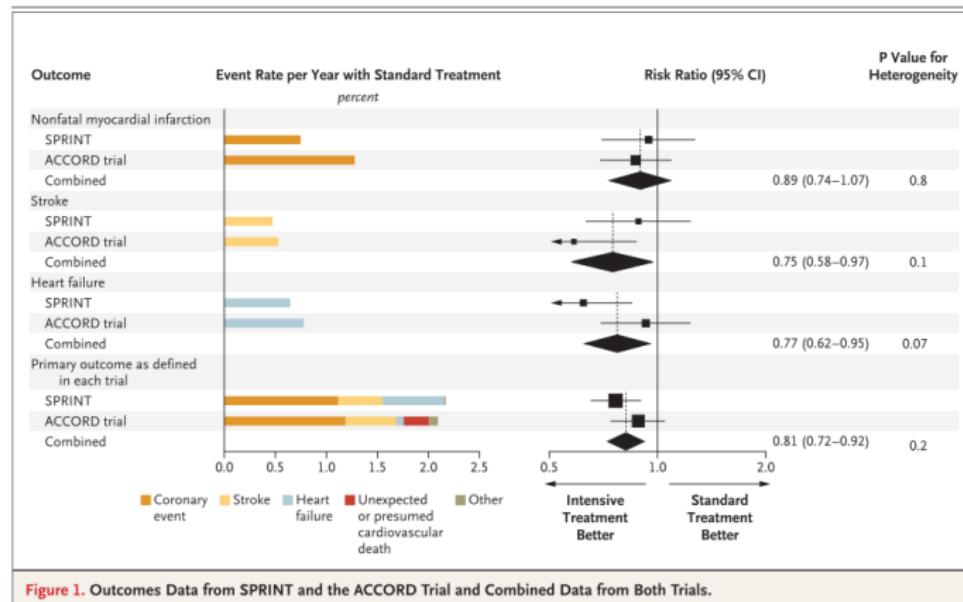
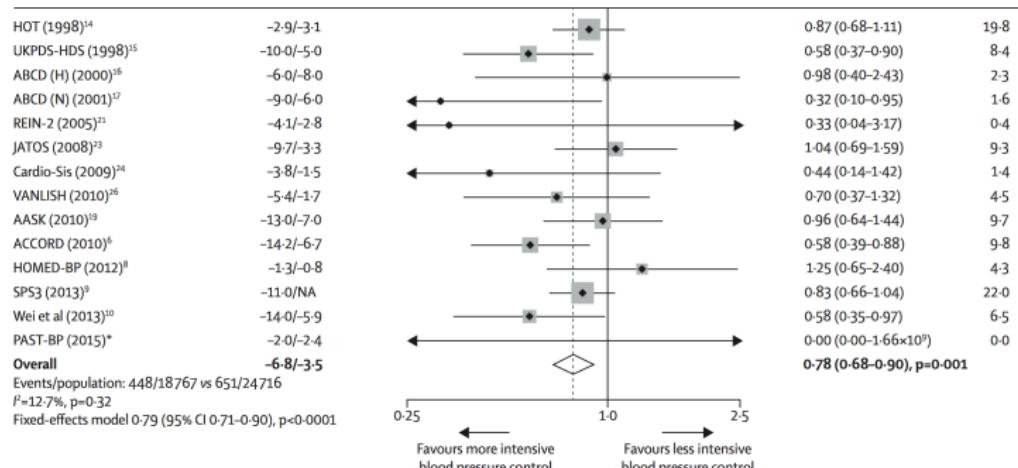


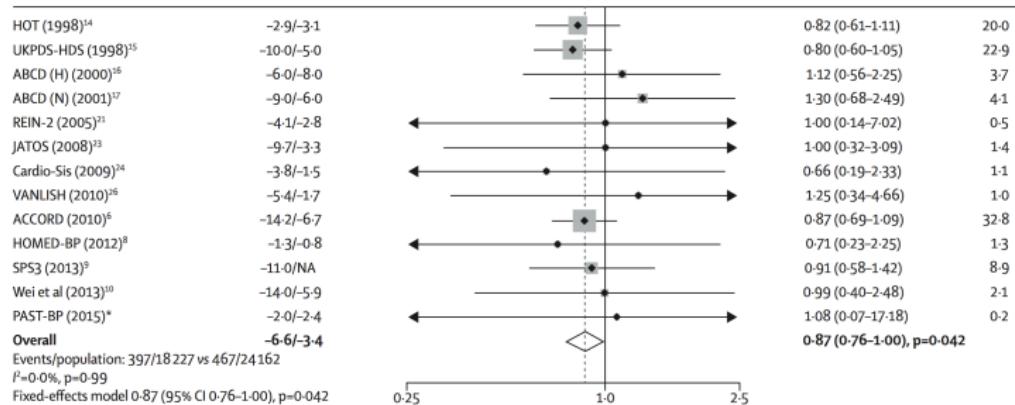
Figure 1. Outcomes Data from SPRINT and the ACCORD Trial and Combined Data from Both Trials.

Effect of intensive BP lowering on Stroke



133/76 mm Hg vs. 140/81 mm Hg

Effect of intensive BP lowering on MI



133/76 mm Hg vs. 140/81 mm Hg

Hypertension in 2017

└ BP Goal

└ HOPE-3

HOPE-3



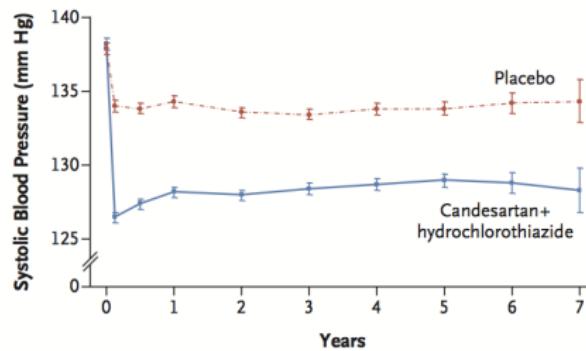
Blood-Pressure Lowering in Intermediate-Risk Persons without Cardiovascular Disease

Eva M. Lonn, M.D., Jackie Bosch, Ph.D., Patricio López-Jaramillo, M.D., Ph.D., Jun Zhu, M.D., Lisheng Liu, M.D.,

HOPE-3

Characteristic	Candesartan + Hydrochlorothiazide (N=6356)	Placebo (N=6349)
Age — yr	65.7±6.4	65.8±6.4
Female sex — no. (%)	2910 (45.8)	2964 (46.7)
Cardiovascular risk factor — no. (%)		
Elevated waist-to-hip ratio	5511 (86.7)	5523 (87.0)
Recent or current smoking	1782 (28.0)	1742 (27.4)
Low concentration of HDL cholesterol	2297 (36.1)	2291 (36.1)
Impaired fasting glucose or impaired glucose tolerance	799 (12.6)	817 (12.9)
Early diabetes mellitus	386 (6.1)	345 (5.4)
Family history of premature coronary heart disease	1668 (26.2)	1667 (26.3)
Early renal dysfunction	184 (2.9)	166 (2.6)
Hypertension	2398 (37.7)	2416 (38.1)
Blood pressure — mm Hg		
Systolic	138.2±14.7	137.9±14.8
Diastolic	82.0±9.4	81.8±9.3

HOPE-3

**No. at Risk**

Candesartan+hydro-chlorothiazide	6356	5907	5667	5446	5213	3862	1437	350
Placebo	6347	5879	5623	5442	5186	3822	1424	334

ACCORD, SPRINT, and HOPE-3

	ACCORD	SPRINT	HOPE-3
Population	4733 DM	9631 non-DM	12705
Intervention	<120 vs. <140	<120 vs. <140	drug vs. placebo
Primary outcome	MI, Stroke, CV death	+ HF, other ACS	= ACCORD
SBP at 1yr	119 vs. 134	121 vs. 136	≈ 128 vs. ≈ 134
Outcome/yr	1.87% vs. 2.09%	1.65% vs. 2.19% *	4.1% vs. 4.4%
All cause death/yr	1.28% vs. 1.19%	1.03% vs. 1.40% *	5.4% vs. 5.5%
Stroke	0.32% vs. 0.53% *	0.41% vs. 0.47%	1.2% vs. 1.5%

HOPE-3: event rates during follow-up (median f/u 5.6year)

Guidelines Debate

Is It Time to Reappraise Blood Pressure Thresholds and Targets?

A Statement From the International Society
of Hypertension—A Global Perspective

Michael A. Weber, Neil R. Poulter, Aletta E. Schutte, Louise M. Burrell, Masatsugu Horiuchi,
Dorairaj Prabhakaran, Agustin J. Ramirez, Ji-Guang Wang, Ernesto L. Schiffrin, Rhian M. Touyz

Taking into consideration the global target population of interest to the International Society of Hypertension, together with evidence derived from SPRINT and other recent meta-analyses and clinical trials, the practical message from the International Society of Hypertension is to strive for a systolic blood pressure target of 130 mmHg in most patients with hypertension. This is especially important considering that

Take-Home Message

- ▶ Stroke and Hypertension are big health issues in rapidly aging societies like Korea.
- ▶ Therapeutic target of BP in patients with stroke should be individualized.
- ▶ The practical therapeutic goal of SBP in patients with hypertension might be **130 mm Hg**.