Target BP in elderly HT

Resurrection of old dispute?

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Hypertension Seoul 2016

Welcome to Seoul, Korea!

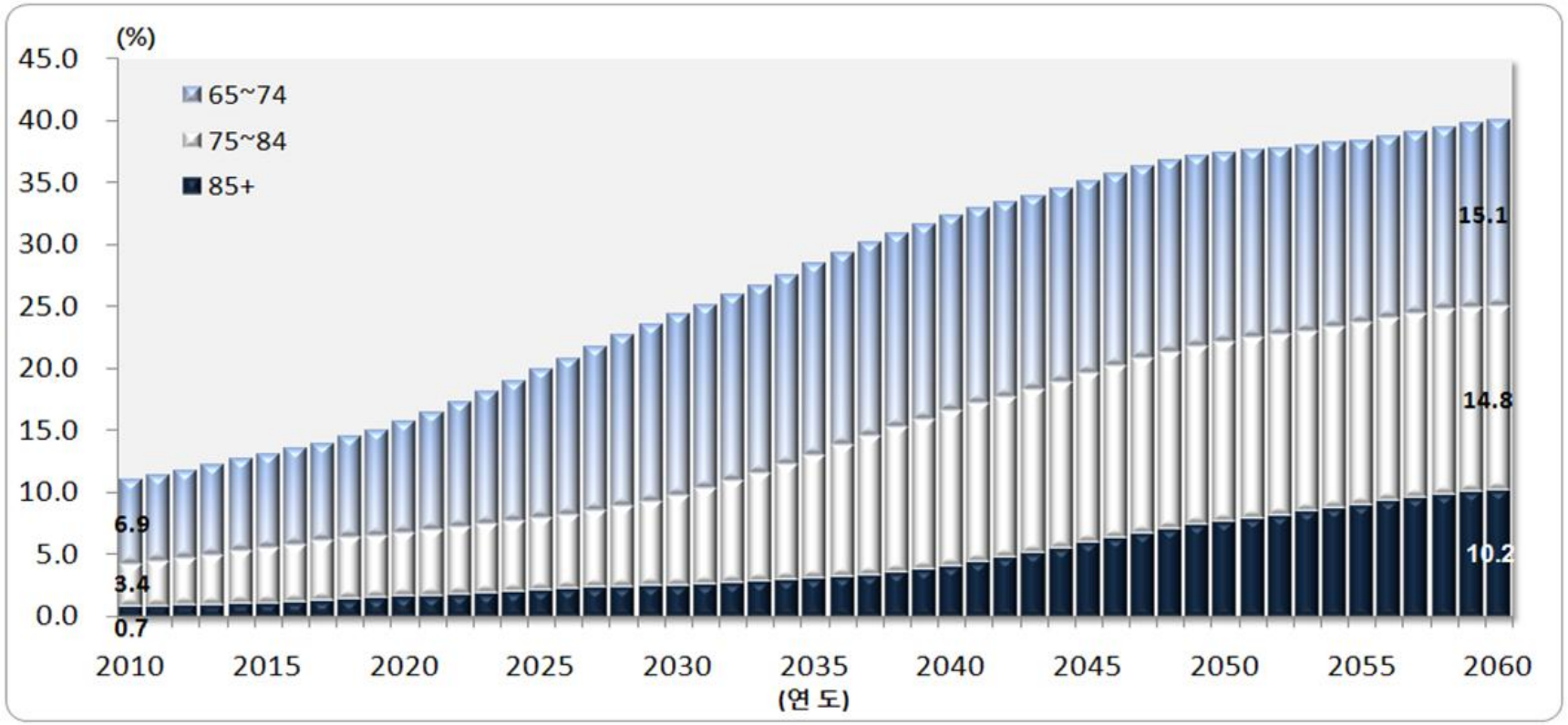
The 26th International Society of Hypertension
Biennial Scientific Meeting 2016

***September 24**(Sat) – **29**(Thu), **2016**, Coex, Seoul, Korea*

www.ish2016.org

Estimated aging of Korean population

Within several years Korean society will be aged, >65 years old more than 14%



Facts and Disputes in elderly HT

FACTS

ISH as 2nd HT; result of aortic dysfunction

ISH as a cause of 3 major CV disease in the elderly such as CAD, HFpsf and Af

3 major CV diseases preventable with management; absolute effect greater than middle aged

IOH more prevalent

SVD in the elderly as a cause of geriatric syndrome

Disputes

How far should it be lowered?

Can SVD be preventable and geriatric syndrome be lessened?

Can lowering BP be effective even in the frail elderly?

Common sense in hypertension?

Common sense; the higher BP, the more CV events regardless of the age

But is it also common sense that the more lowering BP, the lesser CV events?

It may not be common sense because of worry in the presence of J curve phenomenon and also because most of studies were carried to lower BP to certain level

Start of dispute; Whether lowering BP is effective in the elderly over 80yrs-old?

Meta analysis of 7 studies; 1,670 subjects with mean age 83 yrs/ female 70%

Effective in decrease of stroke 34%, heart failure 39%, CV events 22%

Insignificant decrease in coronary events; 22%

Increase of total mortality 6%, CV mortality 1%

Lancet 1999; 353;792-796

Pilot result of HYVET

Stroke decrease 53%

Mortality from stroke decreased 43%

Total mortality increase 23%

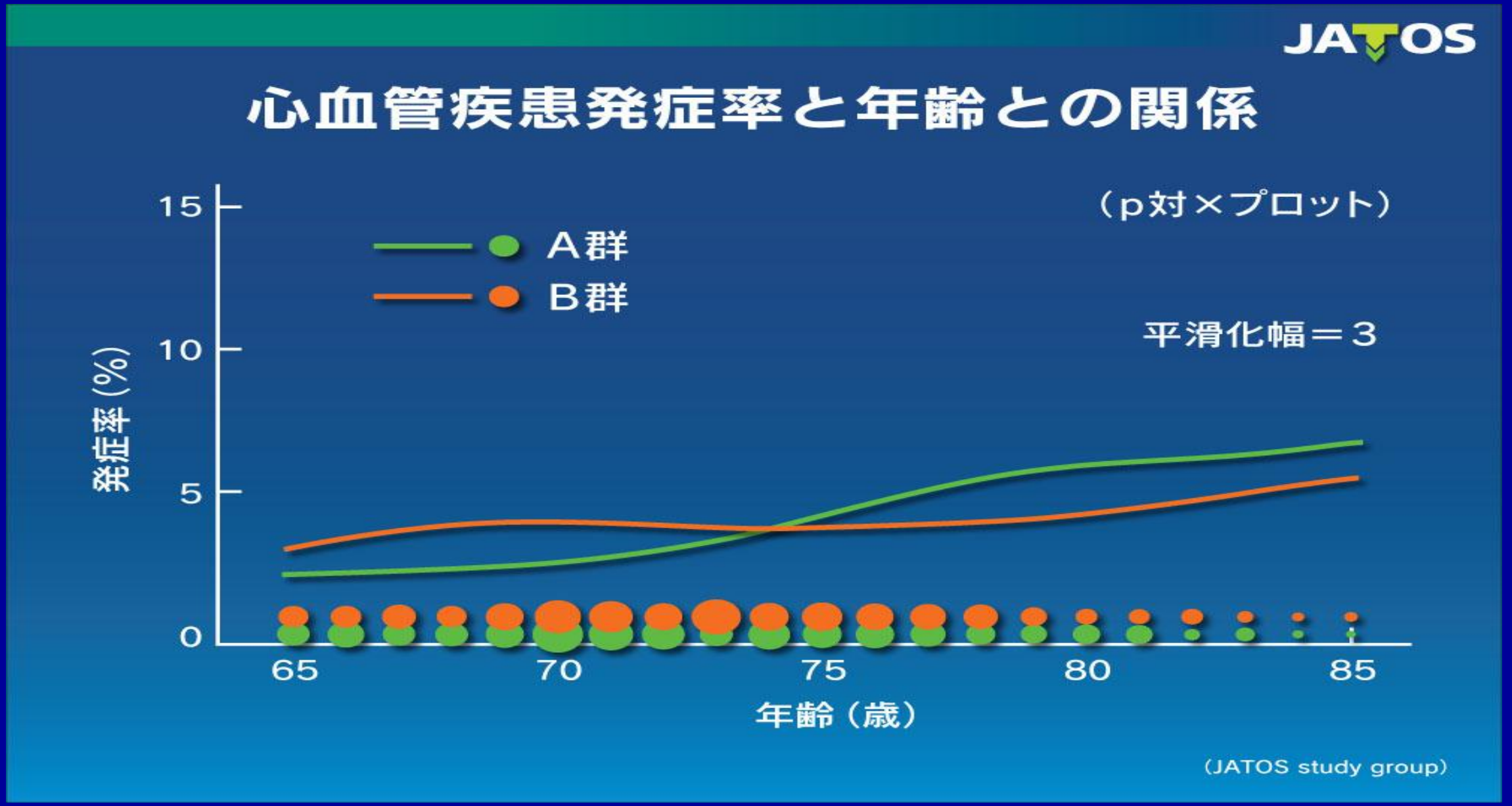
20 stroke events preventable if 1000 subjects managed for 1 years

Two studies in elderly HT

HYVET study was intended to prove the effect of blood pressure lowering in the old-old compared with placebo and showed that lowering BP in the healthy independent elderly is effective enough to reduce stroke as well as heart failure.

JATOS study was intended to compare the effects on CV events between the lower target BP and high target group and showed that there was no significant decrease in 1 end points between two gorups. But lower target was effective in decreasing CV events in the young old whereas lower target was hazardous in the old-old

Cardiovascular events according to age in A and B groups



End of disputes from clinical trials?

Data from HYVET study showed that lowering SBP less than 150mmHg be effective in the elderly

This data confirmed that in the old-old, lowering of BP is necessary but it did not suggest the target BP

Data from JATOS suggested that lowering SBP less than 140mmHg is not more effective than less than 150mmHg

This data suggested that there can be some hazard in lowering BP in the old-old

These studies were critical in making BP target in major guidelines of HT management

Summary of target blood pressure

Situations	Systolic BP (mmHg)	Diastolic BP (mmHg)
Uncomplicated hypertension	140	90
Elderly	140~150	90
Diabetes Mellitus	140	85
Stroke	140	90
Coronary artery disease	140	90
Chronic kidney disease		
without albuminuria*	140	90
with albuminuria	130	80

Clinical Hypertension 2015, 21:2

Peculiar recommendation by so call JNC-8

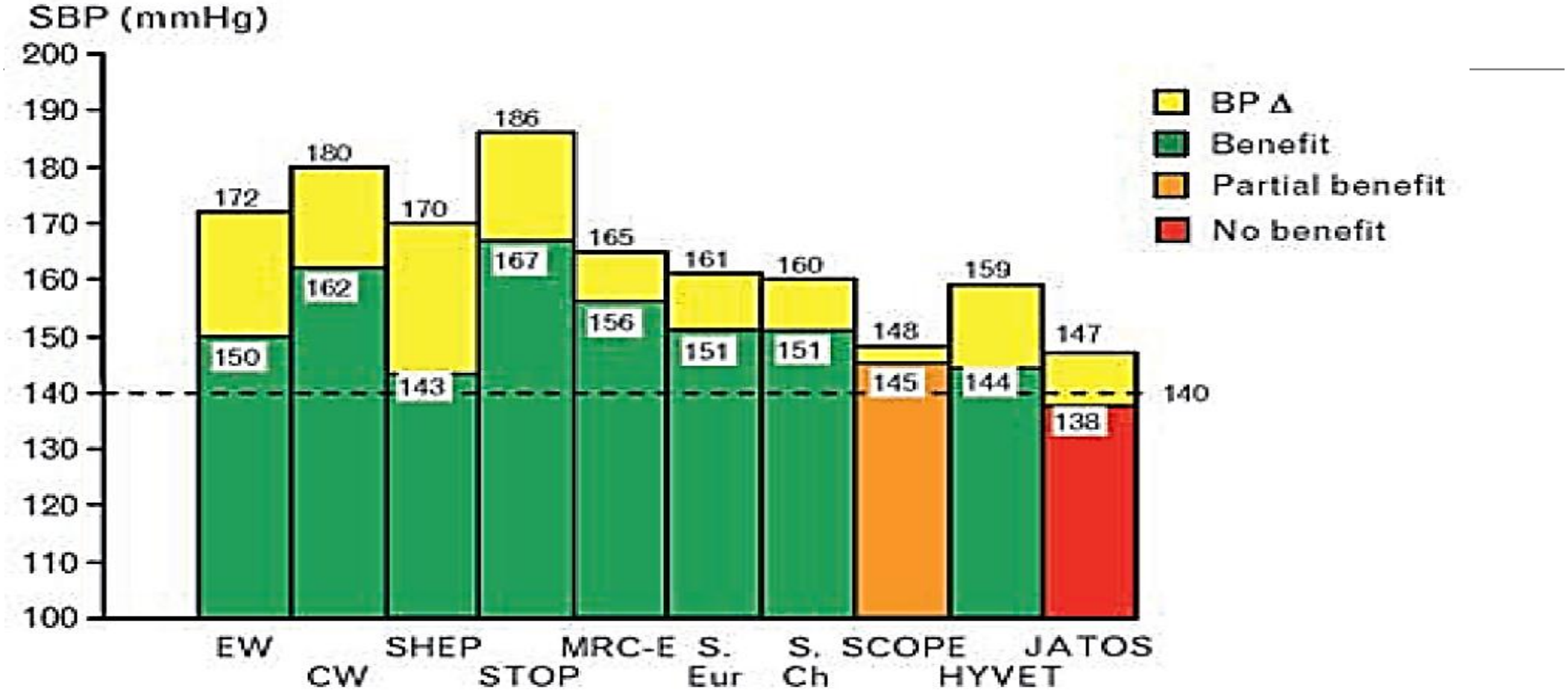
JNC-8 recommended to lower SBP to less than <150mmHg in the aged over 60 years.

This was based on SHEP study.

In most of the clinical trials, elderlies were included and subgroup analysis showed that less than 140mmHg was effective in lowering CV events

It is true that there was no study in which target BP below 140mmHg was achieved except JATOS

Goal BP in elderly hypertension



No further benefit BP <140mmHg on CVD prevention

Resurrection of dispute

SPRINT
Systolic Blood Pressure Intervention Trial

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Randomized Trial of Intensive versus Standard Blood-Pressure Control

The SPRINT Research Group*

Major Inclusion Criteria

- ***≥50 years old***
- ***Systolic blood pressure : 130 – 180 mm Hg*** ***(treated or untreated)***
- ***Additional cardiovascular disease (CVD) risk***
  - ***Clinical or subclinical CVD (excluding stroke)***
  - ***Chronic kidney disease (CKD), defined as eGFR 20 – <60 ml/min/1.73m²***

At least one

  - ***Framingham Risk Score for 10-year CVD risk ≥ 15%***
  - ***Age ≥ 75 years***

Major Exclusion Criteria

- ***Stroke***
- ***Diabetes mellitus***

- ***Polycystic kidney disease***
- ***Congestive heart failure (symptoms or EF < 35%)***
- ***Proteinuria >1g/d***
- ***CKD with eGFR < 20 mL/min/1.73m² (MDRD)***
- ***Adherence concerns***
- ***Hypertensive patients under the age of 50***

SPRINT
Systolic Blood Pressure Intervention Trial

Primary Outcome Composite (CVD)

CVD mortality

Myocardial infarction

Non-MI acute coronary syndrome

Stroke

Heart Failure

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
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

What can be changed after SPRINT?

Possibility of J curve phenomenon can be excluded?

Target BP should be reduced in selected group of hypertensive?

It should consider the difference in method of BP measurement

Blood Pressure Measurement in SPRINT

Blood pressure readings were conducted in a unique manner that is probably not the standard in our office.

Patients were asked to sit quietly for 5 minutes before blood pressure readings were measured by an automated unit.

Three readings were obtained over several minutes with no clinician in the room.

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

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Primary outcome or death	332 (7.1)	2.25	423 (9.0)	2.90	0.78 (0.67–0.90)	<0.001
Participants with CKD at baseline	**(N=1330)**		**(N=1316)**			
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
Participants without CKD at baseline‖	**(N=3332)**		**(N=3345)**			
≥30% reduction in estimated GFR to <60 ml/min/1.73 m^2§	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

* CI denotes confidence interval, and CKD chronic kidney disease.

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
	no. of patients (%)			
Serious adverse event*	1793 (38.3)	1736 (37.1)	1.04	0.25
Conditions of interest				
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

Personal view on SPRINT

Lowering BP target in selected group of HT will be desirable

It is not clear to what level of BP should be beneficial at clinical practice.

Hazard associated with low BP should be balanced with the benefit

J curve phenomenon should be made clear from the data of SPRINT

Blood-pressure targets in patients with recent lacunar stroke: the SPS3 randomised trial

*The SPS3 Study Group**

Summary

Background Lowering of blood pressure prevents stroke but optimum target levels to prevent recurrent stroke are unknown. We investigated the effects of different blood-pressure targets on the rate of recurrent stroke in patients with recent lacunar stroke.

Methods In this randomised open-label trial, eligible patients lived in North America, Latin America, and Spain and had recent, MRI-defined symptomatic lacunar infarctions. Patients were recruited between March, 2003, and April, 2011, and randomly assigned, according to a two-by-two multifactorial design, to a systolic-blood-pressure target of 130–149 mm Hg or less than 130 mm Hg. The primary endpoint was reduction in all stroke (including ischaemic strokes and intracranial haemorrhages). Analysis was done by intention to treat. This study is registered with ClinicalTrials.gov, number NCT 00059306.

Findings 3020 enrolled patients, 1519 in the higher-target group and 1501 in the lower-target group, were followed up for a mean of 3·7 (SD 2·0) years. Mean age was 63 (SD 11) years. After 1 year, mean systolic blood pressure was 138 mm Hg (95% CI 137–139) in the higher-target group and 127 mm Hg (95% CI 126–128) in the lower-target group. Non-significant rate reductions were seen for all stroke (hazard ratio 0·81, 95% CI 0·64–1·03, p=0·08), disabling or fatal stroke (0·81, 0·53–1·23, p=0·32), and the composite outcome of myocardial infarction or vascular death (0·84, 0·68–1·04, p=0·32) with the lower target. The rate of intracerebral haemorrhage was reduced significantly (0·37, 0·15–0·95, p=0·03). Treatment-related serious adverse events were infrequent.

Interpretation Although the reduction in stroke was not significant, our results support that in patients with recent lacunar stroke, the use of a systolic-blood-pressure target of less than 130 mm Hg is likely to be beneficial.

Lancet 2013; 382: 507–15

Published Online
May 29, 2013
http://dx.doi.org/10.1016/S0140-6736(13)60852-1

This online publication has been corrected. The corrected version first appeared at thelancet.com on August 9, 2013

See **Comment** page 482

*Members listed at end of paper

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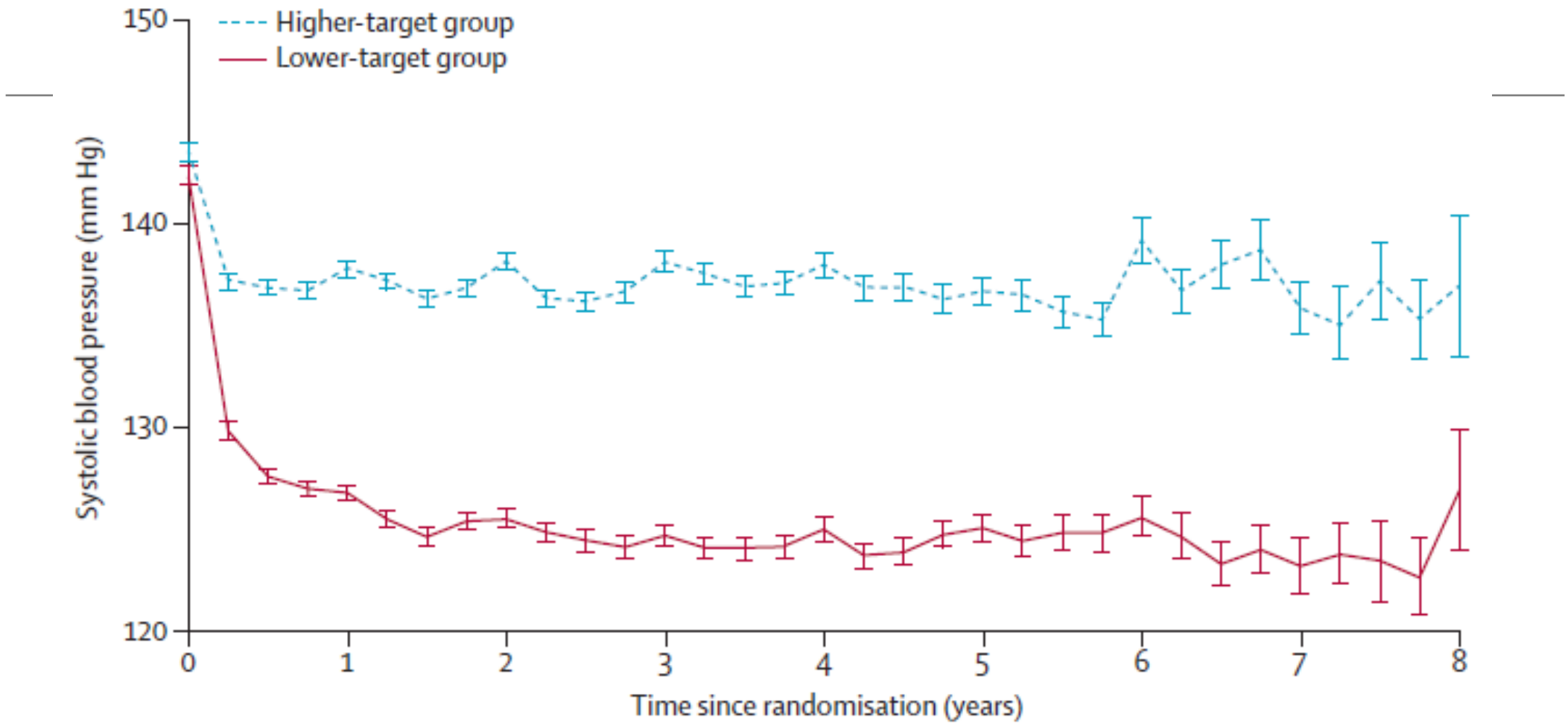
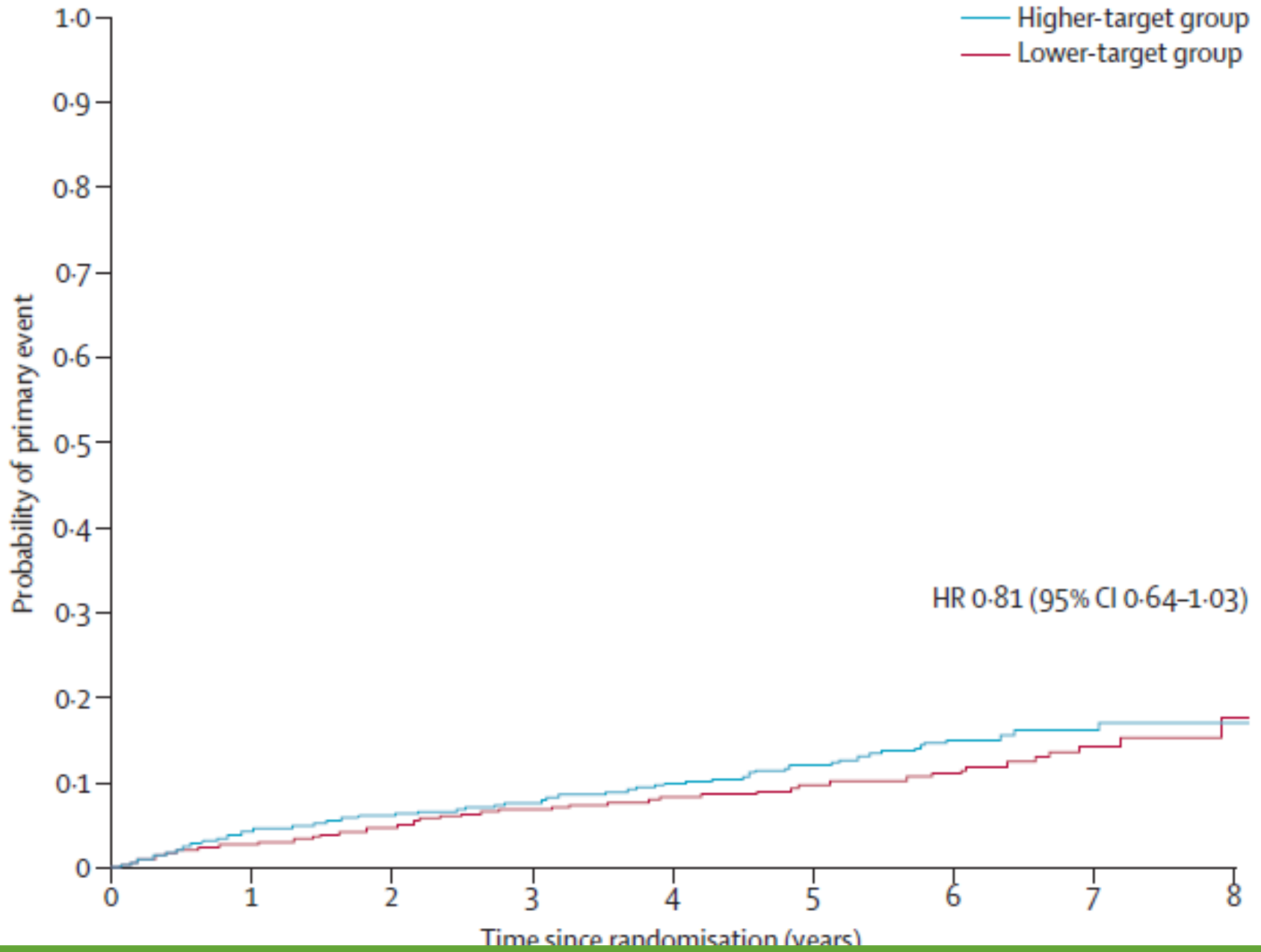

Higher-target group
Lower-target group
Systolic blood pressure (mm Hg)
150
140
130
120
0
1
2
3
4
5
6
7
8
Time since randomisation (years)


Higher-target group
Lower-target group
Probability of primary event
1·0
0·9
0·8
0·7
0·6
0·5
0·4
0·3
0·2
0·1
0
HR 0·81 (95% CI 0·64–1·03)
0
1
2
3
4
5
6
7
8
Time since randomisation (years)

	Higher-target group (n=1519)		Lower-target group (n=1501)		Hazard ratio (95% CI)	p value
	Number of patients	Rate (% per patient-year)	Number of patients	Rate (% per patient-year)		
Stroke						
All stroke	152	2·77%	125	2·25%	0·81 (0·64–1·03)	0·08
Ischaemic stroke or unknown	131	2·4%	112	2·0%	0·84 (0·66–1·09)	0·19
Intracranial haemorrhage						
All	21*	0·38%	13†	0·23%	0·61 (0·31–1·22)	0·16
Intracerebral	16	0·29%	6	0·11%	0·37 (0·15–0·95)	0·03
Subdural or epidural	5	0·091%	6	0·11%	1·18 (0·36–3·88)	0·78
Other	2	0·036%	4	0·072%	1·97 (0·36–10·74)	0·43
Disabling or fatal stroke‡	49	0·89%	40	0·72%	0·81 (0·53–1·23)	0·32
Myocardial infarction	40	0·70%	36	0·62%	0·88 (0·56–1·39)	0·59
Major vascular event*	188	3·46%	160	2·91%	0·84 (0·68–1·04)	0·10

How to compromise SPRINT with SPS3?

Why event rate in the lower BP group in SPS3 study did not decrease?

Due to insufficient number of subjects?

Due to insufficient decline of SBP in SPS3? 120 vs 140 mmHg in SPRINT, 130 vs 150 in SPS3

Due to difference in subjects group?

Due to different methods of BP measurement?

Conclusion and perspective

Target BP in the elderly can not be lowered with SPRINT.

We need more data for reducing target BP in the elderly.

Otherwise we should change the method of measuring BP to totally eliminating white coat effect

The target BP in the guideline is reasonable except JNC-8