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Target Blood Pressure For Asian Population

Management of Elderly Hypertension beyond Target Blood Pressure

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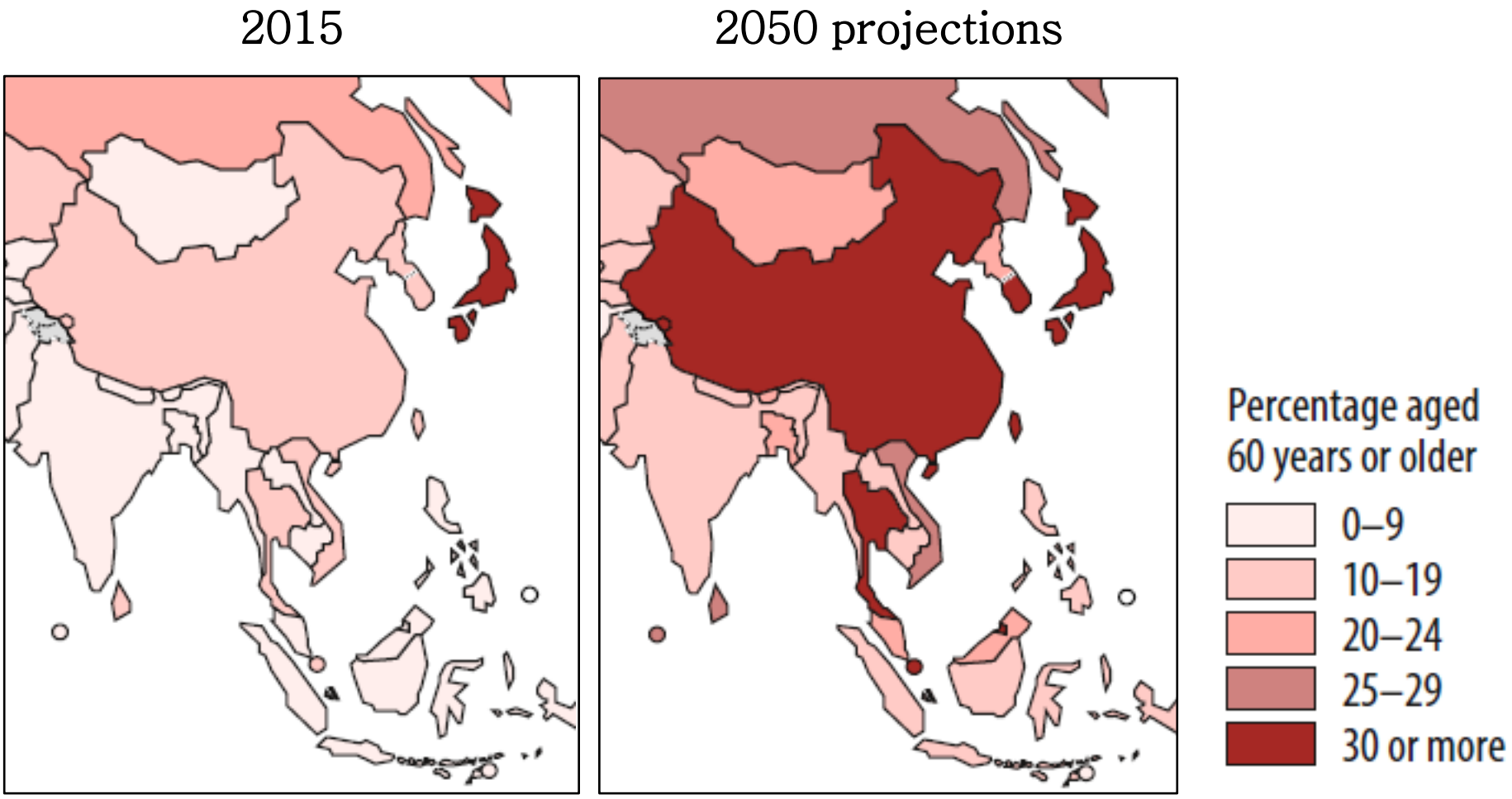
COI Disclosure

Hiromi Rakugi, Osaka University

The author has no actual or potential conflicts of interest to disclose in relation to the presentation.

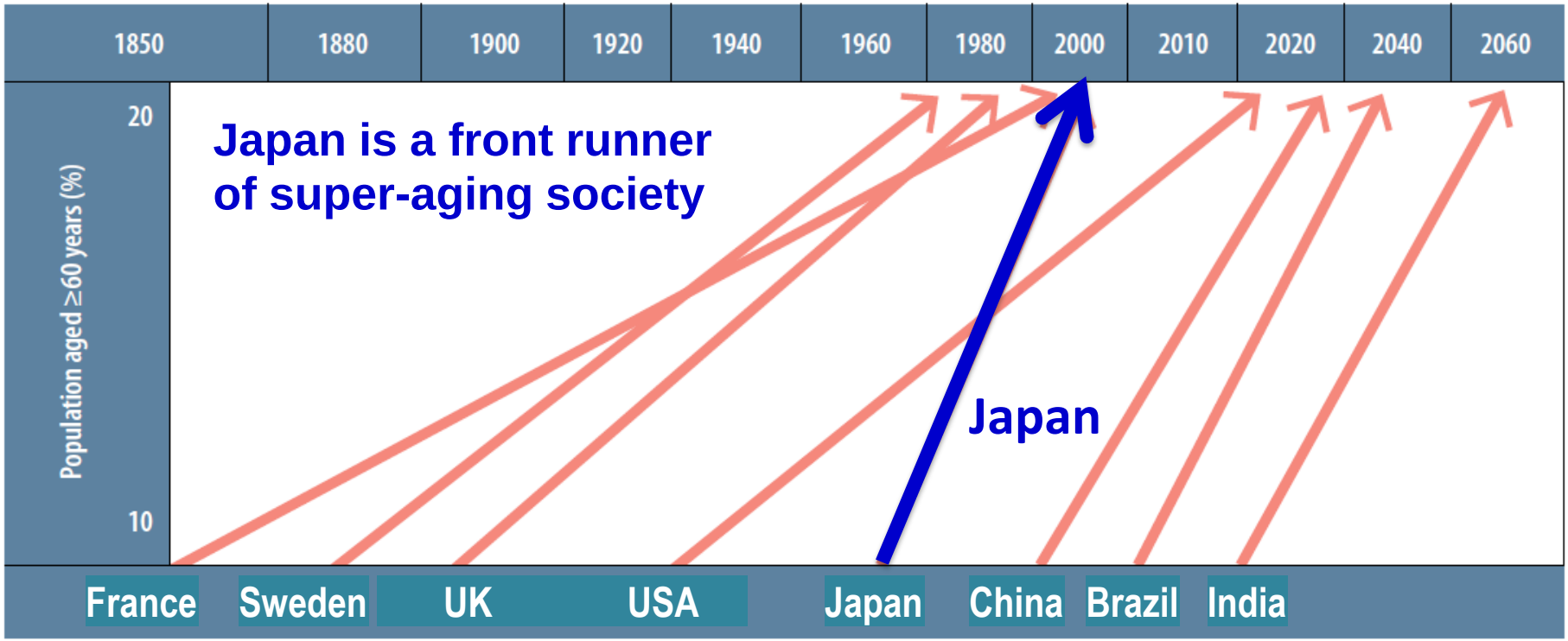
Proportion of population aged 60 years or older, by country
In East Asia and South Asia



World report on ageing and health. World Health Organization 2015

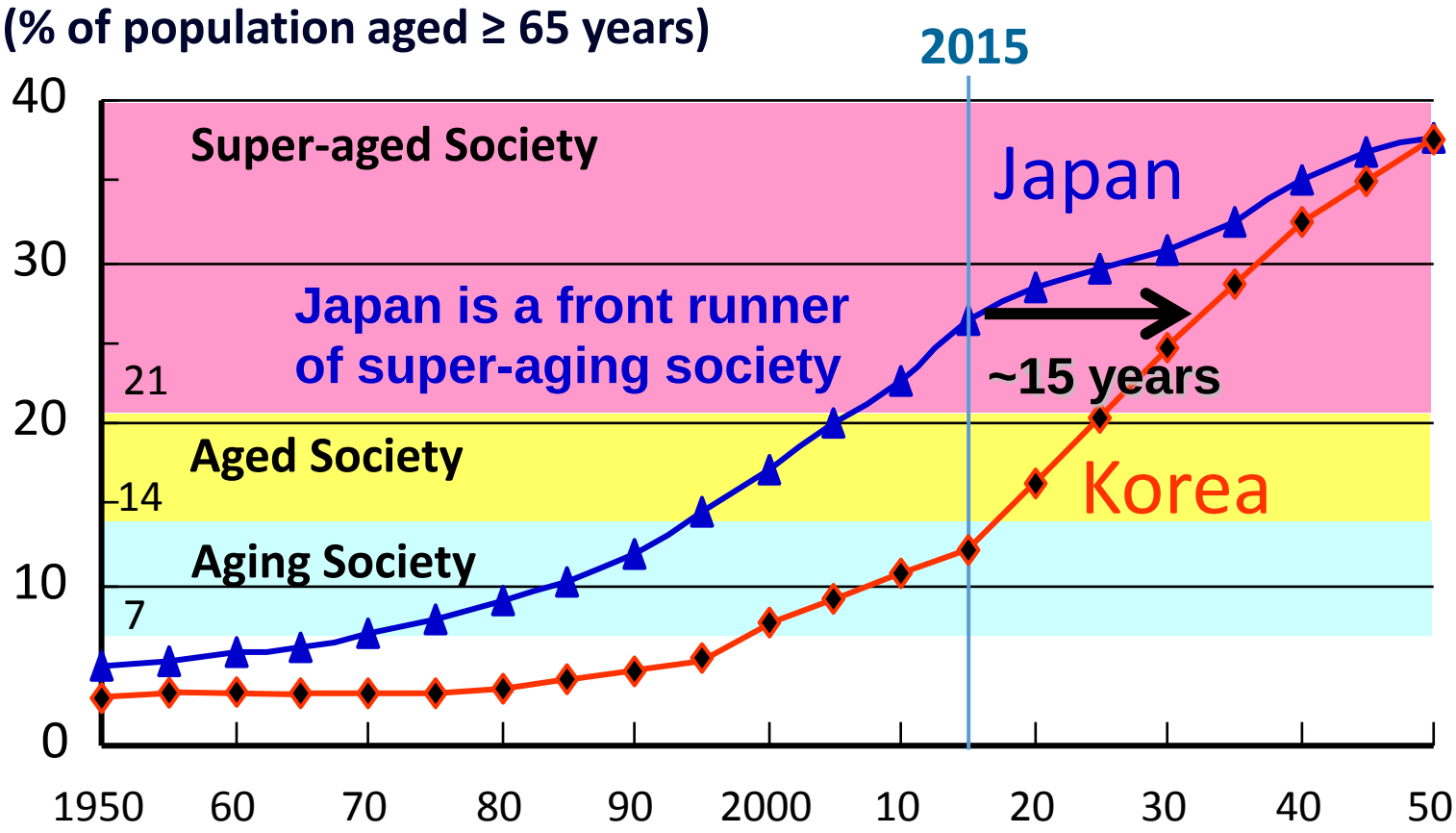
Period required or expected for the percentage of the population aged 60 years and older to rise from 10% to 20%

World report on ageing and health. WHO 2015



	Year at aging/aged society			Years required	
	7%	14%	20%	7%→14%	14%→20%
Japan	1970	1994	2006	24 years	12 years
Korea	2000	2018	2026	18 years	8 years

Only 15 years later, Korea will reach to the same level of society aging in Japan now.



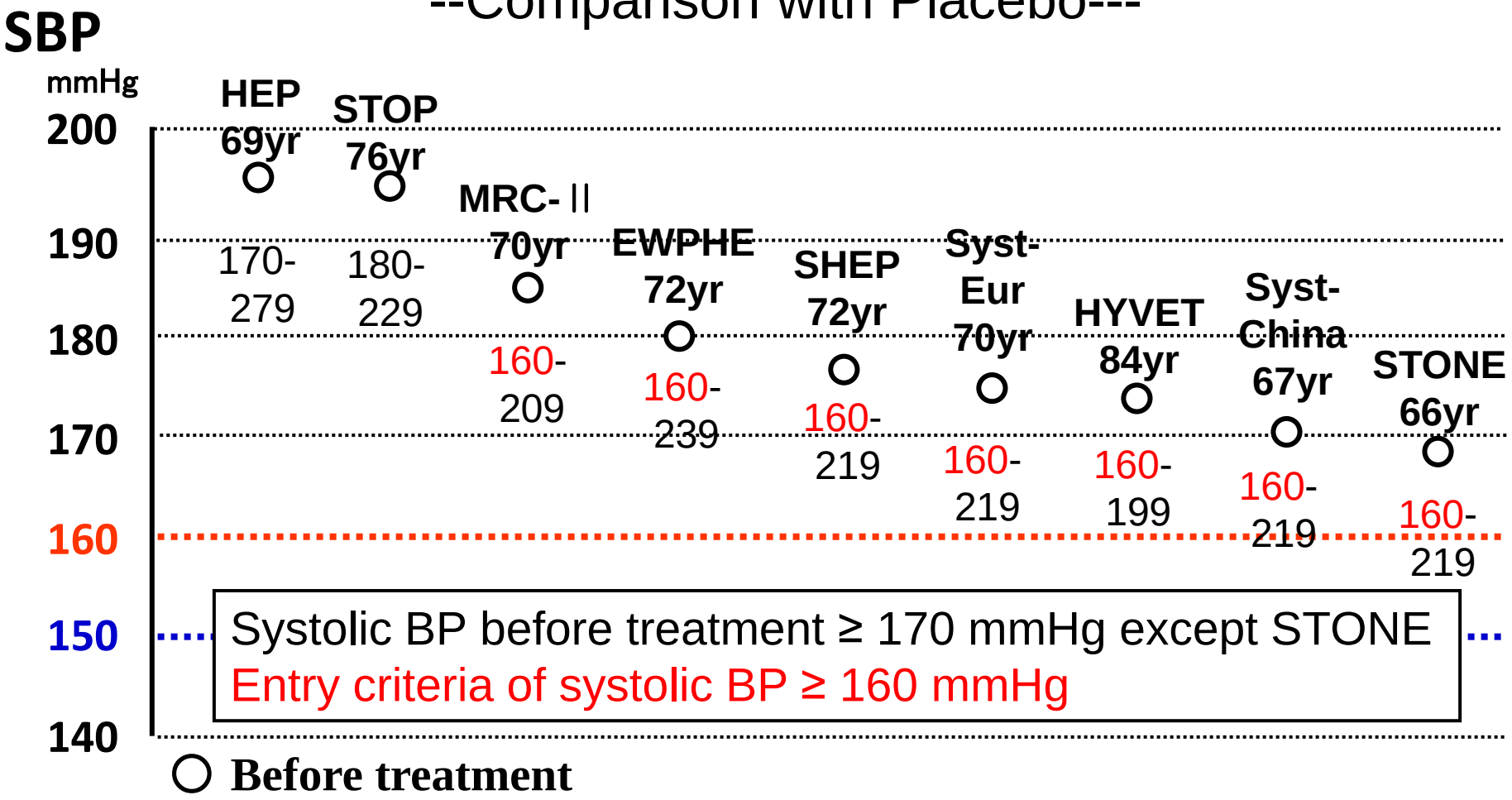
Chapter of JSH2014 guideline for elderly hypertension would be also useful in Korea

Who should be treated with antihypertensive drugs?

- Levels of blood pressure
  - ≥140, ≥150, ≥160 mmHg
- Health condition
  - Fit elderly, frail elderly
- Age category in the elderly
  - Young-old, old-old, oldest-old

Clinical Trials In Elderly Hypertension

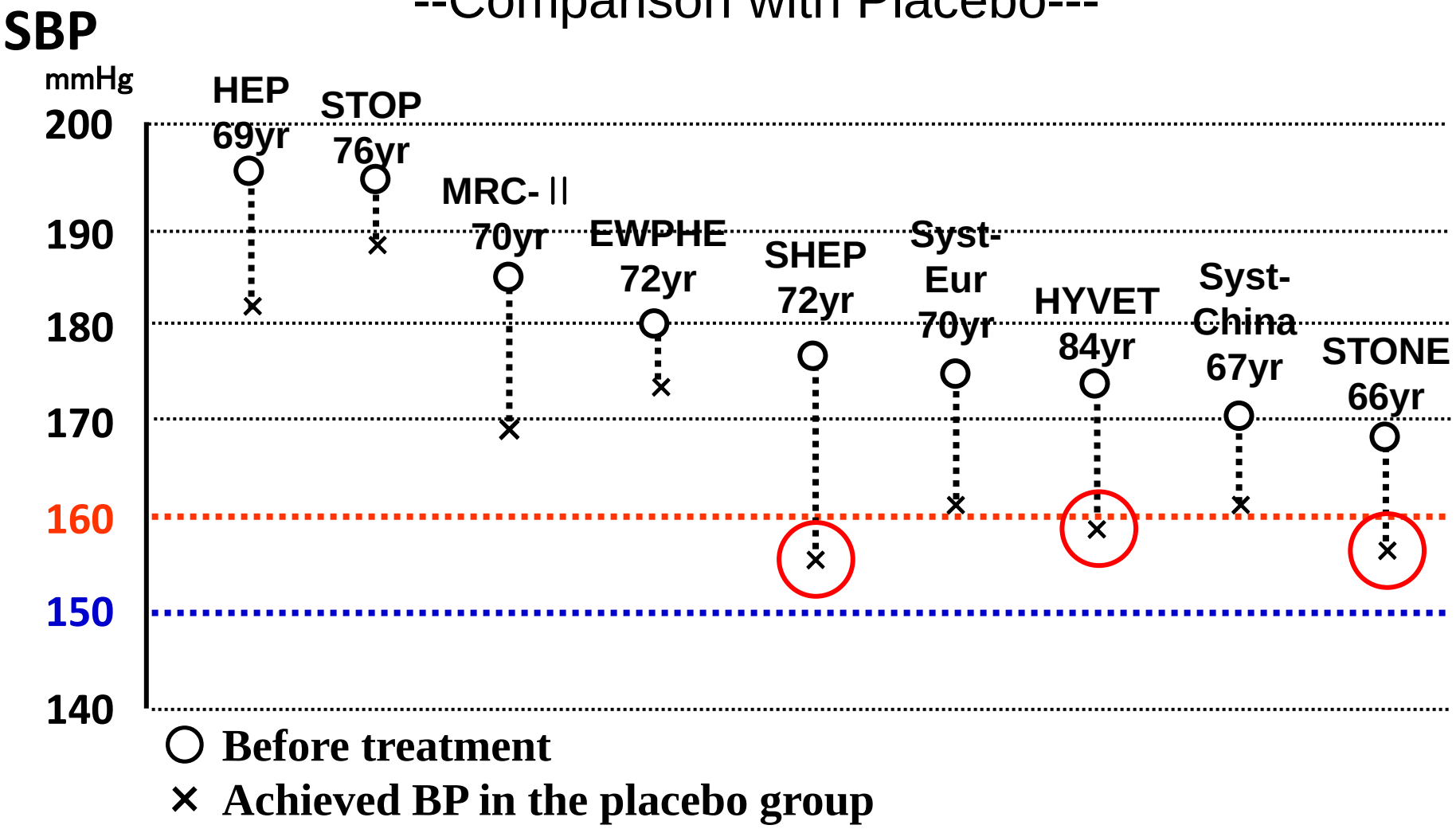
--Comparison with Placebo---



Beneficial effects of antihypertensive drugs have been elucidated only in patients with systolic BP ≥ 160 mmHg.

Clinical Trials In Elderly Hypertension

--Comparison with Placebo---



At least, patients with BP > 150 mmHg should be treated.

The Impact of Frailty on the Association of High Blood Pressure With Mortality in Elderly Adults

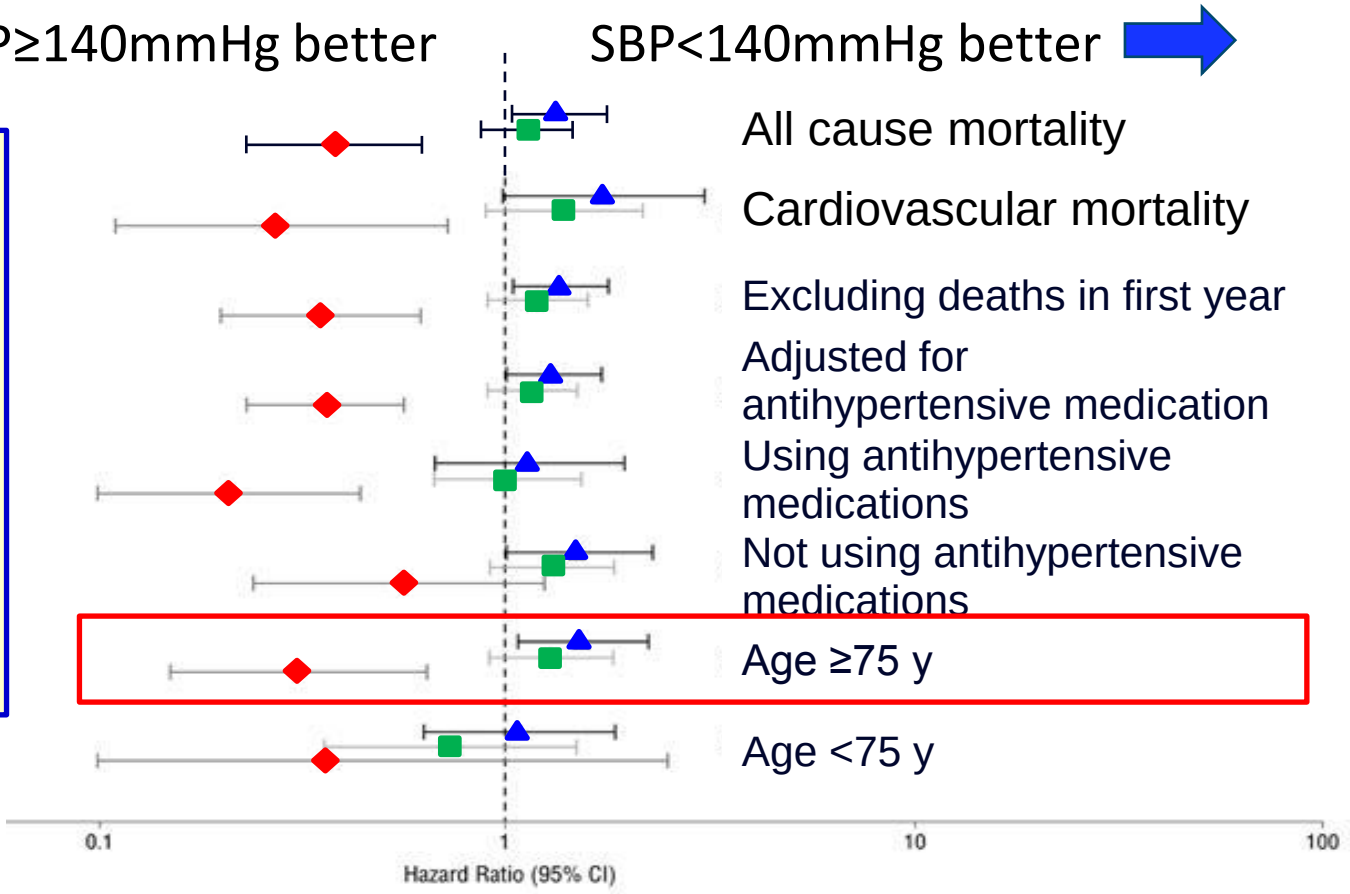
Age and comprehensive characteristics should be considered.

NHANES

Age ≥65 y, n=**2340**

6m **walking speed**

- Faster walkers (≥0.8 m/s), n=1307
- Slower walkers (<0.8 m/s), n=790
- Did not complete, n=243



Odden MC, et al. *Arch Intern Med*. 2012;172:1162-1168

JSH2014

Initiation of antihypertensive drugs

Drug therapy should be indicated for patients with BP ≥ 140/90mmHg in principle.

However, treatment indication must be **individually assessed** in persons,

- aged **over 75 years**, with a systolic blood pressure of 140–149mmHg or
- **frail elderly**, such as subjects who are unable to accomplish 6m walking.

(Recommendation grade: B, Evidence level: II)

Optimal target BP for prevention of cardiovascular events in the elderly patients with hypertension

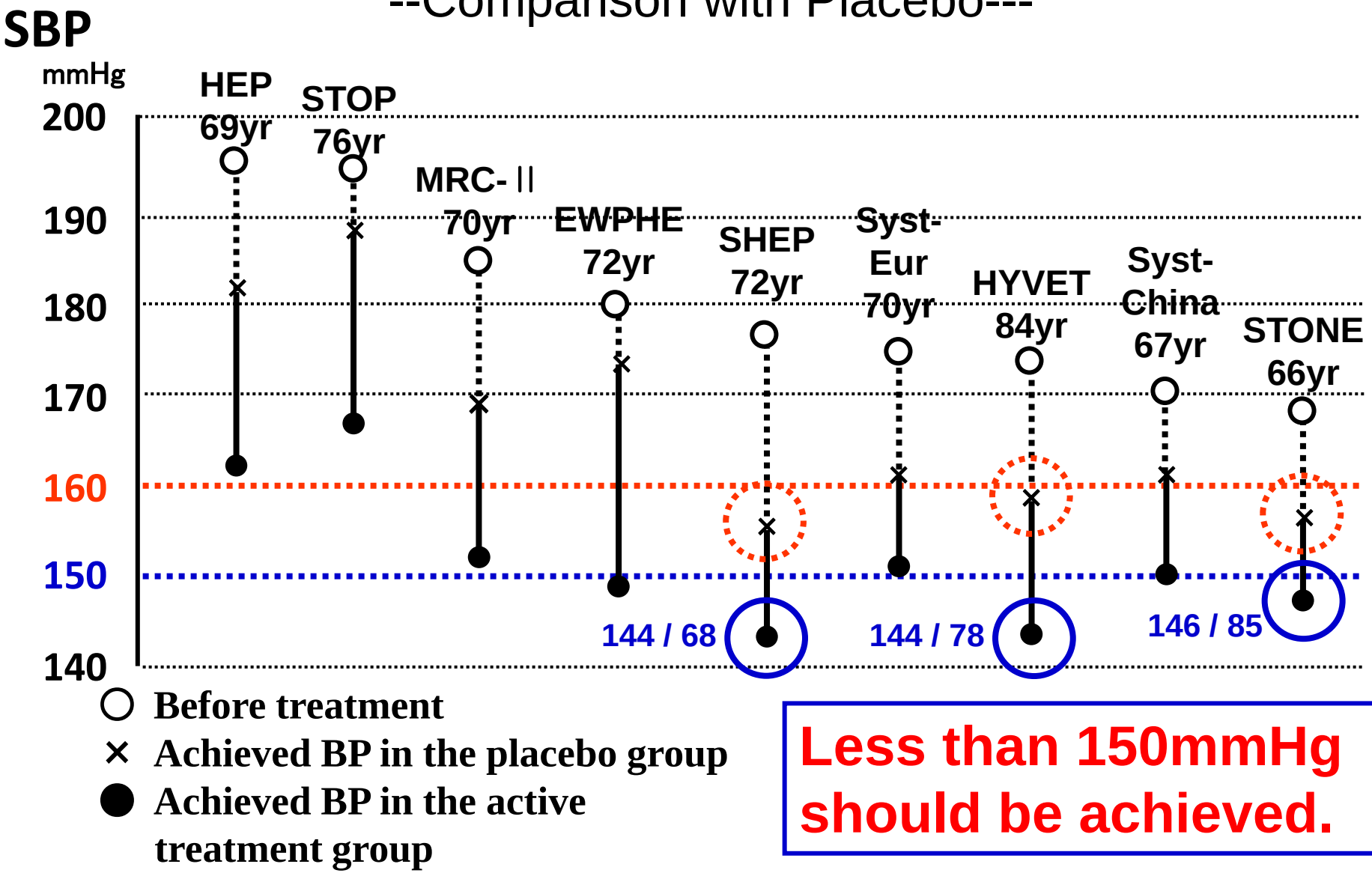
Optimal target BP would be estimated based on

(1) achieved BP in the RCTs and

(2) target BPs which was compared between two groups in the RCTs.

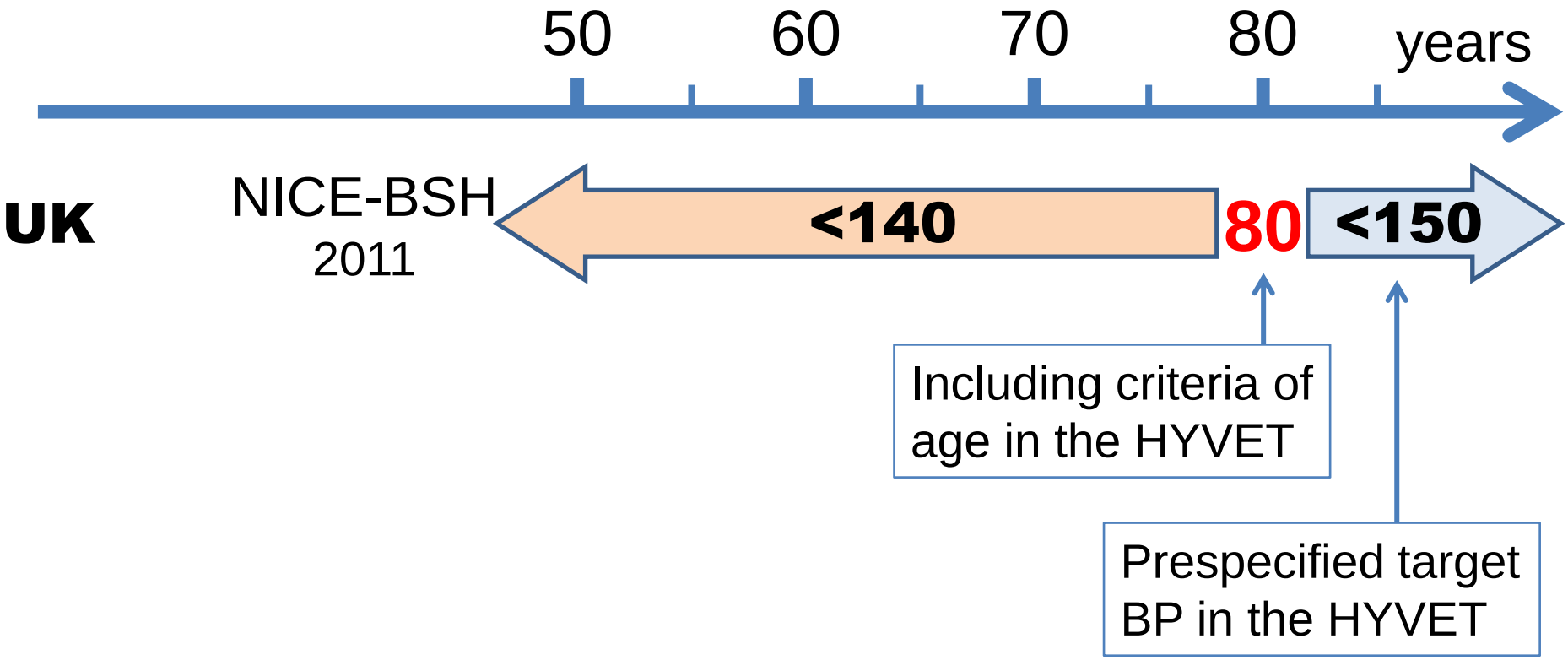
Clinical Trials In Elderly Hypertension

--Comparison with Placebo---



Less than 150mmHg should be achieved.

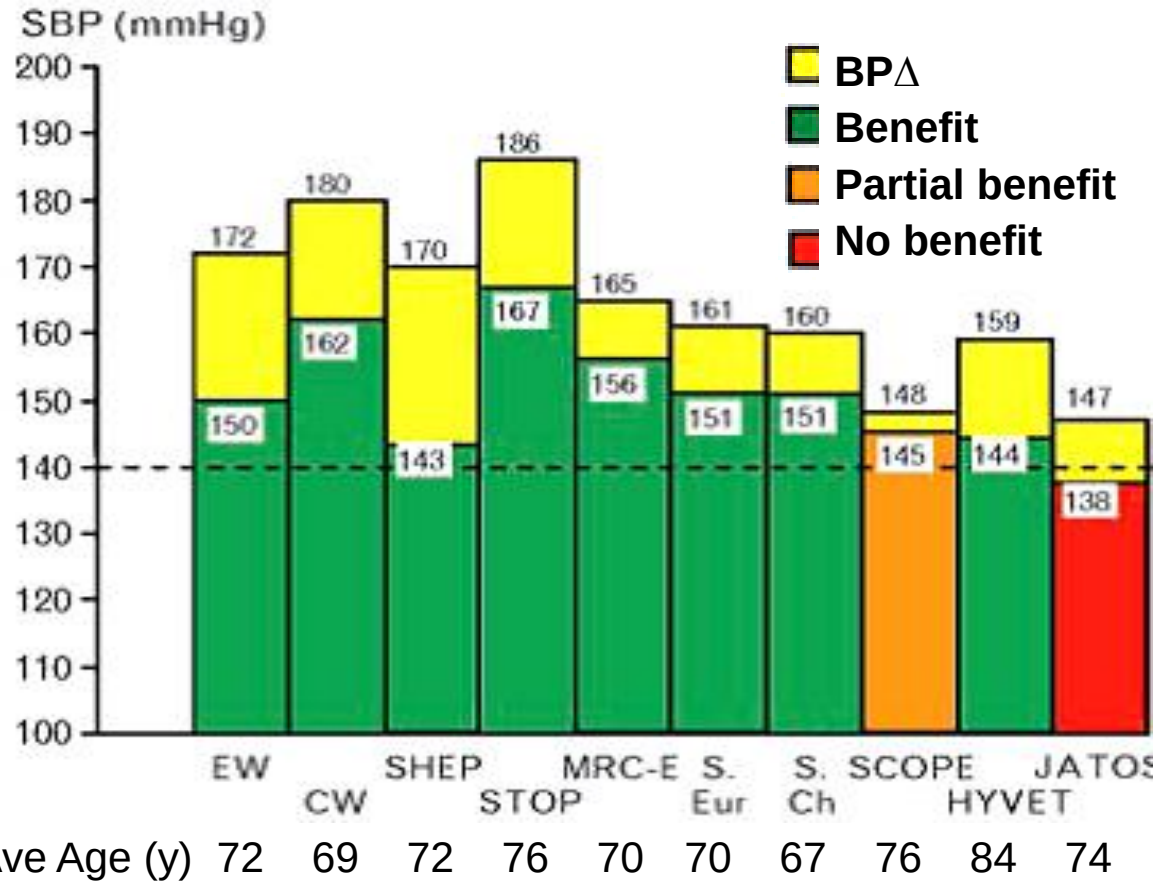
Target BP recommended by the guidelines
the elderly and the very elderly



RCTs cannot support the concept, "the lower, the better" in elderly hypertension

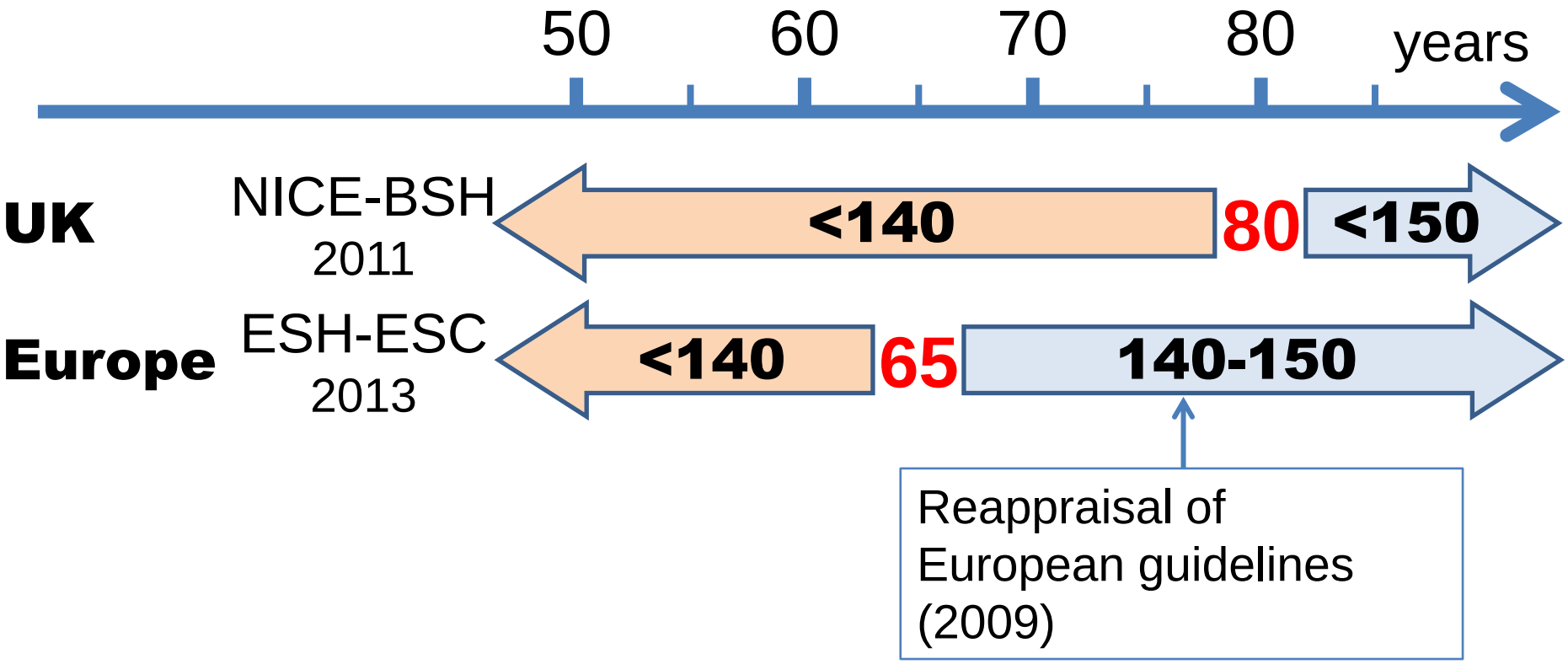
Reappraisal of European guidelines on hypertension management.

J Hypertens. 2009, 27:2121–58, Original reference: Zanchetti et al. JH 2009, 27:923–934



There is no trial evidence in support of the guidelines recommendation to adopt the less than 140 mmHg SBP target in elderly patients.

Target BP recommended by the guidelines
the elderly and the very elderly



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)

James PA et al JAMA on line Dec 18, 2013

Recommendation 1

duces stroke, heart failure, and coronary heart disease (CHD). There is also evidence (albeit low quality) from evidence statement 6, question 2 that setting a goal SBP of lower than 140 mm Hg in this age group provides no additional benefit compared with a higher goal SBP of 140 to 160 mm Hg or 140 to 149 mm Hg.[9,10]

To answer question 2 about goal BP, the panel reviewed all RCTs that met the eligibility criteria and that either compared treatment with a particular goal vs no treatment or placebo or compared treatment with one BP goal with treatment to another BP goal. The trials on which these evidence statements and this recommendation are based include HYVET, Syst-Eur, SHEP, JATOS, VALISH, and CARDIO-SIS.[1-3,9-11]

HYVET, Syst-Eur, SHEP, JATOS, VALISH, CARDIO-SIS

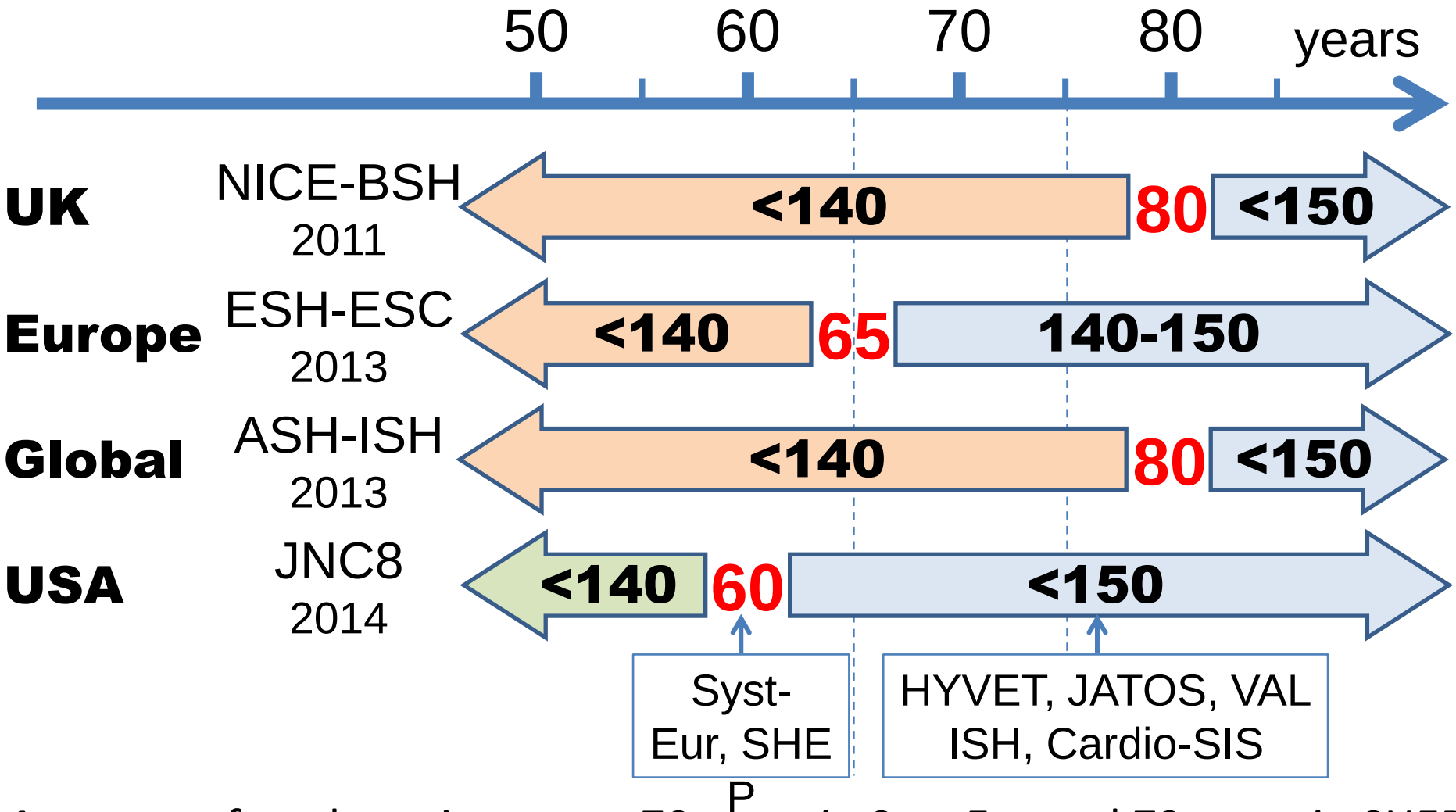
References

9. JATOS Study Group. Principal results of the Japanese trial to assess optimal systolic blood pressure in elderly hypertensive patients (JATOS). *Hypertens Res*. 2008;31(12):2115-2127.

10. Ogihara T, Saruta T, Rakugi H, et al; Valsartan in Elderly Isolated Systolic Hypertension Study Group. Target blood pressure for treatment of isolated systolic hypertension in the elderly: Valsartan in Elderly Isolated Systolic Hypertension Study. *Hypertension*. 2010;56(2):196-202.

11. Verdecchia P, Staessen JA, Angeli F, et al; Cardio-Sis investigators. Usual versus tight control of systolic blood pressure in non-diabetic patients with hypertension (Cardio-Sis): an open-label randomised trial. *Lancet*. 2009;374(9689):525-533.

Target BP recommended by the guidelines
the elderly and the very elderly



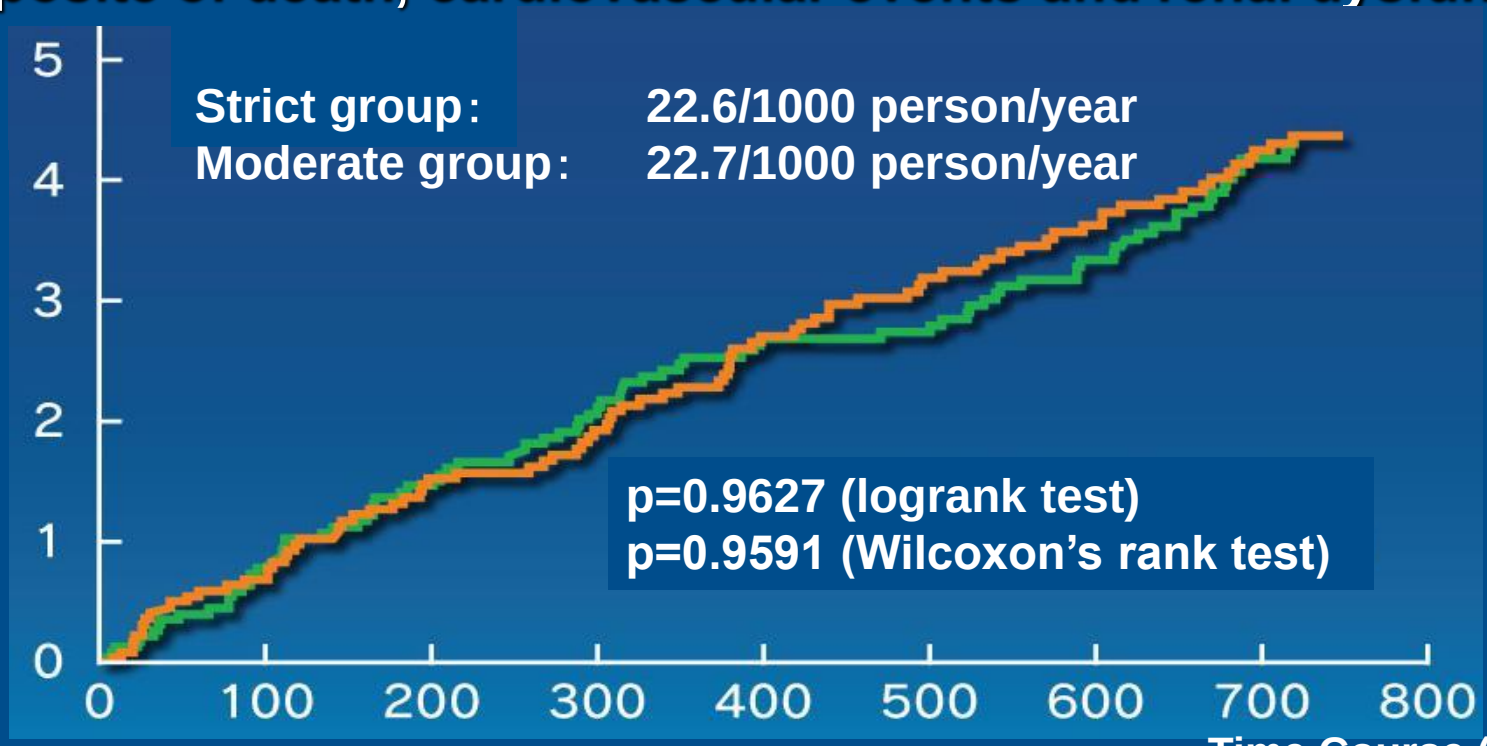
Mean age of study patients was 70 years in Syst-Eur and 72 years in SHEP.

JATOS

The Japanese Trial to Assess Optimal Systolic Blood Pressure in Elderly Hypertensive Patients

- Strict-treatment group: < 140 mmHg (136/75 mmHg)
- Moderate-treatment group: 140-160mmHg (146/78 mmHg)

Composite of death, cardiovascular events and renal dysfunction



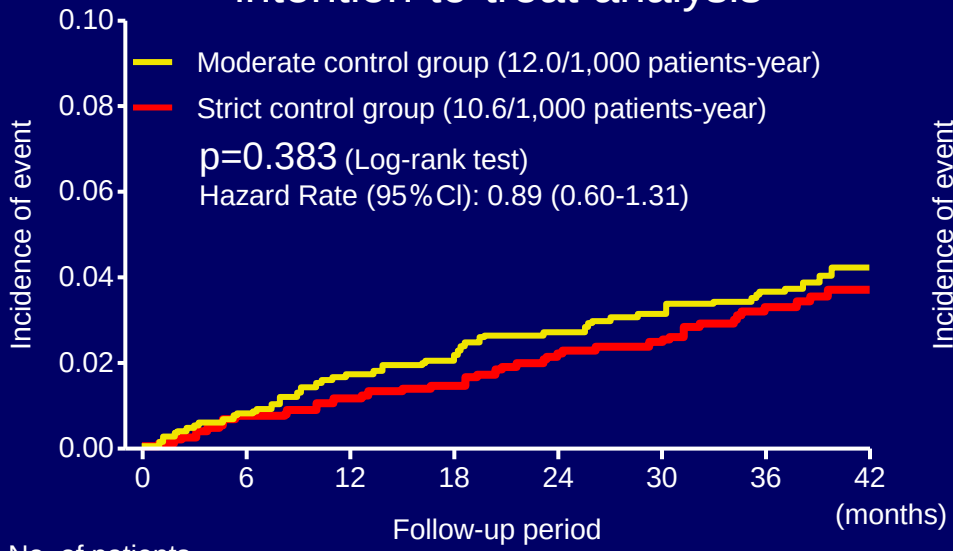
JATOS study group *Hypertension Research* 2008

VALISH study (70-84 years with ISH)

Primary endpoint: composite of cardiovascular and renal events

- Moderate control (<150mmHg) Achieved BP=142.0/76.5 mmHg
- Strict control (<140mmHg) Achieved BP=136.6/74.8 mmHg

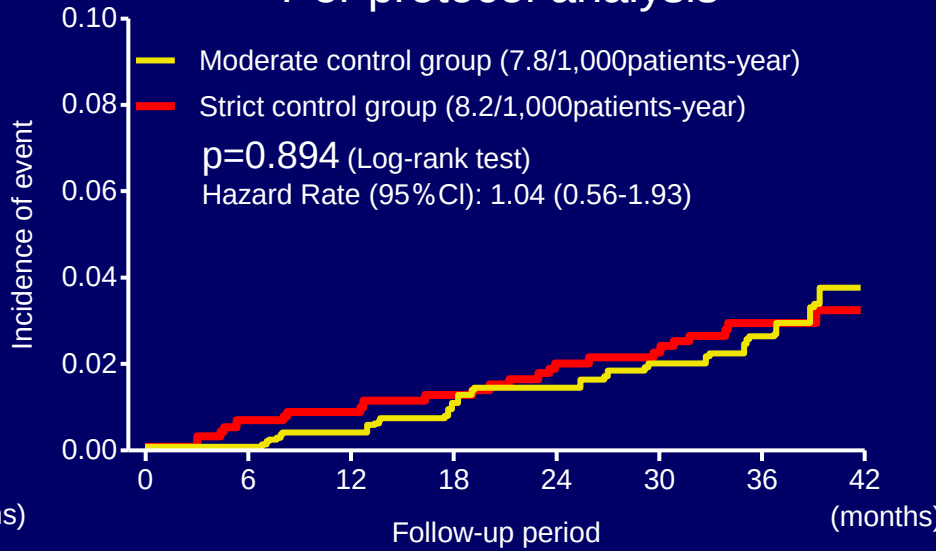
intention-to-treat analysis



No. of patients

Strict	1,545	1,482	1,408	1,336	1,306	1,295	924	336
Moderate	1,534	1,461	1,375	1,304	1,279	1,265	902	335

Per protocol analysis

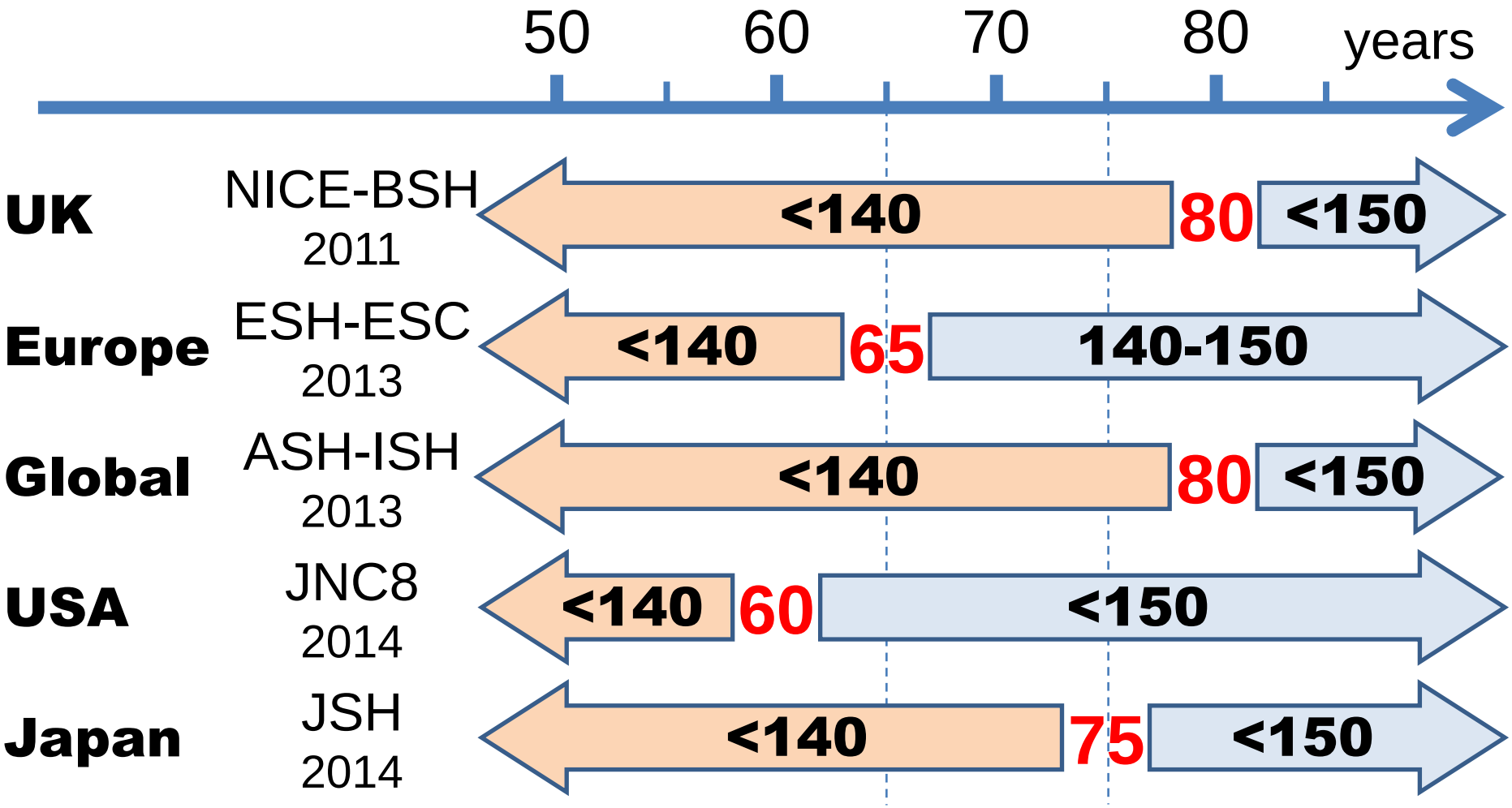


	1,043	1,012	969	932	914	906	624	225
	733	719	686	653	646	638	437	182

Ogihara T et al: Hypertension 2010;56:196-202, www.clinicaltrials.gov (identifier NCT00151229).

(Top paper published in *Hypertension* for 2010, Clinical Science Category)

Target BP recommended by the guidelines
the elderly and the very elderly

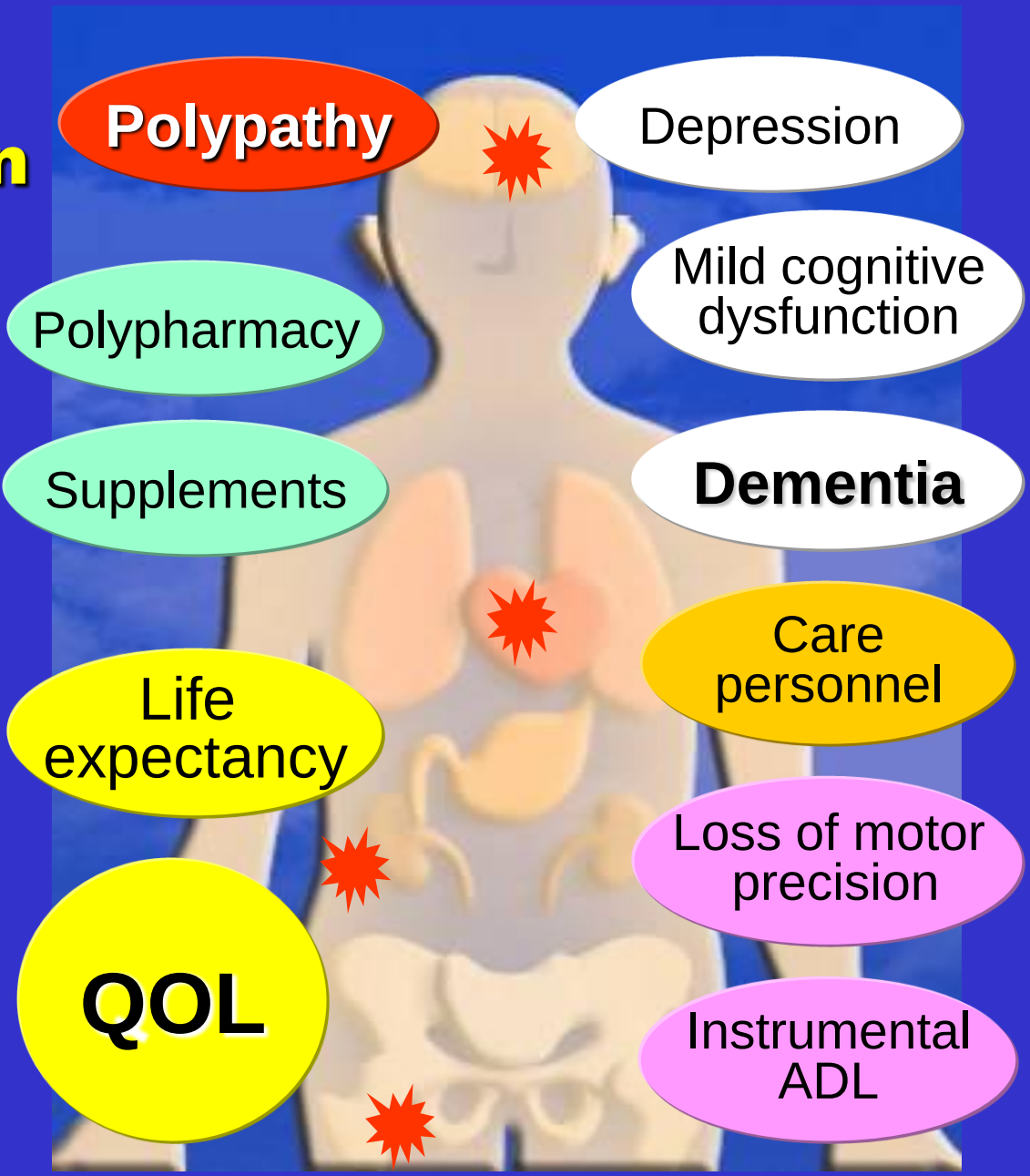


Goal of the treatment of HT in the very elderly

Successful aging

- Avoiding disease and disability
- High cognitive and physical function
- Engagement with life

Rowe and Kahn, The Gerontologist, 1997



What are the goals of antihypertensive treatment for the elderly?

1. Prevention of cardiovascular events
2. Prevention of decline in cognitive function
3. Prevention of fall/fracture
4. Prevention of serious adverse events such as acute kidney disease

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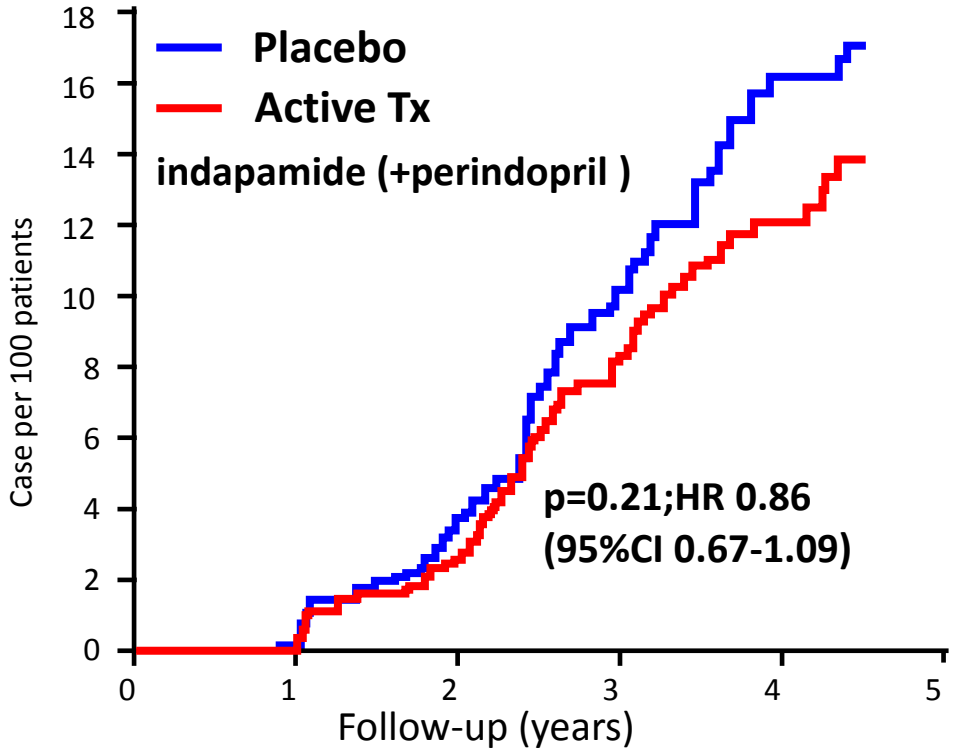
HYVET-COG

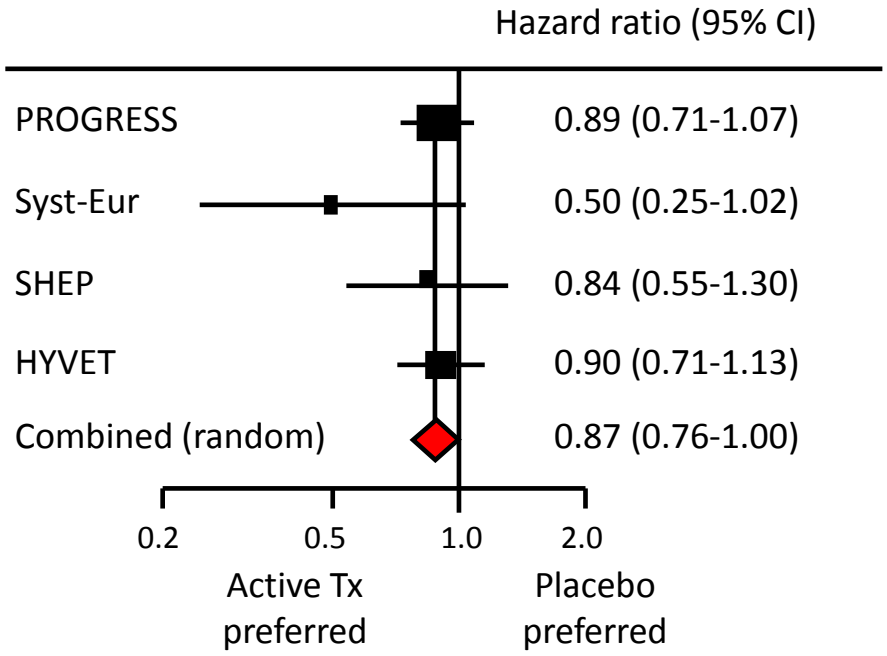
Hypertension in the Very Elderly Trial cognitive function assessment

3336 HYVET participants (age 83.5 years、baseline SBP 173 mmHg)

Target BP : SBP < 150 mmHg and DBP < 80 mmHg

Cumulative incident of patients with dementia





Test for overall effect; p=0.045

Peters R, et al. Lancet Neurology, July 8, 2008

Chapter 9. Dementia

1. Hypertension in **middle age** is a risk factor for senile dementia, and it should be aggressively treated from the perspective of dementia prevention. (Recommendation grade: C1, Evidence level: VI)
2. The prevention of dementia by antihypertensive medication in **the elderly** has not been proved, but no study has suggested that antihypertensive drugs reduce the cognitive function. Accordingly, antihypertensive drug therapy should be performed. (Recommendation grade: C1, Consensus)
3. There is little evidence about the effects of antihypertensive drugs on cognitive function in hypertensive **patients with dementia**, but antihypertensive treatment should be considered. (Recommendation grade: C1, Consensus)

What are the goals of antihypertensive treatment for the elderly?

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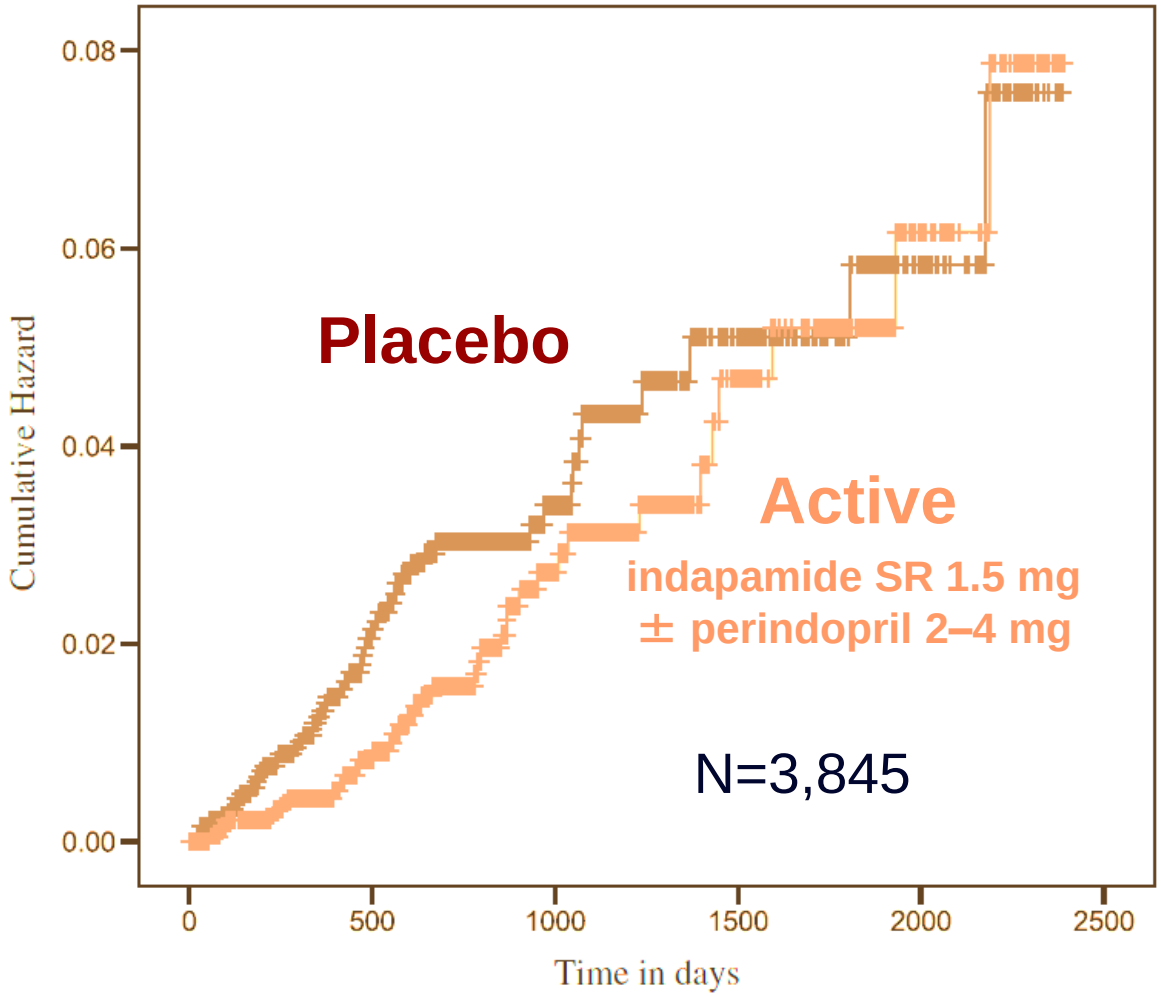
The effect of treatment based on a diuretic ± ACE inhibitor on fractures in the Hypertension in the Very Elderly Trial (HYVET)



Incidence of Fracture

Active: 42 cases

Placebo: 60 cases

Cox proportional hazard regression, adjusted for key baseline risk factors

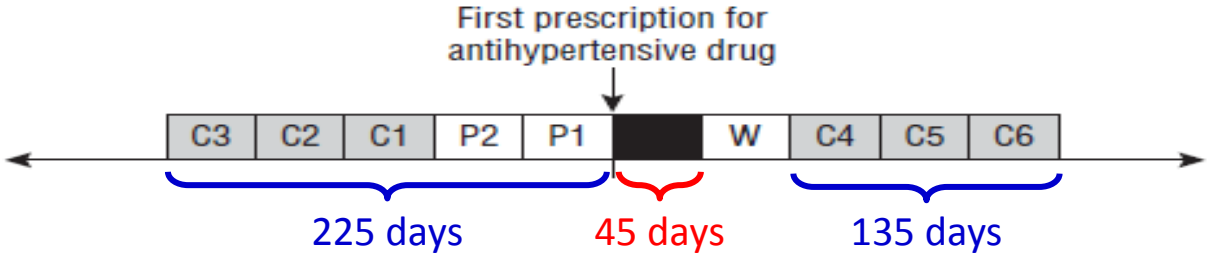
HR: 0.58

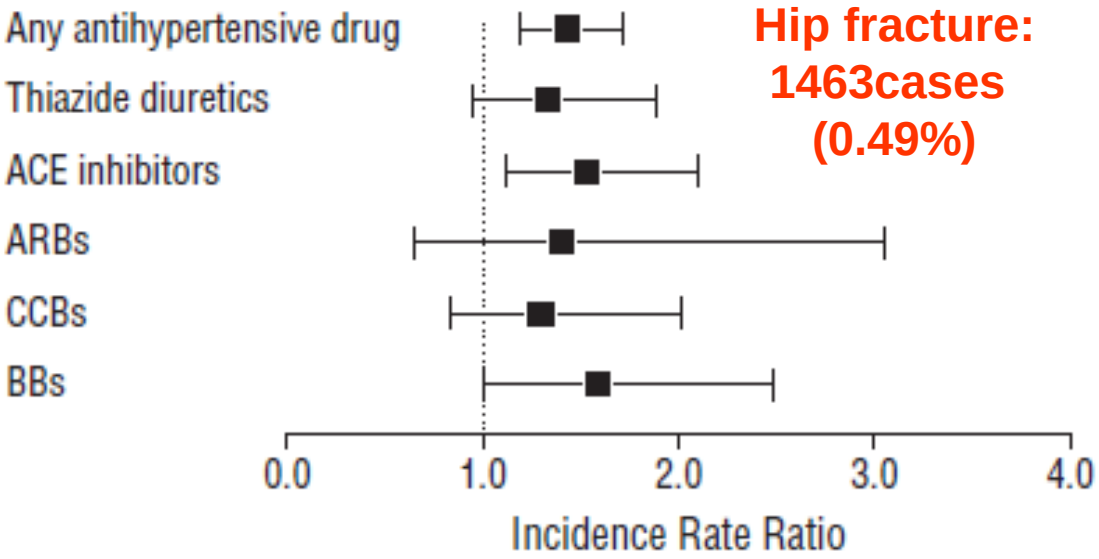
(95% CI 0.33–1.00)

P=0.0498

Peters R, et al.
Age and Ageing
2010; 39: 609–616

The risk of Hip Fracture increased 43% during the first 45 days after newly initiation of antihypertensive drugs in the elderly





Hip fracture: 1463cases (0.49%)

Inclusion:

Ontario Drug Benefit Program prescription drugs Database, Age ≥ 66 years, n=301,591

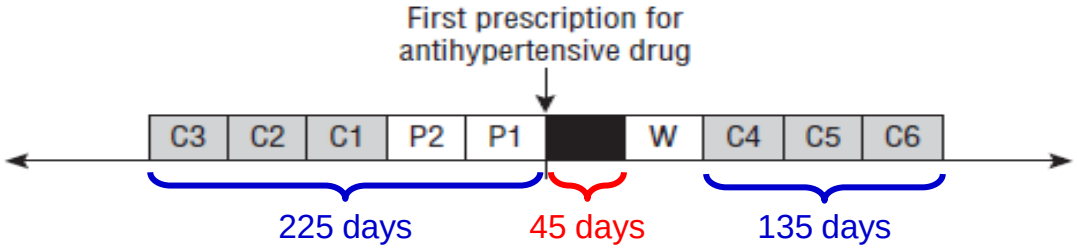
Exclusion:

DM, CVD, renal disease, prescription of antihypertensive drugs due to diseases other than hypertension, residents in long-term care homes

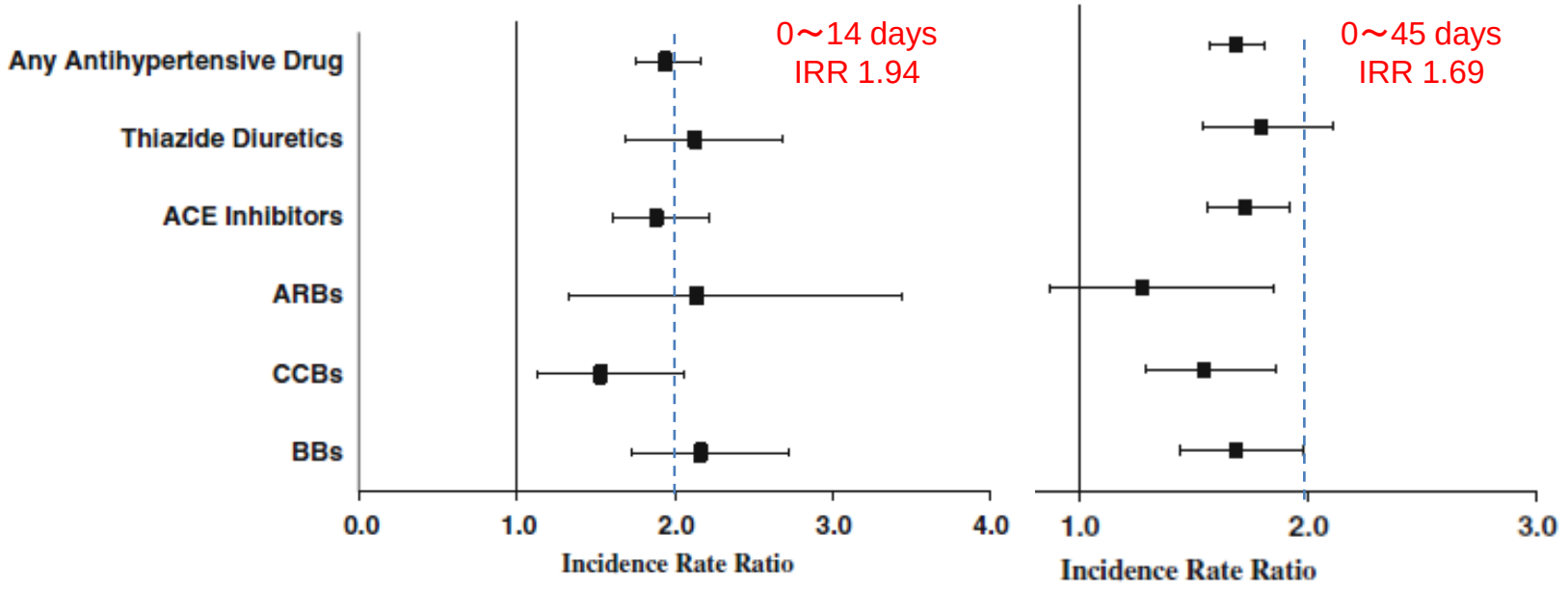
Butt DA, et al. published online November 19, 2012 in the *Archives of Internal Medicine*

The risk of falls on initiation of antihypertensive drugs in the elderly

New users had a 69 % increased risk of having an injurious fall during the first 45 days following antihypertensive treatment (IRR = 1.69; 95 % CI, 1.57-1.81).



Subjects：543,572
(Age 80 years)
Fall：8,893人
Incidence:1.6%



Butt DA, et al. Osteoporos Int (2013) 24:2649–2657

JSH2014: Precautions associated with the prevention of fall/fracture

- **An inquiry on a history of fall within 1 year should be conducted.** If the history is present, intrinsic and extrinsic factors should be examined.
- Osteoporosis should be evaluated and treatment should be performed according to guidelines.
- If there is no antihypertensive drug to be aggressively indicated, thiazide diuretics should be used for osteoporosis.
- Blood pressure should be gradually reduced regardless of the presence or absence of orthostatic hypotension.
- When antihypertensive drug therapy is newly started or changed, the risk of fracture may increase.

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1. Prevention of cardiovascular events
2. Prevention of decline in cognitive function
3. Prevention of fall/fracture
4. Prevention of serious adverse events such as acute kidney disease

The SPRINT Trial

KEY POINTS FROM

A Randomized Trial of Intensive versus Standard Blood-Pressure Control

by the SPRINT Research Group

NOVEMBER 9, 2015

<120 mm Hg (Intensive)

<140 mm Hg (Standard)

121.5 mm Hg

134.6 mm Hg

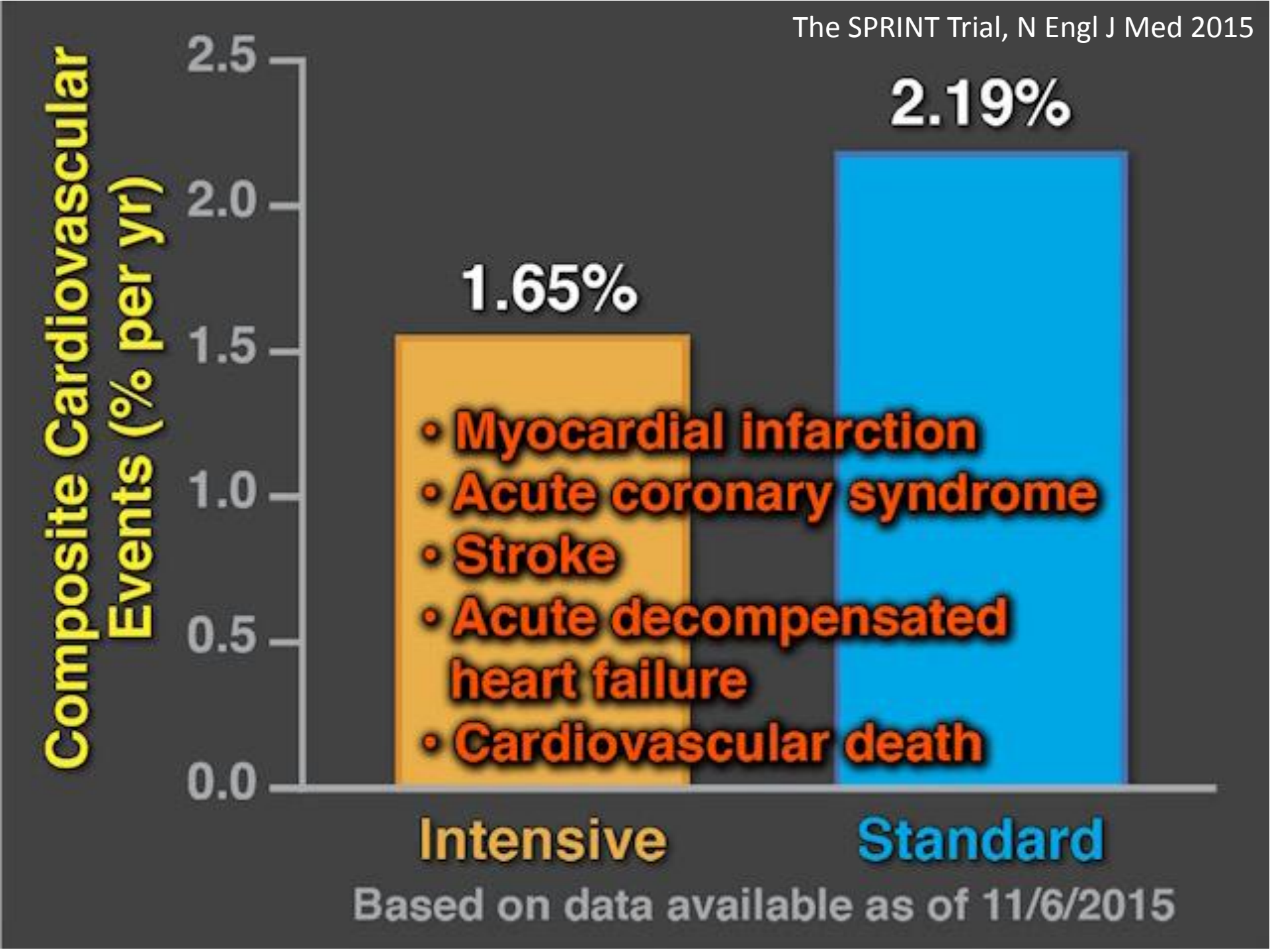
Automated Office BP Measurement

2.8 Medications

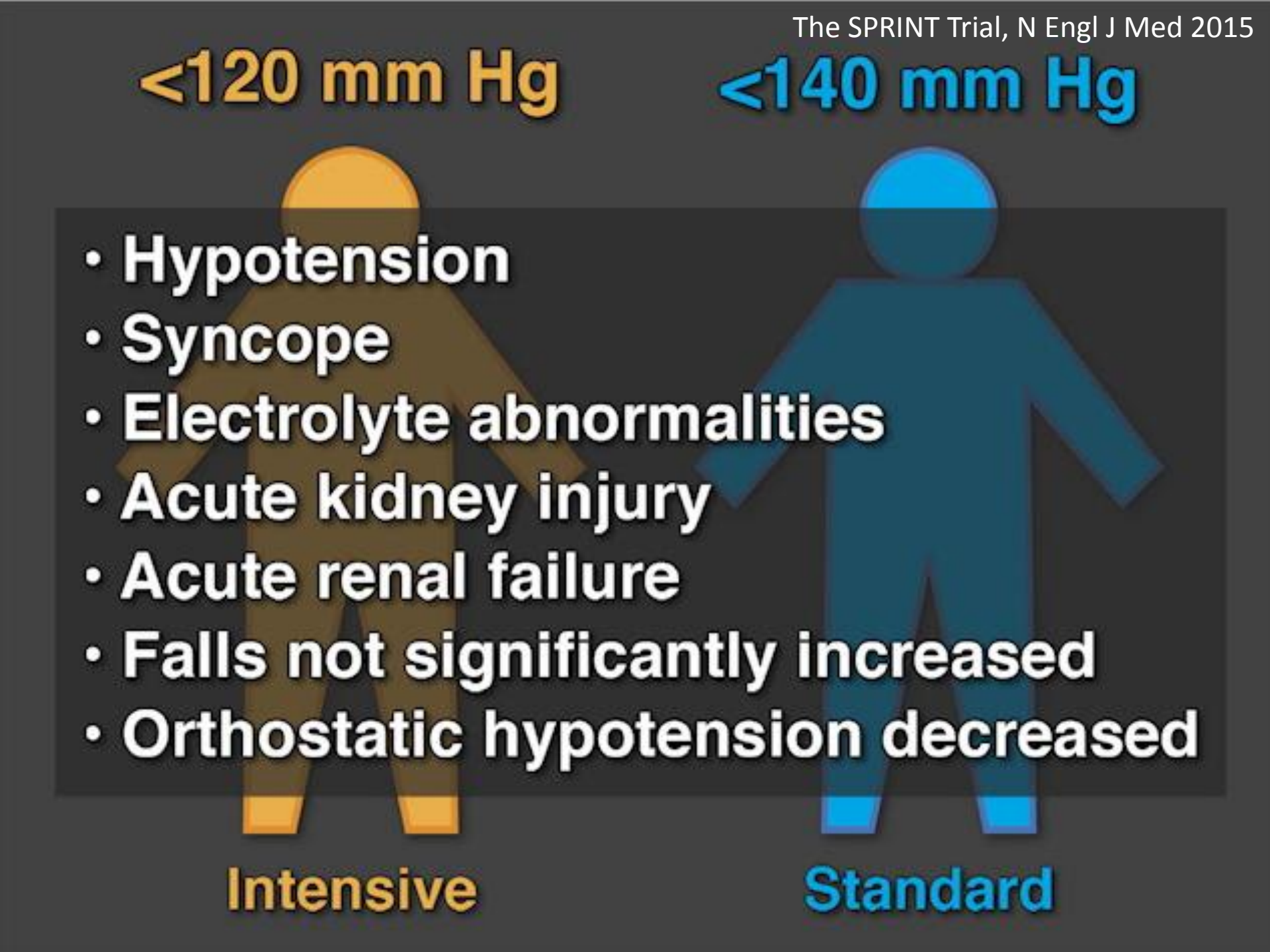
1.8 Medications

The SPRINT Trial, N Engl J Med 2015

The SPRINT Trial, N Engl J Med 2015



The SPRINT Trial, N Engl J Med 2015



Three Things to Know About the Sprint Blood Pressure Trial

By KRUMHOLZ HM, M.D. ***The New York Times***. NOVEMBER 9, 2015

First, the results should not be considered a mandate for people to run out and get treated so their BP are below 120.

- **Over all, about one in 12 (about 17 million adults) would have been considered eligible for the study.**
- **Of those already being treated, one in six patients**
- **BP was measured with patients sitting in a quiet area for five minutes, with no doctor present, using an automated machine that took three readings.**

Second, the potential benefits of lowering BP must be weighed against harms.

- **Benefits: Avoid one CV event every 200 people treated per year, and one death every 300 people treated per year.**
- **Harms: one more life-threatening low BP, one more fainted and two more had severe kidney problems for every 100 people treated to achieve the lower BP over the 3.3 years of follow-up.**

Third, we need more information about the balance of risks and benefits for each person so that the choice can be personalized.

Dehydration- or environmental change-matched guidance for drug therapy

- Excessive salt restriction or dehydration (diarrhea, fever, excessive sweating in the summer, a decrease in dietary intake) sometimes enhances the responses to antihypertensive drugs. Patients must be instructed to consult the attending physician if the condition deteriorates with the above symptoms.
- Blood pressure sometimes changes with environmental changes such as admission to a nursing home (including salt restriction related to meals in the nursing home).

Evaluation of drug adherence

Various factors involved in a reduction in adherence

- Insufficient understanding of treatment by the patient
- Cognitive impairment
- Impairment of the visual function or coordinated movement
- Complex prescription, a large number of drugs, recent switching of the prescription

JSH2014

Precautions for the management of drug adherence

- Informed consent with supporting the understanding of treatment by the patient
- **Simplification of prescriptions** (use of long-acting antihypertensive drugs or fixed-combination drugs)
- **One-dose packaging**
- Utilization of **pill calendars/cases**
- **Compliance management by the patient's family or nursing staff**

Precautions in management of hypertension beyond BP lowering in the very elderly and frail patients

1. Precautions in fall/fracture at initiation of drugs
2. Preventions in decline in cognitive function
3. Precautions in serious adverse events
4. Precautions in dehydration or environmental changes which may enhance drug effects
5. Precautions in poor drug adherence