Challenges in Hypertension 2017

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오늘의 내용

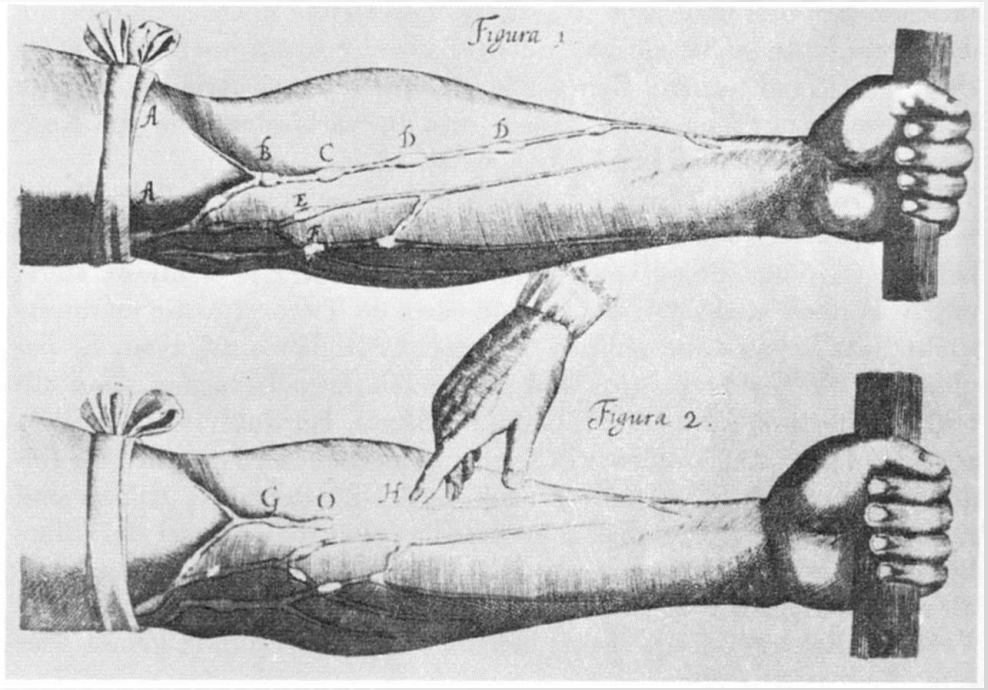
- 고혈압의 간략한 역사 및 임상적 의의
- 적극적 혈압조절의 중요성 (메타분석, SPRINT)
- 고혈압의 치료에서 순응도 문제
- 국내 유일 삼중 고정용량복합제 (Sevikar HCT®)
  - Sevikar HCT trial in Korea

William Harvey (1578-1657, UK)

..I found the task so truly arduous... that I was almost tempted to think... that the movement of the **heart** was only to be comprehended by **God**. For I could neither rightly perceive at first when the systole and when the diastole took place by reason of the rapidity of the movement..."

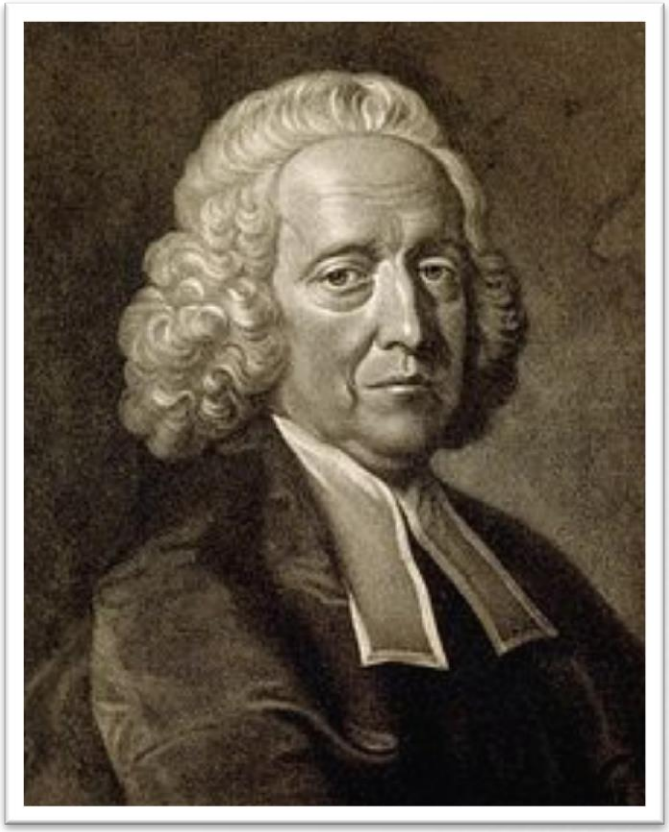

EXERCITATIO
ANATOMICA DE
MOTV CORDIS ET SAN-
GVINIS IN ANIMALI-
BVS,
GVILIELMI HARVEI ANGLI,
Medici Regii, & Professoris Anatomiæ in Col-
legio Medicorum Londinensi.
FRANCOFVRTI,
Sumptibus GVILIELMI FITZERI.
ANNO M. DC. XXVIII.

De Motu Cordis, Published in 1628
"On the Motion of the Heart and Blood"



Stephen Hales (1677-1761)

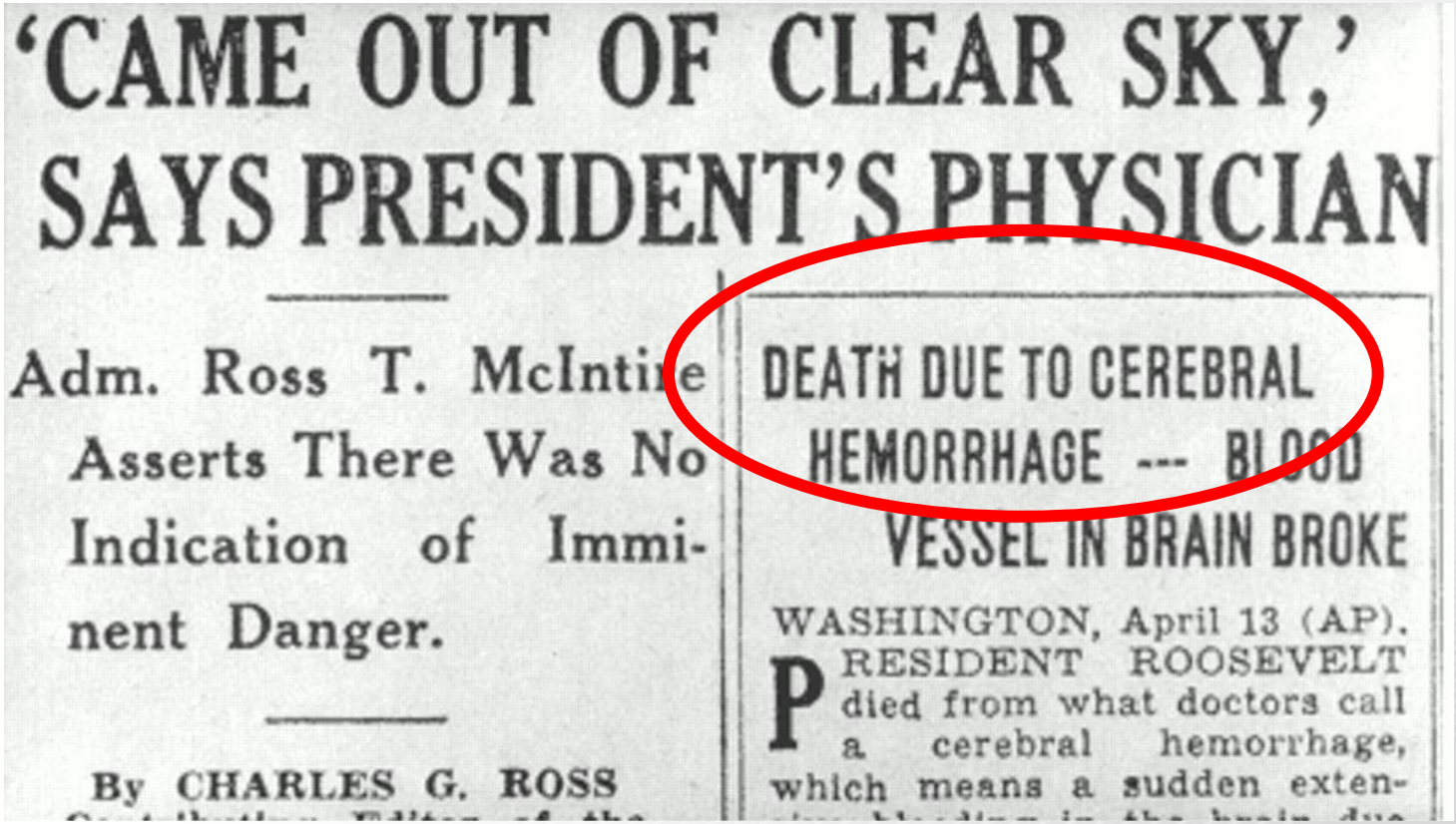
the first person to measure blood pressure in **1733**



Hales, S. Haemastatics, 3rd edition pg 1. 1738

History of Hypertension

- **1911, Eberhard Frank**
  - Described "Essentielle Hypertonie"
- **1928, Keith NM, et al from Mayo Clinic**
  - The syndrome of **malignant** hypertension (Arch Intern Med 1928;41(2):141-88)
- **1931, John Hay; 1937, Paul Dudley White**
  - Hypertension as **benign** condition, ~1950s
- **1970s, results from Framingham Heart Study** (began in 1948 with 5,209 adult)
  - "benign" hypertension increased death and cardiovascular disease
  - The 10-year cardiovascular risk (Framingham Risk Score)



‘CAME OUT OF CLEAR SKY,’ SAYS PRESIDENT’S PHYSICIAN

Adm. Ross T. McIntire Asserts There Was No Indication of Imminent Danger.

By CHARLES G. ROSS

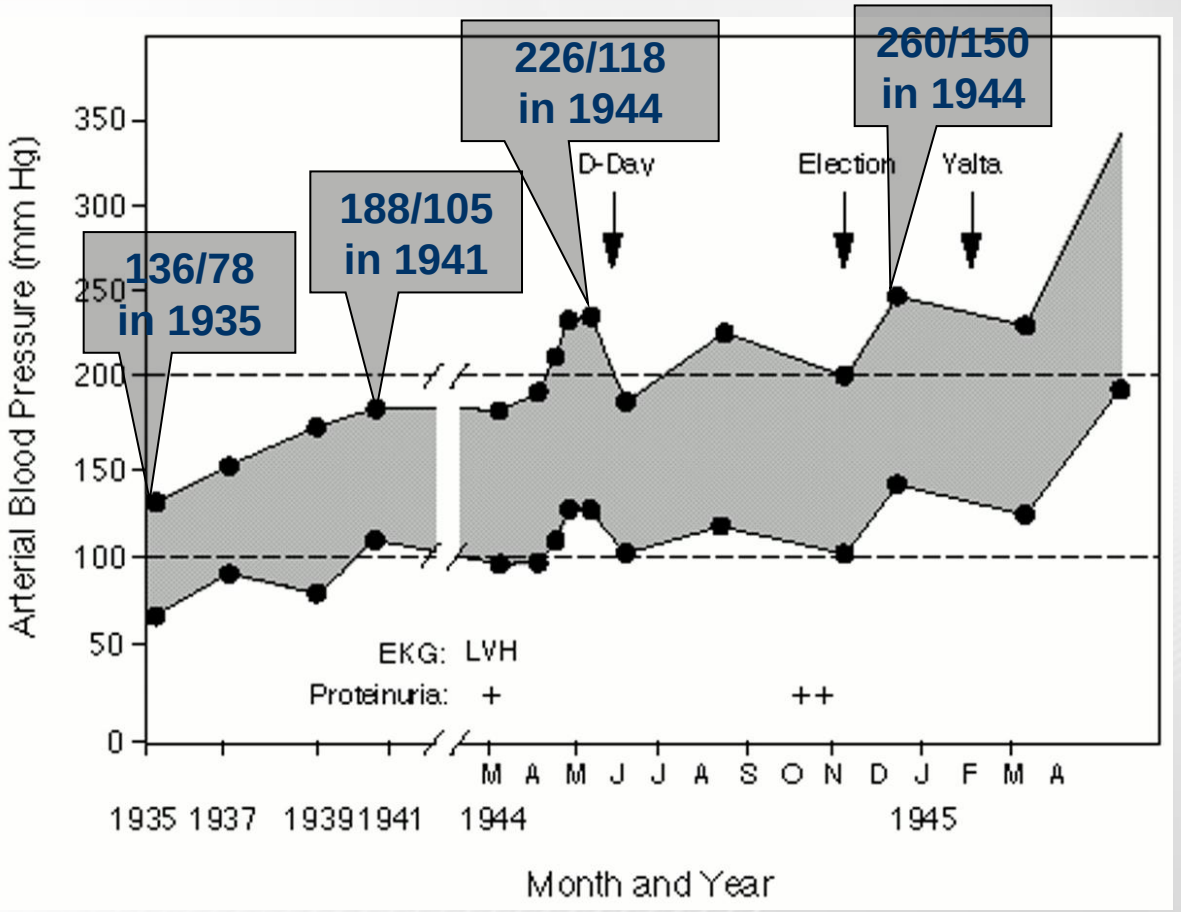
DEATH DUE TO CEREBRAL HEMORRHAGE --- BLOOD VESSEL IN BRAIN BROKE

WASHINGTON, April 13 (AP). PRESIDENT ROOSEVELT died from what doctors call a cerebral hemorrhage, which means a sudden exten-

Headlines of the *St. Louis Post-Dispatch,* April 13, **1945**

1882-1945
Thirty-Second President
(1933-1945)

Franklin D. Roosevelt



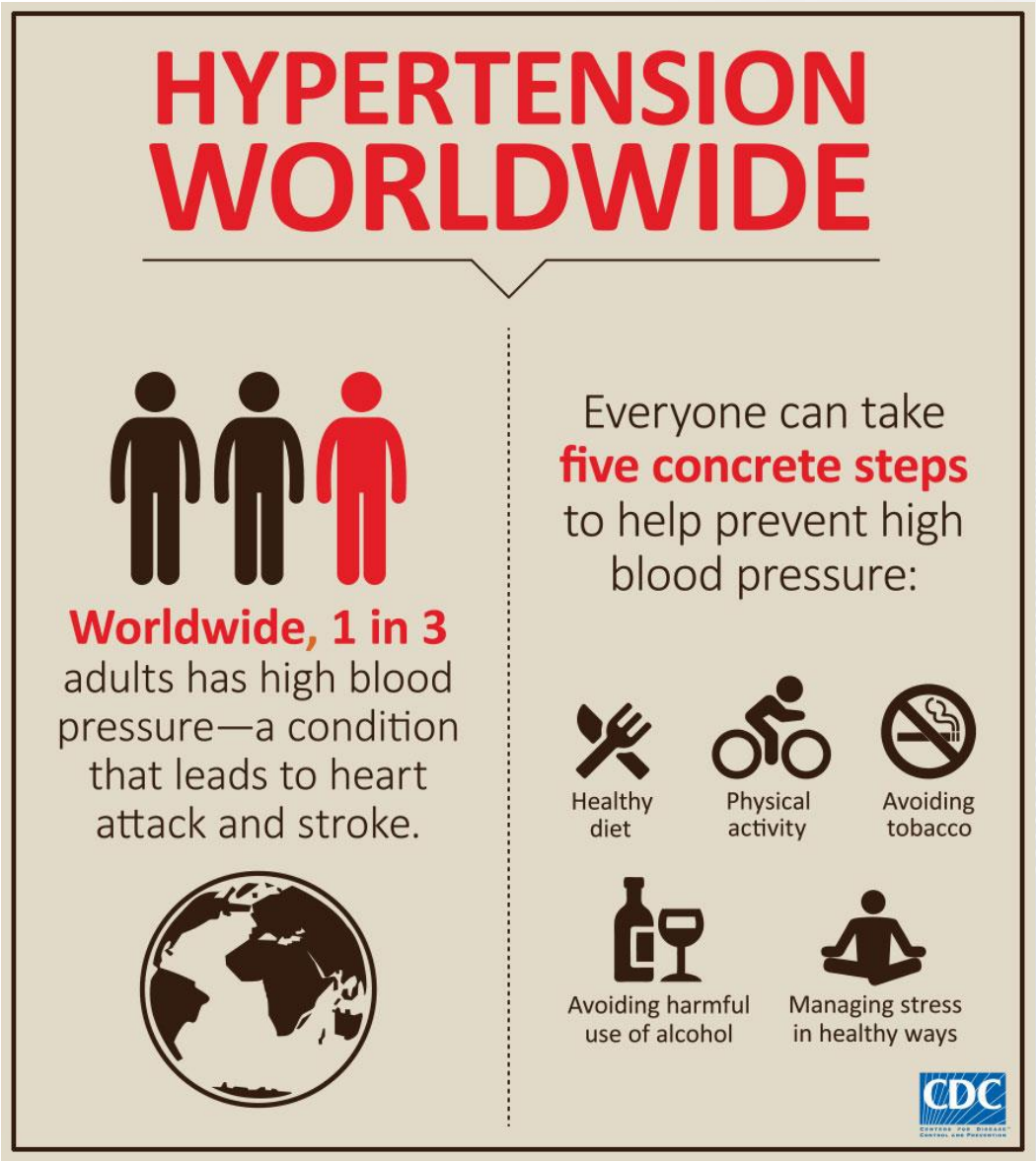
Messerli FH, *N Engl J Med.* 1995

Discovery of Antihypertensive Drugs

Year(s)	Antihypertensive Agent(s)
1900	Sodium thiocyanate
1931	Reserpine
1947–1950	Ganglion blocking drugs
1958	Thiazide-type diuretics
1950s	Hydralazine
1950s	Guanethidine
1957	Spironolactone
1960	Methyldopa
1973	β-Receptor blockers (eg, propranolol)
1970s	Central α_2 agonists (eg, clonidine)
1975	Peripheral α_1 receptor blockers (eg, prazosin)
1977	ACE inhibitors (eg, captopril)
1977	Calcium channel blockers (eg, verapamil, nifedipine)
1993	Angiotensin II receptor blockers (eg, losartan)
2000	Renin inhibitors (eg, aliskiren)

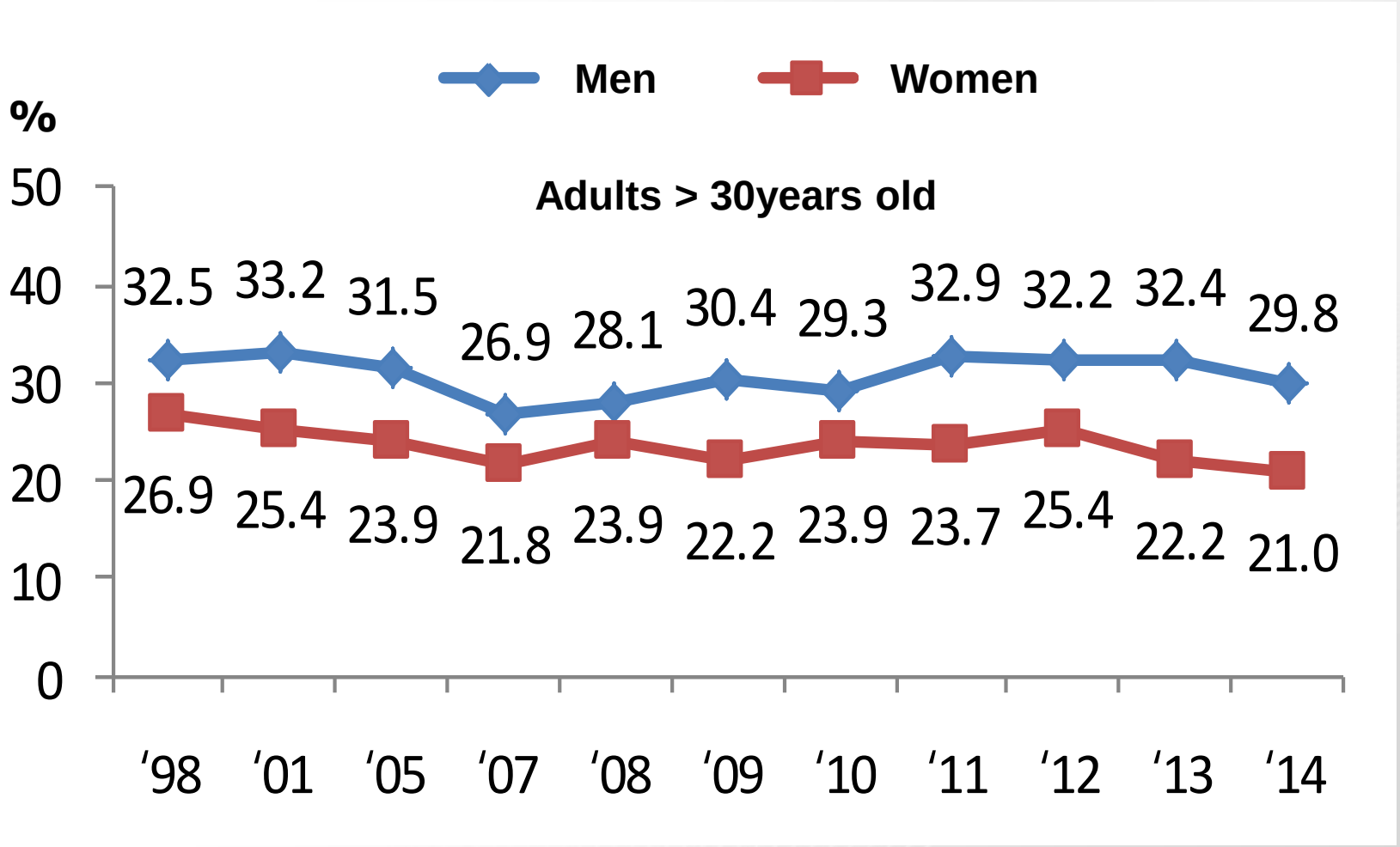
Fries E. A history of hypertension treatment. In: Oparil S, Weber MA, eds. Hypertension: Companion to Brenner & Rector's The Kidney. 2nd ed. Philadelphia, PA: Elsevier/Saunders; 2005:1–6 (chapter 1).

Hypertension Worldwide



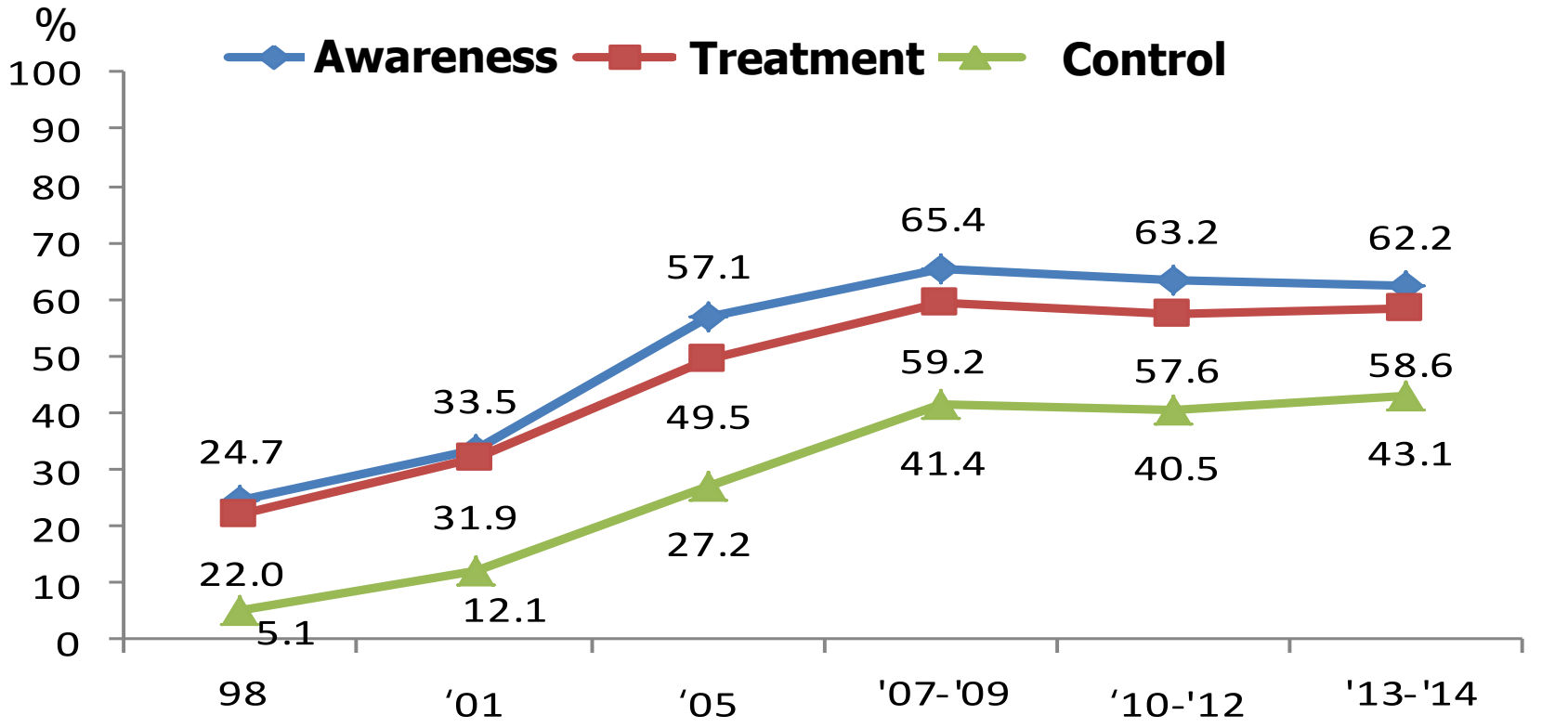
https://www.cdc.gov/globalhealth/images/infographics/hypertension-inforgraphic-lg.jpg

국내 고혈압 유병률, 1998-2014



2014 Korea National Health & Nutrition Examination Survey

국내 고혈압의 인지율, 치료율, 조절률, 1998-2014



2014 Korea National Health & Nutrition Examination Survey

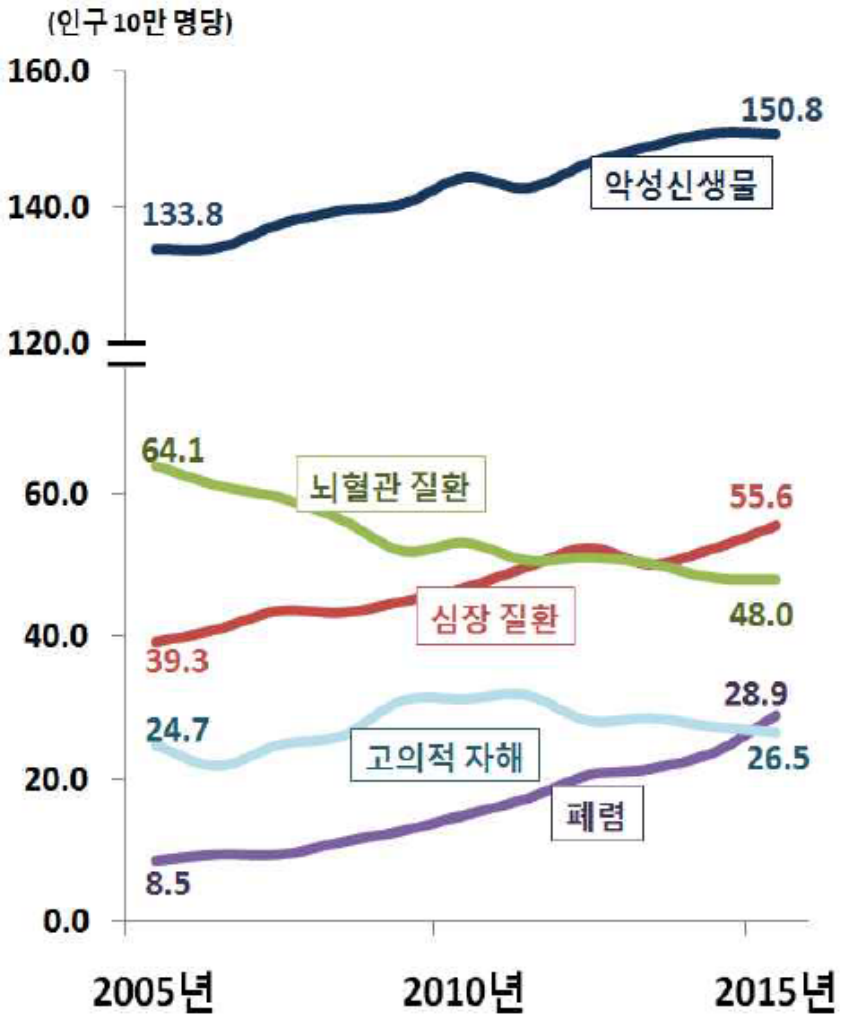
한국 사망원인

10대 사망원인 순위 및 사망률, 2015년

(인구 10만 명 당)

순위	사망원인	사망률	'14년 순위 대비
1	악성신생물(암)	150.8	-
2	심장 질환	55.6	-
3	뇌혈관 질환	48.0	-
4	폐렴	28.9	⬆(+1)
5	고의적 자해(자살)	26.5	⬇(-1)
6	당뇨병	20.7	-
7	만성 하기도 질환	14.8	-
8	간 질환	13.4	-
9	운수사고	10.9	-
10	고혈압성 질환	9.9	-

5대 사망원인 사망률 추이, 2005-2015년



2016 통계청

국내 사망원인 2위, 심장질환

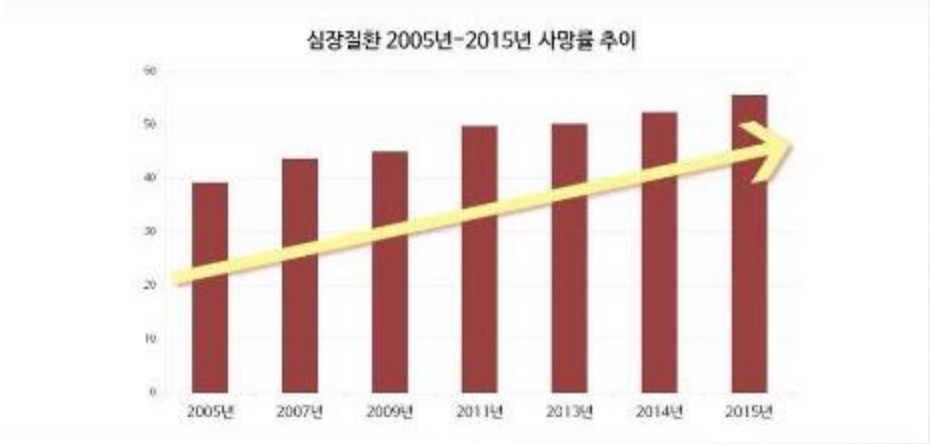
교통사고를 포함한 운수사고보다

사망자 수 5배 더 많아

교통사고보다 위험한 심장 질환,
최근 10년 새 사망률은 41.6%나 증가했습니다.

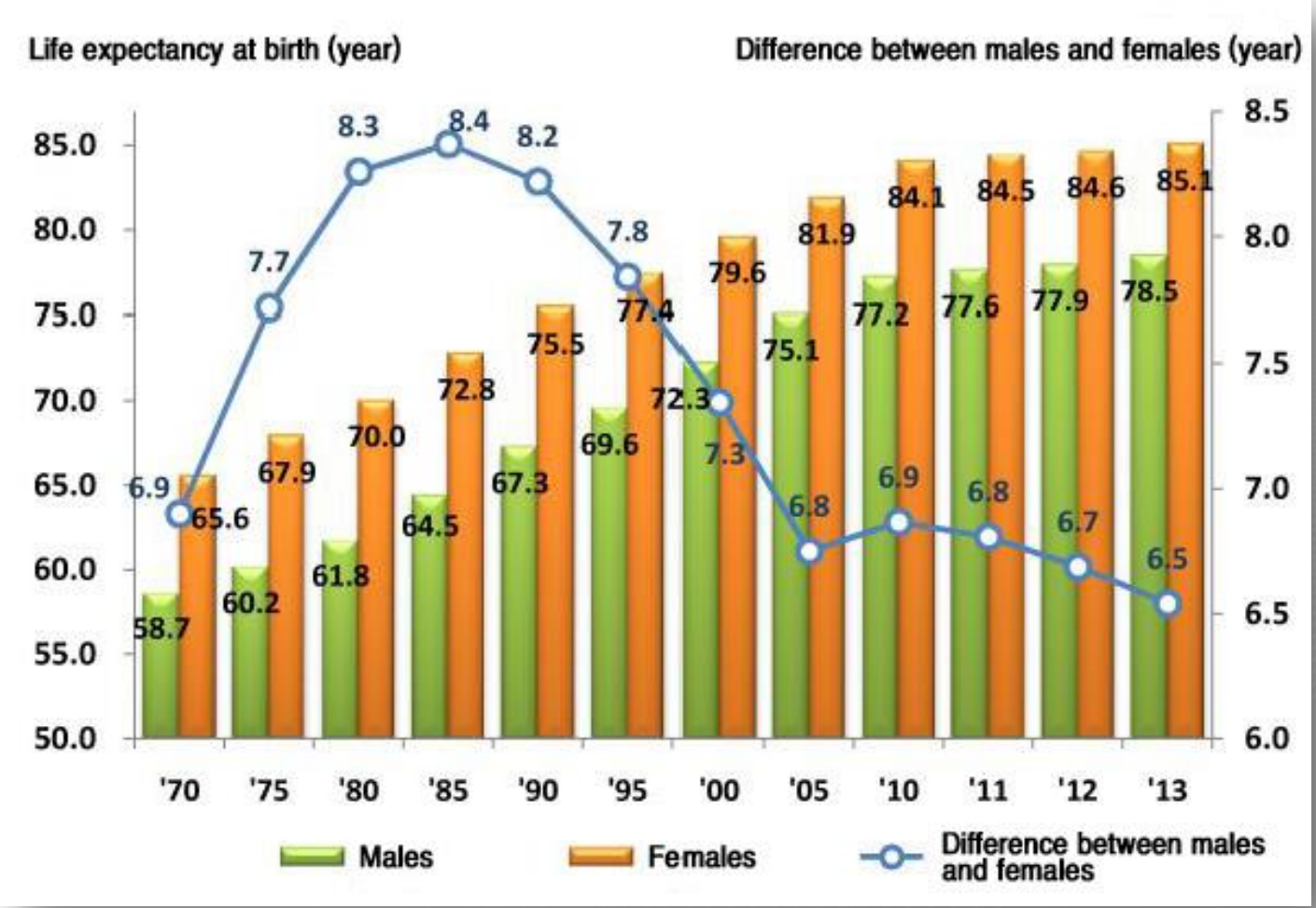
당신의 심장은 건강하신가요?

쿠키뉴스



2017 대한심장학회 뉴스

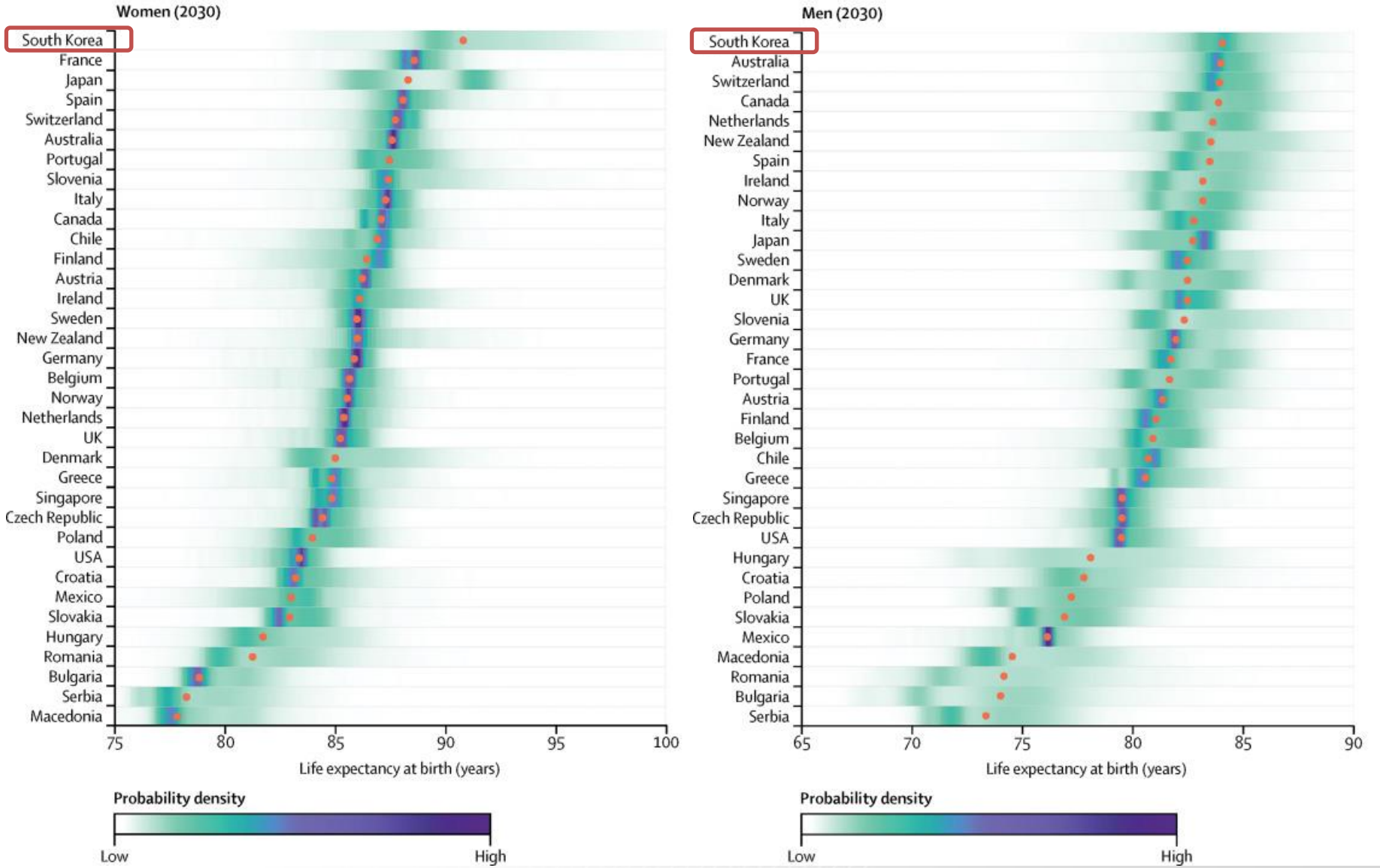
Life Expectancy at Birth, 81.9 yrs



* Average of OECD member countries (year)
Total **80.2** Males 77.6 Females 82.8
(South Korea, Males 78.5 Females 85.1)

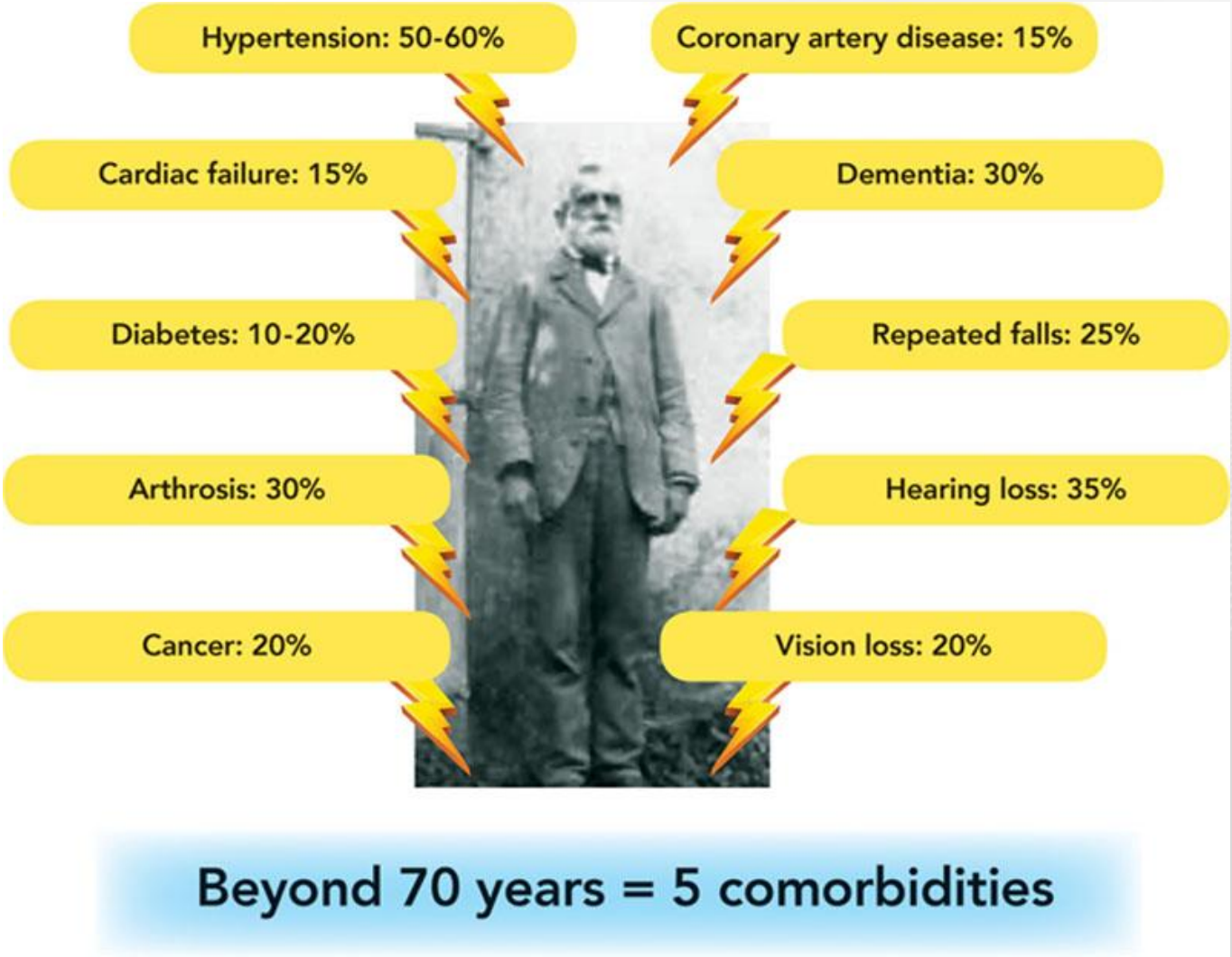
2013 Statistics Korea

Life Expectancy at Birth, 2030



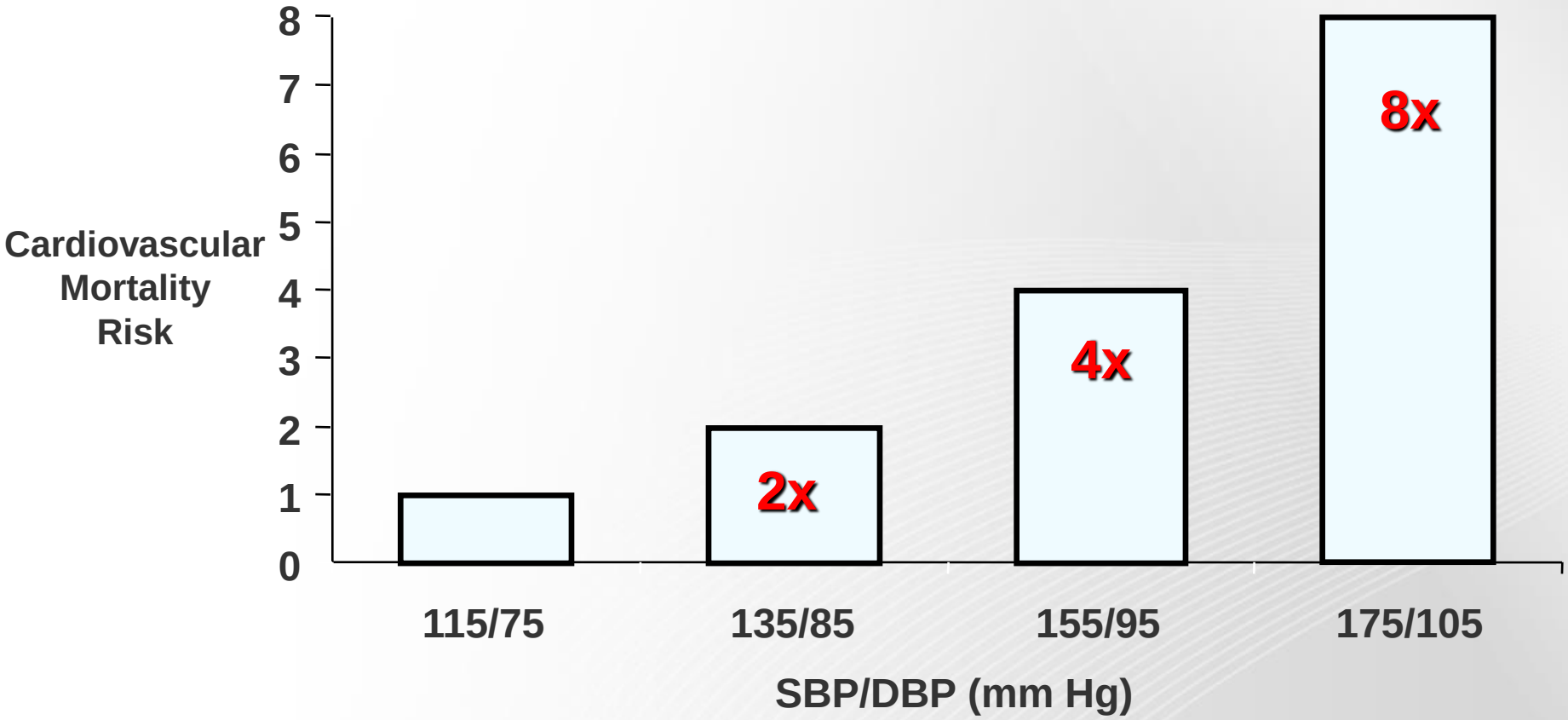
35 industrialised countries with high-quality vital statistics data. Lancet 2017;389:1323

Elderly with co-morbidities



Anesthesiology 2014

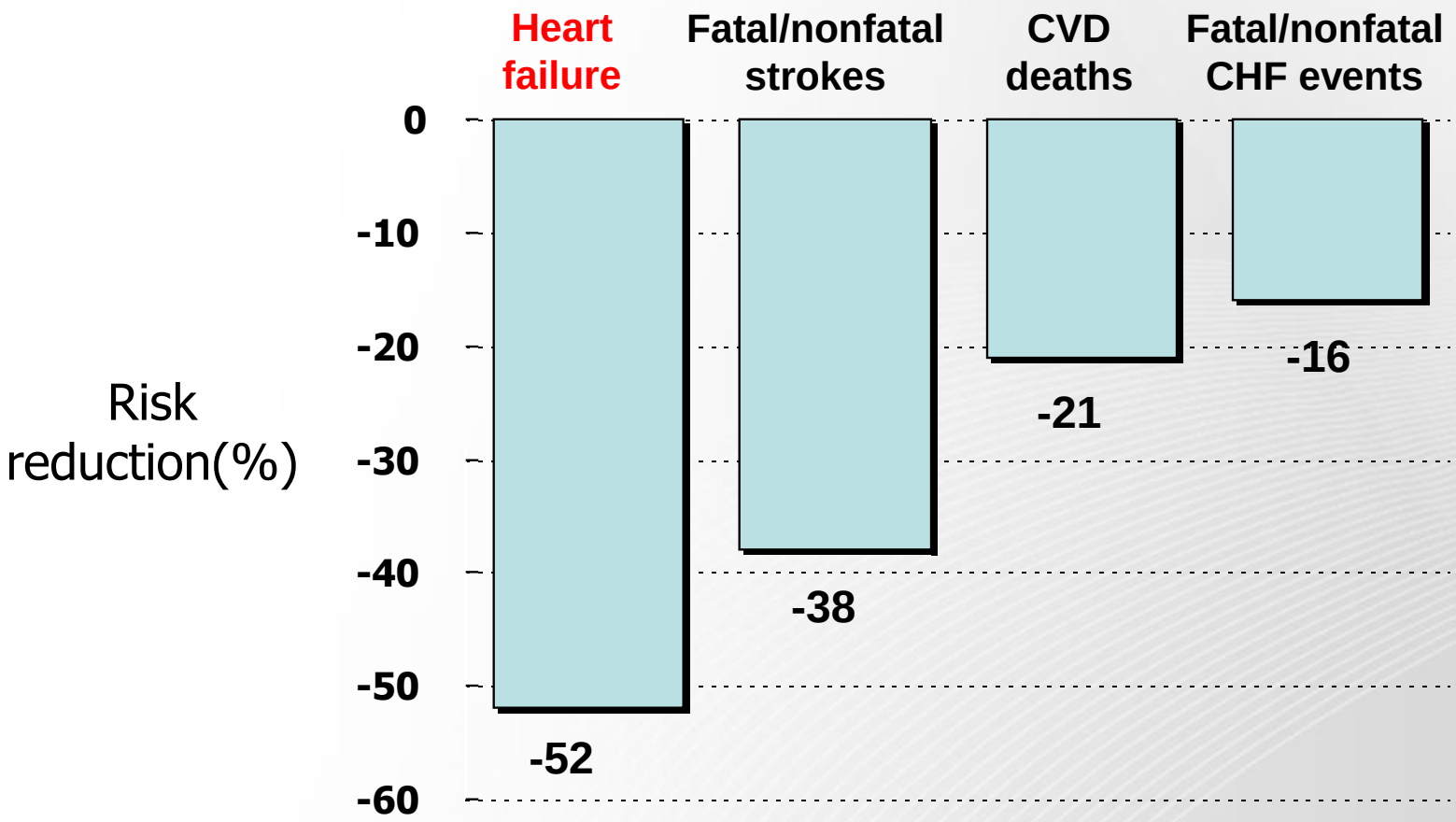
Cardiovascular Mortality Risk Doubles with Each 20/10 mmHg BP Increment*



SBP = systolic blood pressure; DBP = diastolic blood pressure.
*Individuals aged 40-69 years, starting at blood pressure 115/75 mm Hg

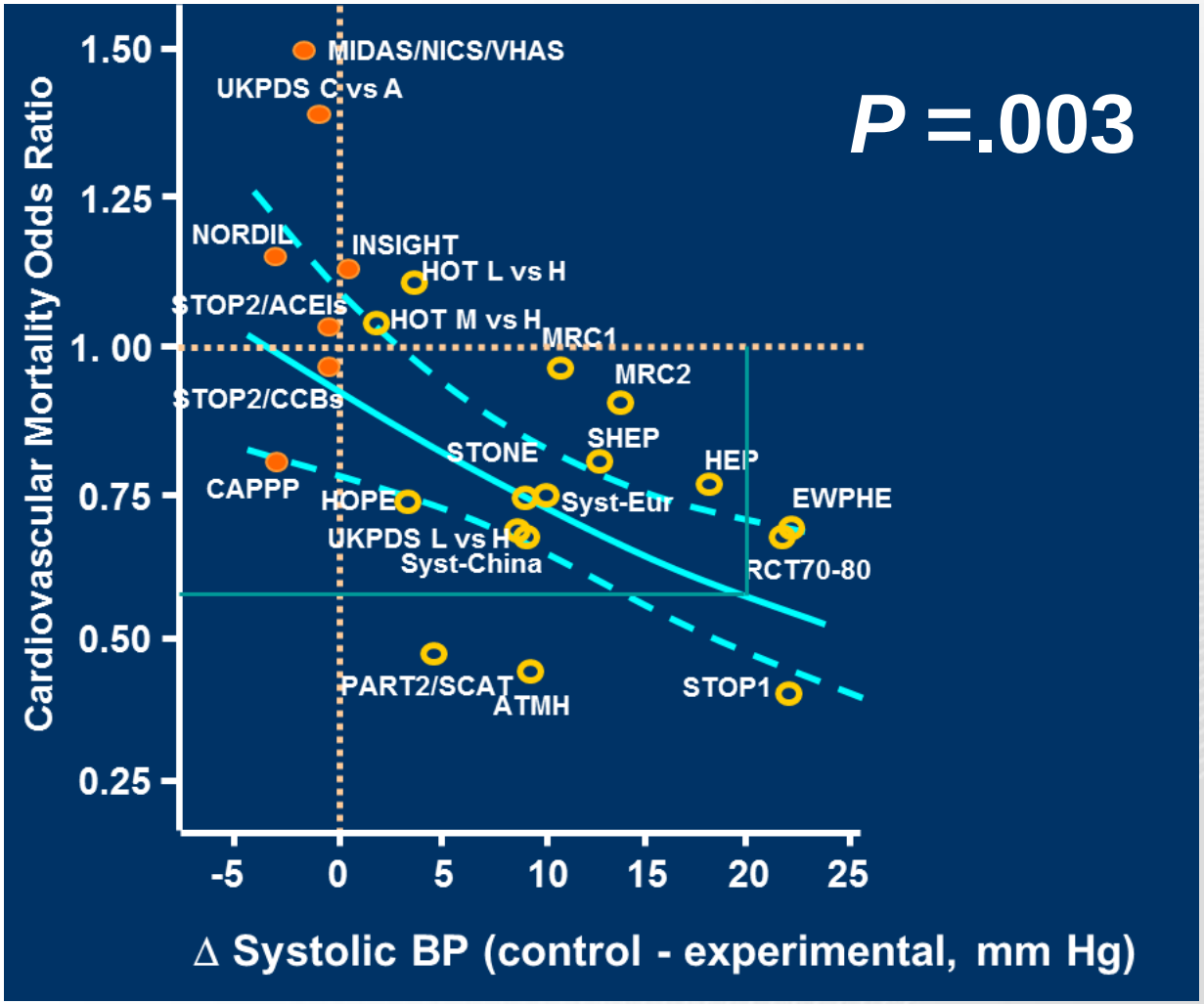
Chobanian AV et al. *JAMA*. 2003;289:2560-2572.
Lewington S et al. *Lancet*. 2002;360:1903-1913.

Antihypertensive therapy, CVD risk



Herbert et al. *Arch Intern Med* 1993

SBP reduction and CVD mortality



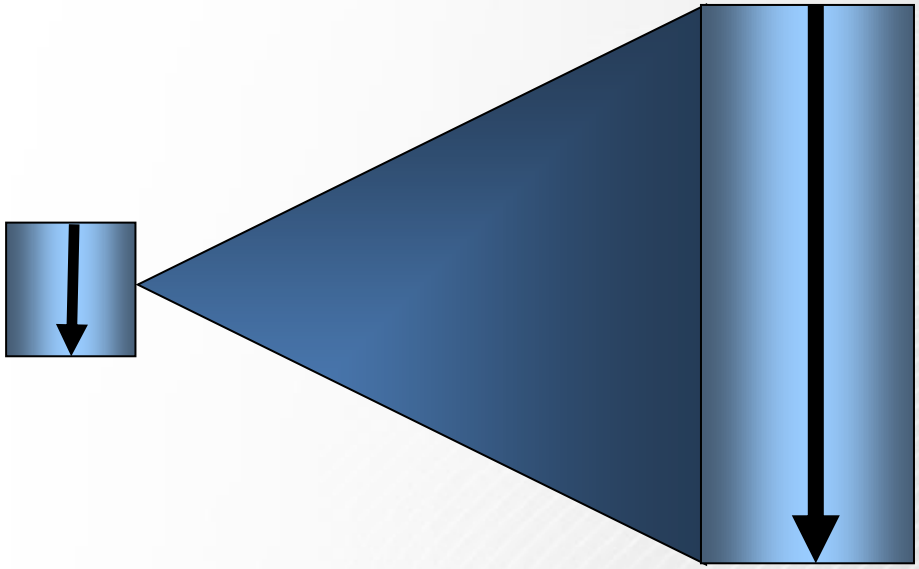
Staessen JA et al. *Lancet.* 2001;358:1305 -1315.

Small Difference Produces Big Impact

Meta-analysis of 61 observational studies

~ 1 million adults

For every 2 mmHg decrease in mean SBP



- **7% reduction in CHD mortality**
- **10% reduction in stroke mortality**

Lewington S et al. *Lancet.* 2002;360:1903-1913.

Meta-analysis

Effects of intensive blood pressure lowering on cardiovascular and renal outcomes: updated systematic review and meta-analysis

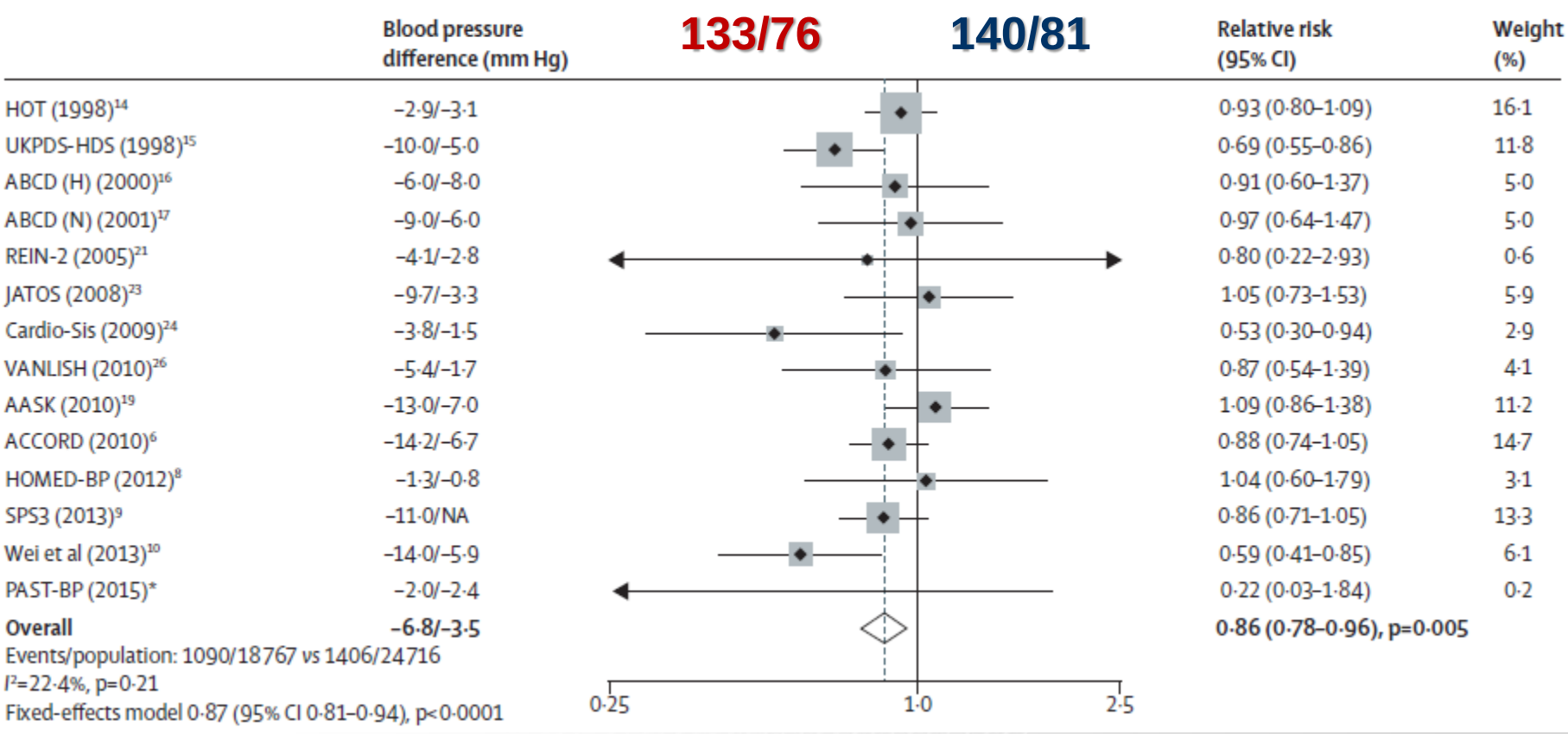
Xinfang Xie, Emily Atkins, Jicheng Lv, Alexander Bennett, Bruce Neal, Toshiharu Ninomiya, Mark Woodward, Stephen MacMahon, Fiona Turnbull, Graham S Hillis, John Chalmers, Jonathan Mant, Abdul Salam, Kazem Rahimi, Vlado Perkovic, Anthony Rodgers

- MEDLINE, Embase, and the Cochrane Library
- Trials published between Jan 1, **1950**, and Nov 3, **2015**
- Included **RCT** with at least 6 months' follow-up
- More **intensive** versus **less intensive** BP lowering treatment
- 19 trials including **44,989** participants, mean 3.8 years of follow-up
- Mean BP **133/76** (intensive BP lowering) vs **140/81** mm Hg (less intensive treatment group)

Lancet 2016; 387: 435–43

Effects of Intensive BP Lowering on Cardiovascular Outcomes

Overall, more intensive blood pressure-lowering regimens reduced the risk of major cardiovascular events by 14% (*P*=0.005)



Lancet 2016; 387: 435–43

BP Goal by Age and Comorbid Conditions by Current Hypertension Guidelines

Guideline	<60yrs	60-79 yrs	≥80 yrs	Diabetes	CKD
AHA/ACC	<140/90	<140/90	<140-145/90	<140/90	<140/90
ASH/ISH	<140/90	<140/90	<150/90	<140/90	<140/90
BHS/NICE	<140/90	<140/90	<150/90	<140/90	<140/90
ESH/ESC	<140/90	<140/90	<150/90	<140/**85**	<140/90 <130/90 (proteinuria)
JNC-8	<140/90	<**150**/90	<150/90	<140/90	<140/90
Korea	<140/90	<**140-150**/90	<140-150/90	<140/**85**	<**130/80** (albuminuria)

AHA/ACC/CDC 2013 (Hypertension online Nov 15, 2013), ASH/ISH 2014 (J Clin Hypertens 2014), BHS/NICE 2011 (www.nice.org.uk/guidance/CG127), ESH/ESC 2013 (J Hypertens, Eur Heart J 2013), JNC 8 (JAMA online Dec 18, 2013), Korea 2013 (Clinical Hypertension 2015)

NEJM

SPRINT
Systolic Blood Pressure Intervention Trial

American Heart Association
SCIENTIFIC SESSIONS 2015

Systolic Blood **Pr**essure **In**tervention **T**rial

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 NOVEMBER 26, 2015 VOL. 373 NO. 22

A Randomized Trial of Intensive versus Standard Blood-Pressure Control

The SPRINT Research Group*

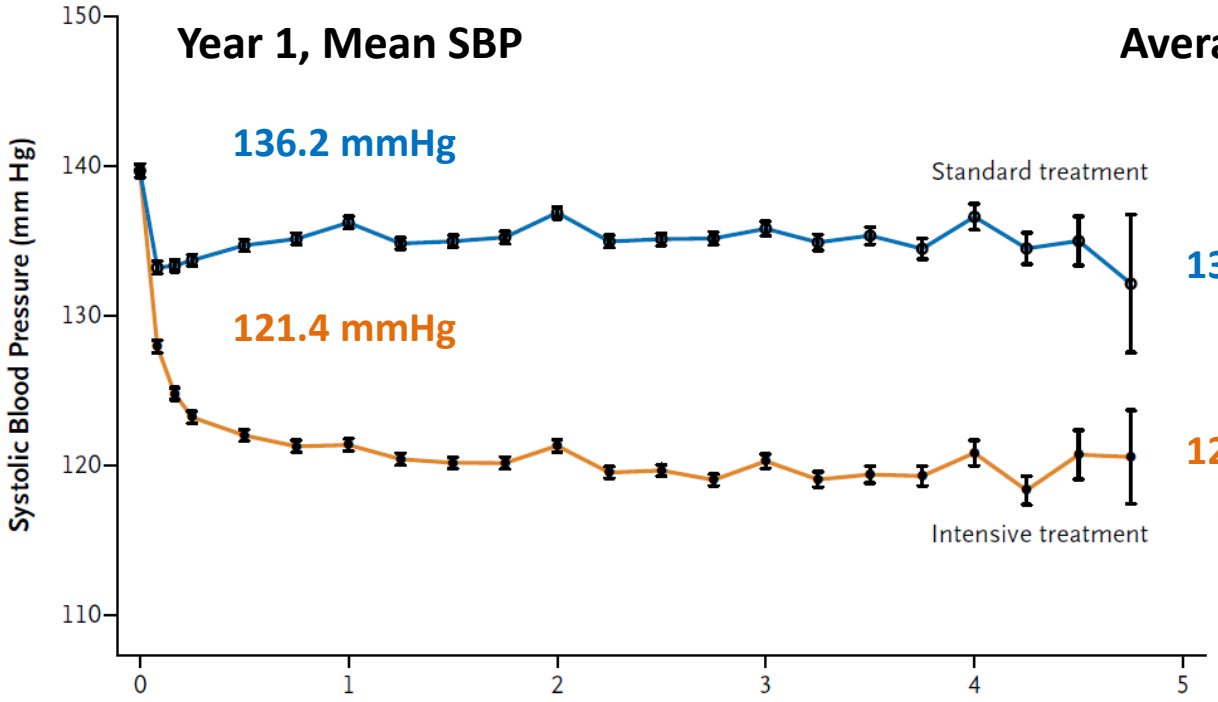
Funded by the National Institutes of Health (NIH);
ClinicalTrials.gov number, NCT01206062

Systolic Blood Pressure Intervention Trial (SPRINT)

- n=9,361 at 102 clinics in US, Puerto Rico
- Inclusion : ≥ 50 yrs, **SBP 130-180 mmHg**, + one of
  - Clinical or subclinical CVD (other than stroke)
  - CKD, eGFR 20-59 ml/min/1.73m^2(excluding PKD)
  - 10yr risk of CVD ≥ 15% by Framingham risk score
  - ≥ 75 years
- Intensive (SBP<120mmHg) vs Standard (SBP<140mmHg)
- Exclusion
  - <50yrs
  - DM
  - Stroke
  - CHF (Sx or EF <35%)
  - Proteinuria >1g/d, ESRD (eGFR <20ml/min/1.73m^2)

Clin Trials. 2014 October ; 11(5): 532–546

Achieved BP reduction



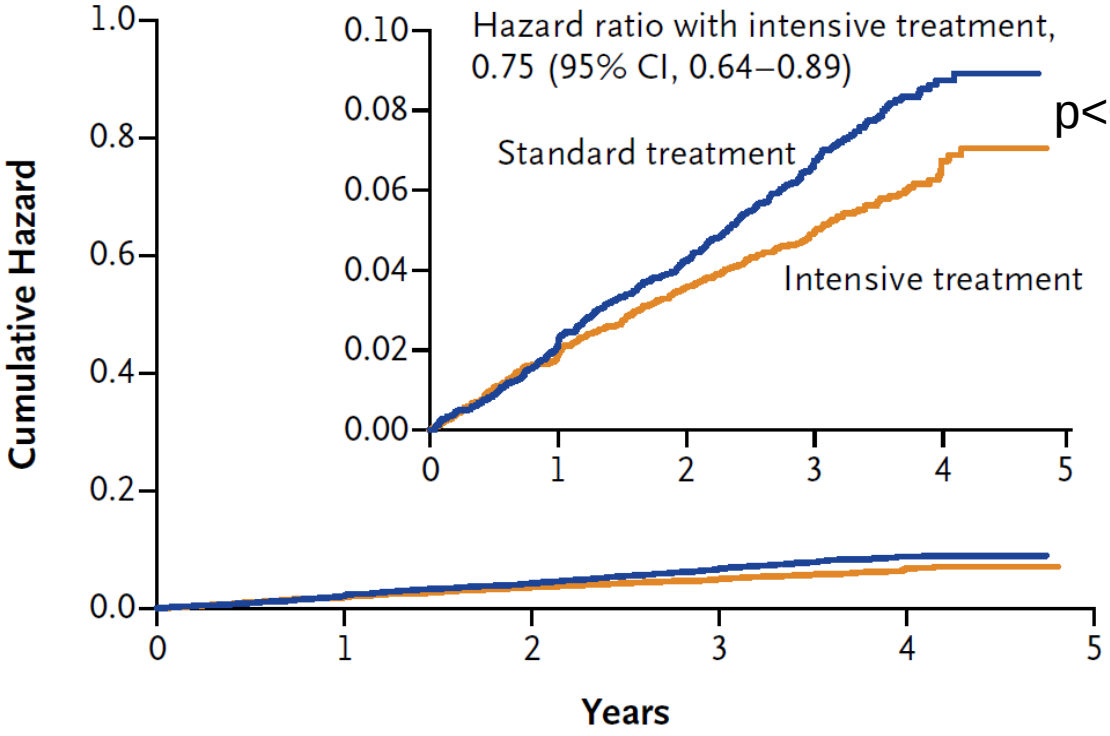
No. with Data										
Standard treatment	4683	4345	4222	4092	3997	3904	3115	1974	1000	274
Intensive treatment	4678	4375	4231	4091	4029	3920	3204	2035	1048	286
Mean No. of Medications										
Standard treatment	1.9	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.9
Intensive treatment	2.3	2.7	2.8	2.8	2.8	2.8	2.8	2.8	2.8	3.0

Median 3.26 years

N Engl J Med. 2015;373(22):2103-16

Intensive treatment, (vs. Standard treatment)
"심혈관 질환발생 및 CVD로 의한 사망" 위험 25% 감소

A Primary Outcome (a composite of MI, ACS, Stroke, HF, CV death)

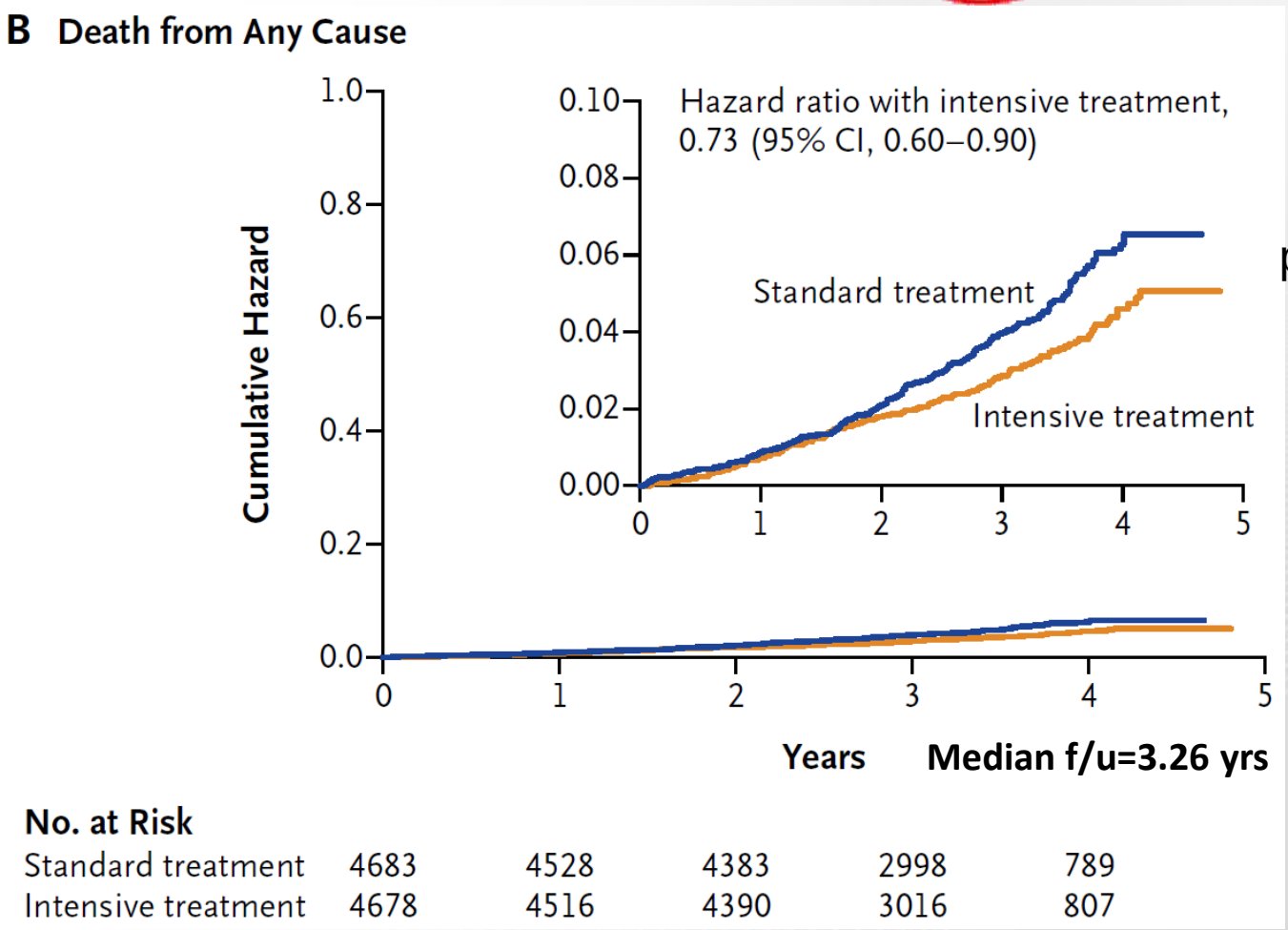


No. at Risk

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

N Engl J Med. 2015;373(22):2103-16

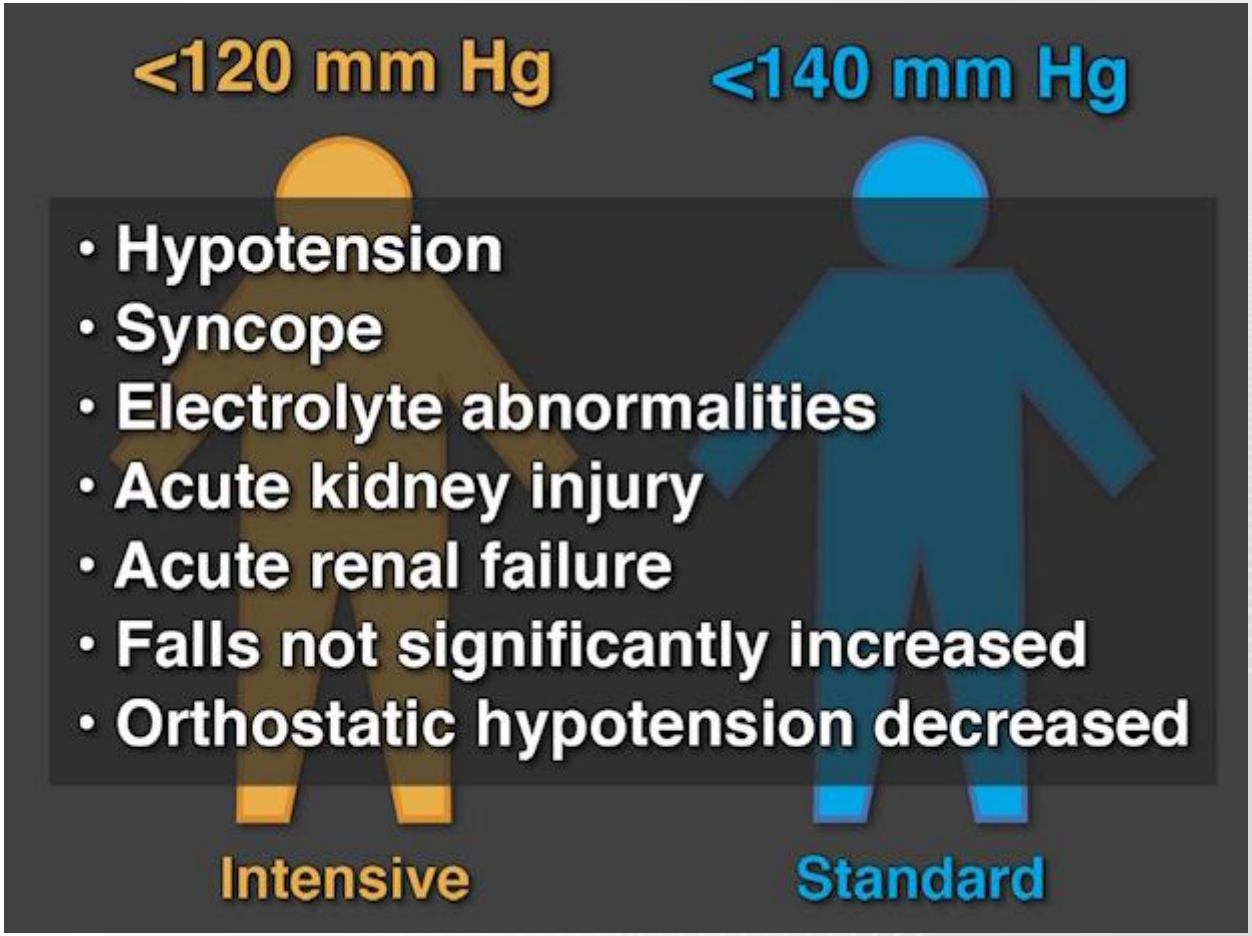
Intensive treatment, (vs. Standard treatment)
"모든 원인으로 인한 사망" 위험 27% 감소



p=0.003

N Engl J Med. 2015;373(22):2103-16

Adverse events of SPRINT

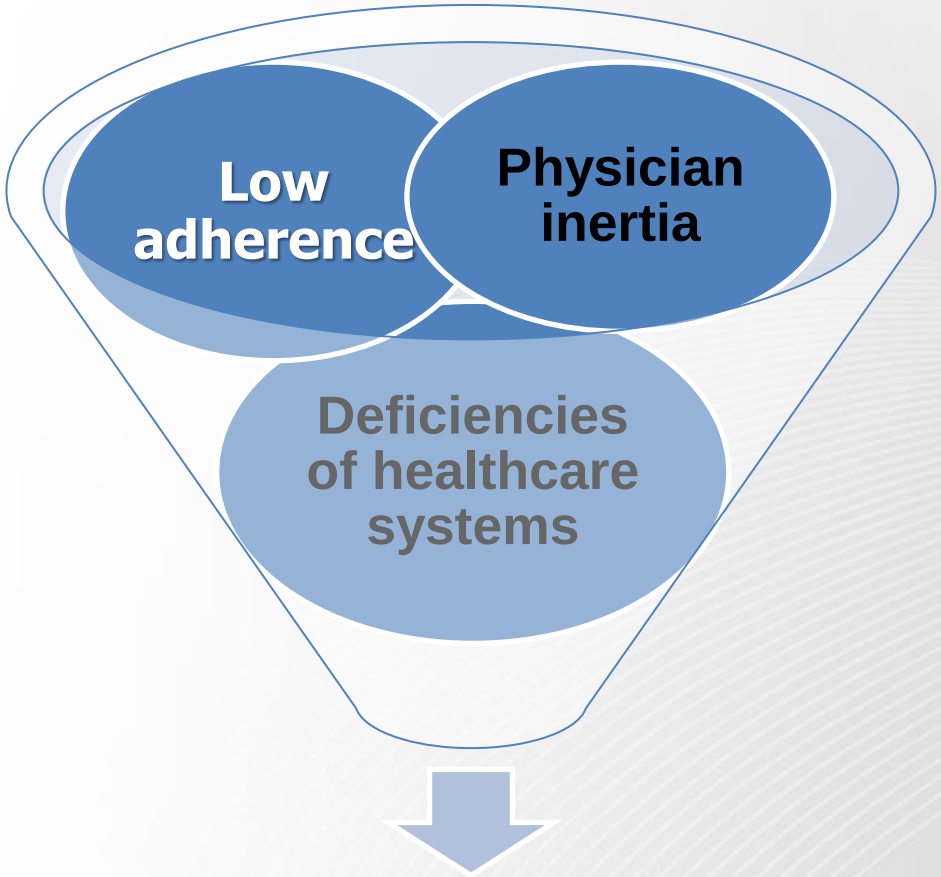


NEJM 2015.DOI: 10.1056/NEJMoa1511939

Lessons from SPRINT

- 50세 이상 고위험 고혈압 환자에서는 적극적 혈압 조절이 예후 개선에 도움이 된다.
- 다만, 저혈압, 실신, 전해질 및 신기능 이상을 잘 모니터 할 필요가 있다.
- 당뇨병, 뇌졸중, 심부전 및 만성콩팥병 환자에서 이득이 있다고 말할 수 없다.

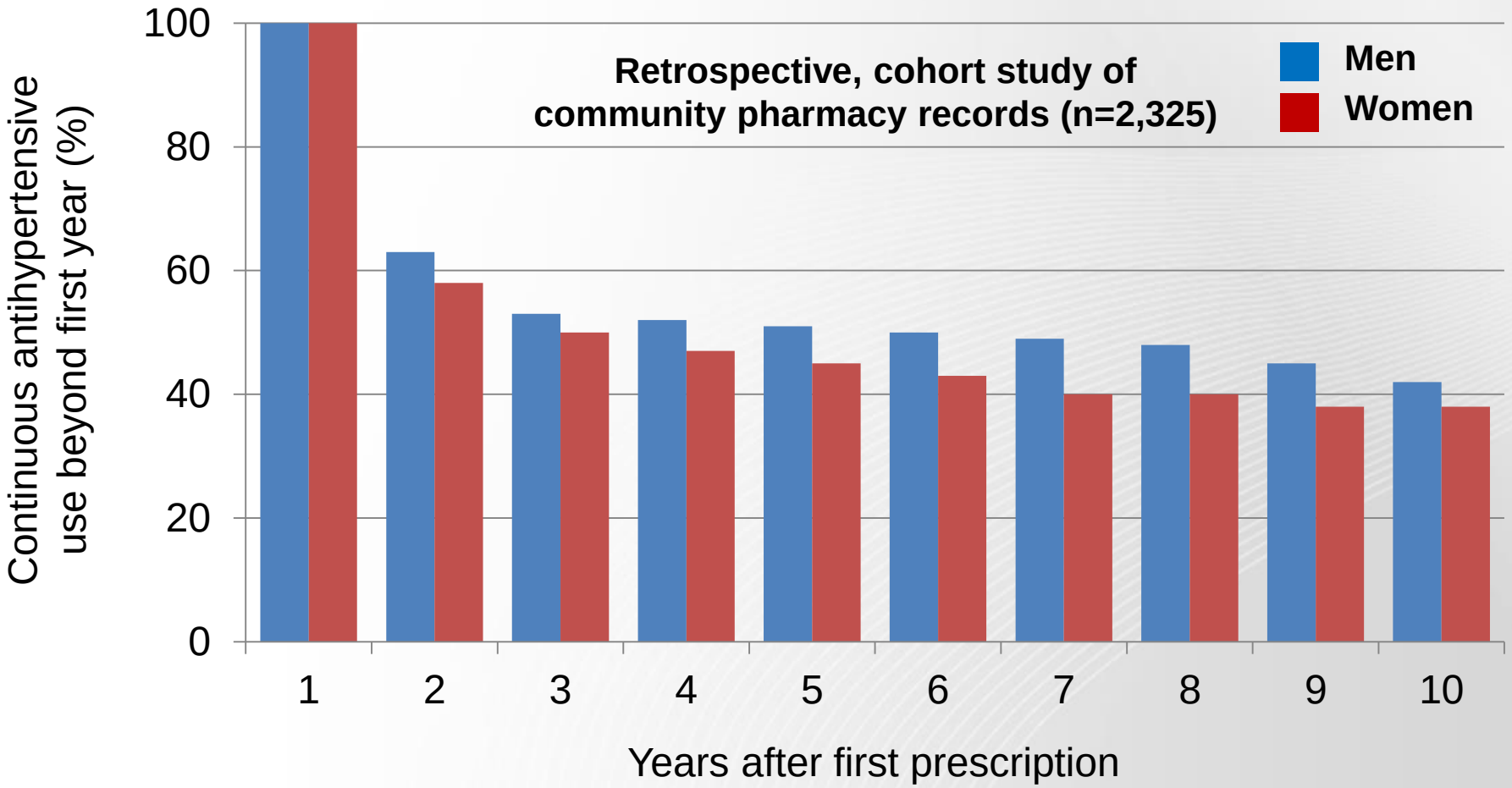
혈압조절이 잘 안 되는 세가지 이유



Low rate of BP control

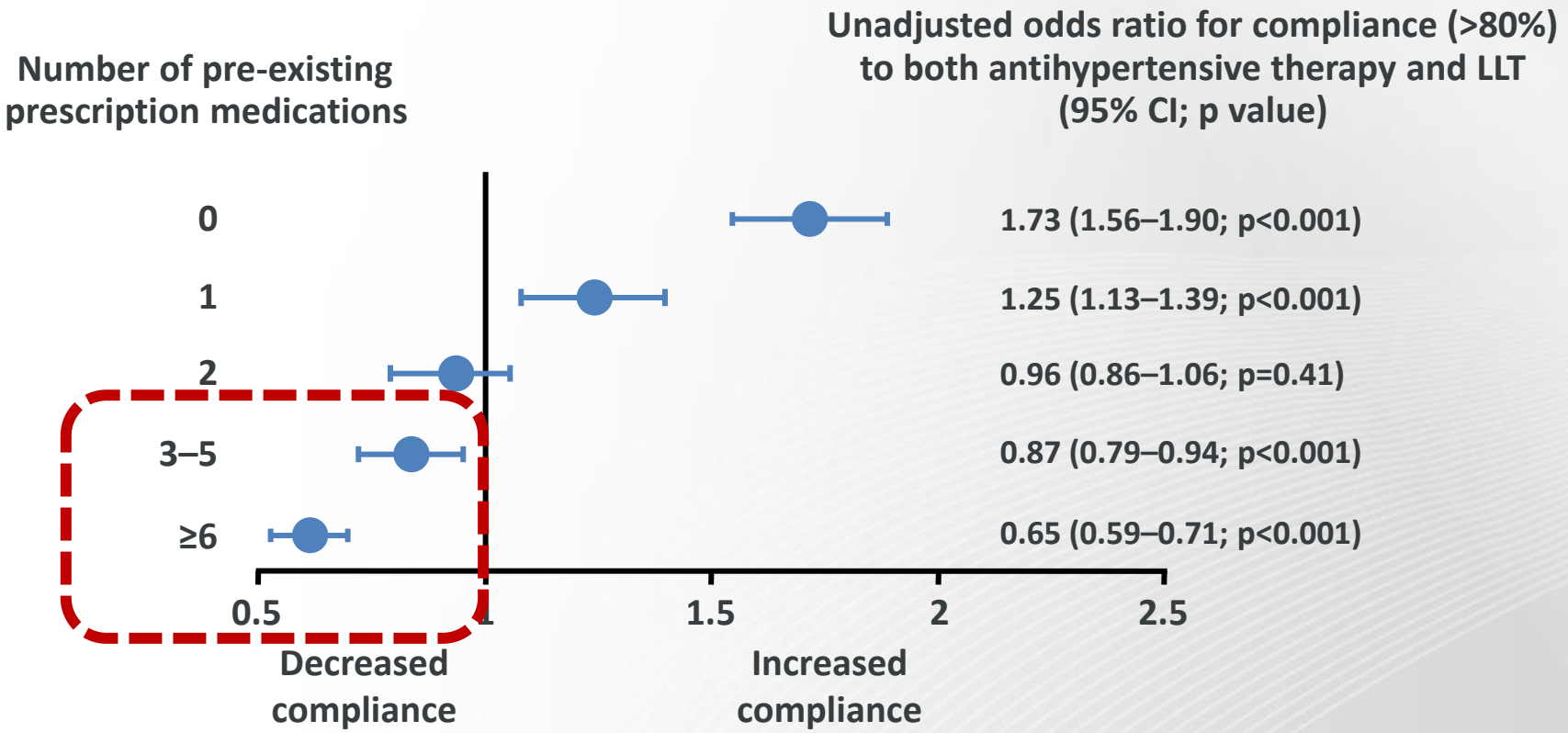
Poor Compliance and Persistence with Antihypertensive Drugs Treatment

치료시작 1년 후부터 1년 사이 절반이 치료를 중단



Van Wijk et al. *J Hypertens* 2005;23:2101–7

약이 많을 수록 순응도는 더 떨어져



Retrospective cohort study of MCO population.
N=8,406 patients with hypertension who added antihypertensive therapy and LLT to existing prescription medications within a 90-day period.
Compliance to concomitant therapy: sufficient antihypertensive and LL prescription medications to cover ≥80% of days per 91-day period
CI=confidence interval; LLT = lipid-lowering therapy

Arch Intern Med 2005;165:1147–52

Medication adherence and CV mortality

Medication Adherence and the Risk of Cardiovascular Mortality and Hospitalization Among Patients With Newly Prescribed Antihypertensive Medications

Soyeun Kim, Dong Wook Shin, Jae Moon Yun, Yunji Hwang, Sue K. Park, Young-Jin Ko, BeLong Cho

Abstract—The importance of adherence to antihypertensive treatments for the prevention of cardiovascular disease has not been well elucidated. This study evaluated the effect of antihypertensive medication adherence on specific cardiovascular disease mortality (ischemic heart disease [IHD], cerebral hemorrhage, and cerebral infarction). Our study used data from a 3% sample cohort that was randomly extracted from enrollees of Korean National Health Insurance. Study subjects were aged ≥20 years, were diagnosed with hypertension, and started newly prescribed antihypertensive medication in 2003 to 2004. Adherence to antihypertensive medication was estimated as the cumulative medication adherence. Subjects were divided into good (cumulative medication adherence, ≥80%), intermediate (cumulative medication adherence, 50%–80%), and poor (cumulative medication adherence, <50%) adherence groups. We used time-dependent Cox proportional hazards models to evaluate the association between medication adherence and health outcomes. Among 33 728 eligible subjects, 670 (1.99%) died of coronary heart disease or stroke during follow-up. Patients with poor medication adherence had worse mortality from IHD (hazard ratio, 1.64; 95% confidence interval, 1.16–2.31; *P* for trend=0.005), cerebral hemorrhage (hazard ratio, 2.19; 95% confidence interval, 1.28–3.77; *P* for trend=0.004), and cerebral infarction (hazard ratio, 1.92; 95% confidence interval, 1.25–2.96; *P* for trend=0.003) than those with good adherence. The estimated hazard ratios of hospitalization for cardiovascular disease were consistent with the mortality end point. Poor medication adherence was associated with higher mortality and a greater risk of hospitalization for specific cardiovascular diseases, emphasizing the importance of a monitoring system and strategies to improve medication adherence in clinical practice.
(***Hypertension***. **2016;67:506-512. DOI: 10.1161/HYPERTENSIONAHA.115.06731.)** ● Online Data Supplement

3% of the total KNHICD (n=1,025,340), 2002.12.31~ 2010.12.31.
The Korea National Health Insurance(KNHI) program
aged ≥20 years, newly diagnosed with hypertension (ICD-10: I10, I11, I12, I13, or I15)
N=33,728 who had their prescriptions filled more than twice during 2 years
Cumulative medication adherence [CMA], good ≥80%; intermediate 50% ≤ <80%, poor <50%

Medication adherence and CV mortality

Medication Adherence and the Risk of Cardiovascular Mortality and Hospitalization Among Patients With Newly Prescribed Antihypertensive Medications

	Good Adherence	Intermediate Adherence	Poor Adherence	
	HR (95% CI)	HR (95% CI)	HR (95% CI)	*P* Trend
All-cause mortality	1.00	1.39 (1.26–1.53)	1.75 (1.58–1.93)	<0.001
Acute myocardial infarction	1.00	1.02 (0.68–1.53)	1.32 (0.87–1.99)	0.210
Ischemic heart disease	1.00	1.11 (0.78–1.57)	1.64 (1.16–2.31)	0.005
Cerebral hemorrhage	1.00	1.35 (0.77–2.35)	2.19 (1.28–3.77)	0.004
Cerebral infarction	1.00	1.49 (0.95–2.35)	1.92 (1.25–2.96)	0.003
Stroke	1.00	1.68 (1.30–2.18)	1.92 (1.47–2.50)	<0.001

Hypertension. 2016;67:506-512

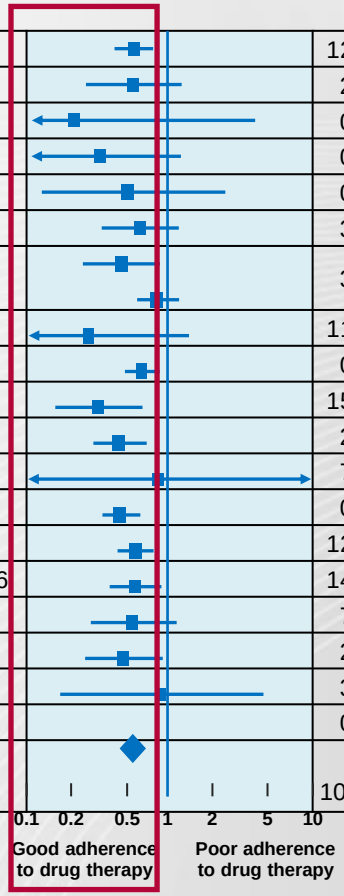
3% of the total KNHICD (n=1,025,340), 2002.12.31~ 2010.12.31.
The Korea National Health Insurance(KNHI) program
aged ≥20 years, newly diagnosed with hypertension (ICD-10: I10, I11, I12, I13, or I15)
N=33,728 who had their prescriptions filled more than twice during 2 years
Cumulative medication adherence [CMA], good ≥80%; intermediate 50% ≤ <80%, poor <50%

순응도가 좋으면 사망률이 감소

[For participants with good adherence to beneficial drug therapy, the risk of mortality was about half that of participants with poor adherence.]

Beneficial drug therapy

Coronary Drug Project Research Group 1980[w1]	106/708	88/357	12.11	0.54 (0.39 to 0.74)
Wei et al 2002[w5]	14/272	14/155	2.06	0.55 (0.25 to 1.18)
Cotter et al 2004[w6]	1/52	1/12	0.15	0.22 (0.01 to 3.72)
β blocker heart attack trial (men) 1990[w2]	14/1009	3/72	0.75	0.32 (0.09 to 1.15)
β blocker heart attack trial (women) 1993[w3]	11/242	2/23	0.49	0.50 (0.10 to 2.41)
Wei et al 2004[w7]	24/226	26/160	3.43	0.61 (0.34 to 1.11)
Candian amiodarone myocardial infarction arrhythmia trial 1999[w8]	33/445	19/128	3.35	0.46 (0.25 to 0.84)
San Andres Rebollo et al 2004[w9]	69/197	300/753	11.39	0.81 (0.59 to 1.13)
Cohn et al 2002[w10]	8/585	2/41	0.49	0.27 (0.06 to 1.32)
Garcia de Olalla et al 2002[w11]	156/831	105/388	15.13	0.62 (0.47 to 0.83)
Grimwade et al 2005[w12]	12/743	27/545	2.56	0.31 (0.16 to 0.63)
Hogg et al 2002[w13]	62/955	44/327	7.29	0.45 (0.30 to 0.67)
Paterson et al 2000[w14]	0/23	1/58	0.12	0.82 (0.03 to 20.75)
Wood et al 2003[w15]	117/1067	76/355	12.04	0.45 (0.33 to 0.62)
Physicians health study 1994[w16]	89/6608	102/4396	14.80	0.57 (0.43 to 0.77)
West of Scotland prevention study 1997[w17]	66/2435	40/867	7.59	0.58 (0.39 to 0.86)
Howell et al 2004[w19]	24/654	14/215	2.65	0.55 (0.28 to 1.08)
Miura et al 2001[w20]	17/218	32/213	3.15	0.48 (0.26 to 0.89)
Dobbels et al 2004w[21]	9/84	2/17	0.46	0.90 (0.18 to 4.59)
Total (95% CI)	17 354	9082	100.00	0.55 (0.49 to 0.62)



Total events: 832 (good adherence), 898 (poor adherence)

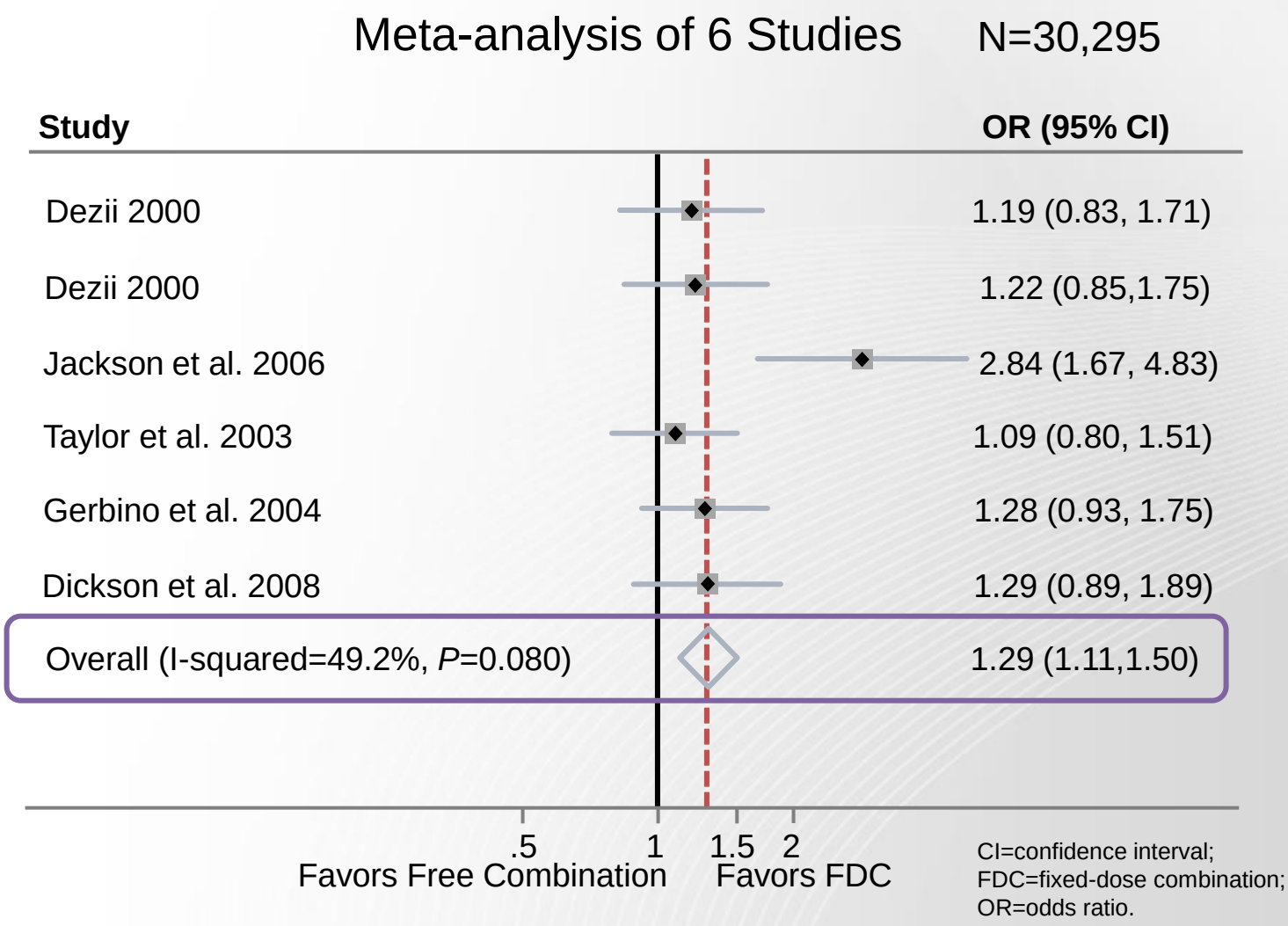
Test for heterogeneity: χ^2=14.34, df=18, P=0.71,I^2=0%

Test for overall effect: z=10.54, P<0.0001

Simson *SH,et al.BMJ,*doi:10.1136/bmj.38875.675486.55 (published 21 June 2006).

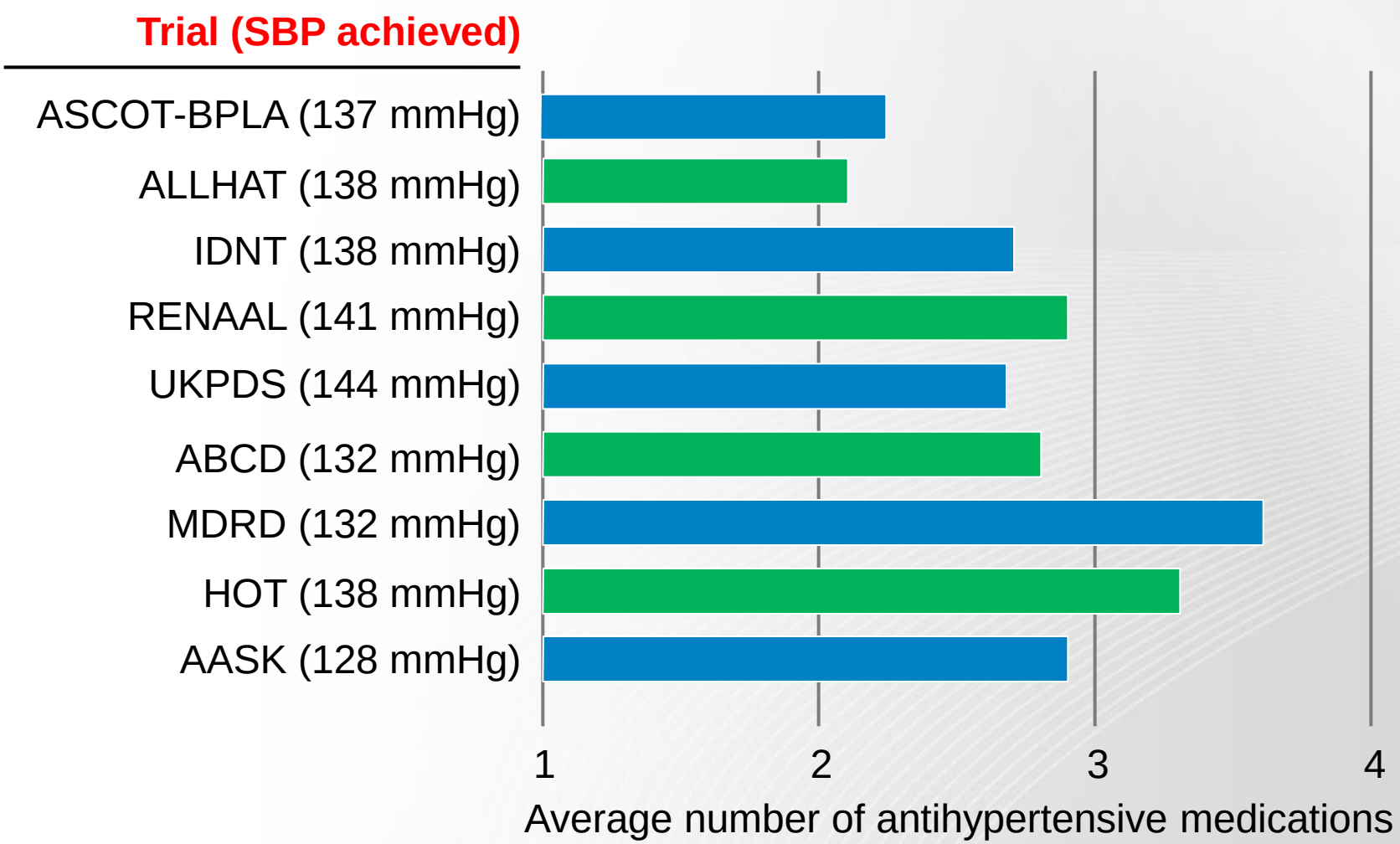
고정용량복합제(FDC)가 순응도를 좋게 해준다

FDC *vs* free-drug combination, **29%** Improvement in Adherence (*P*=0.080)



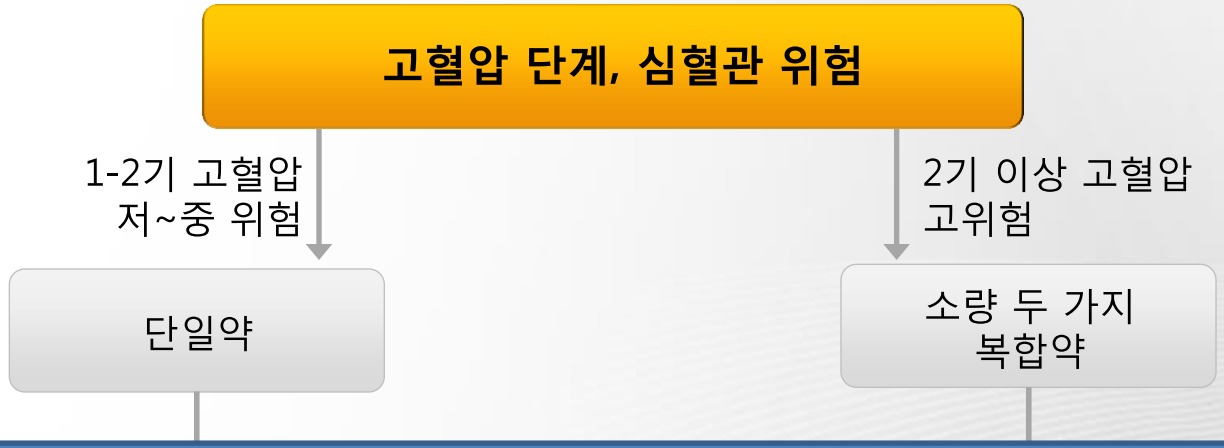
Gupta AK, et al. *Hypertension.* 2010;55:399-407

대부분의 고혈압 환자들이 목표혈압에 도달하기 위해 2제 이상의 혈압약 필요



Bakris et al. *Am J Med.* 2004;116(5A):30S–38S; Dahlöf et al. *Lancet.* 2005;366:895–906.

대한고혈압학회 고혈압진료지침 2013



혈압이 160/100 mmHg 이상이거나 목표혈압보다 20/10 mmHg 이상 높은 경우는 강압효과를 극대화하고 혈압을 빠르게 조절하기 위해 **처음부터 고혈압약을 병용 투여**할 수 있다.
또한 **고정용량복합제**는 **강압효과를 상승**시키고 **부작용을 줄이고**, **환자의 약 순응도를 증가**시켜, 심뇌혈관질환과 무증상장기손상을 방지하는 데 도움이 된다.

대한고혈압학회진료지침 2013

병합요법의 장점, 고정용량복합제

2013 유럽고혈압가이드라인

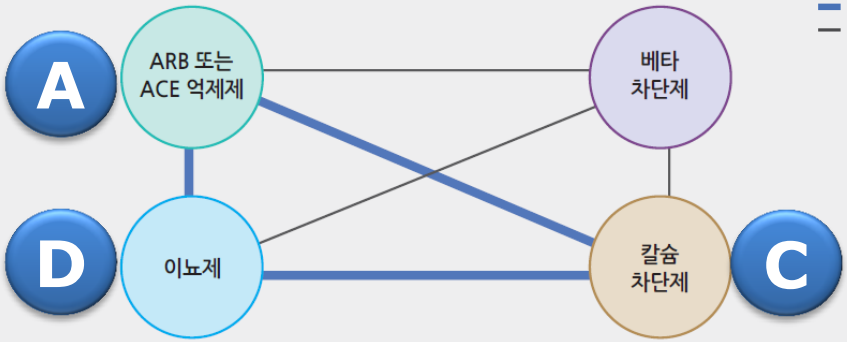
- 많은 환자에서 **빠른 혈압조절**이 가능 (고위험 환자에서 이득)
- **목표 혈압**에 더 잘 도달
- 잦은 혈압약 변경으로 인한 **순응도** 저하가 적다.
- 2가지 이상 혈압약을 한 알로 만든 **고정용량복합제**가 순응도를 개선시킨다.

Mancia et al. J Hypertens 2013;31:1281–1357

Korea and Japan

2013 대한고혈압학회 고혈압 진료지침

권장되는 병용요법

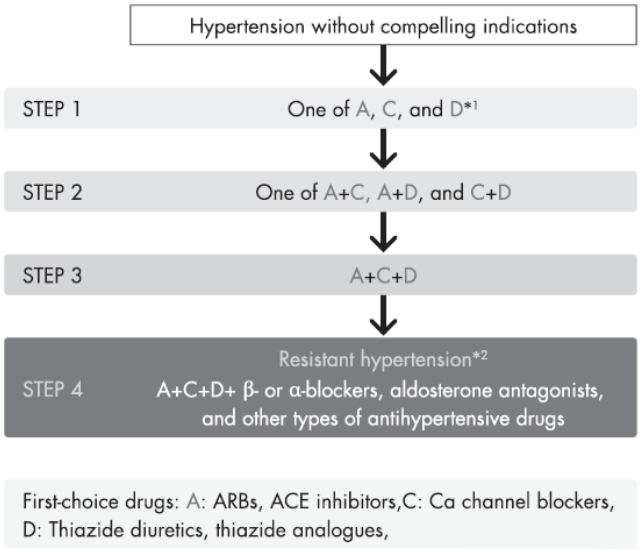


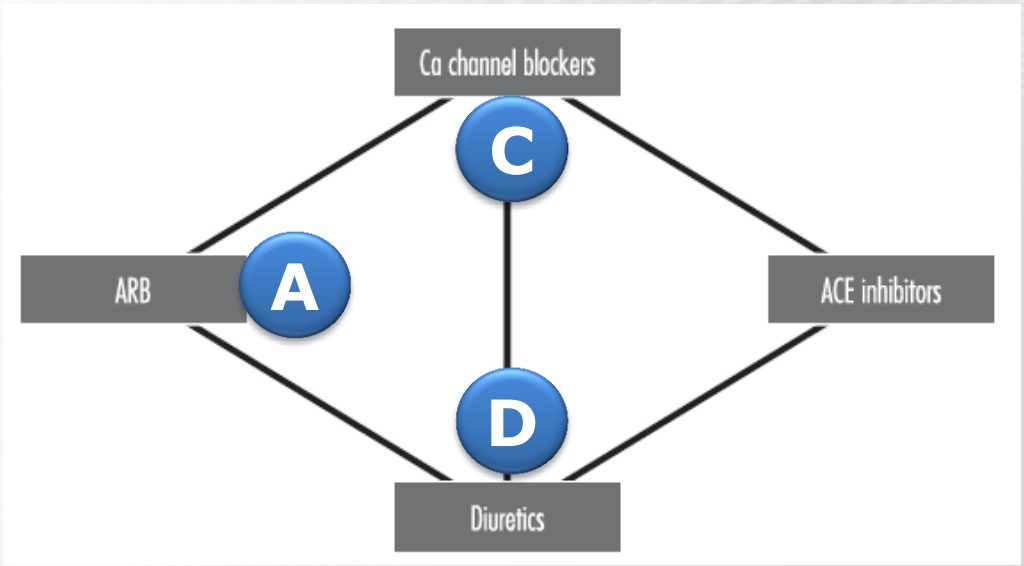
A + C *or* **A + D**

Then

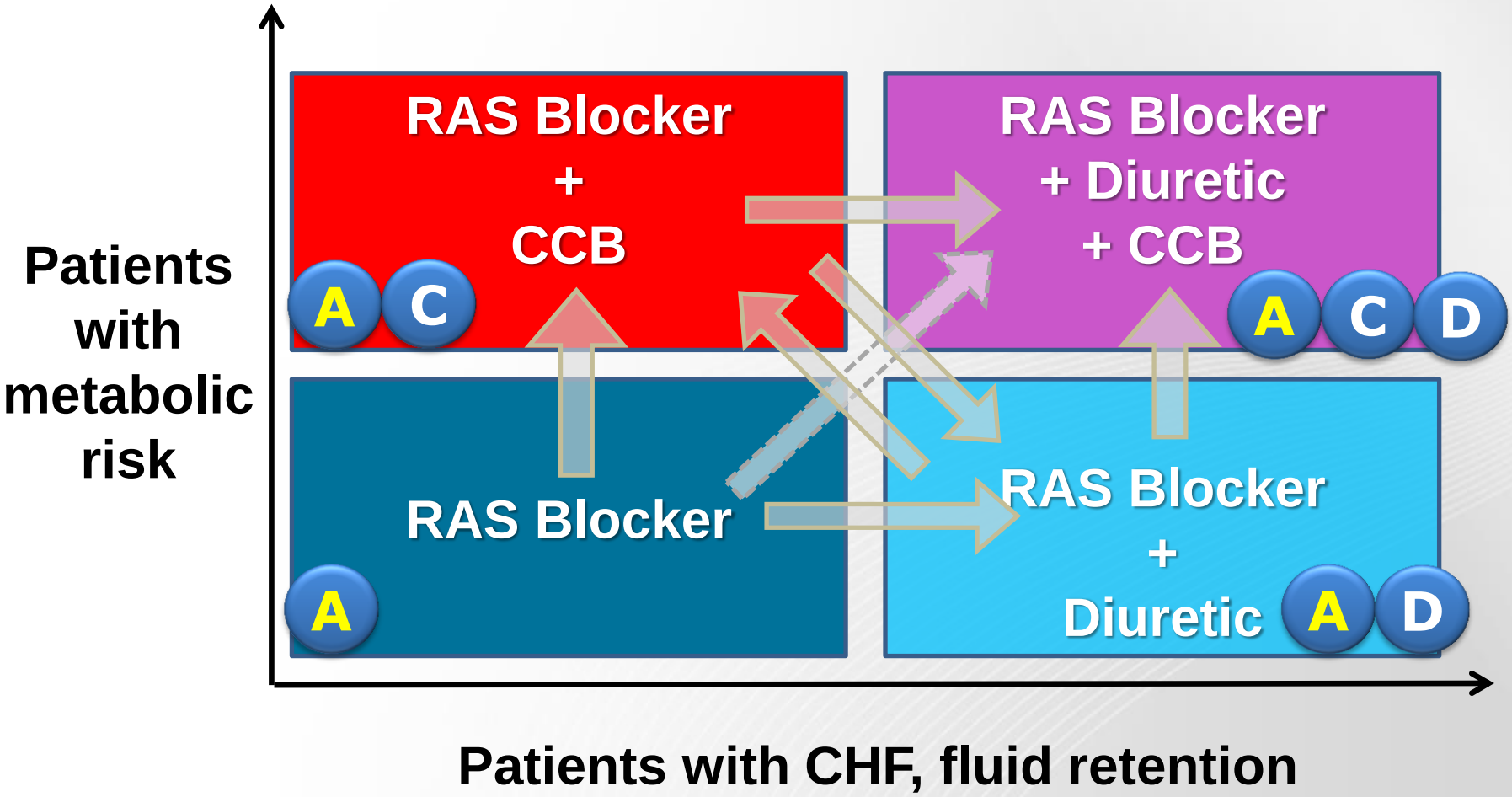
A + C + D

2014 일본고혈압학회 (JSH) Guideline, *Hypertension Research* (2014) 37, 291–300





BP Goal: Proposal for Simple Solution



Only ARB having single pill of triple combination

[Only one Olmesartan with full range dosage with one pill by not giving price burden and increasing patient adherence]

SEVIKAR®

6.2 mm	8.2 mm	8.2 mm
		
5/20 mg	5/40 mg	10/40 mg
696원	758원	814원

SEVIKAR HCT®

8 mm	9 mm	9 mm
		
5/20/12.5 mg	5/40/12.5 mg	10/40/12.5 mg
777원	999원	1,071원

Olmetec®

5.5 mm	8.7 mm	15.4 mm
		 7.2 mm
10 mg	20 mg	40 mg
277원	416원	478원

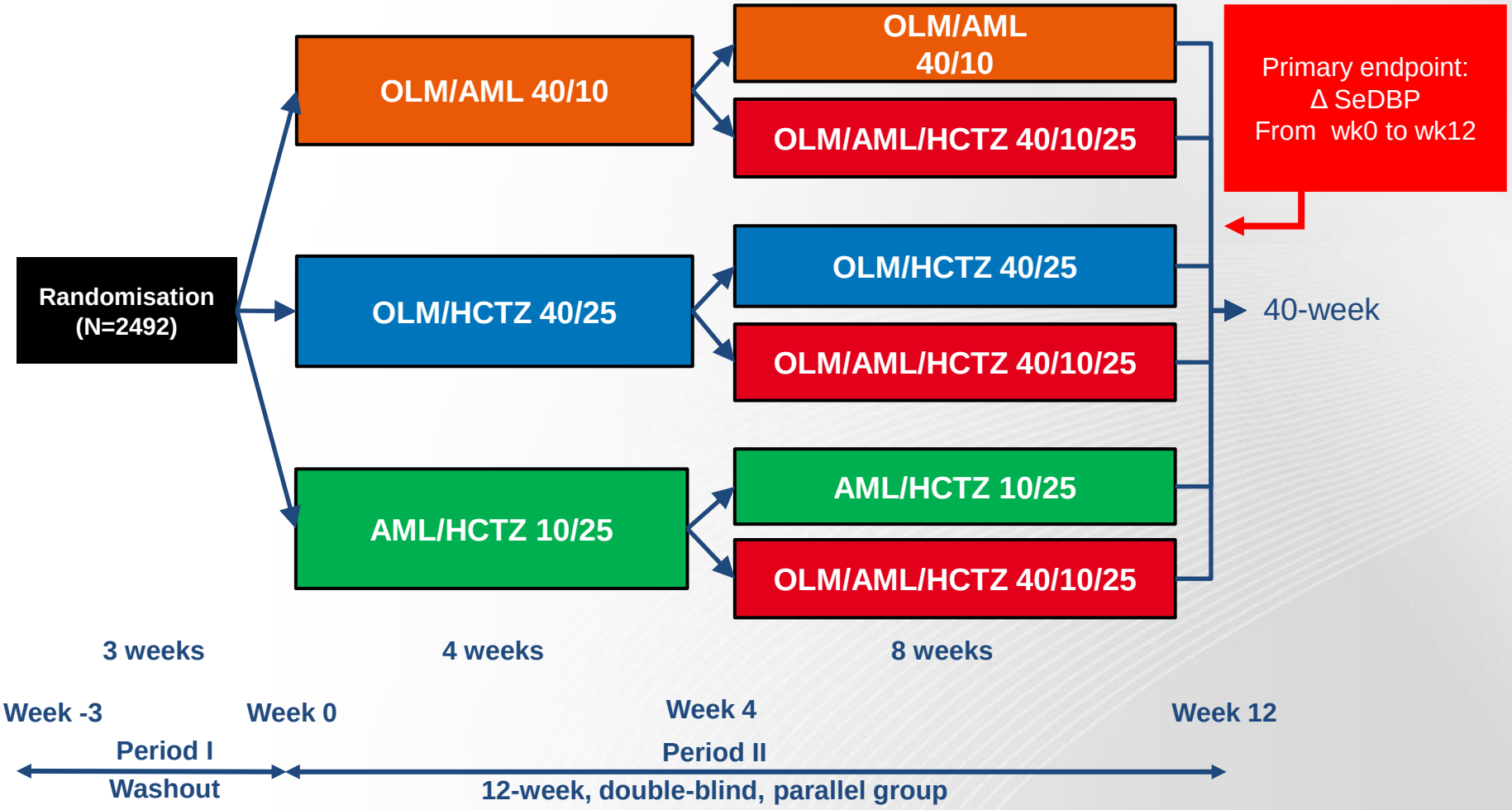
Olmetec Plus®

8.7 mm

20/12.5 mg

417원

Triple Therapy with High Dose Olmesartan/AML /HCTZ in the TRINITY Study



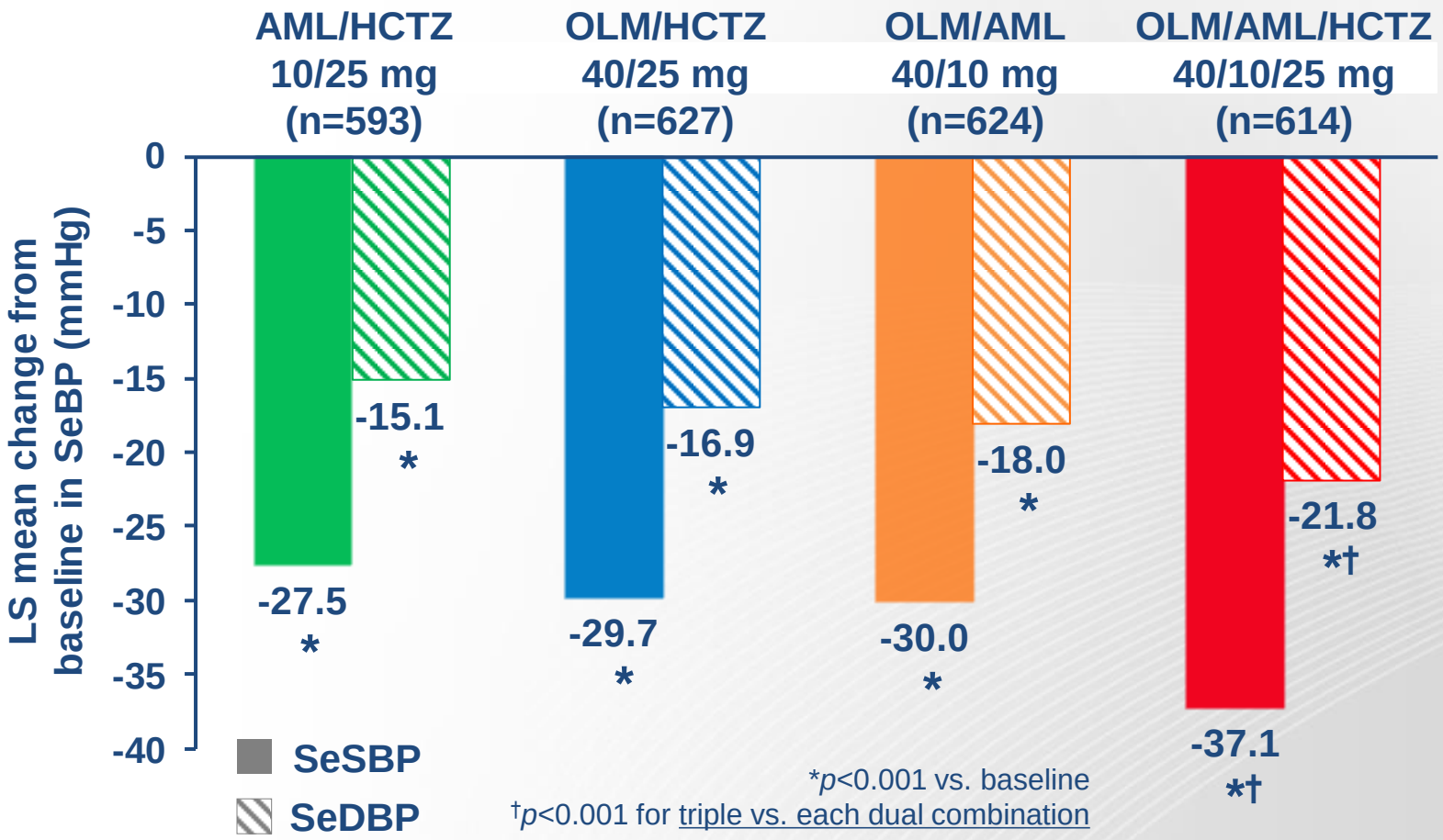
BP was measured using an automated BP monitor (Omron HEM-705CP, Omron Healthcare, Inc., Bannockburn, Illinois)

Oparil et al. Clin Ther 2010;32:1252–69

With Dr. Suzanne Oparil

Hypertension Seoul 2016, Coex

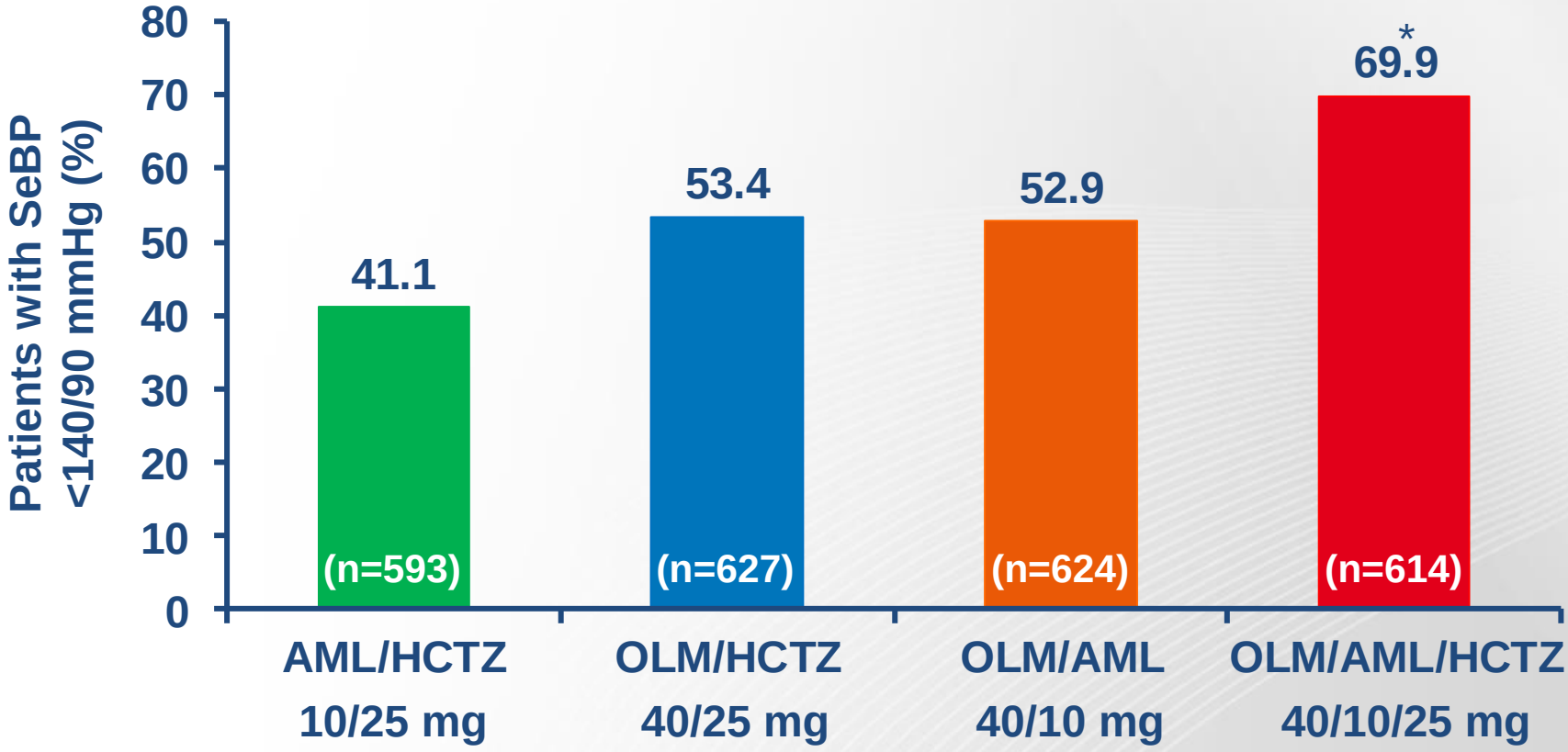
High Dose OLM/AML/HCTZ Triple Combination Therapy is Superior to Dual Combination at Lowering BP



In patients with baseline mean SeBP 168.5/100.9 mmHg, after 12 weeks of treatment

Oparil et al. Clin Ther 2010;32:1252–69

High Dose OLM/AML/HCTZ Provides Significantly Better BP Threshold Achievement than Dual Therapy (TRINITY study)



*p<0.001 for triple vs. each dual combination

In patients with baseline mean SeBP 168.5/100.9 mmHg, after 12 weeks of treatment

Oparil et al. Clin Ther 2010;32:1252–69

국내(아시안)에서 현실적인 저용량 FDC의 효과

Am J Cardiovasc Drugs
DOI 10.1007/s40256-015-0156-x

CrossMark

ORIGINAL RESEARCH ARTICLE

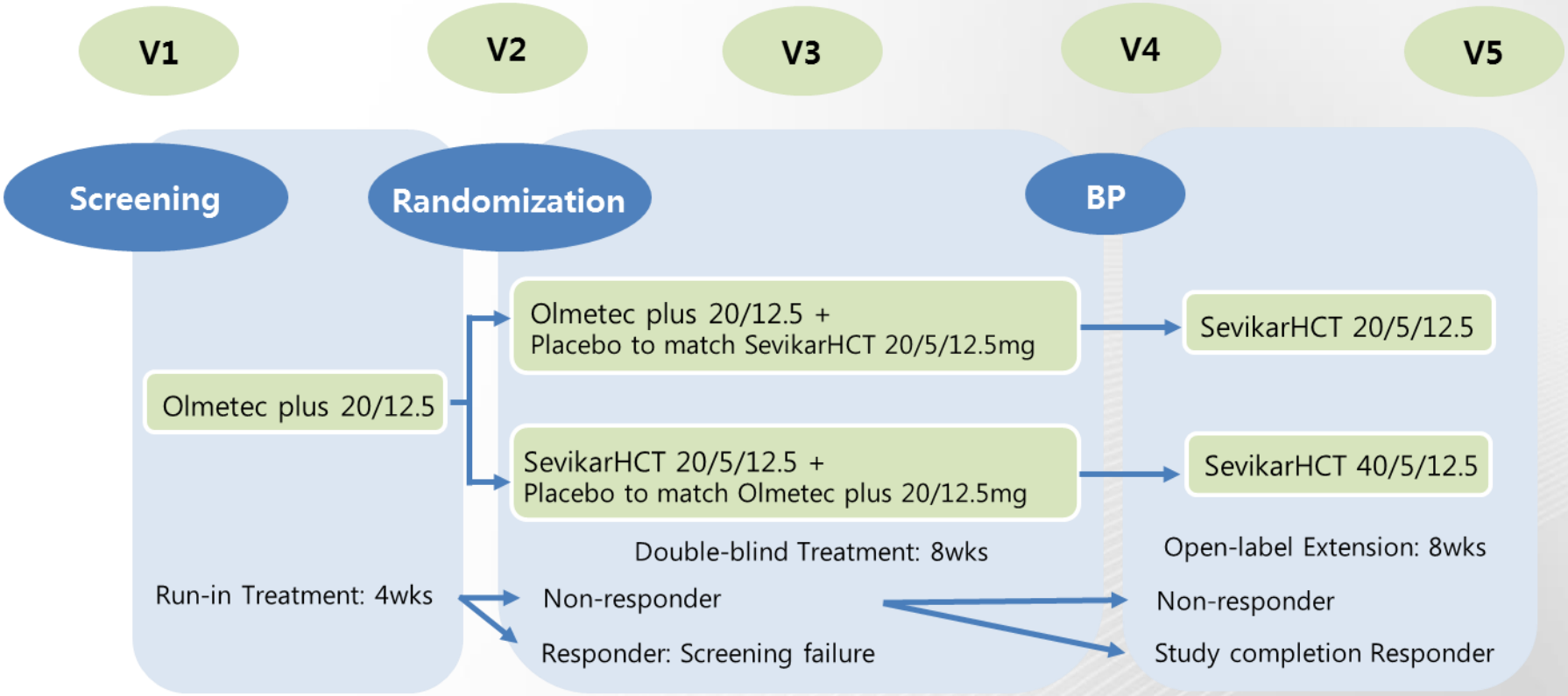
Efficacy and Safety Study of Olmesartan Medoxomil, Amlodipine, and Hydrochlorothiazide Combination Therapy in Patients with Hypertension Not Controlled with Olmesartan Medoxomil and Hydrochlorothiazide Combination Therapy: Results of a Randomized, Double-Blind, Multicenter Trial

Il Suk Sohn[1] · Chong-Jin Kim[1] · Byung-Hee Oh[2] · Taek-Jong Hong[3] · Chang-Gyu Park[4] · Byung-Soo Kim[5] · Woo-Baek Chung[6] · For the Investigators

A+D 로 혈압조절 안 될 때 저용량 **A+C+D**의 효과

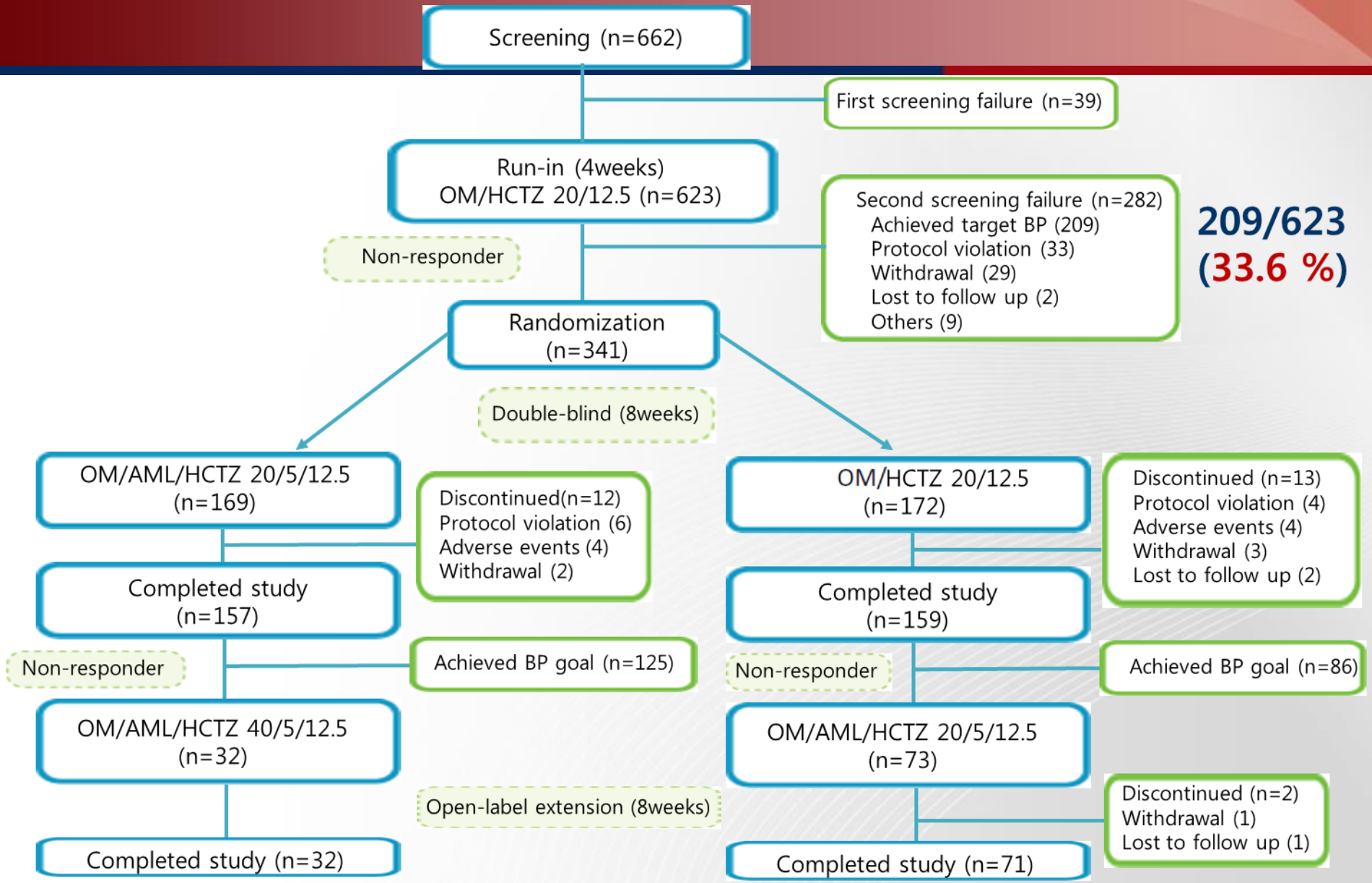
Am J Cardiovasc Drugs. 2016;16:129-38

국내(아시안)에서 현실적인 저용량 FDC의 효과



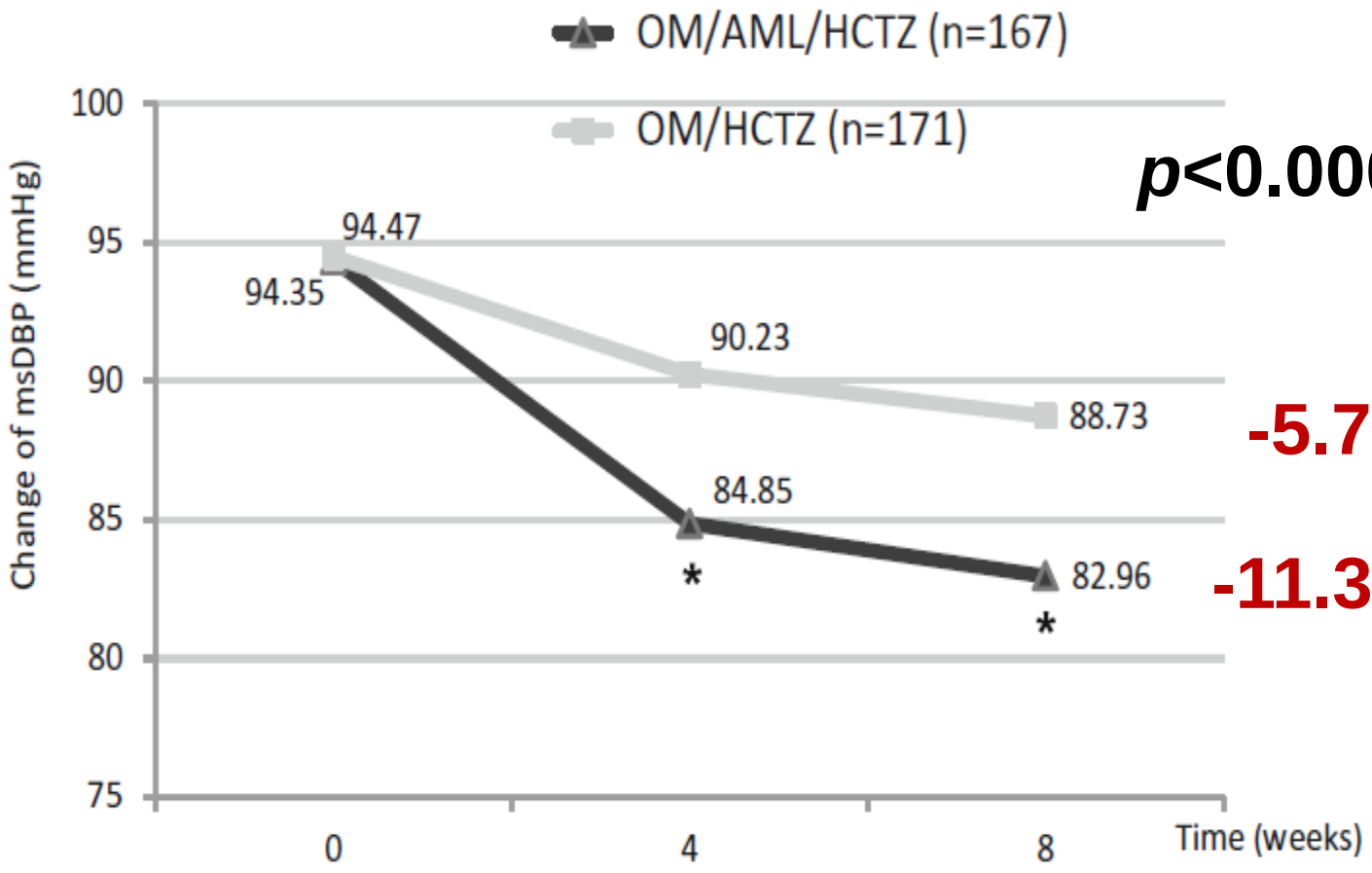
V2, V4 Non-responder: msSBP ≥ 140 mmHg and msDBP ≥ 90 mmHg
msSBP/DBP < 140/90 mmHg
msSBP/DBP < 130/80 mmHg for the patients with diabetes or chronic renal disease

Am J Cardiovasc Drugs. 2016;16:129-38



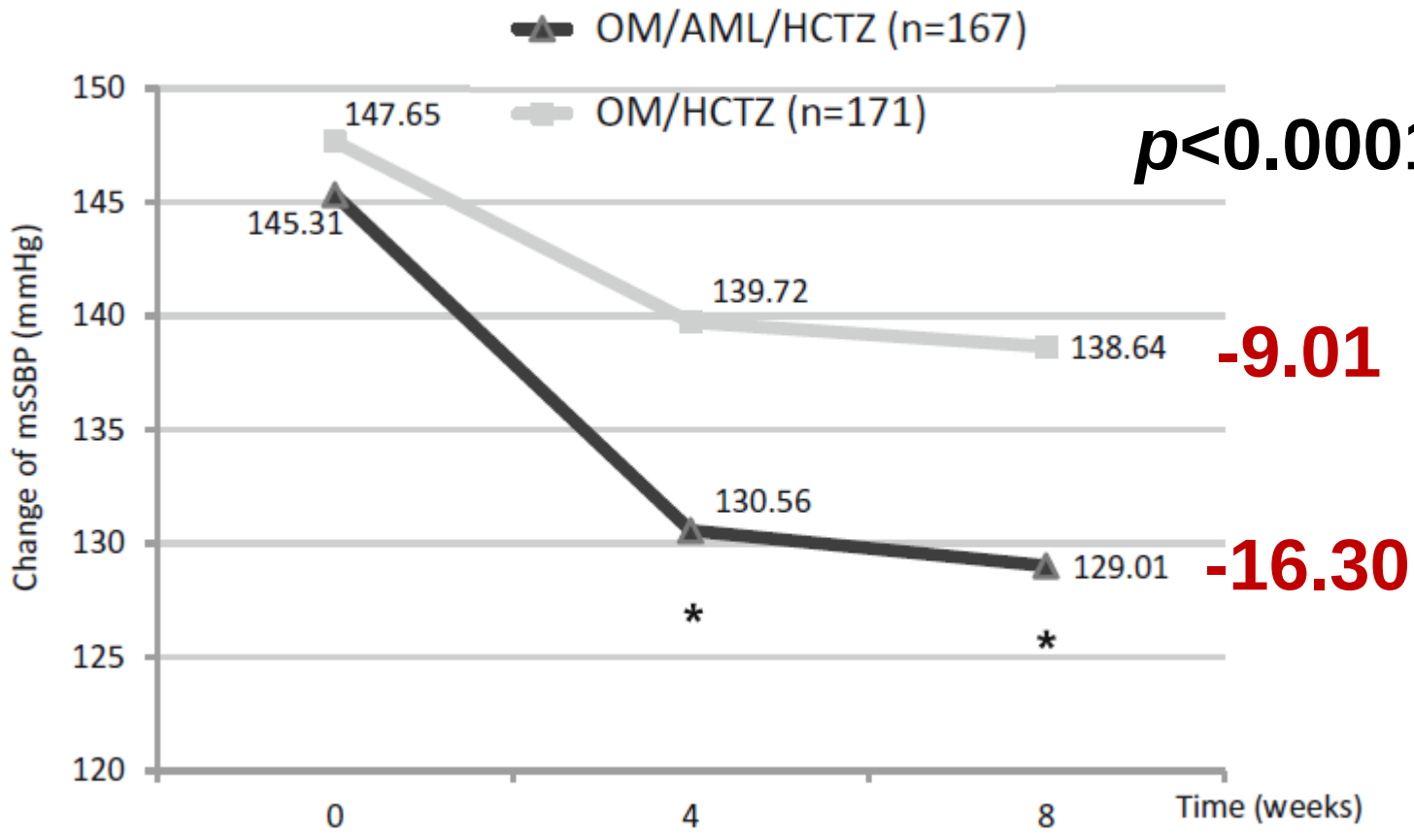
Am J Cardiovasc Drugs. 2016;16:129-38

8주 동안 msDBP의 변화



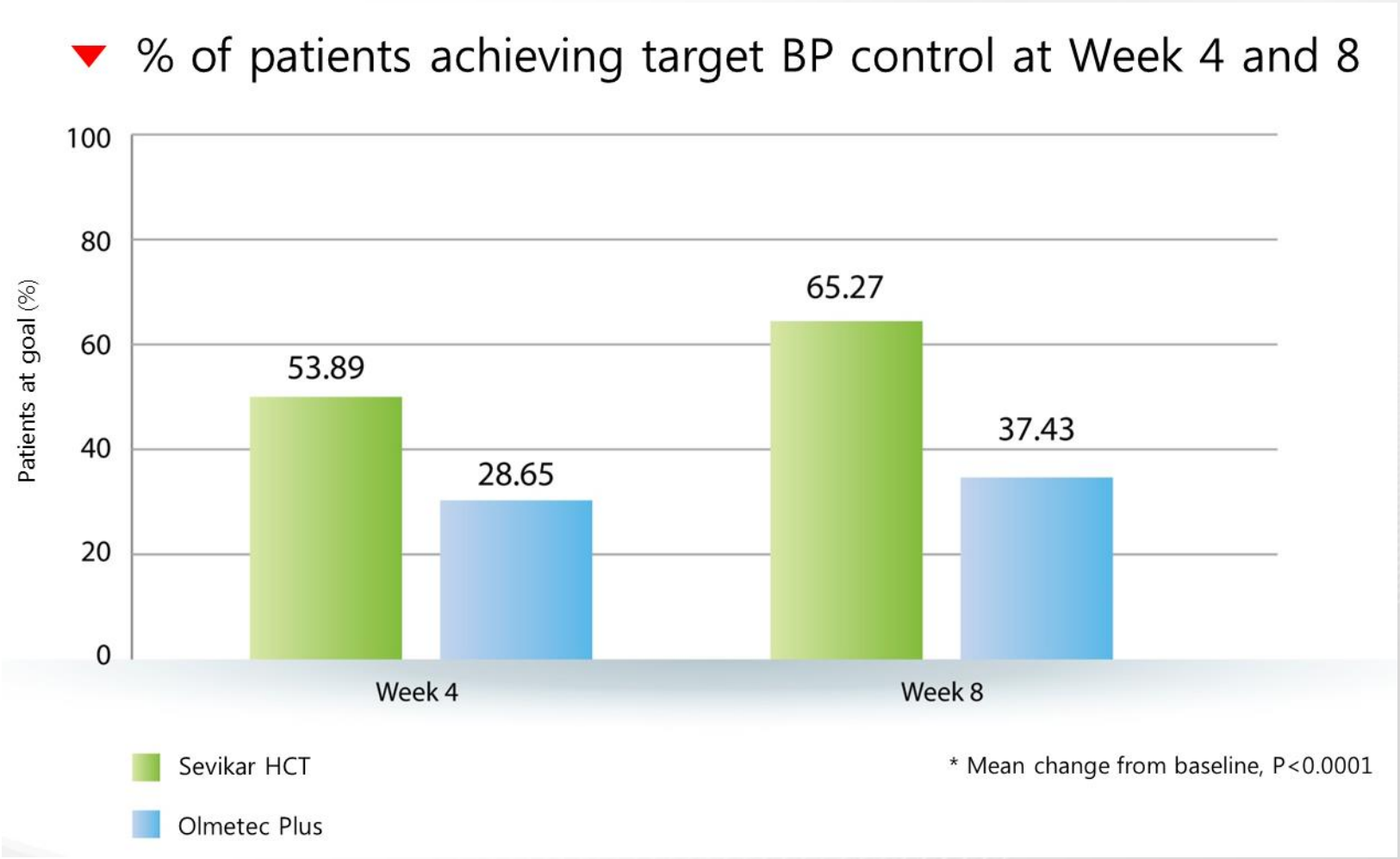
Am J Cardiovasc Drugs. 2016;16:129-38

8주 동안 msSBP의 변화



Am J Cardiovasc Drugs. 2016;16:129-38

4주, 8주에 목표 혈압에 도달한 환자 비율



Am J Cardiovasc Drugs. 2016;16:129-38

Adverse events

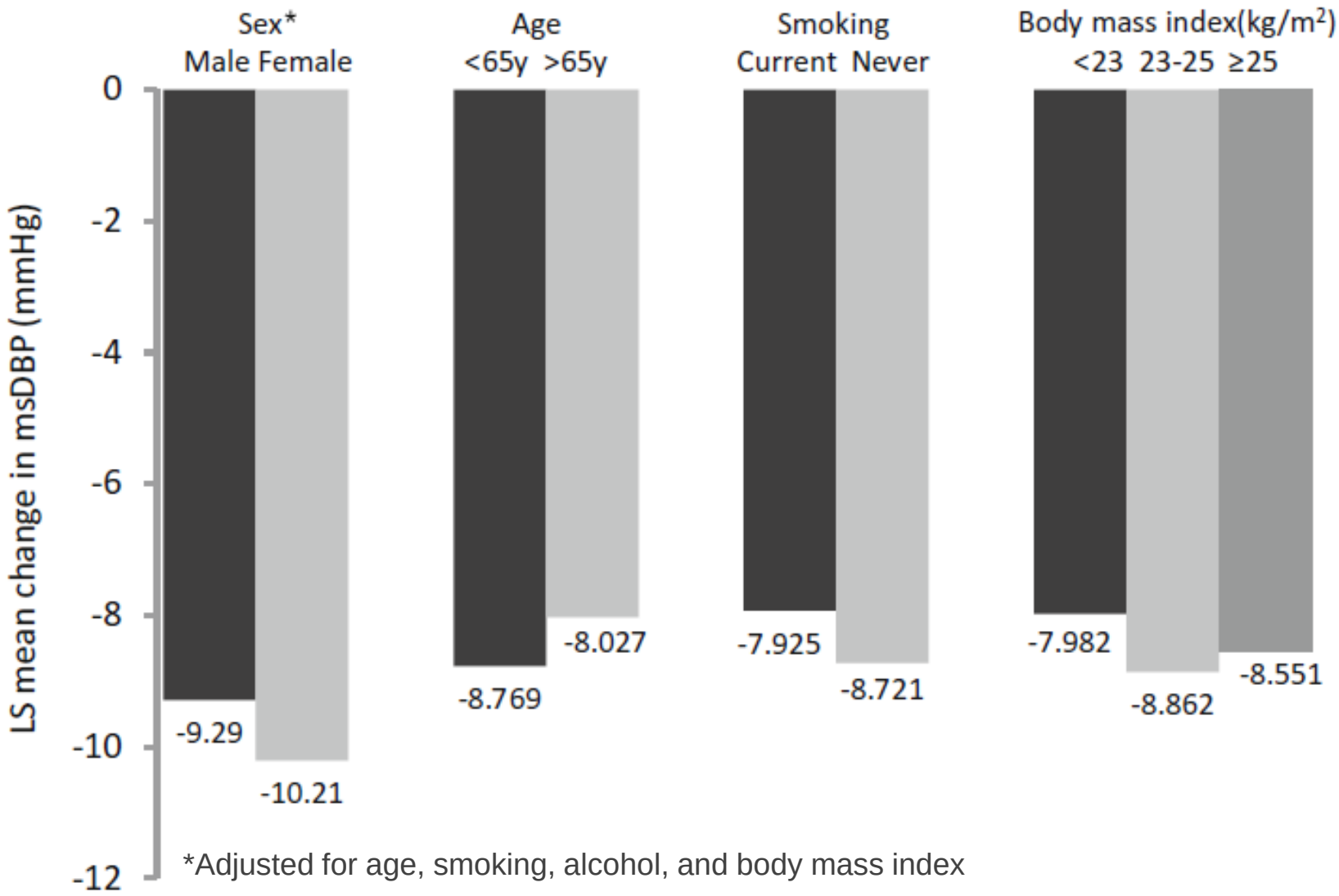
Adverse events	Sevikar HCT 20/5/12.5(n=168)	Olmetec Plus 20/12.5(n=172)
Any adverse events	33 (19.64)[a], 46 events	34 (19.77)[a], 51 events
Severity		
Mild	41(24.40)	40(23.36)
Moderate	5(2.98)	10(5.81)
Severe	0	1(0.58)
Causality		
Related	6 (3.57)	8(4.65)
Certainly/probably/possibly/unassessable	2/1/2/1	0/1/5/2
Not related	40 (23.81)	43 (25.00)
Unlikely/not related	14/26	11/32
Adverse drug reactions	5 (2.98)[a], 6 events	6 (3.49)[a], 8 events
Dizziness	2 (1.19)	2 (1.16)
Pre-syncope	1 (0.60)	0
Syncope	0	1(0.58)
Peripheral edema	0	2(1.16)
Generalized edema	0	1(0.58)
Fatigue	1(0.60)	0
Constipation	0	1(0.58)
Cough	1(0.60)	0
Pruritus	0	1(0.58)
Hypotension	1(0.60)	0
Serious adverse events	2(1.19)[b], 2 events	1 (0.58)[c], 3 events

Data are presented as n (%) patients
AML amlodipine, ***HCTZ*** hydrochlorothiazide, ***OM*** olmesartan medoxomil
a Some patients had more than one event
b One had acute tonsillitis and one underwent minor surgery for cervical polyp
c The patient died after sudden cardiac arrest with hyperkalemia and the diagnosis of probable acute myocardial infarction

For tolerability, only 8 of 340 patients (2.35 %) discontinued their medications.

Am J Cardiovasc Drugs. 2016;16:129-38

Changes in msDBP by subgroup



*Adjusted for age, smoking, alcohol, and body mass index

Am J Cardiovasc Drugs. 2016;16:129-38

국내(아시안)에서 현실적인 저용량 FDC의 효과

KEY POINTS

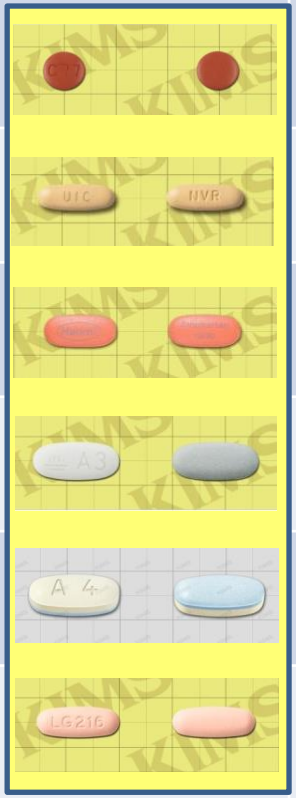
In Korean patients with moderate hypertension not controlled with **dual fixed-dose combination (FDC)** as first-line therapy, **switching to triple FDC** therapy is **safe and effective** in reaching target blood pressure.

Triple FDC therapy can be a safe and effective alternative for Asian patients with hypertension not controlled with a dual FDC, including thiazide, in **real-world clinical practice**.

Am J Cardiovasc Drugs. 2016;16:129-38

국내 CCB + ARB 복합제

CCB	+	ARB	Brand name	ARB high dose	Cost (원)*
Amlodipine		**Olmesartan**	**Sevikar**	10/40	814
Amlodipine		Valsartan	Exforge	10/160	1,128
Amlodipine		Losartan	Amosartan	10/50	1,126
Amlodipine		Telmisartan	Twynsta	5/80	853
S-amlodipine		Telmisartan	Telminuvo	5/80	987
Lercanidipine		Valsartan	Levacalm	20/160	1,037



* 2017.4.20 기준. kimsonline.co.kr

요약

- 고혈압은 적극적 관리가 예후 개선에 중요
- 환자-순응도는 고혈압 조절 및 예후와 밀접한 관계
- 의사-순응도 개선을 위해 **초기 병합 요법** 혹은 약 개수를 줄이는 **고정용량복합제**가 중요

- **Sevikar HCT**
  - 국내 유일 삼중 고정용량복합제(triple FDC)
  - ARB (olmesartan) + CCB (AML) + HCTZ
  - TRINITY study – 고용량 병합. dual< triple
  - 국내 임상 – 저용량 병합. dual → triple

Sevikar HCT, Who will benefit from it?

- 단일 혹은 이중 병용요법으로 조절 안되는 환자
- 저항성 고혈압
- 여러 질환 동반으로 약 개수가 많은 환자
- 순응도 좋지 않은 환자
- 초기 빠르고 적극적인 혈압조절 필요한 고위험

All for one, one for all

"Athos, Porthos, Aramis & D'Artagnan" Image by Maurice Leloir, 1894
Alexandre Dumas, Les Trois Mousquetaires (French), 1844