Ways to Improve Blood Pressure Control in Hypertension Patients

SEVIKAR/SEVIKAR HCT Trial in Korean with Hypertension

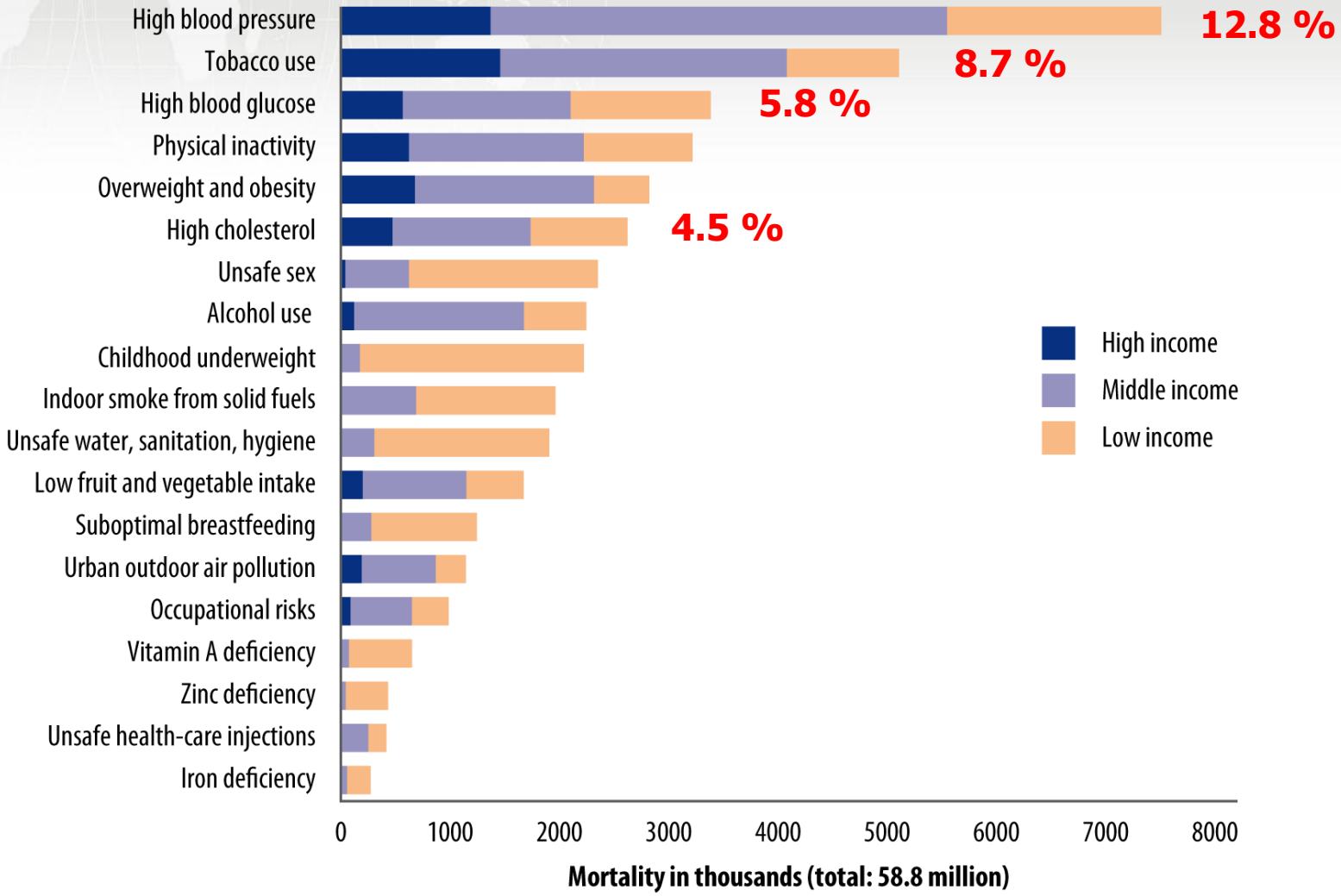
강동경희대병원 심장혈관내과

손 일 석

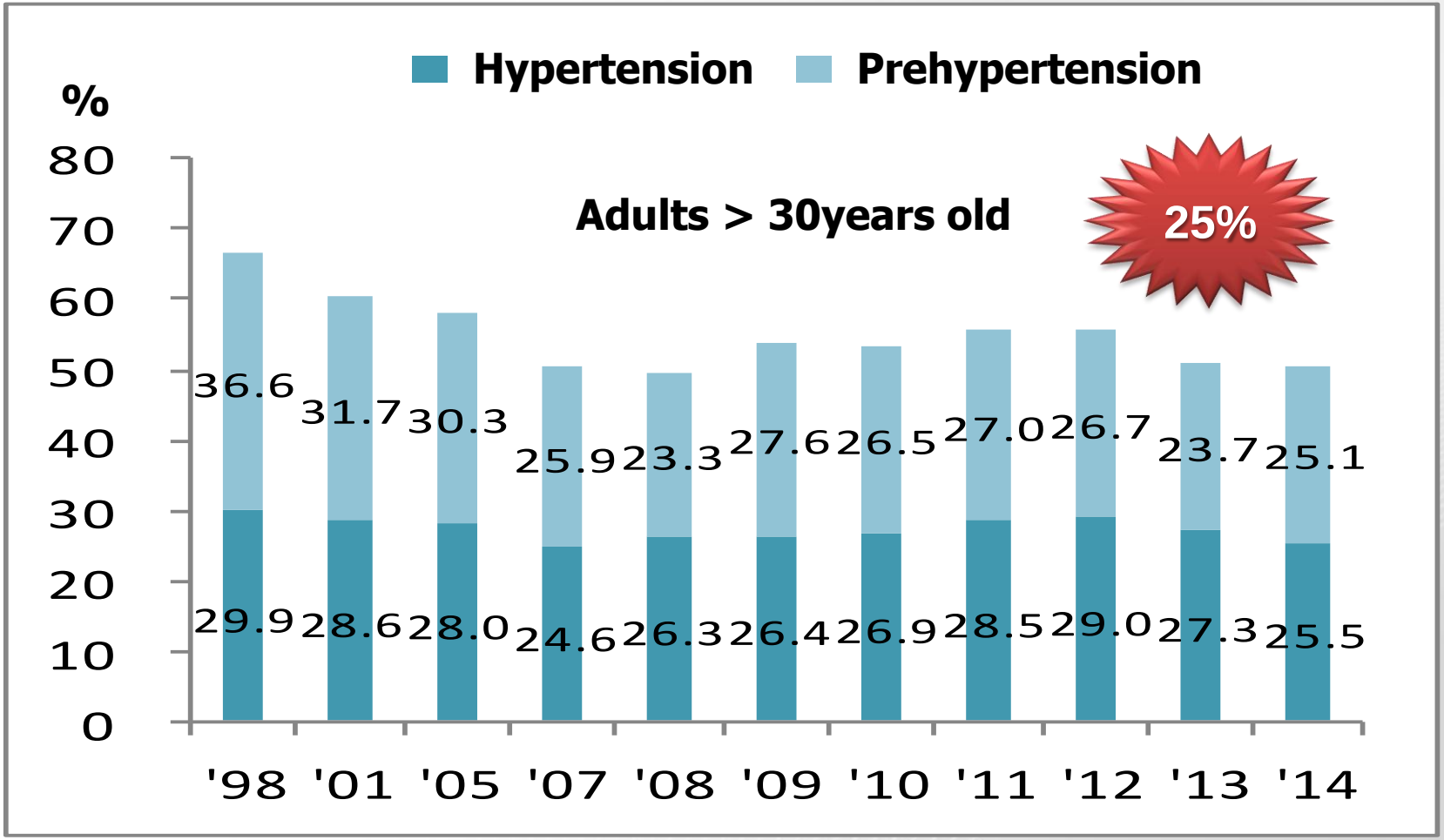
오늘의 내용

- 고혈압의 치료에서 순응도의 중요성
- 이중 고정용량복합제 (Sevikar®)
  - ACE-HY
- 국내 유일 삼중 고정용량복합제 (Sevikar HCT®)
  - Sevikar HCT trial in Korea

Deaths attributed to 19 leading factors, by country income level, 2004



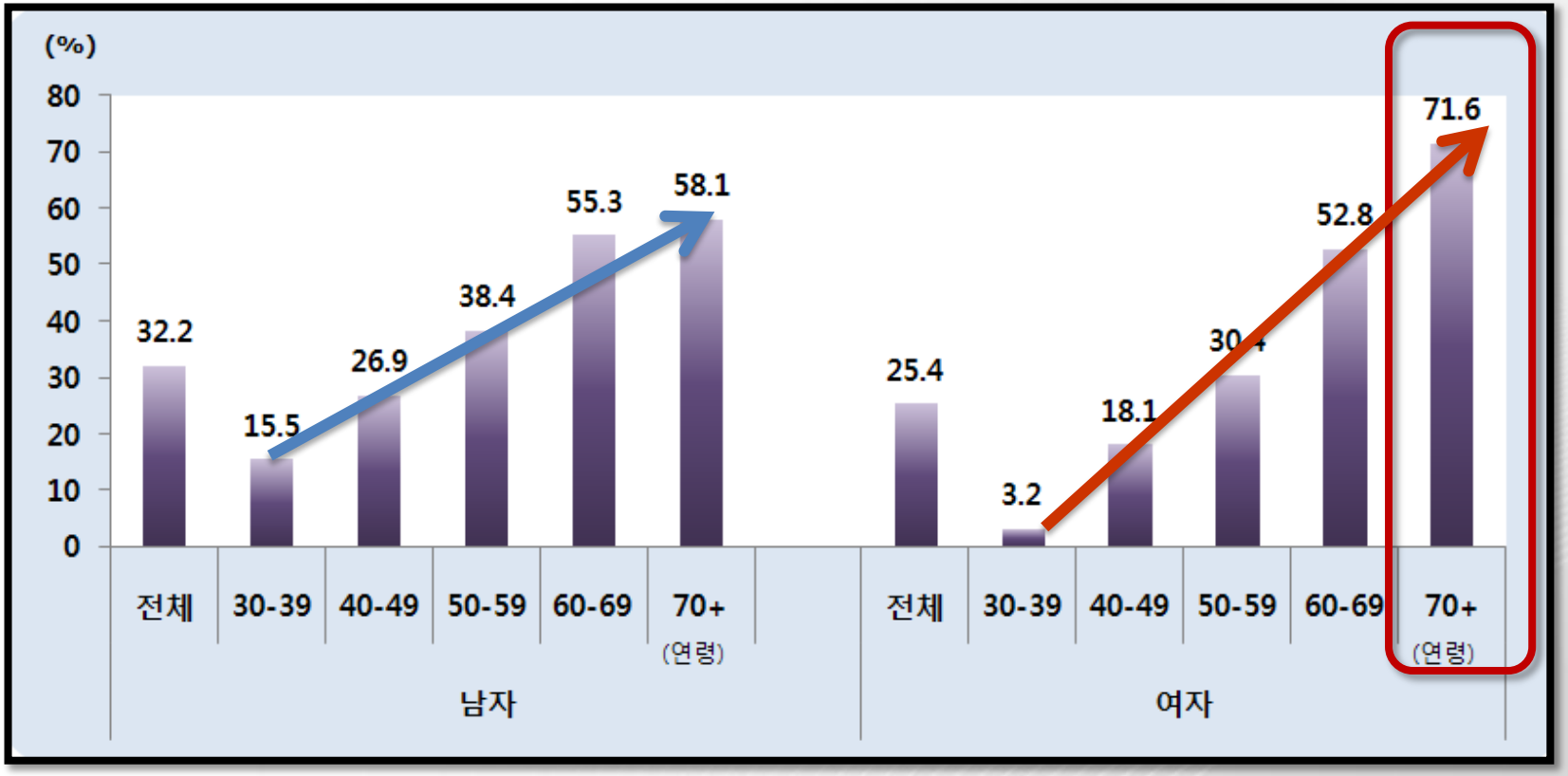
Prevalence of Hypertension and Prehypertension in South Korea



2014 Korea National Health & Nutrition Examination Survey

국내 고혈압 유병률 (만 30세 이상)

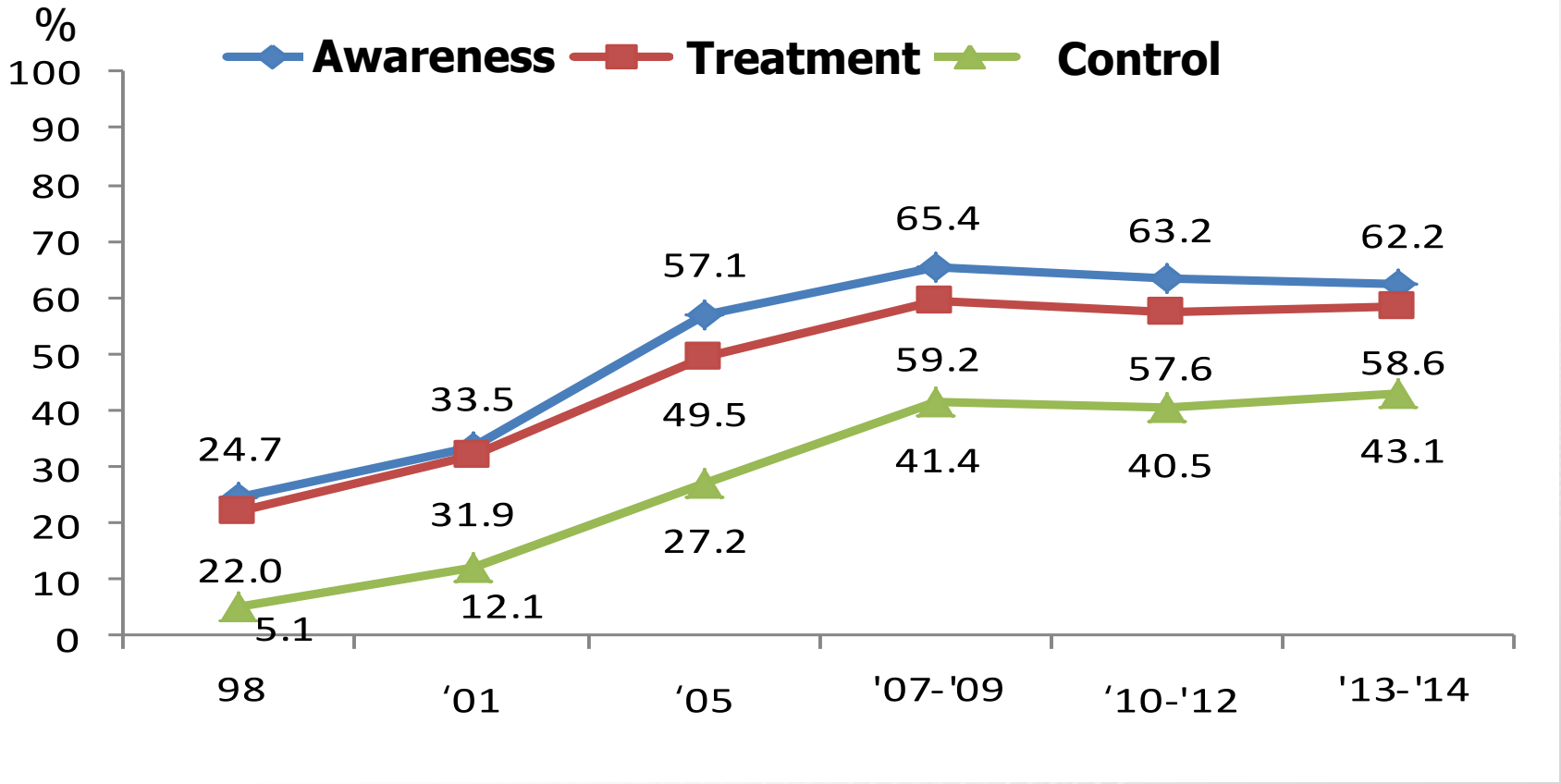
30세 이상 남자 3명 중 1명, 여자 4명 중 1명 고혈압 유병자



고혈압 유병률 : 수축기혈압이 140mmHg 이상이거나 이완기혈압이 90mmHg 이상 또는 고혈압 약물을 복용한 분율, 만30세 이상

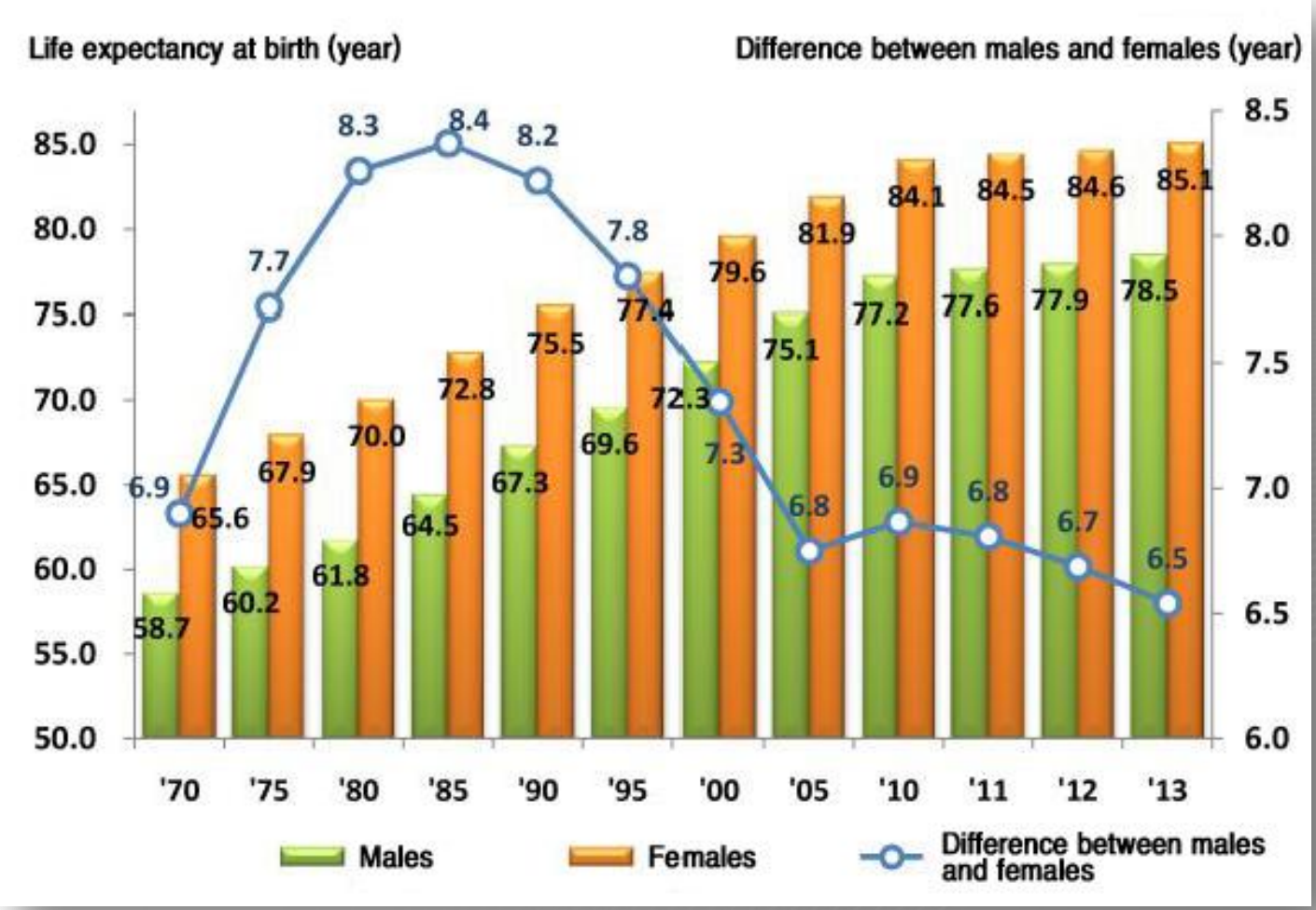
2012 국민건강영양조사. 보건복지부

Trends in Awareness, Treatment, and Control of Hypertension in South Korea, 1998-2014



2014 Korea National Health & Nutrition Examination Survey

Life Expectancy at Birth, 81.9 yrs

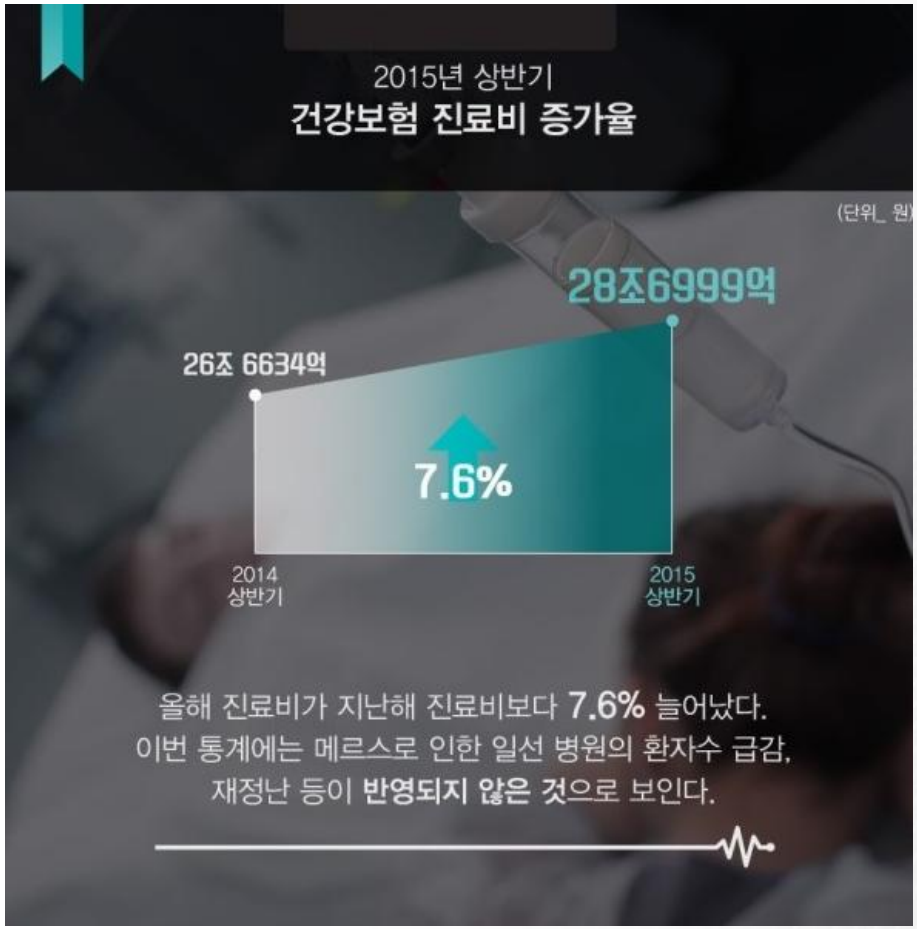


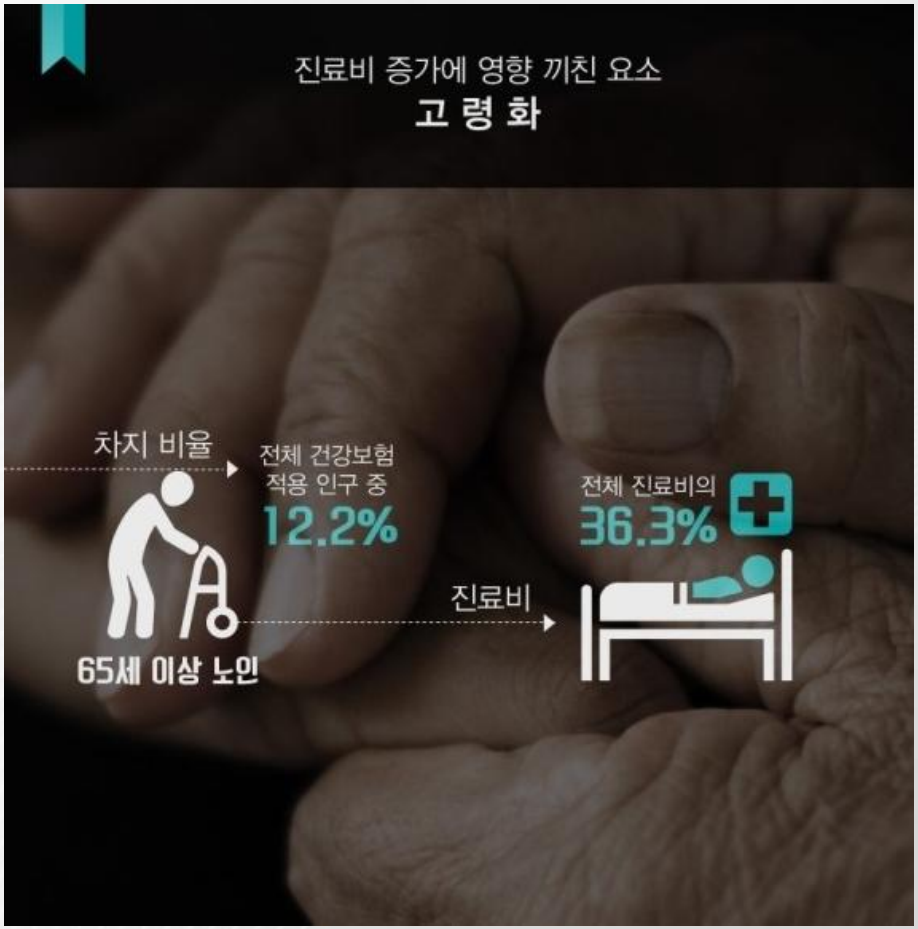
* Average of OECD member countries (year)
Total **80.2** Males 77.6 Females 82.8

2013 Statistics Korea

고령화와 국내 의료

2015년 상반기 건강보험 진료비...지난해比 7.6% 증가

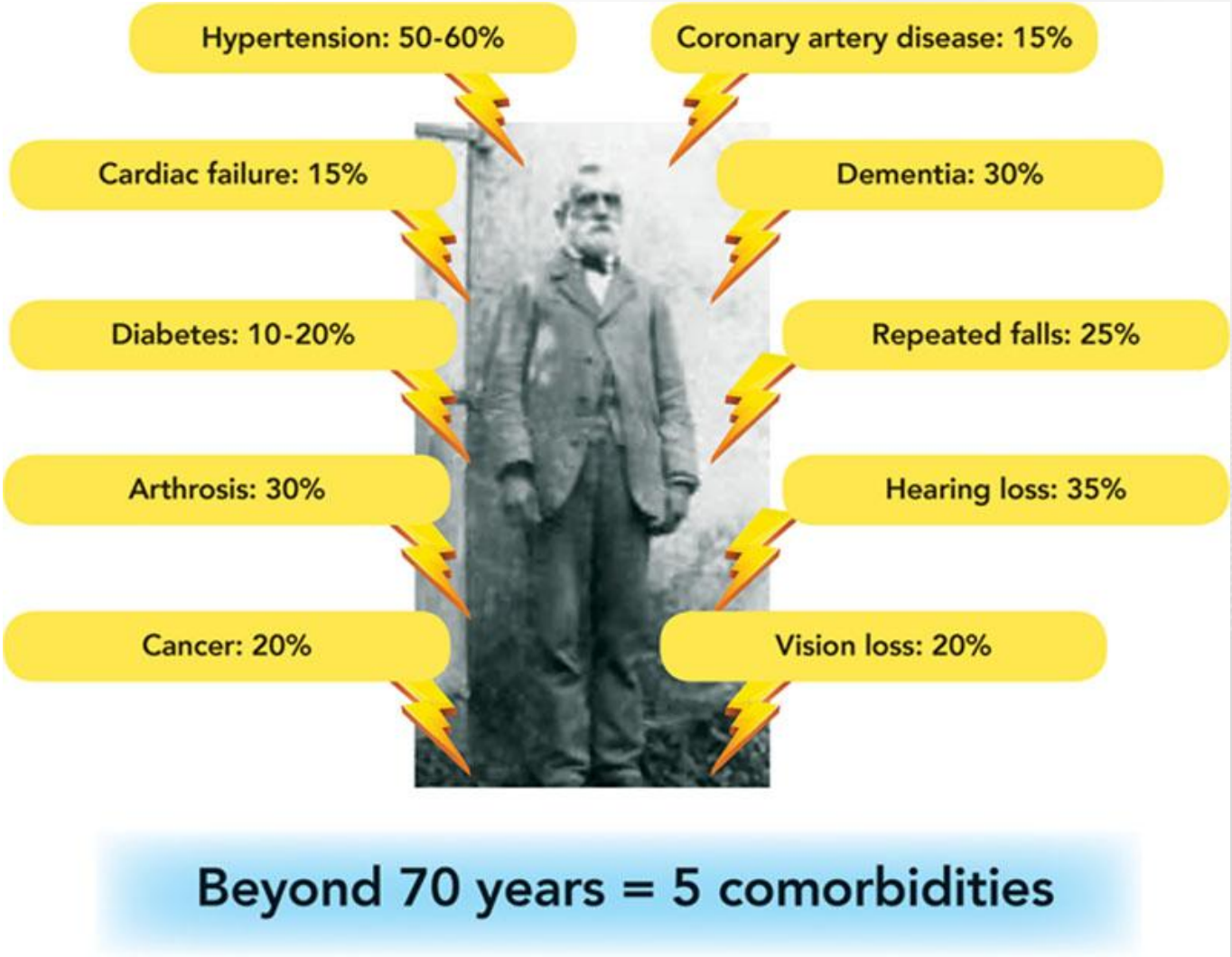




http://news.visualdive.co.kr/?p=95039

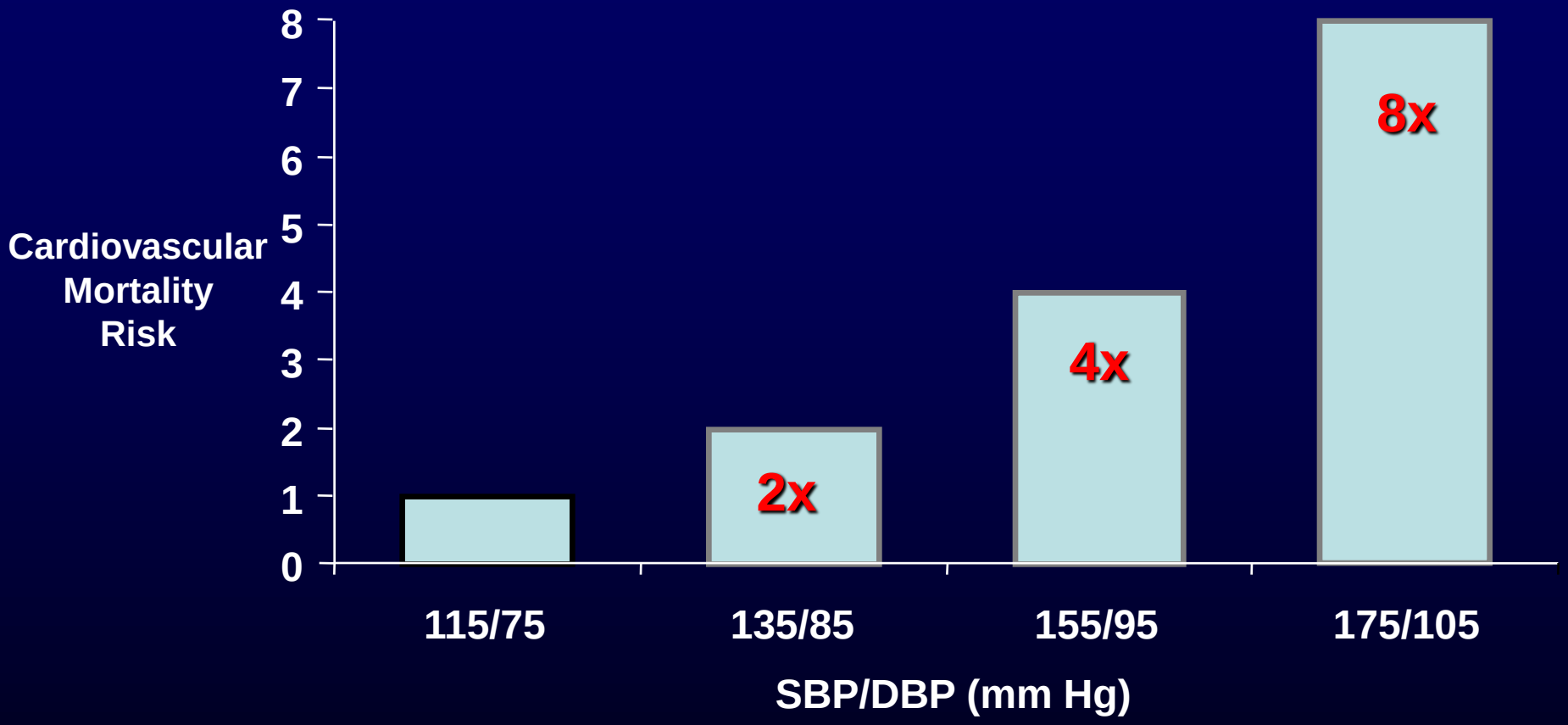
자료: 국민건강보험공단

Elderly with co-morbidities



Anesthesiology 2014

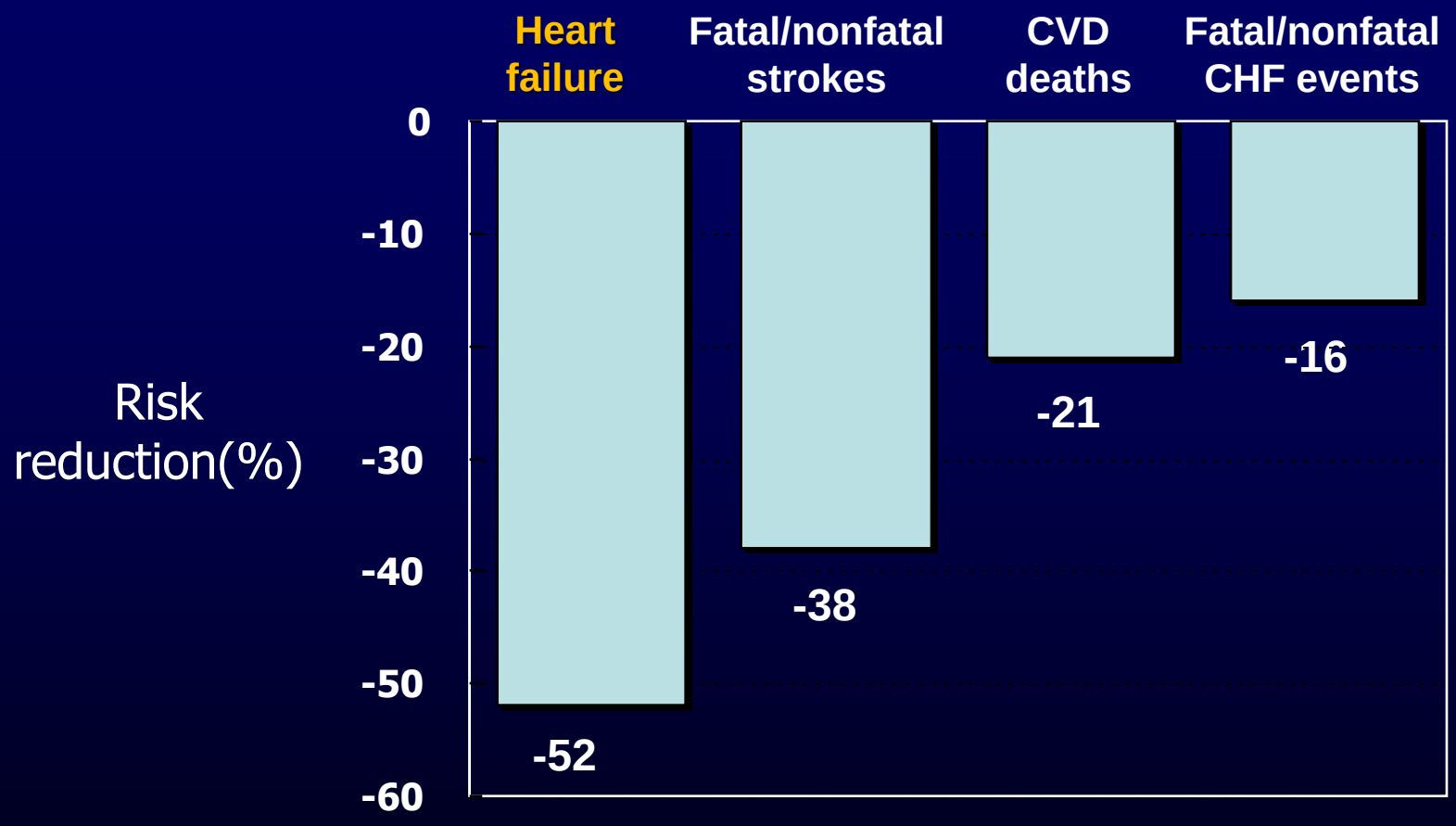
Cardiovascular Mortality Risk Doubles with Each 20/10 mmHg BP Increment*



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

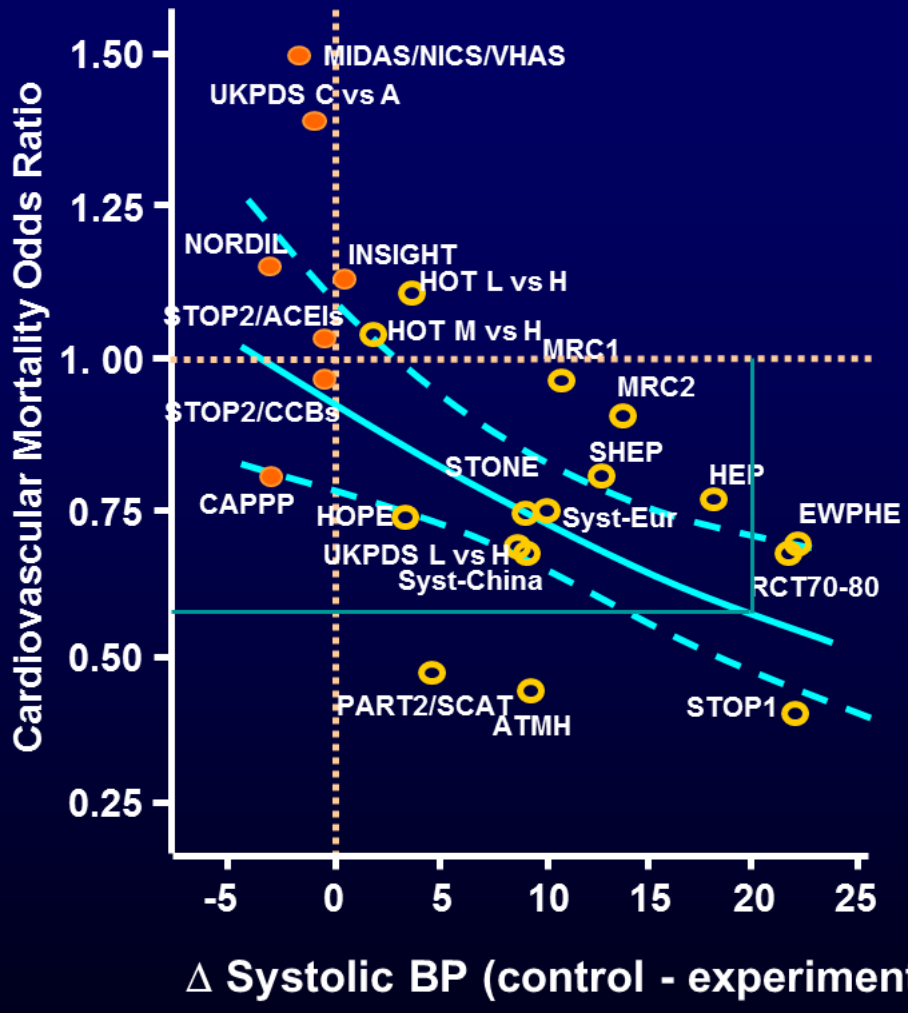
Chobanian AV et al. *JAMA*. 2003;289:2560-2572.
Lewington S et al. *Lancet*. 2002;360:1903-1913.

Antihypertensive therapy, CVD risk



Herbert et al. *Arch Intern Med* 1993

SBP reduction and CVD mortality



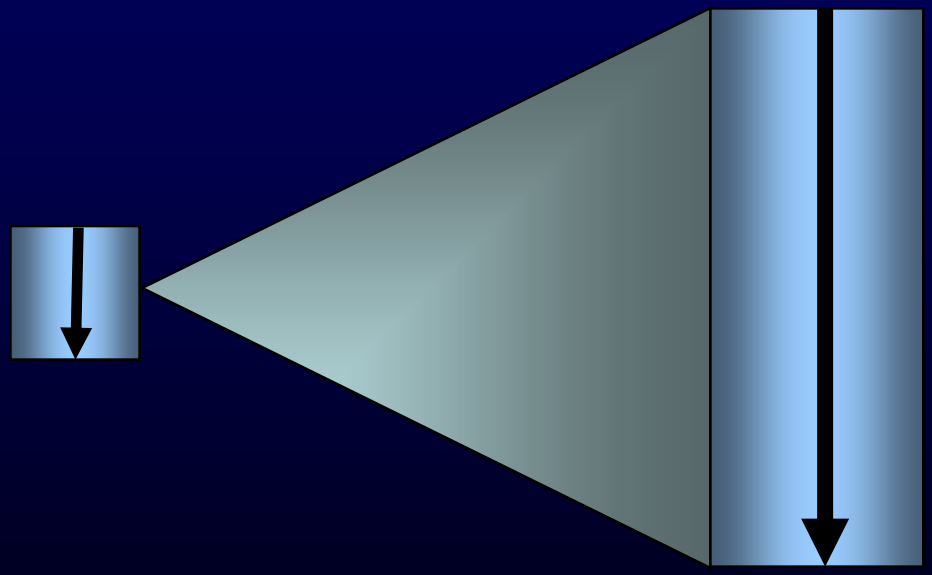
P =.003

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 mm Hg** 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

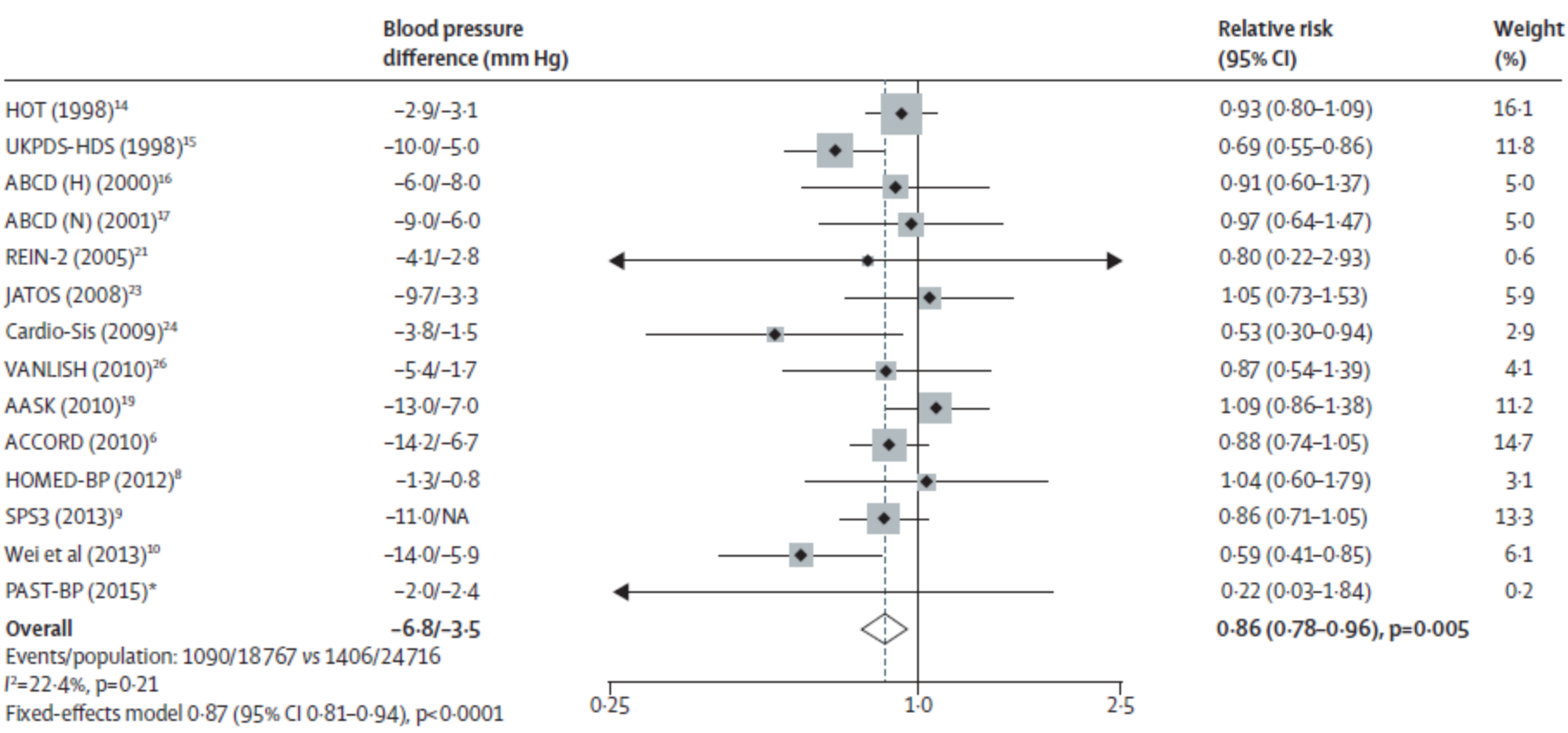
Effects of intensive blood pressure lowering on cardiovascular and renal outcomes: updated systematic review and meta-analysis

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

Hypertension Seoul 2016

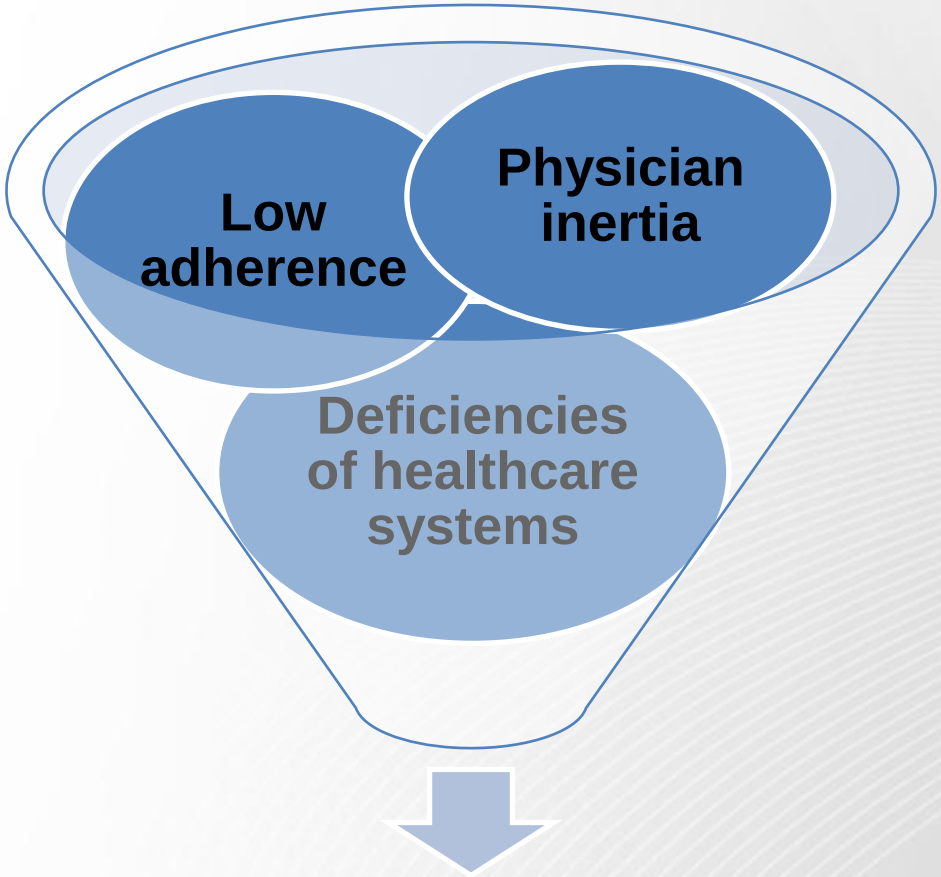
Welcome to Seoul, Korea!

The 26th International Society of Hypertension
Biennial Scientific Meeting 2016

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

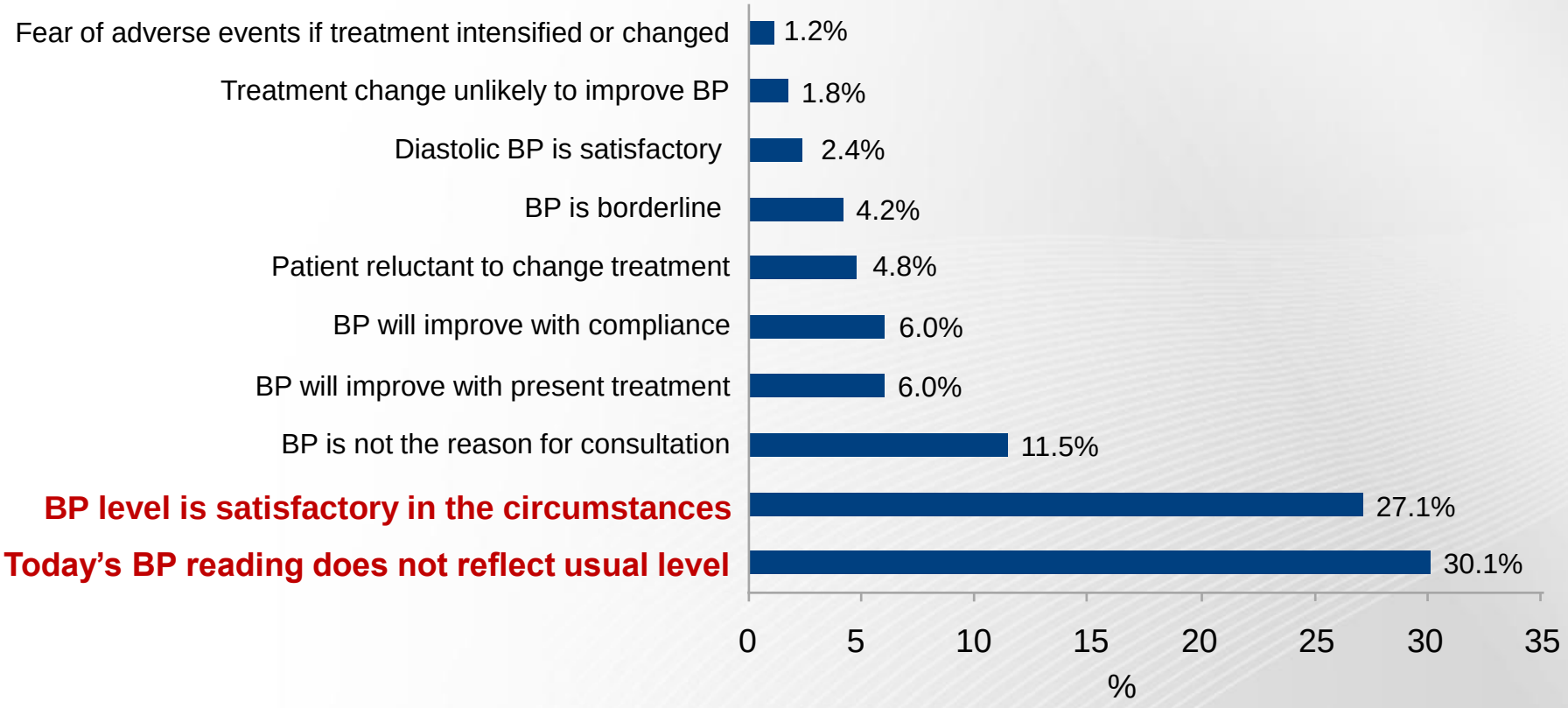
www.ish2016.org

Three Main Causes of The Low Rate of BP Control



Low rate of BP control

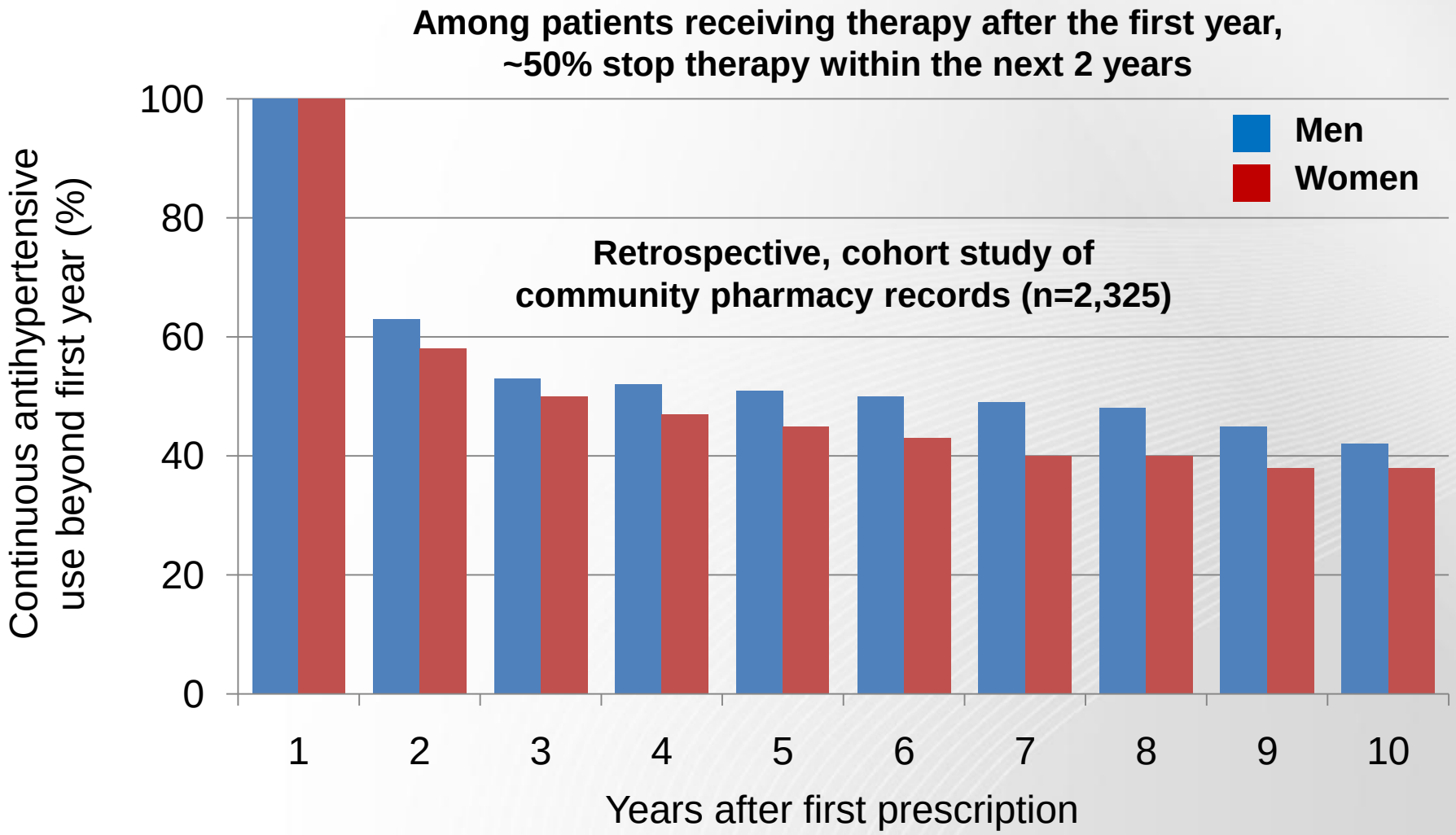
Reasons Given by Physicians for Not Changing Treatment in Uncontrolled HTN



A total of 479 hypertensive patients were included in this cross-sectional study.
Limitations include that the participation rate of general practitioners was 52% (27 general practitioners participated, all from southwestern France).

Nicodeme R, et al. *Arch Cardiovasc Dis*. 2009;102:477-483

Poor Compliance and Persistence with Antihypertensive Drugs



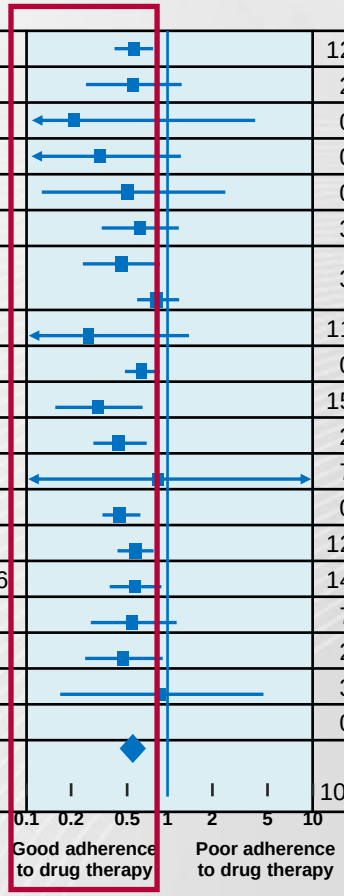
Van Wijk et al. *J Hypertens* 2005;23:2101–7

Good adherence is associated with low mortality

[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)

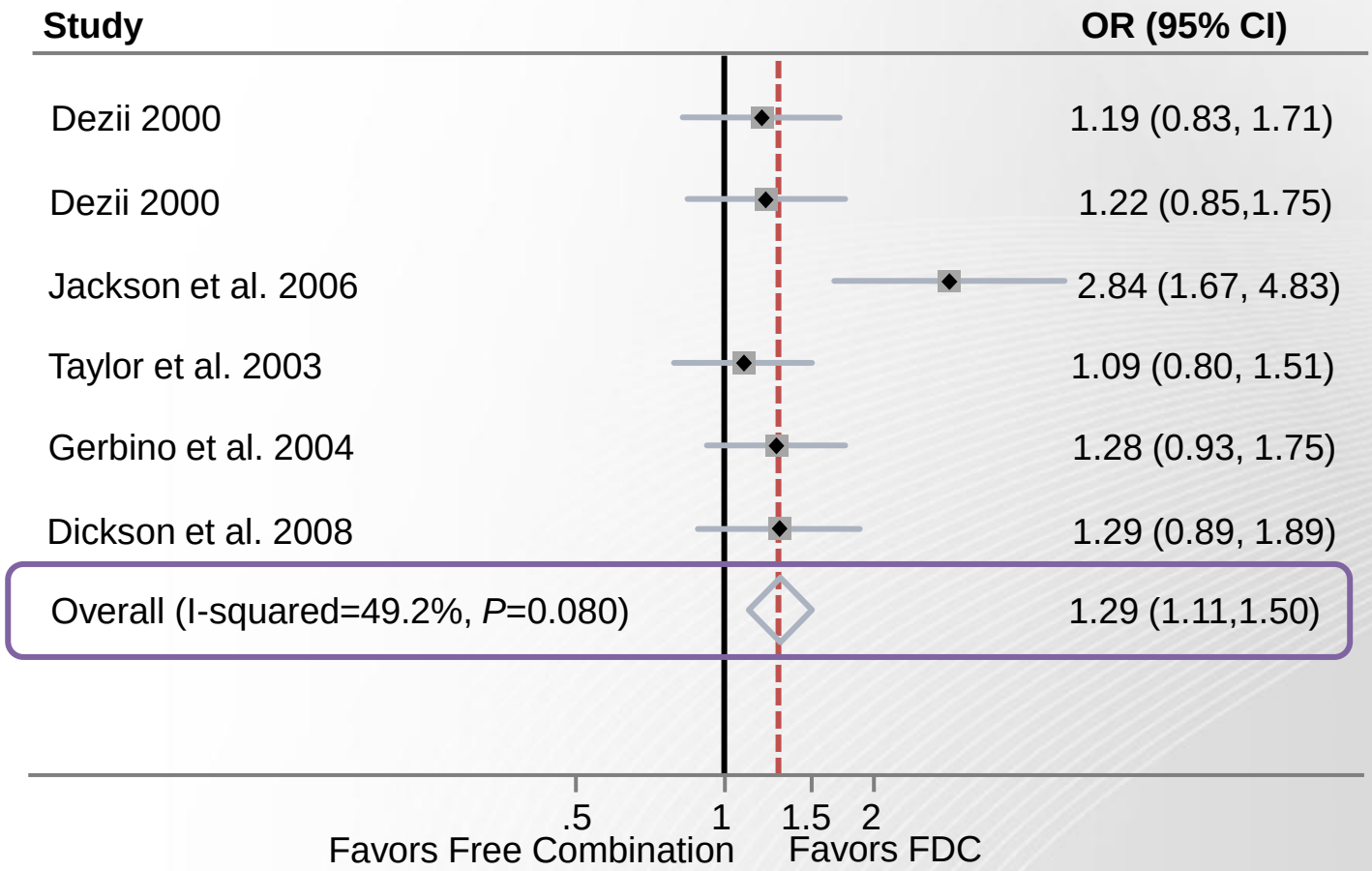
Test for heterogeneity: χ^2=14.34, df=18, P=0.71,I^2=0%

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).

Fixed-Dose Combinations Resulted in Increased Persistence and Compliance

Meta-analysis of 6 Studies N=30,295



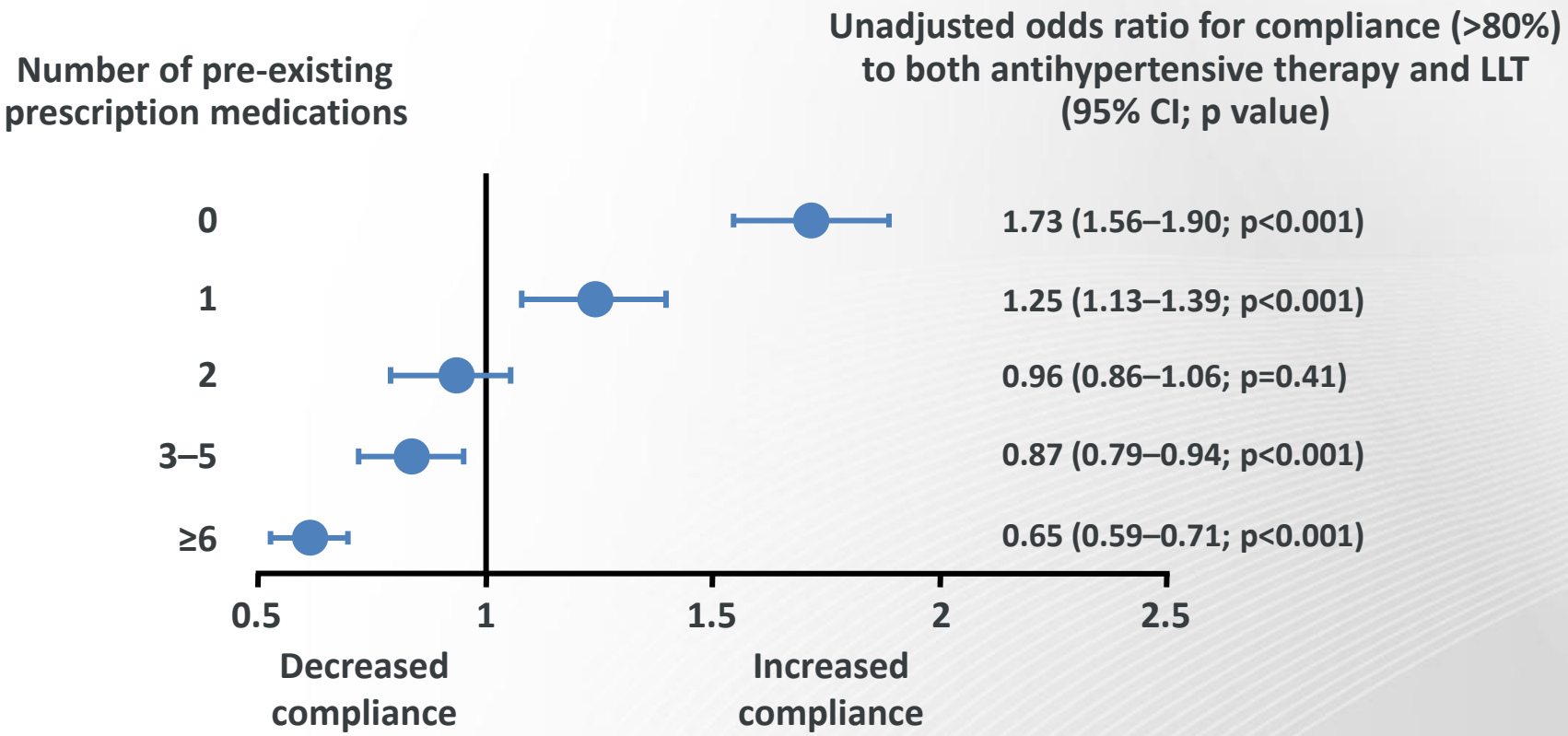
CI=confidence interval; FDC=fixed-dose combination; OR=odds ratio.

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

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

Compliance Decreases

as the Number of Medications Increases



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

Korean Hypertension Guideline

1-2기 고혈압
저~중 위험

2기 이상 고혈압
고위험

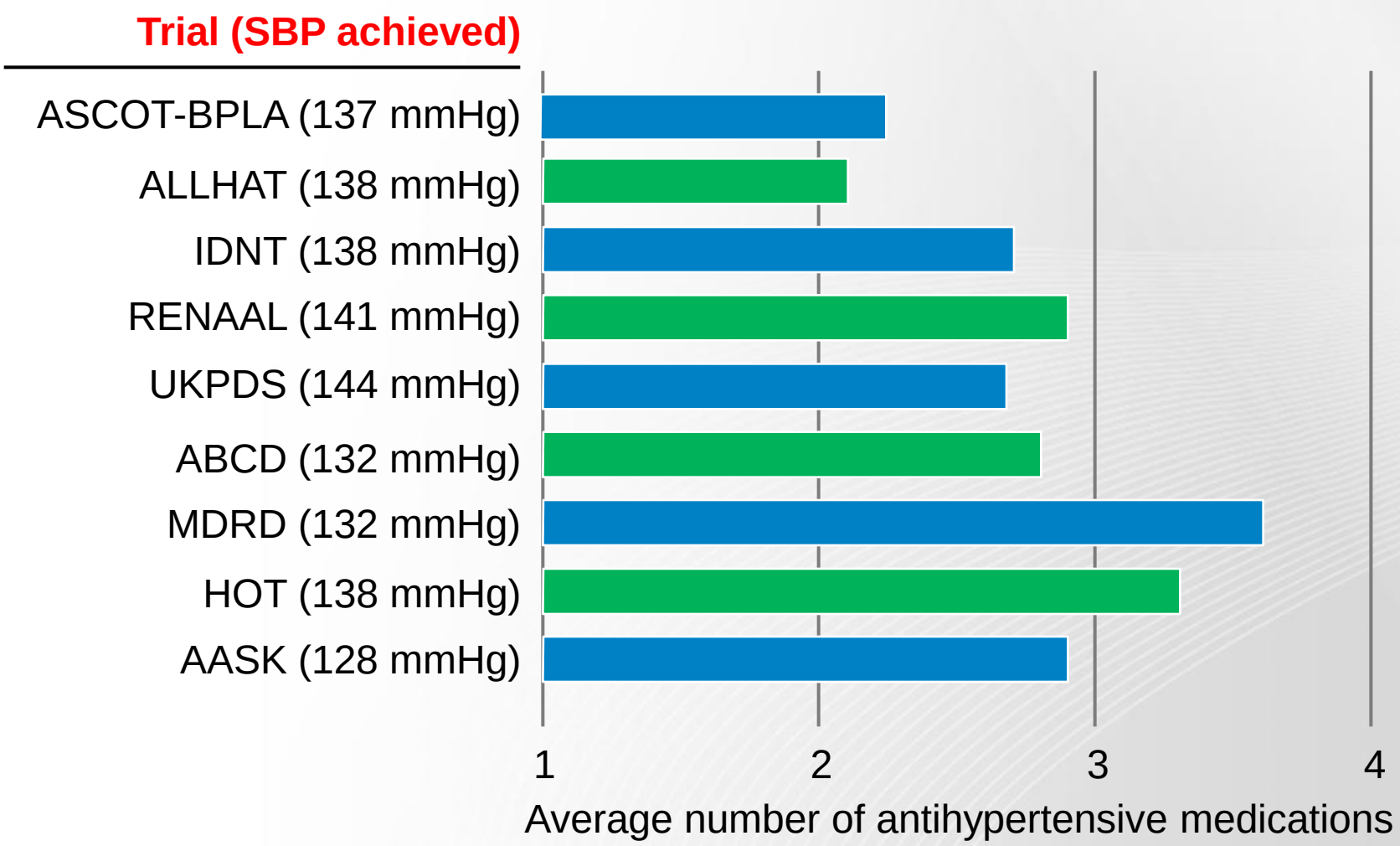
단일약

소량 두 가지
복합약

주의해야 한다[41]. 혈압이 160/100 mmHg 이상이거나 목표 혈압보다 20/10 mmHg 이상 높은 경우는 강압효과를 극대화하고 혈압을 빠르게 조절하기 위해 처음부터 고혈압약을 병용 투여할 수 있다[41]. 또한 고정용량복약제는 강압효과를 상승시키고 부작용을 줄이고, 환자의 약 순응도를 증가시켜, 심뇌혈관질환과 무증상장기손상을 방지하는 데 도움이 된다[41].

대한고혈압학회진료지침 2013

The Majority of Hypertensive Patients Need Combination Therapy to Achieve BP Goals



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

병합요법의 장점, 고정용량복합제

2013 유럽고혈압가이드라인

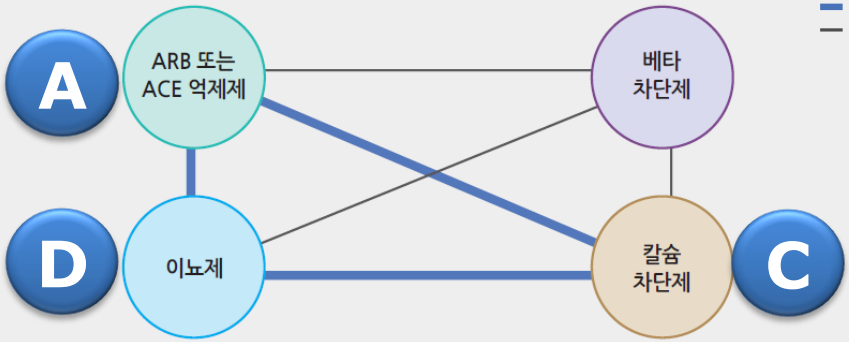
- 많은 환자에서 **빠른 혈압조절**이 가능 (고위험 환자에서 이득)
- **목표 혈압**에 더 잘 도달
- 잦은 혈압약 변경으로 인한 **순응도** 저하가 적다.
- 2가지 이상 혈압약을 한 알로 만든 **고정용량복합제**가 순응도를 개선시킨다.

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

Korea and Japan

2013 대한고혈압학회 고혈압 진료지침

권장되는 병용요법

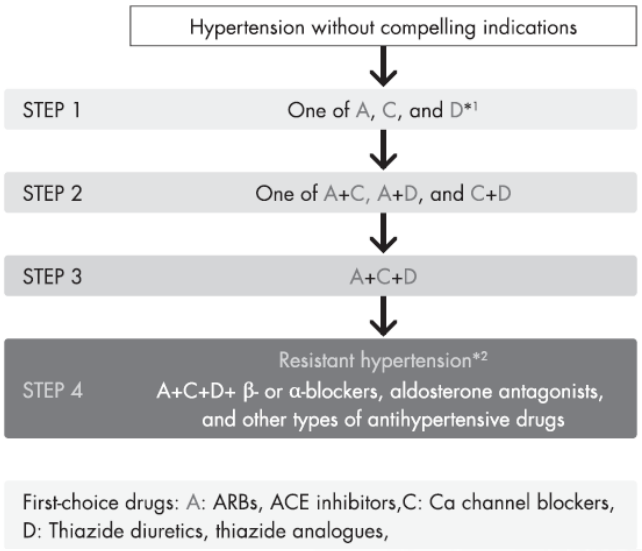


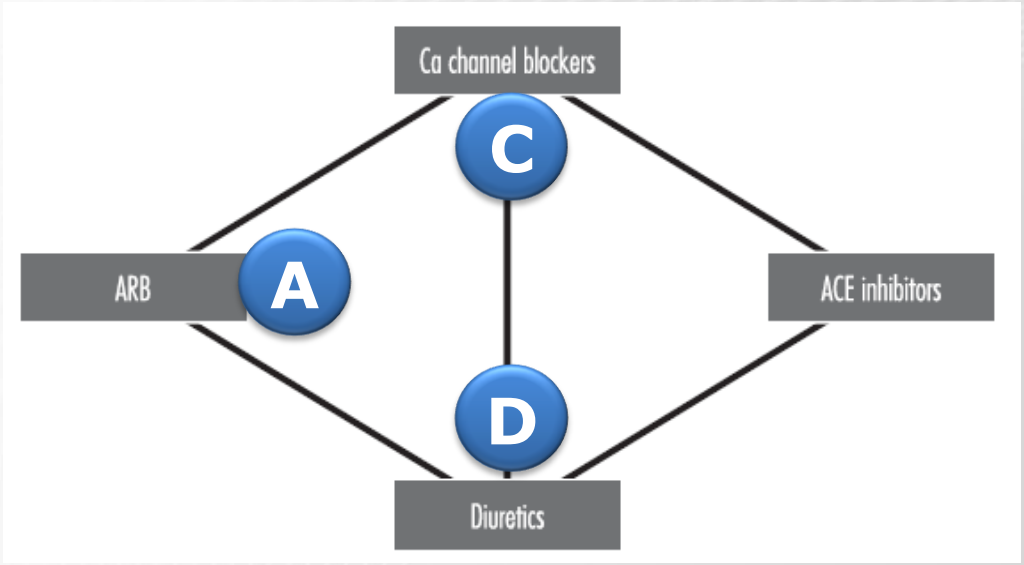
A + C *or* **A + D**

Then

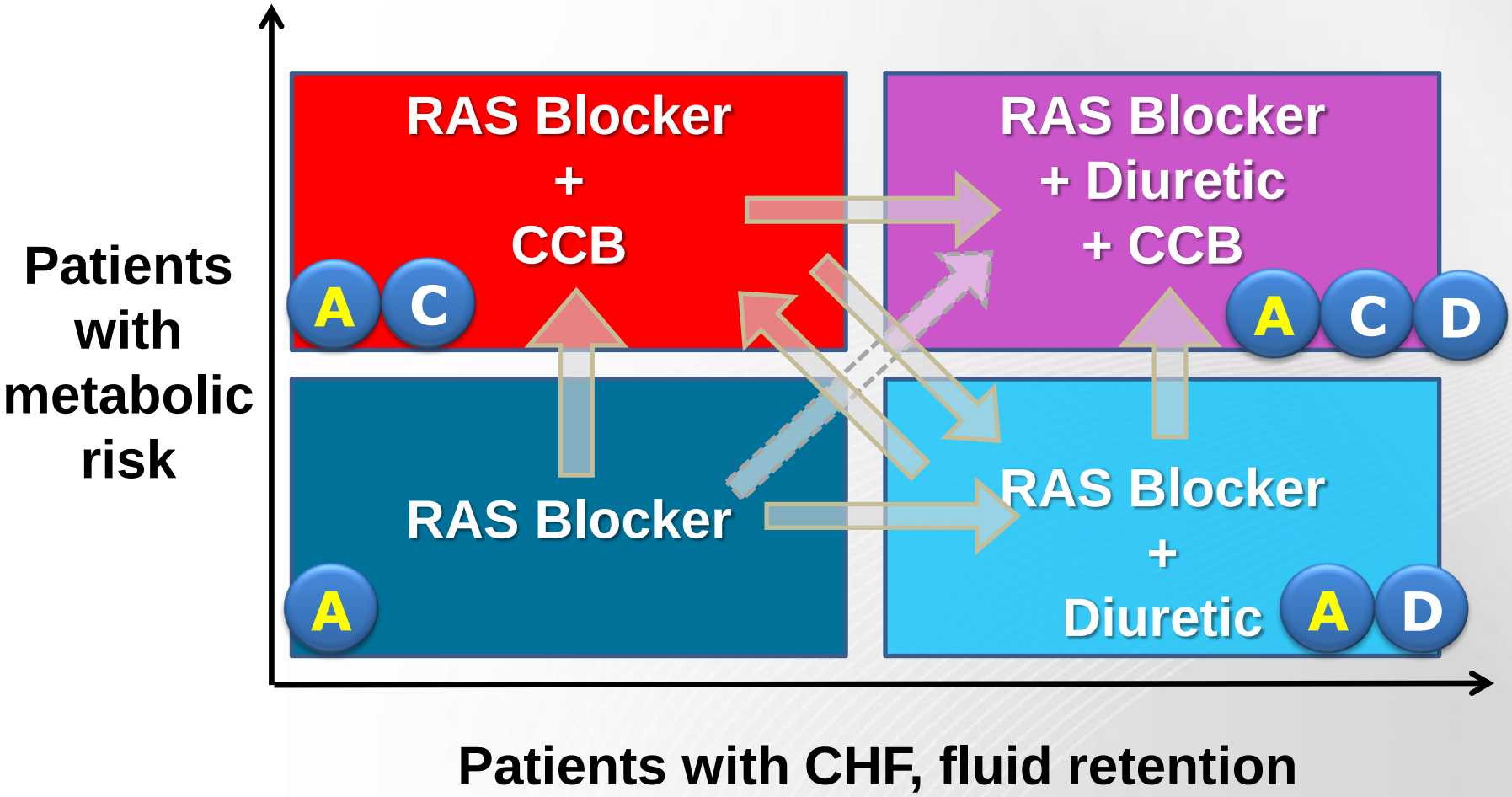
A + C + D

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

SEVIKAR Trial in Korean with Hypertension

ACE-HY study

Assured dual Combination Evaluation with korean HYpertensives

Clinical and Experimental HYPERTENSION

http://informahealthcare.com/ceh
ISSN: 1064-1963 (print), 1525-6006 (electronic)

Clin Exp Hypertens, Early Online: 1–8
 DOI: 10.3109/10641963.2015.1013119

informa healthcare

A multicenter, non-comparative study to evaluate the efficacy and safety of fixed-dose olmesartan/amlodipine in Korean patients with hypertension who are naïve or non-responders to anti-hypertensive monotherapy (ACE-HY study)

Hee-Won Jung[1]*, Kwang-il Kim[1]*, Chang Gyu Park[2], Duk-Hyun Kang[3], Youngkeun Ahn[4], Jang Ho Bae[5], and Cheol-Ho Kim[1]

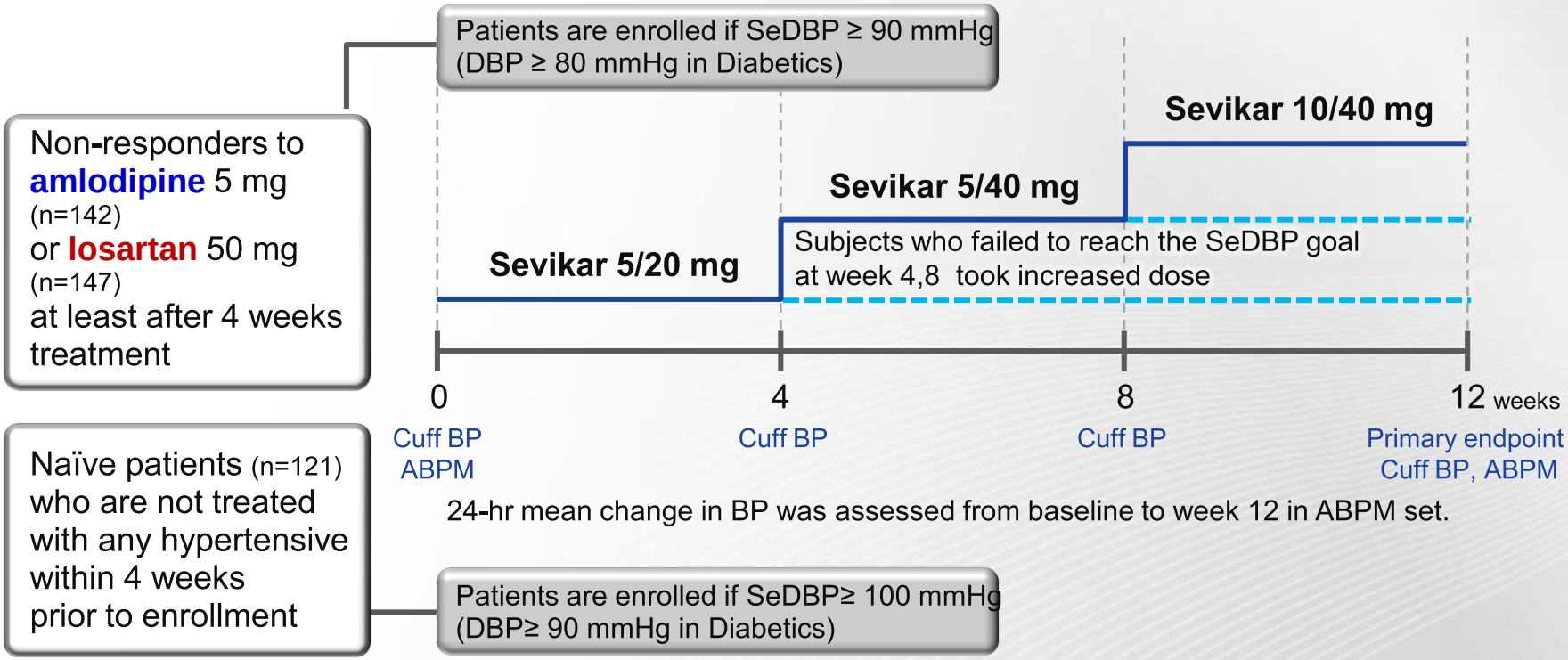
Clin Exp Hypertens. 2015;37(6):482-9

ACE-HY study

- **Multi-center, non-comparative clinical study during 12 weeks**
- **Period**
  - 04 Apr 2010 - 04 Feb 2012
- **Medication**
  - Sevikar® Tablet 5/20 mg, 5/40 mg, 10/40 mg
    Fixed-dose combination of **amlodipine** besylate and **olmesartan** medoxomil
- **Study center**
  - Total of 21 sites
- **Objectives**
  - To evaluate the efficacy of Sevikar® in treatment of Korean hypertensive subjects who were naïve or not controlled to anti-hypertensive monotherapy (amlodipine or losartan)

Clin Exp Hypertens. 2015;37(6):482-9

Study design



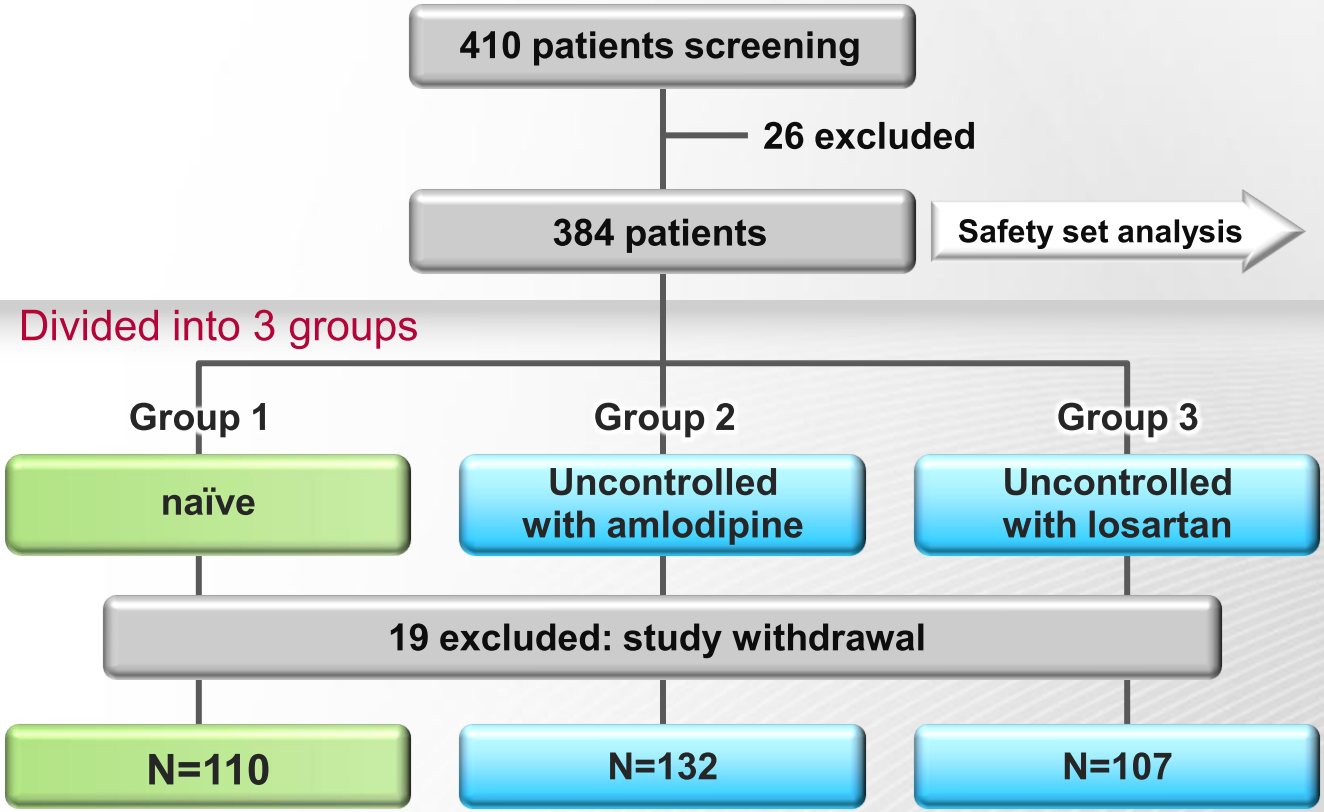
24-hr mean change in BP was assessed from baseline to week 12 in ABPM set.

Patients were up-titrated with SeDBP≥ 90 mmHg (DBP ≥ 80 mmHg in diabetics).
If target BP is achieved, the patient stays in the same dose.

SeDBP: seated diastolic blood pressure
ABPM: ambulatory blood pressure monitoring

Clin Exp Hypertens. 2015;37(6):482-9

Subject status: 376 patients analyzed



[**ITT analysis: total 376**]

ITT: intent-to-treat

Clin Exp Hypertens. 2015;37(6):482-9

Baseline characteristics (ITT group)

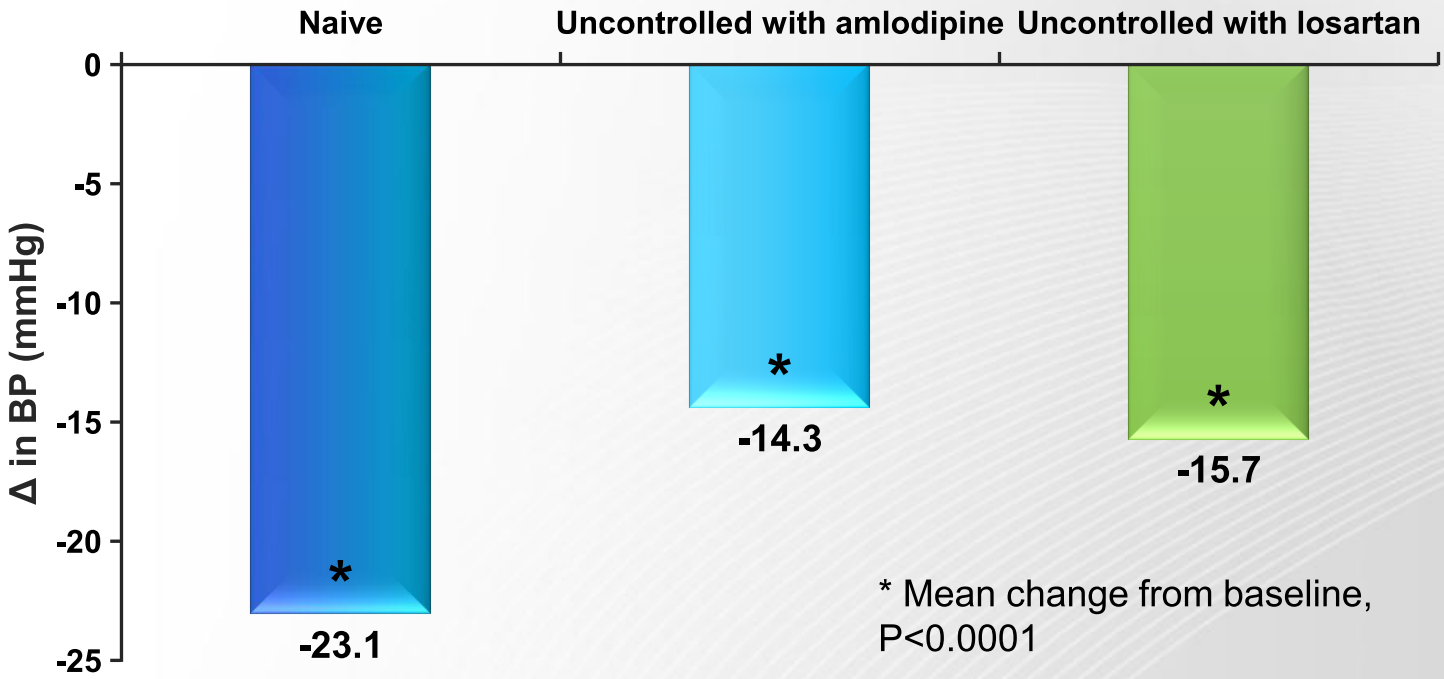
	Naïve (n=134)	Non-responders to amlodipine (n=132)	Non-responders to losartan (n=110)	Total (N=376)
Male, n (%)	75 (68.18)	76 (57.58)	73 (54.48)	**224 (59.57)**
Age (Mean±SD)	48.04 ± 10.14	55.23 ± 11.28	53.23 ± 12.28	**52.41 ± 11.68**
BMI (kg/m^2)	25.31 ± 3.29	25.38 ± 3.16	25.22 ± 3.15	**25.30 ± 3.19**
Seated systolic BP (mmHg) (Mean±SD)	154.61 ± 11.91	143.12 ± 11.50	143.10 ± 10.27	**146.47 ± 12.34**
Seated diastolic BP (mmHg) (Mean±SD)	103.27 ± 2.9	94.63 ± 5.14	94.60 ± 4.82	**97.15 ± 5.97**
Duration of hypertension (Months) (Mean±SD)	21.1 ± 36.47	52.05 ± 56.97	41.93 ± 54.30	**39.43 ± 52.21**
Family history of Hypertension, n (%)	55 (50.0)	73 (55.3)	68 (50.75)	**196 (52.13)**
Current smoker, n (%)	32 (29.09)	22 (16.67)	25 (18.66)	**79 (21.01)**
Abnormal in electro-cardiogram, n (%)	66 (60.00)	72 (54.55)	59 (43.28)	**196 (52.13)**

Clin Exp Hypertens. 2015;37(6):482-9

DBP reduction after 12 weeks administration

› Primary Endpoint

- Change of seDBP after 12 weeks

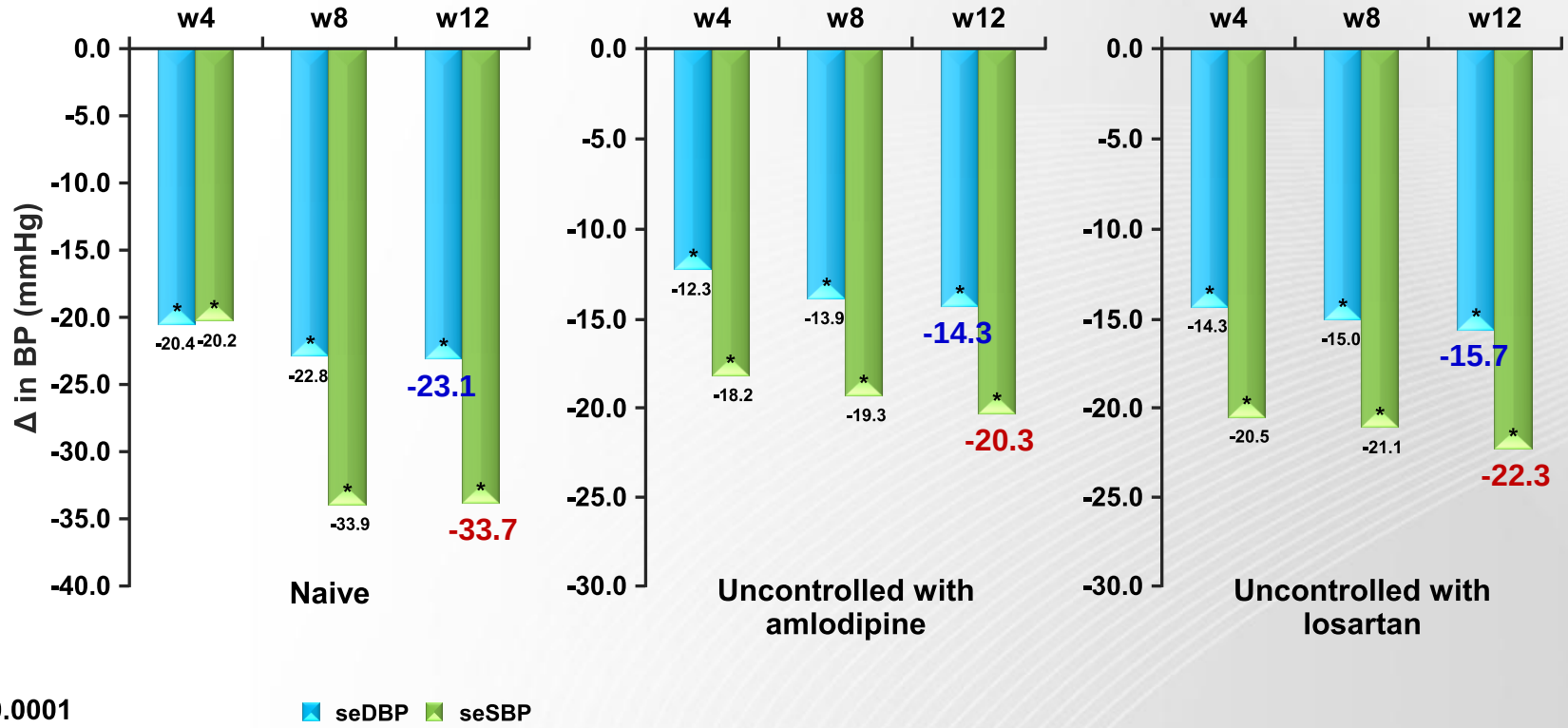


Clin Exp Hypertens. 2015;37(6):482-9

Reduction in SBP as well as DBP

Secondary Endpoint

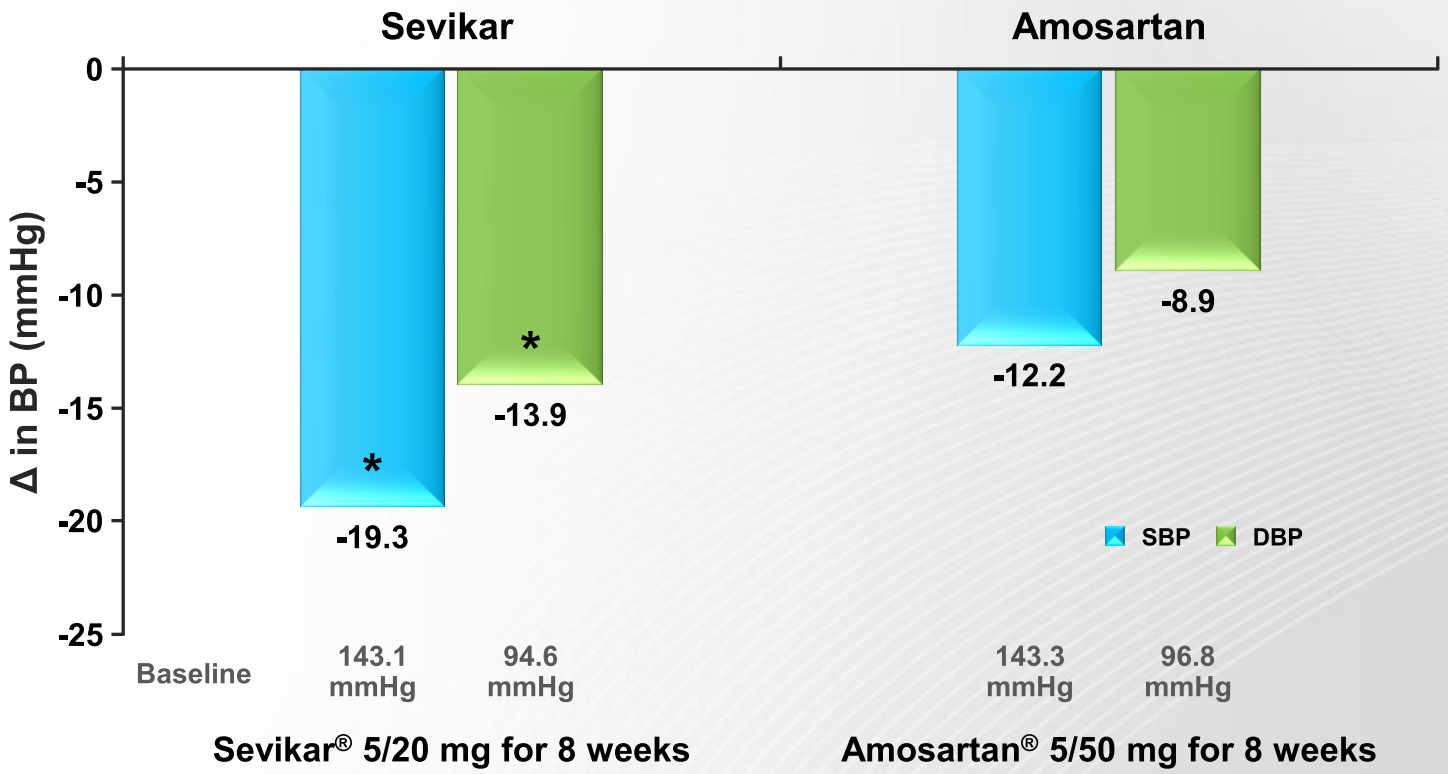
- Change of BP at week 4, 8 and 12



Clin Exp Hypertens. 2015;37(6):482-9

Sevikar®: Superior efficacy in amlodipine-uncontrolled patients- compared with Amosartan®

- **BP change in non-responders to amlodipine 5 mg monotherapy**
  - Comparison of 2 clinical trials (not head-to-head study)



*P<0.0001

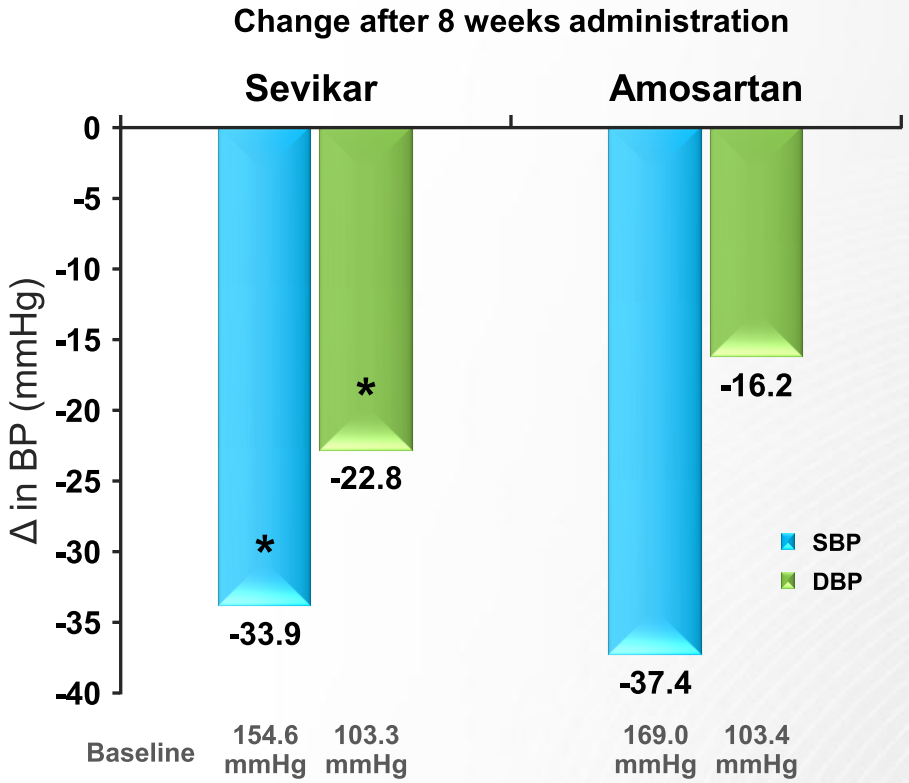
Data of amlodipine from 8-week, multicenter, randomized, double-blind phase III non-inferiority study

Kang S, *et al. Clinical Therapeutics*.2011;33(1):1953-1963.

Sevikar®: Effective as initial treatment for stage 2 hypertension- compared with Amosartan®

› Comparison of BP control in naïve patients

- Comparison of 2 clinical trials (not head-to-head study)



	Sevikar® Group	Amosartan® Group
Study Duration	12 weeks	8 weeks
Study Design	Sevikar® Tablet 5/20 mg 5/40 mg 10/40 mg *dose titration at week 4, week 8	Amosartan® Tablet 5/50 mg 10/50 mg ***dose titration at week 2, week 4** ***hydrochlorothiazide 12.5 mg added at week 4, optionally**

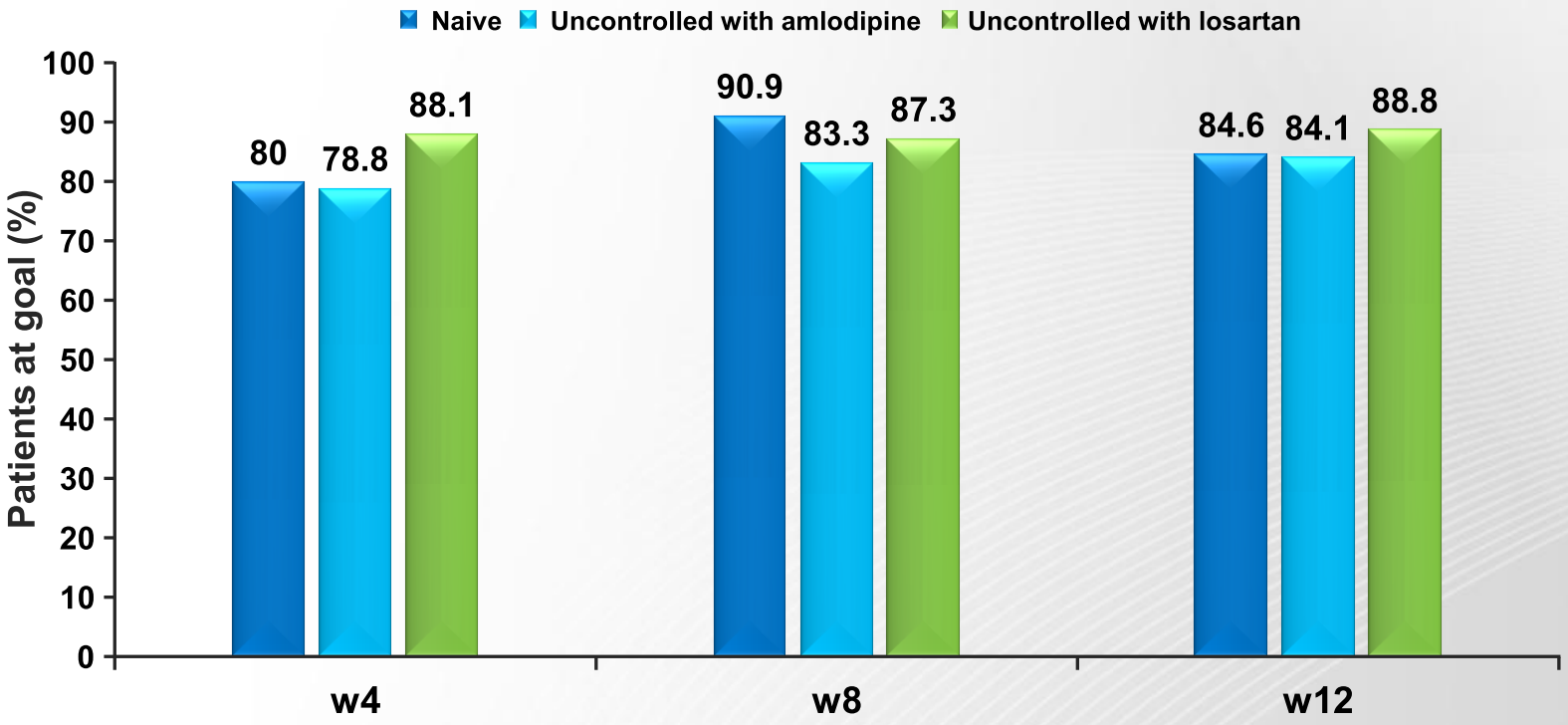
***P<0.0001**

Data of amlodipine from
Efficacy of fixed-dose amlodipine and losartan combination compared with amlodipine monotherapy in stage 2 hypertension:a randomized, double blind, multicenter study

Kim S, *et al. BMC Research Notes*. 2011.4:461

Success in achieving the BP goal over 80% at any time, any patients

› % of patients achieving target BP control rate at week 4, 8, and 12

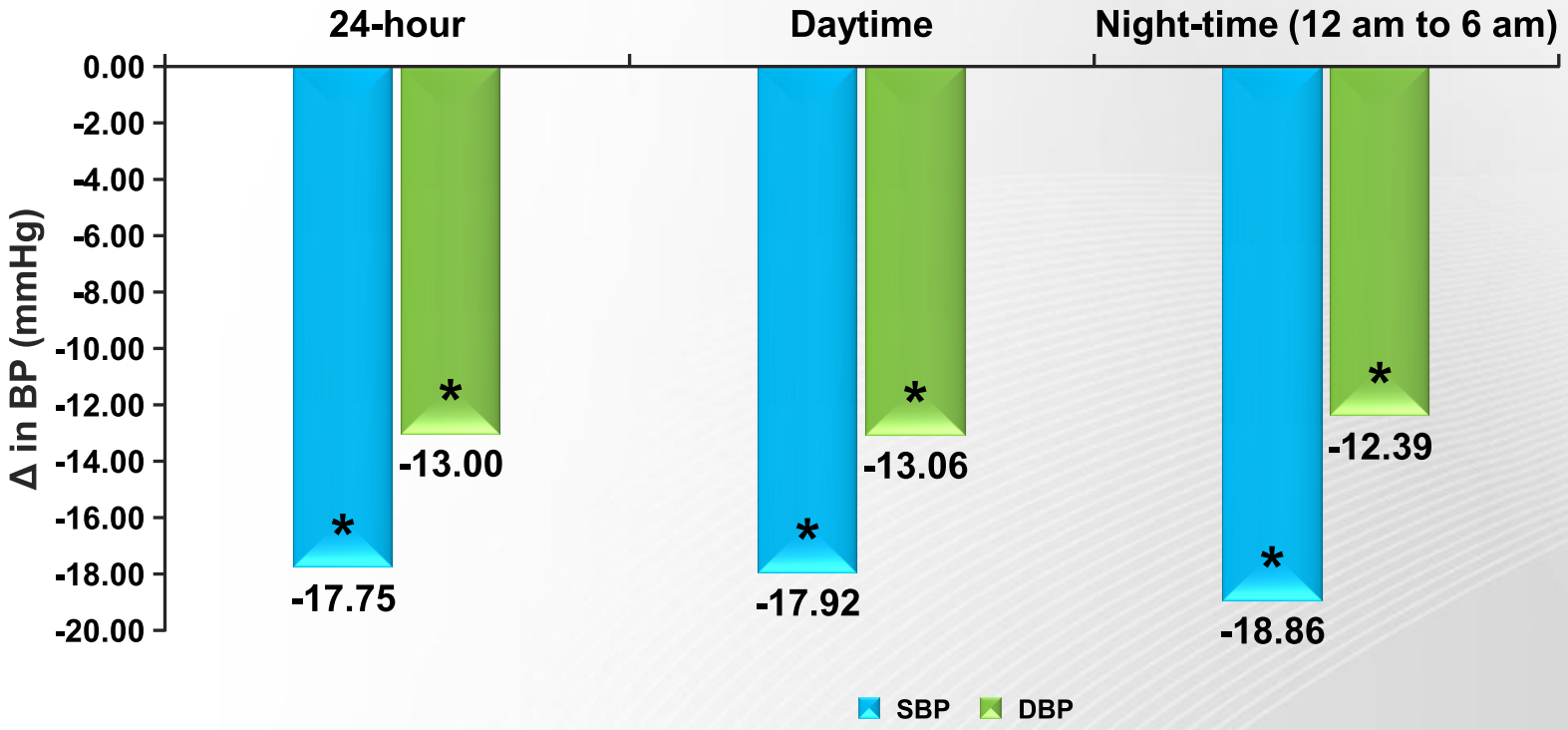


Target BP: SeDBP< 90mmHg and SeSBP< 140mmHg
SeDBP< 80mmHg and SeSBP< 130mmHg for patients with diabetes

Clin Exp Hypertens. 2015;37(6):482-9

24-hour successful BP control at any time

- Hourly mean change in SBP/DBP by ABPM at week 12 (N=36)



*P<0.0001

Clin Exp Hypertens. 2015;37(6):482-9

Safety profile (1)

Summary of adverse events (safety set)

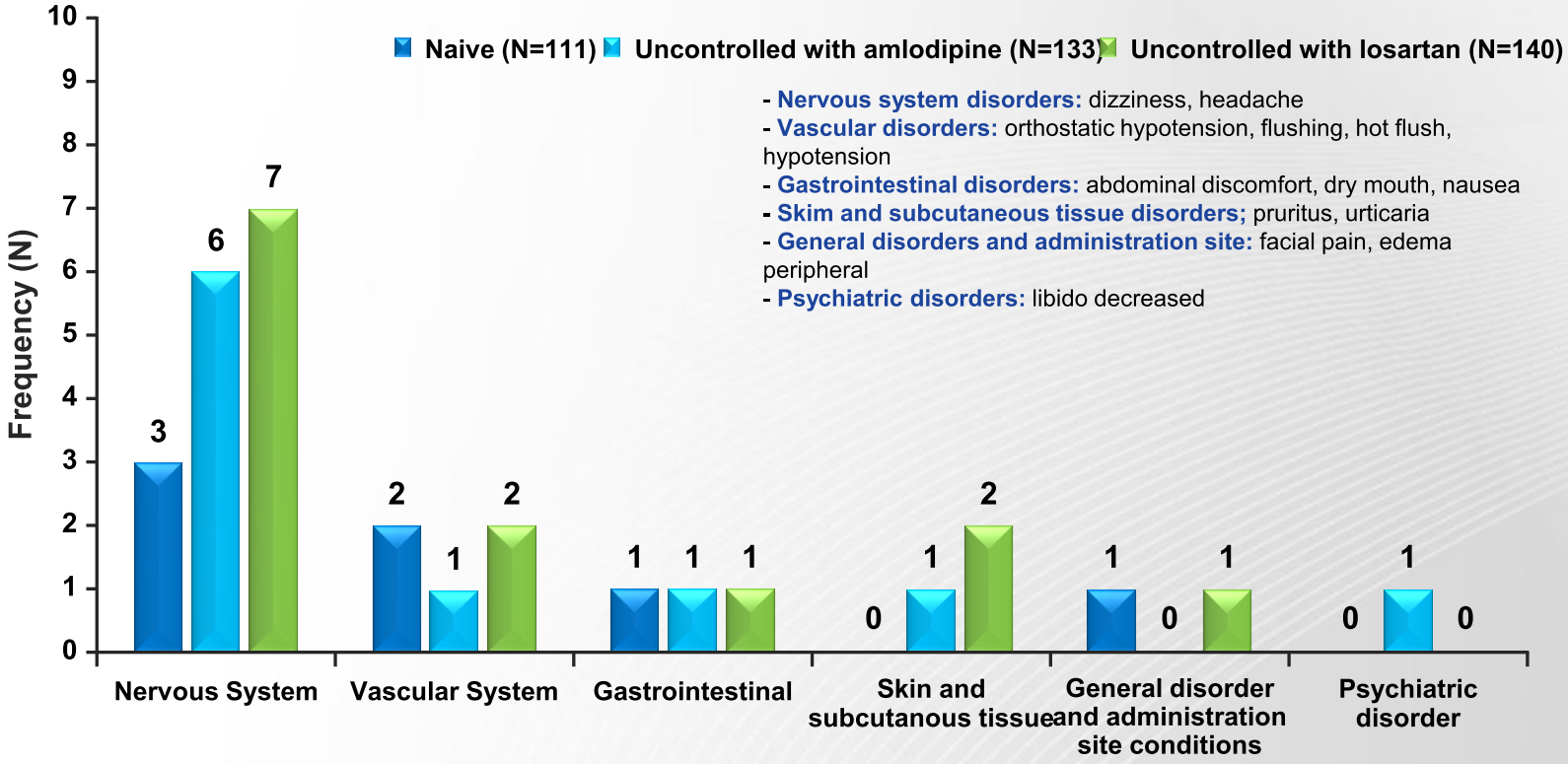
Adverse events	Naive		Uncontrolled with amlodipine		Uncontrolled with losartan		Total	
	N=111		N=133		N=140		N=384	
	n(%)	[event]	n(%)	[event]	n(%)	[event]	n(%)	[event]
Treatment-Emergent Adverse Event (TEAE)	31(27.93)	[52]	31(23.31)	[54]	46(32.86)	[63]	**108(28.13)**	[169]
Adverse Drug Reaction (ADR)	6(5.41)	[7]	8(6.02)	[10]	12(8.57)	[15]	**26(6.77)**	[32]
Serious Adverse Event (SAE)	0(0.00)	[0]	1(0.75)	[1]	1(0.71)	[2]	**2(0.52)**	[3]

- There was no AE with moderate maximum intensity in Group 1 and 2.
- One case of AE with moderate maximum intensity occurred in Group 3. However, there was no causal relationship between study medications.

Clin Exp Hypertens. 2015;37(6):482-9

Safety profile (2)

The frequency and proportion of subjects with ADRs by system organ class
(Safety set, N=384)



Adverse events based upon the SOC classification

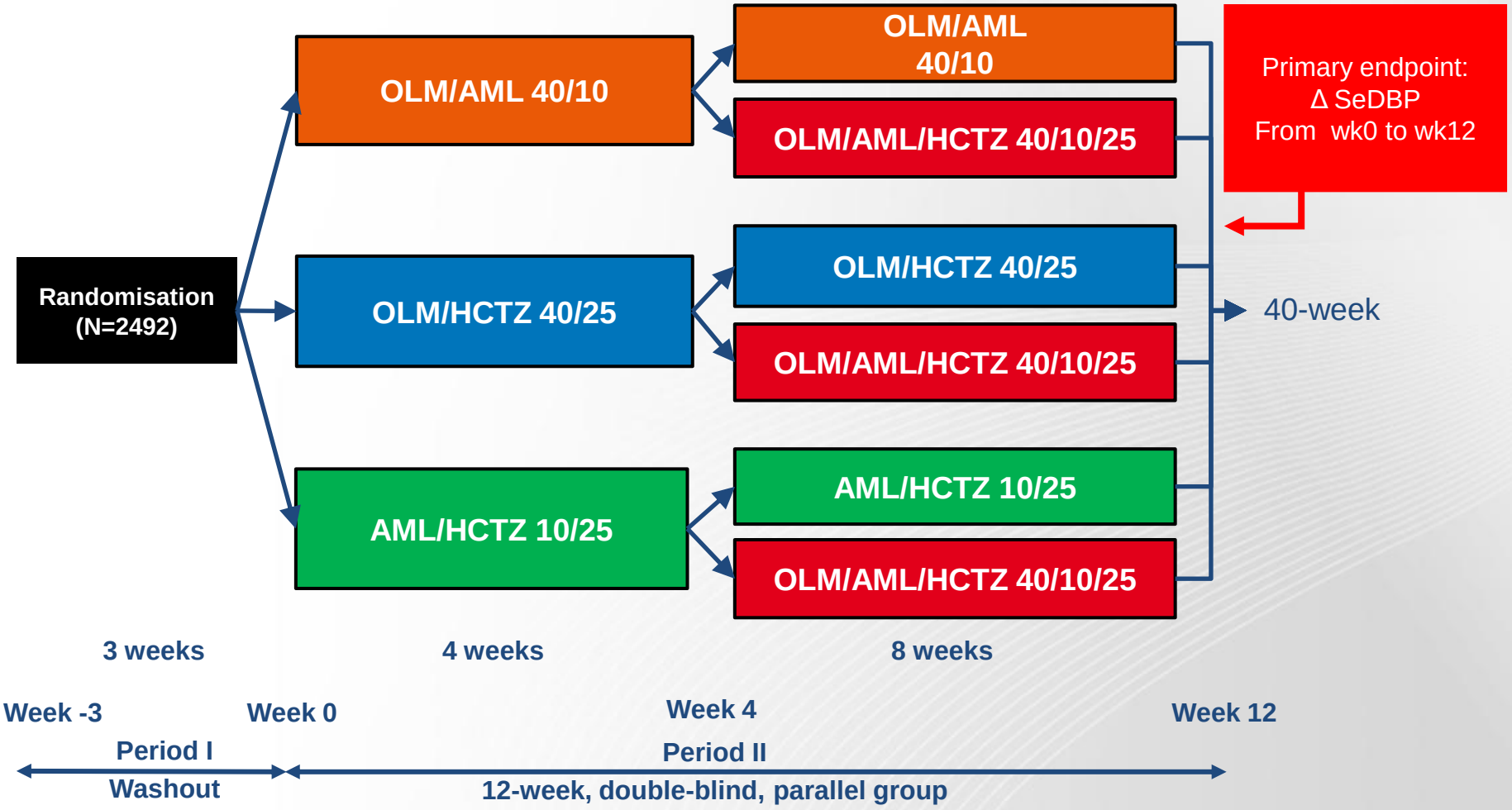
Clin Exp Hypertens. 2015;37(6):482-9

Conclusion

- **ACE-HY study demonstrated Sevikar®s strong BP lowering effect in Korea.**
- **Sevikar® achieved BP goal rates more than 80% at all periods in all group.**
- **Sevikar® provided effective BP control across the entire 24-hour dosing period.**
- **Sevikar® exhibited favorable safety profile.**

Clin Exp Hypertens. 2015;37(6):482-9

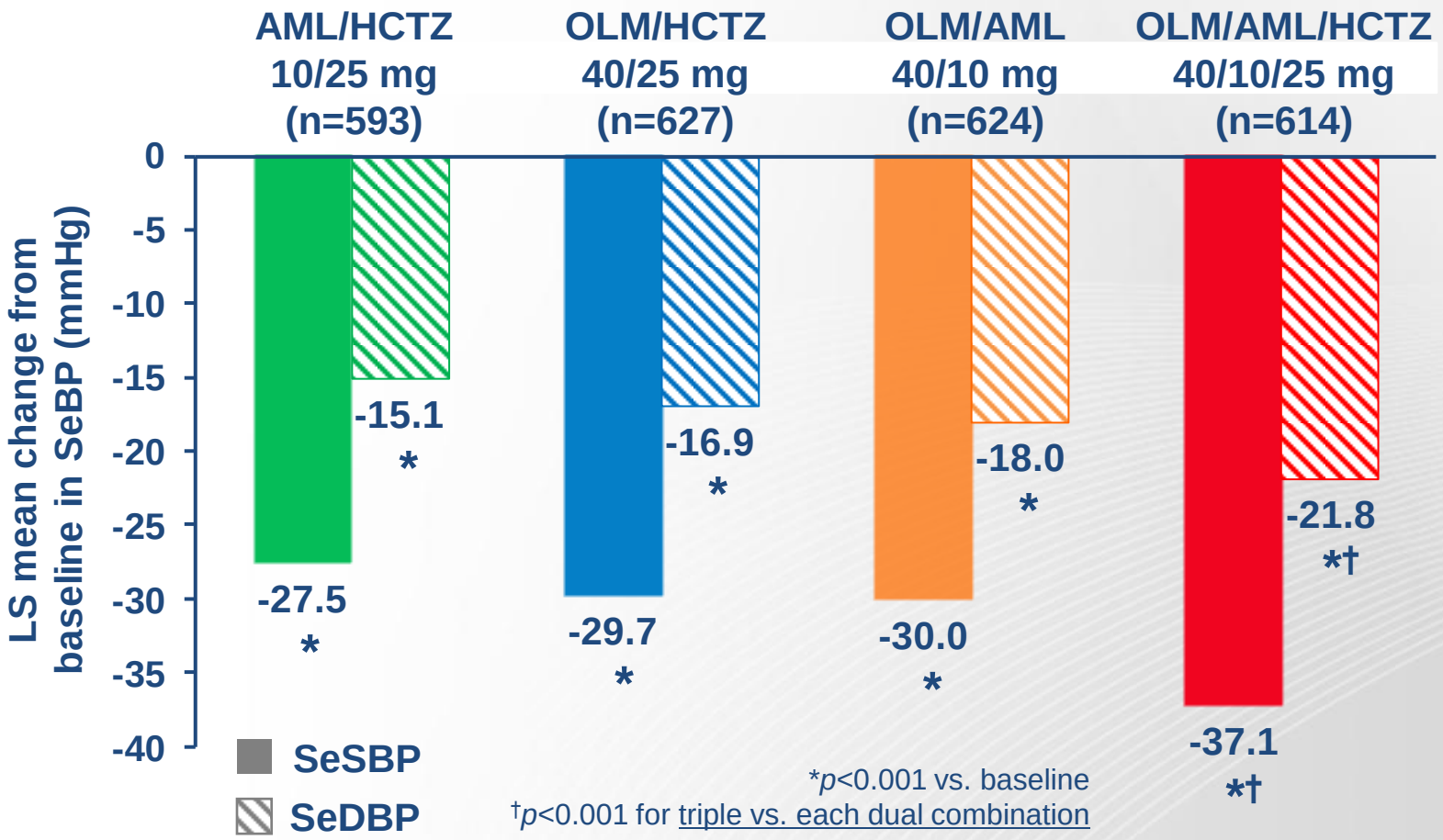
Triple Therapy with High Dose Olmesartan/AML /HCTZ in the TRINITY Study



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

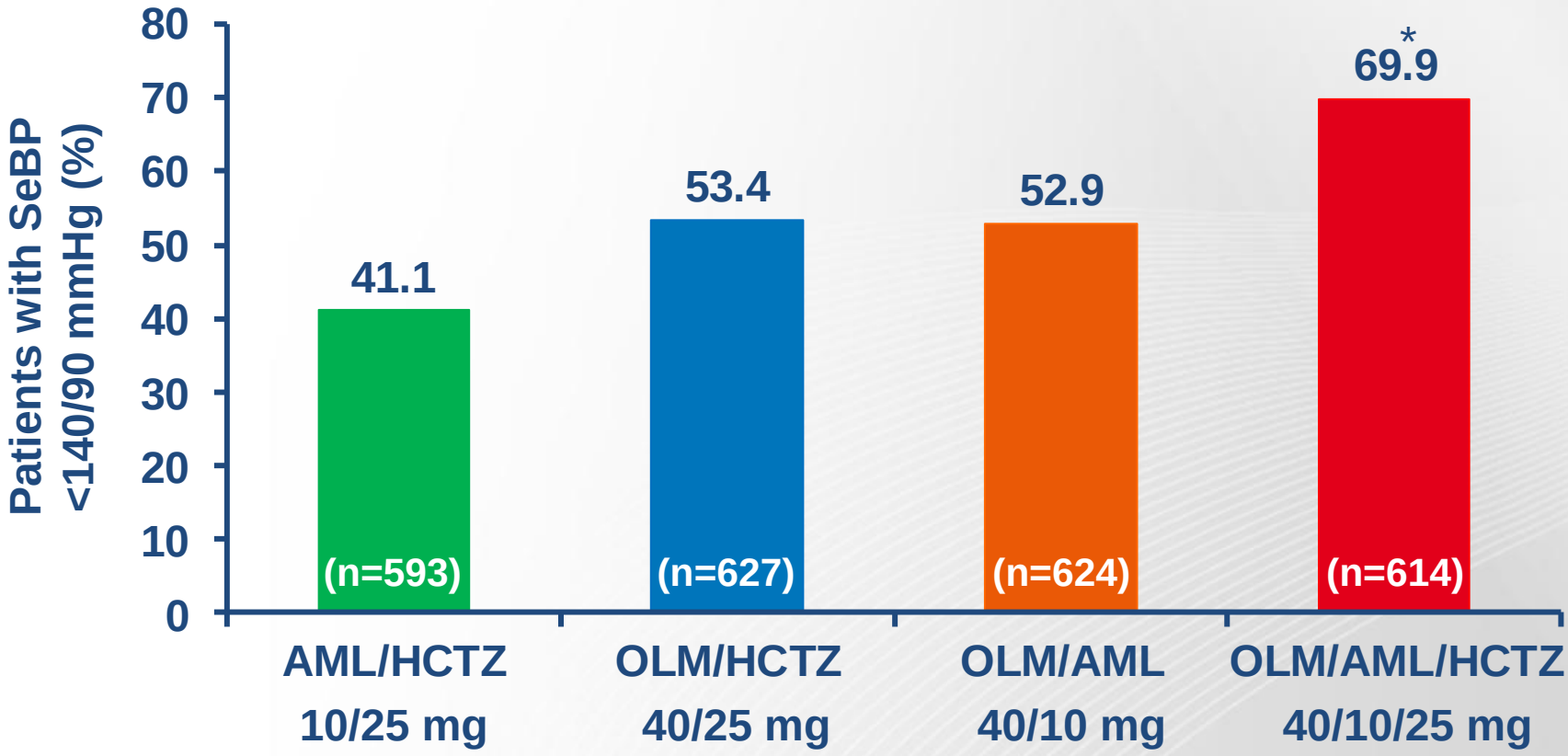
High Dose OLM/AML/HCTZ Triple Combination Therapy is Superior to Dual Combination at Lowering BP



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

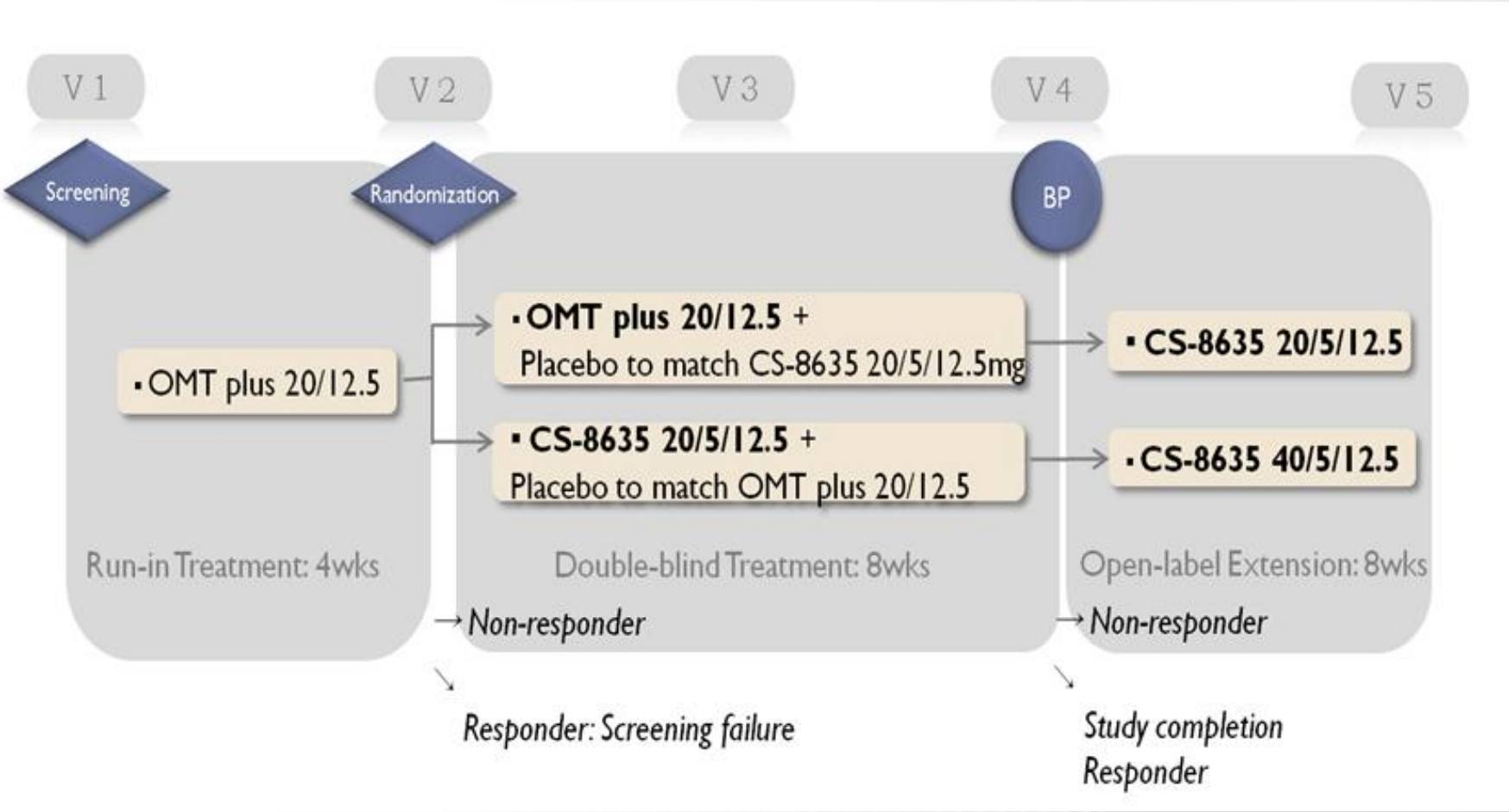
Efficacy and Safety Study of Olmesartan Medoxomil, Amlodipine, and Hydrochlorothiazide Combination Therapy in Patients with Hypertension Not Controlled with Olmesartan Medoxomil and Hydrochlorothiazide Combination Therapy: Results of a Randomized, Double-Blind, Multicenter Trial

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

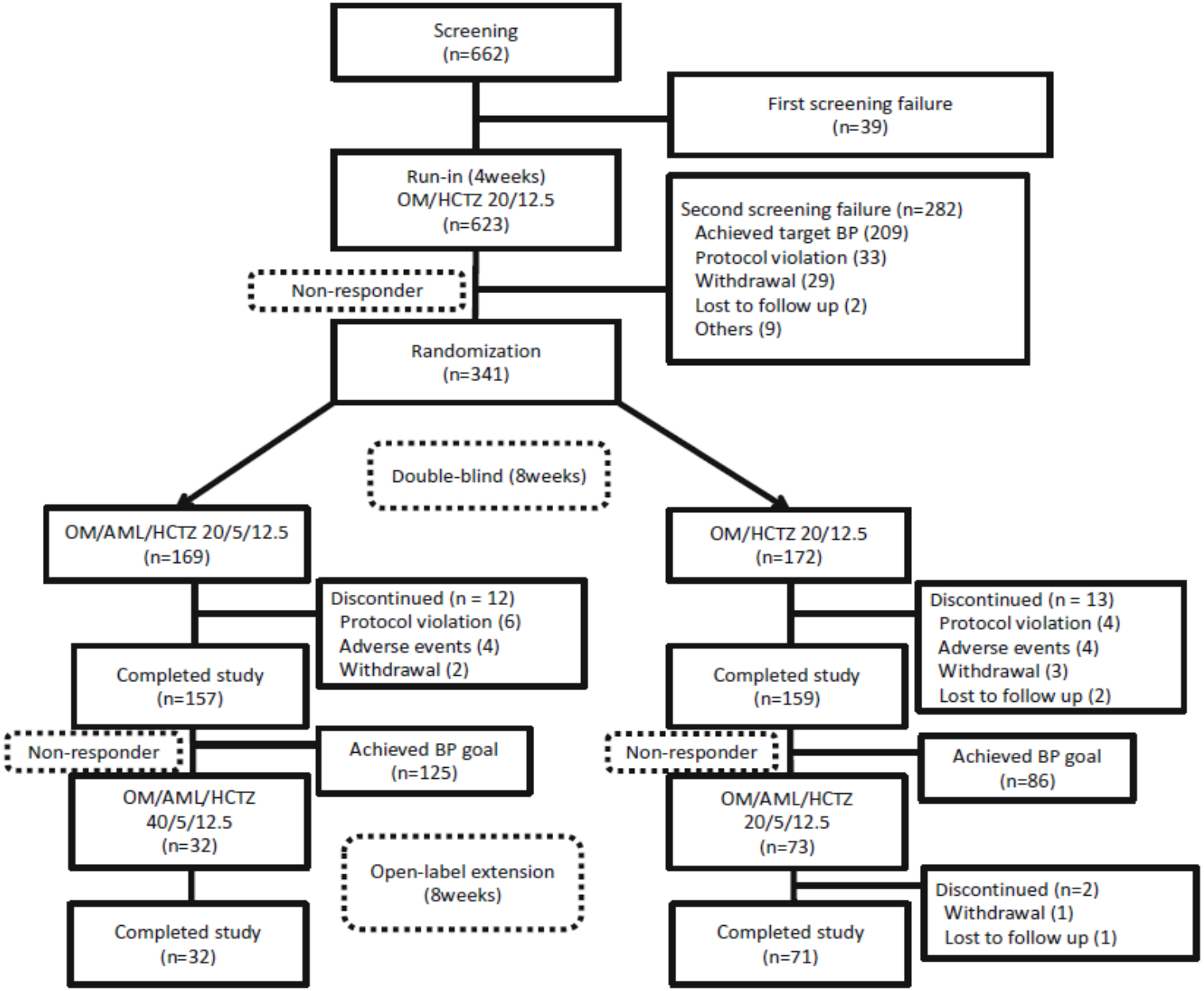
국내(아시안)에서 현실적인 저용량 FDC의 효과



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



OM : olmesartan medoxomil

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

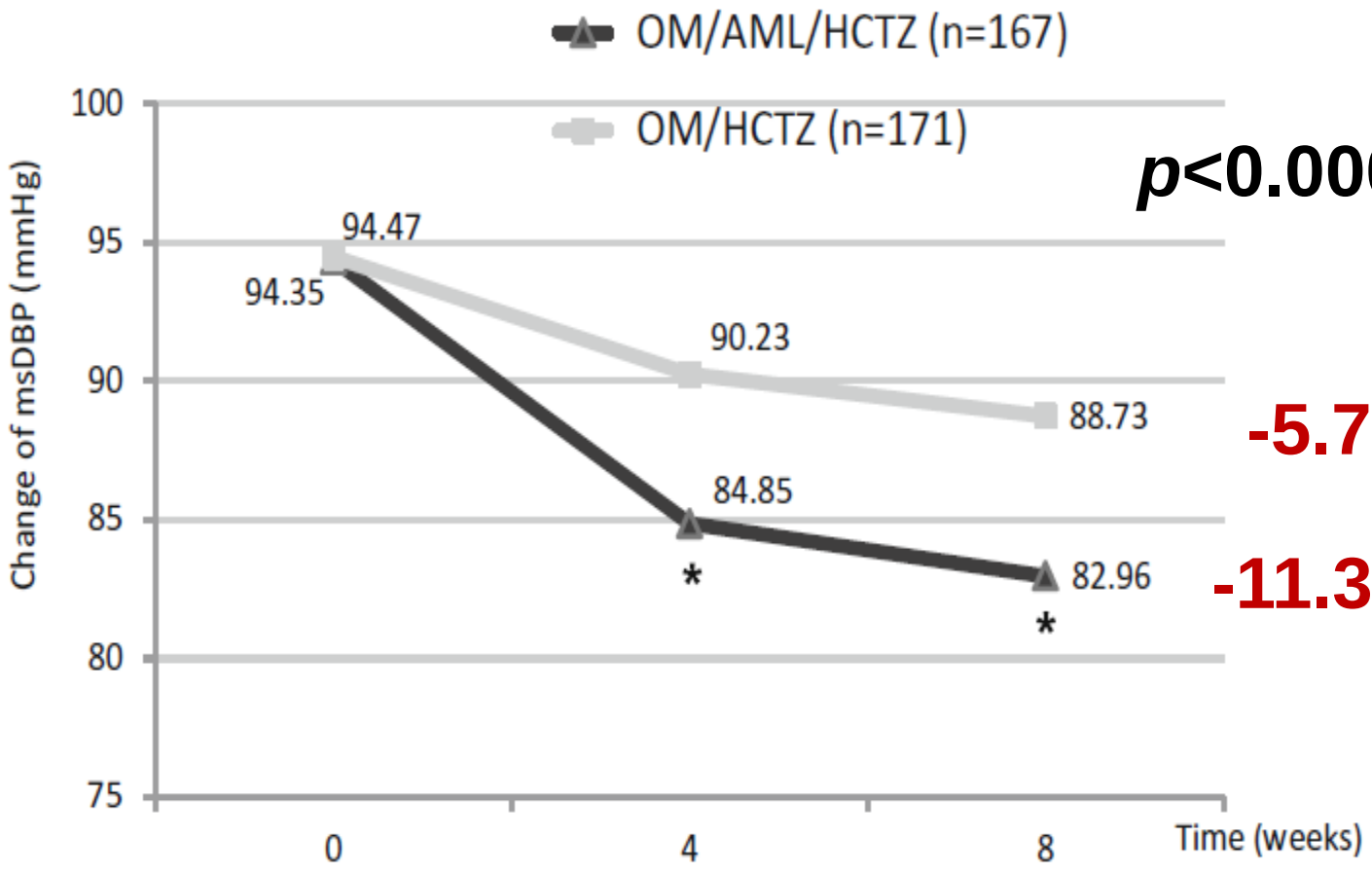
Baseline characteristics

Characteristics	OM/AML/HCTZ 20/5/12.5 (n = 167)	OM/HCTZ 20/12.5 (n = 171)	All patients (n = 338)
Age, years	56.1 ± 10.1	56.4 ± 10.7	56.3 ± 10.4
Female	52 (31.1)	51 (29.8)	103 (30.5)
Weight, kg	73.6 ± 12.3	73.8 ± 11.4	73.7 ± 11.8
Height, cm	166.3 ± 8.3	165.6 ± 8.1	165.9 ± 8.2
BMI, kg/m^2	26.5 ± 3.3	26.8 ± 3.3	26.7 ± 3.3
msDBP, mmHg	94.4 ± 6.2	94.5 ± 6.1	94.4 ± 6.1
msSBP, mmHg	145.3 ± 8.7	147.7 ± 11.0	146.5 ± 10.0
Heart rate, rate/minute	73.8 ± 9.6	74.0 ± 9.5	73.2 ± 9.5
Smoking history			
Current	35 (21.0)	32 (18.7)	67 (19.8)
Past	36 (21.6)	42 (24.6)	78 (23.1)
Never	96 (57.5)	97 (56.7)	193 (57.1)
Alcohol intake			
Current	97 (58.1)	87 (50.9)	184 (54.4)
Past	10 (6.0)	10 (5.8)	20 (5.9)
None	60 (35.9)	74 (43.3)	134 (39.6)
Duration of hypertension, years	8.2 ± 7.2	9.4 ± 8.6	8.8 ± 8.0
Family history of hypertension	81 (48.5)	80 (46.8)	161 (47.6)
History of antihypertensive drugs	128 (76.6)	125 (73.1)	253 (74.9)
Monotherapy	25 (19.5)	23 (18.4)	48 (19.0)
Double combination	57 (44.5)	65 (52.0)	122 (48.2)
Triple combination	46 (35.9)	37 (29.6)	83 (32.8)
Diabetes mellitus	33 (19.8)	33 (19.3)	66 (19.5)
Chronic kidney disease	3 (1.8)	8 (4.7)	11 (3.3)

Data are presented as mean ± SD or n (%), SD standard deviation

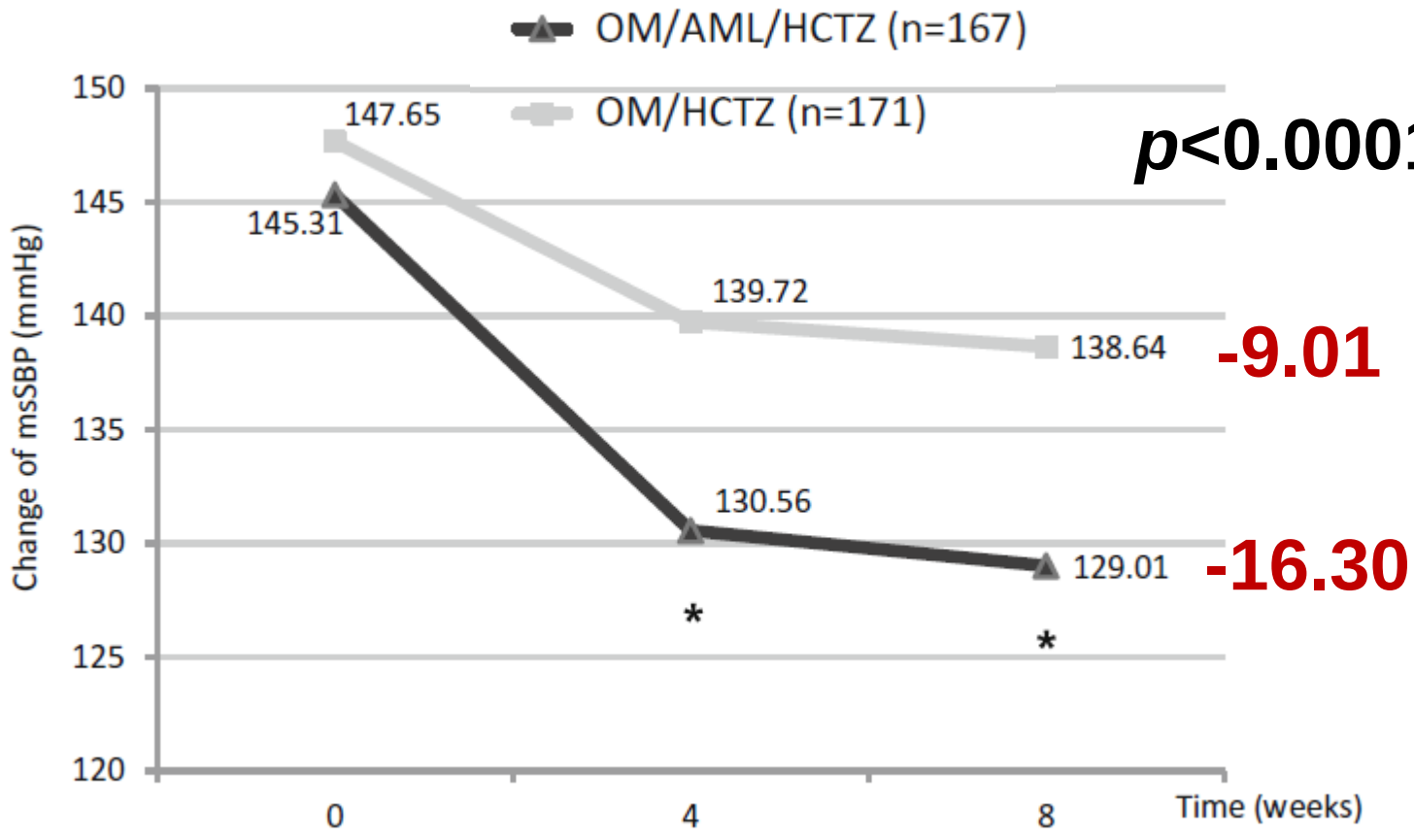
Am J Cardiovasc Drugs. 2016;16:129-38

8주 동안 msDBP의 변화



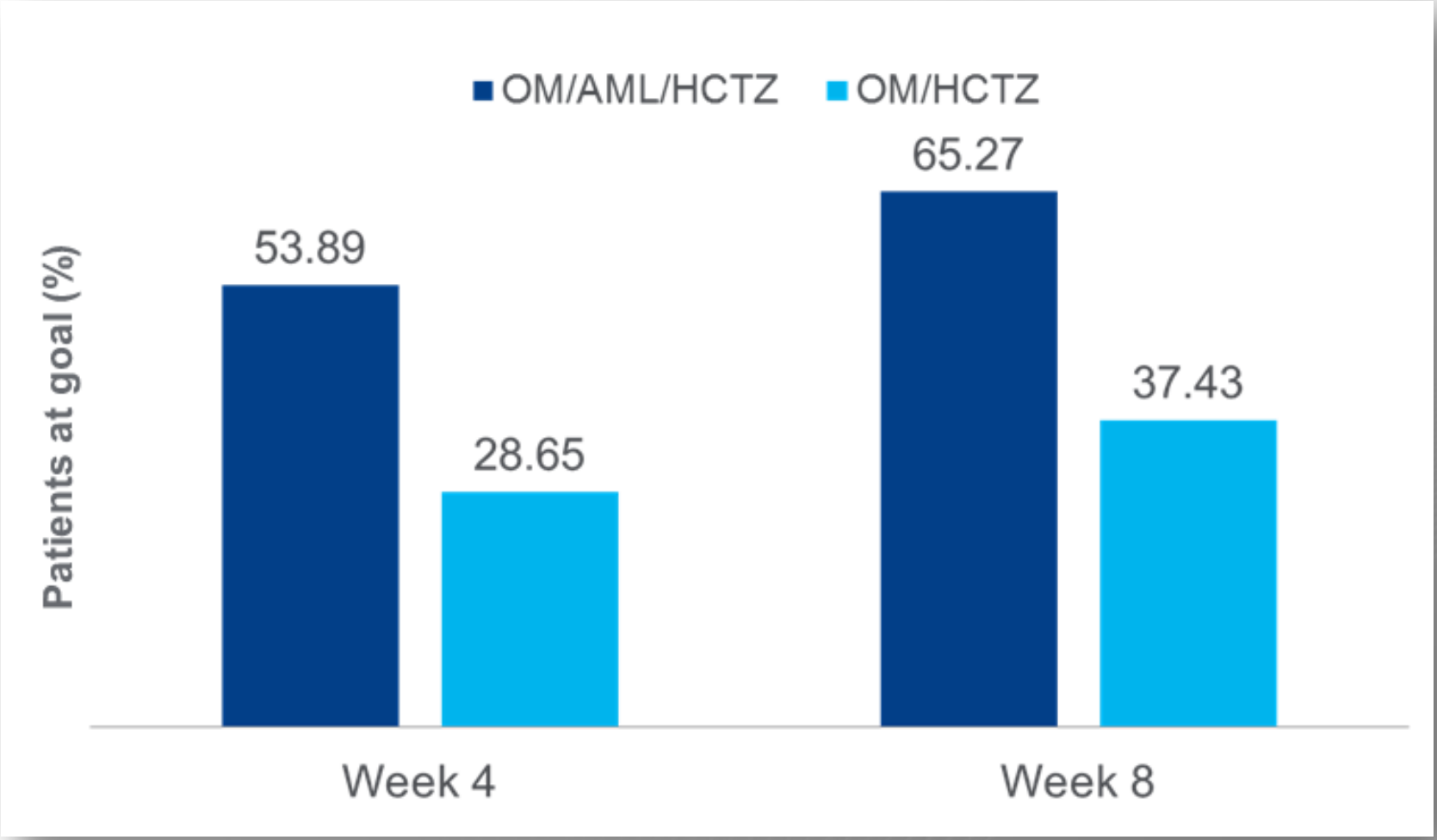
Am J Cardiovasc Drugs. 2016;16:129-38

8주 동안 msSBP의 변화



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

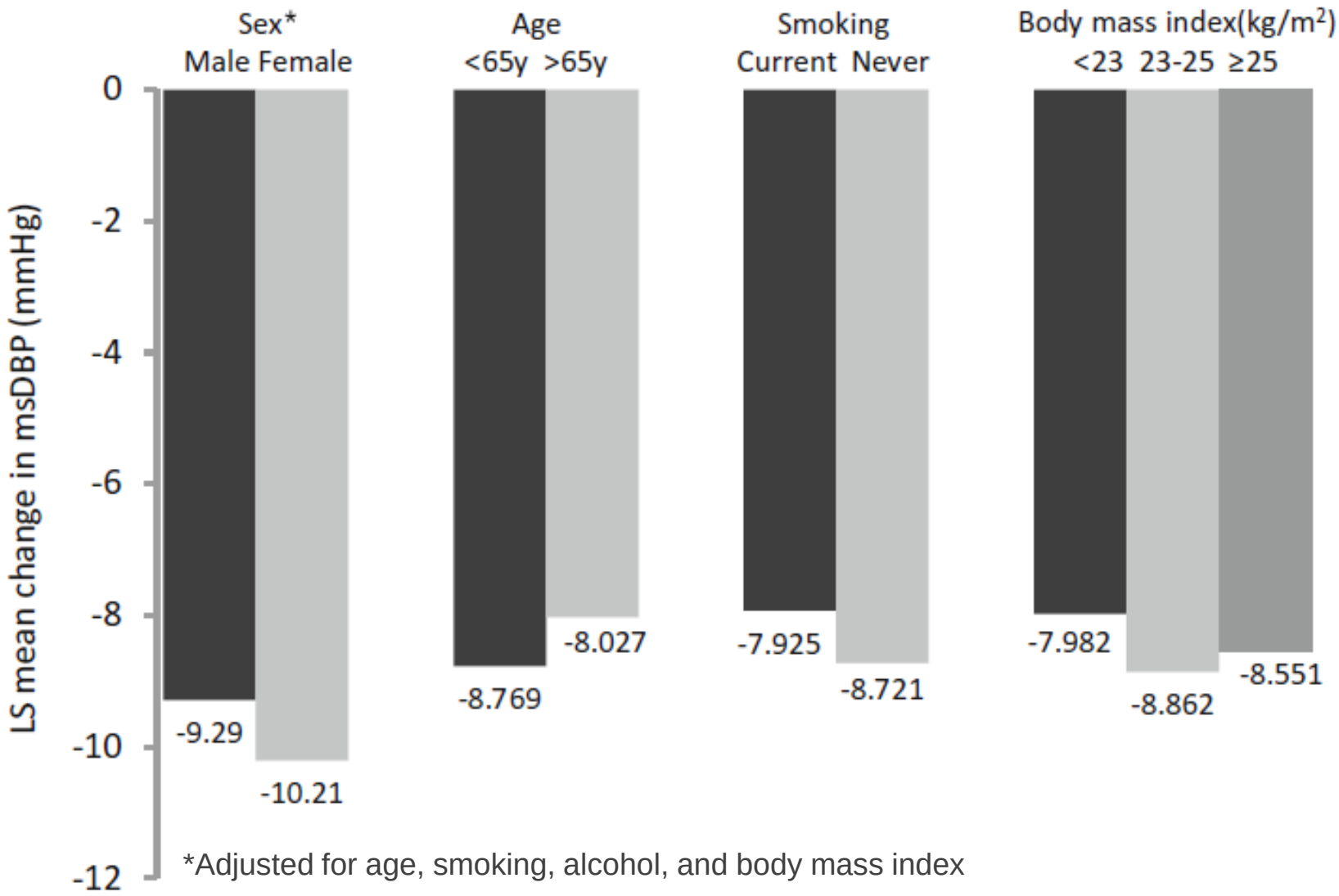
Patients achieving target BP at Week 4, 8



* Mean change from baseline, P<0.0001

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

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

All for one, one for all

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

Olmesartan and enteropathy

- Olmesartan – approved by FDA on Apr 25, **2002**
- Olmesartan-induced sprue-like enteropathy
  - 1st report in Aug **2012** from **Mayo Clinic**
    - Aug 1, 2008~ Aug 1, 2011, **22** pts (13 women) (21 white, 1 black)
    - Median age 69.5 yr (47-81 yrs), Most taking **40mg**/d (10~40mg)
    - Chronic diarrhea and weight loss, Enteropathy on intestinal biopsy
    - Clinical improvement after discontinuation of olmesartan
    - *Mayo Clin Proc*. 2012;87(8):732–738
  - **FDA label** change in July **2013**

Olmesartan and enteropathy

- **French** nationwide observational cohort study, 4,546,680 Pts
  - Intestinal malabsorption, 218 events (87 ACEi, **48** OLM, 83 other ARB)
  - increased risk of hospitalisation for intestinal malabsorption and coeliac disease
- Reported in **23**pts among ~2 million Pts in **US** (2012)
- Develop **months to years** after starting olmesartan
- Drug-induced or associated, ***not*** causality?
- Mechanism- **unknown**

ACG CASE REPORTS JOURNAL

CASE REPORT | SMALL BOWEL

A Case of Severe Sprue-Like Enteropathy Associated With Valsartan

Margot L. Herman, MD,[1] Alberto Rubio-Tapia, MD,[2] Tsung-Teh Wu, MD, PhD,[3] and Joseph A. Murray, MD[2]

[1]*Department of Medicine, Division of Gastroenterology, University of Washington, Seattle, WA*
[2]*Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN*
[3]*Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, MN*

Celiac disease (Sprue)

- Intestinal **autoimmune** disorder
- **Gluten** in diet (밀,보리) → **소장 점막에 염증**
  → **만성 설사, 흡수장애**, 영양결핍, 체중감소
- In genetically susceptible (HLA-DQ2+)
- Treatment: gluten-free diet

- ~1% in Europe and US, very rare in Asia
- Only **TWO** cases in Korea
  - 47yo lady. *Endocrinol Metab* (Seoul). 2015;30(1):105–109
  - 36yo lady. *Korean J Gastroenterol*. 2013;61:338–342

그렇다면 우리는..

- 대략 **10만 명 중에 한 명** 정도로 보고됨
- 지금까지 보고된 **국내 사례가 없다**
- 혈압조절 잘된다면 먹던 **약 끊을 필요는 없다**
- 복용중인 환자가 원인 불명의 **만성설사, 체중감소** 있다면 한번쯤 의심해 볼만 → 정확한 원인 위해 소화기내과 의뢰

Hypertension Seoul 2016

The 26th Scientific Meeting of the International Society of Hypertension

in collaboration with the 12th Congress of the Asian Pacific Society of Hypertension (APSH)
the 25th Annual Scientific Meeting of the Korean Society of Hypertension (KSH)

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



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