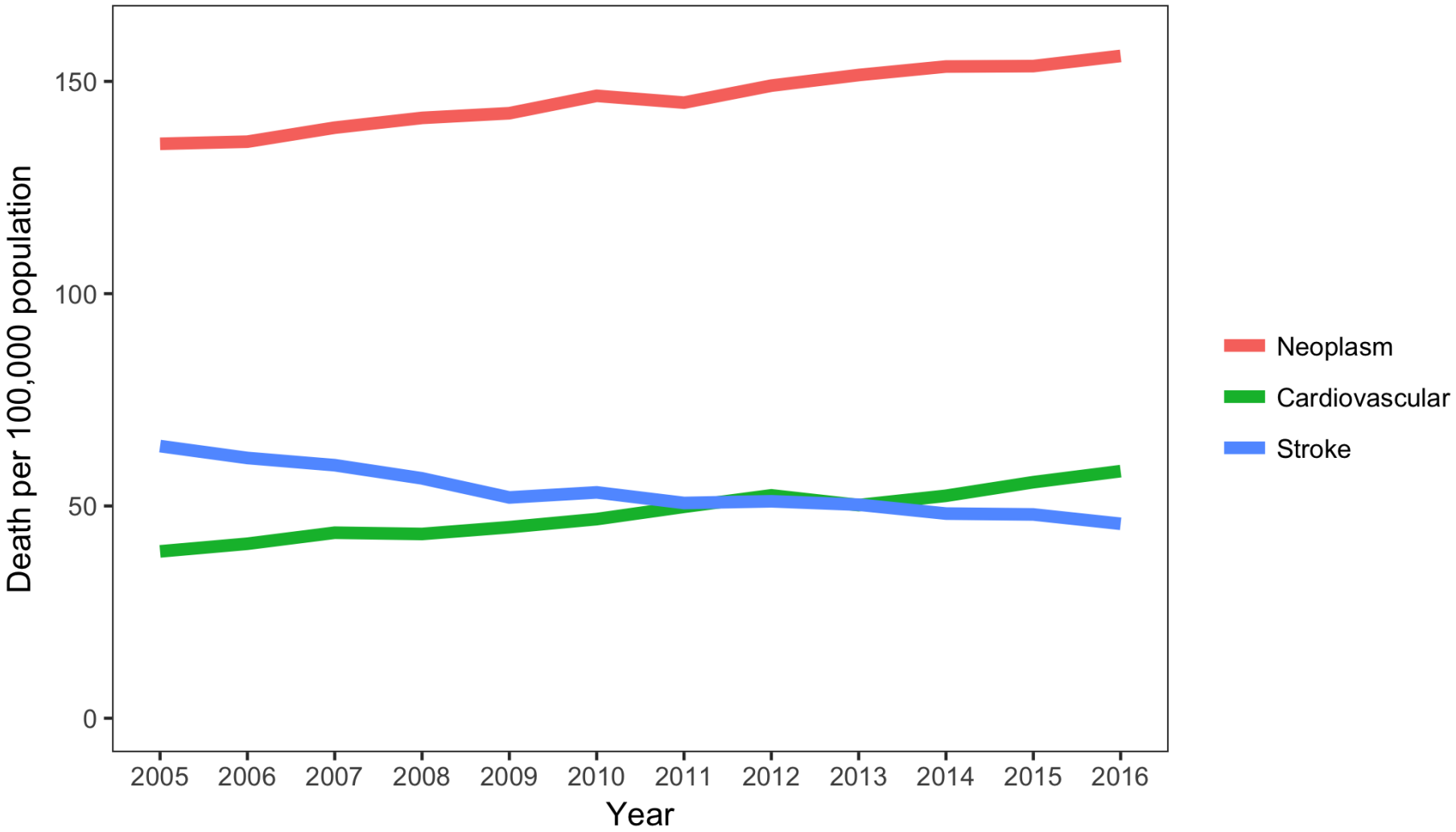
뉴로 Symposium

Differential Benefit and Real World Clinical Practices of Edarbi

Kwang-Yeol Park

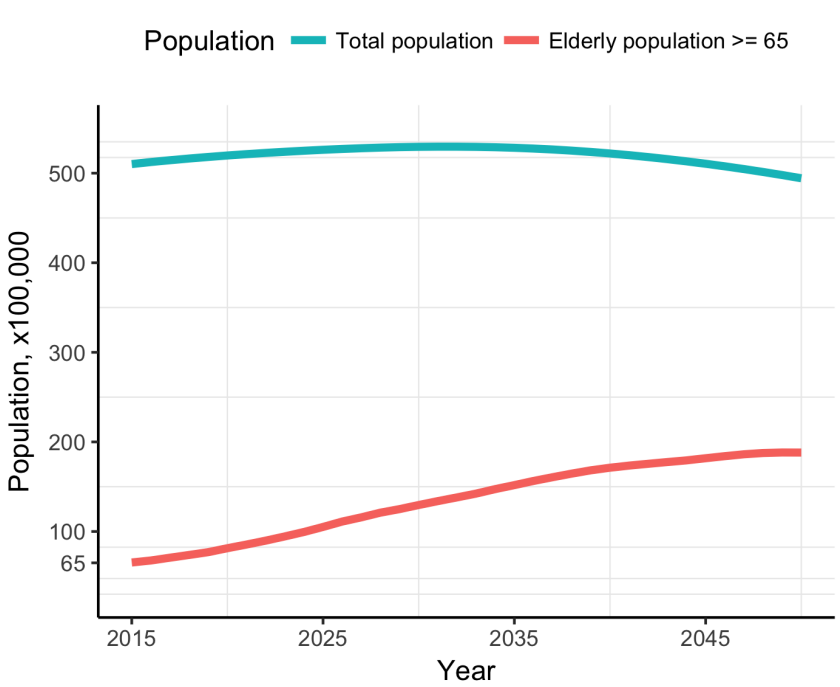
Dep. of Neurology, Chung-Ang University, Seoul South Korea

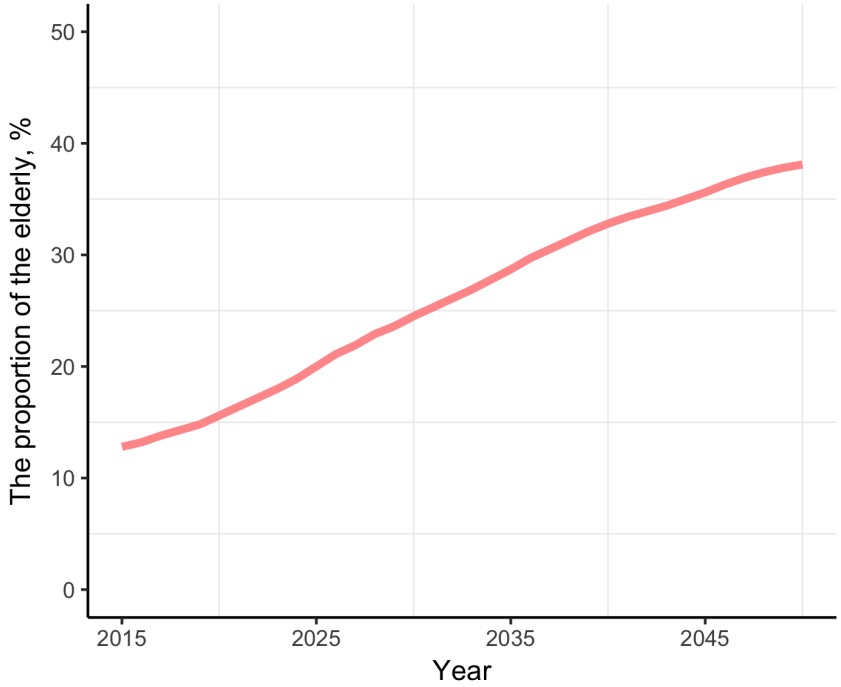
Secular trend of mortality in Korea



http://www.index.go.kr/potal/main/EachDtlPageDetail.do?idx_cd=1012 accessed on Aug. 26, 2018

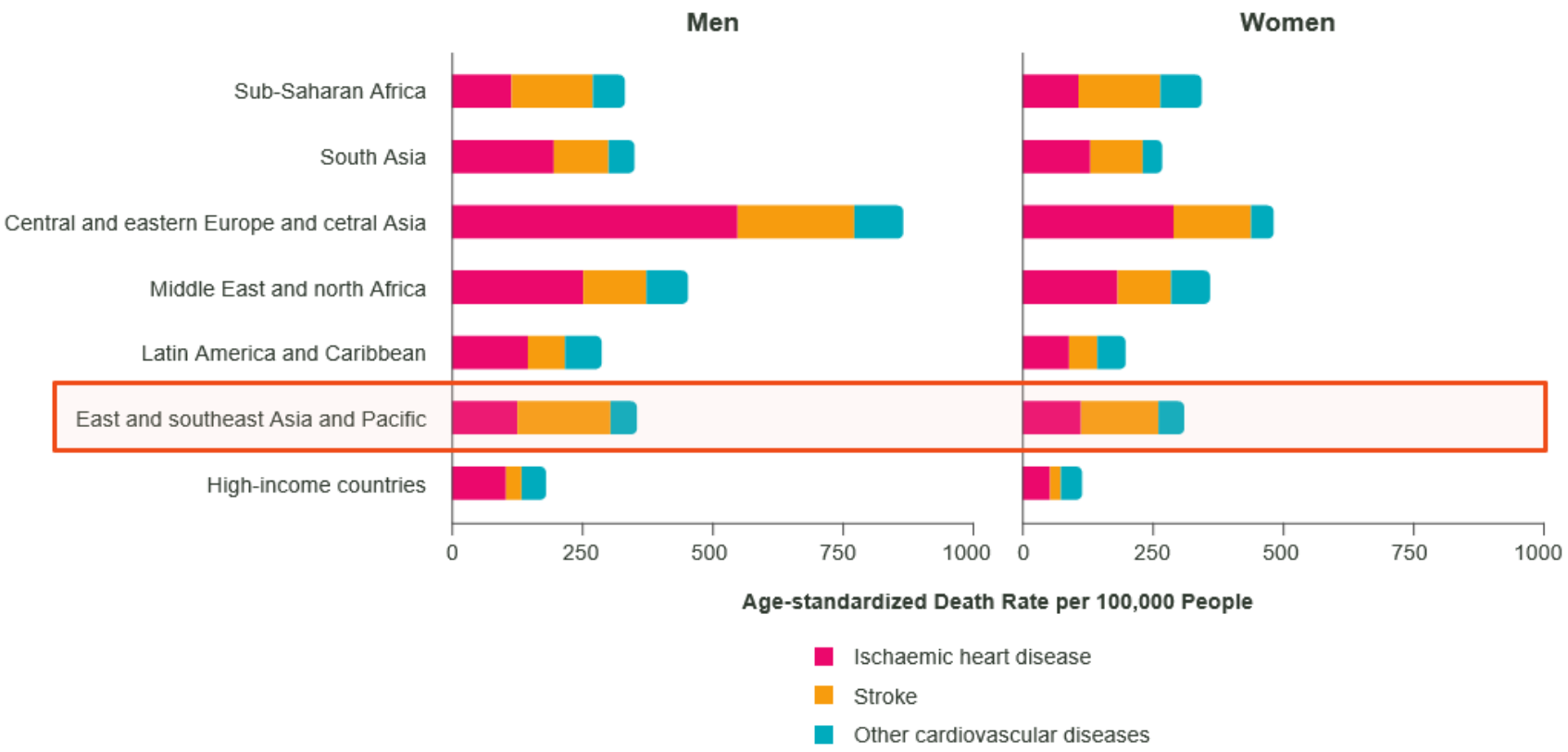
Rapid increase of Korean elderly population





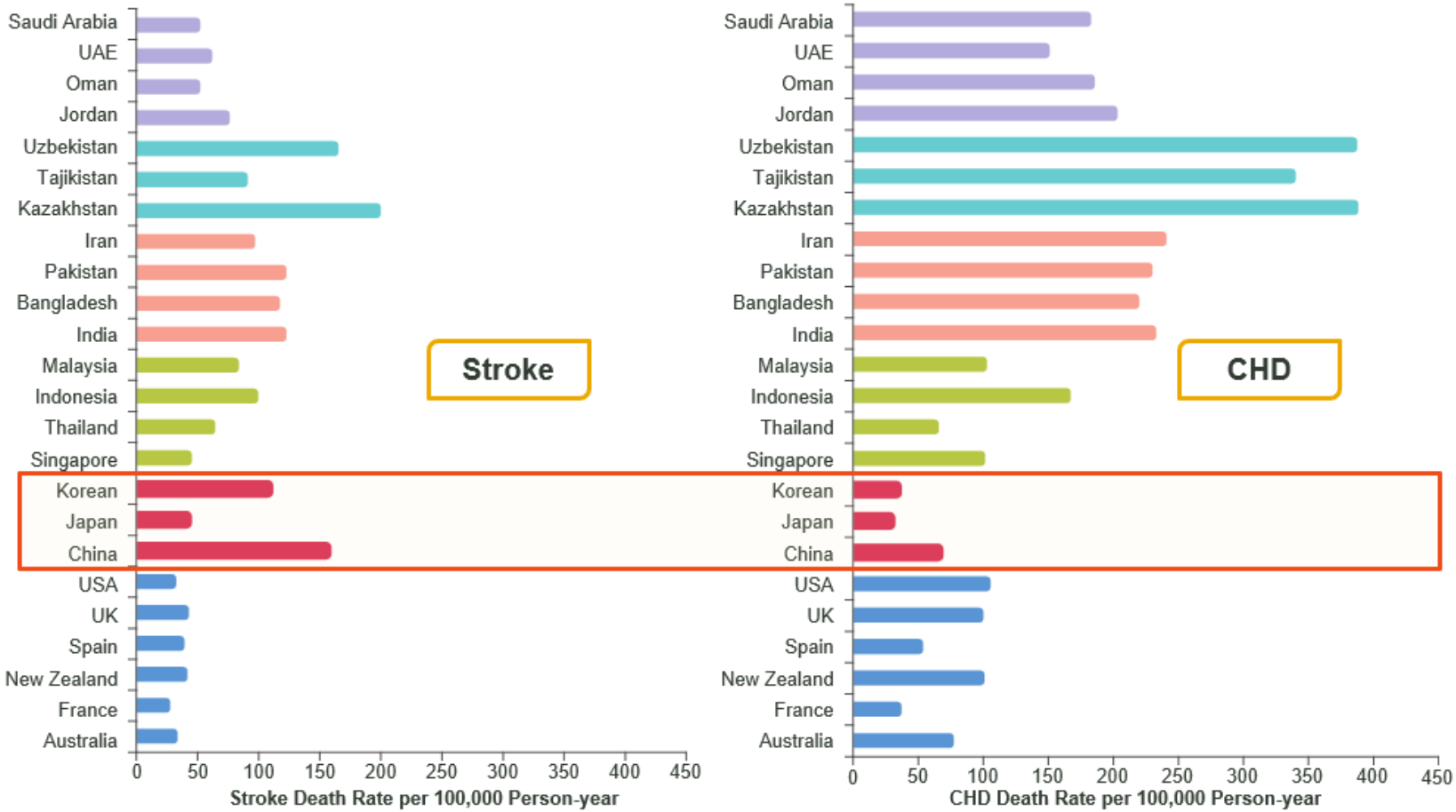
http://kosis.kr/visual/populationKorea/

다른 지역에 비해 동아시아에서 높은 발병률을 보이는 Stroke (1)



1. Tzoulaki I, et al. Worldwide Exposures to Cardiovascular Risk Factors and Associated Health Effects: Current Knowledge and Data Gaps. *Circulation*. 2016;133:2314-2333.

다른 지역에 비해 동아시아에서 높은 발병률을 보이는 Stroke (2)



UAE=United Arab Emirates; USA=United States of America; UK=United Kingdom; CHD=coronary heart disease.

1. Ueshima H, et al. Cardiovascular Disease and Risk Factors in Asia: A Selected Review. *Circulation*. 2008;118:2702-2709.

Table of contents

Risk factors for Stroke

Non-modifiable factors

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

Modifiable factors

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

IHD vs Stroke and SBP

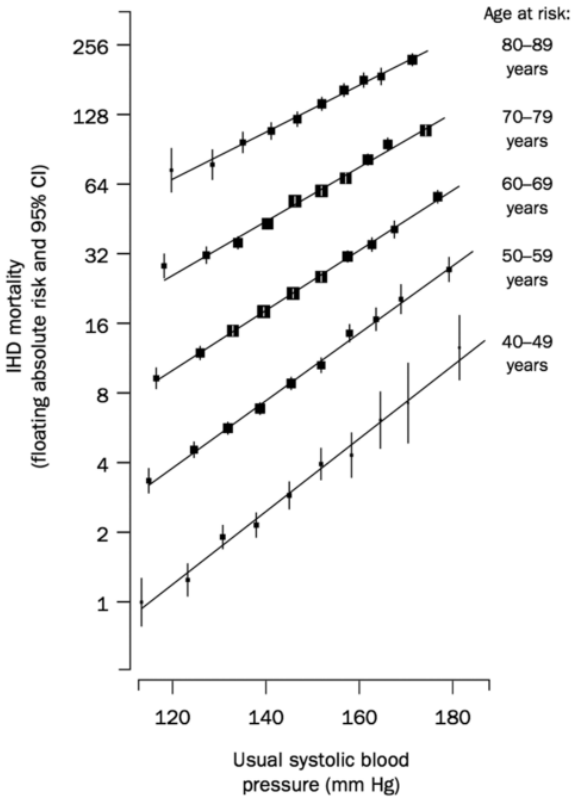


Figure 1. Ischemic heart disease (IHD) mortality

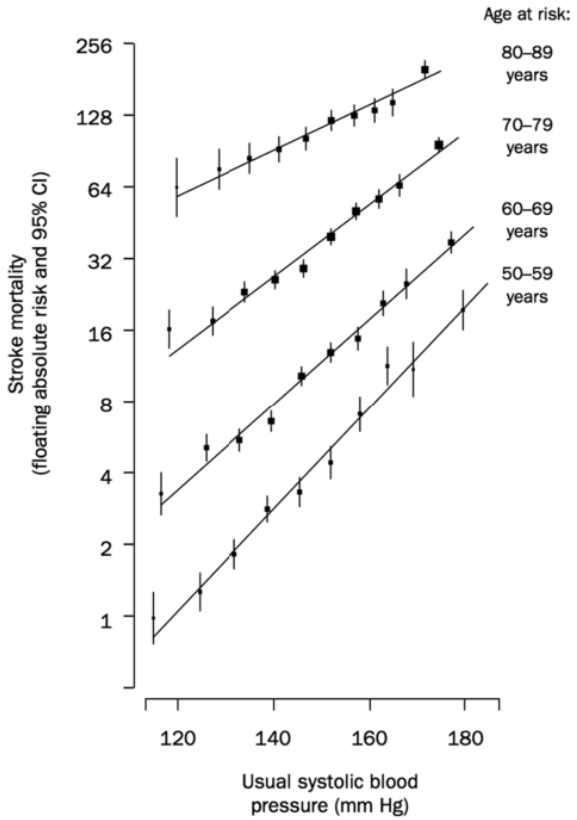
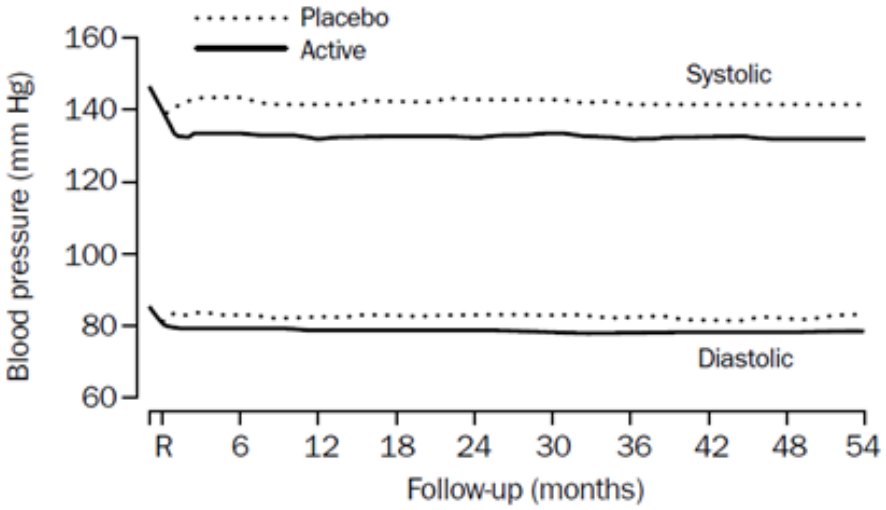


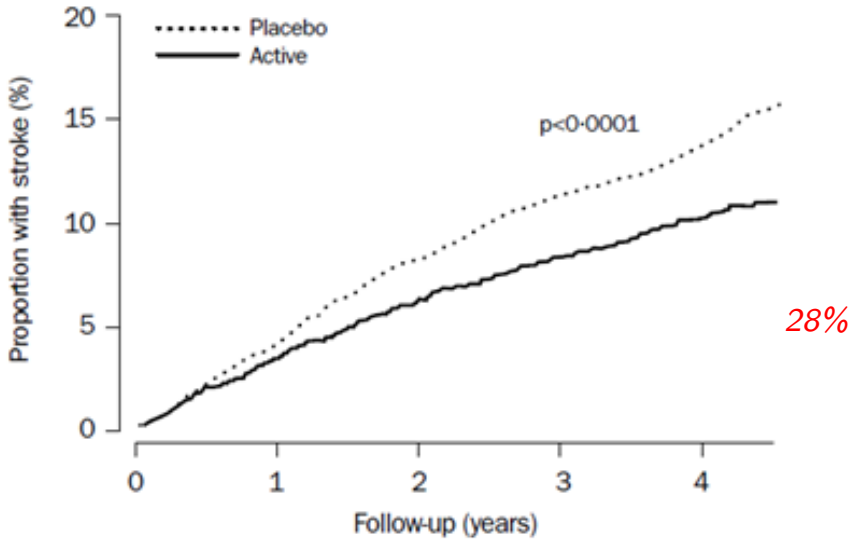
Figure 2. Stroke mortality

Rahimi, K et al. Cir Res 2015

PROGRESS

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





28%

BP difference: 9/4 mm Hg

Cumulative incidence of Stroke

PROGRESS Collaborative Group et al. Lancet 2001;358:1033-41

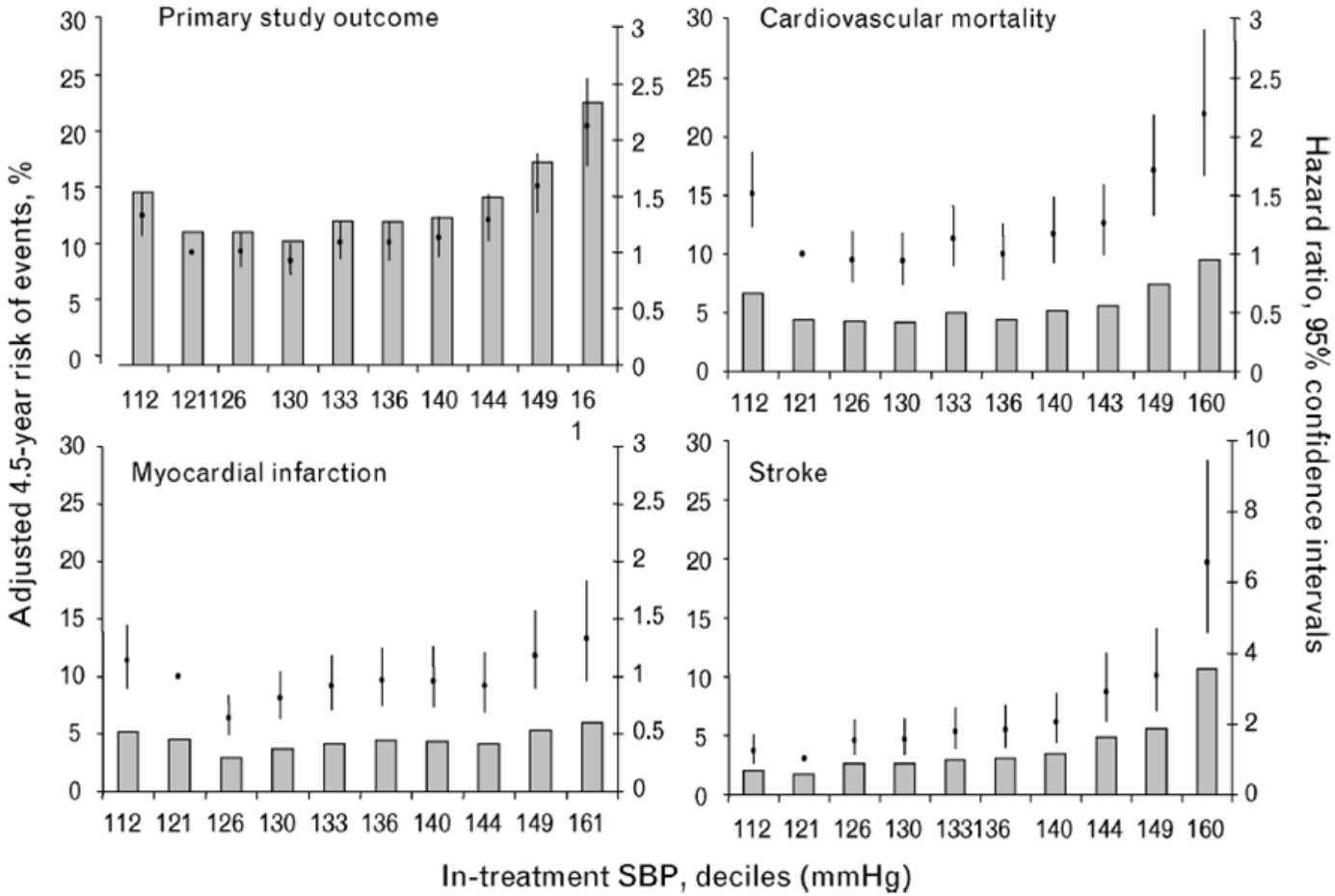
미국 및 유럽 이뇨제 단일제 사용현황

	USD (actual exchange rate/MNF)		
	FY 2017		
	Volume - Absolute	Share	%Growth
USA	229,241,833		-6.7%
C03A3 : THIAZIDES AND ANALOGUES PLAIN	229,241,833	100.0%	-6.7%
CHLORTALIDONE	128,377,880	56.0%	-4.2%
METOLAZONE	39,914,726	17.4%	-9.4%
HYDROCHLOROTHIAZIDE	33,875,024	14.8%	-13.1%
CHLOROTHIAZIDE	19,581,824	8.5%	0%
INDAPAMIDE	6,940,927	3.0%	-18.0%
METHYCLOTHIAZIDE	551,452	0.2%	-20.8%
BENDROFLUMETHIAZIDE	0	0.0%	
POLYTHIAZIDE	0	0.0%	

	USD (actual exchange rate/MNF)		
	FY 2017		
	Volume - Absolute	Share	%Growth
Europe & Canada	217,641,370		1.1%
C03A3 : THIAZIDES AND ANALOGUES PLAIN	217,641,370	100.0%	1.1%
INDAPAMIDE	119,963,659	55.1%	1.6%
HYDROCHLOROTHIAZIDE	52,278,247	24.0%	6.1%
BENDROFLUMETHIAZIDE	14,671,102	6.7%	-17.8%
CHLORTALIDONE	11,021,874	5.1%	10.0%
BENDROFLUMETHIAZIDE + POTASSIUM	10,671,011	4.9%	-3.3%
XIPAMIDE	5,121,483	2.4%	-0.7%
METOLAZONE	2,407,018	1.1%	8.0%
CLOPAMIDE	559,391	0.3%	-1.8%
CHLOROTHIAZIDE	449,720	0.2%	-3.7%
AMILORIDE + HYDROCHLOROTHIAZIDE	353,185	0.2%	-7.6%
METIPAMIDE	144,576	0.1%	-5.3%
CYCLOPENTHIAZIDE	103	0.0%	-68.5%

Data Source : IMS MIDAS, 2017, FY2017; 2017.4~2018.3.

Ontarget study

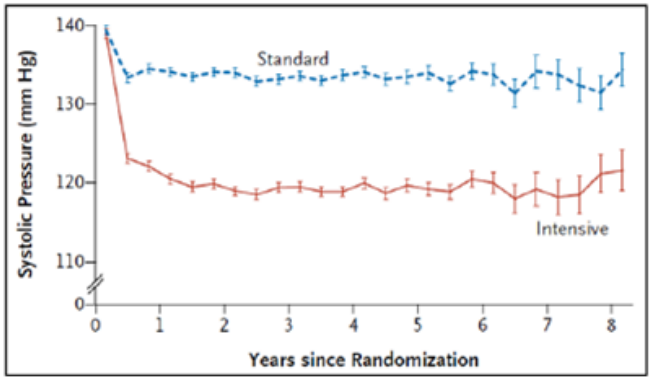


Journal of Hypertension 2009, 27:1360 - 1369

The lower BP looks beneficial in stroke: ACCORD

- 4733 patients with type 2 DM
- SBP

  < 140 mm Hg vs. < 120 mm Hg



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

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

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

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

Post-hoc analysis of PRoFESS trial: U-shaped Relationship between Mean BP and Subsequent Vascular Events

Adjusted risk of clinical outcomes by mean SBP Level in 20,330 patients with a recent ischemic stroke

	Mean SBP Level, mmHg				
	High-Normal (130-<140; n=6,004)	**Very Low-Normal** (<120; n=1,919)	**Low-Normal** (120-<130; n=3,982)	**High** (140-<150; n=4,520)	**Very High** (≥150; n=3,905)
AHR (95% CI)					
Stroke*	1.00	1.29 (1.07-1.56)	1.10 (0.95-1.28)	1.23 (1.07-1.41)	2.08 (1.83-2.37)
Stroke, MI, or vascular death†	1.00	1.31 (1.13-1.52)	1.16 (1.03-1.31)	1.24 (1.11-1.39)	1.94 (1.74-2.16)
Fatal Stroke‡	1.00	0.63 (0.26-1.49)	1.01 (0.64-1.89)	1.50 (0.94-2.40)	2.51 (1.62-3.09)

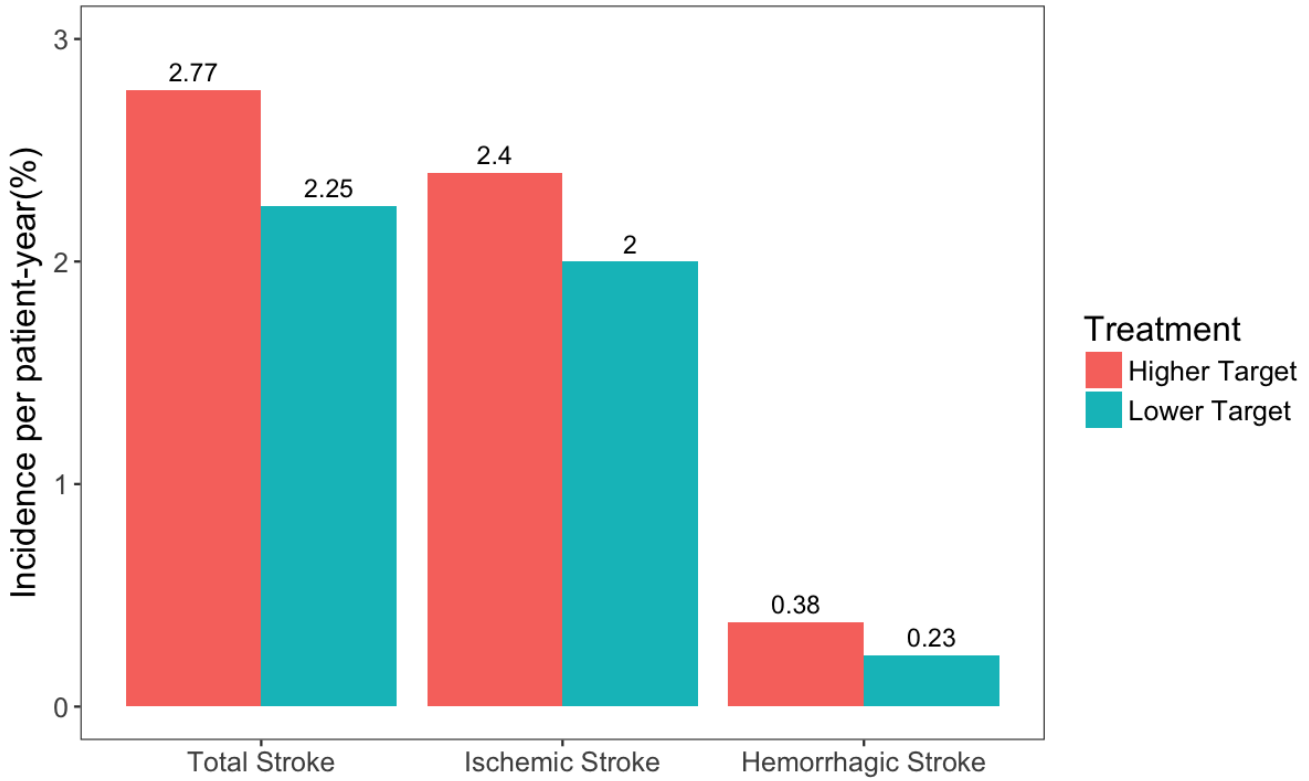
*Adjusted for age, sex, previous stroke, congestive heart failure, diabetes, MI, hypertension, current smoking status, baseline National Institutes of Health Stroke Scale score, qualifying stroke due to small vessel disease, previous transient ischemic attack, and Asian ethnicity; †Adjusted for age, sex, previous stroke, congestive heart failure, diabetes, MI, hyperlipidemia, coronary artery disease, current smoking status, antihypertensive medication use at baseline, baseline National Institutes of Health Stroke Scale score, qualifying stroke due to small vessel disease, body mass index (calculated as weight in kilograms divided by height in meters squared), black race, white race, previous transient ischemic attack, and Asian ethnicity; ‡Adjusted for age, sex, previous stroke, congestive heart failure, diabetes, MI, treatment with angiotensin receptor blocker, antiplatelet treatment at baseline, baseline National Institutes of Health Stroke Scale score, body mass index (calculated as weight in kilograms divided by height in meters squared), and previous transient ischemic attack.

BP, blood pressure; PRoFESS=The Prevention Regimen for Effectively Avoiding Second Strokes; AHR=adjusted hazard ratio; MI=myocardial infarction; SBP=systolic blood pressure; CI=confidence interval.

1. Ovbiagele B, et al. Level of systolic blood pressure within the normal range and risk of recurrent stroke. *JAMA*. 2011;306:2137-2144.

BP targets in recent lacunar stroke: SPS3

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



The SPS3 Study Group. Lancet 2013;382:507-15

2014 AHA/ASA 2ndary Prevention of Stroke Guideline

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

Kernan WN et al. Stroke. 2014;45

SPRINT and ACCORD

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

N Engl J Med. 2010 362(17):1575-85; N Engl J Med. 2015 Nov 26;373(22)89mm:2103-16

SPRINT and ACCORD

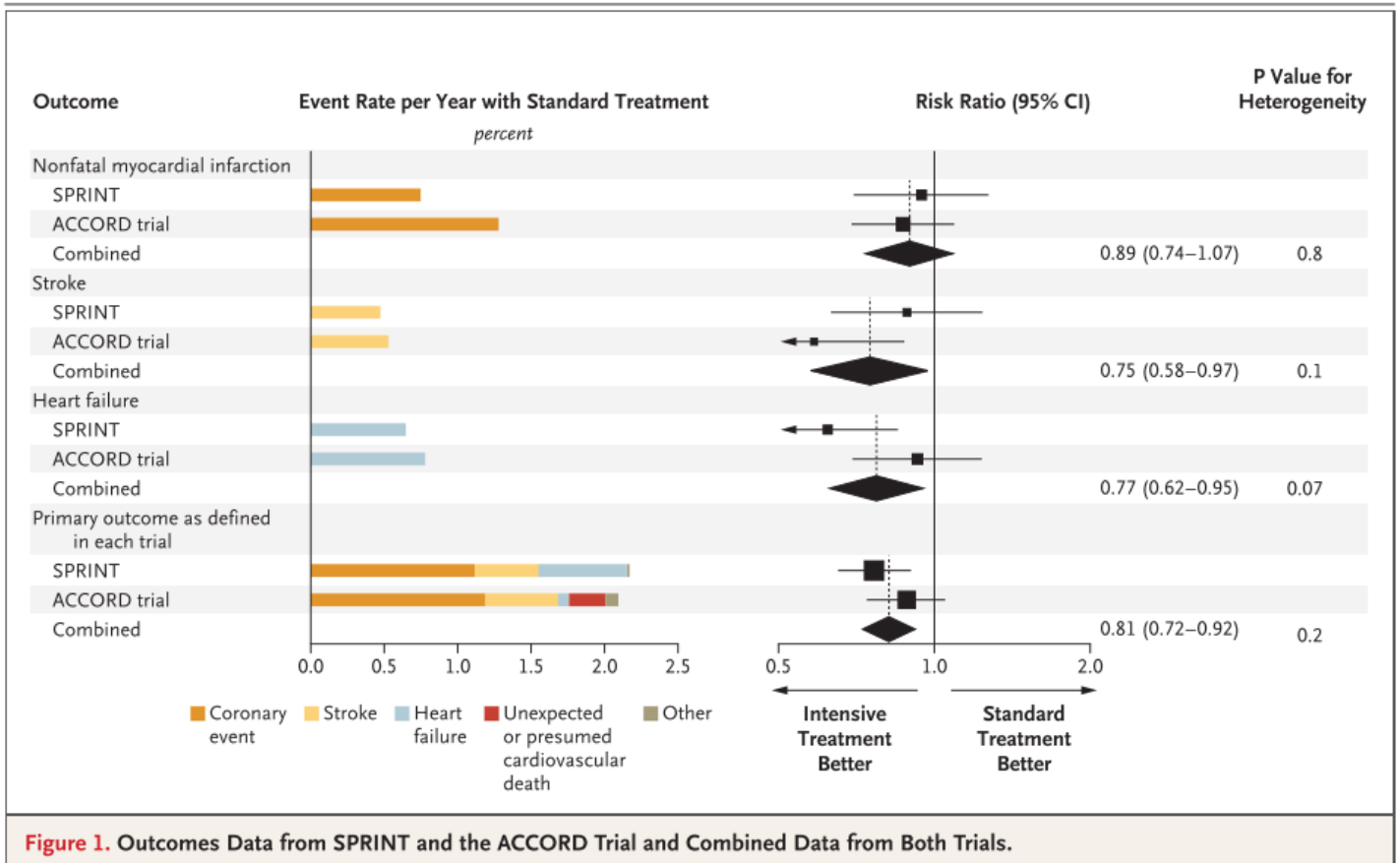


Figure 1. Outcomes Data from SPRINT and the ACCORD Trial and Combined Data from Both Trials.

Perkovic V, Rodgers A. N Engl J Med. 2015 Nov 26;373(22):2175-8

2017 US - 2018 Korea and Europe

Whelton PK, et al.
2017 High Blood Pressure Clinical Practice Guideline

2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

WRITING COMMITTEE MEMBERS

Paul K. Whelton, MB, MD, MSc, FAHA, *Chair*
Robert M. Carey, MD, FAHA, *Vice Chair*

Wilbert S. Aronow, MD, FACC, FAHA*
Donald E. Casey, Jr, MD, MPH, MBA, FAHA†
Karen J. Collins, MBA‡
Cheryl Dennison Himmelfarb, RN, ANP, PhD, FAHA§
Sondra M. DePalma, MHS, PA-C, CLS, AACC‖
Samuel Gidding, MD, FACC, FAHA¶
Kenneth A. Jamerson, MD#
Daniel W. Jones, MD, FAHA†
Eric J. MacLaughlin, PharmD**
Paul Muntner, PhD, FAHA†
Bruce Ovbiagele, MD, MSc, MAS, MBA, FAHA†
Sidney C. Smith, Jr, MD, MACC, FAHA††
Crystal C. Spencer, JD‡
Randall S. Stafford, MD, PhD‡‡
Sandra J. Taler, MD, FAHA§§
Randal J. Thomas, MD, MS, FACC, FAHA‖‖
Kim A. Williams, Sr, MD, MACC, FAHA†
Jeff D. Williamson, MD, MHS¶¶
Jackson T. Wright, Jr, MD, PhD, FAHA##

ACC/AHA TASK FORCE MEMBERS

Glenn N. Levine, MD, FACC, FAHA, *Chair*
Patrick T. O'Gara, MD, MACC, FAHA, *Chair-Elect*
Jonathan L. Halperin, MD, FACC, FAHA, *Immediate Past Chair*
Sana M. Al-Khatib, MD, MHS, FACC, FAHA
Joshua A. Beckman, MD, MS, FAHA
Kim K. Birtcher, MS, PharmD, AACC
Biykem Bozkurt, MD, PhD, FACC, FAHA***
Ralph G. Brindis, MD, MPH, MACC***
Joaquin E. Cigarroa, MD, FACC
Lesley H. Curtis, PhD, FAHA***
Anita Deswal, MD, MPH, FACC, FAHA
Lee A. Fleisher, MD, FACC, FAHA
Federico Gentile, MD, FACC
Samuel Gidding, MD, FAHA***
Zachary D. Goldberger, MD, MS, FACC, FAHA
Mark A. Hlatky, MD, FACC, FAHA
John Ikonomidis, MD, PhD, FAHA
José A. Joglar, MD, FACC, FAHA
Laura Mauri, MD, MSc, FAHA
Susan J. Pressler, PhD, RN, FAHA***
Barbara Riegel, PhD, RN, FAHA
Duminda N. Wijeysundera, MD, PhD

Hypertension

THE KOREAN SOCIETY OF HYPERTENSION

2018년 고혈압 진료지침

대한고혈압학회
The Korean Society of Hypertension

ESC European Society of Cardiology

European Heart Journal (2018) **00**, 1–98
doi:10.1093/eurheartj/ehy339

ESC/ESH GUIDELINES

2018 ESC/ESH Guidelines for the management of arterial hypertension

The Task Force for the management of arterial hypertension of the European Society of Cardiology (ESC) and the European Society of Hypertension (ESH)

Authors/Task Force Members: Bryan Williams* (ESC Chairperson) (UK), Giuseppe Mancia* (ESH Chairperson) (Italy), Wilko Spiering (The Netherlands), Enrico Agabiti Rosei (Italy), Michel Azizi (France), Michel Burnier (Switzerland), Denis L. Clement (Belgium), Antonio Coca (Spain), Giovanni de Simone (Italy), Anna Dominiczak (UK), Thomas Kahan (Sweden), Felix Mahfoud (Germany), Josep Redon (Spain), Luis Ruilope (Spain), Alberto Zanchetti† (Italy), Mary Kerins (Ireland), Sverre E. Kjeldsen (Norway), Reinhold Kreutz (Germany), Stephane Laurent (France), Gregory Y. H. Lip (UK), Richard McManus (UK), Krzysztof Narkiewicz (Poland), Frank Ruschitzka (Switzerland), Roland E. Schmieder (Germany), Evgeny Shlyakhto (Russia), Costas Tsioufis (Greece), Victor Aboyans (France), Ileana Desormais (France)

* Corresponding authors. Bryan Williams, Institute of Cardiovascular Science, University College London, Maple House, 1st Floor, Suite A, 149 Tottenham Court Road, London W1T 7DN, UK. Tel: +44 (0) 20 3108 7907, E-mail: bryanwilliams@ucl.ac.uk. Giuseppe Mancia, University of Milano-Bicocca, Milan, Italy; and Hypertension Center Istituto Universitario Policlinico di Monza, Verano (MB), Piazza dei Daini, 4 – 20126 Milan, Italy. Tel: +39 347 4327142, E-mail: giuseppe.mancia@unimib.it

† Professor Zanchetti died towards the end of the development of these Guidelines, in March 2018. He contributed fully to the development of these Guidelines, as a member of the Guidelines' Task Force and as a section co-ordinator. He will be sadly missed by colleagues and friends.

The two chairpersons contributed equally to the document.

ESC Committee for Practice Guidelines (CPG), European Society of Hypertension (ESH) Council, ESC National Cardiac Societies having participated in the review process, ESH National Hypertension Societies having participated in the review process: listed in the Appendix.

ESC entities having participated in the development of this document:

Associations: European Association of Cardiovascular Imaging (EACVI), European Association of Preventive Cardiology (EAPC), European Association of Percutaneous Cardiovascular Interventions (EAPCI), European Heart Rhythm Association (EHRA), Heart Failure Association (HFA).

Councils: Council for Cardiology Practice, Council on Cardiovascular Nursing and Allied Professions, Council on Cardiovascular Primary Care, Council on Hypertension,

2017 ACC/AHA 가이드라인 진단 기준=고혈압 정의

- ✓ 14년만에 고혈압 정의를 개정함
- ✓ 낮아진 고혈압 경계치, **130-139/80-89mmHg = 고혈압 1단계**

SBP, DBP(mmHg)	JNC7	2017 ACC/AHA
<120 and <80	Normal BP	Normal BP
120–129 and <80	Prehypertension	**Elevated BP**
130–139 or 80–89	Prehypertension	**Stage 1 hypertension**
140–159 or 90–99	Stage 1 hypertension	**Stage 2 hypertension**
≥160 or ≥100	Stage 2 hypertension	Stage 2 hypertension

JNC=Joint National Committee; ACC=The American College of Cardiology; AHA=American Heart Association; BP=blood pressure; SBP=systolic blood pressure; DBP=diastolic blood pressure.

1. Whelton PK, et al. *Hypertension*. 2017 Nov 13. [Epub ahead of print]

2017 ACC/AHA 가이드라인:
BP Threshold and BP Goal

Clinical Condition(s)	BP Threshold (mmHg)	BP Goal (mmHg)
General		
Clinical CVD or 10-year ASCVD risk ≥10%	**≥130/80**	**<130/80**
No clinical CVD and 10-year ASCVD risk <10%	**≥140/90**	**<130/80**
Older persons (≥65 years of age; noninstitutionalized, ambulatory, community-living adults)	**≥130(SBP)**	**<130(SBP)**
Specific comorbidities		
Diabetes mellitus	≥130/80	<130/80
Chronic kidney disease	≥130/80	<130/80
Chronic kidney disease after renal transplantation	≥130/80	<130/80
Heart failure	≥130/80	<130/80
Stable ischemic heart disease	≥130/80	<130/80
Secondary stroke prevention	≥140/90	<130/80
Secondary stroke prevention(lacunar)	≥130/80	<130/80
Peripheral arterial disease	≥130/80	<130/80

ACC=The American College of Cardiology; AHA=American Heart Association; ASCVD=atherosclerotic cardiovascular disease; BP=blood pressure; CVD=cardiovascular disease; SBP=systolic blood pressure.

1. Whelton PK, et al. *Hypertension*. 2017 Nov 13. [Epub ahead of print]

2017 ACC/AHA 가이드라인:
Recommendation for Out-of-Office and Self-Monitoring

COR	LOE*	Recommendation
I	A^{SR}	Out-of-office BP measurements are recommended to confirm the diagnosis of hypertension and for titration of BP-lowering medication, in conjunction with telehealth counseling or clinical interventions.

Clinic	HBPM	Daytime ABPM	Nighttine ABPM	24-Hour ABPM
120/80	120/80	120/80	100/65	115/75
130/80	130/80	130/80	110/65	125/75
140/90	135/85	135/85	120/70	130/80
160/100	145/90	145/90	140/85	145/90

*The method of assessing quality is evoving, including the application of standardized, widely used, and preferably validated evidence grading tools; and for systematic reviews, the incorporation of an Evidence Review Committee.

ACC=The American College of Cardiology; AHA=American Heart Association; COR=class of recommendation; LOE=level of evidence; SR=systematic review; BP=blood pressure; HBPM=home blood pressure monitoring; ABPM= ambulatory blood pressure monitoring.

1. Whelton PK, et al. *Hypertension*. 2017 Nov 13. [Epub ahead of print]

KSH Guideline 2013 vs 2018

2013				2018			
혈압 분류	SBP (mmHg)		DBP (mmHg)	혈압분류	SBP (mmHg)		DBP (mmHg)
정상	<120	그리고	<80	정상	<120	그리고	<80
고혈압전단계 1기	120-129	또는	80-84	주의혈압	120-129	그리고	<80
고혈압전단계 2기	130-139	또는	85-89	고혈압 전단계	130-139	또는	80-89
고혈압1기	140-159	또는	90-99	고혈압1기	140-159	또는	90-99
고혈압2기	≥160	또는	≥100	고혈압2기	≥160	또는	≥100

SBP=systolic blood pressure; DBP=diastolic blood pressure.

1. KSH Treatment Guideline 2013. 2. KSH Treatment Guideline 2018 보도자료.

Korea Target BP Goal 2018

상황	SBP (mmHg)	DBP (mmHg)
단순고혈압	140	90
고위험군*	130	80
심혈관질환**	130	80
노인 고혈압	140	90
당뇨병		
심혈관질환 없음	140	85
심혈관질환† 있음	130	80
만성콩팥병		
알부민뇨 없음	140	90
알부민뇨 동반됨	130	80
뇌졸중	140	90

*10년 심뇌혈관질환 발생률 > 15%, 노인은 노인 기준에 따름; †관상동맥질환, 말초혈관질환, 대동맥질환, 심부전 및 좌심실비대.
SBP=systolic blood pressure; DBP=diastolic blood pressure.
1. KSH Treatment Guideline 2018 보도자료.

Europe guideline

Summary - Office BP Thresholds for Treatment

ESC European Society of Cardiology

European Society of Hypertension

Age group	Office SBP treatment threshold (mmHg)					Diastolic treatment Threshold (mmHg)
	Hypertension	+ Diabetes	+ CKD	+ CAD	+ Stroke/ TIA	
18–65 years	≥ 140	≥ 140	≥ 140	≥ 140[a]	≥ 140[a]	≥ 90
65–79 years	≥ 140	≥ 140	≥ 140	≥ 140[a]	≥ 140[a]	≥ 90
≥ 80 years	≥ 160	≥ 160	≥ 160	≥ 160	≥ 160	≥ 90
Diastolic treatment threshold (mmHg)	≥ 90	≥ 90	≥ 90	≥ 90	≥ 90	

[a]Treatment may be considered in these very high-risk patients with high–normal SBP (i.e. SBP 130–140 mmHg)

www.escardio.org/guidelines

Williams B, Mancia G et al. Eur Heart J (2018); doi:10.1093/eurheartj/ehy339
Williams B, Mancia G et al. J Hypertens (2018); doi:10.1097/HJH0000000000001940

Summary - Office BP Target Ranges

ESC European Society of Cardiology

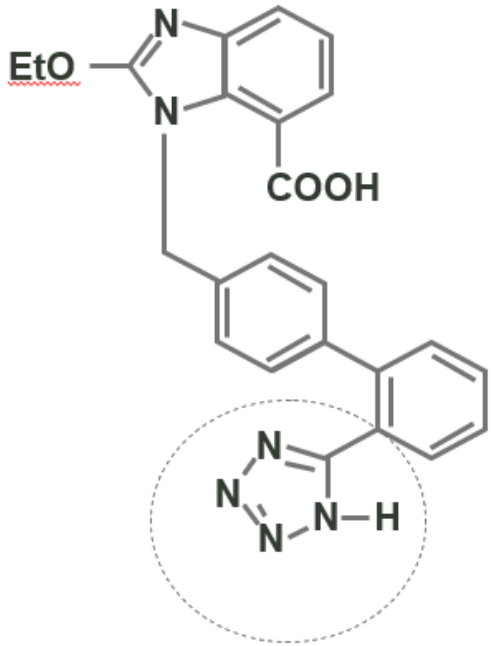
ESH European Society of Hypertension

Age group	Office SBP treatment target ranges (mmHg)					DBP treatment target range (mmHg)
	Hypertension	+ Diabetes	+ CKD	+ CAD	+ Stroke/ TIA	
18–65 years	Target to 130 *or lower if tolerated* Not <120	Target to 130 *or lower if tolerated* Not <120	Target to <140 to 130 *if tolerated*	Target to 130 *or lower if tolerated* Not <120	Target to 130 *or lower if tolerated* Not <120	<80 to 70
65–79 years	Target to <140 to 130 *if tolerated*	Target to <140 to 130 *if tolerated*	Target to <140 to 130 *if tolerated*	Target to <140 to 130 *if tolerated*	Target to <140 to 130 *if tolerated*	<80 to 70
≥ 80 years	Target to <140 to 130 *if tolerated*	Target to <140 to 130 *if tolerated*	Target to <140 to 130 *if tolerated*	Target to <140 to 130 *if tolerated*	Target to <140 to 130 *if tolerated*	<80 to 70
DBP treatment target range (mmHg)	< 80 to 70	< 80 to 70	< 80 to 70	< 80 to 70	< 80 to 70	

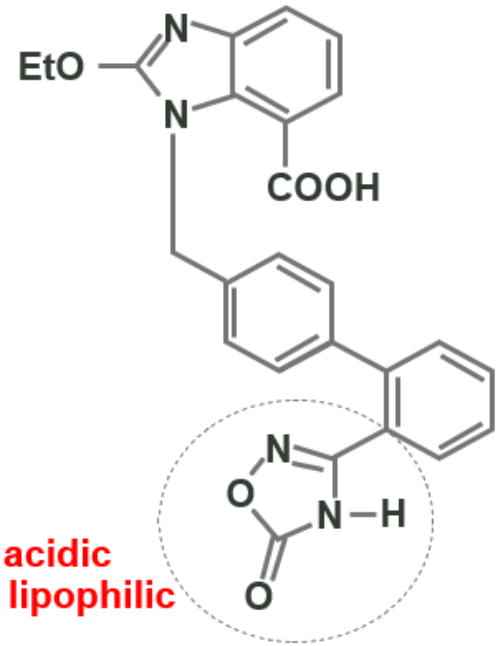
www.escardio.org/guidelines

Azilsartan 개발 History

Candesartan



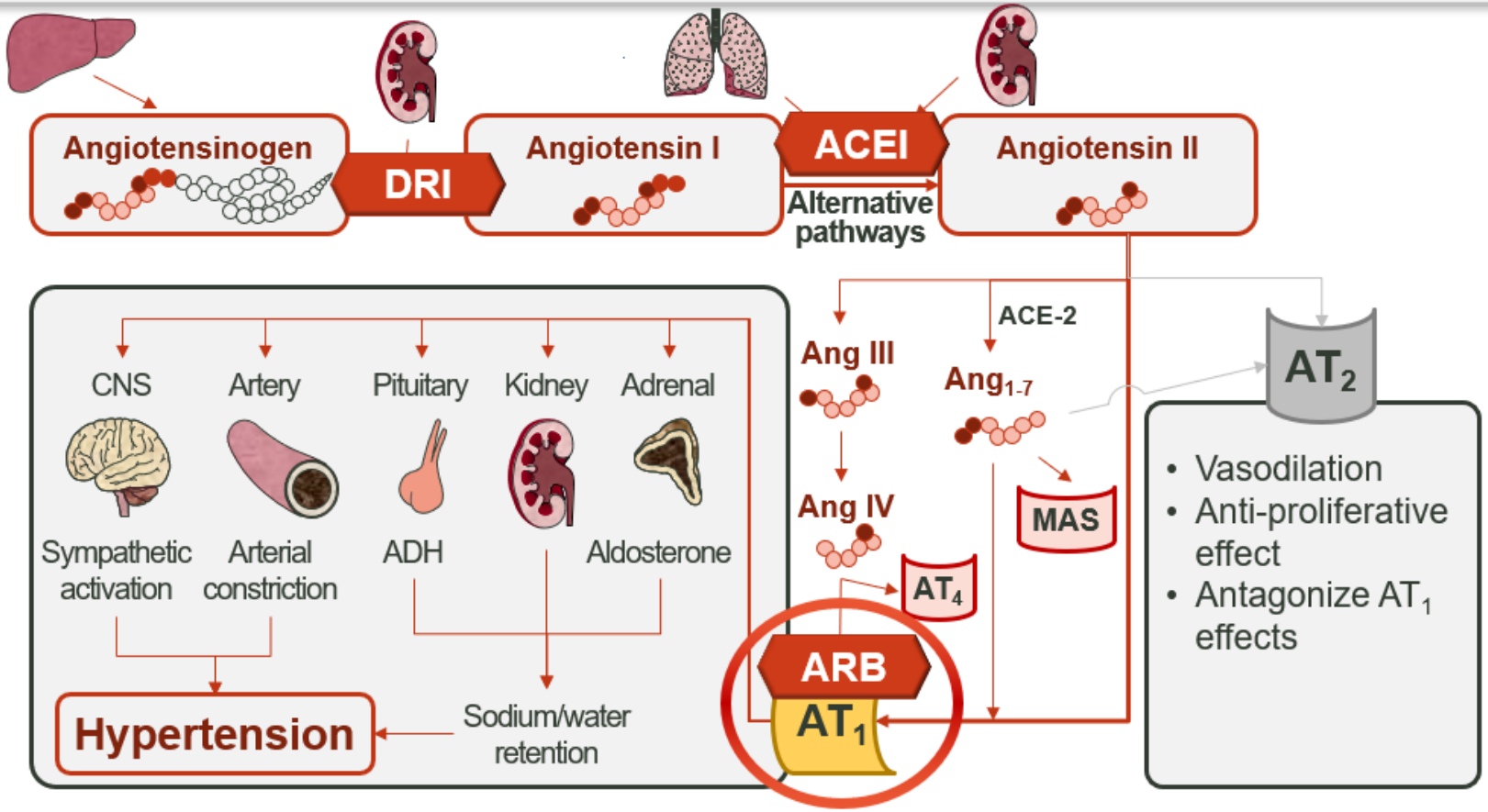
Azilsartan



Less acidic
More lipophilic

1. Kurts TW, et al. Differential pharmacology and benefit/risk of azilsartan compared to other sartans. *Vasc Health Risk Manag.* 2012;8:133-143.

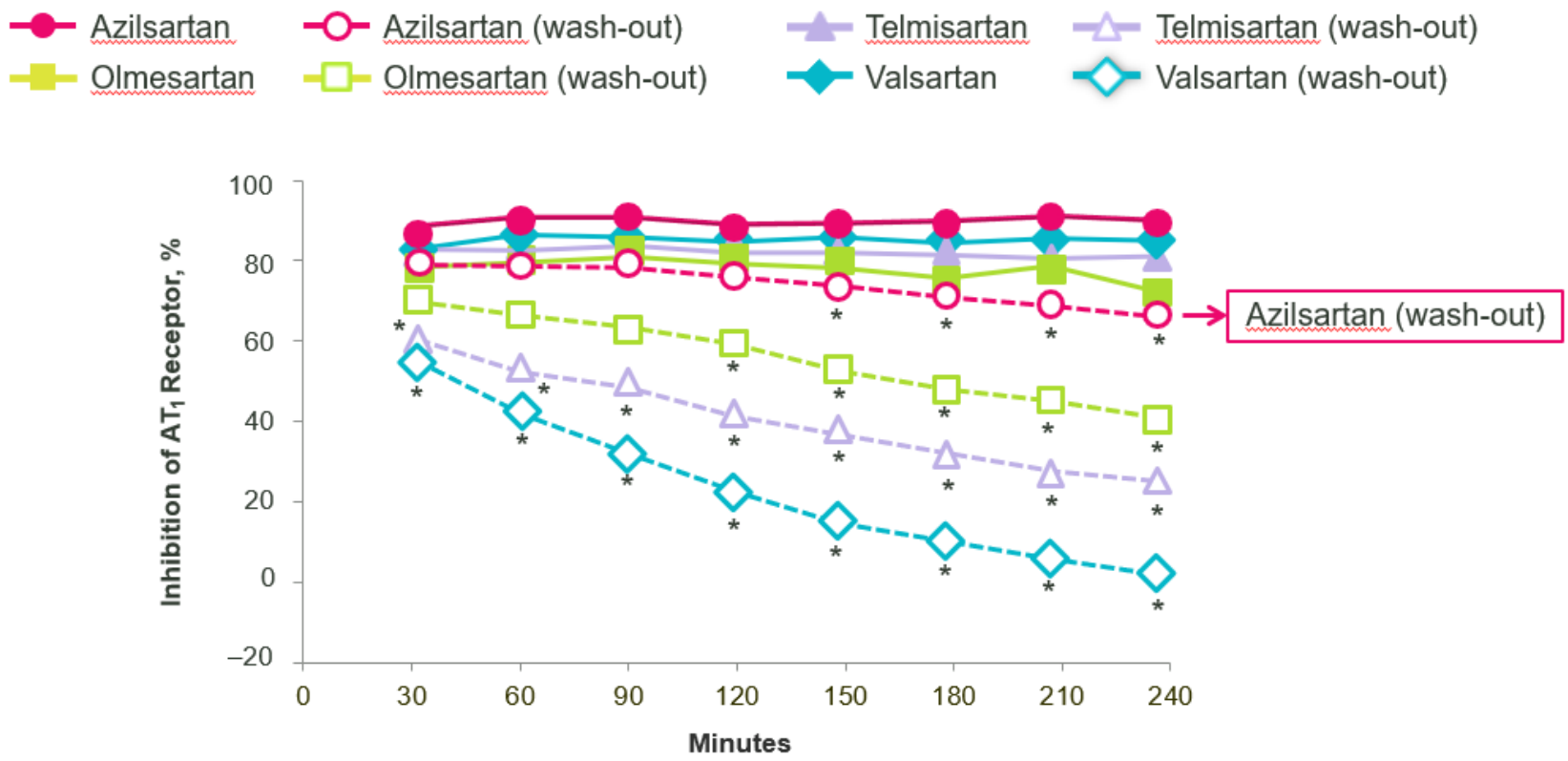
RAAS 수용체 차단제



ACE=angiotensin converting enzyme; ACEI=ACE inhibitor; ADH=antidiuretic hormone; Ang=angiotensin; ARB=angiotensin receptor blocker; AT$_{1-4}$=angiotensin II type 1-4 receptor; DRI=direct renin inhibitor; RAAS=renin-angiotensin-aldosterone-system.

1. Victor RG. In: Bonow RO, et al, eds. *Braunwald's Heart Disease*. 9th edition. Volume I. 2. Philadelphia, PA: Elsevier; 2012:935-954. 3. Santos PCJL, et al. *J Pharmacol Sci*. 2012;120:77-88. 4. Volpe M, et al. *Vasc Health Risk Manag*. 2012;8:371-380. 5. Becari C, et al. *Braz J Med Biol Res*. 2011;44:914-919.

Rate of Dissociation of ARBs from AT_1 Receptor



Statistically significant difference. Azilsartan Medoxomil is a prodrug of Azilsartan.

*P<0.05; **P<0.01 vs presence of the compound.

ARB=angiotensin receptor blocker; AT_1=angiotensin II type 1 receptor.

1. Ojima M, et al. *J Pharmacol Exp Ther*. 2011;336:801-808.

SPRINT Formulary

Class	Drug	Available Strengths	Usual Dose Range / day	Usual Daily Frequency
Diuretic	Chlorthalidone	25 mg	12.5-25 mg	1
	Furosemide	20 mg, 40 mg, 80 mg	20-80 mg	2
	Spironolactone	25 mg	25-50 mg	1
	Triamterene/HCTZ	75/50 mg	37.5/25 – 75/50 mg	1
	Amiloride	5 mg	5-10 mg	1-2
Ace Inhibitor	Lisinopril	5 mg, 10 mg, 20 mg, 40 mg	5-40 mg	1
Angiotensin Receptor Blocker	Losartan	25 mg, 50 mg, 100 mg	25-100 mg	1-2
	Azilsartan	40 mg, 80 mg	40-80 mg	1
	Azilsartan/ chlorthalidone	40/12.5 mg, 40/25 mg	40/12.5 – 40/25 mg	1
Calcium Channel Blockers	Diltiazem	120 mg, 180 mg, 240 mg, 300 mg	120-540 mg	1
	Amlodipine	2.5mg, 5mg, 10mg	2.5-10 mg	1
Beta Blockers	Metoprolol Tartate	25mg, 50mg, 100mg	50-200 mg	1-2
	Atenolol	25mg, 50mg, 100mg	25-100 mg	1
	Atenolol/ Chlorthalidone	50/25 mg	50/25 mg	1
Vasodilators	Hydralazine	25 mg, 50 mg, 100 mg	50/25 mg	2
	Minoxidil	2.5 mg, 10 mg	2.5-80 mg	1-2
Alpha 2 Agonist	Guanfacine	1 mg, 2 mg	0.5-2 mg	1
Alpha Blockers	Doxazosin	1 mg, 2 mg, 4 mg, 8 mg	1-16 mg	1
Potassium Supplements	KCL tablets	20 mEq	20-80 mEq	1-2
	KCL oral solution (10%)	20 mEq/15 ml	20-80 mEq	1-2

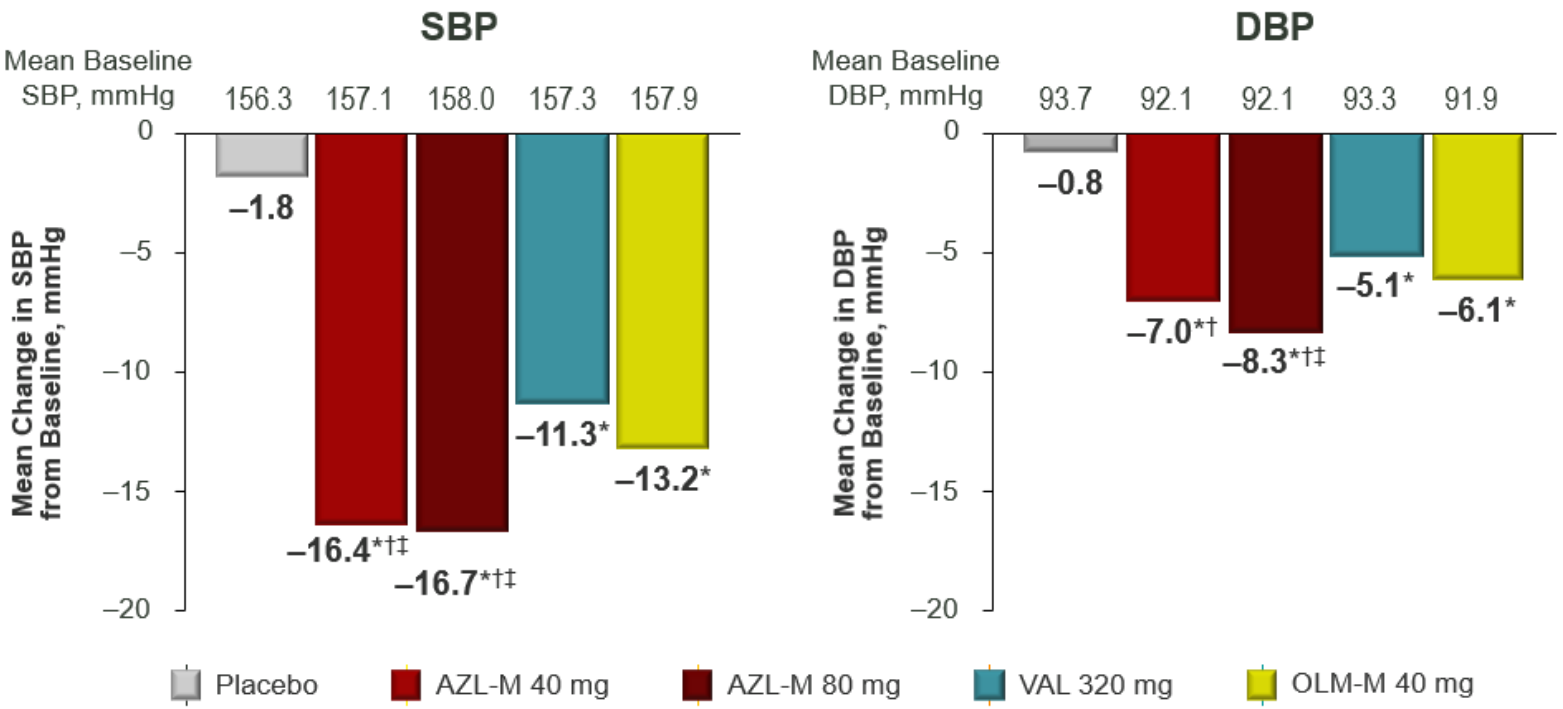
For more detailed information of SPRINT formulary, please refer to "Table S1. SPRINT Formulary" in the Supplementary Appendix.

1. SPRINT Research Group. A Randomized Trial of Intensive versus Standard Blood-Pressure Control. *N Engl J Med* . 2015;373:2103-2116.

Azilsartan medoxoil vs Olmesartan and Valsartan:

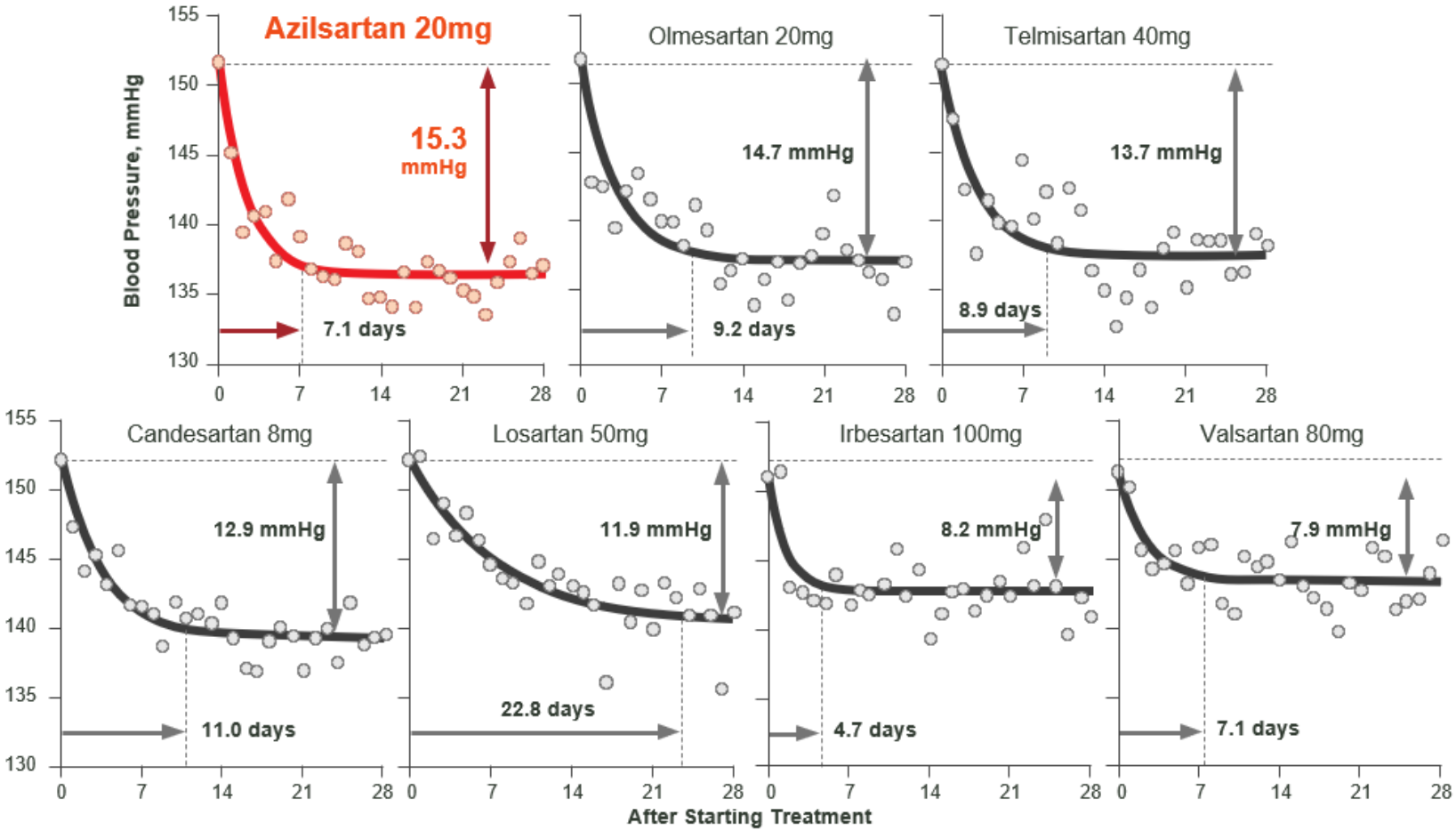
*Change in **Clinic BP** at Week 6*

Change From Baseline to Week 6 in Clinic BP (N=1,291)



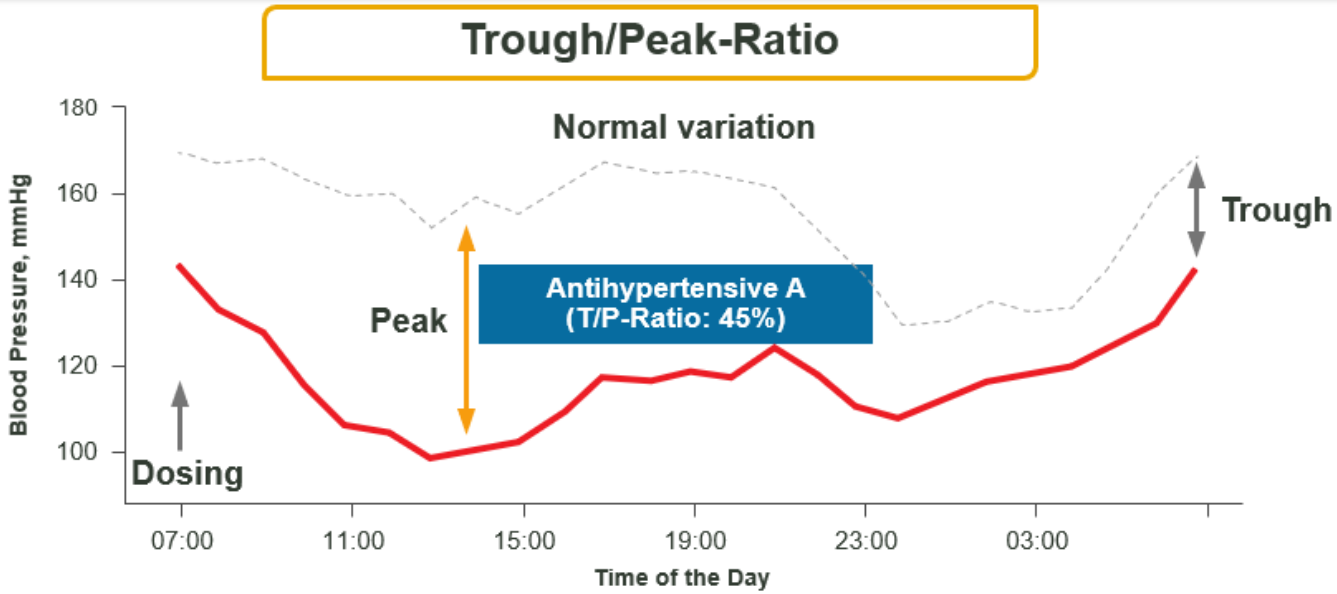
*Statistically significant difference ($P<0.05$) vs placebo; †Statistically significant difference ($P<0.05$) vs VAL; ‡Statistically significant difference ($P<0.05$) vs OLM-M.
AZL-M=azilsartan medoxomil; BP=blood pressure; DBP=diastolic blood pressure; OLM-M=olmesartan medoxomil; SBP=systolic blood pressure; VAL=valsartan.
1. White WB, et al. *Hypertension*. 2011;57:413-420. 2.White WB, et al. Presented at: 25th ASH Annual Scientific Meeting; May 1-4, 2010. New York, NY. Poster PO-242.

Blood Pressure-lowering Effect and Stabilization Time



1. Satoh M, et al. The velocity of antihypertensive effects of seven angiotensin II receptor blockers determined by home blood pressure measurements. *J Hypertens.* 2016;34:1218-1223.

고혈압 치료제 효과의 일관성 평가, T/P Ratio



- ✓ 다음 약물 복용까지 **얼마나 낮은 혈압으로 잘 유지되는지**를 나타내는 지표
- ✓ 개별 환자에서 **약제의 선택, 용량, 투약 시간 관리 등을 결정**하는 데 유용
- ✓ **FDA** 가이드라인에 따르면, 고혈압 치료제 **최소 T/P ratio는 0.5 이상**

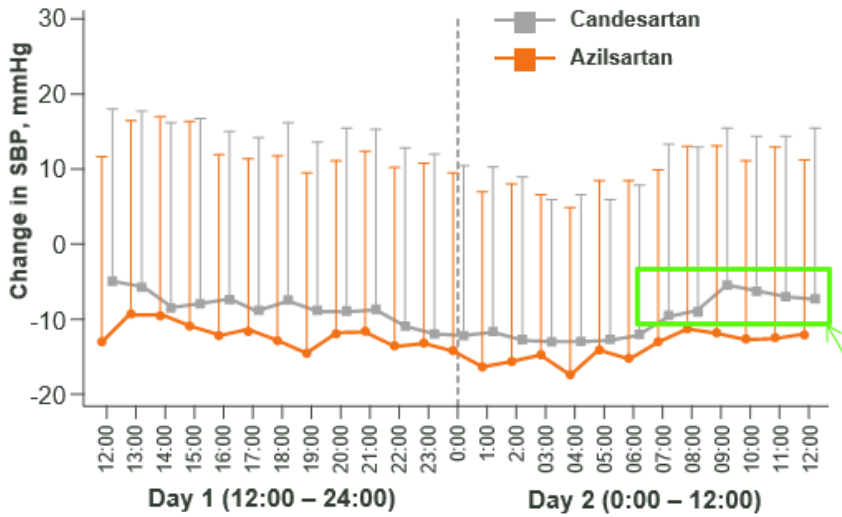
항고혈압 반응의 일관성을 나내는 유용한 지표!

T/P=through-to-peak; FDA=food and drug administration.

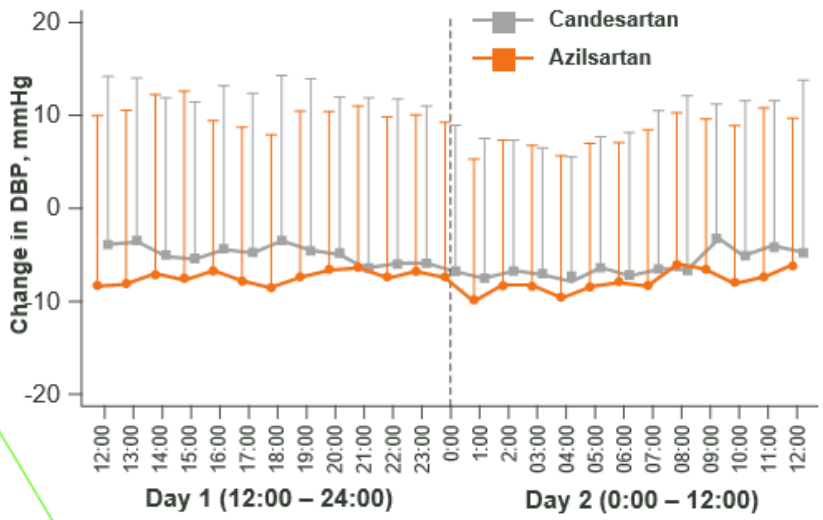
1. Morgan T, et al. Trough to peak ratio as a guide to BP control: measurement and calculation. *J Hum Hypertens.* 1998;12:49-53. 2. Elliott HL. Trough: peak ratio and twenty-four-hour blood pressure control. *J Hypertens Suppl.* 1994;12:S29-S33. 3. Meredith PA. ACE inhibition and AT(1) receptor blockers: efficacy and duration in hypertension. *Heart.* 2000;84(Suppl I):i39-i41.

AZL vs CAND:
24-Hour Time Course BP

Change in SBP from baseline at week 14 on ABPM



Change in DBP from baseline at week 14 on ABPM



Morning surge

Parameter	Azilsartan (n=311)	Candesartan (n=309)
Trough-to-peak ratio at week 14		
DBP	0.97	0.75
SBP	0.95	0.82

1. Rakugi H, et al. *Hypertens Res.* 2012;35:552-558.

SBP T/P Ratios & Half Life for Antihypertensives

Drug class	Monotherapy	SBP T/P ratio or range thereof	$T_{1/2}$ or range thereof (h)
ARB	**Azilsartan**	0.95*	11
	Telmisartan	0.92†	up to 24
	Candesartan	0.82*	9
	Olmesartan	0.60-0.80‡	13
	Valsratan	0.65*	6
	Losartan	0.62*	2 (6-9 for metabolite)
	Irbesartan	0.57*	11-15
CCB	Amlodipine	0.85*	35-50
ACEi	Ramipril	0.50-0.63*	2

가장 안정적으로 혈압강하효과를 지속하는
Azilsartan !

*Mean values; †Ratio of reduction in trough BP to reduction in maximal diurnally-adjusted BP; ‡Not mentioned.
T/P=through-to-peak; SBP=systolic blood pressure; ARB=angiotensin receptor blocker; CCB=calcium channel blocker; ACEi=angiotensin converting enzyme inhibitor; $T_{1/2}$=half life.

1. Parati G, et al. *Hypertens Res.* 2014;37:187-193.

Take-Home Message

- Stroke and Hypertension are big health issues in rapidly aging societies like Korea.
- Therapeutic target of BP is lowered in new guidelines.
- Initiation of antihypertensive drug therapy with 2 first-line agents of different classes, as a single pill combination, is recommended in all guideline.