

2019 Pfizer Medical Forum

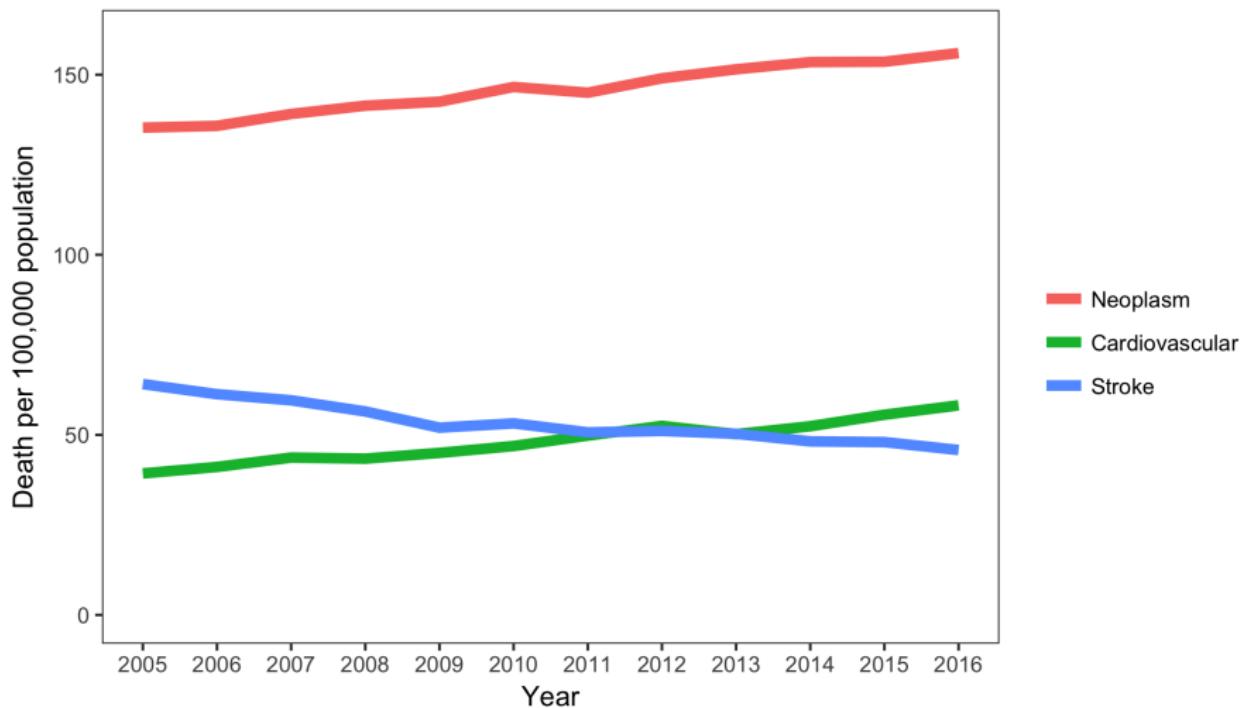
## Management of Stroke Patients in Primary Care



Kwang-Yeol Park

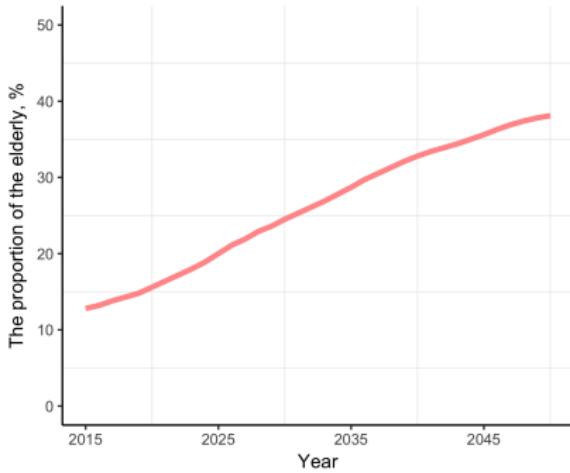
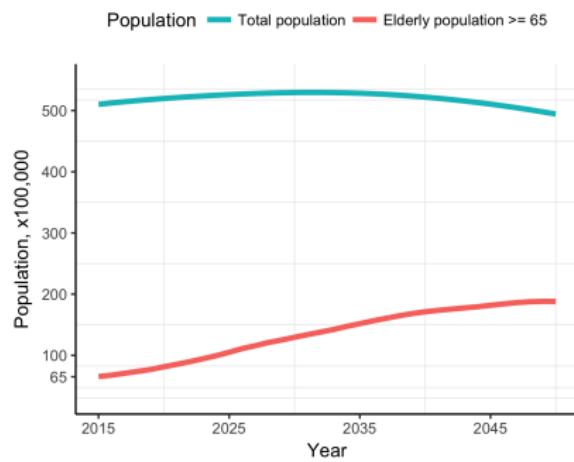
Dep. of Neurology, Chung-Ang University, Seoul South Korea

# Secular trend of mortality in Korea



[http://www.index.go.kr/potal/main/EachDtlPageDetail.do?idx\\_cd=1012](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/>

# 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

# Stroke has diverse etiologies

## Ischemic Stroke

- Atherosclerosis
- Lacunar infarction
- Cardiac disease causing embolism
- Other causes such as moyamoya disease

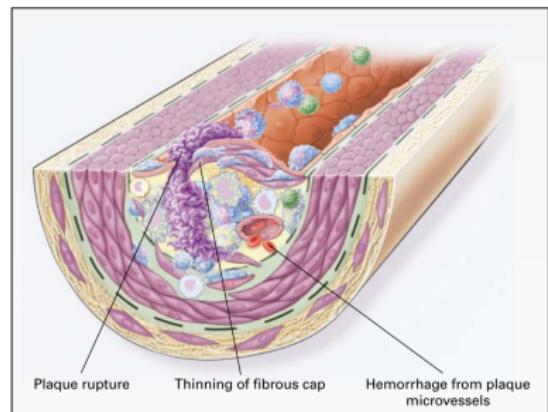
## Hemorrhagic Stroke

- Hypertensive hemorrhage
- Cerebral amyloid angiopathy
- Arteriovenous malformations
- Subarachnoid hemorrhage

Treatment should be decided according to the etiologies

# Atherosclerosis: Leading cause of ischemic stroke

- Artery wall thickens as a result of invasion and accumulation of white blood cells with cholesterol fatty substances, calcium and fibrin.
- Intima of medium and large sized systemic arteries are involved.



Ross R. N Engl J Med 1999

# Cerebral small vessel disease

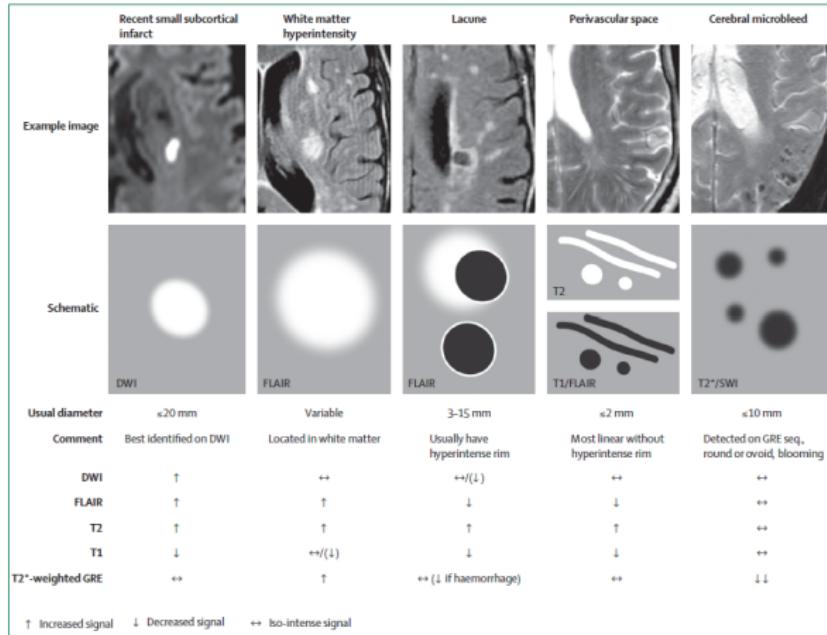


Figure 2: MRI findings for lesions related to small vessel disease

Wardlaw JM et al. Lancet Neurol 2013; 12: 822–38

# Cardioembolic stroke

- 비판막성 심방세동
- 인공판막
- 좌심실 혈전증
- 점액종
- 감염성 심뇌막염

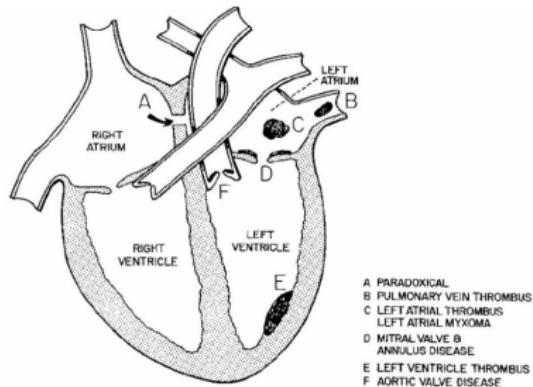


Figure 1. Cardiac causes of stroke (Adapted from Barnett et al)

## Chain of Events

**Dyslipidemia, DM, HTN, Aging**



**Atherosclerosis, Arterial stiffness  
Atrial fibrillation**



**Coronary artery disease  
Ischemic stroke  
Peripheral arterial disease**

# Table of contents

- 1 Atrial fibrillation and stroke
- 2 Recent lipid guidelines
- 3 Statin for Atherosclerotic stroke or Any stroke ?
- 4 Hypertension and Stroke
- 5 Hypertension Guidelines
- 6 Summary

# Risk factors for Stroke

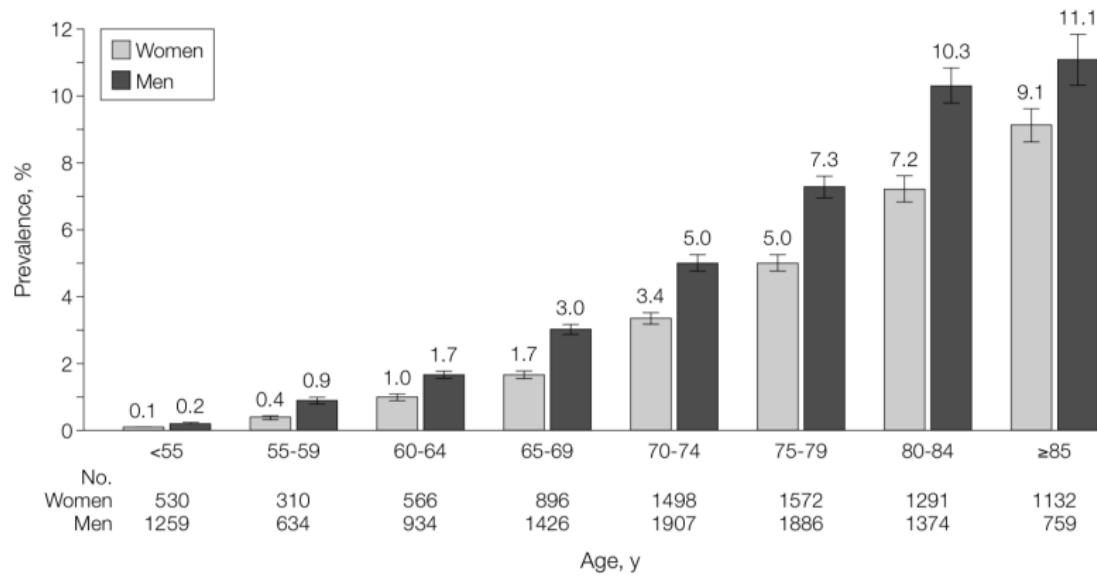
## Non-modifiable factors

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

## Modifiable factors

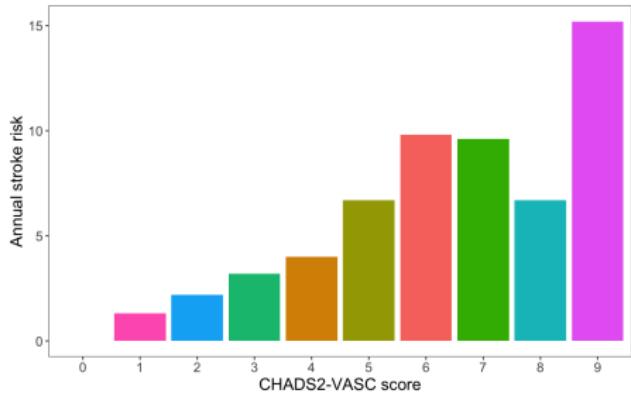
- ① Hypertension
- ② Diabetes
- ③ Dyslipidemia
- ④ Smoking
- ⑤ Carotid disease
- ⑥ Cardiac disease such as **atrial fibrillation**
- ⑦ Obesity
- ⑧ Inactivity

# Prevalence of AF by age



# Thromboembolic risk of AF

<i>CHA<sub>2</sub>DS<sub>2</sub>-VASc</i> criteria	Score
CHF	1
Hypertension	1
Age $\geq$ 75 years	2
Diabetes mellitus	1
Stroke/TIA or embolism	2
Vascular disease	1
Age 65-74 years	1
Sex category (female)	1



Gage BF et al. JAMA 2001;285:2864–70; Lip G et al. Chest 2010;137:263–72  
 January, C. T., et al. Circulation 2014

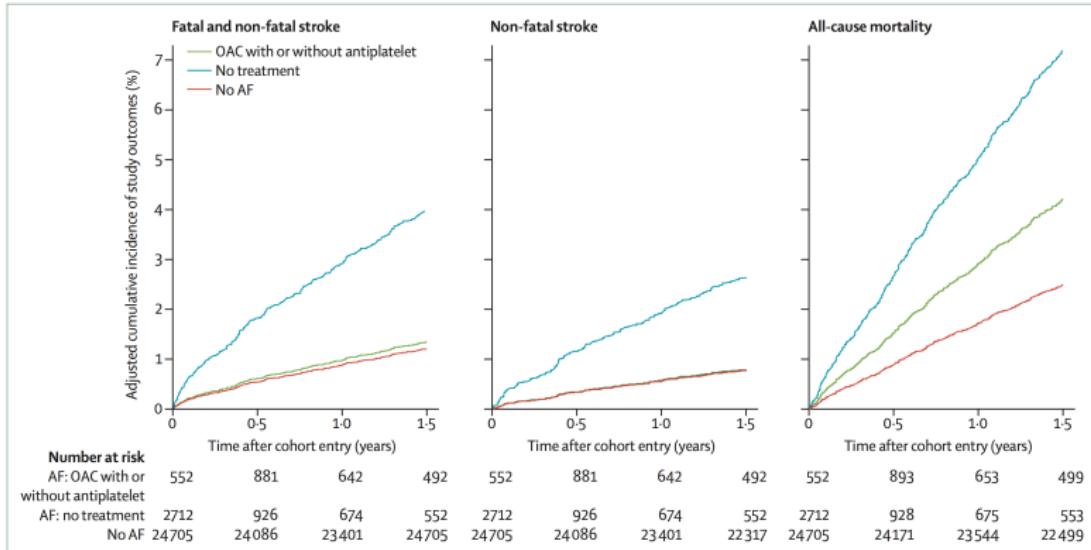
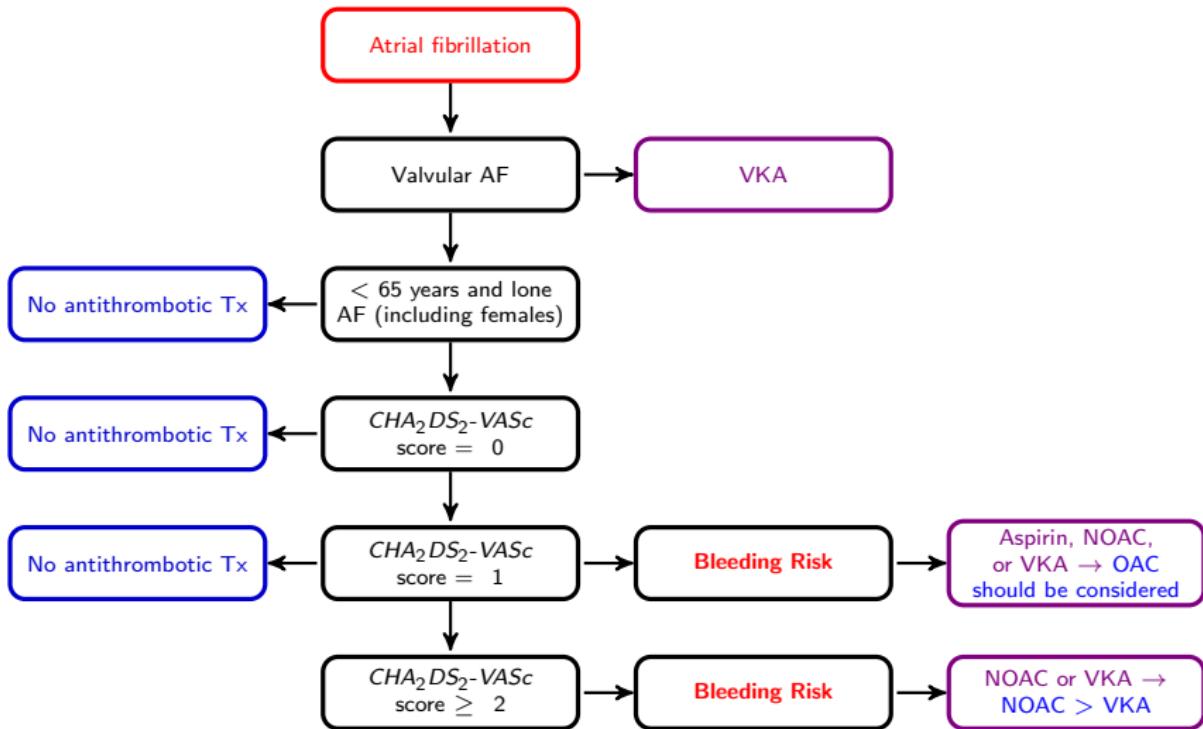


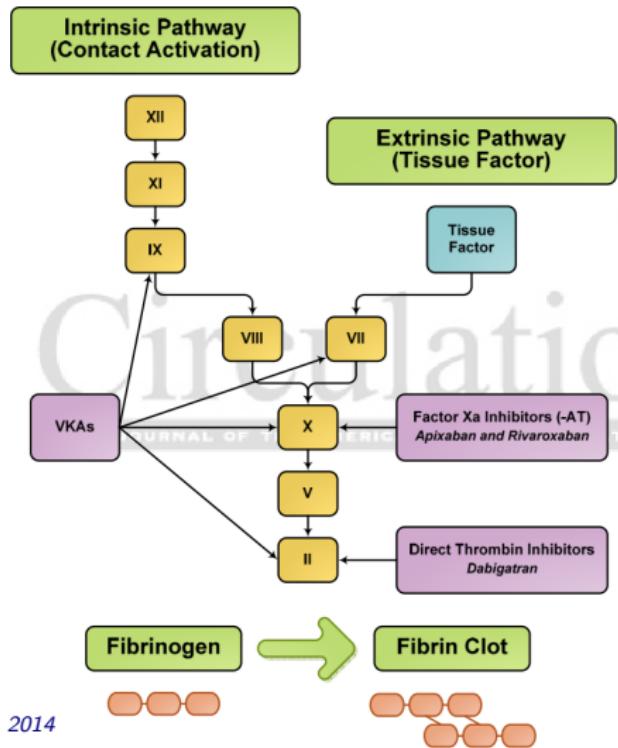
Figure 2: Effect of treatment on incidentally detected atrial fibrillation

AF=atrial fibrillation. OAC=oral anticoagulant. Reproduced with permission from Freedman and colleagues.<sup>21</sup>



Camm, A. J., et al. Eur Heart J. 2012; Meschia, J. F., et al. Stroke 2014; Kirchhof et al. Eur Heart J 2016

# Selection of anticoagulants



January, C. T., et al. Circulation 2014

# VKA has been underused

- Narrow therapeutic margin
- Slow onset and offset of action
- Interindividual variability in anticoagulant effect
- Numerous food and drug interaction
- Frequent INR testing

## In-Depth Review

# Vitamin K-dependent Proteins, Warfarin, and Vascular Calcification

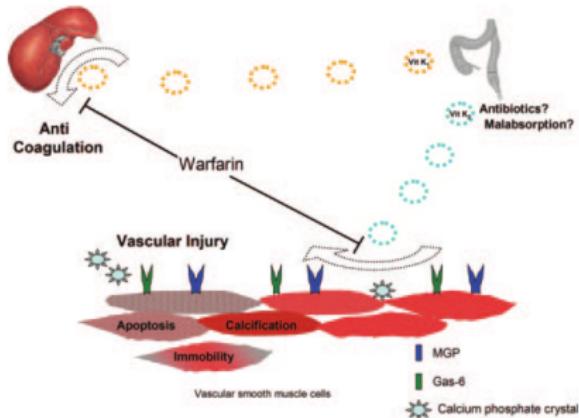
John Danziger

*Renal Division, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts*

Vitamin K-dependent proteins (VKDPs) require carboxylation to become biologically active. Although the coagulant factors are the most well-known VKDPs, there are many others with important physiologic roles. Matrix Gla Protein (MGP) and Growth Arrest Specific Gene 6 (Gas-6) are two particularly important VKDPs, and their roles in vascular biology are just beginning to be understood. Both function to protect the vasculature; MGP prevents vascular calcification and Gas-6 affects vascular smooth muscle cell apoptosis and movement. Unlike the coagulant factors, which undergo hepatic carboxylation, MGP and Gas-6 are carboxylated within the vasculature. This peripheral carboxylation process is distinct from hepatic carboxylation, yet both are inhibited by warfarin administration. Warfarin prevents the activation of MGP and Gas-6, and in animals, induces vascular calcification. The relationship of warfarin to vascular calcification in humans is not fully known, yet observational data suggest an association. Given the high risk of vascular calcification in those patients with chronic kidney disease, the importance of understanding warfarin's effect on VKDPs is paramount. Furthermore, recognizing the importance of VKDPs in vascular biology will stimulate new areas of research and offer potential therapeutic interventions.

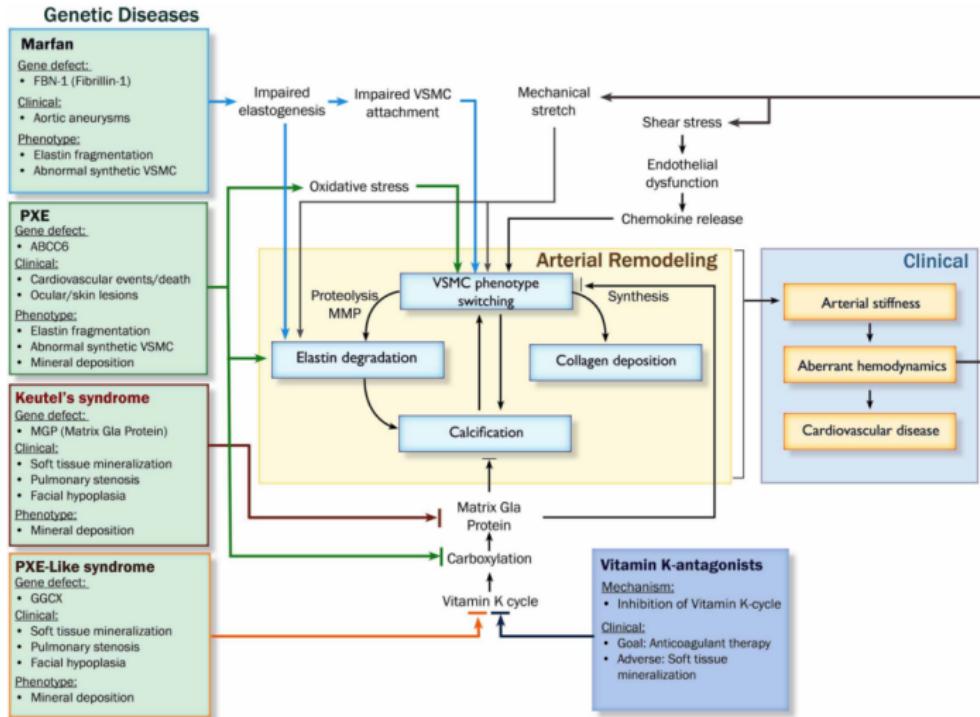
*Clin J Am Soc Nephrol* 3: 1504–1510, 2008. doi: 10.2215/CJN.00770208

Danziger J. *J Am Soc Nephrol*. 2008



**Warfarin inhibits hepatic and peripheral carboxylation.** Warfarin prevents vitamin K from participating in the carboxylation process, inhibiting both hepatic and peripheral production of VKDPs. The well-known therapeutic effect is anticoagulation. However, warfarin also inhibits activation of MGP and Gas-6, interrupting the protective mechanisms of these proteins. Vascular smooth muscle cells are unable to respond to injury in a normal manner, and potentially, cell death and eventual calcification ensue.

Danzier J. J Am Soc Nephrol. 2008

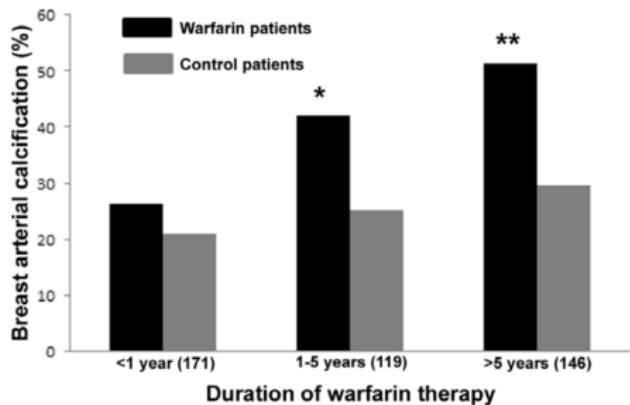


**FIGURE 3 | Pathophysiological pathways leading to arterial remodeling in genetic and cardiovascular disease.** Abbreviations: PXE, pseudoxanthoma elasticum; MMP, matrix metalloproteinases; VSMC, vascular smooth muscle cell; GGCX, gamma glutamyl transferase.

van Varik BJ, et al. *Frontiers in genetics*. 2012

## Increased Vascular Calcification in Patients Receiving Warfarin

Ekamol Tantisattamo, Kum Hyun Han, W. Charles O'Neill

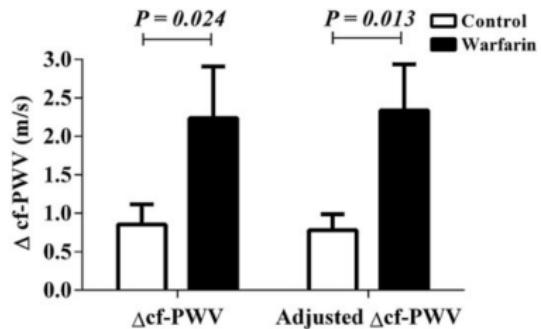


**Figure 3.** Effect of warfarin duration on breast arterial calcification. Control patients (no warfarin therapy) were matched for age and diabetes mellitus status. The number of patients is given in parentheses. \* $P=0.009$ ; \*\* $P=0.0002$ .

Tantisattamo, E., et al. (2015). *Arterioscler Thromb Vasc Biol* 35(1): 237-242.

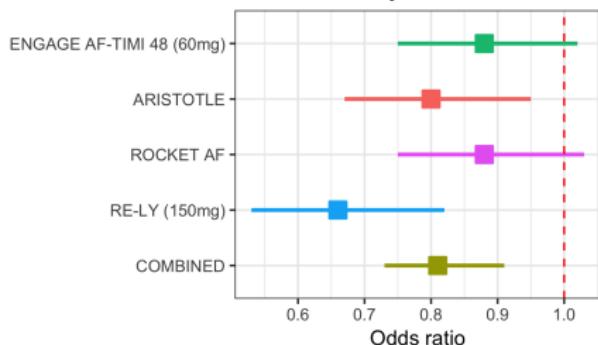
## The impact of warfarin on the rate of progression of aortic stiffness in hemodialysis patients: a longitudinal study

Fabrice Mac-Way<sup>1,2</sup>, Aurélie Poulin<sup>1,2</sup>, Mihai Silviu Utescu<sup>1,2</sup>, Sacha A. De Serres<sup>1,2</sup>, Karine Marquis<sup>1</sup>, Pierre Douville<sup>3,4</sup>, Simon Desmeules<sup>1,2</sup>, Richard Larivière<sup>1,2</sup>, Marcel Lebel<sup>2</sup> and Mohsen Agharazii<sup>1,2</sup>

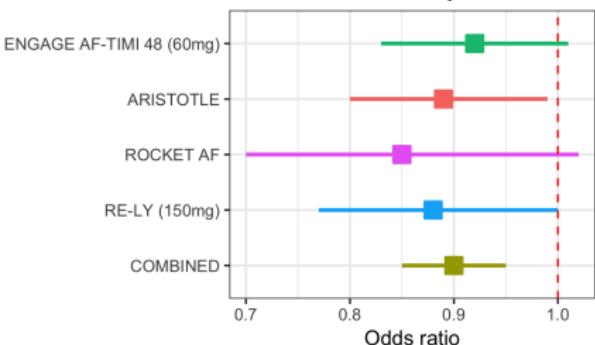


**FIGURE 1:** Changes in aortic stiffness. Changes in aortic stiffness as measured by changes (open triangle) in carotid-femoral pulse wave velocity (cf-PWV) are shown in the control (open square) and the warfarin groups (filled square), as raw data (left part of graph) and adjusted (right part of graph) for a duration of follow-up of 1.2 years and adjusted for changes in MBP. Values are mean  $\pm$  SEM.

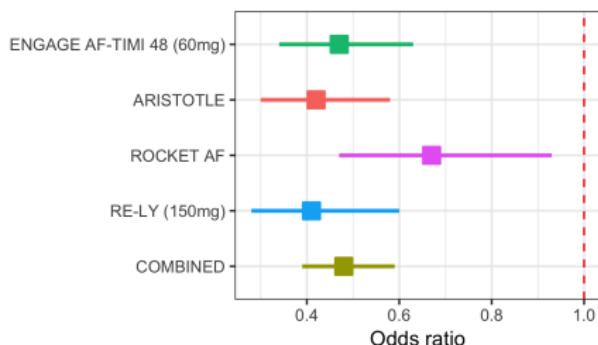
## Stroke and systemic embolism



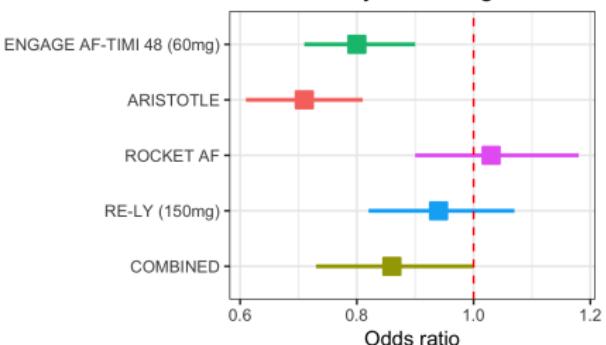
## Mortality



## ICH



## Major bleeding



# Risk factors for Stroke

## Non-modifiable factors

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

## Modifiable factors

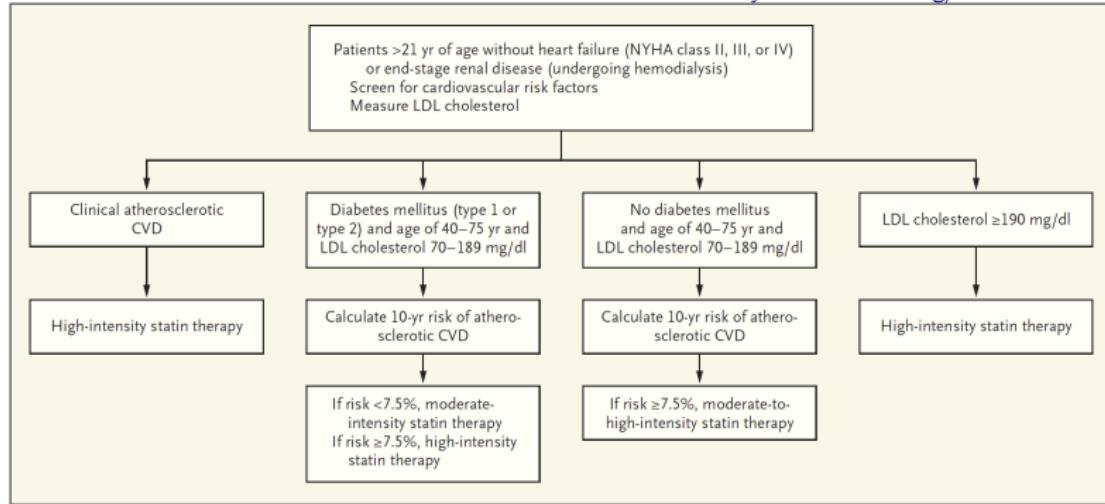
- ① Hypertension
- ② Diabetes
- ③ **Dyslipidemia**
- ④ Smoking
- ⑤ Carotid disease
- ⑥ Cardiac disease such as atrial fibrillation
- ⑦ Obesity
- ⑧ Inactivity

# Guidelines

- 2013 American College of Cardiology/American Heart Association (ACC/AHA)
- 2014 United Kingdom's National Institute for Health and Care Excellence (NICE)
- 2016 Canadian Cardiovascular Society (CCS),  
U.S. Preventive Services Task Force (USPSTF), and  
European Society of Cardiology/European Atherosclerosis Society (ESC/EAS)
- 2017 Japan Atherosclerosis Society Guidelines
- 2018 American Stroke Association (Secondary Prevention)
- 2018 Korean Society of Lipid and Atherosclerosis (KSoLA)
- 2018 American Heart Association

# 2013 ACC/AHA Guideline on the Tx of Blood Chol. to Reduce Atherosclerotic CV Risk in Adults

[my.americanheart.org/cvriskcalculator](http://my.americanheart.org/cvriskcalculator)



Stone NJ, et al. JACC. 2013; Keaney JF, et al. N Engl J Med. 2013

# 2013 ACC/AHA Guideline on the Tx of Blood Chol. to Reduce Atherosclerotic CV Risk in Adults

**Table 1.** High-Intensity and Moderate-Intensity Statin Therapy, According to 2013 American College of Cardiology–American Heart Association (ACC-AHA) Cholesterol Guidelines.

### High-intensity statin therapy

Daily dose lowers LDL cholesterol level by approximately  $\geq 50\%$  on average

Recommended: atorvastatin, 40 to 80 mg; rosuvastatin, 20 to 40 mg

### Moderate-intensity statin therapy

Daily dose lowers LDL cholesterol level by approximately 30 to  $< 50\%$  on average

Recommended: atorvastatin, 10 to 20 mg; rosuvastatin, 5 to 10 mg; simvastatin, 20 to 40 mg; pravastatin, 40 to 80 mg; lovastatin, 40 mg; extended-release fluvastatin, 80 mg; fluvastatin, 40 mg twice a day; pitavastatin, 2 to 4 mg

## AHA/ASA Guideline

# 2018 Guidelines for the Early Management of Patients With Acute Ischemic Stroke

**A Guideline for Healthcare Professionals From the American Heart  
Association/American Stroke Association**

*Reviewed for evidence-based integrity and endorsed by the American Association of Neurological  
Surgeons and Congress of Neurological Surgeons*

*Endorsed by the Society for Academic Emergency Medicine*

<b>CLASS III: No Benefit (MODERATE)</b> <i>(Generally, LOE A or B use only)</i>	<b>Benefit = Risk</b>
Suggested phrases for writing recommendations: <ul style="list-style-type: none"><li>■ Is not recommended</li><li>■ Is not indicated/useful/effective/beneficial</li><li>■ Should not be performed/administered/other</li></ul>	
<b>CLASS III: Harm (STRONG)</b>	<b>Risk &gt; Benefit</b>
Suggested phrases for writing recommendations: <ul style="list-style-type: none"><li>■ Potentially harmful</li><li>■ Causes harm</li><li>■ Associated with excess morbidity/mortality</li><li>■ Should not be performed/administered/other</li></ul>	

## 6.5. Cholesterol

6.5. Cholesterol	COR	LOE	New, Revised, or Unchanged
1. Routine measurement of blood cholesterol levels in all patients with ischemic stroke presumed to be of atherosclerotic origin who are not already taking a high-intensity statin is not recommended.	III: No Benefit	B-R	New recommendation.
2. Measurement of blood cholesterol levels in patients with ischemic stroke presumed to be of atherosclerotic origin who are already taking an optimized regimen of statin therapy may be useful for identifying patients who would be candidates for outpatient proprotein convertase subtilisin/kexin type 9 inhibitor treatment to reduce the risk of subsequent cardiovascular death, MI, or stroke.	IIb	B-R	New recommendation.

Level of LDL-cholesterol is not important in patients with atherosclerotic stroke.

The “2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults” recommend statin therapy for secondary prevention for adults with clinical atherosclerotic cardiovascular disease (ASCVD), including stroke presumed to be of atherosclerotic origin. No data were identified for treatment or titration to a specific low-density lipoprotein cholesterol (LDL-C) goal.<sup>7</sup> The 2016 European Society of Cardiology/European Atherosclerosis Society guidelines for the management of dyslipidemias and the 2014 guidelines from the UK National Institute for Health Care Excellence also contain recommendations based on clinical factors and not blood cholesterol measurements.<sup>305,306</sup> Thus, statin therapy can be recommended in patients with stroke presumed to be of atherosclerotic origin without measurement of blood cholesterol. For patients with ischemic stroke that is presumed to be the result of nonatherosclerotic disease such as arterial dissection, measurement of blood cholesterol may be of value because the primary prevention guidelines are based on LDL-C levels.<sup>7</sup> It is of note that the 2012 Canadian Cardiovascular

# 2016 ESC/EAS guideline



EUROPEAN  
SOCIETY OF  
CARDIOLOGY®

European Heart Journal (2016) **37**, 2999–3058  
doi:10.1093/eurheartj/ehw272

**ESC/EAS GUIDELINES**

## **2016 ESC/EAS Guidelines for the Management of Dyslipidaemias**

**The Task Force for the Management of Dyslipidaemias of the  
European Society of Cardiology (ESC) and European Atherosclerosis  
Society (EAS)**

**Developed with the special contribution of the European Association  
for Cardiovascular Prevention & Rehabilitation (EACPR)**

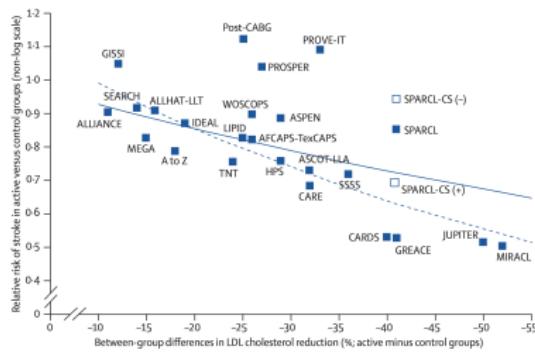
**Authors/Task Force Members: Alberico L. Catapano\* (Chairperson) (Italy),**

# Treatment goal in ESC

**Table 10 Treatment targets and goals for cardiovascular disease prevention**

<b>Smoking</b>	No exposure to tobacco in any form.
<b>Diet</b>	Healthy diet low in saturated fat with a focus on whole grain products, vegetables, fruit and fish.
<b>Physical activity</b>	2.5–5 h moderately vigorous physical activity per week or 30–60 min most days.
<b>Body weight</b>	BMI 20–25 kg/m <sup>2</sup> ; waist circumference <94 cm (men) and <80 cm (women).
<b>Blood pressure</b>	<140/90 mmHg <sup>a</sup>
<b>Lipids LDL-C is the primary target<sup>b</sup></b>	<b>Very high-risk:</b> LDL-C <1.8 mmol/L (70 mg/dL) or a reduction of at least 50% if the baseline <sup>c</sup> is between 1.8 and 3.5 mmol/L (70 and 135 mg/dL).
	<b>High-risk:</b> LDL-C <2.6 mmol/L (100 mg/dL) or a reduction of at least 50% if the baseline <sup>c</sup> is between 2.6 and 5.2 mmol/L (100 and 200 mg/dL).
	<b>Low to moderate risk:</b> LDL-C <3.0 mmol/L (115 mg/dL).
	Non-HDL-C secondary targets are <2.6, 3.4 and 3.8 mmol/L (100, 130 and 145 mg/dL) for very high-, high- and moderate-risk subjects, respectively.
	HDL-C: no target, but >1.0 mmol/L (40 mg/dL) in men and >1.2 mmol/L (48 mg/dL) in women indicates lower risk.
<b>Diabetes</b>	TG: no target but <1.7 mmol/L (150 mg/dL) indicates lower risk and higher levels indicate a need to look for other risk factors.
	HbA1c: <7% (<53 mmol/mol).

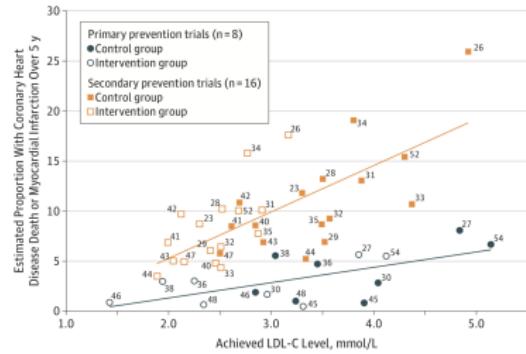
# Dose-response relationship in Stroke/IHD and LDL-C



## Estimates of relative risk reduction

- 10% LDL reduction: relative risk reduction 7.5% (2.3-12.5) overall  
relative risk reduction 13.5% (7.7-18.8) for primary prevention of stroke
- 1 mmol/l (39 mg/dl) LDL reduction: relative risk reduction 21.1% (6.3-33.5) overall  
relative risk reduction 35.9% (21.7-47.6) for primary prevention of stroke

Figure 4. Association Between Achieved Low-Density Lipoprotein Cholesterol (LDL-C) and Major Coronary Event Rates From 24 Trials of Established Interventions That Lower LDL-C Predominantly Through Upregulation of LDL Receptor Expression



Amarenco et al. Lancet Neurol 2009;8:453-463; Silverman MG et al. JAMA 2016

# Reason: Treatment goal

- Systematic reviews confirming the dose-dependent reduction in CVD with LDL-C lowering;  
the greater the LDL-C reduction, the greater the CV risk reduction
- The benefits related to LDL-C reduction are not specific for statin therapy.
- The use of goals can also aid patient–doctor communication.

**Very high-risk**

Subjects with any of the following:

- Documented cardiovascular disease (CVD), clinical or unequivocal on imaging. Documented CVD includes previous myocardial infarction (MI), acute coronary syndrome (ACS), coronary revascularisation (percutaneous coronary intervention (PCI), coronary artery bypass graft surgery (CABG)) and other arterial revascularization procedures, stroke and transient ischaemic attack (TIA), and peripheral arterial disease (PAD). Unequivocally documented CVD on imaging is what has been shown to be strongly predisposed to clinical events, such as significant plaque on coronary angiography or carotid ultrasound.
- DM with target organ damage such as proteinuria or with a major risk factor such as smoking, hypertension or dyslipidaemia.
- Severe CKD (GFR <30 mL/min/1.73 m<sup>2</sup>).
- A calculated SCORE ≥10% for 10-year risk of fatal CVD.

# Intensive statin for non-cardioembolic stroke or TIA

**Table 33 Recommendations for lipid-lowering drugs for primary and secondary prevention of stroke**

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>	Ref <sup>c</sup>
Statin therapy to reach established treatment goals is recommended in patients at high or very high CV risk for primary prevention of stroke.	I	A	64, 65, 422, 426
Lipid-lowering therapy is recommended in patients with other manifestations of CVD for primary prevention of stroke.	I	A	63–65, 422, 426
Intensive statin therapy is recommended in patients with a history of non-cardioembolic ischaemic stroke or TIA for secondary prevention of stroke	I	A	422, 428

CVD = cardiovascular disease; TIA = transient ischaemic attack.

<sup>a</sup>Class of recommendation.

<sup>b</sup>Level of evidence.

<sup>c</sup>Reference(s) supporting recommendations.

# Treatment goal

## 9.12.2 Secondary prevention of stroke

Following stroke or TIA, patients are at risk not only of recurrent cerebrovascular events, but also of other major CV events, including MI. Secondary prevention therapy with statins reduces the risk of recurrent stroke (by 12%), MI and vascular death.<sup>422,428</sup> Statin pre-treatment at TIA onset was associated with reduced recurrent early stroke risk in patients with carotid stenosis in a pooled data analysis, supporting an as-early-as-possible initiation of statins after stroke.<sup>429</sup> However, the aetiology of stroke may influence the response to statins, and those patients with evidence of atherosclerosis underlying their cerebrovascular events appear to benefit most, while those with haemorrhagic stroke may not benefit.<sup>422</sup>

THE KOREAN SOCIETY OF LIPID AND ATHEROSCLEROSIS

2018

<http://www.lipid.or.kr>

# 이상지질혈증 치료지침

제4판

Korean Guidelines for the Management of Dyslipidemia 4th ed

한국지질·동맥경화학회 진료지침위원회

Committee of Clinical Practice Guideline of The Korean Society of Lipid and Atherosclerosis (KSoLA)

한국지질동맥경화학회, 2018



# 위험도 분류에 따른 LDL 콜레스테롤 및 Non-HDL 콜레스테롤의 치료 목표치

위험도	LDL 콜레스테롤 (mg/dL)	Non-HDL 콜레스테롤 (mg/dL)
초고위험군	관상동맥질환	
	죽상경화성 혈관뇌졸증 및 일과성뇌혈관발작	< 70
	말초혈관질환	< 100
고위험군	경동맥질환 <sup>1)</sup>	
	복부동맥류	< 100
	당뇨병 <sup>2)</sup>	< 130
중등도 위험군	주요위험인자 <sup>3)</sup> 2개 이상	< 130
저위험군	주요위험인자 <sup>3)</sup> 1개 이하	< 160
		< 190

1) 유의한 경동맥 협착이 확인된 경우

2) 표적장기손상 혹은 심혈관질환의 주요위험인자를 가지고 있는 경우 환자에 따라서 목표치를 하향조정할 수 있다.

3) 연령(남 ≥ 45세, 여 ≥ 55세), 관상동맥질환 조기발병 가족력, 고혈압, 흡연, 저HDL 콜레스테롤

# 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA.. Guideline on the Management of Blood Cholesterol

Figure 1. Secondary Prevention in Patients With Clinical ASCVD

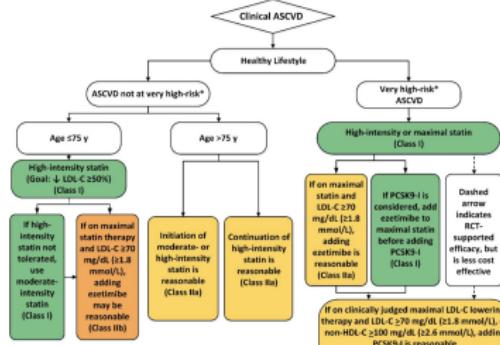
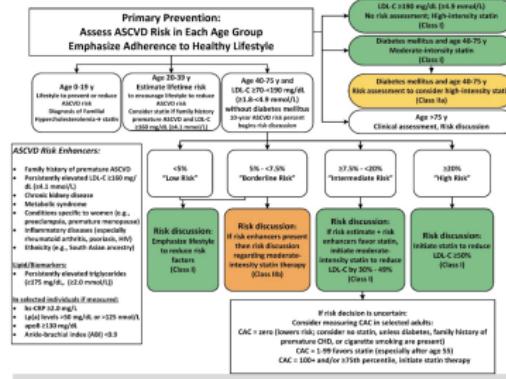


Figure 2. Primary Prevention



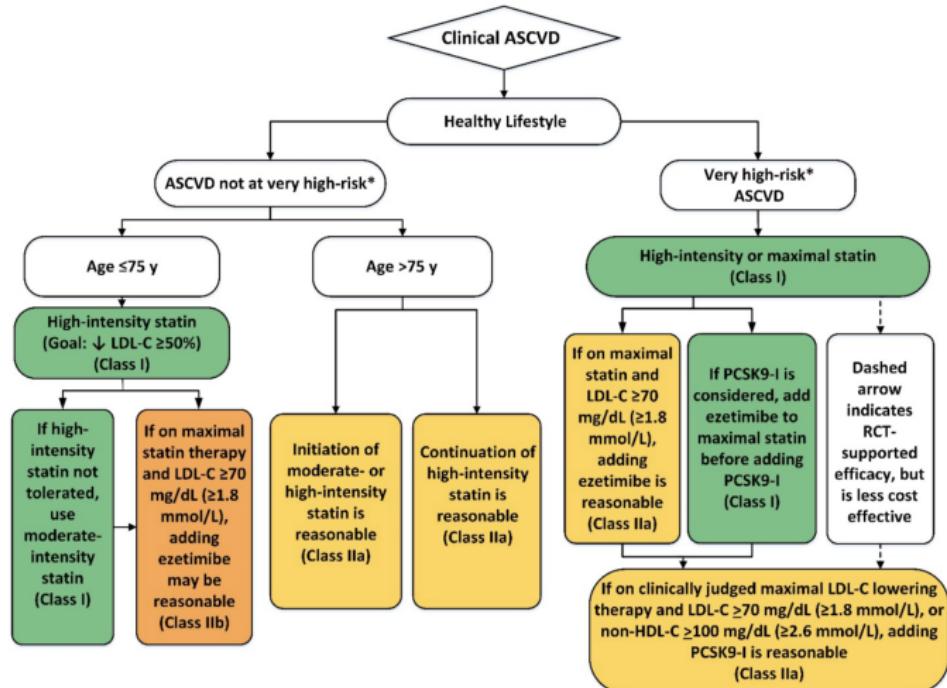
Grundy SM, et al. 10 Nov 2018 Circulation. 2018;0:CIR.0000000000000625

**Table 4. Very High-Risk\* of Future ASCVD Events**

<b>Major ASCVD Events</b>
Recent ACS (within the past 12 mo)
History of MI (other than recent ACS event listed above)
History of ischemic stroke
Symptomatic peripheral arterial disease (history of claudication with ABI <0.85, or previous revascularization or amputation (S4.1-39))
<b>High-Risk Conditions</b>
Age ≥65 y
Heterozygous familial hypercholesterolemia
History of prior coronary artery bypass surgery or percutaneous coronary intervention outside of the major ASCVD event(s)
Diabetes mellitus
Hypertension
CKD (eGFR 15-59 mL/min/1.73 m <sup>2</sup> ) (S4.1-15, S4.1-17)
Current smoking
Persistently elevated LDL-C (LDL-C ≥100 mg/dL [≥2.6 mmol/L]) despite maximally tolerated statin therapy and ezetimibe
History of congestive HF



\*Very high-risk includes a history of multiple major ASCVD events or one major ASCVD event and multiple high-risk conditions.

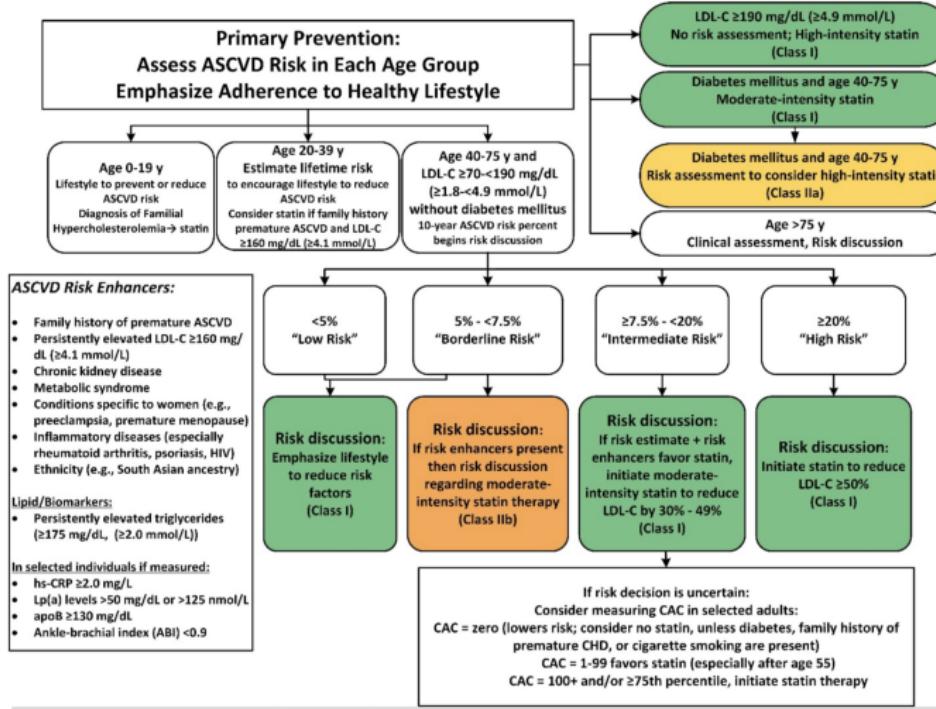
**Figure 1. Secondary Prevention in Patients With Clinical ASCVD**

Colors correspond to Class of Recommendation in Table 2.

Clinical ASCVD consists of acute coronary syndrome (ACS), those with history of myocardial infarction (MI), stable or unstable angina or coronary other arterial revascularization, stroke, transient ischemic attack (TIA), or peripheral artery disease (PAD) including aortic aneurysm, all of atherosclerotic origin.

Grundy SM, et al. 10 Nov 2018 Circulation. 2018;0:CIR.0000000000000625

Figure 2. Primary Prevention





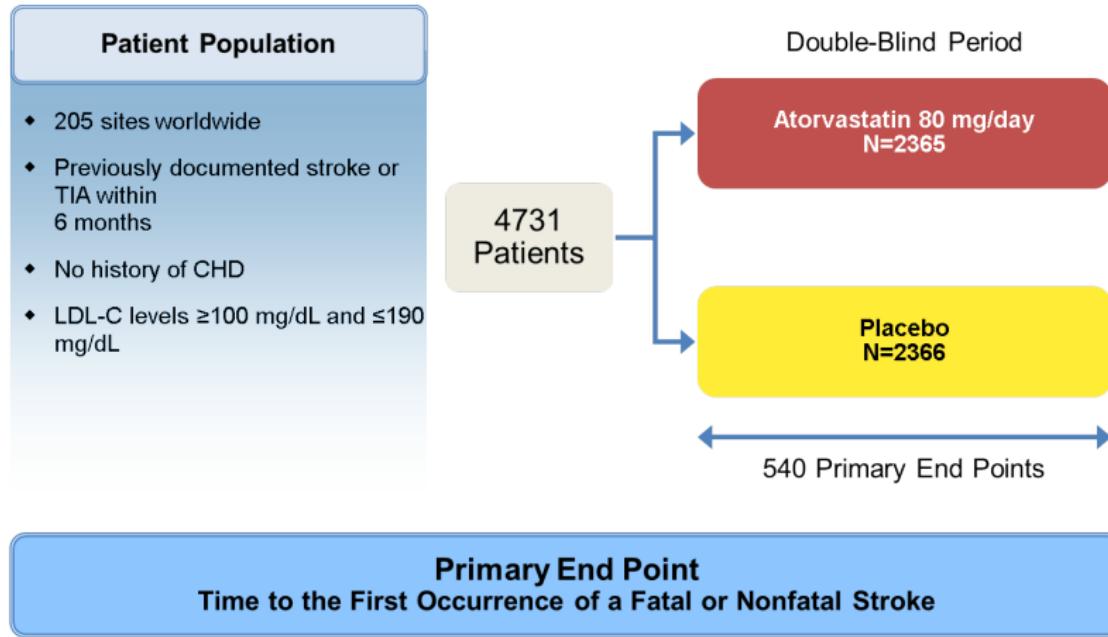
#### 4.4.3. Monitoring in Response to LDL-C-Lowering Therapy

##### Recommendation for Monitoring

Referenced studies that support the recommendation are summarized in [Online Data Supplement 17](#).

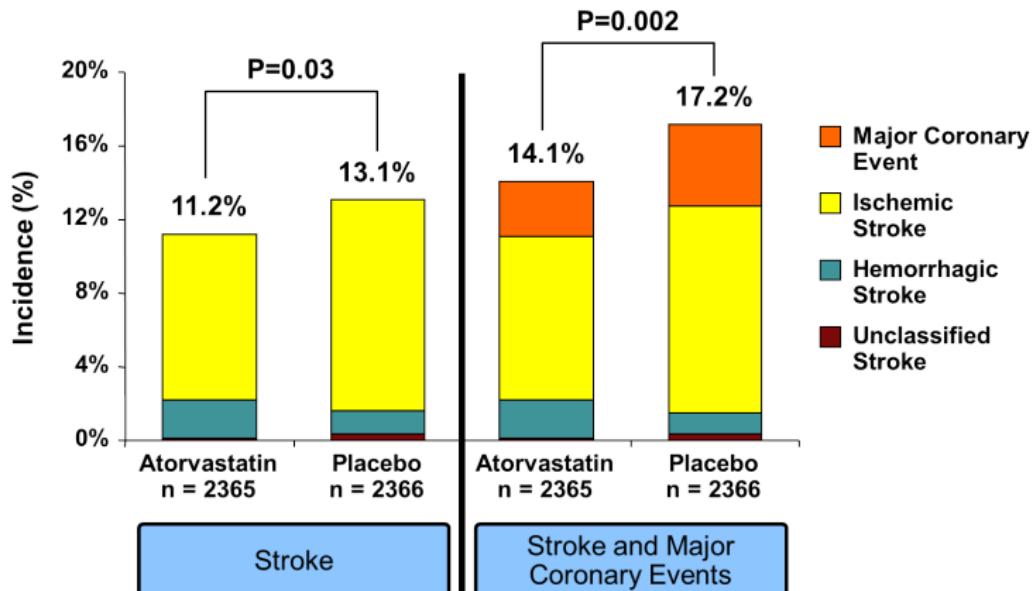
COR	LOE	Recommendation
I	A	<ol style="list-style-type: none"><li>1. Adherence to changes in lifestyle and effects of LDL-C-lowering medication should be assessed by measurement of fasting lipids and appropriate safety indicators 4 to 12 weeks after statin initiation or dose adjustment and every 3 to 12 months thereafter based on need to assess adherence or safety (S4.4.3-1–S4.4.3-3).</li></ol>

# SPARCL design



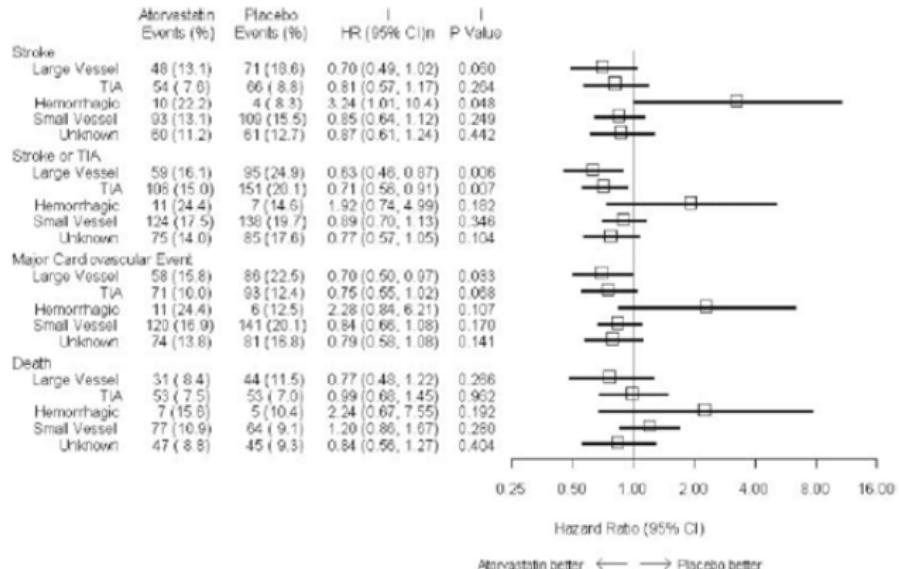
SPARCL investigator. *N Engl J Med* 2006; 355:549-559

## SPARCL: Atorvastatin 80mg vs. placebo



SPARCL investigator. N Engl J Med 2006; 355:549-559

# The Effectiveness of statin by stroke subtype ?



**Figure 1.** Risk of recurrent stroke by entry event stroke subtypes, relative to large vessel disease entry event group. HR indicates hazard ratio; CI, confidence interval; TIA, transient ischemic attack.

# 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

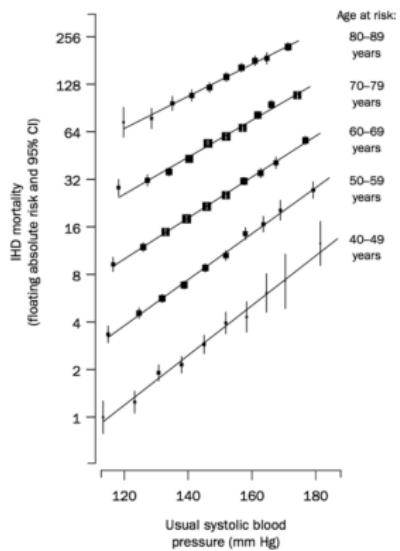


Figure 1. Ischemic heart disease (IHD) mortality

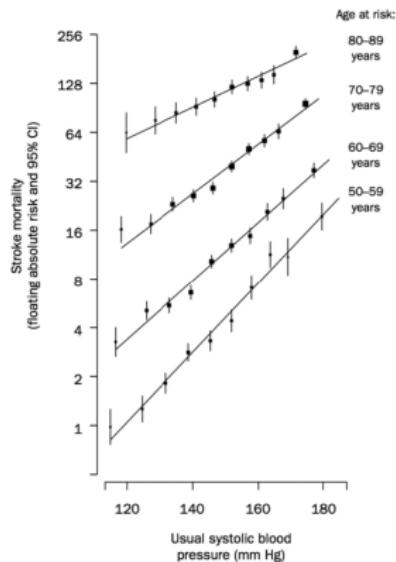
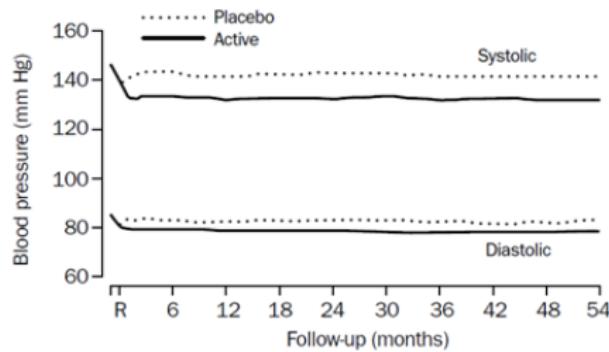


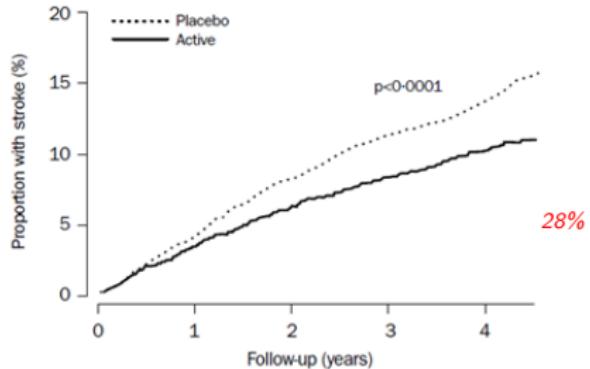
Figure 2. Stroke mortality

# PROGRESS

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



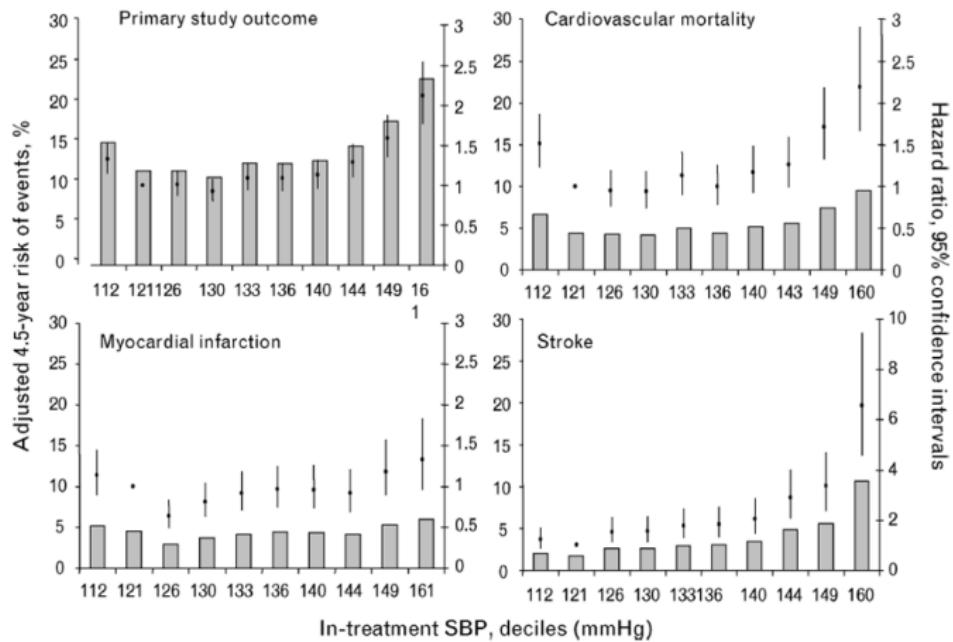
BP difference: 9/4 mm Hg



Cumulative incidence of Stroke

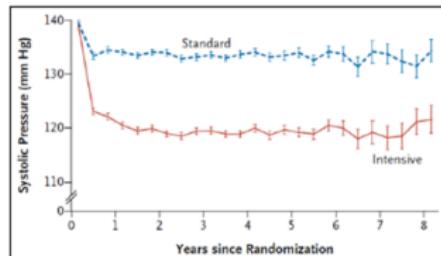
PROGRESS Collaborative Group et al. Lancet 2001;358:1033-41

# Ontarget study



# The lower BP looks beneficial in stroke: ACCORD

- 4733 patients with type 2 DM
- SBP  
< 140 mm Hg vs. < 120 mm Hg



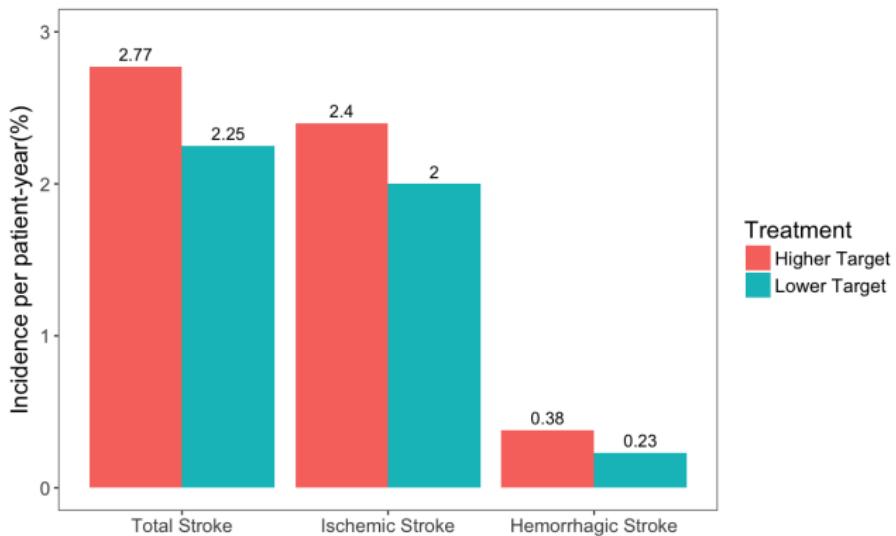
Outcome	Intensive Therapy (N=2363)		Standard Therapy (N=2371)		Hazard Ratio (95% CI)	P Value
	no. of events	%/yr	no. of events	%/yr		
Primary outcome*	208	1.87	237	2.09	0.88 (0.73–1.06)	0.20
Prespecified secondary outcomes						
Nonfatal myocardial infarction	126	1.13	146	1.28	0.87 (0.68–1.10)	0.25
Stroke						
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% *

# 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

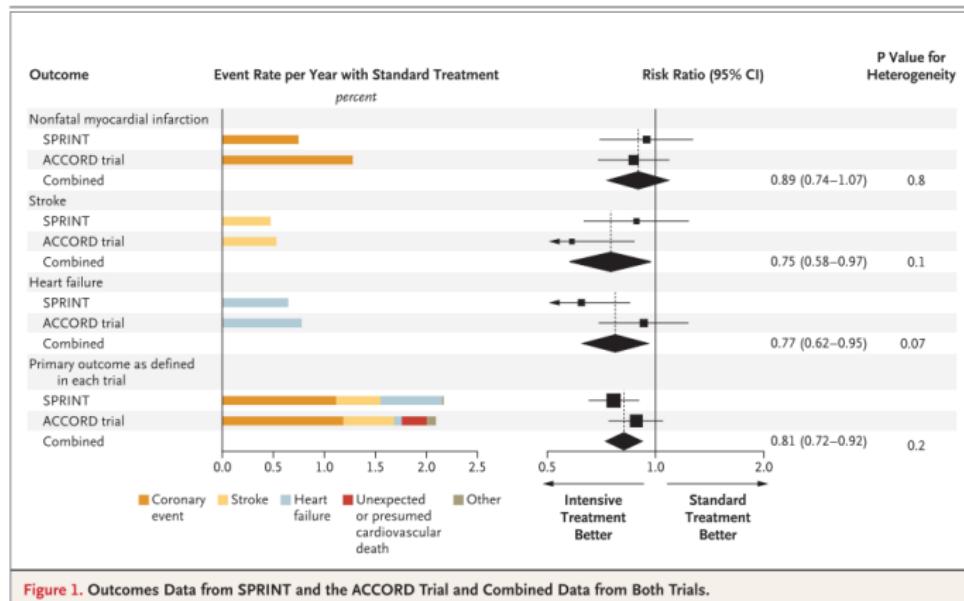
**For patients with a recent lacunar stroke, it might be reasonable to target an SBP of <130 mmHg (Class IIb; Level of Evidence B).  
(Revised recommendation)**

# 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



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



New AHA/ACC Guideline, Nov 13 2017

# Blood Pressure Categories



BLOOD PRESSURE CATEGORY	SYSTOLIC mm Hg (upper number)		DIASTOLIC mm Hg (lower number)
NORMAL	LESS THAN 120	and	LESS THAN 80
ELEVATED	120 – 129	and	LESS THAN 80
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 1	130 – 139	or	80 – 89
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 2	140 OR HIGHER	or	90 OR HIGHER
HYPERTENSIVE CRISIS (consult your doctor immediately)	HIGHER THAN 180	and/or	HIGHER THAN 120



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## BP Thresholds for and Goals of Pharmacological Therapy in Patients With Hypertension According to Clinical Conditions

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

ASCVD indicates atherosclerotic cardiovascular disease; BP, blood pressure; CVD, cardiovascular disease; and SBP, systolic blood pressure.



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## 11.8.3. 이차 예방

권고 내용	권고 등급	근거 수준	참고 문헌
• 치료를 받던 고혈압 환자는 뇌졸중 또는 일과성 허혈발작이 발생하면 뇌졸중 및 혈관질환 재발 방지를 위해 발병 수일 후 고혈압 약물치료를 재개할 것을 권고한다.	I	A	257,340, 341
• 뇌졸중 또는 일과성 허혈발작 환자의 고혈압 조절을 위해 ACE억제제/안지오텐신차단제, 티아지드계 이뇨제 또는 ACE억제제/안지오텐신차단제와 티아지드계 이뇨제의 병용치료를 권고한다.	I	A	110,257, 340
• 뇌졸중 또는 일과성 허혈발작 환자의 고혈압 조절을 위해 칼슘차단제를 고려한다.	IIa	C	310,342
• 고혈압 치료를 받지 않았던 환자는 뇌졸중 또는 일과성 허혈발작이 발생한 후 혈압이 140/90 mmHg 이상으로 지속되면 뇌졸중 및 혈관질환 재발 방지를 위해 발병 수일 후 고혈압 약물치료를 시작할 것을 권고한다.	I	B	110,340, 341
• 고혈압 치료를 받지 않았던 환자는 뇌졸중 또는 일과성 허혈발작이 발생한 후 혈압이 140/90 mmHg 이하인 경우 고혈압 치료의 유용성은 확립되어 있지 않다.	IIb	C	81
• 열공성 뇌경색 환자는 목표 수축기혈압을 130mmHg 미만으로 고려할 수 있다.	IIb	B	343

**Table 23** Office blood pressure treatment target range

Age group	Office SBP treatment target ranges (mmHg)					Office DBP treatment target range (mmHg)
	Hypertension	+ Diabetes	+ CKD	+ CAD	+ Stroke <sup>a</sup> /TIA	
18 - 65 years	<b>Target to 130</b> or lower if tolerated Not <120	<b>Target to 130</b> or lower if tolerated Not <120	<b>Target to &lt;140 to 130</b> if tolerated	<b>Target to 130</b> or lower if tolerated Not <120	<b>Target to 130</b> or lower if tolerated Not <120	70–79
65 - 79 years <sup>b</sup>	<b>Target to 130-139</b> if tolerated	<b>Target to 130-139</b> if tolerated	<b>Target to 130-139</b> if tolerated	<b>Target to 130-139</b> if tolerated	<b>Target to 130-139</b> if tolerated	70–79
≥80 years <sup>b</sup>	<b>Target to 130-139</b> if tolerated	<b>Target to 130-139</b> if tolerated	<b>Target to 130-139</b> if tolerated	<b>Target to 130-139</b> if tolerated	<b>Target to 130-139</b> if tolerated	70–79
<b>Office DBP treatment target range (mmHg)</b>	70–79	70–79	70–79	70–79	70–79	

CAD = coronary artery disease; CKD = chronic kidney disease (includes diabetic and non-diabetic CKD); DBP = diastolic blood pressure; SBP = systolic blood pressure; TIA = transient ischaemic attack.

<sup>a</sup>Refers to patients with previous stroke and does not refer to blood pressure targets immediately after acute stroke.

<sup>b</sup>Treatment decisions and blood pressure targets may need to be modified in older patients who are frail and independent.

## Take-Home Message

- In patients with non-valvular atrial fibrillation, NOAC might be a better option than warfarin.
- Dyslipidemia should be intensively treated in patients with atherosclerotic stroke.
- However, the effectiveness of lipid lowering treatment on non-atherosclerotic stroke has not been determined yet.
- Stroke and Hypertension are big health issues in rapidly aging societies like Korea.
- Therapeutic target of BP is lowered in new guidelines.