

MASTER CLASS Web Symposium  
**Personalized treatment strategies  
for stroke prevention in AF**



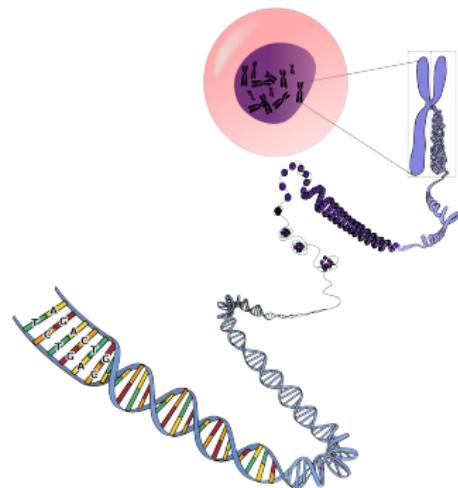
중앙대학교 의과대학 신경과학교실  
박 광 열

## Prologue

## Introduction

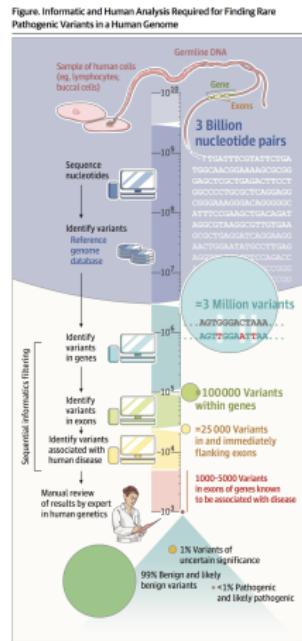
### Stroke in Asian and Korean Subtypes of ischemic stroke

## Summary



# In clinics, we are not prepared for precision medicine yet

- ▶ Cost
- ▶ Interpretation of information
  - ▶ 3,000,000,000 base pairs
  - ▶ 3,000,000 SNPs
  - ▶ 100,000 variants in exon



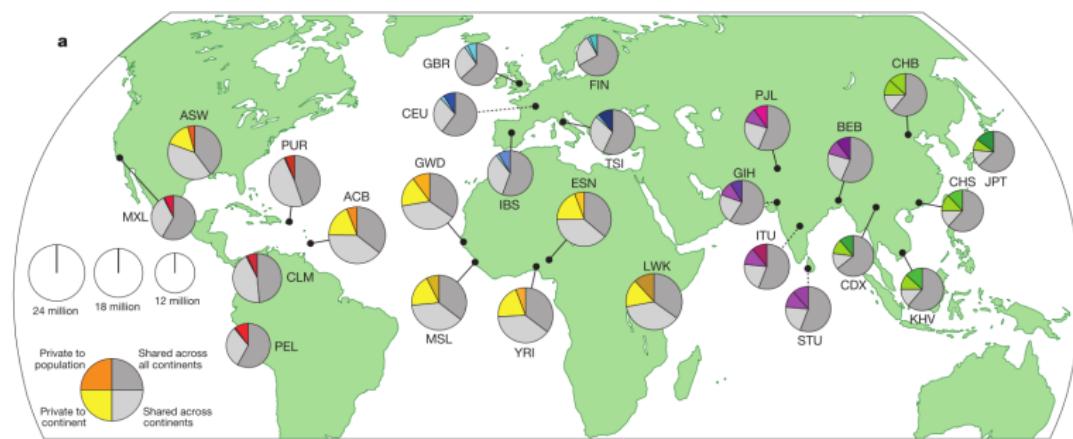
### IGSR and the 1000 Genomes Project



Populations: ● - African; ● - American; ● - East Asian; ● - European; ● - South Asian;

2,504 individuals from 26 populations

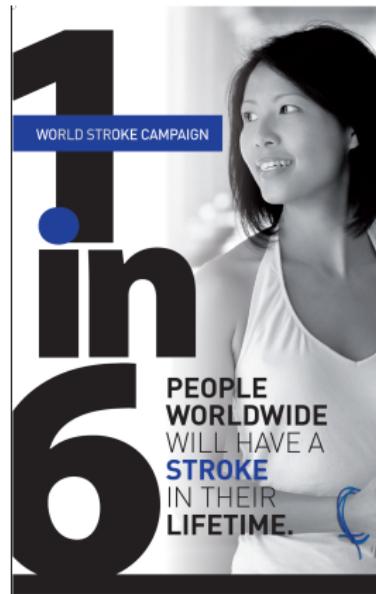
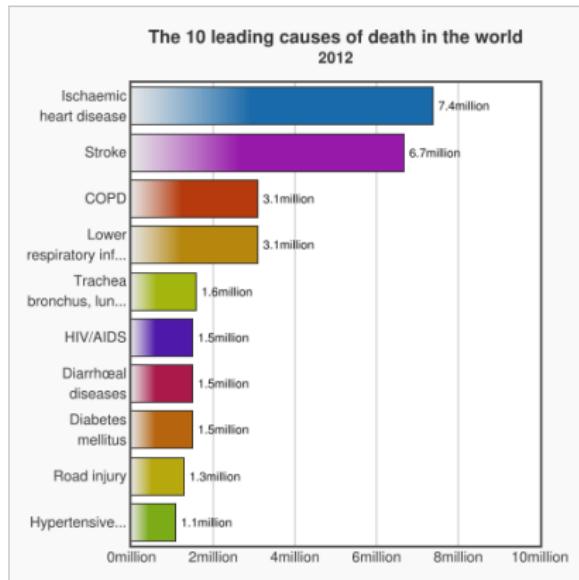
# A global reference for human genetic variation



## 뇌졸중이란?

- ▶ 중풍(中風)
- ▶ 뇌졸중(腦卒中)
- ▶ 뇌혈관질환
- ▶ 뇌에 혈액을 공급하는 혈관이 막히거나 터져서 뇌 손상이 오고 그에 따른 신체장애가 나타나는 질환.

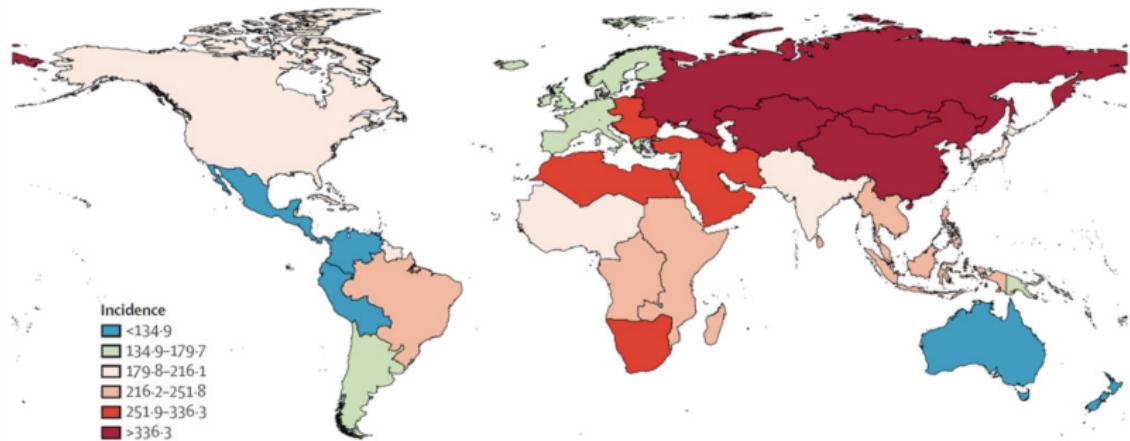
## Global burden of stroke



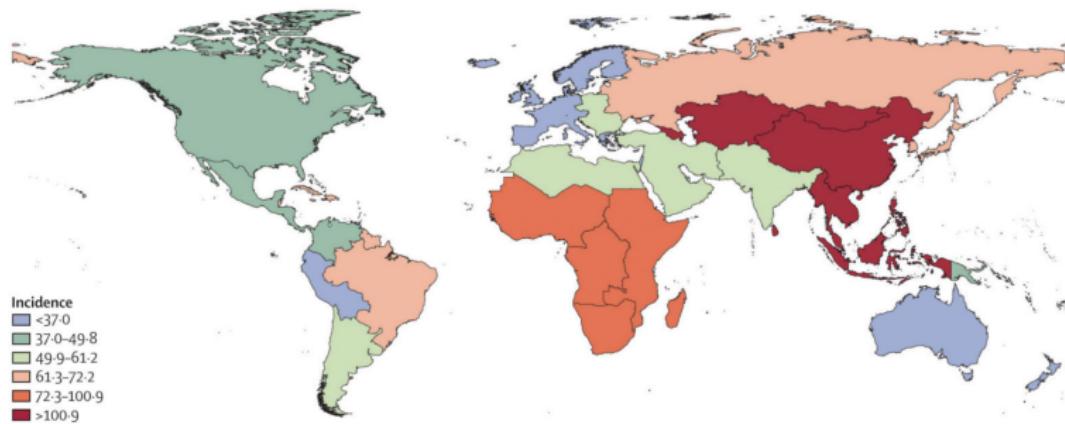
<http://www.who.int/mediacentre/factsheets/fs310/en/> accessed on Jan 16, 2016

<http://www.worldstrokecampaign.org/get-involved/2015-08-20-01-49-19/campaign-posters.html>

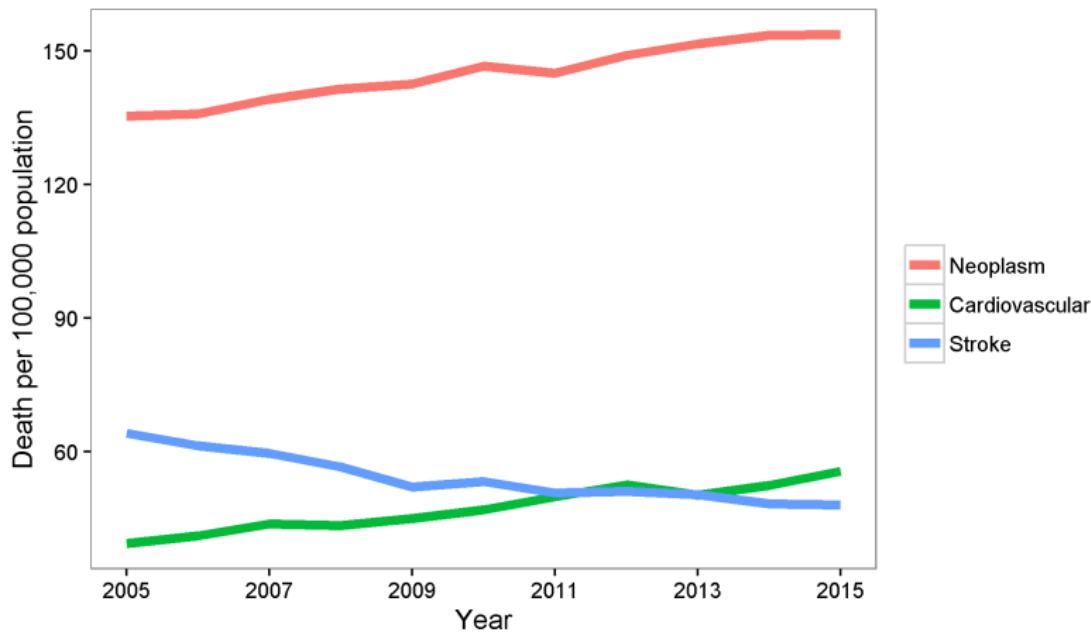
## Age-standardised stroke incidence per 100 000 person-years for 2010



## Age-standardised incidence of haemorrhagic stroke per 100 000 person-years for 2010



## Secular trend of mortality in Korea



## Etiologies of stroke

### Ischemic Stroke

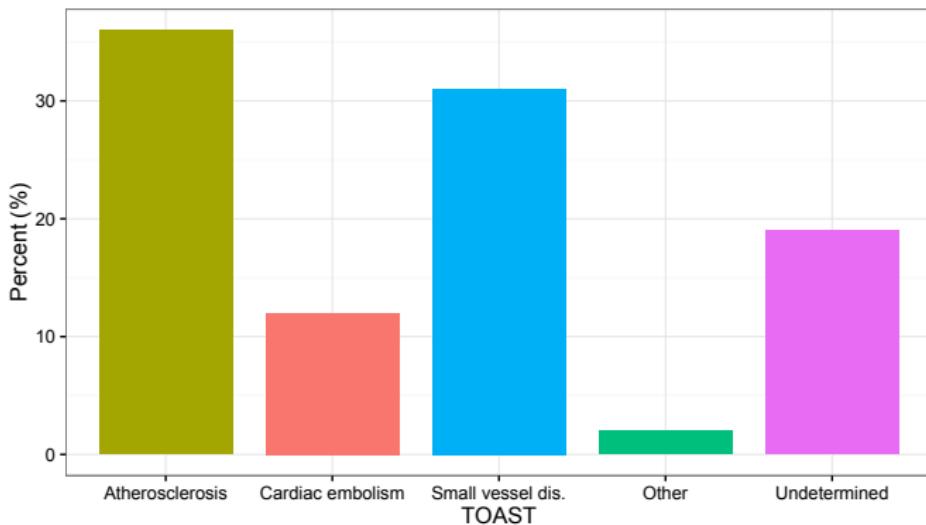
- ▶ Atherosclerosis
- ▶ Small artery occlusion
- ▶ Cardiac disease causing embolism
- ▶ Other causes such as moyamoya disease

### Hemorrhagic Stroke

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

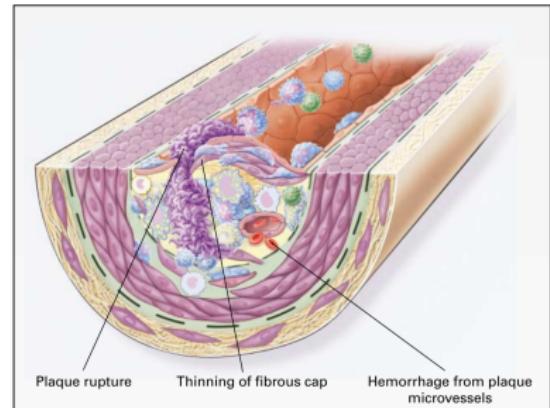
## 한국의 허혈성 뇌졸중:

### Analysis of 10,861 cases in Korean Stroke Registry



## Atherosclerosis

- ▶ 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.

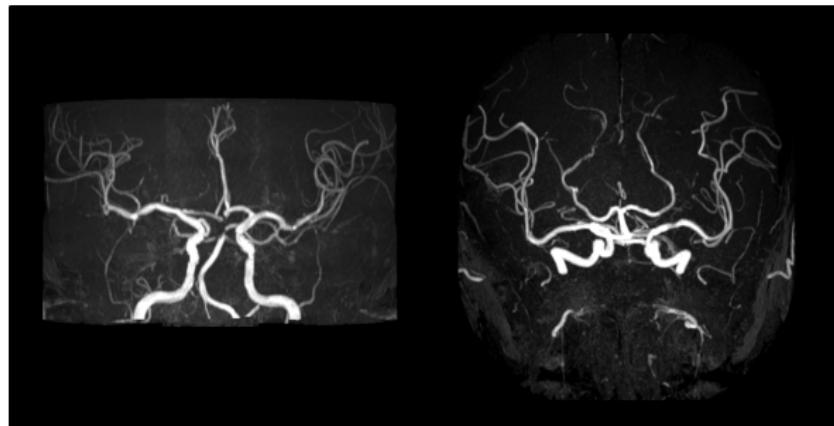


Stroke prevention in AF

└ Stroke in Asian and Korean

└ Subtypes of ischemic stroke

## Atherosclerotic stenosis on MRA



## Lacunar infarction by small vessel disease

- ▶ 대개 직경 1.5 cm 이하의 작고 둥근 형태의 뇌경색
- ▶ 보통 100-400  $\mu\text{m}$  직경의 관통동맥이 막혀서 생기는 것으로 여겨짐.
- ▶ 혈관
  - ▶ 전, 중간대뇌동맥의 렌즈핵줄무늬(lenticulostriate) 가지로부터 나오는 혈관
  - ▶ 후대뇌동맥으로부터 나오는 thalamoperforating 가지
  - ▶ 기저동맥의 paramedian 가지
- ▶ 주된 위험인자: 고혈압, 당뇨

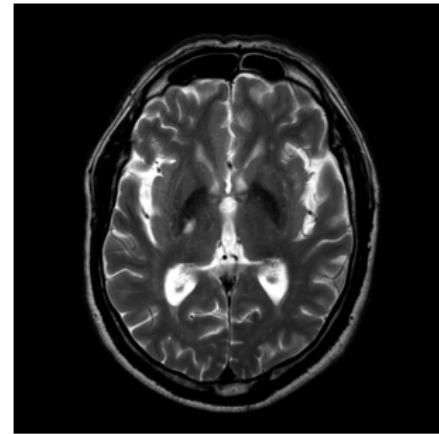
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## Small vessel disease

- ▶ Involved vessels:
  - ▶ small artery and arteriole
  - ▶ capillary and venules ?
- ▶ Parenchymal lesions as a surrogate marker
- ▶ Both ischemic and hemorrhagic lesions



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# MRI findings of small vessel disease

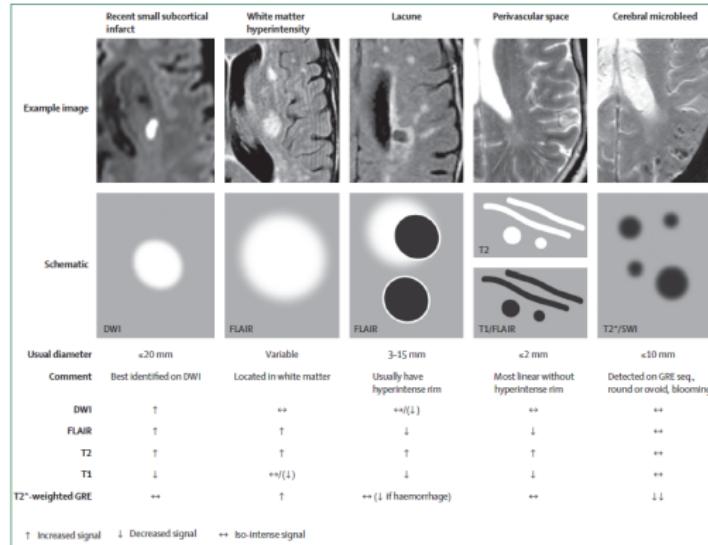


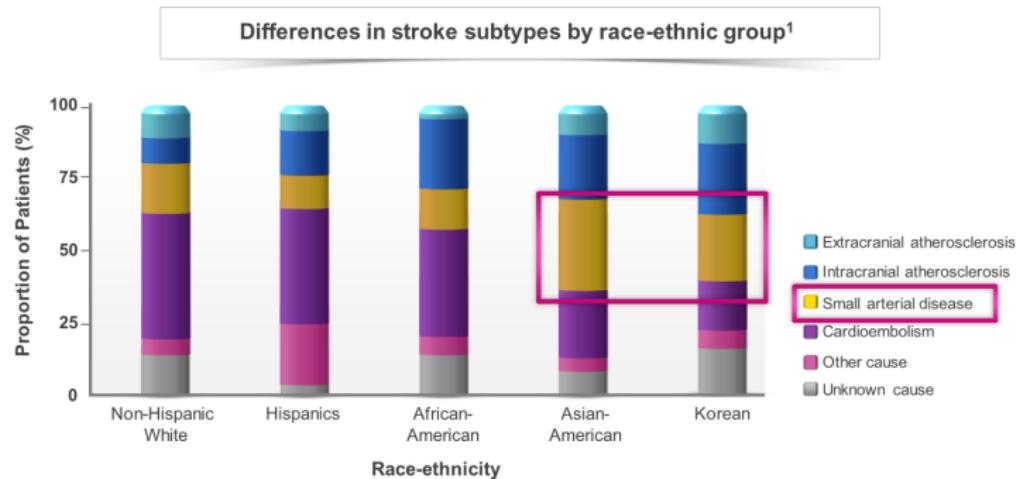
Figure 2: MRI findings for lesions related to small vessel disease

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# SVD is more prevalent in Asians than Western populations



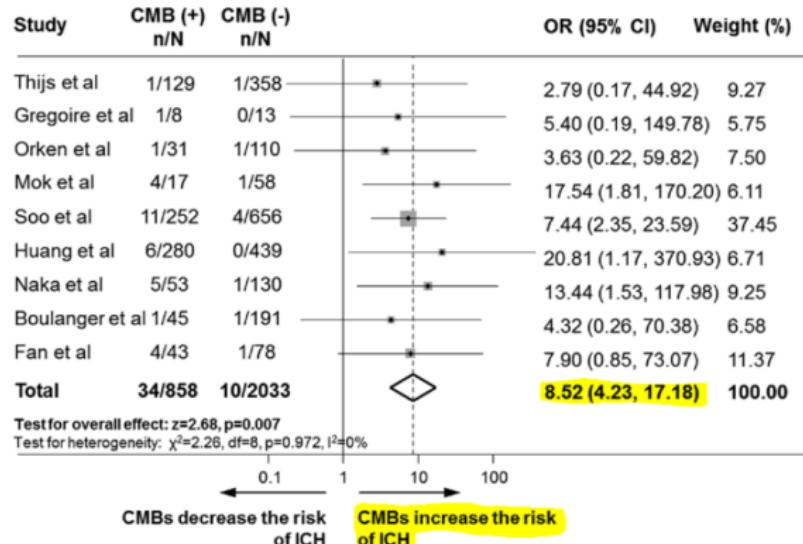
Data collected over 4 yr-period in prospectively maintained registries on 3,053 subjects with ischemic cerebrovascular events (1,982 South Korean & 1,071 Southern Californian).

1. Bang OY, et al. Cerebrovasc Dis 2009;27:13–21. 2. Kim BJ, et al. J Stroke 2014;16:8–17.

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# Stroke prevention in AF

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### Subtypes of ischemic stroke

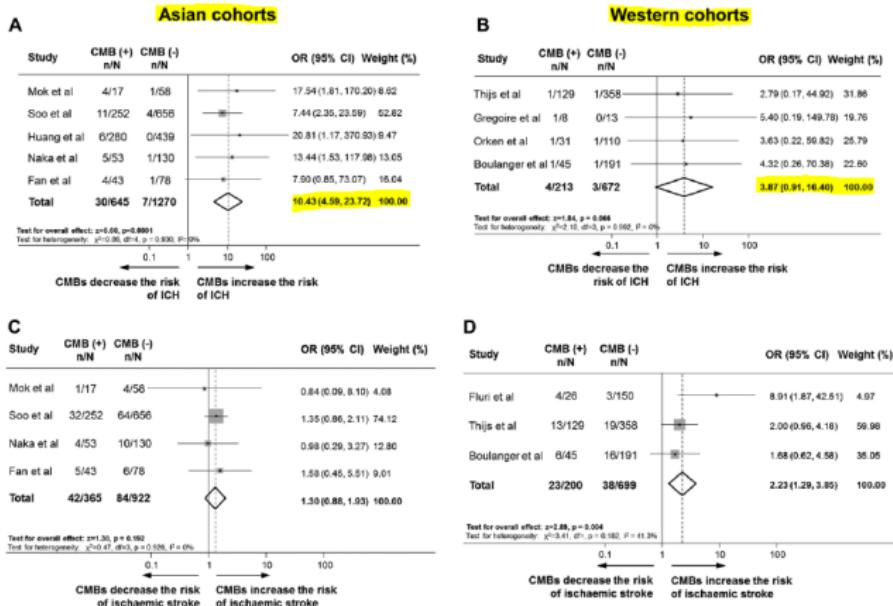
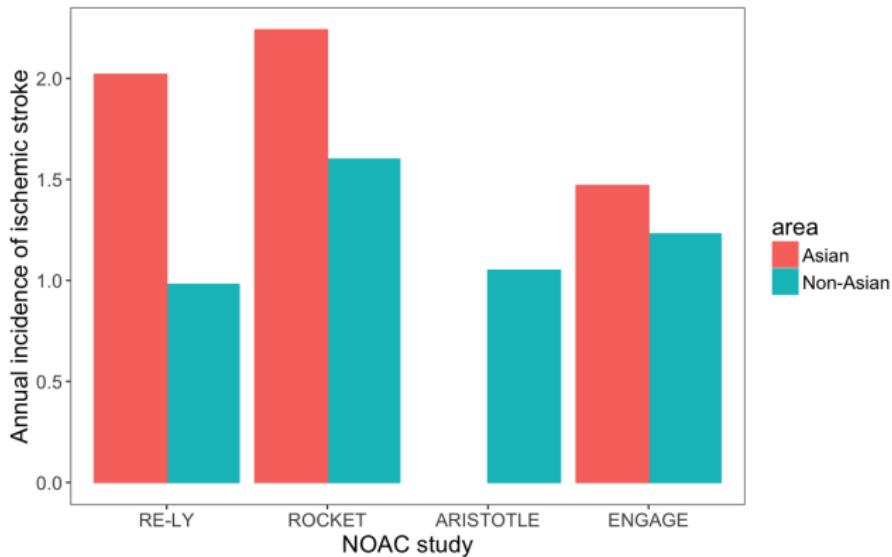
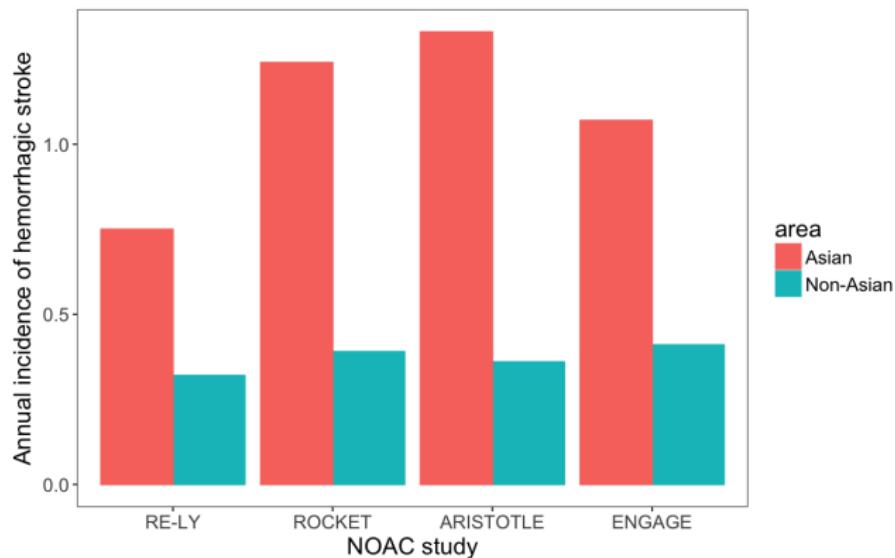


Figure 4. Meta-analysis of the risk of spontaneous intracerebral hemorrhage (ICH; A and B) and ischemic stroke (C and D) stratified by the dominant ethnicity of subjects included in each cohort as Asian or Western (white), with and without cerebral microbleeds (CMBs).

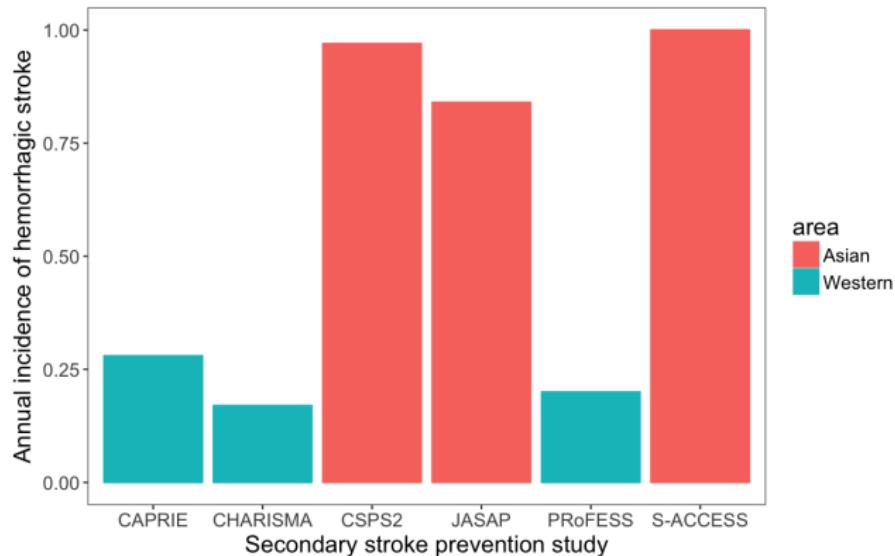
## Ischemic stroke on warfarin



## hemorrhagic stroke on warfarin



## Incidence of Cerebral Hemorrhage with Aspirin



## 심장질환에 의한 뇌졸중

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

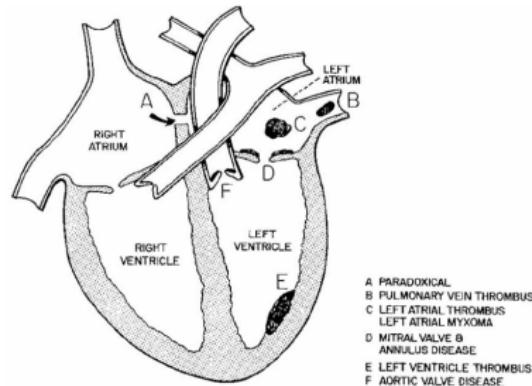


Figure 1. Cardiac causes of stroke (Adapted from Barnett et al)

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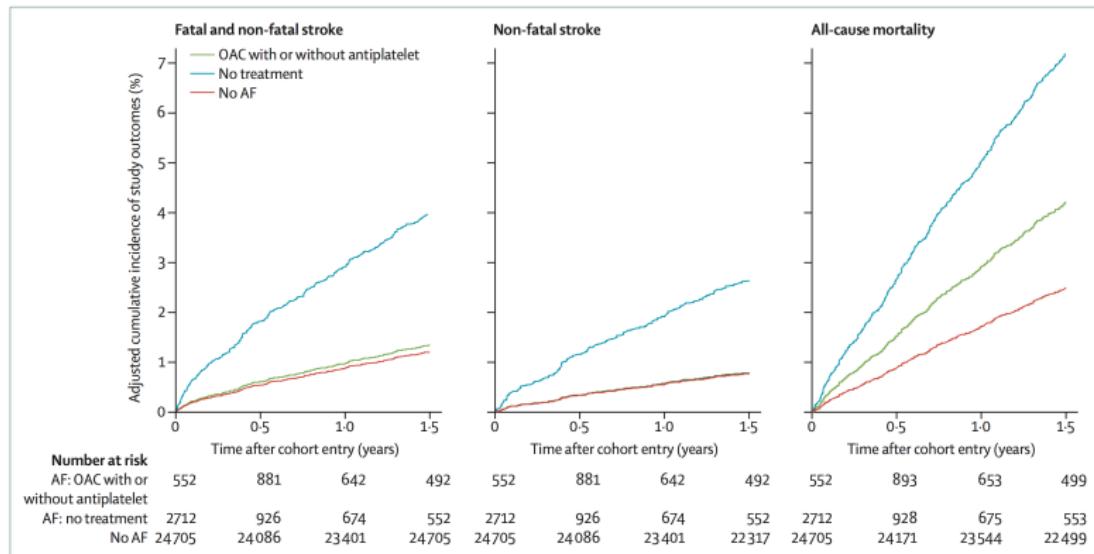
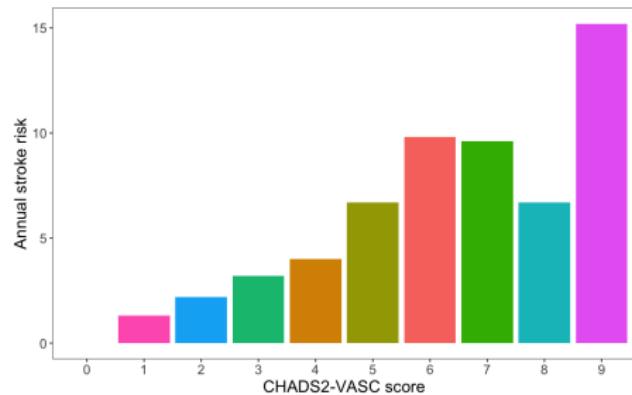


Figure 2: Effect of treatment on incidentally detected atrial fibrillation

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

# 심방세동환자에서의 색전증 위험도

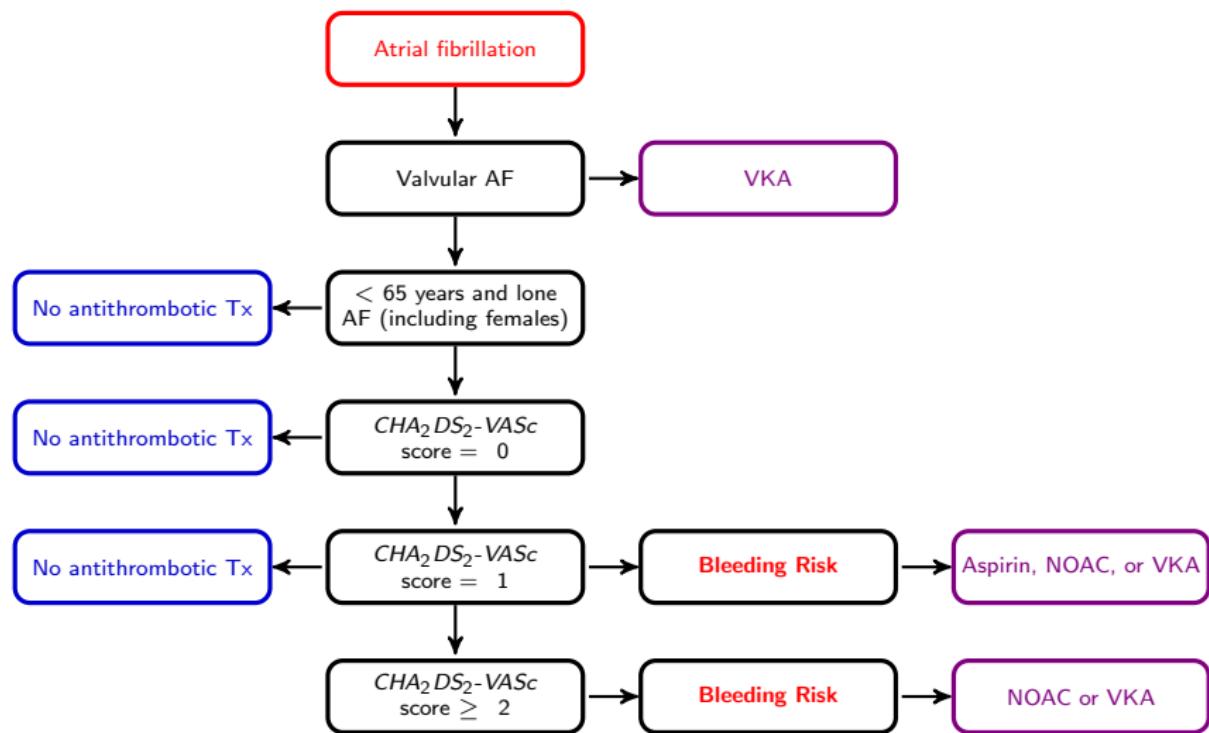
<i>CHA<sub>2</sub>DS<sub>2</sub>-VASc criteria</i>	Score
CHF	1
Hypertension	1
Age $\geq$ 75 years	2
Diabetes mellitus	1
Stroke or TIA	2
Vascular disease	1
Age 65-74 years	1
Sex category (female)	1



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The image shows the front cover of the 2016 ESC Guidelines for the management of atrial fibrillation. The cover features a red heart icon with the text "European Society of Cardiology". At the top right, it says "ESC GUIDELINES". Below that, the title reads "2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS". Underneath the title, it says "The Task Force for the management of atrial fibrillation European Society of Cardiology (ESC)". It also mentions "Developed with the special contribution of the European Rhythm Association (EHRA) of the ESC". The bottom left corner says "Endorsed by the European Stroke Organisation (ESO)". The bottom right corner contains the journal information: "Europace (2016) 38, 1609–1678 doi:10.1093/europace/euw295".

**2016 European guidance:**  
OAC therapy to prevent thromboembolism is recommended in all patients with a  $\text{CHA}_2\text{DS}_2\text{-VASc}$  score of  $\geq 2$  (men) or  $\geq 3$  (women)

A NOAC is recommended in preference to a VKA in patients who are eligible for NOACs

## Assessment of bleeding risk ?

HAS-BLED	Score
Hypertension	1
Abnormal renal function	1
Abnormal liver function	1
Stroke, previous	1
Prior major Bleeding or bleeding predisposition	1
Labile INR (TTR < 60%)	1
Elderly (old age > 65y)	1
Drugs: antiplatelet or NSAID	1
Excessive alcohol use	1

## Stroke in Asian

### Ischemic Stroke

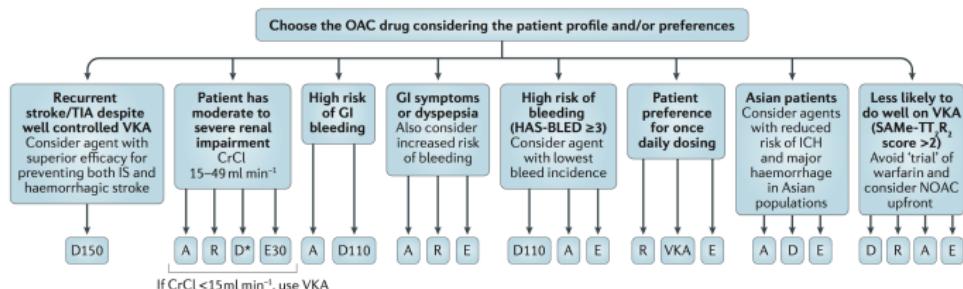
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Higher risk of hemorrhagic stroke should be considered when choosing the anti-thrombotic medication in Asians.

# Choice of NOAC



**Figure 8 | Selection of oral anticoagulant drugs.** A schematic representation of decision making in the selection of an oral anticoagulant (OAC) drug based on patient and drug characteristics using illustrative examples. A, apixaban; CrCl, creatinine clearance; D, dabigatran (D75, dabigatran 75 mg two times per day, available in the United States only; D110, dabigatran 110 mg, not available in the United States for AF; D150, dabigatran 150 mg); E, edoxaban (E30, edoxaban 30 mg); GI, gastrointestinal; ICH, intracranial haemorrhage; IS, ischaemic stroke; NOAC, non-vitamin K antagonist oral anticoagulant; R, rivaroxaban; TIA, transient ischaemic attack; VKA, vitamin K antagonist. \*D110 for patients with a CrCl 30–49 ml min<sup>-1</sup> (most countries); in the United States only, D75 for patients with CrCl 15–29 ml min<sup>-1</sup> (and only 150 mg b.i.d. dose available in the United States, for CrCl >30 ml min<sup>-1</sup>). Figure adapted with permission from REF. 250, Wiley.

## Take-Home Message

- ▶ Stroke is the second leading cause of death in Korea.
- ▶ Stroke is caused by various etiologies.
- ▶ In Asian countries, small vessel disease is prevalent and the risk of hemorrhagic stroke are higher than Western countries.
- ▶ NOAC has been proven to be more effective and safer treatment than warfarin in patients with NVAF in several RCTs.