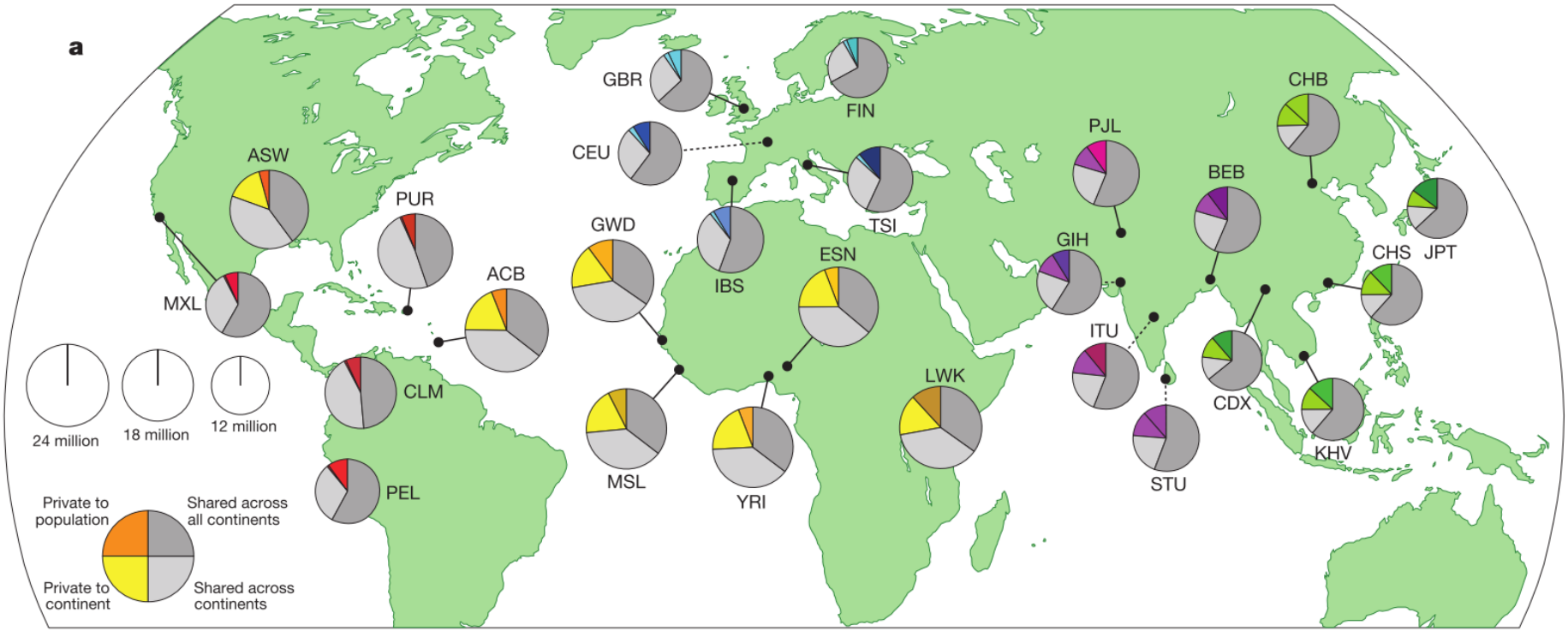
CPBMI

Variations in Vitamine D Related Genes Among Races

CPBMI 1조: 강민규, 김혜원, 박광열, 이은솔, 조인영, 한현욱

17 Dec 2016

A global reference for human genetic variation



The Genomes Project. Nature 2015

Stroke has diverse etiologies

Ischemic Stroke

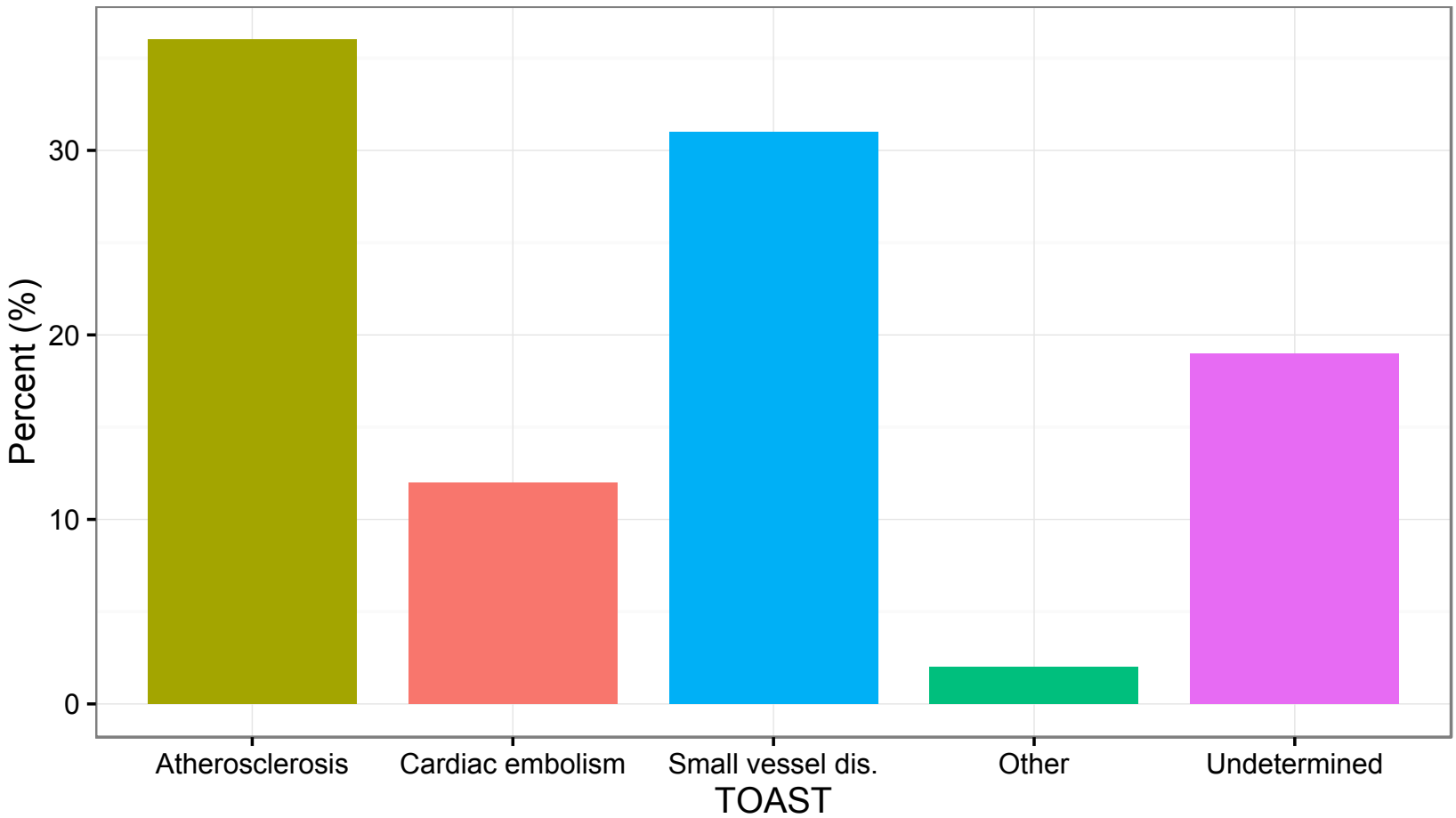
- Atherosclerosis
- Small artery occlusion
- Cardiac disease causing embolism
- Other causes such as moyamoya disease

Hemorrhagic Stroke

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

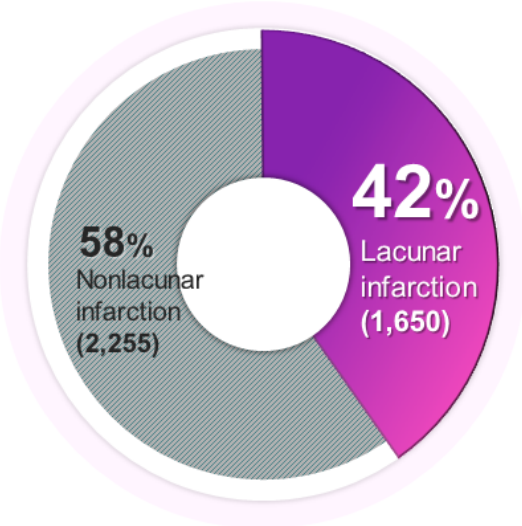
Ischemic stroke in Korea

Analysis of 10,861 cases in Korean Stroke Registry



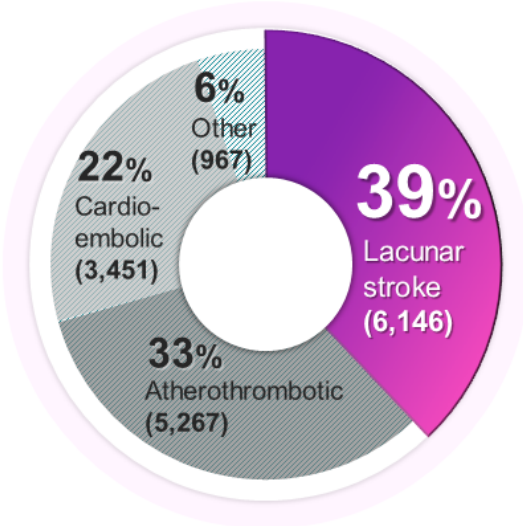
Yu KH et al. J Korean Neurol Society 2006

Lacunar stroke is one of the frequent stroke subtypes



Proportion of lacunar infarction in China[1]

Prospective registry data (n=3,905) entered within 1 month after a first-ever stroke between March 2002 and March 2007 were used from 4 Chinese hospitals.

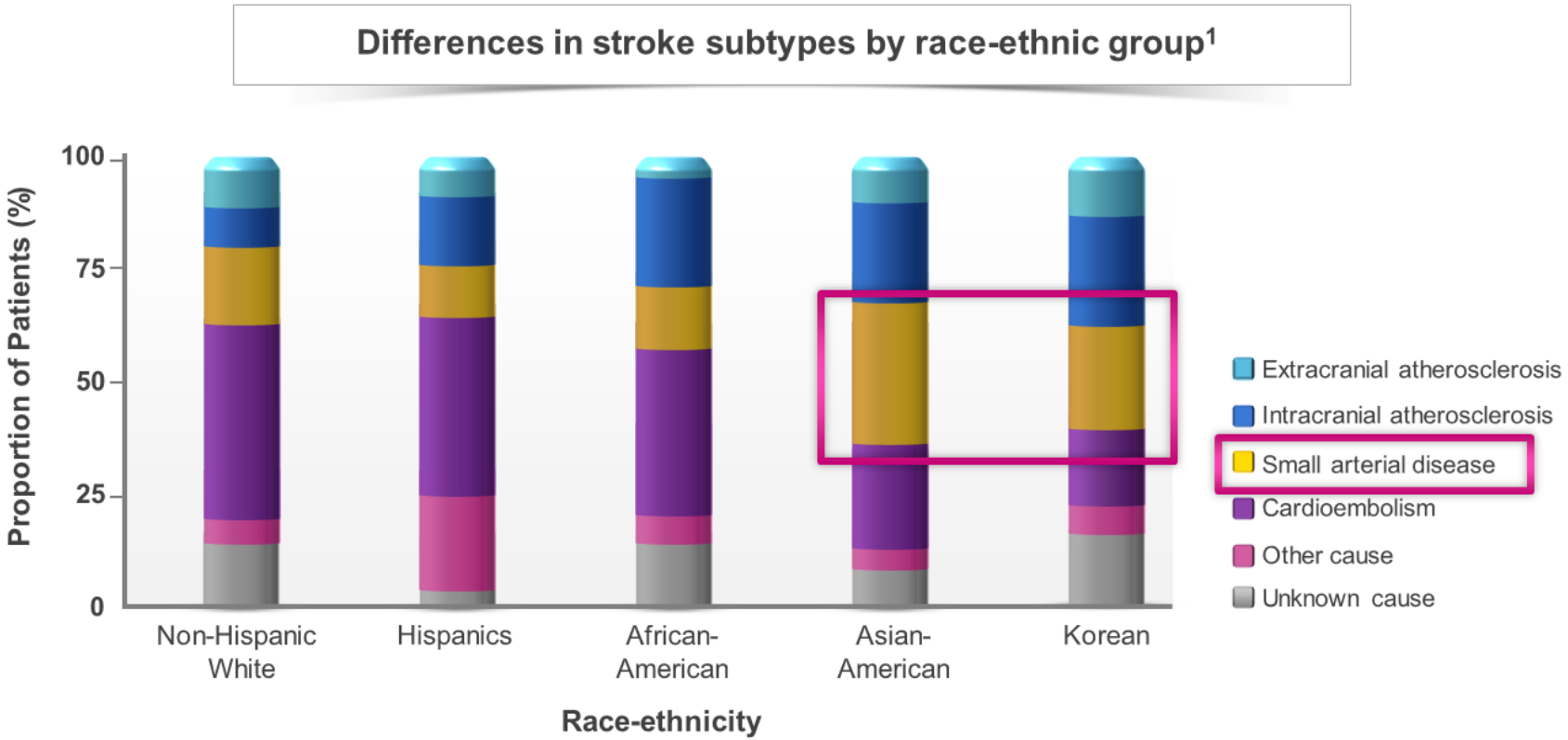


Stroke subtype in Japan[2]

Prospective registry data (n=15,831) entered within 7 days after acute ischemic stroke from May 1999 to April 2000 were used from 156 Japanese hospitals.

1. Wu B, et al. Cerebrovasc Dis 2010;29:181–7. 2. Kimura K, et al. Cerebrovasc Dis 2004;18:47–56

SVD is more prevalent in Asians than Western populations

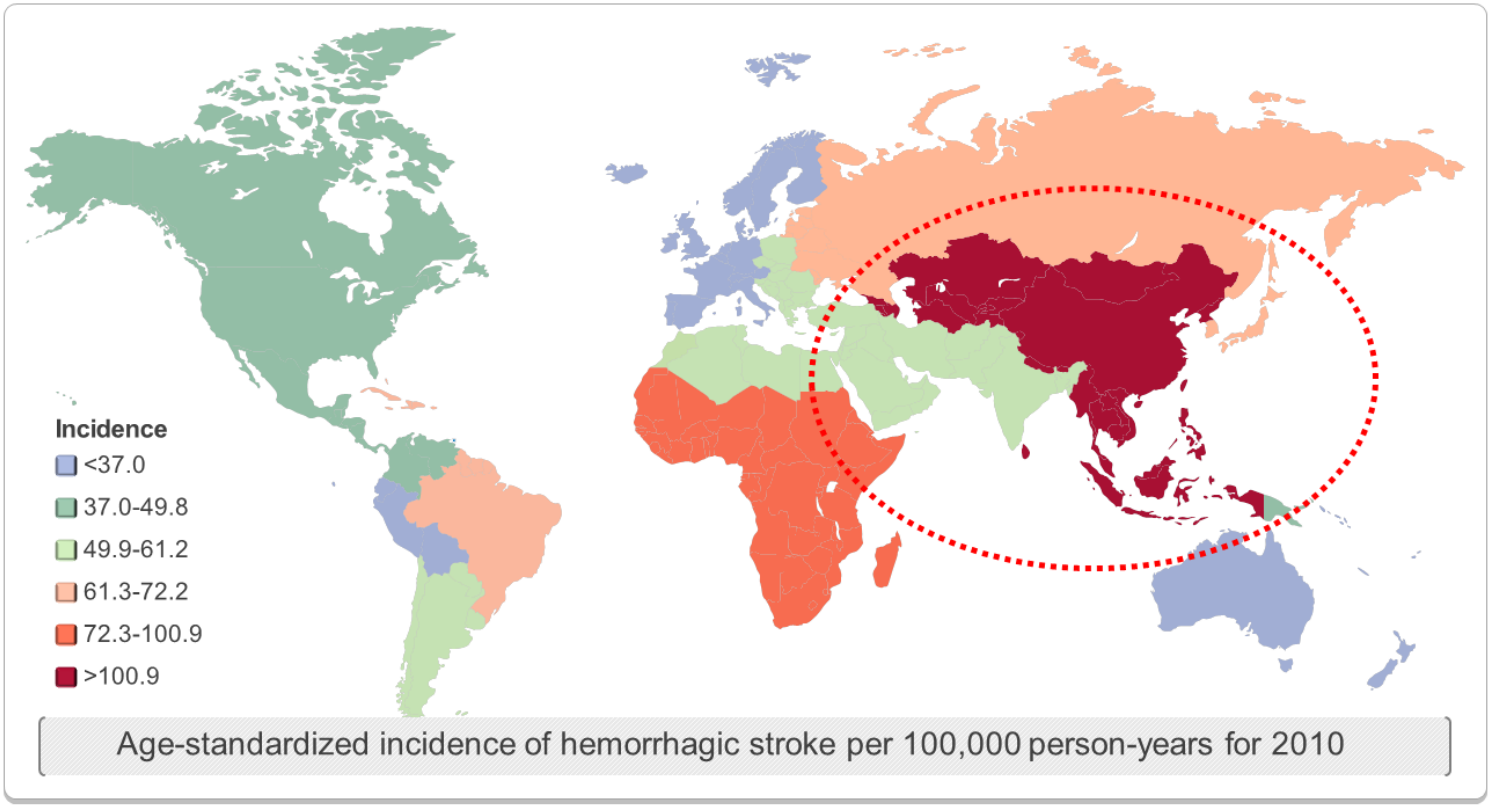


Data collected over 4 yr-period in prospectively maintained registries on 3,053 subjects with ischemic cerebrovascular events (1,982 South Korean & 1,071 Southern Californean).

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

Burden of Hemorrhagic Stroke in Asia

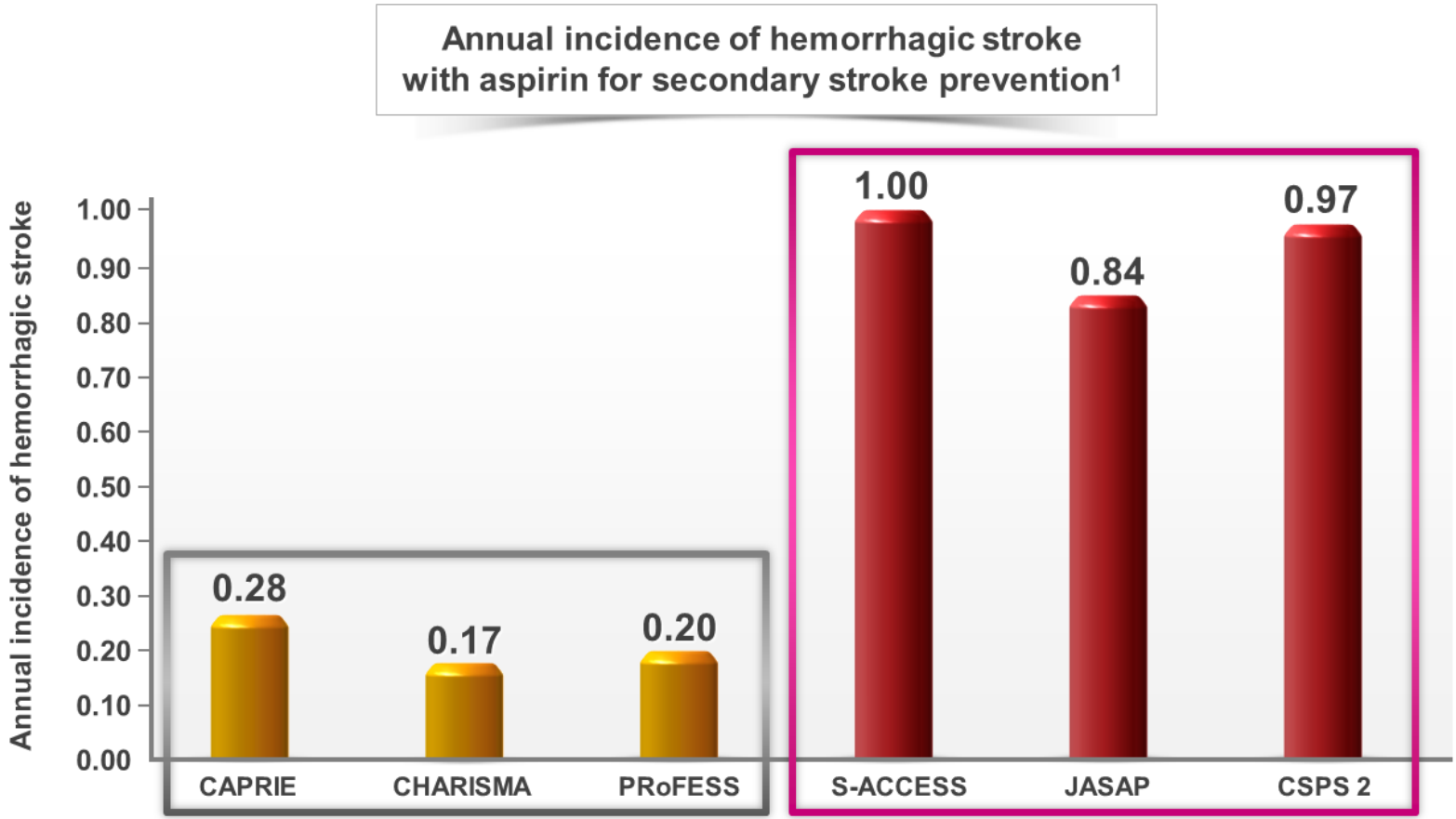
In 2010, incidence of hemorrhagic stroke was highest in central and east Asia (101–158/100,000 person-years).[1]



1. Krishnamurthi RV, et al. Lancet Glob Health 2013;1:e259-81.

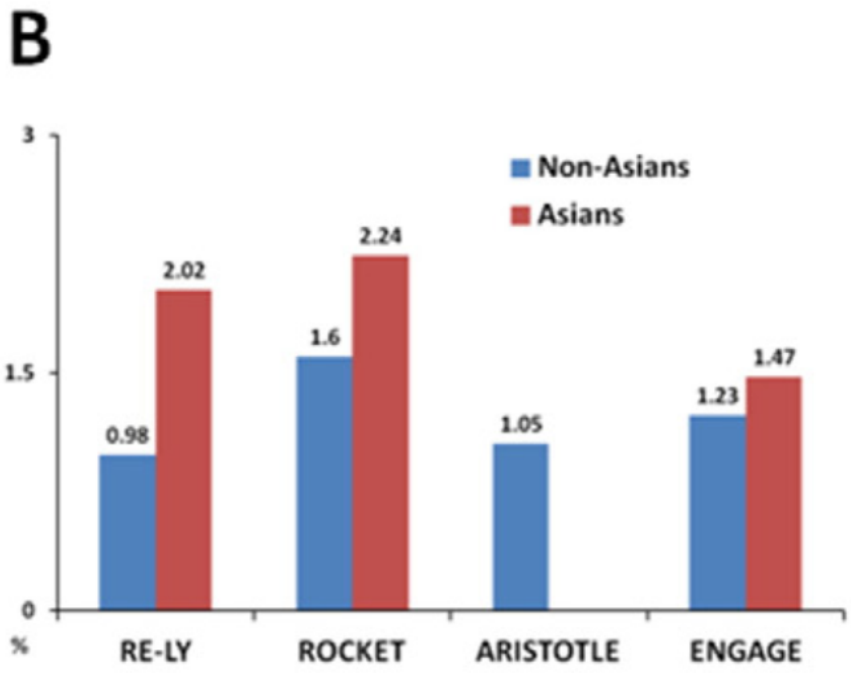
Incidence of Cerebral Hemorrhage with Aspirin

Incidence of hemorrhagic stroke with aspirin was much higher in Asian trials.

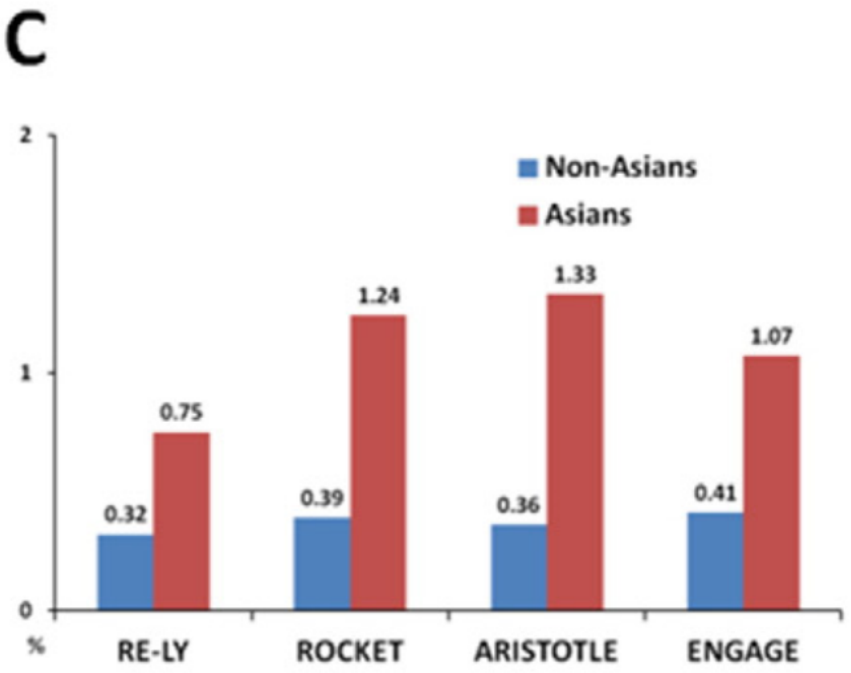


1. Kim JS, et al. Int J Stroke 2015;10 Suppl 1:1-9.

Cerebral hemorrhage with new oral anticoagulant

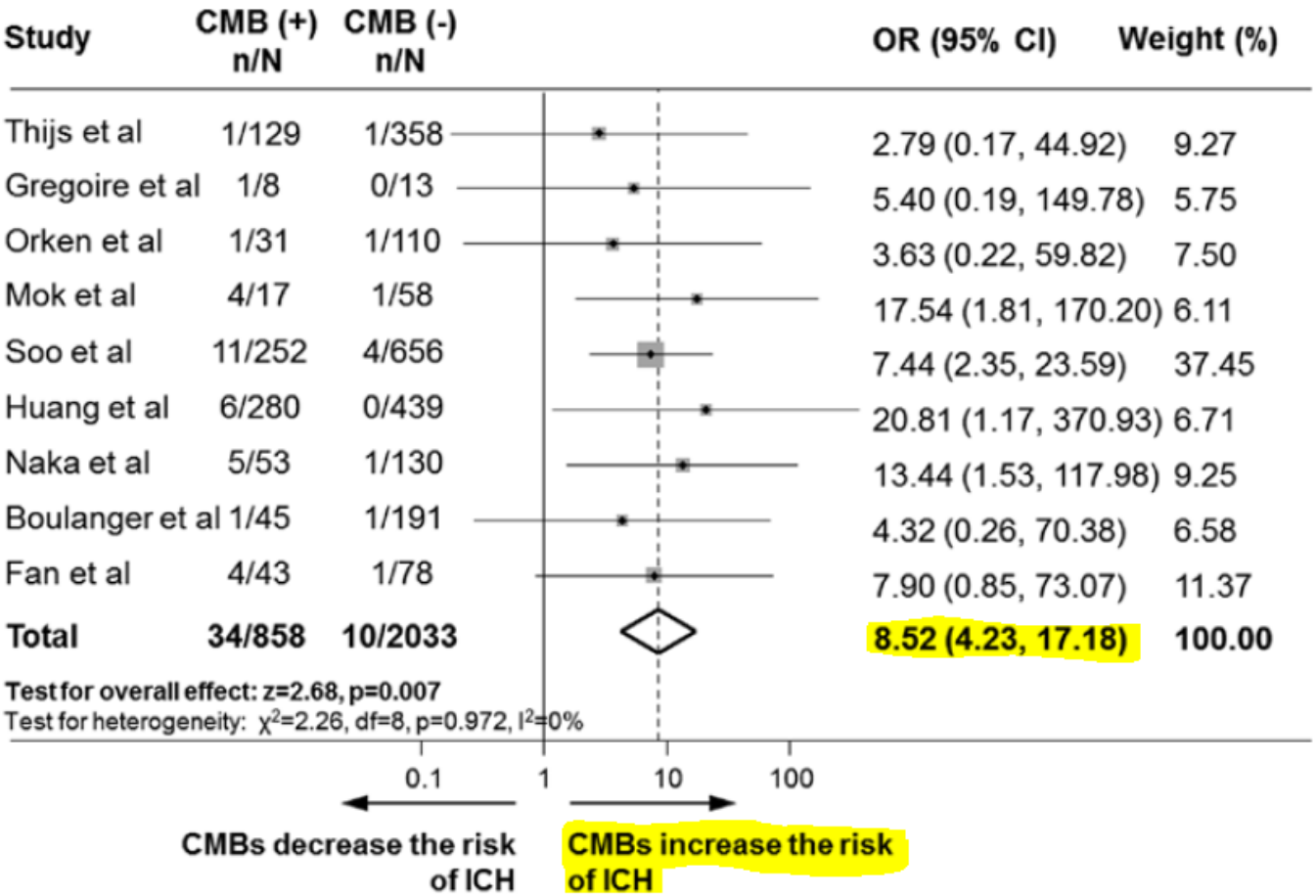


Ischemic stroke



Hemorrhagic stroke

Lip GYH et al, Int J Cardiol 2015;180:246



Charidimou A et al. Am J Cardiol 2013;112:1230e1234

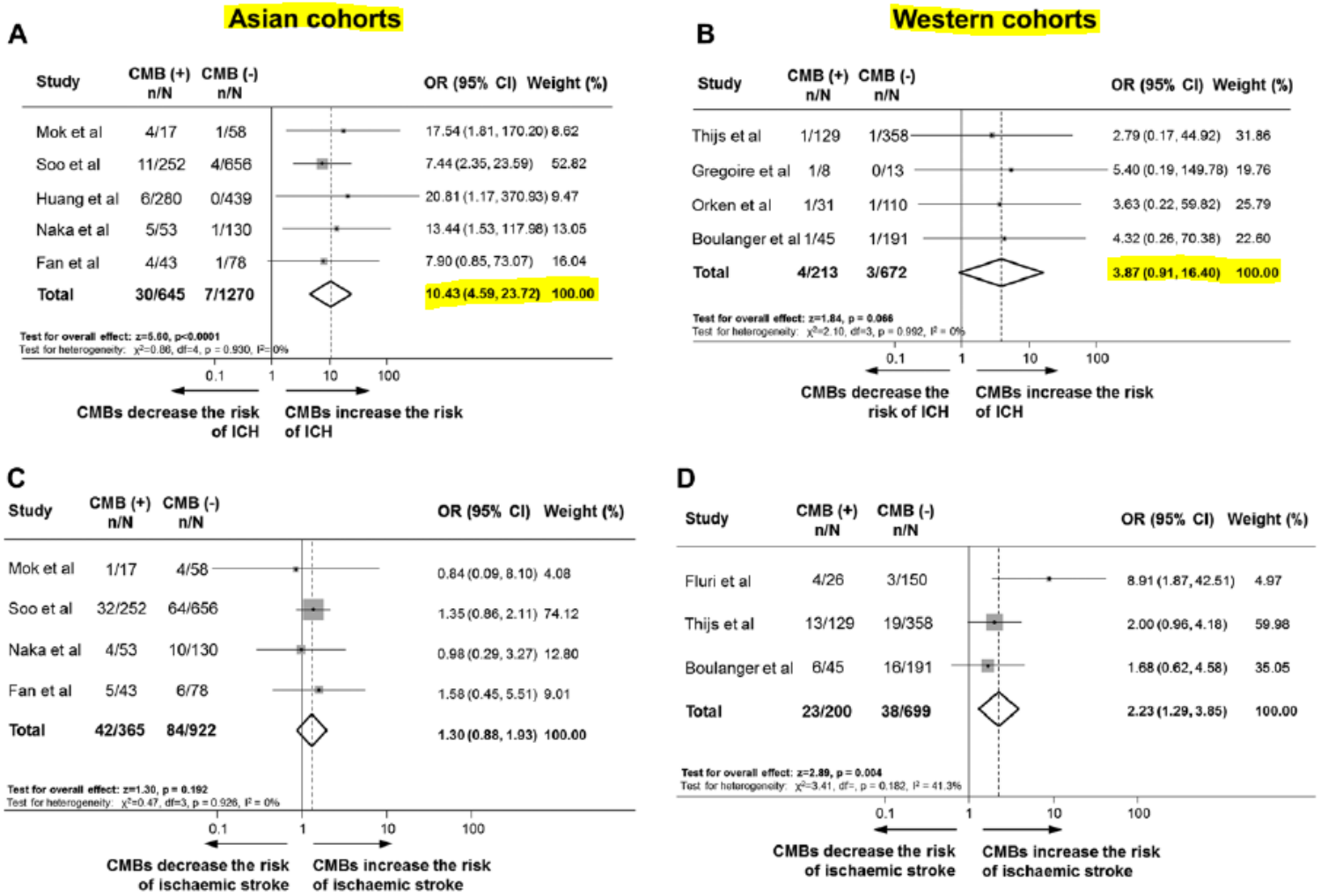
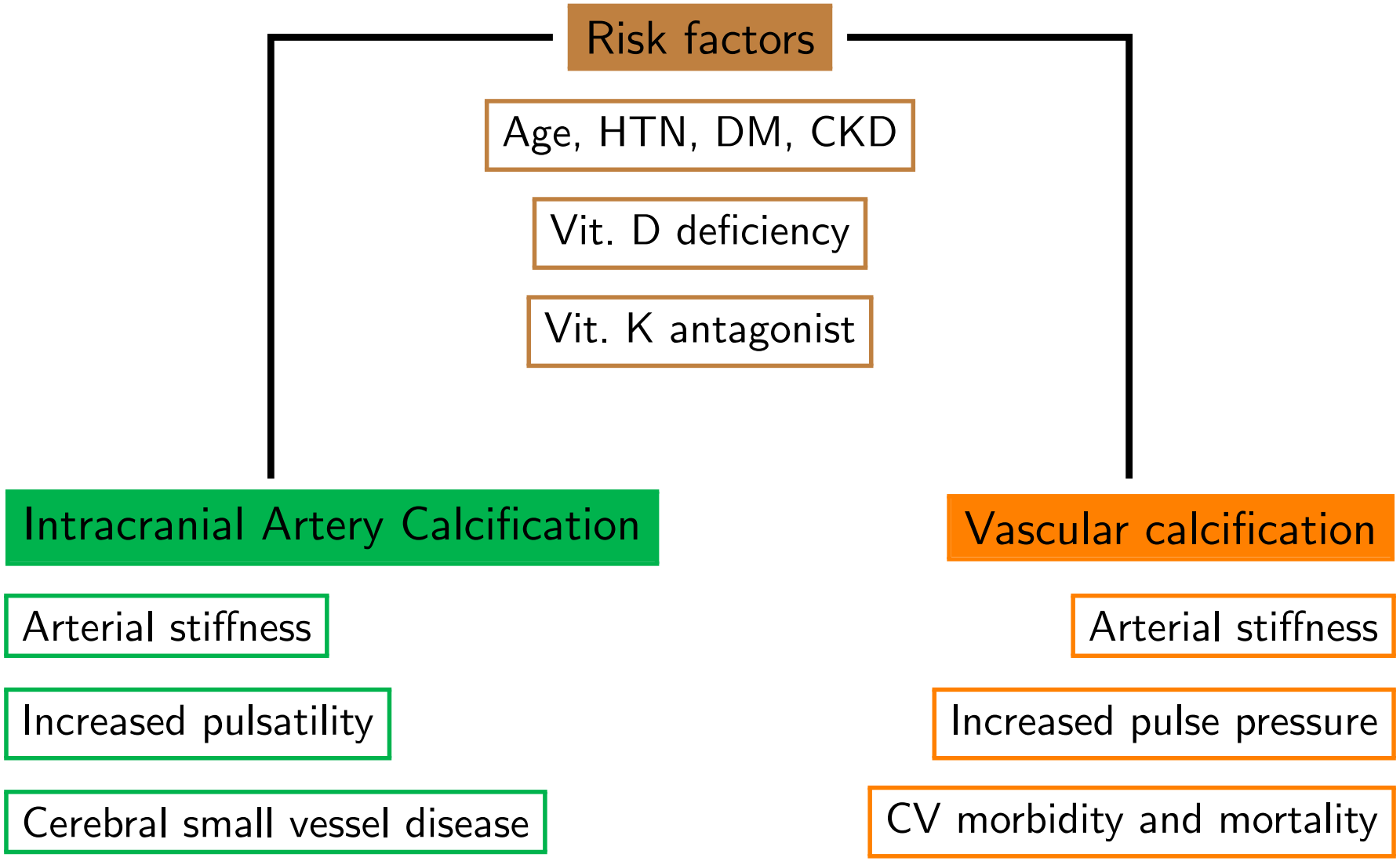


Figure 4. Meta-analysis of the risk of spontaneous intracerebral hemorrhage (ICH; **A** and **B**) and ischemic stroke (**C** and **D**) stratified by the dominant ethnicity of subjects included in each cohort as Asian or Western (white), with and without cerebral microbleeds (CMBs).

Charidimou A et al. Am J Cardiol 2013;112:1230e1234


Risk factors
Age, HTN, DM, CKD
Vit. D deficiency
Vit. K antagonist
Intracranial Artery Calcification
Arterial stiffness
Increased pulsatility
Cerebral small vessel disease
Vascular calcification
Arterial stiffness
Increased pulse pressure
CV morbidity and mortality

25-Hydroxyvitamin D Status Is Associated With Chronic Cerebral Small Vessel Disease

Pil-Wook Chung, MD; Kwang-Yeol Park, MD; Jeong-Min Kim, MD; Dong-Woo Shin, MD; Moo-Seok Park, MD; Yun Jae Chung, MD; Sam-Yeol Ha, MD; Suk-Won Ahn, MD; Hae-Won Shin, MD; Yong Bum Kim, MD; Heui-Soo Moon, MD

Background and Purpose—The aim of this study was to determine the association between 25-hydroxyvitamin D (25(OH) D) and neuroimaging correlates of cerebral small vessel disease.

Methods—We identified 759 consecutive patients with acute ischemic stroke or transient ischemic attack. Lacunes, white matter hyperintensity, and cerebral microbleed (CMB) were assessed using MR images. Deep CMB was defined as the presence of CMB in basal ganglia, thalamus, or brain stem. The association between 25(OH)D and small vessel disease was tested using linear and logistic regression analyses.

Results—Mean age was 68 (±13) years. Mean level of 25(OH)D was 34.1±17.8 nmol/L. On bivariate analysis, a 25-nmol/L decrease in 25(OH)D was associated with lacunes (regression coefficient, 0.23; 95% confidence interval [CI], 0.02–0.45), severe white matter hyperintensity (odds ratio, 2.05; 95% CI, 1.41–3.08), and deep CMB (odds ratio, 1.28; 95% CI, 1.01–1.63). Also, 25(OH)D deficiency (≤25 nmol/L) was associated with lacunes (regression coefficient, 0.5; 95% CI, 0.04–0.95), severe white matter hyperintensity (odds ratio, 2.74; 95% CI, 1.31–6.45), and deep CMB (odds ratio, 1.68; 95% CI, 1.03–2.78). The association remained significant even after multivariable adjustment and in the subgroup of previously healthy patients.

Conclusions—25(OH)D is inversely associated with lacunes, white matter hyperintensity, and deep CMB. Our findings suggest that 25(OH)D is linked to small vessel disease, and in future trials it should be tested whether 25(OH)D supplementation can prevent small vessel disease. **(*Stroke*. 2015;46:00-00. DOI: 10.1161/STROKEAHA.114.007706)**

Chung PW et al. Stroke 2015

Vitamin D

- Calcium homeostasis and bone metabolism

Vitamin D

- Calcium homeostasis and bone metabolism
- Atherosclerosis
- Blood pressure
- Inflammation
- Metabolic syndrome
- Vascular calcification
- Arterial stiffness

Vitamin D related genes

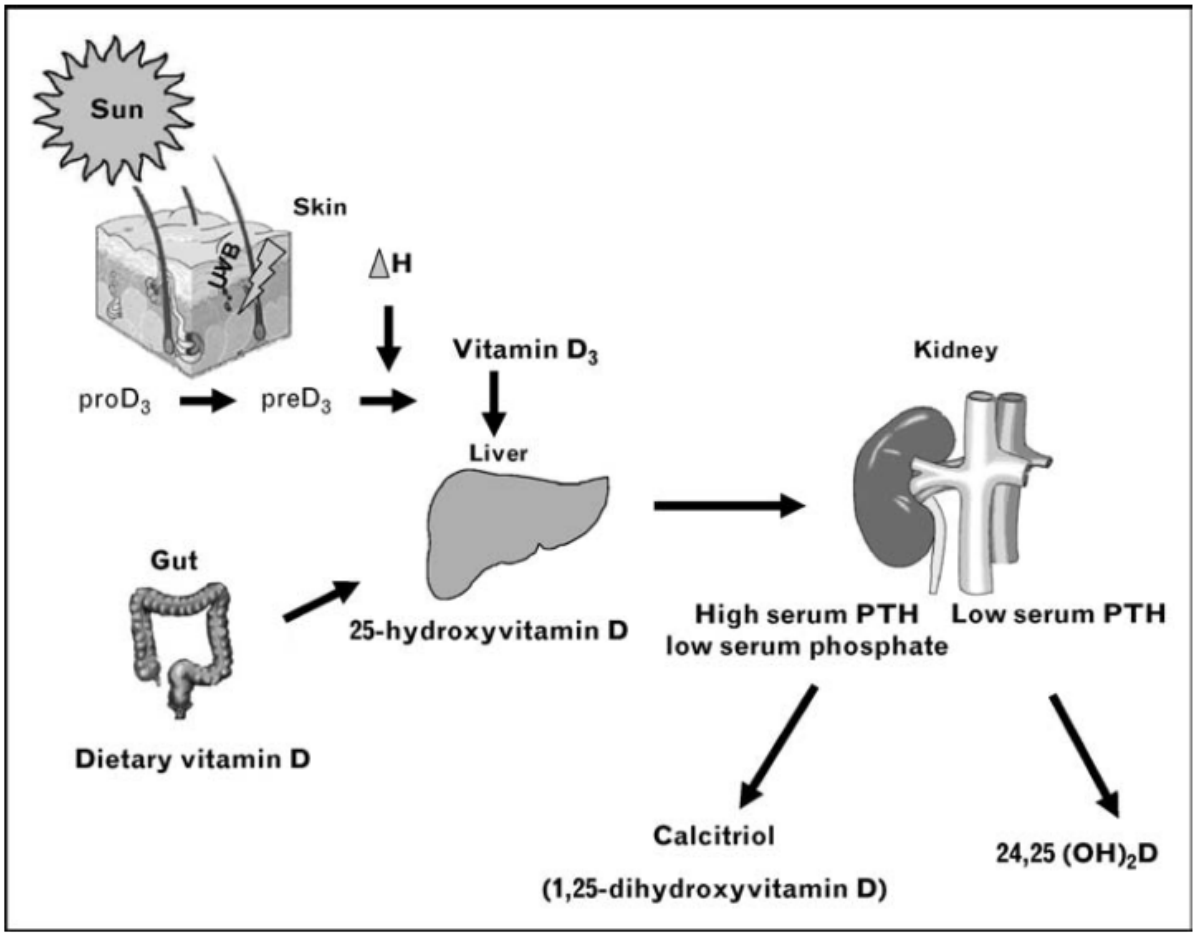
- KEGG pathway, Reactome pathway, AmiGO
- Pubmed search
- rs ID: dbSNP, SNPedia

1000 Genome Project

- Variation detection of vitamin D related genes
  - Base variation: SNP, short InDel
  - Structural variation: CNV, Duplication, InDel, Translocation, Inversion
- Racial and geographic difference

Figure 1 Vitamin D physiology

PTH, parathyroid hormone. Adapted with permission [1].



Zittermann A. et al. Curr Opin Lipidol 2007

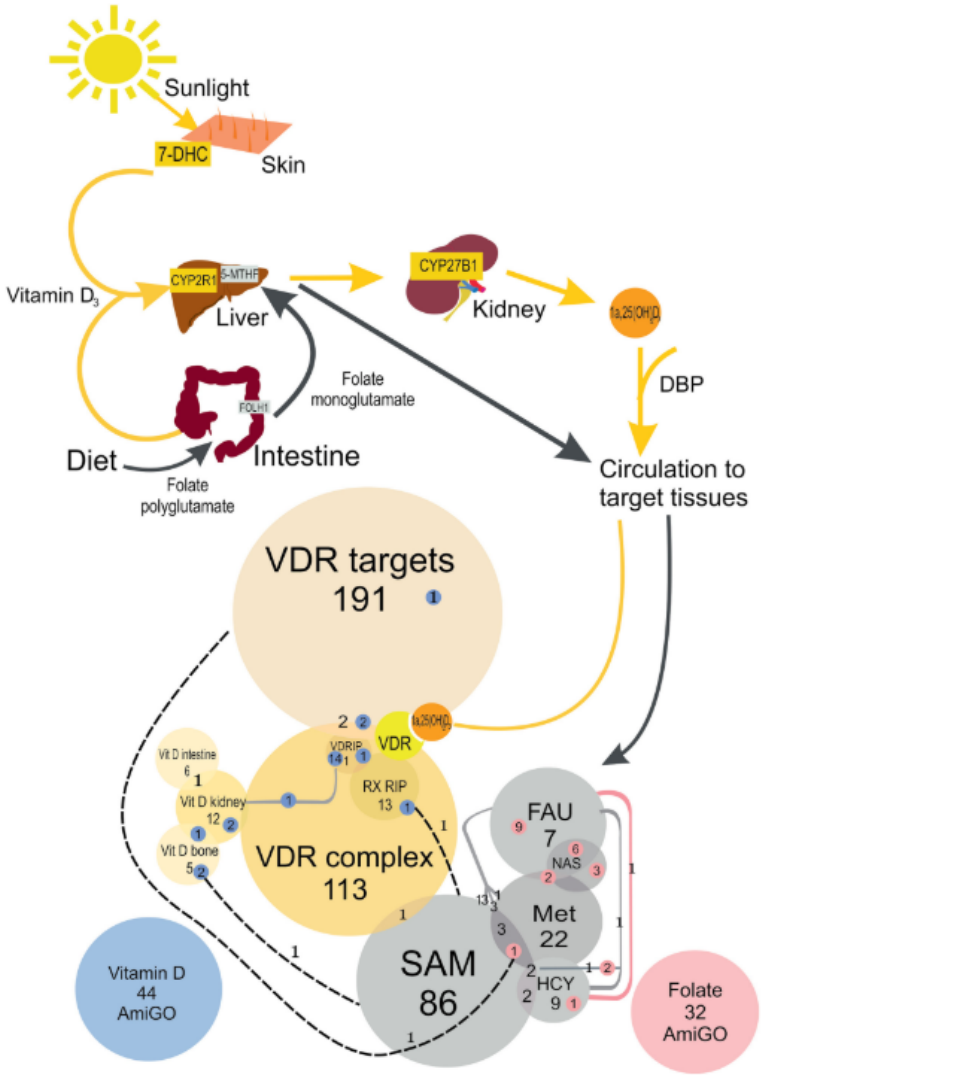


Fig 1. Vitamin D and folate acquisition, metabolism and gene sets analyzed in this study. The upper part shows metabolism of vitamin D (yellow

Arciero E et al. PLOS ONE 2015

IGSR and the 1000 Genomes Project

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

2,504 individuals from 26 populations

http://www.internationalgenome.org/

내용	12월		1월				2월			
	3주	4주	1주	2주	3주	4주	1주	2주	3주	4주
연구 설계										
Vitamin D 유전체 데이터 수집										
Vitamin D SNP 데이터 수집										
1000 genome 데이터 구조 분석 (VCF File)										
Vitamin D 유전체 Variant Detection										
인종별 Vitamin D 유전체 특성분석										
보고서 작성 및 프리젠테이션 준비										