Variations in Vitamine D Related Genes Among Races

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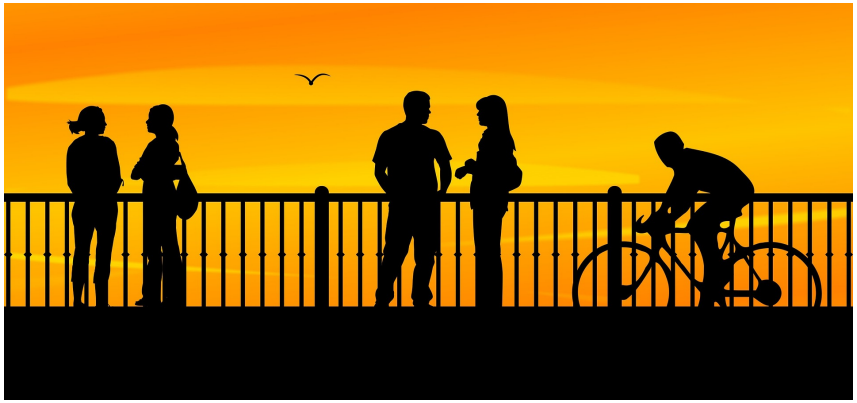
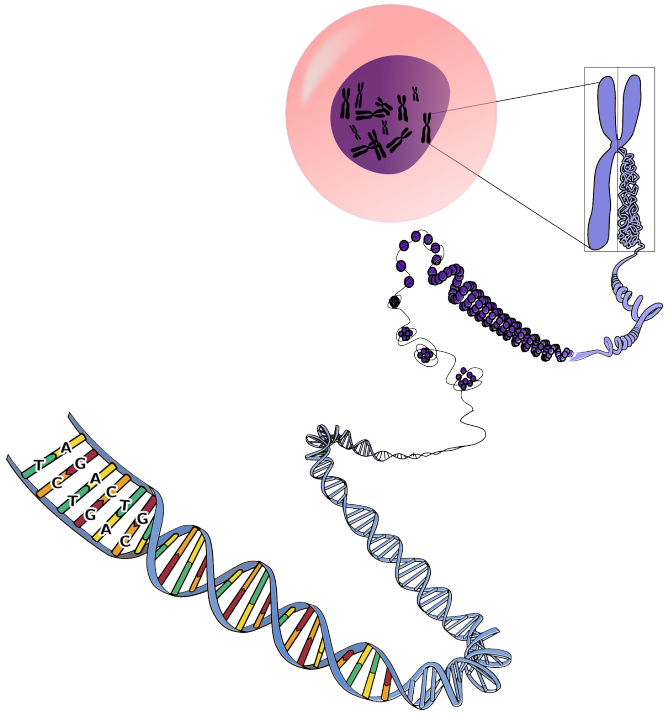
I am a Novice, too.

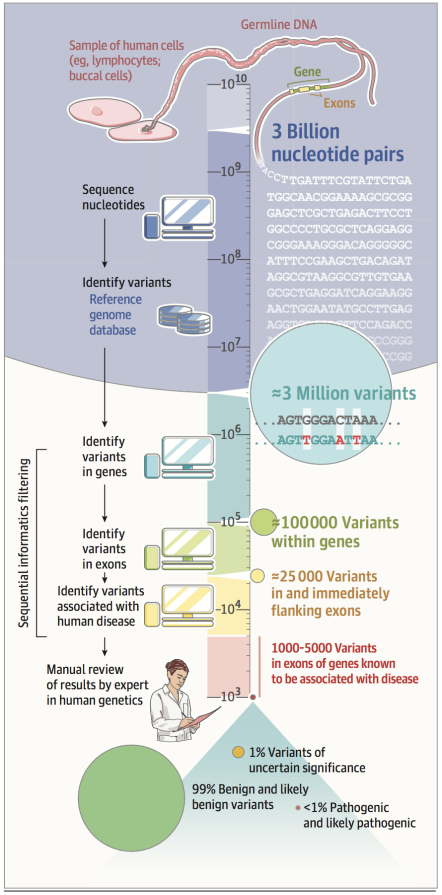




Gene-disease association

- Amount of information
  - 3,000,000,000 base pairs
  - 3,000,000 SNPs
  - 100,000 variants in exon
- The majority of variants are very rare.
- Characterization of functional meaning of genetic variation needs various kinds of data.

Figure. Informatic and Human Analysis Required for Finding Rare Pathogenic Variants in a Human Genome



Evans JP et al. JAMA May 9, 2017 Volume 317, Number 18

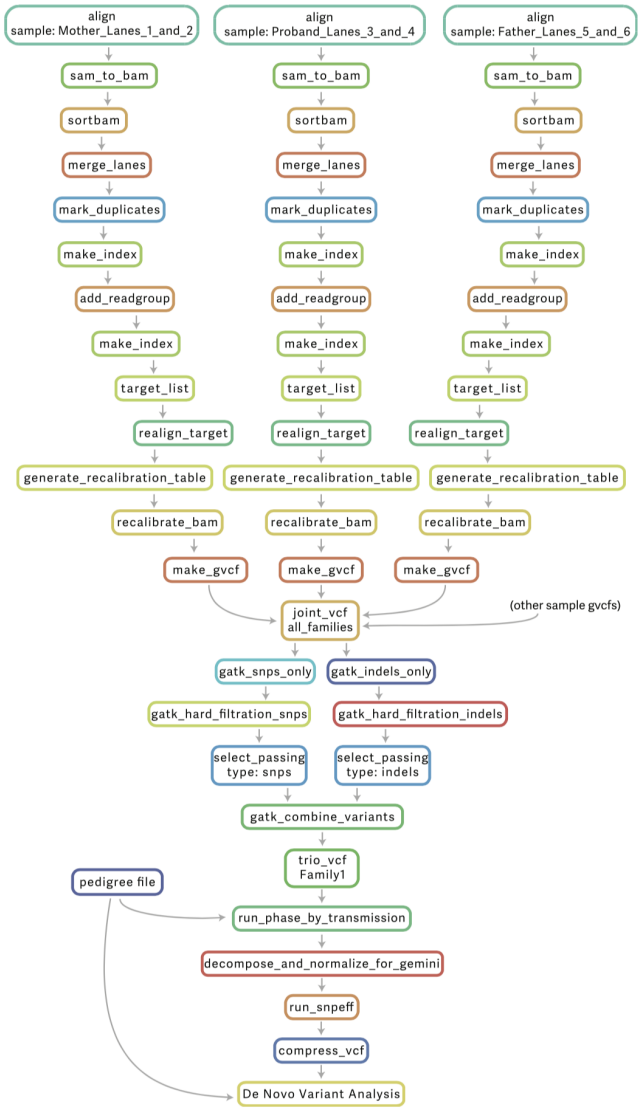


Figure 1. A DAG (Directed Acyclic Graph) depicting a trio analysis pipeline for detecting *de novo* mutations.

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Table 1. A classification of modern pipeline frameworks

Syntax	Paradigm	Interaction	Example	Ease of Development	Ease of Use	Performance
Implicit	Convention	CLI	Snakemake, Nextflow, BigDataScript	★★★½	★★★★½	★★★
Explicit	Convention	CLI	Ruffus, bpipe	★★★★	★★★★	★★★
Explicit	Configuration	CLI	Pegasus	★★½	★★★	★★★★
Explicit	Class	CLI	Queue, Toil	★★½	★★★	★★★★★
Implicit	Class	CLI	Luigi	★★★	★★★½	★★★★★
Explicit	Configuration	Open Source Server Workbench	Galaxy, Taverna	★★★	★★★★½	★★★
Explicit	Configuration	Commercial Cloud Workbench	DNAnexus, SevenBridges	★★½	★★★★★	★★★★½
Explicit	Configuration	Open Source Cloud API	Arvados, Agave	★★★	★★★★	★★★★½

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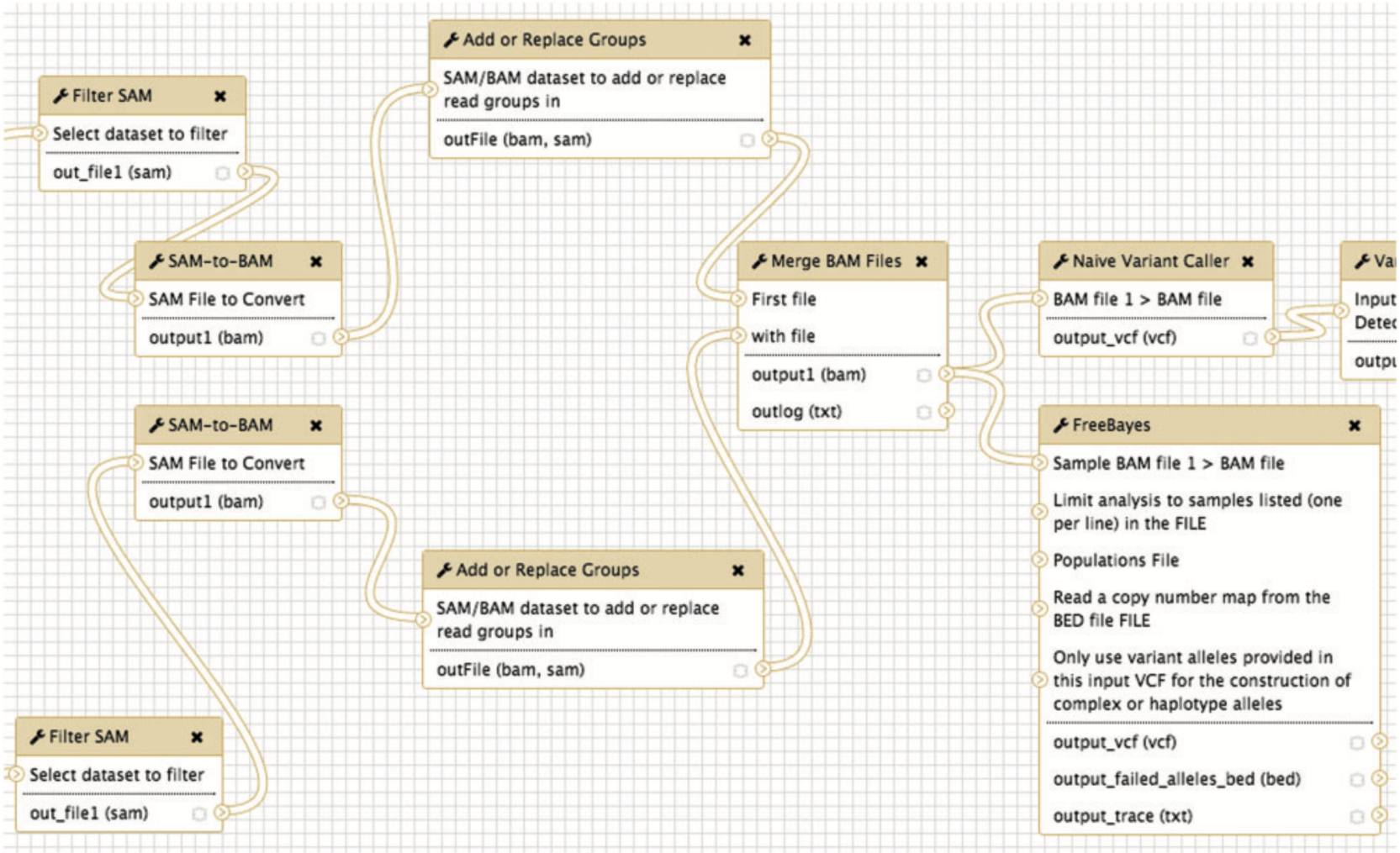

Figure 7. The Galaxy Workflow Editor allows users to link inputs, outputs and tools on a graphical canvas.

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Tools that I am using are

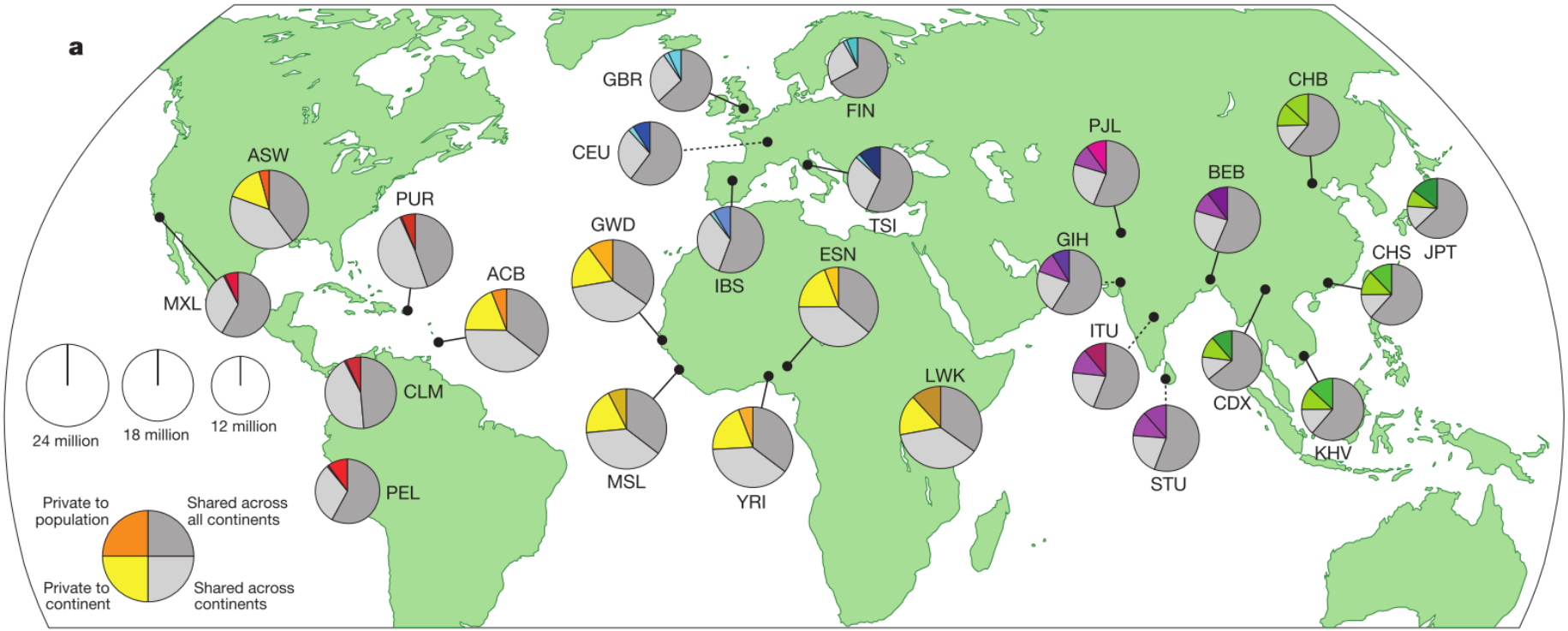
- R
- Git
- GitHub
- Python
- Unix Shell Commands
- Softwares downloaded from the Web
- Amazon Web Service
- SQL

IGSR and the 1000 Genomes Project

2,504 individuals from 26 populations

http://www.internationalgenome.org/

A global reference for human genetic variation



The 1000 Genomes Project. Nature 2015

Stroke has diverse etiologies

Ischemic Stroke

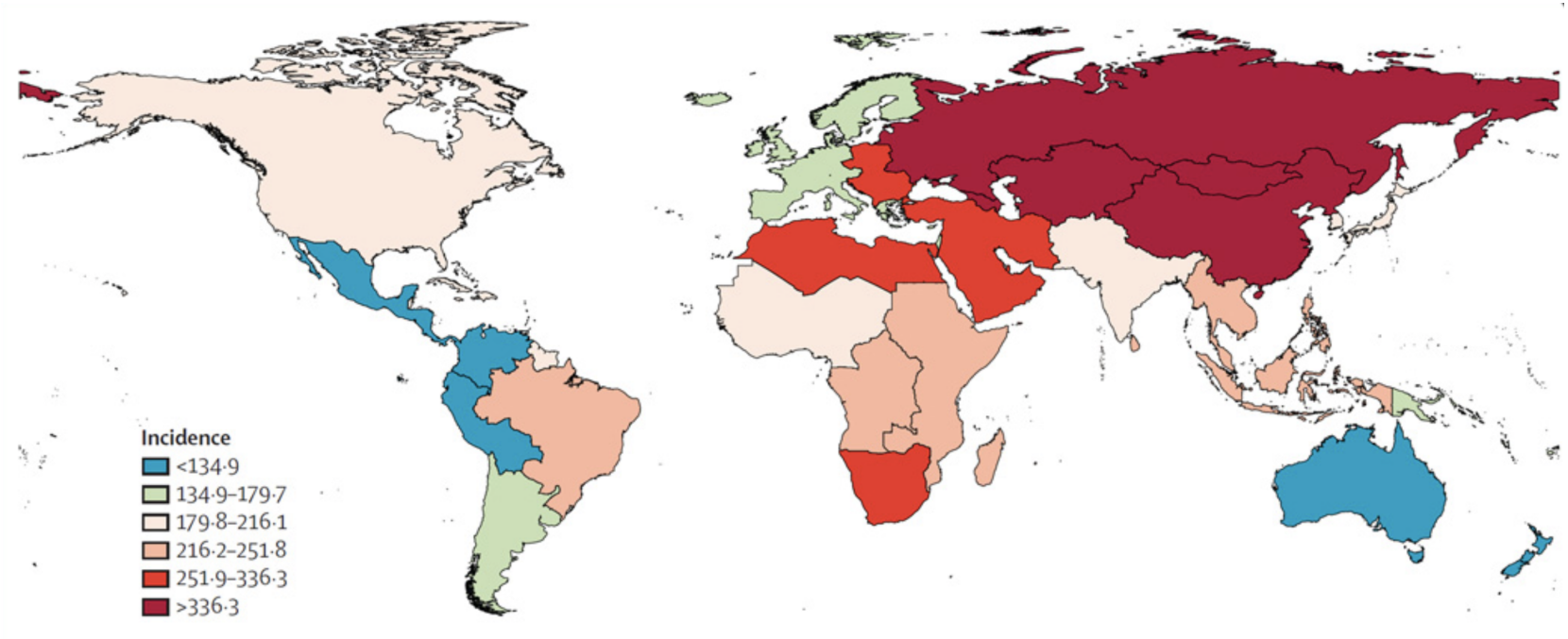
- Atherosclerosis
- Small artery occlusion
- Cardiac disease causing embolism
- Other causes such as moyamoya disease

Hemorrhagic Stroke

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

Age-standardised stroke incidence

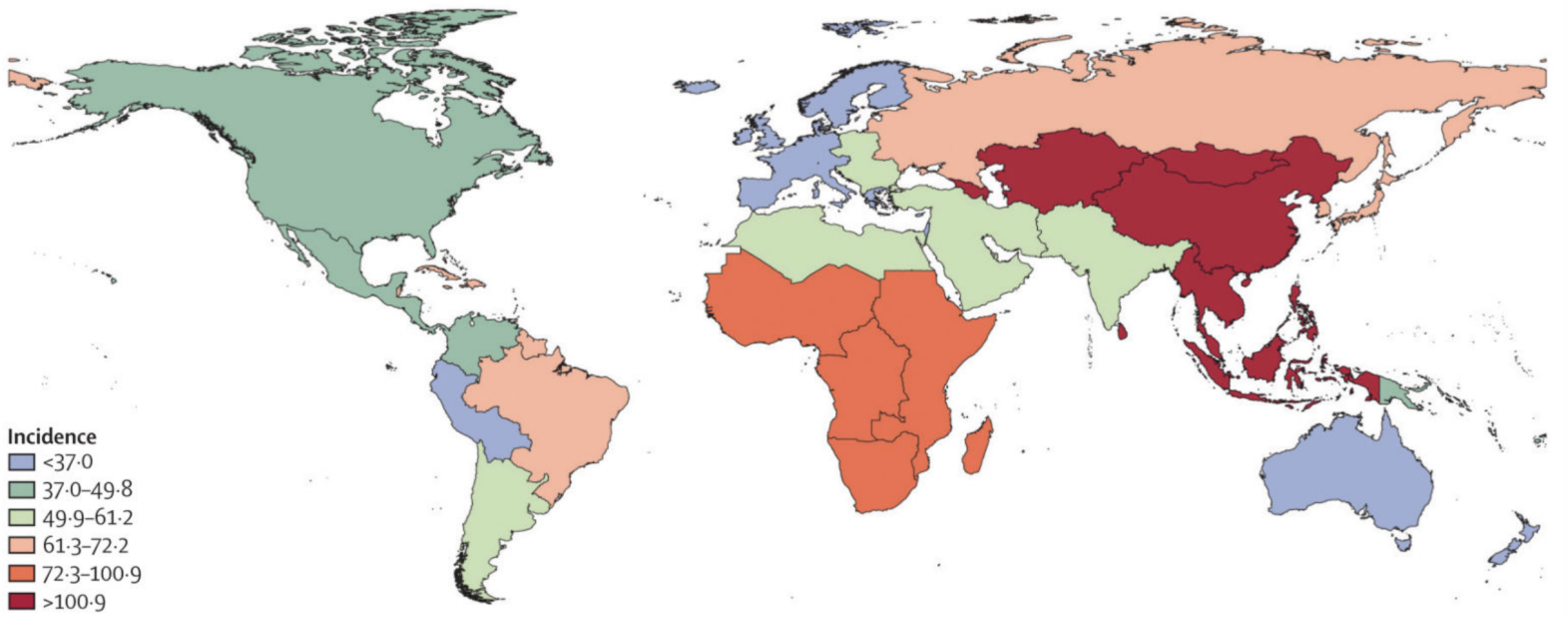
per 100 000 person-years for 2010



Lancet Neurol. 2014 383(9913): 245–254.

Age-standardised incidence of haemorrhagic stroke

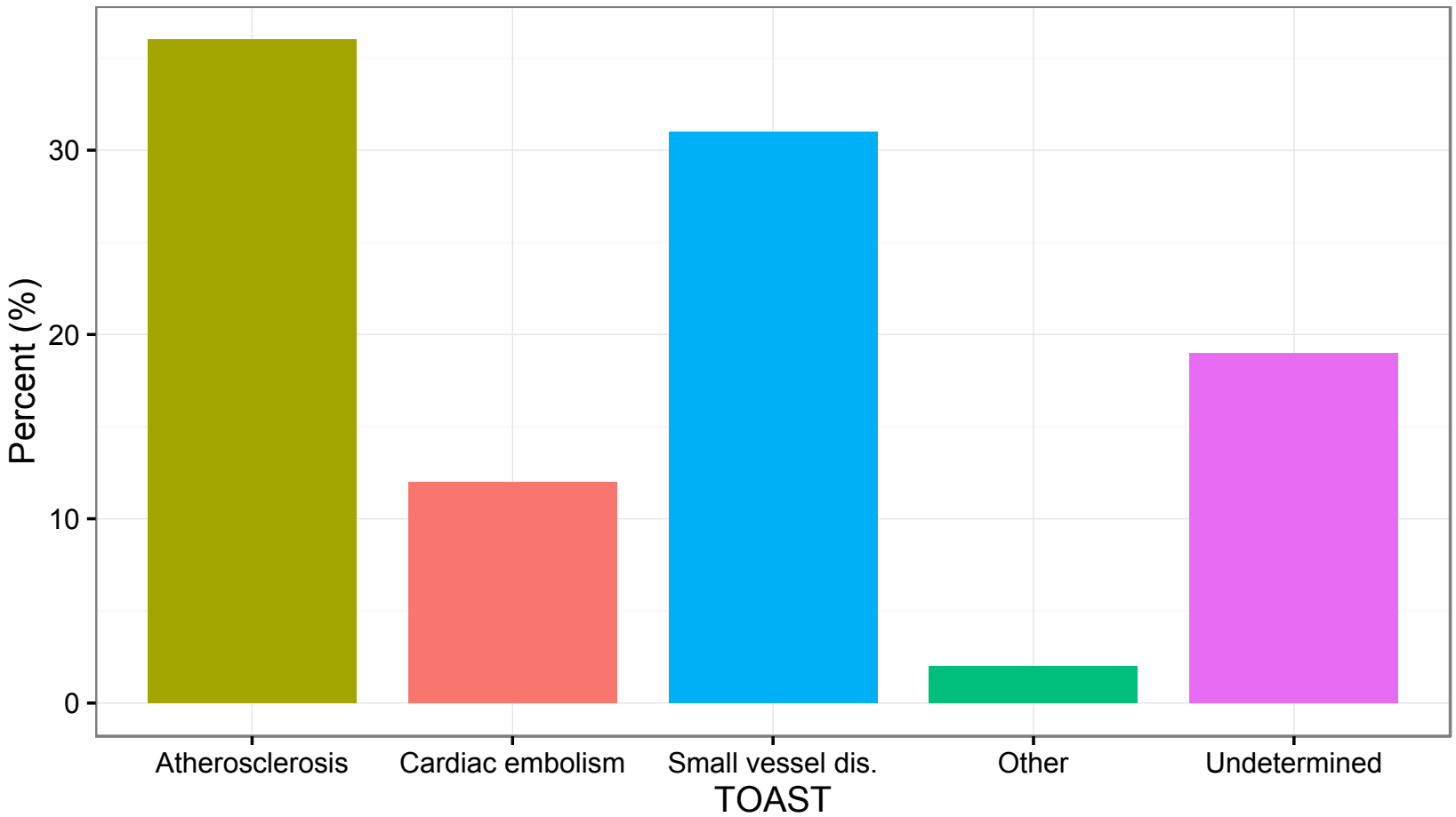
per 100 000 person-years for 2010



Lancet Glob Health. 2013 Nov; 1(5): e259–e281.

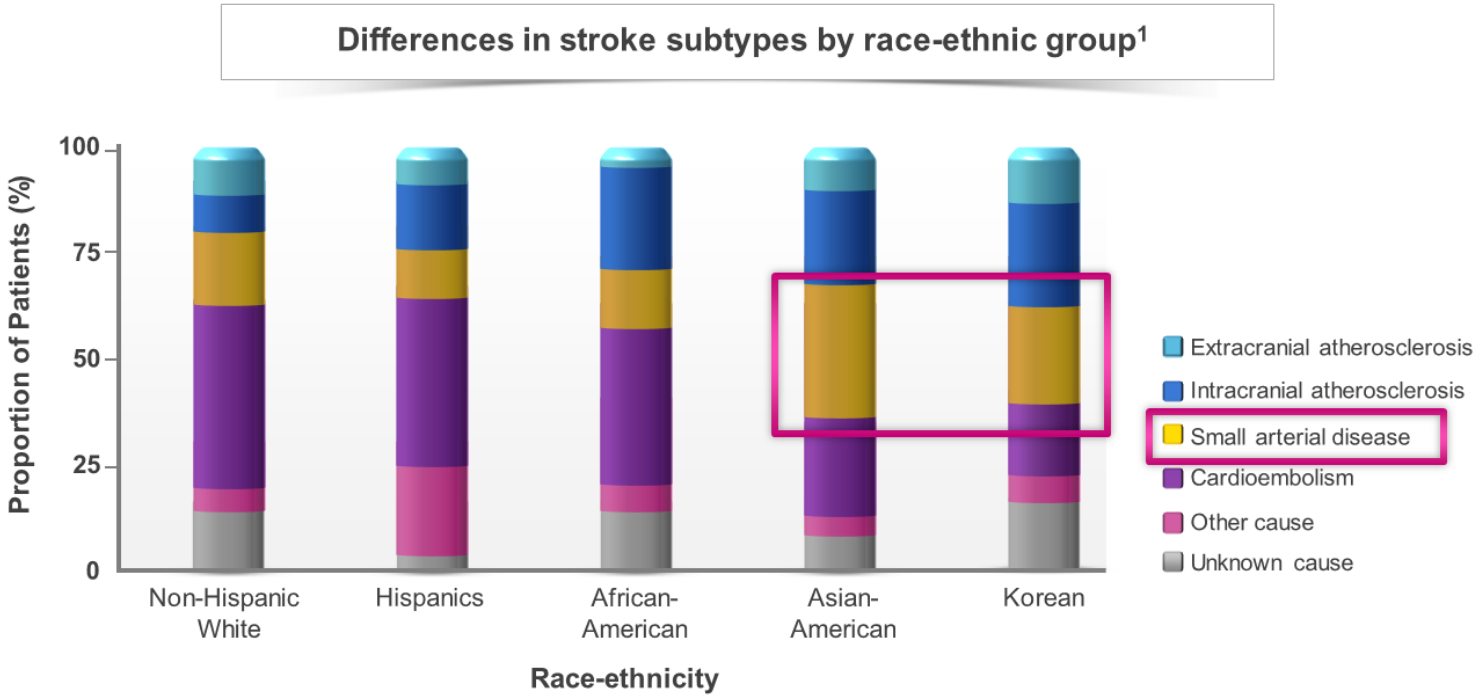
Ischemic stroke in Korea

Analysis of 10,861 cases in Korean Stroke Registry



Yu KH et al. J Korean Neurol Society 2006

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.

MRI findings of small vessel disease

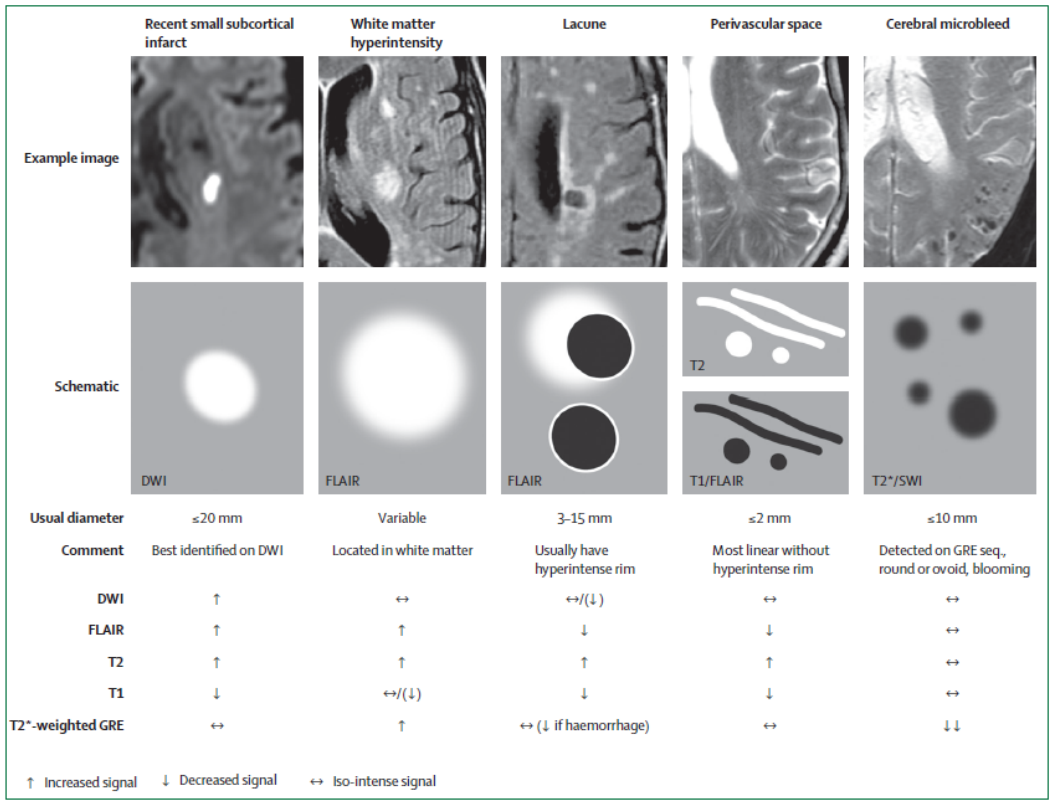
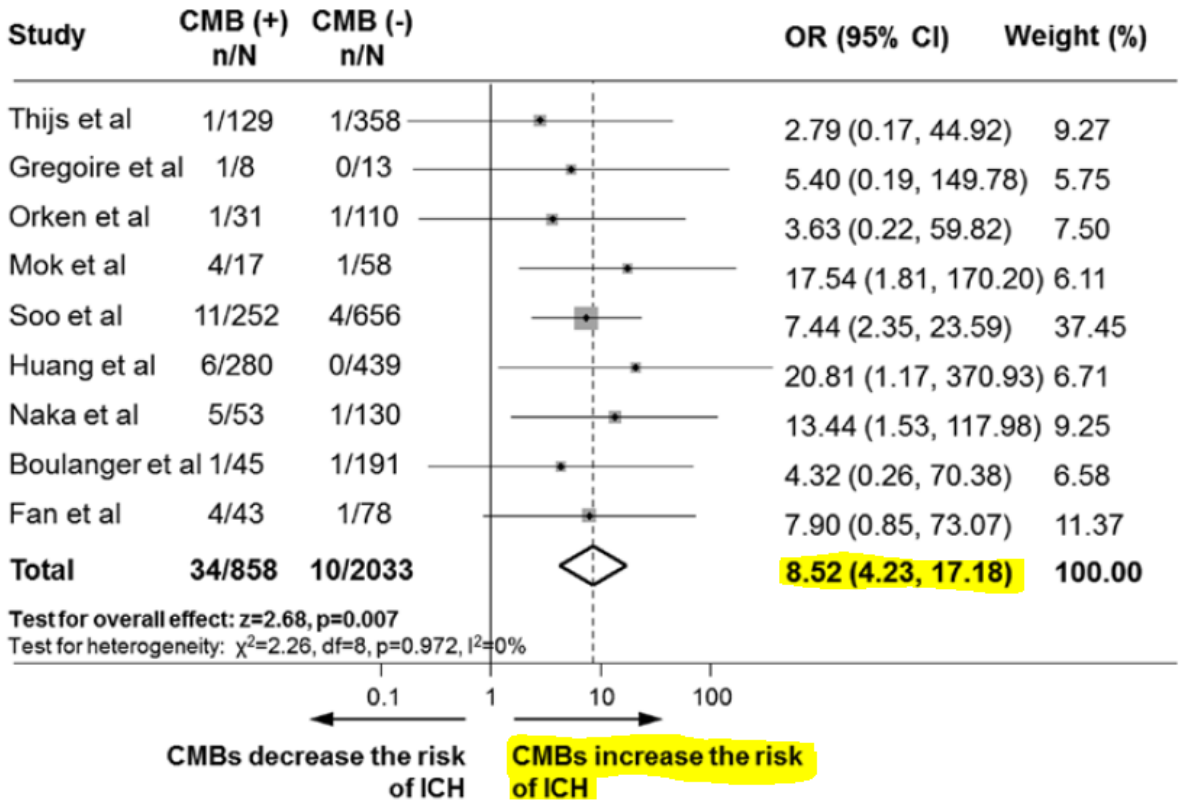


Figure 2: **MRI findings for lesions related to small vessel disease**

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



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

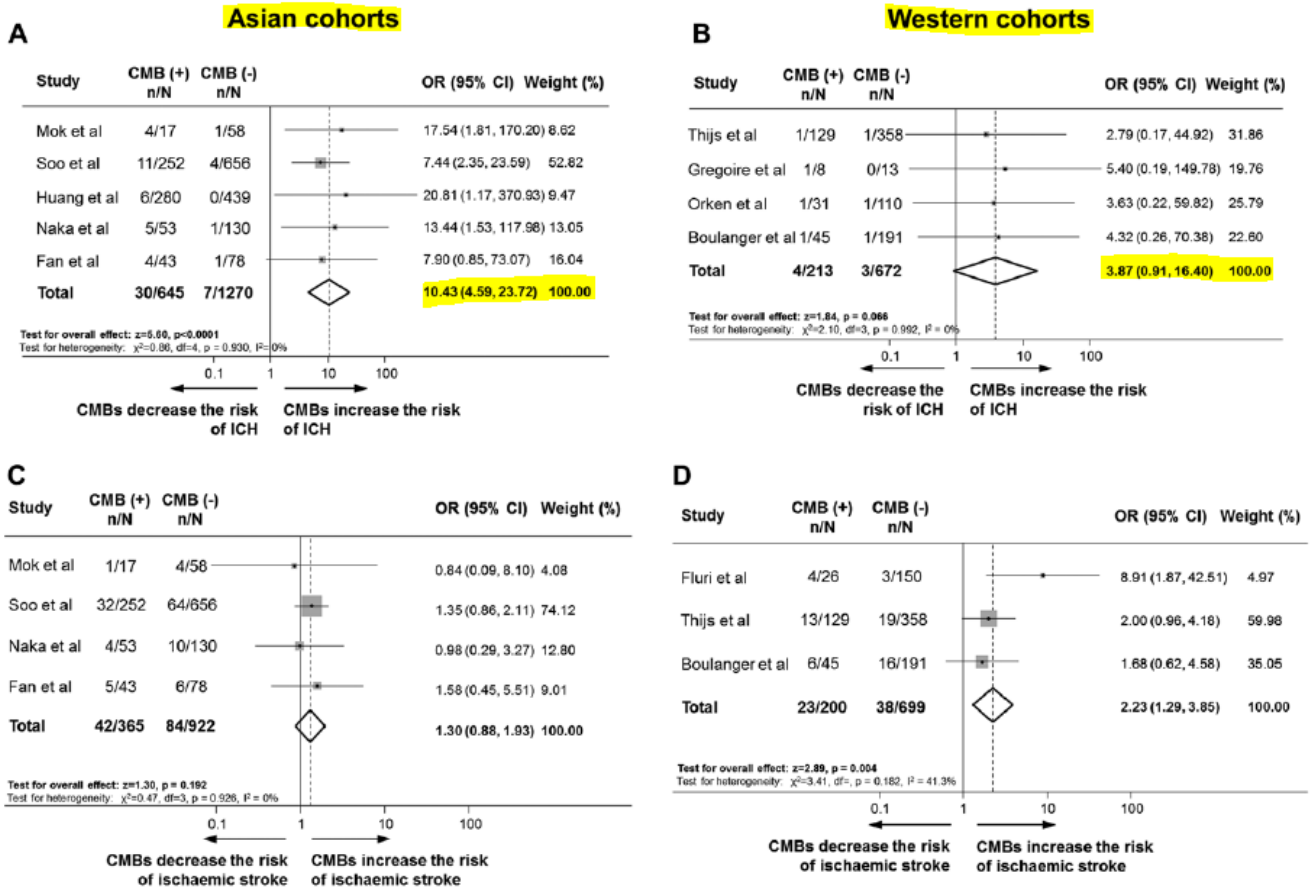
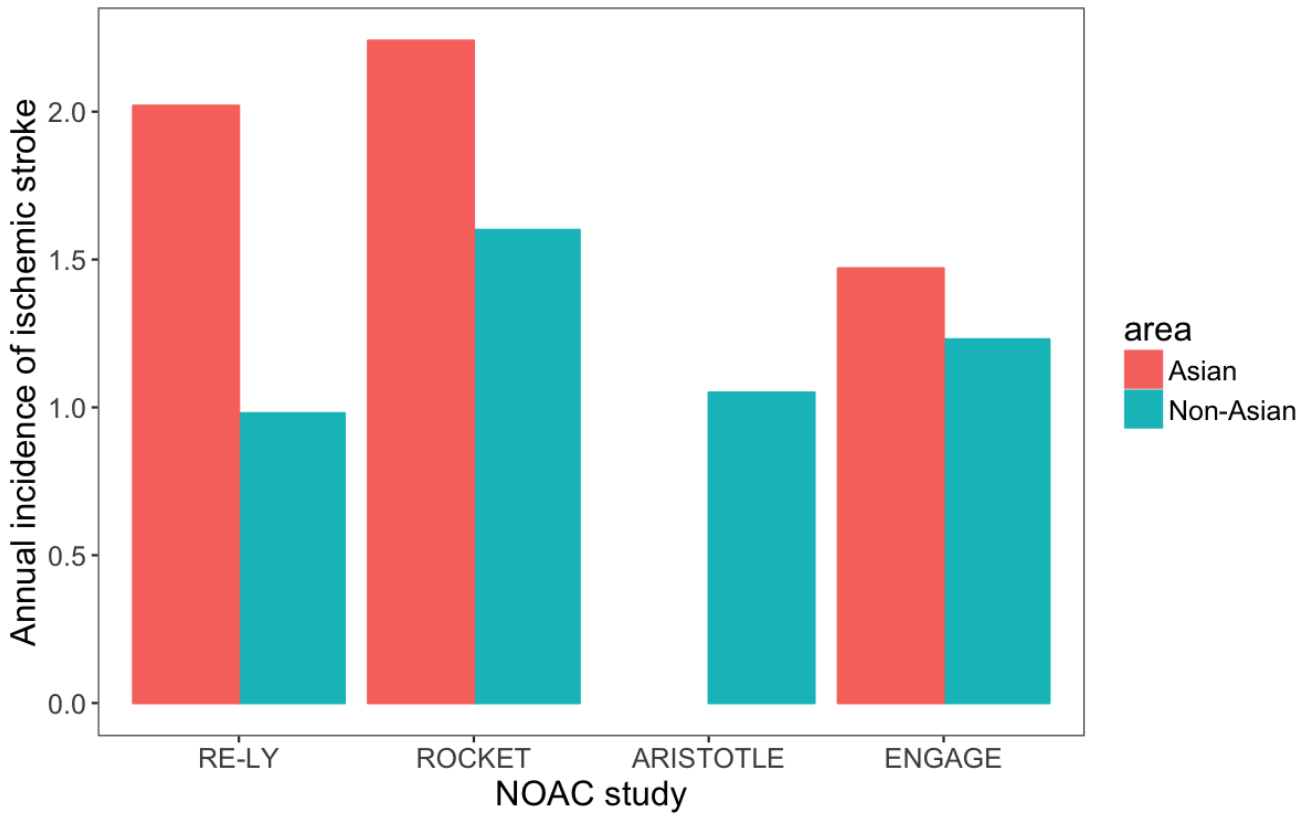


Figure 4. Meta-analysis of the risk of spontaneous intracerebral hemorrhage (ICH; **A** and **B**) and ischemic stroke (**C** and **D**) stratified by the dominant ethnicity of subjects included in each cohort as Asian or Western (white), with and without cerebral microbleeds (CMBs).

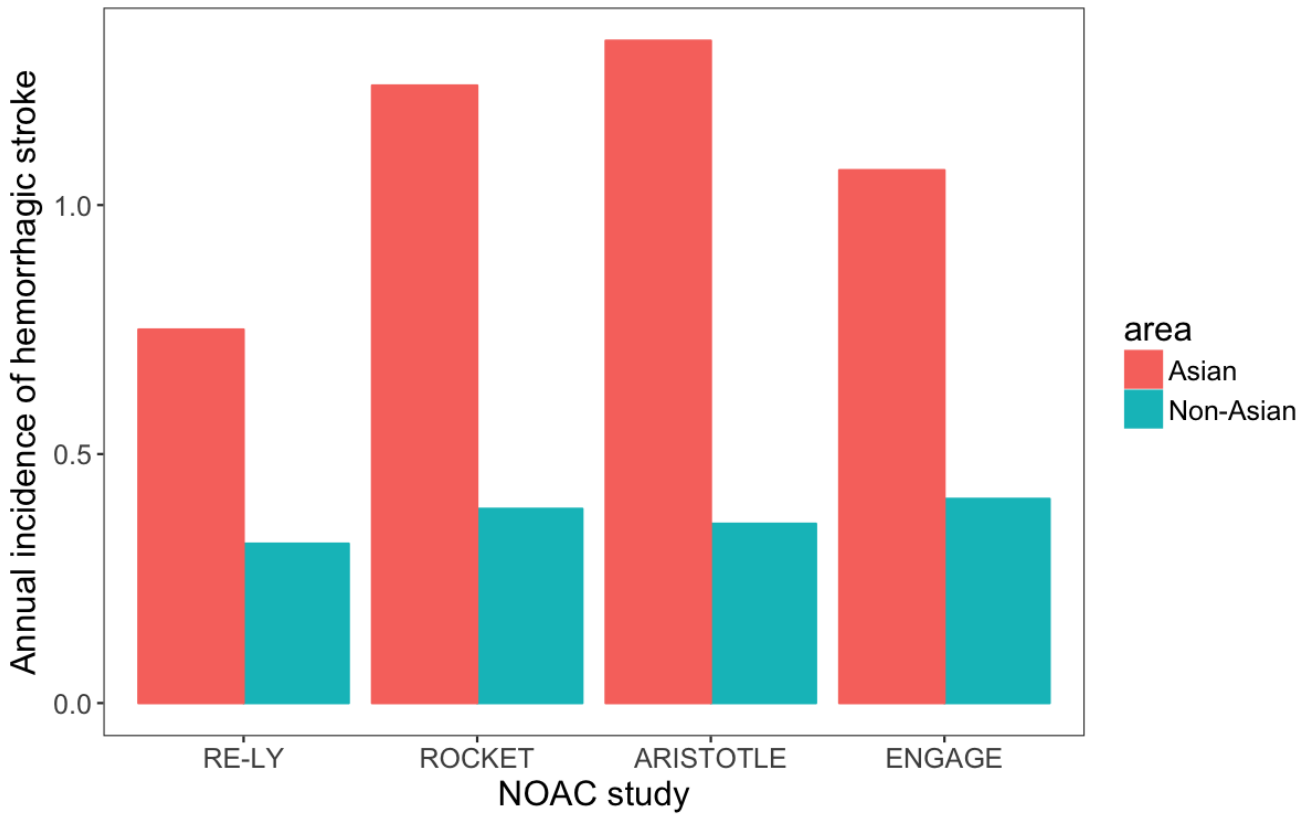
Charidimou A et al. Am J Cardiol 2013;112:1230e1234

Ischemic stroke on warfarin



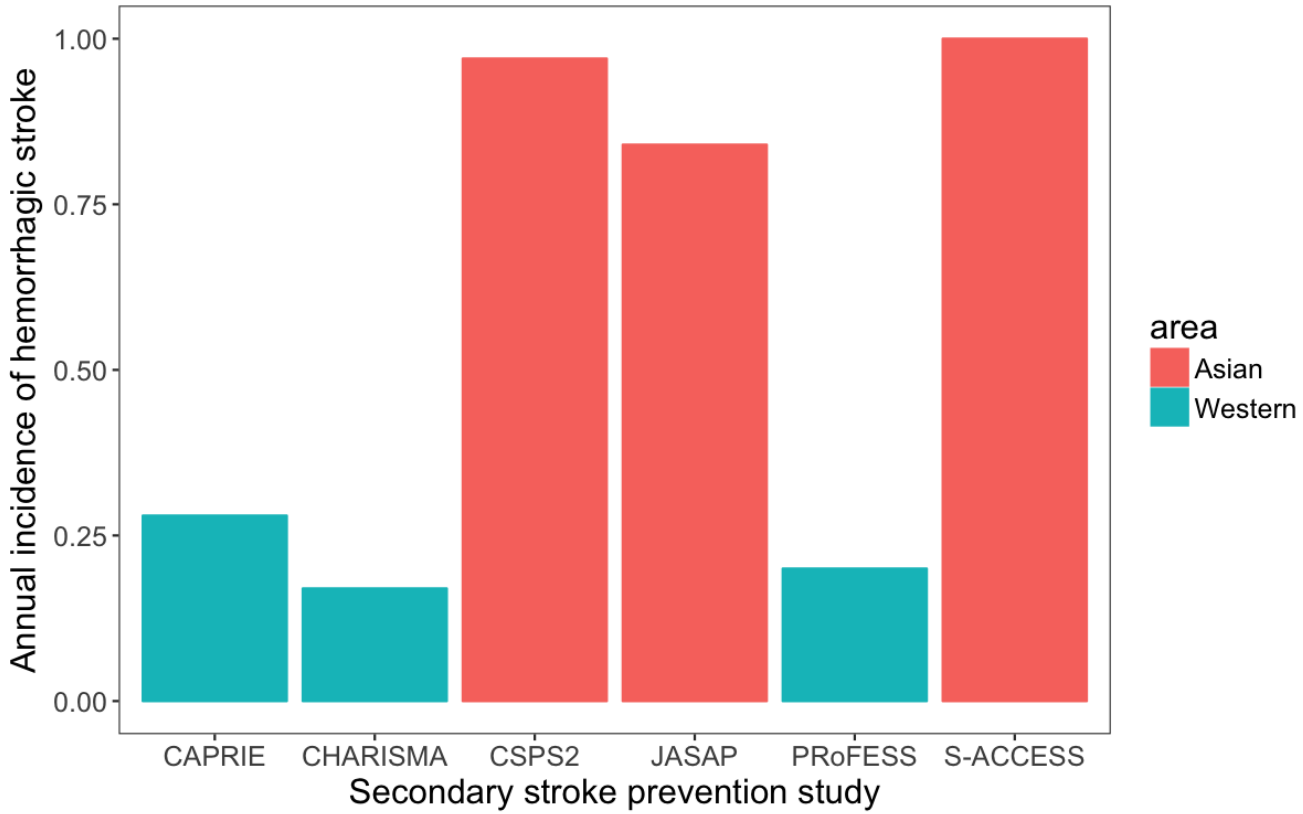
Lip GYH et al, Int J Cardiol 2015;180:246

hemorrhagic stroke on warfarin

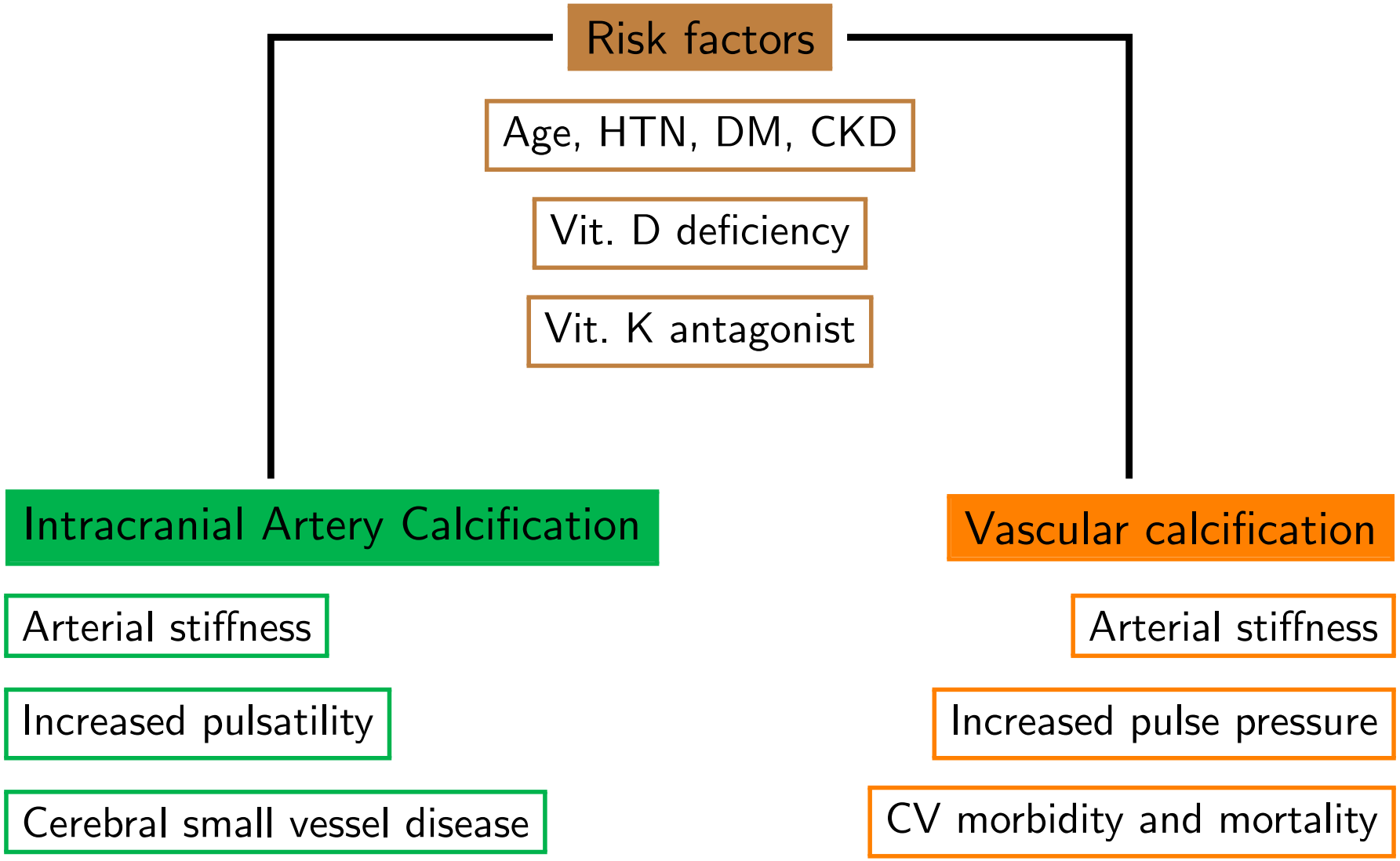


Lip GYH et al, Int J Cardiol 2015;180:246

Incidence of Cerebral Hemorrhage with Aspirin



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


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

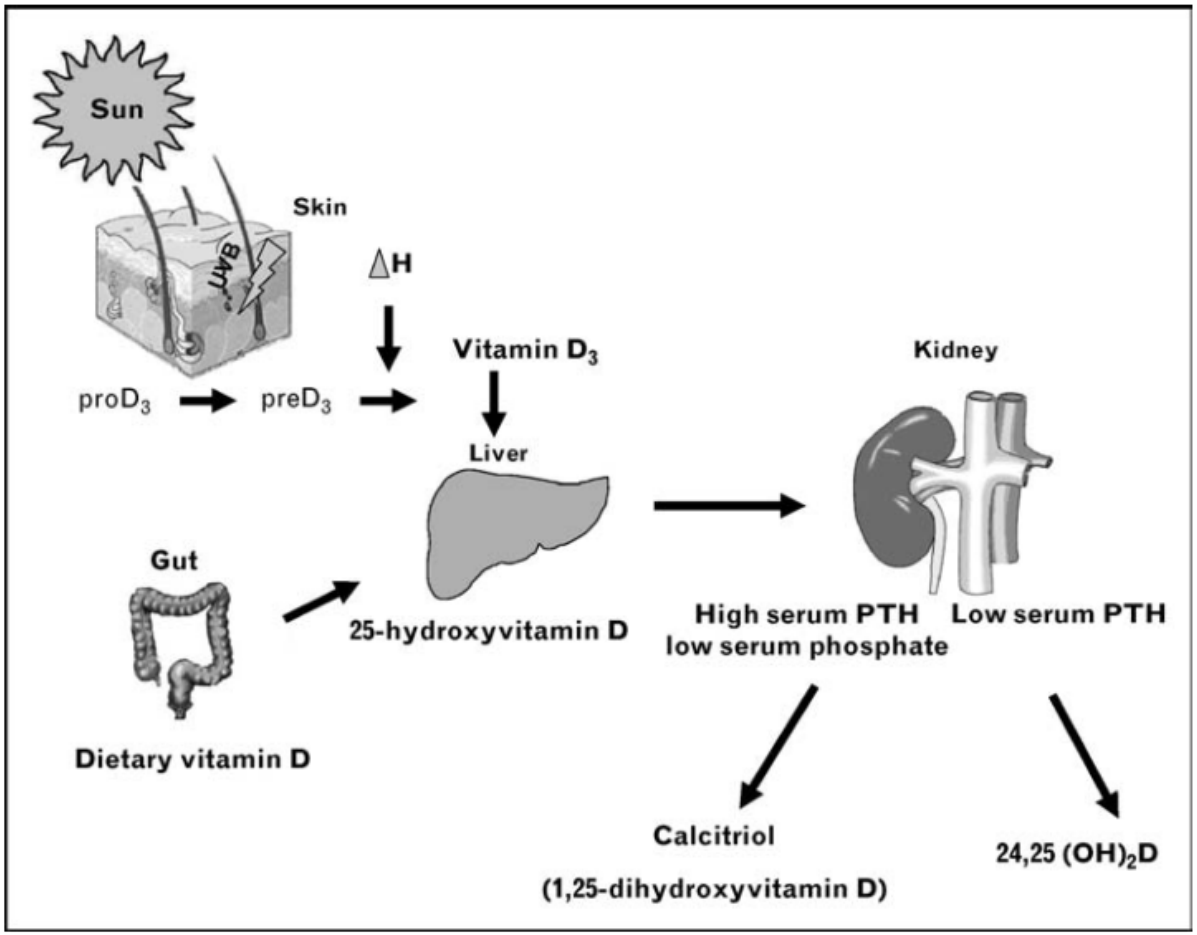
- Calcium homeostasis and bone metabolism

Vitamin D

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

Figure 1 Vitamin D physiology

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



Zittermann A. et al. Curr Opin Lipidol 2007

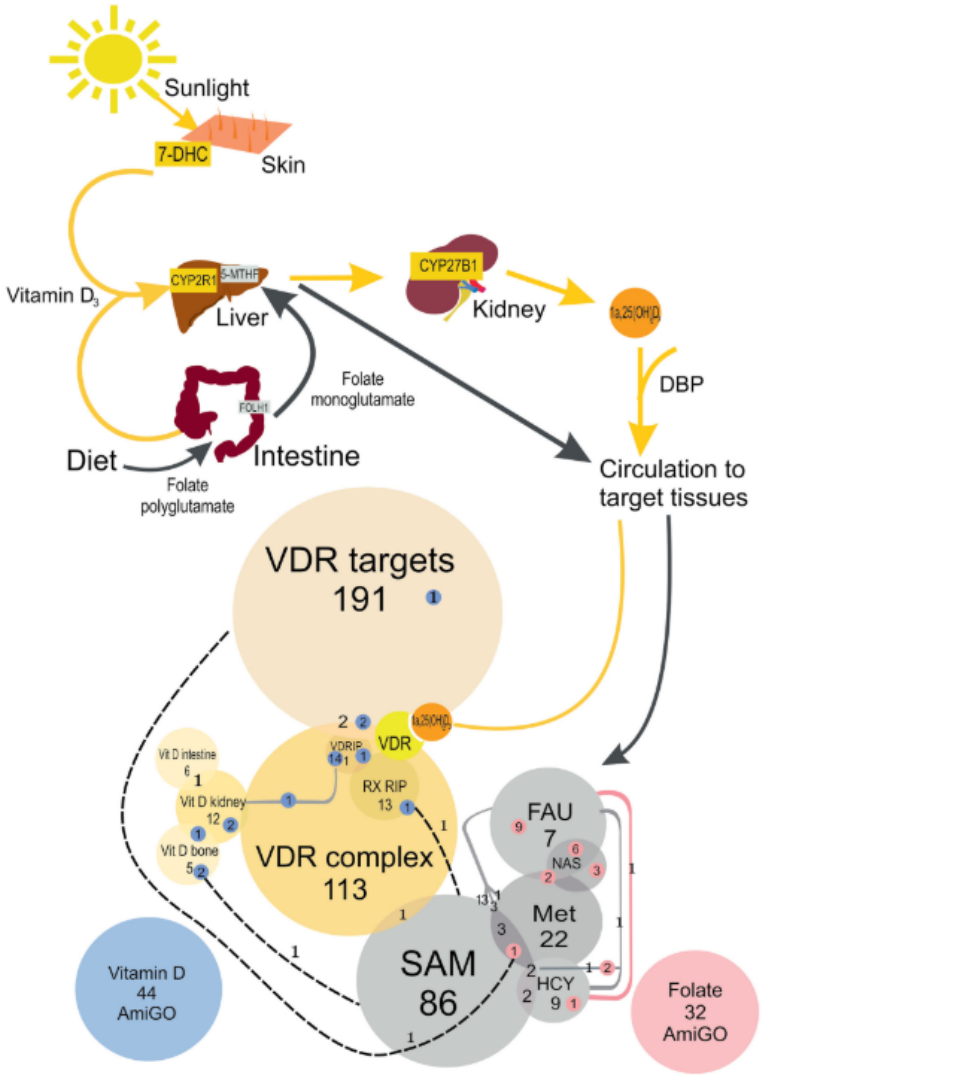


Fig 1. Vitamin D and folate acquisition, metabolism and gene sets analyzed in this study. The upper part shows metabolism of vitamin D (yellow

Arciero E et al. PLOS ONE 2015