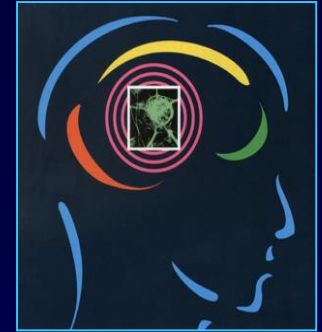




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Race/Ethnic Variations In Cerebral Microbleeds

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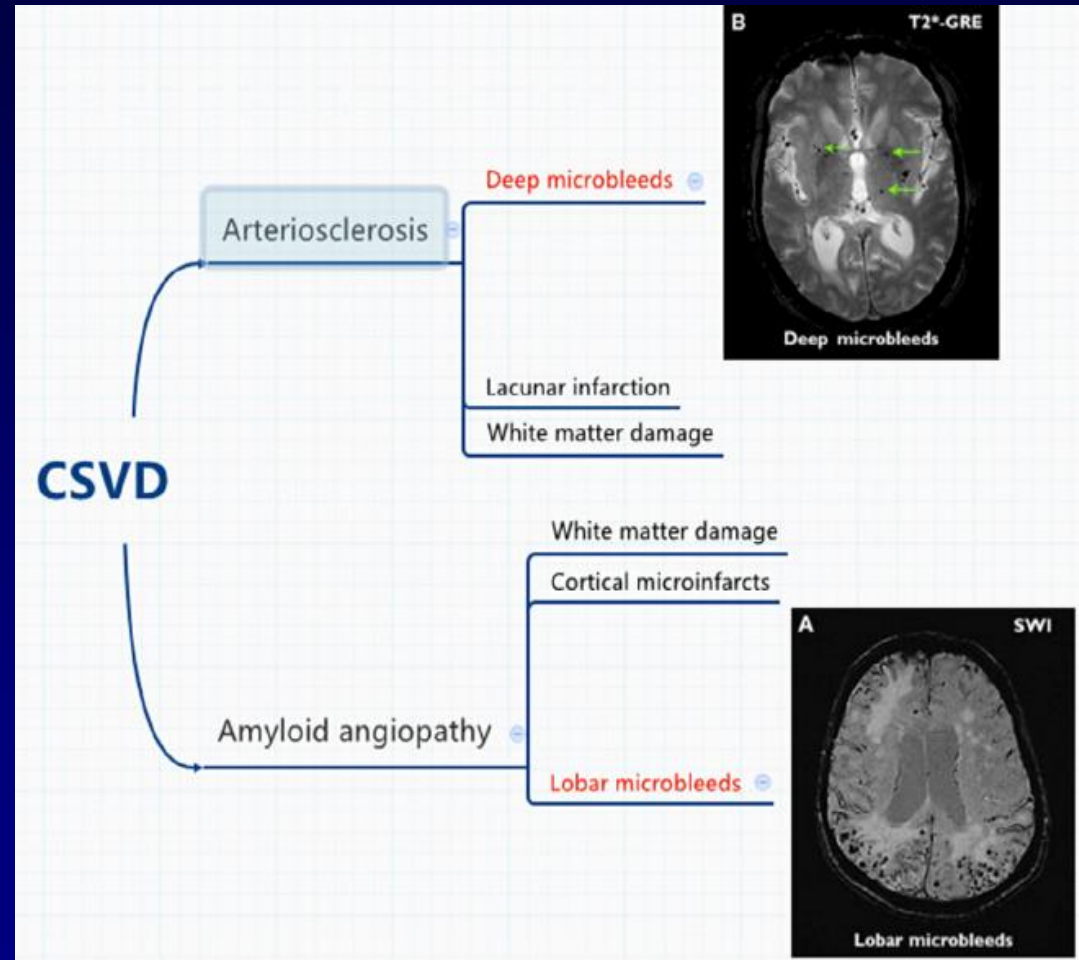
Stanford University

Disclosures

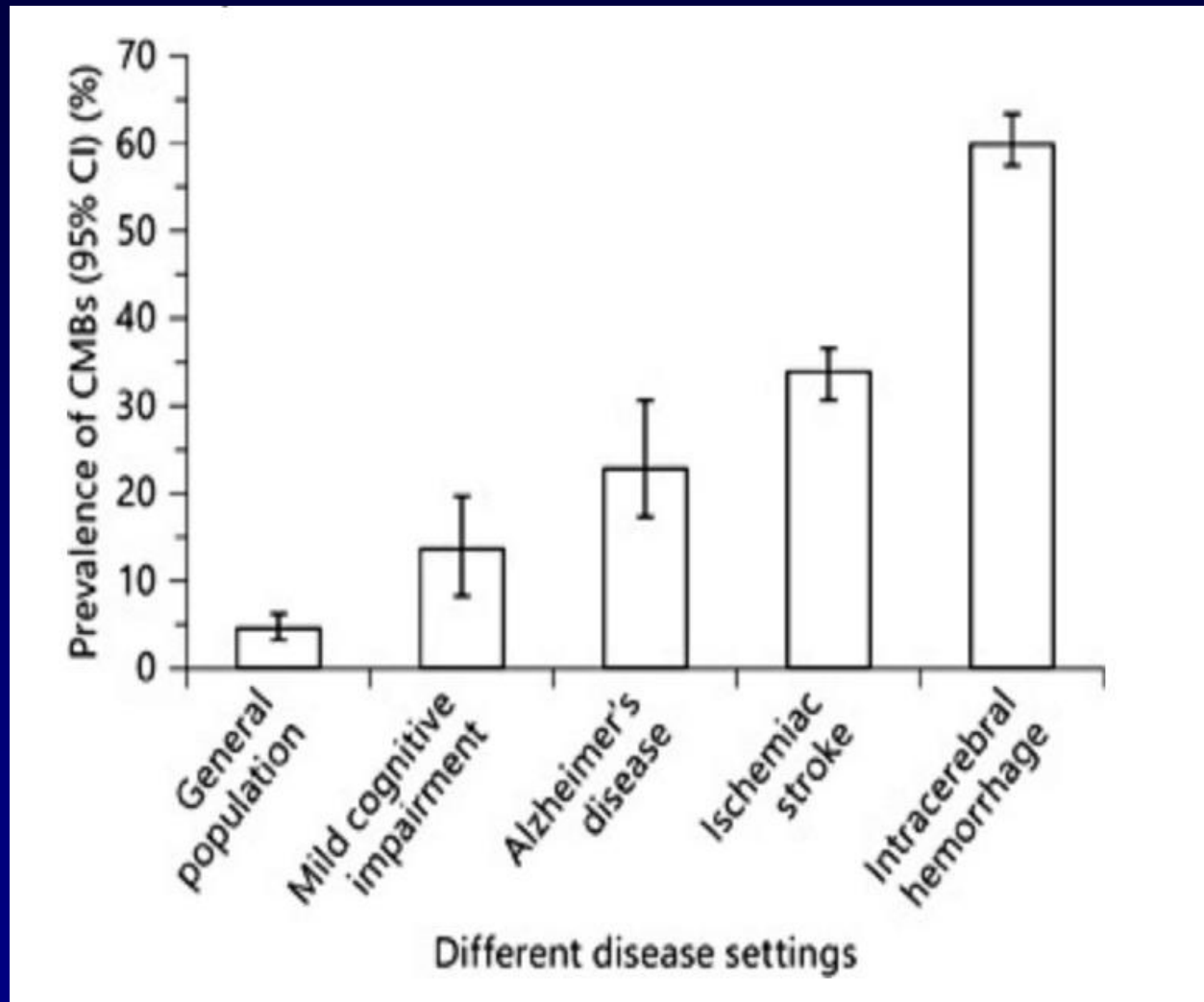
- My favorite MRI sequences are GRE and SWI 😊

Cerebral microbleeds

- Small well demarcated hypointense foci
- T_2^* GRE or SWI
- Cortical, subcortical or deep
- Perivascular hemosiderin laden macrophages
- hemorrhage prone state (e.g. HTN, CAA)
- Marker for SVD
- Risk with age, HTN, CAA, COL4A1, statin etc.
- Influence on outcome (ICH, cognitive dysfunction)



Prevalence of CMB in health and disease



Are there Race/Ethnic
differences in CMB prevalence
in healthy populations?

Non-Asian Vs. Asian cohorts Prevalence of CMB in health

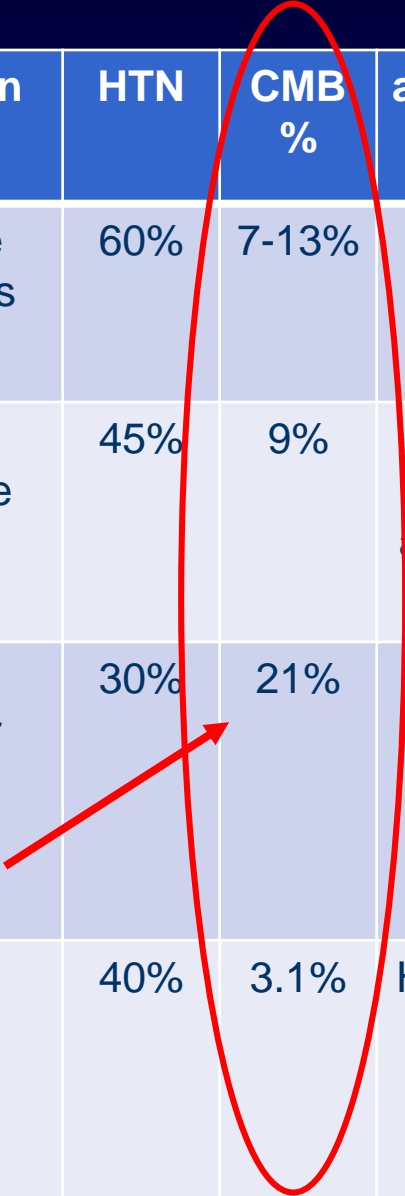
4.5% Asian vs. 5.3% Western

Table 1 Prevalence of cerebral microbleeds (CMB) among subjects without cerebrovascular disease

Refer	Western	Cohort characteristics	Max. CMB size, mm	Age \pm SD (range), y	% HTN	n	% CMB
15		Randomly selected asymptomatic individuals without a history of neuropsychiatric disease	5	60 (44–79)	32	280	6.4
16		Healthy elderly individuals	NR	62 (55–77)	0	66	4.5
17		Patients with headache or vertigo, >60 y	NR	72 \pm 8	31	65	7.7
18		Patients with headache or “dizziness”	NR	76 \pm 7	33	55	7.3
19		Patients with headache or “dizziness”	NR	75 \pm 8	34	59	8.5
20		Subjects “without a history of cerebrovascular disease”	10	56 \pm 16	NR	1,718	3.7
21		Participants of a screening program for “asymptomatic brain diseases”	7	56 \pm 8	46	209	7.7
22		Framingham Study Offspring and Cohort	9	64 \pm 12	29	472	4.7
Total						2,924	4.7

CMB in healthy Asian cohorts

Study	n	Mean age	ethnicity	population	HTN	CMB %	association
Wang et al 2017	139	66	South Indian (kerala)	Cognitive complaints	60%	7-13%	Lacunar infarcts
Cho et al 2016	1215	65	Korean	Disease preventive health checkup	45%	9%	Age, HTN, SVD,GFR, albuminuria
Kim et al 2015	300	56	Korean	Healthy adults for checkup	30%	21%	Age, male, statin, AT
Japanese screening study 2002	450	53	Japanese	Healthy adults	40%	3.1%	HTN, heavy smoking



CMB in healthy non-Asian cohorts

Study	n	Mean age	population	HTN%	CMB %	association
AGES Reykjavik 2008	1962	76	Iceland, Population based	78%	11.1%	Age, male, APOE e4/e4, retinal lesions, DM
Rotterdam Scan Study 2010	3979	60	Dutch, population based	55%	15%	Age, HTN, smoking, low cholesterol, APOe4/- SVD
Del Brutto 2016	311	71	Mestizo, Atahualpa, Ecuador	50%	13%	Age, HTN, poorer diet

Northern Manhattan Study

N= 935, mean age = 70, 70% Hispanics, 15% each Blacks, Whites
Overall prevalence of CMB 5%, lower in Hispanics (4.4%) but not statistically different

	All N=935	With CMB N=46	Without CMB N=889	P Value [†]	Only Deep N=17	Mixed N=7	Only Lobar N=22	P Value [†]
Frequency (%)								
Sex								
Male	369 (39)	17 (37)	352 (40)	0.721	6 (35)	2 (29)	9 (41)	0.920
Female	566 (61)	29 (63)	537 (60)		11 (65)	5 (71)	13 (59)	
Race/ethnicity								
Black	138 (15)	8 (17)	130 (14)	0.784	3 (18)	2 (29)	3 (14)	0.218
Hispanic	652 (70)	29 (63)	623 (70)		12 (71)	4 (57)	13 (59)	
White	127 (14)	8 (17)	119 (13)		2 (12)	—	6 (27)	
Other	18 (2)	1 (2)	17 (2)		—	1 (14)	—	

WHICAP study

N= 243, mean age = 84.5, 1/3rd each Hispanics, Blacks and Whites
Overall prevalence of CMB 28%, lower in Hispanics (22%)
compared to others (30%)

	<u>No microbleeds</u>	<u>Any microbleeds</u>	<u>Total sample</u>
N	176	67	243
Age, mean yrs (SD)	84.27 (5.36)	85.22 (5.29)	84.50 (5.34)
Sex, N women (%)	125 (71%)	44 (65.6%)	169 (69.5%)
Mean (SD), education years, not available for 2 subjects	10.90 (4.849)	11.36 (5.459)	11.04 (5.006)
Ethnicity N (%)			
White/non-Hisp or other	52 (29.5%)	23 (34.3%)	75 (30.9%)
Black/non-Hisp	60 (34.1%)	26 (38.8%)	86 (35.4%)
Hispanic	64 (36.4%)	18 (26.9%)	82 (33.7%)

Wiegman et al, Cerebral microbleeds in a multiethnic elderly community:demographic and clinical correlates. J Neurological Sciences 2014

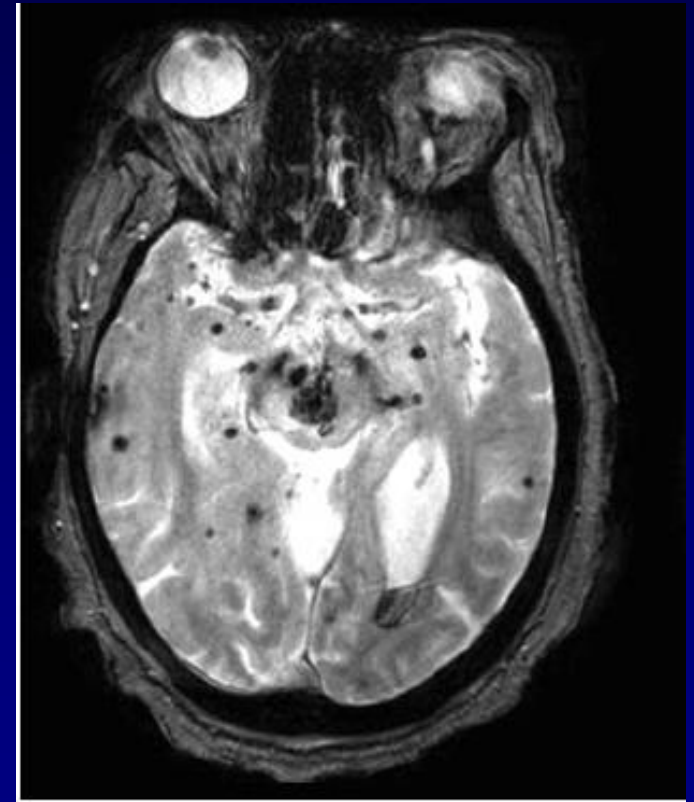
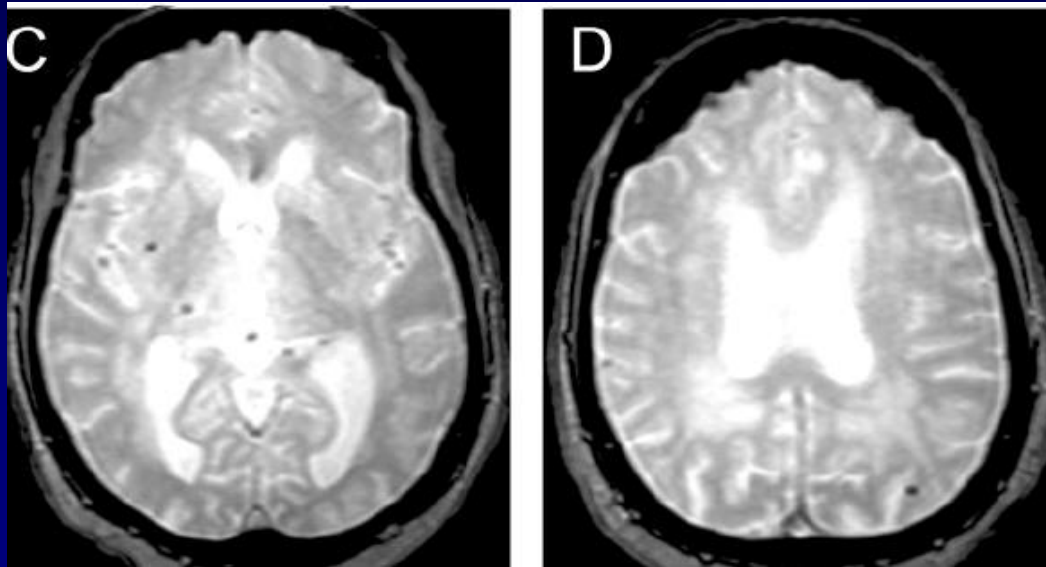
Are there Race/Ethnic
differences in CMB in patients
with ICH?

CMB in ICH- Race associated with CMB presence and burden

	Black (n = 42)	White (n = 45)	p Value
Age, mean	63	73	<0.001*
Women (%)	24 (57)	23 (51)	0.668
Hyperter			0.001*
Untreate			0.007*
Diabetes			0.271
CAD (%)			0.215
Hyperlipi			0.795
Prior stro			0.356
Tobacco			0.236
Antiplate			0.225
Anticoag			0.349
Heavy alk			0.117
One or m			0.005*
No. of mi (interquartile range)			0.002*
ICH volume, mean cc (interquartile range)	20.0 (4.05-25.2)	24.9 (4.5-32.6)	0.346
Primary ICH lobar (%)	12 (29)	16 (36)	0.502
Moderate-severe leukoaraiosis (%)	29 (69)	13 (29)	<0.001*
Chronic hematomas (%)	13 (31)	7 (16)	0.088

	OR	95% CI	p Value
Race	3.308	1.144-9.571	0.027*
Alcohol	5.284	1.062-26.280	0.042*
Age	0.997	0.957-1.038	0.878
Hypertension	1.092	0.354-2.266	0.878

Topographical differences in CMB



CMB in ICH- Asian vs. Western cohorts

Asian cohorts had higher prevalence of (n=780, 68.4%) compared to Western cohorts (N = 203, 56.2%). Likely related to HTN

Table 2 Prevalence of cerebral microbleeds (CMB) among patients with spontaneous intracerebral hemorrhages (ICH)

Reference	Cohort characteristics	Max. CMB size, mm	Age \pm SD (range), y	% HTN	n	% CMB
12	Patients with spontaneous ICH	5	60 (43–77)	83	30	57
→23	Consecutive patients with spontaneous ICH	5	65 (22–91)	62	109	54
16	Consecutive patients with acute ICH and hypertension	NR	64 (24–86)	100	130	65
17	Patients with acute or chronic ICH	NR	72 \pm 11	63	35	71
20	Patients with acute or chronic ICH	10	63 \pm 10	NR	69	71
24	Consecutive patients with acute ICH	5	62 (17–91)	67	107	70
25	Consecutive patients with acute ICH and hypertension	5	65 \pm 9	100	51	73
26	Consecutive patients with acute ICH	5	66 \pm 11	74	83	80
→27	Consecutive patients with acute lobar ICH	5	>55	49	94	59
28	Consecutive patients with first-ever acute ICH	NR	69 \pm 13	NR	36	47
29	Acute non-lobar ICH	7	66 \pm 11	85	199	77
Total					943	68

CMB in ICH-ATACH-II

- 120/157 had at least one CMB (76%)
- Asians and Blacks had higher prevalence of CMB compared to Whites ($p=0.09$)
- Associated with degree of WMD, and renal function.

Are there Race/Ethnic
differences in AIS associated
CMB?

CMB in AIS- Asian vs. Non-Asian cohorts

Asian cohorts had higher prevalence of (43%) compared to Western cohorts (25%). Likely a function of stroke etiology?

Table 3 Prevalence of cerebral microbleeds (CMB) among patients with ischemic cerebrovascular disease

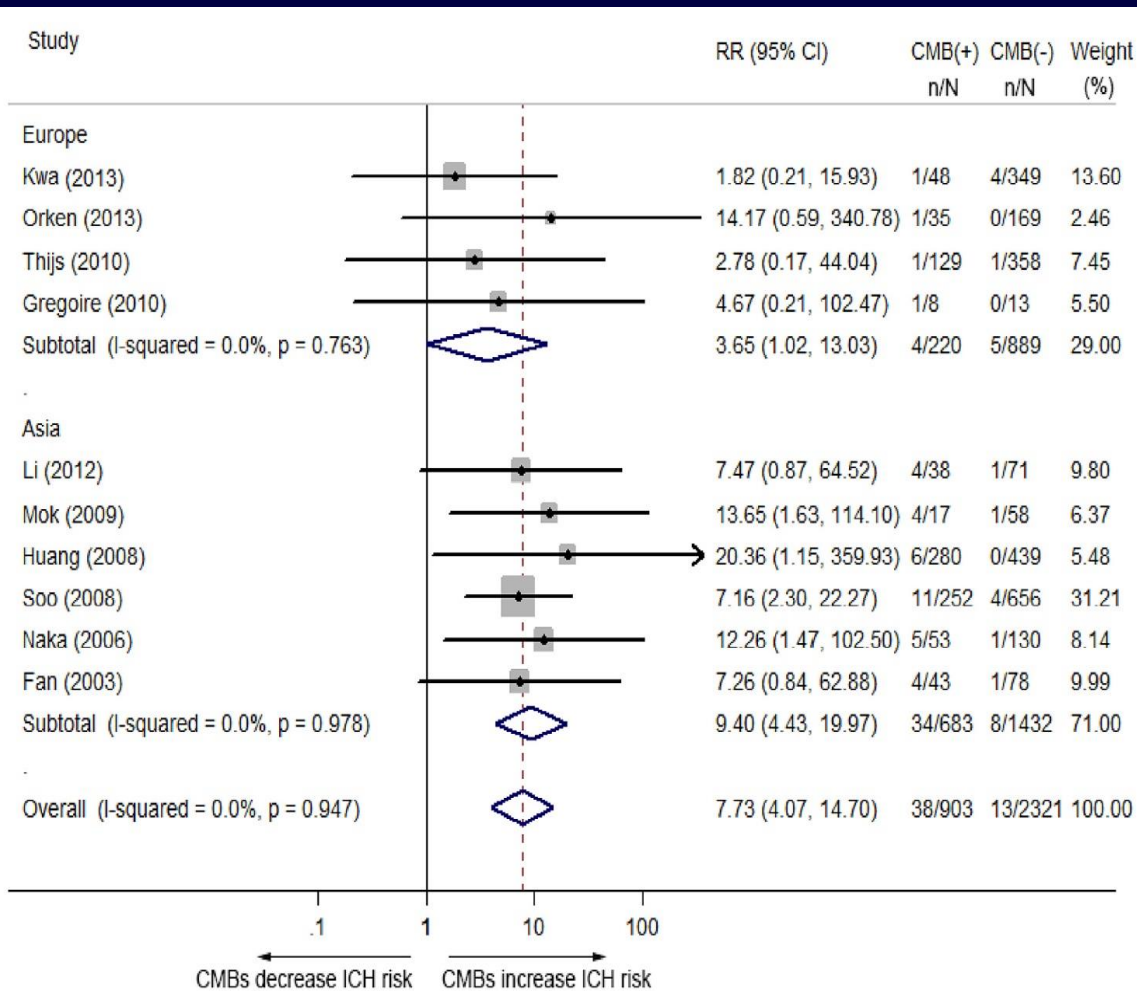
Reference	Cohort characteristics	Max. CMB size, mm	Age \pm SD (range), y	% HTN	n	% CMB
16	Patients with multiple lacunes and hypertension	NR	69 (55–88)	100	68	71
17	Acute or chronic ischemic stroke	NR				
	Lacunar		74 \pm 9	71	66	62
	Atherothrombotic		74 \pm 10	46	24	21
	Cardioembolic		77 \pm 6	39	23	30
36	Vascular dementia and microangiopathic lesions on MRI	NR	74 \pm 6	79	67	78
20	History of ischemic stroke	10	NR	NR	232	18
19	Patients with multiple lacunes or Binswanger's disease	NR	76 \pm 8	77	81	60
39	Consecutive patients with acute ischemic stroke	NR	68 \pm 11	69	121	36
25	Consecutive patients with acute ischemic stroke and HTN	5	65 \pm 9	100	113	65
26	Consecutive patients with acute ischemic stroke	5	65 \pm 9	84	144	35
28	Acute first ever ischemic stroke	NR	69 \pm 13	NR		
	Lacunar				31	23
	Atherothrombotic				22	23
	Cardioembolic				13	0
29	Acute lacunar infarction	7	66 \pm 9	72	138	51
40	Acute TIA or ischemic stroke	NR	>50 y	NR	203	25
Total					1,346	40

Are there Race/Ethnic
differences in response to
therapy in patients with CMB?

CMB and post tpa hemorrhage

Study	n	Mean age	population	CMB %	sICH	association
Turc, 2015	717	74	Western	21%	3.8-9% (depending on definition)	multivariate no increase in groups
Dannenberg 2014	326	76	Western	25%	3%	52% CAA, increased sICH
Gratz 2015	392	68	Western	20%	5%	11% CMB-, 26% CMB +
Shi 2015	206	67	Western	18%	3%	n/a
Tokai 2012	71	73	Japanese	20%	n/a (hemorrhagic transformation 23%)	n/a
Kimura 2013	224	76	Japanese	32%	2.7%	n/a
Yan, 2015	333	67	Chinese	40%	2%	24% had > 5 CMB, 24% CAA Worse 3 m outcome with CMB

ICH associated with anti platelets/warfarin - Higher risk in Asians with multiple CMB



N=3224; 28% CMB; Asian cohorts had higher crude RR (9.40) vs 3.65 for Western cohorts; more pronounced for multiple CMB.

Figure 2. Summary of the RRs for subsequent ICH among patients with CMBs versus those without CMBs. The pooled RRs of Asian and European cohorts for ICH are shown, respectively. Abbreviations: CMB, cerebral microbleed; ICH, intracerebral hemorrhage; RR, relative ratio.

Are there Race/Ethnic
differences in recurrent stroke
risk in patients with CMB?

CMB and recurrent stroke in AIS patients

N=3067, 30% CMB,

OR of 2.2 of any recurrent stroke in Asian/Western cohorts
 ICH substantially increased for Asian and AIS for Western

Risk of recurrent ICH

Risk of recurrent AIS

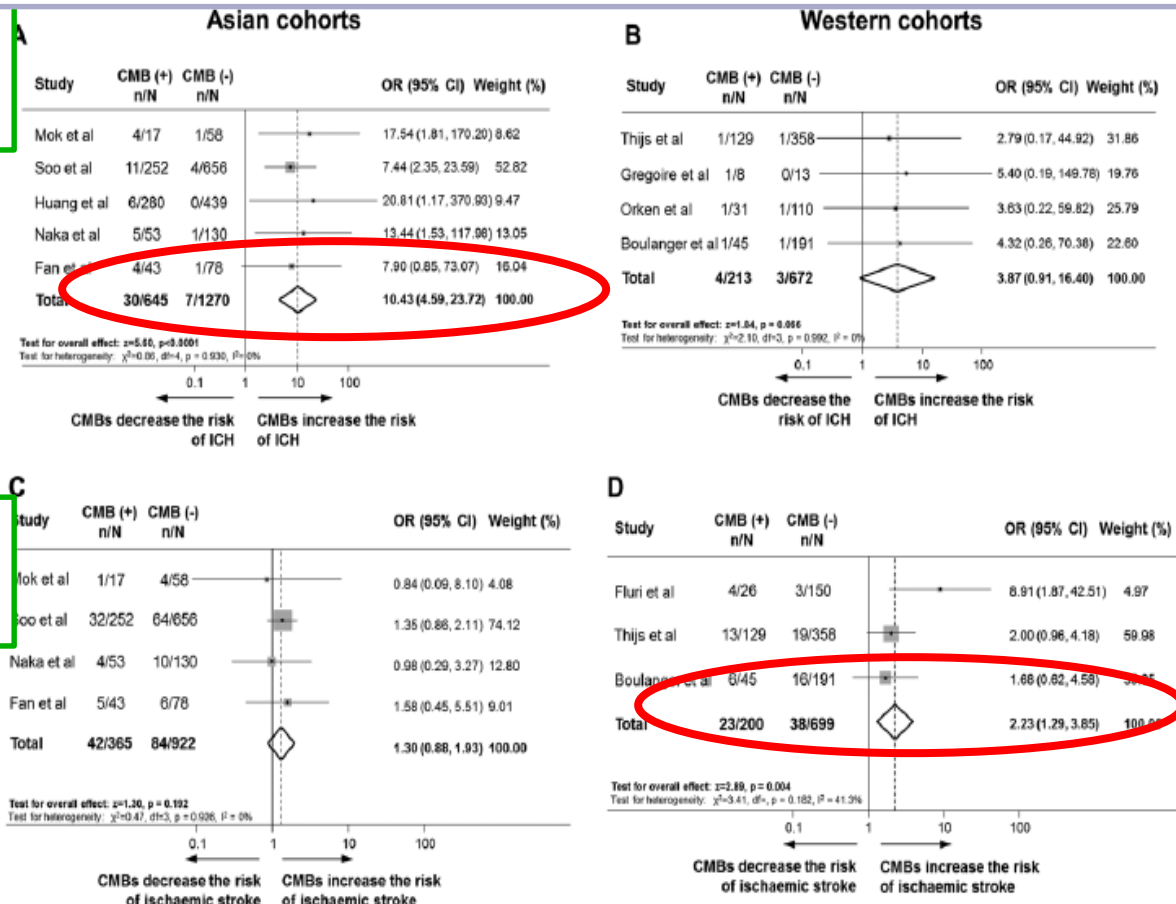


Figure 4. Meta-analysis of the risk of spontaneous intracerebral hemorrhage (ICH; A and B) and ischemic stroke (C and D) stratified by the d

Conclusions and Future research

- Prevalence of CMB in healthy non Asian cohorts slightly higher; trend to lower CMB in Hispanics;
- However, in ICH and AIS, Asians and Blacks have higher CMB prevalence, likely due to underlying HTN
- In the setting of antithrombotic use in AIS and ICH, Asians tend to have higher CMB prevalence, higher # of CMB and increased risk of initial and subsequent ICH.

Outstanding questions

- Better details of race/ethnicity in studies (need multicenter systematic data collection)
- Fully explore how much of the CMB differences are driven by race/ethnicity versus genetic differences, environmental factors, risk factors, drug metabolism and treatment practices.