Web extra material

	Countries	Total number of partipants (n)	N with clinical follow-up	Ethnic origins (n, %)	Endpoints	Age at base-line (years)	Men (%)[&]	Time between first and second utrasound scan (mean, years)	Clinical follow-up after ultrasound scan 2 (mean, years)	Segments	Measure-ments	Intima media thickness definition
Atherosclerosis Risk of Rural Areas in Korea General Population (ARIRANG)[1]	Korea	5,020	unknown	Asian	MI, stroke, death	40-70	693 of 1,795 (40·4)	3·0	3·0	CCA	Far wall	Mean
Carotid-Femoral morphology and cardiovascular events (CAFES-CAVE)[2]	Italy	13,221	10,000	White	MI, stroke, death, vascular death	35-65	6,055[§] (60·6)	2·0	8·0	BIF	Far wall, left+right	Maximal categories
Chin-Shan Community Cardiovascular Cohort Study (CCCC)[3]	Taiwan	3,602	3,602	Asian (3602, 100·0%)*	MI, stroke, vascular death, death	>35	1,702 (47.3)	5·0	5·0	CCA	Far wall, left+right	max
Perth Carotid Ultrasound Disease Assessment Study (CUDAS)[4]	Australia	1,111	779*	White	MI, CVD	27-77	558 (50·2)	3·0*	7·0*	CCA	Far wall, left+right	mean
Hoorn Study[5]	Nether-lands	581	400*	White (581, 100·0%)	MI, stroke, death, vascular death*	50-75	285 (49·0)	5·0	5·0	CCA	Far wall, right	mean
Multi-Ethnic Study of Atherosclerosis (MESA)[6]	USA	6,814	5,028	White (1986, 39·5%) African American (1292, 25·7%) Hispanic (1106, 22·0%) Asian (644, 12·8%)	Mi, stroke, vascular death, death	45-84	2,411 (48.0)	2.6	3.2	CCA, ICA	Far wall, left+right	mean, max

CCA=common carotid artery; BIF=bifurcation of carotid artery; ICA=internal carotid artery; [&]total sample; [§]only those with clinical follow up; *personal communication

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Webtable A1: **Description of eligible studies not included**

Cohort	N total	N excluded* due to ..			N after exclusion*
		.. event before 2nd ultrasound	.. lost to ultrasound follow-up	.. lost to clinical follow-up	
Atherosclerosis and Insulin Resistance study	391	91	52	40	297
Atherosclerosis Risk In Communities	14,289	1,229	940	0	12,221
Bogalusa Heart Study	1,399	29	596	229	558
Bruneck study	821	82	145	0	633
Carotid Atherosclerosis Progression Study	6,972	280	3,549	0	3,284
Cardiovascular Health Study, cohort 1	5,201	908	1,048	0	3,551
Cardiovascular Health Study, cohort 2	687	140	336	0	297
Edinburgh Artery Study	1,605	138	899	0	613
Etude sur le vieillissement artériel	1,040	101	12	7	922
Interventionsprojekt zerebrovaskuläre Erkrankungen und Demenz im Landkreis Ebersberg	3,908	354	1,154	1	2,534
Kuopio Ischemic Heart Disease Study	1,399	222	370	0	849
Northern Manhattan Study/The Oral Infections and Vascular Disease Epidemiology Study	784	30	101	0	653
Prospective Investigation of the Vasculature in Uppsala Seniors	1,017	158	223	190	680
Progression of Lesions in the Intima of the Carotid	1,782	58	146	43	1,538
Rotterdam Study	7,983	1,239	4,903	22	2,611
Study of Health in Pomerania	4,308	91	2,478	0	1,751
Tromsø Study	4,821	667	191	0	3,992

* These numbers do not necessarily add up to N total, as subjects may have been excluded due to more than one reason

Webtable A2: **Sample size and number of exclusions by reason of exclusion**

	Sampling strategy	Identification of endpoints	Were the subjects informed of their IMT results ?
Atherosclerosis and Insulin Resistance study	Subset of an age-stratum of a random sample from the male general population, selected by quintiles of a BMI/blood glucose score. Exclusion of subjects with cardiovascular disease, other established disease, cardiovascular drug treatment.	National death register National registers of diagnoses at hospitalizations	Yes
Atherosclerosis Risk In Communities	Probability sampling or area sampling.	Annual telephone questionnaire three-year examinations community-wide surveillance procedures	Yes
Bogalusa Heart Study	Recruited from schools in Bogalusa.	Death endpoint: newspaper obituaries information from families, friends and colleagues of the deceased	No
Bruneck study	Sex- and age-stratified random sample from the official population registry	Self-reported medical history in quinquennial visits medical records provided by the general practitioners death certificates reviews of the Bruneck Hospital databases, which is the only hospital in the district	Only plaques
Carotid Atherosclerosis Progression Study	Geografic sample of members of a company health insurance.	Primary healthcare scheme records	Yes
Cardiovascular Health Study	Age, gender and race-stratified random samples from sampling frames from Medicare eligibility lists; exclusion of wheelchair-bound persons and subjects receiving hospice treatment, radiation therapy or chemotherapy for cancer.	Semiannual contacts, alternating between telephone interviews clinic visits	Yes
Edinburgh Artery Study	Age and sex stratified random sample from 10 general practices serving a range of socioeconomic and geographical areas.	General practitioners Information and Statistics Division of the Scottish Office Home and Health Department Hospital notes Annual participant questionnaires United Kingdom National Health Service Central Registry	No
Etude sur le vieillissement artériel	Mostly recruited from the electoral rolls (random sample from population register) and to a lesser extent via information campaigns. When a subject was recruited, his or her spouse was systematically asked to participate if or she was in the required age range.	French National Registry of Death (INSEE)	No
Interventionsprojekt zerebrovaskuläre Erkrankungen und Demenz im Landkreis Ebersberg	All members of the largest health insurance company living in the community of Ebersberg > 55 years at baseline were invited.	2-Year visit Health insurance database	Yes
Kuopio Ischemic Heart Disease Study	Age strata of male residents; exclusion in case of serious disease or migration.	National hospital discharge register Finnish national death registry	No
Northern Manhattan Study/The Oral Infections and Vascular Disease Epidemiology Study	Random digit dialing, older than 39 years and resided in northern Manhattan for more than 3 months; exclusion of previous stroke.	Annual telephone interviews	No
Prospective Investigation of the Vasculature in Uppsala Seniors	Age stratum, random sample of community register.	National death register	Only severe stenosis
Progression of Lesions in the Intima of the Carotid	Random sample of GP patient lists	Visits every third year phone interview every year	Yes
Rotterdam Study	Age stratified sample of community register.	Files from general practitioners in the study area Municipal health authorities	Only severe stenosis
Study of Health in Pomerania	Age and gender stratified random sample from official inhabitant data files.	Follow-up examinations Participant questionnaires	Only plaques and stenoses
Tromsø Study	Age and gender stratified sample of inhabitants in Tromsø, Norway. Exclusion of subjects with known myocardial infarction or ischemic stroke.	National and local diagnosis registries	No

Webtable A3: **Study procedures by cohort**

	Avoid plaques	ECG gated	Angle control	Multiple scans	Same ultrasound machine	Same sono-grapher	Central reading	Edge-detection algorithm[+]	Other
Atherosclerosis and Insulin Resistance study	no	yes	no	no	no	no	yes	yes	
Atherosclerosis Risk In Communities	no	yes	yes	for CCA[§]	no	no	yes	no	
Bogalusa Heart Study	no	yes	no	no	no	no	no[#]	no	
Bruneck study	yes	yes	yes	no	no	yes	no	no	Rereading of baseline at follow-up
Carotid Atherosclerosis Progression Study	n.s.	no	no	no	yes	no	yes	yes	
Cardiovascular Health Study	no*	no	no	for ICA[§]	yes	no	yes	no	Rereading of baseline at follow-up
Edinburgh Artery Study	yes	no	vessel wall parallel to transducer face	no	no	no	yes	no	yes
Etude sur le vieillissement artériel	yes	no	internal landmarks [++]	no	yes	no	yes	yes	
Interventions-projekt zerebrovaskuläre Erkrankungen und Demenz im Landkreis Ebersberg	yes	no	yes	yes	yes	yes	yes	yes	
Kuopio Ischemic Heart Disease Study	no	no	no	no	no	no	yes	yes	
Northern Manhattan Study/The Oral Infections and Vascular Disease Epidemiology Study	yes	no	internal landmarks [++]	no	yes	yes	yes	yes	Same depth and angle at follow-up
Prospective Investigation of the Vasculature in Uppsala Seniors	n.s.	yes	no	no	yes	yes	yes	yes	
Progression of Lesions in the Intima of the Carotid	yes	no	no	no	yes	yes	yes	no	
Rotterdam Study	no	yes	no	yes	yes	no	yes	yes	
Study of Health in Pomerania	no	no	no	no	yes	no	yes	yes	Observer recertifi-cation; re-reading
Tromsø Study	no*	yes	no	yes	yes	no	yes	yes	

n.s. = not specified in ultrasound instructions; [+] semiautomated algorithm to reliably detect the surface of the lumen-intima and the intima-media interfaces, instead of manual caliper measurement; [§] Multiple scans under different angles were used in ARIC for the CCA (anterior, posterior and optimal angle) and in CHS for the ICA (anterior, lateral and posterior angle); [#] central reading for baseline, but not for follow-up scans; [++] creation and storing of a mask outlining the internal vessel surface of the both neck sides during baseline scan; and recalling the mask during follow-up scan as a navigation aid; * plaques purposely included

Webtable A4: **Measures taken to improve assessment of cIMT progression by included studies**

	Specific definition of the endpoint			Number of events* (event rate+)			
	Myocardial infaction (MI)	Stroke	Vascular death (VD)	MI	stroke	VD	death
Atherosclerosis and Insulin Resistance study	Criteria of the Seven Country Study[1]: 1) ECG findings 2) Clinical judgment of heart disease 3) Etiology specified as MI (by history) based on medical records	Ischemic stroke was verified by the following criteria: 1) Clinical event with sudden or rapid onset 2) Lasting more than 24h or death 3) Neurological findings Non-ischemic stroke was verified from CT based on medical records	Fatal MI based on medical records	9 (5·4)	5 (3·0)	2 (1·2)	9 (5·4)
Atherosclerosis Risk In Communities	Definite hospitalized MI: One or more criteria fulfilled: 1) Cardiac pain 2) Diagnostic ECG pattern 3) Abnormal enzymes based on medical records	National Survey of Stroke criteria [2] 1) Clinical event with sudden or rapid onset 2) Lasting for more than 24 hours, or death 3) Neurological findings 4) Vascular origins limited to a. thrombotic or embolic occlusion of a cerebral artery resulting in infarction b. spontaneous rupture of a vessel resulting in intracerebral or subarachnoid hemorrhage based on medical records	not assessed	447 (4·4)	275 (2·7)	-	772 (7·7)
Bogalusa Heart Study	not assessed	not assessed	fatal MI, fatal stroke, other vascular death based on medical records and death certificates	-	-	3 (1·2)	12 (4·8)
Bruneck Study	WHO criteria[3] 1) Diagnostic ECG pattern 2) Typical history 3) Abnormal enzymes based on medical records	same as ARIC based on medical records	fatal MI, fatal stroke, fatal ICH, sudden cardiac death, and death due to rupture of aortic aneurysm based on medical records and death certificates	33 (5·7)	52 (9·0)	29 (5·0)	129 (22·4)
Carotid Atherosclerosis Progression Study	Based on ICD codes ICD-9: 410 ICD-10: I21, I22	Based on ICD codes ICD-9: 430, 431, 433, 434, 436 ICD: I60-64	not assessed	38 (2·2)	61 (3·5)	-	37 (2·1)
Cardiovascular Health Study, cohort1	same as ARIC based on medical records	Modified Systolic Hypertension in the Elderly Program (SHEP) criteria[4]: 1) Clinical event on rapid onset of neurologic deficit or subarachnoid hemorrhage 2) Greater than 24 hours unless death 3) CT/MRI lesion 4) Not secondary to brain trauma, tumor or infection based on medical records	fatal MI, fatal stroke, fatal coronary heart disease based on medical records and death certificates	502 (14·3)	469 (13·4)	643 (18·3)	1,797 (51·3)
Cardiovascular Health Study, cohort 2	see CHS cohort 1	see CHS cohort 1	see CHS cohort 1	26 (15·6)	34 (20·4)	28 (16·8)	79 (47·4)
Edinburgh Artery Study	criteria of the American Heart Association[5]: Two of the following criteria: 1) Cardiac pain 2) Diagnostic ECG pattern 3) Abnormal enzymes based on medical records	criteria of the American Heart Association one of the following criteria: 1) History of onset of symptoms of less than 48 hours, plus clinical confirmation of a focal or global disturbance of cerebral function lasting more than 24 hours 2) CT lesion based on medical records	definite fatal MI, definite fatal stroke, other cardiovascular causes based on autopsy records, hospital records, or UK National Health Service Central Registry	8 (2·3)	12 (3·5)	17 (4·9)	53 (15·2)
Etude sur le vieillissement artériel	not assessed	not assessed	based on National Statistics of Causes of Death records	-	-	33 (2·5)	173 (13·3)

(Continues on next page)

	Specific definition of the endpoint			Number of events* (event rate+)			
	Myocardial infaction (MI)	Stroke	Vascular death (VD)	MI	stroke	VD	death
(Continued from previous page)							
Interventions-projekt zerebrovasku-läre Erkrankungen und Demenz im Landkreis Ebersberg	according to[6] one of the following criteria: 1) cardiac enzyme abnormalities (troponin, CK-MB) plus one of the following two criteria a. ischemic symptoms b. electrocardiogram abnormalities 2) postmortem findings of an acute MI." based on medical records, autopsy records and death certificates	WHO criteria[7]: 1) "rapidly developed clinical signs of focal or global disturbance of cerebral function, lasting more than 24 hours or until death, with no apparent non-vascular cause" 2) postmortem findings of an acute stroke based on medical records, autopsy records and death certificates	not assessed	22 (2·1)	67 (6·5)	-	172 (16·8)
Kuopio Ischemic Heart Disease Study	WHO MONICA/MORGAM criteria[7]; 1) clinical symptoms and signs 2) electrocardiograms 3) cardiac biomarkers based on medical records, autopsy records and death certificates	WHO MONICA criteria[7]: "rapidly developed clinical signs of focal or global disturbance of cerebral function, lasting more than 24 hours or until death, with no apparent non-vascular cause" based on medical records, autopsy records and death certificates	ICD-10: I00-I99 based on medical records, autopsy records and death certificates	138 (10·3)	71 (5·3)	85 (6·4)	186 (13·9)
Northern Manhattan Study/The Oral Infections and Vascular Disease Epidemiology Study	Criteria adapted from the Cardiac Arrhythmia Suppression Trial and the Lipid Research Clinics Coronary Primary Prevention Trial [8,9] Two of the following three criteria: 1) cardiac pain determined to be typical angina; 2) cardiac enzyme abnormalities (CPK-MB fraction or troponin values); 3) electrocardiogram abnormalities based on medical records	WHO criteria[7]: "rapidly developed clinical signs of focal or global disturbance of cerebral function, lasting more than 24 hours or until death, with no apparent non-vascular cause" based on medical records	Fatal MI, fatal ischemic stroke, heart failure, pulmonary embolus, cardiac arrhythmia, other vascular causes based on information from family, medical records, death certificates	0 (0·0)	8 (4·1)	13 (6·7)	34 (17·6)
Prospective Investigation of the Vasculature in Uppsala Seniors	not assessed	not assessed	not assessed	-	-	-	26 (20·6)
Progression of Lesions in the Intima of the Carotid	Self reported physician's diagnosis of MI, and confirmed by physician	Self reported physician's diagnosis of stroke and confirmed by physician	not assessed	10 (1·6)	10 (1·6)	5 (0·8)	17 (2·7)
Rotterdam Study	According to the International Classification of Diseases, 10th Edition (ICD-10) From general practitioners and letters and discharge reports from medical specialists	Typical symptoms that lasted longer than 24 hours From general practitioners and letters and discharge reports from medical specialists, diagnosis reviewed and verified by stroke neurologist	not assessed	71 (4·7)	146 (9·6)	-	397 (26·2)
Study of Health in Pomerania	Self reported physician's diagnosis of MI	Self reported physician's diagnosis of stroke	not assessed	15 (1·5)	10 (1·0)	-	167 (16·2)
Tromsø Study	Slightly modified WHO[7] criteria; 1) clinical symptoms and signs 2) electrocardiograms 3) cardiac biomarkers based on medical records	same as NOMAS/INVEST based on medical records	fatal MI, fatal stroke based on medical records, autopsy records, death certificates	200 (11·4)	119 (6·8)	62 (3·5)	208 (11·9)

* beginning after the 2nd ultrasound visit, after exclusion of subjects with previous events; +event rate per 1000 person years

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Webtable A5: **Endpoint event definitions and number of events in included studies**

	Mean (SD) {n} of mean CCA-IMT [mm]				Mean (SD) {n} of maximal CCA-IMT [mm]				Mean (SD) {n} of meanmax IMT [mm]				Pearsons correlation of two occasions		
	Visit 1	Visit 2	Mean of visits 1 and 2	Annual progression	Visit 1	Visit 2	Mean of visits 1 and 2	Annual progression	Visit 1	Visit 2	Mean of visits 1 and 2	Annual progression	between mean CCA-IMT[†] and annual mean IMT progression	of mean CCA-IMT	of annual mean CCA-IMT progression
Atherosclerosis and Insulin Resistance study	0·794 (0·121) {297}	0·798 (0·136) {297}	0·796 (0·121) {297}	0·001 (0·028) {297}	0·958 (0·155) {297}	1·002 (0·184) {297}	0·980 (0·156) {297}	0·010 (0·044) {297}	1·157 (0·230) {297}	1·196 (0·252) {297}	1·177 (0·233) {297}	0·009 (0·040) {297}	0·16	0·76	n.a.
Atherosclerosis Risk In Communities	0·644 (0·127) {12,221}	0·676 (0·129) {12,221}	0·660 (0·116) {12,221}	0·011 (0·038) {12,221}	0·749 (0·150) {12,221}	0·793 (0·150) {12,221}	0·771 (0·135) {12,221}	0·015 (0·045) {12,221}	0·867 (0·257) {7,507}	0·906 (0·254) {9,535}	0·895 (0·232) {6,451}	0·016 (0·076) {6,451}	0·07	0·64	-0·02[#]
Bogalusa Heart Study	N/A	N/A	N/A	N/A	0·756 (0·134) {558}	0·758 (0·143) {558}	0·757 (0·125) {558}	0·001 (0·052) {558}	0·816 (0·173) {558}	0·836 (0·174) {558}	0·826 (0·164) {558}	0·008 (0·053) {558}	0·09*	0·63*	n.a.
Bruneck study	0·838 (0·164) {633}	N/A	N/A	N/A	0·888 (0·204) {633}	1·024 (0·183) {633}	0·956 (0·182) {633}	0·027 (0·270) {633}	0·862 (0·186) {633}	0·965 (0·157) {633}	0·914 (0·161) {633}	0·021 (0·025) {633}	-0·16*	0·76*	n.a.
Carotid Atherosclerosis Progression Study	0·732 (0·148) {3,283}	0·735 (0·137) {3,283}	0·733 (0·131) {3,283}	0·001 (0·036) {3,283}	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	-0·11	0·69	n.a.
Cardiovascular Health Study, cohort 1	0·859 (0·155) {3,551}	0·873 (0·169) {3,551}	0·866 (0·147) {3,551}	0·005 (0·047) {3,551}	1·031 (0·197) {3,551}	1·059 (0·220) {3,551}	1·045 (0·188) {3,551}	0·010 (0·063) {3,551}	1·192 (0·316) {3,551}	1·231 (0·336) {3,551}	1·211 (0·305) {3,551}	0·013 (0·079) {3,551}	0·12	0·65	n.a.
Cardiovascular Health Study, cohort 2	0·901 (0·165) {297}	0·955 (0·195) {297}	0·928 (0·160) {297}	0·009 (0·029) {297}	1·093 (0·197) {297}	1·098 (0·240) {297}	1·095 (0·193) {297}	0·001 (0·035) {297}	1·218 (0·284) {297}	1·355 (0·431) {297}	1·286 (0·329) {297}	0·023 (0·053) {297}	0·21	0·56	n.a.
Edinburgh Artery Study	0·753 (0·278) {613}	0·949 (0·187) {613}	0·851 (0·188) {613}	0·030 (0·044) {613}	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	-0·38	0·27	n.a.
Etude sur le vieillissement artériel	0·658 (0·111) {922}	0·670 (0·114) {922}	0·664 (0·103) {922}	0·006 (0·045) {922}	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	0·04[#]	0·69	n.a.
Interventions-projekt zerebrovaskuläre Erkrankungen und Demenz im Landkreis Ebersberg	0·806 (0·191) {2,534}	0·827 (0·193) {2,534}	0·816 (0·174) {2,534}	0·010 (0·076) {2,534}	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	0·01[#]	0·64	-0·04[#]

(Continues on next page)

	Mean (SD) {n} of mean CCA-IMT [mm]				Mean (SD) {n} of maximal CCA-IMT [mm]				Mean (SD) {n} of meanmax IMT [mm]				Pearsons correlation of two occasions		
	Visit 1	Visit 2	Mean of visits 1 and 2	Annual pro-gres-sion	Visit 1	Visit 2	Mean of visits 1 and 2	Annual pro-gres-sion	Visit 1	Visit 2	Mean of visits 1 and 2	Annual pro-gres-sion	bet-ween mean CCA-IMT† and annual mean IMT pro-gres-sion	of mean CCA-IMT	of annual mean CCA-IMT progres sion
(Continued from previous page)															
Kuopio Ischemic Heart Disease Study	0·713 (0·154) {849}	0·862 (0·186) {849}	0·805 (0·158) {849}	0·028 (0·033) {849}	0·929 (0·205) {849}	1·190 (0·266) {849}	1·059 (0·219) {849}	0·065 (0·049) {849}	N/A	N/A	N/A	N/A	0·16	0·72	-0·06#
Northern Manhattan Study/The Oral Infections and Vascular Disease Epidemiology Study	0·712 (0·086) {653}	0·747 (0·108) {653}	0·729 (0·083) {653}	0·008 (0·030) {653}	0·921 (0·963) {653}	0·956 (0·115) {653}	0·938 (0·091) {653}	0·009 (0·032) {653}	0·892 (0·072) {653}	0·934 (0·100) {653}	0·913 (0·071) {653}	0·011 (0·030) {653}	0·25	0·47	n.a.
Prospective Investigation of the Vasculature in Uppsala Seniors	0·905 (0·157) {680}	0·949 (0·168) {680}	0·927 (0·144) {680}	0·009 (0·029) {680}	1·025 (0·186) {680}	1·103 (0·208) {680}	1·064 (0·173) {680}	0·015 (0·037) {680}	N/A	N/A	N/A	N/A	0·08	0·58	n.a.
Progression of Lesions in the Intima of the Carotid	0·647 (0·140) {1,538}	0·680 (0·138) {1,538}	0·663 (0·133) {1,538}	0·014 (0·036) {1,538}	0·726 (0·154) {1,538}	0·745 (0·152) {1,538}	0·735 (0·146) {1,538}	0·009 (0·043) {1,538}	N/A	N/A	N/A	N/A	-0·03#	0·84	n.a.
Rotterdam Study	0·757 (0·136) {2,610}	0·867 (0·148) {2,610}	0·812 (0·131) {2,610}	0·017 (0·017) {2,610}	0·975 (0·175) {2,324}	1·074 (0·188) {2,324}	1·025 (0·168) {2,324}	0·016 (0·023) {2,324}	N/A	N/A	N/A	N/A	0·14	0·69	n.a.
Study of Health in Pomerania	0·771 (0·153) {1,751}	0·803 (0·164) {1,751}	0·787 (0·148) {1,751}	0·006 (0·022) {1,751}	0·902 (0·195) {1,751}	0·906 (0·219) {1,751}	0·904 (0·191) {1,751}	0·001 (0·031) {1,751}	N/A	N/A	N/A	N/A	0·11	0·74	n.a.
Tromsø Study	0·769 (0·150) {3,992}	0·797 (0·164) {3,992}	0·783 (0·145) {3,992}	0·004 (0·019) {3,992}	0·953 (0·194) {3,992}	0·984 (0·209) {3,992}	0·968 (0·184) {3,992}	0·005 (0·026) {3,992}	1·144 (0·297) {3,776}	1·134 (0·295) {3,702}	1·143 (0·266) {3,532}	-0·0003 (0·043) {3,535}	0·11	0·70	n.a.

† mean of baseline and follow-up; * correlation for maximal CCA-IMT, mean CCA-IMT was not avaiable for both visits; # not significantly different from zero.

Webtable A6: **Estimates of cIMT and cIMT progression following different definitions by study**

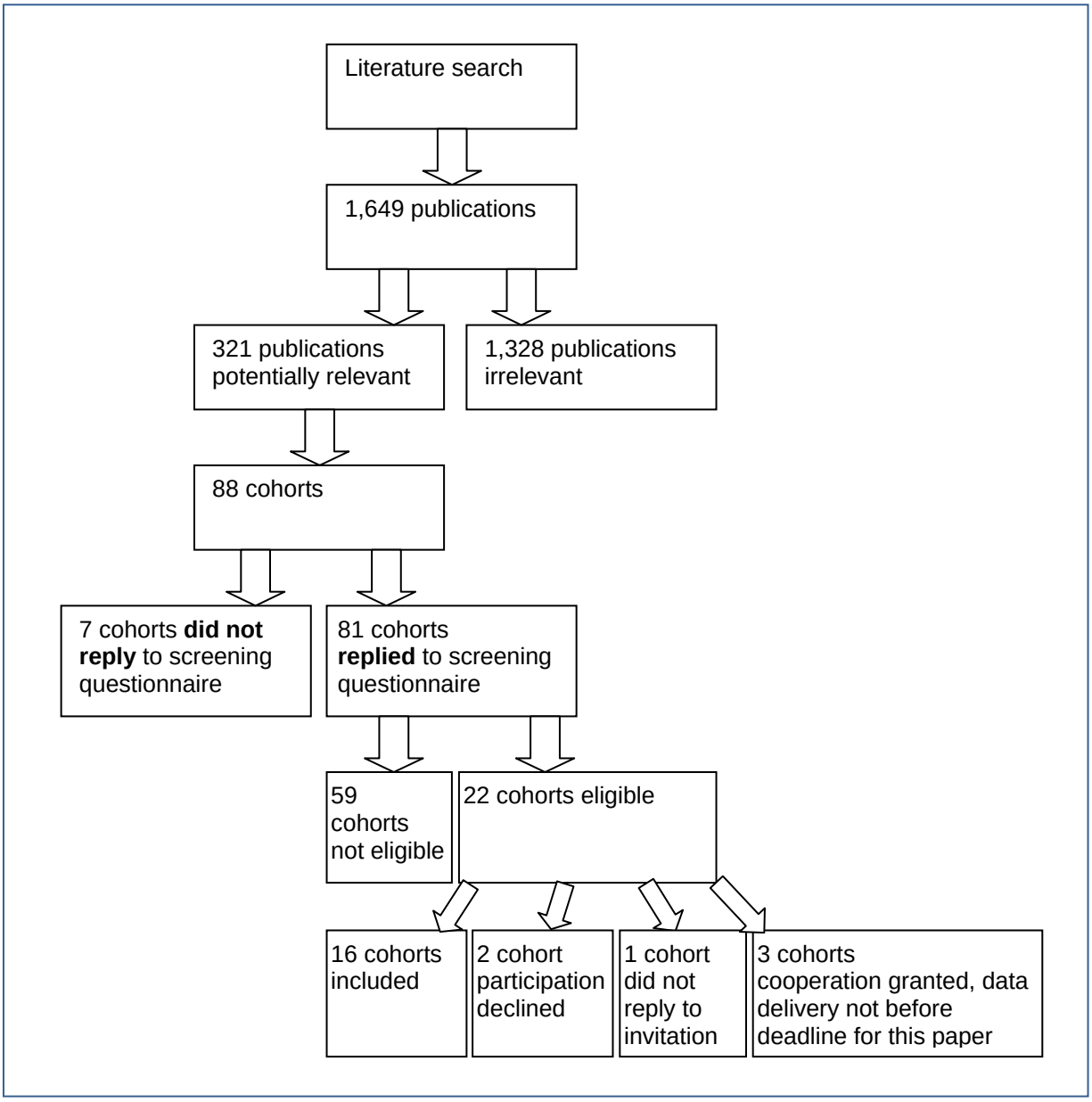
Specific characteristic	Adjustment level*	Endpoint	Studies included	Annual cIMT progression Overall HR (95% CI)	I^2 (p)#	Mean cIMT of scan 1 and 2 Overall HR (95% CI)	I^2 (p)#
Maximal CCA-IMT	model 1	combined	AIR, ARIC, Bruneck, CHS1, CHS2, KIHD, NOMAS/INVEST, PLIC, Rotterdam, SHIP, Tromsø	1·01 (0·97-1·04)	0·0% (0·457)	-	-
	model 2			1·00 (0·95-1·04)	32·8% (0·137)	1·27 (1·19-1·35)	64·5% (0·002)
	model 3			1·00 (0·95-1·04)	33·2% (0·133)	1·26 (1·19-1·33)	53·0% (0·019)
	model 4			0·99 (0·95-1·04)	34·0% (0·127)	1·16 (1·10-1·23)	50·8% (0·026)
Maximal CCA-IMT	model1	death	AIR, AIRC, BHS, Bruneck, CHS1, CHS2, KIHD, NOMAS, PIVUS, PLIC, Rotterdam, SHIP, Tromsø	1·10 (0·98-1·04)	1·9% (0·428)	-	-
	model 2			0·99 (0·96-1·02)	0·0% (0·774)	1·20 (1·13-1·27)	47·8% (0·028)
	model 3			0·99 (0·96-1·03)	0·0% (0·767)	1·19 (1·14-1·24)	22·2% (0·217)
	model 4			0·99 (0·96-1·02)	0·0% (0·788)	1·14 (1·10-1·18)	0·0% (0·469)
Meanmax IMT	model 1	combined	AIR, ARIC, CHS1, NOMAS/INVEST, Tromsø	0·97 (0·92-1·02)	23·6% (0·264)	-	-
	model 2			0·96 (0·91-1·02)	38·5% (0·164)	1·36 (1·25-1·47)	69·9% (0·010)
	model 3			0·96 (0·91-1·02)	37·4% (0·172)	1·35 (1·25-1·47)	67·3% (0·016)
	model 4			0·97 (0·92-1·02)	26·1% (0·248)	1·22 (1·11-1·34)	73·5% (0·004)
Per 0·1mm difference (mean CCA-IMT)	model 1	combined	AIR, ARIC, CAPS, CHS1, CHS2, EAS, INVADE, KIHD, NOMAS/INVEST, PLIC, Rotterdam, SHIP, Tromsø	0·97 (0·88-1·07)	16·1% (0·282)	-	-
	model 2			0·94 (0·87-1·01)	0·0% (0·485)	1·16 (1·10-1·23)	80·8% (<0·001)
	model 3			0·94 (0·87-1·01)	0·0% (0·513)	1·16 (1·10-1·22)	73·0% (<0·001)
	model 4			0·95 (0·88-1·03)	0·0% (0·672)	1·11 (1·07-1·15)	47·8% (0·028)
Non-imputed datasets (mean CCA-IMT)	model 1	combined	AIR, ARIC, CAPS, CHS1, CHS2, EAS, INVADE, KIHD, NOMAS/INVEST, PLIC, Rotterdam, SHIP, Tromsø	0·99 (0·96-1·02)	9·8% (0·347)	-	-
	model 2			0·98 (0·95-1·01)	0·0% (0·478)	1·24 (1·17-1·31)	64·6% (0·001)
	model 3			0·98 (0·96-1·01)	0·0% (0·422)	1·23 (1·17-1·30)	53·7% (0·011)
	model 4			0·98 (0·95-1·01)	0·0% (0·484)	1·14 (1·08-1·21)	46·3% (0·034)
Normalized IMT (progression) variable (mean CCA-IMT)	model 4	combined	AIR, ARIC, CAPS, CHS1, CHS2, EAS, INVADE, KIHD, NOMAS/INVEST, PLIC, Rotterdam, SHIP, Tromsø	0·98 (0·96-1·00)	0·0% (0·520)	1·19 (1·12-1·26)	57·2% (0·005)
Mean CCA-IMT by quintiles+: quintile 2 vs. 1 (lowest)	model 4	combined	AIR, ARIC, CAPS, CHS1, CHS2, EAS, INVADE, KIHD, NOMAS/INVEST, PLIC, Rotterdam, SHIP, Tromsø	0·99 (0·85-1·15)	31·7% (0·133)	1·31 (1·12-1·52)	0·8% (0·434)
quintile 3 vs. 1 (lowest)				0·94 (0·80-1·09)	25·5% (0·187)	1·40 (1·22-1·60)	0·0% (0·636)
quintile 4 vs. 1 (lowest)				0·95 (0·86-1·07)	2·6% (0·419)	1·55 (1·35-1·77)	0·0% (0·662)
quintile 5 vs. 1 (lowest)				0·91 (0·82-1·01)	0·0% (0·576)	1·86 (1·62-2·13)	0·0% (0·476)
Mean CCA-IMT stratified by sex: men	model 4	combined	AIR, ARIC, CAPS, CHS1, CHS2, EAS, INVADE, KIHD, NOMAS/INVEST, PLIC, Rotterdam, SHIP, Tromsø	0·98 (0·94-1·02)	0·0% (0·865)	1·12 (1·05-1·19)	38·6% (0·076)
women			ARIC, CAPS, CHS1, CHS2, EAS, INVADE, KIHD, NOMAS/INVEST, Rotterdam, SHIP, Tromsø	0·97 (0·93-1·02)	0·0% (0·837)	1·16 (1·10-1·21)	38·6% (0·032)
Mean CCA-IMT stratified by ultrasound protocol: Studies avoiding plaques in the IMT measurement	model 4	combined	EAS, INVADE, NOMAS/INVEST, PLIC	0·99 (0·85-1·15)	23·3% (0·271)	1·19 (1·06-1·32)	0·0% (0·583)
Studies including plaques in the IMT measurement			AIR, ARIC, CAPS, CHS1, CHS2, KIHD, Rotterdam, SHIP, Tromsø	0·97 (0·95-1·00)	0·0% (0·841)	1·15 (1·08-1·22)	61·6% (0·008)
Mean CCA-IMT including published results from MESA	model 4	stroke	ARIC, CAPS, CHS1, CHS2, EAS, INVADE, KIHD, NOMAS/INVEST, PLIC, Rotterdam, SHIP, Tromsø, published estimates from MESA	1·02 (0·96-1·09)	19·2% (0·250)	1·18 (1·05-1·31)	63·9% (<0·001)

* model 1:adjusted for age and sex; model 2: adjusted for age, sex and mean cIMT of scan 1 and 2; model 3: adjusted for age, sex, mean cIMT of scan 1 and 2, ethnicity and socioeconomic status; model 4: adjusted for age, sex, mean cIMT of scan 1 and 2, ethnicity, socioeconomic status, systolic blood pressure, antihypertensive treatment, total cholesterol, lipid-lowering treatment, creatinine, hemoglobin, smoking and diabetes; #p-value of test for heterogeneity; + The analysis by quintiles was done on non-imputed data, as the imputation of cIMT values resulted in changing strata and therefore in non-integer sample size per stratum

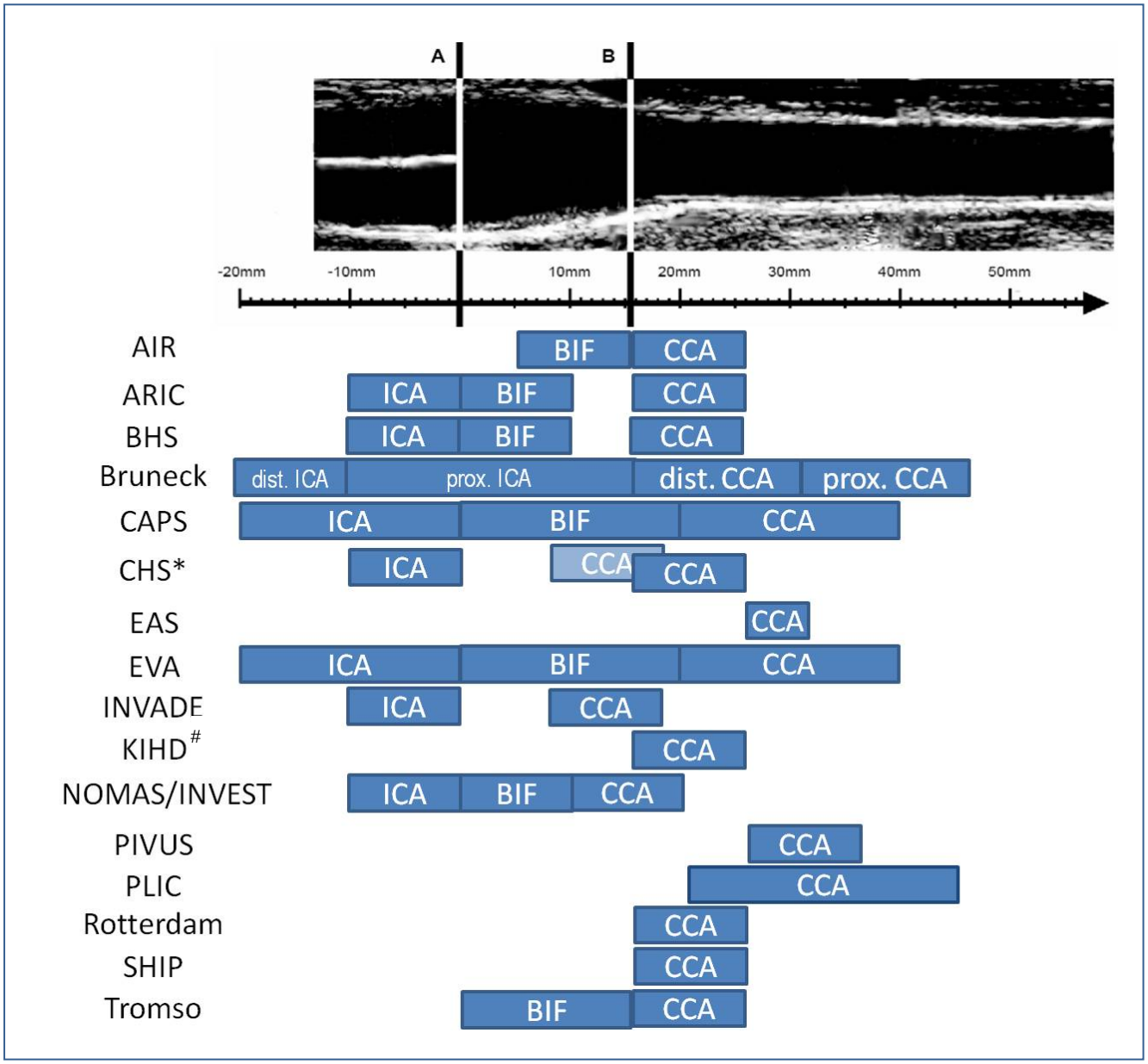
Webtable A7: **Sensitivity analyses: overall hazard ratios (per one SD increase unless otherwise indicated)**

	mean (SD) of common carotid artery intima media thickness progression [mm/year]		
	2 ultrasound visits	derived from 3 ultrasound visits	4 ultrasound visits
Atherosclerosis and Insulin Resistance study (subset with 3 ultrasound visits, n=267)	0·0012 (0·0276)	0·0134 (0·0133)	-
Atherosclerosis Risk In Communities (subset with 3 ultrasound visits, n=6,191)	0·0120 (0·0477)	0·0203 (0·0256)	-
Atherosclerosis Risk In Communities (subset with 4 ultrasound visits, n=1,564)	0·0115 (0·0473)	-	0·0174 (0·0150)
Cardiovascular Health Study, cohort1 (subset with 3 ultrasound visits, n=1,921)	0·0052 (0·0431)	0·0095 (0·0199)	-
Etude sur le vieillissement artériel (subset with 3 ultrasound visits, n=845)	0·0055 (0·0454)	0·0113 (0·0265)	-
Interventionsprojekt zerebrovaskuläre Erkrankungen und Demenz im Landkreis Ebersberg (subset with 3 ultrasound visits, n=1,986)	0·0094 (0·0770)	0·0044 (0·0396)	-
Interventionsprojekt zerebrovaskuläre Erkrankungen und Demenz im Landkreis Ebersberg (subset with 4 ultrasound visits, n=1,309)	0·0113 (0·0747)	-	0·0080 (0·0295)
Kuopio Ischemic Heart Disease Study (subset with 3 ultrasound visits, n=692)	0·0275 (0·0316)	0·0279 (0·0323)	-
Kuopio Ischemic Heart Disease Study (subset with 4 ultrasound visits, n=560)	0·0274 (0·0302)	-	0·0129 (0·0098)
Northern Manhattan Study/The Oral Infections and Vascular Disease Epidemiology Study (subset with 3 ultrasound visits, n=488)	0·0082 (0·0301)	0·0306 (0·0163)	-
Progression of Lesions in the Intima of the Carotid (subset with 3 ultrasound visits, n=1,467)	0·0144 (0·0359)	0·0178 (0·0177)	-
Study of Health in Pomerania (subset with 3 ultrasound visits, n=758	0·0043 (0·0206)	-0·0033 (0·0109)	-
Tromsø Study (subset with 3 ultrasound visits, n=2,407)	0·0048 (0·0178)	0·0114 (0·0096)	-

Webtable A8: **Comparison of cIMT progression estimates derived from 2, 3 or 4 ultrasound visits**

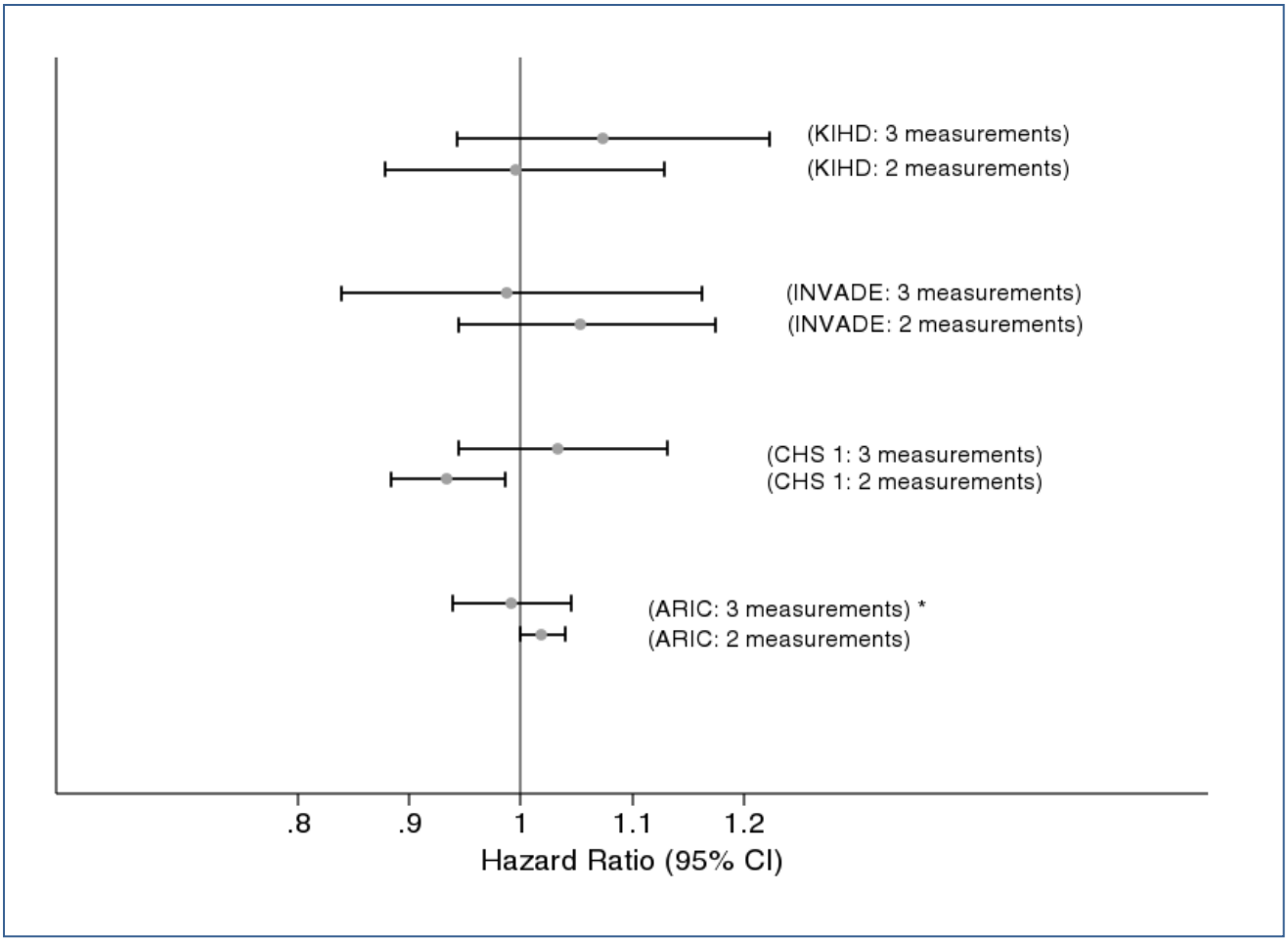


Webfigure A1: **Number of publications and studies screened and included**



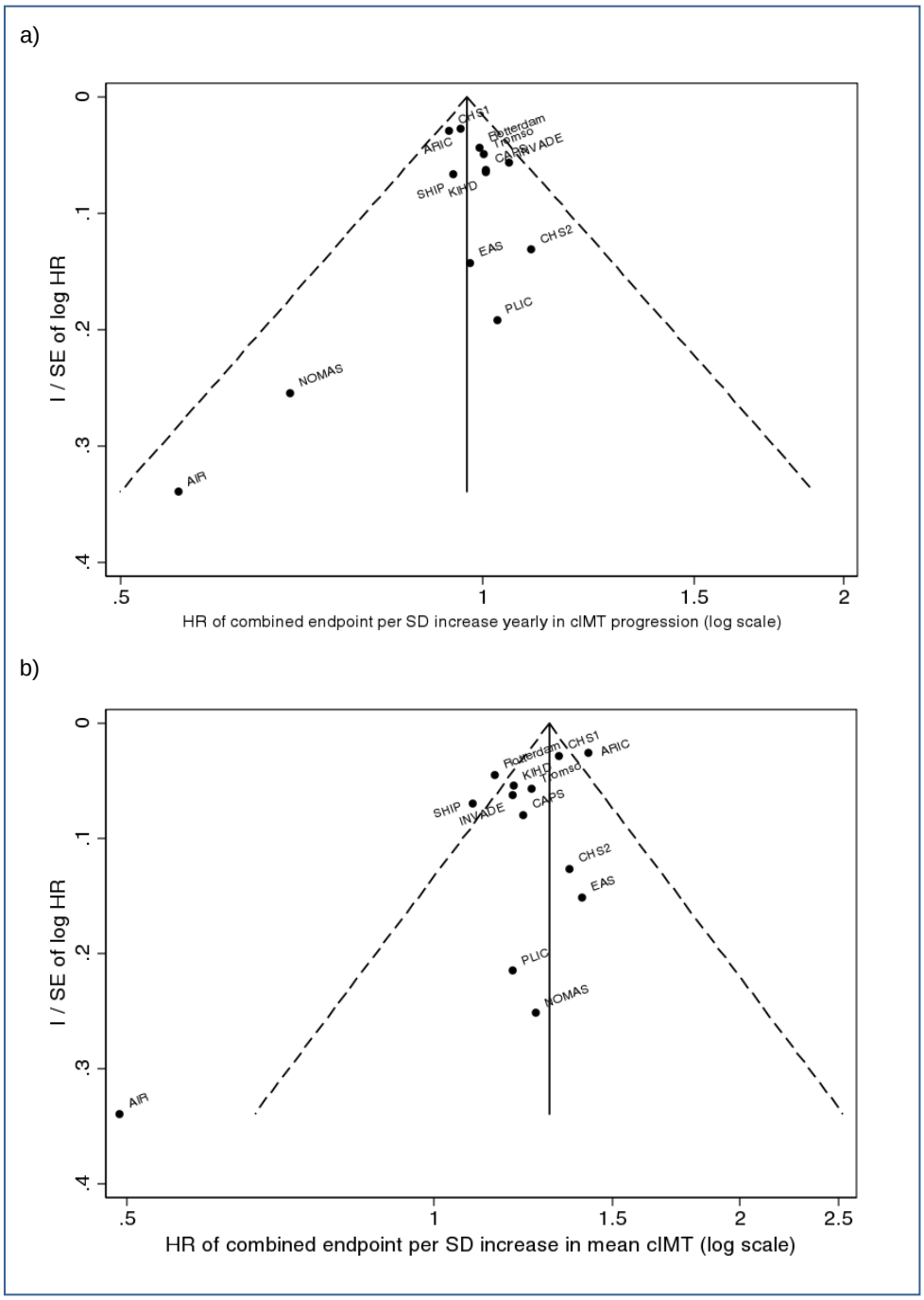
Webfigure A2: **Segment definitions across included studies**

CCA = common carotid artery; BIF = carotid bifurcation; ICA = internal carotid artery; * CCA definition in the CHS: If the beginning of the bulbus widening is determinable, a 1cm segment proximal, else a segment extending from 8 to 18mm proximal to the tip of the flow divider; # CCA definition in the KIHD: A 1 to 1·5cm segment proximal to the bulbar widening.



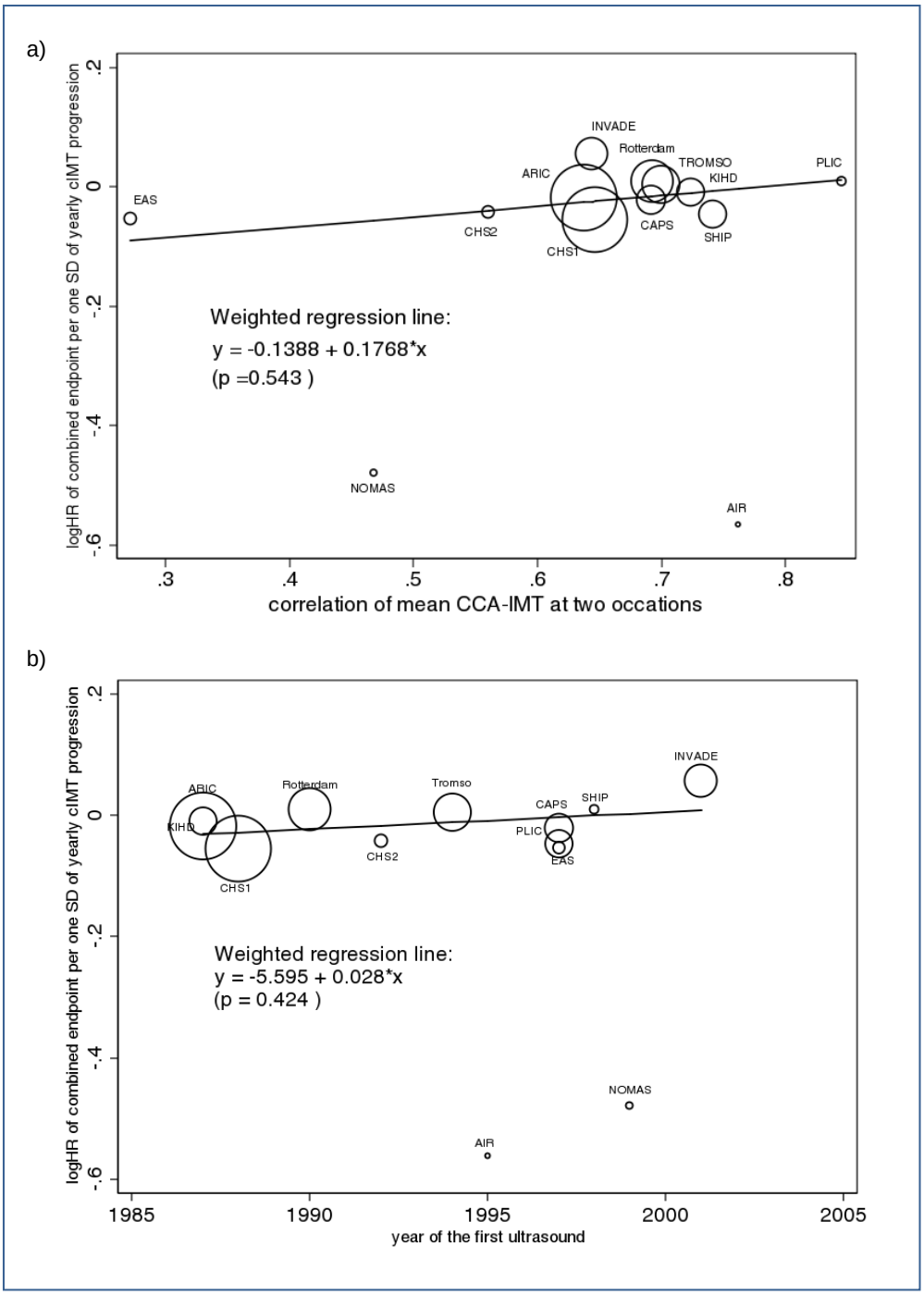
Webfigure A3: **Comparison of overall hazard ratios of combined endpoint per one SD increase in mean common carotid artery intima media thickness progression, based on 2 and 3 ultrasound visits**

Results are adjusted for age, sex and mean IMT (model 2, see text). *In ARIC, a minority of participants was seen at both visits 3 and 4, but most subjects attended visit 3 **or** 4. Therefore, measurements from the visits 1, 2 and 3 or from the visits 1, 2 and 4 were used here.



Webfigure A4: **Funnel plots of the hazard ratio of the combined endpoint per one SD increase in mean common carotid artery intima media thickness progression or mean CCA-IMT**

Results are adjusted for age, sex and mean IMT (model 2, see text), The weight (vertical axis) is the reciprocal of the standard error of the logHR. The dashed lines are pseudo 95% confidence limits.



Webfigure A5: **Meta-regression of the log hazard ratio of the combined outcome per one SD increase in mean CCA-IMT progression vs. a) the reproducibility (correlation of repeated measures) of mean CCA-IMT by study and b) the year of the first ultrasound scan by study**

Hazard ratios are adjusted for vascular risk factors (model 4, see text). The size of the circles is inversely proportional to the variance of the log HR.

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