The Prospective Studies of Atherosclerosis (Proof-ATHERO) consortium: Design and rationale

Tschiderer, Seekircher *et al.*

Electronic Supplementary Material

Table S1. Study acronyms, full study names, and study references in the Proof-ATHERO consortium

Study acronym or first author	Ref.	Full study name
General population		
AIR	[1]	Atherosclerosis and Insulin Resistance Study
ARIC	[2]	Atherosclerosis Risk in Communities Study
BRUN	[3]	Bruneck Study
CAPS	[4]	Carotid Atherosclerosis Progression Study
CCCC	[5]	Chin-Shan Community Cardiovascular Cohort
CHS	[6]	Cardiovascular Health Study
CMCS-BEIJING	[7]	Chinese Multi-Provincial Cohort Study (Beijing)
DIWA	[8]	Diabetes and Insulin Resistance in Women Study
EAS	[9]	Edinburgh Artery Study
EPICARDIAN	[10]	Epidemiología Cardiovascular en los Ancianos en España Study
EVA	[11]	Étude sur la Vieillissement Artériel Study
HOORN	[12]	Hoorn Study
INVADE	[13]	Interventionsprojekt zerebrovaskuläre Erkrankungen und Demenz im Landkreis Ebersberg
JHS	[14]	Jackson Heart Study
KIHD	[15]	Kuopio Ischemic Heart Disease Risk Factor Study
MESA	[16]	Multi-Ethnic Study of Atherosclerosis
NOMAS-INVEST	[17]	Northern Manhattan Study and The Oral Infections and Vascular Disease Epidemiology Study
PIVUS	[18]	Prospective Investigation of the Vasculature in Uppsala Seniors Study
PLIC	[19]	Presence and Progression of Lesions in Carotid Arteries Study
ROTTERDAM	[20]	Rotterdam Study
SAPHIR	[21]	Salzburg Atherosclerosis Prevention Program in Subjects at High Individual Risk
High-risk populations		
BK REGISTRY	[22]	BK Registry Study
CREED	[23]	Cardiovascular Risk Extended Evaluation in Dialysis Patients
CSN	[24]	Campania Salute Network
Ekart	[25]	Study Ekart et al.
HD-IMT	[26]	HD-IMT Study
Honda	[27]	Study Honda et al.
IMPROVE	[28]	Carotid Intima Media Thickness and IMT-Progression as Predictors of Vascular Events in a High Risk European Population Study
Kato	[29]	Study Kato et al.
Landecho	[30]	Study Landecho et al.
NIGUARDA-MONZINO	[31]	Niguarda-Monzino Study
OSACA2	[32]	Osaka Follow-up Study for Carotid Atherosclerosis 2
Papagianni	[33]	Study Papagianni et al.
POPROSTU	[34]	Poznań Prospective Study of Type-1 Diabetic Patients
RIAS	[35]	Resistive Index in Atherosclerosis Study
SPARC	[36]	SPARC Study
3SCO	[37]	Hiroshima-Shobara-Soryo Cohort
Clinical trials		
ACAPS	[38]	Asymptomatic Carotid Artery Progression Study
ALLO-IMT	[39]	ALLO-IMT Study
ASAP-NL	[40]	Atorvastatin vs. Simvastatin on Atherosclerosis Progression Study
ATIC	[41]	Anti-oxidant Therapy in Chronic Renal Insufficiency Study
AUDITOR	[42]	Atherosclerosis Underlying Development Assessed by Intima-Media Thickness in atients on Rimonabant Study
BAS	[43]	Beijing Atherosclerosis Study
BK REGISTRY II	[44]	BK Registry II Study
CAMERA	[45]	Carotid Atherosclerosis - Metformin for Insulin Resistance Study
CAPTIVATE	[46]	Carotid Atherosclerosis Progression Trial Investigating Vascular ACAT Inhibition
CERDIA	[47]	Cerivastatin in Diabetes Trial
CONTRAST	[48]	Convective Transport Study

ENHANCE	[49]	Ezetimibe and Simvastatin in Hypercholesterolemia Enhances Atherosclerosis egression Trial
FACIT	[50]	Folic Acid and Carotid Intima-media Thickness Study
GRACE	[51]	Glucose Reduction and Atherosclerosis Continuing Evaluation Study
Gresele	[52]	Study Gresele at al.
HART	[53]	Homocysteine and Atherosclerosis Reduction Trial
KIMVASC	[54]	KIMVASC Study
LIFE-ICARUS	[55]	Losartan Intervention For Endpoint Reduction in Hypertension - Insulin Carotids US Scandinavia Study
Masia	[56]	Study Masiá et al.
MAVET	[57]	Melbourne Atherosclerosis Vitamin E Trial
MEDICLAS	[58]	Metabolic Effects of Different Classes of Antiretrovirals Study
MG600	[59]	Effects of Magnesium Supplementation on Vascular Structure and Function in Hypertensive Patients Study
Nakamura II	[60]	Study Nakamura et al. II
OPAL	[61]	Osteoporosis Prevention and Arterial Effects of Tibolone Study
PERIOCARDIO	[62]	PerioCardio Study
PREVEND IT	[63]	Prevention of Renal and Vascular Endstage Disease Intervention Trial
RADIANCE I	[64]	Rating Atherosclerosis Disease Change by Imaging with a New CETP Inhibitor 1 Trial
RADIANCE II	[65]	Rating Atherosclerosis Disease Change by Imaging with a New CETP Inhibitor 2 Trial
REGRESS	[66]	Regression Growth Evaluation Statin Study
RIS	[67]	Risk Factor Intervention Study
Safarova	[68]	Study Safarova at al.
SECURE	[69]	Study to Evaluate Carotid Ultrasound Changes in Patients Treated with Ramipril and Vitamin E
STARR	[70]	Study of Atherosclerosis with Ramipril and Rosiglitazone
STOP-NIDDM	[71]	Study to Prevent Non-Insulin-Dependent Diabetes Mellitus
VITAL	[72]	Vital Study
WELCOME	[73]	Wessex Evaluation of Fatty Liver and Cardiovascular Markers in NAFLD with Omacor Therapy Trial

Table S2. Ascertainment of cIMT in the Proof-ATHERO consortium

Study acronym or first author	cIMT definition											Measurement features							
	Section			Side			Wall			Type									
	CCA	BIF	ICA	Right	Left	Average	Near	Far	Average	Mean	Max	Plaque avoided	Multiple scans	ECG gated	Same machine type	Same sonographer	Central reading	Angle control	Edge detection
General population																			
AIR	●	●	○	●	●	●	○	●	●	●	●	–	–	+	+	+	+	–	+[e]
ARIC	●	●	●	●	●	●	●	●	●	●	●	–	+	+	+	–	+	+	–
BRUN	●	●	●	●	●	●	○	●	●	●	●	+	–	+	–	+	–	+	–
CAPS	●	●	●	●	●	●	○	●	●	●	○	–	–	+	+	–	+	–	+[d]
CCCC	●	○	●	●	●	●	○	●	●	○	●	+	+	+	+	–	–	+	–
CHS	●	○	●	●	●	●	●	●	●	○	●	–	+[a]	–	+	–	+	+	–
CMCS-BEIJING	●	●	●	●	●	●	○	○	●	●	●	+	–	–	–	–	+	+	–/+[e]
DIWA	●	●	○	●	●	●	○	●	●	●	●	–	–	+	+	+	+	–	+[e]
EAS	●	○	○	●	●	●	○	●	●	●	●	–	–	–	+	–	+	–	–
EPICARDIAN	●	●	●	●	●	●	○	●	●	●	○	+	+	–	+	+	–	+	–
EVA	●	○	○	●	●	●	○	●	●	●	○	+	–	–	+	–	+	+	+[d]
HOORN	●	○	○	●	○	●	○	●	●	●	○	+	+	+	+	+	+	+	+[d]
INVADE	●	○	○	●	●	●	○	●	●	●	○	+	+	–	+	+	+	+	+[d]
JHS	●	●	●	●	●	●	●	●	●	●	●	–	+	+	+	–	+	+	–
KIHD	●	○	○	●	●	●	○	●	●	●	●	–	–	–	–	–	+	+	+[e]
MESA	●	○	●	●	●	●	○	○	●	●	●	+	+[ab]	+	+	NR	+	+	+[d]
NOMAS-INVEST	●	●	●	●	●	●	●	●	●	●	●	+	+[b]	–	+	+	+	+	+[e]
PIVUS	●	○	○	●	●	●	○	●	●	●	●	NR	–	+	+	+	+	–	+[e]
PLIC	●	○	○	●	●	●	○	●	●	●	●	+	+[b]	+	+	+	+	–	+
ROTTERDAM	●	○	○	●	●	●	●	●	●	●	●	–	+	+	+	–	+	–	–
SAPHIR	●	●	●	●	●	●	○	○	●	●	○	+	+	–	+	+	+	+	–
High-risk populations																			
BK REGISTRY	●	●	○	●	●	●	○	●	●	●	○	+	+	+	+	+	+	+	+[e]
CREED	●	○	○	○	○	●	○	●	●	●	○	+	–	+	+	+	–	+	–
CSN	●	●	●	●	●	●	●	●	●	○	●	–	–	–	+	–	+	–	–
Ekart	●	●	●	●	●	●	○	●	●	●	○	+	+	–	+	+	+	+	–
HD-IMT	●	○	○	●	○	●	○	●	●	○	●	–	–	+	+	+	–	–	–
Honda	●	○	○	●	●	●	○	●	●	●	●	–	–	–	–	–	–	–	–
IMPROVE	●	●	●	●	●	●	○	●	●	●	●	–	+	+[b]	+	–	+	+	+[e]
Kato	●	○	○	○	○	●	○	●	●	●	●	+	–	–	+	+	+	+	+[e]
Landecho	●	○	○	●	●	●	○	○	●	○	●	+	–	–	–	–	–	–	–
NIGUARDA-MONZINO	●	●	●	●	●	●	●	●	●	○	●	–	–	–	–	–	–	+	–
OSACA2	●	●	●	●	●	●	●	●	●	●	●	–	+[b]	–	+	–	+	–	–
Papagianni	○	●	○	●	●	●	○	●	●	●	●	+	–	+	+	+	+	–	–
POPROSTU	●	○	○	●	○	●	○	●	●	●	●	+	+	–	+	+	+	+	+[d]
RIAS	●	○	○	●	●	●	○	●	●	●	○	+	+	+	+	–	–	–	–
SPARC	●	○	○	●	●	●	○	●	●	●	○	+	+	–	NR	NR	+	–	–
3SCO	●	●	●	●	●	●	●	●	●	●	●	–	–	–	+	–	–	–	–
Clinical trials																			
ACAPS	●	●	●	●	●	●	○	○	●	○	●	–	–	+	+	–	+	+	+[e]
ALLO-IMT	●	●	●	●	●	●	●	●	●	●	●	–	–	+	+	+	+	+	+[de]
ASAP-NL	●	●	●	●	●	●	●	●	●	●	○	–	–	–	+	–	+	+	+[e]
ATIC	●	○	○	●	○	●	○	●	●	●	○	+	+	+	+	+	+	–	+[d]
AUDITOR	●	●	●	●	●	●	○	●	●	●	○	–	–	+	+	–	+	+	–
BAS	●	○	○	○	○	●	●	○	●	●	○	+	–	–	+	–	+	–	–
BK REGISTRY II	●	●	●	○	●	●	○	●	●	●	○	+	+	+	+	+	+	+	+[e]
CAMERA	●	○	○	●	●	●	○	●	●	●	○	+	–	+	+	+	+	+	+[e]
CAPTIVATE	●	●	●	●	●	●	●	●	●	●	●	–	+	–	+	–	+	+	+[e]
CERDIA	●	●	●	●	○	●	○	○	●	●	●	+	–	+	+	–	+	+	+[e]
CONTRAST	●	○	○	●	●	●	●	●	●	●	●	–	+	+	–	–	+	+	–

ENHANCE	●	●	●	●	●	●	○	●	●	●	●	–	+[c]	–	+	–	+	+	+[e]
FACIT	●	○	○	○	○	●	○	○	●	●	●	–	+	+	+	–	+	+	+[d]
GRACE	●	●	●	●	●	●	●	●	●	●	●	–	+	–	–	–	+	+	–
Gresele	●	○	○	●	○	●	●	○	●	●	●	+	–	–	+	+	+	+	+[d]
HART	●	●	●	●	●	●	●	●	●	●	●	–	+	–	–	–	+	+	–
KIMVASC	●	○	○	●	●	●	○	●	●	●	○	+	–	–	+	+	+	–	–
LIFE-ICARUS	●	○	○	●	●	●	○	●	●	●	○	+	+[b]	+	+	+	+	+	+[e]
Masia	●	○	○	●	●	●	○	●	●	●	●	NR	NR	NR	NR	NR	NR	NR	NR
MAVET	●	○	○	○	○	●	○	○	●	○	●	NR	+	+	+	+	+	+	–
MEDICLAS	●	○	○	●	○	●	○	○	●	●	○	+	+	–	+	+	+	–	–
MG600	●	○	○	●	●	●	○	○	●	●	●	+	+	+	+	+	–	–	–
Nakamura II	●	●	●	●	●	●	○	●	●	●	●	+	–	+	+	+	+	+	–
OPAL	●	●	●	●	●	●	●	●	●	●	●	–	+	+	+	–	+	+	–
PERIOCARDIO	●	○	○	●	●	●	○	●	●	●	●	–	+	+	+	–	+	+	+[e]
PREVEND IT	●	○	○	○	●	●	○	●	●	●	○	+	+	+	+	–	+	+	+[d]
RADIANCE I	●	●	●	●	●	●	●	●	●	●	●	–	+[c]	+	+	–	+	+	+[e]
RADIANCE II	●	●	●	●	●	●	●	●	●	●	●	–	+[c]	+	+	–	+	+	+[e]
REGRESS	●	●	●	●	●	●	●	●	●	●	●	–	–	–	–	–	+	+	+[d]
RIS	●	●	○	●	○	●	○	●	●	●	●	+	+	+	+	+	+	+	+[d]
Safarova	●	○	○	●	●	●	○	●	●	●	○	+	–	+	+	+	+	+	+[e]
SECURE	●	●	●	●	●	●	●	●	●	○	●	–	+	–	–	–	+	+	–
STARR	●	●	●	●	●	●	●	●	●	●	●	–	+	–	–	–	+	+	–
STOP-NIDDM	●	○	○	●	●	●	○	●	●	●	●	NR	+	+	+	–	NR	NR	NR
VITAL	●	○	○	●	○	●	○	●	●	●	○	NR	NR	NR	NR	NR	NR	NR	NR
WELCOME	●	○	○	●	●	●	○	●	●	●	○	+	+	+	+	+	+	+	+[d]

●=provided, ○=not provided; BIF=carotid bifurcation, CCA=common carotid artery, cIMT=carotid intima-media thickness, ECG=electrocardiography, ICA=internal carotid artery, IMT=intima-media thickness. Full study names and references are provided in **Table S1**. [a]ICA only. [b]Only in a subset of the study population. [c]Only at baseline and final follow-up. [d]Automated. [e]Semi-automated.

Table S3. Ascertainment of carotid plaque in the Proof-ATHERO consortium

Study acronym or first author	Parameters					Detailed information on carotid plaque definition
	Status	Amount	Thickness	Area	Density[a]	
General population						
AIR	●	●	●	●	●	Distinct area with an IMT >50% thicker than that of neighbouring sites
ARIC	●	●	○	○	○	If two of three conditions are met: (1) wall shape (protrusion into the lumen, loss of alignment, rough boundary), (2) wall texture (brighter echoes than adjacent boundaries), and (3) wall thickness (IMT ≥1.5 mm)
BRUN	●	●	●	○	○	Based on (1) wall surface (protrusion into the lumen or roughness of the arterial boundary) and (2) wall texture (echogenicity)
CAPS	●	○	○	○	○	Focal protrusion of ≥1.8 mm
CCCC	●	●	○	○	○	Grading as (1) normal or no observable plaque, (2) one small plaque with diameter stenosis <30%, (3) one medium plaque with 30-49% diameter stenosis or multiple small plaques, (4) one large plaque with 50-99% diameter stenosis or multiple plaques with at least one medium plaque, and (5) 100% occlusion
CHS	●	○	○	○	●	Definition based on the greatest wall protrusion (i.e. IMT) and grading based on lesion surface, echogenicity, and texture characteristics as (1) no plaque (i.e. smooth surface and normal density and morphology), (2) high-risk plaque (i.e. irregular/ulcerated surface, echolucent, or heterogeneous texture), and (3) intermediate-risk plaque (i.e. any other combinations of lesion characteristics)
CMCS-BEIJING	●	○	●	●	○	IMT ≥1.3 mm or focal structure encroaching into arterial lumen of ≥0.5 mm or ≥50% of surrounding IMT
EAS	●	○	●	○	○	IMT >1.2 mm with advanced atherosclerotic plaque defined as IMT >2 mm
EVA	●	●	●	○	○	Localised echo structures encroaching into the vessel lumen with a distance ≥1 mm between media-adventitia interface and lesion surface facing the lumen
INVADE	●	○	○	○	○	Focal structure encroaching into the arterial lumen ≥0.5 mm or ≥50% of the surrounding IMT, or IMT >1.5 mm as measured from the media-adventitia interface to the intima-lumen interface
JHS	●	○	○	○	○	If two of three conditions are met: (1) wall shape (protrusion into the lumen, loss of alignment, rough boundary), (2) wall texture (brighter echoes than adjacent boundaries), and (3) wall thickness (IMT ≥1.5 mm)
KIHD	●	○	○	○	○	Distinct area either with mineralisation (bright echo, often producing a typical echogenic shadow) or with focal protrusion into the lumen
MESA	●	○	○	○	●	Discrete, focal thickening ≥1.5 mm or ≥50% greater than the surrounding IMT
NOMAS-INVEST	●	●	●	●	○	Focal wall thickening or protrusion into the lumen >50% greater than the surrounding thickness
PIVUS	●	○	●	●	○	Local thickening of the intima-media by >50% vs. surrounding IMT
PLIC	●	○	○	○	○	Focal plaque >1.3 mm in longitudinal resolution, lateral, or medial angle
ROTTERDAM	●	○	○	○	○	Focal widening relative to adjacent segments, with protrusion into the lumen with calcified deposits or both calcified and non-calcified material
SAPHIR	●	○	○	○	○	Grading as (1) normal, (2) vessel wall thickening <1 mm, (3) one minimal plaque ≤2 mm, (4) two moderate plaques ≤3 mm, (5) severe plaque >3 mm, and (6) completely obstructed lumen
High-risk populations						
BK REGISTRY	●	○	●	○	○	Focal structure encroaching into arterial lumen by ≥50% of surrounding IMT or thickness >1.2 mm
CSN	●	○	○	○	○	IMT >1.5 mm
IMPROVE	●	●	●	●	○	IMT ≥1.5 mm
Kato	●	○	○	○	○	IMT >1 mm
Landecho	●	○	○	○	○	Echogenic structures encroaching on the vessel's lumen with a distinct area 50% greater than the IMT of neighbouring sites
NIGUARDA-MONZINO	●	●	●	○	○	IMT ≥1.5 mm
Papagianni	●	○	○	○	○	Faint grey echoes or bright white echoes protruding into the arterial lumen
SPARC	●	○	○	●	○	Focal thickening >1 mm
Clinical trials						
BK REGISTRY II	●	○	●	○	○	Localised thickening >1.2 mm not involving the whole carotid artery
CAMERA	●	●	○	○	○	IMT ≥1.5 mm or focal encroachment into the arterial lumen ≥0.5 mm

CONTRAST	●	●	○	○	○	Grading as (1) no plaque, (2) minimal plaque, (3) moderate plaque, and (4) severe plaque, where a moderate or severe plaque was generally defined as a focal structure that encroaches into the arterial lumen or demonstrates a thickness >1.5 mm
ENHANCE	●	○	○	○	○	IMT >1.3 mm
LIFE-ICARUS	●	○	○	○	○	Semi-quantitative grading of the amount of atherosclerotic lesions as (1) none, (2) very few, (3) few, (4) some, and (5) several
Masia	●	○	○	○	○	NR
MG600	●	○	○	○	○	IMT ≥1.5 mm
WELCOME	●	○	○	○	○	Focal thickening ≥50% greater than the surrounding wall or focal region with IMT >1.5 mm protruding into the lumen distinct from adjacent boundary

● =provided, ○ =not provided; IMT=intima-media thickness. Full study names and references are provided in **Table S1**.
[a]Density according to the Gray-Weale classification.

Table S4. Assessment of prevalent and incident disease in the Proof-ATHERO consortium

Study acronym or first author	Prevalent disease			Incident events		
	CHD	Stroke	Diabetes	CHD	Stroke	Death
General population						
AIR	+	+	++	++	++	*
ARIC	++	++	++	++	++	**
BRUN	++	++	++	++	++	**
CAPS	+	+	+	++	++	**
CCCC	++	++	++	NR	++	*
CHS	++	++	++	++	++	**
CMCS-BEIJING	++	++	++	++	++	**[c]
DIWA	+	+	++	++	++	*
EAS	++	+	+	++	++	**[c]
EPICARDIAN	++	++	++	++	++	*
EVA	+	+	++	++[b]	++[b]	**
HOORN	+/++	+/++	++	++	++	**
INVADE	++	++	++	++	++	**
JHS	+	+	++	+	+	–[a]
KIHD	++	+	++	++	++	**
MESA	+	–[a]	++	++	++	**
NOMAS-INVEST	+	+	++	++	++	**
PIVUS	+	+	+/++	++	++	**
PLIC	NR	NR	++	NR	NR	NR
ROTTERDAM	++	++	++	++	++	**
SAPHIR	++	++	++	++	++	**
High–risk populations						
BK REGISTRY	++	–	++	++	++	*/**
CREED	NR	NR	NR	++	++	**
CSN	++	++	++	++	++	**
Ekart	NR	–	NR	NR	NR	NR
HD-IMT	NR	NR	NR	NR	NR	NR
Honda	NR	++	NR	++[b]	++[b]	**
IMPROVE	++	++	++	++	++	**
Kato	++	++	++	++	++	**
Landecho	++	++	++	++	++	**
NIGUARDA-MONZINO	++	++	++	++	++	**
OSACA2	+	+	++	++	++	*
Papagianni	++	+	++	++	+	*/**
POPROSTU	++	+	++	++	++	*
RIAS	++	++	++	++	++	**
SPARC	NR	NR	NR	++	++	**
3SCO	++	++	++	++	++	**
Clinical trials						
ACAPS	+	+	+	++	++	**
ALLO-IMT	+	++	+	++	++	*
ASAP-NL	–	–	++	–	–	–
ATIC	+/++	+/++	+/++	–[a]	–[a]	–[a]
AUDITOR	–	–	++	–	–	–
BAS	+	+	+	–	+	–
BK REGISTRY II	++	–	++	++	++	*/**
CAMERA	++	+	++	++	++	**
CAPTIVATE	–	–	++	–	–	–
CERDIA	++	–	++	++	++	**
CONTRAST	+	+	+	++	++	**
ENHANCE	–[a]	++	++	++	++	**
FACIT	+	+	+	–	–	*
GRACE	++	++	++	++	++	**
Gresele	++	++	++	++	++	**
HART	++	++	++	++	++	**
KIMVASC	–[a]	–[a]	NR	NR	–	NR
LIFE-ICARUS	++	++	++	++	++	**
Masia	NR	NR	++	NR	–	NR

MAVET	–[a]	–[a]	–[a]	–	–	–
MEDICLAS	–	–	–	+	+	*
MG600	++	++	++	++	++	**
Nakamura II	NR	NR	NR	NR	NR	NR
OPAL	+	+	+	+	+	*
PERIOCARDIO	+	+	+	+	+	**
PREVEND IT	+	–[a]	+	++	++	*
RADIANCE I	+	–	++	++	++	**
RADIANCE II	+	–	++	++	++	**
REGRESS	++	–	++	–[a]	–[a]	–[a]
RIS	++	++	++	++	++	**
Safarova	++	++	++	++	++	*
SECURE	++	++	++	++	++	**
STARR	++	++	++	++	++	**
STOP-NIDDM	++	NR	++	++	++	NR
VITAL	+	+	++	++	++	**
WELCOME	++	++	++	++	++	**

–, not provided; +, self-report only; ++, self-report supplemented by objective criteria (e.g.: electrocardiography, echocardiography, enzymes, imaging); *, based on death certificate only; **, based on death certificate supplemented by medical record; CHD, coronary heart disease; NR, not reported; Full study names and references are provided in **Table S1**. [a]recorded but not provided. [b]fatal events only. [c]cardiovascular disease only.

Supplementary References

1 Hulthe J, Bokemark L, Wikstrand J, Fagerberg B: The Metabolic Syndrome, LDL Particle Size, and Atherosclerosis. Arterioscler Thromb Vasc Biol 2000;20:2140–2147.

2 The ARIC Investigators: The Atherosclerosis Risk in Communities (ARIC) Study: design and objectives. Am J Epidemiol 1989;129:687–702.

3 Kiechl S, Willeit J: In a Nutshell: Findings from the Bruneck Study. Gerontology 2019;65:9–19.

4 Lorenz MW, Kegler S von, Steinmetz H, Markus HS, Sitzer M: Carotid intima-media thickening indicates a higher vascular risk across a wide age range: prospective data from the Carotid Atherosclerosis Progression Study (CAPS). Stroke 2006;37:87–92.

5 Chien K-L, Su T-C, Jeng J-S, Hsu H-C, Chang W-T, Chen M-F, et al.: Carotid artery intima-media thickness, carotid plaque and coronary heart disease and stroke in Chinese. PLoS ONE 2008;3:e3435.

6 Fried LP, Borhani NO, Enright P, Furberg CD, Gardin JM, Kronmal RA, et al.: The Cardiovascular Health Study: design and rationale. Ann Epidemiol 1991;1:263–276.

7 Li Y, Liu J, Wang W, Zhao D: The association between within-visit blood pressure variability and carotid artery atherosclerosis in general population. PLoS ONE 2014;9:e97760.

8 Brohall G, Behre C-J, Hulthe J, Wikstrand J, Fagerberg B: Prevalence of diabetes and impaired glucose tolerance in 64-year-old Swedish women: experiences of using repeated oral glucose tolerance tests. Diabetes Care 2006;29:363–367.

9 Allan PL, Mowbray PI, Lee AJ, Fowkes FGR: Relationship Between Carotid Intima-Media Thickness and Symptomatic and Asymptomatic Peripheral Arterial Disease. Stroke 1997;28:348–353.

10 Gabriel Sánchez R, Novella Arribas B, Alonso Arroyo M, Vega Quiroga S, López García I, Suárez Fernández C, et al.: El proyecto Epicardian: un estudio de cohortes sobre enfermedades y factores de riesgo cardiovasculares en ancianos españoles: consideraciones metodológicas y principales hallazgos demográficos. Rev Esp Salud Publica 2004;78:243–255.

11 Bonithon-Kopp C, Touboul P-J, Berr C, Leroux C, Mainard F, Courbon D, et al.: Relation of Intima-Media Thickness to Atherosclerotic Plaques in Carotid Arteries. Arterioscler Thromb Vasc Biol 1996;16:310–316.

12 Rutters F, Nijpels G, Elders P, Stehouwer CDA, van der Heijden AA, Groeneveld L, et al.: Cohort Profile: The Hoorn Studies. Int J Epidemiol 2018;47:396-396j.

13 Bickel H, Ander K-H, Brönner M, Etgen T, Gnahn H, Gotzler O, et al.: Reduction of Long-Term Care Dependence After an 8-Year Primary Care Prevention Program for Stroke and Dementia: The INVADE Trial. J Am Heart Assoc 2012;1:e000786.

14 Taylor HA, Wilson JG, Jones DW, Sarpong DF, Srinivasan A, Garrison RJ, et al.: Toward resolution of cardiovascular health disparities in African Americans: design and methods of the Jackson Heart Study. Ethn Dis 2005;15:S6-4-17.

15 Salonen JT: Is there a continuing need for longitudinal epidemiologic research? The Kuopio Ischaemic Heart Disease Risk Factor Study. Ann Clin Res 1988;20:46–50.

16 Bild DE: Multi-Ethnic Study of Atherosclerosis: Objectives and Design. Am J Epidemiol 2002;156:871–881.

17 Rundek T, Blanton SH, Bartels S, Dong C, Raval A, Demmer RT, et al.: Traditional risk factors are not major contributors to the variance in carotid intima-media thickness. Stroke 2013;44:2101–2108.

18 Rodriguez-Macias KA, Lind L, Naessen T: Thicker carotid intima layer and thinner media layer in subjects with cardiovascular diseases. An investigation using noninvasive high-frequency ultrasound. Atherosclerosis 2006;189:393–400.

19 Norata GD, Garlaschelli K, Ongari M, Raselli S, Grigore L, Benvenuto F, et al.: Effect of the Toll-like receptor 4 (TLR-4) variants on intima-media thickness and monocyte-derived macrophage response to LPS. J Intern Med 2005;258:21–27.

20 Hofman A, Grobbee DE, Jong PT de, van den Ouweland FA: Determinants of disease and disability in the elderly: the Rotterdam Elderly Study. Eur J Epidemiol 1991;7:403–422.

21 Esterbauer H, Schneitler C, Oberkofler H, Ebenbichler C, Paulweber B, Sandhofer F, et al.: A common polymorphism in the promoter of UCP2 is associated with decreased risk of obesity in middle-aged humans. Nat Genet 2001;28:178–183.

22 Yuk HB, Park HW, Jung IJ, Kim WH, Kim K-H, Yang D-J, et al.: Analysis of Carotid Ultrasound Findings on Cardiovascular Events in Patients with Coronary Artery Disease during Seven-Year Follow-Up. Korean Circ J 2015;45:28–37.

23 Benedetto FA, Mallamaci F, Tripepi G, Zoccali C: Prognostic value of ultrasonographic measurement of carotid intima media thickness in dialysis patients. J Am Soc Nephrol 2001;12:2458–2464.

24 Izzo R, Mancusi C, Stefano G de, Albano G, Losi M-A, Trimarco V, et al.: Achievement of target SBP without attention to decrease in DBP can increase cardiovascular morbidity in treated arterial hypertension: the Campania Salute Network. J Hypertens 2019;37:1889–1897.

25 Ekart R, Hojs R, Hojs-Fabjan T, Balon BP: Predictive value of carotid intima media thickness in hemodialysis patients. Artif Organs 2005;29:615–619.

26 Stolić R, Trajković G, Jovanović A, Stolić D, Perić V, Sovtić S, et al.: Carotid ultrasonographic parameters as markers of atherogenesis and mortality rate in patients on hemodialysis. Vojnosanit Pregl 2010;67:916–922.

27 Honda H, Ueda M, Kojima S, Mashiba S, Michihata T, Takahashi K, et al.: Oxidized high-density lipoprotein as a risk factor for cardiovascular events in prevalent hemodialysis patients. Atherosclerosis 2012;220:493–501.

28 Baldassarre D, Nyyssönen K, Rauramaa R, Faire U de, Hamsten A, Smit AJ, et al.: Cross-sectional analysis of baseline data to identify the major determinants of carotid intima-media thickness in a European population: the IMPROVE study. Eur Heart J 2010;31:614–622.

29 Kato A, Ishida J, Endo Y, Takita T, Furuhashi M, Maruyama Y, et al.: Association of abdominal visceral adiposity and thigh sarcopenia with changes of arteriosclerosis in haemodialysis patients. Nephrol Dial Transplant 2011;26:1967–1976.

30 Landecho MF, Colina I, Huerta A, Fortuño A, Zalba G, Beloqui O: Relación entre las fases precoces de la enfermedad renal y el síndrome metabólico. Rev Esp Cardiol 2011;64:373–378.

31 Baldassarre D, Amato M, Bondioli A, Sirtori CR, Tremoli E: Carotid artery intima-media thickness measured by ultrasonography in normal clinical practice correlates well with atherosclerosis risk factors. Stroke 2000;31:2426–2430.

32 Kitagawa K, Hougaku H, Yamagami H, Hashimoto H, Itoh T, Shimizu Y, et al.: Carotid intima-media thickness and risk of cardiovascular events in high-risk patients. Results of the Osaka Follow-Up Study for Carotid Atherosclerosis 2 (OSACA2 Study). Cerebrovasc Dis 2007;24:35–42.

33 Papagianni A, Kalovoulos M, Kirmizis D, Vainas A, Belechri A-M, Alexopoulos E, et al.: Carotid atherosclerosis is associated with inflammation and endothelial cell adhesion molecules in chronic haemodialysis patients. Nephrol Dial Transplant 2003;18:113–119.

34 Araszkiewicz A, Zozulinska-Ziolkiewicz D, Trepinska M, Wierusz-Wysocka B: Knowledge after five-day teaching program in intensive insulin therapy performed at the onset of type 1 diabetes influence the development of late diabetic complications. Diabetes Res Clin Pract 2008;81:61–67.

35 Frauchiger B, Schmid HP, Roedel C, Moosmann P, Staub D: Comparison of Carotid Arterial Resistive Indices With Intima-Media Thickness as Sonographic Markers of Atherosclerosis. Stroke 2001;32:836–841.

36 Wannarong T, Parraga G, Buchanan D, Fenster A, House AA, Hackam DG, et al.: Progression of carotid plaque volume predicts cardiovascular events. Stroke 2013;44:1859–1865.

37 Nagai M, Hoshide S, Ishikawa J, Shimada K, Kario K: Visit-to-visit blood pressure variations: new independent determinants for carotid artery measures in the elderly at high risk of cardiovascular disease. J Am Soc Hypertens 2011;5:184–192.

38 The ACAPS Group: Rationale and design for the Asymptomatic Carotid Artery Plaque Study (ACAPS). Control Clin Trials 1992;13:293–314.

39 Higgins P, Walters MR, Murray HM, McArthur K, McConnachie A, Lees KR, et al.: Allopurinol reduces brachial and central blood pressure, and carotid intima-media thickness progression after ischaemic stroke and transient ischaemic attack: a randomised controlled trial. Heart 2014;100:1085–1092.

40 Smilde TJ, Trip MD, Wollersheim H, van Wissen S, Kastelein JJ, Stalenhoef AF: Rationale, Design and Baseline Characteristics of a Clinical Trial Comparing the Effects of Robust vs Conventional Cholesterol Lowering and Intima Media Thickness in Patients with Familial Hypercholesterolaemia: The Atorvastatin versus Simvastatin on Atherosclerosis Progression (ASAP) Study. Clin Drug Investig 2000;20:67–79.

41 Nanayakkara PWB, Teerlink T, Stehouwer CDA, Allajar D, Spijkerman A, Schalkwijk C, et al.: Plasma asymmetric dimethylarginine (ADMA) concentration is independently associated with carotid intima-media thickness and plasma soluble vascular cell adhesion molecule-1 (sVCAM-1) concentration in patients with mild-to-moderate renal failure. Kidney Int 2005;68:2230–2236.

42 O'Leary DH, Reuwer AQ, Nissen SE, Després J-P, Deanfield JE, Brown MW, et al.: Effect of rimonabant on carotid intima-media thickness (CIMT) progression in patients with abdominal obesity and metabolic syndrome: the AUDITOR Trial. Heart 2011;97:1143–1150.

43 Zou Z-Y, Xu X-R, Lin X-M, Zhang H-B, Xiao X, Ouyang L, et al.: Effects of lutein and lycopene on carotid intima-media thickness in Chinese subjects with subclinical atherosclerosis: a randomised, double-blind, placebo-controlled trial. Br J Nutr 2014;111:474–480.

44 Bae J-H, Bassenge E, Kim K-Y, Synn Y-C, Park K-R, Schwemmer M: Effects of low-dose atorvastatin on vascular responses in patients undergoing percutaneous coronary intervention with stenting. J Cardiovasc Pharmacol Ther 2004;9:185–192.

45 Preiss D, Lloyd SM, Ford I, McMurray JJ, Holman RR, Welsh P, et al.: Metformin for non-diabetic patients with coronary heart disease (the CAMERA study): a randomised controlled trial. Lancet Diabetes Endocrinol 2014;2:116–124.

46 Meuwese MC, Groot E de, Duivenvoorden R, Trip MD, Ose L, Maritz FJ, et al.: ACAT inhibition and progression of carotid atherosclerosis in patients with familial hypercholesterolemia: the CAPTIVATE randomized trial. JAMA 2009;301:1131–1139.

47 Beishuizen ED, van de Ree MA, Jukema JW, Tamsma JT, van der Vijver JCM, Meinders AE, et al.: Two-year statin therapy does not alter the progression of intima-media thickness in patients with type 2 diabetes without manifest cardiovascular disease. Diabetes Care 2004;27:2887–2892.

48 Grooteman MPC, van den Dorpel MA, Bots ML, Penne EL, van der Weerd NC, Mazairac AHA, et al.: Effect of online hemodiafiltration on all-cause mortality and cardiovascular outcomes. J Am Soc Nephrol 2012;23:1087–1096.

49 Kastelein JJP, Sager PT, Groot E de, Veltri E: Comparison of ezetimibe plus simvastatin versus simvastatin monotherapy on atherosclerosis progression in familial hypercholesterolemia. Design and rationale of the Ezetimibe and Simvastatin in Hypercholesterolemia Enhances Atherosclerosis Regression (ENHANCE) trial. Am Heart J 2005;149:234–239.

50 Durga J, Bots ML, Schouten EG, Grobbee DE, Kok FJ, Verhoef P: Effect of 3 y of folic acid supplementation on the progression of carotid intima-media thickness and carotid arterial stiffness in older adults. Am J Clin Nutr 2011;93:941–949.

51 Lonn EM, Bosch J, Diaz R, Lopez-Jaramillo P, Ramachandran A, Hâncu N, et al.: Effect of insulin glargine and n-3FA on carotid intima-media thickness in people with dysglycemia at high risk for cardiovascular events: the glucose reduction and atherosclerosis continuing evaluation study (ORIGIN-GRACE). Diabetes Care 2013;36:2466–2474.

52 Gresele P, Migliacci R, Arosio E, Bonizzoni E, Minuz P, Violi F: Effect on walking distance and atherosclerosis progression of a nitric oxide-donating agent in intermittent claudication. J Vasc Surg 2012;56:1622-8, 1628.e1-5.

53 Held C, Sumner G, Sheridan P, McQueen M, Smith S, Dagenais G, et al.: Correlations between plasma homocysteine and folate concentrations and carotid atherosclerosis in high-risk individuals: baseline data from the Homocysteine and Atherosclerosis Reduction Trial (HART). Vasc Med 2008;13:245–253.

54 Fulton RL, McMurdo MET, Hill A, Abboud RJ, Arnold GP, Struthers AD, et al.: Effect of Vitamin K on Vascular Health and Physical Function in Older People with Vascular Disease--A Randomised Controlled Trial. J Nutr Health Aging 2016;20:325–333.

55 Olsen MH, Fossum E, Hjerkinn E, Wachtell K, Høieggen A, Nesbitt SD, et al.: Relative influence of insulin resistance versus blood pressure on vascular changes in longstanding hypertension. ICARUS, a LIFE sub study. Insulin Carotids US Scandinavia. J Hypertens 2000;18:75–81.

56 Masiá M, Bernal E, Padilla S, García N, Escribano JC, Martínez E, et al.: A pilot randomized trial comparing an intensive versus a standard intervention in stable HIV-infected patients with moderate-high cardiovascular risk. J Antimicrob Chemother 2009;64:589–598.

57 Magliano D, McNeil J, Branley P, Shiel L, Demos L, Wolfe R, et al.: The Melbourne Atherosclerosis Vitamin E Trial (MAVET): a study of high dose vitamin E in smokers. Eur J Cardiovasc Prev Rehabil 2006;13:341–347.

58 van Vonderen MGA, Hassink EAM, van Agtmael MA, Stehouwer CDA, Danner SA, Reiss P, et al.: Increase in carotid artery intima-media thickness and arterial stiffness but improvement in several markers of endothelial function after initiation of antiretroviral therapy. J Infect Dis 2009;199:1186–1194.

59 Cunha AR, Medeiros F, Umbelino B, Oigman W, Touyz RM, Neves MF: Altered vascular structure and wave reflection in hypertensive women with low magnesium levels. J Am Soc Hypertens 2013;7:344–352.

60 Nakamura T, Kawagoe Y, Matsuda T, Ueda Y, Shimada N, Ebihara I, et al.: Oral adsorbent AST-120 decreases carotid intima-media thickness and arterial stiffness in patients with chronic renal failure. Kidney Blood Press Res 2004;27:121–126.

61 Bots ML, Evans GW, Riley W, McBride KH, Paskett ED, Helmond FA, et al.: The effect of tibolone and continuous combined conjugated equine oestrogens plus medroxyprogesterone acetate on progression of carotid intima-media thickness: the Osteoporosis Prevention and Arterial effects of tiboLone (OPAL) study. Eur Heart J 2006;27:746–755.

62 Skilton MR, Maple-Brown LJ, Kapellas K, Celermajer DS, Bartold M, Brown A, et al.: The effect of a periodontal intervention on cardiovascular risk markers in Indigenous Australians with periodontal disease: the PerioCardio study. BMC Public Health 2011;11:729.

63 Diercks GF, Janssen WM, van Boven AJ, Bak AA, Jong PE de, Crijns HJ, et al.: Rationale, design, and baseline characteristics of a trial of prevention of cardiovascular and renal disease with fosinopril and pravastatin in nonhypertensive, nonhypercholesterolemic subjects with microalbuminuria (the Prevention of REnal and Vascular ENdstage Disease Intervention Trial PREVEND IT). Am J Cardiol 2000;86:635–638.

64 Kastelein JJP, van Leuven SI, Burgess L, Evans GW, Kuivenhoven JA, Barter PJ, et al.: Effect of torcetrapib on carotid atherosclerosis in familial hypercholesterolemia. N Engl J Med 2007;356:1620–1630.

65 Bots ML, Visseren FL, Evans GW, Riley WA, Revkin JH, Tegeler CH, et al.: Torcetrapib and carotid intima-media thickness in mixed dyslipidaemia (RADIANCE 2 study): a randomised, double-blind trial. The Lancet 2007;370:153–160.

66 Jukema JW, Bruschke AVG, van Boven AJ, Reiber JHC, Bal ET, Zwinderman AH, et al.: Effects of Lipid Lowering by Pravastatin on Progression and Regression of Coronary Artery Disease in Symptomatic Men With Normal to Moderately Elevated Serum Cholesterol Levels. Circulation 1995;91:2528–2540.

67 Agewall S, Fagerberg B, Berglund G, Schmidt C, Wendelhag I, Wikstrand J: Multiple risk intervention trial in high risk hypertensive men: comparison of ultrasound intima-media thickness and clinical outcome during 6 years of follow-up. J Intern Med 2001;249:305–314.

68 Safarova MS, Trukhacheva EP, Ezhov MV, Afanas'eva OI, Afanas'eva MI, Tripoten' MI, et al.: Pleiotropic effects of nicotinic acid therapy in men with coronary heart disease and elevated lipoprotein(a) levels. Kardiologiia 2011;51:9–16.

69 Lonn EM, Yusuf S, Dzavik V, Doris CI, Yi Q, Smith S, et al.: Effects of Ramipril and Vitamin E on Atherosclerosis. Circulation 2001;103:919–925.

70 Lonn EM, Gerstein HC, Sheridan P, Smith S, Diaz R, Mohan V, et al.: Effect of ramipril and of rosiglitazone on carotid intima-media thickness in people with impaired glucose tolerance or impaired fasting glucose: STARR (STudy of Atherosclerosis with Ramipril and Rosiglitazone). J Am Coll Cardiol 2009;53:2028–2035.

71 Temelkova-Kurktschiev T, Fischer S, Koehler C, Mennicken G, Henkel E, Hanefeld M: Intima-Media-Dicke bei Gesunden ohne Risikofaktoren für Arteriosklerose. Dtsch Med Wochenschr 2001;126:193–197.

72 Nieuwkerk PT, Nierman MC, Vissers MN, Locadia M, Greggers-Peusch P, Knape LPM, et al.: Intervention to improve adherence to lipid-lowering medication and lipid-levels in patients with an increased cardiovascular risk. Am J Cardiol 2012;110:666–672.

73 Scorletti E, Bhatia L, McCormick KG, Clough GF, Nash K, Hodson L, et al.: Effects of purified eicosapentaenoic and docosahexaenoic acids in nonalcoholic fatty liver disease: results from the Welcome* study. Hepatology 2014;60:1211–1221.