Supplemental material

Supplemental Table 1: Medline search strategy.

1	chd risk assessment$.mp.
2	cvd risk assessment$.mp.
3	heart disease risk assessment$.mp.
4	coronary disease risk assessment$.mp.
5	cardiovascular disease risk assessment$.mp.
6	cardiovascular risk assessment$.mp.
7	cv risk assessment$.mp.
8	cardiovascular disease$ risk assessment$.mp.
9	coronary risk assessment$.mp.
10	coronary risk scor$.mp.
11	heart disease risk scor$.mp.
12	chd risk scor$.mp.
13	cardiovascular risk scor$.mp.
14	cardiovascular disease$ risk scor$.mp.
15	cvd risk scor$.mp.
16	cv risk scor$.mp.
17	or/1-16
18	cardiovascular diseases/
19	coronary disease/
20	cardiovascular disease$.mp.
21	heart disease$.mp.
22	coronary disease$.mp.
23	cardiovascular risk?.mp.
24	coronary risk?.mp.
25	exp hypertension/
26	exp hyperlipidemia/
27	or/18-26
28	risk function.mp.
29	Risk Assessment/mt
30	risk functions.mp.
31	risk equation$.mp.
32	risk chart?.mp.
33	(risk adj3 tool$).mp.
34	risk assessment function?.mp.
35	risk assessor.mp.
36	risk appraisal$.mp.
37	risk calculation$.mp.
38	risk calculator$.mp.
39	risk factor$ calculator$.mp.
40	risk factor$ calculation$.mp.
41	risk engine$.mp.
42	risk equation$.mp.
43	risk table$.mp.
44	risk threshold$.mp.
45	risk disc?.mp.
46	risk disk?.mp.
47	risk scoring method?.mp.

48 scoring scheme?.mp.
49 risk scoring system?.mp.
50 risk prediction?.mp.
51 predictive instrument?.mp.
52 project$ risk?.mp.
53 cdss.mp.
54 or/28-53
55 27 and 54
56 17 or 55
57 new zealand chart$.mp.
58 sheffield table$.mp.
59 procam.mp.
60 General Rule to Enable Atheroma Treatment.mp.
61 dundee guideline$.mp.
62 shaper scor$.mp.
63 (brhs adj3 score$).mp.
64 (brhs adj3 risk$).mp.
65 copenhagen risk.mp.
66 precard.mp.
67 (framingham adj1 (function or functions)).mp.
68 (framingham adj2 risk).mp.
69 framingham equation.mp.
70 framingham model$.mp.
71 (busselton adj2 risk$).mp.
72 (busselton adj2 score$).mp.
73 erica risk score$.mp.
74 framingham scor$.mp.
75 dundee scor$.mp.
76 brhs scor$.mp.
77 British Regional Heart study risk scor$.mp.
78 brhs risk scor$.mp.
79 dundee risk scor$.mp.
80 framingham guideline$.mp.
81 framingham risk?.mp.
82 new zealand table$.mp.
83 ncep guideline?.mp.
84 smac guideline?.mp.
85 copenhagen risk?.mp.
86 or/57-85
87 56 or 86
88 exp decision support techniques/
89 Diagnosis, Computer-Assisted/
90 Decision Support Systems,Clinical/
91 algorithms/
92 algorithm?.mp.
93 algorythm?.mp.
94 decision support?.mp.
95 predictive model?.mp.
96 treatment decision?.mp.
97 scoring method$.mp.
98 (prediction$ adj3 method$).mp.

99 or/88-98
100 Risk Factors/
101 exp Risk Assessment/
102 (risk? adj1 assess$).mp.
103 risk factor?.mp.
104 or/100-103
105 27 and 99 and 104
106 87 or 105
107 stroke.mp.
108 exp Stroke/
109 cerebrovascular.mp. or exp Cerebrovascular Circulation/
110 limit 106 to ed=20040101-20130601
111 107 or 108 or 109
112 111 and 54
113 111 and 99 and 104
114 112 or 113
115 106 or 114

Supplemental Table 2: List of articles in which the development of a model was presented, the number of models that were developed in these articles and references of papers in which these models were externally validated or incremental value was assessed.

First author, publication year	**Number of models developed**	**Number of articles in which model is validated**
Adult Treatment Panel III 2002[1]	2	19[2-20]
Alssema 2012[21]	2	-
Anderson 1991a[22]	12	28[23-50]
Anderson 1991b[51]	4	10[9 25 52-59]
Arima 2009[60]	1	-
Asayama 2008[61]	2	-
Asia Pacific Cohort Studies Collaboration 2006[62]	2	-
Asia Pacific Cohort Studies Collaboration 2007[63]	4	1[63]
Aslibekyan 2011[64]	2	1[64]
Assmann 2002[65]	1	6[5 7 66-69]
Assmann 2007[70]	3	1[71]
Assmann 2008[66]	1	-
Balkau 2004[72]	8	-
Bastuji 2002[23]	6	-
Beer 2011[73]	1	-
Bell 2012[74]	4	-
Berard 2011[75]	1	-
Boland 2004[76]	1	1[76]
Bolton 2013[77]	1	-
Boudik 2006[52]	1	-
Brand 1976[78]	1	-
Braun 2013[79]	6	1[79]
Brautbar 2009[80]	2	-
Brindle 2006[81]	32	-

First author, publication year	Number of models developed	Number of articles in which model is validated
Chamberlain 2011[3]	2	-
Chambless 2003[82]	4	3[83-85]
Chen 2009[27]	2	1[27]
Chien 2010[71]	2	-
Chien 2012[67]	3	1[67]
Ciampi 2001[86]	10	-
Conroy 2003[87]	12	21[24 27 43 44 55 85 88-102]
Cook 2006[4]	1	-
Cooper 2005[5]	1	-
Cross 2012[103]	1	1[103]
D'Agostino 1994[104]	2	1[105]
D'Agostino 2000[106]	2	-
D'Agostino 2008[107]	4	15[6 20 28 43 50 53 73 108-115]
Davies 2010[116]	1	-
De Ruijter 2009[31]	5	-
Donfrancesco 2010[117]	2	-
Dunder 2004[7]	1	-
Duprez 2011[8]	1	-
Empana 2011[118]	1	-
Faeh 2013[119]	2	-
Ferrario 2005[69]	1	-
Folsom 2003[120]	1	1[3]
Friedland 2009[121]	7	1[121]
Gaziano 2008[122]	4	1[43]
Glynn 2002[123]	2	-
Hesse 2005[124]	1	1[124]
Hippisley-Cox 2007[34]	2	4[28 29 33 35]
Hippisley-Cox 2008b[35]	2	1[30]
Hippisley-Cox 2010[125]	2	1[30]
Hoes 1993[126]	2	-
Houterman 2002[127]	2	-
Ishikawa 2009[128]	3	-
Janssen 2005[129]	1	-
Kannel 1976[130]	2	-
Keys 1972[131]	4	1[131]
Knuiman 1997[132]	4	-
Knuiman 1998[133]	2	-
Koller 2012[10]	4	-
L'Italien 2000[134]	1	1[134]
Larson 1995[135]	3	-
Leaverton 1987[136]	4	2[132 136]
Lee 2006[137]	2	-

First author, publication year	Number of models developed	Number of articles in which model is validated
Lee 2008[138]	4	-
Levy 1990[139]	4	1[132]
Liu 2004[140]	2	-
Lloyd-Jones 2006[141]	2	1[47]
Lumley 2002[142]	2	1[143]
Macfarlane 2007[144]	1	-
Mainous 2007[93]	3	-
Mannan 2010[145]	2	-
Mannan 2011[146]	1	-
Mannan 2013[147]	2	-
Matsumoto 2009[148]	2	-
May 2006[37]	2	-
May 2007[149]	1	-
McGorrian 2011[150]	4	1[150]
McNeil 2001[151]	1	-
Menotti 1990[152]	1	-
Menotti 1994[153]	1	1[153]
Menotti 2000[154]	3	-
Menotti 2002[155]	3	-
Menotti 2005[156]	2	-
Merry 2012[94]	1	-
Moons 2002[157]	3	-
Nelson 2012[40]	1	1[40]
Nippon Data Research Group 2006[158]	6	-
Noda 2010[159]	3	-
Nordestgaard 2010[160]	1	-
Odell 1994[161]	9	-
Onat 2012[162]	2	-
Panagiotakos 2007[96]	2	-
Pencina 2009[163]	1	-
Petersson 2009[164]	2	-
Plichart 2011[165]	2	-
Pocock 2001[166]	1	1[41]
Polonsky 2010[167]	2	-
Prati 2011[168]	1	-
Qiao 2012[169]	8	-
Ridker 2007[15]	2	1[20]
Ridker 2008[16]	4	1[20]
Schnabel 2009[170]	1	1[3]
Shaper 1986[171]	2	-
Simons 2003[18]	2	1[41]
Smith 2010[172]	2	-

First author, publication year	Number of models developed	Number of articles in which model is validated
Tanabe 2010[173]	2	-
Teramoto 2008[174]	1	-
Thomsen 2001[175]	1	-
Thorsen 1979[176]	1	-
Truett 1967[177]	2	1[78]
Tsang 2003[178]	1	1[178]
Tunstall-Pedoe 1991[179]	2	1[179]
Vergnaud 2008[180]	1	-
Voss 2002[181]	2	1[182]
Wilson 1987[183]	2	1[67]
Wilson 1998[184]	2	41[2 3 15 54 68 69 88-90 93-95 98 101 103 107 138 140 180 182 185-205]
Wolf 1991[206]	2	5[71 142 143 207 208]
Woodward 2007[48]	2	2[34 53]
Wu 2006[209]	2	1[209]
Wu 2011[210]	2	-
Yip 2004[211]	1	-
Zhang 2005[49]	3	-
Framingham unspecified*	-	3[84 85 212]

*If authors explicitly stated they determined incremental value on top of the variables from a Framingham model without referencing this specific model, they were categorized under Framingham unspecified.

Supplemental Table 3: Main categories of outcomes that were used in the developed models.

Outcome	**N (%)**
Fatal or nonfatal CHD	118 (33%)
Fatal or nonfatal CVD	95 (26%)
Fatal CVD	40 (11%)
Fatal or nonfatal stroke	29 (8%)
Fatal or nonfatal MI	23 (6%)
Fatal CHD	21 (6%)
All-cause mortality	9 (2%)
Atrial fibrillation	4 (1%)
Fatal nonCHD	4 (1%)
Fatal or nonfatal stroke, TIA	4 (1%)
Ischemic stroke	3 (1%)
Fatal stroke	2 (1%)
Hemorrhagic stroke	2 (1%)
Nonfatal MI	2 (1%)
Claudication	1 (<0.5%)
Coronary artery bypass grafting	1 (<0.5%)
Heart failure	1 (<0.5%)
Ischemic stroke, TIA	1 (<0.5%)
Nonfatal CHD	1 (<0.5%)
Percutaneous transluminal coronary angioplasty	1 (<0.5%)
TIA	1 (<0.5%)
Total	363

CHD=coronary heart disease; CVD=cardiovascular disease; MI=myocardial infarction; TIA=transient ischemic attack.

Supplemental Table 4: Outcome definitions as extracted by reviewers, and category in which these were placed of developed models.

Outcome category	**Definition**
Fatal or nonfatal CHD (n=118)	Any fatal/non-fatal coronary event: death from CHD or definite myocardial infarction, and any CHD, classical angina pectoris, clinical judgment of definite heart disease and etiology specified as myocardial infarction by history, and (3) follow-up clinical diagnosis of possible heart disease with etiology specified by history as myocardial infarction and any of Minnesota ECG codes17 1.2, 1.3, 5.1, 5.2, 6.1, 6.2, 7.1, 7.2, 7.4, or 8.3 at the 5-year examination, or Minnesota ECG codes 1.2 or 1.3 + 5.1 or 1.3 + 5.2 at the 5-year examination but not at entry.
	CHD death or hospitalization: ICD-9 410-414
	CHD event: a validate definite or probable hospitalized myocardial infarction, a definite CHD death, an unrecognised myocardial infarction defined by ARIC ECG readings, or coronary revascularization.
	CHD hard criteria: CHD death (ICD-9 410-414 or code 428.0-1), definite MI
	CHD-any criterion: CHD death (ICD-9 410-414 or code 428.0-1), fatal or non-fatal MI, angina pectoris, chronic heart disease of possible coronary origin, coronary bypass surgery, coronary angioplasty
	CHD: all definite myocardial infarction, coronary insufficiency, angina pectoris and death from coronary heart disease.
	CHD: death from CHD (sudden or non-sudden), myocardial infarction, angina pectoris and coronary insufficiency
	CHD: definite or probable myocardial infarction, silent myocardial infarction between examinations (indicated by ECG), definite CHD death, coronary revascularization
	CHD: fatal and non-fatal myocardial infarction, angina pectoris, cardiac/sudden death, and angioplasty

Outcome category	Definition
	CHD: fatal and non-fatal myocardial infarction, cardiovascular death, angina pectoris
	CHD: ICD-9: 410-414
	CHD: presence of angina pectoris, a history of myocardial infarction with or without accompanying Minnesota codes of the ECG, a history of myocardial revascularisation, death from heart failure of coronary origin and fatal coronary event
	CHD: sudden coronary death, fatal acute myocardial infarction, nonfatal acute myocardial infarction, new major Q wave on the ECG after 5 years of follow-up (Minnesota codes 11, 12.1 to 12.7, and 12.8 plus 51 or 52) surgery for angina pectoris with CHD angiographically demonstrated
	CHD: validated definite or probable hospitalized MI, a definite CHD death, an unrecognized MI defined by ARIC ECG readings, or coronary revascularization. The criteria for definite or probable hospitalized MI were based on combinations of chest pain symptoms, ECG changes, and cardiac enzyme levels [33,34]. The criteria for definite fatal CHD were based on chest pain symptoms, underlying cause of death from the death certificate, and any other associated hospital information or medical history, including that from the ARIC clinic visit
	Coronary artery disease
	Coronary artery disease or coronary artery disease death (angina pectoris, myocardial infarction, coronary insufficiency)
	Coronary death, MI, angina, coronary insufficiency
	Coronary deaths, underlying causes of death ICD-IX codes 410-414, 798, 799, 250, 428, 440 in association with 410-414 codes in other causes were considered as suspected coronary deaths Non fatal coronary events: ICD IX 410–411 codes for suspected acute infarction and ICD IX CM 36.0-9 codes for coronary surgery revascularization.
	Coronary heart disease
	Coronary heart disease (MI, CHD death, angina pectoris, coronary insufficiency)
	Coronary heart disease events: myocardial infarction or death from coronary heart disease (ICD-9 codes 410-414).
	Coronary heart disease: angina pectoris, coronary insufficiency (unstable angina), myocardial infarction, and sudden death
	Coronary heart disease: angina pectoris, coronary insufficiency, myocardial infarction (recognized or not), sudden death
	Coronary heart disease: angina pectoris, recognized and unrecognized myocardial infarction, coronary insufficiency, and coronary heart disease death
	Coronary heart disease: coronary revascularization or fatal or nonfatal myocardial infarction
	Coronary heart disease: hospitalization for angina pectoris, myocardial infarction, or a CHD death (I210–I219, I251–I259, I461 and R960 ICD-10 codes), or a revascularization procedure (percutaneous intervention or coronary artery bypass- grafting).
	Coronary heart disease: MI or acute coronary death
	Coronary heart disease: MI, aorto-coronary bypass, angina, other forms of specifically defined ischemic cardiopathies or cardiac complications before or after surgery
	Coronary heart disease: myocardial infarction, death due to CHD, resuscitated cardiac arrest, definite or probable angina followed by coronary revascularization, and definite angina not followed by coronary revascularization
	Coronary mortality, non-fatal myocardial infarction
	Definite fatal coronary heart disease or definite nonfatal myocardial infarction
	Fatal and nonfatal CHD: angina pectoris and myocardial infarction (ICD-9 Codes: 410–414.9)
	Fatal or non-fatal myocardial infarction, angioplasty, coronary artery bypass surgery
	Fatal or nonfatal CHD: nonfatal definite MI, definite CHD, ECG-evident definite MI, fatal definite MI, definite CHD, possible CHD (87% fatal), and sudden death due to CHD
	First coronary heart disease event
	First major coronary event (definition reported in unavailable article)
	Hard CHD: acute myocardial infarction, sudden death, and other coronary deaths
	hard CHD: death from CHD or definite myocardial infarction, and any CHD (classical angina pectoris, (2) clinical judgment of definite heart disease and etiology specified as myocardial infarction by history, and (3) follow-up clinical diagnosis of possible heart disease with etiology specified by history as myocardial

Outcome category	Definition
	infarction and any of Minnesota ECG codes17 1.2, 1.3, 5.1, 5.2, 6.1, 6.2, 7.1, 7.2, 7.4, or 8.3 at the 5-year examination, or Minnesota ECG codes 1.2 or 1.3 + 5.1 or 1.3 + 5.2 at the 5-year examination but not at entry).
	Hard CHD: myocardial infarction + CHD death
	Incident cases of coronary heart disease: death with an underlying or contributing cause of CHD (International classification of diseases, 10 revision codes I20–I25, I51.6) or a myocardial infarction, diagnosis of angina or coronary artery bypass or angioplasty identified in the follow-up medical record review.
	Incident coronary heart disease: a clinical diagnosis of an acute myocardial infarction, unstable angina pectoris, a percutaneous transluminal coronary angioplasty, or coronary artery bypass grafting according to the Cardiology information system or coronary heart disease as primary or secondary cause of death according to Statistics Netherlands (ICD9 410–414 or ICD10 I20–I25).
	Incident coronary heart disease: fatal and nonfatal myocardial infarction, percutaneous coronary intervention, coronary artery bypass graft
	Incident coronary heart disease: myocardial infarction, fatal coronary heart disease, cardiac procedure
	Ischemic cardiovascular disease: acute myocardial infarction, coronary death, ischemic cardiac arrest, ischemic stroke (brain infarction due to occlusion of precerebral arteries or embolic brain infarction, ICD-9 433-434)
	Major coronary event: sudden cardiac death or definite fatal or nonfatal myocardial infarction on the basis of ECG and/or cardiac enzyme changes
	Major coronary event: sudden cardiac death, definite fatal or non-fatal myocardial infarction on the basis of ECG and/or cardiac enzyme changes. The detailed criteria for defining a sudden coronary death and a definite fatal or non-fatal myocardial infarction have been previously published.
	Major coronary events: nonfatal MI and coronary deaths
	Major coronary events: sudden coronary death, non-sudden coronary death, definite non-fatal myocardial infarction, fatal myocardial infarction, definite fatal chronic ischemic heart disease, surgery of coronary arteries
	Myocardial infarction, undergone coronary artery bypass grafting, had percutaneous coronary intervention, or had a coronary angiography or computed tomography angiography demonstrating a stenosis of at least 50% in at least 1 epicardial vessel
	Non-fatal myocardial infarction (ECG and/or cardiac enzyme changes), fatal MI (MI 28 d before death and no known nonatherosclerotic cause of death), atherosclerotic CHD death (Chest pain 72 h before death and no known nonatherosclerotic cause of death; History of chronic ischemic heart disease in the absence of valvular heart disease or nonischemic cardiomyopathy and no known nonatherosclerotic cause of death; Death certificate consistent with atherosclerotic CHD death and no known nonatherosclerotic cause of death; Coronary death related to CHD procedures, such as PCI or CABG)
Fatal or nonfatal CVD (n=95)	Atherosclerotic CVD: ICD-8 D410-D414, D427, D430-438, D440-444
	Cardiovascular disease
	Cardiovascular disease event: coronary heart disease (CHD) and stroke
	Cardiovascular disease event: coronary heart disease (CHD) and stroke - Definition: referred to 5 references with different definitions
	Cardiovascular disease: coronary heart disease (angina and myocardial infarction), stroke, or transient ischaemic attacks in the term cardiovascular disease but not peripheral vascular disease. ICD-10 codes I20-I25, I63-I64.
	Cardiovascular disease: coronary heart disease, congestive heart failure, cerebrovascular disease, intermittent claudication
	Cardiovascular disease: includes coronary heart disease (angina and myocardial infarction), stroke, or transient ischaemic attacks, but not peripheral vascular disease.
	Cardiovascular disease: myocardial infarction, coronary heart disease, stroke, and transient ischaemic attack.
	Cardiovascular disease: myocardial infarction, coronary insufficiency, death resulting from coronary heart disease, angina pectoris, atherothrombotic stroke, intermittent claudication, or other cardiovascular death
	Cardiovascular disease: stroke or coronary heart disease including acute myocardial infarction, silent myocardial infarction, sudden cardiac death within 1 h after onset of acute illness, coronary artery disease followed by coronary artery bypass surgery or angioplasty. Cardiovascular disease was defined as first-ever development of coronary heart disease or stroke. The criteria for a diagnosis of coronary heart disease included first-ever acute myocardial infarction, silent myocardial infarction, sudden cardiac death within 1 h after the onset of acute illness, or coronary artery disease followed by coronary artery bypass surgery or

Outcome category	Definition
	angioplasty. Acute myocardial infarction was diagnosed when a subject met at least two of the following criteria: (1) typical symptoms, including prolonged severe anterior chest pain; (2) abnormal cardiac enzymes more than twice the upper limit of the normal range; (3) evolving diagnostic electrocardiographic changes; and (4) morphological changes, including local asynergy of cardiac wall motion on echocardiography, persistent perfusion defect on cardiac scintigraphy, or myocardial necrosis or scars 41 cm long accompanied by coronary atherosclerosis at autopsy. Silent myocardial infarction was defined as myocardial scarring without any historical indication of clinical symptoms or abnormal cardiac enzyme changes, and was detected by electrocardiography, echocardiography, cardiac scintigraphy or autopsy. Stroke was defined as a sudden onset of nonconvulsive and focal neurological deficit persisting for 424 h. The diagnosis of stroke and the determination of its pathological type were based on the clinical history, neurological examination and all available clinical data, including brain CT/MRI and autopsy findings.
	Cardiovascular events (myocardial infarction, ischemic stroke, coronary revascularization, cardiovascular death).
	CHD, ischemic stroke and MI (ICD codes of 433–434 (I63), 410–414 (I20–I25) and 410–411 (I21–I22, I24))
	CHF, AF, MI, coronary revascularisation, stroke, transient ischemic attack and CVD death.
	CVD including coronary heart disease, stroke, or peripheral vascular disease
	CVD-any criterion: CHD death (ICD-9 410-414 or code 428.0-1), fatal or non-fatal MI, angina pectoris, chronic heart disease of possible coronary origin, coronary bypass surgery, coronary angioplasty, cerebrovascular death (ICD-9 430-438), stroke, TIA, peripheral artery disease, intermitted claudication, aortic aneurysm, arterial surgical procedures
	CVD: cardiovascular death, non-fatal myocardial infarction or non-fatal cerebrovascular event
	CVD: CHD (coronary death, myocardial infarction, coronary insufficiency, and angina), cerebrovascular events (including ischaemic stroke, haemorrhagic stroke, and transient ischaemic attack), peripheral artery disease (intermittent claudication), and heart failure
	CVD: CHD (coronary death, myocardial infarction, coronary insufficiency, and angina), cerebrovascular events (ischemic stroke, haemorrhagic stroke, transient ischemic attack), peripheral artery disease (intermittent claudication), heart failure.
	CVD: coronary heart disease (angina pectoris, coronary insufficiency, myocardial infarction, sudden or non-sudden death attributed to coronary disease), cerebrovascular accident (stroke, transient ischaemia, cerebral embolism, intracerebral or subarachnoid haemorrhage), intermittent claudication, and congestive heart failure
	CVD: death from CHD (sudden or non-sudden), myocardial infarction, angina pectoris, coronary insufficiency, stroke and transient ischemia
	CVD: death, myocardial infarction, stroke, congestive heart failure, and coronary revascularisation including coronary artery bypass grafting and percutaneous transluminal coronary angioplasty
	CVD: fatal and non-fatal myocardial infarction, cardiovascular death, angina pectoris, fatal and non-fatal stroke, transient ischaemic attack and subarachnoid haemorrhage, fatal and non-fatal heart failure and cerebrovascular death of other origin
	CVD: MI, CHD death, angina pectoris, coronary insufficiency, stroke, congestive heart failure. peripheral vascular disease
	CVD: myocardial infarction, angina, stroke, coronary artery bypass surgery, percutaneous coronary intervention, heart failure, peripheral vascular disease
	CVD: myocardial infarction, angina, stroke, left ventricular or congestive cardiac failure, peripheral vascular event, sudden/rapid cardiac death, heart failure death or other coronary or cardiovascular death
	CVD: myocardial infarction, coronary death or stroke. This outcome (effectively “hard” CHD) excluded other, non-fatal forms of CHD, but included transient ischaemic attack.
	CVD: myocardial infarction, ischemic stroke, coronary revascularization procedures, deaths from cardiovascular causes
	Deaths from cardiovascular causes (ICD-9 codes 390–459, ICD-10 codes I00-I99) or any hospital discharge diagnosis post recruitment (potentially several per admission) for coronary heart disease (ICD-9 410–414, ICD-10 I20-I25) or cerebrovascular disease (ICD-9 430–438, ICD-10 G45, I60-I69),10 11 or for coronary artery interventions (CABG or PTCA).
	Fatal and non-fatal stroke, fatal and non-fatal myocardial infarction. The International Classification of Disease codes for stroke and TIA were 362.3, 430, 431, 433.x1, 434.x1, 435, 436, G45, H34.1, I60, I61, and I6-7 and for MI were 410, 411, and I21x.
	Fatal or nonfatal CVD (myocardial infarction, percutaneous transluminal coronary angioplasty, coronary artery bypass graft, angina pectoris, stroke, claudication intermittent, peripheral intervention, or heart failure), sudden death, type 2 diabetes, and/or CKD. Cardiovascular death was defined as death due to diseases of the cardiovascular system (ICD-10: I00–I99) and sudden death (ICD-10: R96). CKD was defined

Outcome category	Definition
	by estimated glomerular filtration rate,60 mL/min/1.73 m2
	Fatal/nonfatal cardiovascular events: ICD-8 and ICD-9: 410–414, 431, 433, 434, 435, 436, 437, 440, 441, ICD-10: I20–I25, I61, I63-I66, I70–I72
	First major cardiovascular event: hard coronary event (definition reported in unavailable article), hard cerebrovascular event (definition reported in unavailable article), major peripheral artery disease (manifested as fatal peripheral artery disease, or as fatal or non-fatal gangrene of the extremities, or as fatal or non-fatal aneurysm of the aorta in any anatomical site, or as surgical procedures for aortic aneurysm or for lower limb artery disease, or as any other fatal cardiovascular event attributed to arteriosclerosis)
	First occurrence of cardiovascular disease: myocardial infarction, stroke, death from cardiovascular causes, percutaneous transluminal coronary angioplasty, or coronary artery bypass graft surgery.
	Hard cardiovascular disease: recognized MI, sudden death, or atherothrombotic brain infarction
	Hard CV events: coronary death, myocardial infarction, stroke
	Incident cardiovascular disease (CHD or stroke): death with an underlying or contribution cause coded as I20–I25, I51.6,I60–I69 or G45 or a new CHD or stroke event in any woman's medical record review.
	Major cardiovascular events: major coronary events (sudden coronary death, non-sudden coronary death, definite non-fatal myocardial infarction, fatal myocardial infarction, definite fatal chronic ischemic heart disease, surgery of coronary arteries) and cerebrovascular events (definite fatal and non-fatal haemorrhagic and thrombotic stroke, surgery of carotid arteries), plus major peripheral artery events comprising fatal and non-fatal aortic aneurysms, fatal lower limbs artery disease, surgery of aorta or lower limb arteries.
	Myocardial infarction (recognized or unrecognized), coronary heart disease, and cardiovascular disease. Specification in reference.
	Myocardial infarction, stroke, coronary revascularization procedures, or cardiovascular death
	Recognized myocardial infarction (MI) or atherothrombotic brain infarction (ABI)
Fatal CVD (n=40)	Cardiovascular death: ICD-10 codes I00-I99
	Cardiovascular death: ICD-9 codes 401–414 and 426–443, with the exception of the 430.0. 798.1 and 798.2. Instantaneous death (ICD-9, 798.1) and death within 24 h of symptoms onset (ICD-9, 798.2)
	Cardiovascular disease mortality: myocardial infarction (definite), angina pectoris (definite), intermittent claudication (definite), stroke (definite), TIA (definite) or heart failure
	Cardiovascular mortality (ICD-10: I10 to I79)
	Cardiovascular mortality: ICD-9 codes 401 through 414 and 426 through 443, with the exception of the following ICD-9 codes for definitely non-atherosclerotic causes of death: 426.7, 429.0, 430.0, 432.1, 437.3, 437.4, and 437.5. We also classified 798.1 (instantaneous death) and 798.2 (death within 24h of symptom onset) as cardiovascular deaths.
	Cause-specific death from all CVD
	CVD death: death from MI, CHD death, angina pectoris, coronary insufficiency, stroke, congestive heart failure, peripheral vascular disease
	Fatal cardiovascular events: deaths with an underlying cause given as ICD-10 codes I10 through I15, I20 through I25, R96.0, R96.1 and I44 through I73, with the exception of I45.6, I51.4, I52, I60, I62, I67.1, I67.5 and I67.7
	Fatal CVD
	Fatal CVD event: ICD-8:390–458, until 1994; ICD-10: I00-I99, since 1995
	Fatal CVD: all deaths due to ischaemic heart disease (ICD-9 410–414) and cerebrovascular accidents (ICD-9 430–438)
	Fatal CVD: ICD-8: 390–458, ICD-10: I00-I99
	Sudden death
Fatal or nonfatal stroke (n=29)	fatal/non-fatal stroke of all types
	fatal/non-fatal stroke: Atherothrombotic brain infarction, Transient ischemic attack, Cerebral embolus, Intracerebral haemorrhage, Subarachnoid haemorrhage
	First major cerebrovascular event (definition reported in unavailable article)
	Major cerebrovascular events: definite fatal and non-fatal haemorrhagic and thrombotic stroke, surgery of carotid arteries
	nonfatal ischemic stroke, transient ischemic attack (TIA) or all-causes vascular death

Outcome category	Definition
	Stroke
	Stroke: a clinical event of rapid onset consisting of neurological deficit lasting more than 24 hours unless death supervenes, or if it lasts less than 24 hours, an appropriate lesion to explain the deficit is seen in a brain image. The event could not be directly caused by trauma to the brain, tumour, or infection. Based on the information present, the neurologist classified the event into first and recurrent stroke, and into subarachnoid haemorrhage, intracranial haemorrhage, intracerebral infarction, or unspecified stroke. Cerebral infarction was classified according to internationally accepted criteria.22 23 In addition, the certainty of the diagnosis was assessed in definite, probable, possible and no stroke. The present analysis is restricted to definite and probable strokes
	Stroke: a focal, nonconvulsive neurological deficit of sudden onset that persisted for at least 24 hours. Stroke subtypes, ie, cerebral haemorrhage (CH), cerebral infarction (CI), and subarachnoid hemorrhage (SAH), were determined by using the criteria of the National Institute of Neurological Disorder and Stroke.23 Symptomatic lacuna infarction was defined as a CI.
	Stroke: a sudden neurological symptom of vascular origin that lasted 24 hours with supporting evidence from the image study; fatal stroke cases were included. Transient ischemic attacks were not included in this study.
	Stroke: ICD-9-CM, 430-437, or ICD-10 I60-I69
	Stroke: including transient ischemia
	Stroke: subarachnoid haemorrhage or a neurological deficit of rapid onset lasting more than 24 hours unless death supervenes or, if less than 24 hours, an appropriate lesion to explain the deficit was seen on brain imaging
Fatal or nonfatal MI (n=23)	Acute MI
	Acute MI: based on chest pain, cardiac enzyme levels, and electrocardiograms. These criteria were based on criteria from the MONICA study 28 or from the World Health Organization
	Fatal or non-fatal major ischaemic heart disease: A fatal case was considered to have occurred if ischaemic heart disease (ICD codes 410-414) was recorded as the underlying cause of death. In non-fatal cases a myocardial infarction was diagnosed according to World Health Organisation criteria
	Fatal or nonfatal MI
	Fatal or nonfatal MI: Fatal myocardial infarction was defined as cause of death with ICD-8 code 410 in the Danish National Register of Causes of Death. The nonfatal myocardial infarctions were defined as first-ever hospital admission with ICD-8 code 410 in the National Patient Register
	Fatal or nonfatal MI: Myocardial infarction was classified as bdefiniteQ or bsuspect,Q but within these categories, further subdivisions of recognized, unrecognized, and silent were made. Truly silent MI was diagnosed based on definite ECG changes (new Minnesota Code 1) without any supporting clinical history; unrecognized MI was diagnosed based on electrocardiographic changes accompanied by symptoms, which, in retrospect, were consistent with acute MI but which had not been recognized as such at the time by either the patient or his general practitioner. The diagnosis of recognized MI was based on clinical data with or without accompanying electrocardiographic abnormalities.
	Heart attack: recognized MI or sudden death
	MI
	MI (ICD 410/I21)
	MI: WHO; International Classification of Diseases, 8th edition: codes 410; 10th edition: codes I21- I22
	Myocardial infarction case: criteria from MONICA project
	Myocardial infarction: including silent and unrecognized MI
	Nonfatal or fatal definite myocardial infarction or possible myocardial infarction according to the criteria of the World Health Organization Multinational Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA) Project
	Recognized myocardial infarction (MI)
Fatal CHD (n=21)	Cause-specific death from CHD
	CHD death: ICD-9 410-414
	Coronary death: ICD-9 410-414
	Coronary heart disease death (ICD-8 410, 411, 412.1 or 412.3)
	Coronary heart disease death (ICD-9 410, 411, 412 or 414)

Outcome category	Definition
	Coronary heart disease death: death from MI, CHD death, angina pectoris, coronary insufficiency
	Coronary heart disease mortality: death from myocardial infarction (definite) or angina pectoris (definite)
	Fatal coronary heart disease
	Fatal coronary heart disease (ICD 410-414)
	Nonsudden/sudden coronary death
All-cause mortality (n=9)	All-cause mortality
Nonfatal CHD (n=5)	Fatal nonCHD: ICD-9 codes 401 through 409 and 426 through 443, with the exception of the following ICD-9 codes for definitely non-atherosclerotic causes of death: 426.7, 429.0, 430.0, 432.1, 437.3, 437.4, and 437.5. We also classified 798.1 (instantaneous death) and 798.2 (death within 24h of symptom onset).
	Non-fatal, acute myocardial infarction (ICD-9: 410.xx and 412.xx) or hospitalization for unstable angina (ICD-9: 411.1)
Fatal or nonfatal stroke, TIA (n=4)	Fatal and non-fatal stroke, transient ischaemic attack and subarachnoid haemorrhage
	Stroke, transient ischaemic attack. The diagnostic criteria of stroke, TIA, and their subtypes were based on the system for the Classification of Cerebrovascular Disease III by the National Institute of Neurological Disorders and Stroke
Atrial fibrillation (n=4)	Atrial fibrillation: ICD-9 427.31 or 427.32
	Atrial fibrillation: 427.92 (ICD-8), 427D (ICD-9), and I48 (ICD-10)
	First event of atrial fibrillation: atrial flutter or atrial fibrillation was present on an electrocardiograph
Ischemic stroke (n=3)	Atherothrombotic brain infarction
	Ischemic stroke
	Cerebral Infarction: criteria of the National Institute of Neurological Disorder and Stroke
Fatal stroke (n=2)	Cause-specific death from stroke
Haemorrhagic stroke (n=2)	Haemorrhagic stroke
	Cerebral haemorrhage: criteria of the National Institute of Neurological Disorder and Stroke
Nonfatal MI (n=2)	Non-fatal acute myocardial infarction
Heart failure (n=1)	Heart failure: 427.00 (ICD-8), 427.10 (ICD-9), and 428.99 (ICD-10)
Ischemic stroke, TIA (n=1)	Stroke: TIA, ischaemic stroke. A transient ischaemic attack (TIA) was defined as focal neurological symptoms of ischaemic cause that lasted less than 24 h. A definite stroke was defined as a focal neurological deficit that lasted longer than 24 h and was attributable to a vascular event. Strokes were independently classified by two neurologists into ischaemic and haemorrhagic subtypes on the basis of mode of onset, clinical findings and magnetic resonance imaging and/or computerized tomography
TIA (n=1)	TIA
Claudication (n=1)	Claudication
CABG (n=1)	Coronary artery bypass grafting
PTCA (n=1)	Percutaneous transluminal coronary angioplasty

CHD=coronary heart disease; CVD=cardiovascular disease; MI=myocardial infarction; TIA=transient ischemic attack; AF=atrial fibrillation; ECG=electrocardiography; ICD=International Classification of Disease; PCI= percutaneous coronary intervention; CABG=Coronary artery bypass grafting; PTCA=Percutaneous transluminal coronary angioplasty.

Supplemental Table 5: Modelling method used to develop the prediction models.

Method	**N (%)**
Cox proportional hazards regression	160 (44%)
Accelerated failure time analysis	77 (21%)
Logistic regression	71 (20%)
Other parametric survival model	7 (2%)
Competing risk model	4 (1%)
Conditional logistic regression	2 (1%)
Poisson regression	2 (1%)
Expert weighing	1 (<0.5%)
Neural network	1 (<0.5%)
Other e.g. counted number of risk factors	2 (1%)
Not reported	36 (10%)
Total	363

Supplemental Table 6: Prediction horizons used for developed models.

Prediction horizon	**N (%)**
<5 years	3 (1%)
5 years	47 (13%)
5-10 years	25 (7%)
10 years	209 (58%)
10-20 years	14 (4%)
20-30 years	14 (4%)
>30 years	2 (1%)
Not reported	49 (13%)
Total	363

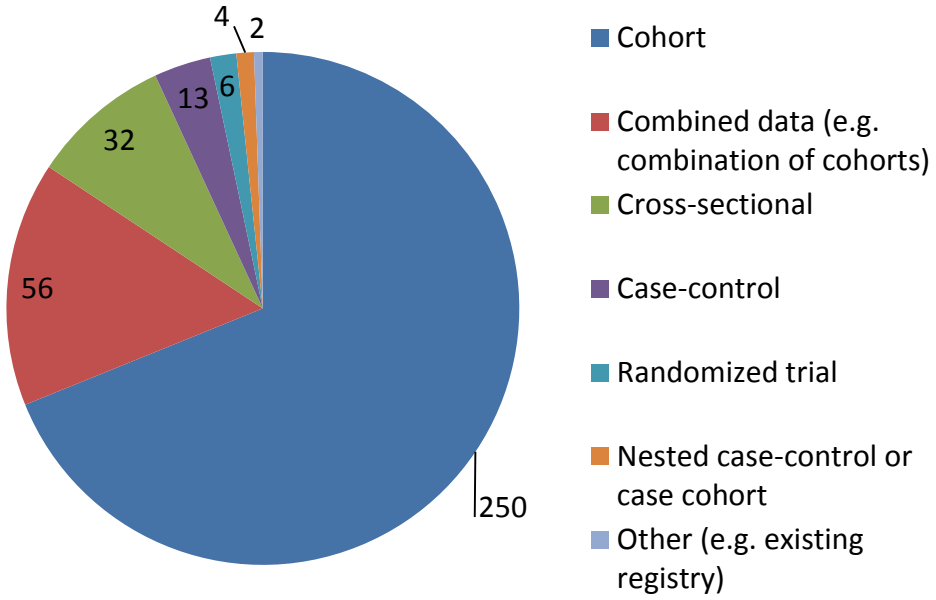
Supplemental Table 7: Characteristics of developed models that were and were not externally validated.

		Validated (n=132) N (%)	Not validated (n=231) N (%)
Study design	Longitudinal data (e.g. cohort)	123 (93%)	187 (81%)
	Cross-sectional data (e.g. case-control)	9 (7%)	44 (19%)
Gender	Men	52 (39%)	90 (39%)
	Women	41 (31%)	67 (29%)
	Men and women	39 (30%)	74 (32%)
Prediction horizon	<10 years	26 (20%)	49 (21%)
	10 years	88 (67%)	121 (52%)
	>10 years	4 (3%)	26 (11%)
	Not reported	14 (11%)	35 (15%)
Modelling method	Survival model	88 (67%)	149 (65%)
	Logistic regression	32 (24%)	39 (17%)
	Other	8 (6%)	11 (5%)
	Not reported	4 (3%)	22 (10%)
Internal validation	Yes	45 (34%)	35 (15%)
	No	87 (66%)	196 (85%)
Presentation	Model can be used for individual risk predictions	110 (83%)	161 (70%)
	Model cannot be used for individual risk predictions	22 (17%)	70 (30%)
Performance reported	Discrimination	46 (35%)	117 (51%)
	Calibration	34 (26%)	82 (35%)
	Overall performance	27 (20%)	8 (3%)
	Any performance measure	61 (46%)	130 (56%)

	N reported	Median	N reported	Median
Publication year	132	2003	231	2006
Impact factor	125	6.2	220	4.2
Number of participants	113	4,890	226	3,513
Number of events	80	364	209	181
Lower age limit	124	35	213	35
Upper age limit	124	74	213	74
Number of predictors	130	7	227	6

Supplemental figures

A



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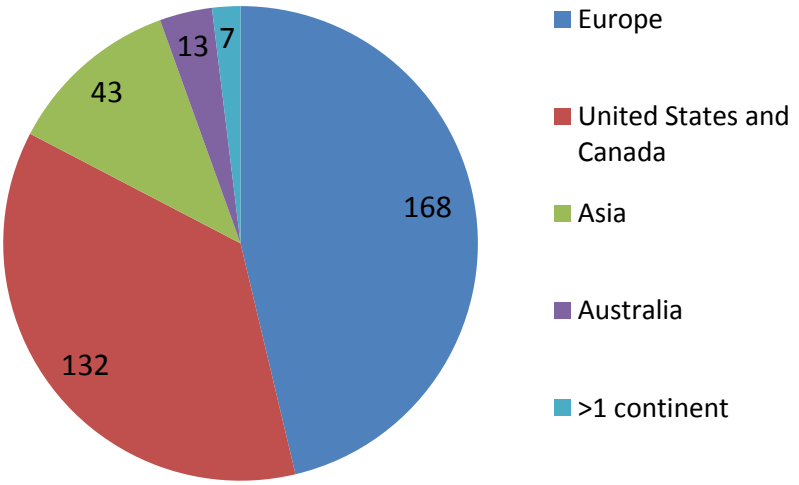

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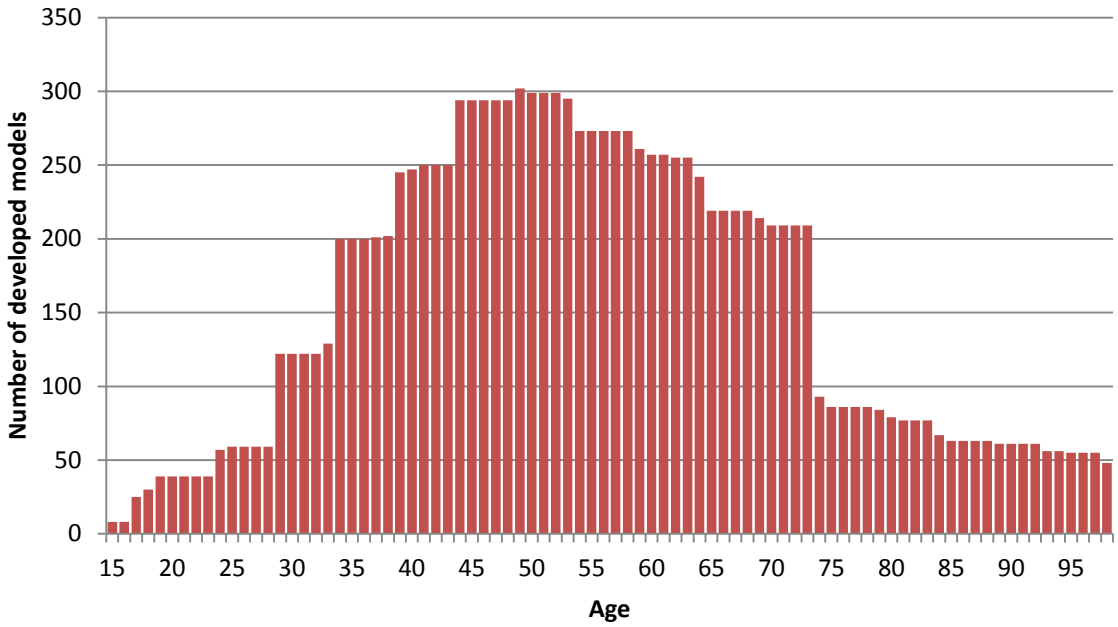
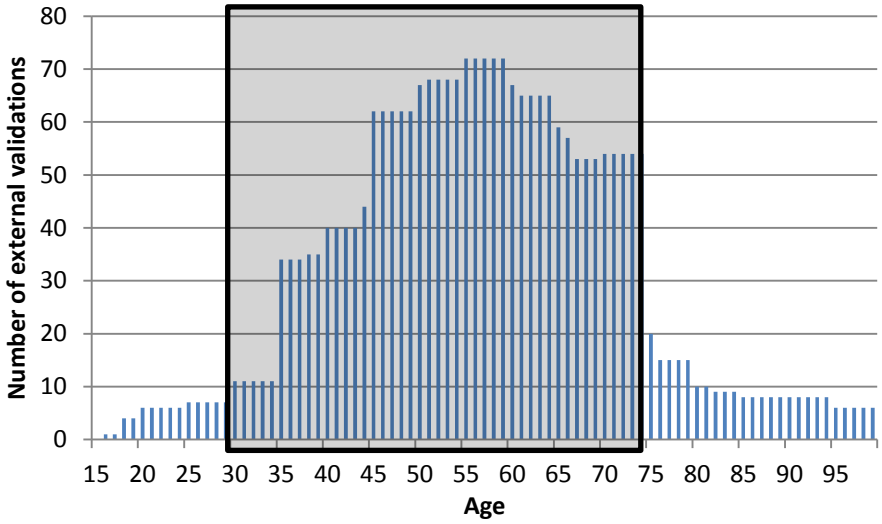


Supplemental Figure 1: Study design, location and age of included participants of all developed models. A: study design, B: location, C: age; bars indicate the number of models developed for that specific age. Models developed for e.g. age >16 were assumed to include people up to 99 years of age.

A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Age

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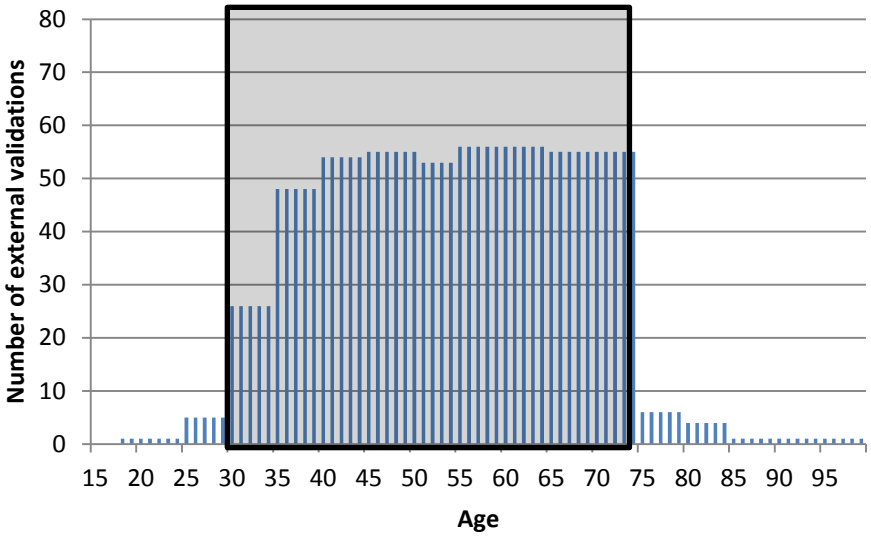
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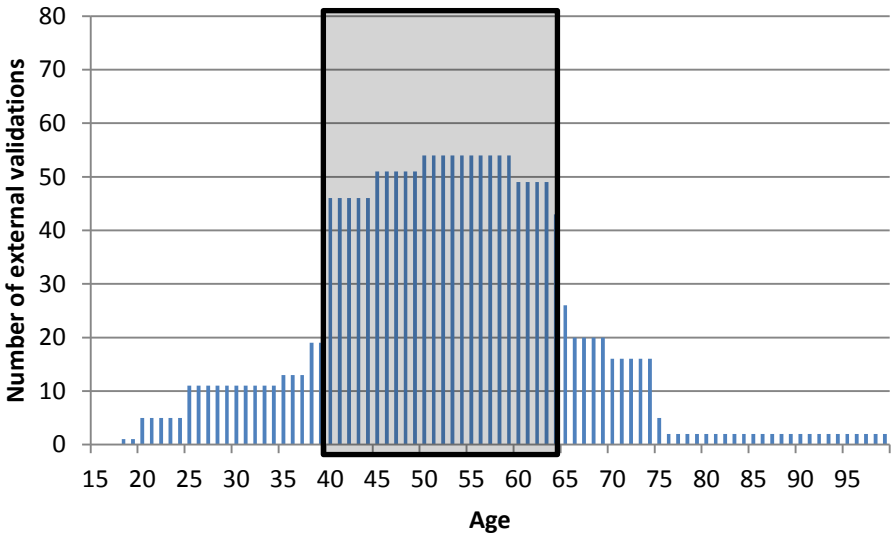
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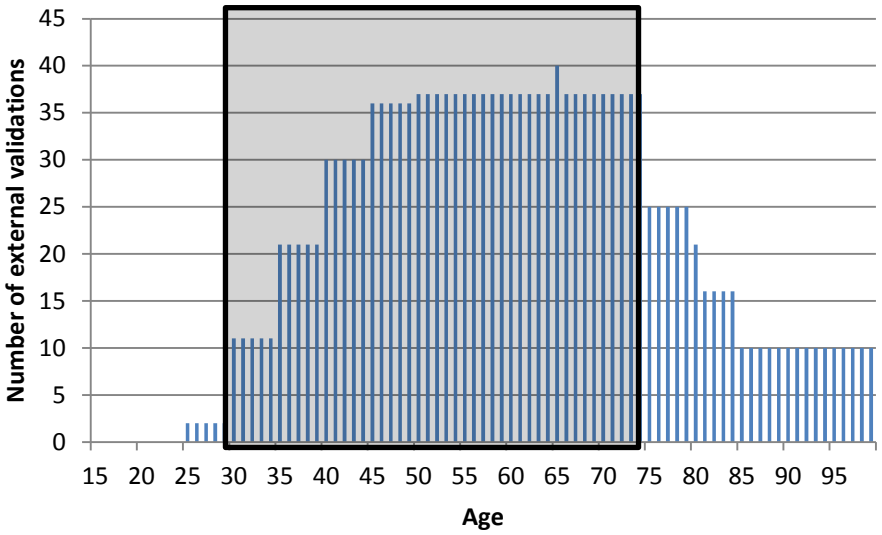
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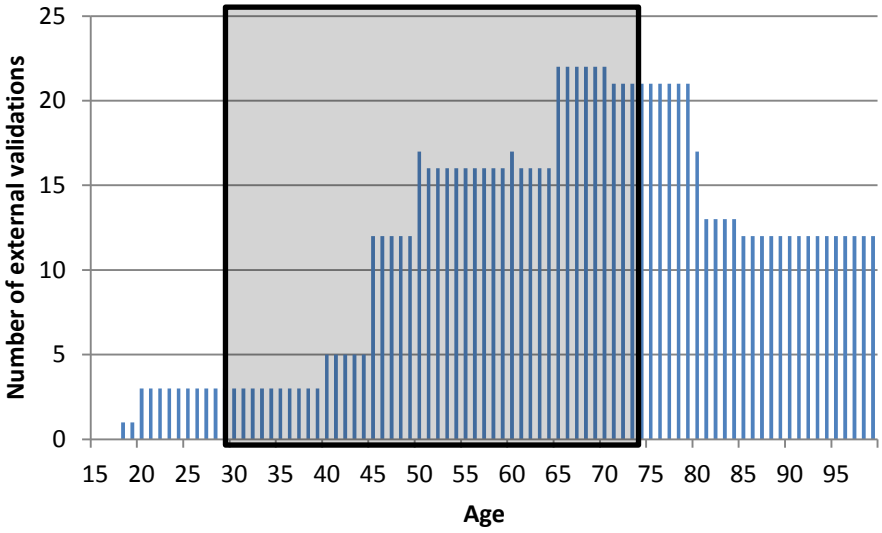
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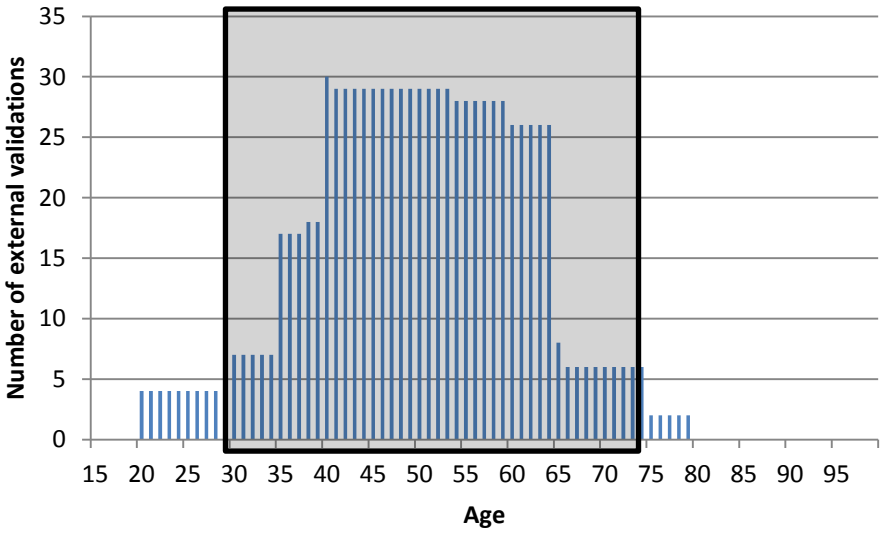
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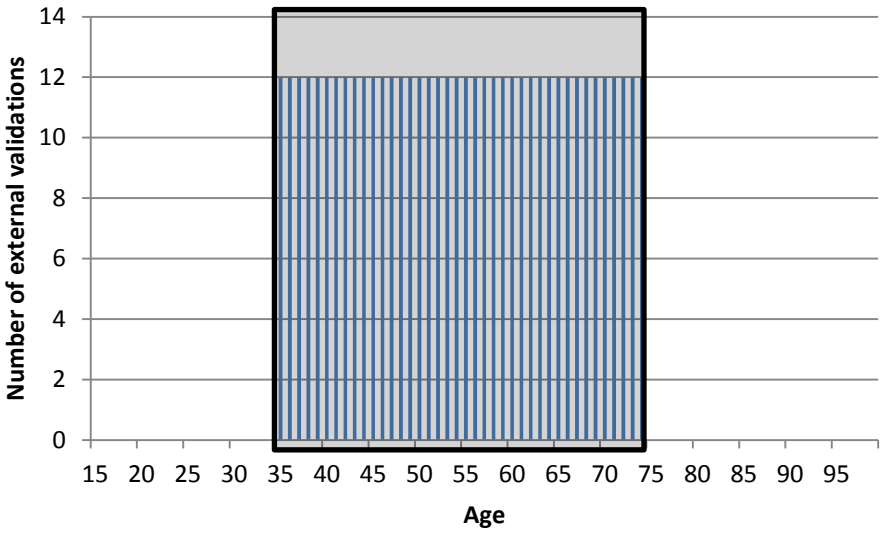

Supplemental Figure 2: Ages of people included in external validations of the 7 most often validated models (see Table 3). The grey area indicates the age range in the original development study. A: Framingham Wilson 1998,[184] B: Framingham Anderson 1991a,[22] C: SCORE Conroy 2003,[87] D: Framingham D'Agostino 2008,[107] E: Framingham ATP III 2002,[1] F: Framingham Anderson 1991b,[51] G: QRISK Hippisley-Cox 2007.[34]

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