

Appendix 1: Supplementary tables [posted as supplied by author]

Table A - First-incident hard atherosclerotic cardiovascular events during follow-up

	Rotterdam Study I n = 6045			Rotterdam Study II n = 2374	
	Total n = 8419	Men n = 2287	Women n = 3758	Men n = 1006	Women n = 1368
First-incident event:					
hard atherosclerotic cardiovascular disease	1700 (20.2)	660 (28.9)	836 (22.2)	102 (10.1)	102 (7.5)
hard coronary heart disease	766 (9.1)	348 (15.2)	316 (8.4)	63 (6.3)	39 (2.9)
• <i>myocardial infarction</i>	565 (6.7)	256 (11.2)	219 (5.8)	53 (5.3)	37 (2.7)
• <i>definite fatal coronary heart disease</i>	201 (2.4)	92 (4.0)	97 (2.6)	10 (1.0)	2 (0.1)
non-haemorrhagic stroke	869 (10.3)	280 (12.2)	494 (13.1)	36 (3.6)	59 (4.3)
• <i>ischaemic stroke</i>	528 (6.3)	180 (7.9)	275 (7.3)	29 (2.9)	44 (3.2)
• <i>unspecified stroke</i>	341 (4.1)	100 (4.4)	219 (5.8)	7 (0.7)	15 (1.1)
other atherosclerotic cardiovascular death	65 (0.8)	32 (1.4)	26 (0.7)	3 (0.3)	4 (0.3)
non-atherosclerotic death	2486 (29.5)	897 (39.2)	1328 (35.3)	133 (13.2)	128 (9.4)
no event (censored alive)	4233 (50.3)	730 (31.9)	1594 (42.4)	771 (76.6)	1138 (83.2)
Follow-up time:					
total person-time, yrs	96,363	26,760	49,032	8540	12,032
median (25th to 75th percentile), y	10.5 (7.9 to 17.0)	12.8 (6.3 to 17.5)	15.5 (8.1 to 18.0)	9.2 (8.0 to 10.1)	9.3 (8.3 to 10.1)
median (25th to 75th percentile), y *	16.0 (9.7 to 18.1)	17.9 (17.0 to 18.7)	18.0 (17.4 to 18.9)	9.7 (8.7 to 10.2)	9.6 (8.7 to 10.2)

Values are number of participants (percentages) unless stated otherwise.

* Median follow-up for participants censored alive.

Table B - Age of first-incident cardiovascular event or non-cardiovascular death

First-incident event	Men n = 3293	Women n = 5126	P-value *
cardiovascular disease	75.8 (8.3)	80.2 (8.9)	< 0.001
coronary heart disease	73.1 (8.1)	78.7 (9.5)	< 0.001
cerebrovascular disease	76.4 (8.0)	79.8 (8.8)	0.009
heart failure	78.1 (7.8)	81.7 (8.2)	0.006
other CVD death	80.0 (8.4)	84.0 (7.4)	0.17
non-cardiovascular death	78.8 (8.4)	82.7 (9.5)	< 0.001

Values are mean (standard deviation) age in years of occurrence of first-incident cardiovascular event or competing non-cardiovascular death during follow-up among men and women. Coronary heart disease was defined as myocardial infarction, coronary revascularisation, or death due to coronary heart disease. Cerebrovascular disease was defined as stroke, transient ischaemic attack, or carotid revascularisation. Other cardiovascular death included all cardiovascular mortality other than fatal coronary heart disease or stroke.

* Adjusted for age at start of follow-up and cohort.

Table C - Hazard ratios for cardiovascular disease and non-cardiovascular death for women compared to men by cohort

	Rotterdam Study I n = 6045		Rotterdam Study II n = 2374	
	Traditional Cox model HR (95% CI)	Competing risks model * HR (95% CI)	Traditional Cox model HR (95% CI)	Competing risks model * HR (95% CI)
Model 1:				
cardiovascular disease	0.75 (0.69 to 0.81)	0.81 (0.75 to 0.87)	0.76 (0.62 to 0.94)	0.78 (0.63 to 0.97)
coronary heart disease	0.49 (0.43 to 0.57)	0.54 (0.47 to 0.63)	0.39 (0.27 to 0.57)	0.40 (0.28 to 0.58)
cerebrovascular disease	0.93 (0.82 to 1.06)	1.08 (0.93 to 1.22)	1.56 (1.09 to 2.22)	1.65 (1.16 to 2.36)
heart failure	0.87 (0.74 to 1.01)	0.98 (0.84 to 1.14)	0.53 (0.32 to 0.87)	0.55 (0.34 to 0.90)
other cardiovascular death	0.59 (0.39 to 0.89)	0.69 (0.46 to 1.04)	2.63 (0.56 to 12.43) †	2.88 (0.62 to 13.50) †
non-cardiovascular death	0.70 (0.63 to 0.78)	0.80 (0.72 to 0.89)	0.55 (0.40 to 0.74)	0.57 (0.42 to 0.77)
Model 2:				
cardiovascular disease	0.61 (0.56 to 0.67)	0.73 (0.67 to 0.80)	0.68 (0.54 to 0.85)	0.72 (0.57 to 0.91)
coronary heart disease	0.44 (0.38 to 0.51)	0.53 (0.46 to 0.62)	0.35 (0.24 to 0.51)	0.36 (0.24 to 0.53)
cerebrovascular disease	0.77 (0.68 to 0.88)	1.02 (0.90 to 1.16)	1.36 (0.94 to 1.99)	1.42 (1.00 to 2.04)
heart failure	0.64 (0.54 to 0.75)	0.83 (0.71 to 0.98)	0.44 (0.27 to 0.75)	0.53 (0.30 to 0.91)
other cardiovascular death	0.44 (0.28 to 0.67)	0.62 (0.41 to 0.94)	2.90 (0.58 to 14.52) †	NA
non-cardiovascular death	0.52 (0.46 to 0.58)	0.69 (0.62 to 0.77)	0.49 (0.35 to 0.68)	0.50 (0.36 to 0.70)
Model 3:				
cardiovascular disease	0.67 (0.61 to 0.75)	0.76 (0.69 to 0.85)	0.74 (0.57 to 0.95)	0.77 (0.60 to 0.99)
coronary heart disease	0.46 (0.38 to 0.55)	0.53 (0.44 to 0.64)	0.41 (0.26 to 0.63)	0.43 (0.28 to 0.66)
cerebrovascular disease	0.92 (0.78 to 1.07)	1.13 (0.97 to 1.32)	1.38 (0.90 to 2.09)	1.45 (0.99 to 2.14)
heart failure	0.64 (0.52 to 0.78)	0.77 (0.63 to 0.95)	0.52 (0.28 to 0.97)	0.56 (0.30 to 1.05)
other cardiovascular death	0.57 (0.33 to 0.98)	0.77 (0.48 to 1.23)	5.40 (0.81 to 36.13) †	NA
non-cardiovascular death	0.64 (0.56 to 0.73)	0.78 (0.68 to 0.90)	0.56 (0.39 to 0.81)	0.55 (0.38 to 0.81)

Values are hazard ratios (95% confidence intervals) for the risk of a first-incident cardiovascular event or competing non-cardiovascular death associated with sex, where men served as the reference category. All regression analyses used follow-up time as the time scale. Coronary heart disease was defined as myocardial infarction, coronary revascularisation, or death due to coronary heart disease. Cerebrovascular disease was defined as stroke, transient ischaemic attack, or carotid revascularisation. Other cardiovascular death included all cardiovascular mortality other than fatal coronary heart disease or stroke. NA = not applicable due to non-converging models (only 2 events in men).

Model 1: unadjusted.

Model 2: adjusted for age (linear covariate) and level of education.

Model 3: adjusted for age (linear covariate), level of education, systolic and diastolic blood pressure, total and HDL-cholesterol levels, diabetes mellitus, smoking status, family history of premature myocardial infarction, body mass index, C-reactive protein level, use of blood pressure lowering medication, and use of statins.

* Fine and Gray methodology for subdistribution regression with competing risks.²⁰

† Interpret with caution, only 2 events in men.

Table D - Age of first-incident hard atherosclerotic cardiovascular event or non-atherosclerotic death

First-incident event	Men n = 3293	Women n = 5126	P-value *
hard atherosclerotic cardiovascular disease	76.6 (8.6)	81.5 (8.7)	< 0.001
hard coronary heart disease	75.3 (8.6)	79.9 (9.1)	< 0.001
non-haemorrhagic stroke	78.0 (8.5)	82.4 (8.4)	0.022
other atherosclerotic cardiovascular death	78.7 (7.7)	84.0 (6.8)	0.016
non-atherosclerotic death	80.0 (8.1)	84.0 (9.1)	< 0.001

Values are mean (standard deviation) age in years of occurrence of first-incident hard atherosclerotic cardiovascular event or competing non-atherosclerotic death during follow-up among men and women. Hard coronary heart disease was defined as myocardial infarction or death due to coronary heart disease. Other atherosclerotic cardiovascular death included all atherosclerotic cardiovascular mortality other than fatal coronary heart disease or non-haemorrhagic stroke.

* Adjusted for age at start of follow-up and cohort.

Table E - Remaining lifetime risks of nonfatal and fatal first-incident manifestation of cardiovascular disease at different ages

	Lifetime Risk		P-value	Excess events per 1000 women
	Men	Women		
Risk at 55 years of age:	n = 3293	n = 5126		
cardiovascular disease	67.1% (64.7 to 69.5)	66.4% (64.2 to 68.7)	0.34	-7
nonfatal event	55.1% (52.3 to 57.8)	52.6% (49.9 to 55.2)	0.101	-25
fatal event	12.1% (10.5 to 13.6)	13.9% (12.4 to 15.3)	0.047	18
Risk at 65 years of age:	n = 3001	n = 4832		
cardiovascular disease	63.4% (61.1 to 65.7)	65.6% (63.7 to 67.5)	0.077	22
nonfatal event	50.5% (48.1 to 52.9)	50.4% (48.5 to 52.4)	0.49	-1
fatal event	12.9% (11.3 to 14.5)	15.1% (13.7 to 16.5)	0.021	22
Risk at 75 years of age:	n = 1648	n = 3180		
cardiovascular disease	58.7% (55.8 to 61.6)	63.4% (61.2 to 65.6)	0.006	48
nonfatal event	42.9% (40.0 to 45.9)	46.4% (44.1 to 48.7)	0.033	35
fatal event	15.8% (13.6 to 17.9)	17.0% (15.3 to 18.8)	0.182	13
Risk at 85 years of age:	n = 438	n = 1296		
cardiovascular disease	52.0% (46.6 to 57.3)	57.1% (53.9 to 60.3)	0.054	51
nonfatal event	33.9% (28.8 to 39.0)	36.1% (33.0 to 39.2)	0.23	22
fatal event	18.1% (14.0 to 22.2)	21.0% (18.4 to 23.6)	0.123	29

Values are remaining lifetime risks (95% confidence interval) of occurrence of first-incident nonfatal or fatal cardiovascular event adjusted for competing non-cardiovascular death among men and women at different ages. A first-incident manifestation of cardiovascular disease was considered fatal if death occurred within 28 days of the event and death was attributed to cardiovascular disease. Excess risk was computed as the absolute difference in remaining lifetime risk between men and women