

Supplementary tables and figures

Table A. Classification of vascular and nonvascular outcomes in the Reykjavik cohort study using codes from both 9th and 10th revisions of International Classification of Diseases (ICD 9 and 10)

Outcome	ICD 9 Codes	ICD 10 Codes
Myocardial infarction	410, 412	I21, I22
Other CHD	411, 414	I23-I25
Ischaemic stroke	433, 434	I63
Subarachnoid haemorrhage (SAH)	430	I60
Haemorrhagic stroke (excl. SAH)	431	I61
Unclassified stroke	436	I64
Other cerebrovascular events (excl. unclassified stroke)	432, 437, 438	F01, I62, I65-I69
Other vascular events	093, 391, 393-398, 416-426, 440, 442-459, 745-747	I01, I05-I09, I27-I46, I52, I70, I72-I74, I77-I89, I95-I99, Q20-Q28
Cancers deaths	140-141, 143-151, 155, 157, 160-162, 180, 188, 189, 205, 152-154, 156, 174, 175, 182, 183, 185, 186, 193, 142, 158, 159, 163-173, 176-179, 181, 184, 187, 190-192, 194-204, 206-239	C00-C06, C09-C16, C22, C25, C30-C34, C64, C53, C65, C67, C92, C17-C21, C23, C24, C50, C54-C56, C61-C62, C73, C07, C08, C26, C37-C49, C51, C52, C57-C60, C63, C66, C68-C72, C74-C85, C88-C91, C93-D48
Nonvascular noncancer deaths	460-478, 490-496, 500-519, 001-066, 071-092, 094-139, 480-486, 290-359, 530-579, 580-637, 001-092, 094-139, 240-390, 392, 454-457, 460-487, 500-744, 748-760, 779, 800-999	J00-J11, J20-J47, J60-J99, A00-B99, J12-J18, F00, F02-F99, G00-G37, G40-G44, G46, G47, G50-G99, K00-K67, K70-K77, K80-K99, N00-N99, A00-B99, D50-F00, F02-F99, G00-G44, G46-I00, I02, I83-I86, I88, I89, J00-J39, J60-Q18, Q30-Q99, U04-Z99, S00-T98
Unclassified deaths	780-797, 799	R00-R95, R98, R99

Table B. Baseline correlates of eGFR levels by 4-variable MDRD equation

	No of subjects	Mean (SD) or %	Pearson correlation r (95% CI)	Difference (95% CI) in eGFR levels per 1 SD increase or compared to reference category§	z values§
eGFR by 4-variable MDRD equation	16,958	79 (14)			
Demographic factors					
Age, years	16,958	52 (9)	-0.26 (-0.27 to -0.25)	-3.49 (-3.69 to -3.29)	-33.7***
Sex	16,958				
Male	8,237	49%	-	7.04 (6.63 to 7.44)	34.0***
Female	8,721	51%	-	Ref	
Established risk factors					
Systolic Blood Pressure, mmHg	16,957	138 (22)	-0.07 (-0.08 to -0.05)	-0.57 (-0.78 to -0.36)	-5.3***
Diastolic Blood Pressure, mmHg	16,956	87 (12)	-0.02 (-0.04 to -0.01)	-0.93 (-1.14 to -0.72)	-8.8***
BMI, kg/m ²	16,895	25 (4)	-0.07 (-0.08 to -0.05)	-0.92 (-1.12 to -0.71)	-8.8***
Smoking status	16,958				
Current	8,013	47%	-	2.08 (1.67 to 2.50)	9.9***
Other	8,945	53%			
History of diabetes	16,958				
Yes	400	2%	-	2.26 (0.92 to 3.59)	3.3**
No	16,558	98%			
Blood based factors					
Total cholesterol, mmol/l	16,942	6.5 (1.2)	-0.11 (-0.12 to -0.09)	-0.75 (-0.96 to -0.55)	-7.2***
Log triglycerides, mmol/l	16,447	0.02 (0.45)	-0.09 (-0.11 to -0.08)	-1.55 (-1.76 to -1.34)	-14.5***
Fasting glucose, mmol/l	16,905	4.48 (0.74)	0.05 (0.04 to 0.07)	0.50 (0.29 to 0.70)	4.7***
Socioeconomic factors					
Occupation	10,889				
Nonmanual	5,841	54%	-	-1.78 (-2.31 to -1.26)	-6.7***
Manual	5,048	46%			
Education beyond high school	16,958				
Yes	2,558	15%	-	-2.08 (-2.65 to -1.50)	-7.1***
No	14,400	85%			
Physical activity	16,958				
Active	2,561	15%	-	0.59 (0.02 to 1.15)	2.0*
Not active	14,397	85%			
Renal function markers					
Creatinine clearance - Cockcroft-Gault method	16,895	83 (16)	0.82 (0.82 to 0.83)	13.43 (13.30 to 13.56)	205.4***
Creatinine (mg/dL)	16,958	0.95 (0.18)	-0.61 (-0.62 to -0.60)	-13.45 (-13.56 to -13.34)	-237.5***
Proteinuria	16,958				
Present	241	1%	-	-0.93 (-2.64 to 0.79)	-1.1
Absent	16,717	99%			

§adjusted for sex and age; eGFR, estimated glomerular filtration rate; MDRD, Modification of Diet for Renal Disease; *p<0.05; **p<0.001; ***p<0.0001

Table C. Association of renal function with coronary heart disease and nonvascular mortality (unadjusted analysis)

	No. of participants	Coronary Heart Disease (CHD)		Nonvascular Mortality	
		No. of events	Crude HR (95% CI)	No. of events	Crude HR (95% CI)
Participants without chronic kidney disease					
eGFR ≥90 mL/min/1.73m ²	3,265	872	1.09 (1.01 to 1.16)	803	1.04 (0.97 to 1.12)
eGFR 75-89 mL/min/1.73m ²	6,031	1,478	1.00 (0.95 to 1.05)	1,404	1.00 (0.95 to 1.05)
eGFR 60-74 mL/min/1.73m ²	5,902	1,319	0.96 (0.91 to 1.02)	1,346	1.05 (1.00 to 1.11)
Participants with chronic kidney disease†					
					1.27 (0.74 to 2.19)
Stage 1 (eGFR ≥90 mL/min/1.73m ² + proteinuria)	63	22	1.97 (1.30 to 2.99)	13	1.23 (0.80 to 1.88)
Stage 2 (eGFR 60-89 mL/min/1.73m ² + proteinuria)	125	54	2.83 (2.17 to 3.70)	21	1.78 (1.58 to 2.01)
Stage 3a (eGFR 45-59 mL/min/1.73m ²)	908	240	1.50 (1.32 to 1.70)	258	3.86 (2.63 to 5.67)
Stage 3b (eGFR 30-44 mL/min/1.73m ²)	63	20	2.57 (1.66 to 3.98)	26	5.45 (2.04 to 14.51)
Stage 4 (eGFR 15-29 mL/min/1.73m ²)	12	5	5.80 (2.41 to 13.93)	4	1.04 (0.97 to 1.12)

Analysis restricted to 16,369 participants with complete information on smoking status, history of diabetes, total cholesterol, triglycerides (log transformed), systolic blood pressure, and body mass index

† No participants in this cohort were in stage 5 or kidney failure stage (ie, eGFR <15 mL/min/1.73m²).

Table D. Association of renal function* with coronary heart disease and nonvascular mortality

	No. of participants	Coronary Heart Disease (CHD)			Nonvascular Mortality		
		No. of events	Age and sex adjusted	Further adjusted‡	No. of events	Age and sex adjusted	Further adjusted‡
Participants without chronic kidney disease							
eGFR ≥90 mL/min/1.73m ²	3,265	872	1.09 (1.02 to 1.17)	1.11 (1.03 to 1.19)	803	1.15 (1.07 to 1.24)	1.13 (1.05 to 1.21)
eGFR 75-89 mL/min/1.73m ²	6,031	1,478	1.00 (0.95 to 1.05)	1.00 (0.95 to 1.06)	1,404	1.00 (0.95 to 1.06)	1.00 (0.95 to 1.06)
eGFR 60-74 mL/min/1.73m ²	5,902	1,319	1.04 (0.99 to 1.10)	1.02 (0.97 to 1.08)	1,346	0.94 (0.89 to 0.99)	0.95 (0.88 to 1.00)
Participants with chronic kidney disease†							
Stage 1 (eGFR ≥90 mL/min/1.73m ² + proteinuria)	63	22	1.77 (1.16 to 2.69)	1.55 (1.02 to 2.35)	13	1.37 (0.79 to 2.36)	1.33 (0.77 to 2.29)
Stage 2 (eGFR 60-89 mL/min/1.73m ² + proteinuria)	125	54	1.94 (1.49 to 2.54)	1.72 (1.31 to 2.24)	21	0.83 (0.54 to 1.27)	0.76 (0.50 to 1.17)
Stage 3 (eGFR 30-59 mL/min/1.73m ²)	971	260	1.48 (1.30 to 1.68)	1.42 (1.24 to 1.61)	284	1.07 (0.94 to 1.21)	1.11 (0.98 to 1.25)
Stage 4 (eGFR 15-29 mL/min/1.73m ²)	12	5	6.46 (2.69 to 15.5)	4.29 (1.78 to 10.3)	4	6.40 (2.40 to 17.1)	5.97 (2.24 to 15.9)

Analysis restricted to 16,369 participants with complete information on smoking status, history of diabetes, total cholesterol, triglycerides (log transformed), systolic blood pressure, and body mass index

* In accordance to the National Kidney Foundation KDOQI Clinical Practice Guidelines

† No participants in this cohort were in stage 5 or kidney failure stage (ie, eGFR <15 mL/min/1.73m²).

‡ Additionally adjusted for smoking status, history of diabetes, total cholesterol, triglycerides (log transformed), systolic blood pressure, and body mass index

Table E. Association of renal function with coronary heart disease and nonvascular mortality using Chronic Kidney Disease epidemiology Collaboration (CKD-EPI) prediction equation

	No. of participants	Coronary Heart Disease (CHD)			Nonvascular Mortality		
		No. of events	Age and sex adjusted	Further adjusted‡	No. of events	Age and sex adjusted	Further adjusted‡
Participants without chronic kidney disease							
eGFR _{epi} ≥90 mL/min/1.73m ²	4,212	1,086	1.13 (1.05 to 1.21)	1.13 (1.05 to 1.21)	931	1.08 (1.01 to 1.17)	1.06 (0.98 to 1.14)
eGFR 75-89 mL/min/1.73m ²	6,083	1,441	1.00 (0.95 to 1.06)	1.00 (0.95 to 1.06)	1,456	1.00(0.95 to 1.06)	1.00 (0.94 to 1.06)
eGFR 60-74 mL/min/1.73m ²	4,969	1,149	1.08 (1.02 to 1.15)	1.04 (0.98 to 1.10)	1,177	0.90 (0.85 to 0.95)	0.91 (0.86 to 0.96)
Participants with chronic kidney disease†							
Stage 1 (eGFR ≥90 mL/min/1.73m ² + proteinuria)	70	26	1.92 (1.31 to 2.82)	1.63 (1.11 to 2.40)	14	1.31 (0.77 to 2.21)	1.27 (0.75 to 2.16)
Stage 2 (eGFR 60-89 mL/min/1.73m ² + proteinuria)	118	50	1.93 (1.46 to 2.55)	1.70 (1.29 to 2.24)	19	0.75 (0.48 to 1.18)	0.69 (0.44 to 1.08)
Stage 3a (eGFR 45-59 mL/min/1.73m ²)	832	228	1.47 (1.28 to 1.67)	1.39 (1.22 to 1.59)	244	0.99 (0.88 to 1.13)	1.03 (0.91 to 1.17)
Stage 3b (eGFR 30-44 mL/min/1.73m ²)	72	25	2.49 (1.68 to 3.70)	2.29 (1.54 to 3.4)	29	1.63 (1.13 to 2.35)	1.64 (1.14 to 2.37)
Stage 4 (eGFR 15-29 mL/min/1.73m ²)	13	5	4.61 (1.91 to 11.07)	3.03 (1.26 to 7.29)	5	3.10 (1.29 to 7.46)	2.98 (1.23 to 7.18)

Analysis restricted to 16,369 participants with complete information on smoking status, history of diabetes, total cholesterol, triglycerides (log transformed), systolic blood pressure, and body mass index

[‡] Additionally adjusted for smoking status, history of diabetes, total cholesterol, triglycerides (log transformed), systolic blood pressure, body mass index, and stratified for periods of enrolment

[†] No participants in this cohort were in stage 5 or kidney failure stage (ie, eGFR <15 mL/min/1.73m²).

Table F. Association of renal function with vascular and nonvascular mortality using competing risk model

Outcome	No. of events	Sub-hazard ratio (95% CI)	
		Age and sex adjusted	Further adjusted‡
Coronary deaths	1,143	1.14 (0.92 to 1.40)	1.07 (0.87 to 1.32)
Other vascular deaths	1,221	0.96 (0.78 to 1.18)	0.94 (0.76 to 1.16)
Cancer	2,289	0.85 (0.71 to 1.00)	0.87 (0.73 to 1.03)
Non-Cancer	1,586	1.10 (0.93 to 1.32)	1.14 (0.95 to 1.36)

Analysis restricted to 16,369 participants with complete information on smoking status, history of diabetes, total cholesterol, triglycerides (log transformed), systolic blood pressure, and body mass index

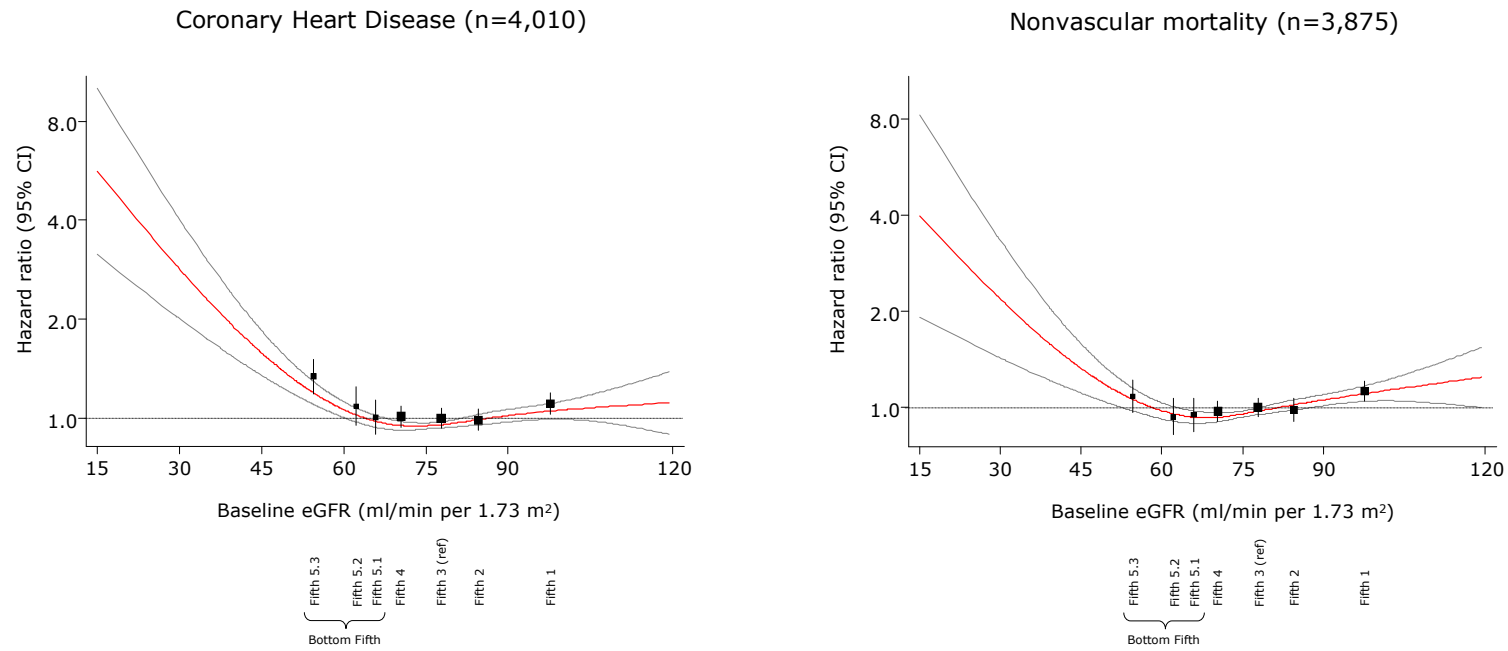
‡ Additionally adjusted for smoking status, history of diabetes, total cholesterol, triglycerides (log transformed), systolic blood pressure, body mass index, and stratified for periods of enrolment

Table G. Reclassification of individuals between predicted 10-year CHD risk categories upon addition of CKD status

Model without CKD*	Model with CKD				Reclassified into new risk category	
	0-5%	5-10%	10-20%	≥20%	Lower	Higher
0-5%						
Cases, n	151	8	0	0	0	8
Controls, n	8915	138	0	0	0	138
5-10%						
Cases, n	11	296	29	0	11	29
Controls, n	158	3762	128	0	158	128
10-20%						
Cases, n	0	15	306	13	15	13
Controls, n	0	115	1557	40	115	40
≥20%						
Cases, n	0	0	14	110	14	0
Controls, n	0	0	32	240	32	0
Total						
Cases, n	159	336	334	124	50	40
Controls, n	9073	4015	1717	280	306	305

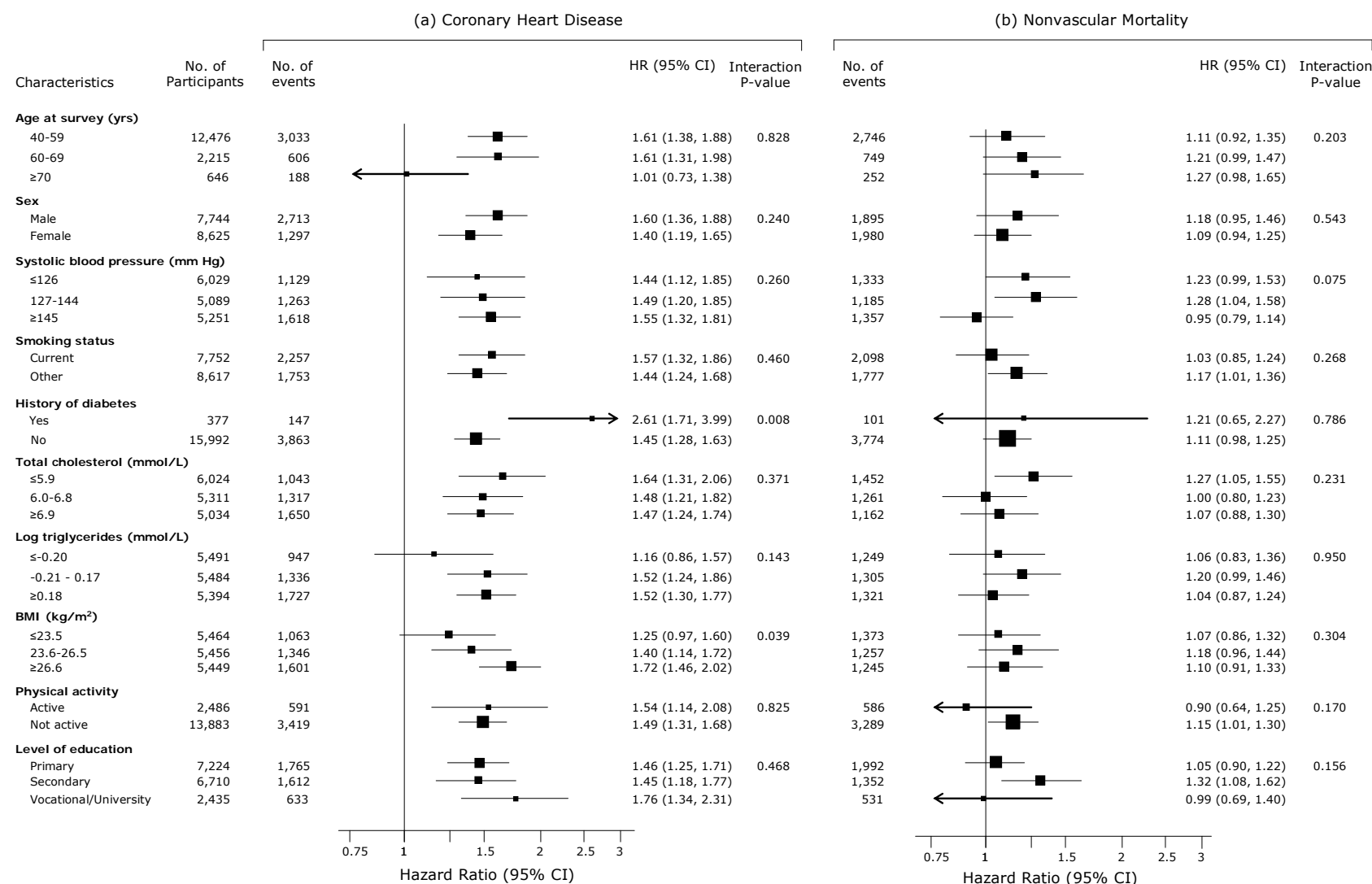
The model with conventional risk factors (stratified by sex) includes age, smoking status (current vs other), history of diabetes (yes vs no), total cholesterol, systolic blood pressure.

Figure A. Renal function and risk of coronary heart disease and nonvascular mortality



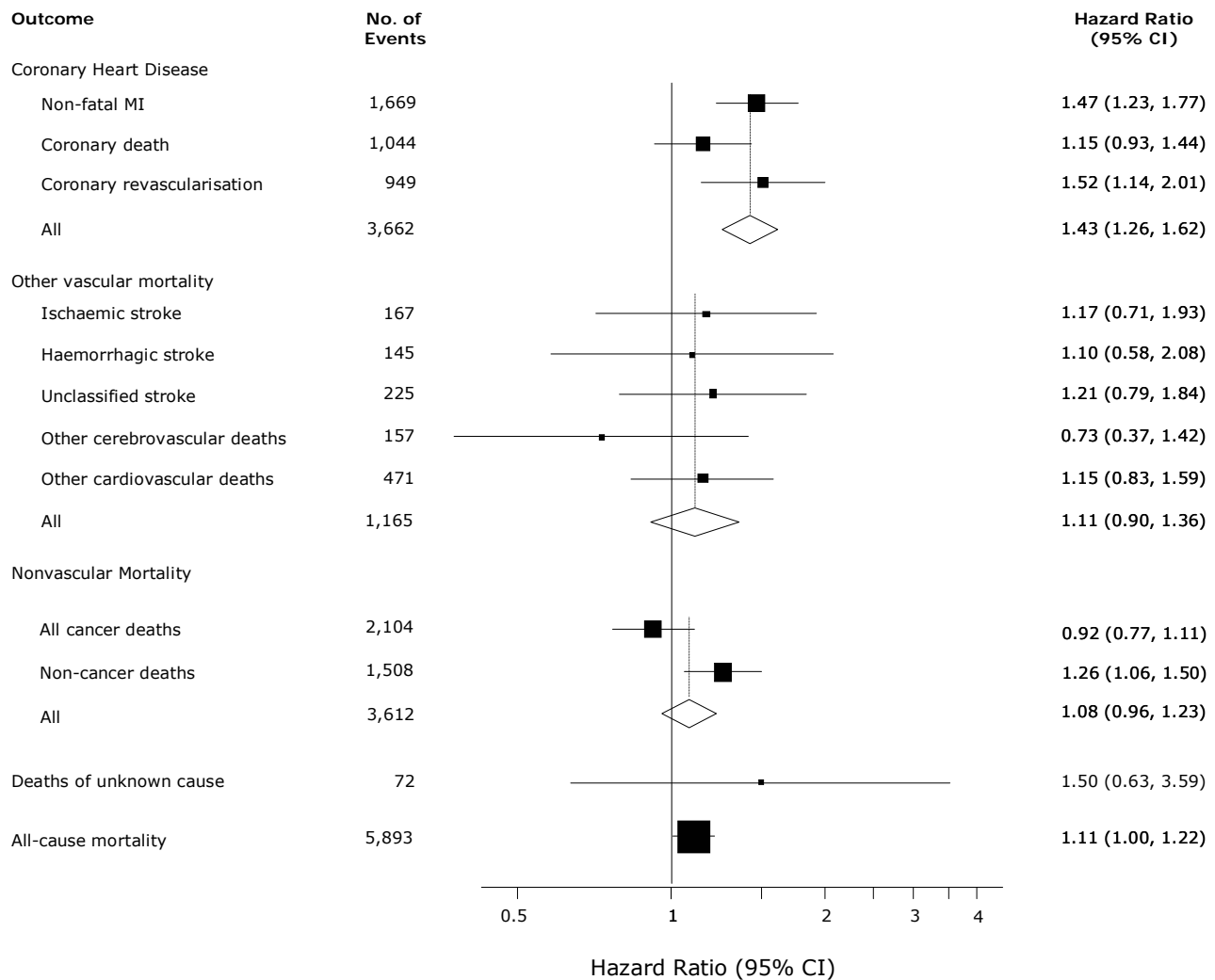
Multivariate regression spline was used to model the exposure association (cubic function, with 3 equally spaced knots placed at 25th, 50th and 75th centiles)
Hazard ratios presented are adjusted for age, sex, smoking status, history of diabetes, total cholesterol, triglycerides (log transformed), systolic blood pressure, and body mass index
The size of the data markers is proportional to the inverse of the variance of the hazard ratios. CI are calculated using floating-variance
Estimated GFR (eGFR) was calculated using the MDRD equation

Figure B. Risk of vascular and nonvascular outcomes in people with chronic kidney disease compared with people without chronic kidney disease, grouped by several individual characteristics



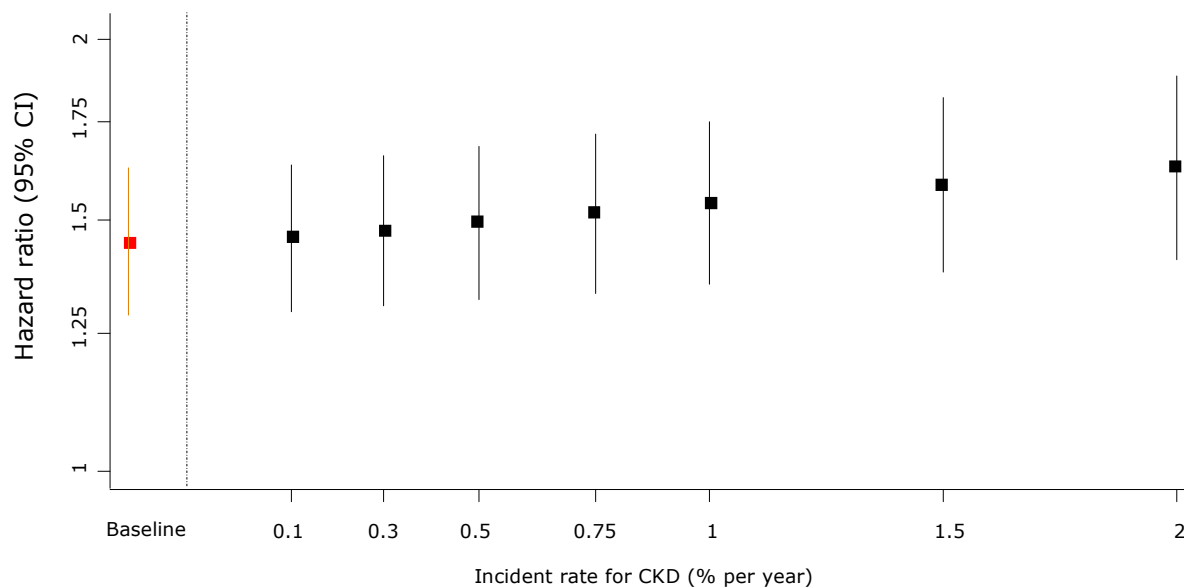
Hazard ratios presented are adjusted for age, sex, smoking status, history of diabetes, systolic blood pressure, total cholesterol, log triglycerides and body mass index
The size of the data markers is proportional to the inverse of the variances of the hazard ratios. Estimated GFR (eGFR) was calculated using the MDRD equation

Figure C. Risk of vascular and nonvascular outcomes in people with chronic kidney disease compared with people without chronic kidney disease, excluding events occurring in first five years of follow-up



Hazard ratios presented are adjusted for age, sex, smoking status, history of diabetes, systolic blood pressure, total cholesterol, log triglycerides and body mass index. The size of the data markers is proportional to the inverse of the variances of the hazard ratios. COPD, chronic obstructive pulmonary disease; estimated GFR (eGFR) was calculated using the MDRD equation

Figure D. Hazard ratios for coronary heart disease in people with chronic kidney disease compared with people without, allowing for time-dependent chronic kidney disease status



In the baseline analyses (indicated by red markers) CKD status was defined only according to the baseline measurement. In the other analyses, CKD status was modelled as a time dependent continuous variable to represent the probability of having CKD (range between 0 and 1). Participants classified as having CKD kept CKD status of 1 until time of event. For participants with no known CKD, the probability of having CKD was calculated according to the incident rates of CKD (% per year) based on the cumulative exponential distribution.