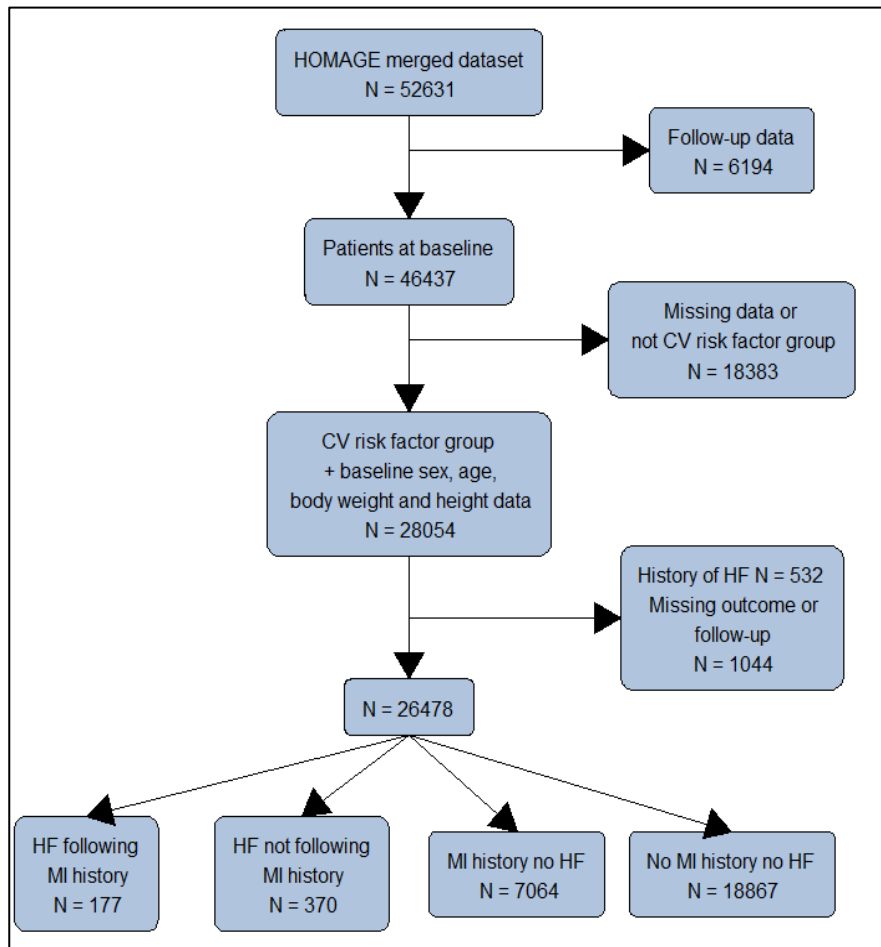
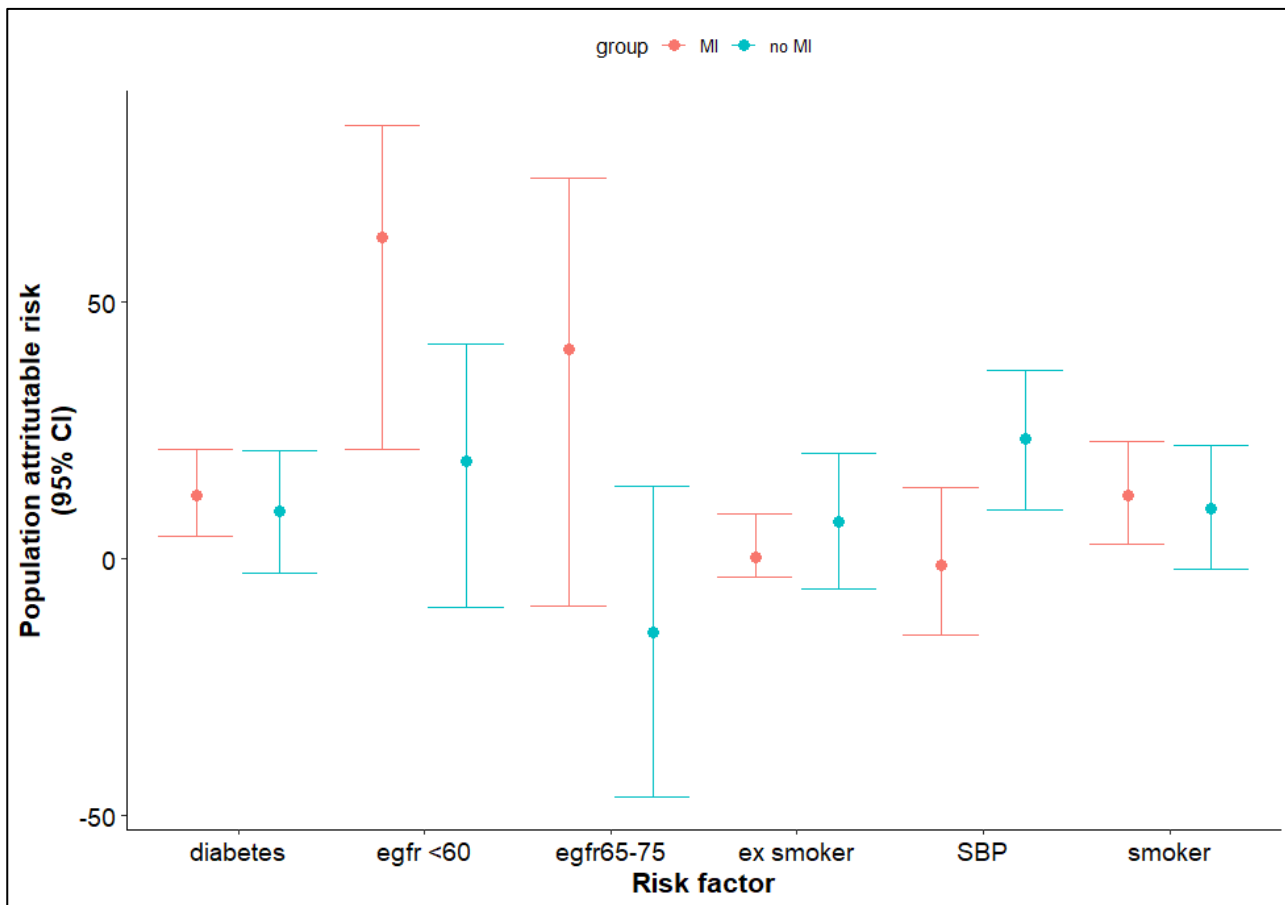


Supplementary information

Supplementary figure 1: Study flowchart for HOMAGE cohort



Supplementary Figure 2: Population attributable risk associated with modifiable risk variables in people with or without MI in HOMAGE



PAR: population attributable risk; x-axis: PAR percentage; y-axis: modifiable risk factors; error bars: confidence interval

Supplementary table 1: Definition of HF in the included cohorts (1,2,3)

Name of the cohort	Criteria for diagnosing HF
ASCOT trial	HF onset was confirmed by clinical signs and symptoms or diagnosis by attending physician
PROSPER trial	HF onset was confirmed by review of hospital records
HVC	Investigator judgement
DYDA trial	Investigator judgement Systolic LVD was defined as LV ejection fraction (LVEF) $\leq 50\%$ or Midwall fractional shortening $\leq 15\%$. Diastolic LVD was defined as E/A ratio (transmitral flow by Doppler) between 0.75 and 1.5 and deceleration time of E wave >140 msec.
UK Biobank	International Classification of Diseases-10 codes

Study description of UK Biobank

Study design and participants

Between 2007 and 2010, UK Biobank recruited 502,493 participants (aged 37–73 years) from the general population. Participants attended one of 22 assessment centres across England, Scotland, and Wales where they completed a self-administered, touch-screen questionnaire and face-to-face interview, and trained staff took a series of measurements including: height, weight, and blood pressure. Ethnicity, education level, sleep duration, smoking status, and alcohol intake were self-reported. Townsend area deprivation index was derived from postcode of residence using aggregated data on unemployment, car and home ownership, and household overcrowding.(4) Blood pressure was measured by a trained nurse. Hours of physical activity were self-reported using the validated International Physical Activity Questionnaire.(5) Height was measured to the nearest centimetre, using a Seca 202 stadiometer, body weight to the nearest 0.1 kg, using a Tania BC-418 body composition analyser, and waist circumference (WC) and hip circumference to the nearest 1 mm using a standard scale. BMI was calculated as $\text{weight}/\text{height}^2$ and the World Health Organization's criteria were used to classify BMI into: underweight (<18.5), normal weight (18.5 to <25), overweight (25 to <30), and obese (≥ 30). Biochemistry measures were performed at a dedicated central laboratory between 2014 and 2017. All of these tests were externally verified with acceptable distribution. Details of these measurements and assay performances can be found in the UK Biobank online showcase and protocol (6).

Outcome ascertainment

Clinical endpoints were ascertained through data linkage in the UK Biobank. Date and cause of death was obtained from death certificates held within the National Health Service Information Centre (England and Wales) and the National Health Service Central Register Scotland (Scotland). Date and cause of hospital admissions were obtained through record linkage to Health Episode Statistics (England and Wales) and Scottish Morbidity Records (Scotland). Detailed information about the linkage procedures can be found at <http://content.digital.nhs.uk/services>. At the time of analysis, mortality data

were available up to 30 June 2020 and hospital admission data were available up to 31 May 2020 for participants in England and 31 March 2017 for those in Scotland and Wales.

Supplementary Table 2: Baseline characteristics in relation to history of MI and the occurrence of HF during follow-up in UK Biobank (validation cohort)

	Prior MI at baseline		No MI at baseline		P	
	Overall (N=500001)	No incident HF (N=3875)	Incident HF (N=680)	No incident HF (N=481910)		Incident HF (N=13536)
Total n (%)						
Age, years, mean (SD)	56.50 (8.09)	60.87 (6.41)	62.21 (5.75)	56.31 (8.09)	61.95 (6.32)	< 0.0001
Male	227224 (45.45)	3150 (81.29)	550 (80.88)	215100 (44.64)	8424 (62.23)	< 0.0001
Smoking						< 0.0001
Never	272630 (54.85)	1301 (33.84)	174 (25.82)	265718 (55.46)	5437 (40.54)	
Smoker	52653 (10.59)	523 (13.61)	126 (18.69)	49881 (10.41)	2123 (15.83)	
Ex-smoker	171788 (34.56)	2020 (52.55)	374 (55.49)	163544 (34.13)	5850 (43.62)	
Units/week of alcohol intake	16.28 (18.90)	18.42 (20.90)	17.09 (20.92)	16.20 (18.74)	18.34 (23.27)	< 0.0001
BMI, kg/m ² , mean (SD)	27.42 (4.79)	27.34 (4.74)	29.82 (5.89)	28.80 (4.45)	29.90 (5.34)	< 0.0001
Hypertension	252917 (52.87)	3288 (85.87)	588 (87.89)	238693 (51.81)	10348 (78.46)	< 0.0001
SBP, mmHg, mean (SD)	137.84 (18.67)	137.68 (18.59)	144.53 (20.02)	135.32 (18.33)	135.23 (19.73)	< 0.0001
Diabetes	28084 (6.03)	606 (16.67)	183 (28.28)	24862 (5.54)	2433 (19.23)	< 0.0001
HbA1c, nmol/mol, mean (SD)	36.09 (6.76)	39.66 (8.80)	42.66 (12.16)	35.94 (6.52)	39.99 (11.17)	< 0.0001
eGFR, mean (SD)	91.86 (17.14)	81.17 (17.11)	73.67 (19.40)	92.37 (16.86)	77.61 (19.15)	< 0.0001
Cholesterol lowering medication	85126 (17.03)	3604 (93.01)	625 (91.91)	75386 (15.64)	5511 (40.71)	< 0.0001
Total cholesterol, mmol/L, mean (SD)	5.70 (1.14)	4.29 (0.91)	4.32 (0.98)	5.72 (1.13)	5.31 (1.25)	< 0.0001
LDL-c, mmol/L, mean (SD)	3.56 (0.87)	2.57 (0.66)	2.60 (0.72)	3.58 (0.86)	3.30 (0.93)	< 0.0001
HDL-c, mmol/L, mean (SD)	1.45 (0.38)	1.18 (0.29)	1.16 (0.30)	1.46 (0.38)	1.33 (0.38)	< 0.0001
Triglyceride, mmol/L, mean (SD)	1.75 (1.04)	1.87 (1.07)	1.88 (0.99)	1.74 (1.03)	1.95 (1.16)	< 0.0001

BMI; Body Mass Index; FU: follow-up; HF: Heart failure; MI: Myocardial Infarction; SBP: Systolic Blood Pressure; eGFR: estimated Glomerular Filtration Rate

T2DM defined by either self-report diagnosis, medication, or A1c>48 nmol/mol

Hypertension defined by self-report diagnosis, medication, or SBP>140 mmHg

Supplementary Table 3: Univariable and multivariable (using backward selection) Cox regression models for HF event with or without history of MI in the HOMAGE cohort

Variable	Patients with history of MI				Patients without history of MI				P-value interaction
	Univariable model		Multivariable model		Univariable model		Multivariable model		
	HR (95%CI)	P-value	HR (95%CI)	P-value	HR (95%CI)	P-value	HR (95%CI)	P-value	
Sex (Female)	0.85 (0.63 - 1.15)	0.296	0.63 (0.45 - 0.88)	0.008	1.00 (0.79 - 1.27)	0.996	0.71 (0.54 - 0.93)	0.015	0.803
Age class (ref: age <55 years)		<0.001		<0.001		<0.001		<0.001	<0.001
55-65 yrs	0.92 (0.39 - 2.17)	0.842	0.79 (0.26 - 2.41)	0.681	1.52 (0.84 - 2.77)	0.167	1.52 (0.7 - 3.27)	0.29	
65-75 yrs	3.47 (1.66 - 7.26)	0.001	2.94 (1.13 - 7.64)	0.027	3.34 (1.89 - 5.92)	<0.001	3.22 (1.52 - 6.84)	0.002	
> 75 yrs	7.58 (3.5 - 16.4)	<0.001	6.84 (2.52 - 18.59)	<0.001	5.84 (3.24 - 10.52)	<0.001	4.83 (2.2 - 10.6)	<0.001	
BMI (5 kg/cm²)	1.12 (0.95 - 1.33)	0.189	-	-	1.15 (1.04 - 1.28)	0.006	1.15 (1.02 - 1.31)	0.027	0.107
Smoking status (ref: non-smokers)		0.258		0.002		0.011			< 0.001
Smoker	1.36 (0.94 - 1.96)	0.105	2.00 (1.36 - 2.94)	<0.001	0.91 (0.7 - 1.18)	0.47	-	-	
Ex-smoker	1.26(0.71 - 2.23)	0.428	1.21 (0.61 - 2.41)	0.583	1.38 (1.05 - 1.83)	0.022	-	-	
Diabetes	1.88 (1.29 - 2.75)	0.001	1.96 (1.29 - 2.99)	0.002	1.95 (1.57 - 2.43)	<0.001	-	-	0.164
SBP class >160 mmHg	1.03 (0.76 - 1.41)	0.84	-	-	1.74 (1.4 - 2.15)	<0.001	1.59 (1.23 - 2.05)	<0.001	< 0.001

Variable	Patients with history of MI				Patients without history of MI				P-value interaction
	Univariable model		Multivariable model		Univariable model		Multivariable model		
			c-index = 0.708				c-index = 0.692		
	HR (95%CI)	P-value	HR (95%CI)	P-value	HR (95%CI)	P-value	HR (95%CI)	P-value	
Heart rate (10 bpm)	1.13 (1 - 1.27)	0.047	1.16 (1.02 - 1.32)	0.02	1.1 (1.01 - 1.19)	0.026	1.12 (1.02 - 1.23)	0.022	0.139
Blood glucose (mmol/L)	1.05 (0.96 - 1.15)	0.314	-	-	1.13 (1.09 - 1.17)	<0.001	1.14 (1.09 - 1.18)	<0.001	0.016
eGFR class (ml/min/1.73 m²) (ref: ≥75)		<0.001		0.002		<0.001		0.006	0.002
< 60	3.71 (1.89 - 7.3)	<0.001	3.13 (1.54 - 6.37)	0.002	1.7 (1.23 - 2.35)	0.001	1.3 (0.9 - 1.87)	0.159	
60 - 75	2.05 (1.01 - 4.16)	0.046	2 (0.96 - 4.14)	0.063	0.93 (0.66 - 1.31)	0.68	0.81 (0.55 - 1.18)	0.264	

BMI; Body Mass Index; FU: follow-up; HF: Heart failure; MI: Myocardial Infarction; SBP: Systolic Blood Pressure; eGFR: estimated Glomerular Filtration Rate

Values for univariable association not shown for alcohol intake, hypertension, HDL, LDL cholesterol because they were not retained in backward selection procedure of multivariable analysis in both the group.

Interaction were tested in models containing only the interaction and main effects (i.e. with no adjustment variables).

Supplementary Table 4: Head-to-head comparison of risk factors for HF onset in multivariable survival models in participants with and without a history of MI in the HOMAGE cohort, after forcing the adjustment for beta-blockers and ACEi/ARBs use.

Variable	Group	Multivariable MI+ c-index = 0.704		Multivariable MI- c-index = 0.699		Interaction in multivariable model
		HR (CI)	P-value	HR (CI)	P-value	P-value interaction
Sex			0.014		0.029	0.763
	M	Reference		Reference		
	F	0.64 (0.45 - 0.91)	0.014	0.72 (0.54 - 0.97)	0.029	
Age class			<0.001		<0.001	0.004
	<= 55 yrs	Reference		Reference		
	> 75 yrs	7.11 (2.1 - 24.06)	0.002	4.59 (1.97 - 10.7)	<0.001	
	55-65 yrs	0.87 (0.23 - 3.31)	0.839	1.4 (0.61 - 3.21)	0.429	
	65-75 yrs	2.99 (0.93 - 9.62)	0.066	3.13 (1.39 - 7.03)	0.006	
BMI (5 kg/cm ²)		1.02 (0.83 - 1.26)	0.838	1.16 (1.02 - 1.32)	0.024	0.032
Smoking status			0.008		0.105	0.055
	Non-smoker	Reference		Reference		
	Smoker	1.92 (1.27 - 2.91)	0.002	1.4 (1.02 - 1.92)	0.039	
	Ex-smoker	1.2 (0.51 - 2.79)	0.675	1.27 (0.87 - 1.85)	0.214	
Diabetes			0.003		0.137	0.395
	No	Reference		Reference		
	Yes	2.37 (1.35 - 4.14)	0.003	1.32 (0.91 - 1.91)	0.137	
SBP class			0.908		<0.001	0.005
	<= 160 mmHg	Reference		Reference		
	> 160 mmHg	0.98 (0.69 - 1.39)	0.908	1.75 (1.34 - 2.27)	<0.001	
Heart rate (10 bpm)		1.17 (1.01 - 1.34)	0.033	1.11 (1 - 1.23)	0.041	0.55
Blood glucose (mmol/L)		0.9 (0.78 - 1.04)	0.154	1.07 (1.01 - 1.15)	0.033	0.013
eGFR class			0.022		0.004	0.04

Variable	Group	Multivariable MI+ c-index = 0.704		Multivariable MI- c-index = 0.699		Interaction in multivariable model
		HR (CI)	P-value	HR (CI)	P-value	P-value interaction
	>= 75 ml/min/1,73 m ²	Reference		Reference		
	60-75 ml/min/1,73 m ²	1.79 (0.83 - 3.86)	0.136	0.78 (0.53 - 1.17)	0.233	
	< 60 ml/min/1,73 m ²	2.57 (1.23 - 5.38)	0.012	1.31 (0.9 - 1.93)	0.162	
ACEi and/or ARB use			<0.001		0.011	0.774
	No	Reference		Reference		
	Yes	2.12 (1.47 - 3.05)	<0.001	1.44 (1.09 - 1.9)	0.011	
Beta-blockers use			0.748		0.604	0.711
	No	Reference		Reference		
	Yes	1.06 (0.73 - 1.56)	0.748	0.92 (0.68 - 1.25)	0.604	

Supplementary Table 5: Multivariable Cox proportional model for the risk of HF onset depending on the MI history in the validation cohort (UK Biobank)

	Prevalent MI at baseline		No MI at baseline		P value of interaction
	HR (95% CI)	P	HR (95% CI)	P	
Model 0					
Age in year	1.04 (1.03-1.05)	< 0.0001	1.12 (1.11-1.12)	< 0.0001	< 0.0001
Male	1.00 (0.83-1.21)	0.97	2.06 (1.99-2.13)	< 0.0001	< 0.0001
Non-white ethnicity	1.49 (1.11-1.98)	0.007	0.96 (0.89-1.04)	0.37	0.04
Model 1					
Deprivation	1.20 (1.12-1.29)	< 0.0001	1.31 (1.28-1.33)	< 0.0001	0.61
Model 2					
MET-min/week	0.85 (0.77-0.93)	0.0008	0.89 (0.88-0.91)	< 0.0001	0.13
TV viewing	1.13 (1.06-1.21)	0.0003	1.24 (1.22-1.26)	< 0.0001	0.003
Fruit/veg intake	0.98 (0.91-1.06)	0.6	0.96 (0.94-0.97)	< 0.0001	0.46
Red meat intake	1.10 (1.02-1.18)	0.008	1.07 (1.06-1.09)	< 0.0001	0.69
Processed meat intake	1.06 (0.90-1.24)	0.51	1.21 (1.16-1.25)	< 0.0001	0.053
Low oily fish intake	1.15 (0.91-1.47)	0.25	1.29 (1.22-1.36)	< 0.0001	0.69
Former smoker	1.36 (1.13-1.63)	0.0009	1.32 (1.27-1.37)	< 0.0001	0.74
Current smoker	1.88 (1.48-2.38)	< 0.0001	1.97 (1.87-2.08)	< 0.0001	0.59
Alcohol intake	0.98 (0.90-1.06)	0.56	1.01 (1.00-1.03)	0.12	0.1
Model 3					
BMI	1.22 (1.12-1.33)	< 0.0001	1.49 (1.46-1.51)	< 0.0001	0.0005
WHR	1.28 (1.14-1.44)	< 0.0001	1.57 (1.54-1.61)	< 0.0001	< 0.0001
Model 4					
Grip strength	0.80 (0.71-0.89)	< 0.0001	0.75 (0.73-0.77)	< 0.0001	0.49
Hypertension	1.15 (0.89-1.50)	0.29	1.61 (1.54-1.69)	< 0.0001	0.0005
SBP	0.97 (0.89-1.06)	0.53	1.06 (1.04-1.08)	< 0.0001	0.15
CRP	1.14 (1.08-1.22)	< 0.0001	1.16 (1.14-1.17)	< 0.0001	0.02
Type 2 diabetes	1.50 (1.22-1.84)	0.0001	1.81 (1.72-1.91)	< 0.0001	0.03
HbA1c	1.13 (1.07-1.20)	< 0.0001	1.19 (1.17-1.20)	< 0.0001	0.03
Cystatin C	1.30 (1.21-1.39)	< 0.0001	1.39 (1.37-1.41)	< 0.0001	0.0002
eGFR	0.73 (0.67-0.81)	< 0.0001	0.67 (0.66-0.69)	< 0.0001	< 0.0001
GGT	1.12 (1.05-1.19)	0.0003	1.14 (1.12-1.16)	< 0.0001	0.02

Adjusted for all factors in the prior model. E.g. factors in Model 1 adjusted for factors in Model 0
Continuous variables were standardised to per-SD increase

Table 6: Multivariable Fine-Gray competing risks models for HF event with or without prior MI (with non-HF death as competing risk) using variables selected in both backwards procedure)

Variable	Multivariable MI+ c-index = 0.826		Multivariable MI- c-index = 0.704		Multiplicative interaction in multivariable model
	HR (CI)	P-value	HR (CI)	P-value	P-value interaction
Sex (male)	1.79 (1.26 - 2.54)	0.001	1.16 (0.88 - 1.54)	0.29	0.323
Age class (ref: age ≤ 55 yrs)		<0.001		<0.001	< 0.001
55-65	0.61 (0.18 - 2.06)	0.423	1.66 (0.75 - 3.67)	0.214	
65-75	4.05 (1.61 - 10.22)	0.003	4.33 (2.03 - 9.21)	<0.001	
> 75	12.06 (4.64 - 31.32)	<0.001	7.92 (3.62 - 17.32)	<0.001	
BMI (5 kg/m ²)	1.03 (0.85 - 1.26)	0.734	1.16 (1.03 - 1.31)	0.014	0.022
Smoking status (ref: Non-smoker)		0.001		0.127	0.019
Smoker	1.73 (1.18 - 2.54)	0.005	1.17 (0.87 - 1.58)	0.297	
Ex-smoker	0.47 (0.23 - 0.95)	0.035	0.83 (0.61 - 1.13)	0.242	
Diabetes	2.71 (1.56 - 4.7)	<0.001	1.12 (0.79 - 1.59)	0.521	0.672
SBP class > 160 mmHg	0.8 (0.56 - 1.13)	0.204	1.42 (1.11 - 1.82)	0.006	0.002
Heart rate (10 bpm)	1.1 (0.97 - 1.24)	0.144	1.09 (0.99 - 1.21)	0.089	0.247
Blood glucose (mmol/L)	0.86 (0.73 - 1.02)	0.076	1.09 (1.02 - 1.17)	0.012	0.01
eGFR class (ref: ≥ 75 ml/min/1.73 m ²)		0.004		0.002	0.015
60-75	1.91 (0.86 - 4.27)	0.114	0.76 (0.52 - 1.1)	0.141	
< 60	3.28 (1.46 - 7.37)	0.004	1.3 (0.9 - 1.88)	0.155	

Supplementary References

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