Figure S1. Cumulative incidence of non-CV death (panel A), CV death (panel B), MACE (panel C) and HHF (panel D) according to Copeptin level quintile derived from the unadjusted cause-specific hazard estimates (model A) by application of the Aalen-Johansen estimator

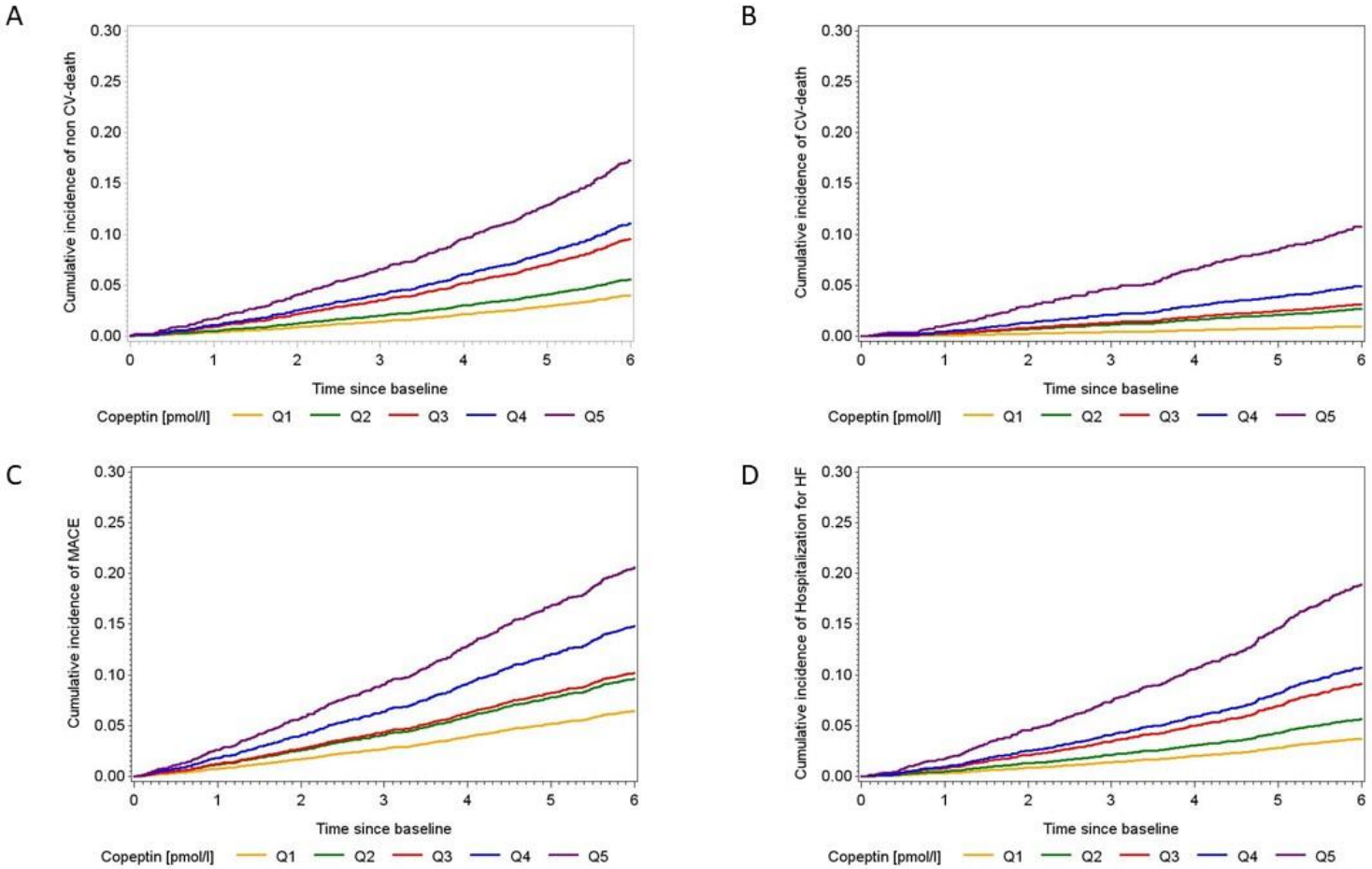

Figure S2. Cumulative incidence of non-CV death (panel A), CV death (panel B), MACE (panel C) and HHF (panel D) according to MR-proANP level quintile derived from the unadjusted cause-specific hazard estimates (model A) by application of the Aalen-Johansen estimator

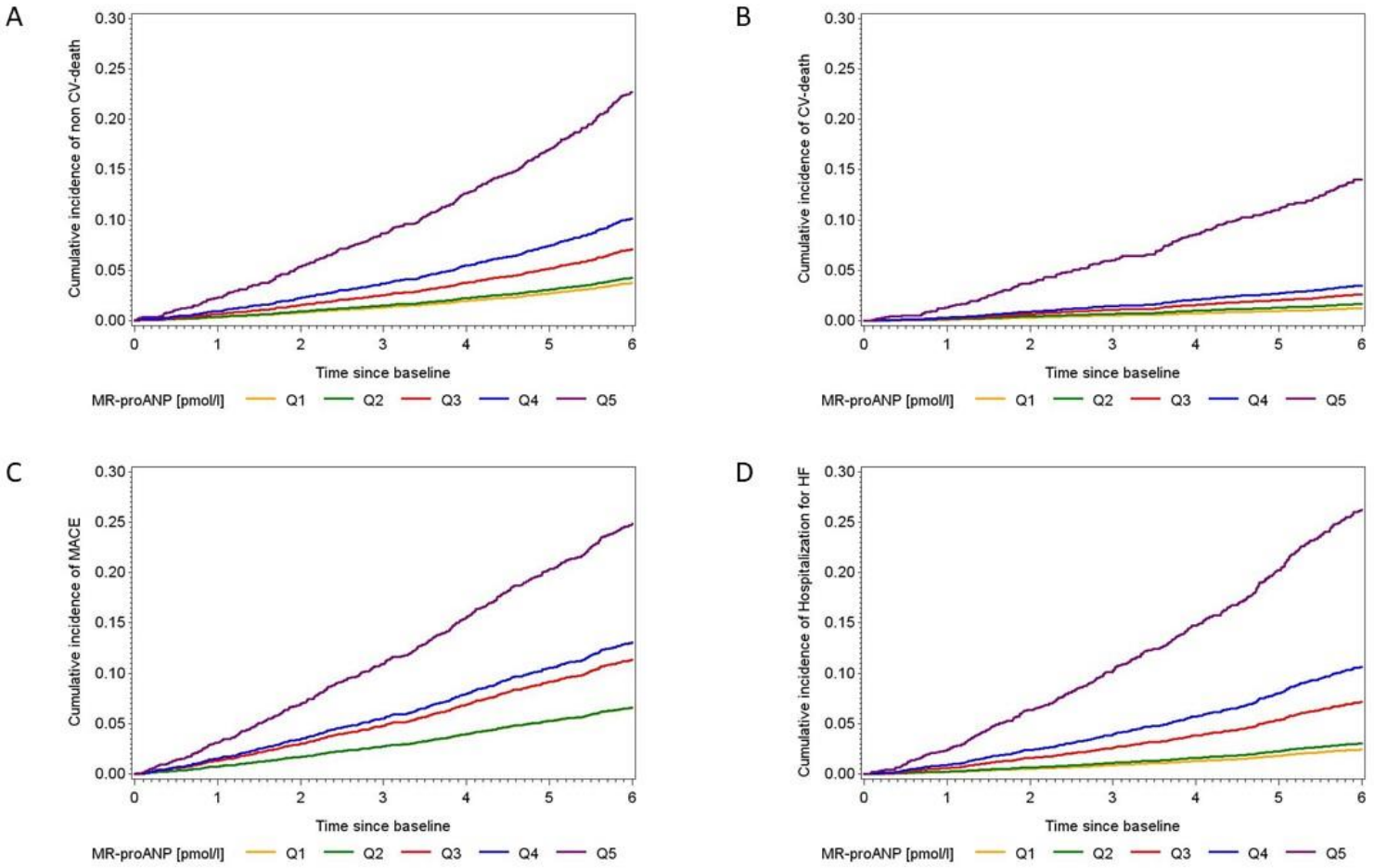

Figure S3. Cumulative incidence of non-CV death (panel A), CV death (panel B), MACE (panel C) and HHF (panel D) according to NT-proBNP level quintile derived from the unadjusted cause-specific hazard estimates (model A) by application of the Aalen-Johansen estimator

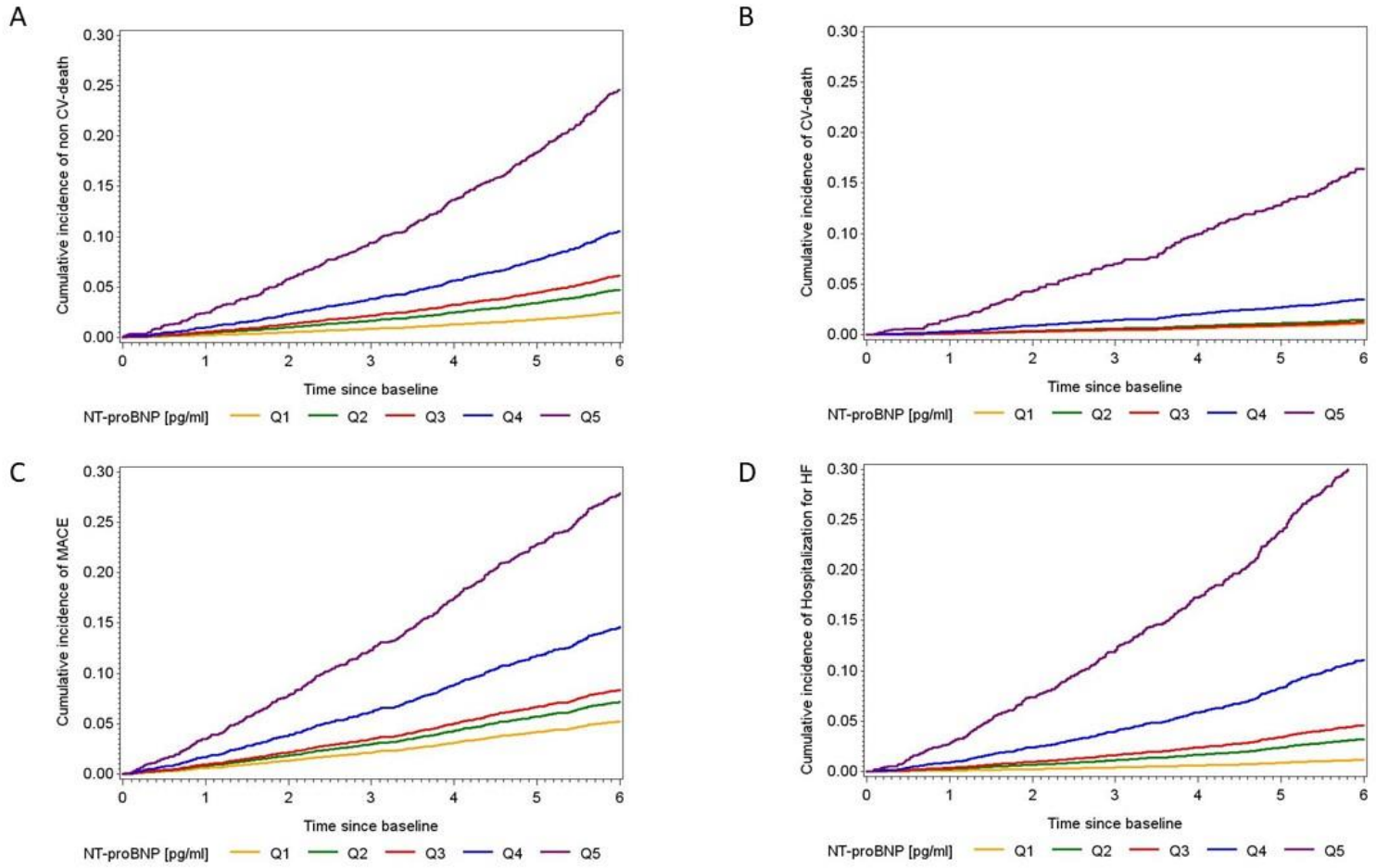

Table S1 Demographics and clinical parameters at baseline stratified by MR-proANP quintiles

		MR-proANP (pmol/l)				
	Total Cohort	Q1 (≤ 69)	Q2 (> 69 - ≤ 102)	Q3 (> 102 - ≤ 144)	Q4 (> 144 - ≤ 213)	Q5 (> 213)
N (%)	4417	843 (19.1)	883 (20.0)	891 (20.2)	899 (20.4)	901 (20.4)
Demographics						
Age (ys)	61 ± 12	53.4 ± 13.4	57.9 ± 11.4	61.9 ± 10.5	64.0 ± 9.0	66.0 ± 8.2
Male	2681 (61)	534 (63)	502 (57)	501 (56)	546 (61)	598 (66)
Regional center						
AA – Aachen	446 (10)	76 (9)	74 (8)	91 (10)	95 (11)	110 (12)
BE – Berlin	372 (8)	63 (7)	68 (8)	69 (8)	87 (10)	85 (9)
ER - Erlangen	801 (18)	182 (22)	160 (18)	163 (18)	139 (15)	157 (17)
FR – Freiburg	300 (7)	60 (7)	71 (8)	512 (6)	62 (7)	56 (6)
HA - Hannover	376 (8)	76 (9)	72 (8)	78 (9)	74 (8)	76 (8)
HE – Heidelberg	404 (9)	68 (8)	79 (9)	74 (8)	94 (10)	89 (10)
JE – Jena	575 (13)	91 (11)	123 (14)	126 (14)	113 (13)	122 (14)
MU – München	425 (10)	96 (11)	88 (10)	100 (11)	83 (9)	58 (6)
WU - Würzburg	718 (16)	131 (16)	148 (17)	139 (16)	152 (17	148 (16)
Laboratory Measures						
eGFR (ml/min per 1.73 m^2)	49 ± 17	60.8 ± 22.0	53.2 ± 16.2	48.3 ± 14.4	43.9 ± 12.6	38.8 ± 11.3
UACR (mg/g)	47 (9-366)	52.4 (7.5-498.6)	33.9 (6.7-284.0)	30.6 (8.8-218.2)	46.5 (9.8-309.7)	85.8 (15.8-562.7)
hsCRP (mg/dl)	2 (1-5)	1.9 (1.0-4.4)	2.1 (1.0-4.8)	2.2 (1.0-4.7)	2.4 (1.1-5.3)	2.9 (1.3-6.6)
LDL cholesterol (mg/dl)	113 (88-143)	122.6 (96.1-149.6)	118.1 (93.5-142.7)	114.0 (88.6-145.9)	107.8 (85.5-136.9)	103.9 (81.3-133.7)
HDL cholesterol (mg/dl)	48 (39-60)	47.2 (38.3-59.2)	48.7 (39.5-60.9)	49.3 (40.3-61.5)	48.3 (38.9-61.6)	47.5 (38.6-61.1)
CVD risk factors						
Systolic BP (mmHg)	140 ± 21	135.0 ± 17.1	138.3 ± 18.1	139.5 ± 19.5	142.9 ± 21.2	142.9 ± 24.3
Diastolic BP (mmHg)	79 ± 12	81.4 ± 10.9	81.0 ± 10.9	79.2 ± 11.4	78.1 ± 11.9	75.9 ± 12.9
BMI (kg/m^2)	30 ± 6	29.8 ± 5.9	29.5 ± 5.9	30.1 ± 6.1	30.1 ± 5.7	30.4 ± 6.2
Diabetes	1645 (37)	235 (28)	274 (31)	345 (39)	369 (41)	422 (47)
Previous CVD	1180 (27)	95 (11)	154 (17)	199 (22)	327 (36)	405 (45)

Heart Failure	836 (19)	80 (9)	104 (12)	140 (16)	219 (24)	293 (33)
Smoking history						
never	1813 (41)	336 (40)	363 (41)	396 (44)	376 (42)	342 (38)
former	1918 (44)	334 (40)	362 (41)	377 (42)	394 (44)	451 (50)
current	673 (15)	170 (20)	155 (18)	115 (13)	126 (14)	107 (12)
Medication Use						
RASi	3713 (84)	704 (84)	724 (82)	729 (82)	784 (87)	772 (86)
Statins	2155 (49)	324 (38)	379 (43)	428 (48)	492 (55)	532 (59)
Anti-platelet agents	1564 (36)	173 (21)	266 (30)	329 (37)	405 (45)	391 (43)
Beta-blockers	2480 (57)	238 (28)	374 (42)	492 (55)	653 (73)	723 (80)
MRA	364 (8)	57 (7)	56 (6)	68 (8)	73 (8)	110 (12)

Continuous variables are presented as mean and standard deviation or median and interquartile range.
Categorical variables are presented as numbers with percentages in the overall study population.
eGFR=estimated glomerular filtration rate, UACR=urinary albumin excretion rate, hsCRP=high sensitive C-reactive protein, LDL=low density lipoprotein, HDL=high density lipoprotein, BP=blood pressure, BMI=body mass index, CVD=cardiovascular disease, RASi=renin angiotensin system inhibitor, MRA=mineralocorticoid receptor antagonist

Table S2: Demographics and clinical parameters at baseline stratified by NT-proBNP quintiles

		NT-proBNP (pg/ml)				
	Total Cohort	Q1 (≤ 74)	Q2 (> 74 - ≤ 136)	Q3 (> 136 - ≤ 250)	Q4 (> 250 - ≤ 532)	Q5 (> 532)
N (%)	4417	879 (19.9)	868 (19.7)	873 (19.8)	902 (20.4)	895 (20.3)
Demographics						
Age (ys)	61 ± 12	53.8 ± 12.9	59.2 ± 11.4	61.1 ± 11.3	63.6 ± 9.8	65.9 ± 8.0
Male	2681 (61)	617 (70)	503 (58)	484 (55)	495 (55)	582 (65)
Reginal center						
AA – Aachen	446 (10)	90 (10)	86 (10)	83 (10)	87 (10)	100 (11)
BE – Berlin	372 (8)	63 (7)	61 (7)	79 (9)	96 (11)	73 (8)
ER - Erlangen	801 (18)	177 (20)	160 (18)	152 (17)	145 (16)	167 (19)
FR – Freiburg	300 (7)	60 (7)	56 (6)	48 (6)	70 (8)	66 (7)
HA - Hannover	376 (9)	87 (10)	73 (8)	75 (9)	75 (8)	66 (7)
HE – Heidelberg	404 (9)	75 (9)	72 (8)	95 (11)	80 (9)	82 (9)
JE – Jena	575 (13)	92 (10)	118 (14)	118 (14)	116 (13)	131 (15)
MU – München	425 (10)	96 (11)	96 (11)	87 (10)	87 (10)	80 (9)
WU - Würzburg	718 (16)	139 (16)	146 (17)	136 (16)	167 (19)	130 (15)
Laboratory Measures						
eGFR (ml/min per 1.73 m^2)	49 ± 17	58.4 ± 21.0	51.3 ± 16.9	48.3 ± 14.9	45.5 ± 14.9	40.7 ± 13.0
UACR (mg/g)	47 (9-366)	52.4 (7.2-416.4)	37.3 (7.0-276.9)	34.8 (8.5-318.9)	41.6 (9.9-305.7)	77.3 (15.5-531.5)
hsCRP (mg/dl)	2 (1-5)	1.7 (0.8-3.8)	2.1 (1.0-4.7)	2.2 (1.0-4.5)	2.6 (1.1-5.4)	3.2 (1.5-7.9)
LDL cholesterol (mg/dl)	113 (88-143)	122.7 (94.9-148.0)	118.2 (94.4-147.3)	113.5 (90.2-142.7)	110.5 (86.1-140.5)	101.8 (80.3-131.2)
HDL cholesterol (mg/dl)	48 (39-60)	46.8 (38.1-57.4)	48.7 (40.3-60.9)	49.8 (40.7-62.4)	49.2 (40.6-62.8)	47.0 (37.3-59.8)
CVD risk factors						
Systolic BP (mmHg)	140 ± 21	134.8 ± 16.3	137.9 ± 19.1	138.8 ± 18.8	143.1 ± 21.6	143.0 ± 24.4
Diastolic BP (mmHg)	79 ± 12	81.4 ± 10.4	80.7 ± 11.6	78.9 ± 11.4	78.3 ± 12.1	76.3 ± 12.6
BMI (kg/m^2)	30 ± 6	29.8 ± 5.7	29.8 ± 6.1	29.5 ± 5.9	30.0 ± 6.1	30.5 ± 6.2
Diabetes	1645 (37)	250 (28)	258 (30)	316 (36)	345 (38)	476 (53)
Previous CVD	1180 (27)	92 (10)	144 (17)	190 (22)	314 (35)	440 (49)
Heart Failure	836 (19)	68 (8)	106 (12)	126 (14)	210 (23)	326 (36)
Smoking history						
never	1813 (41)	350 (40)	366 (42)	391 (45)	384 (43)	322 (36)
former	1918 (44)	371 (42)	362 (42)	369 (42)	376 (42)	440 (49)
current	673 (15)	157 (18)	138 (16)	108 (12)	140 (16)	130 (15)
Medication Use						
RASi	3713 (84)	739 (84)	724 (83)	711 (81)	778 (86)	761 (85)
Statins	2155 (49)	349 (40)	391 (45)	403 (46)	485 (54)	527 (59)
Anti-platelet agents	1564 (36)	180 (20)	253 (29)	332 (38)	400 (44)	399 (45)
Beta-blockers	2480 (57)	263 (30)	376 (43)	499 (57)	624 (69)	718 (80)
MRA	364 (8)	53 (6)	50 (6)	53 (6)	79 (9)	129 (14)

Continuous variables are presented as mean and standard deviation or median and interquartile range.
Categorical variables are presented as numbers with percentages in the overall study population.
eGFR=estimated glomerular filtration rate, UACR=urinary albumin excretion rate, hsCRP=high sensitive C-reactive protein, LDL=low density lipoprotein, HDL=high density lipoprotein, BP=blood pressure, BMI=body mass index, CVD=cardiovascular disease, RASi=renin angiotensin system inhibitor, MRA=mineralocorticoid receptor antagonist

Table S3 Models A and Models B for Copeptin (showing all included variables)

		Non-cardiovascular death	Cardiovascular death	Major adverse cardiovascular event	Hospitalization for Heart Failure
		HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
Adjusted model A[a]					
Copeptin HR per SD increase		1.31 [1.24; 1.39]	1.39 [1.28; 1.49]	1.24 [1.16; 1.32]	1.35 [1.28; 1.43]
Age (ys)		1.07 [1.06; 1.09]	1.08 [1.06; 1.11]	1.05 [1.04; 1.06]	1.08 [1.06; 1.09]
gender	female	0.70 [0.56; 0.87]	0.47 [0.32; 0.69]	0.54 [0.44; 0.66]	0.80 [0.64; 0.99]
Copeptin (pmol/l)	Q2	1.27 [0.82; 1.96]	2.29 [1.02; 5.17]	1.31 [0.94; 1.85]	1.42 [0.90; 2.25]
	Q3	2.10 [1.40; 3.13]	2.49 [1.12; 5.54]	1.29 [0.92; 1.82]	2.27 [1.48; 3.47]
	Q4	2.35 [1.58; 3.49]	3.68 [1.70; 7.95]	1.81 [1.30; 2.51]	2.60 [1.72; 3.95]
	Q5	3.70 [2.54; 5.41]	8.08 [3.86; 16.87]	2.54 [1.86; 3.48]	4.72 [3.18; 7.02]
Age (ys)		1.07 [1.06; 1.08]	1.08 [1.06; 1.10]	1.05 [1.04; 1.06]	1.07 [1.06; 1.09]
gender	female	0.76 [0.60; 0.95]	0.54 [0.38; 0.78]	0.57 [0.46; 0.70]	0.87 [0.70; 1.09]
Adjusted model B[b]					
Copeptin HR per SD increase		1.19 [1.08; 1.32]	1.29 [1.12; 1.48]	1.10 [1.00; 1.21]	1.30 [1.18; 1.43]
Age (ys)		1.06 [1.04; 1.08]	1.05 [1.02; 1.08]	1.03 [1.02; 1.04]	1.06 [1.04; 1.08]
gender	female	0.79 [0.62; 1.02]	0.56 [0.36; 0.84]	0.60 [0.48; 0.76]	0.89 [0.70; 1.14]
Heart Failure	unknown	1.33 [0.86; 2.06]	0.79 [0.36; 1.72]	1.10 [0.74; 1.63]	1.87 [1.24; 2.80]
	yes	1.93 [1.52; 2.44]	1.50 [1.06; 2.11]	1.31 [1.06; 1.62]	2.17 [1.72; 2.74]
BMI (kg/m²)		1.00 [0.98; 1.02]	1.00 [0.98; 1.03]	1.00 [0.98; 1.02]	1.03 [1.02; 1.05]
Systolic BP (mmHg)		1.00 [1.00; 1.01]	1.00 [1.00; 1.01]	1.00 [1.00; 1.01]	1.00 [1.00; 1.01]
LDL cholesterol (mg/dl)		1.00 [1.00; 1.00]	1.00 [1.00; 1.00]	1.00 [1.00; 1.00]	1.00 [1.00; 1.00]
Diabetes	yes	1.78 [1.42; 2.23]	2.44 [1.70; 3.49]	1.71 [1.40; 2.08]	1.72 [1.36; 2.18]
eGFR (ml/min per 1.73 m²)		0.99 [0.98; 1.00]	0.98 [0.96; 0.99]	0.99 [0.98; 0.99]	0.99 [0.98; 1.00]
UACR (mg/g)		1.00 [1.00; 1.00]	1.00 [1.00; 1.00]	1.00 [1.00; 1.00]	1.00 [1.00; 1.00]
Previous CVD	yes	1.23 [0.96; 1.56]	2.03 [1.42; 2.90]	1.73 [1.40; 2.14]	1.62 [1.28; 2.05]
Smoking history	current smoker	2.71 [1.98; 3.70]	1.27 [0.76; 2.11]	1.39 [1.06; 1.84]	1.77 [1.28; 2.45]
	former smoker	1.34 [1.04; 1.72]	0.95 [0.66; 1.35]	0.97 [0.78; 1.19]	1.01 [0.78; 1.30]
hsCRP (mg/dl)		1.02 [1.00; 1.02]	1.02 [1.00; 1.03]	1.01 [1.00; 1.02]	1.01 [1.00; 1.02]
Statins	yes	0.70 [0.56; 0.89]	0.74 [0.52; 1.06]	0.93 [0.76; 1.14]	0.88 [0.70; 1.13]
RASi	yes	0.76 [0.58; 1.02]	1.40 [0.80; 2.45]	1.14 [0.84; 1.53]	1.27 [0.88; 1.82]
Anti-platelet agents	yes	0.83 [0.66; 1.05]	1.08 [0.76; 1.53]	1.39 [1.12; 1.71]	0.84 [0.66; 1.06]
Beta-blockers	yes	1.18 [0.92; 1.49]	1.40 [0.94; 2.08]	1.25 [1.02; 1.55]	1.72 [1.32; 2.26]
MRA	yes	1.08 [0.78; 1.50]	2.23 [1.50; 3.31]	1.14 [0.84; 1.53]	1.73 [1.30; 2.30]
regional center	AA	1.02 [0.68; 1.54]	0.58 [0.30; 1.16]	0.60 [0.40; 0.91]	0.59 [0.38; 0.93]
	BE	1.07 [0.72; 1.59]	0.64 [0.34; 1.17]	1.03 [0.74; 1.44]	0.68 [0.46; 1.01]
	FR	1.06 [0.66; 1.67]	1.14 [0.62; 2.13]	0.79 [0.52; 1.20]	0.67 [0.40; 1.10]
	HA	0.97 [0.60; 1.56]	0.59 [0.28; 1.27]	0.79 [0.52; 1.22]	0.52 [0.30; 0.88]
	HE	1.49 [1.00; 2.21]	0.29 [0.10; 0.82]	0.62 [0.40; 0.96]	0.47 [0.26; 0.81]
	JE	0.89 [0.62; 1.30]	0.80 [0.48; 1.35]	0.90 [0.66; 1.23]	0.79 [0.56; 1.11]
	MU	0.78 [0.50; 1.23]	0.98 [0.54; 1.76]	0.91 [0.64; 1.31]	0.87 [0.58; 1.31]
	WU	0.93 [0.66; 1.30]	0.95 [0.60; 1.48]	1.14 [0.88; 1.49]	0.77 [0.56; 1.06]
Copeptin (pmol/l)	Q2	1.02 [0.64; 1.64]	1.31 [0.56; 3.02]	1.05 [0.74; 1.51]	1.06 [0.66; 1.72]

	Q3	1.58 [1.02; 2.44]	1.31 [0.58; 2.98]	0.90 [0.62; 1.29]	1.47 [0.94; 2.32]
	Q4	1.53 [0.98; 2.37]	1.94 [0.88; 4.30]	1.28 [0.90; 1.83]	1.56 [0.98; 2.46]
	Q5	2.01 [1.30; 3.14]	2.91 [1.32; 6.44]	1.39 [0.96; 2.01]	2.36 [1.50; 3.74]
Age (ys)		1.06 [1.04; 1.08]	1.05 [1.02; 1.08]	1.03 [1.02; 1.04]	1.06 [1.04; 1.08]
gender	female	0.82 [0.64; 1.06]	0.59 [0.38; 0.90]	0.62 [0.48; 0.78]	0.91 [0.70; 1.17]
Heart Failure	unknown	1.35 [0.88; 2.09]	0.78 [0.36; 1.70]	1.09 [0.74; 1.61]	1.90 [1.26; 2.85]
	yes	1.93 [1.52; 2.44]	1.48 [1.06; 2.09]	1.31 [1.06; 1.61]	2.18 [1.72; 2.75]
BMI (kg/m²)		1.00 [0.98; 1.02]	1.00 [0.98; 1.03]	1.00 [0.98; 1.02]	1.03 [1.02; 1.05]
Systolic BP (mmHg)		1.00 [1.00; 1.01]	1.00 [1.00; 1.01]	1.00 [1.00; 1.01]	1.00 [1.00; 1.01]
LDL cholesterol (mg/dl)		1.00 [1.00; 1.00]	1.00 [1.00; 1.00]	1.00 [1.00; 1.00]	1.00 [1.00; 1.00]
Diabetes	yes	1.73 [1.38; 2.17]	2.30 [1.60; 3.31]	1.68 [1.38; 2.05]	1.66 [1.32; 2.11]
eGFR (ml/min per 1.73 m²)		0.99 [0.98; 1.00]	0.98 [0.96; 0.99]	0.99 [0.98; 0.99]	0.99 [0.98; 1.00]
UACR (mg/g)		1.00 [1.00; 1.00]	1.00 [1.00; 1.00]	1.00 [1.00; 1.00]	1.00 [1.00; 1.00]
Previous CVD	yes	1.21 [0.96; 1.54]	1.99 [1.40; 2.84]	1.73 [1.40; 2.14]	1.58 [1.24; 2.01]
Smoking history	current smoker	2.63 [1.92; 3.59]	1.24 [0.74; 2.05]	1.38 [1.04; 1.83]	1.72 [1.24; 2.38]
	former smoker	1.34 [1.04; 1.73]	0.96 [0.68; 1.37]	0.97 [0.78; 1.19]	1.01 [0.80; 1.30]
hsCRP (mg/dl)		1.02 [1.00; 1.02]	1.02 [1.00; 1.03]	1.01 [1.00; 1.02]	1.01 [1.00; 1.02]
Statins	yes	0.71 [0.56; 0.90]	0.75 [0.52; 1.07]	0.92 [0.74; 1.13]	0.90 [0.70; 1.15]
RASi	yes	0.75 [0.56; 1.00]	1.38 [0.80; 2.42]	1.14 [0.84; 1.54]	1.24 [0.86; 1.78]
Anti-platelet agents	yes	0.84 [0.66; 1.06]	1.12 [0.80; 1.58]	1.41 [1.14; 1.75]	0.85 [0.68; 1.07]
Beta-blockers	yes	1.16 [0.92; 1.47]	1.37 [0.92; 2.03]	1.24 [1.00; 1.54]	1.69 [1.30; 2.22]
MRA	yes	1.07 [0.78; 1.49]	2.14 [1.44; 3.18]	1.12 [0.84; 1.51]	1.70 [1.28; 2.26]
regional center	AA	1.01 [0.66; 1.52]	0.57 [0.30; 1.14]	0.59 [0.38; 0.89]	0.59 [0.38; 0.92]
	BE	1.06 [0.72; 1.56]	0.63 [0.34; 1.15]	1.02 [0.72; 1.42]	0.68 [0.46; 1.00]
	FR	1.03 [0.64; 1.63]	1.08 [0.58; 2.01]	0.78 [0.52; 1.19]	0.63 [0.38; 1.04]
	HA	0.95 [0.58; 1.53]	0.57 [0.26; 1.24]	0.78 [0.50; 1.21]	0.51 [0.30; 0.86]
	HE	1.46 [0.98; 2.16]	0.27 [0.10; 0.77]	0.60 [0.38; 0.94]	0.45 [0.26; 0.78]
	JE	0.88 [0.60; 1.27]	0.77 [0.46; 1.30]	0.89 [0.64; 1.22]	0.77 [0.54; 1.09]
	MU	0.78 [0.50; 1.24]	0.95 [0.52; 1.72]	0.90 [0.62; 1.30]	0.87 [0.58; 1.30]
	WU	0.94 [0.68; 1.31]	0.94 [0.60; 1.47]	1.13 [0.86; 1.48]	0.77 [0.56; 1.06]

Results are presented as hazard ratios with 95%-confidence intervals given in parentheses

[a] model A: all models adjusted for age, gender,

[b] model B: all models adjusted for age, gender, BMI, systolic BP, LDL cholesterol, diabetes, eGFR, UACR, smoking, hs-CRP, preexisting CVD, history of heart failure, CV medication, i.e. use of statins, RASi, anti-platelet agents, beta-blockers, and mineralocorticoid receptor antagonists and regional center.

[c] SD Copeptin 11.7 pmol/l (whole population),

[d] SD for MR-proANP 109.04 pmol/l (whole population),

[e] SD for NT-proBNP 1073.4 pg/ml (whole population)

Table S4 Models A and Models B for MR-proANP (showing all included variables)

		Non-cardiovascular death	Cardiovascular death	Major adverse cardiovascular event	Hospitalization for Heart Failure
		HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
Adjusted model A[a]					
MR-proANP HR per SD increase		1.51 [1.42; 1.60]	1.68 [1.56; 1.82]	1.40 [1.32; 1.49]	1.68 [1.58; 1.79]
Age (ys)		1.06 [1.04; 1.07]	1.06 [1.04; 1.08]	1.04 [1.04; 1.05]	1.06 [1.04; 1.07]
gender	female	0.65 [0.52; 0.81]	0.45 [0.32; 0.65]	0.51 [0.42; 0.62]	0.75 [0.60; 0.93]
MR-proANP (pmol/l)	Q2	0.98 [0.62; 1.58]	1.17 [0.52; 2.65]	0.91 [0.62; 1.31]	1.08 [0.60; 1.93]
	Q3	1.45 [0.94; 2.23]	1.62 [0.76; 3.44]	1.44 [1.04; 2.02]	2.25 [1.36; 3.76]
	Q4	1.91 [1.26; 2.89]	1.92 [0.92; 3.99]	1.51 [1.08; 2.11]	3.11 [1.90; 5.09]
	Q5	4.20 [2.84; 6.20]	7.30 [3.74; 14.24]	2.83 [2.08; 3.88]	7.77 [4.84; 12.48]
Age (ys)		1.05 [1.04; 1.06]	1.05 [1.04; 1.08]	1.04 [1.02; 1.05]	1.05 [1.04; 1.06]
gender	female	0.63 [0.52; 0.78]	0.43 [0.30; 0.61]	0.50 [0.40; 0.61]	0.71 [0.58; 0.88]
Adjusted model B[b]					
MR-proANP HR per SD increase		1.41 [1.30; 1.52]	1.54 [1.38; 1.71]	1.25 [1.16; 1.36]	1.58 [1.46; 1.71]
Age (ys)		1.06 [1.04; 1.07]	1.05 [1.02; 1.07]	1.03 [1.02; 1.04]	1.05 [1.04; 1.07]
gender	female	0.75 [0.58; 0.95]	0.52 [0.34; 0.79]	0.59 [0.46; 0.73]	0.83 [0.64; 1.06]
Heart Failure	unknown	1.24 [0.80; 1.92]	0.81 [0.38; 1.76]	1.11 [0.76; 1.65]	1.87 [1.24; 2.8]
	yes	1.77 [1.40; 2.24]	1.45 [1.04; 2.03]	1.27 [1.02; 1.57]	2.04 [1.62; 2.57]
BMI (kg/m²)		1.01 [1.00; 1.03]	1.02 [0.98; 1.05]	1.00 [0.98; 1.02]	1.05 [1.02; 1.06]
Systolic BP (mmHg)		1.00 [1.00; 1.01]	1.00 [1.00; 1.01]	1.00 [1.00; 1.01]	1.00 [1.00; 1.00]
LDL cholesterol (mg/dl)		1.00 [1.00; 1.00]	1.00 [1.00; 1.00]	1.00 [1.00; 1.00]	1.00 [1.00; 1.00]
Diabetes	yes	1.91 [1.52; 2.40]	2.71 [1.90; 3.87]	1.75 [1.44; 2.14]	1.96 [1.56; 2.47]
eGFR (ml/min per 1.73 m²)		0.99 [0.98; 1.00]	0.98 [0.98; 1.00]	0.99 [0.98; 1.00]	1.00 [0.98; 1.01]
UACR (mg/g)		1.00 [1.00; 1.00]	1.00 [1.00; 1.00]	1.00 [1.00; 1.00]	1.00 [1.00; 1.00]
Previous CVD	yes	1.11 [0.88; 1.42]	1.78 [1.24; 2.55]	1.64 [1.32; 2.03]	1.44 [1.12; 1.83]
Smoking history	current smoker	2.85 [2.08; 3.89]	1.38 [0.82; 2.30]	1.43 [1.08; 1.89]	1.92 [1.38; 2.67]
	former smoker	1.33 [1.04; 1.71]	0.92 [0.64; 1.31]	0.95 [0.78; 1.18]	0.98 [0.76; 1.25]
hsCRP (mg/dl)		1.01 [1.00; 1.02]	1.01 [1.00; 1.03]	1.01 [1.00; 1.02]	1.01 [1.00; 1.02]
Statins	yes	0.70 [0.56; 0.89]	0.72 [0.50; 1.03]	0.92 [0.74; 1.13]	0.88 [0.68; 1.12]
RASi	yes	0.76 [0.58; 1.01]	1.43 [0.82; 2.49]	1.15 [0.86; 1.54]	1.30 [0.90; 1.87]
Anti-platelet agents	yes	0.93 [0.74; 1.17]	1.21 [0.86; 1.71]	1.45 [1.18; 1.78]	0.94 [0.74; 1.19]
Beta-blockers	yes	0.98 [0.76; 1.25]	1.09 [0.74; 1.63]	1.12 [0.90; 1.39]	1.35 [1.02; 1.77]
MRA	yes	1.04 [0.76; 1.45]	2.10 [1.42; 3.11]	1.11 [0.82; 1.49]	1.68 [1.26; 2.23]
regional center	AA	1.07 [0.70; 1.63]	0.68 [0.34; 1.35]	0.63 [0.40; 0.96]	0.67 [0.42; 1.06]
	BE	1.20 [0.82; 1.78]	0.81 [0.44; 1.49]	1.13 [0.80; 1.58]	0.83 [0.56; 1.23]
	FR	1.18 [0.74; 1.87]	1.42 [0.76; 2.67]	0.86 [0.56; 1.30]	0.80 [0.48; 1.33]
	HA	1.04 [0.64; 1.68]	0.66 [0.30; 1.42]	0.85 [0.54; 1.30]	0.61 [0.36; 1.03]
	HE	1.54 [1.04; 2.28]	0.30 [0.10; 0.84]	0.64 [0.40; 0.99]	0.52 [0.30; 0.90]
	JE	0.97 [0.66; 1.40]	0.94 [0.56; 1.60]	0.96 [0.70; 1.32]	0.93 [0.66; 1.32]
	MU	0.83 [0.52; 1.31]	1.18 [0.64; 2.15]	0.96 [0.66; 1.39]	0.97 [0.64; 1.47]
	WU	0.99 [0.70; 1.39]	1.05 [0.66; 1.65]	1.21 [0.92; 1.58]	0.88 [0.64; 1.20]

MR-proANP (pmol/l)	Q2	0.87 [0.54; 1.42]	1.14 [0.50; 2.57]	0.80 [0.54; 1.17]	1.23 [0.68; 2.25]
	Q3	1.14 [0.72; 1.80]	1.26 [0.60; 2.71]	1.15 [0.80; 1.63]	2.08 [1.20; 3.60]
	Q4	1.47 [0.94; 2.28]	1.13 [0.52; 2.42]	1.00 [0.70; 1.43]	2.74 [1.60; 4.69]
	Q5	2.72 [1.76; 4.20]	3.70 [1.82; 7.51]	1.66 [1.16; 2.36]	6.03 [3.54; 10.28]
Age (ys)		1.05 [1.04; 1.07]	1.04 [1.02; 1.07]	1.03 [1.02; 1.04]	1.05 [1.04; 1.07]
gender	female	0.74 [0.58; 0.95]	0.51 [0.34; 0.76]	0.58 [0.46; 0.73]	0.81 [0.64; 1.04]
Heart Failure	unknown	1.27 [0.82; 1.97]	0.79 [0.36; 1.72]	1.11 [0.76; 1.65]	1.76 [1.18; 2.64]
	yes	1.80 [1.42; 2.28]	1.49 [1.06; 2.10]	1.29 [1.04; 1.59]	2.05 [1.62; 2.58]
BMI (kg/m²)		1.01 [0.98; 1.03]	1.01 [0.98; 1.03]	1.00 [0.98; 1.02]	1.04 [1.02; 1.06]
Systolic BP (mmHg)		1.00 [1.00; 1.01]	1.00 [1.00; 1.01]	1.00 [1.00; 1.01]	1.00 [1.00; 1.00]
LDL cholesterol (mg/dl)		1.00 [1.00; 1.00]	1.00 [1.00; 1.00]	1.00 [1.00; 1.00]	1.00 [1.00; 1.00]
Diabetes	yes	1.86 [1.48; 2.33]	2.58 [1.80; 3.69]	1.74 [1.42; 2.12]	1.86 [1.48; 2.35]
eGFR (ml/min per 1.73 m²)		0.99 [0.98; 1.00]	0.98 [0.96; 0.99]	0.99 [0.98; 1.00]	1.00 [1.00; 1.01]
UACR (mg/g)		1.00 [1.00; 1.00]	1.00 [1.00; 1.00]	1.00 [1.00; 1.00]	1.00 [1.00; 1.00]
Previous CVD	yes	1.11 [0.88; 1.42]	1.82 [1.26; 2.60]	1.65 [1.34; 2.05]	1.40 [1.10; 1.78]
Smoking history	current smoker	2.85 [2.08; 3.90]	1.29 [0.78; 2.16]	1.42 [1.08; 1.88]	1.96 [1.40; 2.72]
	former smoker	1.31 [1.02; 1.69]	0.89 [0.62; 1.28]	0.96 [0.78; 1.18]	1.01 [0.78; 1.29]
hsCRP (mg/dl)		1.01 [1.00; 1.02]	1.02 [1.00; 1.03]	1.01 [1.00; 1.02]	1.01 [1.00; 1.02]
Statins	yes	0.71 [0.56; 0.90]	0.74 [0.52; 1.06]	0.92 [0.74; 1.13]	0.89 [0.70; 1.13]
RASi	yes	0.79 [0.60; 1.06]	1.50 [0.86; 2.62]	1.16 [0.86; 1.56]	1.36 [0.96; 1.95]
Anti-platelet agents	yes	0.90 [0.72; 1.13]	1.24 [0.88; 1.75]	1.45 [1.18; 1.79]	0.96 [0.76; 1.21]
Beta-blockers	yes	0.96 [0.74; 1.23]	1.09 [0.72; 1.64]	1.13 [0.90; 1.42]	1.22 [0.92; 1.61]
MRA	yes	1.05 [0.76; 1.46]	2.24 [1.50; 3.32]	1.12 [0.84; 1.51]	1.62 [1.22; 2.16]
regional center	AA	1.04 [0.68; 1.59]	0.60 [0.30; 1.18]	0.60 [0.40; 0.92]	0.60 [0.38; 0.94]
	BE	1.09 [0.74; 1.61]	0.65 [0.36; 1.19]	1.06 [0.76; 1.48]	0.71 [0.48; 1.05]
	FR	1.06 [0.68; 1.68]	1.16 [0.62; 2.17]	0.80 [0.52; 1.22]	0.66 [0.40; 1.10]
	HA	1.00 [0.62; 1.61]	0.63 [0.30; 1.37]	0.81 [0.52; 1.25]	0.53 [0.32; 0.90]
	HE	1.43 [0.96; 2.13]	0.27 [0.10; 0.77]	0.60 [0.38; 0.94]	0.44 [0.26; 0.77]
	JE	0.92 [0.64; 1.34]	0.84 [0.50; 1.41]	0.92 [0.66; 1.26]	0.86 [0.60; 1.21]
	MU	0.82 [0.52; 1.30]	1.15 [0.64; 2.08]	0.93 [0.64; 1.35]	0.92 [0.62; 1.39]
	WU	0.92 [0.66; 1.28]	0.92 [0.58; 1.44]	1.15 [0.88; 1.51]	0.77 [0.56; 1.06]

Results are presented as hazard ratios with 95%-confidence intervals given in parentheses

[a] model A: all models adjusted for age, gender,

[b] model B: all models adjusted for age, gender, BMI, systolic BP, LDL cholesterol, diabetes, eGFR, UACR, smoking, hs-CRP, preexisting CVD, history of heart failure, CV medication, i.e. use of statins, RASi, anti-platelet agents, beta-blockers, and mineralocorticoid receptor antagonists and regional center.

[c] SD Copeptin 11.7 pmol/l (whole population),

[d] SD for MR-proANP 109.04 pmol/l (whole population),

[e] SD for NT-proBNP 1073.4 pg/ml (whole population)

Table S5 Models A and Models B for NT-proBNP (showing all included variables)

		Non-cardiovascular death	Cardiovascular death	Major adverse cardiovascular event	Hospitalization for Heart Failure
		HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
Adjusted model A[a]					
NT-proBNP HR per SD increase		1.20 [1.16; 1.24]	1.28 [1.24; 1.32]	1.23 [1.20; 1.27]	1.38 [1.32; 1.42]
Age (ys)		1.07 [1.06; 1.08]	1.08 [1.06; 1.10]	1.05 [1.04; 1.06]	1.07 [1.06; 1.09]
gender	female	0.60 [0.48; 0.75]	0.38 [0.26; 0.54]	0.49 [0.40; 0.60]	0.69 [0.56; 0.86]
NT-proBNP (pg/ml)	Q2	1.67 [1.00; 2.80]	1.19 [0.50; 2.85]	1.27 [0.86; 1.87]	2.40 [1.16; 4.97]
	Q3	2.06 [1.24; 3.39]	0.94 [0.38; 2.34]	1.45 [1.00; 2.11]	3.30 [1.64; 6.63]
	Q4	3.35 [2.10; 5.38]	2.56 [1.20; 5.48]	2.45 [1.72; 3.47]	7.66 [3.96; 14.81]
	Q5	7.59 [4.82; 11.96]	11.26 [5.60; 22.69]	4.56 [3.26; 6.36]	21.96 [11.52; 41.82]
Age (ys)		1.05 [1.04; 1.06]	1.05 [1.02; 1.07]	1.03 [1.02; 1.05]	1.04 [1.02; 1.06]
gender	female	0.60 [0.48; 0.75]	0.42 [0.30; 0.60]	0.48 [0.40; 0.58]	0.66 [0.54; 0.82]
Adjusted model B[b]					
NT-proBNP HR per SD increase		1.14 [1.08; 1.19]	1.25 [1.18; 1.32]	1.17 [1.12; 1.23]	1.32 [1.26; 1.37]
Age (ys)		1.06 [1.04; 1.08]	1.05 [1.02; 1.08]	1.03 [1.02; 1.04]	1.06 [1.04; 1.08]
gender	female	0.72 [0.56; 0.92]	0.47 [0.30; 0.70]	0.57 [0.46; 0.72]	0.77 [0.60; 0.99]
Heart Failure	unknown	1.24 [0.80; 1.94]	0.71 [0.32; 1.58]	1.11 [0.76; 1.64]	1.87 [1.24; 2.80]
	yes	1.90 [1.50; 2.41]	1.46 [1.04; 2.04]	1.26 [1.02; 1.56]	2.11 [1.68; 2.66]
BMI (kg/m²)		1.01 [0.98; 1.03]	1.02 [0.98; 1.05]	1.01 [0.98; 1.02]	1.05 [1.02; 1.07]
Systolic BP (mmHg)		1.00 [1.00; 1.01]	1.00 [1.00; 1.01]	1.00 [1.00; 1.01]	1.00 [1.00; 1.00]
LDL cholesterol (mg/dl)		1.00 [1.00; 1.00]	1.00 [1.00; 1.00]	1.00 [1.00; 1.00]	1.00 [1.00; 1.00]
Diabetes	yes	1.85 [1.48; 2.32]	2.55 [1.78; 3.65]	1.69 [1.38; 2.06]	1.76 [1.40; 2.22]
eGFR (ml/min per 1.73 m²)		0.98 [0.98; 0.99]	0.98 [0.96; 0.99]	0.99 [0.98; 0.99]	0.99 [0.98; 1.00]
UACR (mg/g)		1.00 [1.00; 1.00]	1.00 [1.00; 1.00]	1.00 [1.00; 1.00]	1.00 [1.00; 1.00]
Previous CVD	yes	1.19 [0.94; 1.51]	1.87 [1.30; 2.68]	1.65 [1.34; 2.04]	1.49 [1.16; 1.89]
Smoking history	current smoker	2.63 [1.92; 3.6]	1.18 [0.70; 1.97]	1.36 [1.02; 1.80]	1.71 [1.22; 2.38]
	former smoker	1.31 [1.02; 1.69]	0.88 [0.62; 1.26]	0.94 [0.76; 1.16]	0.99 [0.76; 1.27]
hsCRP (mg/dl)		1.01 [1.00; 1.02]	1.01 [1.00; 1.02]	1.01 [1.00; 1.02]	1.01 [1.00; 1.02]
Statins	yes	0.72 [0.58; 0.92]	0.78 [0.54; 1.12]	0.94 [0.76; 1.17]	0.92 [0.72; 1.18]
RASi	yes	0.76 [0.56; 1.01]	1.45 [0.82; 2.54]	1.14 [0.84; 1.53]	1.28 [0.90; 1.84]
Anti-platelet agents	yes	0.85 [0.68; 1.07]	1.14 [0.80; 1.61]	1.43 [1.16; 1.76]	0.92 [0.72; 1.17]
Beta-blockers	yes	1.12 [0.88; 1.42]	1.24 [0.84; 1.84]	1.19 [0.96; 1.47]	1.55 [1.18; 2.03]
MRA	yes	1.07 [0.78; 1.49]	2.11 [1.42; 3.12]	1.09 [0.82; 1.47]	1.59 [1.20; 2.12]
regional center	AA	1.02 [0.68; 1.55]	0.65 [0.32; 1.29]	0.64 [0.42; 0.99]	0.64 [0.40; 1.01]
	BE	1.16 [0.78; 1.71]	0.81 [0.44; 1.50]	1.17 [0.84; 1.64]	0.82 [0.56; 1.21]
	FR	1.10 [0.70; 1.74]	1.36 [0.72; 2.56]	0.87 [0.56; 1.32]	0.74 [0.44; 1.23]
	HA	1.05 [0.64; 1.69]	0.73 [0.34; 1.60]	0.88 [0.58; 1.36]	0.62 [0.36; 1.05]
	HE	1.61 [1.08; 2.39]	0.36 [0.12; 1.01]	0.68 [0.44; 1.06]	0.55 [0.32; 0.96]
	JE	0.94 [0.64; 1.37]	0.95 [0.56; 1.62]	0.98 [0.72; 1.35]	0.89 [0.64; 1.26]
	MU	0.83 [0.52; 1.31]	1.18 [0.64; 2.14]	0.99 [0.68; 1.43]	0.96 [0.64; 1.45]
	WU	0.97 [0.70; 1.35]	1.06 [0.68; 1.66]	1.23 [0.94; 1.61]	0.81 [0.60; 1.11]

NT-proBNP (pg/ml)	Q2	1.80 [1.02; 3.16]	0.98 [0.40; 2.35]	1.08 [0.72; 1.60]	1.87 [0.90; 3.94]
	Q3	2.11 [1.22; 3.66]	0.66 [0.26; 1.67]	1.09 [0.74; 1.61]	2.58 [1.26; 5.26]
	Q4	2.99 [1.76; 5.07]	1.44 [0.66; 3.18]	1.61 [1.10; 2.33]	5.21 [2.64; 10.25]
	Q5	5.73 [3.38; 9.68]	4.99 [2.36; 10.53]	2.56 [1.76; 3.72]	12.72 [6.50; 24.88]
Age (ys)		1.05 [1.04; 1.07]	1.04 [1.02; 1.07]	1.02 [1.02; 1.04]	1.04 [1.02; 1.06]
gender	female	0.68 [0.54; 0.87]	0.48 [0.32; 0.72]	0.56 [0.44; 0.70]	0.72 [0.56; 0.92]
Heart Failure	unknown	1.22 [0.80; 1.90]	0.75 [0.34; 1.64]	1.06 [0.72; 1.56]	1.69 [1.12; 2.53]
	yes	1.66 [1.32; 2.10]	1.32 [0.94; 1.86]	1.20 [0.98; 1.49]	1.85 [1.46; 2.33]
BMI (kg/m²)		1.01 [1.00; 1.03]	1.01 [0.98; 1.04]	1.00 [0.98; 1.02]	1.04 [1.02; 1.06]
Systolic BP (mmHg)		1.00 [1.00; 1.00]	1.00 [1.00; 1.01]	1.00 [1.00; 1.01]	1.00 [1.00; 1.00]
LDL cholesterol (mg/dl)		1.00 [1.00; 1.00]	1.00 [1.00; 1.00]	1.00 [1.00; 1.00]	1.00 [1.00; 1.00]
Diabetes	yes	1.79 [1.42; 2.24]	2.43 [1.70; 3.47]	1.72 [1.40; 2.09]	1.79 [1.42; 2.25]
eGFR (ml/min per 1.73 m²)		0.99 [0.98; 1.00]	0.98 [0.96; 0.99]	0.99 [0.98; 1.00]	1.00 [0.98; 1.00]
UACR (mg/g)		1.00 [1.00; 1.00]	1.00 [1.00; 1.00]	1.00 [1.00; 1.00]	1.00 [1.00; 1.00]
Previous CVD	yes	1.02 [0.80; 1.31]	1.58 [1.10; 2.27]	1.53 [1.24; 1.90]	1.23 [0.96; 1.57]
Smoking history	current smoker	2.55 [1.86; 3.49]	1.16 [0.70; 1.93]	1.33 [1.00; 1.75]	1.63 [1.18; 2.26]
	former smoker	1.28 [1.00; 1.65]	0.88 [0.62; 1.26]	0.94 [0.76; 1.17]	0.96 [0.74; 1.24]
hsCRP (mg/dl)		1.01 [1.00; 1.02]	1.01 [1.00; 1.03]	1.01 [1.00; 1.02]	1.01 [1.00; 1.02]
Statins	yes	0.71 [0.56; 0.90]	0.75 [0.52; 1.08]	0.92 [0.74; 1.13]	0.86 [0.68; 1.10]
RASi	yes	0.79 [0.60; 1.05]	1.53 [0.88; 2.67]	1.17 [0.88; 1.58]	1.43 [1.00; 2.05]
Anti-platelet agents	yes	0.91 [0.72; 1.15]	1.33 [0.94; 1.87]	1.47 [1.20; 1.81]	1.01 [0.80; 1.28]
Beta-blockers	yes	0.91 [0.72; 1.17]	1.01 [0.68; 1.52]	1.06 [0.86; 1.33]	1.13 [0.86; 1.49]
MRA	yes	0.96 [0.70; 1.34]	1.88 [1.26; 2.80]	1.03 [0.76; 1.39]	1.42 [1.06; 1.89]
regional center	AA	1.12 [0.74; 1.70]	0.61 [0.30; 1.23]	0.63 [0.42; 0.96]	0.66 [0.42; 1.03]
	BE	1.21 [0.82; 1.78]	0.77 [0.42; 1.41]	1.12 [0.80; 1.57]	0.80 [0.54; 1.17]
	FR	0.98 [0.62; 1.55]	1.01 [0.54; 1.89]	0.74 [0.48; 1.13]	0.58 [0.34; 0.96]
	HA	1.03 [0.64; 1.67]	0.65 [0.30; 1.40]	0.83 [0.54; 1.27]	0.56 [0.32; 0.95]
	HE	1.45 [0.98; 2.16]	0.27 [0.10; 0.78]	0.59 [0.38; 0.93]	0.43 [0.24; 0.75]
	JE	0.92 [0.64; 1.33]	0.83 [0.48; 1.40]	0.92 [0.66; 1.26]	0.83 [0.58; 1.17]
	MU	0.78 [0.50; 1.23]	0.97 [0.54; 1.75]	0.91 [0.62; 1.31]	0.86 [0.58; 1.30]
	WU	0.93 [0.66; 1.31]	0.93 [0.60; 1.46]	1.16 [0.88; 1.51]	0.77 [0.56; 1.06]

Results are presented as hazard ratios with 95%-confidence intervals given in parentheses

[a] model A: all models adjusted for age, gender,

[b] model B: all models adjusted for age, gender, BMI, systolic BP, LDL cholesterol, diabetes, eGFR, UACR, smoking, hs-CRP, preexisting CVD, history of heart failure, CV medication, i.e. use of statins, RASi, anti-platelet agents, beta-blockers, and mineralocorticoid receptor antagonists and regional center.

[c] SD Copeptin 11.7 pmol/l (whole population),

[d] SD for MR-proANP 109.04 pmol/l (whole population),

[e] SD for NT-proBNP 1073.4 pg/ml (whole population)