Supplemental material

Table S1. Characteristics of all included patients grouped according to quartiles of BNP

	BNP (5-49 pg/ml) n=1381	BNP (50-105 pg/ml) n=1383	BNP (106-218 pg/ml) n=1378	BNP (218-4231 pg/ml) n=1383	P value
randomized to lixisenatide	666 (48.2%)	745 (53.9%)	696 (50.5%)	669 (48.4%)	0.009
age (yrs)	56.7 ± 9.3	59.5 ± 9.1	61.3 ± 9.2	63.5 ± 9.7	<0.001
male (%)	1019 (73.8%)	968 (70.0%)	982 (71.3%)	896 (64.8%)	<0.001
BMI (kg/m2)	30.8 ± 5.7	30.3 ± 5.8	29.9 ± 5.6	29.3 ± 5.6	<0.001
Race					0.020
Asian	204 (14.8%)	186 (13.4%)	183 (13.3%)	157 (11.4%)	
Black	57 (4.1%)	44 (3.2%)	33 (2.4%)	55 (4.0%)	
Other	102 (7.4%)	115 (8.3%)	117 (8.5%)	137 (9.9%)	
White	1018 (73.7%)	1038 (75.1%)	1045 (75.8%)	1034 (74.8%)	
ethnicity – hispanic	375 (27.2%)	407 (29.4%)	413 (30.0%)	451 (32.6%)	0.019
Region					<0.001
Africa/Near East	86 (6.2%)	71 (5.1%)	58 (4.2%)	54 (3.9%)	
Asia Pacific	184 (13.3%)	175 (12.7%)	172 (12.5%)	138 (10.0%)	
Eastern Europe	290 (21.0%)	332 (24.0%)	377 (27.4%)	414 (29.9%)	
North America	219 (15.9%)	181 (13.1%)	181 (13.1%)	135 (9.8%)	
South and Centr. America	421 (30.5%)	438 (31.7%)	449 (32.6%)	516 (37.3%)	
Western Europe	181 (13.1%)	186 (13.4%)	141 (10.2%)	126 (9.1%)	
Systolic blood pressure (mmHg)	128.4 ± 15.1	129.9 ± 17.0	130.0 ± 17.8	129.9 ± 19.3	0.035
Diastolic blood pressure (mmHg)	78.0 ± 9.2	77.0 ± 9.6	77.2 ± 10.5	76.5 ± 10.8	0.003
heart rate (bpm)	70.5 ± 9.9	69.0 ± 10.3	69.5 ± 10.5	71.3 ± 10.9	<0.001
current smoker	194 (14.0%)	174 (12.6%)	134 (9.7%)	125 (9.0%)	<0.001
former smoker	656 (47.5%)	614 (44.4%)	640 (46.4%)	612 (44.3%)	0.24
Medical history					
MI	252 (18.2%)	299 (21.6%)	314 (22.8%)	393 (28.4%)	<0.001
HF	172 (12.5%)	245 (17.7%)	304 (22.1%)	514 (37.2%)	<0.001
atrial fibrillation/flutter	30 (2.2%)	63 (4.6%)	96 (7.0%)	172 (12.4%)	<0.001
PAD	65 (4.7%)	86 (6.2%)	111 (8.1%)	151 (10.9%)	<0.001
TIA	29 (2.1%)	33 (2.4%)	23 (1.7%)	42 (3.0%)	0.11
ventricular tachycardia	13 (0.9%)	14 (1.0%)	21 (1.5%)	26 (1.9%)	0.10
stroke	45 (3.3%)	68 (4.9%)	67 (4.9%)	112 (8.1%)	<0.001
CABG	51 (3.7%)	101 (7.3%)	157 (11.4%)	151 (10.9%)	<0.001
implanted pacemaker	17 (1.2%)	23 (1.7%)	43 (3.1%)	60 (4.3%)	<0.001
carotid disease	28 (2.0%)	28 (2.0%)	39 (2.8%)	44 (3.2%)	0.12
hypertension	1001 (72.5%)	1068 (77.2%)	1062 (77.1%)	1079 (78.0%)	0.002
Index event					<0.001
STEMI	458 (33.2%)	591 (42.7%)	684 (49.6%)	710 (51.3%)	
NSTEMI	591 (42.8%)	559 (40.4%)	505 (36.6%)	479 (34.6%)	
UAP	332 (24.0%)	233 (16.8%)	189 (13.7%)	194 (14.0%)	
PCI treatment at index ACS	903 (65.4%)	906 (65.5%)	870 (63.1%)	727 (52.6%)	<0.001
insulin-treated	463 (33.5%)	539 (39.0%)	555 (40.3%)	602 (43.5%)	<0.001
duration of diabetes (yrs)	7.8 ± 7.2	9.2 ± 8.2	9.4 ± 8.3	10.7 ± 9.0	<0.001
retinopathy	122 (8.8%)	134 (9.7%)	141 (10.2%)	194 (14.0%)	<0.001
neuropathy	215 (15.6%)	224 (16.2%)	209 (15.2%)	271 (19.6%)	0.007
asthma	33 (2.4%)	53 (3.8%)	36 (2.6%)	32 (2.3%)	0.05
COPD	42 (3.0%)	59 (4.3%)	79 (5.7%)	69 (5.0%)	0.005
HbA1c (%)	7.7 ± 1.3	7.7 ± 1.3	7.7 ± 1.3	7.7 ± 1.2	0.64
HDL(mg/dl)	1.1 ± 0.3	1.1 ± 0.3	1.1 ± 0.3	1.1 ± 0.3	0.58
LDL (mg/dl)	2.1 ± 0.9	2.0 ± 1.0	2.0 ± 0.9	2.0 ± 0.9	0.17
eGFR (ml/min/1.73m^2)	82.6 ± 20.4	78.6 ± 20.8	74.4 ± 21.0	68.1 ± 20.2	<0.001
Albuminuria					<0.001
normoalbuminuria	1134 (82.1%)	1074 (77.7%)	1019 (73.9%)	875 (63.3%)	
microalbuminura	200 (14.5%)	249 (18.0%)	269 (19.5%)	345 (24.9%)	
macroalbuminuria	47 (3.4%)	60 (4.3%)	90 (6.5%)	163 (11.8%)	
Hemoglobin (g/dL)	14.1 ± 1.4	13.9 ± 1.3	13.8 ± 1.4	13.3 ± 1.5	<0.001
Na (mmol/l)	140.2 ± 2.7	140.3 ± 2.8	140.5 ± 3.0	140.5 ± 3.2	0.033
albumin (g/dl)	41.6 ± 3.2	40.9 ± 3.1	40.4 ± 3.5	39.3 ± 4.0	<0.001
CRP (mg/dl)	1.9 (1.8-2.0)	1.9 (1.8-2.0)	2.1 (2.0-2.3)	2.4 (2.3-2.6)	<0.001
BNP (pg/ml)	28 (27-28)	73 (72-74)	150 (148-152)	431 (419-443)	
NT-proBNP (pg/ml)	78 (74-81)	208 (200-215)	470 (453-487)	1541 (1468-1618)	

Table S2. Linear regression of BNP and NT-proBNP with all variables listed in the model

	BNP	P value	NT-proBNP	P value
randomized to lixisenatide	0.0 (-14.0, 14.0)	0.996	16.2 (-66.4, 98.8)	0.701
age (yrs)	1.9 (1.0, 2.9)	<0.001	7.2 (1.6, 12.8)	0.012
male (%)	15.0 (-3.6, 33.6)	0.113	8.2 (-101.4, 117.9)	0.883
BMI (kg/m2)	-7.0 (-8.4, -5.6)	<0.001	-46.8 (-55.2, -38.4)	<0.001
Race				
Black vs. white	19.4 (-20.4, 59.2)	0.340	27.7 (-207.3, 262.8)	0.817
Asian vs. white	-37.9 (-64.6, -11.2)	0.005	-225.1 (-382.7, -67.4)	0.005
other vs. white	-1.0 (-27.3, 25.4)	0.943	127.4 (-28.3, 283.2)	0.109
ethnicity – hispanic	19.8 (0.7, 38.9)	0.042	169.9 (57.0, 282.8)	0.003
Systolic blood pressure (mmHg)	-1.0 (-1.6, -0.5)	<0.001	-5.3 (-8.6, -2.0)	0.002
Diastolic blood pressure (mmHg)	1.3 (0.4, 2.2)	0.007	6.6 (1.1, 12.2)	0.019
heart rate (bpm)	2.1 (1.4, 2.8)	<0.001	13.8 (9.7, 18.0)	<0.001
current smoker	-5.0 (-29.9, 19.8)	0.692	-78.0 (-224.8, 68.8)	0.298
former smoker	3.0 (-13.0, 18.9)	0.717	-31.9 (-126.2, 62.5)	0.508
Medical history				
MI	28.5 (10.4, 46.5)	0.002	35.3 (-71.3, 141.9)	0.516
HF	114.2 (95.7, 132.7)	<0.001	648.8 (539.4, 758.2)	<0.001
atrial fibrillation/flutter	34.2 (4.4., 64.0)	0.024	232.8 (57.0, 408.7)	0.009
PAD	27.7 (-0.5, 56.0)	0.054	290.0 (123.2, 456.7)	0.001
TIA	2.5(-44.8, 49.9)	0.916	-48.3 (-327.7, 231.2)	0.735
ventricular tachycardia	82.3 (20.9, 143.6)	0.009	182.8 (-179.4, 545.0)	0.323
stroke	42.7 (10.6, 74.7)	0.009	105.2 (-84.0, 294.4)	0.276
CABG	-5.0 (-32.3, 22.4)	0.722	-166.9 (-328.3, -5.5)	0.043
implanted pacemaker	6.5 (-39.1, 52.1)	0.781	-20.6 (-289.9, 248.8)	0.881
carotid disease	-28.1 (-74.8, 18.6)	0.239	-120.8 (-396.6, 154.9)	0.390
hypertension	-20.6 (-38.8, -2.3)	0.027	-95.5 (-203.4, 12.4)	0.083
Index event				
STEMI	103.0 (81.2, 124.8)	<0.001	579.6 (451.0, 708.3)	<0.001
NSTEMI	50.0 (28.8, 71.2)	<0.001	294.5 (169.3, 419.6)	<0.001
PCI treatment at index ACS	-41.0 (-56.7, -25.3)	<0.001	-179.6 (-272.2, -86.9)	<0.001
insulin-treated	-12.7 (-29.1, 3.7)	0.130	-17.6 (-114.5, 79.3)	0.722
duration of diabetes (yrs)	-0.1 (-1.1, 1.0)	0.900	-4.6 (-10.7, 1.5)	0.137
Retinopathy	-12.1 (-37.1, 12.9)	0.343	-68.3 (-215.9, 79.2)	0.364
neuropathy	-19.3 (-40.0, 1.4)	0.068	-12.6 (-135.0, 109.8)	0.840
asthma	0.8 (-42.7, 44.4)	0.970	-46.0 (-303.1, 211.1)	0.726
COPD	-2.1 (-32.2, 32.9)	0.905	-67.4 (-274.5, 139.7)	0.523
HbA1c (%)	-3.6 (-9.7, 2.6)	0.254	-51.8 (-88.1, -15.5)	0.005
HDL(mg/dl)	-10.5 (-37.7, 16.7)	0.449	-91.0 (-251.5, 69.5)	0.267
LDL (mg/dl)	1.4 (7.0, 9.7)	0.750	2.0 (-47.3, 51.2)	0.938
eGFR (ml/min/1.73m^2)	-1.8 (-2.1, -1.4)	<0.001	-14.4 (-16.7, -12.2)	<0.001
micro vs. Normoalbuminuria	67.3 (48.7, 85.9)	<0.001	443.7 (334, 553.4)	<0.001
macro vs. Normoalbuminuria	89.6 (57.6, 121.6)	<0.001	661.0 (472.2, 849.9)	<0.001
Hemoglobin (g/dL)	-21.4 (-27.4, -15.4)	<0.001	-98.3 (-133.6, -63.1)	<0.001
Na (mmol/l)	2.4 (-0.2, 4.9)	0.072	-5.1 (-20.3, 10.0)	0.506
albumin (g/dl)	-13.8 (-16.1, -11.5)	<0.001	-85.4 (-99.1, -71.8)	<0.001

Table S3. Variables independently associated with BNP/NT-proBNP concentrations, and corresponding r^2 values for regression models with the 5 listed variables

	1st	**2nd**	**3rd**	**4th**	**5th**
log_2BNP	**Albumin**	**Age (per 10 years)**	**Prior HF**	**STEMI**	**BMI (per 5 kg/m^2)**
(r^2=0.20)	(χ^2:318, coeff:- 0.09)	(χ^2:316, coeff: -0.35)	(χ^2: 312, coeff: 0.78)	(χ^2:227, coeff: 0.57)	(χ^2:80, coeff: -0.15)
log_2NT-proBNP	**eGFR**	**Albumin**	**STEMI**	**BMI (per 5 kg/m^2)**	**prior HF**
(r^2=0.28)	(χ^2:672, coeff: 0.27)	(χ^2:527, coeff: -0.14)	(χ^2: 381, coeff: 0.87)	(χ^2:305, coeff: -0.34)	(χ^2:262, coeff: 0.86)

Table S4. Unadjusted estimates of predictors of outcomes found significant in multivariate models using base variables and BNP (n=5525)

Outcome	1st	2nd	3rd	4th	5th
Death (397 events)	**log_2BNP** HR 1.90 (1.78-2.03)	**AF** HR 2.90 (2.22-3.79)	**NSTEMI** HR 1.53 (1.26-1.86)	**Na*** HR 1.10 (1.05-1.16)	**HR per 10** HR 1.21 (1.11-1.34)
CV death (286 events)	**log_2BNP** HR 2.01 (1.87-2.17)	**HbA1c** HR 1.23 (1.13-1.34)	**AF** HR 3.14 (2.31-4.25)	**NSTEMI** HR 1.61 (1.28-2.04)	**HR per 10** HR 1.25 (1.12-1.40)
MI (473 events)	**prior MI** HR 2.63 (2.19-3.16)	**log_2BNP** HR 1.33 (1.25-1.41)	**NSTEMI** HR 1.90 (1.59-2.28)	**prior stroke** HR 2.50 (1.89-3.33)	**PAD** HR 2.52 (1.94-3.29)
HF (221 events)	**log_2BNP** HR 1.96 (1.80-2.14)	**BMI per 5** HR 1.31 (1.19-1.43)	**HR per 10** HR 1.34 (1.18-1.51)	**prior HF** HR 4.16 (3.19-5.42)	**prior MI** HR 3.09 (2.37-4.03)
Stroke (115 events)	**log_2BNP** HR 1.49 (1.33-1.68)	**prior TIA** HR 4.90 (2.69-8.91)	**macroalbuminuria** HR 3.05 (1.86-4.99)	**Age per 10** HR 1.61 (1.32-1.95)	**LDL per 10** HR 1.07 (1.02-1.12)

Table S5. Unadjusted estimated of predictors of outcomes found significant in multivariate models using base variables and NT-proBNP (n=5525)

Outcome	1st	2nd	3rd	4th	5th
Death (397 events)	**log_2NT-proBNP** HR 1.64 (1.56-1.73)	**NSTEMI** HR 1.53 (1.26-1.86)	**PCI** HR 0.52 (0.42-0.63)	**DBP#** HR 1.04 (1.02-1.06)	**Na*** HR 1.10 (1.05-1.16)
CV death (286 events)	**log_2NT-proBNP** HR 1.72 (1.62-1.83)	**HbA1c** HR 1.23 (1.13-1.34)	**NSTEMI** HR 1.61 (1.28-2.04)	**AF** HR 3.14 (2.31-4.25)	**prior HF** HR 2.87 (2.27-3.62)
MI (473 events)	**prior MI** HR 2.63 (2.19-3.16)	**log_2NT-proBNP** HR 1.23 (1.18-1.29)	**NSTEMI** HR 1.90 (1.59-2.28)	**prior stroke** HR 2.50 (1.89-3.33)	**PAD** HR 2.52 (1.94-3.29)
HF (221 events)	**log_2NT-proBNP** HR 1.68 (1.57-1.80)	**BMI per 5** HR 1.31 (1.19-1.43)	**NSTEMI** HR 1.91 (1.47-2.49)	**prior HF** HR 4.16 (3.19-5.42)	**prior MI** HR 3.09 (2.37-4.03)
Stroke (115 events)	**log_2NT-proBNP** HR 1.34 (1.22-1.48)	**prior TIA** HR 4.90 (2.69-8.91)	**macroalbuminuria** HR 3.05 (1.86-4.99)	**Age per 10** HR 1.61 (1.32-1.95)	**LDL per 10** HR 1.07 (1.02-1.12)

Table S6. Predictors of outcomes ranked according to χ^2 value using base variables and BNP and stratified according to history of heart failure (No prior HF, n=4290; Prior HF, n=1235)

Outcome		1st	2nd	3rd
Death (397 events)	**No prior HF**	**log_2BNP** (χ^2:108, HR 1.68)	**HR per 10** (χ^2:11, HR 1.24)	**Age per 10** (χ^2:9, HR 1.28)
	Prior HF	**log_2BNP** (χ^2:108, HR 1.72)	**AF** (χ^2:13, HR 1.93)	**Race** (χ^2:13, HR 1.42)
CV death (286 events)	**No prior HF**	**log_2BNP** (χ^2:101, HR 1.80)	**AF** (χ^2:12, HR 2.45)	**NSTEMI** (χ^2:9, HR 1.64)
	Prior HF	**log_2BNP** (χ^2:95, HR 1.84)	**CABG** (χ^2:10, HR 2.03)	**PAD** (χ^2:9, HR 1.90)
MI (473 events)	**No prior HF**	**log_2BNP** (χ^2:29, HR 1.23)	**prior MI** (χ^2:27, HR 1.86)	**PAD** (χ^2:21, HR 2.03)
	Prior HF	**log_2BNP** (χ^2:26, HR 1.34)	**prior MI** (χ^2:17, HR 2.10)	**NSTEMI** (χ^2:15, HR 2.00)
HF (221 events)	**No prior HF**	**log_2BNP** (χ^2:52, HR 1.70)	**HR per 10** (χ^2:22, HR 1.53)	**macroalbuminuria** (χ^2:13, HR 2.78)
	Prior HF	**log_2BNP** (χ^2:100, HR 1.94)	**BMI per 5** (χ^2:28, HR 1.39)	**DBP*** (χ^2:12, HR 1.06)
Stroke (115 events)	**No prior HF**	**log_2BNP** (χ^2:15, HR 1.40)	**macroalbuminuria** (χ^2:12, HR 2.98)	**TIA** (χ^2:10, HR 3.98)
	Prior HF	**log_2BNP** (χ^2:8, HR 1.31)	**TIA** (χ^2:6, HR 2.46)	**MI** (χ^2:5, HR 2.20)

Hazard ratio's reflect 1 unit changes if nothing else is stated. For log_2BNP that translates into a doubling of the untransformed BNP concentrations. Macroalbuminuria: >300 mg albumin excretion/24 h. *per 1 mmHg decrease below ≥75 mmHg.. AF- atrial fibrillation/flutter. NSTEMI – non-ST elevation myocardial infarction at index event. HR – heart rate. PAD – peripheral artery disease. TIA – transient ischemic attack. Duration of T2D is per year since diagnosis. All variables are significant, $p<0.05$.

Table S7. Discriminatory changes in best risk models with and without BNP stratified according to history of heart failure (No prior HF, n=4290; Prior HF, n=1235)

C statistics in each model (n=5525)

		Base model	BNP in model	NRI	IDI
Death (397 events)	No prior HF	0.77 (0.73-0.80)	0.80 (0.77-0.84)*	25.7% (17.3-34.7)*	4.0% (2.4-6.8)*
	Prior HF	0.69 (0.64-0.73)	0.78 (0.75-0.81)*	38.5% (28.7-45.4)*	7.8% (4.4-11.4)*
CV death (286 events)	No prior HF	0.76 (0.72-0.80)	0.81 (0.77-0.85)*	27.4% (17.7-35.6)*	3.7% (1.9-6.8)*
	Prior HF	0.73 (0.68-0.77)	0.82 (0.79-0.85)*	39.6% (28.6-51.1)*	6.9% (3.6-11.6)*
MI (473 events)	No prior HF	0.72 (0.69-0.75)	0.73 (0.70-0.75)#	13.7% (5.6-19.4)*	0.8% (0.2-1.9)*
	Prior HF	0.71 (0.66-0.76)	0.73 (0.68-0.77)	21.7% (8.4-30.9)*	2.4% (0.9-4.7)*
HF (221 events)	No prior HF	0.83 (0.79-0.87)	0.86 (0.83-0.90)*	29.4% (15.3-39.4)*	3.4% (1.4-6.7)*
	Prior HF	0.75 (0.71-0.80)	0.81 (0.77-0.85)*	38.8% (26.6-46.6)*	9.0% (5.1-13.3)*
Stroke (115 events)	No prior HF	0.76 (0.71-0.82)	0.79 (0.73-0.84)	17.6% (1.8-31.1)*	0.1% (-0.6-1.6)
	Prior HF	0.67 (0.58-0.75)	0.69 (0.61-0.76)	21.3% (0.0-35.2)*	1.0% (0.1-3.9)*

*$p<0.05$, comparison between base model and BNP model. #$p=0.053$, comparison between base model and BNP model. NRI – Net Reclassification Index. IDI – Integrated Discrimination Index. NRI and IDI summarized as mean percent improvement ±95%CI..

Table S8. Discriminatory changes in best risk models without BNP compared to BNP alone, in all patients (n=5525) and stratified according to history of heart failure (No prior HF, n=4290; Prior HF, n=1235).

	All patients		**No prior HF**		**Prior HF**	
Outcome	**Base model**	**BNP**	**Base model**	**BNP**	**Base model**	**BNP**
Death (397 events)	0.77 (0.74-0.79)	0.77 (0.75-0.80)	0.77 (0.74-80)	0.75 (0.71-0.78)	0.71 (0.67-0.74)	**0.76 (0.73-0.80)***
CV death (286 events)	0.77 (0.74-0.80)	0.79 (0.76-0.82)	0.76 (0.72-0.80)	0.76 (0.72-0.81)	0.73 (0.68-0.77)	0.78 (0.74-0.82)
MI (473 events)	**0.71 (0.68-0.73)**	0.63 (0.61-0.66)*	**0.72 (0.69-0.75)**	0.62 (0.59-0.65)*	0.71 (0.66-0.76)	0.66 (0.61-0.70)
HF (221 events)	**0.84 (0.81-0.86)**	0.78 (0.75-0.81)*	**0.83 (0.79-0.87)**	0.76 (0.72-0.80)*	0.75 (0.71-0.80)	0.74 (0.69-0.78)
Stroke (115 events)	**0.75 (0.70-0.79)**	0.67 (0.62-0.72)*	**0.76 (0.71-0.82)**	0.67 (0.60-0.74)*	0.67 (0.58-0.75)	0.61 (0.52-0.70)

*$p<0.05$, significant difference between base model compared to BNP model.

Table S9. Predictors of outcomes ranked according to χ^2 value using base variables and BNP in patients without prior CV disease (n=2899)

Outcome	1st	2nd	3rd
Death (112 events)	**log_2BNP** (χ^2:81, HR 1.78)	**DBP*** (χ^2:14, HR 1.05)	**Na#** (χ^2:7, HR 0.84)
CV death (74 events)	**log_2BNP** (χ^2:81, HR 2.04)	**DBP*** (χ^2:16, HR 1.06)	**duration of T2D** (χ^2:10, HR 1.04)
MI (153 events)	**log_2BNP** (χ^2:18, HR 1.27)	**macroalbuminuria** (χ^2:12, HR 2.34)	**hypertension** (χ^2:10, HR 1.89)
HF (39 events)	**log_2BNP** (χ^2:31, HR 1.87)	**duration of T2D** (χ^2:13, HR 1.06)	**albumin** (χ^2:6, HR 0.91)
Stroke (31 events)	**carotid disease** (χ^2:41, HR 34.79)	**microalbuminuria** (χ^2:16, HR 5.08)	**DBP*** (χ^2:16, HR 1.09)

Hazard ratio's reflect 1 unit changes if nothing else is stated. For log_2BNP that translates into a doubling of the untransformed BNP concentrations. Microalbuminuria ≥30-300 mg albumin excretion/24h. Macroalbuminuria: >300 mg albumin excretion/24h.. *per 1 mmHg decrease below ≥75 mmHg.. T2D – Type 2 diabetes (years). All variables are significant, $p<0.05$.

Table S10. Predictors of outcomes ranked according to χ^2 value using base variables and NT-proBNP in patients without prior CV disease (n=2899)

Outcome	1st	2nd	3rd
Death (112 events)	**log_2proBNP** (χ^2:81, HR 1.61)	**DBP*** (χ^2:16, HR 1.05)	**age per 10** (χ^2:8, HR 1.36)
CV death (74 events)	**log_2proBNP** (χ^2:81, HR 1.81)	**DBP*** (χ^2:16, HR 1.06)	**duration of T2D** (χ^2:10, HR 1.04)
MI (153 events)	**log_2proBNP** (χ^2:18, HR 1.21)	**macroalbuminuria** (χ^2:11, HR 2.23)	**hypertension** (χ^2:10, HR 1.92)
HF (39 events)	**log_2proBNP** (χ^2:53, HR 1.91)	**duration of T2D** (χ^2:14, HR 1.06)	**NSTEMI** (χ^2:5, HR 2.06)
Stroke (31 events)	**carotid disease** (χ^2:37, HR 29.09)	**microalbuminuria** (χ^2:16, HR 5.06)	**DBP*** (χ^2:15, HR 1.08)

Hazard ratio's reflect 1 unit changes if nothing else is stated. For log_2BNP that translates into a doubling of the untransformed BNP concentrations. Microalbuminuria ≥30-300 mg albumin excretion/24h. Macroalbuminuria: >300 mg albumin excretion/24h. DBP* diastolic blood pressure per 1 mmHg decrease below ≥75 mmHg. NSTEMI – non-ST elevation myocardial infarction at index event. T2D – Type 2 diabetes (years). All variables are significant, $p<0.05$.

Table S11. Predictors of outcomes ranked according to χ^2 value using base variables and BNP with and without adding information on LVEF (n=3390)

Outcome		1st	2nd	3rd
Death (236 events)	**Variables**	**log_2BNP** (χ^2:99, HR 1.60)	**Duration of T2D** (χ^2:17, HR 1.03)	**male** (χ^2:9, HR 1.59)
	Variables +LVEF	**log_2BNP** (χ^2:108, HR 1.60)	**Duration of T2D** (χ^2:17, HR 1.03)	**male** (χ^2:9, HR 1.59)
CV death (166 events)	**Variables**	**log_2BNP** (χ^2:131, HR 1.86)	**HbA1c** (χ^2:10, HR 1.22)	**Duration of T2D** (χ^2:10, HR 1.03)
	Variables +LVEF	**log_2BNP** (χ^2:95, HR 1.79)	**HbA1c** (χ^2:11, HR 1.23)	**Duration of T2D** (χ^2:10, HR 1.03)
MI (290 events)	**Variables**	**prior MI** (χ^2:43, HR 2.21)	**NSTEMI** (χ^2:24, HR 1.81)	**log_2BNP** (χ^2:23, HR 1.21)
	Variables +LVEF	**prior MI** (χ^2:43, HR 2.21)	**NSTEMI** (χ^2:24, HR 1.81)	**log_2BNP** (χ^2:23, HR 1.21)
HF (148 events)	**Variables**	**log_2BNP** (χ^2:97, HR 1.80)	**BMI per 5** (χ^2:25, HR 1.33)	**HR per 10** (χ^2:20, HR 1.43)
	Variables +LVEF	**log_2BNP** (χ^2:97, HR 1.80)	**BMI per 5** (χ^2:25, HR 1.33)	**HR per 10** (χ^2:20, HR 1.43)
Stroke (70 events)	**Variables**	**log_2BNP** (χ^2:21, HR 1.42)	**TIA** (χ^2:11, HR 3.59)	**LDL per 10** (χ^2:7, HR 1.08)
	Variables +LVEF	**log_2BNP** (χ^2:21, HR 1.42)	**TIA** (χ^2:11, HR 3.59)	**LDL per 10** (χ^2:7, HR 1.08)

Table S12. Predictors of outcomes ranked according to χ^2 value using base variables and NT-proBNP with and without adding information on LVEF at index ACS (n=3390)

Outcome		1st	2nd	3rd
Death (236 events)	**Variables**	**log_2NT-proBNP** (χ^2:107, HR 1.46)	**COPD** (χ^2:9, HR 1.81)	**Male** (χ^2:9, HR 1.58)
	Variables +LVEF	**log_2NT-proBNP** (χ^2:107, HR 1.46)	**COPD** (χ^2:9, HR 1.81)	**Male** (χ^2:9, HR 1.58)
CV death (166 events)	**Variables**	**log_2NT-proBNP** (χ^2:115, HR 1.57)	**HbA1c** (χ^2:14, HR 1.27)	**Male** (χ^2:9, HR 1.71)
	Variables +LVEF	**log_2NT-proBNP** (χ^2:68, HR 1.49)	**HbA1c** (χ^2:13, HR 1.26)	**AF** (χ^2:10, HR 1.92)
MI (290 events)	**Variables**	**prior MI** (χ^2:44, HR 2.24)	**log_2NT-proBNP** (χ^2:30, HR 1.18)	**NSTEMI** (χ^2:25, HR 1.18)
	Variables +LVEF	**prior MI** (χ^2:44, HR 2.24)	**log_2NT-proBNP** (χ^2:30, HR 1.18)	**NSTEMI** (χ^2:25, HR 1.18)
HF (148 events)	**Variables**	**log_2NT-proBNP** (χ^2:86, HR 1.56)	**BMI per 5** (χ^2:25, HR 1.33)	**CABG** (χ^2:19, HR 2.48)
	Variables +LVEF	**log_2NT-proBNP** (χ^2:86, HR 1.56)	**BMI per 5** (χ^2:25, HR 1.33)	**CABG** (χ^2:19, HR 2.48)
Stroke (70 events)	**Variables**	**log_2NT-proBNP** (χ^2:14, HR 1.26)	**TIA** (χ^2:10, HR 3.36)	**LDL per 10** (χ^2:6, HR 1.07)
	Variables +LVEF	**log_2NT-proBNP** (χ^2:14, HR 1.26)	**TIA** (χ^2:10, HR 3.36)	**LDL per 10** (χ^2:6, HR 1.07)

Table S13. Discriminatory changes in best risk models with and without BNP and NT-proBNP with LVEF and coronary intervention procedure added to base model

C statistics in each model (n=3390)

		Base model	BNP/ NT-proBNP in model	NRI	IDI
Death (236 events)	BNP	0.75 (0.72-0.78)	0.79 (0.76-0.82)*	31.8% (25.1-37.4)*	5.3% (3.5-7.4)*
	NT-proBNP		0.79 (0.75-0.82)*	25.5% (19.4-31.9)*	3.5% (2.3-5.1)*
CV death (166 events)	BNP	0.77 (0.73-0.81)	0.83 (0.80-0.86)*	34.8% (28.0-41.7)*	5.7% (3.7-8.4)*
	NT-proBNP		0.82 (0.79-0.85)*	29.9% (22.4-36.8)*	3.9% (2.3-6.2)*
MI (290 events)	BNP	0.70 (0.67-0.73)	0.71 (0.67-0.74)	14.3% (9.3-19.5)*	1.2% (0.6-2.1)*
	NT-proBNP		0.71 (0.68-0.74)	10.6% (5.7-16.6)*	0.8% (0.3-1.6)*
HF (148 events)	BNP	0.86 (0.83-0.89)	0.88 (0.85-0.90)*	35.4% (24.7-40.6)*	5.0% (3.0-7.6)*
	NT-proBNP		0.88 (0.85-0.90)*	29.9% (21.8-36.6)*	3.8% (2.2-5.8)*
Stroke (70 events)	BNP	0.72 (0.66-0.78)	0.76 (0.70-0.82)	19.3% (8.8-29.9)*	0.4% (0-1.2)
	NT-proBNP		0.75 (0.70-0.81)	17.2% (6.3-28.1)*	0.2% (0-0.8)

*$p<0.05$, comparison between base model and /NT-proBNP model. NRI – Net Reclassification Index. IDI – Integrated Discrimination Index. NRI and IDI summarized as mean percent improvement ±95%CI.

Myocardial infarction summary criteria for positive adjudication:

Spontaneous MI: Elevated cardiac markers (CM) and either new electrocardiographic (ECG) changes or a clinical presentation consistent with an acute MI.
○PCI-related MI: Elevated CM (or other criteria in the absence of elevated CM).
○Coronary artery bypass graft (CABG)–related MI: Elevated CM and new ECG changes (or other criteria).
Detailed criteria for positive adjudication:
a. Spontaneous MI:
Cardiac markers:
○Troponin$_p$>upper limit of normal (ULN) or
○CK-MB>ULN

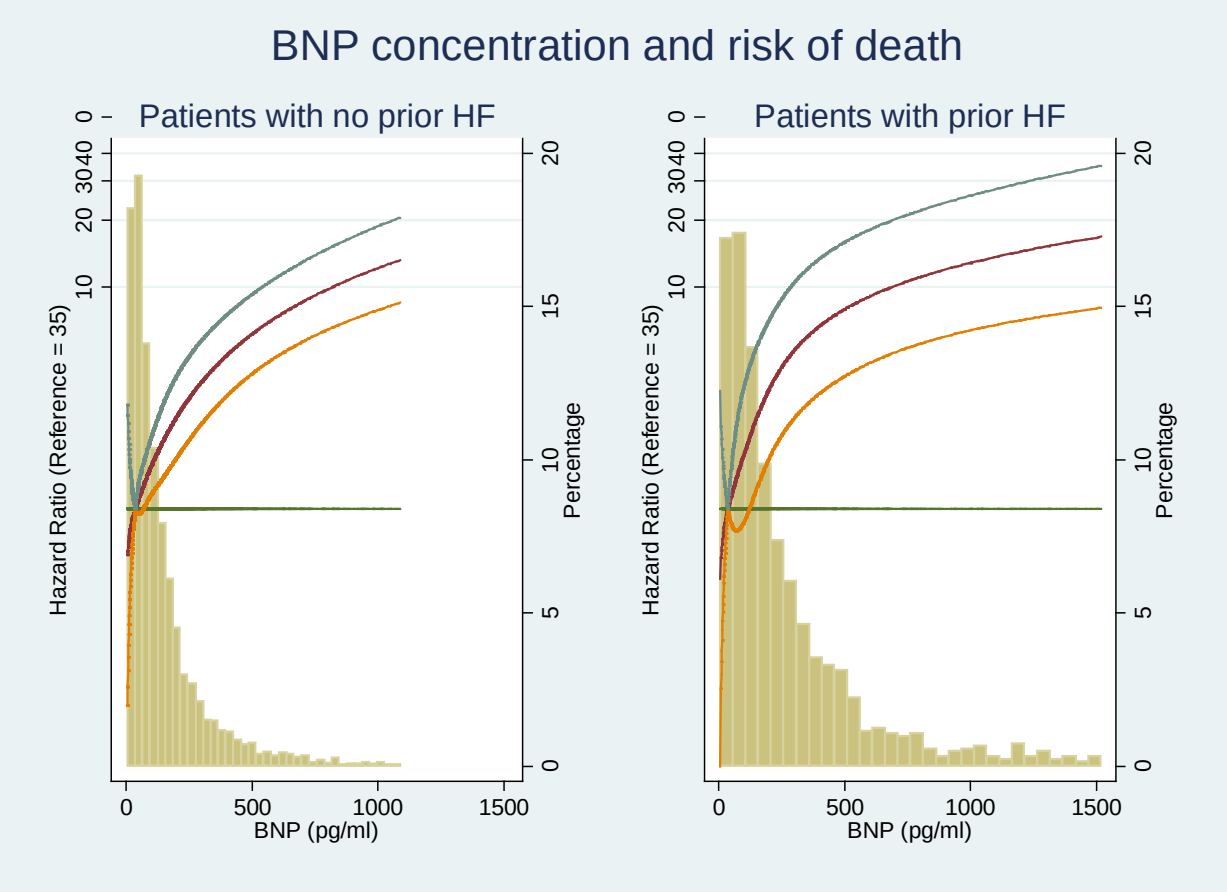
and at least 1 of the following:
○Ischemic symptoms: rest or accelerated symptoms (pain, dyspnea, and pressure) consistent with myocardial ischemia.
○ECG changes consistent with infarction:
•New significant Q waves (or R waves in V_1-V_2)in 2 contiguous leads in absence of previous left ventricular hypertrophy or conduction abnormalities. OR
•Evolving ST-segment to T-wave changes in≥2 contiguous leads.
•Development of new left bundle-branch block.
•ST-segment elevation requiring thrombolytics or PCI.
b. PCI-related MI:
Cardiac markers$_q$:
1. Assuming baseline value>ULN
2. Within 48 hours of procedure
a. Troponin$_p$>3× ULN OR
b. CK-MB>3× ULN
c. CABG-related MI:
Cardiac markers:
1. Assuming baseline value>ULN
2. Within 72 hours of procedure
a. Troponin$_p$>5× ULN OR
b. CK-MB>5× ULN
AND
c. New pathologic Q waves or left bundle-branch block, new native or graft vessel occlusion, or imaging evidence of loss of viable myocardium.
3. Hospitalization for UA
a. Unplanned hospitalization for worsening angina defined as rest or accelerated symptoms (pain, dyspnea, and pressure) consistent with myocardialischemia AND
b. Cardiac markers (CK-MB or troponin) suggestive of myocardial injury but not meeting MI criteria. Note: if abnormal troponin, value must be in the suggestive (middle) range and below the threshold for MI.

Baseline variables used in risk models:

Log_2BNP, Log_2NT-proBNP

Race, ethnicity, region, randomization to lixisenatide, PCI at index ACS, age, gender, BMI, systolic blood pressure, diastolic blood pressure (above/below 70 mmHg), heart rate, smoking (current/never/former), history of MI, history of HF, history of AF, history of PAD, history of TIA, history of stroke, history of ventr. tachycardia, history of CABG, pacemaker implanted, carotid disease, history of hypertension, index ACS (STEMI, NSTEMI, UAP), insulin use (yes/no), duration of T2D, retinopathy, neuropathy, asthma, COPD, albuminuria (no/micro/macro), logCRP, HbA1c, HDL, LDL, eGFR, Hgb, Na (above/below 140 mmol/L), albumin.

Figure S1. The association of BNP concentrations and risk of all-cause death according to history of heart failure



The hazard of death is depicted with 95%CI. The Cox spline model was fully adjusted for all significant variables. The reference of HR=1.0 corresponds to a BNP concentration of 35 pg/ml.