

SUPPLEMENTARY DATA

Supplementary Table 1. Baseline characteristics classified according to baseline NT-proBNP level.

	NT-proBNP (pg/ml)												
	1 st : ≤35			2 nd : >35 - ≤90			3 rd : >90 - ≤223			4 th : >223			p-trend
	n=976			n=959			n=963			n=964			
Males – n (%)	648	66.4%		568	59.2%		553	57.4%		587	60.9%		0.0086
Current Smokers – n (%)	190	19.5%		150	15.6%		141	14.6%		100	10.4%		<0.0001
History of macrovascular event – n (%)	220	22.5%		247	25.8%		370	38.4%		508	52.7%		<0.0001
Age (years) – Mean (SD)	64.05	6.11		66.47	6.12		67.53	6.40		69.53	6.61		<.0001
Duration of diabetes (years) – Mean (SD)	7.11	5.84		7.53	6.09		7.91	6.42		8.90	7.11		<.0001
BMI (kg/m ²) – Mean (SD)	29.81	4.92		30.15	5.42		30.46	5.32		29.81	5.36		0.6493
History of heart failure – n (%)	18	1.8%		13	1.4%		36	3.7%		114	11.8%		<.0001
Participation in moderate or vigorous activity* – n (%)	533	54.6%		492	51.3%		441	45.8%		405	42.0%		<.0001
Aspirin or other antiplatelet agent – n (%)	399	40.9%		441	46.0%		505	52.4%		566	58.7%		<.0001
Statin or other lipid lowering agent – n (%)	376	38.5%		418	43.6%		473	49.1%		448	46.5%		<.0001
Beta blocker – n (%)	156	16.0%		236	24.6%		347	36.0%		435	45.1%		<.0001
ACE inhibitor or angiotensin receptor blocker – n (%)	515	52.8%		531	55.4%		566	58.8%		667	69.2%		<.0001
Blood pressure (mmHg) – Mean (SD)													
- systolic	142.64	18.80		146.79	20.68		148.87	22.35		151.99	23.53		<.0001
- diastolic	82.05	9.92		81.52	10.69		81.65	11.11		81.22	11.73		0.1316
Cholesterol (mmol/L) – Mean (SD)													
	5.22	1.25		5.13	1.10		5.13	1.19		5.06	1.13		0.0036

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- total													
- HDL	1.20	0.32		1.24	0.33		1.24	0.35		1.21	0.33		0.409
Triglycerides (mmol/L) – Median (Q1, Q3)	1.73	1.27	2.50	1.70	1.20	2.30	1.67	1.20	2.38	1.60	1.20	2.24	0.0007
HbA1c (% / mmol/mol)– Mean (SD)	7.45 / 58	1.37 / 15.0		7.38 / 57	1.33 / 14.5		7.38 / 57	1.47 / 16.1		7.45 / 58	1.54 / 16.8		0.9925
Urinary ACR (µ/mg) – Median (Q1, Q3)	12.38	6.10	30.0 0	11.63	5.88	30.9 4	14.76	6.72	38.9 0	22.98	8.84	74.1 7	<.0001
Glucose (mmol/L) – Mean (SD)	8.66	2.67		8.48	2.53		8.45	2.70		8.32	2.97		0.0089
Egfr – Mean (SD)	77.49	14.92		73.93	15.36		70.82	16.24		63.62	17.64		<.0001
CRP (mg/L) – Median (Q1, Q3)	1.54	0.80	3.53	1.62	0.82	3.53	2.00	0.95	4.36	2.17	1.02	4.75	<.0001
hs-cTnT (ng/L) – Median (Q1, Q3)	1.5	1.5	6	4	1.5	9	6	1.5	11	11	5	19	<.0001
NT-proBNP (pg/ml) – Median (Q1, Q3)	15	2.5	25	58	46	72	136	110	168	463	306	819. 5	<.0001

The characteristic of participants are presented in four categories of NT-proBNP levels, defined by their quartiles.

* participation in moderate and/or vigorous exercise for >15 minutes at least once weekly. SD, standard deviation; BMI, body mass index; ACE, angiotensin converting enzyme; HbA1c, hemoglobin A1c; ACR, albumin:creatinine ratio; eGFR, estimated glomerular filtration rate; hs-CRP, high sensitivity C-reactive protein, hs-cTnT, high sensitivity cardiac troponin T; NT-proBNP, N-terminal pro-B-type natriuretic peptide.

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Supplementary Table 2. Baseline characteristics classified according to baseline high sensitivity troponin T level.

	High sensitivity troponin T (ng/L)												
	1 st : <3			2 nd : ≥3 - <7			3 rd : ≥7 - <14			4 th : ≥14			p-trend
	n=1,369			n=848			n=915			n=730			
Males – n (%)	589	43.0%		537	63.3%		666	72.8%		564	77.3%		<0.0001
Current Smokers – n (%)	246	18.0%		120	14.2%		127	13.9%		88	12.1%		0.0002
History of macrovascular event – n (%)	375	27.4%		288	34.0%		343	37.5%		339	46.4%		<0.0001
Age (years) – Mean (SD)	64.95	6.08		66.35	6.08		68.18	6.59		69.51	6.95		<.0001
Duration of diabetes (years) – Mean (SD)	7.18	5.87		7.40	5.99		8.16	6.50		9.29	7.44		<.0001
BMI (kg/m ²) – Mean (SD)	30.08	5.41		30.25	5.44		29.87	4.87		30.03	5.23		0.502
History of heart failure – n (%)	30	2.2%		20	2.4%		42	4.6%		89	12.2%		<.0001
Participation in moderate or vigorous activity [*] – n (%)	682	49.8%		426	50.2%		453	49.5%		310	42.5%		0.0061
Aspirin or other antiplatelet agent – n (%)	622	45.4%		394	46.5%		478	52.2%		417	57.1%		<.0001
Statin or other lipid lowering agent – n (%)	614	44.9%		371	43.8%		396	43.3%		334	45.8%		0.9255
Beta blocker – n (%)	395	28.9%		263	31.0%		291	31.8%		225	30.8%		0.2140
ACE inhibitor or angiotensin receptor blocker – n (%)	734	53.6%		484	57.1%		575	62.8%		486	66.6%		<.0001
Blood pressure (mmHg) – Mean (SD)													
- systolic	143.73	20.27		148.13	21.12		149.50	22.20		151.64	23.04		<.0001
- diastolic	80.95	10.57		82.22	10.64		82.27	11.23		81.33	11.21		0.152
Cholesterol (mmol/L) – Mean (SD)													
	5.28	1.25		5.12	1.16		5.05	1.11		4.98	1.08		<.0001

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- total													1
- HDL	1.26	0.34		1.23	0.33		1.20	0.32		1.19	0.33		<.0001
Triglycerides (mmol/L) – Median (Q1, Q3)	1.70	1.20	2.40	1.70	1.20	2.30	1.68	1.20	2.33	1.69	1.20	2.40	0.5841
HbA1c (% / mmol/mol)– Mean (SD)	7.33 / 57	1.34 / 14.6		7.39 / 57	1.41 / 15.4		7.49 / 58	1.45 / 15.8		7.51 / 59	1.57 / 17.2		0.0011
Urinary ACR (µ/mg) – Median (Q1, Q3)	11.50	6.19	28.29	15.03	6.01	38.01	15.91	7.07	45.00	25.64	8.84	86.27	<.0001
Glucose (mmol/L) – Mean (SD)	8.38	2.58		8.47	2.63		8.60	2.68		8.51	3.12		0.1256
eGFR – Mean (SD)	75.60	15.12		73.43	15.51		70.02	16.41		63.33	18.82		<.0001
CRP (mg/L) – Median (Q1, Q3)	1.81	0.87	4.05	1.78	0.85	4.07	1.87	0.90	3.98	1.82	0.90	4.21	0.0061
hs-cTnT (ng/L) – Median (Q1, Q3)	1.5	1.5	1.5	5	4	6	9	8	11	20	16	28	<.0001
NT-proBNP (pg/ml) – Median (Q1, Q3)	51	20	116	82	33	171	110	49	270	257	102	707	<.0001

The characteristics of patients are presented in categories of hs-cTnT levels defined using the cut-off values of <3ng/L (the lower detection limit of the assay), ≥14ng/L (the 99th percentile value in a healthy population) and divided around the median level between these two values (7ng/L).

* participation in moderate and/or vigorous exercise for >15 minutes at least once weekly.

SD, standard deviation; BMI, body mass index; ACE, angiotensin converting enzyme; HbA1c, hemoglobin A1c; ACR, albumin:creatinine ratio; eGFR, estimated glomerular filtration rate; hs-CRP, high sensitivity C-reactive protein, hs-cTnT, high sensitivity cardiac troponin T; NT-proBNP, N-terminal pro-B-type natriuretic peptide.

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Supplementary Table 3. Comparison of C-statistic, IDI, RIDI and NRI between total cholesterol, high sensitivity cTnT and NT-proBNP.

	Cardiovascular events*	Death
Base model[†] C-statistic	0.704 (0.673, 0.734)	0.713 (0.682, 0.744)
Base + Total Cholesterol		
C-statistic	0.704 (0.673, 0.734) vs base, p=0.855	0.713 (0.682, 0.744) vs base, p=0.615
IDI	-0.003 (-0.004, -0.002) p<0.001	-0.0007 (-0.0009, -0.0004) p<0.001
Relative IDI (%)	-3.0 (-4.0, -2.0)	-0.8 (-1.0, -0.5)
NRI-continuous	-0.103 (-0.226, 0.018) p=0.098	-0.126 (-0.250, -0.003) p=0.046
NRI – categorical	-0.009 (-0.033, 0.016) p=0.432	-0.011 (-0.035, 0.014) p=0.388
Base + hs-cTnT		
C-statistic	0.727 (0.697, 0.757) vs base, p=0.001	0.734 (0.704, 0.764) vs base, p=0.004
IDI	0.029 (0.021, 0.038) p<0.001	0.028 (0.021, 0.036) p<0.001
Relative IDI (%)	32.8 (23.0, 43.0)	31.6 (23.3, 39.9)
NRI-continuous	0.445 (0.324, 0.569) p<0.001	0.430 (0.309, 0.549) p<0.001
NRI – categorical	0.120 (0.060, 0.175) p<0.001	0.069 (0.003, 0.129) p=0.046
Base + NT-proBNP		
C-statistic	0.744 (0.715, 0.773) vs base, p<0.001	0.757 (0.729, 0.785) vs base, p<0.001
IDI	0.056 (0.044, 0.069) p<0.001	0.061 (0.049, 0.075) p<0.001
Relative IDI (%)	64.1 (48.7, 79.1)	67.9 (53.2, 83.6)
NRI-continuous	0.364 (0.243, 0.484) p<0.001	0.419 (0.309, 0.533) p<0.001
NRI – categorical	0.121 (0.057, 0.188) p<0.001	0.116 (0.053, 0.180) p=0.002

Results are derived from the random sub-cohort (n=3,500); * cardiovascular death, non-fatal myocardial infarction or non-fatal stroke

[†] Base model includes age, sex, randomized treatment allocations, prior history of vascular disease, duration of diabetes, current smoking, systolic blood pressure, body mass index, albumin:creatinine ratio, estimated glomerular filtration rate, hemoglobin A1c, glucose, HDL-cholesterol, triglycerides, high sensitivity CRP, aspirin or other antiplatelet agent, statin or other lipid lowering agent, beta blocker, angiotensin converting enzyme inhibitor or angiotensin receptor blocker, history of heart failure and participation in moderate or vigorous activity (>15 minutes at least once weekly).

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Supplementary Table 4. Comparison of C-statistic, IDI, RIDI and NRI between high sensitivity CRP, high sensitivity cTnT and NT-proBNP.

	Cardiovascular events*	Death
Base model[†] C-statistic	0.702 (0.671, 0.733)	0.710 (0.679, 0.740)
Base + high sensitivity CRP		
C-statistic	0.704 (0.673, 0.734), p=0.400 vs base	0.713 (0.682, 0.744), p=0.386 vs base
IDI	0.004 (0.002, 0.006), p<0.001	0.010 (0.006, 0.014) p<0.001
Relative IDI (%)	4.4 (2.2, 6.8)	12.9 (8.4, 17.6)
NRI-continuous	0.089 (-0.034, 0.210), p=0.156	0.132 (0.015, 0.264) p=0.030
NRI – categorical	-0.013 (-0.042, 0.017), p=0.386	0.009 (-0.037, 0.052) p=0.612
Base + hs-cTnT		
C-statistic	0.727 (0.697, 0.757), p<0.001 vs base	0.732 (0.701, 0.762), p=0.003 vs base
IDI	0.036 (0.028, 0.045) p<0.001	0.034 (0.027, 0.041) p<0.001
Relative IDI (%)	43.8 (33.3, 54.8)	42.8 (33.3, 52.2)
NRI-continuous	0.480 (0.365, 0.600) p<0.001	0.498 (0.383, 0.617) p<0.001
NRI – categorical	0.105 (0.049, 0.159) p<0.001	0.078 (0.017, 0.138) p=0.016
Base + NT-proBNP		
C-statistic	0.744 (0.715, 0.773), p<0.001 vs base	0.758 (0.730, 0.785), p<0.001 vs base
IDI	0.064 (0.052, 0.078) p<0.001	0.068 (0.056, 0.082) p<0.001
Relative IDI (%)	78.6 (62.9, 95.2)	86.0 (69.6, 103.7)
NRI-continuous	0.409 (0.302, 0.525) p<0.001	0.459 (0.355, 0.576) p<0.001
NRI – categorical	0.124 (0.056, 0.194) p=0.002	0.123 (0.058, 0.183) p<0.001

Results are derived from the random sub-cohort (n=3,500); * cardiovascular death, non-fatal myocardial infarction or non-fatal stroke

[†] Base model includes age, sex, randomized treatment allocations, prior history of vascular disease, duration of diabetes, current smoking, systolic blood pressure, body mass index, albumin:creatinine ratio, estimated glomerular filtration rate, hemoglobin A1c, glucose, HDL-cholesterol, total cholesterol, triglycerides, aspirin or other antiplatelet agent, statin or other lipid lowering agent, beta blocker, angiotensin converting enzyme inhibitor or angiotensin receptor blocker, history of heart failure and participation in moderate or vigorous activity (>15 minutes at least once weekly).