

# **High Sensitivity Cardiac Troponin I and B-type Natriuretic Peptide as Predictors of Vascular Events in Primary Prevention: Impact of Statin Therapy**

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## **SUPPLEMENTAL MATERIAL**

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**Supplement Table 1. Baseline characteristics of the subcohort with samples assayed for high-sensitivity troponin I compared to the remainder of the JUPITER cohort**

Characteristic*	JUPITER participants with samples available	JUPITER participants without samples available	P-value
N	12956	4846	-
Age	66 (60-71)	66 (61-71)	0.0001
Female sex	4696 (36.3)	2105 (43.4)	<0.0001
Race or ethnic group, n (%)			<0.0001
White	10594 (81.8)	2089 (43.1)	
Black	944 (7.3)	1280 (26.4)	
Hispanic	1122 (8.7)	1139 (23.5)	
Other	294 (2.3)	338 (7.0)	
Hypertension, N (%)	7208 (55.7)	3000 (61.9)	<0.0001
Systolic blood pressure, mm Hg	134 (124-146)	135 (125-145)	0.47
Diastolic blood pressure, mm Hg	80 (75-86)	80 (76-89)	<0.0001
Body mass index (kg/m <sup>2</sup> )	28.4 (25.4-32.0)	28.1 (24.9-32.1)	<0.0001
Current smoking, N (%)	1952 (15.1)	868 (17.9)	<0.0001
Family history of premature MI, N (%)	1651 (12.8)	394 (8.2)	<0.0001
Diabetes, n (%)	64 (0.5)	14 (0.3)	0.07
Metabolic syndrome, n (%)	5219 (40.6)	2156 (44.7)	<0.0001
Impaired fasting glucose, N (%)	4214 (32.6)	1355 (28.1)	<0.0001
HbA1c (Q1-Q3), %	5.7 (5.4-5.9)	5.8 (5.5-6.0)	<0.0001
Fasting glucose, mg/dL	95 (88-102)	93 (86-101)	<0.0001
Total cholesterol (Q1-Q3), mg/dL	186 (170-200)	183 (165-198)	<0.0001
LDL cholesterol (Q1-Q3), mg/dL	109 (95-119)	107 (91-118)	<0.0001
HDL cholesterol (Q1-Q3), mg/dL	49 (41-60)	47 (39-58)	<0.0001
hsCRP (Q1-Q3), mg/L	4.1 (2.8-6.9)	4.3 (2.9-7.1)	<0.0001
Estimated GFR (Q1-Q3), mL/min	73.3 (64.6-82.8)	74.1 (64.5-88.4)	<0.0001
Framingham risk score (Q1-Q3)	10 (6-16)	11 (6-16)	0.0003
Reynolds risk score (Q1-Q3)	10 (6-16)	10 (6-16)	0.56
Random allocation to rosuvastatin, N (%)	6491 (50.1)	2410 (49.7)	0.66

\* Continuous variables are presented as median [quartile 1 (Q1)-quartile 3 (Q3)] and categorical variables are presented as N (%).

Abbreviations: BNP, B-type natriuretic peptide; GFR, glomerular filtration rate; HbA1c, hemoglobin A1c; HDL, high-density lipoprotein; hsCRP, high-sensitivity C-reactive protein; hsTnI, high-sensitivity cardiac troponin I; LDL, low density lipoprotein; Q1-Q3, value at the 25<sup>th</sup> (Q1) and 75<sup>th</sup> (Q3) percentiles

**Supplement Table 2. Baseline characteristics of the study population stratified by B-type natriuretic peptide tertile**

Characteristic*	BNP Tertile 1	BNP Tertile 2	BNP Tertile 3	P-value
Range in men, ng/L	<20	20 to <28.6	≥28.6	
Range in women, ng/L	<20	20 to <44.4	≥44.4	
N events/N at risk, men	54/3594	26/1096	88/2331	
N events/N at risk, women	10/1391	16/1303	42/1342	
Median (Q1-Q3) time to event, years	1.9 (1.5-2.2)	1.9 (1.5-2.3)	2.0 (1.5-2.4)	<0.0001
Age	63 (58-68)	66 (62-71)	69 (64-74)	<0.0001
Race or ethnic group, n (%)				<0.0001
White	4080 (81.9)	1908 (79.5)	3020 (82.2)	
Black	398 (8.0)	169 (7.0)	244 (6.6)	
Hispanic	380 (7.6)	275 (11.5)	334 (9.1)	
Other	126 (2.5)	47 (2.0)	74 (2.0)	
Hypertension, N (%)	2560 (51.4)	1344 (56.1)	2292 (62.4)	
Systolic blood pressure, mm Hg	132 (122-144)	134 (124-146)	138 (126-150)	<0.0001
Diastolic blood pressure, mm Hg	80 (76-88)	80 (74-86)	80 (74-87)	<0.0001
Body mass index (kg/m <sup>2</sup> )	28.7 (25.8-32.2)	28.4 (25.4-31.8)	27.9 (24.9-31.5)	<0.0001
Current smoking, N (%)	879 (17.6)	326 (13.6)	483 (13.2)	<0.0001
Family history of premature MI, N (%)	608 (12.3)	295 (12.3)	457 (12.5)	0.94
Diabetes, n (%)	27 (0.5)	12 (0.5)	14 (0.4)	0.56
Metabolic syndrome, n (%)	2142 (43.4)	938 (39.5)	1345 (36.9)	<0.0001
Impaired fasting glucose, N (%)	1728 (34.8)	755 (31.6)	1086 (29.6)	<0.0001
HbA1c (Q1-Q3), %	5.7 (5.4-5.9)	5.7 (5.5-5.9)	5.6 (5.4-5.9)	0.0001
Fasting glucose, mg/dL	95 (89-103)	94 (88-102)	94 (87-101)	<0.0001
Total cholesterol (Q1-Q3), mg/dL	186 (170-200)	189 (173-203)	184 (168-198)	<0.0001
LDL cholesterol (Q1-Q3), mg/dL	109 (95-119)	110 (97-120)	107 (93-119)	<0.0001
HDL cholesterol (Q1-Q3), mg/dL	47 (40-58)	52 (43-63)	51 (42-62)	<0.0001
hsCRP (Q1-Q3), mg/L	4.1 (2.7-6.6)	4.0 (2.8-6.7)	4.2 (2.8-6.9)	0.12
Estimated GFR (Q1-Q3), mL/min	75.9 (66.6-87.9)	73.3 (64.7-82.2)	70.8 (62.1-81.3)	<0.0001
Framingham risk score (Q1-Q3)	10 (6-16)	8 (5-14)	12 (8-17)	<0.0001
Reynolds risk score (Q1-Q3)	9 (5-14)	8 (5-14)	12 (7-21)	<0.0001
Random allocation to rosuvastatin, N (%)	2510 (50.4)	1195 (49.8)	1829 (49.8)	0.84

\* Continuous variables are presented as median [quartile 1 (Q1)-quartile 3 (Q3)]

Abbreviations: BNP, B-type natriuretic peptide; GFR, glomerular filtration rate; HbA1c, hemoglobin A1c; HDL, high-density lipoprotein; hsCRP, high-sensitivity C-reactive protein; hsTnI, high-sensitivity cardiac troponin I; LDL, low density lipoprotein; MI, myocardial infarction; Q1-Q3, value at the 25th (Q1) and 75th (Q3) percentiles

**Supplement Table 3. Spearman correlations of biomarkers in men enrolled in JUPITER**

	BNP	Total cholesterol	LDL-C	HDL-C	hsCRP	HbA1c	eGFR
hsTnI	0.30*	0.07*	0.08*	0.01	0.07*	0.05*	-0.18*
BNP		-0.07*	-0.05*	0.11*	0.04†	-0.04‡	-0.14*
Total cholesterol			0.73*	0.25*	-0.09*	0.02	-0.02§
LDL-C				0.02§	-0.07*	0.04‡	-0.06*
HDL-C					-0.05*	-0.11*	0.16*
hsCRP						0.10*	0.02
HbA1c							-0.03‡

\*P&lt;0.0001; †P&lt;0.001; ‡P&lt;0.01; §P&lt;0.05

Abbreviations: BNP, B-type natriuretic peptide; eGFR, estimated glomerular filtration rate; HbA1c, hemoglobin A1c; HDL-C, high-density lipoprotein cholesterol; hsCRP, high-sensitivity C-reactive protein; hsTnI, high-sensitivity cardiac troponin I; LDL-C, low density lipoprotein cholesterol

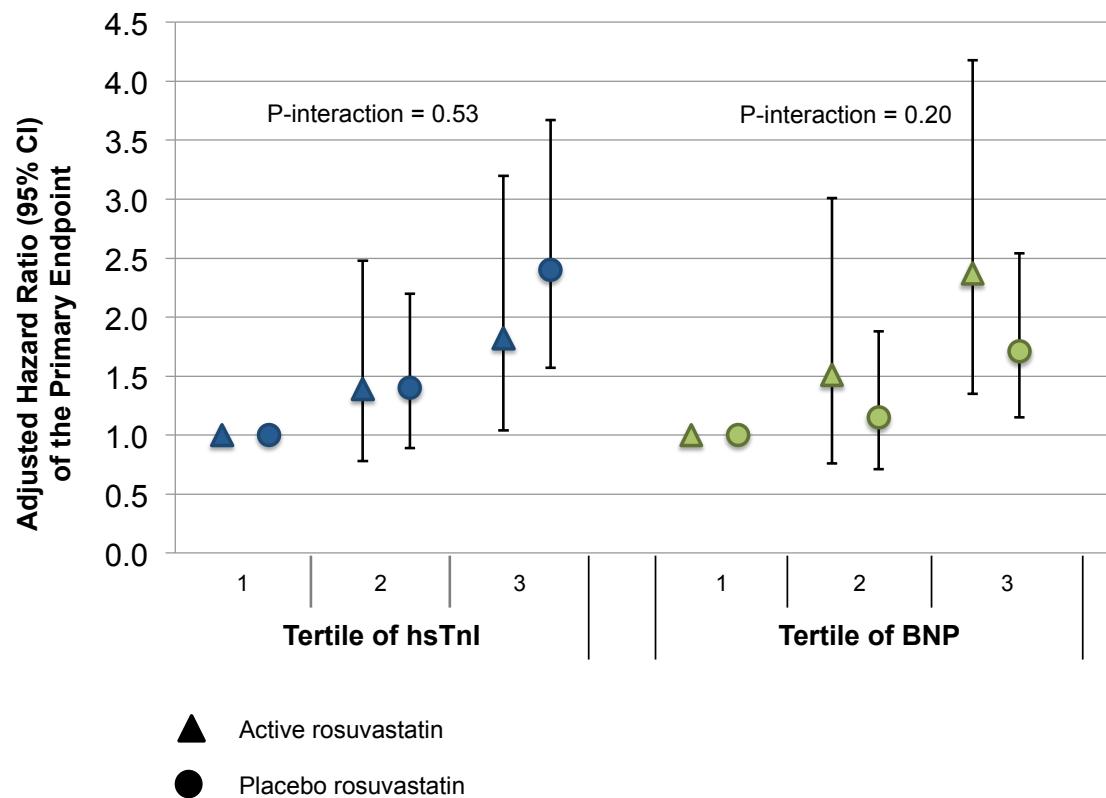
**Supplement Table 4. Spearman correlations of biomarkers in women enrolled in JUPITER**

	BNP	Total cholesterol	LDL-C	HDL-C	hsCRP	HbA1c	eGFR
hsTnI	0.25*	0.01	0.05†	-0.05†	0.04‡	0.04‡	-0.16*
BNP		-0.06†	-0.04§	0.03	-0.04§	-0.07*	-0.18*
Total cholesterol			0.74*	0.41*	-0.10*	-0.08*	-0.07*
LDL-C				0.04‡	-0.06†	-0.01	-0.04‡
HDL-C					-0.14*	-0.21*	0.04‡
hsCRP						0.15*	-0.01
HbA1c							0.03§

\*P&lt;0.0001; †P&lt;0.001; ‡P&lt;0.01; §P&lt;0.05

Abbreviations: BNP, B-type natriuretic peptide; eGFR, estimated glomerular filtration rate; HbA1c, hemoglobin A1c; HDL-C, high-density lipoprotein cholesterol; hsCRP, high-sensitivity C-reactive protein; hsTnI, high-sensitivity cardiac troponin I; LDL-C, low density lipoprotein cholesterol

**Supplement Figure 1. Risk of the JUPITER primary endpoint according to baseline category of high sensitivity cardiac troponin I (blue) and B-type natriuretic peptide (light green) stratified by random allocation to active rosuvastatin (triangles) or placebo (circles). Models are adjusted for age, race, sex, body mass index, history of hypertension, current smoking, family history of myocardial infarction, total cholesterol, high-density lipoprotein cholesterol, and high-sensitivity C-reactive protein.**



**Supplement Figure 2. Adjusted relative risk of a first major cardiovascular event, according to random allocation to rosuvastatin 20 mg daily versus placebo.** A first major cardiovascular event is defined as the JUPITER primary endpoint (non-fatal myocardial infarction, non-fatal stroke, hospitalization for unstable angina, arterial revascularization, or death from cardiovascular causes). There was no statistically significant evidence for heterogeneity of the effect of rosuvastatin across baseline categories of high-sensitivity troponin I ( $P$ -interaction = 0.53) or B-type natriuretic peptide ( $P$ -interaction = 0.20). Relative risk estimates were adjusted for age, sex, race, hypertension, smoking, body mass index, total cholesterol, high-density lipoprotein cholesterol, family history of coronary heart disease, and high-sensitivity C-reactive protein at baseline. The summary estimate is for the 12,956 participants with an hsTnI measure available.

