Supplemental Material

Online Table I: Baseline clinical and biochemical variables by GlycA quartile in JUPITER.

	Quartiles of GlycA, umol/L			
	<364 (n=3,196)	364-404 (n=3,091)	404-449 (n=3,130)	>449 (n=3,110)
Age, years	66 (60, 71)	65 (60, 71)	66 (60, 71)	66 (61, 71)
Women, %	24.0	33.7	40.5	47.1
Race/ethnicity, %				
White	86	85	84	73
Black	3.1	4.2	5.9	15
Asian	1.8	1.1	1.4	1.6
Hispanic	9.1	8.9	8.4	8.9
Other/unknown	0.4	0.7	0.9	1.2
BMI, kg/m^2	28 (25, 31)	29 (26, 32)	29 (26, 33)	28 (25, 33)
Hypertension	51.1	53.9	58.1	60.8
HbA1c, %	5.6 (5.3, 5.8)	5.6 (5.4, 5.9)	5.7 (5.5, 5.9)	5.8 (5.5, 6.0)
hsCRP, mg/L	3.0 (2.3, 4.4)	3.6 (2.6, 5.4)	4.4 (3.1, 6.9)	7.1 (4.3,13.2)
Family history CHD, %	12.6	12.5	12.7	12.7
LDL-c, mg/dL	109 (95, 119)	110 (97, 120)	110 (96, 120)	107 (92, 118)
HDL-c, mg/dL	50 (41, 61)	49 (41, 60)	49 (41, 60)	49 (40, 60)
Triglycerides, mg/dL	101 (74, 140)	114 (83, 162)	124 (91, 180)	129 (94, 186)
Smoker*, %	10.3	13.7	15.5	20.8
Alcohol†, %	23.9	23.7	21.9	18.1

Abbreviations: BMI = body-mass index, BP = blood pressure, CHD = coronary heart disease, hsCRP = high sensitivity C-reactive protein, LDL-c = low density cholesterol. Data presented as median (25^{th}, 75^{th} percentile) otherwise as percent where indicated. *Current or former. †Alcohol consumption ≥1 drink/day. By Wilcoxon rank sum or $\chi 2$ test, $p \leq 0.01$ except for HDL ($p=0.10$) and family history of CHD ($p=0.99$).

Online Table II: Hazard ratios per-standard deviation increment associated with GlycA and hsCRP and mortality in JUPITER based on 12-month (on-treatment) measurement of GlycA and hsCRP after 12 months' of rosuvastatin 20 mg (N= 4,926 participants with 52 deaths).

	HR (95% CI)	P-value
	GlycA	
All-Cause Mortality		
Unadjusted	1.85 (1.59, 2.15)	<0.0001
Adjusted for clinical variables*	1.70 (1.42, 2.04)	<0.0001
Adjusted for clinical variables*(and CRP**	1.67 (1.36, 2.06)	<0.0001
	hsCRP	
All-Cause Mortality		
Unadjusted	1.37 (1.15, 1.64)	0.001
Adjusted for clinical variables*	1.31 (1.08, 1.58)	0.005
Adjusted for clinical variables* and GlycA	1.04 (0.85, 1.27)	0.728

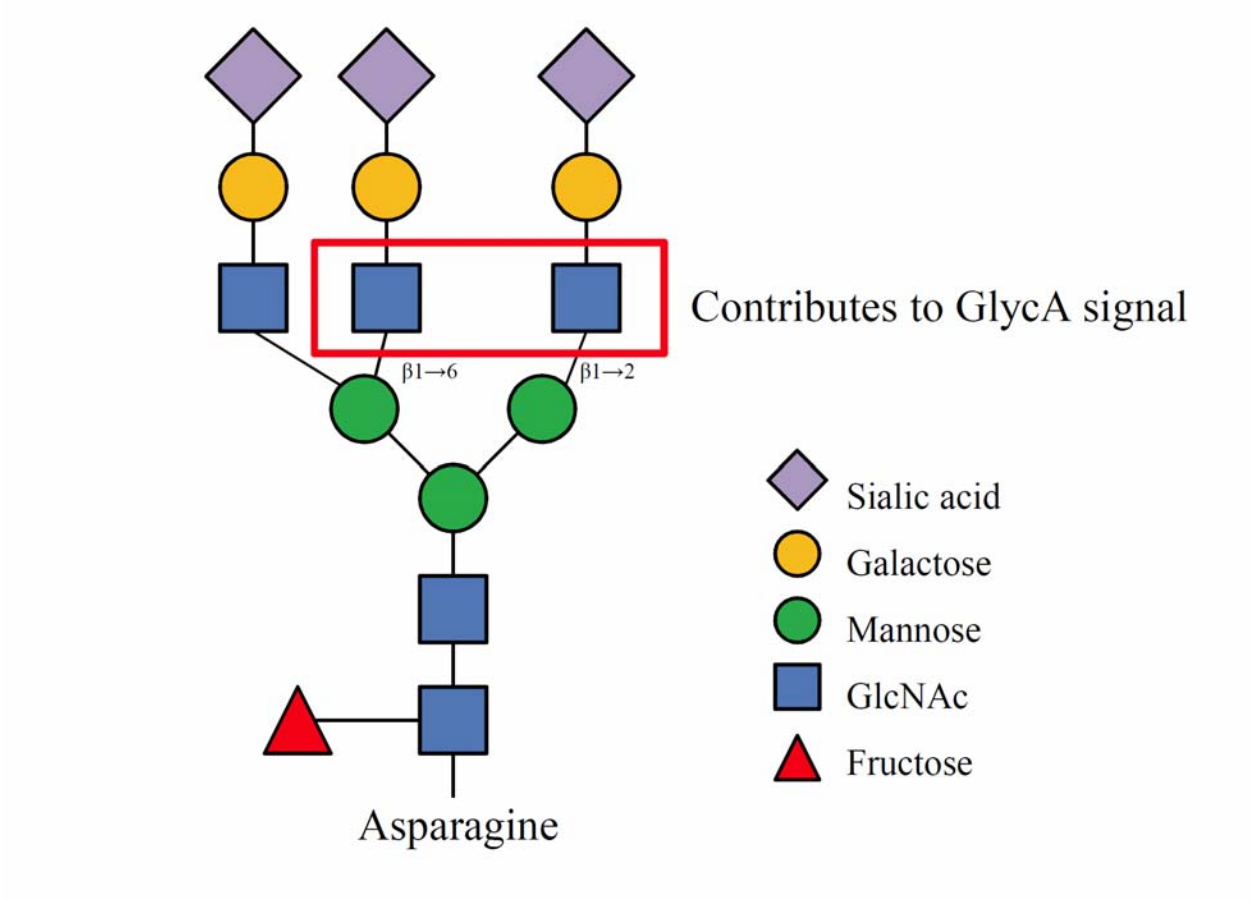
Abbreviations: CI = confidence interval, HR = hazard ratio, hsCRP = high sensitivity C-reactive protein. *Models adjusted for age, race, family history of coronary heart disease, hypertension, smoking, alcohol use, body mass index, HbA1c, LDLc, HDLc, log-transformed triglycerides, and randomization arm. **Natural log-transformed.

Online Table III: All-cause mortality risk at times of biomarker (GlycA or hsCRP) discordance: risk associated with GlycA when hsCRP is <25th percentile and for hsCRP when GlycA is <25th percentile, in WHS.

	Q1	Q2	Q3	Q4	P for trend
HR (95% CI) for GlycA among individuals in the lowest quartile† of hsCRP (N=6,918)					
	<326 µmol/L (n=3,832)	326-369 µmol/L (n=1,940)	369-416 µmol/L (n=888)	>416 µmol/L (n=258)	
All-Cause Mortality (647 deaths)					
Unadjusted	Ref.	1.19 (0.99, 1.44)	1.72 (1.38, 2.13)	2.76 (2.05, 3.73)	<0.0001
Model 1	Ref.	0.96 (0.79, 1.17)	1.28 (1.01, 1.63)	1.49 (1.05, 2.11)	0.013
CVD Mortality (104 deaths)					
Unadjusted	Ref.	0.70 (0.42, 1.16)	1.35 (0.79, 2.32)	2.89 (1.48, 5.66)	0.031
Model 1	Ref.	0.48 (0.28, 0.83)	0.74 (0.40, 1.37)	0.75 (0.32, 1.75)	0.220
Cancer Mortality (208 deaths)					
Unadjusted	Ref.	1.09 (0.79, 1.50)	1.51 (1.03, 2.21)	1.87 (1.03, 3.40)	0.010
Model 1	Ref.	0.99 (0.70, 1.39)	1.37 (0.90, 2.09)	1.52 (0.77, 3.00)	0.119
HR (95% CI) for hsCRP among individuals in the lowest quartile† of GlycA (N=6,996)**					
	<0.81 mg/L (n=3,832)	0.81-2.1 mg/L (n=2,013)	2.1-4.4 mg/L (n=869)	>4.4 mg/L (n=282)	
All-Cause Mortality (664 deaths)					
Unadjusted	Ref.	1.41 (1.18, 1.68)	1.63 (1.31, 2.03)	1.81 (1.28, 2.54)	<0.0001
Model 1	Ref.	1.08 (0.90, 1.31)	1.01 (0.79, 1.29)	1.05 (0.72, 1.52)	0.790
CVD Mortality (103 deaths)					
Unadjusted	Ref.	0.82 (0.51, 1.32)	1.21 (0.68, 2.13)	1.79 (0.82, 3.93)	0.297
Model 1	Ref.	0.60 (0.36, 1.01)	0.69 (0.37, 1.29)	0.99 (0.42, 2.34)	0.378
Cancer Mortality (237 deaths)					
Unadjusted	Ref.	1.55 (1.16, 2.06)	1.92 (1.35, 2.74)	0.83 (0.36, 1.88)	0.005
Model 1	Ref.	1.37 (1.01, 1.86)	1.51 (1.02, 2.23)	0.64 (0.27, 1.50)	0.467

Abbreviations: CI = confidence interval, HR = hazard ratio, hsCRP = high sensitivity C-reactive protein. Model 1 is adjusted for age, race, family history of myocardial infarction, hypertension, smoking, alcohol use (≥ 1 drink/day), body mass index, HbA1c, LDLc, HDLc, log-transformed triglycerides, and randomization arm. Further adjustment of GlycA and hsCRP (Model 2) for each other produced no appreciable change in the results. *During maximal follow-up. **Natural-log transformed for regression analyses. †For consistency, quartiles are a used in the primary analyses.

Online Figure I: Schematic example of tri-antennary N-acetyl linked glycan chain, with N-acetylglucosamine (GlcNAc) contributing to the GlycA signal (red box). GlycA identifies bi-, tri-, and tetra-antennary N-linked glycan chains with β1→2 and β1→6 mannose-GlcNAc linkage. Asparagine represents the universal amino acid site for N-glycosylation. (Modified from Otvos *et al*. *Clinical Chemistry* 2015.[10])



Online Figure II: Median (25th, 75th percentile) percentage change in hsCRP and GlycA after 12 months of rosuvastatin therapy in JUPITER.