Glycosylation profile of Immunoglobulin G is cross-sectionally associated with cardiovascular disease risk score and subclinical atherosclerosis in two independent cohorts

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Supplementary Material

OnlineTable I. Description of 24 quantitative IgG glycosylation traits and 52 derived trait and association between all tested glycans and derived traits with the 10-year ASCVD risk score in the discovery cohort. Analyses adjusted by age, BMI and family relatedness. Significance cut-off: P< $6.58x10^{-4}$

				10-year ASCVD risk score	
GROUP	**Glycan**	**DESCRIPTION***	**FORMULA***	**Beta(SE)**	**P**
Total IgG glycans (neutral + charged)	GP1	*The percentage of FA1 glycan in total IgG glycans*	*GP1 / GP* 100*	0.002(0.01)	8.46E-01
	GP2	*The percentage of A2 glycan in total IgG glycans*	*GP2 / GP* 100*	0.051(0.01)	3.45E-07
	GP4	*The percentage of FA2 glycan in total IgG glycans*	*GP4 / GP* 100*	-0.005(0.011)	6.36E-01
	GP5	*The percentage of M5 glycan in total IgG glycans*	*GP5 / GP* 100*	0.037(0.01)	1.53E-04
	GP6	*The percentage of FA2B glycan in total IgG glycans*	*GP6 / GP* 100*	0.072(0.011)	1.30E-10
	GP7	*The percentage of A2G1 glycan in total IgG glycans*	*GP7 / GP* 100*	0.028(0.009)	2.52E-03
	GP8	*The percentage of FA2[6]G1 glycan in total IgG glycans*	*GP8 / GP* 100*	-0.046(0.009)	8.06E-07
	GP9	*The percentage of FA2[3]G1 glycan in total IgG glycans*	*GP9 / GP* 100*	-0.052(0.009)	1.76E-08
	GP10	*The percentage of FA2[6]BG1 glycan in total IgG glycans*	*GP10 / GP* 100*	0.048(0.009)	1.93E-07
	GP11	*The percentage of FA2[3]BG1 glycan in total IgG glycans*	*GP11 / GP* 100*	0.054(0.01)	3.42E-08
	GP12	*The percentage of A2G2 glycan in total IgG glycans*	*GP12 / GP* 100*	0(0.01)	9.66E-01
	GP13	*The percentage of A2BG2 glycan in total IgG glycans*	*GP13 / GP* 100*	-0.01(0.009)	2.80E-01
	GP14	*The percentage of FA2G2 glycan in total IgG glycans*	*GP14 / GP* 100*	-0.063(0.012)	1.49E-07

	GP15	*The percentage of FA2BG2 glycan in total IgG glycans*	*GP15 / GP* 100*	0.005(0.011)	6.35E-01
	GP16	*The percentage of FA2G1S1 glycan in total IgG glycans*	*GP16 / GP * 100*	-0.049(0.009)	1.32E-07
	GP17	*The percentage of A2G2S1 glycan in total IgG glycans*	*GP17/ GP * 100*	0.012(0.009)	1.84E-01
	GP18	*The percentage of FA2G2S1 glycan in total IgG glycans*	*GP18 / GP * 100*	-0.077(0.012)	5.59E-11
	GP19	*The percentage of FA2BG2S1 glycan in total IgG glycans*	*GP19 / GP * 100*	-0.013(0.009)	1.55E-01
	GP20+GP21		*(GP20+GP21)/GP * 100*	0.017(0.009)	6.23E-02
	GP22	*The percentage of A2BG2S2 glycan in total IgG glycans*	*GP22 / GP * 100*	0.022(0.009)	8.87E-03
	GP23	*The percentage of FA2G2S2 glycan in total IgG glycans*	*GP23 / GP * 100*	-0.071(0.01)	1.43E-13
	GP24	*The percentage of FA2BG2S2 glycan in total IgG glycans*	*GP24 / GP * 100*	-0.003(0.009)	7.04E-01
Total IgG glycans - derived parameters	FGS/(FG+FGS)	*The percentage of sialylation of fucosylated galactosylated structures without bisecting GlcNAc in total IgG glycans*	*SUM(GP16 + GP18 + GP23) / SUM(GP16 + GP18 + GP23 + GP8 + GP9 + GP14)* 100*	-0.034(0.01)	5.36E-04
	FBGS/(FBG+FBGS)	*The percentage of sialylation of fucosylated galactosylated structures with bisecting GlcNAc in total IgG glycans*	*SUM(GP19 + GP24) / SUM(GP19 + GP24 + GP10 + GP11 + GP15)* 100*	-0.031(0.009)	4.26E-04
	FGS/(F+FG+FGS)	*The percentage of sialylation of all fucosylated structures without bisecting GlcNAc in total IgG glycans*	*SUM(GP16 + GP18 + GP23) / SUM(GP16 + GP18 + GP23 + GP4 + GP8 + GP9 + GP14)* 100*	-0.042(0.011)	1.31E-04
	FBGS/(FB+FBG+FBGS)	*The percentage of sialylation of all fucosylated structures with bisecting GlcNAc in total*	*SUM(GP19 + GP24) / SUM(GP19 + GP24 + GP6 + GP10 + GP11*	-0.042(0.009)	4.47E-06

		IgG glycans	*+ GP15)* 100*		
	FG1S1/(FG1+FG1S1)	*The percentage of monosialylation of fucosylated monogalactosylated structures in total IgG glycans*	*GP16 / SUM(GP16 + GP8 + GP9)* 100*	-0.005(0.009)	5.89E-01
	FG2S1/(FG2+FG2S1+FG2S2)	*The percentage of monosialylation of fucosylated digalactosylated structures in total IgG glycans*	*GP18 / SUM(GP18 + GP14 + GP23)* 100*	-0.021(0.009)	1.93E-02
	FG2S2/(FG2+FG2S1+FG2S2)	*The percentage of disialylation of fucosylated digalactosylated structures in total IgG glycans*	*GP23 / SUM(GP23 + GP14 + GP18)* 100*	-0.027(0.009)	2.99E-03
	FBG2S1/(FBG2+FBG2S1+FBG2S2)	*The percentage of monosialylation of fucosylated digalactosylated structures with bisecting GlcNAc in total IgG glycans*	*GP19 / SUM(GP19 + GP15 + GP24)* 100*	-0.018(0.009)	5.64E-02
	FBG2S2/(FBG2+FBG2S1+FBG2S2)	*The percentage of disialylation of fucosylated digalactosylated structures with bisecting GlcNAc in total IgG glycans*	*GP24 / SUM(GP24 + GP15 + GP19)* 100*	-0.001(0.009)	9.00E-01
	$F^{total}S1/F^{total}S2$	*Ratio of all fucosylated (+/- bisecting GlyNAc) monosialylated and disialylated structures in total IgG glycans*	*SUM(GP16 + GP18 + GP19) / SUM(GP23 + GP24)*	-0.009(0.009)	3.29E-01
	FS1/FS2	*Ratio of fucosylated (without bisecting GlcNAc) monosialylated and disialylated structures in total IgG glycans*	*SUM(GP16 + GP18) / GP23*	0.028(0.009)	1.50E-03

	FBS1/FBS2	*Ratio of fucosylated (with bisecting GlcNAc) monosialylated and disialylated structures in total IgG glycans*	*GP19 / GP24*	-0.01(0.009)	2.65E-01
	FBS^{total}/FS^{total}	*Ratio of all fucosylated sialylated structures with and without bisecting GlcNAc*	*SUM(GP19 + GP24) / SUM(GP16 + GP18 + GP23)*	0.053(0.01)	4.18E-07
	FBS1/FS1	*Ratio of fucosylated monosialylated structures with and without bisecting GlcNAc*	*GP19 / SUM(GP16 + GP18)*	0.041(0.01)	6.08E-05
	FBS1/(FS1+FBS1)	*The incidence of bisecting GlcNAc in all fucosylated monosialylated structures in total IgG glycans*	*GP19 / SUM(GP16 + GP18 + GP19)*	0.042(0.01)	5.97E-05
	FBS2/FS2	*Ratio of fucosylated disialylated structures with and without bisecting GlcNAc*	*GP24 / GP23*	0.101(0.01)	9.48E-23
	FBS2/(FS2+FBS2)	*The incidence of bisecting GlcNAc in all fucosylated disialylated structures in total IgG glycans*	*GP24 / SUM(GP23 + GP24)*	0.101(0.011)	2.23E-21
Neutral IgG glycans	$GP1^n$	*The percentage of FA1 glycan in total neutral IgG glycans (GP^n)*	*GP1 / GP^n* 100*	0.009(0.01)	3.48E-01
	$GP2^n$	*The percentage of A2 glycan in total neutral IgG glycans (GP^n)*	*GP2 / GP^n* 100*	0.055(0.01)	3.34E-08
	$GP4^n$	*The percentage of FA2 glycan in total neutral IgG glycans (GP^n)*	*GP4 / GP^n* 100*	0.007(0.012)	5.32E-01
	$GP5^n$	*The percentage of M5 glycan in total neutral IgG glycans (GP^n)*	*GP5 / GP^n* 100*	0.046(0.01)	2.01E-06

	GP6^{n}	*The percentage of FA2B glycan in total neutral IgG glycans (GP^{n})*	*GP6 / GP^{n}* 100*	0.096(0.012)	7.93E-17
	GP7^{n}	*The percentage of A2G1 glycan in total Ineutral IgG glycans (GP^{n})*	*GP7 / GP^{n}* 100*	0.032(0.009)	5.28E-04
	GP8^{n}	*The percentage of FA2[6]G1 glycan in total neutral IgG glycans (GP^{n})*	*GP8 / GP^{n}* 100*	-0.044(0.01)	4.31E-06
	GP9^{n}	*The percentage of FA2[3]G1 glycan in total neutral IgG glycans (GP^{n})*	*GP9 / GP^{n}* 100*	-0.047(0.009)	2.58E-07
	GP10^{n}	*The percentage of FA2[6]BG1 glycan in total neutral IgG glycans (GP^{n})*	*GP10 / GP^{n}* 100*	0.062(0.009)	1.99E-11
	GP11^{n}	*The percentage of FA2[3]BG1 glycan in total neutral IgG glycans (GP^{n})*	*GP11 / GP^{n}* 100*	0.067(0.01)	4.19E-12
	GP12^{n}	*The percentage of A2G2 glycan in total neutral IgG glycans (GP^{n})*	*GP12 / GP^{n}* 100*	0.006(0.01)	5.30E-01
	GP13^{n}	*The percentage of A2BG2 glycan in total neutral IgG glycans (GP^{n})*	*GP13 / GP^{n}* 100*	0.003(0.01)	7.79E-01
	GP14^{n}	*The percentage of FA2G2 glycan in total neutral IgG glycans (GP^{n})*	*GP14 / GP^{n}* 100*	-0.047(0.012)	9.50E-05
	GP15^{n}	*The percentage of FA2BG2 glycan in total neutral IgG glycans (GP^{n})*	*GP15 / GP^{n}* 100*	0.017(0.011)	1.14E-01
Neutral IgG glycans - derived parameters	G0^{n}	*The percentage of agalactosylated structures in total neutral IgG glycans*	*SUM(GP1^{n}: GP6^{n})*	0.036(0.012)	3.07E-03
	G1^{n}	*The percentage of*	*SUM(GP7^{n}: GP11^{n})*	-0.026(0.009)	4.69E-03

		monogalactosylated structures in total neutral IgG glycans			
	$G2^n$	*The percentage of digalactosylated structures in total neutral IgG glycans*	*SUM($GP12^n$: $GP15^n$)*	-0.037(0.012)	1.72E-03
	$F^{n\ total}$	*The percentage of all fucosylated (+/- bisecting GlcNAc) structures in total neutral IgG glycans*	*SUM($GP1^n$+ $GP4^n$+ $GP5^n$+ $GP6^n$+ $GP8^n$+ $GP9^n$+ $GP10^n$+ $GP11^n$+ $GP14^n$+ $GP15^n$)*	-0.028(0.009)	1.55E-03
	$FG0^{n\ total}/G0^n$	*The percentage of fucosylation of agalactosylated structures*	*SUM($GP1^n$+ $GP4^n$+ $GP5^n$+ $GP6^n$) / $G0^n$ * 100*	-0.038(0.008)	6.61E-06
	$FG1^{n\ total}/G1^n$	*The percentage of fucosylation of monogalactosylated structures*	*SUM($GP8^n$+ $GP9^n$+ $GP10^n$+ $GP11^n$) / $G1^n$ * 100*	-0.031(0.009)	4.04E-04
	$FG2^{n\ total}/G2^n$	*The percentage of fucosylation of digalactosylated structures*	*SUM($GP14^n$+ $GP15$) / $G2^n$ * 100*	-0.026(0.009)	3.56E-03
	F^n	*The percentage of fucosylated (without bisecting GlcNAc) structures in total neutral IgG glycans*	*SUM($GP1^n$+ $GP4^n$+ $GP5^n$+ $GP8^n$+ $GP9^n$+ $GP14^n$)*	-0.084(0.009)	3.68E-19
	$FG0^n/G0^n$	*The percentage of fucosylation (without bisecting GlcNAc) of agalactosylated structures*	*SUM($GP1^n$+ $GP4^n$+ $GP5^n$) / $G0^n$ * 100*	-0.074(0.009)	2.22E-16
	$FG1^n/G1^n$	*The percentage of fucosylation (without bisecting GlcNAc) of monogalactosylated structures*	*SUM($GP8^n$+ $GP9^n$) / $G1^n$ * 100*	-0.082(0.009)	1.60E-18

	$FG2^n/G2^n$	*The percentage of fucosylation (without bisecting GlcNAc) of digalactosylated structures*	$GP14^n/ G2^n * 100$	-0.058(0.01)	1.51E-09
	FB^n	*The percentage of fucosylated (with bisecting GlcNAc) structures in total neutral IgG glycans*	$SUM(GP6^n + GP10^n + GP11^n + GP15^n)$	0.09(0.01)	7.75E-20
	$FBG0^n/G0^n$	*The percentage of fucosylation (with bisecting GlcNAc) of agalactosylated structures*	$GP6^n/ G0^n * 100$	0.073(0.009)	4.22E-15
	$FBG1^n/G1^n$	*The percentage of fucosylation (with bisecting GlcNAc) of monogalactosylated structures*	$SUM(GP10^n + GP11^n) / G1^n * 100$	0.08(0.01)	5.72E-17
	$FBG2^n/G2^n$	*The percentage of fucosylation (with bisecting GlcNAc) of digalactosylated structures*	$GP15) / G2^n * 100$	0.072(0.01)	1.90E-12
	FB^n/F^n	*Ratio of fucosylated structures with and without bisecting GlcNAc*	$FB^n/ F^n * 100$	0.09(0.01)	3.70E-20
	$FB^n/F^{n\ total}$	*The incidence of bisecting GlcNAc in all fucosylated structures in total neutral IgG glycans*	$FB^n/ F^{n\ total} * 100$	0.09(0.01)	6.23E-20
	$F^n/(B^n + FB^n)$	*Ratio of fucosylated non-bisecting GlcNAc structures and all structures with bisecting GlcNAc*	$F^n/(GP13^n + FB^n)$	-0.089(0.01)	7.74E-20
	$B^n/(F^n + FB^n)$	*Ratio of structures with bisecting GlcNAc and all fucosylated structures (+/-*	$GP13^n/ (F^n + FB^n) * 1000$	0.004(0.009)	6.61E-01

		bisecting GlcNAc)			
	FBG2^{n}/FG2^{n}	*Ratio of fucosylated digalactosylated structures with and without bisecting GlcNAc*	*GP15^{n}/GP14^{n}*	0.074(0.01)	4.86E-13
	FBG2^{n}/(FG2^{n} + FBG2^{n})	*The incidence of bisecting GlcNAc in all fucosylated digalactosylated structures in total neutral IgG glycans*	*GP15^{n}/(GP14^{n} + GP15^{n}) * 100*	0.074(0.01)	5.73E-13
	FG2^{n}/(BG2^{n} + FBG2^{n})	*Ratio of fucosylated digalactosylated non-bisecting GlcNAc structures and all digalactosylated structures with bisecting GlcNAc*	*GP14^{n}/(GP13^{n} + GP15^{n})*	-0.074(0.01)	1.23E-12
	BG2^{n}/(FG2^{n} + FBG2^{n})	*Ratio of digalactosylated structures with bisecting GlcNAc and all fucosylated digalactosylated structures (+/- bisecting GlcNAc)*	*GP15^{n}/(GP14^{n} + GP15^{n}) * 1000*	0.038(0.01)	2.18E-04

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Online Table II. Descriptive characteristics of the male population included in the validation analysis.

Phenotype	TwinsUK Mean(SD)	ORCADES Mean(SD)
n	189	656
Males %	100%	100%
Age	57.21(10.88)	54.51(14.76)
10-years ASCVD Risk Score	11.04(9.29)	12.19(13.59)
BMI	26.70(3.71)	28.03(5.51)
DBP, mmHG	82.03(9.79)	72.67(9.23)
HDL Cholesterol, mmol/l	1.24(0.35)	1.33(0.37)
SBP, mmHG	133.19(16.13)	132.07(16.26)
Current smokers,%	2.65%	8.52%
Total Cholesterol, mmol/l	5.24(1.20)	5.32(1.12)
T2D, %	0%	4.71%

Online Table III. Glycan traits associated with the 10-years ASCVD risk score and their association with smoking, HDL and total cholesterol, systolic blood pressure, type 2 diabetes and insulin resistance adjusting for age, BMI and family relatedness in the discovery cohort.

	ASCVD		SMK		HDL		TC		SBP		T2D		HOMA	
Glycan	**Beta (SE)**	**P**	**Beta (SE)**	**P**	**Beta (SE)**	**P**	**Beta (SE)**	**P**	**Beta (SE)**	**P**	**Beta (SE)**	**P**	**Beta (SE)**	**P**
GP6	0.07 (0.01)	1.30×10^{-10}	0.52 (0.08)	2.08×10^{-10}	-0.04 (0.01)	4.07×10^{-6}	0.07 (0.03)	1.51×10^{-2}	-0.13 (0.34)	7.01×10^{-1}	0.18 (0.14)	1.90×10^{-1}	0.06 (0.02)	9.63×10^{-4}
GP14	-0.06 (0.01)	1.49×10^{-7}	-0.13 (0.1)	1.80×10^{-1}	0.03 (0.01)	7.50×10^{-4}	-0.15 (0.03)	9.48×10^{-8}	-0.21 (0.36)	5.56×10^{-1}	-0.11 (0.19)	5.71×10^{-1}	-0.03 (0.02)	1.91×10^{-1}
GP18	-0.08 (0.01)	5.59×10^{-11}	-0.19 (0.09)	4.71×10^{-2}	0.05 (0.01)	8.92×10^{-8}	-0.15 (0.03)	2.94×10^{-8}	-0.32 (0.35)	3.55×10^{-1}	-0.13 (0.16)	3.92×10^{-1}	-0.05 (0.02)	4.20×10^{-3}
FGS/(F+FG+FGS)	-0.04 (0.01)	1.31×10^{-4}	-0.01 (0.09)	8.71×10^{-1}	0.05 (0.01)	1.27×10^{-8}	-0.06 (0.03)	2.10×10^{-2}	-0.35 (0.33)	2.77×10^{-1}	-0.01 (0.14)	9.40×10^{-1}	-0.07 (0.02)	3.15×10^{-5}
FBStotal/FStotal	0.05 (0.01)	4.18×10^{-7}	0.22 (0.09)	1.03×10^{-2}	-0.03 (0.01)	1.31×10^{-3}	0.08 (0.02)	8.22×10^{-4}	-0.14 (0.31)	6.46×10^{-1}	0.07 (0.15)	6.66×10^{-1}	0.01 (0.02)	7.19×10^{-1}
FBS1/FS1	0.04 (0.01)	6.08×10^{-5}	0.12 (0.08)	1.62×10^{-1}	-0.03 (0.01)	4.25×10^{-4}	0.07 (0.02)	3.56×10^{-3}	-0.1 (0.31)	7.50×10^{-1}	0.01 (0.15)	9.38×10^{-1}	0.02 (0.02)	3.27×10^{-1}
FBS1/(FS1+FBS1)	0.04 (0.01)	5.97×10^{-5}	0.11 (0.08)	1.76×10^{-1}	-0.03 (0.01)	5.63×10^{-4}	0.07 (0.02)	2.55×10^{-3}	-0.11 (0.31)	7.24×10^{-1}	0.01 (0.16)	9.31×10^{-1}	0.02 (0.02)	3.36×10^{-1}
GP6n	0.1 (0.01)	7.93×10^{-17}	0.73 (0.09)	3.33×10^{-15}	-0.04 (0.01)	4.85×10^{-5}	0.13 (0.03)	5.57×10^{-6}	-0.24 (0.35)	4.99×10^{-1}	0.28 (0.16)	7.94×10^{-2}	0.04 (0.02)	3.19×10^{-2}
GP9n	-0.05 (0.01)	2.58×10^{-7}	-0.54 (0.06)	6.40×10^{-18}	0.02 (0.01)	1.43×10^{-2}	0.02 (0.02)	3.25×10^{-1}	0.27 (0.27)	3.23×10^{-1}	-0.18 (0.12)	1.23×10^{-1}	-0.02 (0.01)	3.02×10^{-1}
GP14n	-0.05 (0.01)	9.50×10^{-5}	-0.01 (0.1)	9.31×10^{-1}	0.04 (0.01)	2.03×10^{-5}	-0.1 (0.03)	8.11×10^{-4}	-0.29 (0.36)	4.24×10^{-1}	-0.05 (0.16)	7.76×10^{-1}	-0.05 (0.02)	6.75×10^{-3}
GlycA*	0.13 (0.01)	9.34×10^{-21}	0.24 (0.09)	9.39×10^{-3}	-0.09 (0.01)	3.31×10^{-14}	0.23 (0.03)	9.70×10^{-12}	1.06 (0.42)	0.01	0.55 (0.17)	1.30×10^{-3}	0.13 (0.02)	5.10×10^{-13}

ASCVD=10-year atherosclerotic cardiovascular disease risk score adjusting for age, BMI and family relatedness; **SMK**= smoking, **HDL**= HDL cholesterol, **TC**= total cholesterol, **SBP**= systolic blood pressure; **T2D**=type 2 diabetes; **HOMA**=insulin resistance. *GlycA was measured in mmol/L by the NMR metabolomics provider Nightingale inc under the name GP. GlycA has been standardised to have mean 0 and SD 1.

Online Table IV. Association of glycan traits with the 10-year ASCVD risk score overall and adjusting for smoking, HDL cholesterol, total cholesterol and HOMA respectively in the discovery cohort.

	ASCVD		ASCVD_adj_SMK		ASCVD_adj_HDL		ASCVD_adj_TC		ASCVD_adj_HOMA	
Glycan	**Beta (SE)**	**P**	**Beta (SE)**	**P**	**Beta (SE)**	**P**	**Beta (SE)**	**P**	**Beta (SE)**	**P**
GP6	0.07 (0.01)	$1.30x10^{-10}$	0.05 (0.01)	$4.68x10^{-7}$	0.05 (0.01)	$4.58x10^{-7}$	0.06 (0.01)	$4.54x10^{-9}$	0.05 (0.01)	$1.57x10^{-4}$
GP14	-0.06 (0.01)	$1.49x10^{-7}$	-0.06 (0.01)	$6.18x10^{-9}$	-0.05 (0.01)	$1.39x10^{-5}$	-0.04 (0.01)	$1.84x10^{-4}$	-0.05 (0.01)	$9.02x10^{-4}$
GP18	-0.08 (0.01)	$5.59x10^{-11}$	-0.07 (0.01)	$1.86x10^{-11}$	-0.05 (0.01)	$6.31x10^{-7}$	-0.06 (0.01)	$4.03x10^{-7}$	-0.06 (0.01)	$1.24x10^{-5}$
FGS/(F+FG+FGS)	-0.04 (0.01)	$1.31x10^{-4}$	-0.04 (0.01)	$2.96x10^{-5}$	-0.02 (0.01)	$5.59x10^{-2}$	-0.03 (0.01)	$1.11x10^{-3}$	-0.02 (0.01)	$9.62x10^{-2}$
FBStotal/FStotal	0.05 (0.01)	$4.18x10^{-7}$	0.05 (0.01)	$1.12x10^{-6}$	0.04 (0.01)	$2.55x10^{-5}$	0.04 (0.01)	$2.73x10^{-5}$	0.05 (0.01)	$2.13x10^{-5}$
FBS1/FS1	0.04 (0.01)	$6.08x10^{-5}$	0.04 (0.01)	$1.87x10^{-5}$	0.03 (0.01)	$2.72x10^{-3}$	0.03 (0.01)	$1.20x10^{-3}$	0.04 (0.01)	$8.25x10^{-4}$
FBS1/(FS1+FBS1)	0.04 (0.01)	$5.97x10^{-5}$	0.04 (0.01)	$1.56x10^{-5}$	0.03 (0.01)	$2.43x10^{-3}$	0.03 (0.01)	$1.34x10^{-3}$	0.04 (0.01)	$1.01x10^{-3}$
GP6n	0.1 (0.01)	$7.93x10^{-17}$	0.07 (0.01)	$5.69x10^{-11}$	0.08 (0.01)	$2.90x10^{-13}$	0.08 (0.01)	$6.75x10^{-13}$	0.08 (0.01)	$7.35x10^{-9}$
GP9n	-0.05 (0.01)	$2.58x10^{-7}$	-0.02 (0.01)	$9.94x10^{-3}$	-0.04 (0.01)	$6.14x10^{-6}$	-0.05 (0.01)	$6.92x10^{-9}$	-0.05 (0.01)	$2.30x10^{-6}$
GP14n	-0.05 (0.01)	$9.50x10^{-5}$	-0.05 (0.01)	$3.02x10^{-6}$	-0.03 (0.01)	$1.08x10^{-2}$	-0.03 (0.01)	$3.10x10^{-3}$	-0.02 (0.01)	$9.85x10^{-2}$
GlycA	0.13 (0.01)	$9.34 x10^{-21}$	0.11 (0.01)	$1.19x10^{-16}$	0.09 (0.01)	$2.27x10^{-11}$	0.11 (0.01)	$4.35x10^{-15}$	0.11 (0.02)	$2.33x10^{-12}$

ASCVD=10-year atherosclerotic cardiovascular disease risk score adjusting for age, BMI and family relatedness; **ASCVD_adj_SMK**= 10-years ASCVD score adjusting for age, BMI, family relatedness and smoking, **ASCVD_adj_HDL**= 10-years ASCVD scor adjusting for age, BMI, family relatedness and HDL cholesterol, **ASCVD_adj_TC**= 10-years ASCVD scor adjusting for age, BMI, family relatedness and total cholesterol, **ASCVD_adj_HOMA2IR**= 10-years ASCVD scor adjusting for age, BMI, family relatedness and HOMA2IR. Glycan traits in italics do not remain statistically significant after adjustment

for individual risk factors. *****GlycA was measured in mmol/L by the NMR metabolomics provider Nightingale inc under the name GP. GlycA has been standardised to have mean 0 and SD 1.

Online Table V. Glycan traits associated with the 10-year ASCVD risk score and their association with femoral and carotid plaque in TwinsUK females.

	Femoral plaque		Femoral plaque adj SMK		Carotid plaque		Carotid plaque adj SMK	
Glycan	**Beta(SE)**	**P**	**Beta(SE)**	**P**	**Beta(SE)**	**P**	**Beta(SE)**	**P**
GP6	0.387(0.152)	**0.01**	0.359(0.158)	**0.02**	0.467(0.154)	**$2.40x10^{-3}$**	0.453(0.157)	**$3.92x10^{-3}$**
GP14	-0.174(0.165)	0.29	-0.177(0.166)	0.29	-0.213(0.155)	0.17	-0.221(0.156)	0.16
GP18	-0.128(0.162)	0.43	-0.144(0.165)	0.38	-0.494(0.147)	**$7.70x10^{-4}$**	-0.524(0.152)	**$5.81x10^{-4}$**
FBStotal/FStotal	0.021(0.149)	0.89	0.022(0.149)	0.89	0.173(0.133)	0.19	0.177(0.132)	0.18
FBS1/FS1	-0.03(0.148)	0.84	-0.003(0.15)	0.98	0.123(0.127)	0.33	0.154(0.13)	0.23
FBS1/(FS1+FBS1)	-0.041(0.149)	0.78	-0.014(0.152)	0.93	0.12(0.13)	0.35	0.152(0.133)	0.25
GP6n	0.48(0.154)	**$1.88x10^{-3}$**	0.427(0.159)	**0.01**	0.39(0.152)	**0.01**	0.347(0.155)	**0.03**
GP9n	-0.252(0.128)	**0.05**	-0.211(0.129)	0.10	-0.297(0.119)	**0.01**	-0.264(0.121)	**0.03**
GlycA*	0.317(0.105)	**0.002**	0.313(0.107)	**0.003**	0.194(0.099)	**0.05**	0.298(0.15)	**0.049**

*GlycA was measured in mmol/L by the NMR metabolomics provider Nightingale inc under the name GP. GlycA has been standardised to have mean 0 and SD 1.

Online Table VI. Pearson's correlation and p-value between the 8 IgG glycans reproducibly and the NMR GlycA measure in TwinsUK

Pearson Correlations	GlycA*	GP6	GP14	GP18	FBStotal/ FStotal	FBS1/FS1	FBS1/ (FS1+FBS1)	GP6n	GP9n
GlycA	1								
GP6	0.21 $7.7x10^{-18}$	1							
GP14	-0.22 $3.4x10^{-20}$	-0.69 $2.5x10^{-233}$	1						
GP18	-0.21 $2.5x10^{-18}$	-0.74 $5.4x10^{-284}$	0.87 $<10^{-300}$	1					
FBStotal/FStotal	0.17 $4.5x10^{-12}$	0.50 $8.1x10^{-103}$	-0.73 $4.8x10^{-273}$	-0.76 $<10^{-300}$	1				
FBS1/FS1	0.16 $2.2x10^{-11}$	0.50 $4.1x10^{-102}$	-0.70 $7.4x10^{-244}$	-0.77 $<10^{-300}$	0.97 $<10^{-300}$	1			
FBS1/(FS1+FBS1)	0.16 $2.2x10^{-11}$	0.50 $7.0x10^{-104}$	-0.70 $2.1x10^{-244}$	-0.77 $<10^{-300}$	0.97 $<10^{-300}$	0.99 $<10^{-300}$	1		
GP6n	0.20 $9.8x10^{-17}$	0.94 $<10^{-300}$	-0.78 $<10^{-300}$	-0.76 $<10^{-300}$	0.55 $3.2x10^{-128}$	0.51 $3.7x10^{-111}$	0.52 $9.6x10^{-113}$	1	
GP9n	-0.06 $2.4x10^{-2}$	-0.30 $8.0x10^{-36}$	0.1369 $2.7x10^{-8}$	0.111 $2.0x10^{-5}$	-0.10 $2.1x10^{-5}$	-0.08 $1.1x10^{-3}$	-0.08 $2.1x10^{-3}$	-0.34 $2.2x10^{-45}$	1

*GlycA was measured in mmol/L by the NMR metabolomics provider Nightingale inc under the name GP. GlycA has been standardised to have mean 0 and SD 1.

Online Table VII. Association between GP18 and various measures of cholesterol, lipoproteins and triglycerides in serum from TwinsUK females

Lipid trait	Beta	SE	P
Apolipoprotein A-I	0.069	0.055	2.09×10^{-1}
Apolipoprotein B	-0.148	0.052	4.86×10^{-3}
Concentration of chylomicrons and extremely large VLDL particles	-0.210	0.053	9.73×10^{-5}
Concentration of IDL particles	-0.070	0.052	1.80×10^{-1}
Concentration of large HDL particles	0.149	0.054	5.70×10^{-3}
Concentration of large LDL particles	-0.083	0.053	1.19×10^{-1}
Concentration of large VLDL particles	-0.226	0.053	2.29×10^{-5}
Concentration of medium HDL particles	0.093	0.050	6.36×10^{-2}
Concentration of medium LDL particles	-0.082	0.054	1.30×10^{-1}
Concentration of medium VLDL particles	-0.228	0.052	1.56×10^{-5}
Concentration of small LDL particles	-0.089	0.053	9.23×10^{-2}
Concentration of small VLDL particles	-0.213	0.050	2.25×10^{-5}
Concentration of very large HDL particles	0.095	0.055	8.66×10^{-2}
Concentration of very large VLDL particles	-0.224	0.054	3.49×10^{-5}
Concentration of very small VLDL particles	-0.149	0.049	2.64×10^{-3}
Remnant cholesterol (non-HDL, non-LDL -cholesterol)	-0.138	0.049	5.16×10^{-3}
Sphingomyelins	-0.045	0.058	4.41×10^{-1}
Triglycerides in chylomicrons and extremely large VLDL	-0.209	0.053	9.24×10^{-5}
Triglycerides in HDL	-0.079	0.045	8.26×10^{-2}
Triglycerides in IDL	-0.086	0.046	6.48×10^{-2}
Triglycerides in large HDL	0.092	0.047	4.93×10^{-2}
Triglycerides in large LDL	-0.060	0.047	2.07×10^{-1}
Triglycerides in large VLDL	-0.223	0.052	1.85×10^{-5}
Triglycerides in LDL	-0.063	0.049	1.97×10^{-1}
Triglycerides in medium HDL	-0.093	0.048	5.38×10^{-2}
Triglycerides in medium LDL	-0.038	0.050	4.51×10^{-1}
Triglycerides in medium VLDL	-0.227	0.051	1.31×10^{-5}
Triglycerides in small LDL	-0.106	0.048	2.94×10^{-2}

Triglycerides in small VLDL	-0.213	0.050	$2.81x10^{-5}$
Triglycerides in very large HDL	-0.048	0.050	$3.37x10^{-1}$
Triglycerides in very large VLDL	-0.223	0.053	$2.71x10^{-5}$
Triglycerides in very small VLDL	-0.165	0.048	$6.04x10^{-4}$
Triglycerides in VLDL	-0.197	0.048	$5.10x10^{-5}$

Online Figure I. Glycan traits significantly associated with 10-years ASCVD risk in females and validation in males.