Supplementary Materials: A gene-diet interaction-based score predicts response to dietary fat in the Women's Health Initiative

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Supplementary

Table 1: Sample size necessary to achieve power of 0.8

GxE variance explained (%)	N (nominal)	N (suggestive)	N (genome-wide)
0.05	14046	49488	70866
0.10	7021	24737	35423
0.50	1401	4936	7069
1.00	699	2461	3524

Power calculations were undertaken using the Quanto tool, with parameters set as follows: additive model, SNP main effect of 0.5% of trait variance, binary environment with 50% prevalence, and environmental effect explaining 10% of the trait variance.

Table 2: Responder score effects on CRF changes in DM trial participants across main-effect filter thresholds

CRF	N[1]	All variants			Nominal main effect (p<0.05)			Suggestive main effect (p<1e-5)		
		# SNPs[2]	SES[3]	P-value	# SNPs[2]	SES[3]	P-value	# SNPs[2]	SES[3]	P-value
BMI	1988	158365	0.058	0.009	6042	0.029	0.189	569	0.027	0.221
SBP	2004	153942	-0.016	0.473	1536	0.034	0.125	6	-0.003	0.899
LDL-C	145	156313	0.124	0.337	1760	-0.191	0.02	46	0	1
HDL-C	150	153942	0.031	0.611	1731	-0.083	0.32	42	0.086	0.244
TG	150	152006	-0.067	0.66	1774	-0.146	0.055	47	-0.034	0.661
FG	281	161906	-0.056	0.64	1924	0.011	0.853	7	0.004	0.952

[1] Sample size available with 1-year follow-up for each CRF

[2] Number of SNPs selected by the pruning-and-thresholding algorithm for each CRF-threshold combination

[3] Standardized effect size (SES) represents the regression coefficient estimate in terms of CRF standard deviation per responder

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Table 3: Responder score effects on CRF changes in DM trial participants across ancestries

CRF	All combined			Black			Hispanic		
	N[1]	SES[2]	P-value	N[1]	SES[2]	P-value	N[1]	SES[2]	P-value
BMI	3606	-0.019	0.263	1214	0.002	0.941	404	0.019	0.714
SBP	3645	0.046	0.005	1230	0.011	0.692	411	-0.016	0.744
LDL-C	422	0.084	0.068	206	0.06	0.373	71	0.124	0.24
HDL-C	430	-0.059	0.24	206	-0.087	0.242	74	-0.032	0.815
TG	430	-0.073	0.122	206	-0.02	0.778	74	-0.1	0.424
FG	572	0.077	0.048	214	-0.01	0.876	77	0.006	0.961

[1] Sample size available with 1-year follow-up measurements for each CRF

[2] Std. effect size represents the regression coefficient estimate in terms of CRF standard deviation per responder score standard deviation

Table 4: LDpred-based responder score effects on CRF changes in DM trial participants across causal variant fractions (F)

CRF	F = 0.001		F = 0.01		F = 0.1	
	SES[1]	P-value	SES[1]	P-value	SES[1]	P-value

BMI	0.001	0.969	0.003	0.906	0.003	0.906
SBP	-0.016	0.478	-0.011	0.617	-0.011	0.625
LDL-C	-0.038	0.652	-0.051	0.555	-0.053	0.533
HDL-C	0.059	0.484	0.069	0.422	0.071	0.409
TG	0.015	0.863	0.019	0.828	0.018	0.832
FG	0.038	0.538	0.051	0.399	0.052	0.395

[1] Standardized effect size (SES) represents the regression coefficient estimate in terms of CRF standard deviation per responder score standard deviation

Table 5: LDL-FRS effects on alternate CRF changes in DM trial participants

Outcome risk factor	# SNPs in risk score	N[1]	Std. effect size[2]	P-value
BMI	1760	1988	-0.02	0.48
SBP	1760	2004	0.00	0.85
HDL-C	1760	150	-0.07	0.40
TG	1760	150	0.11	0.18
FG	1760	281	0.01	0.93

[1] Sample size available with 1-year follow-up measurements for each CRF

[2] Std. effect size represents the regression coefficient estimate in terms of CRF standard deviation per responder score standard deviation

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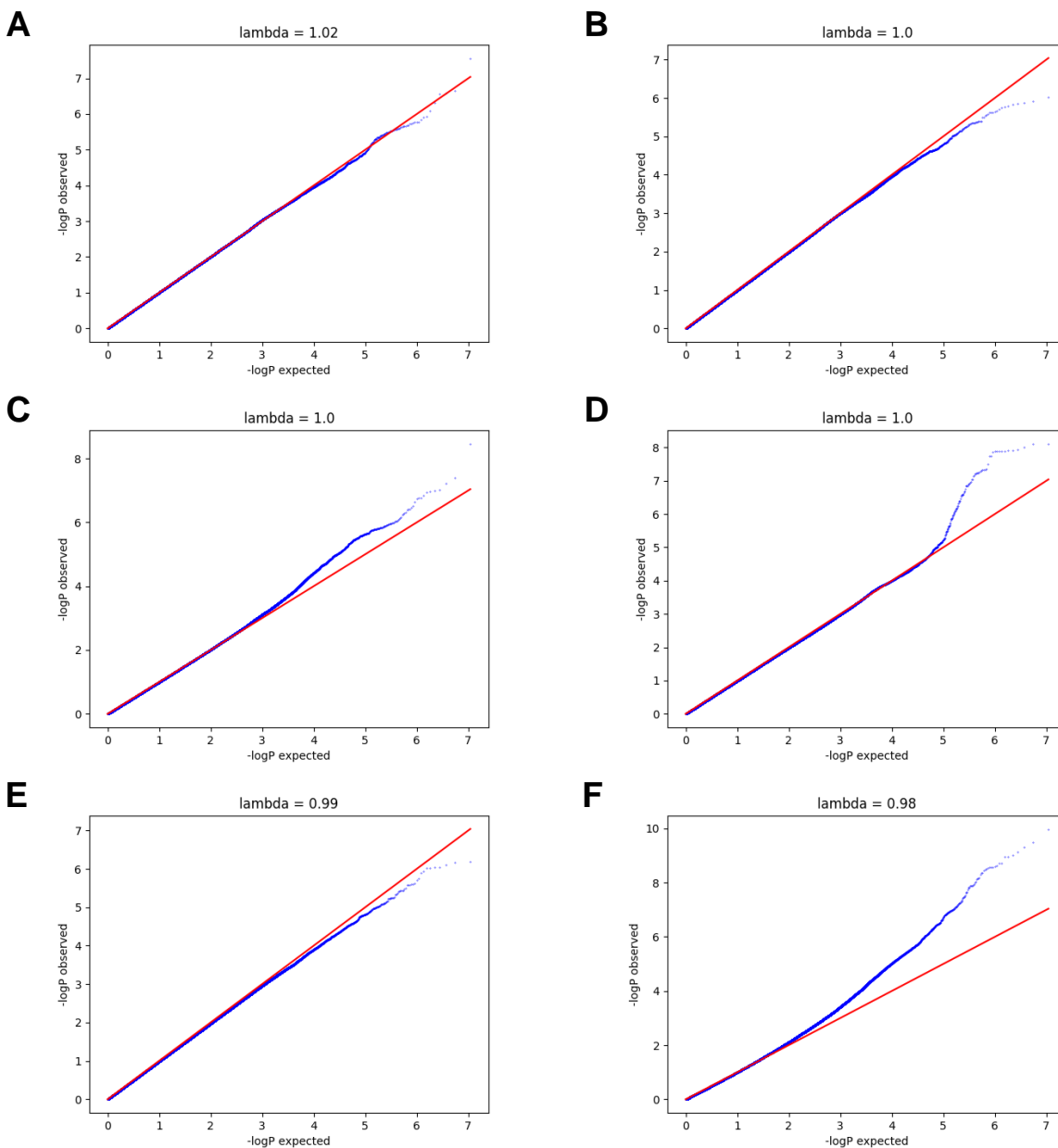

Figure 1: Q-Q plots from individual CRF GWIS. The distribution of p-values from each GWIS is plotted against the expected uniform p-value distribution. Plots correspond to: A) BMI, B) SBP, C) LDL-C, D) HDL-C, E) TG, and F) FG. Lambda values above each plot represent genomic inflation estimates. BMI: body mass index, SBP: systolic blood pressure, LDL-C: LDL cholesterol, HDL-C: HDL cholesterol, TG: triglycerides, FG: fasting glucose.