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

Table S1: 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 S2: 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	0.049	0.026	6042	0.027	0.221	569	0.027	0.236
FG	281	161906	-0.078	0.495	1924	0.016	0.791	7	0.006	0.92
HDL-C	150	153942	0.028	0.63	1731	-0.06	0.471	42	0.085	0.258
LDL-C	145	156313	0.035	0.729	1760	-0.179	0.026	46	0.01	0.901
SBP	2004	153942	-0.016	0.473	1536	0.029	0.196	6	0	0.999
TG	150	152006	-0.184	0.203	1774	-0.139	0.066	47	-0.043	0.573

[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 score standard deviation

Table S3: Responder score effects on CRF changes in DM trial participants across ancestries

CRF	All combined			Black			Hispanic		
	N	SES[1]	P-value	N	SES[1]	P-value	N	SES[1]	P-value
BMI	3606	-0.02	0.24	1214	0	0.994	404	0.018	0.719
FG	572	0.08	0.043	214	-0.004	0.955	77	-0.014	0.901
HDL-C	430	-0.06	0.224	206	-0.096	0.182	74	-0.057	0.66
LDL-C	422	0.084	0.066	206	0.055	0.412	71	0.126	0.227
SBP	3645	0.041	0.015	1230	0	0.991	411	-0.008	0.868
TG	430	-0.075	0.112	206	-0.023	0.743	74	-0.098	0.433

[1] Standardized effect size (SES) represents the regression coefficient estimate in terms of CRF standard deviation per responder score standard deviation
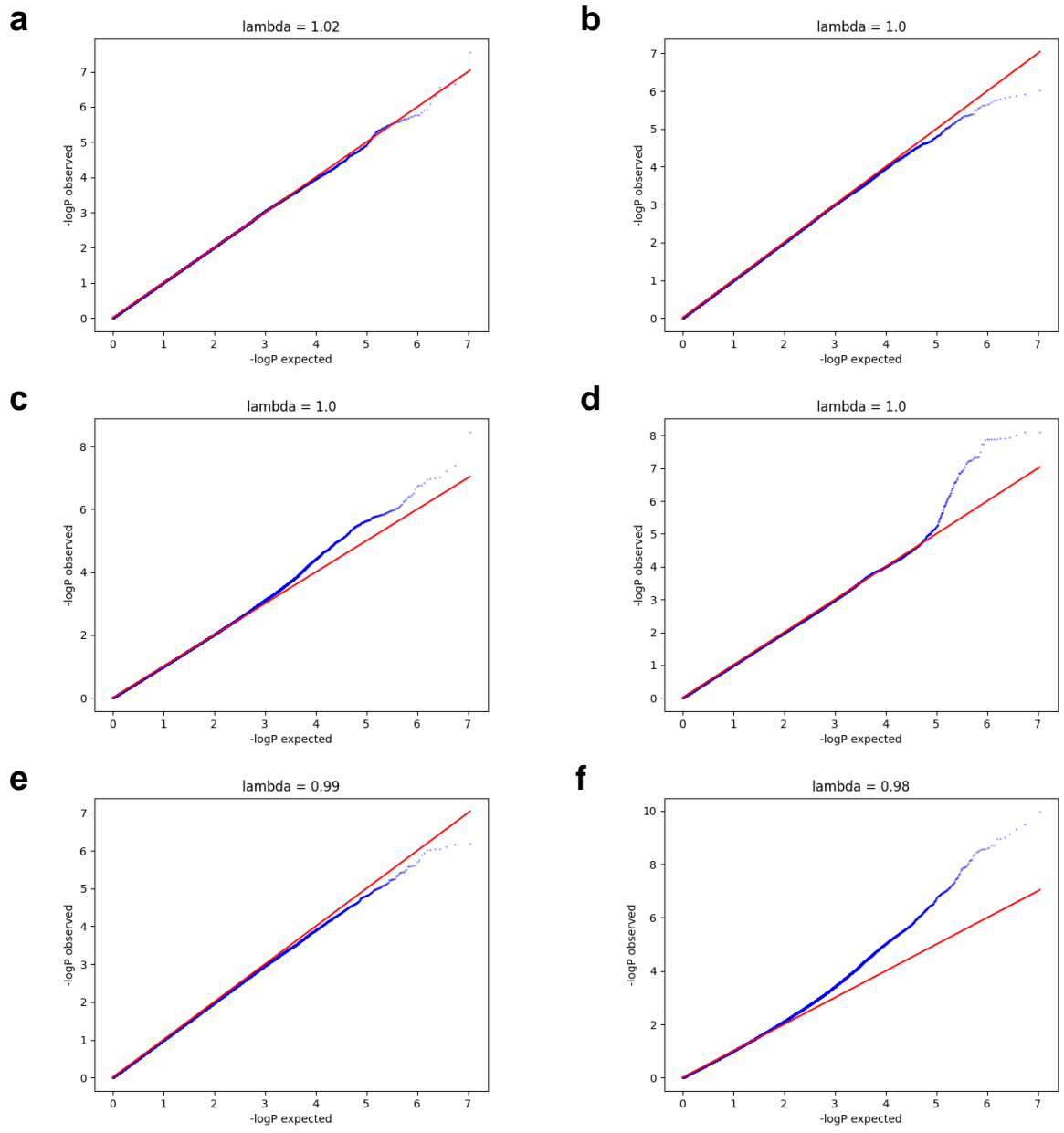
Figure S1: Q-Q plots from individual CRF GWIS. The distribution of p-values from each GWIS is plotted against the expected uniform p-value distribution. Plots correspond to: a) BMI, b) SBP, c) LDL-C, d) HDL-C, e) TG, and f) FG.

Table S4: LDL-FRS effects on alternate CRF changes in DM trial participants

Outcome risk factor	# SNPs in risk score	Sample size	Std. effect size[1]	P-value
BMI	1747	1988	-0.02	0.36
SBP	1747	2004	0.00	0.83
HDL-C	1747	150	-0.07	0.39
TG	1747	150	0.11	0.16
FG	1747	281	0.01	0.82

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