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

		All variants			Nominal main effect (p<0.05)			Suggestive main effect (p<1e-5)		
CRF	N[1]	# 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

	All combined			Black			Hispanic		
CRF	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

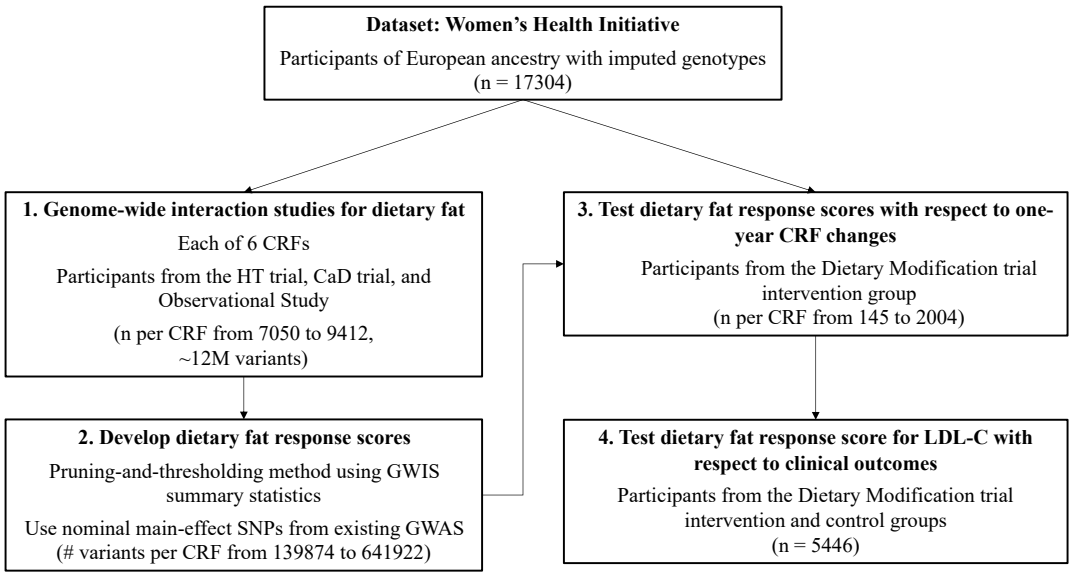

Figure S1: Workflow of the study. First, a series of genome-wide interaction studies (GWIS) were conducted with dietary fat as the exposure for each of six cardiovascular risk factors (CRFs). Next, dietary fat response scores were developed using GWIS summary statistics and tested for the prediction of one-year CRF changes in the Dietary Modification trial intervention arm. Finally, the LDL-C score was tested for the prediction of differential effects on chronic disease development over approximately twenty years of follow-up.

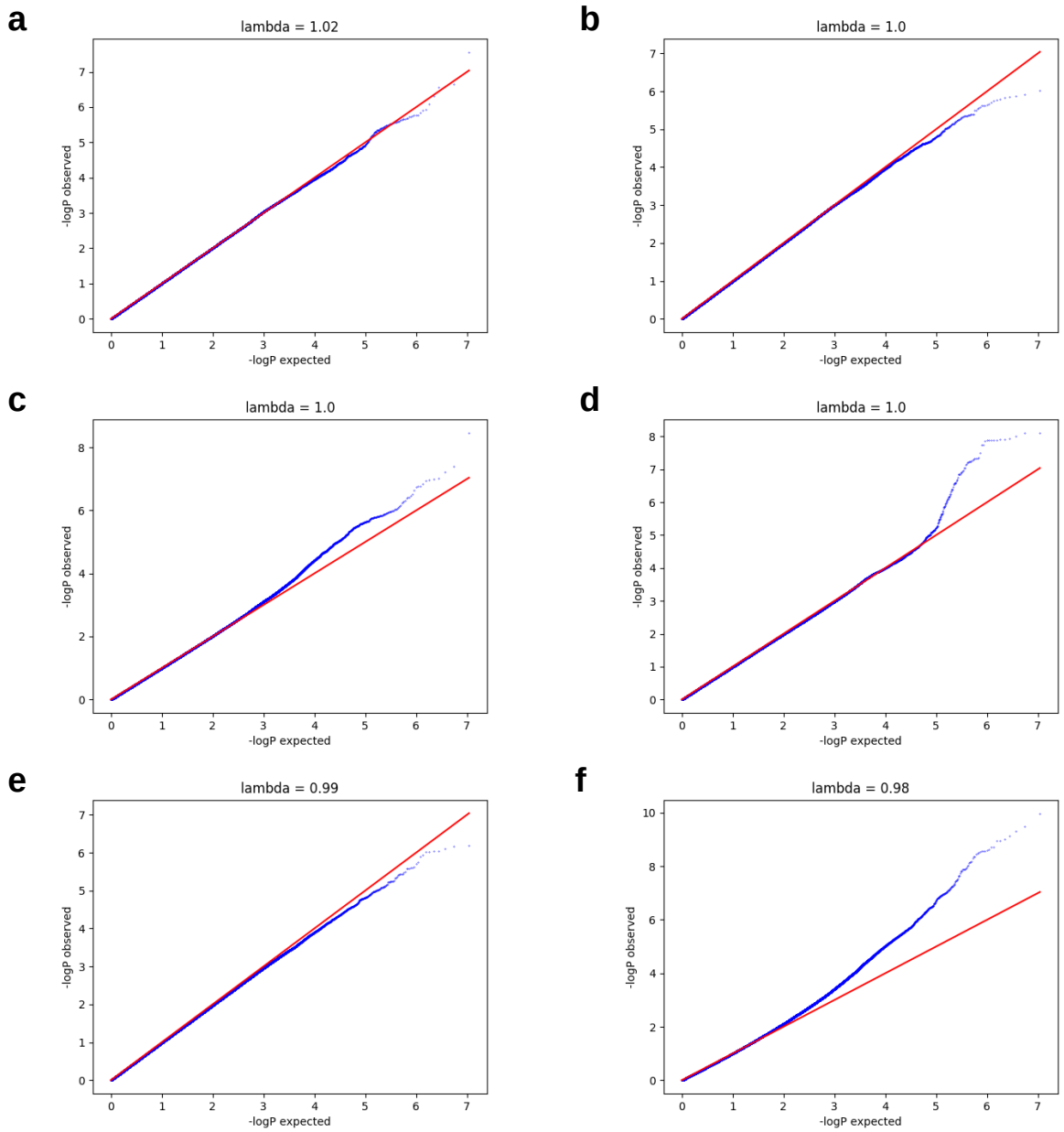

Figure S2: Q-Q plots from individual CRF GWIS. The distribution of p-values from each GWIS is plotted against the expected uniform p-value distribution. Plots correspond to: a) BMI, b) SBP, c) LDL-C, d) HDL-C, e) TG, and f) FG.

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