Supplemental Data Information

Supplemental Materials and Methods

WHI-OS and WHI- SHARe

Women's Health Initiative (WHI) represents one of the largest (n=161,808) studies of women's health conducted in the U.S. with two components: (i) a Clinical Trial (CT) component that enrolled and randomized 68,132 women ages 50 –79 into at least one of three placebo-control clinical trials (hormone therapy, dietary modification, and calcium/vitamin D); and (ii) an Observational Study (OS) component that enrolled 93,676 women of the same age range into a parallel prospective cohort study(1). The WHI OS is a longitudinal study designed to investigate the association of clinical, socioeconomic, behavioral, and dietary risk factors with the subsequent incidences of health outcomes, which includes T2D and cardiovascular disease. Details regarding the prospective observational study design have been described elsewhere(1, 2). Of the 93,676 postmenopausal women enrolled in the WHI-OS, 82,069 had no history of type 2 diabetes (T2D) at baseline. T2D was self-reported by treatments with diet, oral hypoglycemic agents, or insulin. Incident T2D cases were identified from post-baseline self-reports of first-time use of oral hypoglycemic agents or insulin or from hospitalizations for previously unreported T2D. We followed the principle of risk-set sampling (3) to randomly select controls for each new case from women who remained free of T2D at the time the case was identified during follow-up. We individually matched 1,543 incident cases with 2,170 controls by age ($\pm$2.5 years), ethnic group, clinical center (geographic location), time of blood draw ($\pm$ 0.10 h), and length of follow-up. From 1993-1998, 26,045 (17%) women from minority groups were recruited at 40 clinical centers across the U.S. Of the CT and OS minority participants enrolled in WHI, 12,157 (including 8,515 self identified African American and 3,642 self identified Hispanic subjects) who had consented to genetic research were eligible for the NHLBI's WHI SNP Health Association Resource (SHARe) Genome-Wide Association Study (GWAS) project. DNA

was extracted by the Specimen Processing Laboratory at the Fred Hutchinson Cancer research Center (FHCRC) using specimens that were collected at the time of enrollment. Specimens were stored at -80°C(4). The WHI-SHARe cohort originally included 4,477 African American and 1,821 Hispanic American postmenopausal women enrolled in WHI-Clinical Trial (CT) whose self-reported ethnicity was either African American or Hispanic American with raw genotyping data available (909,622 genotypes were produced by the Affymetrix Genome-wide Human SNP Array 6.0, Santa Clara, CA).

Tag single nucleotide polymorphism selection, genotyping methods, and quality control (QC)

In WHI-OS, we implemented a two-stage approach for selecting tag single nucleotide polymorphisms (tagSNPs) for genotyping, which was described elsewhere previously(5, 6). In the first stage, the National Center for Biotechnology Information database SNP (NCBI dbSNP) and the HapMap database were used to conduct a comprehensive review of common genetic variation. A high-density common SNP set covering the *PPARG* gene's exons, introns, 5' and 3' untranslated regions (UTRs), as well as its 30 kb 5' upstream and 30 kb 3' downstream regions was genotyped in 244 samples, i.e., 61 individuals from each ethnic group (African American, European American, Hispanic American, and Asian American) randomly selected from the WHI-OS source population. In second stage, based on linkage disequilibrium (LD) patterns, we selected LD-based 24 tagSNPs that account for most of the genetic variation within the *PPARG* locus across the four ethnic groups and genotyped these in larger WHI-OS matched case-control samples with the TaqMan allelic-discrimination method. After PCR amplification, the end-point fluorescence was read with the Applied Biosystems Primer 7900HT Fast Real-Time PCR instrument and genotypes were attained with the aid of SDS 2.2.2 Allelic Differentiation Software (Applied Biosystems, Foster City, CA). To estimate reproducibility, 138 duplicated samples were randomly selected and genotyped in a blinded fashion.

In WHI-SHARe, we excluded samples on the basis of genotyping failure and quality control (n = 149), relatedness (n = 56), discordance between self-identified race and genetic ancestry (n = 56), and missing phenotypic information (n = 40). In case of related individuals, the relative with the highest call rate was retained, while other family members were excluded.

Statistical Analysis

In WHI-OS matched case-control sample, we first estimated the minor allele frequencies (MAFs) of the 24 tagSNPs among WHI-OS controls in each ethnic group. We tested for heterogeneity of genotype distributions across ethnicities using the χ^2 test. Then, single-SNP and haplotype-based analyses of the data based on multivariate logistic regression models were performed to calculate odds ratios (ORs) and 95% confidence intervals (95% CIs) for each genetic variant with T2D risk. Specifically, we made adjustments for potential confounders [body mass index, fasting glucose and insulin levels in logarithmic scale, cigarette smoking (never, past, and current), alcohol intake (never, past, and current), hormone-replacement therapy use (never, past, and current), family history of T2D, and values of the total metabolic equivalent (MET) value from the individual's recreational physical activity per week at baseline] in multivariate and conditional logistic regression models. In addition, we adjusted for the matching factors (age, clinical center, time of blood draw, and ethnicity) in the multivariate logistic regression models.

In WHI-OS matched case-control sample, single-SNP analyses were performed by coding each SNP either as an additive, dominant, or recessive genetic model. Because multiple *PPARG* SNPs are examined simultaneously, correction for multiple testing is needed, and the conventional Bonferroni control of family-wise error rate (FWER) could be overly conservative. A widely used procedure for controlling FDR is the Benjamini-Hochberg (BH) procedure, which is demonstrated to be more powerful than the Bonferroni method that controls FWER(7). In practice, a prudently chosen trade-off is needed

between type I and type II errors when selecting a significance threshold. A *more stringent* significance threshold increases confidence but reduces statistical power, whereas a *less stringent* significance threshold reduces confidence but increases power. In our study, we reported both raw p-values (i.e., without Bonferroni correction) and FDR adjusted P-value using Benjamini and Hochberg procedure (8) in the single-SNP analysis. Although FDR adjusted P-value threshold of 0.05 is typically applied, a *low-stringency* FDR adjusted P-value threshold of 0.25 has also been applied in previous genetic studies (7, 9). In haplotype-based analyses, only haplotypes with estimated frequencies ≥ 5% were included for analyses. To increase the genomic coverage, we utilized a sliding-window (3-SNP) haplotype-based analysis. For each window, we used an omnibus likelihood ratio test (LRT), which was a χ^2 test (degrees of freedom = number of haplotypes in a particular window – 1). The LRT compared the two nested logistic regression models: (i) the full model that contains the haplotype covariates with matching factors (age, clinical center, time of blood draw, and ethnicity), body mass index, fasting glucose and insulin levels in logarithmic scale, cigarette smoking, alcohol intake, hormone-replacement therapy use, family history of T2D, and values of total MET, and (ii) the reduced model that does not contain the haplotype covariates, i.e., age, clinical center, time of blood draw, ethnicity, body mass index, fasting glucose and insulin levels in logarithmic scale, cigarette smoking, alcohol intake, hormone-replacement therapy use, family history of T2D, and values of total MET. $-\log_{10}P > 2.64$ (P-value < 0.0023) was used as the global significance threshold using Bonferroni correction for 22 3-SNP window frames. These above haplotype analyses (i.e., omnibus association analysis and association between selected haplotypes) were performed using the SAS HAPPY macro (http://www.hsph.harvard.edu/faculty/peter-kraft/software/).

We made adjustment for potential confounders [body mass index, fasting glucose and insulin levels in logarithmic scale, cigarette smoking (never, past, and current), alcohol intake (never, past, and current), hormone-replacement therapy use (never, past, and current), family history of T2D, and values of the total metabolic equivalent (MET) value from the individual's recreational physical activity per week at baseline] in multivariate and conditional logistic regression models. In addition, we adjusted for

the matching factors (age, clinical center, time of blood draw, and ethnicity) in multivariate logistic regression models. Overall, the models had good fit of the data (P-values for LRT of χ^2 statistics < 0.001). In sliding window-based haplotype-analysis, we assessed interaction effects by ethnicity by fitting a model with haplotype*ethnicity interaction term. The statistical significance of the association of each SNP with T2D risk was determined using an omnibus LRT, which was a χ^2 test (degrees of freedom = number of haplotypes in a particular window – 1).

To validate results of WHI-OS, in WHI-SHARe unmatched case-control sample consisting of 5,642 individuals by excluding participants who enrolled in the WHI-OS, only single-SNP analyses of data from the study of WHI-SHARe were performed (given the sparseness of the distribution of the 8 tagSNPs) to obtain OR and associated 95% CI estimates for each SNP under additive, dominant, or recessive genetic model (R, version 2.13) with adjustment for the same set of covariates of WHI-OS, as well as global ancestry using 3 principal components computed with EIGENSTRAT(10). Because cases and controls were not matched within each of the two minority groups, unconditional multivariate logistic regression model was employed. We also performed a statistical analysis of candidate T2D-related pathways (i.e., pathways involved in beta cell function, insulin signaling, leptin, PPAR signaling, signaling of WNT (structurally related genes that encode secreted signaling proteins), glucose transport and metabolism, adipocytokine signaling, glucokinase regulation, triglyceride activity, neuronal activity, inflammatory response, and endothelial activity)(11) using the Gene Set Enrichment Algorithm (GSEA), with the 871,309 SNPs remained after genotype cleaning, provided by the MAGENTA program(12) with adjustment for age, region of clinical center, and global ancestry.

References:

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Supplemental Table 1. Minor allele frequencies (MAFs) of the 24 tagSNPs in the *PPARG* gene.

dbSNP ID	SNP ID	Genome Coordinate[a]	Major/ Minor Allele	MAF (%)[b]					P-value for heterogeneity[c]
				European American	African American	Hispanic American	Asian American	Combined	
				(n=968)	(n=754)	(n=282)	(n=166)	(n=2,170)	
rs9878908	SNP1	12242462	*T/C*	0.2022	0.1122	0.1178	0.3302	0.1695	<.0001
rs6798713	SNP2	12245587	*T/C*	0.1812	0.1938	0.1137	0.3282	0.1881	<.0001
rs6809631	SNP3	12275647	*A/T*	0.2607	0.2889	0.3073	0.4785	0.2934	<.0001
rs9817428	SNP4	12280267	*C/A*	0.2593	0.3616	0.3147	0.4697	0.3186	<.0001
rs10510411	SNP5	12286849	*G/A*	0.2603	0.3038	0.3105	0.2638	0.2822	0.1039
rs12629293	SNP6	12291746	*A/G*	0.2641	0.2293	0.3011	0.2813	0.2581	0.0577
rs12636454	SNP7	12300214	*T/C*	0.2611	0.2969	0.3032	0.2719	0.2799	0.3227
rs4518111	SNP8	12317344	*C/A*	0.4033	0.1835	0.3859	0.5123	0.3328	<.0001
rs10510418	SNP9	12328563	*A/C*	0.3259	0.111	0.2744	0.2284	0.2369	<.0001
rs1801282	SNP10	12333125	*C/G*	0.1192	0.0255	0.0655	0.0494	0.0742	<.0001
rs1373640	SNP12	12342601	*C/T*	0.339	0.1198	0.2591	0.1883	0.2403	<.0001
rs2972162	SNP13	12364793	*C/T*	0.5207	0.3351	0.5345	0.4286	0.4505	<.0001
rs10510419	SNP14	12366936	*G/T*	0.1457	0.1159	0.2527	0.0123	0.1391	<.0001
rs2959272	SNP16	12382833	*C/A*	0.5277	0.4158	0.5469	0.4294	0.4837	<.0001
rs709150	SNP18	12391337	*C/G*	0.4721	0.2255	0.4063	0.5648	0.3845	<.0001
rs709157	SNP19	12402024	*G/A*	0.3047	0.0875	0.2364	0.0245	0.1983	<.0001
rs1175540	SNP20	12405243	*C/A*	0.3607	0.6514	0.317	0.4146	0.4607	<.0001
rs1175544	SNP21	12407044	*C/T*	0.3231	0.1292	0.2473	0.3742	0.2495	<.0001
rs1797912	SNP22	12410239	*A/C*	0.3672	0.1523	0.2726	0.4146	0.2846	<.0001
rs1152002	SNP23	12411871	*G/A*	0.4856	0.4298	0.3727	0.4479	0.4486	0.0001
rs3856806	SNP24	12415557	*C/T*	0.1303	0.0643	0.074	0.1933	0.1047	<.0001
rs1152003	SNP25	12417055	*C/G*	0.3383	0.6171	0.5163	0.5185	0.4725	<.0001
rs1152007	SNP26	12427547	*C/G*	0.3455	0.1808	0.3327	0.4634	0.2955	<.0001
rs709167	SNP28	12442955	*A/C*	0.4601	0.2917	0.4076	0.8025	0.4204	<.0001

[a]: Genome coordinate was according to chromosome 3 genomic contig (reference assembly) NT_022517.18.

[b]: MAF was estimated in the controls only (The minor allele was defined based on the entire control population).

[c]: The P-value was estimated based on a χ^2 test (d.f. = 6) for genotype distribution across the four ethnicities.

Supplemental Table 2. Association between the *PPARG* non-synonymous SNP (rs1801282) and T2D risk by genotype[a] in Women's Health Initiative Observational Study nested case-control sample (n=3,713).

Genotype	European American (954/968)[b]	African American (369/754)	Hispanic American (141/282)	Asian American (79/166)	Combined (1,543/2,170)
rs1801282					
CC	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
CG	0.60(0.32-1.14)	0.59(0.15-2.31)	**0.17(0.04-0.77)[d]**	0.13(0.01-1.27)	**0.51(0.31-0.83)[e]**
GG	0.58(0.03-10.8)	---[c]	---[e]	---[c]	0.77(0.07-8.02)

[a]: Adjusted OR (95% CI) for each tagSNP was estimated under the dominant genetic model, using conditional logistic regression models with adjustments for age, body mass index (BMI), ln(fasting insulin), ln(fasting glucose), cigarette smoking (never, past and current), alcohol intake (never, past and current), hormone replacement therapy (HRT) usage (never, past, current), T2D family history (presence/absence), and physical activity per week at baseline. Due to the small Asian population size, BMI, ln(fasting insulin), ln(fasting glucose) were excluded to cause the model to converge.

[b]: Sample size is presented as cases/controls.

[c]: Participants do not possess this genotype.

[d]: P-value = 0.02.

[e]: P-value = 0.006.

Supplemental Table 3. Single-SNP association studies of the 24 tagSNPs in the *PPARG* gene with T2D risk under dominant genetic model[a] in Women's Health Initiative Observational Study nested case-control sample (n=3,713).

dbSNP ID	European American	African American	Hispanic American	Asian American	Combined	P-value (Combined)
	(954/968)[b]	(369/754)	(141/282)	(79/166)	(1,543/2,170)	
rs9878908	0.89(0.51-1.54)	0.78(0.35-1.76)	1.13(0.41-3.10)	1.04(0.53-2.06)	0.90(0.62-1.31)	0.58
rs6798713	0.74(0.43-1.28)	0.98(0.53-1.80)	1.37(0.49-3.82)	1.10(0.55-2.20)	0.90(0.64-1.27)	0.55
rs6809631	0.71(0.40-1.23)	0.67(0.36-1.22)	0.54(0.21-1.35)	0.57(0.25-1.30)	**0.67(0.48-0.95)**	**0.03[h]**
rs9817428	0.76(0.44-1.31)	0.61(0.34-1.12)	0.53(0.21-1.34)	0.55(0.24-1.24)	**0.68(0.48-0.96)**	**0.03[i]**
rs10510411	0.69(0.40-1.20)	0.63(0.33-1.22)	0.69(0.28-1.72)	0.98(0.51-1.88)	**0.65(0.46-0.93)**	**0.02[j]**
rs12629293	0.69(0.39-1.21)	0.78(0.45-1.36)	0.68(0.28-1.65)	0.97(0.51-1.85)	**0.70(0.50-0.98)**	**0.04[k]**
rs12636454	0.72(0.42-1.24)	0.74(0.43-1.29)	0.65(0.27-1.56)	1.08(0.57-2.04)	**0.71(0.51-0.99)**	**0.05[l]**
rs4518111	1.41(0.78-2.53)	1.15(0.64-2.09)	1.73(0.61-4.87)	1.07(0.50-2.27)	1.34(0.94-1.90)	0.10
rs10510418	1.00(0.60-1.68)	0.68(0.35-1.32)	1.23(0.42-3.56)	0.83(0.41-1.64)	1.00(0.71-1.40)	0.99
rs1801282	0.60(0.32-1.12)	0.59(0.15-2.31)	**0.19(0.04-0.81)[d]**	0.21(0.04-1.04)	**0.51(0.32-0.83)**	**0.01[m]**
rs1373640	1.07(0.65-1.77)	0.83(0.43-1.60)	1.77(0.63-4.99)	0.59(0.27-1.28)	1.10(0.78-1.54)	0.58
rs2972162	0.97(0.51-1.84)	1.09(0.64-1.87)	2.02(0.61-6.71)	0.99(0.45-2.16)	1.17(0.82-1.68)	0.38
rs10510419	1.28(0.68-2.39)	1.13(0.58-2.21)	0.87(0.30-2.53)	1.49(0.19-11.5)	1.11(0.75-1.64)	0.60
rs2959272	0.85(0.44-1.65)	1.03(0.56-1.88)	1.62(0.50-5.20)	1.20(0.54-2.66)	1.10(0.75-1.60)	0.63
rs709150	**0.43(0.22-0.85)[c]**	0.78(0.43-1.43)	1.94(0.58-6.52)	0.93(0.38-2.29)	0.75(0.52-1.09)	0.13
rs709157	1.29(0.78-2.14)	0.67(0.33-1.39)	1.18(0.45-3.06)	---[g]	1.04(0.74-1.48)	0.81
rs1175540	1.03(0.61-1.73)	0.84(0.33-2.14)	1.42(0.55-3.65)	1.17(0.53-2.59)	1.12(0.78-1.62)	0.54
rs1175544	1.18(0.70-2.00)	0.79(0.40-1.55)	1.42(0.53-3.79)	1.20(0.58-2.51)	1.18(0.83-1.66)	0.36
rs1797912	1.13(0.67-1.92)	0.84(0.45-1.60)	1.57(0.56-4.34)	0.96(0.46-1.97)	1.16(0.82-1.63)	0.41
rs1152002	0.84(0.45-1.57)	0.88(0.49-1.61)	**4.51(1.28-15.9)[e]**	0.79(0.39-1.56)	1.12(0.78-1.60)	0.55
rs3856806	0.94(0.50-1.77)	0.52(0.22-1.22)	**0.22(0.05-0.97)[f]**	0.79(0.39-1.59)	0.70(0.46-1.07)	0.10
rs1152003	1.01(0.59-1.72)	0.75(0.36-1.58)	1.77(0.59-5.33)	1.00(0.43-2.32)	1.01(0.70-1.45)	0.97
rs1152007	1.14(0.64-2.04)	0.76(0.41-1.42)	0.99(0.32-3.09)	0.94(0.46-1.93)	0.94(0.66-1.35)	0.74
rs709167	1.24(0.70-2.21)	1.28(0.70-2.36)	2.08 (0.59, 7.37)	0.75(0.17-3.27)	1.23(0.85-1.77)	0.27

[a]: Adjusted OR (95% CI) for each tagSNP was estimated under the dominant genetic model, using conditional logistic regression models with adjustments for age, body mass index (BMI), ln(fasting insulin), ln(fasting glucose), cigarette smoking (never, past and current), alcohol intake (never, past and current), hormone replacement therapy (HRT) usage (never, past, current), T2D family history (presence/absence), and physical activity per week at baseline. Due to the small Asian population size, BMI, ln(fasting insulin), ln(fasting glucose) were excluded to cause the model to converge.

[b]: Sample size is presented as cases/controls.

[c]: P-value = 0.02, with FDR adjusted P-value = 0.37 using the method of Benjamini and Hochberg.

[d]: P-value = 0.03, with FDR adjusted P-value = 0.30 using the method of Benjamini and Hochberg.
[e]: P-value = 0.02, with FDR adjusted P-value = 0.30 using the method of Benjamini and Hochberg.
[e]: P-value = 0.05, with FDR adjusted P-value = 0.37 using the method of Benjamini and Hochberg.
[g]: Result is difficult to interpret because of small sample size within strata.
[h]: P-value = 0.03, with FDR adjusted P-value = 0.16 using the method of Benjamini and Hochberg.
[i]: P-value = 0.03, with FDR adjusted P-value = 0.16 using the method of Benjamini and Hochberg.
[j]: P-value = 0.02, with FDR adjusted P-value = 0.16 using the method of Benjamini and Hochberg.
[k]: P-value = 0.04, with FDR adjusted P-value = 0.18 using the method of Benjamini and Hochberg.
[l]: P-value = 0.05, with FDR adjusted P-value = 0.18 using the method of Benjamini and Hochberg.
[m]: P-value = 0.01, with FDR adjusted P-value = 0.16 using the method of Benjamini and Hochberg.

Supplemental Table 4. Single-SNP association studies of the 24 tagSNPs in the *PPARG* gene with T2D risk under recessive genetic model[a] in Women's Health Initiative Observational Study nested case-control sample (n=3,713).

dbSNP ID	European American	African American	Hispanic American	Asian American	Combined	P-value (Combined)
	(954/968)[b]	(369/754)	(141/282)	(79/166)	(1,543/2,170)	
rs9878908	0.59(0.20-1.73)	---[d]	---[d]	0.91(0.35-2.36)	0.71(0.31-1.66)	0.43
rs6798713	0.50(0.14-1.79)	0.91(0.17-5.00)	---[d]	1.07(0.44-2.62)	0.72(0.30-1.71)	0.45
rs6809631	0.48(0.17-1.34)	0.93(0.33-2.64)	0.91(0.18-4.77)	0.98(0.45-2.16)	0.79(0.44-1.43)	0.44
rs9817428	0.54(0.18-1.57)	1.05(0.46-2.39)	0.89(0.18-4.32)	0.96(0.44-2.08)	0.85(0.49-1.47)	0.56
rs10510411	0.41(0.14-1.21)	0.49(0.14-1.76)	0.91(0.19-4.42)	1.43(0.48-4.24)	0.55(0.29-1.04)	0.07
rs12629293	0.33(0.11-1.01)	0.54(0.14-2.00)	0.95(0.19-4.84)	1.39(0.47-4.12)	**0.51(0.26-0.99)**	**0.05**[e]
rs12636454	0.33(0.11-1.02)	0.70(0.26-1.88)	1.00(0.20-5.09)	1.32(0.46-3.82)	0.55(0.30-1.03)	0.06
rs4518111	1.66(0.79-3.48)	0.71(0.16-3.16)	1.32(0.36-4.87)	1.49(0.68-3.29)	1.15(0.70-1.87)	0.59
rs10510418	1.83(0.70-4.81)	1.08(0.15-7.63)	0.38(0.06-2.33)	---[d]	1.23(0.63-2.41)	0.55
rs1801282	0.60(0.03-11.3)	---[d]	---[d]	---[d]	0.79(0.08-8.37)	0.85
rs1373640	1.87(0.73-4.76)	0.82(0.15-4.56)	0.38(0.06-2.30)	---[d]	1.27(0.66-2.42)	0.48
rs2972162	1.76(0.92-3.39)	1.81(0.75-4.40)	0.53(0.16-1.78)	0.96(0.36-2.57)	1.30(0.85-1.99)	0.22
rs10510419	**14.4(1.71-121)**[c]	4.32(0.58-32.0)	1.80(0.16-20.4)	---[d]	**3.83(1.15-12.82)**	**0.03**[f]
rs2959272	1.90(1.00-3.62)	1.40(0.67-2.94)	0.58(0.17-2.00)	1.00(0.40-2.50)	1.35(0.90-2.00)	0.14
rs709150	0.87(0.45-1.67)	0.65(0.17-2.45)	0.49(0.14-1.67)	0.92(0.42-2.03)	0.74(0.47-1.17)	0.20
rs709157	1.98(0.73-5.43)	0.30(0.02-5.56)	0.44(0.07-2.85)	---[d]	1.34(0.65-2.75)	0.43
rs1175540	1.64(0.67-4.02)	1.13(0.65-1.97)	0.24(0.04-1.55)	1.34(0.52-3.45)	1.09(0.71-1.65)	0.70
rs1175544	1.67(0.68-4.10)	0.78(0.12-4.97)	0.28(0.04-1.94)	1.58(0.61-4.12)	1.05(0.58-1.90)	0.88
rs1797912	1.59(0.69-3.69)	1.07(0.30-3.84)	0.33(0.05-2.37)	1.07(0.42-2.76)	1.16(0.66-2.04)	0.61
rs1152002	0.99(0.54-1.83)	1.00(0.47-2.16)	0.83(0.18-3.78)	0.83(0.32-2.11)	1.02(0.67-1.54)	0.94
rs3856806	0.46(0.01-23.8)	---[d]	---[d]	0.83(0.17-4.08)	0.62(0.06-6.13)	0.68
rs1152003	1.44(0.63-3.34)	1.08(0.62, 1.87)	2.43(0.73-8.07)	1.02(0.49-2.14)	1.21(0.81-1.80)	0.35
rs1152007	1.37(0.51-3.65)	0.42(0.10-1.73)	1.45(0.28-7.48)	0.71(0.32-1.60)	0.79(0.43-1.45)	0.45
rs709167	0.90(0.47-1.71)	0.64(0.20-2.04)	0.51(0.11-2.31)	0.85(0.39-1.83)	0.86(0.55-1.36)	0.53

[a]: Adjusted OR (95% CI) for each tagSNP was estimated under the recessive genetic model, using conditional logistic regression models with adjustments for age, body mass index (BMI), ln(fasting insulin), ln(fasting glucose), cigarette smoking (never, past and current), alcohol intake (never, past and current), hormone replacement therapy (HRT) usage (never, past, current), T2D family history (presence/absence), and physical activity per week at baseline. Due to the small Asian population size, BMI, ln(fasting insulin), ln(fasting glucose) were excluded to cause the model to converge.

[b]: Sample size is presented as cases/controls.
[c]: P-value = 0.01, with FDR adjusted P-value = 0.32 using the method of Benjamini and Hochberg.
[d]: Result is difficult to interpret because of small sample size within strata.
[e]: P-value = 0.05, with FDR adjusted P-value = 0.40 using the method of Benjamini and Hochberg.
[f]: P-value = 0.03, with FDR adjusted P-value = 0.40 using the method of Benjamini and Hochberg.

Supplemental Table 5. Single-SNP association studies of the 8 tagSNPs in the *PPARG* gene with T2D risk under additive genetic model[a] in Women's Health Initiative SHARe case-control sample (n=5,642).

dbSNP ID	SNP name	Reference allele	African American (582/3,359)[b]	Hispanic American (241/1,460)[b]	Combined	P-value (Combined) [c]
rs9878908	SNP_A-1875778	C	0.74(0.44-1.26)	0.94(0.43-2.02)	0.84(0.55-1.29)	0.43
rs9817428	SNP_A-1949196	A	1.01(0.73-1.39)	**0.52(0.28-0.96)[e]**	0.88(0.66-1.16)	0.36
rs10510418	SNP_A-1971789	C	1.08(0.66-1.76)	1.04(0.56-1.95)	1.01(0.69-1.46)	0.97
rs1801282	SNP_A-1971790	G	0.81(0.27-2.41)	**0.25(0.08-0.77)[f]**	0.51(0.24-1.07)	0.08
rs2972162	SNP_A-1946610	T	0.92(0.66-1.28)	1.11(0.65-1.90)	0.99(0.75-1.30)	0.93
rs10510419	SNP_A-4209319	T	0.93(0.56-1.53)	1.87(0.92-3.82)	1.22(0.82-1.81)	0.33[f]
rs1175544	SNP_A-8304334	T	1.11(0.71-1.75)	1.40(0.74-2.63)	1.16(0.81-1.66)	0.43
rs1152003	SNP_A-2140799	G	1.19(0.85-1.65)	0.84(0.51-1.40)	1.08(0.83-1.42)	0.56

[a]: Adjusted OR (95% CI) for each tagSNP was estimated under the additive genetic model, using logistic regression adjustments for global ancestry (3 PCs), age, ethnicity (combined analysis only), body mass index (BMI), ln(insulin), ln(glucose), cigarette smoking (never, past and current), alcohol intake (never, past and current), hormone replacement therapy (HRT) usage (never, past, current), T2D family history (presence/absence), and physical activity per week at baseline.

[b]: Sample sizes for each ethnic group are presented as cases/controls.

[c]: Ethnic interaction was estimated by fitting a model with ethnicity*SNP interaction term and adjusting for global ancestry using 3 PCs.

[d]: The likelihood ratio test compared model with SNP versus model without SNP.

[e]: P-value = 0.04, with FDR adjusted P-value = 0.15 using the method of Benjamini and Hochberg.

[f]: P-value = 0.02, with FDR adjusted P-value = 0.12 using the method of Benjamini and Hochberg.

Supplemental Table 6. Single-SNP association studies of the 8 tagSNPs in the *PPARG* gene with T2D risk under dominant genetic model[a] in Women's Health Initiative SHARe case-control sample (n=5,642).

dbSNP ID	SNP name	Reference allele	African American (582/3,359)[b]	Hispanic American (241/1,460)[b]	Combined	P-value (Combined) [c]
rs9878908	SNP_A-1875778	C	0.73(0.41-1.32)	0.85(0.37-1.96)	0.82(0.52-1.31)	0.41
rs9817428	SNP_A-1949196	A	1.11(0.71-1.74)	0.59(0.28-1.26)	0.97(0.66-1.42)	0.88
rs10510418	SNP_A-1971789	C	1.09(0.63-1.90)	1.04(0.49-2.23)	1.03(0.67-1.59)	0.88
rs1801282	SNP_A-1971790	G	0.82(0.27-2.48)	**0.25(0.08-0.77)[e]**	0.51(0.24-1.08)	0.08
rs2972162	SNP_A-1946610	T	0.92(0.46-1.86)	1.12(0.45-2.74)	1.02(0.60-1.75)	0.93
rs10510419	SNP_A-4209319	T	---[f]	---[f]	---[f]	---[f]
rs1175544	SNP_A-8304334	T	1.17(0.70-1.97)	1.93(0.89-4.21)	1.33(0.88-2.03)	0.18
rs1152003	SNP_A-2140799	G	1.05(0.57-1.90)	0.76(0.33-1.72)	0.96(0.60-1.54)	0.87

[a]: Adjusted OR (95% CI) for each tagSNP was estimated under the dominant genetic model, using logistic regression adjustments for global ancestry (3 PCs), age, ethnicity (combined analysis only), body mass index (BMI), ln(insulin), ln(glucose), cigarette smoking (never, past and current), alcohol intake (never, past and current), hormone replacement therapy (HRT) usage (never, past, current), T2D family history (presence/absence), and physical activity per week at baseline.
[b]: Sample sizes for each ethnic group are presented as cases/controls.
[c]: Ethnic interaction was estimated by fitting a model with ethnicity*SNP interaction term and adjusting for global ancestry using 3 PCs.
[d]: The likelihood ratio test compared model with SNP versus model without SNP.
[e]: P-value = 0.02, with FDR adjusted P-value = 0.12 after the method of Benjamini and Hochberg.
[f]: Result is difficult to interpret because of small sample size within strata.

Supplemental Table 7. Single-SNP association studies of the 8 tagSNPs in the *PPARG* gene with T2D under recessive model[a] in Women's Health Initiative SHARe case-control sample (n=5,642).

dbSNP ID	SNP name	Reference allele	African American (582/3,359)[b]	Hispanic American (24/1,460)[b]	Combined	P-value (Combined) [c]
rs9878908	SNP_A-1875778	C	0.53(0.07-4.12)	2.50(0.21-30.0)	0.85(0.18-4.15)	0.85
rs9817428	SNP_A-1949196	A	0.81(0.40-1.61)	**0.17(0.03-0.89)[e]**	0.60(0.32-1.11)	0.10
rs10510418	SNP_A-1971789	C	1.03(0.18-5.96)	1.09(0.22-5.47)	0.85(0.26-2.73)	0.78
rs1801282	SNP_A-1971790	G	---[f]	---[f]	---[f]	---[f]
rs2972162	SNP_A-1946610	T	0.88(0.56-1.38)	1.18(0.52-2.71)	0.96(0.65-1.43)	0.86
rs10510419	SNP_A-4209319	T	0.85(0.51-1.43)	1.77(0.82-3.81)	1.11(0.73-1.70)	0.62
rs1175544	SNP_A-8304334	T	0.81(0.16-4.01)	0.30(0.003-3.30)	0.49(0.14-1.76)	0.28
rs1152003	SNP_A-2140799	G	1.39(0.86-2.22)	0.83(0.36-1.90)	1.24(0.82-1.85)	0.31

[a]: Adjusted OR (95% CI) for each tagSNP was estimated under the recessive genetic model, using logistic regression adjustments for global ancestry (3 PCs), age, ethnicity (combined analysis only), body mass index (BMI), ln(insulin), ln(glucose), cigarette smoking (never, past and current), alcohol intake (never, past and current), hormone replacement therapy (HRT) usage (never, past, current), T2D family history (presence/absence), and physical activity per week at baseline.

[b] Sample sizes for each ethnic group are presented as cases/controls.

[c] Ethnic interaction was estimated by fitting a model with ethnicity*SNP interaction term and adjusting for global ancestry using 3 PCs.

[d] The likelihood ratio test compared model with SNP versus model without SNP.

[e]: P-value = 0.04, with FDR adjusted P-value = 0.29 after the method of Benjamini and Hochberg.

[f] Result is difficult to interpret because of small sample size within strata.

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