

SUPPLEMENTARY DATA

The Health Professionals Follow-up Study (HPFS)

The HPFS is a prospective cohort study of 51,529 U.S. male health professionals aged 40 to 75 years at study initiation in 1986. Information about health and disease is assessed biennially by a self-administered questionnaire. Between 1993 and 1999, 18,159 men provided blood samples. The present study was approved by the institutional review board of the Brigham and Women's Hospital and the Human Subjects Committee Review Board of Harvard School of Public Health. HPFS participants for the current study were selected among those with a blood sample using a "nested" case-control study design. Diabetes cases were defined as self-reported diabetes confirmed by a validated supplementary questionnaire. For cases before 1998, diagnosis was made using criteria consistent with those proposed by the National Diabetes Data Group (NDDG) (1). We used the American Diabetes Association diagnostic criteria for diagnosis of diabetes cases during the 1998 and 2000 cycles (2). 98% of self-reported cases were confirmed by medical records review in both cohorts (3). Controls were defined as those free of diabetes at the time of diagnosis of the case and remained unaffected through follow-up (2006). Although controls were originally matched per case (by gender, year of birth, month of blood collection, and fasting status), matched pairs were broken because not all subjects gave informed consent for submission of their GWAS data to dbGaP.

Genome-Wide Scans of Type 2 Diabetes in the NHS and HPFS

The NHS and HPFS T2D GWA scans are a component of the Gene Environment-Association Studies (GENEVA) under the NIH Genes, Environment and Health Initiative (GEI). Genotyping for 2,745 patients with T2D and 3,148 healthy controls from NHS and HPFS was done at the Broad Center for Genotyping and Analysis using the Affymetrix Genome-Wide Human 6.0 array (Santa Clara, CA). Genotype data was subsequently released for further quality control (QC) to the GENEVA Coordinating Center at the University of Washington. A total of 704,409 SNPs for NHS samples and 706,040 SNPs for HPFS samples passed QC (4; 5). After applying quality control filters, 3,221 (1,467 cases, 1,754 controls) women and 2,422 (1,124 cases, 1,298 controls) men of genetically inferred European ancestry were included in the analysis for the associations with type 2 diabetes.

References

1. Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance. National Diabetes Data Group. *Diabetes* 28:1039-1057, 1979
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3. Hu FB, Leitzmann MF, Stampfer MJ, Colditz GA, Willett WC, Rimm EB: Physical activity and television watching in relation to risk for type 2 diabetes mellitus in men. *Arch Intern Med* 161:1542-1548, 2001
4. Qi L, Cornelis MC, Kraft P, Stanya KJ, Linda Kao WH, Pankow JS, Dupuis J, Florez JC, Fox CS, Pare G, Sun Q, Girman CJ, Laurie CC, Mirel DB, Manolio TA, Chasman DI, Boerwinkle E, Ridker PM, Hunter DJ, Meigs JB, Lee CH, Hu FB, van Dam RM: Genetic variants at 2q24 are associated with susceptibility to type 2 diabetes. *Hum Mol Genet* 19:2706-2715
5. Qi L, Cornelis MC, Kraft P, Jensen M, van Dam RM, Sun Q, Girman CJ, Laurie CC, Mirel DB, Hunter DJ, Rimm E, Hu FB: Genetic variants in ABO blood group region, plasma soluble E-selectin levels and risk of type 2 diabetes. *Hum Mol Genet* 19:1856-1862

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Supplementary Table 1. Characteristics of the participants in GWAS and replication samples

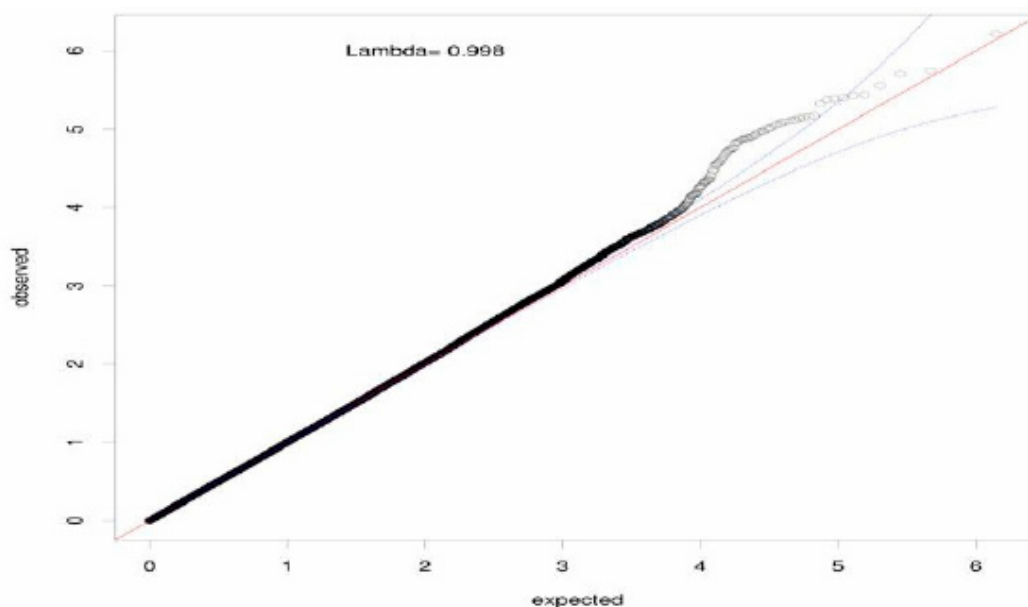
Variables	NHS	Italian	
		Men	Women
Study design	Nested case-control	Family based	
Genotyping	Affymetrix Genome- Wide Human 6.0 array	Taqman SNP allelic discrimination technique	
N, participants	1,591	240	386
Age, y	56 (8)	40.3 (14.9)	40.2 (14.3)
BMI, kg/m ²	28.2 (5.8)	26.5 (4.0)	26.1 (4.9)
Diabetes, n (%)	698 (43.9%)	0	0
HMW adiponectin, g/mL	6.46 (4.91)	3.2 (2.0)	4.9 (3.1)
HMW adiponectin measurement	Enzyme-linked immunosorbent assay	Enzyme-linked immunosorbent assay	

Continuous variables are presented as mean (SD)

BMI, body mass index; HMW, high molecule weight; GWAS, genome-wide association study

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Supplementary Figure 1: Quantile-quantile plots of the trend test statistic for the genome-wide association analyses on serum HMW adiponectin levels in NHS.



Supplementary Figure 2: Genome-wide associations of serum HMW adiponectin levels in NHS, graphed by chromosome position and $-\log_{10}$ p value.

