SUPPLEMENTARY DATA

Supplementary Table 1. Quantitative Score of Adherence to the Mediterranean Diet (14-items).

	Foods and frequency of consumption	Criteria for 1 point*
1	Do you use olive oil as main culinary fat?	Yes
2	How much olive oil do you consume in a given day (including oil used for frying, salads, out of house meals, etc.)?	4 or more tablespoons
3	How many vegetable servings do you consume per day? (1 serving = 200g - consider side dishes as 1/2 serving)	2 or more (at least 1 portion raw or as salad)
4	How many fruit units (including natural fruit juices) do you consume per day?	3 or more
5	How many servings of red meat, hamburger, or meat products (ham, sausage, etc.) do you consume per day? (1 serving = 100-150 g)	Less than 1
6	How many servings of butter, margarine, or cream do you consume per day? (1 serving = 12 g)	Less than 1
7	How many sweet/carbonated beverages do you drink per day?	Less than 1
8	How much wine do you drink per week?	7 or more glasses
9	How many servings of legumes do you consume per week? (1 serving = 150 g)	3 or more
10	How many servings of fish or shellfish do you consume per week? (1 serving: 100-150 g fish, or 4-5 units or 200 g shellfish)	3 or more
11	How many times per week do you consume commercial sweets or pastries (not homemade), such as cakes, cookies, biscuits, or custard?	Less than 3
12	How many servings of nuts (including peanuts) do you consume per week? (1 serving = 30 g)	3 or more
13	Do you preferentially consume chicken, turkey or rabbit meat instead of veal, pork, hamburger or sausage?	Yes
14	How many times per week do you consume vegetables, pasta, rice, or other dishes seasoned with sofrito (sauce made with tomato and onion, leek, or garlic, simmered with olive oil)?	2 or more

* 0 points if these criteria are not met.

SUPPLEMENTARY DATA

Supplementary Table 2. Association between the TCF7L2 -rs7903146 polymorphism and fasting glucose, plasma lipid concentrations and type 2 diabetes at baseline*

	TCF7L2 genotypes				
	CC (n=2,770)	CT (n=3,249)	TT (n=999)		
Parameter	Mean SD	Mean SD	Mean SD	P†	P‡
Age (years)	67.0 ± 6.0	67.0 ± 6.1	66.7 ± 6.3	0.392	
BMI (kg/m^2)	30.2 ± 3.9	29.9 ± 3.8	29.6 ± 3.6	0.004	0.003
Waist circumference (cm)	100.7 ± 10.7	100.2 ± 10.4	100.1 ± 9.8	0.147	0.193
Fasting glucose§ (mg/dL)	117.5 ± 39.0	124.2 ± 42.7	128.1 ± 43.6	1.18×10^{-12}	0.021
Total cholesterol§ (mg/dL)	211.6 ± 39.7	210.6 ± 40.0	211.7 ± 38.6	0.587	0.275
LDL-C§ (mg/dL)	130.6 ± 34.4	130.2 ± 36.5	130.0 ± 34.1	0.901	0.509
HDL-C§ (mg/dL)	53.4 ± 14.0	53.9 ± 14.2	54.4 ± 13.6	0.204	0.098
Triglycerides§ (mg/dL)	139.0 ± 86.0	137.0 ± 77.0	133.9 ± 69.1	0.494	0.520
Type 2 diabetes: n (%)	1158 (41.8)	1680 (51.7)	573 (57.4)	3.1×10^{-21}	
Type 2 diabetes risk (OR and 95% CI)	Ref.	1.50 (1.35-1.65)	1.87 (1.62-2.17)	3.3×10^{-21}	5.4×10^{-21}
Female sex : n, %	1609 (58.1)	1961 (57.3)	555 (55.6)	0.380	0.491
Current smokers: n, %	414 (14.9)	439 (13.5)	136 (13.6)	0.194	0.378
Hypertension: n, %	2340 (84.5)	2664 (82.0)	797 (79.9)	0.001	0.579
Dyslipidemia: n, %	2042 (73.7)	2298 (70.7)	723 (72.4)	0.110	0.164
Energy intake (kcal/d)	2309 ± 615.0	2253 ± 599.0	2262 ± 602.0	0.001	0.061
Total fat (% energy)	39.2 ± 6.6	39.1 ± 6.9	39.3 ± 7.0	0.819	0.934
Saturated fat (% energy)	10.0 ± 2.2	10.0 ± 2.3	10.0 ± 2.3	0.633	0.799
MUFA (% energy)	19.5 ± 4.4	19.5 ± 4.6	19.4 ± 4.8	0.878	0.940
Proteins (% energy)	16.4 ± 2.8	16.7 ± 2.8	16.7 ± 2.9	0.003	0.273
Carbohydrates (% energy)	41.9 ± 7.0	41.8 ± 7.2	41.7 ± 7.4	0.496	0.268
Glycemic index	53.8 ± 5.7	53.5 ± 5.9	53.5 ± 5.8	0.097	0.167
Glycemic load (g)	132.7 ± 52.3	128.3 ± 50.9	128.0 ± 49.8	0.002	0.084
Adherence to the MedDiet	8.7 ± 2.0	8.7 ± 2.8	8.5 ± 1.9	0.081	0.248
Alcohol consumption (g/d)	8.4 ± 13.8	8.3 ± 14.1	8.4 ± 15.3	0.921	0.994
Physical activity (kcal/d)	230.9 ± 244.7	233.2 ± 232.6	228.7 ± 253.2	0.871	0.806

*: Values are means ± SD for continuous variables and number (%) for categorical variables, or odds ratio, OR and 95% confidence intervals (95% CI)

†: Unadjusted P values for mean comparison among genotypes, total energy intake, alcohol consumption, smoking and physical activity.

‡: P values adjusted for sex, age, center, type 2 diabetes, BMI, medications (anti-diabetic drugs, lipid-lowering and antihypertensive drugs), total energy intake, alcohol consumption, smoking and physical activity.

§: Fasting glucose, total cholesterol, LDL-C, HDL-C and triglycerides were obtained for n= 6201, n=6568, n=6465, n=6497, n=6492 subjects, respectively

SUPPLEMENTARY DATA

Supplementary Table 3. Interaction between the TCF7L2- rs7903146 polymorphism and pre-randomization adherence to the Mediterranean diet in determining plasma lipid concentrations. Multivariate* adjusted means and P values.

Parameter (mg/dL) / Adherence to Mediterranean Diet	*TCF7L2* genotypes CC+CT Mean (SE)	*TCF7L2* genotypes TT Mean (SE)	P† *TCF7L2* Genotype	P‡ Interaction Genotype x Diet
Total cholesterol				0.005
Low (<9) (n=2992)	206.2 ± 3.5	211.3 ± 3.9	0.005	
High (>=9) (n=3576)	208.7 ± 3.5	206.5 ± 3.8	0.251	
LDL-C				0.003
Low (<9) (n=2946)	124.1 ± 3.2	128.7 ± 3.5	0.005	
High (>=9) (n=3529)	125.9 ± 3.2	124.5 ± 3.4	0.167	
HDL-C				0.628
Low (<9) (n=2968)	54.0 ± 1.3	54.9 ± 1.4	0.151	
High (>=9) (n=3529)	54.4 ± 1.3	55.8 ± 1.4	0.037	
Triglycerides				0.046
Low (<9) (n=2964)	142.5 ± 7.8	143.2 ± 8.5	0.528	
High (>=9) (n=3528)	139.2 ± 7.7	130.4 ± 8.4	0.036	

*: Values are multivariate adjusted means (mg/dL) and standard errors (SE)

†: P value for the TCF7L2 genotype in each strata after multivariate adjustment for sex, age, center, type 2 diabetes, BMI, medications, total energy intake, alcohol consumption, smoking and physical activity

‡: P value for the interaction term between the TCF7L2 polymorphism and adherence to the Mediterranean diet in the multivariate adjusted model for each lipid parameter analyzed

SUPPLEMENTARY DATA

Supplementary Table 4. Incidence rates and hazard ratios (HR) for total cardiovascular events and stroke according to the TCF7L2-rs7903146 polymorphism depending on the pre-randomization adherence to the Mediterranean strata at baseline. Multivariate adjusted models.

	Adherence to Mediterranean diet									
	Low Adherence (n=3,199)					High Adherence (n=3,972)				
	Cases	Incidence* rate/1000 person-y	HR	95% CI	P value	Cases	Incidence* rate/1000 person-y	HR	95% CI	P value
Outcome	**Total cardiovascular events†**									
	<9 points					**>=9 points**				
TCF7L2 (Model 1)										
CC	44	8.5	1.00	(reference)		53	7.9	1.00	(reference)	
CT	68	11.2	1.29	(0.88-1.89)	0.194	52	6.4	0.82	(0.56-1.21)	0.346
TT	27	12.9	1.43	(0.89-2.31)	0.146	18	8.2	1.11	(0.65-1.91)	0.607
TCF7L2 (Model 2)										
CC			1.00	(reference)				1.00	(reference)	
CT			1.22	(0.83-1.79)	0.332			0.79	(0.54-1.17)	0.253
TT			1.34	(0.83-2.17)	0.251			1.06	(0.62-1.83)	0.801
Outcome	**Stroke‡**									
	<9 points					**>=9 points**				
TCF7L2 (Model 1)										
CC	19	3.7	1.00	(reference)		26	3.9	1.00	(reference)	
CT	33	5.4	1.52	(0.86-2.69)	0.149	26	3.2	0.83	(0.48-1-42)	0.483
TT	18	8.6	2.36	1.24-4.52)	0.009	8	3.6	1.03	(0.46-2.28)	0.948
TCF7L2 (Model 2)										
CC			1.00	(reference)				1.00	(reference)	
CT			1.48	(0.84-2.41)	0.179			0.79	(0.54-1.17)	0.253
TT			2.27	(1.19-4.39)	0.014			1.06	(0.62-1.83)	0.801

*: Crude incidence rates were expressed per 1000 pers on-years of follow-up

†: Total cardiovascular events is a composite end point including incident non-fatal myocardial infarction, non-fatal stroke and cardiovascular deaths

‡: Total stroke incidence

Model 1: Multivariate model adjusted for sex, age, center and dietary intervention group.

Model 2: Variables in model 1 plus type 2 diabetes, BMI, total energy intake, smoking, drinking and total energy intake at baseline.

SUPPLEMENTARY DATA

Supplementary Figure 1. Interaction between the TCF7L2-rs7903146 polymorphism and adherence to the Mediterranean diet in determining fasting glucose concentration in PREDIMED participants at baseline: A) Adjusted means of fasting glucose depending on the TCF7L2-rs7903146 polymorphism (three genotypes) and two strata of adherence to the Mediterranean diet (AdMEDiet) (<9 points and >=9 points). Values are adjusted means ± SEM. Models were adjusted for age, sex, BMI, type 2 diabetes, total energy intake, alcohol consumption, smoking, physical activity, and medications (anti-diabetic drugs, lipid-lowering and antihypertensive drugs). P values for mean comparison in each saturated fat stratrum were also adjusted for covariates. B) Predicted values of fasting glucose by the TCF7L2- rs7903146 polymorphism (recessive model) in the PREDIMED study plotted against the adherence to the Mediterranean diet score. Predicted values were calculated from the regression models adjusted for age, sex, BMI, type 2 diabetes, total energy intake, alcohol consumption, smoking, physical activity, and medications (anti-diabetic drugs, lipid-lowering and antihypertensive drugs). The P value for the interaction term between adherence to the Mediterranean diet and the polymorphism was obtained in the hierarchical multivariate adjusted interaction model. In addition, adjusted regression coefficients (B), SE, correlation coefficients (r) and P-values are included for each genotype.