

SUPPLEMENTARY DATA

Supplementary Table 1. Association between genetic variation in APOE and phenotypes of familial longevity at middle age

	rs7412		rs429358	
	β (SE)	P-Value	β (SE)	P-Value
Glucose-insulin homeostasis^a				
Glucose in mmol/L	0.03 (0.06)	0.63	-0.01 (0.05)	0.91
Insulin in mU/L ^c	0.01 (0.04)	0.87	-0.04 (0.04)	0.27
Serum lipid levels^b				
Triglycerides in mmol/L ^c	0.06 (0.03)	0.08	0.03 (0.03)	0.20
HDL cholesterol in mmol/L	0.05 (0.03)	0.08	-0.03 (0.02)	0.08
Other serum levels				
25-hydroxyvitamin D in nmol/L ^c	-0.02 (0.02)	0.28	0.02 (0.02)	0.21
Disease history				
Diabetes, yes	0.41 (0.21)	0.04	-0.23 (0.23)	0.33
Hypertension, yes	-0.01 (0.13)	0.97	-0.18 (0.11)	0.12
Myocardial infarction, yes	0.45 (0.27)	0.10	-0.25 (0.30)	0.40

^a) Participants with diabetes were excluded. ^b) Participants using lipid-lowering agents were excluded. ^c) Depicted beta is log transformed. Analyses were adjusted for age, gender, and corrected for familial relationships using clustered robust. Beta estimates are depicted as the additive effect of the effect alleles of the polymorphisms on the outcome. P-values <0.05 are presented in bold.

Supplementary Table 2. Comparison offspring and controls for the phenotypes associated with familial longevity restricted to individuals with the APOE $\epsilon 3/\epsilon 3$ variant

	Offspring N=921	Controls N=448	P-Value
Glucose-insulin homeostasis^a			
Glucose in mmol/L	5.7 \pm 1.0	5.8 \pm 1.1	0.037
Insulin in mU/L, median (IQR)	16.0 (9.0-28.0)	17.0 (9.0-28.0)	0.34
Serum lipid levels^b			
Triglyceride in mmol/L, median (IQR)	1.4 (1.0-2.1)	1.5 (1.1-2.3)	0.002
HDL cholesterol in mmol/L	1.5 \pm 0.4	1.4 \pm 0.4	0.016
Other serum levels			
25-hydroxyvitamin D in nmol/L median (IQR)	63.9 (51.0-79.6)	68.3 (55.8-82.9)	0.001
Disease History			
Diabetes Mellitus, yes	35 (3.8)	36 (8.0)	0.002
Hypertension, yes	219 (23.8)	154 (34.4)	<0.001
Myocardial infarction, yes	18 (2.0)	15 (3.3)	0.15

Abbreviations: n, number of participants; IQR, interquartile range; SD, Standard deviation. Data presented as the mean \pm SD unless indicated otherwise. ^a) Participants with diabetes were excluded. ^b) Participants using lipid lowering agents were excluded. Comparisons between offspring and partners were adjusted for age and gender, and corrected for familial relationships using clustered robust. P-values <0.05 are presented in bold.

Supplementary Table 3. Association (*APOE* variant-adjusted) residuals and LLS offspring/control status

	Model 1		Model 2	
	OR (95% CI)	P-Value	OR (95% CI)	P-Value
Glucose-insulin homeostasis^a				
Glucose	0.88 (0.83 – 0.92)	<0.001	0.87 (0.83 – 0.92)	<0.001
Insulin	0.85 (0.76 – 0.95)	0.003	0.84 (0.76 – 0.94)	0.003
Serum lipid levels^b				
Triglyceride	0.73 (0.62 – 0.87)	<0.001	0.75 (0.63 – 0.89)	0.001
HDL cholesterol	1.32 (1.05 – 1.67)	0.017	1.27 (1.01 – 1.61)	0.042
Other serum levels				
25-hydroxyvitamin D	0.56 (0.43 – 0.73)	<0.001	0.58 (0.44 – 0.75)	<0.001