

1 **SUPPLEMENTAL MATERIAL**
2

3 **SUPPLEMENTARY METHODS**

4

5 **Quality control of the samples analyzed with the Illumina MethylationEPIC**

6 **BeadChip**

7 We removed the samples with a detection p-value >0.05 in at least 1% of the probes
8 using the pfilter function of the waterMelon R package available through the
9 Bioconductor repository. We also discarded those samples that did not cluster in the
10 correspondent sex cluster based on the DNA methylation levels in the X chromosome
11 using methylumi R package available through the Bioconductor repository.

12

13 **Quality control of the CpGs analyzed with the Illumina MethylationEPIC**

14 **BeadChip**

15 We excluded those probes with both a detection p-value >0.05 in at least 1% of the
16 samples and a beadcount < 3 in at least 5% of the samples using waterMelon R
17 package available through the Bioconductor repository. We further removed those
18 probes reported by Illumina to be discarded due to underperformance (n=1,031) and
19 changes in the manufacturing process (n=977). Also, we excluded those probes
20 corresponding to a methylation site different from a CpG site and those that could
21 hybridize in more than one genomic region (n=43,979).

22

23 **SUPPLEMENTARY RESULTS**

24

25 **Quality control of data**

26 In the secondary analysis considering BMI as a covariate, due to missing data, we
27 used 617 participants from the discovery sample, and 1,732 and 190 from the
28 validation samples (Framingham and REGICOR, respectively).

29 In the sensitivity analyses, we did not discard the individuals with TPA=0. In the
30 sensitivity analysis of the main analysis (without BMI as a covariate), we included 643
31 individuals from the discovery sample, and 1,737 and 192 from the validation samples
32 (Framingham and REGICOR, respectively). In the sensitivity analysis considering BMI
33 as a covariate, we included 641 individuals from the discovery sample, and 1,734 and
34 192 from the validation samples (Framingham and REGICOR, respectively).