**Supplementary Table 1:** Participating study characteristics

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study sample** | **Participants** | **Male, N (%)** | **Age\*,mean ± SD** | **Age\*, range** | **Current Smokers, N (%)** | **Diabetes,N (%)** | **Hypertension,** **N (%)** | **History of MI,** **N (%)** |
| **Randomized controlled trials** | ***N Overall*** |  |  |  |  |  |  |  |
| PROSPER Cases Controls  | 52445904654 | 2524 (48)356 (60)2168 (47) | 75.3 ± 3.375.7 ± 3.475.3 ± 3.3 | 70-8370-8370-83 | 1392 (27)152 (26)1240 (27) | 544 (10)83 (14)461 (10) | 3257 (62)361 (61)2896( 62) | 708 (14)153 (26)555 (12) |
| ASCOT UK RCT Cases Controls | 1971681903 | 1754 (89)60 (89)1754 (89) | 64.1 ± 8.265.8 ± 8.464.0 ± 8.1 | 41-8044-8041-80 | 24.726.524.6 | 23.335.322.9 | 100100100 | 000 |
| **Observational studies** | ***N Overall*** |  |  |  |  |  |  |  |
| ARIC | 624 | 450 (72) | 61.1 **±** 6.0 | 45-74 | 136 (22) | 183 (29) | 334 (54) | 155 (25) |
| ASCOT UK OBS  | 82 | 82.9  | 65.5 ± 7.3 | 46-78 | 24.4 | 32.9 | 100 | 0 |
| CHS | 484 | 222 (46) | 72.1 ± 4.64 | 65-88 | 47 (10) | 68 (14) | 295 (61) | 0 by design |
| FHS | 263 | 158 (60) | 69.3 ± 12.4 | 34-97 | 58 (22) | 66 (25) | 160 (61) | 30 (11) |
| HVH1 | 1228 | 566 (46) | 66.2 ± 9.40 | 32-80 | 218 (18) | 308 (25) | 940 (77) | 0 by design |
| HVH2 | 290 | 149 (51) | 65.0 ± 9.27 | 40-80 | 45 (16) | 75 (26) | 243 (84) | 0 by design |
| Rotterdam Study | 555 | 322 (58) | 77.0 ± 8.0 | 56-99 | 156 (28) | 72 (13) | 435 (78) | 81 (15) |
| **Second stage studies** | ***N Overall*** |  |  |  |  |  |  |  |
| ASCOT Scandinavia (OBS)Ascot Scandinavia (RCT) Cases Controls | 441391461345 | 84.178.587.078.2 | 60.8 ± 9.461.0 ± 8.863.9 ± 8.260.9 ± 8.8 | 44-7840-8043-7940-80 | 54.544.047.843.9 | 27.323.430.423.1 | 100100100100 | 0000 |
| MESA | 90 | 55 (61) | 67.0 ± 10.4 | 45-84 | 54 (60.0) | 26 (28.9) | 74 (82) | 0 |
| \*Age at DNA collection |  |

**Supplementary Table 2:** Genotyping characteristics

| **Study sample** | **Participants** | **Genotyping platform** | **Calling algorithm** | **NCBI build** | **Imputation software** | **Analysis software** | **Exclusion criteria used** |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **RCTs** | ***N Overall*** |  |  |  |  |  |  |
| PROSPER |  | Illumina Human 660\_Quadv1 | Beadstudio | 36.22 | MACH v1.0 16 | ProbABEL | Sample call rate>=97.5%, SNP call rate >=98%, SNP MAF>0.01 |
| ASCOT UK RCT | 1971 | Illumina Human 370CNV | Beadstudio | 36.22 | MACH v1.0 16 | ProbABEL | Sample call rate <=95%, SNP call rate <=97%, HWE<=10E-7, relatedness |
| **Observational**  | ***N Overall*** |  |  |  |  |  |  |
| ARIC | 624 | Affymetrix 6.0 | Birdseed | 36 | MACH v1.0.16 | ProbABEL | MAF <1%, call rate <95%, HWE<10E-5 |
| ASCOT UK OBS | 82 | Illumina Human 370CNV | Beadstudio | 36.22 | MACH v1.0 16 | ProbABEL | Sample call rate <=95%, SNP call rate <=97%, HWE<=10E-7, relatedness |
| CHS | 484 | Illumina Human 370CNV | BeadStudio | 36 | BIMBAM | R | Samples excluded for sex mismatch, discordance with prior genotyping, or call rate < 95%SNPs excluded for: call rate < 97%, HWE P < 10-5, > 2 duplicate errors or Mendelian inconsistencies (for reference CEPH trios), heterozygote frequency = 0, SNP not found in HapMap.  |
| FHS |  | Affymetrix 250K Sty, 250K Nsp & MIPS 50K Gene Centric | BRLMM | 36.22 | MACH v1.0.15 | R 2.6.1 with lmekin | Sample call rate ≤ 97%,SNP call rate ≤ 95%, SNP >1000 Mendelian errors, Heterozygosity 5 SD from Mean (<25.758% or >29.958%) |
| HVH1 | 1228 | Illumina Human 370CNV | BeadStudio | 36 | BIMBAM | R | Samples excluded for sex mismatch or call rate < 95%. SNP exclusions: call rate < 97%, HWE P < 10-5, > 2 duplicate errors or Mendelian inconsistencies (for reference CEPH trios), heterozygote frequency = 0, SNP not found in HapMap, inconsistencies across genotyping batches. |
| HVH2 | 290 | Illumina Omni Express | GenomeStudio | 36 | MaCH | R | Samples excluded for sex mismatch or call rate < 95%. SNP exclusions: call rate < 97%, HWE P < 10-5, > 2 duplicate errors or Mendelian inconsistencies (for reference CEPH trios), heterozygote frequency = 0, SNP not found in HapMap, inconsistencies across genotyping batches. |
| Rotterdam Study | 555 | Illumina HumanHap 550K | Illumina GenomeStudio | 36.22 | MACH v1.0.15 | ProbABEL | Call rate <98%, HWE P<10-6, or MAF<1%  |
| **Second stage** |  |  |  |  |  |  |  |
| ASCOT Scandinavia | RCT: 1391OBS: 44 | Illumina Human Omni Exome Express v8.1 | BeadStudio, followed by zCall | 37 | MACH v1.0.18 | R | GWAS: Exclude samples with: Discrepant sex, duplicate samples, relatedness at IBD pi\_hat 0.25, <99% call- rate, heterozygosity +/- 3 SD from Mean, separately for MAF > 1% / < 1%. Excluded SNPs with: 0% MAF, <98% call rate, HWE p<10-6 |
| MESA | 90 | Affymetrix Genome-Wide Human SNP Array 6.0 | Affymetrix | 36.24 | IMPUTE v2.1.0 | SNPTEST  | SNP call rate >=95%, Imputation information>0.30, SNP MAF>0.01 |

Supplementary Figure 1: Quantile-quantile plots of the expected versus observed -logP values for all studies participating in the first discovery stage.



