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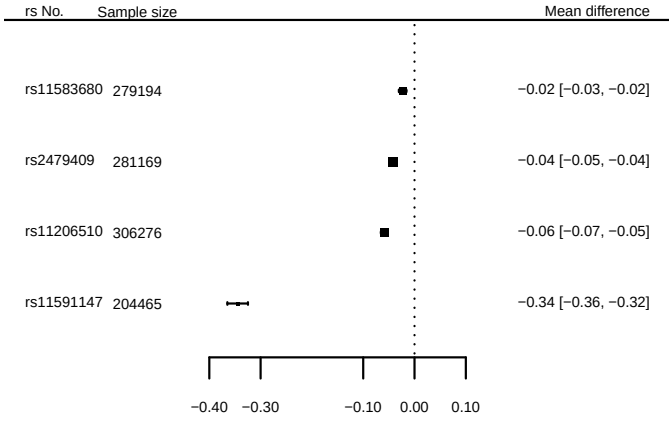
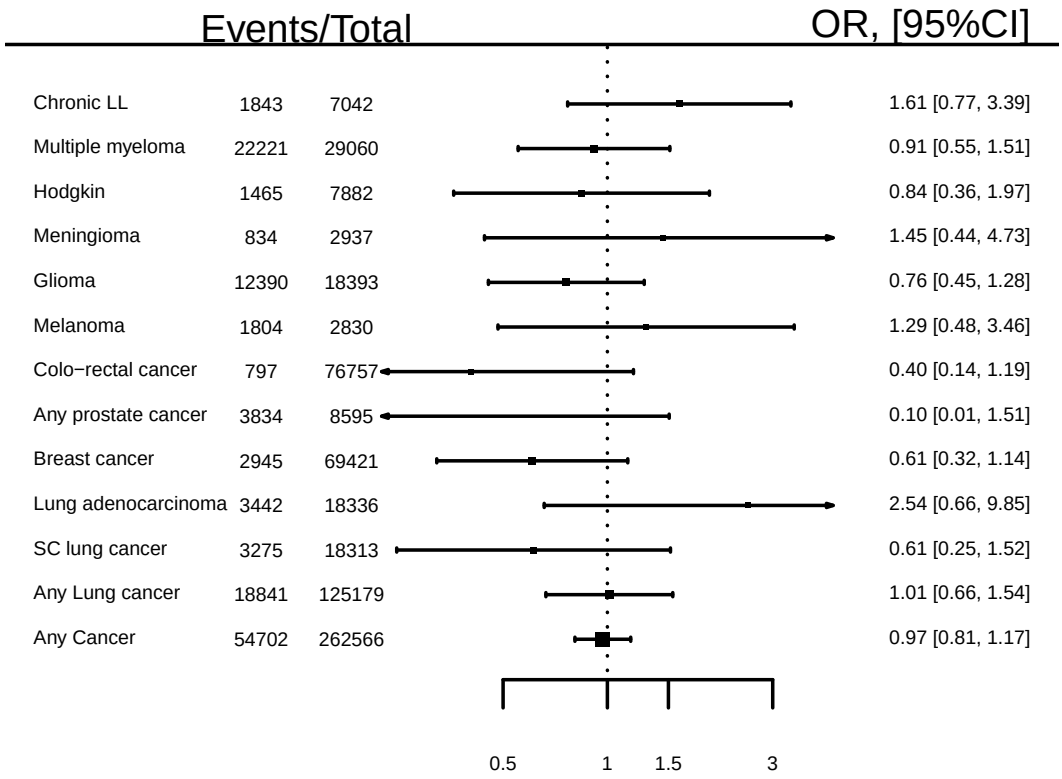
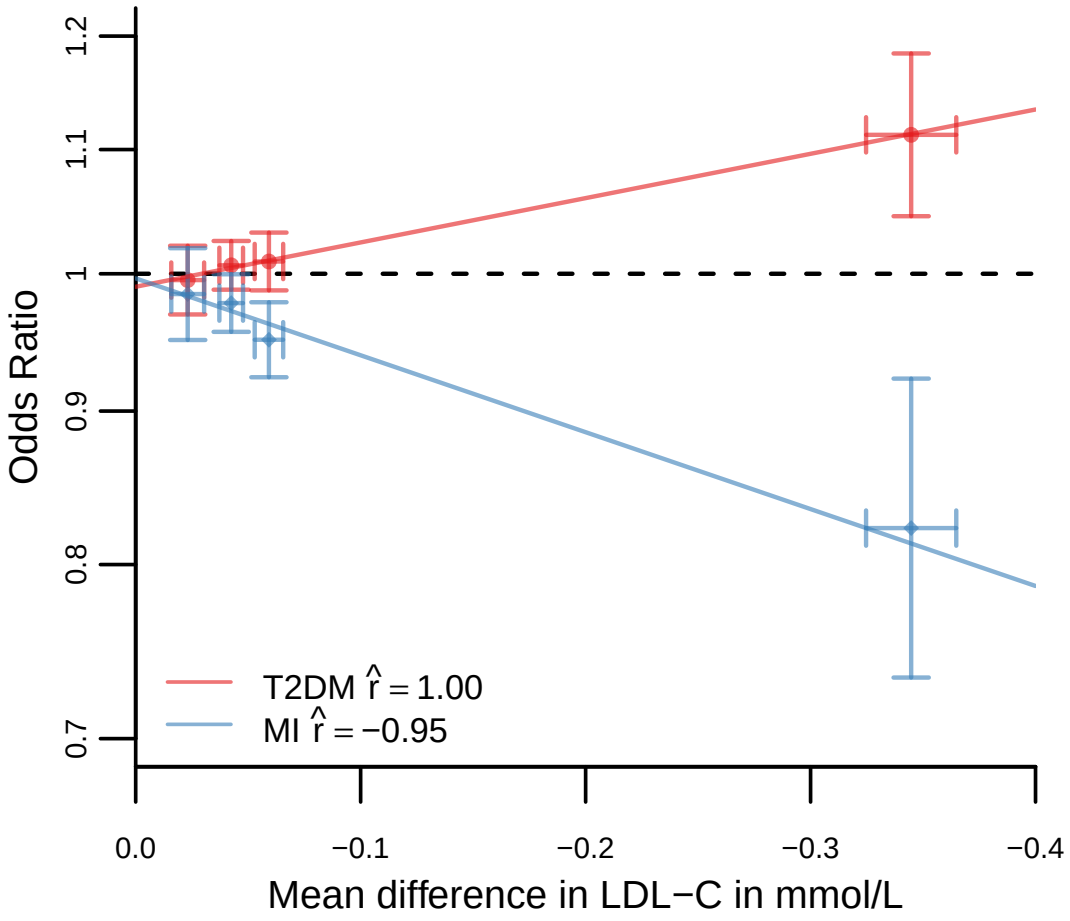
Phenome-wide association analysis of LDL-cholesterol lowering genetic variants in *PCSK9*



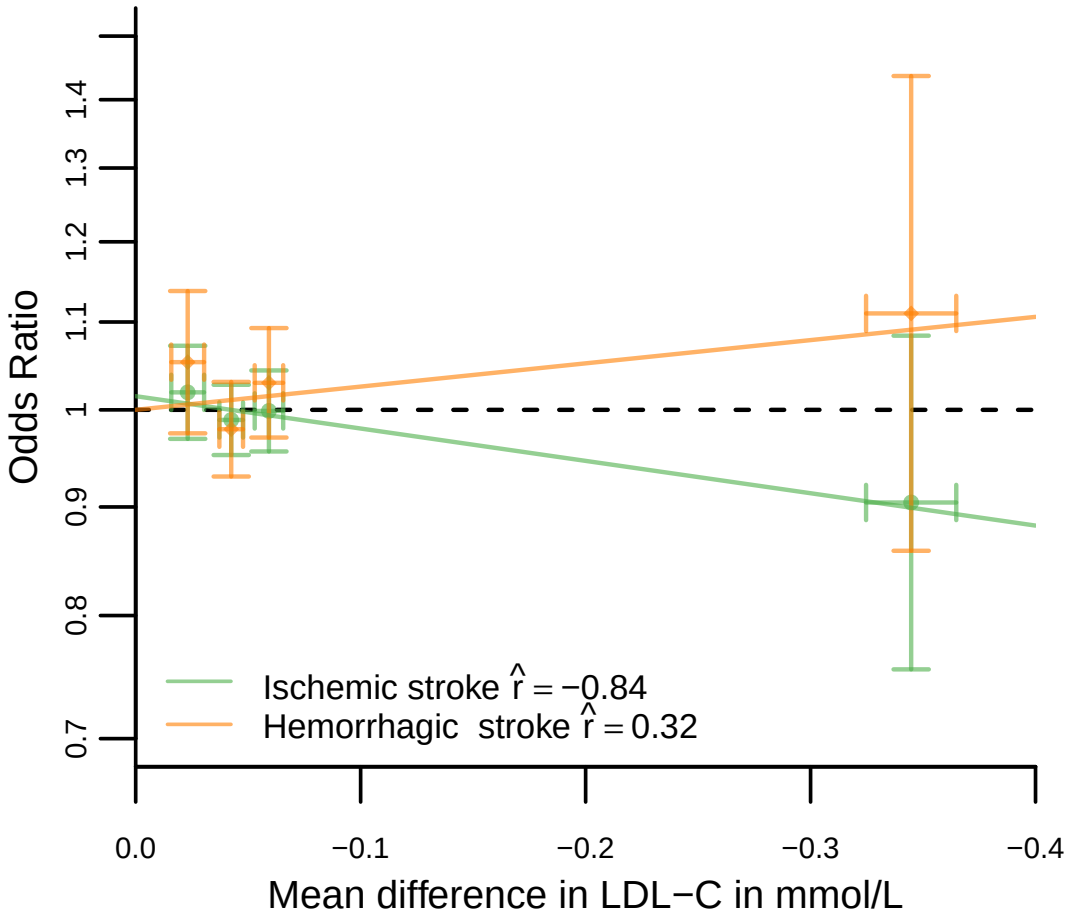
Appendix Figure 1: The LDL-C (mmol/L) effect of 4 *PCSK9* SNPs per LDL-C decreasing allele.



Appendix Figure 2: Associations of a PCSK9 gene-centric score (GS) with cancers. Effect estimates are presented as odds ratios (OR), with 95% confidence interval (CI) scaled to a mmol/L decrease in LDL-C (mmol/L). Results are pooled using a fixed effect model. The size of the black squares are proportional to the inverse of the variance.



Appendix Figure 3: Associations of a PCSK9 gene-centric score (GS) with myocardial infarction or type 2 diabetes, and LDL-C. Effect estimates are presented as odds ratios (OR) or mean differences, with 95% confidence interval (CI). r = Pearson's correlation coefficient was estimated using a weighted linear regression.



Appendix Figure 4: Associations of a PCSK9 gene-centric score (GS) with ischemic or hemorrhagic stroke, and LDL-C. Effect estimates are presented as odds ratios (OR) or mean differences, with 95% confidence interval (CI). r = Pearson's correlation coefficient was estimated using a weighted linear regression.

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Online only methods

International Genomics of Alzheimer's Project (IGAP) is a large two-stage study based upon genome-wide association studies (GWAS) on individuals of European ancestry. In stage 1, IGAP used genotyped and imputed data on 7,055,881 single nucleotide polymorphisms (SNPs) to meta-analyse four previously-published GWAS datasets consisting of 17,008 Alzheimer's disease cases and 37,154 controls (The European Alzheimer's disease Initiative - EADI the Alzheimer Disease Genetics Consortium - ADGC The Cohorts for Heart and Aging Research in Genomic Epidemiology consortium - CHARGE The Genetic and Environmental Risk in AD consortium - GERAD). In stage 2, 11,632 SNPs were genotyped and tested for association in an independent set of 8,572 Alzheimer's disease cases and 11,312 controls. Finally, a meta-analysis was performed combining results from stages 1 & 2.