# Supplemental Online Content

Zhao SS, Yiu ZZN, Barton A, Bowes J. Association of lipid-lowering drugs with risk of psoriasis: a mendelian randomization study. *JAMA Dermatol*. Published online January 25, 2023. doi:10.1001/jamadermatol.2022.6051



This supplemental material has been provided by the authors to give readers additional information about their work.

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eMethods.

**MR concept and assumptions**

Mendelian randomization (MR) provides evidence about putative causal relationships between modifiable exposures and disease outcomes, using genetic variants that are associated with exposure variation at a population level [1–4]. A genetic variant can be considered as a valid instrumental variable for an exposure if it satisfies the instrumental variable assumptions: it is associated with the exposure in a specific way (assumption 1) that does not affect the outcome except via the exposure (assumption 3), and it is not associated with the outcome due to confounding (assumption 2) (**Figure S1**).

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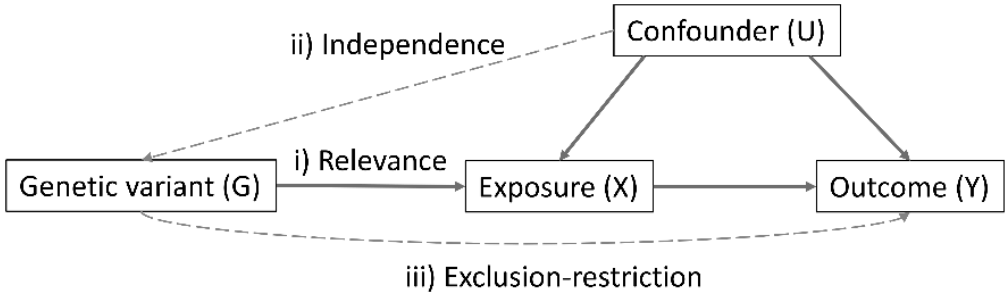
**eFigure 1: Illustration of instrumental variable assumptions.**




We used the Wald ratio method for the single variant instrument. If instrumental variable assumptions are met, the exposure-outcome estimate ($B_{XY}$) can be derived from the variant-outcome association ($B_{GY}$) divided by the variant-exposure association ($B_{GX}$). $B_{GX}$ can be obtained from genome-wide association study (GWAS) of the exposure, and $B_{GY}$ from GWAS of the outcome. $B_{GY}=B_{GX} * B_{XY}$, thus the exposure-outcome association can be derived as $B_{GY} / B_{GX}$, the Wald ratio.

**Psoriasis GWAS using the UK Biobank study**

We performed a GWAS of 6,495 psoriasis cases vs 25,980 controls using UK Biobank data. We excluded related participants (kinship coefficient ≥0.0884), those of non-white British ancestry or had discrepant reported and genetic sex. Quality control of UK Biobank genotype data has been described previously [5]. GWAS was performed using SNPTEST v2.5.4, adjusting for the first four principal components derived using cases and controls (FlashPCA for 64-bit Linux). Variants with minor allele frequency of <0.01 and INFO score of <0.5 were excluded. QQ, PCA and Manhattan plots are shown in Figure S2.

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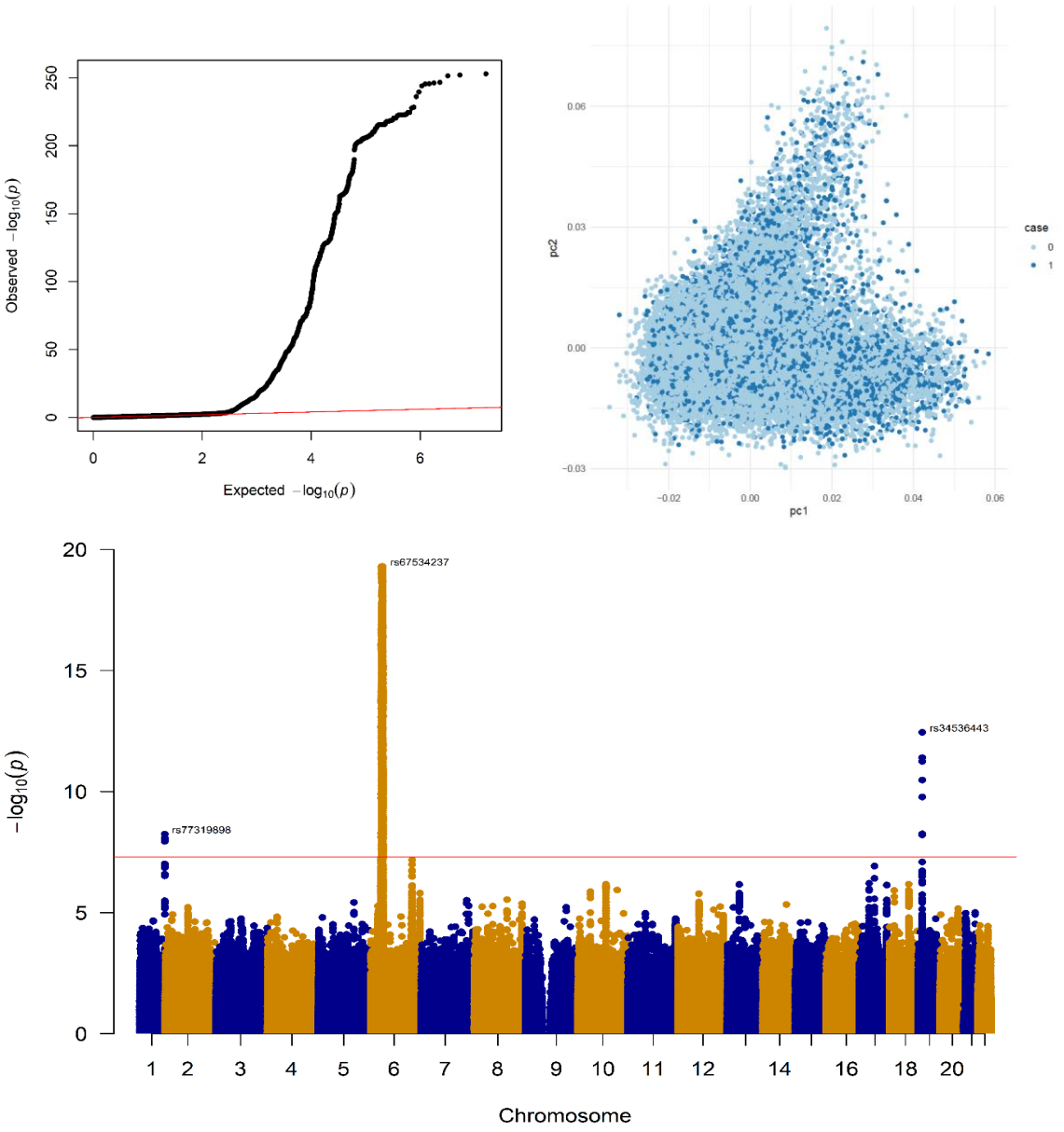
**eFigure 2: Plots from the psoriasis GWAS using UK Biobank data.**




Top left: QQ plot (genomic inflation factor 1.047); Top right: Overlap of principal components 1 and 2 between cases and controls; Botton: Manhattan plot.

**Genetic correlation using linkage disequilibrium score (LDSC) regression**

Cross-trait LDSC estimates genetic correlation from GWAS summary statistics. The method is detailed in [6]. In brief, LDSC is based on the concept that SNPs with high LD will have higher GWAS test statistics on average than SNPs with low LD. The z statistic for the genetic association of each variant with one trait are multiplied with those of the other trait. The product is regressed against the LD scores, with the coefficient representing genetic correlation.

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The software derives LD scores for each SNP using individuals of European ancestry from the 1000 Genomes project, excluding SNPS from the major histocompatibility complex (MHC) region (i.e. SNPs between 26Mb and 34Mb on chromosome 6) and those with minor allele frequency of <1%.

**Colocalization**

Colocalization as a sensitivity analysis in the context of MR is discussed in detail in reference [7]. In brief, MR can produce false positive exposure-outcome associations due to genetic confounding, that is, a variant that causes the outcome via a non-lipid pathway being closely correlated with the true causal variant. Bayesian colocalization was used with the default prior probabilities of $10^{-4}$, $10^{-4}$ and $10^{-5}$ for a variant within the relevant genomic locus being associated with the exposure trait, outcome trait, or both traits, respectively. The outputs of interest are posterior probability of distinct causal variants (H3), shared causal variant (H4), and the probability of colocalization conditional on the presence of a causal variant for the outcome (H4/(H3+H4)). Prior probabilities stated above were originally recommended for analyses of expression quantitative trait loci (eQTL) [8] and are conservative for hypothesis driven analyses. In the absence of evidence supporting colocalization, posterior probabilities will resemble the priors.

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**eTable 1. Variants in the HMGCR gene associated with body composition traits excluded in sensitivity analyses.**

| | rs116211124 | rs151000110 | rs17738989 | rs2112653 | rs4703665 | rs62366588 | rs6895057 |
|---|---|---|---|---|---|---|---|
| Arm fat-free mass left | 0 | 0 | 1 | 1 | 1 | 0 | 0 |
| Arm fat-free mass right | 0 | 0 | 1 | 1 | 1 | 0 | 0 |
| Arm fat mass left | 0 | 0 | 1 | 1 | 1 | 0 | 1 |
| Arm fat mass right | 0 | 0 | 1 | 1 | 1 | 0 | 1 |
| Arm fat percentage left | 0 | 0 | 1 | 1 | 0 | 0 | 0 |
| Arm fat percentage right | 0 | 0 | 1 | 1 | 0 | 0 | 0 |
| Arm predicted mass left | 0 | 0 | 1 | 1 | 1 | 0 | 0 |
| Arm predicted mass right | 0 | 0 | 1 | 1 | 1 | 0 | 0 |
| Basal metabolic rate | 0 | 1 | 1 | 1 | 1 | 0 | 0 |
| Body fat percentage | 0 | 0 | 1 | 1 | 0 | 0 | 0 |
| Body mass index | 1 | 0 | 1 | 1 | 1 | 0 | 1 |
| Body mass index males | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| Comparative body size at age 10 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| Hip circumference | 0 | 0 | 1 | 1 | 1 | 0 | 1 |
| Impedance of arm left | 0 | 0 | 1 | 1 | 0 | 0 | 0 |
| Impedance of arm right | 0 | 0 | 1 | 1 | 0 | 0 | 1 |
| Impedance of leg left | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| Impedance of leg right | 0 | 0 | 1 | 1 | 0 | 0 | 0 |
| Impedance of whole body | 0 | 0 | 1 | 1 | 0 | 0 | 0 |
| Leg fat-free mass left | 0 | 1 | 1 | 1 | 1 | 0 | 0 |
| Leg fat-free mass right | 0 | 1 | 1 | 1 | 1 | 0 | 0 |
| Leg fat mass left | 1 | 0 | 1 | 1 | 1 | 1 | 1 |
| Leg fat mass right | 0 | 0 | 1 | 1 | 1 | 1 | 1 |
| Leg fat percentage left | 0 | 0 | 1 | 1 | 0 | 0 | 1 |
| Leg fat percentage right | 0 | 0 | 1 | 1 | 0 | 0 | 1 |
| Leg predicted mass left | 0 | 1 | 1 | 1 | 1 | 0 | 0 |

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| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Leg predicted mass right | 0 | 1 | 1 | 1 | 1 | 0 | 0 |
| Low density lipoprotein | 0 | 0 | 0 | 1 | 0 | 0 | 1 |
| Medication for cholesterol, blood pressure or diabetes: cholesterol lowering medication | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| Self-reported high cholesterol | 0 | 1 | 1 | 1 | 0 | 0 | 1 |
| Total cholesterol | 0 | 0 | 0 | 1 | 0 | 0 | 1 |
| Treatment with cholesterol lowering medication | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| Trunk fat-free mass | 0 | 0 | 1 | 1 | 1 | 0 | 0 |
| Trunk fat mass | 0 | 0 | 1 | 1 | 0 | 0 | 0 |
| Trunk fat percentage | 0 | 0 | 1 | 1 | 0 | 0 | 0 |
| Trunk predicted mass | 0 | 0 | 1 | 1 | 1 | 0 | 0 |
| Waist circumference | 0 | 0 | 1 | 1 | 1 | 0 | 1 |
| Weight | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Whole body fat-free mass | 0 | 1 | 1 | 1 | 1 | 0 | 0 |
| Whole body fat mass | 0 | 0 | 1 | 1 | 1 | 0 | 1 |
| Whole body water mass | 0 | 1 | 1 | 1 | 1 | 0 | 0 |
| 1 indicates an association with the trait at $p<5x10^{-5}$ and 0 no such association. | | | | | | | |

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**eTable 2. Associations between genetically proxied exposures (drug targets and LDL) and outcomes (psoriasis using UK Biobank and FinnGen and control outcomes).**

| Outcome | Exposure | Method | No. SNPs | OR | Lower 95% CI | Upper 95% CI | p-value |
|---|---|---|---|---|---|---|---|
| **Psoriasis (UKB)** | **PCSK9** | **IVW** | 33 | 0.69 | 0.55 | 0.88 | **2.62E-03** |
| Psoriasis (UKB) | PCSK9 | MR Egger | 33 | 0.97 | 0.59 | 1.59 | 0.90 |
| Psoriasis (UKB) | PCSK9 | Weighted median | 33 | 0.76 | 0.52 | 1.09 | 0.14 |
| Psoriasis (UKB) | PCSK9 | Weighted mode | 33 | 0.80 | 0.55 | 1.15 | 0.24 |
| Psoriasis (UKB) | HMGCR | IVW | 14 | 0.84 | 0.64 | 1.09 | 0.18 |
| Psoriasis (UKB) | HMGCR | MR Egger | 14 | 0.63 | 0.10 | 3.89 | 0.62 |
| Psoriasis (UKB) | HMGCR | Weighted median | 14 | 0.84 | 0.50 | 1.42 | 0.52 |
| Psoriasis (UKB) | HMGCR | Weighted mode | 14 | 0.82 | 0.46 | 1.47 | 0.52 |
| Psoriasis (UKB) | NPC1L1 | IVW | 8 | 0.55 | 0.25 | 1.23 | 0.15 |
| Psoriasis (UKB) | NPC1L1 | MR Egger | 8 | 0.05 | 0.00 | 1.05 | 0.10 |
| Psoriasis (UKB) | NPC1L1 | Weighted median | 8 | 0.58 | 0.24 | 1.45 | 0.25 |
| Psoriasis (UKB) | NPC1L1 | Weighted mode | 8 | 0.60 | 0.24 | 1.48 | 0.30 |
| Psoriasis (UKB) | LDL | IVW | 266 | 0.90 | 0.79 | 1.02 | 0.09 |
| Psoriasis (UKB) | LDL | MR Egger | 266 | 0.91 | 0.76 | 1.09 | 0.30 |
| Psoriasis (UKB) | LDL | Weighted median | 266 | 0.97 | 0.81 | 1.16 | 0.73 |
| Psoriasis (UKB) | LDL | Weighted mode | 266 | 0.93 | 0.78 | 1.11 | 0.44 |
| **Psoriasis (FinnGen)** | **PCSK9** | **IVW** | **33** | **0.77** | **0.66** | **0.91** | **1.46E-03** |
| Psoriasis (FinnGen) | PCSK9 | MR Egger | 33 | 0.80 | 0.62 | 1.02 | 0.08 |
| **Psoriasis (FinnGen)** | **PCSK9** | **Weighted median** | **33** | **0.74** | **0.58** | **0.93** | **0.01** |
| **Psoriasis (FinnGen)** | **PCSK9** | **Weighted mode** | **33** | **0.76** | **0.60** | **0.95** | **0.02** |
| Psoriasis (FinnGen) | HMGCR | IVW | 20 | 0.98 | 0.64 | 1.50 | 0.94 |
| Psoriasis (FinnGen) | HMGCR | MR Egger | 20 | 1.08 | 0.14 | 8.16 | 0.94 |
| Psoriasis (FinnGen) | HMGCR | Weighted median | 20 | 0.85 | 0.47 | 1.53 | 0.59 |
| Psoriasis (FinnGen) | HMGCR | Weighted mode | 20 | 0.88 | 0.51 | 1.51 | 0.64 |
| Psoriasis (FinnGen) | NPC1L1 | IVW | 9 | 0.67 | 0.32 | 1.40 | 0.28 |

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|---|---|---|---|---|---|---|---|
| Psoriasis (FinnGen) | NPC1L1 | MR Egger | 9 | 1.34 | 0.09 | 19.47 | 0.84 |
| Psoriasis (FinnGen) | NPC1L1 | Weighted median | 9 | 0.57 | 0.25 | 1.31 | 0.19 |
| Psoriasis (FinnGen) | NPC1L1 | Weighted mode | 9 | 0.54 | 0.22 | 1.35 | 0.22 |
| Psoriasis (FinnGen) | LDL | IVW | 372 | 0.97 | 0.85 | 1.10 | 0.62 |
| Psoriasis (FinnGen) | LDL | MR Egger | 372 | 0.92 | 0.76 | 1.11 | 0.39 |
| Psoriasis (FinnGen) | LDL | Weighted median | 372 | 0.87 | 0.73 | 1.04 | 0.14 |
| Psoriasis (FinnGen) | LDL | Weighted mode | 372 | 0.87 | 0.73 | 1.04 | 0.12 |
| **CAD** | **PCSK9** | **IVW** | **29** | **0.51** | **0.44** | **0.60** | **3.13E-17** |
| **CAD** | **PCSK9** | **MR Egger** | **29** | **0.48** | **0.35** | **0.65** | **7.26E-05** |
| **CAD** | **PCSK9** | **Weighted median** | **29** | **0.49** | **0.39** | **0.61** | **2.87E-10** |
| **CAD** | **PCSK9** | **Weighted mode** | **29** | **0.47** | **0.37** | **0.59** | **3.63E-07** |
| **CAD** | **HMGCR** | **IVW** | **19** | **0.70** | **0.55** | **0.89** | **3.08E-03** |
| CAD | HMGCR | MR Egger | 19 | 0.50 | 0.13 | 1.87 | 0.32 |
| CAD | HMGCR | Weighted median | 19 | 0.81 | 0.60 | 1.09 | 0.16 |
| CAD | HMGCR | Weighted mode | 19 | 0.78 | 0.59 | 1.02 | 0.09 |
| **CAD** | **NPC1L1** | **IVW** | **10** | **0.48** | **0.34** | **0.69** | **6.26E-05** |
| CAD | NPC1L1 | MR Egger | 10 | 1.31 | 0.32 | 5.32 | 0.72 |
| **CAD** | **NPC1L1** | **Weighted median** | **10** | **0.56** | **0.34** | **0.90** | **0.02** |
| **CAD** | **NPC1L1** | **Weighted mode** | **10** | **0.58** | **0.36** | **0.92** | **0.04** |
| **CAD** | **LDL** | **IVW** | **380** | **0.57** | **0.52** | **0.63** | **4.80E-35** |
| **CAD** | **LDL** | **MR Egger** | **380** | **0.52** | **0.45** | **0.60** | **4.07E-18** |
| **CAD** | **LDL** | **Weighted median** | **380** | **0.58** | **0.52** | **0.64** | **6.75E-28** |
| **CAD** | **LDL** | **Weighted mode** | **380** | **0.58** | **0.52** | **0.65** | **7.20E-19** |
| Psoriasis (UKB) | HMGCR excl* | IVW | 10 | 0.92 | 0.58 | 1.48 | 0.74 |
| Psoriasis (UKB) | HMGCR excl* | MR Egger | 10 | 0.83 | 0.01 | 75.87 | 0.94 |
| Psoriasis (UKB) | HMGCR excl* | Weighted median | 10 | 0.90 | 0.41 | 1.99 | 0.80 |
| Psoriasis (UKB) | HMGCR excl* | Weighted mode | 10 | 1.14 | 0.38 | 3.45 | 0.82 |
| Psoriasis (FinnGen) | HMGCR excl* | IVW | 15 | 1.11 | 0.53 | 2.33 | 0.79 |
| Psoriasis (FinnGen) | HMGCR excl* | MR Egger | 15 | 2.62 | 0.05 | 142.37 | 0.64 |
| Psoriasis (FinnGen) | HMGCR excl* | Weighted median | 15 | 1.07 | 0.38 | 3.04 | 0.89 |

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| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Psoriasis (FinnGen) | HMGCR excl* | Weighted mode | 15 | 0.98 | 0.29 | 3.28 | 0.97 |
| **CAD** | **HMGCR excl*** | **IVW** | **13** | **0.52** | **0.31** | **0.89** | **0.02** |
| CAD | HMGCR excl* | MR Egger | 13 | 0.18 | 0.01 | 2.73 | 0.24 |
| **CAD** | **HMGCR excl*** | **Weighted median** | **13** | **0.48** | **0.24** | **0.94** | **0.03** |
| CAD | HMGCR excl* | Weighted mode | 13 | 0.53 | 0.18 | 1.60 | 0.28 |

*excluding potentially pleiotropic variants. Bold text highlights results with p<0.05.
IVW, multiplicative random effects inverse variance weighted method; CAD, coronary artery disease; HMGCR, HMG-CoA reductase; PCSK9, proprotein convertase subtilisin/kexin type 9; NPC1L1, Niemann-Pick C1-Like 1; LDL, low-density lipoprotein.

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**eTable 3. MR Egger intercepts.**

| Outcome | Exposure | Egger intercept | p-value |
|---|---|---|---|
| Psoriasis (UKB) | HMGCR | -0.02 | 0.75 |
| Psoriasis (UKB) | LDL | 0.00 | 0.82 |
| Psoriasis (UKB) | NPC1L1 | -0.08 | 0.16 |
| Psoriasis (UKB) | PCSK9 | 0.02 | 0.13 |
| Psoriasis (FinnGen) | HMGCR | 0.03 | 0.61 |
| Psoriasis (FinnGen) | LDL | 0.00 | 0.74 |
| Psoriasis (FinnGen) | NPC1L1 | 0.00 | 0.64 |
| Psoriasis (FinnGen) | PCSK9 | 0.00 | 0.93 |
| CAD | HMGCR | 0.03 | 0.19 |
| CAD | LDL | 0.00 | 0.60 |
| CAD | NPC1L1 | 0.00 | 0.07 |
| CAD | PCSK9 | -0.02 | 0.62 |
| Psoriasis (UKB) | HMGCR excl* | -0.01 | 0.96 |
| Psoriasis (FinnGen) | HMGCR excl* | 0.04 | 0.67 |
| CAD | HMGCR excl* | -0.05 | 0.44 |

*excluding potentially pleiotropic variants. CAD, coronary artery disease; HMGCR, HMG-CoA reductase; PCSK9, proprotein convertase subtilisin/kexin type 9; NPC1L1, Niemann-Pick C1-Like 1; LDL, low-density lipoprotein.

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**eTable 4. Colocalization results.**

| H0 | H1 | H2 | H3 | H4 | H4/(H4+H3) |
|---|---|---|---|---|---|
| 2.96E-323 | 0.00E+00 | 9.56E-01 | 0.00E+00 | 9.12E-03 | 7.94E-01 |

Posterior probability for
H0: neither trait has a genetic association in the region;
H1: only trait 1 has a genetic association in the region;
H2: only trait 2 has a genetic association in the region;
H3: both traits are associated, but with different causal variants;
H4: both traits are associated and share a single causal variant.
H4/(H3+H4) represents the probability of colocalization conditional on the presence of a causal variant for the outcome

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**eTable 5. Associations between circulating PCSK9 level and psoriasis risk.**

| Outcome | Exposure | Method | No. SNPs | OR | Lower 95% CI | Upper 95% CI | p-value |
|---|---|---|---|---|---|---|---|
| Psoriasis (UKB) | PCSK9 (cis-pQTL) | IVW | 2 | 0.86 | 0.49 | 1.51 | 0.61 |
| **Psoriasis (FinnGen)** | **PCSK9 (cis-pQTL)** | **IVW** | **3** | **0.83** | **0.74** | **0.93** | **1.03E-03** |
| Psoriasis (FinnGen) | PCSK9 (cis-pQTL) | MR Egger | 3 | 0.60 | 0.15 | 2.37 | 0.60 |
| Psoriasis (FinnGen) | PCSK9 (cis-pQTL) | Weighted median | 3 | 0.81 | 0.58 | 1.14 | 0.23 |
| Psoriasis (FinnGen) | PCSK9 (cis-pQTL) | Weighted mode | 3 | 0.80 | 0.55 | 1.17 | 0.37 |
| Sensitivity methods were not possible for 2 variants in the UKB analysis. Bold text highlights results with p<0.05. | | | | | | | |

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**eTable 6. Genetic variants used to instrument LDL and each lipid lowering drug target for the primary analysis.**

| Exposure | SNP | EA/OA | EAF | beta | p-value | F |
|---|---|---|---|---|---|---|
| HMGCR | rs375392181 | T/G | 0.010 | 0.048 | 5.11E-09 | 34 |
| HMGCR | rs2112653 | C/T | 0.441 | 0.063 | 1.00E-200 | 1342 |
| HMGCR | rs4703665 | T/C | 0.130 | -0.034 | 4.17E-32 | 139 |
| HMGCR | rs35122945 | C/A | 0.067 | -0.043 | 2.76E-32 | 140 |
| HMGCR | rs75240579 | T/C | 0.036 | -0.048 | 1.65E-23 | 100 |
| HMGCR | rs112672253 | T/A | 0.008 | 0.065 | 8.59E-11 | 42 |
| HMGCR | rs17238568 | T/G | 0.065 | 0.044 | 8.94E-39 | 170 |
| HMGCR | rs17244939 | C/A | 0.013 | -0.057 | 2.48E-11 | 45 |
| HMGCR | rs3761740 | A/C | 0.099 | 0.056 | 1.96E-93 | 420 |
| HMGCR | rs115169875 | A/G | 0.025 | -0.039 | 5.44E-12 | 48 |
| HMGCR | rs62366588 | A/C | 0.054 | -0.043 | 1.05E-27 | 119 |
| HMGCR | rs74695562 | G/T | 0.040 | -0.039 | 2.83E-17 | 71 |
| HMGCR | rs144083983 | T/C | 0.066 | -0.048 | 9.34E-38 | 165 |
| HMGCR | rs181668591 | T/C | 0.011 | 0.070 | 4.10E-17 | 71 |
| HMGCR | rs114253542 | C/T | 0.007 | 0.079 | 7.86E-14 | 56 |
| HMGCR | rs180755046 | A/C | 0.013 | -0.054 | 2.08E-10 | 40 |
| HMGCR | rs182826525 | G/A | 0.023 | 0.104 | 1.79E-33 | 145 |
| HMGCR | rs151000110 | A/G | 0.056 | 0.067 | 1.39E-72 | 325 |
| HMGCR | rs200823803 | C/T | 0.021 | 0.060 | 7.95E-18 | 74 |
| NPC1L1 | rs7808295 | T/C | 0.041 | -0.025 | 1.15E-08 | 33 |
| NPC1L1 | rs10260606 | C/G | 0.201 | 0.043 | 1.50E-91 | 412 |
| NPC1L1 | rs77517259 | T/C | 0.011 | 0.051 | 7.27E-10 | 38 |
| NPC1L1 | rs117623941 | T/C | 0.016 | -0.040 | 1.21E-08 | 32 |
| NPC1L1 | rs2289051 | T/C | 0.028 | 0.030 | 2.25E-08 | 31 |
| NPC1L1 | rs217370 | G/A | 0.466 | -0.027 | 1.44E-60 | 270 |
| NPC1L1 | rs79836087 | A/G | 0.045 | -0.024 | 4.22E-09 | 35 |
| NPC1L1 | rs79854399 | T/C | 0.019 | -0.047 | 3.15E-14 | 58 |
| NPC1L1 | rs143116067 | A/G | 0.065 | -0.021 | 6.98E-09 | 34 |
| PCSK9 | rs12138834 | T/C | 0.348 | 0.012 | 3.81E-12 | 48 |
| PCSK9 | rs12043403 | C/T | 0.098 | -0.028 | 8.70E-22 | 92 |
| PCSK9 | rs12409233 | C/G | 0.086 | -0.025 | 1.56E-17 | 73 |
| PCSK9 | rs890576 | G/C | 0.200 | -0.015 | 2.08E-13 | 54 |
| PCSK9 | rs12123143 | C/T | 0.229 | 0.013 | 5.57E-09 | 34 |
| PCSK9 | rs12732125 | T/C | 0.018 | -0.206 | 1.00E-200 | 1055 |
| PCSK9 | rs145075626 | G/C | 0.017 | -0.046 | 1.86E-12 | 50 |
| PCSK9 | rs146480899 | G/A | 0.019 | -0.048 | 9.43E-15 | 60 |
| PCSK9 | rs77875082 | A/G | 0.030 | 0.045 | 1.08E-18 | 78 |
| PCSK9 | rs12117661 | G/C | 0.240 | -0.069 | 1.00E-200 | 1237 |
| PCSK9 | rs374459115 | A/G | 0.016 | 0.074 | 2.66E-19 | 81 |
| PCSK9 | rs28775984 | C/T | 0.432 | -0.019 | 2.18E-10 | 40 |
| PCSK9 | rs2479420 | C/T | 0.261 | 0.034 | 1.70E-58 | 260 |

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| | | | | | | |
|---|---|---|---|---|---|---|
| PCSK9 | rs181331606 | G/C | 0.087 | 0.027 | 1.38E-13 | 55 |
| PCSK9 | rs12739979 | T/C | 0.232 | -0.032 | 1.64E-46 | 205 |
| PCSK9 | rs11810371 | A/G | 0.042 | -0.046 | 1.73E-24 | 104 |
| PCSK9 | rs72660548 | G/C | 0.021 | 0.074 | 1.49E-37 | 164 |
| PCSK9 | rs2479409 | G/A | 0.338 | 0.048 | 9.06E-160 | 725 |
| PCSK9 | rs10888896 | G/C | 0.237 | -0.042 | 7.92E-95 | 427 |
| PCSK9 | rs499718 | T/C | 0.178 | -0.016 | 3.35E-14 | 58 |
| PCSK9 | rs2495477 | G/A | 0.399 | -0.054 | 1.00E-200 | 921 |
| PCSK9 | rs41294825 | T/A | 0.042 | -0.042 | 3.28E-25 | 108 |
| PCSK9 | rs150119739 | A/G | 0.040 | 0.067 | 3.85E-52 | 231 |
| PCSK9 | rs7525503 | T/G | 0.024 | 0.065 | 7.04E-29 | 124 |
| PCSK9 | rs11206517 | G/T | 0.039 | 0.081 | 1.40E-79 | 357 |
| PCSK9 | rs41297885 | G/C | 0.036 | -0.038 | 3.47E-17 | 71 |
| PCSK9 | rs28385715 | G/T | 0.022 | 0.050 | 1.33E-16 | 68 |
| PCSK9 | rs77011887 | T/C | 0.016 | 0.058 | 1.00E-15 | 64 |
| PCSK9 | rs142116310 | A/G | 0.010 | 0.057 | 1.81E-10 | 41 |
| PCSK9 | rs115465289 | A/G | 0.030 | -0.047 | 1.08E-19 | 82 |
| PCSK9 | rs530804537 | A/G | 0.013 | -0.290 | 1.00E-200 | 1103 |
| PCSK9 | rs12031153 | A/G | 0.054 | 0.039 | 1.84E-19 | 81 |
| PCSK9 | rs55817205 | A/G | 0.012 | 0.069 | 1.24E-15 | 64 |
| PCSK9 | rs139003571 | A/C | 0.028 | -0.062 | 1.14E-34 | 151 |
| LDL | rs1123571 | A/G | 0.473 | -0.011 | 5.26E-11 | 43 |
| LDL | rs75907879 | T/C | 0.121 | 0.020 | 2.14E-14 | 58 |
| LDL | rs1136348 | T/C | 0.154 | -0.013 | 1.31E-08 | 32 |
| LDL | rs10903129 | A/G | 0.458 | -0.025 | 1.94E-51 | 228 |
| LDL | rs79778025 | G/A | 0.176 | -0.016 | 1.33E-11 | 46 |
| LDL | rs79598313 | T/C | 0.024 | 0.074 | 2.94E-45 | 199 |
| LDL | rs113046963 | G/C | 0.090 | -0.020 | 3.19E-12 | 49 |
| LDL | rs72660594 | C/T | 0.015 | -0.252 | 1.00E-200 | 1327 |
| LDL | rs146346813 | C/A | 0.029 | -0.061 | 1.94E-33 | 145 |
| LDL | rs148742777 | C/T | 0.010 | 0.065 | 3.91E-12 | 48 |
| LDL | rs2270690 | T/C | 0.040 | 0.081 | 3.70E-79 | 355 |
| LDL | rs12750160 | T/C | 0.007 | -0.322 | 1.00E-200 | 988 |
| LDL | rs150088310 | A/G | 0.014 | 0.044 | 5.32E-10 | 39 |
| LDL | rs115449167 | C/A | 0.024 | 0.050 | 1.55E-18 | 77 |
| LDL | rs76488758 | G/A | 0.021 | -0.054 | 2.65E-19 | 81 |
| LDL | rs113654127 | A/G | 0.012 | -0.049 | 6.54E-10 | 38 |
| LDL | rs598253 | C/T | 0.330 | -0.039 | 2.08E-103 | 466 |
| LDL | rs7515577 | C/A | 0.207 | -0.025 | 5.67E-35 | 152 |
| LDL | rs189974330 | A/G | 0.007 | 0.056 | 2.18E-08 | 31 |
| LDL | rs4970829 | A/G | 0.072 | -0.110 | 1.00E-200 | 1198 |
| LDL | rs6670347 | C/T | 0.040 | -0.115 | 3.18E-166 | 755 |
| LDL | rs17036094 | C/A | 0.011 | -0.121 | 6.83E-57 | 253 |
| LDL | rs10858093 | T/C | 0.023 | 0.050 | 2.74E-16 | 67 |
| LDL | rs41279736 | G/A | 0.029 | 0.032 | 1.38E-08 | 32 |
| LDL | rs115458560 | C/T | 0.014 | -0.047 | 3.49E-10 | 39 |

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|---|---|---|---|---|---|---|
| LDL | rs116276872 | T/C | 0.019 | -0.055 | 2.26E-17 | 72 |
| LDL | rs267733 | G/A | 0.153 | -0.019 | 1.07E-17 | 73 |
| LDL | rs4390169 | A/G | 0.487 | 0.013 | 1.48E-14 | 59 |
| LDL | rs6682862 | A/G | 0.162 | -0.014 | 8.30E-11 | 42 |
| LDL | rs1689801 | A/G | 0.322 | 0.015 | 2.62E-17 | 72 |
| LDL | rs2296288 | T/C | 0.442 | -0.011 | 1.58E-11 | 45 |
| LDL | rs2642438 | A/G | 0.293 | -0.025 | 3.82E-45 | 199 |
| LDL | rs6426060 | A/T | 0.119 | -0.014 | 4.98E-08 | 30 |
| LDL | rs7544869 | A/T | 0.458 | -0.010 | 2.20E-09 | 36 |
| LDL | rs553427 | C/T | 0.469 | -0.038 | 1.83E-116 | 526 |
| LDL | rs10910522 | A/G | 0.433 | -0.011 | 4.59E-11 | 43 |
| LDL | rs3738622 | T/G | 0.203 | -0.016 | 3.81E-15 | 62 |
| LDL | rs3820897 | T/C | 0.198 | 0.016 | 7.26E-15 | 61 |
| LDL | rs880973 | G/A | 0.223 | -0.012 | 2.22E-09 | 36 |
| LDL | rs4075673 | T/C | 0.442 | 0.059 | 1.00E-200 | 1264 |
| LDL | rs1712249 | T/C | 0.249 | -0.072 | 1.00E-200 | 1430 |
| LDL | rs13005230 | A/C | 0.096 | -0.020 | 1.54E-09 | 36 |
| LDL | rs13403394 | T/C | 0.032 | -0.028 | 1.72E-09 | 36 |
| LDL | rs1260326 | T/C | 0.390 | 0.021 | 1.41E-36 | 160 |
| LDL | rs745763 | C/T | 0.168 | 0.018 | 1.16E-14 | 60 |
| LDL | rs56266464 | A/G | 0.062 | -0.109 | 1.00E-200 | 1020 |
| LDL | rs140488605 | T/C | 0.042 | 0.075 | 4.10E-63 | 281 |
| LDL | rs55726838 | A/G | 0.009 | 0.070 | 3.19E-14 | 58 |
| LDL | rs548088667 | T/C | 0.018 | 0.076 | 1.61E-23 | 100 |
| LDL | rs360804 | A/G | 0.316 | -0.022 | 2.70E-35 | 154 |
| LDL | rs10193634 | C/A | 0.391 | -0.012 | 6.22E-13 | 52 |
| LDL | rs2970902 | C/G | 0.344 | 0.012 | 6.30E-12 | 47 |
| LDL | rs2465956 | C/T | 0.195 | 0.019 | 2.57E-20 | 85 |
| LDL | rs150474434 | A/G | 0.092 | -0.042 | 7.99E-50 | 220 |
| LDL | rs17050272 | A/G | 0.426 | -0.020 | 5.50E-31 | 134 |
| LDL | rs1375131 | C/T | 0.341 | 0.021 | 9.67E-23 | 96 |
| LDL | rs10184376 | T/C | 0.074 | -0.027 | 2.12E-18 | 77 |
| LDL | rs10184673 | G/A | 0.409 | 0.020 | 4.55E-31 | 134 |
| LDL | rs189527671 | A/G | 0.023 | 0.039 | 2.14E-09 | 36 |
| LDL | rs10932008 | G/A | 0.184 | -0.025 | 1.26E-28 | 123 |
| LDL | rs1250259 | T/A | 0.264 | -0.017 | 2.35E-20 | 85 |
| LDL | rs887829 | T/C | 0.328 | -0.016 | 1.09E-19 | 82 |
| LDL | rs1177809 | G/A | 0.344 | -0.024 | 3.82E-42 | 185 |
| LDL | rs6792725 | A/G | 0.325 | 0.016 | 5.38E-18 | 75 |
| LDL | rs9837622 | A/T | 0.073 | -0.035 | 1.23E-27 | 119 |
| LDL | rs71311871 | G/A | 0.081 | -0.036 | 2.57E-34 | 149 |
| LDL | rs55921103 | G/T | 0.364 | -0.011 | 2.37E-10 | 40 |
| LDL | rs10936349 | T/C | 0.341 | 0.011 | 5.07E-10 | 39 |
| LDL | rs3732359 | G/A | 0.236 | 0.014 | 4.35E-13 | 52 |
| LDL | rs12054451 | G/T | 0.260 | 0.015 | 7.04E-16 | 65 |
| LDL | rs9824581 | G/A | 0.267 | -0.011 | 2.58E-09 | 35 |

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|---|---|---|---|---|---|---|
| LDL | rs78946096 | G/A | 0.047 | -0.041 | 1.65E-26 | 114 |
| LDL | rs6794351 | C/T | 0.240 | -0.012 | 1.47E-09 | 37 |
| LDL | rs9653945 | A/G | 0.344 | -0.011 | 3.61E-11 | 44 |
| LDL | rs1584688 | C/T | 0.449 | 0.013 | 2.98E-14 | 58 |
| LDL | rs56118251 | G/A | 0.155 | 0.015 | 5.06E-12 | 48 |
| LDL | rs16861497 | T/G | 0.395 | -0.010 | 4.37E-09 | 34 |
| LDL | rs13108218 | A/G | 0.387 | 0.016 | 3.87E-21 | 89 |
| LDL | rs4234798 | T/G | 0.393 | -0.010 | 2.72E-09 | 35 |
| LDL | rs112575086 | T/C | 0.121 | -0.015 | 6.91E-10 | 38 |
| LDL | rs34707604 | C/T | 0.242 | 0.030 | 3.42E-38 | 167 |
| LDL | rs13112099 | G/T | 0.471 | 0.011 | 8.50E-10 | 38 |
| LDL | rs72647039 | T/C | 0.020 | 0.037 | 1.40E-09 | 37 |
| LDL | rs342467 | T/C | 0.401 | -0.010 | 8.75E-09 | 33 |
| LDL | rs17586023 | G/A | 0.113 | 0.016 | 1.02E-09 | 37 |
| LDL | rs28497720 | T/C | 0.250 | -0.018 | 6.75E-22 | 92 |
| LDL | rs17617028 | A/G | 0.223 | 0.015 | 8.56E-14 | 56 |
| LDL | rs138204164 | G/C | 0.135 | -0.014 | 1.20E-08 | 32 |
| LDL | rs2085723 | G/T | 0.342 | -0.011 | 9.85E-10 | 37 |
| LDL | rs72729610 | G/A | 0.167 | -0.013 | 5.99E-09 | 34 |
| LDL | rs793900 | T/C | 0.408 | 0.011 | 1.03E-10 | 42 |
| LDL | rs77704739 | C/T | 0.036 | -0.049 | 1.27E-28 | 123 |
| LDL | rs3010265 | A/G | 0.212 | -0.017 | 1.17E-16 | 69 |
| LDL | rs141234987 | G/A | 0.028 | -0.029 | 3.55E-08 | 30 |
| LDL | rs11957820 | T/C | 0.063 | 0.025 | 1.95E-14 | 59 |
| LDL | rs4704221 | A/T | 0.391 | 0.066 | 1.00E-200 | 1475 |
| LDL | rs16873292 | C/T | 0.064 | 0.019 | 2.01E-08 | 31 |
| LDL | rs13189347 | C/A | 0.448 | -0.017 | 2.15E-23 | 99 |
| LDL | rs6894249 | G/A | 0.389 | 0.016 | 1.05E-20 | 87 |
| LDL | rs13161656 | C/T | 0.108 | 0.022 | 2.71E-17 | 72 |
| LDL | rs543486395 | A/C | 0.024 | -0.042 | 2.59E-08 | 31 |
| LDL | rs12657266 | C/T | 0.365 | -0.033 | 3.05E-82 | 369 |
| LDL | rs13357800 | C/T | 0.426 | -0.009 | 4.06E-08 | 30 |
| LDL | rs241056 | A/G | 0.256 | -0.011 | 5.50E-09 | 34 |
| LDL | rs113371168 | A/G | 0.068 | -0.018 | 1.39E-08 | 32 |
| LDL | rs7746081 | A/G | 0.330 | -0.031 | 1.42E-71 | 320 |
| LDL | rs80215559 | C/T | 0.062 | -0.058 | 2.84E-63 | 282 |
| LDL | rs71536537 | C/T | 0.473 | -0.026 | 1.86E-12 | 50 |
| LDL | rs6689 | G/A | 0.210 | 0.041 | 1.98E-72 | 324 |
| LDL | rs62399909 | A/C | 0.087 | 0.016 | 1.67E-08 | 32 |
| LDL | rs11754773 | G/A | 0.098 | -0.027 | 3.61E-23 | 98 |
| LDL | rs6940814 | A/G | 0.416 | 0.014 | 1.70E-16 | 68 |
| LDL | rs17665178 | G/C | 0.304 | -0.018 | 4.93E-23 | 98 |
| LDL | rs6458949 | T/G | 0.259 | 0.013 | 1.30E-12 | 50 |
| LDL | rs9496567 | A/G | 0.233 | -0.019 | 6.07E-22 | 93 |
| LDL | rs240762 | C/T | 0.406 | 0.013 | 1.50E-14 | 59 |
| LDL | rs4946713 | A/C | 0.443 | -0.011 | 1.03E-10 | 42 |

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|---|---|---|---|---|---|---|
| LDL | rs1556857 | C/T | 0.399 | -0.015 | 1.80E-20 | 86 |
| LDL | rs72971192 | C/T | 0.237 | -0.013 | 1.70E-10 | 41 |
| LDL | rs7758845 | C/A | 0.279 | -0.025 | 1.06E-41 | 183 |
| LDL | rs75393372 | C/T | 0.078 | 0.020 | 1.43E-10 | 41 |
| LDL | rs112170089 | A/G | 0.016 | 0.055 | 4.86E-13 | 52 |
| LDL | rs12208357 | T/C | 0.069 | 0.059 | 2.62E-78 | 351 |
| LDL | rs146534110 | T/G | 0.011 | 0.075 | 5.73E-20 | 84 |
| LDL | rs74907759 | G/A | 0.009 | -0.059 | 8.54E-11 | 42 |
| LDL | rs117733303 | G/A | 0.017 | 0.142 | 7.13E-111 | 501 |
| LDL | rs118039278 | A/G | 0.064 | 0.111 | 1.00E-200 | 1078 |
| LDL | rs12055389 | T/C | 0.059 | -0.028 | 4.64E-16 | 66 |
| LDL | rs10263252 | A/G | 0.208 | -0.021 | 4.98E-26 | 111 |
| LDL | rs34927723 | T/C | 0.157 | -0.014 | 3.09E-09 | 35 |
| LDL | rs55696093 | G/A | 0.206 | 0.038 | 4.70E-80 | 359 |
| LDL | rs896311 | G/A | 0.303 | -0.018 | 5.37E-24 | 102 |
| LDL | rs56001710 | A/T | 0.426 | -0.018 | 7.38E-17 | 70 |
| LDL | rs10951769 | T/C | 0.474 | -0.022 | 1.80E-37 | 164 |
| LDL | rs4724315 | G/A | 0.100 | 0.027 | 4.85E-21 | 89 |
| LDL | rs42122 | A/G | 0.161 | 0.015 | 7.41E-11 | 42 |
| LDL | rs2302434 | T/C | 0.177 | 0.012 | 1.99E-08 | 32 |
| LDL | rs56223611 | A/C | 0.142 | -0.014 | 7.07E-10 | 38 |
| LDL | rs6967728 | A/G | 0.182 | -0.016 | 2.97E-13 | 53 |
| LDL | rs564449 | T/G | 0.114 | 0.027 | 1.07E-25 | 110 |
| LDL | rs10229853 | G/A | 0.087 | 0.018 | 3.34E-09 | 35 |
| LDL | rs11761517 | T/C | 0.458 | -0.010 | 1.18E-09 | 37 |
| LDL | rs2911971 | C/G | 0.374 | -0.012 | 2.07E-11 | 45 |
| LDL | rs9987289 | A/G | 0.092 | -0.057 | 1.34E-92 | 417 |
| LDL | rs6601302 | T/G | 0.248 | 0.015 | 1.38E-15 | 64 |
| LDL | rs900776 | C/A | 0.167 | -0.019 | 3.01E-18 | 76 |
| LDL | rs17526980 | T/C | 0.030 | 0.030 | 4.34E-10 | 39 |
| LDL | rs28615248 | C/T | 0.195 | 0.025 | 3.03E-32 | 140 |
| LDL | rs9297994 | G/A | 0.339 | 0.032 | 9.24E-75 | 335 |
| LDL | rs62509311 | T/A | 0.277 | -0.015 | 3.60E-16 | 66 |
| LDL | rs368280 | A/C | 0.253 | 0.011 | 4.46E-09 | 34 |
| LDL | rs2737252 | A/G | 0.276 | -0.022 | 1.48E-33 | 146 |
| LDL | rs2954017 | T/C | 0.472 | 0.051 | 1.00E-200 | 932 |
| LDL | rs11787335 | T/C | 0.353 | 0.024 | 9.48E-43 | 188 |
| LDL | rs3780181 | G/A | 0.071 | -0.035 | 8.09E-27 | 115 |
| LDL | rs28498684 | A/G | 0.410 | 0.013 | 6.64E-14 | 56 |
| LDL | rs12551960 | T/C | 0.079 | 0.033 | 3.04E-26 | 112 |
| LDL | rs615552 | C/T | 0.438 | 0.011 | 7.52E-11 | 42 |
| LDL | rs10814052 | A/C | 0.162 | 0.012 | 4.93E-08 | 30 |
| LDL | rs7864568 | A/G | 0.321 | -0.016 | 7.53E-17 | 70 |
| LDL | rs7046887 | T/C | 0.464 | 0.013 | 1.14E-15 | 64 |
| LDL | rs9410207 | C/T | 0.066 | -0.021 | 3.25E-10 | 40 |
| LDL | rs1571536 | T/C | 0.485 | 0.009 | 4.26E-08 | 30 |

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|---|---|---|---|---|---|---|
| LDL | rs2297400 | C/T | 0.125 | 0.016 | 6.10E-10 | 38 |
| LDL | rs2740488 | C/A | 0.260 | -0.021 | 6.65E-30 | 129 |
| LDL | rs10818580 | A/G | 0.263 | 0.011 | 5.78E-09 | 34 |
| LDL | rs6478851 | A/G | 0.234 | -0.015 | 1.54E-14 | 59 |
| LDL | rs2519093 | T/C | 0.189 | 0.073 | 1.00E-200 | 1275 |
| LDL | rs76643124 | A/G | 0.029 | -0.030 | 1.94E-09 | 36 |
| LDL | rs11999532 | C/G | 0.267 | -0.015 | 8.71E-16 | 65 |
| LDL | rs7903259 | G/C | 0.417 | 0.017 | 4.85E-25 | 107 |
| LDL | rs1031101 | G/A | 0.142 | 0.013 | 2.16E-08 | 31 |
| LDL | rs10761750 | A/G | 0.488 | 0.015 | 1.52E-19 | 82 |
| LDL | rs11000443 | A/C | 0.043 | -0.023 | 8.28E-09 | 33 |
| LDL | rs1870140 | A/G | 0.159 | -0.013 | 2.13E-08 | 31 |
| LDL | rs2068888 | A/G | 0.452 | -0.015 | 1.11E-20 | 87 |
| LDL | rs61886346 | T/C | 0.059 | -0.022 | 2.96E-10 | 40 |
| LDL | rs603424 | A/G | 0.169 | 0.014 | 2.02E-10 | 40 |
| LDL | rs78531123 | A/G | 0.058 | 0.020 | 2.52E-08 | 31 |
| LDL | rs2792751 | T/C | 0.285 | 0.023 | 2.29E-38 | 168 |
| LDL | rs60847460 | T/C | 0.138 | -0.018 | 1.12E-14 | 60 |
| LDL | rs4751995 | A/G | 0.470 | -0.016 | 2.20E-22 | 95 |
| LDL | rs9423289 | C/T | 0.423 | -0.022 | 4.71E-40 | 175 |
| LDL | rs12271225 | T/A | 0.133 | 0.016 | 2.76E-11 | 44 |
| LDL | rs11601507 | A/C | 0.070 | 0.040 | 4.36E-37 | 162 |
| LDL | rs10832956 | T/C | 0.279 | -0.021 | 4.94E-31 | 134 |
| LDL | rs61882680 | T/C | 0.030 | -0.029 | 2.51E-09 | 36 |
| LDL | rs174546 | T/C | 0.347 | -0.044 | 9.15E-143 | 647 |
| LDL | rs77631946 | A/C | 0.090 | -0.017 | 2.60E-09 | 35 |
| LDL | rs642803 | T/C | 0.452 | 0.012 | 1.63E-13 | 54 |
| LDL | rs77860716 | G/A | 0.048 | 0.023 | 2.50E-08 | 31 |
| LDL | rs2072560 | T/C | 0.065 | 0.044 | 1.21E-40 | 178 |
| LDL | rs45505501 | A/G | 0.137 | 0.018 | 3.27E-14 | 58 |
| LDL | rs76970536 | A/G | 0.071 | 0.059 | 1.42E-78 | 352 |
| LDL | rs34019521 | C/G | 0.252 | 0.019 | 1.52E-21 | 91 |
| LDL | rs147654565 | A/G | 0.032 | -0.028 | 1.35E-09 | 37 |
| LDL | rs12320328 | G/A | 0.082 | -0.026 | 7.23E-18 | 74 |
| LDL | rs11175540 | A/T | 0.065 | 0.026 | 2.09E-14 | 58 |
| LDL | rs2251024 | T/C | 0.339 | -0.017 | 2.63E-22 | 94 |
| LDL | rs9795910 | G/A | 0.376 | -0.012 | 1.42E-12 | 50 |
| LDL | rs7300593 | C/T | 0.172 | 0.013 | 1.34E-09 | 37 |
| LDL | rs61754230 | T/C | 0.014 | 0.042 | 7.46E-09 | 33 |
| LDL | rs11105294 | A/G | 0.339 | 0.012 | 2.33E-12 | 49 |
| LDL | rs4760388 | T/C | 0.478 | -0.010 | 1.50E-09 | 37 |
| LDL | rs7955221 | C/A | 0.453 | -0.012 | 1.02E-11 | 46 |
| LDL | rs3184504 | T/C | 0.468 | -0.025 | 4.56E-53 | 235 |
| LDL | rs1169288 | C/A | 0.326 | 0.035 | 9.94E-91 | 408 |
| LDL | rs2247139 | A/G | 0.136 | 0.014 | 3.15E-09 | 35 |
| LDL | rs825474 | G/A | 0.416 | -0.009 | 4.46E-08 | 30 |

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|---|---|---|---|---|---|---|
| LDL | rs11057841 | T/C | 0.142 | 0.021 | 5.48E-18 | 75 |
| LDL | rs77502095 | A/G | 0.141 | 0.016 | 1.08E-10 | 42 |
| LDL | rs7327867 | G/A | 0.474 | 0.019 | 2.01E-31 | 136 |
| LDL | rs207637 | G/T | 0.385 | 0.011 | 3.08E-10 | 40 |
| LDL | rs17532301 | A/G | 0.068 | -0.018 | 2.83E-08 | 31 |
| LDL | rs9805560 | G/A | 0.465 | 0.011 | 3.84E-11 | 44 |
| LDL | rs9524538 | A/G | 0.235 | 0.017 | 1.38E-19 | 82 |
| LDL | rs551473284 | T/C | 0.367 | -0.015 | 4.78E-13 | 52 |
| LDL | rs6602909 | C/T | 0.332 | 0.016 | 2.37E-19 | 81 |
| LDL | rs12016920 | C/T | 0.192 | -0.017 | 4.72E-15 | 61 |
| LDL | rs11621792 | T/C | 0.448 | 0.021 | 9.39E-35 | 151 |
| LDL | rs11846704 | T/C | 0.267 | -0.012 | 2.42E-11 | 45 |
| LDL | rs11846741 | G/A | 0.074 | 0.017 | 4.83E-08 | 30 |
| LDL | rs11620731 | T/C | 0.147 | -0.025 | 1.07E-26 | 114 |
| LDL | rs13379043 | C/T | 0.268 | -0.016 | 2.03E-18 | 77 |
| LDL | rs11159099 | G/A | 0.461 | -0.010 | 1.17E-08 | 33 |
| LDL | rs17776811 | A/C | 0.403 | 0.011 | 2.42E-10 | 40 |
| LDL | rs28929474 | T/C | 0.017 | 0.065 | 1.62E-25 | 109 |
| LDL | rs17580 | A/T | 0.034 | 0.054 | 8.39E-33 | 142 |
| LDL | rs28375625 | A/C | 0.459 | -0.009 | 2.33E-08 | 31 |
| LDL | rs79391862 | C/A | 0.023 | -0.065 | 1.00E-26 | 115 |
| LDL | rs11635502 | A/G | 0.306 | 0.013 | 1.62E-12 | 50 |
| LDL | rs11638576 | A/G | 0.396 | 0.015 | 1.14E-16 | 69 |
| LDL | rs2469204 | G/T | 0.379 | -0.009 | 4.27E-08 | 30 |
| LDL | rs8041391 | T/C | 0.154 | 0.015 | 5.72E-10 | 38 |
| LDL | rs756559 | G/A | 0.310 | -0.011 | 9.42E-10 | 37 |
| LDL | rs12445804 | A/G | 0.077 | 0.029 | 4.59E-20 | 84 |
| LDL | rs11075253 | A/C | 0.302 | 0.011 | 6.27E-09 | 34 |
| LDL | rs16967478 | A/G | 0.157 | -0.012 | 4.74E-08 | 30 |
| LDL | rs7184567 | T/C | 0.375 | 0.011 | 6.27E-11 | 43 |
| LDL | rs247617 | A/C | 0.319 | -0.035 | 2.97E-87 | 392 |
| LDL | rs7206039 | A/C | 0.371 | 0.012 | 5.90E-12 | 47 |
| LDL | rs12924886 | T/A | 0.192 | 0.054 | 3.81E-150 | 681 |
| LDL | rs7202323 | G/T | 0.227 | -0.021 | 2.93E-26 | 112 |
| LDL | rs7404072 | C/T | 0.289 | -0.011 | 8.52E-09 | 33 |
| LDL | rs67890964 | C/T | 0.385 | -0.019 | 7.87E-27 | 115 |
| LDL | rs576285576 | G/A | 0.111 | -0.024 | 3.33E-09 | 35 |
| LDL | rs55714927 | T/C | 0.187 | -0.035 | 6.56E-58 | 257 |
| LDL | rs150688657 | A/G | 0.103 | 0.021 | 1.14E-14 | 60 |
| LDL | rs10462024 | G/A | 0.415 | 0.010 | 2.16E-09 | 36 |
| LDL | rs28811342 | C/T | 0.200 | 0.013 | 8.32E-10 | 38 |
| LDL | rs9909417 | A/G | 0.288 | 0.010 | 2.01E-08 | 31 |
| LDL | rs704 | A/G | 0.478 | 0.020 | 2.10E-35 | 154 |
| LDL | rs67777803 | T/G | 0.168 | -0.015 | 3.63E-11 | 44 |
| LDL | rs6505220 | T/A | 0.468 | -0.014 | 2.57E-13 | 54 |
| LDL | rs11650379 | G/A | 0.013 | -0.047 | 6.70E-10 | 38 |

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| | | | | | | |
|---|---|---|---|---|---|---|
| LDL | rs62075782 | C/G | 0.226 | -0.012 | 1.33E-08 | 32 |
| LDL | rs72836561 | T/C | 0.030 | -0.037 | 1.21E-14 | 60 |
| LDL | rs11870935 | G/A | 0.491 | 0.025 | 1.38E-51 | 228 |
| LDL | rs62075819 | T/C | 0.358 | 0.010 | 8.50E-09 | 33 |
| LDL | rs2665404 | C/T | 0.459 | -0.011 | 6.43E-11 | 43 |
| LDL | rs1801689 | C/A | 0.024 | 0.095 | 1.06E-74 | 334 |
| LDL | rs17647249 | T/C | 0.499 | 0.013 | 2.14E-15 | 63 |
| LDL | rs59593290 | A/G | 0.084 | 0.017 | 4.48E-09 | 34 |
| LDL | rs77542162 | G/A | 0.018 | 0.169 | 1.57E-160 | 729 |
| LDL | rs72631343 | G/C | 0.131 | -0.041 | 1.34E-64 | 288 |
| LDL | rs2125345 | C/T | 0.291 | -0.018 | 1.71E-23 | 100 |
| LDL | rs12451056 | T/C | 0.143 | -0.020 | 1.38E-18 | 77 |
| LDL | rs77960347 | G/A | 0.012 | 0.064 | 5.71E-18 | 75 |
| LDL | rs4939883 | T/C | 0.175 | -0.016 | 4.65E-14 | 57 |
| LDL | rs12454507 | G/A | 0.288 | 0.011 | 2.01E-08 | 31 |
| LDL | rs1618633 | G/C | 0.353 | 0.014 | 1.17E-10 | 42 |
| LDL | rs4804815 | G/C | 0.264 | -0.012 | 1.05E-09 | 37 |
| LDL | rs144900553 | T/C | 0.014 | -0.158 | 3.52E-95 | 428 |
| LDL | rs1109375 | G/C | 0.170 | -0.071 | 1.00E-200 | 1059 |
| LDL | rs2738445 | C/T | 0.430 | -0.053 | 1.00E-200 | 1012 |
| LDL | rs7250652 | G/A | 0.439 | 0.025 | 1.65E-50 | 223 |
| LDL | rs3745686 | A/G | 0.042 | -0.030 | 1.30E-12 | 50 |
| LDL | rs58542926 | T/C | 0.075 | -0.099 | 1.00E-200 | 1019 |
| LDL | rs76738473 | C/T | 0.028 | -0.027 | 3.98E-08 | 30 |
| LDL | rs28677840 | A/C | 0.069 | -0.022 | 3.08E-12 | 49 |
| LDL | rs62119267 | C/A | 0.020 | -0.233 | 1.00E-200 | 1542 |
| LDL | rs531660643 | T/G | 0.016 | -0.413 | 1.00E-200 | 3160 |
| LDL | rs140365836 | A/G | 0.004 | 0.113 | 8.95E-11 | 42 |
| LDL | rs113330691 | A/G | 0.033 | -0.230 | 1.00E-200 | 2557 |
| LDL | rs111654618 | A/G | 0.009 | 0.079 | 3.48E-18 | 76 |
| LDL | rs148601586 | G/C | 0.011 | 0.138 | 1.75E-63 | 283 |
| LDL | rs41289514 | G/A | 0.010 | 0.216 | 3.04E-140 | 636 |
| LDL | rs146275714 | A/G | 0.028 | 0.174 | 1.00E-200 | 1041 |
| LDL | rs182824418 | T/G | 0.005 | 0.143 | 7.81E-27 | 115 |
| LDL | rs117264457 | A/G | 0.020 | -0.049 | 7.70E-15 | 60 |
| LDL | rs72654437 | A/G | 0.030 | 0.066 | 1.31E-34 | 151 |
| LDL | rs79429216 | A/G | 0.009 | 0.087 | 2.02E-21 | 90 |
| LDL | rs204473 | A/G | 0.022 | -0.055 | 4.51E-22 | 93 |
| LDL | rs35313547 | C/T | 0.158 | -0.015 | 5.83E-11 | 43 |
| LDL | rs34503352 | A/G | 0.161 | -0.029 | 4.27E-37 | 162 |
| LDL | rs73066228 | G/A | 0.164 | 0.017 | 9.29E-15 | 60 |
| LDL | rs6107650 | G/A | 0.390 | -0.011 | 1.94E-10 | 41 |
| LDL | rs438568 | A/G | 0.392 | -0.013 | 2.84E-15 | 62 |
| LDL | rs969075 | T/C | 0.334 | -0.015 | 9.98E-18 | 74 |
| LDL | rs2618566 | G/T | 0.339 | 0.040 | 8.46E-111 | 500 |
| LDL | rs1044573 | G/A | 0.495 | 0.010 | 4.28E-09 | 34 |

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| | | | | | | |
|---|---|---|---|---|---|---|
| LDL | rs61016611 | A/G | 0.101 | -0.032 | 1.36E-32 | 141 |
| LDL | rs1883711 | C/G | 0.032 | 0.128 | 5.99E-145 | 657 |
| LDL | rs6093446 | A/G | 0.269 | 0.024 | 2.78E-38 | 167 |
| LDL | rs1800961 | T/C | 0.035 | -0.049 | 8.47E-28 | 119 |
| LDL | rs4239702 | T/C | 0.282 | -0.011 | 1.27E-09 | 37 |
| LDL | rs2295027 | A/G | 0.321 | 0.012 | 4.86E-11 | 43 |
| LDL | rs117590445 | T/C | 0.014 | -0.044 | 8.48E-09 | 33 |
| LDL | rs35046559 | G/A | 0.246 | 0.012 | 3.05E-10 | 40 |
| LDL | rs8121509 | C/T | 0.452 | -0.014 | 3.75E-15 | 62 |
| LDL | rs60417583 | T/G | 0.165 | 0.015 | 5.92E-10 | 38 |
| LDL | rs16988435 | T/C | 0.051 | 0.032 | 2.53E-17 | 72 |
| LDL | rs414850 | C/A | 0.411 | -0.012 | 7.89E-12 | 47 |
| LDL | rs235343 | A/C | 0.436 | -0.009 | 3.19E-08 | 31 |
| LDL | rs5746498 | C/T | 0.237 | 0.014 | 6.60E-12 | 47 |
| LDL | rs5752963 | A/G | 0.036 | 0.029 | 2.01E-11 | 45 |
| LDL | rs4465 | C/T | 0.358 | 0.014 | 6.62E-17 | 70 |
| LDL | rs138335 | C/G | 0.347 | 0.013 | 9.17E-13 | 51 |
| LDL | rs3747207 | A/G | 0.226 | -0.014 | 1.03E-12 | 51 |
| LDL | rs13057311 | A/G | 0.267 | -0.012 | 2.22E-10 | 40 |
| EA/OA: effect allele/other allele; EAF: effect allele frequency. | | | | | | |

**Analysis R code**

```
library(TwoSampleMR)
library(coloc)
library(phenoscanner)

#read in summary statistics
temp<-fread("LDL_exp_dat_EUR.tsv")
temp$pval=2*pnorm(-abs(temp$beta / temp$se))

HMGCR<-temp[chr ==5 &
          pos > 74632154 - 1 - 100*1000 &
          pos < 74657929 + 1 + 100*1000,]
NPC1L1<-temp[chr ==7 &
           pos > 44552134 - 1 - 100*1000 &
           pos < 44580914 + 1 + 100*1000,]
PCSK9<-temp[chr ==1 &
          pos > 55505221 - 1 - 100*1000 &
          pos < 55530525 + 1 + 100*1000,]

#r2 threshold for cis-MR
r2=0.1

#drug target instruments
HMGCR_iv<-filter(HMGCR, pval<5e-8)
HMGCR_iv<-clump_data(format_data(HMGCR_iv), clump_r2 =r2)
HMGCR_iv$exposure <-"HMGCR"
```

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```
NPC1L1_iv<-filter(NPC1L1, pval<5e-8)
NPC1L1_iv<-clump_data(format_data(NPC1L1_iv), clump_r2 =r2)
NPC1L1_iv$exposure <-"NPC1L1"

PCSK9_iv<-filter(PCSK9, pval<5e-8)
PCSK9_iv<-clump_data(format_data(PCSK9_iv), clump_r2 =r2)
PCSK9_iv$exposure <-"PCSK9"

#instruments for LDL
ldl_iv<-filter(temp,pval<5e-8)
exc_list=c(HMGCR$SNP, NPC1L1$SNP, PCSK9$SNP)
ldl_iv <- ldl_iv[ ! ldl_iv$SNP %in% exc_list, ]
ldl_iv<-clump_data(format_data(ldl_iv))
ldl_iv$exposure<-"LDL"

exp_dat<-bind_rows(HMGCR_iv,NPC1L1_iv,PCSK9_iv,ldl_iv)
exp_dat$F<-(exp_dat$beta.exposure/exp_dat$se.exposure)^2

#F statistic approximation
F_hmgcr = sum (exp_dat$F[exp_dat$exposure=="HMGCR"]) /
length(exp_dat$F[exp_dat$exposure=="HMGCR"])
F_npc1l1 = sum (exp_dat$F[exp_dat$exposure=="NPC1L1"]) /
length(exp_dat$F[exp_dat$exposure=="NPC1L1"])
F_pcsk = sum (exp_dat$F[exp_dat$exposure=="PCSK9"]) /
length(exp_dat$F[exp_dat$exposure=="PCSK9"])
F_ldl = sum (exp_dat$F[exp_dat$exposure=="LDL"]) / length(exp_dat$F[exp_dat$exposure=="LDL"])

#Phenoscanner
list<-exp_dat$SNP[exp_dat$exposure=="HMGCR"]
pheno_hmgcr<-phenoscanner(snpquery=list,catalogue = "GWAS", pvalue = 1e-05, proxies = "None",
build=37)
pheno_hmgcr=pheno_hmgcr$results
table(pheno_hmgcr$trait, pheno_hmgcr$snp)

list<-exp_dat$SNP[exp_dat$exposure=="NPC1L1"]
pheno_npc1l1<-phenoscanner(snpquery=list,catalogue = "GWAS", pvalue = 1e-05, proxies = "None",
build=37)
pheno_npc1l1=pheno_npc1l1$results
table(pheno_npc1l1$trait, pheno_npc1l1$snp)

list<-exp_dat$SNP[exp_dat$exposure=="PCSK9"]
pheno_pcsk9<-phenoscanner(snpquery=list,catalogue = "GWAS", pvalue = 1e-05, proxies = "None",
build=37)
pheno_pcsk9=pheno_pcsk9$results
table(pheno_pcsk9$trait, pheno_pcsk9$snp)

#MR analysis - note instruments differ between each of the three outcomes (due to exclusion of
sample overlap)
out_dat_ukb <- read_outcome_data(snps = exp_dat$SNP, filename = "ukb_pso_6495_25980.tsv",
sep = "\t")
```

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```
exp_h_ukb <- harmonise_data(exp_dat, out_dat_ukb, action=1)
exp_h_ukb$outcome<-"Psoriasis (UKB)"

out_dat_finn <- read_outcome_data(snps = exp_dat$SNP, filename = "pso_r6fin_gwas.txt",  sep =
"\t")
out_dat_finn$outcome <- "Psoriasis (FinnGen)"
exp_h_pso <- harmonise_data(exp_dat,out_dat_finn,action=1)

out_dat_cad <- extract_outcome_data(
  snps = exp_dat$SNP, outcomes = "ebi-a-GCST003116",
  rsq = 0.9
)
cont_h <- harmonise_data(exp_dat,out_dat_cad,action=1)

exp_h <- bind_rows(exp_h_pso, exp_h_ukb, cont_h)

res<-try(mr(exp_h , method_list = c('mr_ivw_mre'
                                    , "mr_wald_ratio"
                                    ,'mr_egger_regression',
                                    'mr_weighted_median',
                                    'mr_weighted_mode'
)))

res$b<- -1*res$b
res<-generate_odds_ratios(res)
hp <- mr_pleiotropy_test(exp_h)

#coloc
PCSK9_ukb <- fread("ukb_pso_6495_25980.tsv")
d <- PCSK9[PCSK9_ukb, on = c("pos" = "pos"), nomatch = NULL]
d<-d[chr ==1 & pos >= 55505221  & pos <= 55530525 ,]

d[,"EA_exp_aligned" := ifelse(eaf < 0.5, effect_allele, other_allele)]
d[,"NEA_exp_aligned" := ifelse(eaf < 0.5, other_allele, effect_allele)]
d[,"MAF_exp" := ifelse(eaf < 0.5, eaf, 1 - eaf)]
d[,"BETA_exp_aligned" := ifelse(eaf < 0.5, beta, -beta)]

d[,"EA_out_aligned" := ifelse(i.eaf < 0.5, i.effect_allele, i.other_allele)]
d[,"NEA_out_aligned" := ifelse(i.eaf < 0.5, i.other_allele, i.effect_allele)]
d[,"MAF_out" := ifelse(i.eaf < 0.5, i.eaf, 1 - i.eaf)]
d[,"BETA_out_aligned" := ifelse(i.eaf < 0.5, i.beta, -i.beta)]

d[,"flipped" := (EA_exp_aligned != EA_out_aligned)*1]

D1 <- list(
  type = "quant",
  beta = d$BETA_exp_aligned,
  varbeta = d$se^2,
  N = 842660, #excluding
ukb   MAF_exp,
  snp = d$SNP,
```

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```
  sdY = 1
)

D2 <- list(
  type = "cc",
  beta = d$BETA_out_aligned,
  varbeta = d$i.se^2,
  N = (6495+ 25980),
  s = 6495/25980,
  MAF_out,
  snp = d$SNP
)

coloc_pso <- coloc.abf(D1, D2, p1 = 1e-4, p2 = 1e-4, p12 = 1e-5)
```

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**eTable 7: STROBE-MR checklist of recommended items to address in reports of Mendelian randomization studies.**

| Item No. | Section | Checklist item | Page No. | Relevant text from manuscript |
|---|---|---|---|---|
| 1 | **TITLE and ABSTRACT** | Indicate Mendelian randomization (MR) as the study's design in the title and/or the abstract if that is a main purpose of the study | 1 | Mendelian randomization study in subtitle |
| | **INTRODUCTION** | | | |
| 2 | **Background** | Explain the scientific background and rationale for the reported study. What is the exposure? Is a potential causal relationship between exposure and outcome plausible? Justify why MR is a helpful method to address the study question | 4 | Exposure: 3 lipid lowering drug targets;<br>Outcome: psoriasis and psoriatic arthritis (PsA). |
| 3 | **Objectives** | State specific objectives clearly, including pre-specified causal hypotheses (if any). State that MR is a method that, under specific assumptions, intends to estimate causal effects | 4 | Does genetically proxied inhibition of 3 lipid lowering drug targets reduce psoriasis and PsA. |
| | **METHODS** | | | |
| 4 | **Study design and data sources** | Present key elements of the study design early in the article. Consider including a table listing sources of data for all phases of the study. For each data source contributing to the analysis, describe the following: | | |
| | a) | Setting: Describe the study design and the underlying population, if possible. Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection, when available. | 5 | Detailed in Methods with references provided. |
| | b) | Participants: Give the eligibility criteria, and the sources and methods of selection of participants. Report the sample size, and whether any power or sample size calculations were carried out prior to the main analysis | 5 | Detailed in Methods with references provided. |
| | c) | Describe measurement, quality control and selection of genetic variants | 5-6 | Detailed in Methods with references provided. |
| | d) | For each exposure, outcome, and other relevant variables, describe methods of assessment and diagnostic criteria for diseases | 5 | Detailed in Methods with references provided. |

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| | | | | |
|---|---|---|---|---|
| | e) | Provide details of ethics committee approval and participant informed consent, if relevant | 5 | Ethical approval had been obtained in all original studies |
| 5 | **Assumptions** | Explicitly state the three core IV assumptions for the main analysis (relevance, independence and exclusion restriction) as well assumptions for any additional or sensitivity analysis | 6-7 and Fig S1 | Detailed discussion in Methods and supplementary materials |
| 6 | **Statistical methods: main analysis** | Describe statistical methods and statistics used | | |
| | a) | Describe how quantitative variables were handled in the analyses (i.e., scale, units, model) | 6 | scaled to one standard deviation ~6.7mmol/mol reduction in LDL |
| | b) | Describe how genetic variants were handled in the analyses and, if applicable, how their weights were selected | n/a | |
| | c) | Describe the MR estimator (e.g. two-stage least squares, Wald ratio) and related statistics. Detail the included covariates and, in case of two-sample MR, whether the same covariate set was used for adjustment in the two samples | 6 | Ratio method |
| | d) | Explain how missing data were addressed | n/a | |
| | e) | If applicable, indicate how multiple testing was addressed | 6 | p-value threshold of 0.05/3 = 0.017 |
| 7 | **Assessment of assumptions** | Describe any methods or prior knowledge used to assess the assumptions or justify their validity | 6-7 | Each assumption discussed |
| 8 | **Sensitivity analyses and additional analyses** | Describe any sensitivity analyses or additional analyses performed (e.g. comparison of effect estimates from different approaches, independent replication, bias analytic techniques, validation of instruments, simulations) | 6-7 | Pleiotropy robust methods and colocalization. |
| 9 | **Software and preregistration** | | | |
| | a) | Name statistical software and package(s), including version and settings used | 7 | Analyses were performed in R using the TwoSampleMR and coloc packages |
| | b) | State whether the study protocol and details were pre-registered (as well as when and where) | n/a | The protocol was not pre-registered but was pre-determined |

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| | | | | |
|---|---|---|---|---|
| | **RESULTS** | | | |
| 10 | **Descriptive data** | | | |
| | a) | Report the numbers of individuals at each stage of included studies and reasons for exclusion. Consider use of a flow diagram. | n/a | Not applicable for summary statistics. |
| | b) | Report summary statistics for phenotypic exposure(s), outcome(s), and other relevant variables (e.g. means, SDs, proportions) | n/a | Not applicable for summary statistics. |
| | c) | If the data sources include meta-analyses of previous studies, provide the assessments of heterogeneity across these studies | 7 | Not feasible to list all details within word limit, but references are provided. |
| | d) | For two-sample MR:<br>i. Provide justification of the similarity of the genetic variant-exposure associations between the exposure and outcome samples<br>ii. Provide information on the number of individuals who overlap between the exposure and outcome studies | 6-7 | Overlap discussed and accounted for |
| 11 | **Main results** | | | |
| | a) | Report the associations between genetic variant and exposure, and between genetic variant and outcome, preferably on an interpretable scale | supp materials | All instruments listed in Table S6. Full details for all traits not practical to include |
| | b) | Report MR estimates of the relationship between exposure and outcome, and the measures of uncertainty from the MR analysis, on an interpretable scale, such as odds ratio or relative risk per SD difference | 7-8 | Summarised in Figures |
| | c) | If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | n/a | |
| | d) | Consider plots to visualize results (e.g. forest plot, scatterplot of associations between genetic variants and outcome versus between genetic variants and exposure) | Figs 1-3 | |
| 12 | **Assessment of assumptions** | | | |
| | a) | Report the assessment of the validity of the assumptions | 7 | results of detailed sensitivity analyses provided in supp materials |

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| | | | | |
|---|---|---|---|---|
| | b) | Report any additional statistics (e.g., assessments of heterogeneity across genetic variants, such as $I^2$, Q statistic or E-value) | Fig 1 | |
| 13 | **Sensitivity analyses and additional analyses** | | | |
| | a) | Report any sensitivity analyses to assess the robustness of the main results to violations of the assumptions | 7 | . |
| | b) | Report results from other sensitivity analyses or additional analyses | 7 and Fig2 | |
| | c) | Report any assessment of direction of causal relationship (e.g., bidirectional MR) | n/a | |
| | d) | When relevant, report and compare with estimates from non-MR analyses | n/a | Limitations of comparison given in Discussion section |
| | e) | Consider additional plots to visualize results (e.g., leave-one-out analyses) | n/a | Not included |
| | **DISCUSSION** | | | |
| 14 | **Key results** | Summarize key results with reference to study objectives | 8 | |
| 15 | **Limitations** | Discuss limitations of the study, taking into account the validity of the IV assumptions, other sources of potential bias, and imprecision. Discuss both direction and magnitude of any potential bias and any efforts to address them | 10 | |
| 16 | **Interpretation** | | | |
| | | Meaning: Give a cautious overall interpretation of results in the context of their limitations and in comparison with other studies | 9 | |
| | | Mechanism: Discuss underlying biological mechanisms that could drive a potential causal relationship between the investigated exposure and the outcome, and whether the gene-environment equivalence assumption is reasonable. Use causal language carefully, clarifying that IV estimates may provide causal effects only under certain assumptions | 9 | |

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| | | | | |
|---|---|---|---|---|
| | | Clinical relevance: Discuss whether the results have clinical or public policy relevance, and to what extent they inform effect sizes of possible interventions | 9 | |
| 17 | **Generalizability** | Discuss the generalizability of the study results (a) to other populations, (b) across other exposure periods/timings, and (c) across other levels of exposure | 10 | |
| | **OTHER INFORMATION** | | | |
| 18 | **Funding** | Describe sources of funding and the role of funders in the present study and, if applicable, sources of funding for the databases and original study or studies on which the present study is based | 11 | |
| 19 | **Data and data sharing** | Provide the data used to perform all analyses or report where and how the data can be accessed, and reference these sources in the article. Provide the statistical code needed to reproduce the results in the article, or report whether the code is publicly accessible and if so, where | 11 | |
| 20 | **Conflicts of Interest** | All authors should declare all potential conflicts of interest. | 11 | |
| Note that page numbers will differ between author submitted and published versions. | | | | |

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