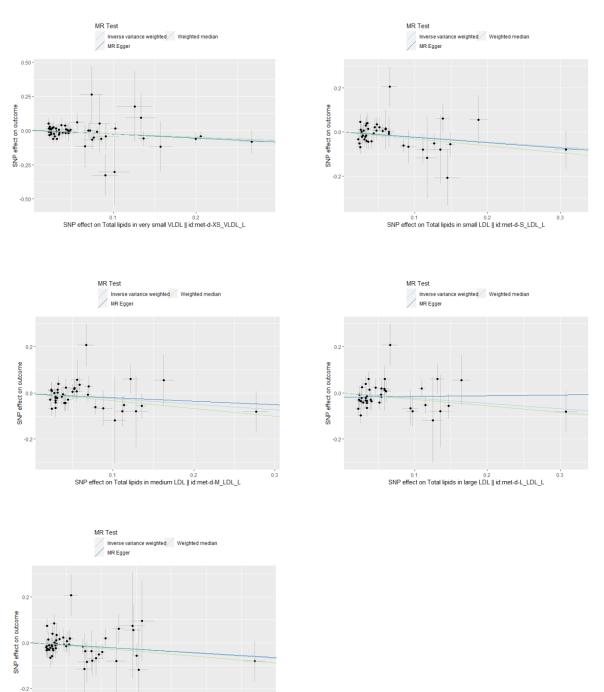
Supplementary materials

Supplementary Figures S1-S3: Pages 2-24

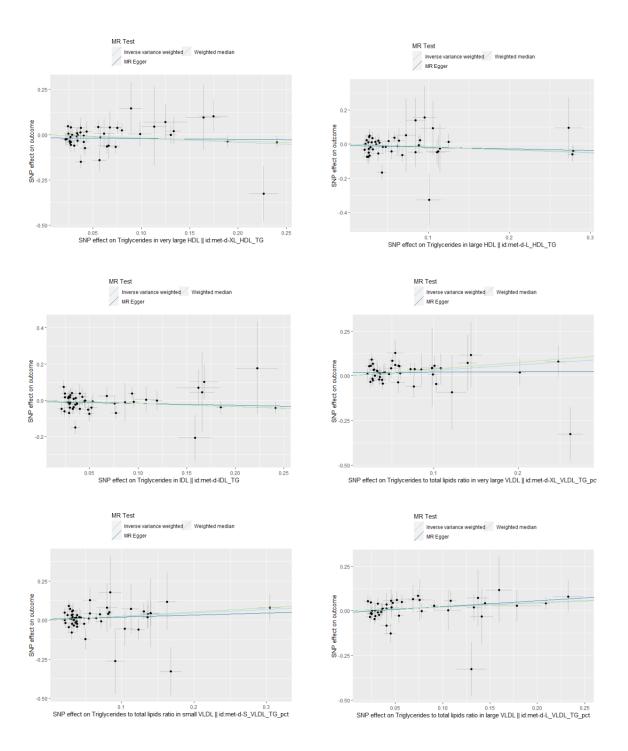
Supplementary Figures S1-S3

Supplementary Figure S1. Scatter plot results of IVW, weighted median and MR-Egger. Pages 1-11.

Total lipids



Triglycerides

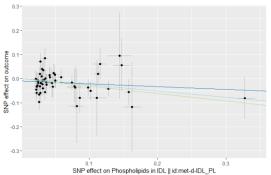


Phospholipids

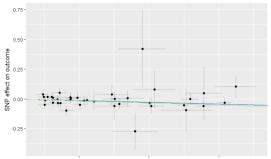
MR Test

Inverse variance weighted Weighted median MR Egger 0.25 SNP effect on outcome 52.0--0.50 0.1 0.2 SNP effect on Phospholipids in very small VLDL || id:met-d-XS_VLDL_PL

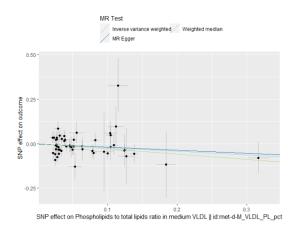


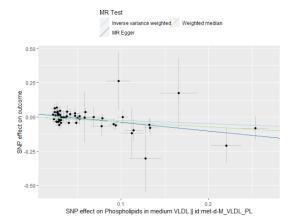




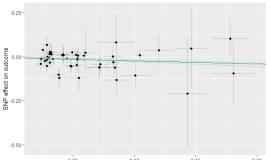


0.05 0.10 0.15 SNP effect on Phospholipids to total lipids ratio in IDL || id:met-d-IDL_PL_pct

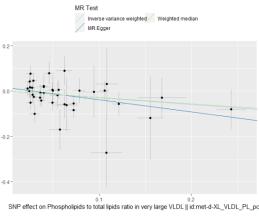




MR Test Inverse var ce weighted Weighted median MR Egger

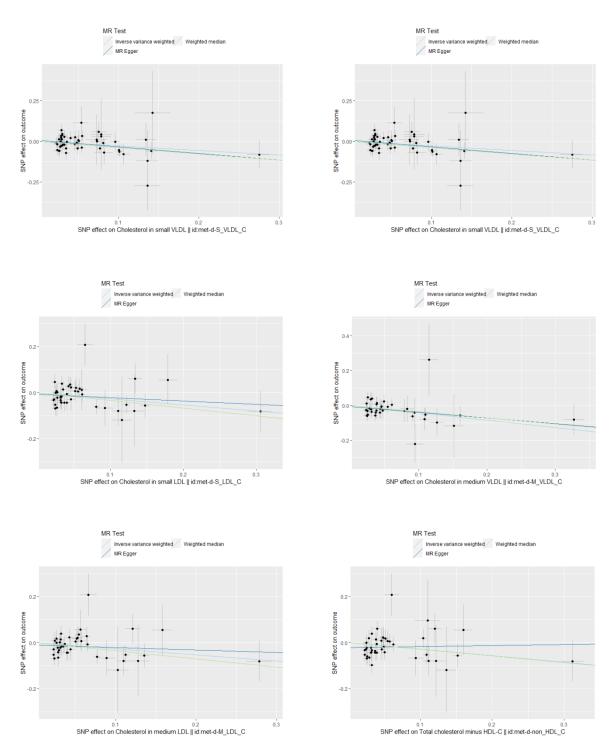


0.05 0.10 0.15 0.20 SNP effect on Phospholipids to total lipids ratio in very small VLDL || id:met-d-XS_VLDL_PL_pc

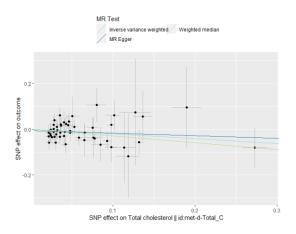


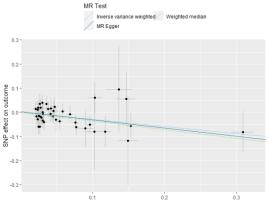
SNP effect on outcome

Cholesterol



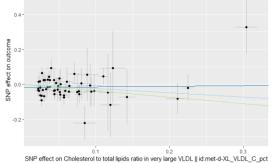
Cholesterol - continued

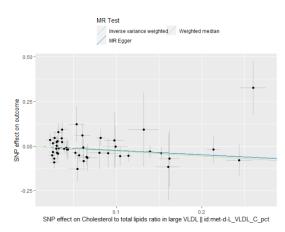


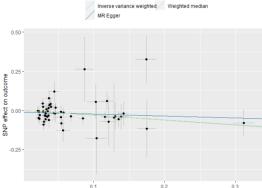


0.1 0.2 0.3 SNP effect on Remnant cholesterol (non-HDL, non-LDL -cholesterol) || id:met-d-Remnant_C





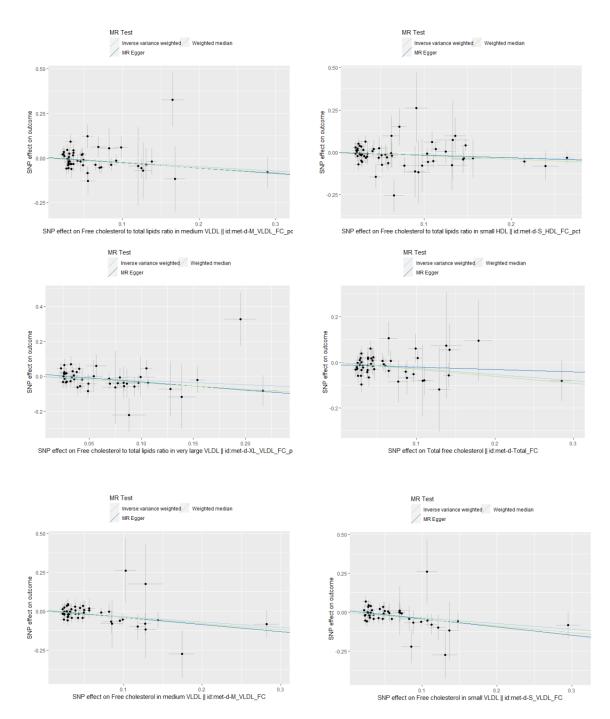




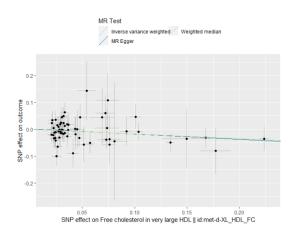
MR Test

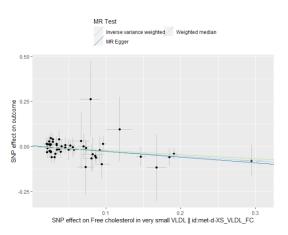


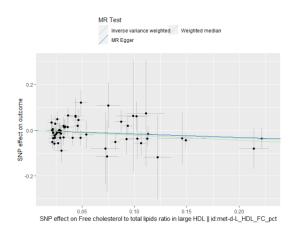
Free cholesterol



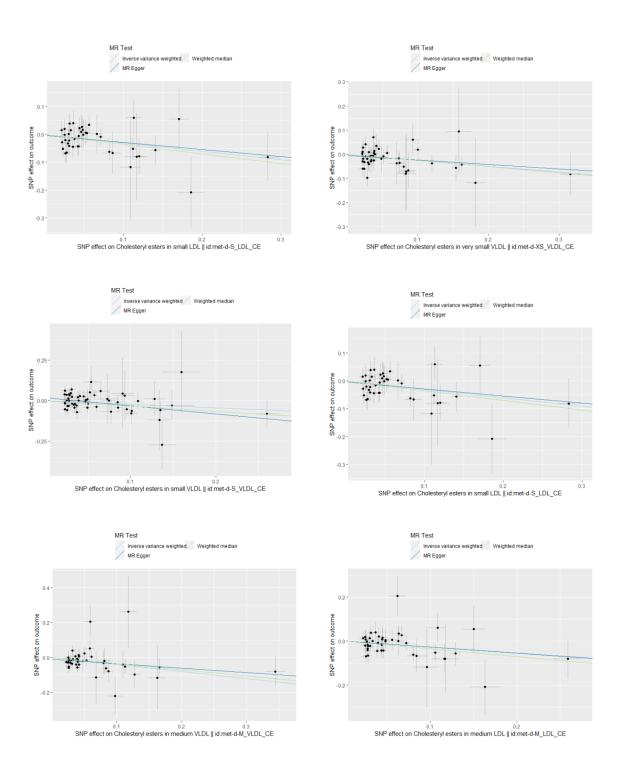
Free cholesterol - continued



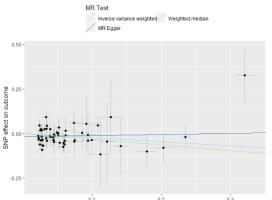




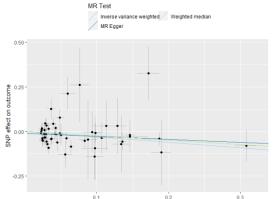
Cholesteryl esters



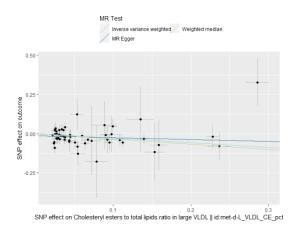
Cholesteryl esters - continued

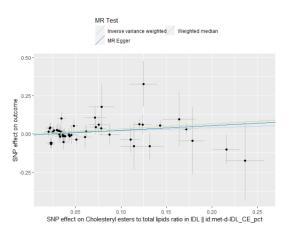


0.1 0.2 0.3 SNP effect on Cholesteryl esters to total lipids ratio in very large VLDL || id:met-d-XL_VLDL_CE_

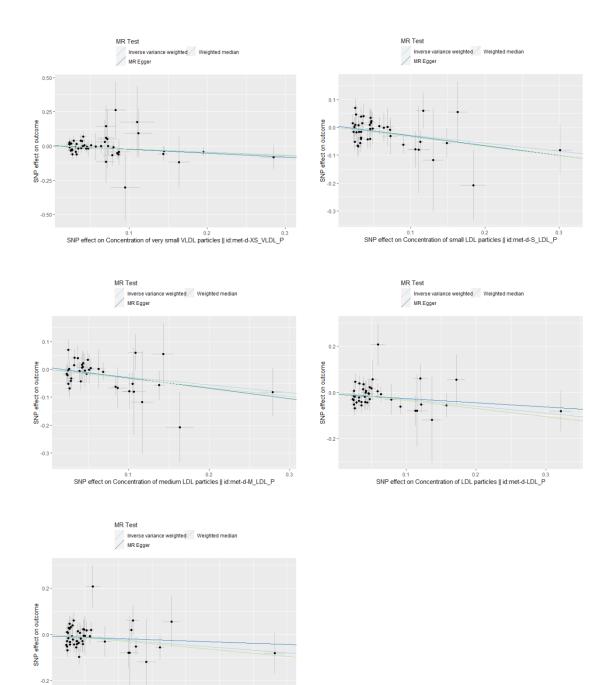


0.1 0.2 0.3 SNP effect on Cholesteryl esters to total lipids ratio in small VLDL || id:met-d-S_VLDL_CE_pc



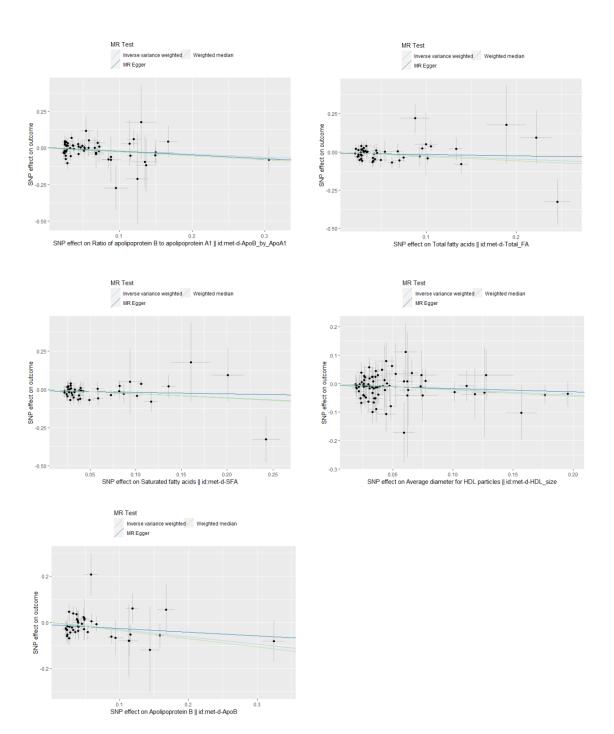


Lipoprotein



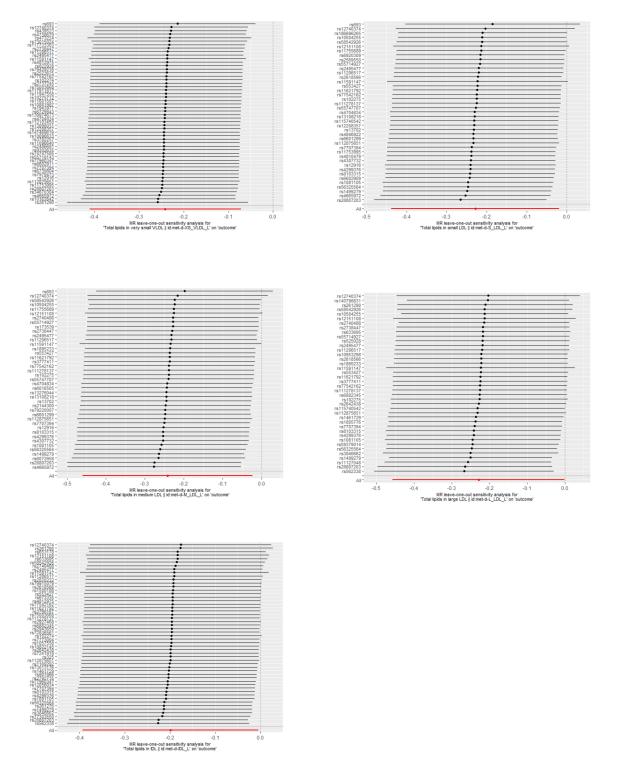
0.1 0.2 0.3 SNP effect on Concentration of large LDL particles || id:met-d-L_LDL_P

Other

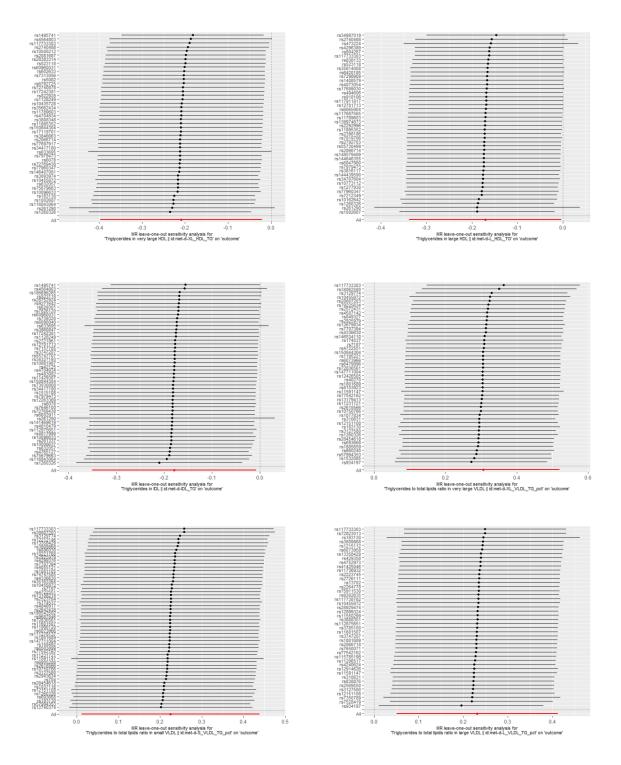


Supplementary Figure S2. Leave-one-out results of IVW, weighted median and MR-Egger. Pages 12-22.

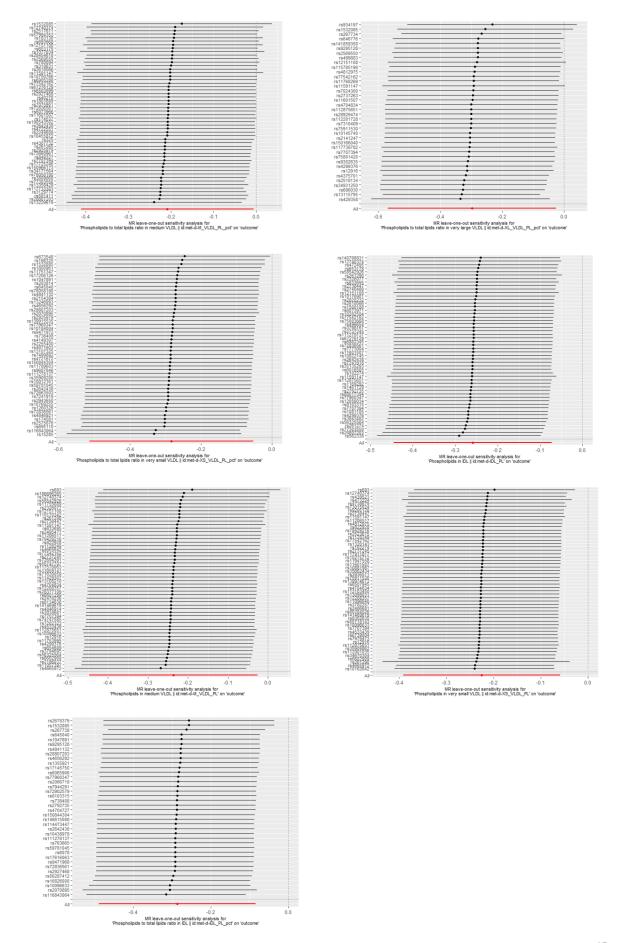




Triglycerides

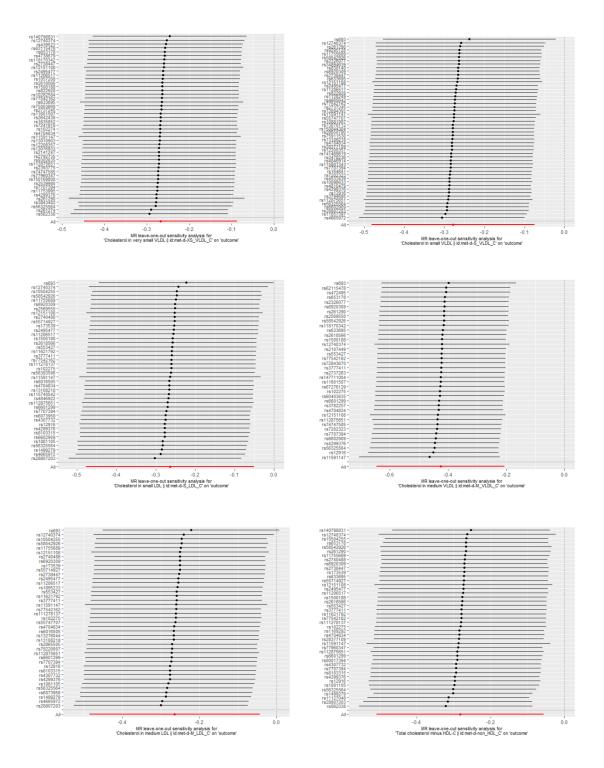


Phospholipids

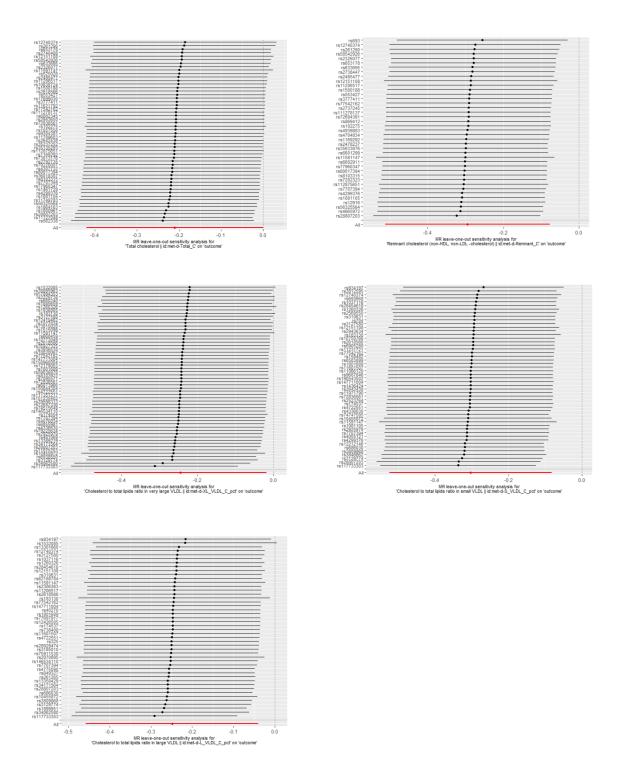


Supplementary Figure S2. Leave-one-out results of IVW, weighted median and MR-Egger. ¹⁵

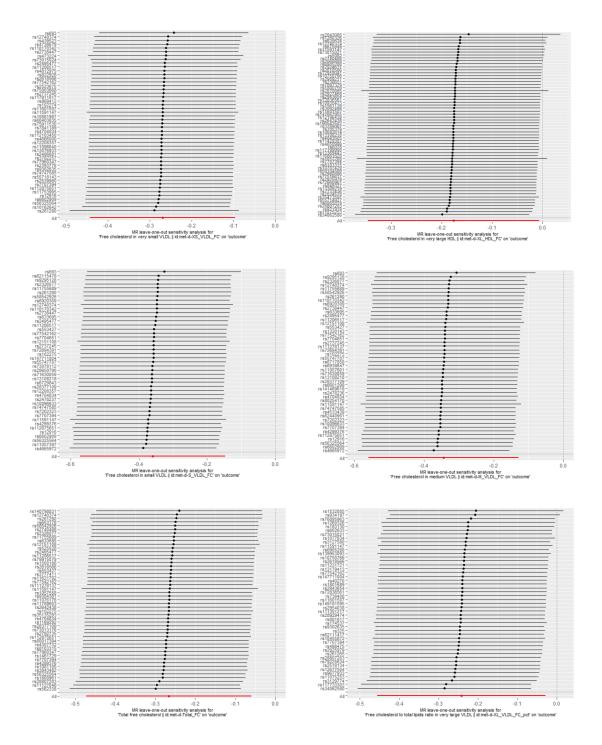
Cholesterol



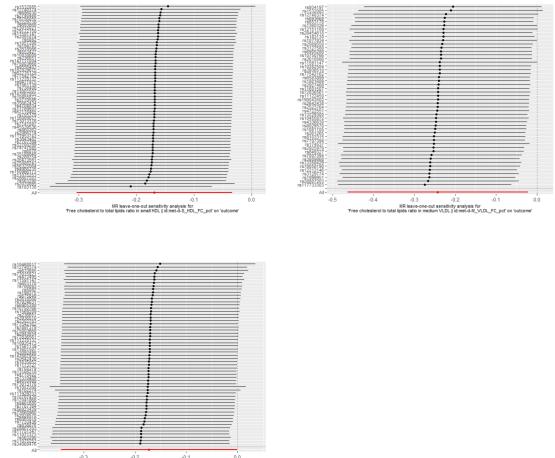
Cholesterol - continued



Free cholesterol

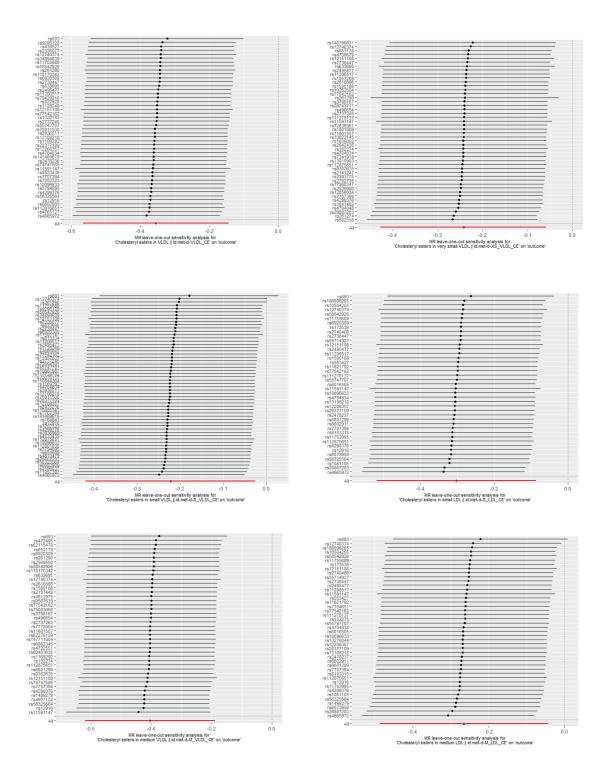


Free cholesterol - continued

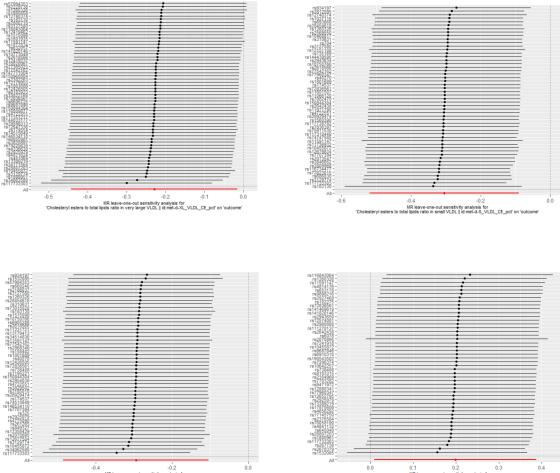


MR leave-one-out sensitivity analysis for 'Free cholesterol to total lipids ratio in large HDL || id::met-d-L_HDL_FC_pct' on 'outcome

Cholesteryl esters

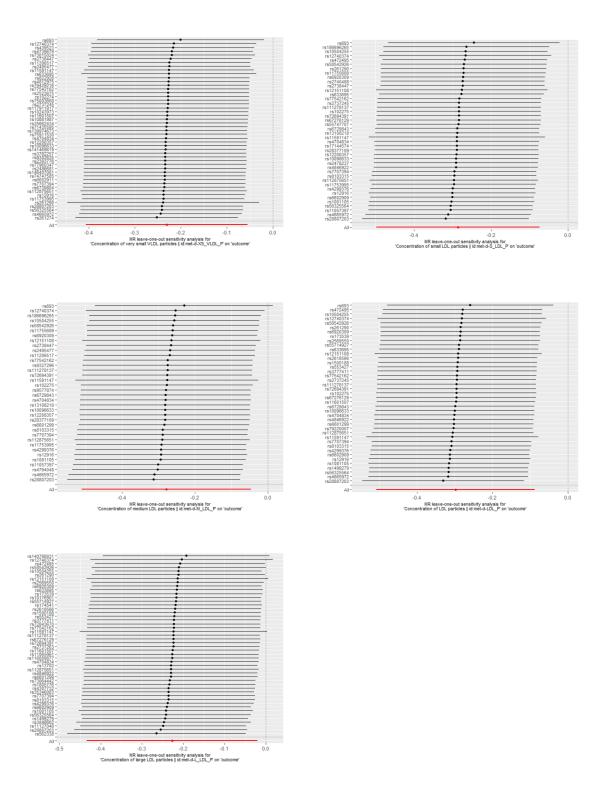


Cholesteryl esters - continued

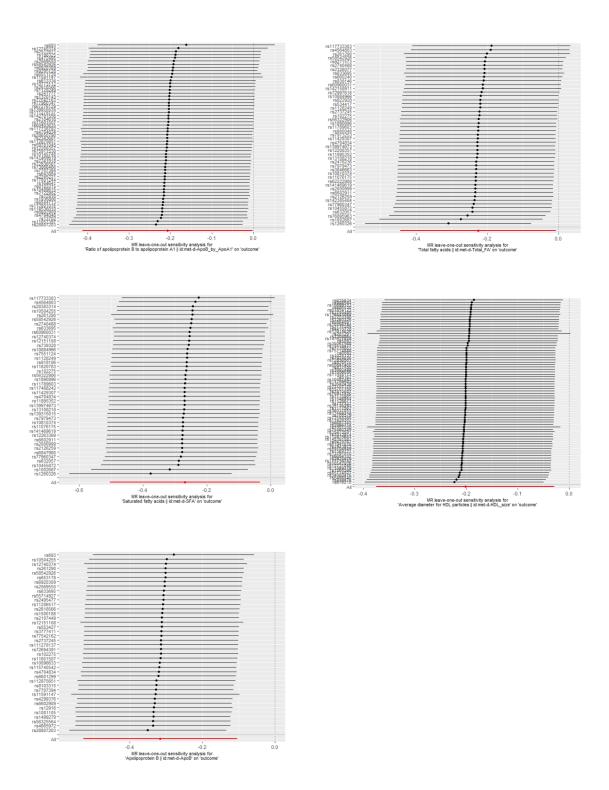


Supplementary Figure S2. Leave-one-out results of IVW, weighted median and MR-Egger. ²¹

Lipoprotein



Other



Supplementary Figure S3. Lipids remained significant after multivariable MR.

| Category | SNP | OR(95%CI) | Р | OR(95%CI) |
|---|-----|-----------------|-------|--------------|
| Total lipids in very small VLDL | 31 | 0.79(0.66-0.95) | 0.010 | |
| Triglycerides in very large HDL | 24 | 0.84(0.70-1.00) | 0.046 | |
| Triglycerides in large HDL | 29 | 0.84(0.72-0.99) | 0.036 | |
| Phospholipids in very small VLDL | 31 | 0.81(0.68-0.96) | 0.018 | — |
| Phospholipids in medium VLDL | 30 | 0.75(0.6-00.95) | 0.018 | _ |
| Phospholipids in IDL | 30 | 0.80(0.65-0.99) | 0.037 | |
| Cholesterol in very small VLDL | 28 | 0.79(0.65-0.96) | 0.018 | |
| Cholesterol in small VLDL | 31 | 0.74(0.59-0.93) | 0.010 | — |
| Cholesterol in medium VLDL | 23 | 0.68(0.54-0.87) | 0.002 | — |
| Remnant cholesterol (non-HDL, non-LDL -cholesterol) | 28 | 0.74(0.59-0.94) | 0.012 | — |
| Cholesterol to total lipids ratio in small VLDL | 27 | 0.75(0.58-0.98) | 0.034 | |
| Free cholesterol in very small VLDL | 28 | 0.75(0.63-0.91) | 0.003 | |
| Free cholesterol in small VLDL | 27 | 0.70(0.56-0.89) | 0.003 | — |
| Free cholesterol in medium VLDL | 26 | 0.74(0.58-0.94) | 0.013 | — |
| Total free cholesterol | 29 | 0.76(0.60-0.96) | 0.019 | _ |
| Cholesteryl esters in VLDL | 29 | 0.71(0.57-0.90) | 0.004 | — |
| Cholesteryl esters in very small VLDL | 27 | 0.81(0.67-1.00) | 0.045 | -+ |
| Cholesteryl esters in small VLDL | 33 | 0.76(0.61-0.95) | 0.015 | — |
| Cholesteryl esters in medium VLDL | 23 | 0.72(0.56-0.92) | 0.008 | — |
| Cholesteryl esters to total lipids ratio in IDL | 28 | 1.26(1.00-1.58) | 0.046 | ⊢ •── |
| Concentration of very small VLDL particles | 30 | 0.80(0.66-0.96) | 0.017 | |
| Concentration of medium LDL particles | 22 | 0.77(0.60-1.00) | 0.049 | |
| Total fatty acids | 25 | 0.75(0.60-0.95) | 0.017 | |
| | | | | |

0.0 0.5 1.0 1.5 2.0