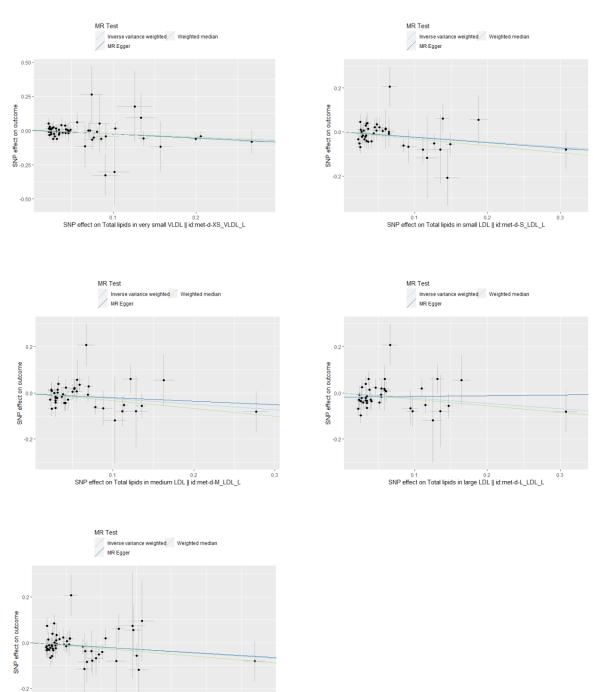
# **Supplementary materials**

**Supplementary Figures S1-S3: Pages 2-24** 

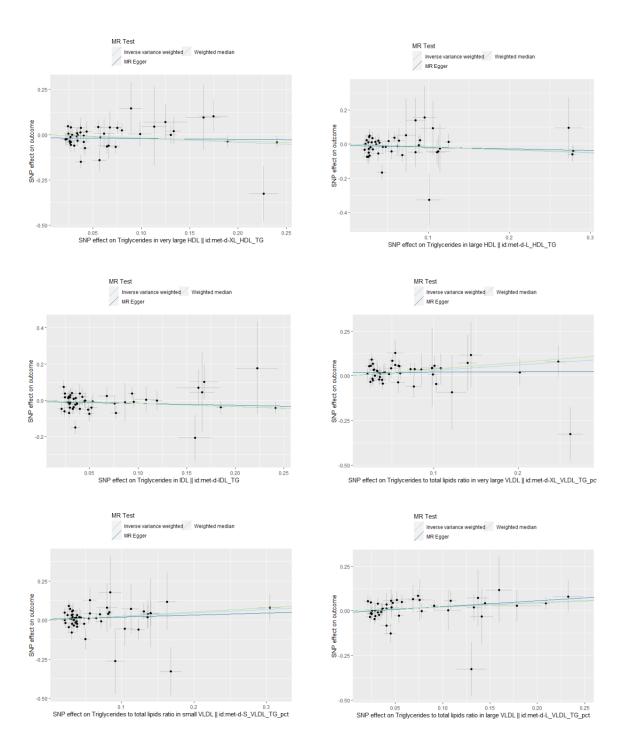
# **Supplementary Figures S1-S3**

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

#### **Total lipids**



# Triglycerides

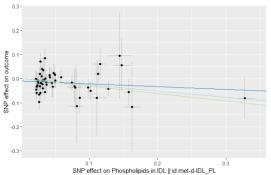


# Phospholipids

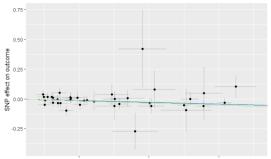
MR Test

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

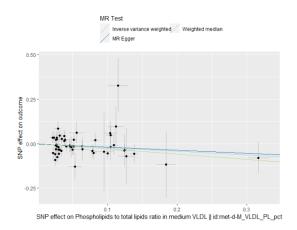


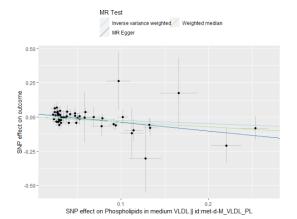




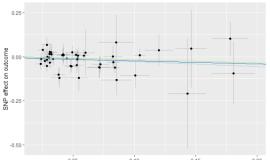


0.05 0.10 0.15 SNP effect on Phospholipids to total lipids ratio in IDL || id:met-d-IDL\_PL\_pct

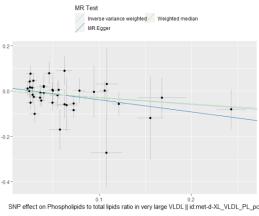




MR Test Inverse var ce weighted Weighted median MR Egger

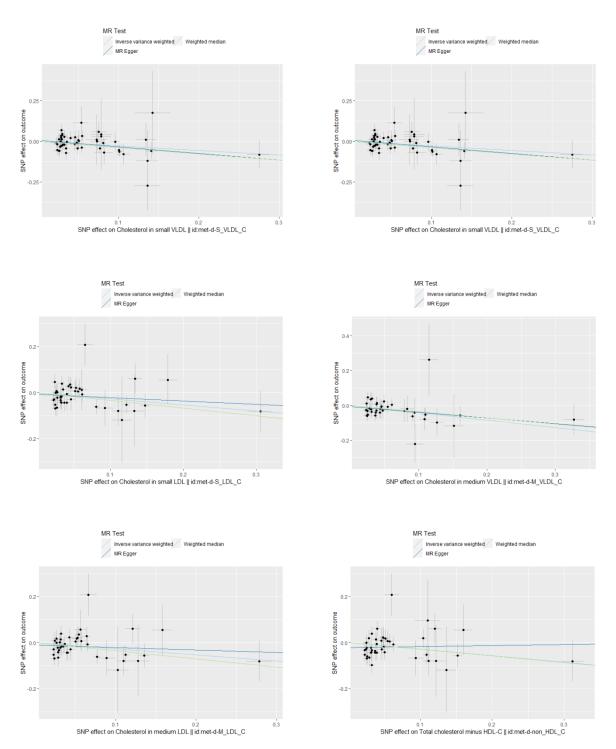


0.05 0.10 0.15 0.20 SNP effect on Phospholipids to total lipids ratio in very small VLDL || id:met-d-XS\_VLDL\_PL\_pc

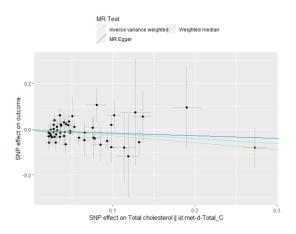


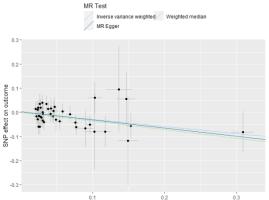
SNP effect on outcome

#### Cholesterol



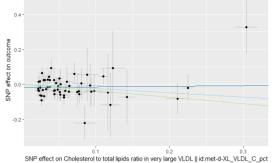
#### **Cholesterol - continued**

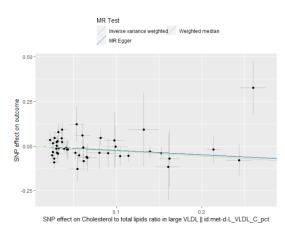


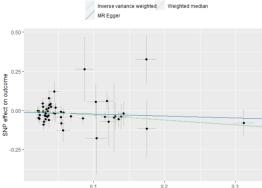


0.1 0.2 0.3 SNP effect on Remnant cholesterol (non-HDL, non-LDL -cholesterol) || id:met-d-Remnant\_C





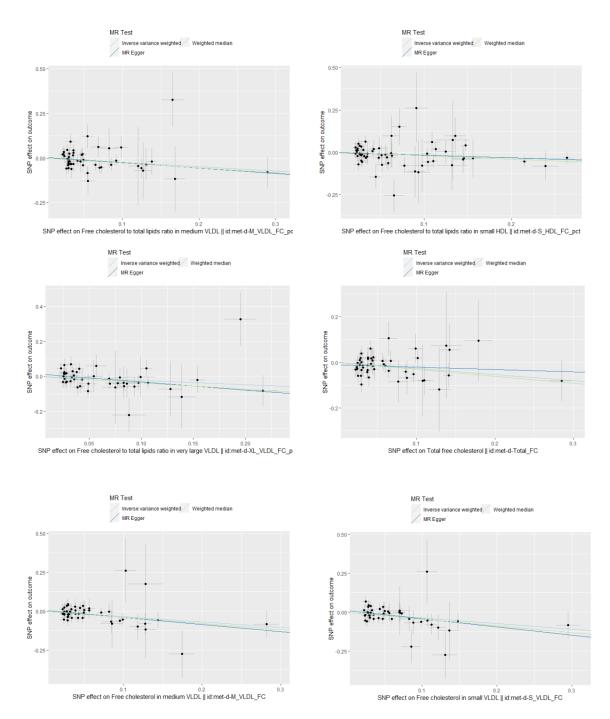




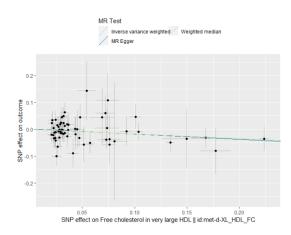
MR Test

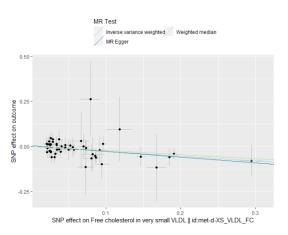


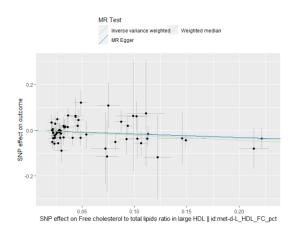
#### **Free cholesterol**



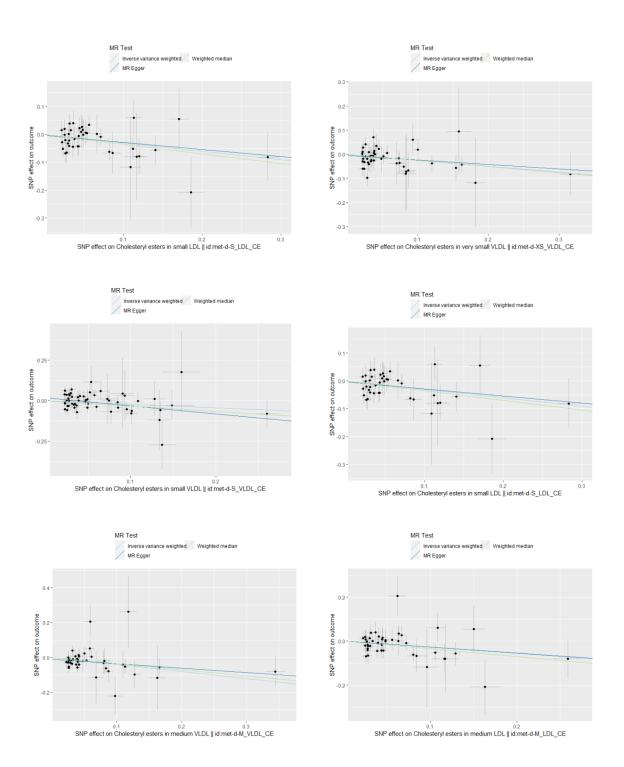
#### **Free cholesterol - continued**



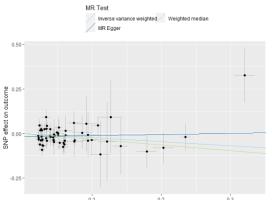




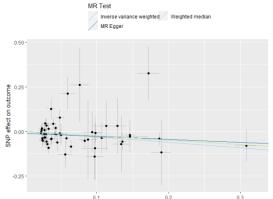
# **Cholesteryl esters**



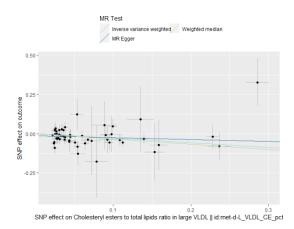
#### **Cholesteryl esters - continued**

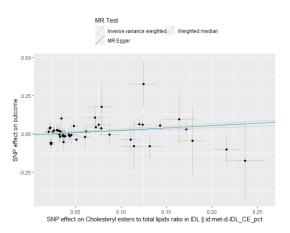


0.1 0.2 0.3 SNP effect on Cholesteryl esters to total lipids ratio in very large VLDL || id:met-d-XL\_VLDL\_CE\_

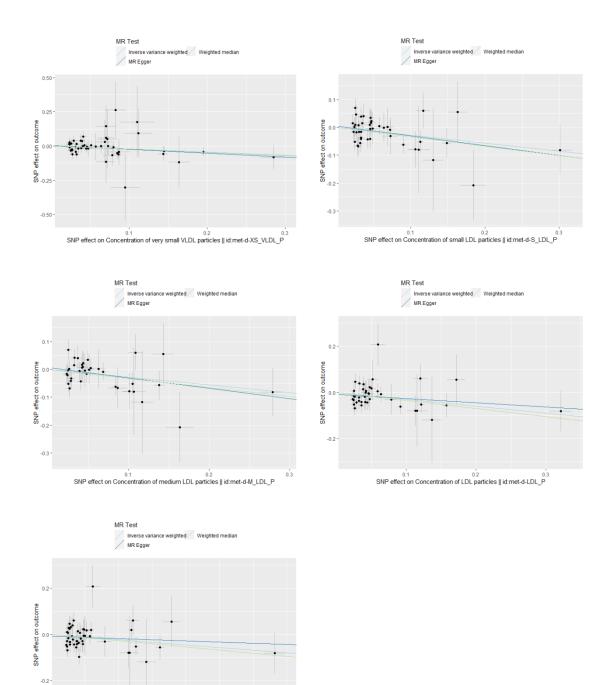


0.1 0.2 0.3 SNP effect on Cholesteryl esters to total lipids ratio in small VLDL || id:met-d-S\_VLDL\_CE\_pc



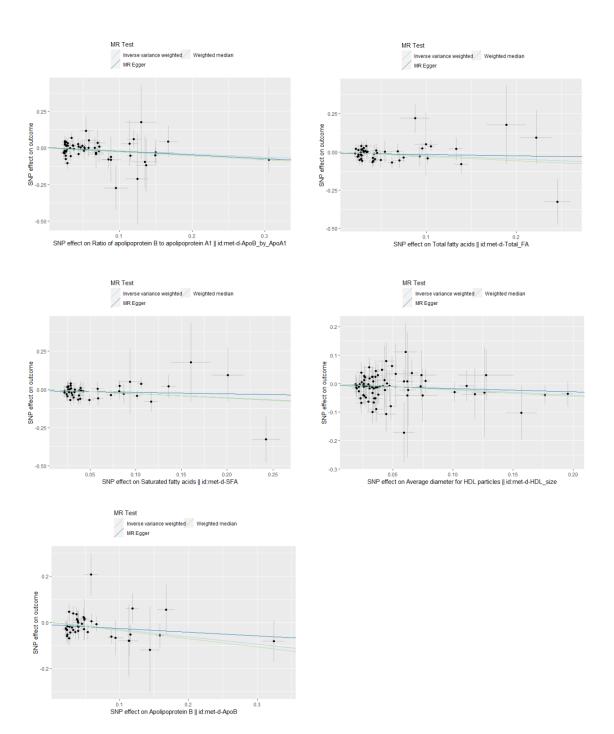


# Lipoprotein



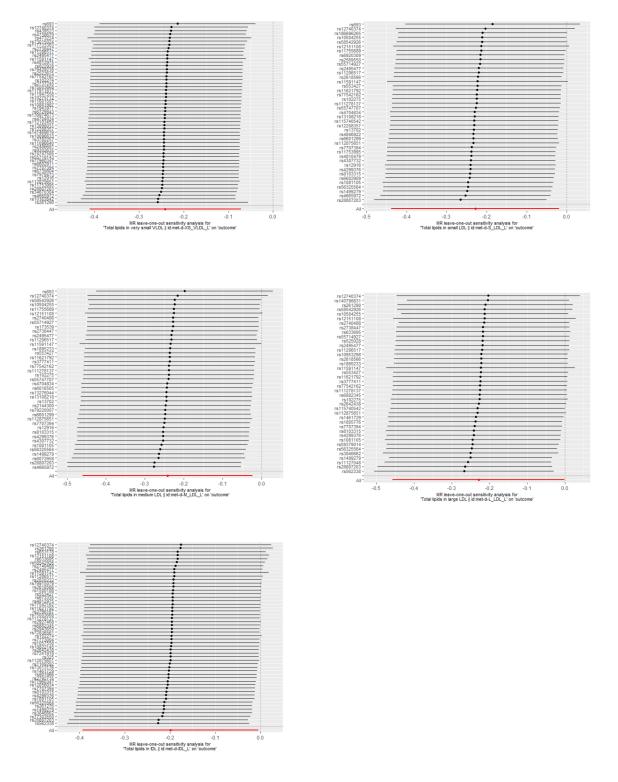
0.1 0.2 0.3 SNP effect on Concentration of large LDL particles || id:met-d-L\_LDL\_P

# Other

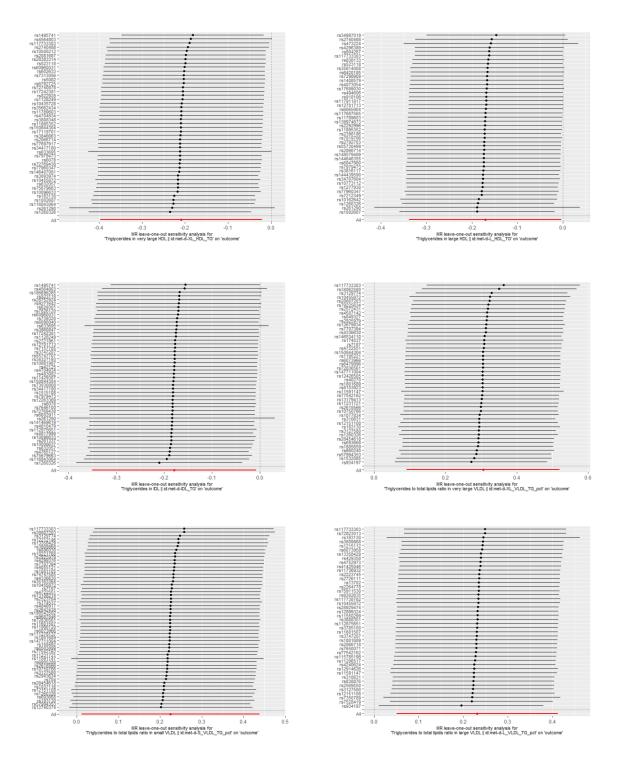


**Supplementary Figure S2.** Leave-one-out results of IVW, weighted median and MR-Egger. Pages 12-22.

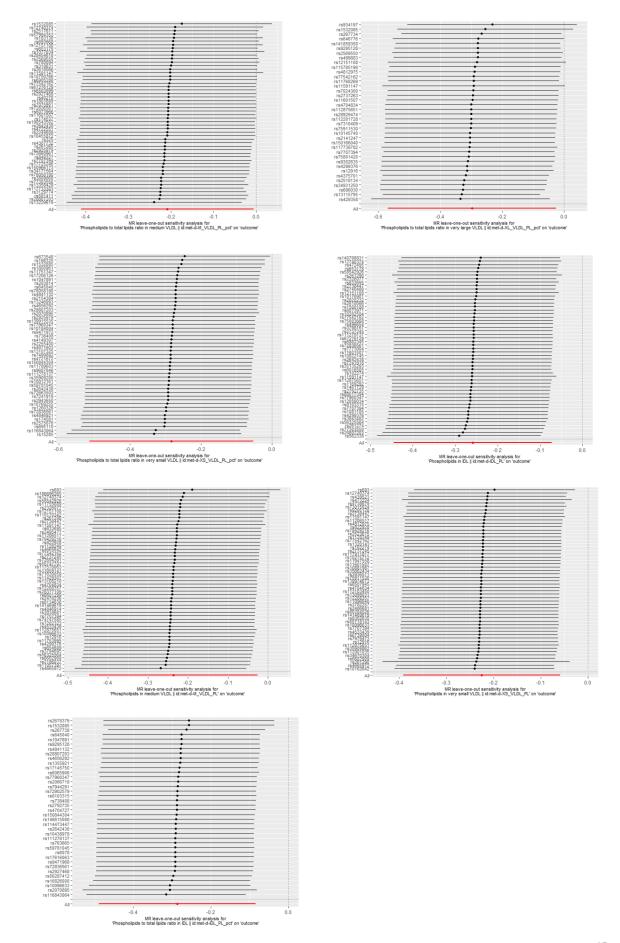




# Triglycerides

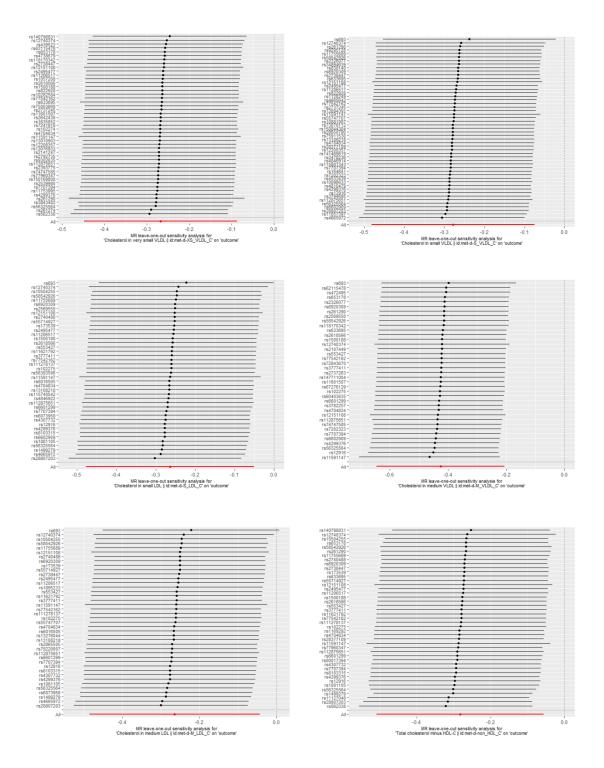


# Phospholipids

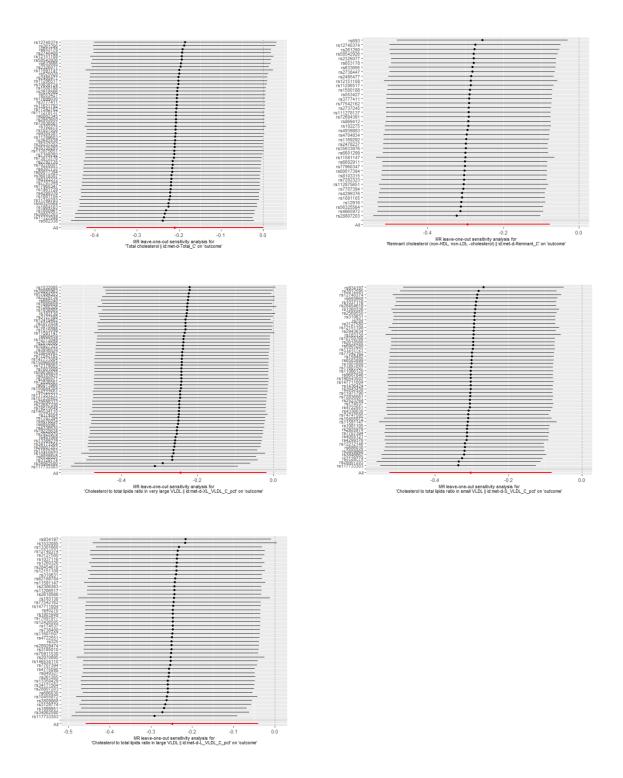


Supplementary Figure S2. Leave-one-out results of IVW, weighted median and MR-Egger. <sup>15</sup>

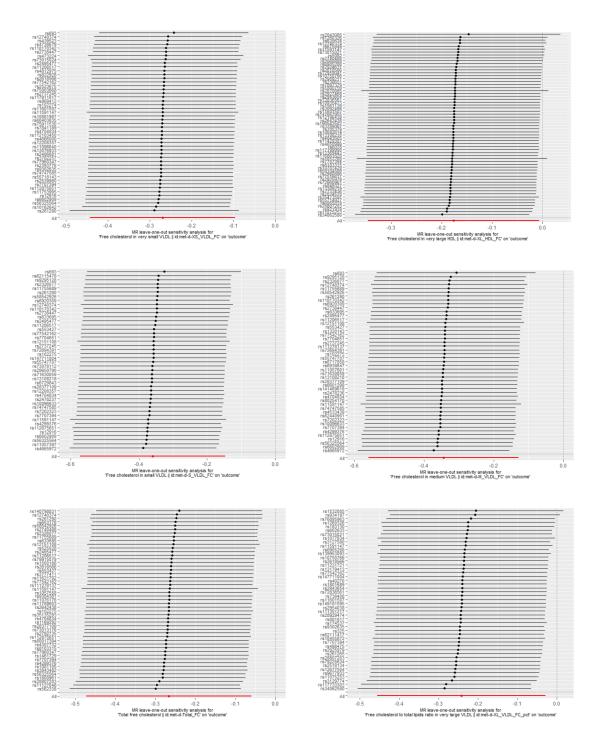
# Cholesterol



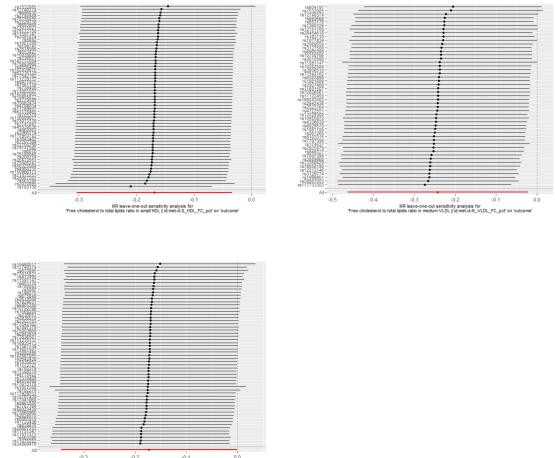
#### **Cholesterol - continued**



#### **Free cholesterol**

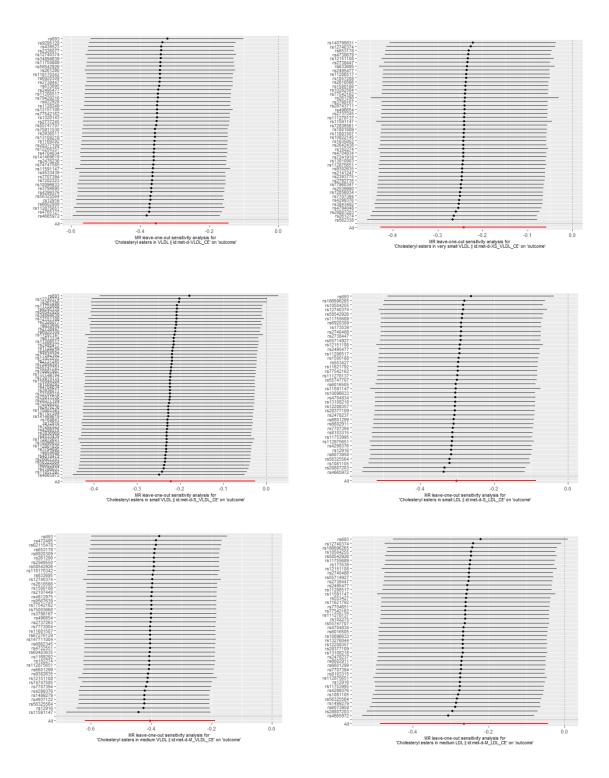


## **Free cholesterol - continued**

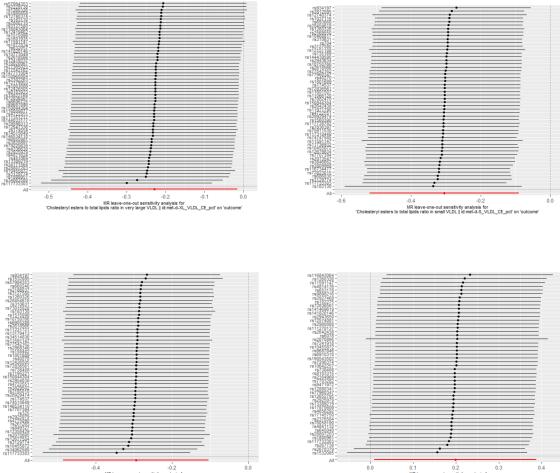


MR leave-one-out sensitivity analysis for 'Free cholesterol to total lipids ratio in large HDL || id::met-d-L\_HDL\_FC\_pct' on 'outcome

# **Cholesteryl esters**

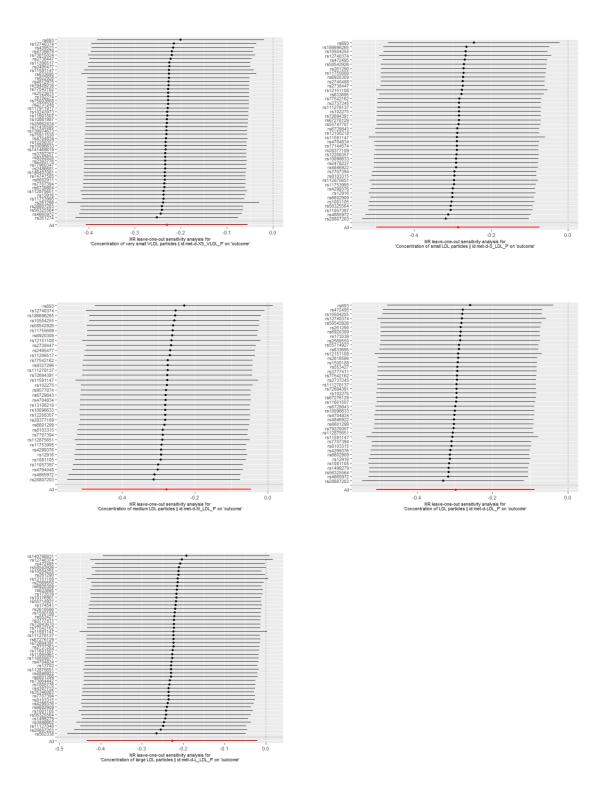


# **Cholesteryl esters - continued**

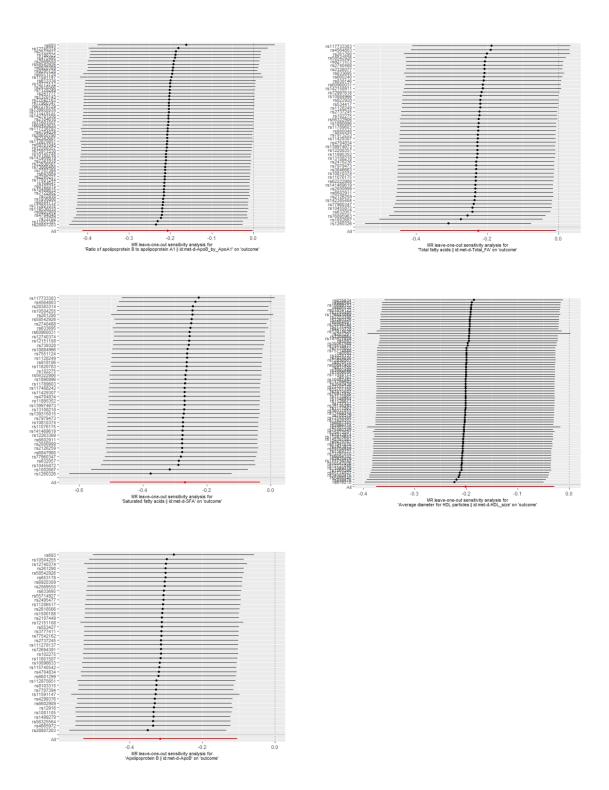


Supplementary Figure S2. Leave-one-out results of IVW, weighted median and MR-Egger. <sup>21</sup>

# 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	<b>—</b>
Phospholipids in medium VLDL	30	0.75(0.6-00.95)	0.018	<b>_</b>
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	<b>—</b>
Cholesterol in medium VLDL	23	0.68(0.54-0.87)	0.002	<b>—</b>
Remnant cholesterol (non-HDL, non-LDL -cholesterol)	28	0.74(0.59-0.94)	0.012	<b>—</b>
Cholesterol to total lipids ratio in small VLDL	27	0.75(0.58-0.98)	0.034	<b></b>
Free cholesterol in very small VLDL	28	0.75(0.63-0.91)	0.003	<b></b>
Free cholesterol in small VLDL	27	0.70(0.56-0.89)	0.003	<b>—</b>
Free cholesterol in medium VLDL	26	0.74(0.58-0.94)	0.013	<b>—</b>
Total free cholesterol	29	0.76(0.60-0.96)	0.019	<b>_</b>
Cholesteryl esters in VLDL	29	0.71(0.57-0.90)	0.004	<b>—</b>
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	<b>—</b>
Cholesteryl esters in medium VLDL	23	0.72(0.56-0.92)	0.008	<b>—</b>
Cholesteryl esters to total lipids ratio in IDL	28	1.26(1.00-1.58)	0.046	<b>⊢</b> •──
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	<b></b>

0.0 0.5 1.0 1.5 2.0