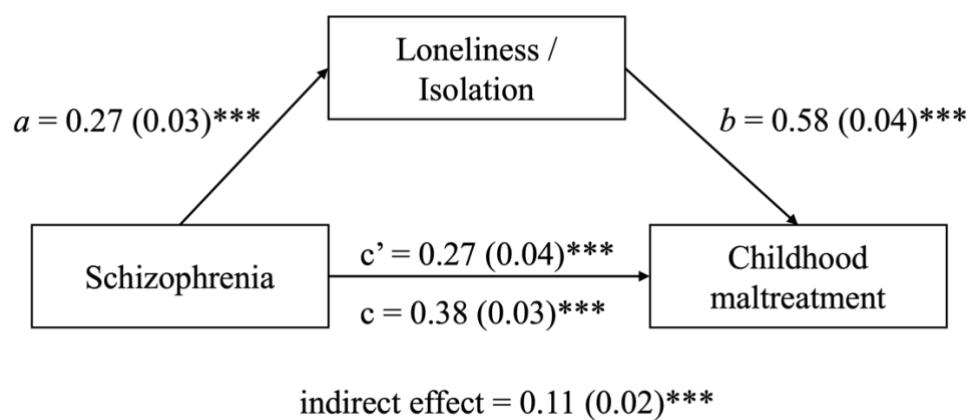


Supplementary Figures for The Role of Loneliness and Social Isolation in Mediating the Relationship Between Childhood Maltreatment and Schizophrenia: A Genetically Informed Approach

Supplementary Figure 1

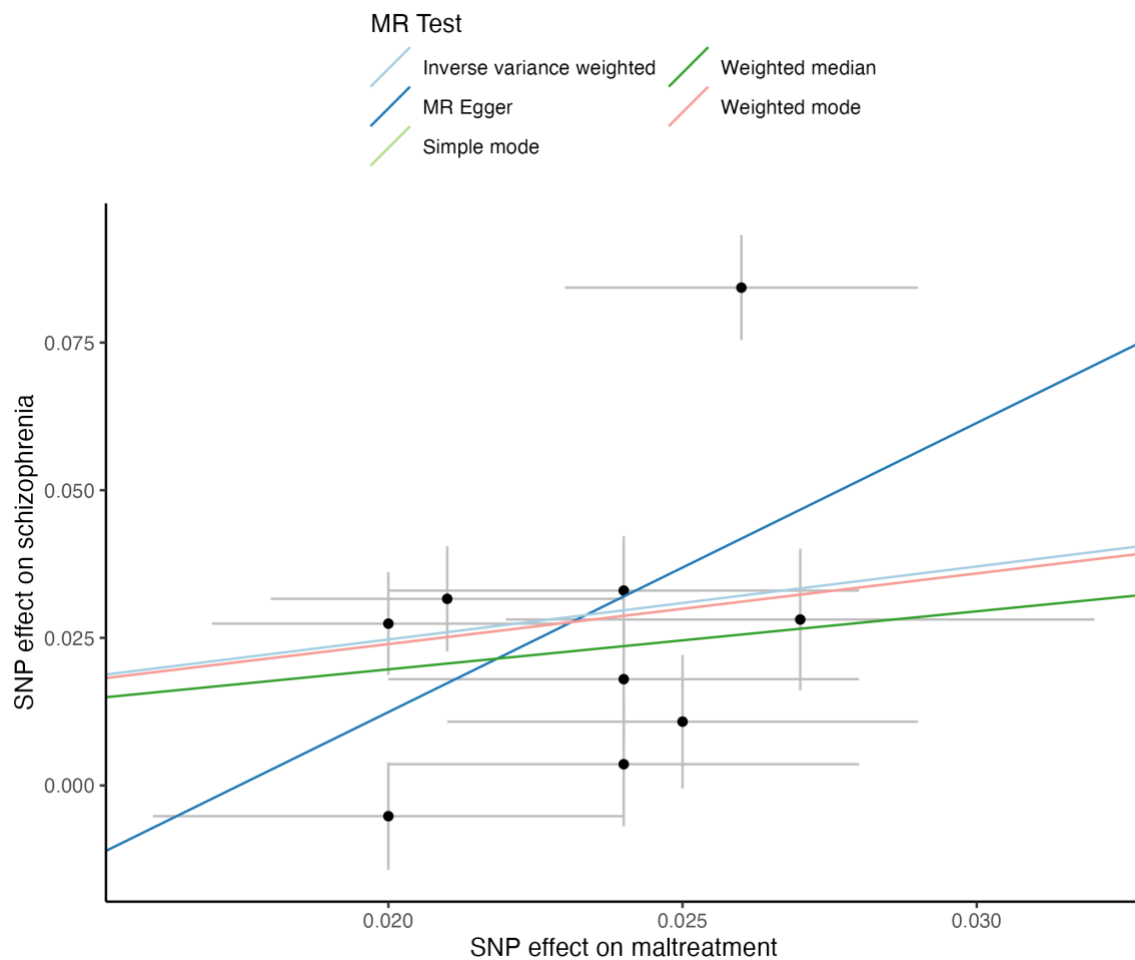
Genetic Mediation Analysis Estimating the Mediating Effect of Loneliness/Isolation in the Relationship between Schizophrenia and Childhood Maltreatment



Note. Standardised regression weights and the corresponding standard errors (in parentheses) are reported. a path = effect of the predictor (schizophrenia) on the mediator (loneliness/isolation); b path = effect of the mediator (loneliness/isolation) on the outcome (childhood maltreatment); c' path = direct effect of schizophrenia on childhood maltreatment; c path = total effect of schizophrenia on childhood maltreatment. *** $p < 0.001$.

Supplementary Figure 2

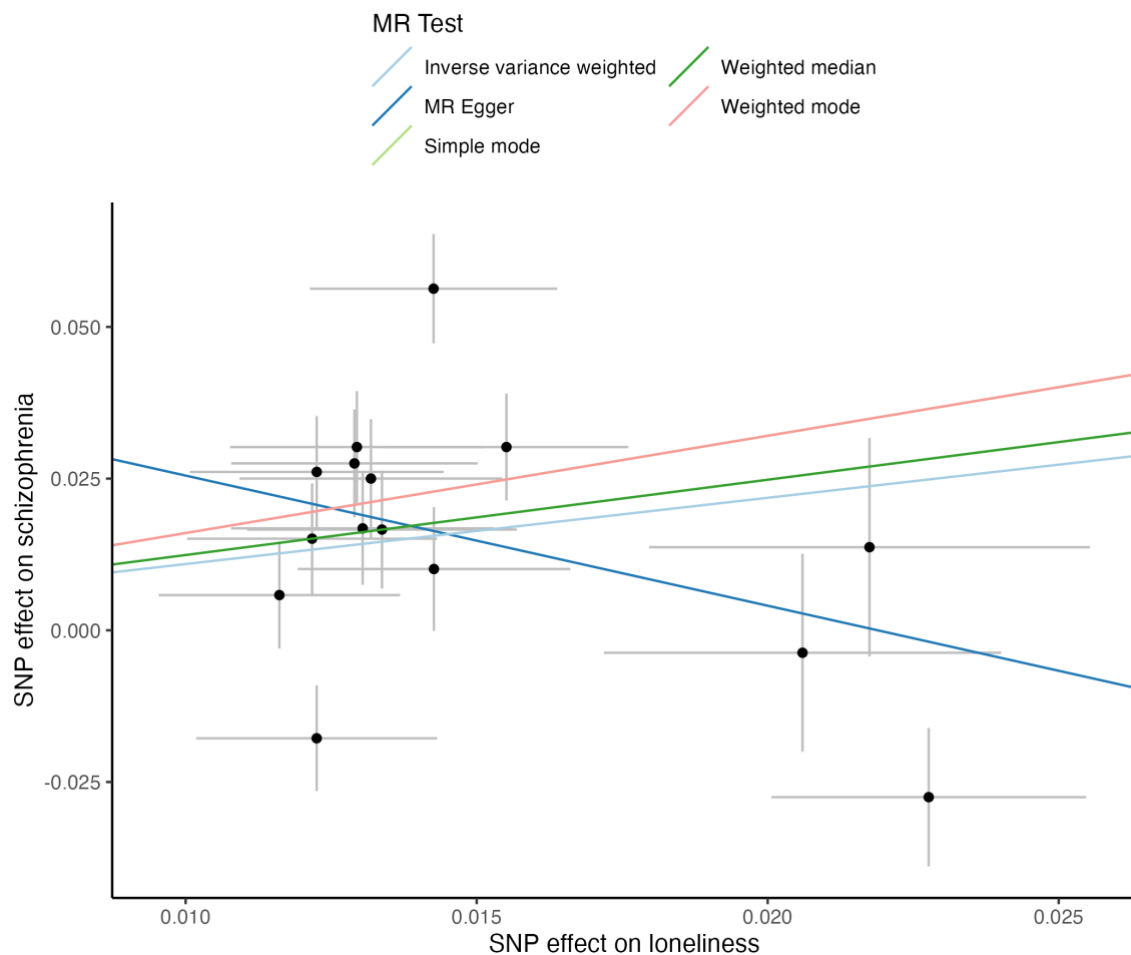
Scatter Plot of the SNP Effects of Childhood Maltreatment on Schizophrenia from Univariable Mendelian Randomisation Analysis



Note. Slopes represent estimates from the primary inverse variance weighted analysis and four sensitivity analyses: MR Egger, weighted median, simple mode, weighted median, weighted mode. Units of association are log odds ratios. MR = Mendelian randomisation; SNP = single nucleotide polymorphism.

Supplementary Figure 3

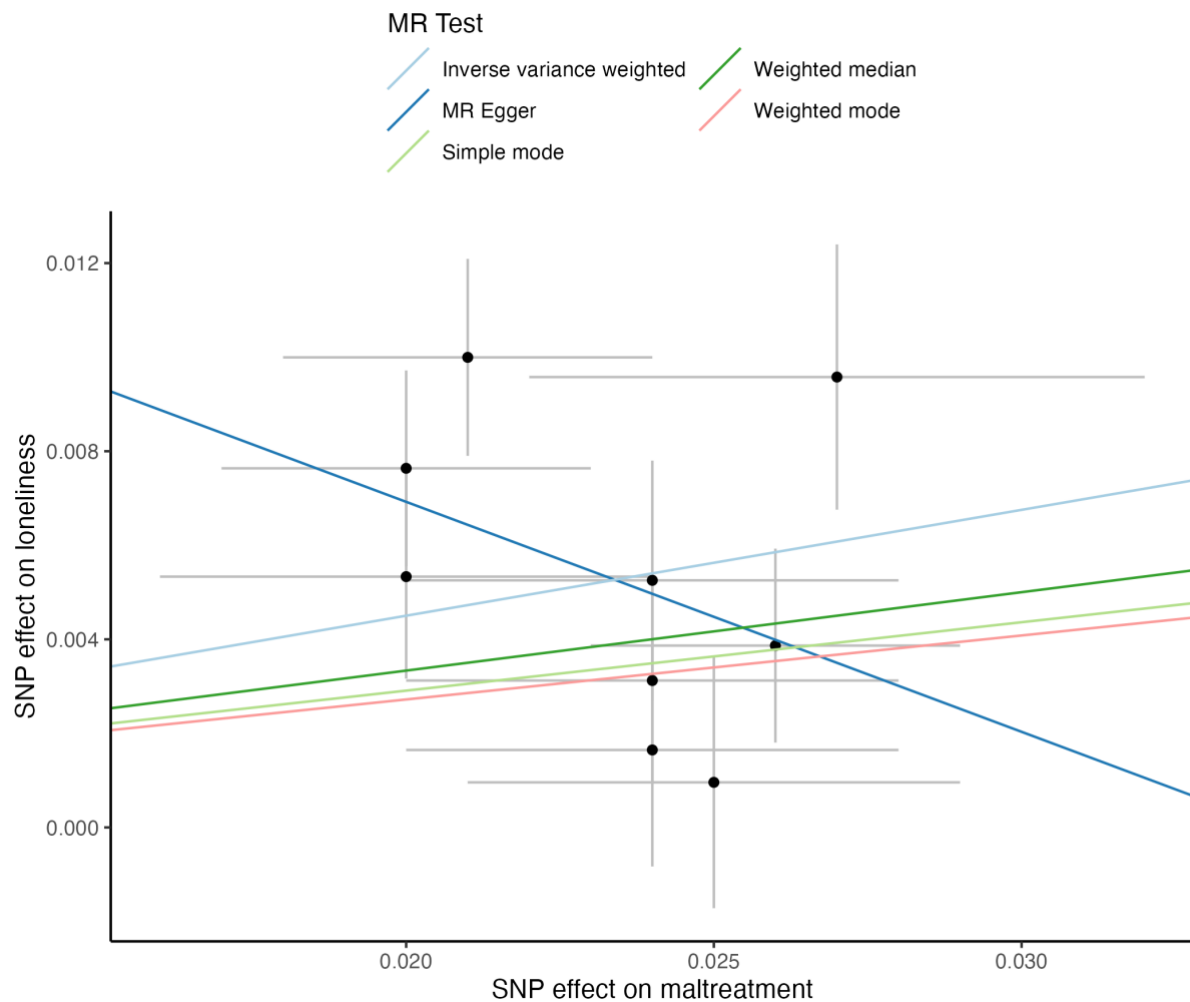
Scatter Plot of the SNP Effects of Loneliness/Isolation on Schizophrenia from Univariable Mendelian Randomisation Analysis



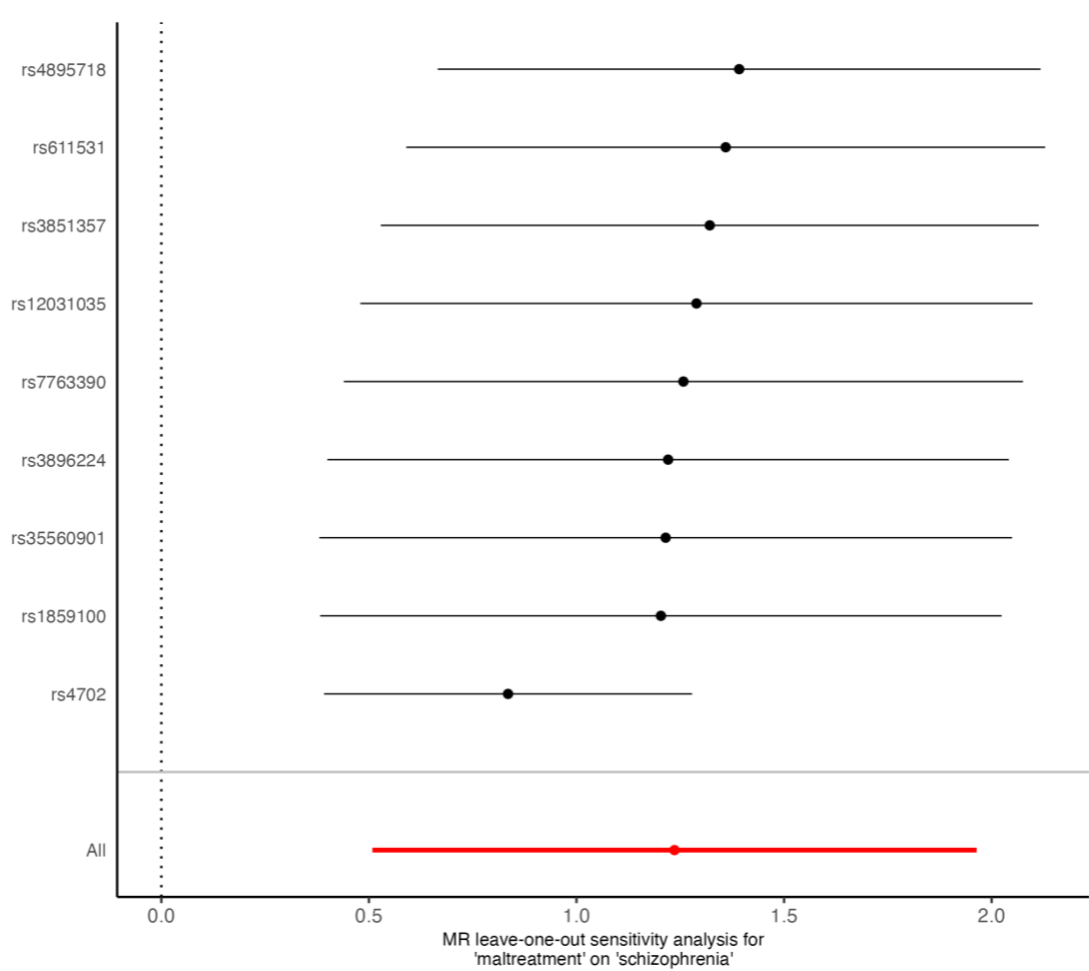
Note. Slopes represent estimates from the primary inverse variance weighted analysis and four sensitivity analyses: MR Egger, weighted median, simple mode, weighted median, weighted mode. Units of association are log odds ratios. MR = Mendelian randomisation; SNP = single nucleotide polymorphism.

Supplementary Figure 4

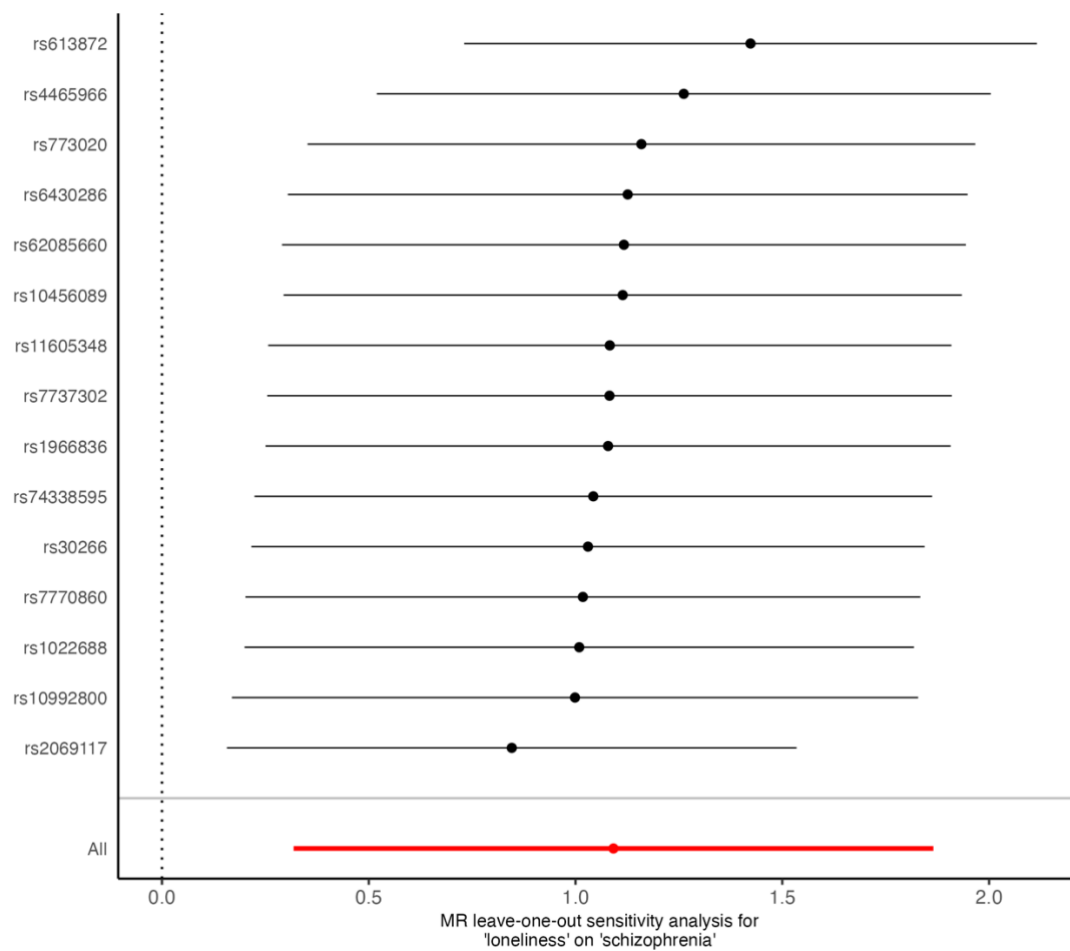
Scatter Plot of the SNP Effects of Childhood Maltreatment on Loneliness/Isolation from Univariable Mendelian Randomisation Analysis



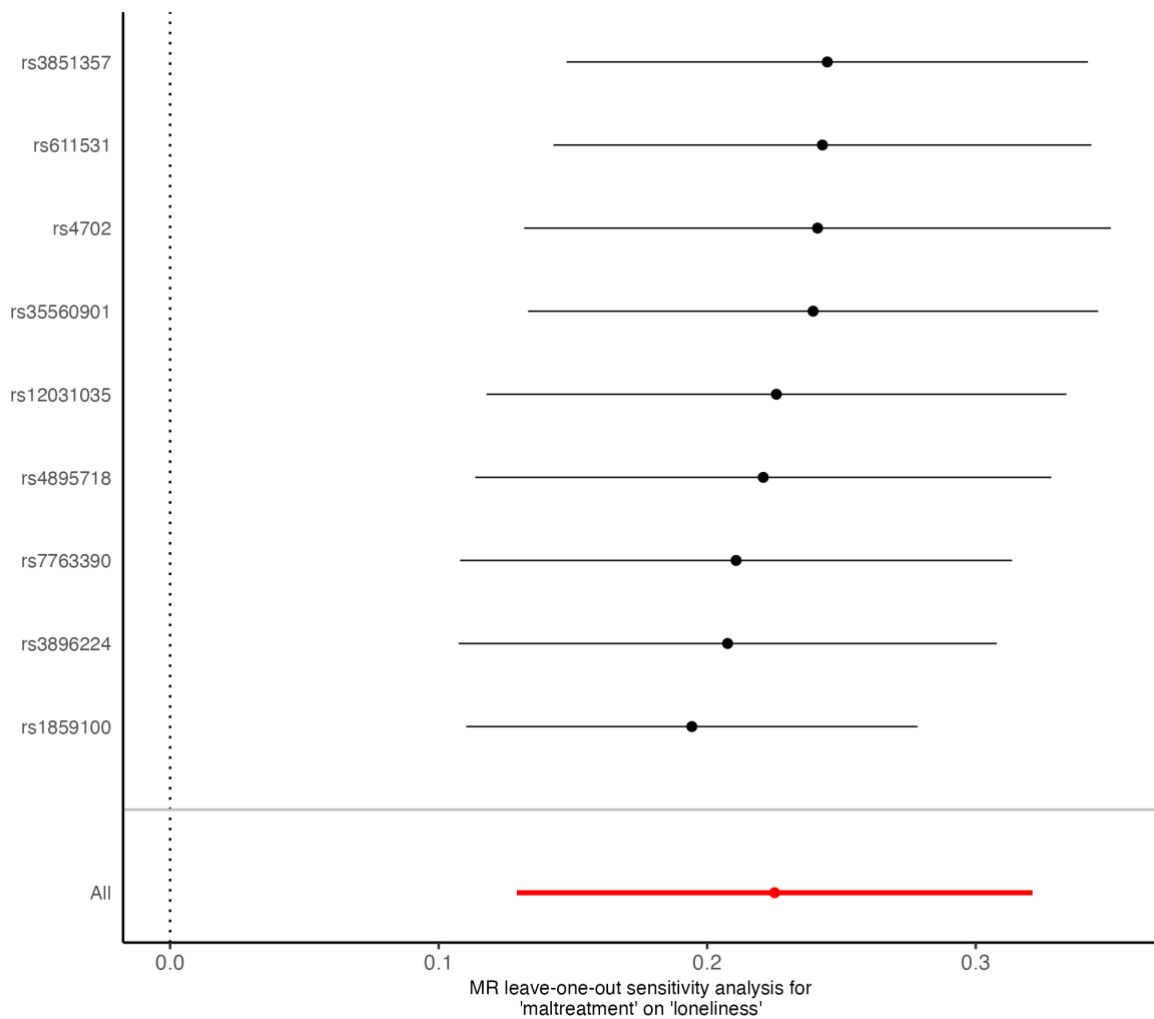
Note. Slopes represent estimates from the primary inverse variance weighted analysis and four sensitivity analyses: MR Egger, weighted median, simple mode, weighted median, weighted mode. Units of association are standard deviation. MR = Mendelian randomisation; SNP = single nucleotide polymorphism.

Supplementary Figure 5*Leave-One-Out Plot for the SNP Effects of Childhood Maltreatment on Schizophrenia*

Note. The estimated effect of each excluded SNP is depicted in black. The overall estimate including all SNPs is depicted in red. Error bars indicate the 95% confidence interval. MR = Mendelian randomisation; SNP = single nucleotide polymorphism.

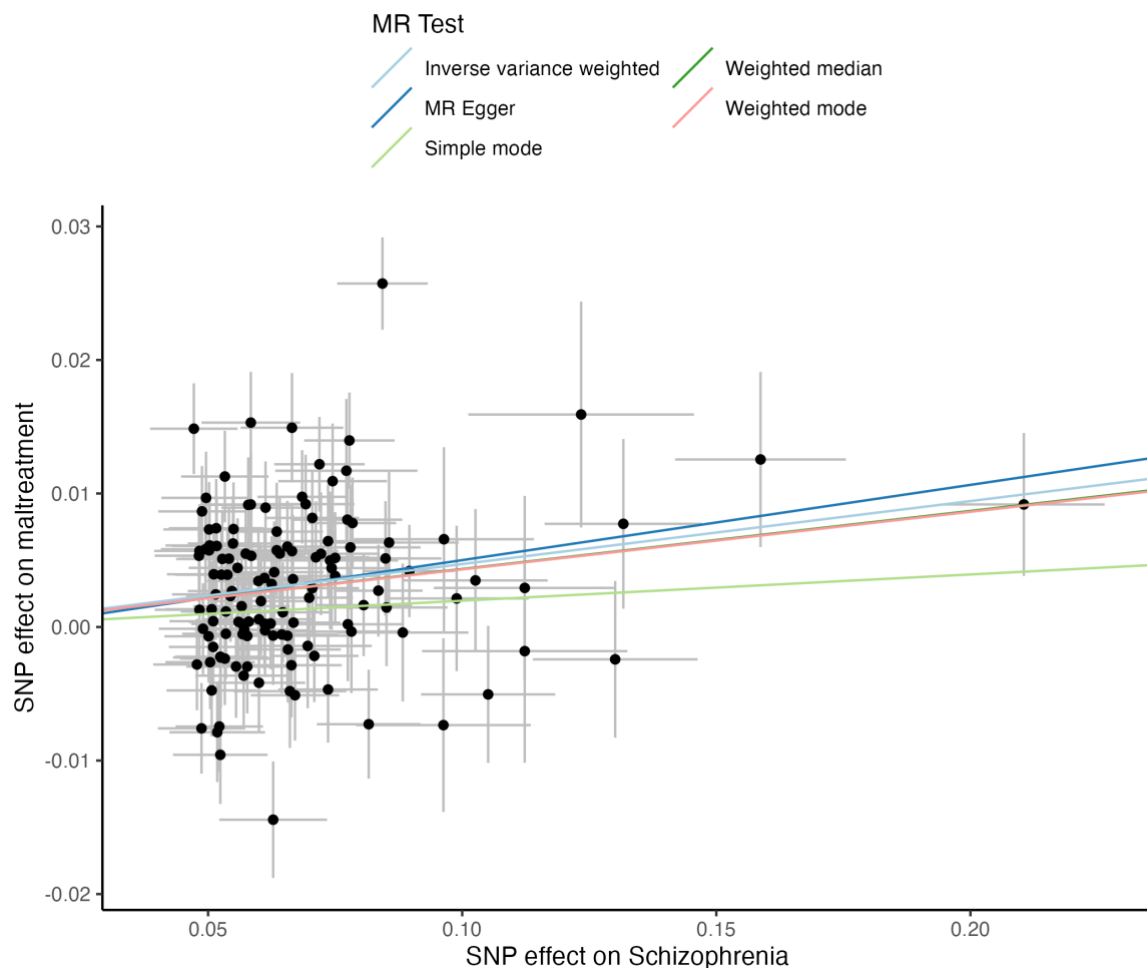
Supplementary Figure 6*Leave-One-Out Plot for the SNP Effects of Loneliness/Isolation on Schizophrenia*

Note. The estimated effect of each excluded SNP is depicted in black. The overall estimate including all SNPs is depicted in red. Error bars indicate the 95% confidence interval. MR = Mendelian randomisation; SNP = single nucleotide polymorphism.

Supplementary Figure 7*Leave-One-Out Plot for the SNP Effects of Childhood Maltreatment on Loneliness/Isolation*

Supplementary Figure 8

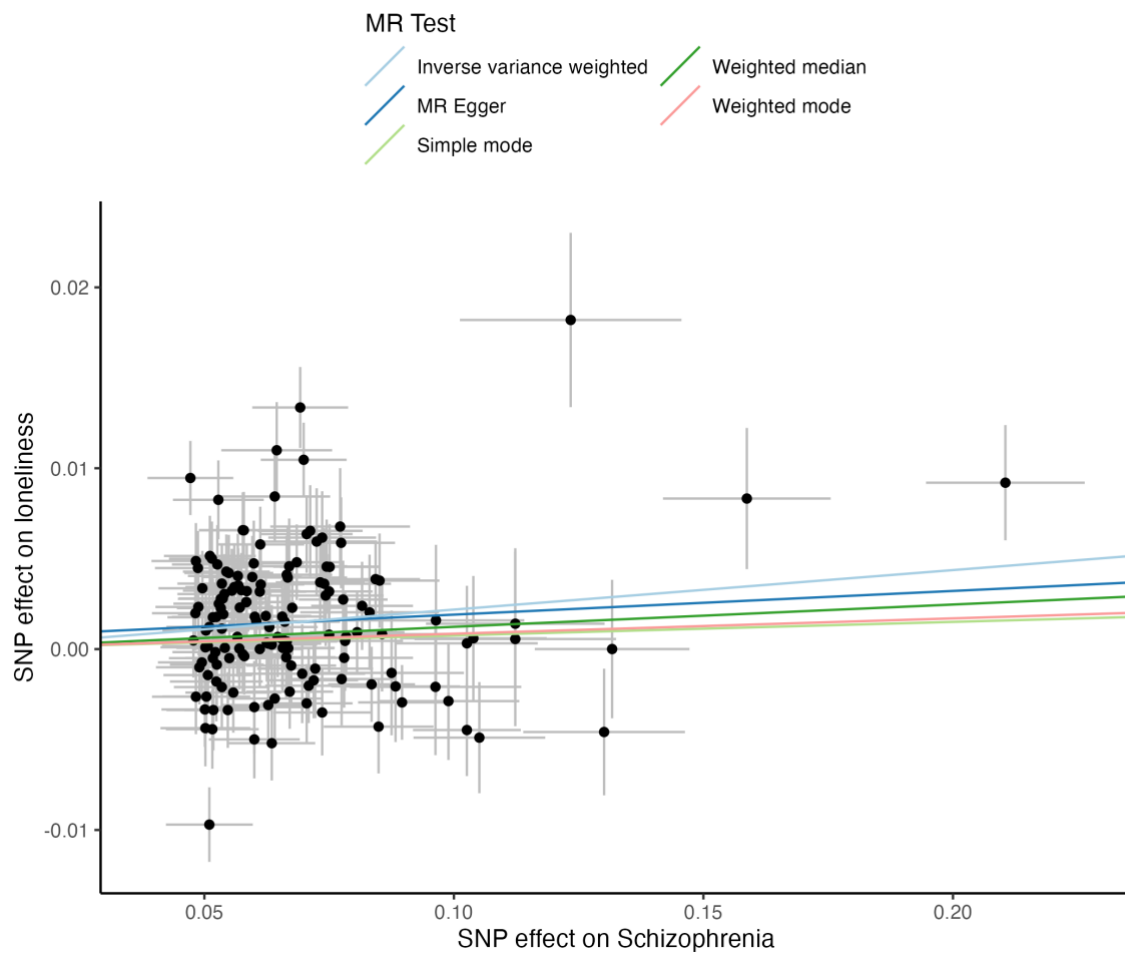
Scatter Plot of the SNP Effects of Schizophrenia on Childhood Maltreatment from Reverse Univariable Mendelian Randomisation Analysis



Note. Slopes represent estimates from the primary inverse variance weighted analysis and four sensitivity analyses: MR Egger, weighted median, simple mode, weighted median, weighted mode. All four sensitivity analyses are directionally concordant with the IVW estimate but two of them (MR Egger and simple mode) are not significant. Units of association are betas. MR = Mendelian randomisation; SNP = single nucleotide polymorphism.

Supplementary Figure 9

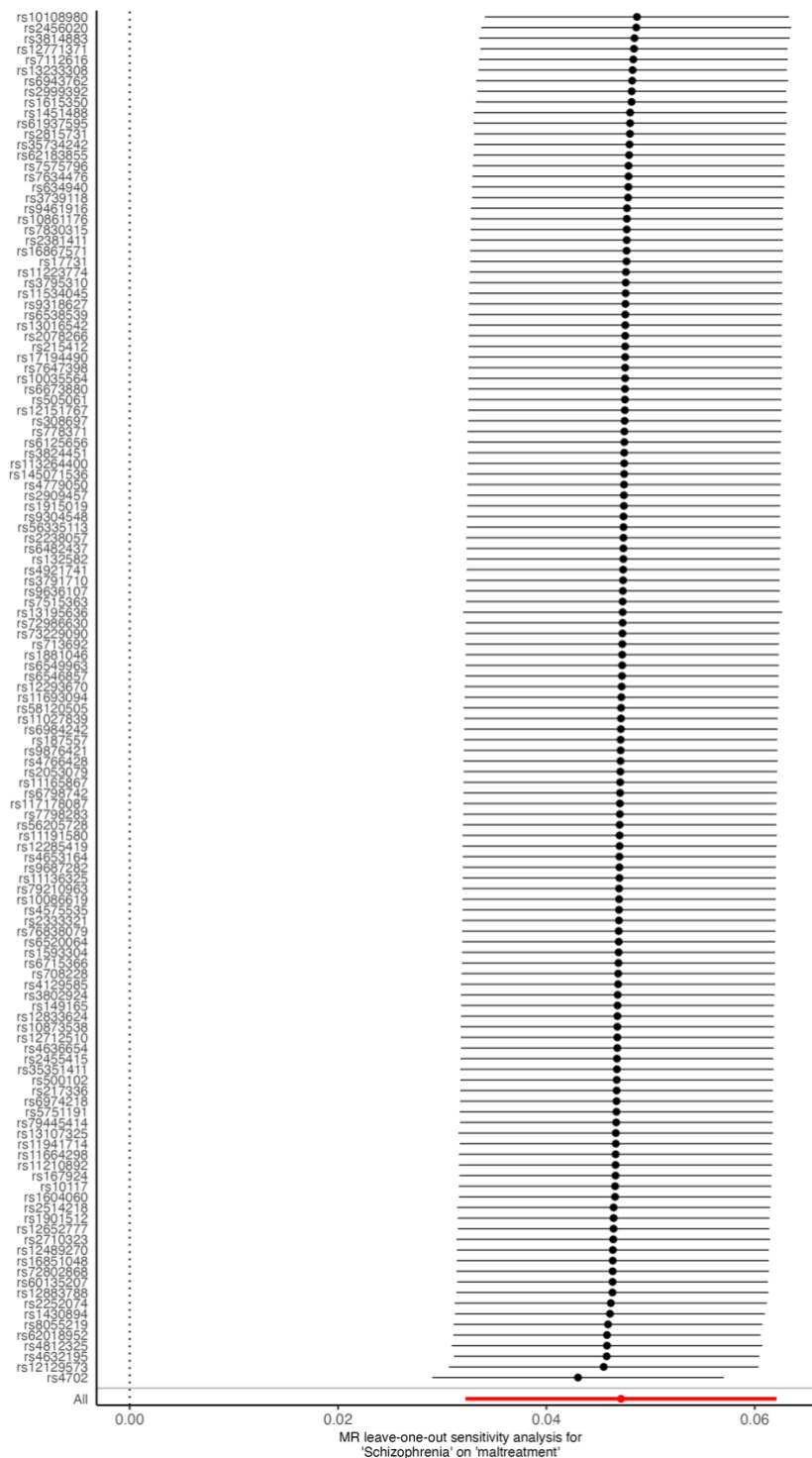
Scatter Plot of the SNP Effects of Schizophrenia on Loneliness/Isolation from Reverse Univariable Mendelian Randomisation Analysis



Note. Slopes represent estimates from the primary inverse variance weighted analysis and four sensitivity analyses: MR Egger, weighted median, simple mode, weighted median, weighted mode. Units of association are betas. MR = Mendelian randomisation; SNP = single nucleotide polymorphism.

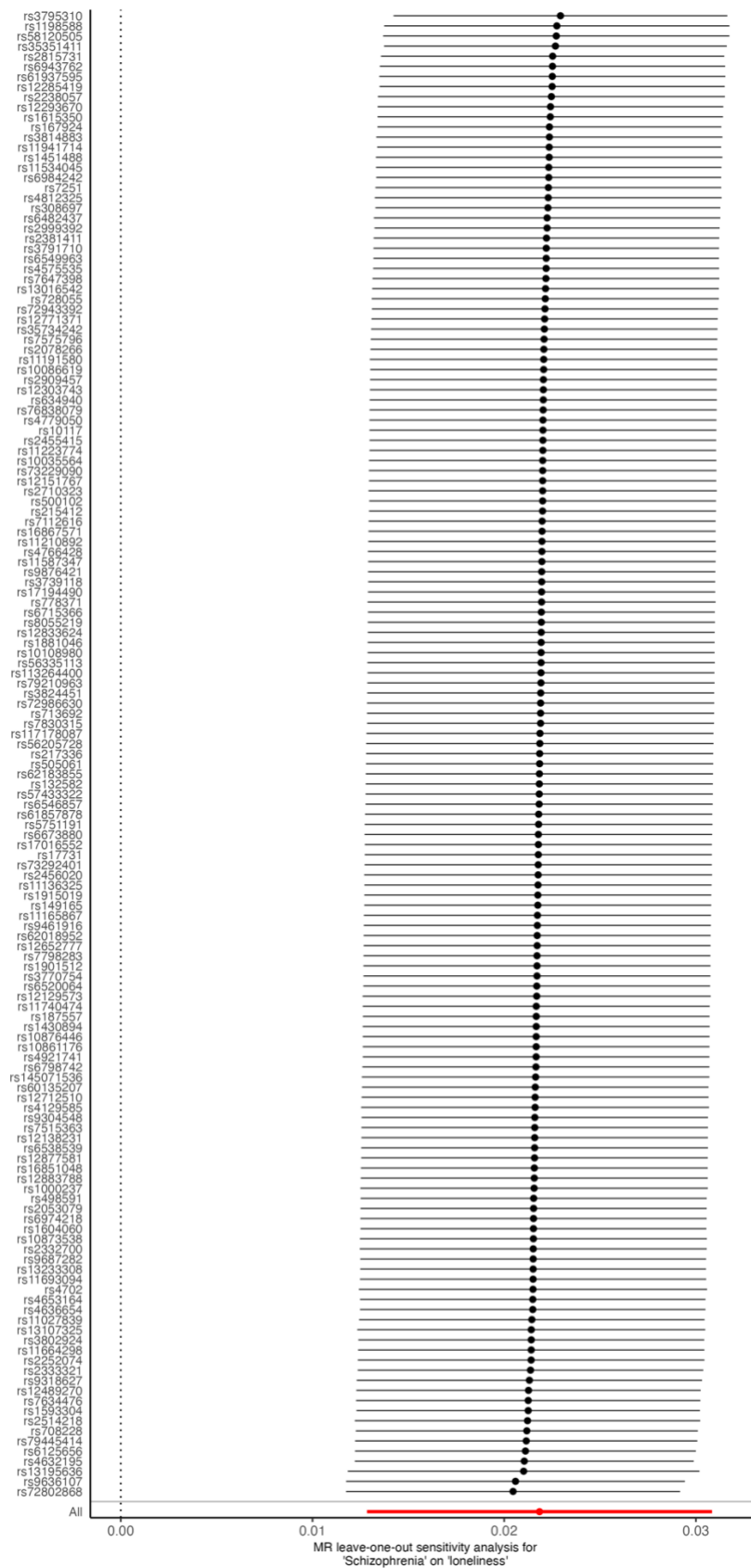
Supplementary Figure 10

Leave-One-Out Plot for the SNP Effects of Schizophrenia on Childhood Maltreatment



Note. The estimated effect of each excluded SNP is depicted in black. The overall estimate including all SNPs is depicted in red. Error bars indicate the 95% confidence interval. MR = Mendelian randomisation; SNP = single nucleotide polymorphism.

Supplementary Figure 11

Leave-One-Out Plot for the SNP Effects of Schizophrenia on Loneliness/Isolation

Note. The estimated effect of each excluded SNP is depicted in black. The overall estimate including all SNPs is depicted in red. Error bars indicate the 95% confidence interval. MR = Mendelian randomisation; SNP = single nucleotide polymorphism.