

## **Supplementary Materials**

### **Shared genetic architecture between brain imaging-derived phenotypes and osteoporosis: a large-scale genetic correlation study**

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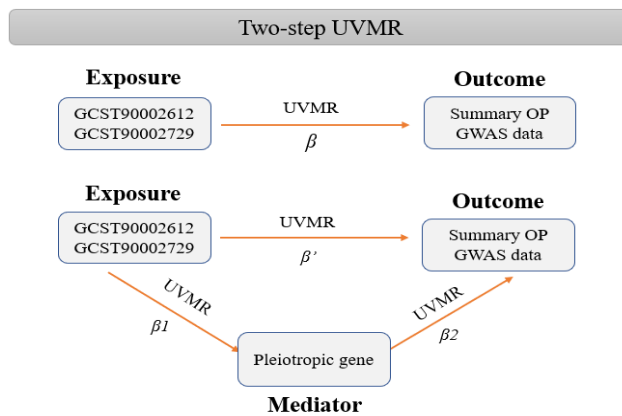
#### **Supplementary Figures 1-48**

**Supplementary Figure 1.** Flow chart of two-step UVMR mediation analysis.

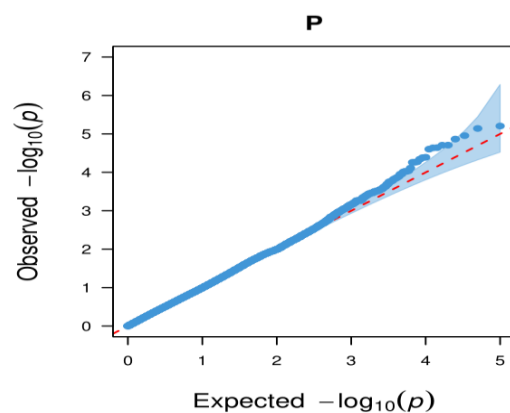
**Supplementary Figure 2.** Quantile-quantile (Q-Q) plot of OP GWAS.

**Supplementary Figure 3.** MR analysis of eQTL and OP summary data of 6 Pleiotropic genes.

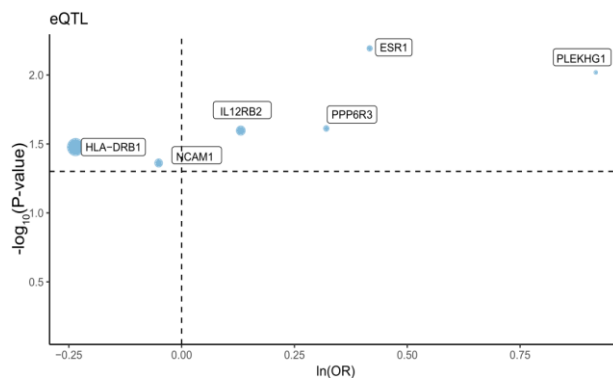
**Supplementary Figures 4-48.** Scatter plot, funnel plot and leave-one-out plot with IDPs as exposure and OP, Forearm BMD, Femoral neck BMD, Lumbar spine BMD, Total body BMD and Heel BMD as outcome.



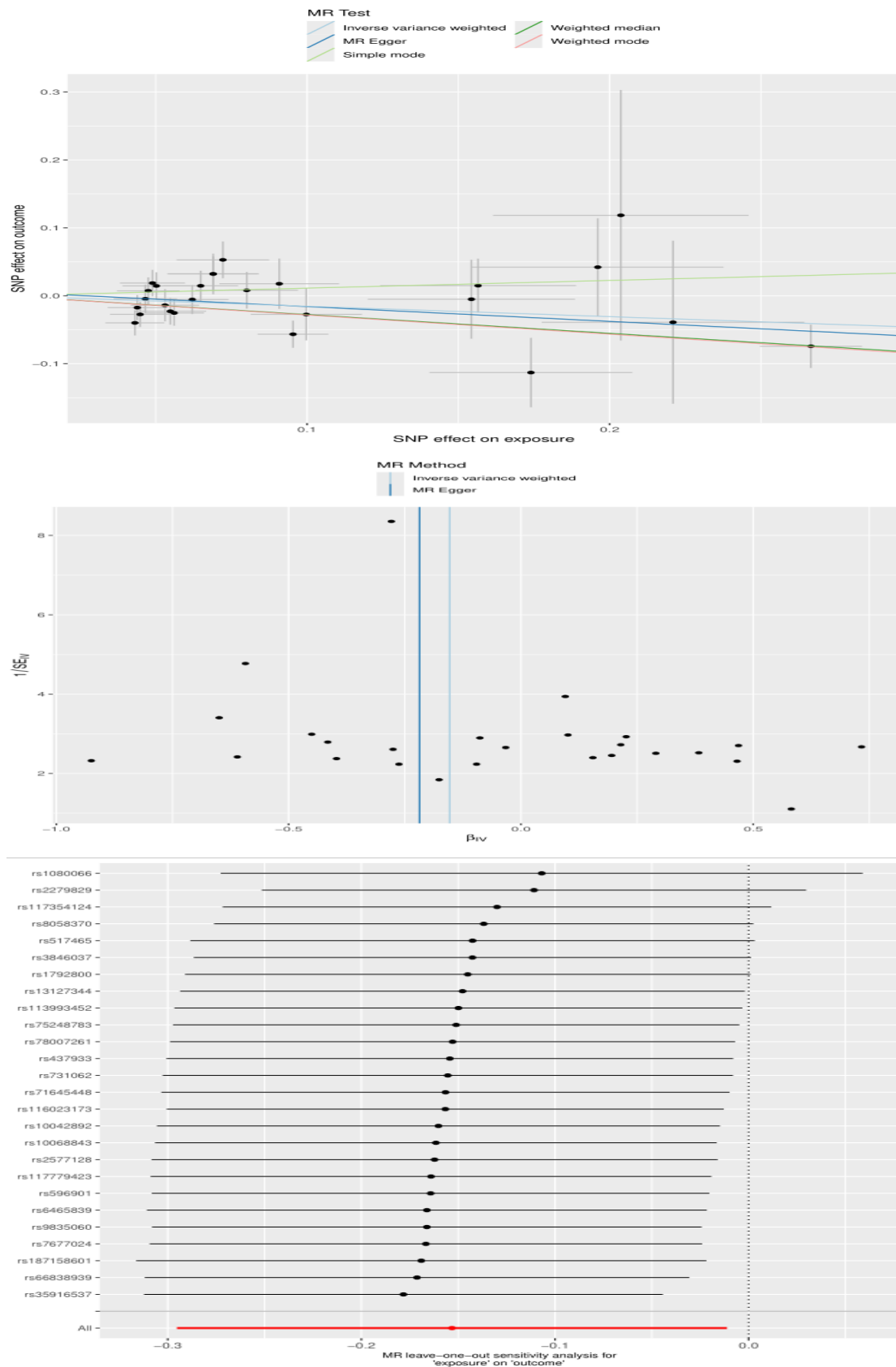
**Supplementary Figure 1.** Flow chart of two-step UVMR mediation analysis.



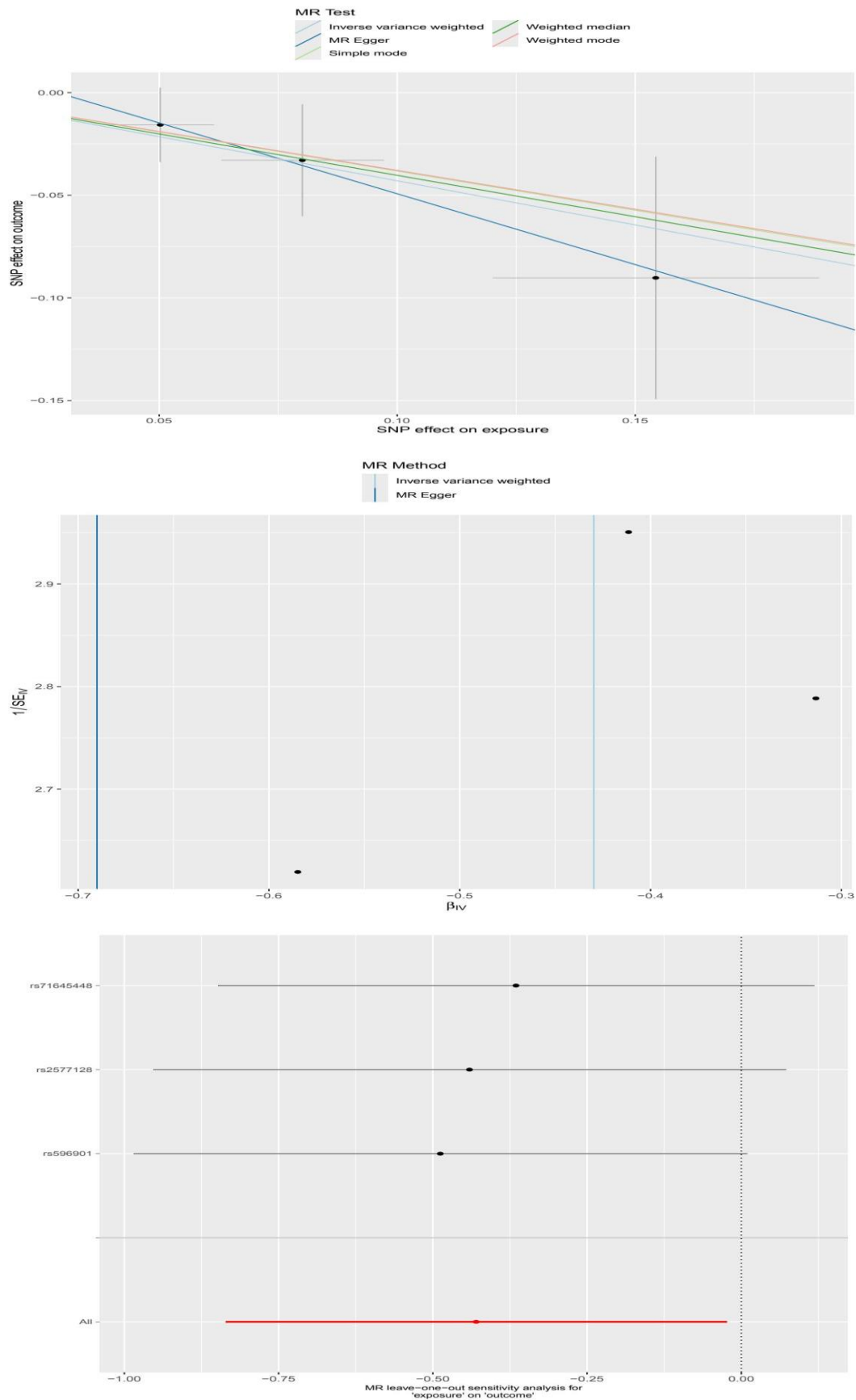
**Supplementary Figure 2.** Quantile-quantile (Q-Q) plot of OP GWAS. The Q-Q plot demonstrates the number and magnitude of observed associations between genotyped SNPs and OP compared to the expected association statistics under the null hypothesis that there is no association. The identity line is shown in red. Observed association statistics (y-axis) and expected association statistics (x-axis) are on a  $-\log$   $P$  scale.



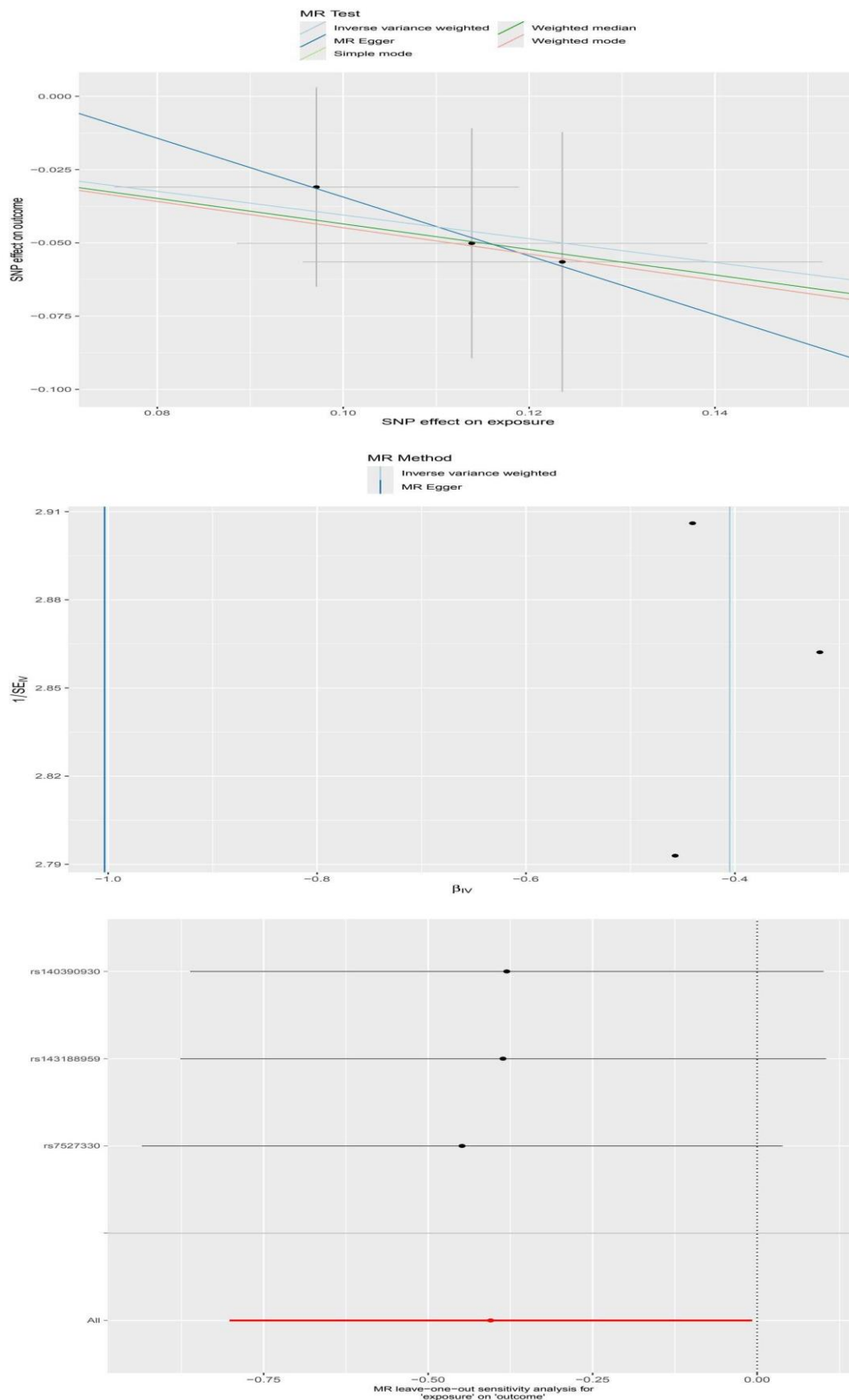
**Supplementary Figure 3.** MR analysis of eQTL and OP summary data of 6 Pleiotropic genes.



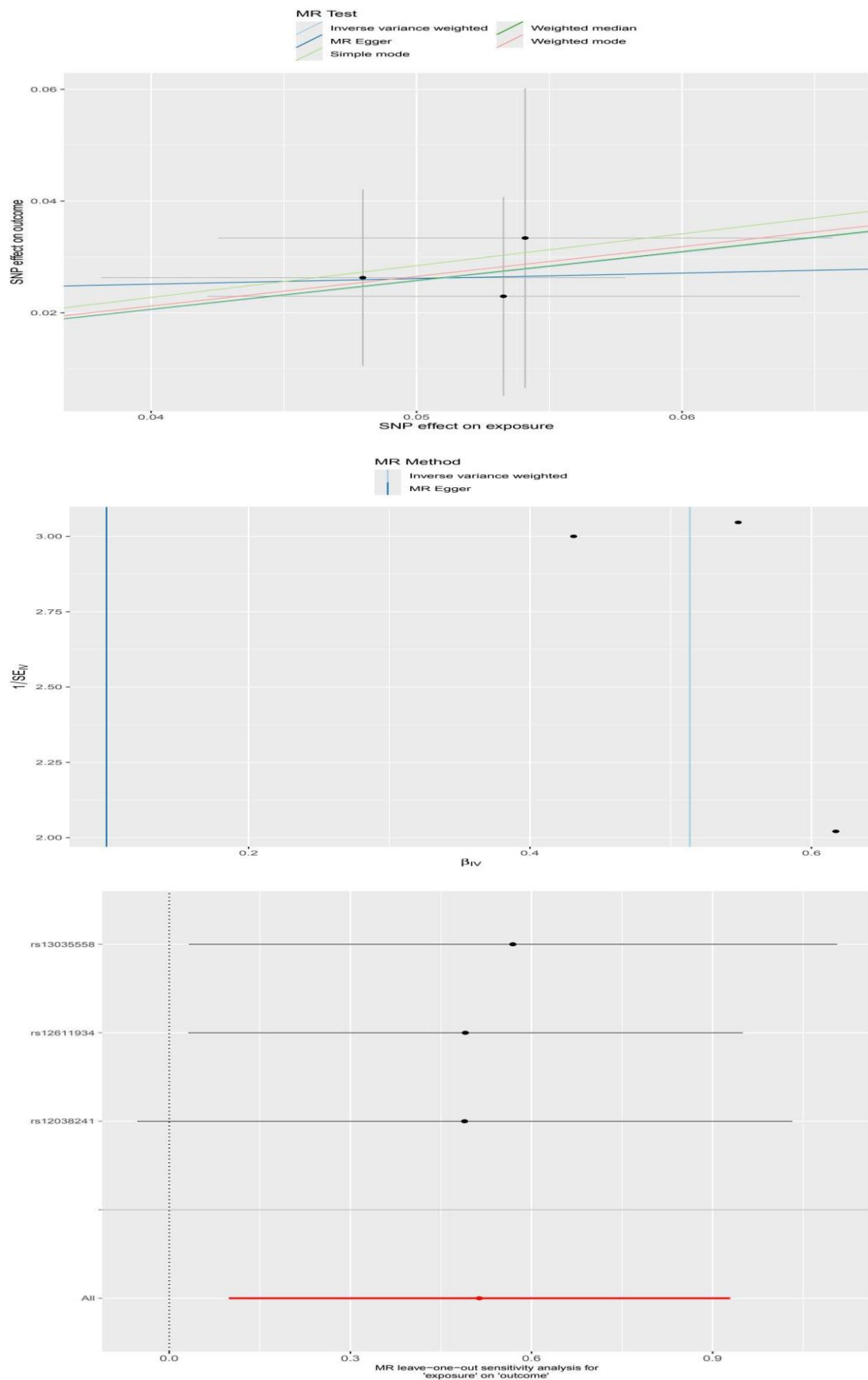
**Supplementary Figure 4.** Scatter plot, funnel plot and leave-one-out plot with GCST90003162 as exposure and OP as outcome.



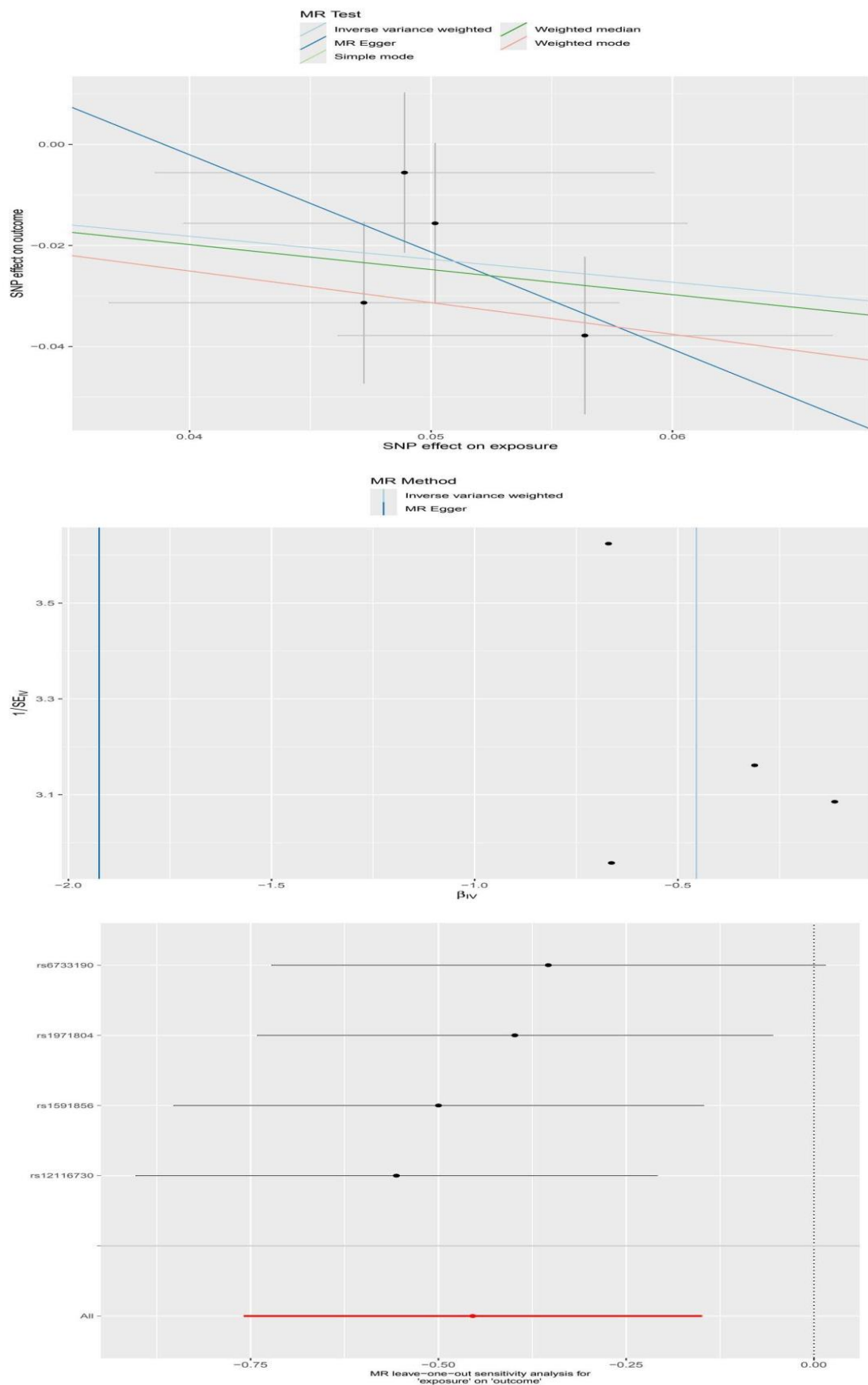
**Supplementary Figure 5.** Scatter plot, funnel plot and leave-one-out plot with GCST90003162 as exposure and Forearm BMD as outcome.



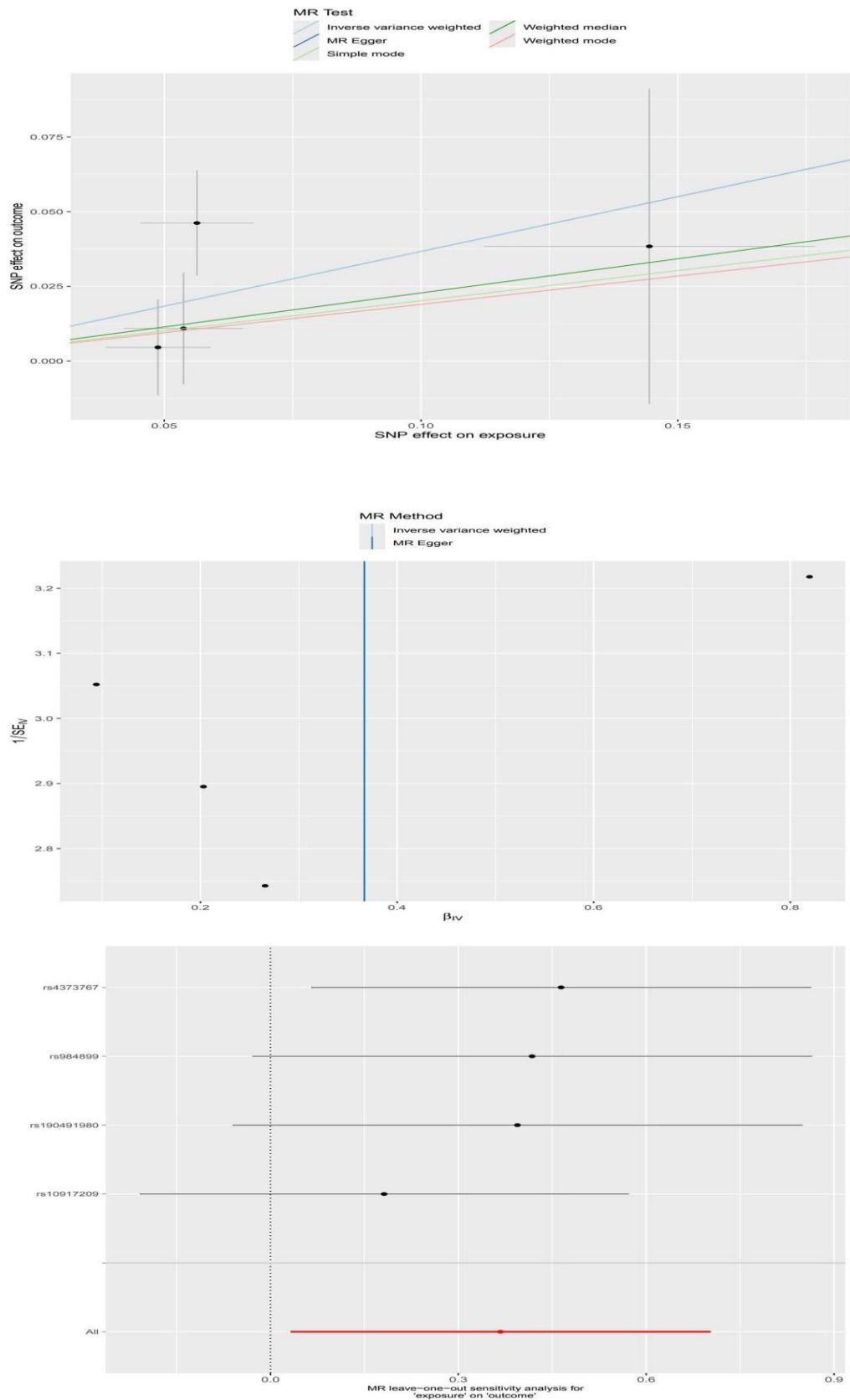
**Supplementary Figure 6.** Scatter plot, funnel plot and leave-one-out plot with GCST90003158 as exposure and Forearm BMD as outcome.



**Supplementary Figure 7.** Scatter plot, funnel plot and leave-one-out plot with GCST90002612 as exposure and Forearm BMD as outcome.

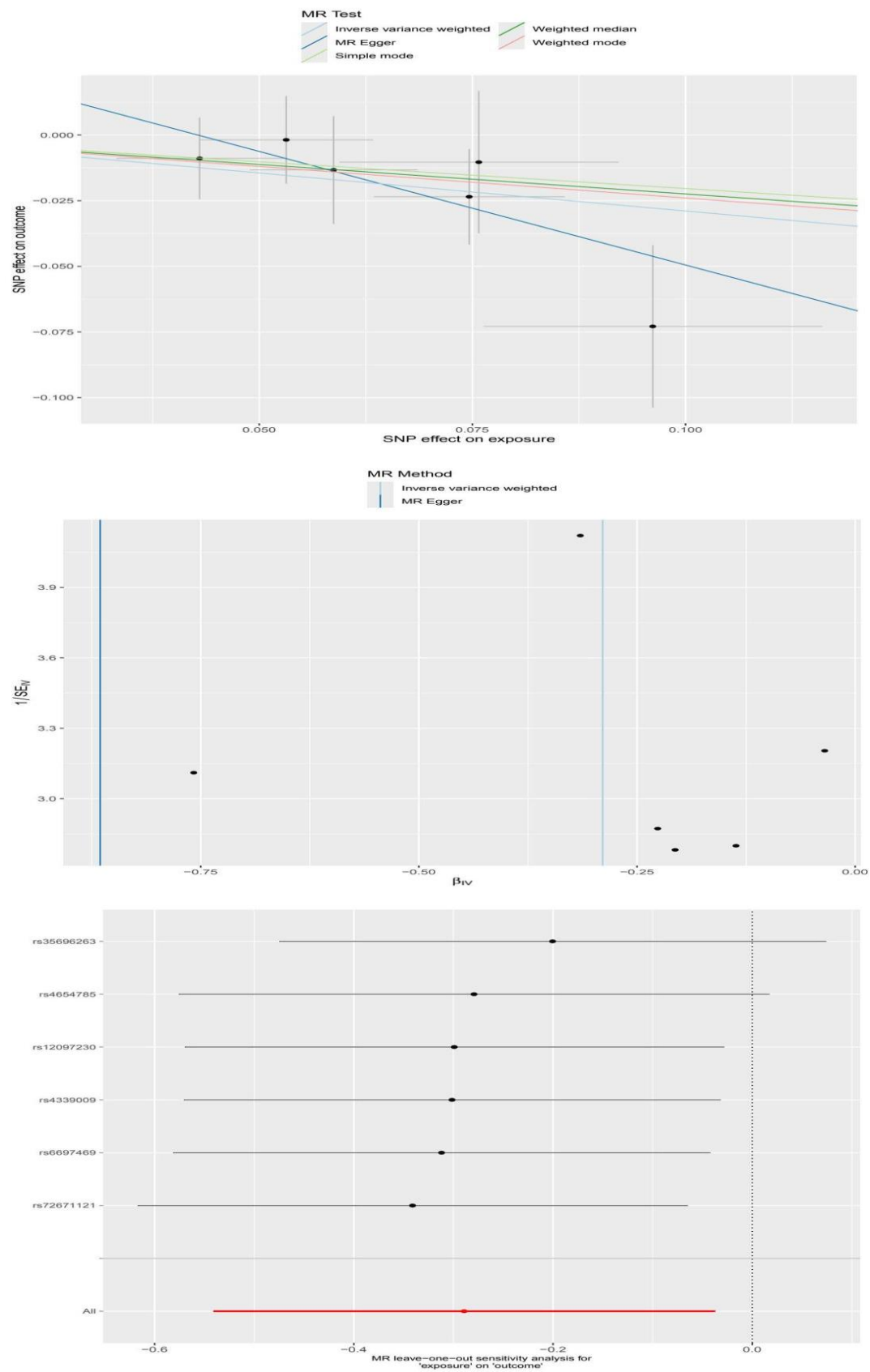


**Supplementary Figure 8.** Scatter plot, funnel plot and leave-one-out plot with GCST90006352 as exposure and Forearm BMD as outcome.

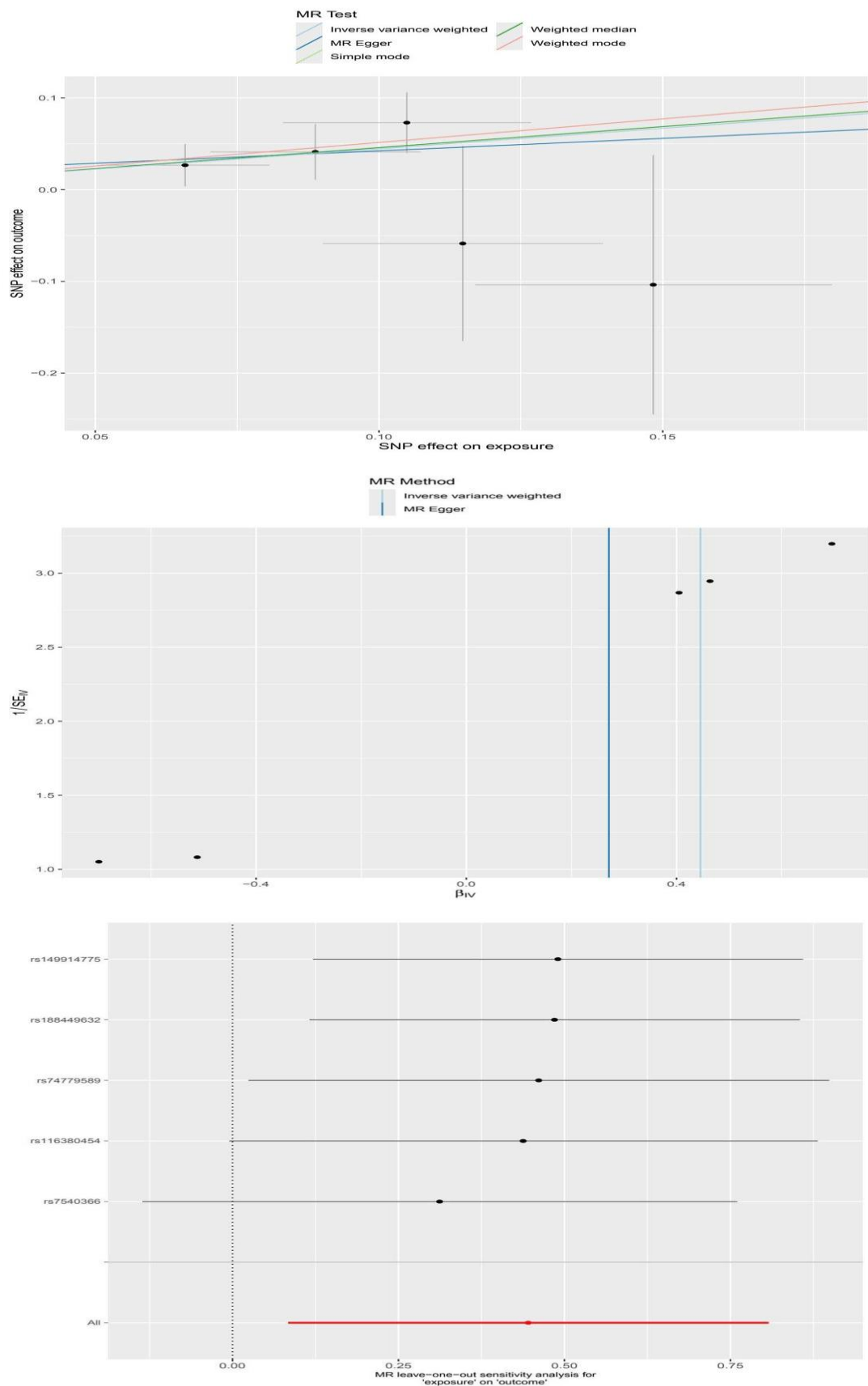


**Supplementary Figure 9.** Scatter plot, funnel plot and leave-one-out plot with GCST90002729 as exposure and Forearm BMD as outcome.

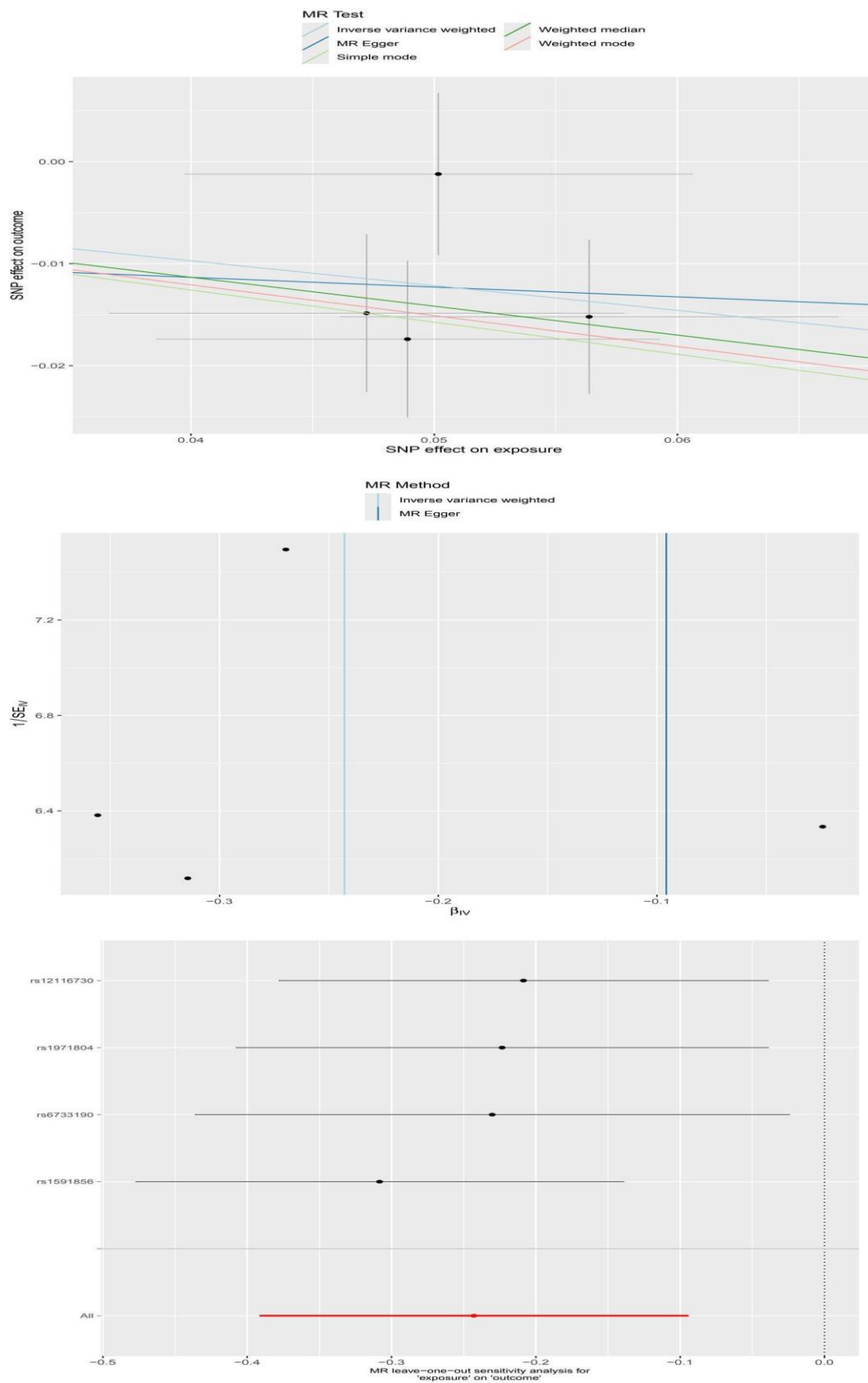




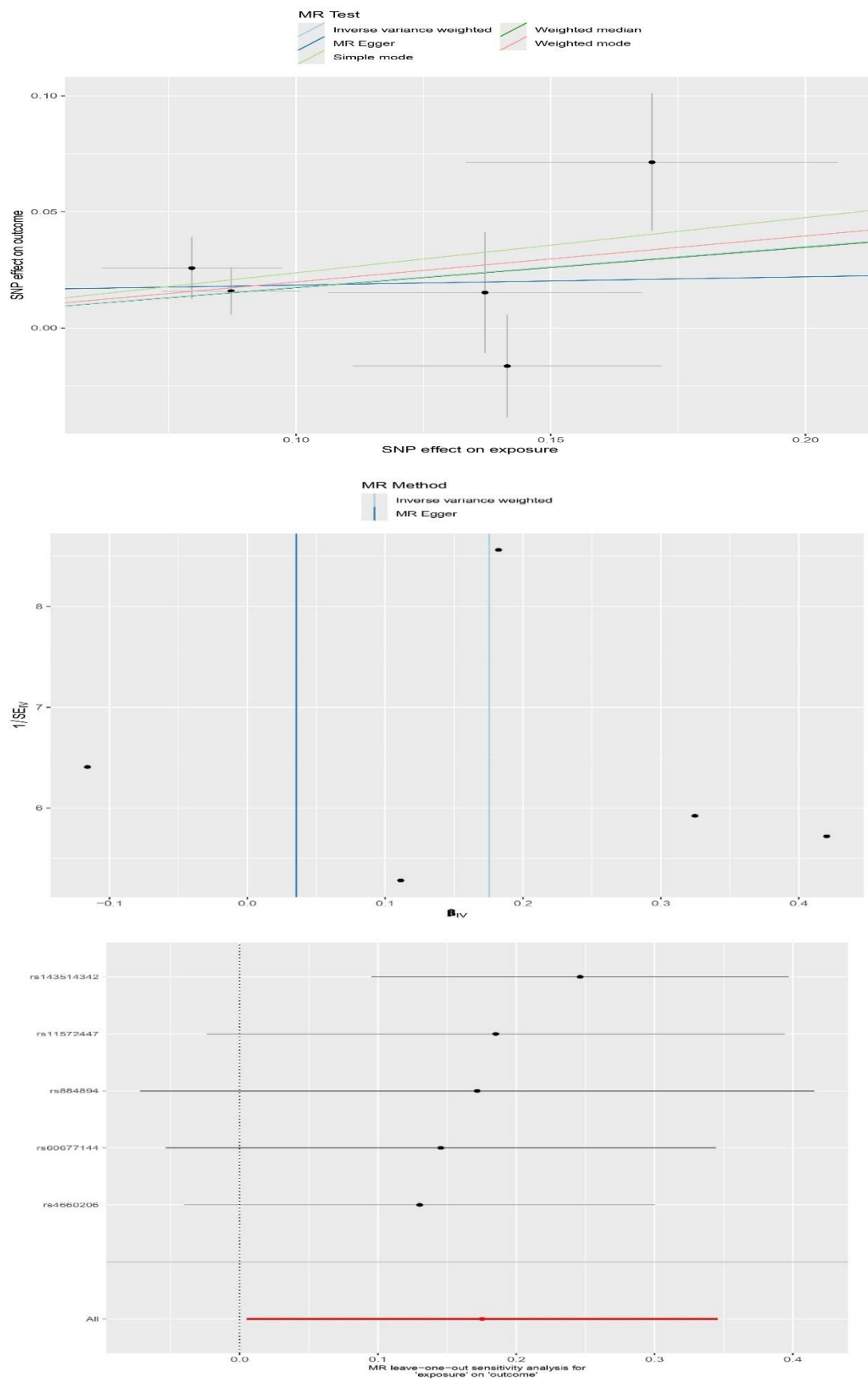
**Supplementary Figure 10.** Scatter plot, funnel plot and leave-one-out plot with GCST90003361 as exposure and Forearm BMD as outcome.



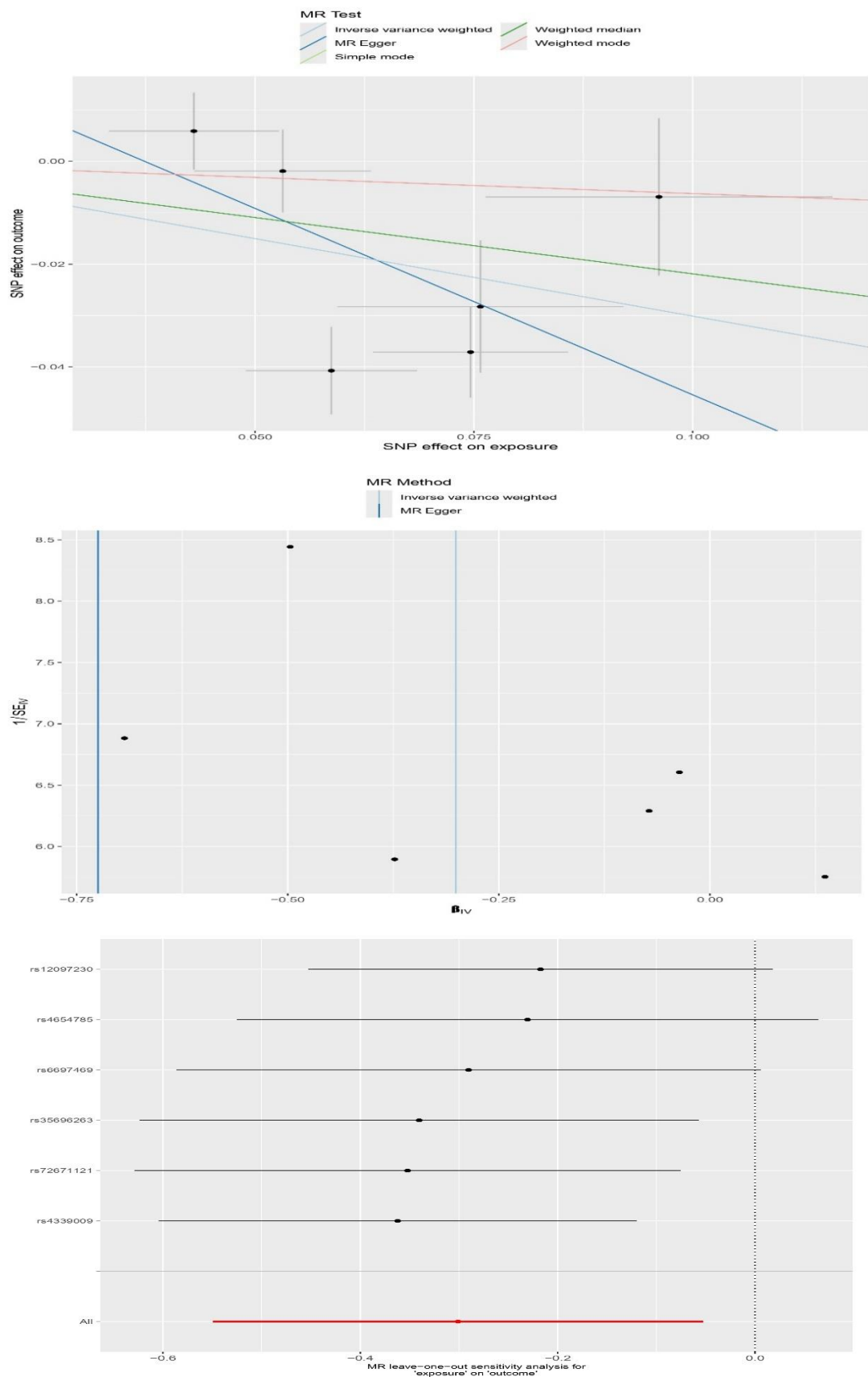
**Supplementary Figure 11.** Scatter plot, funnel plot and leave-one-out plot with GCST90003764 as exposure and Forearm BMD as outcome.



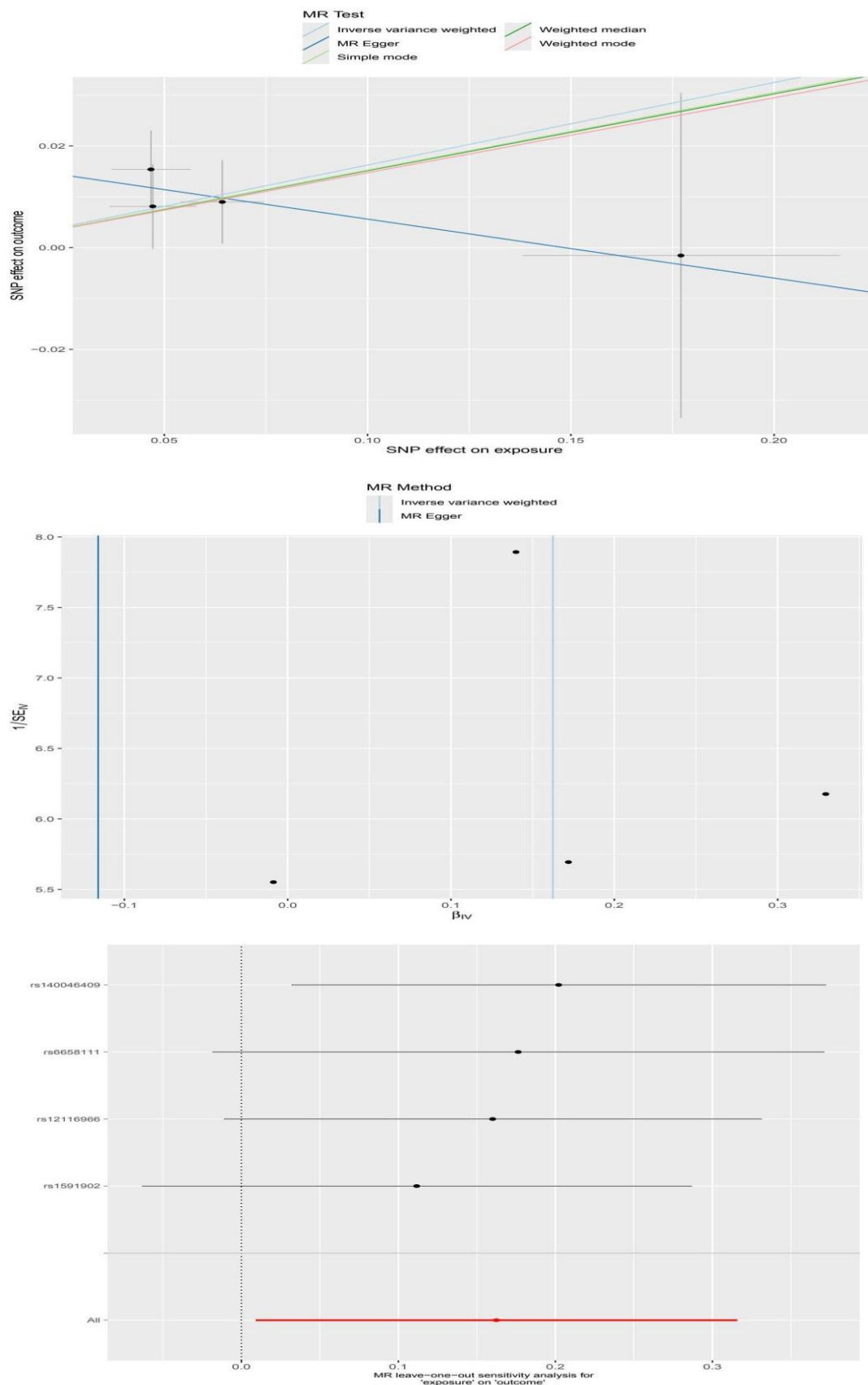
**Supplementary Figure 12.** Scatter plot, funnel plot and leave-one-out plot with GCST90006352 as exposure and Femoral neck BMD as outcome.



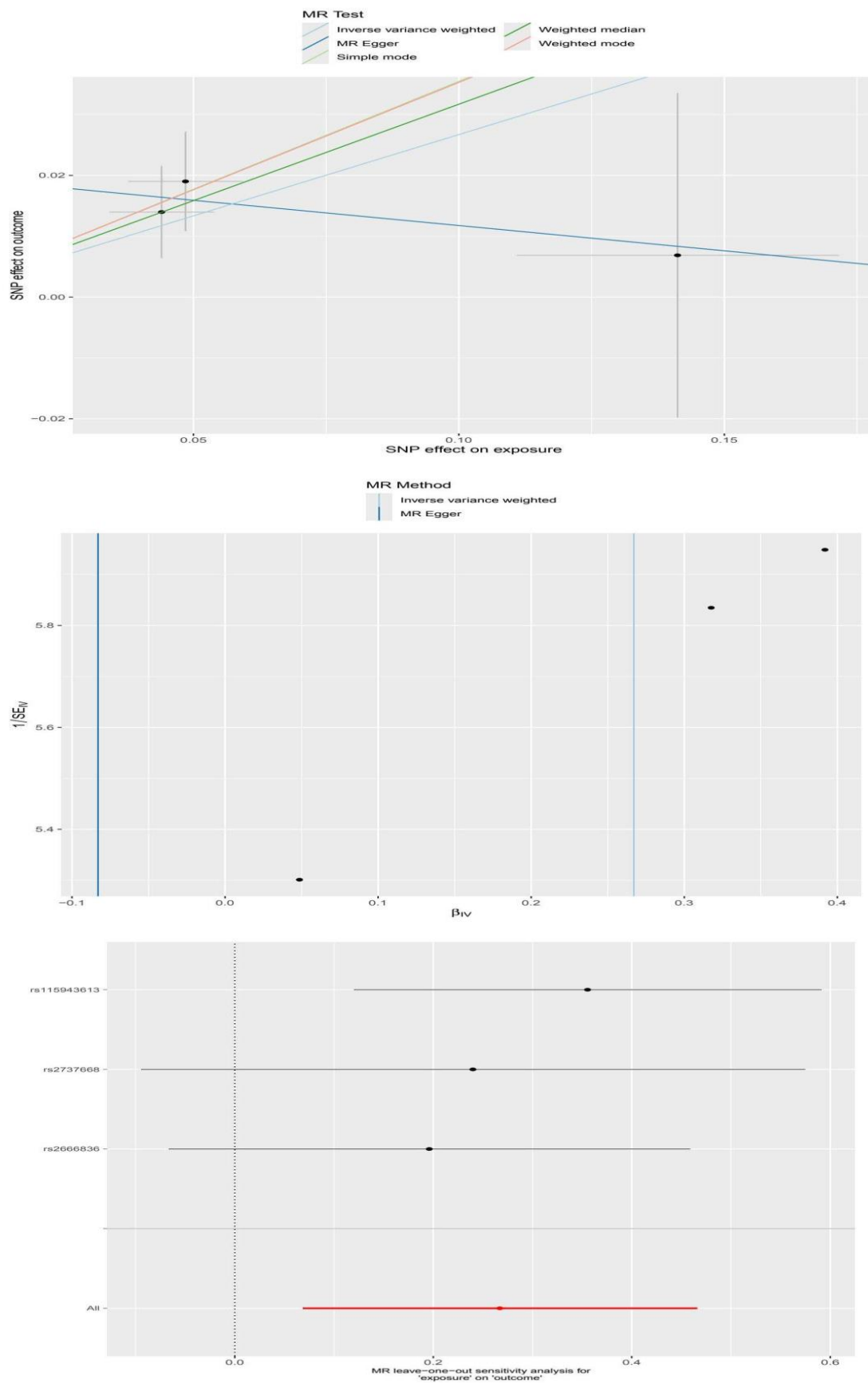
**Supplementary Figure 13.** Scatter plot, funnel plot and leave-one-out plot with GCST90002729 as exposure and Femoral neck BMD as outcome.



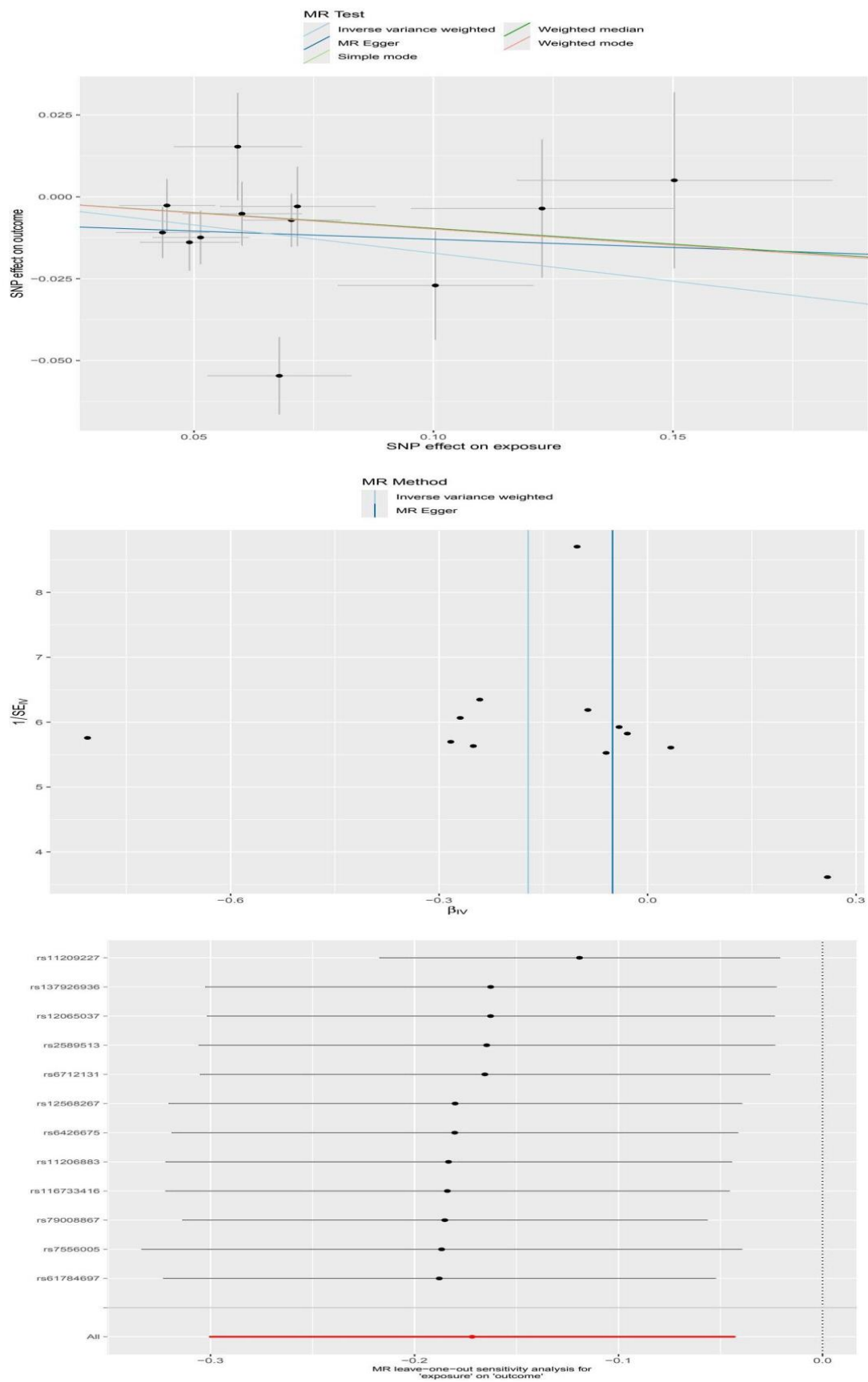
**Supplementary Figure 14.** Scatter plot, funnel plot and leave-one-out plot with GCST90003122 as exposure and Femoral neck BMD as outcome.



**Supplementary Figure 15.** Scatter plot, funnel plot and leave-one-out plot with GCST90002612 as exposure and Femoral neck BMD as outcome.

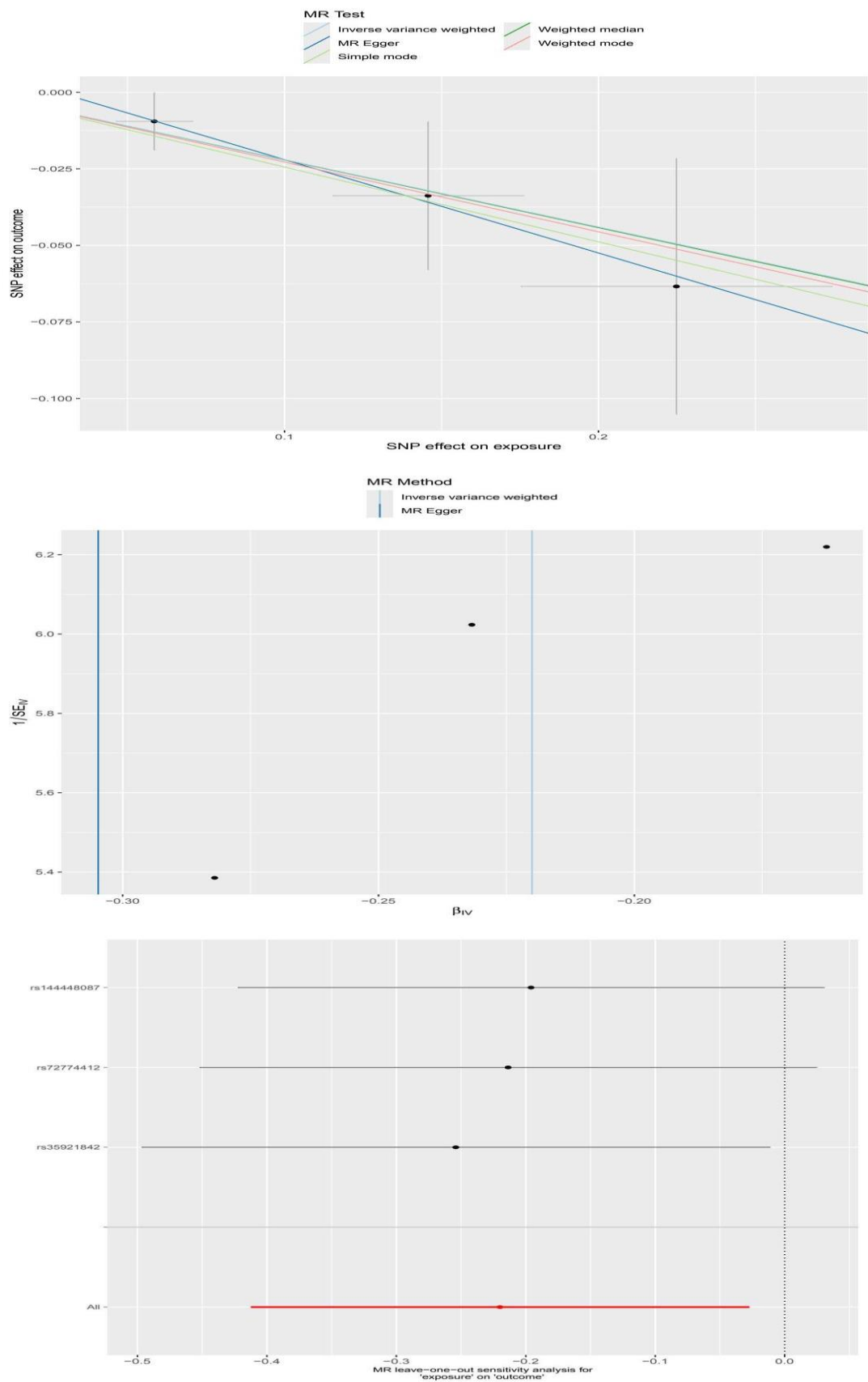


**Supplementary Figure 16.** Scatter plot, funnel plot and leave-one-out plot with GCST90003883 as exposure and Femoral neck BMD as outcome.

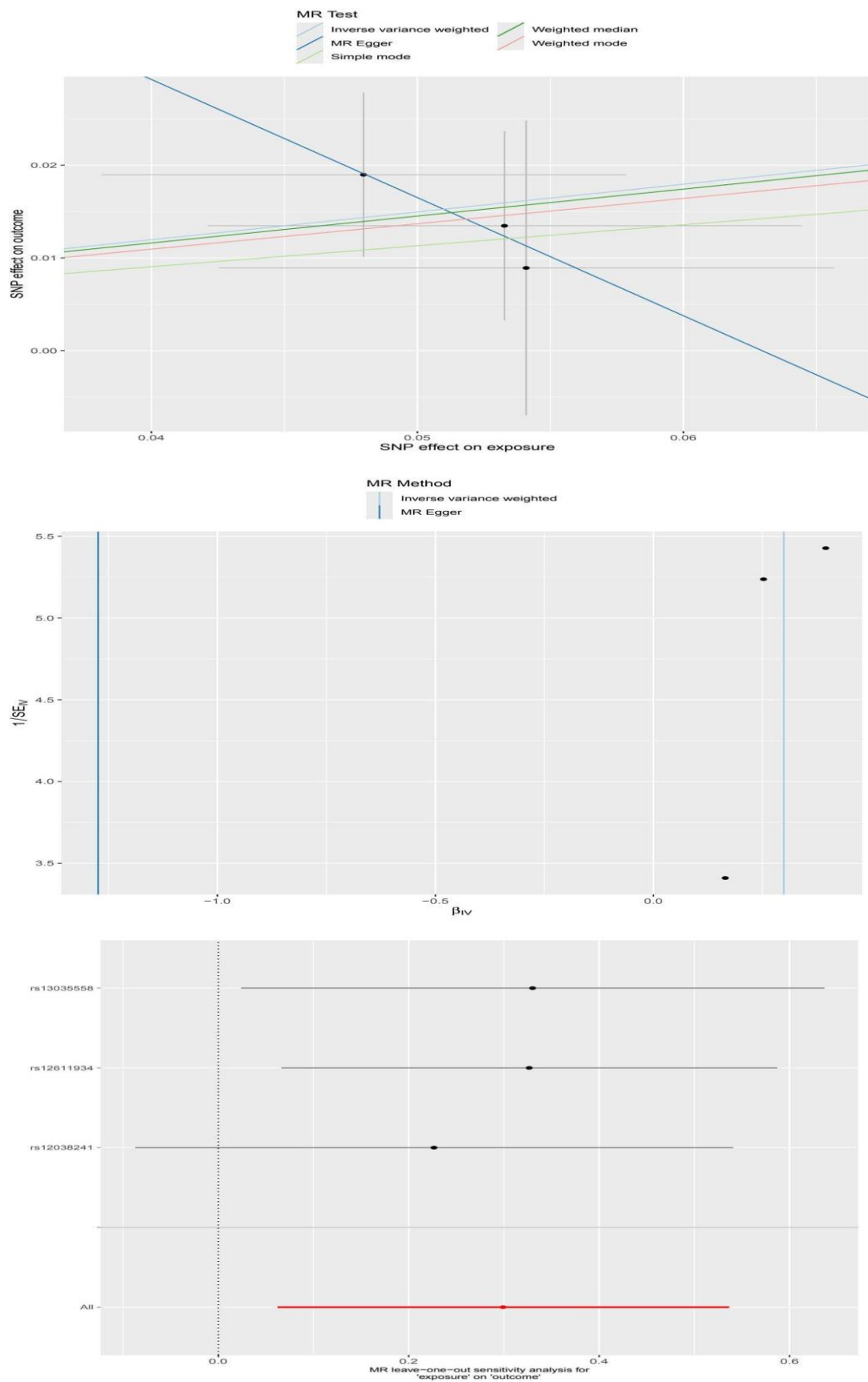


**Supplementary Figure 17.** Scatter plot, funnel plot and leave-one-out plot with GCST90006346 as exposure and Femoral neck BMD as outcome.

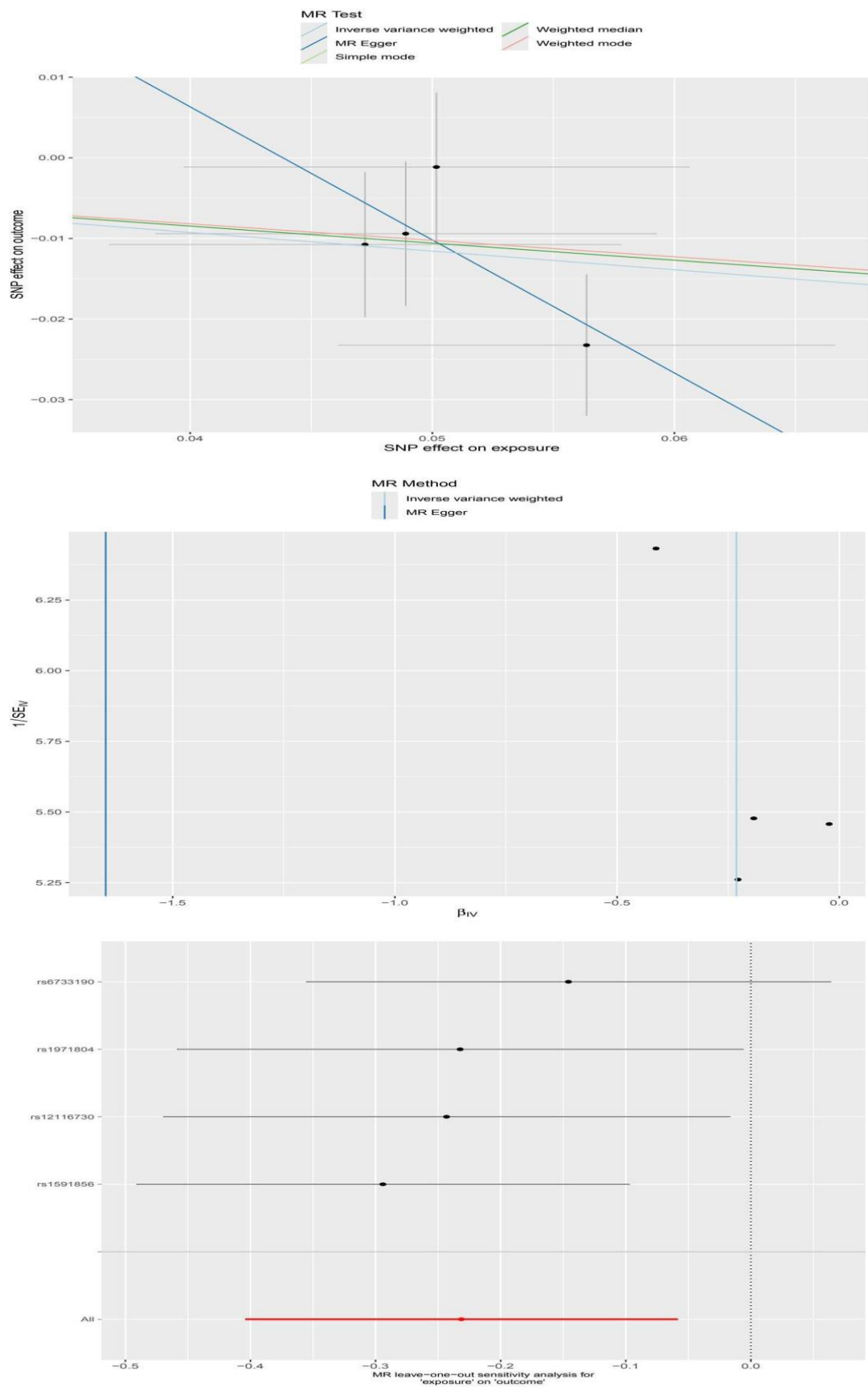




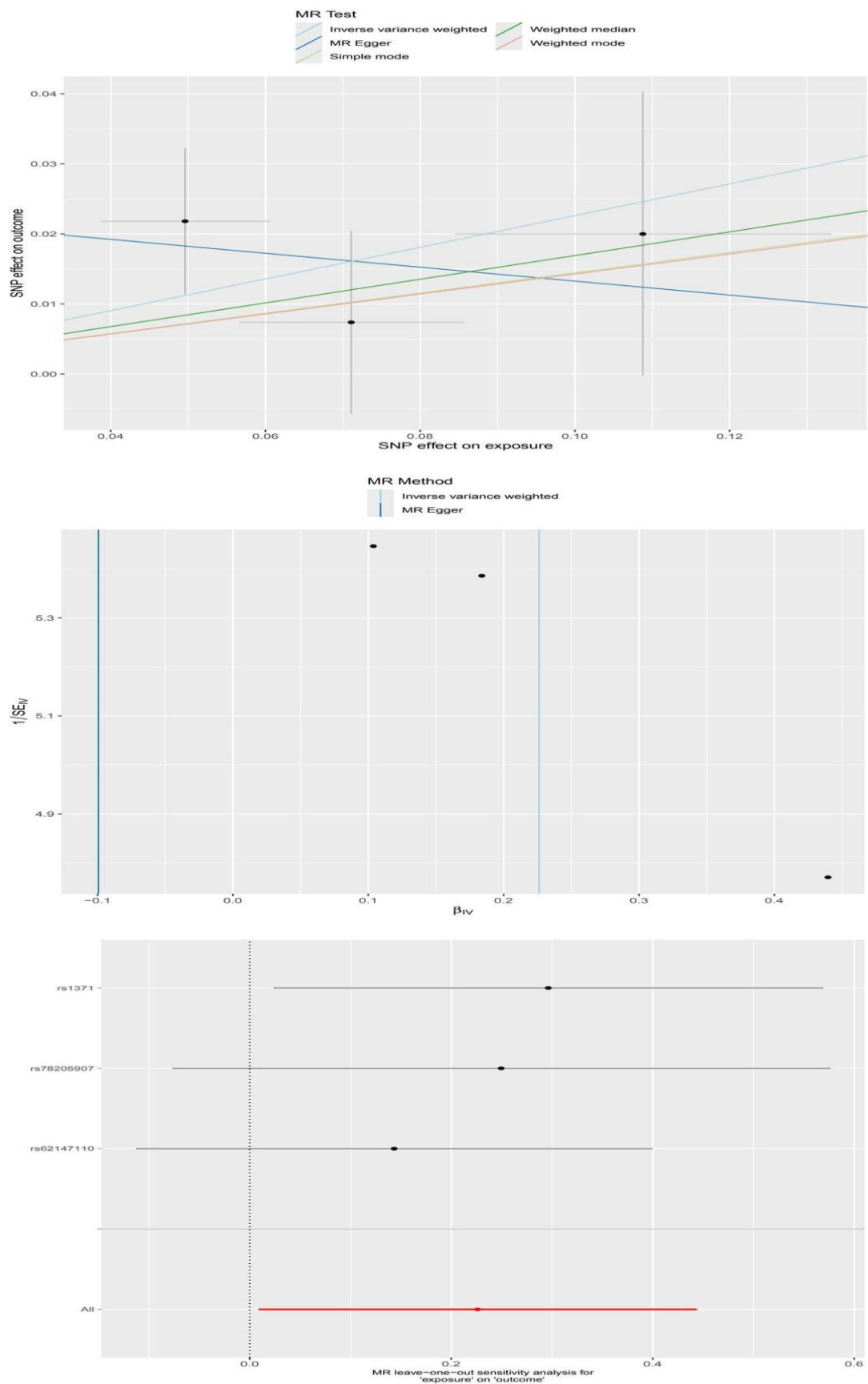
**Supplementary Figure 18.** Scatter plot, funnel plot and leave-one-out plot with GCST90003670 as exposure and Femoral neck BMD as outcome.



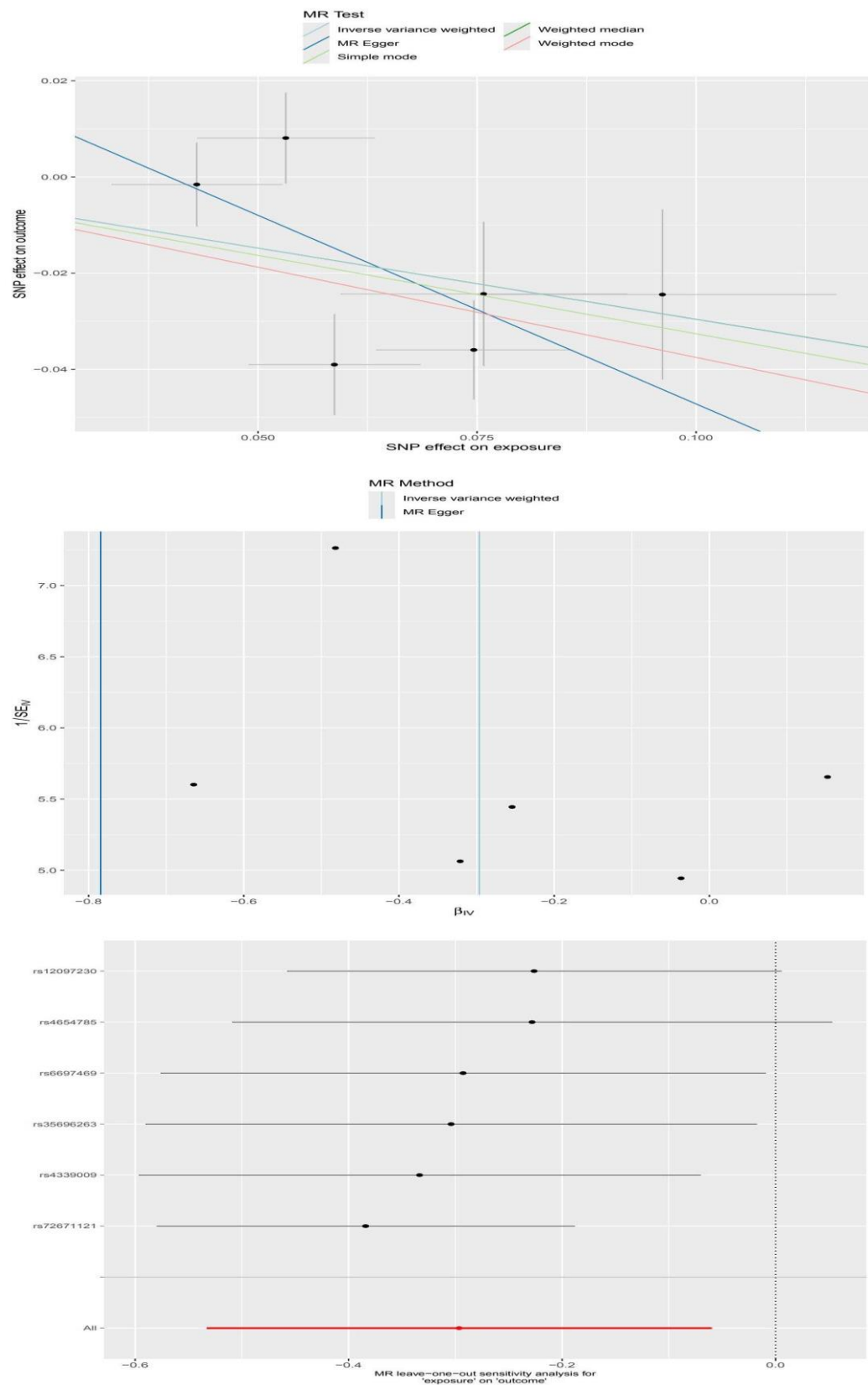
**Supplementary Figure 19.** Scatter plot, funnel plot and leave-one-out plot with GCST90002612 as exposure and Lumbar spine BMD as outcome.



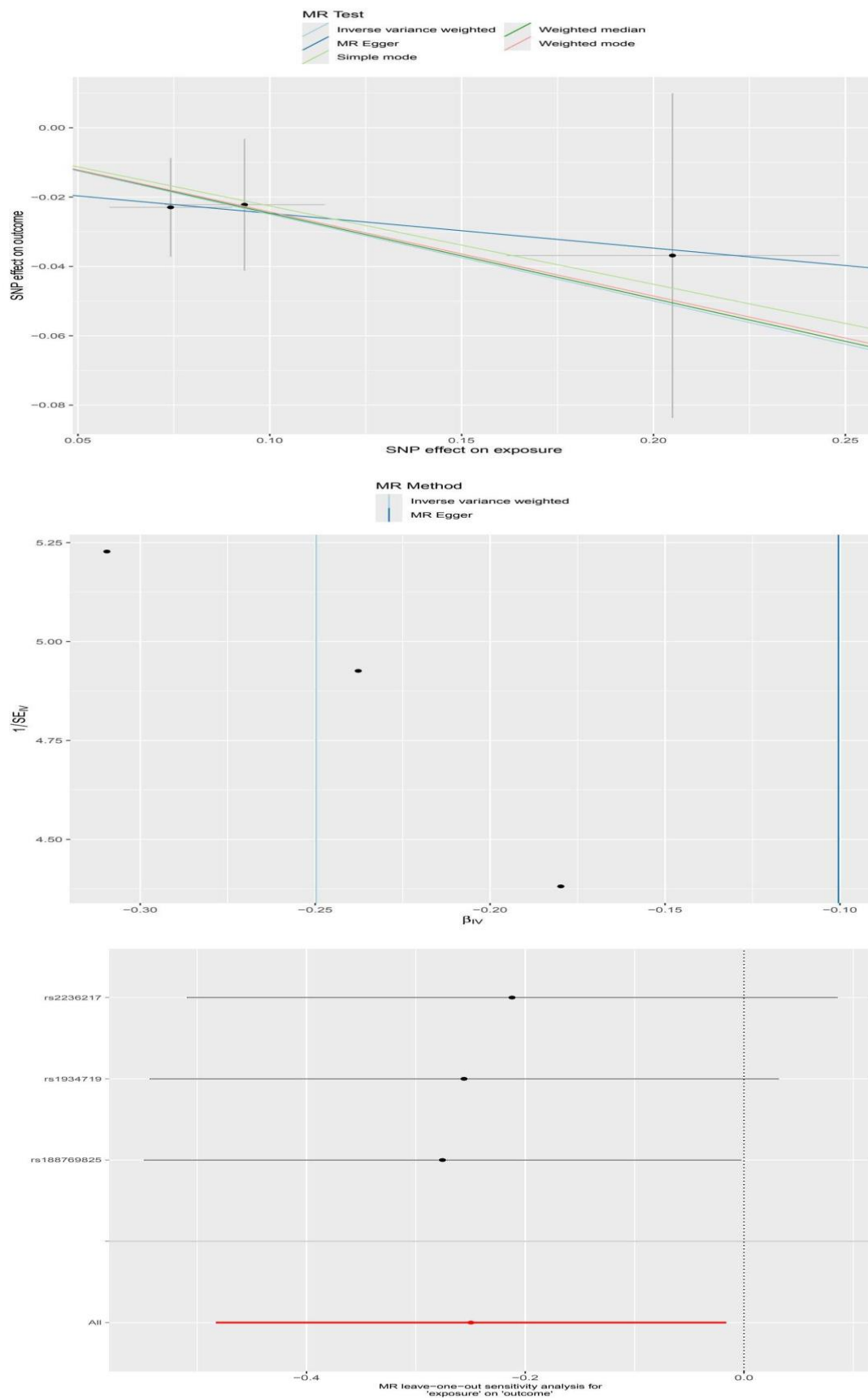
**Supplementary Figure 20.** Scatter plot, funnel plot and leave-one-out plot with GCST90006352 as exposure and Lumbar spine BMD as outcome.



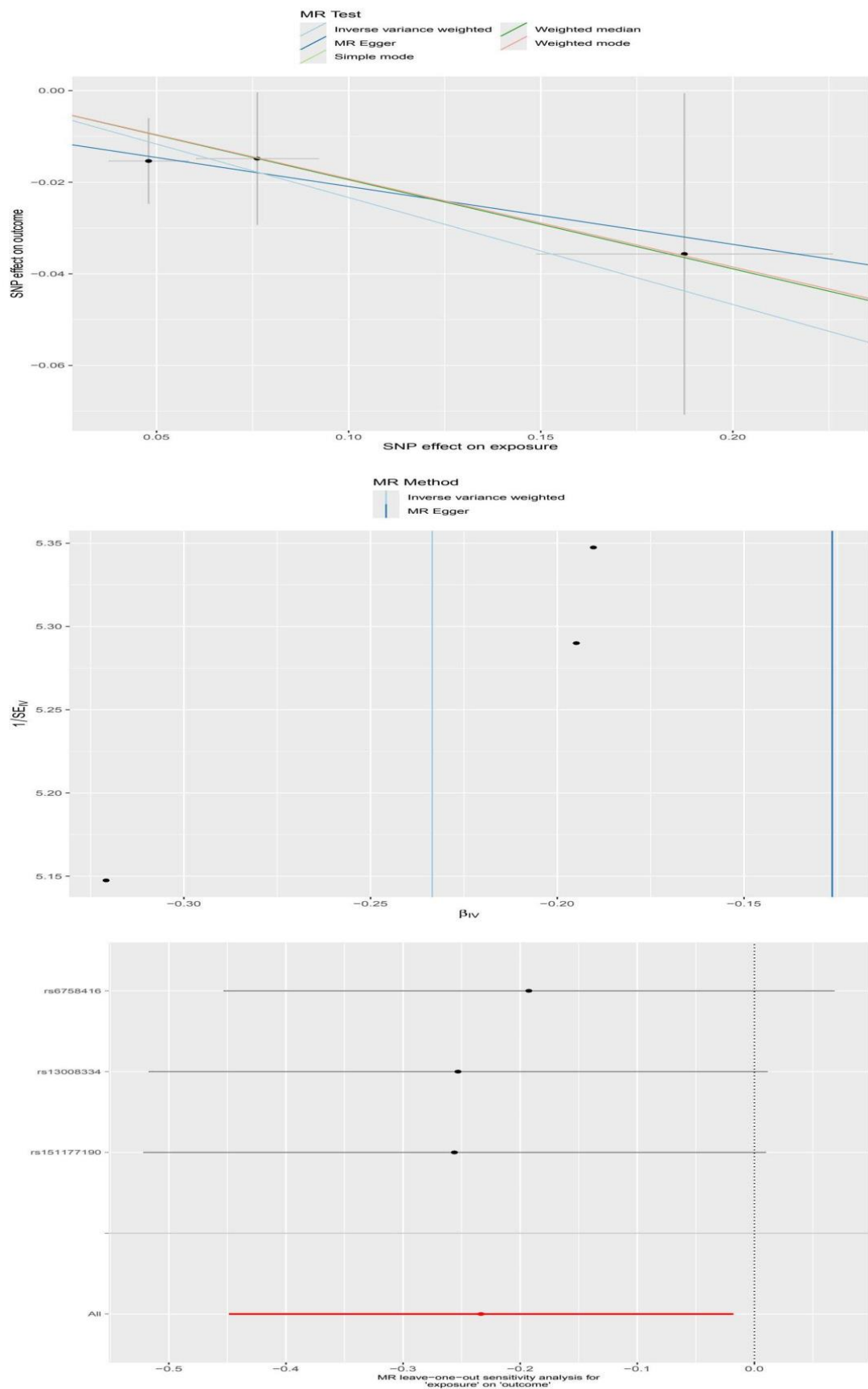
**Supplementary Figure 21.** Scatter plot, funnel plot and leave-one-out plot with GCST90002729 as exposure and Lumbar spine BMD as outcome.



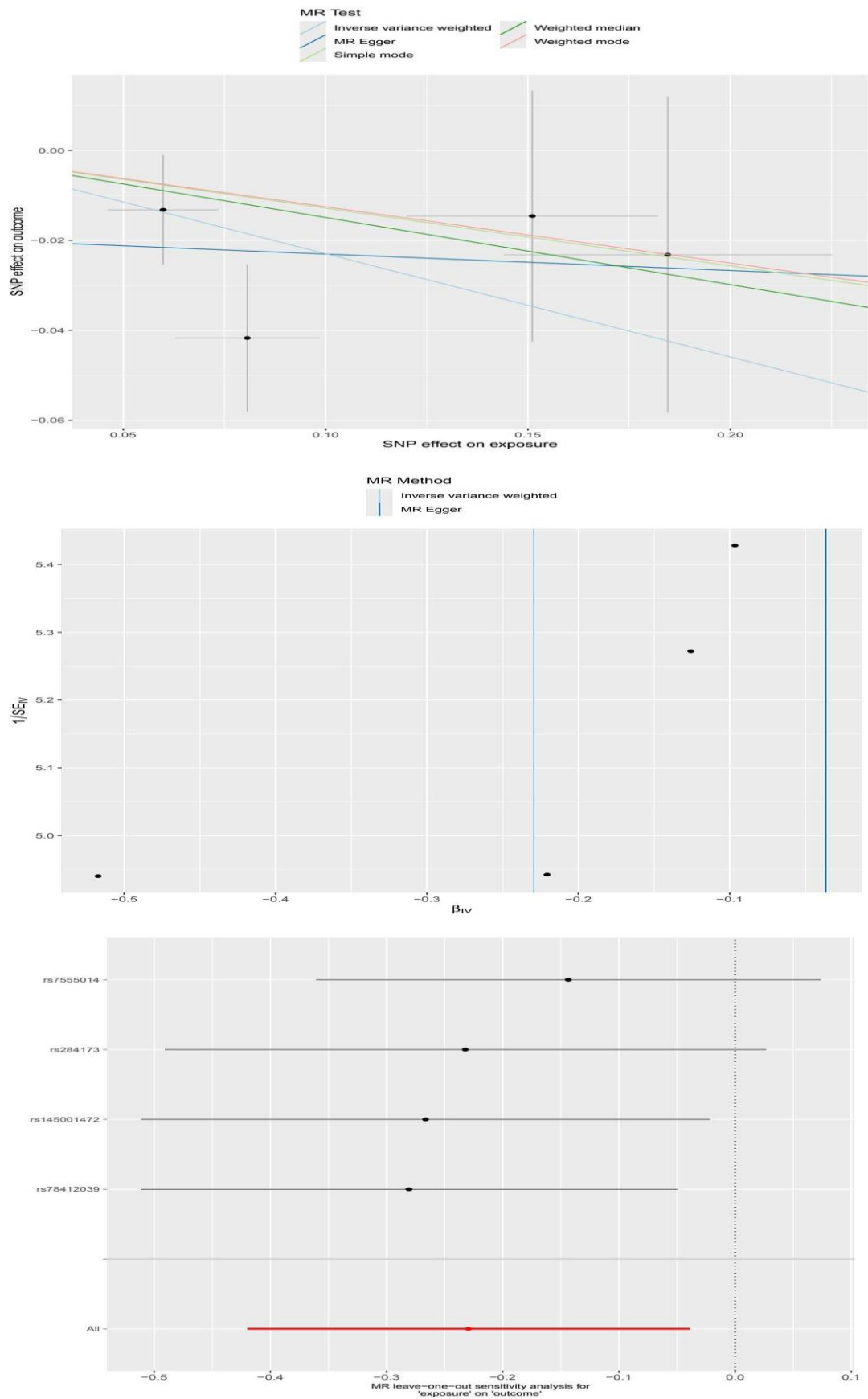
**Supplementary Figure 22.** Scatter plot, funnel plot and leave-one-out plot with GCST90003361 as exposure and Lumbar spine BMD as outcome.



**Supplementary Figure 23.** Scatter plot, funnel plot and leave-one-out plot with GCST90002686 as exposure and Lumbar spine BMD as outcome.

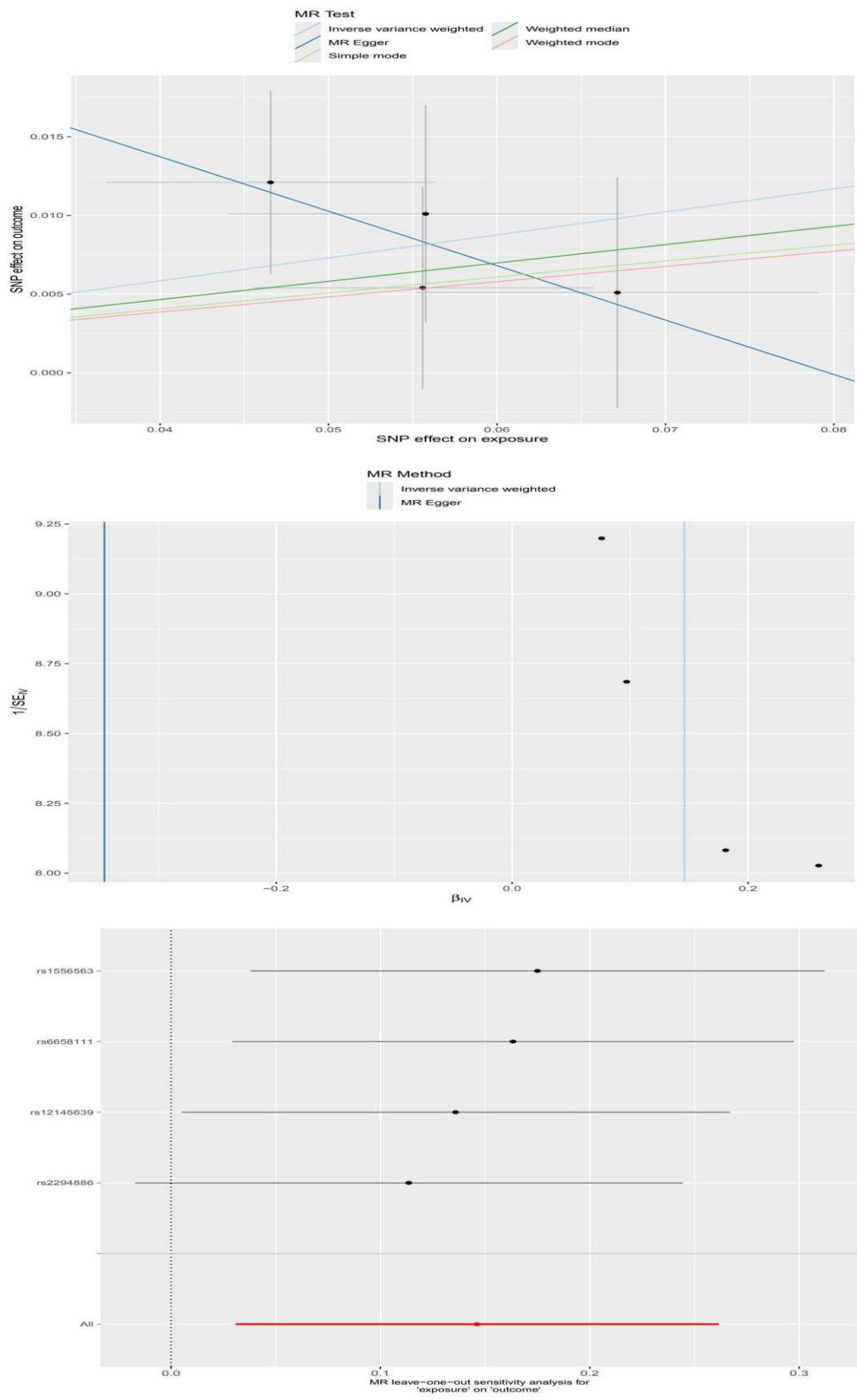


**Supplementary Figure 24.** Scatter plot, funnel plot and leave-one-out plot with GCST90004325 as exposure and Lumbar spine BMD as outcome.

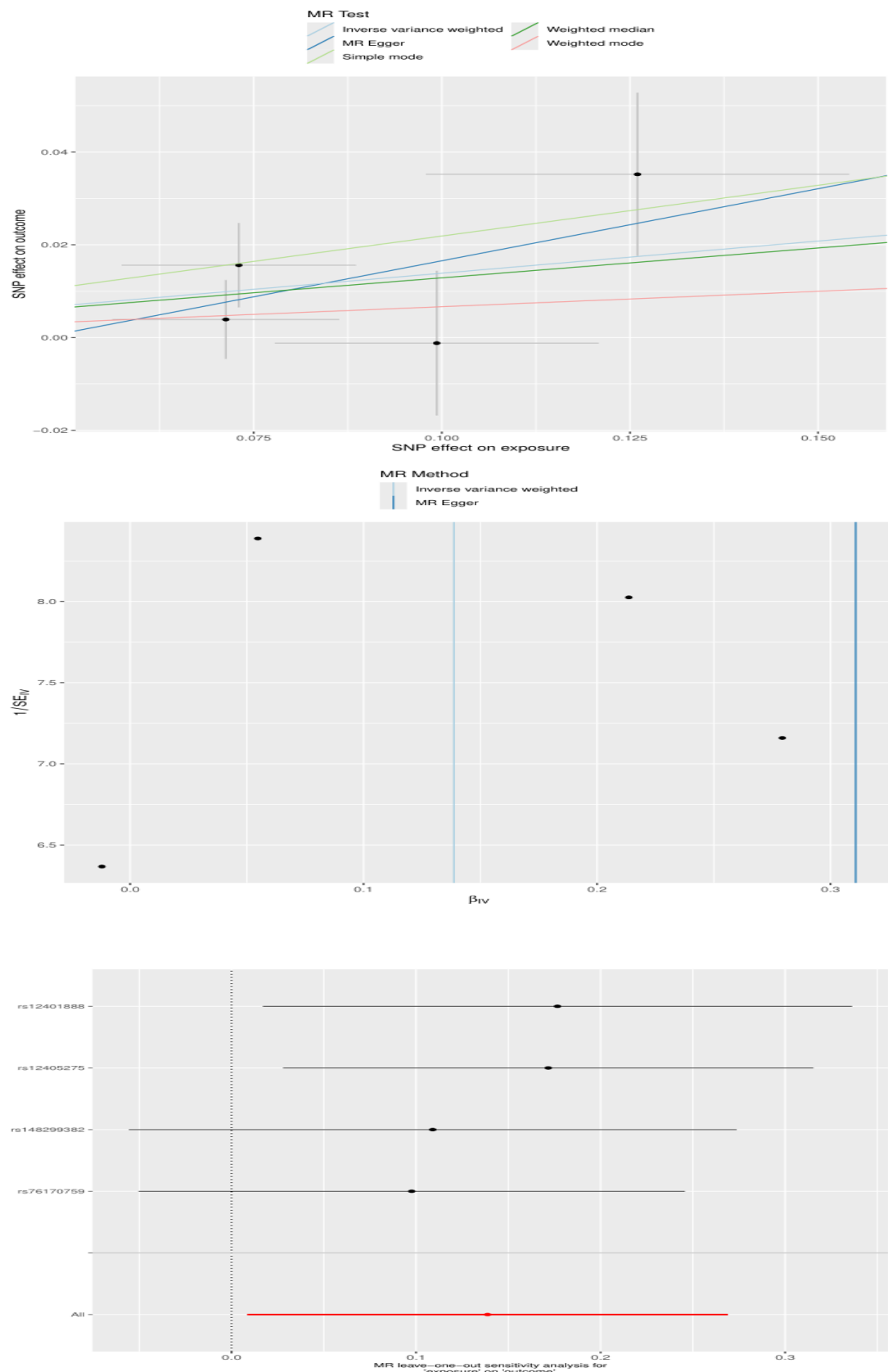


**Supplementary Figure 25.** Scatter plot, funnel plot and leave-one-out plot with GCST90004235 as exposure and Lumbar spine BMD as outcome.

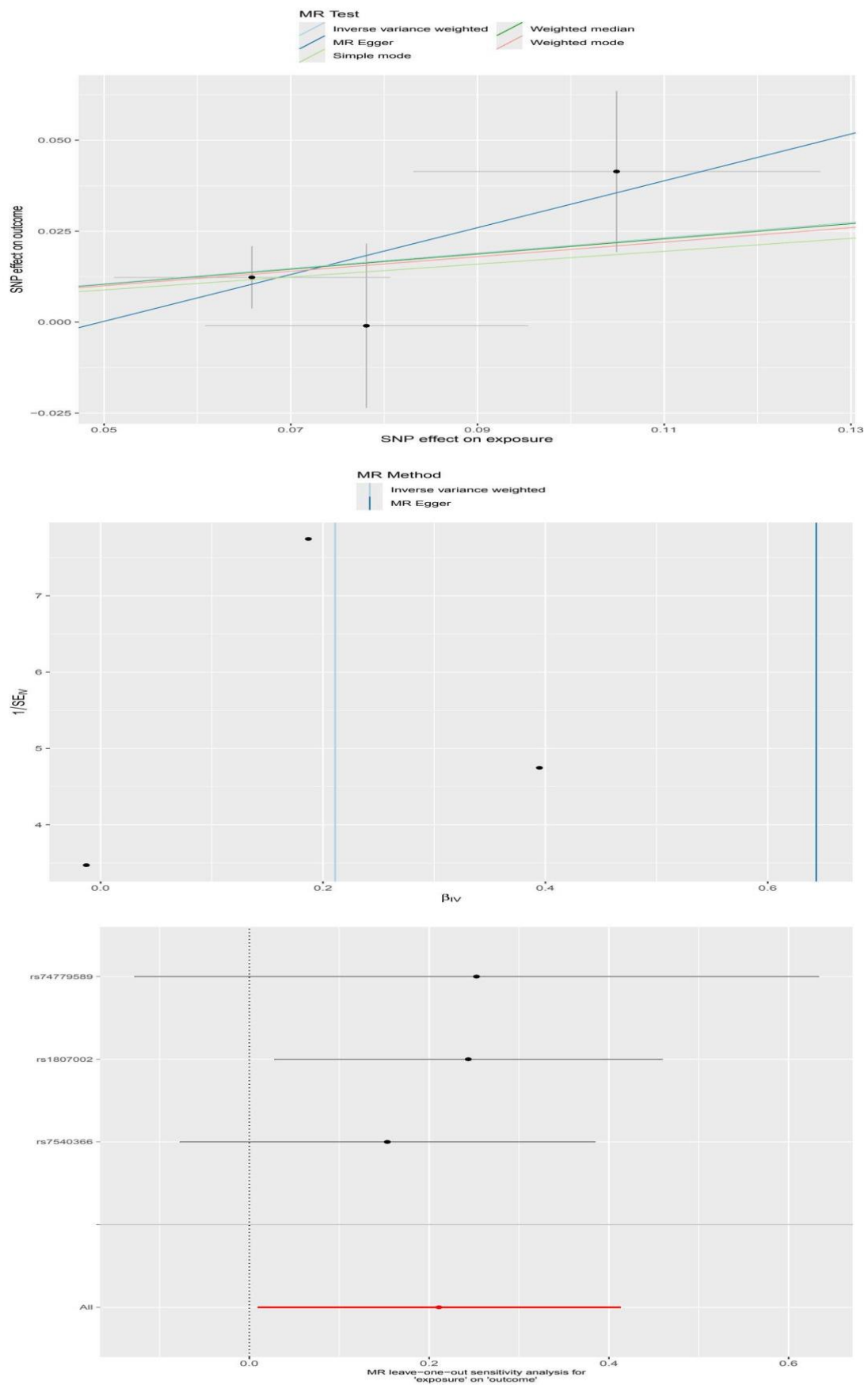




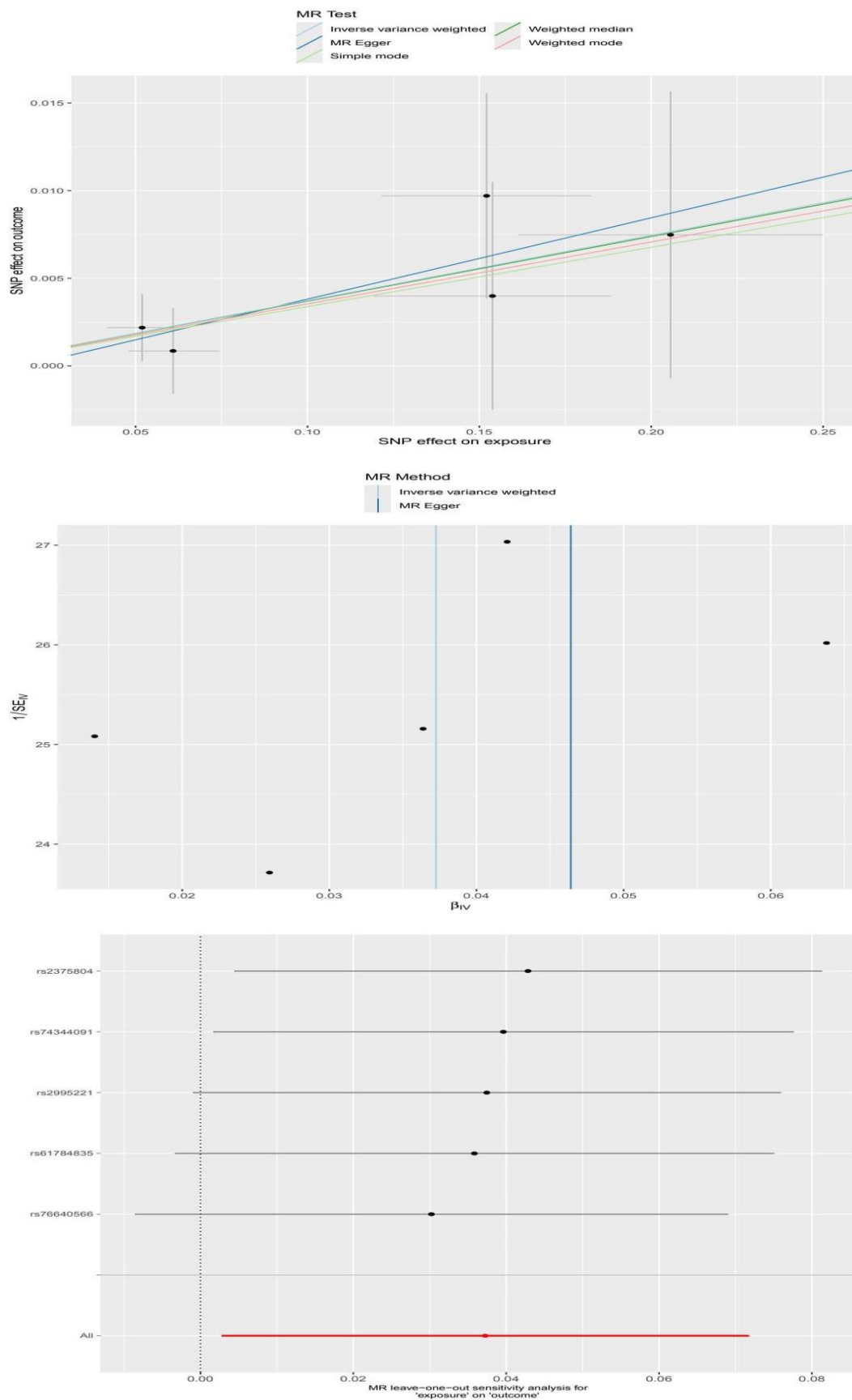
**Supplementary Figure 26.** Scatter plot, funnel plot and leave-one-out plot with GCST90002729 as exposure and TOTAL BODY BMD as outcome.



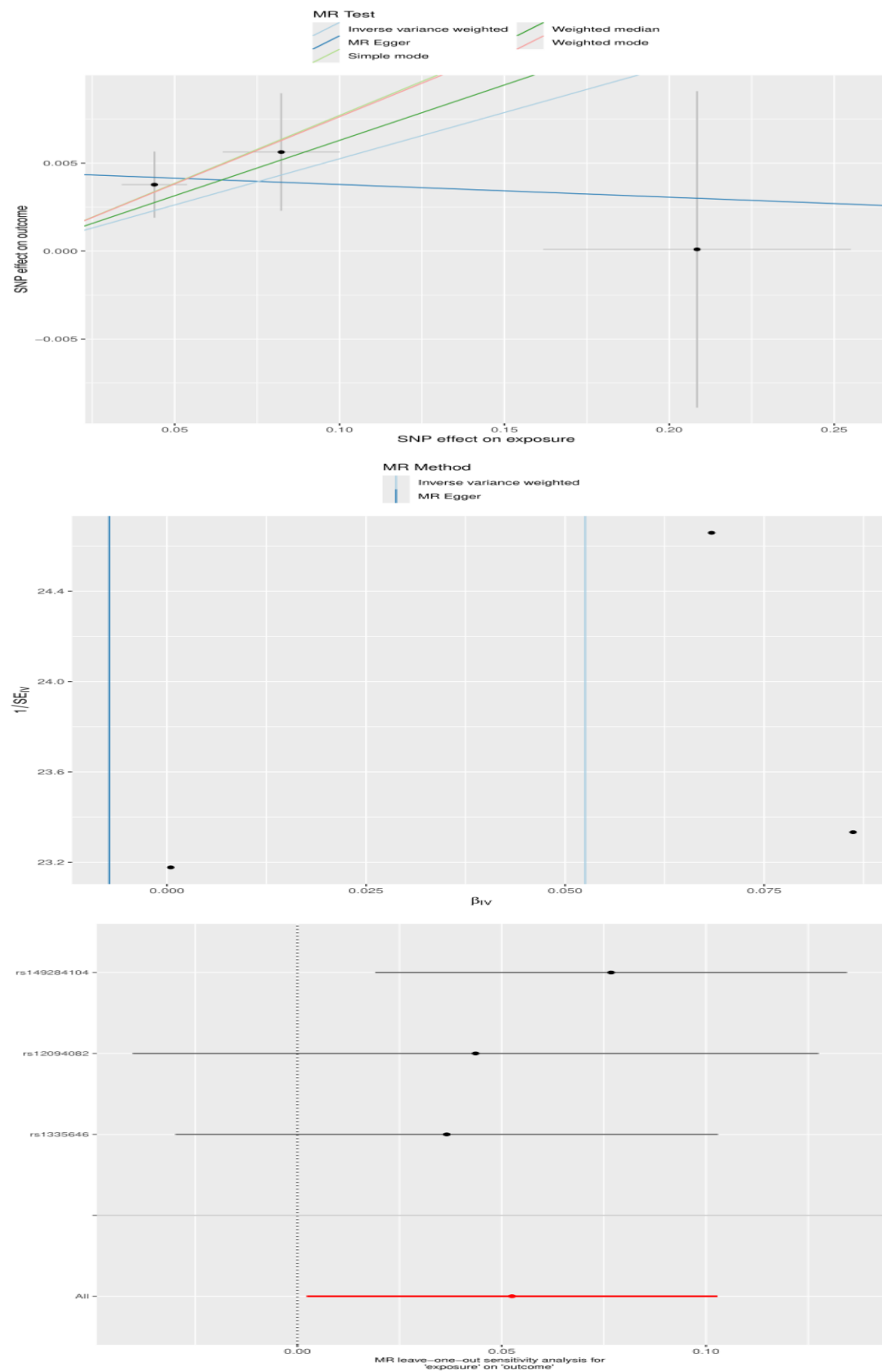
**Supplementary Figure 27.** Scatter plot, funnel plot and leave-one-out plot with GCST90002612 as exposure and TOTAL BODY BMD as outcome.



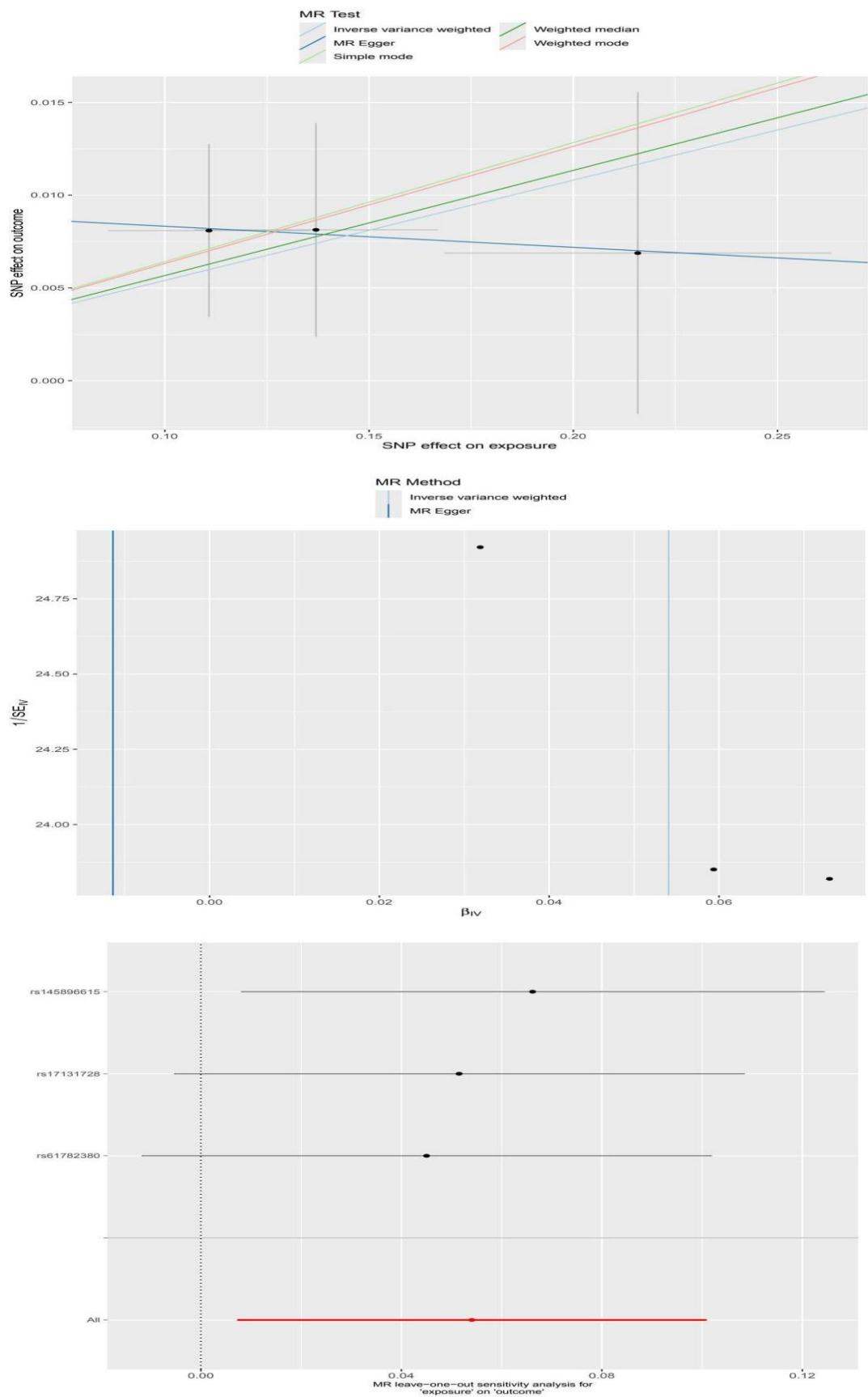
**Supplementary Figure 28.** Scatter plot, funnel plot and leave-one-out plot with GCST90003764 as exposure and TOTAL BODY BMD as outcome.



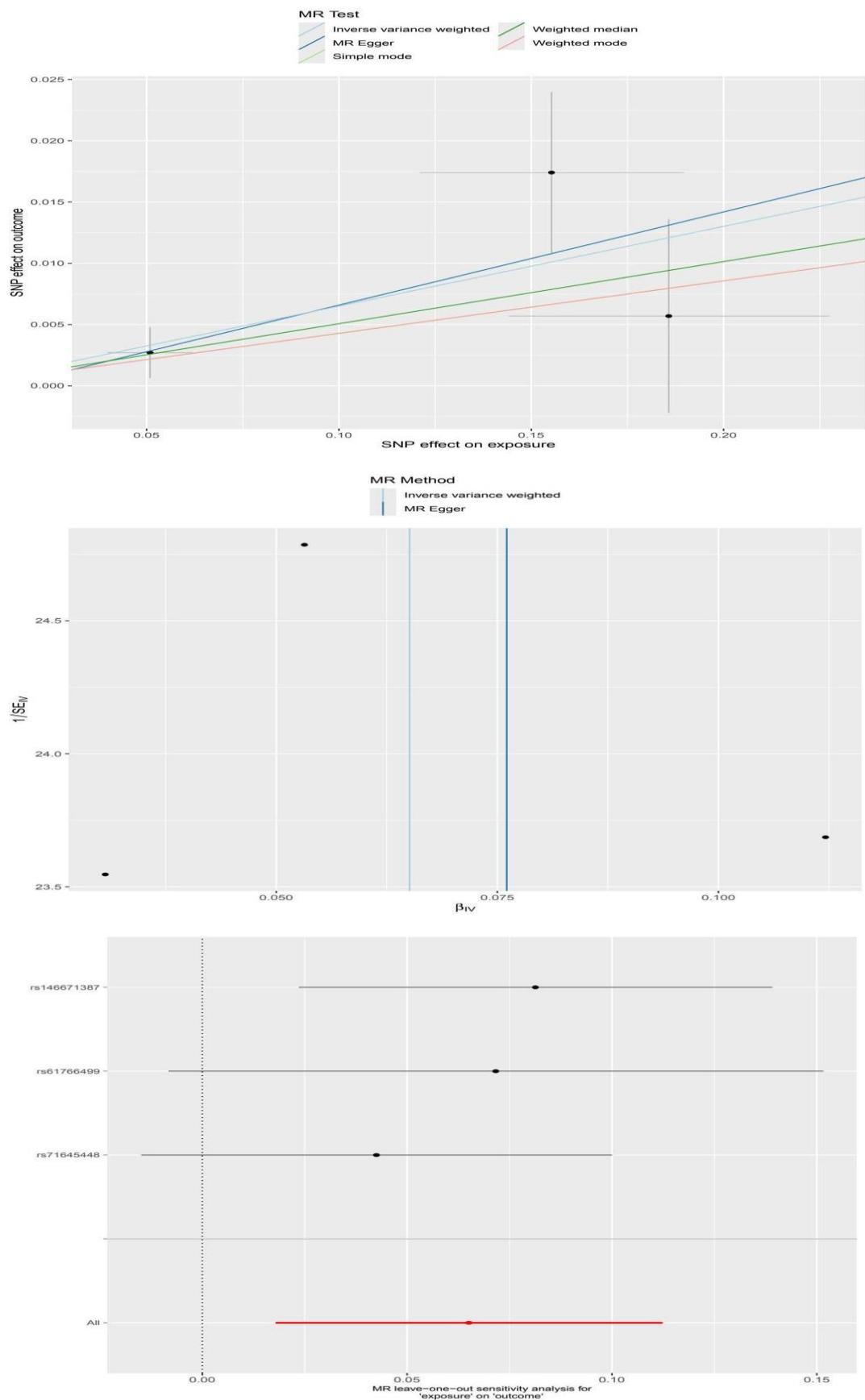
**Supplementary Figure 29.** Scatter plot, funnel plot and leave-one-out plot with GCST90002729 as exposure and HEEL BMD as outcome.



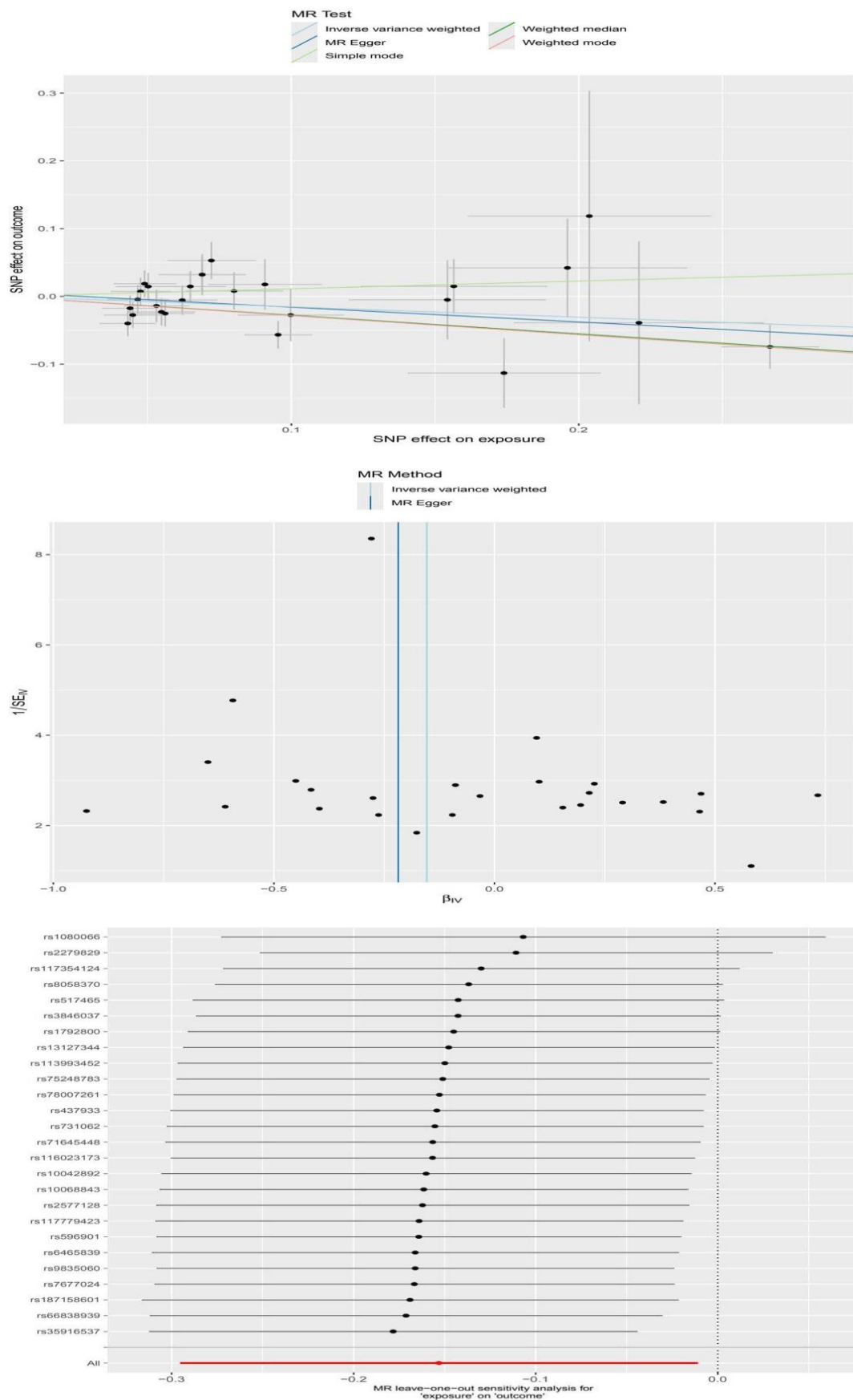
**Supplementary Figure 30.** Scatter plot, funnel plot and leave-one-out plot with GCST90002612 as exposure and HEEL BMD as outcome.



**Supplementary Figure 31.** Scatter plot, funnel plot and leave-one-out plot with GCST90002953 as exposure and HEEL BMD as outcome.

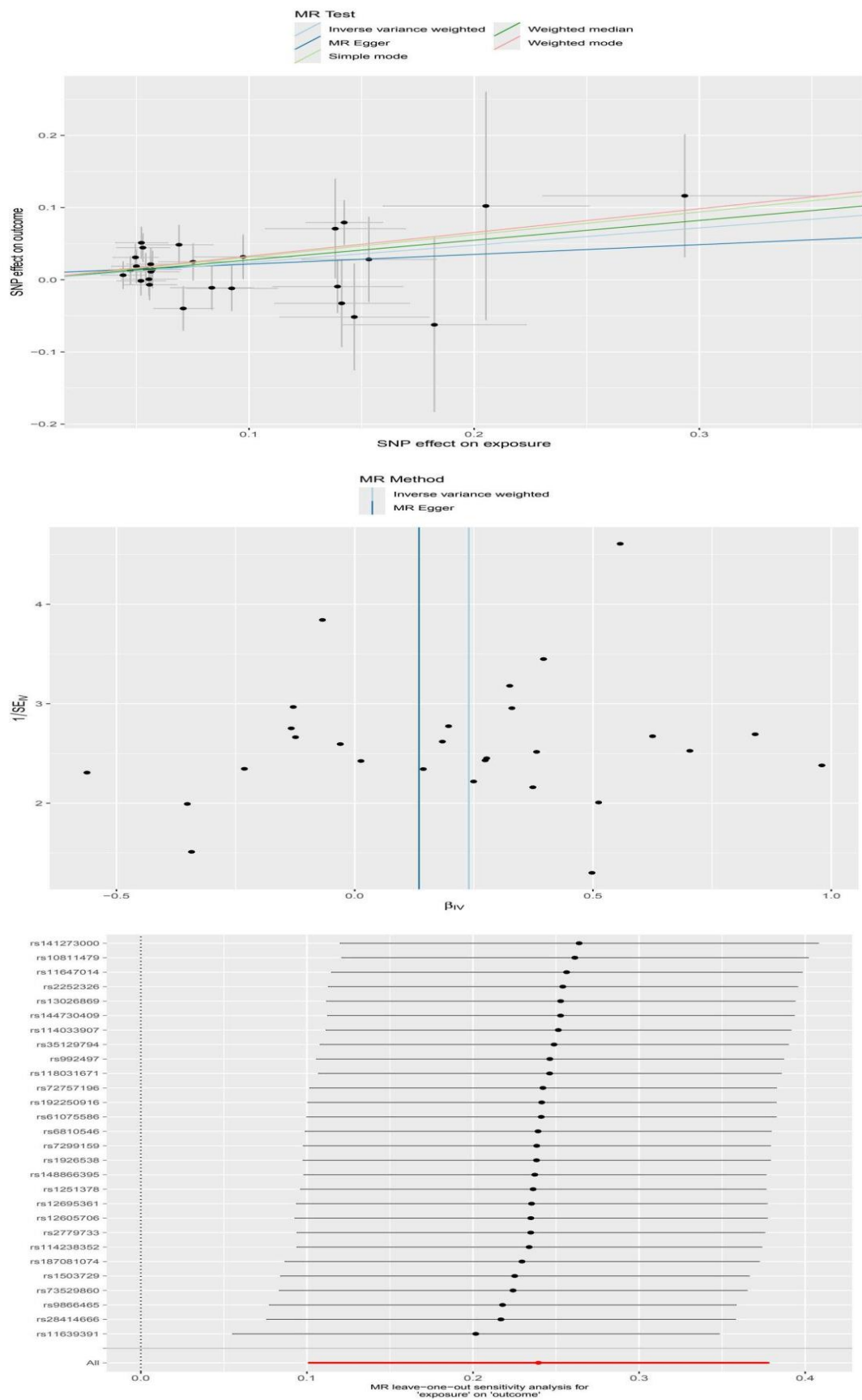


**Supplementary Figure 32.** Scatter plot, funnel plot and leave-one-out plot with GCST90002789 as exposure and HEEL BMD as outcome.

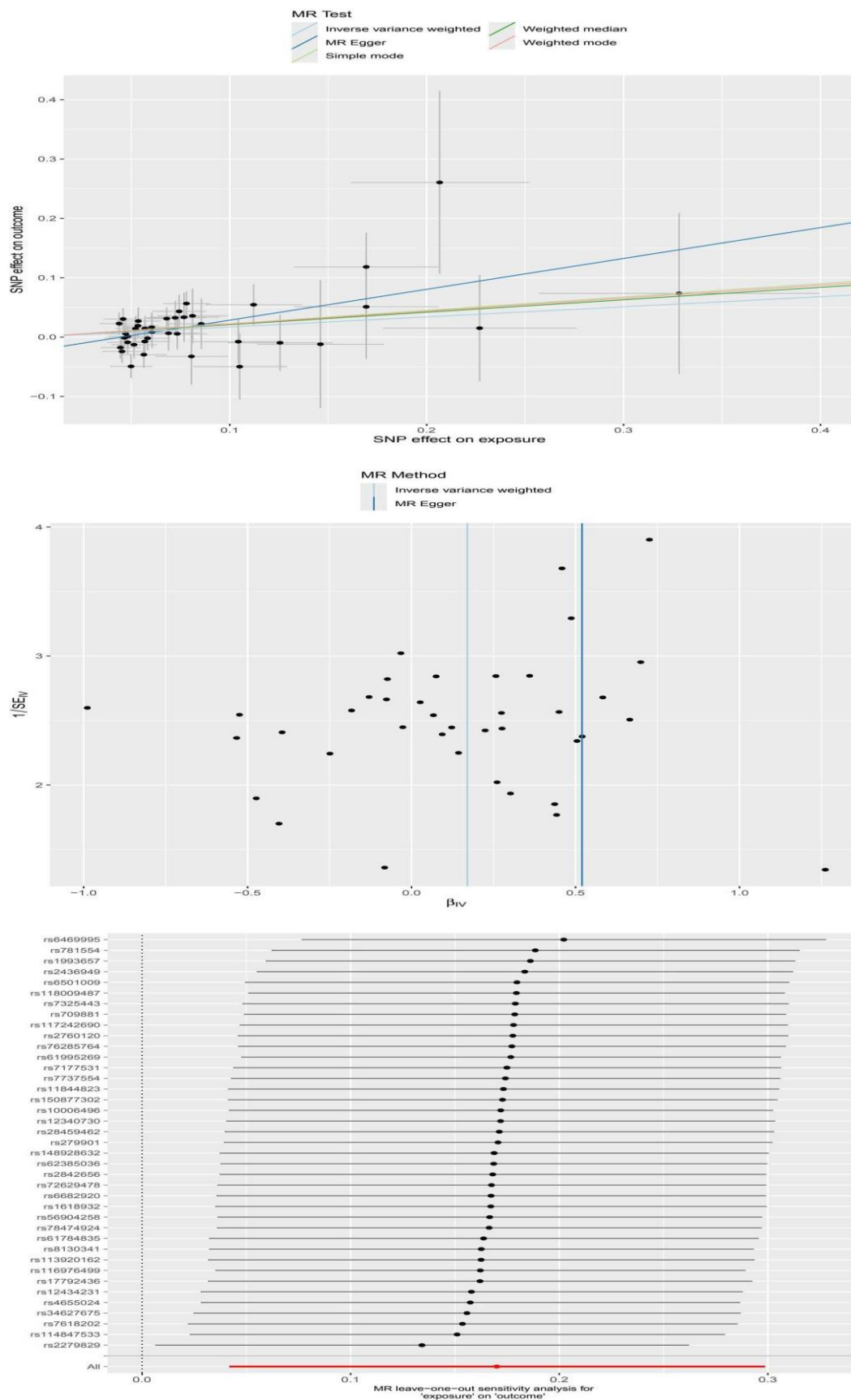


**Supplementary Figure 33.** Scatter plot, funnel plot and leave-one-out plot with GCST90003162 as exposure and OP as outcome.

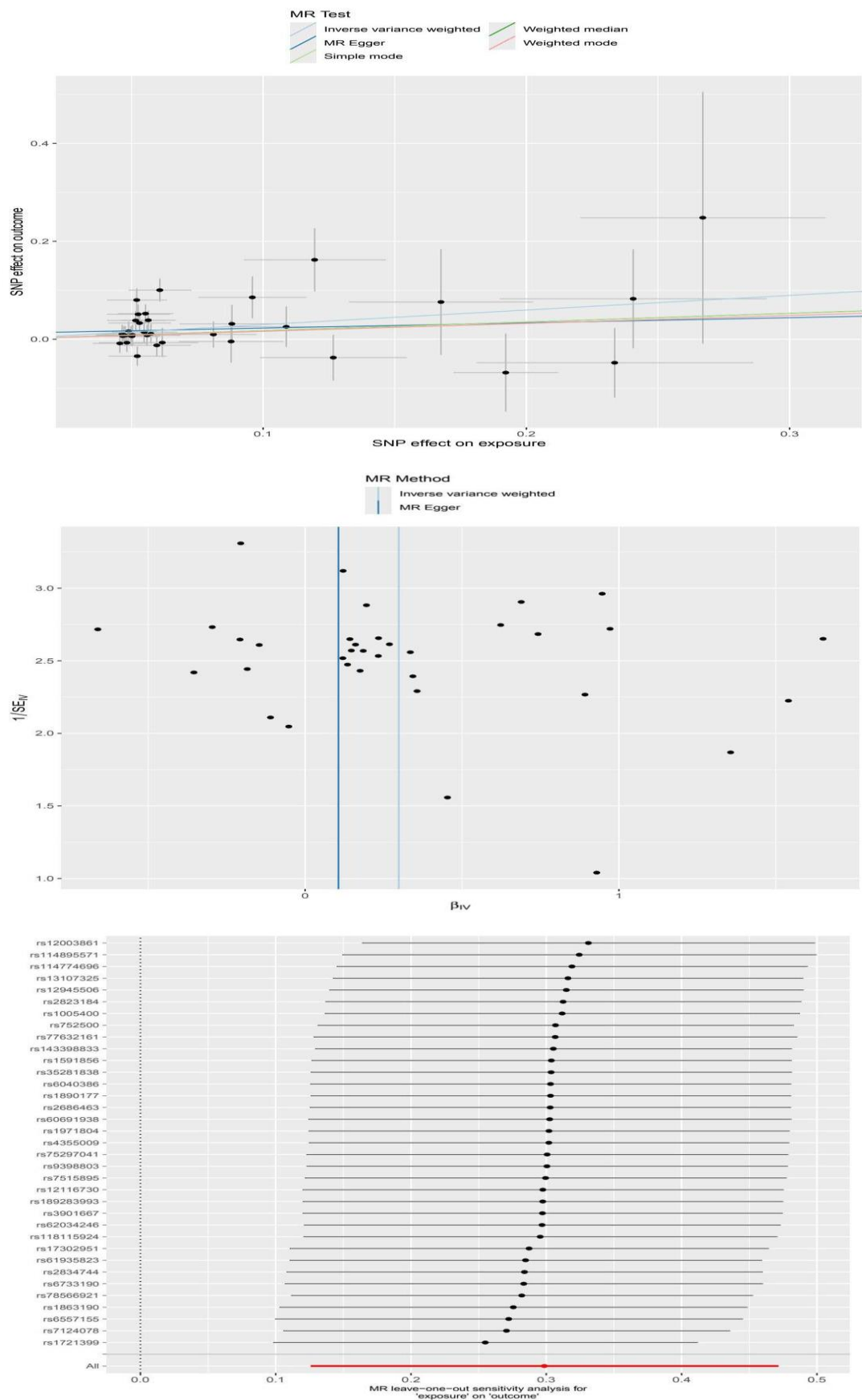




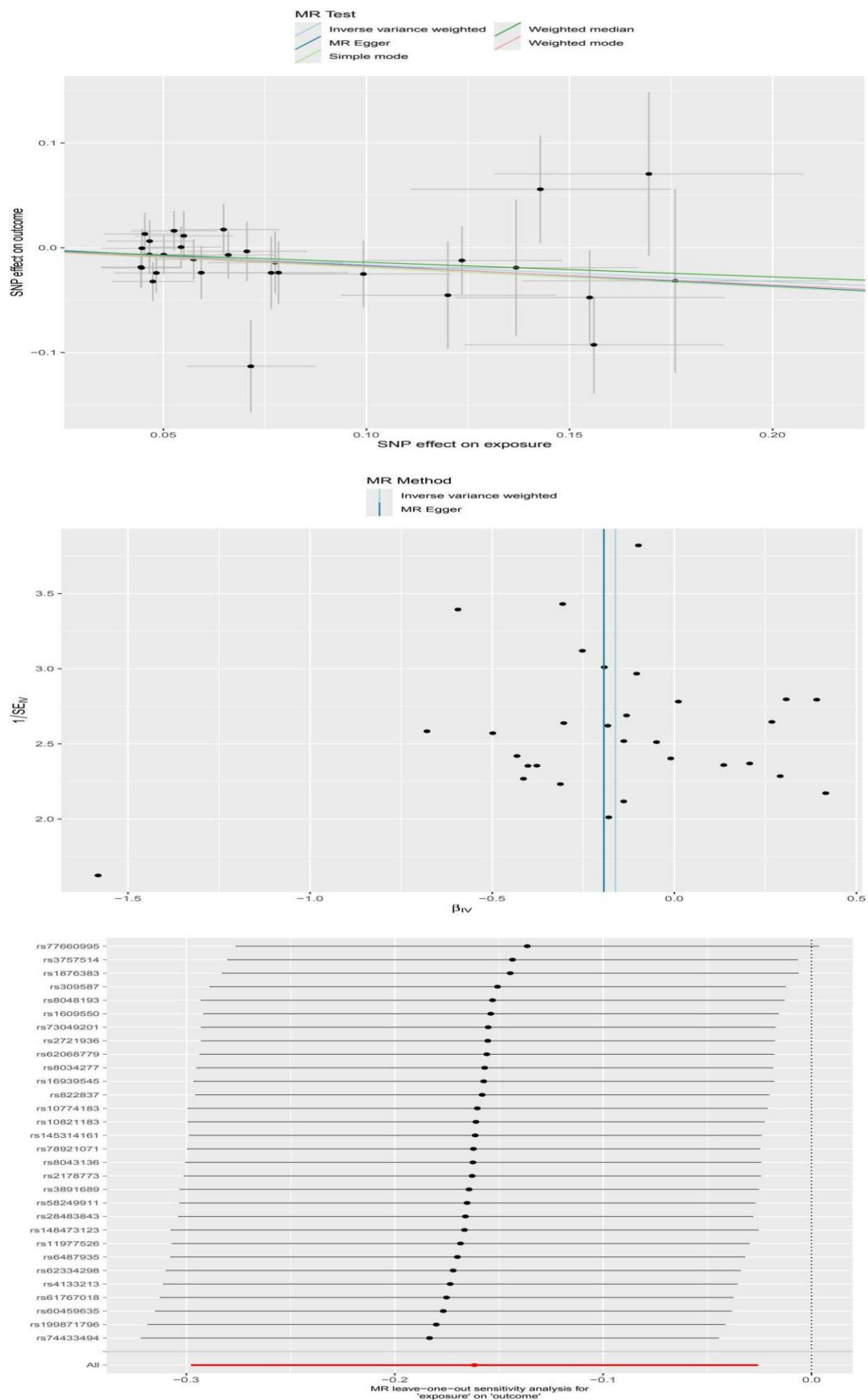
**Supplementary Figure 34.** Scatter plot, funnel plot and leave-one-out plot with GCST90003158 as exposure and OP as outcome.



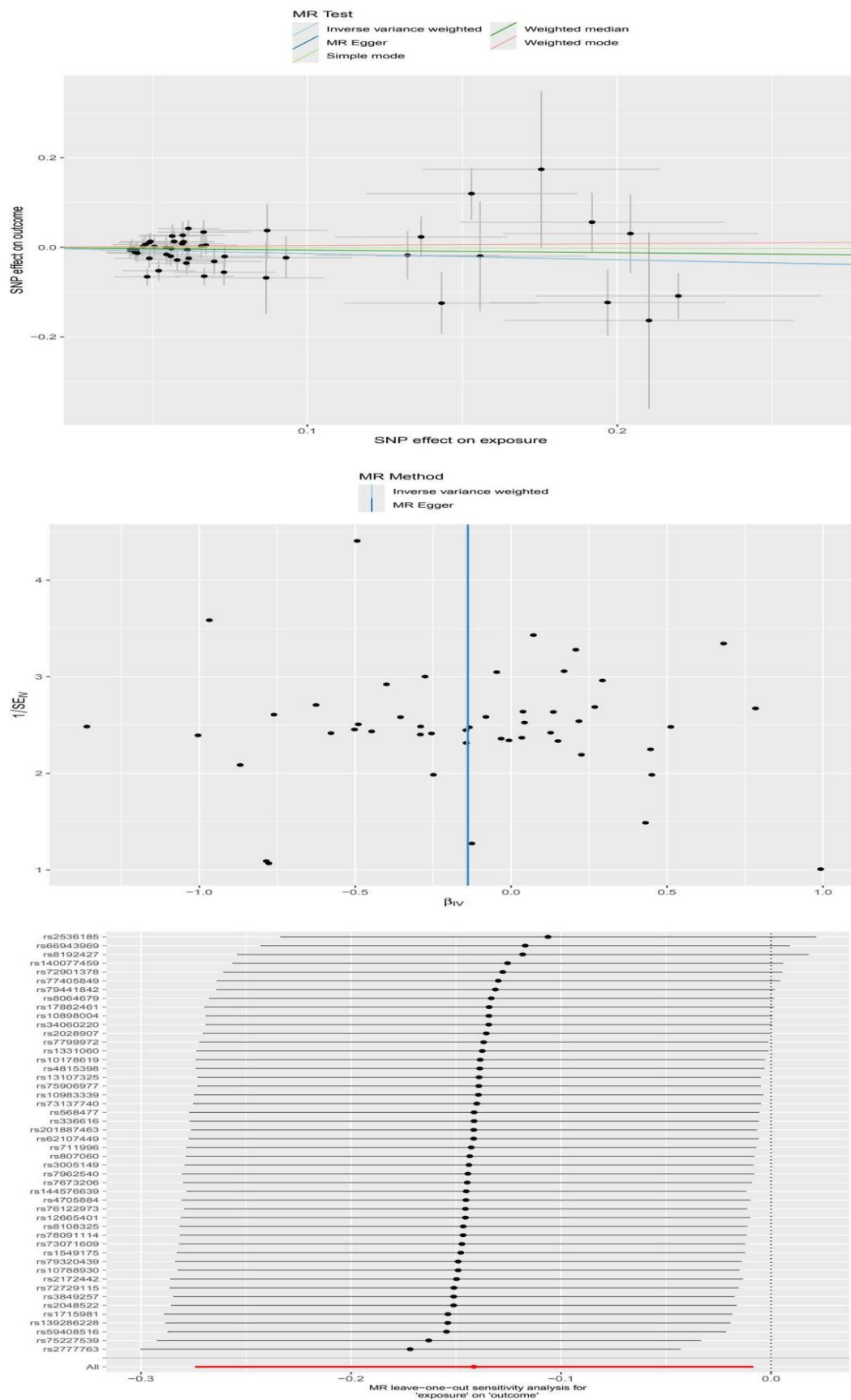
**Supplementary Figure 35.** Scatter plot, funnel plot and leave-one-out plot with GCST90003361 as exposure and OP as outcome.



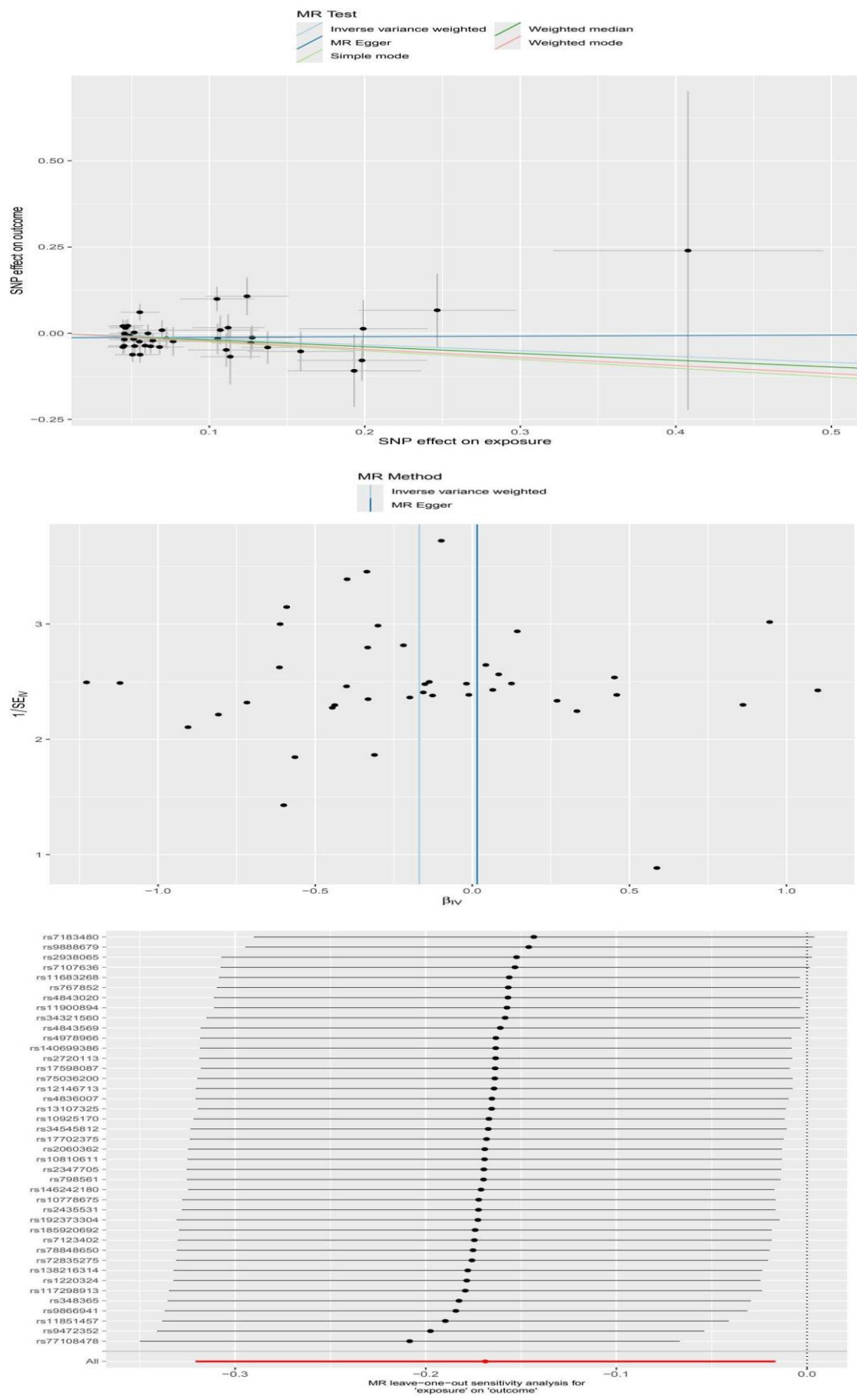
**Supplementary Figure 36.** Scatter plot, funnel plot and leave-one-out plot with GCST90006352 as exposure and OP as outcome.



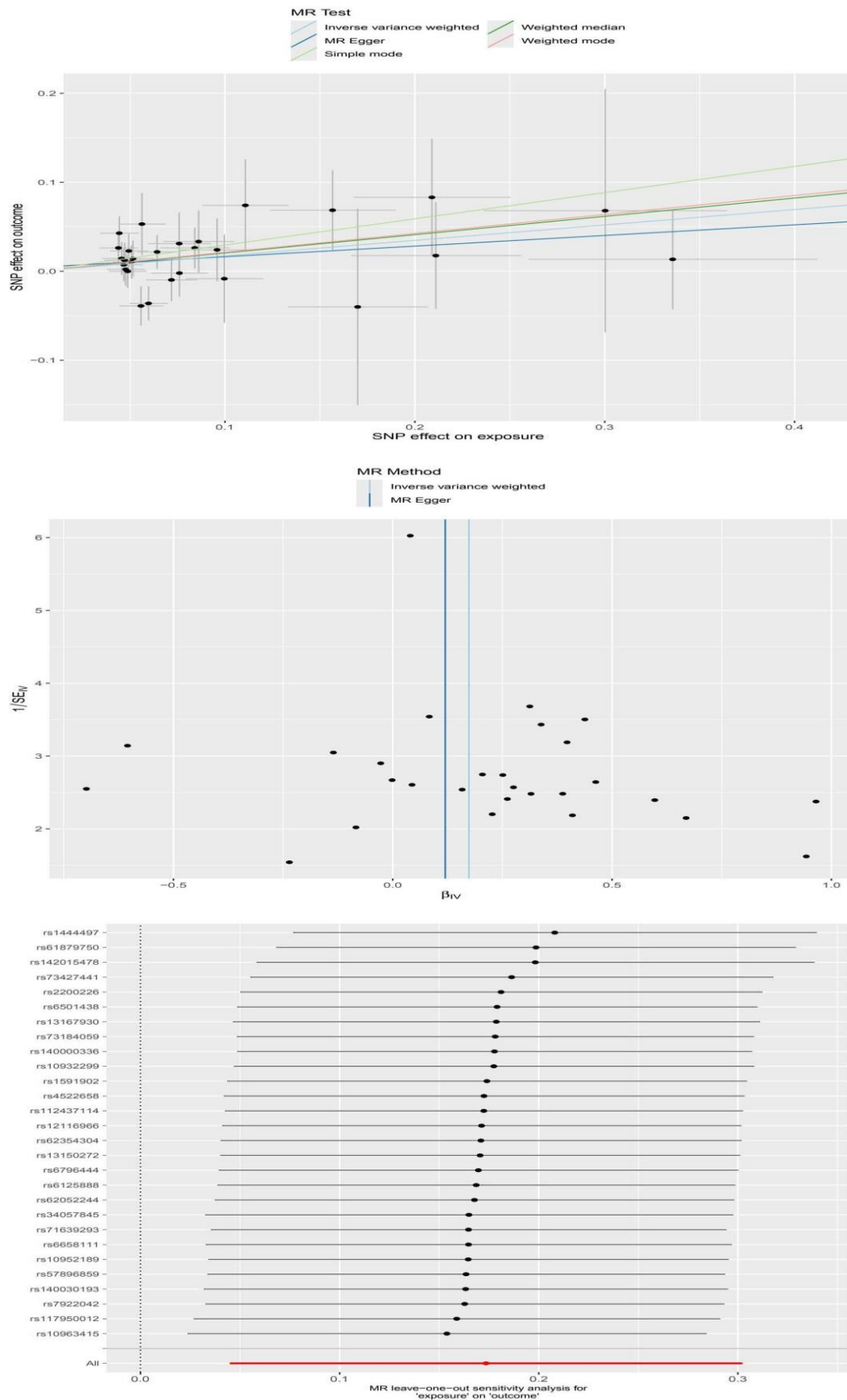
**Supplementary Figure 37.** Scatter plot, funnel plot and leave-one-out plot with GCST90002729 as exposure and OP as outcome.



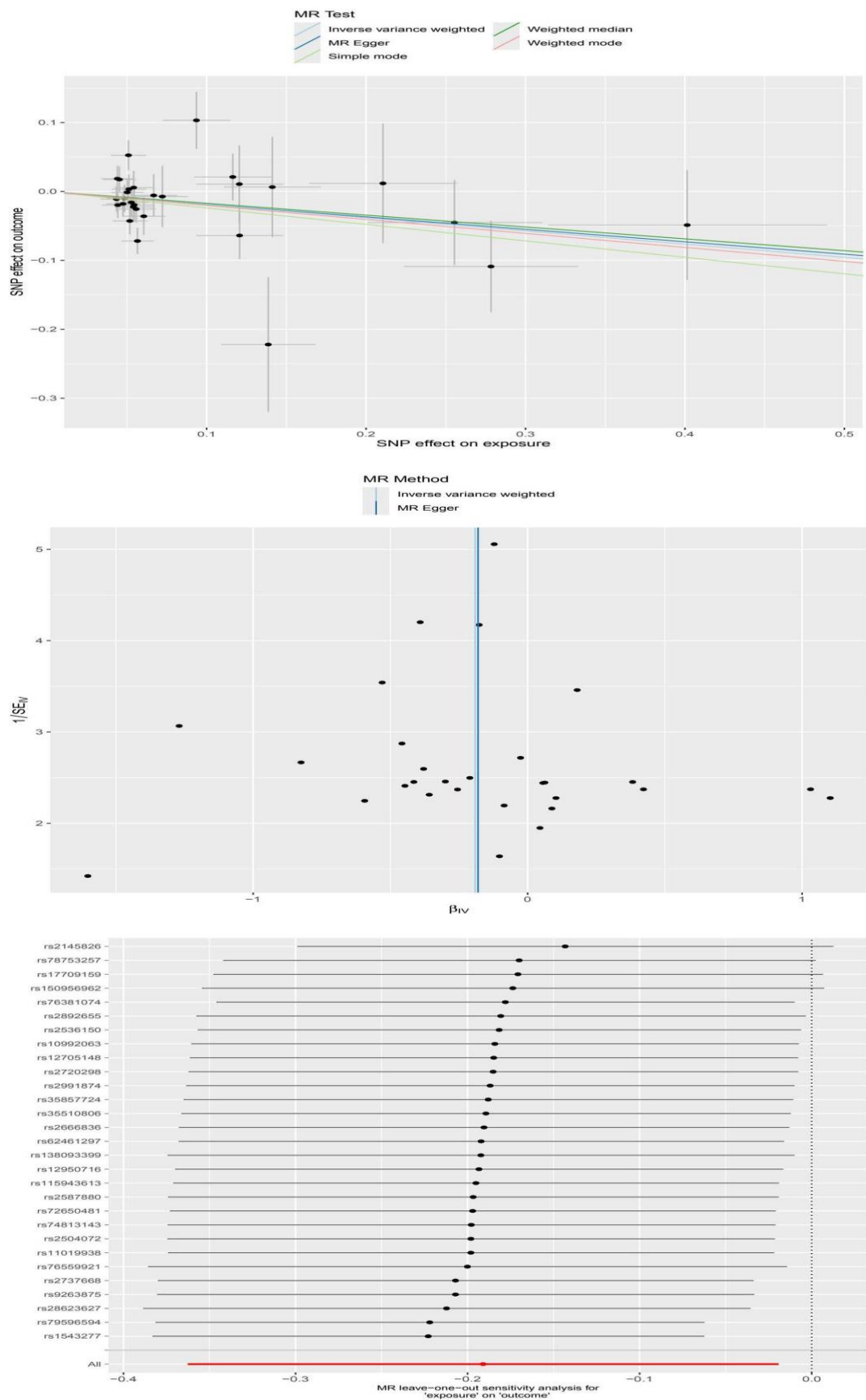
**Supplementary Figure 38.** Scatter plot, funnel plot and leave-one-out plot with GCST90002612 as exposure and OP as outcome.



**Supplementary Figure 39.** Scatter plot, funnel plot and leave-one-out plot with GCST90003764 as exposure and OP as outcome.

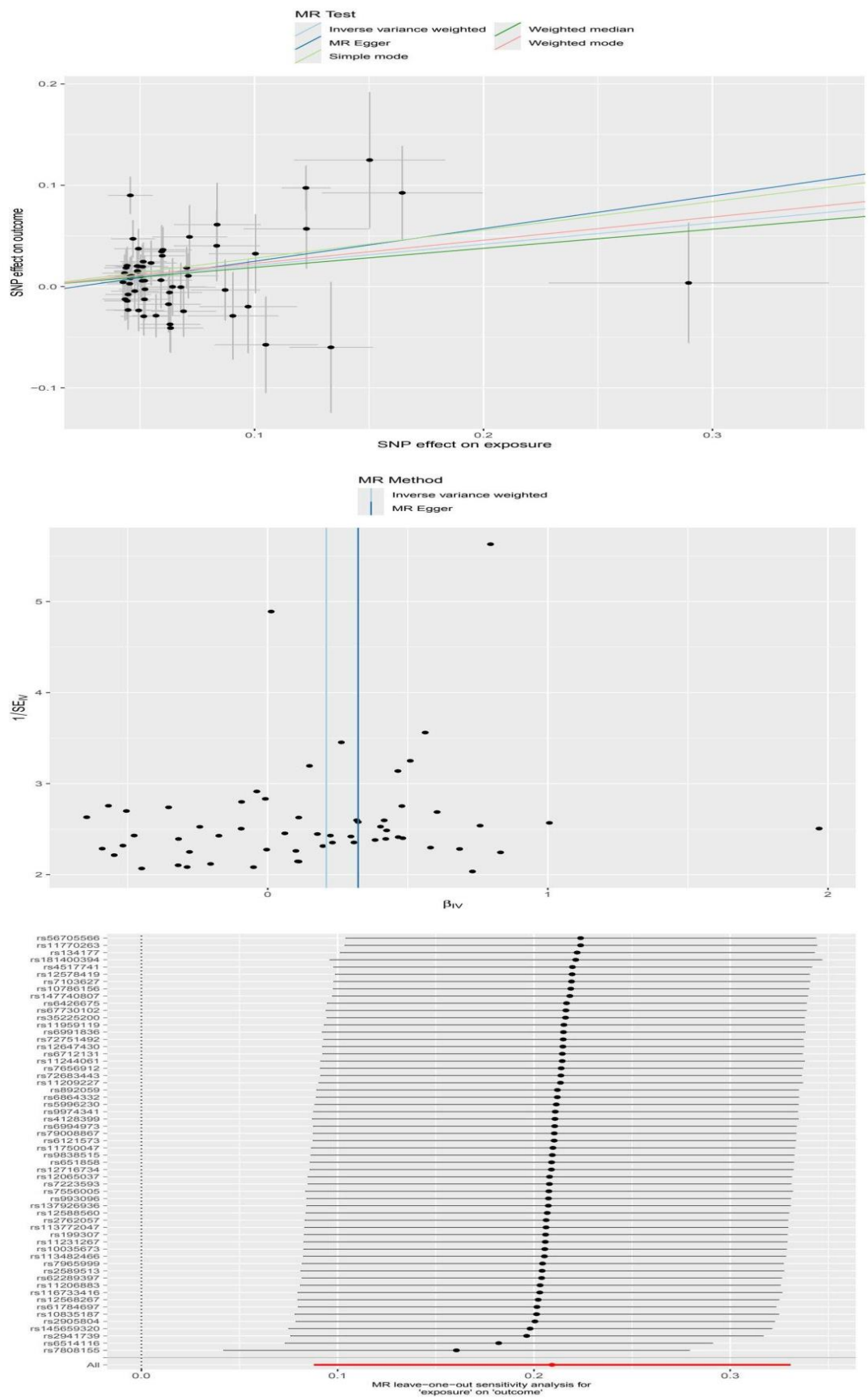


**Supplementary Figure 40.** Scatter plot, funnel plot and leave-one-out plot with GCST90003122 as exposure and OP as outcome.

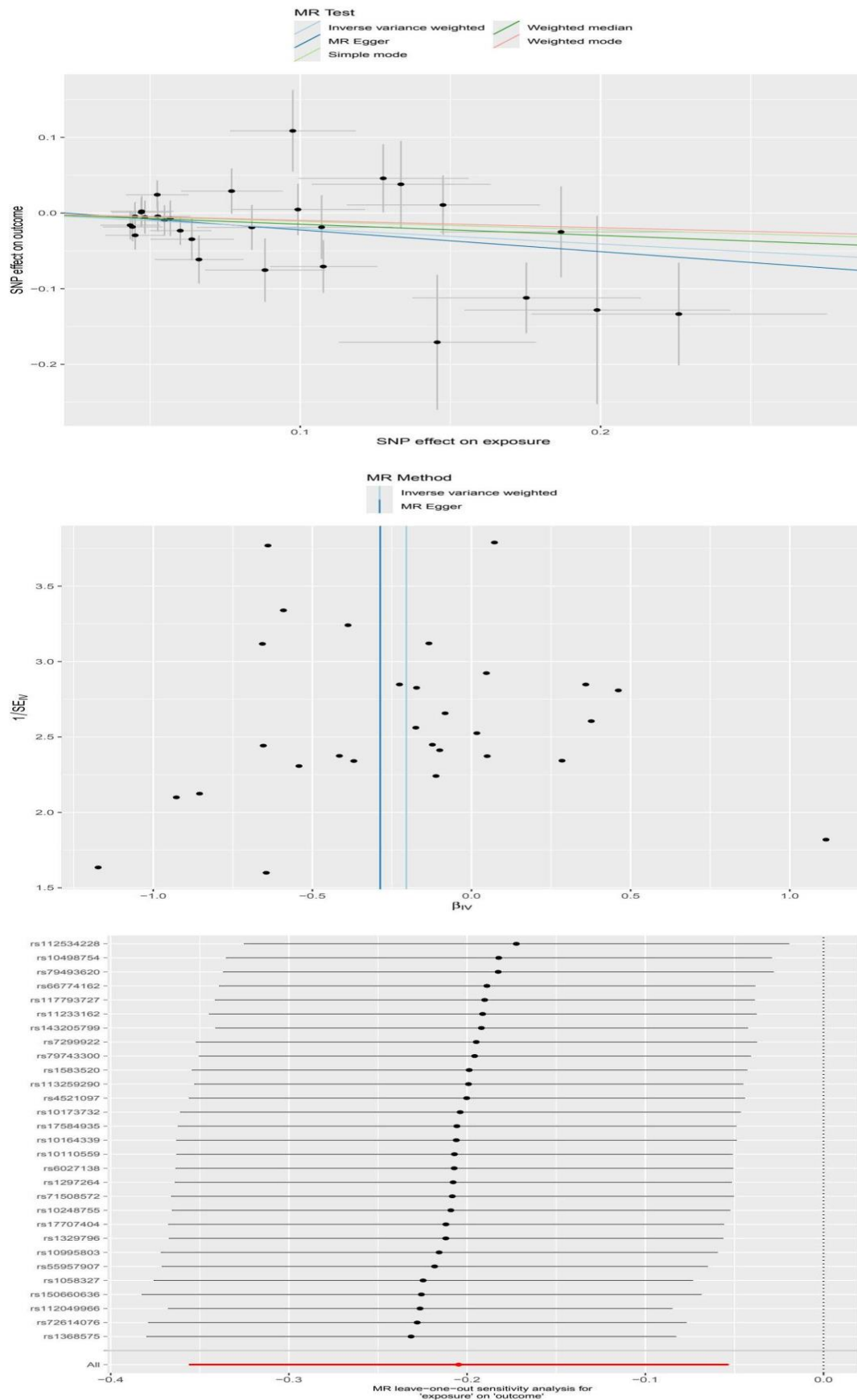


**Supplementary Figure 41.** Scatter plot, funnel plot and leave-one-out plot with GCST90003883 as exposure and OP as outcome.

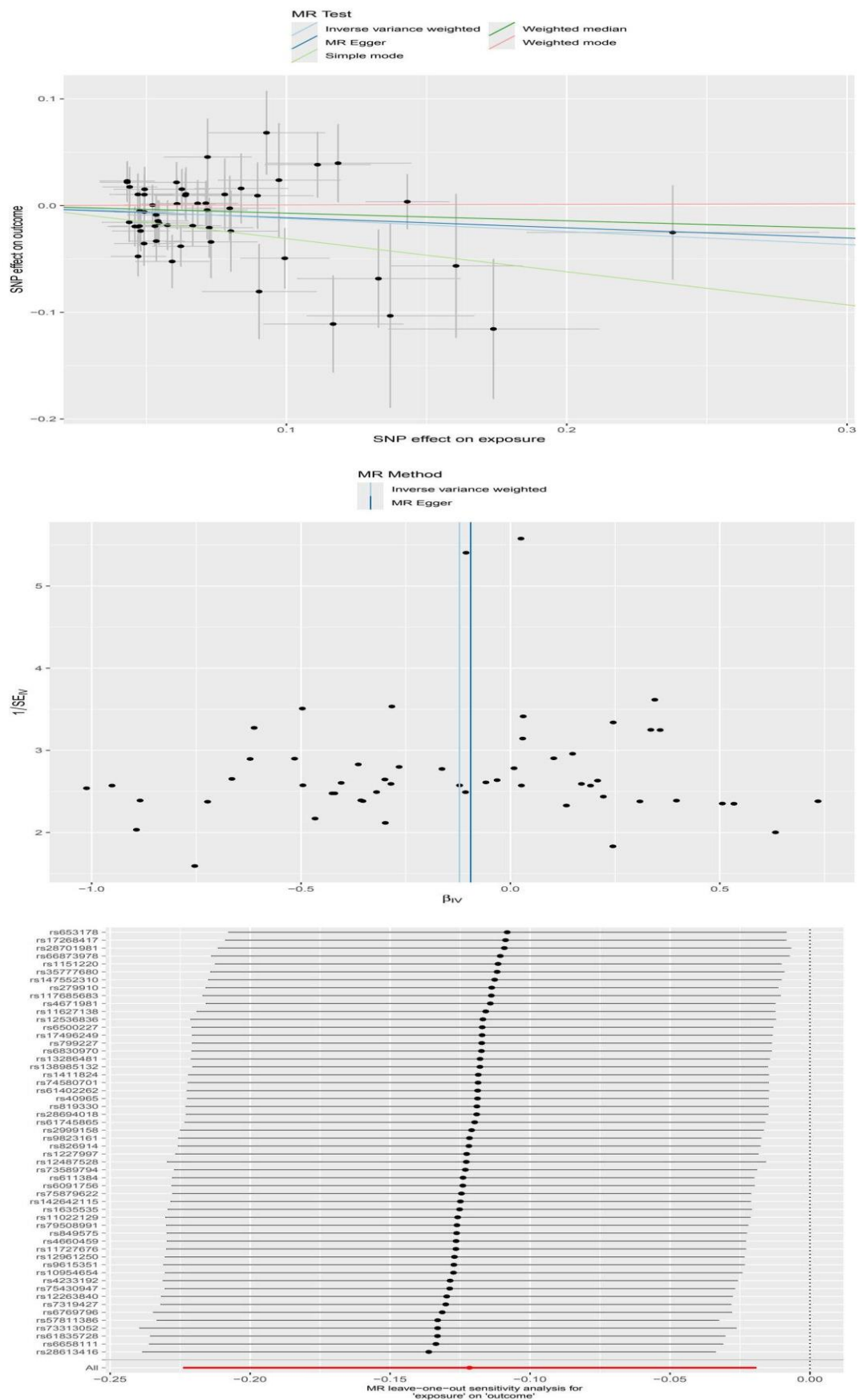




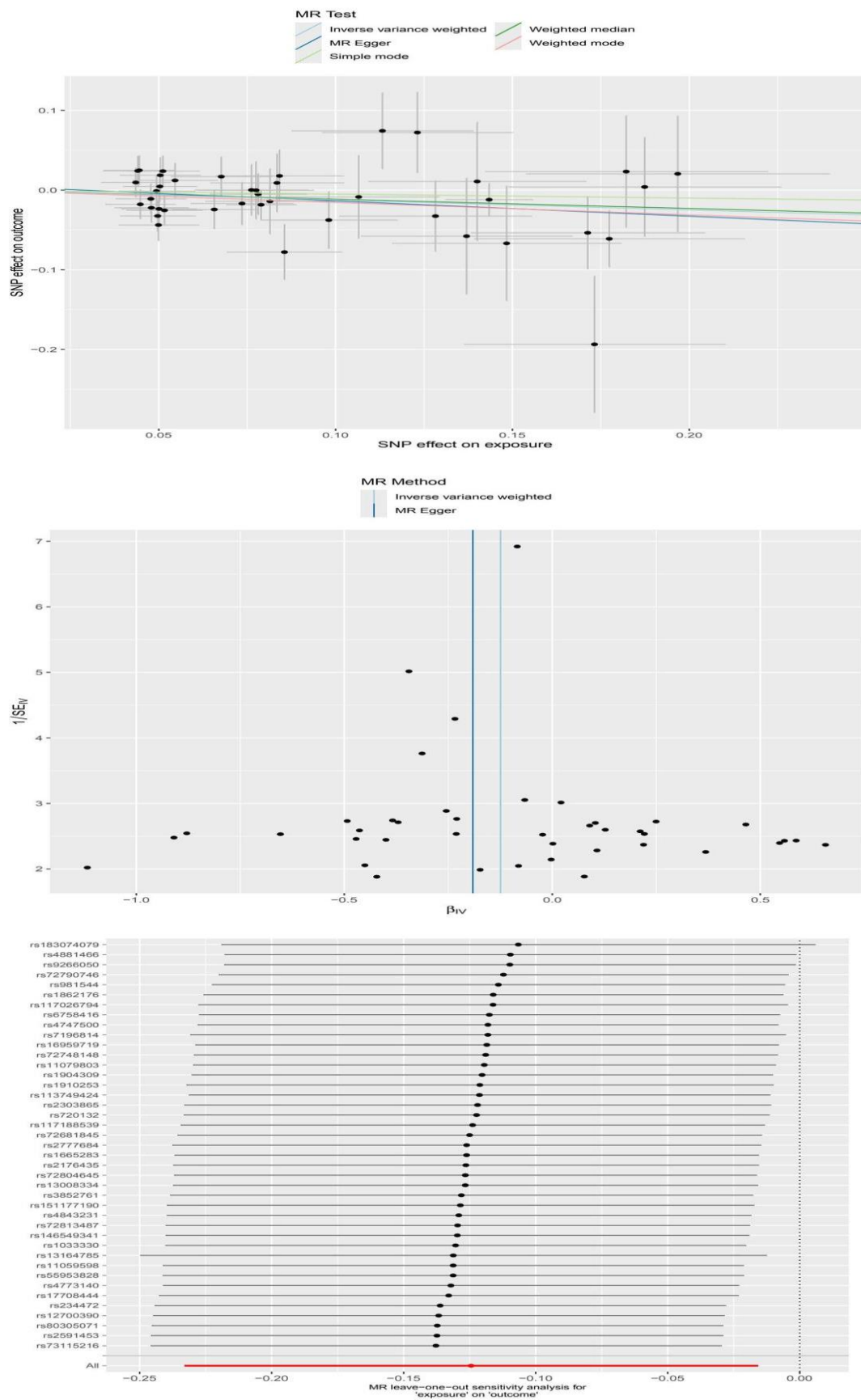
**Supplementary Figure 42.** Scatter plot, funnel plot and leave-one-out plot with GCST90006346 as exposure and OP as outcome.



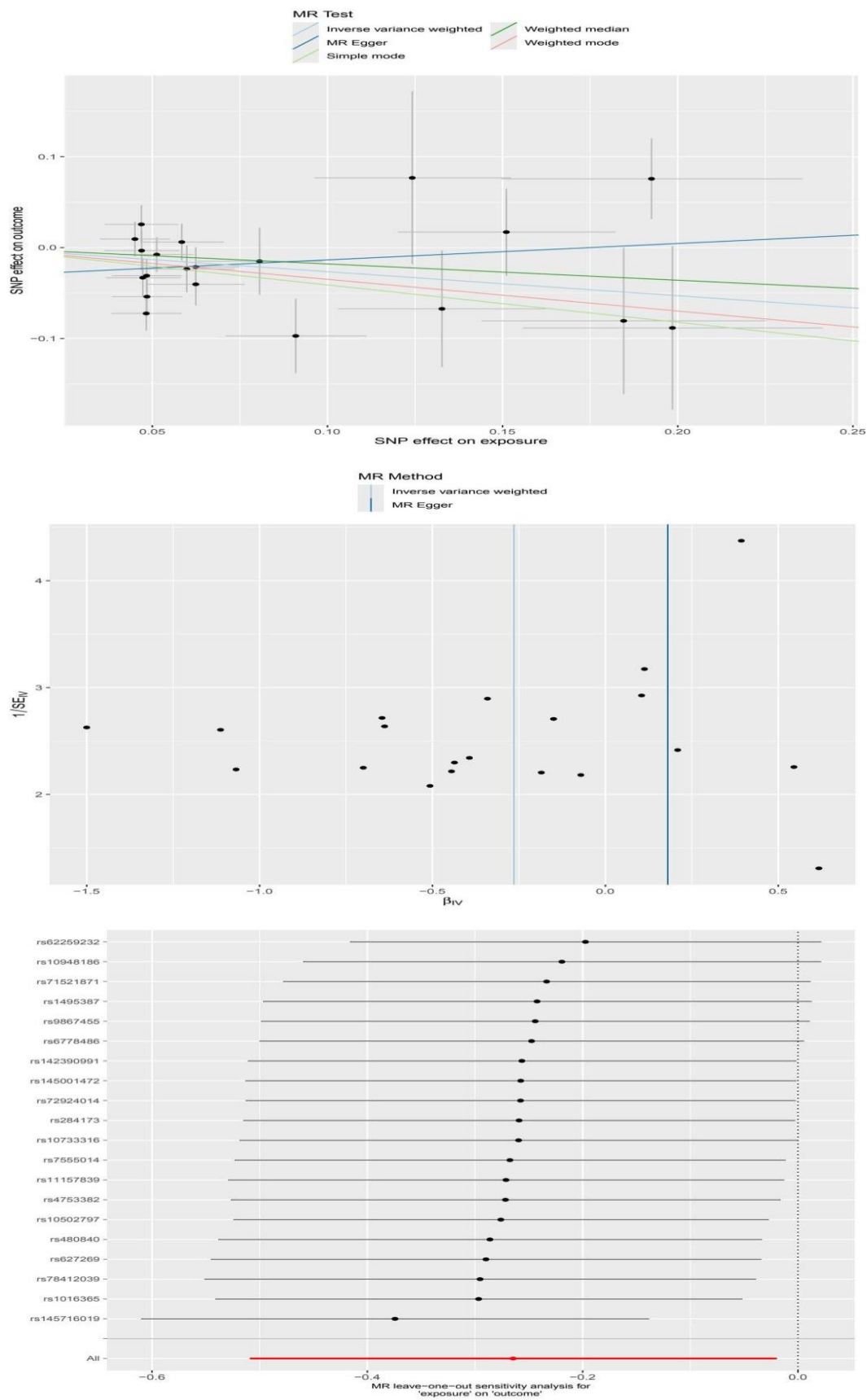
**Supplementary Figure 43.** Scatter plot, funnel plot and leave-one-out plot with GCST90003670 as exposure and OP as outcome.



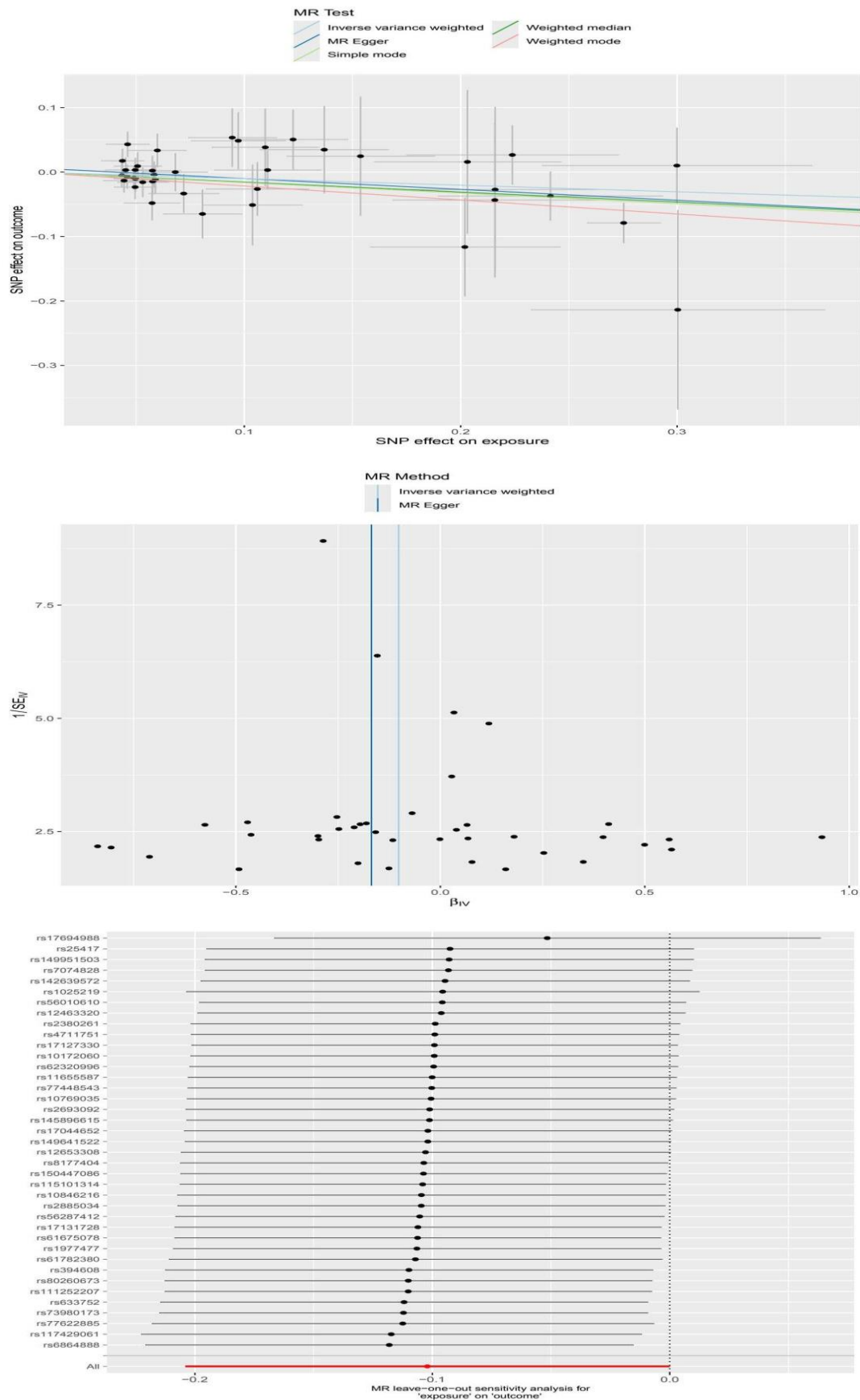
**Supplementary Figure 44.** Scatter plot, funnel plot and leave-one-out plot with GCST90002686 as exposure and OP as outcome.



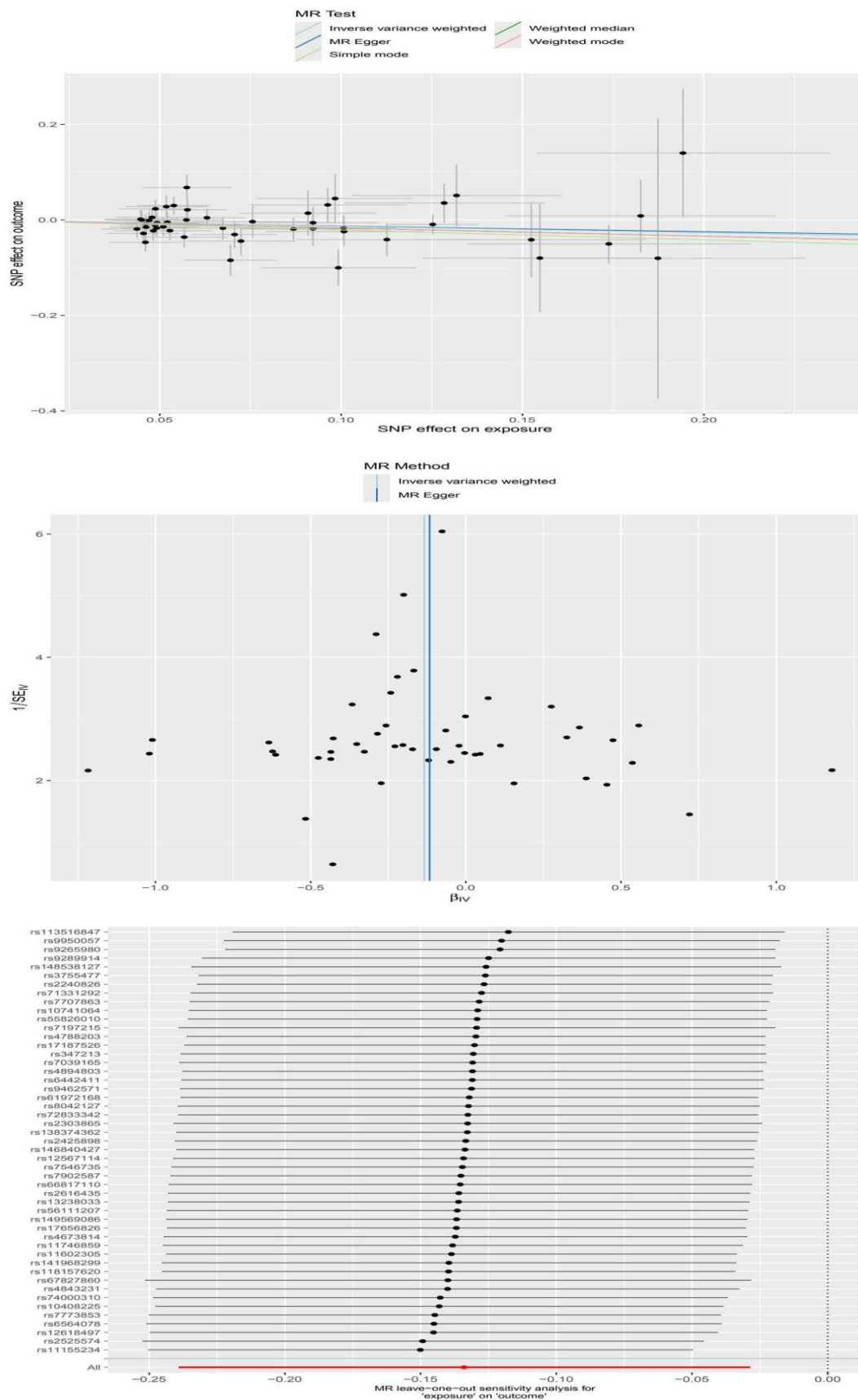
**Supplementary Figure 45.** Scatter plot, funnel plot and leave-one-out plot with GCST90004325 as exposure and OP as outcome.



**Supplementary Figure 46.** Scatter plot, funnel plot and leave-one-out plot with GCST90004235 as exposure and OP as outcome.



**Supplementary Figure 47.** Scatter plot, funnel plot and leave-one-out plot with GCST90002953 as exposure and OP as outcome.



**Supplementary Figure 48.** Scatter plot, funnel plot and leave-one-out plot with GCST90002789 as exposure and OP as outcome.