Supplementary File 2: Effect of corrected insulin response on cardiometabolic parameters

Exposure: Corrected Insulin Response Outcome: Waist-to-Hip Ratio

Results from two sample MR:

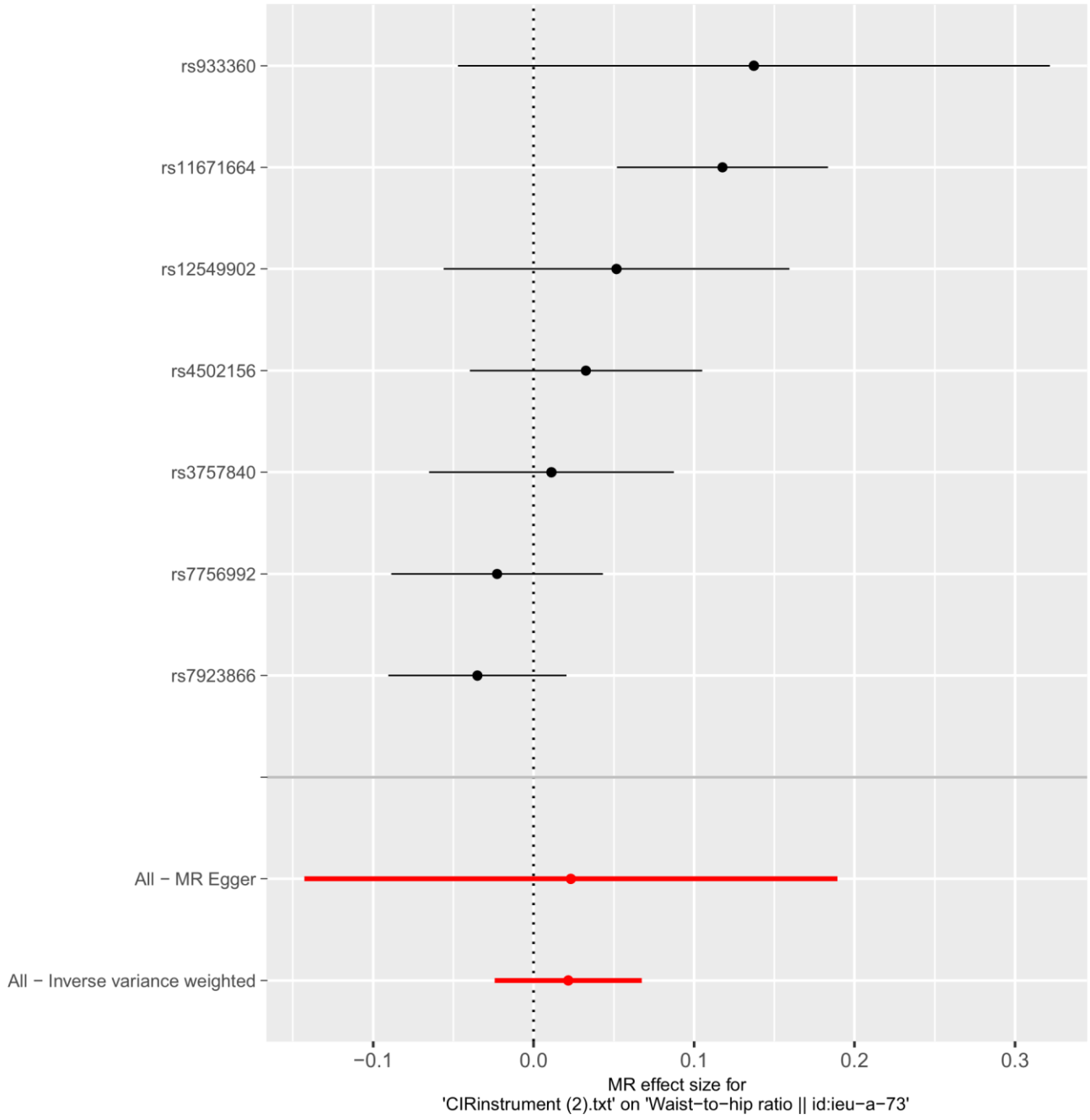
method	nsnp	b	se	pval
MR Egger	7	0.0321250	0.0833561	0.7157958
Weighted median	7	-0.0133751	0.0137789	0.3317033
Inverse variance weighted	7	0.0095089	0.0239154	0.6909220
Simple mode	7	-0.0179172	0.0255213	0.5089538
Weighted mode	7	-0.0307832	0.0123619	0.0471514

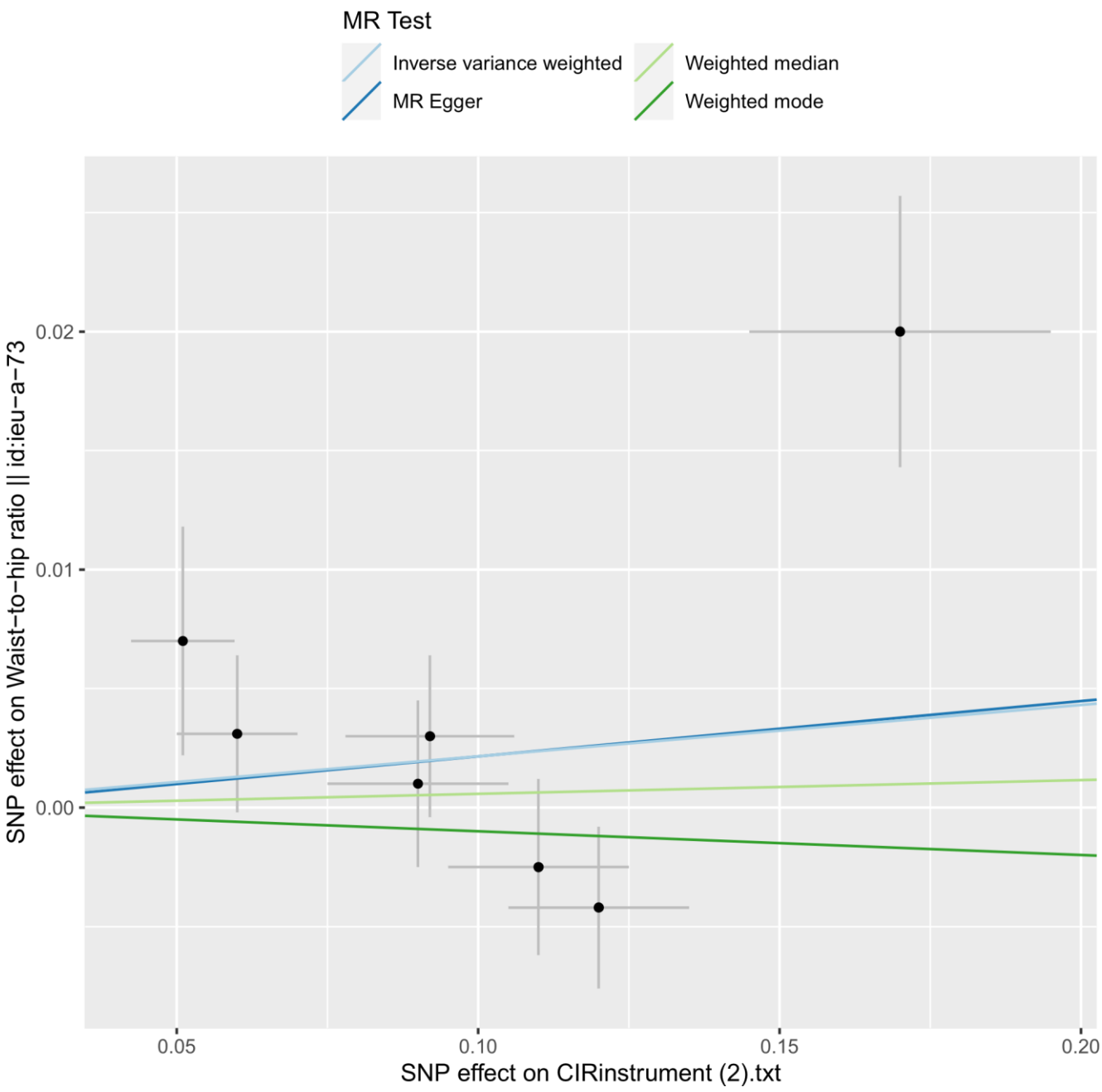
Heterogeneity tests

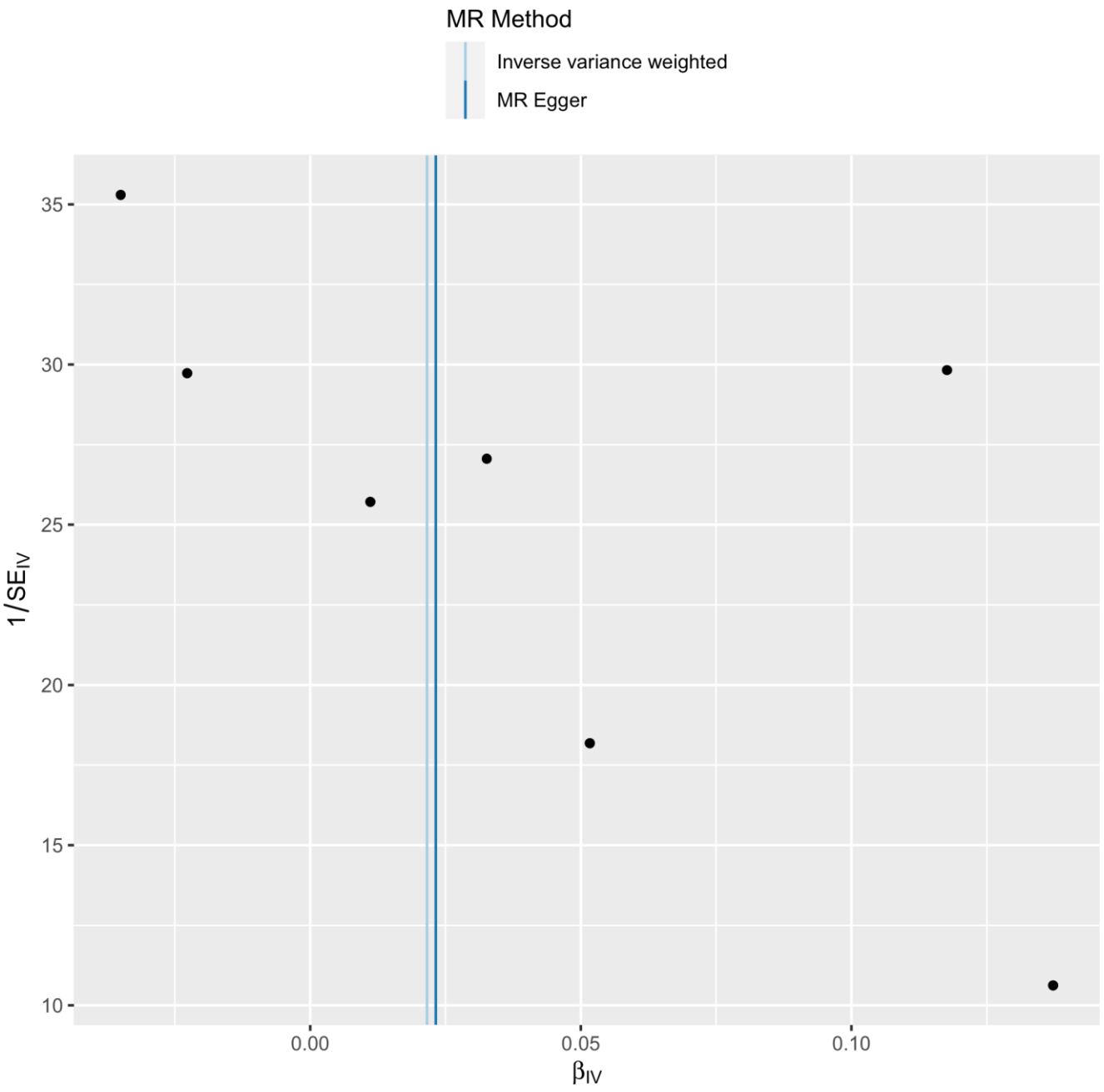
method	Q	Q_df	Q_pval
MR Egger	66.34434	5	0
Inverse variance weighted	67.42627	6	0

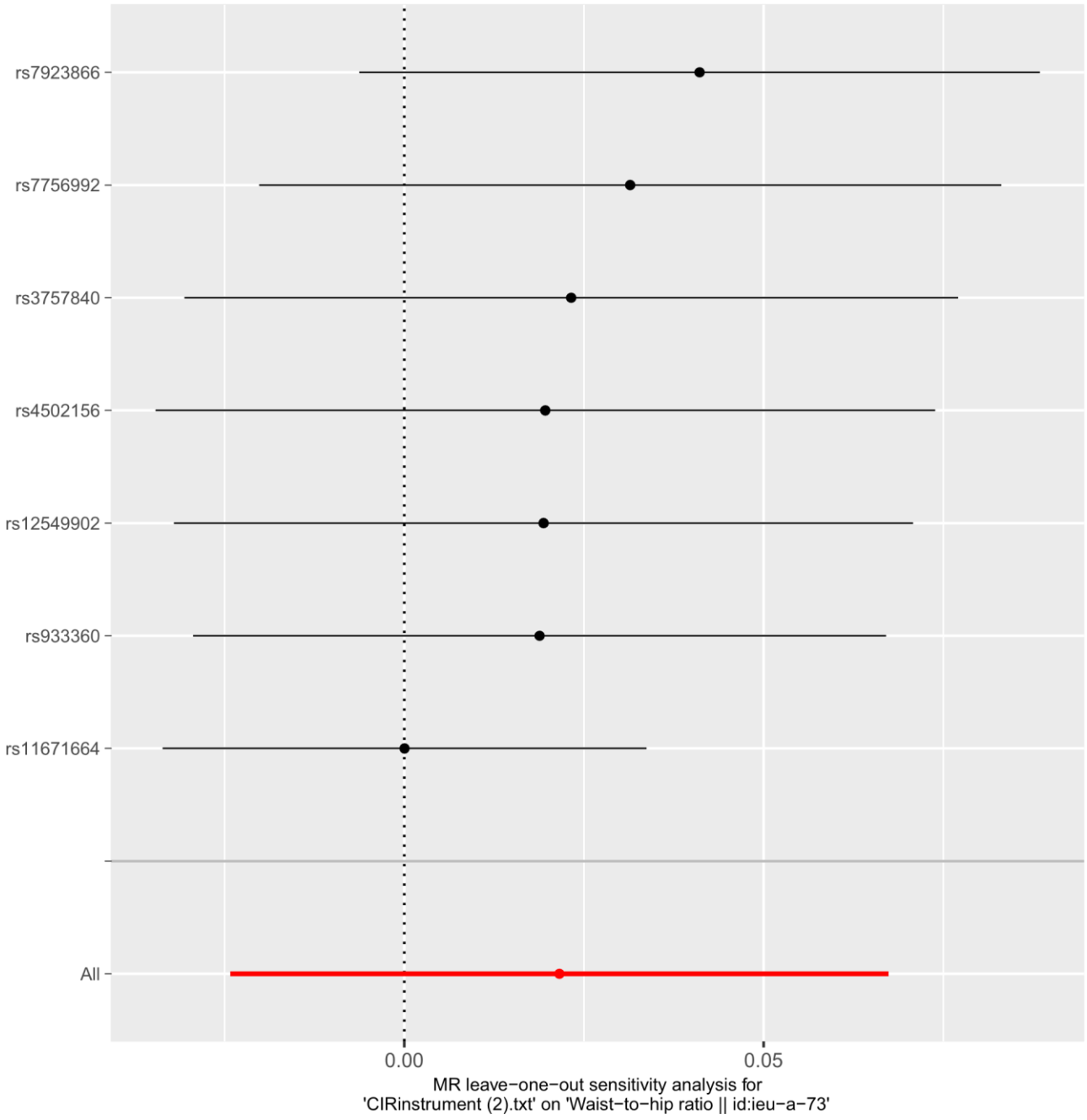
Test for directional horizontal pleiotropy

egger_intercept	se	pval
-0.0023367	0.0081833	0.7866736


rs933360
rs11671664
rs12549902
rs4502156
rs3757840
rs7756992
rs7923866
All − MR Egger
All − Inverse variance weighted
−0.1
0.0
0.1
0.2
0.3
MR effect size for
'CIRinstrument (2).txt' on 'Waist−to−hip ratio || id:ieu−a−73'


MR Test
Inverse variance weighted
MR Egger
Weighted median
Weighted mode
SNP effect on Waist−to−hip ratio || id:ieu−a−73
0.02
0.01
0.00
0.05
0.10
0.15
0.20
SNP effect on CIRinstrument (2).txt


MR Method
Inverse variance weighted
MR Egger
35
30
25
20
15
10
1/SE_IV
0.00
0.05
0.10
β_IV


rs7923866
rs7756992
rs3757840
rs4502156
rs12549902
rs933360
rs11671664
All
0.00
0.05
MR leave−one−out sensitivity analysis for
'CIRinstrument (2).txt' on 'Waist−to−hip ratio || id:ieu−a−73'

Exposure: Corrected Insulin Response, Outcome: Waist-to-Hip Ratio adjusted for Body Mass Index

Results from two sample MR:

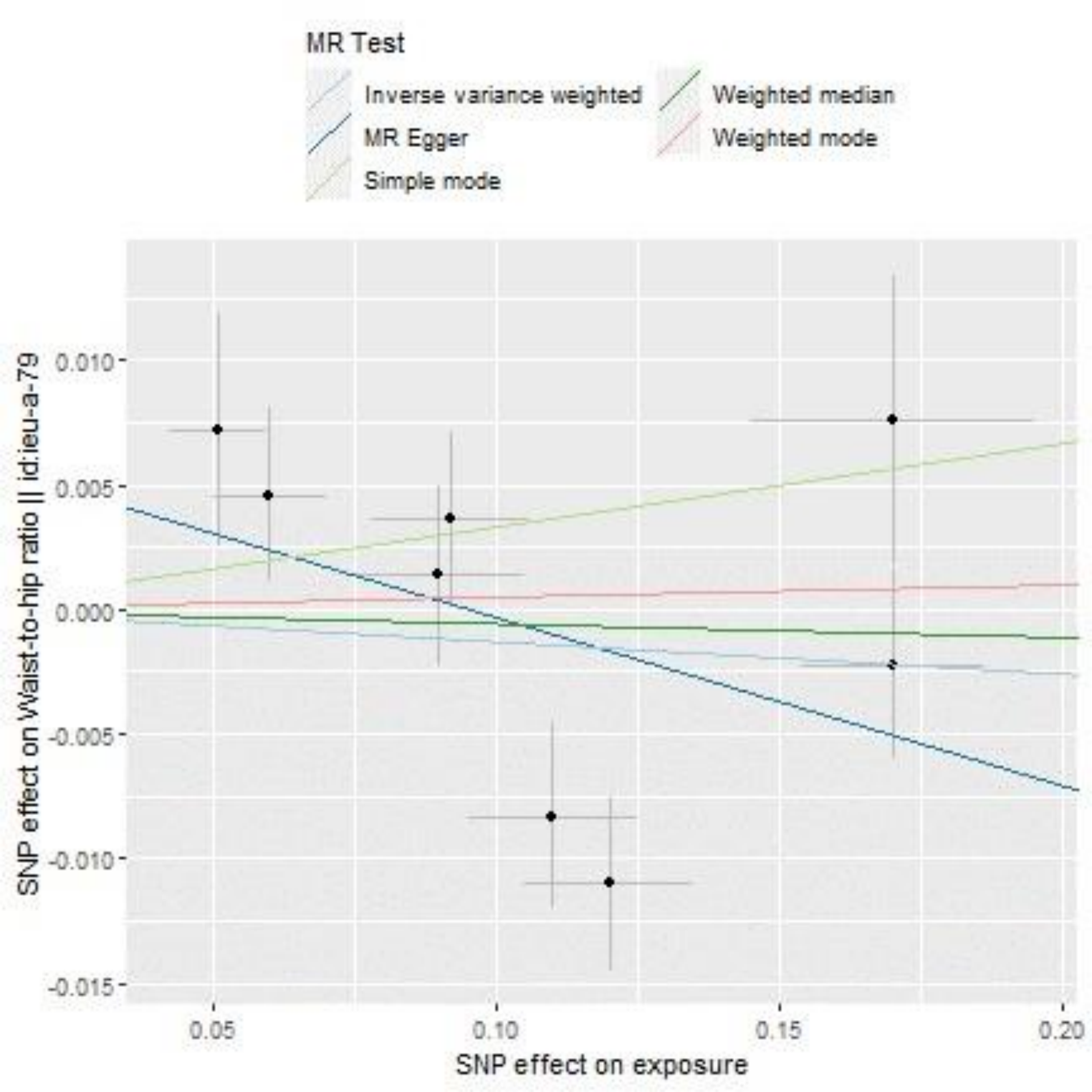
method	nsnp	b	se	pval
MR Egger	7	-0.0676635	0.0851654	0.4629326
Weighted median	7	0.0090489	0.0140206	0.5186665
Inverse variance weighted	7	-0.0181022	0.0253012	0.4743184
Simple mode	7	0.0420798	0.0177506	0.0554743
Weighted mode	7	0.0347674	0.0207333	0.1445785

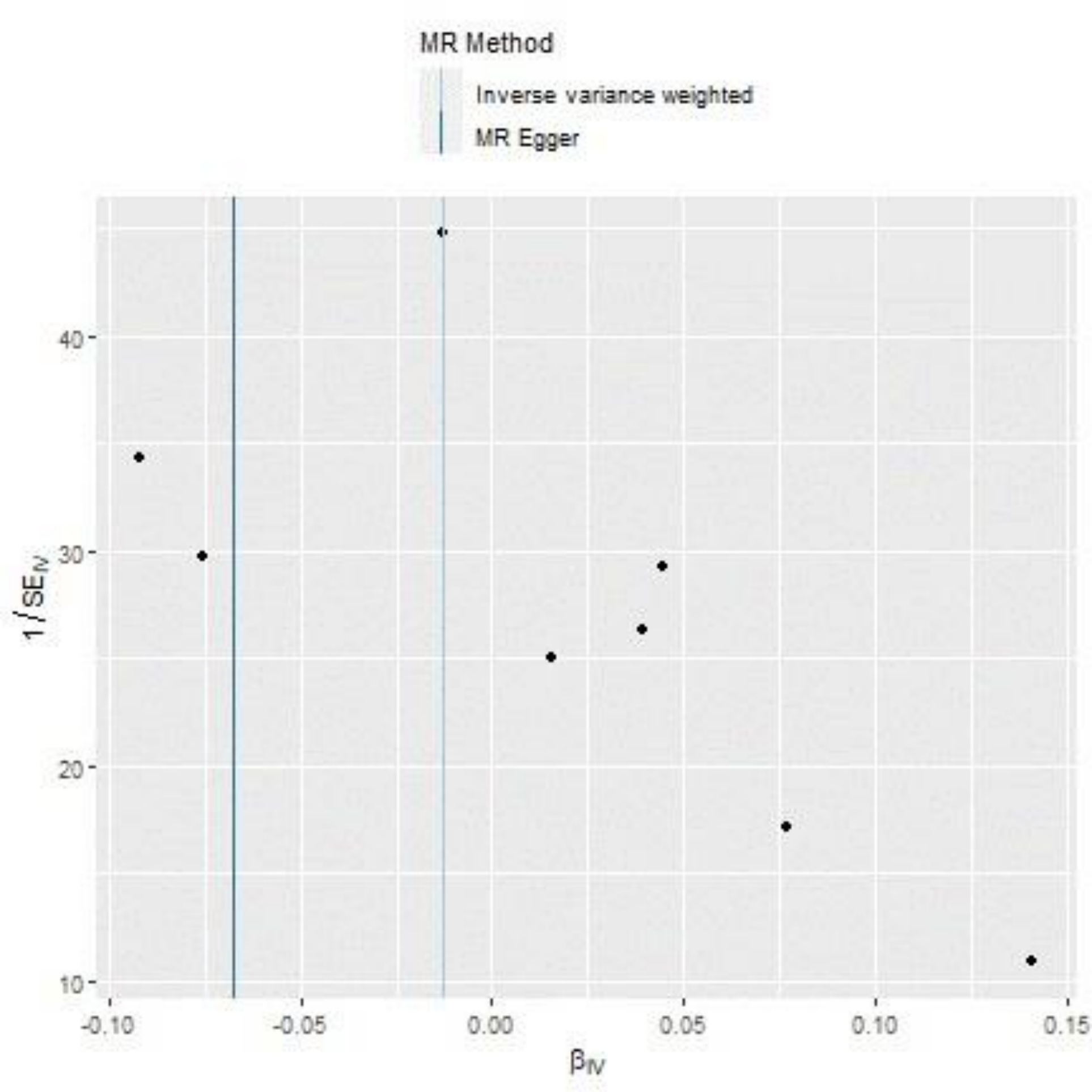
Heterogeneity tests

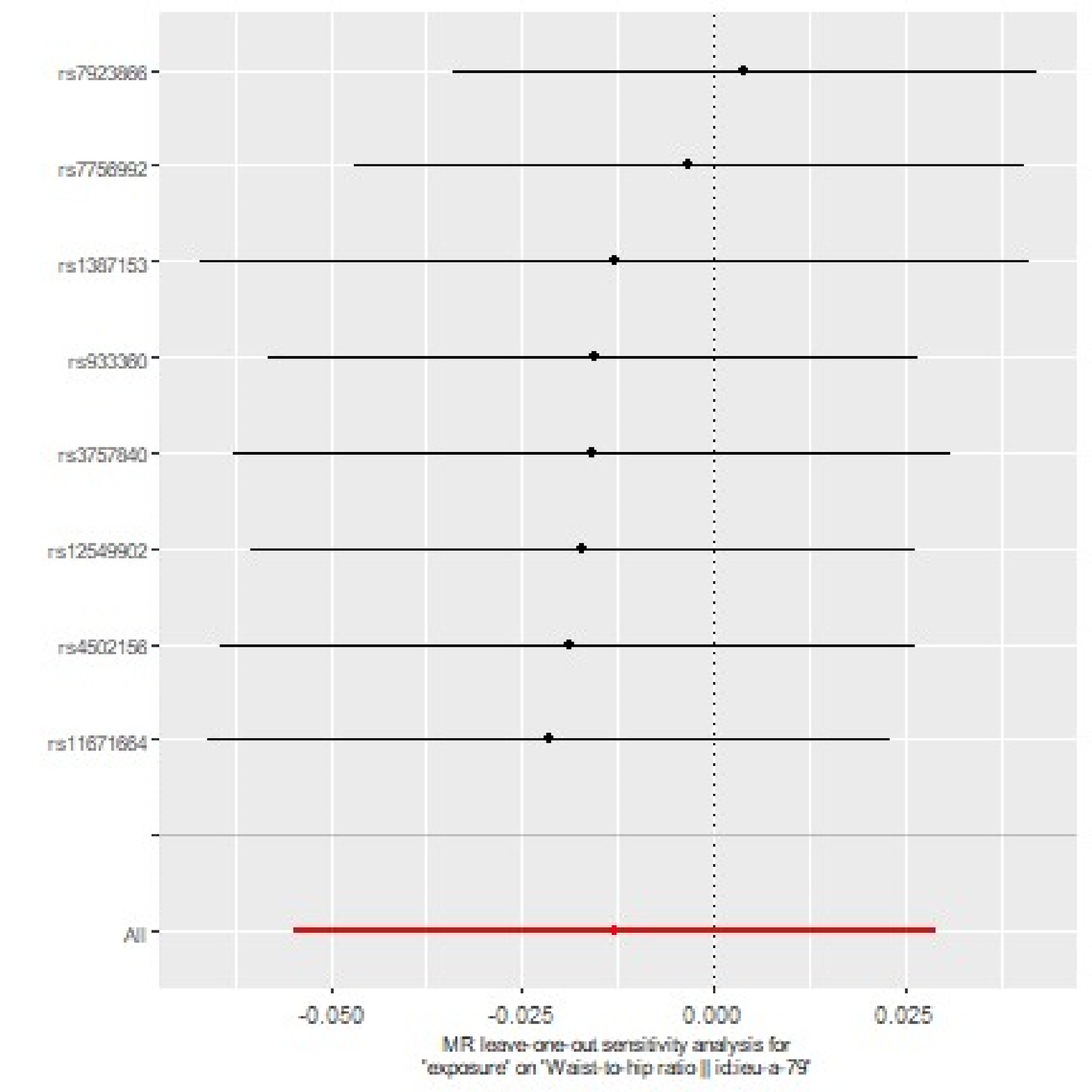
method	Q	Q_df	Q_pval
MR Egger	68.26968	5	0
Inverse variance weighted	73.39894	6	0

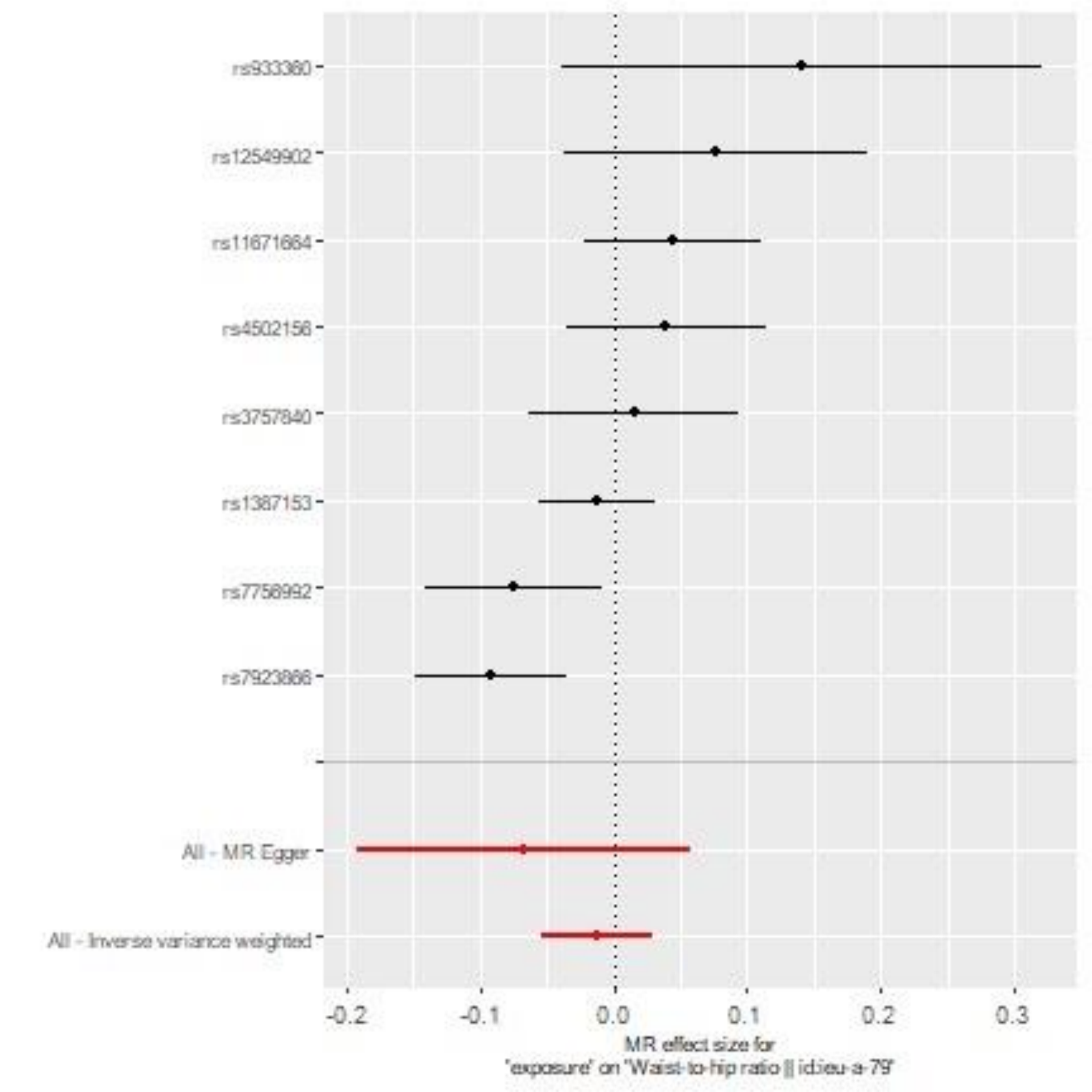
Test for directional horizontal pleiotropy

egger_intercept	se	pval
0.0051008	0.0083222	0.566737


MR Test
Inverse variance weighted
MR Egger
Simple mode
Weighted median
Weighted mode
SNP effect on Waist-to-hip ratio || id:ieu-a-79
0.010
0.005
0.000
-0.005
-0.010
-0.015
0.05
0.10
0.15
0.20
SNP effect on exposure


MR Method
Inverse variance weighted
MR Egger
40
30
20
10
$1/SE_{IV}$
-0.10
-0.05
0.00
0.05
0.10
0.15
β_{IV}


rs7923866
rs7756992
rs1397153
rs933360
rs3757840
rs12549902
rs4502156
rs11671664
All
-0.050
-0.025
0.000
0.025
MR leave-one-out sensitivity analysis for
"exposure" on "Waist-to-hip ratio || id:ieu-a-79"


rs933360
rs12549902
rs11671664
rs4502156
rs3757840
rs1387153
rs7758992
rs7923866
All - MR Egger
All - Inverse variance weighted
-0.2
-0.1
0.0
0.1
0.2
0.3
MR effect size for
'exposure' on "Waist-to-hip ratio || id:ieu-a-79"

Exposure: Corrected Insulin Response, Outcome: Right Leg Fat Percentage

Results from two sample MR:

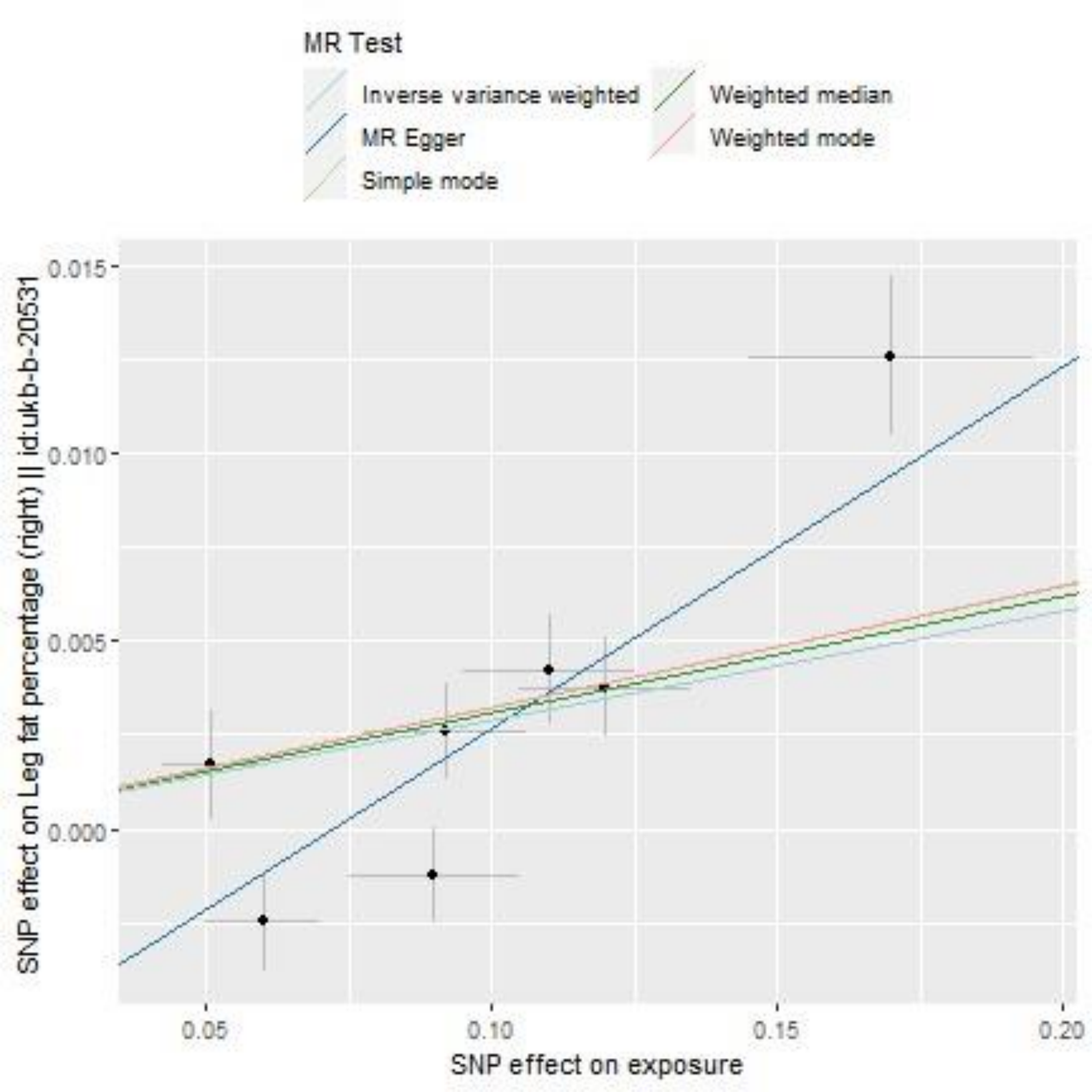
method	nsnp	b	se	pval
MR Egger	7	0.0963049	0.0310484	0.0267994
Weighted median	7	0.0308977	0.0080142	0.0001156
Inverse variance weighted	7	0.0289189	0.0127660	0.0234937
Simple mode	7	0.0324867	0.0120228	0.0354770
Weighted mode	7	0.0321854	0.0098808	0.0173058

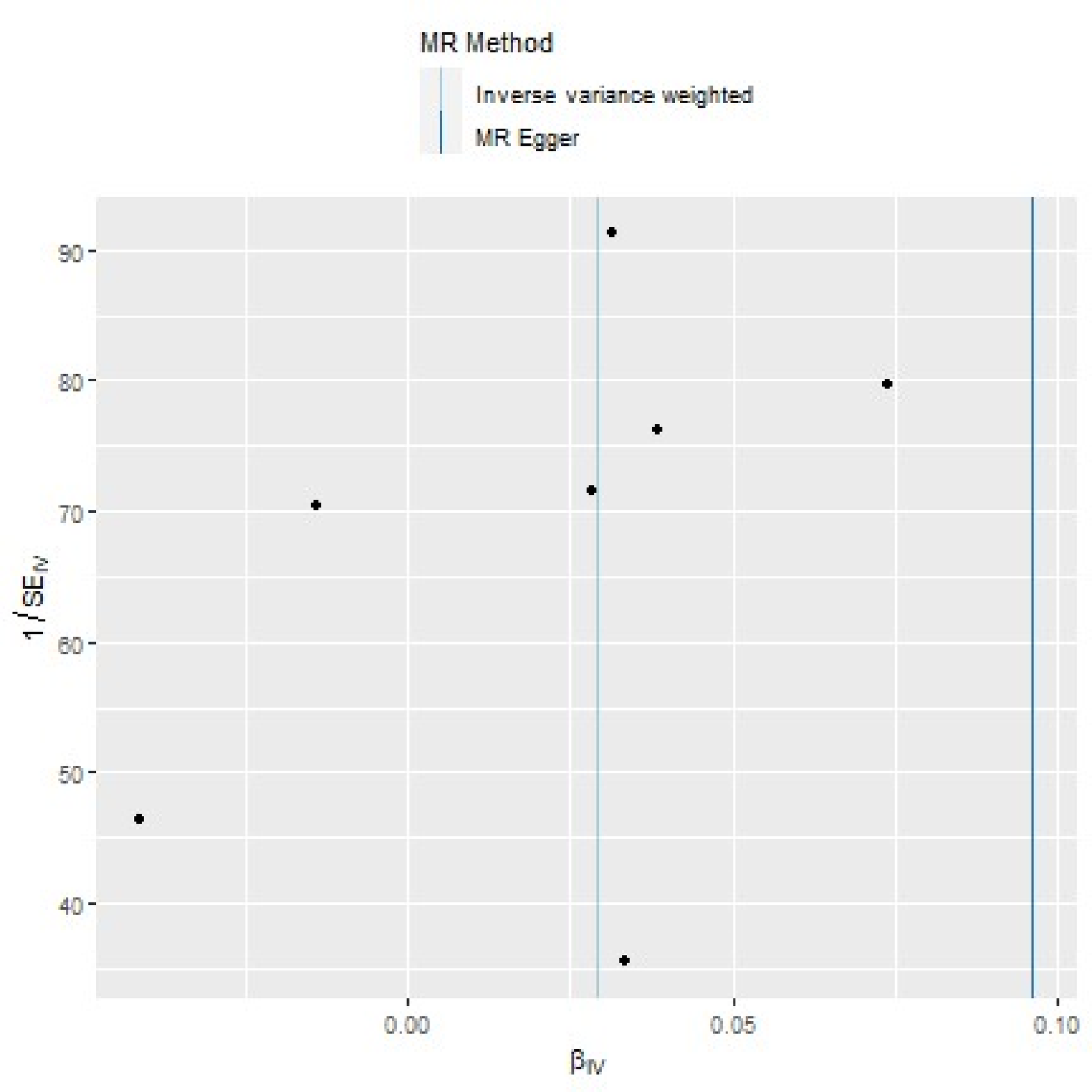
Heterogeneity tests

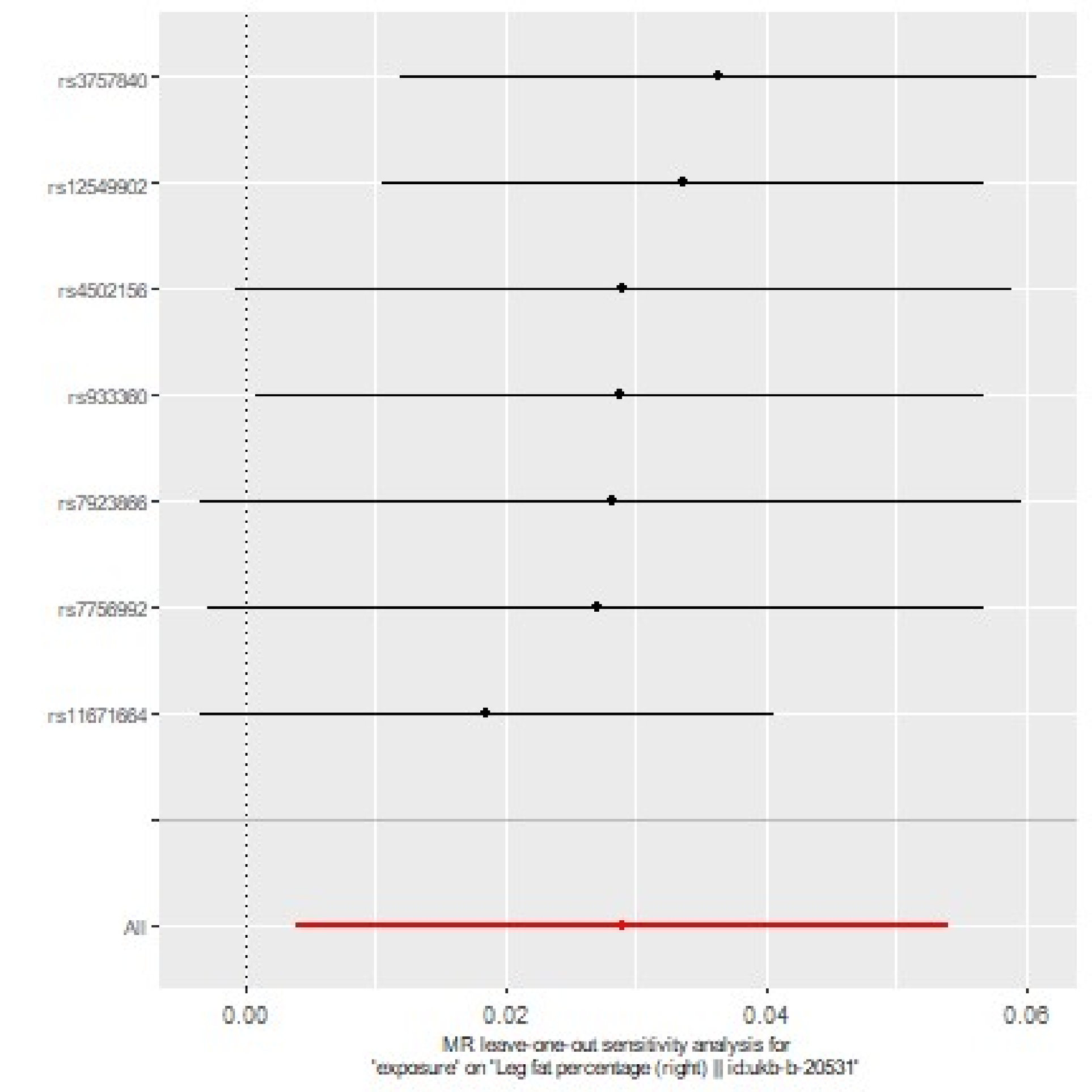
method	Q	Q_df	Q_pval
MR Egger	16.24640	5	0.0061747
Inverse variance weighted	33.23677	6	0.0000094

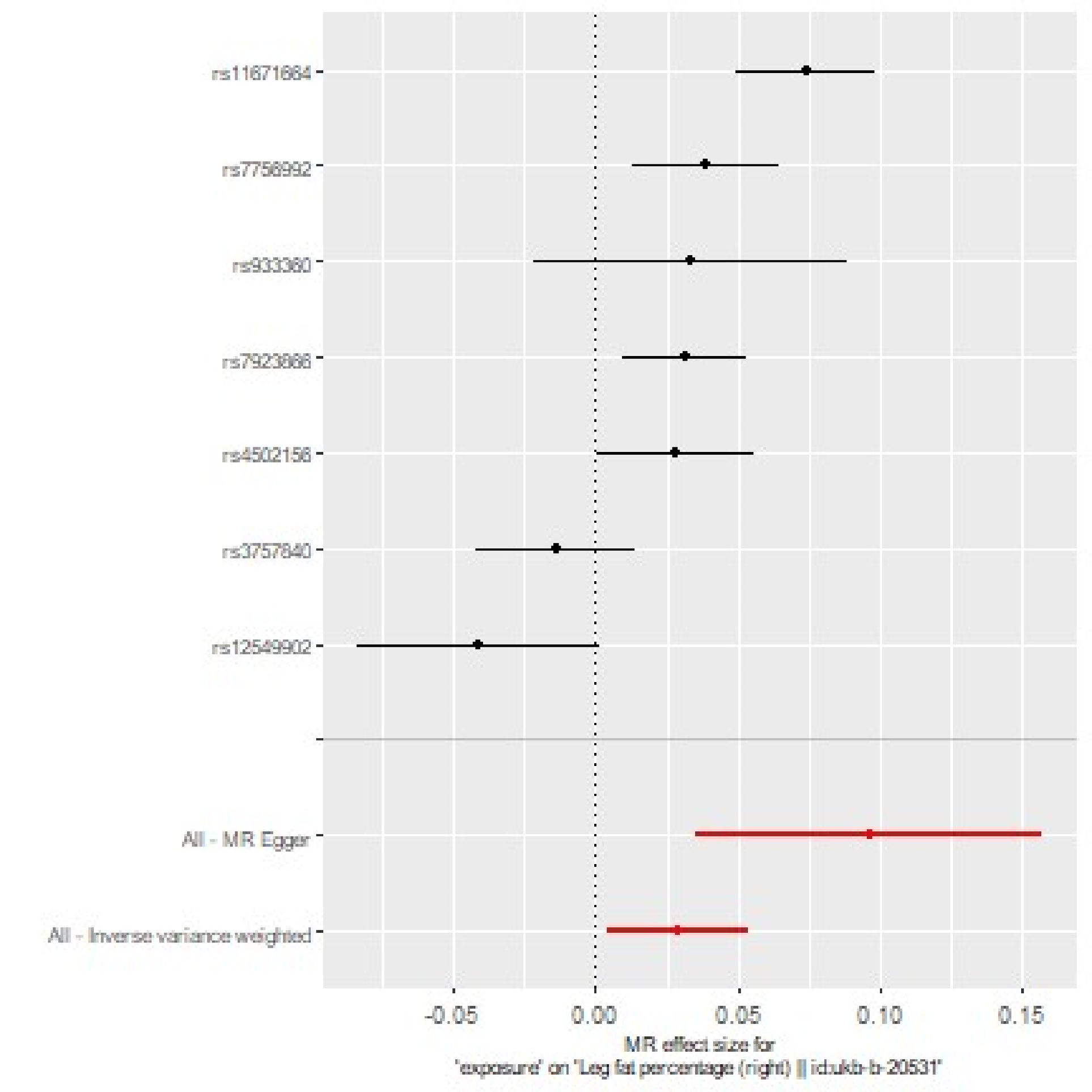
Test for directional horizontal pleiotropy

egger_intercept	se	pval
-0.0069221	0.0030271	0.0709419


MR Test
Inverse variance weighted
MR Egger
Simple mode
Weighted median
Weighted mode
SNP effect on Leg fat percentage (right) || id:ukb-b-20531
0.015
0.010
0.005
0.000
0.05
0.10
0.15
0.20
SNP effect on exposure


MR Method
Inverse variance weighted
MR Egger
90
80
70
60
50
40
1 / SE_IV
0.00
0.05
0.10
β_IV


rs3757840
rs12549902
rs4502156
rs933360
rs7923866
rs7756992
rs11671664
All
0.00
0.02
0.04
0.06
MR leave-one-out sensitivity analysis for
"exposure" on "Leg fat percentage (right) || id:ukb-b-20531"


rs11671664
rs7756992
rs933360
rs7923866
rs4502158
rs3757840
rs12549902
All - MR Egger
All - Inverse variance weighted
-0.05
0.00
0.05
0.10
0.15
MR effect size for
'exposure' on 'Leg fat percentage (right) || id:ukb-b-20531'

Exposure: Corrected Insulin Response, Outcome: Liver Fat

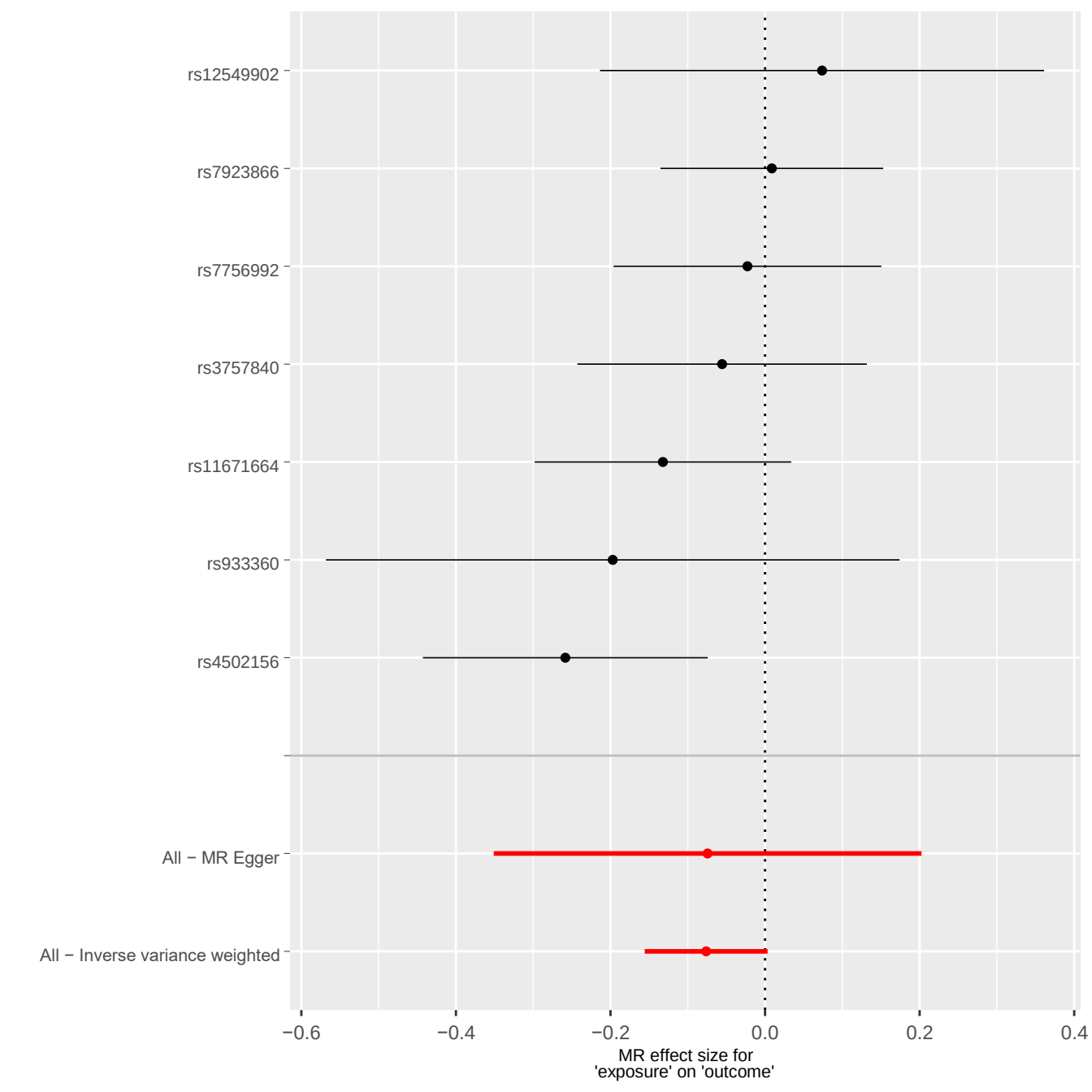
Method	nsnp	beta	se	pval
MR Egger	7	-0.074	0.141	0.621
Weighted median	7	-0.041	0.05	0.405
Inverse variance weighted	7	-0.076	0.04	0.06
Simple mode	7	-0.026	0.07	0.723
Weighted mode	7	-0.026	0.064	0.7

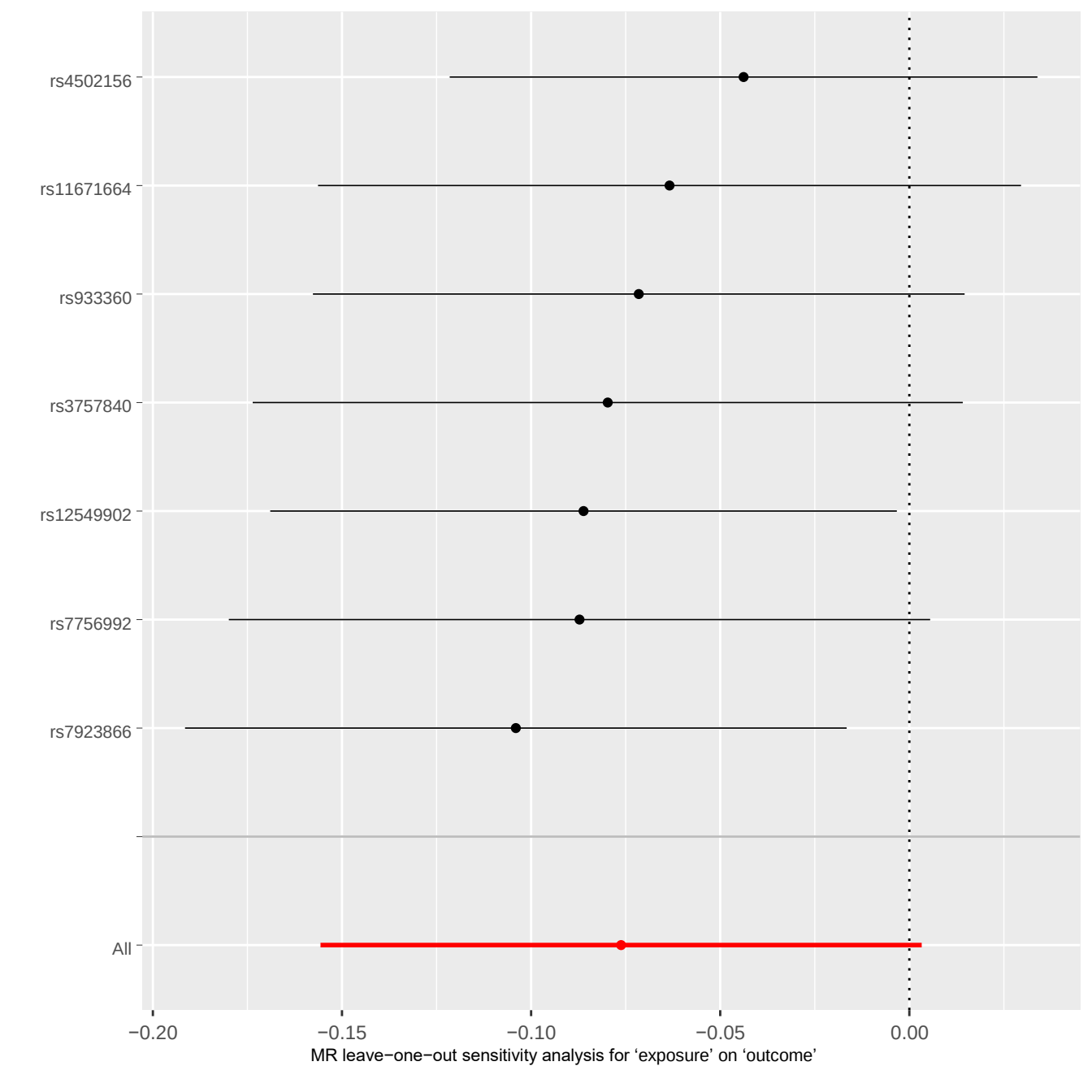
Heterogeneity tests:

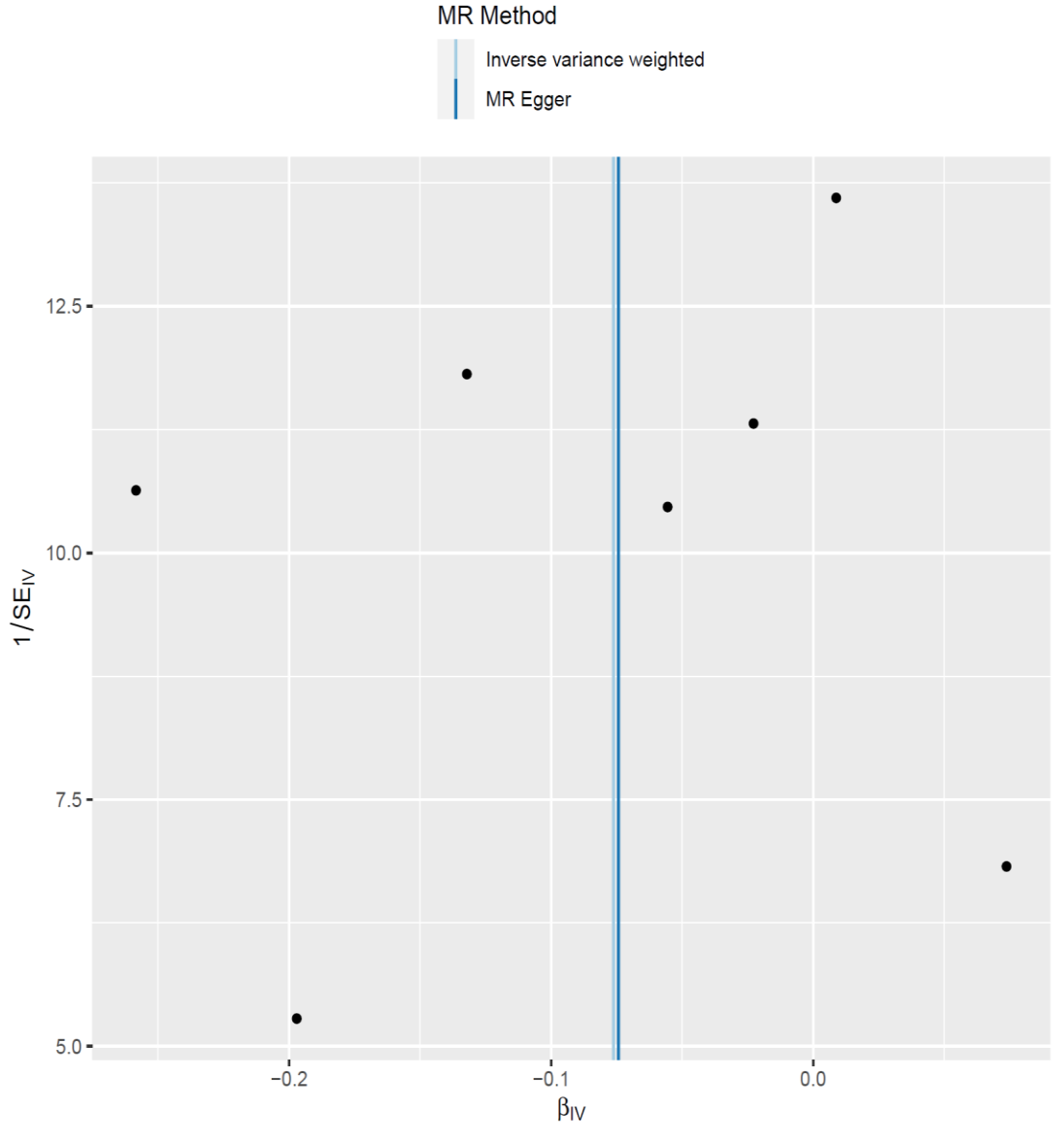
Method	Q	Q_df	Q_pval
MR Egger	7.39	5	0.193
Inverse variance weighted	7.39	6	0.286

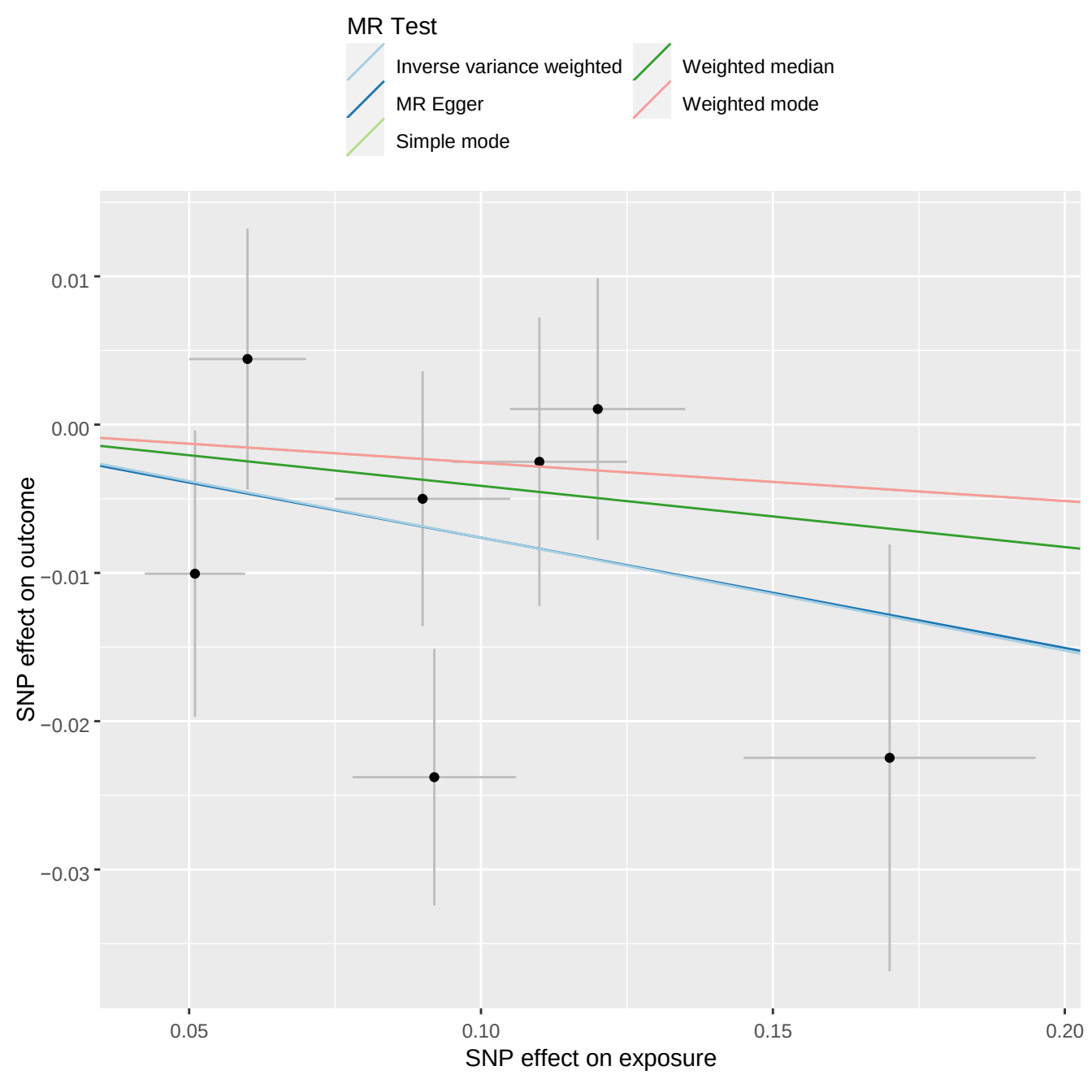
Test for directional horizontal pleiotropy:

Egger_intercept	se	pval
-0.00019	0.014	0.98


rs12549902
rs7923866
rs7756992
rs3757840
rs11671664
rs933360
rs4502156
All − MR Egger
All − Inverse variance weighted
−0.6
−0.4
−0.2
0.0
0.2
0.4
MR effect size for
'exposure' on 'outcome'


rs4502156
rs11671664
rs933360
rs3757840
rs12549902
rs7756992
rs7923866
All
−0.20
−0.15
−0.10
−0.05
0.00
MR leave−one−out sensitivity analysis for ‘exposure’ on ‘outcome’


MR Method
Inverse variance weighted
MR Egger
12.5
10.0
7.5
5.0
1/SE_IV
−0.2
−0.1
0.0
β_IV


MR Test
Inverse variance weighted
MR Egger
Simple mode
Weighted median
Weighted mode
SNP effect on outcome
0.01
0.00
−0.01
−0.02
−0.03
0.05
0.10
0.15
0.20
SNP effect on exposure

Exposure: Corrected Insulin Response, Outcome: Hypertension

Results from two sample MR:

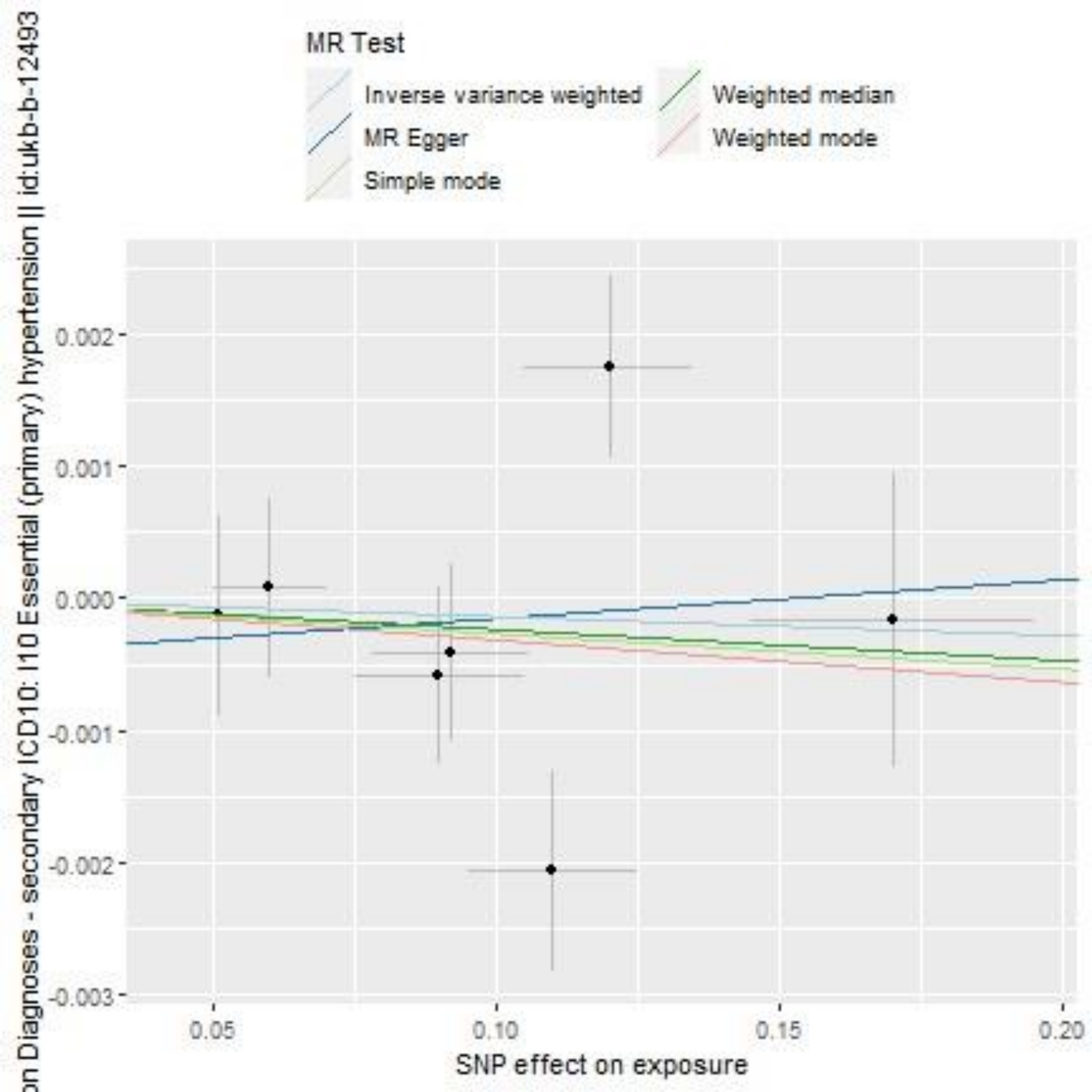
method	nsnp	b	se	pval
MR Egger	7	0.0029412	0.0154000	0.8560500
Weighted median	7	-0.0023705	0.0043531	0.5860614
Inverse variance weighted	7	-0.0014397	0.0044674	0.7472460
Simple mode	7	-0.0026606	0.0067889	0.7086691
Weighted mode	7	-0.0031927	0.0076392	0.6905387

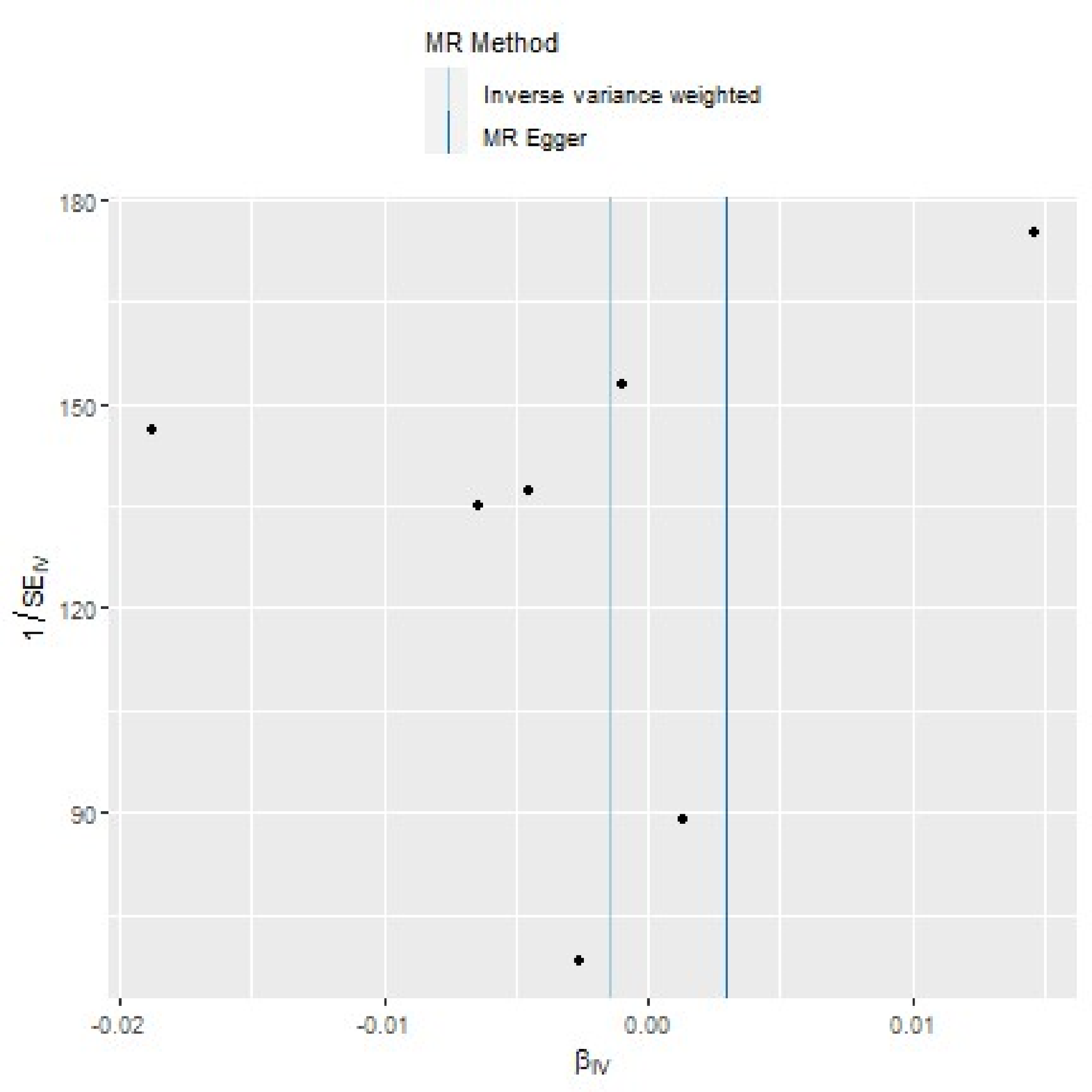
Heterogeneity tests

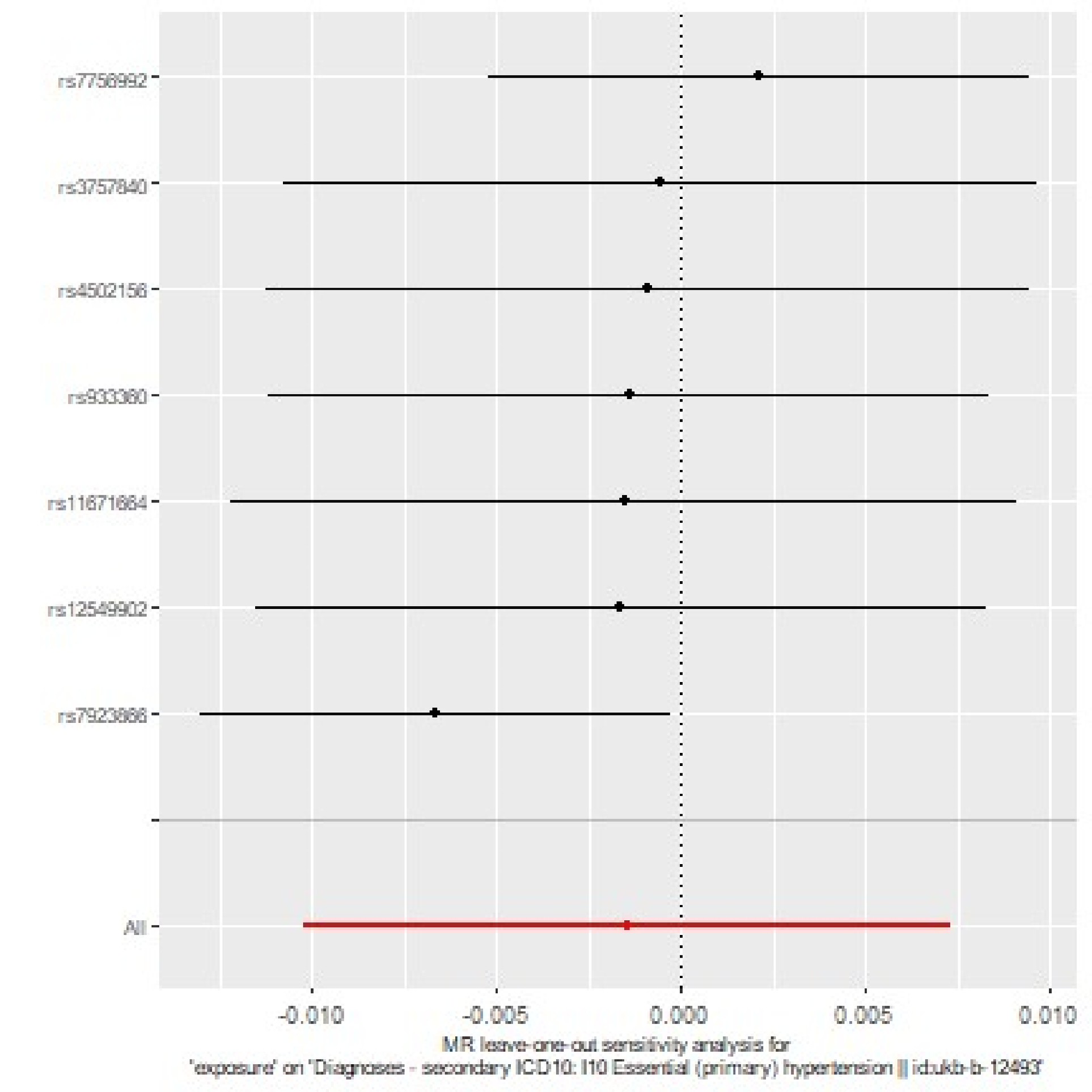
method	Q	Q_df	Q_pval
MR Egger	14.70558	5	0.0116973
Inverse variance weighted	14.96980	6	0.0204929

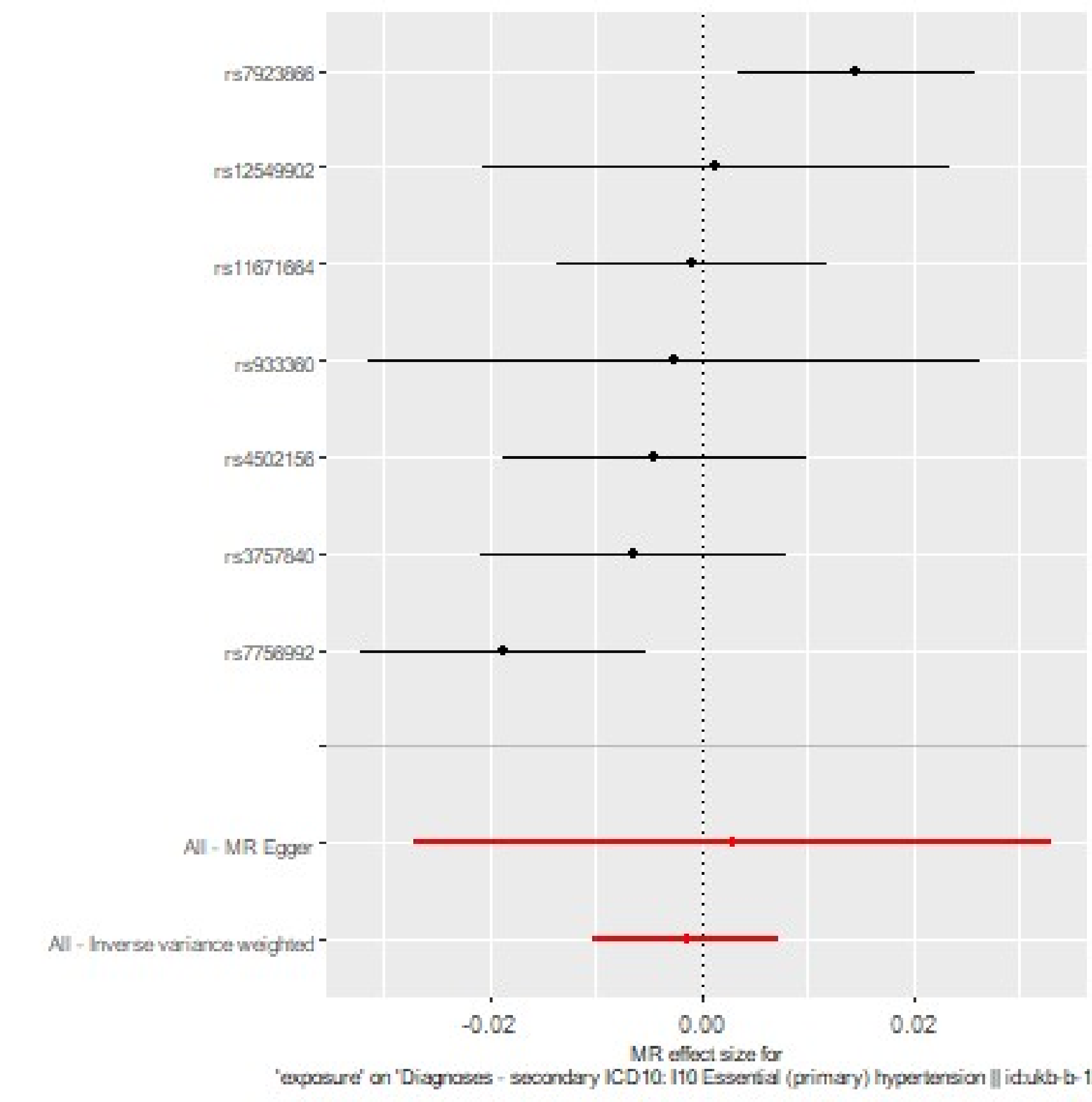
Test for directional horizontal pleiotropy

egger_intercept	se	pval
-0.0004501	0.0015016	0.7764451


MR Test
Inverse variance weighted
MR Egger
Simple mode
Weighted median
Weighted mode
0.002
0.001
0.000
-0.001
-0.002
-0.003
0.05
0.10
0.15
0.20
SNP effect on exposure
on Diagnoses - secondary ICD10: I10 Essential (primary) hypertension || id:ukb-b-12493


MR Method
Inverse variance weighted
MR Egger
180
150
120
90
1 / SE_IV
-0.02
-0.01
0.00
0.01
β_IV


rs7756992
rs3757840
rs4502156
rs933360
rs11671664
rs12549902
rs7923866
All
-0.010
-0.005
0.000
0.005
0.010
MR leave-one-out sensitivity analysis for
'exposure' on 'Diagnoses - secondary ICD10: I10 Essential (primary) hypertension || id:ukb-b-12493'


rs7923868
rs12549902
rs11671664
rs933360
rs4502158
rs3757840
rs7756992
All - MR Egger
All - Inverse variance weighted
-0.02
0.00
0.02
MR effect size for
'exposure' on 'Diagnoses - secondary ICD10: I10 Essential (primary) hypertension || id:ukb-b-12

Exposure: Corrected Insulin Response, Outcome: Systolic Blood Pressure

Results from two sample MR:

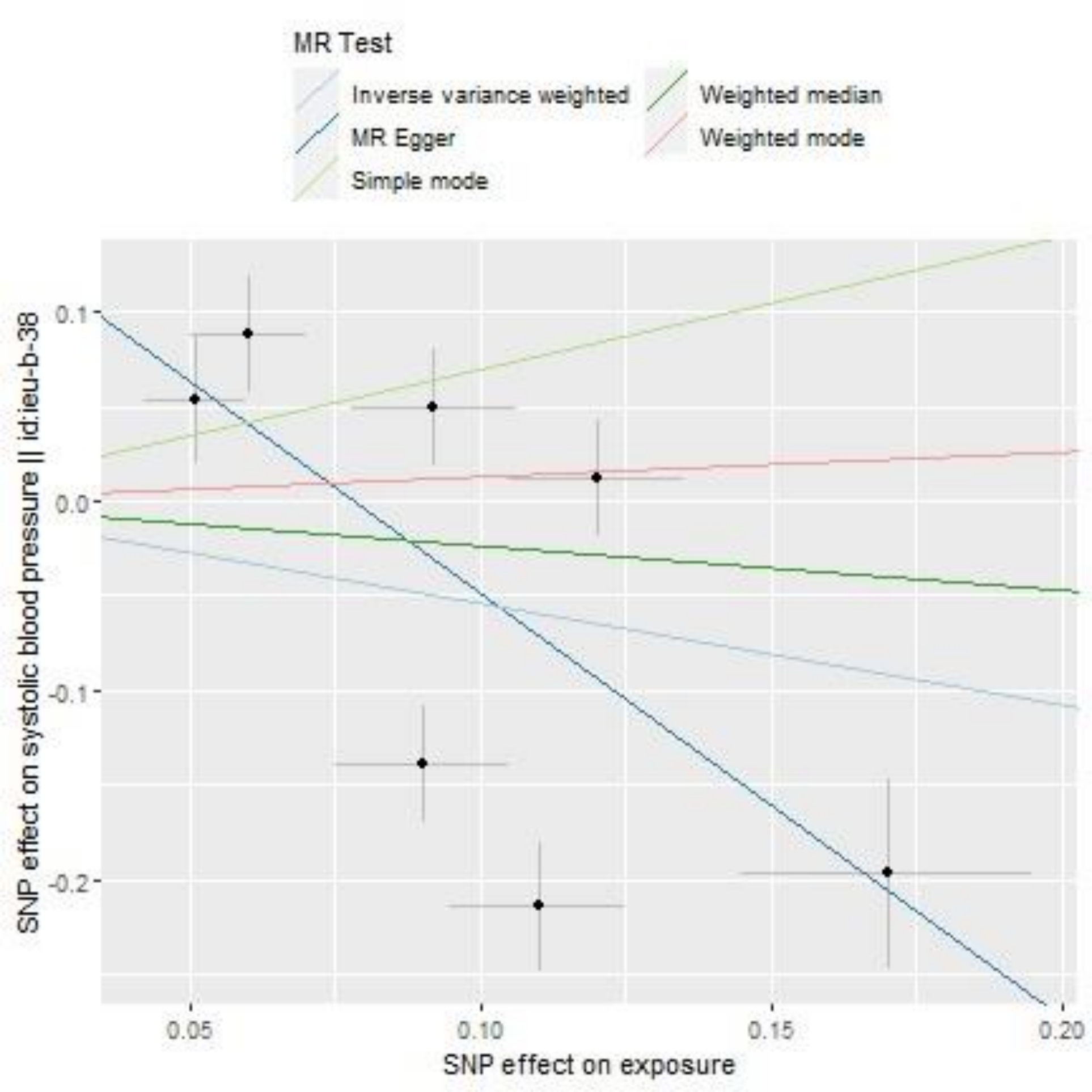
method	nsnp	b	se	pval
MR Egger	7	-2.2430229	1.3158998	0.1489994
Weighted median	7	-0.2343501	0.2532287	0.3547327
Inverse variance weighted	7	-0.5365593	0.4438628	0.2267242
Simple mode	7	0.6986504	0.6607231	0.3310306
Weighted mode	7	0.1286353	0.3593088	0.7325956

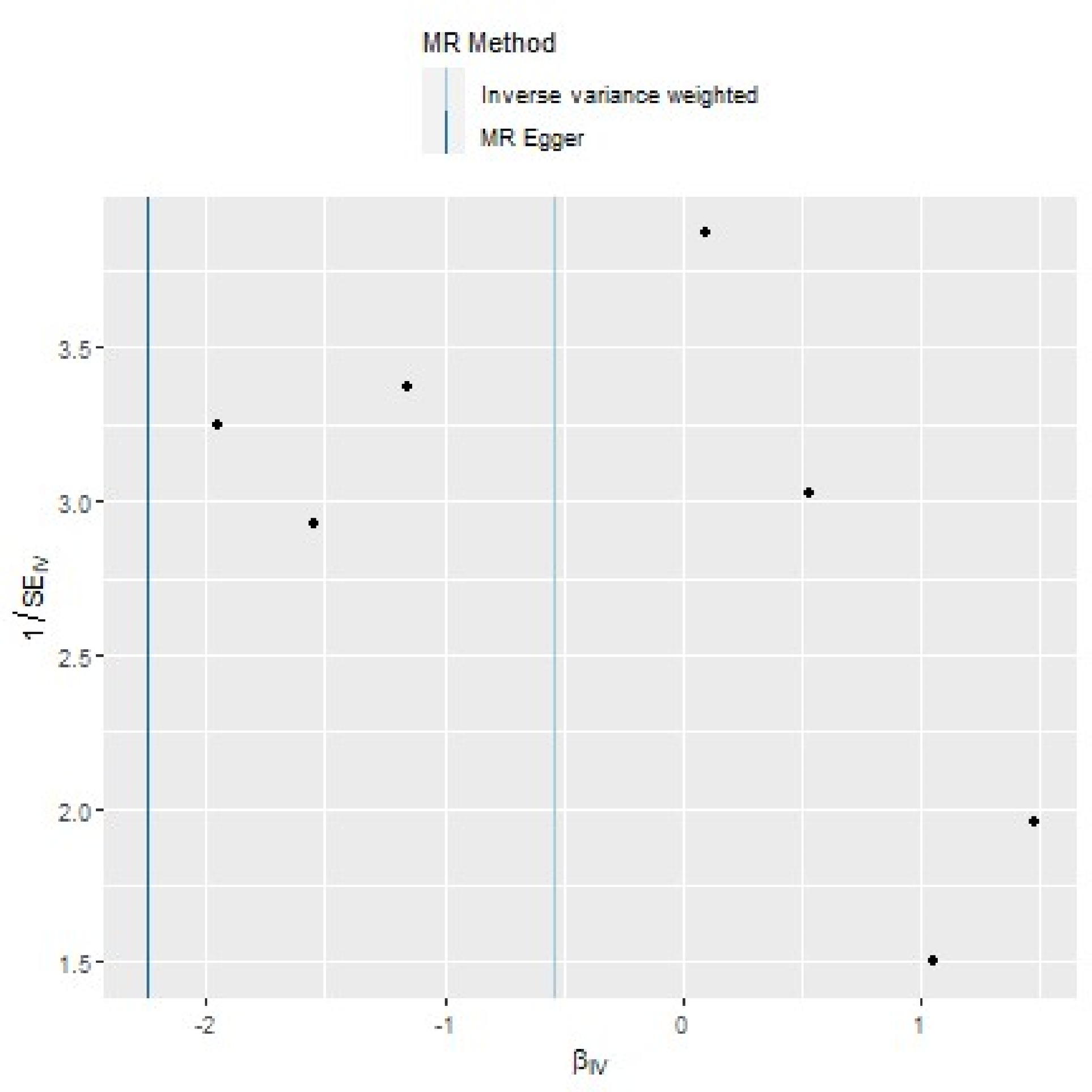
Heterogeneity tests

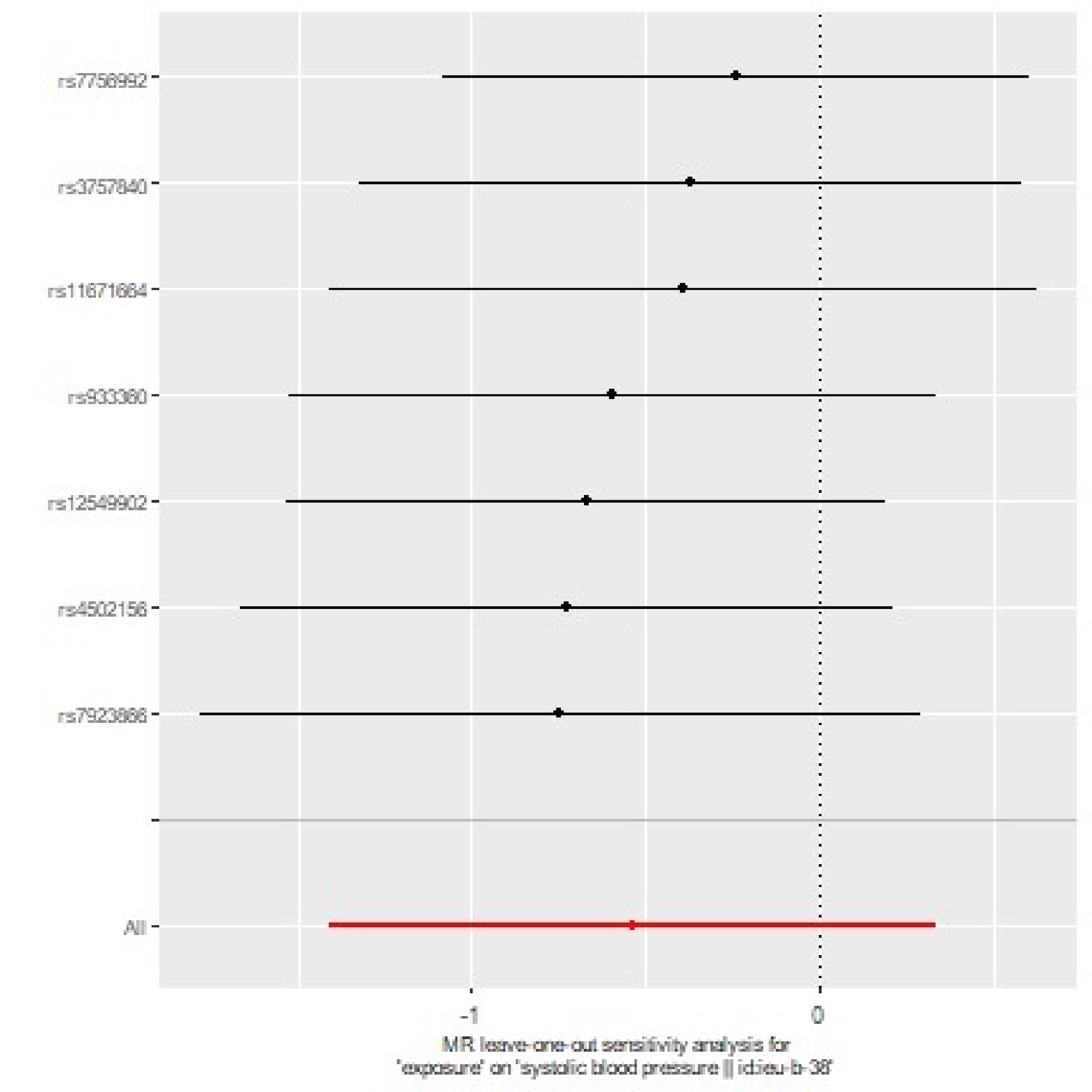
method	Q	Q_df	Q_pval
MR Egger	52.25330	5	0
Inverse variance weighted	71.76807	6	0

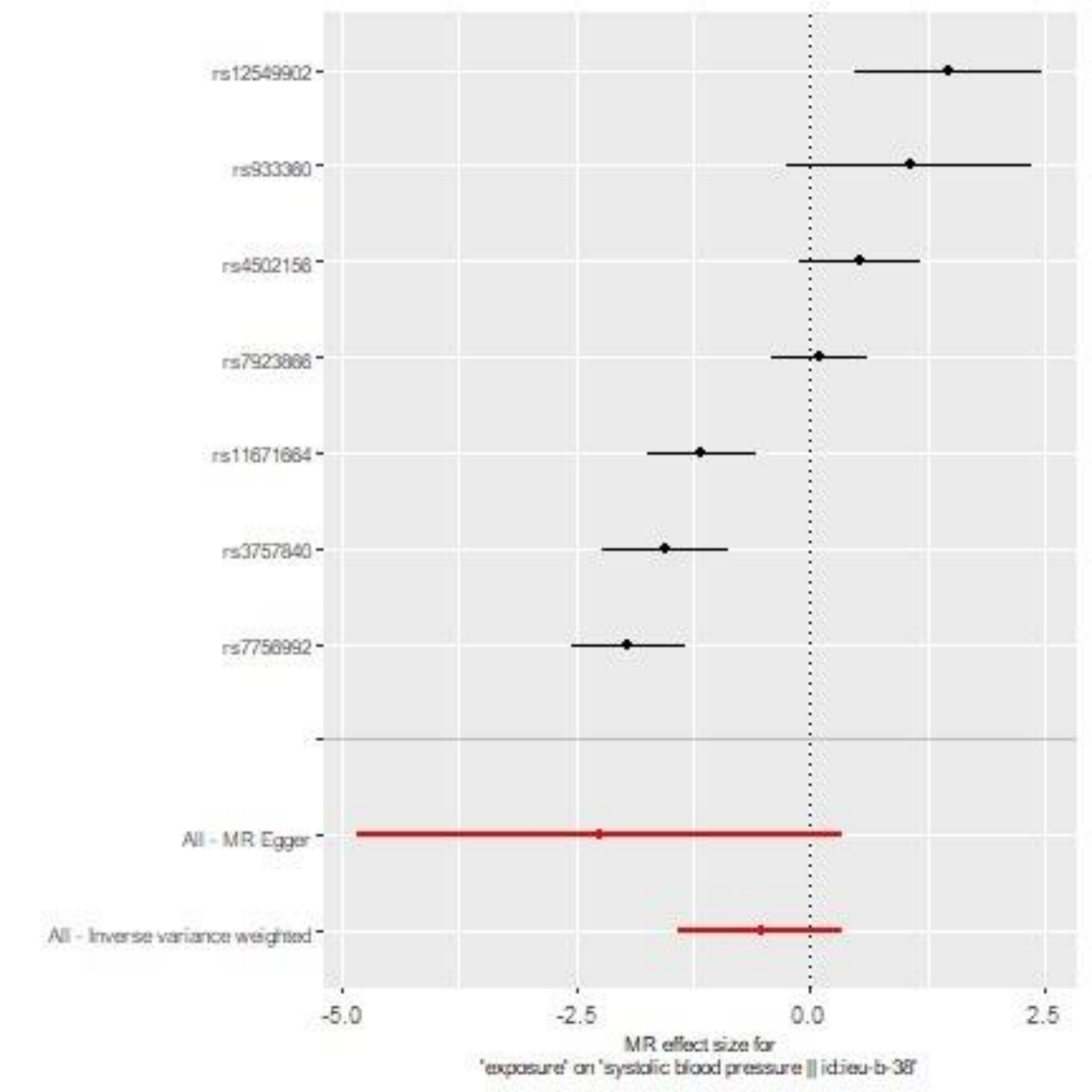
Test for directional horizontal pleiotropy

egger_intercept	se	pval
0.1755021	0.1284318	0.2300257


MR Test
Inverse variance weighted
MR Egger
Simple mode
Weighted median
Weighted mode
SNP effect on systolic blood pressure || id:ieu-b-38
0.1
0.0
-0.1
-0.2
0.05
0.10
0.15
0.20
SNP effect on exposure


MR Method
Inverse variance weighted
MR Egger
3.5
3.0
2.5
2.0
1.5
1 / SE_IV
-2
-1
0
1
β_IV


rs7756992
rs3757840
rs11671664
rs933360
rs12549902
rs4502156
rs7923866
All
-1
0
MR leave-one-out sensitivity analysis for
'exposure' on 'systolic blood pressure || id:ieu-b-38'


rs12549902
rs933360
rs4502156
rs7923866
rs11671664
rs3757840
rs7756992
All - MR Egger
All - Inverse variance weighted
-5.0
-2.5
0.0
2.5
MR effect size for
'exposure' on 'systolic blood pressure || id:ieu-b-38'

Exposure: Corrected Insulin Response, Outcome: Diastolic Blood Pressure

Results from two sample MR:

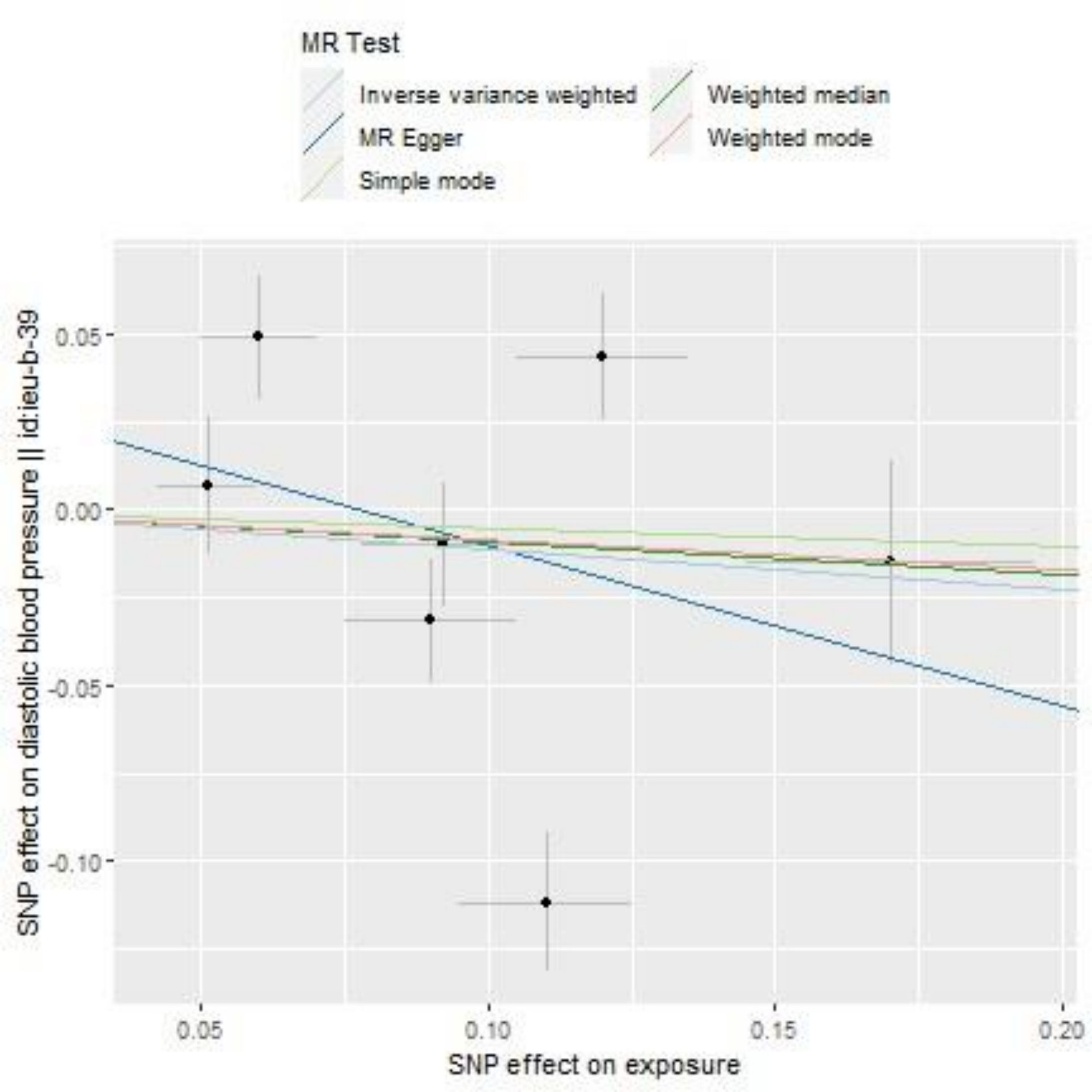
method	nsnp	b	se	pval
MR Egger	7	-0.4564535	0.7074576	0.5472303
Weighted median	7	-0.0933277	0.1209776	0.4404425
Inverse variance weighted	7	-0.1135097	0.2088032	0.5867027
Simple mode	7	-0.0523889	0.1868643	0.7886184
Weighted mode	7	-0.0842812	0.1578549	0.6125922

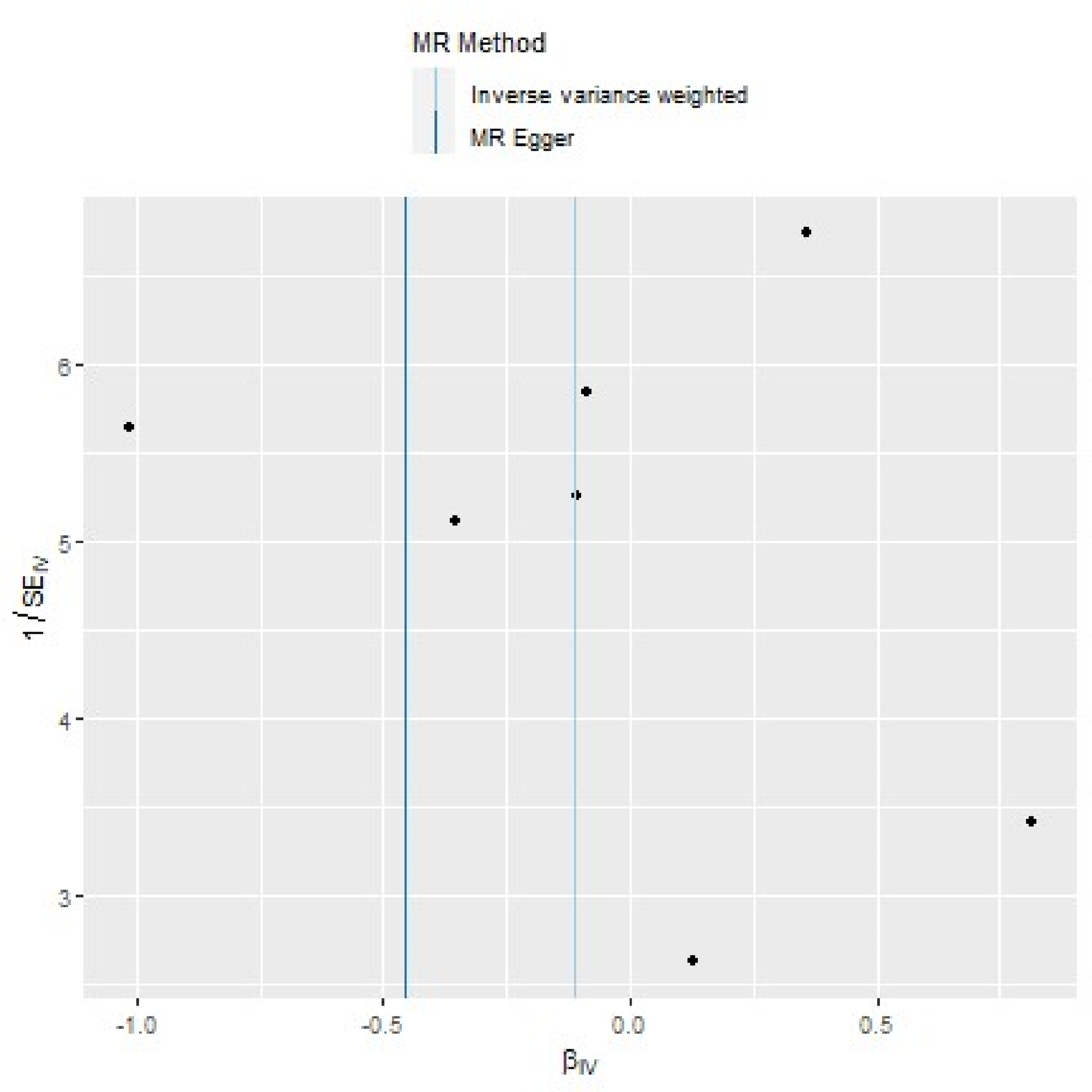
Heterogeneity tests

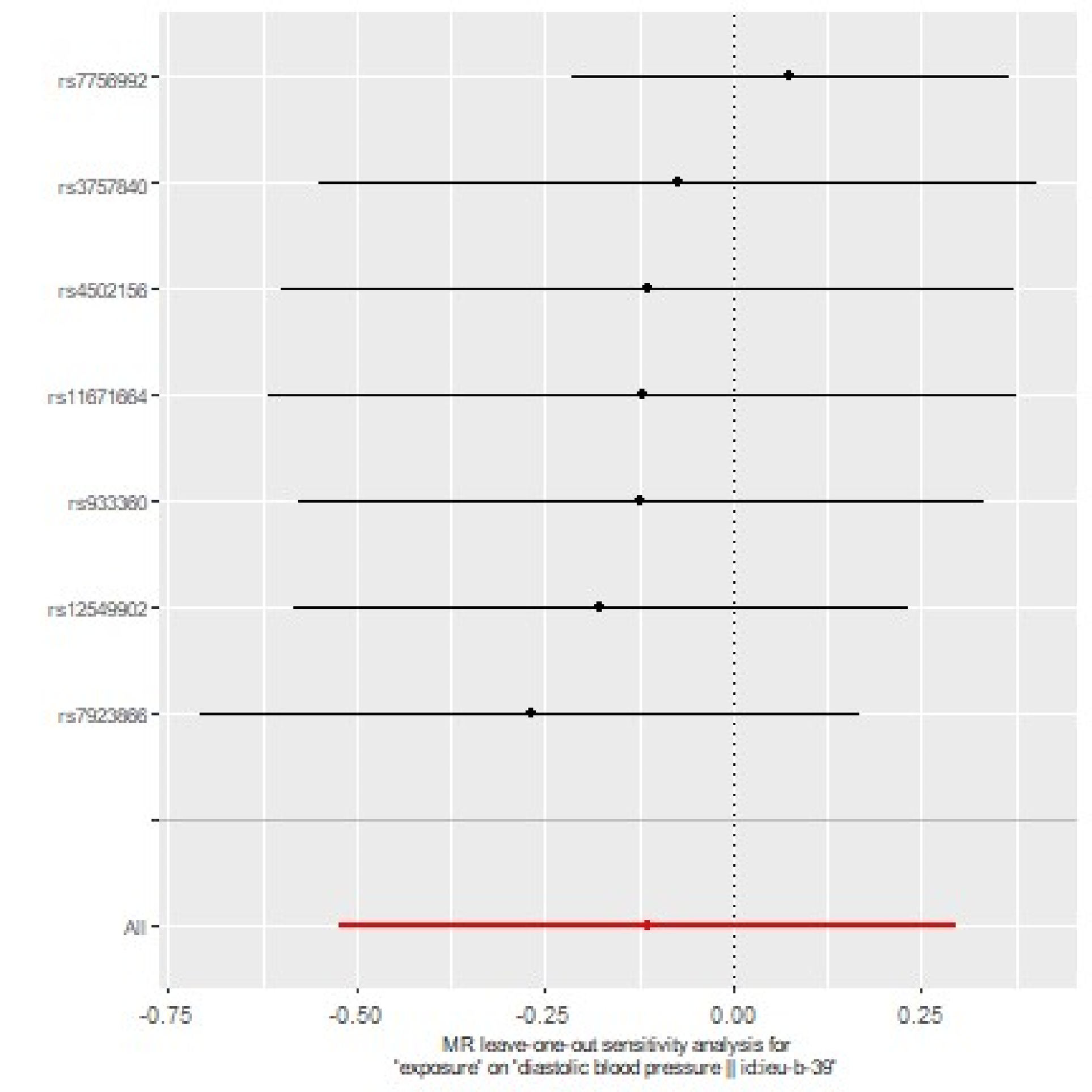
method	Q	Q_df	Q_pval
MR Egger	45.65820	5	0
Inverse variance weighted	48.04072	6	0

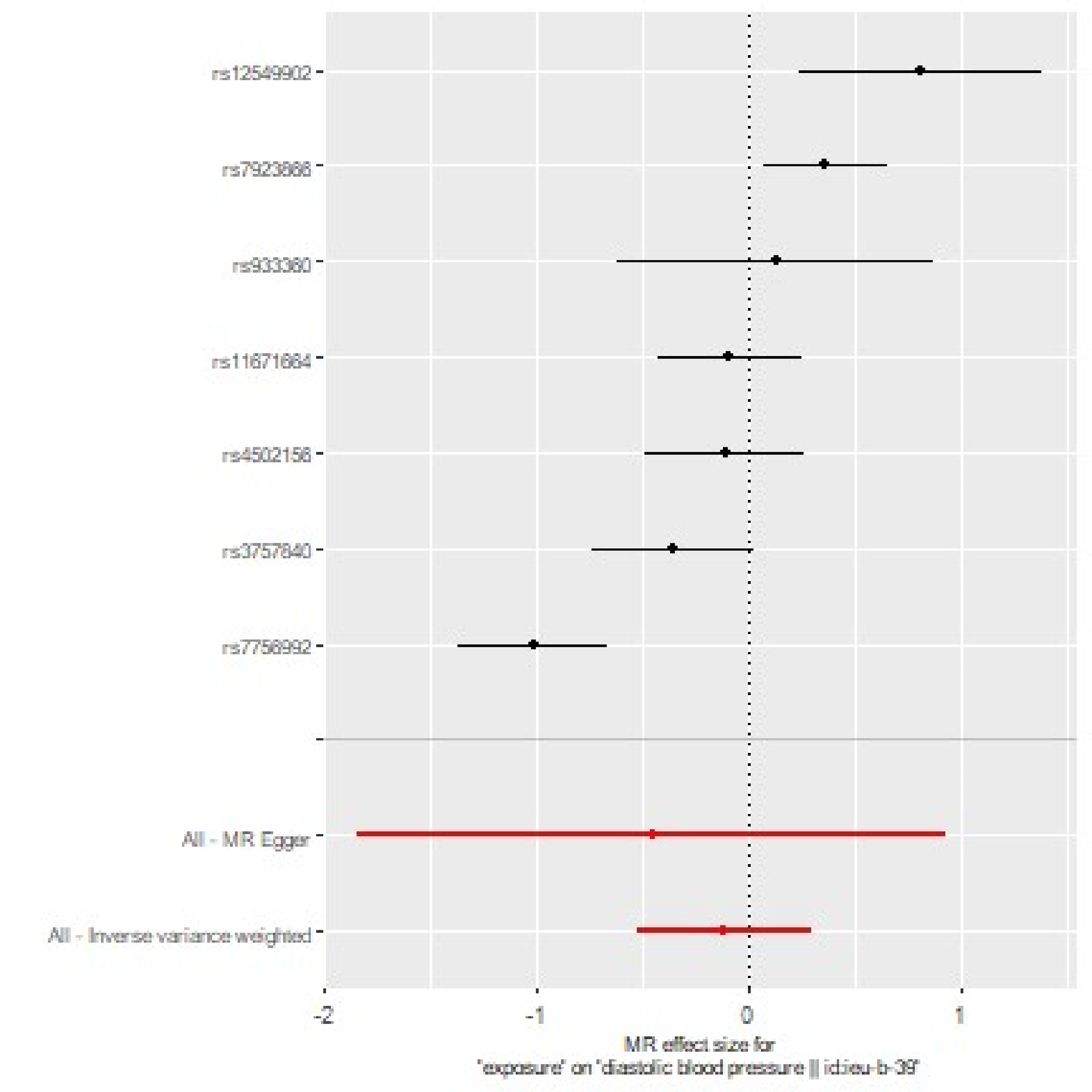
Test for directional horizontal pleiotropy

egger_intercept	se	pval
0.0352329	0.0689769	0.6312429


MR Test
Inverse variance weighted
MR Egger
Simple mode
Weighted median
Weighted mode
SNP effect on diastolic blood pressure || id:ieu-b-39
0.05
0.00
-0.05
-0.10
0.05
0.10
0.15
0.20
SNP effect on exposure


MR Method
Inverse variance weighted
MR Egger
6
5
4
3
1 / SE_IV
-1.0
-0.5
0.0
0.5
β_IV


rs7756992
rs3757840
rs4502156
rs11671664
rs933360
rs12549902
rs7923866
All
-0.75
-0.50
-0.25
0.00
0.25
MR leave-one-out sensitivity analysis for
"exposure" on "diastolic blood pressure || id:ieu-b-39"


rs12549902
rs7923868
rs933360
rs11671664
rs4502158
rs3757840
rs7756992
All - MR Egger
All - Inverse variance weighted
-2
-1
0
1
MR effect size for
"exposure" on "diastolic blood pressure || id:ieu-b-39"

Exposure: Corrected Insulin Response, Outcome: Coronary Artery Disease

Results from two sample MR:

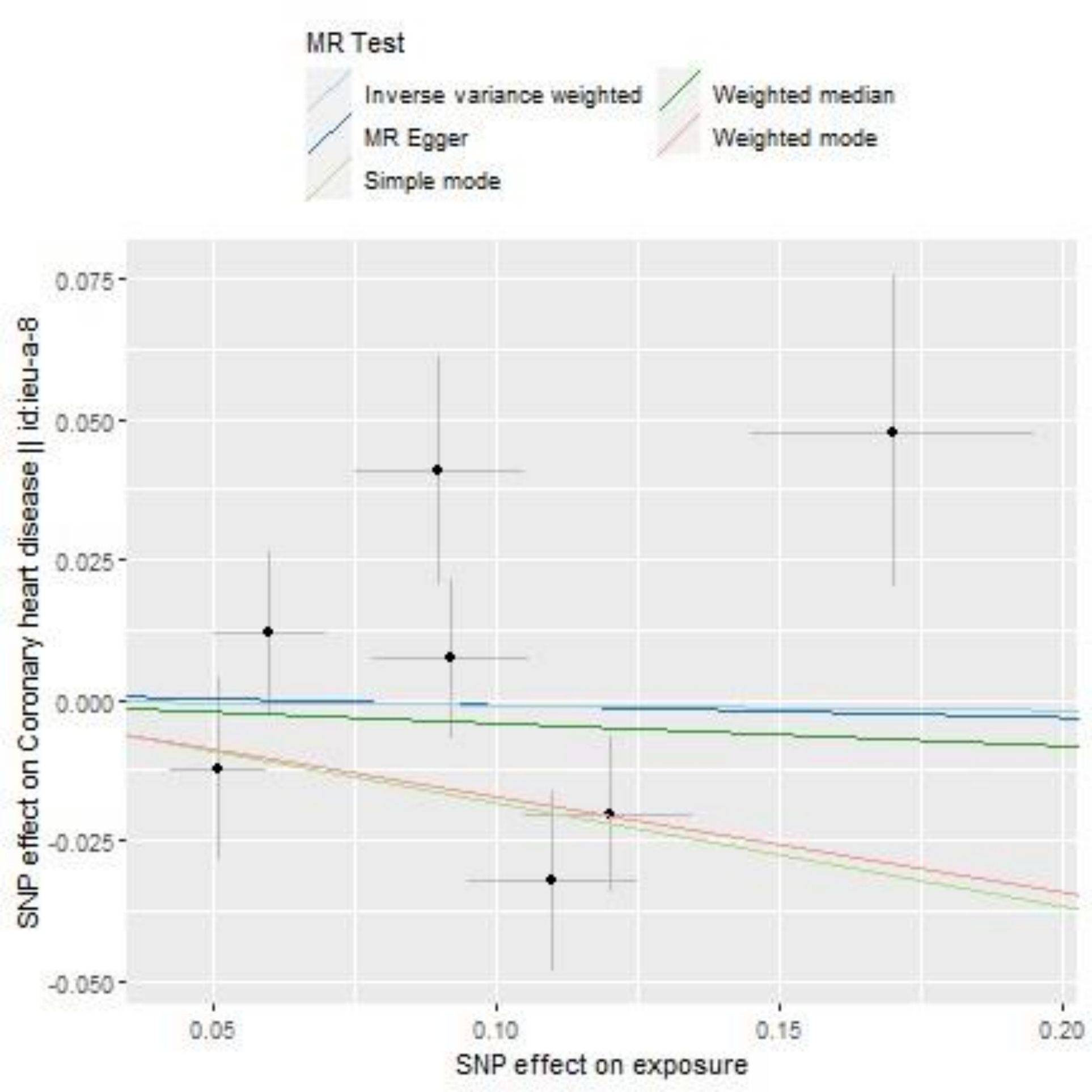
method	nsnp	b	se	pval
MR Egger	7	-0.0225323	0.3474347	0.9508038
Weighted median	7	-0.0409994	0.0956883	0.6683102
Inverse variance weighted	7	-0.0091031	0.0998871	0.9273860
Simple mode	7	-0.1839868	0.2037766	0.4013794
Weighted mode	7	-0.1699464	0.1231637	0.2168506

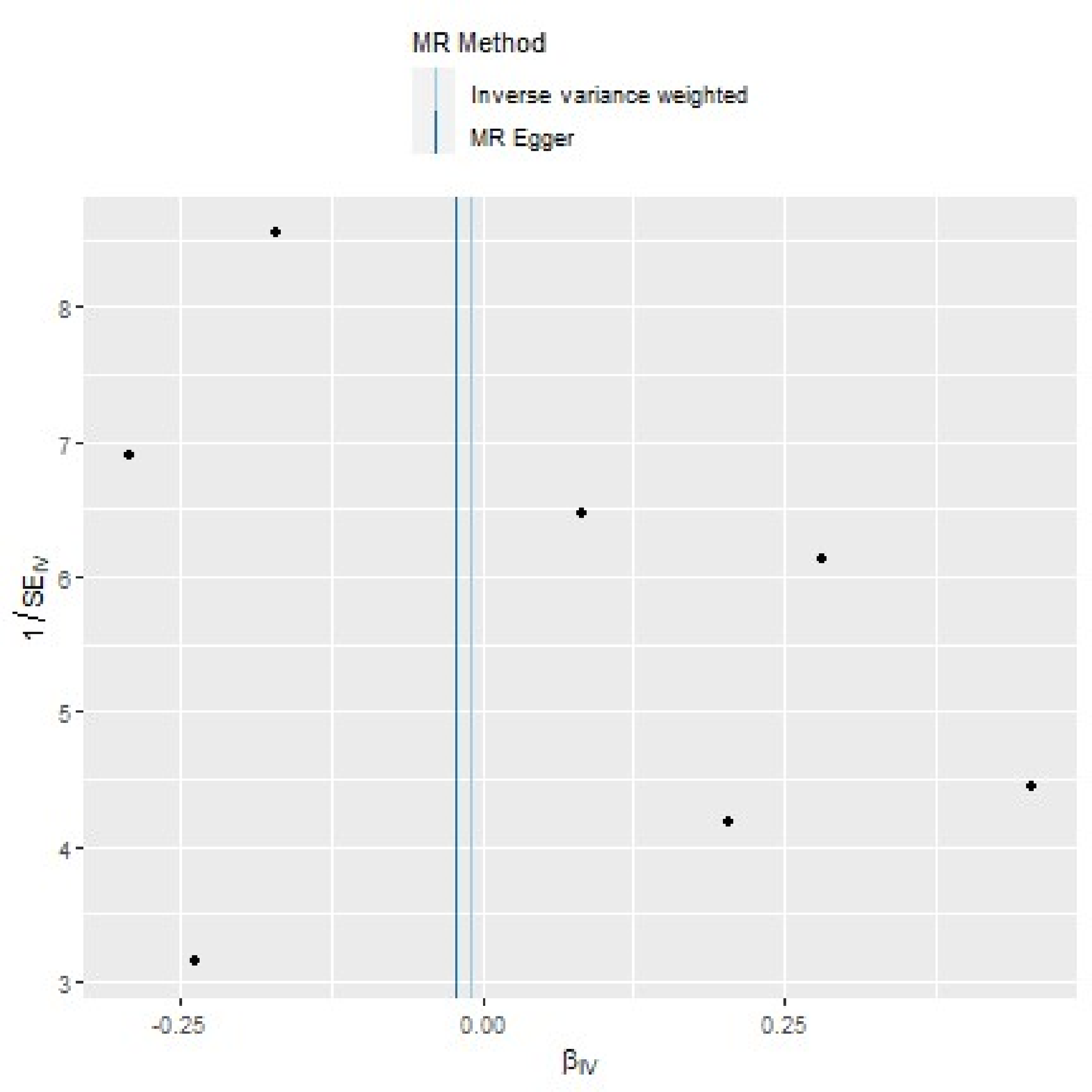
Heterogeneity tests

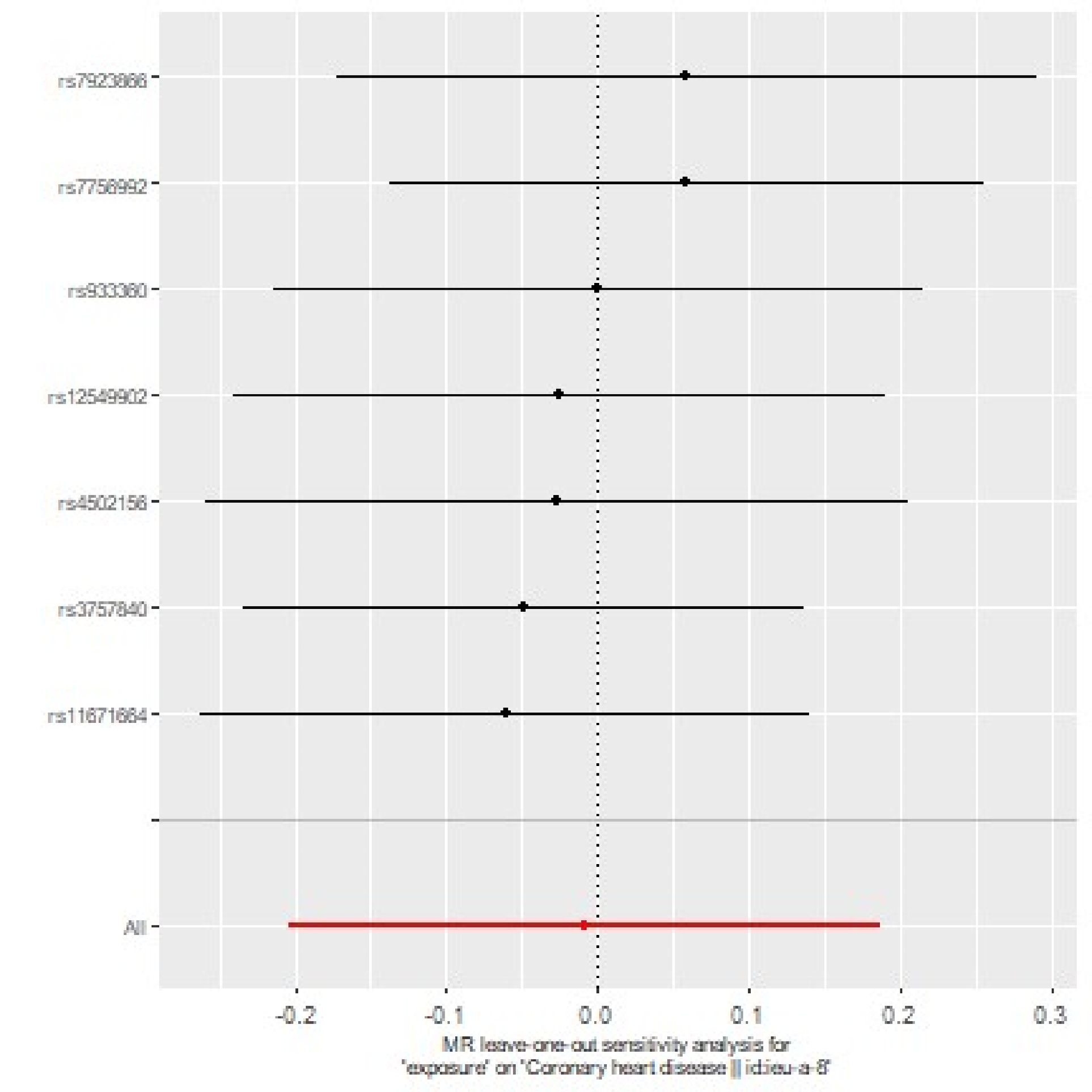
method	Q	Q_df	Q_pval
MR Egger	14.78573	5	0.0113182
Inverse variance weighted	14.79063	6	0.0219491

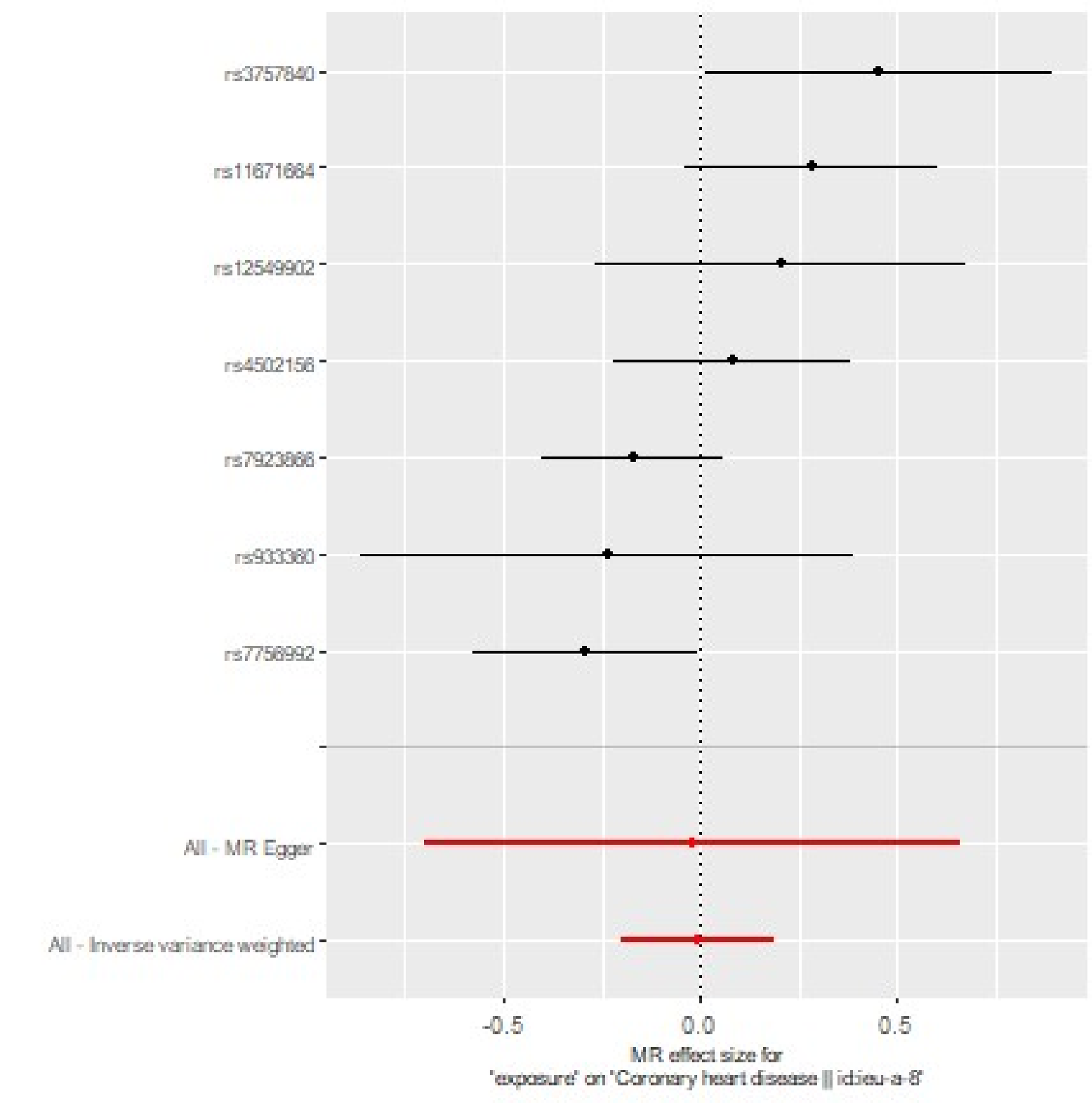
Test for directional horizontal pleiotropy

egger_intercept	se	pval
0.0013708	0.0336602	0.969092


MR Test
Inverse variance weighted
MR Egger
Simple mode
Weighted median
Weighted mode
SNP effect on Coronary heart disease || id:ieu-a-8
0.075
0.050
0.025
0.000
-0.025
-0.050
0.05
0.10
0.15
0.20
SNP effect on exposure


MR Method
Inverse variance weighted
MR Egger
8
7
6
5
4
3
1 / SE_IV
-0.25
0.00
0.25
β_IV


rs7923866
rs7756992
rs933360
rs12549902
rs4502156
rs3757840
rs11671664
All
-0.2
-0.1
0.0
0.1
0.2
0.3
MR leave-one-out sensitivity analysis for
'exposure' on 'Coronary heart disease || id:ieu-a-8'


rs3757840
rs11671664
rs12549902
rs4502156
rs7923866
rs933360
rs7756992
All - MR Egger
All - Inverse variance weighted
-0.5
0.0
0.5
MR effect size for
"exposure" on "Coronary heart disease || id:ieu-a-8"

Exposure: Corrected Insulin Response, Outcome: Major Coronary Heart Disease Event

Results from two sample MR:

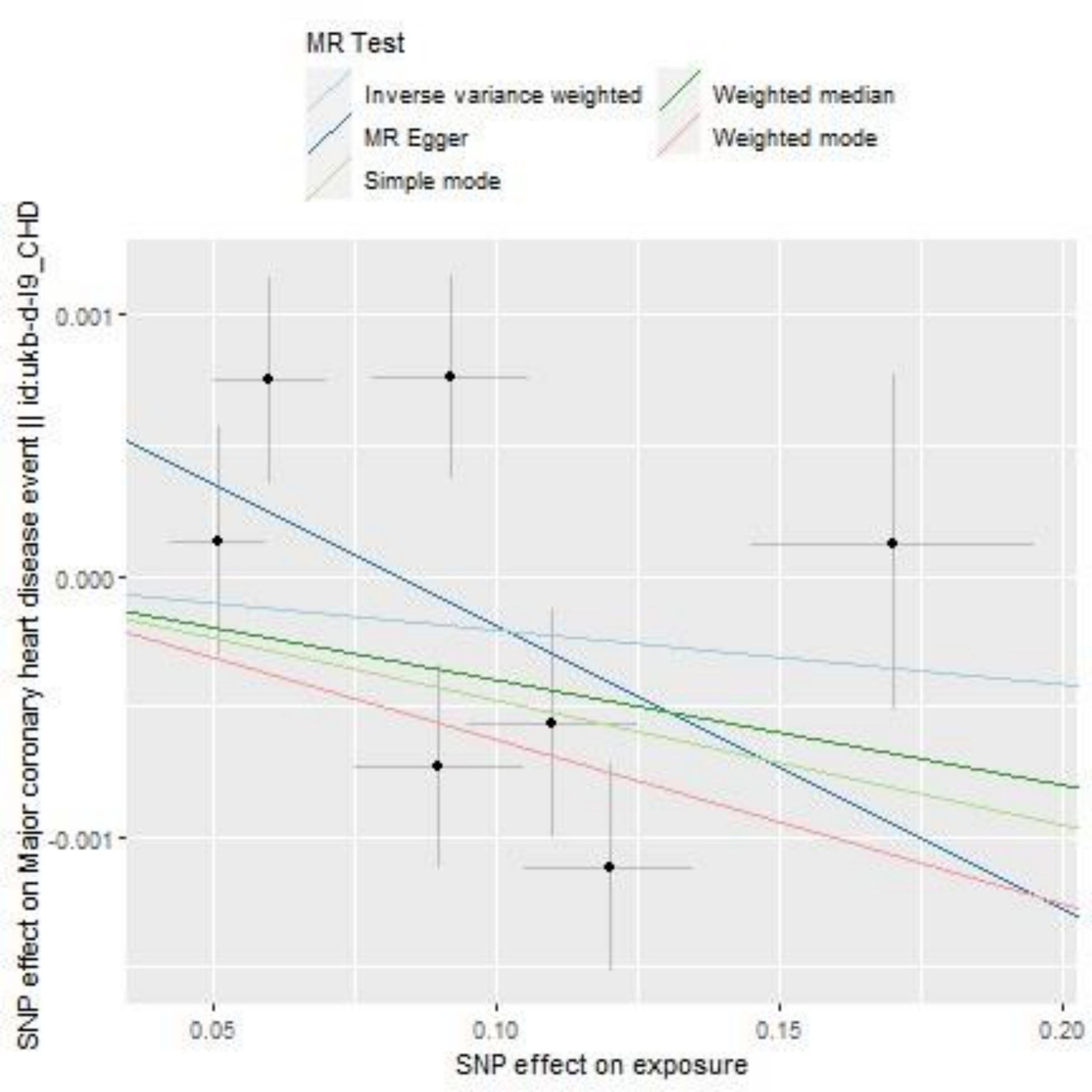
method	nsnp	b	se	pval
MR Egger	7	-0.0108608	0.0093130	0.2961308
Weighted median	7	-0.0040163	0.0025176	0.1106519
Inverse variance weighted	7	-0.0020739	0.0029300	0.4790536
Simple mode	7	-0.0047685	0.0047456	0.3537661
Weighted mode	7	-0.0062940	0.0034029	0.1138593

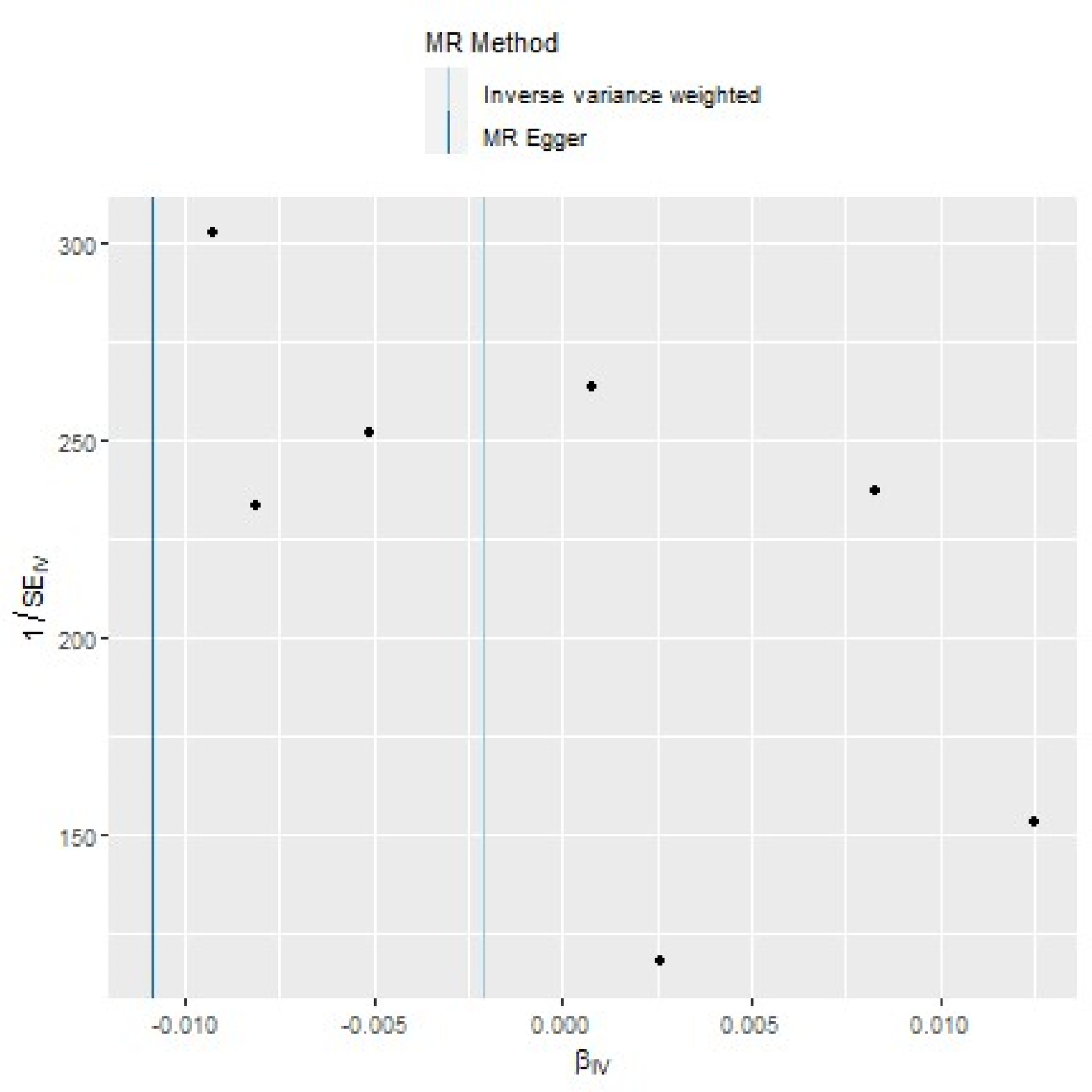
Heterogeneity tests

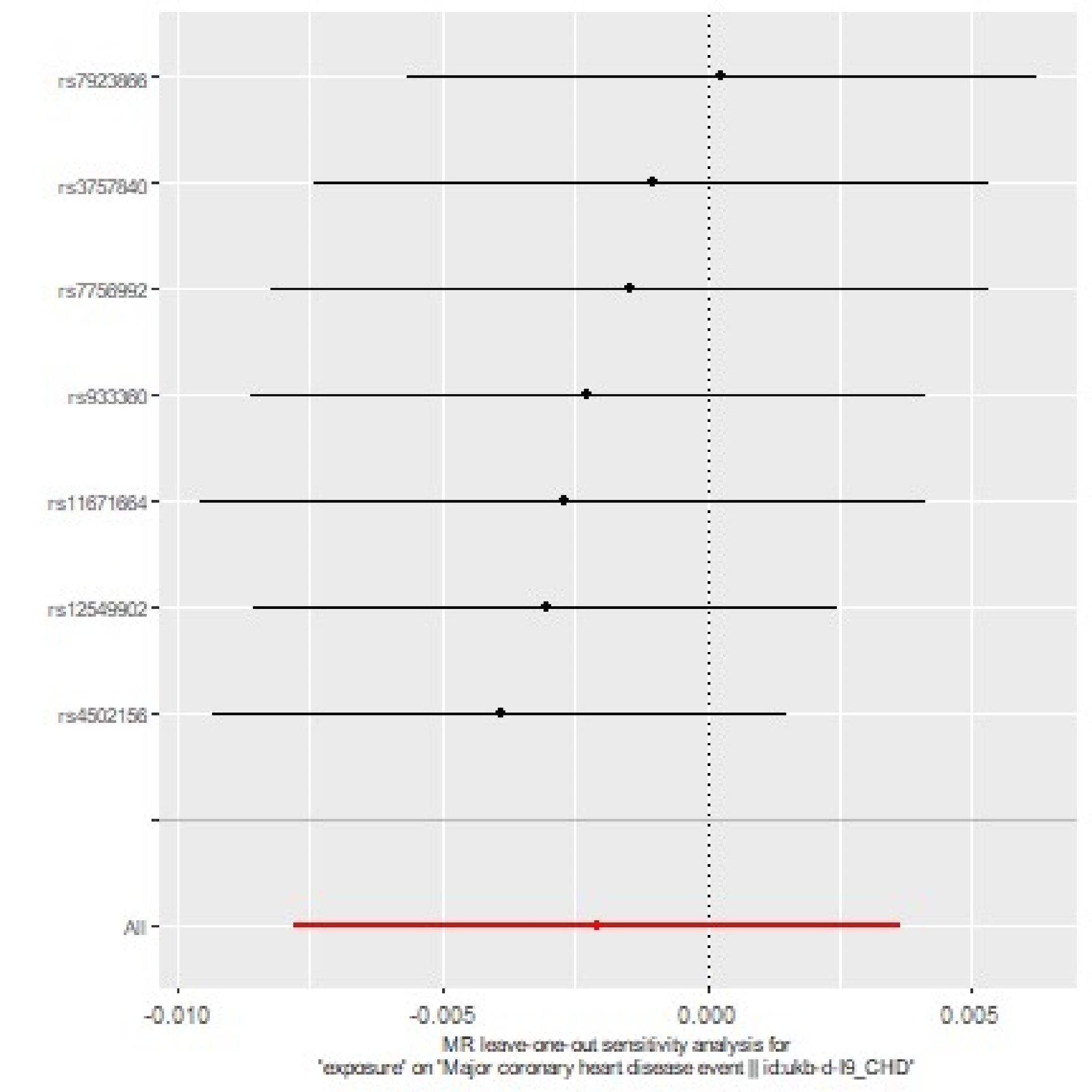
method	Q	Q_df	Q_pval
MR Egger	16.03256	5	0.0067517
Inverse variance weighted	19.20126	6	0.0038369

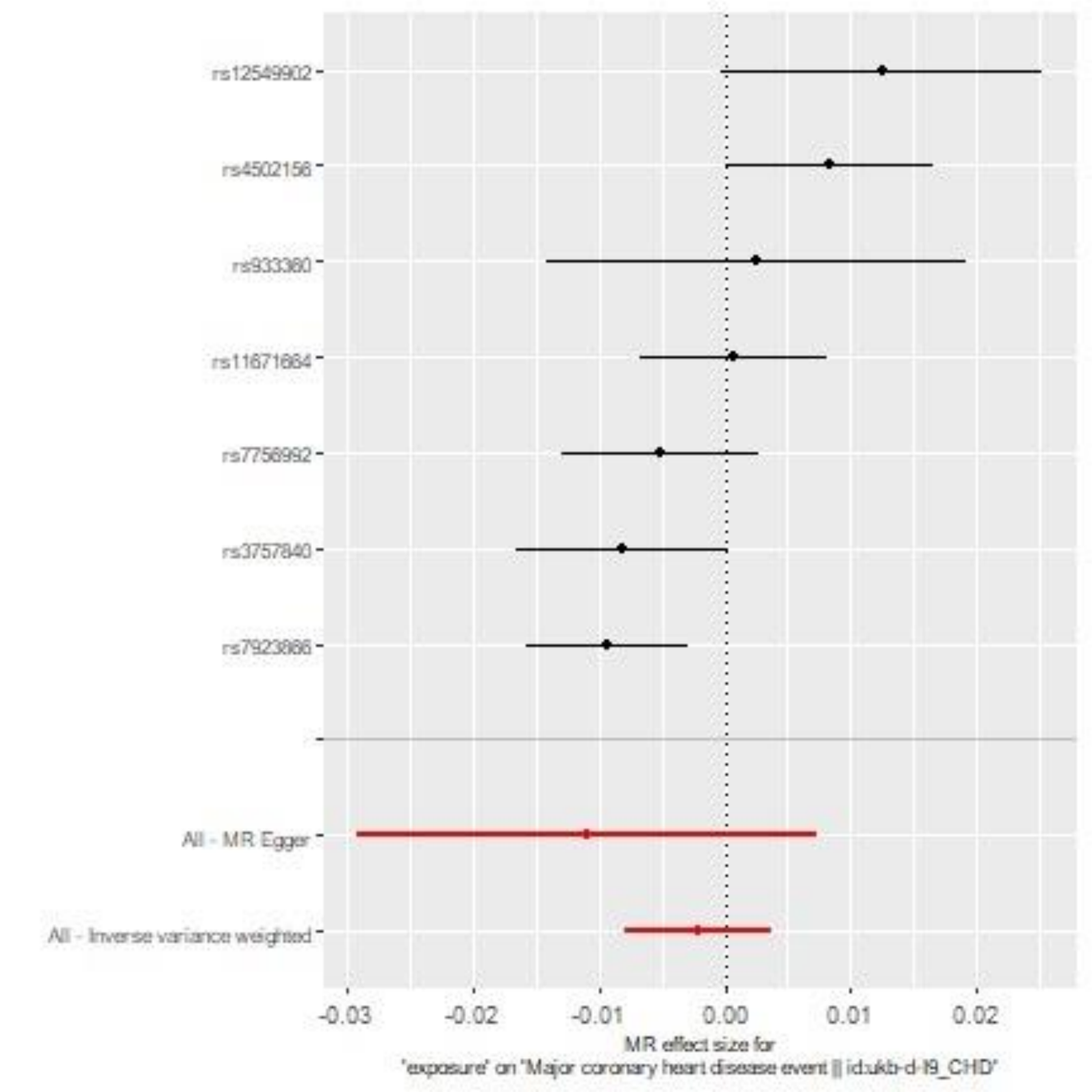
Test for directional horizontal pleiotropy

egger_intercept	se	pval
0.000902	0.0009074	0.3658237


MR Test
Inverse variance weighted
MR Egger
Simple mode
Weighted median
Weighted mode
SNP effect on Major coronary heart disease event || id:ukb-d-I9_CHD
0.001
0.000
-0.001
0.05
0.10
0.15
0.20
SNP effect on exposure


MR Method
Inverse variance weighted
MR Egger
300
250
200
150
1 / SE_IV
-0.010
-0.005
0.000
0.005
0.010
β_IV


rs7923866
rs3757840
rs7756992
rs933360
rs11671664
rs12549902
rs4502156
All
-0.010
-0.005
0.000
0.005
MR leave-one-out sensitivity analysis for
'exposure' on 'Major coronary heart disease event || id:ukb-d-I9_CHD'


rs12549902
rs4502156
rs933380
rs11671664
rs7756992
rs3757840
rs7923866
All - MR Egger
All - Inverse variance weighted
-0.03
-0.02
-0.01
0.00
0.01
0.02
MR effect size for
"exposure" on "Major coronary heart disease event || id:ukb-d-I9_CHD"