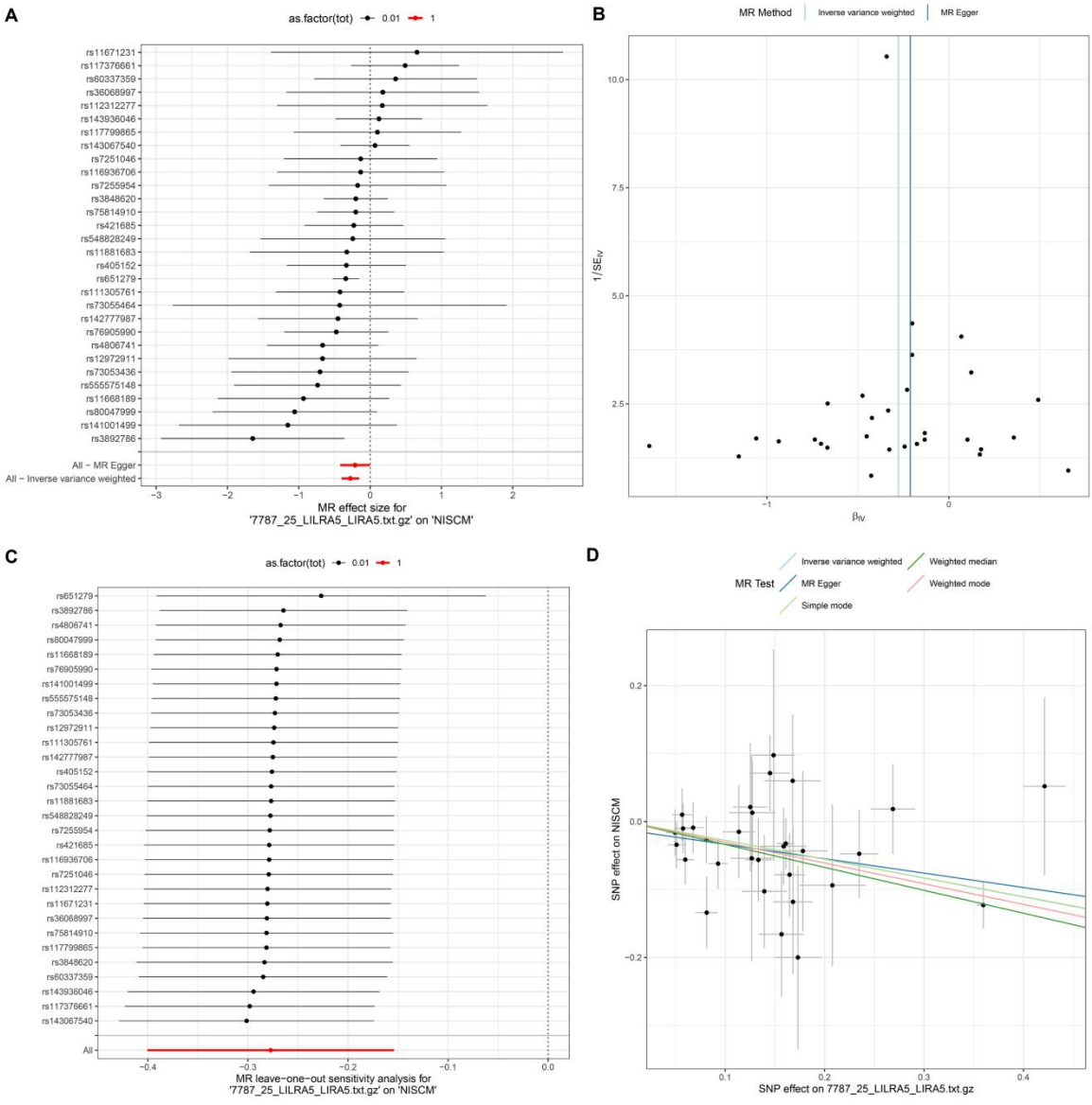
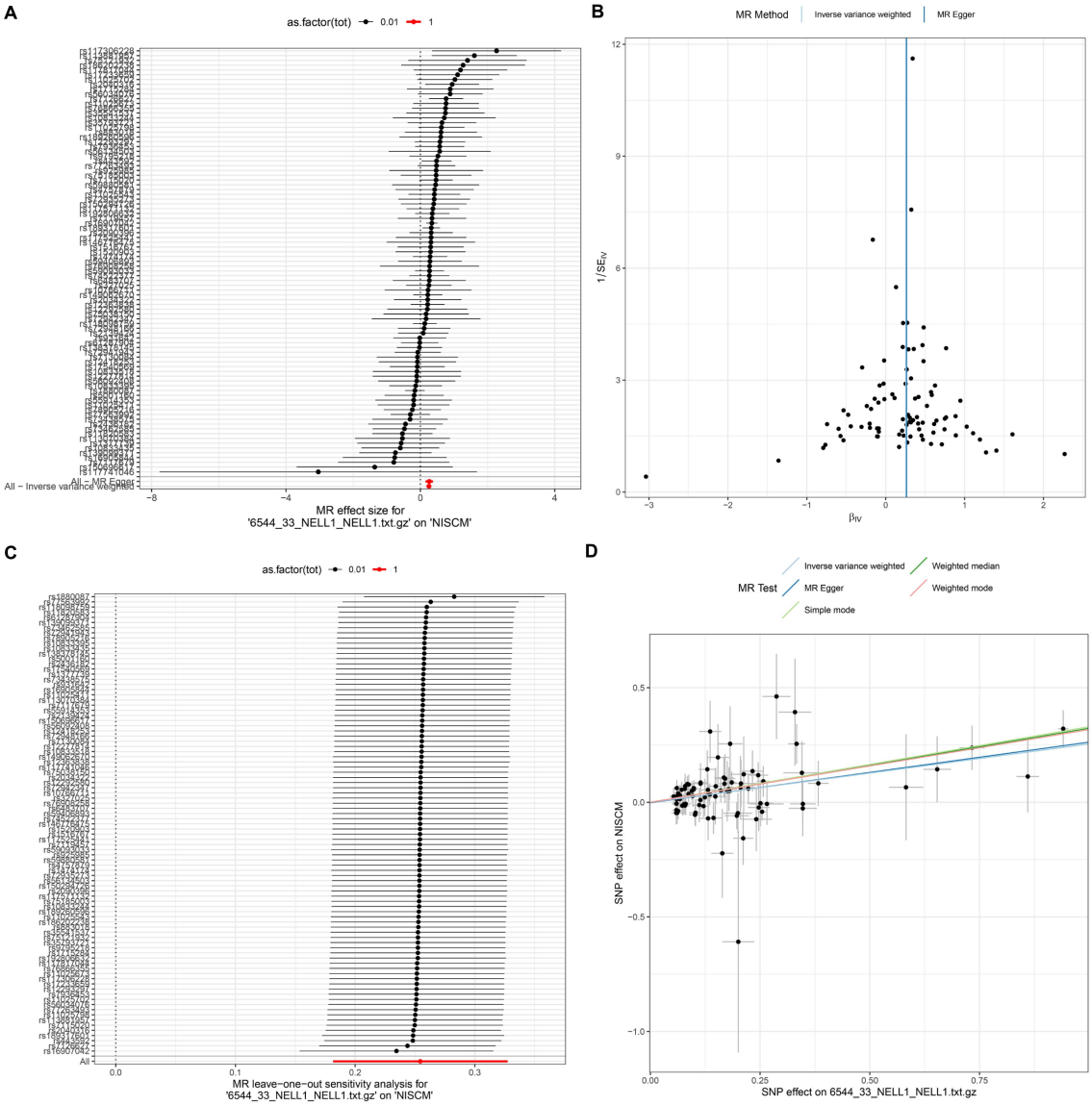
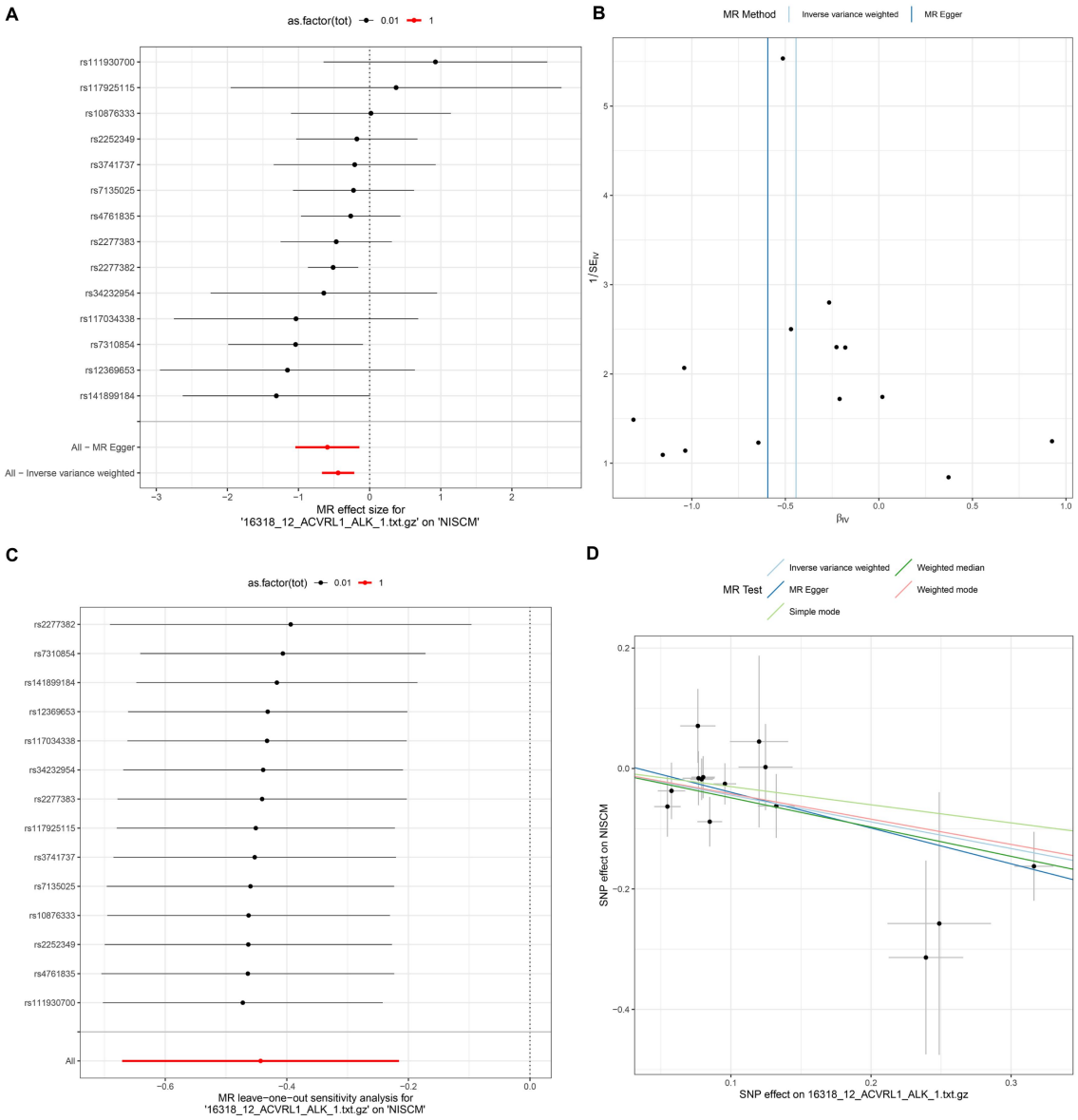
Figure S1. Heterogeneity or pleiotropy for the 16 identified plasma proteins. (*A*) Variant-specific inverse-variance forest plots were used to estimate the causal relationships between each of the 16 circulating plasma proteins and nonischemic cardiomyopathy (NISCM) separately. (*B*) Funnel plot of causal association between between each of the 16 circulating plasma proteins and NISCM separately. (*C*) Leave-one-out plot was used to separately assess if a single variant is driving the association between each of the 16 circulating plasma proteins and NISCM. (*D*) Mendelian Randomization sensitivity plots of the causal effect of each of the 16 circulating plasma proteins on NISCM.



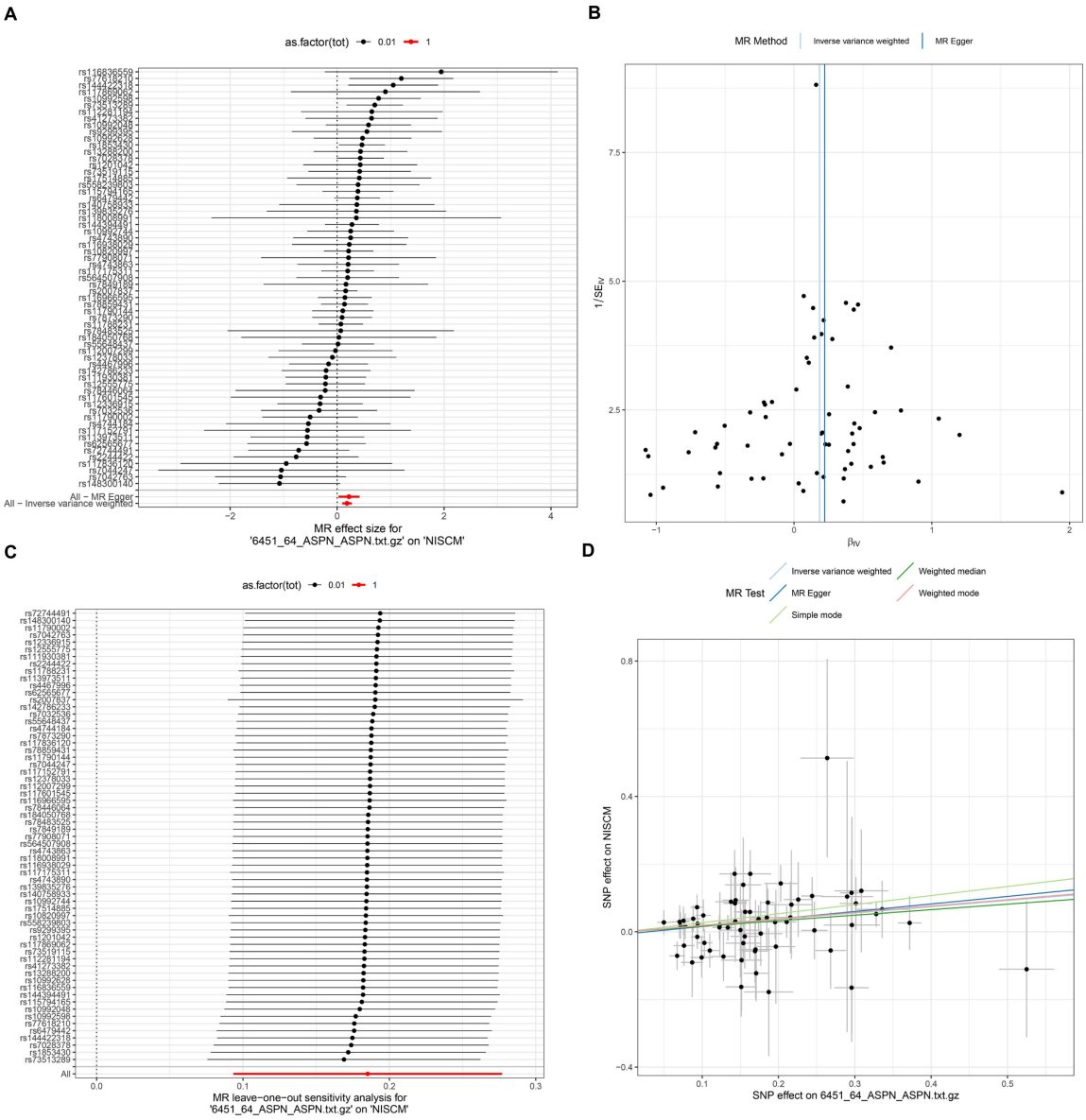
LILRA5


A
as.factor(tot) 0.01 1
All − Inverse variance weighted
All − MR Egger
MR effect size for
'6544_33_NELL1_NELL1.txt.gz' on 'NISCM'
B
MR Method
Inverse variance weighted
MR Egger
1/SE_IV
β_IV
C
as.factor(tot) 0.01 1
All
MR leave−one−out sensitivity analysis for
'6544_33_NELL1_NELL1.txt.gz' on 'NISCM'
D
MR Test
Inverse variance weighted
MR Egger
Simple mode
Weighted median
Weighted mode
SNP effect on NISCM
SNP effect on 6544_33_NELL1_NELL1.txt.gz

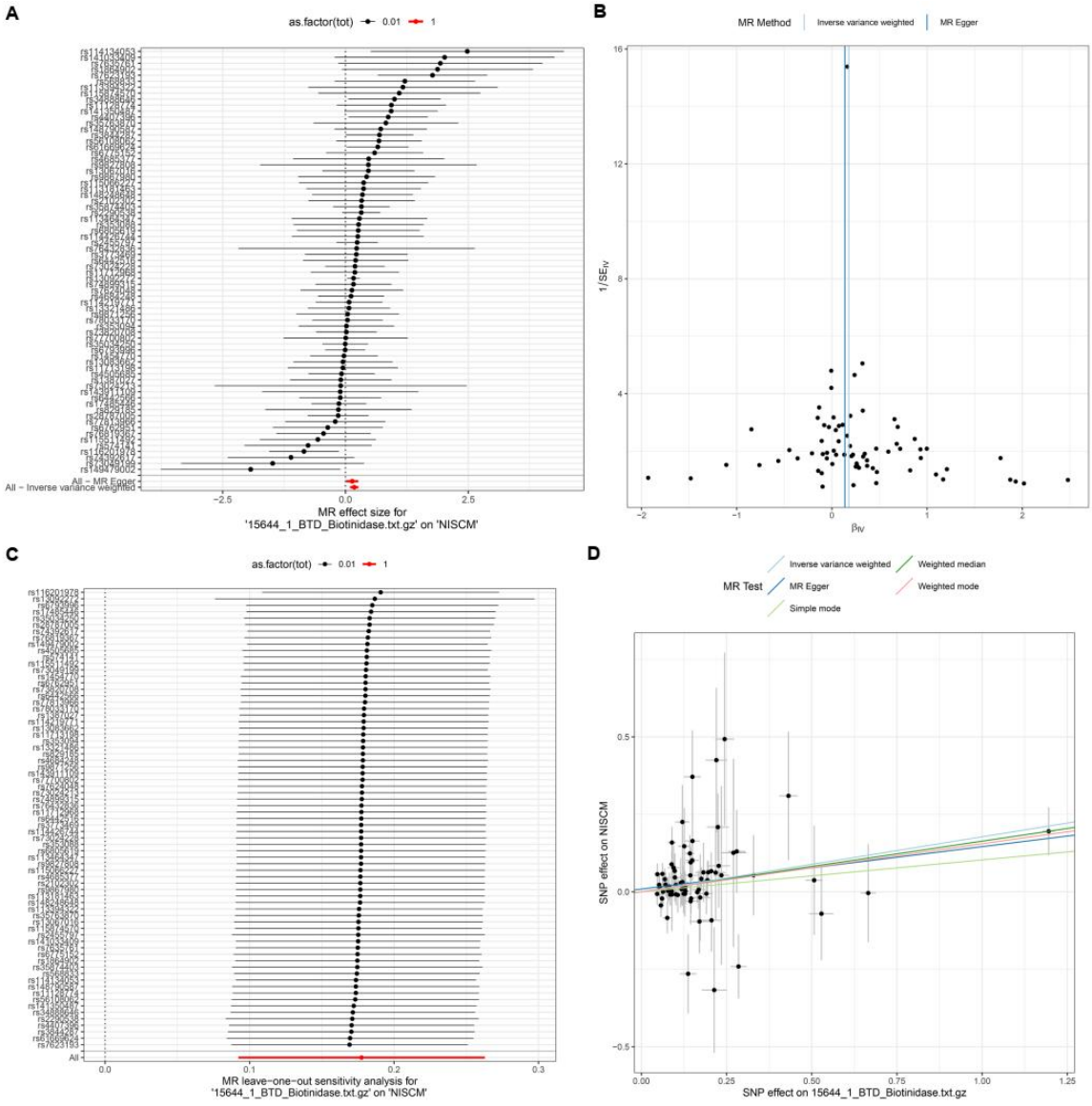
NELL1


A
as.factor(tot) 0.01 1
rs111930700
rs117925115
rs10876333
rs2252349
rs3741737
rs7135025
rs4761835
rs2277383
rs2277382
rs34232954
rs117034338
rs7310854
rs12369653
rs141899184
All − MR Egger
All − Inverse variance weighted
MR effect size for
'16318_12_ACVRL1_ALK_1.txt.gz' on 'NISCM'
B
MR Method
Inverse variance weighted
MR Egger
1/SE_IV
β_IV
C
as.factor(tot) 0.01 1
rs2277382
rs7310854
rs141899184
rs12369653
rs117034338
rs34232954
rs2277383
rs117925115
rs3741737
rs7135025
rs10876333
rs2252349
rs4761835
rs111930700
All
MR leave−one−out sensitivity analysis for
'16318_12_ACVRL1_ALK_1.txt.gz' on 'NISCM'
D
MR Test
Inverse variance weighted
MR Egger
Simple mode
Weighted median
Weighted mode
SNP effect on NISCM
SNP effect on 16318_12_ACVRL1_ALK_1.txt.gz

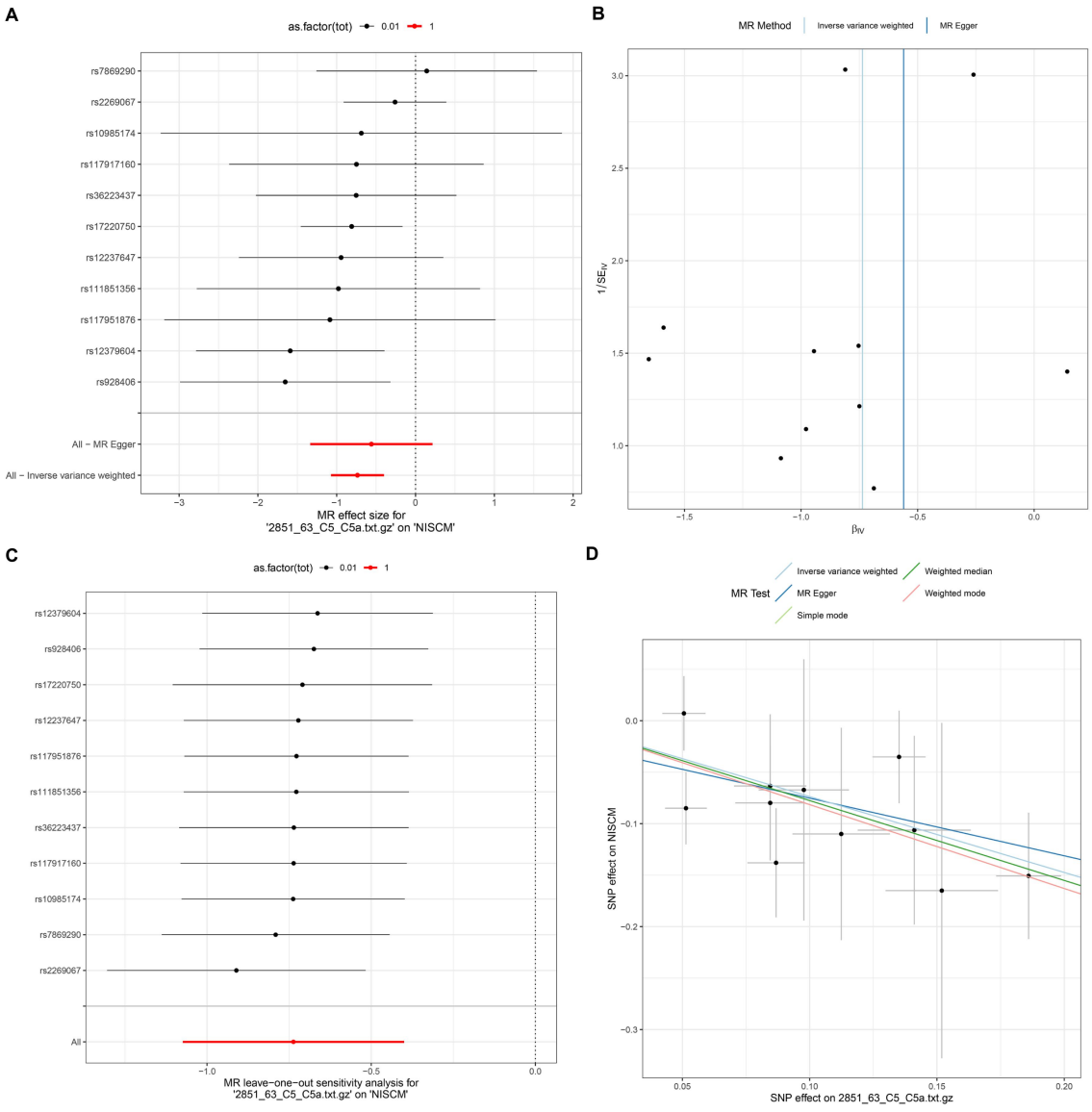
ACVRL1


A
as.factor(tot) 0.01 1
All − MR Egger
All − Inverse variance weighted
MR effect size for
'6451_64_ASPN_ASPN.txt.gz' on 'NISCM'
B
MR Method
Inverse variance weighted
MR Egger
1/SE_IV
β_IV
C
as.factor(tot) 0.01 1
All
MR leave−one−out sensitivity analysis for
'6451_64_ASPN_ASPN.txt.gz' on 'NISCM'
D
MR Test
Inverse variance weighted
MR Egger
Simple mode
Weighted median
Weighted mode
SNP effect on NISCM
SNP effect on 6451_64_ASPN_ASPN.txt.gz

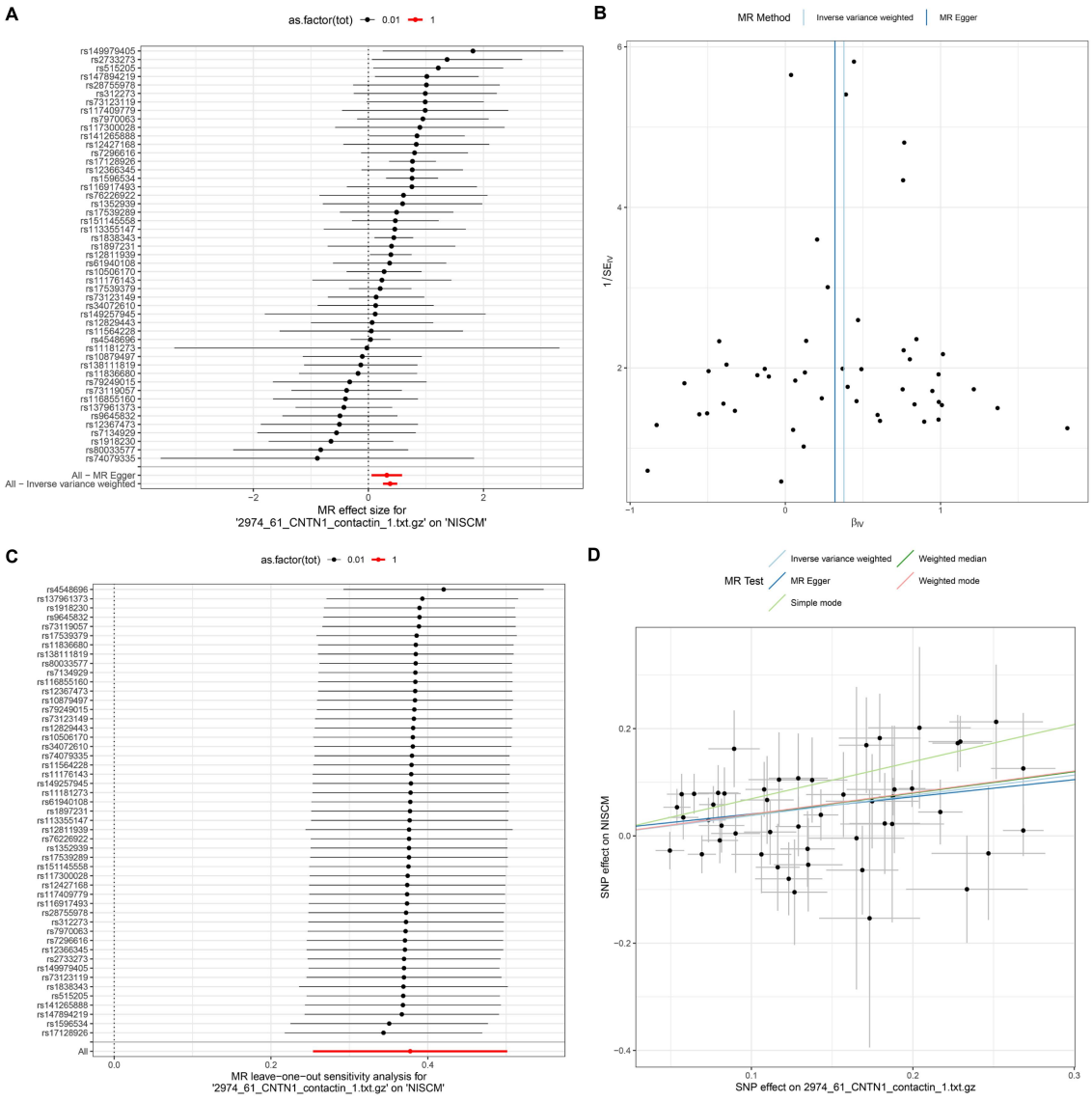
ASPN


A
as.factor(tot) 0.01 1
All − MR Egger
All − Inverse variance weighted
MR effect size for
'15644_1_BTD_Biotinidase.txt.gz' on 'NISCM'
B
MR Method
Inverse variance weighted
MR Egger
1/SE_IV
β_IV
C
as.factor(tot) 0.01 1
All
MR leave−one−out sensitivity analysis for
'15644_1_BTD_Biotinidase.txt.gz' on 'NISCM'
D
MR Test
Inverse variance weighted
MR Egger
Simple mode
Weighted median
Weighted mode
SNP effect on NISCM
SNP effect on 15644_1_BTD_Biotinidase.txt.gz

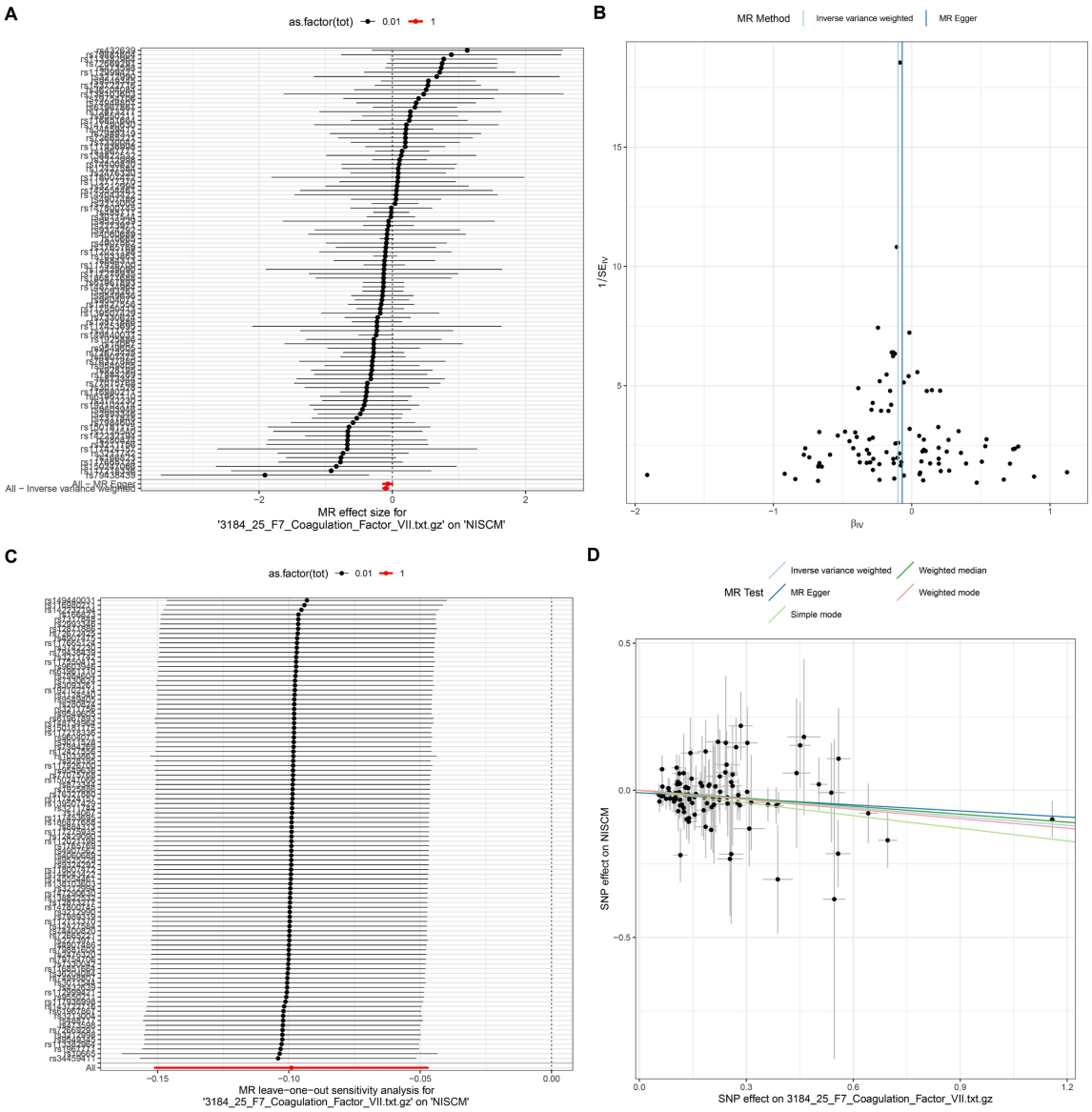
BTD


A
as.factor(tot) 0.01 1
rs7869290
rs2269067
rs10985174
rs117917160
rs36223437
rs17220750
rs12237647
rs111851356
rs117951876
rs12379604
rs928406
All − MR Egger
All − Inverse variance weighted
MR effect size for
'2851_63_C5_C5a.txt.gz' on 'NISCM'
B
MR Method
Inverse variance weighted
MR Egger
1/SE_IV
β_IV
C
as.factor(tot) 0.01 1
rs12379604
rs928406
rs17220750
rs12237647
rs117951876
rs111851356
rs36223437
rs117917160
rs10985174
rs7869290
rs2269067
All
MR leave−one−out sensitivity analysis for
'2851_63_C5_C5a.txt.gz' on 'NISCM'
D
MR Test
Inverse variance weighted
MR Egger
Simple mode
Weighted median
Weighted mode
SNP effect on NISCM
SNP effect on 2851_63_C5_C5a.txt.gz

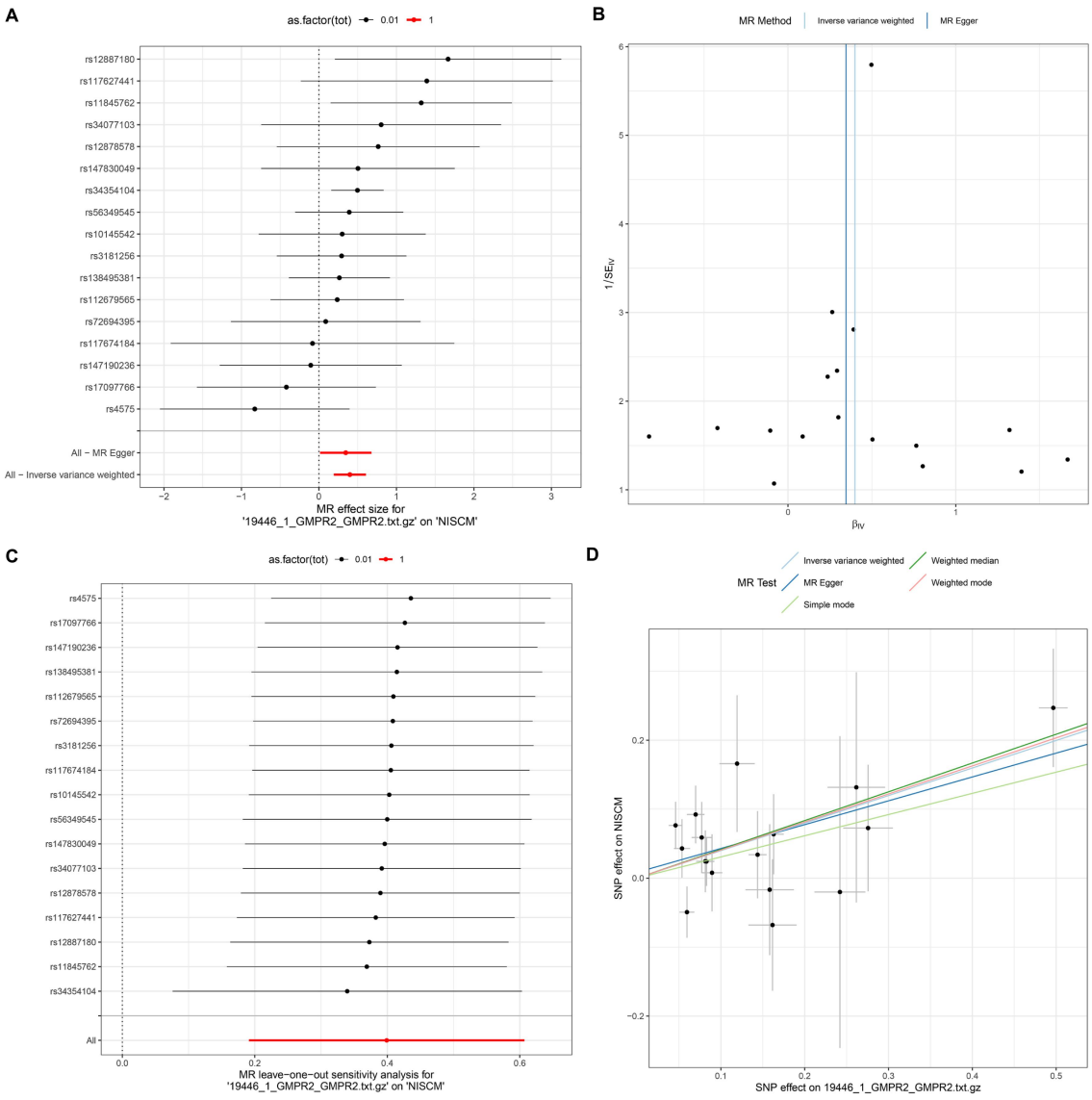
C5


A
as.factor(tot) 0.01 1
All − MR Egger
All − Inverse variance weighted
MR effect size for
'2974_61_CNTN1_contactin_1.txt.gz' on 'NISCM'
B
MR Method
Inverse variance weighted
MR Egger
1/SE_IV
β_IV
C
as.factor(tot) 0.01 1
All
MR leave−one−out sensitivity analysis for
'2974_61_CNTN1_contactin_1.txt.gz' on 'NISCM'
D
MR Test
Inverse variance weighted
MR Egger
Simple mode
Weighted median
Weighted mode
SNP effect on NISCM
SNP effect on 2974_61_CNTN1_contactin_1.txt.gz

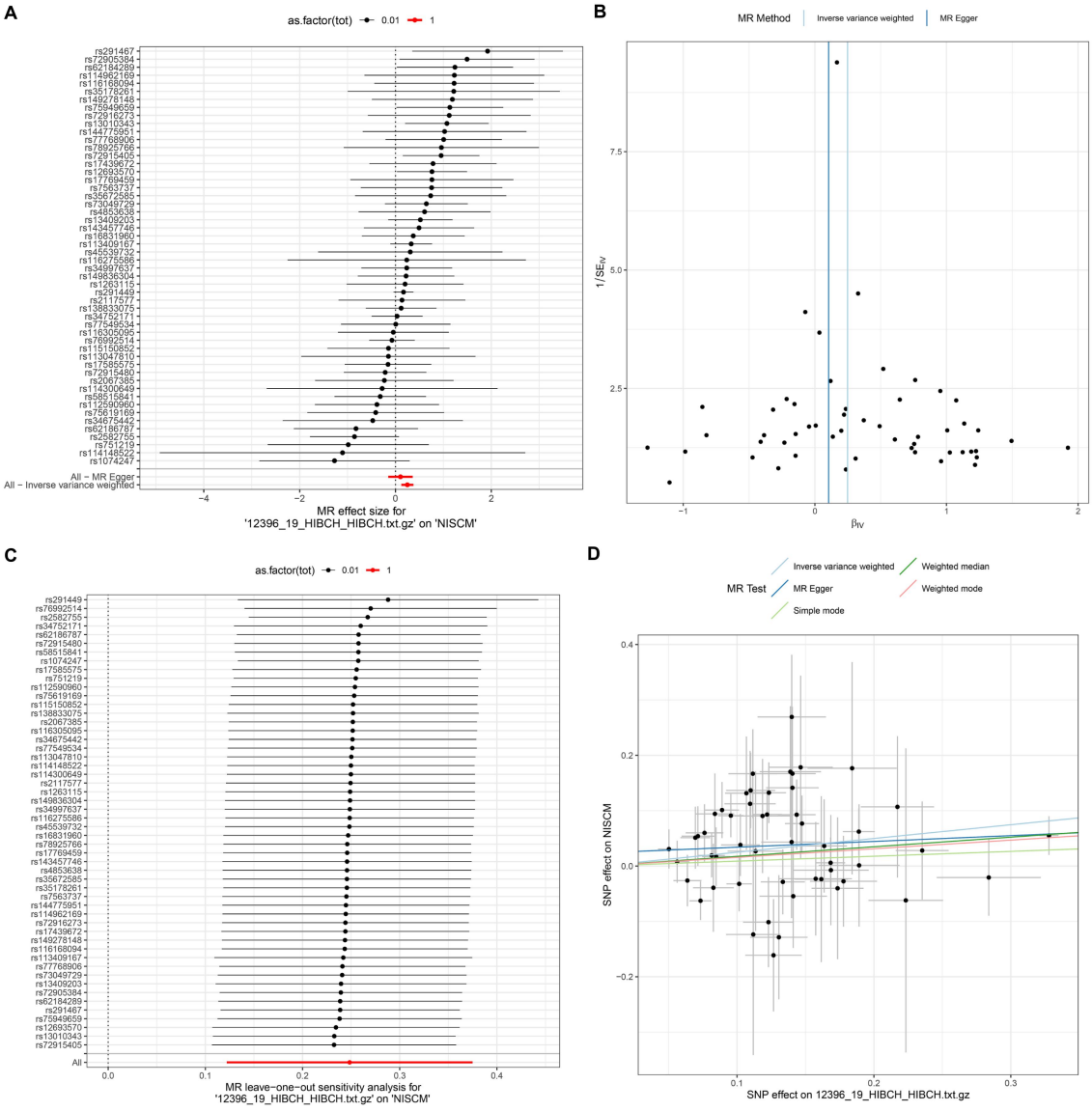
CNTN1



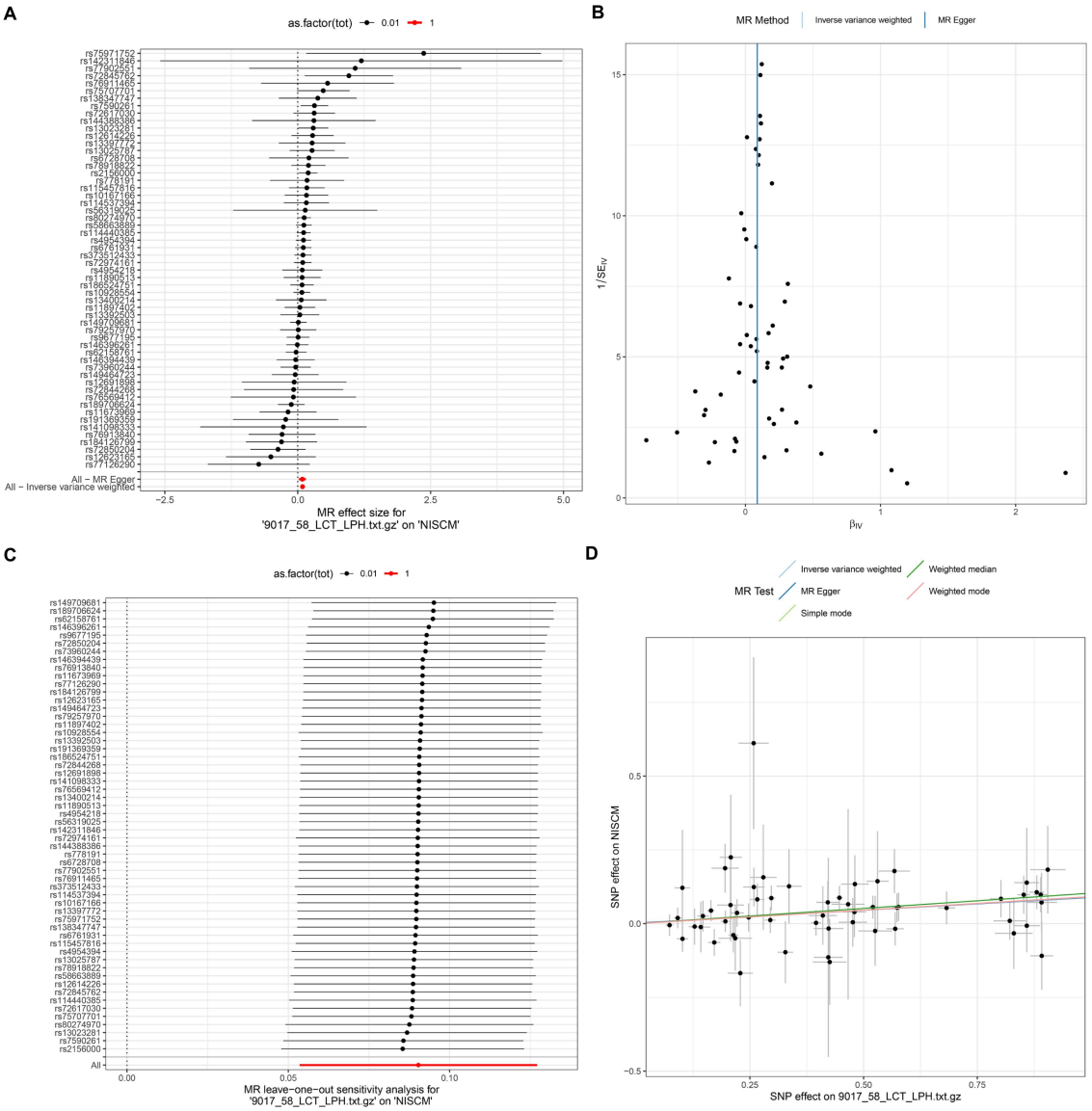
F7-Coagulation_Factor VII


A
as.factor(tot) 0.01 1
rs12887180
rs117627441
rs11845762
rs34077103
rs12878578
rs147830049
rs34354104
rs56349545
rs10145542
rs3181256
rs138495381
rs112679565
rs72694395
rs117674184
rs147190236
rs17097766
rs4575
All − MR Egger
All − Inverse variance weighted
−2 −1 0 1 2 3
MR effect size for
'19446_1_GMPR2_GMPR2.txt.gz' on 'NISCM'
B
MR Method
Inverse variance weighted
MR Egger
1/SE_IV
β_IV
C
as.factor(tot) 0.01 1
rs4575
rs17097766
rs147190236
rs138495381
rs112679565
rs72694395
rs3181256
rs117674184
rs10145542
rs56349545
rs147830049
rs34077103
rs12878578
rs117627441
rs12887180
rs11845762
rs34354104
All
0.0 0.2 0.4 0.6
MR leave−one−out sensitivity analysis for
'19446_1_GMPR2_GMPR2.txt.gz' on 'NISCM'
D
MR Test
Inverse variance weighted
MR Egger
Simple mode
Weighted median
Weighted mode
SNP effect on NISCM
SNP effect on 19446_1_GMPR2_GMPR2.txt.gz

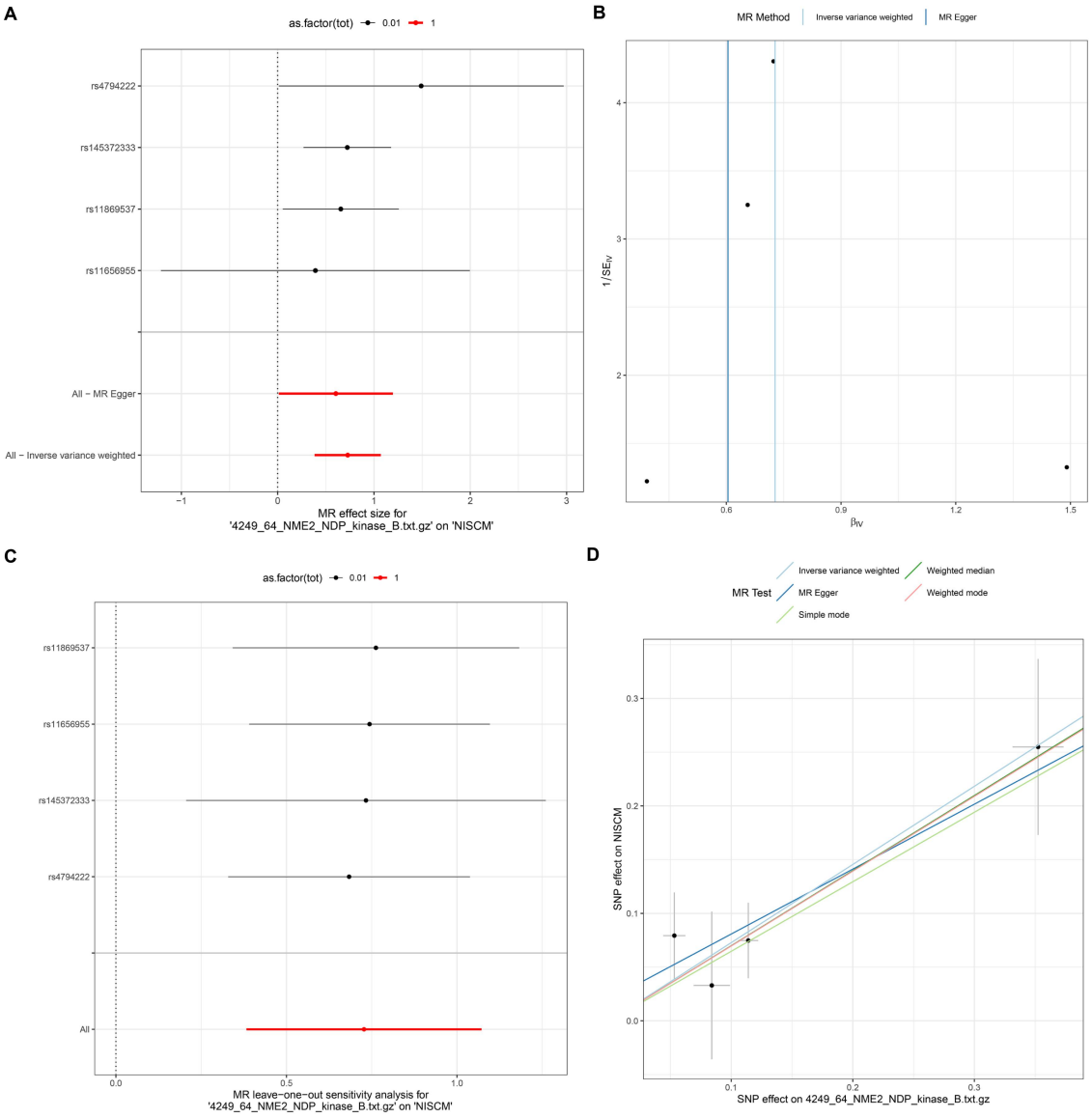
GMPR2


A
as.factor(tot) 0.01 1
All − MR Egger
All − Inverse variance weighted
MR effect size for
'12396_19_HIBCH_HIBCH.txt.gz' on 'NISCM'
B
MR Method
Inverse variance weighted
MR Egger
1/SE_IV
β_IV
C
as.factor(tot) 0.01 1
All
MR leave−one−out sensitivity analysis for
'12396_19_HIBCH_HIBCH.txt.gz' on 'NISCM'
D
MR Test
Inverse variance weighted
MR Egger
Simple mode
Weighted median
Weighted mode
SNP effect on NISCM
SNP effect on 12396_19_HIBCH_HIBCH.txt.gz

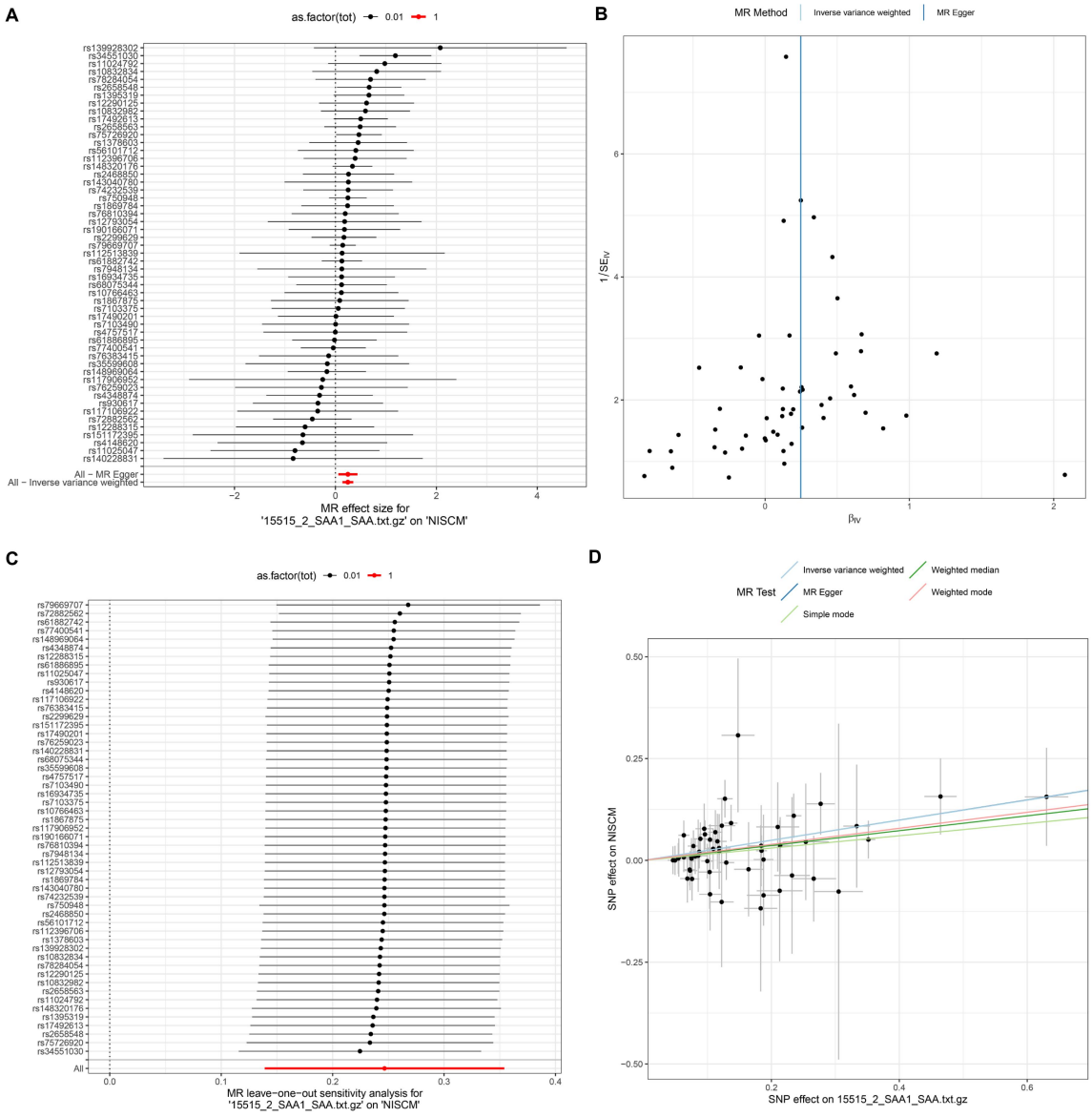
HIBCH


A
as.factor(tot) 0.01 1
All − MR Egger
All − Inverse variance weighted
−2.5
0.0
2.5
5.0
MR effect size for
'9017_58_LCT_LPH.txt.gz' on 'NISCM'
B
MR Method
Inverse variance weighted
MR Egger
1/SE_IV
β_IV
C
as.factor(tot) 0.01 1
All
0.00
0.05
0.10
MR leave−one−out sensitivity analysis for
'9017_58_LCT_LPH.txt.gz' on 'NISCM'
D
MR Test
Inverse variance weighted
MR Egger
Simple mode
Weighted median
Weighted mode
SNP effect on NISCM
SNP effect on 9017_58_LCT_LPH.txt.gz

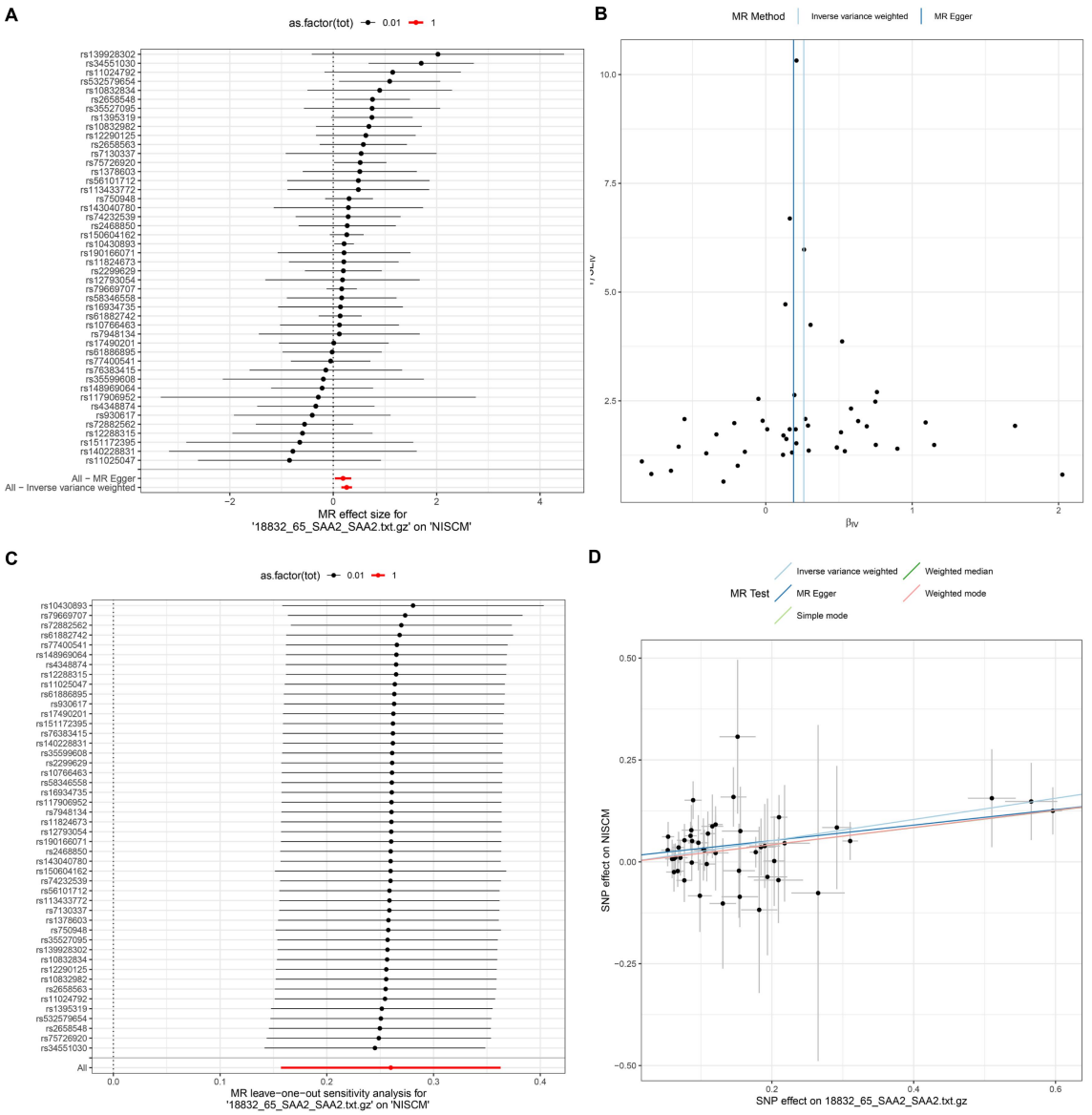
LCT


A
as.factor(tot) 0.01 1
rs4794222
rs145372333
rs11869537
rs11656955
All − MR Egger
All − Inverse variance weighted
MR effect size for
'4249_64_NME2_NDP_kinase_B.txt.gz' on 'NISCM'
B
MR Method
Inverse variance weighted
MR Egger
1/SE_IV
β_IV
C
as.factor(tot) 0.01 1
rs11869537
rs11656955
rs145372333
rs4794222
All
MR leave−one−out sensitivity analysis for
'4249_64_NME2_NDP_kinase_B.txt.gz' on 'NISCM'
D
MR Test
Inverse variance weighted
MR Egger
Simple mode
Weighted median
Weighted mode
SNP effect on NISCM
SNP effect on 4249_64_NME2_NDP_kinase_B.txt.gz

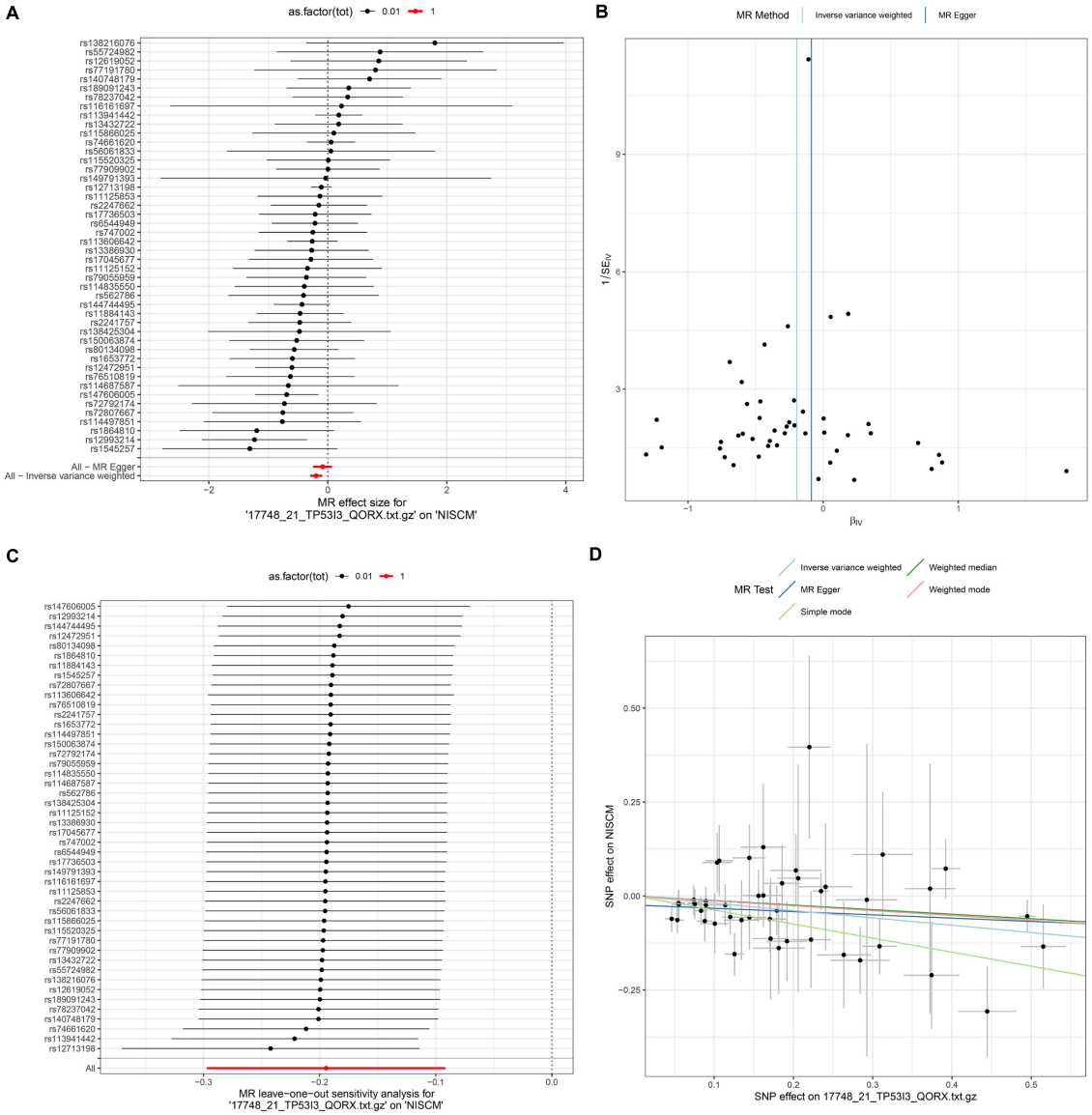
NME2


A
as.factor(tot) 0.01 1
All − MR Egger
All − Inverse variance weighted
MR effect size for
'15515_2_SAA1_SAA.txt.gz' on 'NISCM'
B
MR Method
Inverse variance weighted
MR Egger
1/SE_IV
β_IV
C
as.factor(tot) 0.01 1
All
MR leave−one−out sensitivity analysis for
'15515_2_SAA1_SAA.txt.gz' on 'NISCM'
D
MR Test
Inverse variance weighted
MR Egger
Simple mode
Weighted median
Weighted mode
SNP effect on NISCM
SNP effect on 15515_2_SAA1_SAA.txt.gz

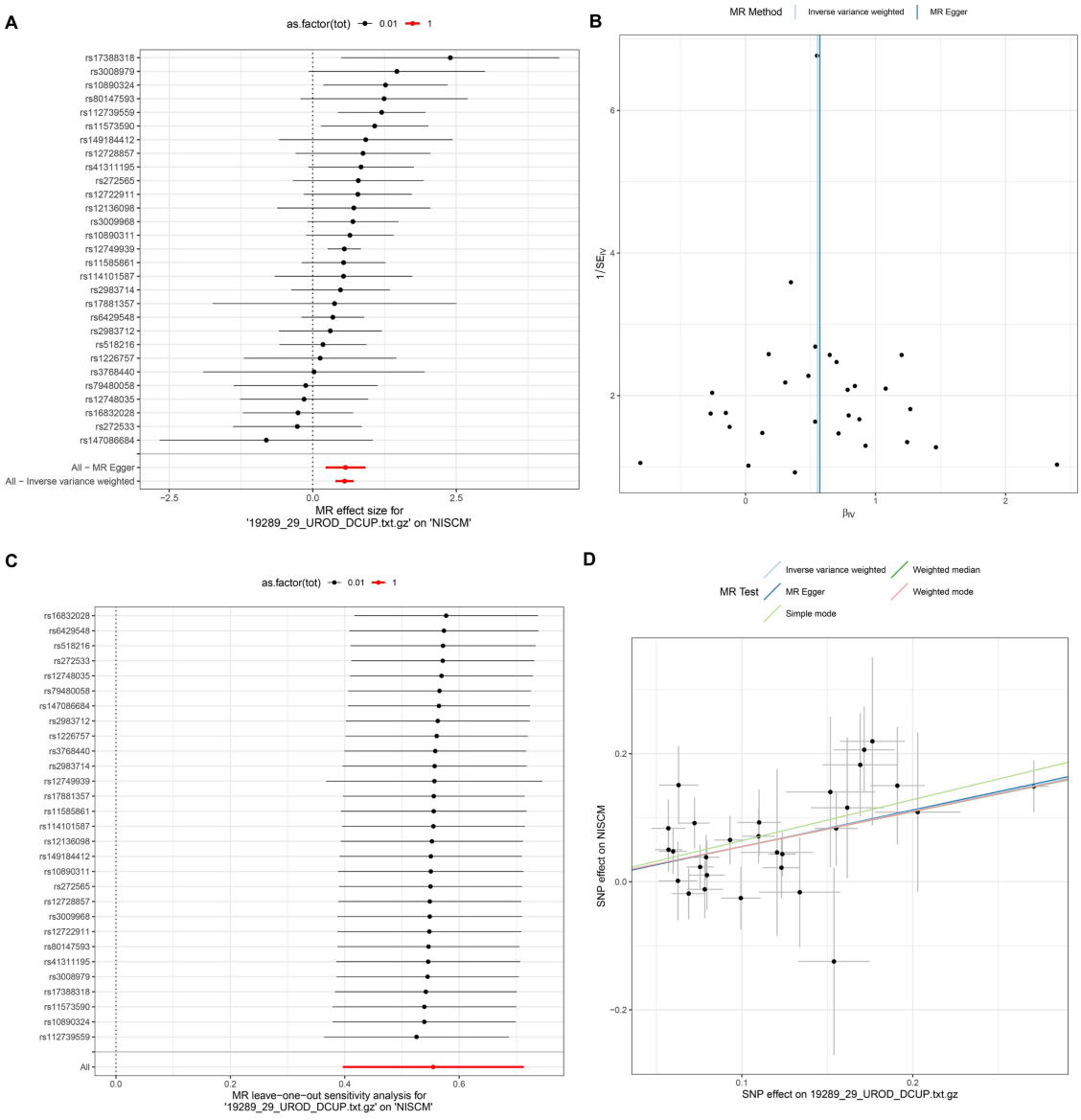
SAA1


A
as.factor(tot) 0.01 1
rs139928302
rs34551030
rs11024792
rs532579654
rs10832834
rs2658548
rs35527095
rs1395319
rs10832982
rs12290125
rs2658563
rs7130337
rs75726920
rs1378603
rs56101712
rs113433772
rs750948
rs143040780
rs74232539
rs2468850
rs150604162
rs10430893
rs190166071
rs11824673
rs2299629
rs12793054
rs79669707
rs58346558
rs16934735
rs61882742
rs10766463
rs7948134
rs17490201
rs61886895
rs77400541
rs76383415
rs35599608
rs148969064
rs117906952
rs4348874
rs930617
rs72882562
rs12288315
rs151172395
rs140228831
rs11025047
All − MR Egger
All − Inverse variance weighted
−2
0
2
4
MR effect size for
'18832_65_SAA2_SAA2.txt.gz' on 'NISCM'
B
MR Method
Inverse variance weighted
MR Egger
10.0
7.5
5.0
2.5
0
1
2
β_{IV}
C
as.factor(tot) 0.01 1
rs10430893
rs79669707
rs72882562
rs61882742
rs77400541
rs148969064
rs4348874
rs12288315
rs11025047
rs61886895
rs930617
rs17490201
rs151172395
rs76383415
rs140228831
rs35599608
rs2299629
rs10766463
rs58346558
rs16934735
rs117906952
rs7948134
rs11824673
rs12793054
rs190166071
rs2468850
rs143040780
rs150604162
rs74232539
rs56101712
rs113433772
rs7130337
rs1378603
rs750948
rs35527095
rs139928302
rs10832834
rs12290125
rs10832982
rs2658563
rs11024792
rs1395319
rs532579654
rs2658548
rs75726920
rs34551030
All
0.0
0.1
0.2
0.3
0.4
MR leave−one−out sensitivity analysis for
'18832_65_SAA2_SAA2.txt.gz' on 'NISCM'
D
MR Test
Inverse variance weighted
MR Egger
Simple mode
Weighted median
Weighted mode
0.50
0.25
0.00
−0.25
−0.50
SNP effect on NISCM
0.2
0.4
0.6
SNP effect on 18832_65_SAA2_SAA2.txt.gz

SAA2


A
as.factor(tot) 0.01 1
All − MR Egger
All − Inverse variance weighted
MR effect size for
'17748_21_TP53I3_QORX.txt.gz' on 'NISCM'
B
MR Method
Inverse variance weighted
MR Egger
1/SE_IV
β_IV
C
as.factor(tot) 0.01 1
All
MR leave−one−out sensitivity analysis for
'17748_21_TP53I3_QORX.txt.gz' on 'NISCM'
D
MR Test
Inverse variance weighted
MR Egger
Simple mode
Weighted median
Weighted mode
SNP effect on NISCM
SNP effect on 17748_21_TP53I3_QORX.txt.gz

TP53I3


A
as.factor(tot) 0.01 1
rs17388318
rs3008979
rs10890324
rs80147593
rs112739559
rs11573590
rs149184412
rs12728857
rs41311195
rs272565
rs12722911
rs12136098
rs3009968
rs10890311
rs12749939
rs11585861
rs114101587
rs2983714
rs17881357
rs6429548
rs2983712
rs518216
rs1226757
rs3768440
rs79480058
rs12748035
rs16832028
rs272533
rs147086684
All − MR Egger
All − Inverse variance weighted
−2.5
0.0
2.5
MR effect size for
'19289_29_UROD_DCUP.txt.gz' on 'NISCM'
B
MR Method
Inverse variance weighted
MR Egger
1/SE_IV
6
4
2
0
1
2
β_IV
C
as.factor(tot) 0.01 1
rs16832028
rs6429548
rs518216
rs272533
rs12748035
rs79480058
rs147086684
rs2983712
rs1226757
rs3768440
rs2983714
rs12749939
rs17881357
rs11585861
rs114101587
rs12136098
rs149184412
rs10890311
rs272565
rs12728857
rs3009968
rs12722911
rs80147593
rs41311195
rs3008979
rs17388318
rs11573590
rs10890324
rs112739559
All
0.0
0.2
0.4
0.6
MR leave−one−out sensitivity analysis for
'19289_29_UROD_DCUP.txt.gz' on 'NISCM'
D
MR Test
Inverse variance weighted
MR Egger
Simple mode
Weighted median
Weighted mode
SNP effect on NISCM
0.2
0.0
−0.2
0.1
0.2
SNP effect on 19289_29_UROD_DCUP.txt.gz

UROD