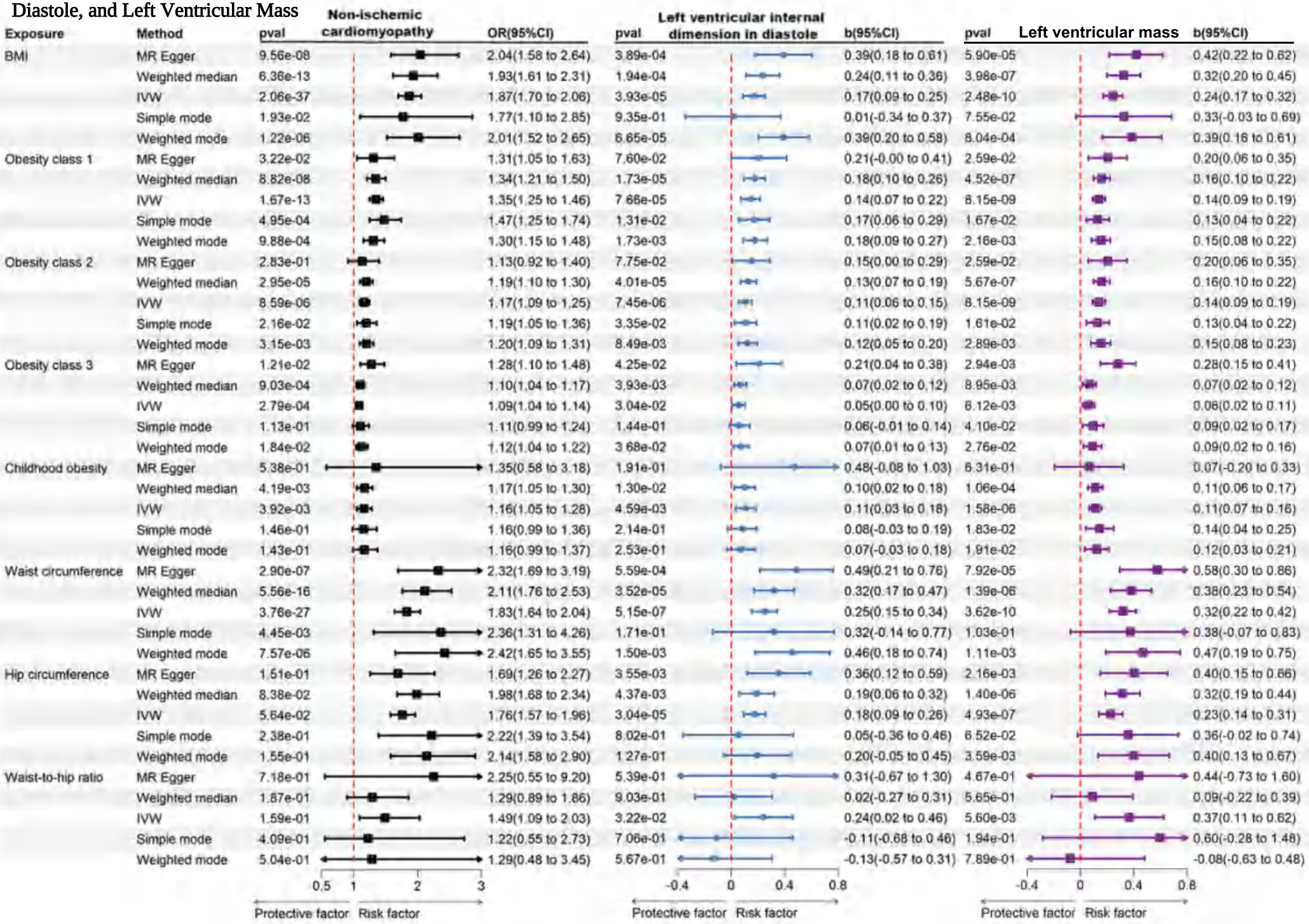
Directory

Fig S1 Genetically Predicted Eight Obesity-related Traits Associations with Risk of Non-Ischemic Cardiomyopathy, Left Ventricular Internal Dimension in Diastole, and Left Ventricular Mass



Exposure	Method	pval	OR(95%CI)	pval	b(95%CI)	pval	b(95%CI)
BMI	MR Egger	9.56e-08	2.04(1.58 to 2.64)	3.89e-04	0.39(0.18 to 0.61)	5.90e-05	0.42(0.22 to 0.62)
	Weighted median	6.36e-13	1.93(1.61 to 2.31)	1.94e-04	0.24(0.11 to 0.36)	3.98e-07	0.32(0.20 to 0.45)
	IVW	2.06e-37	1.87(1.70 to 2.06)	3.93e-05	0.17(0.09 to 0.25)	2.48e-10	0.24(0.17 to 0.32)
	Simple mode	1.93e-02	1.77(1.10 to 2.85)	9.35e-01	0.01(-0.34 to 0.37)	7.55e-02	0.33(-0.03 to 0.69)
	Weighted mode	1.22e-06	2.01(1.52 to 2.65)	6.65e-05	0.39(0.20 to 0.58)	8.04e-04	0.39(0.16 to 0.61)
Obesity class 1	MR Egger	3.22e-02	1.31(1.05 to 1.63)	7.60e-02	0.21(-0.00 to 0.41)	2.59e-02	0.20(0.06 to 0.35)
	Weighted median	8.82e-08	1.34(1.21 to 1.50)	1.73e-05	0.18(0.10 to 0.26)	4.52e-07	0.16(0.10 to 0.22)
	IVW	1.67e-13	1.35(1.25 to 1.46)	7.66e-05	0.14(0.07 to 0.22)	8.15e-09	0.14(0.09 to 0.19)
	Simple mode	4.95e-04	1.47(1.25 to 1.74)	1.31e-02	0.17(0.06 to 0.29)	1.67e-02	0.13(0.04 to 0.22)
	Weighted mode	9.88e-04	1.30(1.15 to 1.48)	1.73e-03	0.18(0.09 to 0.27)	2.16e-03	0.15(0.08 to 0.22)
Obesity class 2	MR Egger	2.83e-01	1.13(0.92 to 1.40)	7.75e-02	0.15(0.00 to 0.29)	2.59e-02	0.20(0.06 to 0.35)
	Weighted median	2.95e-05	1.19(1.10 to 1.30)	4.01e-05	0.13(0.07 to 0.19)	5.67e-07	0.16(0.10 to 0.22)
	IVW	8.59e-06	1.17(1.09 to 1.25)	7.45e-06	0.11(0.06 to 0.15)	8.15e-09	0.14(0.09 to 0.19)
	Simple mode	2.16e-02	1.19(1.05 to 1.36)	3.35e-02	0.11(0.02 to 0.19)	1.61e-02	0.13(0.04 to 0.22)
	Weighted mode	3.15e-03	1.20(1.09 to 1.31)	8.49e-03	0.12(0.05 to 0.20)	2.89e-03	0.15(0.08 to 0.23)
Obesity class 3	MR Egger	1.21e-02	1.28(1.10 to 1.48)	4.25e-02	0.21(0.04 to 0.38)	2.94e-03	0.28(0.15 to 0.41)
	Weighted median	9.03e-04	1.10(1.04 to 1.17)	3.93e-03	0.07(0.02 to 0.12)	8.95e-03	0.07(0.02 to 0.12)
	IVW	2.79e-04	1.09(1.04 to 1.14)	3.04e-02	0.05(0.00 to 0.10)	6.12e-03	0.06(0.02 to 0.11)
	Simple mode	1.13e-01	1.11(0.99 to 1.24)	1.44e-01	0.06(-0.01 to 0.14)	4.10e-02	0.09(0.02 to 0.17)
	Weighted mode	1.84e-02	1.12(1.04 to 1.22)	3.68e-02	0.07(0.01 to 0.13)	2.76e-02	0.09(0.02 to 0.16)
Childhood obesity	MR Egger	5.38e-01	1.35(0.58 to 3.18)	1.91e-01	0.48(-0.08 to 1.03)	6.31e-01	0.07(-0.20 to 0.33)
	Weighted median	4.19e-03	1.17(1.05 to 1.30)	1.30e-02	0.10(0.02 to 0.18)	1.06e-04	0.11(0.06 to 0.17)
	IVW	3.92e-03	1.16(1.05 to 1.28)	4.59e-03	0.11(0.03 to 0.18)	1.58e-06	0.11(0.07 to 0.16)
	Simple mode	1.46e-01	1.16(0.99 to 1.36)	2.14e-01	0.08(-0.03 to 0.19)	1.83e-02	0.14(0.04 to 0.25)
	Weighted mode	1.43e-01	1.16(0.99 to 1.37)	2.53e-01	0.07(-0.03 to 0.18)	1.91e-02	0.12(0.03 to 0.21)
Waist circumference	MR Egger	2.90e-07	2.32(1.69 to 3.19)	5.59e-04	0.49(0.21 to 0.76)	7.92e-05	0.58(0.30 to 0.86)
	Weighted median	5.56e-16	2.11(1.76 to 2.53)	3.52e-05	0.32(0.17 to 0.47)	1.39e-06	0.38(0.23 to 0.54)
	IVW	3.76e-27	1.83(1.64 to 2.04)	5.15e-07	0.25(0.15 to 0.34)	3.62e-10	0.32(0.22 to 0.42)
	Simple mode	4.45e-03	2.36(1.31 to 4.26)	1.71e-01	0.32(-0.14 to 0.77)	1.03e-01	0.38(-0.07 to 0.83)
	Weighted mode	7.57e-06	2.42(1.65 to 3.55)	1.50e-03	0.46(0.18 to 0.74)	1.11e-03	0.47(0.19 to 0.75)
Hip circumference	MR Egger	1.51e-01	1.69(1.26 to 2.27)	3.55e-03	0.36(0.12 to 0.59)	2.16e-03	0.40(0.15 to 0.66)
	Weighted median	8.38e-02	1.98(1.68 to 2.34)	4.37e-03	0.19(0.06 to 0.32)	1.40e-06	0.32(0.19 to 0.44)
	IVW	5.64e-02	1.76(1.57 to 1.96)	3.04e-05	0.18(0.09 to 0.26)	4.93e-07	0.23(0.14 to 0.31)
	Simple mode	2.38e-01	2.22(1.39 to 3.54)	8.02e-01	0.05(-0.36 to 0.46)	6.52e-02	0.36(-0.02 to 0.74)
	Weighted mode	1.55e-01	2.14(1.58 to 2.90)	1.27e-01	0.20(-0.05 to 0.45)	3.59e-03	0.40(0.13 to 0.67)
Waist-to-hip ratio	MR Egger	7.18e-01	2.25(0.55 to 9.20)	5.39e-01	0.31(-0.67 to 1.30)	4.67e-01	0.44(-0.73 to 1.60)
	Weighted median	1.87e-01	1.29(0.89 to 1.86)	9.03e-01	0.02(-0.27 to 0.31)	5.65e-01	0.09(-0.22 to 0.39)
	IVW	1.59e-01	1.49(1.09 to 2.03)	3.22e-02	0.24(0.02 to 0.46)	5.60e-03	0.37(0.11 to 0.62)
	Simple mode	4.09e-01	1.22(0.55 to 2.73)	7.06e-01	-0.11(-0.68 to 0.46)	1.94e-01	0.60(-0.28 to 1.48)
	Weighted mode	5.04e-01	1.29(0.48 to 3.45)	5.67e-01	-0.13(-0.57 to 0.31)	7.89e-01	-0.08(-0.63 to 0.48)

Fig S2 Forestplot for BMI and Cardiac MRI

Outcome	nsnp	beta	adjustP	beta(95%CI)
AA	378	0.20	4.09e−13	0.20 (0.15 to 0.25)
DA	378	0.27	1.05e−32	0.27 (0.23 to 0.32)
LA	378	−0.08	2.61e−37	−0.08 (−0.09 to −0.07)
LPDSR	361	−0.07	2.08e−05	−0.07 (−0.09 to −0.04)
LV	378	0.25	5.23e−30	0.25 (0.20 to 0.29)
LVEDV	378	0.20	3.76e−19	0.20 (0.16 to 0.24)
LVEF	378	−0.08	3.60e−03	−0.08 (−0.13 to −0.03)
LVESV	378	0.17	9.14e−14	0.17 (0.13 to 0.22)
LVM	378	12.86	1.36e−98	12.86 (11.68 to 14.05)
LVSV	378	0.24	8.19e−24	0.24 (0.20 to 0.29)
PA	378	0.20	1.78e−13	0.20 (0.15 to 0.25)
RA	378	0.02	4.69e−01	0.02 (−0.03 to 0.07)
RPDSR	378	−0.26	7.45e−07	−0.26 (−0.36 to −0.16)
RVEDV	378	0.24	1.04e−33	0.24 (0.21 to 0.28)
RVEF	378	−0.06	1.43e−02	−0.06 (−0.11 to −0.02)
RVSV	378	0.22	1.81e−21	0.22 (0.18 to 0.27)

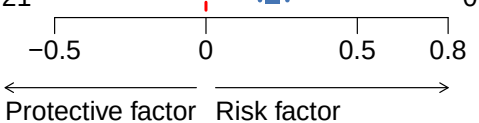


Fig S3 Forestplot for Childhood obesity and Cardiac MRI

Outcome	nsnp	beta	adjustP	beta(95%CI)
AA	5	0.04	0.35	0.04 (−0.03 to 0.10)
DA	5	0.07	0.003	0.07 (0.02 to 0.11)
LA	5	−0.01	0.09	−0.01 (−0.03 to 0.00)
LPDSR	5	0.005	0.76	0.01 (−0.02 to 0.03)
LV	5	0.08	0.02	0.08 (0.02 to 0.14)
LVEDV	5	0.09	0.0003	0.09 (0.04 to 0.13)
LVEF	5	−0.03	0.12	−0.03 (−0.06 to 0.00)
LVESV	5	0.07	0.0002	0.07 (0.04 to 0.11)
LVM	5	3.31	0.003	3.31 (1.25 to 5.37)
LVSV	5	0.06	0.06	0.06 (0.00 to 0.12)
PA	5	0.06	0.05	0.06 (0.01 to 0.11)
RA	5	0.05	0.03	0.05 (0.01 to 0.09)
RPDSR	5	−0.04	0.31	−0.04 (−0.12 to 0.03)
RVEDV	5	0.07	0.008	0.07 (0.02 to 0.13)
RVEF	5	−0.03	0.12	−0.03 (−0.06 to 0.00)
RVSV	5	0.06	0.03	0.06 (0.01 to 0.12)

P < 0.05 was considered statistically significant

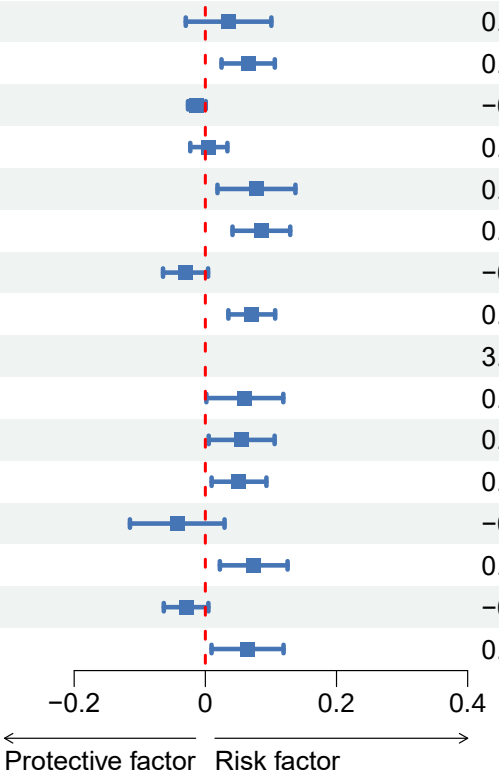


Fig S4 Forestplot for Hip circumference and Cardiac MRI

Outcome	nsnp	beta	adjustP	beta(95%CI)
AA	365	0.25	2.59e−16	0.25 (0.19 to 0.31)
DA	364	0.32	1.21e−37	0.32 (0.27 to 0.37)
LA	365	−0.11	5.76e−50	−0.11 (−0.12 to −0.09)
LPDSR	348	0.01	6.76e−01	0.01 (−0.02 to 0.04)
LV	365	0.41	2.23e−51	0.41 (0.35 to 0.46)
LVEDV	364	0.39	5.38e−46	0.39 (0.33 to 0.44)
LVEF	364	−0.10	3.54e−04	−0.10 (−0.15 to −0.05)
LVESV	364	0.30	1.36e−30	0.30 (0.25 to 0.35)
LVM	365	13.61	4.21e−78	13.61 (12.20 to 15.02)
LVSV	365	0.39	6.10e−44	0.39 (0.34 to 0.45)
PA	364	0.28	7.53e−22	0.28 (0.22 to 0.33)
RA	365	0.26	1.80e−20	0.26 (0.21 to 0.32)
RPDSR	365	0.00	9.96e−01	0.00 (−0.11 to 0.12)
RVEDV	364	0.38	2.30e−50	0.38 (0.33 to 0.43)
RVEF	364	−0.03	3.43e−01	−0.03 (−0.08 to 0.02)
RVSV	364	0.38	1.82e−45	0.38 (0.33 to 0.43)

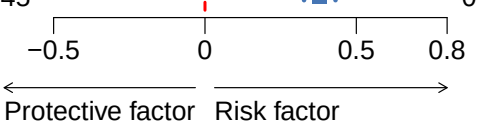


Fig S5 Forestplot for Obesity 1 and Cardiac MRI

Outcome	nsnp	beta	adjustP	beta(95%CI)
AA	14	0.04	3.07e−01	0.04 (−0.03 to 0.10)
DA	14	0.10	6.32e−08	0.10 (0.06 to 0.13)
LA	14	−0.02	2.05e−03	−0.02 (−0.03 to −0.01)
LPDSR	14	−0.01	6.34e−01	−0.01 (−0.04 to 0.02)
LV	14	0.11	1.07e−06	0.11 (0.07 to 0.15)
LVEDV	14	0.11	7.74e−09	0.11 (0.07 to 0.15)
LVEF	14	−0.03	1.74e−01	−0.03 (−0.06 to 0.01)
LVESV	14	0.09	2.23e−07	0.09 (0.05 to 0.12)
LVM	14	4.88	1.88e−18	4.88 (3.81 to 5.95)
LVSV	14	0.11	6.31e−05	0.11 (0.06 to 0.16)
PA	14	0.09	2.52e−03	0.09 (0.03 to 0.14)
RA	14	0.04	1.65e−02	0.04 (0.01 to 0.08)
RPDSR	14	−0.04	3.77e−01	−0.04 (−0.13 to 0.04)
RVEDV	14	0.11	1.84e−08	0.11 (0.07 to 0.14)
RVEF	14	−0.03	8.81e−02	−0.03 (−0.07 to 0.00)
RVSV	14	0.10	1.55e−05	0.10 (0.05 to 0.14)

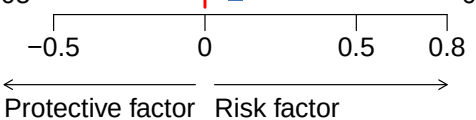


Fig S6 Forestplot for Obesity 2 and Cardiac MRI

Outcome	nsnp	beta	adjustP	beta(95%CI)
AA	11	0.04	4.19e−02	0.04 (0.00 to 0.08)
DA	11	0.08	3.75e−12	0.08 (0.06 to 0.10)
LA	11	−0.01	4.11e−04	−0.01 (−0.02 to −0.01)
LPDSR	11	0.00	8.20e−01	0.00 (−0.02 to 0.01)
LV	11	0.10	1.89e−12	0.10 (0.07 to 0.13)
LVEDV	11	0.09	3.30e−13	0.09 (0.07 to 0.12)
LVEF	11	−0.02	2.25e−01	−0.02 (−0.05 to 0.01)
LVESV	11	0.07	2.83e−08	0.07 (0.05 to 0.09)
LVM	11	4.06	3.49e−35	4.06 (3.43 to 4.70)
LVSV	11	0.10	5.89e−09	0.10 (0.06 to 0.13)
PA	11	0.05	4.32e−02	0.05 (0.00 to 0.09)
RA	11	0.05	2.83e−03	0.05 (0.02 to 0.08)
RPDSR	11	−0.02	4.96e−01	−0.02 (−0.08 to 0.03)
RVEDV	11	0.09	1.78e−13	0.09 (0.07 to 0.11)
RVEF	11	0.00	7.93e−01	0.00 (−0.03 to 0.02)
RVSV	11	0.09	1.03e−13	0.09 (0.07 to 0.12)

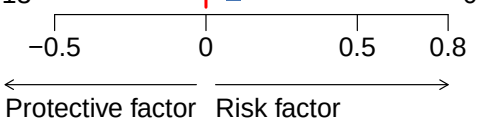


Fig S7 Forestplot for Obesity 3 and Cardiac MRI

Outcome	nsnp	beta	adjustP	beta(95%CI)
AA	10	0.03	8.85e−02	0.03 (−0.00 to 0.06)
DA	10	0.04	9.31e−05	0.04 (0.02 to 0.07)
LA	10	−0.01	2.51e−02	−0.01 (−0.01 to −0.00)
LPDSR	10	−0.01	4.70e−01	−0.01 (−0.02 to 0.01)
LV	10	0.05	1.43e−05	0.05 (0.03 to 0.08)
LVEDV	10	0.05	3.55e−09	0.05 (0.04 to 0.07)
LVEF	10	−0.01	3.36e−01	−0.01 (−0.03 to 0.01)
LVESV	10	0.04	1.67e−05	0.04 (0.02 to 0.06)
LVM	10	2.19	2.42e−13	2.19 (1.62 to 2.76)
LVSV	10	0.05	2.33e−04	0.05 (0.03 to 0.08)
PA	10	0.05	3.00e−03	0.05 (0.02 to 0.08)
RA	10	0.03	6.88e−04	0.03 (0.02 to 0.05)
RPDSR	10	−0.03	2.39e−01	−0.03 (−0.07 to 0.01)
RVEDV	10	0.05	1.40e−04	0.05 (0.02 to 0.07)
RVEF	10	0.00	7.63e−01	0.00 (−0.02 to 0.02)
RVSV	10	0.05	5.50e−05	0.05 (0.03 to 0.07)

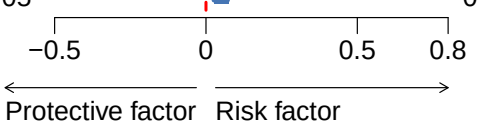


Fig S8 Forestplot for Waist circumference and Cardiac MRI

Outcome	nsnp	beta	adjustP	beta(95%CI)
AA	365	0.25	2.51e−16	0.25 (0.19 to 0.31)
DA	364	0.32	1.14e−37	0.32 (0.27 to 0.37)
LA	365	−0.11	5.12e−50	−0.11 (−0.12 to −0.09)
LPDSR	348	0.01	6.70e−01	0.01 (−0.02 to 0.04)
LV	365	0.41	1.78e−51	0.41 (0.35 to 0.46)
LVEDV	364	0.39	4.89e−46	0.39 (0.33 to 0.44)
LVEF	364	−0.10	3.49e−04	−0.10 (−0.15 to −0.05)
LVESV	364	0.30	1.30e−30	0.30 (0.25 to 0.35)
LVM	365	13.61	2.81e−78	13.61 (12.20 to 15.02)
LVSV	365	0.39	5.69e−44	0.39 (0.34 to 0.45)
PA	364	0.28	7.25e−22	0.28 (0.22 to 0.33)
RA	365	0.26	1.74e−20	0.26 (0.21 to 0.32)
RPDSR	365	0.00	9.88e−01	0.00 (−0.11 to 0.12)
RVEDV	364	0.38	1.97e−50	0.38 (0.33 to 0.43)
RVEF	364	−0.03	3.40e−01	−0.03 (−0.08 to 0.02)
RVSV	364	0.38	1.68e−45	0.38 (0.33 to 0.43)

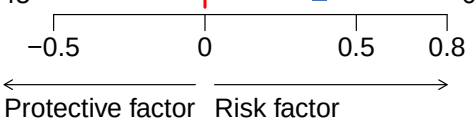


Fig S9 Forestplot for Waist-to-hip ratio and Cardiac MRI

Outcome	nsnp	beta	adjustP	beta(95%CI)
AA	29	0.07	0.46900	0.07 (−0.08 to 0.21)
DA	29	0.18	0.02910	0.18 (0.03 to 0.33)
LA	29	−0.05	0.02430	−0.05 (−0.08 to −0.01)
LPDSR	27	−0.01	0.82600	−0.01 (−0.12 to 0.09)
LV	29	0.03	0.78900	0.03 (−0.15 to 0.21)
LVEDV	29	−0.01	0.89600	−0.01 (−0.19 to 0.16)
LVEF	29	0.10	0.22400	0.10 (−0.04 to 0.24)
LVESV	29	−0.06	0.53900	−0.06 (−0.23 to 0.10)
LVM	29	8.45	0.00379	8.45 (3.04 to 13.87)
LVSV	29	0.07	0.47000	0.07 (−0.09 to 0.23)
PA	29	0.13	0.15000	0.13 (−0.03 to 0.28)
RA	29	−0.04	0.66800	−0.04 (−0.20 to 0.12)
RPDSR	29	−0.10	0.63100	−0.10 (−0.46 to 0.25)
RVEDV	29	0.05	0.60600	0.05 (−0.12 to 0.23)
RVEF	29	−0.04	0.53500	−0.04 (−0.15 to 0.07)
RVSV	29	0.04	0.70800	0.04 (−0.13 to 0.21)

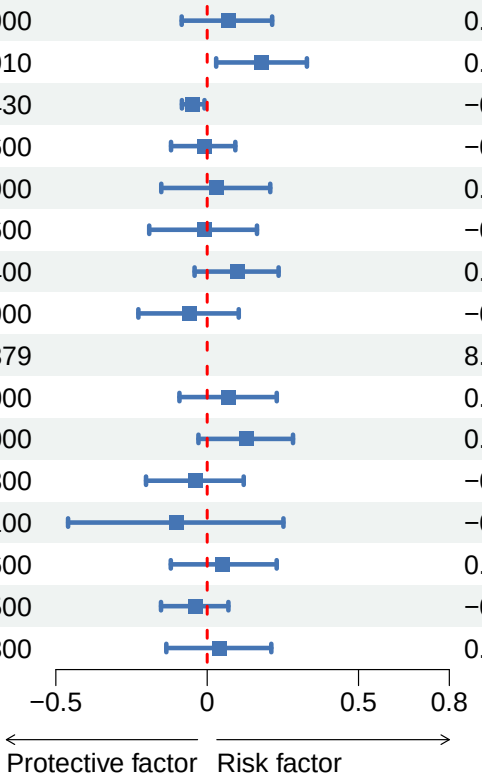
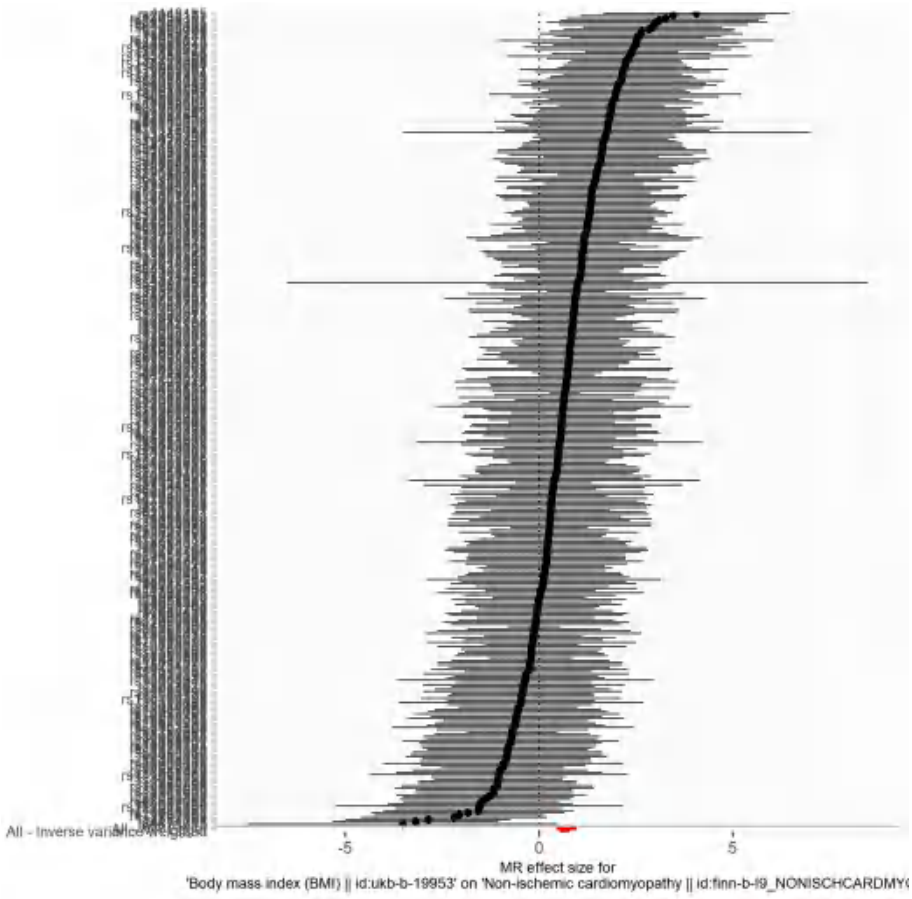
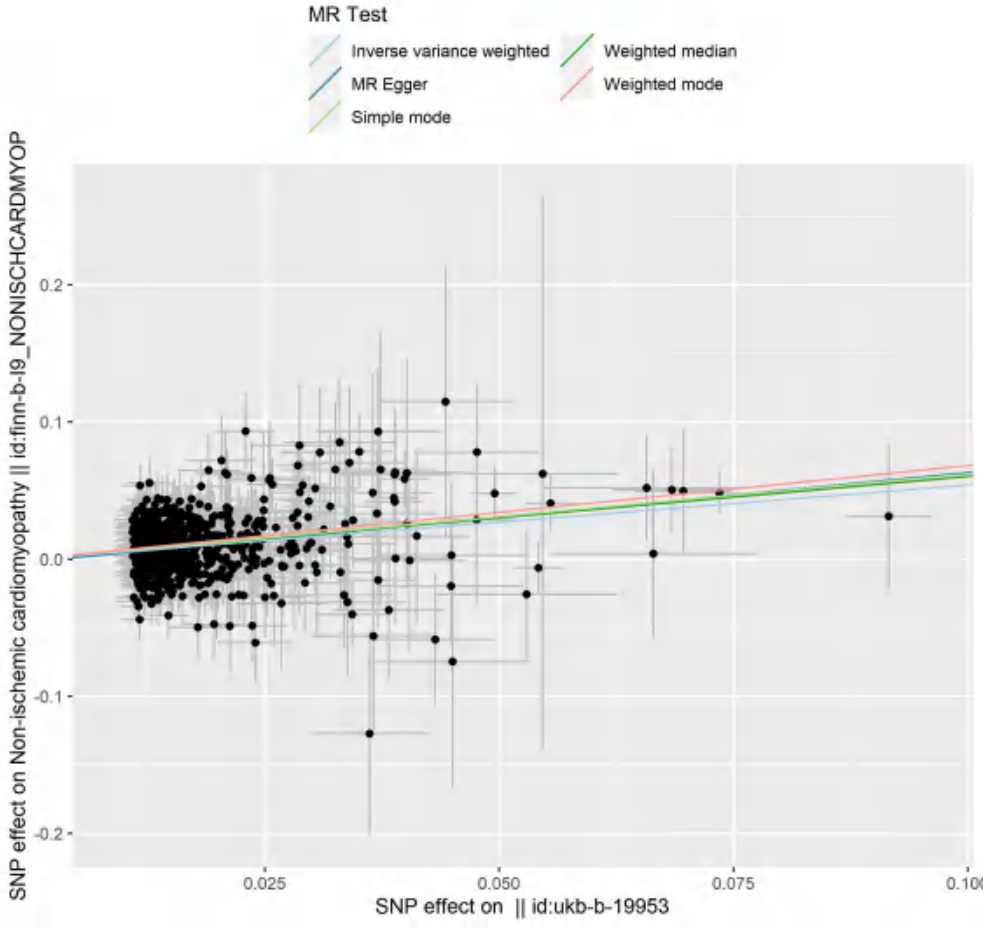


Figure S10. Visualisation of mendelian randomization for causal associations between BMI and non-ischemic cardiomyopathy. A: Forest plot of MR effect size using MR-Egger and IVW methods; B: Pleiotropy analysis; C : Stability analysis of leave-one-out method; D: funnel plot.

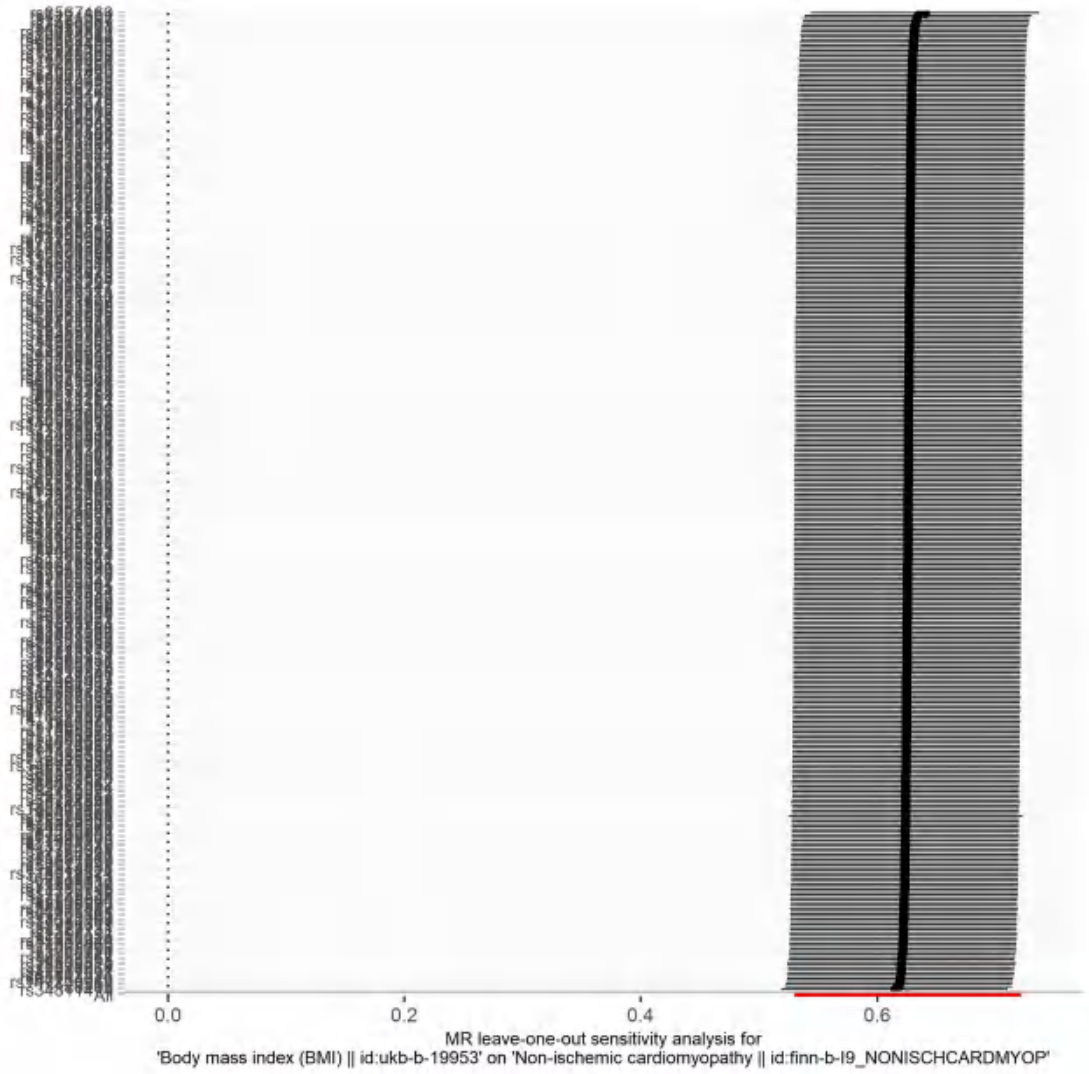
A



B



C


0.0
0.2
0.4
0.6
MR leave-one-out sensitivity analysis for
'Body mass index (BMI) || id:ukb-b-19953' on 'Non-ischemic cardiomyopathy || id:finn-b-I9_NONISCHCARDMYOP'

D

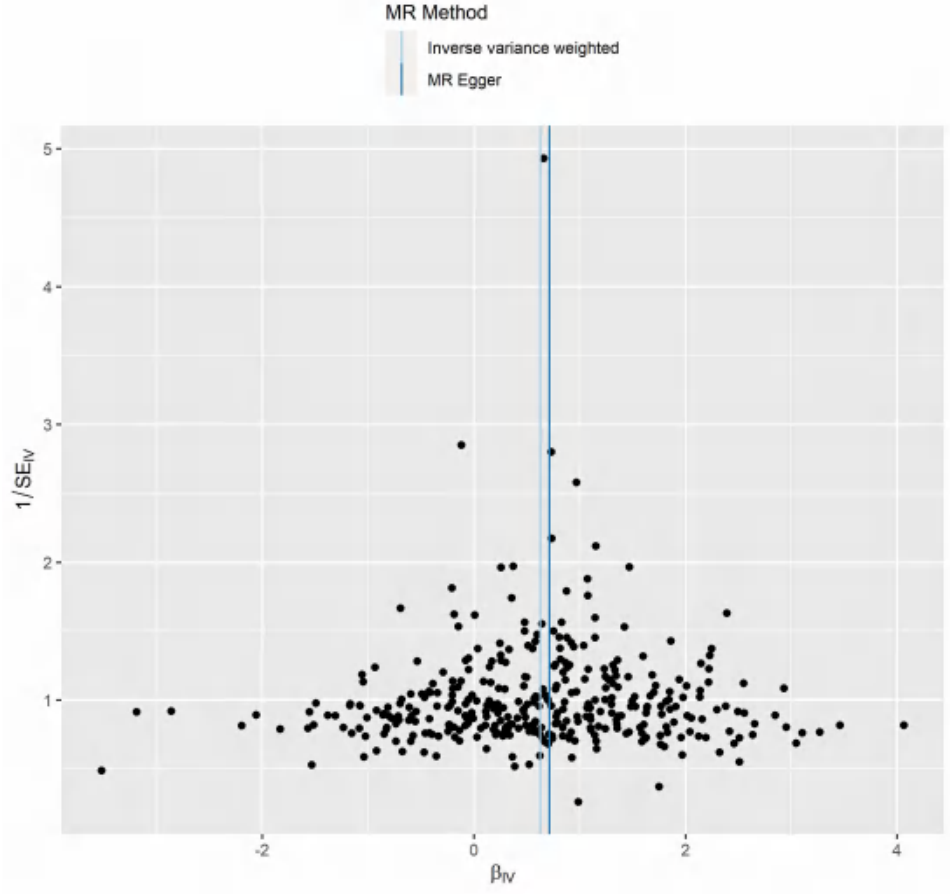
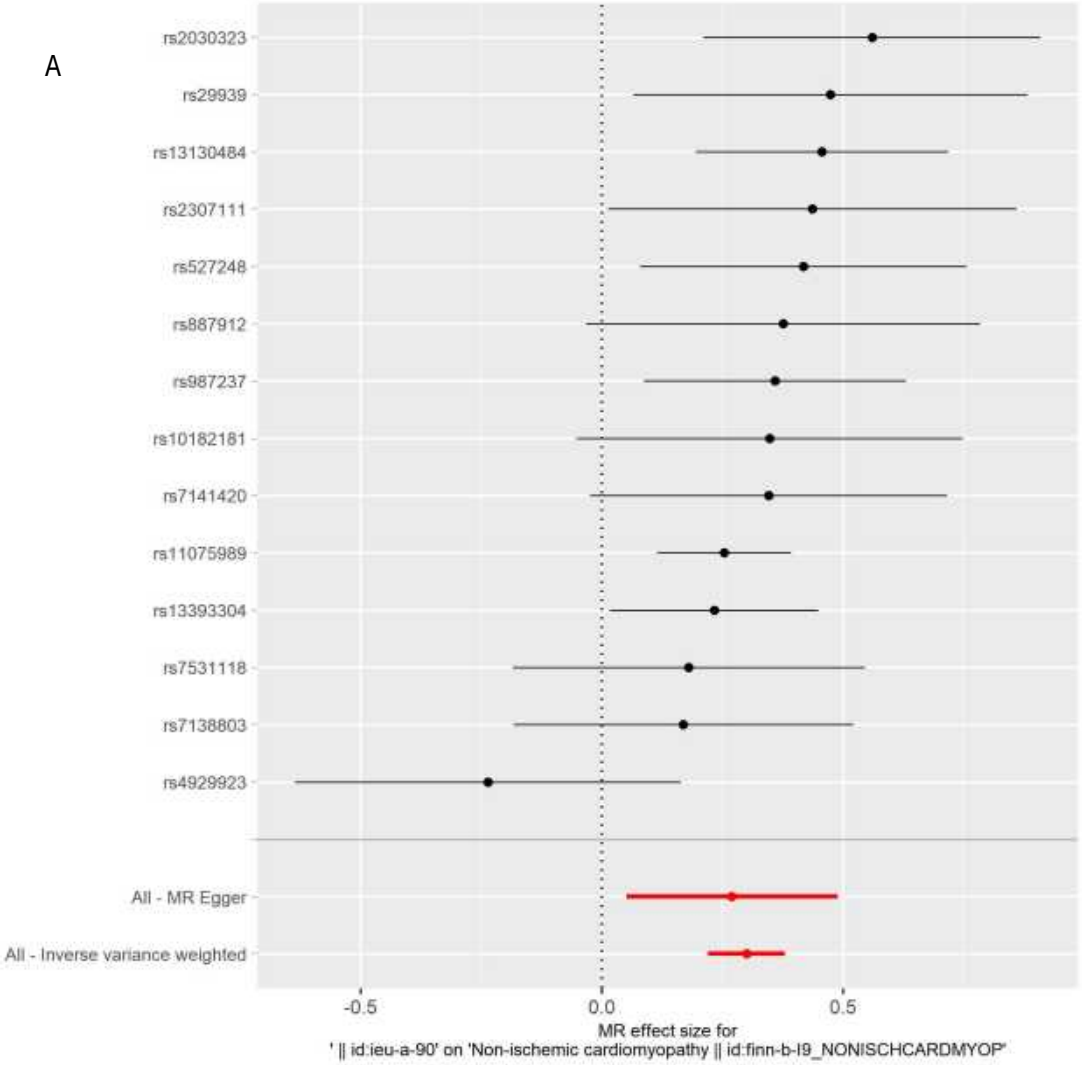
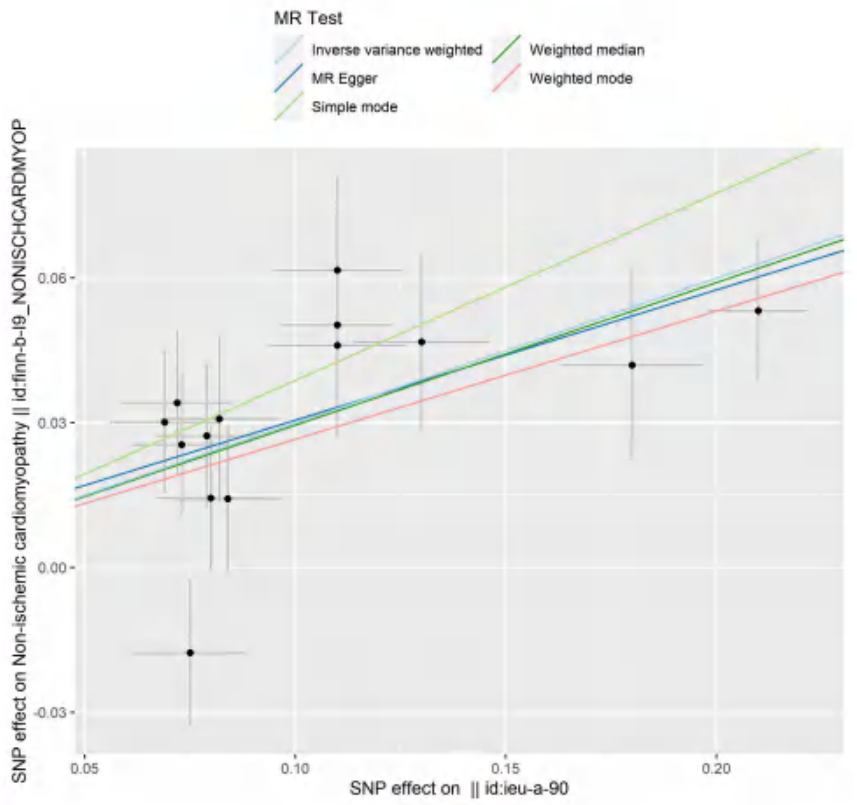

MR Method
Inverse variance weighted
MR Egger
5
4
3
2
1
1/SE_IV
-2
0
2
4
β_IV

Figure S11. Visualisation of mendelian randomization for causal associations between obesity class 1 and non-ischemic cardiomyopathy. A: Forest plot of MR effect size using MR-Egger and IVW methods; B: Pleiotropy analysis; C :Stability analysis of leave-one-out method; D: funnel plot.

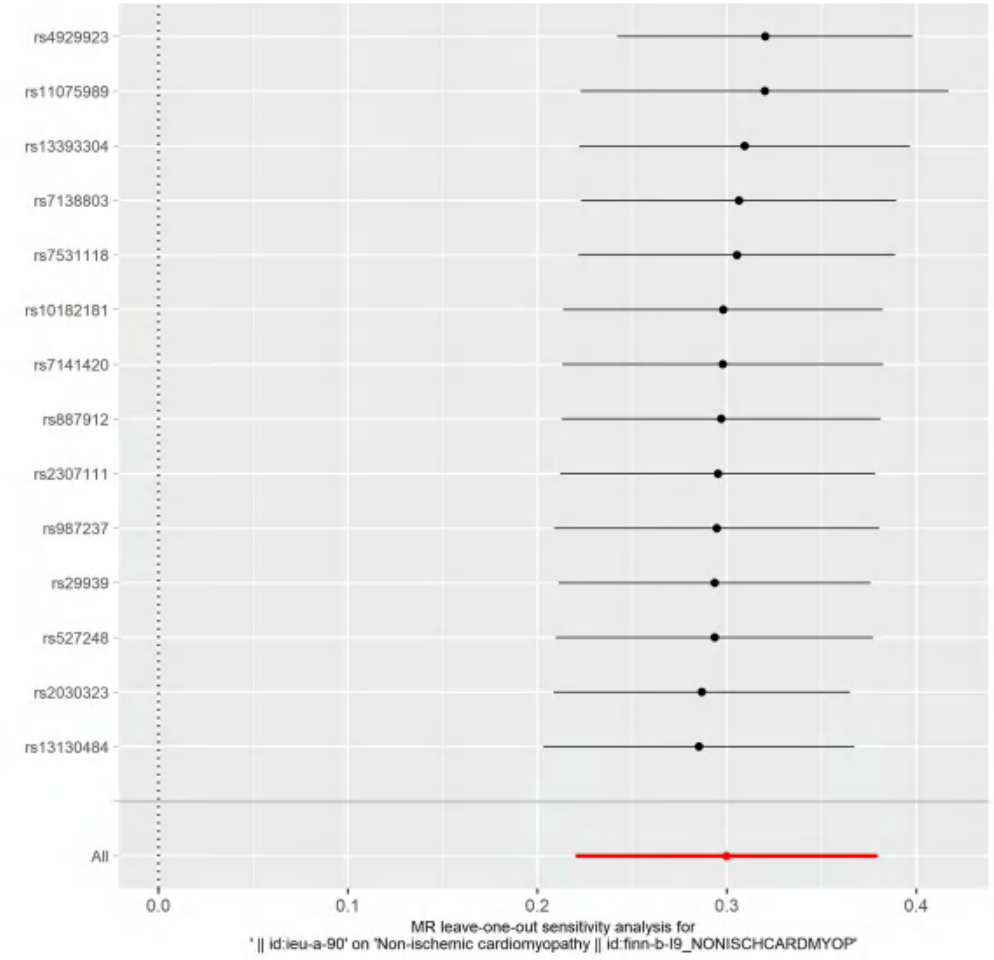
A



B



C


rs4929923
rs11075989
rs13393304
rs7138803
rs7531118
rs10182181
rs7141420
rs887912
rs2307111
rs987237
rs29939
rs527248
rs2030323
rs13130484
All
0.0
0.1
0.2
0.3
0.4
MR leave-one-out sensitivity analysis for
' || id:ieu-a-90' on 'Non-ischemic cardiomyopathy || id:finn-b-I9_NONISCHCARDMYOP'

D

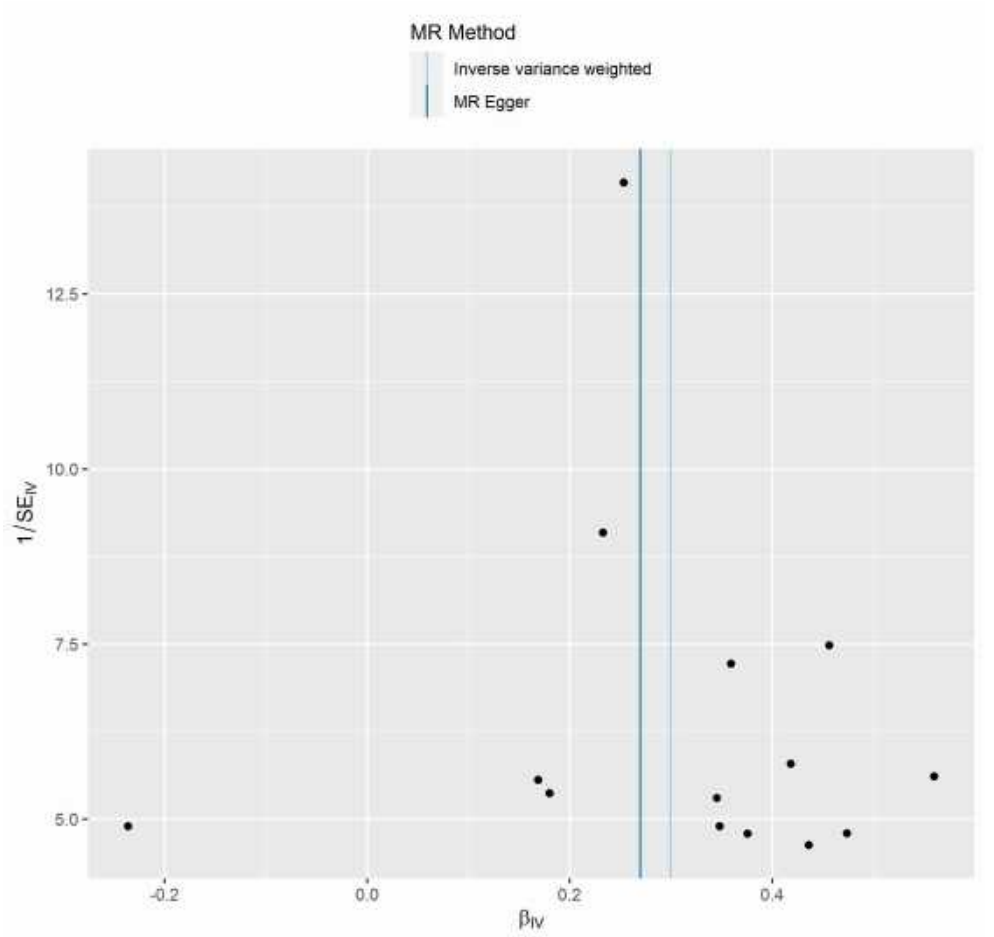
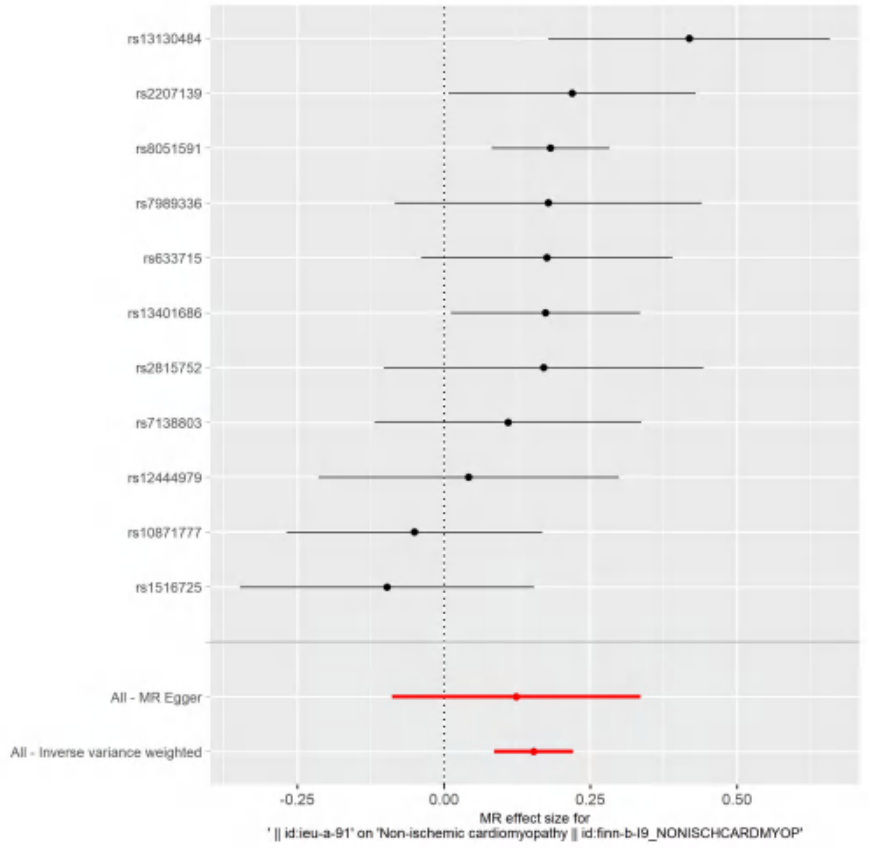
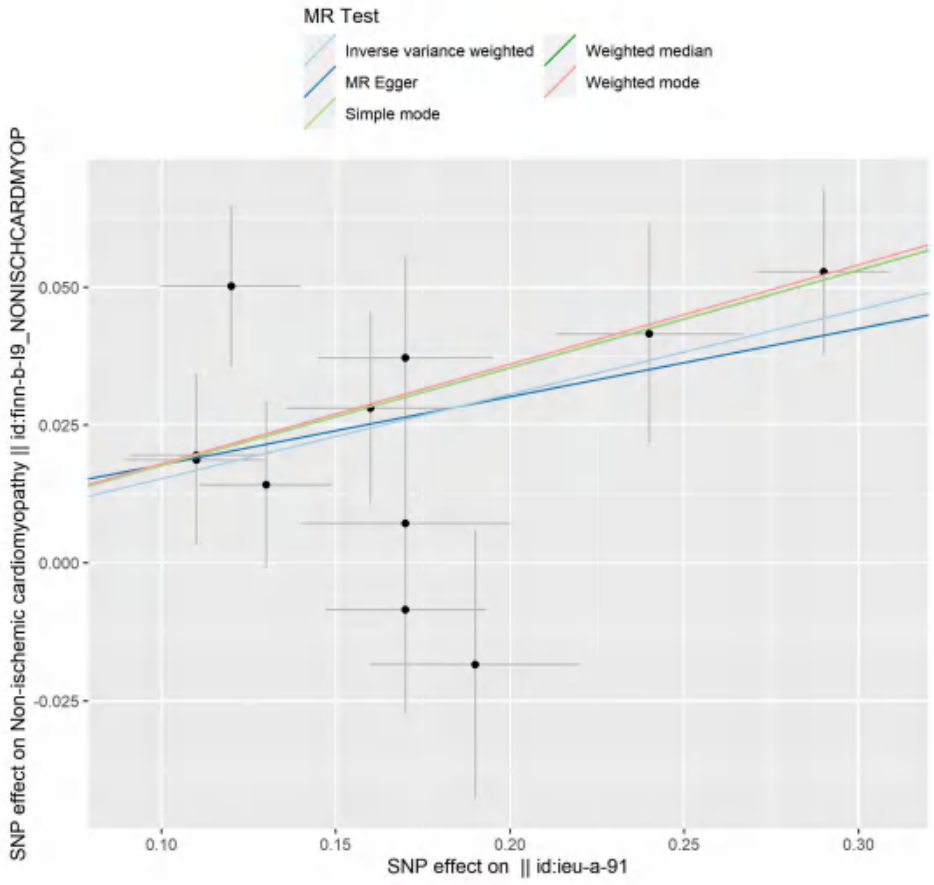

MR Method
Inverse variance weighted
MR Egger
12.5
10.0
7.5
5.0
1/SEiv
-0.2
0.0
0.2
0.4
βiv

Figure S12. Visualisation of mendelian randomization for causal associations between obesity class 2 and non-ischemic cardiomyopathy. A: Forest plot of MR effect size using MR-Egger and IVW methods; B: Pleiotropy analysis; C : Stability analysis of leave-one-out method; D: funnel plot.

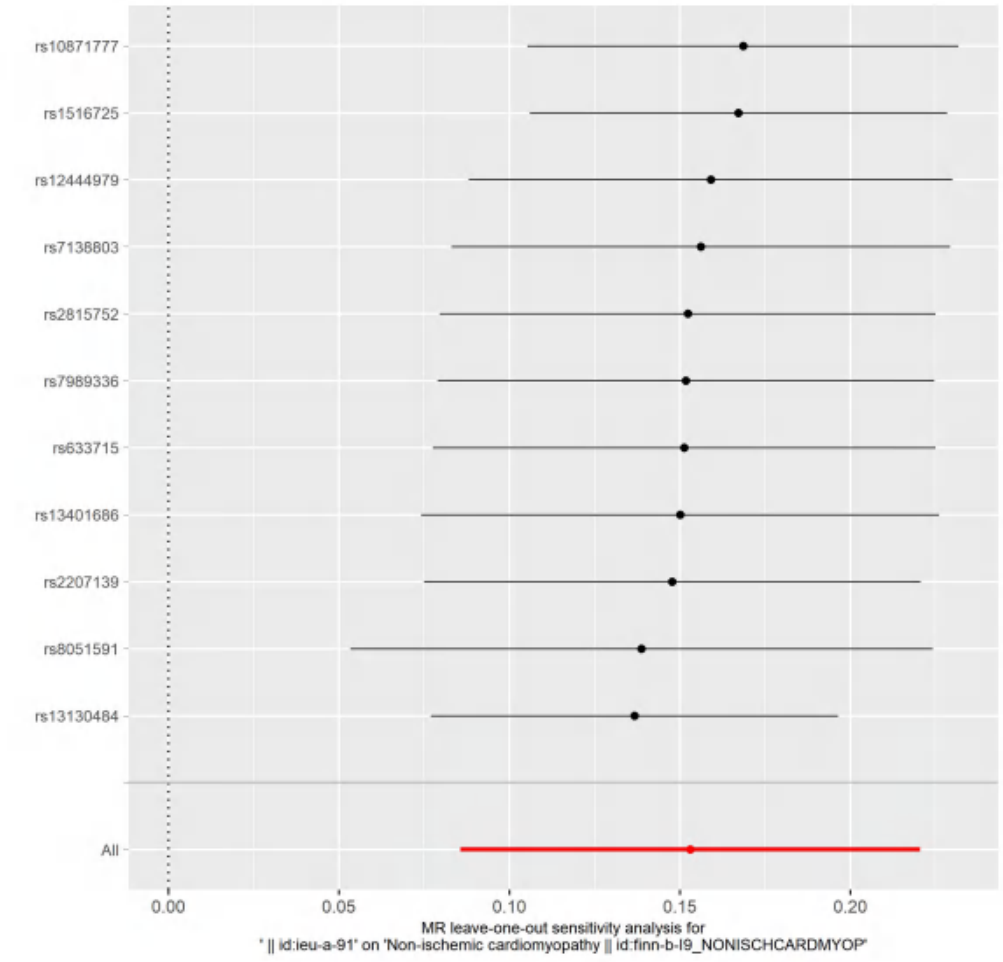
A



B



C


rs10871777
rs1516725
rs12444979
rs7138803
rs2815752
rs7989336
rs633715
rs13401686
rs2207139
rs8051591
rs13130484
All
0.00
0.05
0.10
0.15
0.20
MR leave-one-out sensitivity analysis for
' || id:ieu-a-91' on 'Non-ischemic cardiomyopathy || id:finn-b-I9_NONISCHCARDMYOP'

D

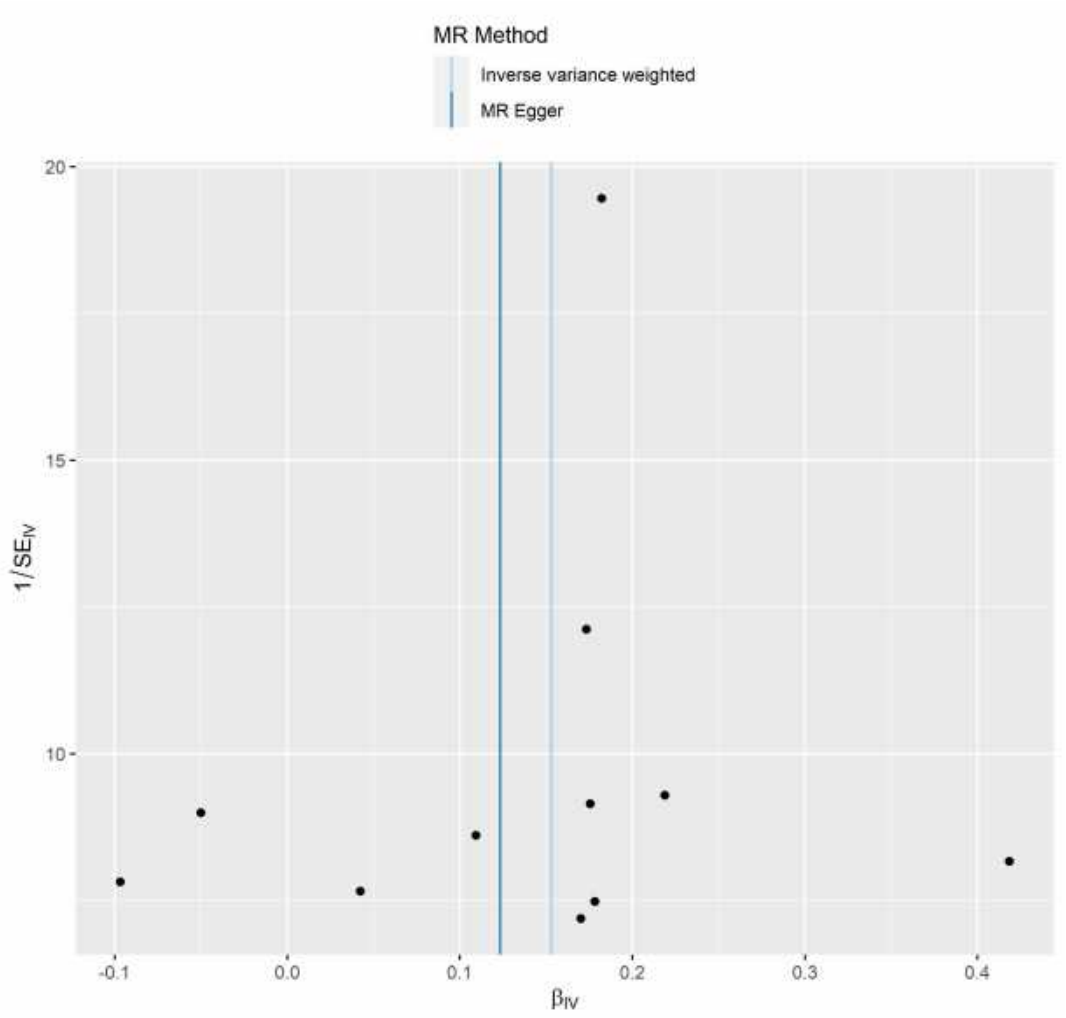
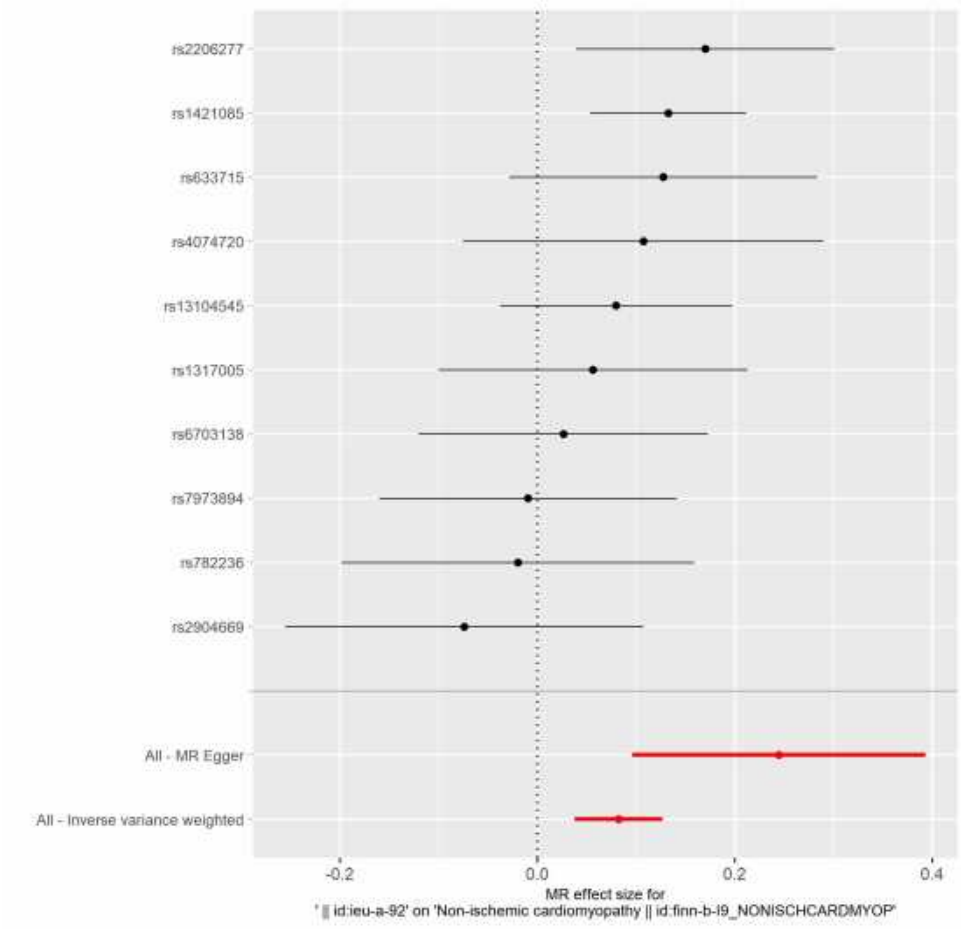
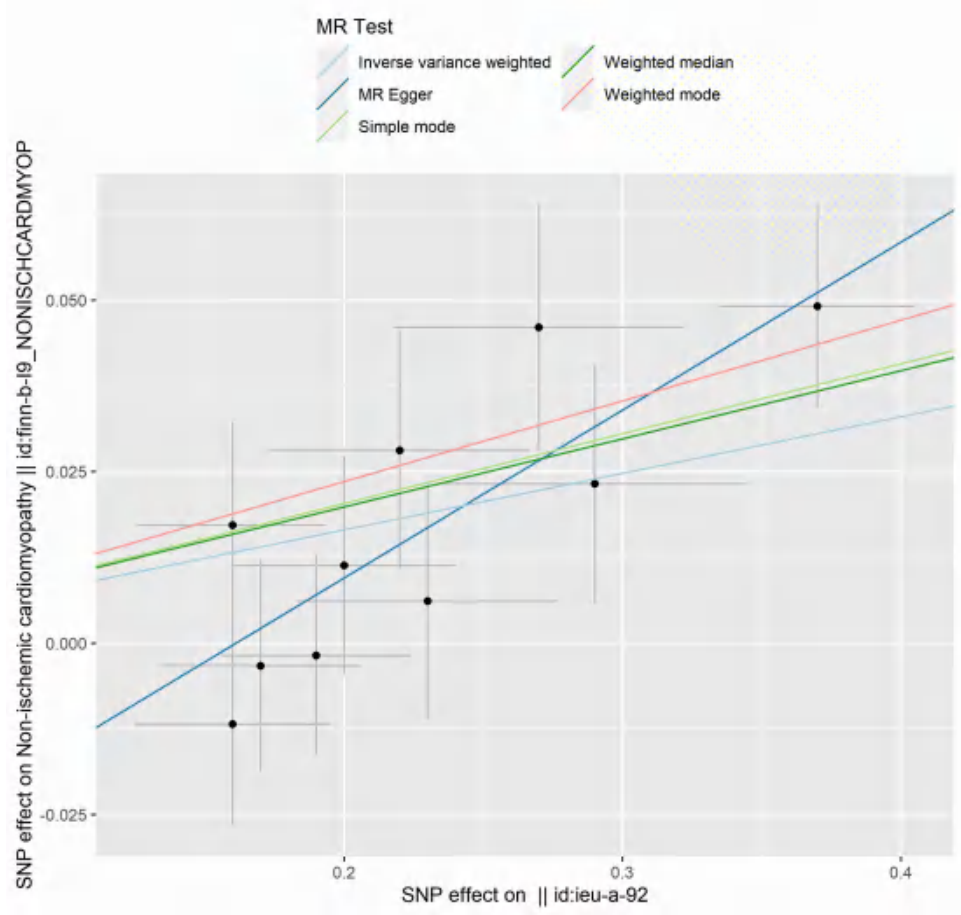

MR Method
Inverse variance weighted
MR Egger
20
15
10
1/SE_IV
-0.1
0.0
0.1
0.2
0.3
0.4
β_IV

Figure S13. Visualisation of mendelian randomization for causal associations between obesity class 3 and non-ischemic cardiomyopathy. A: Forest plot of MR effect size using MR-Egger and IVW methods; B: Pleiotropy analysis; C : Stability analysis of leave-one-out method; D: funnel plot.

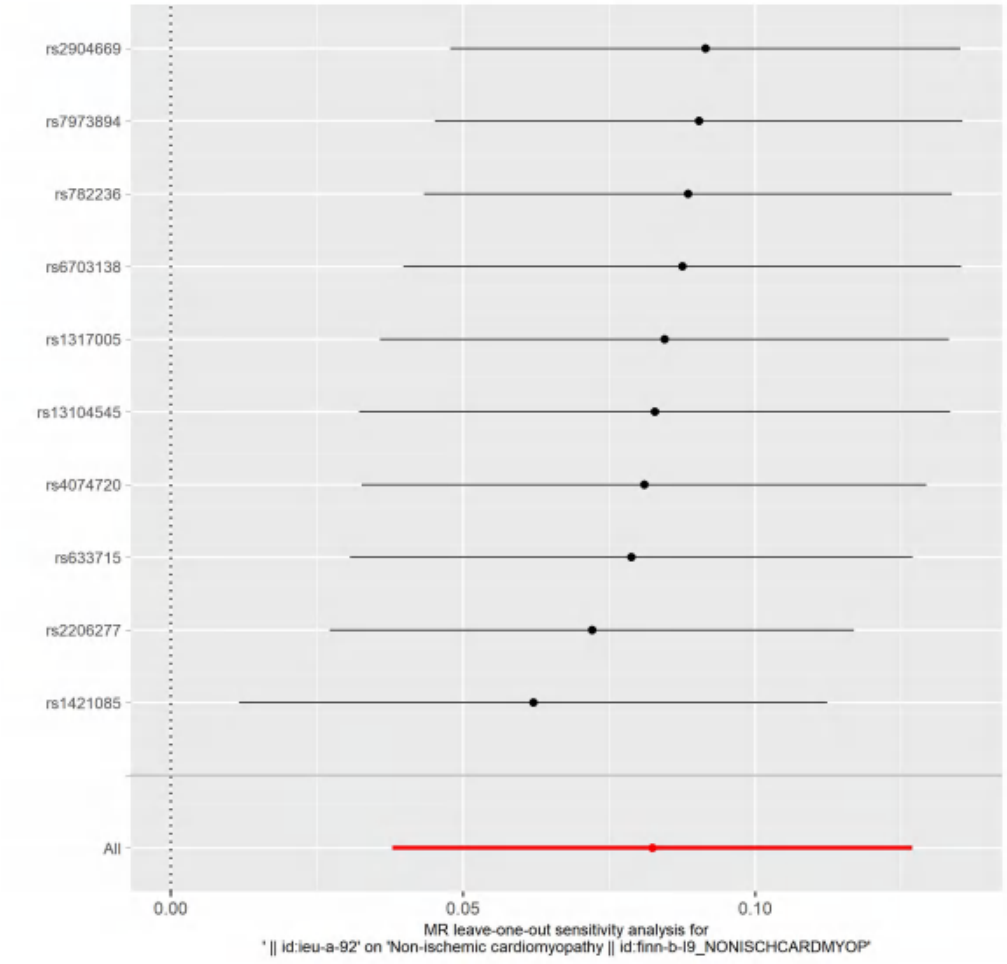
A



B



C


rs2904669
rs7973894
rs782236
rs6703138
rs1317005
rs13104545
rs4074720
rs633715
rs2206277
rs1421085
All
0.00
0.05
0.10
MR leave-one-out sensitivity analysis for
' || id:ieu-a-92' on 'Non-ischemic cardiomyopathy || id:finn-b-I9_NONISCHCARDMYOP'

D

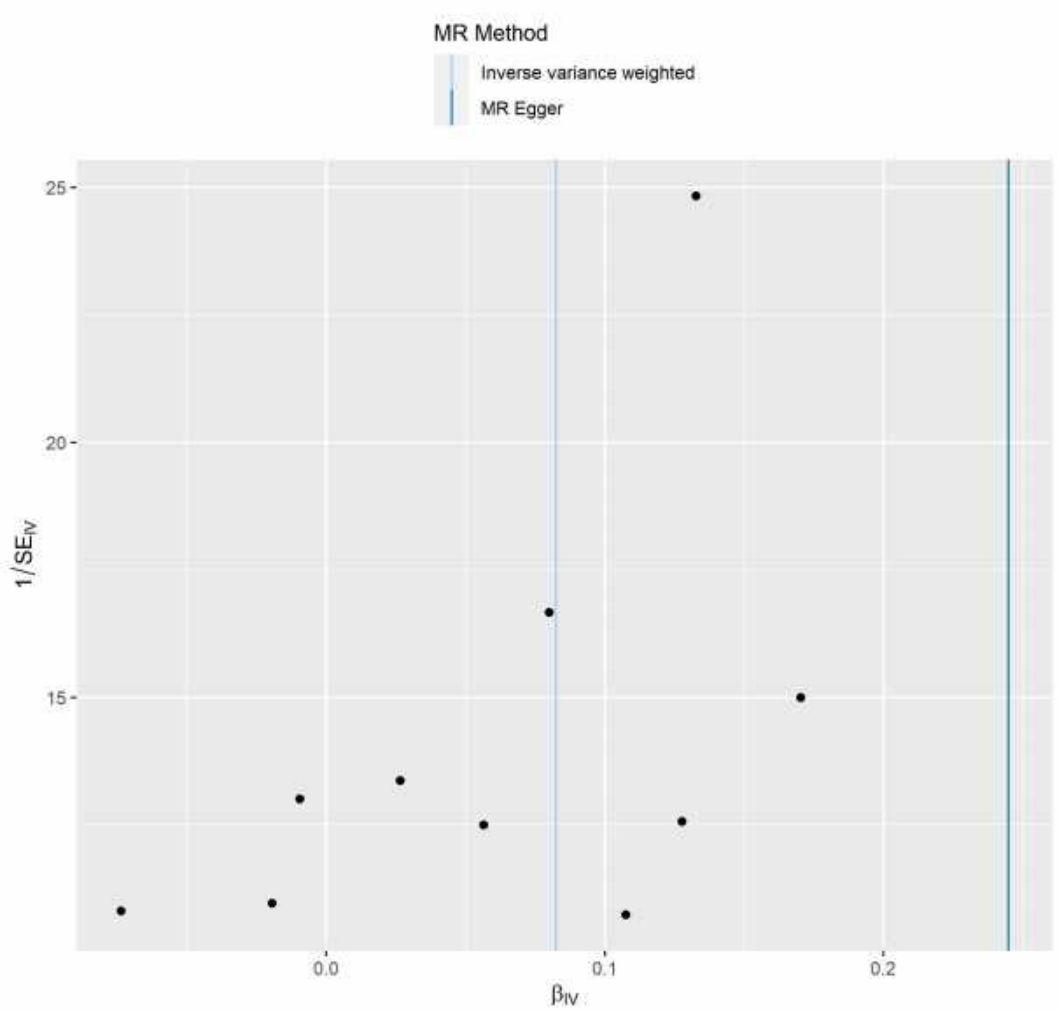
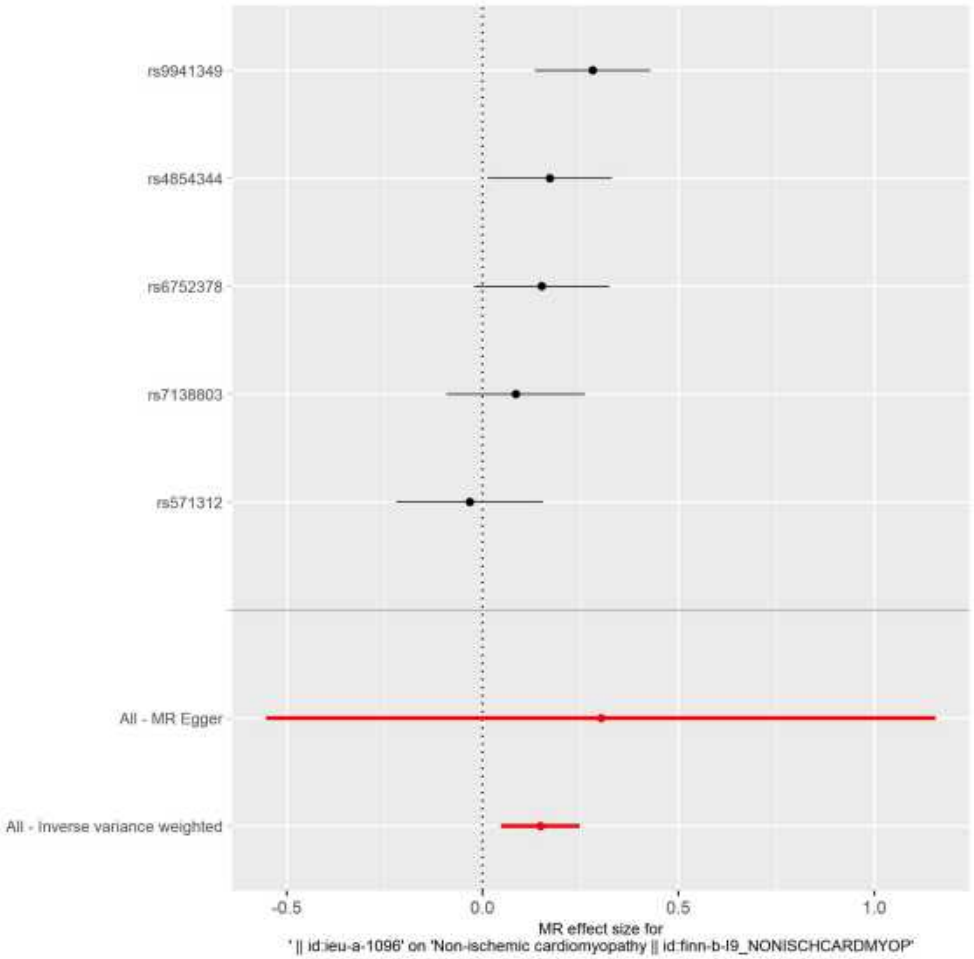
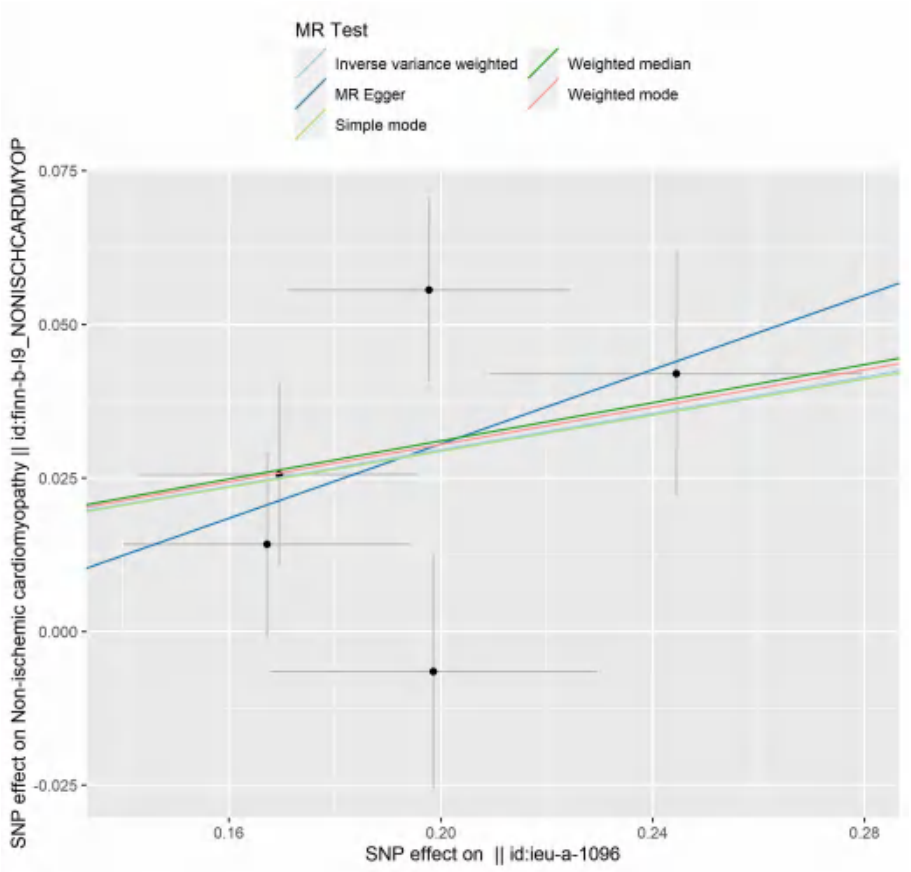

MR Method
Inverse variance weighted
MR Egger
25
20
15
1/SE_IV
0.0
0.1
0.2
β_IV

Figure S14. Visualisation of mendelian randomization for causal associations between childhood obesity and non-ischemic cardiomyopathy. A: Forest plot of MR effect size using MR-Egger and IVW methods; B: Pleiotropy analysis; C : Stability analysis of leave-one-out method; D: funnel plot.

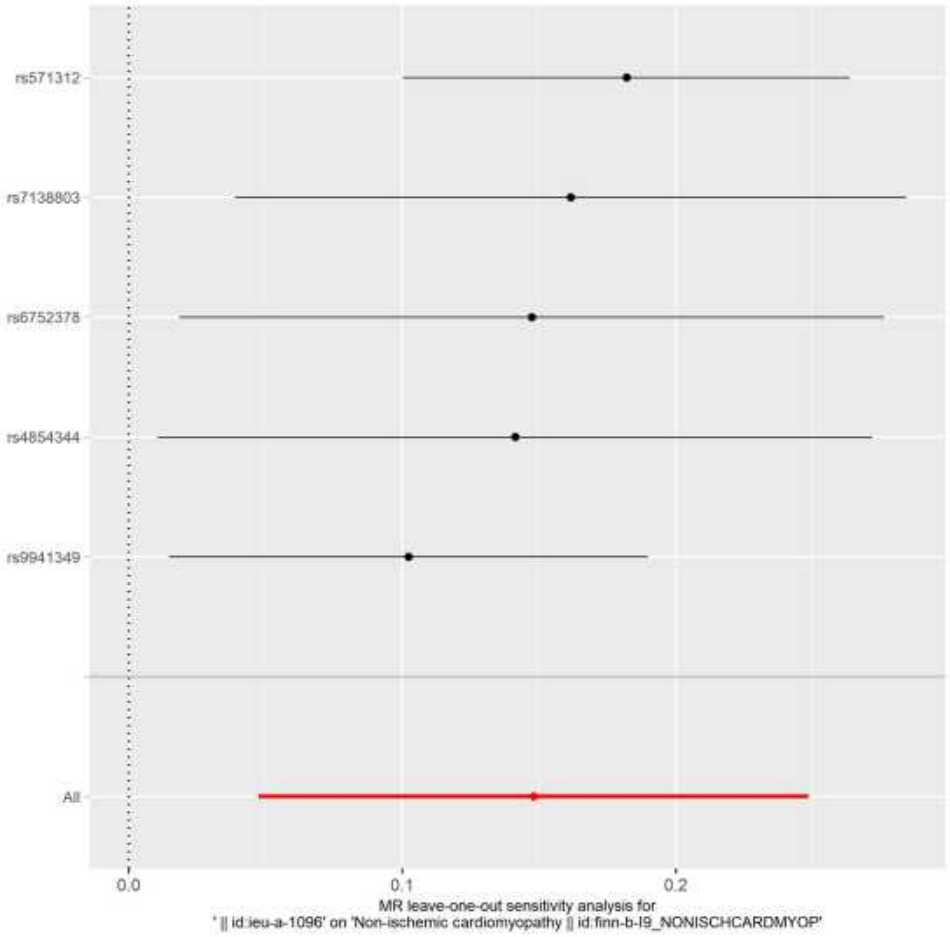
A



B



C


rs571312
rs7138803
rs6752378
rs4854344
rs9941349
All
0.0
0.1
0.2
MR leave-one-out sensitivity analysis for
' || id:ieu-a-1096' on 'Non-ischemic cardiomyopathy || id:finn-b-I9_NONISCHCARDMYOP'

D

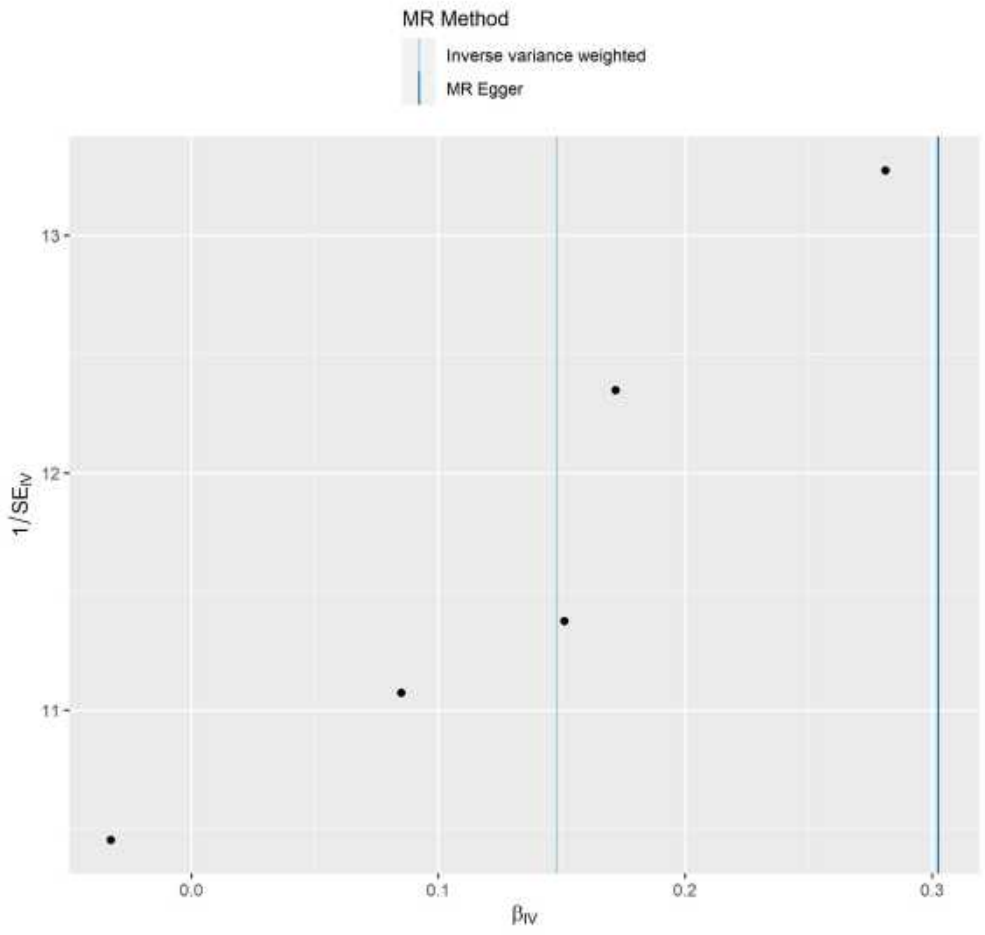
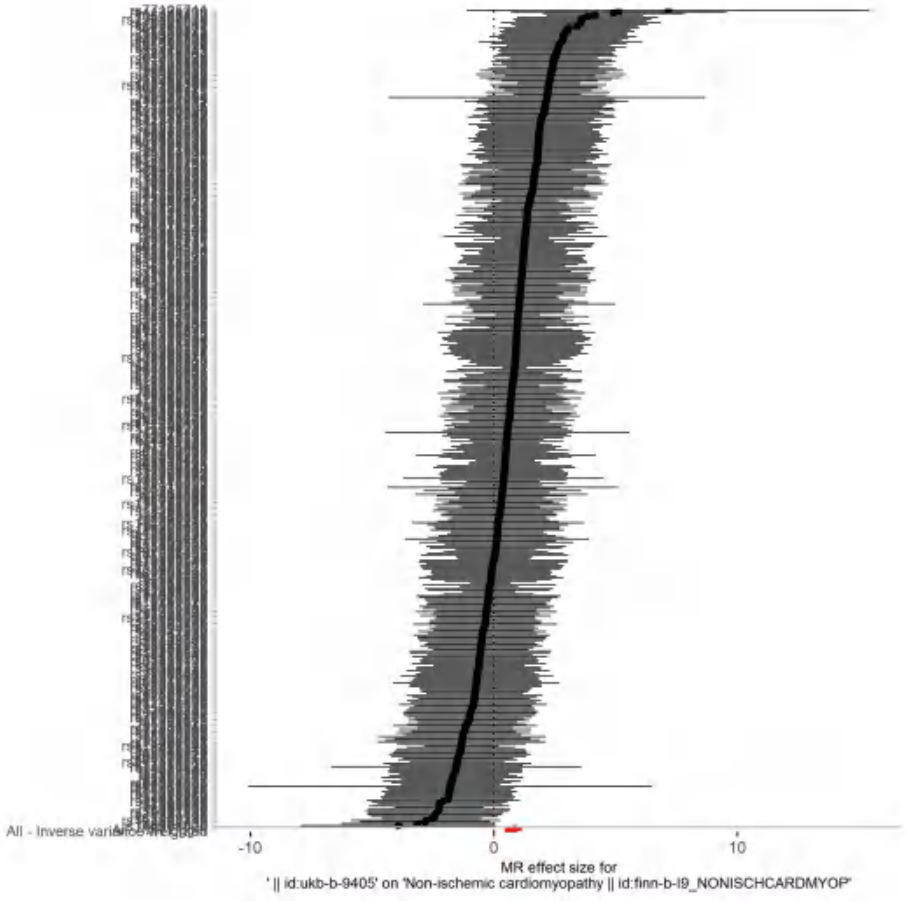
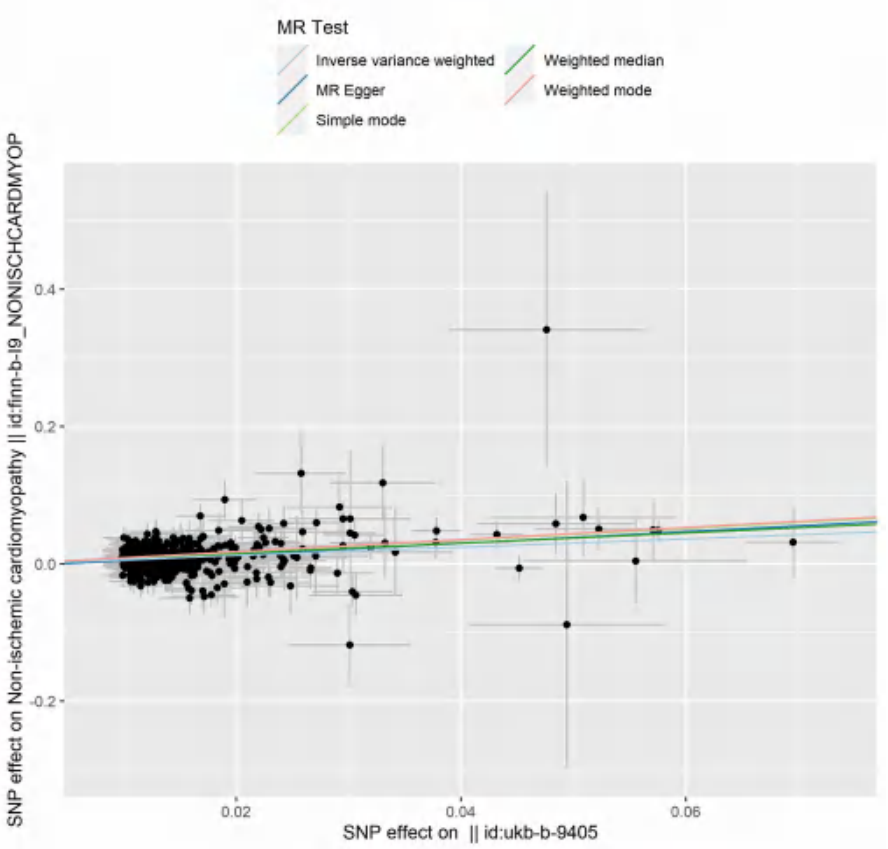

MR Method
Inverse variance weighted
MR Egger
13
12
11
1/SE_IV
0.0
0.1
0.2
0.3
β_IV

Figure S15 Visualisation of mendelian randomization for causal associations between waist circumference and non-ischemic cardiomyopathy. A: Forest plot of MR effect size using MR-Egger and IVW methods; B: Pleiotropy analysis; C: Stability analysis of leave-one-out method; D: funnel plot.

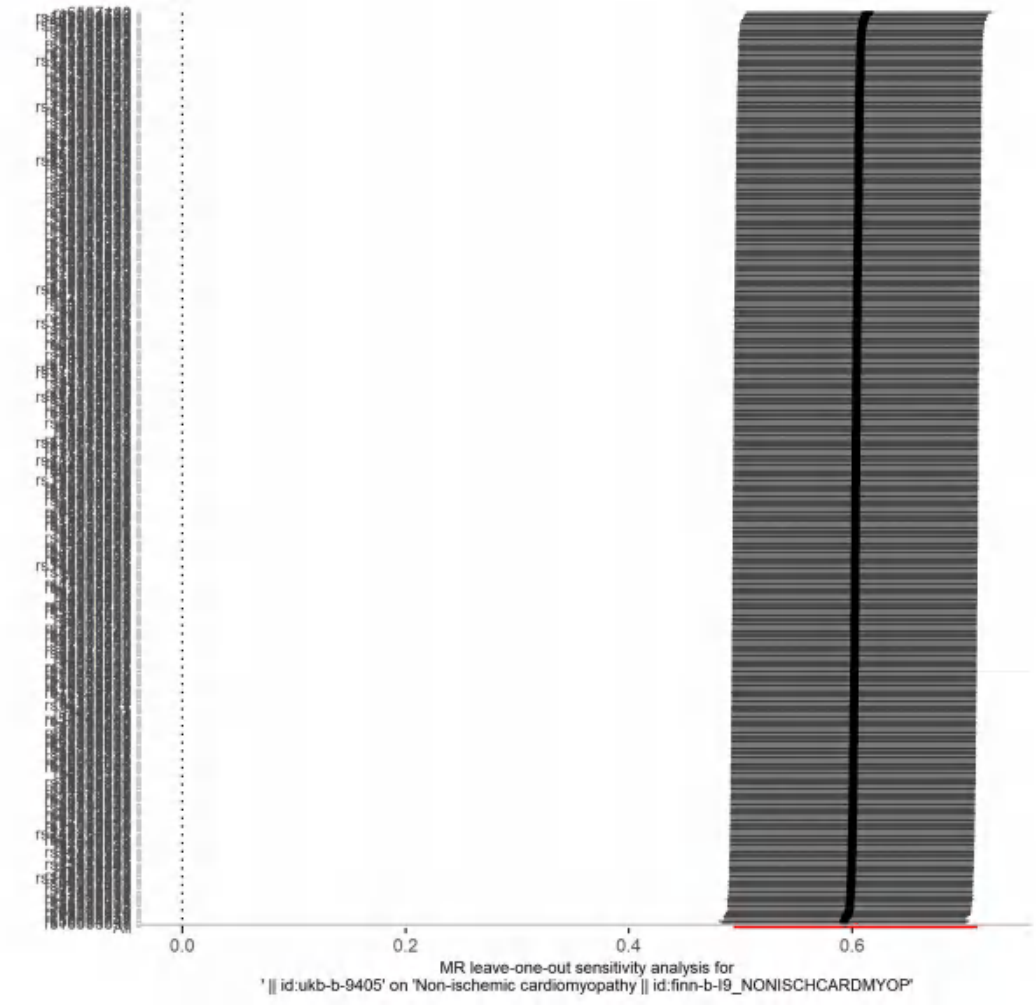
A



B



C


0.0
0.2
0.4
0.6
MR leave-one-out sensitivity analysis for
' || id:ukb-b-9405' on 'Non-ischemic cardiomyopathy || id:finn-b-I9_NONISCHCARDMYOP'

D

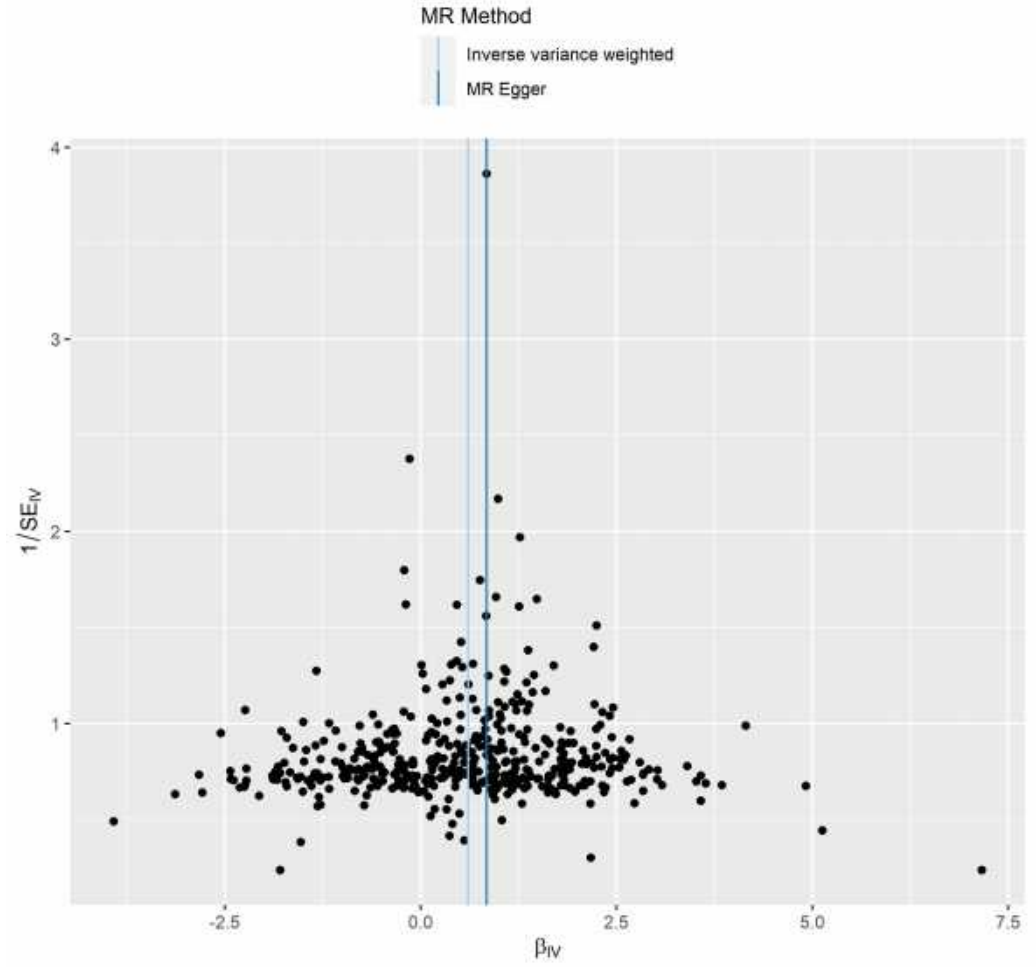
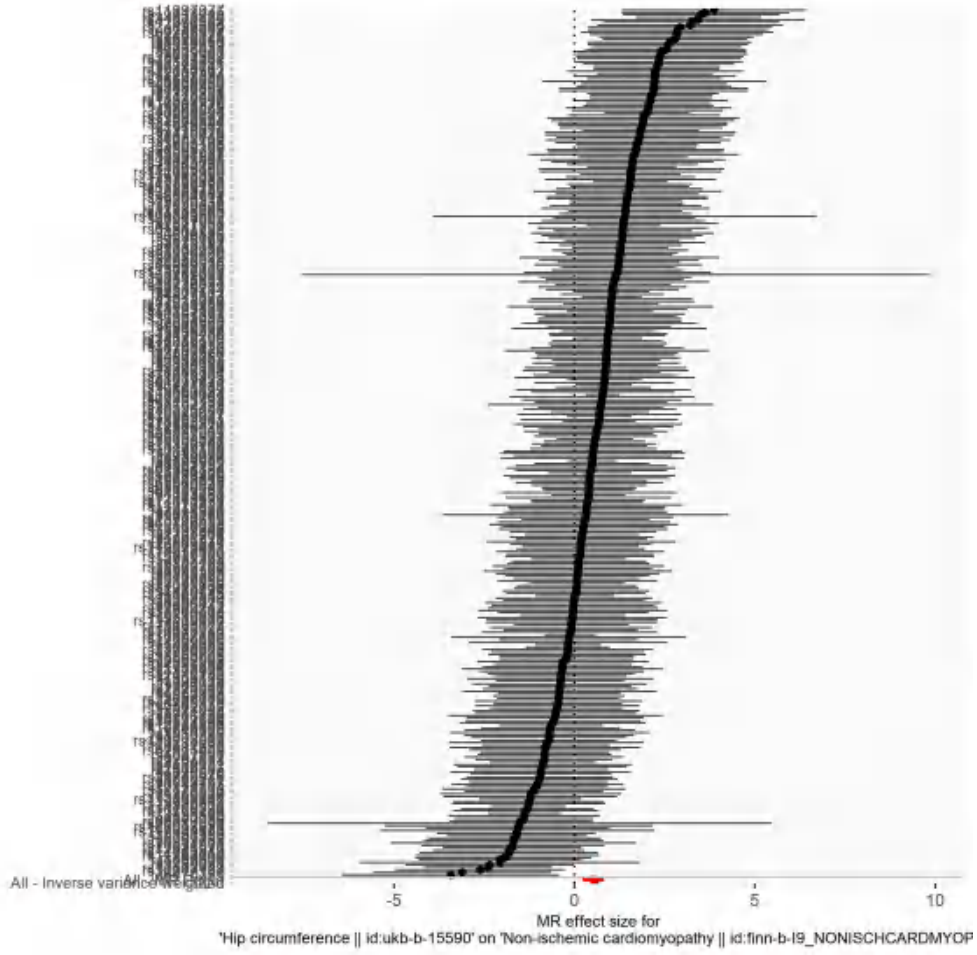
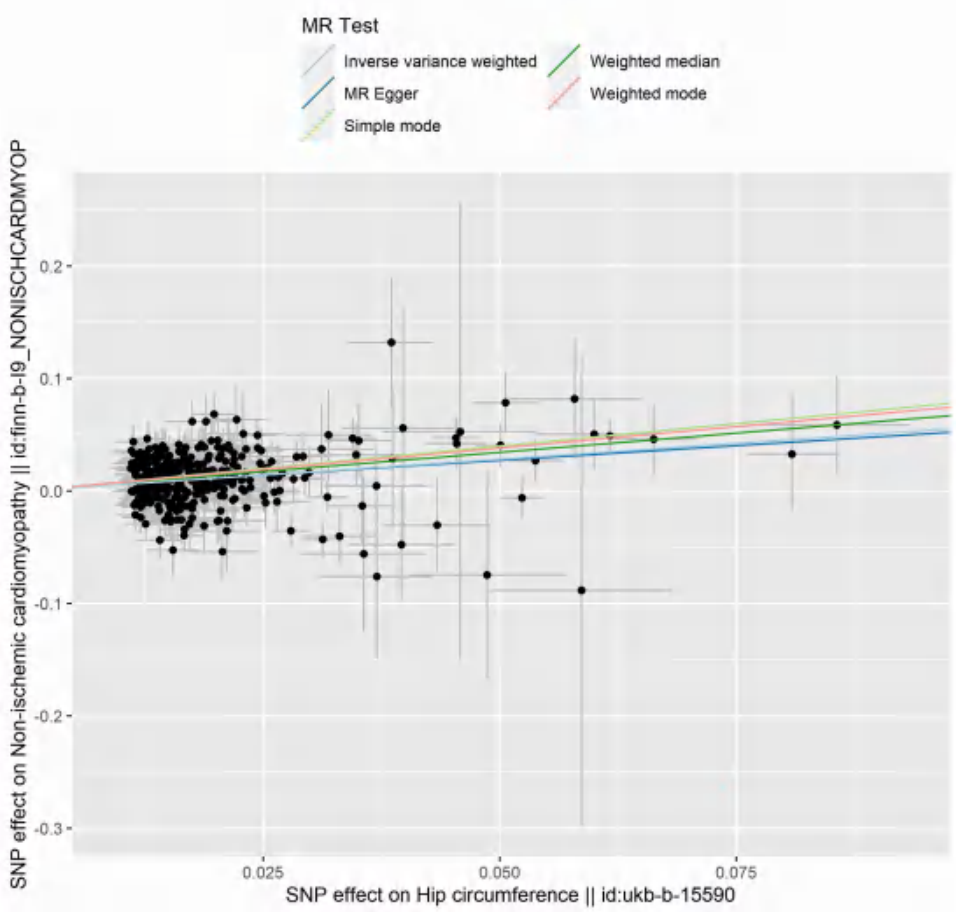

MR Method
Inverse variance weighted
MR Egger
4
3
2
1
1/SE_IV
-2.5
0.0
2.5
5.0
7.5
β_IV

Figure S16. Visualisation of mendelian randomization for causal associations between hip circumference and non-ischemic cardiomyopathy. A: Forest plot of MR effect size using MR-Egger and IVW methods; B: Pleiotropy analysis; C : Stability analysis of leave-one-out method; D: funnel plot.

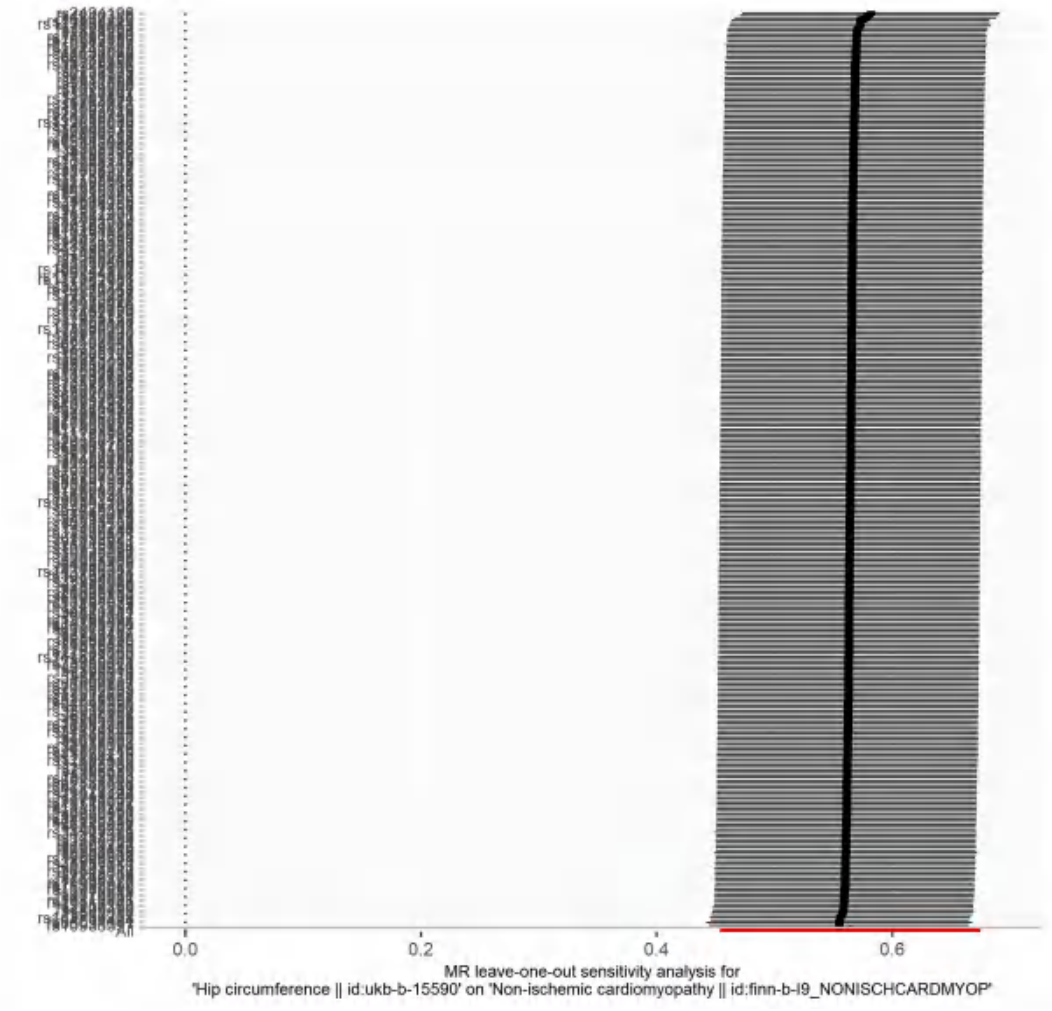
A



B



C


0.0
0.2
0.4
0.6
MR leave-one-out sensitivity analysis for
"Hip circumference || id:ukb-b-15590" on "Non-ischemic cardiomyopathy || id:finn-b-I9_NONISCHCARDMYOP"

D

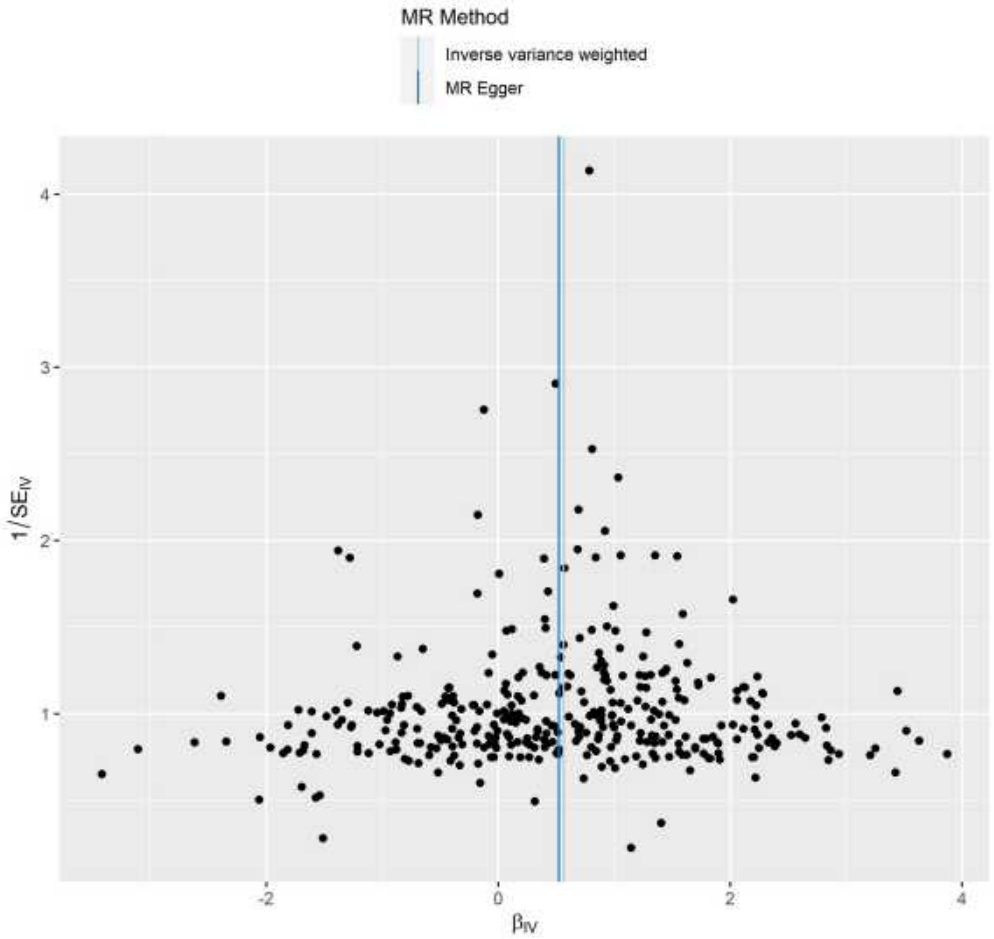
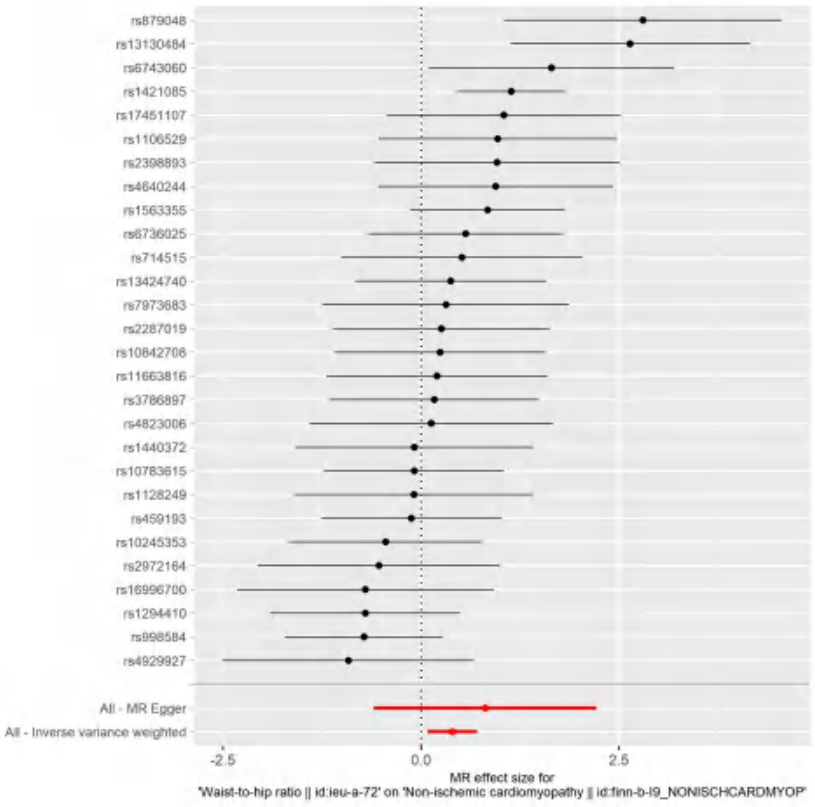
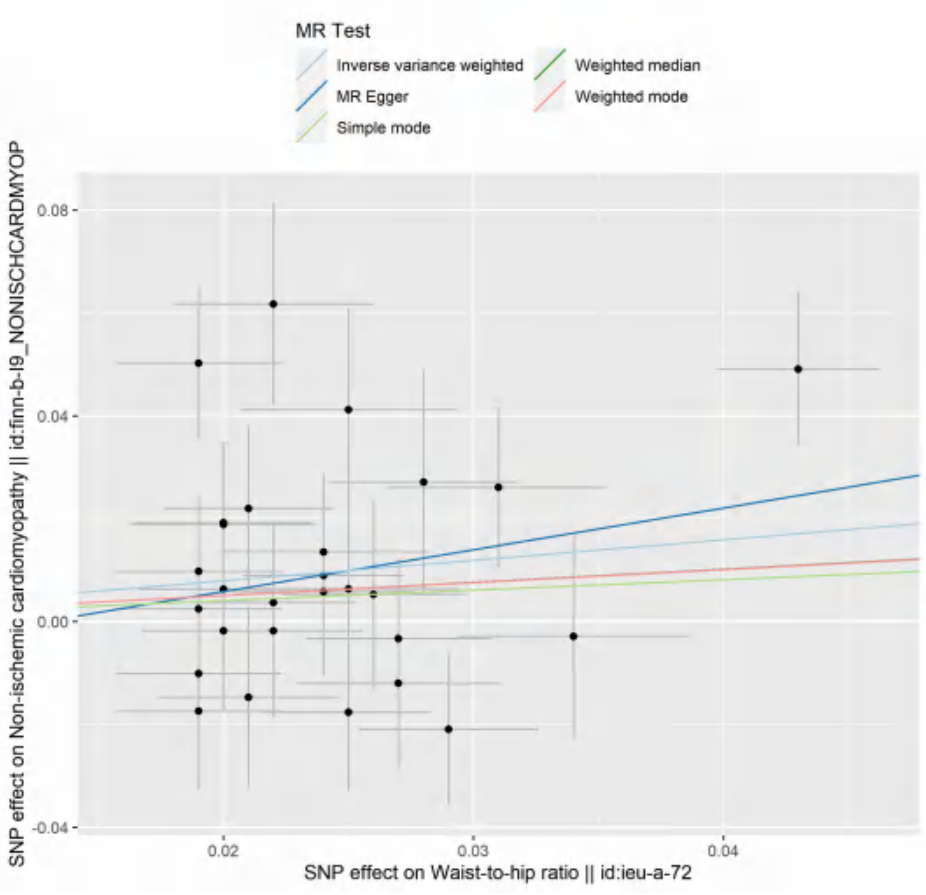

MR Method
Inverse variance weighted
MR Egger
4
3
2
1
1/SE_IV
-2
0
2
4
β_IV

Figure S17. Visualisation of mendelian randomization for causal associations between waist-hip ratio and non-ischemic cardiomyopathy. A: Forest plot of MR effect size using MR-Egger and IVW methods; B: Pleiotropy analysis; C: Stability analysis of leave-one-out method; D: funnel plot.

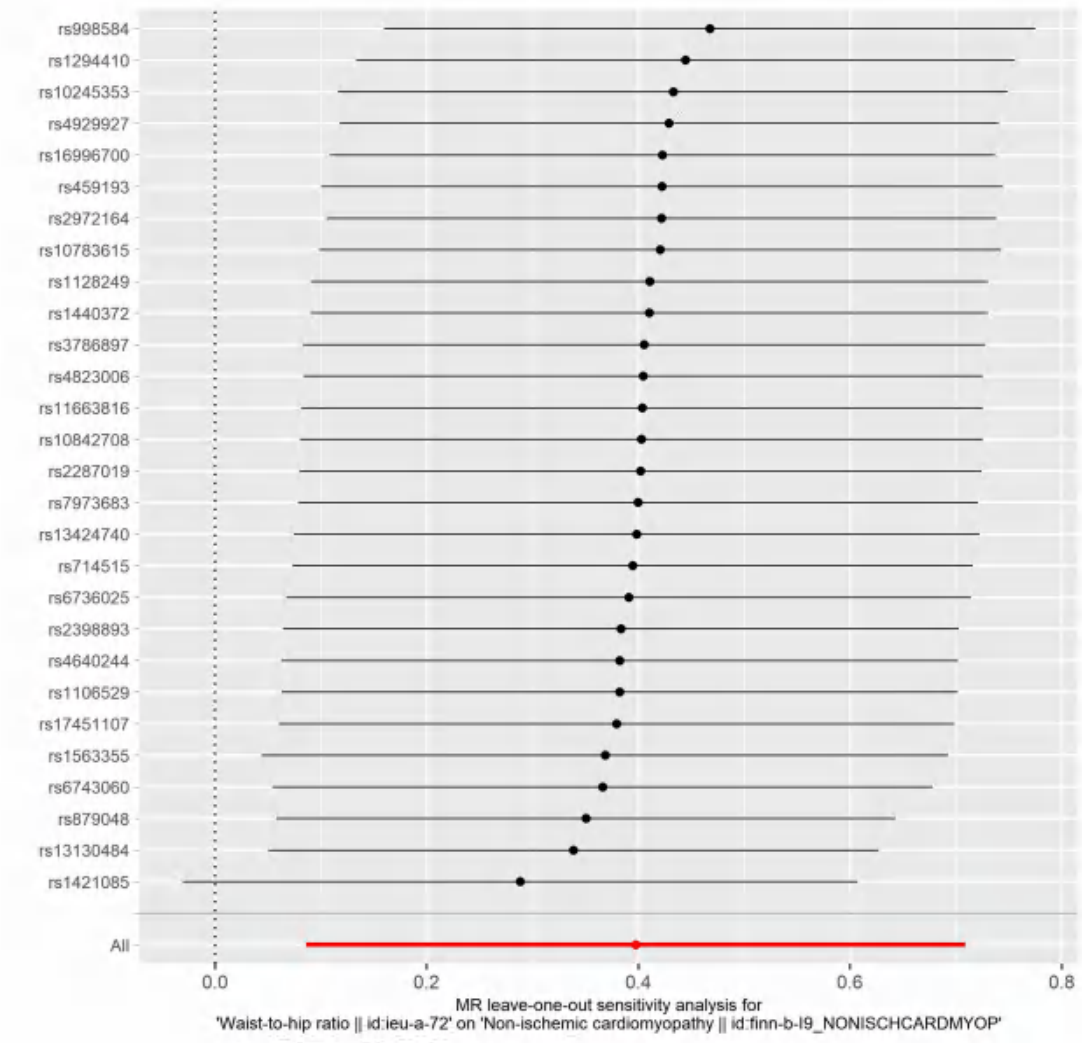
A



B



C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rs1294410
rs10245353
rs4929927
rs16996700
rs459193
rs2972164
rs10783615
rs1128249
rs1440372
rs3786897
rs4823006
rs11663816
rs10842708
rs2287019
rs7973683
rs13424740
rs714515
rs6736025
rs2398893
rs4640244
rs1106529
rs17451107
rs1563355
rs6743060
rs879048
rs13130484
rs1421085
All
0.0
0.2
0.4
0.6
0.8
MR leave-one-out sensitivity analysis for
'Waist-to-hip ratio || id:ieu-a-72' on 'Non-ischemic cardiomyopathy || id:finn-b-I9_NONISCHCARDMYOP'

D

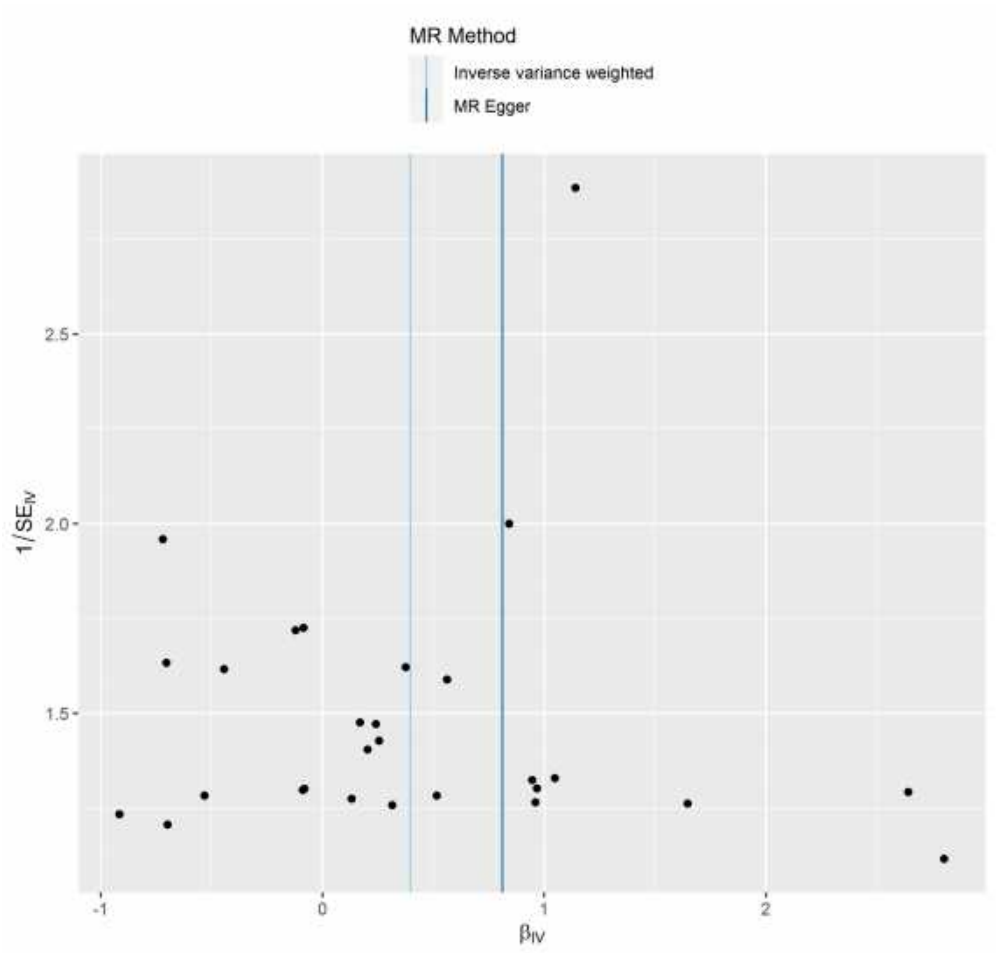
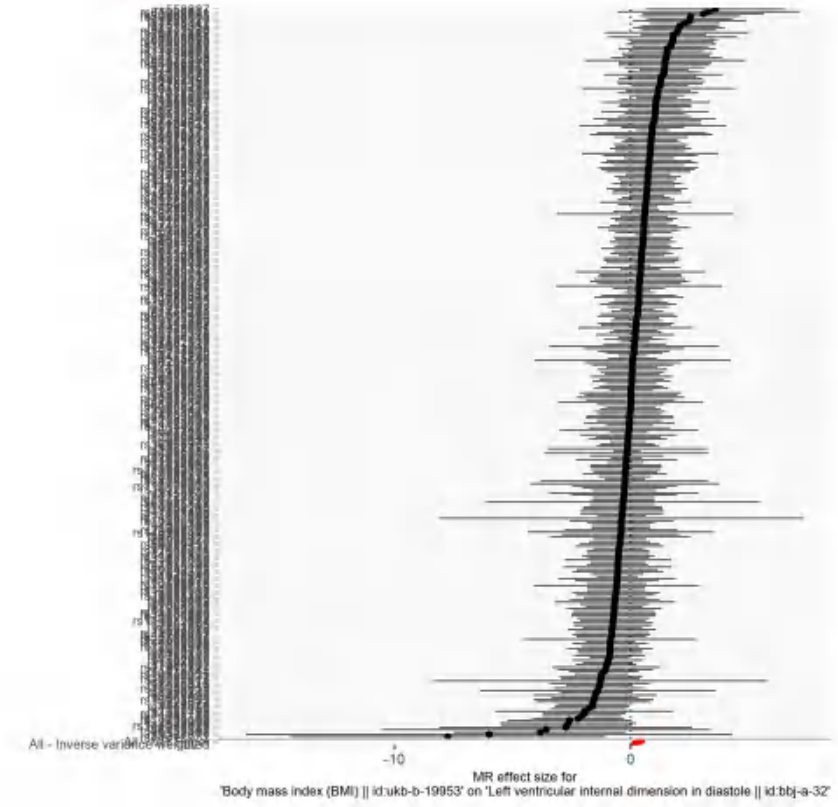
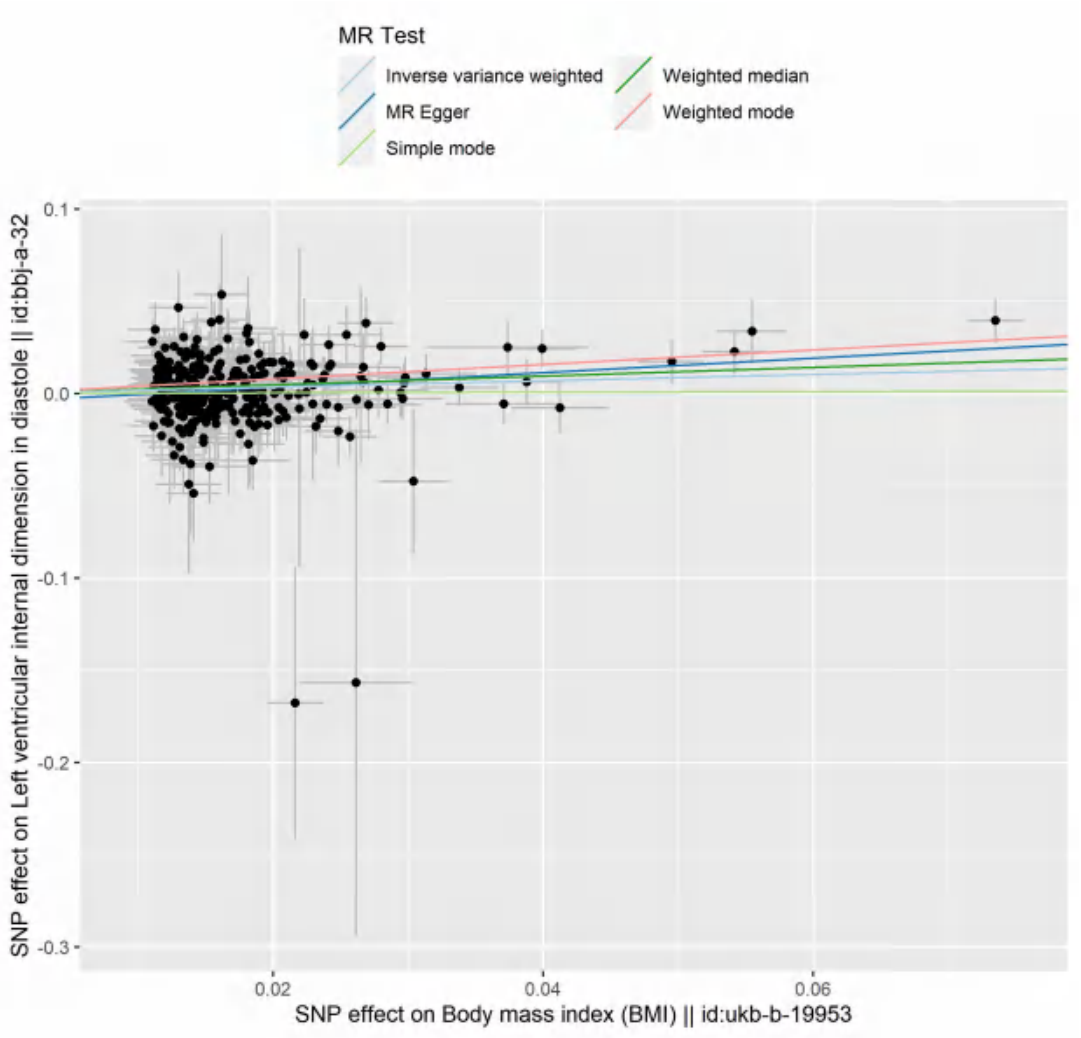

MR Method
Inverse variance weighted
MR Egger
2.5
2.0
1.5
1/SE_IV
-1
0
1
2
β_IV

Figure S18 Visualisation of mendelian randomization for causal associations between BMI and left ventricular internal dimension in diastole. A: Forest plot of MR effect size using MR-Egger and IVW methods; B: Pleiotropy analysis; C:Stability analysis of leave-one-out method; D: funnel plot.

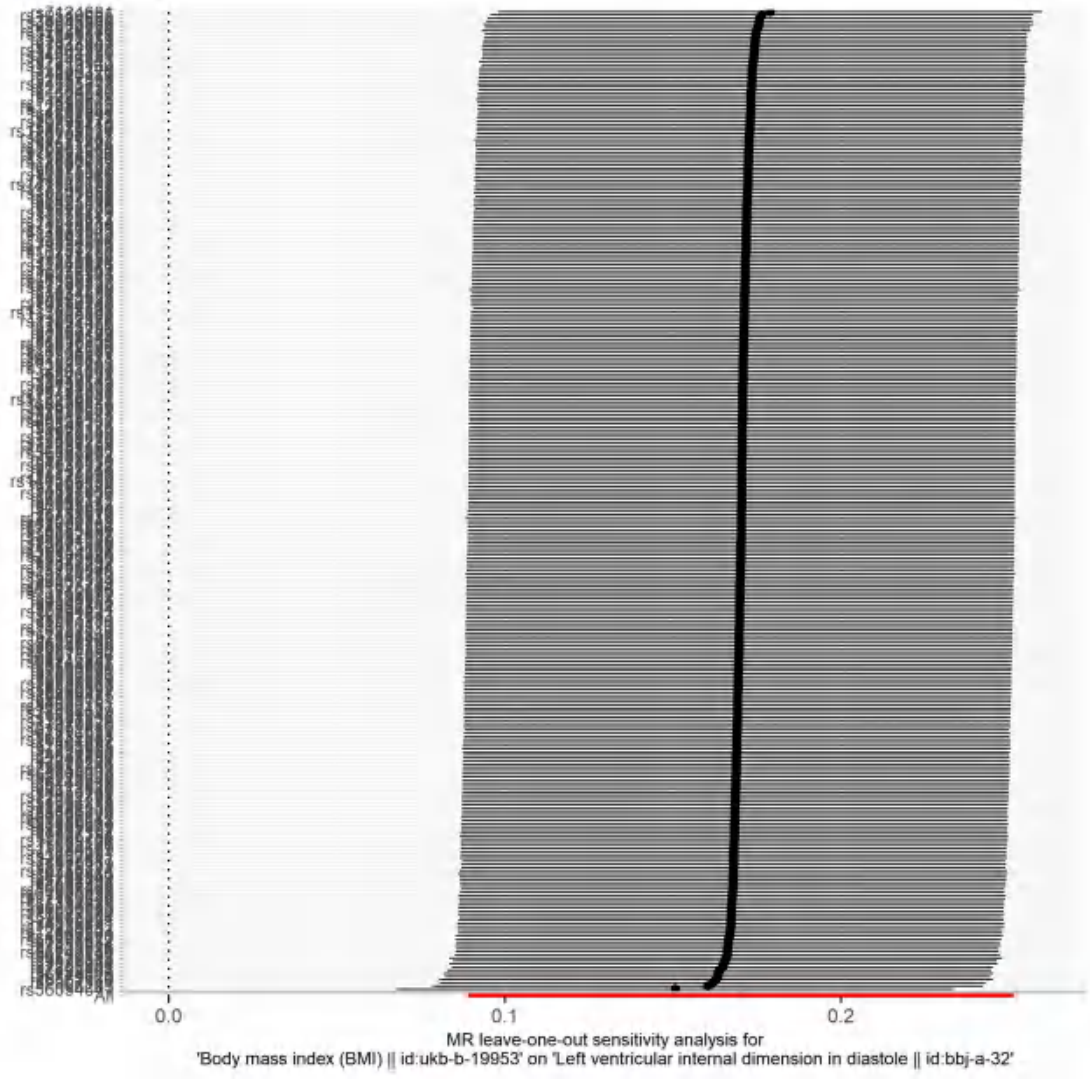
A



B



C


0.0
0.1
0.2
MR leave-one-out sensitivity analysis for
'Body mass index (BMI) || id:ukb-b-19953' on 'Left ventricular internal dimension in diastole || id:bbj-a-32'

D

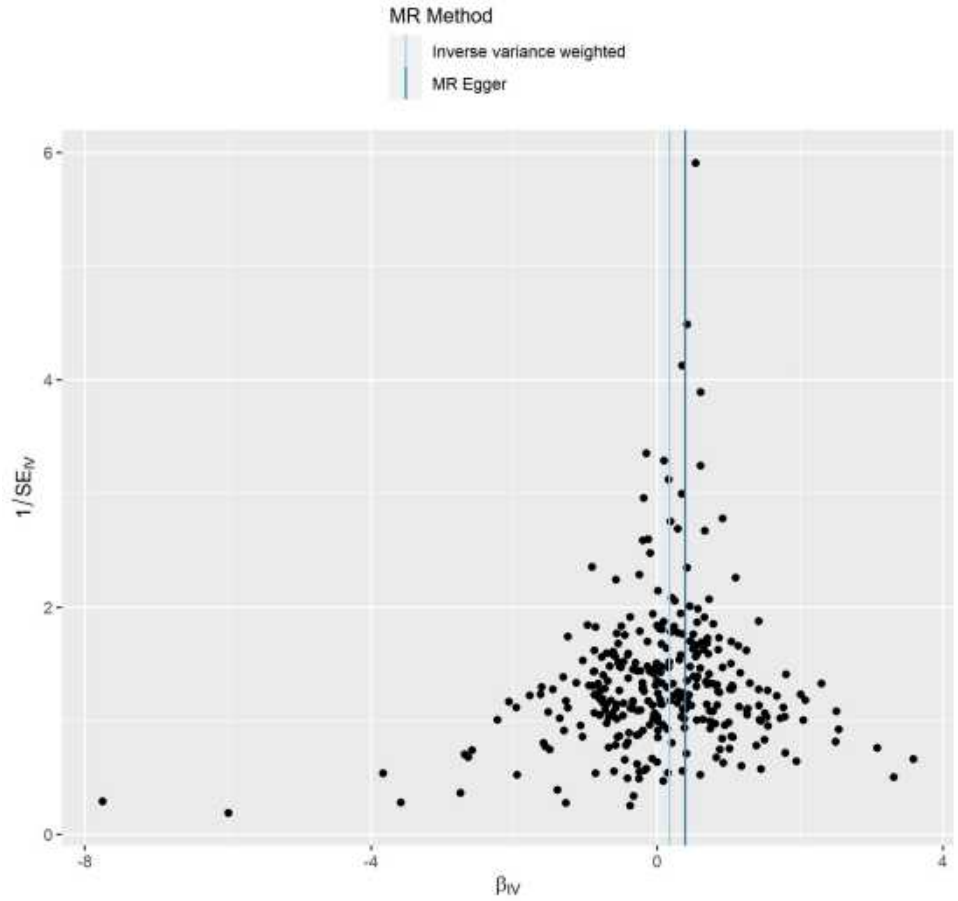
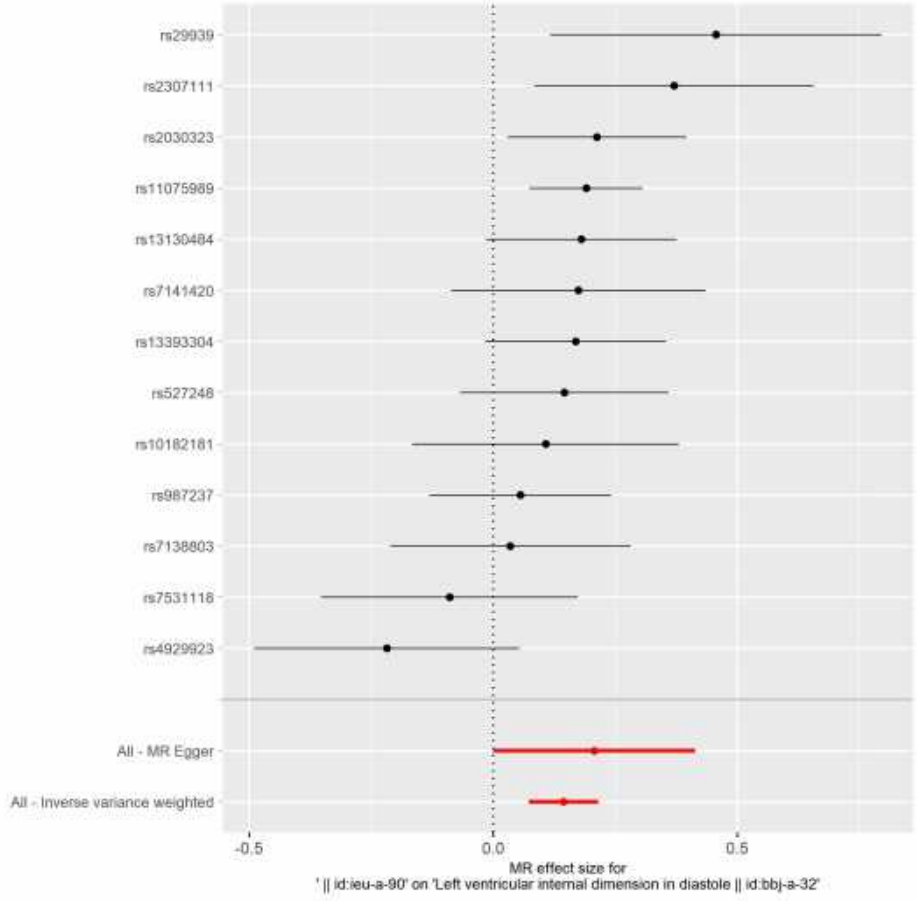
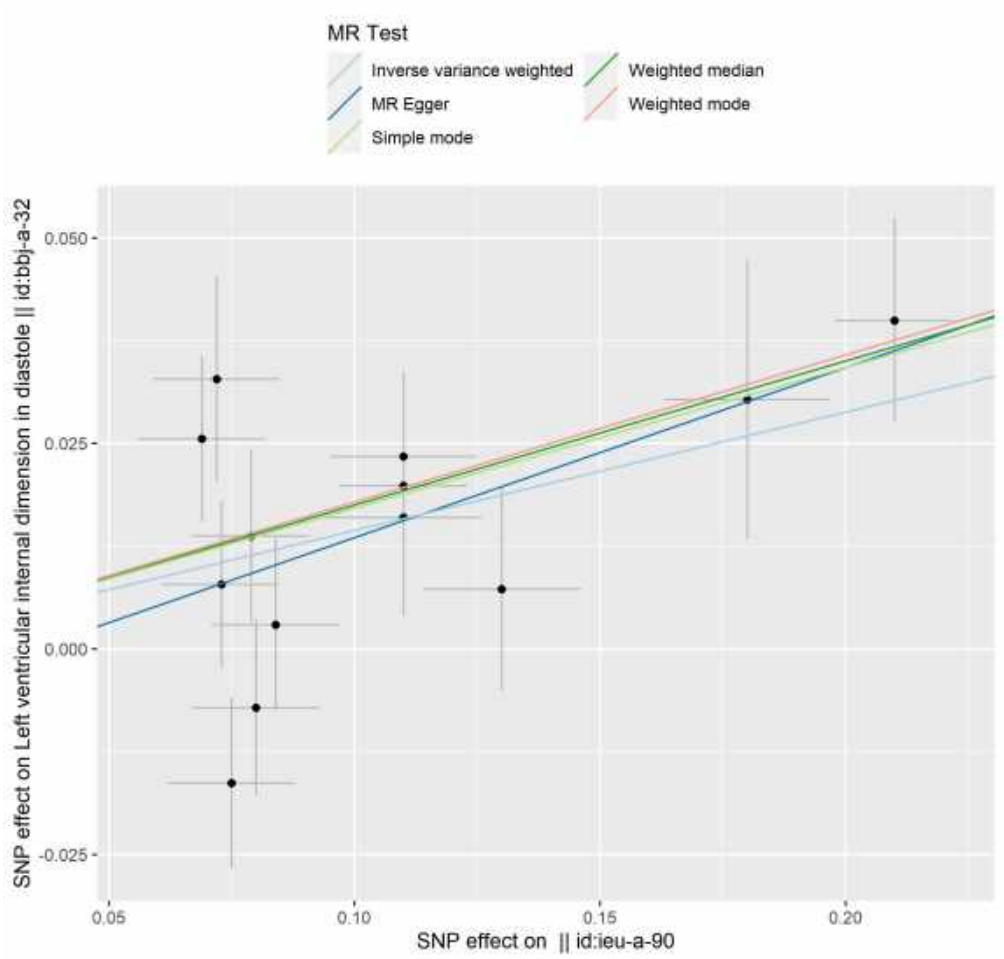

MR Method
Inverse variance weighted
MR Egger
6
4
2
0
1/SE_IV
-8
-4
0
4
β_IV

Figure S19. Visualisation of mendelian randomization for causal associations between obesity class 1 and left ventricular internal dimension in diastole. A: Forest plot of MR effect size using MR-Egger and IVW methods; B: Pleiotropy analysis; C: Stability analysis of leave-one-out method; D: funnel plot.

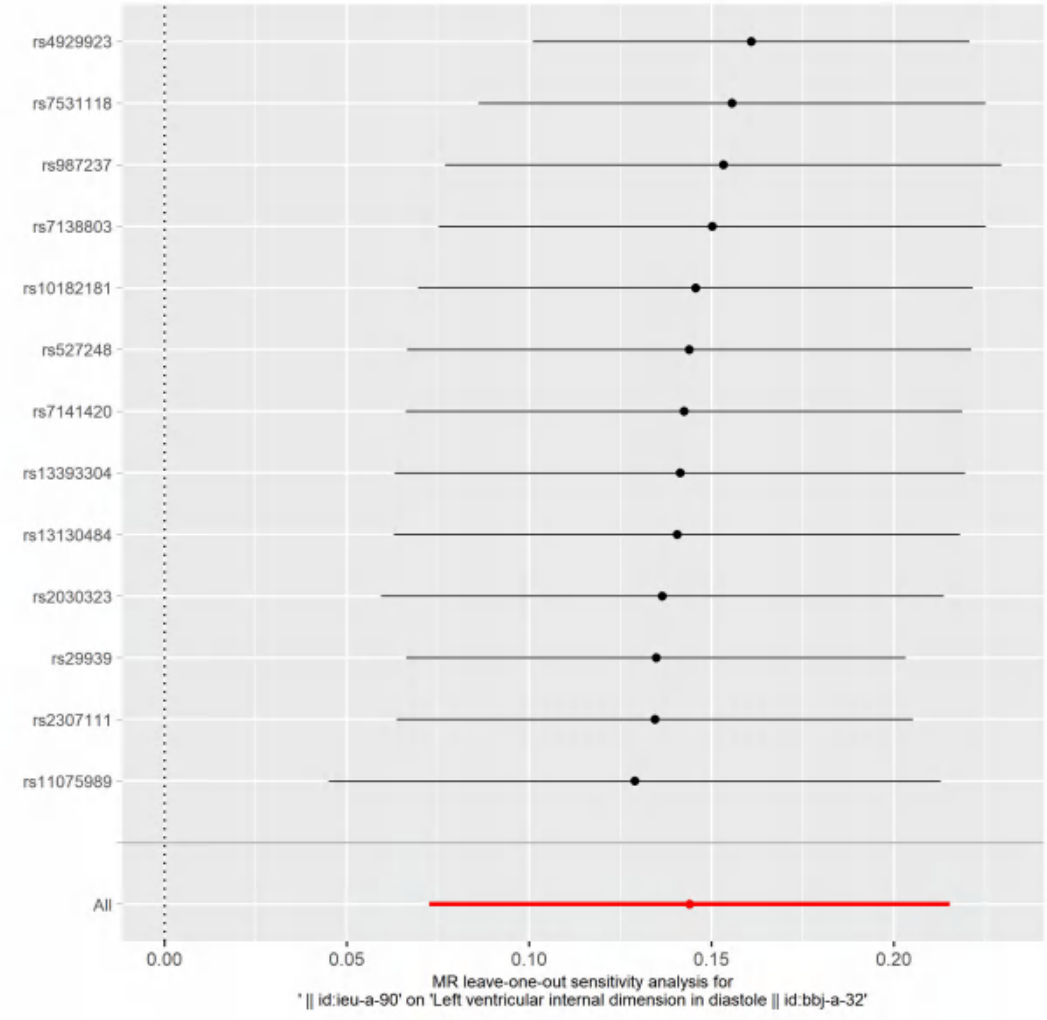
A



B



C


rs4929923
rs7531118
rs987237
rs7138803
rs10182181
rs527248
rs7141420
rs13393304
rs13130484
rs2030323
rs29939
rs2307111
rs11075989
All
0.00
0.05
0.10
0.15
0.20
MR leave-one-out sensitivity analysis for
' || id:ieu-a-90' on 'Left ventricular internal dimension in diastole || id:bbj-a-32'

D

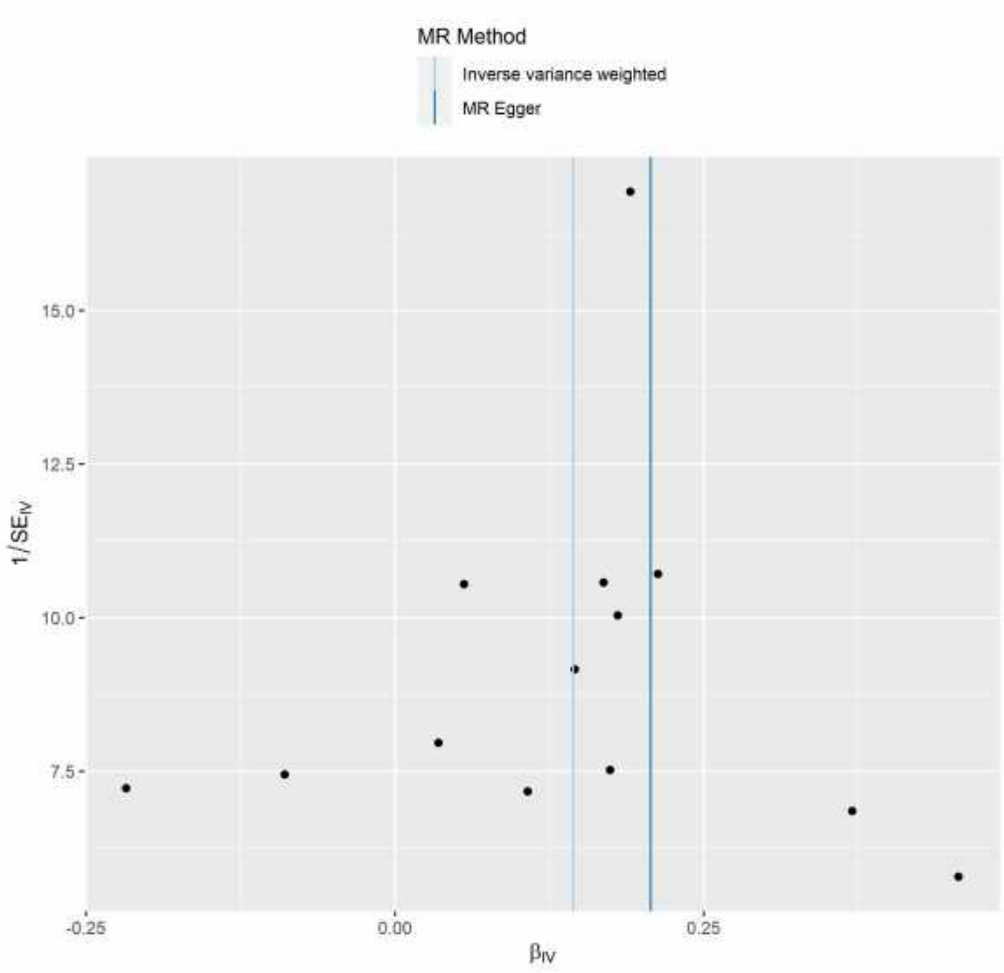
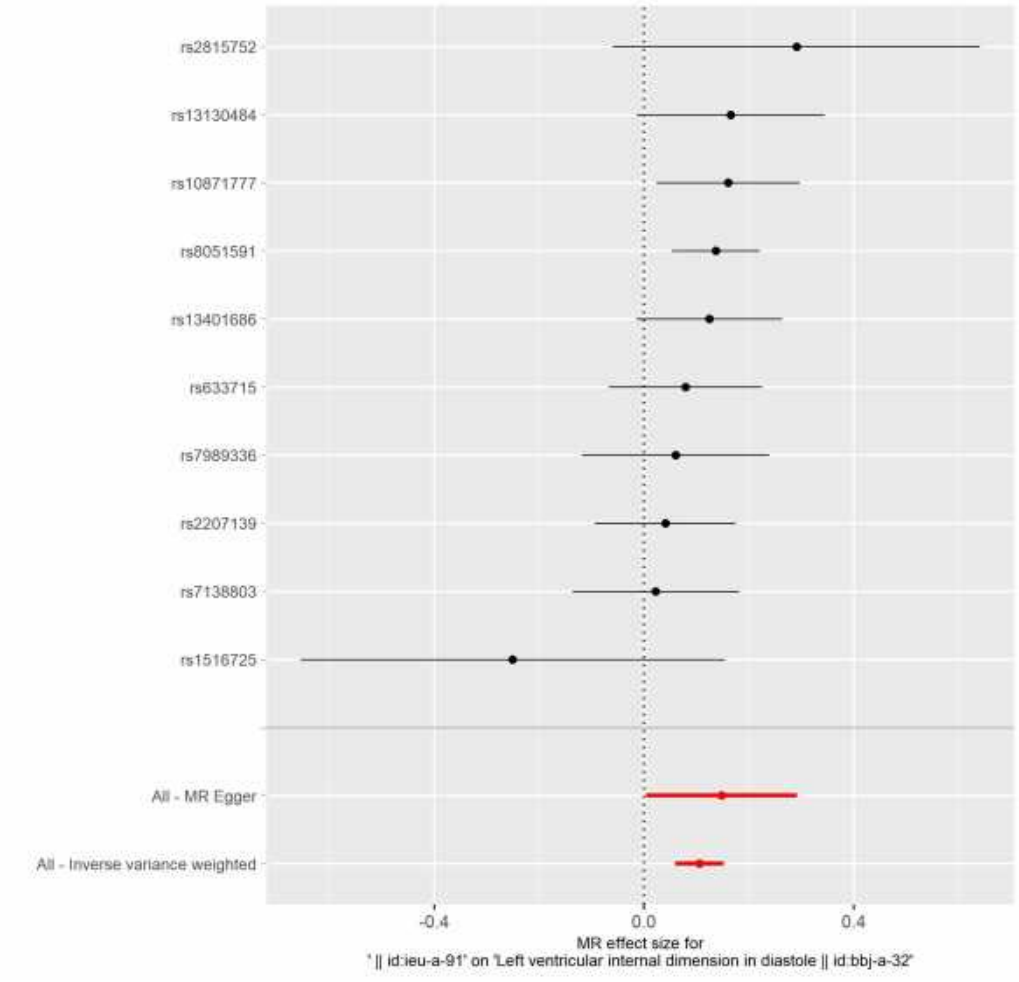
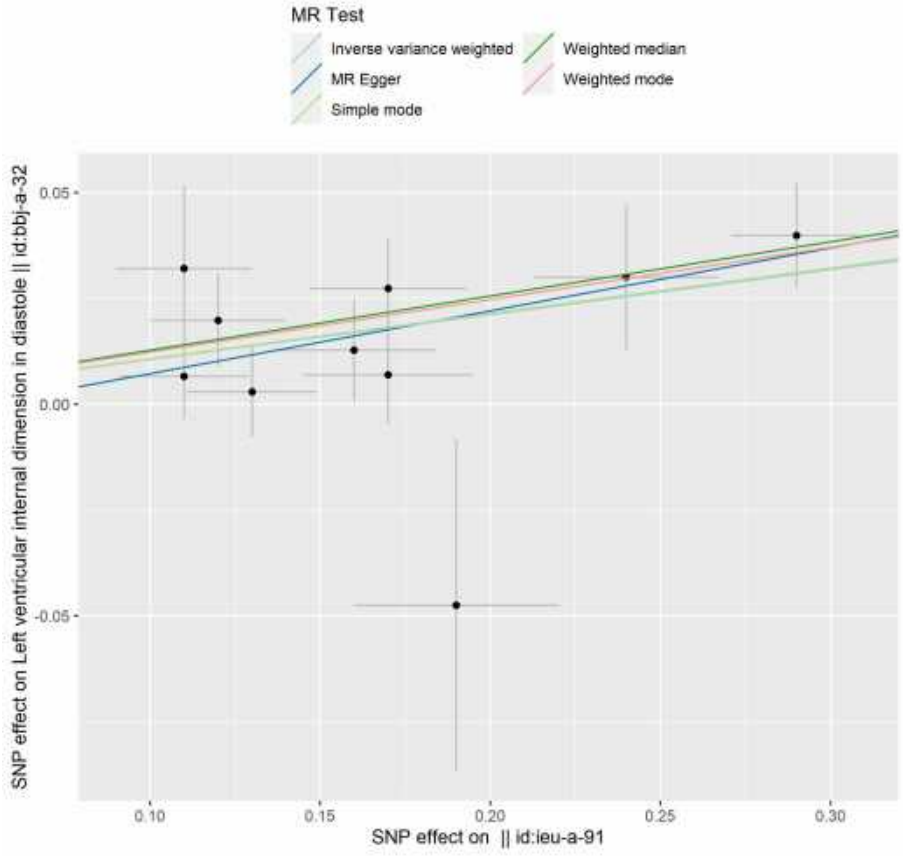

MR Method
Inverse variance weighted
MR Egger
15.0
12.5
10.0
7.5
1/SE_IV
-0.25
0.00
0.25
β_IV

Figure S20. Visualisation of mendelian randomization for causal associations between obesity class 2 and left ventricular internal dimension in diastole. A: Forest plot of MR effect size using MR-Egger and IVW methods; B: Pleiotropy analysis ;C: Stability analysis of leave-one-out method; D: funnel plot.

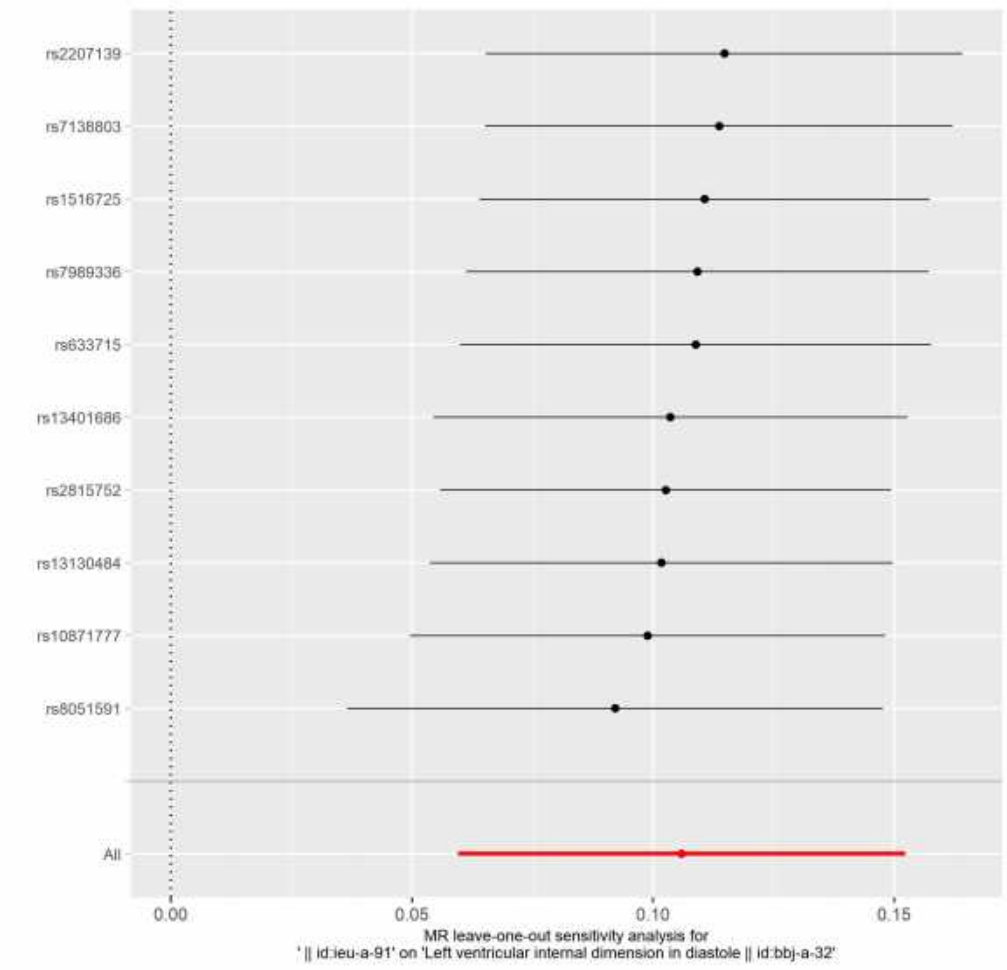
A



B



C


rs2207139
rs7138803
rs1516725
rs7989336
rs633715
rs13401686
rs2815752
rs13130484
rs10871777
rs8051591
All
0.00
0.05
0.10
0.15
MR leave-one-out sensitivity analysis for
' || id:ieu-a-91' on 'Left ventricular internal dimension in diastole || id:bbj-a-32'

D

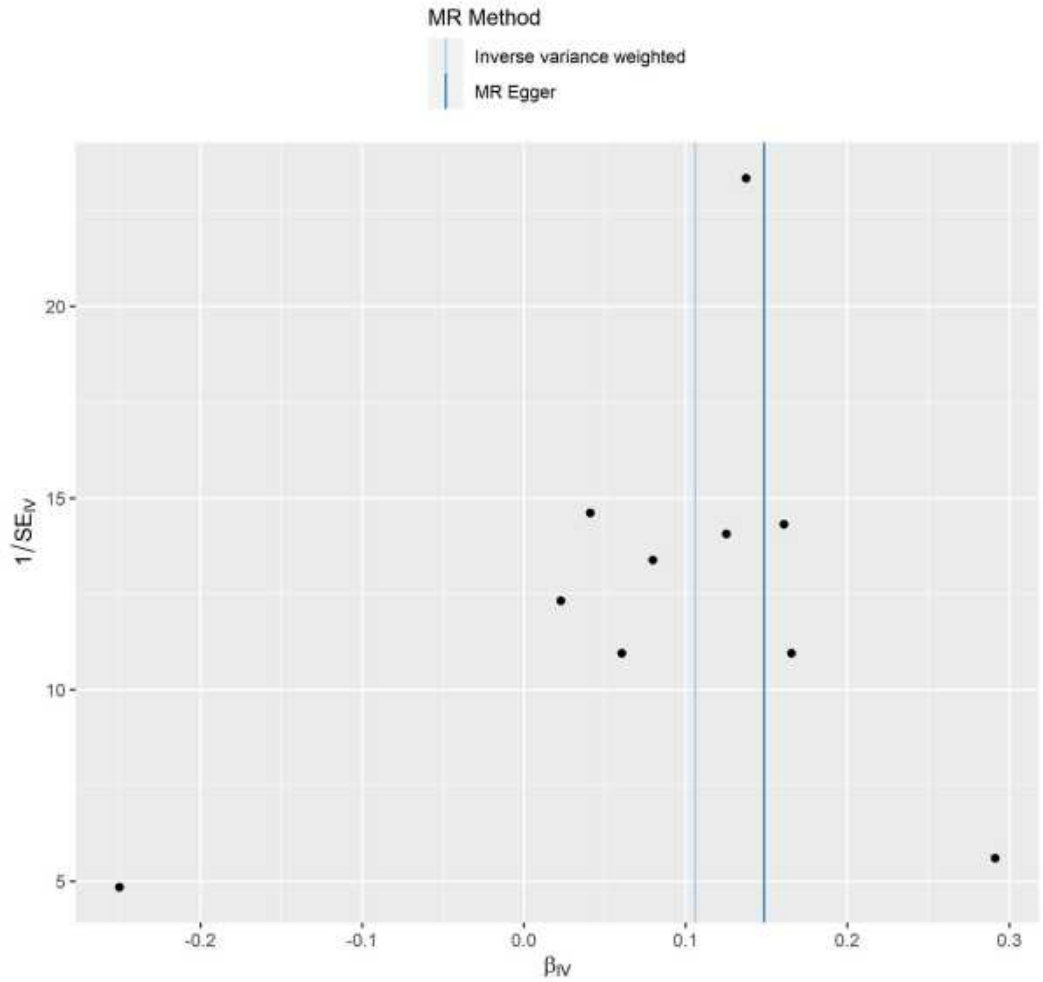
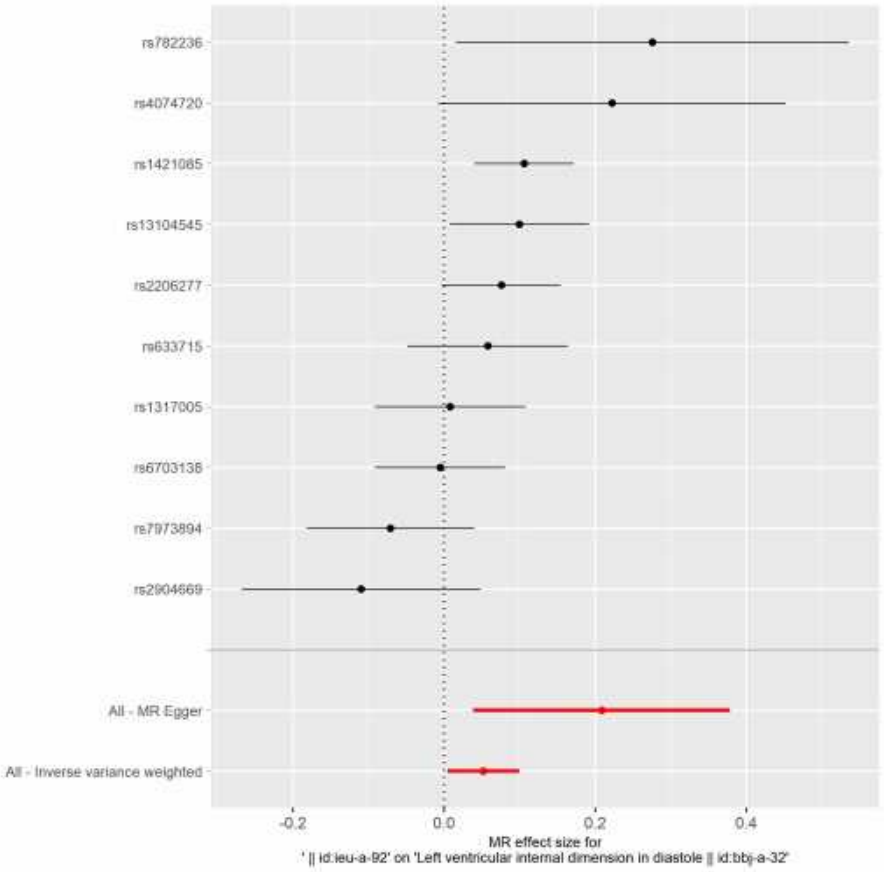
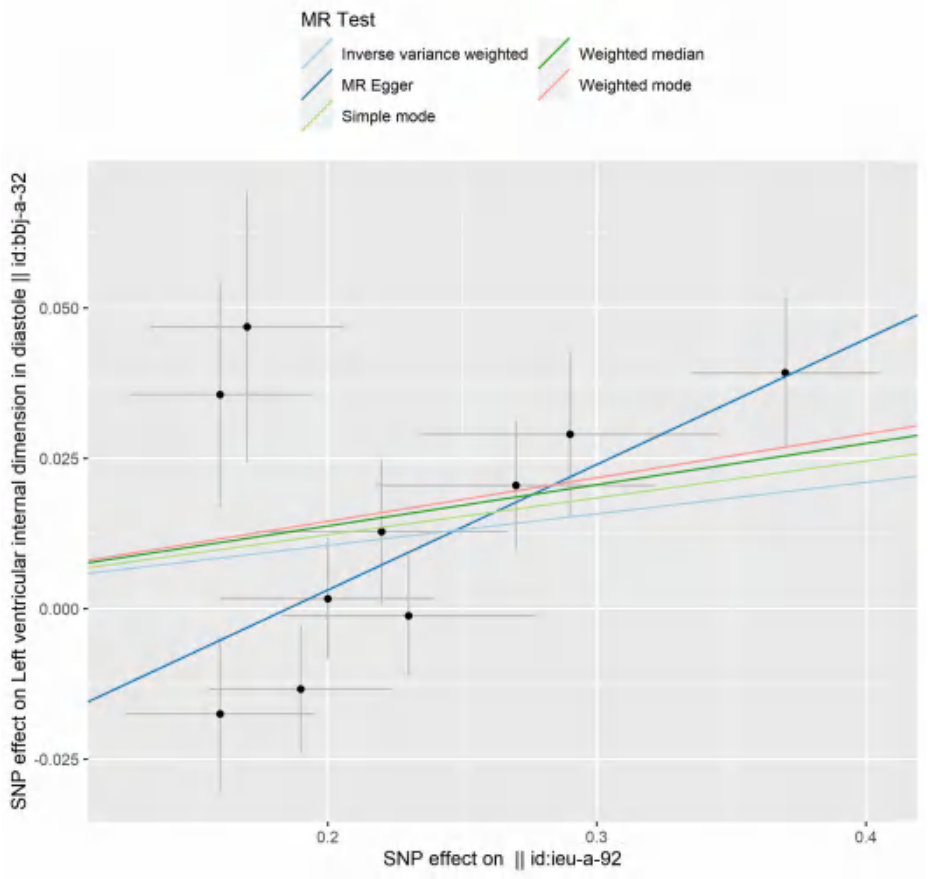

MR Method
Inverse variance weighted
MR Egger
20
15
10
5
1/SE_IV
-0.2
-0.1
0.0
0.1
0.2
0.3
β_IV

Figure S21. Visualisation of mendelian randomization for causal associations between obesity class 3 and left ventricular internal dimension in diastole. A: Forest plot of MR effect size using MR-Egger and IVW methods; B: Pleiotropy analysis ;C: Stability analysis of leave-one-out method; D: funnel plot.

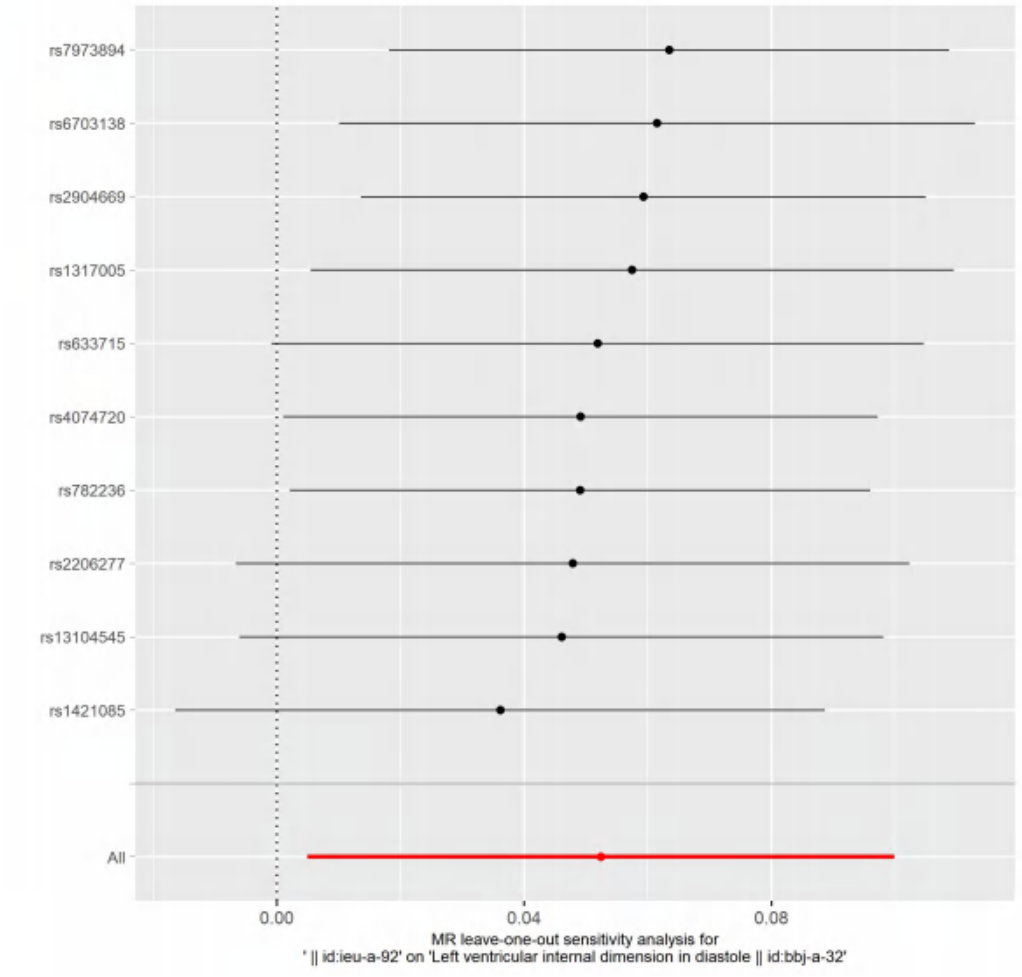
A



B



C


rs7973894
rs6703138
rs2904669
rs1317005
rs633715
rs4074720
rs782236
rs2206277
rs13104545
rs1421085
All
0.00
0.04
0.08
MR leave-one-out sensitivity analysis for
' || id:ieu-a-92' on 'Left ventricular internal dimension in diastole || id:bbj-a-32'

D

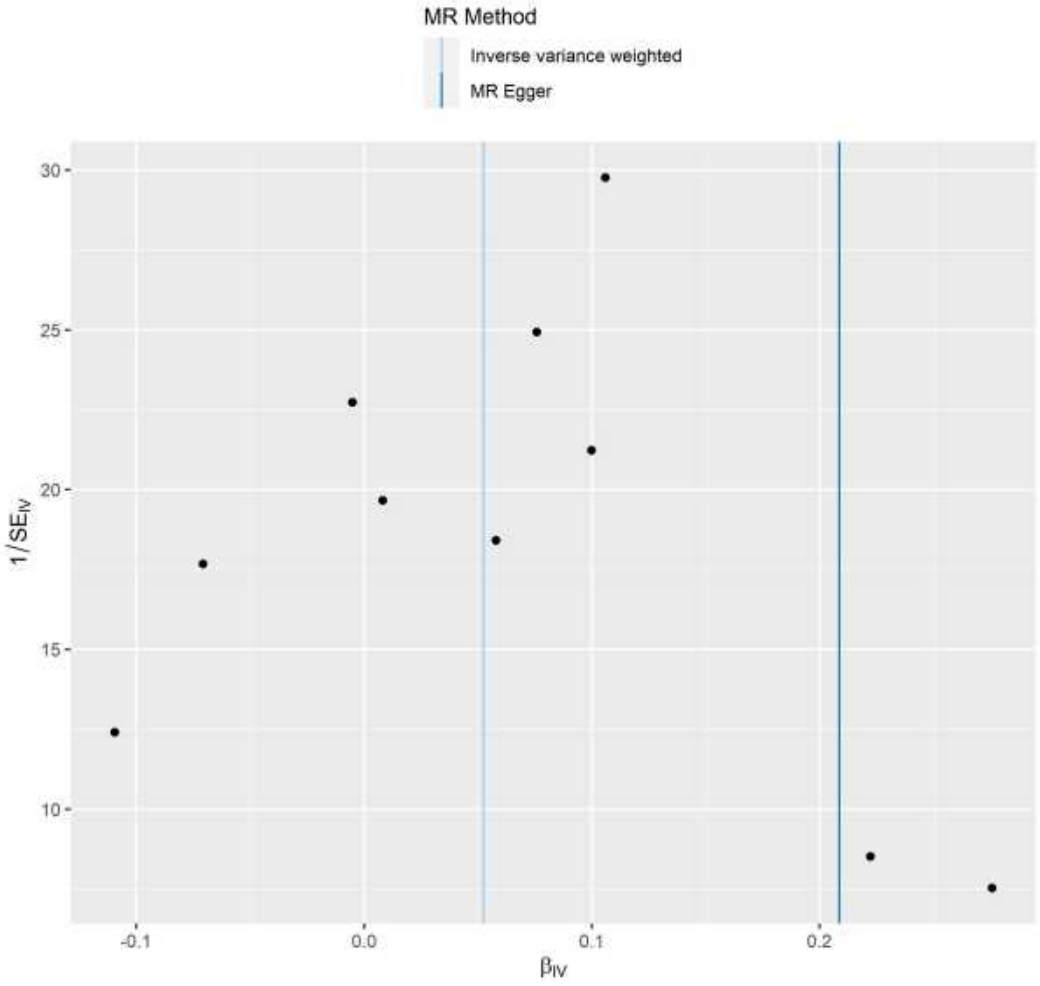
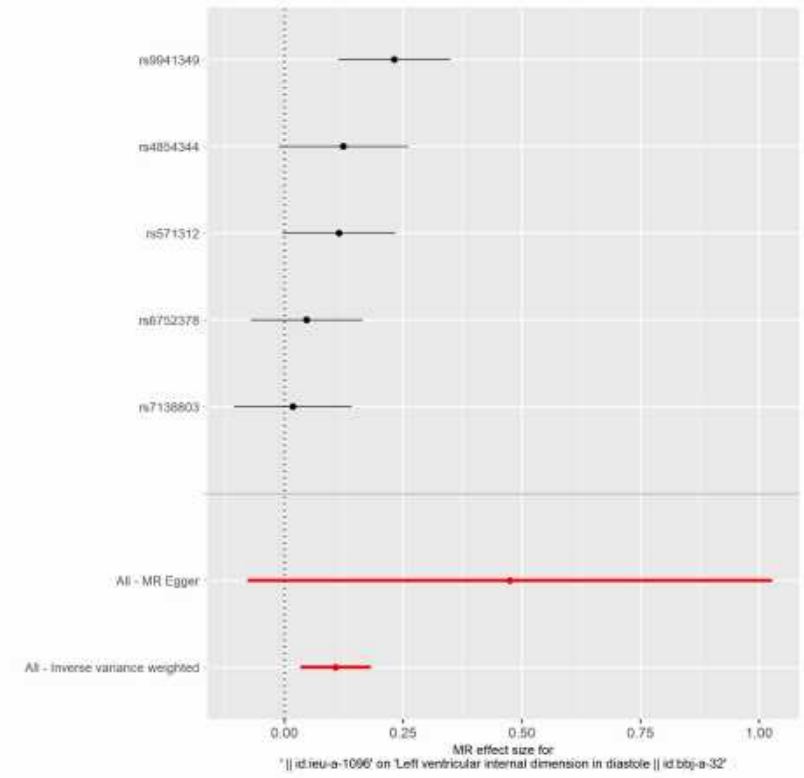
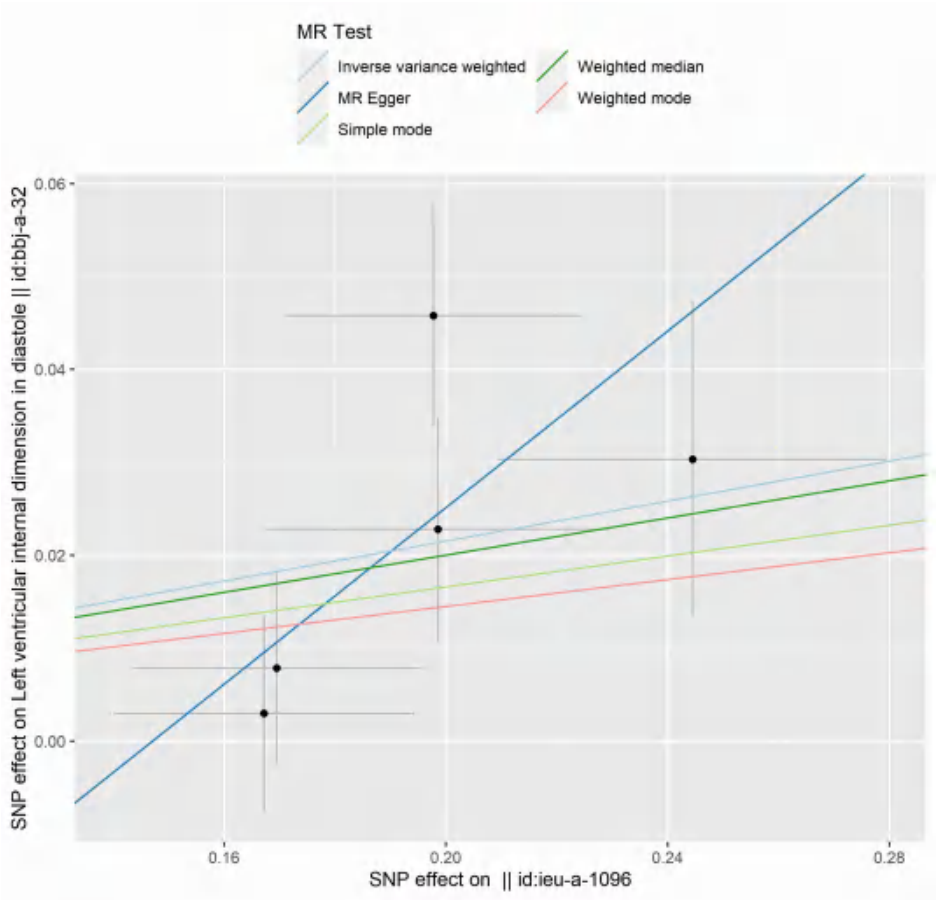

MR Method
Inverse variance weighted
MR Egger
30
25
20
15
10
1/SE_IV
-0.1
0.0
0.1
0.2
β_IV

Figure S22. Visualisation of mendelian randomization for causal associations between childhood obesity and left ventricular internal dimension in diastole. A: Forest plot of MR effect size using MR-Egger and IVW methods; B: Pleiotropy analysis; C: Stability analysis of leave-one-out method; D: funnel plot.

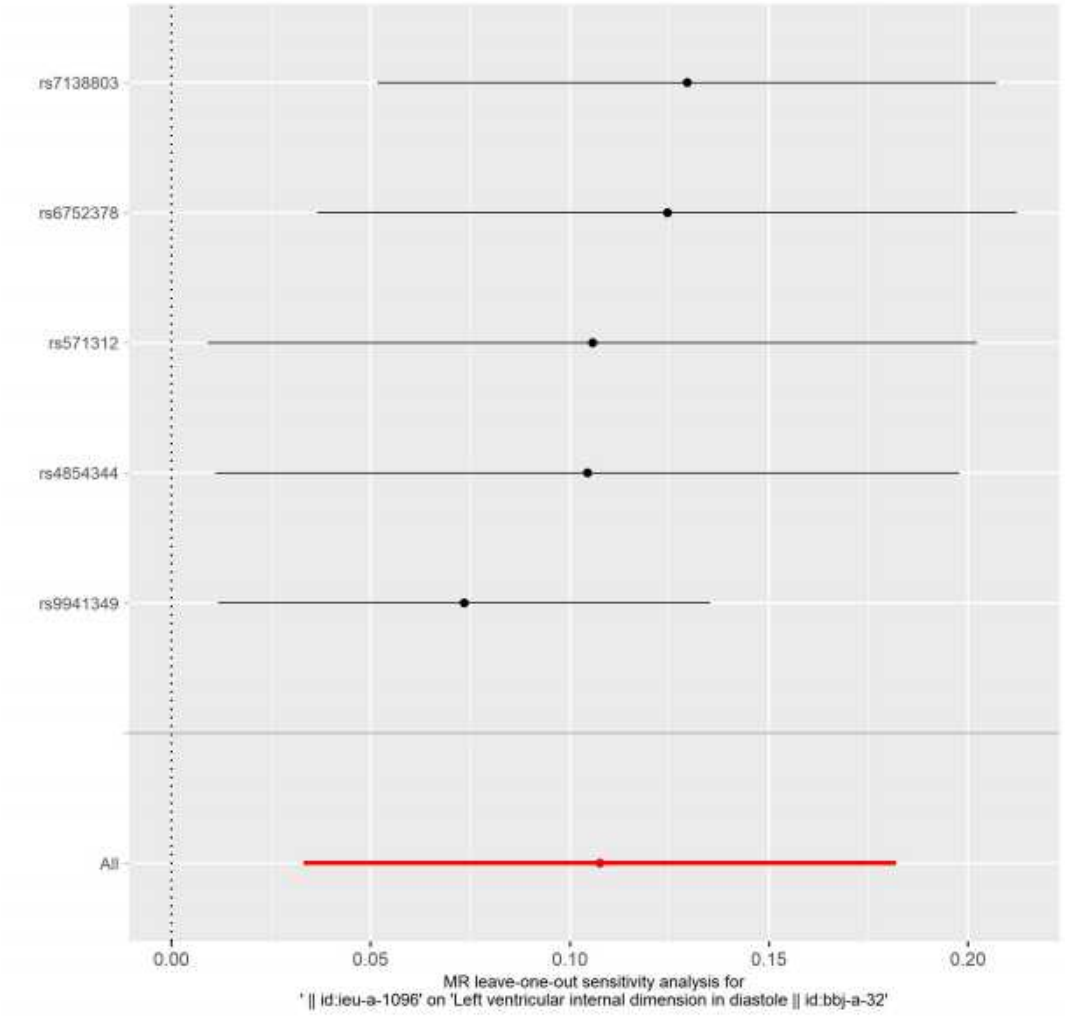
A



B



C


rs7138803
rs6752378
rs571312
rs4854344
rs9941349
All
0.00
0.05
0.10
0.15
0.20
MR leave-one-out sensitivity analysis for
' || id:ieu-a-1096' on 'Left ventricular internal dimension in diastole || id:bbj-a-32'

D

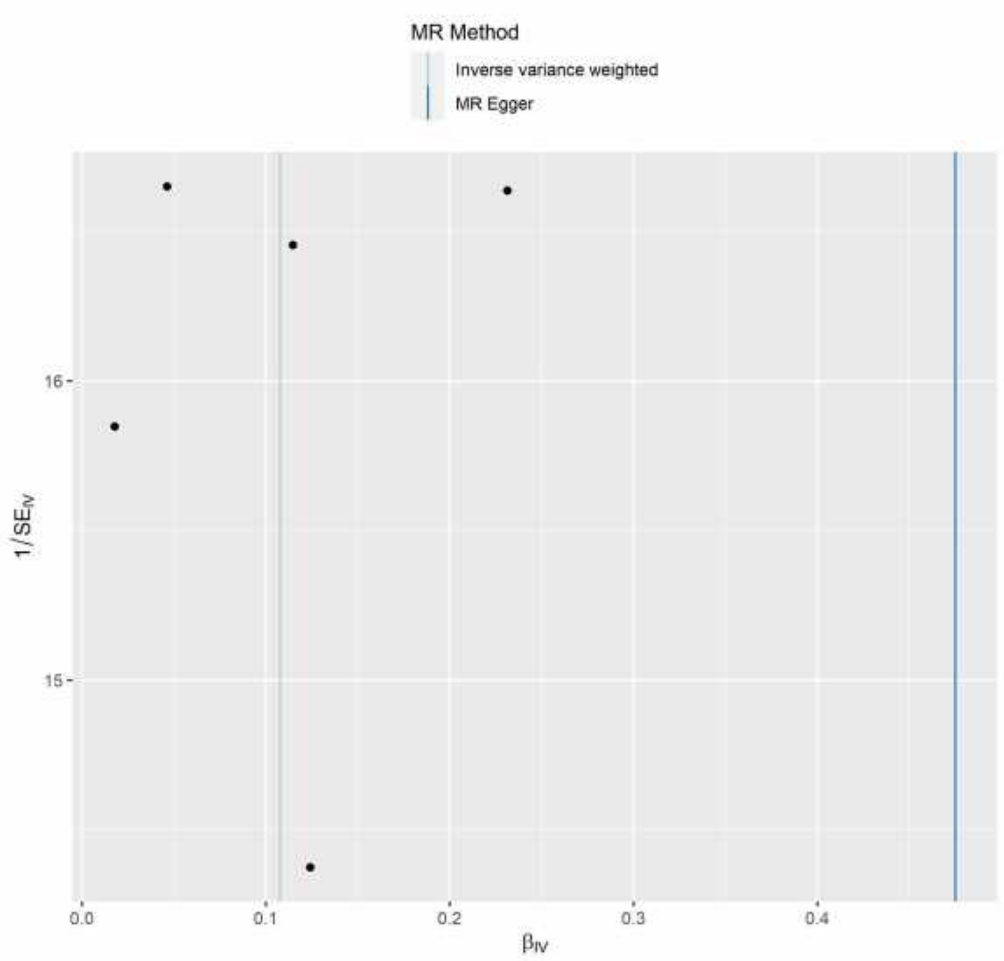
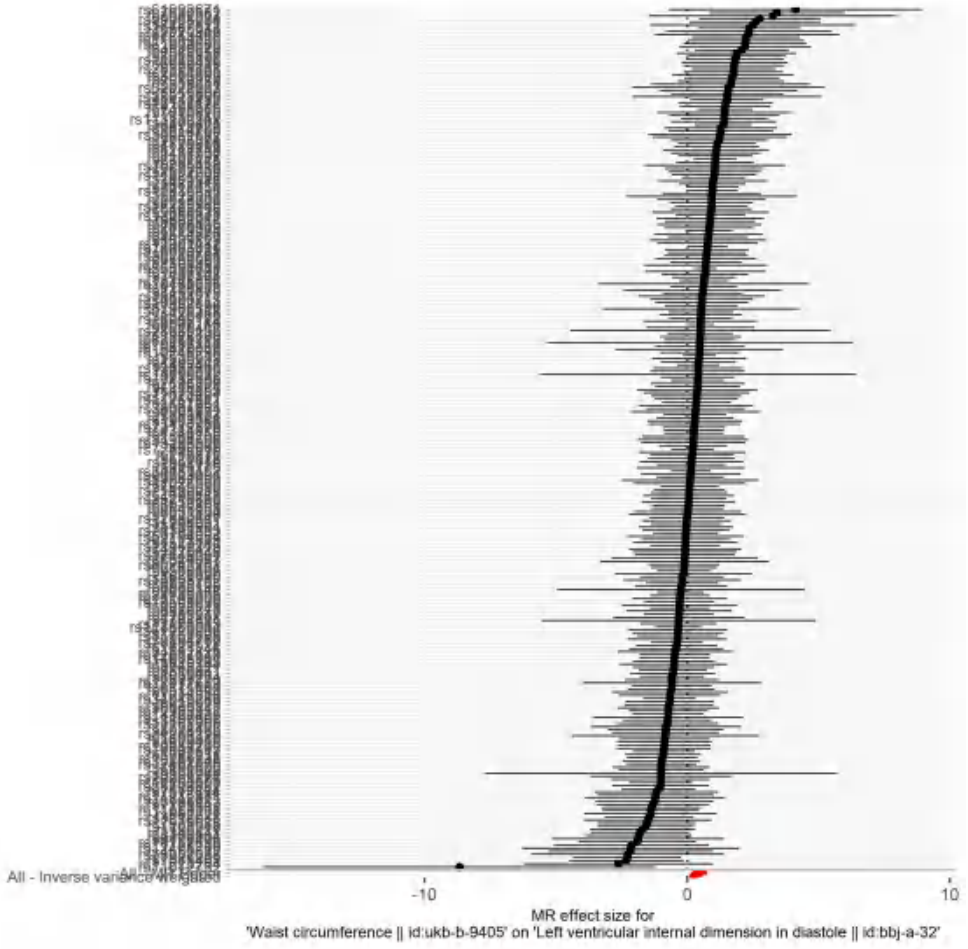
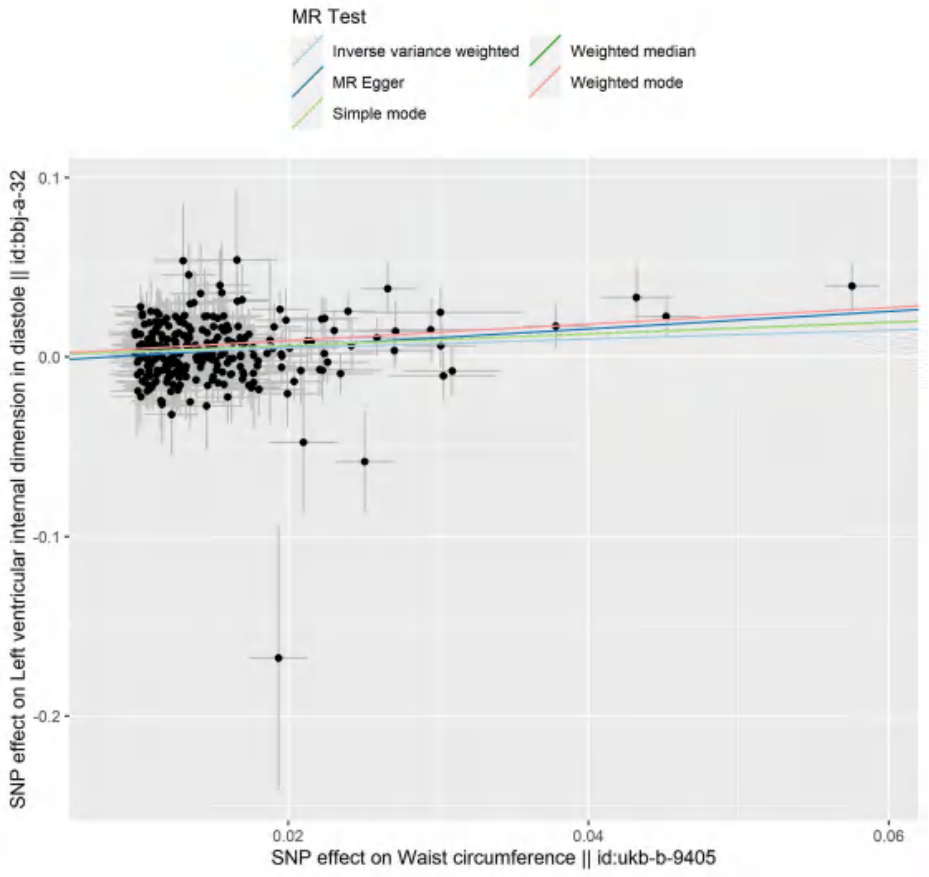

MR Method
Inverse variance weighted
MR Egger
16
15
1/SE_IV
0.0
0.1
0.2
0.3
0.4
β_IV

Figure S23. Visualisation of mendelian randomization for causal associations between waist circumference and left ventricular internal dimension in diastole. A: Forest plot of MR effect size using MR-Egger and IVW methods; B: Pleiotropy analysis; C: Stability analysis of leave-one-out method; D: funnel plot.

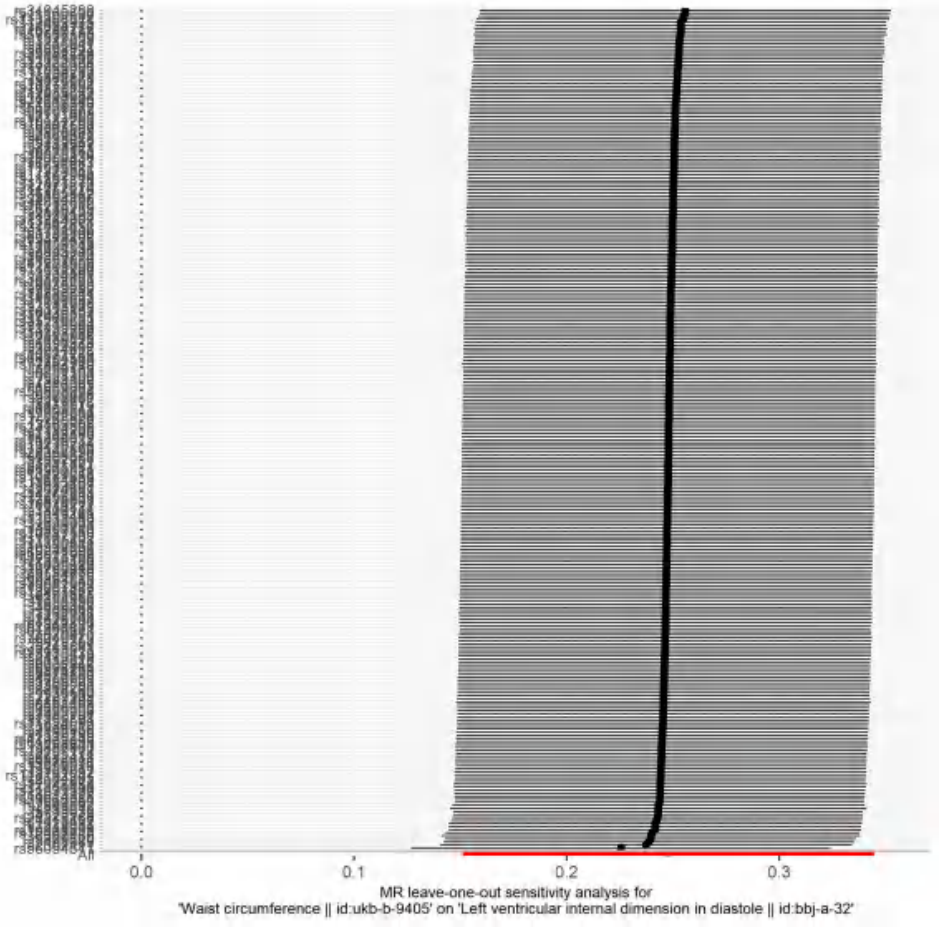
A



B



C


All
0.0
0.1
0.2
0.3
MR leave-one-out sensitivity analysis for
'Waist circumference || id:ukb-b-9405' on 'Left ventricular internal dimension in diastole || id:bbj-a-32'

D

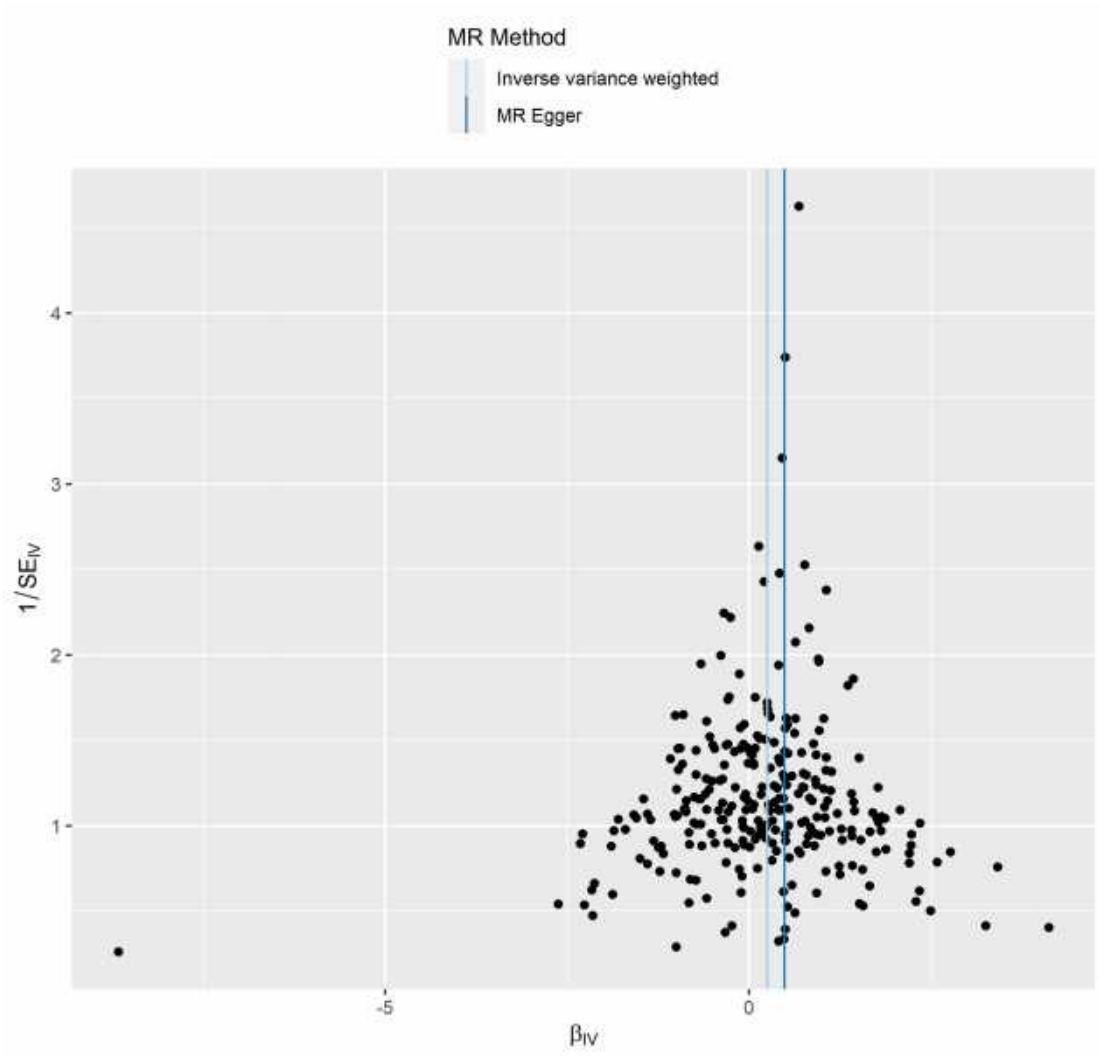
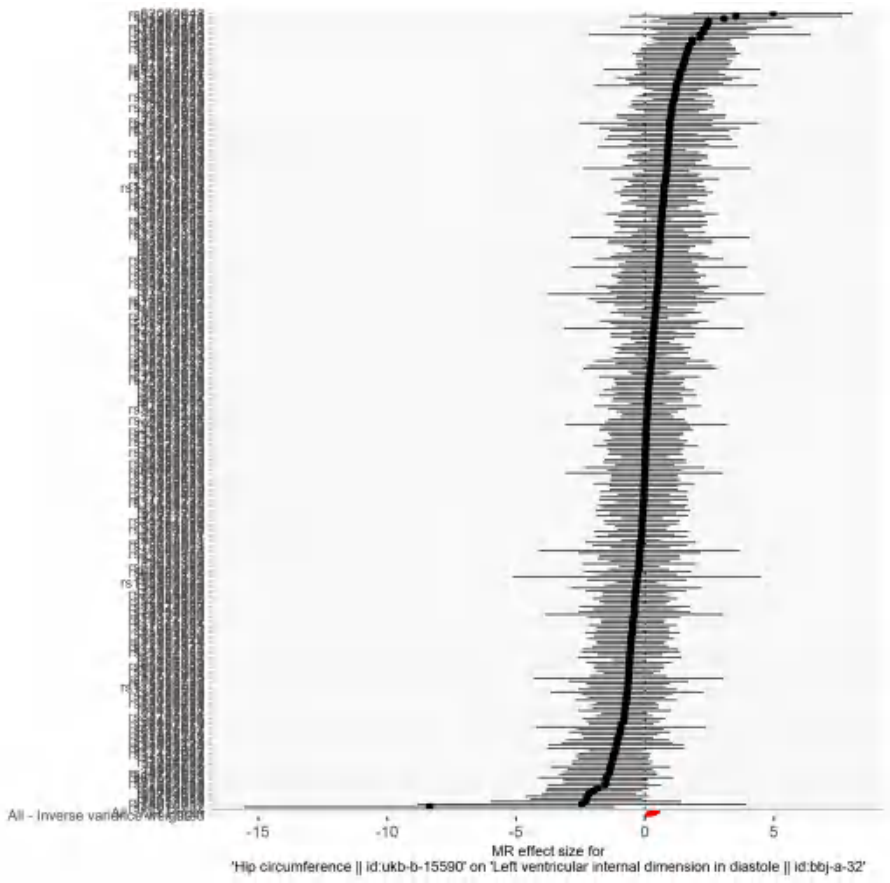
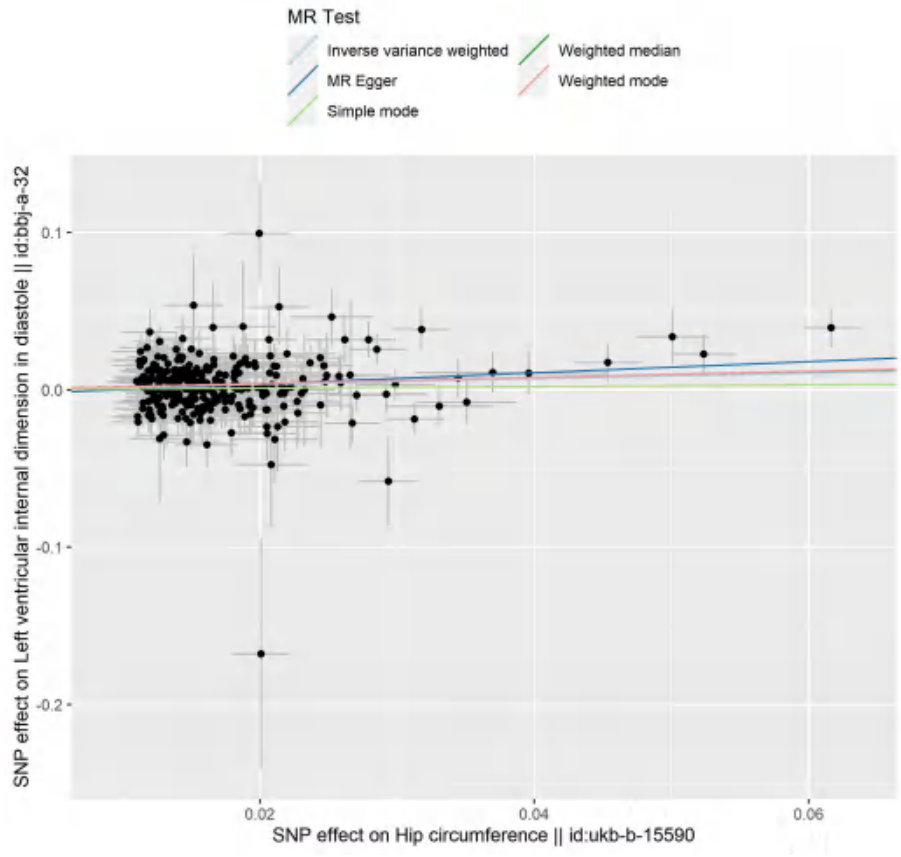

MR Method
Inverse variance weighted
MR Egger
4
3
2
1
1/SE_IV
-5
0
β_IV

Figure S24. Visualisation of mendelian randomization for causal associations between hip circumference and left ventricular internal dimension in diastole. A: Forest plot of MR effect size using MR-Egger and IVW methods; B: Pleiotropy analysis; C: Stability analysis of leave-one-out method; D: funnel plot.

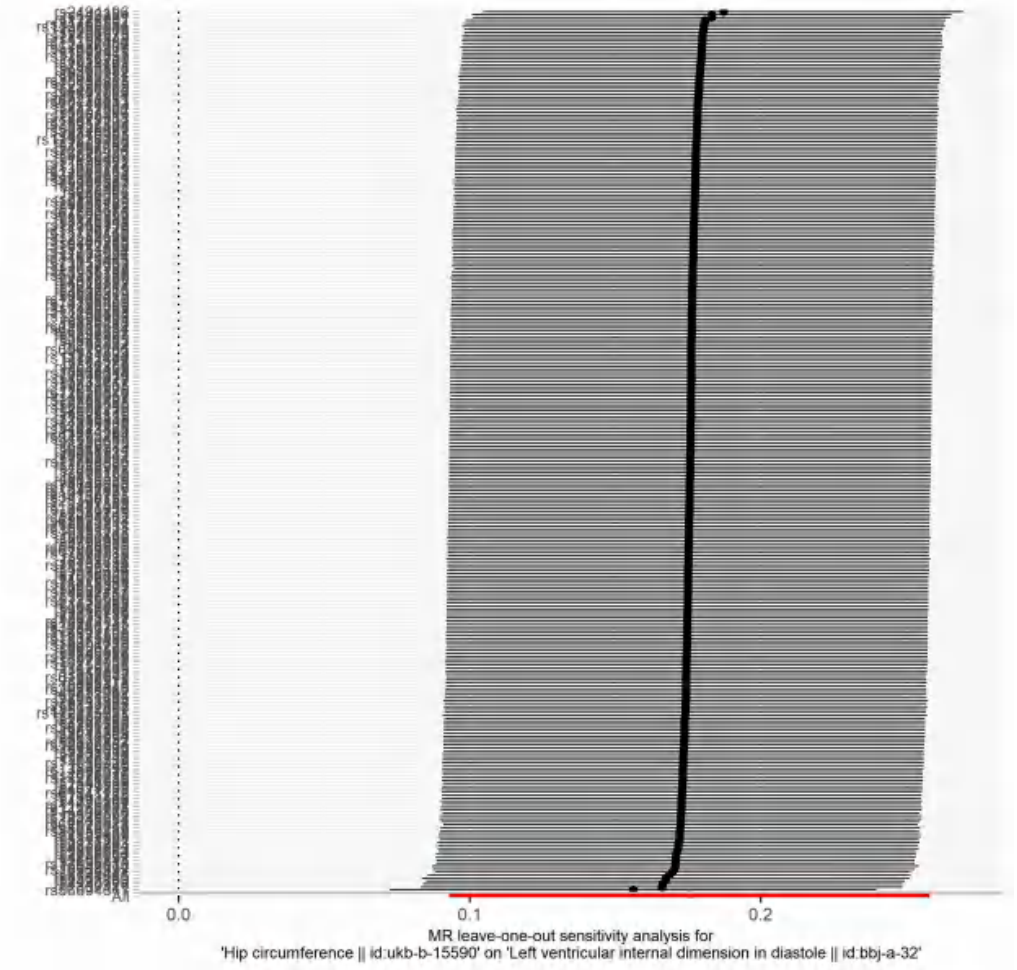
A



B



C


0.0
0.1
0.2
MR leave-one-out sensitivity analysis for
'Hip circumference || id:ukb-b-15590' on 'Left ventricular internal dimension in diastole || id:bbj-a-32'

D

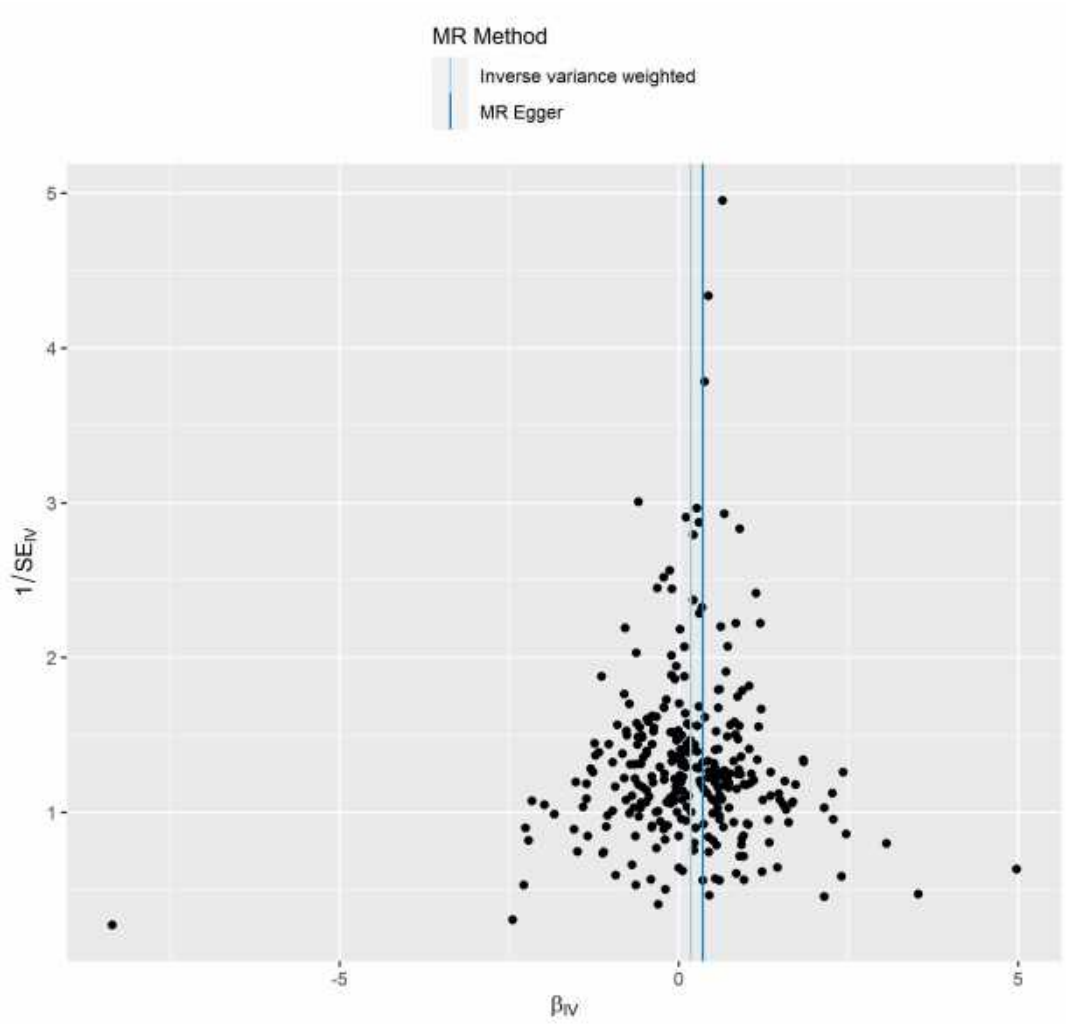
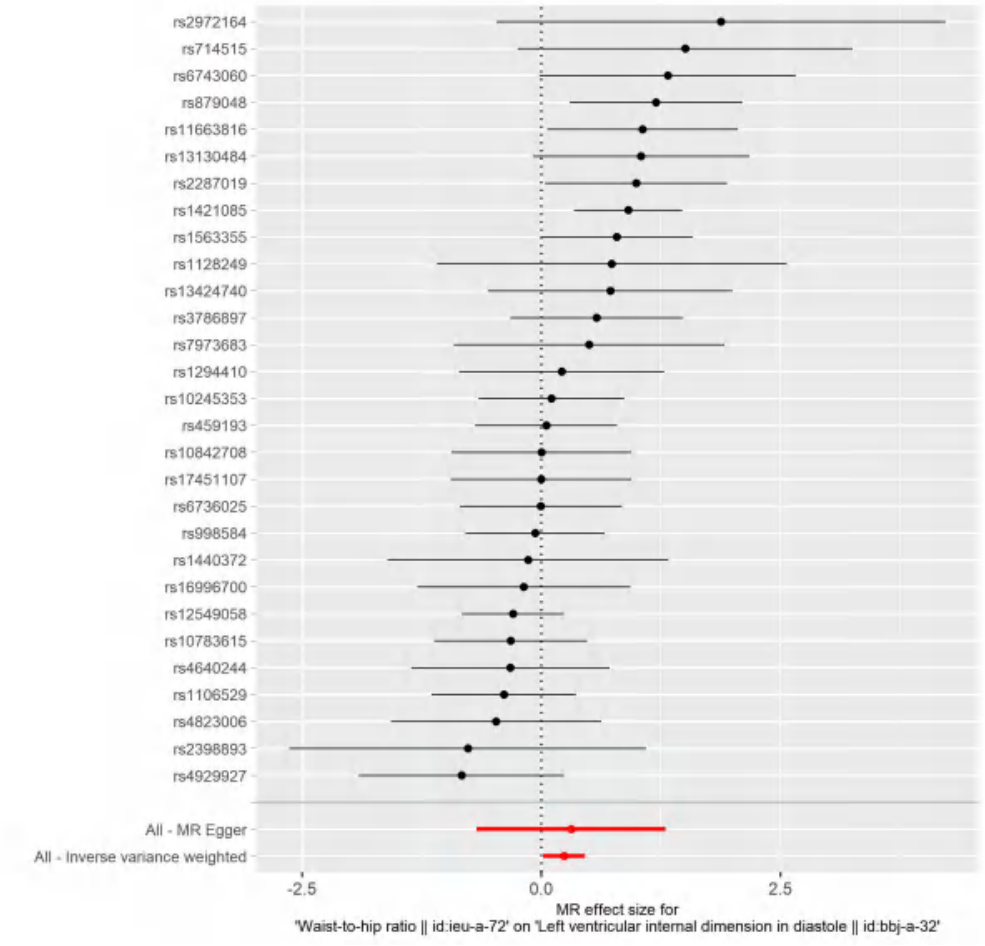
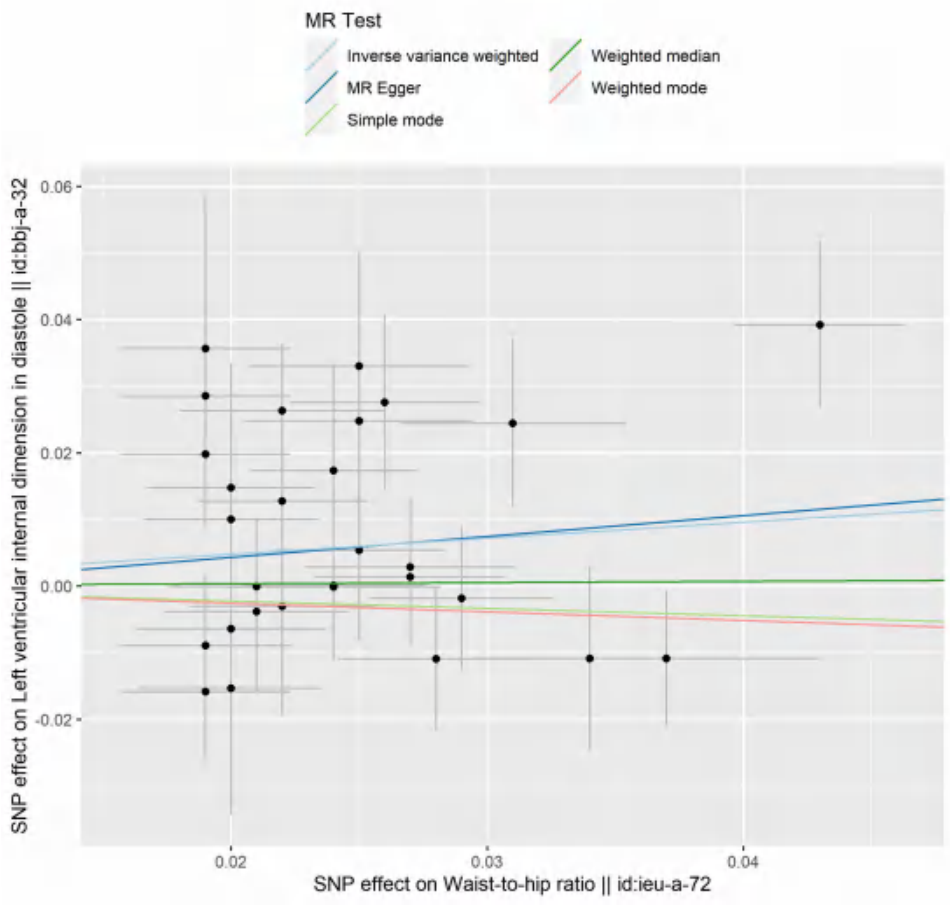

MR Method
Inverse variance weighted
MR Egger
5
4
3
2
1
1/SE_IV
-5
0
5
β_IV

Figure S25. Visualisation of mendelian randomization for causal associations between waist-hip ratio and left ventricular internal dimension in diastole. A: Forest plot of MR effect size using MR-Egger and IVW methods; B: Pleiotropy analysis ;C: Stability analysis of leave-one-out method; D: funnel plot.

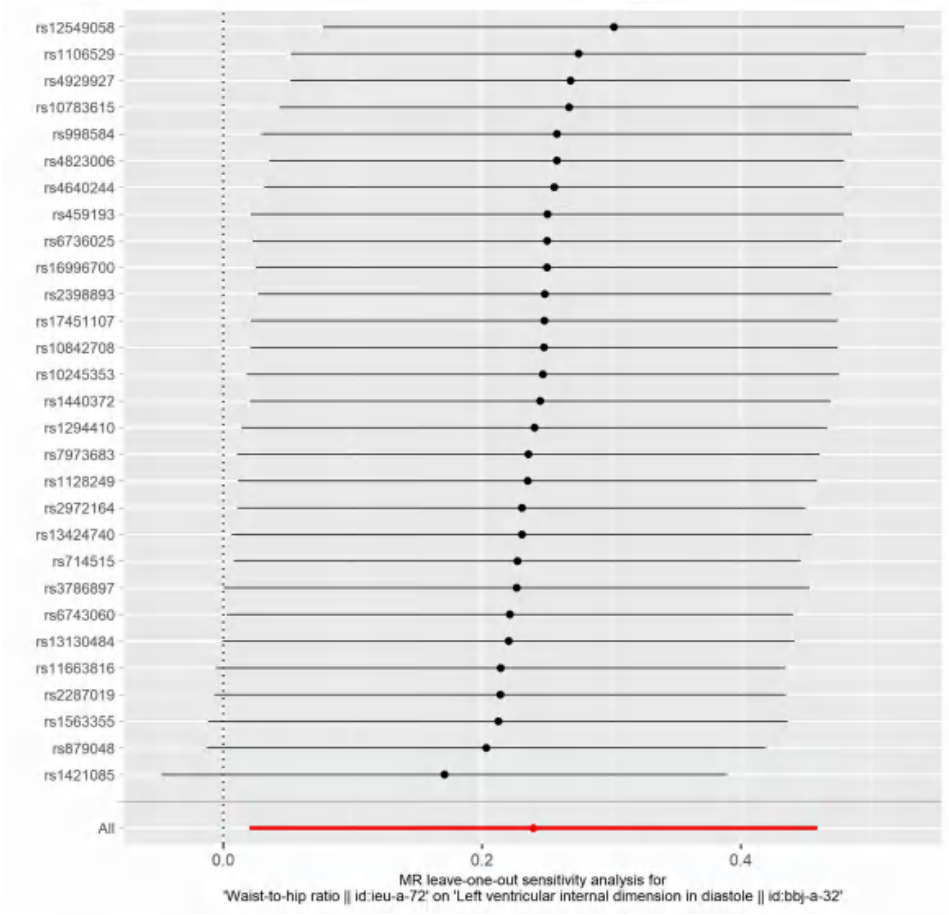
A



B



C


rs12549058
rs1106529
rs4929927
rs10783615
rs998584
rs4823006
rs4640244
rs459193
rs6736025
rs16996700
rs2398893
rs17451107
rs10842708
rs10245353
rs1440372
rs1294410
rs7973683
rs1128249
rs2972164
rs13424740
rs714515
rs3786897
rs6743060
rs13130484
rs11663816
rs2287019
rs1563355
rs879048
rs1421085
All
0.0
0.2
0.4
MR leave-one-out sensitivity analysis for
'Waist-to-hip ratio || id:ieu-a-72' on 'Left ventricular internal dimension in diastole || id:bbj-a-32'

D

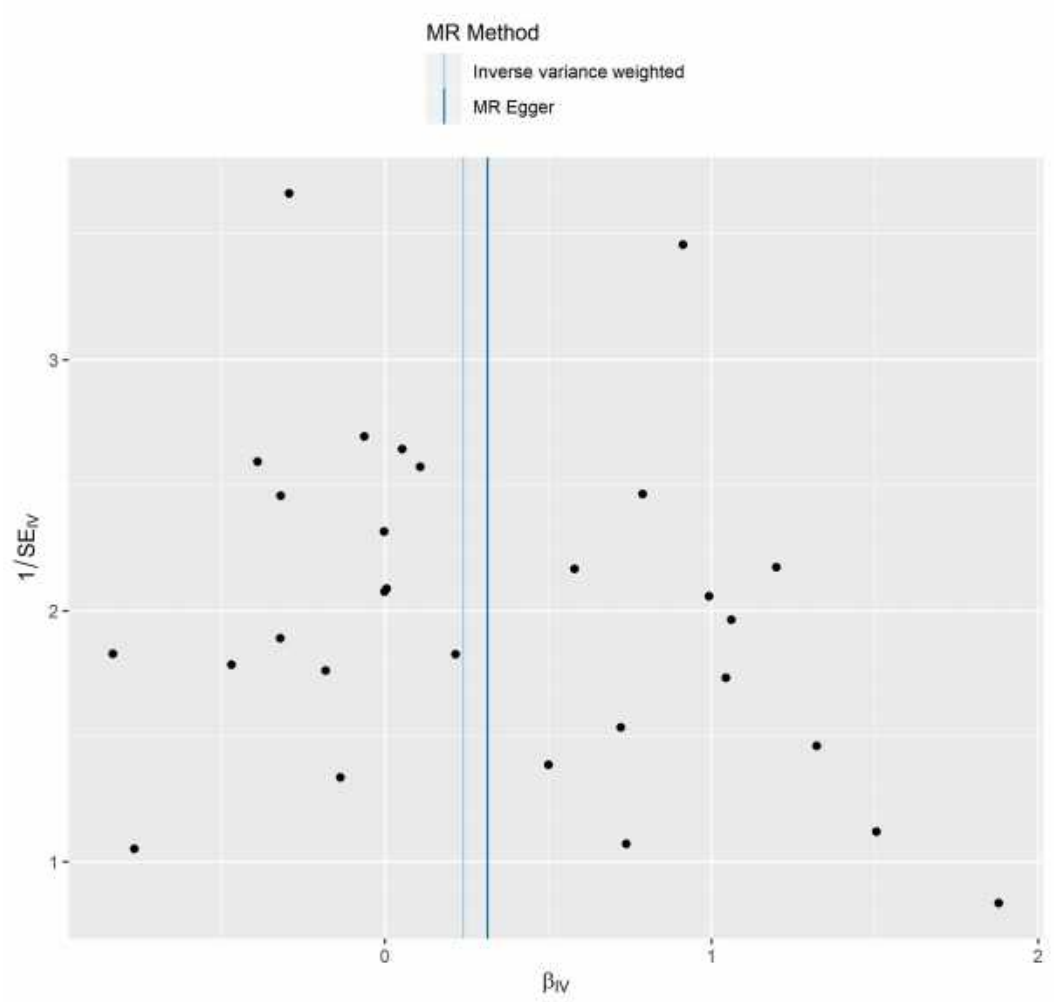
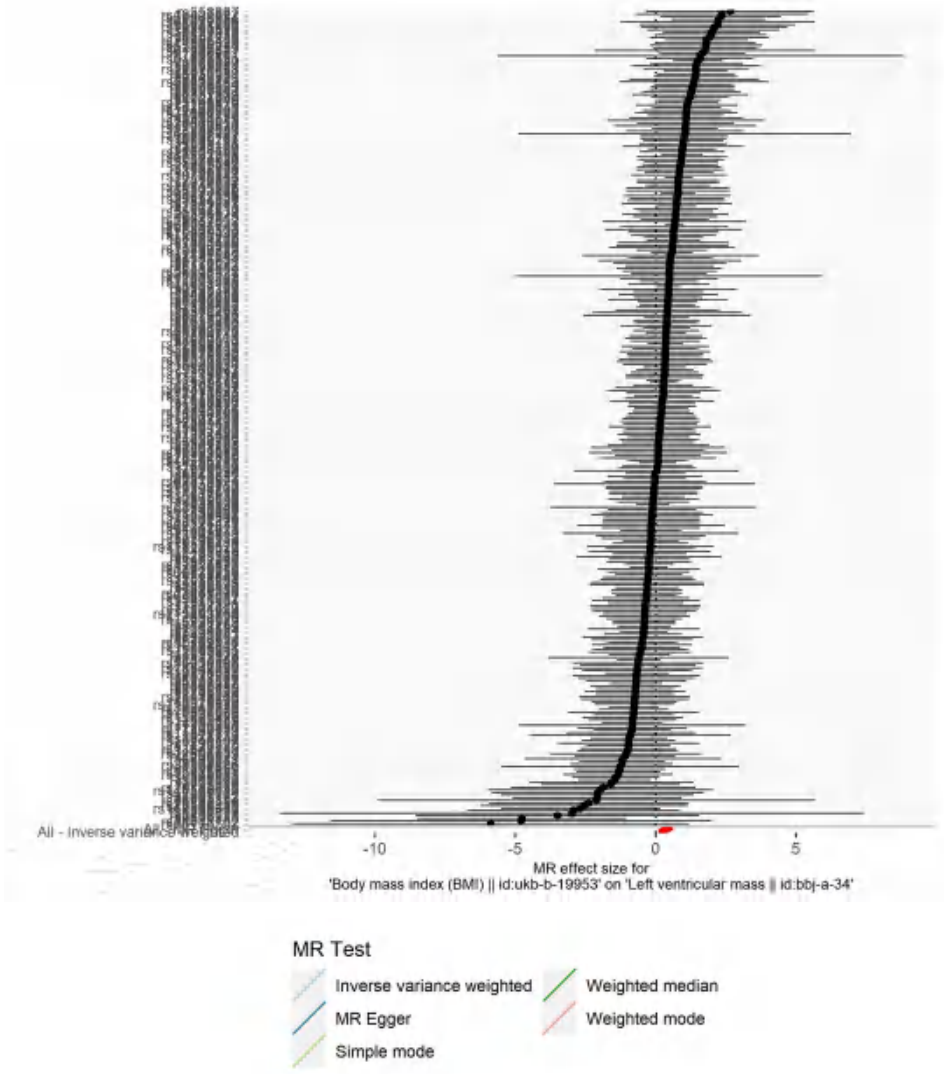
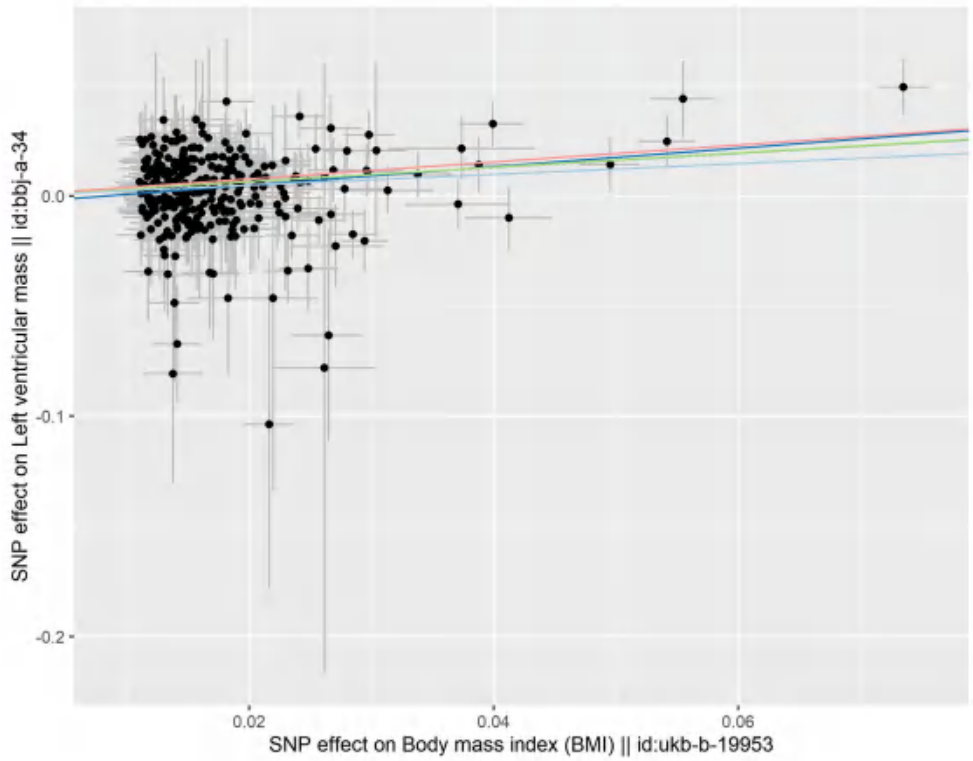

MR Method
Inverse variance weighted
MR Egger
1/SE_IV
3
2
1
0
1
2
β_IV

Figure S26. Visualisation of mendelian randomization for causal associations between BMI and left ventricular mass. A: Forest plot of MR effect size using MR-Egger and IVW methods; B: Pleiotropy analysis; C: Stability analysis of leave-one-out method; D: funnel plot.

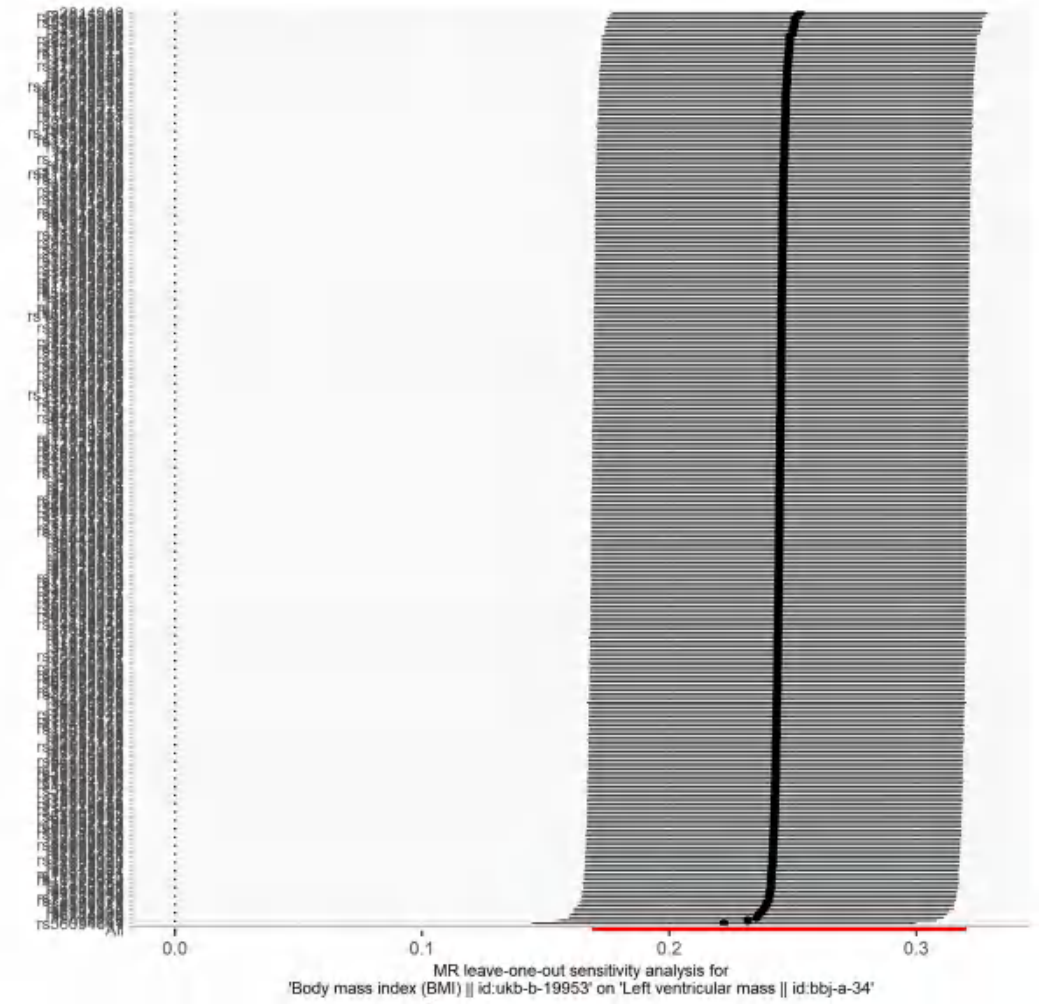
A



B



C


0.0
0.1
0.2
0.3
MR leave-one-out sensitivity analysis for
'Body mass index (BMI) || id:ukb-b-19953' on 'Left ventricular mass || id:bbj-a-34'

D

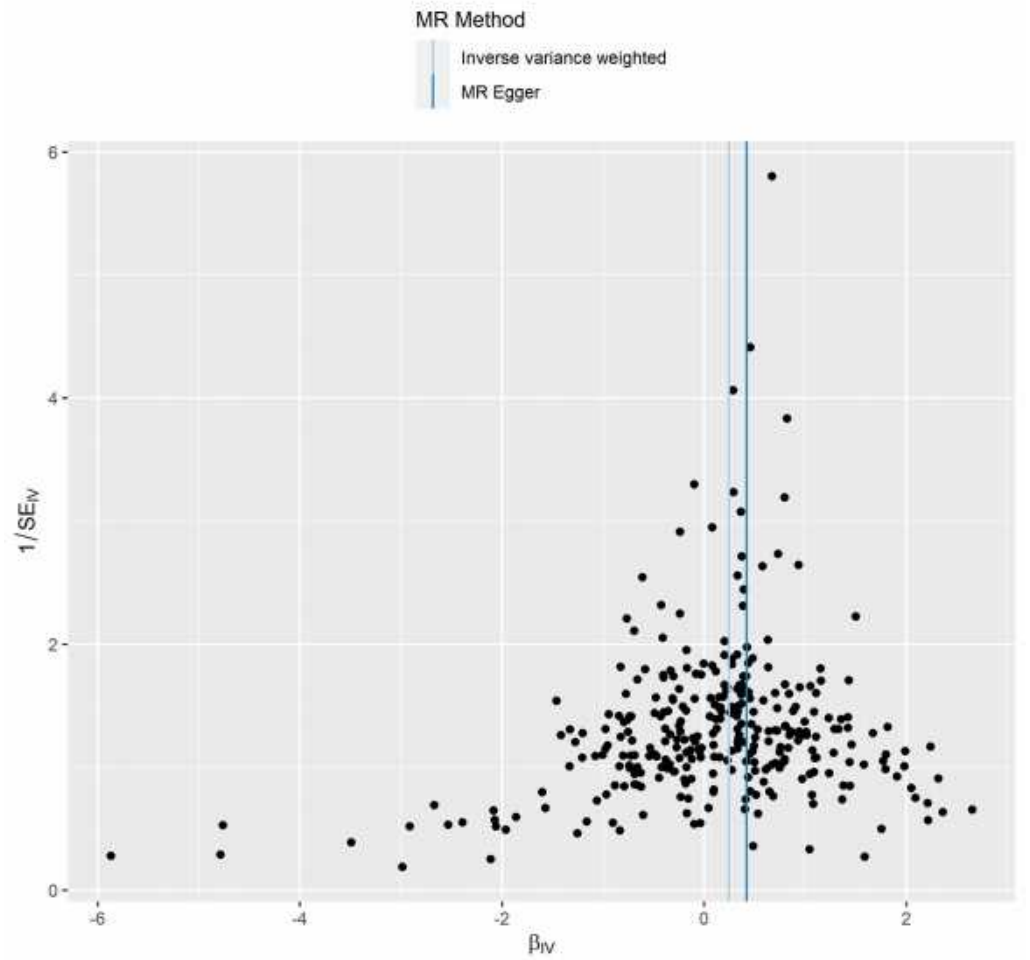
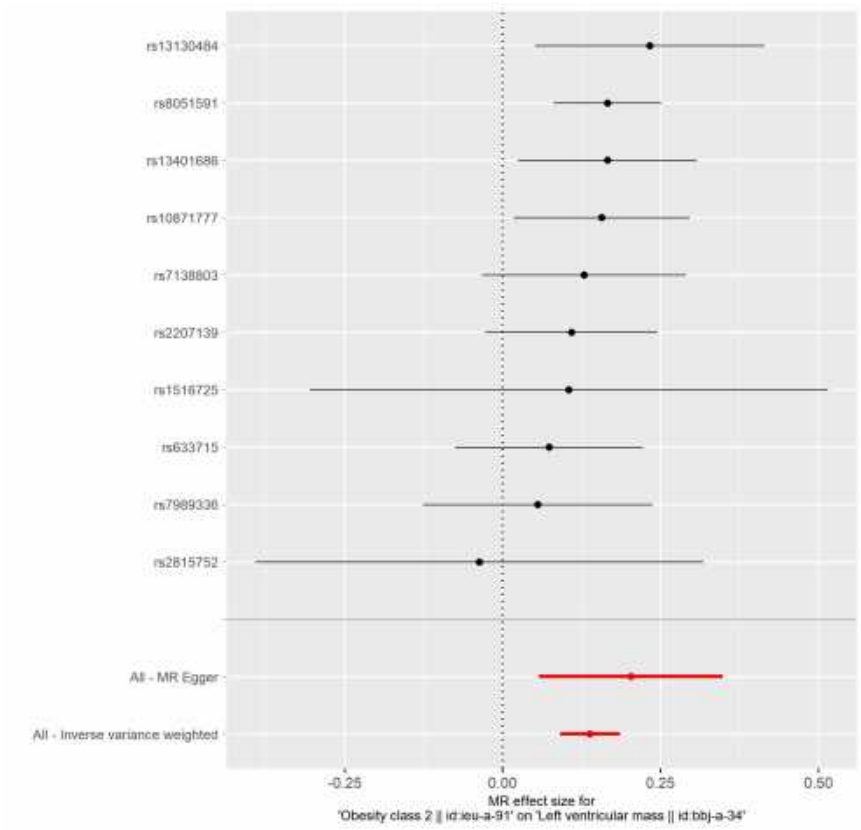
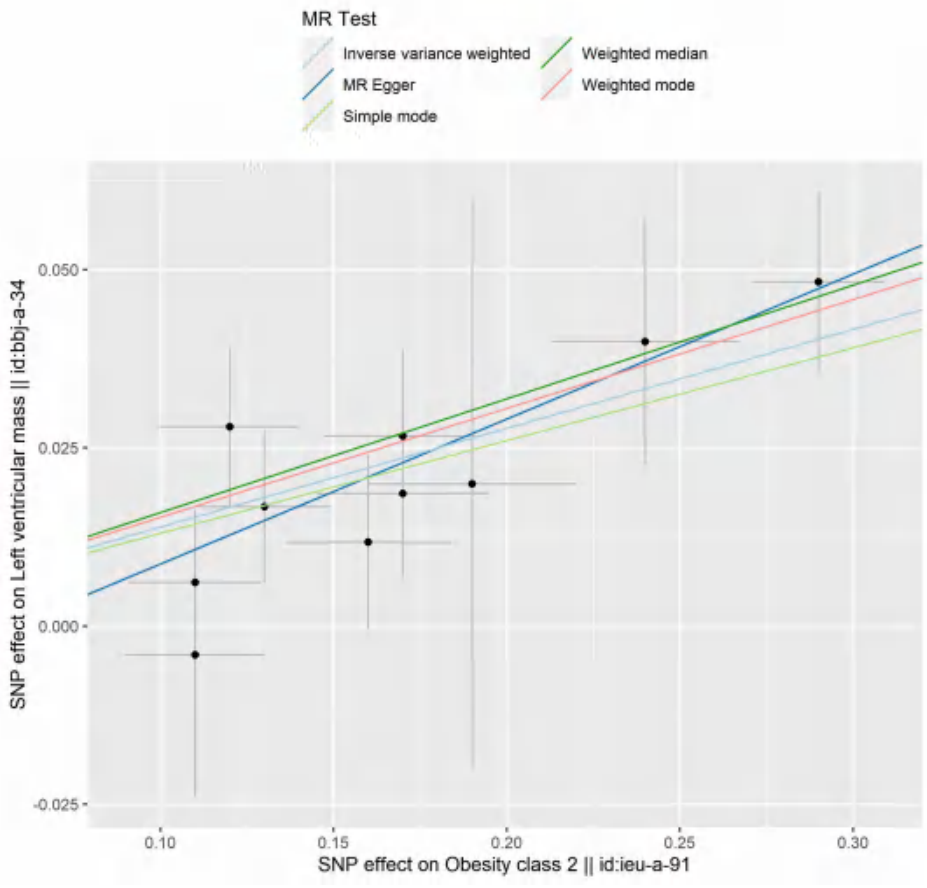

MR Method
Inverse variance weighted
MR Egger
6
4
2
0
1/SE_IV
-6
-4
-2
0
2
β_IV

Figure S27. Visualisation of mendelian randomization for causal associations between obesity class 1 and left ventricular mass. A: Forest plot of MR effect size using MR-Egger and IVW methods; B: Pleiotropy analysis; C: Stability analysis of leave-one-out method; D: funnel plot.

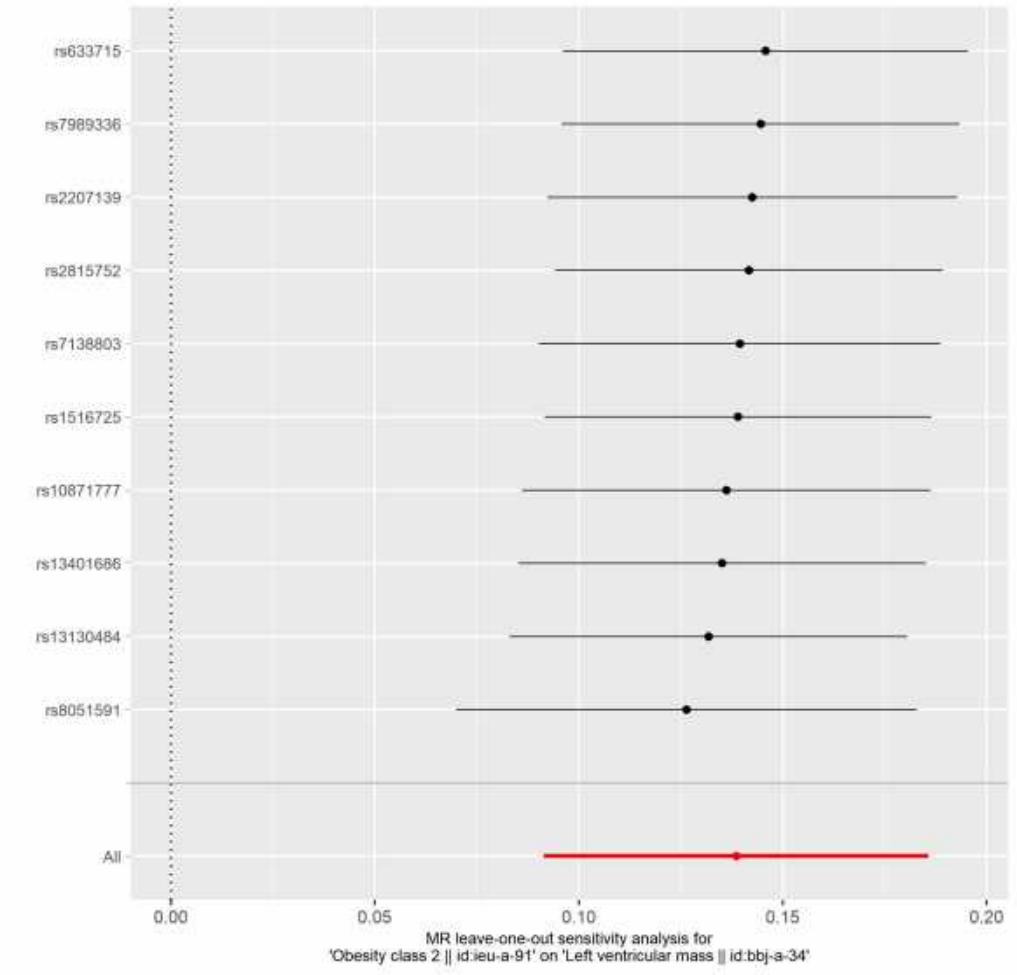
A



B



C


rs633715
rs7989336
rs2207139
rs2815752
rs7138803
rs1516725
rs10871777
rs13401686
rs13130484
rs8051591
All
0.00
0.05
0.10
0.15
0.20
MR leave-one-out sensitivity analysis for
'Obesity class 2 || id:ieu-a-91' on 'Left ventricular mass || id:bbj-a-34'

D

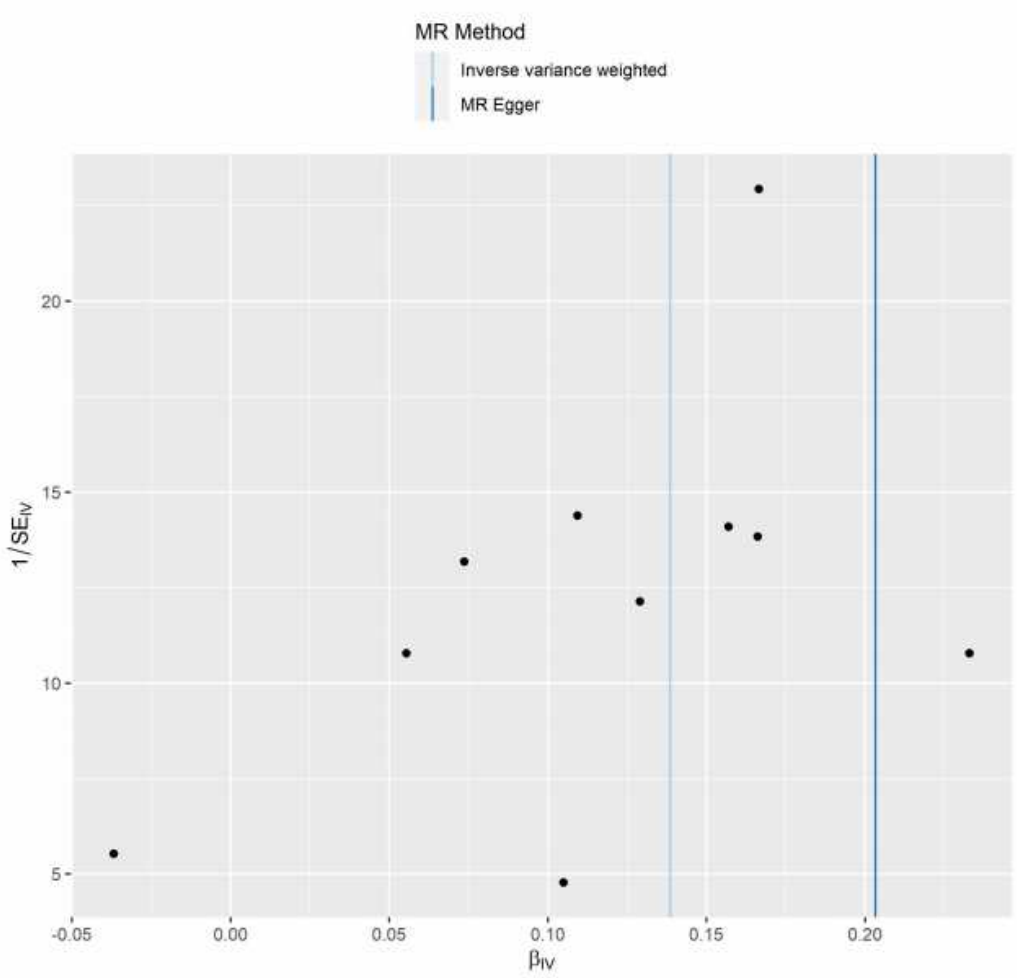
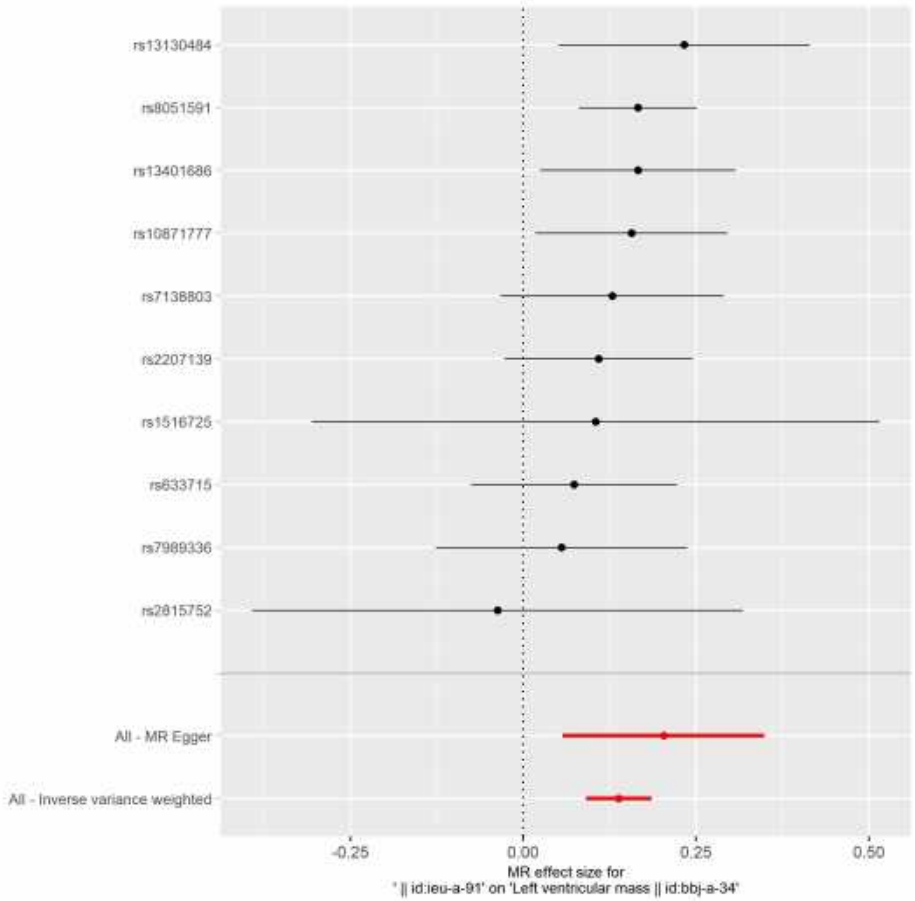
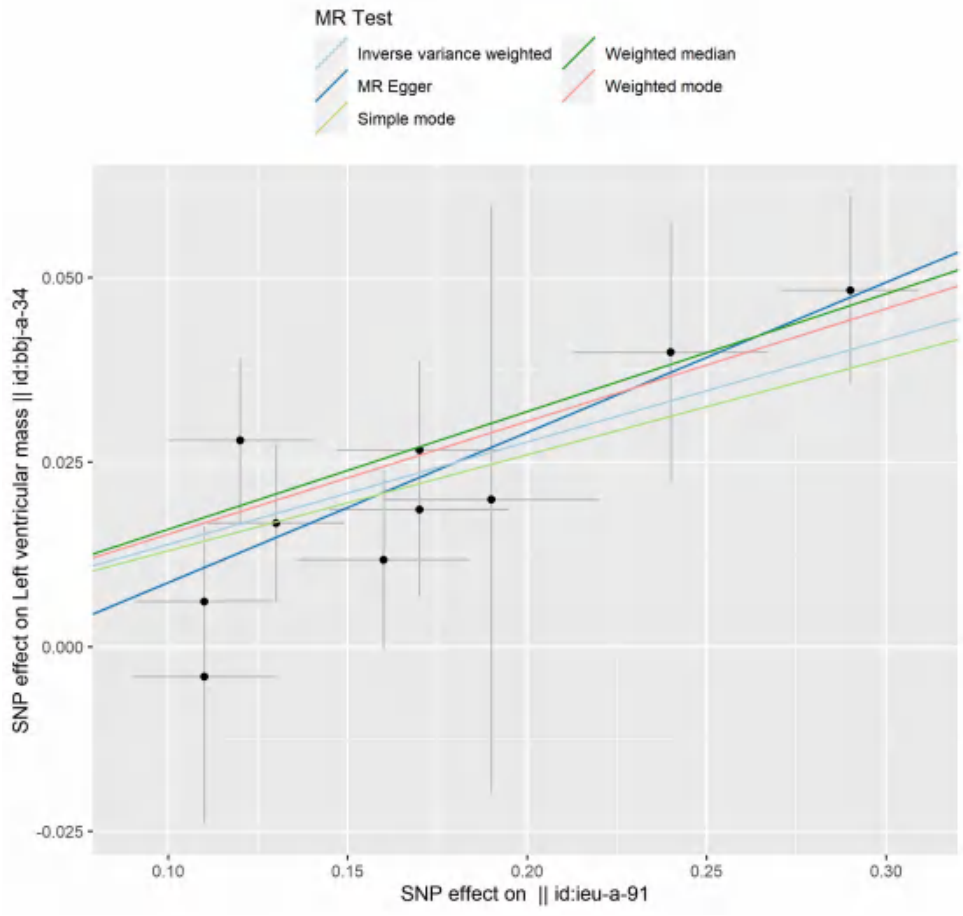

MR Method
Inverse variance weighted
MR Egger
20
15
10
5
1/SEIV
-0.05
0.00
0.05
0.10
0.15
0.20
βIV

Figure S28. Visualisation of mendelian randomization for causal associations between obesity class 2 and left ventricular mass. A: Forest plot of MR effect size using MR-Egger and IVW methods; B: Pleiotropy analysis; C: Stability analysis of leave-one-out method; D: funnel plot.

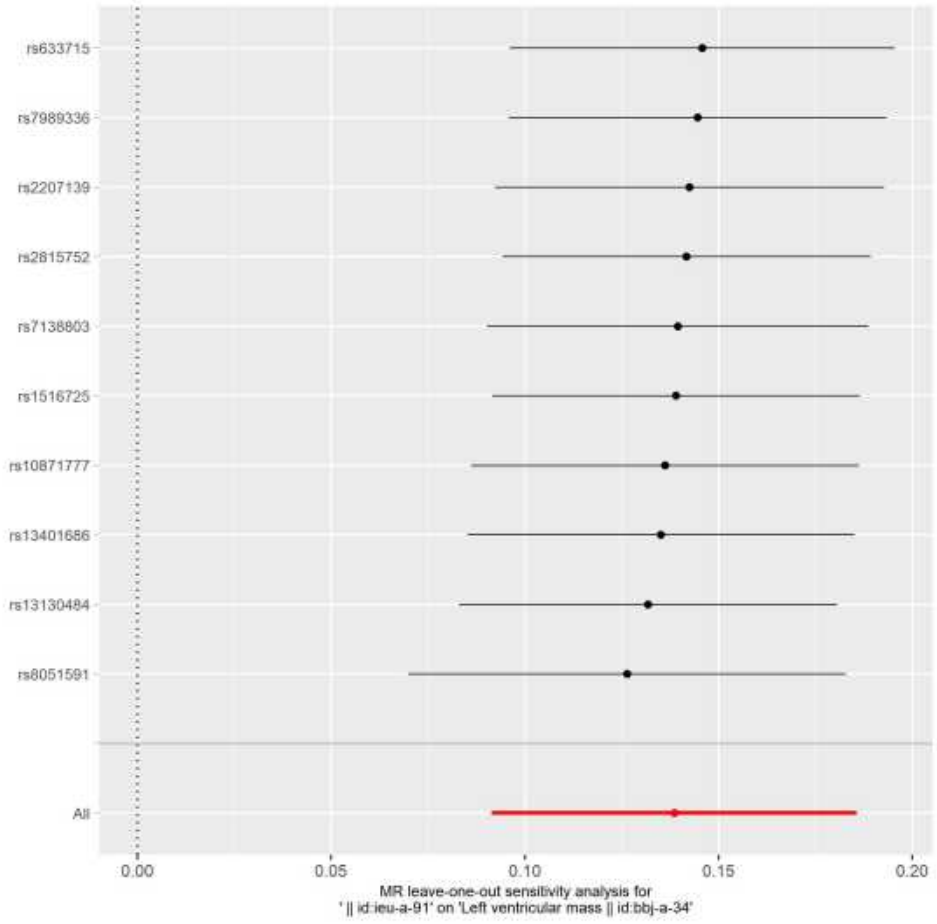
A



B



C


rs633715
rs7989336
rs2207139
rs2815752
rs7138803
rs1516725
rs10871777
rs13401686
rs13130484
rs8051591
All
0.00
0.05
0.10
0.15
0.20
MR leave-one-out sensitivity analysis for
' || id:ieu-a-91' on 'Left ventricular mass || id:bbj-a-34'

D

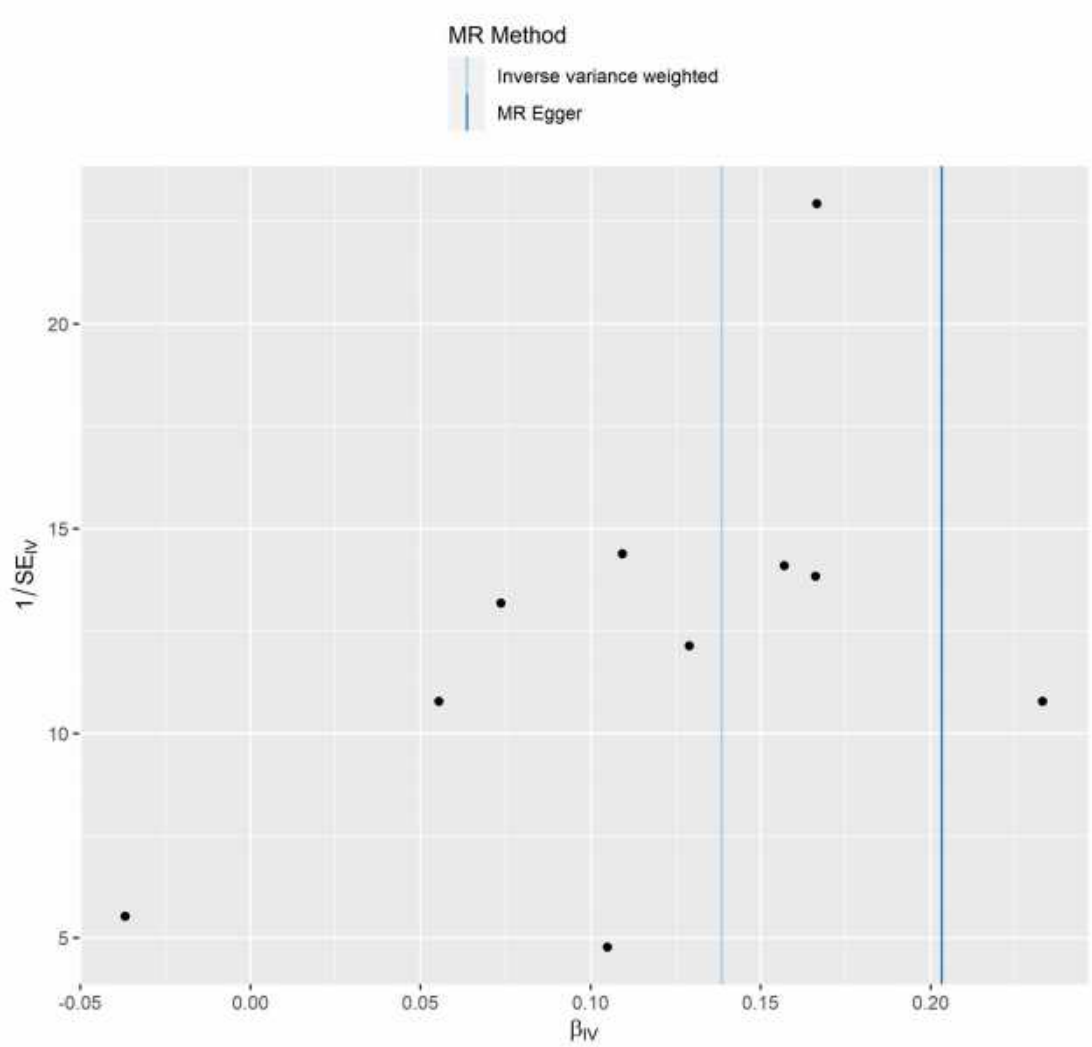
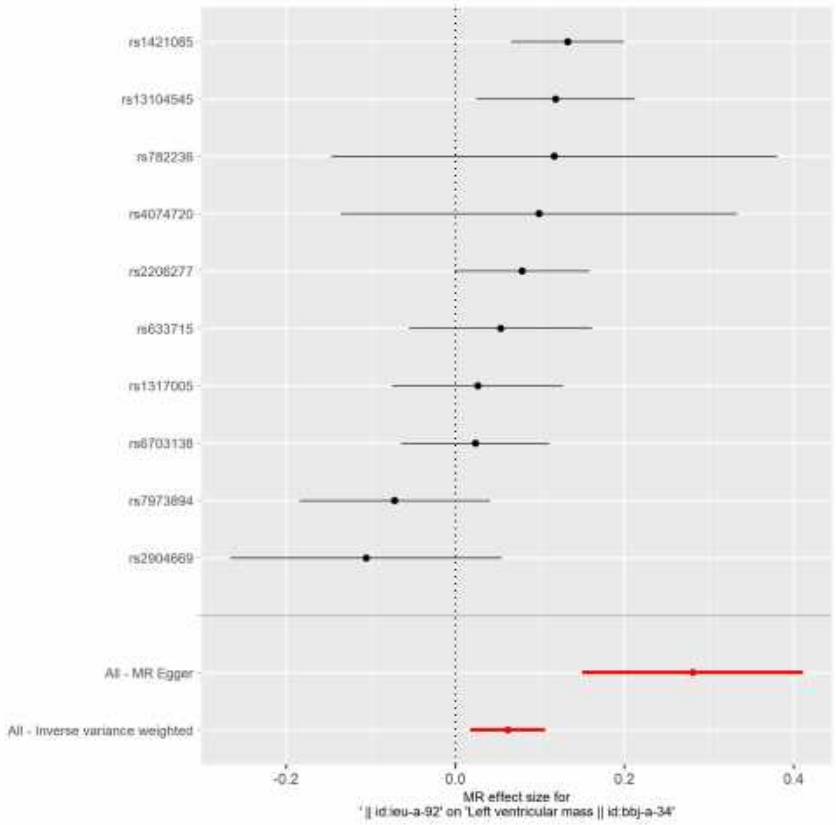
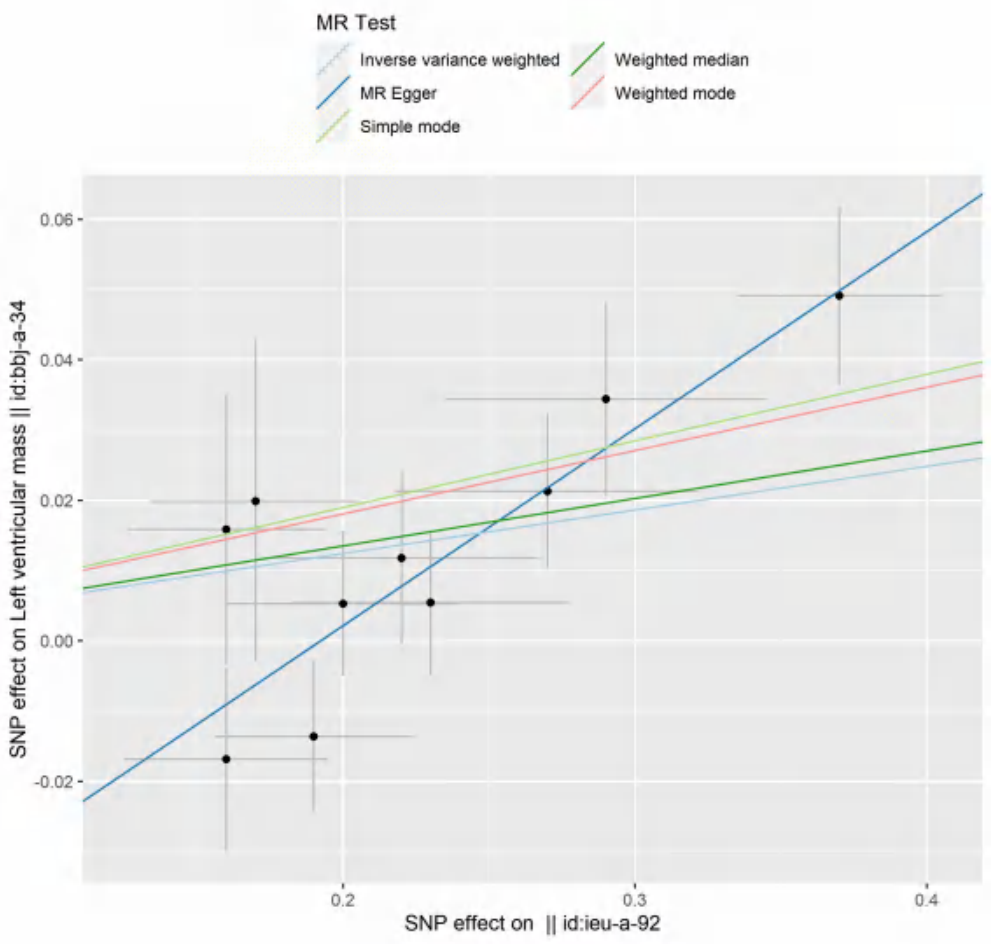

MR Method
Inverse variance weighted
MR Egger
20
15
10
5
1/SEIV
-0.05
0.00
0.05
0.10
0.15
0.20
βIV

Figure S29. Visualisation of mendelian randomization for causal associations between obesity class 3 and left ventricular mass. A: Forest plot of MR effect size using MR-Egger and IVW methods; B: Pleiotropy analysis; C: Stability analysis of leave-one-out method; D: funnel plot.

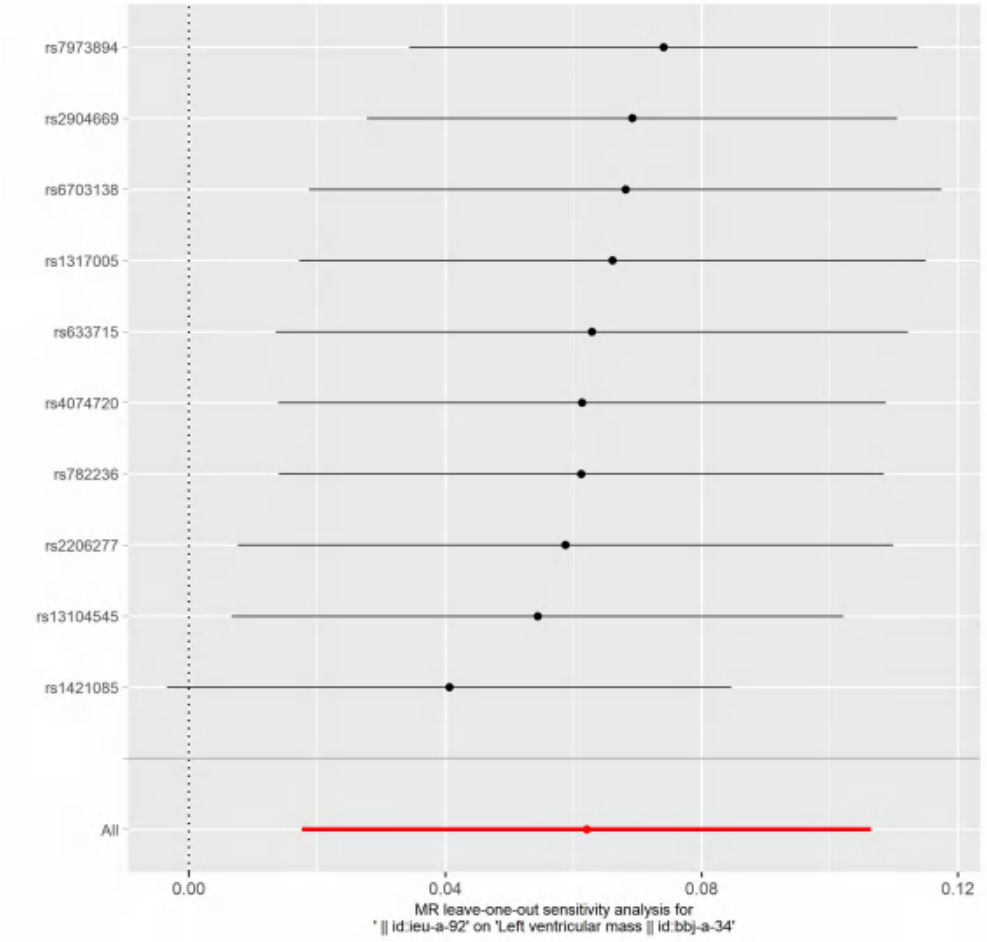
A



B



C


rs7973894
rs2904669
rs6703138
rs1317005
rs633715
rs4074720
rs782236
rs2206277
rs13104545
rs1421085
All
0.00
0.04
0.08
0.12
MR leave-one-out sensitivity analysis for
' || id:ieu-a-92' on 'Left ventricular mass || id:bbj-a-34'

D

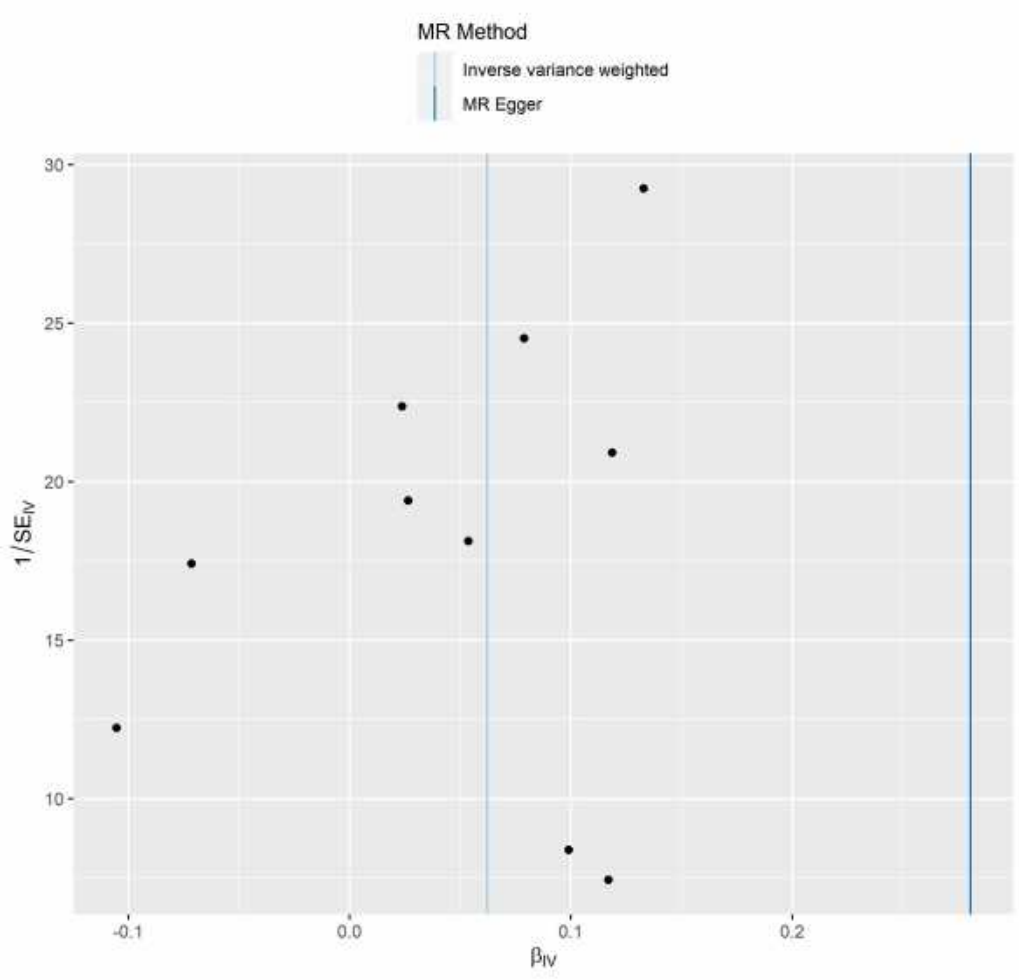
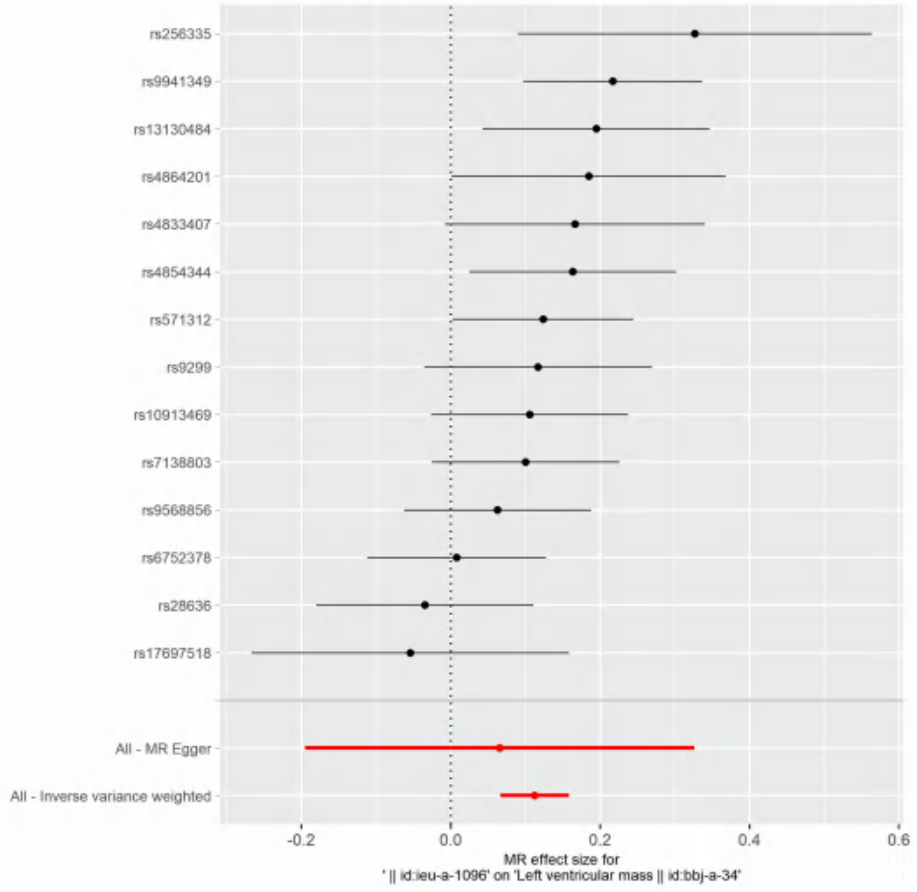
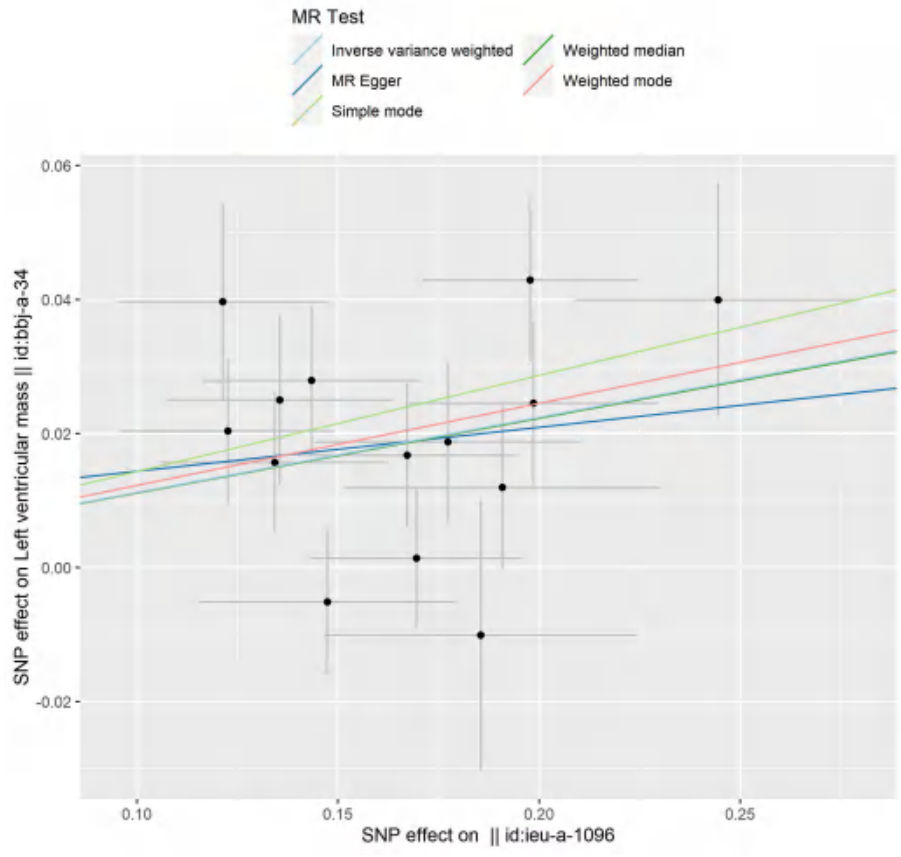

MR Method
Inverse variance weighted
MR Egger
30
25
20
15
10
1/SEIV
-0.1
0.0
0.1
0.2
βIV

Figure S30. Visualisation of mendelian randomization for causal associations between childhood obesity and left ventricular mass. A: Forest plot of MR effect size using MR-Egger and IVW methods; B: Pleiotropy analysis; C: Stability analysis of leave-one-out method; D: funnel plot.

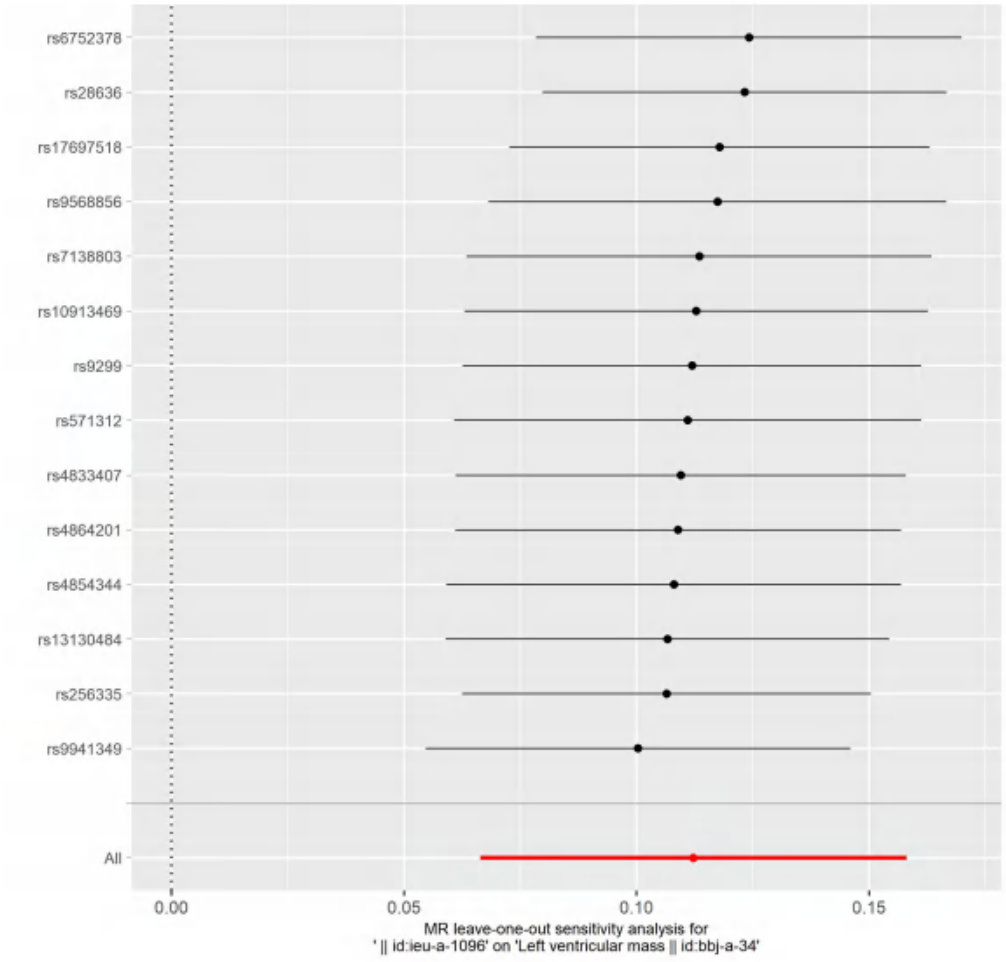
A



B



C


rs6752378
rs28636
rs17697518
rs9568856
rs7138803
rs10913469
rs9299
rs571312
rs4833407
rs4864201
rs4854344
rs13130484
rs256335
rs9941349
All
0.00
0.05
0.10
0.15
MR leave-one-out sensitivity analysis for
' || id:ieu-a-1096' on 'Left ventricular mass || id:bbj-a-34'

D

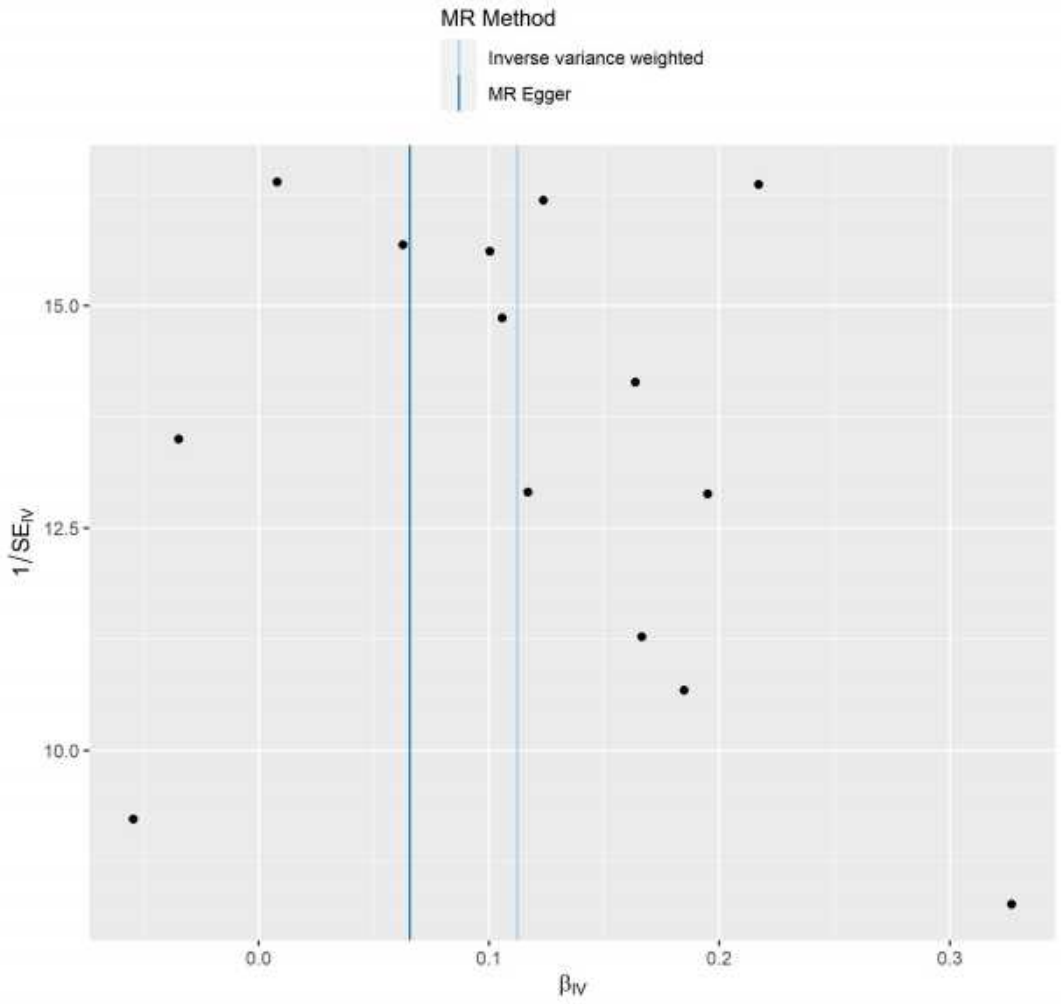
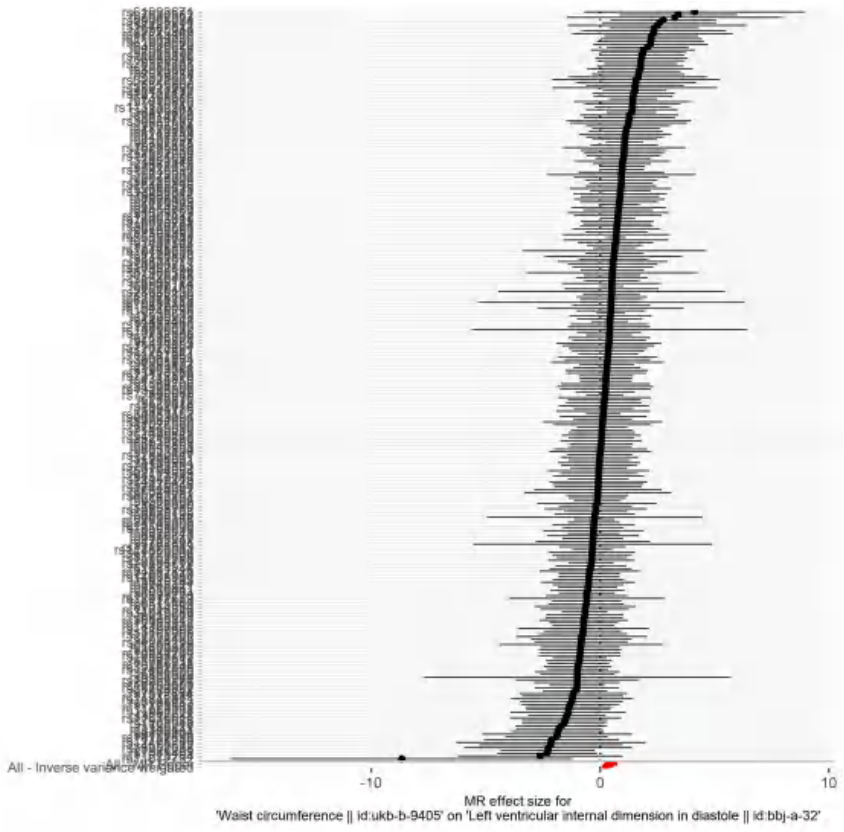
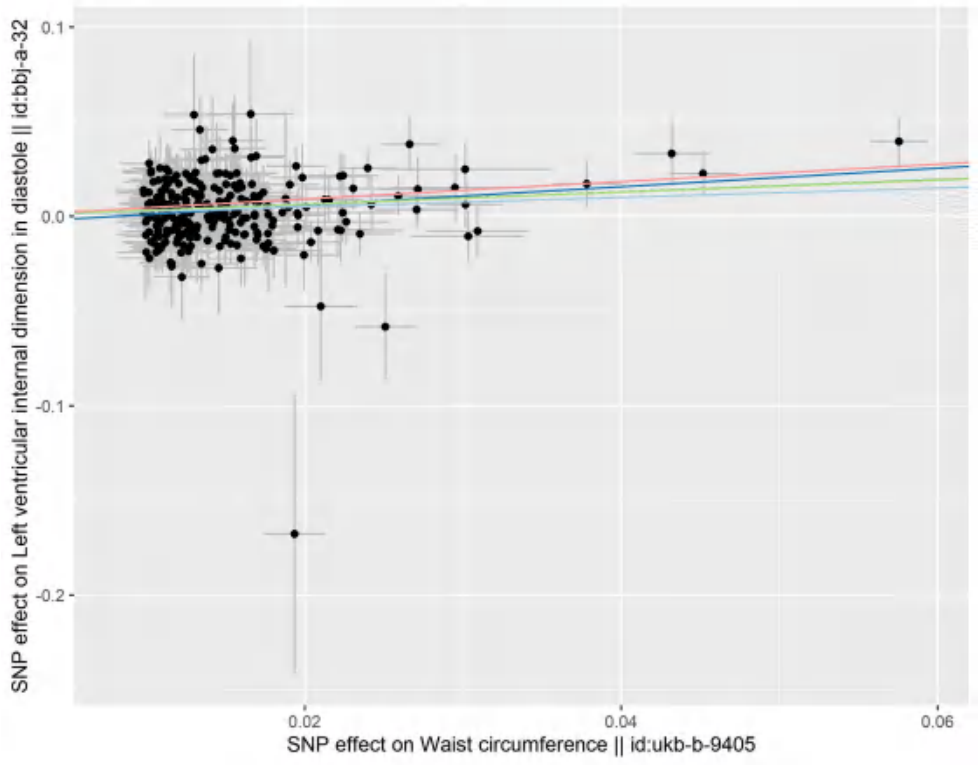

MR Method
Inverse variance weighted
MR Egger
15.0
12.5
10.0
1/SE_IV
0.0
0.1
0.2
0.3
β_IV

Figure S31. Visualisation of mendelian randomization for causal associations between waist circumference and left ventricular mass. A: Forest plot of MR effect size using MR-Egger and IVW methods; B: Pleiotropy analysis; C: Stability analysis of leave-one-out method; D: funnel plot.

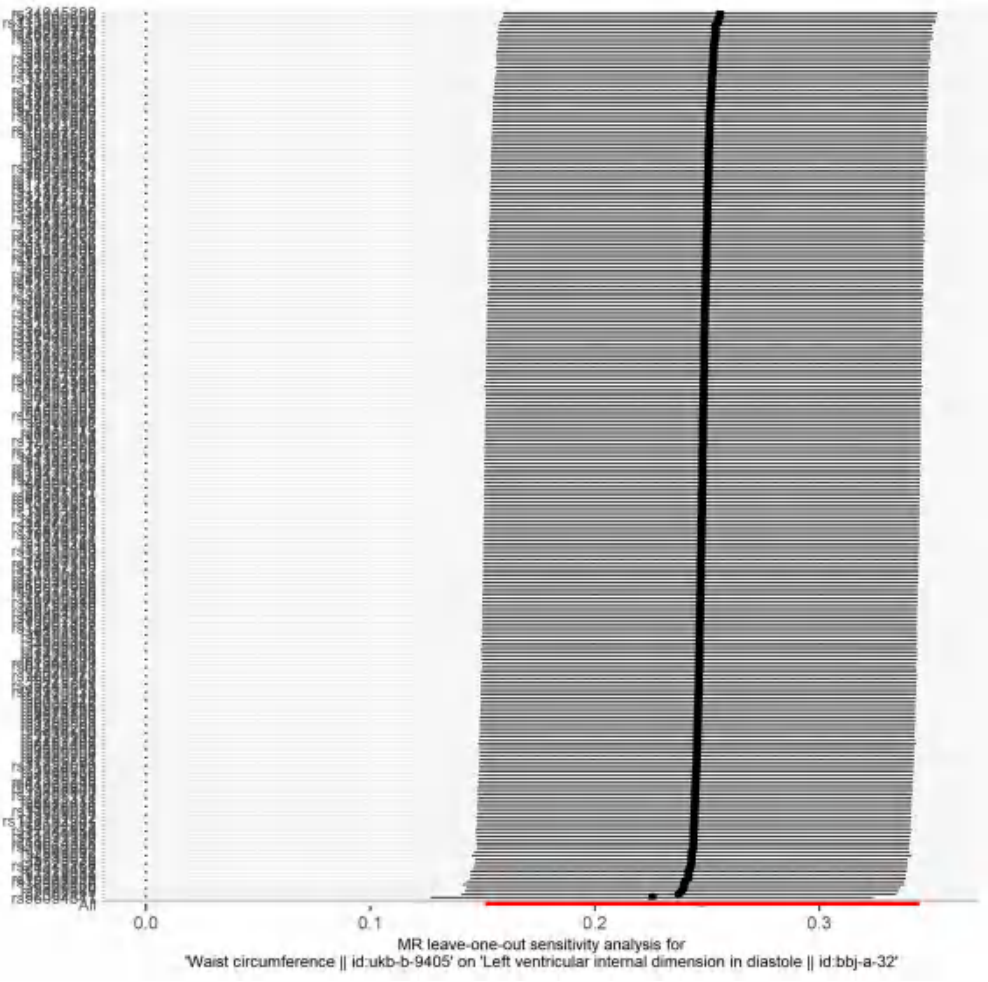
A



B



C


All
0.0
0.1
0.2
0.3
MR leave-one-out sensitivity analysis for
'Waist circumference || id:ukb-b-9405' on 'Left ventricular internal dimension in diastole || id:bbj-a-32'

D

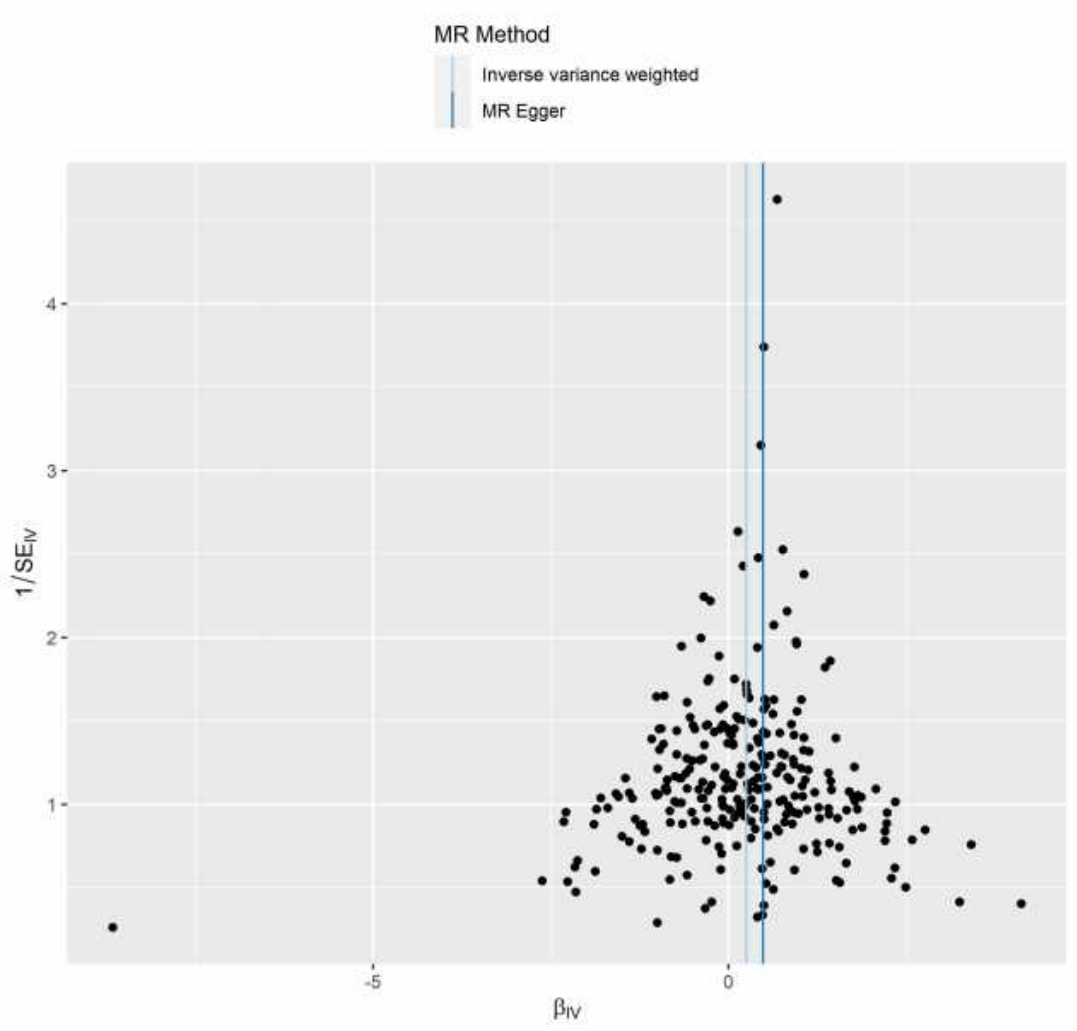
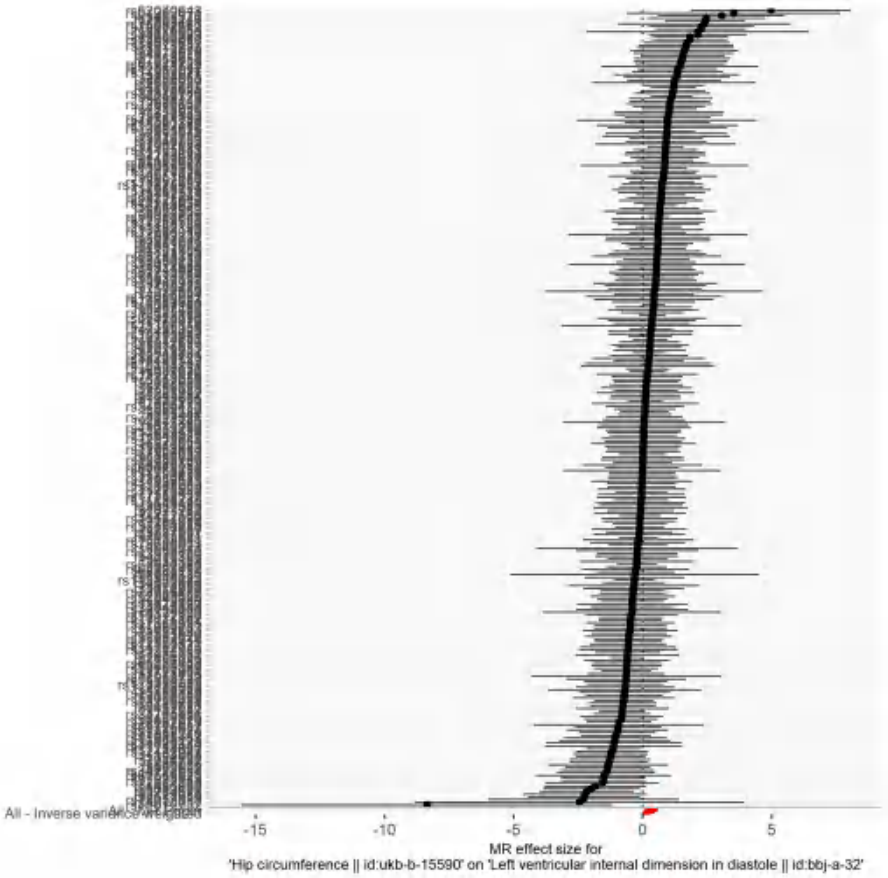
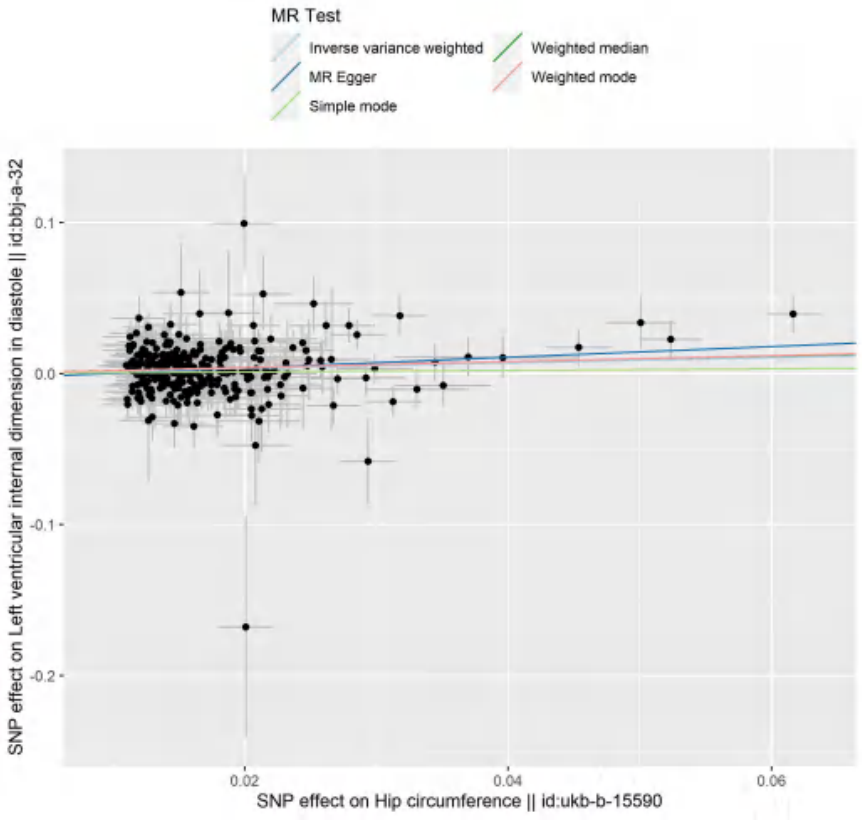

MR Method
Inverse variance weighted
MR Egger
4
3
2
1
1/SE_IV
-5
0
β_IV

Figure S32. Visualisation of mendelian randomization for causal associations between hip circumference and left ventricular mass. A: Forest plot of MR effect size using MR-Egger and IVW methods; B: Pleiotropy analysis; C: Stability analysis of leave-one-out method; D: funnel plot.

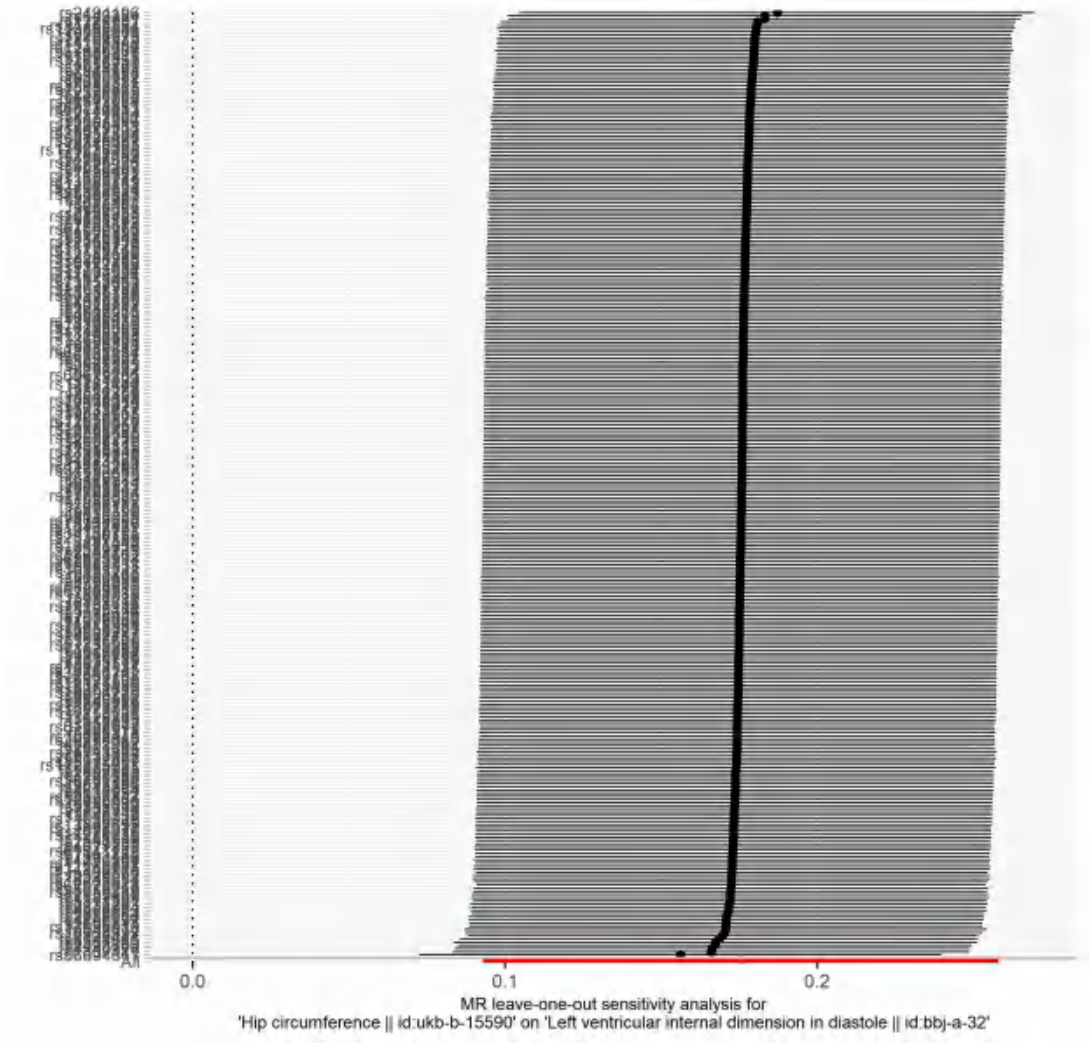
A



B



C


0.0
0.1
0.2
MR leave-one-out sensitivity analysis for
'Hip circumference || id:ukb-b-15590' on 'Left ventricular internal dimension in diastole || id:bbj-a-32'

D

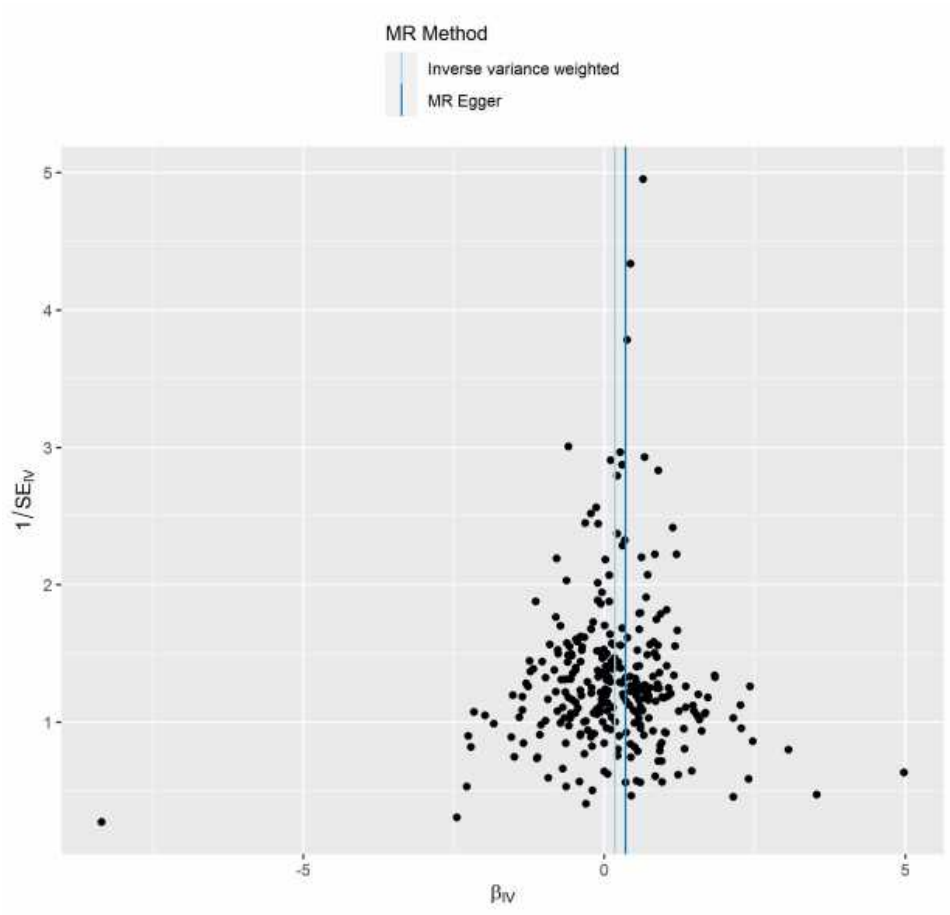
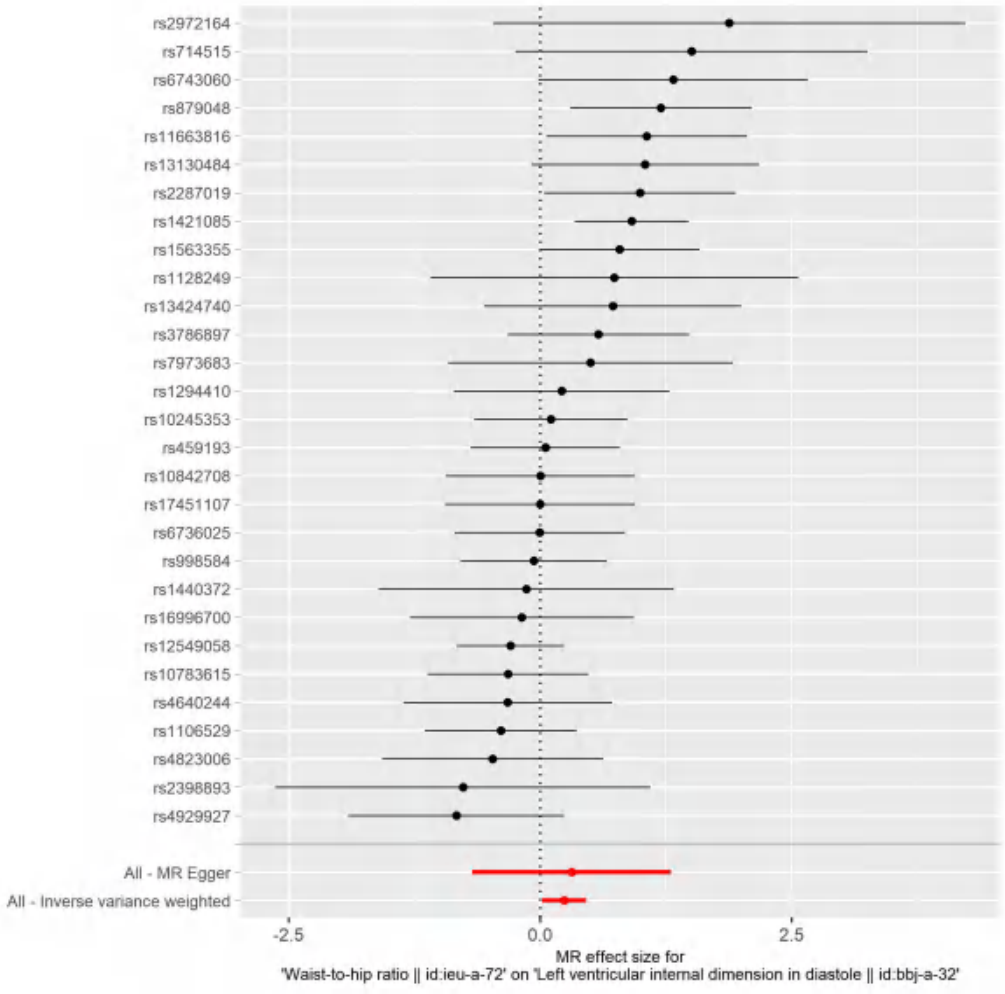
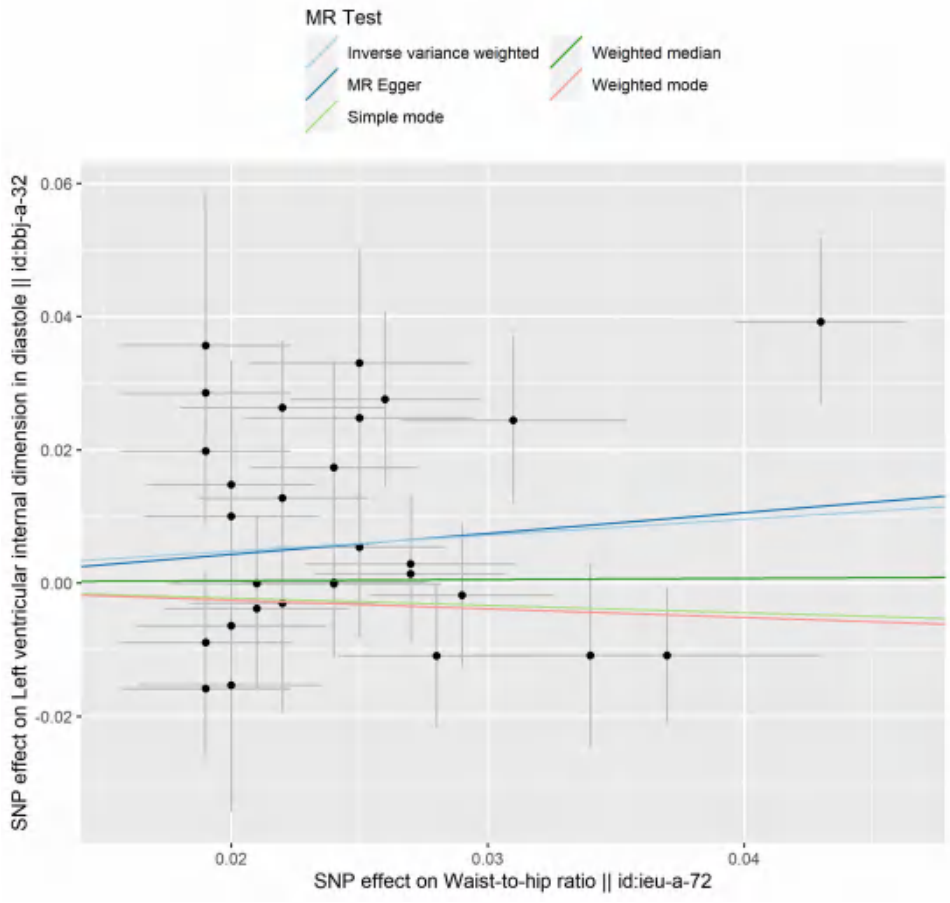

MR Method
Inverse variance weighted
MR Egger
1/SE_IV
β_IV
5
4
3
2
1
-5
0
5

Figure S33. Visualisation of mendelian randomization for causal associations between waist-hip ratio and left ventricular mass. A: Forest plot of MR effect size using MR-Egger and IVW methods; B: Pleiotropy analysis; C: Stability analysis of leave-one-out method; D: funnel plot.

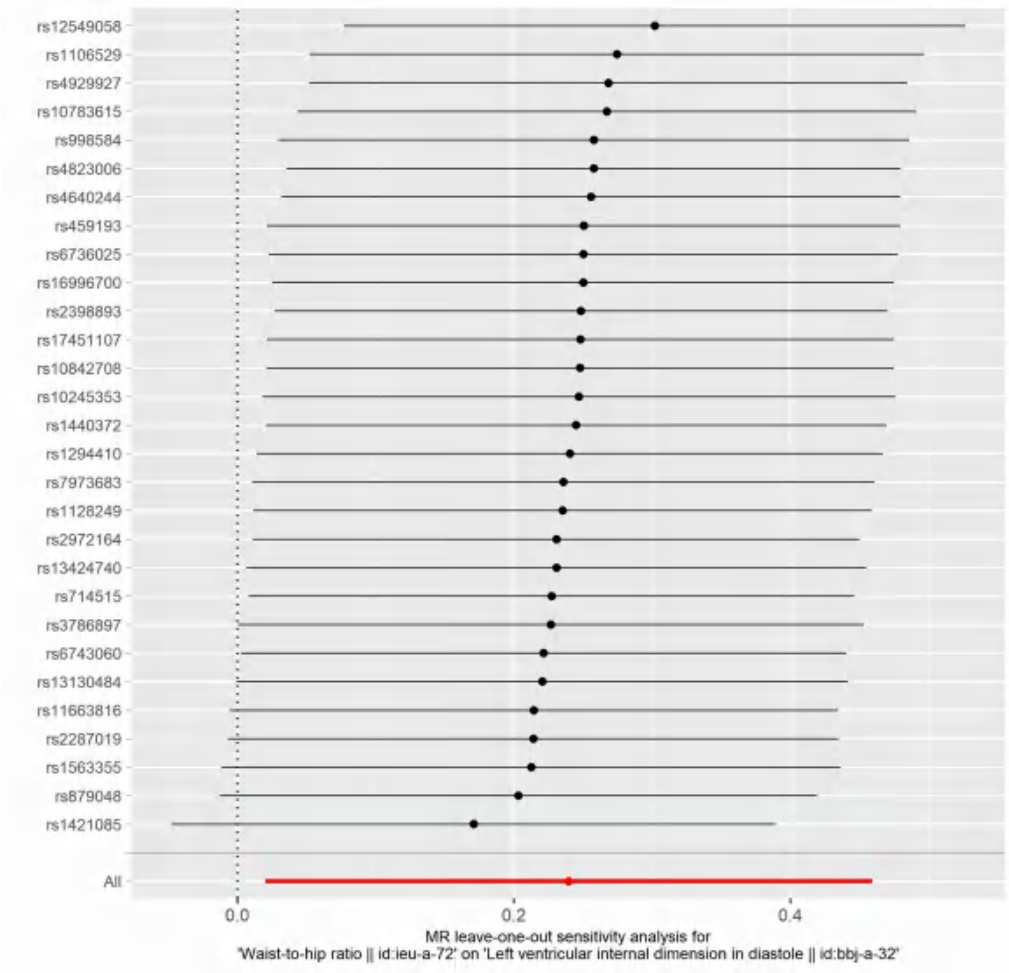
A



B



C


rs12549058
rs1106529
rs4929927
rs10783615
rs998584
rs4823006
rs4640244
rs459193
rs6736025
rs16996700
rs2398893
rs17451107
rs10842708
rs10245353
rs1440372
rs1294410
rs7973683
rs1128249
rs2972164
rs13424740
rs714515
rs3786897
rs6743060
rs13130484
rs11663816
rs2287019
rs1563355
rs879048
rs1421085
All
0.0
0.2
0.4
MR leave-one-out sensitivity analysis for
'Waist-to-hip ratio || id:ieu-a-72' on 'Left ventricular internal dimension in diastole || id:bbj-a-32'

D

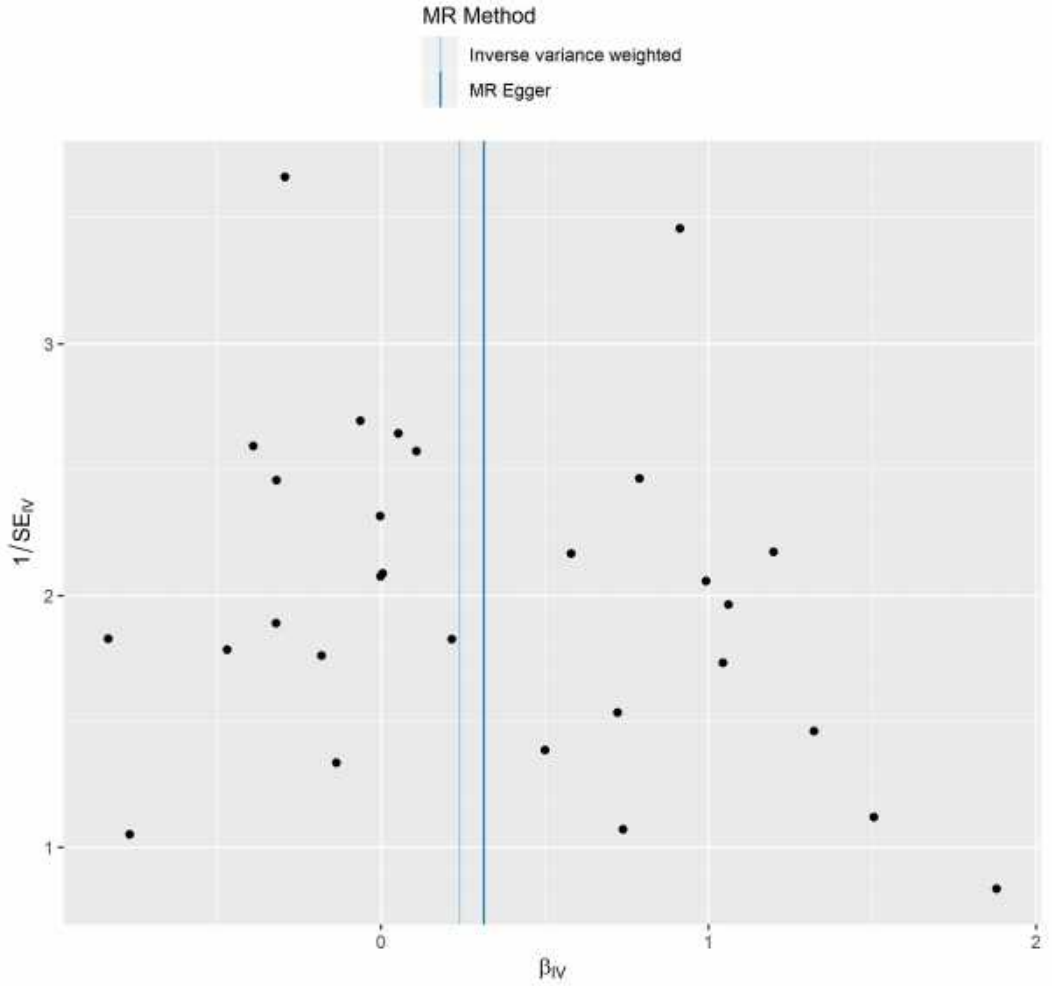

MR Method
Inverse variance weighted
MR Egger
1/SE_IV
3
2
1
0
1
2
β_IV

Fig S34 Univariate and Multivariate Mendelian Randomization Analysis of Potential Metabolism-related Confounding Factors and Their Association with Non-Ischemic Cardiomyopathy

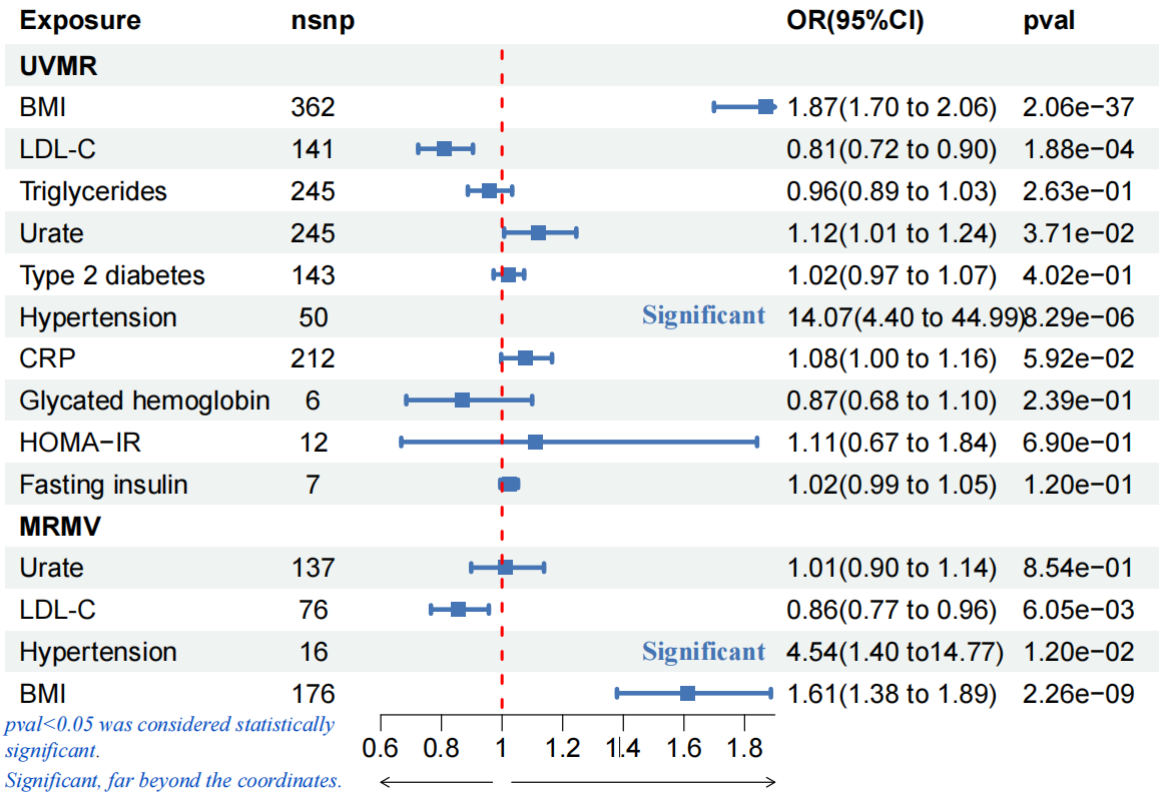


Table 1: Information on data included in the study

Phenotypes/ID	Data source	Study information/PMID	Cases/controls	Author/Year
Non-ischemic cardiomyopathy: I9_NONISCHCARDMYOP	FinnGen	European	11,400/175,752	NA/2021
LVIDd(MRI): bbj-a-32	BBJ	East Asian /29403010	19,676	M. Kanai/2018
LVM (MRI):bbj-a-34	BBJ	East Asian /29403010	19,076	M. Kanai/2018
Hypertension: ukb-b-12493	UKB	European	54,358/408,652	Ben Elsworth/2018
Coronary heart disease: ieu-a-7	CARDIoGRAMplusC4D	Mixed/26343387	60,801/123,504	M . Nikpay/2015
LDL cholesterol: ieu-b-110	UKB	European/32203549	440,546	Richardson, Tom/2020
Triglycerides: ieu-b-111	UKB	European/32203549	441,016	Richardson, Tom/2020
Urate levels: ebi-a-GCST90014015	UKB	European/34017140	389404	J. Marchini/2021
Body mass index ukb-b-19953	UKB	European	461460	Ben Elsworth/2018
C-reactive protein levels ebi-a-GCST90029070	UKB and CHARGE	European/35459240	575,531	Said S/2022
Type 2 diabetes ebi-a-GCST90018926	UKB and FinnGen	European/34594039	38,841/24,167,560	Sakaue S/2021
Obesity class 1: ieu-a-90	GIANT	European/23563607	32,858/65,839	Berndt SI/2013
Obesity class 2: ieu-a-91	GIANT	European/23563607	9889/62,657	Berndt SI/2013
Obesity class 3: ieu-a-92	GIANT	European/23563607	2896/47468	Berndt SI/2013
Childhood obesity: ieu-a-1096	EGG	European/22484627	5,530/8,318	Bradfield JP/2012
Waist circumference: ukb-b-9405	UKB	European	462,166	Ben Elsworth /2018
Hip circumference: ukb-b-15590	UKB	European	462,117	Ben Elsworth /2018
Waist-to-hip ratio: ieu-a-72	GIANT	Mixed/25673412	224,459	Shungin D/2015
Glycated hemoglobin ebi-a-GCST004939	UK-HLS	European/28887542	9436	Prins BP/2017
Fasting insulin ebi-a-GCST90002237	Meta-analysis*	East Asian/34059833	29792	Chen J/2021
HOMA-IR ieu-b-118	MAGIC	European/20081858	37037	Dupuis J/2021
13 cardiac MRI indicators	CVDKP	Multi-Ethnic Study/32382064, 35697867	36,000	Pirruccello J, et al/2020 and 2022
Left ventricular diastolic	UKB	European/35479509	23,321	Thanaj M/2022

Phenotypes/ID	Data source	Study information/PMID	Cases/controls	Author/Year
function measurement(MRI) GCST90019012-GCST90019014				
16 cardiac MRI indicators	CVDKP	Multi-Ethnic Study/32382064, 35697867	36,000	Pirruccello J, et al/2020 and 2022

LVIDd, Left ventricular internal dimension in diastole. LVM, Left ventricular mass. GIANT, The Genetic Investigation of ANthropometric Traits. UK-HLS, the UK Household Longitudinal Study. EGG, Early Growth Genetics Consortium. BBJ, BioBank Japan Project. UKB, UKBiobank. *, meta-analysis, code：GCST90002225-GCST90002248. MAGIC, Mauritius Africa Genetic Innovation Center. CVDKP, Cardiovascular disease knowledge portal. Left ventricular diastolic function measurement: Longitudinal peak diastolic strain rate, Radial peak diastolic strain rate, left atrial maximum volume. Summary statistics from GWAS for hypertension, body mass index, waist circumference, and hip circumference were obtained from the FinnGen consortium and the UKB. Researchers can access the corresponding data and metadata using the accession codes provided in this table via the IEU OpenGWAS platform: https://gwas.mrcieu.ac.uk/datasets/.