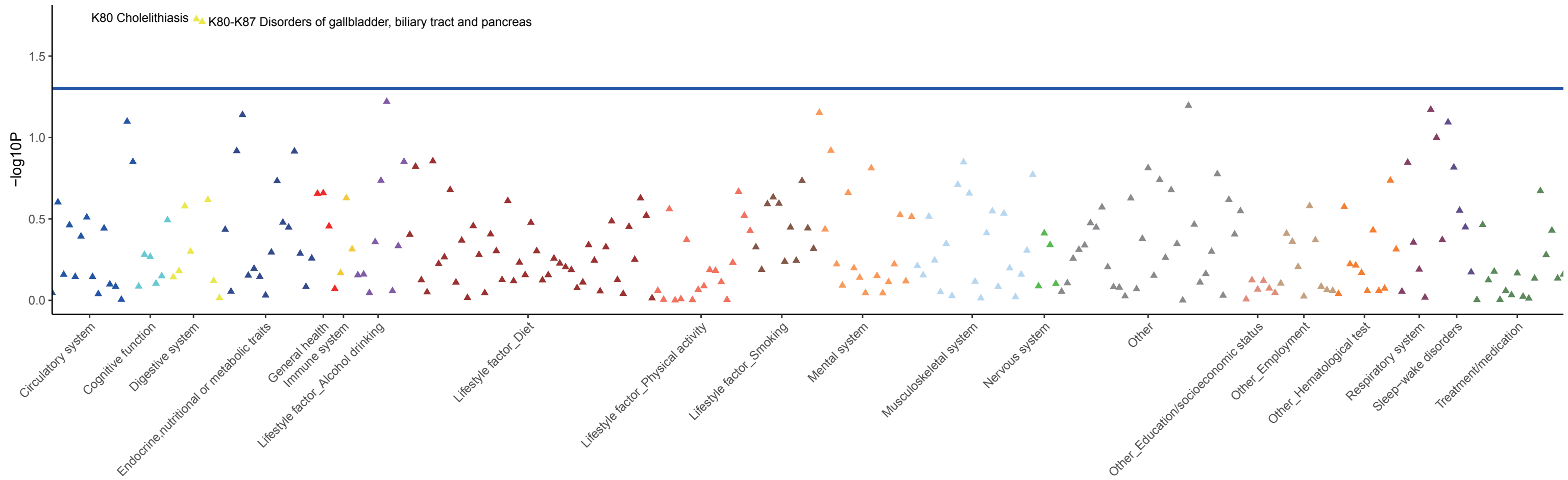


Fig. S1 The data filtering process.

A



B

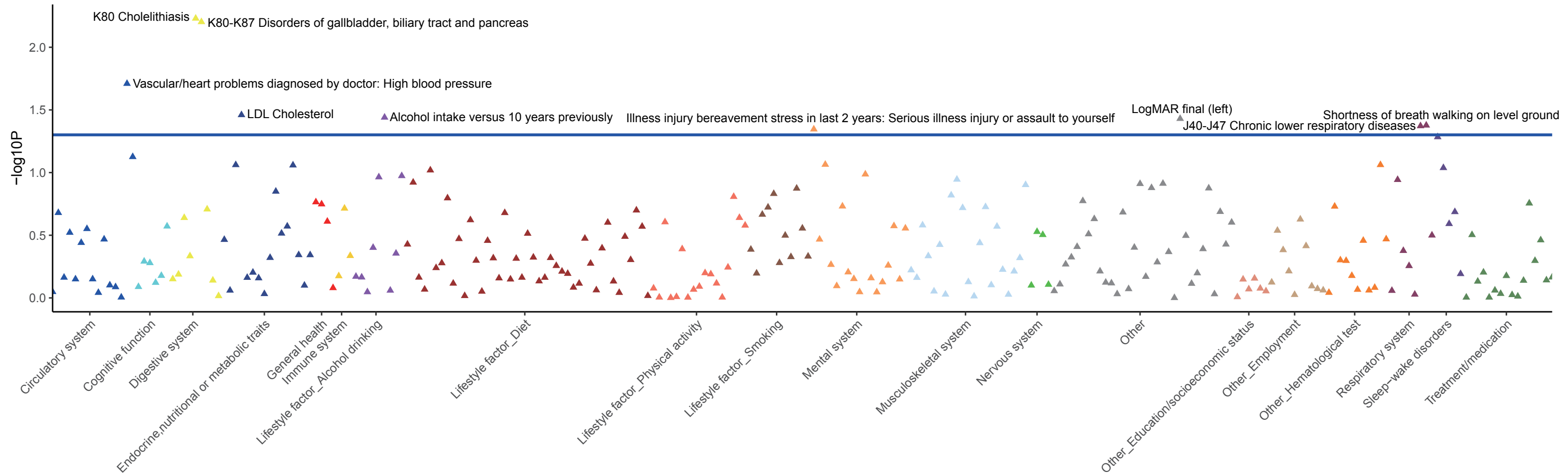


Fig. S2 Manhattan plot showing the pleiotropy assessment results for MR-Egger intercept test (A) and Q-Q' test (B). For each plot, the blue horizontal line represents the threshold for significance ( $P < 0.05$ ).

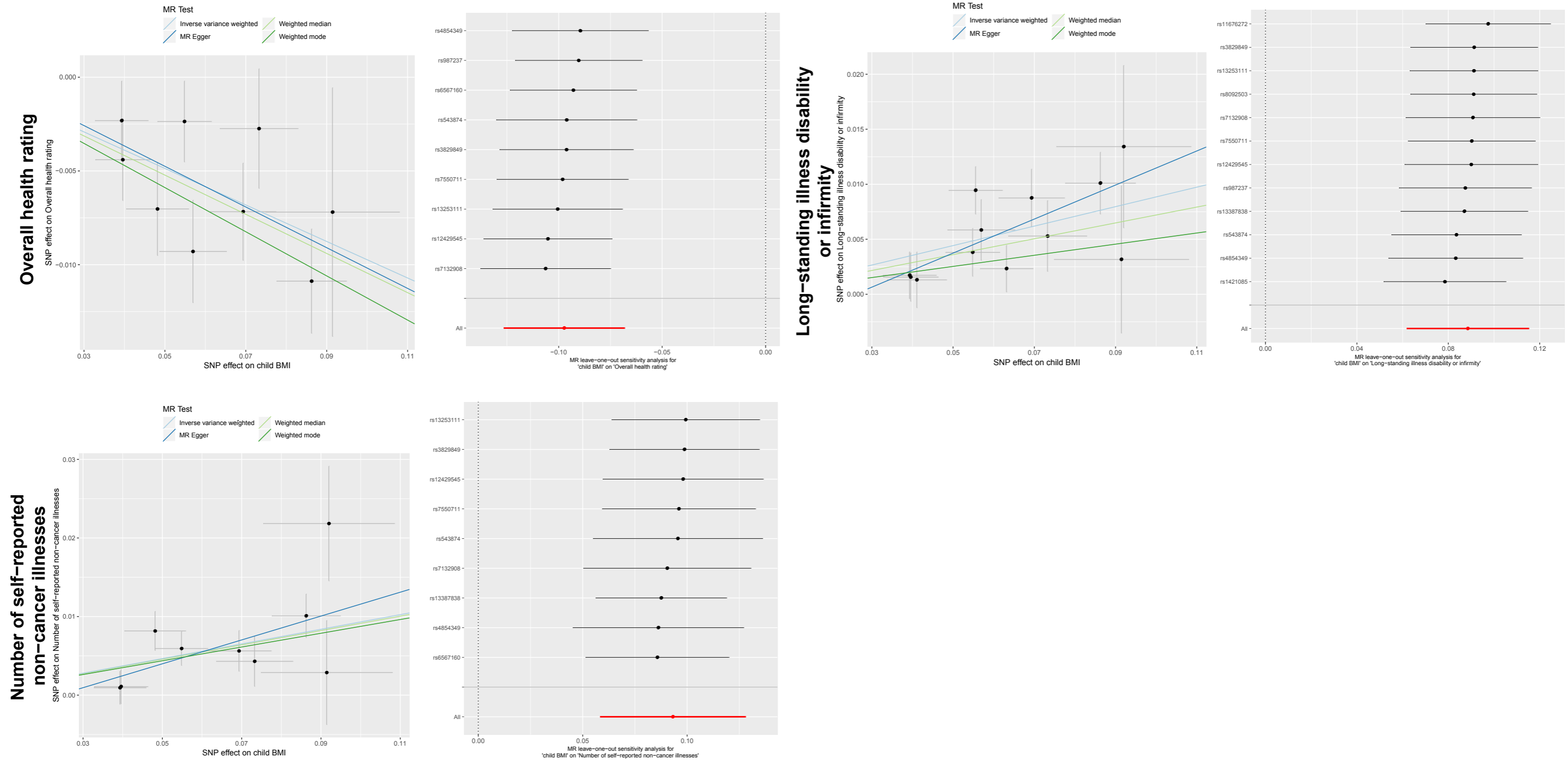
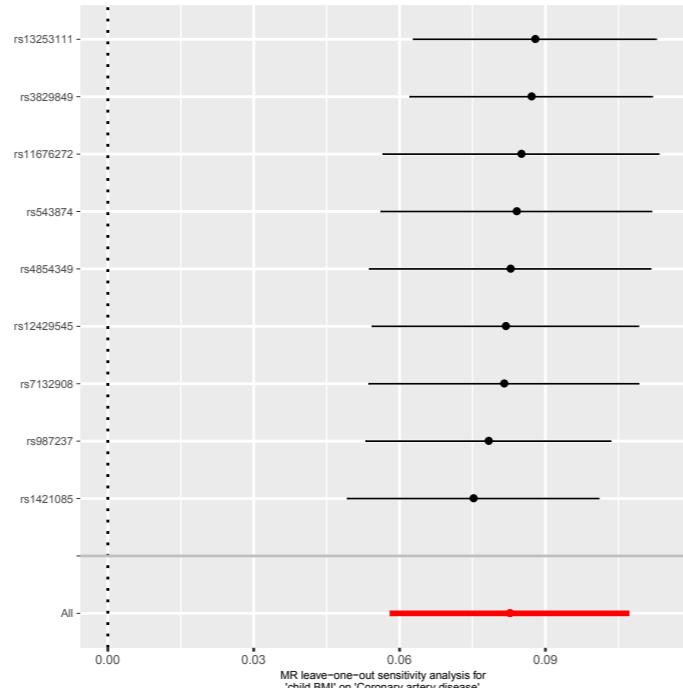
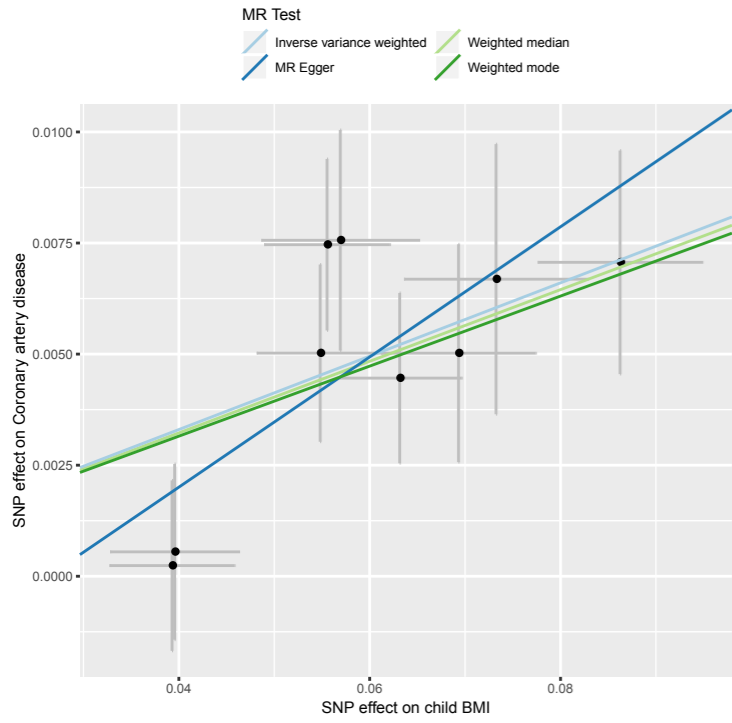
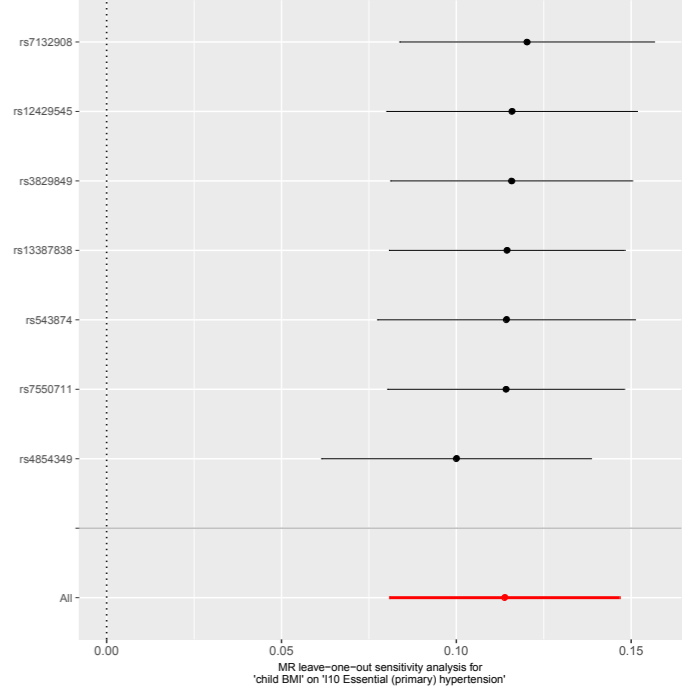
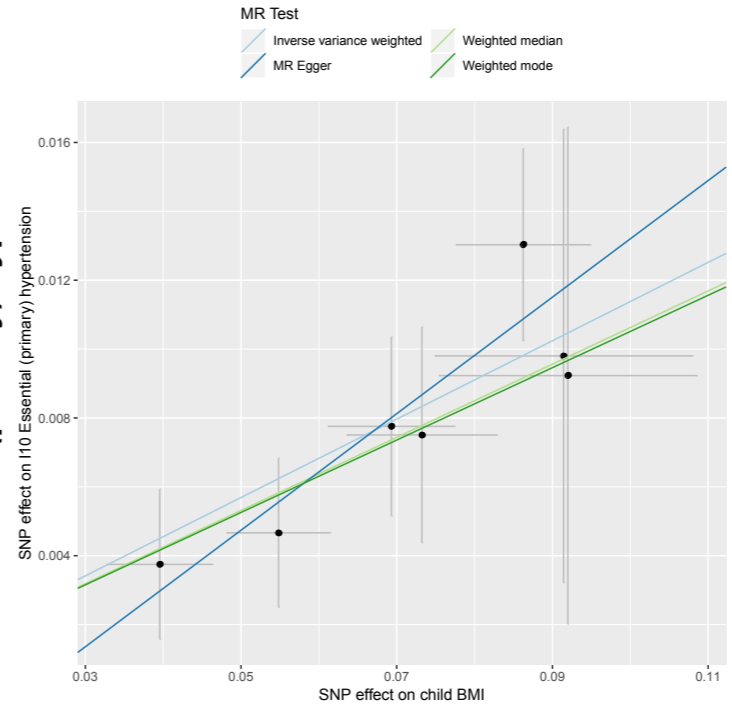


Fig. S3 Scatter plot and leave one out analysis plot for overall health rating, long-standing illness disability or infirmity, and number of self-reported non-cancer illnesses.

### Coronary artery disease



### I10 Essential (primary) hypertension



### Vascular/heart problems diagnosed by doctor: High blood pressure

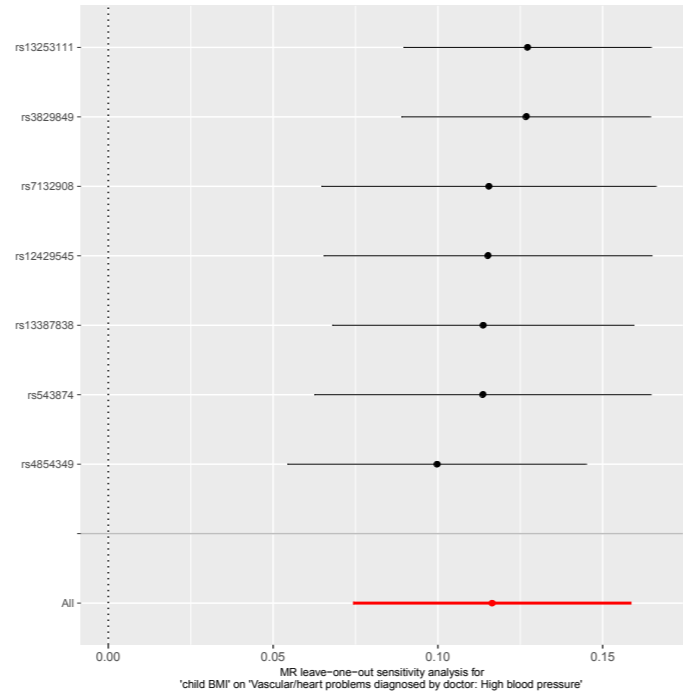
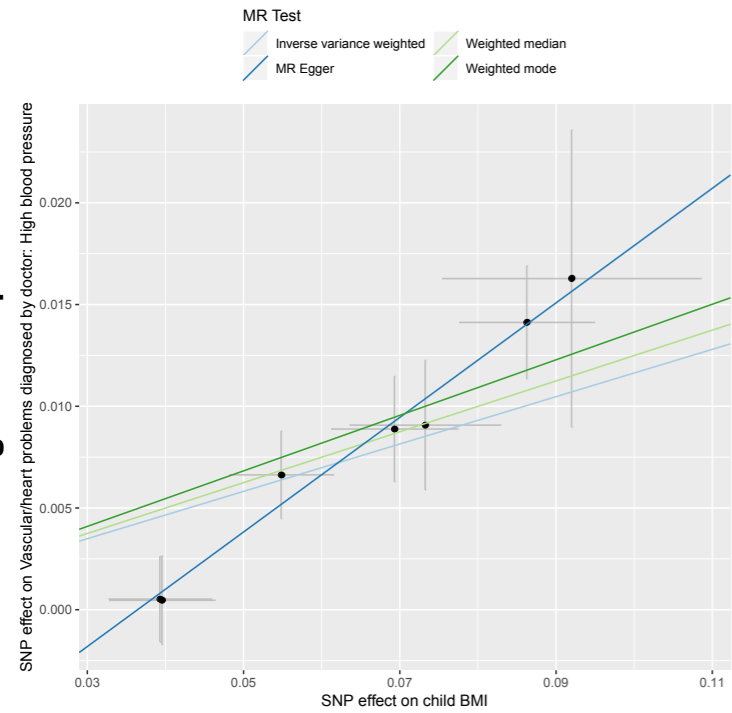
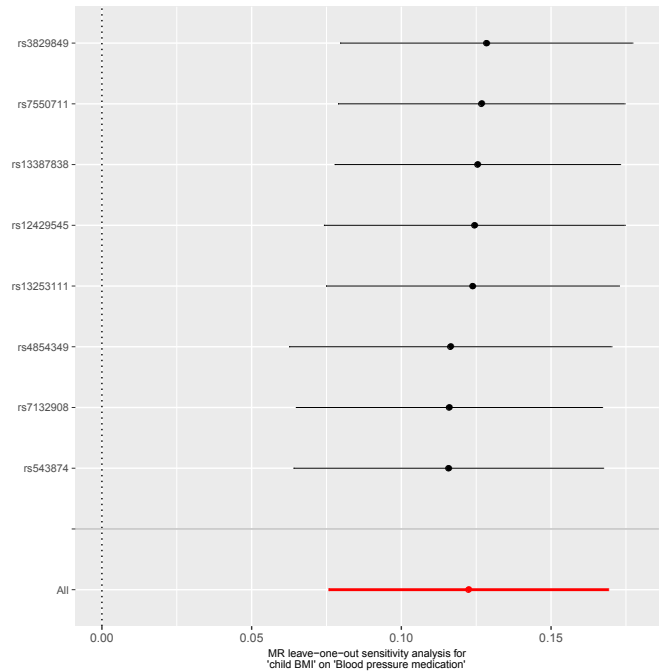
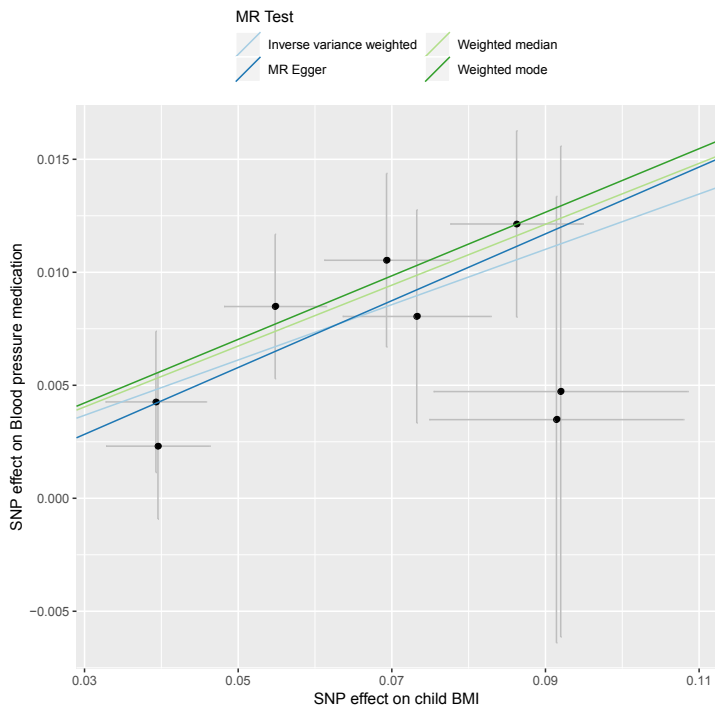


Fig. S4 Scatter plot and leave one out analysis plot for circulatory system traits.

# Blood pressure medication



# Metformin

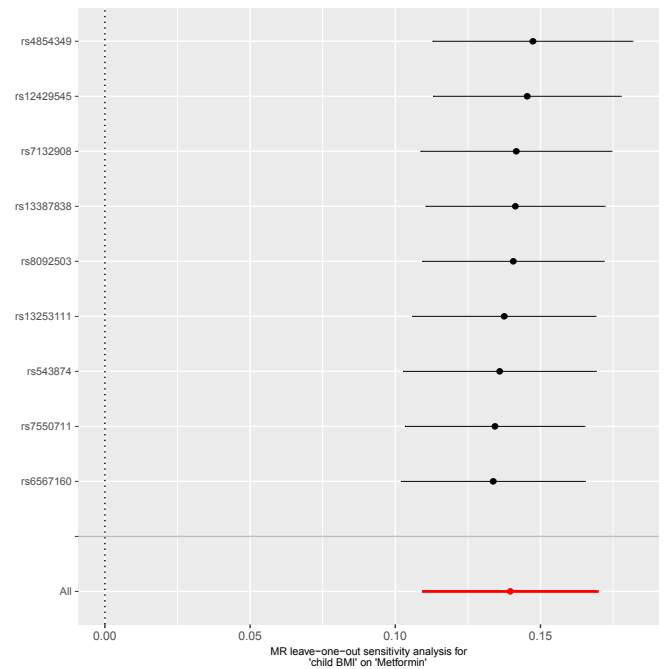
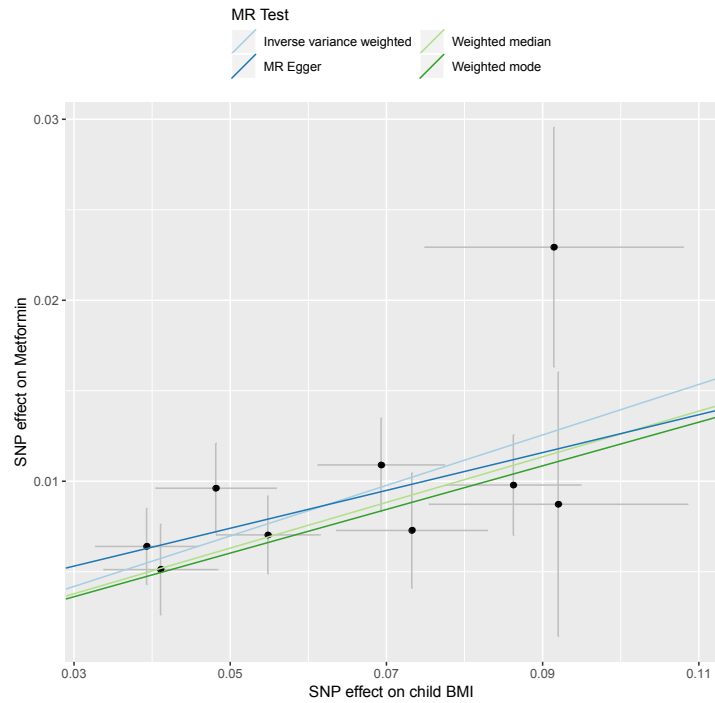


Fig. S5 Scatter plot and leave one out analysis plot for traits of received treatment/medication.

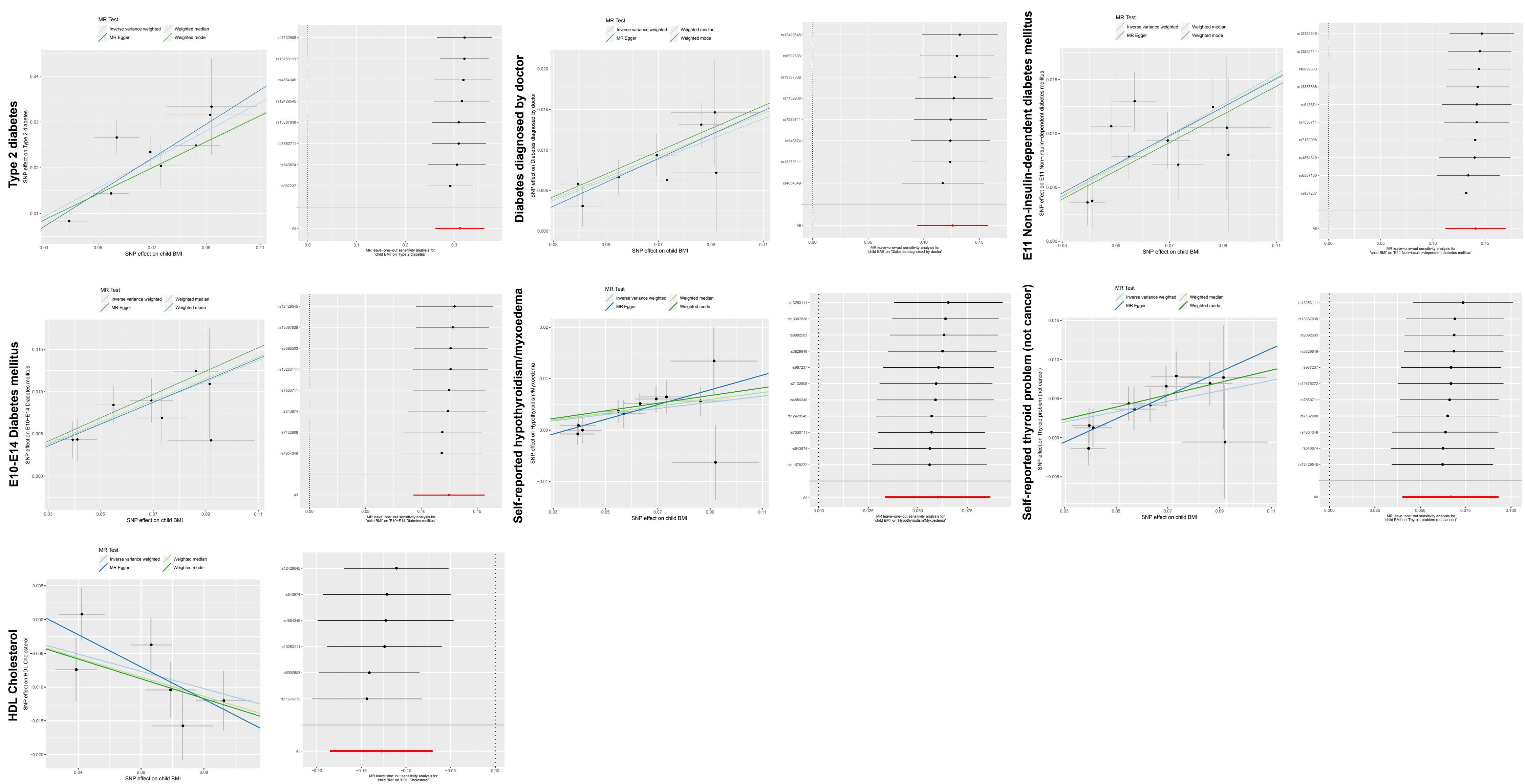


Fig. S6 Scatter plot and leave one out analysis plot for endocrine, nutritional or metabolic traits.

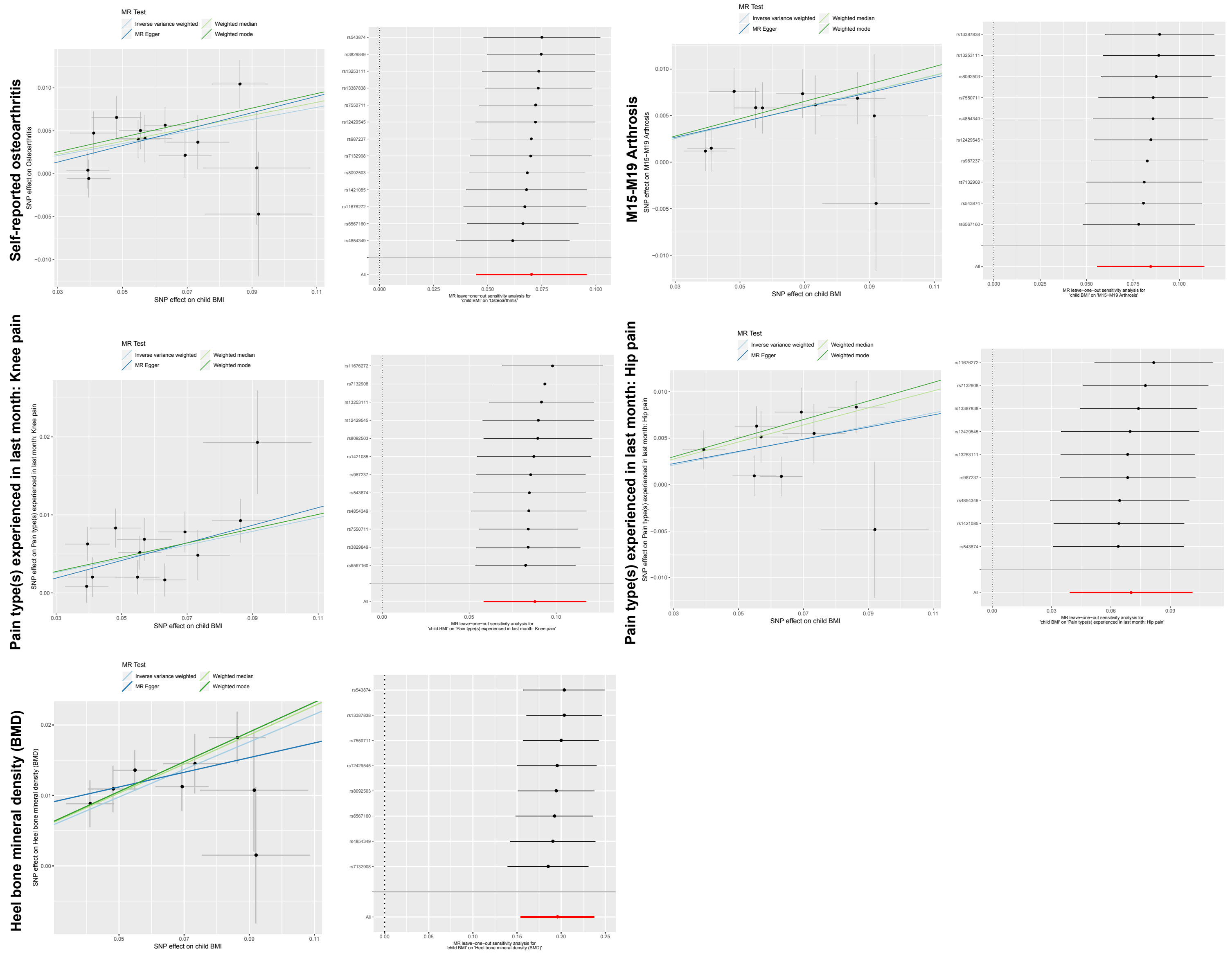
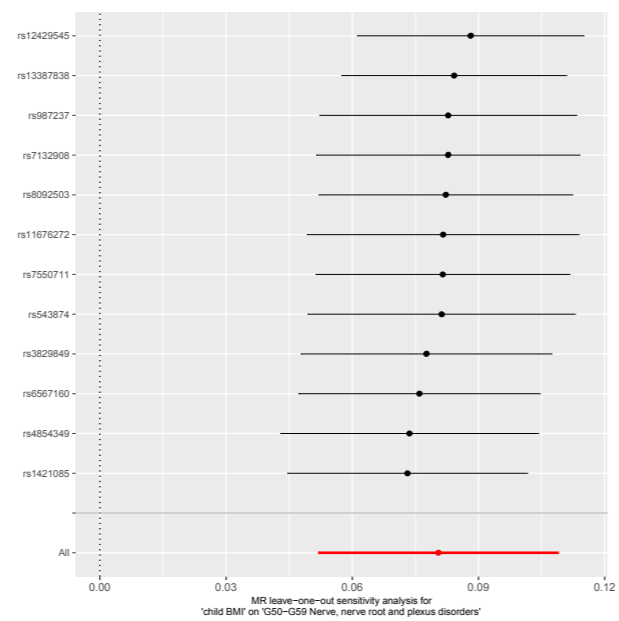
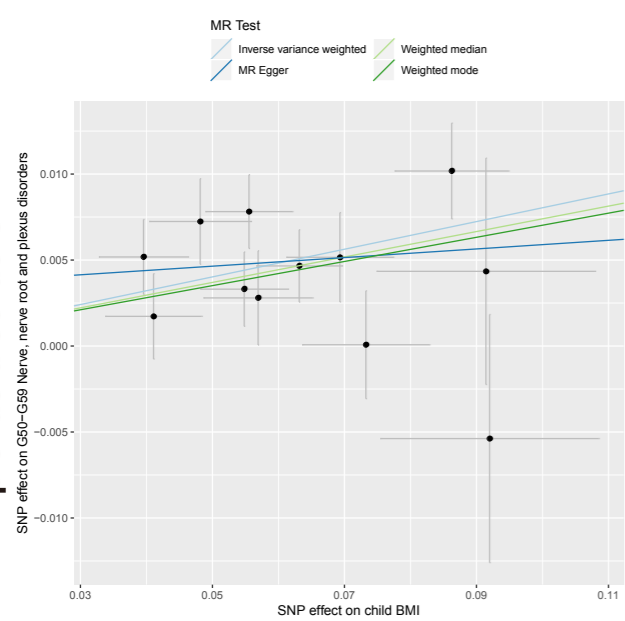
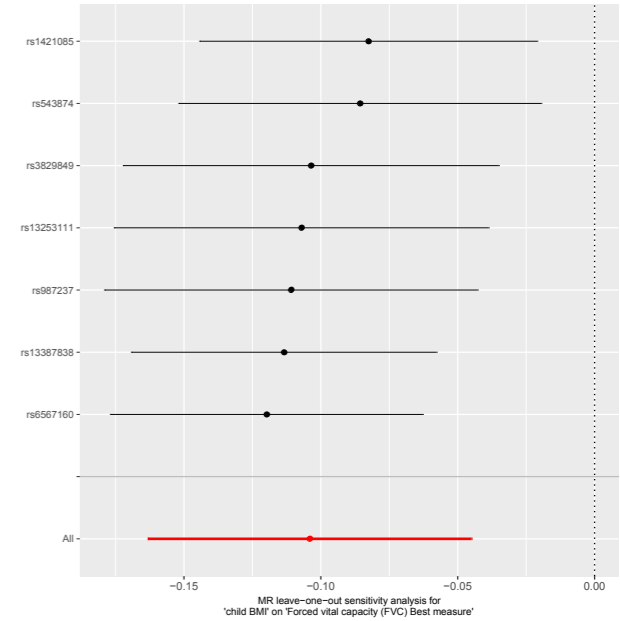
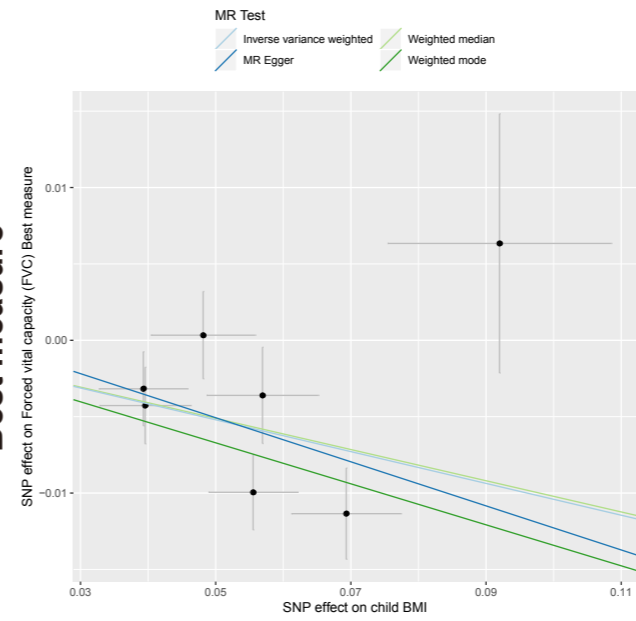


Fig. S7 Scatter plot and leave one out analysis plot for musculoskeletal system traits.

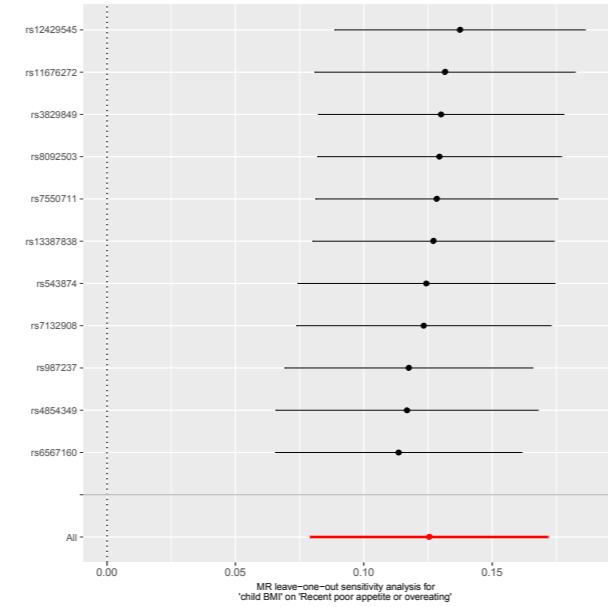
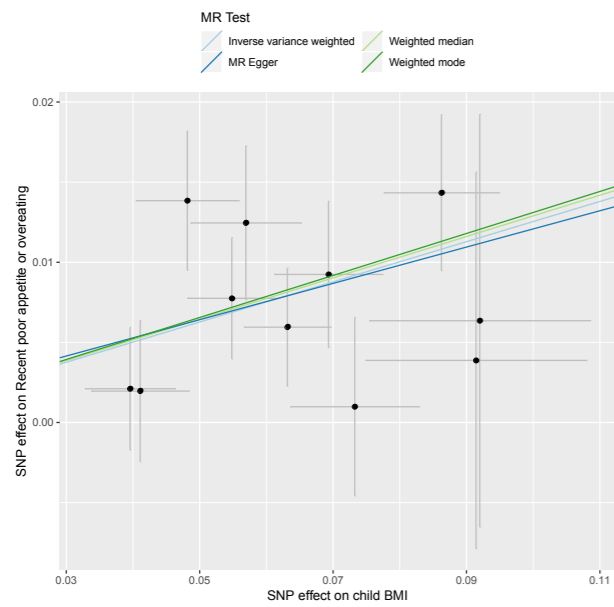
### G50-G59 Nerve, nerve root and plexus disorders



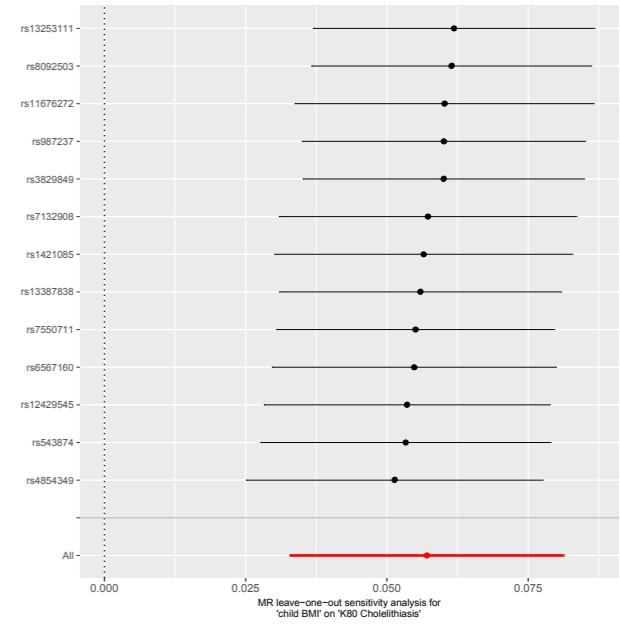
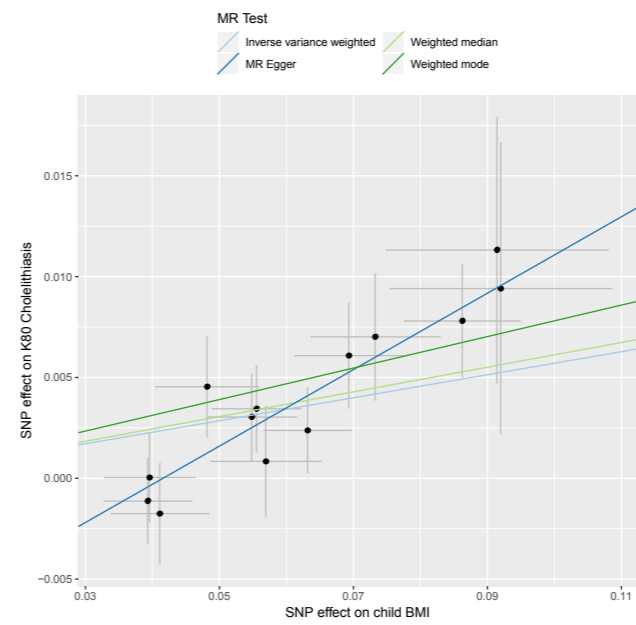
### Forced vital capacity (FVC) Best measure



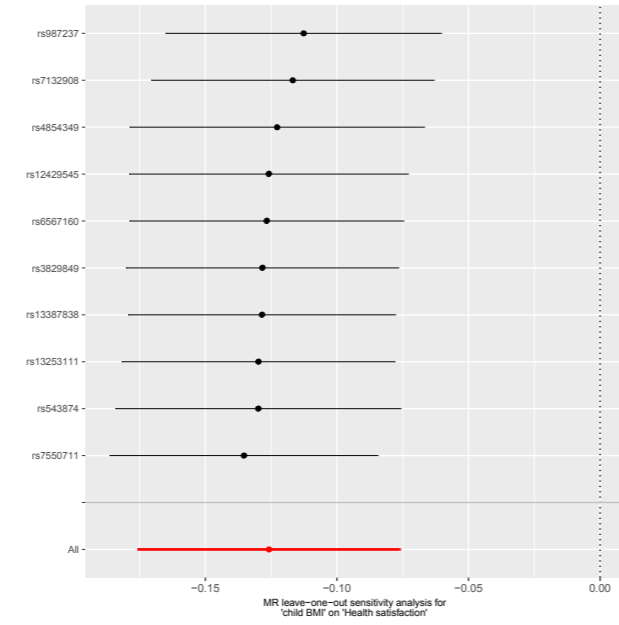
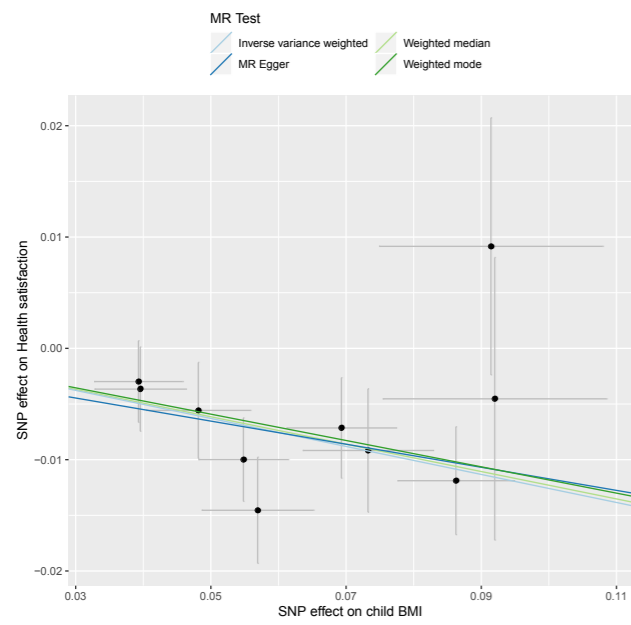
### Recent poor appetite or overeating



### K80 Cholelithiasis



### Health satisfaction



### Weight change during worst episode of depression: Gained weight

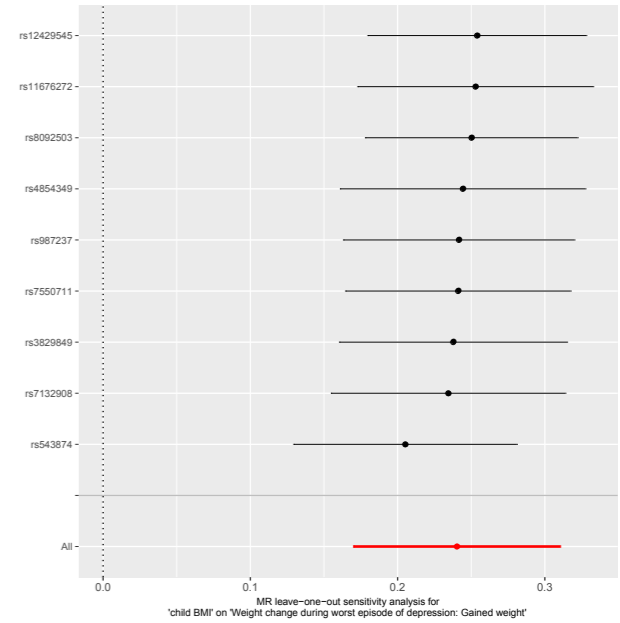
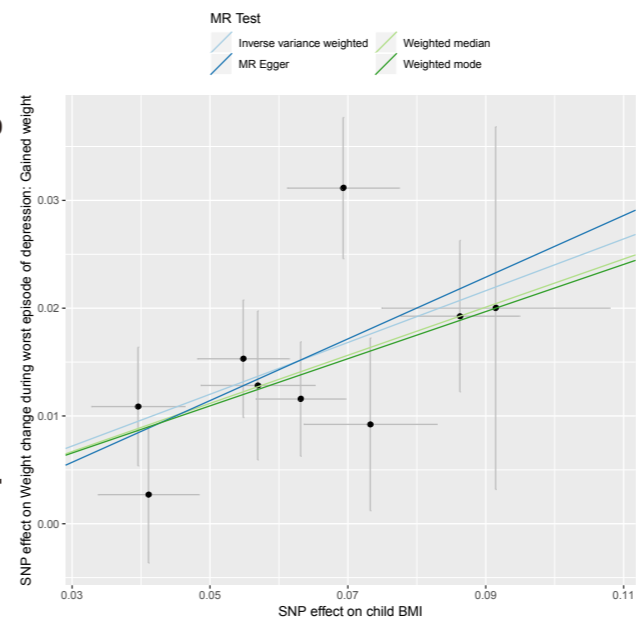
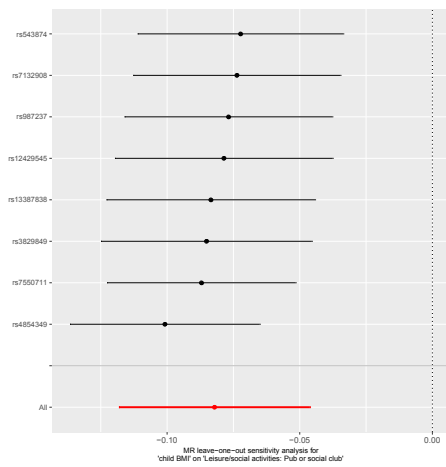
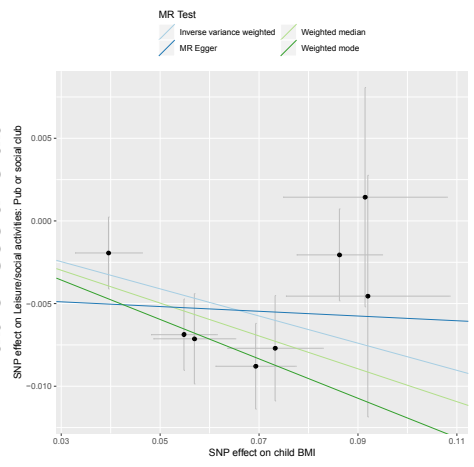


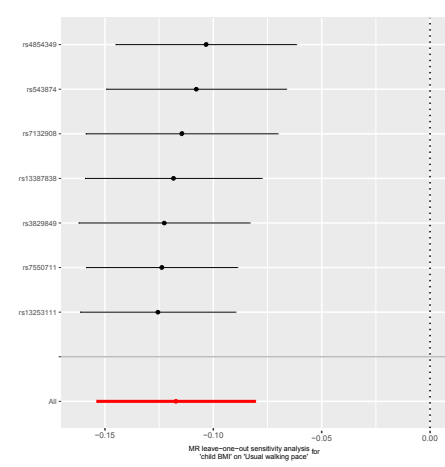
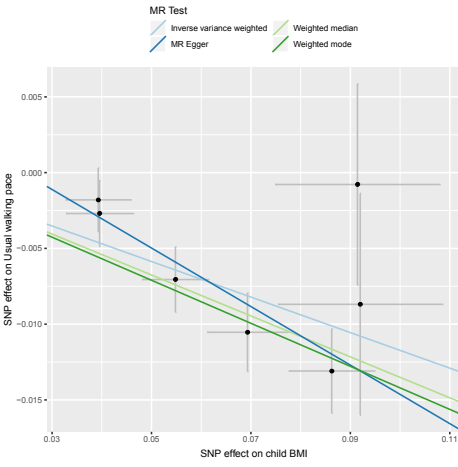
Fig. S8 Scatter plot and leave one out analysis plot for the rest disease-related traits.



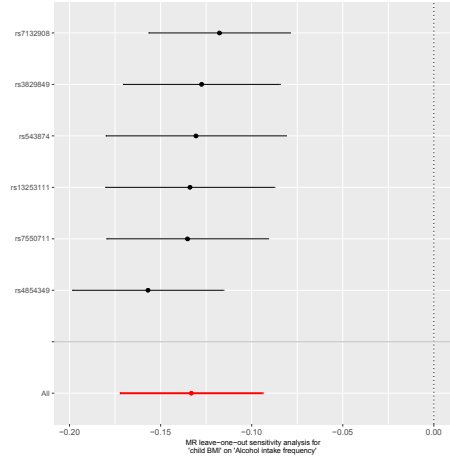
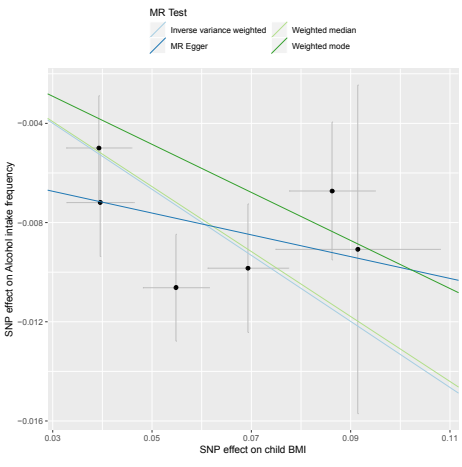
### Leisure/social activities: Pub or social club



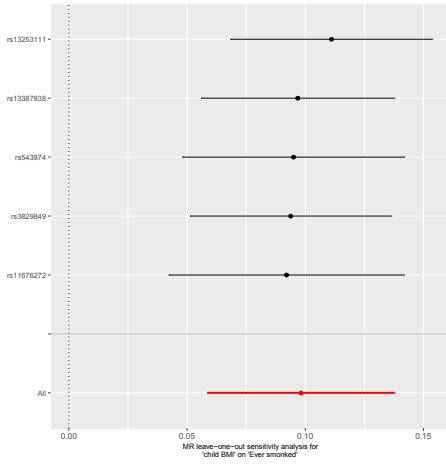
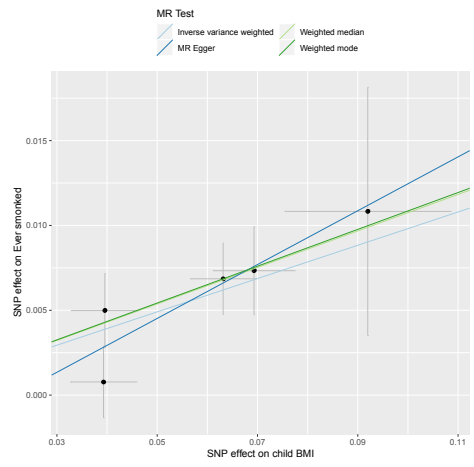
### Usual walking pace



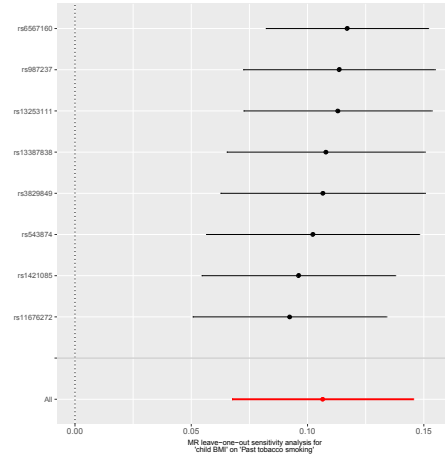
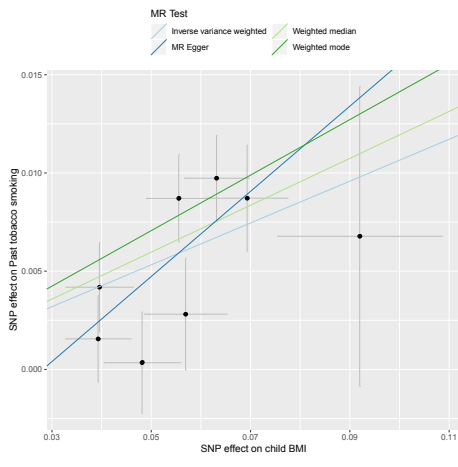
### Alcohol intake frequency



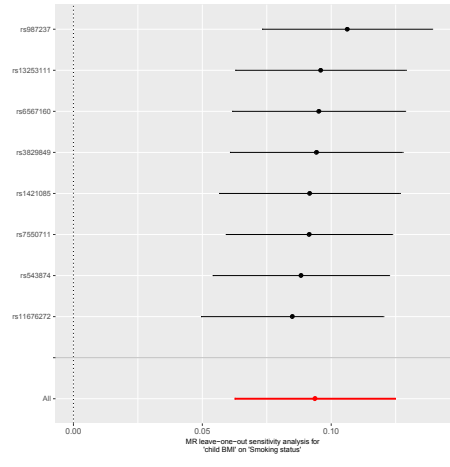
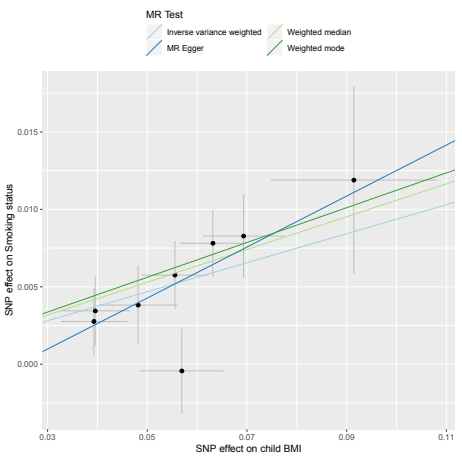
### Ever smoked



### Past tobacco smoking



### Smoking status



### Smoking status: Never

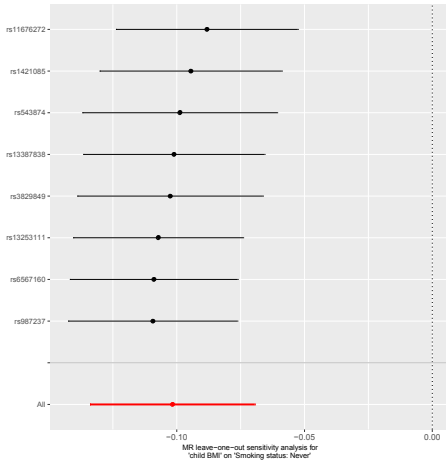
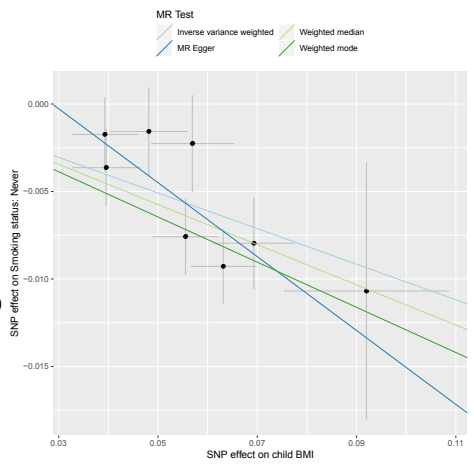
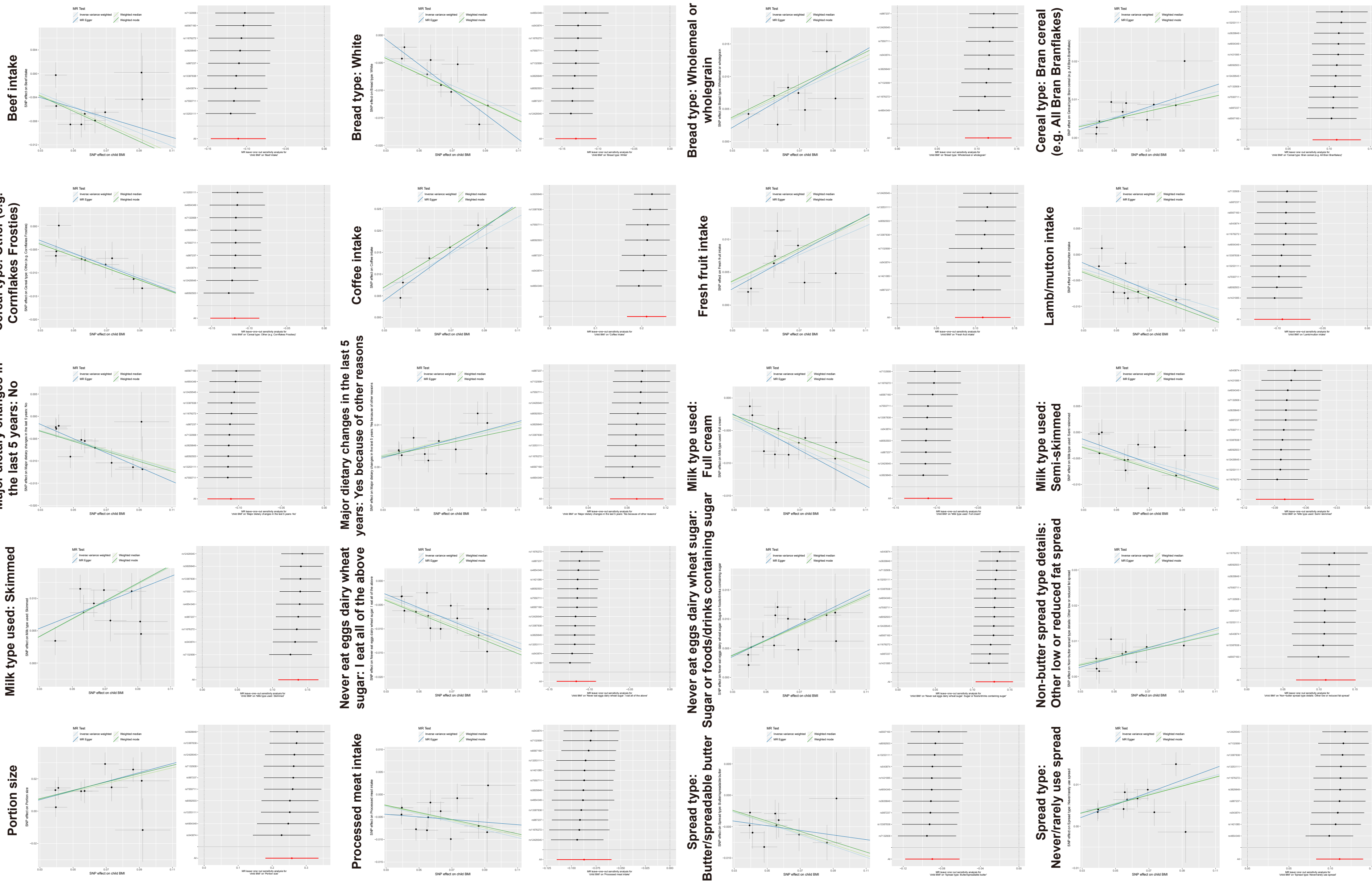


Fig. S9 Scatter plot and leave one out analysis plot for physical activity, smoking behaviors, and alcohol intake frequency.

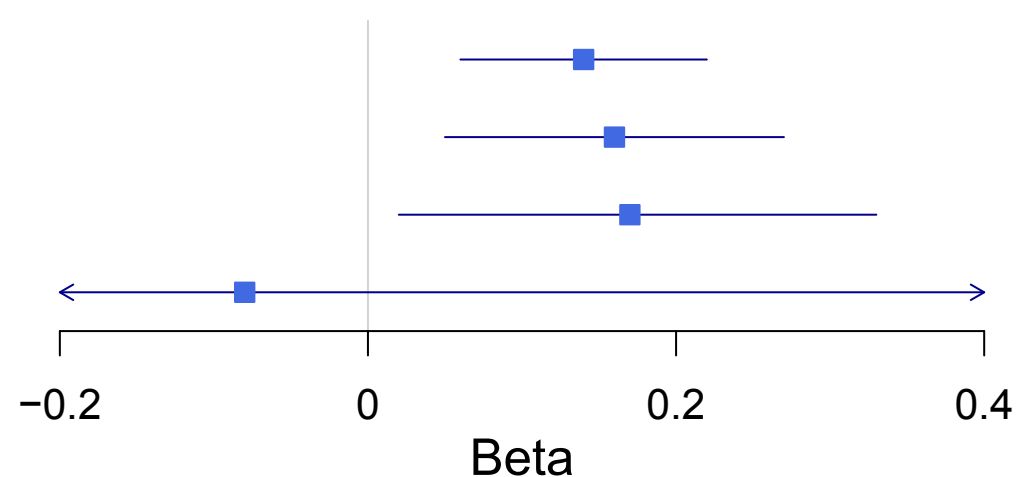
Fig. S10 Scatter plot and leave one out analysis plot for dietary habits.



## Disease count

### Method

Inverse variance weighted  
Weighted median  
Weighted mode  
MR-Egger (SIMEX)



### Beta (95% CI)

0.14 (0.06 to 0.22)

0.16 (0.05 to 0.27)

0.17 (0.02 to 0.33)

-0.08 (-0.63 to 0.46)

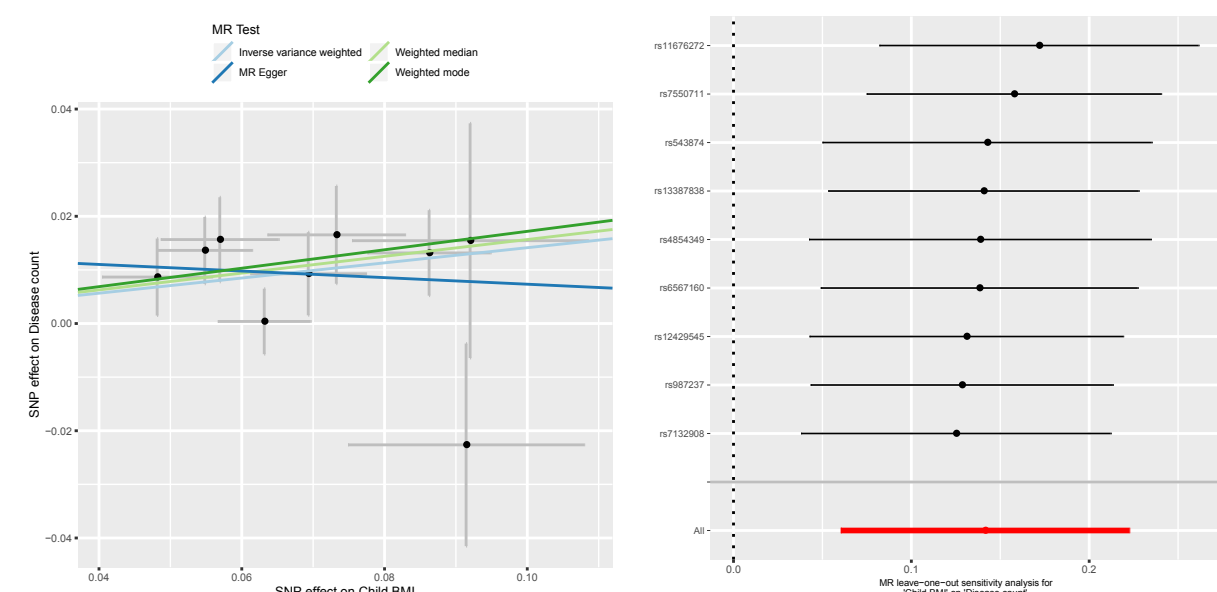
### P value

$6.32 \times 10^{-4}$

$5.72 \times 10^{-3}$

$6.17 \times 10^{-2}$

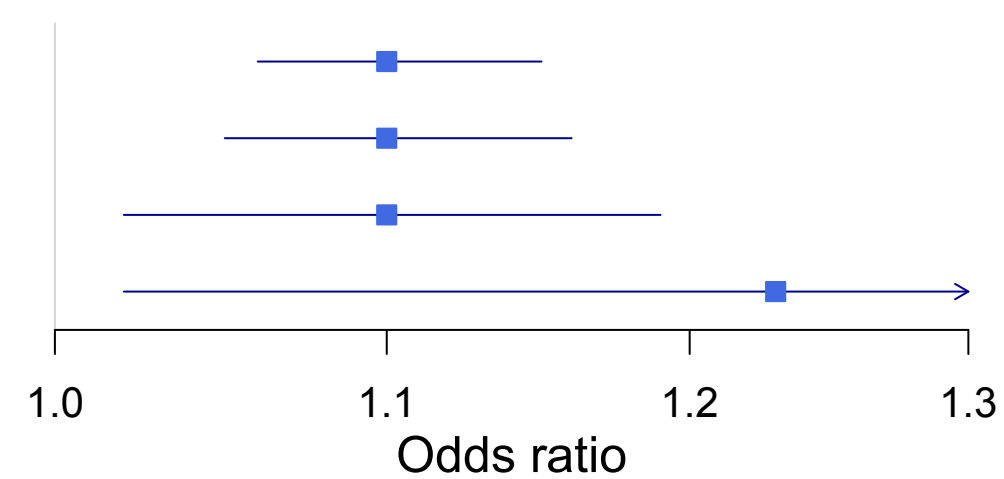
$7.76 \times 10^{-1}$



## Coronary artery disease

### Method

Inverse variance weighted  
Weighted median  
Weighted mode  
MR-Egger (SIMEX)



### Odds ratio (95% CI)

1.10 (1.06 to 1.15)

1.10 (1.05 to 1.16)

1.10 (1.02 to 1.19)

1.23 (1.02 to 1.49)

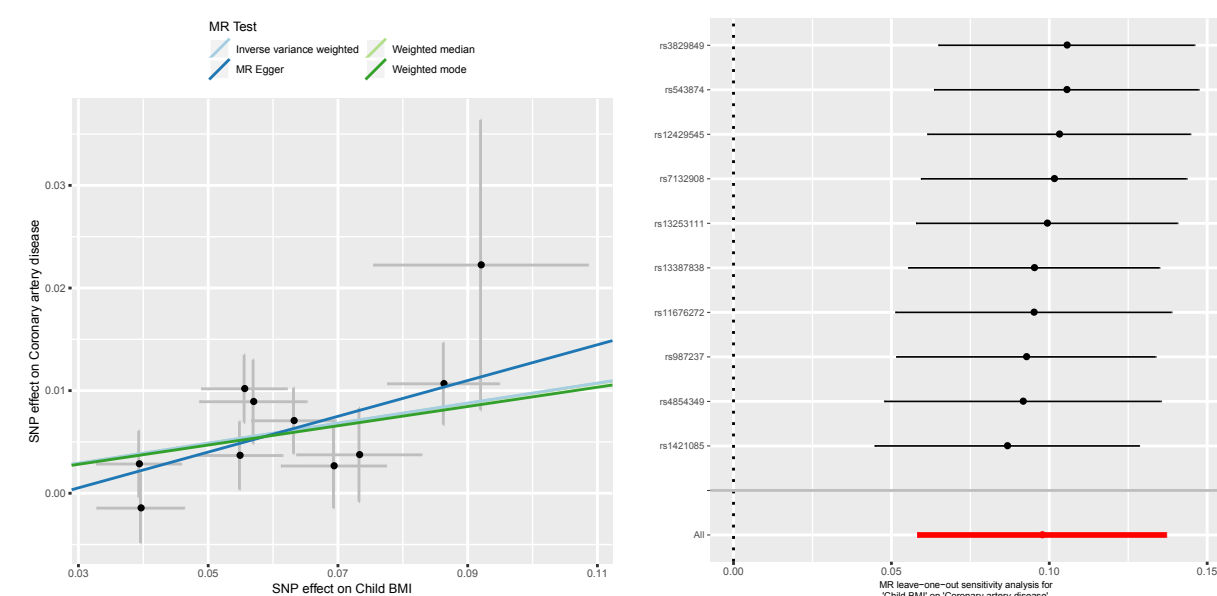
### P value

$1.20 \times 10^{-6}$

$2.65 \times 10^{-4}$

$4.16 \times 10^{-2}$

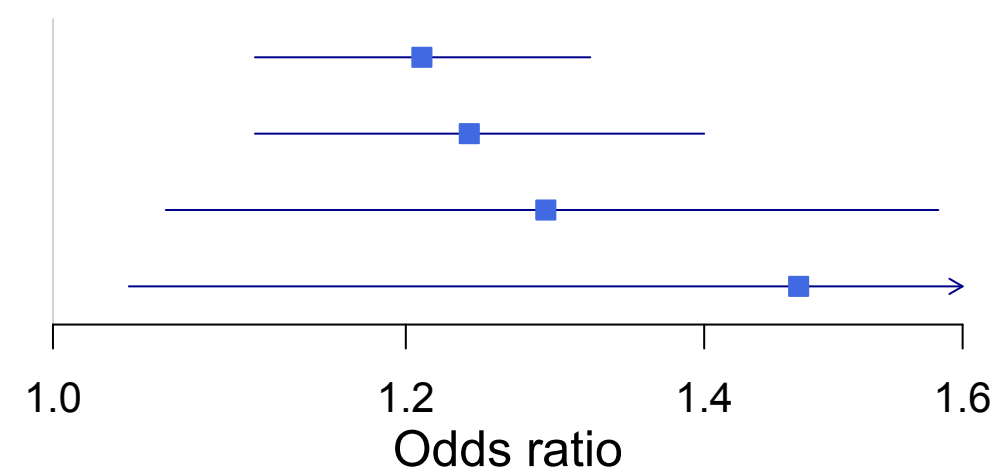
$5.99 \times 10^{-2}$



## Hypertensive Disease

### Method

Inverse variance weighted  
Weighted median  
Weighted mode  
MR-Egger (SIMEX)



### Odds ratio (95% CI)

1.21 (1.11 to 1.32)

1.24 (1.11 to 1.40)

1.29 (1.06 to 1.58)

1.47 (1.04 to 2.09)

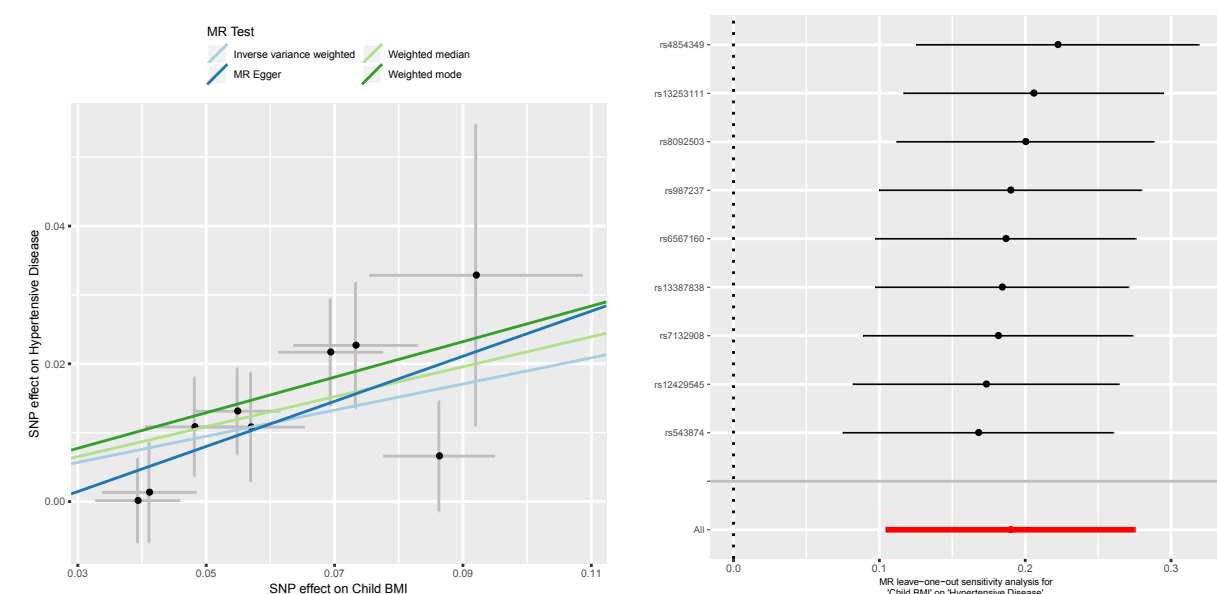
### P value

$1.33 \times 10^{-5}$

$2.78 \times 10^{-4}$

$3.30 \times 10^{-2}$

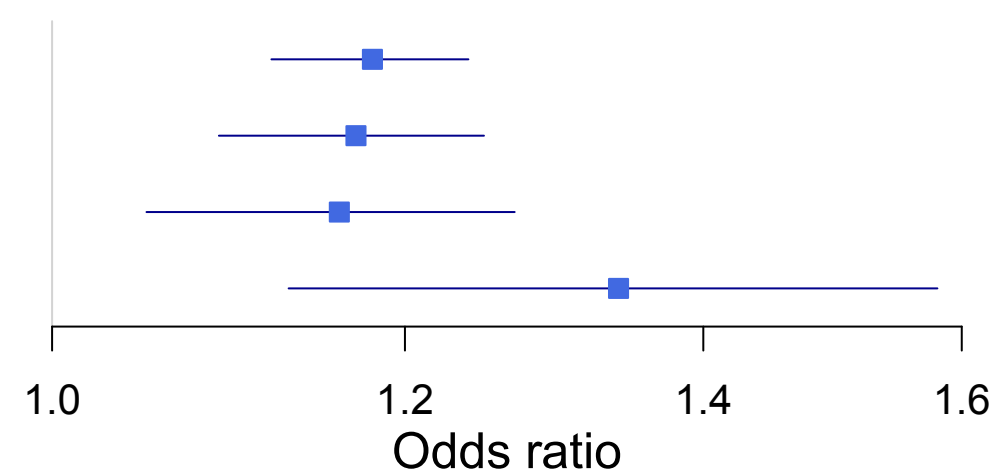
$6.84 \times 10^{-2}$



## Type 2 diabetes

### Method

Inverse variance weighted  
Weighted median  
Weighted mode  
MR-Egger (SIMEX)



### Odds ratio (95% CI)

1.18 (1.12 to 1.24)

1.17 (1.09 to 1.25)

1.16 (1.05 to 1.27)

1.34 (1.13 to 1.58)

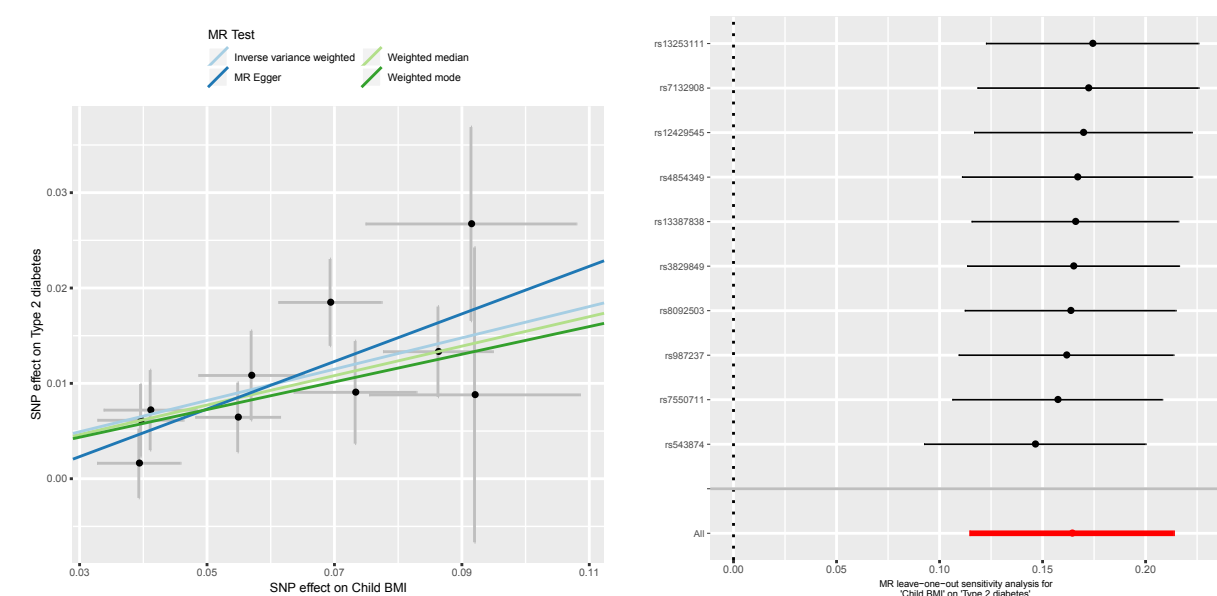
### P value

$8.85 \times 10^{-11}$

$2.33 \times 10^{-5}$

$1.29 \times 10^{-2}$

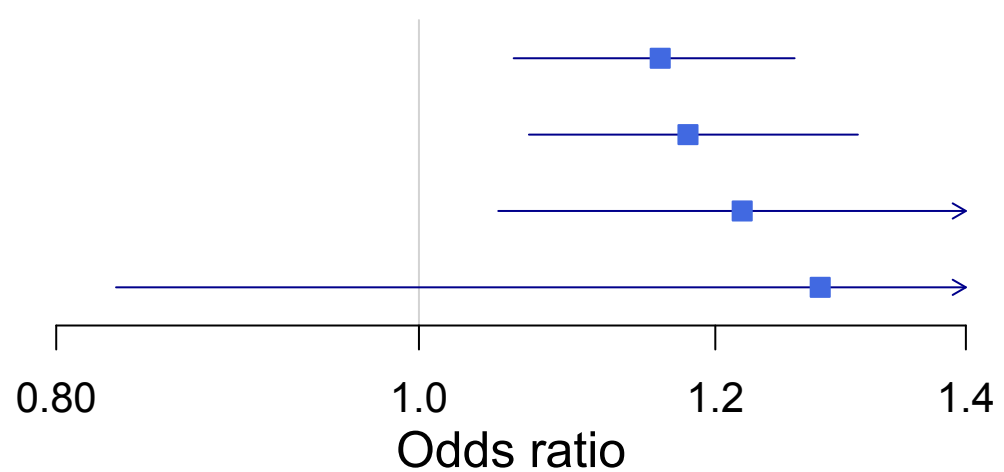
$9.24 \times 10^{-3}$



## Osteoarthritis

### Method

Inverse variance weighted  
Weighted median  
Weighted mode  
MR-Egger (SIMEX)



### Odds ratio (95% CI)

1.16 (1.06 to 1.26)

1.18 (1.07 to 1.31)

1.22 (1.05 to 1.41)

1.28 (0.83 to 1.99)

### P value

$1.04 \times 10^{-3}$

$1.40 \times 10^{-3}$

$2.53 \times 10^{-2}$

$2.93 \times 10^{-1}$

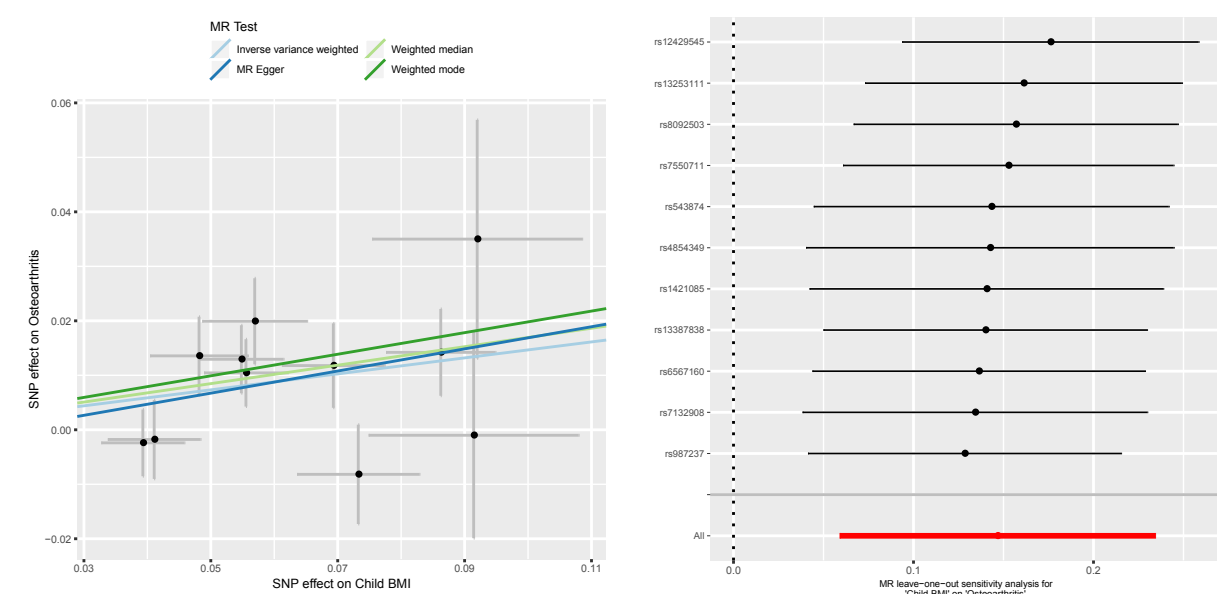
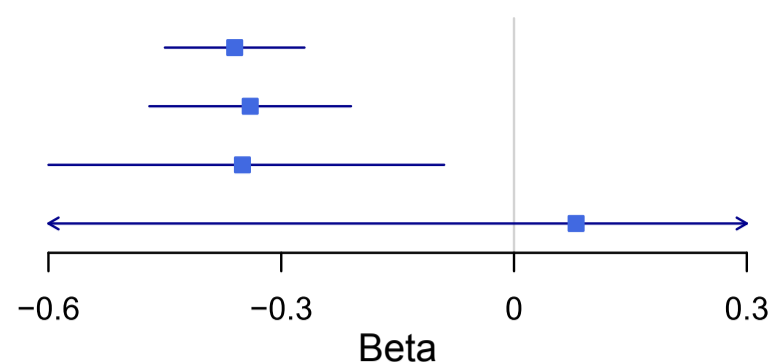


Fig. S11 Summary Mendelian randomization (MR) estimates derived from the inverse-variance weighted, MR-Egger, weighted median and weighted mode -based methods for additional datasets. Childhood BMI was used as exposure and significant associations were detected for these traits. Scatter plot and leave one out analysis plot for each trait are also shown.

## Overall health rating

### Method

Inverse variance weighted  
Weighted median  
Weighted mode  
MR-Egger (SIMEX)

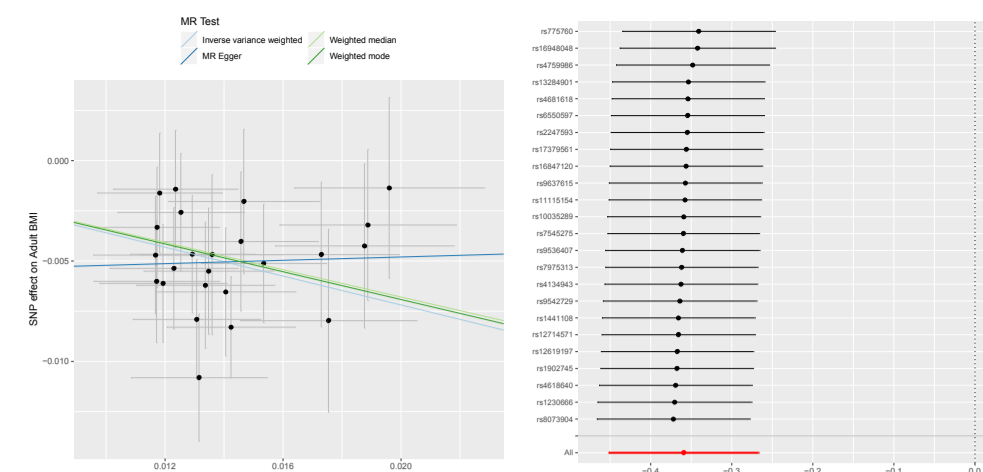


### Beta (95% CI)

-0.36 (-0.45 to -0.27)  
-0.34 (-0.47 to -0.21)  
-0.35 (-0.60 to -0.09)  
0.08 (-0.65 to 0.81)

### P value

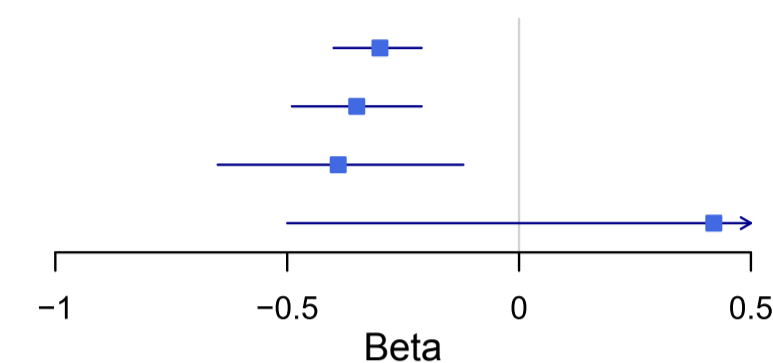
$2.41 \times 10^{-14}$   
 $1.91 \times 10^{-7}$   
 $1.31 \times 10^{-2}$   
 $8.39 \times 10^{-1}$



## Alcohol intake frequency

### Method

Inverse variance weighted  
Weighted median  
Weighted mode  
MR-Egger (SIMEX)

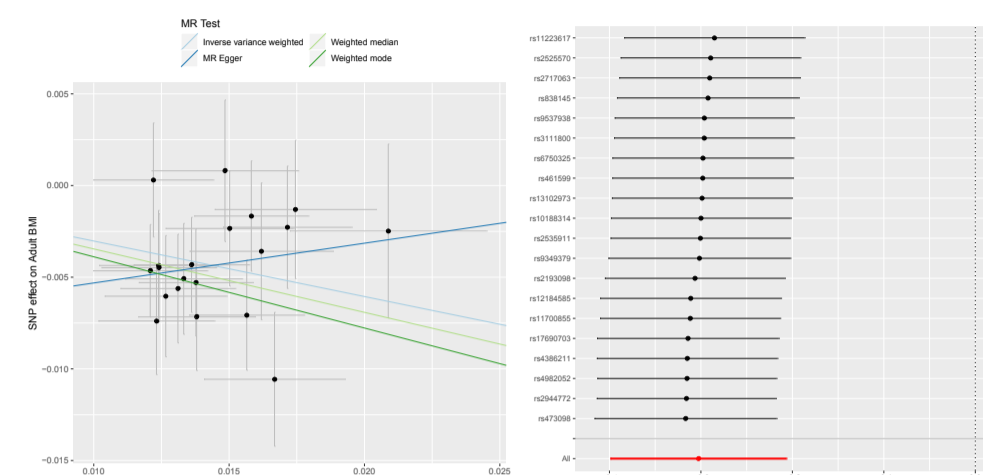


### Beta (95% CI)

-0.30 (-0.40 to -0.21)  
-0.35 (-0.49 to -0.21)  
-0.39 (-0.65 to -0.12)  
0.42 (-0.50 to 1.35)

### P value

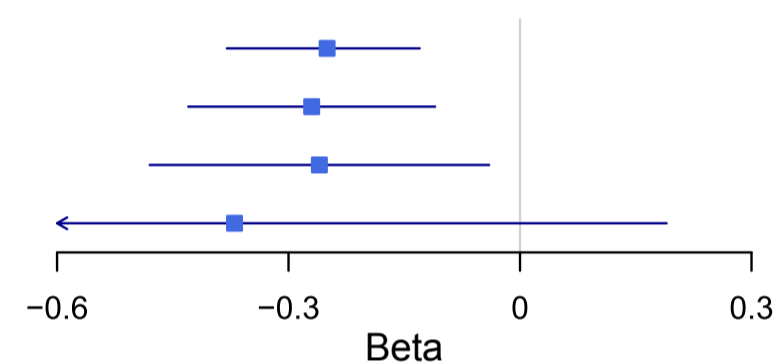
$6.86 \times 10^{-10}$   
 $1.16 \times 10^{-6}$   
 $9.97 \times 10^{-3}$   
 $3.83 \times 10^{-1}$



## Usual walking pace

### Method

Inverse variance weighted  
Weighted median  
Weighted mode  
MR-Egger (SIMEX)

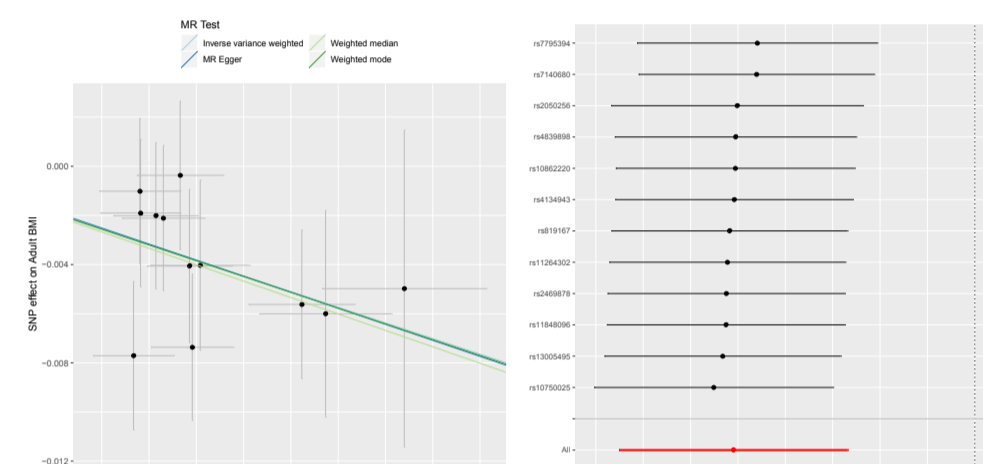


### Beta (95% CI)

-0.25 (-0.38 to -0.13)  
-0.27 (-0.43 to -0.11)  
-0.26 (-0.48 to -0.04)  
-0.37 (-0.94 to 0.19)

### P value

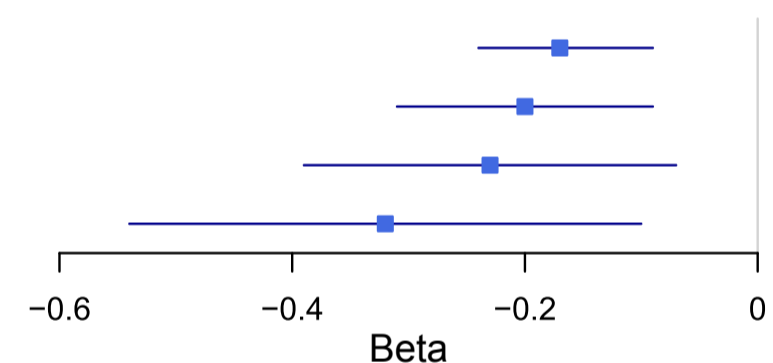
$3.53 \times 10^{-5}$   
 $1.23 \times 10^{-3}$   
 $4.29 \times 10^{-2}$   
 $2.26 \times 10^{-1}$



## Diabetes diagnosed by doctor

### Method

Inverse variance weighted  
Weighted median  
Weighted mode  
MR-Egger (SIMEX)

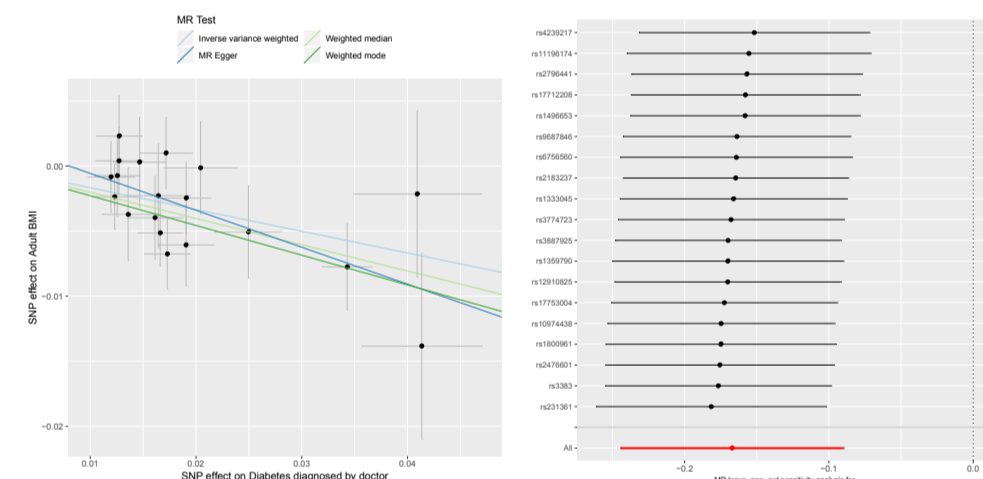


### Beta (95% CI)

-0.17 (-0.24 to -0.09)  
-0.20 (-0.31 to -0.09)  
-0.23 (-0.39 to -0.07)  
-0.32 (-0.54 to -0.10)

### P value

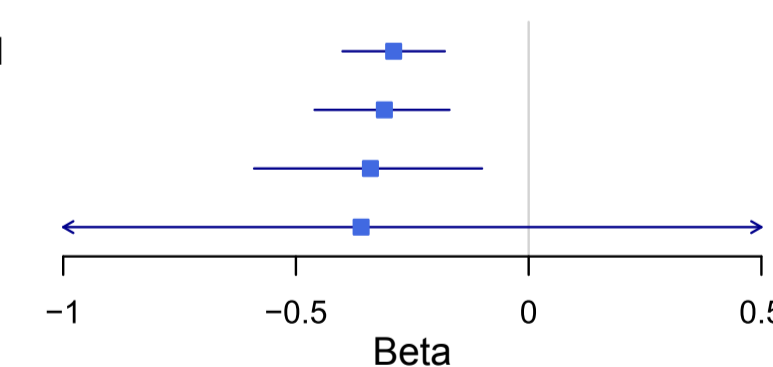
$2.22 \times 10^{-5}$   
 $3.24 \times 10^{-4}$   
 $1.09 \times 10^{-2}$   
 $9.98 \times 10^{-3}$



## E10-E14 Diabetes mellitus

### Method

Inverse variance weighted  
Weighted median  
Weighted mode  
MR-Egger (SIMEX)

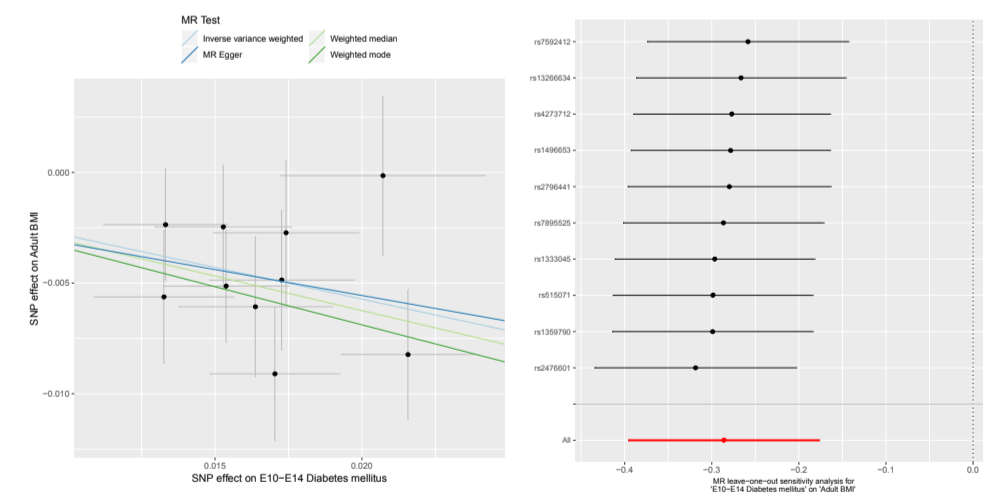


### Beta (95% CI)

-0.29 (-0.40 to -0.18)  
-0.31 (-0.46 to -0.17)  
-0.34 (-0.59 to -0.10)  
-0.36 (-1.33 to 0.60)

### P value

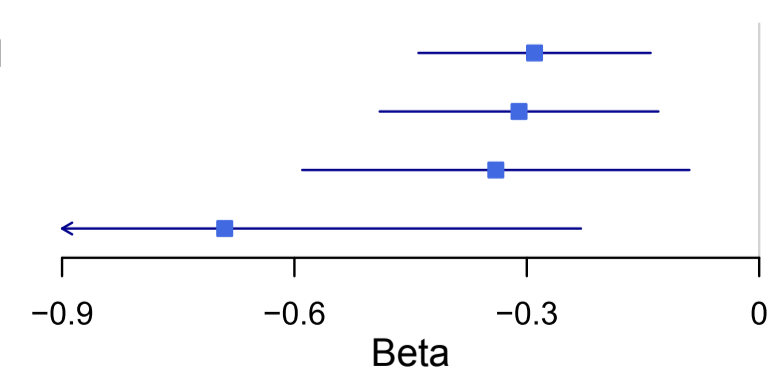
$3.05 \times 10^{-7}$   
 $2.53 \times 10^{-5}$   
 $2.24 \times 10^{-2}$   
 $4.84 \times 10^{-1}$



## E11 Non-insulin-dependent diabetes mellitus

### Method

Inverse variance weighted  
Weighted median  
Weighted mode  
MR-Egger (SIMEX)



### Beta (95% CI)

-0.29 (-0.44 to -0.14)  
-0.31 (-0.49 to -0.13)  
-0.34 (-0.59 to -0.09)  
-0.69 (-1.16 to -0.23)

### P value

$1.26 \times 10^{-4}$   
 $7.79 \times 10^{-4}$   
 $5.61 \times 10^{-2}$   
 $6.25 \times 10^{-2}$

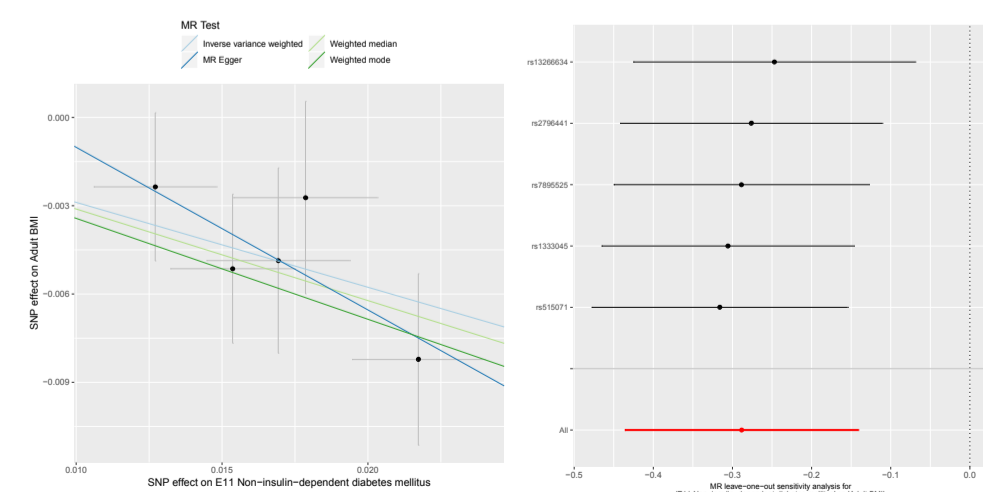


Fig. S12 Summary Mendelian randomization (MR) estimates derived from the main inverse-variance weighted, MR-Egger, weighted median and weighted mode-based methods for reverse analyses using adulthood BMI as outcome. Scatter plot and leave one out analysis plot for each trait are also shown.