

*Insulin Secretion at 30 minutes on Body Mass Index*

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**Results from two sample MR:**

| method                    | nsnp | b         | se        | pval      |
|---------------------------|------|-----------|-----------|-----------|
| MR Egger                  | 3    | 0.8460177 | 0.5951939 | 0.3903035 |
| Weighted median           | 3    | 0.0655322 | 0.0161267 | 0.0000483 |
| Inverse variance weighted | 3    | 0.1432858 | 0.0753950 | 0.0573718 |
| Simple mode               | 3    | 0.0760232 | 0.0243668 | 0.0892001 |
| Weighted mode             | 3    | 0.0572572 | 0.0155849 | 0.0667551 |

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**Heterogeneity tests**

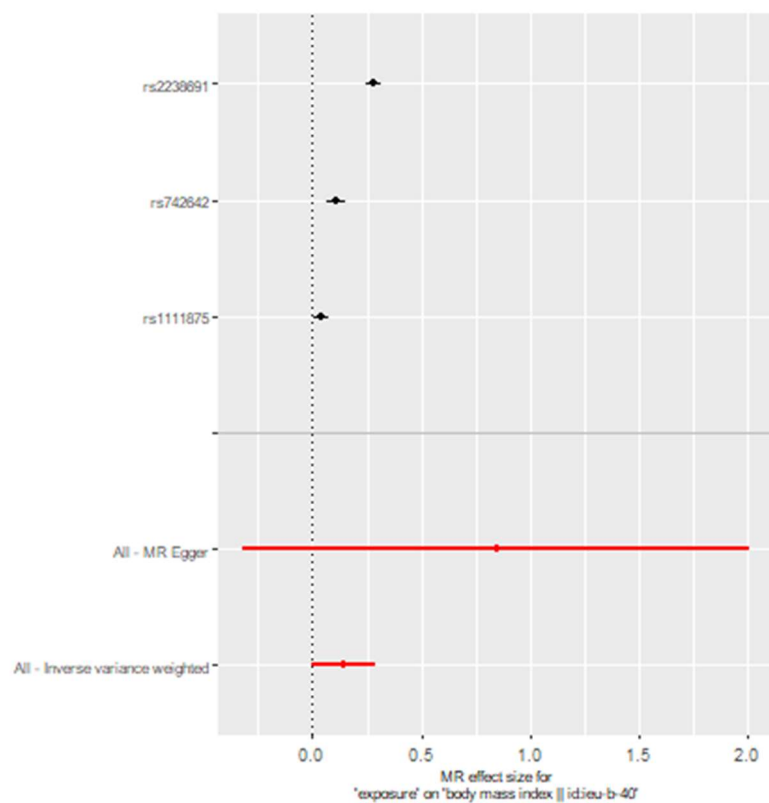
| method                    | Q         | Q_df | Q_pval |
|---------------------------|-----------|------|--------|
| MR Egger                  | 43.77679  | 1    | 0      |
| Inverse variance weighted | 105.62422 | 2    | 0      |

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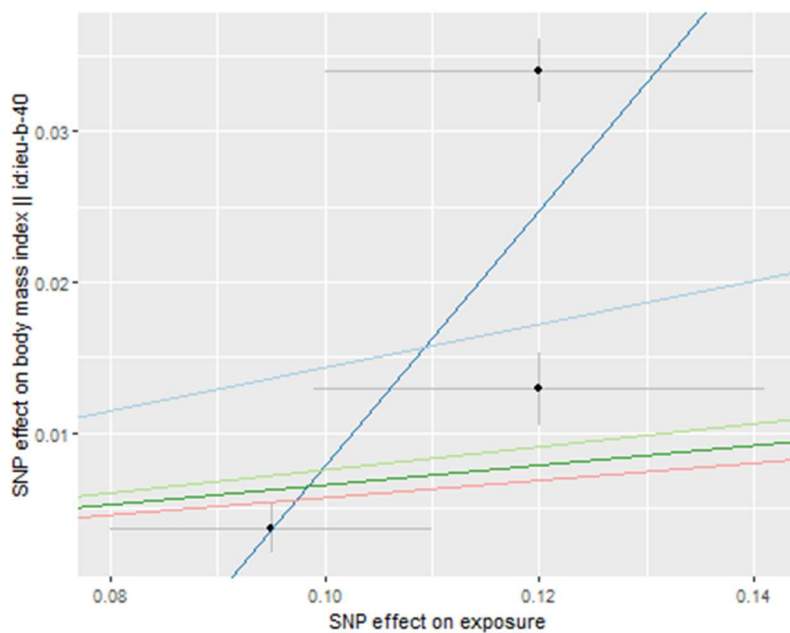
**Test for directional horizontal pleiotropy**

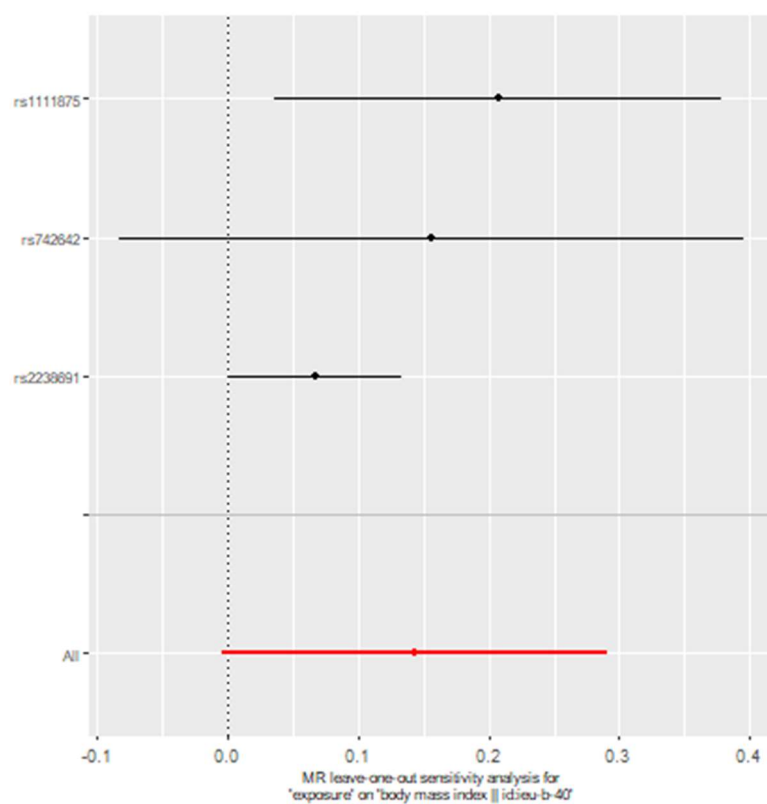
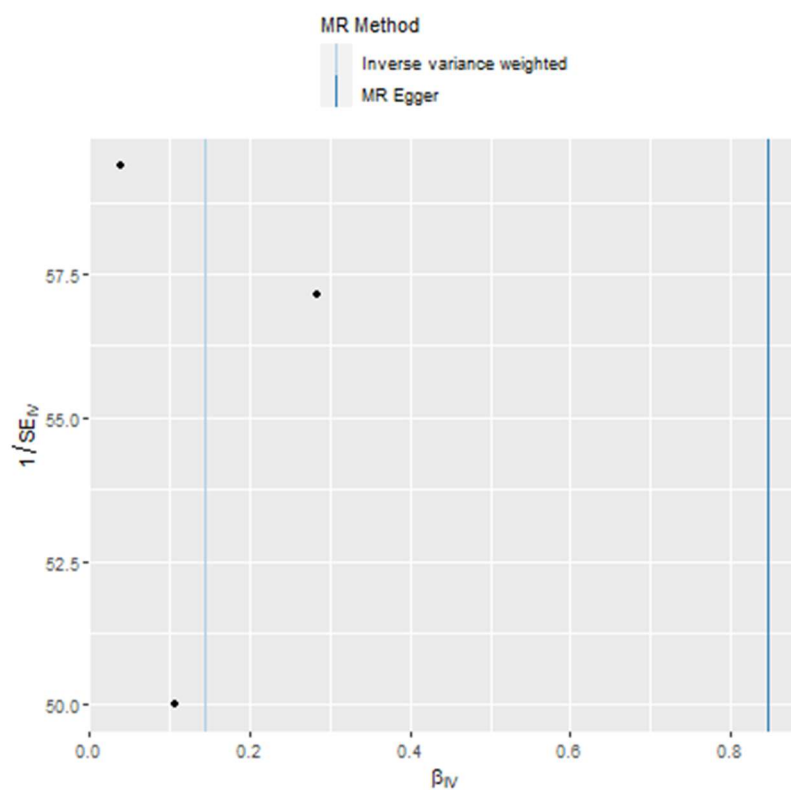
| egger_intercept | se        | pval     |
|-----------------|-----------|----------|
| -0.0766717      | 0.0645054 | 0.445273 |

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#### MR Test





### *Insulin Secretion at 30 minutes on Waist-to-Hip Ratio*

## Results from two sample MR:

| method                    | nsnp | b          | se        | pval      |
|---------------------------|------|------------|-----------|-----------|
| MR Egger                  | 3    | 0.6760108  | 0.6718693 | 0.4980439 |
| Weighted median           | 3    | -0.0411342 | 0.0169318 | 0.0151236 |
| Inverse variance weighted | 3    | 0.0253663  | 0.0763485 | 0.7397050 |
| Simple mode               | 3    | -0.0500881 | 0.0171729 | 0.1001934 |
| Weighted mode             | 3    | -0.0500881 | 0.0146561 | 0.0759884 |

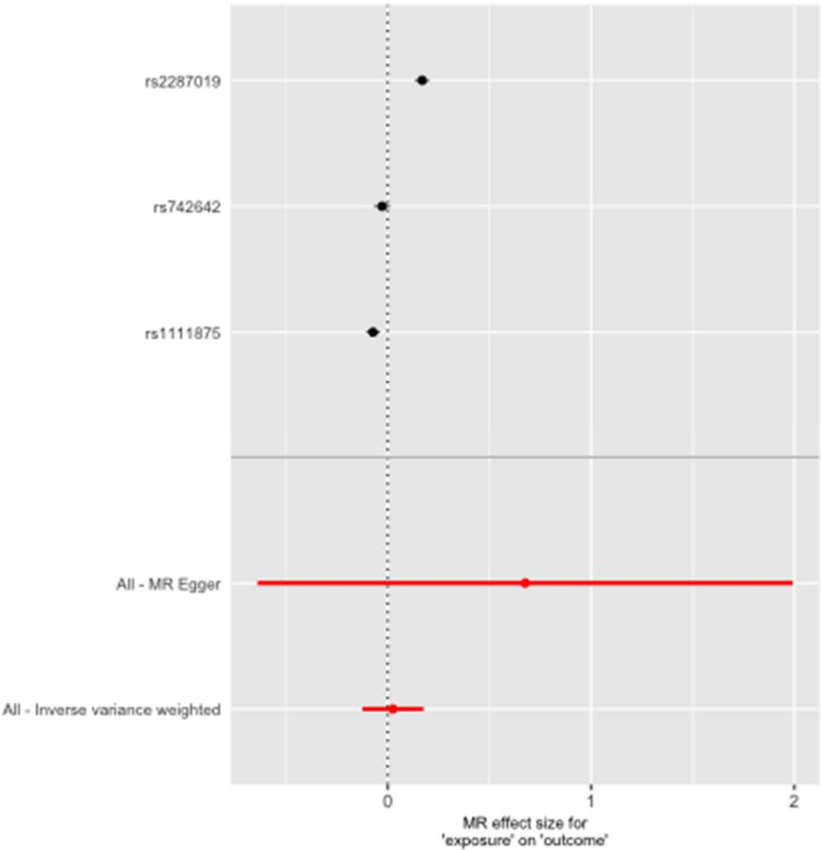
## Heterogeneity tests

| method                    | Q        | Q_df | Q_pval |
|---------------------------|----------|------|--------|
| MR Egger                  | 50.22182 | 1    | 0      |
| Inverse variance weighted | 97.95270 | 2    | 0      |

## Test for directional horizontal pleiotropy

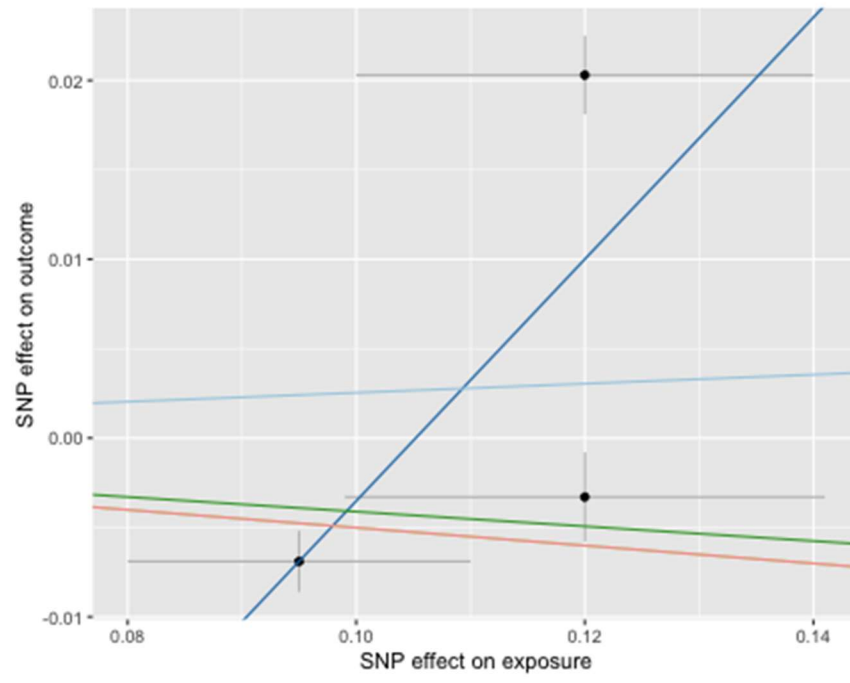
| egger_intercept | se        | pval      |
|-----------------|-----------|-----------|
| -0.071121       | 0.0729532 | 0.5080955 |

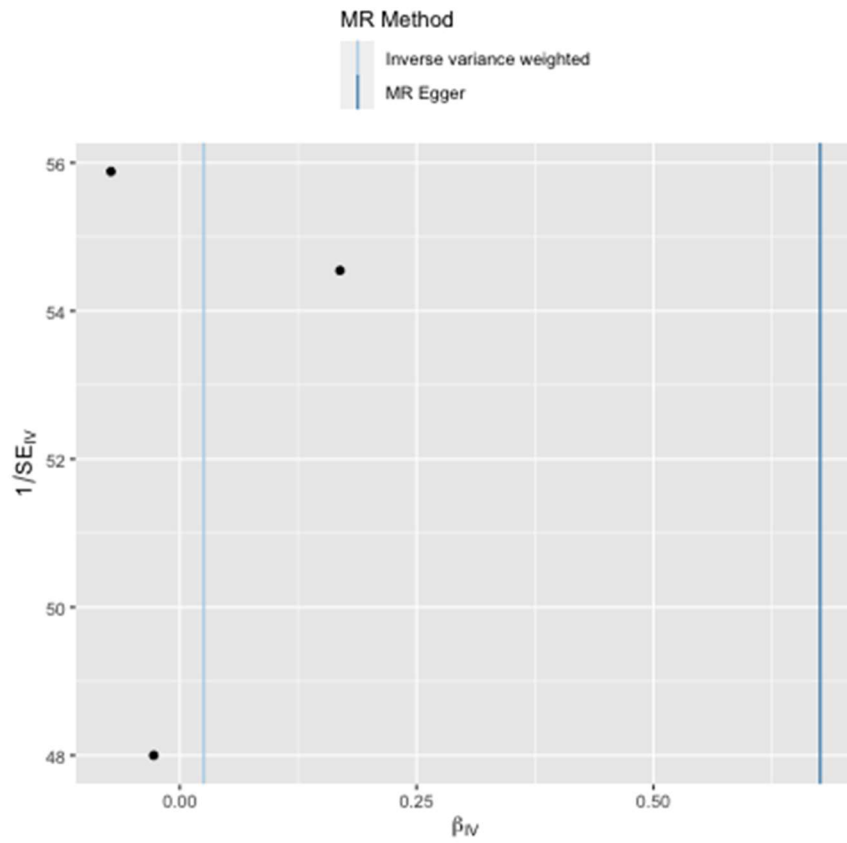
# Forest plot of single SNP MR



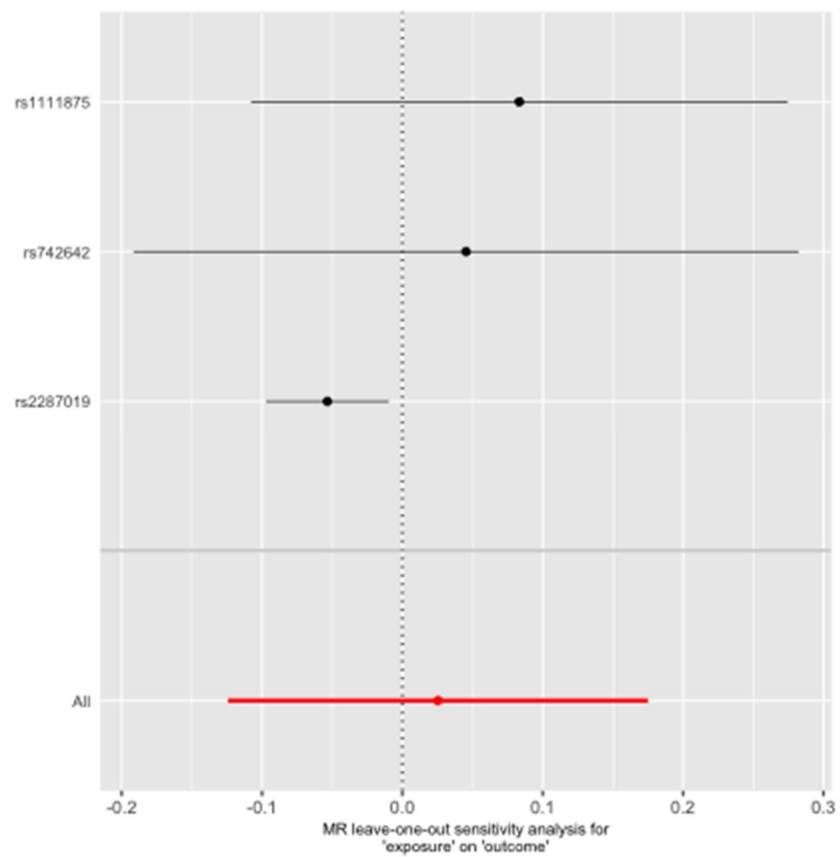
# MR Test

- Inverse variance weighted
- MR Egger
- Simple mode
- Weighted median
- Weighted mode





## Leave-one-out sensitivity analysis





## *Insulin Secretion at 30 minutes on Waist-to-Hip Ratio adjusted for Body Mass Index*

### Results from two sample MR:

| method                    | nsnp | b          | se        | pval      |
|---------------------------|------|------------|-----------|-----------|
| MR Egger                  | 3    | 0.3172964  | 0.3615689 | 0.5414587 |
| Weighted median           | 3    | -0.0560162 | 0.0176360 | 0.0014920 |
| Inverse variance weighted | 3    | -0.0619744 | 0.0429254 | 0.1488035 |
| Simple mode               | 3    | -0.1013431 | 0.0224816 | 0.0458531 |
| Weighted mode             | 3    | -0.1006563 | 0.0568591 | 0.2186994 |

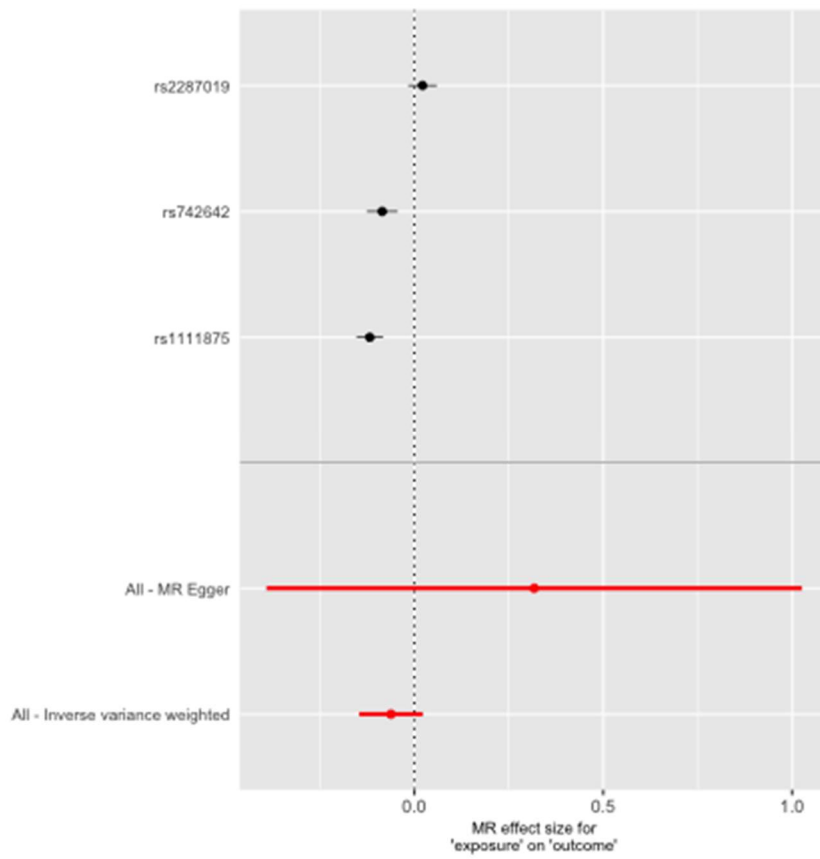
### Heterogeneity tests

| method                    | Q        | Q_df | Q_pval    |
|---------------------------|----------|------|-----------|
| MR Egger                  | 14.19757 | 1    | 0.0001646 |
| Inverse variance weighted | 30.03037 | 2    | 0.0000003 |

### Test for directional horizontal pleiotropy

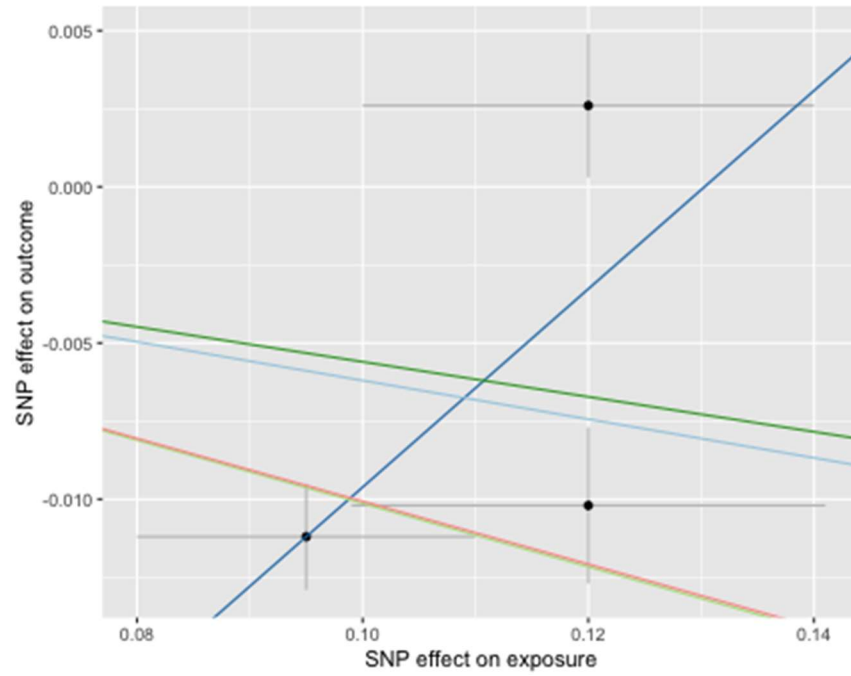
| egger_intercept | se      | pval      |
|-----------------|---------|-----------|
| -0.0413432      | 0.03915 | 0.4826587 |

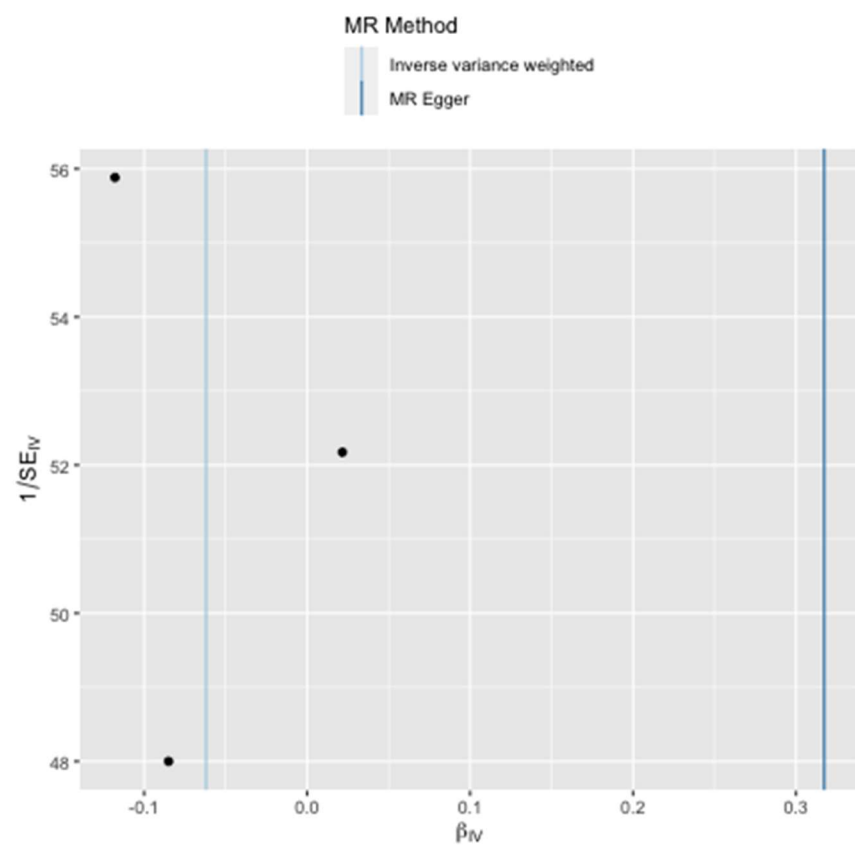
# Forest plot of single SNP MR

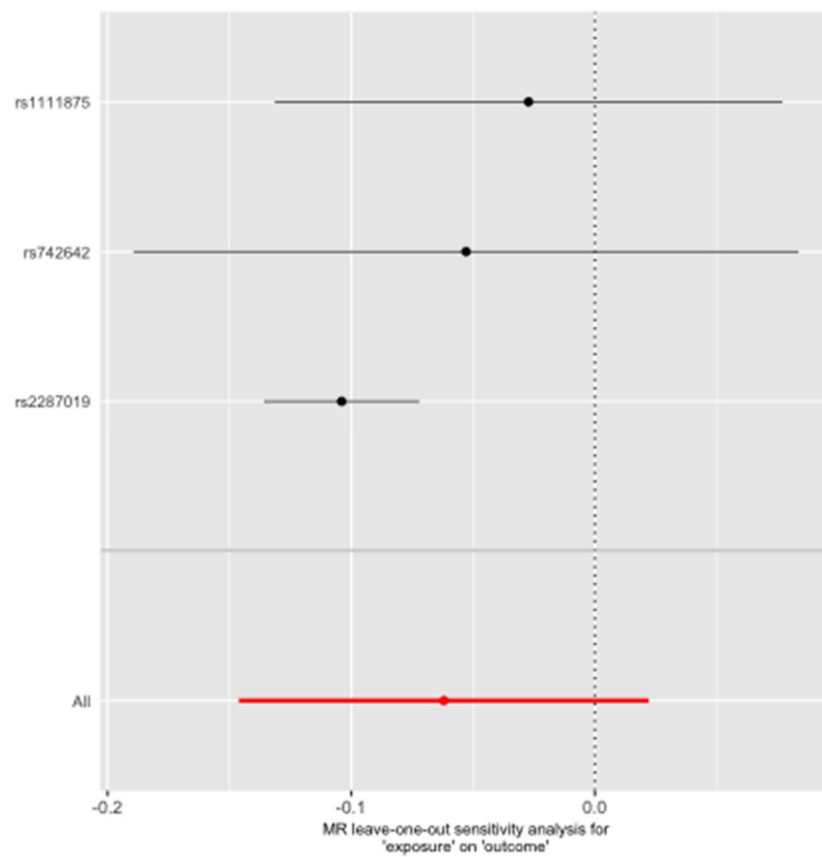


### MR Test

- Inverse variance weighted
- MR Egger
- Simple mode
- Weighted median
- Weighted mode







### *Insulin Secretion at 30 minutes on Left leg fat percentage*

#### Results from two sample MR:

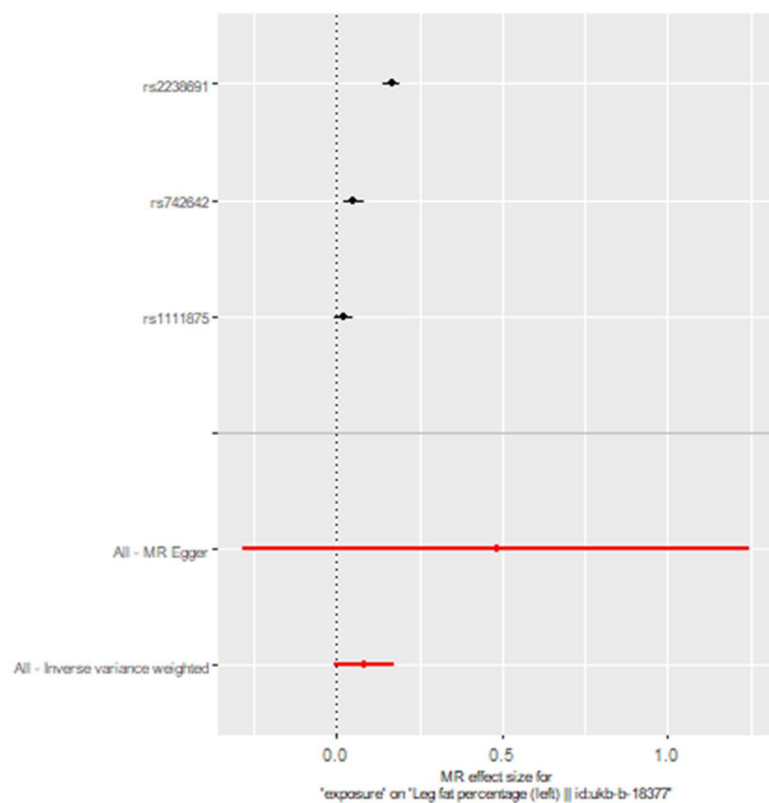
| method                    | nsnp | b         | se        | pval      |
|---------------------------|------|-----------|-----------|-----------|
| MR Egger                  | 3    | 0.4830297 | 0.3911664 | 0.4333466 |
| Weighted median           | 3    | 0.0361370 | 0.0120660 | 0.0027449 |
| Inverse variance weighted | 3    | 0.0826049 | 0.0455331 | 0.0696513 |
| Simple mode               | 3    | 0.0365972 | 0.0134170 | 0.1122272 |
| Weighted mode             | 3    | 0.0313276 | 0.0110387 | 0.1049716 |

#### Heterogeneity tests

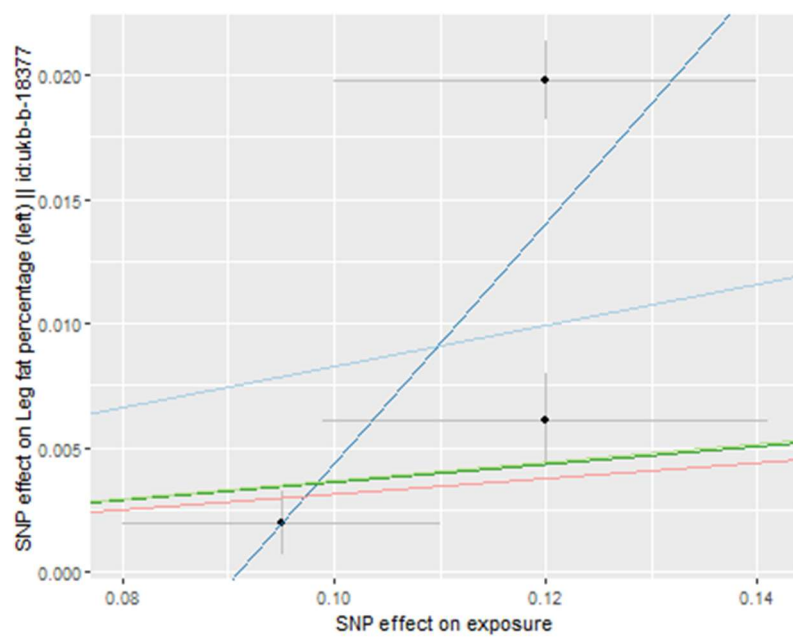
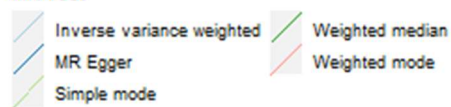
| method                    | Q        | Q_df | Q_pval |
|---------------------------|----------|------|--------|
| MR Egger                  | 30.63897 | 1    | 0      |
| Inverse variance weighted | 63.17309 | 2    | 0      |

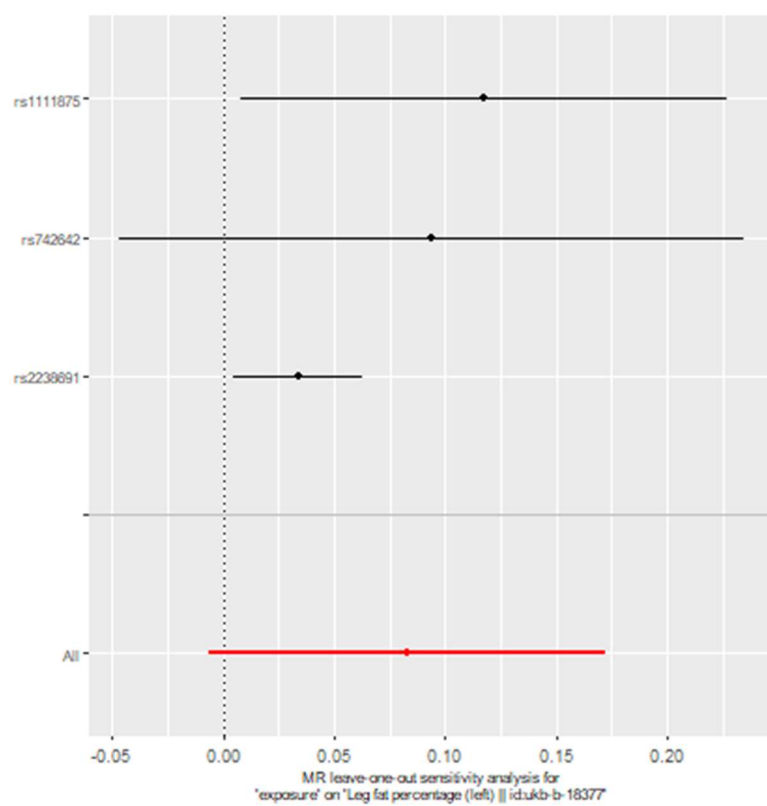
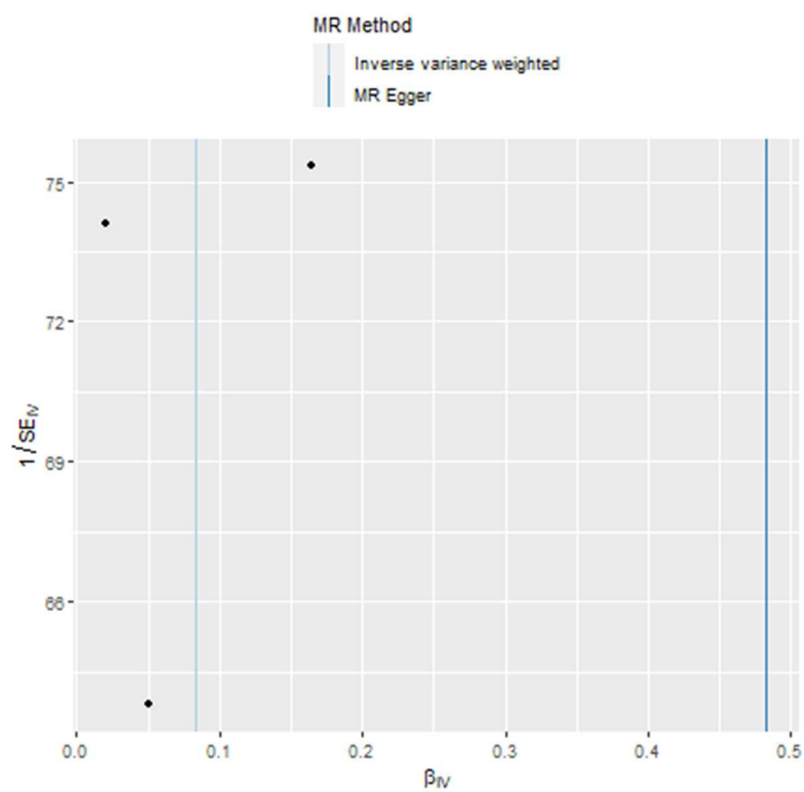
#### Test for directional horizontal pleiotropy

| egger_intercept | se        | pval      |
|-----------------|-----------|-----------|
| -0.0438876      | 0.0425902 | 0.4904495 |



#### MR Test







### *Insulin secretion at 30 mins on Right leg fat percentage*

#### Results from two sample MR:

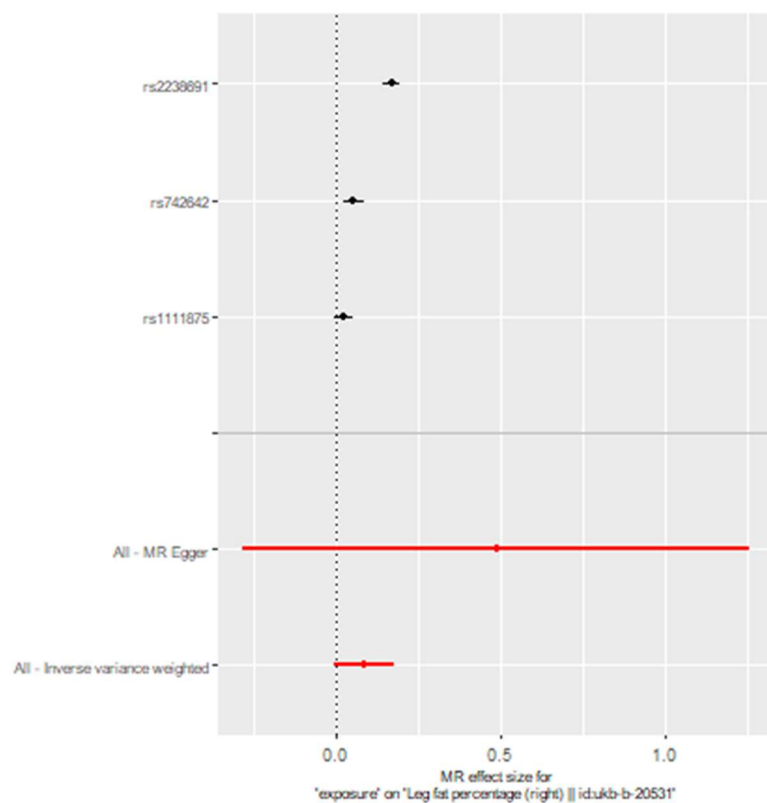
| method                    | nsnp | b         | se        | pval      |
|---------------------------|------|-----------|-----------|-----------|
| MR Egger                  | 3    | 0.4871950 | 0.3925124 | 0.4317436 |
| Weighted median           | 3    | 0.0388031 | 0.0122350 | 0.0015167 |
| Inverse variance weighted | 3    | 0.0854518 | 0.0456856 | 0.0614240 |
| Simple mode               | 3    | 0.0392972 | 0.0149153 | 0.1189057 |
| Weighted mode             | 3    | 0.0340109 | 0.0113437 | 0.0955635 |

#### Heterogeneity tests

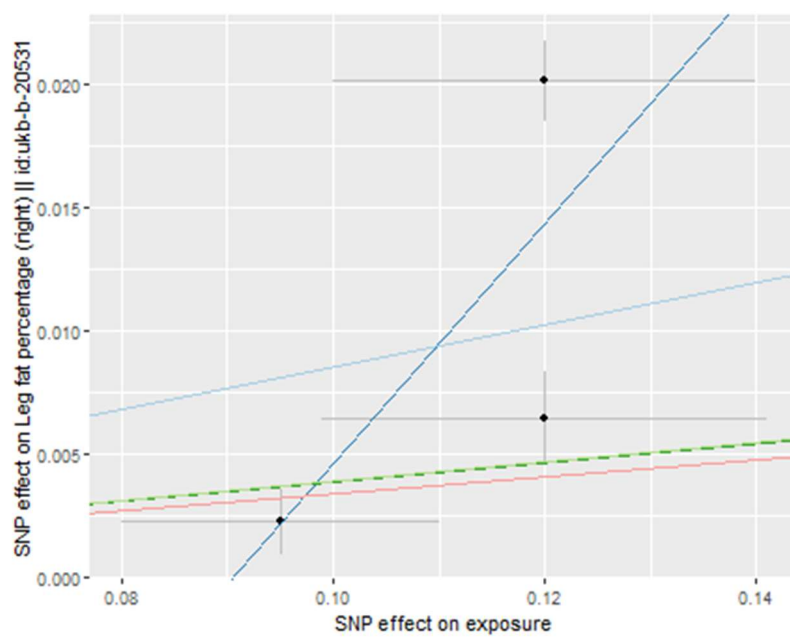
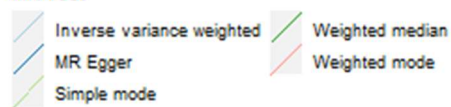
| method                    | Q       | Q_df | Q_pval |
|---------------------------|---------|------|--------|
| MR Egger                  | 30.0652 | 1    | 0      |
| Inverse variance weighted | 61.9806 | 2    | 0      |

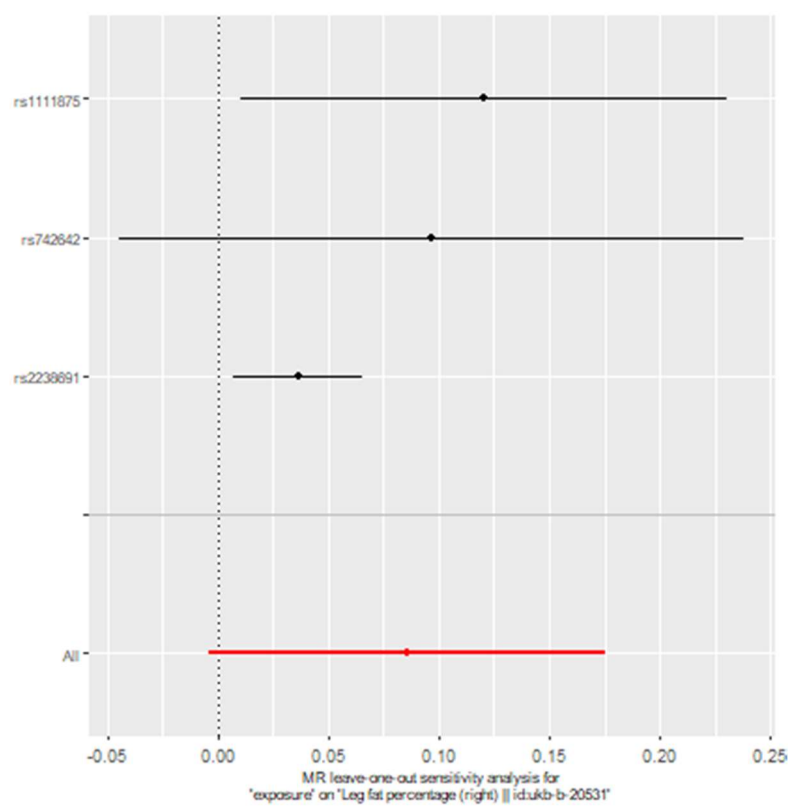
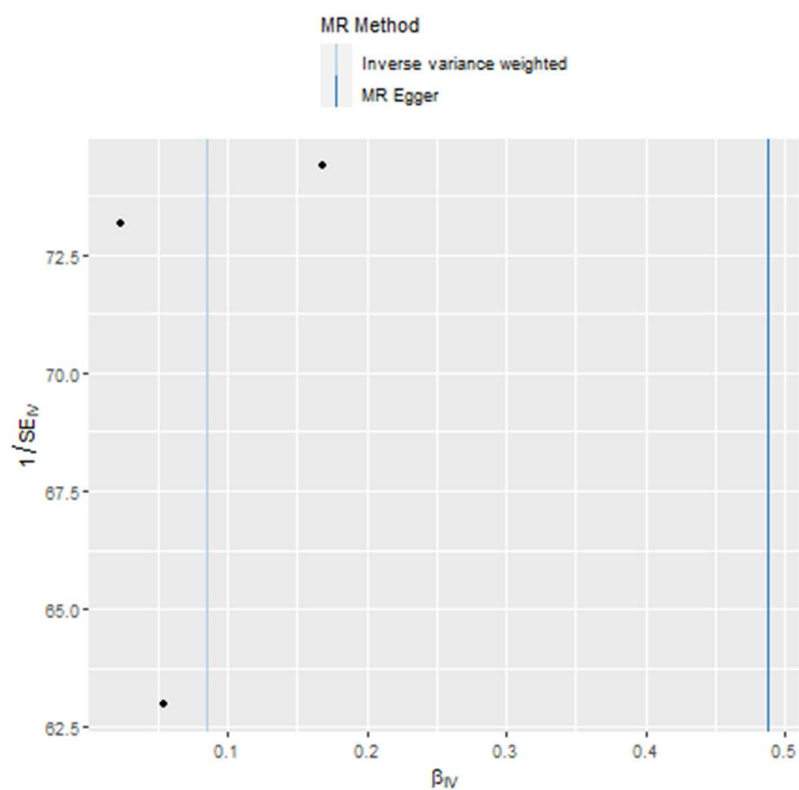
#### Test for directional horizontal pleiotropy

| egger_intercept | se        | pval      |
|-----------------|-----------|-----------|
| -0.0440325      | 0.0427372 | 0.4904967 |



#### MR Test





Insulin secretion at 30 minutes on Triglycerides

Results from two sample MR:

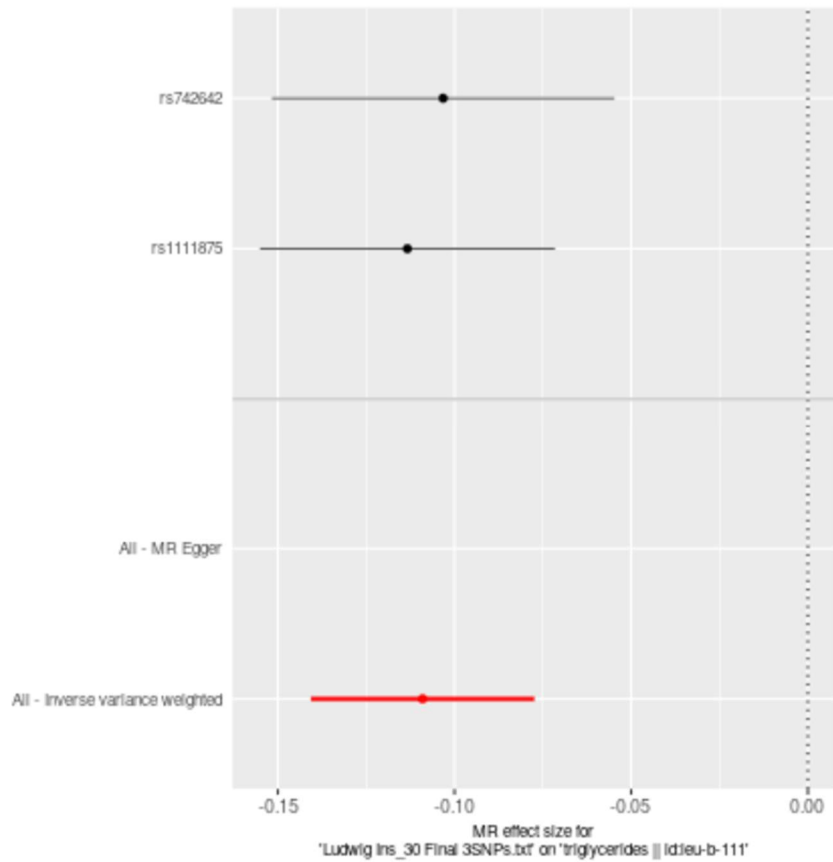
| method                    | nsnp | b          | se        | pval |
|---------------------------|------|------------|-----------|------|
| Inverse variance weighted | 2    | -0.1090188 | 0.0161361 | 0    |

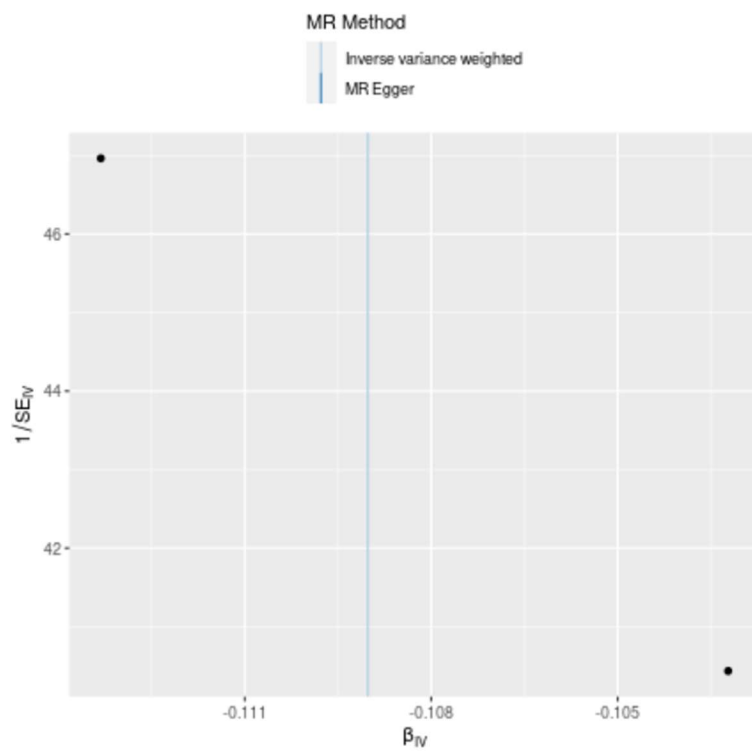
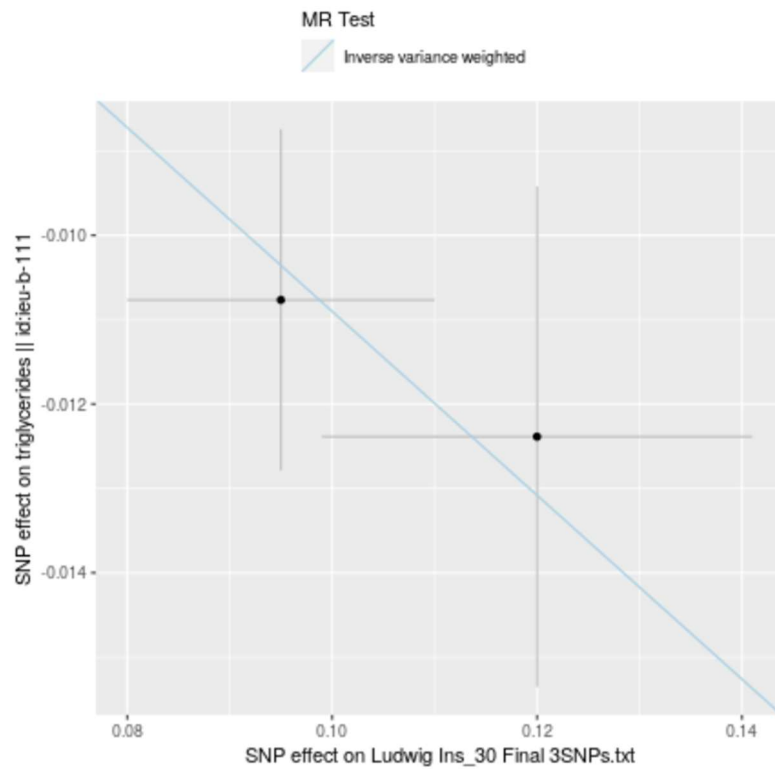
Heterogeneity tests

| method                    | Q         | Q_df | Q_pval    |
|---------------------------|-----------|------|-----------|
| Inverse variance weighted | 0.0956942 | 1    | 0.7570592 |

Test for directional horizontal pleiotropy

| egger_intercept | se | pval |
|-----------------|----|------|
| NA              | NA | NA   |





Insulin secretion at 30 minutes on High-density Lipoprotein

Results from two sample MR:

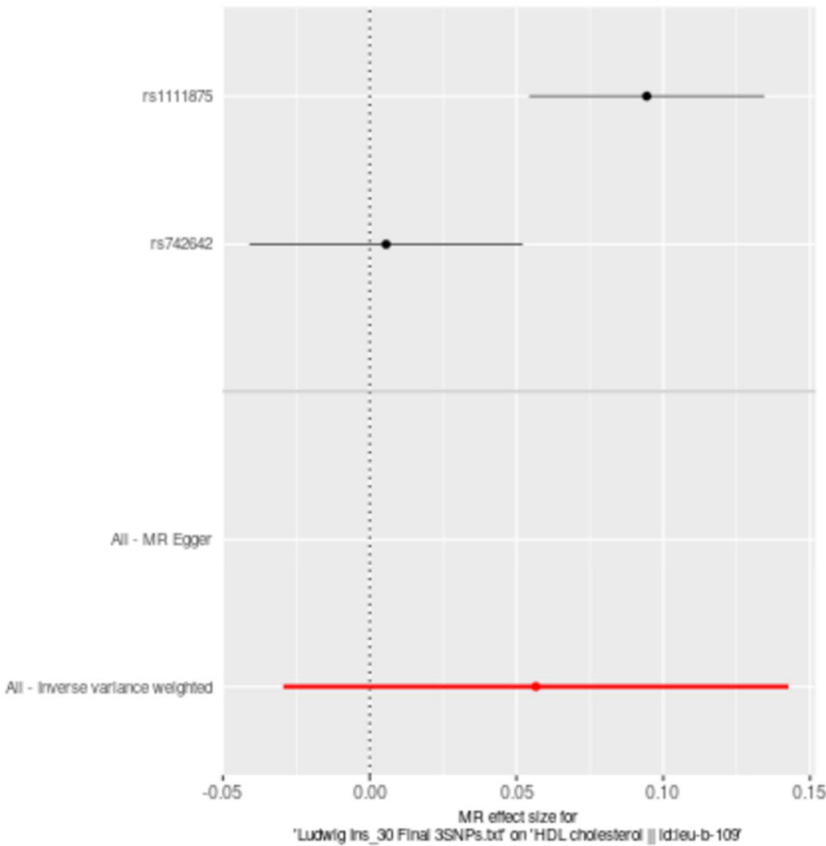
| method                    | nsnp | b         | se        | pval      |
|---------------------------|------|-----------|-----------|-----------|
| Inverse variance weighted | 2    | 0.0566153 | 0.0438974 | 0.1971483 |

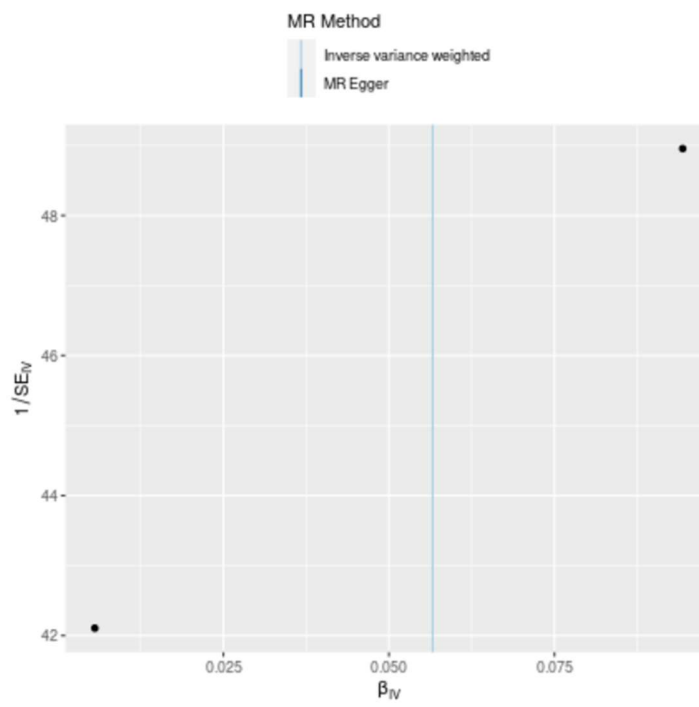
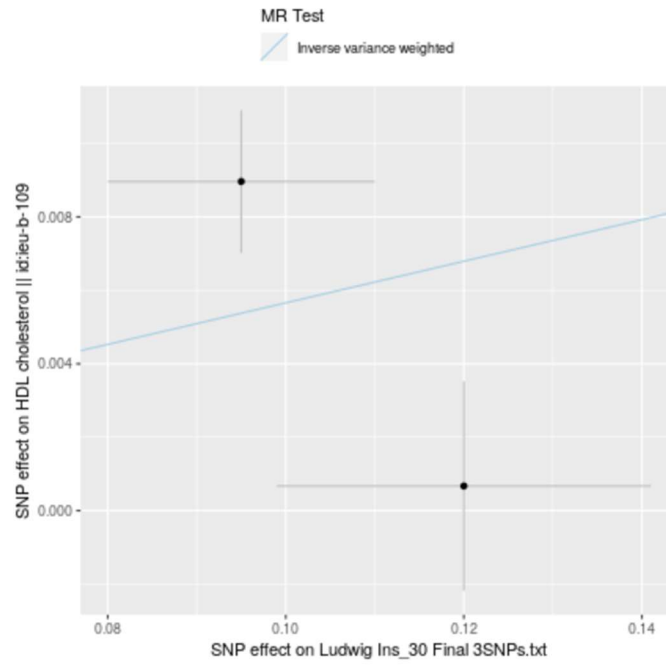
Heterogeneity tests

| method                    | Q        | Q_df | Q_pval    |
|---------------------------|----------|------|-----------|
| Inverse variance weighted | 8.034319 | 1    | 0.0045899 |

Test for directional horizontal pleiotropy

| egger_intercept | se | pval |
|-----------------|----|------|
| NA              | NA | NA   |





### *Insulin secretion at 30 minutes on Type 2 diabetes*

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#### Results from two sample MR:

| method                    | nsnp | b          | se        | pval |
|---------------------------|------|------------|-----------|------|
| Inverse variance weighted | 2    | -0.9800601 | 0.0575195 | 0    |

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#### Heterogeneity tests

| method                    | Q         | Q_df | Q_pval    |
|---------------------------|-----------|------|-----------|
| Inverse variance weighted | 0.1305961 | 1    | 0.7178148 |

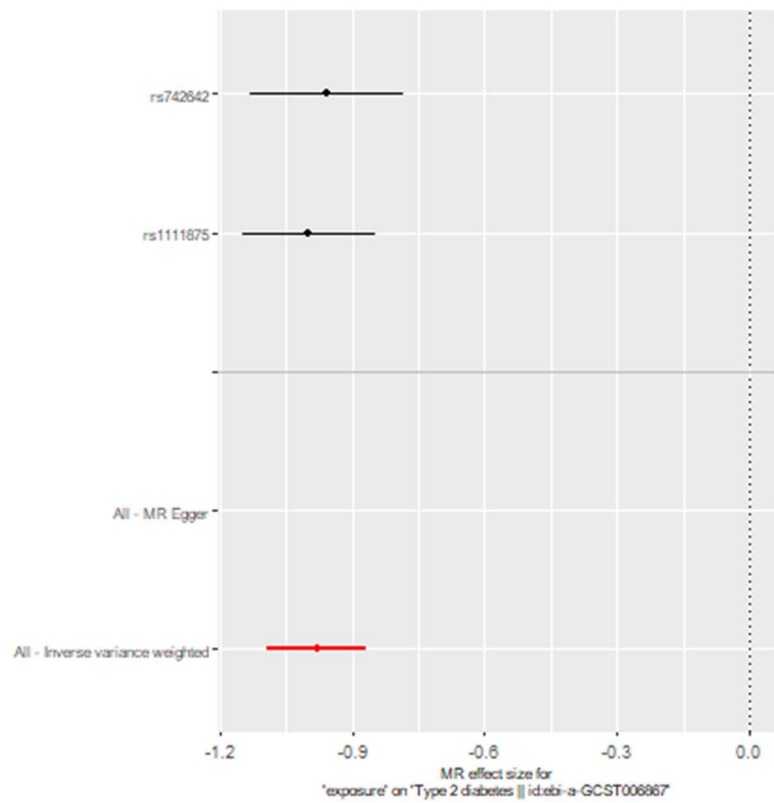
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#### Test for directional horizontal pleiotropy

| egger_intercept | se | pval |
|-----------------|----|------|
| NA              | NA | NA   |

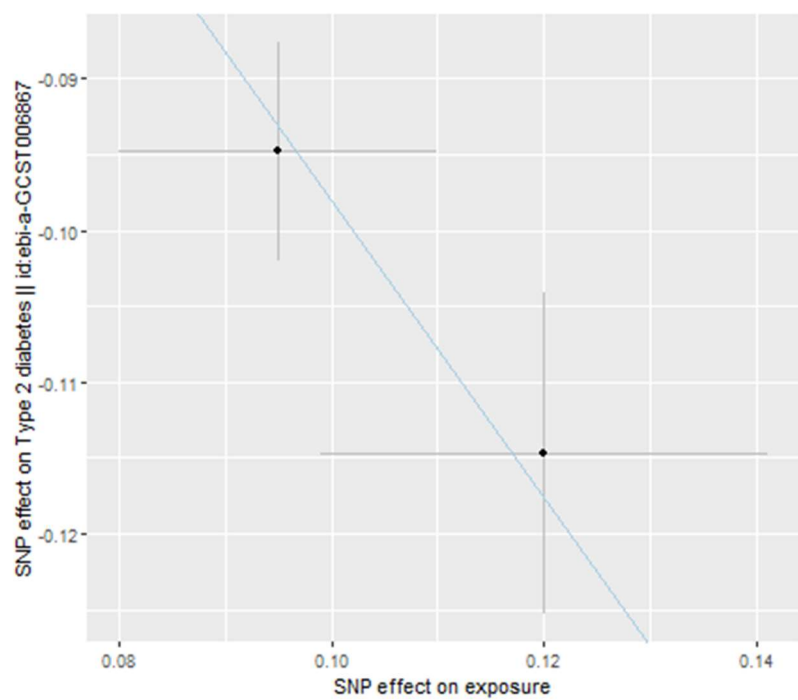
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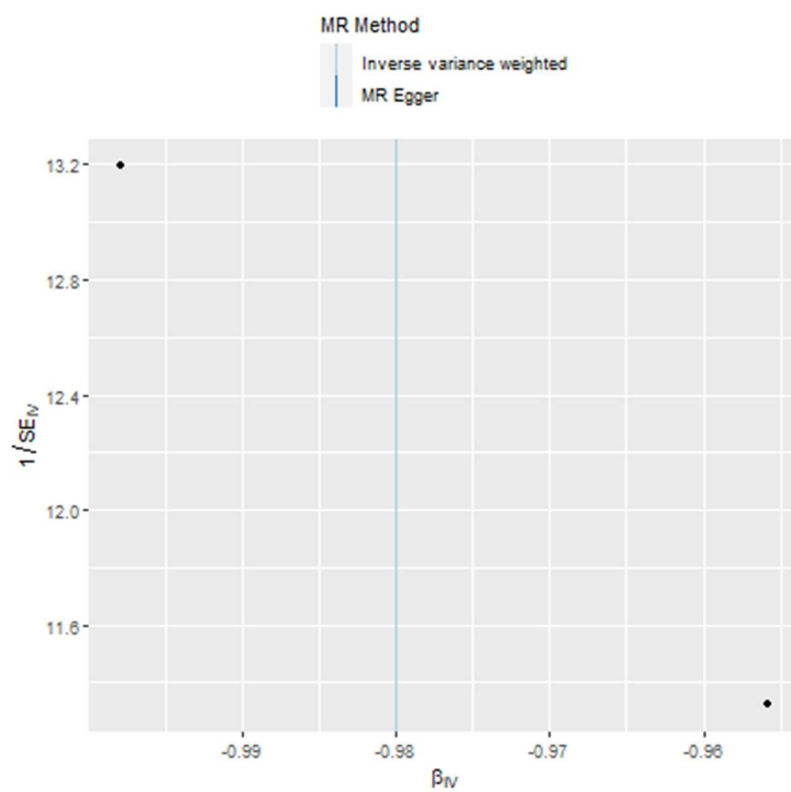




MR Test

Inverse variance weighted





### *Insulin secretion at 30 minutes on Hypertension*

#### Results from two sample MR:

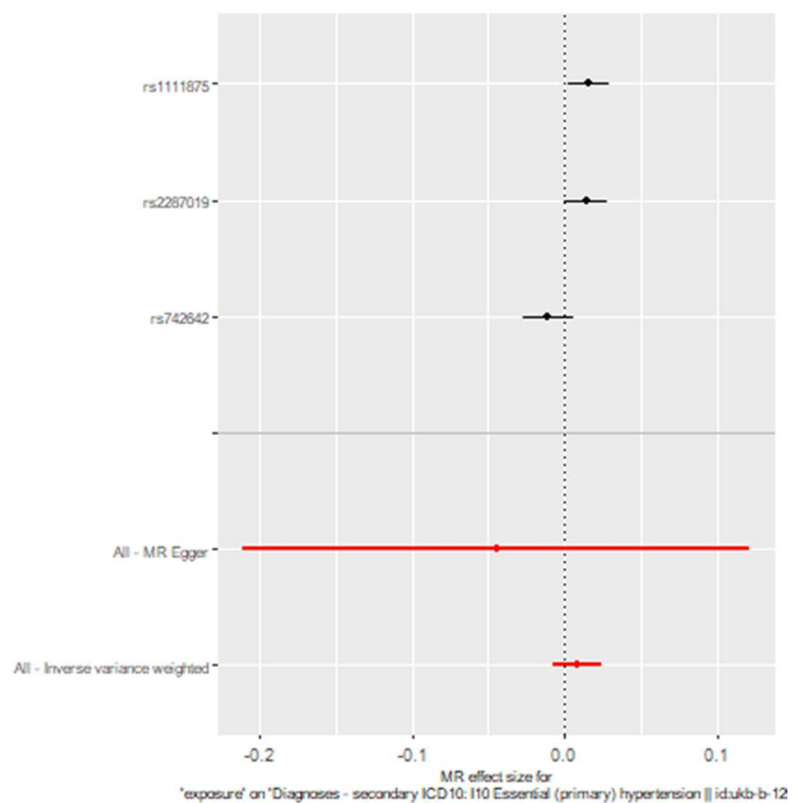
| method                    | nsnp | b          | se        | pval      |
|---------------------------|------|------------|-----------|-----------|
| MR Egger                  | 3    | -0.0444945 | 0.0848004 | 0.6923794 |
| Weighted median           | 3    | 0.0141477  | 0.0060294 | 0.0189539 |
| Inverse variance weighted | 3    | 0.0079012  | 0.0081170 | 0.3303473 |
| Simple mode               | 3    | 0.0148657  | 0.0063758 | 0.1449850 |
| Weighted mode             | 3    | 0.0148657  | 0.0068846 | 0.1634550 |

#### Heterogeneity tests

| method                    | Q        | Q_df | Q_pval    |
|---------------------------|----------|------|-----------|
| MR Egger                  | 5.076932 | 1    | 0.0242462 |
| Inverse variance weighted | 7.041077 | 2    | 0.0295835 |

#### Test for directional horizontal pleiotropy

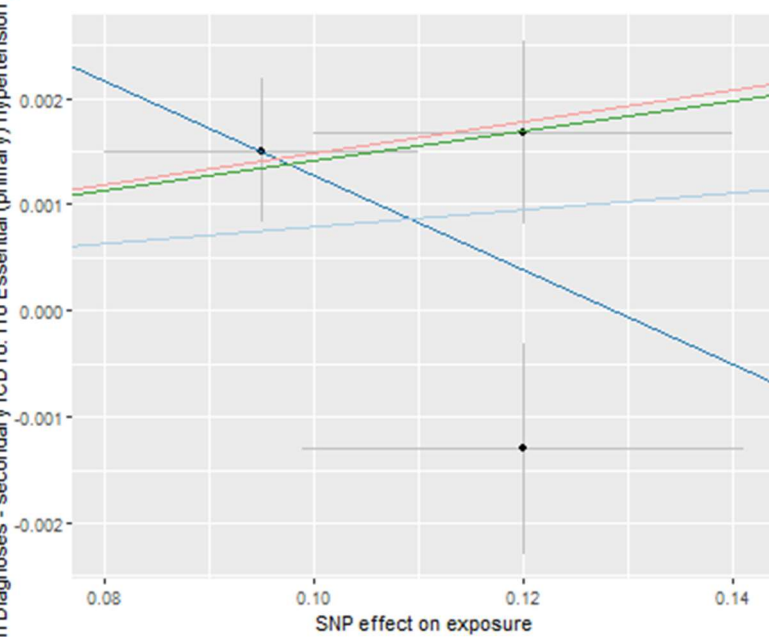
| egger_intercept | se        | pval      |
|-----------------|-----------|-----------|
| 0.0057321       | 0.0092157 | 0.6457627 |

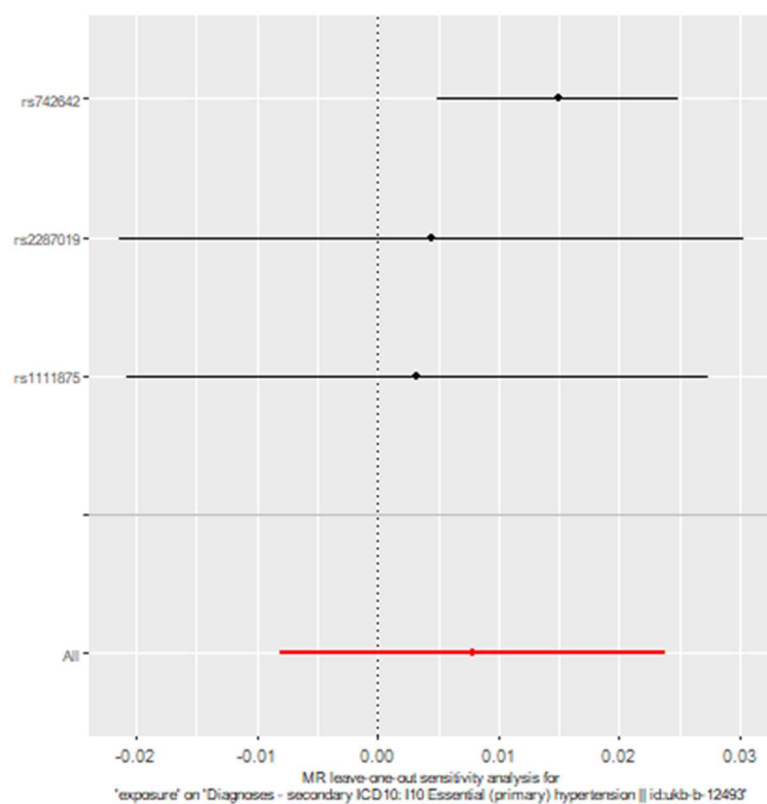
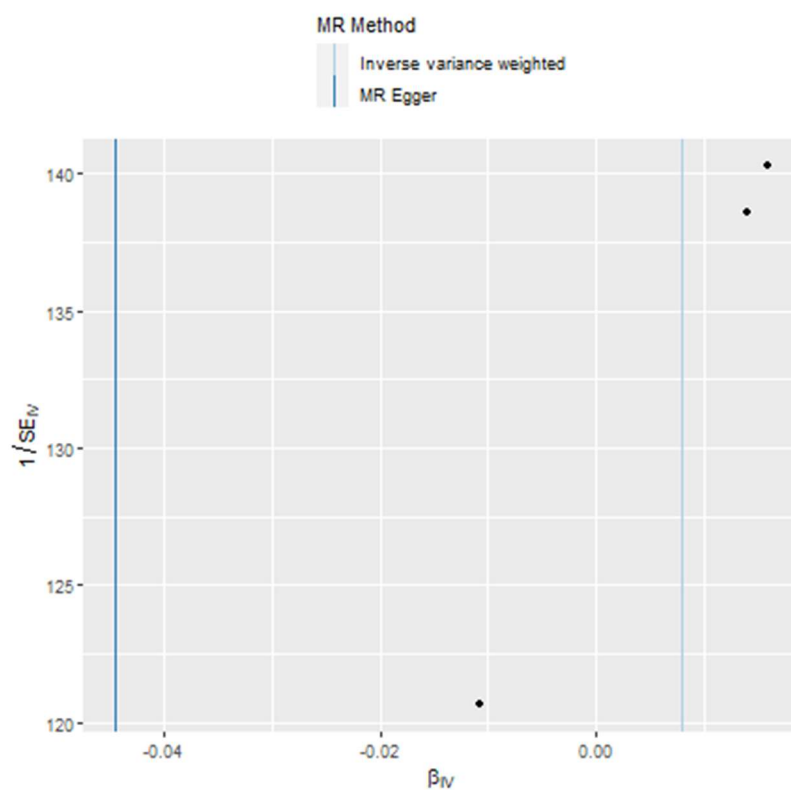


Diagnoses - secondary ICD10: I10 Essential (primary) hypertension || id.ukb-b-12493

#### MR Test

- Inverse variance weighted
- MR Egger
- Simple mode
- Weighted median
- Weighted mode





## *Insulin secretion at 30 minutes on coronary artery disease*

### Results from two sample MR:

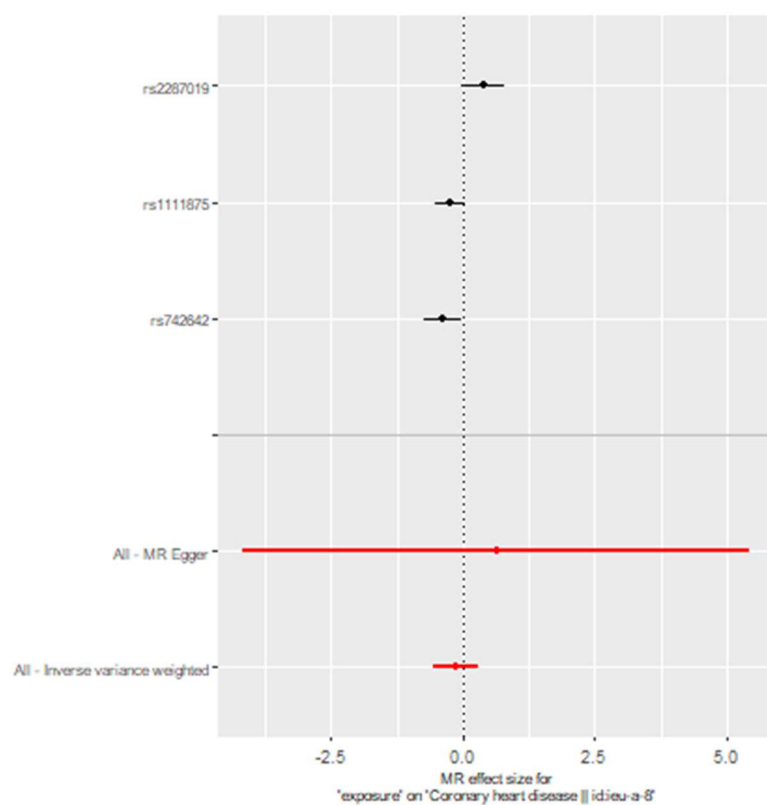
| method                    | nsnp | b          | se        | pval      |
|---------------------------|------|------------|-----------|-----------|
| MR Egger                  | 3    | 0.6378290  | 2.4540175 | 0.8381166 |
| Weighted median           | 3    | -0.2497082 | 0.1374939 | 0.0693490 |
| Inverse variance weighted | 3    | -0.1375311 | 0.2117229 | 0.5159630 |
| Simple mode               | 3    | -0.3151879 | 0.1658046 | 0.1976749 |
| Weighted mode             | 3    | -0.2943264 | 0.1460788 | 0.1814980 |

### Heterogeneity tests

| method                    | Q        | Q_df | Q_pval    |
|---------------------------|----------|------|-----------|
| MR Egger                  | 8.155188 | 1    | 0.0042938 |
| Inverse variance weighted | 8.980460 | 2    | 0.0112181 |

### Test for directional horizontal pleiotropy

| egger_intercept | se        | pval      |
|-----------------|-----------|-----------|
| -0.083239       | 0.2616647 | 0.8039273 |



#### MR Test

