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|  | Description and assumptions | Interpretation of results |
| MR-all | Includes all age at menarche SNPs | Assumes no horizontal pleiotropy via BMI. Estimates would be biased if there is asymmetric horizontal pleiotropy (blue dashed arrows). |
| MR-child | Excludes child BMI SNPs | Assumes all horizontal pleiotropy acts between excluded child BMI SNPs and the outcome. Childhood BMI is used a proxy for pre-pubertal BMI. Less likely to be biased by paths with blue dashed arrows. May have reduced power as some of the variance in menarche explained by the genetic IV will be due to SNP effects on age menarche via child BMI. |
| MR-adult | Excludes adult BMI SNPs | Assumes that all horizontal pleiotropy acts between the excluded adult BMI SNPs and the outcome. Adult BMI is used as a proxy for post-pubertal BMI. Estimates could be biased towards the null by removing causal effects that are via adult BMI (green dot and dashed arrows). |
| MR-Steiger | Excludes SNPs that predict BMI more strongly than age at menarche | Assumes that SNPs more strongly predictive of adult BMI than age at menarche are the ones most likely to cause horizontal pleiotropy. If correct removing these should be less biased than either MR-adult or MR-child. |
| MV-MR | Estimates the independent association of age at menarche and adult BMI | Estimates represent the direct causal effect of age at menarche on the outcome. Hence, estimates may be biased towards the null if adult BMI mediates an effect of age at menarche on the outcome. |