

Supplemental Information Directory for:

Testing bidirectional associations of major depressive disorder with medical conditions:
Two-sample Mendelian randomization study

Yu Fang, et al.

Supplementary Figure 1. Two-sample Mendelian randomization tests and decision flow chart.

Supplementary Figure 2. Forest plots of the estimated causal effects of MDD on 182 other traits, organized by phecode group.

Supplementary Figure 3. Scatter plots of Mendelian randomization tests in the direction of MDD causing other traits, for the 29 most strongly-associated traits (FDR-corrected p-value < 1×10^{-10}).

Supplementary Figure 4. Scatter plots of bidirectional Mendelian randomization tests between MDD and 10 MDD-PRS associated traits, in the direction of MDD causing other traits (AA to AJ) and the direction of other traits causing MDD (BA to BJ).

The accompanying Supplementary Data Excel file includes the following:

Supplementary Data 1. 246 phecode traits from published MDD-PRS EHR PheWAS studies

Supplementary Data 2. Candidate and final keywords for phecode - GWAS dataset matching

Supplementary Data 3. Summary of causal effects of MDD on other traits, by phecode group

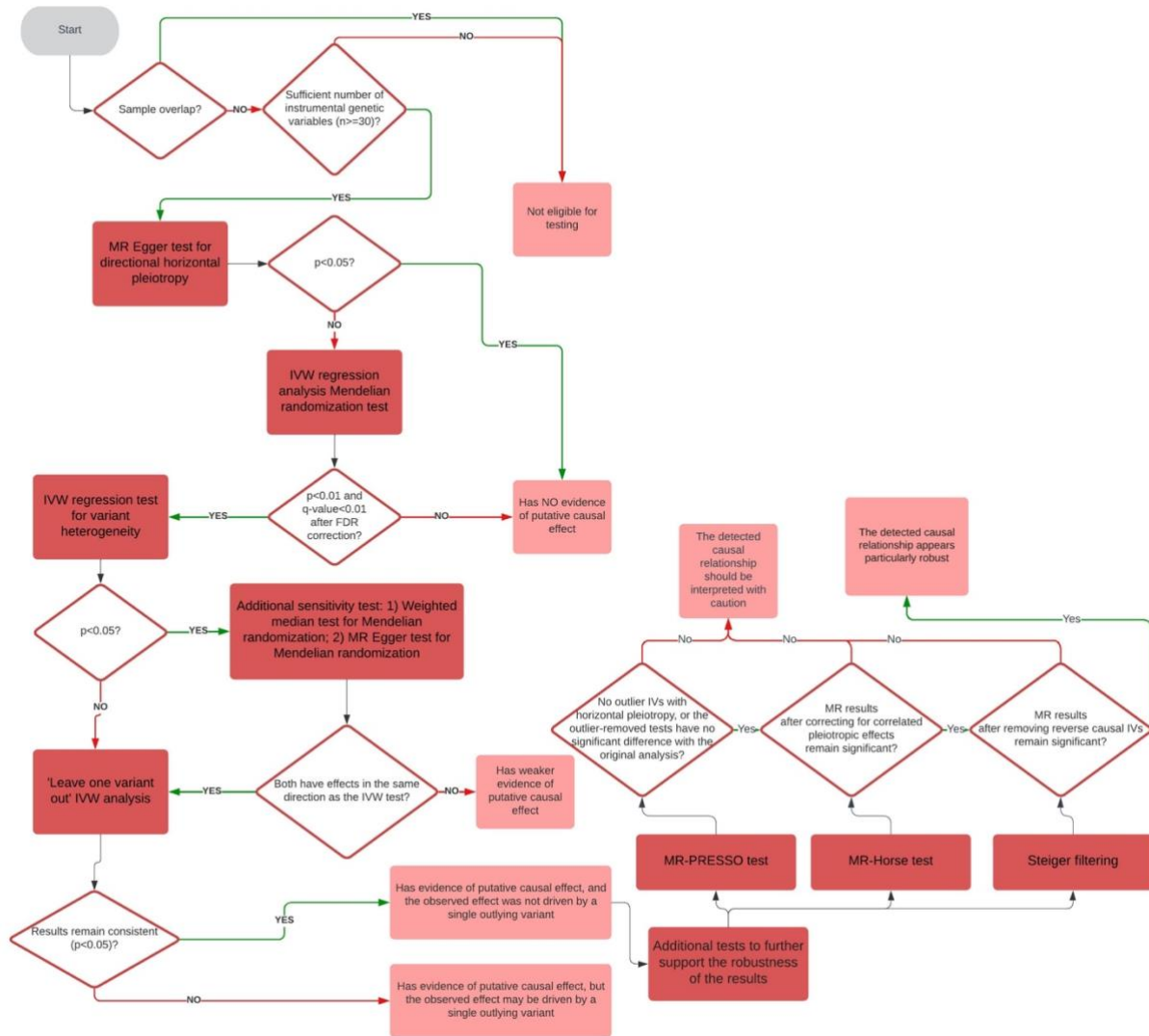
Supplementary Data 4. Tests of causal effects of MDD on 182 other traits

Supplementary Data 5. Tests of causal effects of 10 other traits on MDD

Supplementary Data 6. Negative control: Tests of causal effects of height on 183 traits

Supplementary Figures

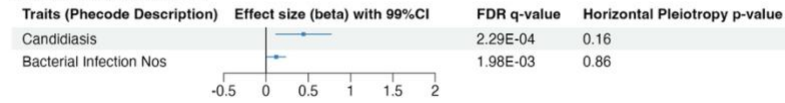
Supplementary Figure 1. Two-sample Mendelian randomization tests and decision flow chart.



Supplementary Figure 2. Forest plots of the estimated causal effects of MDD on 182 other traits, organized by phecode group.

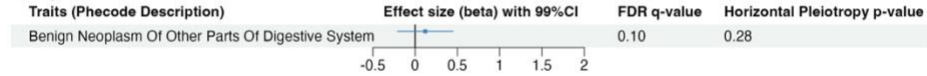
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Infectious Diseases



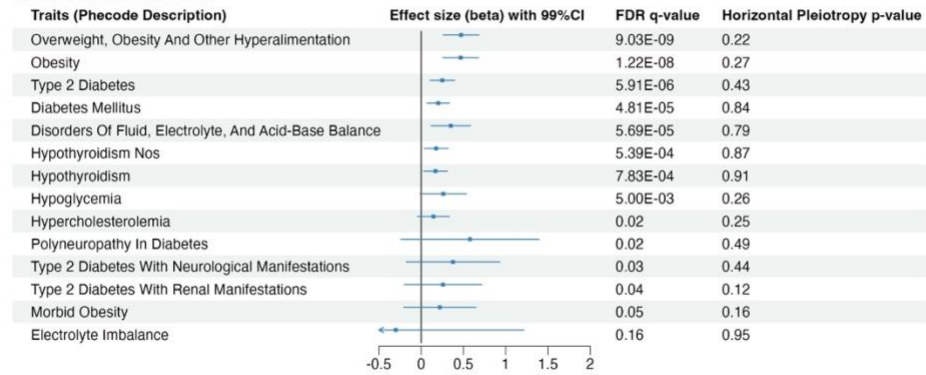
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Neoplasms



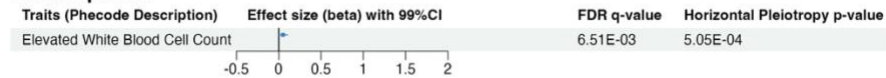
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Endocrine/Metabolic



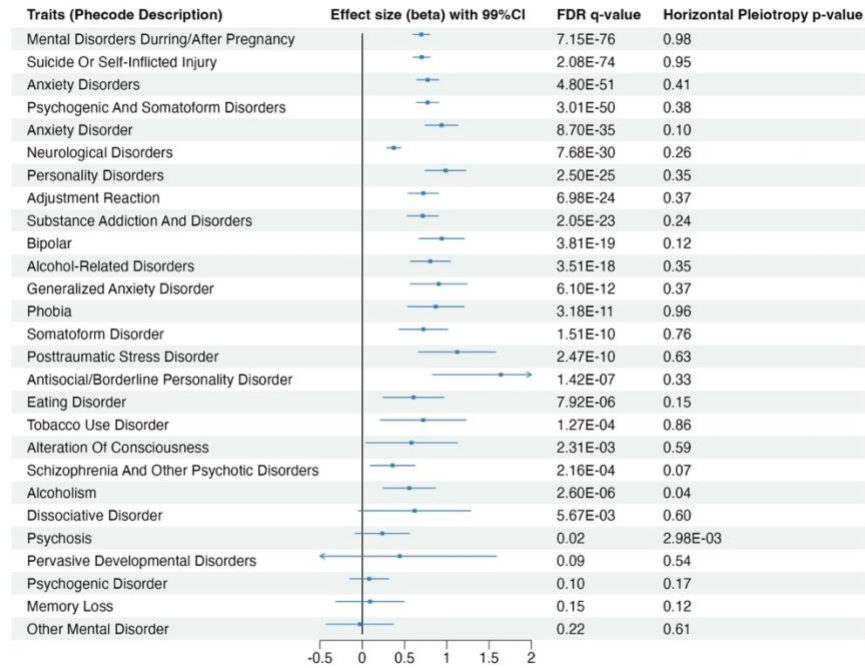
D.

Hematopoietic



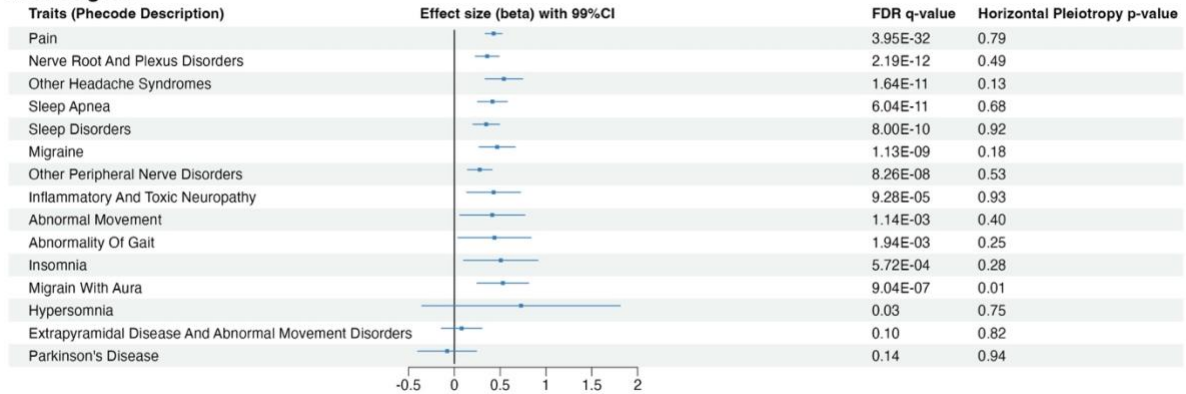
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Mental Disorders



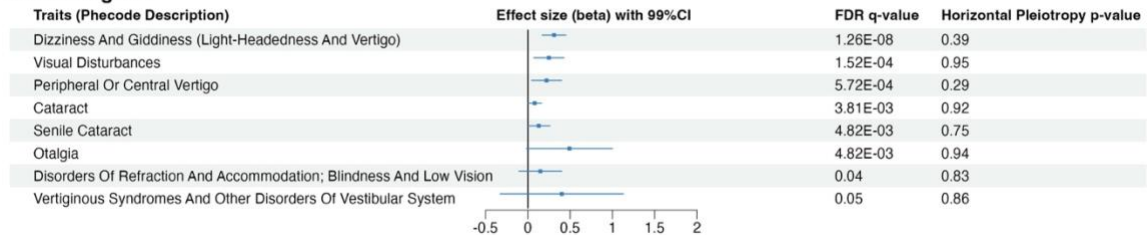
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Neurological



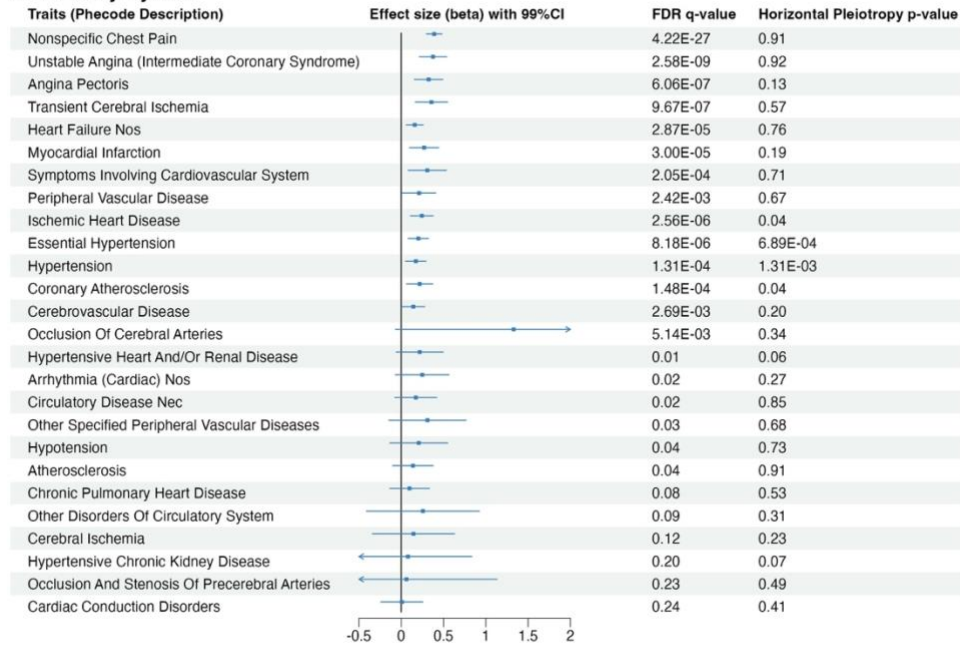
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Sense Organs



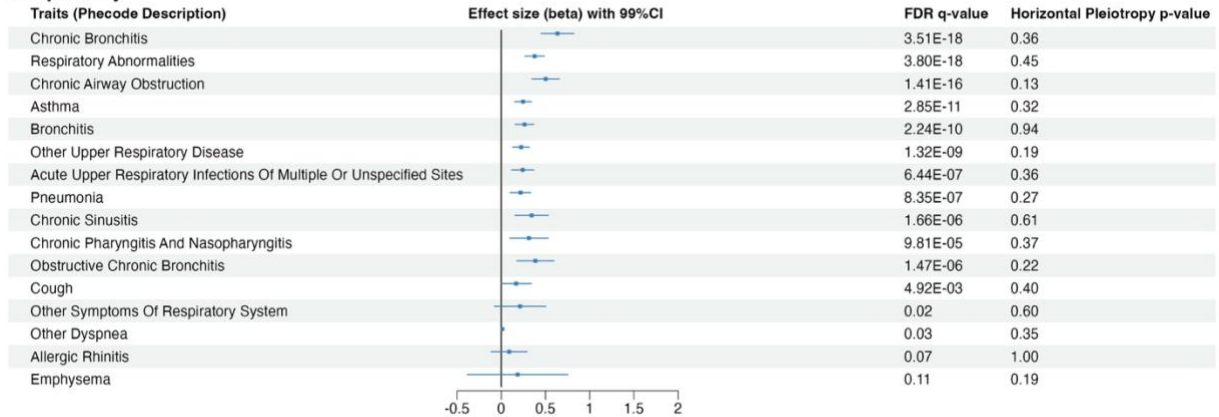
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Circulatory System



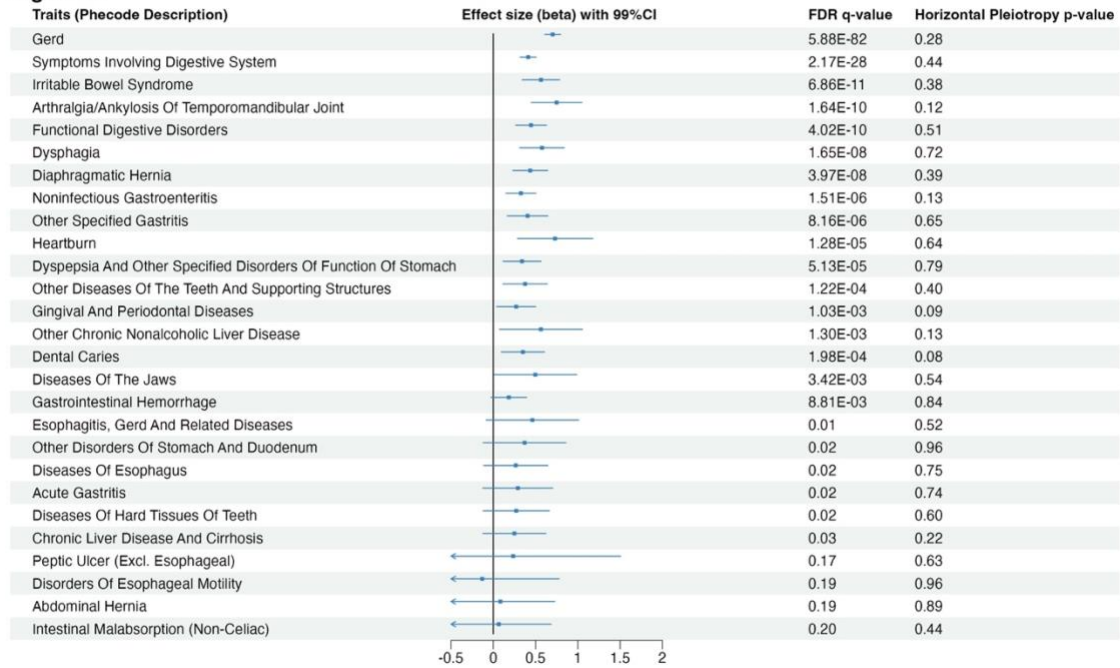
I.

Respiratory



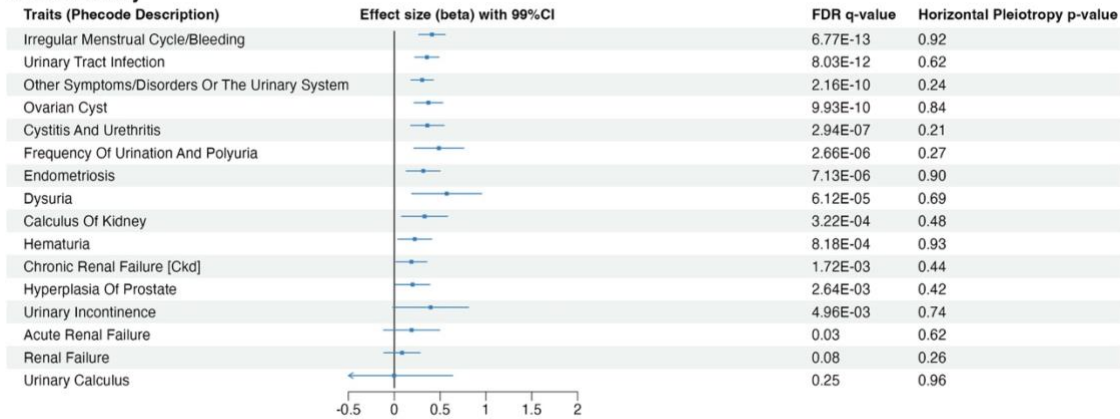
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Digestive



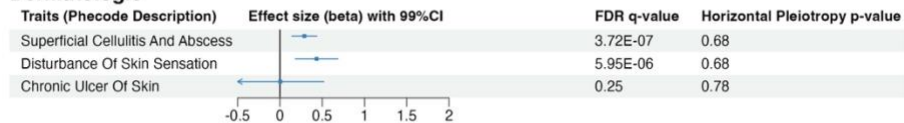
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Genitourinary



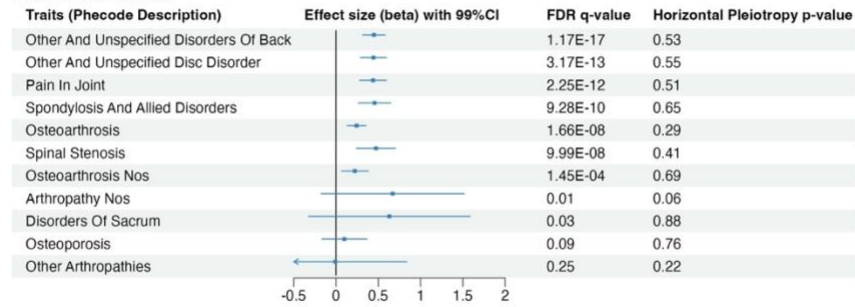
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Dermatologic



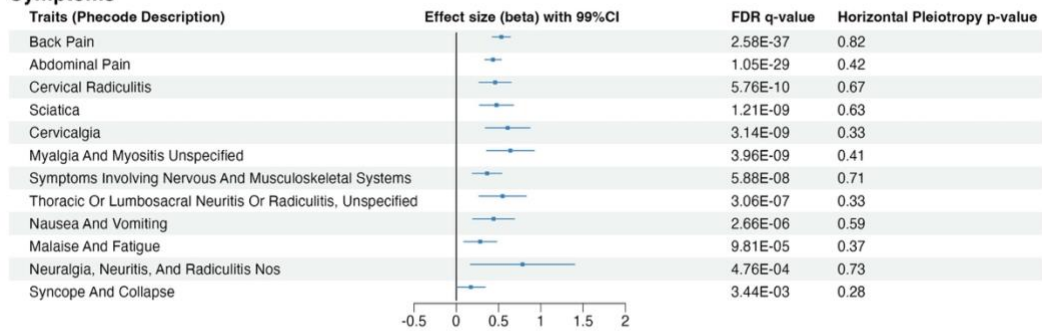
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Musculoskeletal



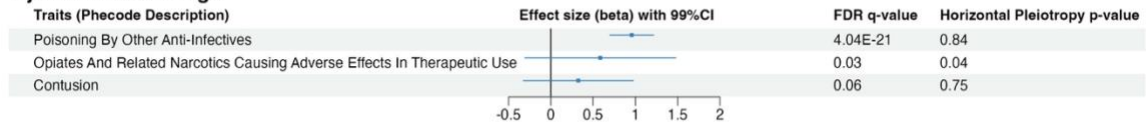
N.

Symptoms



O.

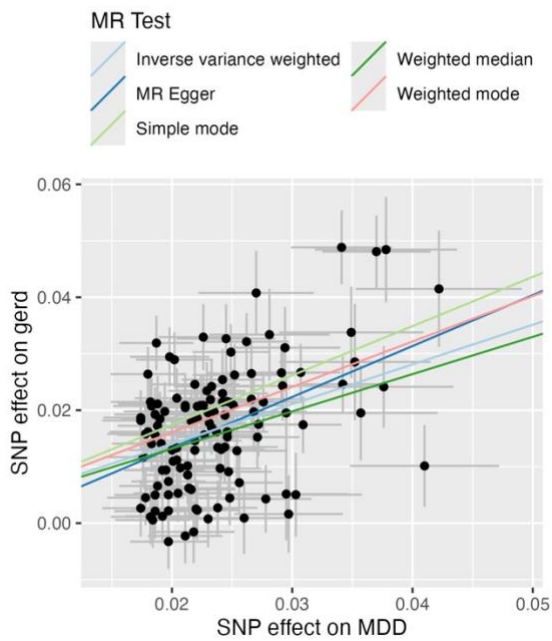
Injuries & Poisonings



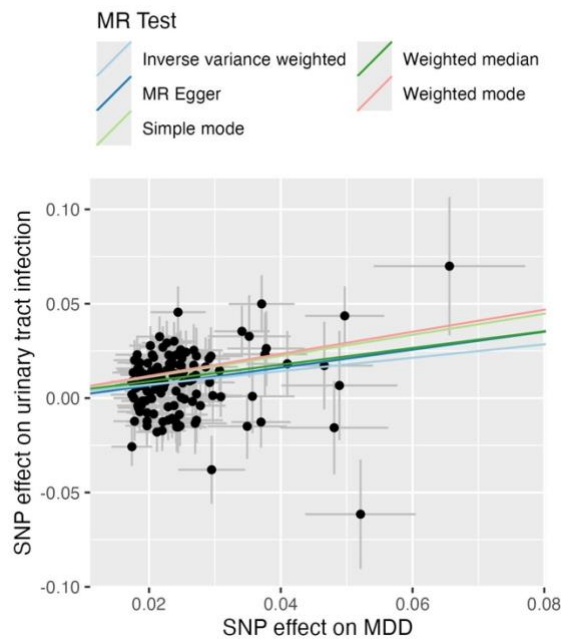
A. Infectious Diseases. B. Neoplasms. C. Endocrine/Metabolic. D. Hematopoietic. E. Mental Disorders. F. Neurological. G. Sense Organs. H. Circulatory System. I. Respiratory. J. Digestive. K. Genitourinary. L. Dermatologic. M. Musculoskeletal. N. Symptoms. O. Injuries & Poisonings. Causal-effect estimates are presented as beta coefficients with 99% confidence intervals. All traits are binary, with the exception of “elevated white blood cell count” (continuous). Odds ratios for associations with binary traits are shown in **Supplementary Data 4**.

Supplementary Figure 3. Scatter plots of Mendelian randomization tests in the direction of MDD causing other traits, for the 29 most strongly-associated traits (FDR-corrected p-value < 1×10^{-10}).

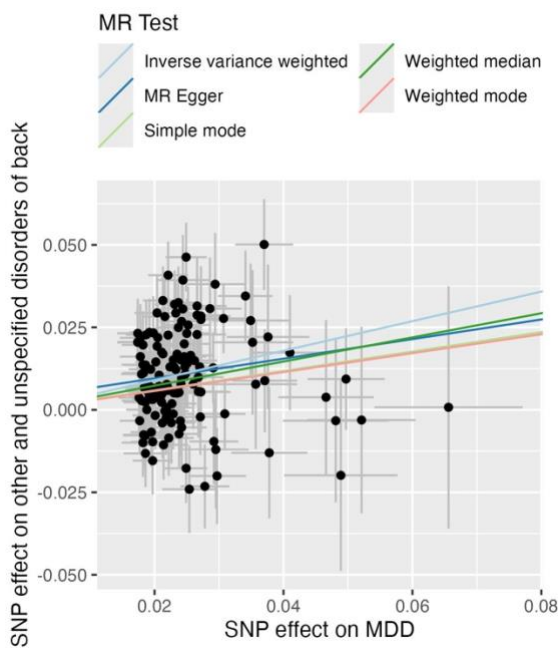
A. GERD



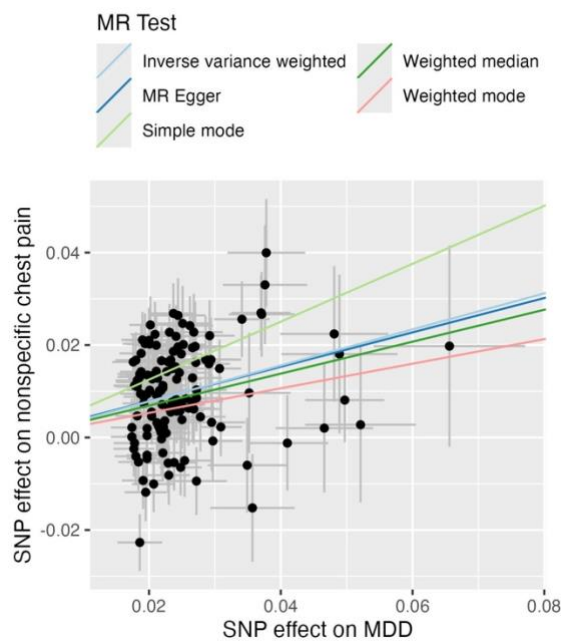
B. Urinary Tract Infection



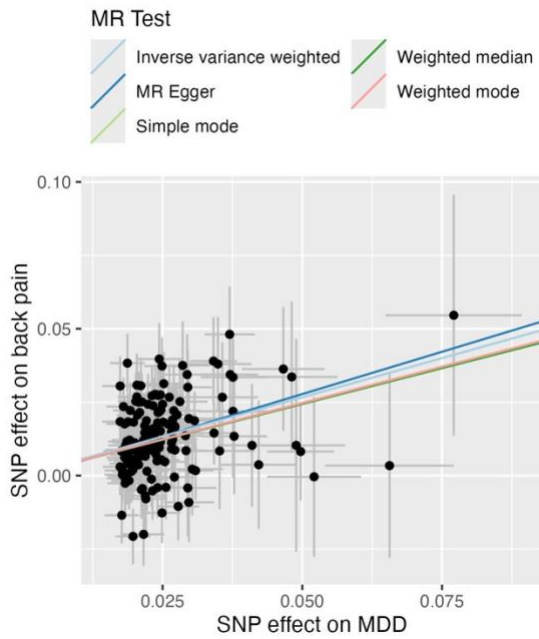
C. Other And Unspecified Disorders Of Back



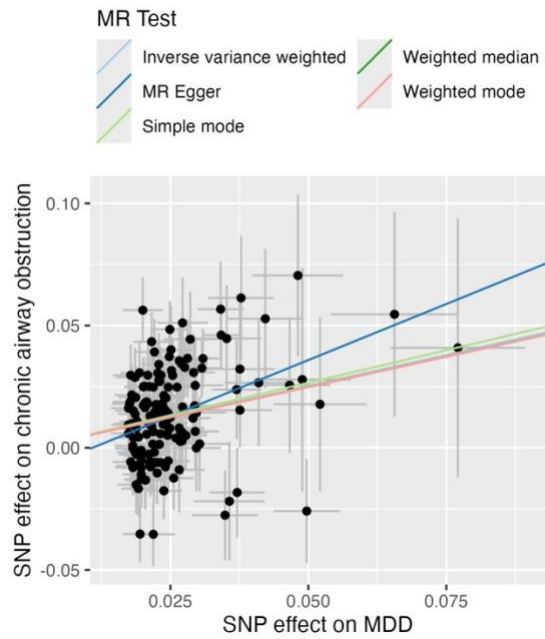
D. Nonspecific Chest Pain



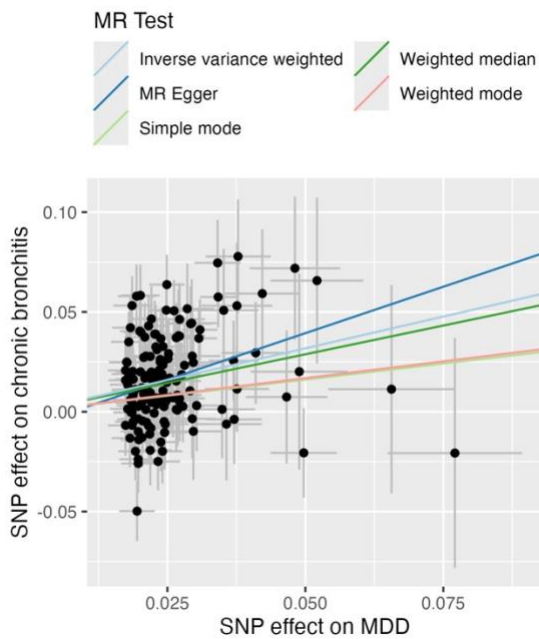
E.Back Pain



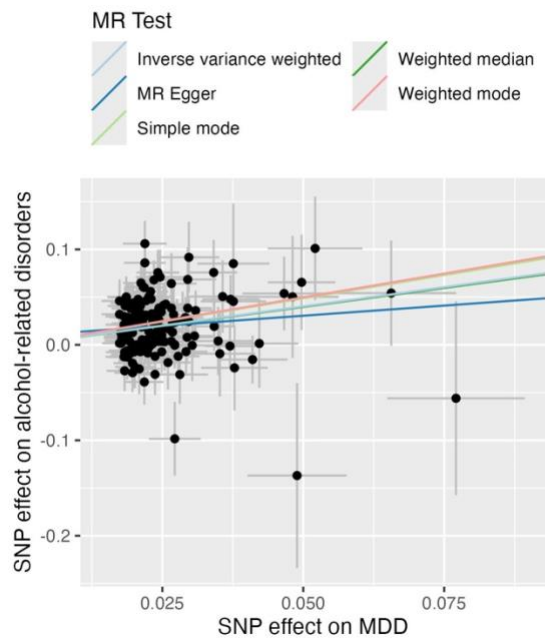
F.Chronic Airway Obstruction



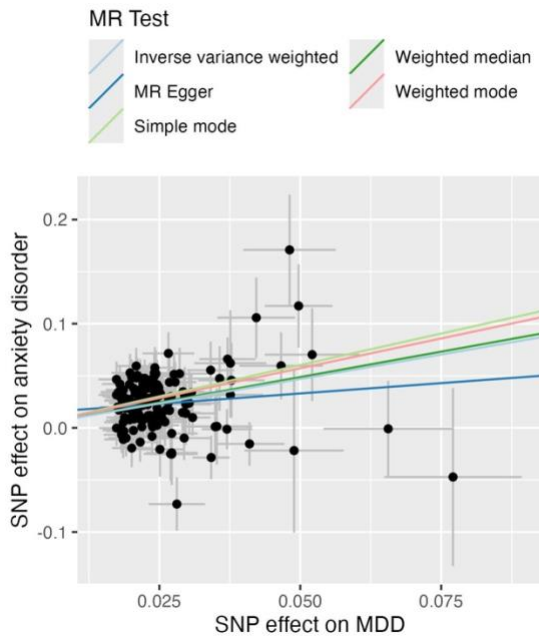
G.Chronic Bronchitis



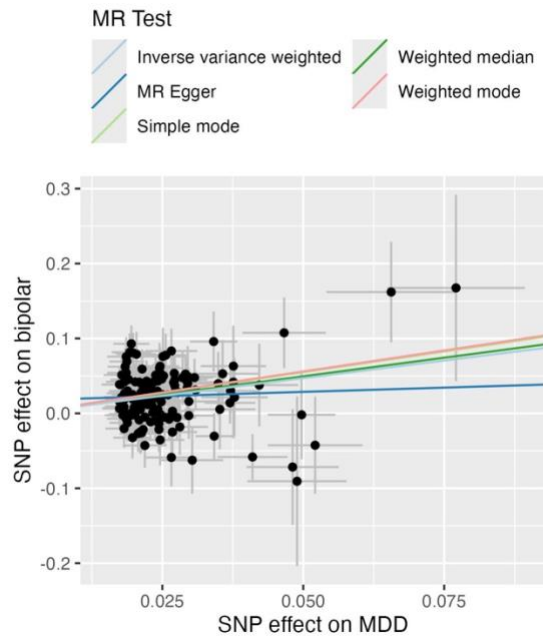
H.Alcohol-Related Disorders



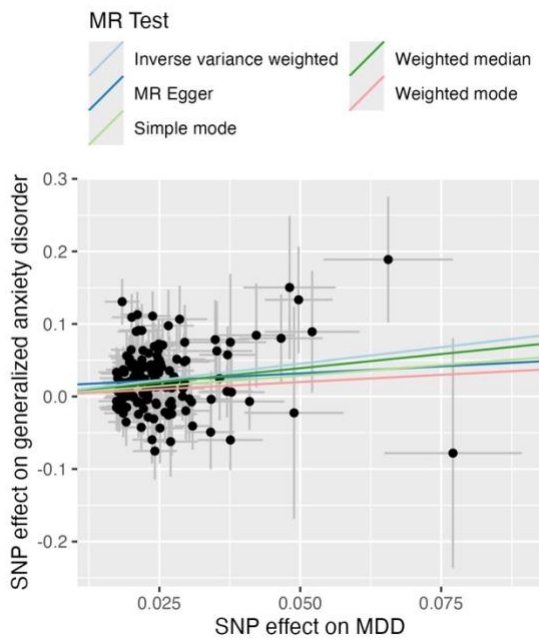
I. Anxiety Disorder



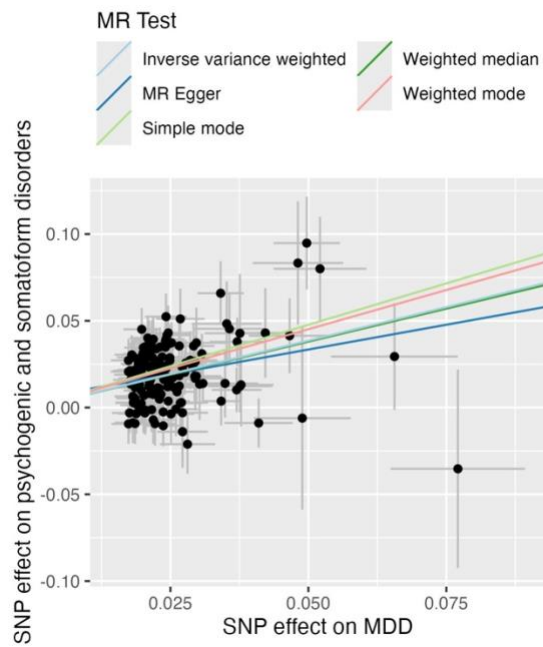
J. Bipolar



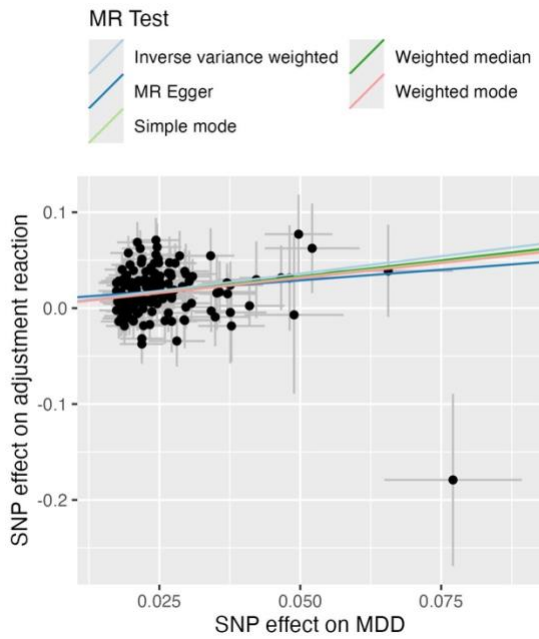
K. Generalized Anxiety Disorder



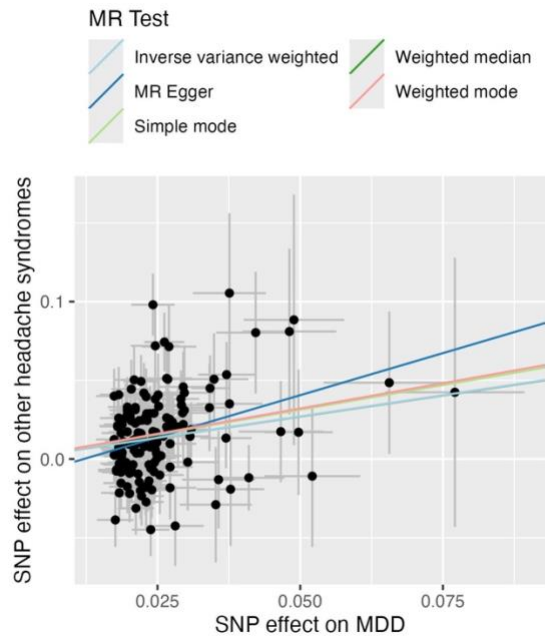
L. Psychogenic And Somatoform Disorders



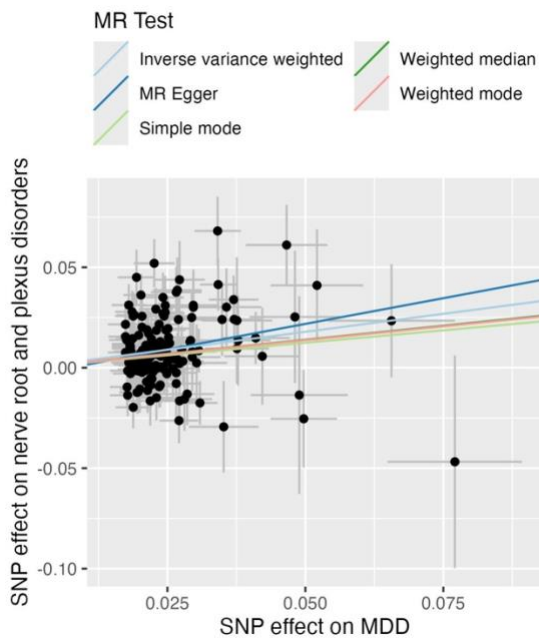
M. Adjustment Reaction



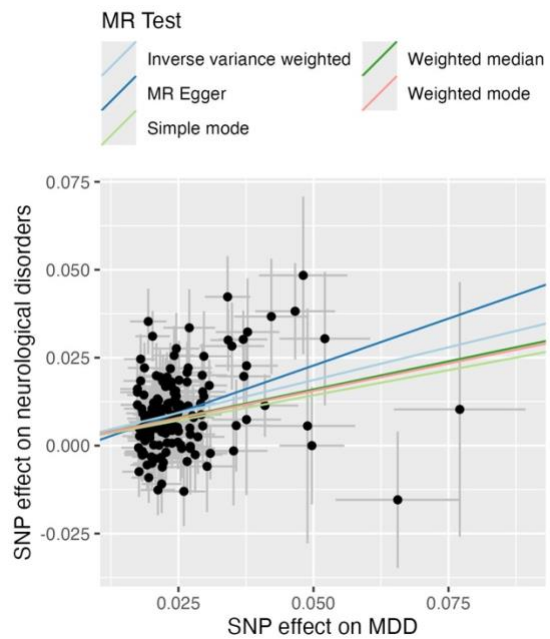
N. Other Headache Syndromes



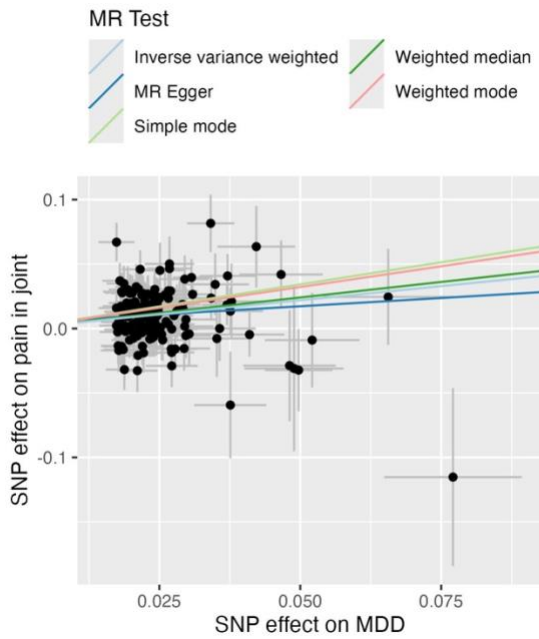
O. Nerve Root And Plexus Disorders



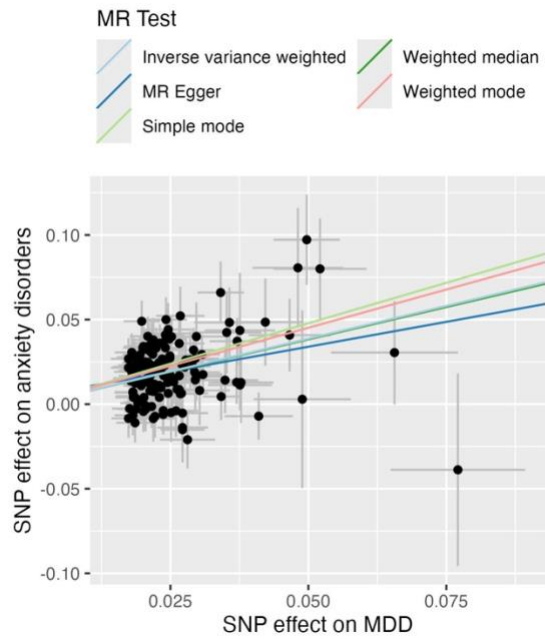
P. Neurological Disorders



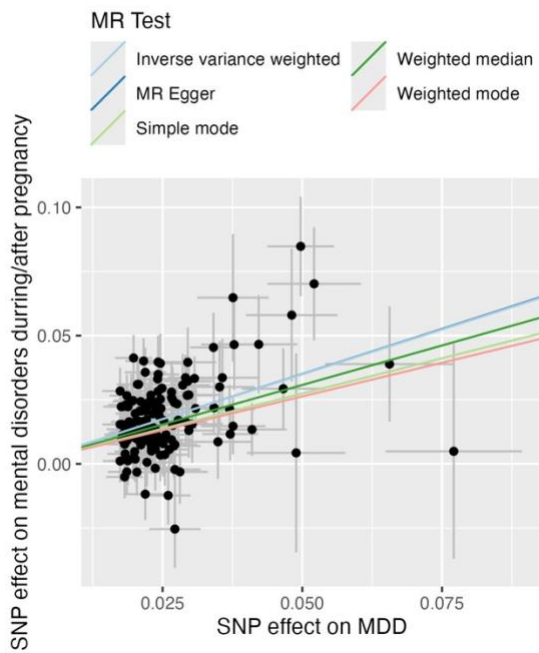
Q. Pain In Joint



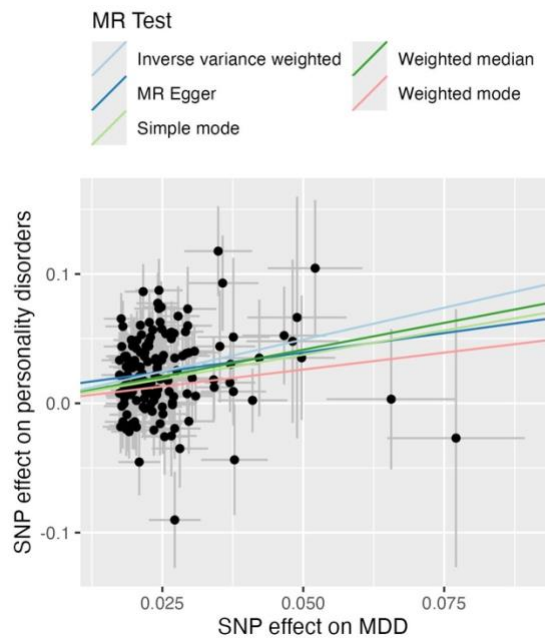
R. Anxiety Disorders



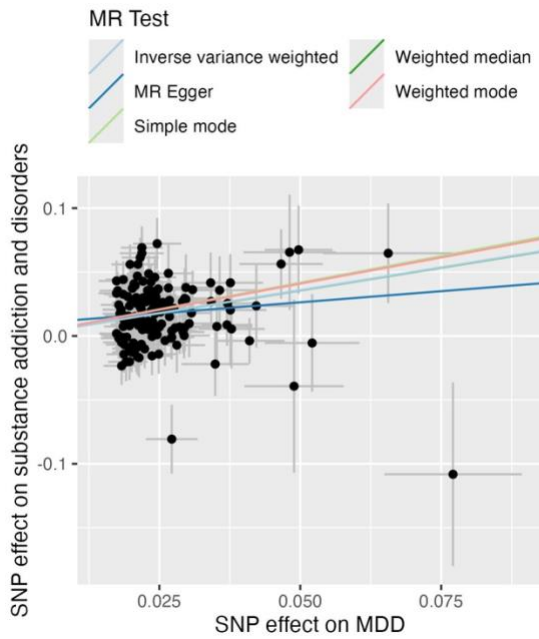
S. Mental Disorders Durring/After Pregnancy



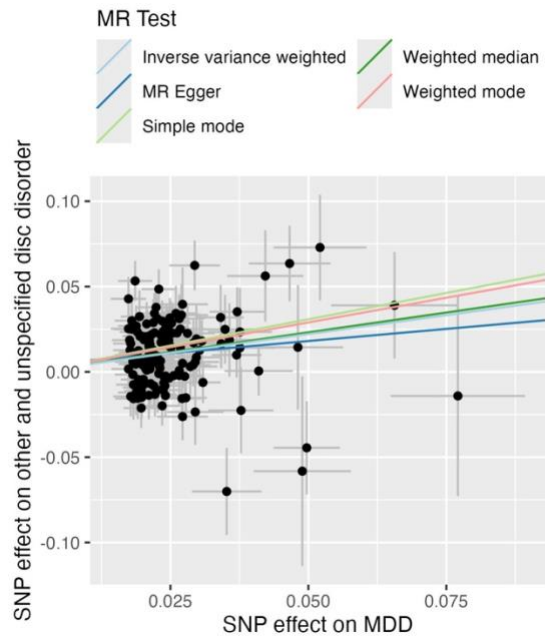
T. Personality Disorders



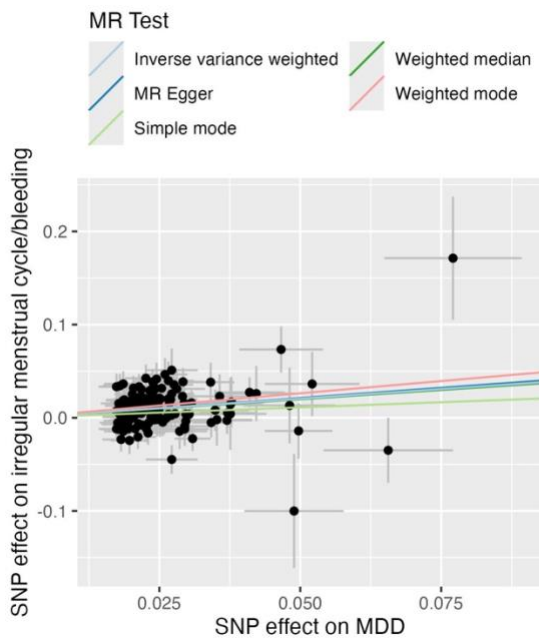
U. Substance Addiction And Disorders



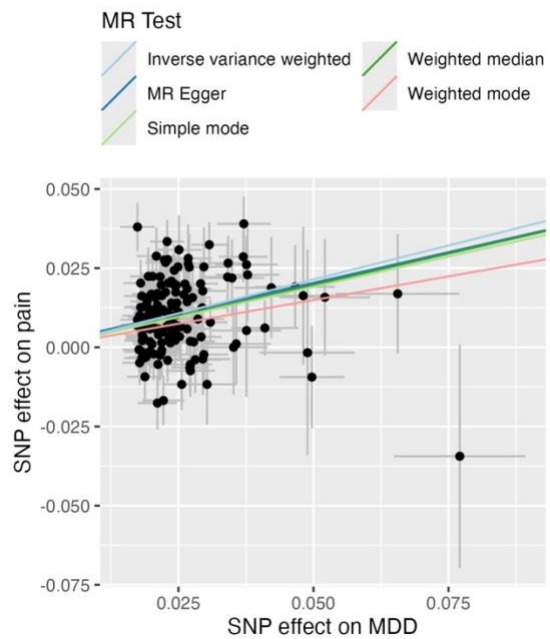
V. Other And Unspecified Disc Disorder



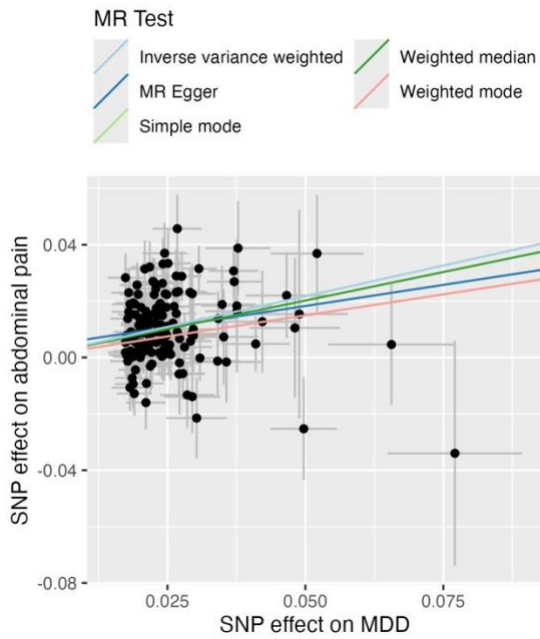
W. Irregular Menstrual Cycle/Bleeding



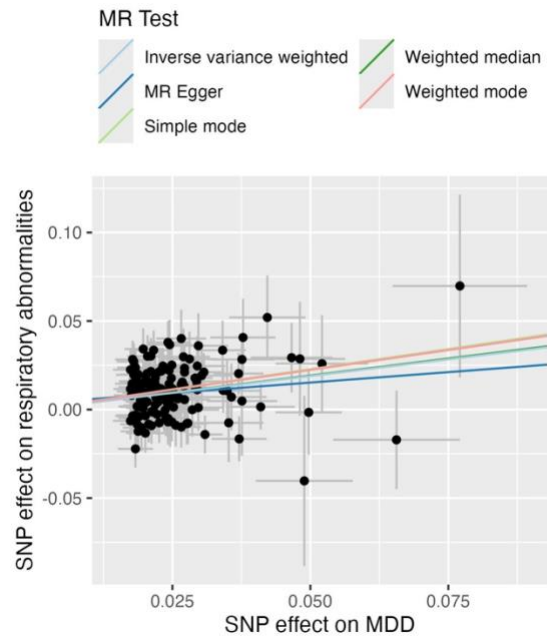
X. Pain



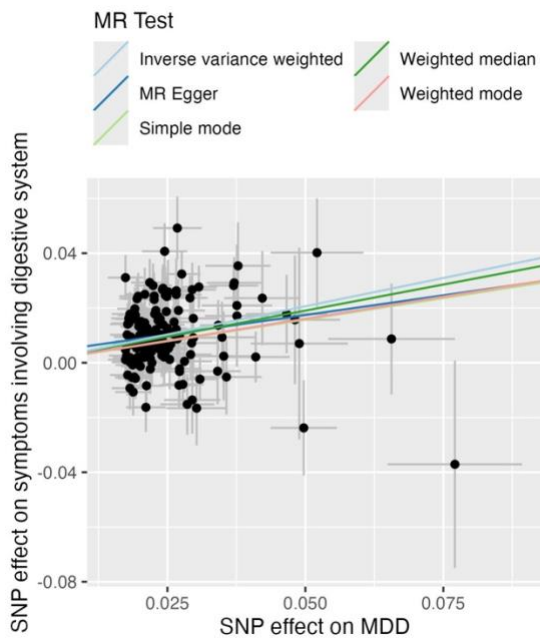
Y.Abdominal Pain



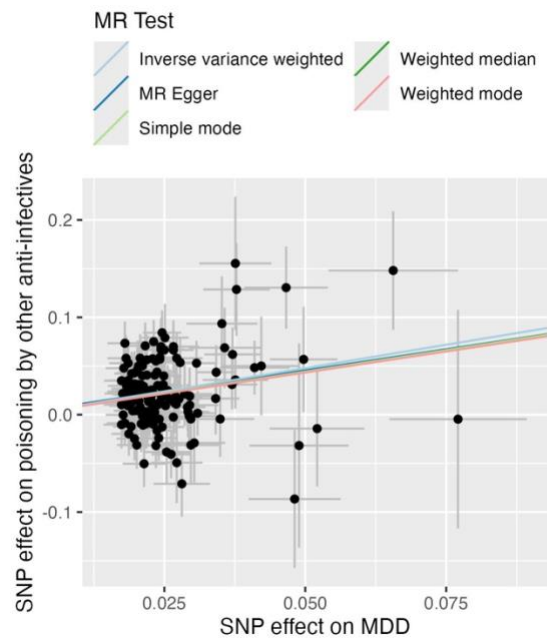
Z.Respiratory Abnormalities



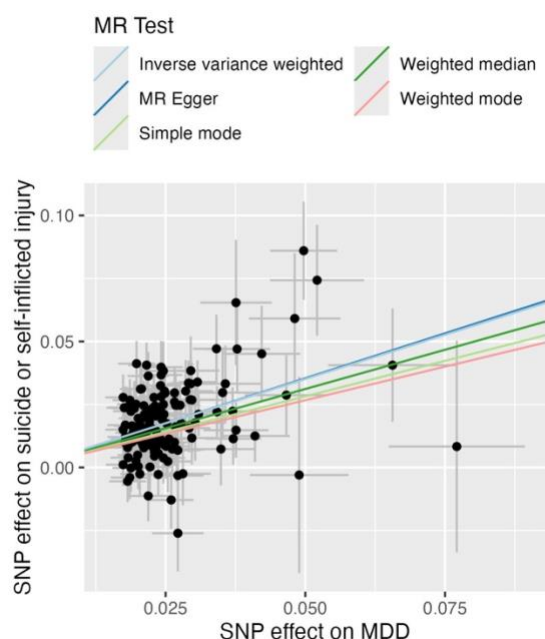
AA.Symptoms Involving Digestive System



AB.Poisoning By Other Anti-Infectives



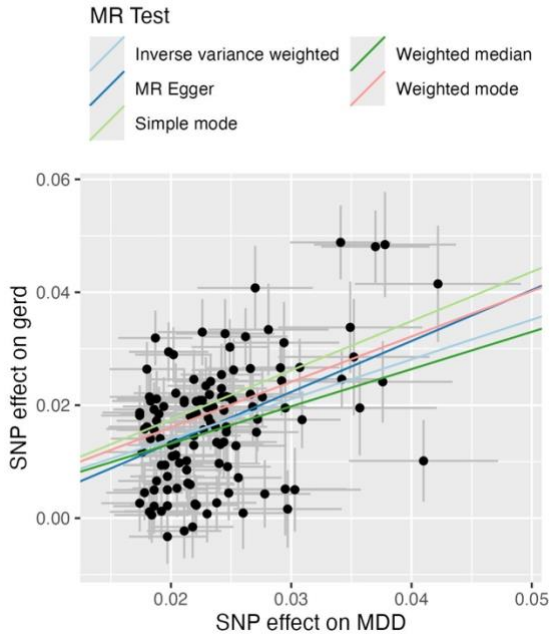
AC.Suicide Or Self-Inflicted Injury



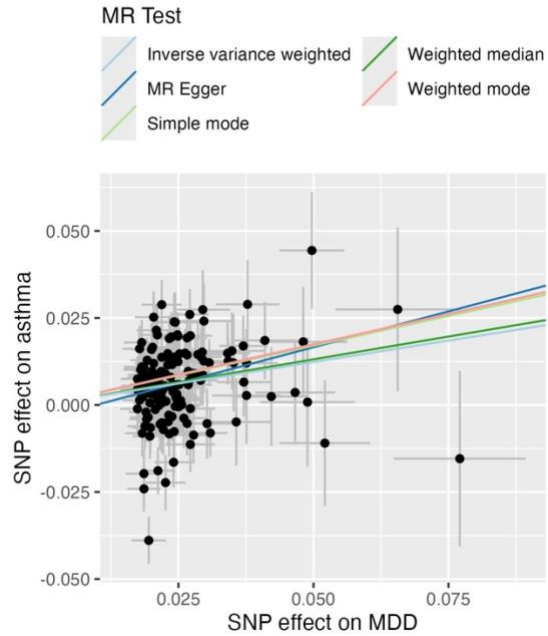
A. GERD. B. Urinary Tract Infection. C. Other and Unspecified Disorders of Back. D. Nonspecific Chest Pain. E. Back Pain. F. Chronic Airway Obstruction. G. Chronic Bronchitis. H. Alcohol-Related Disorders. I. Anxiety Disorder. J. Bipolar. K. Generalized Anxiety Disorder. L. Psychogenic and Somatoform Disorders. M. Adjustment Reaction. N. Other Headache Syndromes. O. Nerve Root and Plexus Disorders. P. Neurological Disorders. Q. Pain in Joint. R. Anxiety Disorders. S. Mental Disorders during/after Pregnancy. T. Personality Disorders. U. Substance Addiction and Disorders. V. Other and Unspecified Disc Disorder. W. Irregular Menstrual Cycle/Bleeding. X. Pain. Y. Abdominal Pain. Z. Respiratory Abnormalities. AA. Symptoms Involving Digestive System. AB. Poisoning by other Anti-infectives. AC. Suicide or Self-inflicted Injury. The slope of each line corresponds to the estimated MR effect per method.

Supplementary Figure 4. Scatter plots of bidirectional Mendelian randomization tests between MDD and 10 MDD-PRS associated traits, in the direction of MDD causing other traits (**AA to AJ**) and the direction of other traits causing MDD (**BA to BJ**).

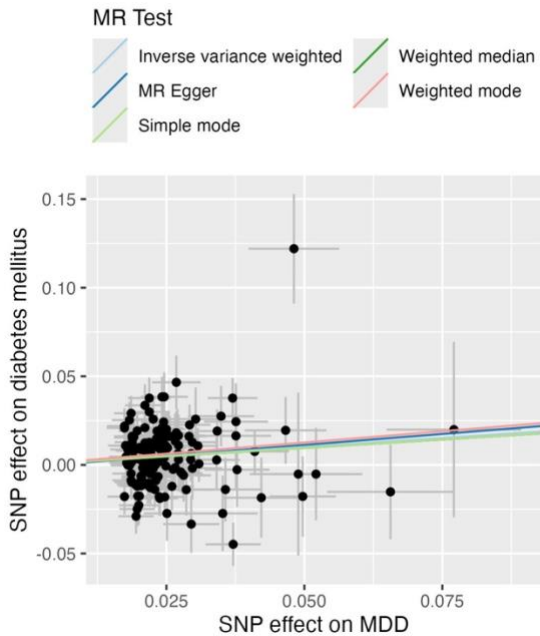
AA.MDD→GERD



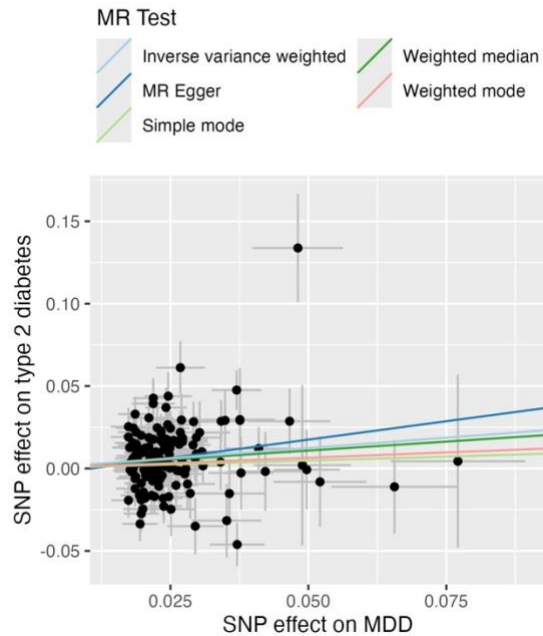
AB.MDD→Asthma



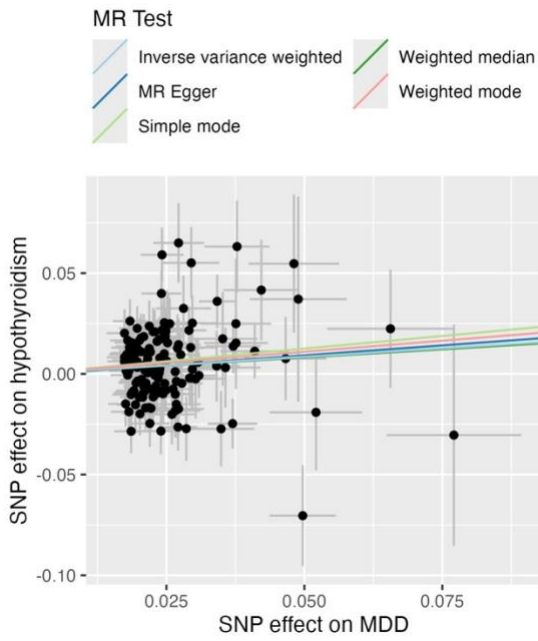
AC.MDD→Diabetes Mellitus



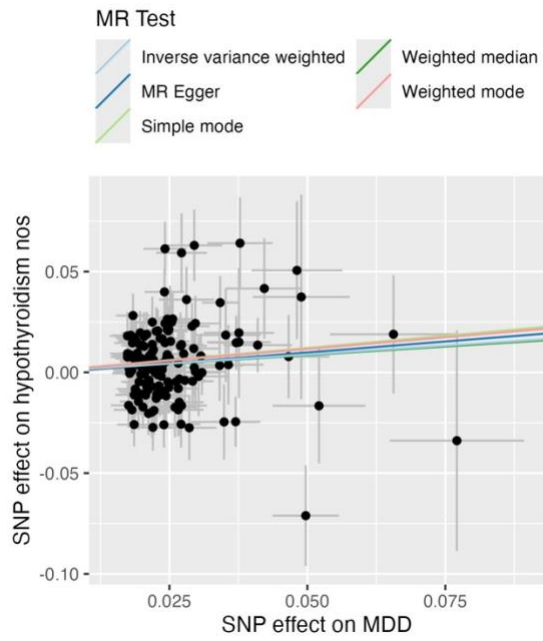
AD.MDD→Type 2 Diabetes



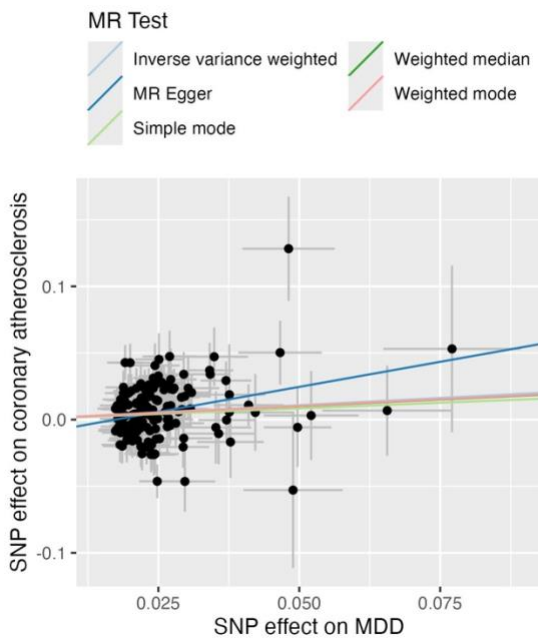
AE.MDD→Hypothyroidism



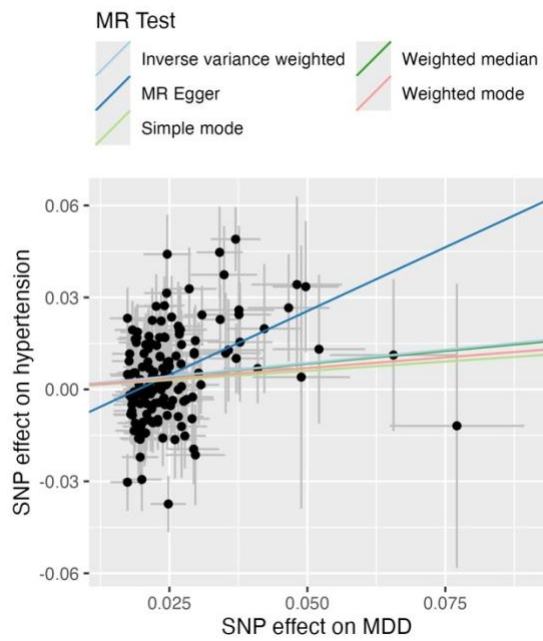
AF.MDD→Hypothyroidism Nos



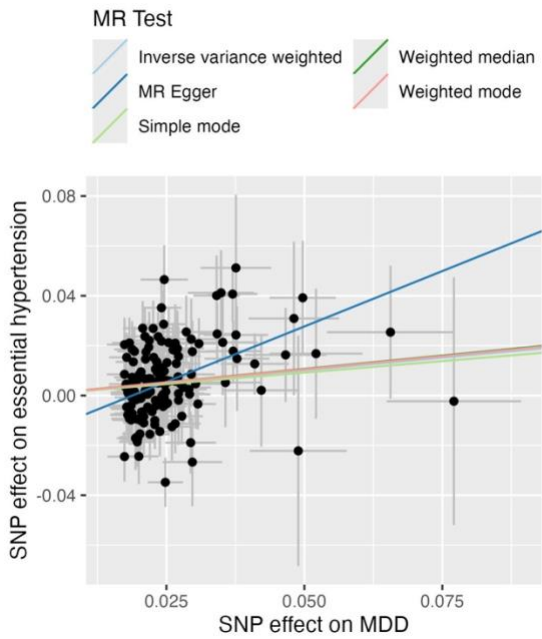
AG.MDD→Coronary Atherosclerosis



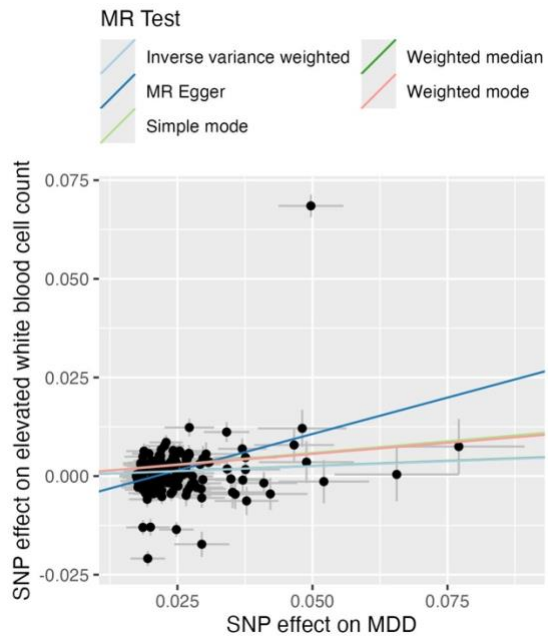
AH.MDD→Hypertension



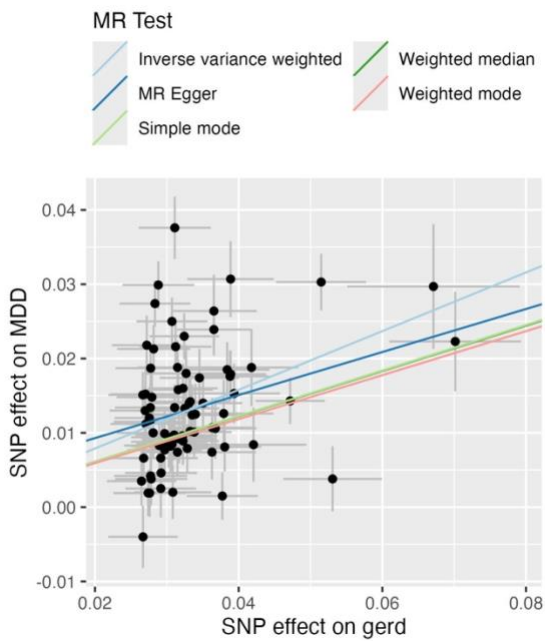
AI.MDD→Essential Hypertension



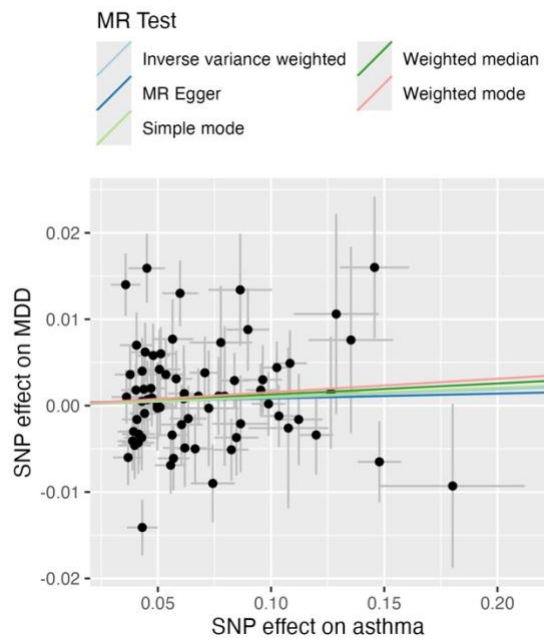
AJ.MDD→Elevated White Blood Cell Count



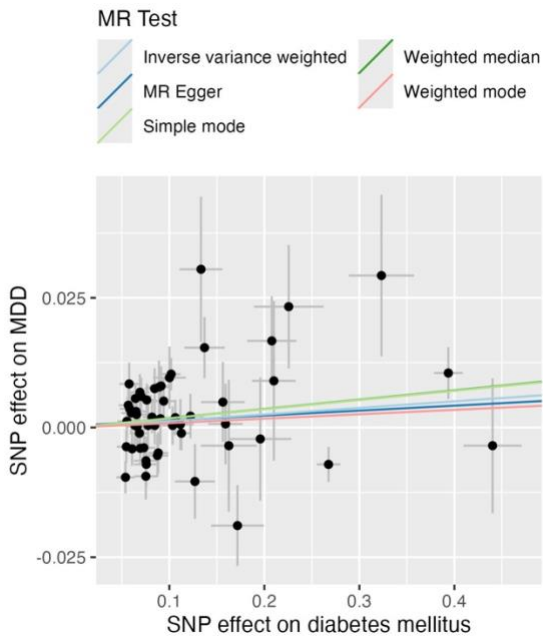
BA.GERD→MDD



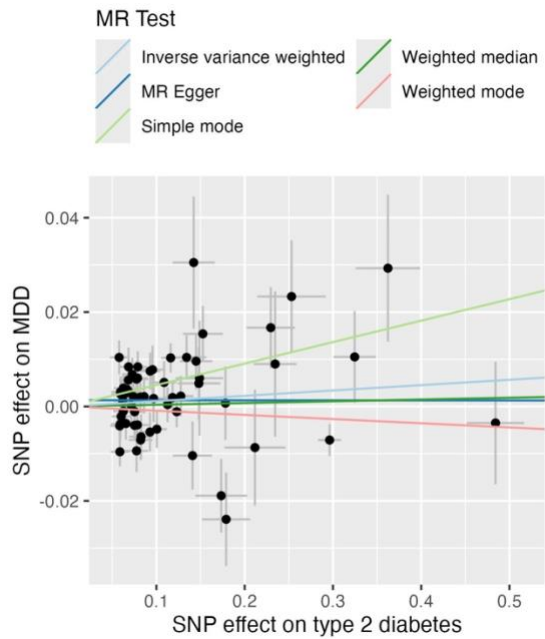
BB.Asthma→MDD



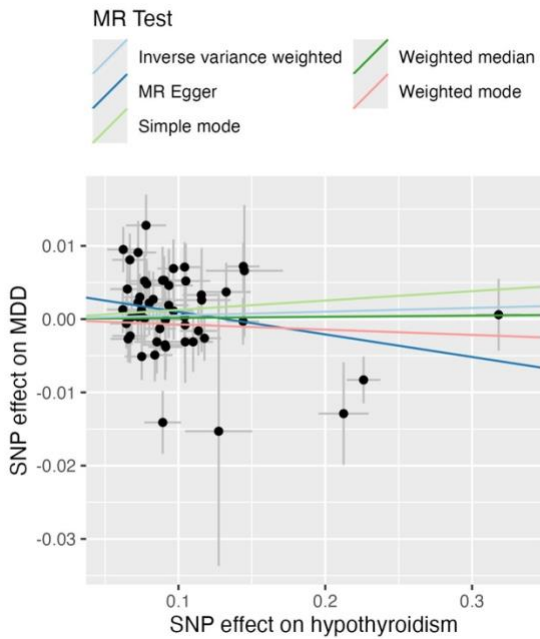
BC.Diabetes Mellitus→MDD



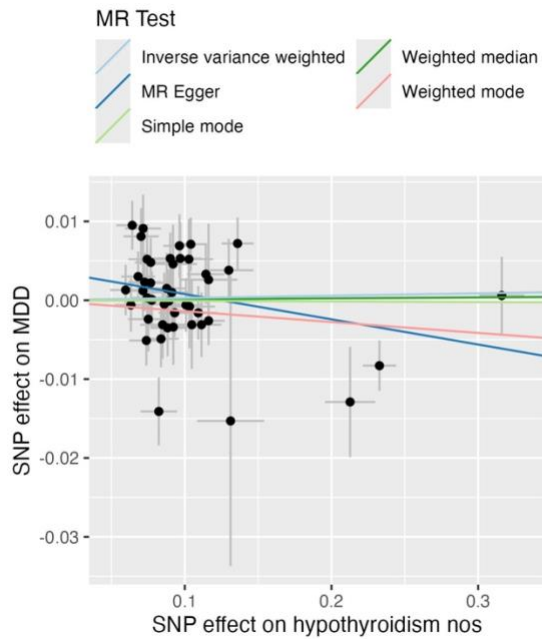
BD.Type 2 Diabetes→MDD



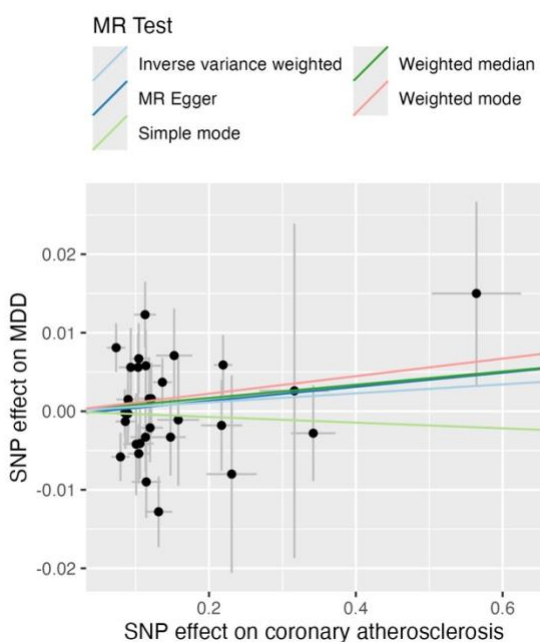
BE.Hypothyroidism→MDD



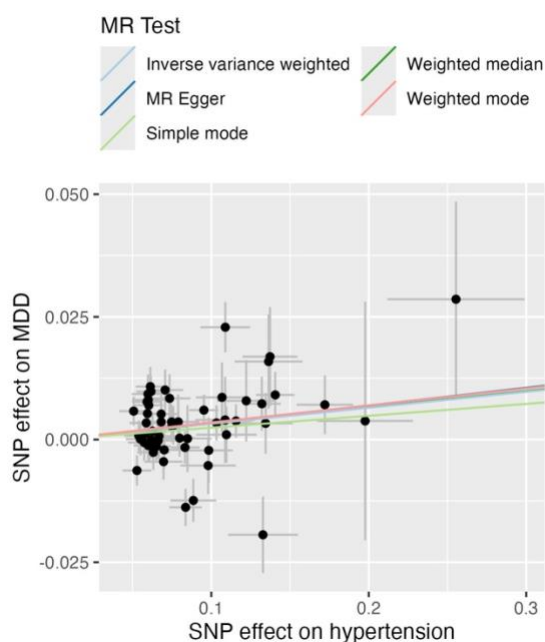
BF.Hypothyroidism Nos→MDD



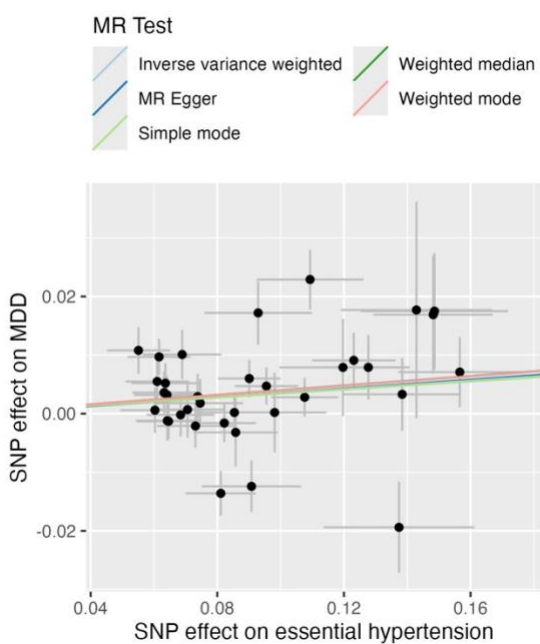
BG. Coronary Atherosclerosis → MDD



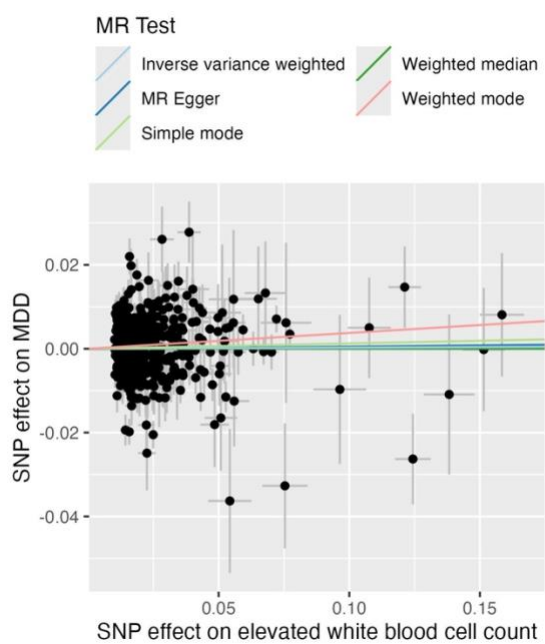
BH. Hypertension → MDD



BI. Essential Hypertension → MDD



BJ. Elevated White Blood Cell Count → MDD



AA. MDD → GERD. AB. MDD → Asthma. AC. MDD → Diabetes Mellitus. AD. MDD → Type 2 Diabetes. AE. MDD → Hypothyroidism. AF. MDD → Hypothyroidism NOS. AG. MDD → Coronary Atherosclerosis. AH. MDD → Hypertension. AI. MDD → Essential Hypertension. AJ. MDD → Elevated White Blood Cell Count. BA. GERD → MDD. BB. Asthma → MDD. BC. Diabetes Mellitus → MDD. BD. Type 2 Diabetes → MDD. BE. Hypothyroidism → MDD. BF. Hypothyroidism NOS → MDD. BG. Coronary

Atherosclerosis →MDD. BH. Hypertension →MDD. BI. Essential Hypertension →MDD. BJ. Elevated White Blood Cell Count →MDD. The slope of each line corresponds to the estimated MR effect per method.