

The Causal Effects between Mood Swings and Gastrointestinal Diseases: A Mendelian Randomization Study

ABSTRACT

Background: Numerous studies have examined the links between mental disorders such as depression and bipolar disorder, and gastrointestinal (GI) diseases. However, few studies have investigated the link between mood swings and GI diseases. Given the impact of mood swings on various conditions and the growing comprehension of the gut-brain axis, this study aims to explore their causal relationship using Mendelian randomization (MR) methods.

Methods: Single-nucleotide polymorphisms (SNPs) associated with mood swings were obtained from a recent study. SNPs associated with GI diseases were identified from the FinnGen project. We conducted two-sample bidirectional MR analyses using three methods, primarily the inverse variance weighting (IVW) method. Furthermore, we performed sensitivity analyses and false discovery rate (FDR) analysis to validate the accuracy and robustness of the results.

Results: Bidirectional MR analysis revealed significant causal effects between mood swings and GI diseases according to the IVW method (odds ratio (OR): 1.213; 95% confidence interval (CI): 1.118-1.316; $P=3.490e-6$; $P_{FDR}=8.730e-5$). Mood swings were linked to an increased risk for 11 of 24 diseases, including five upper GI diseases (gastroesophageal reflux disease (GERD), acute gastritis, gastroduodenal ulcer, duodenal ulcer, and functional dyspepsia), two lower GI diseases (diverticular disease of the intestine and irritable bowel syndrome (IBS)) and four hepatobiliary and pancreatic diseases (nonalcoholic fatty liver disease (NAFLD), chronic pancreatitis, acute pancreatitis, and pancreatic cancer). Inverse MR analysis showed no causal relationship between 24 GI diseases and mood swings.

Conclusions: This comprehensive MR analysis suggests that genetically predicted mood swings may be a risk factor in the development of GI diseases. Interventions for mood swings may help to treat GI diseases.

Keywords: Mendelian randomization, mood swings, gastrointestinal diseases

Introduction

It is well known that emotions are closely related to almost all diseases, such as cardiovascular and cerebrovascular diseases, mental diseases, digestive diseases, and endocrine diseases. Numerous studies¹⁻³ have explored the intricate interplay between gastrointestinal (GI) diseases and various psychological factors. For example, up to one-third of people with irritable bowel syndrome (IBS) also experience anxiety or depression.⁴ The discovery of the gut-brain axis has prompted many researchers to focus on the link between GI diseases and the psychophysiological aspects of the brain.^{5,6} However, while the association between psychotic illness and GI diseases such as inflammatory bowel disease (IBD) and IBS has been extensively documented, evidence on the relationship between personality traits, such as mood swings, and these diseases are limited.



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Received: May 9, 2024
Revision Requested: June 3, 2024
Last Revision Received: June 9, 2024
Accepted: July 2, 2024
Publication Date: September 5, 2024

Cite this article as: Wang K, Wang S, Chen X. The causal effects between mood swings and gastrointestinal diseases: A Mendelian randomization study. *Alpha Psychiatry*. 2024;25(4):533-540.



Mood instability is a common personality trait characterized by frequent, sudden, and unpredictable emotional changes.⁷ Numerous studies have shown a strong association between mood instability and mental illnesses, including bipolar disorder, schizophrenia, major depressive disorder, and anxiety disorders.⁷⁻⁹ A common symptom of individuals with mood instability is mood swings.¹⁰ In the UK-Biobank, mood swings are defined by the answer to the question, "Does your mood often go up and down?"¹¹ Obvious mood swings, defined as high mood instability, are considered a key risk factor in psychopathology.¹² Therefore, mood swings may be associated with an increased risk of diseases in patients with mood instability. It is worth noting that several studies have shown that mood swings may be a risk factor for cardiovascular diseases and cerebrovascular diseases.¹³⁻¹⁵ However, very few studies have focused on the relationship between mood swings and GI diseases. A Mendelian randomization (MR) study suggested that mood swings, high tension, and anxious feelings, are causally related to an increased risk of developing gastroesophageal reflux disease (GERD).¹⁶ IBS patients are commonly reported to have mood swings.¹⁷ Overall, mood swings are a relatively new field in GI disease research, with limited studies.

MR is an analytical method for assessing causal relationships between exposures and clinical outcomes. MR studies can use genetic variation to explore causality when randomized controlled trials cannot test for causality, or when observational studies are susceptible to confounding or reverse causality. Single-nucleotide polymorphisms (SNPs) are a type of genetic variation that is known to be valuable. In this study, SNPs were used as instrumental variables (IVs). Given that previous studies have focused on IBS, GERD, and IBD, our bidirectional MR analysis mainly focused on exploring the causal association between mood swings and GERD as well as IBS. At the same time, the relationships between mood swings and other GI diseases were also examined, with the aim of better understanding the causal relationship between mood swings and full-blown GI diseases and to provide sound recommendations for public health programs.

MAIN POINTS

- This study is the first to explore the bidirectional causal association between mood swings and gastrointestinal (GI) diseases. The advantage of utilizing the Mendelian randomization design is its capability to directly detect causality, which is superior to observational studies as it helps to avoid confounders and reverse causality.
- Almost all common systemic GI diseases were included in this study. This approach provides the most systematic risk assessment of mood swings with 24 GI diseases.
- We performed false discovery rate correction to ensure the reliability of the results.
- Our findings suggest that mood swings could increase the risk of developing various GI diseases, including gastroesophageal reflux disease, acute gastritis, chronic gastritis, gastroduodenal ulcer, gastric ulcer, duodenal ulcer, diverticular disease of the intestine, nonalcoholic fatty liver disease, chronic pancreatitis, acute pancreatitis, irritable bowel syndrome, pancreatic cancer, and functional dyspepsia. Our results offer insights for the early screening of GI diseases and the potential development of new treatments.

Materials and Methods

Study Design

In MR research, the IVs must meet three fundamental assumptions: (1) IVs must be directly associated with exposure factors, (2) IVs are not affected by any potential confounding factors, and (3) IVs do not influence the outcomes other than exposure pathways that affect outcomes (Figure 1).¹⁸ The mood swings sample information was sourced from the UK Biobank. The GI disease sample information was sourced from the FinnGen project. The outcomes in this study were total GI diseases and 24 GI subtypes, including 10 upper GI diseases, five lower GI diseases, eight hepatobiliary and pancreatic diseases, and other diseases such as acute appendicitis.

Data Sources for Mood Swings

Candidate gene tools for mood swings were obtained from the most recent genome-wide association study (GWAS), which included 445 274 participants from the UK Biobank (201 373 cases and 243 901 controls).¹⁹ GWAS summary statistics can be downloaded from the GWAS Catalog at <https://www.ebi.ac.uk>. The UK Biobank study is an ongoing cohort study initiated by recruiting approximately 500 000 adults aged between 40 and 69 from 2006 to 2010. It is a large-scale open database containing hundreds of thousands of individuals' genotype data paired with electronic health records and survey measures.¹¹ Mood swings are defined as answering yes to the question "Does your mood often go up and down?". Detailed information is shown in Table 1 and Supplementary Table S1.

Data Sources for GI Diseases

We selected European samples in all cases to avoid multiplicity bias across geographical regions. In addition, the FinnGen project (<https://www.finnngen.fi/en>)²⁰ was chosen for the GI disease samples. This choice was made because the exposure SNPs were sourced from the UK Biobank, thus preventing any overlap with the samples. The FinnGen study is a large-scale genomics initiative that has analyzed over 500 000 Finnish biobank samples. It correlates genetic variation with health data to understand disease mechanisms and predispositions. The project is a collaboration between research organizations and biobanks within Finland and international industry partners (<https://www.finnngen.fi/en>).²⁰ Detailed information is shown in Table 1 and Supplementary Table S1.

Selection of Instrumental Variables

The screening criteria for candidate IVs were as follows: (1) genome-wide significant SNPs were extracted from the GWAS pooled data ($P < 5e-8$), and SNPs with long physical distances ($\geq 10\,000$ kb) and low probability of linkage disequilibrium ($R^2 < 0.001$) were reserved; (2) we chose robust IVs with F -statistics greater than 10.²¹ The F -statistic was calculated as $F = \beta^2/SE^2$ (Supplementary Table S2 and Supplementary Table S7)²²; (3) SNPs with minor allele frequencies (MAF ≥ 0.01) were excluded; (4) we removed the palindrome sequence from the tool variable; and (5) we excluded SNPs directly associated with GI diseases and some of the recognized confounders associated with GI disease such as smoking,²³ drinking,²³ depression,²⁴ and body mass index (BMI),²⁵ based on LD trait (<https://ldlink.nci.nih.gov/?tab=ldtrait>).²⁶ The specific excluded SNPs and their associated traits are detailed in Supplementary Table S3. Finally, before each MR analysis, outliers were removed using the MR-PRESSO test.

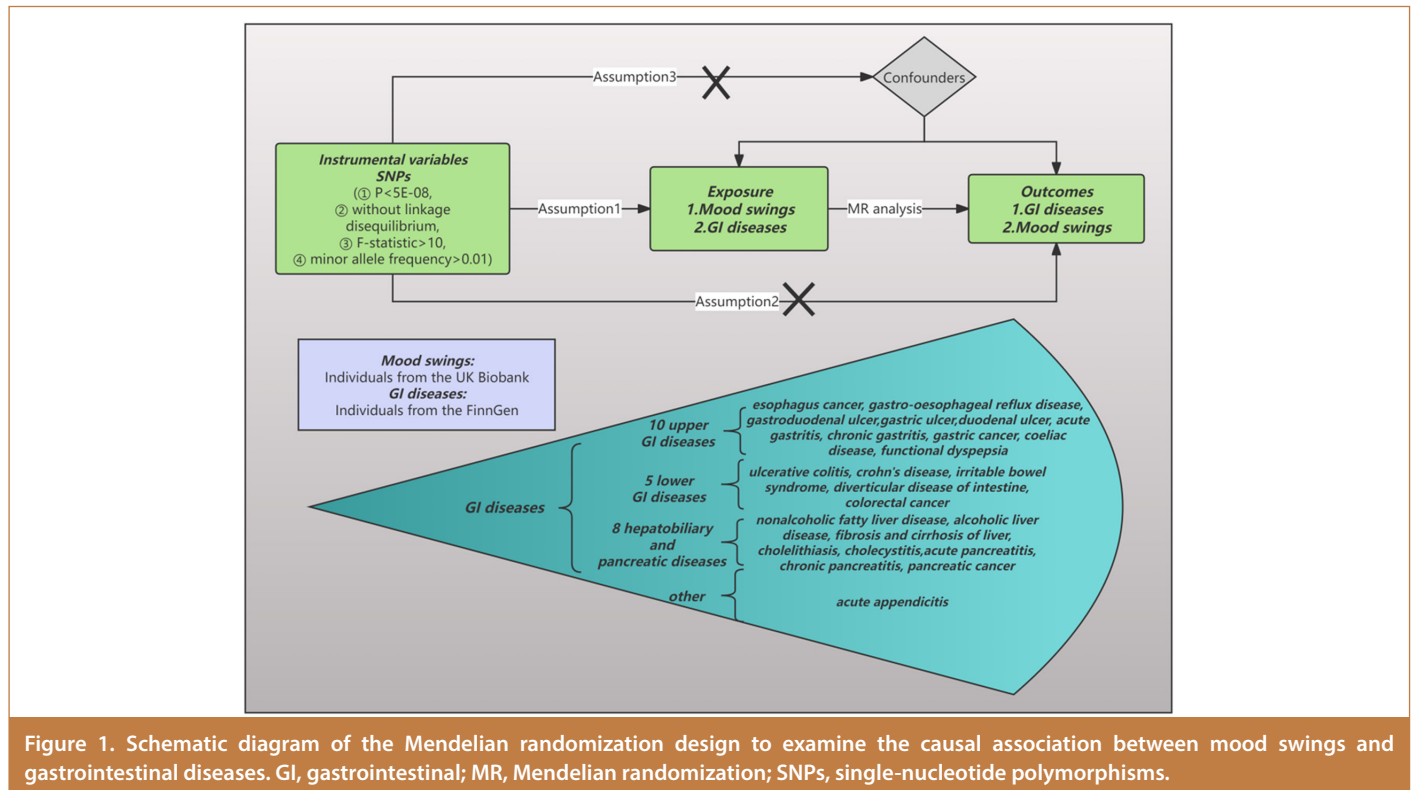


Figure 1. Schematic diagram of the Mendelian randomization design to examine the causal association between mood swings and gastrointestinal diseases. GI, gastrointestinal; MR, Mendelian randomization; SNPs, single-nucleotide polymorphisms.

MR Analysis

In this study, we utilized the inverse variance weighting (IVW) method as the primary method for estimating causal effects. The IVW model is considered the most powerful method for detecting causality in two-sample MR analysis.²⁷ The MR-Egger and weighted median methods were used to support and complement the findings obtained through the IVW results. Cochran's Q -test was performed to evaluate the heterogeneity of the IVW model. Cochran's Q -test of $P < .05$ indicates heterogeneity.²⁸ If no heterogeneity was present, a fixed-effects model was used. Otherwise, a random effects model was used.²⁹ The MR-Egger intercept test was performed to assess whether the included SNPs were potentially horizontally pleiotropic, and a P -value of $< .05$ indicated the presence of pleiotropy.³⁰ The leave-one-out sensitivity test was used to eliminate SNPs to determine the sensitivity of individual SNPs in this MR study. This study also used scatter, forest, and funnel plots for visualization and analysis.³¹ Finally, to fully and accurately represent the causal relationship between mood swings and GI diseases, we applied FDR correction to refine the causal relationship. $P < .05$ was considered statistically significant (two-sided). Odds ratio (OR) and 95% confidence interval (CI) were used to describe the relative risk between mood swings and GI diseases.

The above analyses were performed in R version 4.3.1. The "TwoSampleMR" (<https://mrcieu.github.io/TwoSampleMR/>) and "MR-PRESSO" (<https://github.com/rondolab/MR-PRESSO>) packages were used. TwoSampleMR, which includes various analysis methods, is a package used for conducting MR with GWAS summary data. There are three uses for MR-PRESSO: (1) detecting cross-sectional multicollinearity, (2) correcting for cross-sectional multicollinearity by removing outliers, and (3) testing for significant differences in causal estimates before and after the removal of outliers.³²

Results

MR Analysis Results between 24 GI Diseases and Mood Swings

The exposure sample information was from the UK-Biobank (201 373 cases and 243 901 controls),¹⁹ and the GI diseases sample information was from the FinnGen project.²⁰ A P -value of $< 5 \times 10^{-8}$ was chosen as the screening criterion for mood swing-associated SNPs. After a rigorous IV selection process of removing SNPs with linkage disequilibrium and unsatisfactory MAFs ($MAF < 0.01$), 56 strong IVs were finally chosen, all of which had F -statistics exceeding 10 (Supplementary Table S2).

After FDR correction, we found a significant causal association between mood swings and GI diseases ($OR = 1.213$, 95% $CI = 1.118-1.316$, $P = 3.490 \times 10^{-6}$, $P_{FDR} = 8.730 \times 10^{-5}$). When subtypes of GI diseases were taken into account, mood swings were significantly causally positively associated with 11 GI diseases (Figure 2 and Supplementary Table S4). In detail, mood swings were a significant risk factor for GERD ($OR = 1.294$, 95% $CI = 1.145-1.463$, $P = 3.870 \times 10^{-5}$, $P_{FDR} = 4.838 \times 10^{-4}$), acute gastritis ($OR = 1.664$, 95% $CI = 1.242-2.229$, $P = 6.406 \times 10^{-4}$, $P_{FDR} = 5.339 \times 10^{-3}$), gastroduodenal ulcer ($OR = 1.303$, 95% $CI = 1.113-1.524$, $P = 9.771 \times 10^{-4}$, $P_{FDR} = 4.071 \times 10^{-3}$), duodenal ulcer ($OR = 1.435$, 95% $CI = 1.116-1.846$, $P = 4.896 \times 10^{-3}$, $P_{FDR} = 1.360 \times 10^{-2}$), diverticular disease of the intestine ($OR = 1.190$, 95% $CI = 1.030-1.374$, $P = 1.791 \times 10^{-2}$, $P_{FDR} = 4.071 \times 10^{-2}$), nonalcoholic fatty liver disease (NAFLD; $OR = 1.507$, 95% $CI = 1.107-2.050$, $P = 9.088 \times 10^{-3}$, $P_{FDR} = 2.272 \times 10^{-2}$), chronic pancreatitis ($OR = 1.541$, 95% $CI = 1.194-1.988$, $P = 8.787 \times 10^{-4}$, $P_{FDR} = 5.492 \times 10^{-3}$), acute pancreatitis ($OR = 1.368$, 95% $CI = 1.133-1.651$, $P = 1.096 \times 10^{-3}$, $P_{FDR} = 3.914 \times 10^{-3}$), IBS ($OR = 1.375$, 95% $CI = 1.139-1.661$, $P = 9.414 \times 10^{-4}$, $P_{FDR} = 4.707 \times 10^{-3}$), pancreatic cancer ($OR = 1.553$, 95% $CI = 1.078-2.236$, $P = 1.810 \times 10^{-2}$, $P_{FDR} = 3.770 \times 10^{-2}$), and functional dyspepsia ($OR = 1.327$, 95% $CI = 1.114-1.582$,

Table 1. Genome-Wide Association Study Summary Data Details

| Phenotypes | Data sources | Sample size | Population |
|-----------------------------------|---------------|------------------------------------|------------|
| Mood swings | GWAS catalog | 201 373 cases and 243 901 controls | European |
| Gastrointestinal diseases | FinnGen (R7) | 159 111 cases and 150 043 controls | European |
| Gastro-esophageal reflux disease | FinnGen (R10) | 28 859 cases and 350 064 controls | European |
| Acute gastritis | FinnGen (R10) | 2558 cases and 350 064 controls | European |
| Chronic gastritis | FinnGen (R10) | 3875 cases and 361 641 controls | European |
| Gastric ulcer | FinnGen (R10) | 6459 cases and 350 064 controls | European |
| Duodenal ulcer | FinnGen (R10) | 3795 cases and 350 064 controls | European |
| Gastroduodenal ulcer | FinnGen (R10) | 10 021 cases and 350 064 controls | European |
| Crohn's disease | FinnGen (R10) | 2033 cases and 409 940 controls | European |
| Ulcerative colitis | FinnGen (R10) | 5931 cases and 405 386 controls | European |
| Diverticular disease of intestine | FinnGen (R10) | 33 619 cases and 329 381 controls | European |
| Acute pancreatitis | FinnGen (R10) | 6787 cases and 361 641 controls | European |
| Chronic pancreatitis | FinnGen (R10) | 3875 cases and 361 641 controls | European |
| Irritable bowel syndrome | FinnGen (R10) | 10 329 cases and 329 381 controls | European |
| Functional dyspepsia | FinnGen (R10) | 9680 cases and 3 500 641 controls | European |
| Coeliac disease | FinnGen (R10) | 4115 cases and 394 391 controls | European |
| Acute appendicitis | FinnGen (R10) | 31 628 cases and 378 082 controls | European |
| Alcoholic liver disease | FinnGen (R10) | 3047 cases and 400 247 controls | European |
| Nonalcoholic fatty liver disease | FinnGen (R10) | 2568 cases and 409 613 controls | European |
| Fibrosis and cirrhosis of liver | FinnGen (R10) | 2017 cases and 400 247 controls | European |
| Cholelithiasis | FinnGen (R10) | 40 191 cases and 361 641 controls | European |
| Cholecystitis | FinnGen (R10) | 46 971 cases and 361 641 controls | European |
| Esophagus cancer | FinnGen (R10) | 619 cases and 314 193 controls | European |
| Gastric cancer | FinnGen (R10) | 1423 cases and 314 193 controls | European |
| Colorectal cancer | FinnGen (R10) | 6847 cases and 314 193 controls | European |
| Pancreatic cancer | FinnGen (R10) | 1626 cases and 314 193 controls | European |

GWAS, genome-wide association study.

$P=1.555e-03$, $P_{FDR}=4.860e-03$). Moreover, there was a potential causal association between mood swings and gastric ulcer (OR=1.231, 95% CI=1.015-1.494, $P=3.509e-02$, $P_{FDR}=6.265e-02$) and chronic gastritis (OR=1.182, 95% CI=1.013-1.379, $P=3.378e-02$,

$P_{FDR}=6.497e-02$). No causal relationship was found with the other 13 GI diseases. Sensitivity analyses showed that there was no pleiotropy in any of the associations between mood swings and the above 10 GI diseases (Table 2 and Supplementary Table S5). Furthermore, although there was heterogeneity in associations (Table 2 and Supplementary Table S6) between mood swings and GERD ($P_{\text{heterogeneity}}=2.277e-03 < .05$), diverticular disease of the intestine ($P_{\text{heterogeneity}}=1.061e-07 < .05$), IBS ($P_{\text{heterogeneity}}=1.379e-02 < .05$), and functional dyspepsia ($P_{\text{heterogeneity}}=4.882e-02 < .05$), this did not affect the results. Leave-one-out analysis showed similar results (Supplementary Figures). Scatterplots and funnel plots also showed the stability of the results (Supplementary Figures).

Reverse MR Analysis Results between 24 GI Diseases and Mood Swings

The P -value of $<5e-8$ was selected as the screening criterion for SNPs related to GI diseases. All SNPs included in the analysis were powerful IVs (F -statistics > 10). Four GI diseases (acute gastritis, gastroduodenal ulcer, esophageal cancer, and IBS) were excluded from the reverse MR analysis because no SNPs were screened. After applying FDR correction, the reverse MR results (Figure 3 and Supplementary Table S8) indicated no causal association between the other 20 GI diseases and mood swings (all $P_{FDR} > .05$). Horizontal pleiotropy (Supplementary Table S9) was detected in individuals with ulcerative colitis and mood swings ($P_{\text{pleiotropy}}=.005 < .05$). Additionally, although there was heterogeneity (Supplementary Table S10) shown by reverse MR analysis between six GI diseases (cholecystitis, cholelithiasis, coeliac disease, diverticular disease of the intestine, functional dyspepsia, and gastric cancer) and mood swings (IVW method, $P < .05$), this did not affect the results.

Discussion

This bidirectional MR study used the large-scale, publicly available GWAS summary statistics to explore the causal relationship between mood swings and common GI diseases for the first time. Using forward MR analysis (Figure 2), we demonstrated that genetically predicted mood swings could elevate the risk of developing eleven GI diseases, including GERD, acute gastritis, gastroduodenal ulcer, gastric ulcer, duodenal ulcer, diverticular disease of the intestine, NAFLD, chronic pancreatitis, acute pancreatitis, IBS, pancreatic cancer, and functional dyspepsia. Using reverse MR analysis (Figure 3), no causal relationships were detected between these eleven GI diseases and mood swings. In general, our bidirectional MR results imply that mood swings may elevate the risk of developing GI diseases such as GERD, acute gastritis, gastroduodenal ulcer, gastric ulcer, duodenal ulcer, diverticular disease of the intestine, NAFLD, chronic pancreatitis, acute pancreatitis, IBS, pancreatic cancer, and functional dyspepsia, thus providing insights for the early screening for GI diseases and the potential development of new treatments.

Personality traits, especially mood swings, have enduring effects from birth, yet limited research has been conducted to investigate their causal relationship with different diseases. Almost all the literature focuses on the association between mental disorders, such as depression and bipolar disorder. Many clinical observational studies have identified the coexistence and interaction between mental illness and various GI diseases. An increased risk of GI diseases was strongly associated with neurocognitive and psychiatric disorders,³³ such as autism,³⁴ dementia,^{35,36} schizophrenia,³⁷ depression, and anxiety.³⁸ The current MR analysis confirmed the findings

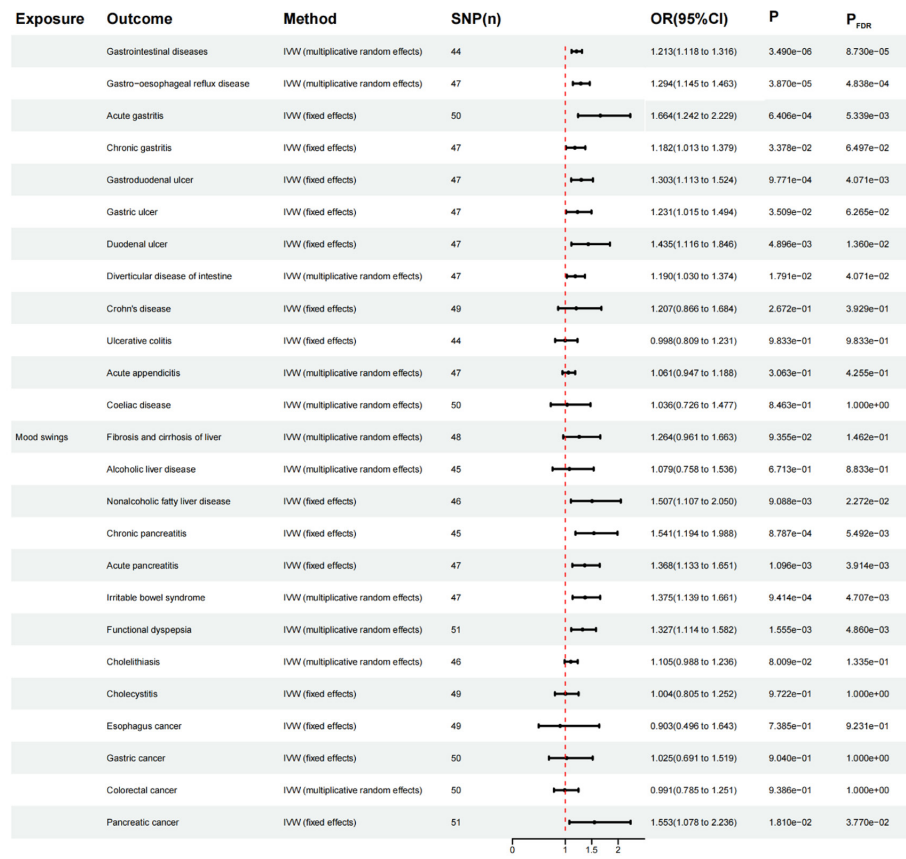


Figure 2. Forest plots of the association between mood swings and GI diseases and final causality. OR, odds ratio; CI, confidence interval; nsnp, number of SNPs; P_{FDR}, P value corrected by false discovery rate (FDR); IWW, inverse variance weighting.

of previous epidemiological studies that depression could increase the risk of IBS,³⁹ NAFLD,⁴⁰ GERD,⁴¹ gastric ulcer, and duodenal ulcer.⁴² However, very few studies have focused on mood swings. An MR study concluded that mood swings and anxious feelings are associated with an increased risk of GERD.¹⁶ Given the growing body of evidence linking mood swings to mental functioning and the fact that mood swings have been recognized as an important factor in understanding clinical and non-clinical emotional states and characteristics,⁴³ we call for more research on mood swings. To our knowledge, our study is the first to examine the causal relationship between mood swings and different GI diseases, which will contribute to a novel perspective on the connection between personality traits and GI diseases.

It is worth noting that the impact of mood swings on the progression of GI disease remains unclear. However, there are some mechanisms that may explain this. First, it is acknowledged that mood swings can induce mental stress,⁴⁴ which may activate the body's defensive response. Consequently, some digestive changes might occur, such as decreased blood flow and increased inflammation,⁴⁵ ultimately damaging the gut lining, disrupting gut motility and secretion, and altering gut microbiota.⁴⁶⁻⁴⁸ Additionally, psychological stress may influence the development of GI diseases through intermediate factors. For instance, stress-triggered GI damage is associated with impaired nutrient absorption.^{49,50} Under psychological stress, individuals are more susceptible to diseases due to the decline in immunity.⁵¹

All of these effects can lead to an increased risk of GI disease. In general, psychological stress can lead to the occurrence of GI diseases.

Considering that mood swings can be a precursor for psychiatric disorders, which are closely linked to GI diseases, early recognition and management of mood swings may decrease the incidence of GI diseases. For instance, it is essential to regularly evaluate mental health using validated questionnaires such as Mood Zoom.⁵² Additionally, individuals experiencing mood swings are also encouraged to do some regular exercise.

A significant amount of effort was invested in preventing IVs from influencing the study results by accounting for confounding factors. We employed stringent criteria for screening SNPs. SNPs associated with GI diseases were excluded if associated with traits such as smoking, alcohol consumption, depression, and body mass index, using the LD trait website. The confounders associated with the diseases mentioned above are well recognized, so we excluded them to prevent unreliable results. Furthermore, we employed the MR-PRESSO method to identify and eliminate aberrant SNPs, Cochran's Q-test to detect heterogeneity, and the MR-Egger intercept test to identify the presence of horizontal pleiotropy. To further demonstrate the stability of our results, we employed the leave-one-out technique and other methods. Finally, we performed FDR to confirm the accuracy and robustness of the results. The methodologies mentioned above are primarily designed to mitigate potential bias and enhance the reliability of the outcomes.

Table 2. Sensitivity Analysis of Causal Associations Between Mood Swings and Gastrointestinal Diseases

| Exposure | Outcome | Cochran Q Statistic | $P_{\text{heterogeneity}}$ | $P_{\text{pleiotropy}}$ |
|-------------|-----------------------------------|---------------------|----------------------------|-------------------------|
| Mood swings | Gastrointestinal diseases | 82.105 | 3.039e-04 | 9.652e-01 |
| | Gastro-esophageal reflux disease | 77.922 | 2.277e-03 | 7.328e-01 |
| | Acute gastritis | 33.706 | 9.529e-01 | 7.985e-01 |
| | Chronic gastritis | 46.827 | 4.383e-01 | 2.023e-01 |
| | Gastroduodenal ulcer | 40.988 | 6.817e-01 | 4.294e-01 |
| | Gastric ulcer | 43.636 | 5.718e-01 | 1.340e-01 |
| | Duodenal ulcer | 46.036 | 4.708e-01 | 9.919e-01 |
| | Diverticular disease of intestine | 114.020 | 1.061e-07 | 2.138e-01 |
| | Crohn's disease | 59.145 | 1.299e-01 | 1.992e-01 |
| | Ulcerative colitis | 56.111 | 8.667e-02 | 1.461e-01 |
| | Acute appendicitis | 73.050 | 6.760e-03 | 6.512e-01 |
| | Coeliac disease | 113.631 | 4.769e-07 | 1.342e-01 |
| | Fibrosis and cirrhosis of liver | 66.823 | 3.014e-02 | 7.400e-01 |
| | Alcoholic liver disease | 66.615 | 1.546e-02 | 3.039e-01 |
| | Nonalcoholic fatty liver disease | 52.375 | 2.095e-01 | 8.788e-01 |
| | Chronic pancreatitis | 43.760 | 4.818e-01 | 2.856e-01 |
| | Acute pancreatitis | 53.681 | 2.036e-01 | 9.245e-01 |
| | Irritable bowel syndrome | 69.638 | 1.379e-02 | 3.930e-01 |
| | Functional dyspepsia | 67.646 | 4.882e-02 | 5.000e-01 |
| | Cholelithiasis | 79.078 | 1.274e-03 | 9.158e-01 |
| | Cholecystitis | 43.009 | 6.771e-01 | 3.519e-02 |
| | Esophagus cancer | 58.311 | 1.464e-01 | 3.710e-01 |
| | Gastric cancer | 47.408 | 5.378e-01 | 6.646e-01 |
| | Colorectal cancer | 79.270 | 3.992e-03 | 2.941e-01 |
| | Pancreatic cancer | 39.164 | 8.655e-01 | 9.055e-01 |

Note: $P_{\text{pleiotropy}} > .05$ indicates pleiotropy. $P_{\text{heterogeneity}}$ indicates heterogeneity.

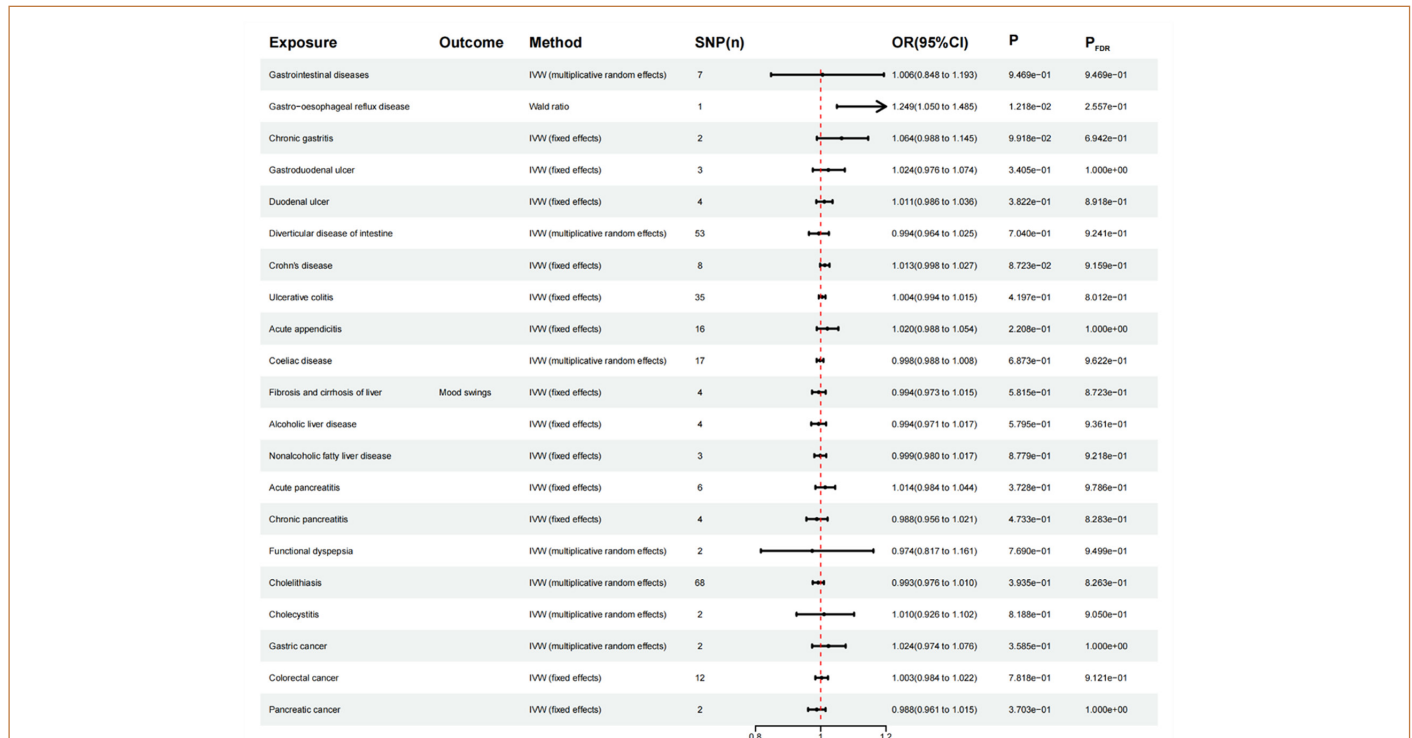


Figure 3. Forest plots of the association between GI diseases and mood swings and final causality. OR, odds ratio; CI, confidence interval; nsnp, number of SNPs; P_{FDR} , P value corrected by false discovery rate (FDR); IWW, inverse variance weighting.

Our study has several advantages. First, this study is the first to assess the causal correlation between mood swings and GI diseases, and the advantage of the MR design in directly detecting causality compared with observational studies is that it helps to avoid confounders and reverse causality. Second, almost all common systemic GI diseases were included in this study. This approach provides the most systematic risk assessment of mood swings in individuals with 24 GI diseases to date. Third, we performed FDR correction to ensure the reliability of the results.

However, there are some limitations to this study. First, the GWAS summary data used in this study were all from the European population, and the generalizability of the results to other populations is limited. To verify our results, further investigation of different populations is necessary. Second, in the UK Biobank cohort, mood swings were self-reported traits, which may have led to phenotypic errors. These factors should be considered in future studies.

Conclusions

This comprehensive MR analysis is the first to suggest that genetically predicted mood swings may be a risk factor in the development of GI diseases. Interventions for mood swings may help to treat GI diseases.

Availability of Data and Material: The original contributions presented in the study are included in the article/Supplementary Material. Further inquiries can be directed to the corresponding author.

Ethics Committee Approval: This MR research utilized only published or publicly available GWAS data.

Informed Consent: N/A.

Peer-Review: Externally peer-reviewed.

Acknowledgments: We express our gratitude to all the genetics consortiums for making the GWAS summary data publicly available. We also express our gratitude to the Core facility and Bioinformatics Laboratory of the Wuhan Union Hospital affiliated with Huazhong University of Science and Technology and the first Hospital of Jilin University for the training and generous sharing of experiences and codes.

Author Contributions: Concept – K.W., S.W.; Design – K.W., S.W., X.C.; Supervision – X.C.; Resources – K.W., S.W.; Materials – S.W.; Data Collection and/or Processing – S.W.; Analysis and/or Interpretation – K.W., S.W.; Literature Search – K.W.; Writing – K.W., S.W., X.C.; Critical Review – K.W., S.W., X.C.

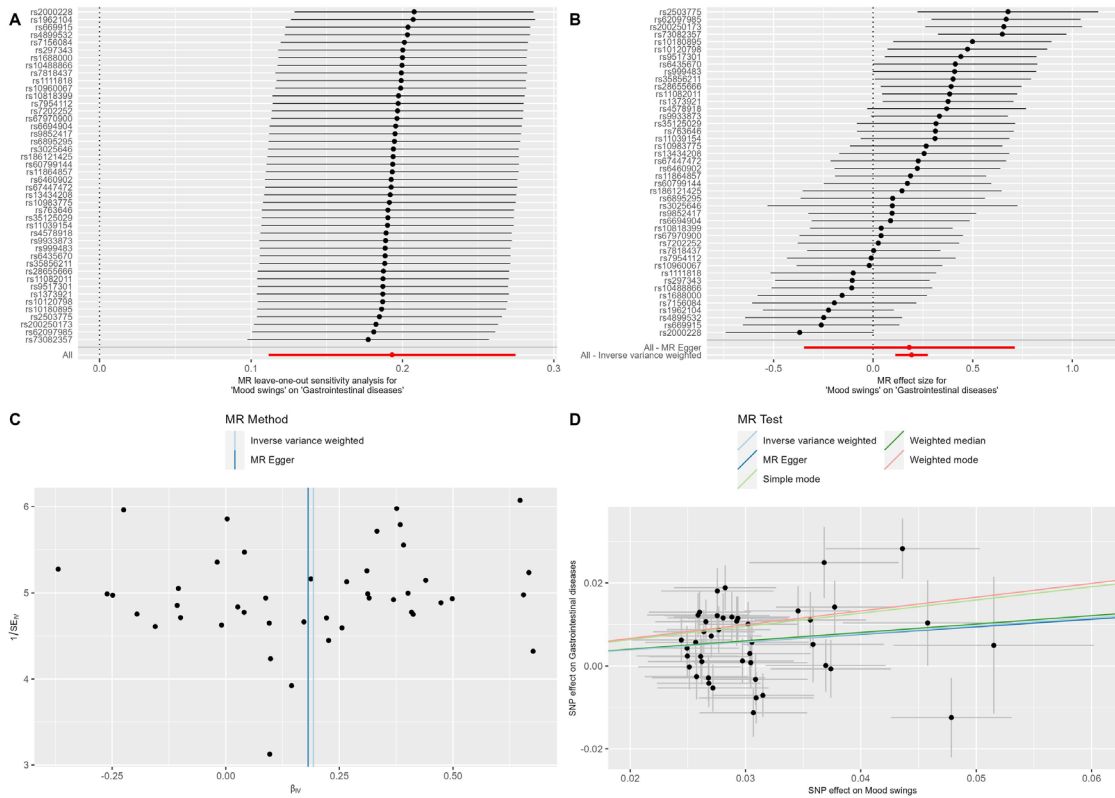
Conflicts of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: This work was supported by the National Key Research and Development Program of China (grant 2018YFC2001802 to X. Chen); National Natural Science Foundation (grant 82071251 to X. Chen); Hubei Province Key Research and Development Program (grant 2021BCA145 to X. Chen).

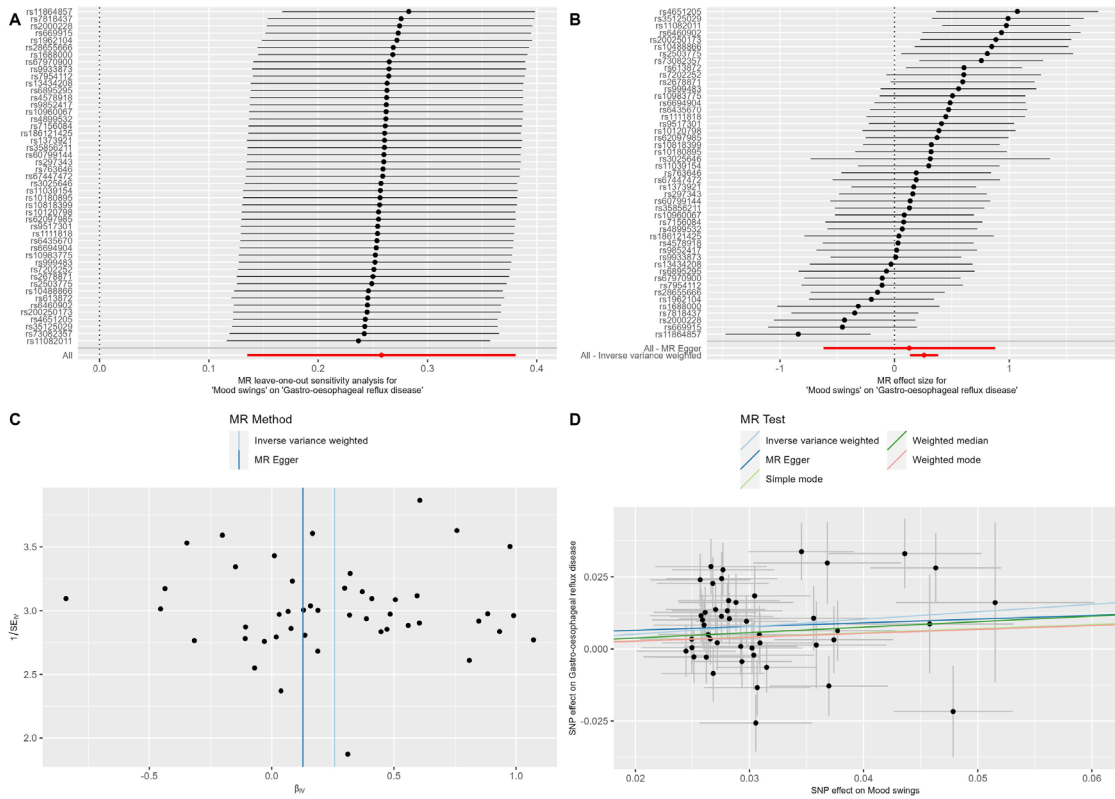
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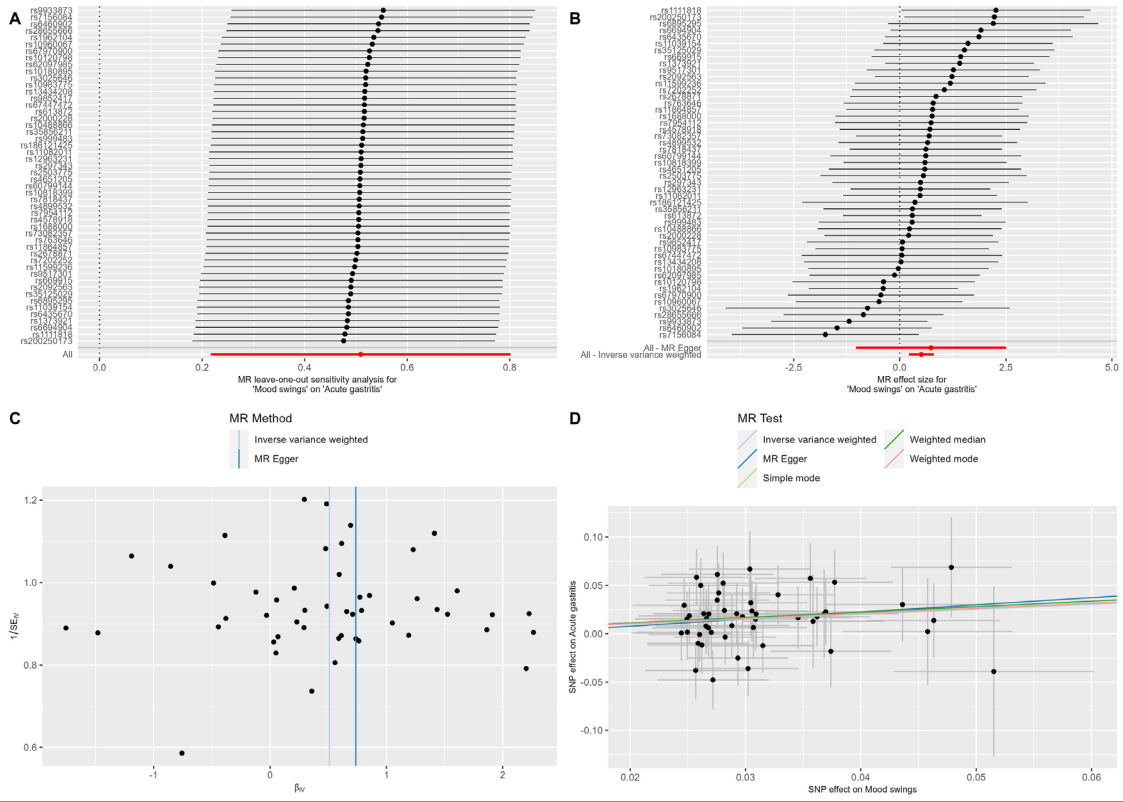
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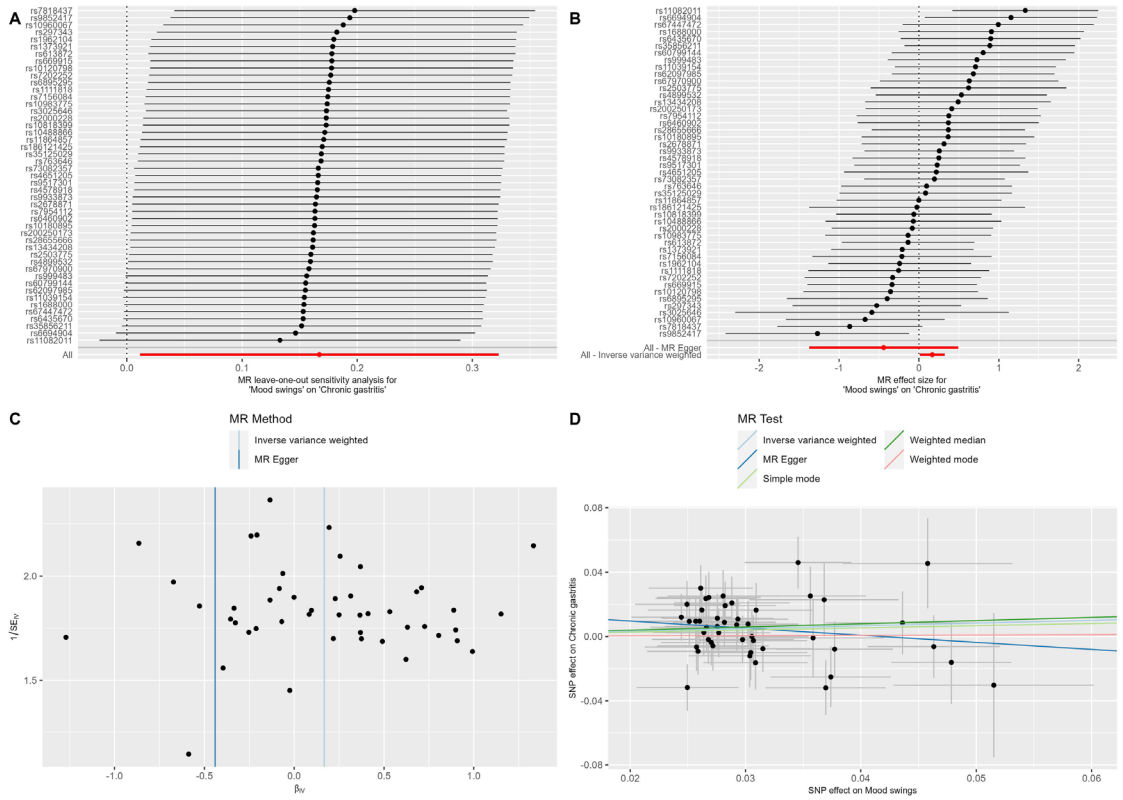
Supplementary Figure 1. Leave-one-out plots, scatter plots, funnel plots and forest plots for mood swings on gastrointestinal diseases.



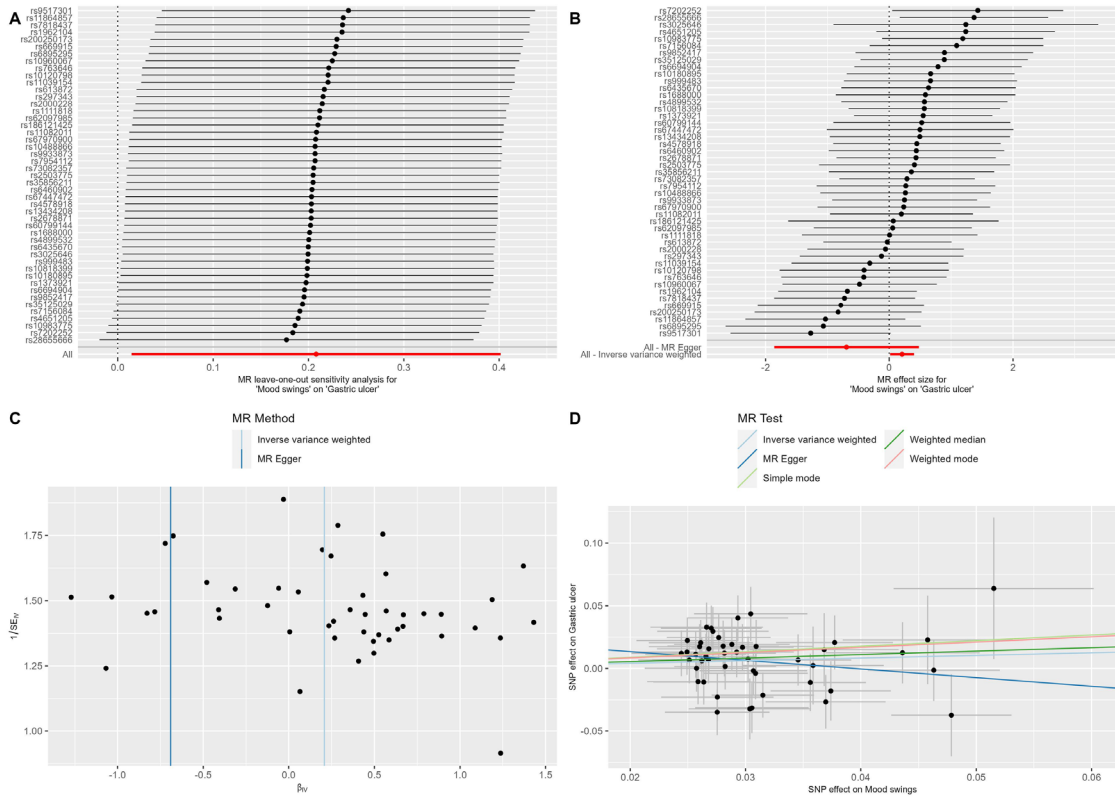
Supplementary Figure 2. Leave-one-out plots, scatter plots, funnel plots and forest plots for mood swings on gastro-esophageal reflux disease.



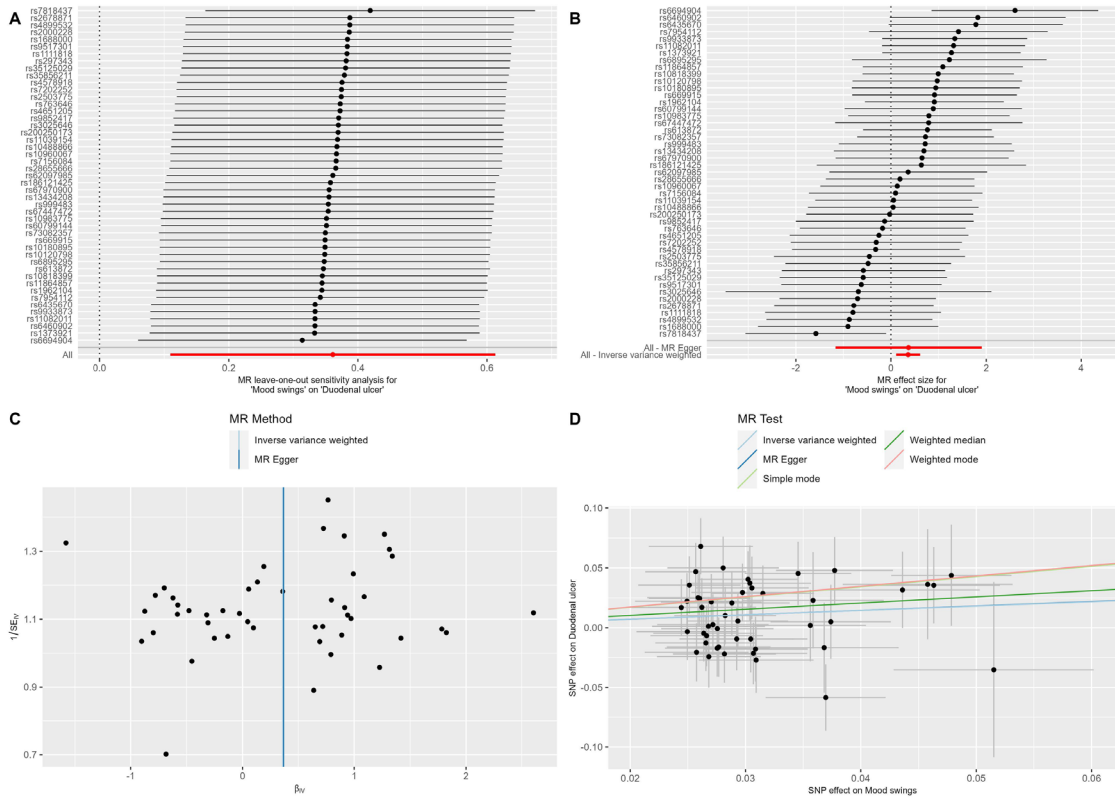
Supplementary Figure 3. Leave-one-out plots, scatter plots, funnel plots and forest plots for mood swings on acute gastritis.



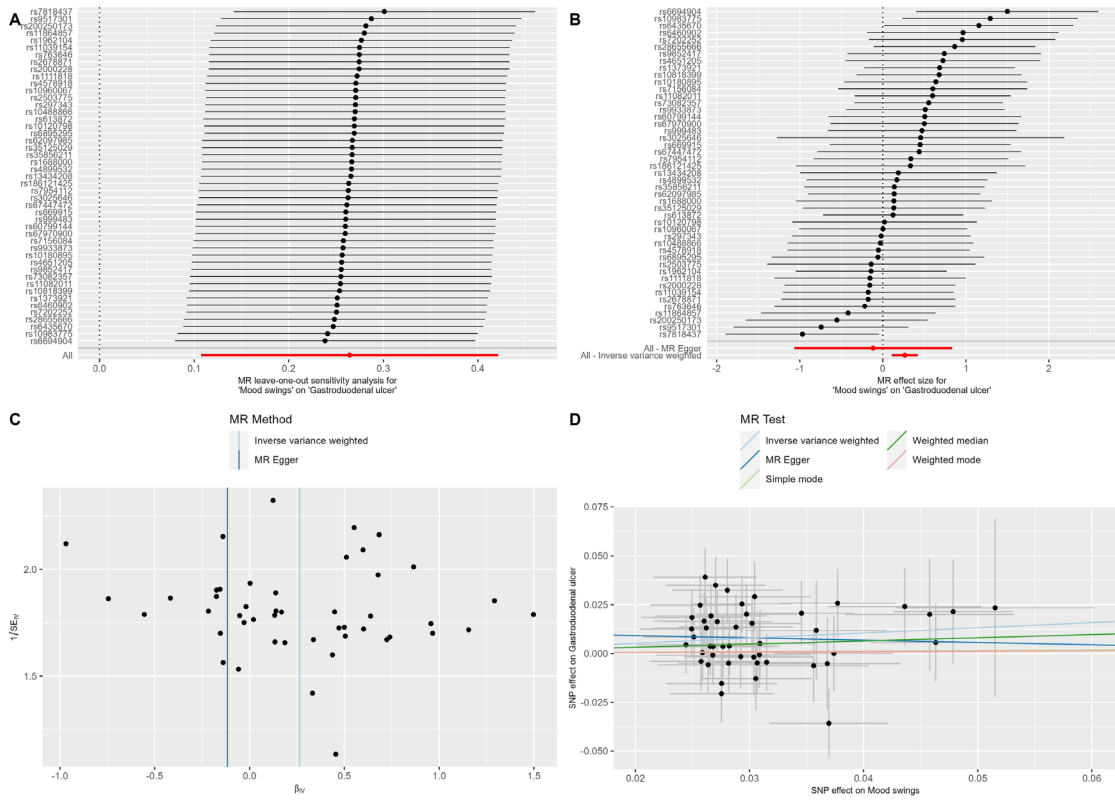
Supplementary Figure 4. Leave-one-out plots, scatter plots, funnel plots and forest plots for mood swings on chronic gastritis.



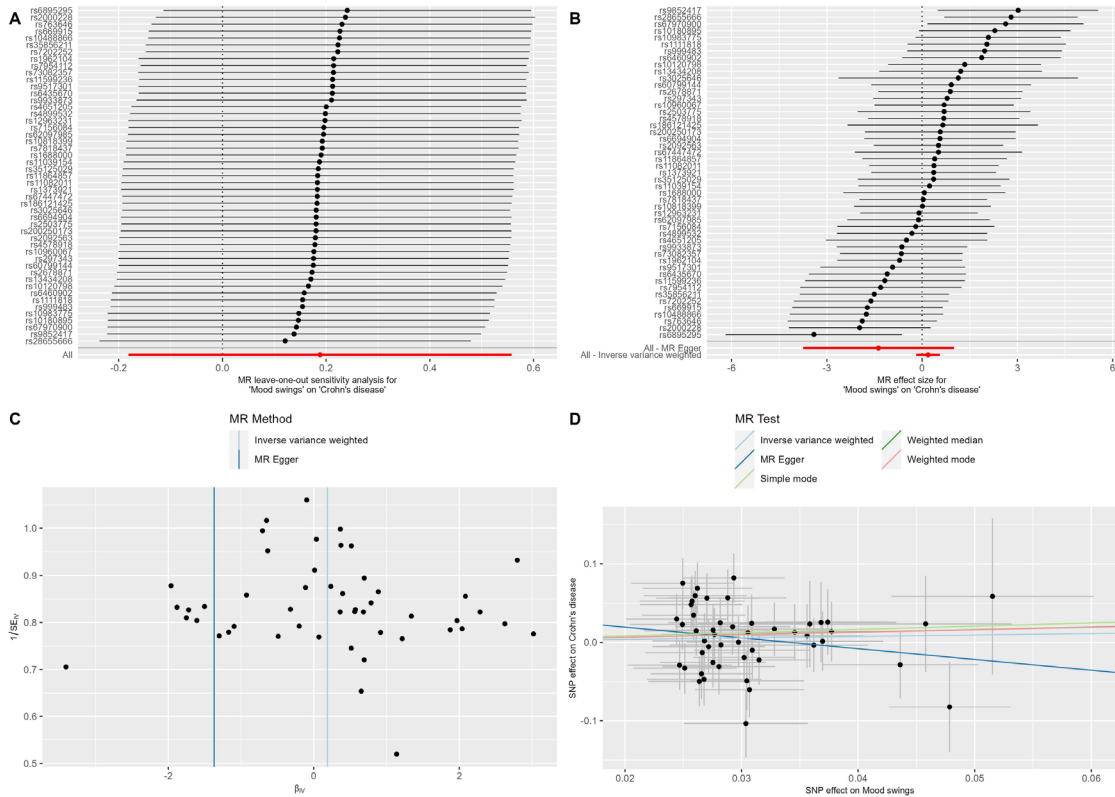
Supplementary Figure 5. Leave-one-out plots, scatter plots, funnel plots and forest plots for mood swings on gastric ulcer.



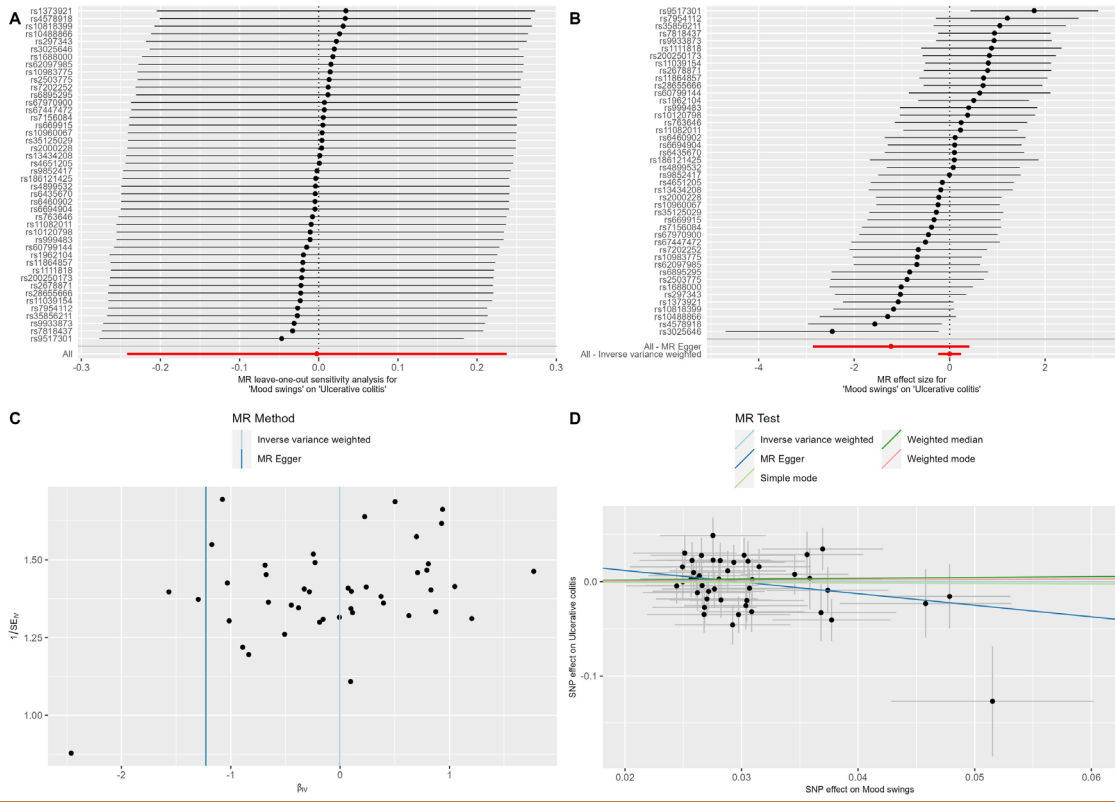
Supplementary Figure 6. Leave-one-out plots, scatter plots, funnel plots and forest plots for mood swings on duodenal ulcer.



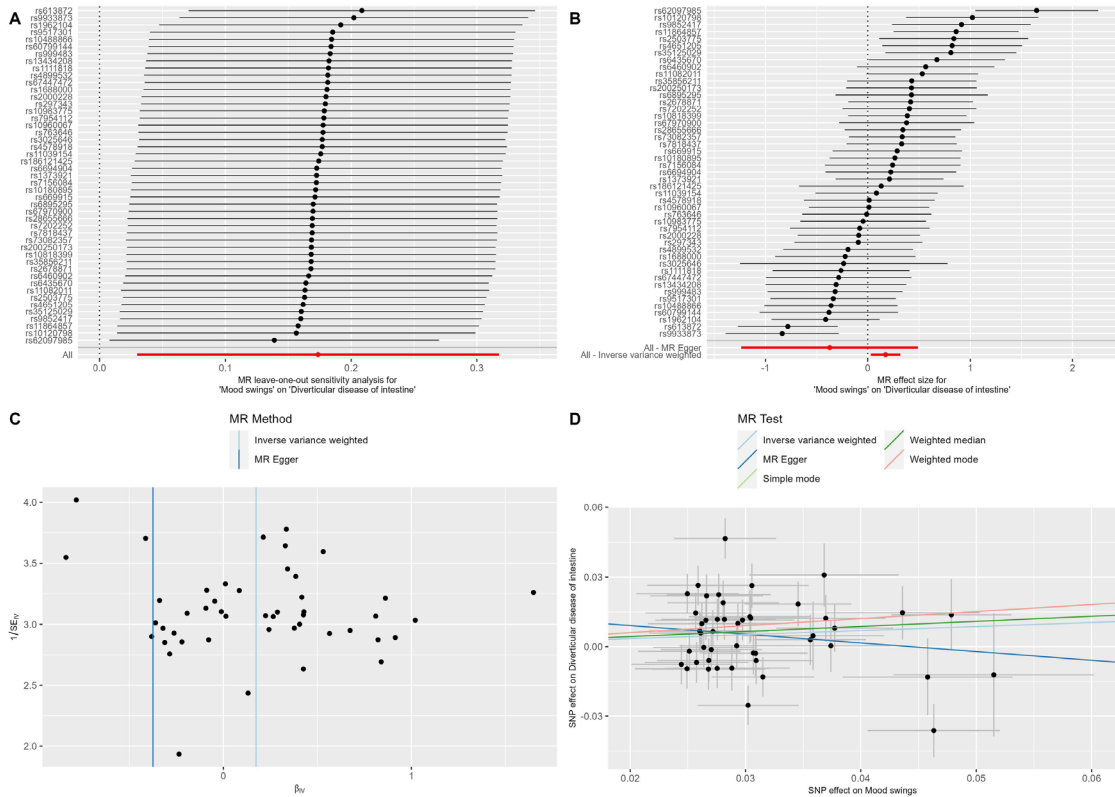
Supplementary Figure 7. Leave-one-out plots, scatter plots, funnel plots and forest plots for mood swings on gastroduodenal ulcer.



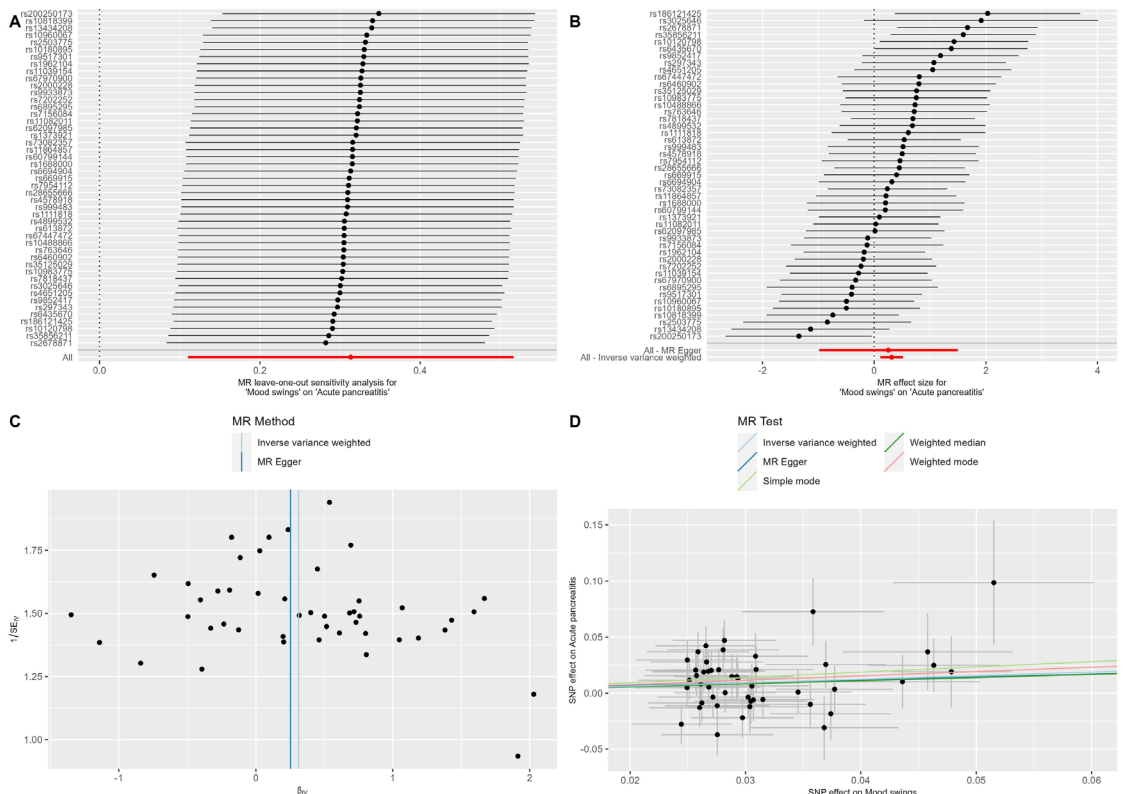
Supplementary Figure 8. Leave-one-out plots, scatter plots, funnel plots and forest plots for mood swings on crohn's disease.



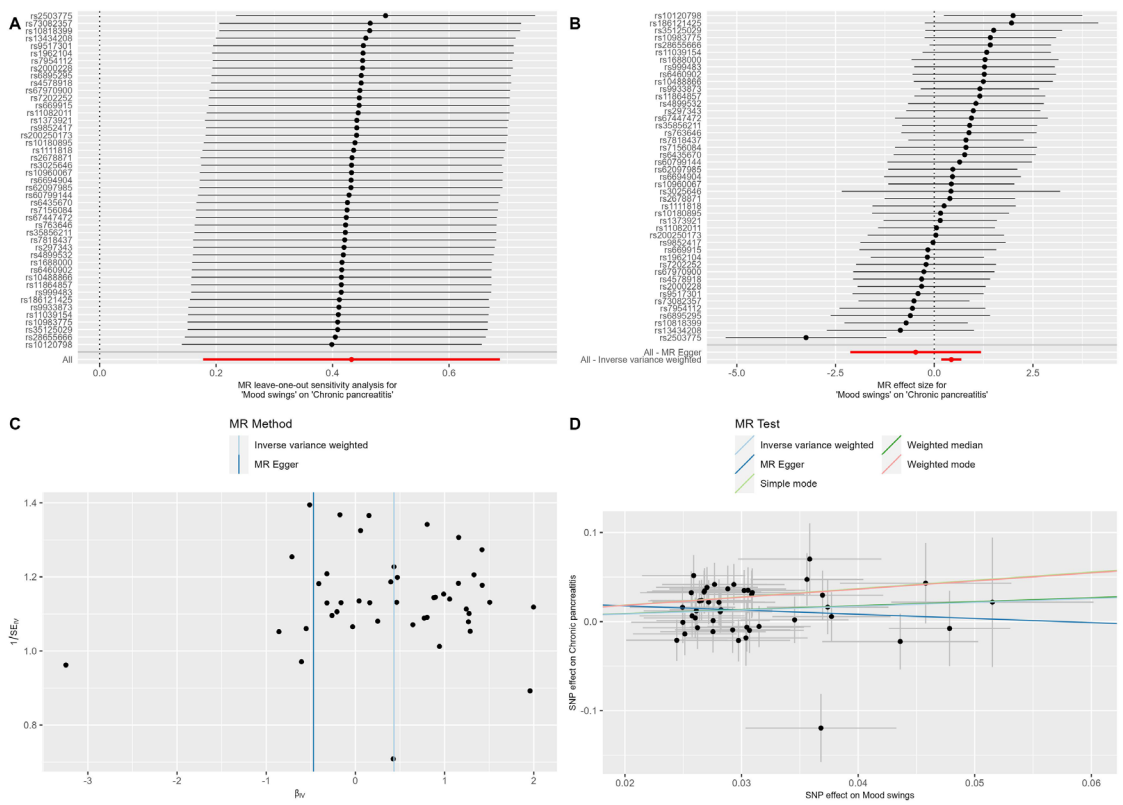
Supplementary Figure 9. Leave-one-out plots, scatter plots, funnel plots and forest plots for mood swings on ulcerative colitis.



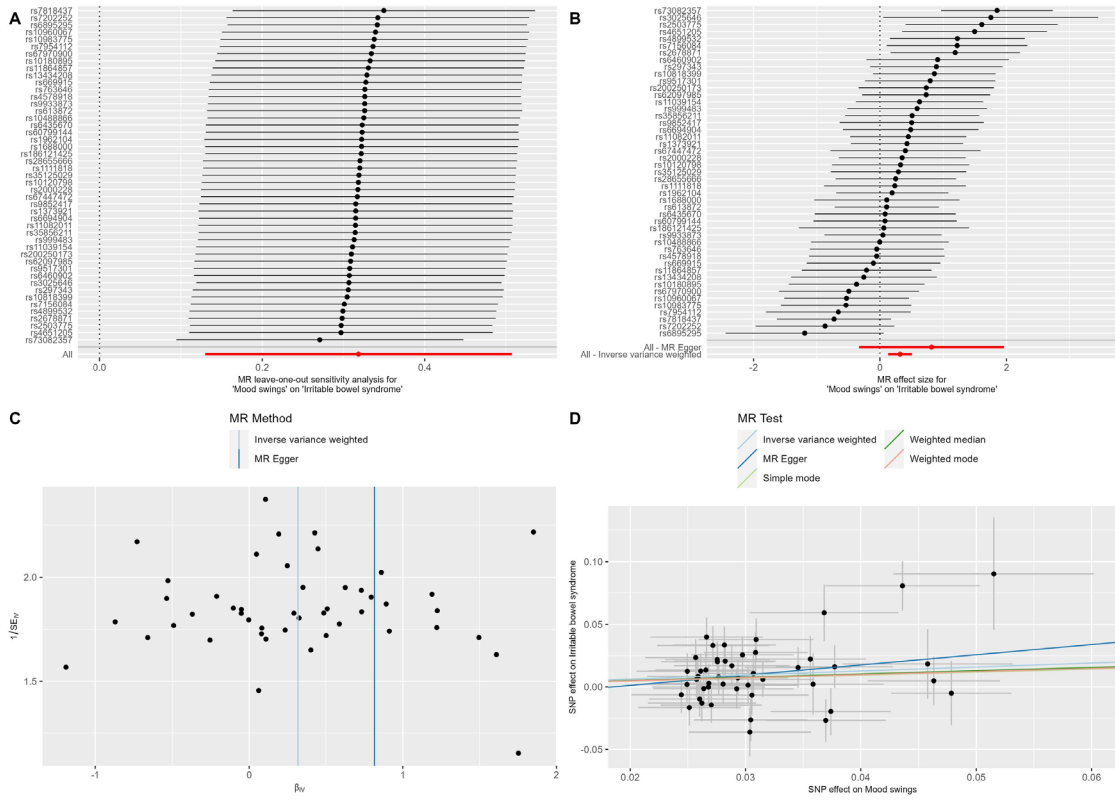
Supplementary Figure 10. Leave-one-out plots, scatter plots, funnel plots and forest plots for mood swings on diverticular disease of intestine.



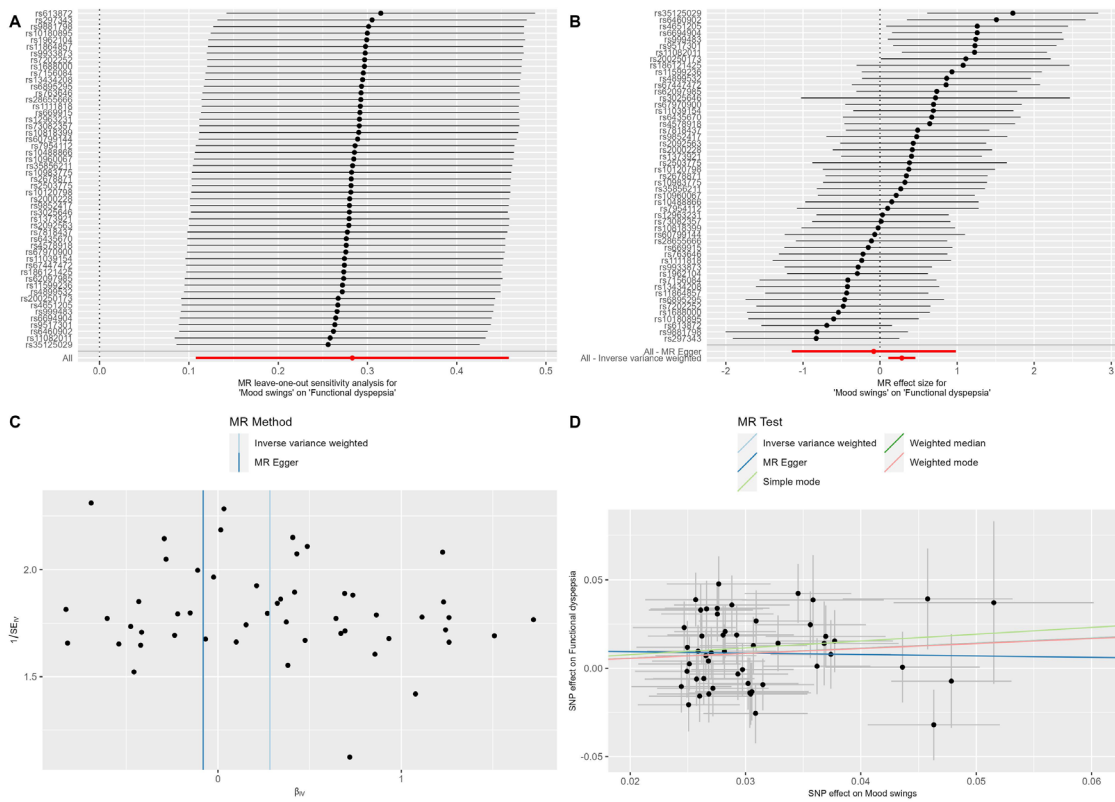
Supplementary Figure 11. Leave-one-out plots, scatter plots, funnel plots and forest plots for mood swings on acute pancreatitis.



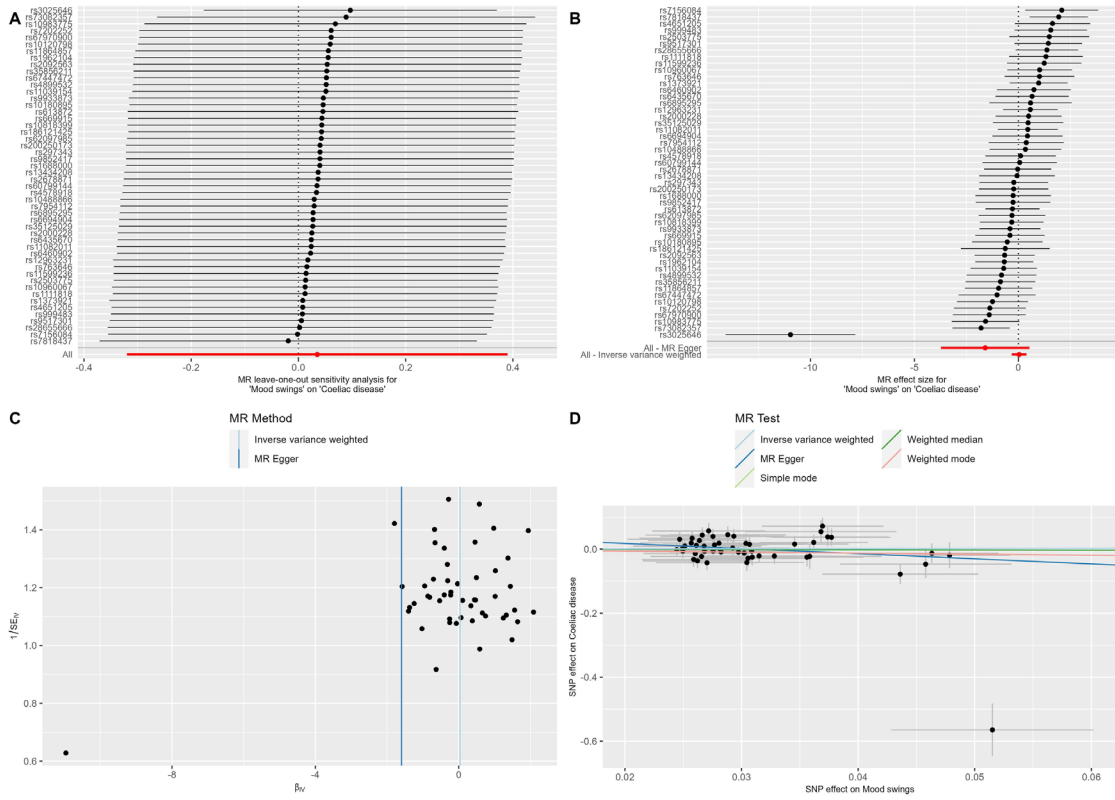
Supplementary Figure 12. Leave-one-out plots, scatter plots, funnel plots and forest plots for mood swings on chronic pancreatitis.



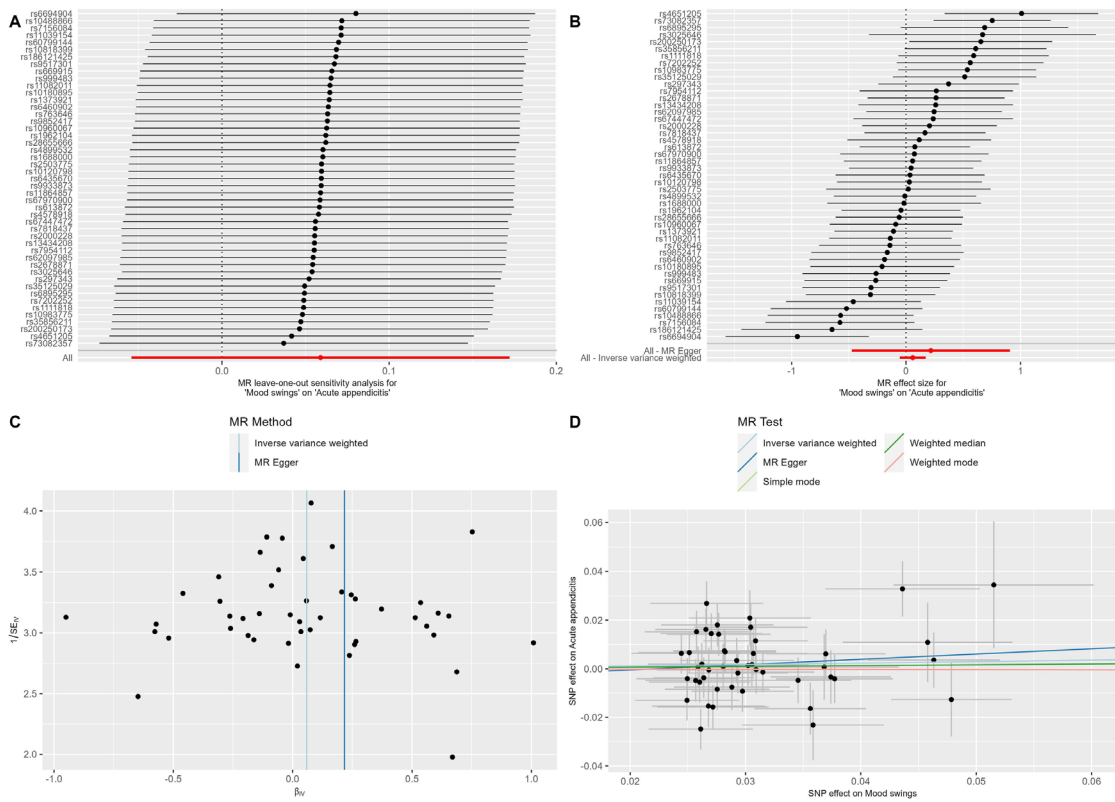
Supplementary Figure 13. Leave-one-out plots, scatter plots, funnel plots and forest plots for mood swings on irritable bowel syndrom.



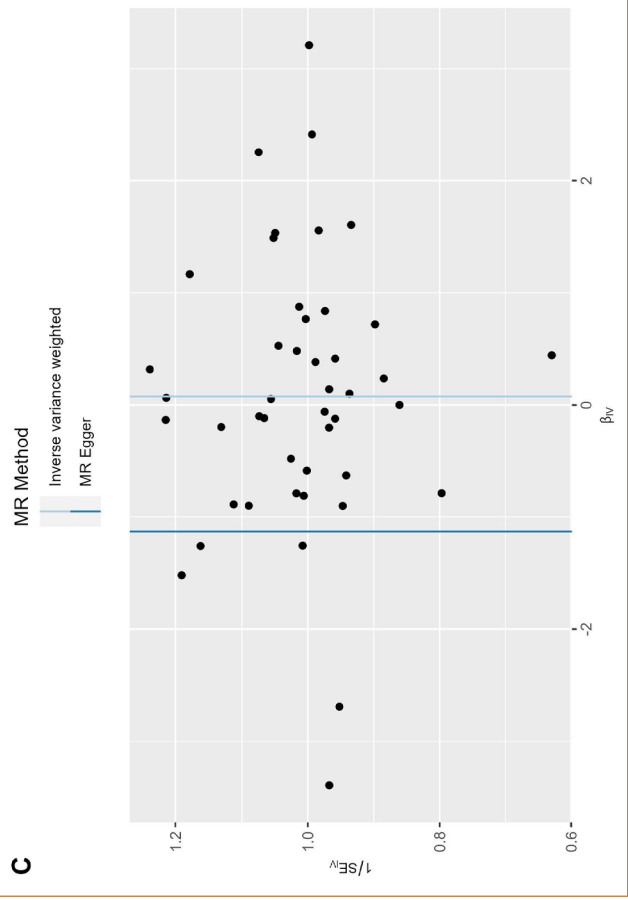
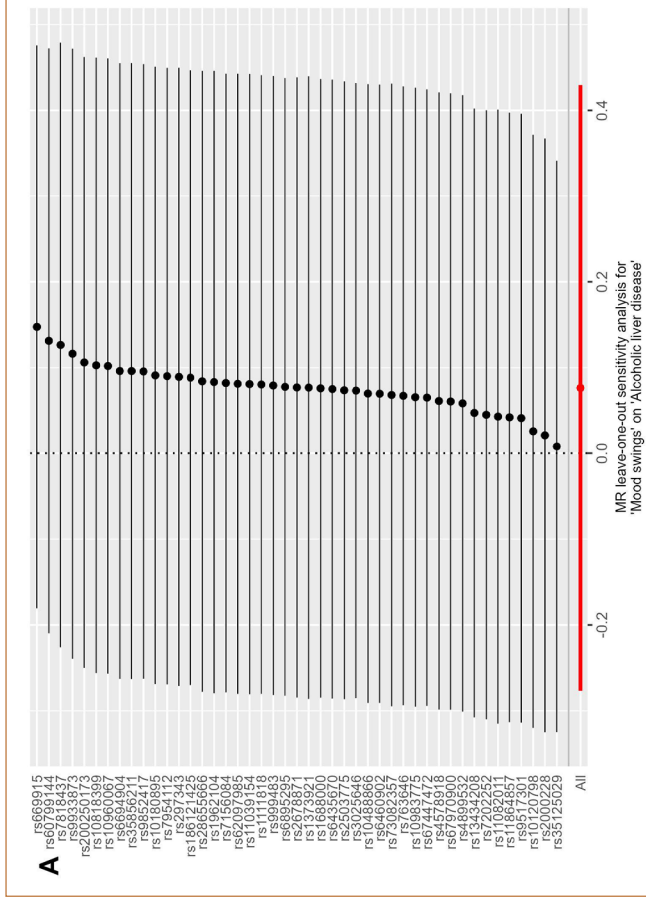
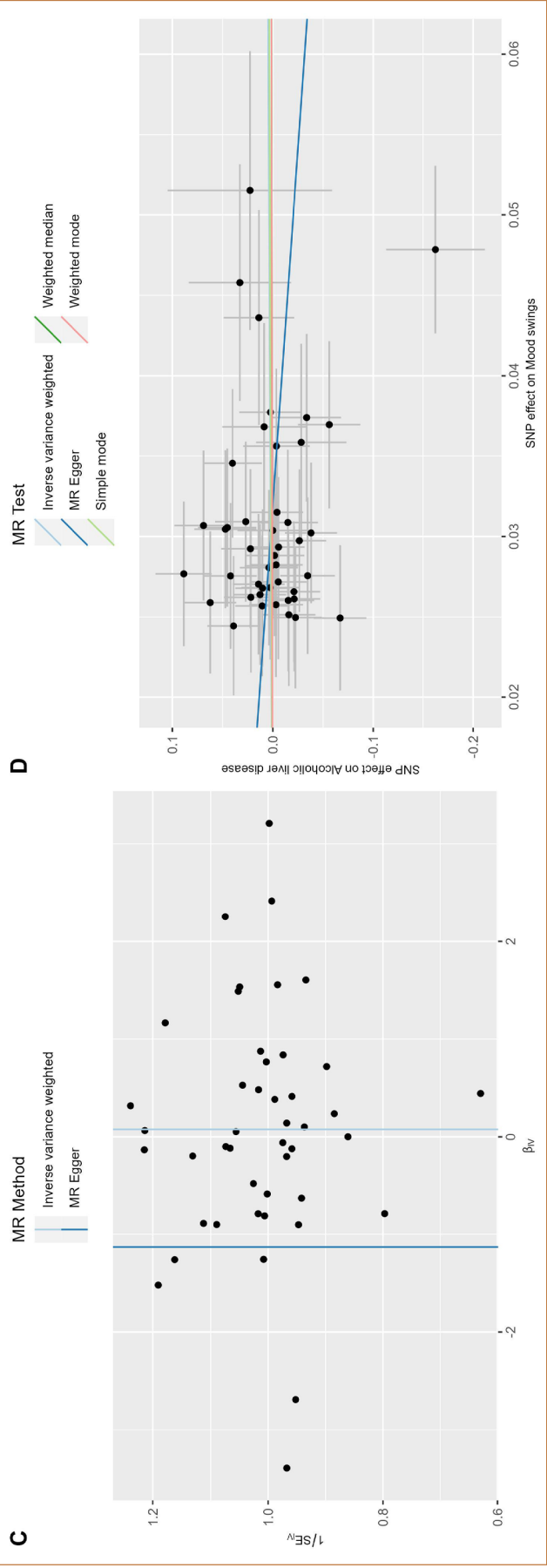
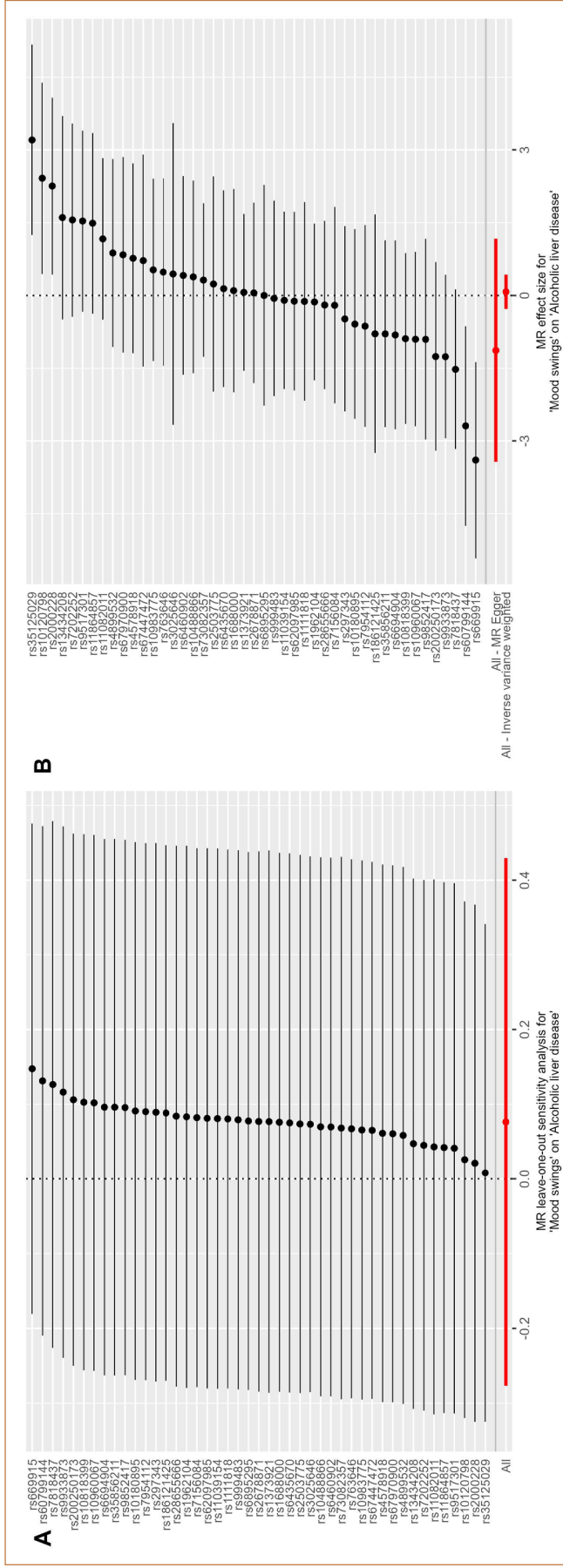
Supplementary Figure 14. Leave-one-out plots, scatter plots, funnel plots and forest plots for mood swings on functional dyspepsia.



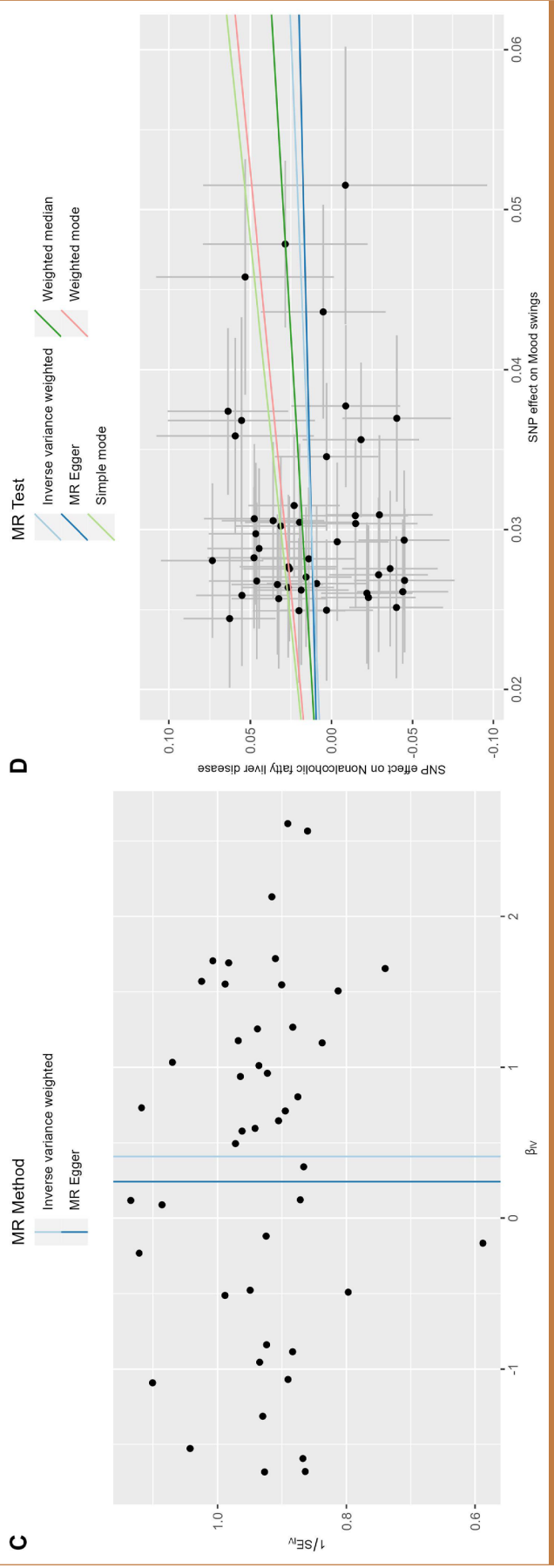
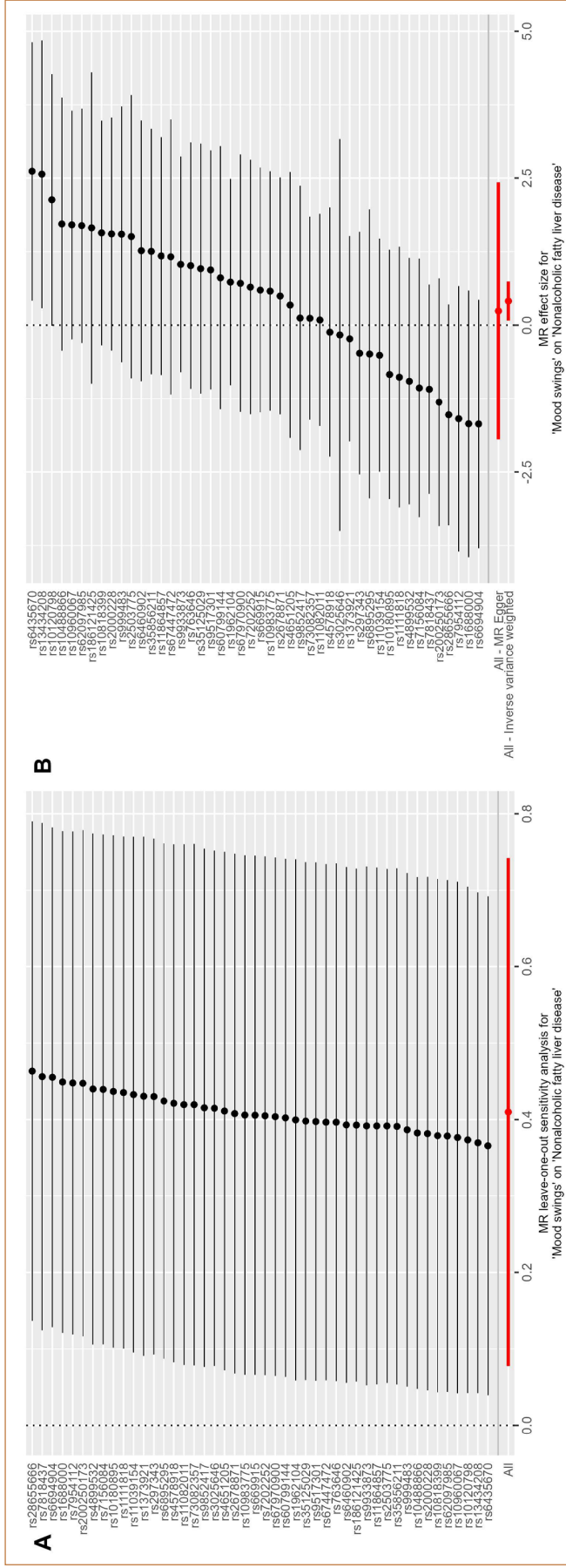
Supplementary Figure 15. Leave-one-out plots, scatter plots, funnel plots and forest plots for mood swings on coeliac disease.



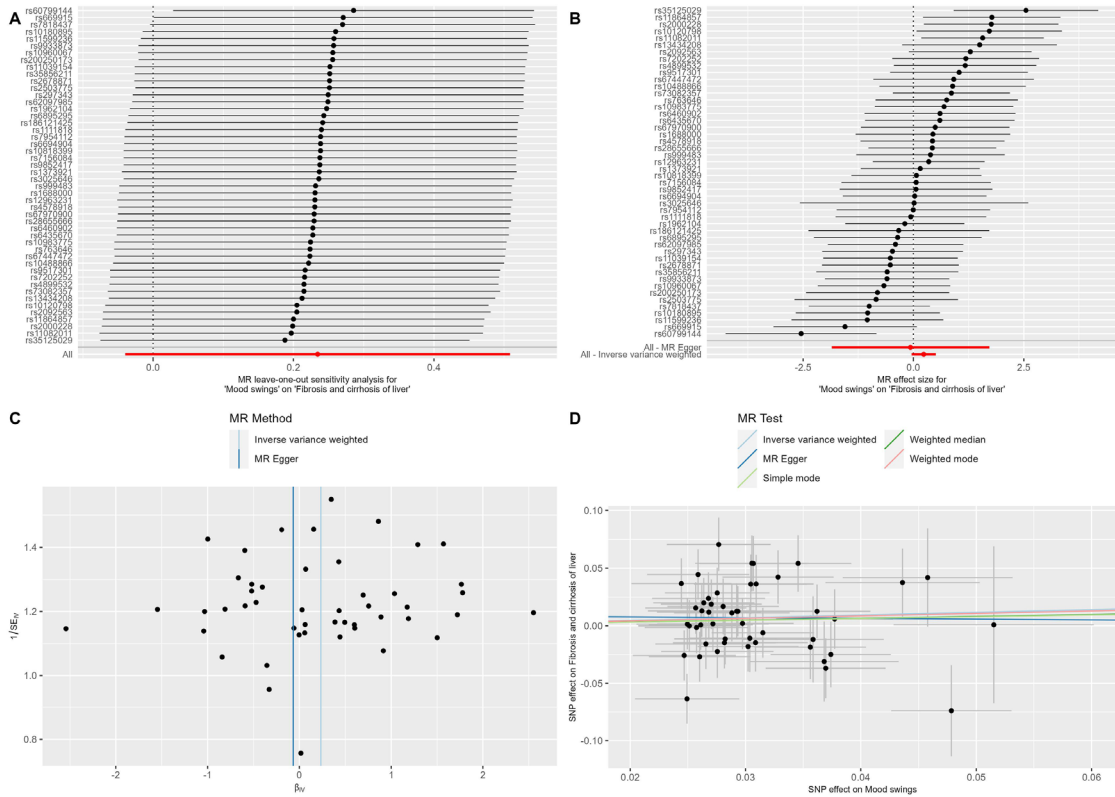
Supplementary Figure 16. Leave-one-out plots, scatter plots, funnel plots and forest plots for mood swings on acute appendicitis.



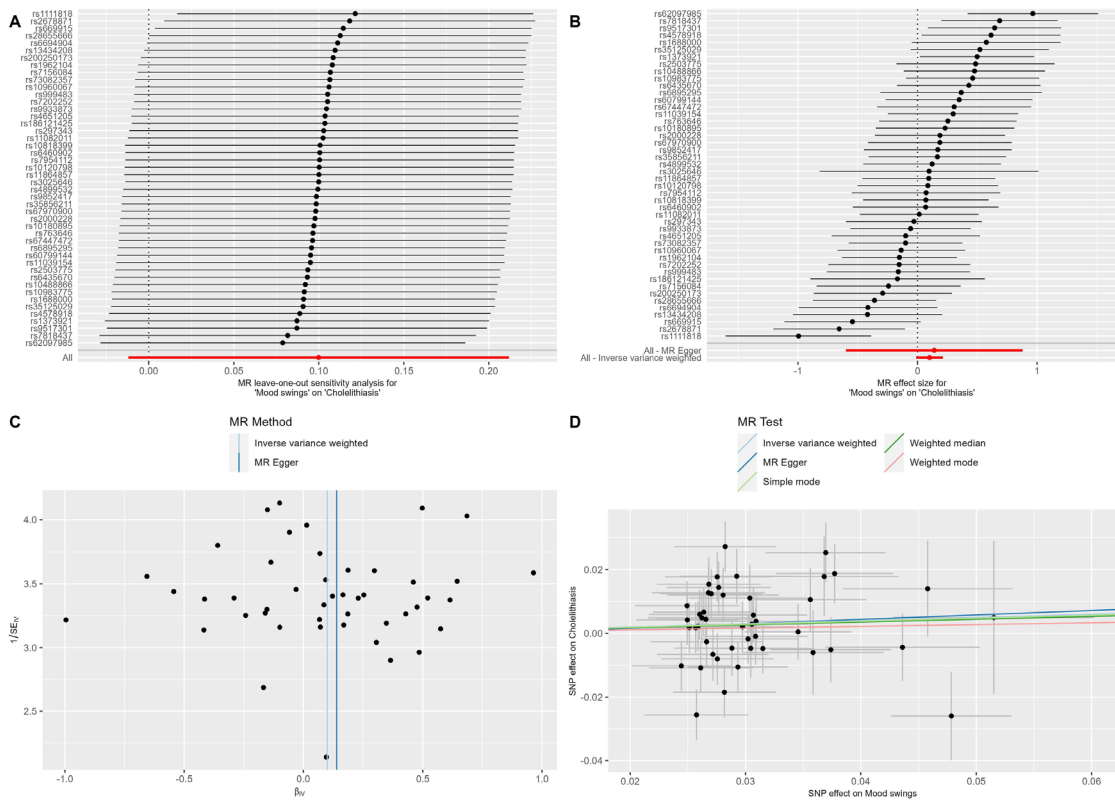
Supplementary Figure 17. Leave-one-out plots, scatter plots, funnel plots and forest plots for mood swings on alcoholic liver disease.



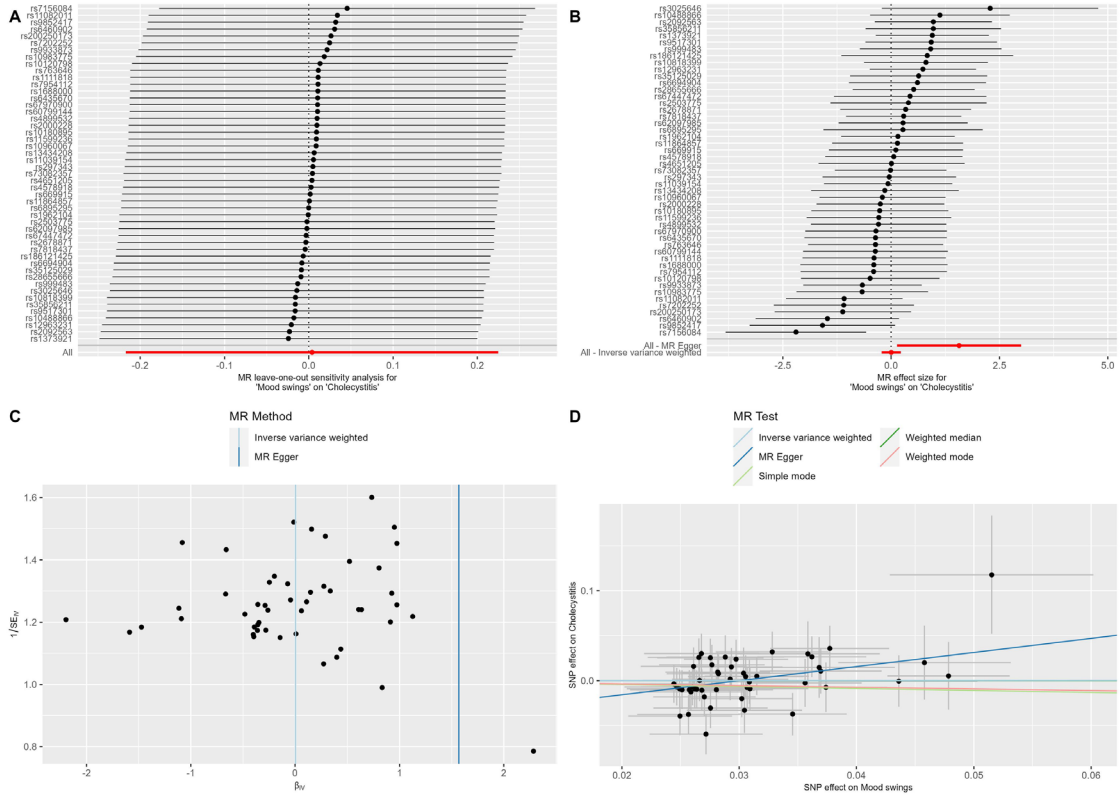
Supplementary Figure 18. Leave-one-out plots, scatter plots, funnel plots and forest plots for mood swings on nonalcoholic fatty liver disease.



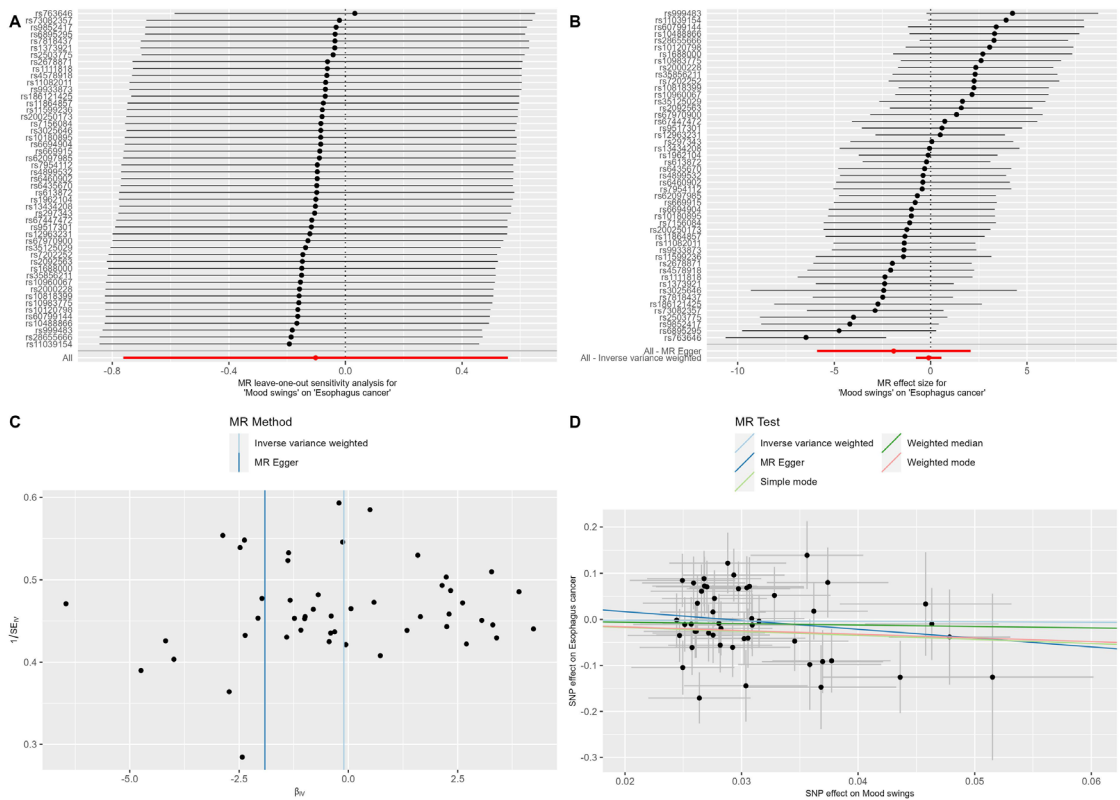
Supplementary Figure 19. Leave-one-out plots, scatter plots, funnel plots and forest plots for mood swings on fibrosis and cirrhosis of liver.



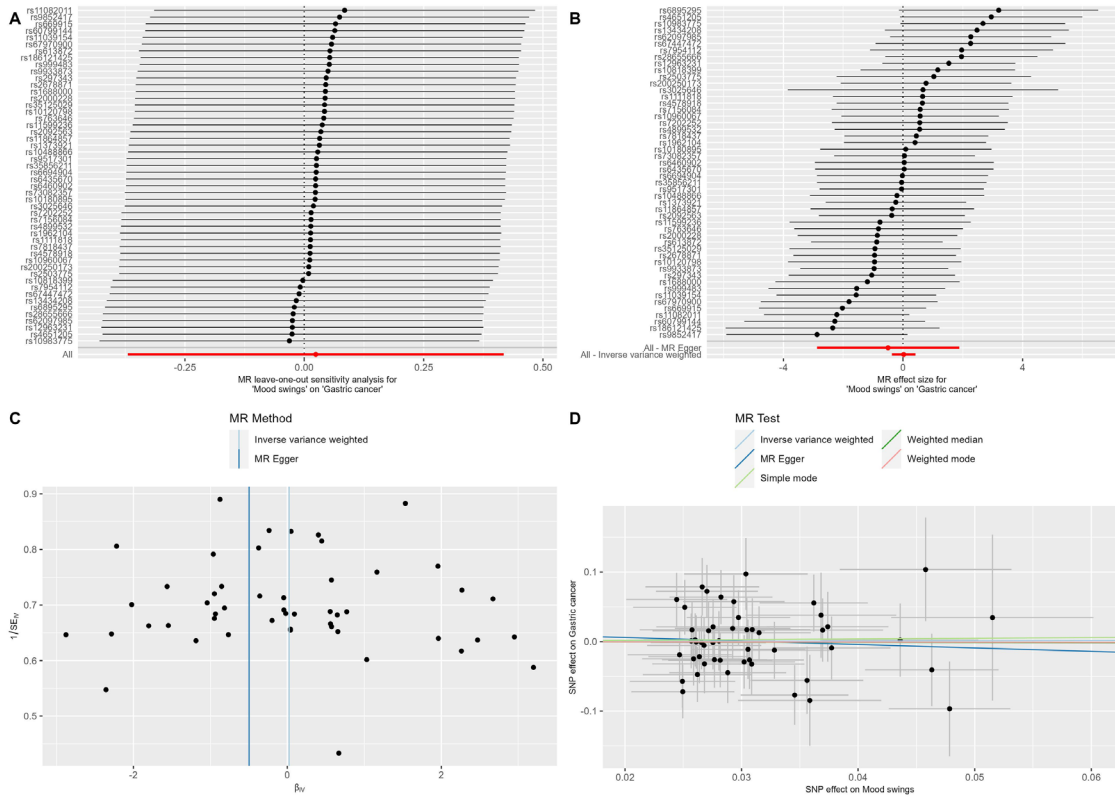
Supplementary Figure 20. Leave-one-out plots, scatter plots, funnel plots and forest plots for mood swings on cholelithiasis.



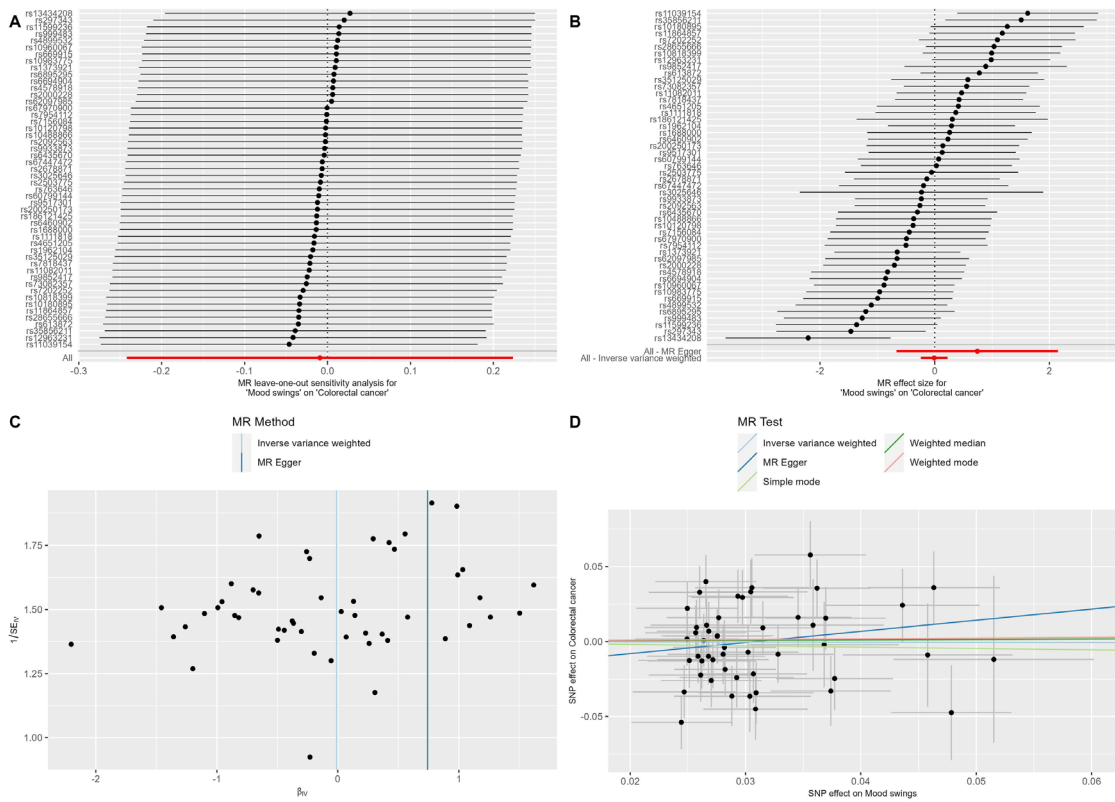
Supplementary Figure 21. Leave-one-out plots, scatter plots, funnel plots and forest plots for mood swings on cholecystitis.



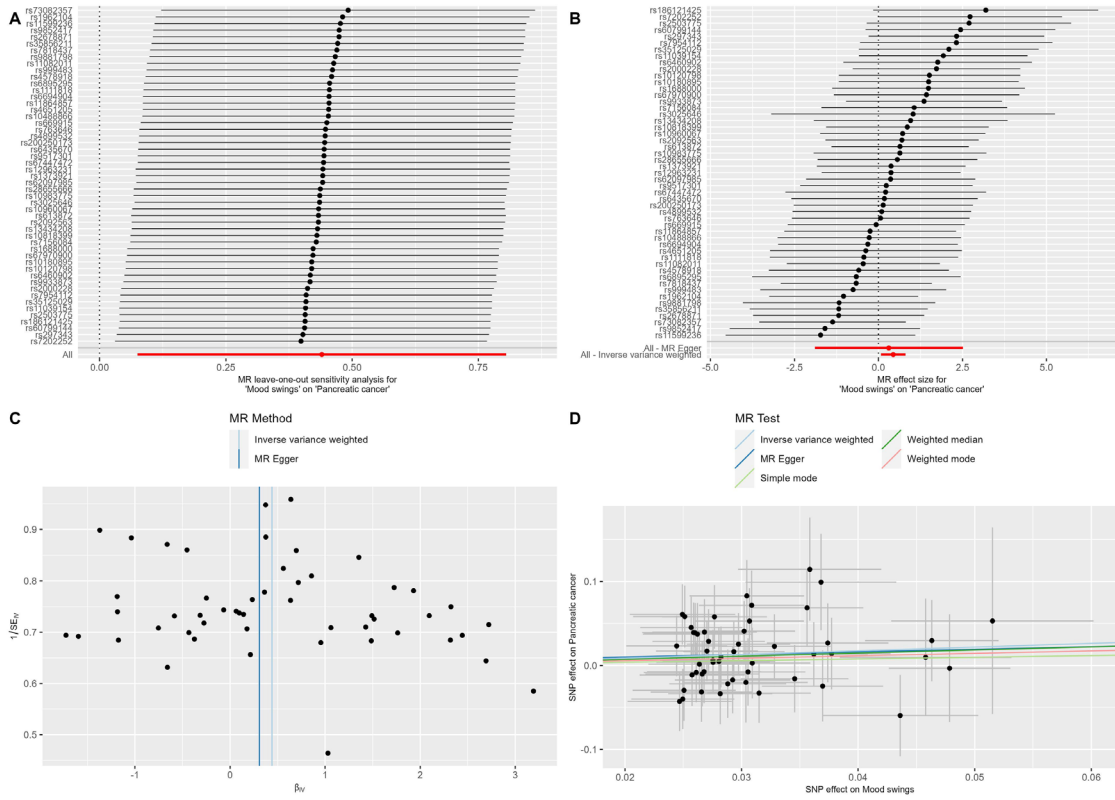
Supplementary Figure 22. Leave-one-out plots, scatter plots, funnel plots and forest plots for mood swings on esophagus cancer.



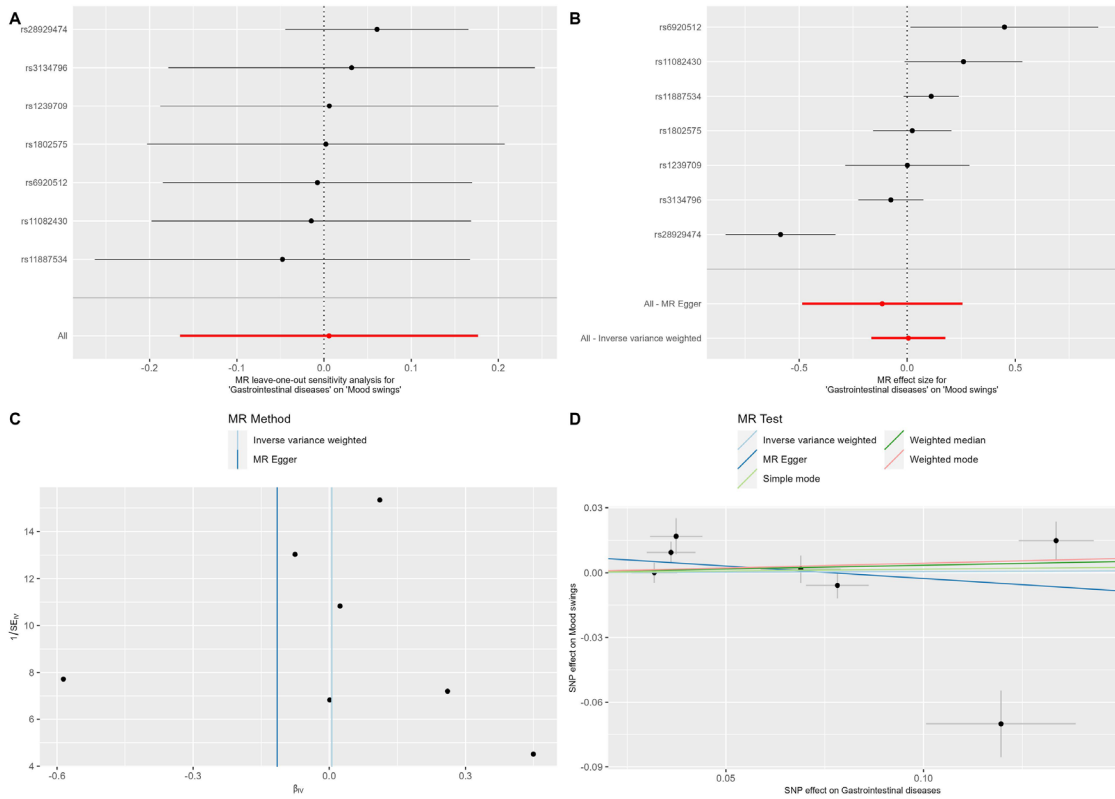
Supplementary Figure 23. Leave-one-out plots, scatter plots, funnel plots and forest plots for mood swings on gastric cancer.



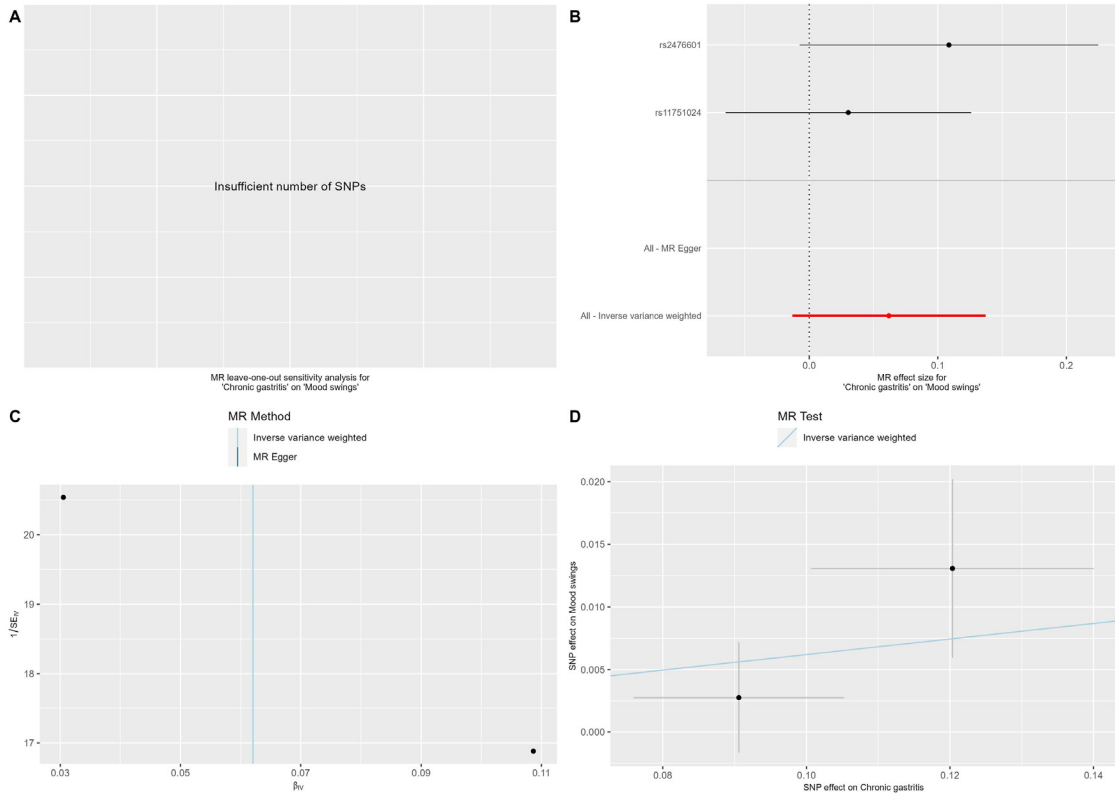
Supplementary Figure 24. Leave-one-out plots, scatter plots, funnel plots and forest plots for mood swings on colorectal cancer.



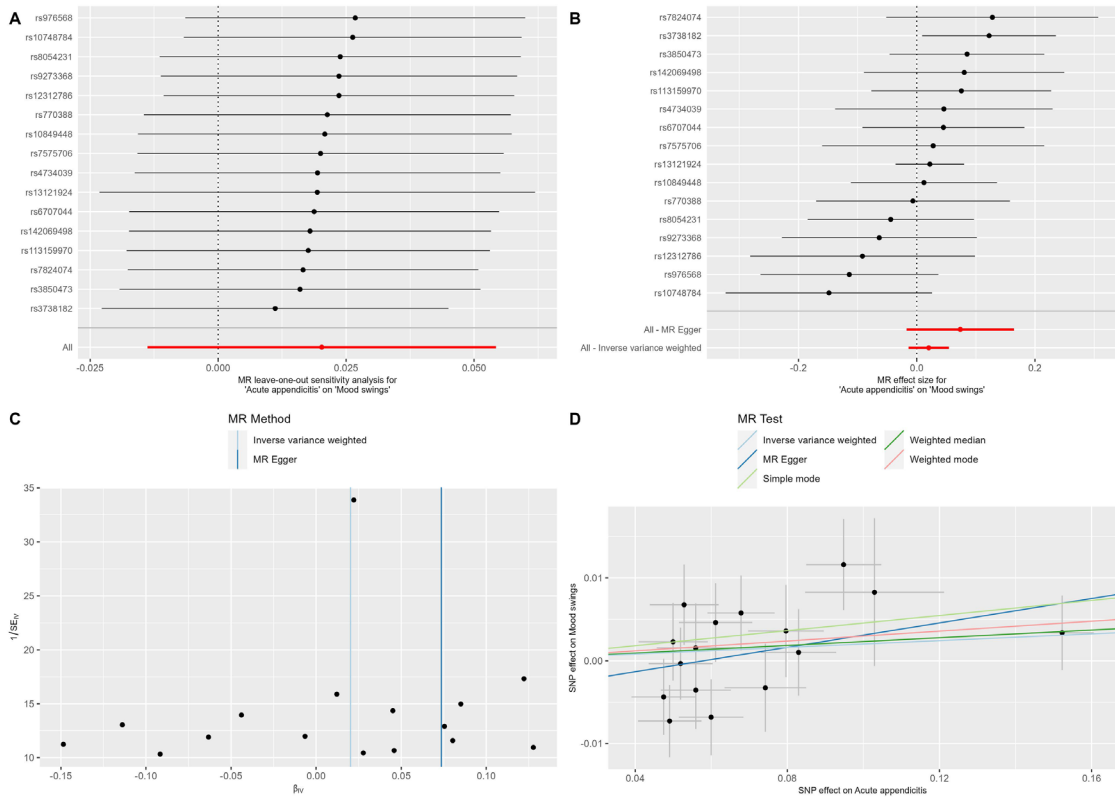
Supplementary Figure 25. Leave-one-out plots, scatter plots, funnel plots and forest plots for mood swings on pancreatic cancer.



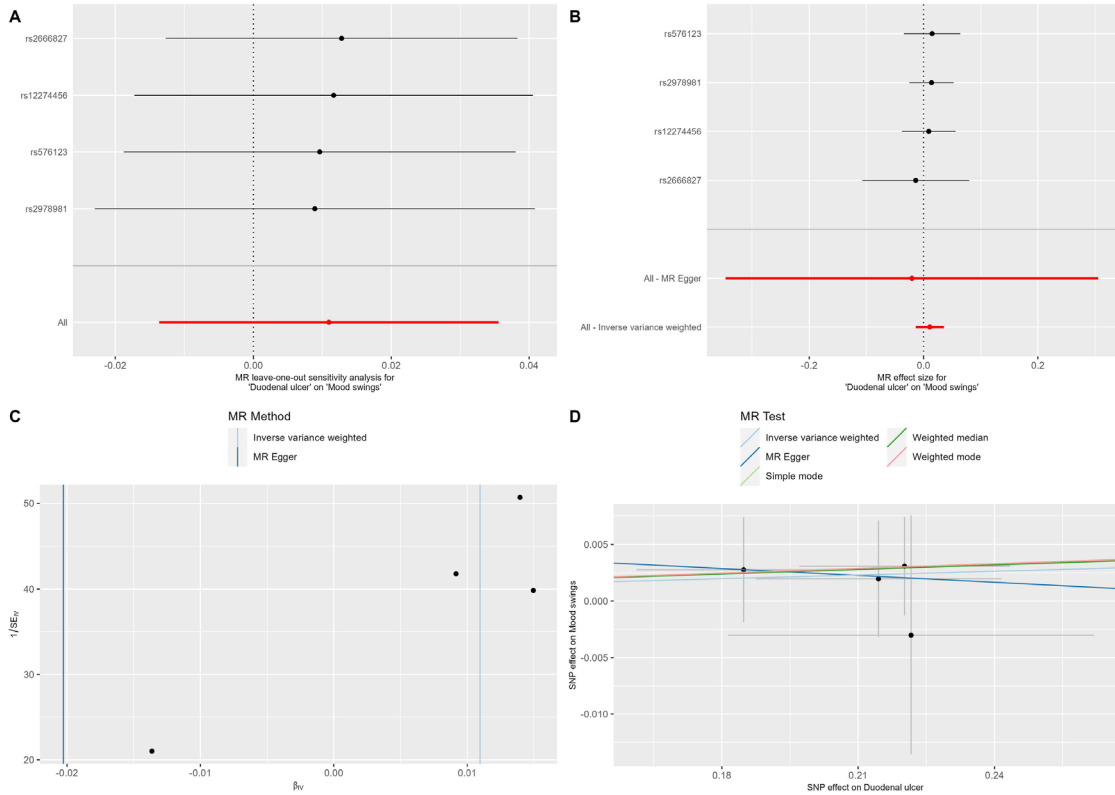
Supplementary Figure 26. Leave-one-out plots, scatter plots, funnel plots and forest plots for gastrointestinal diseases on mood swings.



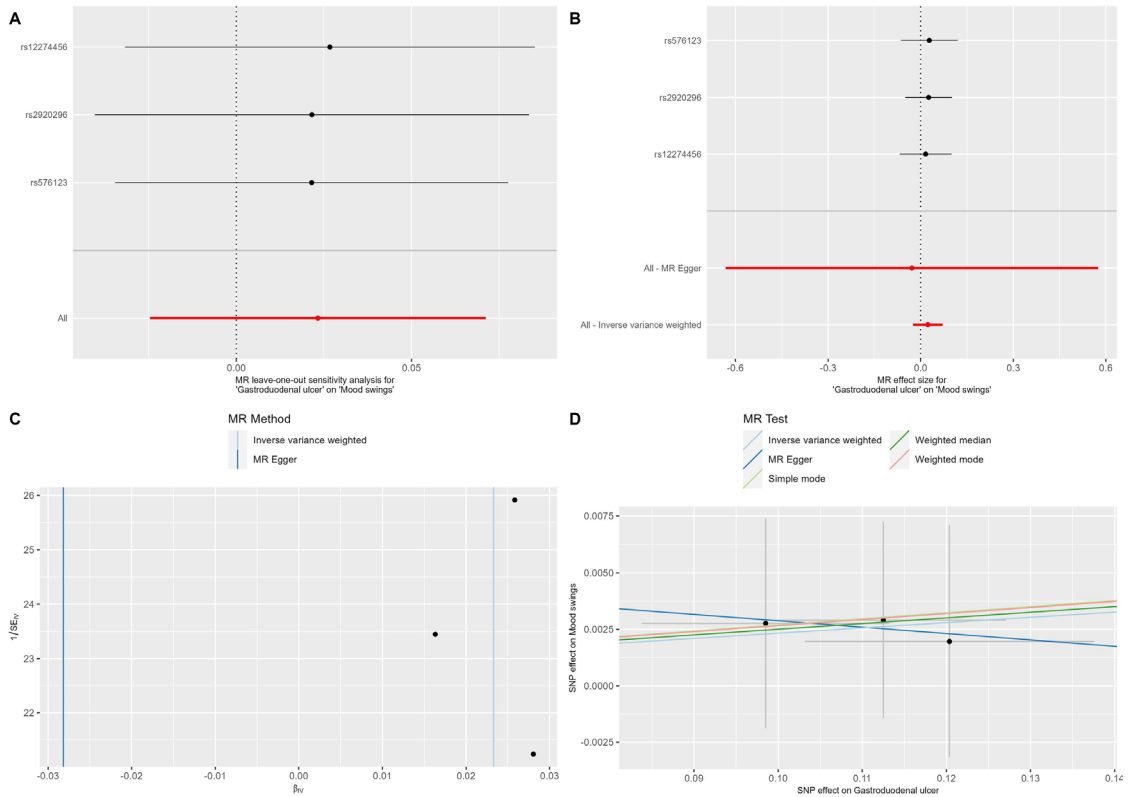
Supplementary Figure 27. Leave-one-out plots, scatter plots, funnel plots and forest plots for chronic gastritis on mood swings.



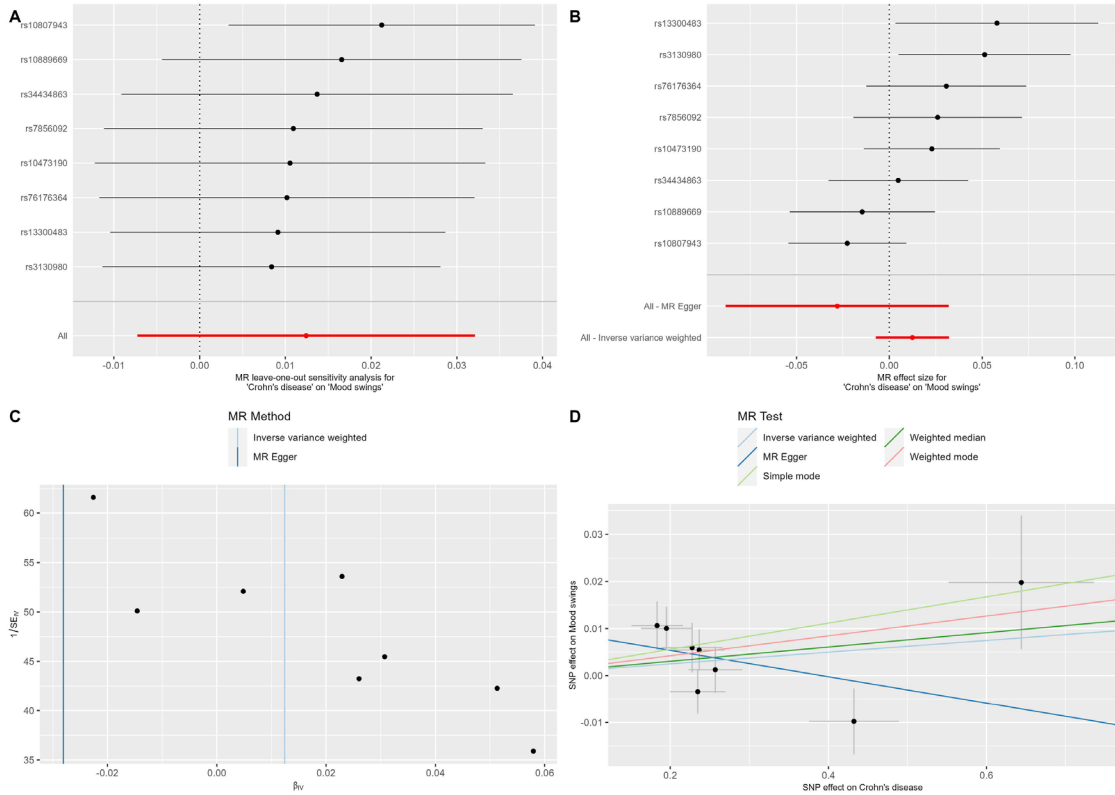
Supplementary Figure 28. Leave-one-out plots, scatter plots, funnel plots and forest plots for acute appendicitis on mood swings.



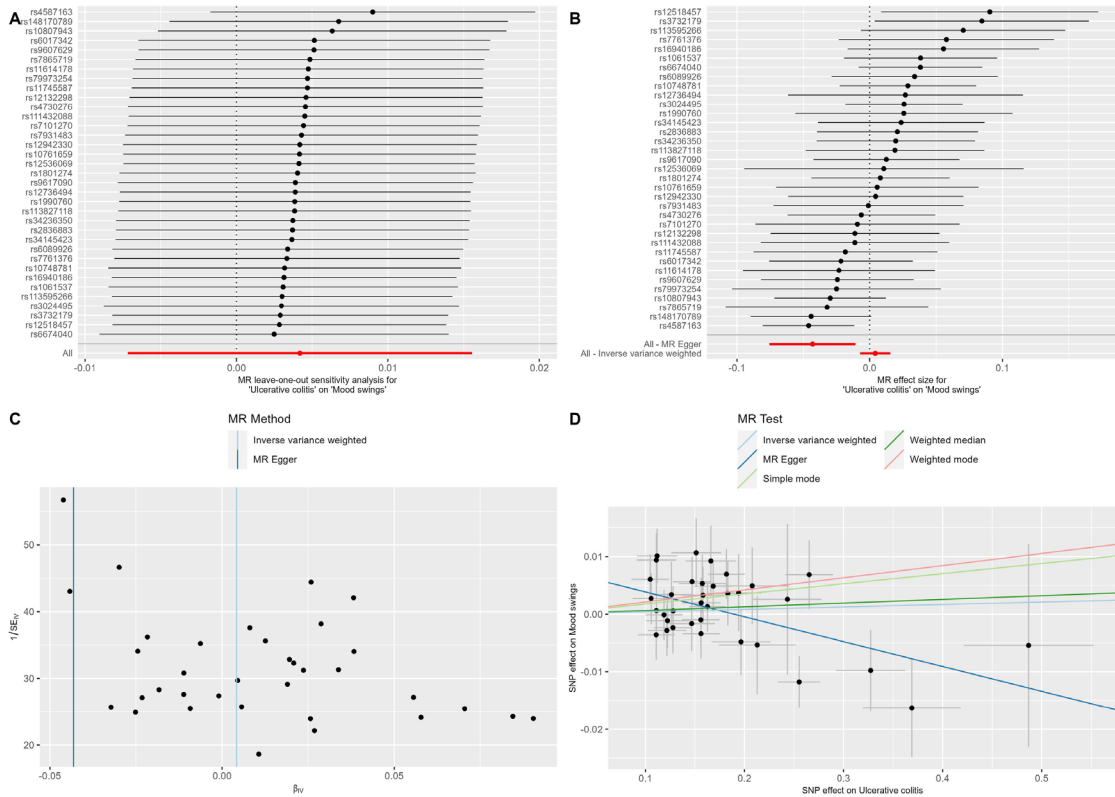
Supplementary Figure 29. Leave-one-out plots, scatter plots, funnel plots and forest plots for duodenal ulcer on mood swings.



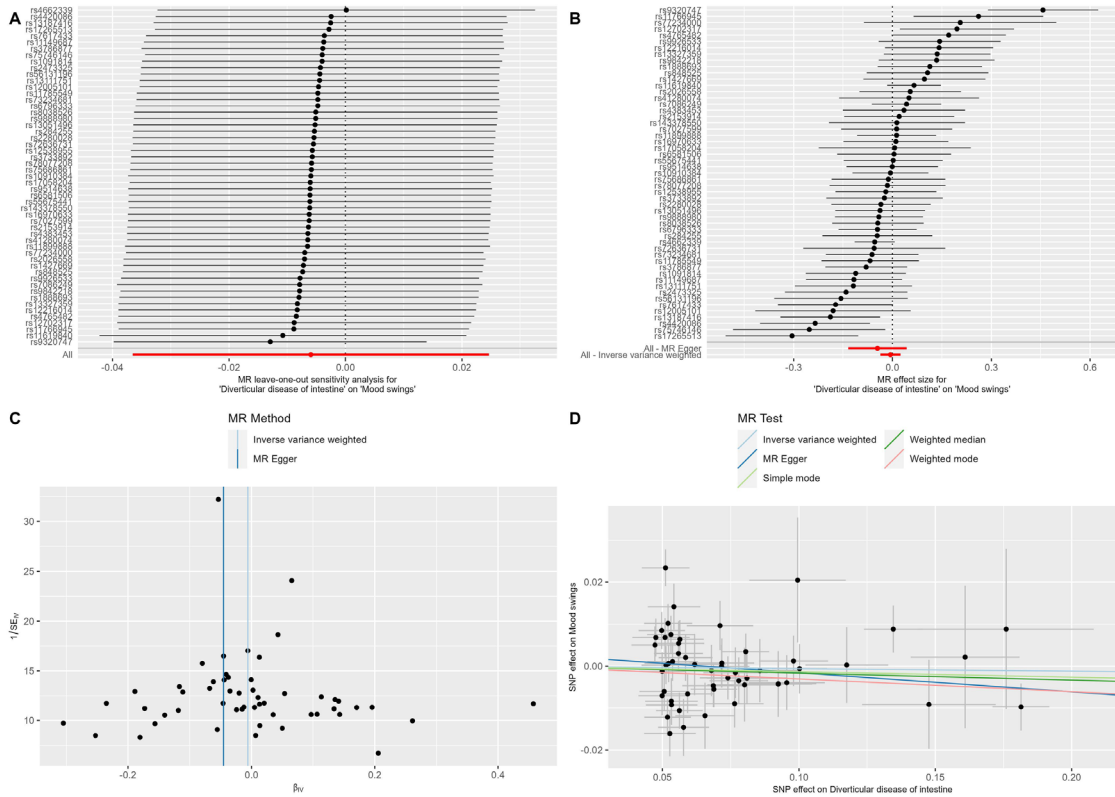
Supplementary Figure 30. Leave-one-out plots, scatter plots, funnel plots and forest plots for gastroduodenal ulcer on mood swings.



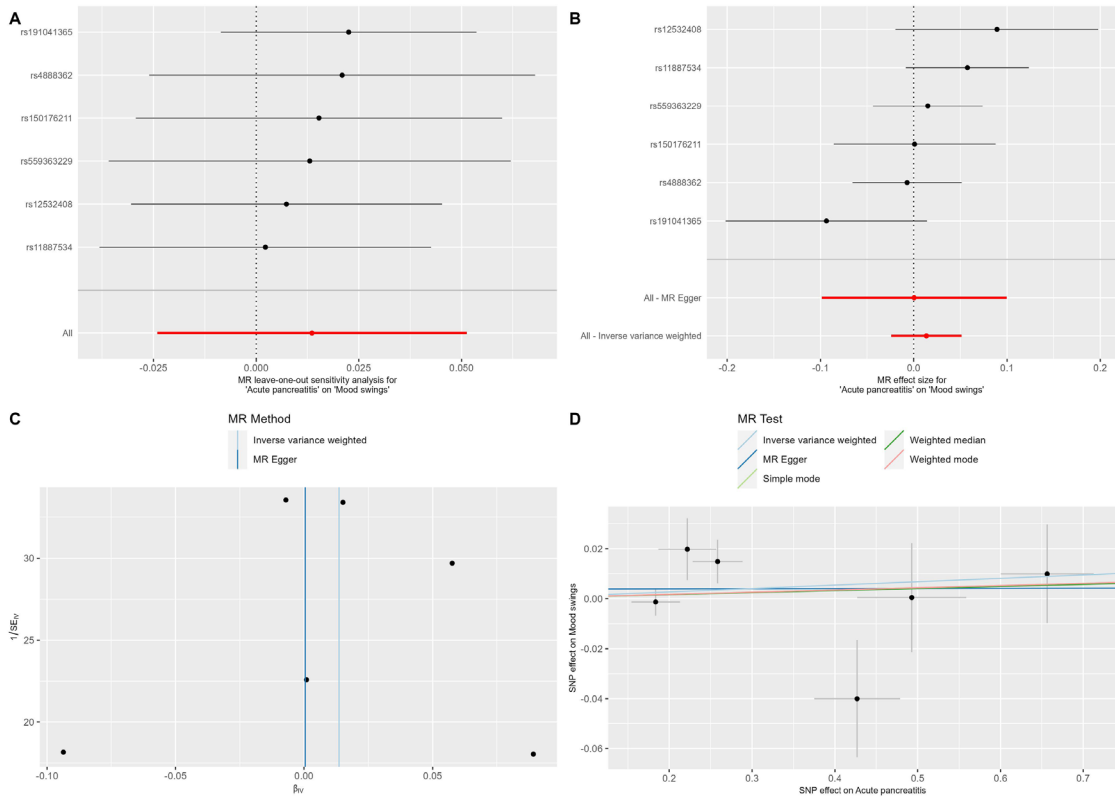
Supplementary Figure 31. Leave-one-out plots, scatter plots, funnel plots and forest plots for crohn's disease on mood swings.



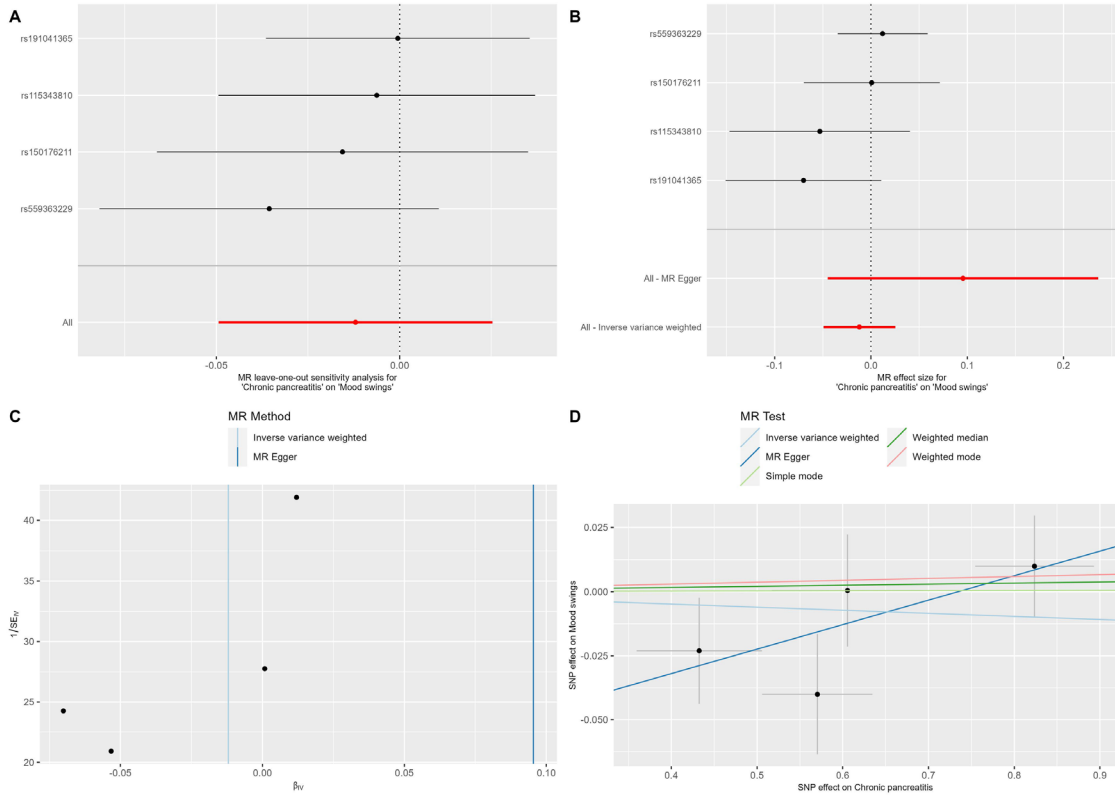
Supplementary Figure 32. Leave-one-out plots, scatter plots, funnel plots and forest plots for ulcerative colitis on mood swings.



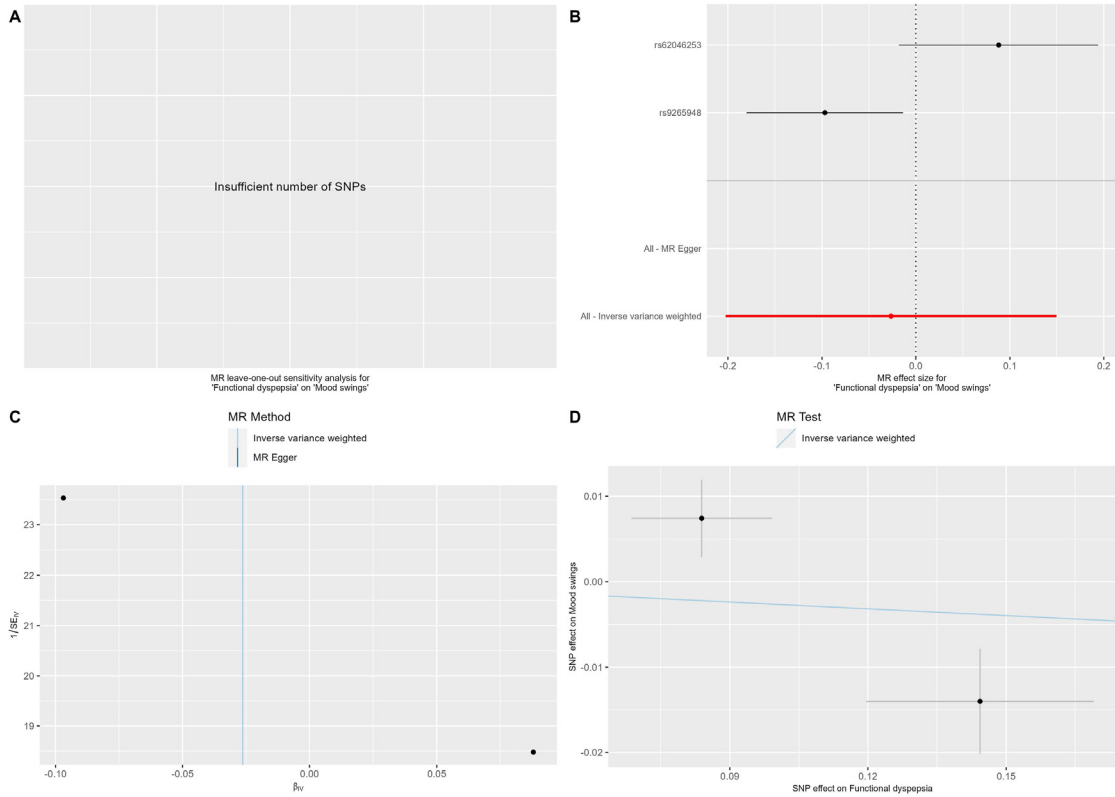
Supplementary Figure 33. Leave-one-out plots, scatter plots, funnel plots and forest plots for diverticular disease of intestine on mood swings.



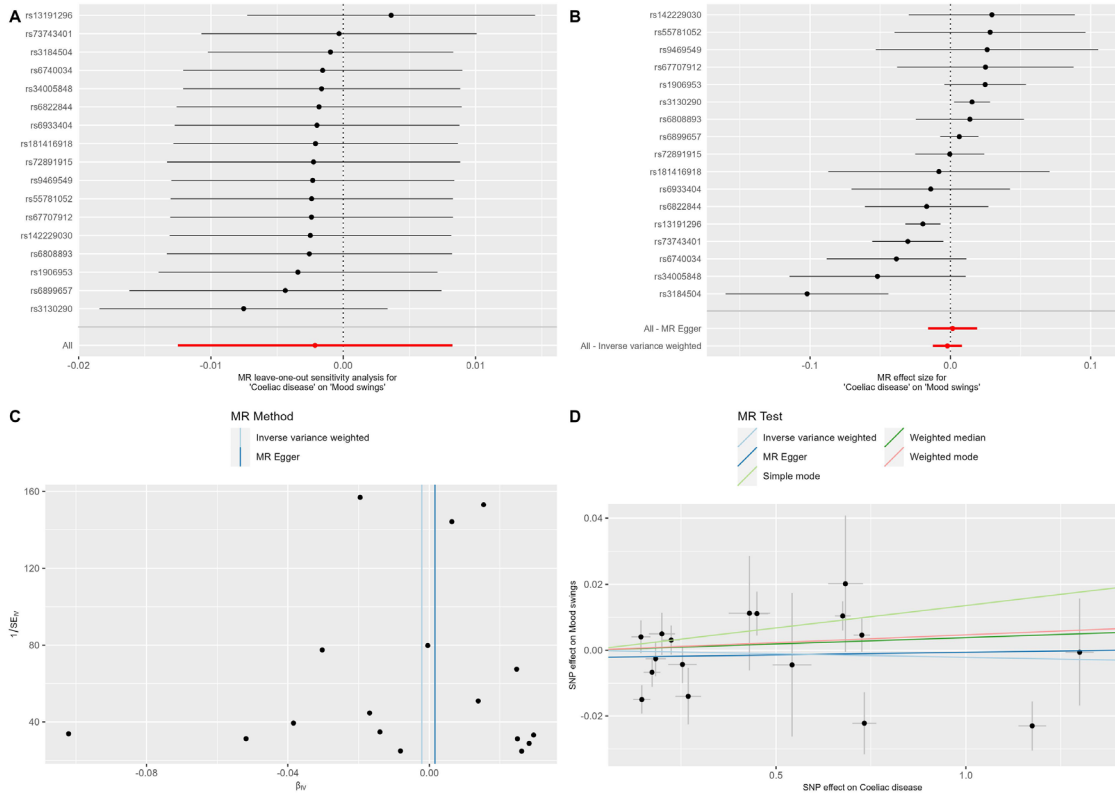
Supplementary Figure 34. Leave-one-out plots, scatter plots, funnel plots and forest plots for acute pancreatitis on mood swings.



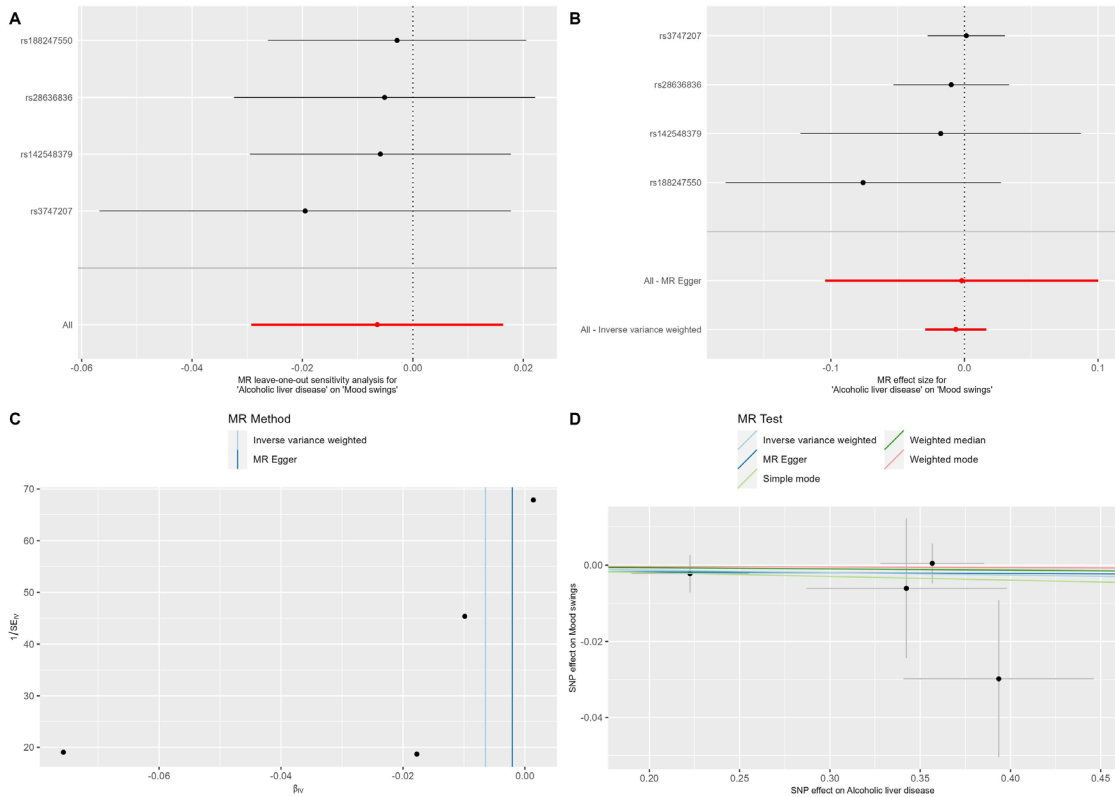
Supplementary Figure 35. Leave-one-out plots, scatter plots, funnel plots and forest plots for chronic pancreatitis on mood swings.



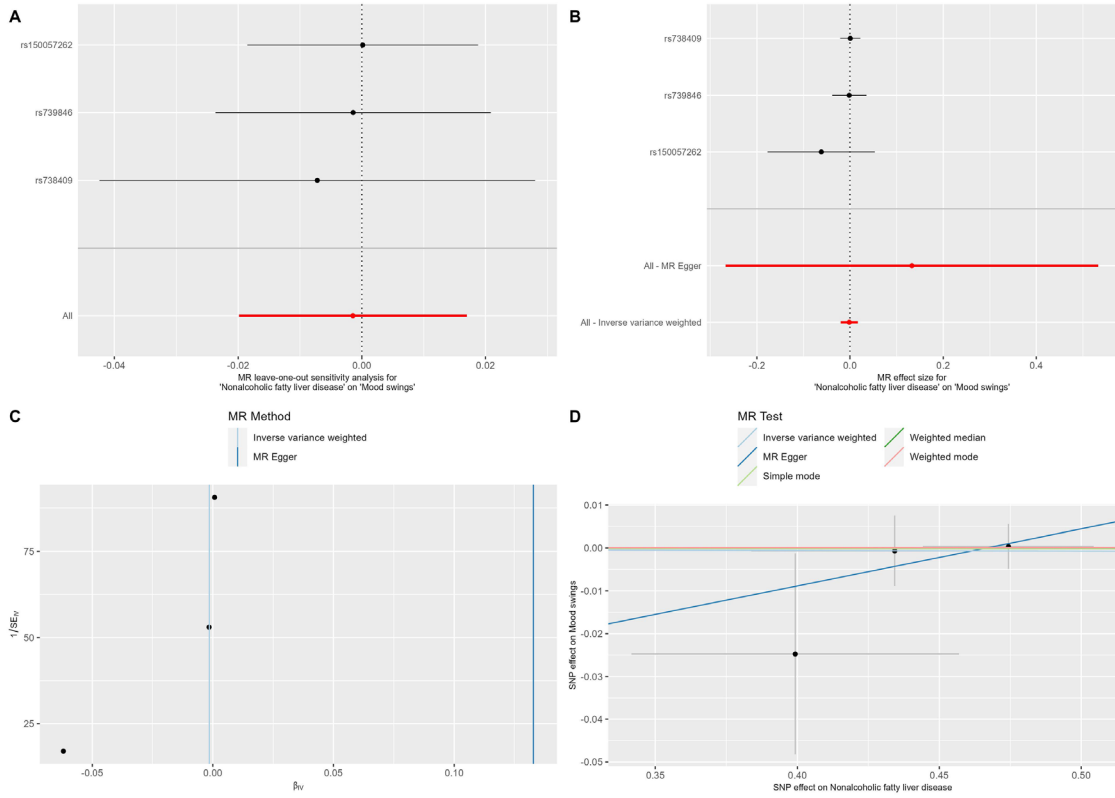
Supplementary Figure 36. Leave-one-out plots, scatter plots, funnel plots and forest plots for functional dyspepsia on mood swings.



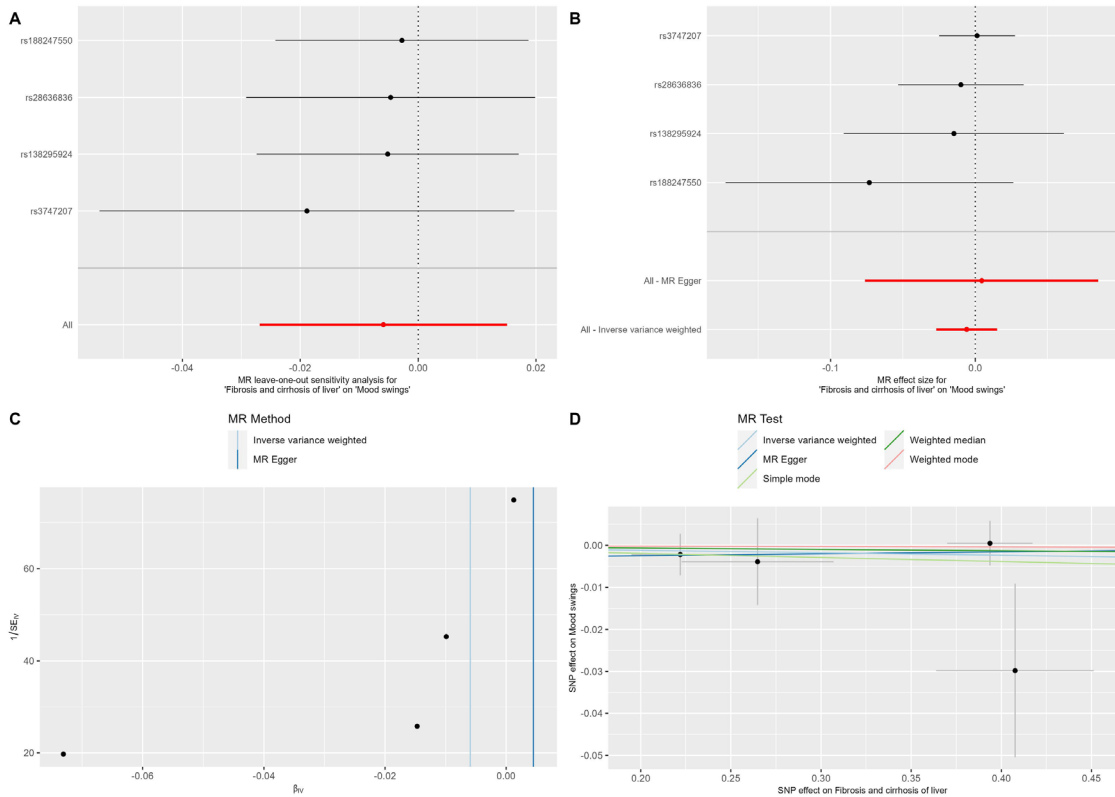
Supplementary Figure 37. Leave-one-out plots, scatter plots, funnel plots and forest plots for coeliac disease on mood swings.



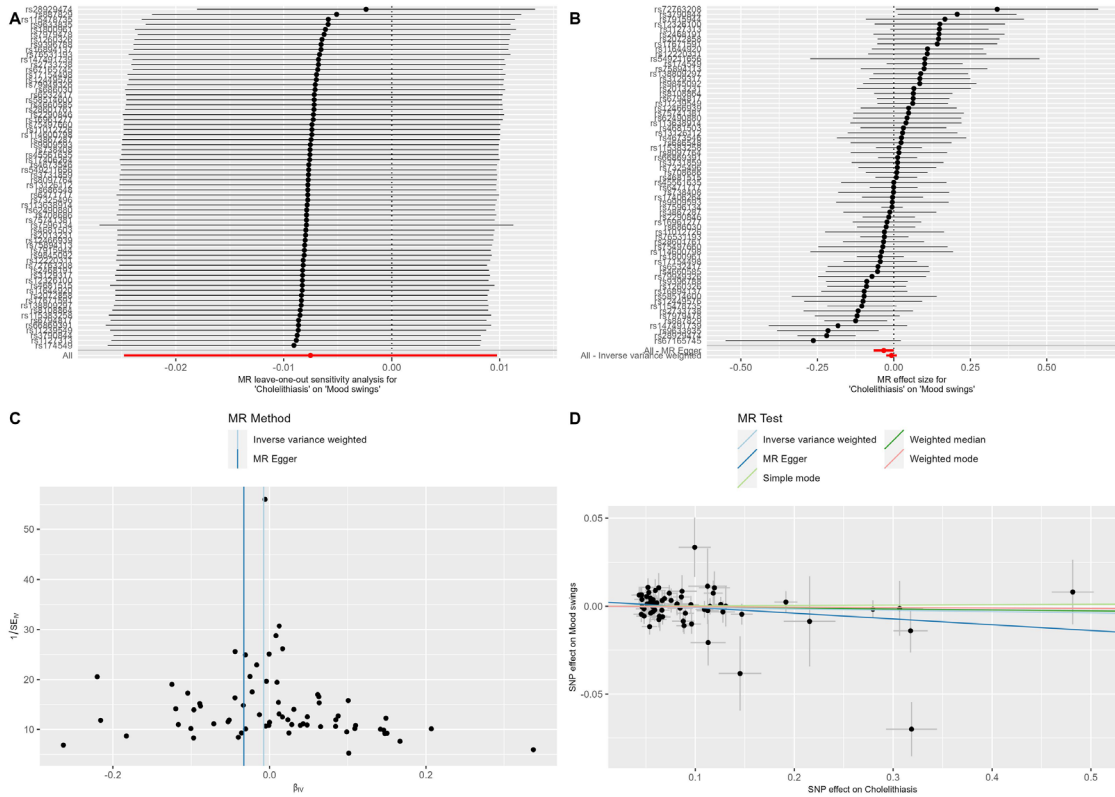
Supplementary Figure 38. Leave-one-out plots, scatter plots, funnel plots and forest plots for alcoholic liver disease on mood swings.



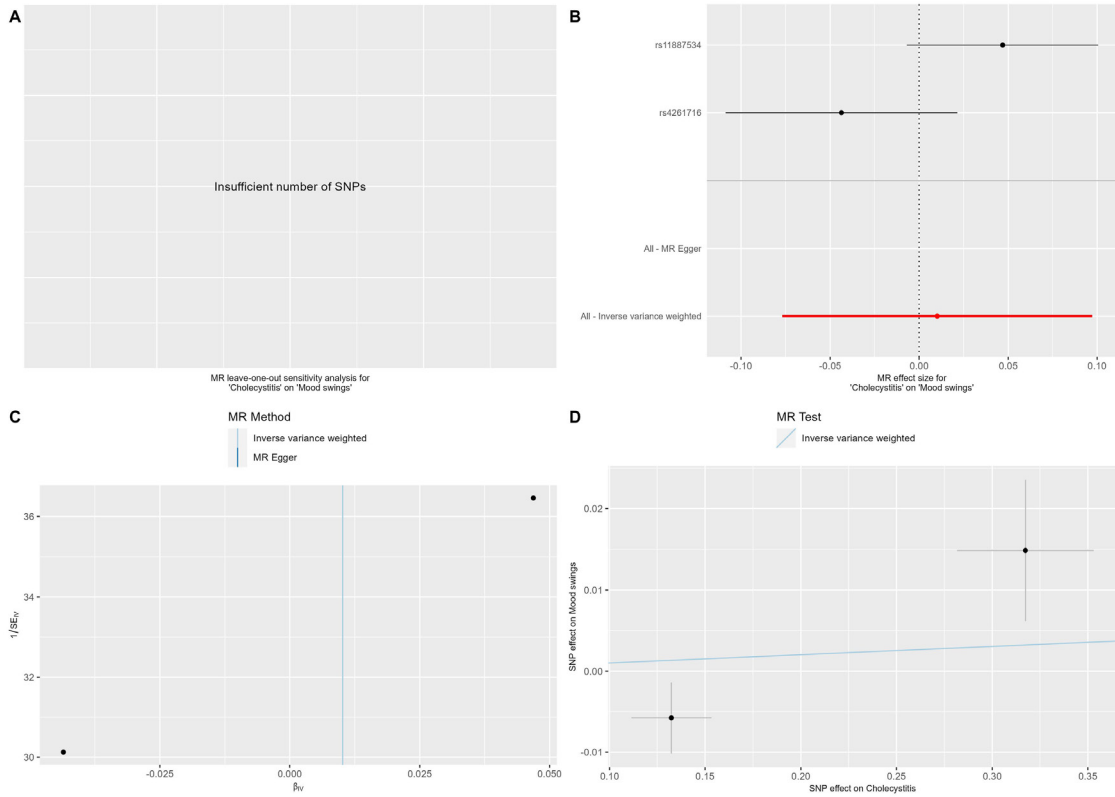
Supplementary Figure 39. Leave-one-out plots, scatter plots, funnel plots and forest plots for nonalcoholic fatty liver disease on mood swings.



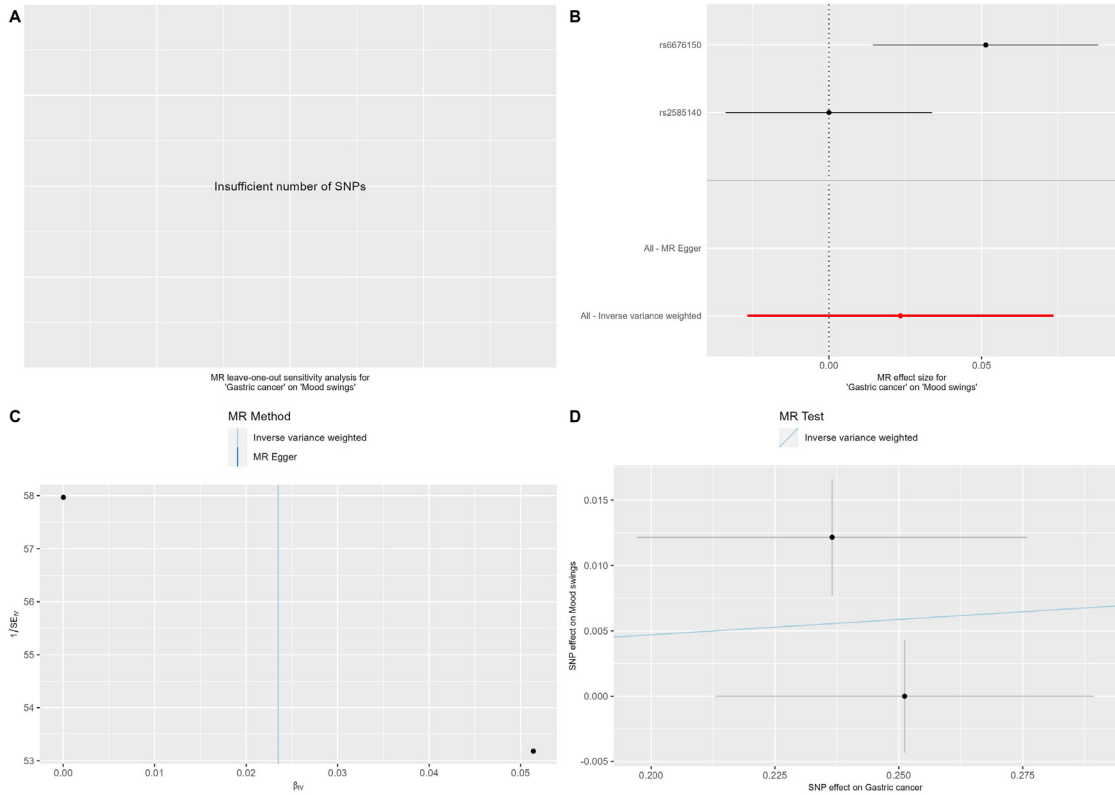
Supplementary Figure 40. Leave-one-out plots, scatter plots, funnel plots and forest plots for fibrosis and cirrhosis of liver on mood swings.



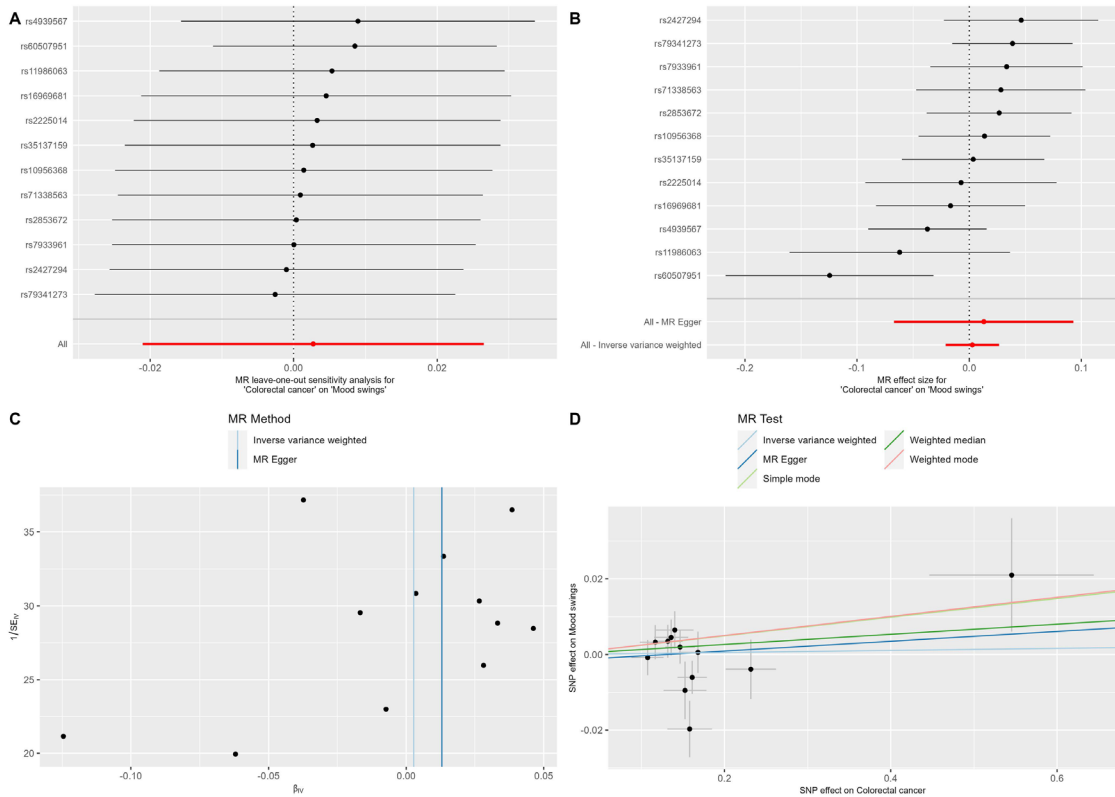
Supplementary Figure 41. Leave-one-out plots, scatter plots, funnel plots and forest plots for cholelithiasis on mood swings.



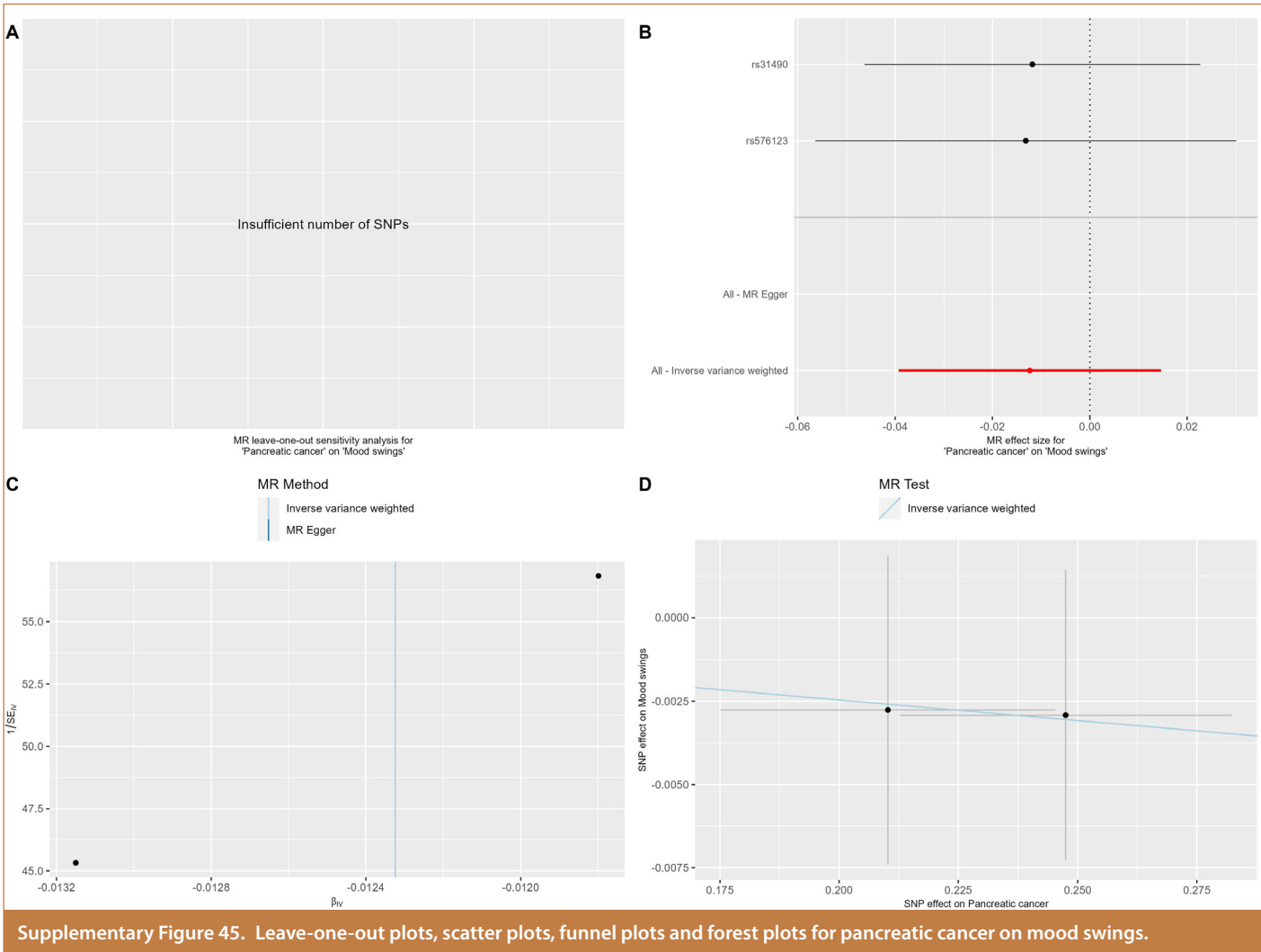
Supplementary Figure 42. Leave-one-out plots, scatter plots, funnel plots and forest plots for cholecystitis on mood swings.



Supplementary Figure 43. Leave-one-out plots, scatter plots, funnel plots and forest plots for gastric cancer on mood swings.



Supplementary Figure 44. Leave-one-out plots, scatter plots, funnel plots and forest plots for colorectal cancer on mood swing.



Supplementary Table 1. Information of Genome-Wide Association Summary Data

| Characteristic | Resource | Sample size | Population | Cases definition | URL |
|-----------------------------------|---------------|------------------------------------|------------|--|---|
| Mood swings | GWAS catalog | 201 373 cases and 243,901 controls | European | UKB:categorical:1920 | http://ftp.ebi.ac.uk/pub/databases/gwas/summary_statistics/GCST90041001-GCST90042000/GCST90041863/harmonised/34737426-GCST90041863-EFO_0008475.h.tsv.gz |
| Gastrointestinal diseases | FinnGen (R7) | 159 111 cases and 150 043 controls | European | Hospital discharge: ICD-10 — K00-K93, K77.0*B96.8 Hospital discharge: ICD-9 — 5[2-7] Hospital discharge: ICD-8 — 5[2-7] Cause of death: ICD-10 — K00-K93, K77.0*B96.8 Cause of death: ICD-9 — 5[2-7] Cause of death: ICD-8 — 5[2-7] | https://storage.googleapis.com/finngen-public-data-r7/summary_stats/finngen_R7_K11_GIDISEASE5.gz |
| Gastro-oesophageal reflux disease | FinnGen (R10) | 28 859 cases and 350 064 controls | European | Hospital discharge: ICD-10 — K21 Hospital discharge: ICD-9 — 5301A Cause of death: ICD-10 — K21 Cause of death: ICD-9 — 5301A | https://storage.googleapis.com/finngen-public-data-r10/summary_stats/finngen_R10_K11_REFLUX.gz |
| Acute gastritis | FinnGen (R10) | 2 558 cases and 350 064 controls | European | Hospital discharge: ICD-10 — K29.0, K29.1 Hospital discharge: ICD-9 — 5350 Hospital discharge: ICD-8 — 5350[0-2] Cause of death: ICD-10 — K29.0, K29.1 Cause of death: ICD-9 — 5350 Cause of death: ICD-8 — 3530[0-2] | https://storage.googleapis.com/finngen-public-data-r10/summary_stats/finngen_R10_K11_ACUTGASTR.gz |
| Chronic gastritis | FinnGen (R10) | 3 875 cases and 361 641 controls | European | Hospital discharge: ICD-10 — K29.3, K29.4, K29.5 Hospital discharge: ICD-9 — 5351 5354 Hospital discharge: ICD-8 — 53503 Cause of death: ICD-10 — K29.3, K29.4, K29.5 Cause of death: ICD-9 — 5351 5354 Cause of death: ICD-8 — 53503 | https://storage.googleapis.com/finngen-public-data-r10/summary_stats/finngen_R10_K11_CHRONGASTR.gz |
| Gastric ulcer | FinnGen (R10) | 6 459 cases and 350 064 controls | European | Hospital discharge: ICD-10 — K25 Hospital discharge: ICD-9 — 531 Cause of death: ICD-10 — K25 Cause of death: ICD-9 — 531 | https://storage.googleapis.com/finngen-public-data-r10/summary_stats/finngen_R10_K11_GULC.gz |
| Duodenal ulcer | FinnGen (R10) | 3 795 cases and 350 064 controls | European | Hospital discharge: ICD-10 — K26 Hospital discharge: ICD-9 — 532 Cause of death: ICD-10 — K26 Cause of death: ICD-9 — 532 | https://storage.googleapis.com/finngen-public-data-r10/summary_stats/finngen_R10_K11_DULC.gz |
| Gastroduodenal ulcer | FinnGen (R10) | 10 021 cases and 350 064 controls | European | Hospital discharge: ICD-10 — K25, K26, K27, K28 Cause of death: ICD-10 — K25, K26, K27, K28 | https://storage.googleapis.com/finngen-public-data-r10/summary_stats/finngen_R10_K11_GASTRODUULC.gz |

Supplementary Table 1. Information of Genome-Wide Association Summary Data (*Continued*)

| Characteristic | Resource | Sample size | Population | Cases definition | URL |
|-----------------------------------|-----------------|--------------------------------------|-------------------|------------------------------------|---|
| Crohn's disease | FinnGen (R10) | 2 033 cases and 409 940 controls | European | Hospital discharge: ICD-10 — K50 | https://storage.googleapis.com/finngen-public-data-r10/summary_stats/finnge_n_R10_K11_CD_STRICT2.gz |
| | | | | Hospital discharge: ICD-9 — 555 | |
| | | | | Hospital discharge: ICD-8 — 5630 | |
| | | | | Cause of death: ICD-10 — K50 | |
| | | | | Cause of death: ICD-9 — 555 | |
| Cause of death: ICD-8 — 5630 | | | | | |
| Ulcerative colitis | FinnGen (R10) | 5 931 cases and 405 386 controls | European | Hospital discharge: ICD-10 — K51 | https://storage.googleapis.com/finngen-public-data-r10/summary_stats/finnge_n_R10_K11_UC_STRICT2.gz |
| | | | | Hospital discharge: ICD-9 — 556 | |
| | | | | Hospital discharge: ICD-8 — | |
| | | | | 5631 569 | |
| | | | | Hospital discharge: excluded ICD-9 | |
| | | | | — 5564A | |
| | | | | Cause of death: ICD-10 — K51 | |
| | | | | Cause of death: ICD-9 — 556 | |
| | | | | Cause of death: ICD-8 — 5631 569 | |
| | | | | Cause of death: excluded ICD-9 — | |
| 5564A | | | | | |
| Diverticular disease of intestine | FinnGen (R10) | 33 619 cases and 329 381 controls | European | Hospital discharge: ICD-10 — K57 | https://storage.googleapis.com/finngen-public-data-r10/summary_stats/finnge_n_R10_K11_DIVERTIC.gz |
| | | | | Hospital discharge: ICD-9 — 562 | |
| | | | | Hospital discharge: ICD-8 — 562 | |
| | | | | Cause of death: ICD-10 — K57 | |
| | | | | Cause of death: ICD-9 — 562 | |
| Cause of death: ICD-8 — 562 | | | | | |
| Acute pancreatitis | FinnGen (R10) | 6787 cases and 361 641 controls | European | Hospital discharge: ICD-10 — K85 | https://storage.googleapis.com/finngen-public-data-r10/summary_stats/finnge_n_R10_K11_ACUTPANC.gz |
| | | | | Hospital discharge: ICD-9 — 5770 | |
| | | | | Hospital discharge: ICD-8 — 5770 | |
| | | | | Cause of death: ICD-10 — K85 | |
| | | | | Cause of death: ICD-9 — 5770 | |
| Cause of death: ICD-8 — 5770 | | | | | |
| Chronic pancreatitis | FinnGen (R10) | 3 875 cases and 361 641 controls | European | Hospital discharge: ICD-10 — | https://storage.googleapis.com/finngen-public-data-r10/summary_stats/finnge_n_R10_K11_CHRONPANC.gz |
| | | | | K86.00, K86.01, K86.08, K86.1 | |
| | | | | Hospital discharge: ICD-9 — 5771 | |
| | | | | Hospital discharge: ICD-8 — 5771 | |
| | | | | Cause of death: ICD-10 — K86.00, | |
| | | | | K86.01, K86.08, K86.1 | |
| | | | | Cause of death: ICD-9 — 5771 | |
| | | | | Cause of death: ICD-8 — 5771 | |
| | | | | KELA reimbursements: KELA codes | |
| | | | | — 133 | |
| Irritable bowel syndrome | FinnGen (R10) | 10 329 cases and 329 381 controls | European | Hospital discharge: ICD-10 — K58 | https://storage.googleapis.com/finngen-public-data-r10/summary_stats/finnge_n_R10_K11_IBS.gz |
| | | | | Hospital discharge: ICD-9 — 5641 | |
| | | | | Hospital discharge: ICD-8 — 56419 | |
| | | | | Cause of death: ICD-10 — K58 | |
| | | | | Cause of death: ICD-9 — 5641 | |
| Cause of death: ICD-8 — 56419 | | | | | |

| Characteristic | Resource | Sample size | Population | Cases definition | URL |
|----------------------------------|---------------|------------------------------------|------------|--------------------------------------|---|
| Functional dyspepsia | FinnGen (R10) | 9 680 cases and 3 500 641 controls | European | Hospital discharge: ICD-10 — K30 | https://storage.googleapis.com/finngen-public-data-r10/summary_stats/finnge_n_R10_K11_FUNC DYSP.gz |
| | | | | Hospital discharge: ICD-9 — 5368A | |
| | | | | Hospital discharge: ICD-8 — 5361 | |
| Coeliac disease | FinnGen (R10) | 4 115 cases and 394 391 controls | European | Cause of death: ICD-10 — K30 | https://storage.googleapis.com/finngen-public-data-r10/summary_stats/finnge_n_R10_K11_COELIAC.gz |
| | | | | Cause of death: ICD-9 — 5368A | |
| | | | | Cause of death: ICD-8 — 5361 | |
| Acute appendicitis | FinnGen (R10) | 31 628 cases and 378 082 controls | European | Hospital discharge: ICD-10 — K35 | https://storage.googleapis.com/finngen-public-data-r10/summary_stats/finnge_n_R10_K11_APPENDACUT.gz |
| | | | | Hospital discharge: ICD-9 — 540 | |
| | | | | Hospital discharge: ICD-8 — 540 | |
| Alcoholic liver disease | FinnGen (R10) | 3 047 cases and 400 247 controls | European | Cause of death: ICD-10 — K35 | https://storage.googleapis.com/finngen-public-data-r10/summary_stats/finnge_n_R10_K11_ALCOLIV.gz |
| | | | | Cause of death: ICD-9 — 540 | |
| | | | | Cause of death: ICD-8 — 540 | |
| Nonalcoholic fatty liver disease | FinnGen (R10) | 2 568 cases and 409 613 controls | European | Hospital discharge: ICD-10 — K70 | https://storage.googleapis.com/finngen-public-data-r10/summary_stats/finnge_n_R10_NAFLD.gz |
| | | | | Hospital discharge: ICD-9 — 571[0-3] | |
| | | | | Hospital discharge: ICD-8 — 5710 | |
| Fibrosis and cirrhosis of liver | FinnGen (R10) | 2 017 cases and 400 247 controls | European | Cause of death: ICD-10 — K70 | https://storage.googleapis.com/finngen-public-data-r10/summary_stats/finnge_n_R10_FIBROCHIRLIV.gz |
| | | | | Cause of death: ICD-9 — 571[0-3] | |
| | | | | Cause of death: ICD-8 — 5710 | |
| Cholelithiasis | FinnGen (R10) | 40 191 cases and 361 641 controls | European | Hospital discharge: ICD-10 — K80 | https://storage.googleapis.com/finngen-public-data-r10/summary_stats/finnge_n_R10_K11_CHOLELITH.gz |
| | | | | Hospital discharge: ICD-9 — 574 | |
| | | | | Hospital discharge: ICD-8 — 574 | |
| Cholecystitis | FinnGen (R10) | 46 971 cases and 361 641 controls | European | Cause of death: ICD-10 — K80 | https://storage.googleapis.com/finngen-public-data-r10/summary_stats/finnge_n_R10_K11_CHOLECYST.GZ |
| | | | | Cause of death: ICD-9 — 574 | |
| | | | | Cause of death: ICD-8 — 574 | |

(Continued)

Supplementary Table 1. Information of Genome-Wide Association Summary Data (Continued)

| Characteristic | Resource | Sample size | Population | Cases definition | URL |
|-------------------|---------------|----------------------------------|------------|--|---|
| Esophagus cancer | FinnGen (R10) | 619 cases and 314 193 controls | European | Hospital discharge: ICD-10 — C15 Hospital discharge: ICD-9 — 150 Hospital discharge: ICD-8 — 150 Cause of death: ICD-10 — C15 Cause of death: ICD-9 — 150 Cause of death: ICD-8 — 150 Cancer registry: Topography ICD-O-3 — C15 Cancer registry: Morphology ICD-O-3 — ANY Cancer registry: Behavior codes — 3 | https://storage.googleapis.com/finngen-public-data-r10/summary_stats/finnge_n_R10_C3_OESOPHAGUS_EXALLC.gz |
| Gastric cancer | FinnGen (R10) | 1 423 cases and 314 193 controls | European | Hospital discharge: ICD-10 — C16 Hospital discharge: ICD-9 — 151 Hospital discharge: ICD-8 — 151 Cause of death: ICD-10 — C16 Cause of death: ICD-9 — 151 Cause of death: ICD-8 — 151 Cancer registry: Topography ICD-O-3 — C16 Cancer registry: Morphology ICD-O-3 — ANY Cancer registry: Behavior codes — 3 | https://storage.googleapis.com/finngen-public-data-r10/summary_stats/finnge_n_R10_C3_STOMACH_EXALLC.gz |
| Colorectal cancer | FinnGen (R10) | 6 847 cases and 314 193 controls | European | ICD-O-3 | https://storage.googleapis.com/finngen-public-data-r10/summary_stats/finnge_n_R10_C3_COLORECTAL_EXALLC.gz |
| Pancreatic cancer | FinnGen (R10) | 1 626 cases and 314 193 controls | European | Hospital discharge: ICD-10 — C25 Hospital discharge: ICD-9 — 157 Hospital discharge: ICD-8 — 157 Cause of death: ICD-10 — C25 Cause of death: ICD-9 — 157 Cause of death: ICD-8 — 157 Cancer registry: Topography ICD-O-3 — C25 Cancer registry: Morphology ICD-O-3 — ANY Cancer registry: Behavior codes — 3 | https://storage.googleapis.com/finngen-public-data-r10/summary_stats/finnge_n_R10_C3_PANCREAS_EXALLC.gz |

Supplementary Table 2. The Summary Information for SNPs of Mood Swings

| Exposure | SNP | chr | pos | effect allele | other allele | eaf | β | SE | P | F |
|-------------|-------------|-----|-----------|---------------|--------------|-----------|------------|------------|------------|-------------|
| Mood swings | rs6694904 | 1 | 67911575 | T | C | 0.634157 | -0.0261214 | 0.00451866 | 7.44e-09 | 33.41747023 |
| Mood swings | rs2000228 | 1 | 72258180 | C | T | 0.313995 | 0.0306801 | 0.00465908 | 4.55e-11 | 43.36238952 |
| Mood swings | rs4651205 | 1 | 174903292 | T | C | 0.271919 | -0.0266305 | 0.00488399 | 4.96e-08 | 29.73097208 |
| Mood swings | rs2678871 | 2 | 57926467 | A | G | 0.593812 | 0.028175 | 0.00445697 | 2.59e-10 | 39.96211155 |
| Mood swings | rs35125029 | 2 | 143504088 | A | G | 0.379778 | -0.0276801 | 0.00449297 | 7.24e-10 | 37.95493675 |
| Mood swings | rs10180895 | 2 | 198630265 | A | C | 0.581921 | -0.026029 | 0.00441923 | 3.86e-09 | 34.69139441 |
| Mood swings | rs6435670 | 2 | 211791160 | T | G | 0.287544 | 0.028063 | 0.00482615 | 6.07e-09 | 33.81166525 |
| Mood swings | rs9881798 | 3 | 16805459 | C | A | 0.404393 | 0.025074 | 0.00442504 | 1.46e-08 | 32.10796947 |
| Mood swings | rs73082357 | 3 | 49046133 | A | G | 0.118454 | -0.043611 | 0.00668905 | 7.04e-11 | 42.50726923 |
| Mood swings | rs9852417 | 3 | 65175479 | A | C | 0.587995 | -0.0249646 | 0.00442571 | 1.69e-08 | 31.81876492 |
| Mood swings | rs539711 | 3 | 107552348 | T | A | 0.259847 | 0.0320546 | 0.00516842 | 5.57e-10 | 38.46494598 |
| Mood swings | rs13434208 | 3 | 117288817 | G | A | 0.525832 | -0.0244442 | 0.00433934 | 1.77e-08 | 31.73250064 |
| Mood swings | rs60799144 | 4 | 21851144 | T | A | 0.601252 | 0.0249364 | 0.00452443 | 3.56e-08 | 30.37664213 |
| Mood swings | rs10488866 | 4 | 104524122 | C | T | 0.267186 | -0.0267895 | 0.00490118 | .000000046 | 29.8763756 |
| Mood swings | rs67970900 | 4 | 146827674 | T | G | 0.307706 | -0.0262217 | 0.00469722 | 2.37e-08 | 31.16304494 |
| Mood swings | rs6882578 | 5 | 104410123 | C | G | 0.512119 | 0.0238142 | 0.00433979 | 4.08e-08 | 30.11165069 |
| Mood swings | rs6895295 | 5 | 108421537 | T | C | 0.214708 | 0.0303752 | 0.00529206 | 9.48e-09 | 32.94494398 |
| Mood swings | rs186121425 | 5 | 117532956 | T | G | 0.145587 | -0.0358465 | 0.00614341 | 5.38e-09 | 34.04666016 |
| Mood swings | rs58746316 | 5 | 148458109 | T | A | 0.589745 | 0.0278641 | 0.00442412 | 3.01e-10 | 39.66762908 |
| Mood swings | rs3025646 | 6 | 29599065 | C | T | 0.0665062 | 0.0515162 | 0.00867373 | 2.86e-09 | 35.27571644 |
| Mood swings | rs200250173 | 6 | 64392217 | T | C | 0.280778 | -0.0275627 | 0.00486132 | 1.43e-08 | 32.14660373 |
| Mood swings | rs2503775 | 6 | 98073724 | G | A | 0.87095 | -0.0368092 | 0.00646842 | 1.27e-08 | 32.38294446 |
| Mood swings | rs67447472 | 6 | 142741079 | T | G | 0.0967712 | 0.0457899 | 0.00735202 | 4.72e-10 | 38.79055832 |
| Mood swings | rs6460902 | 7 | 12215885 | A | G | 0.41808 | 0.0256874 | 0.00438837 | 4.81e-09 | 34.26366554 |
| Mood swings | rs763646 | 7 | 133658600 | T | C | 0.444591 | 0.0263874 | 0.00439284 | 1.89e-09 | 36.08298272 |
| Mood swings | rs7818437 | 8 | 10352113 | C | T | 0.232477 | 0.0369458 | 0.00520265 | 1.24e-12 | 50.42906651 |
| Mood swings | rs1962104 | 8 | 140625230 | C | T | 0.558635 | 0.0315008 | 0.00443214 | 1.18e-12 | 50.5145195 |
| Mood swings | rs10960067 | 9 | 11651144 | G | A | 0.223075 | -0.037386 | 0.00521633 | 7.66e-13 | 51.36743578 |
| Mood swings | rs1111818 | 9 | 23315442 | C | G | 0.631051 | -0.0257611 | 0.00451104 | 1.13e-08 | 32.61185111 |
| Mood swings | rs10120798 | 9 | 93681194 | G | A | 0.592214 | -0.025893 | 0.00443118 | 5.12e-09 | 34.14490893 |
| Mood swings | rs10983775 | 9 | 117758822 | T | C | 0.53444 | -0.0270361 | 0.00436483 | 5.86e-10 | 38.36660943 |
| Mood swings | rs10818399 | 9 | 119894725 | G | C | 0.59583 | 0.0297381 | 0.00442955 | 1.9e-11 | 45.07204035 |
| Mood swings | rs999483 | 9 | 132426002 | G | T | 0.249198 | 0.0288186 | 0.00500489 | 8.51e-09 | 33.1555842 |
| Mood swings | rs11599236 | 10 | 104694914 | C | T | 0.408474 | -0.0246909 | 0.00447242 | 3.38e-08 | 30.47815541 |
| Mood swings | rs297343 | 11 | 16333107 | G | T | 0.638983 | -0.0308684 | 0.00451859 | 8.41e-12 | 46.66834125 |
| Mood swings | rs11039154 | 11 | 47256951 | T | C | 0.277679 | 0.0356116 | 0.00483672 | 1.8e-13 | 54.2102088 |
| Mood swings | rs3133388 | 11 | 113536392 | A | G | 0.315683 | -0.0363991 | 0.0047079 | 1.06e-14 | 59.77599749 |
| Mood swings | rs7954112 | 12 | 16163404 | A | G | 0.418235 | 0.0251362 | 0.00444424 | 1.55e-08 | 31.98926331 |
| Mood swings | rs28655666 | 12 | 121748411 | A | G | 0.55244 | -0.0293402 | 0.00434668 | 1.48e-11 | 45.56284164 |
| Mood swings | rs1373921 | 13 | 58060689 | G | A | 0.238622 | 0.0377152 | 0.00507181 | 1.04e-13 | 55.29767591 |
| Mood swings | rs9517301 | 13 | 98442834 | C | T | 0.376016 | 0.0275496 | 0.00452682 | 1.16e-09 | 37.03771139 |
| Mood swings | rs7156084 | 14 | 71237098 | A | T | 0.707269 | 0.0271777 | 0.00482314 | 1.75e-08 | 31.75160362 |
| Mood swings | rs4899532 | 14 | 74707429 | G | A | 0.745781 | 0.0309192 | 0.00497189 | 5.01e-10 | 38.67349963 |
| Mood swings | rs4243048 | 15 | 77717718 | A | G | 0.560296 | -0.0253962 | 0.00455096 | .000000024 | 31.14092011 |
| Mood swings | rs11864857 | 16 | 5742822 | T | A | 0.277867 | 0.0305537 | 0.00491429 | 5.06e-10 | 38.65503382 |
| Mood swings | rs7202252 | 16 | 24730365 | C | T | 0.733042 | 0.0304521 | 0.00490489 | 5.35e-10 | 38.54570119 |
| Mood swings | rs35856211 | 16 | 74105001 | A | G | 0.540829 | -0.0265702 | 0.00437662 | 1.27e-09 | 36.85631963 |
| Mood swings | rs9933873 | 16 | 87363149 | C | T | 0.439598 | 0.0302215 | 0.0043675 | 4.53e-12 | 47.88132996 |
| Mood swings | rs669915 | 17 | 45646879 | A | G | 0.222411 | 0.0478423 | 0.00520471 | 3.85e-20 | 84.49500339 |
| Mood swings | rs11082011 | 18 | 37565159 | T | C | 0.669366 | -0.0345511 | 0.00462659 | 8.15e-14 | 55.77013906 |
| Mood swings | rs62097985 | 18 | 53284305 | T | C | 0.419319 | 0.0282388 | 0.00440901 | 1.51e-10 | 41.02138388 |
| Mood swings | rs12963231 | 18 | 55100746 | A | C | 0.328391 | 0.0361901 | 0.00464628 | 6.75e-15 | 60.66927565 |
| Mood swings | rs613872 | 18 | 55543071 | T | G | 0.826073 | 0.0463201 | 0.00571822 | 5.48e-16 | 65.61713381 |
| Mood swings | rs1688000 | 19 | 35128262 | G | A | 0.626691 | -0.026825 | 0.0044895 | 2.3e-09 | 35.70125717 |
| Mood swings | rs4578918 | 20 | 46093017 | C | T | 0.739361 | -0.0292367 | 0.00494588 | 3.39e-09 | 34.94375348 |
| Mood swings | rs2092563 | 22 | 41196673 | A | G | 0.285323 | 0.0328158 | 0.00480933 | 8.89e-12 | 46.55827021 |

Supplementary Table 3. Confounding SNPs for Various Phenotypes

| phenotypes | Confounding SNPs | confounders |
|-----------------------------------|--|-------------------------------------|
| Functional dyspepsia | NA | rs9881798:Cigarettes smoked per day |
| Pancreatic cancer | NA | rs3133388:Smoking status |
| Acute gastritis | rs9881798,rs3133388 | rs613872:Body mass index |
| Coeliac disease | rs9881798,rs3133388 | rs11599236:Depression |
| Colorectal cancer | rs9881798,rs3133388 | rs12963231:Depression |
| Gastric cancer | rs9881798,rs3133388 | rs2092563:Depression |
| Cholecystitis | rs9881798,rs3133388,rs613872 | rs4651205:Drinks per week |
| Crohn's disease | rs9881798,rs3133388,rs613872 | |
| Acute appendicitis | rs9881798,rs3133388,rs11599236,rs12963231,rs2092563 | |
| Acute pancreatitis | rs9881798,rs3133388,rs11599236,rs12963231,rs2092563 | |
| Chronic gastritis | rs9881798,rs3133388,rs11599236,rs12963231,rs2092563 | |
| Diverticular disease of intestine | rs9881798,rs3133388,rs11599236,rs12963231,rs2092563 | |
| Duodenal ulcer | rs9881798,rs3133388,rs11599236,rs12963231,rs2092563 | |
| Gastric ulcer | rs9881798,rs3133388,rs11599236,rs12963231,rs2092563 | |
| Gastro-oesophageal reflux disease | rs9881798,rs3133388,rs11599236,rs12963231,rs2092563 | |
| Gastroduodenal ulcer | rs9881798,rs3133388,rs11599236,rs12963231,rs2092563 | |
| Irritable bowel syndrome | rs9881798,rs3133388,rs11599236,rs12963231,rs2092563 | |
| Cholelithiasis | rs9881798,rs3133388,rs11599236,rs12963231,rs2092563,rs613872 | |
| Nonalcoholic fatty liver disease | rs9881798,rs3133388,rs11599236,rs12963231,rs2092563,rs613872 | |
| Ulcerative colitis | rs9881798,rs3133388,rs11599236,rs12963231,rs2092563,rs613872 | |
| Esophagus cancer | rs9881798,rs3133388,rs4651205 | |
| Fibrosis and cirrhosis of liver | rs9881798,rs3133388,rs4651205,rs613872 | |
| Alcoholic liver disease | rs9881798,rs3133388,rs11599236,rs12963231,rs2092563,rs613872,rs4651205 | |
| Chronic pancreatitis | rs9881798,rs3133388,rs11599236,rs12963231,rs2092563,rs613872,rs4651205 | |
| Gastrointestinal diseases | rs9881798,rs3133388,rs11599236,rs12963231,rs2092563,rs613872,rs4651205 | |

Supplementary Table 4. Causal Effects of Mood Swings on Gastrointestinal Diseases Risk

| Exposure | Outcome | Method | SNPs(n) | OR | or_lci95 | or_uci95 | P |
|-------------|----------------------|---|---------|-------------|-------------|-------------|------------|
| Mood swings | Functional dyspepsia | Inverse variance weighted (multiplicative random effects) | 51 | 1.327276515 | 1.113768555 | 1.581713669 | .001555207 |
| Mood swings | Functional dyspepsia | MR Egger | 51 | 0.922429433 | 0.318192477 | 2.674092323 | .882408377 |
| Mood swings | Functional dyspepsia | Weighted median | 51 | 1.328535132 | 1.047927908 | 1.68428151 | .018938843 |
| Mood swings | Pancreatic cancer | Inverse variance weighted (fixed effects) | 51 | 1.552751874 | 1.078043591 | 2.236494333 | .01809513 |
| Mood swings | Pancreatic cancer | MR Egger | 51 | 1.360371272 | 0.150199529 | 12.32101063 | .785433083 |
| Mood swings | Pancreatic cancer | Weighted median | 51 | 1.447901089 | 0.878977065 | 2.385065147 | .1461034 |
| Mood swings | Acute gastritis | Inverse variance weighted (fixed effects) | 50 | 1.664110434 | 1.242203325 | 2.229315829 | .000640629 |
| Mood swings | Acute gastritis | MR Egger | 50 | 2.090887575 | 0.35708651 | 12.24300197 | .41740954 |
| Mood swings | Acute gastritis | Weighted median | 50 | 1.752114433 | 1.178104868 | 2.605799424 | .005616227 |
| Mood swings | Coeliac disease | Inverse variance weighted (multiplicative random effects) | 50 | 1.03571513 | 0.726269568 | 1.477007817 | .846341546 |
| Mood swings | Coeliac disease | MR Egger | 50 | 0.202682311 | 0.024146017 | 1.701320728 | .147968445 |
| Mood swings | Coeliac disease | Weighted median | 50 | 0.945674841 | 0.663933215 | 1.346974189 | .75693425 |
| Mood swings | Colorectal cancer | Inverse variance weighted (multiplicative random effects) | 50 | 0.990887736 | 0.78513237 | 1.250564291 | .938554361 |
| Mood swings | Colorectal cancer | MR Egger | 50 | 2.0988204 | 0.514449635 | 8.562640099 | .306562105 |
| Mood swings | Colorectal cancer | Weighted median | 50 | 1.028268304 | 0.779560823 | 1.356322269 | .843579482 |
| Mood swings | Gastric cancer | Inverse variance weighted (fixed effects) | 50 | 1.024511472 | 0.691083908 | 1.51880798 | .904044646 |
| Mood swings | Gastric cancer | MR Egger | 50 | 0.607455929 | 0.056158135 | 6.570779228 | .683398243 |
| Mood swings | Gastric cancer | Weighted median | 50 | 0.977498149 | 0.550475382 | 1.735777224 | .938079208 |
| Mood swings | Cholecystitis | Inverse variance weighted (fixed effects) | 49 | 1.003934912 | 0.804963745 | 1.252087828 | .972201361 |
| Mood swings | Cholecystitis | MR Egger | 49 | 4.792871387 | 1.14710939 | 20.02565434 | .036888917 |
| Mood swings | Cholecystitis | Weighted median | 49 | 1.000070493 | 0.743267872 | 1.345599655 | .999628543 |
| Mood swings | Crohn's disease | Inverse variance weighted (fixed effects) | 49 | 1.207357194 | 0.865529209 | 1.684185096 | .267168602 |
| Mood swings | Crohn's disease | MR Egger | 49 | 0.253772666 | 0.023571958 | 2.73208392 | .263777011 |

(Continued)

Supplementary Table 4. Causal Effects of Mood Swings on Gastrointestinal Diseases Risk (*Continued*)

| Exposure | Outcome | Method | SNPs(n) | OR | or_lci95 | or_uci95 | P |
|-------------|-----------------------------------|---|---------|-------------|-------------|-------------|-------------|
| Mood swings | Crohn's disease | Weighted median | 49 | 1.384030444 | 0.855120667 | 2.240081833 | .185863958 |
| Mood swings | Acute appendicitis | Inverse variance weighted (multiplicative random effects) | 47 | 1.06080456 | 0.947364126 | 1.187828716 | .306335051 |
| Mood swings | Acute appendicitis | MR Egger | 47 | 1.24243027 | 0.623106055 | 2.477319811 | .54066687 |
| Mood swings | Acute appendicitis | Weighted median | 47 | 1.033845717 | 0.903218393 | 1.183364927 | .629107514 |
| Mood swings | Acute pancreatitis | Inverse variance weighted (fixed effects) | 47 | 1.3681608 | 1.133457518 | 1.651463725 | .001095863 |
| Mood swings | Acute pancreatitis | MR Egger | 47 | 1.288943044 | 0.371833197 | 4.468063057 | .690908318 |
| Mood swings | Acute pancreatitis | Weighted median | 47 | 1.3227648 | 1.003564027 | 1.74349286 | .047116716 |
| Mood swings | Chronic gastritis | Inverse variance weighted (fixed effects) | 47 | 1.181951162 | 1.01289059 | 1.379229468 | .033784437 |
| Mood swings | Chronic gastritis | MR Egger | 47 | 0.643646091 | 0.253043248 | 1.637191637 | .359889614 |
| Mood swings | Chronic gastritis | Weighted median | 47 | 1.21879942 | 0.971005847 | 1.529828097 | .087956681 |
| Mood swings | Diverticular disease of intestine | Inverse variance weighted (multiplicative random effects) | 47 | 1.189722183 | 1.030350384 | 1.373745179 | .017910445 |
| Mood swings | Diverticular disease of intestine | MR Egger | 47 | 0.688058977 | 0.290297512 | 1.630827467 | .40028207 |
| Mood swings | Diverticular disease of intestine | Weighted median | 47 | 1.24413787 | 1.074693232 | 1.44029849 | .003451691 |
| Mood swings | Duodenal ulcer | Inverse variance weighted (fixed effects) | 47 | 1.435095948 | 1.115842944 | 1.845690195 | .004895887 |
| Mood swings | Duodenal ulcer | MR Egger | 47 | 1.446468307 | 0.310714967 | 6.733729589 | .640337757 |
| Mood swings | Duodenal ulcer | Weighted median | 47 | 1.676032272 | 1.167070086 | 2.406954143 | .005163462 |
| Mood swings | Gastric ulcer | Inverse variance weighted (fixed effects) | 47 | 1.231356433 | 1.014658965 | 1.494333286 | .035086628 |
| Mood swings | Gastric ulcer | MR Egger | 47 | 0.50151656 | 0.155684809 | 1.615564559 | .253664183 |
| Mood swings | Gastric ulcer | Weighted median | 47 | 1.318736633 | 1.001794816 | 1.735950595 | .048519925 |
| Mood swings | Gastro-oesophageal reflux disease | Inverse variance weighted (multiplicative random effects) | 47 | 1.29417997 | 1.1445877 | 1.463323251 | 3.87418E-05 |
| Mood swings | Gastro-oesophageal reflux disease | MR Egger | 47 | 1.136924733 | 0.537309584 | 2.405685451 | .738746071 |
| Mood swings | Gastro-oesophageal reflux disease | Weighted median | 47 | 1.207995395 | 1.041563563 | 1.401021431 | .012474329 |
| Mood swings | Gastroduodenal ulcer | Inverse variance weighted (fixed effects) | 47 | 1.302530993 | 1.113140269 | 1.524144831 | .000977064 |
| Mood swings | Gastroduodenal ulcer | MR Egger | 47 | 0.889900732 | 0.344320057 | 2.299962768 | .810823284 |

(Continued)

Supplementary Table 4. Causal Effects of Mood Swings on Gastrointestinal Diseases Risk (*Continued*)

| Exposure | Outcome | Method | SNPs(n) | OR | or_lci95 | or_uci95 | P |
|-------------|----------------------------------|---|---------|-------------|-------------|-------------|------------|
| Mood swings | Gastroduodenal ulcer | Weighted median | 47 | 1.17568386 | 0.931043937 | 1.484605058 | .173911849 |
| Mood swings | Irritable bowel syndrome | Inverse variance weighted (multiplicative random effects) | 47 | 1.375231318 | 1.138609207 | 1.661027475 | .000941411 |
| Mood swings | Irritable bowel syndrome | MR Egger | 47 | 2.260508422 | 0.71923892 | 7.104590959 | .169583749 |
| Mood swings | Irritable bowel syndrome | Weighted median | 47 | 1.296430842 | 1.018156068 | 1.650761588 | .035207975 |
| Mood swings | Cholelithiasis | Inverse variance weighted (multiplicative random effects) | 46 | 1.105122582 | 0.988088558 | 1.236018687 | .080086486 |
| Mood swings | Cholelithiasis | MR Egger | 46 | 1.149675292 | 0.550040696 | 2.403009971 | .71255539 |
| Mood swings | Cholelithiasis | Weighted median | 46 | 1.09247918 | 0.961697524 | 1.241045889 | .173942767 |
| Mood swings | Nonalcoholic fatty liver disease | Inverse variance weighted (fixed effects) | 46 | 1.506685435 | 1.107312199 | 2.050100235 | .009087871 |
| Mood swings | Nonalcoholic fatty liver disease | MR Egger | 46 | 1.272375015 | 0.142857804 | 11.33251478 | .830061008 |
| Mood swings | Nonalcoholic fatty liver disease | Weighted median | 46 | 1.810489127 | 1.159985176 | 2.82578687 | .008965154 |
| Mood swings | Ulcerative colitis | Inverse variance weighted (fixed effects) | 44 | 0.997766606 | 0.808919147 | 1.230701738 | .983336448 |
| Mood swings | Ulcerative colitis | MR Egger | 44 | 0.292832434 | 0.056828745 | 1.508934141 | .149502539 |
| Mood swings | Ulcerative colitis | Weighted median | 44 | 1.093241511 | 0.800248874 | 1.493506633 | .575436148 |
| Mood swings | Esophagus cancer | Inverse variance weighted (fixed effects) | 49 | 0.903048711 | 0.496232378 | 1.643377199 | .73850324 |
| Mood swings | Esophagus cancer | MR Egger | 49 | 0.147922518 | 0.002762501 | 7.920746972 | .351517562 |
| Mood swings | Esophagus cancer | Weighted median | 49 | 0.737776435 | 0.302711669 | 1.798127142 | .503438985 |
| Mood swings | Fibrosis and cirrhosis of liver | Inverse variance weighted (multiplicative random effects) | 48 | 1.264264613 | 0.961197699 | 1.662888927 | .093547272 |
| Mood swings | Fibrosis and cirrhosis of liver | MR Egger | 48 | 0.936125379 | 0.156920156 | 5.584564449 | .942569027 |
| Mood swings | Fibrosis and cirrhosis of liver | Weighted median | 48 | 1.176707184 | 0.822770466 | 1.682899246 | .372729509 |
| Mood swings | Alcoholic liver disease | Inverse variance weighted (multiplicative random effects) | 45 | 1.079429157 | 0.758337441 | 1.536476035 | .671337972 |
| Mood swings | Alcoholic liver disease | MR Egger | 45 | 0.322879151 | 0.032359985 | 3.221600562 | .340825783 |
| Mood swings | Alcoholic liver disease | Weighted median | 45 | 1.023698828 | 0.663417046 | 1.579638776 | .915714378 |
| Mood swings | Chronic pancreatitis | Inverse variance weighted (fixed effects) | 45 | 1.541134436 | 1.194457542 | 1.988430116 | .000878747 |

(Continued)

Supplementary Table 4. Causal Effects of Mood Swings on Gastrointestinal Diseases Risk (*Continued*)

| Exposure | Outcome | Method | SNPs(n) | OR | or_lci95 | or_uci95 | P |
|-------------|---------------------------|---|---------|-------------|-------------|-------------|-------------|
| Mood swings | Chronic pancreatitis | MR Egger | 45 | 0.624931847 | 0.119307245 | 3.273395635 | .580798931 |
| Mood swings | Chronic pancreatitis | Weighted median | 45 | 1.562807859 | 1.091722907 | 2.237168781 | .014708249 |
| Mood swings | Gastrointestinal diseases | Inverse variance weighted (multiplicative random effects) | 44 | 1.213026384 | 1.117995903 | 1.316134526 | 3.4887E-06 |
| Mood swings | Gastrointestinal diseases | MR Egger | 44 | 1.198934312 | 0.706416148 | 2.034839507 | .505106825 |
| Mood swings | Gastrointestinal diseases | Weighted median | 44 | 1.223853473 | 1.109712981 | 1.349733984 | 5.25268E-05 |

Supplementary Table 5. Summary of Pleiotropy

| Exposure | Outcome | Egger_intercept | SE | P |
|-------------|-----------------------------------|-----------------|-------------|------------|
| Mood swings | Functional dyspepsia | 0.011027234 | 0.016229422 | .500044109 |
| Mood swings | Pancreatic cancer | 0.004008184 | 0.033597888 | .9055265 |
| Mood swings | Acute gastritis | -0.006942467 | 0.027043038 | .798492759 |
| Mood swings | Coeliac disease | 0.049571182 | 0.032536567 | .134182276 |
| Mood swings | Colorectal cancer | -0.022825793 | 0.021516907 | .294075646 |
| Mood swings | Gastric cancer | 0.015894319 | 0.036433431 | .664606666 |
| Mood swings | Cholecystitis | -0.046997404 | 0.021669996 | .035192854 |
| Mood swings | Crohn's disease | 0.046884905 | 0.036008175 | .199240147 |
| Mood swings | Acute appendicitis | -0.004788262 | 0.010520828 | .651209625 |
| Mood swings | Acute pancreatitis | 0.001807208 | 0.018953029 | .924458645 |
| Mood swings | Chronic gastritis | 0.018424846 | 0.014240435 | .202322168 |
| Mood swings | Diverticular disease of intestine | 0.01659766 | 0.013160844 | .213757689 |
| Mood swings | Duodenal ulcer | -0.000239222 | 0.023454159 | .991907147 |
| Mood swings | Gastric ulcer | 0.027220319 | 0.017837406 | .134002214 |
| Mood swings | Gastro-oesophageal reflux disease | 0.003926563 | 0.011430501 | .732809976 |
| Mood swings | Gastroduodenal ulcer | 0.011544667 | 0.014478906 | .429438634 |
| Mood swings | Irritable bowel syndrome | -0.015059333 | 0.017460845 | .393005924 |
| Mood swings | Cholelithiasis | -0.001183202 | 0.01112706 | .915799457 |
| Mood swings | Nonalcoholic fatty liver disease | 0.005060606 | 0.03300748 | .87884932 |
| Mood swings | Ulcerative colitis | 0.036424771 | 0.024594783 | .146071332 |
| Mood swings | Esophagus cancer | 0.055131246 | 0.061030944 | .370956093 |
| Mood swings | Fibrosis and cirrhosis of liver | 0.009051175 | 0.027115562 | .740047438 |
| Mood swings | Alcoholic liver disease | 0.036178916 | 0.034765878 | .303856677 |
| Mood swings | Chronic pancreatitis | 0.027065548 | 0.025031732 | .285613012 |
| Mood swings | Gastrointestinal diseases | 0.000351138 | 0.008010722 | .965244872 |

Supplementary Table 6. Summary of Heterogeneity

| Exposure | Outcome | Method | Q | Q_df | Q_pval |
|-------------|-----------------------------------|---------------------------|-------------|------|-------------|
| Mood swings | Functional dyspepsia | MR Egger | 67.01425946 | 49 | 0.044517167 |
| Mood swings | Functional dyspepsia | Inverse variance weighted | 67.64565014 | 50 | 0.048821273 |
| Mood swings | Pancreatic cancer | MR Egger | 39.15026432 | 49 | 0.841862685 |
| Mood swings | Pancreatic cancer | Inverse variance weighted | 39.1644965 | 50 | 0.86552595 |
| Mood swings | Acute gastritis | MR Egger | 33.64001542 | 48 | 0.942278054 |
| Mood swings | Acute gastritis | Inverse variance weighted | 33.70592016 | 49 | 0.952930473 |
| Mood swings | Coeliac disease | MR Egger | 108.3896705 | 48 | 1.45439e-06 |
| Mood swings | Coeliac disease | Inverse variance weighted | 113.631245 | 49 | 4.76918e-07 |
| Mood swings | Colorectal cancer | MR Egger | 77.4544011 | 48 | 0.004499198 |
| Mood swings | Colorectal cancer | Inverse variance weighted | 79.27032199 | 49 | 0.003991869 |
| Mood swings | Gastric cancer | MR Egger | 47.21810796 | 48 | 0.504802479 |
| Mood swings | Gastric cancer | Inverse variance weighted | 47.40842763 | 49 | 0.53782505 |
| Mood swings | Cholecystitis | MR Egger | 38.30536441 | 47 | 0.812996596 |
| Mood swings | Cholecystitis | Inverse variance weighted | 43.00896134 | 48 | 0.677059383 |
| Mood swings | Crohn's disease | MR Egger | 57.08605386 | 47 | 0.148779587 |
| Mood swings | Crohn's disease | Inverse variance weighted | 59.14524198 | 48 | 0.129948283 |
| Mood swings | Acute appendicitis | MR Egger | 72.7153763 | 45 | 0.005523275 |
| Mood swings | Acute appendicitis | Inverse variance weighted | 73.05008715 | 46 | 0.006759791 |
| Mood swings | Acute pancreatitis | MR Egger | 53.6705467 | 45 | 0.176090519 |
| Mood swings | Acute pancreatitis | Inverse variance weighted | 53.68139053 | 46 | 0.203603701 |
| Mood swings | Chronic gastritis | MR Egger | 45.14756809 | 45 | 0.465786702 |
| Mood swings | Chronic gastritis | Inverse variance weighted | 46.82708 | 46 | 0.438335533 |
| Mood swings | Diverticular disease of intestine | MR Egger | 110.1280654 | 45 | 2.21325e-07 |
| Mood swings | Diverticular disease of intestine | Inverse variance weighted | 114.0204142 | 46 | 1.06076e-07 |
| Mood swings | Duodenal ulcer | MR Egger | 46.03545314 | 45 | 0.429151988 |
| Mood swings | Duodenal ulcer | Inverse variance weighted | 46.03555957 | 46 | 0.470792457 |
| Mood swings | Gastric ulcer | MR Egger | 41.30737368 | 45 | 0.629144056 |
| Mood swings | Gastric ulcer | Inverse variance weighted | 43.63612463 | 46 | 0.5717875 |
| Mood swings | Gastro-oesophageal reflux disease | MR Egger | 77.71861108 | 45 | 0.001761405 |
| Mood swings | Gastro-oesophageal reflux disease | Inverse variance weighted | 77.92241241 | 46 | 0.002277032 |
| Mood swings | Gastroduodenal ulcer | MR Egger | 40.35255427 | 45 | 0.668899058 |
| Mood swings | Gastroduodenal ulcer | Inverse variance weighted | 40.98831151 | 46 | 0.6817363 |
| Mood swings | Irritable bowel syndrome | MR Egger | 68.5055095 | 45 | 0.013514189 |
| Mood swings | Irritable bowel syndrome | Inverse variance weighted | 69.63789404 | 46 | 0.013791702 |
| Mood swings | Cholelithiasis | MR Egger | 79.05756908 | 44 | 0.000927048 |
| Mood swings | Cholelithiasis | Inverse variance weighted | 79.07788553 | 45 | 0.001273592 |
| Mood swings | Nonalcoholic fatty liver disease | MR Egger | 52.34701023 | 44 | 0.181642897 |

(Continued)

Supplementary Table 6. Summary of Heterogeneity (Continued)

| Exposure | Outcome | Method | Q | Q_df | Q_pval |
|-----------------|----------------------------------|---------------------------|-------------|-------------|---------------|
| Mood swings | Nonalcoholic fatty liver disease | Inverse variance weighted | 52.37497554 | 45 | 0.209543233 |
| Mood swings | Ulcerative colitis | MR Egger | 53.32598868 | 42 | 0.112995393 |
| Mood swings | Ulcerative colitis | Inverse variance weighted | 56.11080971 | 43 | 0.086672054 |
| Mood swings | Esophagus cancer | MR Egger | 57.3155 | 47 | 0.144017885 |
| Mood swings | Esophagus cancer | Inverse variance weighted | 58.31060674 | 48 | 0.146360474 |
| Mood swings | Fibrosis and cirrhosis of liver | MR Egger | 66.66147175 | 46 | 0.024786323 |
| Mood swings | Fibrosis and cirrhosis of liver | Inverse variance weighted | 66.82294097 | 47 | 0.030136813 |
| Mood swings | Alcoholic liver disease | MR Egger | 64.97898038 | 43 | 0.016793334 |
| Mood swings | Alcoholic liver disease | Inverse variance weighted | 66.61545445 | 44 | 0.015458252 |
| Mood swings | Chronic pancreatitis | MR Egger | 42.59122959 | 43 | 0.488908943 |
| Mood swings | Chronic pancreatitis | Inverse variance weighted | 43.76033015 | 44 | 0.481822623 |
| Mood swings | Gastrointestinal diseases | MR Egger | 82.10111712 | 42 | 0.000211706 |
| Mood swings | Gastrointestinal diseases | Inverse variance weighted | 82.104873 | 43 | 0.000303922 |

Supplementary Table 7. The Summary Information for SNPs of Gastrointestinal Diseases

| Exposure | SNP | chr | pos | effect allele | other allele | eaf | β | SE | P | F |
|-------------------------|-------------|-----|-----------|---------------|--------------|-----------|------------|------------|-------------|-------------|
| Acute appendicitis | rs3738182 | 1 | 220884320 | A | G | 0.24014 | -0.0948389 | 0.0098852 | 8.47032e-22 | 92.04540124 |
| Acute appendicitis | rs7575706 | 2 | 18675186 | A | G | 0.796476 | -0.0559412 | 0.0102314 | 4.56205e-08 | 29.89464694 |
| Acute appendicitis | rs6707044 | 2 | 19290998 | G | A | 0.217912 | 0.0796341 | 0.00992549 | 1.03039e-15 | 64.37159053 |
| Acute appendicitis | rs976568 | 4 | 110629565 | T | G | 0.598844 | -0.0599877 | 0.00847937 | 1.49934e-12 | 50.04921259 |
| Acute appendicitis | rs13121924 | 4 | 110799663 | G | A | 0.530436 | -0.152285 | 0.00829329 | 2.62301e-75 | 337.1790255 |
| Acute appendicitis | rs3850473 | 4 | 111887334 | T | A | 0.658899 | 0.0678463 | 0.0088196 | 1.44079e-14 | 59.17721999 |
| Acute appendicitis | rs9273368 | 6 | 32658698 | A | G | 0.277051 | 0.0559688 | 0.00920476 | 1.19867e-09 | 36.97149839 |
| Acute appendicitis | rs4734039 | 8 | 101728366 | T | C | 0.300434 | -0.0499969 | 0.00912698 | 4.30328e-08 | 30.007648 |
| Acute appendicitis | rs7824074 | 8 | 127576577 | G | T | 0.701058 | -0.052896 | 0.00906707 | 5.41614e-09 | 34.03390064 |
| Acute appendicitis | rs10748784 | 10 | 99560363 | A | G | 0.542533 | 0.0490883 | 0.0083638 | 4.38077e-09 | 34.44678591 |
| Acute appendicitis | rs10849448 | 12 | 6384185 | G | A | 0.756268 | 0.0829448 | 0.00987797 | 4.58247e-17 | 70.50873497 |
| Acute appendicitis | rs12312786 | 12 | 19653137 | A | C | 0.60323 | 0.0475281 | 0.00852101 | 2.43635e-08 | 31.11134281 |
| Acute appendicitis | rs770388 | 13 | 50570629 | A | G | 0.429312 | -0.051964 | 0.0084371 | 7.32116e-10 | 37.93313661 |
| Acute appendicitis | rs113159970 | 15 | 95671001 | A | G | 0.254785 | -0.0611629 | 0.00963316 | 2.16421e-10 | 40.31239406 |
| Acute appendicitis | rs8054231 | 16 | 86134198 | A | G | 0.192565 | -0.0742236 | 0.0107051 | 4.10582e-12 | 48.07314912 |
| Acute appendicitis | rs142069498 | 20 | 51831701 | A | G | 0.057687 | -0.102949 | 0.0182814 | 1.78797e-08 | 31.7121263 |
| Acute pancreatitis | rs11887534 | 2 | 43839108 | C | G | 0.079176 | 0.258431 | 0.0300779 | 8.54476e-18 | 73.82342564 |
| Acute pancreatitis | rs147839099 | 5 | 147654455 | G | A | 0.0486109 | 0.251597 | 0.0385739 | 6.91512e-11 | 42.54257921 |
| Acute pancreatitis | rs559363229 | 5 | 147805265 | T | C | 0.0164175 | 0.65655 | 0.056167 | 1.44644e-31 | 136.638522 |
| Acute pancreatitis | rs191041365 | 5 | 147887437 | T | C | 0.0226971 | 0.426978 | 0.05196 | 2.07922e-16 | 67.52626246 |
| Acute pancreatitis | rs150176211 | 7 | 142780235 | A | G | 0.0246216 | -0.492909 | 0.0657188 | 6.36796e-14 | 56.25410849 |
| Acute pancreatitis | rs12532408 | 7 | 142916804 | A | G | 0.0592276 | 0.221906 | 0.0348656 | 1.95785e-10 | 40.50828002 |
| Acute pancreatitis | rs4888362 | 16 | 75234347 | C | T | 0.892334 | 0.183679 | 0.0294533 | 4.48116e-10 | 38.89117735 |
| Alcoholic liver disease | rs28636836 | 4 | 87310713 | T | C | 0.216269 | -0.222591 | 0.0325205 | 7.66655e-12 | 46.84904827 |
| Alcoholic liver disease | rs142548379 | 11 | 90960263 | G | C | 0.0454412 | 0.342377 | 0.0553852 | 6.33972e-10 | 38.21393036 |
| Alcoholic liver disease | rs188247550 | 19 | 19285807 | T | C | 0.0506347 | 0.393469 | 0.0526723 | 8.01124e-14 | 55.80286253 |
| Alcoholic liver disease | rs3747207 | 22 | 43928975 | A | G | 0.22569 | 0.356707 | 0.0286911 | 1.7374e-35 | 154.5713022 |
| Cholecystitis | rs11887534 | 2 | 43839108 | C | G | 0.0791135 | 0.317358 | 0.0357362 | 6.6512e-19 | 78.86461019 |
| Cholecystitis | rs4261716 | 2 | 233684471 | T | G | 0.480233 | 0.132395 | 0.020951 | 2.62791e-10 | 39.93315779 |
| Cholelithiasis | rs35176086 | 1 | 25512737 | T | A | 0.44867 | 0.0425767 | 0.00774727 | 3.89144e-08 | 30.20275859 |
| Cholelithiasis | rs4660585 | 1 | 41927330 | A | G | 0.702272 | 0.0569994 | 0.00850109 | 2.01465e-11 | 44.95638069 |
| Cholelithiasis | rs1127313 | 1 | 154583949 | A | G | 0.462039 | 0.0528545 | 0.00771818 | 7.48686e-12 | 46.89581977 |
| Cholelithiasis | rs3790844 | 1 | 200038304 | G | A | 0.368021 | 0.0519841 | 0.00801039 | 8.60597e-11 | 42.11470247 |
| Cholelithiasis | rs1260326 | 2 | 27508073 | C | T | 0.6503 | 0.0670143 | 0.00810675 | 1.37975e-16 | 68.33471863 |
| Cholelithiasis | rs115383258 | 2 | 43294374 | G | A | 0.0281622 | 0.481635 | 0.0212013 | 3.0269e-114 | 516.0729495 |
| Cholelithiasis | rs17406264 | 2 | 43361690 | T | C | 0.0234263 | 0.306577 | 0.0236325 | 1.74864e-38 | 168.29058 |
| Cholelithiasis | rs7596134 | 2 | 43825694 | A | C | 0.292582 | 0.279617 | 0.00822479 | 1e-200 | 1155.786207 |
| Cholelithiasis | rs116649224 | 2 | 44226778 | A | G | 0.0199462 | 0.423283 | 0.0252224 | 3.3037e-63 | 281.6364331 |
| Cholelithiasis | rs12466939 | 2 | 45260280 | A | C | 0.49715 | 0.0548306 | 0.00769685 | 1.05003e-12 | 50.74811914 |
| Cholelithiasis | rs114600798 | 2 | 45653845 | G | A | 0.0198978 | 0.21542 | 0.0261179 | 1.61065e-16 | 68.0292266 |
| Cholelithiasis | rs138809297 | 2 | 45795447 | C | T | 0.0616313 | 0.119327 | 0.01569 | 2.84381e-14 | 57.84043589 |

(Continued)

Supplementary Table 7. The Summary Information for SNPs of Gastrointestinal Diseases (Continued)

| Exposure | SNP | chr | pos | effect allele | other allele | eaf | β | SE | P | F |
|----------------|-------------|-----|-----------|---------------|--------------|-----------|------------|------------|-------------|-------------|
| Cholelithiasis | rs4673546 | 2 | 210700968 | T | C | 0.265788 | -0.0511618 | 0.00877306 | 5.48668e-09 | 34.0086531 |
| Cholelithiasis | rs3731859 | 2 | 218259499 | A | G | 0.669906 | 0.0570945 | 0.00819058 | 3.1521e-12 | 48.59138018 |
| Cholelithiasis | rs887829 | 2 | 233759924 | T | C | 0.391913 | 0.0886896 | 0.00782797 | 9.33899e-30 | 128.3651366 |
| Cholelithiasis | rs9845092 | 3 | 56859097 | G | A | 0.452184 | -0.0459243 | 0.00774233 | 3.00034e-09 | 35.18371824 |
| Cholelithiasis | rs4681503 | 3 | 149379523 | A | G | 0.43625 | 0.0611398 | 0.00776989 | 3.58014e-15 | 61.91819486 |
| Cholelithiasis | rs6794817 | 3 | 149465095 | T | C | 0.19327 | 0.118135 | 0.00960316 | 8.86952e-35 | 151.3313275 |
| Cholelithiasis | rs4681515 | 3 | 149494289 | G | A | 0.495776 | -0.125737 | 0.00769296 | 4.76431e-60 | 267.1401957 |
| Cholelithiasis | rs549211656 | 3 | 149713884 | C | G | 0.0445416 | -0.112433 | 0.0194969 | 8.08295e-09 | 33.25496304 |
| Cholelithiasis | rs3129317 | 4 | 3285928 | G | A | 0.260618 | 0.0544365 | 0.0087352 | 4.60935e-10 | 38.83601703 |
| Cholelithiasis | rs2013231 | 4 | 48087441 | T | A | 0.197167 | -0.0573833 | 0.00976444 | 4.18369e-09 | 34.53634371 |
| Cholelithiasis | rs6532417 | 4 | 76484566 | G | T | 0.715308 | 0.057557 | 0.00860194 | 2.21411e-11 | 44.77168927 |
| Cholelithiasis | rs13126112 | 4 | 94918869 | T | C | 0.158987 | 0.059304 | 0.0104591 | 1.42712e-08 | 32.14987906 |
| Cholelithiasis | rs2290846 | 4 | 150277928 | A | G | 0.221765 | 0.109256 | 0.00911195 | 3.99117e-33 | 143.7698888 |
| Cholelithiasis | rs17671591 | 5 | 75319196 | T | C | 0.357067 | 0.0455553 | 0.00801352 | 1.3096e-08 | 32.31700993 |
| Cholelithiasis | rs72763208 | 5 | 76869711 | A | C | 0.0637393 | -0.0994318 | 0.0162143 | 8.65845e-10 | 37.60574481 |
| Cholelithiasis | rs9396788 | 6 | 17676239 | G | A | 0.367057 | -0.0637535 | 0.0080155 | 1.80926e-15 | 63.26256947 |
| Cholelithiasis | rs3132722 | 6 | 29867174 | C | T | 0.663378 | 0.04999 | 0.00818514 | 1.0126e-09 | 37.30044812 |
| Cholelithiasis | rs75894113 | 6 | 104983309 | A | G | 0.0756024 | -0.0866473 | 0.0149514 | 6.82087e-09 | 33.58507695 |
| Cholelithiasis | rs113638914 | 6 | 157981676 | C | T | 0.206817 | 0.0576114 | 0.00943613 | 1.02539e-09 | 37.27597632 |
| Cholelithiasis | rs79949326 | 7 | 6421679 | T | C | 0.226409 | 0.0547111 | 0.00913173 | 2.08142e-09 | 35.89589358 |
| Cholelithiasis | rs147491739 | 7 | 86116958 | C | T | 0.0527181 | -0.112984 | 0.0177238 | 1.8335e-10 | 40.63686637 |
| Cholelithiasis | rs45561635 | 7 | 87404651 | C | A | 0.0425193 | -0.130772 | 0.0196933 | 3.12752e-11 | 44.09532399 |
| Cholelithiasis | rs66869391 | 7 | 87489753 | A | G | 0.135526 | -0.191504 | 0.0116364 | 7.43533e-61 | 270.8434991 |
| Cholelithiasis | rs75741381 | 7 | 101166177 | G | C | 0.152301 | -0.0665724 | 0.0108427 | 8.26133e-10 | 37.69758634 |
| Cholelithiasis | rs17154498 | 7 | 107827680 | A | C | 0.284032 | -0.0900145 | 0.00862959 | 1.79143e-25 | 108.8039399 |
| Cholelithiasis | rs62490880 | 8 | 11556384 | T | C | 0.15274 | -0.0756265 | 0.0109235 | 4.41367e-12 | 47.9318705 |
| Cholelithiasis | rs6471717 | 8 | 58464798 | A | G | 0.615588 | -0.114862 | 0.0078729 | 3.68893e-48 | 212.6175354 |
| Cholelithiasis | rs16894137 | 8 | 95934063 | C | T | 0.130565 | 0.0878145 | 0.011285 | 7.16638e-15 | 60.55211805 |
| Cholelithiasis | rs2468191 | 8 | 119222029 | A | G | 0.582991 | 0.0431407 | 0.00783026 | 3.59898e-08 | 30.35442494 |
| Cholelithiasis | rs28601761 | 8 | 125487789 | G | C | 0.410975 | 0.0663183 | 0.00779217 | 1.72624e-17 | 72.43524481 |
| Cholelithiasis | rs686030 | 9 | 15304784 | A | C | 0.881683 | 0.127897 | 0.0122117 | 1.14551e-25 | 109.69036 |
| Cholelithiasis | rs115478735 | 9 | 133274295 | T | A | 0.198909 | 0.0962828 | 0.00951822 | 4.70977e-24 | 102.3259878 |
| Cholelithiasis | rs11012726 | 10 | 21508343 | C | T | 0.316303 | 0.0479562 | 0.00827716 | 6.88129e-09 | 33.56810499 |
| Cholelithiasis | rs11239549 | 10 | 45523383 | G | A | 0.283438 | 0.0860151 | 0.00845051 | 2.46888e-24 | 103.605678 |
| Cholelithiasis | rs7912893 | 10 | 63402240 | A | T | 0.4727 | 0.049251 | 0.00770933 | 1.67533e-10 | 40.81284159 |
| Cholelithiasis | rs12220311 | 10 | 77921749 | T | C | 0.223217 | 0.0505945 | 0.00918494 | 3.62068e-08 | 30.34268227 |
| Cholelithiasis | rs7915944 | 10 | 100182496 | C | T | 0.126119 | 0.0630824 | 0.0115185 | 4.33541e-08 | 29.99332148 |
| Cholelithiasis | rs58514600 | 11 | 1355653 | T | C | 0.149381 | 0.0642919 | 0.0106923 | 1.82213e-09 | 36.15515686 |
| Cholelithiasis | rs9633835 | 11 | 13324046 | A | G | 0.397664 | -0.0536376 | 0.00790865 | 1.18413e-11 | 45.99747184 |
| Cholelithiasis | rs174549 | 11 | 61803910 | A | G | 0.388125 | 0.0737272 | 0.00785807 | 6.45208e-21 | 88.02857972 |
| Cholelithiasis | rs3867287 | 11 | 69960696 | T | C | 0.0982944 | 0.084642 | 0.0128259 | 4.13143e-11 | 43.55079973 |
| Cholelithiasis | rs75497660 | 12 | 14984781 | T | A | 0.156052 | 0.0590686 | 0.0104756 | 1.71356e-08 | 31.79475929 |
| Cholelithiasis | rs7979478 | 12 | 120982460 | G | A | 0.581426 | 0.0632586 | 0.00786616 | 8.84708e-16 | 64.67159924 |

| Exposure | SNP | chr | pos | effect allele | other allele | eaf | β | SE | P | F |
|----------------------|-------------|-----|-----------|---------------|--------------|-----------|------------|------------|-------------|-------------|
| Cholelithiasis | rs7325496 | 13 | 102847067 | A | C | 0.78466 | -0.0813693 | 0.00926183 | 1.5574e-18 | 77.18404752 |
| Cholelithiasis | rs16961277 | 13 | 103064473 | G | A | 0.139203 | -0.112636 | 0.0113117 | 2.3383e-23 | 99.15136127 |
| Cholelithiasis | rs28929474 | 14 | 94378610 | T | C | 0.0197333 | 0.318602 | 0.0257318 | 3.287e-35 | 153.3051206 |
| Cholelithiasis | rs11644920 | 16 | 11551157 | T | A | 0.324122 | 0.0507302 | 0.00825316 | 7.90788e-10 | 37.78266779 |
| Cholelithiasis | rs7206790 | 16 | 53763996 | G | C | 0.483413 | 0.0519229 | 0.00770869 | 1.6323e-11 | 45.36874011 |
| Cholelithiasis | rs9909593 | 17 | 39813896 | G | A | 0.528206 | -0.0459436 | 0.00771665 | 2.61933e-09 | 35.4480573 |
| Cholelithiasis | rs12449576 | 17 | 79930325 | A | T | 0.621289 | -0.0452691 | 0.00796797 | 1.33607e-08 | 32.27812805 |
| Cholelithiasis | rs12326100 | 18 | 22076747 | A | G | 0.150905 | 0.059595 | 0.0106494 | 2.1926e-08 | 31.3162224 |
| Cholelithiasis | rs8097764 | 18 | 57650664 | A | G | 0.116213 | -0.0816442 | 0.0121353 | 1.72266e-11 | 45.26365726 |
| Cholelithiasis | rs708686 | 19 | 5840608 | T | C | 0.334175 | 0.0955934 | 0.00811191 | 4.70219e-32 | 138.8703627 |
| Cholelithiasis | rs2733738 | 19 | 35554601 | A | G | 0.597709 | -0.0480683 | 0.00784302 | 8.85462e-10 | 37.56218791 |
| Cholelithiasis | rs8108864 | 19 | 45798413 | A | G | 0.297763 | 0.0689141 | 0.00839309 | 2.19685e-16 | 67.41746483 |
| Cholelithiasis | rs67165745 | 19 | 47420724 | A | C | 0.0365428 | -0.145218 | 0.0215056 | 1.45278e-11 | 45.59715803 |
| Cholelithiasis | rs76531193 | 19 | 47857434 | A | T | 0.150579 | -0.146963 | 0.0110753 | 3.48257e-40 | 176.0779688 |
| Cholelithiasis | rs686548 | 20 | 12992873 | T | A | 0.657911 | -0.0526082 | 0.00806999 | 7.07783e-11 | 42.49725629 |
| Cholelithiasis | rs1800961 | 20 | 44413724 | T | C | 0.0454273 | 0.317622 | 0.0173166 | 3.82032e-75 | 336.4309189 |
| Cholelithiasis | rs2072858 | 22 | 40312675 | C | T | 0.393762 | 0.0446305 | 0.00786506 | 1.39072e-08 | 32.20026342 |
| Cholelithiasis | rs738408 | 22 | 43928850 | T | C | 0.226937 | -0.0565375 | 0.00927174 | 1.07515e-09 | 37.18353817 |
| Chronic gastritis | rs2476601 | 1 | 113834946 | G | A | 0.852025 | -0.120346 | 0.0197109 | 1.0244e-09 | 37.27781174 |
| Chronic gastritis | rs11751024 | 6 | 32618459 | A | C | 0.398566 | -0.0905838 | 0.0146894 | 6.97654e-10 | 38.02707811 |
| Chronic pancreatitis | rs115343810 | 5 | 147138130 | G | A | 0.0195196 | 0.432486 | 0.0731619 | 3.39305e-09 | 34.94412385 |
| Chronic pancreatitis | rs147839099 | 5 | 147654455 | G | A | 0.0485444 | 0.287685 | 0.0499717 | 8.56466e-09 | 33.14257046 |
| Chronic pancreatitis | rs559363229 | 5 | 147805265 | T | C | 0.0163691 | 0.823767 | 0.0693697 | 1.59588e-32 | 141.0162455 |
| Chronic pancreatitis | rs191041365 | 5 | 147887437 | T | C | 0.022674 | 0.570242 | 0.0643838 | 8.22621e-19 | 78.44498624 |
| Chronic pancreatitis | rs7744721 | 6 | 76547558 | A | T | 0.493956 | 0.128673 | 0.0231646 | 2.78061e-08 | 30.85497811 |
| Chronic pancreatitis | rs150176211 | 7 | 142780235 | A | G | 0.0246802 | -0.605613 | 0.0886272 | 8.30042e-12 | 46.69348838 |
| Coeliac disease | rs6740034 | 2 | 181172173 | G | A | 0.509444 | 0.173467 | 0.0223741 | 8.97429e-15 | 60.10942669 |
| Coeliac disease | rs34005848 | 3 | 46222254 | T | C | 0.107083 | 0.269027 | 0.03377 | 1.63305e-15 | 63.46431782 |
| Coeliac disease | rs6808893 | 3 | 188415651 | T | C | 0.560215 | 0.224282 | 0.0227241 | 5.62859e-23 | 97.41267217 |
| Coeliac disease | rs6822844 | 4 | 122588266 | T | G | 0.113911 | -0.253943 | 0.0373711 | 1.08168e-11 | 46.17434348 |
| Coeliac disease | rs116673776 | 6 | 22383086 | C | T | 0.013597 | 0.483647 | 0.0824565 | 4.47816e-09 | 34.40386251 |
| Coeliac disease | rs13191296 | 6 | 25684378 | T | C | 0.0455861 | 1.17505 | 0.0366847 | 1e-200 | 1025.989107 |
| Coeliac disease | rs142229030 | 6 | 29320314 | G | A | 0.0387136 | 0.683178 | 0.0461079 | 1.13868e-49 | 219.5417188 |
| Coeliac disease | rs189005954 | 6 | 30539514 | A | G | 0.0294525 | -0.688696 | 0.0798333 | 6.31684e-18 | 74.41953598 |
| Coeliac disease | rs3130290 | 6 | 32207180 | C | T | 0.512175 | 0.676041 | 0.0211719 | 1e-200 | 1019.591962 |
| Coeliac disease | rs6899657 | 6 | 33082446 | A | G | 0.245976 | 0.726413 | 0.0217767 | 1e-200 | 1112.712788 |
| Coeliac disease | rs72891915 | 6 | 33508423 | A | G | 0.0397786 | 1.29981 | 0.0370964 | 1e-200 | 1227.711195 |
| Coeliac disease | rs9469549 | 6 | 33671728 | T | G | 0.0555971 | -0.430024 | 0.0545095 | 3.04719e-15 | 62.23590259 |
| Coeliac disease | rs73743401 | 6 | 33749168 | T | G | 0.0881939 | 0.732927 | 0.0314951 | 8.6896e-120 | 541.5461321 |
| Coeliac disease | rs1906953 | 6 | 34068669 | T | C | 0.127815 | 0.449725 | 0.0296235 | 4.70002e-52 | 230.473673 |
| Coeliac disease | rs181416918 | 6 | 35931587 | T | C | 0.0351565 | 0.542158 | 0.0510108 | 2.20141e-26 | 112.9607252 |
| Coeliac disease | rs67707912 | 6 | 127896629 | C | T | 0.130024 | -0.199779 | 0.0347205 | 8.71907e-09 | 33.10760221 |
| Coeliac disease | rs6933404 | 6 | 137638098 | C | T | 0.189224 | 0.183272 | 0.0270636 | 1.27087e-11 | 45.85863319 |

(Continued)

Supplementary Table 7. The Summary Information for SNPs of Gastrointestinal Diseases (Continued)

| Exposure | SNP | chr | pos | effect allele | other allele | eaf | β | SE | P | F |
|-----------------------------------|-------------|-----|-----------|---------------|--------------|-----------|------------|------------|-------------|--------------|
| Coeliac disease | rs55781052 | 11 | 128581737 | T | C | 0.25974 | 0.144067 | 0.0249489 | 7.71934e-09 | 33.34465442 |
| Coeliac disease | rs3184504 | 12 | 111446804 | C | T | 0.592264 | -0.146296 | 0.0226262 | 1.0077e-10 | 41.80629304 |
| Colorectal cancer | rs2853672 | 5 | 1292868 | A | C | 0.529652 | 0.132033 | 0.0177051 | 8.82877e-14 | 55.61196163 |
| Colorectal cancer | rs11986063 | 8 | 116628076 | T | C | 0.124233 | 0.15268 | 0.0257431 | 3.01266e-09 | 35.17568918 |
| Colorectal cancer | rs10956368 | 8 | 127411405 | C | T | 0.578774 | -0.146741 | 0.0177683 | 1.47401e-16 | 68.20421146 |
| Colorectal cancer | rs2225014 | 10 | 8668752 | T | A | 0.298813 | -0.107513 | 0.019444 | 3.21425e-08 | 30.57389263 |
| Colorectal cancer | rs35137159 | 10 | 99584492 | T | C | 0.160813 | 0.168212 | 0.0230332 | 2.8132e-13 | 53.33415168 |
| Colorectal cancer | rs7933961 | 11 | 111309906 | A | T | 0.231576 | 0.136046 | 0.0204882 | 3.13184e-11 | 44.09242092 |
| Colorectal cancer | rs16969681 | 15 | 32700910 | T | C | 0.0827208 | 0.231703 | 0.0302006 | 1.69161e-14 | 58.86161467 |
| Colorectal cancer | rs4939567 | 18 | 48925503 | A | G | 0.505954 | -0.161297 | 0.0175926 | 4.79844e-20 | 84.06060729 |
| Colorectal cancer | rs79341273 | 19 | 18447707 | A | G | 0.0108056 | -0.545182 | 0.0988457 | 3.47816e-08 | 30.4205775 |
| Colorectal cancer | rs60507951 | 19 | 33053281 | A | G | 0.134689 | -0.158236 | 0.026773 | 3.41547e-09 | 34.93144216 |
| Colorectal cancer | rs71338563 | 20 | 6425097 | T | C | 0.305535 | 0.116934 | 0.0188705 | 5.76766e-10 | 38.39854752 |
| Colorectal cancer | rs2427294 | 20 | 62352201 | A | G | 0.202397 | -0.140375 | 0.0225487 | 4.80286e-10 | 38.75578352 |
| Crohn's disease | rs10889669 | 1 | 67210045 | G | T | 0.244659 | 0.234788 | 0.0349051 | 1.7382e-11 | 45.24535704 |
| Crohn's disease | rs10473190 | 5 | 40412505 | A | C | 0.567765 | 0.236608 | 0.0318849 | 1.1652e-13 | 55.06665936 |
| Crohn's disease | rs3130980 | 6 | 311114627 | T | C | 0.330545 | 0.19529 | 0.0324682 | 1.80098e-09 | 36.17791931 |
| Crohn's disease | rs34434863 | 6 | 32591896 | G | T | 0.336305 | -0.256963 | 0.0339687 | 3.88776e-14 | 57.224675 |
| Crohn's disease | rs10807943 | 7 | 5301033 | C | T | 0.936678 | -0.432494 | 0.0569789 | 3.1886e-14 | 57.61453382 |
| Crohn's disease | rs181316459 | 7 | 5433979 | C | G | 0.0478222 | 0.658972 | 0.0608607 | 2.54859e-27 | 117.2357421 |
| Crohn's disease | rs13300483 | 9 | 114881082 | T | C | 0.327434 | 0.18343 | 0.0327124 | 2.05428e-08 | 31.44241649 |
| Crohn's disease | rs7856092 | 9 | 136493166 | G | A | 0.768037 | 0.227683 | 0.0387581 | 4.24238e-09 | 34.50930814 |
| Crohn's disease | rs76176364 | 16 | 50485831 | G | A | 0.0196732 | 0.64404 | 0.0918429 | 2.34261e-12 | 49.17388326 |
| Diverticular disease of intestine | rs284255 | 1 | 10726749 | A | G | 0.131247 | 0.0924004 | 0.0124225 | 1.02094e-13 | 55.32605342 |
| Diverticular disease of intestine | rs2473325 | 1 | 22052595 | A | G | 0.634514 | -0.049899 | 0.00878113 | 1.32721e-08 | 32.29110234 |
| Diverticular disease of intestine | rs4420086 | 1 | 221029593 | G | T | 0.436872 | -0.0518613 | 0.00856754 | 1.41968e-09 | 36.64160735 |
| Diverticular disease of intestine | rs10910384 | 1 | 234217307 | C | A | 0.221551 | 0.100199 | 0.0100749 | 2.64058e-23 | 98.91115794 |
| Diverticular disease of intestine | rs848525 | 2 | 36518102 | G | A | 0.403636 | -0.0472431 | 0.00866098 | 4.90535e-08 | 29.75381809 |
| Diverticular disease of intestine | rs11899888 | 2 | 55875609 | G | A | 0.125498 | 0.0979911 | 0.0126397 | 8.99912e-15 | 60.1034959 |
| Diverticular disease of intestine | rs4662339 | 2 | 143561263 | C | T | 0.807403 | -0.18138 | 0.0104509 | 1.79267e-67 | 301.21114042 |
| Diverticular disease of intestine | rs1427669 | 2 | 217930633 | G | T | 0.297543 | -0.0559493 | 0.0093642 | 2.30356e-09 | 35.69833437 |
| Diverticular disease of intestine | rs7609897 | 3 | 15461174 | T | G | 0.24867 | -0.0874322 | 0.0100536 | 3.41979e-18 | 75.63095924 |
| Diverticular disease of intestine | rs6796333 | 3 | 52325662 | C | T | 0.105917 | -0.0924184 | 0.0139247 | 3.20037e-11 | 44.04992734 |

| Exposure | SNP | chr | pos | effect allele | other allele | eaf | β | SE | P | F |
|-----------------------------------|-------------|-----|-----------|---------------|--------------|-----------|------------|------------|-------------|-------------|
| Diverticular disease of intestine | rs9842218 | 3 | 55906155 | C | T | 0.330014 | 0.0509731 | 0.00901207 | 1.54864e-08 | 31.99138044 |
| Diverticular disease of intestine | rs7617433 | 3 | 78834329 | A | G | 0.275185 | 0.053335 | 0.00947898 | 1.83734e-08 | 31.6593056 |
| Diverticular disease of intestine | rs4383453 | 3 | 123349512 | A | G | 0.252242 | -0.0584966 | 0.00986825 | 3.071e-09 | 35.13831745 |
| Diverticular disease of intestine | rs77234000 | 3 | 150915691 | A | T | 0.0591778 | 0.0995069 | 0.0177254 | 1.97938e-08 | 31.51478178 |
| Diverticular disease of intestine | rs13327359 | 3 | 151405364 | C | A | 0.145957 | -0.071092 | 0.0121501 | 4.88214e-09 | 34.23590083 |
| Diverticular disease of intestine | rs13111751 | 4 | 119129607 | G | C | 0.31996 | -0.0506569 | 0.00915037 | 3.09357e-08 | 30.64784254 |
| Diverticular disease of intestine | rs75686861 | 4 | 144700176 | A | G | 0.0899344 | -0.0856647 | 0.0151271 | 1.48754e-08 | 32.06951861 |
| Diverticular disease of intestine | rs13187416 | 5 | 37683762 | T | C | 0.551125 | -0.0562251 | 0.00853868 | 4.55617e-11 | 43.35897401 |
| Diverticular disease of intestine | rs3733892 | 5 | 79236265 | C | A | 0.395243 | -0.0499292 | 0.00870166 | 9.58606e-09 | 32.92342399 |
| Diverticular disease of intestine | rs75746146 | 6 | 31723099 | G | C | 0.289835 | 0.0577441 | 0.00931879 | 5.77245e-10 | 38.39690185 |
| Diverticular disease of intestine | rs12216014 | 6 | 80612646 | A | G | 0.369254 | -0.0531247 | 0.00881919 | 1.70416e-09 | 36.28570646 |
| Diverticular disease of intestine | rs9320747 | 6 | 97862415 | G | T | 0.373065 | -0.0511469 | 0.00878867 | 5.89753e-09 | 33.86821572 |
| Diverticular disease of intestine | rs11766945 | 7 | 1848418 | A | G | 0.267224 | -0.0542085 | 0.00965889 | 1.99664e-08 | 31.49780862 |
| Diverticular disease of intestine | rs12702317 | 7 | 47208699 | T | G | 0.369202 | -0.0520697 | 0.00883263 | 3.74326e-09 | 34.7528219 |
| Diverticular disease of intestine | rs55675441 | 7 | 74026655 | C | T | 0.0818384 | 0.117559 | 0.0151976 | 1.0311e-14 | 59.83588886 |
| Diverticular disease of intestine | rs1091814 | 7 | 74075333 | A | C | 0.706566 | 0.0592351 | 0.0093765 | 2.65993e-10 | 39.90954128 |
| Diverticular disease of intestine | rs12538955 | 7 | 102820557 | A | T | 0.150406 | 0.076732 | 0.0117406 | 6.33578e-11 | 42.71421726 |
| Diverticular disease of intestine | rs17058204 | 8 | 27909549 | A | G | 0.172925 | -0.0618024 | 0.0113356 | 4.97943e-08 | 29.72498582 |
| Diverticular disease of intestine | rs11785549 | 8 | 119423465 | C | T | 0.1717 | -0.0686549 | 0.0113777 | 1.59779e-09 | 36.41112697 |
| Diverticular disease of intestine | rs7027599 | 9 | 20782101 | C | T | 0.651132 | 0.0522711 | 0.00892626 | 4.74482e-09 | 34.29132085 |
| Diverticular disease of intestine | rs12005101 | 9 | 124828354 | A | G | 0.81507 | -0.0655973 | 0.0108634 | 1.55675e-09 | 36.46199157 |
| Diverticular disease of intestine | rs143378550 | 9 | 130307462 | A | C | 0.0442174 | 0.16091 | 0.0199185 | 6.56296e-16 | 65.26086258 |
| Diverticular disease of intestine | rs1888693 | 10 | 18151515 | A | G | 0.385816 | -0.056398 | 0.00874874 | 1.14525e-10 | 41.55625343 |

(Continued)

Supplementary Table 7. The Summary Information for SNPs of Gastrointestinal Diseases (Continued)

| Exposure | SNP | chr | pos | effect allele | other allele | eaf | β | SE | P | F |
|-----------------------------------|-------------|-----|-----------|---------------|--------------|-----------|------------|------------|-------------|-------------|
| Diverticular disease of intestine | rs7905216 | 10 | 25425268 | G | C | 0.102872 | -0.0976971 | 0.0142915 | 8.14329e-12 | 46.7312844 |
| Diverticular disease of intestine | rs7086249 | 10 | 25522506 | C | T | 0.440114 | -0.080518 | 0.00854797 | 4.53002e-21 | 88.72785429 |
| Diverticular disease of intestine | rs2026558 | 10 | 51523175 | A | G | 0.657678 | 0.0558826 | 0.00895678 | 4.39977e-10 | 38.92686185 |
| Diverticular disease of intestine | rs2153914 | 10 | 95871294 | C | T | 0.701103 | 0.0537124 | 0.00928944 | 7.37751e-09 | 33.43259199 |
| Diverticular disease of intestine | rs6581506 | 12 | 63763073 | C | T | 0.660152 | 0.0513206 | 0.00904786 | 1.41036e-08 | 32.17301091 |
| Diverticular disease of intestine | rs4765482 | 12 | 124242668 | A | G | 0.513615 | 0.0497471 | 0.00853413 | 5.56968e-09 | 33.97950352 |
| Diverticular disease of intestine | rs73234681 | 13 | 79492033 | C | G | 0.0333227 | -0.147659 | 0.0244565 | 1.56416e-09 | 36.45282883 |
| Diverticular disease of intestine | rs9514638 | 13 | 107249968 | C | G | 0.226623 | -0.0716681 | 0.010229 | 2.44568e-12 | 49.08914012 |
| Diverticular disease of intestine | rs11619840 | 13 | 107566610 | A | C | 0.204769 | -0.134613 | 0.0107277 | 4.06537e-36 | 157.4565626 |
| Diverticular disease of intestine | rs16970633 | 15 | 40350676 | T | G | 0.14891 | 0.0717591 | 0.0118286 | 1.3065e-09 | 36.80334347 |
| Diverticular disease of intestine | rs8038526 | 15 | 76178414 | T | C | 0.799257 | 0.0779589 | 0.0107316 | 3.74714e-13 | 52.77186607 |
| Diverticular disease of intestine | rs9926533 | 16 | 31002858 | T | C | 0.385179 | 0.0475968 | 0.00868954 | 4.3142e-08 | 30.0028104 |
| Diverticular disease of intestine | rs9888980 | 16 | 69848678 | G | C | 0.107313 | -0.0955165 | 0.0139535 | 7.62957e-12 | 46.85872712 |
| Diverticular disease of intestine | rs11149687 | 16 | 84813684 | C | T | 0.805211 | -0.076433 | 0.0106041 | 5.6846e-13 | 51.95342492 |
| Diverticular disease of intestine | rs2280028 | 16 | 86199807 | A | G | 0.0956643 | -0.0809558 | 0.014646 | 3.24833e-08 | 30.55328267 |
| Diverticular disease of intestine | rs41280074 | 17 | 41896746 | T | C | 0.0163803 | 0.175947 | 0.0321421 | 4.39906e-08 | 29.96506587 |
| Diverticular disease of intestine | rs78077208 | 17 | 48126317 | G | A | 0.19112 | -0.0679401 | 0.0108958 | 4.50474e-10 | 38.88070381 |
| Diverticular disease of intestine | rs72636731 | 18 | 10720928 | T | C | 0.114408 | -0.0800808 | 0.0136153 | 4.06191e-09 | 34.59412705 |
| Diverticular disease of intestine | rs2337106 | 18 | 48934533 | G | C | 0.515469 | 0.0481368 | 0.00849369 | 1.45014e-08 | 32.11897076 |
| Diverticular disease of intestine | rs182069332 | 19 | 10074131 | T | C | 0.0303335 | -0.165633 | 0.0256636 | 1.08916e-10 | 41.65417917 |
| Diverticular disease of intestine | rs3786877 | 19 | 38268540 | C | T | 0.554719 | -0.0688446 | 0.00852583 | 6.75772e-16 | 65.20282676 |
| Diverticular disease of intestine | rs56131196 | 19 | 44919589 | A | G | 0.27126 | -0.0532785 | 0.00968626 | 3.78905e-08 | 30.25462219 |
| Diverticular disease of intestine | rs17265513 | 20 | 41203988 | C | T | 0.28276 | -0.0527266 | 0.00949601 | 2.81605e-08 | 30.83026148 |

| Exposure | SNP | chr | pos | effect allele | other allele | eaf | β | SE | P | F |
|-----------------------------------|-------------|-----|-----------|---------------|--------------|-----------|------------|------------|-------------|-------------|
| Diverticular disease of intestine | rs13051496 | 21 | 46003595 | T | C | 0.215182 | 0.0739777 | 0.0102709 | 5.90609e-13 | 51.87816999 |
| Diverticular disease of intestine | rs369935000 | 21 | 46124540 | T | C | 0.605675 | 0.0524851 | 0.00874494 | 1.95187e-09 | 36.02121768 |
| Duodenal ulcer | rs2666827 | 1 | 155711062 | T | C | 0.0835447 | 0.221649 | 0.0402682 | 3.70578e-08 | 30.29752264 |
| Duodenal ulcer | rs2978981 | 8 | 142677719 | T | C | 0.501986 | -0.220209 | 0.0231742 | 2.05258e-21 | 90.29436081 |
| Duodenal ulcer | rs576123 | 9 | 133268896 | T | C | 0.562798 | 0.184782 | 0.0235706 | 4.52376e-15 | 61.45794737 |
| Duodenal ulcer | rs12274456 | 11 | 6234754 | T | C | 0.218173 | 0.214482 | 0.027063 | 2.27615e-15 | 62.81014939 |
| Fibrosis and cirrhosis of liver | rs28636836 | 4 | 87310713 | T | C | 0.215987 | -0.222029 | 0.0271778 | 3.09671e-16 | 66.74070795 |
| Fibrosis and cirrhosis of liver | rs138295924 | 19 | 19283559 | G | A | 0.0606703 | 0.264825 | 0.0420523 | 3.02448e-10 | 39.65869816 |
| Fibrosis and cirrhosis of liver | rs188247550 | 19 | 19285807 | T | C | 0.0508301 | 0.407579 | 0.0436871 | 1.06365e-20 | 87.03965591 |
| Fibrosis and cirrhosis of liver | rs3747207 | 22 | 43928975 | A | G | 0.22649 | 0.393654 | 0.0237257 | 7.98362e-62 | 275.2905276 |
| Functional dyspepsia | rs9265948 | 6 | 31347416 | T | C | 0.0914019 | 0.144331 | 0.0247158 | 5.23215e-09 | 34.10121845 |
| Functional dyspepsia | rs62046253 | 16 | 60610717 | T | C | 0.372802 | -0.0838897 | 0.0152868 | 4.07108e-08 | 30.11508652 |
| Gastric cancer | rs6676150 | 1 | 155151361 | C | G | 0.376152 | -0.236524 | 0.039445 | 2.01878e-09 | 35.95559742 |
| Gastric cancer | rs2585140 | 8 | 142725478 | G | A | 0.434849 | -0.251181 | 0.0382148 | 4.93515e-11 | 43.20265014 |
| Gastro-oesophageal reflux disease | rs1549726 | 2 | 104896566 | G | A | 0.371291 | 0.0502177 | 0.00901917 | 2.57858e-08 | 31.0013417 |
| Gastroduodenal ulcer | rs2920296 | 8 | 142681691 | G | A | 0.501823 | -0.112514 | 0.014524 | 9.4254e-15 | 60.01235211 |
| Gastroduodenal ulcer | rs576123 | 9 | 133268896 | T | C | 0.562937 | 0.0985109 | 0.0147265 | 2.2413e-11 | 44.74757351 |
| Gastroduodenal ulcer | rs12274456 | 11 | 6234754 | T | C | 0.218367 | 0.120356 | 0.0172183 | 2.74916e-12 | 48.86016739 |
| Gastrointestinal diseases | rs11887534 | 2 | 43839108 | C | G | 0.0841502 | 0.133586 | 0.00951419 | 8.79023e-45 | 197.1415884 |
| Gastrointestinal diseases | rs1802575 | 2 | 55866069 | C | G | 0.0730218 | 0.0689153 | 0.010165 | 1.20448e-11 | 45.96386455 |
| Gastrointestinal diseases | rs6920512 | 6 | 28279444 | A | G | 0.802063 | 0.0374104 | 0.00664528 | 1.80605e-08 | 31.69261932 |
| Gastrointestinal diseases | rs3134796 | 6 | 32222144 | G | A | 0.125334 | 0.078193 | 0.00796041 | 8.98669e-23 | 96.48612801 |
| Gastrointestinal diseases | rs1239709 | 13 | 50552741 | G | T | 0.711109 | 0.0318719 | 0.00581324 | 4.19015e-08 | 30.05933731 |
| Gastrointestinal diseases | rs28929474 | 14 | 94378610 | T | C | 0.0196976 | 0.119595 | 0.0189448 | 2.74019e-10 | 39.85162149 |
| Gastrointestinal diseases | rs11082430 | 18 | 45172412 | G | C | 0.236931 | -0.0361152 | 0.00619664 | 5.60338e-09 | 33.96780755 |
| Nonalcoholic fatty liver disease | rs2954029 | 8 | 125478730 | T | A | 0.458823 | -0.16629 | 0.0280625 | 3.10985e-09 | 35.11393897 |
| Nonalcoholic fatty liver disease | rs150057262 | 19 | 19210016 | G | C | 0.0497407 | 0.399234 | 0.0576913 | 4.51128e-12 | 47.88884795 |
| Nonalcoholic fatty liver disease | rs739846 | 19 | 19308262 | A | G | 0.0632336 | 0.434314 | 0.0505004 | 7.95793e-18 | 73.96359669 |
| Nonalcoholic fatty liver disease | rs738409 | 22 | 43928847 | G | C | 0.226988 | 0.474321 | 0.0300889 | 5.50681e-56 | 248.5032563 |
| Pancreatic cancer | rs31490 | 5 | 1344343 | A | G | 0.478804 | 0.247469 | 0.0348531 | 1.24451e-12 | 50.41488514 |
| Pancreatic cancer | rs576123 | 9 | 133268896 | T | C | 0.562561 | -0.21021 | 0.0350771 | 2.06272e-09 | 35.9136365 |
| Ulcerative colitis | rs12736494 | 1 | 8075956 | A | G | 0.264806 | -0.126424 | 0.021438 | 3.69675e-09 | 34.77687233 |
| Ulcerative colitis | rs4655159 | 1 | 19784345 | T | C | 0.634237 | -0.107843 | 0.0192616 | 2.15774e-08 | 31.34723227 |

(Continued)

Supplementary Table 7. The Summary Information for SNPs of Gastrointestinal Diseases (Continued)

| Exposure | SNP | chr | pos | effect allele | other allele | eaf | β | SE | P | F |
|--------------------|-------------|-----|-----------|---------------|--------------|-----------|-----------|-----------|-------------|-------------|
| Ulcerative colitis | rs6674040 | 1 | 19875420 | T | G | 0.490822 | -0.18187 | 0.0185103 | 8.7579e-23 | 96.53731567 |
| Ulcerative colitis | rs34145423 | 1 | 22382523 | A | G | 0.0774263 | -0.207834 | 0.0368378 | 1.68221e-08 | 31.83067299 |
| Ulcerative colitis | rs148170789 | 1 | 67244548 | G | A | 0.046007 | -0.36893 | 0.0492766 | 7.0518e-14 | 56.05398261 |
| Ulcerative colitis | rs1801274 | 1 | 161509955 | G | A | 0.503416 | -0.162744 | 0.0184938 | 1.36867e-18 | 77.4386296 |
| Ulcerative colitis | rs12132298 | 1 | 200905967 | C | T | 0.21262 | -0.146813 | 0.0233183 | 3.05344e-10 | 39.64014693 |
| Ulcerative colitis | rs3024495 | 1 | 206769068 | T | C | 0.15723 | 0.265226 | 0.0240177 | 2.37247e-28 | 121.9465054 |
| Ulcerative colitis | rs3732179 | 2 | 60927190 | C | T | 0.671625 | 0.11123 | 0.0200092 | 2.71431e-08 | 30.90184601 |
| Ulcerative colitis | rs1990760 | 2 | 162267541 | T | C | 0.585139 | -0.1058 | 0.0187436 | 1.65581e-08 | 31.86143414 |
| Ulcerative colitis | rs10931828 | 2 | 198694453 | T | C | 0.44086 | -0.109155 | 0.0187744 | 6.0979e-09 | 33.8029914 |
| Ulcerative colitis | rs34236350 | 2 | 240628909 | T | C | 0.267497 | 0.183297 | 0.0203578 | 2.18072e-19 | 81.06791941 |
| Ulcerative colitis | rs113595266 | 3 | 46430034 | A | G | 0.151292 | 0.151365 | 0.0250788 | 1.58376e-09 | 36.42817602 |
| Ulcerative colitis | rs3197999 | 3 | 49684099 | A | G | 0.39223 | 0.193702 | 0.018728 | 4.50713e-25 | 106.9757669 |
| Ulcerative colitis | rs11745587 | 5 | 132461230 | A | G | 0.405247 | -0.127965 | 0.0190284 | 1.75631e-11 | 45.22492523 |
| Ulcerative colitis | rs12518457 | 5 | 159397502 | T | G | 0.288297 | 0.111957 | 0.0202692 | 3.32307e-08 | 30.50909247 |
| Ulcerative colitis | rs1061537 | 6 | 29970018 | A | G | 0.393366 | -0.147226 | 0.0191264 | 1.38708e-14 | 59.25193768 |
| Ulcerative colitis | rs111432088 | 6 | 31835161 | T | C | 0.0149661 | 0.486843 | 0.0656338 | 1.19289e-13 | 55.02027557 |
| Ulcerative colitis | rs4587163 | 6 | 32625390 | T | C | 0.283395 | -0.255166 | 0.0212016 | 2.32113e-33 | 144.8466109 |
| Ulcerative colitis | rs1042131 | 6 | 33080825 | A | C | 0.502366 | -0.139269 | 0.0185179 | 5.44503e-14 | 56.5620896 |
| Ulcerative colitis | rs7761376 | 6 | 106041095 | G | T | 0.601338 | -0.104791 | 0.0188889 | 2.89374e-08 | 30.77759176 |
| Ulcerative colitis | rs12536069 | 7 | 4869839 | C | T | 0.068463 | 0.243305 | 0.0344247 | 1.57471e-12 | 49.95301885 |
| Ulcerative colitis | rs10807943 | 7 | 5301033 | C | T | 0.936726 | -0.32745 | 0.0349591 | 7.48514e-21 | 87.73431762 |
| Ulcerative colitis | rs181316459 | 7 | 5433979 | C | G | 0.0477545 | 0.604016 | 0.0370107 | 7.1105e-60 | 266.3436135 |
| Ulcerative colitis | rs113827118 | 7 | 5804177 | G | C | 0.186174 | 0.194184 | 0.0230199 | 3.29762e-17 | 71.15739168 |
| Ulcerative colitis | rs4730276 | 7 | 107843992 | A | G | 0.430388 | -0.156065 | 0.0188566 | 1.26911e-16 | 68.49900392 |
| Ulcerative colitis | rs7865719 | 9 | 5082333 | G | A | 0.556917 | 0.111096 | 0.0187342 | 3.02677e-09 | 35.16628896 |
| Ulcerative colitis | rs7101270 | 10 | 11670594 | T | C | 0.24666 | -0.122445 | 0.0219688 | 2.49546e-08 | 31.06486287 |
| Ulcerative colitis | rs10761659 | 10 | 62685804 | G | A | 0.528021 | 0.11128 | 0.0186228 | 2.29419e-09 | 35.70625281 |
| Ulcerative colitis | rs10748781 | 10 | 99523573 | A | C | 0.652091 | -0.168544 | 0.0191946 | 1.62293e-18 | 77.10250017 |
| Ulcerative colitis | rs11190368 | 10 | 100018265 | T | A | 0.444284 | 0.104938 | 0.0187073 | 2.0295e-08 | 31.46613081 |
| Ulcerative colitis | rs7931483 | 11 | 76591023 | A | C | 0.41714 | 0.118971 | 0.0187045 | 2.0102e-10 | 40.45665923 |
| Ulcerative colitis | rs11614178 | 12 | 68114342 | A | G | 0.336586 | 0.121856 | 0.0194308 | 3.58146e-10 | 39.32896096 |
| Ulcerative colitis | rs13379369 | 14 | 105863077 | G | A | 0.875317 | 0.180701 | 0.031494 | 9.6013e-09 | 32.92042745 |
| Ulcerative colitis | rs34399539 | 14 | 106011733 | G | C | 0.138186 | -0.185175 | 0.0293196 | 2.68856e-10 | 39.88858446 |
| Ulcerative colitis | rs79973254 | 15 | 90648210 | A | T | 0.0693439 | -0.212868 | 0.0386677 | 3.6902e-08 | 30.30568317 |
| Ulcerative colitis | rs16940186 | 16 | 85976134 | C | T | 0.145225 | 0.166186 | 0.0253161 | 5.22276e-11 | 43.09186241 |
| Ulcerative colitis | rs12942330 | 17 | 39783586 | T | C | 0.528561 | 0.128182 | 0.0186429 | 6.17021e-12 | 47.27452207 |
| Ulcerative colitis | rs6017342 | 20 | 44436388 | C | A | 0.559222 | 0.15623 | 0.0187875 | 9.12431e-17 | 69.14979204 |
| Ulcerative colitis | rs6089926 | 20 | 63572597 | T | C | 0.208287 | -0.157565 | 0.0236767 | 2.83596e-11 | 44.28709205 |
| Ulcerative colitis | rs2836883 | 21 | 39094818 | A | G | 0.247089 | -0.158251 | 0.0221231 | 8.47813e-13 | 51.16829681 |
| Ulcerative colitis | rs9607629 | 22 | 39274849 | G | A | 0.124865 | -0.196543 | 0.0295736 | 3.0137e-11 | 44.16790221 |
| Ulcerative colitis | rs9617090 | 22 | 50000765 | T | C | 0.371904 | -0.156376 | 0.0194362 | 8.58223e-16 | 64.73176983 |

Supplementary Table 8. Causal Effects of Gastrointestinal Diseases on Mood Swings Risk

| Exposure | Outcome | Method | SNPs(n) | OR | or_lci95 | or_uci95 | P |
|-------------------------|-------------|---|---------|-------------|-------------|-------------|------------|
| Acute appendicitis | Mood swings | Inverse variance weighted (fixed effects) | 16 | 1.020456913 | 0.987907963 | 1.054078264 | .220795315 |
| Acute appendicitis | Mood swings | MR Egger | 16 | 1.076293365 | 0.983019688 | 1.1784173 | .134223461 |
| Acute appendicitis | Mood swings | Weighted median | 16 | 1.023418664 | 0.977323174 | 1.071688249 | .324878788 |
| Acute pancreatitis | Mood swings | Inverse variance weighted (fixed effects) | 6 | 1.013701757 | 0.983812239 | 1.044499358 | .372813941 |
| Acute pancreatitis | Mood swings | MR Egger | 6 | 1.000470726 | 0.906060813 | 1.104717981 | .993020632 |
| Acute pancreatitis | Mood swings | Weighted median | 6 | 1.008218861 | 0.969887192 | 1.048065466 | .678946536 |
| Alcoholic liver disease | Mood swings | Inverse variance weighted (fixed effects) | 4 | 0.99356798 | 0.971146719 | 1.016506889 | .579504844 |
| Alcoholic liver disease | Mood swings | MR Egger | 4 | 0.997943525 | 0.900980612 | 1.105341519 | .972097928 |
| Alcoholic liver disease | Mood swings | Weighted median | 4 | 0.996741508 | 0.971946984 | 1.022168544 | .799533597 |
| Cholecystitis | Mood swings | Inverse variance weighted (multiplicative random effects) | 2 | 1.010228622 | 0.925988197 | 1.102132696 | .818805302 |
| Cholelithiasis | Mood swings | Inverse variance weighted (multiplicative random effects) | 68 | 0.99250706 | 0.975508843 | 1.00980147 | .393467656 |
| Cholelithiasis | Mood swings | MR Egger | 68 | 0.96771347 | 0.936362734 | 1.000113871 | .055034783 |
| Cholelithiasis | Mood swings | Weighted median | 68 | 0.994805064 | 0.970187193 | 1.020047597 | .683711883 |
| Chronic gastritis | Mood swings | Inverse variance weighted (fixed effects) | 2 | 1.063985469 | 0.988364271 | 1.145392554 | .099178372 |
| Chronic pancreatitis | Mood swings | Inverse variance weighted (fixed effects) | 4 | 0.98804189 | 0.956079983 | 1.021072289 | .47334269 |
| Chronic pancreatitis | Mood swings | MR Egger | 4 | 1.100168621 | 0.955942598 | 1.266154472 | .314496107 |
| Chronic pancreatitis | Mood swings | Weighted median | 4 | 1.0042075 | 0.965186031 | 1.044806567 | .835510366 |
| Coeliac disease | Mood swings | Inverse variance weighted (multiplicative random effects) | 17 | 0.997873255 | 0.987581345 | 1.00827242 | .687317441 |
| Coeliac disease | Mood swings | MR Egger | 17 | 1.001579496 | 0.984283033 | 1.019179903 | .861432223 |
| Coeliac disease | Mood swings | Weighted median | 17 | 1.003854752 | 0.993377781 | 1.014442222 | .472297127 |
| Colorectal cancer | Mood swings | Inverse variance weighted (fixed effects) | 12 | 1.002737954 | 0.98352217 | 1.022329172 | .781807974 |
| Colorectal cancer | Mood swings | MR Egger | 12 | 1.013033967 | 0.93514289 | 1.097412843 | .757581141 |
| Colorectal cancer | Mood swings | Weighted median | 12 | 1.013468206 | 0.986502241 | 1.041171283 | .330891825 |

(Continued)

Supplementary Table 8. Causal Effects of Gastrointestinal Diseases on Mood Swings Risk (*Continued*)

| Exposure | Outcome | Method | SNPs(n) | OR | or_lci95 | or_uci95 | P |
|-----------------------------------|-------------|---|---------|-------------|-------------|-------------|------------|
| Crohn's disease | Mood swings | Inverse variance weighted (fixed effects) | 8 | 1.012514618 | 0.998184874 | 1.027050077 | .08723275 |
| Crohn's disease | Mood swings | MR Egger | 8 | 0.972289891 | 0.915586206 | 1.032505323 | .394696578 |
| Crohn's disease | Mood swings | Weighted median | 8 | 1.01528815 | 0.995724196 | 1.035236496 | .126422372 |
| Diverticular disease of intestine | Mood swings | Inverse variance weighted (multiplicative random effects) | 53 | 0.994086527 | 0.964126157 | 1.02497792 | .704042073 |
| Diverticular disease of intestine | Mood swings | MR Egger | 53 | 0.955714277 | 0.874744082 | 1.044179432 | .320663592 |
| Diverticular disease of intestine | Mood swings | Weighted median | 53 | 0.983656097 | 0.952530201 | 1.015799095 | .315145208 |
| Duodenal ulcer | Mood swings | Inverse variance weighted (fixed effects) | 4 | 1.011029893 | 0.986458839 | 1.036212971 | .382183561 |
| Duodenal ulcer | Mood swings | MR Egger | 4 | 0.979929056 | 0.707503671 | 1.357252256 | .914053818 |
| Duodenal ulcer | Mood swings | Weighted median | 4 | 1.013374589 | 0.984509921 | 1.043085534 | .367514284 |
| Fibrosis and cirrhosis of liver | Mood swings | Inverse variance weighted (fixed effects) | 4 | 0.994111433 | 0.973449802 | 1.01521161 | .581534834 |
| Fibrosis and cirrhosis of liver | Mood swings | MR Egger | 4 | 1.004498578 | 0.92673538 | 1.088786957 | .923025517 |
| Fibrosis and cirrhosis of liver | Mood swings | Weighted median | 4 | 0.996763079 | 0.97405014 | 1.020005638 | .78278913 |
| Functional dyspepsia | Mood swings | Inverse variance weighted (multiplicative random effects) | 2 | 0.973957412 | 0.816701674 | 1.16149271 | .768982059 |
| Gastric cancer | Mood swings | Inverse variance weighted (multiplicative random effects) | 2 | 1.023777809 | 0.973689015 | 1.076443285 | .358518904 |
| Gastro-oesophageal reflux disease | Mood swings | Wald ratio | 1 | 1.248520922 | 1.049619822 | 1.485113428 | .012176634 |
| Gastroduodenal ulcer | Mood swings | Inverse variance weighted (fixed effects) | 3 | 1.023580005 | 0.975678725 | 1.073833015 | .340539934 |
| Gastroduodenal ulcer | Mood swings | MR Egger | 3 | 0.972212989 | 0.531592496 | 1.778050111 | .941916068 |
| Gastroduodenal ulcer | Mood swings | Weighted median | 3 | 1.02536582 | 0.970683193 | 1.083128948 | .370330613 |
| Gastrointestinal diseases | Mood swings | Inverse variance weighted (multiplicative random effects) | 7 | 1.005825464 | 0.847736989 | 1.19339474 | .946915884 |
| Gastrointestinal diseases | Mood swings | MR Egger | 7 | 0.891366733 | 0.615048675 | 1.291824019 | .570077797 |
| Gastrointestinal diseases | Mood swings | Weighted median | 7 | 1.035240916 | 0.930168119 | 1.152182849 | .525899805 |
| Nonalcoholic fatty liver disease | Mood swings | Inverse variance weighted (fixed effects) | 3 | 0.998556823 | 0.980326548 | 1.017126111 | .87790209 |
| Nonalcoholic fatty liver disease | Mood swings | MR Egger | 3 | 1.142103092 | 0.765519193 | 1.703940913 | .632642275 |

(Continued)

Supplementary Table 8. Causal Effects of Gastrointestinal Diseases on Mood Swings Risk (*Continued*)

| Exposure | Outcome | Method | SNPs(n) | OR | or_lci95 | or_uci95 | P |
|----------------------------------|-------------|---|---------|-------------|-------------|-------------|------------|
| Nonalcoholic fatty liver disease | Mood swings | Weighted median | 3 | 1.000083466 | 0.980530781 | 1.020026049 | .99338956 |
| Pancreatic cancer | Mood swings | Inverse variance weighted (fixed effects) | 2 | 0.987751617 | 0.961475353 | 1.014745988 | .370315902 |
| Ulcerative colitis | Mood swings | Inverse variance weighted (fixed effects) | 35 | 1.004207852 | 0.994018409 | 1.014501744 | .419675785 |
| Ulcerative colitis | Mood swings | MR Egger | 35 | 0.957756635 | 0.927131386 | 0.989393505 | .013735269 |
| Ulcerative colitis | Mood swings | Weighted median | 35 | 1.006430829 | 0.990881316 | 1.022224355 | .419723011 |

Supplementary Table 9. Summary of Pleiotropy of the Effects of Gastrointestinal Diseases on Mood Swings

| Exposure | Outcome | Egger_intercept | SE | P |
|-----------------------------------|-------------|-----------------|-------------|------------|
| Acute appendicitis | Mood swings | -0.00426141 | 0.003438647 | .235619657 |
| Acute pancreatitis | Mood swings | 0.003882246 | 0.013557547 | .788826697 |
| Alcoholic liver disease | Mood swings | -0.001344825 | 0.015540097 | .938921902 |
| Cholecystitis | Mood swings | NA | NA | NA |
| Cholelithiasis | Mood swings | 0.00262319 | 0.001491849 | .083324098 |
| Chronic gastritis | Mood swings | NA | NA | NA |
| Chronic pancreatitis | Mood swings | -0.070104609 | 0.045458936 | .262982476 |
| Coeliac disease | Mood swings | -0.00218401 | 0.004152708 | .60662959 |
| Colorectal cancer | Mood swings | -0.001664111 | 0.006320322 | .797668558 |
| Crohn's disease | Mood swings | 0.010984896 | 0.007903819 | .213956646 |
| Diverticular disease of intestine | Mood swings | 0.002968446 | 0.003195415 | .357280515 |
| Duodenal ulcer | Mood swings | 0.006522635 | 0.034595304 | .867850567 |
| Fibrosis and cirrhosis of liver | Mood swings | -0.003361346 | 0.012821103 | .817721507 |
| Functional dyspepsia | Mood swings | NA | NA | NA |
| Gastric cancer | Mood swings | NA | NA | NA |
| Gastroduodenal ulcer | Mood swings | 0.005696561 | 0.033971007 | .894230007 |
| Gastrointestinal diseases | Mood swings | 0.008842731 | 0.01215602 | .499579072 |
| Nonalcoholic fatty liver disease | Mood swings | -0.061992117 | 0.094109059 | .629178341 |
| Pancreatic cancer | Mood swings | NA | NA | NA |
| Ulcerative colitis | Mood swings | 0.008182508 | 0.002719348 | .004990303 |

Supplementary Table 10. Summary of Heterogeneity of Effects of Gastrointestinal Diseases on Mood Swings

| Exposure | Outcome | Method | Q | Q_df | Q_pval |
|-----------------------------------|-------------|---------------------------|-------------|------|-------------|
| Acute appendicitis | Mood swings | MR Egger | 14.90076541 | 14 | 0.384971754 |
| Acute appendicitis | Mood swings | Inverse variance weighted | 16.53536692 | 15 | 0.347389694 |
| Acute pancreatitis | Mood swings | MR Egger | 7.760729962 | 4 | 0.100746787 |
| Acute pancreatitis | Mood swings | Inverse variance weighted | 7.919821266 | 5 | 0.160710145 |
| Alcoholic liver disease | Mood swings | MR Egger | 2.083142275 | 2 | 0.352899792 |
| Alcoholic liver disease | Mood swings | Inverse variance weighted | 2.090942608 | 3 | 0.553747308 |
| Cholecystitis | Mood swings | Inverse variance weighted | 4.415427115 | 1 | 0.035615362 |
| Cholelithiasis | Mood swings | MR Egger | 89.01954603 | 66 | 0.03105676 |
| Cholelithiasis | Mood swings | Inverse variance weighted | 93.18969354 | 67 | 0.018914598 |
| Chronic gastritis | Mood swings | Inverse variance weighted | 1.038571984 | 1 | 0.308153823 |
| Chronic pancreatitis | Mood swings | MR Egger | 1.496165678 | 2 | 0.473273024 |
| Chronic pancreatitis | Mood swings | Inverse variance weighted | 3.874399841 | 3 | 0.275349978 |
| Coeliac disease | Mood swings | MR Egger | 43.65816992 | 15 | 0.000124362 |
| Coeliac disease | Mood swings | Inverse variance weighted | 44.46321591 | 16 | 0.000167678 |
| Colorectal cancer | Mood swings | MR Egger | 16.50582476 | 10 | 0.086039354 |
| Colorectal cancer | Mood swings | Inverse variance weighted | 16.62025046 | 11 | 0.119621092 |
| Crohn's disease | Mood swings | MR Egger | 10.11268298 | 6 | 0.119986201 |
| Crohn's disease | Mood swings | Inverse variance weighted | 13.36829798 | 7 | 0.063627374 |
| Diverticular disease of intestine | Mood swings | MR Egger | 114.5245573 | 51 | 8.77298E-07 |
| Diverticular disease of intestine | Mood swings | Inverse variance weighted | 116.4624616 | 52 | 7.64702E-07 |
| Duodenal ulcer | Mood swings | MR Egger | 0.285589682 | 2 | 0.86693191 |
| Duodenal ulcer | Mood swings | Inverse variance weighted | 0.321137414 | 3 | 0.956005298 |
| Fibrosis and cirrhosis of liver | Mood swings | MR Egger | 2.057378259 | 2 | 0.357475257 |
| Fibrosis and cirrhosis of liver | Mood swings | Inverse variance weighted | 2.128084833 | 3 | 0.546251939 |
| Functional dyspepsia | Mood swings | Inverse variance weighted | 7.227644215 | 1 | 0.007178935 |
| Gastric cancer | Mood swings | Inverse variance weighted | 4.053388685 | 1 | 0.04408277 |
| Gastroduodenal ulcer | Mood swings | MR Egger | 0.013273397 | 1 | 0.908278491 |
| Gastroduodenal ulcer | Mood swings | Inverse variance weighted | 0.041392964 | 2 | 0.97951622 |
| Gastrointestinal diseases | Mood swings | MR Egger | 28.95821636 | 5 | 2.36294E-05 |
| Gastrointestinal diseases | Mood swings | Inverse variance weighted | 32.02294354 | 6 | 1.61532E-05 |
| Nonalcoholic fatty liver disease | Mood swings | MR Egger | 0.663336209 | 1 | 0.415384601 |
| Nonalcoholic fatty liver disease | Mood swings | Inverse variance weighted | 1.097256616 | 2 | 0.577741751 |
| Pancreatic cancer | Mood swings | Inverse variance weighted | 0.00229347 | 1 | 0.96180376 |
| Ulcerative colitis | Mood swings | MR Egger | 33.13643235 | 33 | 0.460600981 |
| Ulcerative colitis | Mood swings | Inverse variance weighted | 42.22792368 | 34 | 0.157090851 |