

This is an Open Access document downloaded from ORCA, Cardiff University's institutional repository: <https://orca.cardiff.ac.uk/id/eprint/129993/>

This is the author's version of a work that was submitted to / accepted for publication.

Citation for final published version:

Byrne, Enda, Zhu, Zhihong, Qi, Ting, Skene, Nathan, Bryois, Julien, Pardinias, Antonio, Stahl, Eli, Smoller, Jordon, Rietschel, Marcella, Owen, Michael, Walters, James, O'Donovan, Michael, McGarth, John, Hjerling-Leffler, Jens, Sullivan, Patrick, Goddard, Michael, Visscher, Peter, Yang, Jian and Wray, Naomi 2021. Conditional GWAS analysis to identify disorder-specific SNPs for psychiatric disorders. *Molecular Psychiatry* 26, pp. 2070-2081. 10.1038/s41380-020-0705-9

Publishers page: <http://dx.doi.org/10.1038/s41380-020-0705-9>

Please note:

Changes made as a result of publishing processes such as copy-editing, formatting and page numbers may not be reflected in this version. For the definitive version of this publication, please refer to the published source. You are advised to consult the publisher's version if you wish to cite this paper.

This version is being made available in accordance with publisher policies. See <http://orca.cf.ac.uk/policies.html> for usage policies. Copyright and moral rights for publications made available in ORCA are retained by the copyright holders.



Conditional GWAS analysis to identify disorder-specific SNPs for psychiatric disorders

Enda M Byrne¹, Zhihong Zhu¹, Ting Qi¹, Nathan G Skene², Julien Bryois³, Antonio F Pardinas⁴, Eli Stahl⁵, Jordan W Smoller^{6,7,8,9}, Marcella Rietschel¹⁰, Bipolar Working Group of the Psychiatric Genomics Consortium, Major Depressive Disorder Working Group of the Psychiatric Genomics Consortium, Michael J Owen⁴, James T.R. Walters⁴, Michael C O'Donovan⁴, John G McGrath^{11,12,13}, Jens Hjerling-Leffler², Patrick F Sullivan^{3,14,15}, Michael E Goddard^{16,17}, Peter M Visscher^{1,11}, Jian Yang^{1,11}, Naomi R Wray^{1,11}

1. Institute for Molecular Biosciences, University of Queensland, Brisbane, Australia
2. Laboratory of Molecular Neurobiology, Department of Medical Biochemistry and Biophysics, Karolinska Institutet, Stockholm, Sweden
3. Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden
4. MRC Centre for Neuropsychiatric Genetics and Genomics, Cardiff University, UK
5. Icahn School of Medicine at Mount Sinai, New York, NY, USA
6. Department of Epidemiology, Harvard T. H. Chan School of Public Health, Boston, MA, USA
7. Psychiatric and Neurodevelopmental Genetics Unit, Center for Human Genetic Research, Massachusetts General Hospital, Boston, MA, USA
8. Stanley Center for Psychiatric Research, Broad Institute of MIT and Harvard, Cambridge, MA, USA
9. Department of Psychiatry, Harvard Medical School, Boston, MA, USA
10. Department of Genetic Epidemiology in Psychiatry, Central Institute of Mental Health, Medical Faculty Mannheim, University of Heidelberg, Heidelberg
11. Queensland Brain Institute, University of Queensland, Brisbane, Australia
12. Queensland Centre for Mental Health Research, The Park Centre for Mental Health, Wacol, Australia.
13. National Centre for Register-Based Research, Aarhus University, Aarhus, Denmark
14. Department of Genetics, University of North Carolina, Chapel Hill, NC 27599-7264, USA
15. Department of Psychiatry, University of North Carolina, Chapel Hill, NC 27599-7264, USA
16. Faculty of Veterinary and Agricultural Science, University of Melbourne, Parkville, Victoria, Australia.
17. Biosciences Research Division, Department of Economic Development, Jobs, Transport and Resources, Bundoora, Victoria, Australia.

Abstract

Substantial genetic liability is shared across psychiatric disorders but less is known about risk variants that are specific to a given disorder. We used multi-trait conditional and joint analysis (mtCOJO) to adjust GWAS summary statistics of one disorder for the effects of genetically correlated traits to identify putative disorder-specific SNP associations. We applied mtCOJO to summary statistics for five psychiatric disorders from the Psychiatric Genomics Consortium – schizophrenia (SCZ), bipolar disorder (BIP), major depression (MD), attention-deficit hyperactivity disorder (ADHD) and autism (AUT). Most genome-wide significant variants for these disorders had evidence of pleiotropy (i.e., impact on multiple psychiatric disorders) and hence have reduced mtCOJO conditional effect sizes. However, subsets of genome-wide significant variants had larger conditional effect sizes consistent with disorder-specific effects: 15 of 130 genome-wide significant variants for schizophrenia, 5 of 40 for major depression, 3 of 11 for ADHD and 1 of 2 for autism. We show that decreased expression of *VPS29* in the brain may increase risk to SCZ only and increased expression of *CSE1L* is associated with SCZ and MD, but not with BIP. Likewise, decreased expression of *PCDHA7* in the brain is linked to increased risk of MD but decreased risk of SCZ and BIP.

Introduction

Pervasive sharing of genetic risk factors between common psychiatric disorders (i.e. pleiotropy) has now been unequivocally demonstrated from genome-wide association studies (GWAS), as quantified by estimates of genetic correlation (r_g)^{1,2}. The r_g estimates are highest between schizophrenia and bipolar disorder (0.67, standard error (s.e.) = 0.03) but are > 0.15 for any combination of the five common disorders of schizophrenia (SCZ), bipolar disorder (BIP), ADHD, Major Depression (MD) and autism spectrum disorders (AUT)^{2,3}. Cross-diagnosis analyses can leverage power to identify genetic risk loci shared across classical diagnostic boundaries⁴ and can increase power for risk prediction of disorders in independent samples^{5,6}. The shared genetic basis for psychiatric disorders contributes to an evidence base supporting a trans-diagnostic approach in clinical practice⁷. Nonetheless, traditional diagnostic classes reflect real symptom differences at patient presentation even though it can be difficult to classify some individuals given a high-degree of concurrent and longitudinal comorbidity. Since r_g estimates are higher between data sets of the same disorder than between data sets of different disorders^{4,8} it implies some real biological basis to the classical diagnostic classes. Hence, a key question of importance in psychiatry is identification of genetic factors that are disorder specific rather than those shared across classical diagnostic groupings. Identifying such variants could aid in understanding the biological pathways that underlie the constellation of symptoms seen in each disorder.

One method for identifying disorder-specific variants is to conduct a case-case GWAS with cases of one disorder compared to cases of another. The SCZ/BIP working group of the Psychiatric Genomics Consortium (PGC) conducted an association analysis comparing in logistic regression SCZ (N=23,585) vs BIP (N=15,270) cases to identify variants specific to each disorder. The cases were matched on ancestry and genotyping platform, hence the sample sizes were smaller than those available for the disorder specific GWAS which limits the statistical power. Conducting such analysis requires access to the raw genotypes which is not always feasible for all cohorts due to privacy laws. Methods that use summary statistics can utilise larger sample sizes without the need to provide access to raw data to researchers. In addition, case-case GWAS can identify differences between pairs of disorders⁹, but does not generalize to the multivariate space to identify SNPs primarily associated one disorder.

We conditioned the effect of SNPs estimated for one disorder on those of other disorders using multi-trait, conditional and joint analysis (mtCOJO)¹⁰, a summary-statistics based method that accounts for overlap in samples contributing to the disorder specific

GWAS. We report results from conditional analyses of 5 psychiatric disorders: SCZ, BIP, MD, ADHD and AUT using association summary statistics from meta-analyses conducted by the Psychiatric Genomics Consortium (PGC) including data from 23andMe. Each disorder is conditioned on the other four disorders in one model.

Methods

We applied the mtCOJO method as described in Zhu et al.¹⁰. This method approximates a conditional analysis where the effect of a SNP on a disease is conditioned upon the covariates of the disease, but only requires summary statistics as input. As an example, if we are interested in estimating the effect of a SNP (z) on risk to schizophrenia (y) accounting for the effect of a covarying factor such as bipolar (x), we condition upon the effect of bipolar on schizophrenia \hat{b}_{xy} , as estimated using Generalised Summary-based Mendelian Randomisation (GSMR). This can be extended to condition upon multiple covarying diseases so that the effect of the SNP on risk on the disorder of interest is estimated conditional upon the covariates on the disorder (see **Supplementary Material** for detailed description of the method).

To identify independent genome-wide significant SNPs for use as genetic instruments in mtCOJO analysis, each dataset was clumped to select independent genome-wide significant (GWS) SNPs ($p < 5 \times 10^{-8}$) using 7,762 unrelated individuals from the Atherosclerosis Risk In Community (ARIC) dataset¹¹, imputed to 1000Genomes Phase III as an LD reference sample. GWS SNPs more than 1MB apart or with an r^2 value < 0.05 were considered to be independent. GSMR accounts for any remaining LD between instruments. GSMR analysis with filtering to remove SNPs with outlier pleiotropic effects (compared to other GWS SNPs) using the HEIDI test¹² was performed with each disorder included both as an exposure and an outcome in combination with the other disorders. Owing to having fewer than 10 independent GWS SNPs, independent SNPs significant at $p < 10^{-7}$ were used for GSMR analysis with autism as the exposure variable. In order to compare the estimated effects of one disorder on another from MR, we derived a conversion of the estimated effects from GSMR to the liability scale (see **Supplementary Material, Supplementary Figure 1**).

We performed mtCOJO analysis (implemented in GCTA¹³ (<http://cnsgenomics.com/software/gcta/#mtCOJO>) of 5 genetically correlated psychiatric

disorders using the results from large genome-wide association studies from the Psychiatric GWAS consortium (**Table 1**), running the analysis in turn with each disorder as the outcome with the other disorders as covariates. A total of 5,275,400 SNPs with matching alleles that were in common across the 5 disorders were used for further analysis. Indels were excluded from the analysis.

For each disorder, SNP effects conditional upon the other disorders were calculated. Results were uploaded to FUMA for annotation¹⁴. Ranking SNPs according to the difference between the marginal and conditional effect sizes for each disorder is not necessarily meaningful because, for example, a SNP that has a low estimated marginal effect, so no effect on the outcome trait, will have a large conditional effect if the SNP has a large effect on the covariate traits. For the purposes of identifying which SNPs show evidence of disorder-specificity, we focus on presenting results for SNPs that were GWS with the outcome disorder in the original GWAS. We further estimated whether the difference between the conditional and raw effect size of each SNP was significant (Supplementary Material).

MAGMA gene-set analysis

MAGMA gene-set analysis¹⁵ as implemented in FUMA was used to investigate which sets of biologically related genes show the strongest evidence of association in the conditional analyses.

Genetic Correlation

LD-score regression¹⁶ was used to estimate the genetic correlation between the conditional and unadjusted GWAS results.

Summary Mendelian Randomisation

To investigate the potential functional relevance of SNPs with disorder-specific effects, we applied the SMR approach¹², integrating eQTL (SNP-gene expression association) and mQTL (SNP_DNA methylation association) to the results from the conditional analyses. eQTL data from brain tissue were derived from a meta-analysis of the GTEx study, the Common Mind Consortium (CMC) and the Religious Orders Study and Memory and Aging Project (ROSMAP). The details of the meta-analysis have been described elsewhere¹⁷. Using meta-analysis results across brain tissues and studies is justified owing to the high correlation

in effect sizes between tissues¹⁷. Only genes with a cis-eQTL with $p_{\text{eQTL}} < 5 \times 10^{-8}$ were included in the analysis. Experiment-wide significance accounting for testing multiple SNPs across multiple traits was set at $p_{\text{SMR}} = 1.9 \times 10^{-6}$ and the threshold for no evidence of heterogeneity due to pleiotropy at $p_{\text{HEIDI}} > 0.01$. Individual-level genotypes from the ARIC data ($n = 7,762$ unrelated individuals)¹¹ were used to estimate LD for the HEIDI test.

To test for the effects of disorder-specific variants on DNA methylation, we used SMR to integrating trait association data with meta-analysed brain mQTL data set from Jaffe et al. ($n = 526$) ROSMAP ($n = 486$) and fetal brain mQTL data from Hannon et al.¹⁸. Only probes with at least one cis-mQTL with $p < 5 \times 10^{-8}$ were included in the SMR analysis. Probes that passed the significance threshold of 1.56×10^{-7} and did not show evidence of heterogeneity as indicated by the HEIDI test were considered to be significant.

Cell-type specificity for disorders

To gain insight into the cell types that are important for each disorder, we evaluated whether genes associated with specific brain cell-types are enriched for association with each of the disorders. Using data from single-cell sequencing experiments in mice, the cell-type specificity of each gene was calculated by comparing the expression of a gene in a given cell-type to that across all cell types¹⁹. MAGMA was used to calculate gene-based association statistics and to evaluate whether genes with high specificity in a given cell-type are enriched for association with a disorder. The enrichment analysis was performed for both unadjusted and conditional GWAS for all 5 disorders. To investigate whether there was a significant change in the cell-type enrichment after conditioning, MAGMA analysis was performed using the enrichment Z-scores from the unadjusted GWAS as covariates in the analysis and a conditional enrichment for all level 1 cell types analysed in Skene et al.¹⁹ was estimated.

Code Availability

Scripts used to generate the results are available on request from the corresponding author

Results

Baseline statistics

After merging GWAS summary statistics for the five psychiatric disorders 5,275,400 autosomal SNPs remained (**Table 1**). The number of independent genome-wide significant SNPs annotated by FUMA¹⁴ is much greater for SCZ ($M = 130$) compared to the other

disorders (M =16, 40, 11, 2 for BIP, MD, ADHD, AUT respectively) reflecting mostly sample size, but also genetic architecture, and population risk. Linkage disequilibrium score regression (LDSC) estimates of SNP-based heritability on the liability scale and genetic correlations were all significantly different from zero (**Table 2**). Genetic correlations were highest between SCZ and BIP ($r_g = 0.67$ (s.e. = 0.03)) and lowest between BIP and ADHD ($r_g = 0.15$ (s.e. = 0.04)). The LD-score regression intercept was significantly greater than zero for the majority of pairs of disorders reflecting sample overlap in the GWAS studies. The intercept was highest between ADHD and AUT due to substantial overlap in controls. See Supplementary Material for discussion of interpretation of results in the context of sample overlap.

The GSMR analyses highlights some asymmetries in the estimates of the causal effects of one disorder on another (**Table 3**). In particular, the estimated liability \hat{b}_{xy} when considering MD as an exposure for each trait is higher than the estimates in the reverse direction. One explanation is that since MD is so common and is frequently comorbid with other disorders that MD samples include those diagnosed and undiagnosed with other disorders. However, if model assumptions are violated it may have greater impact when there is a large difference in lifetime risk between the pairs of disorder. However, countering this, we find a higher \hat{b}_{xy} from AUT to ADHD than from ADHD to AUT, but the standard errors on estimates are much higher for these disorders. Interpretation of these \hat{b}_{xy} estimates depends on the nature of the shared genetic contributions to psychiatric disorders that may reflect a complex mix of types of pleiotropy, where some sets shared of variants may have more correlated effect sizes than other sets of shared variants.

Changes in Genetic Correlation

The impact of the conditioning is demonstrated by the changes in the estimates of \hat{r}_g comparing original and conditional GWAS results. The \hat{r}_g between SCZ conditional on the other disorders (denoted SCZ_{cond}) and SCZ remained high at 0.93, while between SCZ_{cond} and BIP it was much reduced (from 0.67 prior to conditioning to 0.36, after conditioning). It is noted that b_{zy} is eliminated in the conditional analysis only if the SNP effect is mediated by trait x . Therefore, there is remaining genetic correlation because of pleiotropic SNP effects. A similar pattern of changes in genetic correlation with other traits was seen for the analyses with the other disorders as the outcome variable (**Supplementary Table 1**).

mtCOJO genome-wide significant SNP results

As expected because of pleiotropy between disorders, conditional analysis leads to a reduction in the mean test statistic across all SNPs in the genome and hence the number of independent SNPs reaching the significance threshold (5×10^{-8}) is reduced (**Table 1**). For each disorder, we present results for all independent SNPs significant in the unadjusted analysis or the conditional analysis (**Supplementary Table 2**). GWS SNPs that are more significantly associated in the conditional analysis than the unadjusted analysis are shown in **Table 4**. A larger conditional effect size suggests that these variants are disorder-specific or have heterogeneous effects across disorders.

Given that SCZ is the disorder with the largest number of significant SNPs and for which the power to detect changes in effects is largest, we focus mostly on the results from the SCZ conditional analysis. Of the 130 SNPs from the unadjusted SCZ GWAS, five were more significant after adjusting for the other disorders (all of which had opposite direction of effects for BIP – **Supplementary Table 2**) and a further eight had a larger estimated effect size after conditioning. Forest plots for the four most significant SCZ SNPs from the conditional analysis (two of which were associated $p < 5 \times 10^{-8}$ in the unadjusted analysis) are shown in **Figure 1**.

For all disorders except for AUT, a number of SNPs surpass the significance threshold that were not significant in the original GWAS. For schizophrenia, ten SNPs that were significant in the conditional analysis and not in the original GWAS (**Table 4**). All 10 SNPs have opposite effects for BIP, so that the allele that predisposes to SCZ is in the protective direction for BIP. Although these opposite effects could be due to ascertainment, among them are variants in or near genes with annotated biological functions that are potentially relevant for SCZ. For instance a SNP that was significant in the conditional analysis (rs2973038 – $p_{\text{adj}} = 1.28 \times 10^{-08}$; $p_{\text{scz}} = 1.72 \times 10^{-06}$) is located in the Glial Cell Derived Neurotrophic Factor (*GDNF*), a gene that encodes a protein that enhances the survival of midbrain dopaminergic neurons²⁰, and is expressed during development²¹.

All SNPs that were associated with BIP at $p < 5 \times 10^{-8}$ in the original GWAS were less significant in the conditional analysis, showing evidence that they have some pleiotropic effect across disorders. Notably, this includes genes involved in calcium signalling, dopaminergic signalling and synaptic plasticity, indicating these processes may be important across psychiatric disorders. Three SNPs that were not significant in the BIP GWAS were

significant in the conditional analysis (**Table 4, Supplementary Table 2, Supplementary Figure 2**).

For each of the remaining disorders (MD, ADHD and AUT), we found that a small proportion of the existing significant SNPs had larger conditional effect sizes and one MD SNP and two ADHD SNPs that were not significant in the original GWAS became significant after conditioning (**Table 4, Supplementary Table 2**). However the difference in effect size after conditioning is not statistically significant for these SNPs, due to low statistical power (Supplementary Table 2). Forest plots for significant SNPs that had increased conditional effect sizes are shown in **Supplementary Figures 3-5**

SMR analysis

Changes in the expression of 9 genes were significantly associated with the 5 disorders (0 for BIP, 5 for SCZ, 3 for MD and 1 for ADHD, 0 for AUT) after conditioning and removal of genes in the MHC (**Supplementary Tables 3-4**), and a total of 72 DNA methylation sites (2 for BIP, 18 for SCZ, 37 for MD, 8 for ADHD, and 6 for AUT) were significantly associated with the 5 conditional traits (**Supplementary Table 3-4**).

Significant SMR results for gene expression where the associated SNP is more significant in the conditional analysis are presented in **Supplementary Table 3**. Three out of 5 significant SMR associations for SCZ were with SNPs where the conditional significance was greater than in the unadjusted analysis. One SNP - rs3759384 – is associated with decreased expression of *VPS29* in the brain and significantly increased risk for SCZ in the unadjusted analysis and has a larger conditional effect size (**Supplementary Figure 6**), indicating that *VPS29* may be linked to the development of SCZ and not other disorders. The *VPS29* protein is a component of the retromer complex which prevents the degradation of certain proteins including signalling receptors, ion channels and small molecule transporters. The complex is essential for maintenance of neurons and has been implicated in the etiology of a number of neurodegenerative disorders²².

One of the three associations for MD was with a SNP (rs7732179) with greater significance in the conditional analysis. The same variant shows evidence of association with SCZ but with opposite directions of effect ($b_{SCZ} = -0.045$; $p_{SCZ} = 1.7 \times 10^{-6}$ and $b_{BIP} = -0.029$; $p_{BIP} = 0.027$). The A allele confers risk to MDD but is protective for SCZ and BIP (**Supplementary Figure 7**). The SNP is associated with expression of *PCDHA7* in the brain. This gene encodes a member of the protocadherin family of genes located together on chromosome 5. A significant association was also found in this region in the DNA

methylation analysis of MD. Little is known about the exact function of these genes, however they are concentrated at the synaptic junction suggesting a key role in neuronal signalling²³.

Out of 72 significant DNA methylation sites, 34 were associated with SNPs with higher significance in the conditional analyses (1 for BIP, 3 for SCZ, 21 for MD, 4 for ADHD and 5 for AUT) (**Supplementary Table 3**). It is noteworthy that one variant (rs2064853) was significantly associated with both SCZ and MD and DNA methylation near the *CSEIL* gene, but with opposite alleles increasing risk to each disorder (**Supplementary Figure 8**).

We investigated whether genes identified in the gene expression SMR or that are the closest gene to a significant methylation site are the primary target for FDA-approved drugs. We identified two genes that are targeted by medications. The serotonin receptor gene *HTR1D* which was identified in the DNA methylation analysis for MD is the primary target of the migraine drug naratriptan. Individuals with migraine are at 2-4 fold higher risk of developing depression and these results may suggest that triptans, used to treat migraines, could also be effective for MD.

The second drug target identified is with *MPL* and ADHD. This gene is targeted by romiplostim, an orphan drug developed for treatment of chronic idiopathic thrombocytopenic purpura.

MAGMA gene-set analyses

We conducted MAGMA gene-set analysis in FUMA to identify pathways and gene-sets that are enriched for association with the disorders after conditional analyses and to identify which sets become more or less significant after conditioning. Results for each disorder are presented in **Supplementary Table 5**. After conservative Bonferroni correction for the number of gene-sets tested for each disorder, three gene sets were significant - two for SCZ conditional analysis and one for AUT. For SCZ, the two significant sets were go:establishment of localization in the cell and GO:Dendrite, of which establishment of localization had a more significant p-value in the conditional analysis (**Supplementary Table 5**). For AUT, the gene-set GO:Dendrite_morphogenesis was significant after multiple testing and had a more significant p-value in the conditional analysis, potentially implicating genes expressed in dendrites in autism-specific pathology.

Cell-type specificity for disorders

The results from the cell-type enrichment analyses of raw and conditional analyses are shown in **Figure 2**. Consistent with previous results, the original SCZ results were enriched in medium spiny neurons (MSNs), pyramidal CA1 cells, pyramidal SS1 cells, interneurons and serotonergic neurons (**Supplementary Table 6**). All of these cell types also show some evidence of association with BIP and to a lesser extent MD, consistent with the genetic correlation between disorders and hence show reduced enrichment in the SCZ conditional analysis. All enriched cell-types for SCZ remained significant after conditioning except for serotonergic neurons, indicating that genes specific to this cell-type may increase risk to all five disorders. Enrichment in interneurons was found for SCZ, BIP and MDD indicating their potential importance across all 3 disorders. After conditioning, this cell-type was still significantly enriched in SCZ and MDD, but not BIP. This may reflect that the sample size of the BIP analysis is smaller than for SCZ and MDD.

Discussion:

Our goal was to identify genetic variants that show disorder specific association by conducting a summary statistics based GWAS analysis for each of five psychiatric disorders conditioning on GWAS results from the other disorders. As expected, given the high degree of pleiotropy across disorders, compared to original GWAS results the number of SNPs associated at the threshold of genome-wide significance is very much reduced for each conditional GWAS. We utilise mtCOJO as a method that uses summary statistics to quickly screen for SNP associations. Functional annotation can help prioritise the associations of most interest. It will be important to understand why a variant increases risk only to that disorder and not to others.

By integrating conditional GWAS results with SNP-gene expression and SNP-methylation results, we identify decreased expression of *VPS29* as a potential biological mechanism underlying schizophrenia. The variant that increases risk to SCZ and is associated with decreased expression of *VPS29* in brain tissue shows no evidence for association with other psychiatric disorders. The retromer complex, of which is *VPS29* is a subunit, is highly conserved across eukaryotes. The complex plays a role in the recycling, delivery and degradation of proteins in the cell and is crucial in the maintenance of cell homeostasis²⁴. Rare exonic mutations in members of the complex have been associated with Parkinson's Disease and post-mortem studies have revealed decreased expression of all members of the complex in the brains of patients with Parkinson's and Alzheimer's disease. The expression

of all three members of the complex is linked such that decreasing expression of one leads to decreased expression of all of them. Knocking down VPS35 using siRNA leads to elevated generation of amyloid-beta and reduced synaptic transmission^{25,26}. There is therefore considerable interest in identifying pharmacological agents that prevent the degradation of the retromer complex as a therapeutic mechanism for neurodegenerative disease. Small molecule screens have identified potential therapeutic agents that have shown promise in vitro²⁷. Our results provide that such compounds may be of interest in targeting biological mechanisms specific to schizophrenia.

Furthermore, SNPs associated with decreased expression of *PCDH7* and decreased methylation near other members of the protocadherin gene family on chromosome 5 may increase risk of MD, but be protective for SCZ and BIP. The protocadherins are a large family of genes involved in cell-cell adhesion that are primarily expressed in the nervous system. They play a major role in the development of the nervous system and in regulating dendritic branching. The *PCDHA7* gene is part of a complex cluster of protocadherin alpha genes in the same genomic locus. The expression of the different isoforms at the locus is controlled by upstream CpG sites. Owing to their functional role in nervous system development and their location in linkage peaks, the *PCDHA* genes have been investigated as candidate genes for bipolar and schizophrenia²⁸. Moreover, an epigenetic study of concordant and discordant MZ twins for depression showed that affected twins had increased variation in methylation in the *PCDHA* region, highlighting instability in this region as a potential mechanism underlying depression²⁹. Further studies of the role of the *PCDHA* gene cluster in psychopathology are warranted.

Methylation in the promoter of the *CSE1L* gene, whose encoded protein influences cellular proliferation and has been linked to progression of a number of cancers, shows evidence of increasing risk to SCZ but being protective for MD.

Consistent with the large degree of pleiotropy between disorders, we found that most of the significant biological pathways for each disorder had reduced significance after conditioning. Pathway analysis of conditional results identified a potential role for genes expressed in dendrites in both autism and schizophrenia. Likewise, for the cell-type enrichment analysis, there was a reduction in the enrichment for most cell types in each disorder after conditioning. For SCZ, the previously identified enrichments in pyramidal SS1 and CA1 cells as well as medium spiny neurons remained significant after conditioning, despite also showing evidence for enrichment in BIP. The largest change in enrichment was

for serotonergic neurons, indicating that genes highly expressed there are important across all psychiatric disorders.

We provide an analysis framework for conditional cross-disorder analyses using summary statistics. Our study was motivated to improve on the SCZ case vs. BIP case analyses that utilised PGC cohorts for which both SCZ and BIP genotyped samples were available³⁰, but which necessarily excluded 28% of cases that could not be allocated into matched cohorts. They identified 5 SNPs associated at $p < 5 \times 10^{-8}$. We conducted an analysis of SCZ conditional on BIP and performed a lookup of those SNPs in the unadjusted and adjusted results. All but one (rs200005157) of their associated SNPs were matched directly or to an LD proxy (**Supplementary Table 7**). All show increased statistical significance in the conditional analysis. We identified more disorder-specific SNPs (10 specific to SCZ) consistent with the larger sample sizes afforded from using summary statistics, highlighting that mtCOJO is an efficient method for screening for disorder-specific SNPs for two or more related disorders. An in depth discussion of the mtCOJO method is given in the **Supplementary Material**.

Limitations

There are a number of limitations to our analyses that should be considered. Although methods that utilise summary statistics have several advantages, they also depend upon the summary statistics being generated accurately. In this instance, all studies have gone through the same quality control and analysis pipeline meaning that systematic differences between studies are unlikely. It is not clear how misdiagnosis of cases would impact upon the results.

There are also substantial differences in sample size between the GWAS of different disorders, with SCZ and MD having a larger sample size than the other disorders, which may disproportionately influence the results. This is shown by most of the significant differences in effect sizes between the raw and conditional results being for SCZ. The disorders that have the most genome-wide significant SNPs will also have the most accurate estimates of their effects on the disorders. As sample sizes increase for some of the other disorders, the results for those disorders will become more accurate.

In order to reduce the burden of multiple testing in the SMR analysis, we only included SNPs that are associated at the genome-wide significant level with gene expression or methylation in cis. Relaxing the statistical threshold for inclusion may have identified more SNPs with effects on gene expression in brain with the trade-off of increasing the experiment-wide significance level.

Conclusion

In conclusion, our results suggest that mtCOJO is an efficient method for identifying variants with disorder-specific effects and they represent a small fraction of variants identified for each disorder to date, reflecting the high degree of pleiotropy between disorders. Nonetheless, we identify several loci that have evidence of being disorder-specific. Further research in human studies should focus on whether the disorder-specific variants associate with specific symptoms in mixed clinical populations.

Acknowledgements

This work is supported by grants from the National Health and Medical Research Council of Australia (1087889, 1145645, 1113400, 1078901,1078037), and the Sylvia & Charles Viertel Charitable Foundation. The PGC has received major funding from the US National Institute of Mental Health and the US National Institute of Drug Abuse (U01 MH109528 and U01 MH1095320). We thank the research participants and employees of 23andMe, Inc. for contributing to this study. This paper would not have been possible without the generosity of participants in the many studies that comprise the final meta-analyses and the dedication of many clinicians and research staff who have collected the data and made them publically available. Acknowledgments for specific datasets are provided in the Supplementary Material.

Conflict of Interest Statement

P.F.S. is on the advisory committee at Lundbeck, is a Scientific Advisory Board member at Pfizer and has received speaker reimbursement and grant funding from Roche. J.H.-L. is a Scientific Advisor at Cartana and has received grant funding from Roche.

References

1. Cross-Disorder Group of the Psychiatric Genomics Consortium, Lee SH, Ripke S, Neale BM, Faraone SV, Purcell SM *et al.* Genetic relationship between five psychiatric disorders estimated from genome-wide SNPs. *Nature genetics* 2013; **45**(9): 984-994.
2. Bulik-Sullivan B, Finucane HK, Anttila V, Gusev A, Day FR, Loh PR *et al.* An atlas of genetic correlations across human diseases and traits. *Nature genetics* 2015; **47**(11): 1236-1241.
3. Grove J, Ripke S, Als TD, Mattheisen M, Walters R, Won H *et al.* Common risk variants identified in autism spectrum disorder. *bioRxiv* 2017.
4. Cross-Disorder Group of the Psychiatric Genomics C. Identification of risk loci with shared effects on five major psychiatric disorders: a genome-wide analysis. *Lancet* 2013; **381**(9875): 1371-1379.
5. Turley P, Walters RK, Maghziyan O, Okbay A, Lee JJ, Fontana MA *et al.* Multi-trait analysis of genome-wide association summary statistics using MTAG. *Nature genetics* 2018.
6. Maier R, Moser G, Chen GB, Ripke S, Cross-Disorder Working Group of the Psychiatric Genomics C, Coryell W *et al.* Joint analysis of psychiatric disorders increases accuracy of risk prediction for schizophrenia, bipolar disorder, and major depressive disorder. *American journal of human genetics* 2015; **96**(2): 283-294.
7. Scott J, Leboyer M, Hickie I, Berk M, Kapczinski F, Frank E *et al.* Clinical staging in psychiatry: a cross-cutting model of diagnosis with heuristic and practical value. *The British journal of psychiatry : the journal of mental science* 2013; **202**(4): 243-245.
8. Wray NR, Ripke S, Mattheisen M, Trzaskowski M, Byrne EM, Abdellaoui A *et al.* Genome-wide association analyses identify 44 risk variants and refine the genetic architecture of major depression. *Nature genetics* 2018; **50**(5): 668-681.
9. Nieuwboer HA, Pool R, Dolan CV, Boomsma DI, Nivard MG. GWIS: Genome-Wide Inferred Statistics for Functions of Multiple Phenotypes. *American journal of human genetics* 2016; **99**(4): 917-927.
10. Zhu Z, Zheng Z, Zhang F, Wu Y, Trzaskowski M, Maier R *et al.* Causal associations between risk factors and common diseases inferred from GWAS summary data. *Nat Commun* 2018; **9**(1): 224.
11. The Atherosclerosis Risk in Communities (ARIC) Study: design and objectives. The ARIC investigators. *American journal of epidemiology* 1989; **129**(4): 687-702.

12. Zhu Z, Zhang F, Hu H, Bakshi A, Robinson MR, Powell JE *et al.* Integration of summary data from GWAS and eQTL studies predicts complex trait gene targets. *Nature genetics* 2016; **48**(5): 481-487.
13. Yang J, Lee SH, Goddard ME, Visscher PM. GCTA: a tool for genome-wide complex trait analysis. *American journal of human genetics* 2011; **88**(1): 76-82.
14. Watanabe K, Taskesen E, van Bochoven A, Posthuma D. Functional mapping and annotation of genetic associations with FUMA. *Nat Commun* 2017; **8**(1): 1826.
15. de Leeuw CA, Mooij JM, Heskes T, Posthuma D. MAGMA: generalized gene-set analysis of GWAS data. *PLoS Comput Biol* 2015; **11**(4): e1004219.
16. Zheng J, Erzurumluoglu AM, Elsworth BL, Kemp JP, Howe L, Haycock PC *et al.* LD Hub: a centralized database and web interface to perform LD score regression that maximizes the potential of summary level GWAS data for SNP heritability and genetic correlation analysis. *Bioinformatics* 2017; **33**(2): 272-279.
17. Qi T, Wu Y, Zeng J, Zhang F, Xue A, Jiang L *et al.* Identifying gene targets for brain-related traits using transcriptomic and methylomic data from blood. *Nat Commun* 2018; **9**(1): 2282.
18. Hannon E, Dempster E, Viana J, Burrage J, Smith AR, Macdonald R *et al.* An integrated genetic-epigenetic analysis of schizophrenia: evidence for co-localization of genetic associations and differential DNA methylation. *Genome Biol* 2016; **17**(1): 176.
19. Skene NG, Bryois J, Bakken TE, Breen G, Crowley JJ, Gaspar HA *et al.* Genetic identification of brain cell types underlying schizophrenia. *Nature genetics* 2018; **50**(6): 825-833.
20. Lin LF, Doherty DH, Lile JD, Bektesh S, Collins F. GDNF: a glial cell line-derived neurotrophic factor for midbrain dopaminergic neurons. *Science* 1993; **260**(5111): 1130-1132.
21. Stromberg I, Bjorklund L, Johansson M, Tomac A, Collins F, Olson L *et al.* Glial cell line-derived neurotrophic factor is expressed in the developing but not adult striatum and stimulates developing dopamine neurons *in vivo*. *Exp Neurol* 1993; **124**(2): 401-412.
22. Wang S, Bellen HJ. The retromer complex in development and disease. *Development* 2015; **142**(14): 2392-2396.
23. Yagi T, Takeichi M. Cadherin superfamily genes: functions, genomic organization, and neurologic diversity. *Genes Dev* 2000; **14**(10): 1169-1180.

24. Vagnozzi AN, Pratico D. Endosomal sorting and trafficking, the retromer complex and neurodegeneration. *Molecular psychiatry* 2019; **24**(6): 857-868.
25. Bhalla A, Vetanovetz CP, Morel E, Chamoun Z, Di Paolo G, Small SA. The location and trafficking routes of the neuronal retromer and its role in amyloid precursor protein transport. *Neurobiol Dis* 2012; **47**(1): 126-134.
26. Zhang H, Huang T, Hong Y, Yang W, Zhang X, Luo H *et al.* The Retromer Complex and Sorting Nexins in Neurodegenerative Diseases. *Front Aging Neurosci* 2018; **10**: 79.
27. Mecozzi VJ, Berman DE, Simoes S, Vetanovetz C, Awal MR, Patel VM *et al.* Pharmacological chaperones stabilize retromer to limit APP processing. *Nat Chem Biol* 2014; **10**(6): 443-449.
28. Pedrosa E, Stefanescu R, Margolis B, Petruolo O, Lo Y, Nolan K *et al.* Analysis of protocadherin alpha gene enhancer polymorphism in bipolar disorder and schizophrenia. *Schizophrenia research* 2008; **102**(1-3): 210-219.
29. Cordova-Palomera A, Fatjo-Vilas M, Gasto C, Navarro V, Krebs MO, Fananas L. Genome-wide methylation study on depression: differential methylation and variable methylation in monozygotic twins. *Transl Psychiatry* 2015; **5**: e557.
30. Bipolar D, Schizophrenia Working Group of the Psychiatric Genomics Consortium. Electronic address drve, Bipolar D, Schizophrenia Working Group of the Psychiatric Genomics C. Genomic Dissection of Bipolar Disorder and Schizophrenia, Including 28 Subphenotypes. *Cell* 2018; **173**(7): 1705-1715 e1716.

FIGURE LEGENDS

Figure 1 – Forest plots for the 4 most significant SNPs in SCZ mtCOJO analysis with larger conditional effect sizes

Figure 2 Results from brain cell-type enrichment analyses of raw and conditional GWAS analyses

Tables

Table 1. Summary of datasets used and results from conditional GWAS analysis

| Disorder | Cases | Controls | No. SNPs in original study | No GWS SNPs in merged data | Study reference | No. GWS SNPs in Published Study | Assumed Lifetime Disease Risk | GWS loci in conditional GWAS | New GWS loci | GWS SNPs from unadjusted GWAS with larger conditional effect size |
|-------------|---------|----------|----------------------------|----------------------------|--------------------------|---------------------------------|-------------------------------|------------------------------|--------------|---|
| SCZ | 40,675 | 64,643 | 5,471,613 | 130 | Pardinas et al 2018 | 145 | 0.01 | 43 | 10 | 15 |
| BIP | 20,352 | 31,358 | 9,498,970 | 16 | Stahl et al 2018 BioRxiv | 19 | 0.01 | 4 | 3 | 0 |
| MD | 135,458 | 344,901 | 10,468,943 | 40 | Wray et al 2018 | 44 | 0.15 | 15 | 1 | 5 |
| ADHD | 19,099 | 34,194 | 6,755,648 | 11 | Demontis et al BioRxiv | 12 | 0.05 | 5 | 2 | 3 |
| AUT | 18,381 | 27,969 | 7,539,669 | 2 | Grove et al BioRxiv | 3 | 0.01 | 1 | 0 | 1 |

Table 2. Estimated SNP-based heritability on the liability scale, genetic correlation and LD-score intercepts estimated from LD-score regression

| | SCZ | BIP | MDD | ADHD | AUT |
|------|--------------------|--------------------|---------------------|---------------------|---------------------|
| SCZ | 0.23 (0.01) | <i>0.21 (0.01)</i> | <i>0.03 (0.01)</i> | 0.02 (0.01) | 0.008 (0.01) |
| BIP | 0.67 (0.02) | 0.19 (0.01) | <i>0.05 (0.007)</i> | <i>0.03 (0.006)</i> | 0.009 (0.008) |
| MD | 0.36 (0.02) | 0.35 (0.02) | 0.08 (0.004) | <i>0.10 (0.008)</i> | <i>0.09 (0.008)</i> |
| ADHD | 0.18 (0.03) | 0.15 (0.04) | 0.43 (0.03) | 0.22 (0.01) | <i>0.35 (0.008)</i> |
| AUT | 0.23 (0.05) | 0.15 (0.05) | 0.43 (0.04) | 0.36 (0.05) | 0.12 (0.01) |

LD-score SNP-based heritability on the liability scale and standard error reported on diagonal

r_g and standard error reported below the diagonal

Bivariate ldsc intercept reported above the diagonal. Value significantly greater than zero (in italics) quantify sample overlap

Table 3. GSMR estimates of causal effect of each psychiatric disorder on the others with

conversion to the log odds ratio and liability scales

| Exposure | Outcome | N SNPs | bxy | bxy_se | bxy_liability | OR | bxy_pval |
|----------|---------|--------|-------|--------|---------------|------|----------|
| SCZ | BIP | 111 | 0.417 | 0.019 | 0.417 | 3.06 | 5.0E-109 |
| SCZ | MD | 111 | 0.074 | 0.007 | 0.109 | 1.22 | 4.9E-26 |
| SCZ | ADHD | 111 | 0.054 | 0.019 | 0.066 | 1.16 | 5.2E-03 |
| SCZ | AUT | 111 | 0.144 | 0.019 | 0.144 | 1.47 | 2.9E-09 |
| BIP | SCZ | 16 | 0.498 | 0.039 | 0.498 | 3.82 | 1.6E-37 |
| BIP | MD | 16 | 0.091 | 0.016 | 0.134 | 1.28 | 2.0E-08 |
| BIP | ADHD | 16 | 0.028 | 0.043 | 0.034 | 1.08 | 5.2E-01 |
| BIP | AUT | 16 | 0.123 | 0.046 | 0.123 | 1.39 | 7.4E-03 |
| MD | SCZ | 40 | 0.414 | 0.059 | 0.281 | 2.13 | 2.7E-12 |
| MD | BIP | 40 | 0.600 | 0.068 | 0.408 | 2.97 | 1.1E-18 |
| MD | ADHD | 40 | 0.402 | 0.072 | 0.339 | 2.09 | 2.9E-08 |
| MD | AUT | 40 | 0.463 | 0.078 | 0.314 | 2.33 | 3.7E-11 |
| ADHD | BIP | 13 | 0.135 | 0.052 | 0.109 | 1.34 | 8.9E-03 |
| ADHD | MD | 13 | 0.086 | 0.019 | 0.102 | 1.21 | 9.1E-06 |
| ADHD | SCZ | 13 | 0.156 | 0.043 | 0.126 | 1.40 | 2.8E-04 |
| ADHD | AUT | 11 | 0.333 | 0.060 | 0.269 | 2.06 | 2.9E-08 |
| AUT | SCZ | 11 | 0.063 | 0.041 | 0.063 | 1.19 | 1.3E-01 |
| AUT | BIP | 11 | 0.053 | 0.057 | 0.053 | 1.15 | 2.9E-01 |
| AUT | MD | 11 | 0.011 | 0.021 | 0.016 | 1.03 | 5.9E-01 |
| AUT | ADHD | 11 | 0.413 | 0.062 | 0.512 | 3.03 | 3.60E-11 |

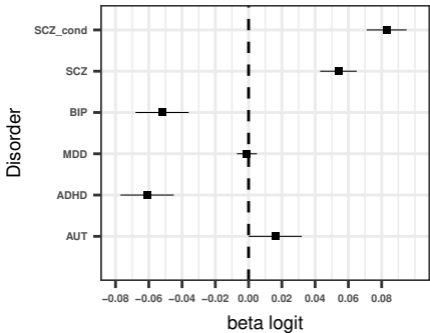
* Estimates using autism as the exposure used instruments with $p < 10E-06$ due to lack of genome-wide significant SNPs for autism

Table 4. Results for SNPs that were genome-wide significant in the conditional analysis and have larger estimated conditional effect sizes than in the original GWAS

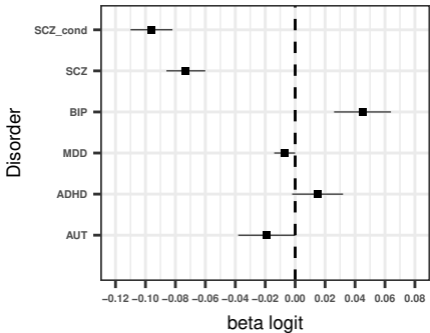
| Disorder | SNP | CHR | Position | A1 | Adjusted beta | SE Adjusted beta | Unadjusted beta | SE Unadjusted beta | Adjusted p-value | Unadjusted p-value | nearestGene |
|----------|-----------|-----|-----------|----|---------------|------------------|-----------------|--------------------|------------------|--------------------|---------------|
| SCZ | rs3764002 | 12 | 108618630 | C | 0.083 | 0.012 | 0.054 | 0.011 | 1.94E-12 | 6.05E-07 | WSCD2 |
| SCZ | rs6095357 | 20 | 47523865 | A | -0.069 | 0.011 | -0.048 | 0.010 | 1.17E-10 | 1.21E-06 | ARFGEF2 |
| SCZ | rs7790864 | 7 | 28478625 | A | -0.062 | 0.011 | -0.044 | 0.010 | 6.33E-09 | 7.18E-06 | CREB5 |
| SCZ | rs1054972 | 19 | 1852582 | A | 0.076 | 0.013 | 0.053 | 0.012 | 6.42E-09 | 1.32E-05 | KLF16 |
| SCZ | rs2867673 | 7 | 71752652 | T | 0.060 | 0.010 | 0.049 | 0.010 | 9.44E-09 | 4.11E-07 | CALN1 |
| SCZ | rs6564668 | 16 | 79457393 | C | -0.060 | 0.010 | -0.038 | 0.010 | 1.05E-08 | 7.94E-05 | RP11-46717.1 |
| SCZ | rs1192276 | 5 | 95047279 | G | -0.060 | 0.010 | -0.044 | 0.010 | 1.22E-08 | 4.36E-06 | RPS18P6 |
| SCZ | rs2973038 | 5 | 37833781 | C | 0.066 | 0.012 | 0.051 | 0.011 | 1.28E-08 | 1.72E-06 | GDNF |
| SCZ | rs1090394 | 5 | 363275 | C | 0.057 | 0.010 | 0.040 | 0.010 | 3.13E-08 | 3.30E-05 | DIP2C |
| SCZ | rs1028293 | 5 | 38703797 | A | 0.058 | 0.011 | 0.041 | 0.010 | 3.97E-08 | 3.17E-05 | TACC1 |
| SCZ | rs6701877 | 1 | 174015259 | G | -0.096 | 0.014 | -0.073 | 0.013 | 1.47E-11 | 2.37E-08 | RP11-160H22.3 |
| SCZ | rs7372313 | 3 | 135872958 | G | -0.069 | 0.010 | -0.062 | 0.010 | 4.26E-11 | 1.54E-10 | MSL2 |
| SCZ | rs1765142 | 11 | 30378559 | C | 0.065 | 0.011 | 0.058 | 0.010 | 1.54E-09 | 1.13E-08 | ARL14EP |
| SCZ | rs5564699 | 3 | 105017864 | G | -0.062 | 0.010 | -0.053 | 0.010 | 2.23E-09 | 3.83E-08 | SRPK2 |
| SCZ | rs1504377 | 60 | 59981768 | A | 0.131 | 0.024 | 0.121 | 0.022 | 3.71E-08 | 4.58E-08 | CCDC175 |
| BIP | rs1255451 | 2 | 23352293 | T | -0.083 | 0.014 | -0.066 | 0.014 | 1.55E-09 | 1.28E-06 | ELAVL2 |
| BIP | rs6891181 | 5 | 80849101 | T | -0.081 | 0.014 | -0.075 | 0.014 | 1.49E-08 | 1.27E-07 | SSBP2 |
| BIP | rs1226891 | 0 | 111878510 | T | -0.097 | 0.018 | -0.091 | 0.018 | 3.29E-08 | 2.73E-07 | ADD3 |

| | | | | | | | | | | | | |
|------|-----------|----|-----------|---|--------|-------|--------|-------|----------|----------|-----------------|--|
| | rs1169737 | | | | | | | | | | | |
| MD | 0 | 20 | 47731767 | T | -0.031 | 0.005 | -0.023 | 0.005 | 3.31E-09 | 3.53E-06 | STAU1 | |
| MD | rs27732 | 5 | 87992576 | A | 0.034 | 0.005 | 0.031 | 0.005 | 1.22E-11 | 1.87E-10 | MEF2C | |
| MD | rs1806153 | 11 | 31850105 | T | 0.037 | 0.006 | 0.036 | 0.006 | 8.78E-10 | 1.18E-09 | RCN1 | |
| MD | rs1354115 | 9 | 2983774 | A | 0.029 | 0.005 | 0.028 | 0.005 | 1.72E-08 | 2.37E-08 | CARM1P1 | |
| MD | rs301799 | 1 | 8489302 | T | -0.028 | 0.005 | -0.026 | 0.005 | 2.49E-08 | 4.68E-08 | RERE | |
| | rs7864810 | | | | | | | | | | | |
| ADHD | 4 | 6 | 50683009 | T | 0.136 | 0.023 | 0.124 | 0.025 | 4.31E-09 | 3.60E-07 | TFAP2D | |
| ADHD | rs2244336 | 10 | 8831827 | C | 0.071 | 0.013 | 0.069 | 0.014 | 3.81E-08 | 3.67E-07 | ENSG00000270234 | |
| | rs1241044 | | | | | | | | | | | |
| ADHD | 4 | 1 | 44188719 | A | 0.107 | 0.014 | 0.106 | 0.015 | 4.23E-15 | 3.85E-13 | ST3GAL3 | |
| | rs1302383 | | | | | | | | | | | |
| ADHD | 2 | 2 | 215219808 | A | 0.133 | 0.020 | 0.117 | 0.021 | 1.23E-11 | 1.62E-08 | SPAG16 | |
| ADHD | rs281320 | 15 | 47769424 | T | -0.080 | 0.013 | -0.074 | 0.013 | 1.84E-10 | 3.14E-08 | SEMA6D | |
| | rs1009910 | | | | | | | | | | | |
| AUT | 0 | 8 | 10576775 | C | 0.084 | 0.014 | 0.084 | 0.015 | 1.20E-09 | 1.07E-08 | SOX7 | |

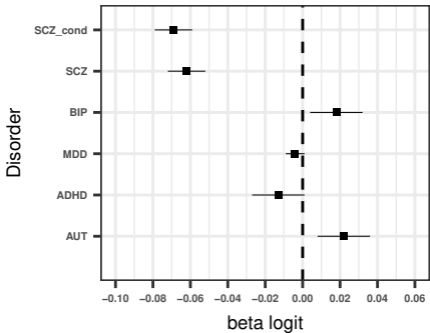
rs3764002 – mtCOJO p-value = 1.9×10^{-12}



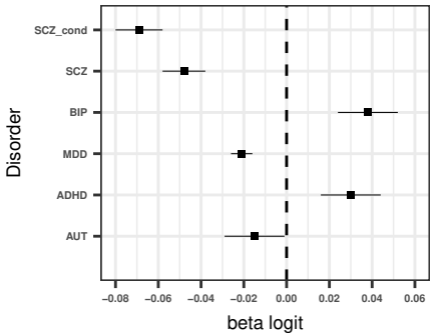
rs6701877 – mtCOJO p-value = 1.47×10^{-11}



rs7372313 – mtCOJO p-value = 4.3×10^{-11}



rs6095357 – mtCOJO p-value = 1.2×10^{-10}



Supplementary Methods

Table of Contents

1. Discussion of mtCOJO method for conditional analysis (Page 1)
2. Discussion of pathway analysis results (Page 4)
3. Summary of estimates of b_{xy} for all combinations of quantitative and binary traits (Page 4)
4. Simulations to confirm derivations (Page 7)
5. Supplementary Figures (Page 10)
6. Acknowledgments (Page 18)

1. Discussion of mtCOJO method for conditional GWAS analysis

Multi-trait, conditional and joint analysis (mtCOJO)

We used the mtCOJO methodology¹ to conduct a conditional GWAS analysis of psychiatric disorders. mtCOJO was developed to generate GWAS summary statistics results for a target trait conditional on a covariate trait, recognising that the covariate trait is frequently not recorded in the individuals measured for the target trait. The mtCOJO method allows conditioning on the exposure by borrowing information from independently collected data, with the data linked through their SNP associations. Briefly, for two traits (y and x) with association effects for SNP z (\hat{b}_{zy} and \hat{b}_{zx} respectively) the association effect estimates for trait y conditional on trait x is estimated as $\hat{b}_{zy}|\hat{b}_{xy} = \hat{b}_{zy} - \hat{b}_{zx}\hat{b}_{xy}$ (see Zhu et al.¹ for details), where \hat{b}_{xy} is the effect of trait x on trait y , as estimated in generalised summary-based Mendelian randomisation (GSMR) analyses. If exposure trait x is causal of the outcome trait y or the two traits are pleiotropically related, we expect the genetic correlation estimated from the conditional GWAS result for trait y and that for trait x to be reduced by a factor proportional to the estimated effect of x on y . In a special case that if traits x and y are genetically identical we expect this correlation to be zero.

Classical MR analyses have the hypothesis of causality of an exposure trait on an outcome trait. Here, when the two disease traits are psychiatric disorders, we have no hypothesis of causality, but rather use GSMR to demonstrate significant bi-directional association of SNPs that are GWS in one disorder with those in another disorder and to estimate the weights for mtCOJO.

mtCOJO allows the analysis conditioning on multiple covarying diseases, so that the effect of a SNP on risk on the disorder of interest conditional upon the covariates on the disorder, is given by $\hat{b}_{zy}|\hat{\mathbf{b}}_{xy} = \hat{b}_{zy} - \hat{\mathbf{b}}_{zx}^t \hat{\mathbf{b}}_{xy}$ where \hat{b}_{zy} is the SNP effect on the disease, $\hat{\mathbf{b}}_{xy}$ is a t -length vector with the i -th element \hat{b}_{x_iy} being the effect of x_i on the disease when all the covariates are fitted jointly, and $\hat{\mathbf{b}}_{zx}$ is a t -length vector of SNP effects on \mathbf{x} . The method is robust to sample overlap between studies.

If the genetic correlation between two disorders is not driven by causality but a large number of pleiotropic effects (generally in the same direction) because of shared genetic pathways, then the GSMR \hat{b}_{xy} reflects an average pleiotropic association between the two disorders. Nonetheless, conditioning on the average effect has meaning, and our conditional results can be used in pathway analyses to identify functionally relevant pathways that are associated with a disorder after accounting for effects of covarying disorders.

While it is possible that differences in quality control analysis or calling/imputation of SNPs across studies could lead to heterogeneity in the results and thus significant effects in the conditional analysis, these datasets were generated using the same analysis pipeline developed by the Psychiatric GWAS Consortium, and hence the likelihood of such heterogeneity is reduced.

Estimating the significance of the difference between raw and conditional estimates.

From Zhu et al, we know that the difference between the raw and the conditional estimates is $\hat{d} = \hat{b}_{zy} - \hat{b}_{zy}|\hat{\mathbf{b}}_{xy} = \hat{\mathbf{b}}_{zx}^t \hat{\mathbf{b}}_{xy}$, where \hat{b}_{zx} , \hat{b}_{zy} and \hat{b}_{xy} are defined the same as above. Therefore, the variance of the difference can be written as $\text{var}(\hat{d}) = \text{var}(\hat{\mathbf{b}}_{zx}^t \hat{\mathbf{b}}_{xy}) = \hat{\mathbf{b}}_{xy}^t \mathbf{V}_{zx} \hat{\mathbf{b}}_{xy}$ with \mathbf{V}_{zx} being the (co)variance matrix of $\hat{\mathbf{b}}_{zx}$ ¹. The significance of the difference can be estimated using the test-statistic $T_d = \hat{d}^2 / \text{var}(\hat{d})$.

If there is a single covariate trait, $\hat{d} = \hat{b}_{zx} \hat{b}_{xy}$ and $\text{var}(\hat{d}) = \text{var}(\hat{b}_{zx} \hat{b}_{xy}) = \hat{b}_{xy}^2 \text{var}(\hat{b}_{zx})$. The significance of the difference can be tested as $T_d = \frac{\hat{d}^2}{\text{var}(\hat{d})} = \frac{(\hat{b}_{zx} \hat{b}_{xy})^2}{\hat{b}_{xy}^2 \text{var}(\hat{b}_{zx})} = \frac{\hat{b}_{zx}^2}{\text{var}(\hat{b}_{zx})}$. Therefore, it suggests the significance of the difference depends on the p-value of SNP effect on the covariate trait. So for a SNP where the estimated effect size in the

covariate traits is very small (no association), we do not expect to see large changes between the raw and conditional estimates.

Interpreting results in the context of sample overlap

From Zhu et al, the joint effects of the covarying traits on the outcome trait are given by

$$\mathbf{b}_{xy} = \mathbf{D}^{-\frac{1}{2}} \mathbf{R}_x^{-1} \mathbf{D}^{\frac{1}{2}} \boldsymbol{\beta}_{xy}$$

where $\mathbf{R}_x = \{r_{g(x_i, x_j)}\}$ is a $t \times t$ matrix with $r_{g(x_i, x_j)}$ being the genetic correlation between covariates i and j , \mathbf{D} is a $t \times t$ diagonal matrix with the i -th diagonal element $h_{SNP(x_i)}^2$ being the SNP-based heritability for the i -th covariate. We estimate $h_{SNP(x_j)}^2$ and $r_{g(x_i, x_j)}$ from GWAS summary data using the LDSC. The calculated genetic correlations are free of bias caused by sample overlap. It is possible that the marginal effects $\boldsymbol{\beta}_{xy}$ could be biased upwards due to sample overlap. However, as we are estimating the joint effects across 4 disorders, any bias would be diluted as the joint effects will be smaller than the marginal effects and the other marginal effects are largely free from bias due to sample overlap.

The sampling variance of the mtCOJO test statistic $\hat{b}_{zy} | \hat{\mathbf{b}}_{xy}$ is approximately $\text{var}(\hat{b}_{zy} | \hat{\mathbf{b}}_{xy}) = \text{var}(\hat{b}_{zy}) + \hat{\mathbf{b}}_{xy}^t \mathbf{V}_{zx} \hat{\mathbf{b}}_{xy} - 2\hat{\mathbf{b}}_{xy}^t \text{cov}(\hat{b}_{zy}, \hat{\mathbf{b}}_{zx})$ where $\mathbf{V}_{zx} = \text{var}(\hat{\mathbf{b}}_{zx})$, and $\text{cov}(\hat{b}_{zy}, \hat{\mathbf{b}}_{zx})$ is a t -length vector with the i -th element $\text{cov}(\hat{b}_{zy}, \hat{b}_{zx_i})$ being the covariance between \hat{b}_{zy} and \hat{b}_{zx_i} . We know from our previous study¹⁷ that $\text{cov}(\hat{b}_{zy}, \hat{b}_{zx_i}) = \rho_{x_i y} r_{p(x_i, y)} \sqrt{\text{var}(\hat{b}_{zx_i}) \text{var}(\hat{b}_{zy})}$ where $\rho_{x_i y}$ is the proportion of sample overlap between x_i and y and $r_{p(x_i, y)}$ is the phenotypic correlation between x_i and y . More generally, if there is a sample overlap between y and \mathbf{x} , $\rho_{x_i y} r_{p(x_i, y)}$ can be approximated by the intercept of a bivariate LDSC analysis between x_i and y (ref³⁰). \mathbf{V}_{zx} is the sampling variance-covariance of $\hat{\mathbf{b}}_{zx}$ with the ij -th element $\text{cov}(\hat{b}_{zx(i)}, \hat{b}_{zx(j)}) = \rho_{x_i x_j} r_{p(x_i, x_j)} \sqrt{\text{var}(\hat{b}_{zx_i}) \text{var}(\hat{b}_{zx_j})}$ where $\rho_{x_i x_j} r_{p(x_i, x_j)}$ can also be approximated by the intercept of a bivariate LDSC analysis between x_i and x_j . Therefore the covariance between traits due to sample overlap is accounted for in estimating the sampling variance of the mtCOJO test-statistic.

Although the test statistic accounts for the sample overlap, the effect size estimate of the effect of trait x conditional on trait y may be conservative (under-estimated) due to sample overlap. The conditional estimate is given by $\hat{b}_{zy} | \hat{\mathbf{b}}_{xy} = \hat{b}_{zy} -$

$\hat{\mathbf{b}}_{zx}^t \hat{\mathbf{b}}_{xy}$. We have shown that any bias in estimating $\hat{\mathbf{b}}_{xy}$ is likely to be small. However, if there is covariance between \hat{b}_{zy} and one or more of the elements of $\hat{\mathbf{b}}_{zx}^t$ this could bias the conditional estimates. However, for positively correlated traits with sample overlap, as is the case for ADHD and autism in this analysis, the bias will be downwards, such that more loci may appear to be shared across disorders, rather than disorder-specific. The implications for the interpretation of these analyses are that if the GWAS studies were conducted in completely independent samples, we may have detected more disorder-specific loci for autism and ADHD. However, given the relatively small sample size of the ADHD and autism studies compared to the other disorders, it is probable that the number of extra loci identified would be small.

2. Discussion of pathway analysis results

Across the five disorders, there were 3 Gene Ontology terms that were more significant after conditioning. The GO Biological Process – Establishment of Localization of the Cell – was more significantly enriched in schizophrenia after conditioning. This is a broad process that includes 1,925 genes and so it is not obvious as to how it may relate to the pathological mechanism of schizophrenia. Among the sub-categories of this process are axonal dopamine secretion, neurotransmitter reuptake and secretion, and postsynaptic neurotransmitter receptor cycle, so it may be of relevance to the pathophysiology of SCZ. *VPS29* which was identified in the SMR analysis is part of this GO category.

Two other GO terms were significant after conditioning and accounting for multiple testing, across all disorders. Both relate to dendrites. The GO category “dendrite” was associated with SCZ but was less significant after conditioning. A related GO biological process “dendrite morphogenesis” was more significantly associated with autism after conditioning ($p_{\text{adj}} = 2.9 \times 10^{-6}$, $p_{\text{unadj}} = 1.9 \times 10^{-04}$). This change in significance does not appear to be driven by the variant near *SOX7* that was more significant after conditioning (Table 4). Decreased branching of dendrites in hippocampal neurons has been found in patients with autism²

3. Summary of estimates of b_{xy} for all combinations of quantitative and binary traits

When estimating b_{xy} using GSMR in instances where the exposure trait and outcome trait are quantitative traits and the effect sizes have been standardised, the effect estimate is directly interpretable as SD units of y per SD unit of x. When using disease traits as exposures, b_{xy} is

estimated on the logit scale and used in mtCOJO. The estimates on the logit scale can be difficult to interpret when disorders have a different prevalence and the proportion of cases and controls used in the GWAS is different from the population prevalence. We derive transformations to make the b_{xy} estimates interpretable when the exposure trait is a disease.

The key transformations of the b_{xy} on the logit scale to the logOR and liability scale are

$$\hat{b}_{xy(\log OR)} = \frac{v_{K_x}}{K_x(1 - K_x)} \hat{b}_{xy(\log it)}$$

$$\hat{b}_{xy(liab)} = \frac{v_{K_x} K_y (1 - K_y)}{v_{K_y} K_x (1 - K_x)} \hat{b}_{xy(\log it)}$$

where K_x is the lifetime risk of the exposure trait and K_y is the lifetime risk of the outcome trait and v_K is the height of the normal distribution at the truncation point on the liability scale corresponding to risk K . $\hat{b}_{xy(\log OR)}$ can be interpreted as the log of the odds ratio of y per 1 SD increase in liability in x . The estimate on the liability scale can be interpreted as the increase in liability in to disorder y per 1 SD increase in liability to x . Note that when two disorders have the same assumed prevalence, as is the case with schizophrenia and bipolar, $\hat{b}_{xy(\log it)} = \hat{b}_{xy(liab)}$. See the derivation below.

For two traits (y and x) with association effect sizes for SNP z (\hat{b}_{zx} and \hat{b}_{zy} , respectively) the association effect size estimates for trait y conditional on trait x ($\hat{b}_{zy|x}$) is estimated as $\hat{b}_{zy|x} \approx \hat{b}_{zy} | \hat{\mathbf{b}}_{xy} = \hat{b}_{zy} - \hat{b}_{zx} \hat{b}_{xy}$, where $\hat{\mathbf{b}}_{xy} = \{\hat{b}_{xy(1)}, \hat{b}_{xy(2)}, \dots, \hat{b}_{xy(m)}\}$ with $\hat{b}_{xy(i)} = \hat{b}_{zy(i)} / \hat{b}_{zx(i)}$, and $\hat{\mathbf{b}}_{xy} \sim N(\mathbf{1} b_{xy}, \mathbf{V})$ where $\mathbf{1}$ is an $m \times 1$ vector of ones and \mathbf{V} is the variance-covariance matrix of $\hat{\mathbf{b}}_{xy}$, and m is the number of genome-wide significant SNPs selected as independently associated with trait x . \hat{b}_{xy} is the effect of trait x on trait y , which can be calculated through GSMR analysis, $\hat{b}_{xy} = (\mathbf{1}' \mathbf{V}^{-1} \mathbf{1})^{-1} \mathbf{1}' \mathbf{V}^{-1} \hat{\mathbf{b}}_{xy}^{-1}$.

When trait x is a dichotomous trait we denote the population lifetime risk as K_x , v_{K_x} as height of the normal curve when truncated at K_x , and the proportion of cases in the samples used to generate the SNP effects as P_x . The effect size estimated from logistic regression of x on SNP

z is on the logit scale $\hat{b}_{zx(\text{logit}(x))}$, such that $\exp(\hat{b}_{zx(\text{logit}(x))})$ is the odds ratio of the SNP for cases of disease x . From Lloyd-Jones et al³, the relationship between $\hat{b}_{zx(\text{logit}(x))}$ and \hat{b}_{zx} on the observed scale from a case-control sample with proportion of cases P_x ($\hat{b}_{zx(01[P_x])}$) is

$$\hat{b}_{zx(01[P_x])} \approx P_x(1 - P_x)\hat{b}_{zx(\text{logit}(x))}$$

From Lee et al. 2011⁴ and Dempster and Lerner⁵ the relationship between \hat{b}_{zx} on the liability scale and ($\hat{b}_{zx(\text{liab})}$) and $\hat{b}_{zx(01[P_x])}$ is

$$\hat{b}_{zx(\text{liab})} = \frac{K_x(1-K_x)}{v_{K_x}P_x(1-P_x)}\hat{b}_{zx(01[P_x])}$$

$$\text{Hence } \hat{b}_{zx(\text{liab})} = \frac{K_x(1-K_x)}{v_{K_x}}\hat{b}_{zx(\text{logit}(x))}$$

So when y is a quantitative trait and x binary, the \hat{b}_{xy} calculated from available summary statistics is $\frac{\hat{b}_{zy}}{\hat{b}_{zx(\text{logit}(x))}} = \hat{b}_{xy(y:\text{logit}(x))}$. A more interpretable regression coefficient is

$$\hat{b}_{xy(\text{liab})} = \frac{\hat{b}_{zy}}{\hat{b}_{zx(\text{liab})}} = \frac{v_{K_x}}{K_x(1-K_x)}\hat{b}_{xy(y:\text{logit}(x))}$$

Similarly, if y is a dichotomous phenotype, the \hat{b}_{xy} calculated from available summary statistics is $\frac{\hat{b}_{zy(\text{logit}(y))}}{\hat{b}_{zx(\text{logit}(x))}} = \hat{b}_{xy(\text{logit}(y):\text{logit}(x))}$, a more interpretable regression coefficient is either as logit of y per phenotypic liability

$$\text{SD unit of } x: \hat{b}_{xy(\text{logit}(y):\text{liab}(x))} = \frac{v_{K_x}}{K_x(1-K_x)}\hat{b}_{xy(\text{logit}(y):\text{logit}(x))}$$

$$\text{SD unit of } y \text{ per phenotypic liability SD unit of } x, \hat{b}_{xy(\text{liab}(y):\text{liab}(x))} = \frac{\hat{b}_{zy(\text{liab})}}{\hat{b}_{zx(\text{liab})}}$$

$$\frac{v_{K_x}K_y(1-K_y)}{v_{K_y}K_x(1-K_x)}\hat{b}_{xy(\text{logit}(y):\text{logit}(x))}$$

So, for schizophrenia and bipolar disorder since we assume $K_x = K_y = 0.01$, then $\hat{b}_{xy(\text{liab}(y):\text{liab}(x))} = \hat{b}_{xy(\text{logit}(y):\text{logit}(x))}$. The interpretation and scaling of \hat{b}_{xy} for any combination of binary and quantitative traits is summarised in **Supplementary Table 9**.

Supplementary Table 9.

| a) Units of \hat{b}_{xy} given $\hat{b}_{xy(i)} = \hat{b}_{zy(i)}/\hat{b}_{zx(i)}$ b) Scale of estimation | Trait y is quantitative Linear regression GWAS \hat{b}_{zy} : Allelic effect in phenotypic SD units of y | Trait y is binary disease Logistic regression GWAS $\hat{b}_{zy(\text{logit}(y))}$: Allelic effect in $\ln(\text{OR})$ of y |
|--|--|--|
| Trait x is quantitative Linear regression GWAS \hat{b}_{zx} : Allelic effect in phenotypic SD units of x | Estimated as \hat{b}_{xy} \hat{b}_{xy} in phenotypic SD units of y per phenotypic SD unit of x | $\hat{b}_{xy(\text{logit}(y):x)}$ \hat{b}_{xy} value is logit SD units for disease y per phenotypic SD of trait x |
| Trait x is binary disease | Estimated as $\hat{b}_{xy(y:\text{logit}(x))}$ | Estimated as $\hat{b}_{xy(\text{logit}(y):\text{logit}(x))}$ |

| | | |
|---|---|--|
| $\hat{b}_{zx(\text{logit}(x))}$: Allelic effect in ln(OR) of x | $\hat{b}_{xy(y:\text{liab}(x))} = \frac{v_{K_x}}{K_x(1-K_x)} \hat{b}_{xy(y:\text{logit}(x))}$ \hat{b}_{xy} in SD unit of y per logit SD unit of x | $\hat{b}_{xy(\text{logit}(y):\text{liab}(x))} = \frac{v_{K_x}}{K_x(1-K_x)} \hat{b}_{xy(\text{logit}(y):\text{logit}(x))}$ \hat{b}_{xy} in logit SD units for disease y per phenotypic liability SD unit of x $= \frac{v_{K_x} K_y (1 - K_y)}{v_{K_y} K_x (1 - K_x)} \hat{b}_{xy(\text{logit}(y):\text{logit}(x))}$ \hat{b}_{xy} in SD units of liability of y per SD unit of liability to x |
|---|---|--|

4. Simulations to confirm derivations

In order to confirm the derivations summarised in Supplementary Table 10, we performed a series of simulations. We simulated 100 SNPs from a binomial distribution $z \sim B(2, p)$ with p being the allele frequency of a SNP $p \sim U(0.01, 0.5)$. We simulated an exposure phenotype under a liability-threshold model in ($n=500,000$ individuals) $x_{\text{liab}} = b_{zx}z + e$, $b_{zx} \sim N(0, 1)$, $e \sim N(0, \sigma_e^2)$, where $\sigma_e^2 = \text{var}(zb_{zx})\left(\frac{1}{R_{zx}^2} - 1\right)$, with R_{zx}^2 was the variance in x explained by z . We set $R_{zx}^2 = 0.2$. x was then standardized with mean 0 and variance 1. Ten different sets of cases and controls were assigned to the underlying simulated liability according to various disease prevalences (K) from 0.01 to 0.1. The sample size of cases was $n_{\text{cases}} = nK$ and that of controls was $n_{\text{controls}} = n_{\text{cases}}\left(\frac{1}{P} - 1\right)$, where P was sample prevalence, $P \sim U(0.1, 0.5)$. The cases and controls were randomly sampled from the whole population. In the simulation, we estimated $\hat{b}_{zx(\text{liab})}$ from the whole population by linear regression and $\hat{b}_{zx(\text{logit})}$ from the ascertained sample by logistic regression. $\hat{b}_{zx(\text{logit})}$ was then transformed to the liability scale. The simulation was replicated 1,000 times. The comparison of estimated and transformed $\hat{b}_{zx(\text{liab})}$ is shown in Supplementary Figure 8.

In the second set of simulations, a dichotomous exposure phenotype was simulated as above with 4 different prevalences ($K_x = 0.01, 0.04, 0.07$ and 0.1) A outcome phenotype y with 200,000 individuals was simulated under the model $y_{\text{liab}} = x_{\text{liab}}b_{xy(\text{liab})} + e_{y(\text{liab})}$, where $e_{y(\text{liab})} \sim N(0, \sigma_{e_{y(\text{liab})}}^2)$. $\sigma_{e_{y(\text{liab})}}^2 = \text{var}(x_{\text{liab}}b_{xy(\text{liab})})\left(\frac{1}{R_{xy}^2} - 1\right)$ with R_{xy}^2 being the variance in y explained by x , $R_{xy}^2 = 0.05$. y was then standardized. We generated an ascertained sample for y using the same method as above. The four prevalences were the same as for disease x , $K_y = (0.01, 0.04, 0.07, 0.1)$. We estimated $\hat{b}_{xy(\text{logit}(y):\text{logit}(x))}$ by GSMR where

$\hat{b}_{zx(\text{logit}(x))}$ and $\hat{b}_{zy(\text{logit}(y))}$ were estimated in the ascertained samples by logistic regression. $\hat{b}_{xy(\text{logit})}$ was then transformed to $\hat{b}_{xy(\text{liab})}$. The simulation was performed 1,000 times.

Because both x and y were standardized, the expected value of $\hat{b}_{xy(\text{liab})} = \sqrt{R_{xy}^2} = 0.223$.

Supplementary Table 10 shows the results from the simulation.

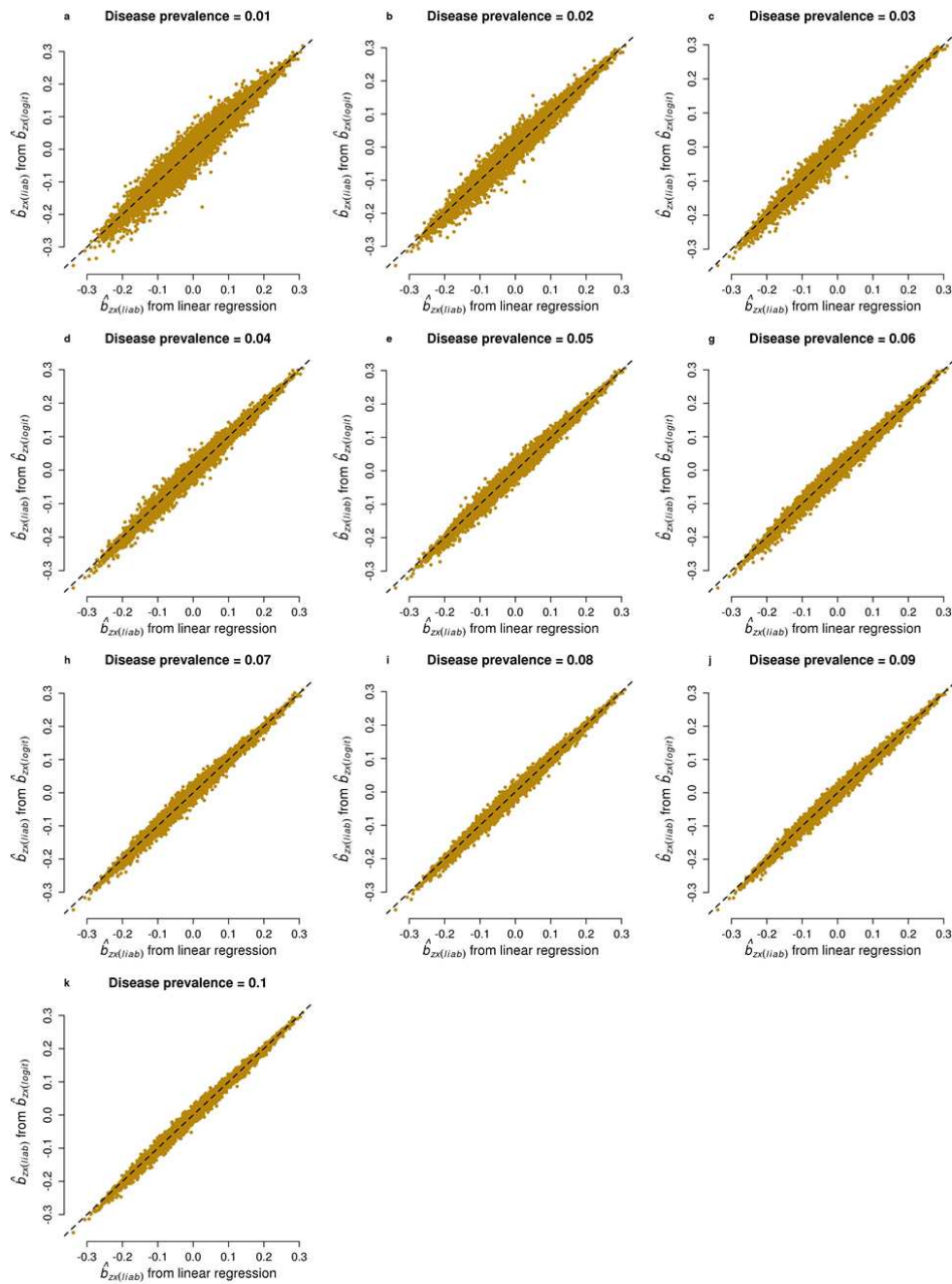
$\hat{b}_{xy(\text{liab})}$ estimated from the logit scale. True $\hat{b}_{xy(\text{liab})}$ is 0.223 which generated $\hat{b}_{xy(\text{logit})}$ ranging from 0.156 to 0.304 depending of K_x, K_y combinations

| Disease prevalence | Scale | $K_y = 0.01$ | $K_y = 0.04$ | $K_y = 0.07$ | $K_y = 0.10$ |
|--------------------|-----------|-------------------|-------------------|-------------------|-------------------|
| $K_x = 0.01$ | logit | 0.214 (0.0007) | 0.180 (0.0004) | 0.165 (0.0003) | 0.156 (0.0002) |
| | liability | 0.214 (0.0007) | 0.215 (0.0004) | 0.216 (0.0004) | 0.216 (0.0003) |
| $K_x = 0.04$ | logit | 0.263 (0.0009) | 0.220 (0.0004) | 0.202 (0.0003) | 0.191 (0.0003) |
| | liability | 0.219 (0.0007) | 0.220 (0.0004) | 0.220 (0.0004) | 0.220 (0.0003) |
| $K_x = 0.07$ | logit | 0.287 (0.0009) | 0.240 (0.0005) | 0.221 (0.0004) | 0.209 (0.0003) |
| | liability | 0.220 (0.0007) | 0.221 (0.0004) | 0.221 (0.0004) | 0.221 (0.0003) |
| $K_x = 0.10$ | logit | 0.304 (0.0010) | 0.254 (0.0005) | 0.234 (0.0004) | 0.221 (0.0003) |
| | liability | 0.220 (0.0007) | 0.221 (0.0004) | 0.221 (0.0004) | 0.221 (0.0003) |

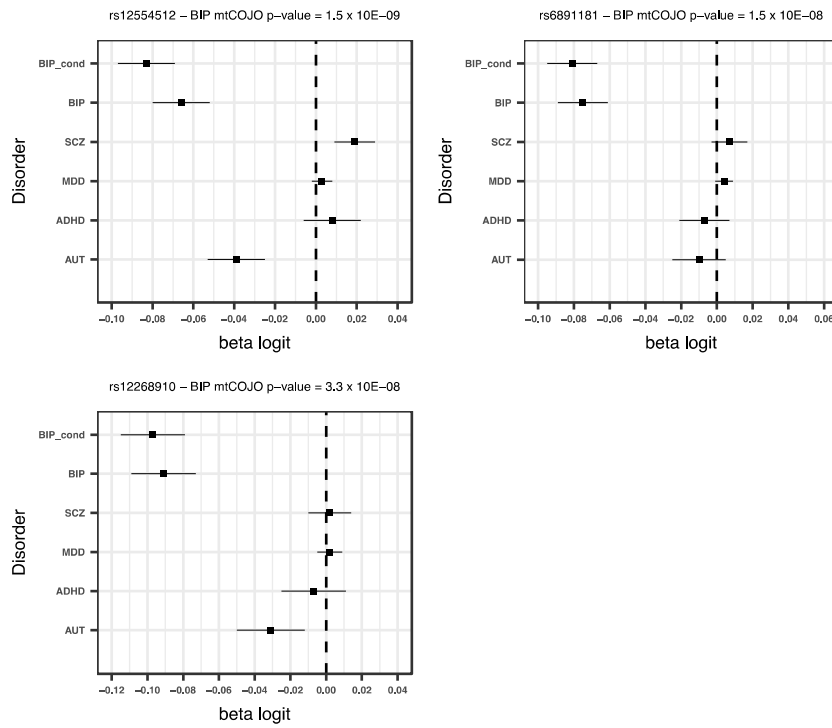
The simulations show that the transformation to the liability scale from the logit scale is a good approximation of the true estimate of $\hat{b}_{xy(liab)}$. The estimate is slightly downward biased and the bias is greater when the prevalence of the exposure trait is low.

Supplementary Figures

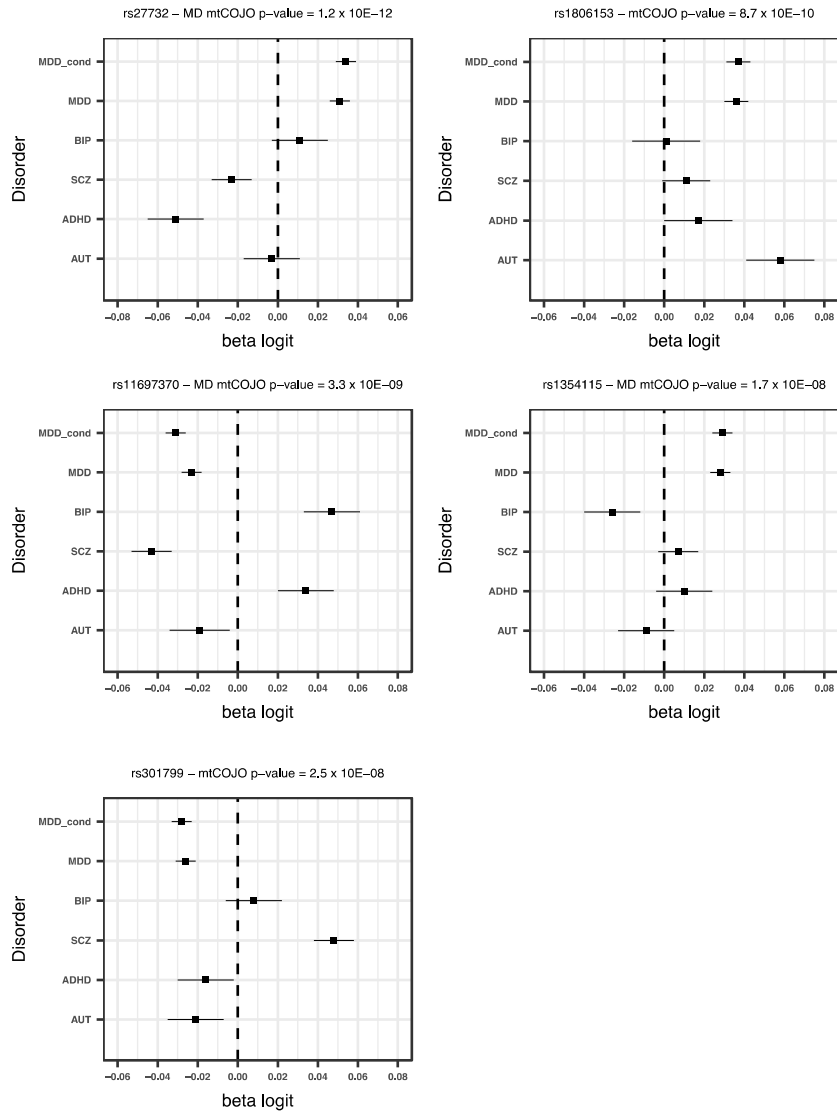
Supplementary Figure 1. Results from simulations to estimate b_{xy} on the liability scale using derived transformation



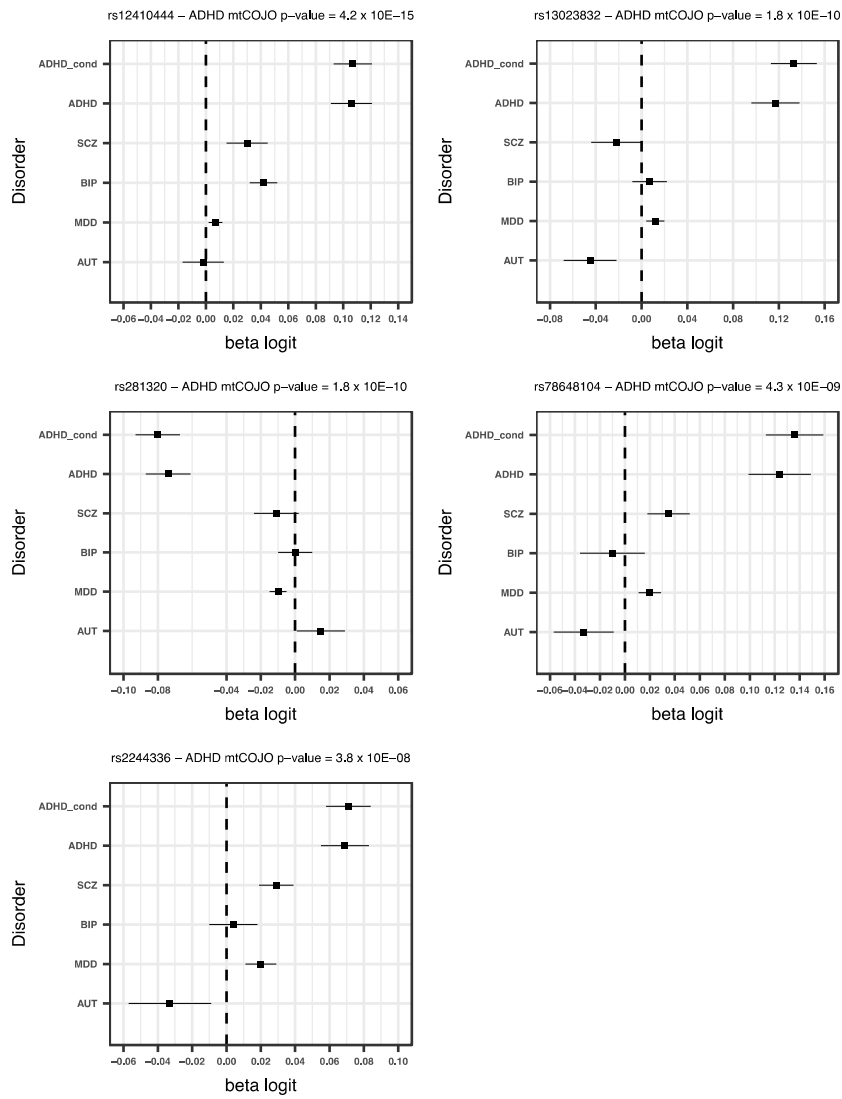
Supplementary Figure 2a-c. Significant SNPs from bipolar conditional analysis. All SNPs were not significant in the raw bipolar GWAS



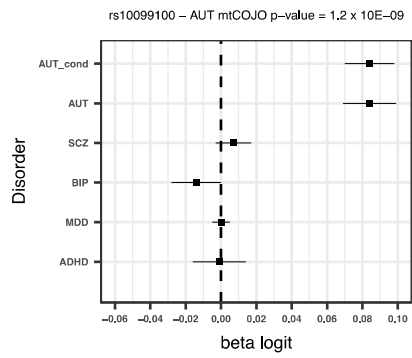
Supplementary Figure 3(a-e) Genome-wide significant SNPs from mtCOJO analysis of major depression with larger conditional effect sizes



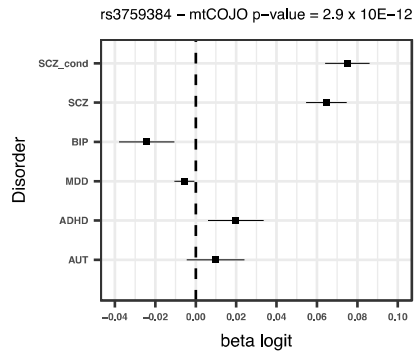
Supplementary Figure 4(a-e) Genome-wide significant SNPs from mtCOJO analysis of ADHD with larger conditional effect sizes.



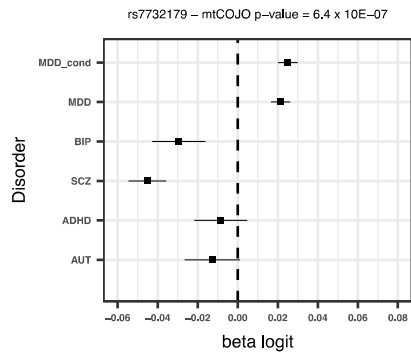
Supplementary Figure 5. Genome-wide significant SNP from mtCOJO analysis of AUT with larger conditional effect size.



Supplementary Figure 6. Forest plot for mtCOJO analysis of rs3759384 – an eQTL for VPS29 – that was significant in SMR analysis.

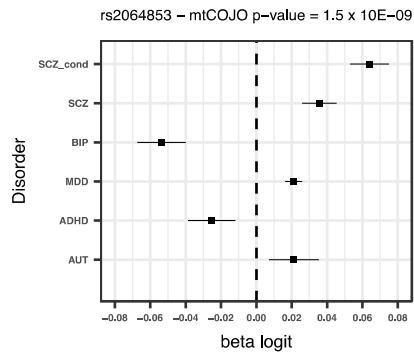


Supplementary Figure 7. Forest plot for mtCOJO analysis of rs2064853
– an eQTL for PCDHA7 in brain– that was significant in SMR analysis and has opposite
effects on MD and SCZ



Supplementary Figure 8. Forest plot for mtCOJO analysis of rs2064853

– an mQTL for DNA methylation in the promotor of the CSE1L gene – that was significant in SMR analysis and has opposite effects on SCZ and BIP



1. Zhu Z, Zheng Z, Zhang F, Wu Y, Trzaskowski M, Maier R *et al.* Causal associations between risk factors and common diseases inferred from GWAS summary data. *Nat Commun* 2018; **9**(1): 224.
2. Arikath J. Molecular mechanisms of dendrite morphogenesis. *Frontiers in Cellular Neuroscience* 2012; **6**(61).
3. Lloyd-Jones LR, Robinson MR, Yang J, Visscher PM. Transformation of Summary Statistics from Linear Mixed Model Association on All-or-None Traits to Odds Ratio. *Genetics* 2018.
4. Lee SH, Wray NR, Goddard ME, Visscher PM. Estimating missing heritability for disease from genome-wide association studies. *American journal of human genetics* 2011; **88**(3): 294-305.
5. Dempster ER, Lerner IM. Heritability of Threshold Characters. *Genetics* 1950; **35**(2): 212-236.

Acknowledgments

ARIC: The Atherosclerosis Risk in Communities Study is carried out as a collaborative study supported by National Heart, Lung, and Blood Institute contracts (HHSN268201100005C, HHSN268201100006C, HHSN268201100007C, HHSN268201100008C, HHSN268201100009C, HHSN268201100010C, HHSN268201100011C, and HHSN268201100012C), R01HL087641, R01HL59367 and R01HL086694; National Human Genome Research Institute contract U01HG004402; and National Institutes of Health contract HHSN268200625226C. The authors thank the staff and participants of the ARIC study for their important contributions. Infrastructure was partly supported by Grant Number UL1RR025005, a component of the National Institutes of Health and NIH Roadmap for Medical Research.

CMC (Synapse accession: syn2759792): CMC data were generated as part of the CommonMind Consortium supported by funding from Takeda Pharmaceuticals Company Limited, F. HoffmanLa Roche Ltd and NIH grants R01MH085542, R01MH093725, P50MH066392, P50MH080405, R01MH097276, RO1-MH-075916, P50M096891, P50MH084053S1, R37MH057881 and R37MH057881S1, HHSN271201300031C, AG02219, AG05138 and MH06692. Brain tissue for the study was obtained from the following brain bank collections: the Mount Sinai NIH Brain and Tissue Repository, the University of

Pennsylvania Alzheimer's Disease Core Center, the University of Pittsburgh NeuroBioBank and Brain and Tissue Repositories and the NIMH Human Brain Collection Core. CMC Leadership: Pamela Sklar, Joseph Buxbaum (Icahn School of Medicine at Mount Sinai), Bernie Devlin, David Lewis (University of Pittsburgh), Raquel Gur, Chang-Gyu Hahn (University of Pennsylvania), Keisuke Hirai, Hiroyoshi Toyoshiba (Takeda Pharmaceuticals Company Limited), Enrico Domenici, Laurent Essioux (F. Hoffman-La Roche Ltd), Lara Mangravite, Mette Peters (Sage Bionetworks), Thomas Lehner, Barbara Lipska (NIMH). GTEx (dbGaP accession: phs000424.v6.p1): The Genotype-Tissue Expression (GTEx) Project was supported by the Common Fund of the Office of the Director of the National Institutes of Health (commonfund.nih.gov/GTEx). Additional funds were provided by the NCI, NHGRI, NHLBI, NIDA, NIMH, and NINDS. Donors were enrolled at Biospecimen Source Sites funded by NCI Leidos Biomedical Research, Inc. subcontracts to the National Disease Research Interchange (10XS170), Roswell Park Cancer Institute (10XS171), and Science Care, Inc. (X10S172). The Laboratory, Data Analysis, and Coordinating Center (LDACC) was funded through a contract (HHSN268201000029C) to the The Broad Institute, Inc. Biorepository operations were funded through a Leidos Biomedical Research, Inc. subcontract to Van Andel Research Institute (10ST1035). Additional data repository and project management were provided by Leidos Biomedical Research, Inc. (HHSN261200800001E). The Brain Bank was supported supplements to University of Miami grant DA006227. Statistical Methods development grants were made to the University of Geneva (MH090941 & MH101814), the University of Chicago (MH090951, MH090937, MH101825, & MH101820), the University of North Carolina - Chapel Hill (MH090936), North Carolina State University (MH101819), Harvard University (MH090948), Stanford University (MH101782), Washington University (MH101810), and to the University of Pennsylvania (MH101822)

GTEx (dbGaP accession: phs000424.v6.p1): The Genotype-Tissue Expression (GTEx) Project was supported by the Common Fund of the Office of the Director of the National Institutes of Health (commonfund.nih.gov/GTEx). Additional funds were provided by the NCI, NHGRI, NHLBI, NIDA, NIMH, and NINDS. Donors were enrolled at Biospecimen Source Sites funded by NCI Leidos Biomedical Research, Inc. subcontracts to the National Disease Research Interchange (10XS170), Roswell Park Cancer Institute (10XS171), and Science Care, Inc. (X10S172). The Laboratory, Data Analysis, and Coordinating Center (LDACC) was funded through a contract (HHSN268201000029C) to the The Broad Institute, Inc. Biorepository operations were funded through a Leidos Biomedical Research, Inc. subcontract to Van Andel Research Institute (10ST1035). Additional data repository and project management were provided by Leidos Biomedical Research, Inc. (HHSN261200800001E). The Brain Bank was supported supplements to University of Miami grant DA006227. Statistical Methods development grants were made to the University of Geneva (MH090941 & MH101814), the University of Chicago (MH090951, MH090937, MH101825, & MH101820), the University of North Carolina - Chapel Hill (MH090936), North Carolina State University (MH101819), Harvard University (MH090948), Stanford University (MH101782), Washington University (MH101810), and to the University of Pennsylvania (MH101822)

Supplementary Table 2. Comparison between conditional and raw results for five psychiatric disorders. Variants that are genome-wide significant in the adjusted analysis and have larger conditional effect sizes than raw effect sizes are SNPs where $b_diff < 0$ are SNPs with larger conditional effect size than raw effect size.

| Disorder | SNP | chr | pos | A1_scz | b_scz_adj | se_scz_adj |
|----------|-------------|-----|-----------|--------|-----------|------------|
| SCZ | rs3764002 | 12 | 108618630 | C | 0.083 | 0.012 |
| SCZ | rs6095357 | 20 | 47523865 | A | -0.069 | 0.011 |
| SCZ | rs7790864 | 7 | 28478625 | A | -0.062 | 0.011 |
| SCZ | rs1054972 | 19 | 1852582 | A | 0.076 | 0.013 |
| SCZ | rs2867673 | 7 | 71752652 | T | 0.060 | 0.010 |
| SCZ | rs6564668 | 16 | 79457393 | C | -0.060 | 0.010 |
| SCZ | rs11922765 | 3 | 95047279 | G | -0.060 | 0.010 |
| SCZ | rs2973038 | 5 | 37833781 | C | 0.066 | 0.012 |
| SCZ | rs10903945 | 10 | 363275 | C | 0.057 | 0.010 |
| SCZ | rs10282935 | 8 | 38703797 | A | 0.058 | 0.011 |
| SCZ | rs6701877 | 1 | 174015259 | G | -0.096 | 0.014 |
| SCZ | rs7372313 | 3 | 135872958 | G | -0.069 | 0.010 |
| SCZ | rs1765142 | 11 | 30378559 | C | 0.065 | 0.011 |
| SCZ | rs55646993 | 7 | 105017864 | G | -0.062 | 0.010 |
| SCZ | rs150437760 | 14 | 59981768 | A | 0.131 | 0.024 |
| SCZ | rs13201681 | 6 | 28394680 | C | -0.196 | 0.019 |
| SCZ | rs2660304 | 1 | 98512127 | G | 0.106 | 0.013 |
| SCZ | rs4766428 | 12 | 110723245 | C | 0.081 | 0.011 |
| SCZ | rs6065094 | 20 | 37453194 | A | -0.074 | 0.011 |
| SCZ | rs12293670 | 11 | 124612932 | A | 0.072 | 0.011 |
| SCZ | rs11783093 | 8 | 27425349 | C | -0.094 | 0.015 |
| SCZ | rs4129585 | 8 | 143312933 | A | 0.066 | 0.010 |
| SCZ | rs2851447 | 12 | 123665113 | G | -0.074 | 0.012 |
| SCZ | rs7432375 | 3 | 136288405 | G | -0.066 | 0.011 |
| SCZ | rs13135092 | 4 | 103198082 | A | -0.125 | 0.020 |
| SCZ | rs34796896 | 3 | 180623255 | G | -0.078 | 0.013 |
| SCZ | rs6002655 | 22 | 42603814 | C | 0.063 | 0.011 |
| SCZ | rs7951870 | 11 | 46373311 | T | -0.082 | 0.014 |
| SCZ | rs11874716 | 18 | 52750688 | T | 0.061 | 0.010 |
| SCZ | rs16867576 | 5 | 88746331 | A | 0.094 | 0.016 |
| SCZ | rs4144797 | 2 | 233562197 | T | 0.063 | 0.011 |
| SCZ | rs12416331 | 10 | 104928914 | T | -0.106 | 0.018 |
| SCZ | rs7632834 | 3 | 17886678 | T | -0.060 | 0.010 |
| SCZ | rs4936215 | 11 | 133852684 | A | 0.075 | 0.013 |
| SCZ | rs12129573 | 1 | 73768366 | C | 0.061 | 0.011 |
| SCZ | rs9461856 | 6 | 33395199 | G | 0.059 | 0.010 |
| SCZ | rs10503253 | 8 | 4180844 | C | 0.071 | 0.013 |
| SCZ | rs62334820 | 4 | 176855221 | C | 0.073 | 0.013 |
| SCZ | rs1353545 | 3 | 60287845 | G | 0.061 | 0.011 |

| | | | | | |
|-----|------------|----|-------------|--------|-------|
| SCZ | rs7632921 | 3 | 71543758 G | -0.058 | 0.011 |
| SCZ | rs2949006 | 2 | 200715388 T | 0.071 | 0.013 |
| SCZ | rs7129727 | 11 | 57484660 G | 0.061 | 0.011 |
| SCZ | rs9607782 | 22 | 41587556 T | 0.067 | 0.012 |
| SCZ | rs17465671 | 16 | 63712719 C | -0.058 | 0.011 |
| SCZ | rs301818 | 1 | 8503242 G | 0.060 | 0.011 |
| SCZ | rs7596038 | 2 | 58383820 C | -0.056 | 0.010 |
| SCZ | rs10148671 | 14 | 29469373 T | -0.059 | 0.011 |
| SCZ | rs12705761 | 7 | 110976264 G | -0.058 | 0.011 |
| SCZ | rs1451488 | 2 | 199990107 A | -0.056 | 0.010 |
| SCZ | rs58950470 | 11 | 65383755 G | 0.059 | 0.011 |
| SCZ | rs2053079 | 19 | 30987423 A | -0.064 | 0.012 |
| SCZ | rs2007044 | 12 | 2344960 A | -0.056 | 0.010 |
| SCZ | rs2917569 | 11 | 132568255 T | 0.056 | 0.010 |
| SCZ | rs1899543 | 11 | 24406419 A | -0.055 | 0.010 |
| SCZ | rs12668848 | 7 | 2020995 G | -0.055 | 0.010 |
| SCZ | rs9403484 | 6 | 143651969 C | 0.064 | 0.012 |
| SCZ | rs14403 | 1 | 243663893 C | -0.065 | 0.013 |
| SCZ | rs36043959 | 8 | 111472014 G | 0.065 | 0.013 |
| SCZ | rs1473594 | 8 | 60696526 T | 0.053 | 0.010 |
| SCZ | rs6680011 | 1 | 95840866 A | -0.073 | 0.014 |
| SCZ | rs1080500 | 3 | 53175017 G | -0.056 | 0.011 |
| SCZ | rs7701440 | 5 | 60620980 T | -0.051 | 0.010 |
| SCZ | rs3743078 | 15 | 78894759 C | -0.060 | 0.012 |
| SCZ | rs12129719 | 1 | 66324512 G | 0.052 | 0.011 |
| SCZ | rs12628643 | 22 | 40015493 C | 0.053 | 0.011 |
| SCZ | rs2332700 | 14 | 72417326 C | 0.057 | 0.012 |
| SCZ | rs7789569 | 7 | 104927586 T | 0.052 | 0.011 |
| SCZ | rs760608 | 6 | 114719447 G | -0.056 | 0.012 |
| SCZ | rs7216638 | 17 | 2156453 T | -0.053 | 0.011 |
| SCZ | rs2905432 | 19 | 19484295 G | -0.051 | 0.011 |
| SCZ | rs1319017 | 9 | 84736303 G | 0.052 | 0.011 |
| SCZ | rs215411 | 4 | 23423603 T | 0.052 | 0.011 |
| SCZ | rs7499750 | 16 | 13749265 A | 0.057 | 0.012 |
| SCZ | rs7801375 | 7 | 131567263 A | -0.067 | 0.014 |
| SCZ | rs10791097 | 11 | 130718630 T | 0.048 | 0.010 |
| SCZ | rs36104021 | 12 | 103361112 C | 0.078 | 0.017 |
| SCZ | rs12704290 | 7 | 86427626 G | -0.075 | 0.016 |
| SCZ | rs1120004 | 12 | 23633432 T | 0.055 | 0.012 |
| SCZ | rs7142769 | 14 | 104228841 C | 0.051 | 0.011 |
| SCZ | rs7893279 | 10 | 18745105 T | 0.077 | 0.017 |
| SCZ | rs10520163 | 4 | 170626552 T | 0.047 | 0.010 |
| SCZ | rs12148337 | 15 | 70589272 T | 0.047 | 0.010 |

| | | | | | |
|-----|------------|----|-------------|--------|-------|
| SCZ | rs281299 | 15 | 47686081 C | 0.048 | 0.011 |
| SCZ | rs6434928 | 2 | 198304577 G | -0.049 | 0.011 |
| SCZ | rs4650963 | 1 | 177309490 G | 0.070 | 0.016 |
| SCZ | rs1191551 | 14 | 30000405 T | 0.056 | 0.013 |
| SCZ | rs6035706 | 20 | 20821005 A | -0.050 | 0.011 |
| SCZ | rs211829 | 7 | 110048893 T | 0.047 | 0.011 |
| SCZ | rs4925114 | 17 | 17711270 A | 0.049 | 0.011 |
| SCZ | rs2514218 | 11 | 113392994 C | -0.049 | 0.011 |
| SCZ | rs2970610 | 1 | 44097530 T | 0.048 | 0.011 |
| SCZ | rs11646127 | 16 | 29966277 G | -0.047 | 0.011 |
| SCZ | rs6800435 | 3 | 10804551 C | 0.070 | 0.016 |
| SCZ | rs324015 | 12 | 57490100 T | -0.054 | 0.012 |
| SCZ | rs2910032 | 5 | 152540354 C | -0.045 | 0.010 |
| SCZ | rs12898315 | 15 | 61854003 G | 0.045 | 0.010 |
| SCZ | rs4240748 | 12 | 92246786 C | -0.046 | 0.011 |
| SCZ | rs17514846 | 15 | 91416550 A | -0.045 | 0.011 |
| SCZ | rs10985817 | 9 | 101071090 T | -0.060 | 0.014 |
| SCZ | rs2161711 | 16 | 71359066 A | 0.058 | 0.014 |
| SCZ | rs1339227 | 6 | 73155701 C | -0.046 | 0.011 |
| SCZ | rs16902086 | 5 | 45285752 A | -0.046 | 0.011 |
| SCZ | rs489939 | 3 | 161470592 G | -0.045 | 0.011 |
| SCZ | rs7010876 | 8 | 89264751 T | -0.048 | 0.012 |
| SCZ | rs10783624 | 12 | 39522907 C | -0.046 | 0.011 |
| SCZ | rs3735025 | 7 | 137074844 T | 0.044 | 0.011 |
| SCZ | rs35346733 | 3 | 2521322 G | 0.055 | 0.013 |
| SCZ | rs704373 | 3 | 63867355 A | 0.045 | 0.011 |
| SCZ | rs6694545 | 1 | 30437268 A | 0.049 | 0.012 |
| SCZ | rs13121251 | 4 | 143829759 T | 0.045 | 0.011 |
| SCZ | rs217287 | 6 | 84407466 C | -0.042 | 0.010 |
| SCZ | rs1975802 | 16 | 68285847 A | -0.053 | 0.014 |
| SCZ | rs783540 | 15 | 83254708 A | -0.040 | 0.010 |
| SCZ | rs11685299 | 2 | 225391296 C | -0.043 | 0.011 |
| SCZ | rs28374258 | 1 | 190949551 T | 0.050 | 0.013 |
| SCZ | rs9881798 | 3 | 16846967 A | -0.040 | 0.011 |
| SCZ | rs133047 | 22 | 41027819 T | 0.066 | 0.017 |
| SCZ | rs12991836 | 2 | 145141541 A | -0.041 | 0.011 |
| SCZ | rs56873913 | 19 | 50091199 T | 0.048 | 0.013 |
| SCZ | rs2077586 | 2 | 73161551 A | 0.045 | 0.012 |
| SCZ | rs12447860 | 16 | 58642638 T | -0.039 | 0.011 |
| SCZ | rs11587347 | 1 | 239198959 C | -0.066 | 0.018 |
| SCZ | rs2410572 | 8 | 18421474 G | -0.038 | 0.010 |
| SCZ | rs10196799 | 2 | 185640728 A | 0.038 | 0.010 |
| SCZ | rs1042992 | 8 | 26269191 C | 0.049 | 0.014 |

| | | | | | | |
|-----|-------------|----|-----------|---|--------|-------|
| SCZ | rs55669358 | 8 | 34312412 | T | -0.065 | 0.018 |
| SCZ | rs9545047 | 13 | 79859456 | A | 0.037 | 0.011 |
| SCZ | rs10156310 | 8 | 38209129 | A | 0.045 | 0.013 |
| SCZ | rs56145559 | 2 | 73623439 | C | 0.044 | 0.013 |
| SCZ | rs634940 | 6 | 93077500 | G | 0.041 | 0.012 |
| SCZ | rs11993663 | 8 | 10032894 | C | 0.036 | 0.011 |
| SCZ | rs7225476 | 17 | 78561603 | G | 0.034 | 0.010 |
| SCZ | rs13169274 | 5 | 137855305 | T | -0.035 | 0.010 |
| SCZ | rs893949 | 11 | 134296384 | C | -0.030 | 0.011 |
| SCZ | rs12908161 | 15 | 85207825 | A | 0.033 | 0.012 |
| SCZ | rs11584091 | 1 | 150101169 | C | -0.038 | 0.014 |
| SCZ | rs75968099 | 3 | 36858583 | C | 0.029 | 0.011 |
| SCZ | rs35604463 | 14 | 99712032 | G | -0.028 | 0.011 |
| SCZ | rs7191183 | 16 | 9900057 | T | -0.029 | 0.011 |
| SCZ | rs112509803 | 7 | 24735004 | G | 0.030 | 0.016 |

| Disorder | SNP | chr | pos | A1_bip | b_bip_adj | se_bip_adj |
|----------|-------------|-----|-----------|--------|-----------|------------|
| BIP | rs12554512 | 9 | 23352293 | T | -0.083 | 0.014 |
| BIP | rs6891181 | 5 | 80849101 | T | -0.081 | 0.014 |
| BIP | rs12268910 | 10 | 111878510 | T | -0.097 | 0.018 |
| BIP | rs9834970 | 3 | 36856030 | T | -0.074 | 0.013 |
| BIP | rs73496688 | 11 | 79156748 | A | 0.103 | 0.019 |
| BIP | rs111444407 | 19 | 19358207 | T | 0.099 | 0.018 |
| BIP | rs11724116 | 4 | 162294038 | T | -0.099 | 0.019 |
| BIP | rs884301 | 17 | 53367464 | T | 0.072 | 0.014 |
| BIP | rs329319 | 5 | 133906609 | A | 0.073 | 0.014 |
| BIP | rs2314398 | 2 | 97413488 | C | 0.071 | 0.014 |
| BIP | rs10455979 | 6 | 166995260 | C | -0.064 | 0.014 |
| BIP | rs174592 | 11 | 61618608 | A | -0.064 | 0.014 |
| BIP | rs55648125 | 6 | 50816718 | A | -0.098 | 0.021 |
| BIP | rs138321 | 22 | 41209304 | A | 0.059 | 0.013 |
| BIP | rs2302417 | 3 | 52814256 | A | -0.058 | 0.014 |
| BIP | rs71395455 | 15 | 85153804 | A | 0.063 | 0.015 |
| BIP | rs13231398 | 7 | 110197412 | C | -0.091 | 0.022 |
| BIP | rs17150022 | 7 | 24771777 | T | -0.078 | 0.020 |
| BIP | rs10744560 | 12 | 2387099 | T | 0.038 | 0.014 |

| Disorder | SNP | chr | pos | A1_mdd | b_md_adj | se_md_adj |
|----------|------------|-----|----------|--------|----------|-----------|
| MD | rs11697370 | 20 | 47731767 | T | -0.031 | 0.005 |
| MD | rs27732 | 5 | 87992576 | A | 0.034 | 0.005 |
| MD | rs1806153 | 11 | 31850105 | T | 0.037 | 0.006 |
| MD | rs1354115 | 9 | 2983774 | A | 0.029 | 0.005 |
| MD | rs301799 | 1 | 8489302 | T | -0.028 | 0.005 |

| | | | | | | |
|----|------------|----|-----------|---|--------|-------|
| MD | rs12552 | 13 | 53625781 | A | 0.040 | 0.005 |
| MD | rs1432639 | 1 | 72813218 | A | 0.038 | 0.005 |
| MD | rs8025231 | 15 | 37648402 | A | -0.031 | 0.005 |
| MD | rs915057 | 14 | 64686207 | A | -0.030 | 0.005 |
| MD | rs11135349 | 5 | 164523472 | A | -0.028 | 0.005 |
| MD | rs12958048 | 18 | 53101598 | A | 0.030 | 0.005 |
| MD | rs4904738 | 14 | 42179732 | T | -0.028 | 0.005 |
| MD | rs12129573 | 1 | 73768366 | A | 0.029 | 0.005 |
| MD | rs12666117 | 7 | 109105611 | A | 0.027 | 0.005 |
| MD | rs159963 | 1 | 8504421 | A | -0.028 | 0.005 |
| MD | rs16854051 | 4 | 42123892 | T | -0.033 | 0.006 |
| MD | rs1363104 | 5 | 103917797 | C | 0.027 | 0.005 |
| MD | rs10149470 | 14 | 104017953 | A | -0.027 | 0.005 |
| MD | rs4261101 | 1 | 90796053 | A | -0.028 | 0.005 |
| MD | rs2389016 | 1 | 80799329 | T | 0.029 | 0.005 |
| MD | rs7430565 | 3 | 158107180 | A | -0.026 | 0.005 |
| MD | rs10959913 | 9 | 11544964 | T | 0.031 | 0.006 |
| MD | rs6905391 | 6 | 28262686 | A | -0.037 | 0.007 |
| MD | rs5758265 | 22 | 41617897 | A | 0.029 | 0.006 |
| MD | rs11643192 | 16 | 72214276 | A | 0.026 | 0.005 |
| MD | rs4074723 | 12 | 23947737 | A | -0.026 | 0.005 |
| MD | rs7198928 | 16 | 7666402 | T | 0.027 | 0.005 |
| MD | rs2005864 | 14 | 75377692 | T | 0.026 | 0.005 |
| MD | rs7029033 | 9 | 126682068 | T | 0.048 | 0.010 |
| MD | rs10950398 | 7 | 12264871 | A | 0.025 | 0.005 |
| MD | rs62099069 | 18 | 36883737 | A | -0.025 | 0.005 |
| MD | rs4869056 | 5 | 166992078 | A | -0.025 | 0.005 |
| MD | rs7856424 | 9 | 119733595 | T | -0.027 | 0.005 |
| MD | rs1226412 | 2 | 157111313 | T | 0.030 | 0.006 |
| MD | rs4143229 | 13 | 44327799 | A | -0.045 | 0.009 |
| MD | rs11682175 | 2 | 57987593 | T | -0.023 | 0.005 |
| MD | rs11663393 | 18 | 50614732 | A | 0.024 | 0.005 |
| MD | rs8063603 | 16 | 6310645 | A | -0.025 | 0.005 |
| MD | rs77135925 | 17 | 27495269 | T | -0.041 | 0.009 |
| MD | rs61867293 | 10 | 106563924 | T | -0.028 | 0.006 |
| MD | rs7200826 | 16 | 13066833 | T | 0.025 | 0.006 |

| Disorder | SNP | chr | pos | A1_adhd | b_adhd_adj | se_adhd_adj | |
|----------|------------|-----|-----|-----------|------------|-------------|-------|
| ADHD | rs78648104 | | 6 | 50683009 | T | 0.136 | 0.023 |
| ADHD | rs2244336 | | 10 | 8831827 | C | 0.071 | 0.013 |
| ADHD | rs12410444 | | 1 | 44188719 | A | 0.107 | 0.014 |
| ADHD | rs13023832 | | 2 | 215219808 | A | 0.133 | 0.020 |
| ADHD | rs281320 | | 15 | 47769424 | T | -0.080 | 0.013 |

| | | | | | | |
|------|------------|----|-----------|---|--------|-------|
| ADHD | rs74760947 | 8 | 34352610 | A | -0.168 | 0.030 |
| ADHD | rs4858241 | 3 | 20669071 | T | 0.071 | 0.013 |
| ADHD | rs1427829 | 12 | 89760744 | A | 0.066 | 0.013 |
| ADHD | rs10262192 | 7 | 114091753 | A | 0.063 | 0.012 |
| ADHD | rs212178 | 16 | 72578131 | A | -0.090 | 0.019 |
| ADHD | rs11591402 | 10 | 106747354 | A | -0.067 | 0.015 |
| ADHD | rs4916723 | 5 | 87854395 | A | -0.050 | 0.013 |
| ADHD | rs2391769 | 1 | 96978961 | A | -0.045 | 0.013 |

| Disorder | SNP | chr | pos | A1_aut | b_aut_adj | se_aut_adj | |
|----------|------------|-----|-----|----------|-----------|------------|-------|
| AUT | rs10099100 | | 8 | 10576775 | C | 0.084 | 0.014 |
| AUT | rs910805 | | 20 | 21248116 | A | 0.077 | 0.015 |

sorders

Effect sizes than raw effect sizes are highlighted in blue

| p_scz_adj | b_scz_unadj | se_scz_unadj | p_scz_unadj | b_scz_diff | se_diff | p_diff |
|-----------|-------------|--------------|-------------|------------|---------|----------|
| 1.94E-12 | 0.054 | 0.011 | 6.05E-07 | -0.029 | 0.007 | 8.68E-05 |
| 1.17E-10 | -0.048 | 0.010 | 1.21E-06 | -0.021 | 0.007 | 1.47E-03 |
| 6.33E-09 | -0.044 | 0.010 | 7.18E-06 | -0.018 | 0.007 | 7.04E-03 |
| 6.42E-09 | 0.053 | 0.012 | 1.32E-05 | -0.024 | 0.008 | 3.93E-03 |
| 9.44E-09 | 0.049 | 0.010 | 4.11E-07 | -0.011 | 0.006 | 8.49E-02 |
| 1.05E-08 | -0.038 | 0.010 | 7.94E-05 | -0.022 | 0.006 | 7.15E-04 |
| 1.22E-08 | -0.044 | 0.010 | 4.36E-06 | -0.015 | 0.006 | 1.82E-02 |
| 1.28E-08 | 0.051 | 0.011 | 1.72E-06 | -0.015 | 0.007 | 3.96E-02 |
| 3.13E-08 | 0.040 | 0.010 | 3.30E-05 | -0.017 | 0.006 | 5.64E-03 |
| 3.97E-08 | 0.041 | 0.010 | 3.17E-05 | -0.017 | 0.006 | 7.55E-03 |
| 1.47E-11 | -0.073 | 0.013 | 2.37E-08 | -0.023 | 0.009 | 9.69E-03 |
| 4.26E-11 | -0.062 | 0.010 | 1.54E-10 | -0.007 | 0.006 | 2.80E-01 |
| 1.54E-09 | 0.058 | 0.010 | 1.13E-08 | -0.008 | 0.007 | 2.27E-01 |
| 2.23E-09 | -0.053 | 0.010 | 3.83E-08 | -0.009 | 0.006 | 1.49E-01 |
| 3.71E-08 | 0.121 | 0.022 | 4.58E-08 | -0.010 | 0.014 | 4.92E-01 |
| 5.98E-26 | -0.235 | 0.017 | 1.32E-41 | 0.039 | 0.011 | 4.71E-04 |
| 1.56E-15 | 0.108 | 0.012 | 2.18E-18 | 0.003 | 0.008 | 7.46E-01 |
| 6.00E-14 | 0.076 | 0.010 | 2.68E-14 | -0.005 | 0.007 | 4.67E-01 |
| 2.03E-11 | -0.085 | 0.010 | 7.91E-17 | 0.011 | 0.007 | 9.75E-02 |
| 6.98E-11 | 0.081 | 0.010 | 1.70E-15 | 0.009 | 0.007 | 1.71E-01 |
| 1.30E-10 | -0.093 | 0.014 | 7.64E-12 | 0.000 | 0.009 | 9.57E-01 |
| 1.62E-10 | 0.082 | 0.010 | 9.26E-18 | 0.016 | 0.006 | 1.26E-02 |
| 2.45E-10 | -0.087 | 0.011 | 5.55E-16 | 0.013 | 0.007 | 6.11E-02 |
| 2.96E-10 | -0.068 | 0.010 | 4.07E-12 | 0.001 | 0.006 | 8.26E-01 |
| 3.58E-10 | -0.149 | 0.018 | 7.87E-16 | 0.024 | 0.012 | 5.20E-02 |
| 1.57E-09 | -0.083 | 0.012 | 3.19E-12 | 0.006 | 0.008 | 4.71E-01 |
| 3.01E-09 | 0.075 | 0.010 | 2.15E-14 | 0.012 | 0.006 | 5.91E-02 |
| 3.16E-09 | -0.093 | 0.013 | 2.99E-13 | 0.012 | 0.008 | 1.72E-01 |
| 3.52E-09 | 0.072 | 0.010 | 8.44E-14 | 0.010 | 0.006 | 1.09E-01 |
| 5.23E-09 | 0.101 | 0.015 | 1.65E-11 | 0.007 | 0.010 | 4.91E-01 |
| 5.87E-09 | 0.082 | 0.010 | 4.33E-16 | 0.019 | 0.007 | 4.76E-03 |
| 7.02E-09 | -0.145 | 0.017 | 7.09E-18 | 0.040 | 0.011 | 3.59E-04 |
| 8.54E-09 | -0.058 | 0.010 | 2.52E-09 | -0.002 | 0.006 | 7.23E-01 |
| 8.72E-09 | 0.091 | 0.012 | 5.32E-14 | 0.016 | 0.008 | 3.69E-02 |
| 8.93E-09 | 0.076 | 0.010 | 8.94E-15 | 0.015 | 0.007 | 1.92E-02 |
| 9.21E-09 | 0.071 | 0.010 | 1.68E-13 | 0.011 | 0.006 | 7.57E-02 |
| 1.52E-08 | 0.066 | 0.012 | 9.60E-09 | -0.005 | 0.008 | 5.35E-01 |
| 1.69E-08 | 0.081 | 0.012 | 9.60E-12 | 0.009 | 0.008 | 2.75E-01 |
| 2.10E-08 | 0.059 | 0.010 | 5.67E-09 | -0.002 | 0.007 | 7.33E-01 |

| | | | | | | |
|----------|--------|-------|----------|--------|-------|----------|
| 4.11E-08 | -0.057 | 0.010 | 9.52E-09 | -0.001 | 0.006 | 8.17E-01 |
| 4.33E-08 | 0.100 | 0.012 | 3.69E-17 | 0.029 | 0.008 | 2.46E-04 |
| 4.50E-08 | 0.063 | 0.010 | 1.47E-09 | 0.001 | 0.007 | 8.71E-01 |
| 4.61E-08 | 0.081 | 0.011 | 5.54E-13 | 0.015 | 0.008 | 5.20E-02 |
| 5.08E-08 | -0.058 | 0.010 | 4.14E-09 | 0.000 | 0.006 | 9.93E-01 |
| 5.10E-08 | 0.060 | 0.010 | 3.79E-09 | 0.000 | 0.007 | 9.82E-01 |
| 5.52E-08 | -0.067 | 0.010 | 2.37E-12 | 0.011 | 0.006 | 8.73E-02 |
| 6.76E-08 | -0.063 | 0.010 | 5.46E-10 | 0.004 | 0.007 | 5.41E-01 |
| 6.96E-08 | -0.066 | 0.010 | 5.11E-11 | 0.007 | 0.007 | 2.61E-01 |
| 7.22E-08 | -0.067 | 0.010 | 4.75E-12 | 0.011 | 0.006 | 9.62E-02 |
| 8.72E-08 | 0.057 | 0.010 | 2.07E-08 | -0.002 | 0.007 | 8.10E-01 |
| 9.65E-08 | -0.071 | 0.011 | 1.82E-10 | 0.007 | 0.007 | 3.67E-01 |
| 9.74E-08 | -0.089 | 0.010 | 5.63E-20 | 0.033 | 0.006 | 3.98E-07 |
| 9.89E-08 | 0.061 | 0.010 | 3.11E-10 | 0.005 | 0.006 | 4.29E-01 |
| 1.05E-07 | -0.058 | 0.009 | 1.23E-09 | 0.003 | 0.006 | 6.28E-01 |
| 1.13E-07 | -0.085 | 0.010 | 1.11E-18 | 0.030 | 0.006 | 3.19E-06 |
| 1.68E-07 | 0.064 | 0.011 | 1.41E-08 | 0.000 | 0.007 | 9.77E-01 |
| 1.80E-07 | -0.074 | 0.012 | 1.71E-10 | 0.009 | 0.008 | 2.58E-01 |
| 2.89E-07 | 0.080 | 0.012 | 4.07E-12 | 0.016 | 0.008 | 4.37E-02 |
| 3.25E-07 | 0.064 | 0.010 | 3.33E-11 | 0.011 | 0.006 | 9.63E-02 |
| 3.98E-07 | -0.074 | 0.013 | 2.83E-08 | 0.001 | 0.009 | 9.50E-01 |
| 5.40E-07 | -0.072 | 0.010 | 2.71E-12 | 0.016 | 0.007 | 2.32E-02 |
| 7.61E-07 | -0.072 | 0.010 | 3.72E-14 | 0.021 | 0.006 | 6.42E-04 |
| 7.82E-07 | -0.078 | 0.011 | 3.11E-12 | 0.018 | 0.007 | 1.42E-02 |
| 9.83E-07 | 0.054 | 0.010 | 3.35E-08 | 0.002 | 0.007 | 7.27E-01 |
| 1.03E-06 | 0.070 | 0.010 | 3.03E-12 | 0.017 | 0.007 | 9.52E-03 |
| 1.37E-06 | 0.070 | 0.011 | 1.52E-10 | 0.013 | 0.007 | 7.99E-02 |
| 1.93E-06 | 0.065 | 0.010 | 7.00E-11 | 0.014 | 0.007 | 3.90E-02 |
| 1.94E-06 | -0.061 | 0.011 | 1.90E-08 | 0.005 | 0.007 | 4.85E-01 |
| 1.98E-06 | -0.065 | 0.010 | 4.59E-10 | 0.011 | 0.007 | 9.52E-02 |
| 2.16E-06 | -0.069 | 0.010 | 6.62E-12 | 0.017 | 0.007 | 8.89E-03 |
| 2.36E-06 | 0.066 | 0.010 | 7.82E-11 | 0.014 | 0.007 | 3.55E-02 |
| 2.70E-06 | 0.058 | 0.010 | 1.40E-08 | 0.006 | 0.007 | 3.51E-01 |
| 2.89E-06 | 0.071 | 0.011 | 4.24E-10 | 0.014 | 0.007 | 6.73E-02 |
| 3.04E-06 | -0.077 | 0.013 | 6.27E-09 | 0.010 | 0.009 | 2.28E-01 |
| 3.12E-06 | 0.063 | 0.010 | 3.29E-11 | 0.015 | 0.006 | 1.72E-02 |
| 3.36E-06 | 0.090 | 0.016 | 7.31E-09 | 0.012 | 0.010 | 2.36E-01 |
| 3.40E-06 | -0.114 | 0.015 | 3.57E-14 | 0.039 | 0.010 | 8.75E-05 |
| 3.41E-06 | 0.062 | 0.011 | 1.42E-08 | 0.007 | 0.007 | 3.19E-01 |
| 3.80E-06 | 0.077 | 0.010 | 4.51E-14 | 0.026 | 0.007 | 1.00E-04 |
| 4.09E-06 | 0.111 | 0.015 | 4.80E-13 | 0.035 | 0.010 | 7.19E-04 |
| 4.87E-06 | 0.053 | 0.010 | 2.81E-08 | 0.006 | 0.006 | 3.55E-01 |
| 5.79E-06 | 0.054 | 0.010 | 1.16E-08 | 0.008 | 0.006 | 2.30E-01 |

| | | | | | | |
|----------|--------|-------|----------|-------|-------|----------|
| 5.87E-06 | 0.055 | 0.010 | 2.19E-08 | 0.007 | 0.007 | 2.98E-01 |
| 6.34E-06 | -0.073 | 0.010 | 3.62E-13 | 0.024 | 0.007 | 4.19E-04 |
| 7.54E-06 | 0.082 | 0.014 | 1.16E-08 | 0.012 | 0.010 | 1.98E-01 |
| 8.02E-06 | 0.073 | 0.012 | 4.12E-10 | 0.017 | 0.008 | 2.97E-02 |
| 8.08E-06 | -0.060 | 0.010 | 7.24E-09 | 0.010 | 0.007 | 1.66E-01 |
| 8.44E-06 | 0.059 | 0.010 | 2.29E-09 | 0.012 | 0.007 | 7.60E-02 |
| 8.59E-06 | 0.057 | 0.010 | 2.64E-08 | 0.008 | 0.007 | 2.40E-01 |
| 8.87E-06 | -0.073 | 0.010 | 2.42E-12 | 0.023 | 0.007 | 4.93E-04 |
| 9.27E-06 | 0.068 | 0.010 | 1.39E-11 | 0.020 | 0.007 | 3.01E-03 |
| 1.04E-05 | -0.071 | 0.010 | 5.52E-13 | 0.024 | 0.007 | 2.22E-04 |
| 1.05E-05 | 0.082 | 0.015 | 2.00E-08 | 0.012 | 0.010 | 2.27E-01 |
| 1.08E-05 | -0.072 | 0.011 | 1.42E-10 | 0.018 | 0.008 | 1.72E-02 |
| 1.18E-05 | -0.063 | 0.010 | 3.72E-11 | 0.018 | 0.006 | 3.93E-03 |
| 1.40E-05 | 0.057 | 0.010 | 2.51E-09 | 0.012 | 0.006 | 5.55E-02 |
| 1.96E-05 | -0.056 | 0.010 | 2.15E-08 | 0.010 | 0.007 | 1.38E-01 |
| 2.03E-05 | -0.069 | 0.010 | 2.55E-12 | 0.023 | 0.007 | 3.97E-04 |
| 2.09E-05 | -0.080 | 0.013 | 1.02E-09 | 0.020 | 0.009 | 2.25E-02 |
| 2.17E-05 | 0.070 | 0.013 | 4.22E-08 | 0.012 | 0.008 | 1.57E-01 |
| 2.23E-05 | -0.063 | 0.010 | 3.76E-10 | 0.017 | 0.007 | 1.15E-02 |
| 2.56E-05 | -0.066 | 0.010 | 5.55E-11 | 0.020 | 0.007 | 2.93E-03 |
| 2.80E-05 | -0.057 | 0.010 | 1.24E-08 | 0.012 | 0.007 | 7.16E-02 |
| 3.11E-05 | -0.062 | 0.011 | 6.51E-09 | 0.014 | 0.007 | 5.16E-02 |
| 3.56E-05 | -0.060 | 0.010 | 5.44E-09 | 0.014 | 0.007 | 4.00E-02 |
| 3.84E-05 | 0.065 | 0.010 | 7.02E-11 | 0.020 | 0.007 | 1.95E-03 |
| 4.27E-05 | 0.087 | 0.012 | 2.42E-12 | 0.032 | 0.008 | 9.34E-05 |
| 4.61E-05 | 0.065 | 0.010 | 1.39E-10 | 0.020 | 0.007 | 3.19E-03 |
| 5.23E-05 | 0.077 | 0.011 | 6.20E-12 | 0.028 | 0.007 | 2.10E-04 |
| 6.08E-05 | 0.057 | 0.010 | 4.06E-08 | 0.012 | 0.007 | 7.80E-02 |
| 6.13E-05 | -0.069 | 0.010 | 9.53E-13 | 0.027 | 0.006 | 2.30E-05 |
| 8.92E-05 | -0.069 | 0.013 | 3.56E-08 | 0.016 | 0.008 | 5.41E-02 |
| 1.04E-04 | -0.059 | 0.010 | 8.45E-10 | 0.019 | 0.006 | 3.73E-03 |
| 1.06E-04 | -0.060 | 0.010 | 3.86E-09 | 0.017 | 0.007 | 1.03E-02 |
| 1.13E-04 | 0.073 | 0.012 | 6.35E-10 | 0.024 | 0.008 | 2.69E-03 |
| 1.31E-04 | -0.054 | 0.010 | 2.81E-08 | 0.014 | 0.006 | 3.34E-02 |
| 1.39E-04 | 0.094 | 0.016 | 3.47E-09 | 0.028 | 0.011 | 9.28E-03 |
| 1.44E-04 | -0.061 | 0.010 | 6.46E-10 | 0.020 | 0.007 | 3.14E-03 |
| 1.56E-04 | 0.070 | 0.012 | 2.58E-09 | 0.022 | 0.008 | 6.46E-03 |
| 1.61E-04 | 0.061 | 0.011 | 2.96E-08 | 0.016 | 0.007 | 2.53E-02 |
| 2.13E-04 | -0.062 | 0.010 | 3.28E-10 | 0.023 | 0.006 | 3.56E-04 |
| 2.19E-04 | -0.103 | 0.017 | 4.82E-10 | 0.037 | 0.011 | 7.69E-04 |
| 2.22E-04 | -0.055 | 0.010 | 1.07E-08 | 0.016 | 0.006 | 9.08E-03 |
| 2.52E-04 | 0.056 | 0.010 | 4.51E-09 | 0.018 | 0.006 | 4.22E-03 |
| 2.75E-04 | 0.073 | 0.012 | 3.67E-09 | 0.024 | 0.008 | 4.21E-03 |

| | | | | | | |
|----------|--------|-------|----------|-------|-------|----------|
| 3.44E-04 | -0.095 | 0.017 | 1.37E-08 | 0.030 | 0.011 | 5.71E-03 |
| 4.01E-04 | 0.056 | 0.010 | 1.15E-08 | 0.019 | 0.006 | 4.09E-03 |
| 4.10E-04 | 0.073 | 0.012 | 5.56E-10 | 0.028 | 0.008 | 4.01E-04 |
| 4.86E-04 | 0.072 | 0.012 | 1.01E-09 | 0.027 | 0.008 | 3.81E-04 |
| 6.73E-04 | 0.063 | 0.011 | 1.30E-08 | 0.023 | 0.007 | 1.91E-03 |
| 7.97E-04 | 0.055 | 0.010 | 3.40E-08 | 0.019 | 0.007 | 4.81E-03 |
| 8.45E-04 | 0.052 | 0.010 | 4.86E-08 | 0.018 | 0.006 | 5.32E-03 |
| 9.01E-04 | -0.060 | 0.010 | 7.06E-10 | 0.025 | 0.006 | 8.66E-05 |
| 3.82E-03 | -0.053 | 0.010 | 2.98E-08 | 0.023 | 0.007 | 5.00E-04 |
| 5.43E-03 | 0.067 | 0.011 | 9.41E-10 | 0.034 | 0.007 | 1.79E-06 |
| 7.39E-03 | -0.081 | 0.013 | 8.63E-10 | 0.043 | 0.009 | 4.68E-07 |
| 8.31E-03 | 0.066 | 0.010 | 9.41E-11 | 0.037 | 0.007 | 2.26E-08 |
| 9.88E-03 | -0.056 | 0.010 | 1.66E-08 | 0.029 | 0.006 | 1.03E-05 |
| 9.91E-03 | -0.060 | 0.010 | 6.31E-09 | 0.031 | 0.007 | 6.25E-06 |
| 6.02E-02 | 0.084 | 0.015 | 2.31E-08 | 0.053 | 0.010 | 6.67E-08 |

| p_bip_adj | b_bip_unadj | se_bip_unadj | p_bip_unadj | b_bip_diff | se_bip_diff | p_bip_diff |
|-----------|-------------|--------------|-------------|------------|-------------|------------|
| 1.55E-09 | -0.066 | 0.014 | 1.28E-06 | -0.016 | 0.005 | 1.034E-03 |
| 1.49E-08 | -0.075 | 0.014 | 1.27E-07 | -0.005 | 0.005 | 3.045E-01 |
| 3.29E-08 | -0.091 | 0.018 | 2.73E-07 | -0.006 | 0.006 | 3.142E-01 |
| 2.52E-08 | -0.101 | 0.013 | 5.53E-14 | 0.027 | 0.005 | 2.934E-08 |
| 5.28E-08 | 0.109 | 0.019 | 1.05E-08 | 0.006 | 0.007 | 4.209E-01 |
| 6.25E-08 | 0.117 | 0.018 | 2.40E-10 | 0.017 | 0.007 | 9.750E-03 |
| 1.37E-07 | -0.104 | 0.019 | 3.27E-08 | 0.005 | 0.007 | 4.042E-01 |
| 1.60E-07 | 0.080 | 0.014 | 5.80E-09 | 0.008 | 0.005 | 9.837E-02 |
| 1.66E-07 | 0.079 | 0.014 | 1.54E-08 | 0.006 | 0.005 | 2.062E-01 |
| 7.83E-07 | 0.084 | 0.014 | 5.92E-09 | 0.013 | 0.005 | 1.015E-02 |
| 2.94E-06 | -0.075 | 0.014 | 4.60E-08 | 0.011 | 0.005 | 2.115E-02 |
| 4.95E-06 | -0.077 | 0.014 | 3.66E-08 | 0.013 | 0.005 | 8.251E-03 |
| 5.00E-06 | -0.117 | 0.022 | 4.92E-08 | 0.019 | 0.008 | 1.241E-02 |
| 1.15E-05 | 0.079 | 0.014 | 4.69E-09 | 0.020 | 0.005 | 2.927E-05 |
| 1.66E-05 | -0.079 | 0.014 | 4.93E-09 | 0.021 | 0.005 | 1.356E-05 |
| 1.75E-05 | 0.082 | 0.015 | 1.93E-08 | 0.020 | 0.005 | 2.065E-04 |
| 3.31E-05 | -0.121 | 0.022 | 3.36E-08 | 0.030 | 0.008 | 1.223E-04 |
| 1.30E-04 | -0.113 | 0.020 | 2.70E-08 | 0.035 | 0.007 | 1.715E-06 |
| 6.26E-03 | 0.083 | 0.014 | 2.92E-09 | 0.045 | 0.005 | 5.766E-19 |

| p_md_adj | b_md_unadj | se_md_unadj | p_md_unadj | b_md_diff | se_md_diff | p_md_diff |
|----------|------------|-------------|------------|-----------|------------|-----------|
| 3.31E-09 | -0.023 | 0.005 | 3.53E-06 | 0.007 | 0.002 | 2.04E-05 |
| 1.22E-11 | 0.031 | 0.005 | 1.87E-10 | 0.003 | 0.002 | 5.96E-02 |
| 8.78E-10 | 0.036 | 0.006 | 1.18E-09 | 0.001 | 0.002 | 5.10E-01 |
| 1.72E-08 | 0.028 | 0.005 | 2.37E-08 | 0.001 | 0.002 | 5.53E-01 |
| 2.49E-08 | -0.026 | 0.005 | 4.68E-08 | 0.001 | 0.002 | 4.70E-01 |

| | | | | | | |
|----------|--------|-------|----------|-------|-------|----------|
| 1.66E-15 | 0.043 | 0.005 | 6.07E-19 | 0.003 | 0.002 | 4.15E-02 |
| 9.37E-14 | 0.039 | 0.005 | 4.55E-15 | 0.001 | 0.002 | 7.61E-01 |
| 3.39E-10 | -0.034 | 0.005 | 2.36E-12 | 0.003 | 0.002 | 9.49E-02 |
| 4.30E-09 | -0.030 | 0.005 | 7.61E-10 | 0.000 | 0.002 | 8.73E-01 |
| 1.08E-08 | -0.029 | 0.005 | 1.09E-09 | 0.001 | 0.002 | 5.48E-01 |
| 1.75E-08 | 0.034 | 0.005 | 3.61E-11 | 0.004 | 0.002 | 1.96E-02 |
| 1.82E-08 | -0.029 | 0.005 | 2.57E-09 | 0.000 | 0.002 | 8.04E-01 |
| 3.35E-08 | 0.034 | 0.005 | 4.01E-12 | 0.006 | 0.002 | 3.91E-04 |
| 4.07E-08 | 0.027 | 0.005 | 1.35E-08 | 0.000 | 0.002 | 9.28E-01 |
| 4.44E-08 | -0.027 | 0.005 | 3.19E-08 | 0.001 | 0.002 | 6.61E-01 |
| 7.02E-08 | -0.035 | 0.006 | 3.58E-09 | 0.002 | 0.002 | 4.23E-01 |
| 7.30E-08 | 0.031 | 0.005 | 7.38E-11 | 0.005 | 0.002 | 4.22E-03 |
| 8.21E-08 | -0.029 | 0.005 | 3.05E-09 | 0.002 | 0.002 | 2.73E-01 |
| 9.60E-08 | -0.029 | 0.005 | 1.04E-08 | 0.001 | 0.002 | 5.90E-01 |
| 1.19E-07 | 0.031 | 0.005 | 1.02E-08 | 0.001 | 0.002 | 4.11E-01 |
| 1.32E-07 | -0.029 | 0.005 | 2.87E-09 | 0.003 | 0.002 | 1.16E-01 |
| 1.39E-07 | 0.033 | 0.006 | 5.06E-09 | 0.002 | 0.002 | 2.15E-01 |
| 1.75E-07 | -0.044 | 0.007 | 1.35E-10 | 0.007 | 0.002 | 2.51E-03 |
| 1.87E-07 | 0.031 | 0.005 | 7.55E-09 | 0.002 | 0.002 | 3.22E-01 |
| 1.88E-07 | 0.027 | 0.005 | 3.36E-08 | 0.001 | 0.002 | 7.15E-01 |
| 2.27E-07 | -0.027 | 0.005 | 3.12E-08 | 0.001 | 0.002 | 6.46E-01 |
| 2.81E-07 | 0.028 | 0.005 | 1.00E-08 | 0.002 | 0.002 | 2.60E-01 |
| 3.09E-07 | 0.028 | 0.005 | 6.73E-09 | 0.002 | 0.002 | 1.68E-01 |
| 5.75E-07 | 0.052 | 0.009 | 2.74E-08 | 0.004 | 0.003 | 2.01E-01 |
| 7.05E-07 | 0.027 | 0.005 | 2.55E-08 | 0.002 | 0.002 | 1.58E-01 |
| 7.90E-07 | -0.028 | 0.005 | 1.31E-08 | 0.003 | 0.002 | 8.82E-02 |
| 9.49E-07 | -0.029 | 0.005 | 6.80E-09 | 0.003 | 0.002 | 4.49E-02 |
| 9.64E-07 | -0.031 | 0.005 | 8.48E-09 | 0.004 | 0.002 | 3.70E-02 |
| 1.17E-06 | 0.033 | 0.006 | 2.38E-08 | 0.004 | 0.002 | 8.27E-02 |
| 1.84E-06 | -0.051 | 0.009 | 2.51E-08 | 0.006 | 0.003 | 4.57E-02 |
| 2.81E-06 | -0.028 | 0.005 | 4.68E-09 | 0.005 | 0.002 | 3.05E-03 |
| 2.88E-06 | 0.028 | 0.005 | 1.65E-08 | 0.004 | 0.002 | 1.29E-02 |
| 4.58E-06 | -0.031 | 0.005 | 6.87E-09 | 0.006 | 0.002 | 1.11E-03 |
| 5.10E-06 | -0.049 | 0.009 | 9.36E-09 | 0.009 | 0.003 | 3.37E-03 |
| 6.33E-06 | -0.037 | 0.006 | 6.97E-10 | 0.009 | 0.002 | 1.15E-05 |
| 1.06E-05 | 0.031 | 0.006 | 2.43E-08 | 0.006 | 0.002 | 2.42E-03 |

| p_adhd_adj | b_adhd_unac | se_adhd_unap | adhd_una | b_adhd_diff | se_adhd_diff | p_adhd_diff |
|------------|-------------|--------------|----------|-------------|--------------|-------------|
| 4.31E-09 | 0.124 | 0.025 | 3.60E-07 | 0.011 | 0.010 | 0.272 |
| 3.81E-08 | 0.069 | 0.014 | 3.67E-07 | 0.001 | 0.006 | 0.843 |
| 4.23E-15 | 0.106 | 0.015 | 3.85E-13 | 0.002 | 0.006 | 0.768 |
| 1.23E-11 | 0.117 | 0.021 | 1.62E-08 | 0.016 | 0.009 | 0.091 |
| 1.84E-10 | -0.074 | 0.013 | 3.14E-08 | 0.006 | 0.006 | 0.279 |

| | | | | | | |
|----------|--------|-------|----------|-------|-------|-------|
| 1.85E-08 | -0.180 | 0.032 | 1.35E-08 | 0.011 | 0.014 | 0.404 |
| 8.95E-08 | 0.079 | 0.014 | 1.74E-08 | 0.008 | 0.006 | 0.160 |
| 1.73E-07 | 0.080 | 0.013 | 1.82E-09 | 0.014 | 0.006 | 0.012 |
| 5.17E-07 | 0.073 | 0.013 | 2.89E-08 | 0.011 | 0.006 | 0.060 |
| 1.70E-06 | -0.115 | 0.020 | 7.68E-09 | 0.025 | 0.009 | 0.005 |
| 1.35E-05 | -0.093 | 0.016 | 1.34E-08 | 0.026 | 0.007 | 0.000 |
| 9.75E-05 | -0.077 | 0.014 | 1.58E-08 | 0.027 | 0.006 | 0.000 |
| 4.55E-04 | -0.075 | 0.014 | 3.96E-08 | 0.030 | 0.006 | 0.000 |

| p_aut_adj | b_aut_unadj | se_aut_unadj | p_aut_unadj | b_aut_diff | se_aut_diff | p_aut_diff |
|-----------|-------------|--------------|-------------|------------|-------------|------------|
| 1.20E-09 | 0.084 | 0.015 | 1.07E-08 | 0.000 | 0.020 | 0.494 |
| 3.22E-07 | -0.096 | 0.016 | 2.04E-09 | -0.004 | 0.022 | 0.447 |

b_mdd_una se_mdd_una p_mdd_una d_b_bip_unadj se_bip_unadj p_bip_unadj b_adhd_unac

| | | | | | | |
|--------|-------|-----------|--------|-------|----------|--------|
| -0.001 | 0.006 | 8.96E-01 | -0.052 | 0.016 | 9.04E-04 | -0.061 |
| -0.021 | 0.005 | 2.98E-05 | 0.038 | 0.014 | 6.28E-03 | 0.030 |
| 0.001 | 0.005 | 8.94E-01 | 0.037 | 0.014 | 7.93E-03 | 0.034 |
| -0.007 | 0.006 | 2.49E-01 | -0.049 | 0.017 | 4.74E-03 | 0.011 |
| -0.002 | 0.005 | 6.44E-01 | -0.019 | 0.014 | 1.73E-01 | -0.058 |
| 0.002 | 0.005 | 6.51E-01 | 0.042 | 0.014 | 2.03E-03 | 0.023 |
| 0.008 | 0.005 | 1.21E-01 | 0.030 | 0.014 | 2.95E-02 | 0.021 |
| 0.009 | 0.006 | 1.09E-01 | -0.029 | 0.015 | 5.63E-02 | 0.009 |
| -0.007 | 0.005 | 1.80E-01 | -0.036 | 0.013 | 8.00E-03 | -0.004 |
| -0.008 | 0.005 | 9.68E-02 | -0.036 | 0.014 | 9.59E-03 | -0.036 |
| -0.007 | 0.007 | 3.44E-01 | 0.045 | 0.019 | 1.73E-02 | 0.015 |
| -0.004 | 0.005 | 4.39E-01 | 0.018 | 0.014 | 1.73E-01 | -0.013 |
| -0.005 | 0.005 | 3.14E-01 | -0.019 | 0.014 | 1.77E-01 | -0.005 |
| -0.004 | 0.005 | 4.16E-01 | 0.019 | 0.013 | 1.49E-01 | -0.034 |
| 0.025 | 0.011 | 1.85E-02 | -0.030 | 0.031 | 3.30E-01 | 0.053 |
| -0.048 | 0.009 | 1.781E-08 | -0.093 | 0.024 | 8.44E-05 | 0.022 |
| -0.001 | 0.006 | 9.402E-01 | 0.012 | 0.017 | 4.72E-01 | -0.019 |
| 0.012 | 0.005 | 1.333E-02 | -0.012 | 0.014 | 3.89E-01 | 0.020 |
| -0.008 | 0.005 | 9.646E-02 | -0.026 | 0.014 | 6.46E-02 | 0.013 |
| 0.006 | 0.005 | 2.251E-01 | 0.021 | 0.014 | 1.44E-01 | 0.027 |
| -0.004 | 0.007 | 5.462E-01 | 0.005 | 0.018 | 7.75E-01 | -0.053 |
| 0.013 | 0.005 | 5.957E-03 | 0.037 | 0.014 | 6.05E-03 | -0.010 |
| 0.005 | 0.006 | 3.560E-01 | -0.032 | 0.015 | 3.49E-02 | 0.032 |
| -0.006 | 0.005 | 2.297E-01 | 0.000 | 0.014 | 9.88E-01 | -0.011 |
| -0.009 | 0.009 | 3.103E-01 | -0.055 | 0.026 | 3.29E-02 | -0.017 |
| 0.004 | 0.006 | 4.913E-01 | -0.011 | 0.017 | 5.09E-01 | 0.002 |
| 0.013 | 0.005 | 8.991E-03 | 0.026 | 0.014 | 5.87E-02 | 0.029 |
| -0.015 | 0.007 | 2.654E-02 | -0.023 | 0.018 | 2.03E-01 | -0.042 |
| 0.022 | 0.005 | 7.027E-06 | 0.021 | 0.014 | 1.17E-01 | 0.019 |
| -0.001 | 0.007 | 9.184E-01 | 0.015 | 0.021 | 4.87E-01 | 0.023 |
| -0.014 | 0.005 | 6.512E-03 | 0.041 | 0.014 | 3.89E-03 | -0.034 |
| -0.034 | 0.009 | 6.645E-05 | -0.081 | 0.024 | 6.45E-04 | -0.049 |
| -0.007 | 0.005 | 1.221E-01 | 0.010 | 0.013 | 4.76E-01 | -0.027 |
| 0.005 | 0.006 | 3.963E-01 | 0.030 | 0.017 | 6.77E-02 | 0.040 |
| 0.034 | 0.005 | 4.006E-12 | 0.031 | 0.014 | 2.36E-02 | 0.043 |
| 0.012 | 0.005 | 1.458E-02 | 0.031 | 0.013 | 1.88E-02 | -0.029 |
| 0.002 | 0.006 | 7.136E-01 | -0.008 | 0.017 | 6.34E-01 | -0.018 |
| 0.018 | 0.006 | 3.814E-03 | 0.017 | 0.017 | 3.12E-01 | 0.036 |
| -0.003 | 0.005 | 6.216E-01 | -0.004 | 0.014 | 7.94E-01 | -0.002 |

| | | | | | | |
|--------|-------|-----------|--------|-------|----------|--------|
| 0.001 | 0.005 | 8.281E-01 | 0.005 | 0.014 | 6.96E-01 | -0.040 |
| 0.014 | 0.006 | 2.073E-02 | 0.063 | 0.017 | 2.10E-04 | 0.003 |
| 0.024 | 0.005 | 3.240E-06 | 0.001 | 0.015 | 9.21E-01 | 0.043 |
| 0.028 | 0.006 | 2.078E-06 | 0.035 | 0.016 | 2.79E-02 | 0.004 |
| -0.004 | 0.005 | 4.192E-01 | 0.002 | 0.014 | 8.71E-01 | -0.017 |
| -0.022 | 0.005 | 2.388E-05 | 0.002 | 0.014 | 8.78E-01 | -0.015 |
| -0.023 | 0.005 | 1.824E-06 | -0.024 | 0.014 | 7.40E-02 | -0.012 |
| -0.007 | 0.005 | 1.701E-01 | -0.009 | 0.014 | 5.34E-01 | 0.013 |
| 0.004 | 0.005 | 4.753E-01 | -0.019 | 0.014 | 1.83E-01 | 0.028 |
| -0.012 | 0.005 | 1.466E-02 | -0.027 | 0.014 | 4.67E-02 | 0.030 |
| 0.000 | 0.005 | 9.645E-01 | 0.001 | 0.014 | 9.48E-01 | -0.014 |
| 0.007 | 0.006 | 2.328E-01 | -0.014 | 0.016 | 3.58E-01 | 0.020 |
| -0.016 | 0.005 | 1.002E-03 | -0.067 | 0.014 | 8.44E-07 | -0.007 |
| 0.001 | 0.005 | 8.327E-01 | 0.011 | 0.014 | 4.45E-01 | 0.011 |
| 0.001 | 0.005 | 7.741E-01 | -0.006 | 0.013 | 6.49E-01 | -0.003 |
| 0.013 | 0.005 | 1.109E-02 | -0.063 | 0.014 | 3.38E-06 | -0.001 |
| 0.004 | 0.006 | 4.755E-01 | 0.006 | 0.016 | 6.87E-01 | -0.021 |
| -0.005 | 0.006 | 4.140E-01 | -0.018 | 0.016 | 2.60E-01 | -0.005 |
| 0.004 | 0.006 | 5.089E-01 | 0.036 | 0.017 | 2.76E-02 | 0.010 |
| -0.011 | 0.005 | 1.866E-02 | 0.024 | 0.014 | 7.17E-02 | -0.013 |
| 0.000 | 0.007 | 9.538E-01 | 0.000 | 0.019 | 9.97E-01 | -0.015 |
| -0.008 | 0.005 | 9.360E-02 | -0.041 | 0.015 | 5.96E-03 | 0.011 |
| 0.000 | 0.005 | 9.827E-01 | -0.043 | 0.013 | 1.42E-03 | -0.002 |
| 0.004 | 0.006 | 4.973E-01 | -0.038 | 0.016 | 1.61E-02 | -0.019 |
| 0.003 | 0.005 | 5.613E-01 | 0.002 | 0.014 | 8.81E-01 | 0.039 |
| 0.010 | 0.005 | 4.392E-02 | 0.036 | 0.014 | 1.10E-02 | 0.002 |
| 0.025 | 0.006 | 6.194E-06 | 0.032 | 0.016 | 3.63E-02 | -0.001 |
| 0.013 | 0.005 | 1.286E-02 | 0.029 | 0.014 | 3.93E-02 | 0.043 |
| -0.001 | 0.005 | 8.141E-01 | -0.011 | 0.015 | 4.81E-01 | -0.010 |
| -0.002 | 0.005 | 7.088E-01 | -0.026 | 0.015 | 7.58E-02 | 0.004 |
| 0.006 | 0.005 | 2.381E-01 | -0.035 | 0.014 | 1.38E-02 | -0.035 |
| 0.008 | 0.005 | 1.029E-01 | 0.028 | 0.014 | 5.09E-02 | 0.033 |
| 0.009 | 0.005 | 7.206E-02 | 0.020 | 0.014 | 1.61E-01 | -0.023 |
| 0.029 | 0.006 | 2.652E-07 | 0.035 | 0.016 | 2.68E-02 | 0.012 |
| -0.003 | 0.007 | 6.161E-01 | -0.028 | 0.018 | 1.26E-01 | 0.021 |
| -0.011 | 0.005 | 2.887E-02 | 0.029 | 0.014 | 3.09E-02 | 0.019 |
| 0.016 | 0.008 | 3.960E-02 | 0.023 | 0.022 | 2.91E-01 | 0.007 |
| 0.007 | 0.007 | 3.183E-01 | -0.088 | 0.021 | 2.39E-05 | 0.020 |
| 0.001 | 0.006 | 8.396E-01 | 0.015 | 0.015 | 3.14E-01 | -0.003 |
| 0.008 | 0.005 | 9.886E-02 | 0.059 | 0.014 | 3.17E-05 | -0.001 |
| 0.007 | 0.008 | 3.722E-01 | 0.075 | 0.022 | 5.49E-04 | 0.033 |
| 0.010 | 0.005 | 3.290E-02 | 0.015 | 0.013 | 2.52E-01 | 0.005 |
| 0.020 | 0.005 | 3.392E-05 | 0.015 | 0.013 | 2.77E-01 | 0.025 |

| | | | | | | |
|--------|-------|-----------|--------|-------|----------|--------|
| 0.010 | 0.005 | 4.959E-02 | 0.012 | 0.014 | 3.83E-01 | 0.023 |
| -0.023 | 0.005 | 8.091E-06 | -0.052 | 0.014 | 2.68E-04 | -0.018 |
| 0.025 | 0.007 | 5.559E-04 | 0.034 | 0.020 | 9.97E-02 | -0.017 |
| 0.007 | 0.006 | 2.030E-01 | 0.033 | 0.016 | 4.13E-02 | 0.042 |
| -0.002 | 0.005 | 7.420E-01 | -0.021 | 0.015 | 1.45E-01 | -0.004 |
| 0.020 | 0.005 | 3.618E-05 | 0.028 | 0.014 | 4.19E-02 | 0.018 |
| -0.014 | 0.005 | 6.005E-03 | 0.018 | 0.014 | 2.01E-01 | -0.039 |
| -0.025 | 0.005 | 4.895E-07 | -0.048 | 0.014 | 6.96E-04 | -0.020 |
| 0.007 | 0.005 | 1.748E-01 | 0.033 | 0.014 | 2.09E-02 | 0.079 |
| -0.008 | 0.005 | 8.274E-02 | -0.053 | 0.014 | 1.33E-04 | -0.018 |
| 0.004 | 0.008 | 5.611E-01 | 0.022 | 0.021 | 3.05E-01 | 0.052 |
| 0.005 | 0.006 | 4.077E-01 | -0.041 | 0.016 | 1.08E-02 | 0.017 |
| -0.002 | 0.005 | 6.684E-01 | -0.039 | 0.013 | 3.26E-03 | -0.022 |
| 0.002 | 0.005 | 7.111E-01 | 0.030 | 0.013 | 2.36E-02 | -0.038 |
| -0.003 | 0.005 | 6.158E-01 | -0.021 | 0.014 | 1.42E-01 | 0.000 |
| -0.018 | 0.005 | 2.199E-04 | -0.047 | 0.014 | 7.60E-04 | -0.040 |
| -0.002 | 0.007 | 7.479E-01 | -0.037 | 0.018 | 4.47E-02 | -0.039 |
| -0.005 | 0.006 | 3.864E-01 | 0.020 | 0.018 | 2.52E-01 | 0.035 |
| -0.015 | 0.005 | 2.895E-03 | -0.037 | 0.014 | 8.24E-03 | -0.016 |
| 0.000 | 0.005 | 9.840E-01 | -0.044 | 0.014 | 2.32E-03 | 0.003 |
| -0.001 | 0.005 | 8.197E-01 | -0.029 | 0.014 | 3.71E-02 | 0.018 |
| 0.007 | 0.005 | 2.121E-01 | -0.027 | 0.015 | 7.19E-02 | -0.011 |
| -0.009 | 0.005 | 7.845E-02 | -0.031 | 0.014 | 3.09E-02 | -0.008 |
| -0.005 | 0.005 | 3.530E-01 | 0.049 | 0.014 | 5.01E-04 | -0.016 |
| 0.009 | 0.006 | 1.665E-01 | 0.068 | 0.017 | 8.75E-05 | 0.013 |
| 0.002 | 0.005 | 6.236E-01 | 0.045 | 0.014 | 1.85E-03 | 0.005 |
| 0.003 | 0.006 | 6.178E-01 | 0.058 | 0.016 | 2.67E-04 | 0.015 |
| 0.015 | 0.005 | 4.842E-03 | 0.026 | 0.015 | 7.82E-02 | 0.005 |
| 0.011 | 0.005 | 2.991E-02 | -0.058 | 0.014 | 2.14E-05 | -0.005 |
| -0.011 | 0.007 | 7.749E-02 | -0.037 | 0.018 | 3.71E-02 | 0.026 |
| -0.007 | 0.005 | 1.486E-01 | -0.040 | 0.014 | 3.33E-03 | -0.007 |
| 0.001 | 0.005 | 8.984E-01 | -0.031 | 0.014 | 3.29E-02 | -0.022 |
| 0.012 | 0.006 | 5.821E-02 | 0.049 | 0.017 | 3.36E-03 | 0.044 |
| 0.002 | 0.005 | 6.768E-01 | -0.029 | 0.014 | 3.20E-02 | -0.032 |
| 0.026 | 0.008 | 7.199E-04 | 0.063 | 0.023 | 5.83E-03 | 0.003 |
| -0.002 | 0.005 | 6.389E-01 | -0.045 | 0.014 | 1.77E-03 | 0.016 |
| -0.010 | 0.006 | 8.187E-02 | 0.045 | 0.017 | 7.07E-03 | 0.004 |
| 0.011 | 0.006 | 3.824E-02 | 0.035 | 0.016 | 2.42E-02 | -0.002 |
| -0.004 | 0.005 | 4.287E-01 | -0.046 | 0.014 | 6.51E-04 | -0.012 |
| -0.021 | 0.008 | 1.149E-02 | -0.088 | 0.023 | 1.63E-04 | 0.030 |
| -0.001 | 0.005 | 8.240E-01 | -0.031 | 0.013 | 2.06E-02 | -0.024 |
| 0.008 | 0.005 | 7.987E-02 | 0.040 | 0.014 | 2.65E-03 | -0.023 |
| 0.002 | 0.006 | 7.320E-01 | 0.055 | 0.018 | 2.25E-03 | -0.017 |

| | | | | | | |
|--------|-------|-----------|--------|-------|----------|--------|
| -0.009 | 0.008 | 2.959E-01 | -0.053 | 0.023 | 2.37E-02 | -0.102 |
| 0.012 | 0.005 | 1.475E-02 | 0.041 | 0.014 | 2.59E-03 | -0.009 |
| 0.013 | 0.006 | 2.861E-02 | 0.060 | 0.017 | 3.40E-04 | 0.036 |
| 0.010 | 0.006 | 9.554E-02 | 0.059 | 0.016 | 3.03E-04 | 0.011 |
| 0.012 | 0.006 | 2.471E-02 | 0.050 | 0.015 | 1.16E-03 | 0.006 |
| -0.009 | 0.005 | 6.844E-02 | 0.033 | 0.014 | 2.01E-02 | 0.020 |
| 0.010 | 0.005 | 3.773E-02 | 0.040 | 0.013 | 2.85E-03 | 0.000 |
| -0.004 | 0.005 | 4.252E-01 | -0.052 | 0.014 | 1.19E-04 | -0.026 |
| 0.005 | 0.005 | 3.036E-01 | -0.052 | 0.014 | 2.30E-04 | 0.016 |
| 0.014 | 0.005 | 9.316E-03 | 0.081 | 0.015 | 7.75E-08 | -0.015 |
| -0.010 | 0.007 | 1.127E-01 | -0.089 | 0.018 | 1.07E-06 | -0.013 |
| -0.005 | 0.005 | 2.872E-01 | 0.081 | 0.014 | 6.44E-09 | -0.024 |
| -0.012 | 0.005 | 1.557E-02 | -0.059 | 0.014 | 1.67E-05 | -0.029 |
| -0.007 | 0.005 | 2.013E-01 | -0.067 | 0.015 | 4.54E-06 | -0.018 |
| 0.028 | 0.008 | 3.286E-04 | 0.114 | 0.021 | 4.92E-08 | 0.055 |

b_mdd_una se_mdd_una p_mdd_una b_scz_unadj se_scz_unadj p_scz_unadj b_adhd_unac

| | | | | | | |
|--------|-------|----------|--------|-------|----------|--------|
| 0.003 | 0.005 | 4.95E-01 | 0.019 | 0.010 | 5.54E-02 | 0.008 |
| 0.004 | 0.005 | 4.94E-01 | 0.007 | 0.010 | 4.94E-01 | -0.007 |
| 0.002 | 0.007 | 8.14E-01 | 0.002 | 0.012 | 8.61E-01 | -0.007 |
| -0.058 | 0.010 | 8.33E-10 | -0.006 | 0.005 | 2.08E-01 | 0.023 |
| 0.032 | 0.014 | 2.24E-02 | 0.006 | 0.007 | 4.20E-01 | -0.004 |
| 0.062 | 0.013 | 3.26E-06 | -0.012 | 0.007 | 7.96E-02 | 0.013 |
| -0.003 | 0.013 | 8.45E-01 | -0.005 | 0.007 | 4.58E-01 | 0.042 |
| 0.010 | 0.010 | 3.29E-01 | 0.006 | 0.005 | 2.48E-01 | 0.016 |
| 0.023 | 0.010 | 2.10E-02 | -0.001 | 0.005 | 8.07E-01 | -0.005 |
| 0.046 | 0.010 | 7.44E-06 | -0.007 | 0.005 | 1.98E-01 | 0.017 |
| -0.027 | 0.010 | 4.70E-03 | -0.009 | 0.005 | 6.41E-02 | -0.002 |
| -0.008 | 0.010 | 4.53E-01 | -0.025 | 0.005 | 4.95E-07 | -0.005 |
| -0.055 | 0.016 | 3.81E-04 | -0.013 | 0.008 | 9.92E-02 | -0.064 |
| 0.039 | 0.010 | 4.96E-05 | 0.019 | 0.005 | 7.06E-05 | -0.006 |
| -0.060 | 0.010 | 3.48E-10 | -0.010 | 0.005 | 3.57E-02 | -0.005 |
| 0.060 | 0.011 | 1.31E-08 | 0.014 | 0.005 | 8.69E-03 | -0.010 |
| -0.046 | 0.016 | 3.10E-03 | -0.013 | 0.008 | 9.46E-02 | -0.017 |
| -0.076 | 0.015 | 1.67E-07 | -0.029 | 0.007 | 8.10E-05 | -0.054 |
| 0.087 | 0.010 | 5.00E-18 | 0.016 | 0.005 | 1.67E-03 | -0.005 |

b_scz_unad se_scz_unadj p_scz_unadj b_bip_unadj se_bip_unadj p_bip_unadj b_adhd_unac

| | | | | | | |
|--------|-------|----------|--------|-------|----------|--------|
| -0.043 | 0.010 | 1.99E-05 | 0.047 | 0.014 | 7.06E-04 | 0.034 |
| -0.023 | 0.010 | 1.94E-02 | 0.011 | 0.014 | 4.19E-01 | -0.051 |
| 0.011 | 0.012 | 3.27E-01 | 0.001 | 0.017 | 9.57E-01 | 0.017 |
| 0.007 | 0.010 | 5.05E-01 | -0.026 | 0.014 | 6.15E-02 | 0.010 |
| 0.048 | 0.010 | 7.12E-07 | 0.008 | 0.014 | 5.60E-01 | -0.016 |

| | | | | | | |
|--------|-------|----------|--------|-------|----------|--------|
| -0.010 | 0.010 | 3.19E-01 | 0.031 | 0.013 | 1.94E-02 | 0.029 |
| 0.026 | 0.010 | 9.00E-03 | 0.008 | 0.014 | 5.44E-01 | 0.016 |
| -0.006 | 0.010 | 5.25E-01 | -0.014 | 0.013 | 2.83E-01 | -0.008 |
| -0.008 | 0.010 | 4.40E-01 | 0.001 | 0.014 | 9.66E-01 | -0.019 |
| -0.010 | 0.010 | 3.03E-01 | 0.003 | 0.014 | 8.27E-01 | -0.006 |
| 0.039 | 0.010 | 1.36E-04 | 0.029 | 0.014 | 4.39E-02 | 0.009 |
| -0.004 | 0.010 | 6.64E-01 | -0.006 | 0.014 | 6.36E-01 | -0.006 |
| 0.076 | 0.010 | 8.94E-15 | 0.031 | 0.014 | 2.36E-02 | 0.043 |
| 0.027 | 0.010 | 5.20E-03 | -0.001 | 0.014 | 9.43E-01 | 0.003 |
| 0.050 | 0.010 | 3.67E-07 | 0.002 | 0.014 | 8.71E-01 | -0.016 |
| -0.032 | 0.012 | 8.70E-03 | -0.015 | 0.017 | 3.78E-01 | -0.037 |
| 0.028 | 0.009 | 3.00E-03 | 0.033 | 0.013 | 1.33E-02 | 0.057 |
| -0.028 | 0.010 | 3.80E-03 | -0.035 | 0.014 | 1.01E-02 | -0.015 |
| -0.002 | 0.010 | 8.47E-01 | -0.010 | 0.014 | 4.93E-01 | -0.007 |
| 0.026 | 0.011 | 1.53E-02 | 0.017 | 0.015 | 2.40E-01 | 0.001 |
| 0.002 | 0.010 | 8.57E-01 | -0.029 | 0.014 | 3.18E-02 | -0.016 |
| -0.012 | 0.011 | 2.72E-01 | 0.018 | 0.016 | 2.69E-01 | -0.007 |
| -0.134 | 0.014 | 2.90E-22 | -0.067 | 0.019 | 4.86E-04 | -0.005 |
| 0.064 | 0.011 | 1.58E-09 | 0.024 | 0.016 | 1.26E-01 | 0.001 |
| 0.009 | 0.010 | 3.82E-01 | 0.047 | 0.014 | 5.48E-04 | -0.025 |
| -0.030 | 0.010 | 2.40E-03 | 0.002 | 0.014 | 8.96E-01 | -0.013 |
| 0.005 | 0.010 | 5.95E-01 | 0.026 | 0.014 | 6.20E-02 | -0.009 |
| 0.030 | 0.010 | 1.80E-03 | 0.009 | 0.014 | 4.88E-01 | 0.016 |
| 0.013 | 0.018 | 4.70E-01 | 0.017 | 0.025 | 5.00E-01 | 0.019 |
| 0.016 | 0.010 | 9.29E-02 | 0.014 | 0.014 | 3.06E-01 | 0.000 |
| -0.014 | 0.010 | 1.62E-01 | -0.024 | 0.014 | 7.64E-02 | -0.012 |
| 0.009 | 0.010 | 3.86E-01 | -0.024 | 0.014 | 8.98E-02 | -0.034 |
| -0.022 | 0.010 | 3.53E-02 | -0.017 | 0.015 | 2.39E-01 | -0.024 |
| 0.011 | 0.012 | 3.60E-01 | 0.024 | 0.017 | 1.42E-01 | 0.023 |
| -0.042 | 0.017 | 1.27E-02 | -0.034 | 0.025 | 1.70E-01 | -0.032 |
| -0.066 | 0.010 | 3.05E-12 | -0.037 | 0.013 | 5.89E-03 | -0.023 |
| 0.041 | 0.010 | 2.70E-05 | 0.017 | 0.014 | 1.99E-01 | 0.028 |
| -0.024 | 0.010 | 2.07E-02 | -0.049 | 0.014 | 6.36E-04 | -0.040 |
| 0.015 | 0.018 | 3.94E-01 | -0.070 | 0.024 | 4.09E-03 | -0.021 |
| -0.057 | 0.012 | 2.97E-06 | -0.045 | 0.017 | 7.56E-03 | -0.085 |
| -0.013 | 0.011 | 2.38E-01 | 0.049 | 0.015 | 1.13E-03 | 0.020 |

| b_mdd_una | se_mdd_una | p_mdd_una | b_scz_unadj | se_scz_unadj | p_scz_unadj | b_bip_unadj |
|-----------|------------|-----------|-------------|--------------|-------------|-------------|
| 0.020 | 0.009 | 2.30E-02 | -0.010 | 0.026 | 6.85E-01 | 0.035 |
| 0.003 | 0.005 | 5.06E-01 | 0.004 | 0.014 | 7.42E-01 | 0.029 |
| 0.007 | 0.005 | 1.74E-01 | 0.042 | 0.010 | 6.51E-05 | 0.030 |
| 0.012 | 0.008 | 1.27E-01 | 0.007 | 0.015 | 6.33E-01 | -0.022 |
| -0.010 | 0.005 | 4.51E-02 | 0.000 | 0.010 | 9.92E-01 | -0.011 |

| | | | | | | |
|--------|-------|----------|--------|-------|----------|--------|
| -0.014 | 0.012 | 2.48E-01 | -0.111 | 0.023 | 1.96E-06 | -0.124 |
| 0.010 | 0.005 | 3.80E-02 | -0.013 | 0.010 | 1.91E-01 | 0.012 |
| 0.007 | 0.005 | 1.28E-01 | -0.016 | 0.010 | 8.71E-02 | 0.003 |
| 0.013 | 0.005 | 8.15E-03 | 0.017 | 0.010 | 6.90E-02 | 0.019 |
| -0.002 | 0.008 | 8.35E-01 | 0.005 | 0.015 | 7.34E-01 | 0.028 |
| -0.027 | 0.006 | 2.47E-06 | -0.045 | 0.012 | 1.23E-04 | -0.042 |
| 0.009 | 0.005 | 5.62E-02 | -0.005 | 0.010 | 5.78E-01 | 0.008 |
| 0.001 | 0.005 | 8.65E-01 | 0.016 | 0.010 | 1.09E-01 | -0.015 |

| se_mdd_un | p_mdd_unad | b_scz_unadj | se_scz_unadj | p_scz_unadj | b_bip_unadj | se_bip_unadj |
|-----------|------------|-------------|--------------|-------------|-------------|--------------|
| 0.005 | 9.34E-01 | 0.007 | 0.010 | 5.10E-01 | -0.014 | 0.014 |
| 0.006 | 0.5195 | -0.032 | 0.011 | 3.90E-03 | -0.003 | 0.016 |

se_adhd_unap_adhd_unac b_aut_unadj se_aut_unad p_aut_unadj nearestGene

| | | | | | |
|-------|----------|--------|-------|----------|---------------|
| 0.016 | 1.34E-04 | 0.016 | 0.016 | 3.08E-01 | WSCD2 |
| 0.014 | 3.05E-02 | -0.015 | 0.014 | 2.90E-01 | ARFGEF2 |
| 0.014 | 1.45E-02 | 0.038 | 0.015 | 8.72E-03 | CREB5 |
| 0.018 | 5.31E-01 | 0.038 | 0.018 | 3.21E-02 | KLF16 |
| 0.013 | 9.76E-06 | -0.029 | 0.014 | 3.44E-02 | CALN1 |
| 0.013 | 8.53E-02 | -0.015 | 0.014 | 2.94E-01 | RP11-467I7.1 |
| 0.013 | 1.21E-01 | -0.004 | 0.014 | 7.91E-01 | RPS18P6 |
| 0.015 | 5.32E-01 | 0.036 | 0.016 | 2.30E-02 | GNDF |
| 0.013 | 7.63E-01 | 0.018 | 0.014 | 1.89E-01 | DIP2C |
| 0.013 | 7.89E-03 | -0.030 | 0.014 | 3.12E-02 | TACC1 |
| 0.017 | 3.99E-01 | -0.019 | 0.019 | 3.11E-01 | RP11-160H22.3 |
| 0.014 | 3.27E-01 | 0.022 | 0.014 | 1.21E-01 | MSL2 |
| 0.014 | 7.20E-01 | -0.022 | 0.015 | 1.27E-01 | ARL14EP |
| 0.014 | 1.36E-02 | -0.047 | 0.014 | 8.06E-04 | SRPK2 |
| 0.029 | 6.22E-02 | -0.027 | 0.029 | 3.63E-01 | CCDC175 |
| 0.022 | 0.326 | -0.035 | 0.023 | 1.29E-01 | ZSCAN23 |
| 0.017 | 0.242 | 0.040 | 0.017 | 2.20E-02 | MIR137HG |
| 0.014 | 0.150 | 0.002 | 0.014 | 8.59E-01 | ATP2A2 |
| 0.014 | 0.374 | -0.001 | 0.015 | 9.31E-01 | PPP1R16B |
| 0.014 | 0.053 | 0.047 | 0.015 | 1.31E-03 | NRGN |
| 0.018 | 0.004 | -0.029 | 0.019 | 1.21E-01 | GULOP |
| 0.013 | 0.469 | 0.008 | 0.014 | 5.90E-01 | TSNARE1 |
| 0.016 | 0.036 | 0.010 | 0.016 | 5.58E-01 | MPHOSPH9 |
| 0.014 | 0.421 | 0.017 | 0.014 | 2.20E-01 | STAG1 |
| 0.029 | 0.565 | -0.061 | 0.029 | 3.44E-02 | SLC39A8 |
| 0.017 | 0.888 | 0.013 | 0.017 | 4.69E-01 | FXR1 |
| 0.014 | 0.040 | 0.031 | 0.014 | 3.05E-02 | TCF20 |
| 0.018 | 0.017 | -0.031 | 0.018 | 9.42E-02 | DGKZ |
| 0.013 | 0.161 | 0.005 | 0.014 | 7.17E-01 | CTD-2171N6.1 |
| 0.019 | 0.240 | 0.033 | 0.020 | 9.65E-02 | MEF2C-AS1 |
| 0.014 | 0.015 | -0.033 | 0.015 | 2.19E-02 | GIGYF2 |
| 0.023 | 0.030 | 0.000 | 0.024 | 9.97E-01 | NT5C2 |
| 0.013 | 0.043 | 0.015 | 0.014 | 2.73E-01 | NA |
| 0.017 | 0.017 | 0.006 | 0.017 | 7.36E-01 | IGSF9B |
| 0.014 | 0.001 | 0.026 | 0.014 | 7.23E-02 | RP4-598G3.1 |
| 0.013 | 0.028 | 0.027 | 0.014 | 5.18E-02 | SYNGAP1 |
| 0.016 | 0.279 | -0.001 | 0.017 | 9.43E-01 | CSMD1 |
| 0.016 | 0.025 | 0.024 | 0.017 | 1.43E-01 | GPM6A |
| 0.015 | 0.903 | 0.011 | 0.015 | 4.47E-01 | FHIT |

| | | | | | |
|-------|-------|--------|-------|----------|------------------|
| 0.014 | 0.004 | -0.036 | 0.014 | 9.87E-03 | FOXP1 |
| 0.017 | 0.839 | -0.005 | 0.018 | 7.80E-01 | FTCDNL1 |
| 0.014 | 0.002 | 0.037 | 0.015 | 1.16E-02 | TMX2:TMX2-CTNND1 |
| 0.016 | 0.791 | 0.025 | 0.016 | 1.16E-01 | ENSG00000231993 |
| 0.014 | 0.222 | -0.001 | 0.014 | 9.51E-01 | ENSG00000259864 |
| 0.014 | 0.282 | 0.011 | 0.015 | 4.48E-01 | RERE |
| 0.013 | 0.376 | -0.011 | 0.014 | 4.43E-01 | VRK2 |
| 0.014 | 0.363 | 0.022 | 0.015 | 1.35E-01 | ENSG00000258028 |
| 0.014 | 0.045 | 0.009 | 0.015 | 5.36E-01 | IMMP2L |
| 0.014 | 0.026 | 0.009 | 0.014 | 5.34E-01 | ENSG00000230407 |
| 0.014 | 0.331 | 0.024 | 0.015 | 9.83E-02 | PCNXL3 |
| 0.016 | 0.204 | 0.023 | 0.016 | 1.59E-01 | ZNF536 |
| 0.014 | 0.611 | 0.030 | 0.014 | 3.59E-02 | CACNA1C |
| 0.013 | 0.402 | 0.011 | 0.014 | 4.45E-01 | OPCML |
| 0.013 | 0.805 | -0.001 | 0.014 | 9.48E-01 | ENSG00000207252 |
| 0.013 | 0.939 | -0.002 | 0.014 | 8.63E-01 | MAD1L1 |
| 0.016 | 0.176 | 0.028 | 0.016 | 9.06E-02 | AIG1 |
| 0.016 | 0.773 | 0.000 | 0.017 | 9.88E-01 | AKT3 |
| 0.016 | 0.557 | 0.038 | 0.017 | 2.36E-02 | ENSG00000253107 |
| 0.014 | 0.321 | 0.004 | 0.014 | 7.96E-01 | ENSG00000253413 |
| 0.019 | 0.415 | -0.008 | 0.020 | 6.68E-01 | ENSG00000237954 |
| 0.015 | 0.449 | -0.047 | 0.015 | 1.27E-03 | RFT1 |
| 0.013 | 0.859 | 0.032 | 0.014 | 2.26E-02 | ZSWIM6 |
| 0.016 | 0.216 | -0.018 | 0.016 | 2.80E-01 | CHRNA3 |
| 0.014 | 0.005 | 0.026 | 0.014 | 6.87E-02 | PDE4B |
| 0.014 | 0.875 | -0.014 | 0.015 | 3.32E-01 | CACNA1I |
| 0.015 | 0.937 | 0.034 | 0.016 | 3.37E-02 | RGS6 |
| 0.014 | 0.002 | 0.050 | 0.015 | 5.61E-04 | SRPK2 |
| 0.015 | 0.492 | -0.014 | 0.016 | 3.82E-01 | RP3-399L15.3 |
| 0.014 | 0.801 | -0.007 | 0.014 | 6.02E-01 | SMG6 |
| 0.014 | 0.010 | -0.027 | 0.014 | 5.55E-02 | GATAD2A |
| 0.014 | 0.022 | 0.017 | 0.015 | 2.62E-01 | ENSG00000235377 |
| 0.014 | 0.099 | 0.026 | 0.015 | 6.98E-02 | RFPL4AP3 |
| 0.016 | 0.448 | 0.057 | 0.017 | 5.67E-04 | ENSG00000262267 |
| 0.018 | 0.246 | -0.026 | 0.019 | 1.60E-01 | ENSG00000233263 |
| 0.013 | 0.148 | 0.000 | 0.014 | 9.76E-01 | ENSG00000254842 |
| 0.021 | 0.735 | -0.031 | 0.022 | 1.52E-01 | ASCL1 |
| 0.020 | 0.314 | -0.030 | 0.021 | 1.57E-01 | GRM3 |
| 0.015 | 0.845 | -0.005 | 0.016 | 7.39E-01 | SOX5 |
| 0.014 | 0.924 | 0.026 | 0.014 | 7.28E-02 | PPP1R13B |
| 0.021 | 0.116 | 0.051 | 0.022 | 2.17E-02 | CACNB2 |
| 0.013 | 0.701 | 0.030 | 0.014 | 2.90E-02 | CLCN3 |
| 0.013 | 0.059 | 0.006 | 0.014 | 6.67E-01 | ENSG00000259503 |

| | | | | | |
|-------|-------|--------|-------|----------|-----------------|
| 0.014 | 0.112 | 0.001 | 0.015 | 9.37E-01 | ENSG00000259221 |
| 0.014 | 0.211 | -0.021 | 0.015 | 1.48E-01 | SF3B1 |
| 0.021 | 0.410 | 0.032 | 0.021 | 1.32E-01 | ENSG00000224968 |
| 0.016 | 0.009 | 0.028 | 0.016 | 8.27E-02 | PRKD1 |
| 0.015 | 0.768 | -0.013 | 0.015 | 3.88E-01 | MRPS11P1 |
| 0.014 | 0.198 | 0.045 | 0.014 | 1.60E-03 | AC003088.1 |
| 0.014 | 0.007 | -0.034 | 0.015 | 1.88E-02 | RAI1 |
| 0.014 | 0.164 | 0.006 | 0.015 | 6.54E-01 | DRD2 |
| 0.014 | 0.000 | 0.010 | 0.015 | 4.92E-01 | PTPRF |
| 0.013 | 0.169 | -0.033 | 0.014 | 1.86E-02 | TMEM219 |
| 0.021 | 0.013 | 0.028 | 0.022 | 2.06E-01 | LINC00606 |
| 0.016 | 0.259 | -0.002 | 0.016 | 8.95E-01 | STAT6 |
| 0.013 | 0.098 | -0.032 | 0.014 | 2.13E-02 | AC091969.1 |
| 0.013 | 0.004 | -0.012 | 0.014 | 4.01E-01 | ENSG00000259616 |
| 0.014 | 0.982 | 0.006 | 0.014 | 6.66E-01 | ENSG00000258224 |
| 0.014 | 0.004 | -0.015 | 0.014 | 2.91E-01 | FURIN |
| 0.018 | 0.026 | 0.002 | 0.019 | 9.18E-01 | GABBR2 |
| 0.018 | 0.058 | 0.002 | 0.019 | 9.26E-01 | ENSG00000221237 |
| 0.014 | 0.249 | -0.026 | 0.015 | 7.58E-02 | RIMS1 |
| 0.014 | 0.813 | -0.002 | 0.015 | 8.89E-01 | HCN1 |
| 0.014 | 0.187 | -0.011 | 0.014 | 4.60E-01 | ENSG00000240354 |
| 0.015 | 0.449 | 0.006 | 0.016 | 6.90E-01 | MMP16 |
| 0.015 | 0.566 | -0.019 | 0.015 | 2.09E-01 | ENSG00000258144 |
| 0.014 | 0.259 | 0.030 | 0.015 | 4.19E-02 | DGKI |
| 0.018 | 0.457 | 0.006 | 0.018 | 7.36E-01 | CNTN4 |
| 0.014 | 0.728 | 0.023 | 0.015 | 1.26E-01 | ATXN7 |
| 0.015 | 0.326 | 0.001 | 0.016 | 9.46E-01 | RP11-111112.1 |
| 0.015 | 0.731 | -0.006 | 0.015 | 7.07E-01 | RP11-284M14.1 |
| 0.013 | 0.708 | -0.009 | 0.014 | 5.01E-01 | SNAP91 |
| 0.018 | 0.153 | 0.018 | 0.019 | 3.28E-01 | PLA2G15 |
| 0.014 | 0.590 | -0.006 | 0.014 | 6.92E-01 | CPEB1 |
| 0.014 | 0.114 | 0.037 | 0.015 | 1.22E-02 | CUL3 |
| 0.016 | 0.007 | 0.037 | 0.017 | 3.22E-02 | HNRNPA1P46 |
| 0.014 | 0.017 | -0.047 | 0.014 | 9.30E-04 | ENSG00000229271 |
| 0.021 | 0.903 | 0.018 | 0.022 | 4.18E-01 | MKL1 |
| 0.014 | 0.257 | 0.006 | 0.015 | 6.98E-01 | ZEB2 |
| 0.016 | 0.786 | 0.004 | 0.016 | 8.06E-01 | NOSIP:PRRG2 |
| 0.015 | 0.883 | -0.012 | 0.015 | 4.24E-01 | EMX1 |
| 0.014 | 0.381 | 0.015 | 0.014 | 2.77E-01 | CNOT1 |
| 0.024 | 0.210 | -0.030 | 0.024 | 2.24E-01 | ENSG00000227854 |
| 0.013 | 0.066 | 0.009 | 0.014 | 5.00E-01 | PSD3 |
| 0.014 | 0.095 | -0.023 | 0.014 | 9.50E-02 | ZNF804A |
| 0.017 | 0.315 | 0.004 | 0.018 | 8.49E-01 | BNIP3L |

| | | | | | |
|-------|-------|--------|-------|----------|-----------------|
| 0.023 | 0.000 | -0.015 | 0.024 | 5.51E-01 | ENSG00000253108 |
| 0.014 | 0.491 | -0.006 | 0.014 | 6.89E-01 | RBM26 |
| 0.016 | 0.021 | 0.044 | 0.017 | 7.30E-03 | WHSC1L1 |
| 0.016 | 0.493 | 0.012 | 0.017 | 4.61E-01 | ALMS1 |
| 0.016 | 0.692 | 0.016 | 0.016 | 3.06E-01 | ENSG00000261038 |
| 0.014 | 0.136 | -0.040 | 0.015 | 5.36E-03 | MSRA |
| 0.013 | 0.996 | 0.016 | 0.014 | 2.35E-01 | RPTOR |
| 0.013 | 0.053 | -0.018 | 0.014 | 1.97E-01 | ETF1 |
| 0.014 | 0.230 | -0.003 | 0.014 | 8.48E-01 | ENSG00000255545 |
| 0.015 | 0.290 | 0.050 | 0.015 | 1.12E-03 | SEC11A |
| 0.018 | 0.476 | 0.029 | 0.018 | 1.18E-01 | VPS45 |
| 0.014 | 0.085 | -0.007 | 0.014 | 6.13E-01 | TRANK1 |
| 0.014 | 0.037 | -0.012 | 0.014 | 3.72E-01 | BCL11B |
| 0.015 | 0.209 | -0.024 | 0.015 | 1.14E-01 | GRIN2A |
| 0.022 | 0.011 | 0.058 | 0.022 | 9.67E-03 | MPP6 |

se_adhd_unap_adhd_unac b_aut_unadj se_aut_unad p_aut_unadj nearestGene

| | | | | | |
|-------|----------|--------|-------|----------|-----------------|
| 0.014 | 5.51E-01 | -0.039 | 0.014 | 6.05E-03 | ELAVL2 |
| 0.014 | 6.08E-01 | -0.010 | 0.015 | 5.10E-01 | SSBP2 |
| 0.018 | 6.89E-01 | -0.031 | 0.019 | 9.76E-02 | ADD3 |
| 0.013 | 8.50E-02 | 0.013 | 0.014 | 3.59E-01 | TRANK1 |
| 0.019 | 8.43E-01 | 0.051 | 0.020 | 9.11E-03 | TENM4 |
| 0.019 | 4.82E-01 | 0.027 | 0.020 | 1.64E-01 | NCAN |
| 0.018 | 1.76E-02 | 0.032 | 0.018 | 8.12E-02 | ENSG00000249568 |
| 0.014 | 2.57E-01 | -0.007 | 0.014 | 6.22E-01 | HLF |
| 0.014 | 7.08E-01 | 0.013 | 0.014 | 3.51E-01 | JADE2 |
| 0.014 | 2.22E-01 | 0.026 | 0.015 | 7.69E-02 | LMAN2L |
| 0.014 | 8.97E-01 | -0.018 | 0.014 | 1.96E-01 | RPS6KA2 |
| 0.014 | 7.03E-01 | 0.008 | 0.014 | 6.04E-01 | FADS2 |
| 0.021 | 2.31E-03 | -0.067 | 0.022 | 1.95E-03 | TFAP2B |
| 0.014 | 6.61E-01 | 0.010 | 0.014 | 4.63E-01 | SLC25A17 |
| 0.013 | 6.79E-01 | -0.042 | 0.014 | 2.60E-03 | ITIH1 |
| 0.014 | 5.06E-01 | 0.051 | 0.015 | 7.29E-04 | ZSCAN2 |
| 0.022 | 4.39E-01 | 0.033 | 0.023 | 1.50E-01 | AC003088.1 |
| 0.021 | 1.09E-02 | -0.053 | 0.022 | 1.55E-02 | DFNA5 |
| 0.014 | 7.44E-01 | -0.025 | 0.015 | 8.50E-02 | CACNA1C-IT3 |

se_adhd_unap_adhd_unac b_aut_unadj se_aut_unad p_aut_unadj nearestGene

| | | | | | |
|-------|----------|--------|-------|----------|---------|
| 0.014 | 1.48E-02 | -0.019 | 0.015 | 1.98E-01 | STAU1 |
| 0.014 | 1.90E-04 | -0.003 | 0.014 | 8.03E-01 | MEF2C |
| 0.017 | 3.10E-01 | 0.058 | 0.017 | 6.59E-04 | RCN1 |
| 0.014 | 4.90E-01 | -0.009 | 0.014 | 5.22E-01 | CARM1P1 |
| 0.014 | 2.48E-01 | -0.021 | 0.014 | 1.41E-01 | RERE |

| | | | | | |
|-------|----------|--------|--------|----------|-----------------|
| 0.013 | 2.91E-02 | 0.032 | 0.0141 | 2.18E-02 | OLFM4 |
| 0.014 | 2.44E-01 | 0.036 | 0.0142 | 1.04E-02 | RPL31P12 |
| 0.013 | 5.39E-01 | 0.014 | 0.014 | 3.15E-01 | ENSG00000259434 |
| 0.013 | 1.51E-01 | -0.026 | 0.014 | 6.74E-02 | ESR2:SYNE2 |
| 0.014 | 6.52E-01 | 0.013 | 0.014 | 3.69E-01 | CTC-340A15.2 |
| 0.014 | 5.16E-01 | -0.004 | 0.0148 | 7.78E-01 | TCF4 |
| 0.014 | 6.75E-01 | -0.013 | 0.014 | 3.46E-01 | LRFN5 |
| 0.014 | 1.49E-03 | 0.026 | 0.0143 | 7.23E-02 | RP4-598G3.1 |
| 0.013 | 8.36E-01 | 0.007 | 0.0139 | 6.22E-01 | ENSG00000234273 |
| 0.014 | 2.54E-01 | -0.021 | 0.0141 | 1.36E-01 | RERE |
| 0.017 | 2.71E-02 | -0.060 | 0.0176 | 6.59E-04 | BEND4 |
| 0.013 | 1.63E-05 | 0.062 | 0.0139 | 7.48E-06 | RP11-6N13.1 |
| 0.014 | 2.86E-01 | -0.056 | 0.0142 | 8.49E-05 | RNU7-160P |
| 0.014 | 6.06E-01 | -0.011 | 0.0144 | 4.67E-01 | RNU6-695P |
| 0.015 | 9.26E-01 | 0.011 | 0.0153 | 4.86E-01 | ENSG00000266033 |
| 0.013 | 2.30E-01 | -0.025 | 0.014 | 7.67E-02 | RSRC1 |
| 0.015 | 6.22E-01 | -0.031 | 0.0161 | 5.80E-02 | ENSG00000230365 |
| 0.019 | 7.77E-01 | -0.025 | 0.0197 | 2.06E-01 | PGBD1 |
| 0.015 | 9.60E-01 | 0.024 | 0.0155 | 1.20E-01 | L3MBTL2 |
| 0.014 | 6.86E-02 | 0.035 | 0.0142 | 1.31E-02 | PMFBP1 |
| 0.014 | 3.37E-01 | -0.010 | 0.0144 | 4.78E-01 | SOX5 |
| 0.014 | 4.89E-01 | -0.005 | 0.0143 | 7.22E-01 | RBFOX1 |
| 0.013 | 2.36E-01 | 0.004 | 0.0141 | 7.50E-01 | RPS6KL1 |
| 0.024 | 4.33E-01 | -0.014 | 0.0253 | 5.87E-01 | DENND1A |
| 0.013 | 9.76E-01 | -0.017 | 0.014 | 2.16E-01 | TMEM106B |
| 0.014 | 3.91E-01 | -0.008 | 0.0144 | 5.53E-01 | LINC00669 |
| 0.014 | 1.33E-02 | -0.025 | 0.0143 | 7.84E-02 | TENM2 |
| 0.015 | 1.02E-01 | 0.000 | 0.0153 | 9.94E-01 | ASTN2 |
| 0.017 | 1.67E-01 | 0.012 | 0.0174 | 4.84E-01 | NR4A2 |
| 0.025 | 1.88E-01 | -0.002 | 0.0271 | 9.35E-01 | ENOX1 |
| 0.013 | 7.85E-02 | -0.024 | 0.014 | 8.48E-02 | ENSG00000271615 |
| 0.013 | 3.44E-02 | 0.005 | 0.0139 | 7.09E-01 | DCC |
| 0.015 | 6.30E-03 | -0.042 | 0.015 | 5.62E-03 | ENSG00000260411 |
| 0.024 | 3.72E-01 | 0.018 | 0.0252 | 4.65E-01 | MYO18A |
| 0.017 | 2.96E-07 | -0.051 | 0.017 | 2.86E-03 | SORCS3 |
| 0.015 | 2.01E-01 | 0.003 | 0.0159 | 8.61E-01 | SHISA9 |

se_bip_unadj p_bip_unadj b_aut_unadj se_aut_unadj p_aut_unadj nearestGene

| | | | | | |
|-------|----------|--------|-------|----------|-----------------|
| 0.017 | 4.69E-02 | -0.033 | 0.024 | 1.69E-01 | TFAP2D |
| 0.010 | 3.60E-03 | -0.003 | 0.014 | 8.11E-01 | ENSG00000270234 |
| 0.015 | 4.32E-02 | -0.002 | 0.015 | 8.73E-01 | ST3GAL3 |
| 0.022 | 3.13E-01 | -0.045 | 0.023 | 4.84E-02 | SPAG16 |
| 0.013 | 4.00E-01 | 0.015 | 0.014 | 2.60E-01 | SEMA6D |

| | | | | | |
|-------|----------|--------|-------|----------|-----------------|
| 0.033 | 1.93E-04 | -0.042 | 0.033 | 2.12E-01 | ENSG00000253108 |
| 0.014 | 3.84E-01 | 0.020 | 0.014 | 1.55E-01 | RNU6-815P |
| 0.013 | 8.09E-01 | 0.035 | 0.014 | 1.25E-02 | ENSG00000271327 |
| 0.014 | 1.59E-01 | 0.026 | 0.014 | 5.78E-02 | FOXP2 |
| 0.022 | 2.09E-01 | -0.057 | 0.021 | 7.26E-03 | AC004158.2 |
| 0.016 | 9.85E-03 | -0.063 | 0.017 | 1.46E-04 | SORCS3 |
| 0.014 | 5.70E-01 | -0.067 | 0.014 | 1.92E-06 | LINC00461 |
| 0.014 | 2.92E-01 | -0.077 | 0.015 | 1.14E-07 | EEF1A1P11 |

p_bip_unadj b_adhd_unacse_adhd_unap_adhd_unacnearestGene

| | | | | |
|----------|--------|-------|----------|---------|
| 3.31E-01 | -0.001 | 0.015 | 9.23E-01 | SOX7 |
| 8.29E-01 | -0.054 | 0.015 | 3.58E-04 | ZNF877P |