

SUPPLEMENTARY NOTE

Large-scale genome-wide association analysis of bipolar disorder identifies a new susceptibility locus near ODZ4

The Psychiatric Genomewide Association Study Consortium Bipolar Disorder Group (PGC-BD)

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Description of individual study sample data contributions, ascertainment and genotyping platforms.

OVERVIEW

The analyses described in this manuscript use BD case-control GWAS datasets from several major international collections and studies (which we will refer to as the “primary studies”), several of which have already been the subject of published analyses. The sample sizes reported in **Supplementary Table 1** and used in the analyses are in several cases smaller than the sample sizes in the primary or published studies because of removal of any sample overlaps across studies. For example, control samples from the NIMH Genetics Repository were used in the STEP-BD, GAIN/BiGS and Pritzker Neuropsychiatric Disorder Research Consortium analyses. There was also an overlap in NIMH repository cases used in the Pritzker Neuropsychiatric Disorders Research Consortium and GAIN/BiGS analyses. There was an overlap in cases used in the GSK and WTCCC analyses. In each case of a sample appearing in more than one dataset, the duplicate in the larger dataset was removed in order that each individual sample appeared only once in any sample used in the analysis. Further details of this procedure are given in the QC sections.

PRIMARY SAMPLE DESCRIPTIONS:

The BOMA-Bipolar Study (uploaded: 681 cases, 1300 controls; post-QC1: 675 cases, 1297 controls). Cases for the BOMA-Bipolar Study were ascertained from consecutive admissions to the inpatient units of the Department of Psychiatry and Psychotherapy at the University of Bonn and at the Central Institute for Mental Health in Mannheim, University of Heidelberg, Germany. DSM-IV lifetime diagnoses of bipolar I disorder were assigned using a consensus best-estimate procedure, based on all available information, including a structured interviews Structured Clinical Interview for DSM-IV-TR-axis I disorders and Schedule of Affective Disorders¹ and Schizophrenia-Lifetime version² (SCID-I, SADS-L), medical records, and the family history method. In addition, the OPCRIT³ system was used for the detailed polydiagnostic documentation of symptoms. Controls were ascertained from three population-based studies in Germany (PopGen, KORA, and Heinz-Nixdorf-Recall Study). Study protocols were reviewed and approved in advance by Institutional Review Boards of the participating institutions. All subjects provided written informed consent. This includes a clause that all data may be shared with the PGC. However, consents does not include permission for depositing of de-identified individual GWAS genotype and phenotype data into the NIMH genetics initiative repository, although these data may be used in specific collaborations for studies of neuropsychiatric disorders. Case Subjects have been previously reported⁴⁻⁷. Control subjects have been previously reported⁸.

Genetic Association Information Network (GAIN)/ The Bipolar Genome Study (BiGS) (uploaded: 1001 cases, 1033 controls, post-QC1: 1001 cases, 1032 controls). The BD sample was collected under the auspices of the NIMH Genetics Initiative for BD (<http://zork.wustl.edu/nimh/>), genotyped as part of GAIN and analyzed as part of a larger GWAS conducted by the BiGS consortium. Approximately half of the GAIN sample was collected as multiplex families or sib pair families (waves 1-4), the remainder were collected as individual cases (wave 5). Subjects were ascertained at 11 sites: Indiana University, John Hopkins University, the NIMH Intramural

Research Program, Washington University at St. Louis, University of Pennsylvania, University of Chicago, Rush Medical School, University of Iowa, University of California, San Diego, University of California, San Francisco, and University of Michigan. All investigations were carried out after the review of protocols by the IRB at each participating institution. At all sites, potential cases were identified from screening admissions to local treatment facilities (systematic ascertainment) and from contacts generated through publicity programs or advocacy groups (nonsystematic ascertainment). Potential cases were evaluated using the Diagnostic Instrument for Genetic Studies⁹ (DIGS), the Family Interview for Genetic Studies (FIGS), and information from relatives and medical records. All information was reviewed through a best estimate diagnostic procedure by two independent and non-interviewing clinicians and a consensus best-estimate diagnosis was reached. In the event of a disagreement, a third review was done to break the tie. Controls are from the NIMH Genetic Repository sample obtained through a contract to Knowledge Networks, Inc. Only individuals with complete or near-complete psychiatric questionnaire data who did not fulfill diagnostic criteria for major depression and denied a history of psychosis or BD were included as controls for BiGS analyses. Controls were matched for gender and ethnicity to the cases. Case samples have been previously reported^{10,11}. Control samples have been previously reported¹⁰⁻¹³.

GlaxoSmithKline (GSK) (uploaded: 899 cases, 904 controls, post-QC1: 892 cases, 902 controls). Cases and controls were recruited from three study sites: the Institute of Psychiatry in London, UK, the Centre for Addiction and Mental Health in Toronto, Canada and the University of Dundee, UK. Cases were recruited through advertisements in hospital, clinics, primary care physician offices, and patient support groups, were ≥ 18 years of age at interview, and reported Caucasian ethnicity. They were interviewed using the Schedules for Clinical Assessment in Neuropsychiatry¹⁴ (SCAN). BD diagnoses were established according to DSM-IV or ICD-10 criteria using the computerized algorithm, (CATEGO) for the SCAN2.1 interview (WHO). Cases were excluded if they received a diagnosis of intravenous drug dependency or reported intravenous drug use or if they had mood incongruent psychotic symptoms, or if manic episodes only occurred in conjunction with or as a result of alcohol, substance abuse, substance dependence, medical illnesses, or medications. Controls were recruited from the same sites and were ≥ 18 years of age, reported Caucasian ethnicity, and denied the presence of any psychiatric disorders in a questionnaire. Case samples have been previously reported¹⁰. Control samples have been previously reported¹⁰.

Pritzker Neuropsychiatric Disorders Research Consortium (NIMH/Pritzker) (uploaded: 1130 cases, 772 controls, post-QC1: 1130 cases, 772 controls). The case and controls samples are from the NIMH Genetics Initiative Genetics Initiative Repository. Cases were diagnosed according to DMS-III or DSM-IV criteria using the DIGS (n=1,081) or FIGS and/or medical record review (n=67), excluding cases with low confidence diagnoses. From each wave 1-5 available non-Ashkenazi European-origin family, two BD I siblings were included when possible and the proband was preferentially included if available (n=946 individuals in 473 sibling pairs); otherwise a single BD I case was included (n=184). The bipolar sibling pairs were retained within the NIMH/Pritzker sample when individuals in more than one study were uniquely assigned to a study set. Controls had non-Ashkenazi European-origin, were aged 20-70 years and reported no diagnosis with or treatment for BD or schizophrenia, and that they had not heard voices that others could not hear. Individuals with suspected major depression were excluded based on answers to questions related to depressive mood. NIMH controls were further selected as the best match(es) to NIMH

cases based on self reported ancestry in the DIGS. Case samples have been previously reported^{10,11}. Control samples have been previously reported¹⁰⁻¹³.

Systematic Treatment Enhancement Program for Bipolar Disorder (STEP1 uploaded: 954 cases, 1498 controls, post-QC1: 927 cases, 1468 controls; *STEP2* uploaded: 665 cases, 192 controls, post-QC1: 659 cases, 192 controls). STEP-BD was a seven-site, national U.S., longitudinal cohort study designed to examine the effectiveness of treatments and their impact on the course of BD that enrolled 4,361 participants who met DSM-IV criteria for bipolar I, bipolar II, bipolar NOS, schizoaffective manic or bipolar type, or cyclothymic disorder based on diagnostic interviews. From the parent study, 2,089 individuals who were over 18 years of age with BD-I and BD-II diagnoses consented to the collection of blood samples for DNA, under IRB-approved protocols at each site with written informed consent that did not prohibit sharing of genotypic data with other scientists. Of the 2,089 STEP-GRP participants 62% had a consensus diagnosis of BDI on both the Affective Disorders Evaluation¹⁵ (ADE) and Mini-international Neuropsychiatric Interview¹⁶ (MINI). Two groups of controls samples from the NIMH repository were used. One comprised DNA samples derived from US Caucasian anonymous cord blood donors. The second were controls who completed the online self-administered psychiatric screen and were ascertained as described above, by Knowledge Networks Inc. For the second sample of controls only those without history of schizophrenia, psychosis, BD or major depression with functional impairment were used. Case samples have been previously reported^{12,13}. Control samples have been previously reported¹⁰⁻¹³.

Thematically Organized Psychoses (TOP) Study (Oslo, Norway) (uploaded: 232 cases, 394 controls, post-QC1: 205 cases, 367 controls). Subjects participated in a large ongoing study on schizophrenia and BD and were recruited from out-patient and in-patient psychiatric units in Norway, from May, 2003 through July, 2008. All participants gave written informed consent, and the study was approved by the Regional Committee for Medical Research Ethics and the Norwegian Data Inspectorate. Diagnosis was established using the SCID-I supplemented by case note review and follow up interviews where available. The healthy controls subjects were randomly selected from statistical records of persons from the same catchment areas as the patient groups. The control subjects were screened by interview and with the Primary Care Evaluation of Mental Disorders¹⁷ (PRIME-MD). None of the control subjects had a history of moderate/severe head injury, neurological disorder, mental retardation or an age outside the age range of 18-60 years. Healthy subjects were excluded if they or any of their close relatives had a lifetime history of a severe psychiatric disorder. Case samples have been previously reported¹⁸. Control samples have been previously reported¹⁹.

Trinity College Dublin (uploaded: 150 cases, 799 controls, post-QC1: 150 cases, 797 controls). Samples were collected as part of a larger study of the genetics of psychotic disorders in the Republic of Ireland, under protocols approved by the relevant IRBs and with written informed consent that permitted repository use. Cases were recruited from Hospitals and Community psychiatric facilities in Ireland by a psychiatrist or psychiatric nurse trained to use the SCID¹⁵. Diagnosis was based on the structured interview supplemented by case note review and collateral history where available. All diagnoses were reviewed by an independent reviewer. Controls were ascertained with informed consent from the Irish GeneBank and represented blood donors who met the same ethnicity criteria as cases. Controls were not specifically screened for psychiatric illness. Case samples have been previously reported¹³, control samples have been previously reported^{13,20,21}.

University College London (UCL) (uploaded: 506 cases, 509 controls, post-QC1: 490 cases, 495 controls). The UCL sample comprised Caucasian individuals who were ascertained and received clinical diagnoses of BD disorder according to UK National Health Service (NHS) psychiatrists at interview using the categories of the International Classification of Disease version 10. In addition bipolar subjects were included only if both parents were of English, Irish, Welsh or Scottish descent and if three out of four grandparents were of the same descent. All volunteers read an information sheet approved by the Metropolitan Medical Research Ethics Committee who also approved the project for all NHS hospitals. Written informed consent was obtained from each volunteer. The UCL control subjects were recruited from London branches of the National Blood Service, from local NHS family doctor clinics and from university student volunteers. All control subjects were interviewed with the SADS-L² to exclude all psychiatric disorders. Case samples have been previously reported^{12,13}. Control samples have been previously reported^{12,13}.

University of Edinburgh (uploaded: 283 cases, 275 controls, post-QC1: 282 cases, 275 controls). This sample comprised Caucasian individuals contacted through the inpatient and outpatient services of hospitals in South East Scotland. A BDI diagnosis was based on an interview with the patient using the SADS-L² supplemented by case note review and frequently by information from medical staff, relatives and care givers. Final diagnoses, based on DSM-IV criteria were reached by consensus between two trained psychiatrists. Ethnically-matched controls from the same region were recruited through the South of Scotland Blood Transfusion Service. Controls were not directly screened to exclude those with a personal or family history of psychiatric illness. The study was approved by the Multi-Centre Research Ethics Committee for Scotland and patients gave written informed consent for the collection of DNA samples for use in genetic studies. Case samples have been previously reported¹². Control samples have been previously reported^{12,13,20,21}.

Wellcome Trust Case Control Consortium, WTCCC (uploaded: 1868 cases, 2938 controls, post-QC1: 1864 cases, 2935 controls). BD cases were all over the age of 16 years, living in mainland UK and of European descent. Recruitment was undertaken by teams based in Aberdeen (8% cases), Birmingham (35% cases), Cardiff (33% cases), London (15% cases) and Newcastle (9% cases), to recruit individuals throughout the UK who had been in contact with mental health services. All subjects were recruited under protocols approved by the appropriate IRBs, and gave written informed consent permitting storage and sharing of de-identified clinical and genotypic data by the WTCCC repository (these genotypes will not be deposited into the NIMH repository). All subjects were interviewed by a trained psychologist or psychiatrist using the SCAN¹⁴. Best-estimate ratings were made based on interview and medical records information, and lifetime diagnoses assigned according to Research Diagnostic Criteria (RDC). Cases have diagnoses of BD-I, BD-II or SA-BD disorders. Controls were recruited from two sources: the 1958 Birth Cohort study and the UK Blood Service (blood donors). Controls (who were not screened to exclude personal or family history of psychiatric illness) were recruited under protocols approved by the appropriate IRBs, and gave written informed consent permitting storage and sharing of de-identified demographic and genotypic data by the WTCCC repository. Case samples have been previously reported^{6,10,13,22,23}. Control samples have been previously reported²².

REPLICATION SAMPLE DESCRIPTIONS (Supplementary Table 5):

French: Patients with BD type I or II and controls were recruited as part of a large study of genetics of BD in France (Paris-Creteil, Bordeaux, Nancy) with a protocol approved by relevant IRBs and with written informed consent. Cases were of French descent for more than 3 generations and have all been assessed by a trained psychiatrist or psychologist with the DIGS⁹ and the FIGS. Diagnosis were based on structured interviews supplemented by medical case notes, mood scales and self rating questionnaire assessing dimensions. Genotyping of controls were provided by the Centre National de Génotypage (M Lathrop, Evry). Patients and controls have been genotyped on the Illumina platform (HumanHap300, HumanHap550, HumanHap 610-quad). Sample QC was performed as described in section S2 (genomic inflation $\lambda = 1.028$). Case and control subjects have not been previously reported.

Bipolar Genome Study / Translational Genomics Institute 1 (BiGS/TGEN1): The TGEN sample is comprised entirely of subjects who were collected as part of wave 5 of the NIMH Genetics Initiative for BD. This collection was conducted at 11 sites where individual unrelated subjects were ascertained for a diagnosis of bipolar I or schizoaffective disorder, bipolar type. All sites were in the United States and varied as to ascertainment method and sites including inpatient and outpatient clinical settings, patient support groups and advertising. Written informed consent was obtained from each subject using consent forms and procedures approved by each site's local human subjects committee. Each consent specifically described the contribution of the subjects data to large repositories in order to facilitate collaborative analyses. Subjects were each individually interviewed using the DIGS⁹. These data and information from medical records and other informants were used to make diagnoses using DSM IV criteria.

FaST STEP2: Samples were collected from individuals at 11 U.S.: Massachusetts General Hospital, University of Pittsburgh Western Psychiatric Institute and Clinic, Stanford University School of Medicine, Case University, University of Pennsylvania, University of Massachusetts Medical Center, Baylor College of Medicine, University of Texas Health Science Center at San Antonio, Portland VA Medical Center, University of Colorado Health Sciences Center, University of Oklahoma College of Medicine. Eligible participants were age 18 or older meeting DSM-IV criteria for Bipolar I or II disorder by consensus diagnosis based on interviews with the ADE¹⁵ and MINI¹⁶. All participants provided written informed consent and the study protocol was approved by IRBs at each site. Collection of phenotypic data and DNA samples were supported by NIMH grants MH063445 (JW Smoller); MH067288 (PI: P Sklar), and MH63420 (PI: V Nimgaonkar). Case subjects have not been previously reported.

Control samples for BiGS/TGEN1 and FaST STEP2:

The cases of BiGS/TGEN1 and FaST STEP2 were combined with NIMH controls that were independent of those that were included in the primary analyses. The control samples were collected by Pablo Gejman and are described in the GAIN/BiGS primary control sample description. Independence of control samples was confirmed by determining eliminating any individual with PLINK pi-hat > 0.2 with another individual in the study. Population stratification was ruled out using principle component analyses. The postimputation $\lambda_{GC} = 1.03$.

ICCBDSBD Bipolar cases were recruited from St. Goran's Hospital in Stockholm, Sweden. All participants gave written informed consent to participate in a genetic study of BD, and the study

was approved by the Regional Ethics Committee of Stockholm. Diagnoses were based on physician-administered ADE¹⁵ and MINI¹⁶.

ICCBD:BiPolaR1 Bipolar cases were identified from the Swedish Bipolar Quality Assurance Registry (BiPolaR). Patient information in the registry includes disease sub-classification, psychosis, age at onset, number of manic and depressive episodes, number of hospitalizations and family history. Participants provided written informed consent to participate in a genetic study of psychiatric disease, and the study was approved by the Regional Ethics Committee of Stockholm.

ICCBD:HDR Bipolar cases were identified from the Swedish Hospital Discharge Registry if they 1) have at least two admissions with discharge diagnoses of BD and 2) born in Sweden or another Nordic country. The register contains a nearly complete register of all individuals hospitalized in Sweden since 1973. Diagnoses were established by the attending physician. The study was approved by the Regional Ethics Committee of Stockholm. Controls were collected in a related study of schizophrenia and were identified from the Swedish Hospital Discharge Register. All participants provided written informed consent to participate in genetic studies of psychotic disorders and were interviewed by a research nurse about other medical conditions.

ICCBD:Sweden/Schalling Bipolar cases were recruited from the Stockholm County catchment area. All patients gave written informed consent to participate in a genetic study of BD, and the study was approved by the Regional Ethics Committee of Stockholm. Diagnoses were made according to the DSM-IV criteria. Cases were not reported previously.

Swedish control samples were obtained from the Swedish Hospital Discharge Registry if they had never received discharge diagnoses of BD, schizophrenia and schizoaffective disorder. Sample QC was performed as described in the online methods (genomic inflation $\lambda = 1.066$). Cases have not been previously reported, controls have not previously been reported (but are included in the replication samples being reported by the PGC schizophrenia group)

BOMA-Bipolar Study rep1 and rep2. Cases for BOMA rep1 and rep2 were again ascertained from consecutive admissions to the inpatient units of the Department of Psychiatry and Psychotherapy at the University of Bonn and at the Central Institute for Mental Health in Mannheim, University of Heidelberg, as well as at other collaborating psychiatric university hospitals in Germany which have joined the BOMA studies. DSM-IV lifetime diagnoses of BD were assigned using a consensus best-estimate procedure, based on all available information, including structured interviews (SCID-I¹, SADS-L²; rep1) or semi-structured interviews (AMDP; rep2), medical records, and the family history method. In addition, the OPCRIT system³, was used for the detailed polydiagnostic documentation of symptoms.

The controls for BOMA rep1 were recruited at the Max Planck Institute of Psychiatry in Munich, Germany, and were selected randomly from a Munich-based community sample. They were collected in the course of genetic studies of major depression, and were therefore screened for the presence of anxiety and affective disorders using the Composite International Diagnostic Screener²⁴ (WHO-CIDI). Only individuals negative for the above-named disorders were included in the sample. All included controls were Caucasian, 93.04% were of German origin. These subjects

thus represent a group of healthy individuals with regard to depression and anxiety. The study was approved by the ethics committee of the Ludwig Maximilians University in Munich, Germany, and written informed consent was obtained from all subjects. These controls were described in detail in the study by Muglia et al. Controls for BOMA rep2 were ascertained from the population-based Heinz Nixdorf Recall Study²⁵ (additional probands to those used in the BOMA-Bipolar Study included in the COMBINED ANALYSIS SAMPLES). Study protocols were reviewed and approved in advance by Institutional Review Boards of the participating institutions. All subjects provided written informed consent. This includes a clause that all data may be shared with collaborating partners such as the PGC. However, consents do not include permission for depositing of de-identified individual GWAS genotype and phenotype data into the NIMH genetics initiative repository, although these data may be used in specific collaborations for studies of neuropsychiatric disorders. All subjects were genotyped using the Illumina platform.

Australian Samples. Subjects were ascertained through two studies – i) a BD pedigree sample (described in McAuley et al.²⁶) and ii) a specialised Sydney Black Dog Institute BD clinic sample (described in Mitchell et al. 2009²⁷). All subjects were interviewed by trained research staff using the DIGS⁹ or SCID¹⁵, using best-estimate DSM-IV diagnoses derived from those instruments, medical records and FIGS. First, for the pedigree sample, only one BD subject per family was included in the case sample. Pedigrees were only included in the original genetic study if there was unilineal inheritance, and at least two BD subjects including at least one with bipolar I disorder. Subjects were ascertained through clinical presentations to the Mood Disorders Unit at Prince of Wales Hospital in Sydney; direct referrals from Australian clinicians; and BD consumer organisations. Second, for the clinic sample, subjects comprised consecutive subjects referred by psychiatrists or general practitioners for specialised clinical review. All patients gave informed consent to participate in this study and the study was approved by the local ethic committee. Patients were included in the BOMA study and genotyped at the Life & Brain Centre in Bonn.

Australian controls were drawn from families participating in the Brisbane Longitudinal Twin Study, an unselected community sample recruited to take part in studies of melanoma risk factors, cognition, and other phenotypes. Subjects were not screened for any phenotype relevant to BD. The study was approved by the ethic committee and all probands gave written informed consent. All were genotyped as a single project by deCODE and have been through an extensive QC process including exclusion for non-european ancestry. The sample is overwhelmingly of northern European origin (mainly British Isles).

Icelandic Samples. The Icelandic sample consisted of 541 subjects with BD and 34,546 population controls. Patients and controls were Icelandic and were recruited throughout Iceland. Diagnoses were assigned according to RDC through the use of the SADS-L for 303 subjects. DSM-IV BD diagnoses were obtained through the use of the Composite International Diagnostic Interview (CIDI-Auto) for 82 subjects. In addition, there were 150 subjects with ICD-9 or ICD-10 BD diagnoses and 9 subjects with DSM-III BD diagnoses.

The 34,546 controls were recruited as a part of various genetic programs at deCODE and were not screened for psychiatric disorders. Approval for the study was granted by the National Bioethics Committee of Iceland and the Icelandic Data Protection Authority and informed consent was obtained for all participants.

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From 2003-2006, the Principal Investigators and Co-Investigators were: NorthShore University HealthSystem, Evanston, IL, R01 MH59571, Pablo V. Gejman, M.D. (Collaboration Coordinator; PI), Alan R. Sanders, M.D.; Emory University School of Medicine, Atlanta, GA, R01 MH59587, Farooq Amin, M.D. (PI); University of California, San Francisco, CA, R01 MH60870, William F. Byerley, M.D. (PI); University of Iowa, IA, R01 MH59566, Donald W. Black, M.D. (PI), Raymond R. Crowe, M.D.; Washington University, St. Louis, MO, R01 MH60879, C. Robert Cloninger, M.D. (PI); University of Colorado, Denver, CO, R01 MH59565, Robert Freedman, M.D. (PI), Ann Olincy, M.D.; Stanford University, Palo Alto, CA, R01 MH61675, Douglas F. Levinson, M.D. (PI); Louisiana State University, New Orleans, LA, R01 MH67257, Nancy G. Buccola, APRN, BC, MSN (PI); University of Queensland, Brisbane, Queensland, Australia, R01 MH59588, Bryan J. Mowry, M.D. (PI); Mt. Sinai School of Medicine, New York, NY, R01 MH59586, Jeremy M. Silverman, Ph.D. (PI).

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Trinity College Dublin: Dublin sample collection was supported by the Health Research Board and Science Foundation Ireland. Controls were supplied by J. McPartlin, Trinity College.

University College London: The UCL clinical and control samples were collected with support from the MDF Bipolar Organization (formerly the UK Manic Depression Fellowship), The Neuroscience Research Charitable Trust, the central London NHS Blood Transfusion Service and by a research lecture-ship from the Priory Hospitals. Processing and genetic analyses of UCL cohort was supported by UK Medical Research Council Project Grants G9623693N and G0500791

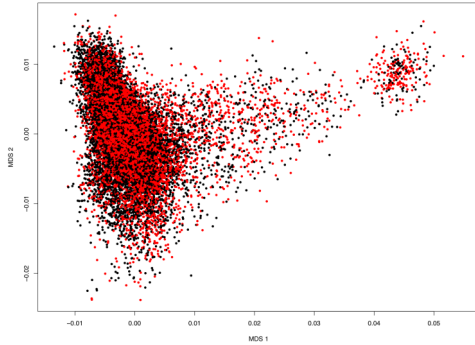
University of Edinburgh: The collection of the Edinburgh cohort was supported by grants from The Wellcome Trust, London, The Chief Scientist Office of the Scottish Executive and the Translational Medicine Research Institute, Glasgow.

Wellcome Trust Case-Control Consortium: We are indebted to all individuals who have participated in our research. We thank MDF-The Bipolar Organization for the help of its staff and members. Funding for recruitment and phenotype assessment has been provided by the Wellcome Trust and the Medical Research Council. The genotype analyses were funded by the Wellcome Trust and undertaken within the context of the Wellcome Trust Case Control Consortium (WTCCC). The members of the WTCCC are listed in the primary paper reporting the SNP GWAS (Nature. Jun 7 2007;447(7145):661-678).

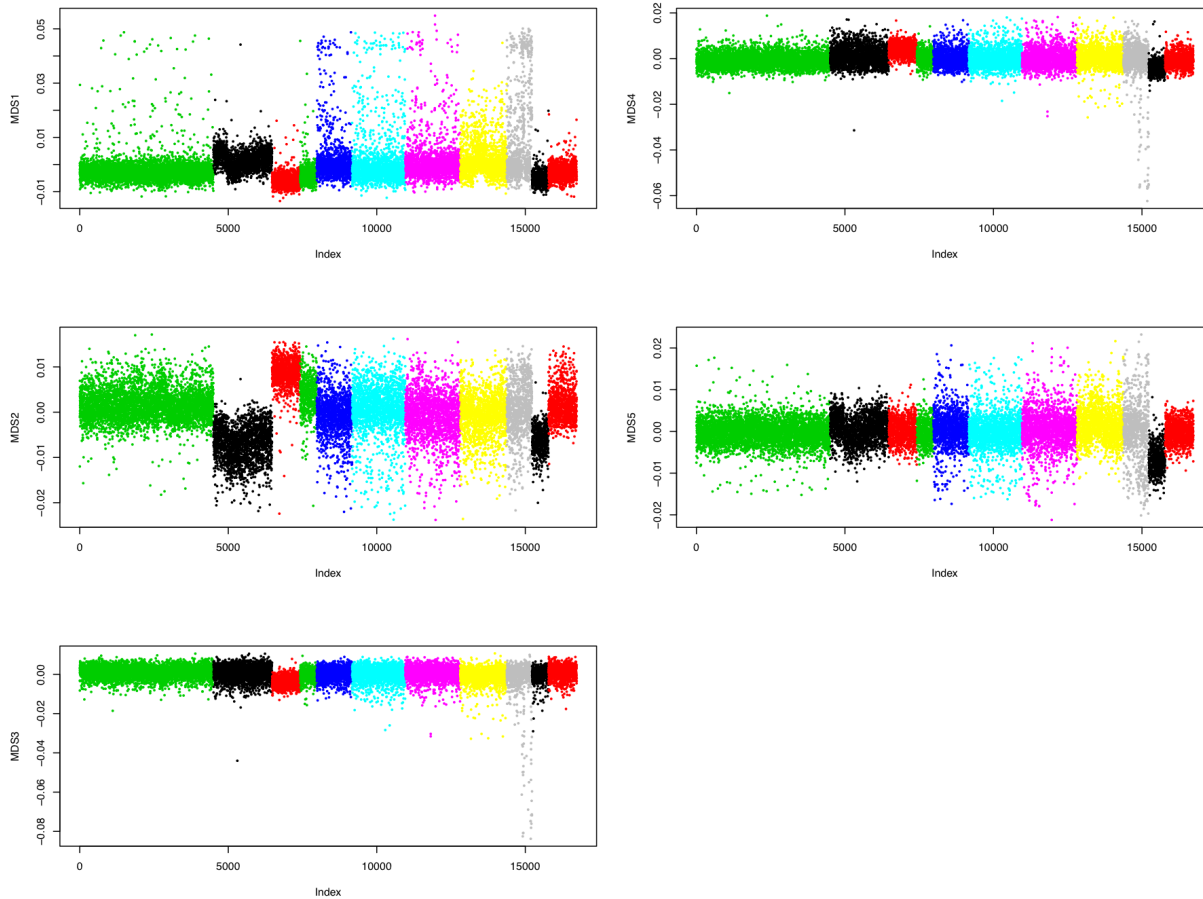
SUPPLEMENTARY FIGURES

Supplementary Figure 1. Multidimensional scaling plot of identity-by state distances

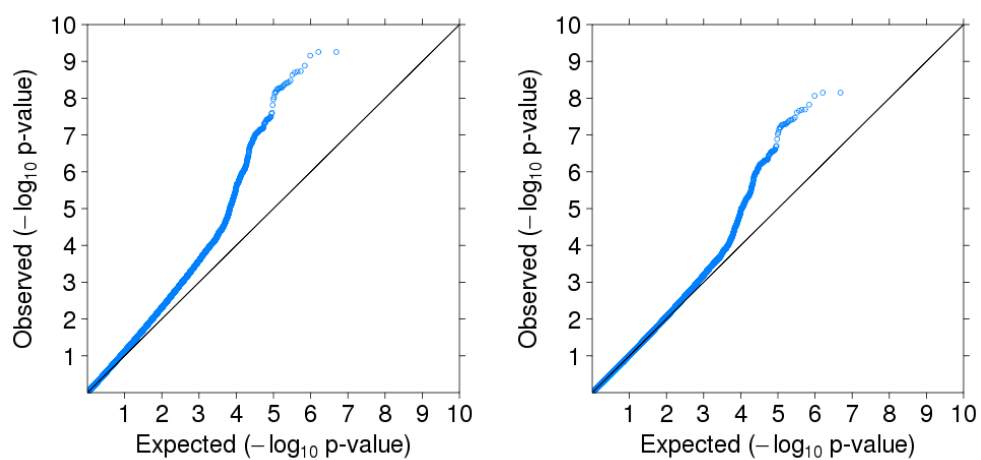
a) Plot of first two MDS components (black=control, red=case).



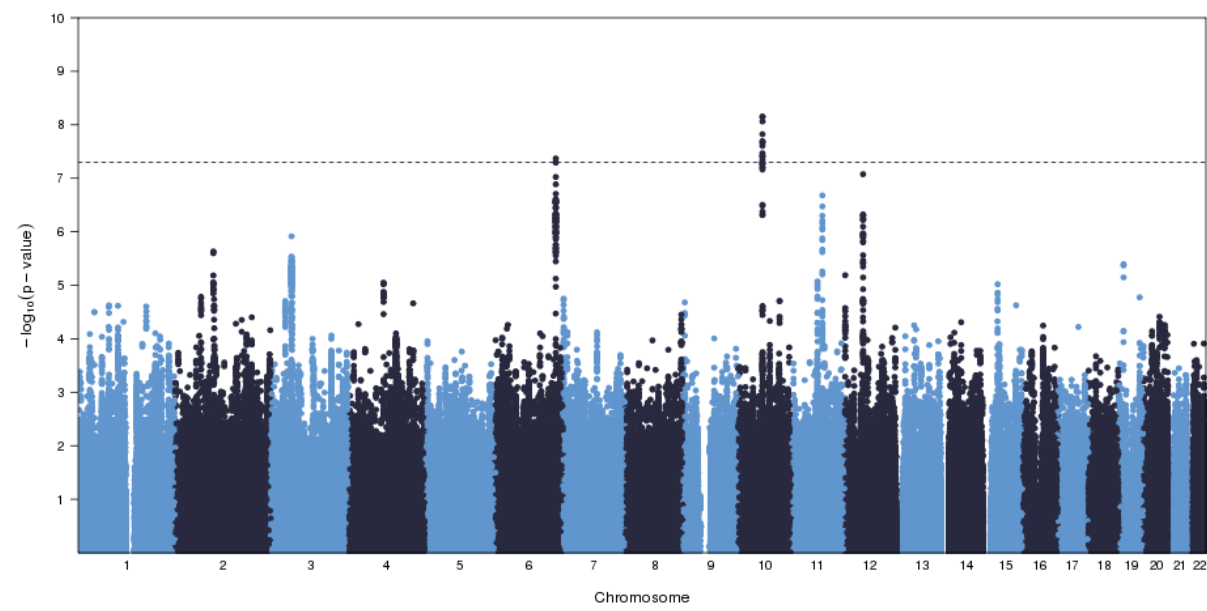
b) All five components, plotted individually against order in sample (x-axis). Samples organized in batches, as follows: Green, WTCCC; Black, BOMA-bipolar study; Red, TRINITY COLLEGE; Green, UEDINBURGH; Blue, GAIN/BiGS; Light-blue, GSK; Pink, NIMH/PRITZKER; Yellow, STEP1; Gray, STEP2; Black, TOP; Red, UCL.



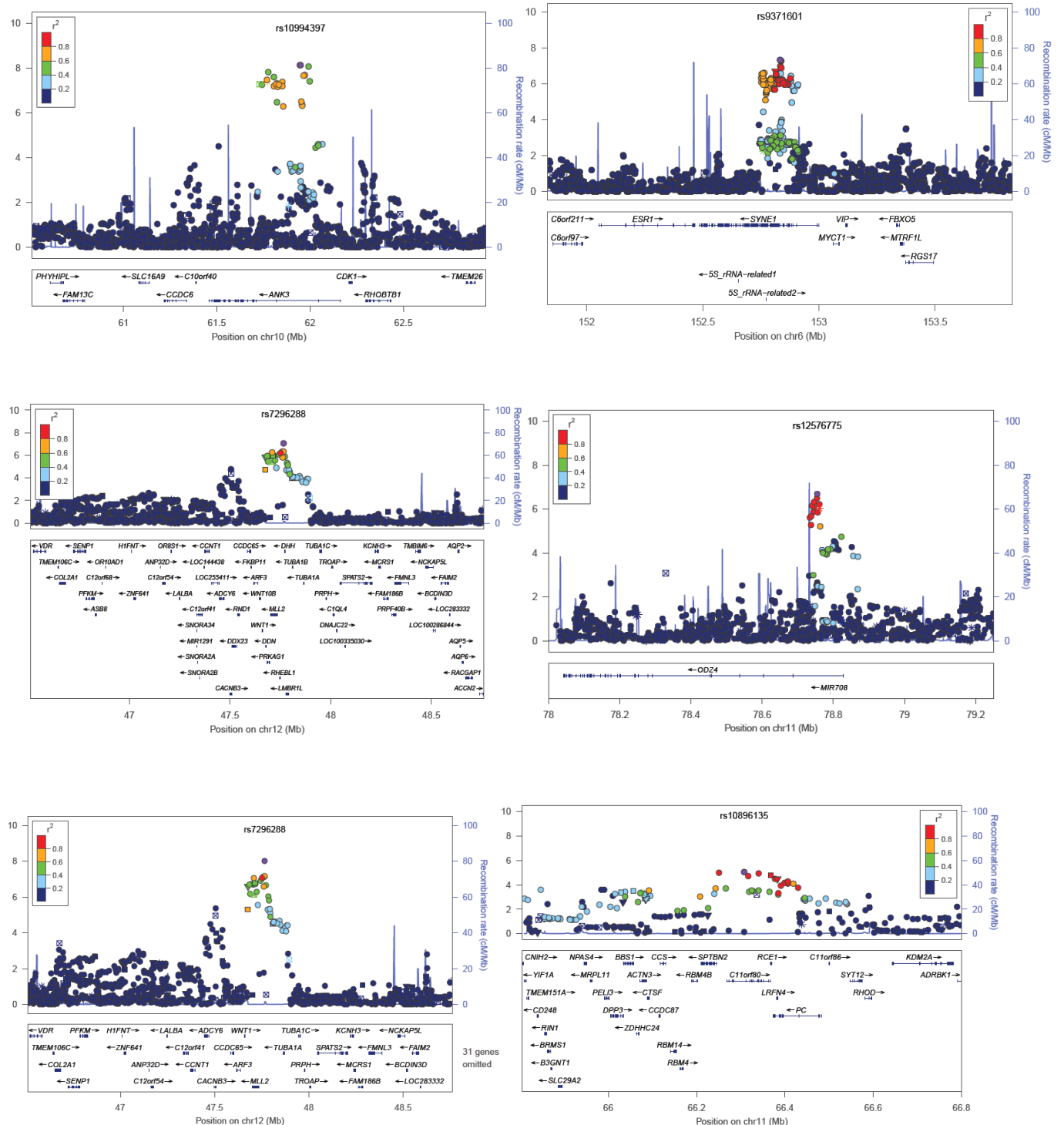
Supplementary Figure 2: Q-Q plot of single SNP statistics, based on SNP allele dosage including covariates described above. Left plot: non-GC corrected; right plot: post-GC correction



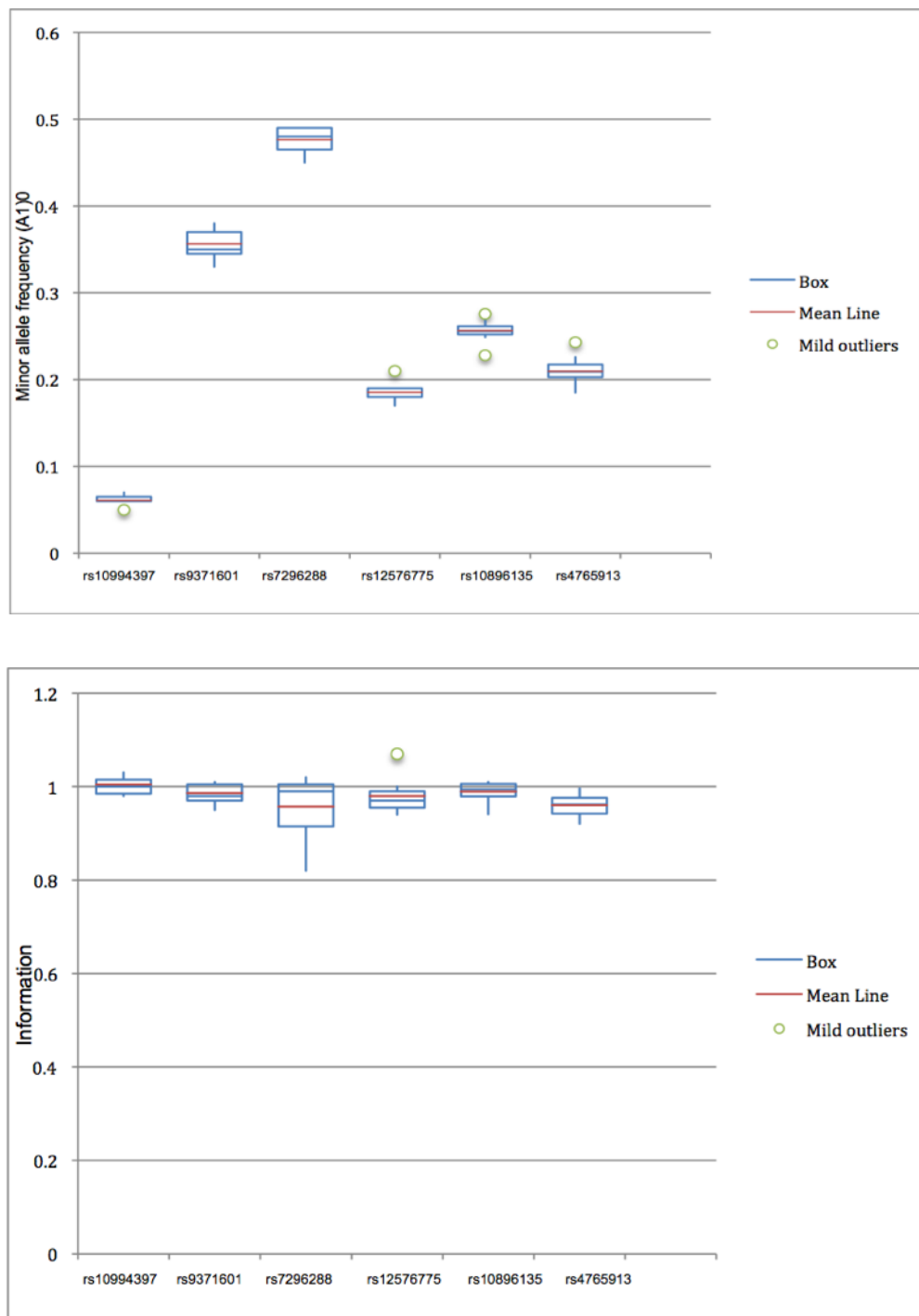
Supplementary Figure 3: Manhattan plot of single SNP test statistics including covariates described above

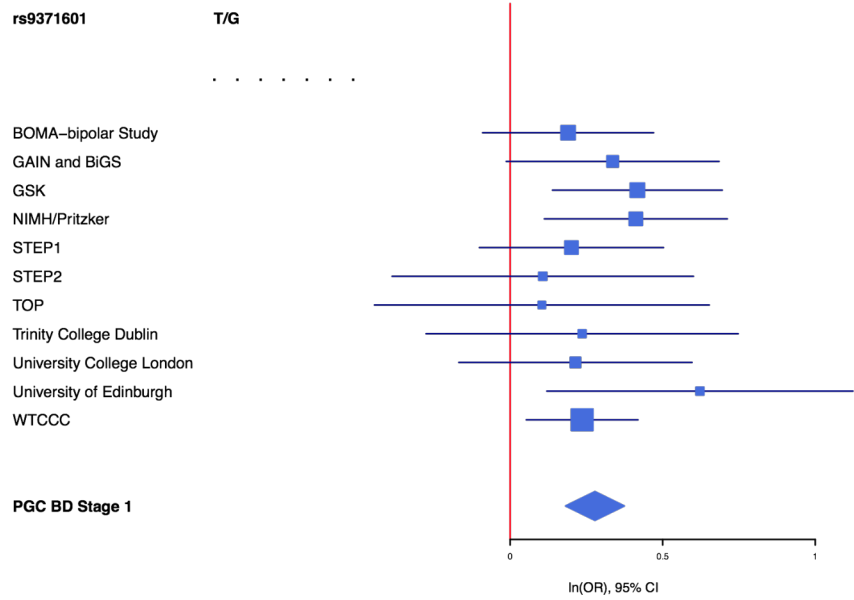
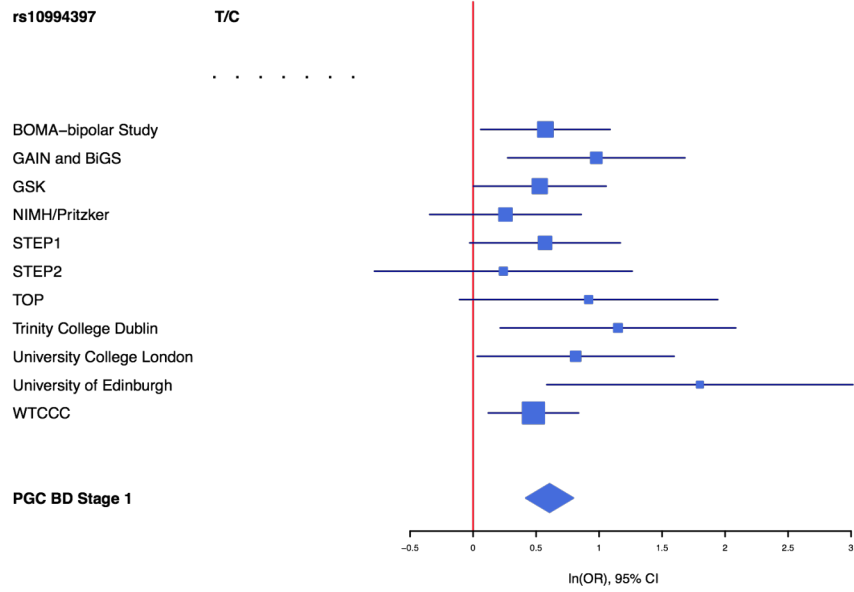


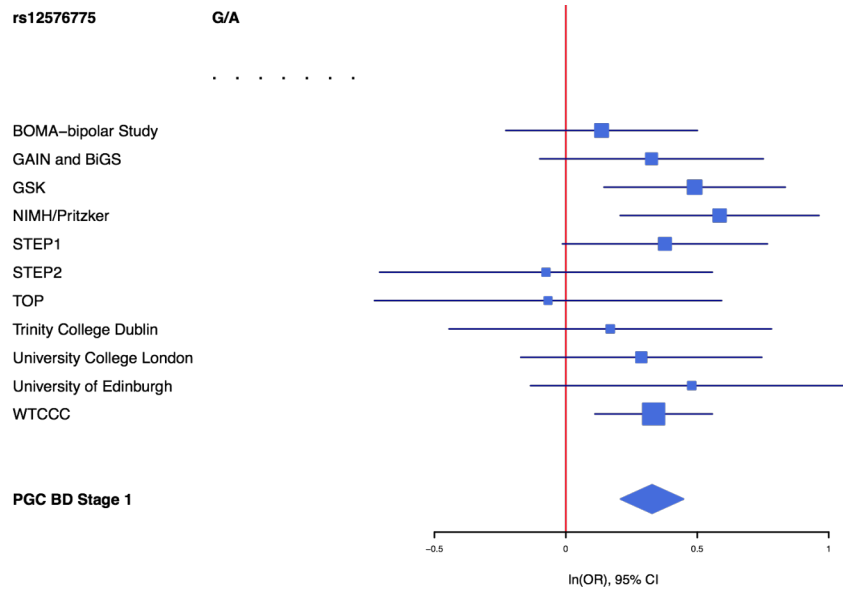
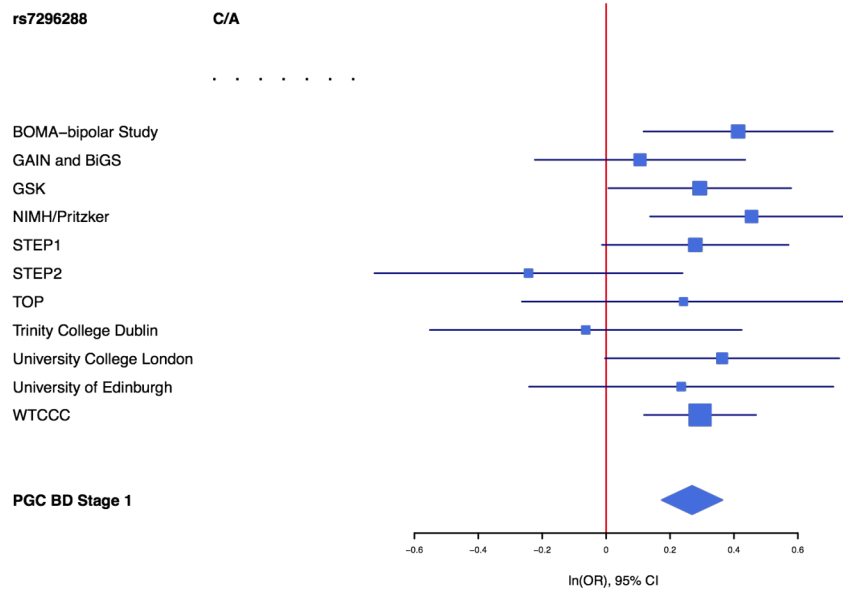
Supplementary Figure 4: Regional plots. Results are shown as P_{gc} ($-\log_{10}(P \text{ value})$) for genotyped and imputed SNPs. The most associated SNP in the primary analysis is shown as a purple circle. The color of the remaining markers reflects r^2 with the most associated SNP. The recombination rate from CEU HapMap (second y axis) is plotted in light blue.

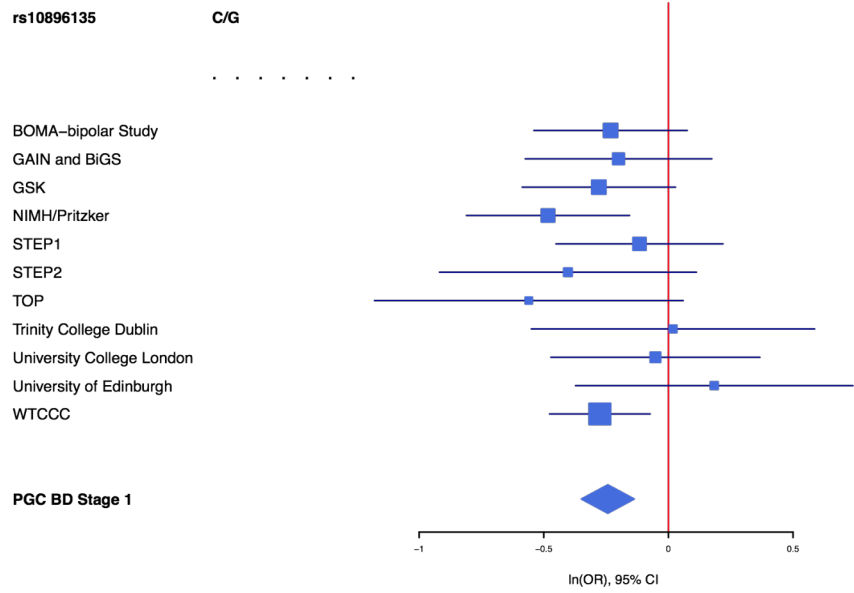
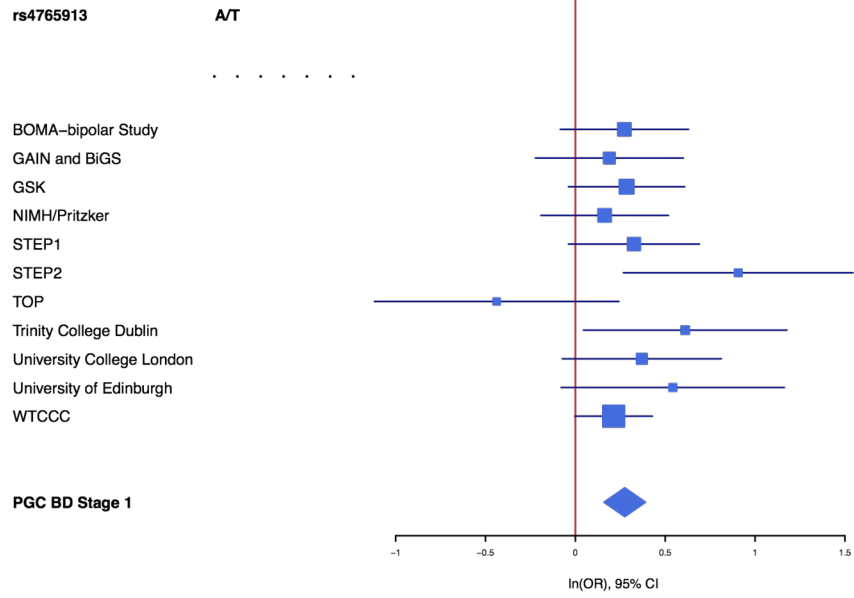


Supplementary Figure 5: Association results by site for imputed SNPs, box plots of information and frequency and forest plots of odds ratios (OR) and 95% confidence intervals (CI)

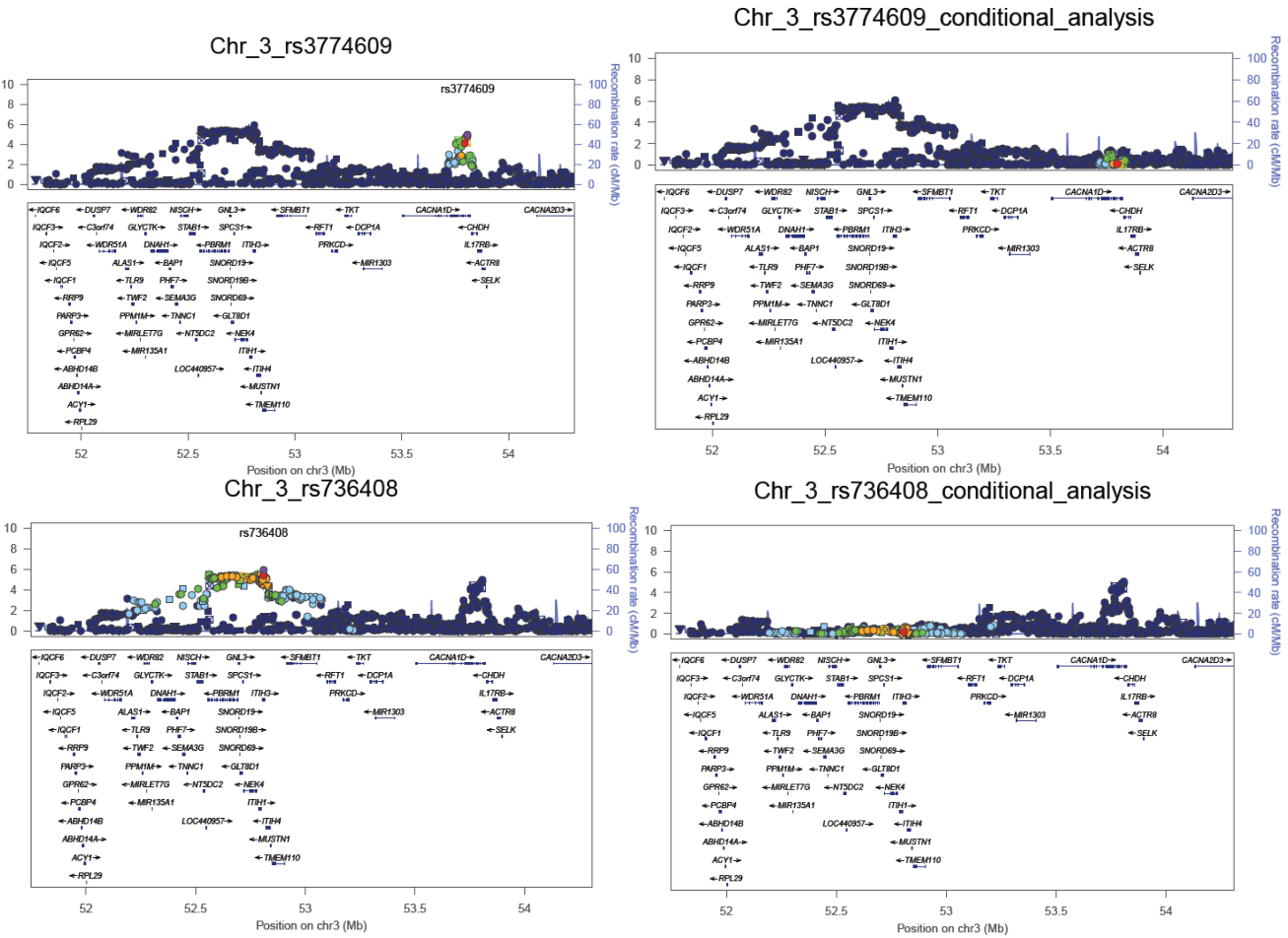




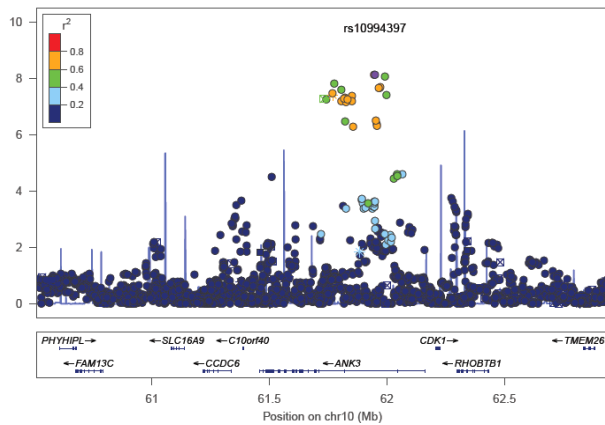




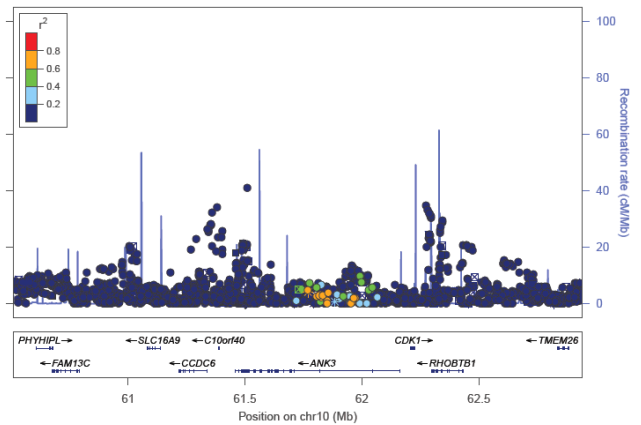
Supplementary Figure 6. Conditional analyses



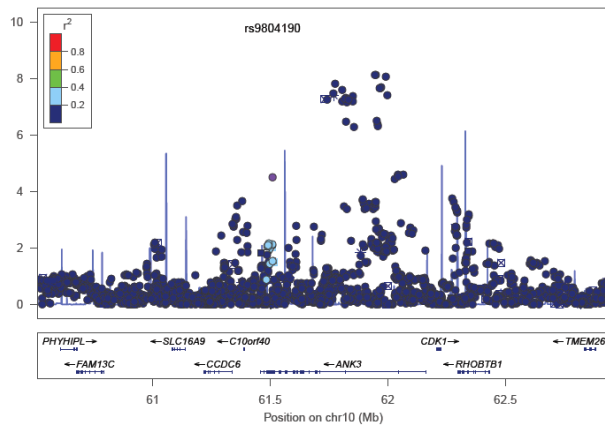
Chr_10_rs10994397



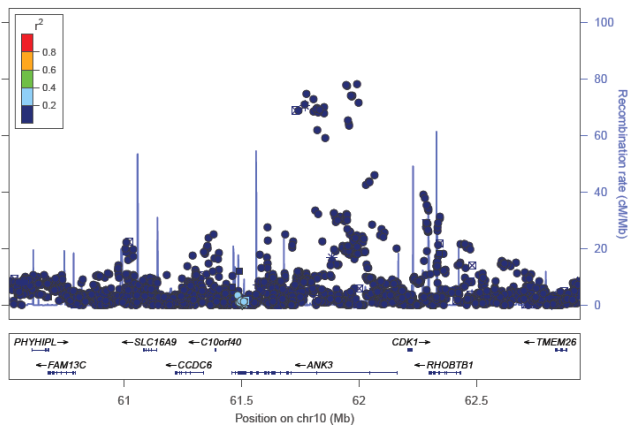
Chr_10_rs10994397_conditional_analysis



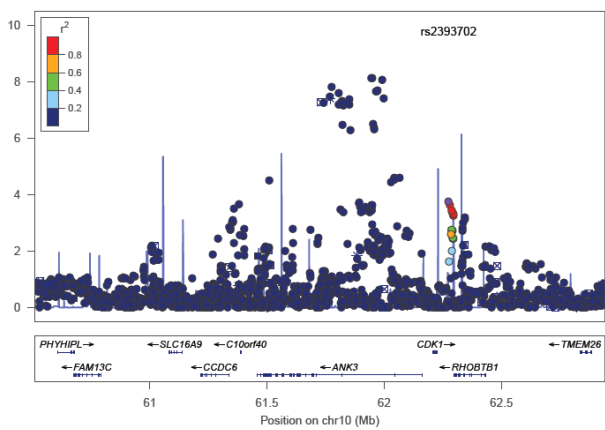
Chr_10_rs9804190



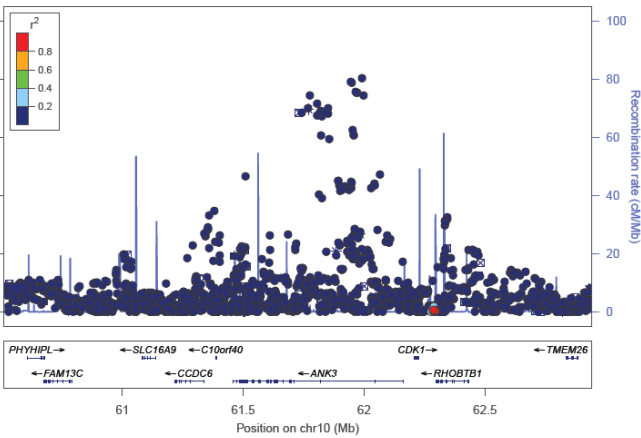
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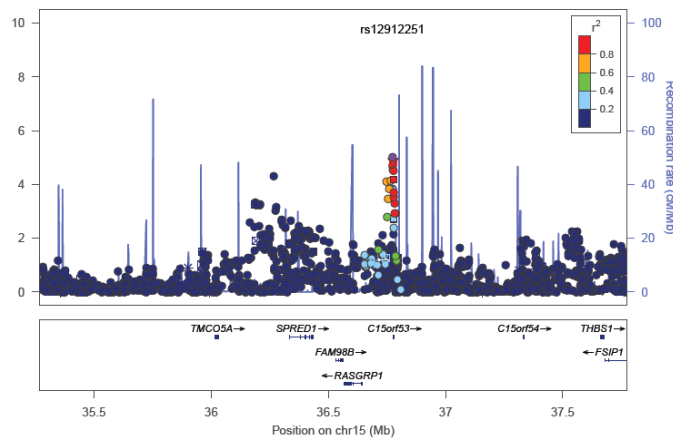
Chr_10_rs2393702



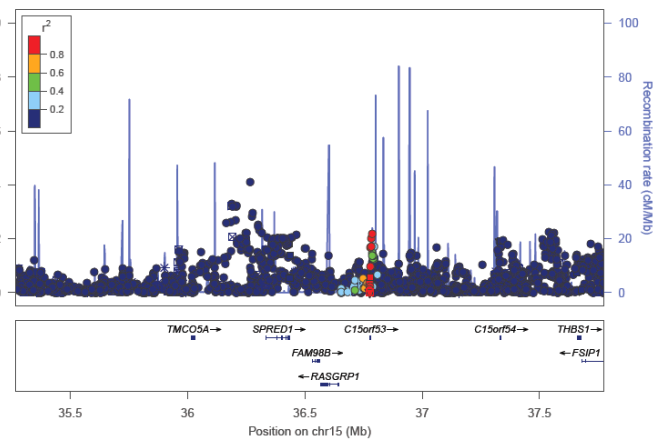
Chr_10_rs10994397_conditional_analysis



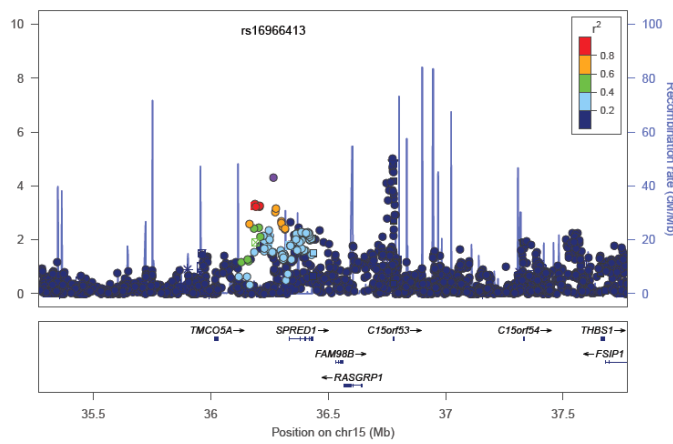
Chr_15_rs12912251



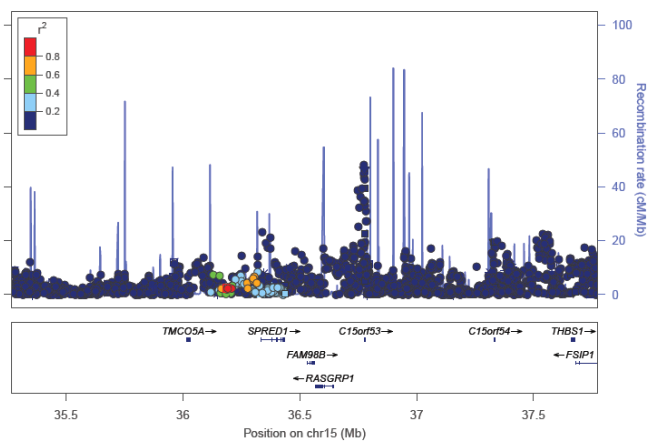
Chr_15_rs12912251_conditional_analysis



Chr_15_rs16966413



Chr_15_rs16966413_conditional_analysis



SUPPLEMENTARY TABLES

Supplementary Table 1: Summary of samples and methods in primary studies used in combined analysis following all QC steps.

Sample	Ancestry	Case (n)	Control (n)	BD1	BD2	SAB	BD-NOS ^a	Diagnosis	Interview	Controls screened	λ
COMBINED ANALYSIS SAMPLES											
BOMA-Bipolar Study	German	675	1297	673 (99.7%)	2 (0.3%)	0	0	DSMIV	SCID	N	1.04
Genetic Association Information Network (GAIN) & Bipolar Genome Study (BiGS)	European-American	542	649	516 (95%)	0	26 (5%)	0	DSMIIR & IV	DIGS	Y	1.03
GlaxoSmithKline (GSK)	British/Canadian/Scottish	890	902	632 (71%)	80 (9%)	134 (15%)	44 (5%)	DSMIV	SCAN	N	1.03
Pritzker Neuropsychiatric Disorders Research Consortium (NIMH/Pritzker)	European-American	1130	718	1130 (100%)	0	0	0	DSMIIR & IV	DIGS	Y	1.02
Systematic Treatment Enhancement Program for Bipolar Disorder (STEP1)	European-American	922	645	922 (100%)	0	0	0	DSMIV	MINI	Y	1.03
Systematic Treatment Enhancement Program for Bipolar Disorder (STEP2)	European-American	659	192	108 (16%)	551 (84%)	0	0	DSMIV	MINI	Y	1.02
Thematically Organized Psychosis (TOP) Study	Norwegian	203	349	119 (59%)	58 (29%)	6 ^b (3%)	20 (9%)	DSMIV	SCID	Y	1.03
Trinity College Dublin	Irish	150	797	150 (100%)	0	0	0	DSMIV	SCID	N	1.02
University College London	British	457	495	457 (100%)	0	0	0	DSMIV	SADS-L	Y	1.01
University of Edinburgh	Scottish	282	275	282 (100%)	0	0	0	DSMIV	SADS	N	1.03
Wellcome Trust Case-Control Consortium (WTCCC)	British	1571	2931	1300 (83%)	133 (8%)	97 (6%)	41 (3%)	RDC	SCAN	N	1.08
COMBINED ANALYSIS TOTAL		7481	9250	6289 (84%)	824 (11%)	263 (4%)	105 (1%)				

^aBD-NOS includes manic disorder; ^bIncludes psychotic depression n=3. SCID^{15,28}; DIGS⁹; SCAN¹⁴; MINI¹⁶; SADS-L²⁸; λ genomic control lambda

Supplementary Table 2: Primary GWAS association analysis for SNPs in regions with a SNP Pgc < 5 x 10⁻⁵.

SNP	CHR	BP	N	CLUMP POSITION	SIZE (kb)	Genes within 20 kb	FREQ A1	A1	A2	OR	(P)GC
rs10994397	10	61949130	60	chr10:61718410..62107916	389.5	ANK3	0.06	T	C	1.35	7.08E-09
rs9371601	6	152832266	144	chr6:152748756..152911419	162.7	SYNE1*	0.36	T	G	1.15	4.27E-08
rs7296288	12	47766235	50	chr12:47675587..47886877	211.3	TUBA1B,TUBA1A,RHEBL1,PRKAG1,MLL2,LMBR1L,DHH,DDN*	0.48	C	A	1.15	8.39E-08
rs12576775	11	78754841	29	chr11:78734745..78869105	134.4	ODZ4	0.18	G	A	1.18	2.09E-07
rs736408	3	52810394	212	chr3:52192744..53203382	1011	WDR82,TWF2,TNNC1,TMEM110,TLR9,STAB1,SPCS1,SNORD69,SNORD19,SNORD19B,SFMBT1,SEMA3G,RFT1,PRKCD,PPM1M,PHF7,PBRM1,NT5DC2,NISCH,NEK4,MUSTN1,LOC440957,ITIH1*,ITIH3,ITIH4,GNL3,GLYCTK,GLT8D1,DNAH1,BAP1,ALAS1	0.34	T	C	0.87	1.22E-06
rs6746896	2	96774676	14	chr2:96715567..96827256	111.7	LMAN2L,FER1L5,CNNM4	0.32	G	A	0.88	2.33E-06
rs11085829	19	13035312	11	chr19:12957285..13035312	78.03	NFIX	0.35	A	G	0.87	4.03E-06
rs4765913	12	2290157	87	chr12:2159912..2310725	150.8	CACNA1C	0.21	A	T	1.15	6.50E-06
rs10896135	11	66307578	127	chr11:65555535..66549905	994.4	ZDHHC24,YIF1A,TMEM151A,SYT12,SPTBN2,SLC29A2,SF3B2,RIN1,RCE1,RBM4B,RBM4,RBM14,RAB1B,PEL13,PC,PACS1,NPAS4,MRPL11,LRFN4,KLC2,GAL3ST3,DPP3,CTSF,CNIH2,CD248,CCS,CCDC87,C11orf86,C11orf80,BRMS1,BBS1,B3GNT1,ACTN3	0.26	C	G	0.88	8.46E-06
rs10028075	4	87186854	47	chr4:87150506..87294783	144.3	MAPK10	0.45	T	C	1.12	8.96E-06
rs12912251	15	36773660	26	chr15:36655206..36787776	132.6	C15orf53*	0.30	T	G	0.88	9.57E-06
rs3774609	3	53807943	55	chr3:53720665..53833581	112.9	CHDH,CACNA1D	0.37	G	T	0.89	1.14E-05
rs3845817	2	65612029	34	chr2:65580381..65654486	74.11		0.39	T	C	1.12	1.65E-05
rs2287921	19	53920084	43	chr19:53808367..53971440	163.1	SPHK2,SEC1,RPL18,RASIP1*,NTN5,MAMSTR,IZUMO1*,FUT2,FUT1,FGF21,FAM83E,DBP,CA11	0.47	T	C	0.89	1.68E-05
rs4332037	7	1917335	35	chr7:1824993..2077043	252.1	MAD1L1	0.18	T	C	1.15	1.78E-05
rs11168751	12	47505405	2	chr12:47477259..47505405	28.15	CACNB3	0.15	G	C	1.19	1.80E-05
rs7578035	2	98749324	157	chr2:98671226..99475683	804.5	TXNDC9,TSGA10,REV1,MRPL30,MITD1,MGAT4A,LYG1,LYG2,LIPT1,EIF5B,C2orf55,C2orf15	0.50	T	G	0.90	1.83E-05
rs2281587	10	105367339	30	chr10:105252560..105510484	257.9	SH3PXD2A,NEURL	0.35	T	C	0.89	1.96E-05
rs6550435	3	36839493	38	chr3:36818153..36939587	121.4	LBA1	0.36	G	T	1.12	1.97E-05
rs3968	9	4931997	7	chr9:4926407..4934004	7.597		0.17	G	C	0.86	2.09E-05
rs17395886	4	162498835	13	chr4:162463932..162573545	109.6	FSTL5	0.16	A	C	0.86	2.18E-05
rs12730292	1	79027350	57	chr1:78919287..79068140	148.9		0.36	G	C	0.89	2.37E-05
rs263906	1	101750922	42	chr1:101647436..101790026	142.6		0.25	T	C	0.88	2.42E-05
rs875326	1	173556022	17	chr1:173555959..173602808	46.85	TNR	0.16	T	C	0.87	2.51E-05
rs11162405	1	78242248	100	chr1:77778712..78490438	711.7	ZZZ3,USP33,NEXN,MGC27382,GIPC2,FUBP1,FAM73A,DNAJB4,AK5	0.42	G	A	1.11	2.54E-05
rs2175420	11	78801531	30	chr11:78801531..78858702	57.17	ODZ4	0.18	T	C	1.15	2.90E-05
rs9804190	10	61509837	11	chr10:61487486..61513457	25.97	ANK3	0.22	T	C	0.86	3.06E-05
rs4660531	1	41612409	6	chr1:41607648..41622769	15.12		0.36	T	G	1.12	3.16E-05
rs7827290	8	142369497	42	chr8:142326560..142443151	116.6	LOC731779,GPR20	0.33	G	T	1.13	3.54E-05
rs13245097	7	2307581	61	chr7:1862167..2307581	445.4	SNX8,NUDT1,MAD1L1,FTSJ2	0.40	T	C	0.88	3.81E-05
rs6102917	20	40652833	18	chr20:40507718..40689191	181.5	PTPR	0.02	G	C	0.69	3.88E-05
rs2176528	2	194580428	76	chr2:194047558..194710792	663.2		0.32	G	C	0.87	3.98E-05
rs2070615	12	47504438	9	chr12:47473717..47547773	74.06	RND1,DDX23,CACNB3	0.44	A	G	0.90	4.00E-05
rs4668059	2	168874528	3	chr2:168800188..168874528	74.34	STK39	0.14	C	T	1.18	4.45E-05
rs780148	10	80605089	54	chr10:80577333..80688954	111.6	ZMIZ1	0.49	G	C	0.89	4.66E-05
rs16966413	15	36267191	107	chr15:36164653..36432881	268.2	SPRED1	0.10	G	A	1.19	4.74E-05
rs10776799	1	115674570	15	chr1:115662788..115679147	16.36	NGF	0.18	G	T	1.15	4.84E-05
rs8006348	14	50595223	16	chr14:50588675..50611358	22.68	TRIM9	0.26	G	A	1.12	4.91E-05

*The following are non-synonymous SNPs have LD > 0.7 with index SNPs above (HapMap 1000G August 2009):

index=rs2287921, rs2287922, r2=0.8298, RASIP1, Arg601Cys
index=rs2287921, rs2307019, r2=0.7594, IZUMO1, Ala333Val
index=rs7296288, rs10783299, r2=0.7143, DDN, Glu607Gly
index=rs12912251, rs7165988, r2= 1, FLJ35695, L3V
index=rs736408, rs1042779, r2=0.70815, ITIH1, Q595R
index=rs9371601, rs214976, r2=0.92857, SYNE1, V1042A

BP=basepair position on Build 36; A1=The OR is predicted to the A1 allele

Supplementary Table 3. Meta-analysis of direct genotypes only for Table 2 SNPs

SNP	CHR	Position	N _S	N _G	P _{raw}	P _{Random}	OR	OR _{Random}	P _{het}	I _{het}
rs9371601	6	152832266	8	11114	0.00004	0.00004	1.13	1.13	0.88	0.00
rs10994397	10	61949130	3	5611	0.00311	0.00311	1.27	1.27	0.71	0.00
rs12576775	11	78754841	3	5611	0.00015	0.00290	1.22	1.22	0.20	38.13
rs7296288	12	47766235	8	11115	0.00013	0.00013	1.12	1.12	0.46	0.00

N_S=number of studies in which SNP was genotyped; rs9371601 and rs7296288 are genotyped in all Affymetrix data; rs10994397 and rs12576775 are genotyped in all Illumina data. N_G=number of genotypes. P_{raw}=Fixed-effects meta-analysis *P* value; P_{Random}=Random-effects meta-analysis *P* value; OR=Fixed-effects summary odds ratio for the minor allele; OR_{Random}=Random-effects summary odds ratio; P_{het}=Cochrane's *Q* *P* value; I_{het}=I² heterogeneity index (0-100).

Supplementary Table 4. Fixed effects meta-analysis of Table 2 SNPs

SNP	CHR	N _s	P _{raw}	P _{gc post}	P _{gc pre}	P _{gc pre post}	P _{Random}	OR	OR _{Random}	P _{het}	I _{het}
rs10994397	10	11	2.9 x 10 ⁻¹⁰	3.0 x 10 ⁻⁹	5.4 x 10 ⁻¹⁰	2.8 x 10 ⁻⁹	2.9 x 10 ⁻¹⁰	1.35	1.35	0.53	0.00
rs9371601	6	11	1.5 x 10 ⁻⁸	1.0 x 10 ⁻⁷	2.5 x 10 ⁻⁸	9.4 x 10 ⁻⁸	1.5 x 10 ⁻⁸	1.15	1.15	0.86	0.00
rs7296288	12	11	2.6 x 10 ⁻⁸	1.6 x 10 ⁻⁷	5.3 x 10 ⁻⁸	1.9 x 10 ⁻⁷	2.6 x 10 ⁻⁸	1.14	1.14	0.47	0.00
rs12576775	11	11	7.6 x 10 ⁻⁸	4.2 x 10 ⁻⁷	1.3 x 10 ⁻⁷	4.3 x 10 ⁻⁷	7.6 x 10 ⁻⁸	1.18	1.18	0.71	0.00

N_s=equals number of studies with imputed data for the SNP. P_{raw}=Fixed-effects meta-analysis *P* value, λ_{gc}=1.13; P_{gc post}=Fixed-effects meta-analysis *P* value, genomic controlled post meta-analysis, λ_{gc}=1; P_{gc pre}=Fixed-effects meta-analysis *P* value, each study genomic controlled prior to meta-analysis, λ_{gc}= 1.09; P_{gc pre post}=Fixed-effects meta-analysis *P* value,each study genomic controlled prior to meta-analysis and post meta-analysis, λ_{gc}=1; P_{Random}=Random-effects meta-analysis *P* value; OR=Fixed-effects summary odds ratio for the minor allele; OR_{Random}=Random-effects summary odds ratio; P_{het}=Cochrane's Q *P* value; I_{het}=I² heterogeneity index (0-100).

Supplementary Table 5. Summary of samples and methods used in replication analyses

Sample	Ancestry	Case (n)	Cont. (n)	BD1	BD2	SAB	BD-NOS	Diagnosis	Interview	Cont. screen	λ
French	French	451	1631	341 (78%)	98 (22%)	0	12	DSMIV	DIGS	N	1.03
Bipolar Genome Study/Translational Genomics Institute (BiGS/TGEN1)	European-American	1188	1112	1111 (93.5%)	0	77 (6.5%)	0	DSMIV	DIGS	Y	1.03
FaST	European-American	494		383 (77.5%)	110 (22.3%)	0	1 (0.2%)	DSMIV	MINI ADE	Y	
International Case-Control Cohort-Bipolar Disorder (ICCBD)	Swedish	825 ^a	2084	489 (82%)	96 (16%)	0	14 ^b (2%)	DSMIV	MINI Hosp record	NA	1.07
BOMA-Bipolar Study rep1	German	488	857	289 (59.2%)	169 (34.6%)	1 (0.2%)	29 (5.9%)	DSMIV	SCID, SADS-L	Y	1.00
BOMA-Bipolar Study rep2	German	180	525	175 (97.2%)	5 (2.8%)	0	0	DSMIV	AMDP	N	1.05
Australian	Australian	326	1787	253 (77.6%)	71 (21.8%)	1 (0.3%)	1 (0.3%)	DSMIV	SCID, DIGS	N	1.00
Icelandic	Icelandic	544 ^c	34426	314 (82%)	71 (18%)	0	0	DSMIV/RDC	SADSL/CITI-Auto	N	1.11
REPLICATION TOTAL		4496	42422								
REPLICATION WITH SUBTYPE AVAILABLE		4111		3355 (81.6%)	620 (15.1%)	79 (1.9%)	57 (1.4%)				
GRAND TOTAL		11977	51672								

^aDiagnoses were made from hospital discharge records 226 of the samples, and thus DSMIV subtypes are unavailable, subtypes are given for 599 of the cases, ^bBDNOS included antidepressant induced mania ^cDSMIV diagnoses were not available for 150 subjects who had been collected under earlier diagnostic criteria and described above. DIGS⁹; MINI¹⁶; ADE; SCID¹; SADS-L²; AMDP; CITI-AUTO; λ =genomic control lambda.

Supplementary Table 6. Meta-analysis results for SNPs tested in replication

SNP	CHR	POS	A1	A2	FRQ(A1)	PRIMARY GWS			REPLICATION META-ANALYSIS					
						P _{GC}	OR	N	P _{REP}	OR	P _{FIXED}	OR _{FIXED}	P _{HET}	I _{REP}
rs4765913	12	2290157	A	T	0.21	6.50E-06	1.150	7	0.00032	1.132	0.00032	1.132	0.912	0
rs10896135	11	66307578	C	G	0.26	8.46E-06	0.880	7	0.00294	0.913	0.00294	0.913	0.552	0
rs2070615*	12	47504438	A	G	0.44	4.00E-05	0.899	7	0.00505	0.926	0.12140	0.938	0.049	53
rs12576775	11	78754841	A	G	0.82	2.09E-07	0.846	7	0.01517	0.917	0.01517	0.917	0.653	0
rs2175420*	11	78801531	C	T	0.82	2.90E-05	0.870	7	0.01559	0.917	0.01559	0.917	0.692	0
rs3845817	2	65612029	C	T	0.61	1.65E-05	0.895	7	0.01796	0.936	0.04512	0.933	0.191	31
rs2176528	2	194580428	C	G	0.68	3.98E-05	1.147	5	0.02084	1.092	0.02084	1.092	0.984	0
rs4660531	1	41612409	G	T	0.64	3.16E-05	0.892	6	0.02219	0.933	0.02219	0.933	0.599	0
rs7578035	2	98749324	G	T	0.50	1.83E-05	1.115	7	0.02588	1.063	0.04496	1.068	0.227	26
rs2287921	19	53920084	C	T	0.53	1.68E-05	1.122	7	0.02729	1.064	0.02729	1.064	0.853	0
rs11168751*	12	47505405	C	G	0.85	1.80E-05	0.841	7	0.02861	0.901	0.02861	0.901	0.889	0
rs7296288	12	47766235	A	C	0.52	8.39E-08	0.872	7	0.03000	0.942	0.04910	0.939	0.278	20
rs7827290	8	142369497	G	T	0.33	3.54E-05	1.134	7	0.03348	1.065	0.03348	1.065	0.540	0
rs12730292	1	79027350	C	G	0.64	2.37E-05	1.125	7	0.03418	1.064	0.05566	1.064	0.325	14
rs12912251	15	36773660	G	T	0.70	9.57E-06	1.130	7	0.04073	1.061	0.19540	1.055	0.081	47
rs4332037	7	1917335	C	T	0.82	1.78E-05	0.867	7	0.05945	0.934	0.19460	0.934	0.065	49
rs6550435	3	36839493	G	T	0.36	1.97E-05	1.118	7	0.06523	1.053	0.11050	1.056	0.209	29
rs17395886	4	162498835	A	C	0.16	2.18E-05	0.860	7	0.07028	0.933	0.07028	0.933	0.765	0
rs6746896	2	96774676	A	G	0.68	2.33E-06	1.136	7	0.07711	1.052	0.11580	1.052	0.294	18
rs736408	3	52810394	C	T	0.66	1.22E-06	1.144	7	0.09293	1.050	0.09293	1.050	0.698	0
rs11162405	1	78242248	A	G	0.58	2.54E-05	0.898	7	0.09519	0.955	0.12310	0.953	0.285	19
rs9804190	10	61509837	C	T	0.78	3.06E-05	1.166	7	0.19260	1.043	0.41780	1.033	0.174	33
rs9371601	6	152832266	G	T	0.64	4.27E-08	0.867	7	0.20690	0.966	0.20690	0.966	0.560	0
rs3774609	3	53807943	G	T	0.37	1.14E-05	0.888	7	0.21400	0.966	0.21400	0.966	0.874	0
rs10994397	10	61949130	C	T	0.94	7.08E-09	0.742	7	0.23190	0.938	0.27150	0.938	0.331	13
rs4668059	2	168874528	C	T	0.14	4.45E-05	1.177	7	0.31540	1.044	0.31540	1.044	0.687	0
rs16966413	15	36267191	A	G	0.90	4.74E-05	0.842	4	0.31600	0.950	0.31600	0.950	0.575	0
rs6102917	20	40652833	C	G	0.98	3.88E-05	1.441	7	0.32930	1.112	0.32930	1.112	0.820	0
rs11085829	19	13035312	A	G	0.35	4.03E-06	0.868	7	0.34950	0.974	0.34950	0.974	0.586	0
rs875326	1	173556022	C	T	0.84	2.51E-05	1.153	7	0.36680	1.034	0.36680	1.034	0.909	0
rs13245097*	7	2307581	C	T	0.60	3.81E-05	1.133	7	0.39240	1.024	0.39240	1.024	0.623	0
rs780148	10	80605089	C	G	0.51	4.66E-05	1.122	7	0.45940	1.027	0.84620	1.009	0.167	34
rs2281587	10	105367339	C	T	0.65	1.96E-05	1.120	7	0.74310	1.009	0.74310	1.009	0.678	0
rs10776799	1	115674570	G	T	0.18	4.84E-05	1.147	7	0.86750	1.006	0.86750	1.006	0.940	0
rs263906	1	101750922	C	T	0.75	2.42E-05	1.131	7	0.88030	1.005	0.88030	1.005	0.607	0
rs10028075	4	87186854	C	T	0.55	8.96E-06	0.894	7	0.51830	1.018	0.50510	1.024	0.150	36
rs3968	9	4931997	C	G	0.83	2.09E-05	1.166	7	0.02554	0.924	0.05668	0.920	0.206	29
rs8006348	14	50595223	A	G	0.74	4.91E-05	0.891	7	0.15070	1.045	0.15070	1.045	0.585	0

POS= basepair position in Build 36. A1=Allele predicted towards for OR N=number of replication studies where the SNP or a proxy was available. SNPs are listed in the order found in Table 3 (1-tailed replication *P* value). P_{REP}=2-tailed *P* value. SNPs marked by an asterisk do not represent independent association signals.

Supplementary Table 7. Replication results by site

This table shows odds ratios for each of the replication datasets. At missing entries, no SNP in the region had a sufficient R^2 in that particular dataset. Odds ratios are reported for the allele given in the discovery sample (**Supplementary Table 2**)

SNP	CHR	POS	A1	AUSTRALIAN	BiGS/TGEN/ FaST	FRENCH	BOMA rep1	BOMA rep2	ICELANDIC	ICCBD- Sweden
rs4765913	12	2290157	A	1.088	1.165	1.095	1.073	1.175	1.074	1.217
rs10896135	11	66307578	C	0.839	0.948	0.875	0.924	1.140	0.845	0.948
rs2070615*	12	47504438	A	0.846	0.953	1.000	1.026	1.272	0.882	0.833
rs12576775	11	78754841	A	0.813	0.915	0.936	0.887	1.275	0.947	0.906
rs2175420*	11	78801531	C	0.973	0.896	0.951	0.850	1.066	1.000	0.841
rs3845817	2	65612029	C	1.050	0.913	0.979	0.829	0.700	0.982	0.955
rs2176528	2	194580428	C	NA	1.107	1.058	NA	1.104	1.117	1.063
rs4660531	1	41612409	G	0.913	0.974	0.814	NA	1.018	0.938	0.947
rs7578035	2	98749324	G	1.056	1.048	1.196	1.210	1.029	1.062	0.954
rs2287921	19	53920084	C	1.030	1.123	1.043	0.967	1.034	1.103	1.045
rs11168751*	12	47505405	C	0.801	0.932	0.945	1.072	0.850	0.900	0.817
rs7296288	12	47766235	A	0.917	1.033	0.973	0.891	0.872	0.977	0.844
rs7827290	8	142369497	G	1.143	1.064	0.957	1.057	0.893	1.155	1.058
rs12730292	1	79027350	C	1.003	1.158	1.225	1.024	0.975	0.995	1.018
rs12912251	15	36773660	G	1.085	1.072	0.872	1.244	0.864	1.118	1.054
rs4332037	7	1917335	C	1.031	0.977	1.024	0.966	0.819	0.731	1.004
rs6550435	3	36839493	G	1.247	1.099	1.021	0.977	1.199	0.953	1.052
rs17395886	4	162498835	A	1.029	0.882	0.892	0.869	0.875	1.029	0.898
rs6746896	2	96774676	A	1.028	1.101	1.186	1.024	1.034	0.921	1.090
rs736408	3	52810394	C	1.103	1.028	0.989	1.053	0.919	1.145	1.029
rs11162405	1	78242248	A	0.970	1.015	0.931	1.031	0.761	0.859	0.985
rs9804190	10	61509837	C	0.876	1.085	0.984	1.079	0.840	1.186	1.023
rs9371601	6	152832266	G	1.082	0.967	1.008	0.856	0.897	0.929	0.997
rs3774609	3	53807943	G	1.034	0.943	0.899	1.026	0.897	0.979	0.973
rs10994397	10	61949130	C	0.925	1.128	1.088	0.917	0.959	0.726	0.899
rs4668059	2	168874528	C	1.031	0.959	1.140	1.163	1.057	1.143	0.947
rs16966413	15	36267191	A	NA	0.889	1.096	NA	NA	0.971	0.914
rs6102917	20	40652833	C	1.379	1.110	1.007	1.008	0.607	1.114	1.255
rs11085829	19	13035312	A	0.979	0.982	0.865	1.015	1.181	1.005	0.947
rs875326	1	173556022	C	1.106	1.026	1.061	1.075	1.065	1.080	0.944
rs13245097*	7	2307581	C	0.945	1.026	0.985	0.963	1.101	1.135	1.013
rs780148	10	80605089	C	0.975	1.040	0.845	0.891	0.794	1.098	1.140
rs2281587	10	105367339	C	0.915	1.039	1.011	1.004	1.226	1.039	0.959
rs10776799	1	115674570	G	0.962	1.014	0.914	1.015	1.065	1.062	1.006
rs263906	1	101750922	C	1.070	0.963	1.164	1.089	1.025	0.928	1.012
rs10028075	4	87186854	C	0.994	0.961	1.222	0.984	1.126	0.945	1.063
rs3968	9	4931997	C	1.069	0.977	0.938	0.950	0.644	0.812	0.945
rs8006348	14	50595223	A	0.897	1.083	1.130	1.053	0.963	0.999	1.088

POS =basepair position in Build 36, A1= Allele predicted towards for OR, SNPs marked by an asterisk do not represent independent association signals.

Supplementary Table 8. Simulation of effects of winner's curse on estimated ORs and replication power

True GRR	Estimated OR (mean)			<i>OR fold-inflation</i>
	<i>All</i>	<i>n.s.</i>	<i>p<5e-8</i>	
1.50	1.508	-	1.508	1.00
1.30	1.304	-	1.304	1.00
1.20	1.203	1.146	1.209	1.03
1.10	1.101	1.100	1.174	1.66
1.08	1.081	1.081	1.172	2.03
1.05	1.051	1.051	1.170	3.16
1.02	1.021	1.021	-	-

Power in replication sample				
<i>Assuming true mean OR</i>				
True GRR	<i>a=0.05</i>	<i>a=0.01</i>	<i>a=0.001</i>	
1.50	100	100	100	
1.30	100	100	100	
1.20	100	100	99	
1.10	82	62	34	
1.08	65	41	17	
1.05	31	13	3	
1.02	9	2	0	

Supplementary Table 9. Variance explained in BD target samples using a BD discovery sample

Discovery <i>P</i> value threshold	<i>R</i> ²	Target <i>P</i> value
0.01	0.0062	0.003206
0.05	0.0164	4.68 x 10 ⁻⁰⁶
0.10	0.0189	1.48 x 10 ⁻⁰⁶
0.20	0.0213	1.58 x 10 ⁻⁰⁷
0.30	0.0210	2.33 x 10 ⁻⁰⁷
0.40	0.0237	4.11 x 10 ⁻⁰⁸
0.50	0.0283	1.71 x 10 ⁻⁰⁹

Supplementary Table10. Association analysis of BD loci in schizophrenia and BD combined

SNP original	SNP proxy	R ²	CHR	Base Pair	A1	A2	Freq A1	Freq A2	COMBINED P value	COMBINED OR
rs4765913	-		12	2219845	C	G	0.35	0.33	7.70E-08	1.110
rs736408	rs2535629	0.88	3	52808259	A	G	0.33	0.35	8.41E-09	0.898
rs10994397	rs10994359	0.86	10	61892113	T	C	0.93	0.94	2.45E-08	0.820
rs12576775	rs17138230	1.00	11	78753500	A	T	0.81	0.83	3.90E-06	0.902
rs9371601	-		6	152832266	T	G	0.36	0.35	1.41E-05	1.081
rs7296288	rs2117028	0.52	12	47767215	A	G	0.43	0.42	1.94E-05	1.108

Base Pair=hg18; SCZ cases = 9375;

Combined cases = 16374; Combined controls = 14044

R² calculated using Hapmap2: rs736408, rs12576775 and HapMap3: rs10994397, rs7296288; rs4765913 did not have an adequate proxy and thus was imputed in the schizophrenia samples using Hapmap2

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