

Supplementary materials

1. Description of individual study samples

The current study combined BD case-control GWAS datasets from 5 previous studies (here designated GAIN-NIMH, TGEN1, BoMA Bipolar, WTCCC1-BD, and STEP-BD).

These are described in detail elsewhere (1-7).

To increase power, we also used SNP array data from 2,072 bipolar patients submitted to the Consortium on Lithium Genetics (ConLiGen) project.(8) Individuals diagnosed by a psychiatrist or clinical psychologist with a DSM-III or DSM-IV diagnosis of BD were included in this study. Most subjects had bipolar I or bipolar II disorder and were treated over a period of at least 6 months with lithium. Further details on this sample have been reported elsewhere (9).

We also obtained SNP array data for 20,998 psychiatrically unscreened controls from dbGaP and WTCCC2 (the 1958 British Birth Cohort and the National Blood Donors Cohort) who were enrolled in studies unrelated to neuropsychiatric disorders. A summary of the dbGaP datasets used (totaling 18,274 individuals) is provided in table S4. The WTCCC2 sample was obtained from Wellcome Trust Case Control Consortium Data Access Committee (EGAD00000000021 and EGAD00000000023). To avoid overlap, only controls who were not included in the WTCCC1 GWAS study (above) were used here.

Data were parsed into 6 sub-studies (Table1), matching cases and controls by genotyping platform. Since exact matching was not possible, Affymetrix platforms, earlier generation, and later generation Illumina platforms were each grouped separately.

2. Supplementary Figures

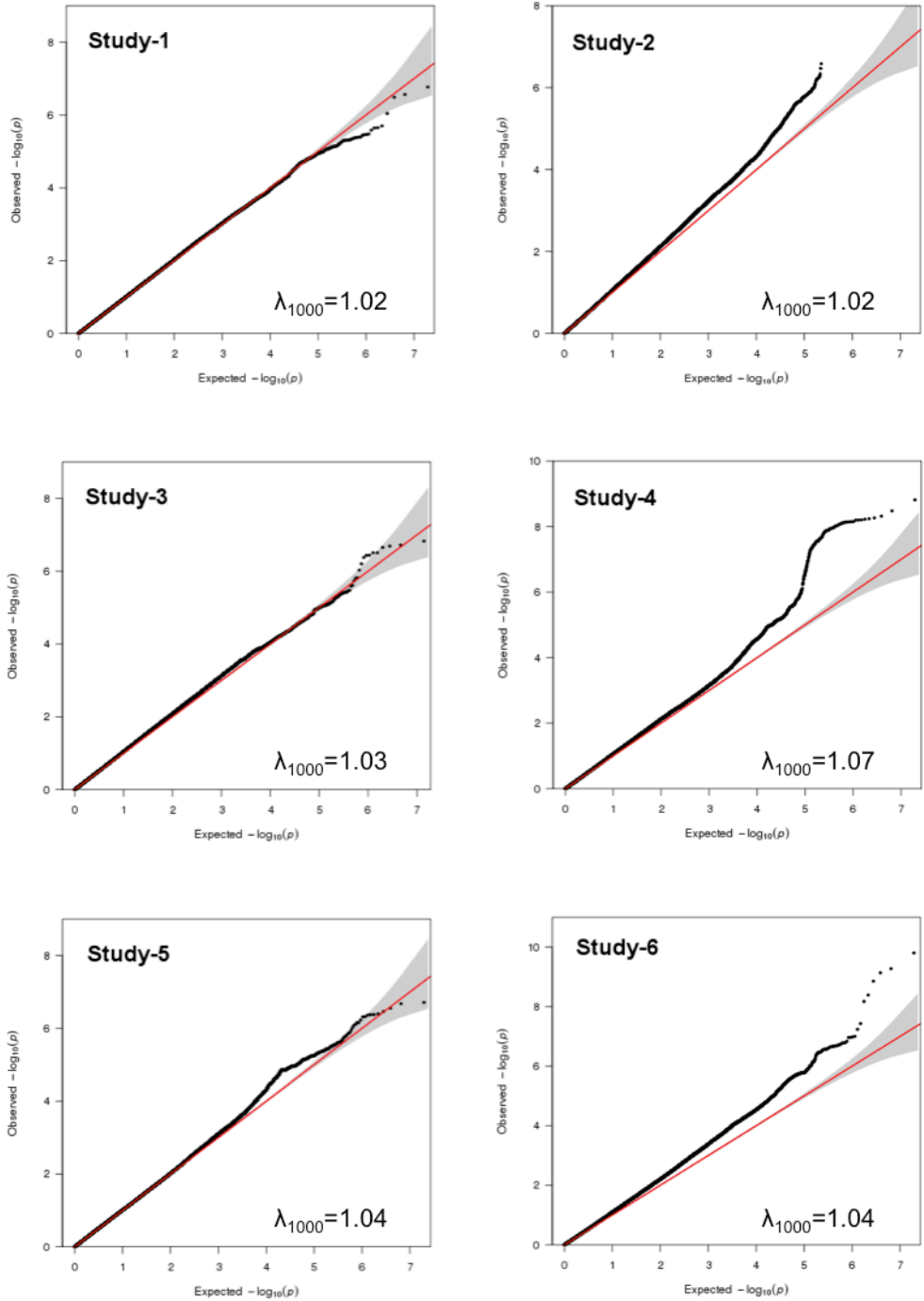


Figure S1: Q-Q plots for stage 1 sub-studies.

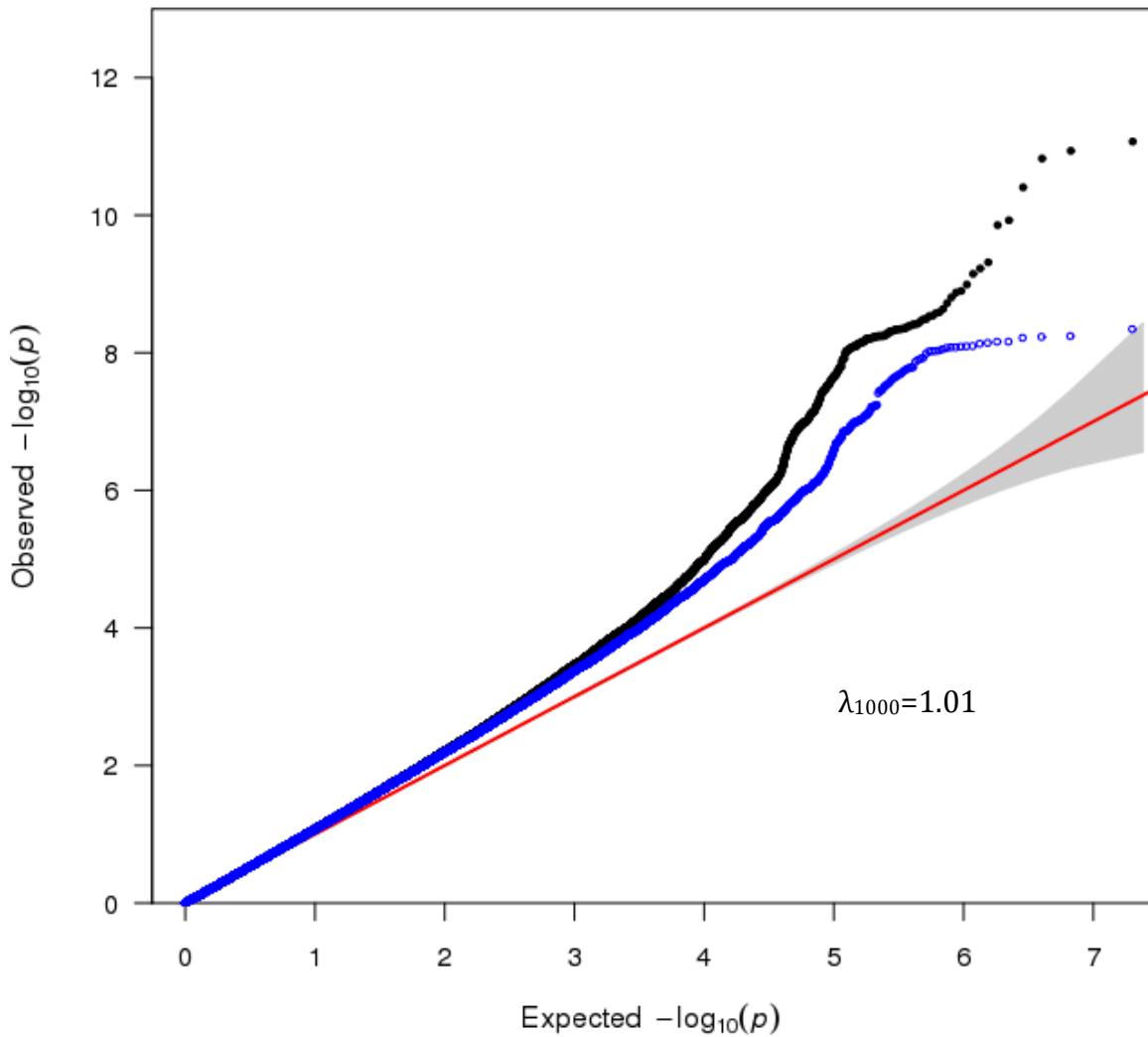


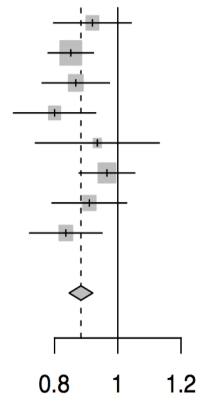
Figure S2. Q-Q plots of the meta-analysis results showing all markers (black) and after excluding previously known loci (blue). The standardized inflation factors (λ_{1000}) were 1.0059 for all markers and 1.0057 after excluding previously known loci.

a: rs9834970 (T)

Study

Study-1
Study-2
Study-3
Study-4
Study-5
Study-6
Swedish sample 1
Swedish sample 2

Fixed effect model



OR 95%-CI W(fixed)

0.92 [0.80; 1.04] 9.3%
0.85 [0.78; 0.92] 27.3%
0.87 [0.76; 0.97] 12.4%
0.80 [0.67; 0.93] 8.3%
0.94 [0.74; 1.13] 3.7%
0.97 [0.88; 1.05] 18.1%
0.91 [0.79; 1.03] 10.1%
0.84 [0.72; 0.95] 10.7%

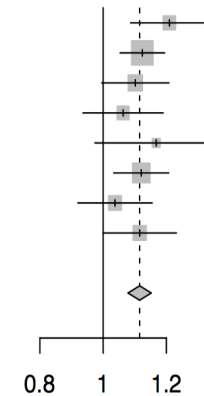
0.88 [0.85; 0.92] 100%

b: rs1487441 (A)

Study

Study-1
Study-2
Study-3
Study-4
Study-5
Study-6
Swedish sample 1
Swedish sample 2

Fixed effect model



OR 95%-CI W(fixed)

1.21 [1.09; 1.33] 9.2%
1.12 [1.05; 1.19] 27.9%
1.10 [1.00; 1.21] 12.2%
1.06 [0.94; 1.19] 8.6%
1.17 [0.97; 1.36] 3.7%
1.12 [1.03; 1.21] 18.3%
1.04 [0.92; 1.15] 10.0%
1.12 [1.00; 1.23] 10.2%

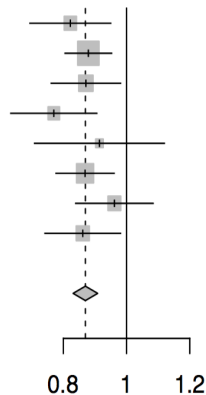
1.12 [1.08; 1.15] 100%

c: rs4236274 (G)

Study

Study-1
Study-2
Study-3
Study-4
Study-5
Study-6
Swedish sample 1
Swedish sample 2

Fixed effect model



OR 95%-CI W(fixed)

0.82 [0.69; 0.95] 9.3%
0.88 [0.81; 0.95] 27.8%
0.87 [0.76; 0.98] 12.6%
0.77 [0.63; 0.91] 8.2%
0.91 [0.71; 1.12] 3.6%
0.87 [0.78; 0.96] 17.9%
0.96 [0.84; 1.08] 10.1%
0.86 [0.74; 0.98] 10.6%

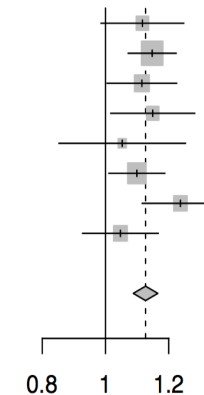
0.87 [0.83; 0.91] 100%

d: rs1054442 (C)

Study

Study-1
Study-2
Study-3
Study-4
Study-5
Study-6
Swedish sample 1
Swedish sample 2

Fixed effect model



OR 95%-CI W(fixed)

1.12 [0.99; 1.25] 8.8%
1.15 [1.07; 1.22] 26.2%
1.12 [1.00; 1.23] 12.5%
1.15 [1.02; 1.28] 8.6%
1.05 [0.85; 1.25] 3.8%
1.10 [1.01; 1.19] 19.3%
1.24 [1.12; 1.36] 10.3%
1.05 [0.93; 1.17] 10.6%

1.13 [1.09; 1.17] 100%

Figure S3: Genetic effect sizes for the most significant SNP of four replicated known BD risk loci.

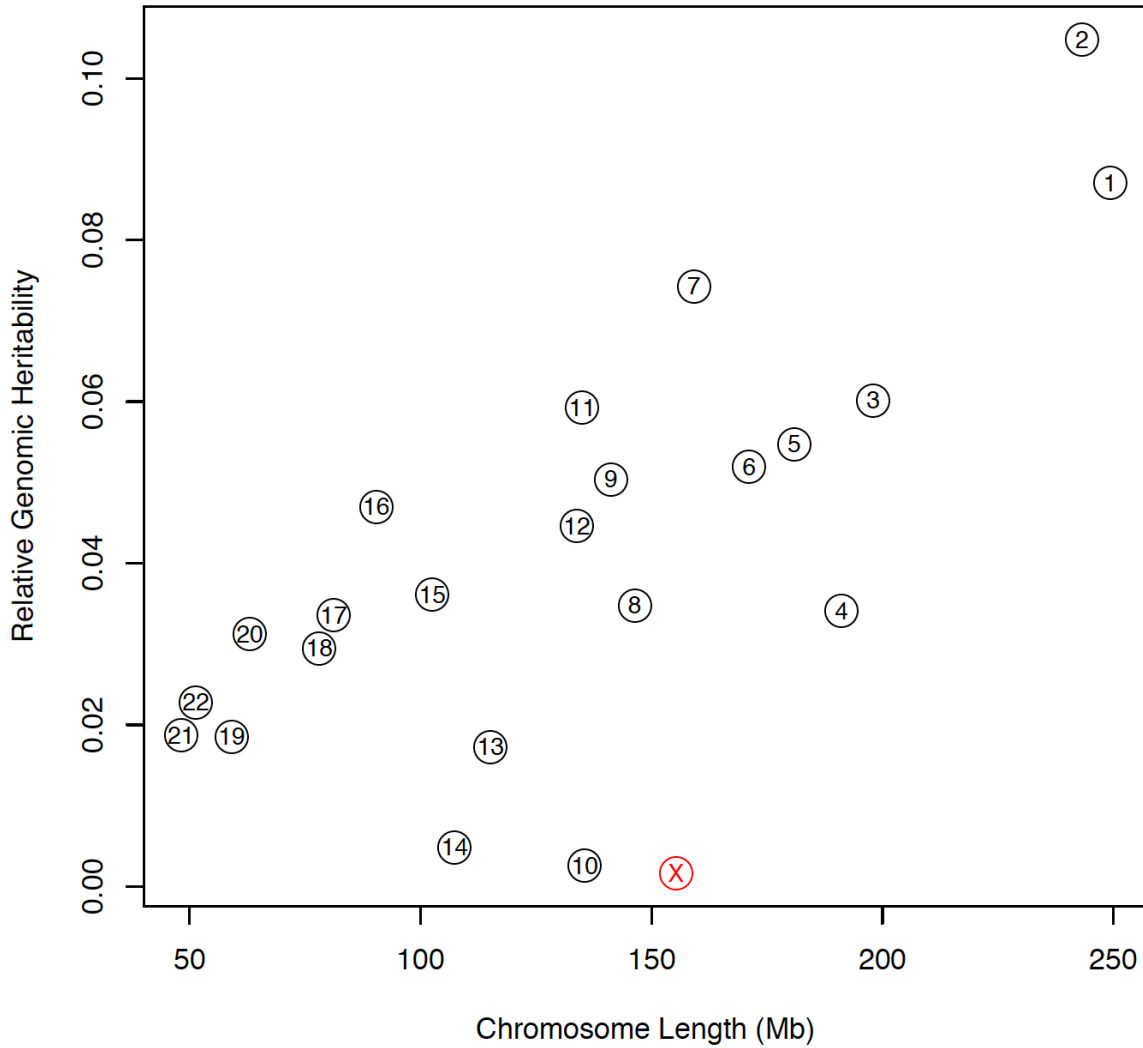
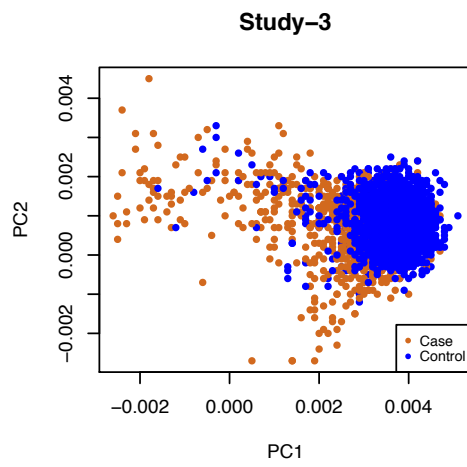
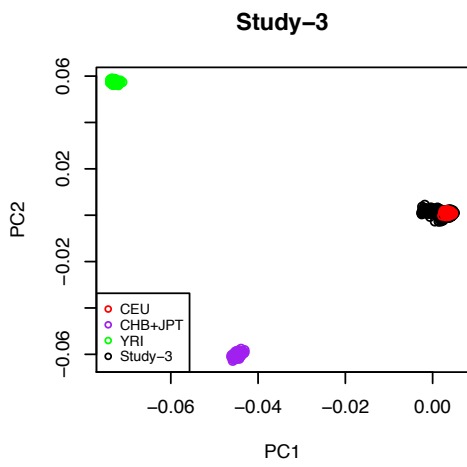
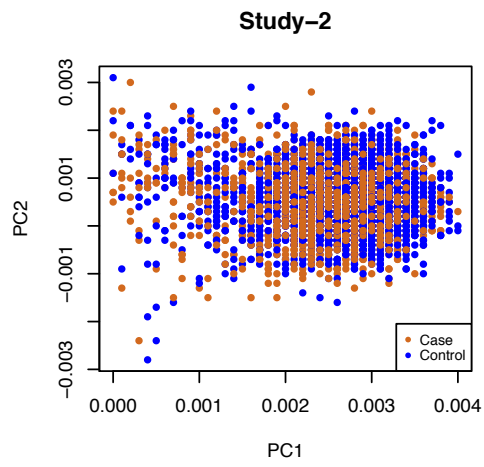
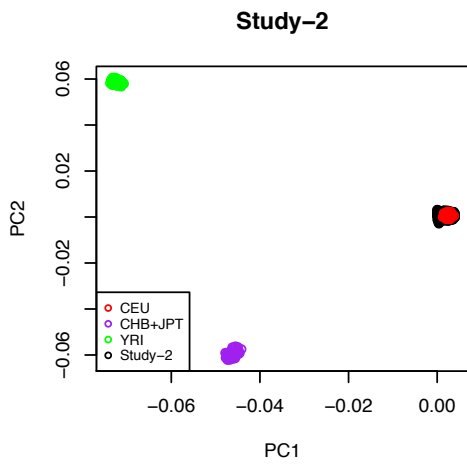
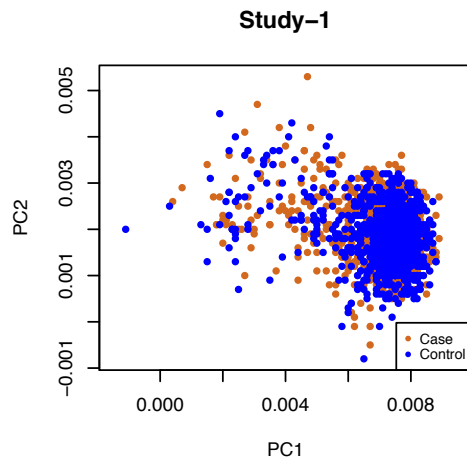
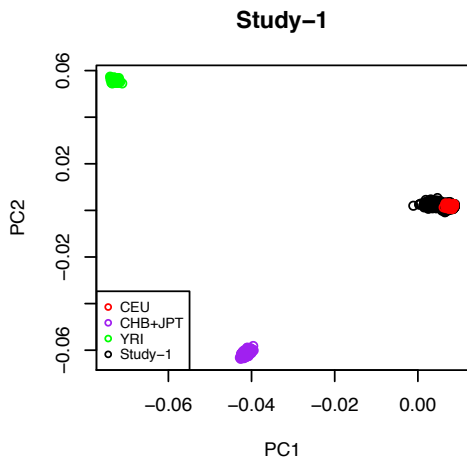


Figure S4 Genomic heritability explained by each chromosome. Relative genomic heritability is defined as the proportion of variance in disease liability attributable to each chromosome, divided by the total genomic heritability. Relative genomic heritability values are shown as medians across study samples. **Markers on X chromosome (highlighted in red) explained an unexpectedly small proportion of the heritability.**



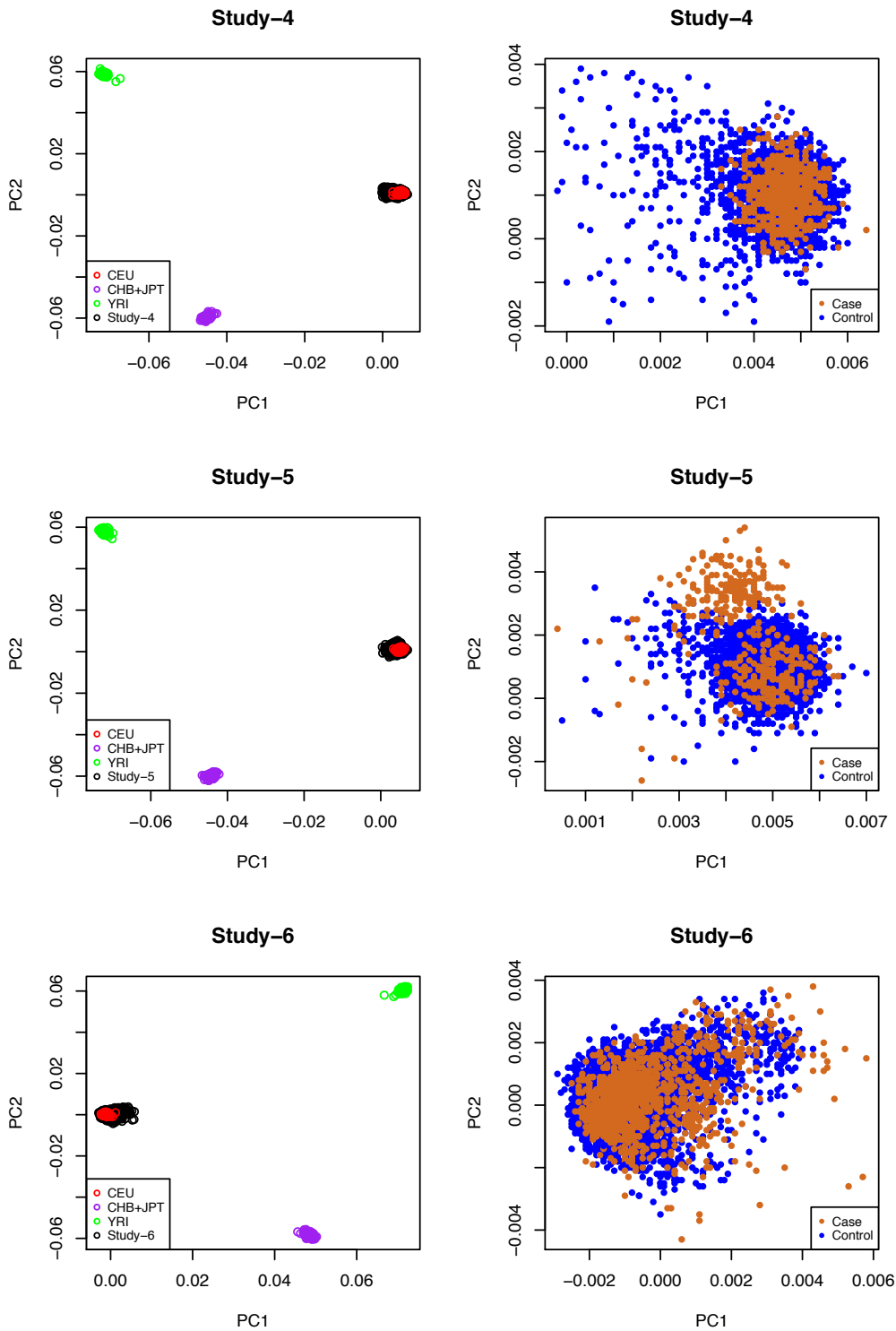


Figure S5: PCA plots for stage 1 sub-studies after removing population outliers. Left: PCA plots for HapMap subjects (red, green, purple) and subjects enrolled in each sub-study (black); Right: PCA plots for subjects enrolled in each sub-study (all are of European ancestry), with points colored by affection status)

3. Supplementary Tables

Table S1: Association analysis results for all SNPs with $P < 1 \times 10^{-6}$ (stage-1 studies only)

CHR	BP	SNP	Alleles	Stage 1		Stage 2	
				P	OR (CI)	P	OR (CI)
1	200975064	rs10920091	A/G	9.38E-07	0.89 (0.85 - 0.93)	8.03E-01	0.99 (0.91 - 1.08)
1	200976145	1:200976145	G/GA C	9.10E-07	0.89 (0.85 - 0.93)	NA	NA
1	231958984	rs201957059	CAT/ C	6.29E-07	1.13 (1.08 - 1.19)	NA	NA
3	36856030	rs9834970	T/C	3.19E-08	0.88 (0.85 - 0.92)	1.12E-03	0.87 (0.80 - 0.95)
3	36859705	rs1553656	T/C	5.13E-07	0.89 (0.86 - 0.93)	1.87E-03	0.87 (0.80 - 0.95)
3	36862680	rs4072458	T/C	3.13E-07	0.89 (0.85 - 0.93)	2.20E-03	0.88 (0.81 - 0.95)
3	36869439	rs4789	T/C	2.71E-07	0.89 (0.85 - 0.93)	1.08E-03	0.87 (0.80 - 0.95)
3	36870230	rs11129735	A/G	2.24E-07	0.89 (0.85 - 0.93)	1.11E-03	0.87 (0.80 - 0.95)
3	36889621	rs9985296	T/C	3.54E-07	0.89 (0.85 - 0.93)	4.34E-04	0.86 (0.79 - 0.93)
3	36892717	rs4441609	T/C	2.29E-07	0.89 (0.85 - 0.93)	4.02E-04	0.86 (0.79 - 0.93)
3	36896270	rs4327336	T/C	3.22E-07	1.12 (1.07 - 1.18)	NA	NA
3	36900944	rs4642070	T/C	8.80E-07	1.12 (1.07 - 1.17)	1.58E-03	1.15 (1.05 - 1.25)
3	36906822	rs28522146	C/G	8.96E-07	0.89 (0.86 - 0.94)	1.78E-03	0.87 (0.80 - 0.95)
3	36915814	rs4296548	T/G	9.70E-07	0.89 (0.86 - 0.94)	1.98E-03	0.87 (0.80 - 0.95)
3	36932703	rs10222527	T/G	7.93E-07	1.12 (1.07 - 1.17)	NA	NA
3	36938180	rs4328757	T/C	6.33E-07	1.12 (1.07 - 1.17)	3.02E-03	1.14 (1.04 - 1.24)
3	36945591	rs9882924	T/C	1.43E-07	0.88 (0.85 - 0.93)	5.03E-03	0.88 (0.81 - 0.96)
3	36948417	rs4678914	T/G	1.72E-07	0.89 (0.85 - 0.93)	2.13E-03	0.87 (0.80 - 0.95)
3	53070755	rs17304995	A/G	9.59E-07	1.14 (1.08 - 1.2)	7.85E-01	1.01 (0.92 - 1.12)
3	53082937	rs7644973	T/C	7.60E-07	0.88 (0.83 - 0.92)	8.46E-01	0.99 (0.90 - 1.09)

3	53085475	rs71301807	C/G	6.81E-07	1.14 (1.08 - 1.2)	8.50E-01	1.01 (0.92 - 1.11)
3	191572842	rs779329	A/G	4.82E-07	1.12 (1.07 - 1.17)	2.75E-01	1.05 (0.96 - 1.14)
3	191575240	rs1083673	T/C	7.20E-07	0.89 (0.85 - 0.93)	2.89E-01	0.96 (0.88 - 1.04)
3	191578101	rs779326	T/C	7.29E-07	0.89 (0.85 - 0.93)	2.70E-01	0.95 (0.88 - 1.04)
6	98547979	rs9385269	T/C	5.92E-07	1.12 (1.07 - 1.16)	2.76E-01	1.05 (0.96 - 1.14)
6	98549801	rs9401593	A/C	7.64E-08	0.89 (0.85 - 0.93)	8.35E-02	0.93 (0.85 - 1.01)
6	98550289	rs1906252	A/C	7.50E-08	1.12 (1.08 - 1.17)	8.52E-02	1.08 (0.99 - 1.17)
6	98553894	rs1487441	A/G	7.12E-08	1.13 (1.08 - 1.17)	8.20E-02	1.08 (0.99 - 1.17)
6	98555272	rs9375188	T/C	9.47E-08	1.12 (1.08 - 1.17)	8.42E-02	1.08 (0.99 - 1.17)
6	98561749	6:98561749	CAAT TT/C	1.34E-07	0.89 (0.85 - 0.93)	NA	NA
6	98562720	rs9375195	A/G	5.13E-07	1.12 (1.07 - 1.17)	2.48E-01	1.05 (0.97 - 1.14)
6	98565211	rs1487445	T/C	1.24E-07	1.12 (1.08 - 1.17)	6.38E-02	1.08 (0.99 - 1.18)
6	98566506	6:98566506	CT/C	1.12E-07	0.89 (0.85 - 0.93)	NA	NA
6	98574560	rs968050	T/C	1.32E-07	1.12 (1.08 - 1.17)	6.75E-02	1.08 (0.99 - 1.18)
6	98576223	rs12202969	A/G	9.32E-08	1.12 (1.08 - 1.17)	7.46E-02	1.08 (0.99 - 1.17)
6	98577689	rs9372734	T/C	1.22E-07	1.12 (1.08 - 1.17)	7.42E-02	1.08 (0.99 - 1.17)
6	98582900	rs12206087	A/G	1.22E-07	1.12 (1.08 - 1.17)	7.29E-02	1.08 (0.99 - 1.17)
6	98583487	rs375282393	CAT/ C	1.83E-07	0.89 (0.85 - 0.93)	NA	NA
6	98583488	rs72934503	A/G	1.79E-07	0.89 (0.85 - 0.93)	NA	NA
6	98584711	6:98584711	T/TA A	1.59E-07	0.89 (0.85 - 0.93)	NA	NA
6	98584713	rs201168005	A/T	1.59E-07	1.12 (1.07 - 1.17)	NA	NA
6	98584715	rs570208294	A/T	1.59E-07	1.12 (1.07 - 1.17)	NA	NA
6	98584717	6:98584717	T/TA	1.59E-07	1.12 (1.07 - 1.17)	NA	NA
6	98584720	rs368928614	T/G	1.23E-07	1.12 (1.08 - 1.17)	NA	NA
6	98584733	rs9320913	A/C	1.24E-07	1.12 (1.08 - 1.17)	8.31E-02	1.08 (0.99 - 1.17)
6	98588281	rs370768052	A/AT	2.16E-07	0.89 (0.85 - 0.93)	NA	NA

			T				
6	98591622	rs2388334	A/G	1.32E-07	0.89 (0.85 - 0.93)	8.36E-02	0.93 (0.85 - 1.01)
7	1858618	rs6950455	T/C	5.66E-07	0.89 (0.85 - 0.93)	9.51E-02	0.93 (0.85 - 1.01)
7	1858898	rs6965294	T/C	6.55E-07	1.12 (1.07 - 1.18)	1.32E-01	1.07 (0.98 - 1.17)
7	1860728	7:1860728	A/AA G	9.16E-08	1.13 (1.08 - 1.18)	NA	NA
7	1861952	rs34120092	A/C	7.13E-08	0.88 (0.84 - 0.92)	1.50E-01	0.94 (0.86 - 1.02)
7	1863164	rs9770241	T/C	3.17E-08	0.88 (0.84 - 0.92)	3.11E-01	0.96 (0.88 - 1.04)
7	1863463	rs56053419	T/C	7.70E-08	0.88 (0.84 - 0.92)	2.43E-01	0.95 (0.87 - 1.04)
7	1866953	rs55948146	C/G	4.15E-08	1.14 (1.09 - 1.19)	2.04E-01	1.06 (0.97 - 1.16)
7	1867680	rs7779512	C/G	7.43E-08	1.13 (1.08 - 1.19)	2.29E-01	1.06 (0.97 - 1.15)
7	1868039	rs7799782	A/G	5.01E-08	0.88 (0.84 - 0.92)	2.48E-01	0.95 (0.87 - 1.04)
7	1868092	rs7799807	A/G	4.14E-08	0.88 (0.84 - 0.92)	2.59E-01	0.95 (0.87 - 1.04)
7	1868761	rs12537430	A/G	5.03E-08	0.88 (0.84 - 0.92)	2.61E-01	0.95 (0.87 - 1.04)
7	1868995	rs12537479	A/G	5.02E-08	0.88 (0.84 - 0.92)	2.62E-01	0.95 (0.87 - 1.04)
7	1869242	rs35935754	T/C	4.98E-08	0.88 (0.84 - 0.92)	1.75E-01	0.94 (0.86 - 1.03)
7	1870592	rs11978270	T/C	5.71E-08	1.13 (1.08 - 1.19)	NA	NA
7	1871062	rs6949160	T/C	5.87E-08	0.88 (0.84 - 0.92)	NA	NA
7	1872132	rs66617818	A/C	7.67E-08	1.13 (1.08 - 1.19)	2.48E-01	1.05 (0.96 - 1.15)
7	1872274	7:1872274:G	G/GA	4.61E-07	0.89 (0.85 - 0.93)	NA	NA
7	1872327	rs559083240	A/G	8.58E-07	0.89 (0.85 - 0.93)	NA	NA
7	1872328	rs577957446	T/C	8.53E-07	0.89 (0.85 - 0.93)	NA	NA
7	1872329	rs540405859	A/G	8.53E-07	1.12 (1.07 - 1.18)	NA	NA
7	1872330	rs561886492	T/C	8.53E-07	0.89 (0.85 - 0.93)	NA	NA
7	1873084	rs4721090	T/C	5.99E-09	1.15 (1.09 - 1.2)	1.93E-01	1.06 (0.97 - 1.16)
7	1873343	rs10237989	A/G	2.93E-09	0.87 (0.83 - 0.91)	1.75E-01	0.94 (0.86 - 1.03)
7	1873879	rs13222183	A/G	3.44E-09	1.15 (1.1 - 1.2)	1.54E-01	1.07 (0.97 - 1.17)
7	1873894	rs13235380	T/C	3.43E-09	0.87 (0.83 - 0.91)	1.54E-01	0.94 (0.86 - 1.03)

7	1874753	7:1874753	CAA/ C	2.74E-08	1.15 (1.09 - 1.2)	NA	NA
7	1877502	rs4719308	T/G	1.50E-09	1.15 (1.1 - 1.2)	1.09E-01	1.08 (0.98 - 1.18)
7	1877503	rs386709275	T/G	1.44E-09	0.87 (0.83 - 0.91)	NA	NA
7	1878453	rs1078112	A/T	2.63E-09	0.87 (0.83 - 0.91)	1.67E-01	0.94 (0.86 - 1.03)
7	1878860	rs13234214	T/C	2.53E-09	0.87 (0.83 - 0.91)	1.74E-01	0.94 (0.86 - 1.03)
7	1878965	rs13233509	T/G	2.40E-09	0.87 (0.83 - 0.91)	1.67E-01	0.94 (0.86 - 1.03)
7	1879779	rs10228057	A/T	2.12E-09	1.15 (1.1 - 1.2)	1.52E-01	1.07 (0.98 - 1.16)
7	1880699	rs10950399	T/C	3.27E-09	0.87 (0.83 - 0.91)	9.52E-02	0.93 (0.85 - 1.01)
7	1881369	rs4236271	T/C	2.01E-09	0.87 (0.83 - 0.91)	1.55E-01	0.94 (0.86 - 1.02)
7	1881813	rs4719311	T/C	2.36E-09	0.87 (0.83 - 0.91)	1.90E-01	0.94 (0.86 - 1.03)
7	1882227	rs12540579	A/C	1.52E-09	0.87 (0.83 - 0.91)	9.63E-02	0.93 (0.85 - 1.01)
7	1882470	rs10950400	T/C	3.24E-09	0.87 (0.83 - 0.91)	1.79E-01	0.94 (0.86 - 1.03)
7	1884630	rs4449693	C/G	3.76E-09	0.87 (0.83 - 0.91)	1.98E-01	0.94 (0.86 - 1.03)
7	1885064	rs58222895	A/G	3.67E-09	0.87 (0.83 - 0.91)	1.49E-01	0.94 (0.86 - 1.02)
7	1885069	rs35729895	T/C	3.67E-09	0.87 (0.83 - 0.91)	1.49E-01	0.94 (0.86 - 1.02)
7	1885144	rs13226911	T/G	2.08E-09	1.15 (1.1 - 1.21)	2.07E-01	1.07 (0.96 - 1.18)
7	1885178	rs140364877	T/C	1.52E-09	0.87 (0.83 - 0.91)	1.39E-01	0.92 (0.83 - 1.03)
7	1885415	rs10233560	T/C	1.13E-09	1.15 (1.1 - 1.21)	1.92E-01	1.06 (0.97 - 1.16)
7	1886388	rs6953693	C/G	1.64E-09	1.15 (1.1 - 1.21)	1.96E-01	1.06 (0.97 - 1.16)
7	1886535	rs6952808	C/G	1.65E-09	0.87 (0.83 - 0.91)	2.11E-01	0.95 (0.87 - 1.03)
7	1886725	rs6977733	A/T	2.52E-09	0.87 (0.83 - 0.91)	2.10E-01	0.95 (0.87 - 1.03)
7	1886865	rs6954521	A/C	2.29E-09	0.87 (0.83 - 0.91)	2.11E-01	0.95 (0.87 - 1.03)
7	1886872	rs6978048	T/G	2.29E-09	1.15 (1.1 - 1.2)	2.11E-01	1.06 (0.97 - 1.16)
7	1886937	rs6954673	T/C	2.47E-09	0.87 (0.83 - 0.91)	2.11E-01	0.95 (0.87 - 1.03)
7	1887362	rs6957894	A/G	1.68E-09	0.87 (0.83 - 0.91)	2.00E-01	0.94 (0.86 - 1.03)
7	1887930	rs4719318	A/G	1.56E-09	0.87 (0.83 - 0.91)	1.97E-01	0.94 (0.86 - 1.03)
7	1888094	rs4719319	A/G	3.07E-09	0.87 (0.83 - 0.91)	2.10E-01	0.95 (0.87 - 1.03)

7	1888180	7:1888180:TC	T/TC	1.94E-09	0.87 (0.83 - 0.91)	NA	NA
7	1888185	rs71531445	A/G	2.16E-09	1.15 (1.1 - 1.2)	NA	NA
7	1889521	rs10260585	A/G	2.97E-09	0.87 (0.83 - 0.91)	1.86E-01	0.94 (0.86 - 1.03)
7	1890764	rs4256490	A/G	2.98E-09	0.87 (0.83 - 0.91)	1.66E-01	0.94 (0.86 - 1.03)
7	1890925	rs4601204	T/C	3.20E-09	0.87 (0.83 - 0.91)	1.50E-01	0.94 (0.86 - 1.02)
7	1892565	rs4721121	T/C	1.33E-09	1.15 (1.1 - 1.21)	1.67E-01	1.06 (0.97 - 1.16)
7	1893311	rs4721122	C/G	2.04E-09	1.15 (1.1 - 1.21)	1.68E-01	1.06 (0.97 - 1.16)
7	1894022	rs12699404	A/T	5.17E-09	1.15 (1.1 - 1.2)	1.67E-01	1.06 (0.97 - 1.16)
7	1894116	rs7810038	T/C	3.56E-09	1.15 (1.1 - 1.2)	1.56E-01	1.07 (0.97 - 1.16)
7	1894884	rs11768541	A/G	4.27E-09	0.87 (0.83 - 0.91)	1.53E-01	0.94 (0.86 - 1.03)
7	1895629	rs10263703	C/G	4.16E-11	0.86 (0.82 - 0.9)	4.25E-02	0.91 (0.84 - 1.00)
7	1895641	rs11762834	T/C	3.64E-09	0.87 (0.83 - 0.91)	1.46E-01	0.94 (0.86 - 1.02)
7	1895666	rs10950407	T/G	1.06E-08	1.14 (1.09 - 1.2)	1.69E-01	1.06 (0.97 - 1.16)
7	1895755	rs12667600	A/C	2.41E-09	0.87 (0.83 - 0.91)	1.60E-01	0.94 (0.86 - 1.03)
7	1896413	rs4236274	A/G	3.57E-11	1.16 (1.11 - 1.22)	3.01E-02	1.10 (1.01 - 1.20)
7	1898075	rs4602777	T/C	9.17E-10	0.87 (0.83 - 0.91)	2.14E-03	0.87 (0.80 - 0.95)
7	1898671	7:1898671	R/I	6.02E-08	0.88 (0.84 - 0.92)	NA	NA
7	1899479	rs12155225	T/C	9.89E-10	1.15 (1.1 - 1.21)	1.87E-02	1.11 (1.02 - 1.21)
7	1899547	rs12155464	C/G	2.91E-07	0.86 (0.82 - 0.91)	NA	NA
7	1899935	rs13312316	T/C	2.85E-08	0.88 (0.84 - 0.92)	4.36E-02	0.91 (0.83 - 1.00)
7	1900003	rs12674189	C/G	8.12E-10	0.87 (0.83 - 0.91)	2.63E-02	0.89 (0.80 - 0.99)
7	1900012	rs13312332	T/C	3.30E-09	0.87 (0.83 - 0.91)	NA	NA
7	1900013	rs12672749	T/G	3.30E-09	1.15 (1.1 - 1.2)	5.66E-02	1.13 (1.00 - 1.28)
7	1900208	rs386709280	T/C	3.40E-10	0.87 (0.83 - 0.91)	NA	NA
7	1903100	rs4610628	T/C	4.70E-08	0.88 (0.84 - 0.92)	7.12E-02	0.92 (0.84 - 1.01)
7	1904709	rs11761670	T/C	3.76E-08	0.88 (0.84 - 0.92)	8.60E-02	0.93 (0.85 - 1.01)
7	1906979	7:1906979	A/AC	2.79E-08	1.14 (1.09 - 1.19)	NA	NA
7	1907009	rs12672286	A/G	6.18E-08	0.88 (0.84 - 0.92)	6.77E-02	0.92 (0.84 - 1.01)

7	1908113	7:1908113	A/AC CCAC	4.76E-08	1.14 (1.09 - 1.19)	NA	NA
7	1908727	rs6949794	A/G	1.63E-07	0.88 (0.85 - 0.93)	8.35E-02	0.93 (0.85 - 1.01)
7	1912057	rs4721134	A/G	2.71E-07	0.89 (0.85 - 0.93)	5.04E-02	0.92 (0.84 - 1.00)
7	1925120	7:1925120	G/GG T	7.36E-07	0.89 (0.86 - 0.94)	NA	NA
7	1926090	rs6967442	A/G	8.65E-07	1.12 (1.07 - 1.17)	9.18E-03	1.12 (1.03 - 1.22)
7	1926577	rs10950422	T/C	8.63E-07	1.12 (1.07 - 1.17)	9.14E-03	1.12 (1.03 - 1.22)
7	1926745	rs12534679	A/G	7.98E-07	0.9 (0.86 - 0.94)	9.13E-03	0.89 (0.82 - 0.97)
7	1979750	rs10950456	A/G	5.27E-07	1.12 (1.07 - 1.17)	5.11E-03	1.13 (1.04 - 1.23)
7	1982181	rs12154473	A/G	4.27E-07	0.89 (0.85 - 0.93)	1.30E-02	0.90 (0.82 - 0.98)
9	23345347	rs11794152	A/G	2.40E-07	0.89 (0.85 - 0.93)	2.18E-02	0.90 (0.83 - 0.98)
9	23346842	rs10429537	C/G	2.51E-07	0.89 (0.85 - 0.93)	2.04E-02	0.90 (0.83 - 0.98)
9	23346850	rs10429582	T/C	2.24E-07	0.89 (0.85 - 0.93)	2.16E-02	0.90 (0.83 - 0.98)
9	23347724	rs12555870	A/G	7.31E-07	0.9 (0.86 - 0.94)	4.40E-02	0.92 (0.84 - 1.00)
9	23347865	rs12553324	C/G	1.53E-07	0.89 (0.85 - 0.93)	2.28E-02	0.90 (0.83 - 0.98)
9	23350420	rs34522021	T/C	8.57E-07	1.12 (1.07 - 1.17)	3.98E-03	1.13 (1.04 - 1.23)
9	23352293	rs12554512	T/C	3.20E-07	0.89 (0.85 - 0.93)	1.50E-02	0.90 (0.82 - 0.98)
9	23354940	rs7467480	A/T	2.55E-07	1.12 (1.07 - 1.17)	1.62E-02	1.11 (1.02 - 1.21)
9	23355310	rs4977839	A/G	2.55E-07	1.12 (1.07 - 1.17)	1.63E-02	1.11 (1.02 - 1.21)
9	23355664	rs4977836	A/C	3.74E-07	1.12 (1.07 - 1.17)	1.56E-02	1.11 (1.02 - 1.21)
9	23357826	rs7868984	T/C	2.76E-07	0.89 (0.85 - 0.93)	1.67E-02	0.90 (0.83 - 0.98)
9	23358081	rs7029201	A/G	3.62E-07	1.12 (1.07 - 1.17)	1.61E-02	1.11 (1.02 - 1.21)
9	23358495	rs7029718	A/G	4.07E-07	1.12 (1.07 - 1.17)	1.62E-02	1.11 (1.02 - 1.21)
9	23358875	rs13294439	A/C	3.77E-07	0.89 (0.85 - 0.93)	1.61E-02	0.90 (0.83 - 0.98)
9	23360417	rs1590949	C/G	3.49E-07	0.89 (0.85 - 0.93)	1.51E-02	0.90 (0.83 - 0.98)
9	23362311	rs11793831	T/G	4.02E-07	1.12 (1.07 - 1.17)	2.05E-02	1.11 (1.02 - 1.21)
9	23362812	9:23362812	<CN0 >/A	4.14E-07	1.12 (1.07 - 1.17)	NA	NA

9	23370987	rs541405065	<CN0 >/A	6.28E-07	1.12 (1.07 - 1.17)	NA	NA
12	49389320	rs1054442	A/C	5.25E-07	0.89 (0.85 - 0.93)	3.97E-03	0.88 (0.81 - 0.96)
16	13309375	rs403898	T/C	8.19E-07	0.89 (0.85 - 0.93)	5.86E-01	1.03 (0.94 - 1.12)
16	13310075	rs386789242	T/G	6.87E-07	1.12 (1.07 - 1.17)	NA	NA
16	13310168	rs377027	C/G	7.55E-07	1.12 (1.07 - 1.17)	3.88E-01	0.96 (0.88 - 1.05)
16	13310535	rs410055	T/C	6.86E-07	0.89 (0.85 - 0.93)	4.00E-01	1.04 (0.95 - 1.13)
16	13312029	rs396357	A/G	8.25E-07	1.12 (1.07 - 1.17)	4.31E-01	0.97 (0.89 - 1.05)
16	13315986	rs1149405	T/C	9.75E-07	1.12 (1.07 - 1.17)	4.85E-01	0.97 (0.89 - 1.06)
16	13316788	rs591066	A/G	5.84E-07	1.13 (1.08 - 1.19)	5.02E-01	0.97 (0.88 - 1.06)
16	64720556	rs976497	A/C	4.30E-07	0.86 (0.81 - 0.91)	5.62E-01	1.04 (0.92 - 1.17)
16	64720943	rs976498	T/C	4.08E-07	1.17 (1.1 - 1.24)	6.30E-01	0.97 (0.86 - 1.09)
16	89706992	rs2052868	T/C	8.65E-07	0.88 (0.83 - 0.92)	1.33E-01	0.92 (0.83 - 1.02)
16	90059336	rs11076649	C/G	8.97E-07	1.17 (1.1 - 1.25)	2.80E-01	1.07 (0.94 - 1.22)
17	37847799	17:37847799	T/TA	8.55E-07	1.12 (1.07 - 1.18)	NA	NA
17	37893484	rs4795393	T/C	6.00E-07	0.89 (0.85 - 0.93)	4.35E-03	0.88 (0.81 - 0.96)
19	13130549	rs7248711	T/G	1.51E-07	1.15 (1.09 - 1.21)	NA	NA
19	13151108	rs1077151	A/G	6.98E-07	1.13 (1.08 - 1.18)	3.36E-01	1.04 (0.96 - 1.14)
19	13153035	rs4926298	A/G	4.65E-07	0.88 (0.84 - 0.93)	3.20E-01	0.96 (0.88 - 1.04)
19	13158678	rs931068	T/C	9.46E-07	1.13 (1.07 - 1.18)	3.36E-01	1.04 (0.96 - 1.14)
19	13159569	rs8104231	A/T	4.57E-07	1.13 (1.08 - 1.19)	3.23E-01	1.04 (0.96 - 1.14)
19	13166480	rs62109902	A/G	3.76E-07	0.8 (0.73 - 0.87)	9.65E-01	1.00 (0.85 - 1.18)
19	13168623	19:13168623	CCT/C	3.67E-07	0.88 (0.84 - 0.93)	NA	NA
19	13174312	rs11085829	A/G	3.29E-07	0.88 (0.84 - 0.93)	3.75E-01	0.96 (0.88 - 1.05)
19	13176815	rs10423745	T/C	4.29E-07	1.13 (1.08 - 1.19)	3.83E-01	1.04 (0.95 - 1.13)
19	13185882	19:13185882	R/I	9.55E-07	1.13 (1.08 - 1.19)	NA	NA
19	13191461	rs8111617	T/C	2.44E-07	0.88 (0.84 - 0.92)	3.95E-01	0.96 (0.88 - 1.05)

Table S2: Meta-analysis results for previous BD GWAS hits *

CH R	BP	SNP	Alleles	P-value	OR	Note
2	97405440	rs2271893	A/G	1.71E-04	0.91 (0.87-0.95)	<i>LMAN2L</i>
2	185533580	rs7597593	T/C	1.09E-02	1.07 (1.02-1.11)	<i>ZNF804A</i>
3	52279594	rs7618915	A/G	9.26E-04	0.92 (0.88-0.97)	3p21
3	52718280	rs10865974	T/G	9.04E-05	0.91 (0.87-0.95)	3p21
3	52733106	rs6765687	T/C	1.67E-04	1.10 (1.05-1.16)	3p21
3	52815905	rs2710323	T/C	1.08E-03	1.08 (1.03-1.13)	3p21
3	52821011	rs1042779	A/G	1.23E-04	1.09 (1.05-1.15)	3p21
3	52833219	rs2535629	A/G	1.36E-04	0.91 (0.87-0.95)	3p21
3	52835354	rs736408	T/C	9.18E-05	0.91 (0.87-0.95)	3p21
5	7519298	rs17826816	A/G	3.51E-03	0.93 (0.88-0.97)	<i>ADCY2</i>
6	152738754	rs17082664	A/G	8.10E-04	0.89 (0.83-0.95)	<i>SYNE1</i>
6	152790573	rs9371601	T/G	2.72E-04	1.10 (1.05-1.15)	<i>SYNE1</i>
6	152791474	rs7747960	A/C	1.86E-03	1.12 (1.05-1.2)	<i>SYNE1</i>
10	62179812	rs10994336	T/C	1.37E-02	1.14 (1.04-1.24)	<i>ANK3</i>
10	62181128	rs10994338	A/G	1.43E-02	1.13 (1.04-1.24)	<i>ANK3</i>
10	62185494	rs4948418	T/C	7.55E-03	1.14 (1.04-1.25)	<i>ANK3</i>
10	62222107	rs10994359	T/C	1.11E-02	0.88 (0.80-0.96)	<i>ANK3</i>
10	62279124	rs10994397	T/C	1.78E-02	1.13 (1.03-1.23)	<i>ANK3</i>
10	62322034	rs10994415	T/C	3.36E-02	0.91 (0.84-0.98)	<i>ANK3</i>
11	79077193	rs12576775	A/G	1.25E-03	0.90 (0.85-0.96)	<i>TENM4</i>
11	79083620	rs12290811	A/T	3.59E-04	1.12 (1.06-1.19)	<i>TENM4</i>
12	2345295	rs1006737	A/G	3.30E-04	1.09 (1.04-1.14)	<i>CACNA1C</i>
12	2419896	rs4765913	A/T	2.28E-04	1.11 (1.05-1.17)	<i>CACNA1C</i>
13	42653437	rs1012053	A/C	2.95E-01	1.04 (0.97-1.10)	<i>DGKH</i>
16	23634026	rs420259	A/G	1.21E-01	1.05 (0.99-1.10)	<i>PALB2</i>
16	23640467	rs249954	A/G	2.72E-01	0.97 (0.92-1.02)	<i>PALB2</i>
19	19361735	rs1064395	A/G	3.36E-04	1.11 (1.05-1.18)	<i>NCAN</i>

*6q16.1, 12q13.1, *TRANK1* and *MAD1L1* were reported in the manuscript so were not included in this table.

Table S3. Results of approximate conditional association analysis

CHR	POS	SNP	Allele	FRQ	BETA	SE	P	P Joint
3	36856030	rs9834970	T	0.50	-0.1261	0.0197	4.83E-10	1.59E-10
6	98553894	rs1487441	A	0.49	0.1087	0.0195	2.58E-08	2.53E-08
7	1896413	rs4236274	G	0.39	-0.1406	0.0205	8.49E-12	7.25E-12
9	23347853	rs10757417	G	0.45	0.1143	0.0198	8.89E-09	7.96E-09
12	49472965	rs11168850	A	0.44	0.1159	0.0199	2.03E-08	5.86E-09
17	37846512	rs2517959	A	0.33	0.1216	0.0209	4.53E-09	6.07E-09

Allele: the effect allele; FRQ: frequency of the effect allele; BETA: beta coefficient; SE: standard error of the beta coefficient; P: p-value from the original meta-analysis; P_Joint: p-value from a joint analysis of all the selected SNPs. For the loci on chromosomes 9 and 12, GCTA selected SNPs that differed from those with the smallest p-value in the meta-analysis. (Default parameters were used for this analysis: --massoc-p 5e-8; --massoc-wind 10000; --massoc-collinear 0.9)

Table S4. Summary of dbGaP GWAS datasets

dbGaP_access_id	Platform	Phenotype	Sample size	Used In
phs000124.v2.p1	HumanHap550	Neuroblastoma	1,662	Study-4
phs000404.v1.p1*	HumanOmni2.5M	Nicotine Dependence	1,527	Study-5
phs000303.v1.p1	HumanOmni2.5M	Refractive Error	1,869	Study-5
phs000203.v1.p1	Human660W	Peripheral Arterial Disease	3,337	Study-6
phs000170.v1.p1#	Human660W	Cataract and HDL	3,947	Study-6
phs000188.v1.p1	Human660W/1M	QRS Duration	2,873	Study-6
phs000237.v1.p1	Human660W/1M	Type 2 Diabetes	3,443	Study-6
phs000234.v1.p1	Human660W	Dementia	1,706	Study-6

* Consent group General Research Use only

Family-based study design

Supplementary References:

- 1 Muhleisen, T.W., Leber, M., Schulze, T.G., Strohmaier, J., Degenhardt, F., Treutlein, J., Mattheisen, M., Forstner, A.J., Schumacher, J., Breuer, R. *et al.* (2014) Genome-wide association study reveals two new risk loci for bipolar disorder. *Nat Commun*, **5**, 3339.
- 2 Green, E.K., Hamshere, M., Forty, L., Gordon-Smith, K., Fraser, C., Russell, E., Grozeva, D., Kirov, G., Holmans, P., Moran, J.L. *et al.* (2013) Replication of bipolar disorder susceptibility alleles and identification of two novel genome-wide significant associations in a new bipolar disorder case-control sample. *Mol. Psychiatry*, **18**, 1302-1307.
- 3 Cichon, S., Muhleisen, T.W., Degenhardt, F.A., Mattheisen, M., Miro, X., Strohmaier, J., Steffens, M., Meesters, C., Herms, S., Weingarten, M. *et al.* (2011) Genome-wide association study identifies genetic variation in neurocan as a susceptibility factor for bipolar disorder. *Am. J. Hum. Genet.*, **88**, 372-381.
- 4 Chen, D.T., Jiang, X., Akula, N., Shugart, Y.Y., Wendland, J.R., Steele, C.J., Kassem, L., Park, J.H., Chatterjee, N., Jamain, S. *et al.* (2013) Genome-wide association study meta-analysis of European and Asian-ancestry samples identifies three novel loci associated with bipolar disorder. *Mol. Psychiatry*, **18**, 195-205.
- 5 Psychiatric GWAS Consortium Bipolar Disorder Working Group. (2011) Large-scale genome-wide association analysis of bipolar disorder identifies a new susceptibility locus near ODZ4. *Nat. Genet.*, **43**, 977-983.
- 6 Ferreira, M.A., O'Donovan, M.C., Meng, Y.A., Jones, I.R., Ruderfer, D.M., Jones, L., Fan, J., Kirov, G., Perlis, R.H., Green, E.K. *et al.* (2008) Collaborative genome-wide association analysis supports a role for ANK3 and CACNA1C in bipolar disorder. *Nat. Genet.*, **40**, 1056-1058.
- 7 Wellcome Trust Case Control Consortium. (2007) Genome-wide association study of 14,000 cases of seven common diseases and 3,000 shared controls. *Nature*, **447**, 661-678.
- 8 Schulze, T.G., Alda, M., Adli, M., Akula, N., Arda, R., Bui, E.T., Chillotti, C., Cichon, S., Czerski, P., Del Zompo, M. *et al.* (2010) The International Consortium on Lithium Genetics (ConLiGen): an initiative by the NIMH and IGSLI to study the genetic basis of response to lithium treatment. *Neuropsychobiology*, **62**, 72-78.
- 9 Hou, L., Heilbronner, U., Degenhardt, F., Adli, M., Akiyama, K., Akula, N., Arda, R., Arias, B., Backlund, L., Banzato, C.E. *et al.* (2016) Genetic variants associated with response to lithium treatment in bipolar disorder: a genome-wide association study. *Lancet*, **387**, 1085-1093.