Supplementary Online Content

Genetics of Personality Consortium. Meta-analysis of genome-wide association studies for neuroticism, and the polygenic association with major depressive disorder. *JAMA Psychiatry*. Published online May 20, 2015. doi:10.1001/jamapsychiatry.2015.0554.

This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix 1. Materials and methods

Cohorts

Approval by local institutional review boards was obtained in all studies and informed consent was obtained from all participants.

1. ALSPAC{Boyd, 2013 #1080} — United Kingdom. The Avon Longitudinal Study of Parents and their Children (ALSPAC) is a longitudinal population-based birth cohort that recruited pregnant women residing in Avon, UK, with an expected delivery date between 1st April 1991 and 31st December 1992. 14 541 pregnant women were initially enrolled with 14 062 children born. Biological samples including DNA have been collected for 10 121 of the children from this cohort. Ethical approval was obtained from the ALSPAC Law and Ethics committee and relevant local ethics committees, and all parents provided written informed consent. In this study, 6 076 children (3 099 females; 51.0%) for whom the IPIP data were available were included. Mean age of the sample was 13.8 years (SD=0.21). The data were collected between 2005 and 2006. The study website contains details of all the data that is available through a fully searchable data dictionary (http://www.bris.ac.uk/alspac/researchers/data-access/data-dictionary).

2. BLSA{Terracciano, 2005 #864} — United States of America. The Baltimore Longitudinal Study of Aging (BLSA) is an ongoing multidisciplinary study of community-dwelling volunteers. For this study, we examined data from 1,917 participants (952 women) of European descent that completed the NEO-PI-R questionnaire. In this sample, mean age was 58.3 years (SD=16.6). The mean age of the men was 56 years (SD=16.7) and of the women 60.7 years (SD=16.3). The data were collected between 1991 and 2010.

3. BRESCIA – Italy. The Brescia cohort consisted of 177 unrelated healthy volunteers (89 female and screened for DSM-IV Axis I disorders by expert psychologists using the Mini-International Neuropsychiatric Interview (M.I.N.I.). Only healthy volunteers without a history of drug or alcohol abuse or dependence and without a personal or first-

degree family history of psychiatric disorders were enrolled in the study. Subjects who obtained a score lower than 27/30 in the Mini Mental State Examination (M.M.S.E.) were excluded as well. Furthermore, only participants with Italian descent (all four grandparents Italian) could participate The personality traits were assessed by the Italian version of the TCI, a 240-item, tru x false self-report questionnaire. The mean age of the sample was 47.58 years (SD=16.30; women M=47.08, SD=17.31, men M=48.09, SD=15.29). The data were collected between 2007 and 2011.

4. CHICAGO – United States of America. (Hart et al. 2012)
The Chicago cohort comes from a genetic study in which 311 healthy Caucasian adults, aged 18-35 years, were tested for response to an acute dose of *d*-amphetamine. They were recruited from the community and underwent medical and psychiatric screening before the study. Participants completed the Multiphasic Personality Inventory- Brief Form during screening, and they were genotyped using the Affymetrix 6.0 array. The sample consisted of 166 men (mean age 23.6, SD=3.7) and 145 women (mean age 22.6, SD 3.2). The data were collected between 2002 and 2010.

5. CILENTO{Colonna, 2007 #146;Colonna, 2009 #147} —Italy. The Cilento study is a population-based study that includes 2,137 individuals from three isolated populations of South Italy. Data from the NEO-PI-R questionnaire were available for 800 participants representing the final sample. Of this sample, 64.4% were women. The mean age of all participants was 54.6 years (SD=19), of the men 54.6 years (SD=19.2) and of the women 54.6 years (SD=19.5). The data were collected between 2009 and 2011.

6. COGEND[5, 6] — United States of America. The Collaboratiove Genetic Study of Nicotine Dependence (COGEND) was initiated as a three-part program project grant funded through the National Cancer Institute (NCI; PI: Laura Bierut). The three projects included a study of the familial transmission of nicotine dependence, a genetic study of nicotine dependence, and a study of the relationship of nicotine dependence with nicotine metabolism. The primary goal is to detect, localize, and characterize genes that predispose or protect an individual with respect to heavy tobacco consumption, nicotine

dependence, and related phenotypes and to integrate these findings with the family transmission and nicotine metabolism findings. As a part of this study, item-level NEO-FFI data were available from 2,712 participants, 1,279 of whom had corresponding genome-wide genotyping successfully performed as part of The Study of Addiction: Genetics and Environment (SAGE). SAGE is part of the Gene Environment Association Studies initiative funded by the National Human Genome Research Institute (NHGRI). The mean age of COGEND participants with both SAGE genotypes and NEO-FFI phenotypes was 36.5 years (SD=5.6) and women constituted 65.1% of the total sample (M=36.6, SD=5.6, versus in men M=36.4, SD=5.5).

7. COGA[34, 35] *— United States of America.* The Collaborative Study on the Genetics of Alcoholism (COGA) is a multi-site study funded by the National Institute on Alcohol Abuse and Alcoholism (NIAAA) and National Institute on Drug Abuse (NIDA) that aims to characterize the familial transmission of alcoholism and related phenotypes and identify susceptibility genes. A total of 649 participants drawn from COGA completed the TCI, 647 of whom had corresponding genome-wide genotyping successfully performed as part of The Study of Addiction: Genetics and Environment (SAGE). SAGE is part of the Gene Environment Association Studies initiative funded by the National Human Genome Research Institute (NHGRI). The mean age of COGA participants with both SAGE genotypes and TCI phenotypes was 40.8 years (SD=10.8) and women constituted 45.6% of the total sample (M=40.9, SD=10.4, versus in men M=40.8, SD=11.1).

8. EGCUT{Metspalu, 2004 #590} — Estonia. The Estonian cohort comes from the population-based biobank of the Estonian Genome Project of University of Tartu (EGCUT). The project is conducted according to the Estonian Gene Research Act and all participants have signed the broad informed consent (www.biobank.ee). In total, 52,000 individuals aged 18 years or older participated in this cohort (33% men, 67% women). General practitioners (GP) and physicians in the hospitals randomly recruited the participants. A Computer-Assisted Personal interview was conducted during 1–2 h at doctors' offices. Data on demographics, genealogy, educational and occupational history,

lifestyle and anthropometric and physiological data were assessed. The personality profile was assayed using NEO-PI-3 questionnaire and was administered to 1 730 participants. In this sample, the age range was 18–88 years (M=42.8 years, SD=16.5). The sample consisted of 740 men (mean age 42 years, SD=16.3) and 991 women (mean age 43.4 years, SD=16.6). The genotyping was carried out in two waves for a random subsamples: 1) 1,183 samples using Illumina Human370CNV array and 2) 120 samples using Illumina OmniExpress array, resulting with an effective sample of 1,303. The data were collected between 2009 and 2012.

9. ERF{Pardo, 2005 #658} — The Netherlands. The Erasmus Rucphen Family (ERF) study is a family-based study including over 3 000 individuals from an isolated population in the Southwest region of the Netherlands. There were 2 400 individuals for whom both NEO personality and GWA data were available. The personality traits were assessed using NEO-FFI. The mean age of all participants was 49.3 years (SD=14.9) and women constituted 55.8% of the total sample (M=49.0, SD=15.1, versus in men M=49.6, SD=14.7).

10+11. FINNISH TWINS EPI AND NEO [9, 10] *— Finland*. The Finnish twin cohort consisted of 1381 genotyped respondents with personality data from two separate twin cohorts: the older Finnish twin cohort consisted of like-sexed twins born before 1958, and FinnTwin12 consisted of twins born in 1983-1987. A total of 568 individuals with available genotyping data (mean age 25.5, SD 4.8; 32.9% women) from the older Finnish twin cohort completed the Eysenck Personality Inventory (EPI; an alternative version of the EPQ) at least once. EPI was assessed in 1975-1976 and for the second time in 1981-1983. Some of the twins from the older Finnish twin cohort were assessed with the NEO-FFI between 2003-2009 as a part of the Nicotine Addiction Genetics (NAG) - Finland study. In addition, NEO-FFI was assessed also in the fourth wave of the FinnTwin12 study in 2005-2009. Combining participants from the NAG and FinnTwin12 studies, the total number of genotyped individuals with the NEO-FFI data was 813 (mean age 30.5, SD 15.3; 49.5% were women). All subjects were genotyped at the Welcome Trust Sanger Institute using the Illumina 670 Custom chip.

12. HBCS{Barker, 2005 #34;Eriksson, 2006 #255;Raikkonen, 2008 #704} — Finland. The Helsinki Birth Cohort Study (HBCS) is composed of 8 760 individuals born between the years 1934 and 1944 in one of the two main maternity hospitals in Helsinki, Finland. Between 2001 and 2003, a randomly selected sample of 928 men and 1 075 women participated in a clinical follow-up study with a focus on cardiovascular, metabolic and reproductive health, cognitive function and depressive symptoms. In 2004, various psychological phenotypes were assessed, including the NEO and TCI personality dimensions. There were 1 698 participants that completed either the NEO and/or the TCI (55.9% women). The mean age of the subjects was 63.4 years (SD=2.9). The mean age of the men was 63.3 years (SD=2.7) and of the women was 63.5 years (SD=3).

13. KORCULA{Polasek, 2009 #687} — Croatia. This study was performed in the eastern part of the island of Korčula, Croatia between March and December 2007. Healthy volunteers aged 18 and over from the town of Korčula and villages Lumbarda, Žrnovo, and Račišće were invited to the study. There was a total of 969 participants included who had a number of quantitative phenotypic traits measured. The EPQ-R was successfully administered to 810 participants (511 female; 63.1%). The mean age was 55.4 years (SD=13.3; female M=54.5, SD=12.8, male M=56.9, SD=14). The data were collected in 2007.

14. LBC1921{Deary, 2011 #191} — United Kingdom. The Lothian Birth Cohort 1921 (LBC1921) study includes 550 individuals born in 1921, most of whom had taken part in the Scottish Mental Survey of 1932. The majority of participants lived independently in the Lothian region (Edinburgh city and surrounding area) of Scotland. Of these, 498 participants were approached to complete the IPIP personality inventory, and 478 participants (283 women; 59.2%) successfully did so. The mean age of both female and male participants was 81.2 (SD=.3). IPIP data were collected twice: in 2002 and between 2007 and 2008. Measurements from the first IPIP assessment were used for 472 individuals, with second assessment measurements used for six individuals. DNA was extracted from blood samples and genotyped using the Illumina610-Quadv1 conducted

by the Genetics Core Laboratory at the Wellcome Trust Clinical Research Facility, Western General Hospital, Scotland. There were 542,050 SNPs remaining after quality control. Genotype and phenotype data were available for 437 individuals.

15. LBC1936{Deary, 2011 #191;Deary, 2004 #189;Deary, 2007 #190} — United Kingdom. The Lothian Birth Cohort 1936 (LBC1936) study comprises 1 091 individuals born in 1936, most of whom had taken part in the Scottish Mental Survey of 1947. The majority of participants lived independently in the Lothian region (Edinburgh city and surrounding area) of Scotland. Participants completed NEO-FFI and IPIP personality questionnaires at a mean age of 69.6 years (SD=.82; women M=69.6, SD=.82, men M=69.6, SD=.82); at 72.5 years (SD=.71; women M=72.5, SD=.72, men M=72.4, SD=.82) the IPIP was re-administered. IPIP data collection occurred between 2004 and 2007, and between 2007 and 2010. First wave measurements were used for 963 individuals, and second wave measurements for 69 individuals. DNA was extracted from blood samples and genotyped using the Illumina610-Quadv1 conducted by the Genetics Core Laboratory at the Wellcome Trust Clinical Research Facility, Western General Hospital, Scotland. There were 542,050 SNPs remaining after quality control exclusions. Genotype and phenotype data were available for 952 individuals.

16. MCTFR United States of America[14,15]. Data from the Minnesota Center for Twin and Family Research (MCTFR) were collected as part of two different longitudinal studies, the Minnesota Twin Family Study (MTFS) and the Sibling Interaction and Behavior Study (SIBS). The MTFS is a study of reared-together, same sex twins and their parents, and the SIBS is a study of families of different types (some include adopted offspring). Both parents and offspring completed the Multidimensional Personality Questionnaire (MPQ) at baseline, and only offspring completed it at subsequent follow-ups of approximately 3 year intervals. The MTFS offspring completed up to 5 follow-up assessments while the SIBS offspring completed up to 2. We selected data from the first assessment with complete data for each individual. The total sample with MPQ data included 9071 participants (53% female), and of those participants 7186 had both IRT-

based neuroticism scores and usable SNP data. The final sample included 3346 males (M age = 31.93, SD = 13.96) and 3840 females (M age = 31.19, SD = 12.97).

17. MGS – United States of America. Data derive from the "control" sample of a large schizophrenia study (Molecular Genetics of Schizophrenia (MGS): PI and Collaboration Coordinator, P.V. Gejman). The available sample consisted of unrelated subjects selected by random digit dialing from approximately 60,000 US households. They were screened for psychotic and bipolar disorders but were not excluded for other common psychiatric disorders seen in the general population. The European American sample (53% female) were adults with a mean age of 50 (SD=16.4) at assessment (Sanders, 2010). Subjects completed an on-line psychiatric screening interview that included the short form of the Eysenck Personality Questionnaire (EPQ-SF). The data were obtained with permission from dbGaP (Database of Genotypes and Phenotypes, http://www.ncbi.nlm.nih.gov/gap, Study Accessions: phs000021.v3.p2 ("GAIN") and phs000167.v1.p1 "nonGAIN"). Data from the GAIN and nonGAIN European American subjects were combined for the current analyses (N=2806).

18. NBS{Kiemeney, 2008 #454} — The Netherlands. In 2000 a study was initiated among the inhabitants of the municipality of Nijmegen by different departments of the Radboud University Nijmegen Medical Centre to research the question what the prevalence of certain risk factors, chronic diseases and genetic variations in the general population are. As a part of this study, the EPQ-R was administered to 1 832 participants. From this sample, 1 823 participants (921 female; 50.5%) completed the test. The mean age of these participants was 61.5 (SD=10.3; women M=56.7, SD=10.8, men M=66.3, SD=7).

19. NESDA{Penninx, 2008 #672} — The Netherlands. The NESDA data for the present study were drawn from the Netherlands Study of Depression and Anxiety{NESDA, #672}, an ongoing longitudinal cohort study aimed at examining the long-term course of depressive and anxiety disorders in different health care settings and phases of illness. A total of 2,981 respondents were recruited from primary care (n=1,610), specialized mental health care (n=807) and the community (n=564), including healthy controls,

respondents with subthreshold symptoms and those with an anxiety and/or depressive disorder. The NEO-FFI was successfully administered to 2 961 participants (1 979 female; 66.8%). The mean age was 41.9 years (SD=13.1; female M=41.1, SD=13.1, male M=43.4, SD=12.9). Baseline data were collected between 2004 and 2007. The NEO-FFI was administered twice, at baseline and two years later. For the NESDA sample, contrary to the other studies with repeated measure data of personality, we first selected the least recent item data. For NESDA, this strategy was deemed most suitable because the first measurement represented the baseline measurement for NESDA which had an overpresentation of MDD cases. So, we choose to measure personality at the time point at which MDD was least prevalent .

20. NTR{Boomsma, 2002 #74;Boomsma, 2006 #76} — The Netherlands.

Data on personality in the Netherlands Twin Register (NTR) were collected as part of a longitudinal study on health, personality and lifestyle in adolescent and adult twins and their relatives (i.e., their non-twin siblings, parents, spouses and children). Eight waves of data collection have been completed (in 1991, 1993, 1995, 1997, 2000, 2002, 2004 and 2009). Twins were invited to participate at all time points, while the parents and siblings could participate on a maximum of 6 time points, spouses on 4 time points and adult children of twins and siblings on 2 time points. The ABV was administered five times in 1991, 1993, 1997, 2000 and 2002, and the NEO-FFI was assessed twice in 2004 and 2009. Of the 31 694 individuals who participated at least once in one of these seven waves, there were 31 259 individuals (58.7% female) with valid personality data (at least one neuroticism item was available on at least one time point). For the analysis in this study, we selected for each individual the ABV item data of the latest time point and the NEO item data of the earliest time point. This ensured that for each individual with data on both the ABV and NEO, the times of measurement were as close as possible. For 21 146 individuals there were NEO data available (of which from 14,880 individuals data came from the 2004 survey and from 6 266 individuals data came from the 2009 survey). For the ABV, data of 6 778 individuals came from survey 2002, 1 803 from 2000, 5,088 from the 1997, 2,208 from 1993, and 2,939 from 1991 (in total 18,816 individuals with ABV data). The mean age of the participants was 37.2 years (SD=15.3) across

assessments. For the GWAS analysis we selected all participants with GWAS data, allowing first-degree relatives (e.g. sibling pairs and parent-offspring pairs), because a genetic relatedness of 0.5 can be accounted for in the GWAS analysis in PLINK by using the –family option. This led to the inclusion of 6,417 participants for the GWAS analysis. For the GCTA analysis, unrelated participants are required. Hence, we randomly selected one individual per family, yielding 3,599 individuals for the GCTA analysis. For the polygenic risk score analysis, we made two selections of participants. In the polygenic analysis where we predicted Neuroticism in the NTR cohort, we were able to deal with any degree of genetic relatedness by applying linear mixed modeling. Therefore, we included all subjects with personality and GWAS data, yielding 8,648 individuals in the analysis. For the polygenic risk score analysis to predict MDD, we combined data from NTR and NESDA and relied to logistic regression, which requires unrelated subjects again. Thus, we selected unrelated subjects with valid information on MDD status.

21. ORCADES{McQuillan, 2008 #582} — United Kingdom. The Orkney Complex Disease Study (ORCADES) is a genetic epidemiology study based in an isolated population in the north of Scotland. It aims to discover the genes and variants in them that influence the risk of common, complex diseases such as diabetes, osteoporosis, stroke, heart disease, myopia, glaucoma, chronic kidney and lung disease. As a part of this study, the EPQ-R was administered to 602 participants (347 female) and all participants all completed the test. The mean age of these participants was 56.8 (SD=13.8; women M=56.5, SD=13.9, men M=57, SD=13.8). The data were collected between 2007 and 2011.

22. PAGES — Germany. In this German cohort, healthy control participants were randomly selected from the general population of Munich, Germany, and contacted by mail. Several screenings were conducted before the volunteers were enrolled in the study. These included screening of medical and psychiatric disorders (in particular psychotic disorders) in the participants and their first-degree relatives by phone and interview and screening for central nervous system and cognitive impairment by neurological examination and cognitive testing. Furthermore, only participants with German descent

(all four grandparents German) could participate. In the resulting sample, a large battery of personality questionnaires was administered as well as data on life events and traumatic events. Data on the NEO-PI-R and TCI were analyzed for the current study. There were 476 individuals (55.7% women) with valid personality data. The mean age of the sample was 45.9 years (SD=15,4; women M=43.4, SD=15,3, men M=49, SD=15,3). The data were collected between 1998 and 2006.

23. QIMR adolescents — Australia Personality data collected between 1992 and 2011 were available for 4,100 adolescents and young adults (51.5% female), of which 2842 (48.6% female) were genotyped. Participants included in the current study (with both phenotypic and genotypic data) ranged in age from 9 to 25 years (M=14.4, SD=2.3). The sample comprised twin pairs (and their siblings) recruited as adolescents as part of the overarching Brisbane Adolescent Twin Study{Wright, 2004 #975} conducted at the QIMR Berghofer Medical Research Institute (QIMR). Recruitment was mostly through primary and secondary schools in south-east Queensland for studies of melanocytic naevi (moles).{Aitken, 1994 #13} JEPQ and/or NEO personality data (NEO-PI-R or NEO-FFI) were collected as part of the melanocytic naevi study (1992-ongoing), the cognition study (in-person testing, 1996-2012){Wright, 2004 #975}, a health and well-being study (a mail/phone study, 2002-2003){Wright, 2004 #975}, and a study of borderline personality disorder (online/paper survey, 2003–2006){Distel, 2008 #218}. JEPQ data were available at 3 time points, NEO-PI-R data at 1 time point, and NEO-FFI data at 2 time points. We first selected the NEO and JEPQ data from the earlier time points, and subsequently selected the data from more recent time points. DNA samples were collected in accordance with standard protocols and were genotyped on the Illumina 610 quad.{Medland, 2009 #1154}

24. QIMR adults — Australia Personality data were available for a large Australian adult sample comprising 26,697 individuals (57.1% female), of which 7305 (38.2% female) were genotyped. Participants included in the current study (with both phenotypic and genotypic data) ranged in age from 17 to 85 years (M=38.1, SD=12.6). Data were collected between 1980 and 2007 in various twin family studies conducted at QIMR.

NEO personality data (NEO-PI-R or NEO-FFI) were collected from a series of studies conducted collaboratively by Nick Martin and Andrew Heath between 2001 and 2006{Pergadia, 2009 #673;Saccone, 2007 #754}, {Distel, 2008 #218}. The EPQ data were obtained from the following sources: (a) The Canberra study (1980-1981){Heath, 1988 #1076}: twins drawn from the Australian Twin Registry and born prior to 1964 ('Cohort 1'); (b) Two twin studies (1988-1991) in which Health and Lifestyle Questionnaires were sent to the members of Cohort 1 and an additional group born from 1964 to 1971 ('Cohort 2')[30]; with similar questionnaires also sent to immediate family members of the twins; (c) The Anxiety and Depression study (assessed twice, once by questionnaire and once by telephone interview)[33] drawn from Cohort 1 and Cohort 2 but selected to include mainly individuals with extreme high or low neuroticism scores from the studies in (b) and members of their immediate families. The TCI data were obtained from two twin studies (1988-1991) from Cohort 1 and 2, and the MPQ data as part of the Gambling Study (cohort 2).{Slutske, 2009 #1078}

Altogether, the EPQ was administered four times, the NEO-FFI twice, and the TCI, NEO-PI-R and MPQ once. We first selected the item data of the EPQ at the first assessment, because the EPQ data were available for the majority of the subjects, the TCI data was obtained at the same time point and the MPQ assessment was close to the EPQ and TCI time points. Subsequently, we selected those time points with NEO item data that were closest in time to the EPQ and TCI assessment. The genotypic data used in the current study are derived from multiple waves of genotyping. DNA samples were collected in accordance with standard protocols and submitted to different genotype centres using different Illumina SNP platforms (317 single, 370 single, 370 duo, 670 quad, 610 quad).{Medland, 2009 #1154} Phenotypic and genotypic data collections were approved by the QIMR Human Research Ethics Committee and informed consent was obtained from all participants.

25. SardiNIA – Italy. The SardiNIA study includes 6148 related individuals from four towns in the Ogliastra province of Sardinia, Italy.[21] These individuals represent 62% of the population in these towns. Valid personality data were available for 5,669 individuals, of which 5,566 were genotyped (56.7% women). The mean age of all participants was

42.8 years (SD=17). The mean age of the men was 43.0 years (SD=18), and of the women 42.4 years (SD=17). The sample has been described in more detail by Terracciano and co-authors.[31]

26. SHIP – Germany. The Study of Health in Pomerania (SHIP) is a cross-sectional survey in West Pomerania, the north-east area of Germany{John, 2001 #1152;Volzke, 2011 #1153}. A sample from the population aged 20 to 79 years was drawn from population registries. First, the three cities of the region (with 17,076 to 65,977 inhabitants) and the 12 towns (with 1,516 to 3,044 inhabitants) were selected, and then 17 out of 97 smaller towns (with less than 1,500 inhabitants), were drawn at random. Second, from each of the selected communities, subjects were drawn at random, proportional to the population size of each community and stratified by age and gender. Only individuals with German citizenship and main residency in the study area were included. Finally, 7,008 subjects were sampled, with 292 persons of each gender in each of the twelve fiv x year age strata. In order to minimize drop-outs by migration or death, subjects were selected in two waves. The net sample (without migrated or deceased persons) comprised 6,267 eligible subjects. Selected persons received a maximum of three written invitations. In case of non-response, letters were followed by a phone call or by home visits if contact by phone was not possible. The SHIP population finally comprised 4,308 participants (corresponding to a final response of 68.8%). From 2007 to 2010, the "Lif x Events and Gen x Environment Interaction in Depression" (LEGEND) study was conducted.{Volzke, 2011 #1153} Until the beginning of LEGEND, 639 participants from the baseline sample SHIP-0 were either deceased (n=383) or refused further participation (n=256). Thus, 3669 participants were invited to take part in the LEGEND study. During the conduction of LEGEND 92 participants were deceased and 1011 subjects refused participation in the LEGEND study. 132 subjects did not respond to repeated efforts of contact (at least three written invitations, 10 telephone calls and five home visits). 35 subjects agreed to participate but missed all appointments. Among the 2400 subjects who participated in the LEGEND study, we excluded 134 subjects from the analyses because of unreliable information or inconsistencies in the interview according

to the judgment of the interviewer and the supervisor. Full data sets (GWAS & neuroticism) were available for n=2213 subjects.

27. STR{Floderus-Myrhed, 1980 #281} — Sweden. For the Swedish Twin Registry (STR) a cohort of twins born in 1926–67 was compiled in 1970, by use of nationalized birth registrations. A register consisting all 50,000 twin births was established. Members of like-sexed pairs from the cohort born in 1926–58 were sent a questionnaire in 1972–73. Responses were received from 36,535 individuals including 14,000 twin pairs. The EPI was included to assess personality and completed by 30,276 individuals (52.3% female). Among these individuals, 22,390 subjects were invited to the TwinGene study conducted between 2004 and 2008. In total, 12,591 (56%) individuals participated by donating blood to the study, and by answering questionnaires about life style and health. DNA from 9,896 individual subjects was sent to Uppsala, Sweden for genome wide genotyping with Illumina OmniExpress bead chip (all available dizygous twins + one twin from each available MZ twin pair). Genotyping results for 9,836 subjects and 731,442 autosomal SNPs passed the initial lab-based quality control (QC). In further QC, SNPs with more than 3% missing information (GENO > 0.03) (n=3,922), a minor allele frequency below 1% (n=79,893), or a Hardy-Weinberg equilibrium (HWE) test p-value <= 1 x 10-07 (n=3,071), were excluded. Individuals with low genotyping success (MIND > 0.03) (n=10), heterozygosity of X-chromosomes in males (n=36), deviations in heterozygosity of more than 5 standard deviations (SD) from the population mean (n=49), or detection of unknown (cryptic) relatedness (n=124), were excluded. After the QC there were 9,617 individuals and 644,556 autosomal SNPs remaining.

28. VIS{Ivkovic, 2007 #400} — Croatia. Adult participants living in the villages of Komiza and Vis on the Croatian island of Vis were recruited in May 2003 and May 2004 for a large genetic study. Croatia has 15 Adriatic Sea islands with populations greater than 1 000. The villages on the islands have unique population histories and have preserved their isolation from other villages and the outside world through many centuries. Informed consents, procedures and questionnaires were reviewed and approved by relevant ethics committees in Scotland and Croatia. All individuals over 18 years old and resident on the Island of Vis were invited to participate in this study. More

information about this sample can be found in {Ivkovic, 2007 #1164}. As a part of the interview participants also completed the Eysenck Personality Questionnair x Revised (short-form; EPQ-R). Seventy percent of the villages' adult population took part in the study, a total of 918 individuals (531 female; 57.8%), 9 of whom have all missing data. The mean age was 56.4 years (SD=15.5; female M=56.7, SD=16, male M=55.9, SD=14.9). The data were collected between 2003 and 2004.

29. YOUNG FINNS{Raitakari, 2008 #706} — Finland. The Young Finns study is an ongoing, population-based prospective cohort study started in 1980 with a baseline sample of 3 596 children and adolescents derived from six birth cohorts aged 3, 6, 9, 12, 15, and 18 years at baseline (http://youngfinnsstudy.utu.fi/). The participants were recruited from five areas according to locations of university cities with a medical school (Helsinki, Kuopio, Oulu, Tampere and Turku). In each location, individuals from urban and surrounding rural areas were selected at random from the population registry (based on their unique personal social security number from) to be invited in the study. Subsequent data collection waves have been carried out in 1983, 1986, 1989, 1992, 1997, 2001, 2007 and 2012. Personality data for the NEO-FFI were collected with mailed questionnaires in 2007 from 2 058 participants of whom 2 057 were included in the study with NEO-FFI data (one participant had all missing data). The mean age of participants was 37.6 years (SD=5) for women and men at the time of personality assessment, and 1 212 participants (58.9%) were female.

30. GENERATION SCOTLAND: Scottish Family Health Study{Smith, 2013 #1172} — Scotland (United Kingdom). The Generation Scotland: Scottish Family Health Study (GS:SFHS) is a collaboration between the Scottish Universities and the NHS, funded by the Chief Scientist Office of the Scottish Government. GS:SFHS is a family-based genetic epidemiology cohort with DNA, other biological samples (serum, urine and cryopreserved whole blood) and socio-demographic and clinical data from ~24,000 volunteers, aged 18-98 years, in ~7,000 family groups. Participants were recruited across Scotland, with some family members from further afield, from 2006 - 2011. Most (87%) participants were born in Scotland and 96% in the UK or Ireland. GS:SFHS operates

under appropriate ethical approvals, and all participants gave written informed consent. From this cohort, 9860 individuals were successfully genotyped using the Illumina OmniExpress + Exome genotyping array. 1000 genomes SNP dosages were imputed using SHAPEIT_v2 and IMPUTE2 in conjunction with the Phase I integrated variant set release (v3) all ethnicities reference panel (MAR 2012). Neuroticism was measured by the Eysenck Personality Questionnaire Revised Short Form, a self-report questionnaire requiring a yes/no response on 24 items. Neuroticism questionnaire data were obtained for 9786 and 9783 individuals respectively who also had 1000G imputed genotype data available. Summed questionnaire scores were used for association analysis of the selected replication SNPs using ProbABEL from the GenABEL suite of programs (www.genabel.org).{Aulchenko, 2007 #28}

Personality assessment

Item data from the following personality inventories were included: the Neuroticism Extraversion Openness to Experience personality inventory revised (NEO-PI-R; 240 items, 48 items for Neuroticism), the abbreviated NEO Five Factor Inventory (NEO-FFI; 60 items, 12 Neuroticism items), the 30-item short version of the NEO-Fiv x Factor Model (NEO-FFI-30), the Eysenck Personality Questionnaire Revised (EPQ-R; 48 items, 12 items for Neuroticism), the Junior EPQ (JEPQ; 81 items, 20 Neuroticism items), the Eysenck Personality Inventory (EPI; 20 items, 10 for Neuroticism), the EPI-based Amsterdamse Biografische Vragenlijst (ABV; 30 Neuroticism items), the Big Five item set of the International Personality Item Pool (IPIP; 50 items, 10 items for Neuroticism), the Temperament and Character Inventory version 9 (TCI; 240 items, of which 35 items were selected for Neuroticism) and the Multidimensional Personality Questionnaire (MPQ; 198 items, of which 27 items were selected for Neuroticism).

Polygenic risk score analysis

To predict neuroticism based on the polygenic risk scores in healthy controls, 8,648 NTR participants with measures for personality and GWA data were selected (participants could be family members, e.g. twins, siblings, parents). Because of the dependency

among observations from the same families, linear mixed modeling was applied, with family as the cluster variable allowing for a random intercept, and with the polygenic risk score and the aforementioned covariates as fixed effects in the model.

The prediction of MDD was based on a sample of 1,859 unrelated MDD cases (1 714 from NESDA and 145 from NTR) and 2,391 unrelated controls (from NESDA and NTR; in NTR one member per family was selected; total sample size 4,250). MDD case-control status was defined as a lifetime DSM-IV diagnosis using the Composite International Diagnostic Interview (CIDI). Binary logistic regression analysis was applied, with MDD (1=case, 0=control) as the dependent variable and the polygenic risk score and the covariates as independent variables.

eAppendix 2. Acknowledgments by cohorts

ALSPAC We are extremely grateful to all the families who took part in this study, the midwives for their help in recruiting them and the whole ALSPAC team, which includes interviewers, computer and laboratory technicians, clerical workers, research scientists, volunteers, managers, receptionists and nurses. The UK Medical Research Council (grant 74882), the Wellcome Trust (grant 076467) and the University of Bristol provide core support for ALSPAC. We thank 23andMe for funding the genotyping of the ALSPAC children's sample.

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COGA & COGEND Funding support for the Study of Addiction: Genetics and Environment (SAGE) was provided through the NIH Genes, Environment and Health Initiative [GEI] (U01 HG004422). SAGE is one of the genome-wide association studies funded as part of the Gene Environment Association Studies (GENEVA) under GEI. Assistance with phenotype harmonization and genotype cleaning, as well as with general study coordination, was provided by the GENEVA Coordinating Center (U01 HG004446). Assistance with data cleaning was provided by the National Center for Biotechnology Information. Support for collection of datasets and samples was provided by the Collaborative Study on the Genetics of Alcoholism (COGA; U10 AA008401) and the Collaborative Genetic Study of Nicotine Dependence (COGEND; P01 CA089392). Funding support for genotyping, which was performed at the Johns Hopkins University Center for Inherited Disease Research, was provided by the NIH GEI (U01HG004438), the National Institute on Alcohol Abuse and Alcoholism, the National Institute on Drug

Abuse, and the NIH contract “High throughput genotyping for studying the genetic contributions to human disease”(HHSN268200782096C). The Collaborative Study on the Genetics of Alcoholism (COGA), Principal Investigators B. Porjesz, V. Hesselbrock, H. Edenberg, L. Bierut, includes ten different centers: University of Connecticut (V. Hesselbrock); Indiana University (H.J. Edenberg, J. Nurnberger Jr., T. Foroud); University of Iowa (S. Kuperman, J. Kramer); SUNY Downstate (B. Porjesz); Washington University in St. Louis (L. Bierut, A. Goate, J. Rice, K. Bucholz); University of California at San Diego (M. Schuckit); Rutgers University (J. Tischfield); Texas Biomedical Research Institute (L. Almasy), Howard University (R. Taylor) and Virginia Commonwealth University (D. Dick). Other COGA collaborators include: L. Bauer (University of Connecticut); D. Koller, S. O’Connor, L. Wetherill, X. Xuei (Indiana University); Grace Chan (University of Iowa); S. Kang, N. Manz, M. Rangaswamy (SUNY Downstate); J. Rohrbaugh, J-C Wang (Washington University in St. Louis); A. Brooks (Rutgers University); and F. Aliev (Virginia Commonwealth University). A. Parsian and M. Reilly are the NIAAA Staff Collaborators. This national collaborative study is supported by NIH Grant U10AA008401 from the National Institute on Alcohol Abuse and Alcoholism (NIAAA) and the National Institute on Drug Abuse (NIDA). The Collaborative Genetic Study of Nicotine Dependence (COGEND) project is a collaborative research group and part of the NIDA Genetics Consortium. Subject collection was supported by NIH grant P01 CA089392 (L.J. Bierut) from the National Cancer Institute. Phenotypic and genotypic data are stored in the NIDA Center for Genetic Studies (NCGS) at http://www.drugabuse.gov/researchers/research-resources/genetics-research-resources/nida-genetics-study-center-biorepository under NIDA Contract HHSN271200477451C (J. Tischfield and J. Rice). Jaime Derringer was supported by NIH T32 MH016880.

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eTable 1. Overview of 29 discovery cohorts and 1 replication cohort of the GPC

	Cohort	**# Subjects ***	**# SNPs ****		**Cohort**	**# Subjects ***	**# SNPs ****
1	ALSPAC	4702	5186454	16	MCTFR	7103	6570007
2	BLSA	820	4989412	17	MGS	2101	5900913
3	BRESCIA	177	3549922	18	NBS	1329	5582155
4	CHICAGO	311	3755621	19	NESDA	2227	4707575
5	CILENTO	627	1123090	20	NTR	6417	5339780
6	COGA	647	5127144	21	ORCADES	1650	5335401
7	COGEND	1279	5932926	22	PAGES	476	4547294
8	EGCUT	1184	5574957	23	QIMR adolescents	2842	5957076

9	ERF	2296	5651599	24	QIMR adults	7203	6343953
10	FINTWIN EPI	568	4870715	25	SardiNIA	5566	6291236
11	FINTWIN NEO	813	5092022	26	SHIP	2213	5913435
12	HBCS	1367	5612810	27	STR	4901	6525398
13	KORCULA	809	5094239	28	VIS	909	5327684
14	LBC1921	437	4363627	29	YFS	1737	5914719
15	LBC1936	952	5168775		***Total***	63661	7480565
				30	Generation Scotland	9 786	NA

* Number of subjects with valid latent score for Neuroticism and SNP data (after imputation and cleaning)

** Number of SNPs (after imputation and cleaning) with valid association results that entered the meta-analysis

NA=Not Applicable for replication cohort because only top hits were sought to replicate.

eTable 2. Genotyping and imputation in the 29 discovery cohorts and 1 replication cohort of the GPC

	Cohort	Genotyping platforms(s)	HWE *P*-value *	SNP call rate *	Sample call rate *	Imputation reference set	Imputation software	Association software
1	ALSPAC	Illumina 550K	>5 x 10-7	>0.95	>0.97	1000G phase 1 v3[1]	MACH	MACH2QTL
2	BLSA	Illumina 550K	≥1 x 10-5	≥0.99	≥0.985	1000G phase 1 v3[2]	MACH	Merlin-offline
3	BRESCIA	Affymetrix 6.0	>1 x 10-6	>0.95	>0.96	1000G phase 1 v3[3]	IMPUTE	SVS 7 GoldenHelix
4	CHICAGO	Affymetrix 6.0	>1 x 10-4	>0.95	>0.90	1000G phase 1 v3	IMPUTE	SNPTEST
5	CILENTO	Illumina 370 K Illumina OmniExpress 700K	NA	>0.95	>0.90	1000G phase 1 v3[2]	MACH /minimac	R, GenABEL /ProbABEL

6	COGA	Illumina 1M	>1 x 10-6	>0.95	>0.95	1000G phase 1 v3[2]	IMPUTE	SNPTEST
7	COGEND	Illumina 1M	>1 x 10-6	>0.95	>0.95	1000G phase 1 v3[2]	IMPUTE	SNPTEST
8	EGCUT	Illumina Human370CNV & OmniExpress770k	>1 x 10-6	>0.95	>.095	1000G phase 1 v3[2]	IMPUTE	SNPTEST
9	ERF	Illumina 318K, 370K, 610K	>1 x 10-6	≥0.95	≥0.95	1000G phase 1 v3	minimac	ProbABEL
10	FINTWIN EPI	Illumina 670K	>1 x 10-6	>0.95	> 0.95	1000G phase 1 v3[3]	IMPUTE	SNPTEST
11	FINTWIN NEO	Illumina 670K	>1 x 10-6	>0.95	>0.95	1000G phase 1 v3[3]	IMPUTE	SNPTEST
12	HBCS	Modified Illumina 610 k	>1 x 10-6	>0.95	>0.95	1000G phase 1 v3[3]	MACH	Plink, ProbABEL

13	KORCULA	Illumina Infinium II HumanCNV370v2	>1 x 10-6	>0.98	>0.97	1000G phase 1 v3[3]	IMPUTE	ProbABEL
14	LBC1921	Illumina610-Quadv1	>1 x 10-3	≥0.98	≥0.95	1000G phase 1 v3[2]	Minimac	MACH2QTL
15	LBC1936	Illumina610-Quadv1	>1 x 10-3	≥0.98	≥0.95	1000G phase 1 v3[2]	Minimac	MACH2QTL
16	MCTFR	Illumina Human660W-Quad Array	>1 x 10-7	>0.99	removed samples with: non-calls in more than 5000 markers; GenCall_10 < .75; GenCall_50 < .9009	1000G phase 1 v3[2]	Beagle / Minimac	RFGLS package for R

17	MGS	Affymetrix 6.0	>1 x 10-6	>0.98	No exclusions; all were > 0.99	1000G phase 1 v3[3]	IMPUTE	ProbABEL
18	NBS	Illumina 317K	>1 x 10-6	>0.95	0.9	1000G phase 1 v3[2]	MACH/minimac	mach2qtl
19	NESDA	Affymetrics 5.0-Perlegen Affymetrix 6.0 Affymetrix 6 907k	>1 x 10-6	>0.95	>0.9	1000G phase 1 v3[1]	IMPUTE	PLINK
20	NTR	Affymetrics 5.0-Perlegen Illumina 370 Illumina 660 Affymetrix 6.0 Affymetrix 6 907k Illumina Omni Express 1M	>1 x 10-6	0.95	0.9	1000G phase 1 v3[1]	IMPUTE	PLINK

21	ORCADES	Illumina HAP300 854 subjs Illumina OmniX 1067 Subjs Illumina Omni1 301 Subjs	>1 x 10-6	>0.97	>0.98	1000G phase 1 v3[3]	IMPUTE	R, GenABEL/ProbABEL
22	PAGES	Illumina Human Hap 300	>1 x 10-6	>0.99	>0.96	1000G phase 1 v3[2]	MACH / minimac	SNPTEST
23	QIMR adolescents	Illumina 610 quad	>1 x 10-6	>0.95	>0.95	1000G phase 1 v3[2]	MACH / minimac	Merlin-offline
24	QIMR adults	Illumina 610 quad Illumina 670 quad Illumina 370 duo Illumina 370 single Illumina 317 single	>1 x 10-6	>0.95	>0.95	1000G phase 1 v3[2]	MACH / minimac	Merlin-offline

25	SardiNIA	Affymetrix 10k, 500k, 1M	≥1 x 10-7	≥0.95	≥0.95	1000G phase 1 v3	MACH	Merlin-offline
26	SHIP	Affymetrix 6.0	>1 x 10-4	>0.8	>0.92	1000G phase 1 v3[2]	IMPUTE	SNPTEST
27	STR	Illumina OmniExpress	>1 x 10-6	>0.97	>0.97	1000G phase 1 v3	MACH/minimac	PLINK
28	VIS	Illumina Infinium II HumanCNV370v1	>1 x 10-6	>0.98	>0.97	1000G phase 1 v3[3]	IMPUTE	ProbABEL
29	YFS	Custom Illumina Human 670k BeadChip	>1 x 10-6	≥0.95	≥0.95	1000G phase 1 v3[2]	IMPUTE	SNPTEST
30	Generation Scotland	Illumina OmniExpress + Exome genotyping array	NA	NA	NA	1000G phase 1 v3[3]	IMPUTE	ProbABEL

* Quality control of genotyped SNPs prior to imputation (Inclusion criteria)

1 Haplotype release date March 14 2012

2 Haplotype release date November 11 2011

3 Haplotype release date September 16 2013 (SHAPEIT)

eTable 3. Genomic inflation factors (lambdas) for neuroticism results in each cohort participating in the GPC

Cohort	**Lambda**	**Cohort**	**Lambda**
ALSPAC	0.97	MCTFR	0.99
BLSA	1.03	MGS	0.96
BRESCIA	0.96	NBS	0.97
CHICAGO	0.97	NESDA	1.00
CILENTO	0.96	NTR	0.99
COGA	0.90	ORCADES	0.97
COGEND	0.89	PAGES	0.97
EGCUT	0.97	QIMR adolescents	0.97
ERF	1.00	QIMR adults	0.98
FINTWIN EPI	0.98	SardiNIA	1.18*
FINTWIN NEO	0.98	SHIP	0.97
HBCS	0.96	STR	0.98
KORCULA	0.98	VIS	0.96
LBC1921	0.95	YFS	0.97
LBC1936	0.96	***Meta-analysis***	1.01

*Genomic control was applied to the results of this cohort prior to meta-analysis

eTable 4. Top 127 SNPs from meta-analysis of GWA results for neuroticism in the GPC ($P < 1*10^{-5}$)[1]

					Results from meta-analysis in 29 discovery cohorts[2]				**Results from 1 replication cohort**			**Results from meta-analysis in all 30 cohorts[3]**
SNP	**Chr_bp[4]**	**A1[5]**	**A2**	**MAF[6]**	**Number of cohorts**	**Effect**	**SE**	**P-value**	**Effect**	**SE**	**P-value**	**P-value**
rs35855737	3_65542856	t	c	.202	29	.040	.007	9.259×10^{09}	.019	.019	.321	2.380×10^{-08}
rs35557878	3_65573858	a	g	.193	29	-.035	.007	4.691×10^{07}	-.003	.019	.870	3.325×10^{-06}
rs2393911	6_27057079	t	c	.192	27	-.039	.008	1.204×10^{06}	-.057	.026	.029	4.846×10^{-07}
rs77337722	18_74935886	t	c	.028	2	.175	.036	1.244×10^{06}	-.044	.047	.351	3.101×10^{-03}
rs1524970	3_65538544	a	c	.258	29	-.031	.006	1.625×10^{06}	-.018	.017	.306	2.319×10^{-06}
rs76457088	18_74936258	a	g	.028	2	.171	.036	2.055×10^{06}	-.043	.047	.359	3.511×10^{-03}
rs1811103	22_34182889	a	t	.171	26	.039	.008	2.334×10^{06}	.002	.020	.933	8.180×10^{-06}
rs10934447	3_118101726	a	g	.180	24	.035	.007	2.530×10^{06}	.016	.018	.386	3.526×10^{-06}

rs4653163	1_36627445	t	g	.041	3	.152	.032	2.696×10^{06}	.022	.034	.524	1.393×10^{-04}
rs56118546	5_164465890	t	g	.166	26	-.039	.008	2.908×10^{06}	-.026	.022	.249	1.480×10^{-06}
rs412701	22_34175587	t	c	.144	25	.040	.009	2.911×10^{06}	-.018	.021	.384	1.799×10^{-05}
rs62188582	2_240175059	t	c	.031	3	-.129	.028	3.636×10^{06}	.010	.045	.818	2.816×10^{-04}
rs9661830	1_23614982	t	c	.139	28	.033	.007	3.761×10^{06}	-.019	.019	.332	4.045×10^{-05}
rs72817567	5_164579303	t	g	.178	27	.035	.008	3.801×10^{06}	.026	.021	.213	2.555×10^{-06}
rs1117999	2_13755118	a	t	.014	22	.047	.010	3.835×10^{06}	.014	.027	.609	2.629×10^{-05}
rs55940235	5_164581837	a	g	.179	27	-.035	.008	3.865×10^{06}	-.026	.021	.218	2.525×10^{-06}
rs72817562	5_164576968	t	g	.178	27	.035	.008	3.941×10^{06}	.026	.021	.211	2.492×10^{-06}
rs72817565	5_164579250	a	g	.178	27	-.035	.008	3.995×10^{06}	-.026	.021	.213	2.675×10^{-06}
rs2112175	5_164580712	t	c	.179	27	-.034	.008	4.036×10^{06}	-.026	.021	.215	2.686×10^{-06}
rs55953354	5_164581366	a	g	.179	27	.034	.008	4.098×10^{06}	.026	.021	.217	2.678×10^{-06}
rs57575916	1_23602620	a	g	.134	28	-.033	.007	4.150×10^{06}	.018	.019	.351	3.939×10^{-05}
rs114293326	5_164471700	a	g	.170	27	.036	.008	4.224×10^{06}	.027	.022	.222	3.382×10^{-06}
rs649915	1_23690876	a	g	.168	29	-.032	.007	4.279×10^{06}	.007	.019	.719	2.620×10^{-05}

rs3753250	1_23669770	a	g	.140	27	-.033	.007	4.287×10^{06}	.016	.019	.419	4.367×10^{-05}
rs2039316	1_23600798	t	c	.133	28	-.033	.007	4.327×10^{06}	.018	.020	.368	3.622×10^{-05}
rs1421698	5_164490019	t	g	.164	27	.036	.008	4.437×10^{06}	.027	.022	.215	3.625×10^{-06}
rs17072113	5_164489105	t	g	.164	27	-.036	.008	4.447×10^{06}	-.027	.022	.215	3.580×10^{-06}
rs1421697	5_164490201	a	g	.164	27	.036	.008	4.453×10^{06}	.027	.022	.215	3.631×10^{-06}
rs140142689	5_164488914	t	c	.164	27	.036	.008	4.545×10^{06}	.027	.022	.215	3.659×10^{-06}
rs72808038	5_164493780	a	g	.164	27	.035	.008	4.566×10^{06}	.026	.022	.225	3.804×10^{-06}
rs61777134	1_23691762	a	g	.176	29	.032	.007	4.578×10^{06}	-.007	.019	.713	2.660×10^{-05}
rs58067912	5_164475990	c	g	.170	27	-.036	.008	4.848×10^{06}	-.027	.022	.216	3.515×10^{-06}
rs72808024	5_164479164	a	c	.170	27	-.036	.008	4.848×10^{06}	-.027	.022	.216	3.432×10^{-06}
rs2413200	22_34191950	t	c	.156	25	.039	.009	4.903×10^{06}	-.005	.021	.811	1.759×10^{-05}
rs644749	1_23687827	t	c	.176	28	.032	.007	4.959×10^{06}	-.005	.019	.778	2.590×10^{-05}
rs7736835	5_164482610	a	g	.164	27	.036	.008	4.975×10^{06}	.028	.022	.211	3.290×10^{-06}
rs72808018	5_164474440	a	g	.170	27	-.036	.008	5.022×10^{06}	-.027	.022	.216	3.589×10^{-06}
rs56013285	6_159210222	a	g	.034	5	.110	.024	5.092×10^{06}	-.038	.041	.358	1.204×10^{-03}

rs618237	1_23693385	t	c	.175	28	.032	.007	5.115×10^{06}	-.007	.019	.729	2.828×10^{-05}
rs605419	9_108413323	a	c	.258	29	-.027	.006	5.160×10^{06}	.000	.016	.983	2.392×10^{-05}
rs678007	1_23600579	t	c	.142	28	-.033	.007	5.258×10^{06}	.013	.019	.492	2.996×10^{-05}
rs6718530	2_13799320	a	c	.077	22	.046	.010	5.266×10^{06}	.015	.026	.574	3.699×10^{-05}
rs72808025	5_164481103	a	g	.167	27	-.036	.008	5.269×10^{06}	-.028	.022	.213	3.607×10^{-06}
rs1421711	5_164575038	t	c	.174	27	.034	.008	5.353×10^{06}	.027	.021	.199	3.595×10^{-06}
rs4916970	7_194947	t	c	.488	27	-.031	.007	5.481×10^{06}	.015	.015	.306	2.466×10^{-04}
rs72808021	5_164476757	a	g	.170	27	-.036	.008	5.527×10^{06}	-.027	.022	.216	3.686×10^{-06}
rs72808022	5_164476789	a	g	.170	27	-.036	.008	5.537×10^{06}	-.027	.022	.216	3.731×10^{-06}
rs61776062	1_25013286	c	g	.194	29	-.036	.008	5.552×10^{06}	.044	.020	.030	7.859×10^{-04}
rs607747	1_23600610	a	g	.227	29	-.031	.007	5.561×10^{06}	.005	.018	.766	1.058×10^{-05}
rs72808036	5_164488789	a	g	.160	27	-.036	.008	5.736×10^{06}	-.027	.022	.228	4.812×10^{-06}
rs75364953	18_43279643	t	c	.035	5	.149	.033	5.788×10^{06}	-.010	.047	.834	9.156×10^{-05}
rs1606045	2_13788408	t	c	.081	22	.046	.010	5.908×10^{06}	.015	.026	.551	3.357×10^{-05}
rs1606039	2_13801366	a	t	.078	22	.046	.010	5.993×10^{06}	.015	.026	.572	4.129×10^{-05}

rs2417651	9_108641054	t	c	.039	7	.090	.020	6.022×10^{06}	.034	.038	.372	1.234×10^{-05}
rs72817557	5_164572551	t	c	.173	27	.034	.008	6.174×10^{06}	.027	.021	.210	4.147×10^{-06}
rs17073151	5_164572747	t	c	.173	27	.034	.008	6.196×10^{06}	.027	.021	.210	4.153×10^{-06}
rs12140750	1_23659141	t	c	.164	28	-.032	.007	6.209×10^{06}	.014	.019	.453	4.902×10^{-05}
rs1421712	5_164575191	a	g	.173	27	-.034	.008	6.226×10^{06}	-.027	.021	.211	4.214×10^{-06}
rs117182615	14_23031439	a	c	.028	8	-.091	.020	6.250×10^{06}	-.012	.041	.760	1.882×10^{-05}
rs113399772	9_10881231	a	t	.080	17	.061	.014	6.361×10^{06}	.050	.028	.073	1.870×10^{-06}
rs10941710	5_45849729	a	t	.382	25	-.032	.007	6.413×10^{06}	-.021	.016	.197	7.895×10^{-06}
rs6720818	2_13774644	t	c	.027	23	.045	.010	6.452×10^{06}	.008	.025	.749	8.102×10^{-05}
rs5754684	22_34202814	a	t	.193	26	.037	.008	6.711×10^{06}	.003	.020	.879	1.889×10^{-05}
rs12111597	7_34870001	a	g	.213	28	-.029	.007	6.825×10^{06}	.003	.018	.855	4.564×10^{-05}
rs1811104	22_34183005	t	c	.181	25	.037	.008	6.954×10^{06}	-.009	.020	.634	4.548×10^{-05}
rs10063439	5_45526983	t	c	.334	25	.036	.008	6.983×10^{06}	-.013	.019	.493	2.027×10^{-04}
rs987276	5_164502640	t	g	.160	27	.034	.008	7.072×10^{06}	.025	.022	.245	5.620×10^{-06}
rs1582420	5_164558173	t	g	.174	27	-.034	.008	7.177×10^{06}	-.026	.021	.214	5.079×10^{-06}

rs572463	9_108417239	a	g	.344	29	.026	.006	7.184×10^{06}	.001	.015	.941	2.970×10^{-05}
rs1421702	5_164584690	t	c	.173	27	.034	.008	7.435×10^{06}	.026	.021	.219	5.004×10^{-06}
rs11782824	8_38781040	a	c	.449	26	-.027	.006	7.461×10^{06}	-.014	.015	.346	4.135×10^{-06}
rs2806552	1_23614479	t	c	.149	28	-.032	.007	7.486×10^{06}	.018	.019	.344	5.986×10^{-05}
rs13056817	22_34180979	t	c	.143	25	-.039	.009	7.506×10^{06}	.000	.021	.984	1.522×10^{-05}
rs35548558	20_12689601	t	c	.353	28	.027	.006	7.668×10^{06}	.018	.016	.253	3.822×10^{-06}
rs4598074	6_46373058	a	c	.198	28	-.034	.008	7.723×10^{06}	.017	.021	.425	1.335×10^{-04}
rs680386	1_23695275	t	g	.174	29	-.031	.007	7.750×10^{06}	.007	.019	.725	4.226×10^{-05}
rs638722	1_23697617	t	c	.168	29	.031	.007	7.784×10^{06}	-.006	.019	.738	4.131×10^{-05}
rs72807971	5_164505399	a	g	.153	27	-.034	.008	7.786×10^{06}	-.025	.022	.246	6.110×10^{-06}
rs6889618	5_164554702	a	g	.174	27	-.034	.008	7.805×10^{06}	-.026	.021	.212	5.469×10^{-06}
rs115313197	18_12178413	a	g	.140	17	.070	.016	7.853×10^{06}	.028	.025	.256	1.265×10^{-05}
rs1510829	2_13792072	t	c	.077	22	-.045	.010	7.876×10^{06}	-.014	.026	.592	4.501×10^{-05}
rs12111600	7_34870101	a	g	.216	28	-.030	.007	7.879×10^{06}	.004	.018	.812	5.726×10^{-05}
rs77124415	11_42225827	c	g	.053	13	.059	.013	7.912×10^{06}	.040	.030	.176	4.949×10^{-06}

rs72808016	5_164473821	a	g	.170	26	.036	.008	7.919×10^{06}	.028	.022	.216	5.276×10^{-06}
rs2861091	5_164552677	t	c	.174	27	-.034	.008	7.920×10^{06}	-.027	.021	.211	5.555×10^{-06}
rs2052453	5_164553369	t	g	.174	27	.034	.008	8.100×10^{06}	.027	.021	.211	5.728×10^{-06}
rs635712	9_108415556	t	c	.334	29	.026	.006	8.247×10^{06}	.003	.015	.868	3.050×10^{-05}
rs10447633	7_32286558	a	t	.132	25	.038	.008	8.319×10^{06}	.015	.021	.481	2.702×10^{-05}
rs112545952	7_32300376	a	c	.132	25	.038	.008	8.357×10^{06}	.015	.021	.477	2.506×10^{-05}
rs4632818	5_164501068	t	c	.166	27	-.034	.008	8.379×10^{06}	-.026	.022	.234	6.558×10^{-06}
rs141712178	4_165733698	t	c	.016	2	.248	.056	8.400×10^{06}	.180	.095	.059	1.410×10^{-04}
rs6960226	7_32291445	a	g	.132	24	.038	.009	8.459×10^{06}	.015	.021	.481	2.554×10^{-05}
rs115280902	5_164552294	t	c	.174	27	.034	.008	8.491×10^{06}	.027	.021	.210	5.936×10^{-06}
rs77288055	7_32289961	a	g	.132	25	-.038	.009	8.493×10^{06}	-.015	.021	.481	2.495×10^{-05}
rs151186946	11_42229793	a	g	.053	13	-.060	.013	8.545×10^{06}	-.039	.030	.189	6.160×10^{-06}
rs72808014	5_164473576	t	c	.170	27	-.035	.008	8.560×10^{06}	-.028	.022	.216	5.641×10^{-06}
rs4331925	5_164488565	t	c	.164	26	-.035	.008	8.600×10^{06}	-.027	.022	.215	5.456×10^{-06}
rs76551066	16_80259391	c	g	.265	27	.028	.006	8.616×10^{06}	-.007	.016	.664	1.268×10^{-04}

rs151278066	11_42232149	a	g	.053	12	-.061	.014	8.672×10^{06}	-.039	.030	.185	6.793×10^{-06}
rs79976237	11_42233805	a	g	.053	12	-.061	.014	8.705×10^{06}	-.040	.030	.182	6.574×10^{-06}
rs72808027	5_164482114	a	t	.164	26	.035	.008	8.876×10^{06}	.028	.022	.206	5.195×10^{-06}
rs72809545	5_164523739	a	g	.168	27	.034	.008	8.884×10^{06}	.031	.022	.150	4.566×10^{-06}
rs72808017	5_164473894	t	c	.170	27	-.035	.008	8.906×10^{06}	-.027	.022	.216	5.894×10^{-06}
rs11228638	11_56308756	c	g	.058	14	.059	.013	8.970×10^{06}	.005	.034	.893	3.491×10^{-05}
rs61225023	5_164529217	c	g	.168	27	-.034	.008	9.020×10^{06}	-.031	.022	.147	4.172×10^{-06}
rs55696446	11_56309373	a	g	.058	14	-.059	.013	9.023×10^{06}	-.005	.034	.893	3.503×10^{-05}
rs56087727	11_56309523	a	g	.058	14	-.059	.013	9.035×10^{06}	-.005	.034	.893	3.519×10^{-05}
rs9840574	3_65530249	t	c	.252	29	-.028	.006	9.036×10^{06}	-.015	.018	.407	1.374×10^{-05}
rs4987595	7_142585006	t	c	.070	23	-.044	.010	9.044×10^{06}	-.046	.028	.095	1.089×10^{-06}
rs1895160	5_164526703	a	t	.166	27	.034	.008	9.065×10^{06}	.031	.022	.150	4.383×10^{-06}
rs192517452	3_146201263	t	c	.074	18	-.065	.015	9.079×10^{06}	.015	.035	.668	3.171×10^{-05}
rs17161087	7_32295769	a	c	.133	25	-.037	.008	9.376×10^{06}	-.015	.021	.456	2.803×10^{-05}
rs72808028	5_164482118	t	c	.161	26	-.035	.008	9.390×10^{06}	-.030	.022	.180	5.352×10^{-06}

rs146120745	11_56264563	t	c	.063	14	-.058	.013	9.446×10^{06}	.009	.034	.800	6.619×10^{-05}
rs1606044	2_13787467	a	t	.083	22	.044	.010	9.452×10^{06}	.012	.026	.641	7.063×10^{-05}
rs148169663	5_164469147	a	g	.161	26	.037	.008	9.489×10^{06}	.027	.023	.231	6.220×10^{-06}
rs9961759	18_74936144	a	g	.028	3	.134	.030	9.538×10^{06}	-.035	.047	.458	2.753×10^{-03}
rs6892403	5_164550274	a	g	.174	27	-.033	.008	9.548×10^{06}	-.027	.021	.208	6.570×10^{-06}
rs7703766	5_164524092	a	g	.166	27	.034	.008	9.604×10^{06}	.031	.022	.148	4.761×10^{-06}
rs6977615	7_32295238	a	g	.133	25	.037	.008	9.640×10^{06}	.015	.021	.458	2.895×10^{-05}
rs57440542	5_164528855	a	g	.167	27	.034	.008	9.688×10^{06}	.031	.022	.147	4.491×10^{-06}
rs1421687	5_164502704	c	g	.157	27	-.034	.008	9.849×10^{06}	-.026	.022	.236	7.636×10^{-06}
rs60354824	5_164528760	a	g	.167	27	-.034	.008	9.861 x 1006	-.031	.022	.149	4.622×10^{-06}
rs6723070	2_13759780	a	t	.008	22	-.046	.010	9.869 x 1006	-.017	.027	.529	4.703×10^{-05}
rs114077592	5_164525315	a	g	.166	27	-.034	.008	9.876 x 1006	-.031	.022	.147	4.933×10^{-06}
rs72870772	1_24962517	a	g	.211	26	.035	.008	9.964 x 1006	-.028	.019	.132	9.326×10^{-04}
rs58828720	5_164545511	a	g	.193	26	.034	.008	9.972 x 1006	.015	.021	.475	1.138×10^{-05}

1 Full list of results from the meta-analysis of 29 discovery cohorts can be downloaded from http://www.tweelingenregister.org/GPC

2 Meta-analysis was inverse weighted variance method in METAL, because neuroticism scores were harmonized scores in all 29 discovery cohorts

3 Meta-analysis was z-score pooling method in METAL, because neuroticism score was sumscore in replication cohort

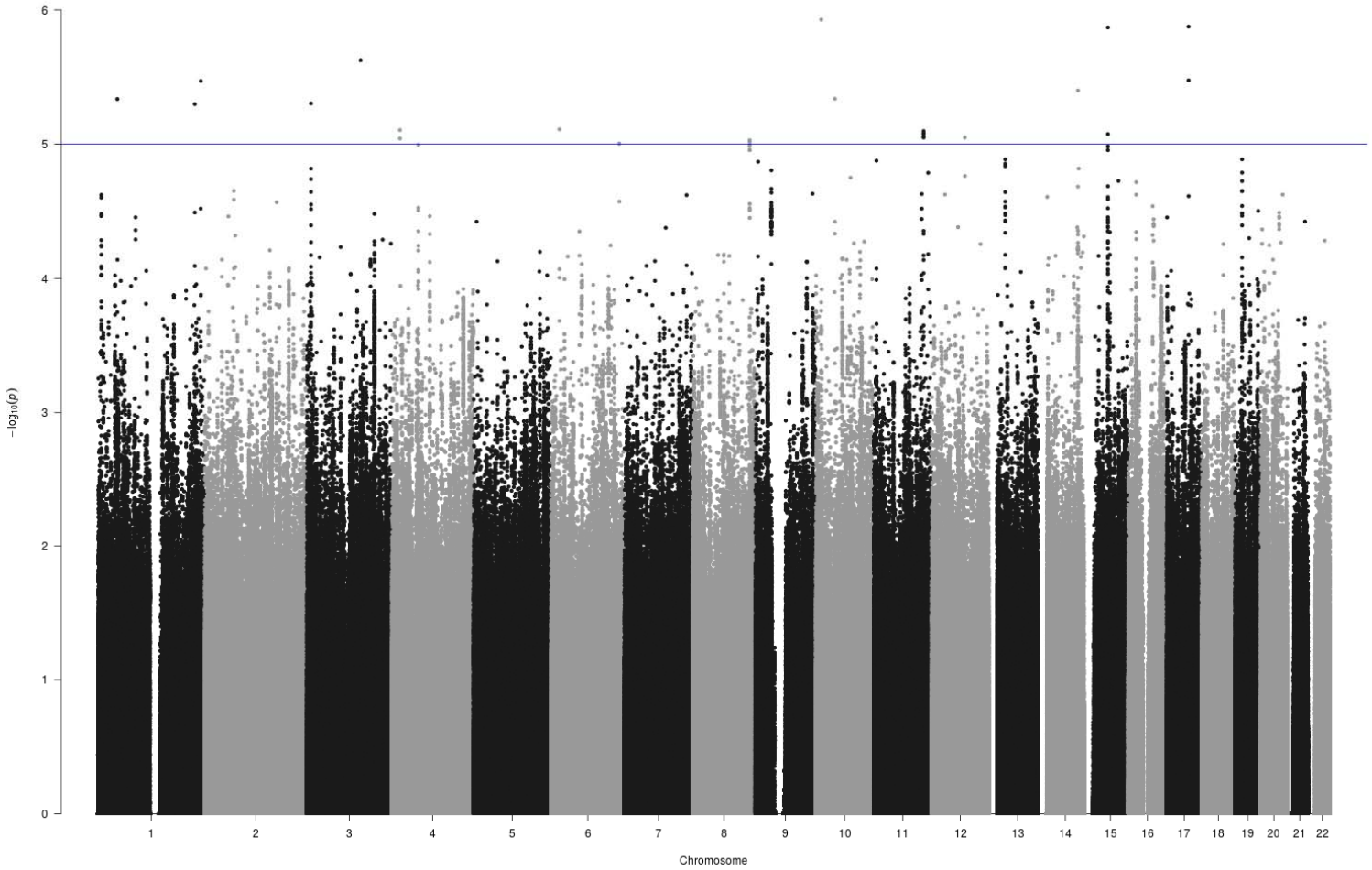
4 Locations taken from build 37 (hg 19)

5 Allele for which effect is reported (Effect allele)

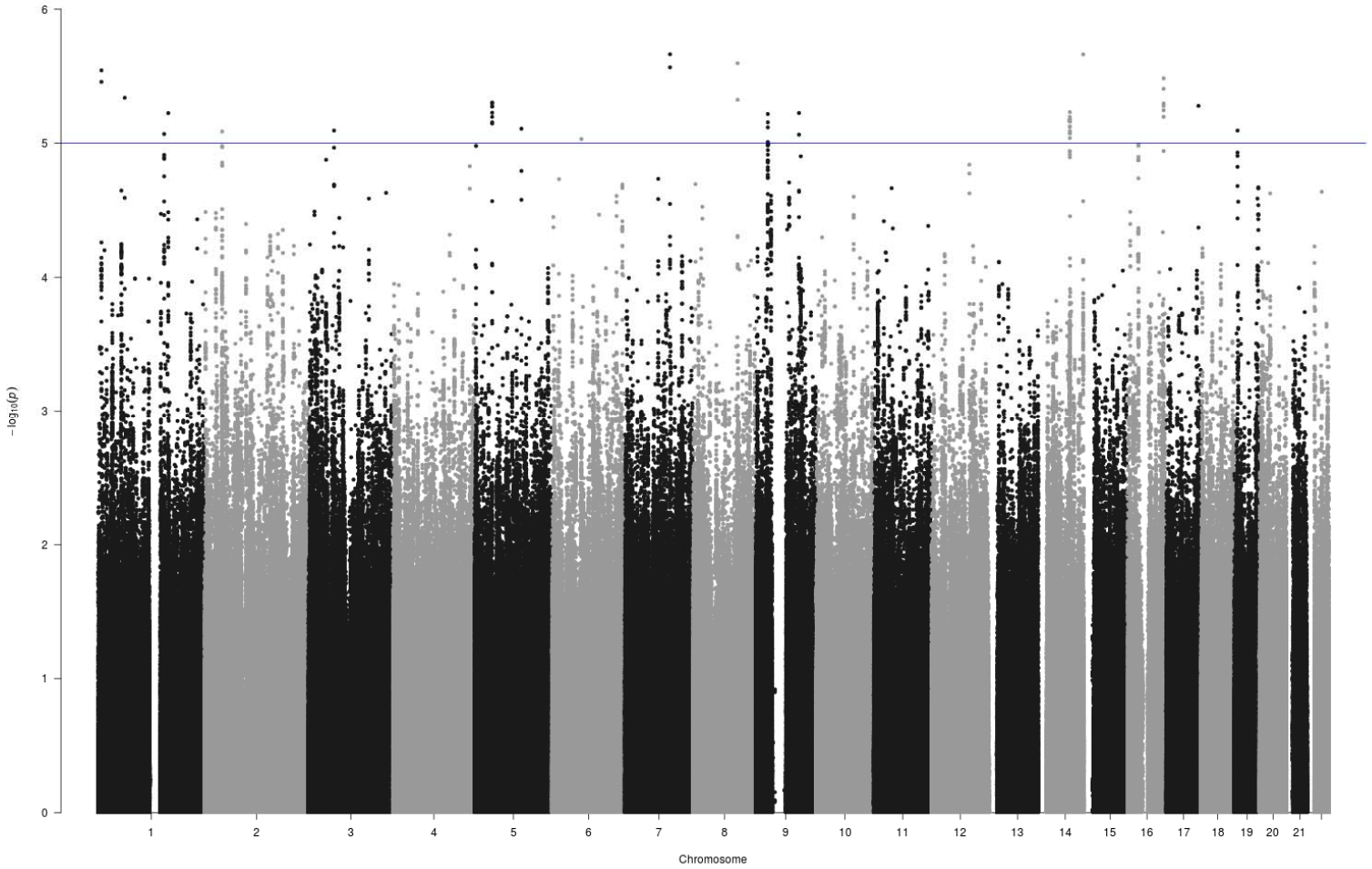
6 MAF based on 1000G reference set

eFigure 1. Manhattan plots for Neuroticism results in each cohort participating in the Genetics of Personality Consortium

ALSPAC



BLSA



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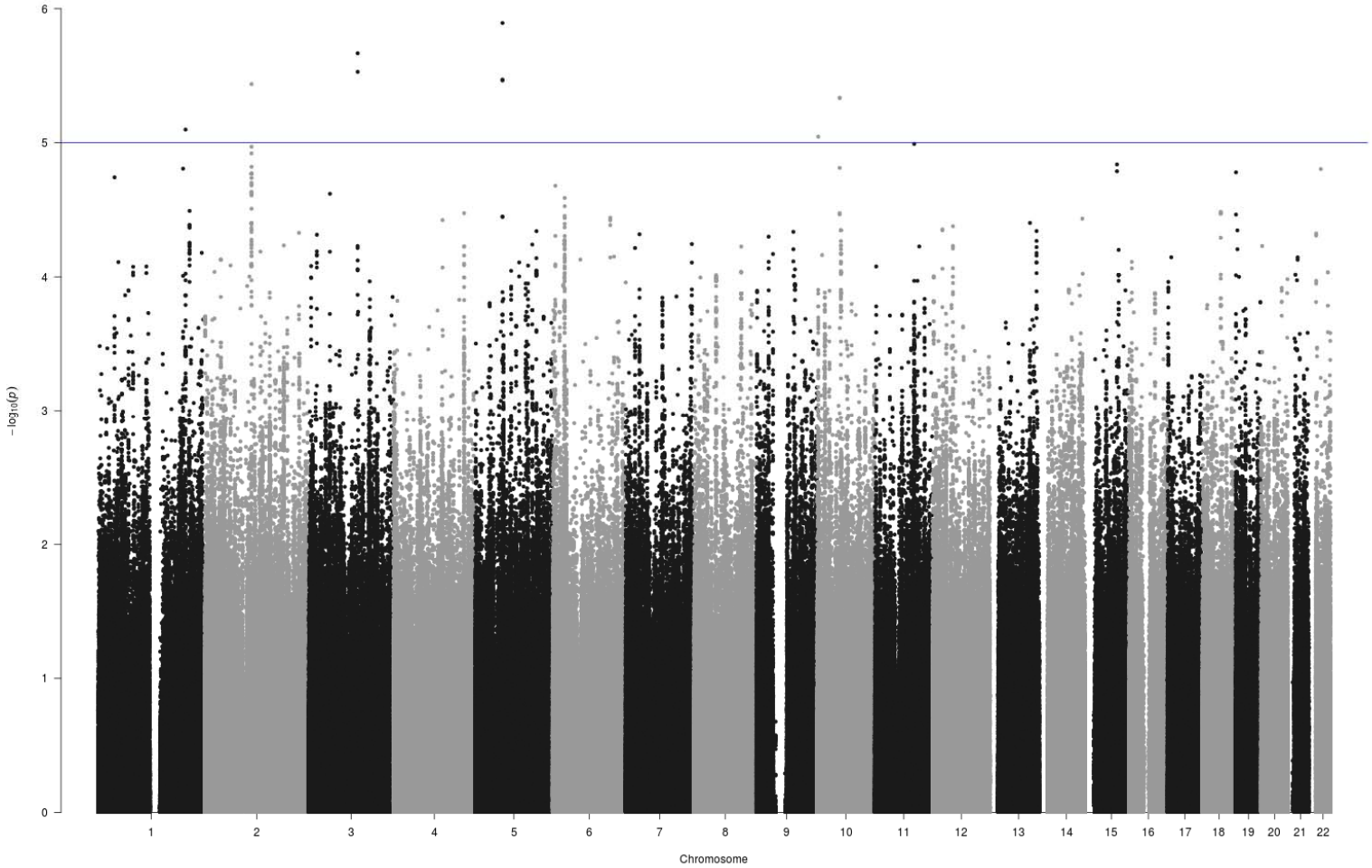

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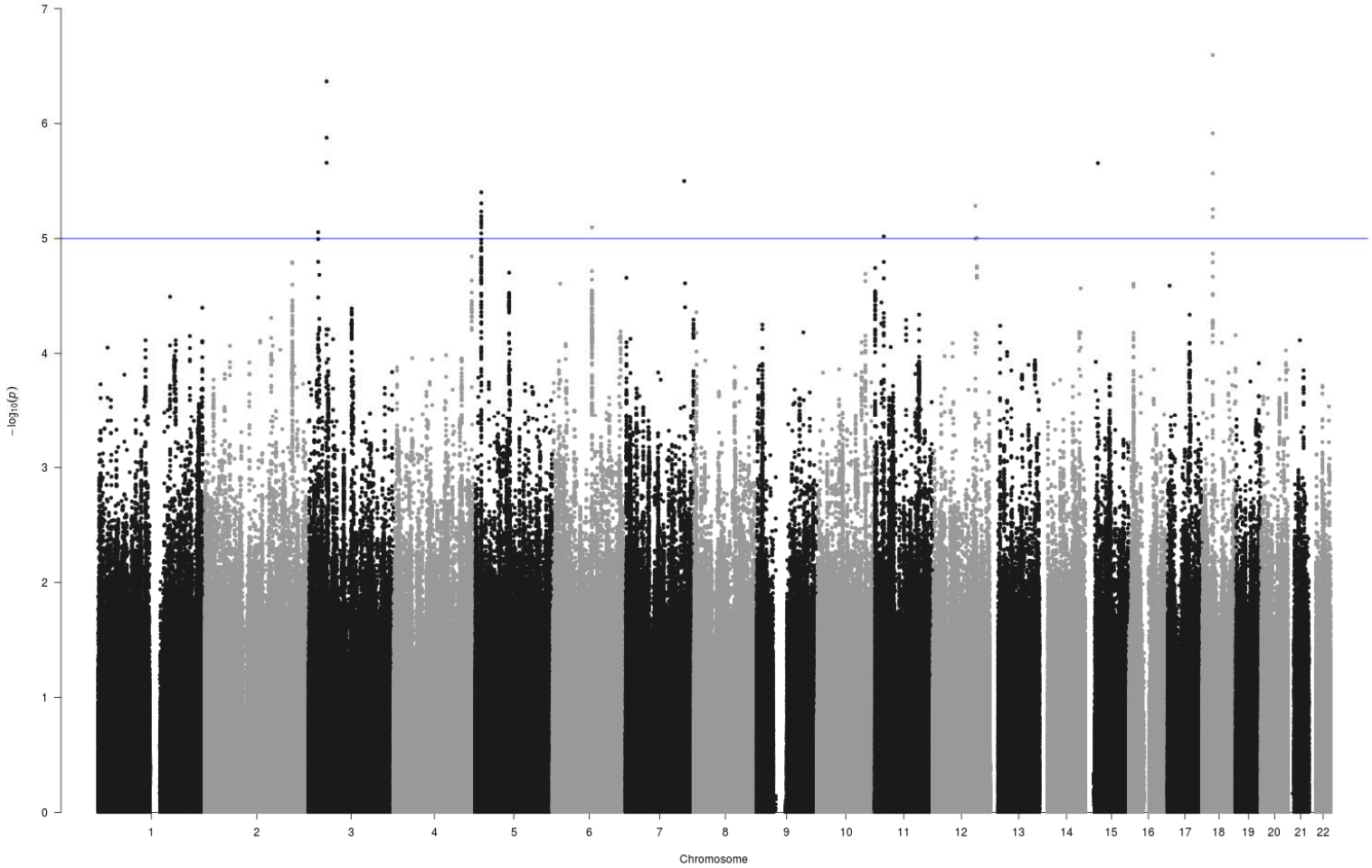

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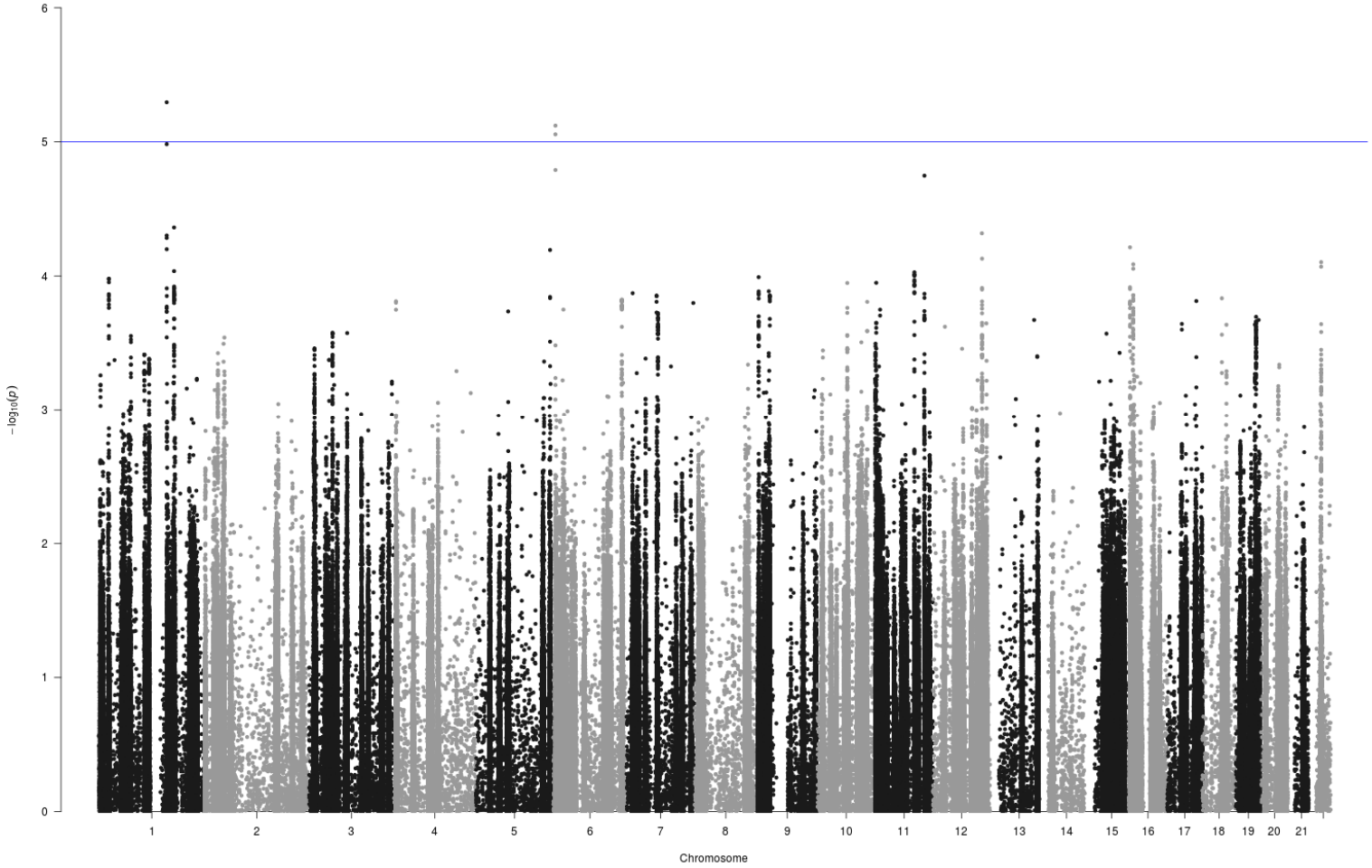

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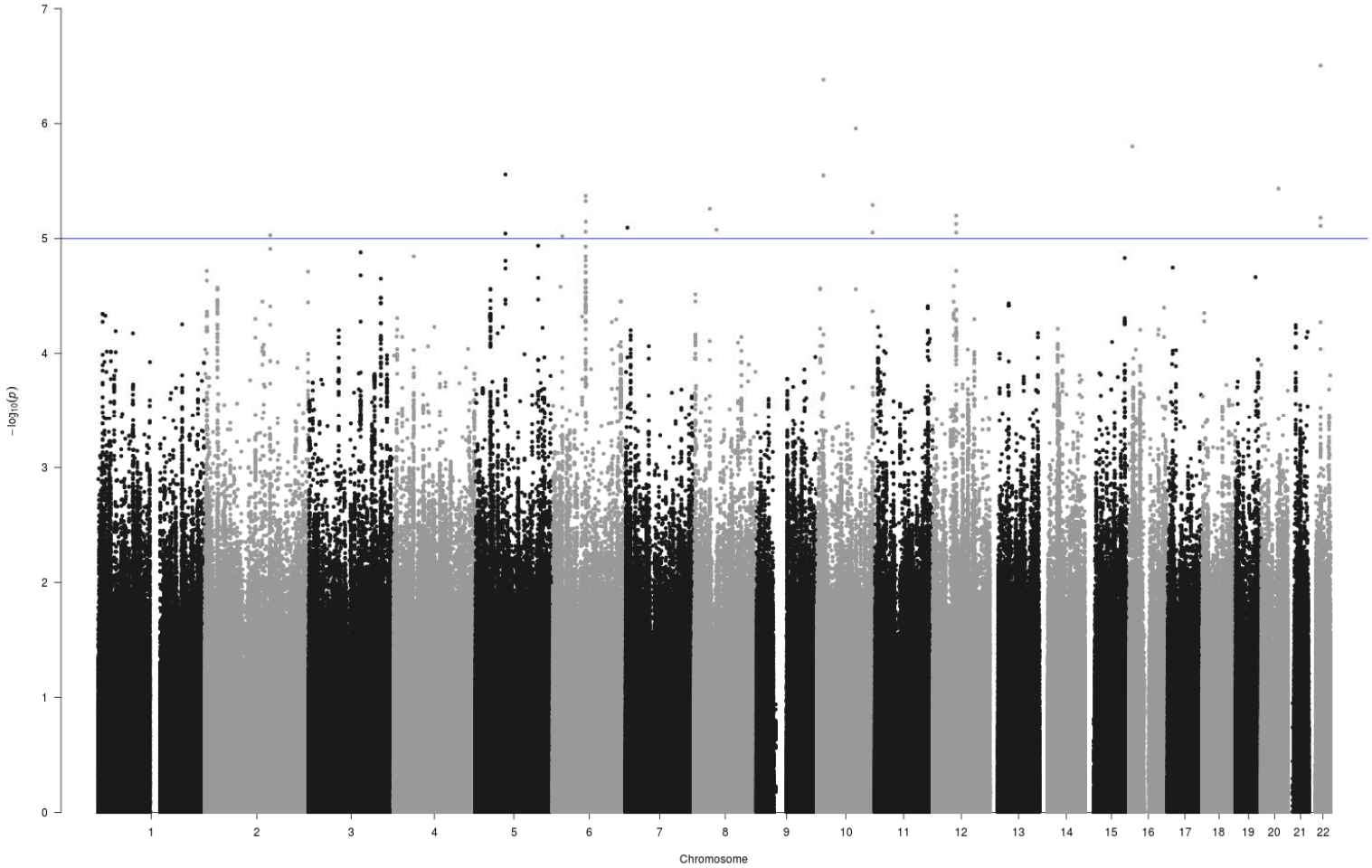

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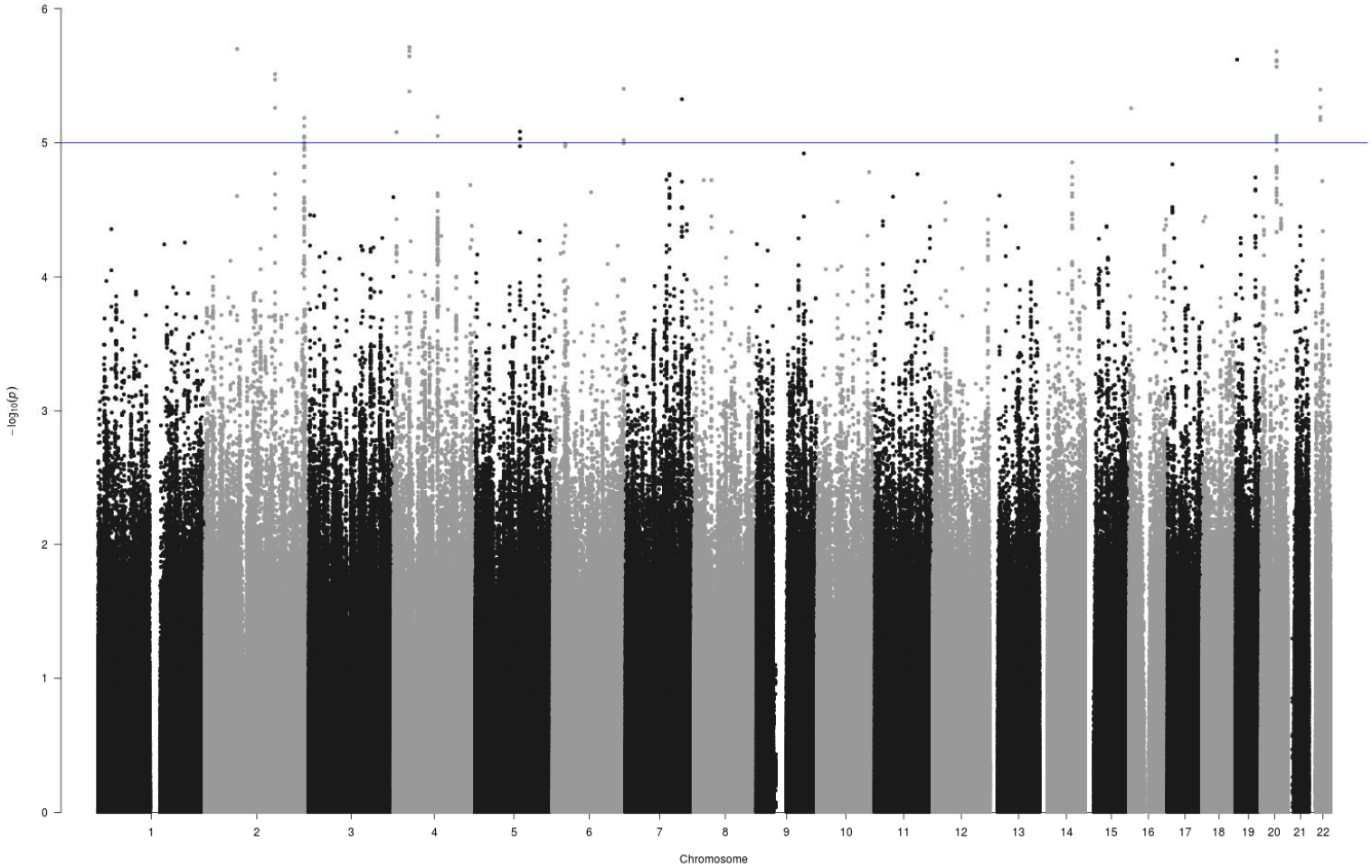

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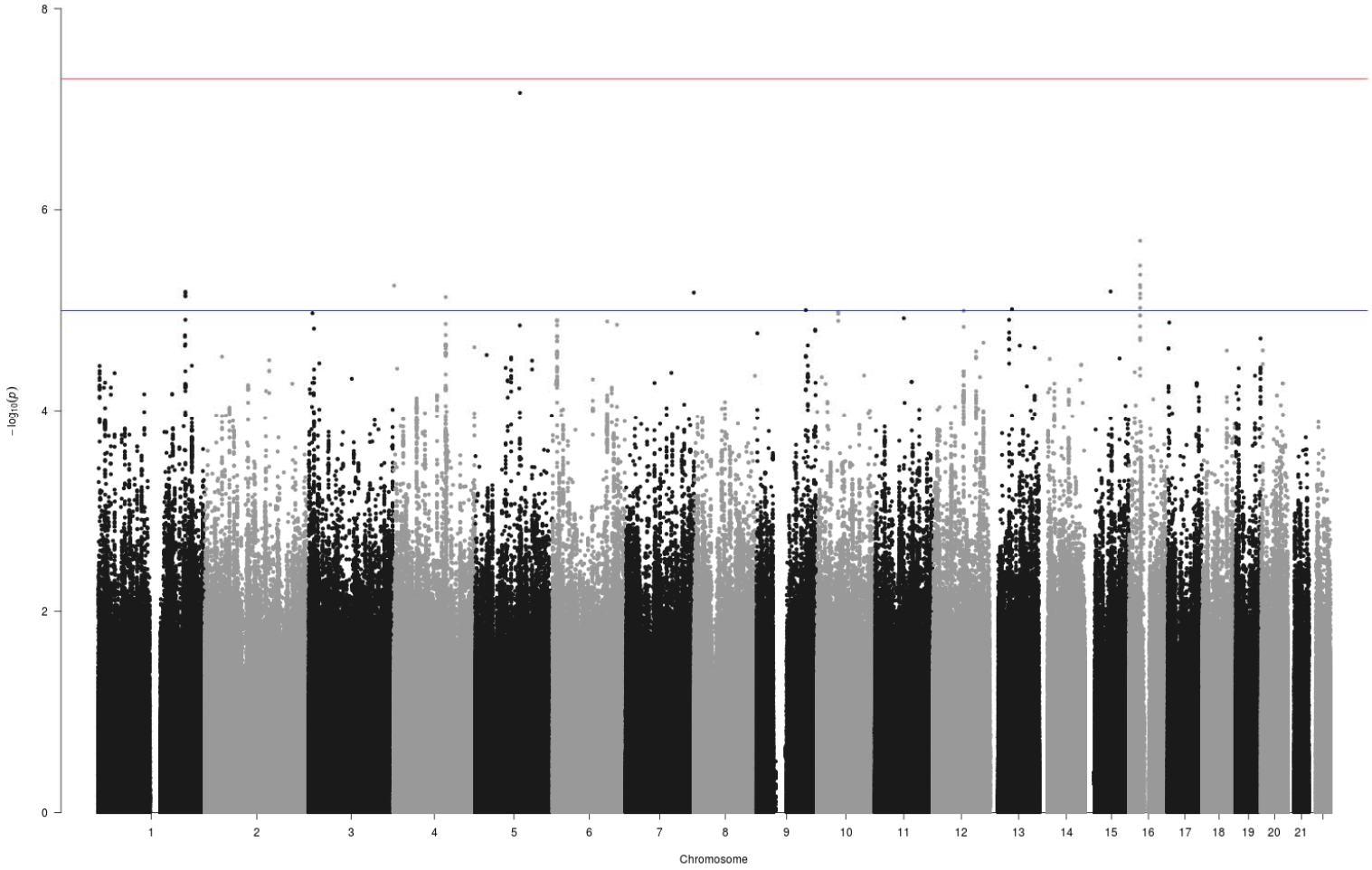

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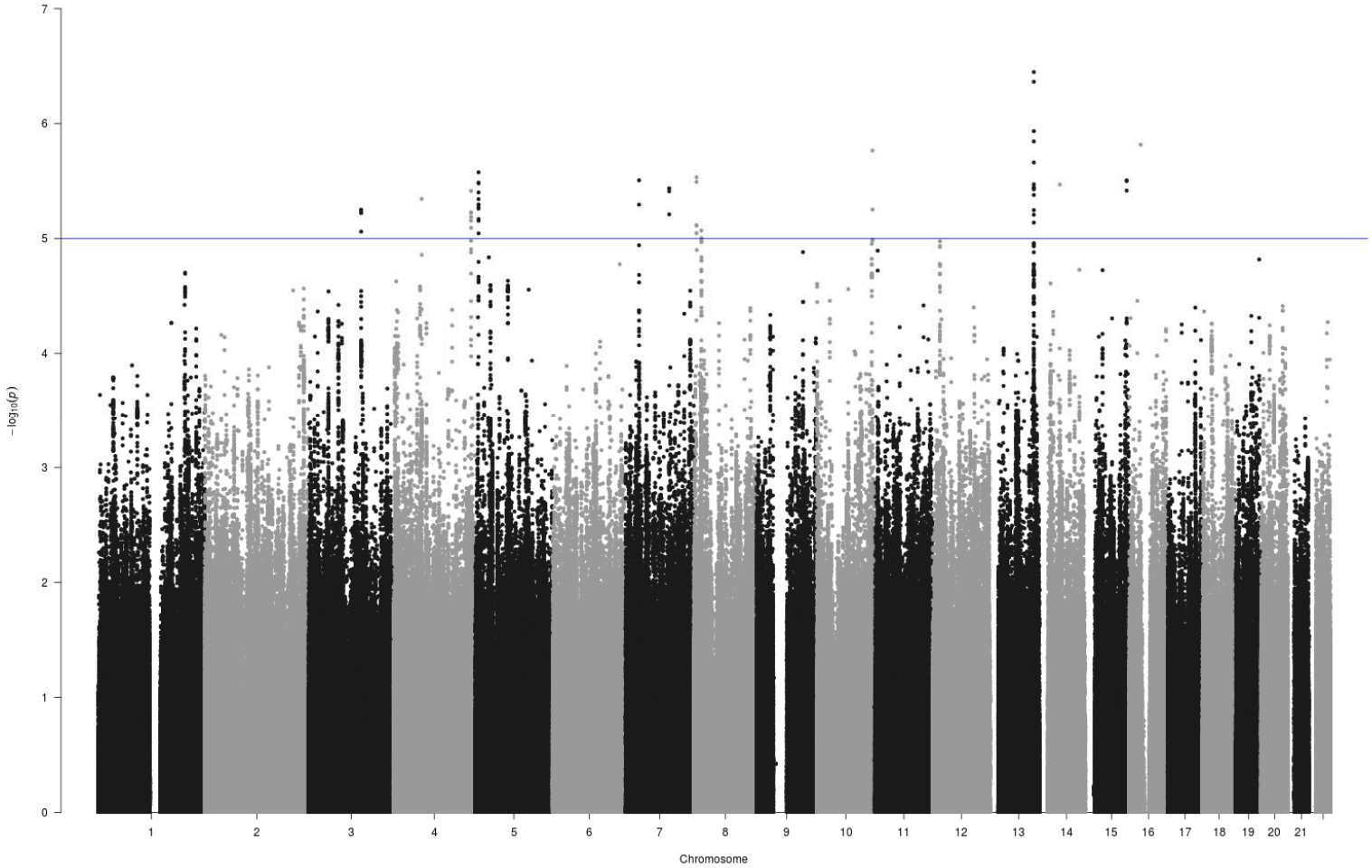

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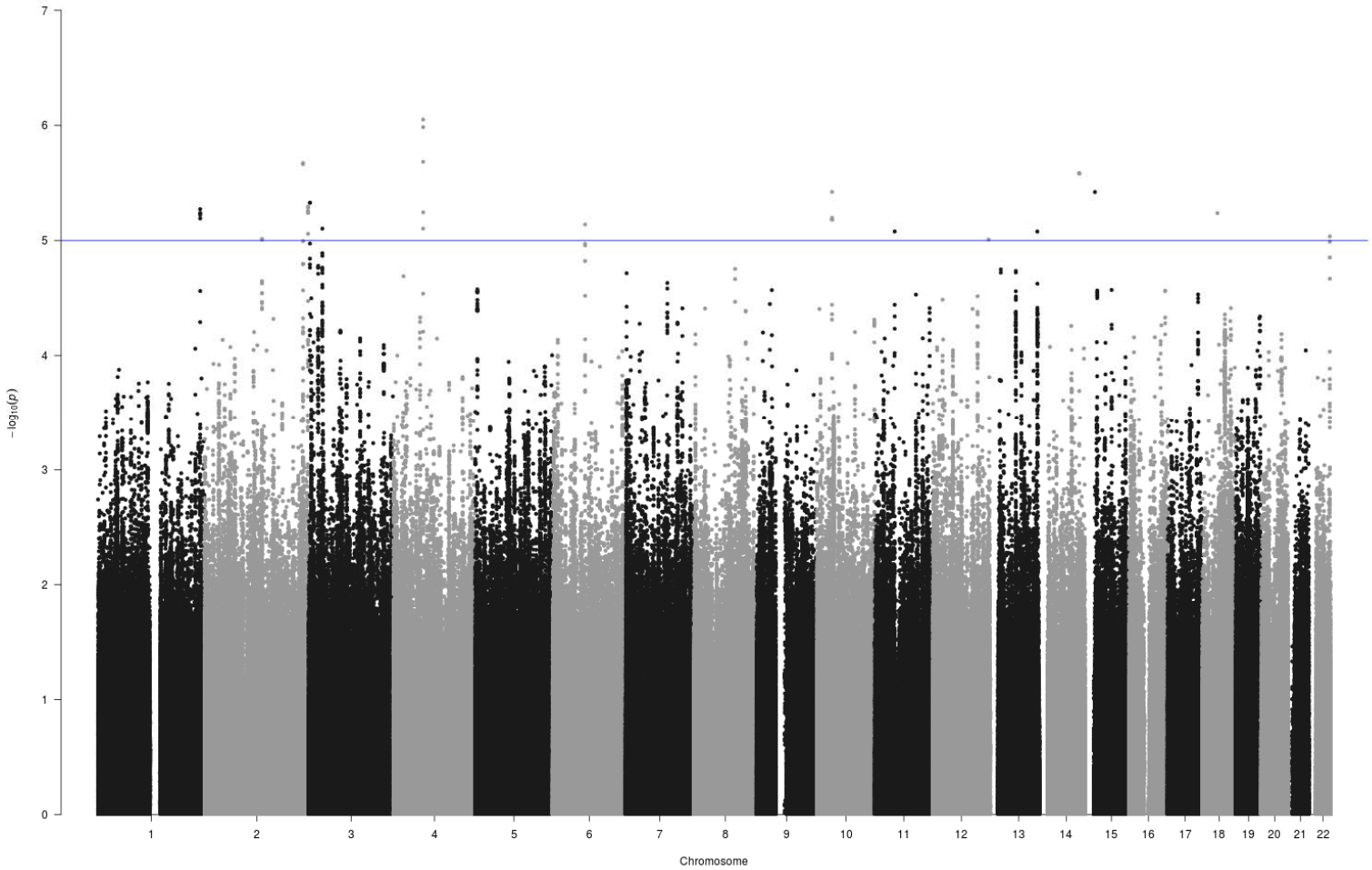

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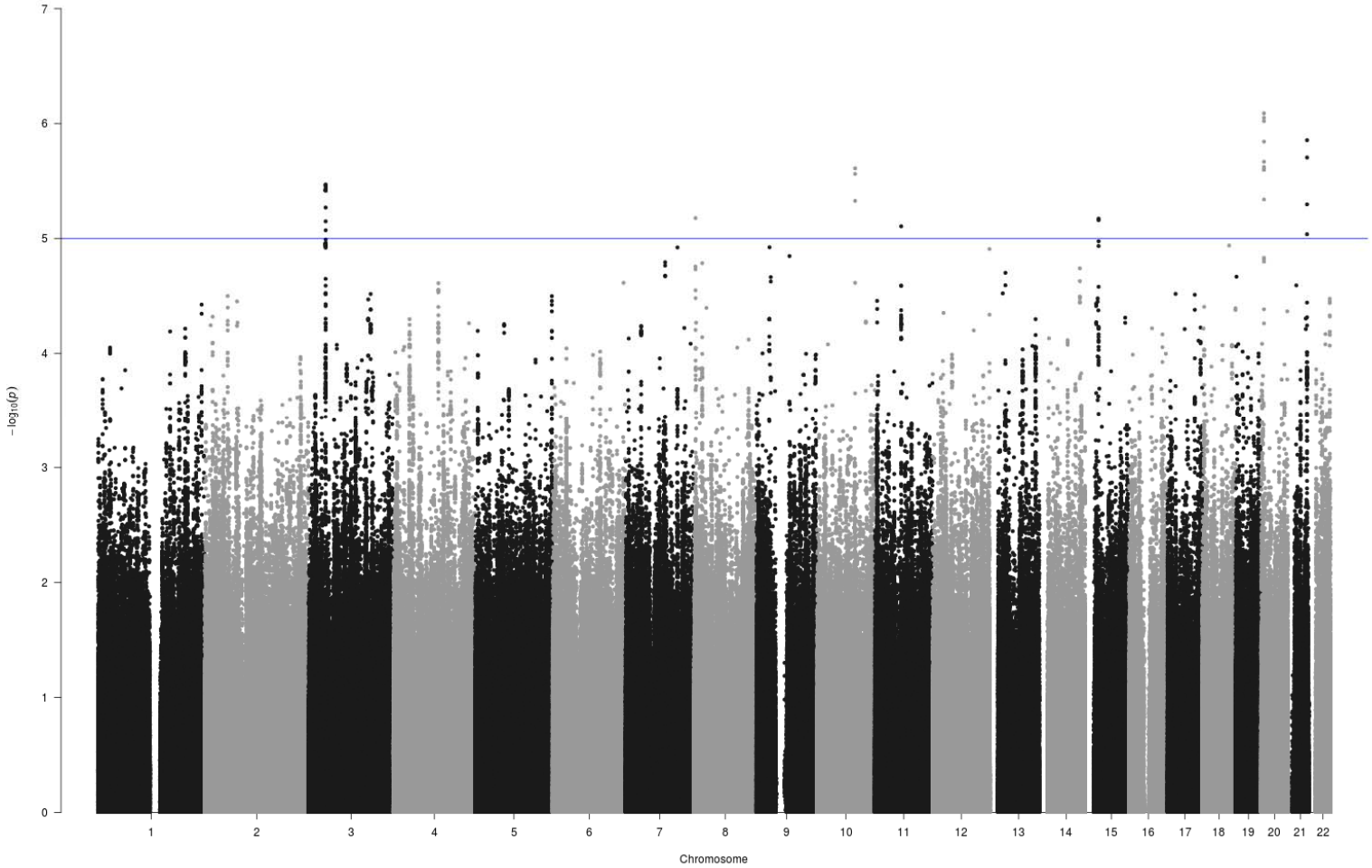
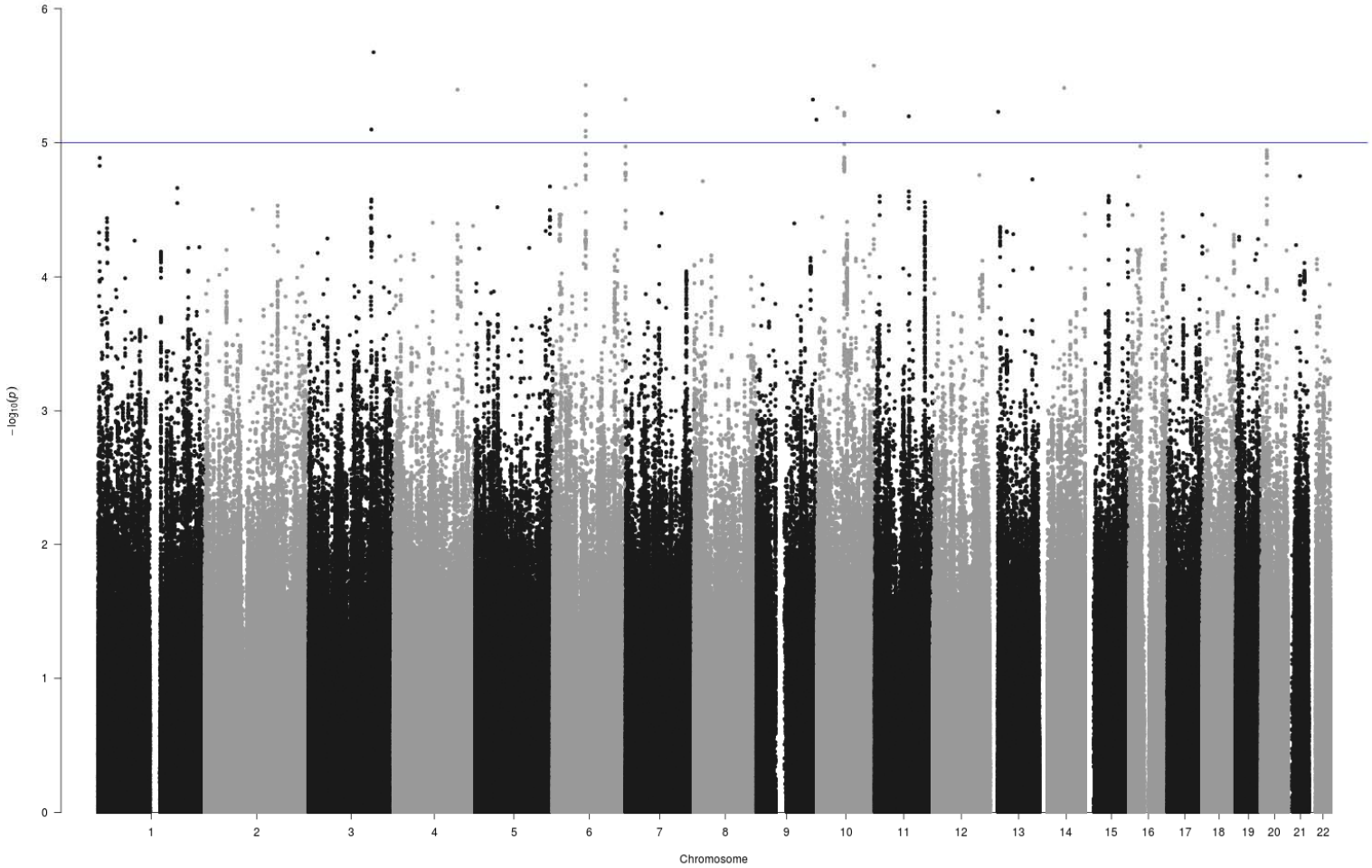


HBCS



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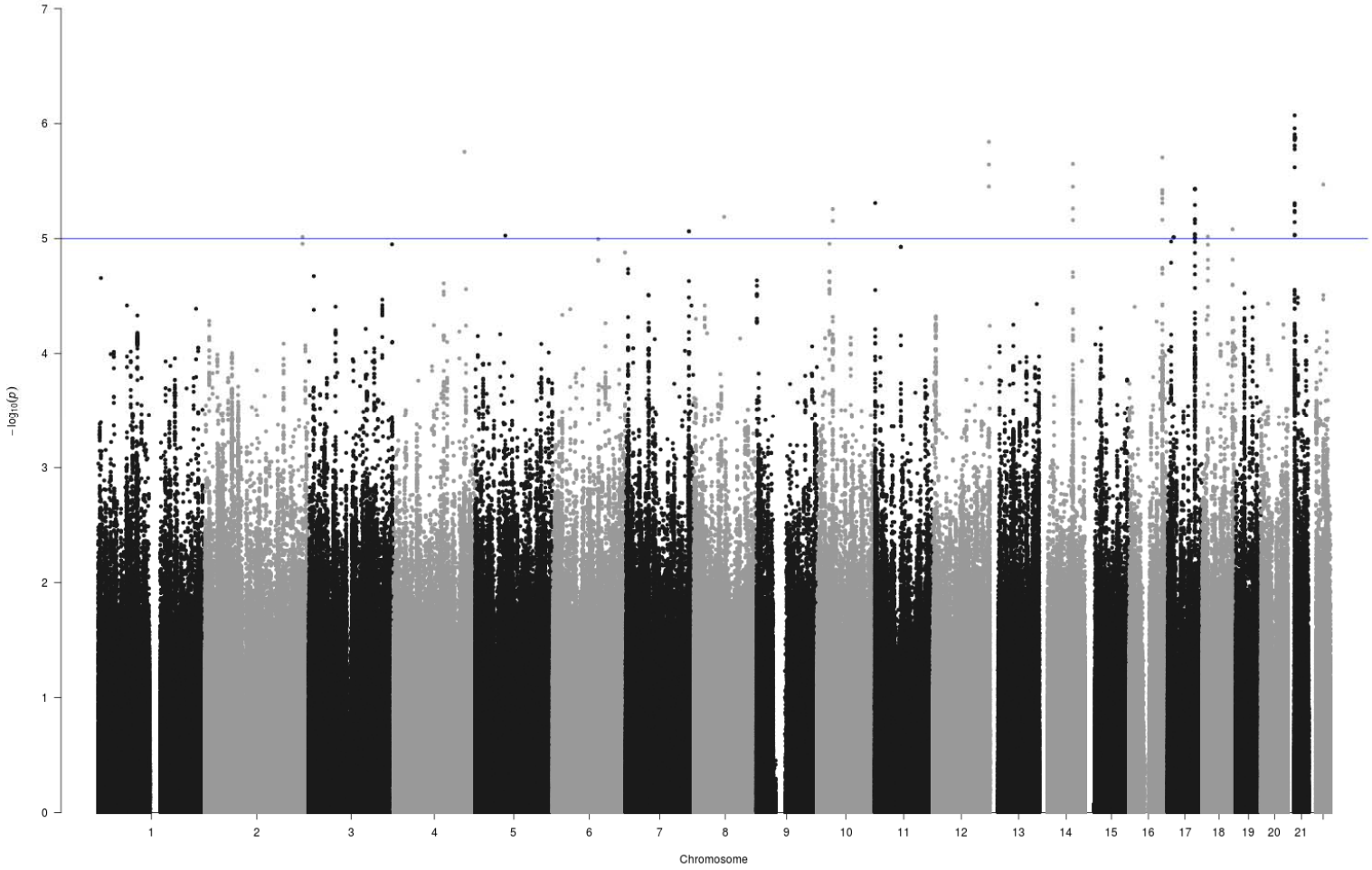

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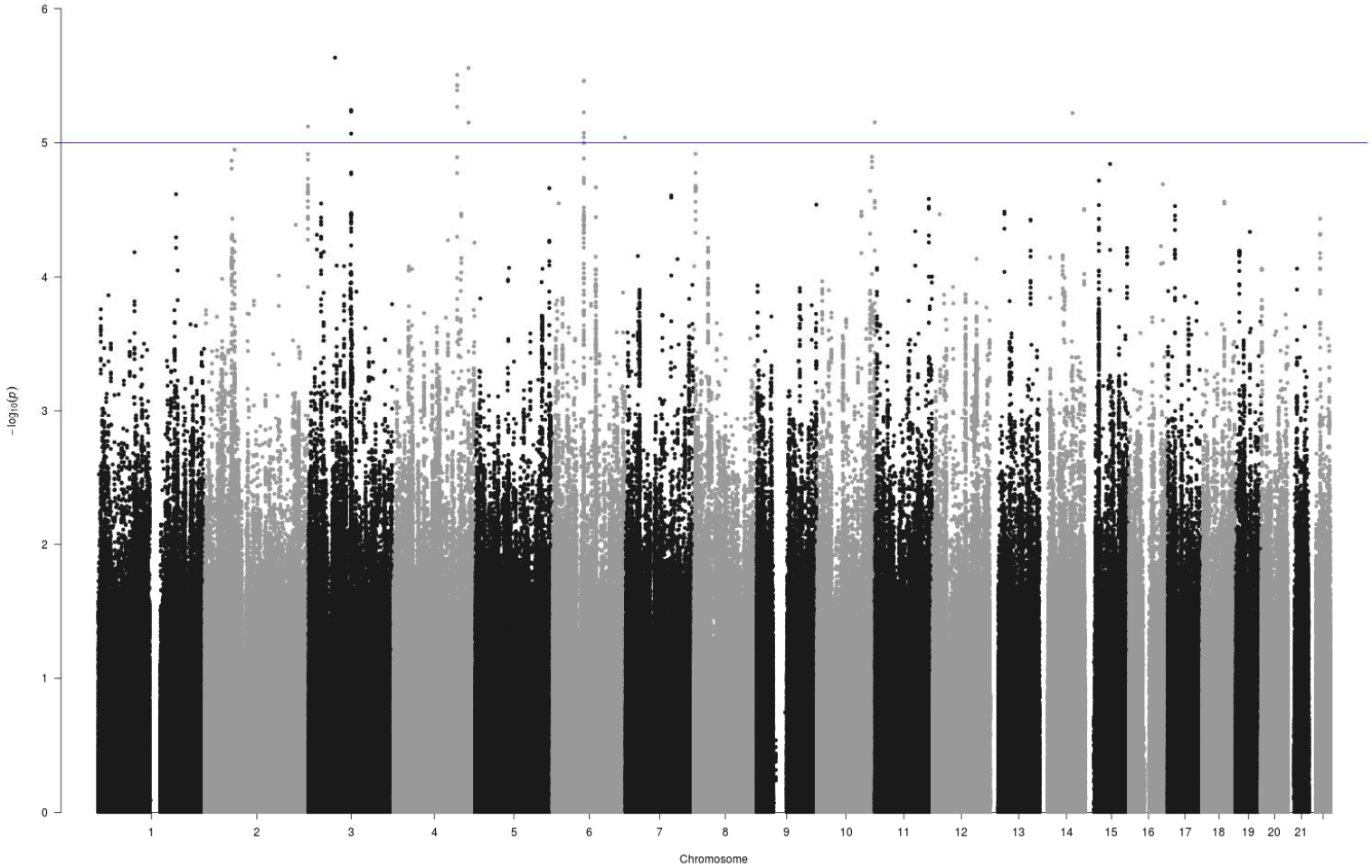

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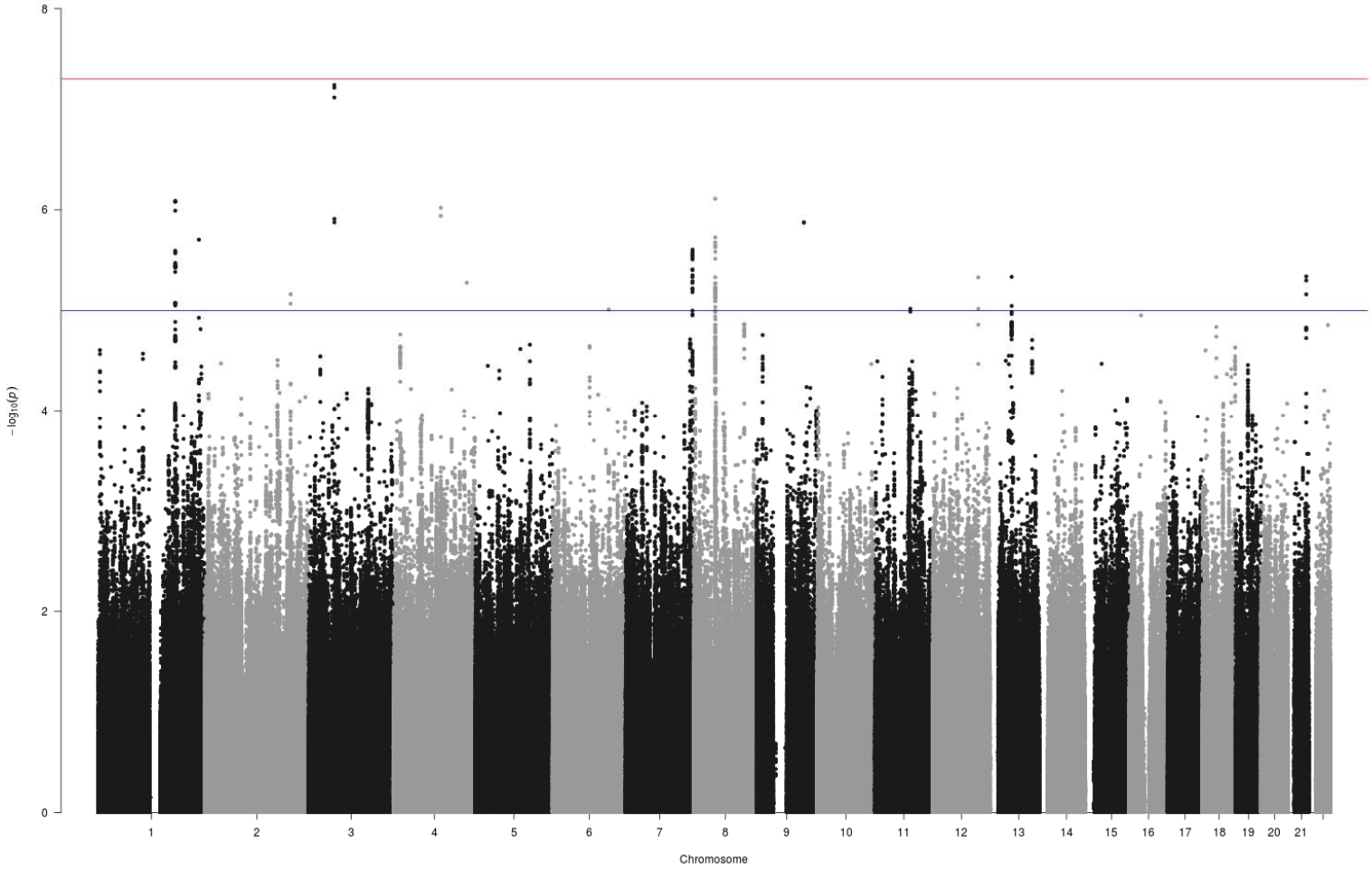

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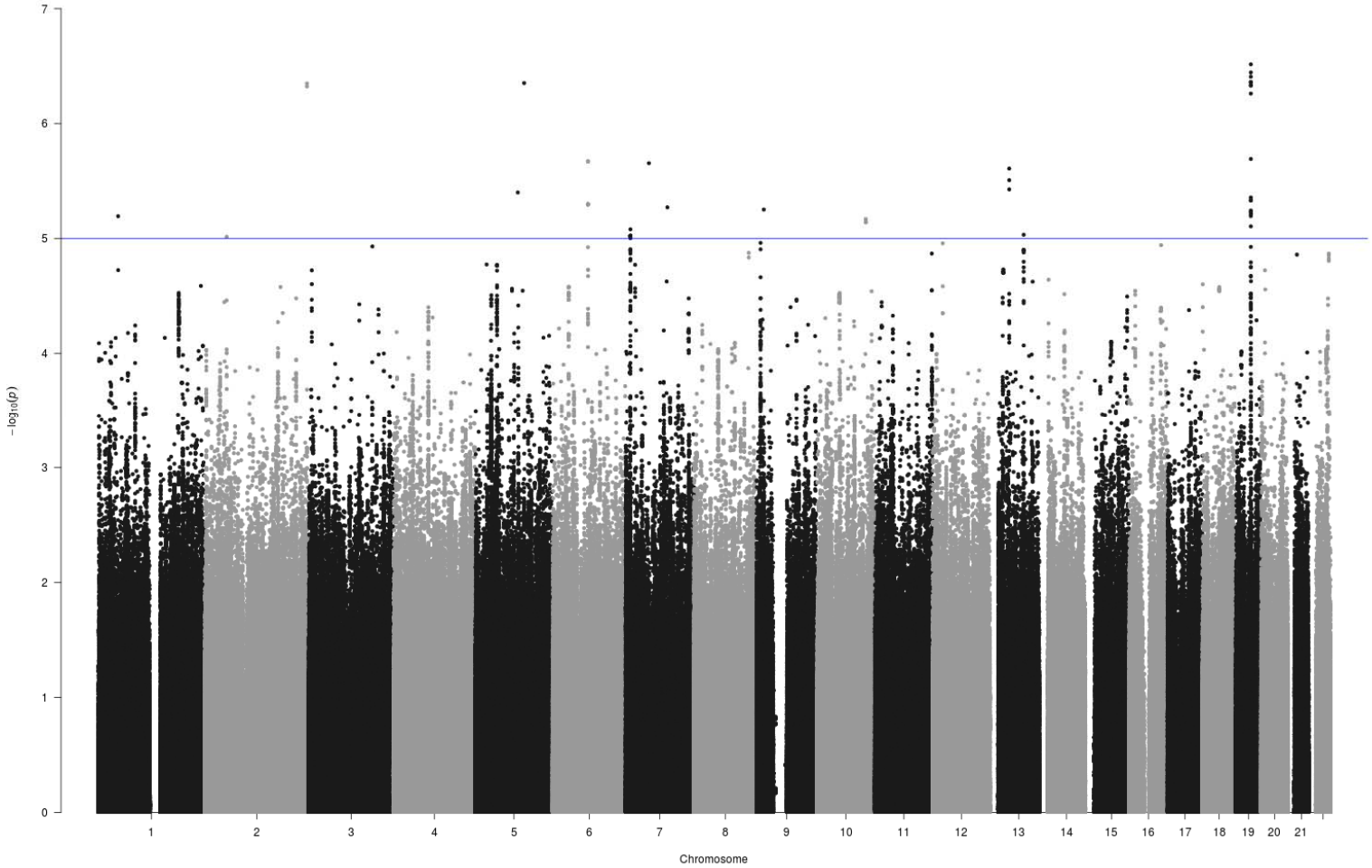

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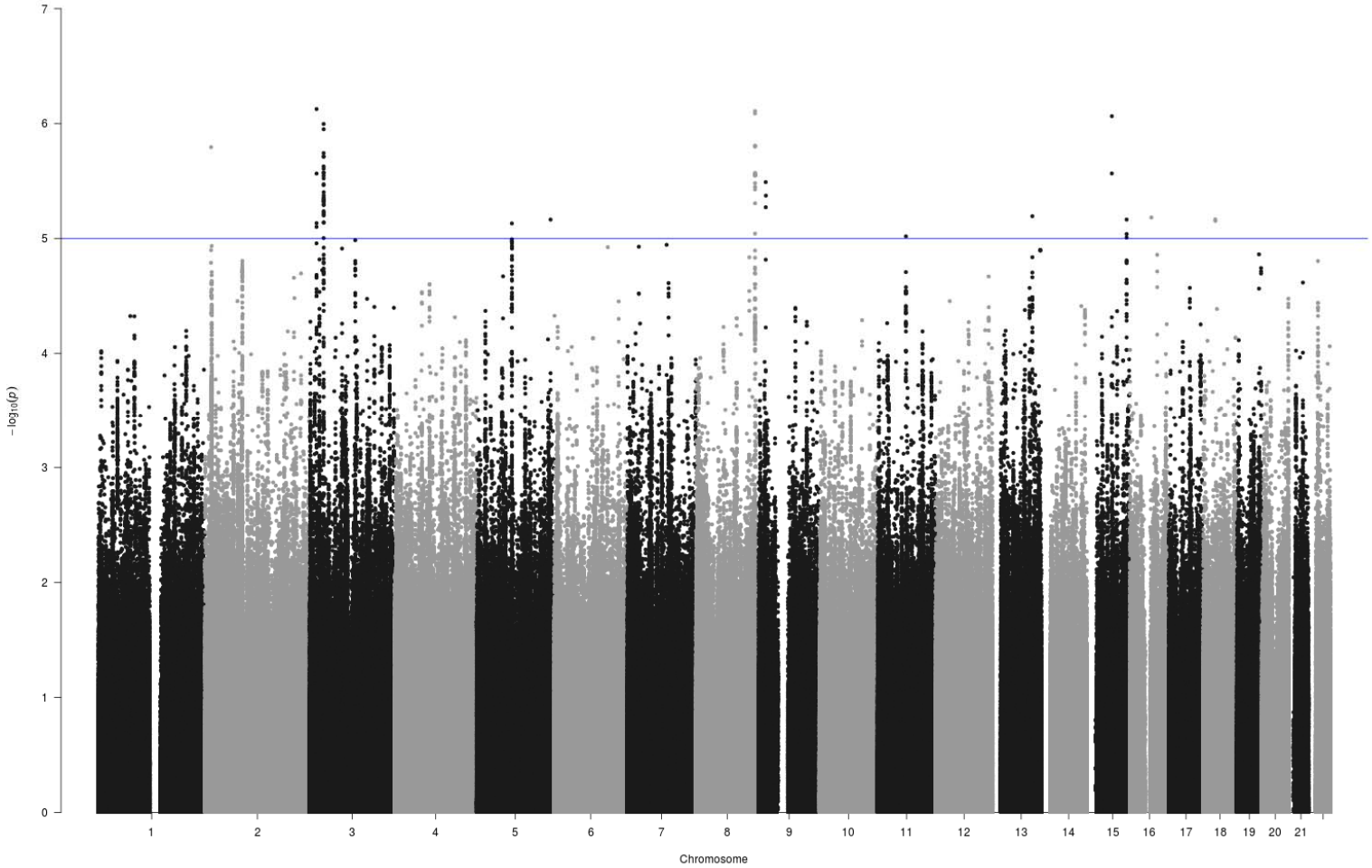

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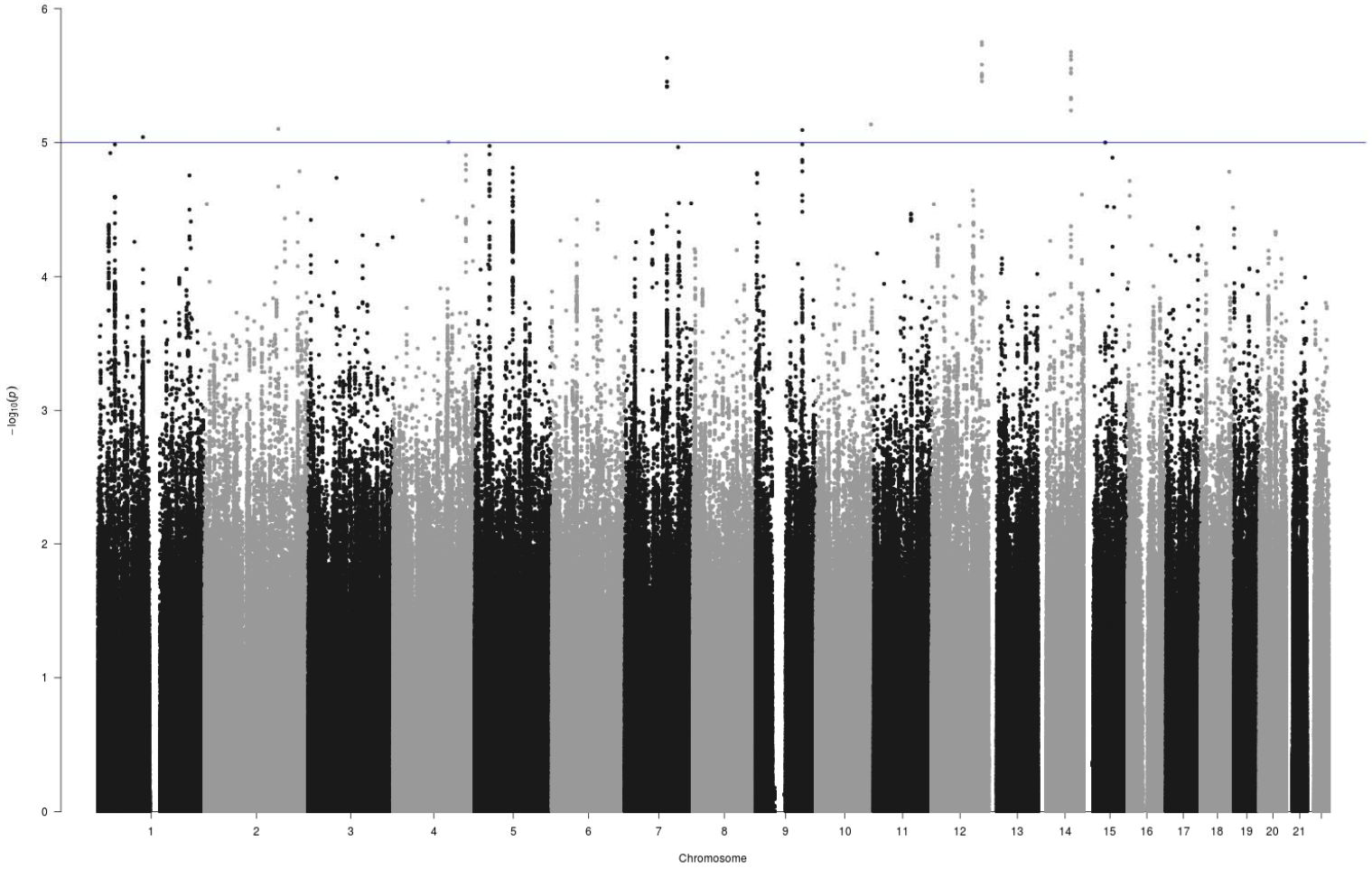

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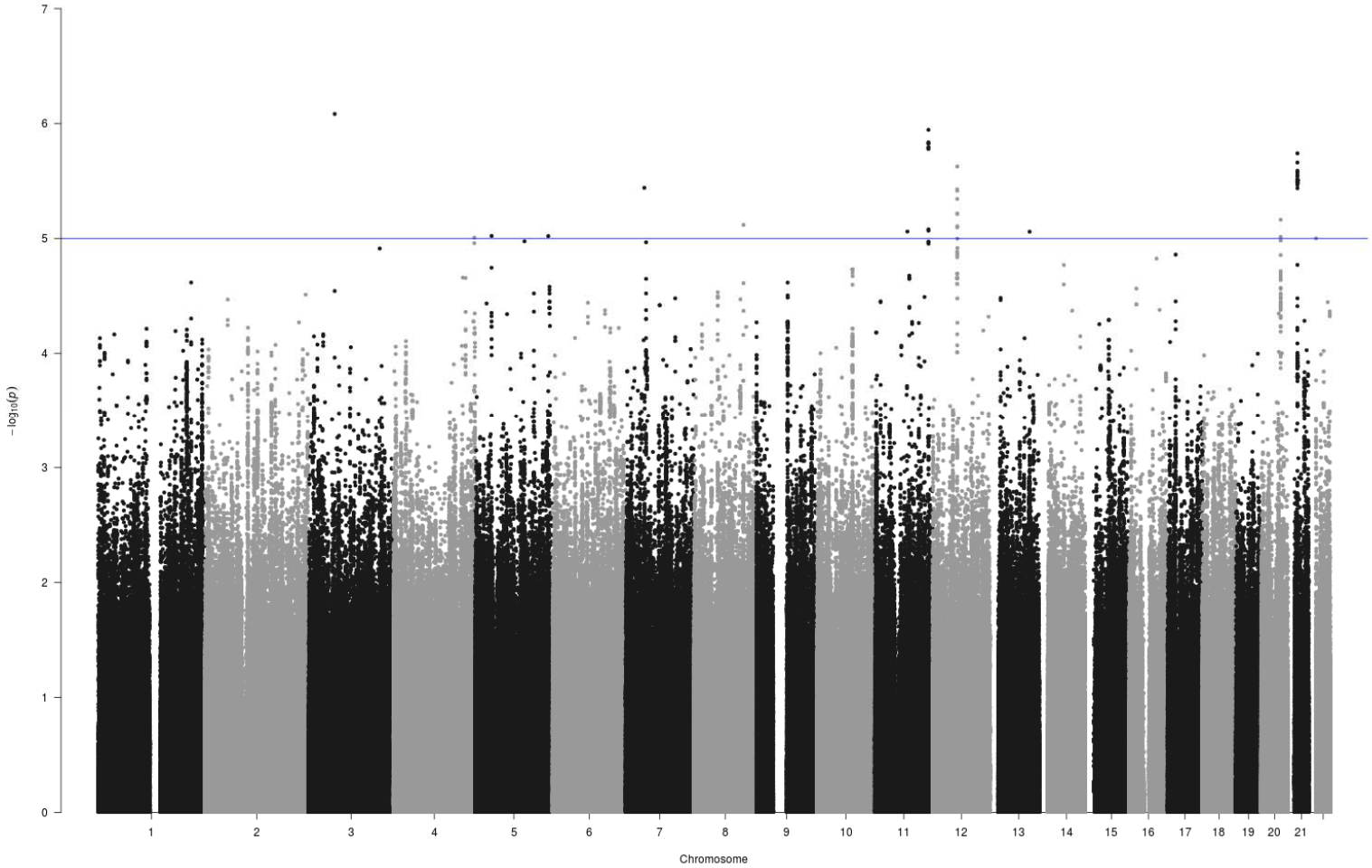

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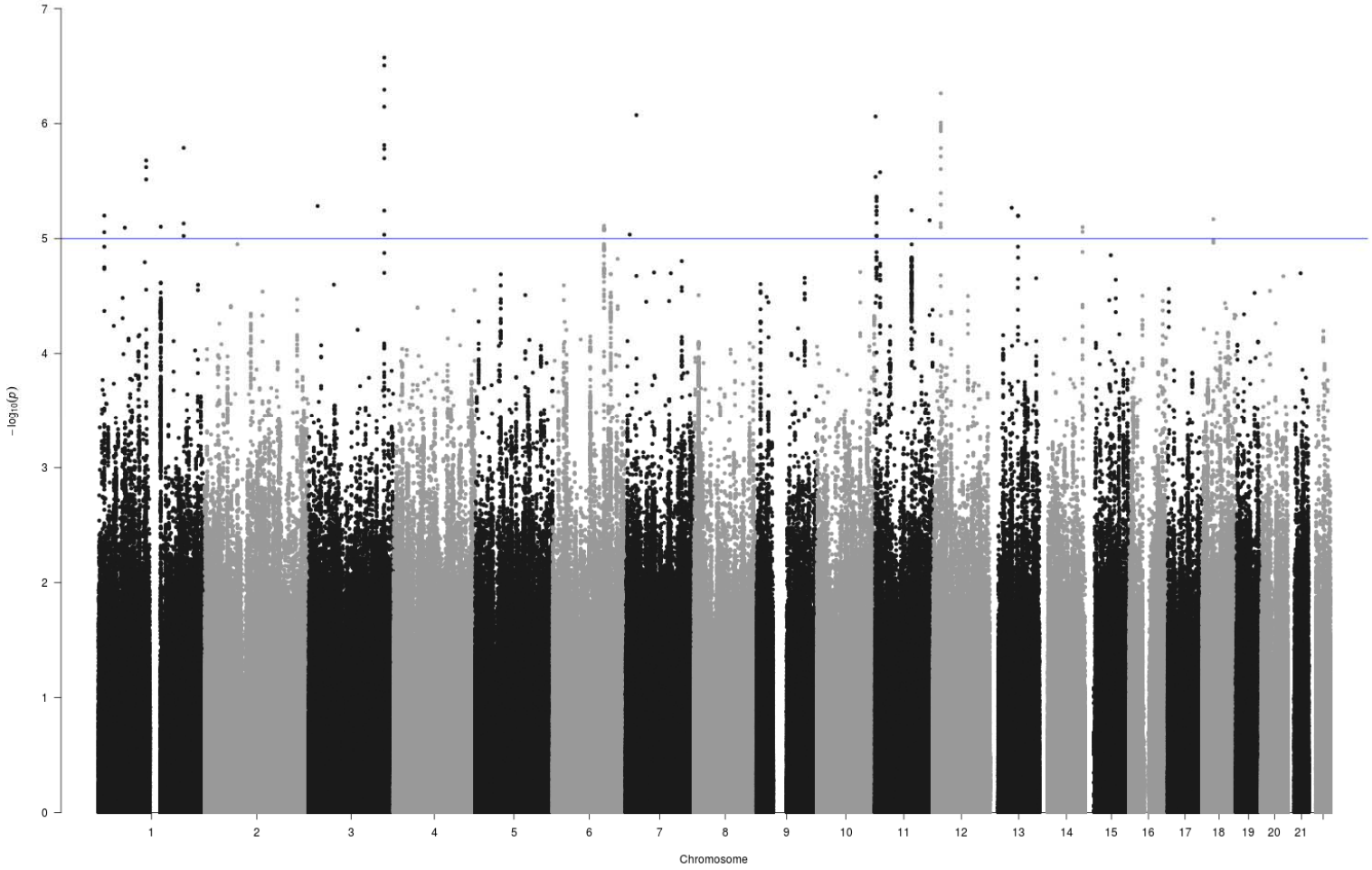

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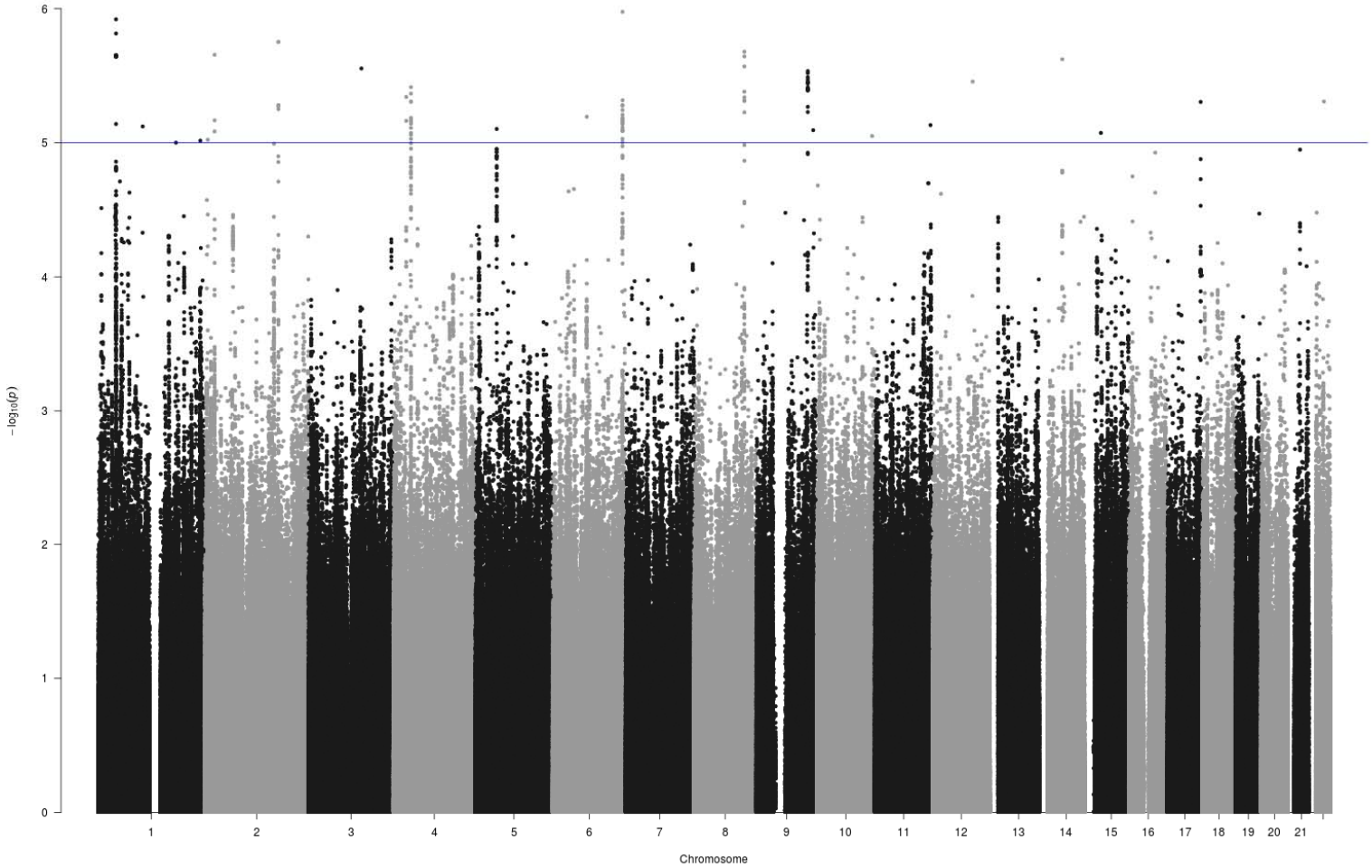

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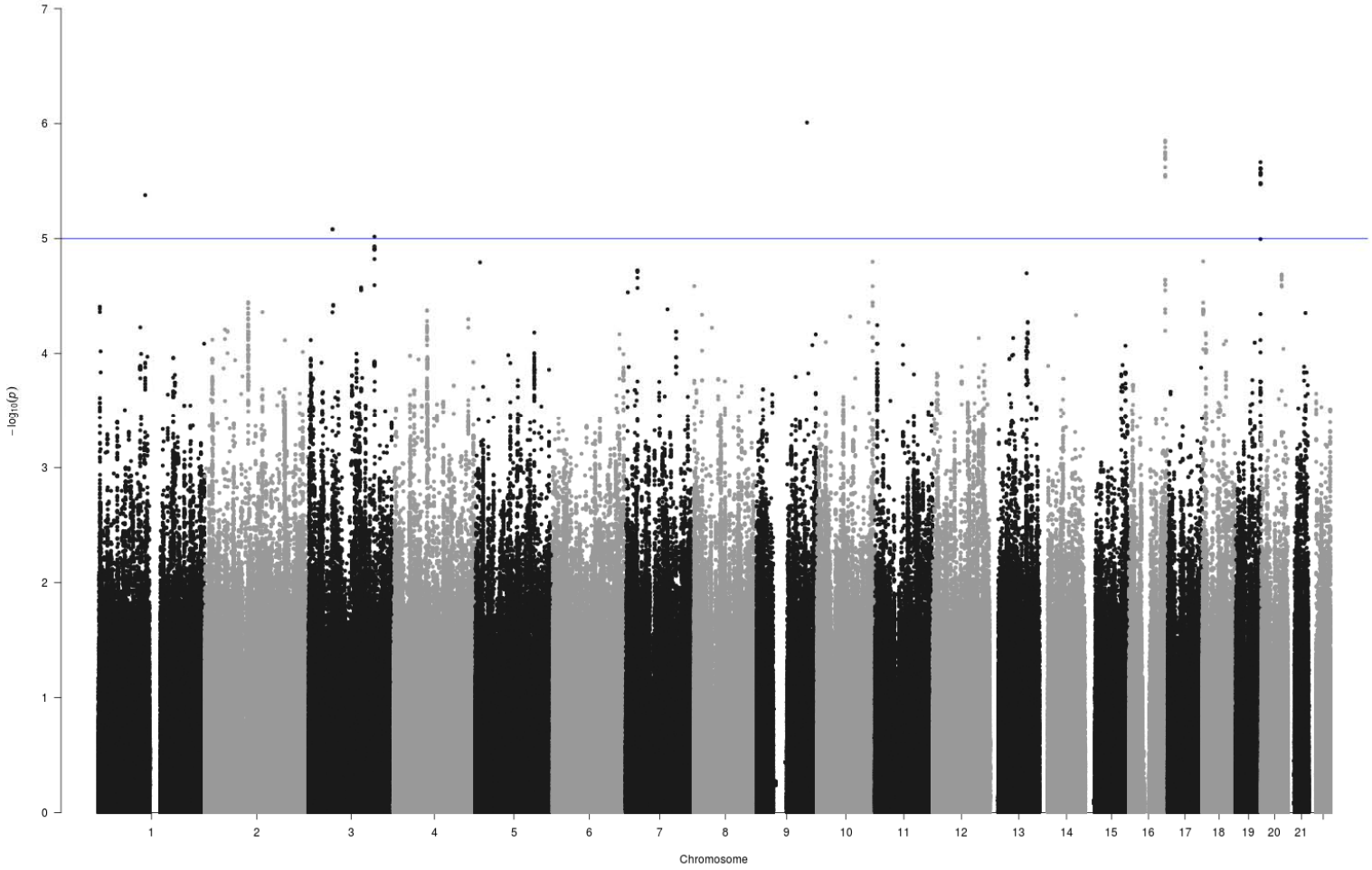

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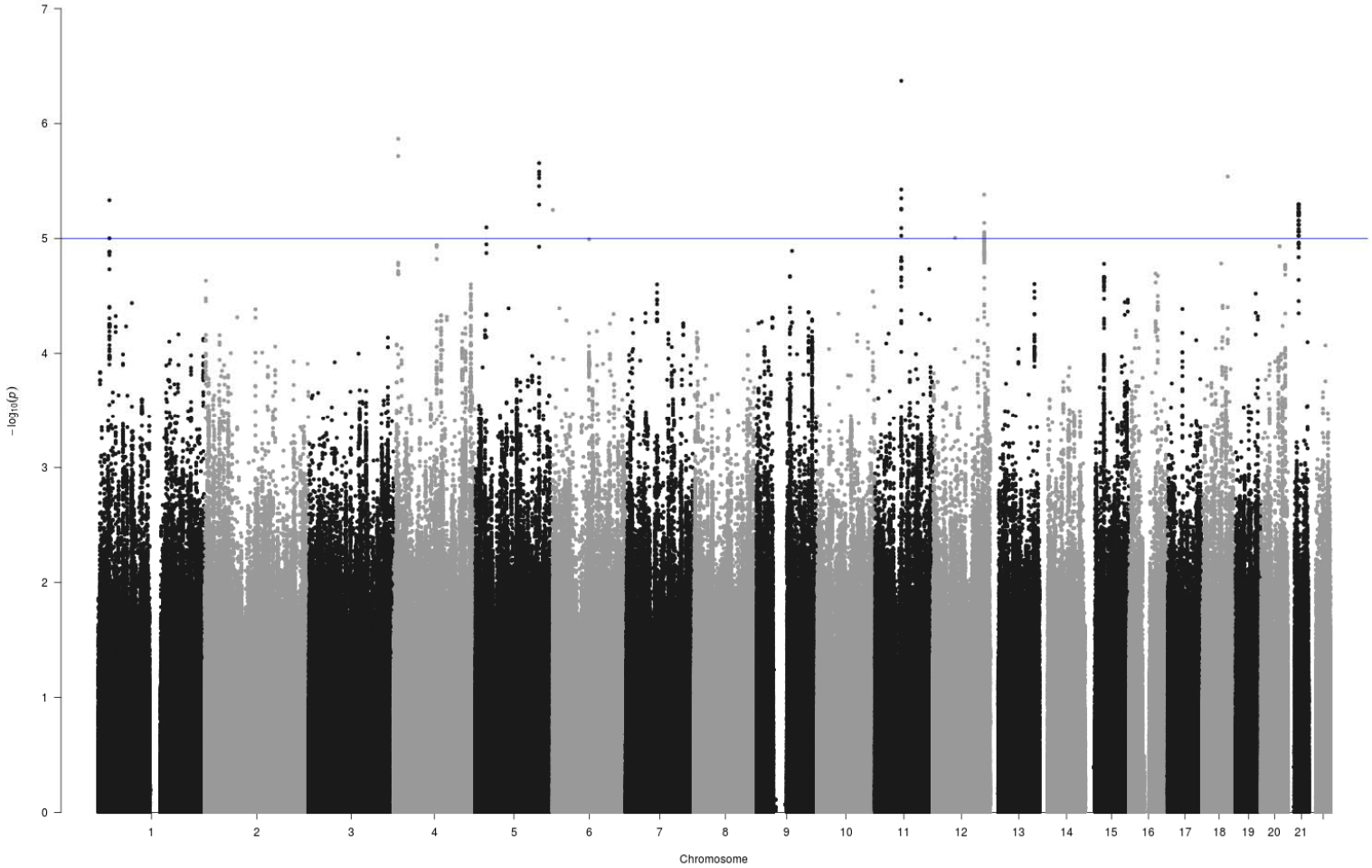

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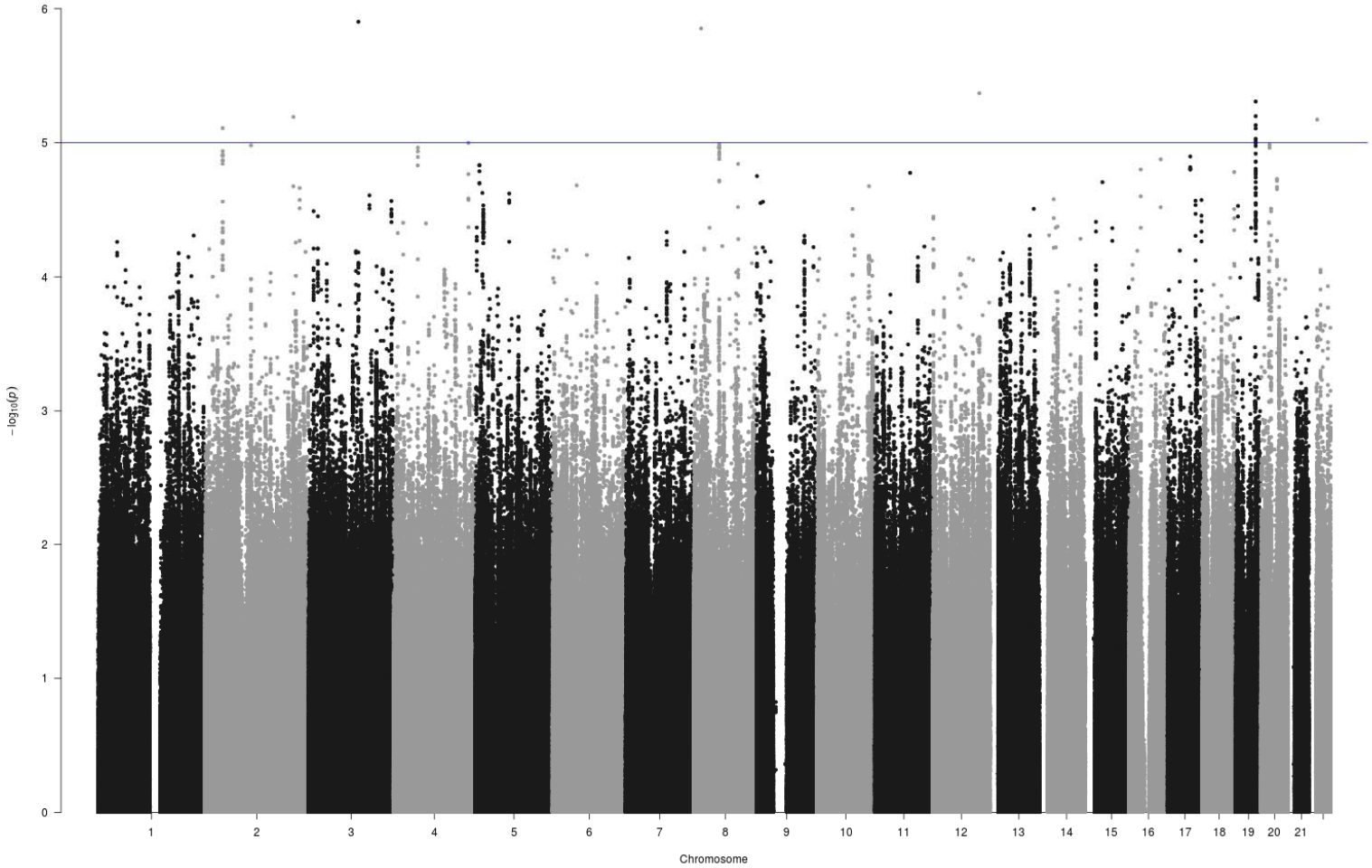

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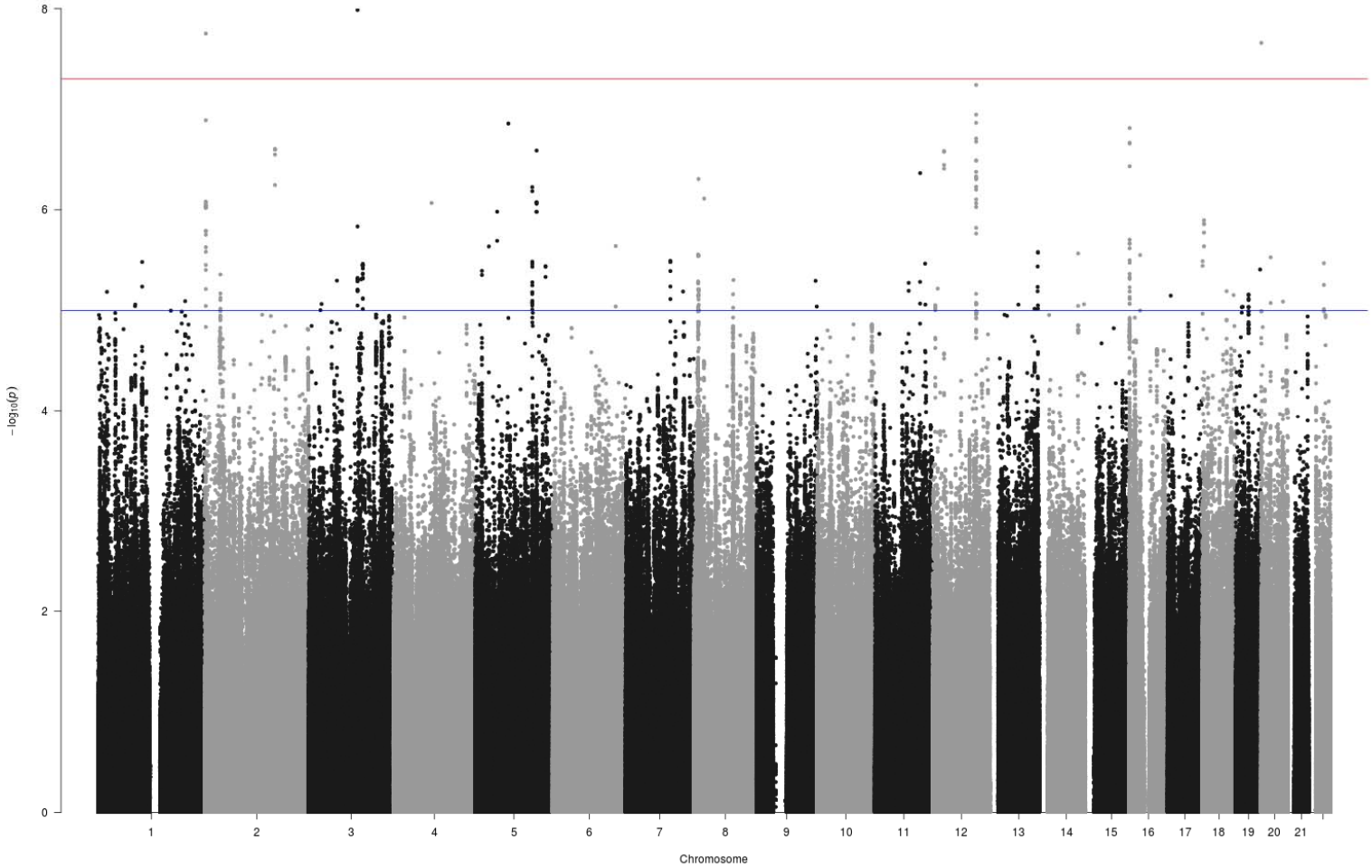

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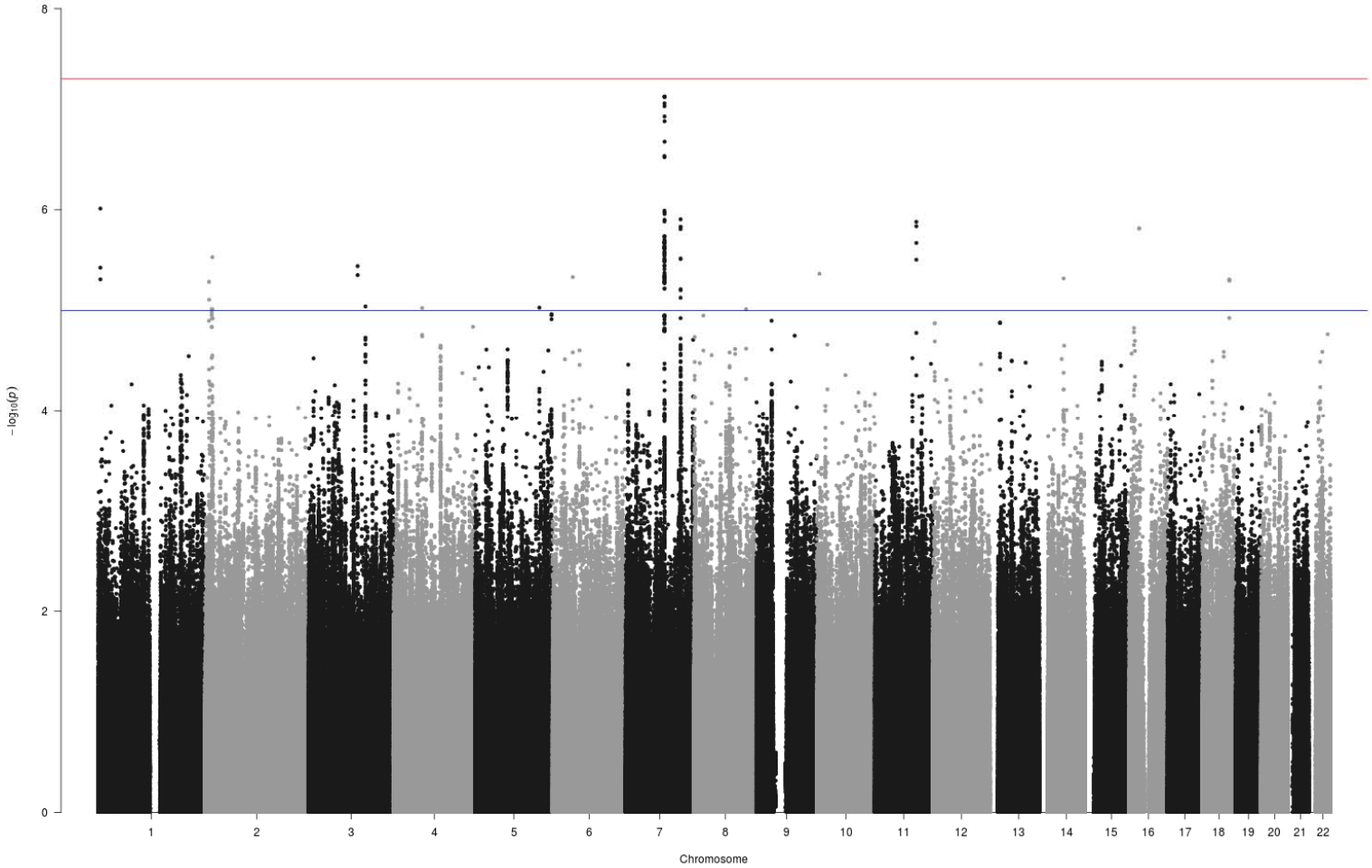

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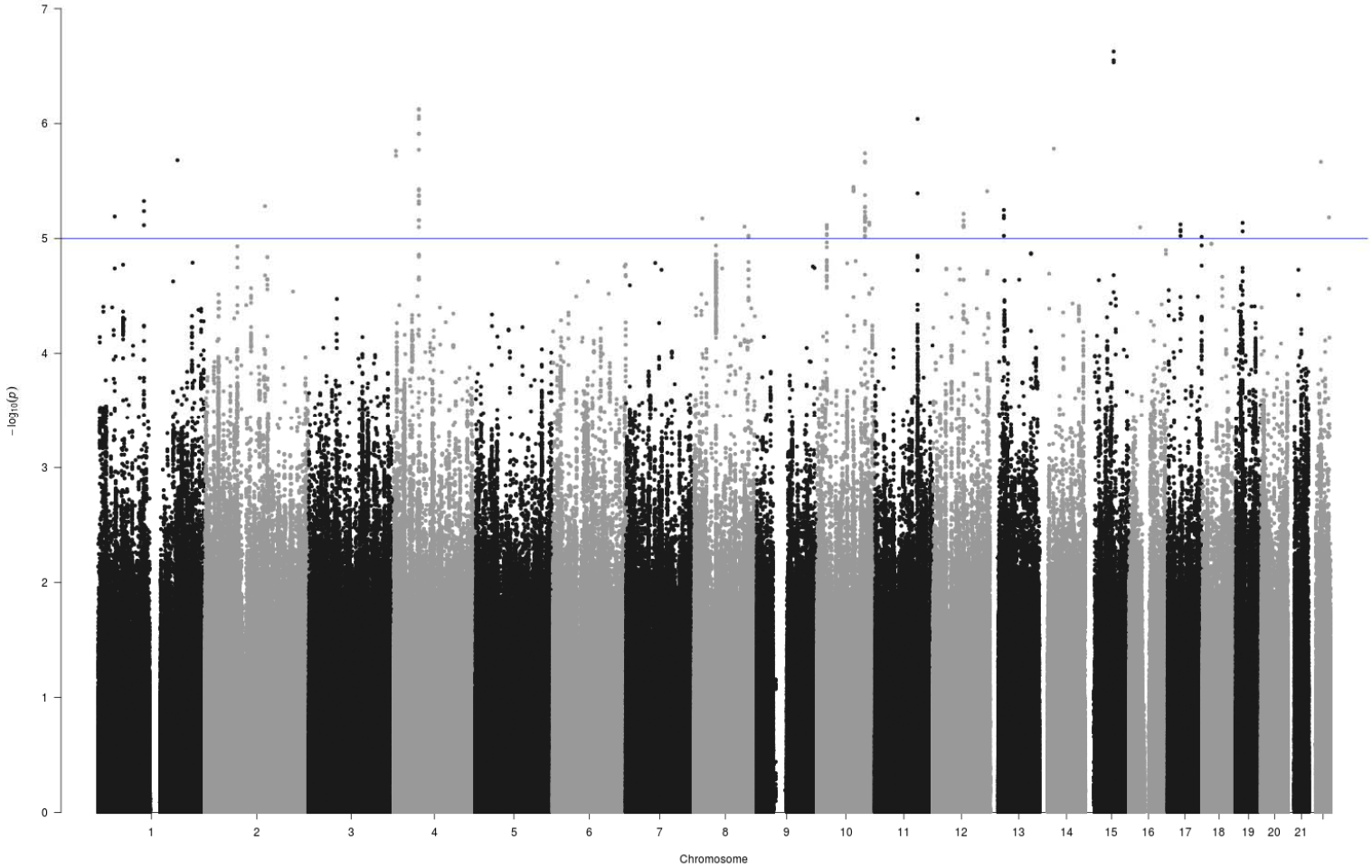

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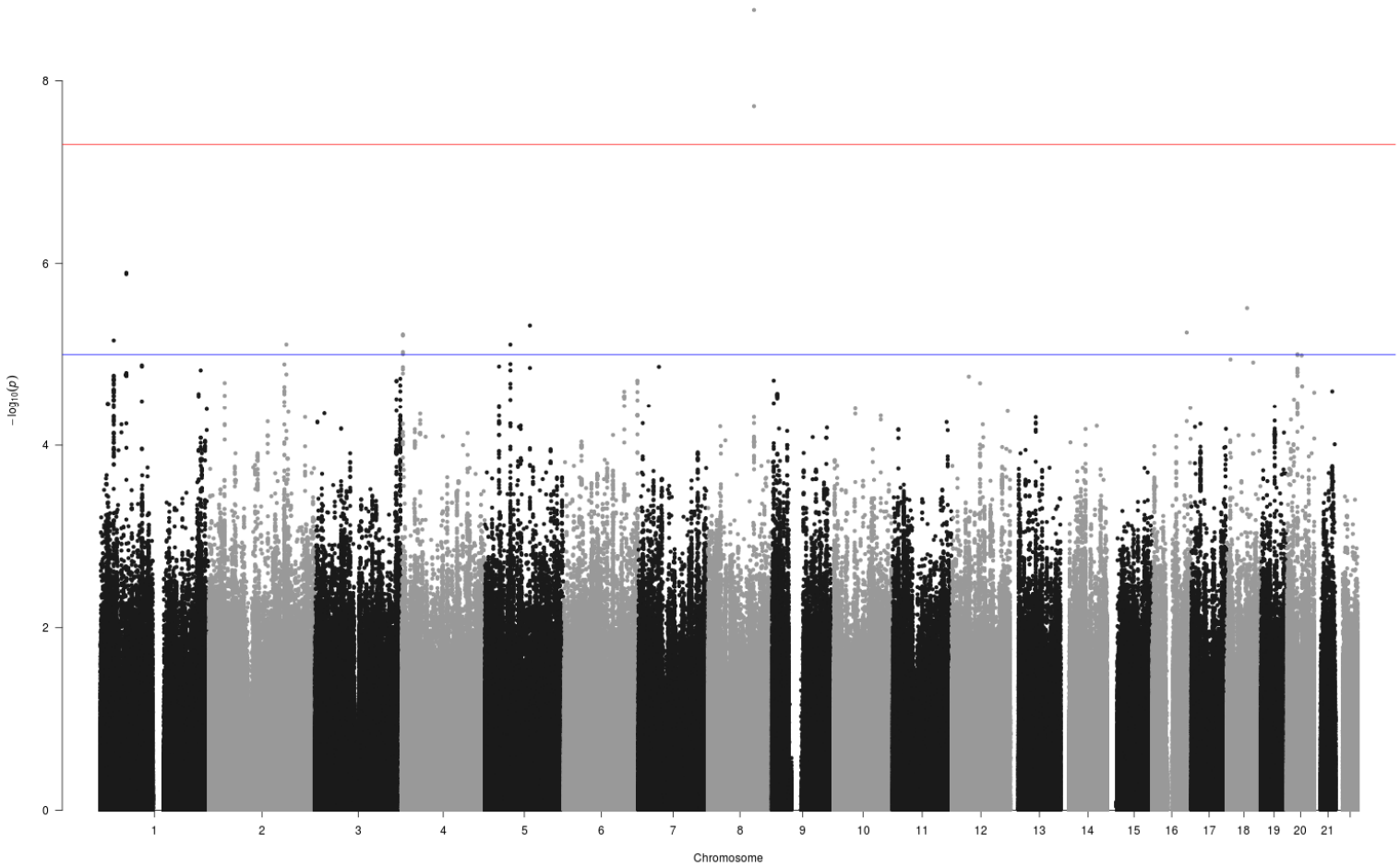

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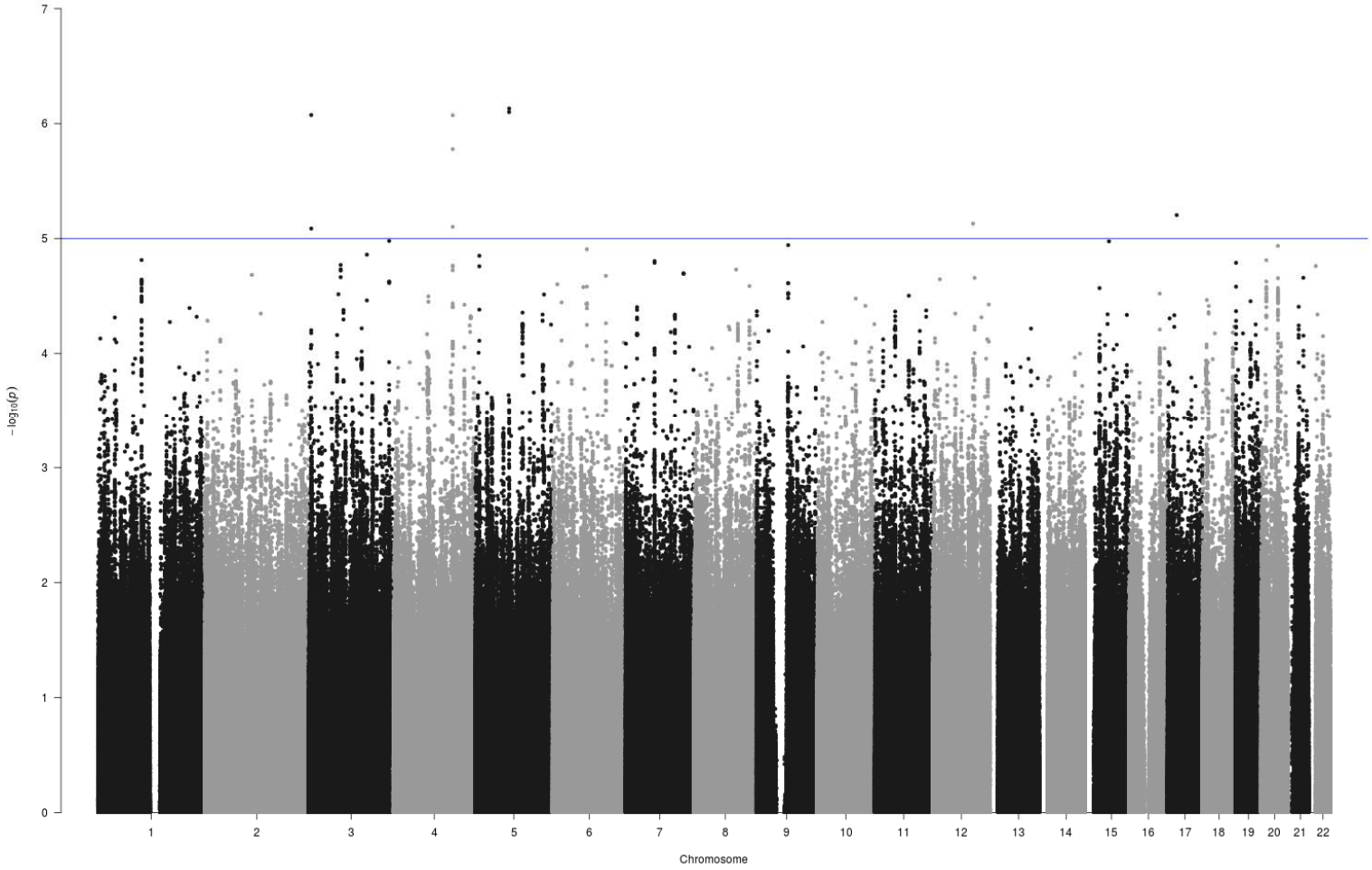

eFigure 2. Quantile-Quantile plots for neuroticism results in each cohort participating in the Genetics of Personality Consortium

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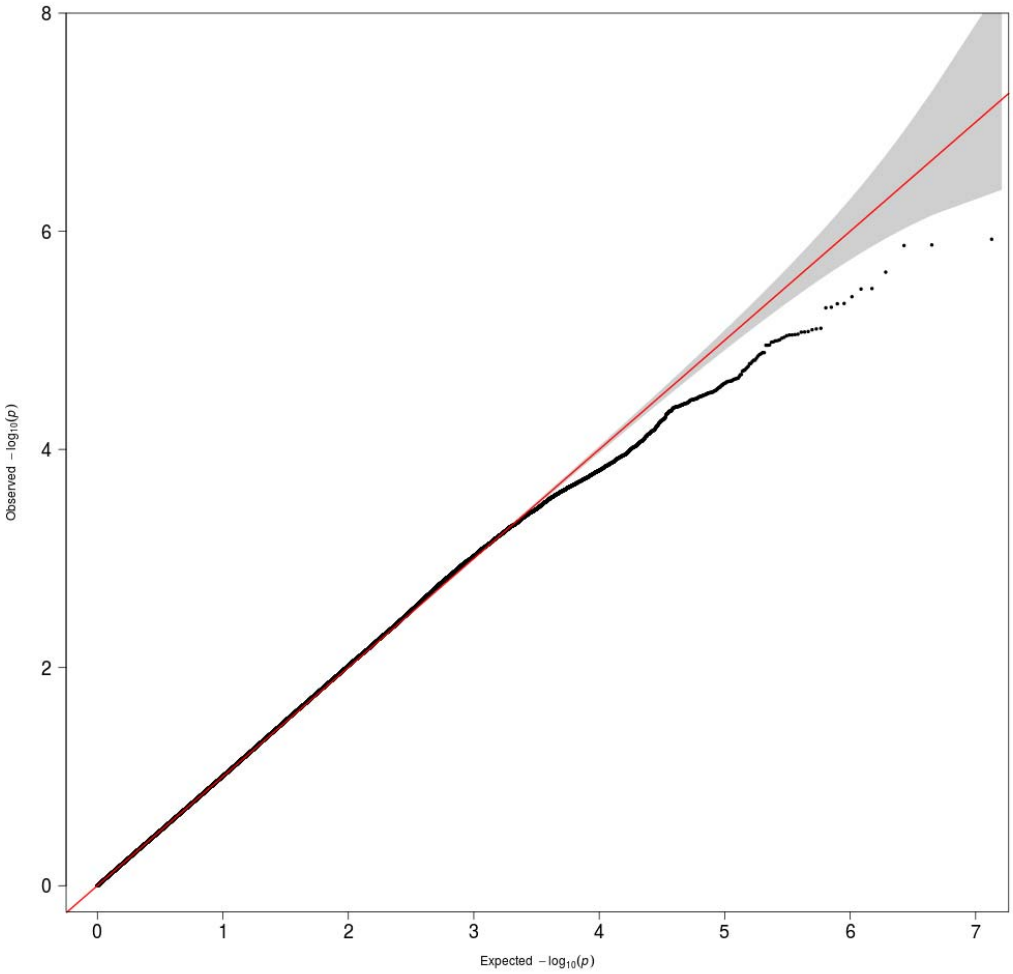

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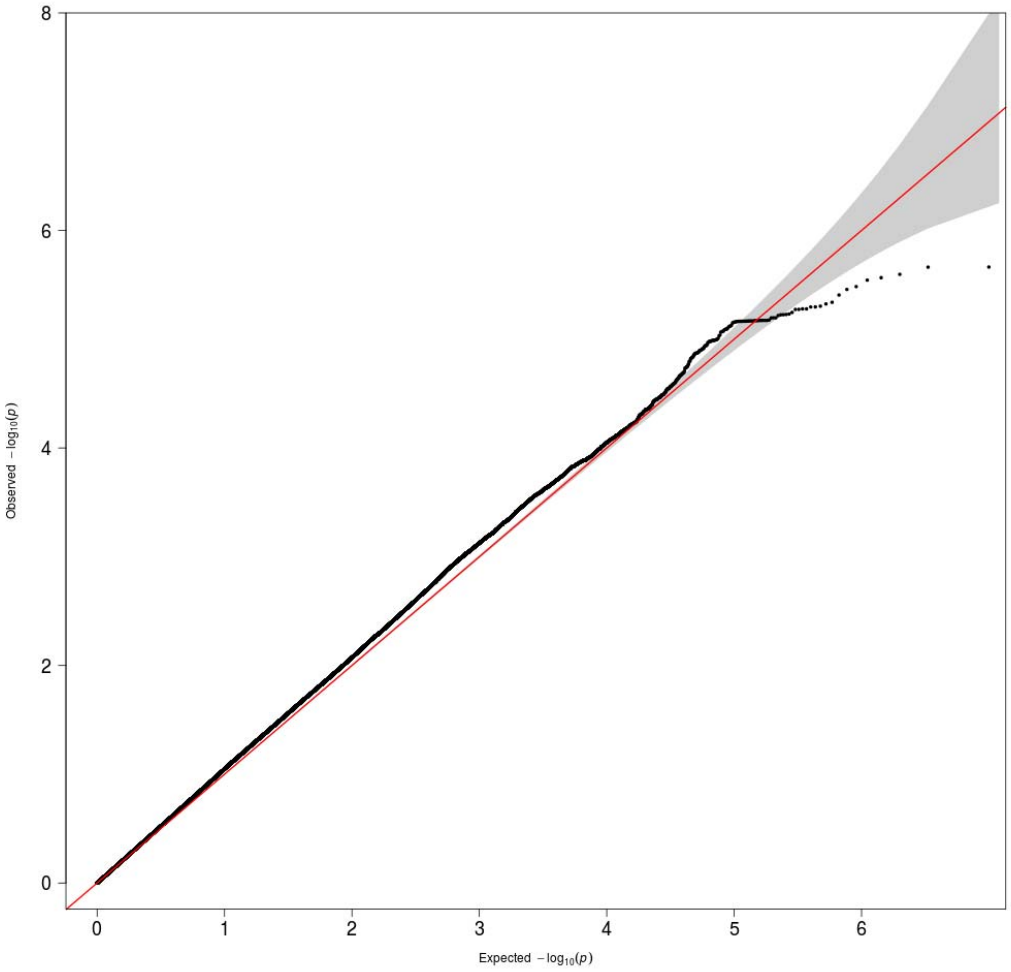

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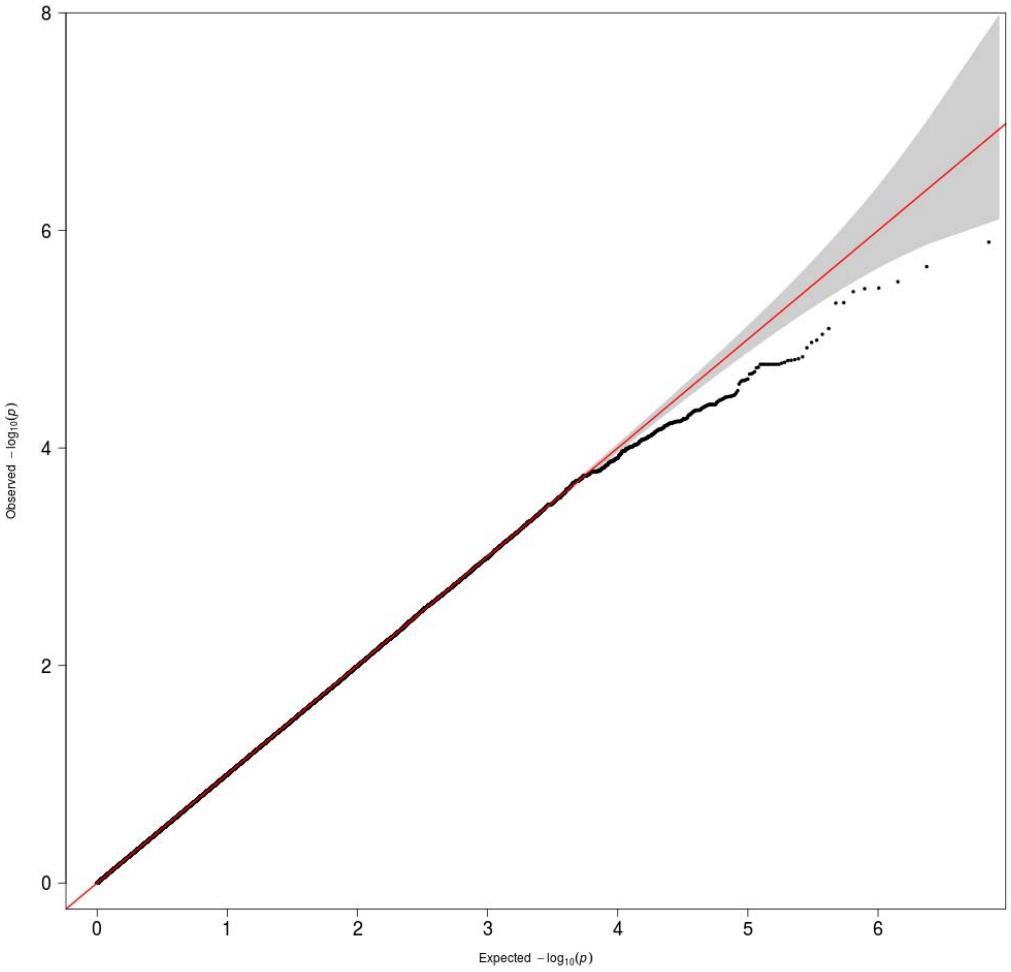

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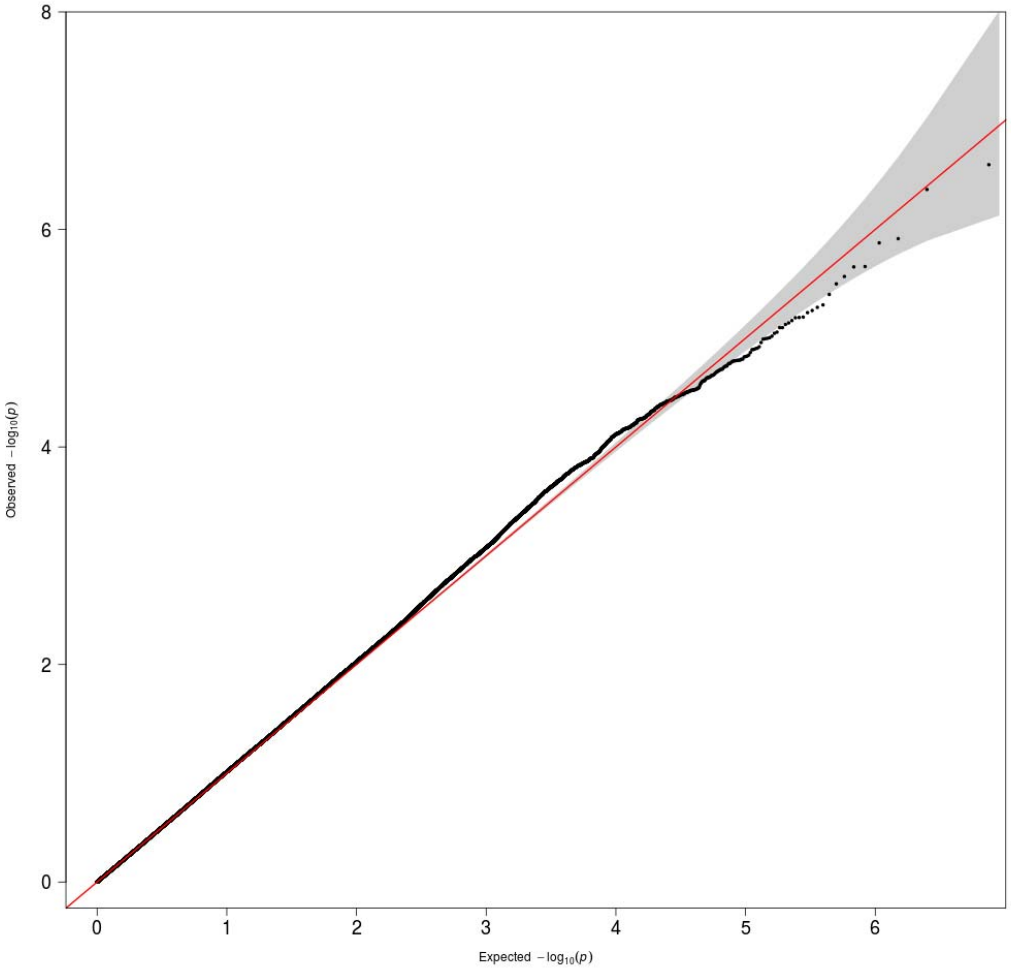

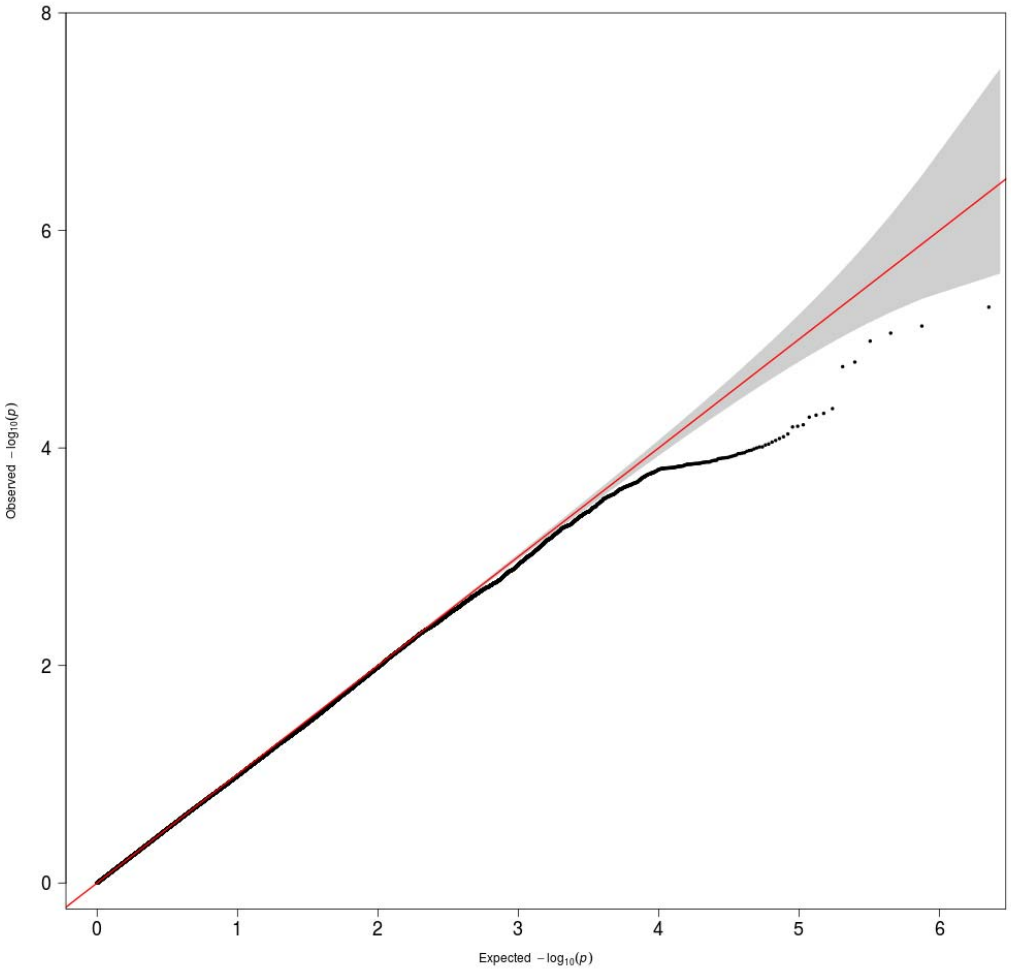

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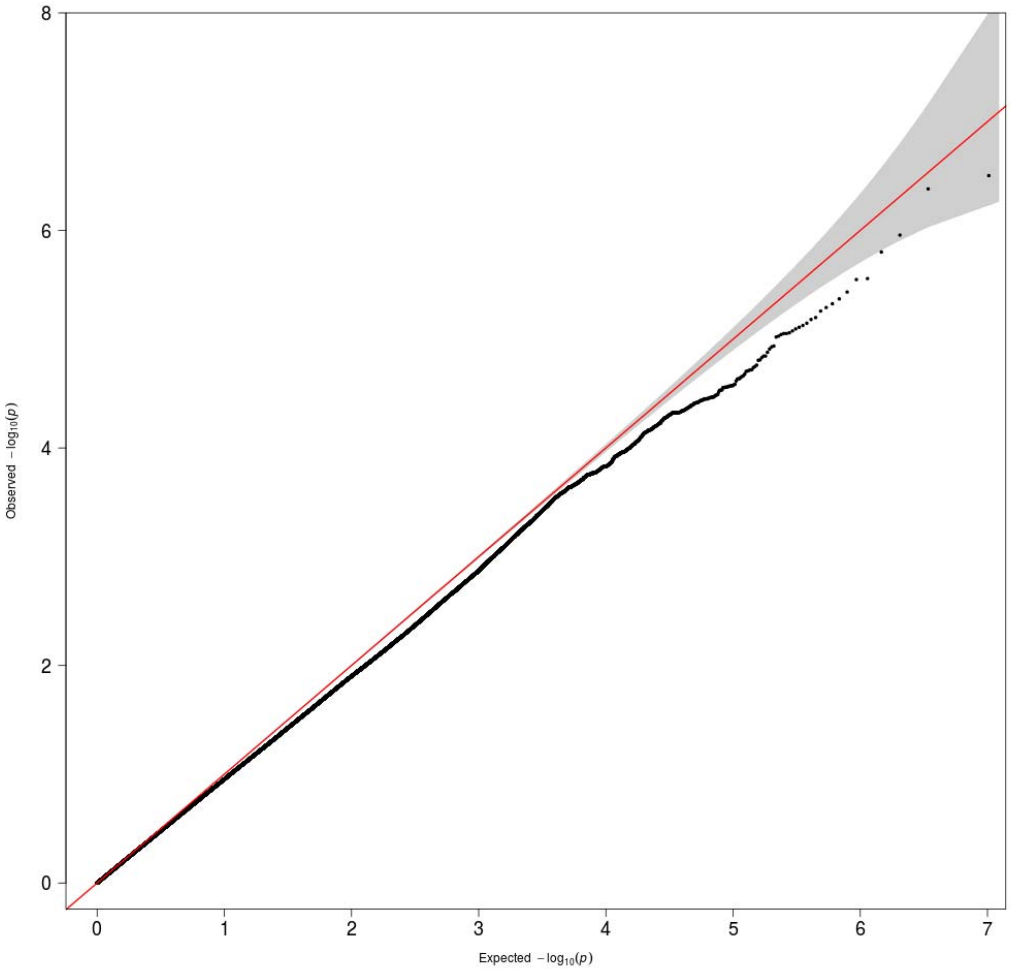

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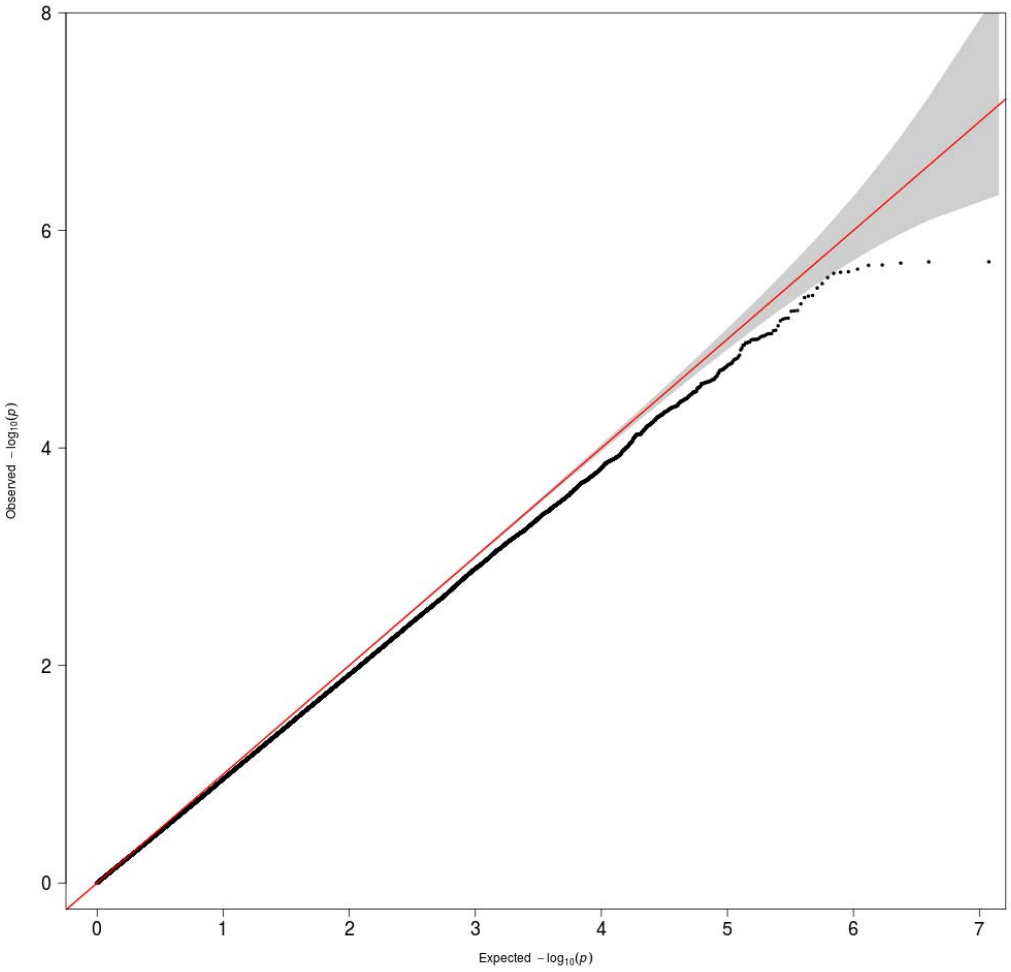

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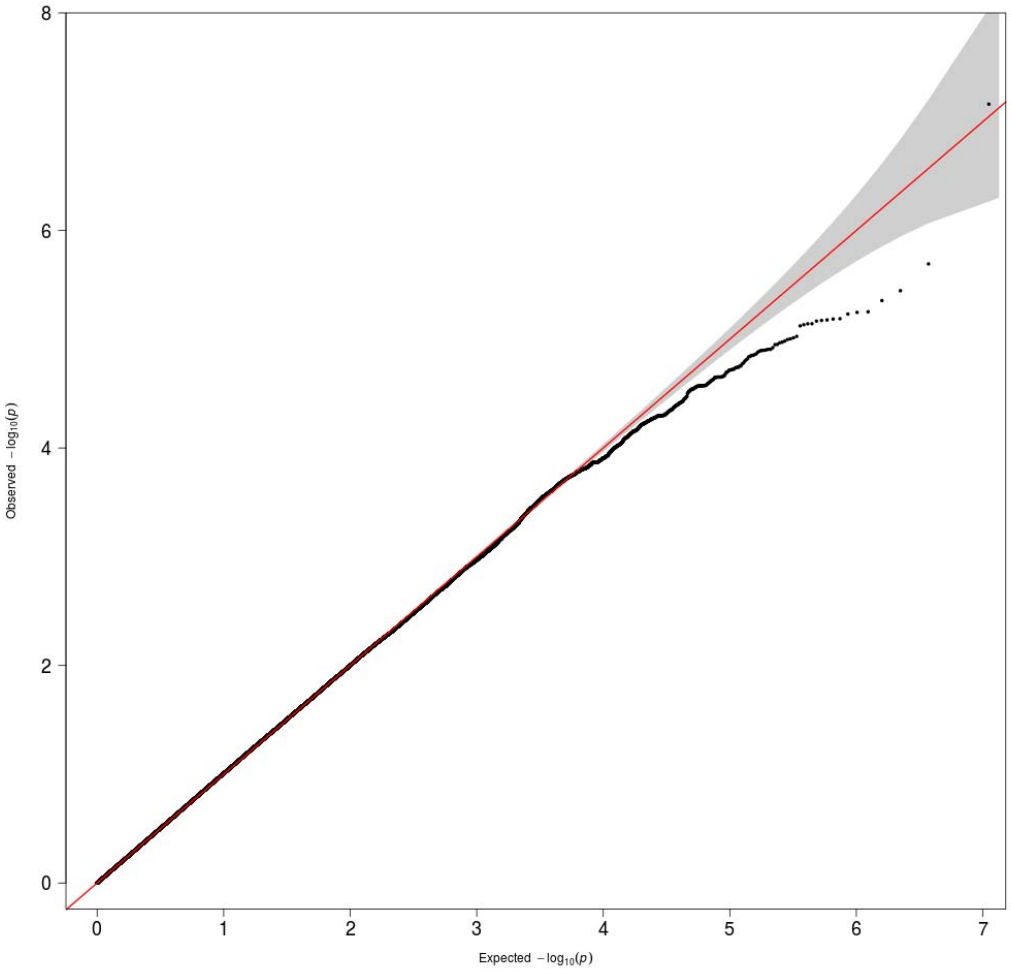

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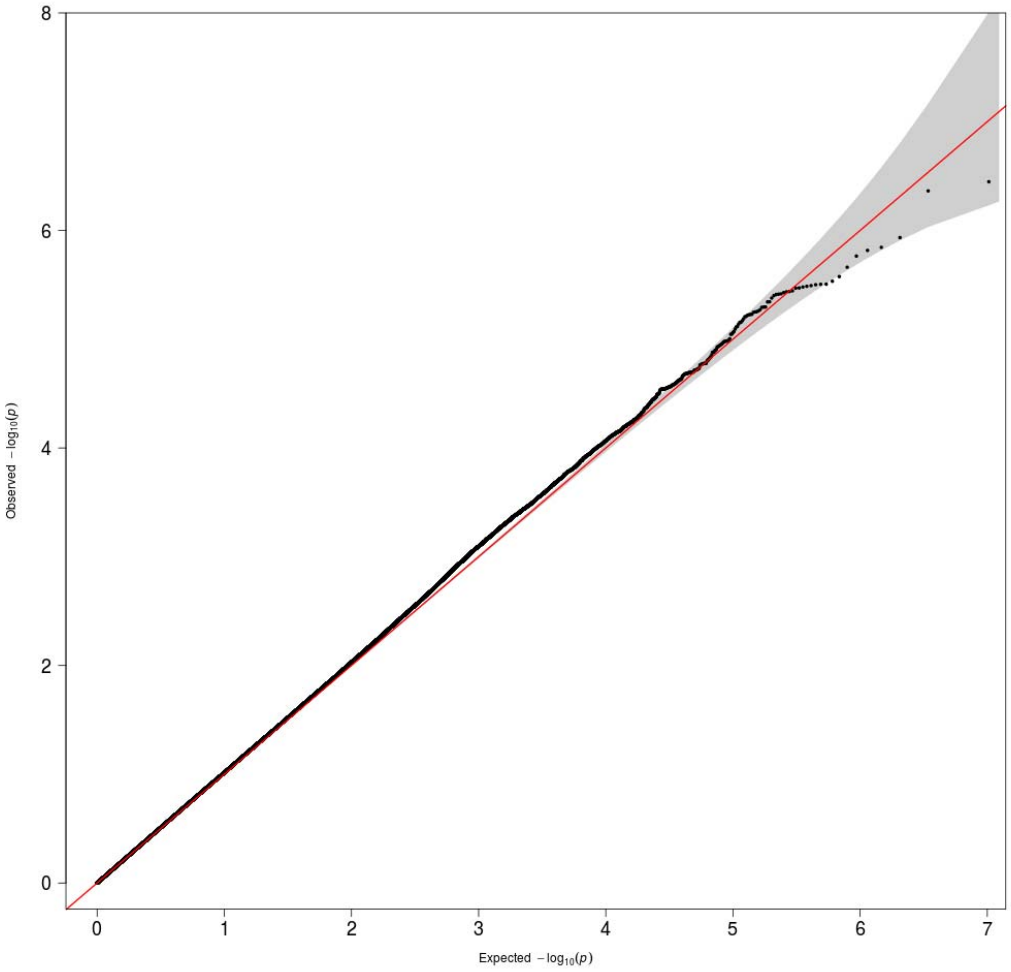

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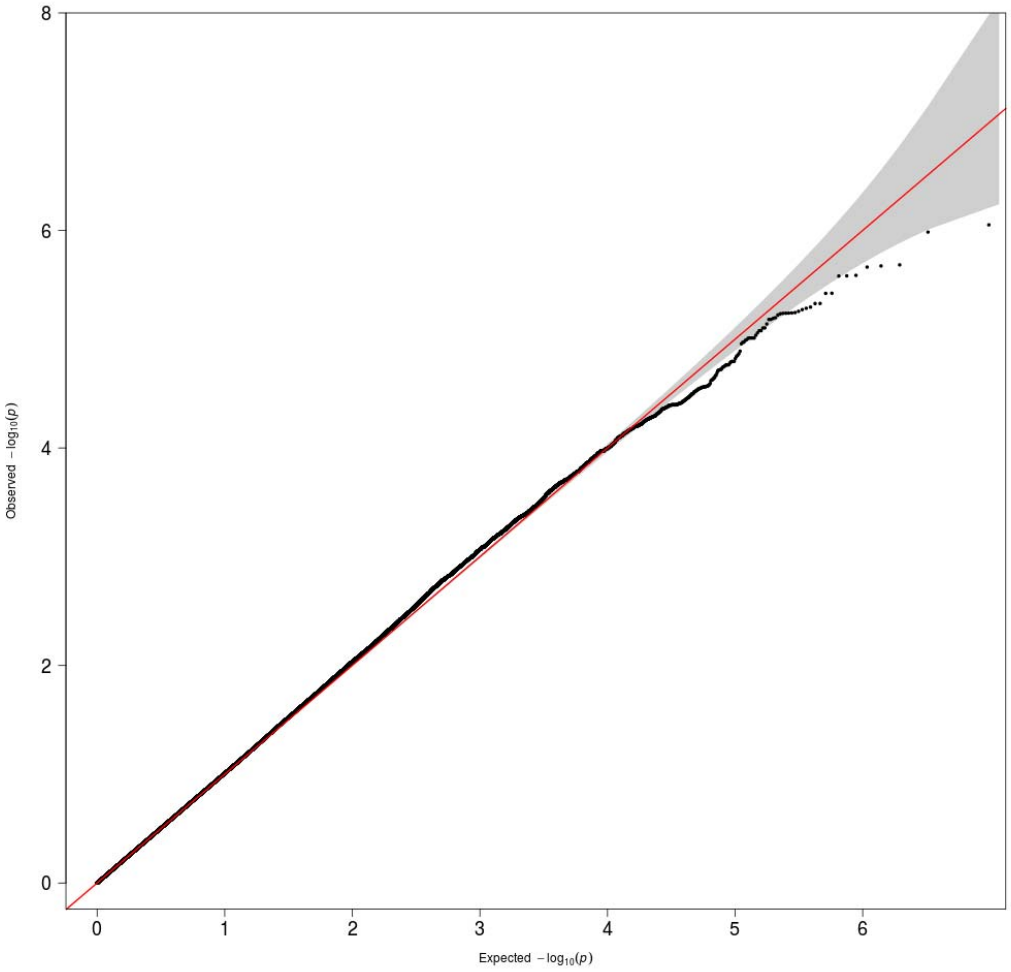

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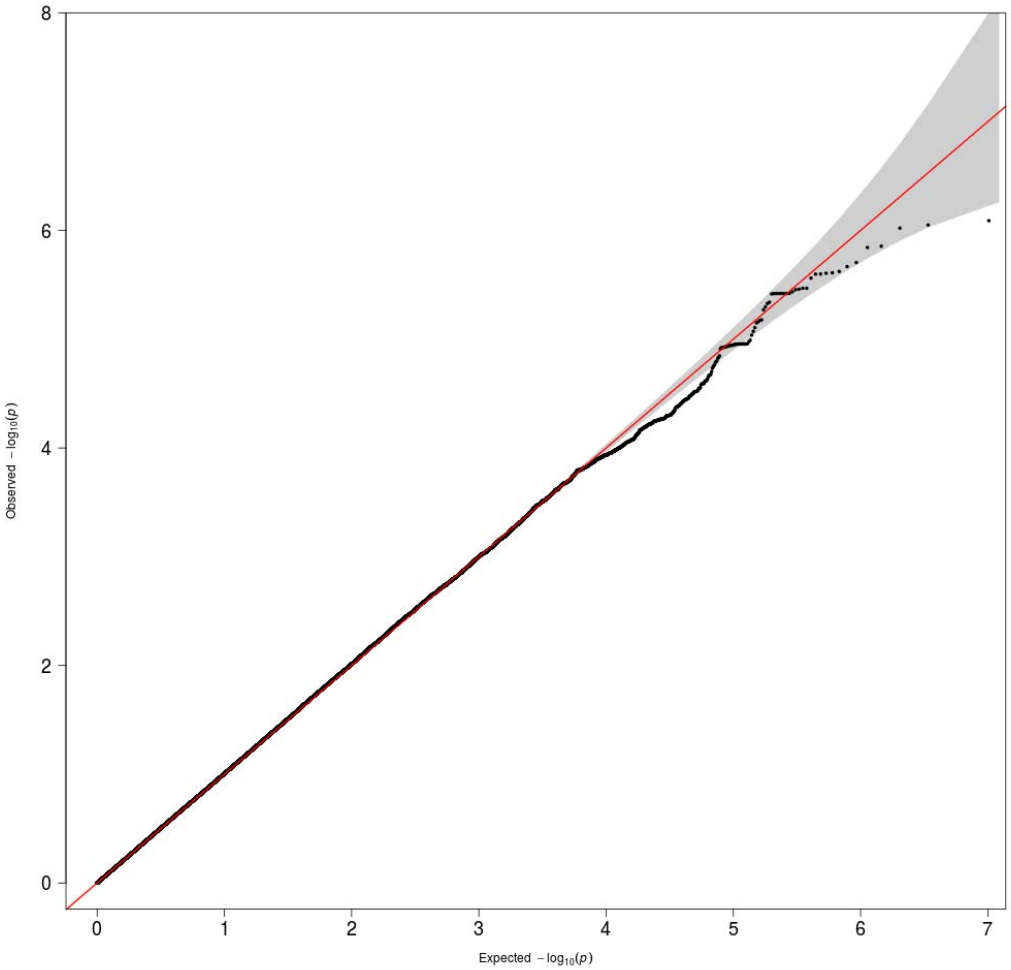

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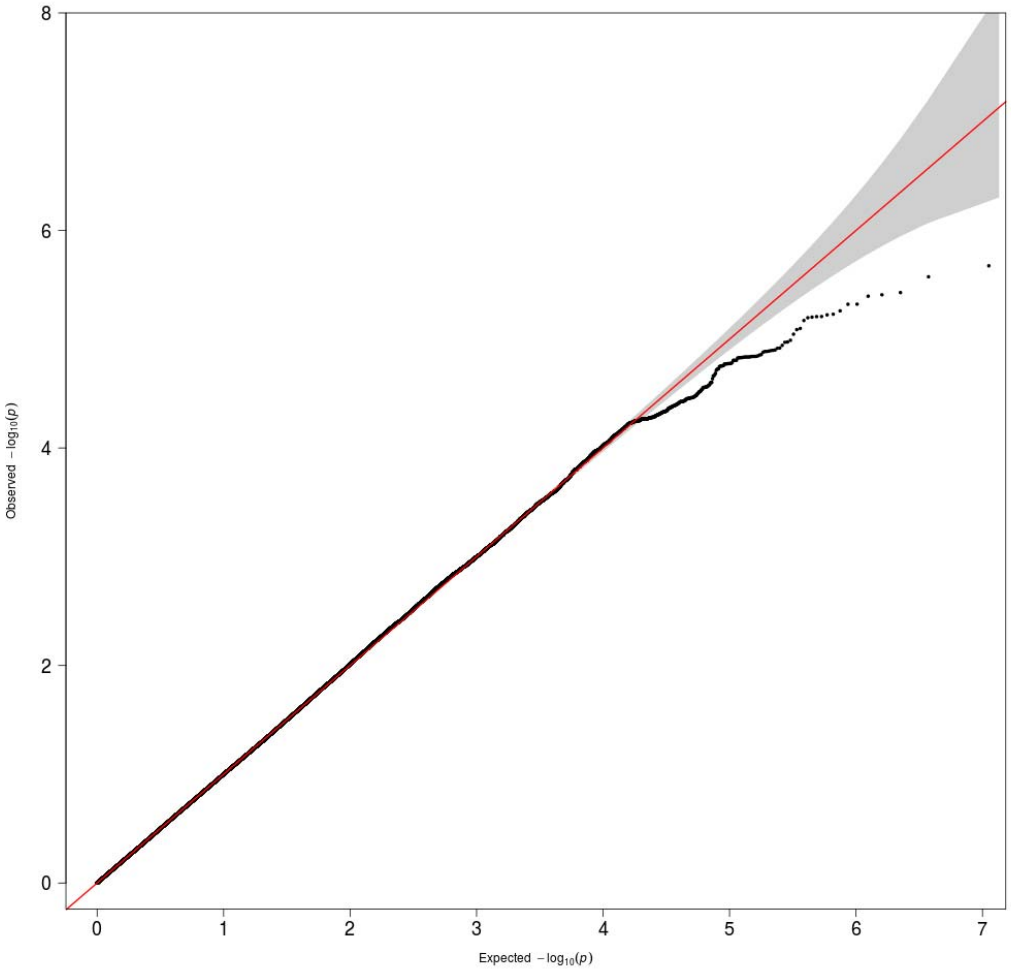

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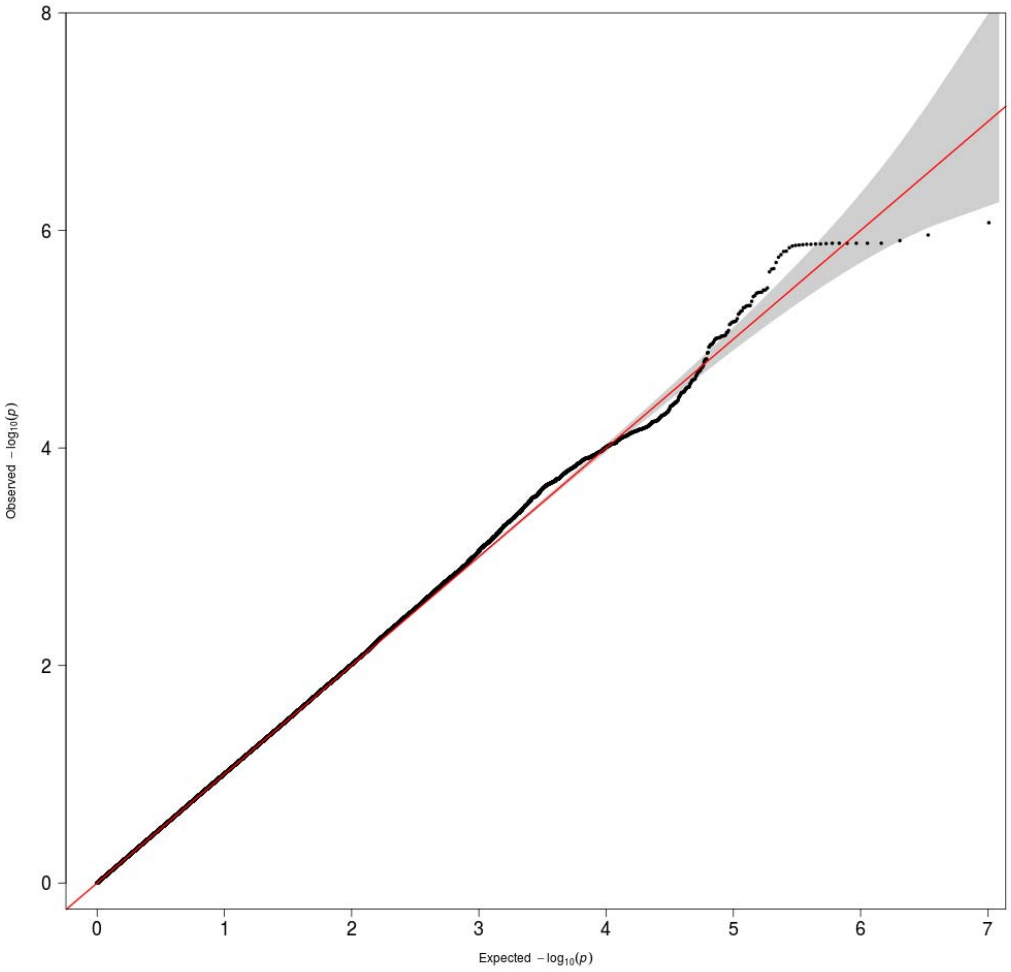

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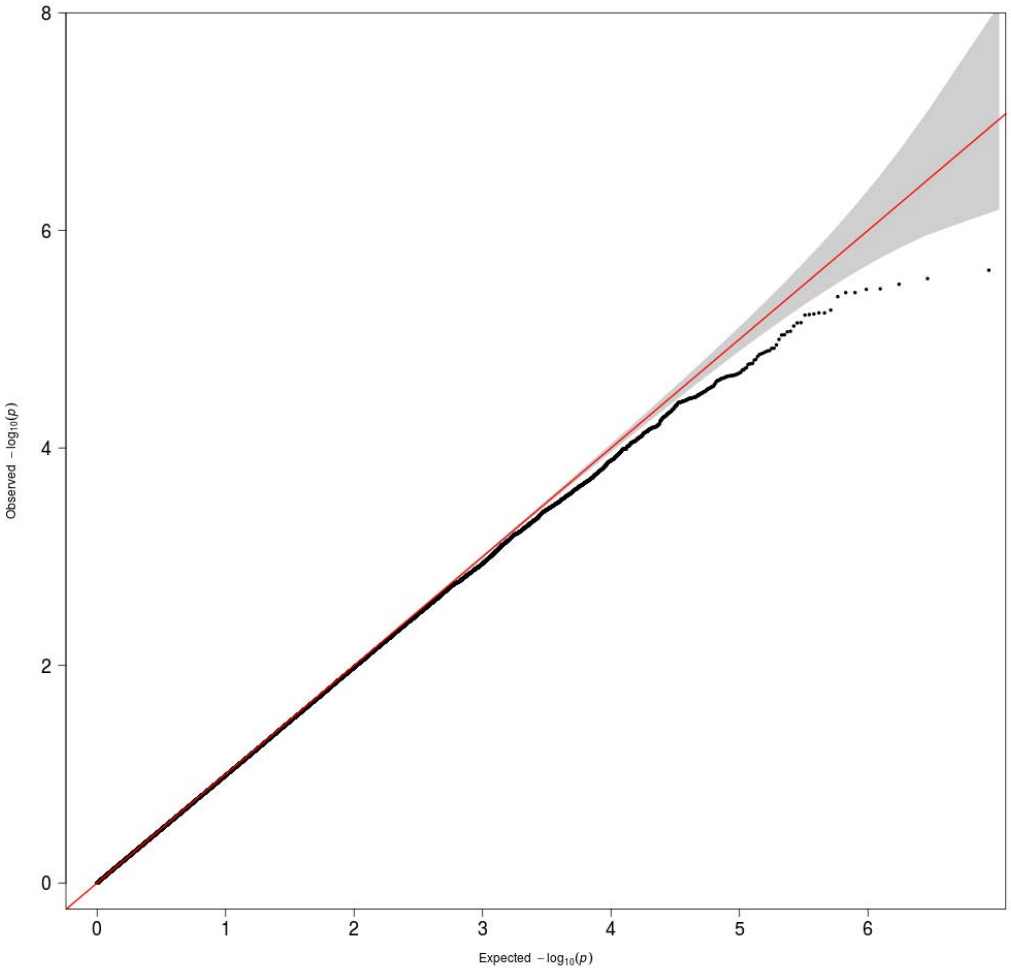

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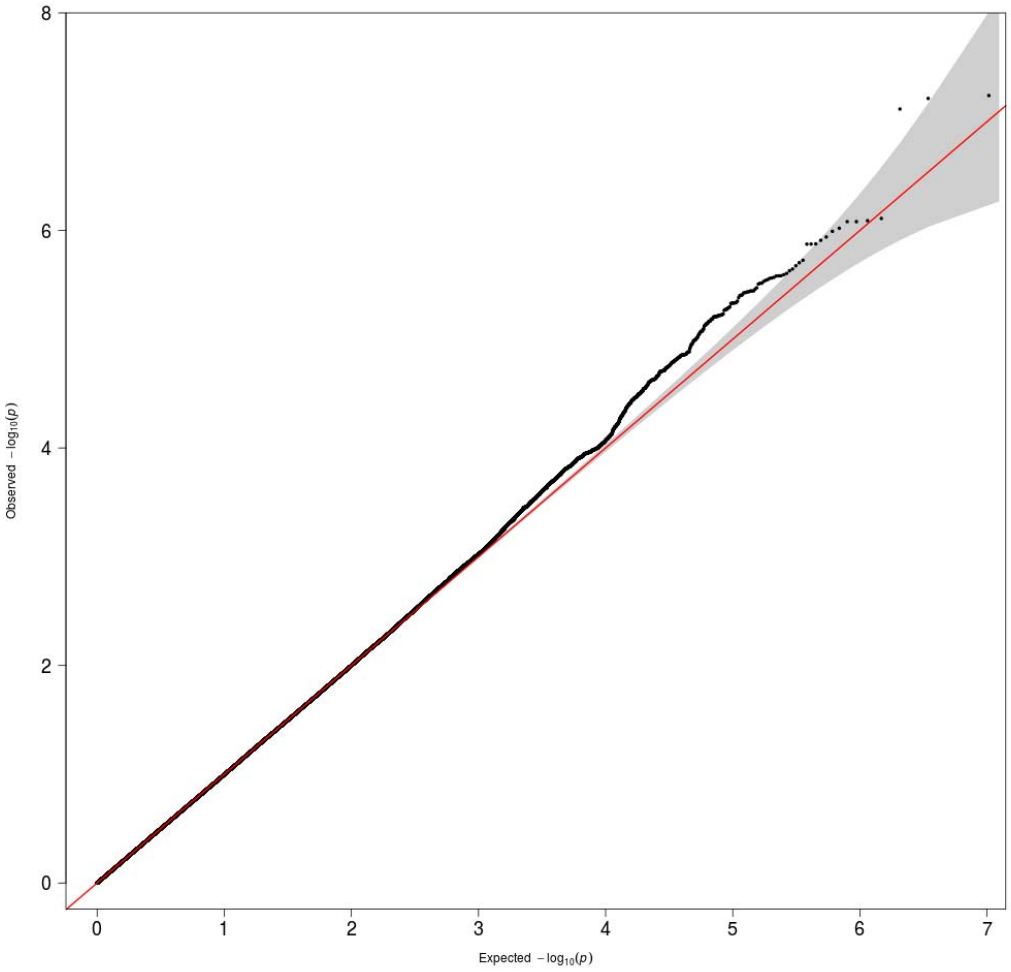

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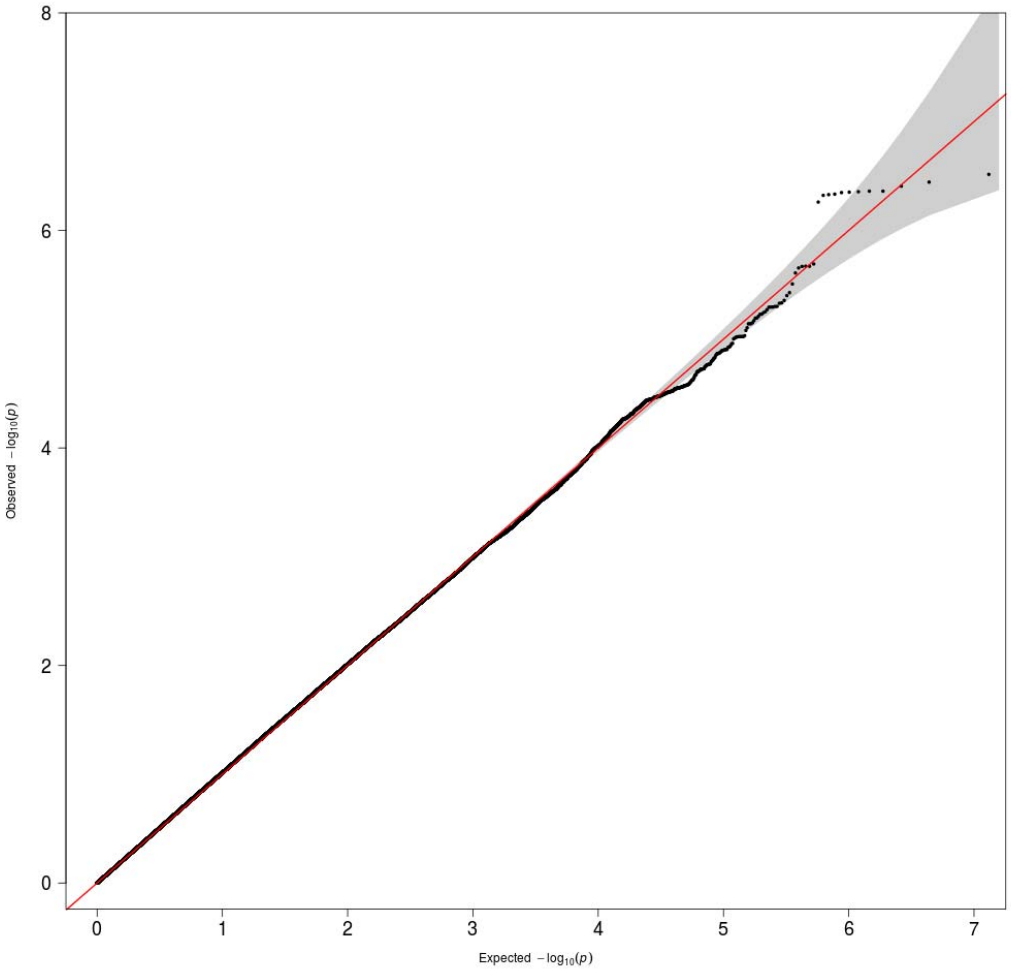

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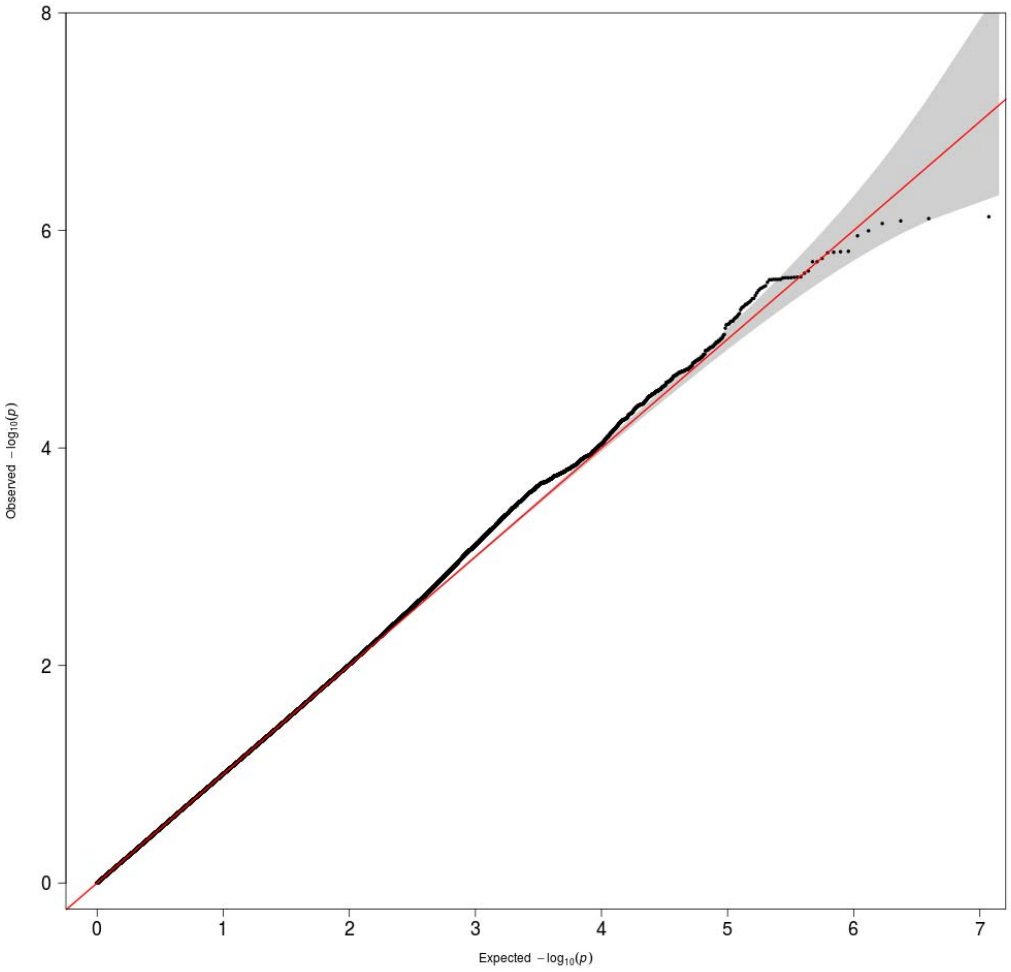

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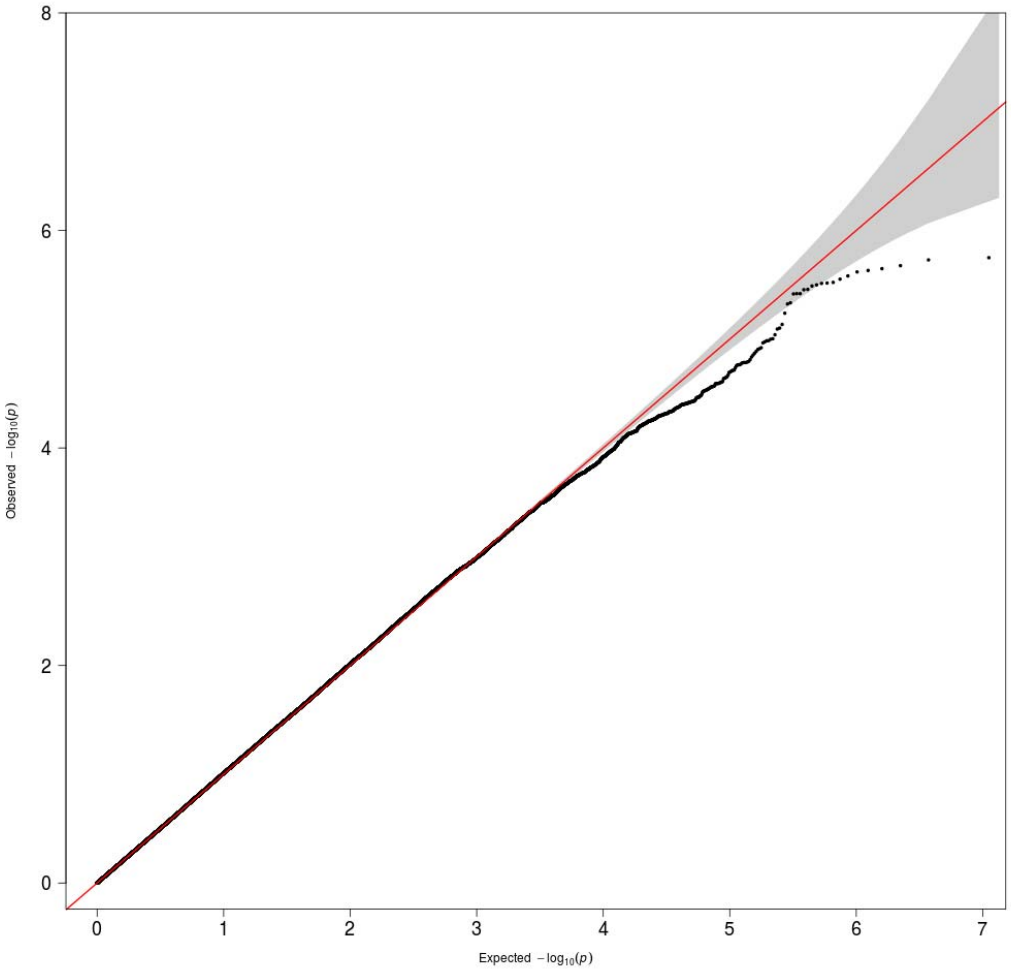

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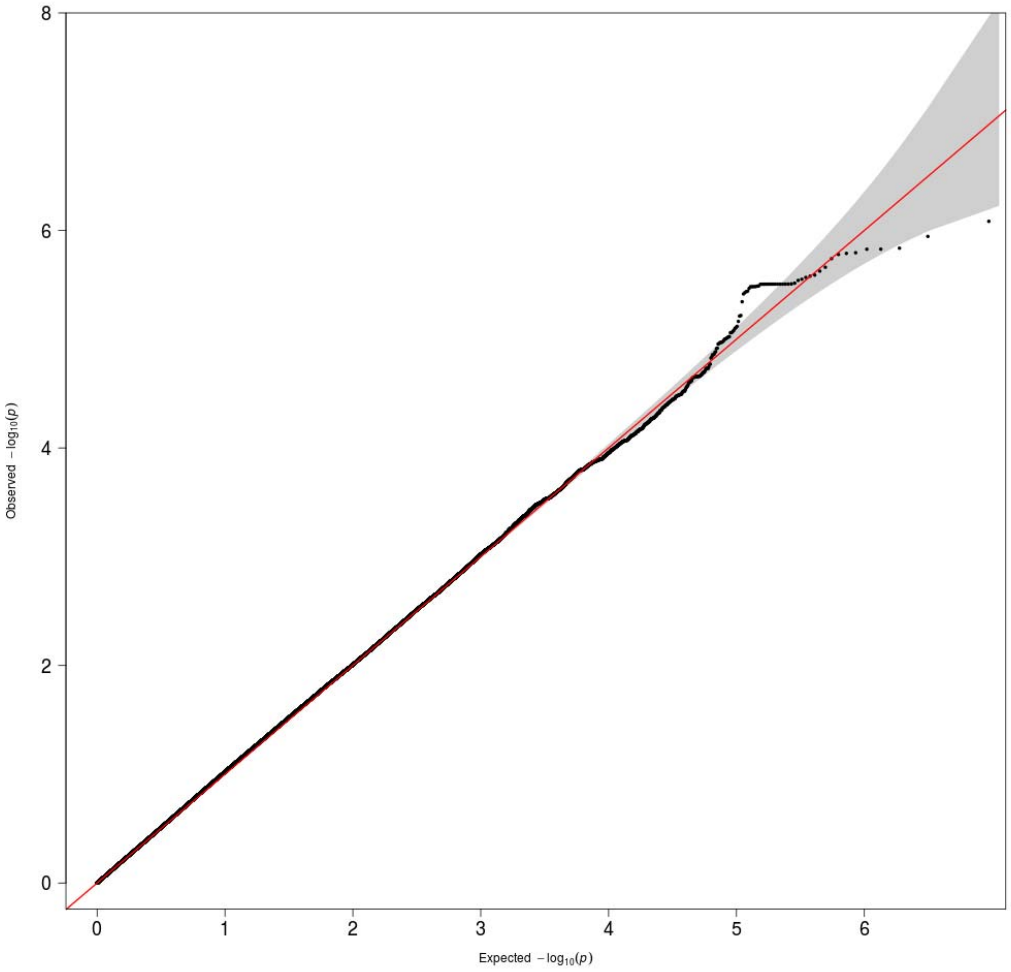

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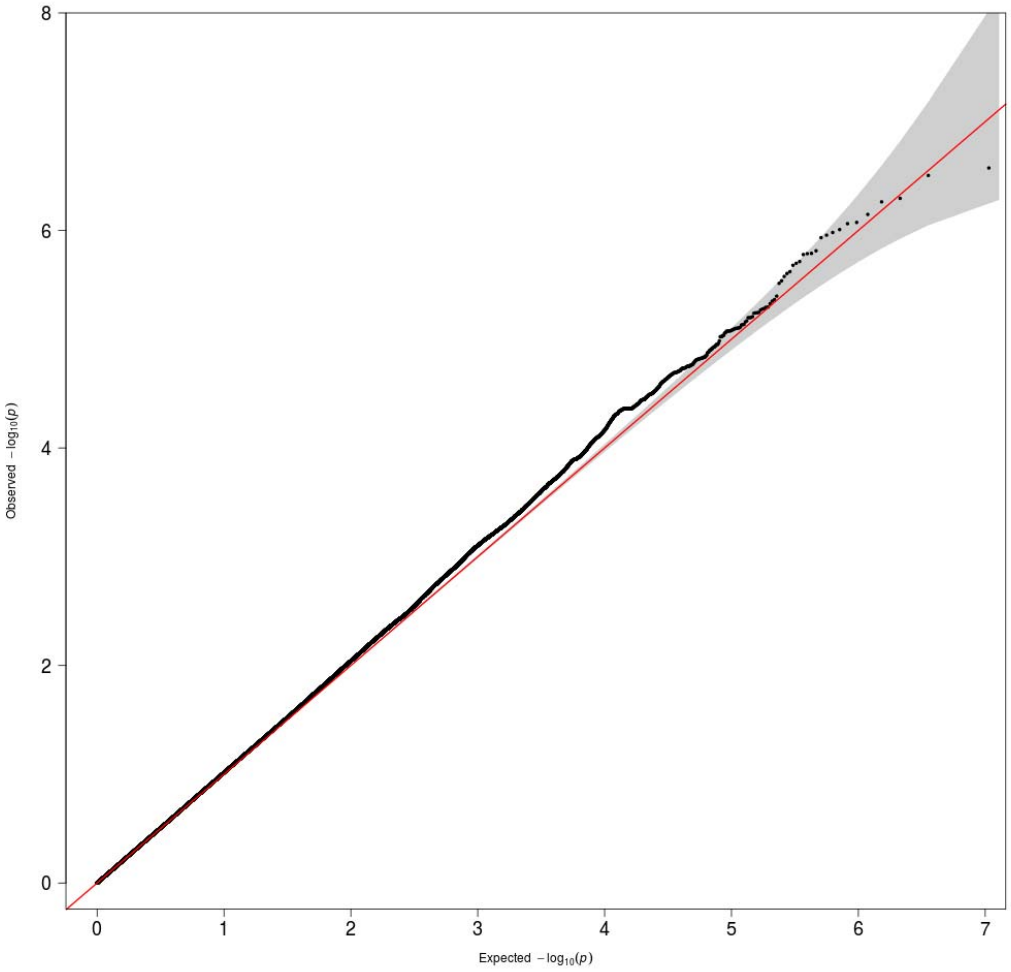

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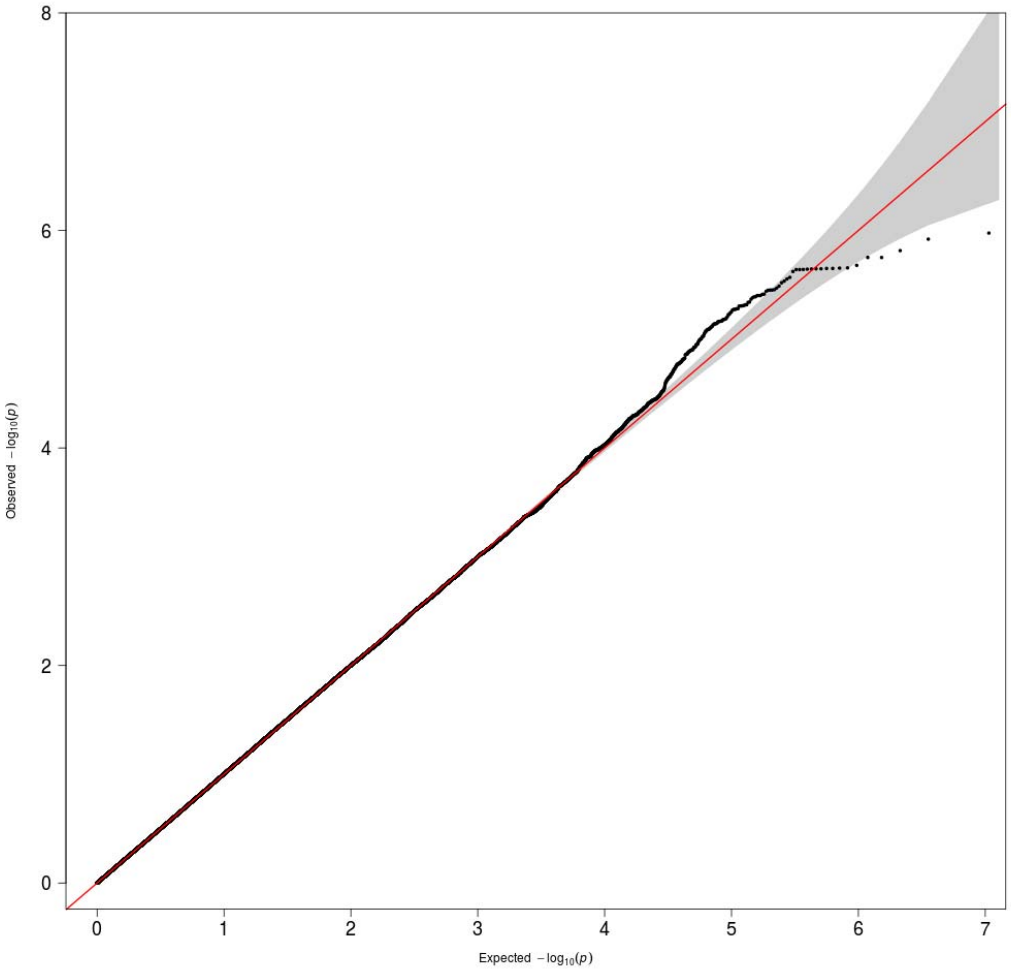

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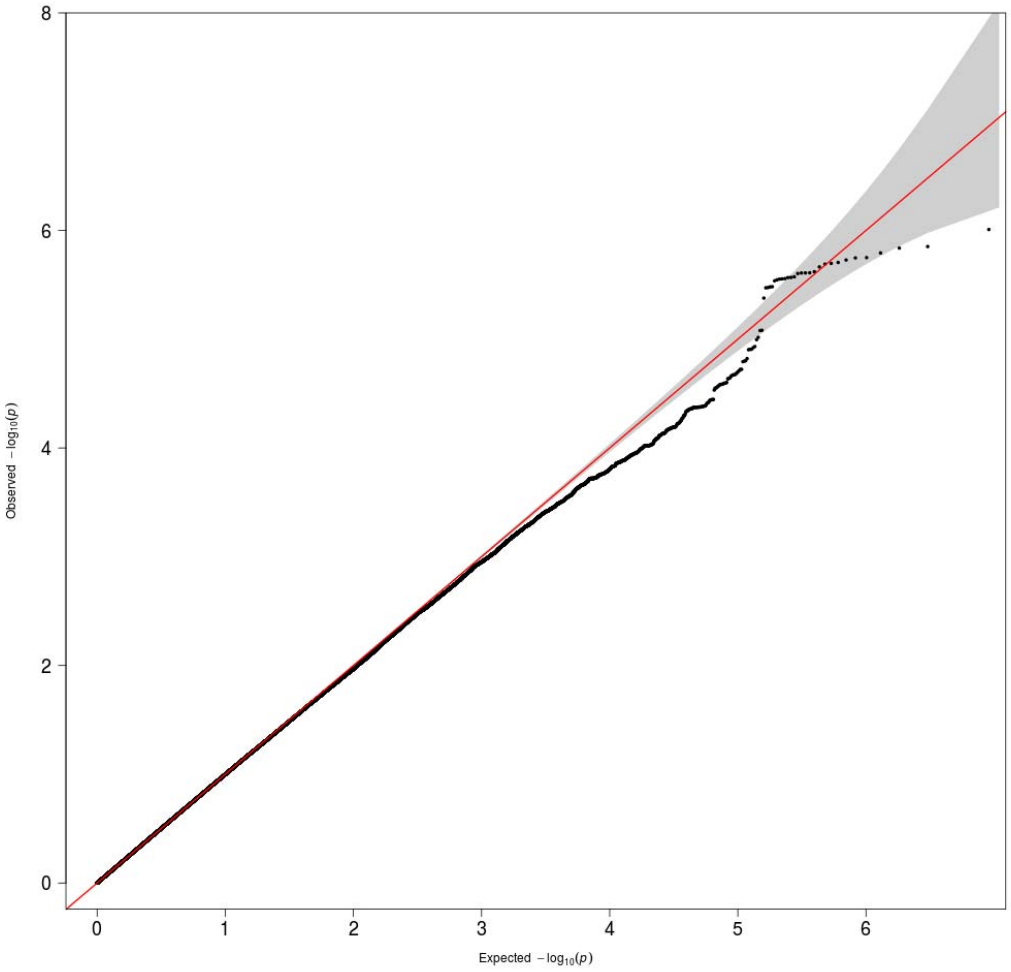

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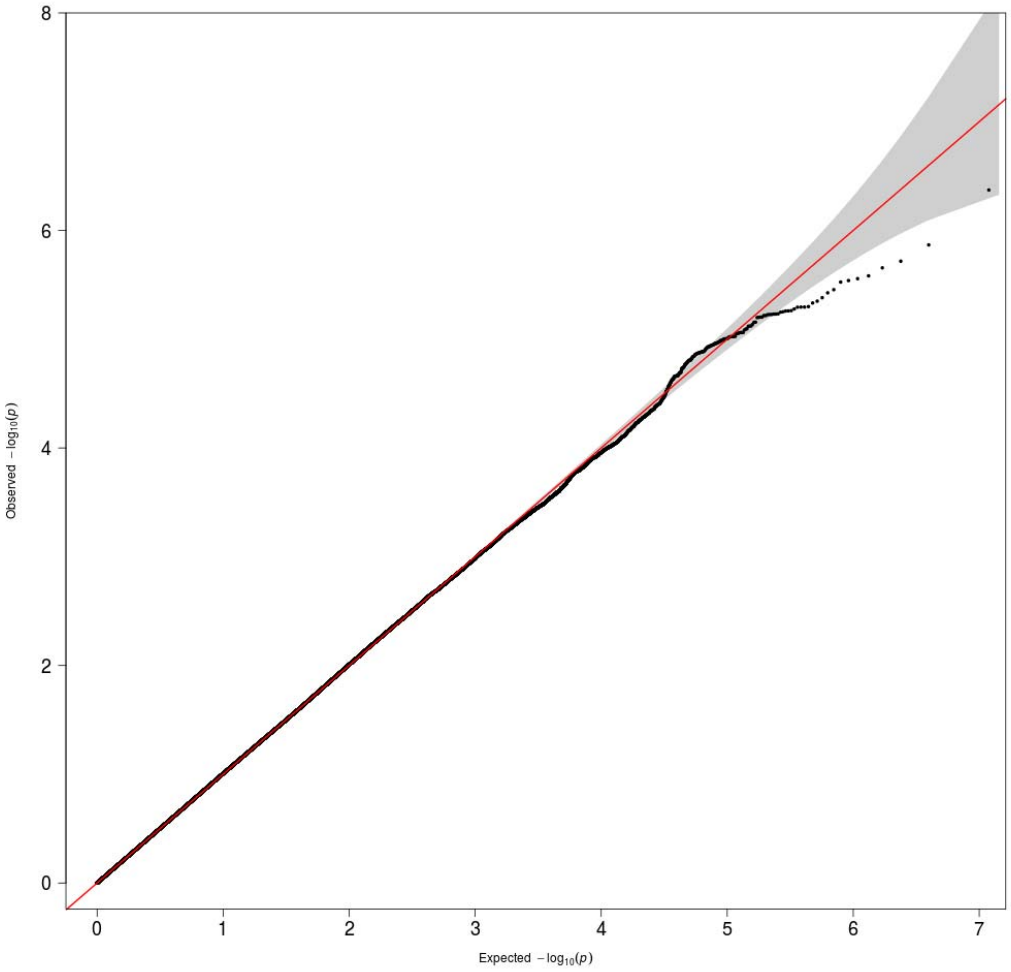

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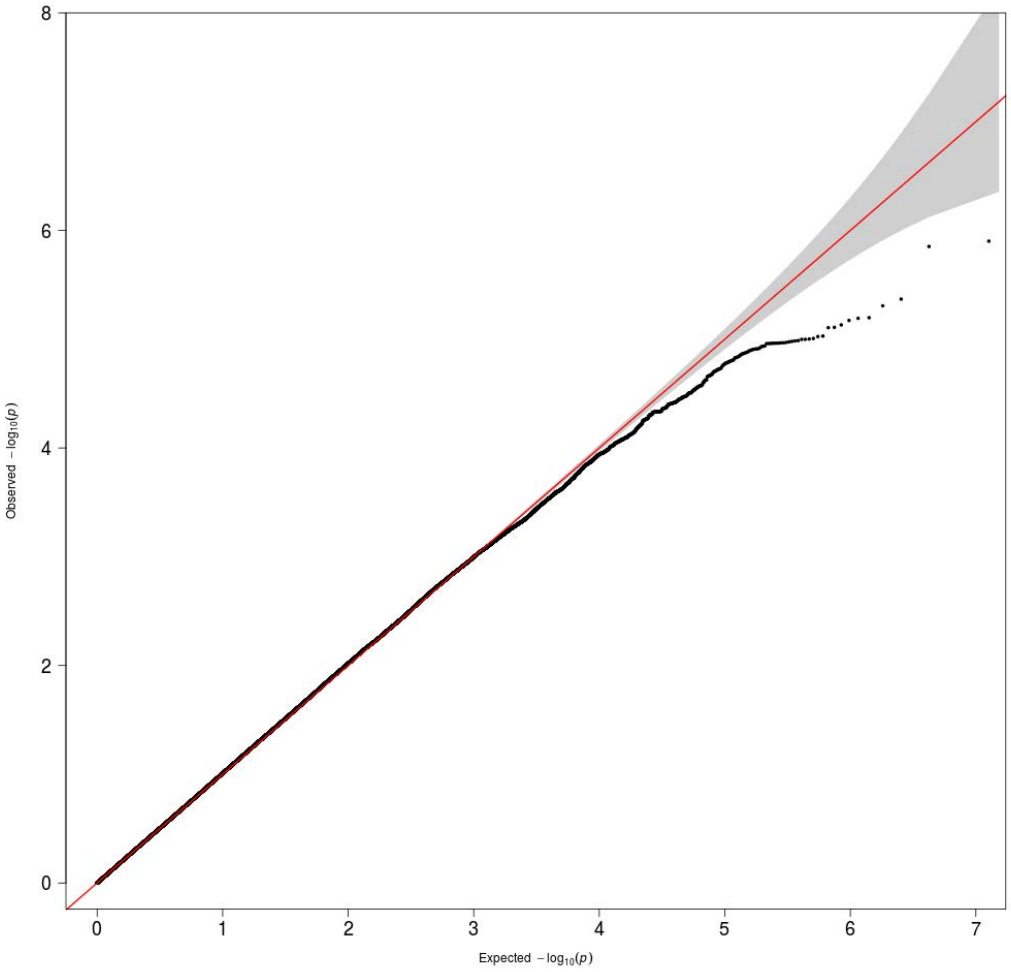

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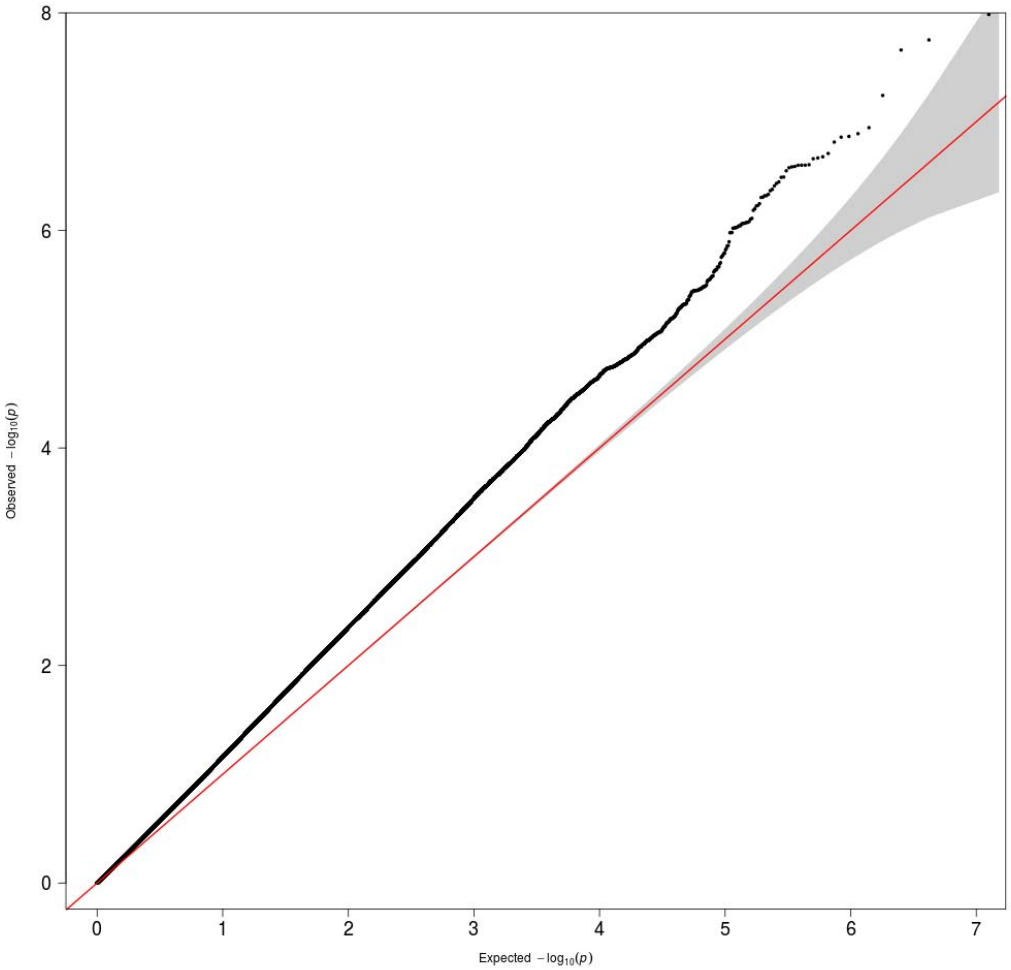

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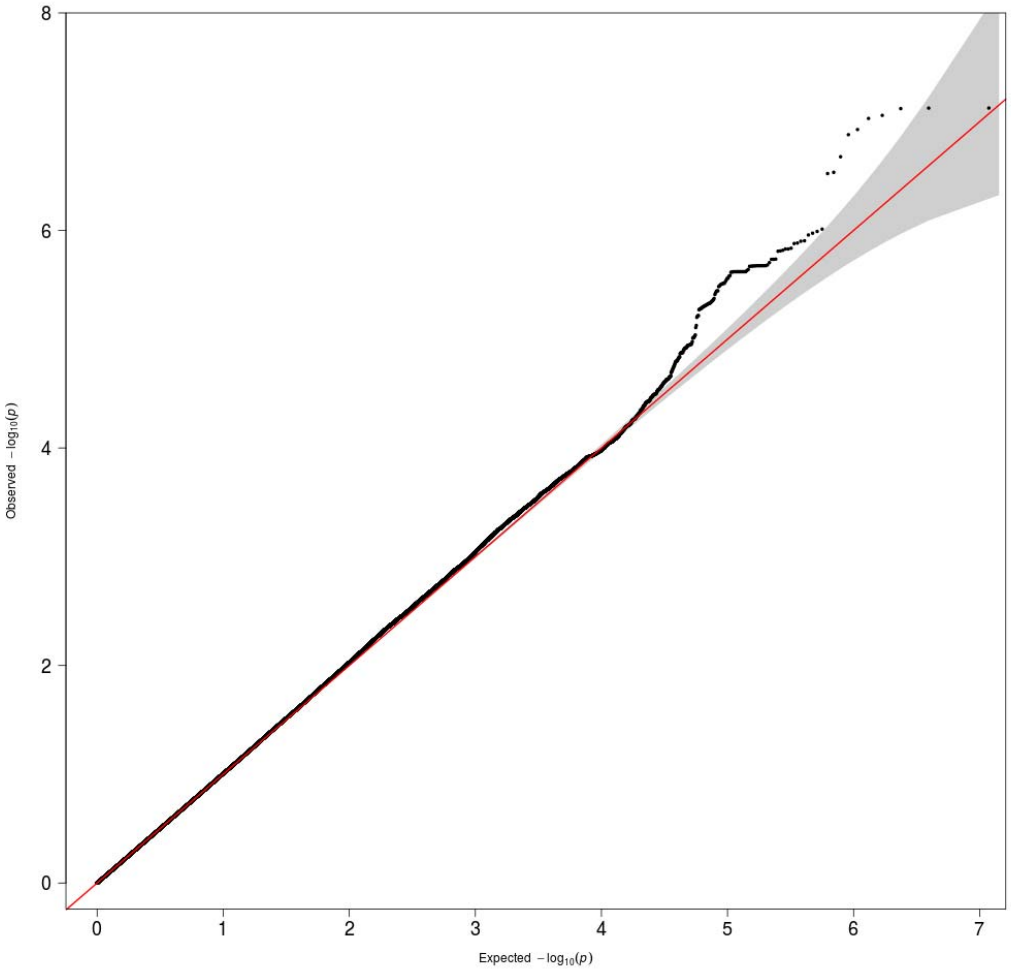

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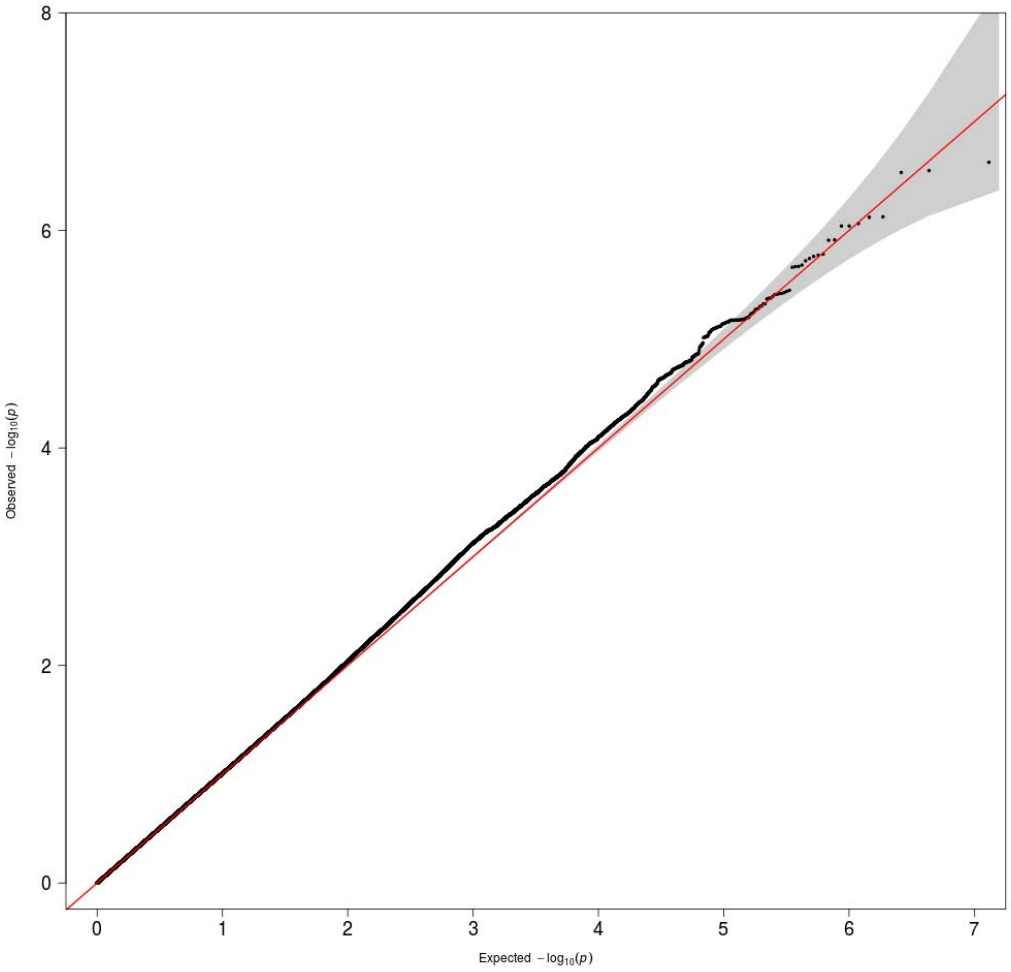

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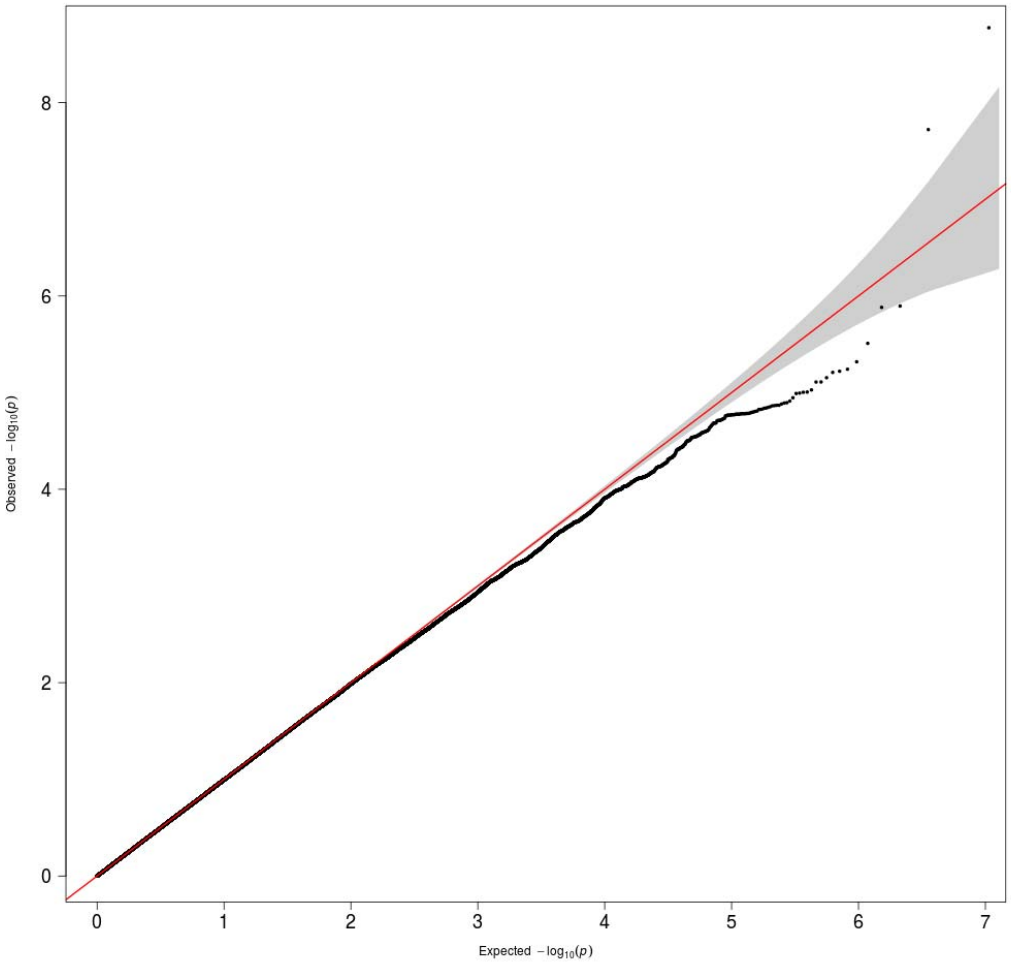

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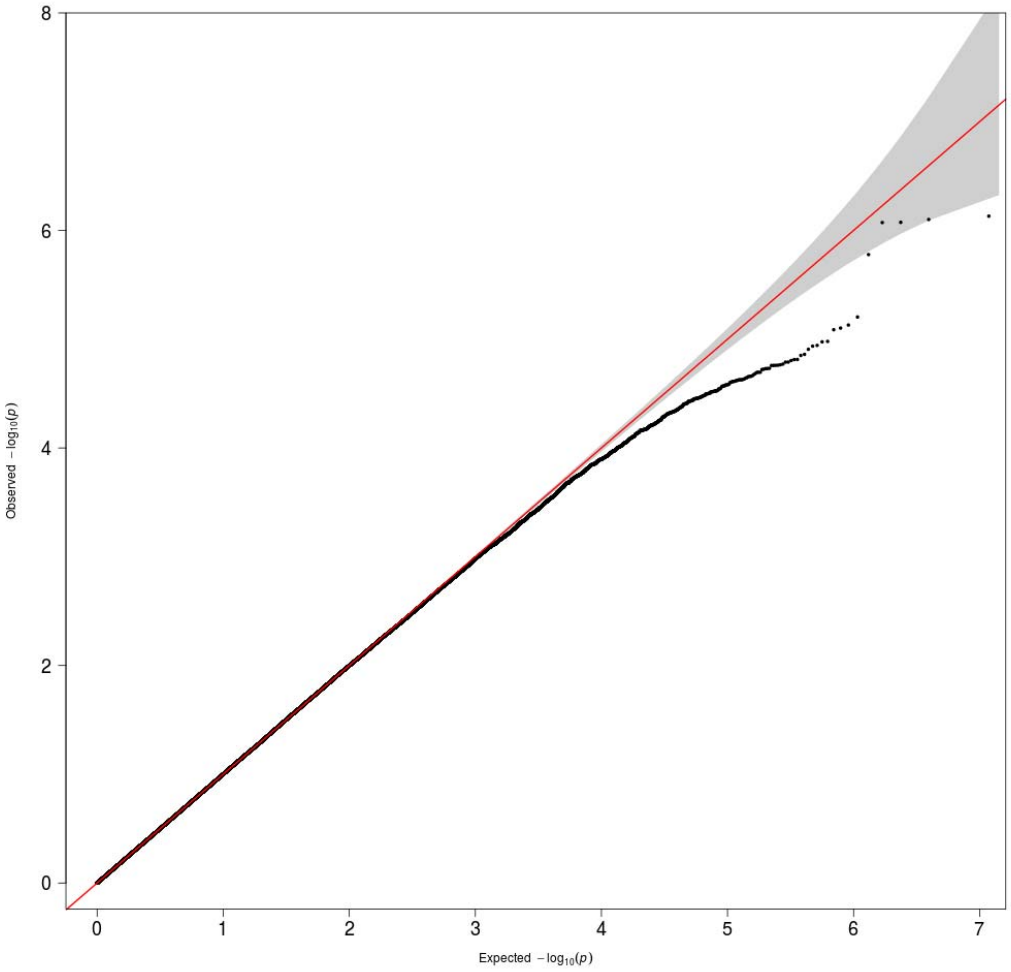

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