Supplementary Information

Supplementary Note

Supplementary Results

Description of novel loci

Three of the 20 loci not previously associated with AR have previously been associated with other atopic traits. These include the locus at 5p13.2 previously associated with eczema[1]. This index SNP is in strong LD with a missense variation in *IL7R* and with meQTLs in blood and lung tissue. IL-7R is necessary for V(D)J recombination of T and B cell receptors, for cellular activation by the type 2 immune inducer TSLP, and *IL7R* polymorphisms have been associated with the autoimmune disease multiple sclerosis[2, 3]. A second locus at 12q24.12 has been associated with blood eosinophil count[4]. A possible functional candidate at this locus, supported by a blood cis-eQTL and a correlated missense variation, is *SH2B3* which is involved in inflammatory pathways and T Cell activation[5]. The third locus at 19q13.11 has previously been associated with eosinophilic esophagitis.[6] We found evidence of enhancer-promotor interaction with *CEBPA* and *CEBPG* in macrophages, monocytes and neutrophils. CEBPA is essential for myeloid cell lineage differentiation[7] while CEBPG function as an enhancer binding protein in *IL4, IL6*, *IL8* and *IGH*, the immunoglobulin heavy chain locus[8].

The majority of the remaining novel loci imply genes with a known role in the immune system. The locus at 11q23 is located near *CXCR5,* a plausible causal candidate supported by cis eQTL and enhancer-promotor interaction in B-cells. *CXCR5* encodes a chemokine receptor that is present on B cells and in a subset of follicular T cells and is involved in B cell migration and facilitates B and T cell interactions within the lymph node[9]. This locus has previously been associated with autoimmune diseases[10,11] and lymphoma[12]. The lead signal at 1q23.3 is located near *FCER1G* and associated with expression of FCER1G in blood and lung tissue. *FCER1G* encodes the gamma chain of the high affinity IgE receptor, a central component in allergic responses, and is thereby a plausible candidate conferring risk of AR at this locus. The locus at 4q24 harbors cis-eQTLs for NFKB1 in monocytes and whole blood and meQTLs in lung tissue. *NFKB1* encodes a subunit of the NF-kappaB complex playing an important role for activation of multiple inflammatory pathways.[13] NF-kappaB activation might also be implicated in the association signal at 10q24.32 with evidence of enhancer-promoter interaction with *NFKB2*, encoding another subunit of the NF-kappaB complex. Other immune related candidates include *BACH2* at 6q15 with a role in antigen-induced formation of memory B cells and memory T cells[1415], *TYRO3* and *LTK* at 15q15.1 modulating TLR signaling[16] and T helper 2 immunity[17], respectively, *VPRBP* at 3p21.2 required for optimal T cell proliferation after antigen recognition and involved in V(D)J recombination during B cell development[18], *SPPL3* and *OASL* at 12q24.31 with potential roles for NK cell maturation[19] and IFN-alpha signaling[20] respectively, *RORA* at 15q22.2 involved in type 2 innate lymphoid cell development and allergic inflammation[21], and *TNFSF11* at 13q14.11 with a role in T cell activation by dendritic cells[22].

Finally, a number of the novel AR loci imply genes with no clear function in AR pathogenesis. These include one of the strongest associated loci in this meta-analysis at 12q24.31 with the top-signal located between *CDK2AP1* and *C12orf65*. This locus harbors cis-eQTLs in blood and/or lung tissue for several genes (*ABCB9, ARL6IP4, C12orf65, CDK2AP1, MPHOSPH9, OGFOD2, PITPNM2, RILPL2, SBNO1, SETD8,* and *SNRNP35*) and shows evidence for enhancer-promoter interaction with *DDX55* in various immune cells, but none of these genes have an obvious function related to AR. The same is the case for *NEGR1* at 1p31.1, *JAZF1* at 7p15.1,

FOSL2 at 2p23.2, and *RERE* at 1p36.32, all supported by cis-eQTLs or me-QTLs in blood and/or lung tissue. No cis-eQTL was identified for the locus at 2q36.3 near *DAW1*. Further studies of these genes and loci might help to understand AR pathogenesis and identify novel drug targets.

Non-allergic rhinitis

Non-allergic rhinitis (NAR), defined as rhinitis symptoms without evidence of allergic sensitization, is a common but poorly understood disease entity.[23] We performed the first GWAS on this phenotype hypothesizing that this might reveal specific rhinitis mechanisms. The analysis included 2,028 cases and 9,606 controls from 9 studies but did not identify any risk loci at the genome-wide significance level. Look-up of the 41 AR top-loci in the non-allergic rhinitis GWAS indicated considerable overlap of susceptibility loci with 33 of 41 loci showing consistent direction of effect and 8 AR loci showing nominal significance ($p<0.05$) in the non-allergic rhinitis GWAS (Supplementary Table 23). In line with this, we found that calculating the population-attributable risk fraction (PARF) for NAR using the risk score from AR showed a highly statistically significant PARF of 48% (95% CI 23%-65%), indicating that a significant proportion of NAR cases can be attributed to AR susceptibility loci. This suggests some genetic commonality between the two phenotypes that can be due to methodological issues, e.g. that some cases of non-allergic rhinitis misdiagnosed due to sensitization not captured by the tests performed, or might have a biological explanation, e.g. the presence of local allergic mechanisms in the nose without presence of systemic allergic sensitization.

Association in non-European populations

We only had data from 3 populations of non-European descent, including populations of African-American (SAPPHIRE, SAGEII) and Latin-American (GALAII) descent. The combined number of individuals was 6,313 providing insufficient statistical power to perform genome-wide association analysis. Look up of the identified novel AR loci was possible for 19 variants. Of these, 13 showed the same direction of effect and two (near RERE and BACH2) reached nominal statistical significance in the random-effects model (Supplementary Table 24). However, the limited statistical power in the non-European sample set does not allow solid interpretations about the potential overlap of AR loci between ethnicities.

Cohort recruitment details, acknowledgements and funding statements

23andme

Recruitment

All individuals included in the analyses provided informed consent and answered surveys online according to our human subjects protocol, which was reviewed and approved by Ethical & Independent Review Services, a private institutional review board (http://www.eandireview.com). Samples were drawn from 23andMe research participants who reported via web-based questionnaires and answered questions about allergic symptoms.

Case/Control definition

23andMe research participants were able to fill out web-based questionnaires whenever they logged into their 23andMe accounts.

For GWAS:

The ”allergic rhinitis” phenotype combines the questions from multiple surveys

(returning all consistent responses, inconsistent responses are set to NA)

1. Survey: "Asthma"

Question: "Have you ever had any of the following? Please check all that apply: "Allergic rhinitis (stuffed or dripping nose caused by allergies)"

2. Samples from ‘Allergies and Asthma’ and “Allergies” surveys that controls are those with no allergies to a broad range of allergens (e.g seasonal_allergies, environmental_allergy, food_allergy and drug_allergy); cases report the allergy to any of these:

[‘grasses’, ‘trees’, ‘weeds’, ‘cats’, ‘dogs’, ‘dust_mite’, ‘mold’],

and had symptoms ‘itchy or runny nose’.

2.1 Survey: "Allergies and Asthma"

Question: "Have you had an allergic reaction to any of the following types of plants?" "Grasses"

2.2 Survey: "Allergies and Asthma"

Question: "What type of reaction did you have after being exposed to grasses? Please check all that apply: "Itchy or runny nose"

2.3 Survey: “Allergies (allergies)"

Question: "Plant Allergies"/"Have you ever had an allergic reaction to any of these types of plants?" "Grasses"

2.4 Survey: "Allergies(allergies)",

Question: "What type of reaction did you have after being exposed to grass? Please check all that apply." : "Itchy or runny nose"

For replication analysis:

The “allergic rhinitis” phenotype combines the questions from multiple surveys

(returning all consistent responses, inconsistent responses are set to NA)

1. Survey: "Asthma"

Question: "Have you ever had any of the following? Please check all that apply: "Allergic rhinitis (stuffed or dripping nose caused by allergies)"

2. New Survey: "Asthma(asthma_background)"

Question: "Have you ever had any of the following? Please check all that apply: “Allergic rhinitis (stuffed or dripping nose caused by allergies)"

3. New Survey: "Asthma(asthma_meds)",

Question: "Have you ever had any of the following? Please check all that apply: "Allergic rhinitis (stuffed or dripping nose caused by allergies)"

4. Samples from allergy surveys that controls are those with no allergies to a broad range of allergens (e.g seasonal_allergies, environmental_allergy, food_allergy and drug_allergy); cases report the allergy to any of these:

['grasses', 'trees', 'weeds', 'cats', 'dogs', 'dust_mite', 'mold'],

and had symptoms 'itchy or runny nose'.

4.1 Survey: "Allergies and Asthma"

Question: "Have you had an allergic reaction to any of the following types of plants?" "Grasses"

4.2 Survey: "Allergies and Asthma"

Question: "What type of reaction did you have after being exposed to grasses? Please check all that apply: "Itchy or runny nose"

4.3 Survey: “Allergies (allergies)"

Question: "Have you ever had an allergic reaction to any of these types of plants?" "Grasses"

4.4 Survey: "Allergies(allergies)",

Question: "What type of reaction did you have after being exposed to grass? Please check all that apply." : "Itchy or runny nose"

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AAGC (QIMR)

Recruitment

As part of the AAGC, we performed a GWAS of allergic rhinitis in unrelated individuals of European ancestry ascertained from the Australian population. Participants provided informed consent to participate in this study, which was approved by the respective ethics committees.

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ALSPAC

Recruitment

ALSPAC recruited 15,247 pregnant women resident in Avon, UK with expected dates of delivery 1st April 1991 to 31st December 1992, resulting in 14,775 live births and 14,701 children who were alive at 1 year of age. Enrolment is described in more detail in the cohort profile paper[24] and via the website http://www.bris.ac.uk/alspac/researchers/data-access/data-dictionary/. Biological samples including DNA have been collected for 10,121 of the children from this cohort. Ethical approval for the study was obtained

from the ALSPAC Ethics and Law Committee and the Local Research Ethics Committees and written and informed consent was provided by the parents.

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B58C (British 1958 birth cohort)

Recruitment

The British 1958 birth cohort is an ongoing follow-up of all persons born in England, Scotland and Wales during one week in 1958. At ages 7, 11, 16, 23, 33 and 42 years, a history of hay fever or allergic rhinitis was obtained by interview with a parent (aged 7-16) or the cohort member (ages 23-42), At the age of 44-45 years, the cohort were followed up with a biomedical examination and blood sampling, from which a DNA collection was established as a nationally representative reference panel, and the presence of circulating IgE antibodies to house dust mite, mixed grass pollen and cat fur was ascertained by Hytec enzyme immunoassay, with a detection threshold of 0.35 kU/L.

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BAMSE

Recruitment

BAMSE is a Swedish birth cohort study. A total number of 4,089 newborn infants were recruited between 1994 and 1996 in the Stockholm area[19]. The first questionnaire data, dealing with parental allergic diseases, socio-economic status and residential characteristics, was obtained when the children were about 2 months. Similar questionnaires, with a focus on the children's symptoms related to asthma and allergic diseases

including eczema, were answered by the parents when the children were approximately 1, 2, 4, 8 and 12 years old. At 8 years of age, all children were invited to clinical testing, and blood samples were obtained from 2,480 children (~60%). DNA was extracted from 2,033 samples after exclusion of samples with too little blood, lack of questionnaire data, or if parental consent to genetic analysis of the sample was not obtained.

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CAMP

Recruitment

The Childhood Asthma Management Program (CAMP) population is composed of non-Hispanic white subjects from a multicenter clinical trial that followed 1,041 children with asthma for four years and 84% of the original participants for 12 years. Stringent inclusion criteria ensured that participants had mild to moderate asthma, which was assessed as having asthma symptoms at least twice per week, using asthma medication daily, or using an inhaled bronchodilator twice per week for six or more months of the year prior to recruitment. CAMP subjects had increased airway responsiveness, as established by a bronchoprovocation test of up to 12.5mg/dl of methacholine resulting in 20% or greater forced expiratory volume in one second (FEV1) reduction.

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CEDAR

Recruitment

The CEDAR cohort comprises 323 healthy individuals of European descent visiting the University of Liège Hospital as part of a national screening for colon cancer. They provided blood samples and intestinal biopsies under full informed consent. The experimental protocol was approved by the ethics committee of the University of Liège Academic Hospital. Informed consent was obtained prior to donation in agreement with the recommendations of the declaration of Helsinki for experiments involving human subjects. We refer to this cohort as CEDAR for Correlated Expression and Disease Association Research.

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COPSAC2000

Recruitment

The COPSAC2000 birth cohort study is a prospective clinical study of a birth cohort of 411 infants born to mothers with a history of asthma. The newborns were enrolled at the age of 1 month, the recruitment of which was previously described in detail.[25] The study was approved by the Ethics Committee for Copenhagen (KF 01- 289/96) and The Danish Data Protection Agency (2008-41-1754) and informed consent was obtained from both parents. For this study, only the parents were included.

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deCODE

Recruitment

Icelandic patients with allergic rhinitis, based on physicians diagnosis, who attended an asthma clinic or emergency room at the National University Hospital of Iceland or the Icelandic Medical Center (Laeknasetrid) during the years 1977 to 2016 were recruited.[2627] All participating subjects who donated biospecimens provided informed consent. Personal identities of the participants and biological samples were encrypted by a third-party system approved and monitored by the Icelandic Data Protection Authority. The study, Genetics of asthma and allergies, was approved by the National Bioethics Committee (VSN-14-099, VS00-135) and the Data Protection Authority (no. PV_2014060841/ÞS) in Iceland.

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ECRHS

Study description

The European Community Respiratory Health Survey (ECRHS) is an international cohort study designed to assess the prevalence of asthma and allergic disease and identify their risk factors (Burney et al. The European Community Respiratory Health Survey.[29] Young adults of European descent were randomly recruited from community-based sampling frames in the ECRHS I (1991-1993) and followed up twice in the 20 years after the first assessment (ECRHS II: 1998-2002; ECRHS III: 2008-2013). Genotyping was performed on blood samples collected at ECRHS II. The current analysis was restricted to participants from centres that took part in the GABRIEL genotyping initiative and were representative of the random sample taken at baseline (i.e. this sample is not enriched with asthmatics). Ethical approval from local research ethics committees and written consent from participants were obtained.

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EVE (CAG/CSGA)

Recruitment

Subjects were from the Chicago Asthma Genetics Study (CAG) and the NHLBI Collaborative Studies on the Genetics of Asthma (CSGA).

CAG included subjects recruited from a) families ascertained through asthma affected sib pairs, b) asthma affected children, c) adults and children with severe persistent asthma, and d) non-asthma controls over 18 years of age. Asthma was defined as 1) a physicals diagnosis, 2) the presence of at least two self-reported symptoms, 3) current use of medications, and 4) bronchial hyperresponsiveness to methacholine or reversibility to inhaled bronchodilator. Controls had no self-reported personal or family history (1st degree relatives) of asthma.

CSGA subjects were recruited from the NHLBI Collaborative Studies on the Genetics of Asthma (CSGA). CSGA cases were recruited and diagnosed as described above for CAG.

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EVE (CHS)

Recruitment

Two cohorts in the Children's Health Study (CHS) including a total of 3000 children (1512 from cohort 1, and 1488 from cohort 2) who were either Hispanic (n=1398) or non-Hispanic white (n=1602) were included in the analysis. The first cohort included children between the ages of 8-14 years recruited from schools in 12 southern California communities in 1993 and 1996. The second cohort included children between the ages of 5-8 years recruited from schools in 13 communities in 2002. A total of 1249 cases were classified as having asthma if the adult completing the questionnaire reported that a doctor had "ever diagnosed the child as having asthma". A total of 1751 controls were selected using frequency matching with cases on sex, ethnicity, cohort, and follow-up time from children without the asthma outcome.

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FINNTWIN (FTC)

Recruitment

The total of 2373 subjects originate within the Finnish Twin Cohort (FTC).[3031] Altogether 1161 of the subjects belong to the Older Finnish Twin Cohort consisting of adult twins born in 1938-1957.[32] Altogether 687 of the subjects belong to the FinnTwin12 cohort, a population-based longitudinal study of five consecutive birth cohorts (1983-1987) of Finnish twins. Altogether 525 of the subjects belong to the FinnTwin16 cohort, a population-based longitudinal study of five consecutive birth cohorts (1975-1979) of Finnish twins and their families.

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GABRIELA

Recruitment

The GABRIELA study (GABRIEL Advanced Studies) was a cross-sectional population-based study in 5 rural regions of Europe: Baden-Württemberg and Bavaria in Germany, North/Central Switzerland, Tyrol in Austria, and Lower Silesia in Poland. In phase 1, a recruitment questionnaire was sent out to 132,518 children age 5 to 13 years through their primary schools. Completed questionnaires were returned by 79,888 (60.3%). With a documented parental consent to dust sampling, blood sampling, and genetic analyses 34,491 children were eligible for phase 2. A stratified random selection process was applied to enrich informative observations. In a first step, 9668 children were selected for phase 2 within 3 exposure strata per center, i.e. farm children, non-farm children with and without farm exposure. In the second step, 1708 children from the Austrian, German, and Swiss centers were selected for genotyping within the mentioned exposure strata and simultaneously stratified for outcome, i.e. asthma, atopic sensitization, and unaffected controls.[33]

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GALA II

Recruitment

The Genes-environments & Admixture in Latino Americans (GALA II) study is an ongoing case-control study of asthma in Latinos that are recruited in five centers throughout the U.S. (Chicago, Illinois; Bronx, New York; Houston, Texas; San Francisco Bay Area, California; and San Juan, Puerto Rico).[34] Participants were eligible if they were aged between 8 to 21 years, had <10 pack-years of smoking history and self-identified all four grandparents as Latino. Subjects were excluded if they reported any of the following: (1) 10 or more pack-years of smoking; (2) any smoking within one year of recruitment date; (3) pregnancy in the third trimester; or (4) history of one of the following conditions: sickle cell disease, cystic fibrosis, sarcoidosis, cerebral palsy, or history of heart or chest surgery. Both children and young adults with physician-diagnosed asthma and non-allergic, non-asthmatic controls were recruited. The presence of allergic rhinitis was defined as a positive response to the question “Has a doctor ever diagnosed the child with hay fever or allergic rhinitis?” According to this, a total of 755 individuals were classified as cases and 2,929 as controls.

All local institutional review boards approved the study and all subjects/parents provided written assent/consent, respectively.

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GENEVA-KORA

Recruitment

A total of 1895 individuals were obtained from an atopic dermatitis case collection recruited from tertiary dermatology clinics based at three centres (Technische Universität Munich, as part of the GENEVA study, University of Kiel, University of Bonn) as well as from two German population-representative cohorts, the PopGen biorepository[35] and the KORA study.[36]

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GENR

Recruitment

The Generation R Study is a population-based prospective cohort study of pregnant women and their children from fetal life onwards in Rotterdam, The Netherlands. All children were born between April 2002 and January 2006, and currently followed until young adulthood. Of all eligible children in the study area, 61% were participating in the study at birth. Cord blood samples including DNA have been collected at birth. The study protocol was approved by the Medical Ethical Committee of the Erasmus Medical Centre, Rotterdam (MEC 217.595/2002/20). Written informed consent was obtained from parents of all participants.

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GENUFAD

Recruitment

All patients were recruited at Charité Universitätsmedizin Berlin for the GENUFAD study (GEnetic analysis of NUclear Families with Atopic Dermatitis) which has been described in a previous GWAS.[37] Briefly, 270 complete nuclear German families were recruited through two siblings affected by eczema with an age of onset below two years. For all family members, eczema, allergic rhinitis, and asthma status was determined by a physician at recruitment. To ensure independent, unrelated cases, all parents with allergic rhinitis were included in this study. If the parents were unaffected, only one child with allergic rhinitis per family was included. Allergic sensitization status was determined for all cases.

German control individuals originated from the Study of Health in Pomerania (SHIP), a population-based cohort from North-Eastern Germany.[38]

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GINI/LISA

Recruitment

The influence of Life-style factors on the development of the Immune System and Allergies in East and West Germany PLUS the influence of traffic emissions and genetics (LISAplus) Study is a population based birth cohort study. A total of 3094 healthy, full-term neonates were recruited between 1997 and 1999 in Munich, Leipzig, Wesel and Bad Honnef. The participants were not preselected based on family history of allergic diseases.[39] A total of 5991 mothers and their newborns were recruited into the German Infant study on the influence of Nutrition Intervention PLUS environmental and genetic influences on allergy development (GINIplus) between September 1995 and June 1998 in Munich and Wesel. Infants with at least one allergic parent and/or sibling were allocated to the interventional study arm investigating the effect of different hydrolysed formulas for allergy prevention in the first year of life.[40] All children without a family history of allergic diseases and children whose parents did not give consent for the intervention were allocated to the non-interventional arm. Detailed descriptions of the LISAplus and GINIplus studies have been published elsewhere1,2. DNA was collected at the age 6 and 10 years and 1511 children from the Munich study center from both studies were genotyped. For both studies, approval by the local Ethics Committees and written consent from participant's families were obtained.

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GOA

Recruitment

Subjects were drawn from the Genetics of Asthma study (GOA) in the Spanish population that have been previously described.[41,42] Cases with rhinitis were diagnosed by a physician, aged ≥5 years, taking medications to control their asthma symptoms, and had an extensive clinical characterization, including allergic sensitization by skin prick tests and specific IgE measurements. Control subjects self-reported absence of personal or familiar history of chronic diseases, and were obtained from the National Genotyping Center (CEGEN-PRB2-ISCIII), Universidad de Santiago de Compostela Node.

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GOYA

Recruitment

The GOYA study (Genetics of Overweight Young Adults) is derived from the genome wide association study (GWAS) on obesity with a case-cohort (obese-non obese) design comprising young men and women of Danish origin.[43]

The GOYA (Male) cohort is a longitudinal case-cohort (obese, non-obese) study comprising a randomly (1%) selected control group and all extremely overweight men identified among 362,200 Caucasian men examined at the mean age of 20 years at the draft boards in Copenhagen and its surrounding areas during 1943–1977. Obesity was defined as 35% overweight relative to a local standard in use at the time (mid 1970's), corresponding to a BMI ≥31.0 kg/m2, which proved to be above the 99th percentile. All of the obese and 50% of the random sampled controls, who were still living in the region, were invited to a follow-up survey in 1992–94 at the mean age of 46 years, at which time the blood samples were taken and genotyping were performed for a total of 673 extremely overweight and 792 controls. With a sampling fraction of 0.5% (50% of 1%), the controls represent about 158,000 men among whom the case group was the most obese.

The GOYA (Female) cohort cohort is nested within the Danish National Birth Cohort (DNBC[43]) which is a collection of data on 92,274 pregnant women recruited between 1996 and 2002, from their first antenatal visit to their general practitioner. Women participated in four telephone interviews (16 and 30 weeks gestation and 6 and 18 months after birth). They also provided two blood samples during pregnancy. The GOYA females were drawn from the 67,863 women within the DNBC who provided information about prepregnancy BMI, gave birth to a live born infant and provided a blood sample during pregnancy. A case sample of the 3.6% most obese women (n=2451) was defined as those with the largest residuals from the regression of BMI on age and parity (all entered as continuous variables). The BMI for these women ranged from 32.6 to 64.4. From the remaining cohort we selected a random sample of similar size (n=2450). Of these, 1,960 extremely overweight and 1,948 control women were genotyped and passed quality control. Information on mother's year of birth and age at first birth derived from national registers. The study was approved by the regional scientific ethics committee and by the Danish Data Protection Board.

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INMA

Recruitment

Population-based birth cohorts were established as part of the INMA – INfancia y Medio Ambiente [Environment and Childhood] Project in several regions of Spain following a common protocol. This analysis uses the INMA subcohort of Menorca established between 1997 and 1998 in Menorca island. This project aims to study the associations between pre- and postnatal environmental exposures and growth, health, and development from early fetal life until adolescence and has been described previously in detail.[44] Pregnant women were enrolled during the 1st trimester of pregnancy at public primary health care centers or public hospitals and children were followed after birth until 18y of age. Informed consent was obtained from all participants and the study was approved by the Hospital Ethics Committee.

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MAAS

Recruitment

The Manchester Asthma and Allergy Study is an unselected (i.e. population-based), birth cohort study. The setting is the maternity catchment area of Wythenshawe and Stepping Hill Hospitals, comprising of 50 square miles of South Manchester and Cheshire, UK, a stable mixed urban-rural population. Study was approved by the Local Research Ethics Committee. Informed consent was obtained from all parents.

Screening & Recruitment

All pregnant women were screened for eligibility at antenatal visits (8th-10th week of pregnancy). The study was explained to the parents, and informed consent for initial questionnaires and skin prick testing was obtained. Both parents completed a questionnaire about their and their partner's history of asthma and allergic diseases and smoking habits. If the pregnant woman's partner was not present at the antenatal clinic visit, an invitation was sent for him to attend an open-access evening clinic for skin prick testing and questionnaire. Once both parents had completed questionnaires and skin prick testing, a full explanation of the proposed future follow-up for the child was given. Of the 1499 couples who met the inclusion criteria

(<10 weeks of pregnancy, maternal age >18 years, questionnaire and skin test data available for both parents), 288 declined to take part in the study. A total of 1185 participants had at least some evaluable data.

Follow-up

The children have been followed prospectively, and attended review clinics at ages 1, 3, 5, 8 and 11 years.

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NFBC1966

Recruitment

The Northern Finland Birth Cohort 1966 is a prospective follow-up study of children from the two northernmost provinces of Finland. Women with expected delivery dates in 1966 were recruited through maternity health centers. Cohort members living in northern Finland or in the capital area were invited to a clinical examination as well as questionnaire at age 31 years. DNA was extracted from blood samples given at the clinical examination. Informed consent for the use of the data including DNA was obtained from all subjects. The study was approved by the ethics committees in Oulu (Finland) and Oxford (UK) universities in accordance with the Declaration of Helsinki.

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NTR

Recruitment

In the Young Netherlands Twin Register (YNTR), twins are followed from birth onwards. Around every two to three years, a survey is sent out inquiring about physical and mental health. At ages 1, 2, 3, 5, 7, 10 and 12 years, the surveys are completed by the parents and/or teachers, from age 14 onward, twins and their non-twin siblings are asked to complete the surveys by themselves. At age 5 years of the twins, parents are asked a series of questions about allergies and rhinitis.[45] Adult and adolescent twins (ANTR) have been recruited through city councils and media, and complete a self-rating survey every few years. Surveys contain a series of questions about doctor diagnosed diseases and disorders. Subsamples of twin families have taken part in biobank and genotyping studies.

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RAINE

Recruitment

The Western Australian Pregnancy Cohort (Raine) Study is a prospective pregnancy cohort where 2900 were recruited from King Edward Memorial Hospital between 1989 and 1991. Data were collected throughout pregnancy and the children have been followed-up at ages 1, 2, 3, 5, 8, 10, 14, 17, 18, 20, and 23. Ethics approval for this study was obtained from King Edward Memorial Hospital and Princess Margaret Hospital. Participants were consented to being involved in this study prior to each follow-up.

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SAGE II

Recruitment

The Study of African Americans, Asthma, Genes & Environments (SAGE II) is an ongoing study of asthma in children and young adults coordinated from the University of California San Francisco. Recruitment protocols and the definition of allergic rhinitis were similar to GALA II with the only differences being that the

recruitment was restricted to San Francisco Bay Area and participants self-identified all four grandparents as African American.[46] In the current study, 385 cases of allergic rhinitis and 978 controls were analyzed.

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SAPALDIA

Recruitment

SAPALDIA is a population-based cohort from Switzerland that recruited subjects aged 18 to 60 from population registries in eight communities, representing the three largest language groups (German, French, Italian) as well as different levels of air pollution and degrees of urbanization**.** Subjects underwent spirometry and answered a detailed questionnaire on respiratory health, allergies, smoking history, and lifestyle factors in the baseline (year 1991) and follow-up (year 2002) examination. 6,055 subjects participated in both examinations and agreed to provide blood for genetic analysis. All subjects that were part of a nested asthma case-control sample subjected for genomewide genotyping in the context of the GABRIEL genome-wide association study on asthma formed the basis of the current study. In the current study, subjects were considered to be a case if they ever reported to have had allergic rhinitis at the baseline or follow-up examination. The analysis included 526 cases of allergic rhinitis and 921 controls.

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SAPPHIRE

Recruitment

The Study of Asthma Phenotypes and Pharmacogenomic Interactions by Race-ethnicity (SAPPHIRE) is an ongoing study that was approved by the Institutional Review Board of Henry Ford Health System. Study individuals included in the current study were members of a large health system, which serves southeast Michigan and all of the Detroit metropolitan statistical area. Individuals were 12-56 years of age and no prior diagnosis of congestive heart failure or chronic obstructive pulmonary disease. Patient recruitment included patients with and without a clinical diagnosis of asthma. Written informed consent was required at the time of enrolment as a condition for study participation. The exam at the time of enrollment included both a staff-administered questionnaire and lung function testing. For the current study, we analyzed only those SAPPHIRE participants who identified themselves as African American.

Acknowledgements and Funding

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UK Biobank

Recruitment

The UK Biobank study is a prospective study of 502,682 volunteer participants aged 40-69 recruited at 22 centers across the UK between 2006 and 2010.[47] A subset of 152,566 individuals with available genotype data were included in the analysis. All particpiants have given informed consent for the storage and use of their data for research.

Acknowledgements and Funding

This research has been conducted using the UK Biobank Resource. L Paternoster was supported by a UK Medical Research Council Fellowship (MR/J012165/1) and works in a unit which receives funding from the UK Medical Research Council (MC_UU_12013/1 & MC_UU_12013/4).

Barcelona Supercomputing Center

Acknowledgements and Funding

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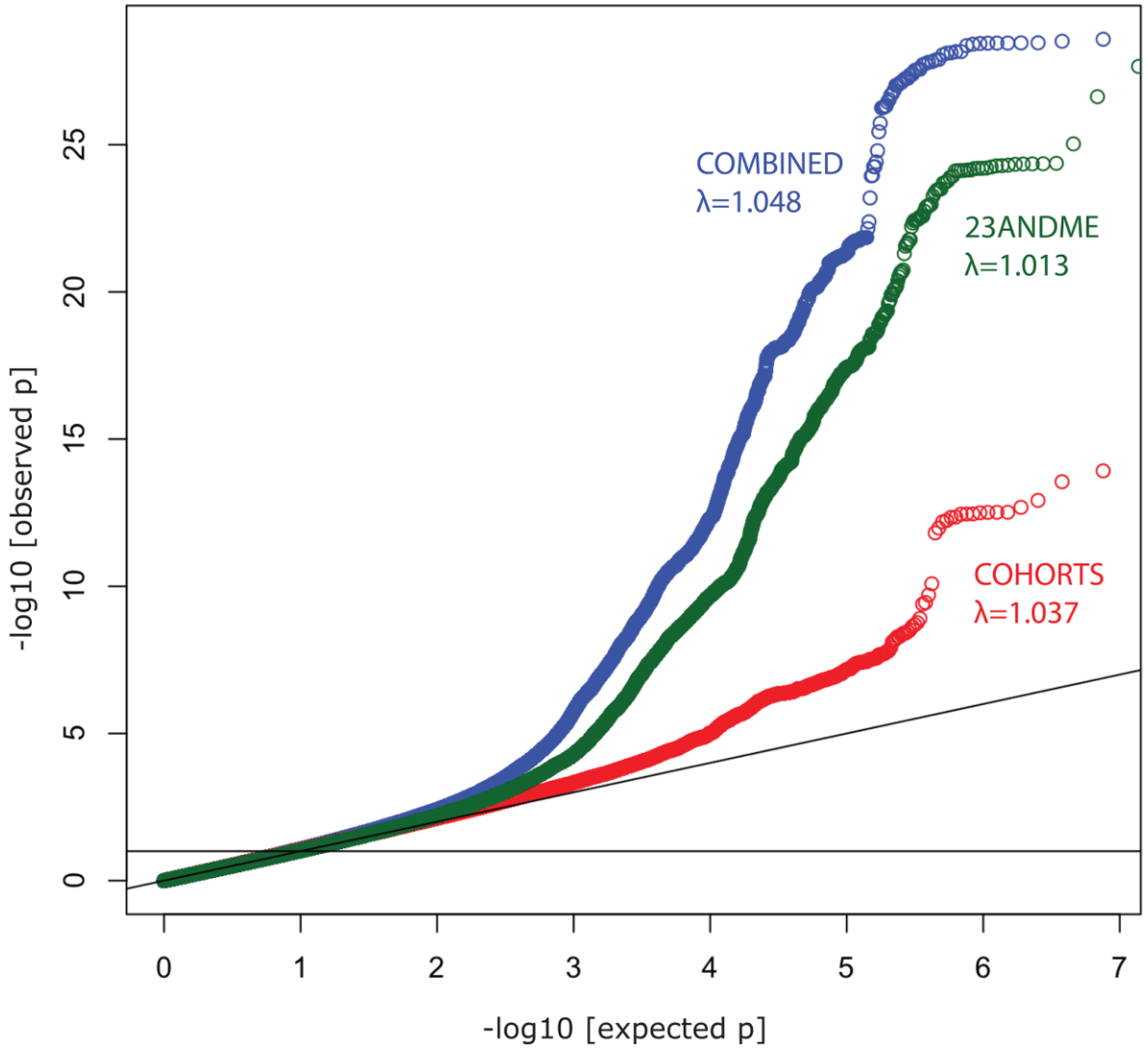
Supplementary Figure 1

QQ-plot for the discovery phase of the allergic rhinitis GWAS, based on p-values from an inverse variance weighted fixed-effect meta-analysis of genetic marker association of 16,531,985 genetic markers to allergic rhinitis from the discovery phase, including 212,120 individuals). λ indicates the genomic inflation rate.



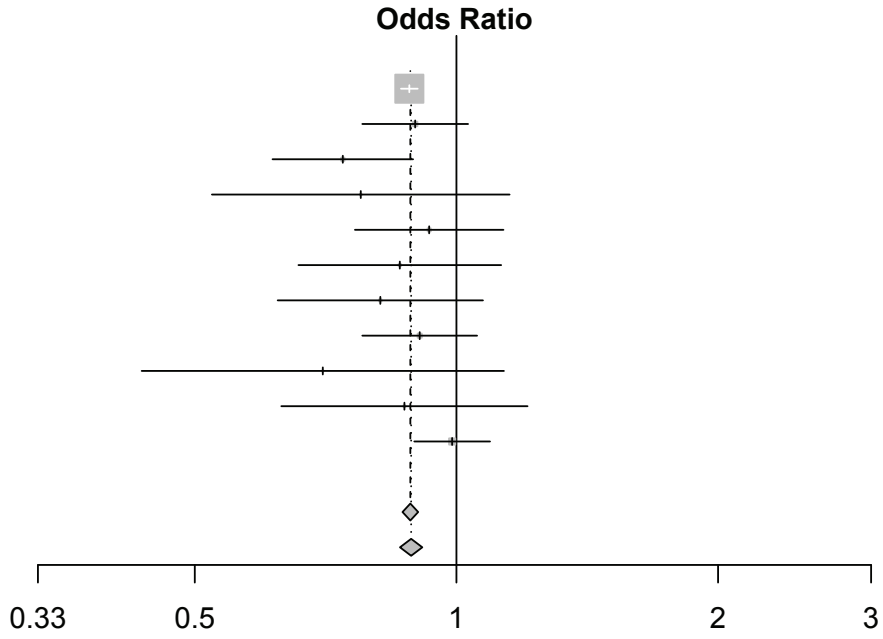
Supplementary Figure 2

Forest plots from the discovery phase for markers previously associated to allergy, including weights, estimates and 95% confidence intervals for inverse variance weighted fixed and random effects meta-analyses from genetic marker association of 16,531,985 genetic markers to allergic rhinitis from the discovery phase, including 212,120 individuals.

rs34004019[G]

Study	Weight (fixed)	Weight (random)	OR	95%−CI
23andme	87.3%	75.0%	0.88	[0.86; 0.90]
AAGC(QIMR)	2.2%	4.3%	0.90	[0.78; 1.03]
ALSPAC	1.2%	2.5%	0.74	[0.61; 0.89]
EVE (CAG/CSGA)	0.3%	0.6%	0.78	[0.52; 1.15]
EVE (CHS)	1.1%	2.2%	0.93	[0.76; 1.13]
GENR	0.6%	1.2%	0.86	[0.66; 1.13]
GINI/LISA	0.6%	1.2%	0.82	[0.62; 1.07]
GOYA	1.9%	3.7%	0.91	[0.78; 1.06]
INMA	0.2%	0.4%	0.70	[0.43; 1.13]
MAAS	0.4%	0.8%	0.87	[0.63; 1.21]
NFBC1966	4.3%	8.2%	0.99	[0.89; 1.09]
Fixed effect model	**100.0%**	**−−**	**0.89**	**[0.87; 0.90]**
Random effects model	**−−**	**100.0%**	**0.89**	**[0.86; 0.91]**

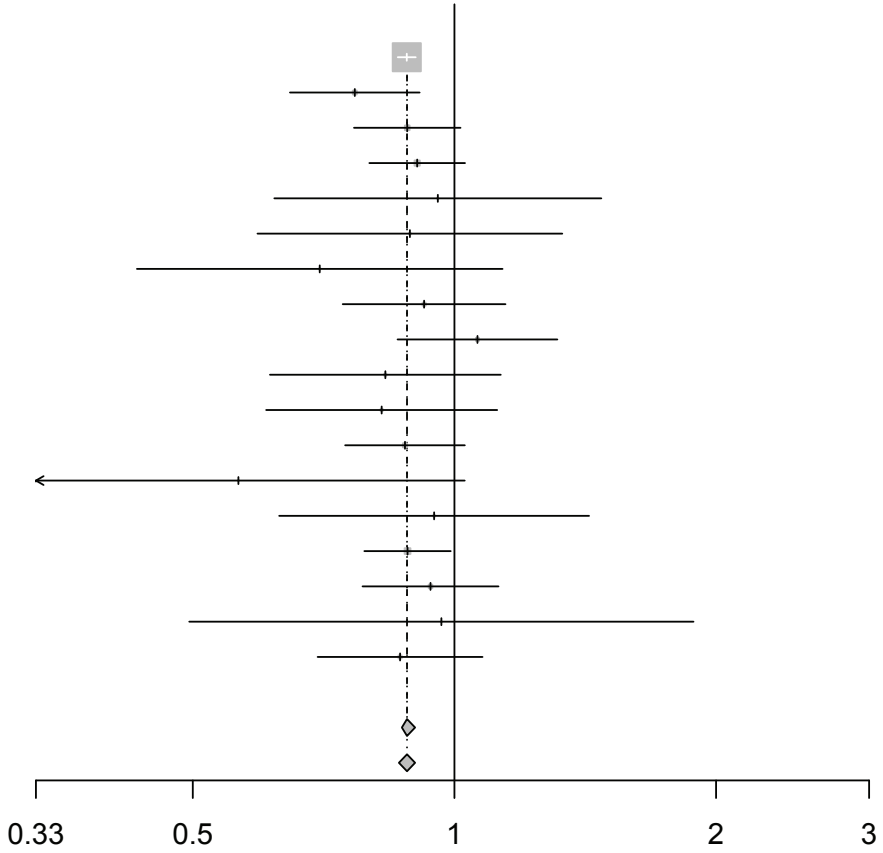
Heterogeneity: I^2 = 4%, p = 0.41



rs950881[T]

Study	Weight (fixed)	Weight (random)	OR	95%−CI
23andme	81.4%	81.4%	0.88	[0.86; 0.90]
AAGC(QIMR)	1.6%	1.6%	0.77	[0.65; 0.91]
ALSPAC	2.3%	2.3%	0.88	[0.77; 1.02]
B58C	2.9%	2.9%	0.91	[0.80; 1.03]
BAMSE	0.2%	0.2%	0.96	[0.62; 1.48]
COPSAC2000	0.3%	0.3%	0.89	[0.59; 1.33]
EVE (CAG/CSGA)	0.2%	0.2%	0.70	[0.43; 1.14]
EVE (CHS)	1.0%	1.0%	0.92	[0.74; 1.14]
GENR	1.0%	1.0%	1.06	[0.86; 1.31]
GENUFAD	0.5%	0.5%	0.83	[0.61; 1.13]
GINI/LISA	0.5%	0.5%	0.82	[0.61; 1.12]
GOYA	1.8%	1.8%	0.88	[0.75; 1.03]
INMA	0.1%	0.1%	0.56	[0.31; 1.03]
MAAS	0.3%	0.3%	0.95	[0.63; 1.43]
NFBC1966	3.5%	3.5%	0.88	[0.79; 0.99]
NTR (adults)	1.4%	1.4%	0.94	[0.78; 1.12]
NTR (children)	0.1%	0.1%	0.97	[0.50; 1.88]
RAINE	1.0%	1.0%	0.87	[0.70; 1.08]
Fixed effect model	**100.0%**	**−−**	**0.88**	**[0.87; 0.90]**
Random effects model	**−−**	**100.0%**	**0.88**	**[0.86; 0.90]**

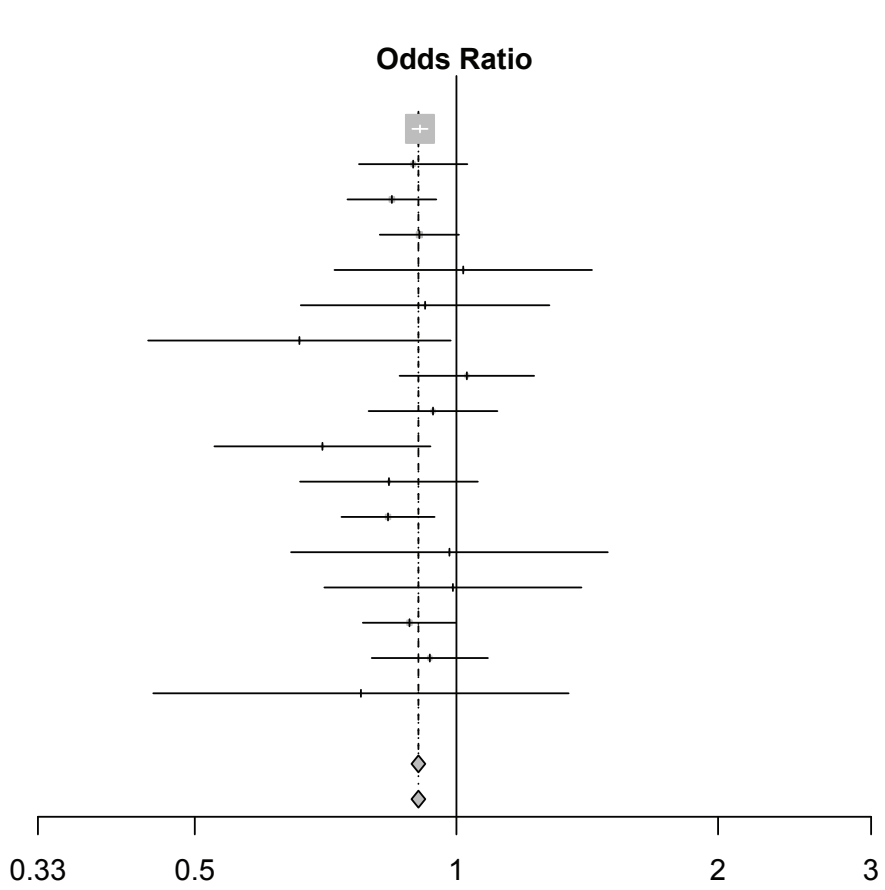
Heterogeneity: I^2 = 0%, p = 0.90



rs5743618[A]

Study	Weight (fixed)	Weight (random)	OR	95%−CI
23andme	82.5%	82.5%	0.91	[0.89; 0.93]
AAGC(QIMR)	1.6%	1.6%	0.89	[0.77; 1.03]
ALSPAC	2.4%	2.4%	0.84	[0.75; 0.95]
B58C	3.0%	3.0%	0.91	[0.82; 1.01]
BAMSE	0.3%	0.3%	1.02	[0.72; 1.43]
COPSAC2000	0.3%	0.3%	0.92	[0.66; 1.28]
EVE (CAG/CSGA)	0.2%	0.2%	0.66	[0.44; 0.98]
EVE (CHS)	1.1%	1.1%	1.03	[0.86; 1.23]
GENR	1.2%	1.2%	0.94	[0.79; 1.11]
GENUFAD	0.4%	0.4%	0.70	[0.53; 0.93]
GINI/LISA	0.6%	0.6%	0.84	[0.66; 1.06]
GOYA	2.2%	2.2%	0.83	[0.74; 0.94]
INMA	0.2%	0.2%	0.98	[0.65; 1.49]
MAAS	0.3%	0.3%	0.99	[0.70; 1.39]
NFBC1966	2.2%	2.2%	0.88	[0.78; 1.00]
NTR (adults)	1.4%	1.4%	0.93	[0.80; 1.09]
NTR (children)	0.1%	0.1%	0.78	[0.45; 1.35]
Fixed effect model	**100.0%**	**−−**	**0.90**	**[0.89; 0.92]**
Random effects model	**−−**	**100.0%**	**0.90**	**[0.89; 0.92]**

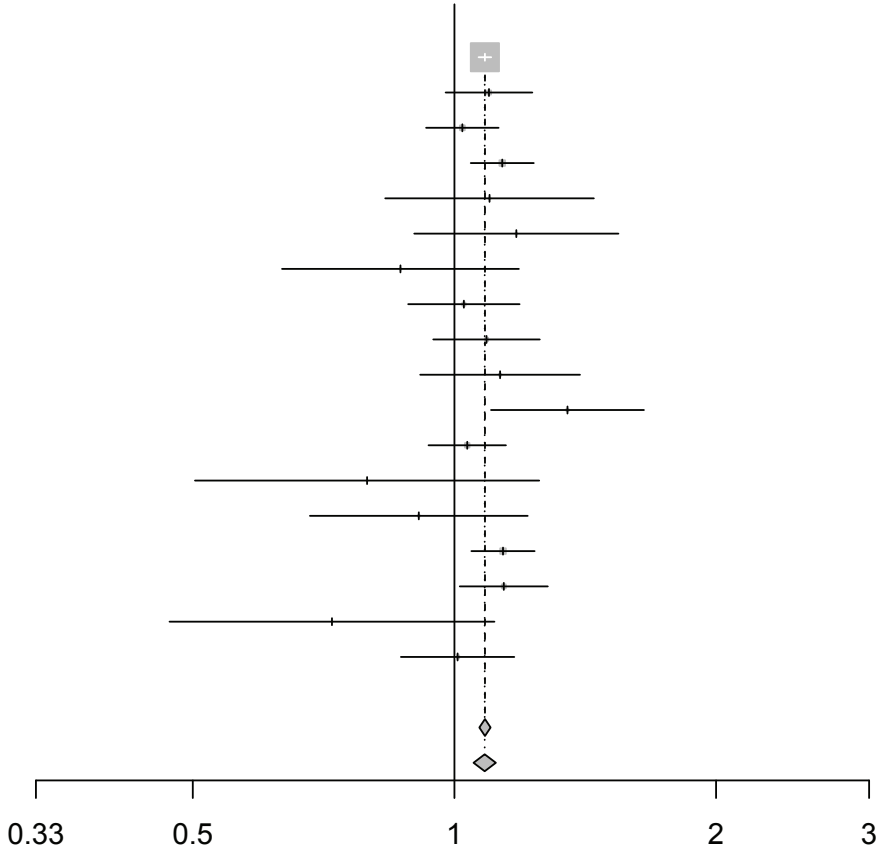
Heterogeneity: I^2 = 0%, p = 0.69



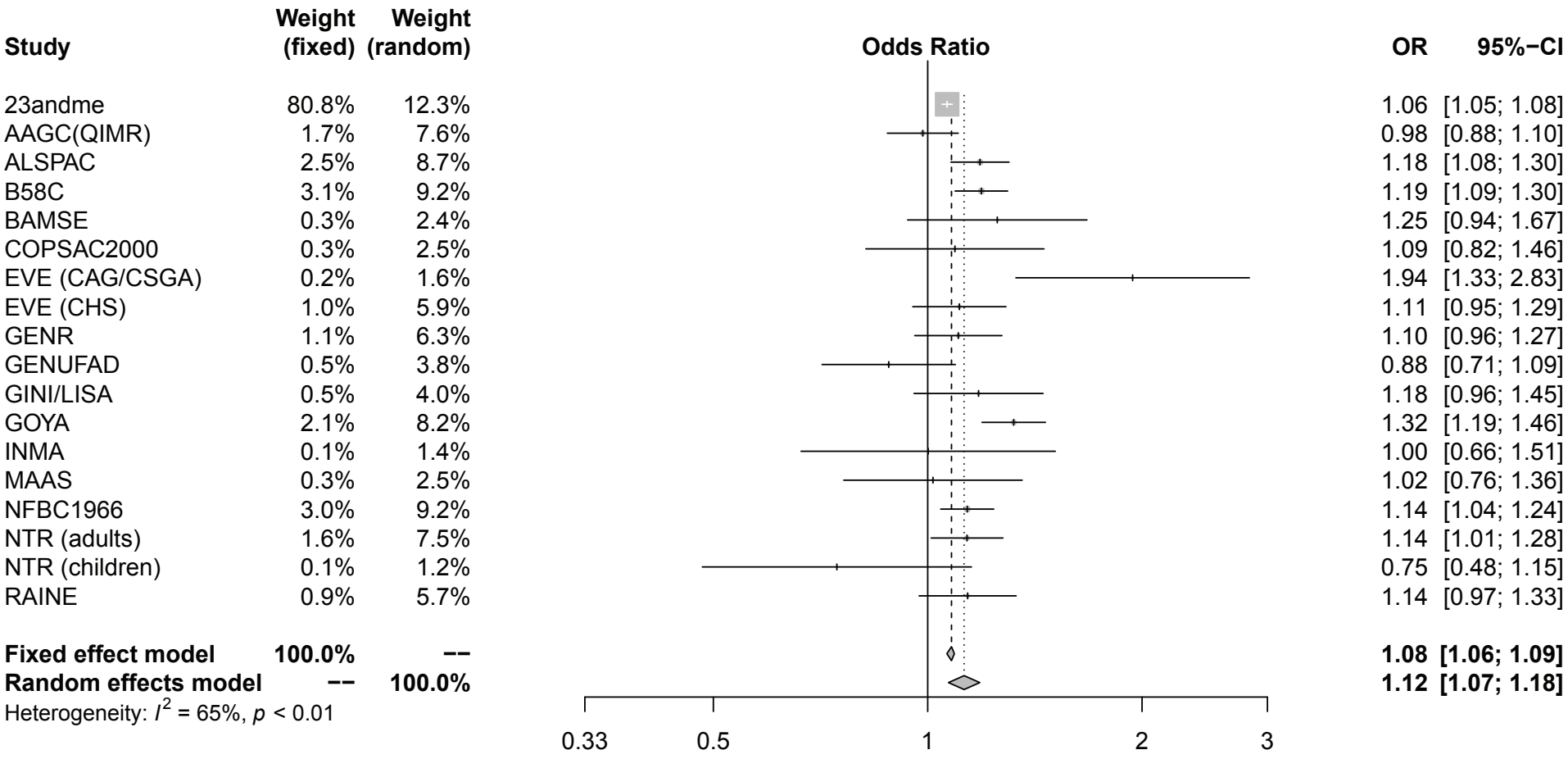
rs1438673[C]

Study	Weight (fixed)	Weight (random)	OR	95%−CI
23andme	80.2%	35.3%	1.08	[1.07; 1.10]
AAGC(QIMR)	1.7%	5.7%	1.10	[0.98; 1.23]
ALSPAC	2.4%	7.6%	1.02	[0.93; 1.12]
B58C	3.2%	9.5%	1.14	[1.04; 1.23]
BAMSE	0.3%	1.1%	1.10	[0.83; 1.45]
COPSAC2000	0.3%	1.2%	1.18	[0.90; 1.54]
EVE (CAG/CSGA)	0.2%	0.9%	0.87	[0.63; 1.19]
EVE (CHS)	1.0%	3.6%	1.03	[0.88; 1.19]
GENR	1.1%	3.9%	1.09	[0.95; 1.25]
GENUFAD	0.5%	1.9%	1.13	[0.91; 1.39]
GINI/LISA	0.5%	2.0%	1.35	[1.10; 1.65]
GOYA	2.1%	6.9%	1.03	[0.93; 1.15]
INMA	0.1%	0.4%	0.79	[0.50; 1.25]
MAAS	0.3%	1.0%	0.91	[0.68; 1.21]
NFBC1966	3.2%	9.5%	1.14	[1.05; 1.24]
NTR (adults)	1.6%	5.5%	1.14	[1.01; 1.28]
NTR (children)	0.1%	0.5%	0.72	[0.47; 1.11]
RAINE	1.0%	3.5%	1.01	[0.87; 1.17]
Fixed effect model	**100.0%**	**−−**	**1.08**	**[1.07; 1.10]**
Random effects model	**−−**	**100.0%**	**1.08**	**[1.05; 1.12]**

Heterogeneity: I^2 = 17%, p = 0.25

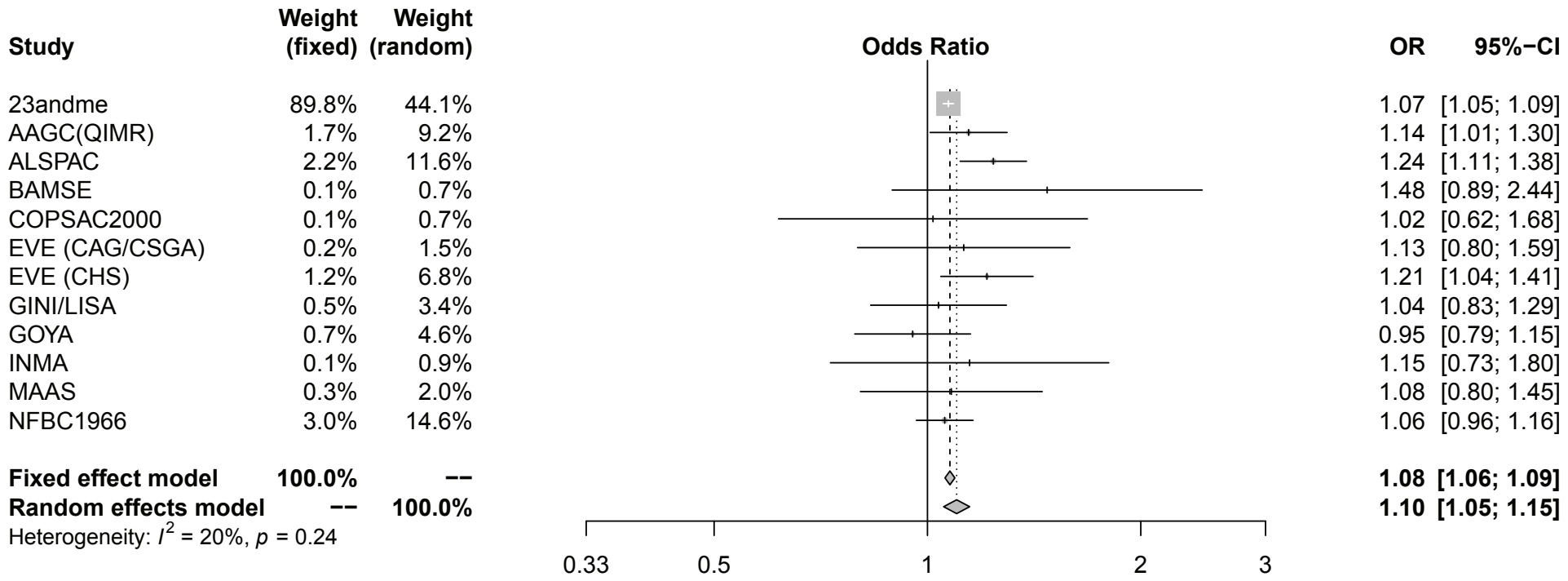


rs7936323[A]

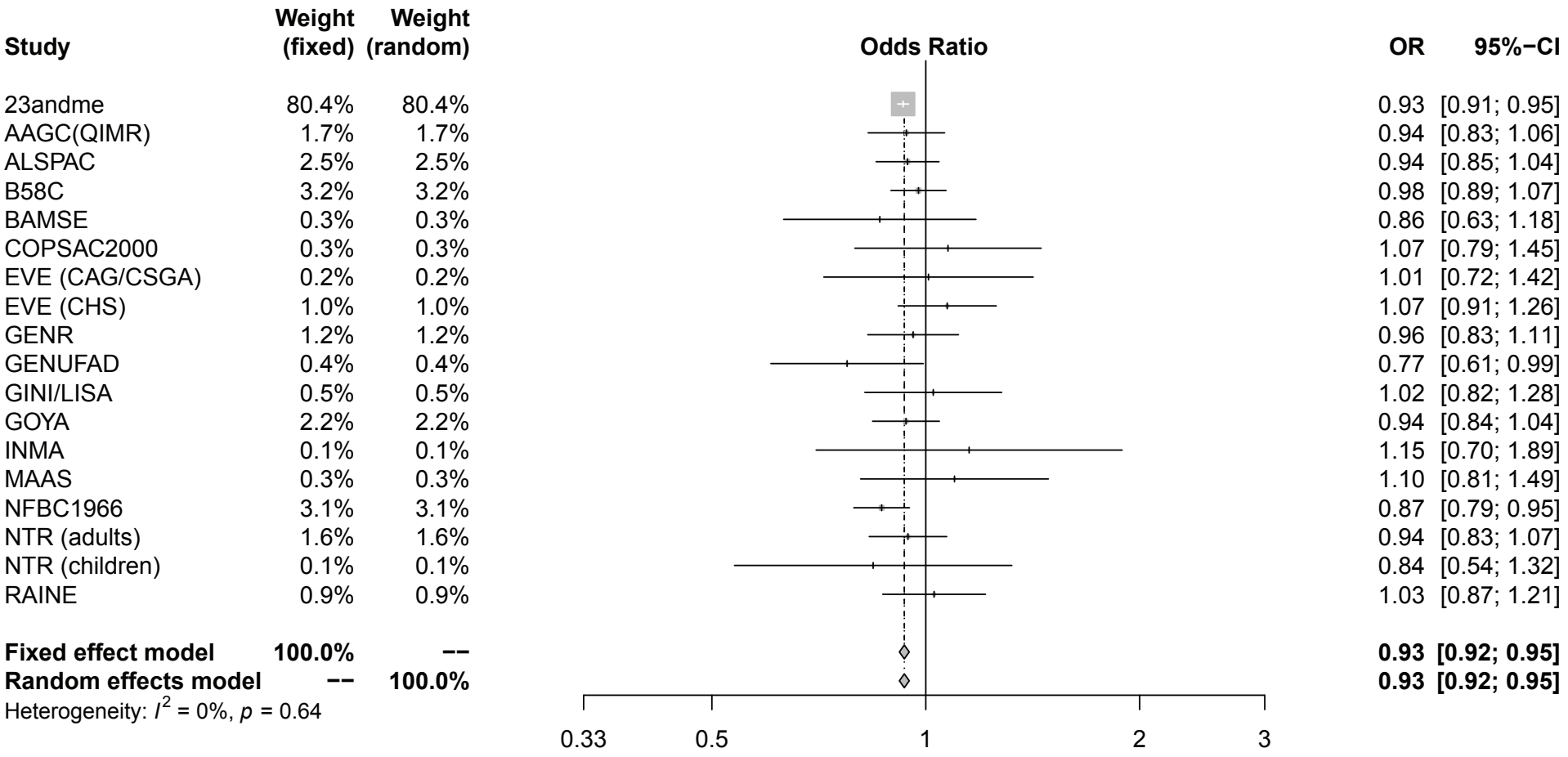


Heterogeneity: I^2 = 65%, p < 0.01

rs2428494[A]


Study
Weight (fixed)
Weight (random)
Odds Ratio
OR
95%−CI
23andme 89.8% 44.1% 1.07 [1.05; 1.09]
AAGC(QIMR) 1.7% 9.2% 1.14 [1.01; 1.30]
ALSPAC 2.2% 11.6% 1.24 [1.11; 1.38]
BAMSE 0.1% 0.7% 1.48 [0.89; 2.44]
COPSAC2000 0.1% 0.7% 1.02 [0.62; 1.68]
EVE (CAG/CSGA) 0.2% 1.5% 1.13 [0.80; 1.59]
EVE (CHS) 1.2% 6.8% 1.21 [1.04; 1.41]
GINI/LISA 0.5% 3.4% 1.04 [0.83; 1.29]
GOYA 0.7% 4.6% 0.95 [0.79; 1.15]
INMA 0.1% 0.9% 1.15 [0.73; 1.80]
MAAS 0.3% 2.0% 1.08 [0.80; 1.45]
NFBC1966 3.0% 14.6% 1.06 [0.96; 1.16]
Fixed effect model 100.0% −− 1.08 [1.06; 1.09]
Random effects model −− 100.0% 1.10 [1.05; 1.15]
Heterogeneity: I^2 = 20%, p = 0.24
0.33
0.5
1
2
3

rs11644510[T]

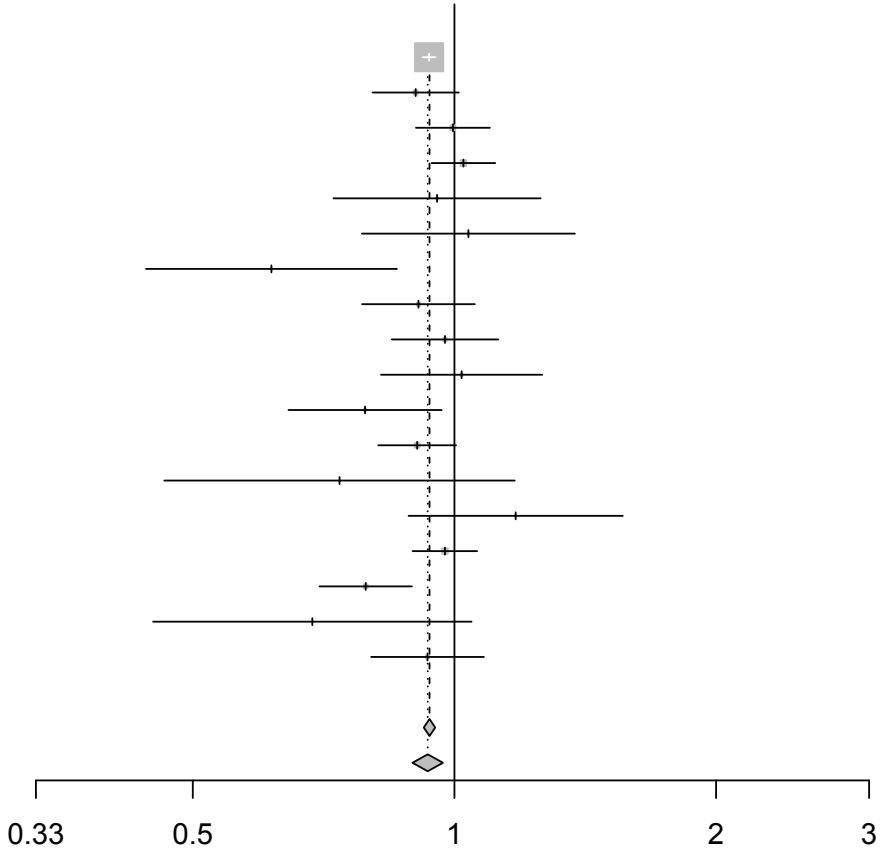


Heterogeneity: I^2 = 0%, p = 0.64

rs12939457[C]

Study	Weight (fixed)	Weight (random)	OR	95%−CI
23andme	79.9%	17.5%	0.94	[0.92; 0.95]
AAGC(QIMR)	1.8%	7.4%	0.90	[0.81; 1.01]
ALSPAC	2.4%	8.8%	1.00	[0.90; 1.10]
B58C	3.3%	10.2%	1.02	[0.94; 1.11]
BAMSE	0.3%	1.9%	0.96	[0.73; 1.26]
COPSAC2000	0.3%	1.8%	1.04	[0.78; 1.38]
EVE (CAG/CSGA)	0.2%	1.4%	0.62	[0.44; 0.86]
EVE (CHS)	1.0%	5.2%	0.91	[0.78; 1.06]
GENR	1.2%	5.7%	0.98	[0.85; 1.12]
GENUFAD	0.5%	3.0%	1.02	[0.82; 1.26]
GINI/LISA	0.6%	3.3%	0.79	[0.64; 0.97]
GOYA	2.2%	8.3%	0.91	[0.82; 1.00]
INMA	0.1%	0.7%	0.74	[0.46; 1.17]
MAAS	0.3%	1.8%	1.18	[0.89; 1.56]
NFBC1966	3.2%	10.0%	0.98	[0.90; 1.06]
NTR (adults)	1.5%	6.8%	0.79	[0.70; 0.89]
NTR (children)	0.1%	0.9%	0.69	[0.45; 1.05]
RAINE	1.0%	5.2%	0.93	[0.80; 1.08]
Fixed effect model	**100.0%**	**−−**	**0.94**	**[0.92; 0.95]**
Random effects model	**−−**	**100.0%**	**0.93**	**[0.89; 0.97]**

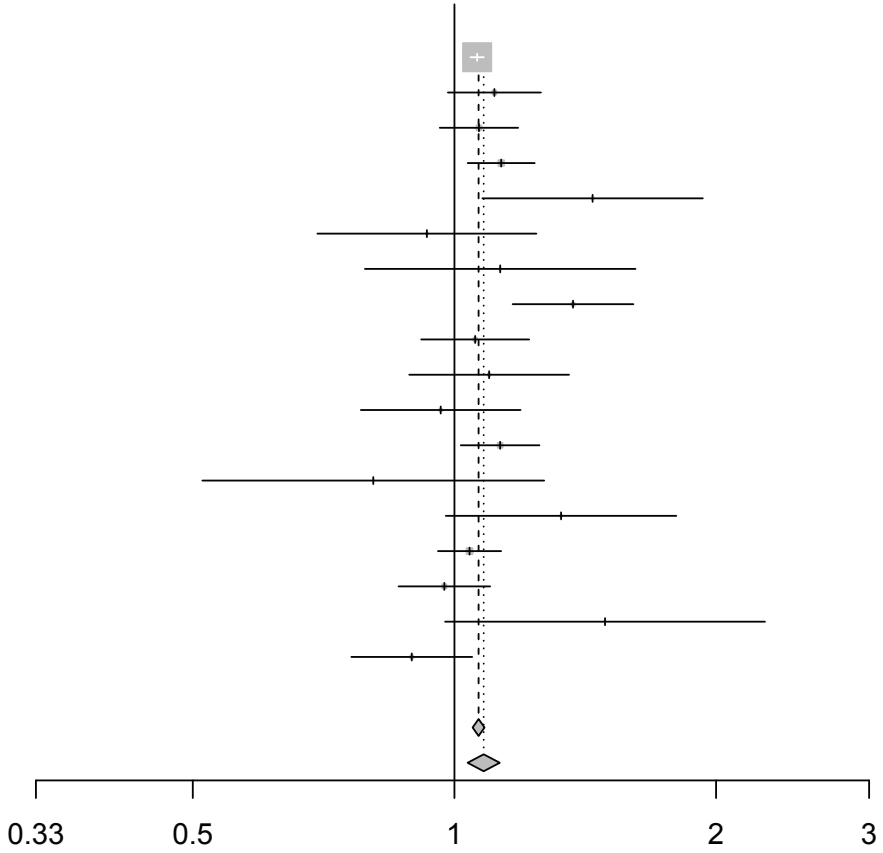
Heterogeneity: I^2 = 45%, p = 0.02



rs148505069[G]

Study	Weight (fixed)	Weight (random)	OR	95%−CI
23andme	79.7%	17.0%	1.06	[1.04; 1.08]
AAGC(QIMR)	1.6%	7.1%	1.11	[0.98; 1.26]
ALSPAC	2.3%	8.6%	1.07	[0.96; 1.18]
B58C	3.2%	9.9%	1.13	[1.04; 1.24]
BAMSE	0.3%	1.9%	1.44	[1.08; 1.93]
COPSAC2000	0.3%	1.9%	0.93	[0.70; 1.24]
EVE (CAG/CSGA)	0.2%	1.3%	1.13	[0.79; 1.62]
EVE (CHS)	1.0%	5.0%	1.37	[1.17; 1.61]
GENR	1.2%	5.9%	1.06	[0.92; 1.22]
GENUFAD	0.6%	3.3%	1.10	[0.89; 1.35]
GINI/LISA	0.6%	3.3%	0.96	[0.78; 1.19]
GOYA	2.3%	8.5%	1.13	[1.02; 1.25]
INMA	0.1%	0.8%	0.81	[0.51; 1.27]
MAAS	0.3%	1.7%	1.33	[0.98; 1.80]
NFBC1966	3.6%	10.4%	1.04	[0.96; 1.13]
NTR (adults)	1.7%	7.2%	0.97	[0.86; 1.10]
NTR (children)	0.1%	1.0%	1.49	[0.98; 2.28]
RAINE	1.0%	5.0%	0.89	[0.76; 1.05]
Fixed effect model	**100.0%**	**--**	**1.07**	**[1.05; 1.08]**
Random effects model	**--**	**100.0%**	**1.08**	**[1.04; 1.13]**

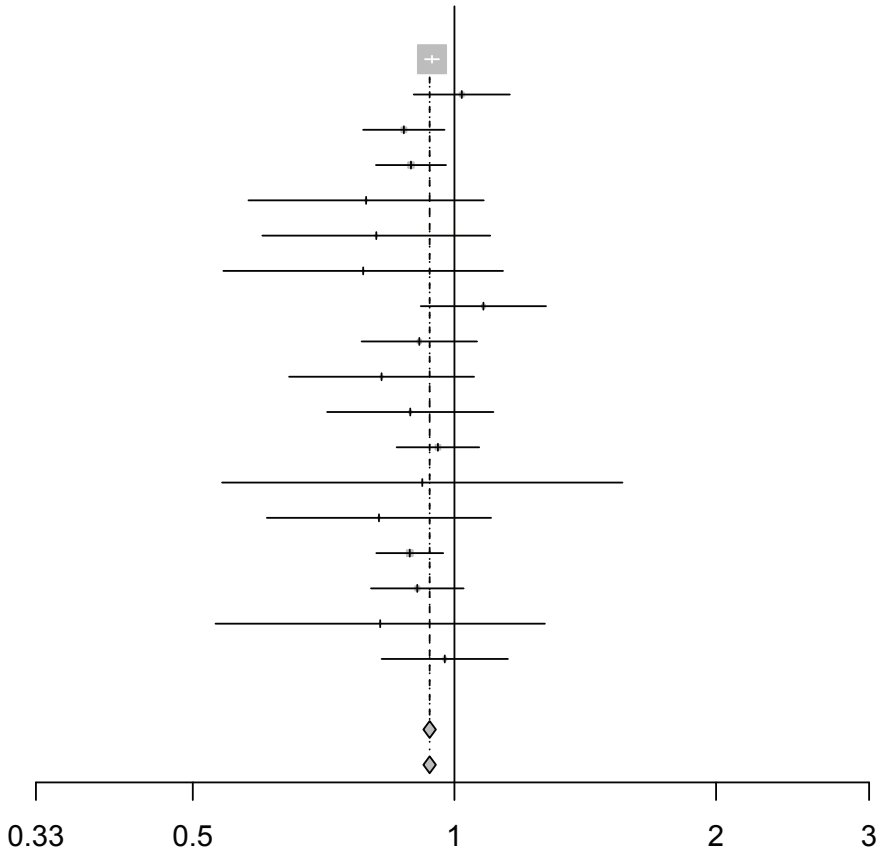
Heterogeneity: I^2 = 47%, p = 0.02



rs13395467[G]

Study	Weight (fixed)	Weight (random)	OR	95%−CI
23andme	79.6%	79.6%	0.94	[0.92; 0.96]
AAGC(QIMR)	1.7%	1.7%	1.02	[0.90; 1.16]
ALSPAC	2.4%	2.4%	0.87	[0.79; 0.97]
B58C	3.2%	3.2%	0.89	[0.81; 0.98]
BAMSE	0.3%	0.3%	0.79	[0.58; 1.08]
COPSAC2000	0.3%	0.3%	0.81	[0.60; 1.10]
EVE (CAG/CSGA)	0.2%	0.2%	0.79	[0.54; 1.14]
EVE (CHS)	1.0%	1.0%	1.08	[0.91; 1.27]
GENR	1.2%	1.2%	0.91	[0.78; 1.06]
GENUFAD	0.5%	0.5%	0.82	[0.65; 1.05]
GINI/LISA	0.6%	0.6%	0.89	[0.71; 1.11]
GOYA	2.3%	2.3%	0.96	[0.86; 1.07]
INMA	0.1%	0.1%	0.92	[0.54; 1.56]
MAAS	0.3%	0.3%	0.82	[0.61; 1.10]
NFBC1966	3.5%	3.5%	0.89	[0.81; 0.97]
NTR (adults)	1.8%	1.8%	0.91	[0.80; 1.02]
NTR (children)	0.1%	0.1%	0.82	[0.53; 1.27]
RAINE	1.0%	1.0%	0.97	[0.82; 1.15]
Fixed effect model	**100.0%**	**−−**	**0.94**	**[0.92; 0.95]**
Random effects model	**−−**	**100.0%**	**0.94**	**[0.92; 0.95]**

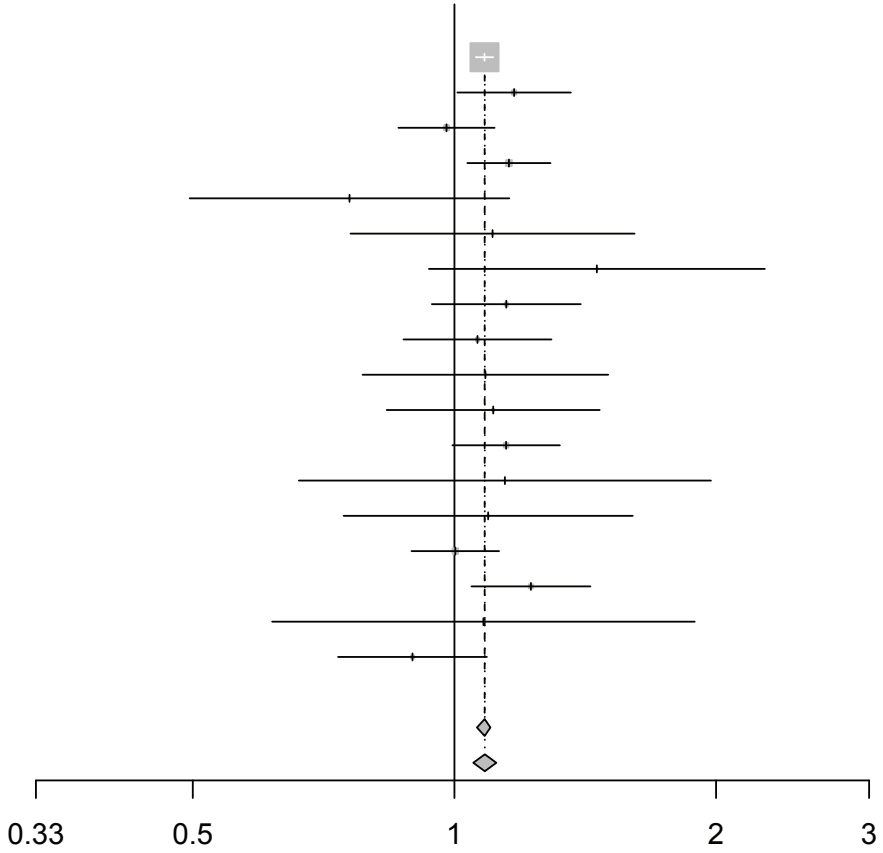
Heterogeneity: I^2 = 0%, p = 0.60



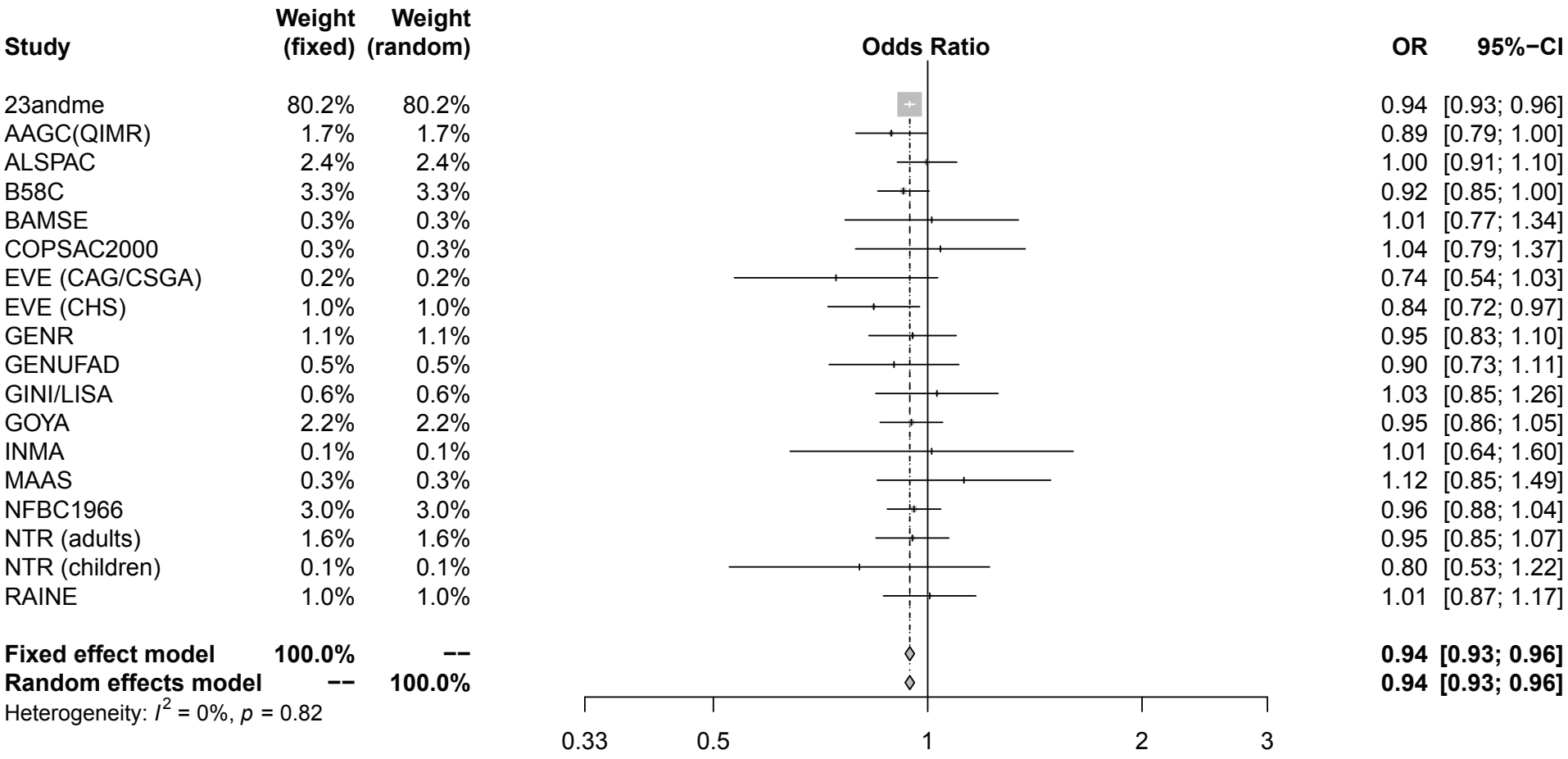
rs9775039[A]

Study	Weight (fixed)	Weight (random)	OR	95%−CI
23andme	79.7%	57.3%	1.08	[1.06; 1.11]
AAGC(QIMR)	1.9%	3.9%	1.17	[1.01; 1.36]
ALSPAC	2.6%	5.4%	0.98	[0.86; 1.11]
B58C	3.5%	7.1%	1.16	[1.03; 1.29]
BAMSE	0.2%	0.5%	0.76	[0.50; 1.16]
COPSAC2000	0.3%	0.7%	1.11	[0.76; 1.61]
EVE (CAG/CSGA)	0.2%	0.5%	1.46	[0.93; 2.28]
EVE (CHS)	1.1%	2.3%	1.15	[0.94; 1.40]
GENR	1.1%	2.4%	1.06	[0.87; 1.29]
GENUFAD	0.4%	0.9%	1.09	[0.78; 1.50]
GINI/LISA	0.5%	1.2%	1.11	[0.84; 1.47]
GOYA	2.1%	4.4%	1.15	[0.99; 1.32]
INMA	0.1%	0.3%	1.14	[0.66; 1.97]
MAAS	0.3%	0.6%	1.09	[0.75; 1.60]
NFBC1966	3.1%	6.4%	1.00	[0.89; 1.13]
NTR (adults)	1.7%	3.6%	1.22	[1.05; 1.43]
NTR (children)	0.1%	0.3%	1.08	[0.62; 1.89]
RAINE	1.1%	2.3%	0.89	[0.73; 1.09]
Fixed effect model	**100.0%**	**−−**	**1.08**	**[1.06; 1.10]**
Random effects model	**−−**	**100.0%**	**1.08**	**[1.05; 1.12]**

Heterogeneity: I^2 = 5%, p = 0.39



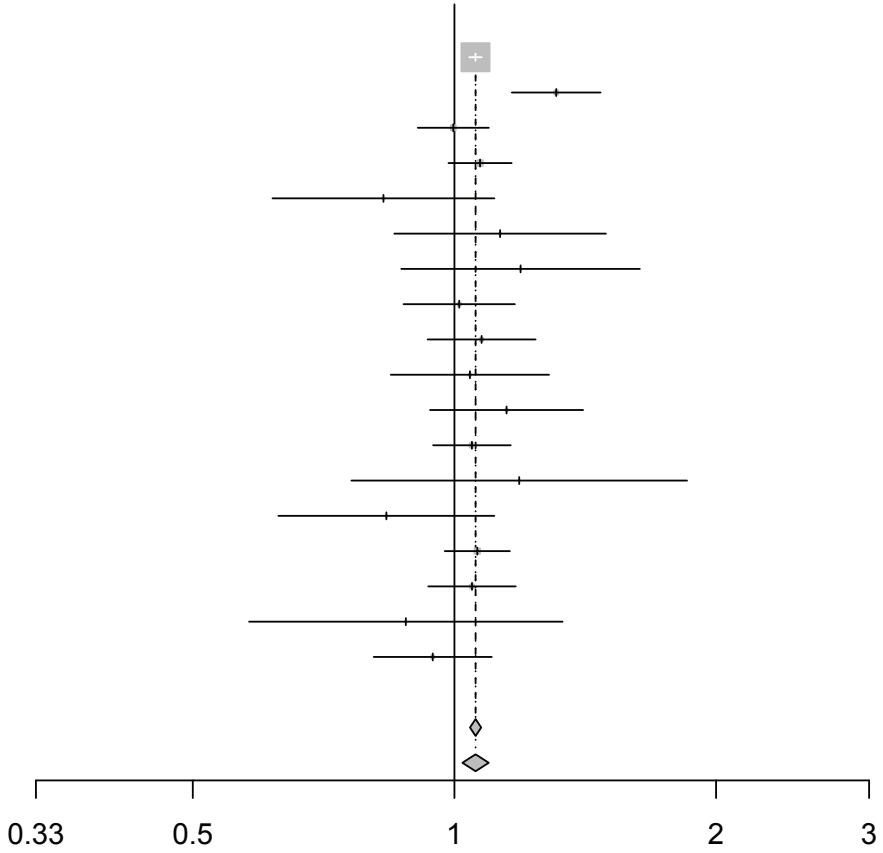
rs2164068[A]


Study
Weight (fixed)
Weight (random)
Odds Ratio
OR
95%−CI
23andme 80.2% 80.2% 0.94 [0.93; 0.96]
AAGC(QIMR) 1.7% 1.7% 0.89 [0.79; 1.00]
ALSPAC 2.4% 2.4% 1.00 [0.91; 1.10]
B58C 3.3% 3.3% 0.92 [0.85; 1.00]
BAMSE 0.3% 0.3% 1.01 [0.77; 1.34]
COPSAC2000 0.3% 0.3% 1.04 [0.79; 1.37]
EVE (CAG/CSGA) 0.2% 0.2% 0.74 [0.54; 1.03]
EVE (CHS) 1.0% 1.0% 0.84 [0.72; 0.97]
GENR 1.1% 1.1% 0.95 [0.83; 1.10]
GENUFAD 0.5% 0.5% 0.90 [0.73; 1.11]
GINI/LISA 0.6% 0.6% 1.03 [0.85; 1.26]
GOYA 2.2% 2.2% 0.95 [0.86; 1.05]
INMA 0.1% 0.1% 1.01 [0.64; 1.60]
MAAS 0.3% 0.3% 1.12 [0.85; 1.49]
NFBC1966 3.0% 3.0% 0.96 [0.88; 1.04]
NTR (adults) 1.6% 1.6% 0.95 [0.85; 1.07]
NTR (children) 0.1% 0.1% 0.80 [0.53; 1.22]
RAINE 1.0% 1.0% 1.01 [0.87; 1.17]
Fixed effect model 100.0% −− 0.94 [0.93; 0.96]
Random effects model −− 100.0% 0.94 [0.93; 0.96]
Heterogeneity: I^2 = 0%, p = 0.82
0.33
0.5
1
2
3

rs2030519[G]

Study	Weight (fixed)	Weight (random)	OR	95%−CI
23andme	80.6%	24.1%	1.06	[1.04; 1.08]
AAGC(QIMR)	1.6%	6.6%	1.31	[1.16; 1.47]
ALSPAC	2.5%	8.9%	1.00	[0.91; 1.10]
B58C	3.2%	10.3%	1.07	[0.98; 1.16]
BAMSE	0.3%	1.3%	0.83	[0.62; 1.11]
COPSAC2000	0.3%	1.5%	1.13	[0.85; 1.49]
EVE (CAG/CSGA)	0.2%	1.2%	1.19	[0.87; 1.63]
EVE (CHS)	1.0%	4.6%	1.01	[0.87; 1.17]
GENR	1.1%	4.8%	1.07	[0.93; 1.24]
GENUFAD	0.5%	2.5%	1.04	[0.84; 1.28]
GINI/LISA	0.5%	2.7%	1.15	[0.94; 1.41]
GOYA	2.1%	7.9%	1.05	[0.95; 1.16]
INMA	0.1%	0.6%	1.19	[0.76; 1.85]
MAAS	0.3%	1.4%	0.84	[0.63; 1.11]
NFBC1966	3.0%	10.0%	1.06	[0.97; 1.16]
NTR (adults)	1.7%	6.7%	1.05	[0.93; 1.18]
NTR (children)	0.1%	0.7%	0.88	[0.58; 1.33]
RAINE	0.9%	4.2%	0.94	[0.81; 1.10]
Fixed effect model	**100.0%**	**−−**	**1.06**	**[1.04; 1.07]**
Random effects model	**−−**	**100.0%**	**1.06**	**[1.02; 1.10]**

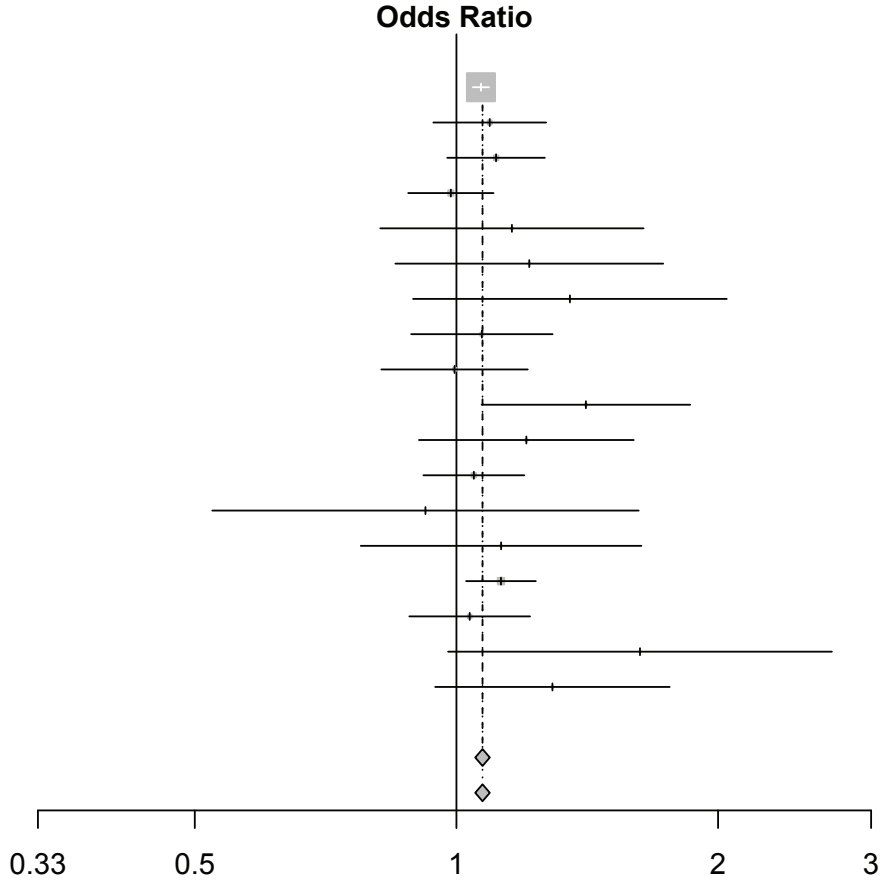
Heterogeneity: I^2 = 30%, p = 0.11



rs11256017[T]

Study	Weight (fixed)	Weight (random)	OR	95%−CI
23andme	80.5%	80.5%	1.07	[1.04; 1.09]
AAGC(QIMR)	1.7%	1.7%	1.09	[0.94; 1.27]
ALSPAC	2.2%	2.2%	1.11	[0.98; 1.26]
B58C	2.9%	2.9%	0.99	[0.88; 1.10]
BAMSE	0.3%	0.3%	1.16	[0.82; 1.64]
COPSAC2000	0.3%	0.3%	1.21	[0.85; 1.73]
EVE (CAG/CSGA)	0.2%	0.2%	1.35	[0.89; 2.05]
EVE (CHS)	1.1%	1.1%	1.07	[0.89; 1.29]
GENR	1.0%	1.0%	1.00	[0.82; 1.21]
GENUFAD	0.5%	0.5%	1.41	[1.07; 1.86]
GINI/LISA	0.5%	0.5%	1.20	[0.91; 1.60]
GOYA	2.1%	2.1%	1.05	[0.92; 1.20]
INMA	0.1%	0.1%	0.92	[0.52; 1.62]
MAAS	0.3%	0.3%	1.13	[0.78; 1.63]
NFBC1966	4.4%	4.4%	1.13	[1.03; 1.23]
NTR (adults)	1.5%	1.5%	1.04	[0.88; 1.22]
NTR (children)	0.1%	0.1%	1.63	[0.98; 2.70]
RAINE	0.4%	0.4%	1.29	[0.95; 1.76]
Fixed effect model	**100.0%**	**−−**	**1.07**	**[1.05; 1.09]**
Random effects model	**−−**	**100.0%**	**1.07**	**[1.05; 1.09]**

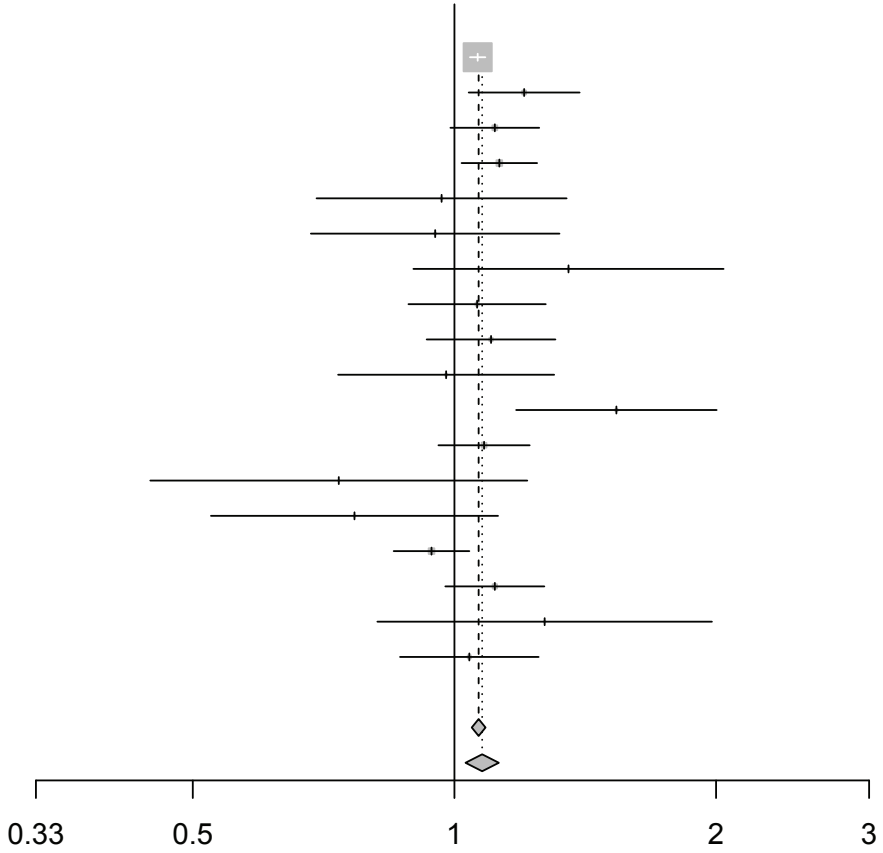
Heterogeneity: I^2 = 0%, p = 0.59



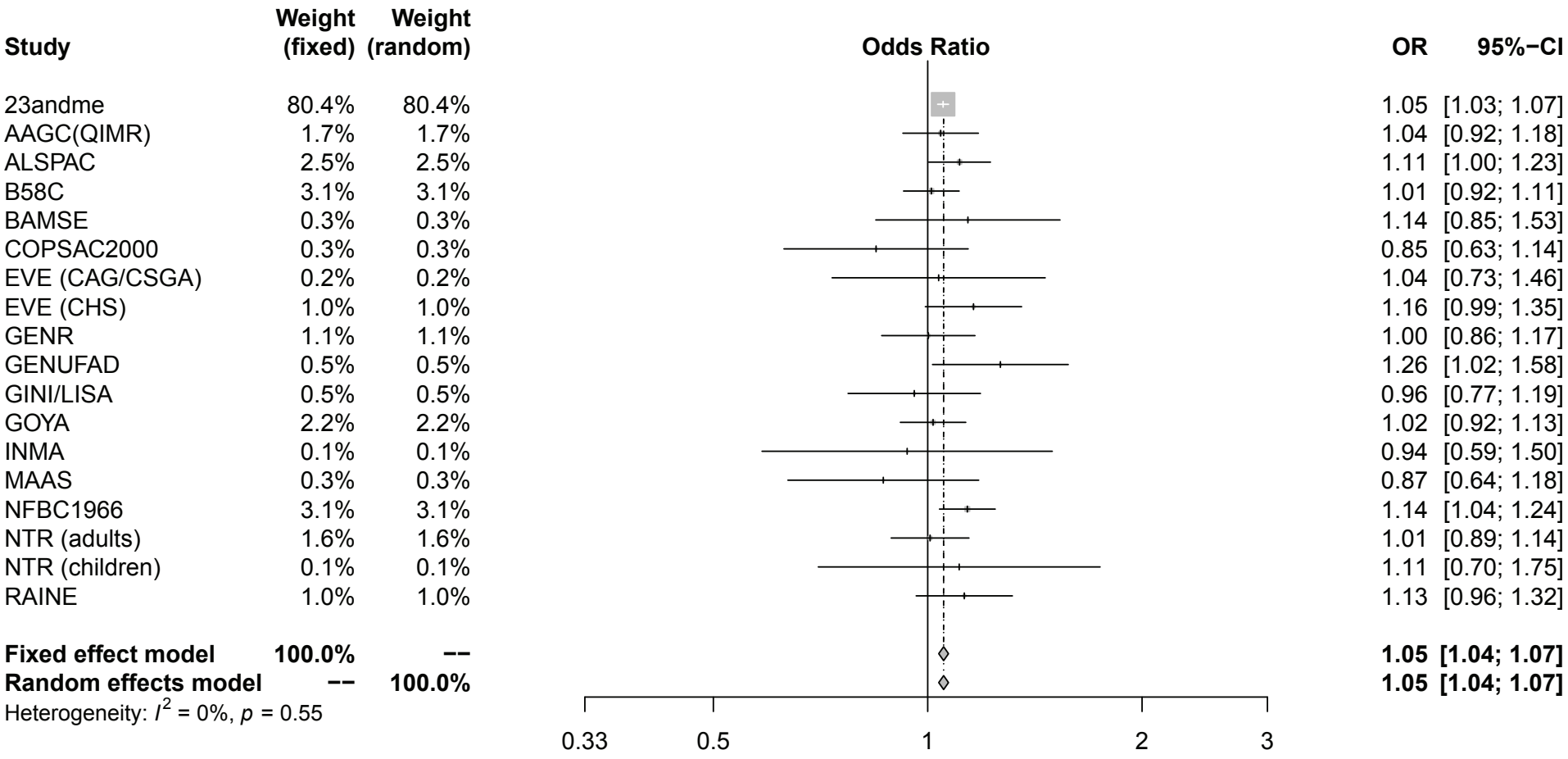
rs17294280[G]

Study	Weight (fixed)	Weight (random)	OR	95%−CI
23andme	79.8%	21.6%	1.06	[1.04; 1.09]
AAGC(QIMR)	1.5%	6.4%	1.20	[1.04; 1.39]
ALSPAC	2.4%	8.7%	1.11	[0.99; 1.25]
B58C	3.3%	10.5%	1.13	[1.02; 1.24]
BAMSE	0.3%	1.6%	0.97	[0.69; 1.35]
COPSAC2000	0.3%	1.7%	0.95	[0.68; 1.32]
EVE (CAG/CSGA)	0.2%	1.1%	1.35	[0.90; 2.04]
EVE (CHS)	1.0%	4.7%	1.06	[0.89; 1.27]
GENR	1.1%	5.2%	1.10	[0.93; 1.31]
GENUFAD	0.4%	2.2%	0.98	[0.73; 1.30]
GINI/LISA	0.5%	2.5%	1.54	[1.18; 2.00]
GOYA	2.3%	8.4%	1.08	[0.96; 1.22]
INMA	0.1%	0.8%	0.74	[0.45; 1.21]
MAAS	0.2%	1.3%	0.77	[0.52; 1.12]
NFBC1966	3.3%	10.4%	0.94	[0.85; 1.04]
NTR (adults)	1.9%	7.5%	1.11	[0.98; 1.27]
NTR (children)	0.2%	0.9%	1.27	[0.82; 1.98]
RAINE	1.0%	4.6%	1.04	[0.87; 1.25]
Fixed effect model	**100.0%**	**−−**	**1.07**	**[1.05; 1.09]**
Random effects model	**−−**	**100.0%**	**1.08**	**[1.03; 1.12]**

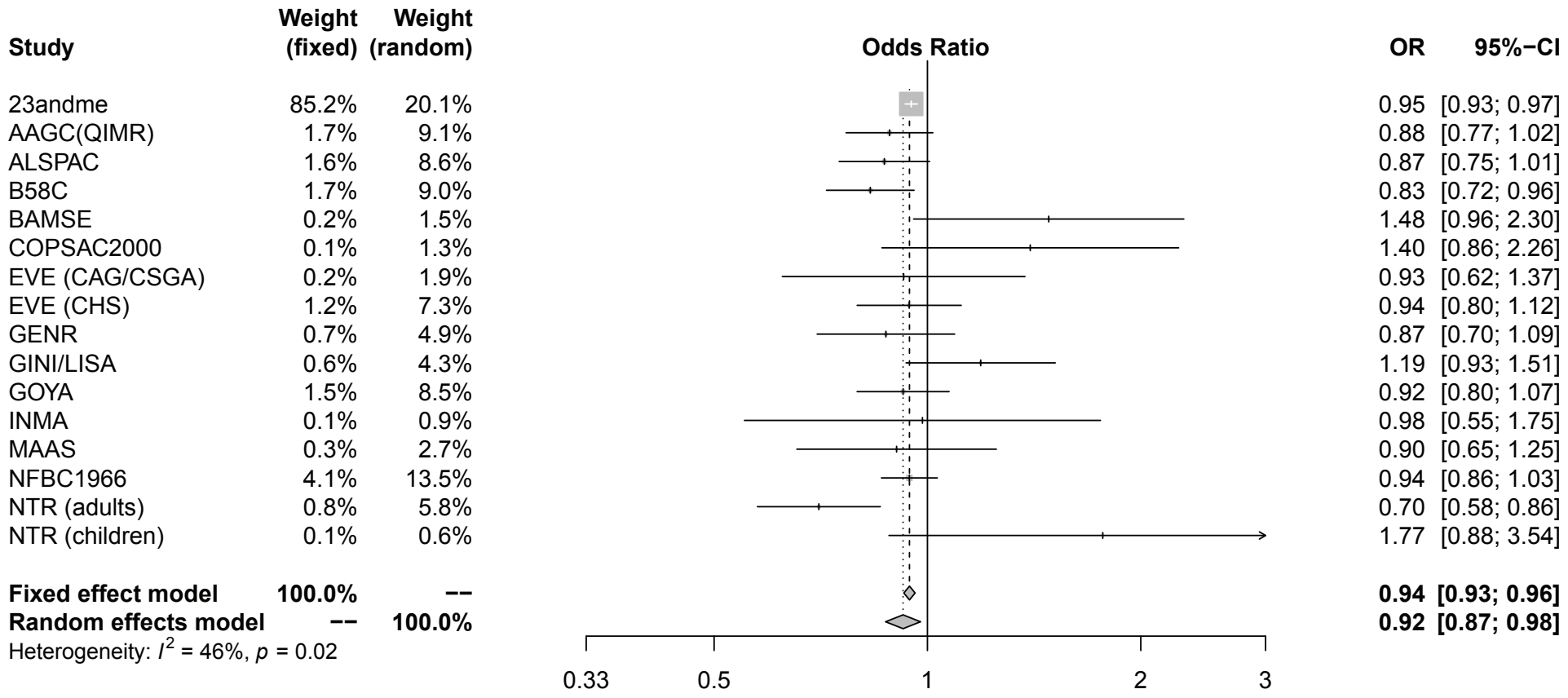
Heterogeneity: I^2 = 35%, p = 0.07



rs7824993[A]


Study
Weight (fixed)
Weight (random)
Odds Ratio
OR
95%−CI
23andme 80.4% 80.4% 1.05 [1.03; 1.07]
AAGC(QIMR) 1.7% 1.7% 1.04 [0.92; 1.18]
ALSPAC 2.5% 2.5% 1.11 [1.00; 1.23]
B58C 3.1% 3.1% 1.01 [0.92; 1.11]
BAMSE 0.3% 0.3% 1.14 [0.85; 1.53]
COPSAC2000 0.3% 0.3% 0.85 [0.63; 1.14]
EVE (CAG/CSGA) 0.2% 0.2% 1.04 [0.73; 1.46]
EVE (CHS) 1.0% 1.0% 1.16 [0.99; 1.35]
GENR 1.1% 1.1% 1.00 [0.86; 1.17]
GENUFAD 0.5% 0.5% 1.26 [1.02; 1.58]
GINI/LISA 0.5% 0.5% 0.96 [0.77; 1.19]
GOYA 2.2% 2.2% 1.02 [0.92; 1.13]
INMA 0.1% 0.1% 0.94 [0.59; 1.50]
MAAS 0.3% 0.3% 0.87 [0.64; 1.18]
NFBC1966 3.1% 3.1% 1.14 [1.04; 1.24]
NTR (adults) 1.6% 1.6% 1.01 [0.89; 1.14]
NTR (children) 0.1% 0.1% 1.11 [0.70; 1.75]
RAINE 1.0% 1.0% 1.13 [0.96; 1.32]
Fixed effect model 100.0% −− 1.05 [1.04; 1.07]
Random effects model −− 100.0% 1.05 [1.04; 1.07]
Heterogeneity: I^2 = 0%, p = 0.55
0.33
0.5
1
2
3

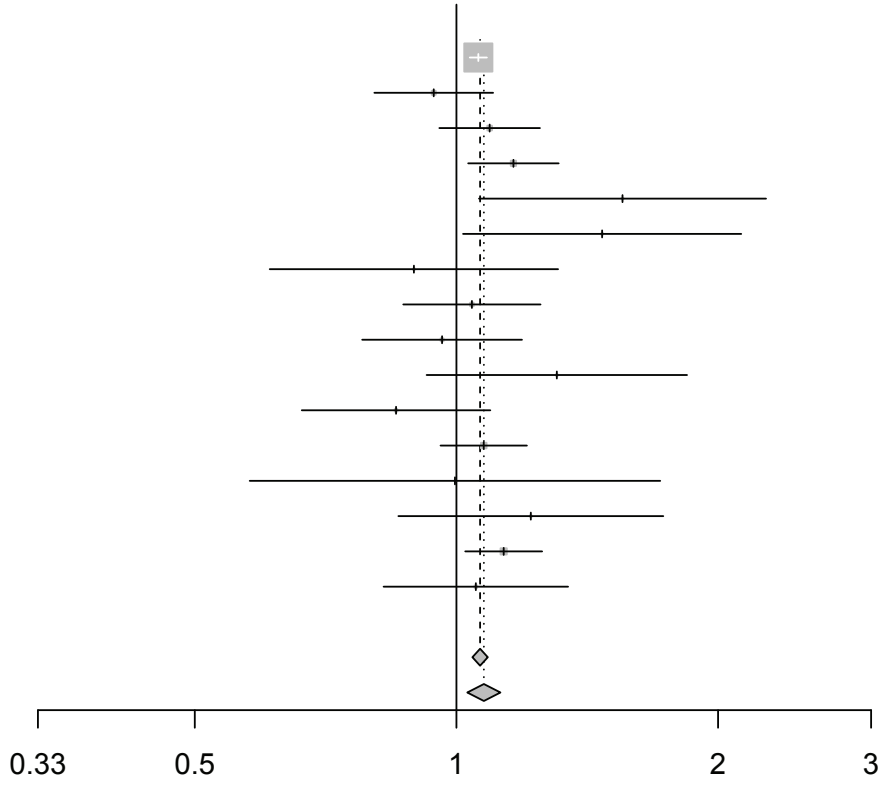
rs9282864[C]


Study
Weight (fixed)
Weight (random)
Odds Ratio
OR
95%−CI
23andme 85.2% 20.1% 0.95 [0.93; 0.97]
AAGC(QIMR) 1.7% 9.1% 0.88 [0.77; 1.02]
ALSPAC 1.6% 8.6% 0.87 [0.75; 1.01]
B58C 1.7% 9.0% 0.83 [0.72; 0.96]
BAMSE 0.2% 1.5% 1.48 [0.96; 2.30]
COPSAC2000 0.1% 1.3% 1.40 [0.86; 2.26]
EVE (CAG/CSGA) 0.2% 1.9% 0.93 [0.62; 1.37]
EVE (CHS) 1.2% 7.3% 0.94 [0.80; 1.12]
GENR 0.7% 4.9% 0.87 [0.70; 1.09]
GINI/LISA 0.6% 4.3% 1.19 [0.93; 1.51]
GOYA 1.5% 8.5% 0.92 [0.80; 1.07]
INMA 0.1% 0.9% 0.98 [0.55; 1.75]
MAAS 0.3% 2.7% 0.90 [0.65; 1.25]
NFBC1966 4.1% 13.5% 0.94 [0.86; 1.03]
NTR (adults) 0.8% 5.8% 0.70 [0.58; 0.86]
NTR (children) 0.1% 0.6% 1.77 [0.88; 3.54]
Fixed effect model 100.0% −− 0.94 [0.93; 0.96]
Random effects model −− 100.0% 0.92 [0.87; 0.98]
Heterogeneity: I^2 = 46%, p = 0.02
0.33
0.5
1
2
3

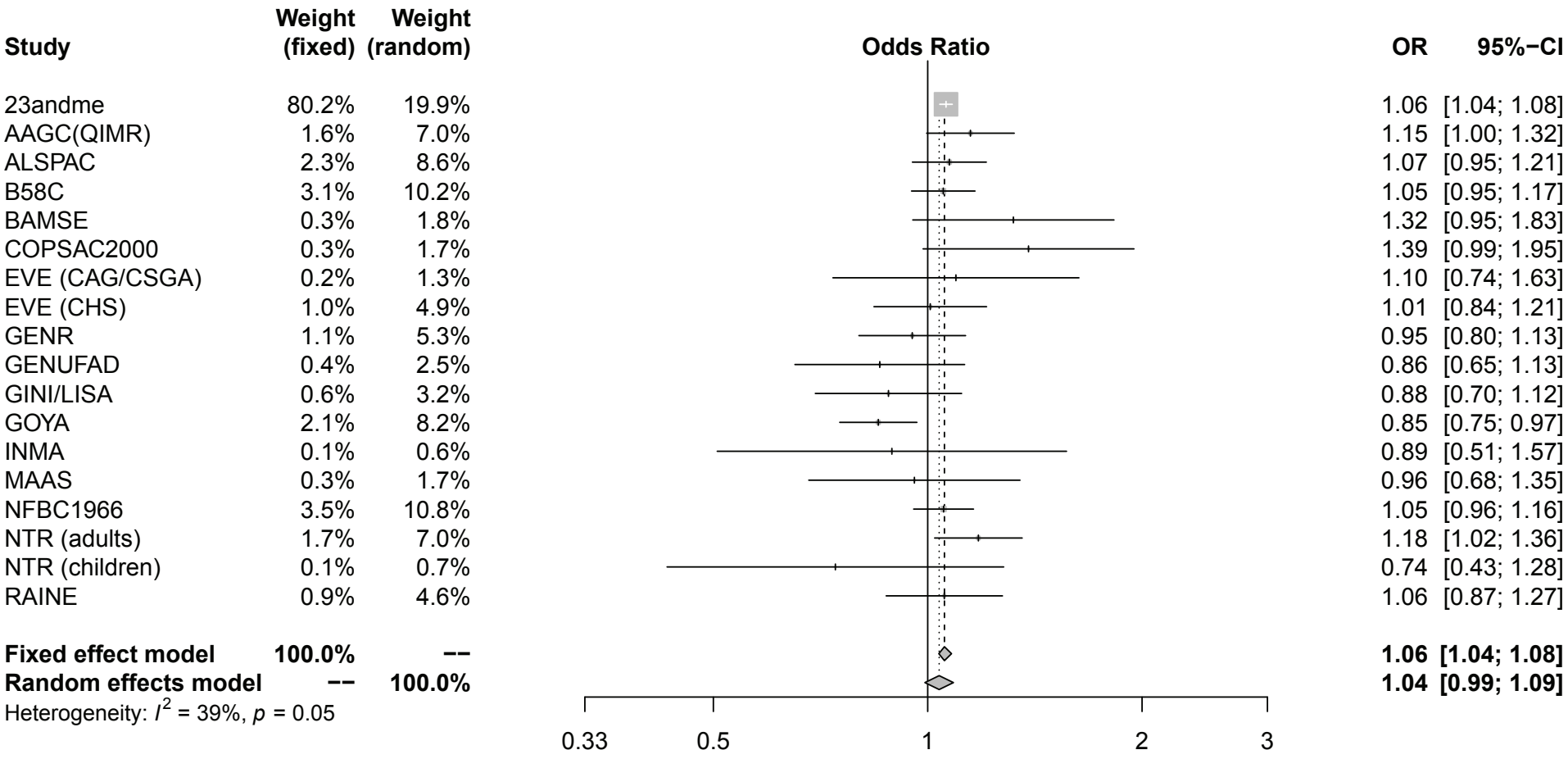
rs9687749[T]

Study	Weight (fixed)	Weight (random)	OR	95%−CI
23andme	80.6%	31.3%	1.06	[1.04; 1.08]
AAGC(QIMR)	1.7%	6.3%	0.94	[0.80; 1.10]
ALSPAC	2.3%	8.2%	1.09	[0.96; 1.25]
B58C	2.9%	9.6%	1.16	[1.03; 1.31]
BAMSE	0.3%	1.3%	1.55	[1.06; 2.27]
COPSAC2000	0.3%	1.4%	1.47	[1.02; 2.13]
EVE (CAG/CSGA)	0.3%	1.3%	0.89	[0.61; 1.31]
EVE (CHS)	1.3%	5.0%	1.04	[0.87; 1.25]
GENR	0.9%	3.8%	0.96	[0.78; 1.19]
GENUFAD	0.3%	1.5%	1.30	[0.92; 1.84]
GINI/LISA	0.7%	2.8%	0.85	[0.66; 1.09]
GOYA	3.2%	10.3%	1.08	[0.96; 1.21]
INMA	0.1%	0.6%	1.00	[0.58; 1.72]
MAAS	0.3%	1.5%	1.22	[0.86; 1.73]
NFBC1966	4.0%	12.0%	1.13	[1.02; 1.25]
RAINE	0.7%	3.0%	1.05	[0.82; 1.34]
Fixed effect model	**100.0%**	**−−**	**1.06**	**[1.04; 1.09]**
Random effects model	**−−**	**100.0%**	**1.08**	**[1.03; 1.12]**

Heterogeneity: I^2 = 24%, p = 0.18



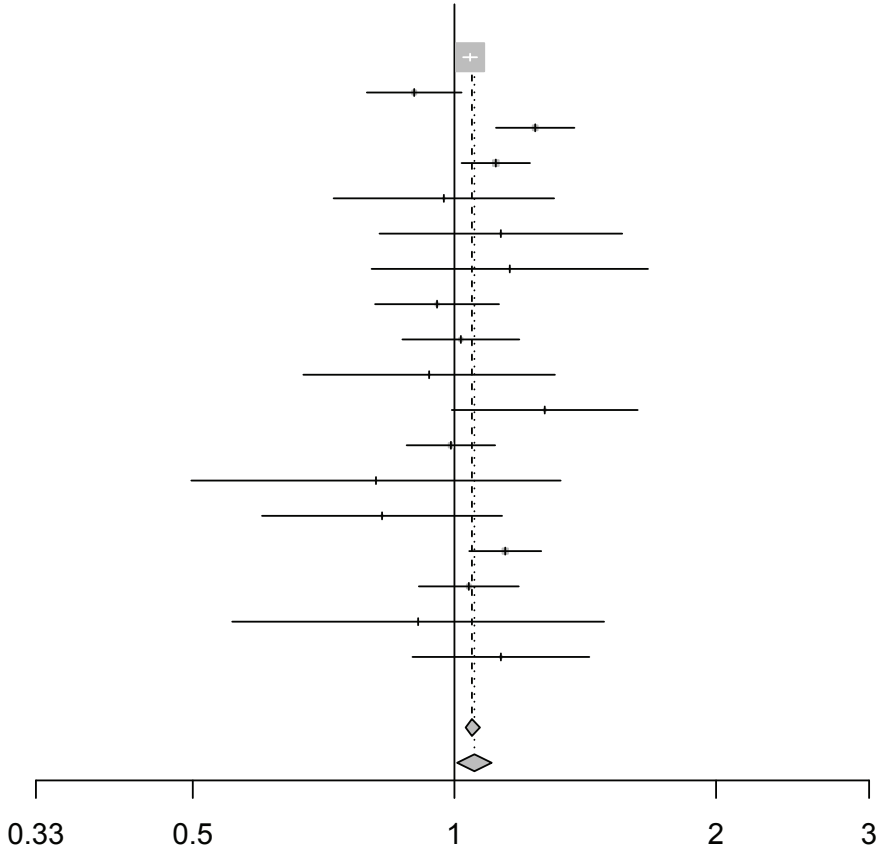
rs61977073[G]



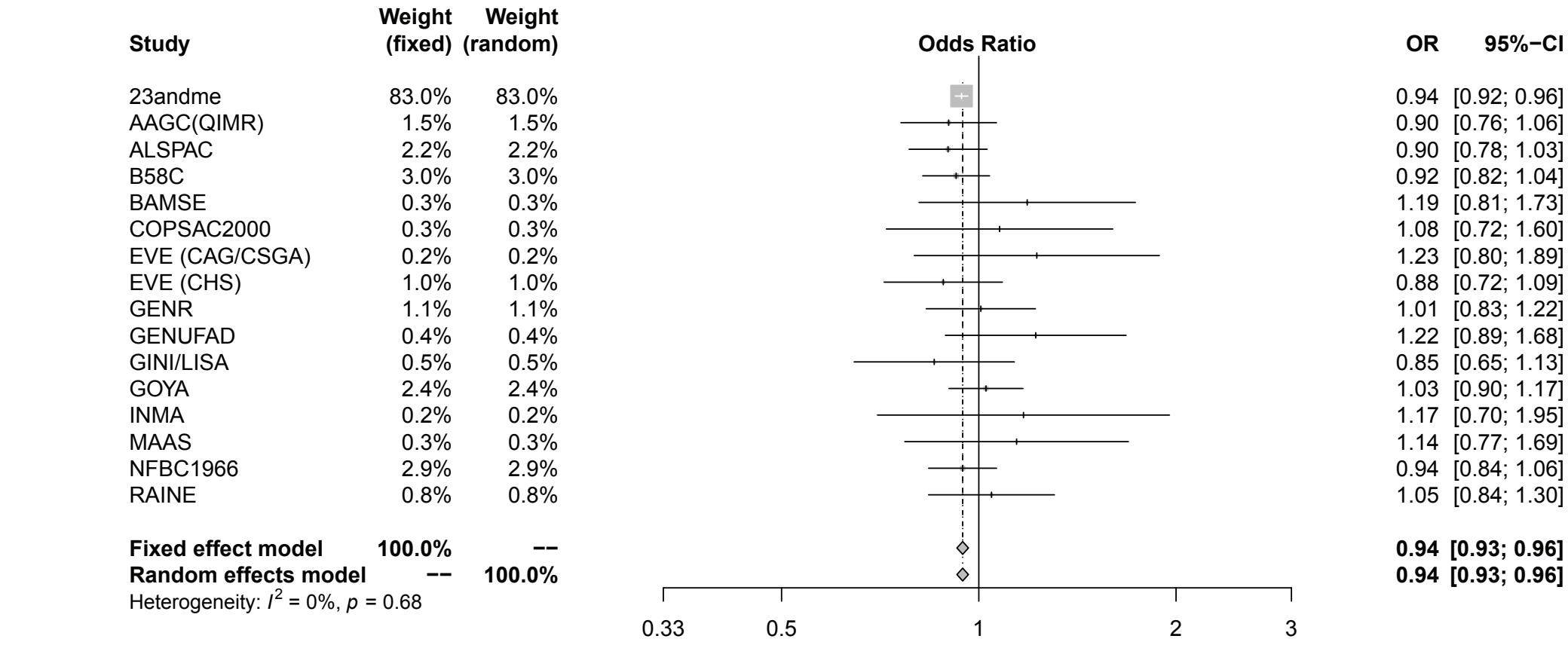
rs6470578[T]

Study	Weight (fixed)	Weight (random)	OR	95%−CI
23andme	81.1%	18.0%	1.04	[1.02; 1.06]
AAGC(QIMR)	1.7%	7.7%	0.90	[0.79; 1.02]
ALSPAC	2.5%	9.5%	1.24	[1.12; 1.37]
B58C	3.4%	10.7%	1.12	[1.02; 1.22]
BAMSE	0.3%	2.2%	0.97	[0.73; 1.30]
COPSAC2000	0.3%	1.8%	1.13	[0.82; 1.56]
EVE (CAG/CSGA)	0.2%	1.4%	1.16	[0.80; 1.67]
EVE (CHS)	1.0%	5.5%	0.96	[0.81; 1.13]
GENR	1.1%	5.9%	1.02	[0.87; 1.19]
GENUFAD	0.2%	1.7%	0.94	[0.67; 1.30]
GINI/LISA	0.5%	2.9%	1.27	[0.99; 1.62]
GOYA	2.0%	8.4%	0.99	[0.88; 1.11]
INMA	0.1%	0.8%	0.81	[0.50; 1.32]
MAAS	0.3%	1.9%	0.83	[0.60; 1.13]
NFBC1966	3.0%	10.3%	1.14	[1.04; 1.26]
NTR (adults)	1.6%	7.3%	1.04	[0.91; 1.19]
NTR (children)	0.1%	0.8%	0.91	[0.56; 1.49]
RAINE	0.5%	3.2%	1.13	[0.89; 1.43]
Fixed effect model	**100.0%**	**−−**	**1.05**	**[1.03; 1.07]**
Random effects model	**−−**	**100.0%**	**1.05**	**[1.01; 1.10]**

Heterogeneity: I^2 = 45%, p = 0.02



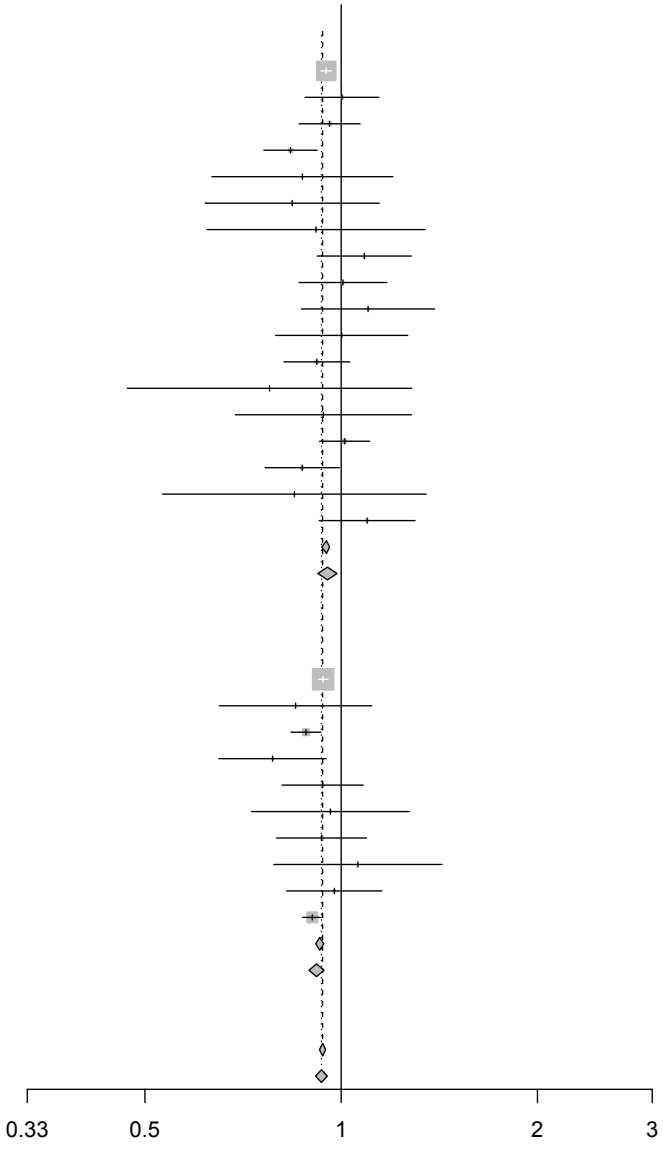
rs3787184[G]


Study
Weight (fixed)
Weight (random)
Odds Ratio
OR
95%−CI
23andme 83.0% 83.0% 0.94 [0.92; 0.96]
AAGC(QIMR) 1.5% 1.5% 0.90 [0.76; 1.06]
ALSPAC 2.2% 2.2% 0.90 [0.78; 1.03]
B58C 3.0% 3.0% 0.92 [0.82; 1.04]
BAMSE 0.3% 0.3% 1.19 [0.81; 1.73]
COPSAC2000 0.3% 0.3% 1.08 [0.72; 1.60]
EVE (CAG/CSGA) 0.2% 0.2% 1.23 [0.80; 1.89]
EVE (CHS) 1.0% 1.0% 0.88 [0.72; 1.09]
GENR 1.1% 1.1% 1.01 [0.83; 1.22]
GENUFAD 0.4% 0.4% 1.22 [0.89; 1.68]
GINI/LISA 0.5% 0.5% 0.85 [0.65; 1.13]
GOYA 2.4% 2.4% 1.03 [0.90; 1.17]
INMA 0.2% 0.2% 1.17 [0.70; 1.95]
MAAS 0.3% 0.3% 1.14 [0.77; 1.69]
NFBC1966 2.9% 2.9% 0.94 [0.84; 1.06]
RAINE 0.8% 0.8% 1.05 [0.84; 1.30]
Fixed effect model 100.0% −− 0.94 [0.93; 0.96]
Random effects model −− 100.0% 0.94 [0.93; 0.96]
Heterogeneity: I^2 = 0%, p = 0.68
0.33
0.5
1
2
3

Supplementary Figure 3

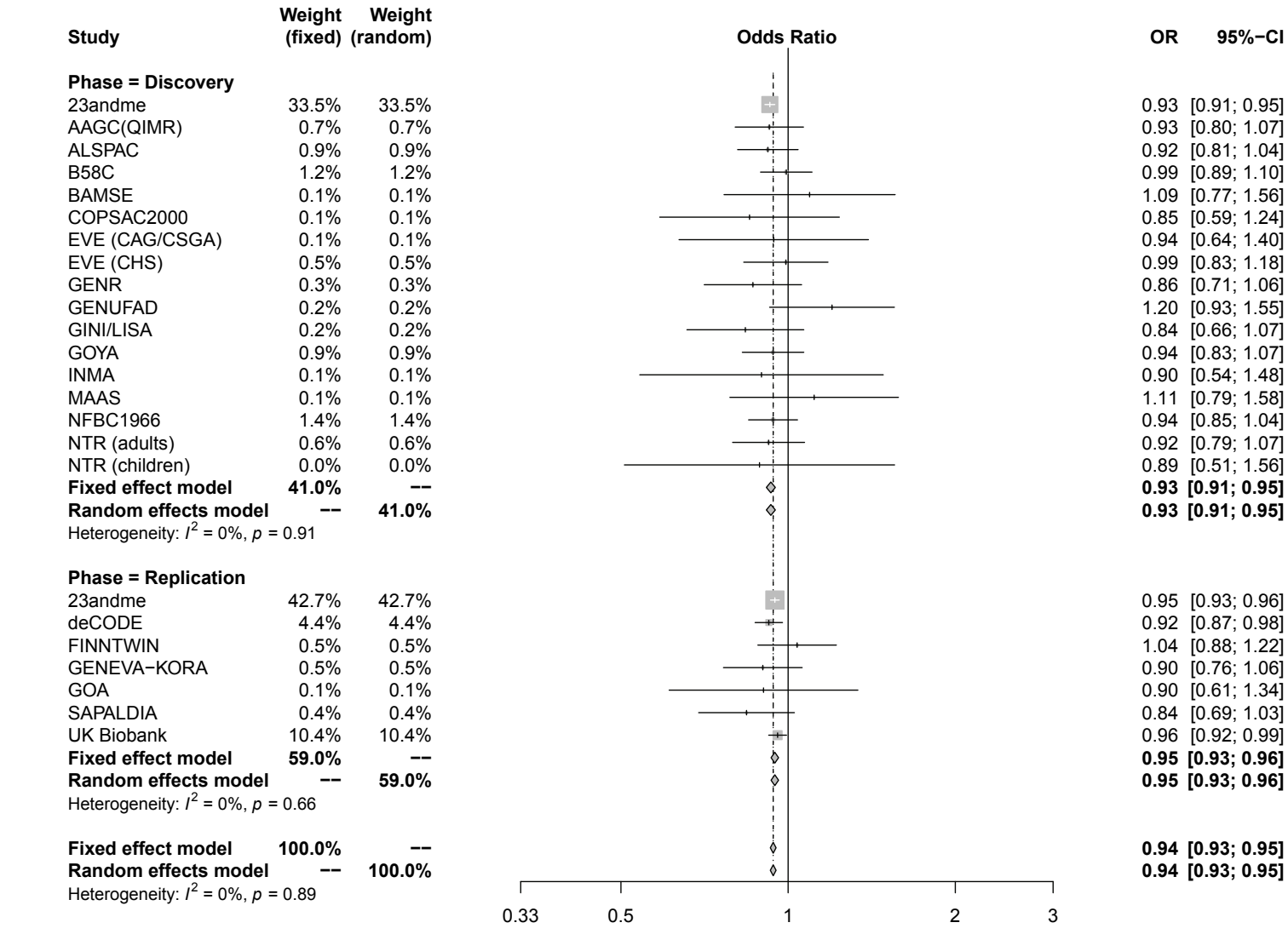
Forest plots from the discovery and replication phase for markers not previously associated to allergic rhinitis, including weights, estimates and 95% confidence intervals for inverse variance weighted fixed and random effects meta-analyses from genetic marker association of 16,531,985 genetic markers to allergic rhinitis from the discovery phase, including 212,120 individuals.

rs7717955[T]

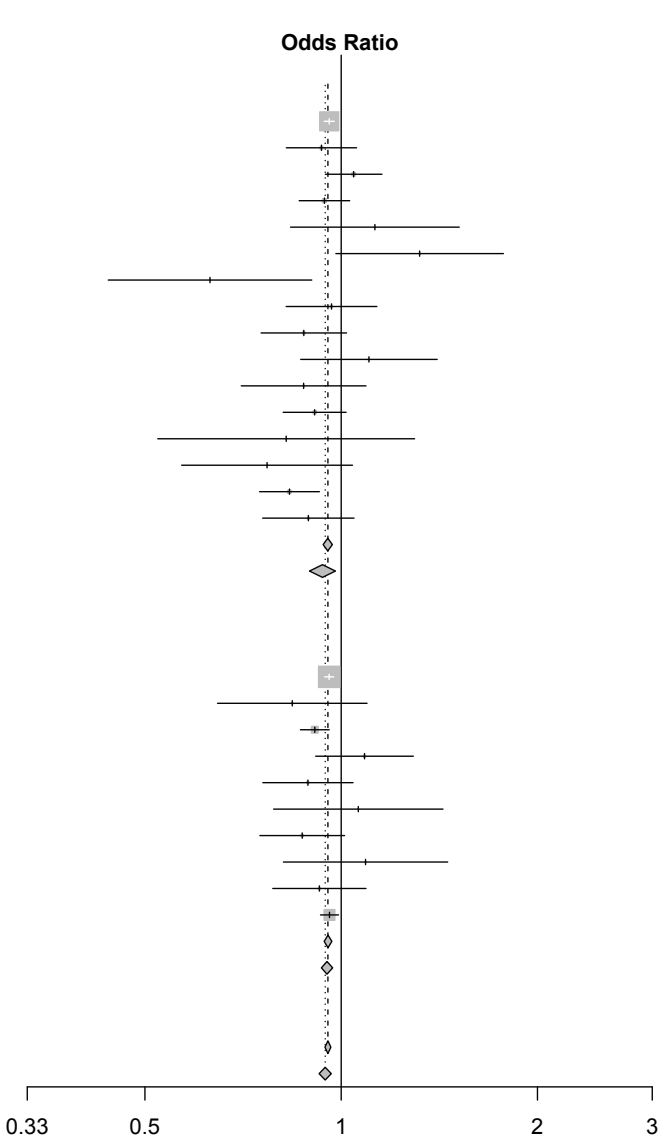


Study	Weight (fixed)	Weight (random)	OR	95%−CI
Phase = Discovery				
23andme	33.8%	20.2%	0.95	[0.93; 0.97]
AAGC(QIMR)	0.7%	2.3%	1.00	[0.88; 1.14]
ALSPAC	1.0%	3.2%	0.96	[0.86; 1.07]
B58C	1.3%	4.0%	0.84	[0.76; 0.92]
BAMSE	0.1%	0.4%	0.87	[0.63; 1.20]
COPSAC2000	0.1%	0.4%	0.84	[0.62; 1.14]
EVE (CAG/CSGA)	0.1%	0.3%	0.91	[0.62; 1.34]
EVE (CHS)	0.4%	1.5%	1.09	[0.92; 1.28]
GENR	0.5%	1.7%	1.01	[0.86; 1.17]
GENUFAD	0.2%	0.8%	1.10	[0.87; 1.39]
GINI/LISA	0.2%	0.8%	1.00	[0.79; 1.27]
GOYA	0.9%	2.8%	0.92	[0.82; 1.03]
INMA	0.0%	0.2%	0.78	[0.47; 1.28]
MAAS	0.1%	0.4%	0.94	[0.69; 1.28]
NFBC1966	1.5%	4.5%	1.01	[0.93; 1.11]
NTR (adults)	0.7%	2.3%	0.87	[0.76; 0.99]
NTR (children)	0.1%	0.2%	0.85	[0.53; 1.35]
RAINE	0.4%	1.4%	1.10	[0.93; 1.30]
Fixed effect model	**42.2%**	**−−**	**0.95**	**[0.93; 0.96]**
Random effects model	**−−**	**47.3%**	**0.95**	**[0.92; 0.99]**
Heterogeneity: I^2 = 19%, p = 0.23				
Phase = Replication				
23andme	40.9%	20.8%	0.94	[0.92; 0.95]
CAMP	0.2%	0.6%	0.85	[0.65; 1.11]
deCODE	4.2%	9.4%	0.88	[0.84; 0.93]
ECRHS	0.3%	1.1%	0.78	[0.65; 0.95]
FINNTWIN	0.6%	1.9%	0.94	[0.81; 1.08]
GABRIELA	0.2%	0.5%	0.96	[0.73; 1.27]
GENEVA−KORA	0.5%	1.6%	0.93	[0.80; 1.09]
GOA	0.1%	0.5%	1.06	[0.79; 1.43]
SAPALDIA	0.4%	1.4%	0.98	[0.83; 1.15]
UK Biobank	10.4%	14.7%	0.90	[0.87; 0.93]
Fixed effect model	**57.8%**	**−−**	**0.93**	**[0.91; 0.94]**
Random effects model	**−−**	**52.7%**	**0.92**	**[0.89; 0.94]**
Heterogeneity: I^2 = 26%, p = 0.21				
Fixed effect model	**100.0%**	**−−**	**0.94**	**[0.93; 0.95]**
Random effects model	**−−**	**100.0%**	**0.93**	**[0.91; 0.95]**
Heterogeneity: I^2 = 28%, p = 0.09				

rs63406760[G]

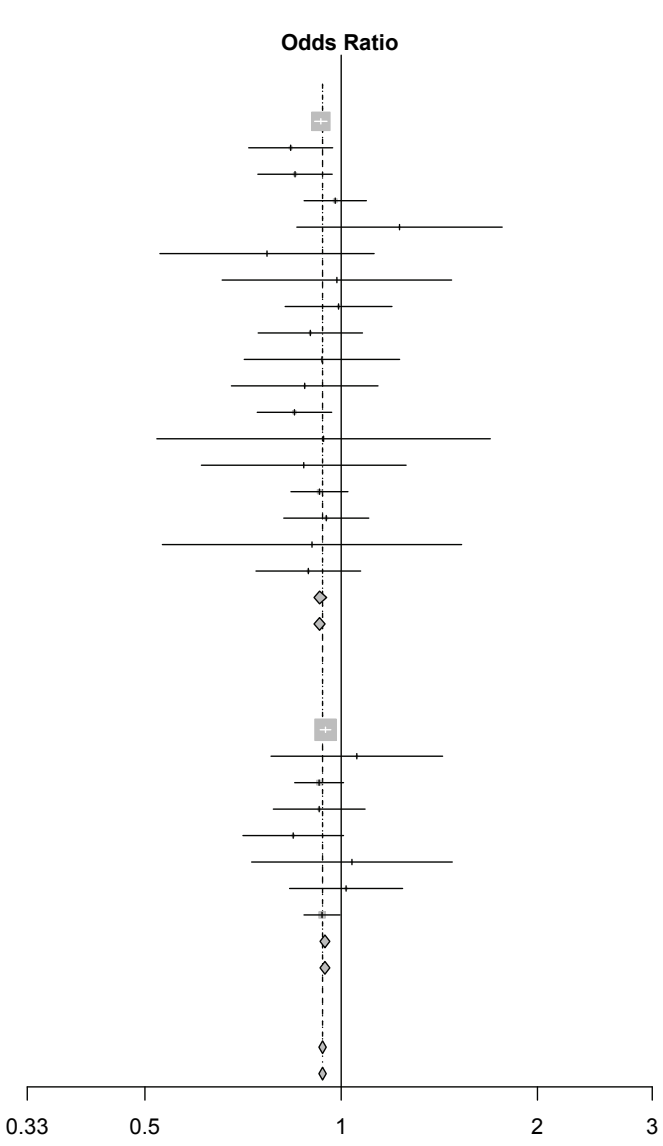


rs1504215[A]



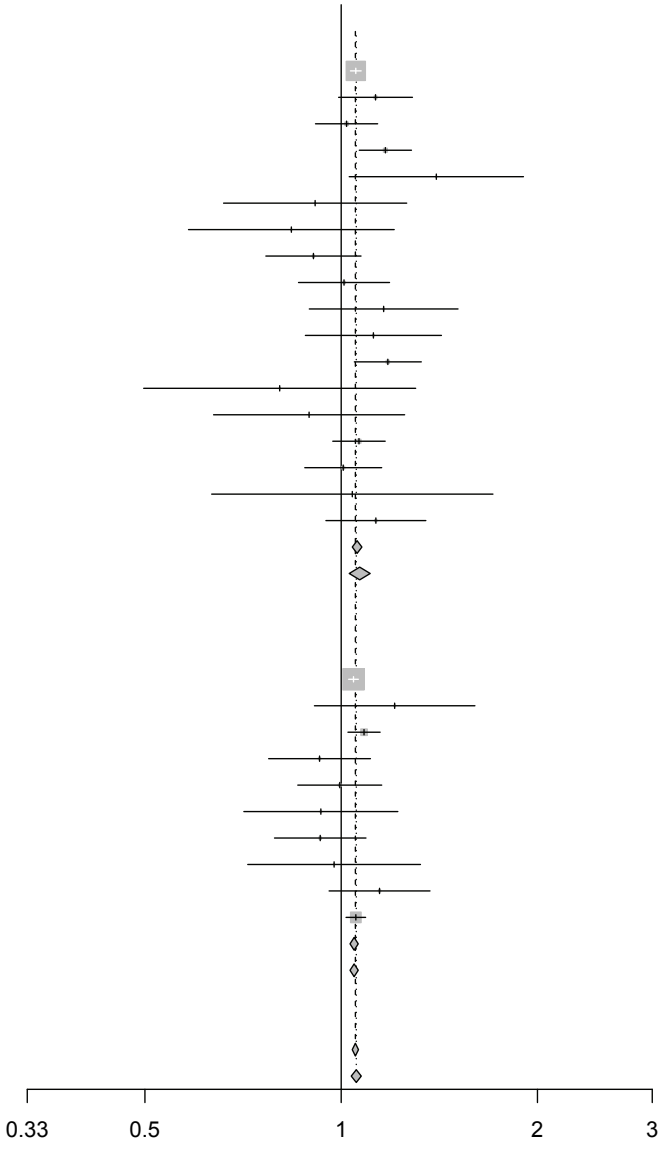
Study	Weight (fixed)	Weight (random)	OR	95%−CI
Phase = Discovery				
23andme	33.5%	19.5%	0.96	[0.94; 0.98]
AAGC(QIMR)	0.7%	2.7%	0.93	[0.82; 1.06]
ALSPAC	1.1%	3.9%	1.04	[0.95; 1.15]
B58C	1.4%	4.6%	0.94	[0.86; 1.03]
BAMSE	0.1%	0.5%	1.13	[0.84; 1.52]
COPSAC2000	0.1%	0.5%	1.32	[0.98; 1.77]
EVE (CAG/CSGA)	0.1%	0.4%	0.63	[0.44; 0.90]
EVE (CHS)	0.4%	1.7%	0.97	[0.82; 1.13]
GENR	0.5%	1.9%	0.88	[0.75; 1.02]
GENUFAD	0.2%	0.8%	1.10	[0.87; 1.40]
GINI/LISA	0.2%	0.9%	0.88	[0.70; 1.09]
GOYA	0.9%	3.2%	0.91	[0.81; 1.02]
INMA	0.1%	0.2%	0.82	[0.52; 1.30]
MAAS	0.1%	0.5%	0.77	[0.57; 1.04]
NFBC1966	1.0%	3.5%	0.83	[0.75; 0.93]
RAINE	0.4%	1.7%	0.89	[0.76; 1.05]
Fixed effect model	**40.8%**	**−−**	**0.95**	**[0.94; 0.97]**
Random effects model	**−−**	**46.4%**	**0.94**	**[0.89; 0.98]**
Heterogeneity: I^2 = 46%, p = 0.02				
Phase = Replication				
23andme	42.1%	20.1%	0.96	[0.94; 0.97]
CAMP	0.2%	0.6%	0.84	[0.65; 1.10]
deCODE	4.2%	10.0%	0.91	[0.87; 0.96]
ECRHS	0.4%	1.5%	1.09	[0.91; 1.29]
FINNTWIN	0.4%	1.7%	0.89	[0.76; 1.04]
GABRIELA	0.1%	0.5%	1.06	[0.79; 1.43]
GENEVA−KORA	0.5%	1.9%	0.87	[0.75; 1.01]
GOA	0.1%	0.5%	1.09	[0.82; 1.46]
SAPALDIA	0.4%	1.6%	0.93	[0.79; 1.09]
UK Biobank	10.8%	15.2%	0.96	[0.93; 0.99]
Fixed effect model	**59.2%**	**−−**	**0.95**	**[0.94; 0.97]**
Random effects model	**−−**	**53.6%**	**0.95**	**[0.93; 0.97]**
Heterogeneity: I^2 = 12%, p = 0.33				
Fixed effect model	**100.0%**	**−−**	**0.95**	**[0.94; 0.96]**
Random effects model	**−−**	**100.0%**	**0.95**	**[0.92; 0.97]**
Heterogeneity: I^2 = 34%, p = 0.05				

rs28361986[A]



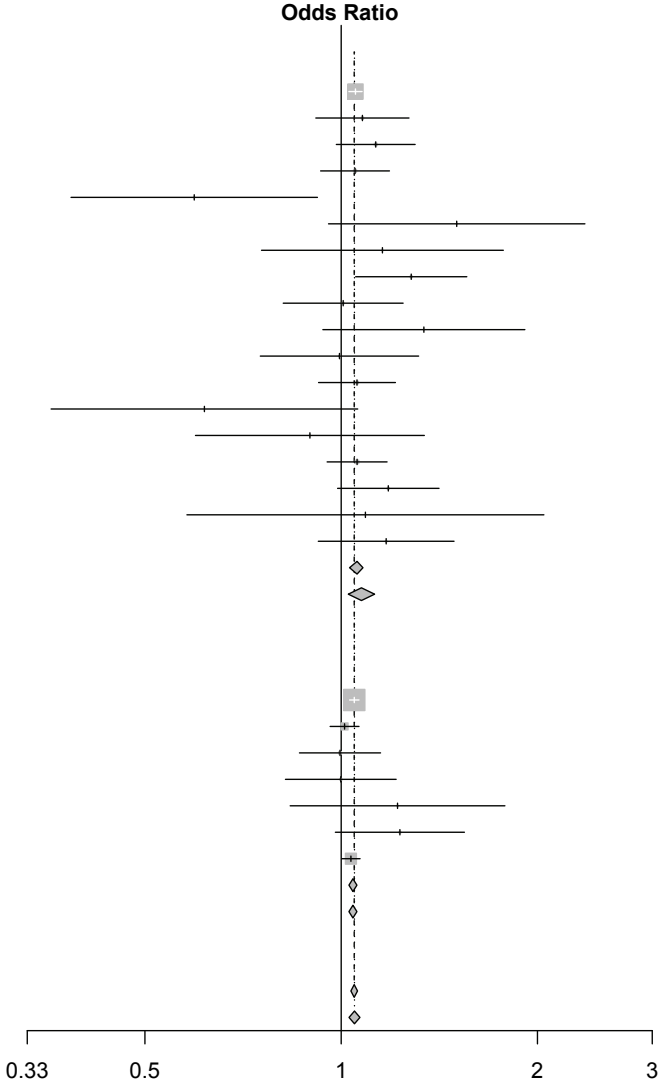
Study	Weight (fixed)	Weight (random)	OR	95%−CI
Phase = Discovery				
23andme	35.1%	35.1%	0.93	[0.91; 0.95]
AAGC(QIMR)	0.8%	0.8%	0.84	[0.72; 0.97]
ALSPAC	1.0%	1.0%	0.85	[0.75; 0.97]
B58C	1.4%	1.4%	0.98	[0.88; 1.09]
BAMSE	0.1%	0.1%	1.23	[0.86; 1.77]
COPSAC2000	0.1%	0.1%	0.77	[0.53; 1.12]
EVE (CAG/CSGA)	0.1%	0.1%	0.98	[0.66; 1.48]
EVE (CHS)	0.5%	0.5%	0.99	[0.82; 1.20]
GENR	0.5%	0.5%	0.90	[0.75; 1.08]
GENUFAD	0.2%	0.2%	0.93	[0.71; 1.23]
GINI/LISA	0.3%	0.3%	0.88	[0.68; 1.14]
GOYA	1.0%	1.0%	0.85	[0.74; 0.97]
INMA	0.0%	0.0%	0.94	[0.52; 1.69]
MAAS	0.1%	0.1%	0.88	[0.61; 1.26]
NFBC1966	1.7%	1.7%	0.93	[0.84; 1.02]
NTR (adults)	0.7%	0.7%	0.95	[0.82; 1.10]
NTR (children)	0.1%	0.1%	0.90	[0.53; 1.53]
RAINE	0.5%	0.5%	0.89	[0.74; 1.07]
Fixed effect model	**44.0%**	**−−**	**0.93**	**[0.91; 0.95]**
Random effects model	**−−**	**44.0%**	**0.93**	**[0.91; 0.94]**
Heterogeneity: I^2 = 0%, p = 0.86				
Phase = Replication				
23andme	47.7%	47.7%	0.95	[0.93; 0.96]
CAMP	0.2%	0.2%	1.06	[0.78; 1.43]
deCODE	2.3%	2.3%	0.93	[0.85; 1.01]
FINNTWIN	0.6%	0.6%	0.93	[0.79; 1.09]
GENEVA−KORA	0.5%	0.5%	0.84	[0.71; 1.01]
GOA	0.1%	0.1%	1.04	[0.73; 1.48]
SAPALDIA	0.4%	0.4%	1.02	[0.83; 1.24]
UK Biobank	4.1%	4.1%	0.93	[0.88; 1.00]
Fixed effect model	**56.0%**	**−−**	**0.94**	**[0.93; 0.96]**
Random effects model	**−−**	**56.0%**	**0.94**	**[0.93; 0.96]**
Heterogeneity: I^2 = 0%, p = 0.86				
Fixed effect model	**100.0%**	**−−**	**0.94**	**[0.92; 0.95]**
Random effects model	**−−**	**100.0%**	**0.94**	**[0.92; 0.95]**
Heterogeneity: I^2 = 0%, p = 0.91				

rs2070902[T]



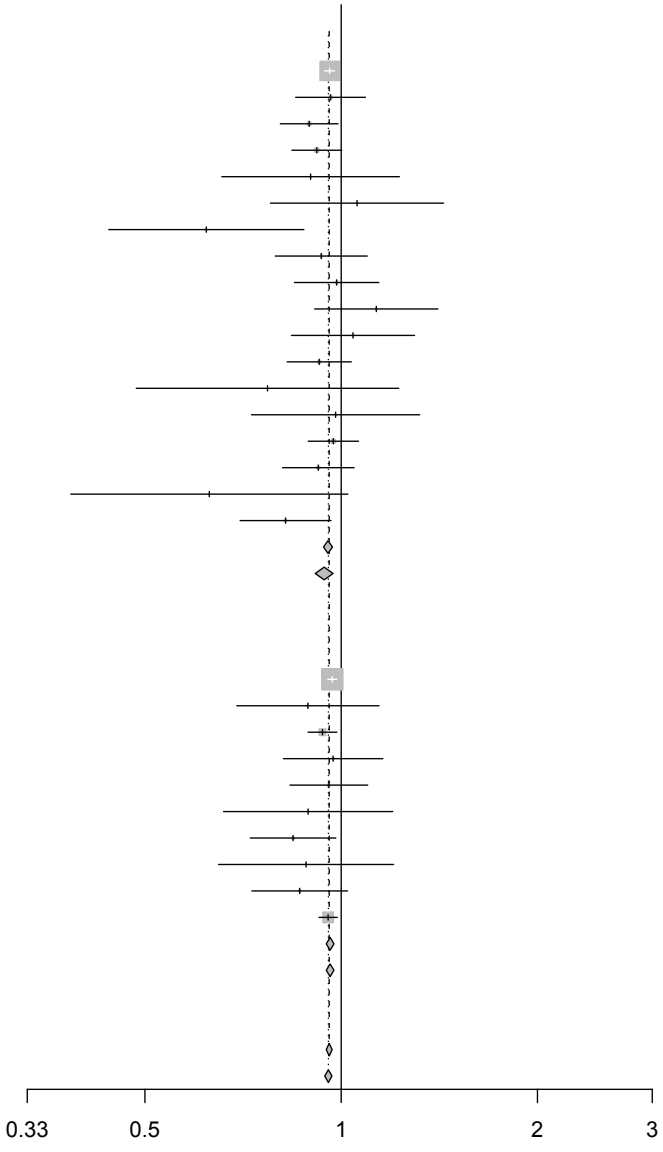
Study	Weight (fixed)	Weight (random)	OR	95%−CI
Phase = Discovery				
23andme	33.9%	25.0%	1.05	[1.03; 1.07]
AAGC(QIMR)	0.7%	1.8%	1.13	[0.99; 1.29]
ALSPAC	1.0%	2.4%	1.02	[0.91; 1.14]
B58C	1.4%	3.4%	1.17	[1.07; 1.28]
BAMSE	0.1%	0.3%	1.40	[1.03; 1.90]
COPSAC2000	0.1%	0.3%	0.91	[0.66; 1.26]
EVE (CAG/CSGA)	0.1%	0.2%	0.84	[0.58; 1.21]
EVE (CHS)	0.4%	1.1%	0.91	[0.77; 1.07]
GENR	0.5%	1.2%	1.01	[0.86; 1.19]
GENUFAD	0.2%	0.5%	1.16	[0.89; 1.51]
GINI/LISA	0.2%	0.5%	1.12	[0.88; 1.42]
GOYA	0.9%	2.1%	1.18	[1.05; 1.33]
INMA	0.1%	0.1%	0.80	[0.50; 1.30]
MAAS	0.1%	0.3%	0.89	[0.64; 1.25]
NFBC1966	1.4%	3.3%	1.06	[0.97; 1.17]
NTR (adults)	0.7%	1.6%	1.01	[0.88; 1.15]
NTR (children)	0.0%	0.1%	1.04	[0.63; 1.71]
RAINE	0.4%	1.0%	1.13	[0.95; 1.35]
Fixed effect model	**42.2%**	**−−**	**1.06**	**[1.04; 1.08]**
Random effects model	**−−**	**45.3%**	**1.07**	**[1.03; 1.11]**
Heterogeneity: I^2 = 24%, p = 0.17				
Phase = Replication				
23andme	41.6%	26.4%	1.04	[1.03; 1.06]
CAMP	0.2%	0.4%	1.21	[0.91; 1.60]
deCODE	3.8%	7.6%	1.08	[1.02; 1.15]
ECRHS	0.4%	0.9%	0.93	[0.77; 1.11]
FINNTWIN	0.6%	1.4%	0.99	[0.86; 1.15]
GABRIELA	0.2%	0.4%	0.93	[0.71; 1.22]
GENEVA−KORA	0.5%	1.2%	0.93	[0.79; 1.09]
GOA	0.1%	0.3%	0.98	[0.72; 1.32]
SAPALDIA	0.4%	1.0%	1.15	[0.96; 1.37]
UK Biobank	10.2%	15.0%	1.05	[1.02; 1.09]
Fixed effect model	**57.8%**	**−−**	**1.05**	**[1.03; 1.06]**
Random effects model	**−−**	**54.7%**	**1.05**	**[1.03; 1.06]**
Heterogeneity: I^2 = 0%, p = 0.45				
Fixed effect model	**100.0%**	**−−**	**1.05**	**[1.04; 1.06]**
Random effects model	**−−**	**100.0%**	**1.05**	**[1.04; 1.07]**
Heterogeneity: I^2 = 16%, p = 0.23				

rs111371454[G]



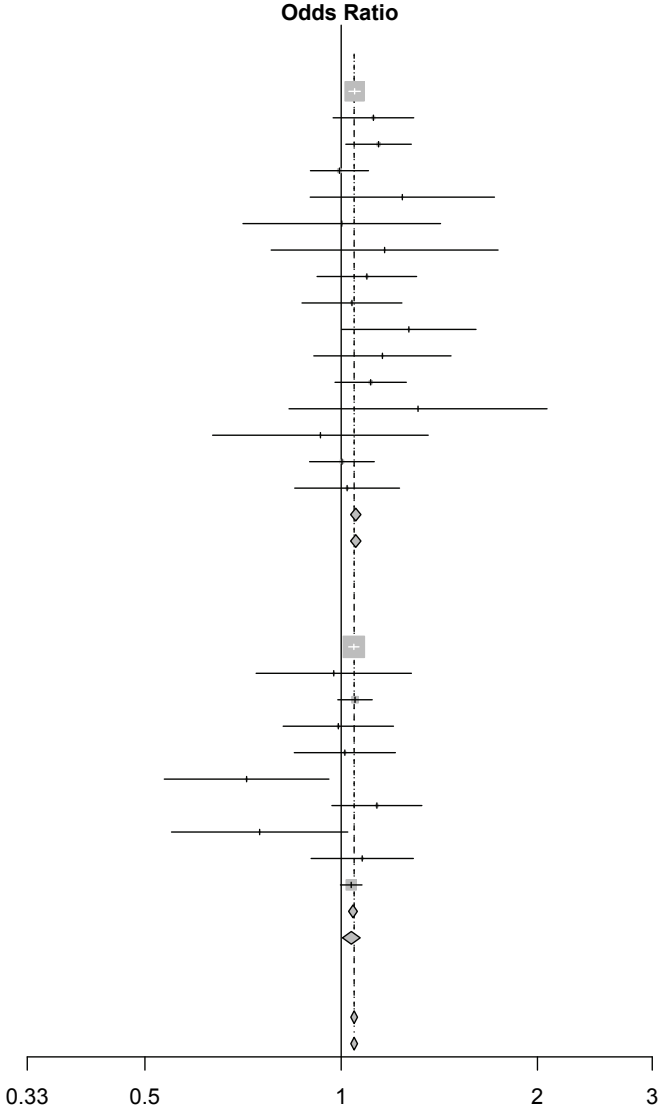
Study	Weight (fixed)	Weight (random)	OR	95%−CI
Phase = Discovery				
23andme	25.2%	23.8%	1.05	[1.03; 1.08]
AAGC(QIMR)	0.5%	1.3%	1.08	[0.91; 1.27]
ALSPAC	0.7%	1.8%	1.13	[0.98; 1.30]
B58C	0.9%	2.4%	1.05	[0.93; 1.19]
BAMSE	0.1%	0.2%	0.60	[0.39; 0.92]
COPSAC2000	0.1%	0.2%	1.50	[0.96; 2.36]
EVE (CAG/CSGA)	0.1%	0.2%	1.16	[0.75; 1.77]
EVE (CHS)	0.4%	0.9%	1.28	[1.05; 1.56]
GENR	0.3%	0.8%	1.01	[0.81; 1.24]
GENUFAD	0.1%	0.3%	1.34	[0.94; 1.91]
GINI/LISA	0.2%	0.5%	0.99	[0.75; 1.31]
GOYA	0.7%	1.9%	1.06	[0.92; 1.21]
INMA	0.0%	0.1%	0.62	[0.36; 1.06]
MAAS	0.1%	0.2%	0.90	[0.60; 1.34]
NFBC1966	1.2%	3.0%	1.06	[0.95; 1.18]
NTR (adults)	0.4%	1.1%	1.18	[0.99; 1.41]
NTR (children)	0.0%	0.1%	1.09	[0.58; 2.05]
RAINE	0.2%	0.6%	1.17	[0.92; 1.49]
Fixed effect model	**31.2%**	**−−**	**1.06**	**[1.03; 1.08]**
Random effects model	**−−**	**39.5%**	**1.07**	**[1.03; 1.13]**
Heterogeneity: I^2 = 25%, p = 0.16				
Phase = Replication				
23andme	49.0%	28.6%	1.05	[1.03; 1.06]
deCODE	5.3%	10.3%	1.01	[0.96; 1.06]
FINNTWIN	0.7%	1.7%	1.00	[0.86; 1.15]
GENEVA−KORA	0.4%	0.9%	1.00	[0.82; 1.21]
GOA	0.1%	0.3%	1.22	[0.84; 1.78]
SAPALDIA	0.3%	0.7%	1.23	[0.98; 1.55]
UK Biobank	13.1%	18.0%	1.03	[1.00; 1.07]
Fixed effect model	**68.8%**	**−−**	**1.04**	**[1.03; 1.06]**
Random effects model	**−−**	**60.5%**	**1.04**	**[1.03; 1.06]**
Heterogeneity: I^2 = 0%, p = 0.54				
Fixed effect model	**100.0%**	**−−**	**1.05**	**[1.03; 1.06]**
Random effects model	**−−**	**100.0%**	**1.05**	**[1.03; 1.07]**
Heterogeneity: I^2 = 17%, p = 0.22				

rs12509403[T]



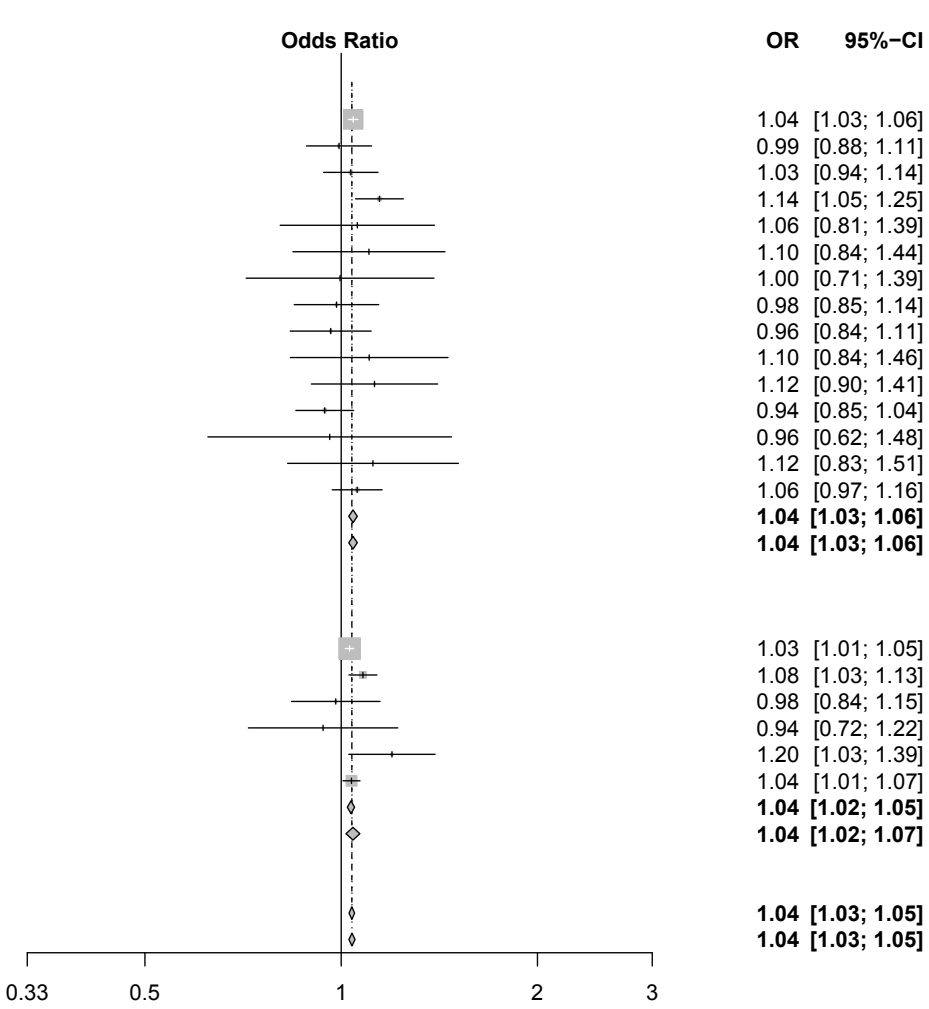
Study	Weight (fixed)	Weight (random)	OR	95%−CI
Phase = Discovery				
23andme	34.0%	31.0%	0.96	[0.94; 0.98]
AAGC(QIMR)	0.7%	1.1%	0.96	[0.85; 1.09]
ALSPAC	1.0%	1.5%	0.89	[0.81; 0.99]
B58C	1.4%	2.0%	0.92	[0.84; 1.00]
BAMSE	0.1%	0.2%	0.90	[0.66; 1.23]
COPSAC2000	0.1%	0.2%	1.06	[0.78; 1.44]
EVE (CAG/CSGA)	0.1%	0.1%	0.62	[0.44; 0.88]
EVE (CHS)	0.4%	0.6%	0.93	[0.79; 1.10]
GENR	0.5%	0.7%	0.98	[0.85; 1.14]
GENUFAD	0.2%	0.3%	1.13	[0.91; 1.41]
GINI/LISA	0.2%	0.3%	1.04	[0.84; 1.30]
GOYA	0.8%	1.2%	0.93	[0.83; 1.04]
INMA	0.0%	0.1%	0.77	[0.48; 1.23]
MAAS	0.1%	0.2%	0.98	[0.73; 1.32]
NFBC1966	1.4%	2.0%	0.97	[0.89; 1.06]
NTR (adults)	0.7%	1.0%	0.92	[0.81; 1.05]
NTR (children)	0.0%	0.1%	0.63	[0.38; 1.02]
RAINE	0.4%	0.6%	0.82	[0.70; 0.96]
Fixed effect model	**42.3%**	**−−**	**0.95**	**[0.94; 0.97]**
Random effects model	**−−**	**43.3%**	**0.94**	**[0.91; 0.97]**
Heterogeneity: I^2 = 16%, p = 0.26				
Phase = Replication				
23andme	41.1%	34.6%	0.97	[0.95; 0.98]
CAMP	0.2%	0.3%	0.89	[0.69; 1.14]
deCODE	4.1%	5.8%	0.94	[0.89; 0.98]
ECRHS	0.3%	0.5%	0.97	[0.82; 1.16]
FINNTWIN	0.6%	0.9%	0.96	[0.83; 1.10]
GABRIELA	0.1%	0.2%	0.89	[0.66; 1.20]
GENEVA−KORA	0.5%	0.7%	0.84	[0.73; 0.98]
GOA	0.1%	0.2%	0.88	[0.65; 1.20]
SAPALDIA	0.4%	0.6%	0.86	[0.73; 1.02]
UK Biobank	10.3%	13.1%	0.95	[0.92; 0.99]
Fixed effect model	**57.7%**	**−−**	**0.96**	**[0.95; 0.97]**
Random effects model	**−−**	**56.7%**	**0.96**	**[0.95; 0.97]**
Heterogeneity: I^2 = 0%, p = 0.58				
Fixed effect model	**100.0%**	**−−**	**0.96**	**[0.95; 0.97]**
Random effects model	**−−**	**100.0%**	**0.96**	**[0.94; 0.97]**
Heterogeneity: I^2 = 5%, p = 0.39				

rs9648346[G]

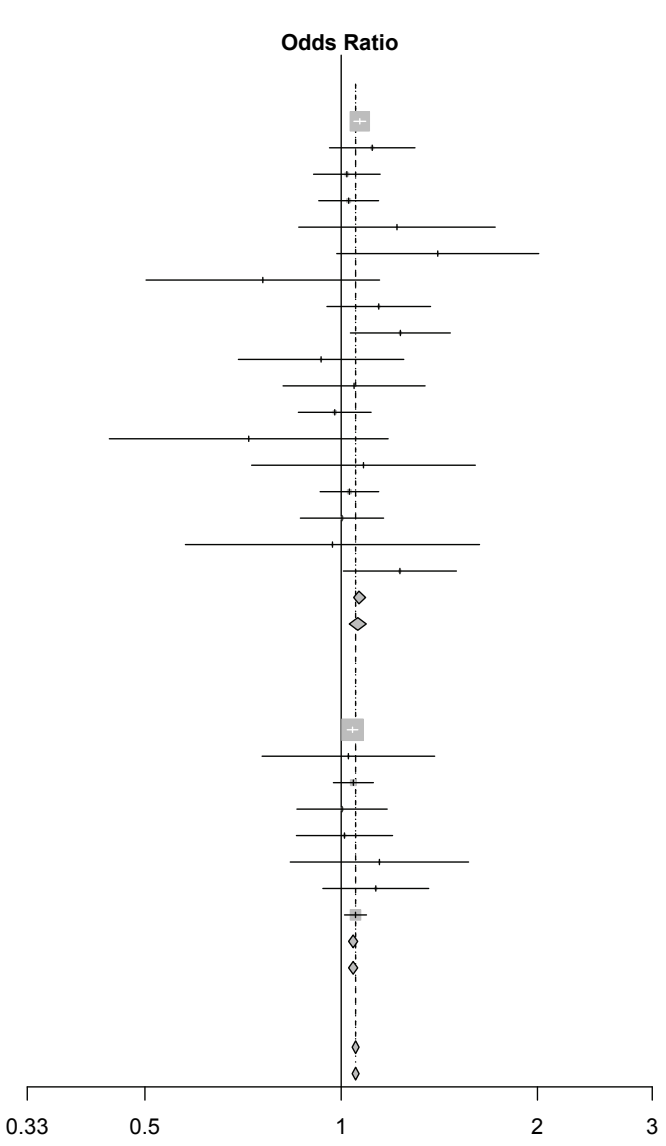


Study	Weight (fixed)	Weight (random)	OR	95%−CI
Phase = Discovery				
23andme	34.6%	34.6%	1.05	[1.03; 1.07]
AAGC(QIMR)	0.7%	0.7%	1.12	[0.97; 1.29]
ALSPAC	1.0%	1.0%	1.14	[1.02; 1.28]
B58C	1.3%	1.3%	0.99	[0.90; 1.10]
BAMSE	0.1%	0.1%	1.24	[0.90; 1.72]
COPSAC2000	0.1%	0.1%	1.00	[0.71; 1.42]
EVE (CAG/CSGA)	0.1%	0.1%	1.17	[0.78; 1.74]
EVE (CHS)	0.5%	0.5%	1.09	[0.92; 1.31]
GENR	0.4%	0.4%	1.04	[0.87; 1.24]
GENUFAD	0.2%	0.2%	1.27	[1.00; 1.61]
GINI/LISA	0.2%	0.2%	1.16	[0.91; 1.47]
GOYA	0.9%	0.9%	1.11	[0.98; 1.26]
INMA	0.1%	0.1%	1.31	[0.83; 2.07]
MAAS	0.1%	0.1%	0.93	[0.64; 1.36]
NFBC1966	1.1%	1.1%	1.00	[0.89; 1.12]
RAINE	0.4%	0.4%	1.02	[0.85; 1.23]
Fixed effect model	**41.9%**	**--**	**1.05**	**[1.03; 1.07]**
Random effects model	**--**	**41.9%**	**1.05**	**[1.03; 1.07]**
Heterogeneity: I^2 = 0%, p = 0.73				
Phase = Replication				
23andme	42.4%	42.4%	1.05	[1.03; 1.06]
CAMP	0.2%	0.2%	0.97	[0.74; 1.28]
deCODE	3.8%	3.8%	1.05	[0.99; 1.12]
ECRHS	0.4%	0.4%	0.99	[0.81; 1.20]
FINNTWIN	0.4%	0.4%	1.01	[0.85; 1.21]
GABRIELA	0.2%	0.2%	0.72	[0.54; 0.96]
GENEVA−KORA	0.6%	0.6%	1.13	[0.97; 1.33]
GOA	0.1%	0.1%	0.75	[0.55; 1.02]
SAPALDIA	0.4%	0.4%	1.08	[0.90; 1.29]
UK Biobank	9.7%	9.7%	1.04	[1.00; 1.08]
Fixed effect model	**58.1%**	**--**	**1.04**	**[1.03; 1.06]**
Random effects model	**--**	**58.1%**	**1.04**	**[1.00; 1.07]**
Heterogeneity: I^2 = 30%, p = 0.17				
Fixed effect model	**100.0%**	**--**	**1.05**	**[1.03; 1.06]**
Random effects model	**--**	**100.0%**	**1.05**	**[1.03; 1.06]**
Heterogeneity: I^2 = 0%, p = 0.48				

rs35350651[C]

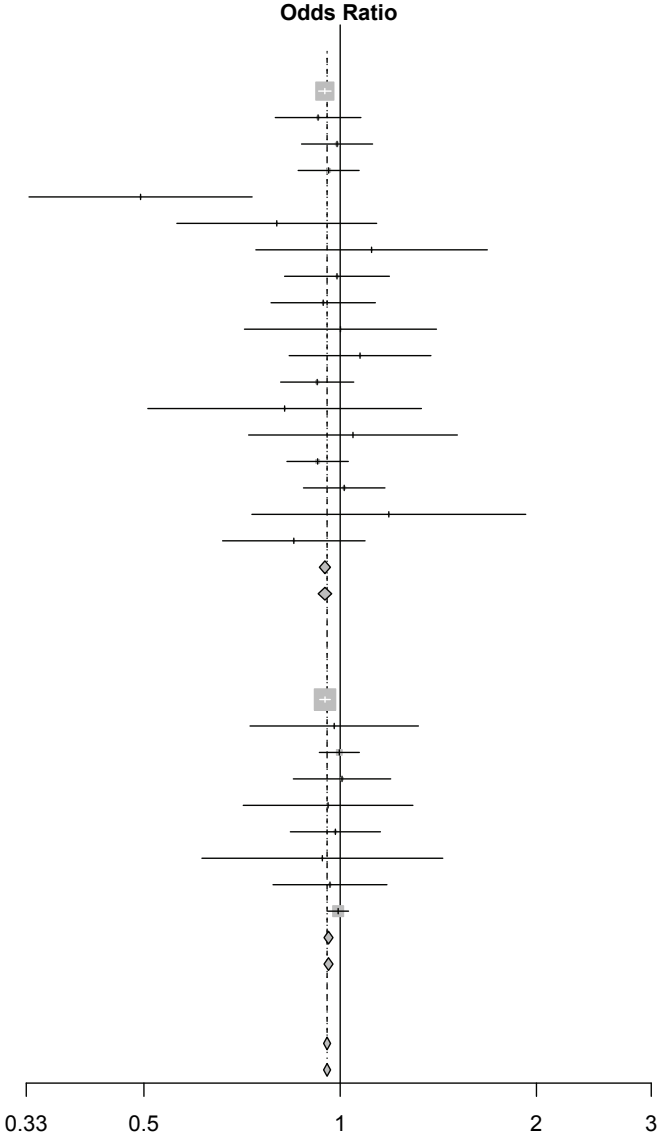


rs2519093[T]



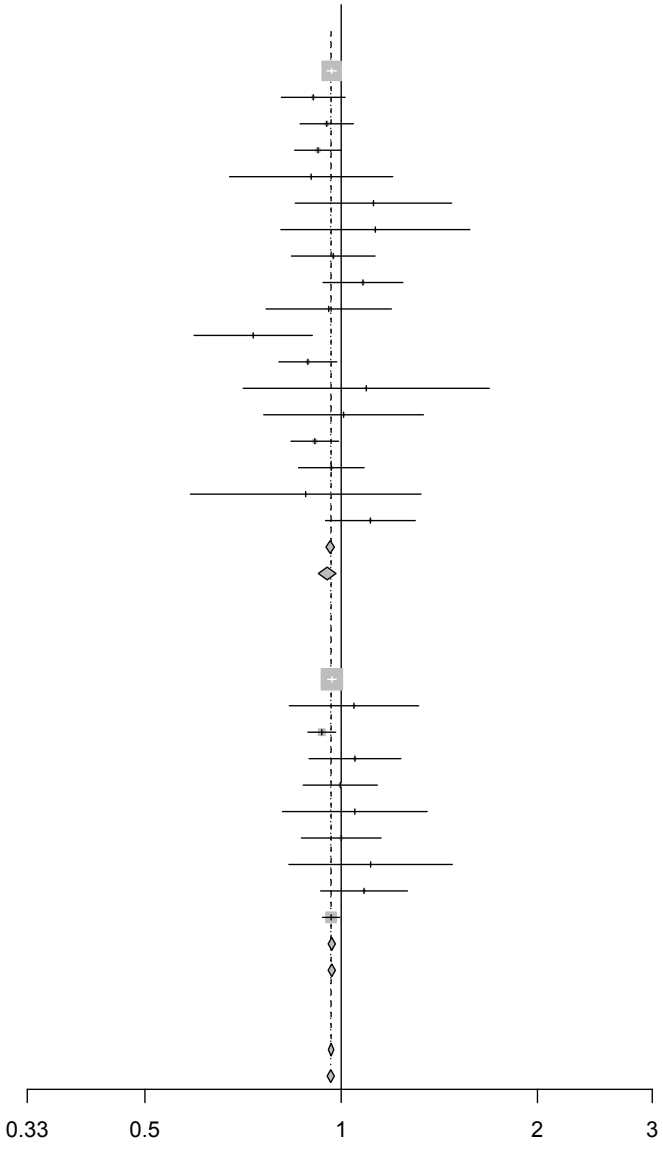
Study	Weight (fixed)	Weight (random)	OR	95%−CI
Phase = Discovery				
23andme	34.5%	34.5%	1.07	[1.05; 1.09]
AAGC(QIMR)	0.7%	0.7%	1.12	[0.96; 1.30]
ALSPAC	1.1%	1.1%	1.02	[0.91; 1.15]
B58C	1.3%	1.3%	1.03	[0.92; 1.14]
BAMSE	0.1%	0.1%	1.22	[0.86; 1.72]
COPSAC2000	0.1%	0.1%	1.41	[0.98; 2.01]
EVE (CAG/CSGA)	0.1%	0.1%	0.76	[0.50; 1.15]
EVE (CHS)	0.4%	0.4%	1.14	[0.95; 1.37]
GENR	0.5%	0.5%	1.23	[1.03; 1.47]
GENUFAD	0.2%	0.2%	0.93	[0.70; 1.25]
GINI/LISA	0.2%	0.2%	1.05	[0.81; 1.34]
GOYA	0.9%	0.9%	0.98	[0.86; 1.11]
INMA	0.1%	0.1%	0.72	[0.44; 1.18]
MAAS	0.1%	0.1%	1.08	[0.73; 1.61]
NFBC1966	1.4%	1.4%	1.03	[0.93; 1.14]
NTR (adults)	0.7%	0.7%	1.00	[0.87; 1.16]
NTR (children)	0.1%	0.1%	0.97	[0.58; 1.63]
RAINE	0.4%	0.4%	1.23	[1.01; 1.50]
Fixed effect model	**42.8%**	**−−**	**1.06**	**[1.04; 1.09]**
Random effects model	**−−**	**42.8%**	**1.06**	**[1.03; 1.09]**
Heterogeneity: I^2 = 7%, p = 0.37				
Phase = Replication				
23andme	42.4%	42.4%	1.04	[1.02; 1.06]
CAMP	0.2%	0.2%	1.03	[0.76; 1.39]
deCODE	3.0%	3.0%	1.04	[0.97; 1.12]
FINNTWIN	0.6%	0.6%	1.00	[0.86; 1.18]
GENEVA−KORA	0.5%	0.5%	1.01	[0.85; 1.20]
GOA	0.2%	0.2%	1.14	[0.84; 1.57]
SAPALDIA	0.4%	0.4%	1.13	[0.94; 1.36]
UK Biobank	9.9%	9.9%	1.05	[1.01; 1.09]
Fixed effect model	**57.2%**	**−−**	**1.04**	**[1.03; 1.06]**
Random effects model	**−−**	**57.2%**	**1.04**	**[1.03; 1.06]**
Heterogeneity: I^2 = 0%, p = 0.98				
Fixed effect model	**100.0%**	**−−**	**1.05**	**[1.04; 1.07]**
Random effects model	**−−**	**100.0%**	**1.05**	**[1.04; 1.07]**
Heterogeneity: I^2 = 0%, p = 0.61				

rs62257549[A]



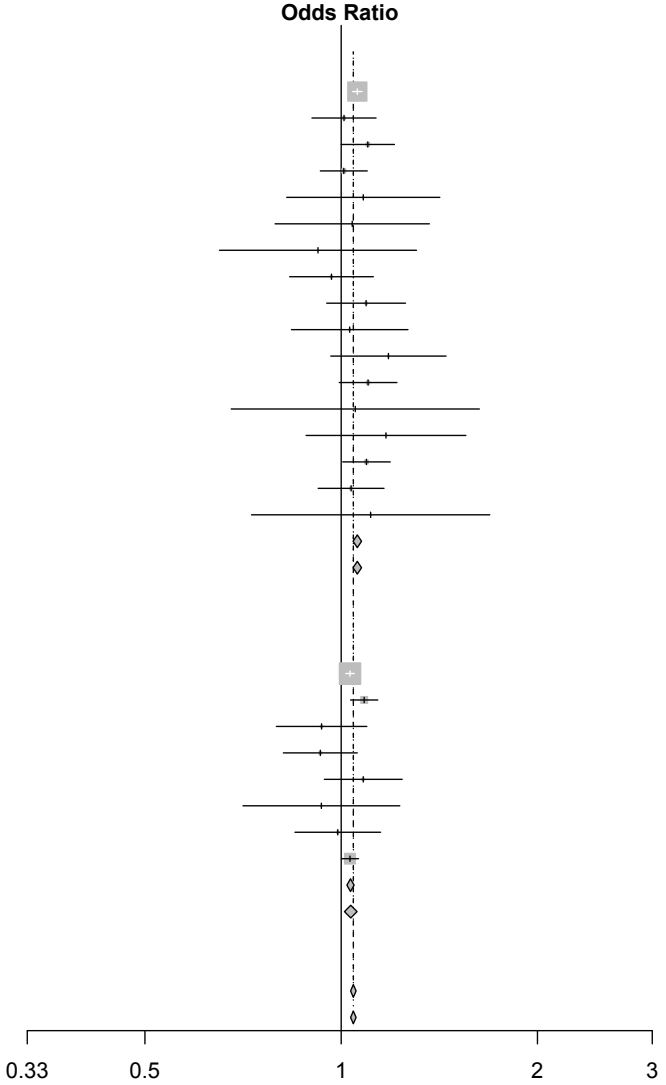
Study	Weight (fixed)	Weight (random)	OR	95%−CI
Phase = Discovery				
23andme	31.6%	31.6%	0.95	[0.93; 0.97]
AAGC(QIMR)	0.7%	0.7%	0.92	[0.80; 1.08]
ALSPAC	1.0%	1.0%	0.99	[0.87; 1.12]
B58C	1.3%	1.3%	0.96	[0.86; 1.07]
BAMSE	0.1%	0.1%	0.49	[0.33; 0.73]
COPSAC2000	0.1%	0.1%	0.80	[0.56; 1.14]
EVE (CAG/CSGA)	0.1%	0.1%	1.12	[0.74; 1.68]
EVE (CHS)	0.4%	0.4%	0.99	[0.82; 1.19]
GENR	0.4%	0.4%	0.94	[0.78; 1.13]
GENUFAD	0.1%	0.1%	1.00	[0.71; 1.41]
GINI/LISA	0.2%	0.2%	1.07	[0.84; 1.38]
GOYA	0.9%	0.9%	0.92	[0.81; 1.05]
INMA	0.1%	0.1%	0.82	[0.51; 1.33]
MAAS	0.1%	0.1%	1.05	[0.72; 1.51]
NFBC1966	1.3%	1.3%	0.92	[0.83; 1.03]
NTR (adults)	0.7%	0.7%	1.01	[0.88; 1.17]
NTR (children)	0.1%	0.1%	1.19	[0.73; 1.93]
RAINE	0.2%	0.2%	0.85	[0.66; 1.09]
Fixed effect model	**39.5%**	**−−**	**0.95**	**[0.93; 0.97]**
Random effects model	**−−**	**39.5%**	**0.95**	**[0.93; 0.97]**
Heterogeneity: I^2 = 2%, p = 0.43				
Phase = Replication				
23andme	44.2%	44.2%	0.95	[0.93; 0.97]
CAMP	0.2%	0.2%	0.98	[0.73; 1.32]
deCODE	3.0%	3.0%	1.00	[0.93; 1.07]
FINNTWIN	0.5%	0.5%	1.01	[0.85; 1.20]
GABRIELA	0.2%	0.2%	0.96	[0.71; 1.29]
GENEVA−KORA	0.6%	0.6%	0.98	[0.84; 1.15]
GOA	0.1%	0.1%	0.94	[0.61; 1.44]
SAPALDIA	0.4%	0.4%	0.96	[0.79; 1.18]
UK Biobank	11.3%	11.3%	0.99	[0.96; 1.03]
Fixed effect model	**60.5%**	**−−**	**0.96**	**[0.94; 0.97]**
Random effects model	**−−**	**60.5%**	**0.96**	**[0.94; 0.97]**
Heterogeneity: I^2 = 0%, p = 0.58				
Fixed effect model	**100.0%**	**−−**	**0.95**	**[0.94; 0.97]**
Random effects model	**−−**	**100.0%**	**0.95**	**[0.94; 0.97]**
Heterogeneity: I^2 = 0%, p = 0.53				

rs11677002[C]



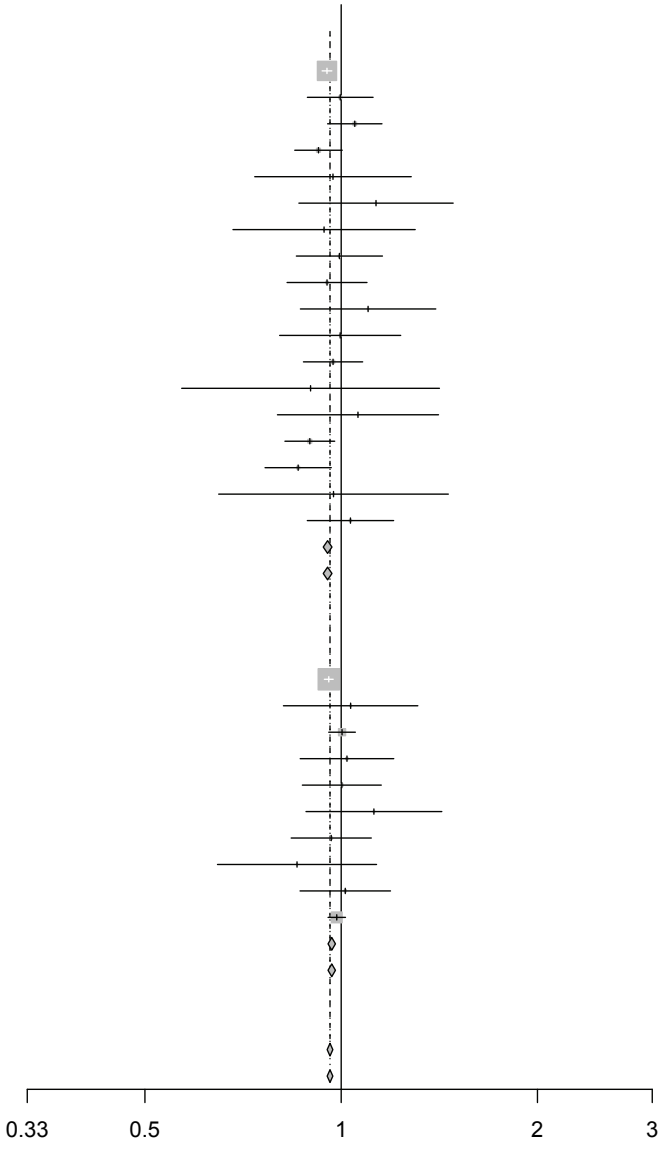
Study	Weight (fixed)	Weight (random)	OR	95%−CI
Phase = Discovery				
23andme	33.8%	29.5%	0.97	[0.95; 0.98]
AAGC(QIMR)	0.7%	1.3%	0.91	[0.81; 1.01]
ALSPAC	1.1%	1.8%	0.95	[0.86; 1.04]
B58C	1.4%	2.3%	0.92	[0.85; 1.00]
BAMSE	0.1%	0.2%	0.90	[0.67; 1.20]
COPSAC2000	0.1%	0.2%	1.12	[0.85; 1.48]
EVE (CAG/CSGA)	0.1%	0.1%	1.13	[0.81; 1.58]
EVE (CHS)	0.4%	0.7%	0.97	[0.84; 1.13]
GENR	0.5%	0.8%	1.08	[0.94; 1.24]
GENUFAD	0.2%	0.3%	0.96	[0.77; 1.19]
GINI/LISA	0.2%	0.4%	0.73	[0.59; 0.90]
GOYA	0.9%	1.5%	0.89	[0.80; 0.98]
INMA	0.1%	0.1%	1.09	[0.71; 1.69]
MAAS	0.1%	0.2%	1.01	[0.76; 1.34]
NFBC1966	1.3%	2.2%	0.91	[0.84; 0.99]
NTR (adults)	0.7%	1.2%	0.97	[0.86; 1.08]
NTR (children)	0.1%	0.1%	0.88	[0.59; 1.33]
RAINE	0.4%	0.7%	1.11	[0.95; 1.30]
Fixed effect model	**42.1%**	**−−**	**0.96**	**[0.95; 0.98]**
Random effects model	**−−**	**43.8%**	**0.95**	**[0.92; 0.98]**
Heterogeneity: I^2 = 21%, p = 0.20				
Phase = Replication				
23andme	41.4%	32.5%	0.97	[0.95; 0.98]
CAMP	0.2%	0.3%	1.05	[0.83; 1.31]
deCODE	3.9%	6.2%	0.93	[0.89; 0.98]
ECRHS	0.4%	0.6%	1.05	[0.89; 1.23]
FINNTWIN	0.6%	0.9%	1.00	[0.87; 1.14]
GABRIELA	0.1%	0.3%	1.05	[0.81; 1.35]
GENEVA−KORA	0.5%	0.8%	1.00	[0.87; 1.15]
GOA	0.1%	0.2%	1.11	[0.83; 1.48]
SAPALDIA	0.4%	0.7%	1.08	[0.93; 1.26]
UK Biobank	10.2%	13.7%	0.97	[0.94; 0.99]
Fixed effect model	**57.9%**	**−−**	**0.97**	**[0.96; 0.98]**
Random effects model	**−−**	**56.2%**	**0.97**	**[0.96; 0.98]**
Heterogeneity: I^2 = 0%, p = 0.61				
Fixed effect model	**100.0%**	**−−**	**0.97**	**[0.96; 0.97]**
Random effects model	**−−**	**100.0%**	**0.96**	**[0.95; 0.98]**
Heterogeneity: I^2 = 7%, p = 0.36				

rs35597970[−]



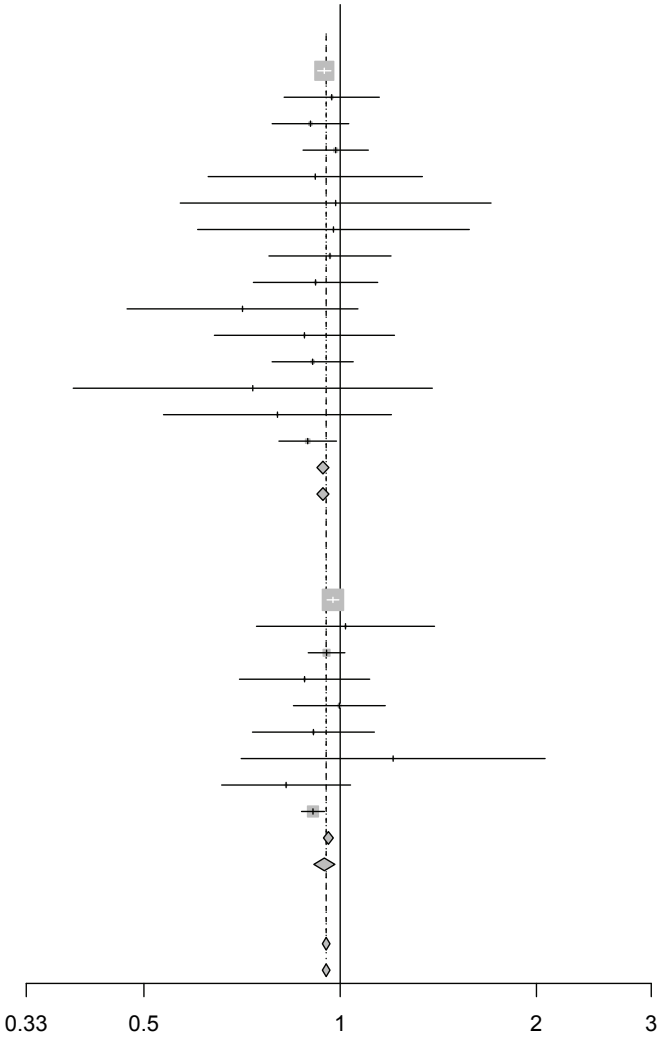
Study	Weight (fixed)	Weight (random)	OR	95%−CI
Phase = Discovery				
23andme	33.7%	33.7%	1.06	[1.04; 1.08]
AAGC(QIMR)	0.7%	0.7%	1.01	[0.90; 1.13]
ALSPAC	1.1%	1.1%	1.10	[1.00; 1.21]
B58C	1.4%	1.4%	1.01	[0.93; 1.10]
BAMSE	0.1%	0.1%	1.08	[0.82; 1.42]
COPSAC2000	0.1%	0.1%	1.04	[0.79; 1.37]
EVE (CAG/CSGA)	0.1%	0.1%	0.92	[0.65; 1.30]
EVE (CHS)	0.4%	0.4%	0.97	[0.83; 1.12]
GENR	0.5%	0.5%	1.09	[0.95; 1.26]
GENUFAD	0.2%	0.2%	1.03	[0.84; 1.27]
GINI/LISA	0.2%	0.2%	1.18	[0.96; 1.45]
GOYA	0.9%	0.9%	1.10	[0.99; 1.22]
INMA	0.0%	0.0%	1.05	[0.68; 1.63]
MAAS	0.1%	0.1%	1.17	[0.88; 1.55]
NFBC1966	1.3%	1.3%	1.09	[1.01; 1.19]
NTR (adults)	0.7%	0.7%	1.04	[0.92; 1.16]
NTR (children)	0.1%	0.1%	1.11	[0.73; 1.69]
Fixed effect model	**41.8%**	**−−**	**1.06**	**[1.04; 1.07]**
Random effects model	**−−**	**41.8%**	**1.06**	**[1.04; 1.07]**
Heterogeneity: I^2 = 0%, p = 0.95				
Phase = Replication				
23andme	41.8%	41.8%	1.03	[1.02; 1.05]
deCODE	4.1%	4.1%	1.08	[1.03; 1.14]
ECRHS	0.4%	0.4%	0.93	[0.80; 1.09]
FINNTWIN	0.6%	0.6%	0.93	[0.82; 1.06]
GENEVA−KORA	0.5%	0.5%	1.08	[0.94; 1.24]
GOA	0.1%	0.1%	0.93	[0.71; 1.23]
SAPALDIA	0.4%	0.4%	0.99	[0.85; 1.15]
UK Biobank	10.4%	10.4%	1.03	[1.00; 1.06]
Fixed effect model	**58.2%**	**−−**	**1.03**	**[1.02; 1.05]**
Random effects model	**−−**	**58.2%**	**1.03**	**[1.01; 1.06]**
Heterogeneity: I^2 = 25%, p = 0.23				
Fixed effect model	**100.0%**	**−−**	**1.04**	**[1.03; 1.05]**
Random effects model	**−−**	**100.0%**	**1.04**	**[1.03; 1.05]**
Heterogeneity: I^2 = 0%, p = 0.53				

rs2815765[T]



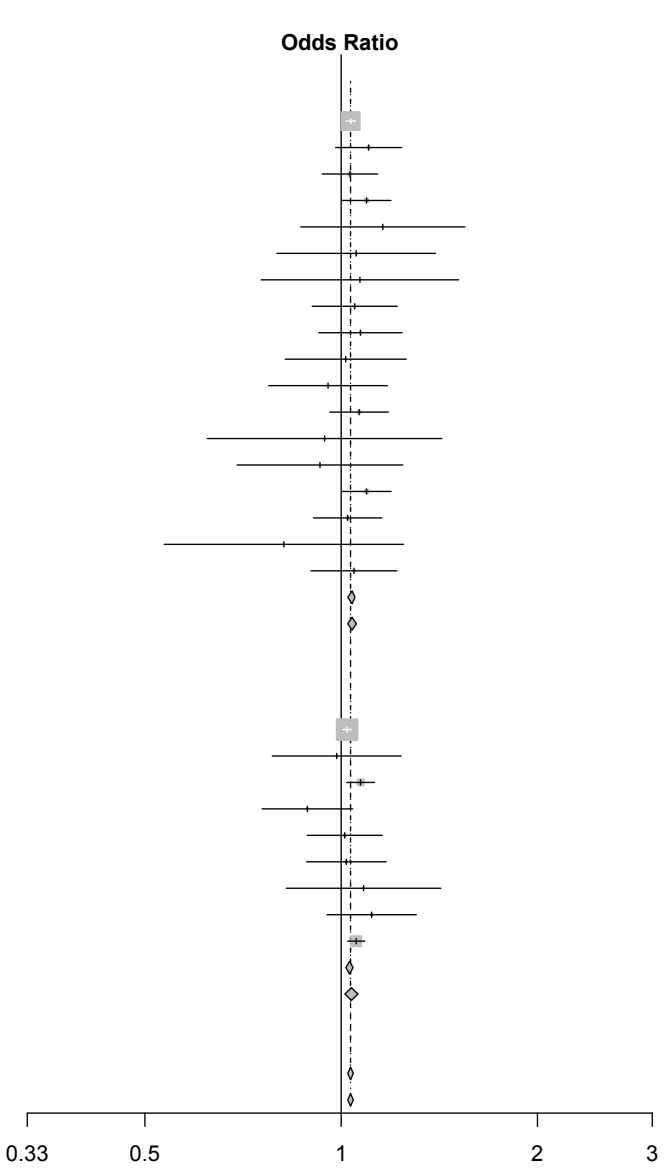
Study	Weight (fixed)	Weight (random)	OR	95%−CI
Phase = Discovery				
23andme	33.4%	33.4%	0.95	[0.93; 0.97]
AAGC(QIMR)	0.7%	0.7%	1.00	[0.89; 1.12]
ALSPAC	1.1%	1.1%	1.05	[0.95; 1.15]
B58C	1.4%	1.4%	0.92	[0.85; 1.00]
BAMSE	0.1%	0.1%	0.97	[0.74; 1.28]
COPSAC2000	0.1%	0.1%	1.13	[0.86; 1.49]
EVE (CAG/CSGA)	0.1%	0.1%	0.94	[0.68; 1.30]
EVE (CHS)	0.4%	0.4%	0.99	[0.85; 1.16]
GENR	0.5%	0.5%	0.95	[0.83; 1.10]
GENUFAD	0.2%	0.2%	1.10	[0.87; 1.40]
GINI/LISA	0.2%	0.2%	1.00	[0.80; 1.23]
GOYA	0.9%	0.9%	0.97	[0.88; 1.08]
INMA	0.0%	0.0%	0.90	[0.57; 1.41]
MAAS	0.1%	0.1%	1.06	[0.80; 1.41]
NFBC1966	1.3%	1.3%	0.90	[0.82; 0.98]
NTR (adults)	0.7%	0.7%	0.86	[0.76; 0.97]
NTR (children)	0.1%	0.1%	0.97	[0.65; 1.46]
RAINE	0.4%	0.4%	1.03	[0.89; 1.20]
Fixed effect model	**41.9%**	**−−**	**0.95**	**[0.94; 0.97]**
Random effects model	**−−**	**41.9%**	**0.95**	**[0.94; 0.97]**
Heterogeneity: I^2 = 0%, p = 0.58				
Phase = Replication				
23andme	40.8%	40.8%	0.96	[0.94; 0.97]
CAMP	0.2%	0.2%	1.03	[0.82; 1.31]
deCODE	4.5%	4.5%	1.00	[0.96; 1.05]
ECRHS	0.4%	0.4%	1.02	[0.87; 1.20]
FINNTWIN	0.5%	0.5%	1.00	[0.87; 1.15]
GABRIELA	0.2%	0.2%	1.12	[0.88; 1.43]
GENEVA−KORA	0.5%	0.5%	0.97	[0.84; 1.11]
GOA	0.1%	0.1%	0.86	[0.65; 1.13]
SAPALDIA	0.4%	0.4%	1.01	[0.86; 1.19]
UK Biobank	10.5%	10.5%	0.98	[0.95; 1.02]
Fixed effect model	**58.1%**	**−−**	**0.97**	**[0.95; 0.98]**
Random effects model	**−−**	**58.1%**	**0.97**	**[0.95; 0.98]**
Heterogeneity: I^2 = 0%, p = 0.45				
Fixed effect model	**100.0%**	**−−**	**0.96**	**[0.95; 0.97]**
Random effects model	**−−**	**100.0%**	**0.96**	**[0.95; 0.97]**
Heterogeneity: I^2 = 0%, p = 0.52				

rs11671925[A]



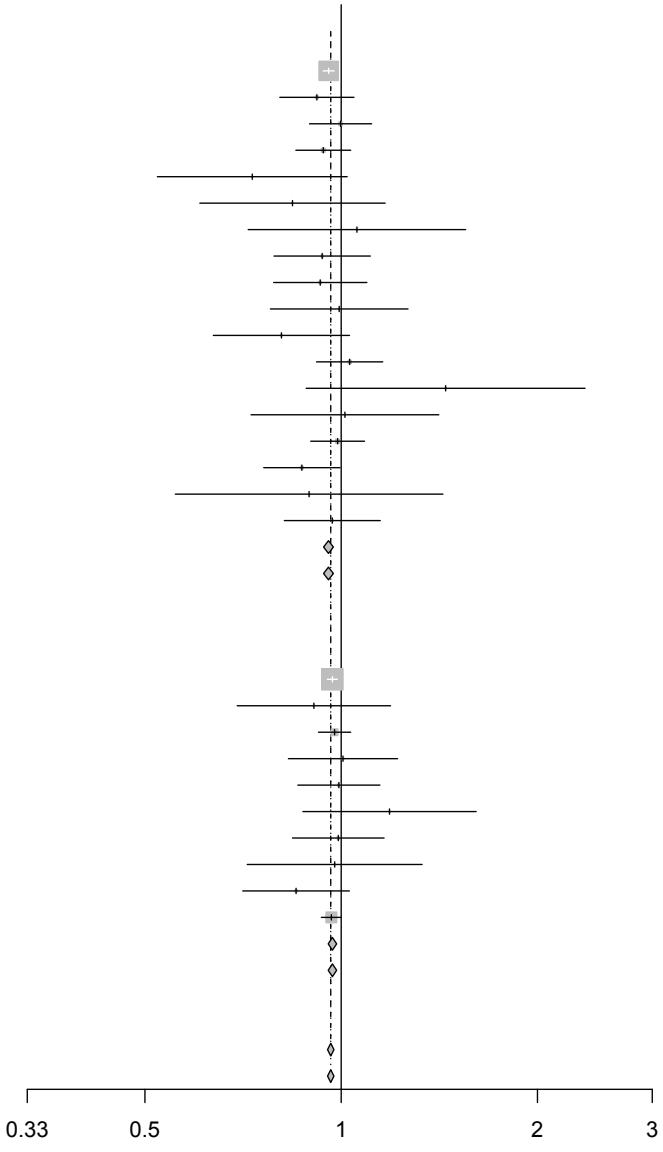
Study	Weight (fixed)	Weight (random)	OR	95%−CI
Phase = Discovery				
23andme	33.4%	33.4%	0.95	[0.92; 0.97]
AAGC(QIMR)	0.6%	0.6%	0.97	[0.82; 1.15]
ALSPAC	1.0%	1.0%	0.90	[0.79; 1.03]
B58C	1.4%	1.4%	0.98	[0.88; 1.10]
BAMSE	0.1%	0.1%	0.92	[0.63; 1.34]
COPSAC2000	0.1%	0.1%	0.98	[0.57; 1.70]
EVE (CAG/CSGA)	0.1%	0.1%	0.98	[0.60; 1.58]
EVE (CHS)	0.4%	0.4%	0.96	[0.78; 1.20]
GENR	0.4%	0.4%	0.92	[0.74; 1.14]
GENUFAD	0.1%	0.1%	0.71	[0.47; 1.06]
GINI/LISA	0.2%	0.2%	0.88	[0.64; 1.21]
GOYA	0.9%	0.9%	0.91	[0.79; 1.05]
INMA	0.0%	0.0%	0.73	[0.39; 1.38]
MAAS	0.1%	0.1%	0.80	[0.54; 1.20]
NFBC1966	1.8%	1.8%	0.89	[0.81; 0.99]
Fixed effect model	**40.5%**	**--**	**0.94**	**[0.92; 0.96]**
Random effects model	**--**	**40.5%**	**0.94**	**[0.92; 0.96]**
Heterogeneity: I^2 = 0%, p = 0.97				
Phase = Replication				
23andme	42.1%	42.1%	0.97	[0.95; 1.00]
CAMP	0.2%	0.2%	1.02	[0.74; 1.40]
deCODE	4.3%	4.3%	0.95	[0.89; 1.02]
ECRHS	0.3%	0.3%	0.88	[0.70; 1.11]
FINNTWIN	0.7%	0.7%	1.00	[0.85; 1.17]
GENEVA−KORA	0.4%	0.4%	0.91	[0.73; 1.13]
GOA	0.1%	0.1%	1.21	[0.70; 2.06]
SAPALDIA	0.3%	0.3%	0.83	[0.66; 1.04]
UK Biobank	11.1%	11.1%	0.91	[0.87; 0.95]
Fixed effect model	**59.5%**	**--**	**0.96**	**[0.94; 0.98]**
Random effects model	**--**	**59.5%**	**0.95**	**[0.91; 0.98]**
Heterogeneity: I^2 = 37%, p = 0.12				
Fixed effect model	**100.0%**	**--**	**0.95**	**[0.94; 0.96]**
Random effects model	**--**	**100.0%**	**0.95**	**[0.94; 0.96]**
Heterogeneity: I^2 = 0%, p = 0.60				

rs2461475[C]



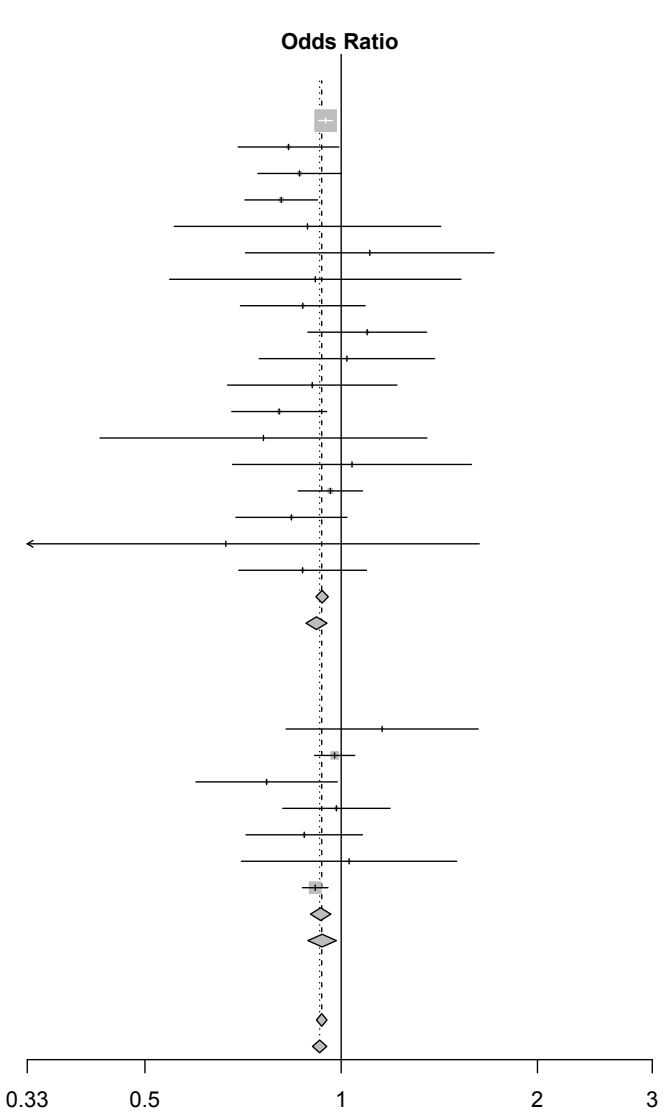
Study	Weight (fixed)	Weight (random)	OR	95%−CI
Phase = Discovery				
23andme	32.7%	32.7%	1.03	[1.02; 1.05]
AAGC(QIMR)	0.7%	0.7%	1.10	[0.98; 1.24]
ALSPAC	1.0%	1.0%	1.03	[0.94; 1.14]
B58C	1.3%	1.3%	1.09	[1.00; 1.19]
BAMSE	0.1%	0.1%	1.16	[0.87; 1.55]
COPSAC2000	0.1%	0.1%	1.05	[0.80; 1.40]
EVE (CAG/CSGA)	0.1%	0.1%	1.07	[0.75; 1.51]
EVE (CHS)	0.4%	0.4%	1.05	[0.90; 1.22]
GENR	0.4%	0.4%	1.07	[0.92; 1.24]
GENUFAD	0.2%	0.2%	1.02	[0.82; 1.26]
GINI/LISA	0.2%	0.2%	0.95	[0.77; 1.18]
GOYA	0.9%	0.9%	1.07	[0.96; 1.18]
INMA	0.1%	0.1%	0.94	[0.62; 1.43]
MAAS	0.1%	0.1%	0.93	[0.69; 1.24]
NFBC1966	1.3%	1.3%	1.09	[1.00; 1.19]
NTR (adults)	0.7%	0.7%	1.02	[0.91; 1.15]
NTR (children)	0.1%	0.1%	0.82	[0.54; 1.25]
RAINE	0.4%	0.4%	1.05	[0.90; 1.22]
Fixed effect model	**40.8%**	**−−**	**1.04**	**[1.02; 1.05]**
Random effects model	**−−**	**40.8%**	**1.04**	**[1.02; 1.06]**
Heterogeneity: I^2 = 0%, p = 0.97				
Phase = Replication				
23andme	42.7%	42.7%	1.02	[1.01; 1.04]
CAMP	0.2%	0.2%	0.98	[0.78; 1.24]
deCODE	4.0%	4.0%	1.07	[1.02; 1.12]
ECRHS	0.4%	0.4%	0.89	[0.76; 1.04]
FINNTWIN	0.5%	0.5%	1.01	[0.89; 1.16]
GENEVA−KORA	0.5%	0.5%	1.02	[0.88; 1.17]
GOA	0.1%	0.1%	1.08	[0.82; 1.42]
SAPALDIA	0.4%	0.4%	1.11	[0.95; 1.30]
UK Biobank	10.5%	10.5%	1.05	[1.02; 1.09]
Fixed effect model	**59.2%**	**−−**	**1.03**	**[1.02; 1.04]**
Random effects model	**−−**	**59.2%**	**1.04**	**[1.01; 1.06]**
Heterogeneity: I^2 = 25%, p = 0.22				
Fixed effect model	**100.0%**	**−−**	**1.03**	**[1.02; 1.04]**
Random effects model	**−−**	**100.0%**	**1.03**	**[1.02; 1.04]**
Heterogeneity: I^2 = 0%, p = 0.83				

rs6738964[G]



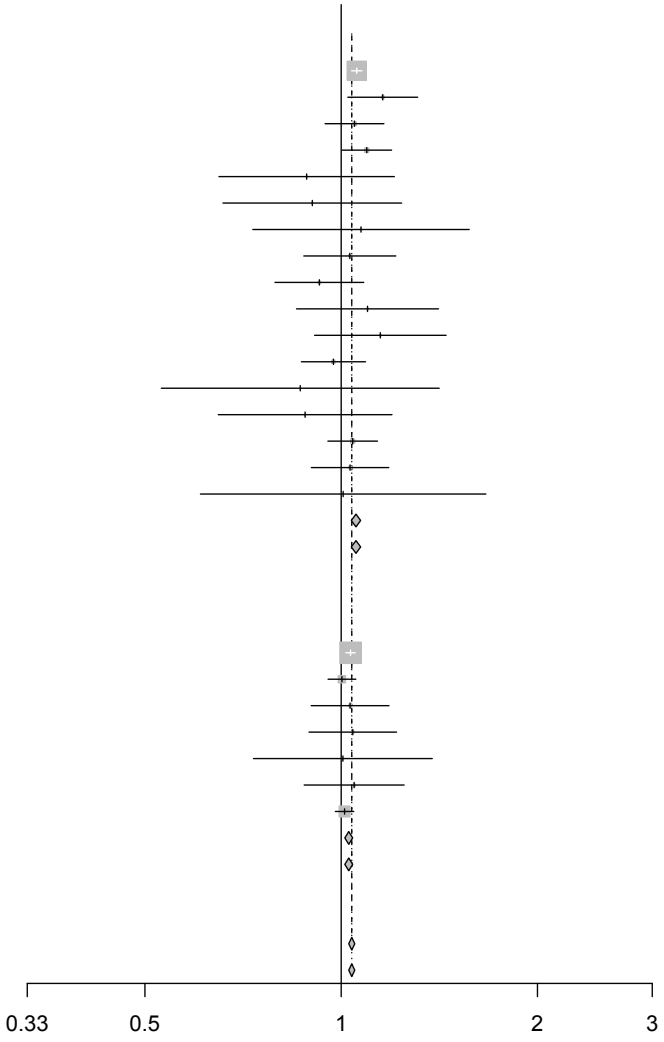
Study	Weight (fixed)	Weight (random)	OR	95%−CI
Phase = Discovery				
23andme	33.8%	33.8%	0.96	[0.94; 0.98]
AAGC(QIMR)	0.7%	0.7%	0.92	[0.81; 1.05]
ALSPAC	1.1%	1.1%	1.00	[0.89; 1.11]
B58C	1.4%	1.4%	0.94	[0.85; 1.03]
BAMSE	0.1%	0.1%	0.73	[0.52; 1.02]
COPSAC2000	0.1%	0.1%	0.84	[0.61; 1.17]
EVE (CAG/CSGA)	0.1%	0.1%	1.06	[0.72; 1.55]
EVE (CHS)	0.4%	0.4%	0.94	[0.79; 1.11]
GENR	0.5%	0.5%	0.93	[0.79; 1.09]
GENUFAD	0.2%	0.2%	0.99	[0.78; 1.27]
GINI/LISA	0.2%	0.2%	0.81	[0.64; 1.03]
GOYA	0.9%	0.9%	1.03	[0.92; 1.16]
INMA	0.1%	0.1%	1.45	[0.88; 2.37]
MAAS	0.1%	0.1%	1.01	[0.73; 1.41]
NFBC1966	1.4%	1.4%	0.99	[0.90; 1.09]
NTR (adults)	0.7%	0.7%	0.87	[0.76; 1.00]
NTR (children)	0.1%	0.1%	0.89	[0.56; 1.43]
RAINE	0.4%	0.4%	0.97	[0.82; 1.15]
Fixed effect model	**42.4%**	**−−**	**0.96**	**[0.94; 0.97]**
Random effects model	**−−**	**42.4%**	**0.96**	**[0.94; 0.97]**
Heterogeneity: I^2 = 0%, p = 0.71				
Phase = Replication				
23andme	41.0%	41.0%	0.97	[0.95; 0.99]
CAMP	0.2%	0.2%	0.91	[0.69; 1.19]
deCODE	4.0%	4.0%	0.98	[0.92; 1.03]
ECRHS	0.3%	0.3%	1.01	[0.83; 1.22]
FINNTWIN	0.6%	0.6%	0.99	[0.86; 1.15]
GABRIELA	0.1%	0.1%	1.19	[0.87; 1.61]
GENEVA−KORA	0.5%	0.5%	0.99	[0.84; 1.16]
GOA	0.1%	0.1%	0.98	[0.72; 1.33]
SAPALDIA	0.4%	0.4%	0.85	[0.71; 1.03]
UK Biobank	10.4%	10.4%	0.97	[0.93; 1.00]
Fixed effect model	**57.6%**	**−−**	**0.97**	**[0.96; 0.98]**
Random effects model	**−−**	**57.6%**	**0.97**	**[0.96; 0.98]**
Heterogeneity: I^2 = 0%, p = 0.91				
Fixed effect model	**100.0%**	**−−**	**0.96**	**[0.95; 0.97]**
Random effects model	**−−**	**100.0%**	**0.96**	**[0.95; 0.97]**
Heterogeneity: I^2 = 0%, p = 0.87				

rs10519067[A]



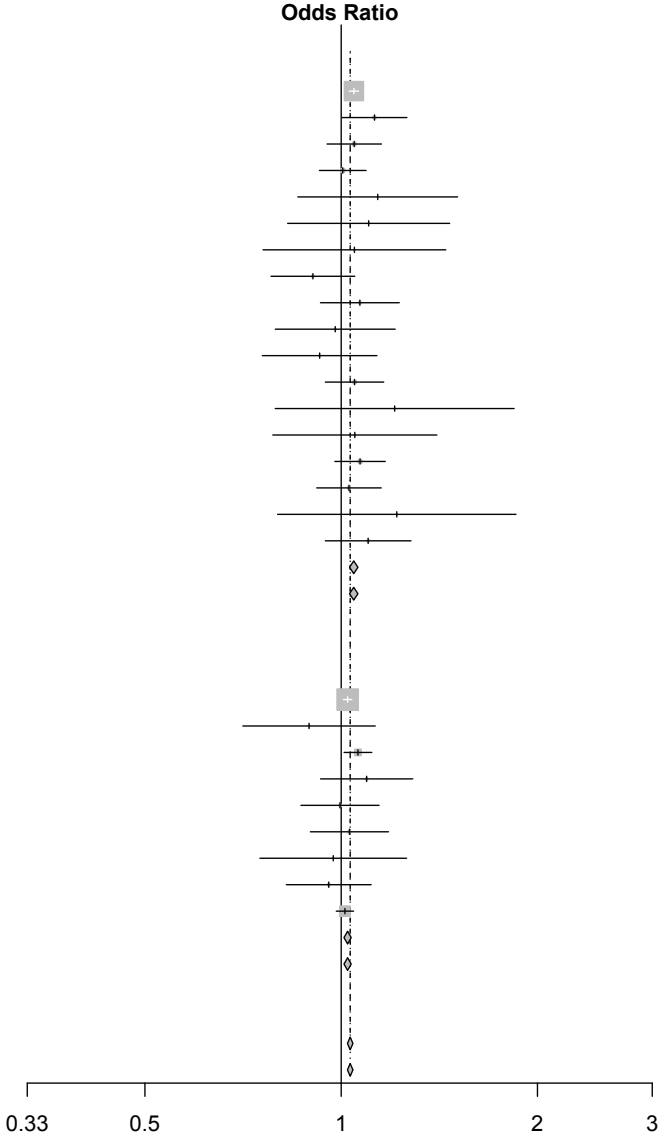
Study	Weight (fixed)	Weight (random)	OR	95%−CI
Phase = Discovery				
23andme	59.4%	39.7%	0.95	[0.92; 0.97]
AAGC(QIMR)	1.1%	2.0%	0.83	[0.69; 0.99]
ALSPAC	1.6%	2.8%	0.86	[0.75; 1.00]
B58C	2.1%	3.7%	0.81	[0.71; 0.92]
BAMSE	0.2%	0.3%	0.89	[0.55; 1.42]
COPSAC2000	0.2%	0.3%	1.11	[0.71; 1.72]
EVE (CAG/CSGA)	0.1%	0.2%	0.91	[0.55; 1.53]
EVE (CHS)	0.7%	1.3%	0.87	[0.70; 1.09]
GENR	0.8%	1.4%	1.10	[0.89; 1.35]
GENUFAD	0.4%	0.7%	1.02	[0.75; 1.39]
GINI/LISA	0.4%	0.7%	0.90	[0.67; 1.22]
GOYA	1.2%	2.2%	0.80	[0.68; 0.95]
INMA	0.1%	0.2%	0.76	[0.43; 1.35]
MAAS	0.2%	0.4%	1.04	[0.68; 1.58]
NFBC1966	2.7%	4.6%	0.96	[0.86; 1.08]
NTR (adults)	0.9%	1.6%	0.84	[0.69; 1.02]
NTR (children)	0.0%	0.1%	0.67	[0.27; 1.63]
RAINE	0.7%	1.2%	0.87	[0.70; 1.09]
Fixed effect model	**72.9%**	**−−**	**0.93**	**[0.91; 0.96]**
Random effects model	**−−**	**63.3%**	**0.92**	**[0.88; 0.95]**
Heterogeneity: I^2 = 8%, p = 0.36				
Phase = Replication				
CAMP	0.3%	0.6%	1.16	[0.82; 1.62]
deCODE	6.9%	10.5%	0.98	[0.91; 1.05]
ECRHS	0.6%	1.0%	0.77	[0.60; 0.99]
FINNTWIN	1.0%	1.7%	0.98	[0.81; 1.19]
GENEVA−KORA	0.8%	1.5%	0.88	[0.71; 1.08]
GOA	0.2%	0.4%	1.03	[0.70; 1.50]
UK Biobank	17.3%	21.0%	0.91	[0.87; 0.95]
Fixed effect model	**27.1%**	**−−**	**0.93**	**[0.90; 0.96]**
Random effects model	**−−**	**36.7%**	**0.93**	**[0.89; 0.98]**
Heterogeneity: I^2 = 18%, p = 0.30				
Fixed effect model	**100.0%**	**−−**	**0.93**	**[0.92; 0.95]**
Random effects model	**−−**	**100.0%**	**0.93**	**[0.90; 0.95]**
Heterogeneity: I^2 = 7%, p = 0.36				

rs138050288[−]



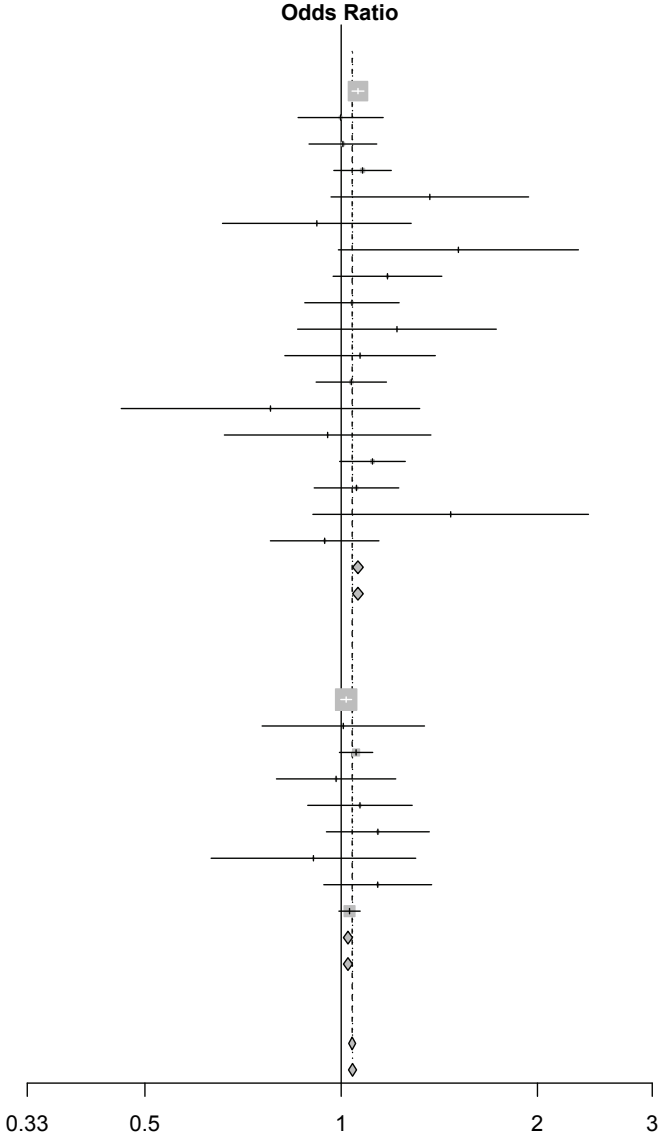
Study	Weight (fixed)	Weight (random)	OR	95%−CI
Phase = Discovery				
23andme	33.6%	33.6%	1.06	[1.04; 1.08]
AAGC(QIMR)	0.7%	0.7%	1.16	[1.02; 1.31]
ALSPAC	1.1%	1.1%	1.05	[0.94; 1.16]
B58C	1.5%	1.5%	1.09	[1.00; 1.19]
BAMSE	0.1%	0.1%	0.89	[0.65; 1.21]
COPSAC2000	0.1%	0.1%	0.90	[0.66; 1.24]
EVE (CAG/CSGA)	0.1%	0.1%	1.07	[0.73; 1.57]
EVE (CHS)	0.4%	0.4%	1.03	[0.88; 1.21]
GENR	0.5%	0.5%	0.93	[0.79; 1.08]
GENUFAD	0.2%	0.2%	1.10	[0.85; 1.41]
GINI/LISA	0.2%	0.2%	1.15	[0.91; 1.45]
GOYA	0.9%	0.9%	0.97	[0.87; 1.09]
INMA	0.0%	0.0%	0.87	[0.53; 1.41]
MAAS	0.1%	0.1%	0.88	[0.65; 1.20]
NFBC1966	1.5%	1.5%	1.04	[0.95; 1.14]
NTR (adults)	0.6%	0.6%	1.03	[0.90; 1.18]
NTR (children)	0.0%	0.0%	1.01	[0.61; 1.67]
Fixed effect model	**41.7%**	**−−**	**1.05**	**[1.04; 1.07]**
Random effects model	**−−**	**41.7%**	**1.05**	**[1.04; 1.07]**
Heterogeneity: I^2 = 0%, p = 0.71				
Phase = Replication				
23andme	41.4%	41.4%	1.03	[1.02; 1.05]
deCODE	4.7%	4.7%	1.00	[0.95; 1.05]
FINNTWIN	0.6%	0.6%	1.03	[0.90; 1.18]
GENEVA−KORA	0.5%	0.5%	1.04	[0.89; 1.22]
GOA	0.1%	0.1%	1.01	[0.73; 1.38]
SAPALDIA	0.4%	0.4%	1.05	[0.88; 1.25]
UK Biobank	10.7%	10.7%	1.01	[0.98; 1.05]
Fixed effect model	**58.3%**	**−−**	**1.03**	**[1.01; 1.04]**
Random effects model	**−−**	**58.3%**	**1.03**	**[1.01; 1.04]**
Heterogeneity: I^2 = 0%, p = 0.89				
Fixed effect model	**100.0%**	**−−**	**1.04**	**[1.03; 1.05]**
Random effects model	**−−**	**100.0%**	**1.04**	**[1.03; 1.05]**
Heterogeneity: I^2 = 0%, p = 0.63				

rs7328203[G]



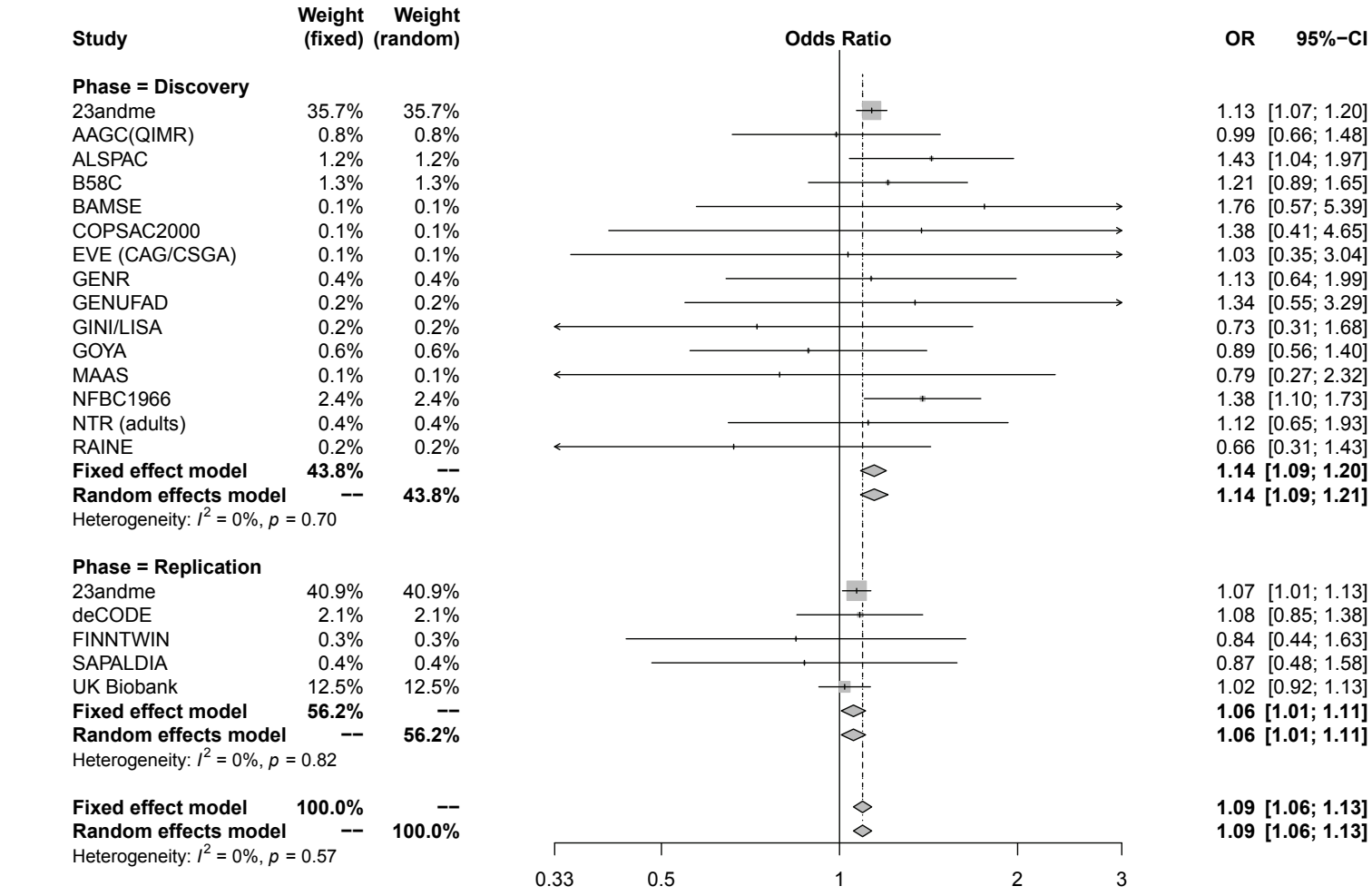
Study	Weight (fixed)	Weight (random)	OR	95%−CI
Phase = Discovery				
23andme	34.1%	34.1%	1.05	[1.03; 1.06]
AAGC(QIMR)	0.7%	0.7%	1.12	[1.00; 1.26]
ALSPAC	1.0%	1.0%	1.05	[0.95; 1.15]
B58C	1.4%	1.4%	1.01	[0.93; 1.09]
BAMSE	0.1%	0.1%	1.14	[0.86; 1.51]
COPSAC2000	0.1%	0.1%	1.10	[0.83; 1.47]
EVE (CAG/CSGA)	0.1%	0.1%	1.05	[0.76; 1.45]
EVE (CHS)	0.4%	0.4%	0.90	[0.78; 1.05]
GENR	0.5%	0.5%	1.07	[0.93; 1.23]
GENUFAD	0.2%	0.2%	0.98	[0.79; 1.21]
GINI/LISA	0.2%	0.2%	0.93	[0.76; 1.13]
GOYA	0.9%	0.9%	1.05	[0.95; 1.16]
INMA	0.1%	0.1%	1.21	[0.79; 1.84]
MAAS	0.1%	0.1%	1.05	[0.79; 1.40]
NFBC1966	1.2%	1.2%	1.07	[0.98; 1.17]
NTR (adults)	0.7%	0.7%	1.03	[0.92; 1.15]
NTR (children)	0.1%	0.1%	1.22	[0.80; 1.85]
RAINE	0.4%	0.4%	1.10	[0.95; 1.28]
Fixed effect model	**42.4%**	**−−**	**1.05**	**[1.03; 1.06]**
Random effects model	**−−**	**42.4%**	**1.05**	**[1.03; 1.06]**
Heterogeneity: I^2 = 0%, p = 0.90				
Phase = Replication				
23andme	41.6%	41.6%	1.02	[1.01; 1.04]
CAMP	0.2%	0.2%	0.89	[0.71; 1.13]
deCODE	3.9%	3.9%	1.06	[1.01; 1.11]
ECRHS	0.4%	0.4%	1.09	[0.93; 1.29]
FINNTWIN	0.5%	0.5%	1.00	[0.87; 1.14]
GENEVA−KORA	0.5%	0.5%	1.03	[0.90; 1.18]
GOA	0.1%	0.1%	0.97	[0.75; 1.26]
SAPALDIA	0.4%	0.4%	0.96	[0.82; 1.11]
UK Biobank	10.0%	10.0%	1.01	[0.98; 1.04]
Fixed effect model	**57.6%**	**−−**	**1.02**	**[1.01; 1.04]**
Random effects model	**−−**	**57.6%**	**1.02**	**[1.01; 1.04]**
Heterogeneity: I^2 = 0%, p = 0.70				
Fixed effect model	**100.0%**	**−−**	**1.03**	**[1.02; 1.04]**
Random effects model	**−−**	**100.0%**	**1.03**	**[1.02; 1.04]**
Heterogeneity: I^2 = 0%, p = 0.78				

rs11169225[A]

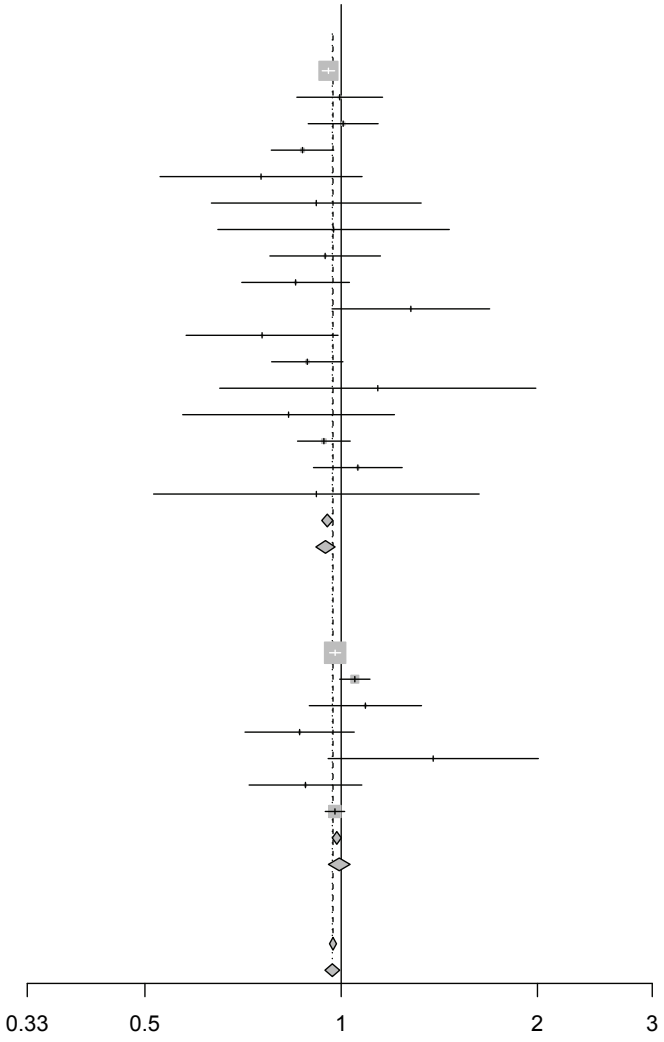


Study	Weight (fixed)	Weight (random)	OR	95%−CI
Phase = Discovery				
23andme	33.9%	32.0%	1.06	[1.04; 1.08]
AAGC(QIMR)	0.7%	0.9%	1.00	[0.86; 1.16]
ALSPAC	1.0%	1.4%	1.01	[0.89; 1.13]
B58C	1.5%	1.9%	1.08	[0.97; 1.19]
BAMSE	0.1%	0.2%	1.37	[0.96; 1.94]
COPSAC2000	0.1%	0.2%	0.92	[0.66; 1.28]
EVE (CAG/CSGA)	0.1%	0.1%	1.51	[0.99; 2.31]
EVE (CHS)	0.4%	0.5%	1.18	[0.97; 1.43]
GENR	0.5%	0.7%	1.04	[0.88; 1.23]
GENUFAD	0.1%	0.2%	1.22	[0.86; 1.73]
GINI/LISA	0.2%	0.3%	1.07	[0.82; 1.39]
GOYA	1.0%	1.3%	1.04	[0.92; 1.17]
INMA	0.1%	0.1%	0.78	[0.46; 1.32]
MAAS	0.1%	0.2%	0.95	[0.66; 1.37]
NFBC1966	1.1%	1.5%	1.12	[0.99; 1.25]
NTR (adults)	0.7%	0.9%	1.06	[0.91; 1.23]
NTR (children)	0.1%	0.1%	1.47	[0.90; 2.39]
RAINE	0.4%	0.5%	0.94	[0.78; 1.14]
Fixed effect model	**42.1%**	**−−**	**1.06**	**[1.04; 1.08]**
Random effects model	**−−**	**42.9%**	**1.06**	**[1.04; 1.08]**
Heterogeneity: I^2 = 0%, p = 0.63				
Phase = Replication				
23andme	41.0%	36.4%	1.02	[1.00; 1.04]
CAMP	0.2%	0.2%	1.01	[0.76; 1.34]
deCODE	4.3%	5.5%	1.05	[0.99; 1.12]
ECRHS	0.3%	0.5%	0.98	[0.80; 1.21]
FINNTWIN	0.4%	0.6%	1.07	[0.89; 1.28]
GENEVA−KORA	0.5%	0.6%	1.14	[0.95; 1.37]
GOA	0.1%	0.2%	0.91	[0.63; 1.30]
SAPALDIA	0.4%	0.6%	1.14	[0.94; 1.38]
UK Biobank	10.6%	12.6%	1.03	[0.99; 1.07]
Fixed effect model	**57.9%**	**−−**	**1.02**	**[1.01; 1.04]**
Random effects model	**−−**	**57.1%**	**1.02**	**[1.01; 1.04]**
Heterogeneity: I^2 = 0%, p = 0.79				
Fixed effect model	**100.0%**	**−−**	**1.04**	**[1.03; 1.05]**
Random effects model	**−−**	**100.0%**	**1.04**	**[1.03; 1.06]**
Heterogeneity: I^2 = 3%, p = 0.42				

rs141023293[A]

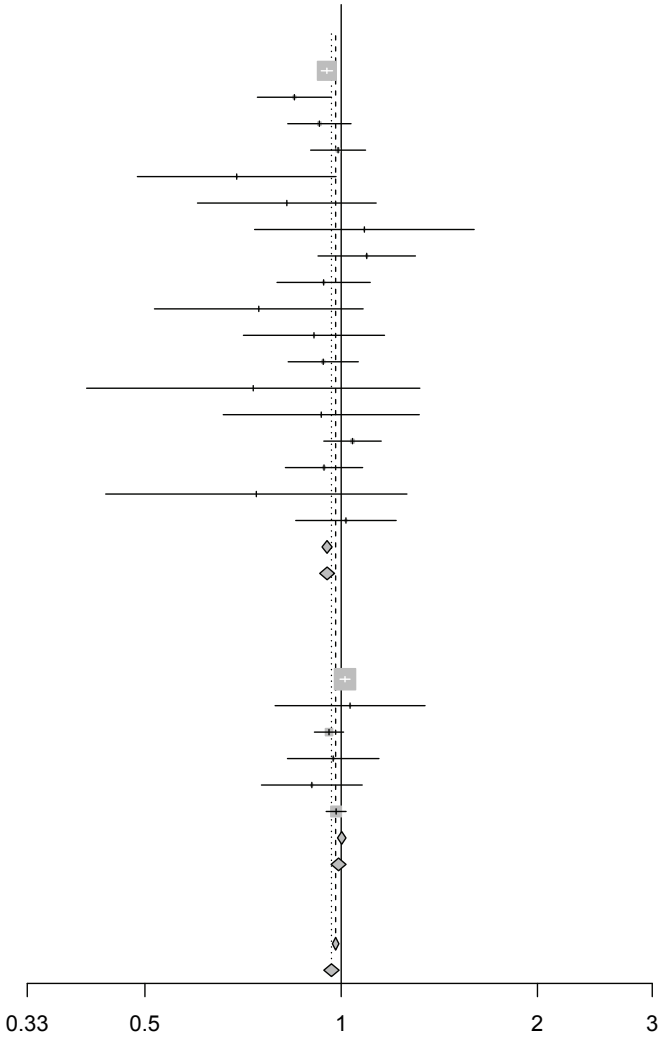


rs201428899[G]



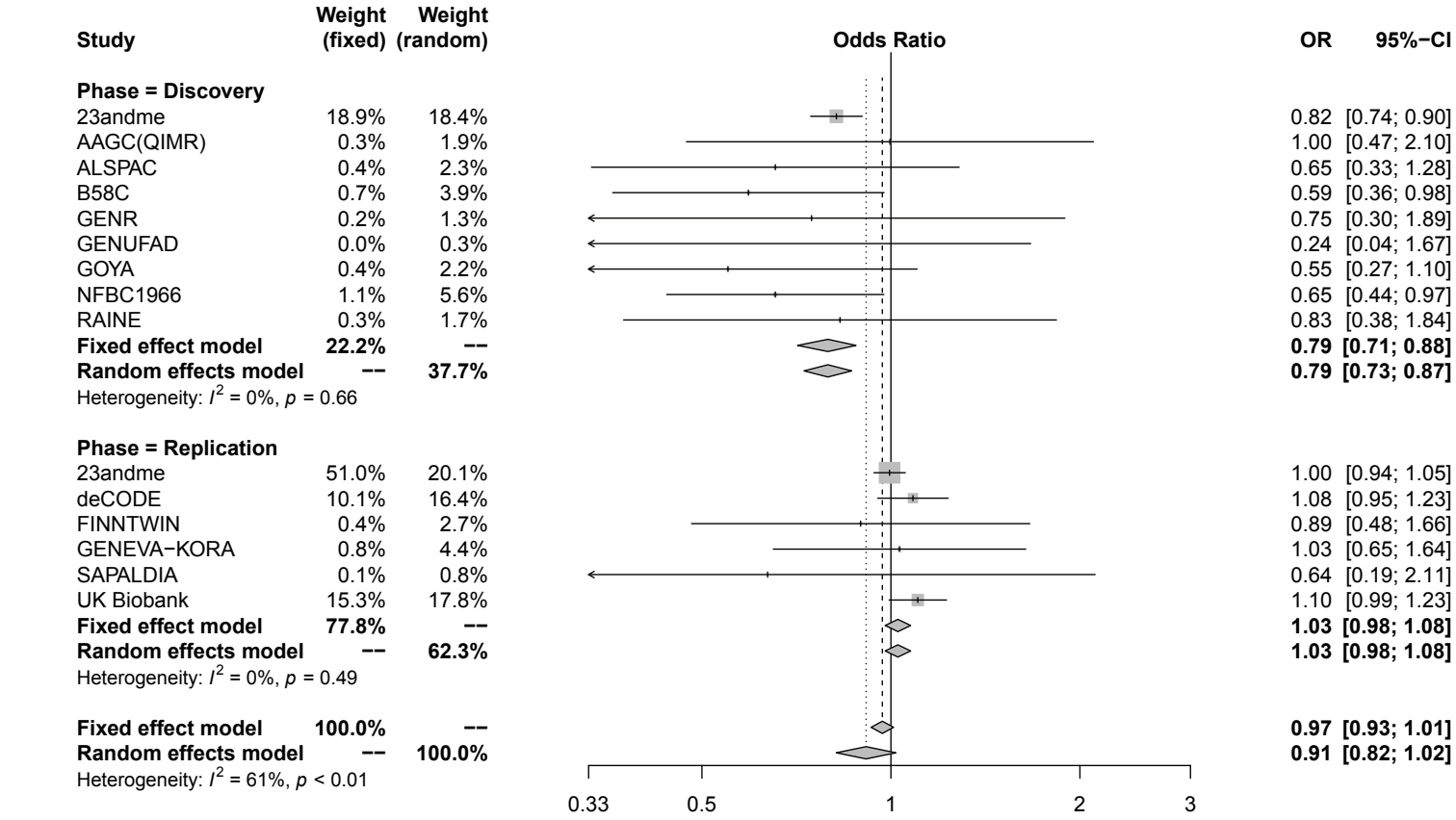
Study	Weight (fixed)	Weight (random)	OR	95%−CI
Phase = Discovery				
23andme	32.0%	18.6%	0.96	[0.94; 0.98]
AAGC(QIMR)	0.7%	2.6%	0.99	[0.86; 1.16]
ALSPAC	1.0%	3.7%	1.01	[0.89; 1.14]
B58C	1.3%	4.4%	0.87	[0.78; 0.97]
BAMSE	0.1%	0.5%	0.75	[0.53; 1.08]
COPSAC2000	0.1%	0.5%	0.92	[0.63; 1.33]
EVE (CAG/CSGA)	0.1%	0.4%	0.97	[0.65; 1.46]
EVE (CHS)	0.4%	1.6%	0.94	[0.78; 1.15]
GENR	0.4%	1.7%	0.85	[0.70; 1.03]
GENUFAD	0.2%	0.8%	1.28	[0.97; 1.69]
GINI/LISA	0.2%	0.9%	0.76	[0.58; 0.99]
GOYA	1.0%	3.6%	0.89	[0.78; 1.01]
INMA	0.0%	0.2%	1.14	[0.65; 1.99]
MAAS	0.1%	0.5%	0.83	[0.57; 1.21]
NFBC1966	1.8%	5.8%	0.94	[0.86; 1.03]
NTR (adults)	0.6%	2.5%	1.06	[0.91; 1.24]
NTR (children)	0.0%	0.2%	0.92	[0.52; 1.63]
Fixed effect model	**40.0%**	**−−**	**0.95**	**[0.93; 0.97]**
Random effects model	**−−**	**48.6%**	**0.95**	**[0.91; 0.98]**
Heterogeneity: I^2 = 10%, p = 0.33				
Phase = Replication				
23andme	40.2%	19.1%	0.98	[0.96; 1.00]
deCODE	5.4%	11.3%	1.05	[0.99; 1.11]
ECRHS	0.4%	1.6%	1.09	[0.89; 1.33]
GENEVA−KORA	0.4%	1.7%	0.86	[0.71; 1.05]
GOA	0.1%	0.5%	1.38	[0.95; 2.01]
SAPALDIA	0.4%	1.6%	0.88	[0.72; 1.08]
UK Biobank	13.0%	15.6%	0.98	[0.95; 1.01]
Fixed effect model	**60.0%**	**−−**	**0.98**	**[0.97; 1.00]**
Random effects model	**−−**	**51.4%**	**0.99**	**[0.96; 1.03]**
Heterogeneity: I^2 = 54%, p = 0.04				
Fixed effect model	**100.0%**	**−−**	**0.97**	**[0.96; 0.98]**
Random effects model	**−−**	**100.0%**	**0.97**	**[0.94; 0.99]**
Heterogeneity: I^2 = 39%, p = 0.03				

rs6011016[C]

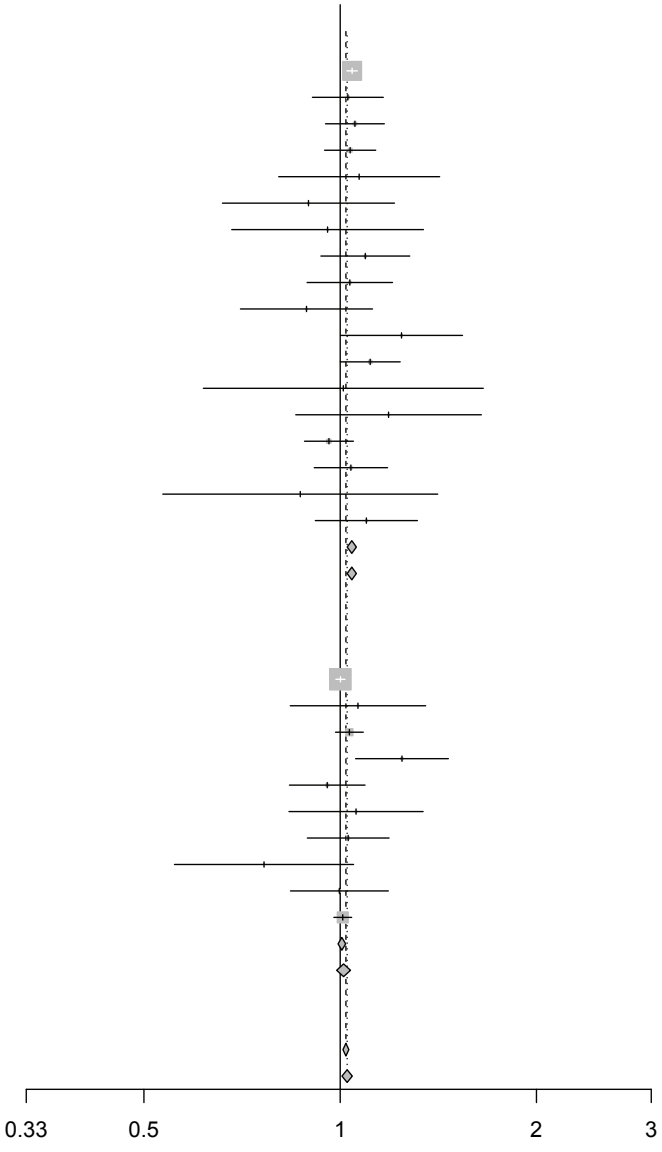


Study	Weight (fixed)	Weight (random)	OR	95%−CI
Phase = Discovery				
23andme	33.2%	16.6%	0.95	[0.93; 0.97]
AAGC(QIMR)	0.8%	3.5%	0.85	[0.74; 0.97]
ALSPAC	1.1%	4.4%	0.93	[0.83; 1.04]
B58C	1.4%	5.4%	0.99	[0.90; 1.09]
BAMSE	0.1%	0.6%	0.69	[0.49; 0.98]
COPSAC2000	0.1%	0.7%	0.83	[0.60; 1.13]
EVE (CAG/CSGA)	0.1%	0.5%	1.09	[0.74; 1.60]
EVE (CHS)	0.4%	2.2%	1.09	[0.92; 1.30]
GENR	0.5%	2.3%	0.94	[0.80; 1.11]
GENUFAD	0.1%	0.5%	0.75	[0.52; 1.08]
GINI/LISA	0.2%	1.1%	0.91	[0.71; 1.17]
GOYA	0.9%	3.8%	0.94	[0.83; 1.06]
INMA	0.0%	0.2%	0.73	[0.41; 1.32]
MAAS	0.1%	0.6%	0.93	[0.66; 1.32]
NFBC1966	1.3%	5.1%	1.04	[0.94; 1.15]
NTR (adults)	0.7%	3.2%	0.94	[0.82; 1.08]
NTR (children)	0.0%	0.3%	0.74	[0.44; 1.26]
RAINE	0.4%	2.0%	1.02	[0.85; 1.21]
Fixed effect model	**41.4%**	**−−**	**0.95**	**[0.93; 0.97]**
Random effects model	**−−**	**52.9%**	**0.95**	**[0.93; 0.98]**
Heterogeneity: I^2 = 5%, p = 0.40				
Phase = Replication				
23andme	41.9%	16.9%	1.01	[1.00; 1.03]
CAMP	0.2%	1.0%	1.03	[0.79; 1.34]
deCODE	4.9%	10.9%	0.96	[0.91; 1.01]
FINNTWIN	0.5%	2.4%	0.97	[0.83; 1.14]
GENEVA−KORA	0.4%	2.0%	0.90	[0.75; 1.08]
UK Biobank	10.6%	13.9%	0.98	[0.95; 1.02]
Fixed effect model	**58.6%**	**−−**	**1.00**	**[0.99; 1.02]**
Random effects model	**−−**	**47.1%**	**0.99**	**[0.97; 1.02]**
Heterogeneity: I^2 = 32%, p = 0.20				
Fixed effect model	**100.0%**	**−−**	**0.98**	**[0.97; 0.99]**
Random effects model	**−−**	**100.0%**	**0.97**	**[0.94; 0.99]**
Heterogeneity: I^2 = 48%, p < 0.01				

rs149341190[C]



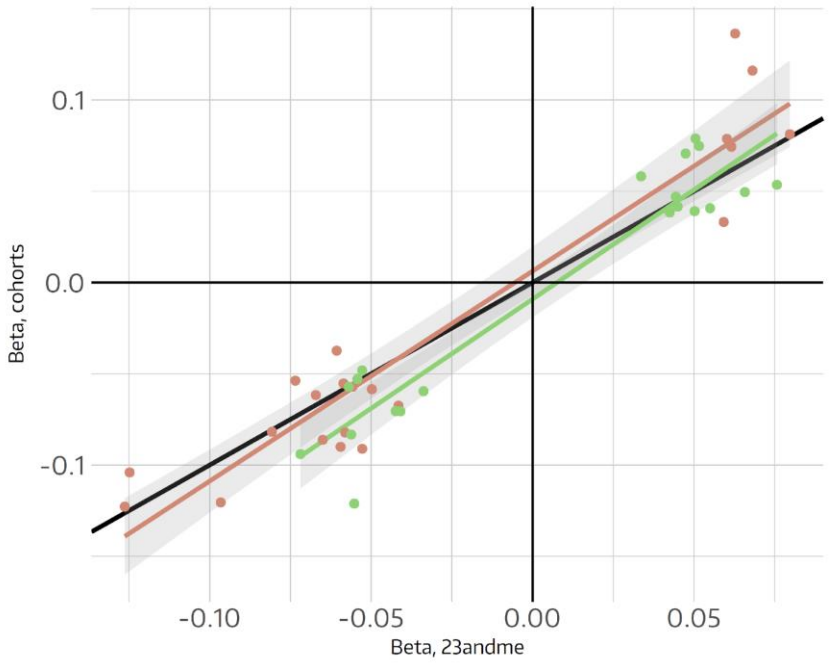
rs10760123[T]



Study	Weight (fixed)	Weight (random)	OR	95%−CI
Phase = Discovery				
23andme	32.5%	21.9%	1.04	[1.02; 1.06]
AAGC(QIMR)	0.7%	2.0%	1.03	[0.91; 1.16]
ALSPAC	1.0%	2.8%	1.05	[0.95; 1.17]
B58C	1.3%	3.6%	1.04	[0.95; 1.13]
BAMSE	0.1%	0.4%	1.07	[0.80; 1.42]
COPSAC2000	0.1%	0.4%	0.89	[0.66; 1.21]
EVE (CAG/CSGA)	0.1%	0.3%	0.96	[0.68; 1.34]
EVE (CHS)	0.4%	1.3%	1.09	[0.93; 1.28]
GENR	0.5%	1.4%	1.03	[0.89; 1.20]
GENUFAD	0.2%	0.6%	0.89	[0.70; 1.12]
GINI/LISA	0.2%	0.7%	1.24	[1.00; 1.54]
GOYA	1.0%	2.7%	1.11	[1.00; 1.24]
INMA	0.0%	0.1%	1.01	[0.62; 1.66]
MAAS	0.1%	0.3%	1.19	[0.85; 1.65]
NFBC1966	1.5%	3.9%	0.96	[0.88; 1.05]
NTR (adults)	0.6%	1.9%	1.04	[0.91; 1.18]
NTR (children)	0.0%	0.1%	0.87	[0.53; 1.41]
RAINE	0.3%	1.0%	1.10	[0.92; 1.31]
Fixed effect model	**40.8%**	**−−**	**1.04**	**[1.02; 1.06]**
Random effects model	**−−**	**45.3%**	**1.04**	**[1.02; 1.06]**
Heterogeneity: I^2 = 0%, p = 0.78				
Phase = Replication				
23andme	41.4%	23.0%	1.00	[0.98; 1.02]
CAMP	0.2%	0.6%	1.06	[0.84; 1.35]
deCODE	4.5%	9.3%	1.03	[0.98; 1.08]
ECRHS	0.4%	1.2%	1.24	[1.06; 1.47]
FINNTWIN	0.6%	1.8%	0.96	[0.84; 1.09]
GABRIELA	0.2%	0.6%	1.06	[0.83; 1.34]
GENEVA−KORA	0.5%	1.5%	1.03	[0.89; 1.19]
GOA	0.1%	0.3%	0.76	[0.56; 1.05]
SAPALDIA	0.4%	1.1%	1.00	[0.84; 1.19]
UK Biobank	10.9%	15.3%	1.01	[0.98; 1.04]
Fixed effect model	**59.2%**	**−−**	**1.01**	**[0.99; 1.02]**
Random effects model	**−−**	**54.7%**	**1.01**	**[0.99; 1.04]**
Heterogeneity: I^2 = 25%, p = 0.22				
Fixed effect model	**100.0%**	**−−**	**1.02**	**[1.01; 1.03]**
Random effects model	**−−**	**100.0%**	**1.02**	**[1.01; 1.04]**
Heterogeneity: I^2 = 22%, p = 0.14				

Supplementary Figure 4

Scatter plot of beta coefficients between 23andme and non-23andme cohorts from the discovery phase of the allergic rhinitis GWAS, from genetic marker association of 16,531,985 genetic markers to allergic rhinitis from the discovery phase, including 212,120 individuals. Only known and replicating novel markers are shown. Red indicates known loci, green indicates novel, replicating loci. The black line represents identity.

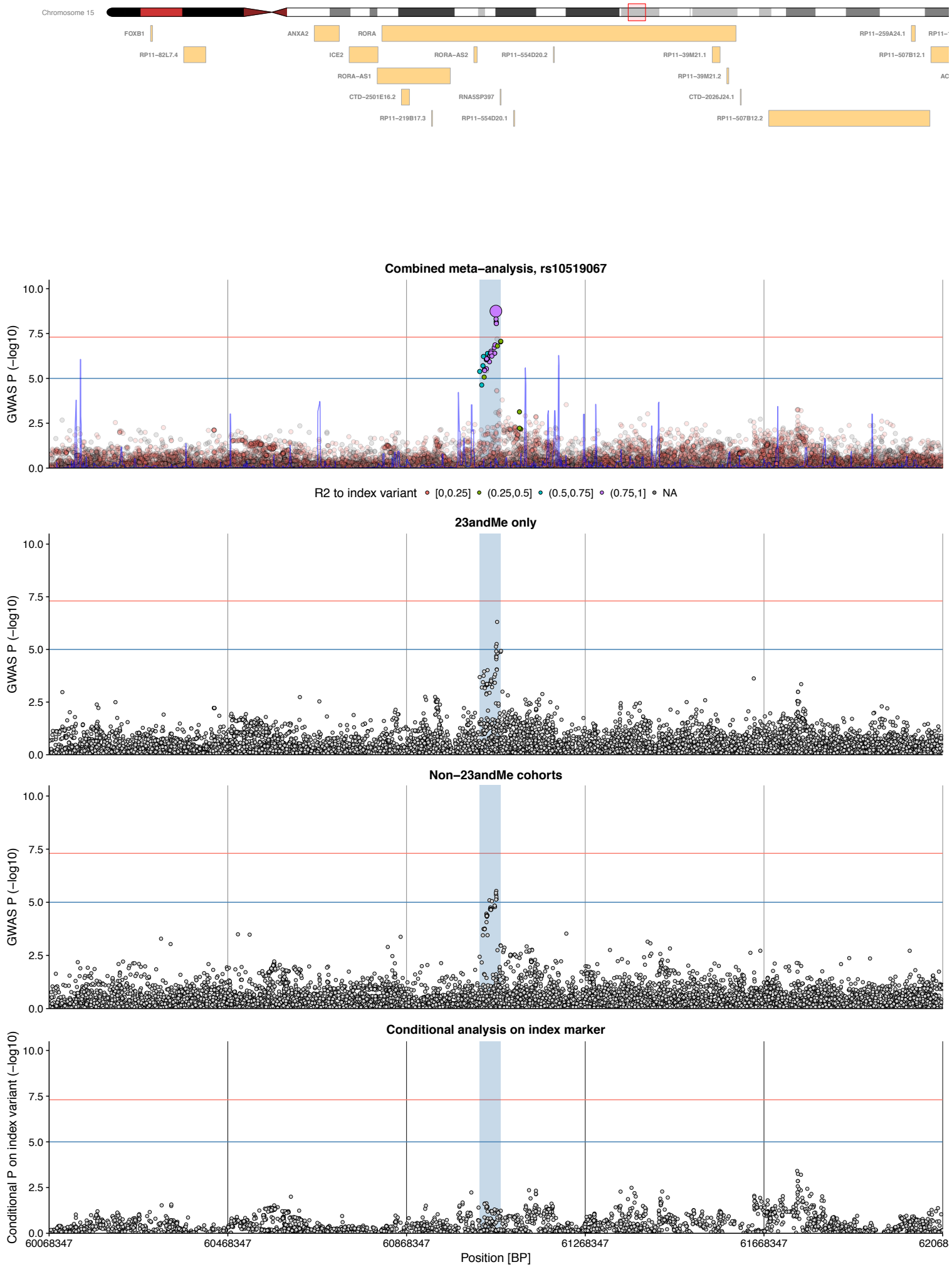


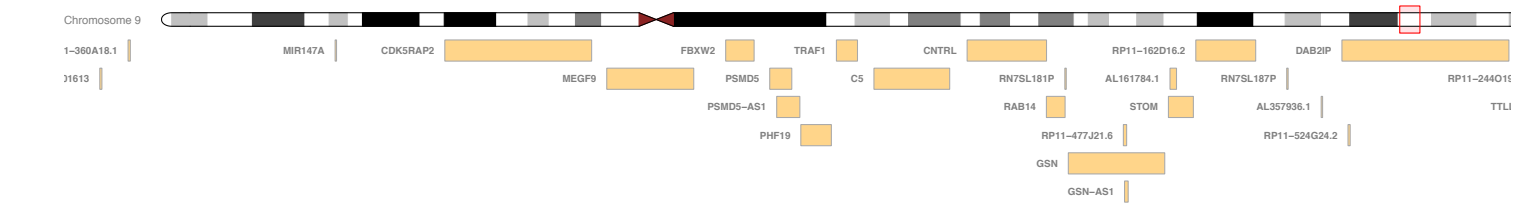
Supplementary Figure 5

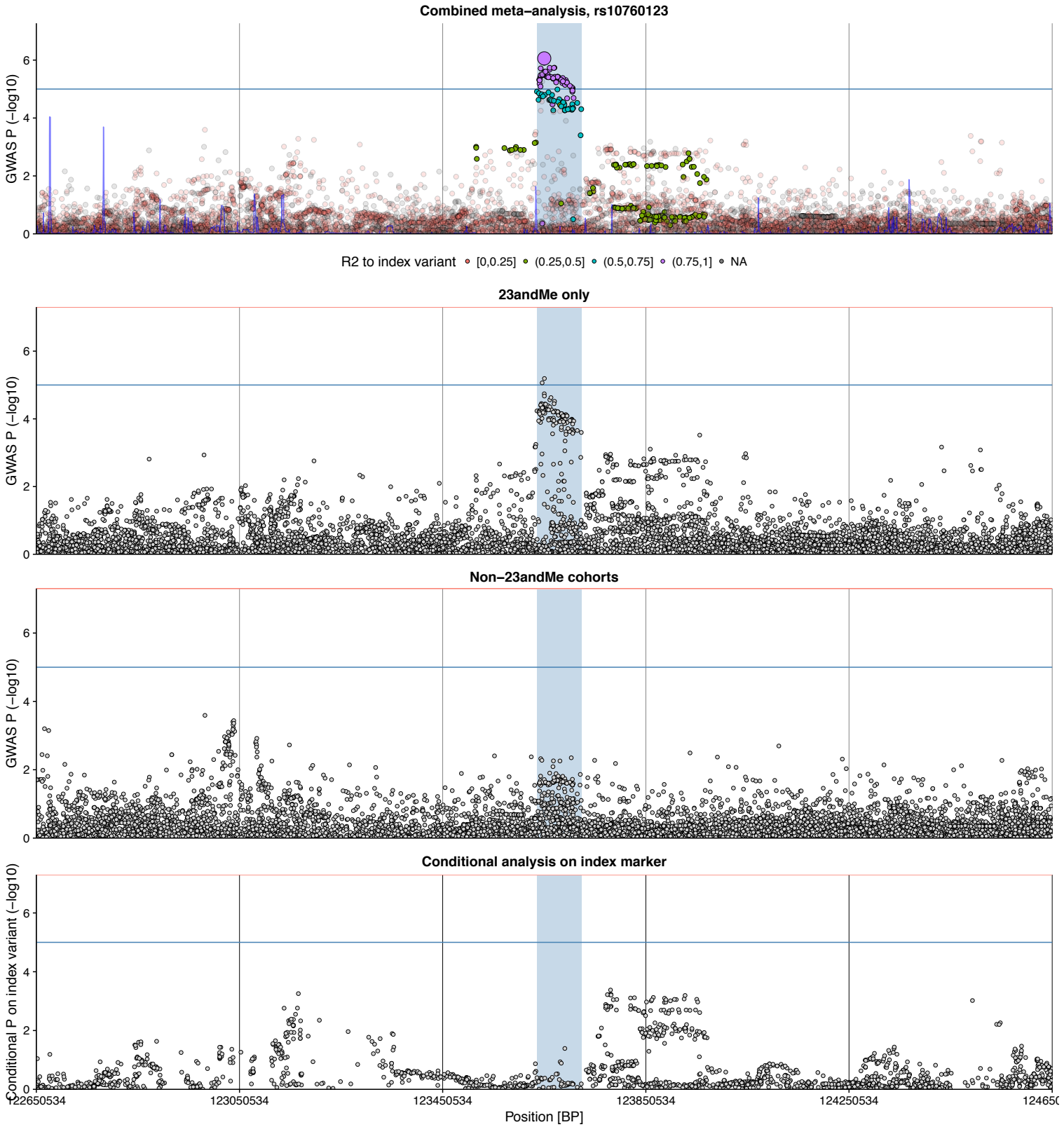
Regional locus plots of allergic rhinitis discovery phase markers. Top panel shows results from the discovery meta-analysis, color coded for 1000g R 2 values. AR discovery markers not present in 1000g are colored in grey ("NA"). Index marker has increased circle size. Locus definition (tag R2 > 0.5 to index) is indicated by blue region. Red line indicates p = 5e-8, blue line indicates p = 1e-5.

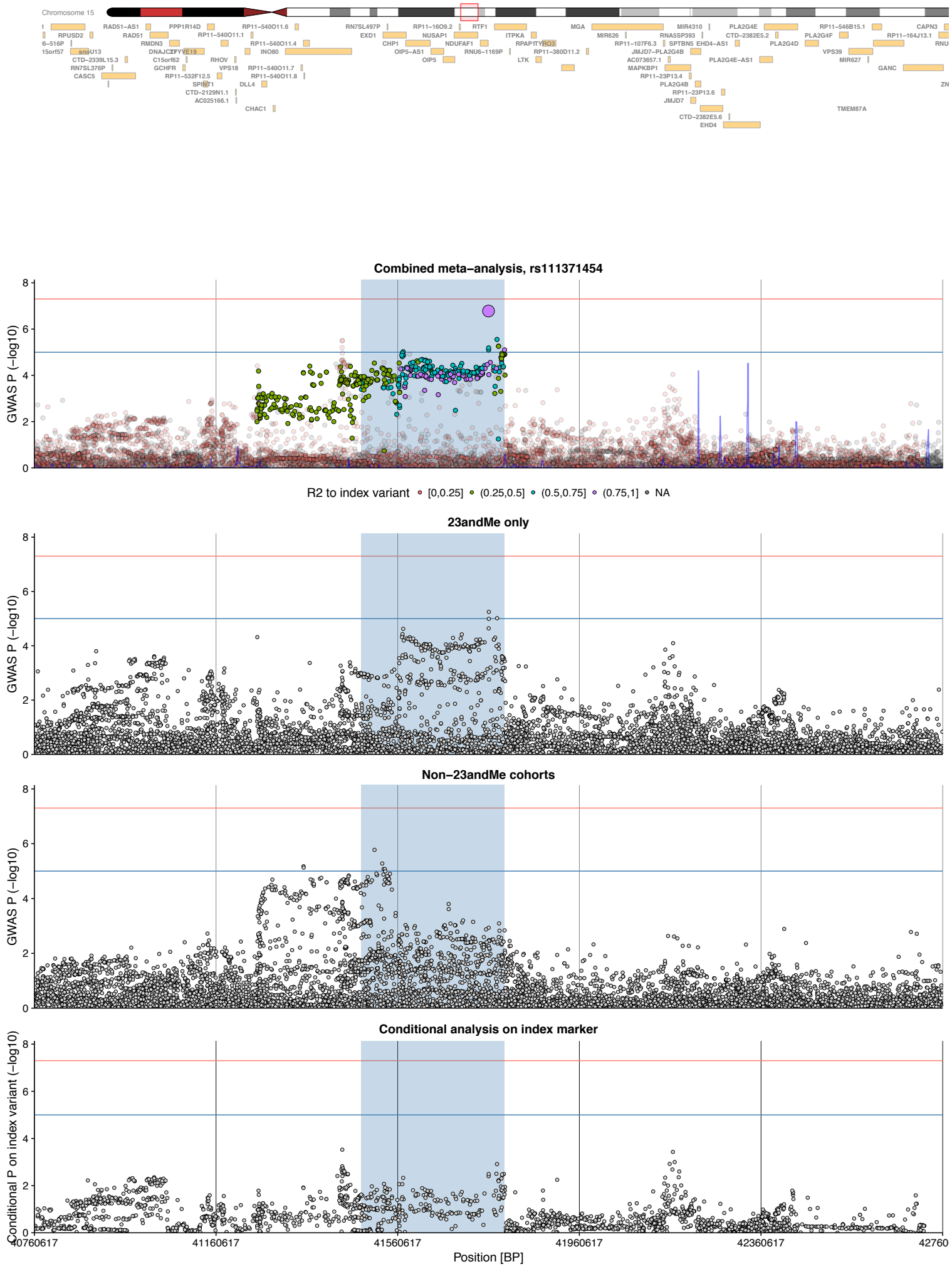
Middle upper panel shows association results for 23andme, and middle lower panel shows association values for non-23andme cohorts.

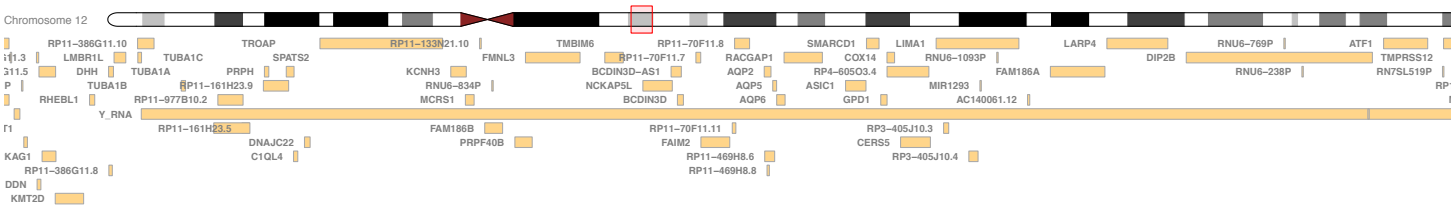
Bottom panel shows results for the conditional analysis on index marker.

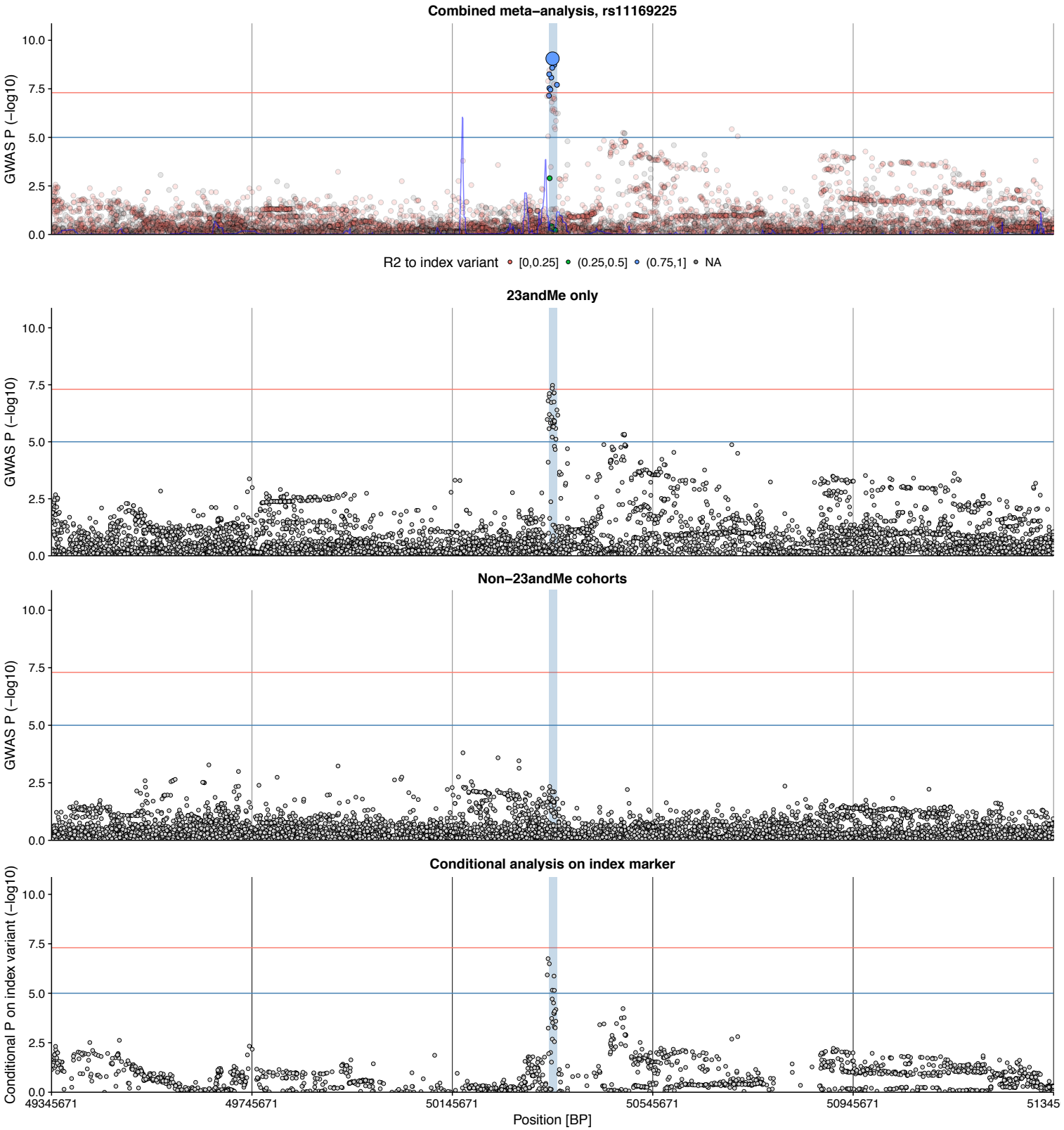

Chromosome 15
FOXB1
ANXA2
RORA
RP11−259A24.1
RP11−82L7.4
ICE2
RORA−AS2
RP11−554D20.2
RP11−39M21.1
RP11−507B12.1
RORA−AS1
RP11−39M21.2
CTD−2501E16.2
RNA5SP397
CTD−2026J24.1
RP11−219B17.3
RP11−554D20.1
RP11−507B12.2
Combined meta−analysis, rs10519067
GWAS P (−log10)
10.0
7.5
5.0
2.5
0.0
R2 to index variant
[0,0.25]
(0.25,0.5]
(0.5,0.75]
(0.75,1]
NA
23andMe only
Non−23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (−log10)
60068347
60468347
60868347
61268347
61668347
62068
Position [BP]

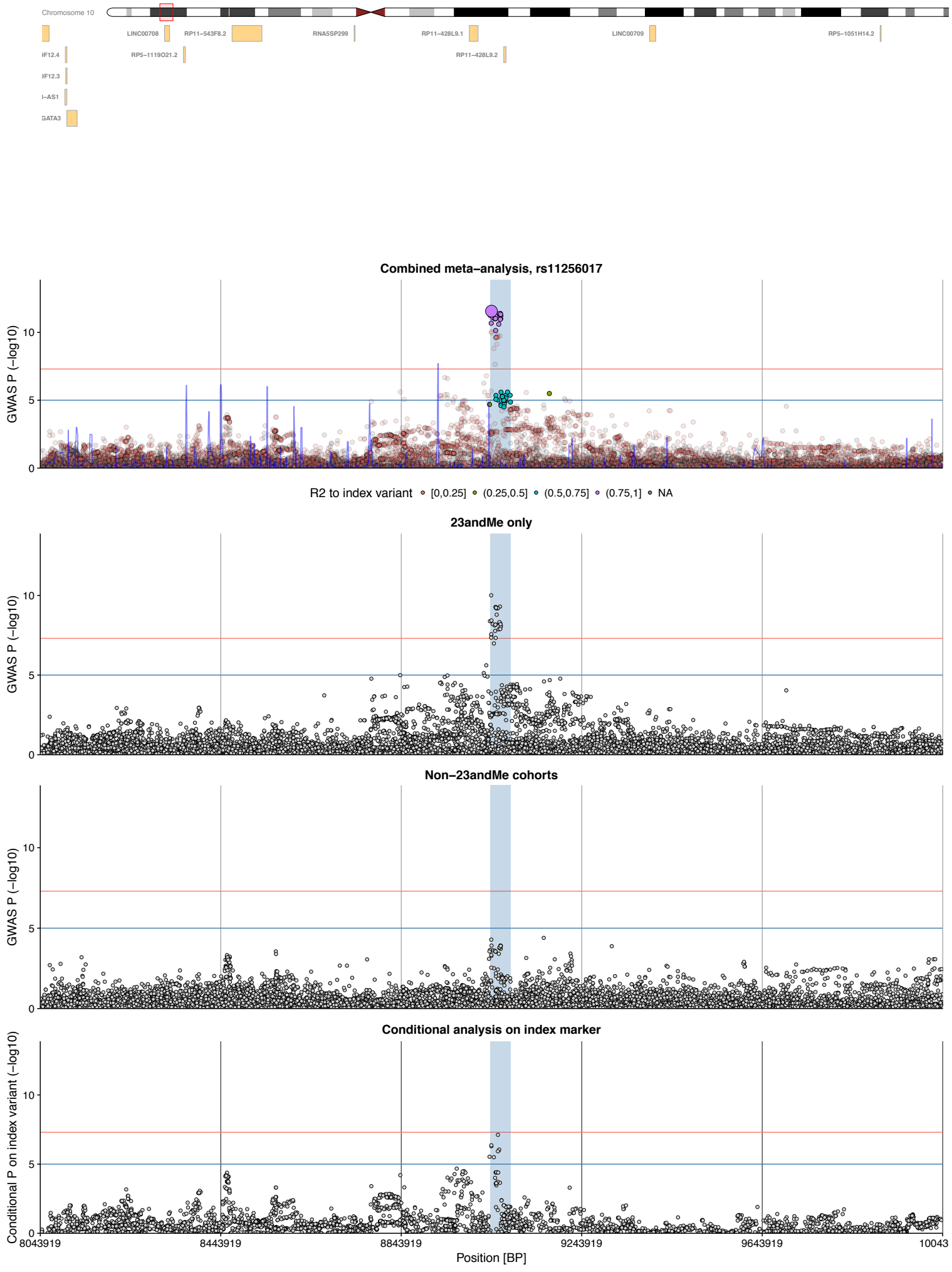

Chromosome 9
1–360A18.1
MIR147A
CDK5RAP2
FBXW2
TRAF1
CNTRL
RP11–162D16.2
DAB2IP
MEGF9
PSMD5
C5
RN7SL181P
AL161784.1
RN7SL187P
PSMD5–AS1
RAB14
STOM
AL357936.1
PHF19
RP11–477J21.6
RP11–524G24.2
GSN
GSN–AS1

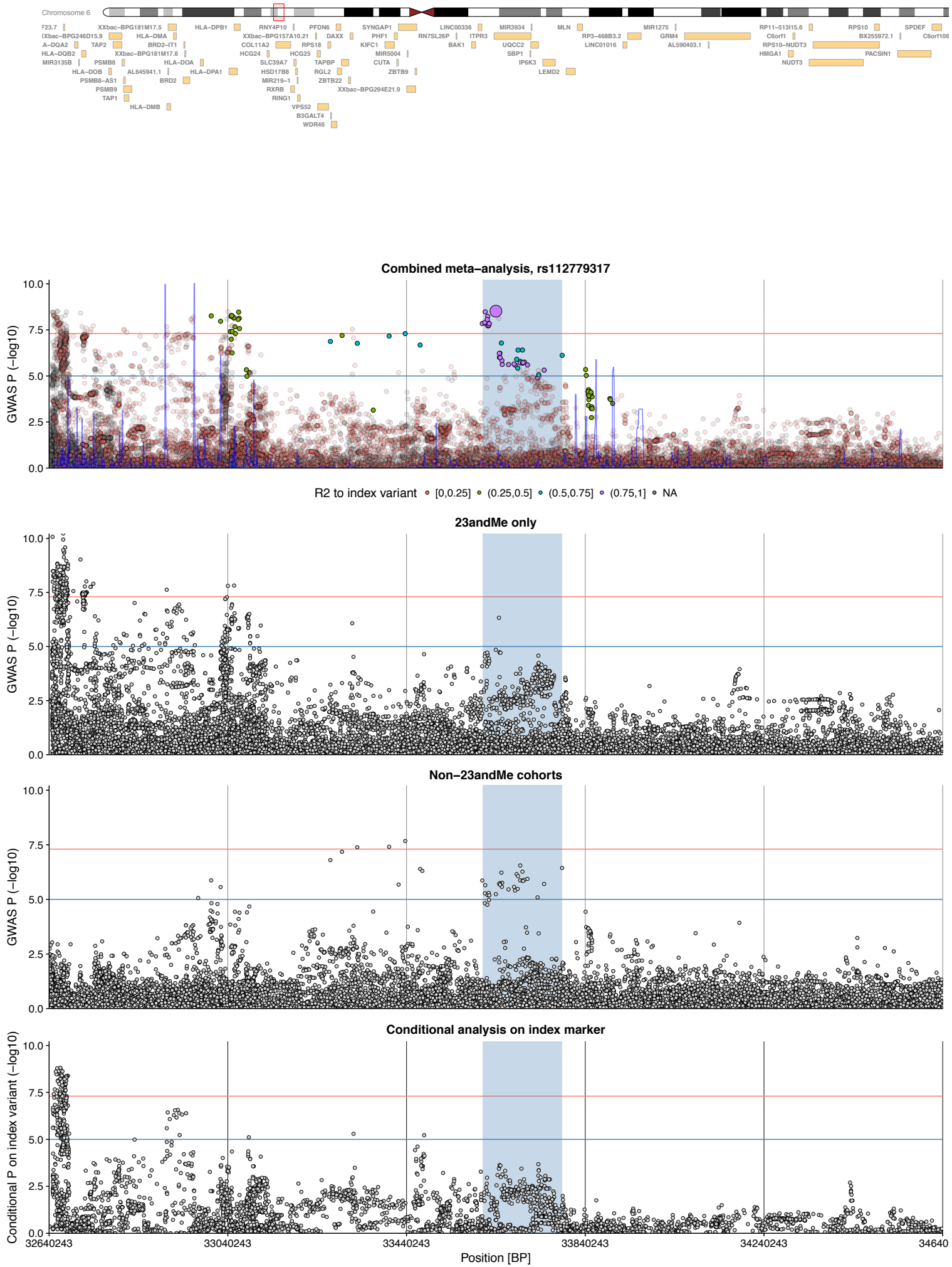

Combined meta–analysis, rs10760123
GWAS P (–log10)
R2 to index variant [0,0.25] (0.25,0.5] (0.5,0.75] (0.75,1] NA
23andMe only
Non–23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (–log10)
122650534
123050534
123450534
123850534
124250534
Position [BP]

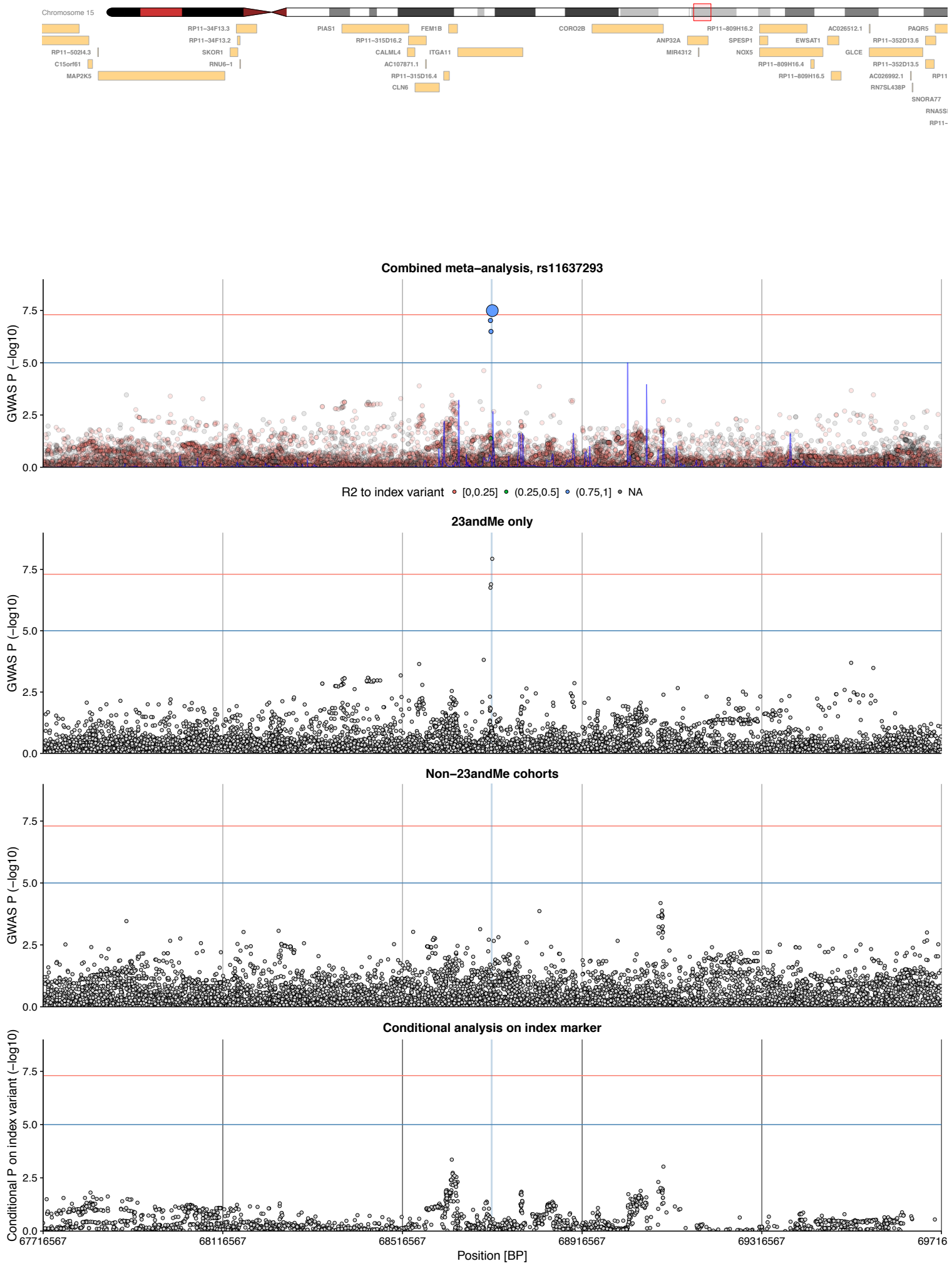

Chromosome 15
Combined meta−analysis, rs111371454
GWAS P (−log10)
R2 to index variant [0,0.25] (0.25,0.5] (0.5,0.75] (0.75,1] NA
23andMe only
Non−23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (−log10)
40760617
41160617
41560617
41960617
42360617
42760
Position [BP]

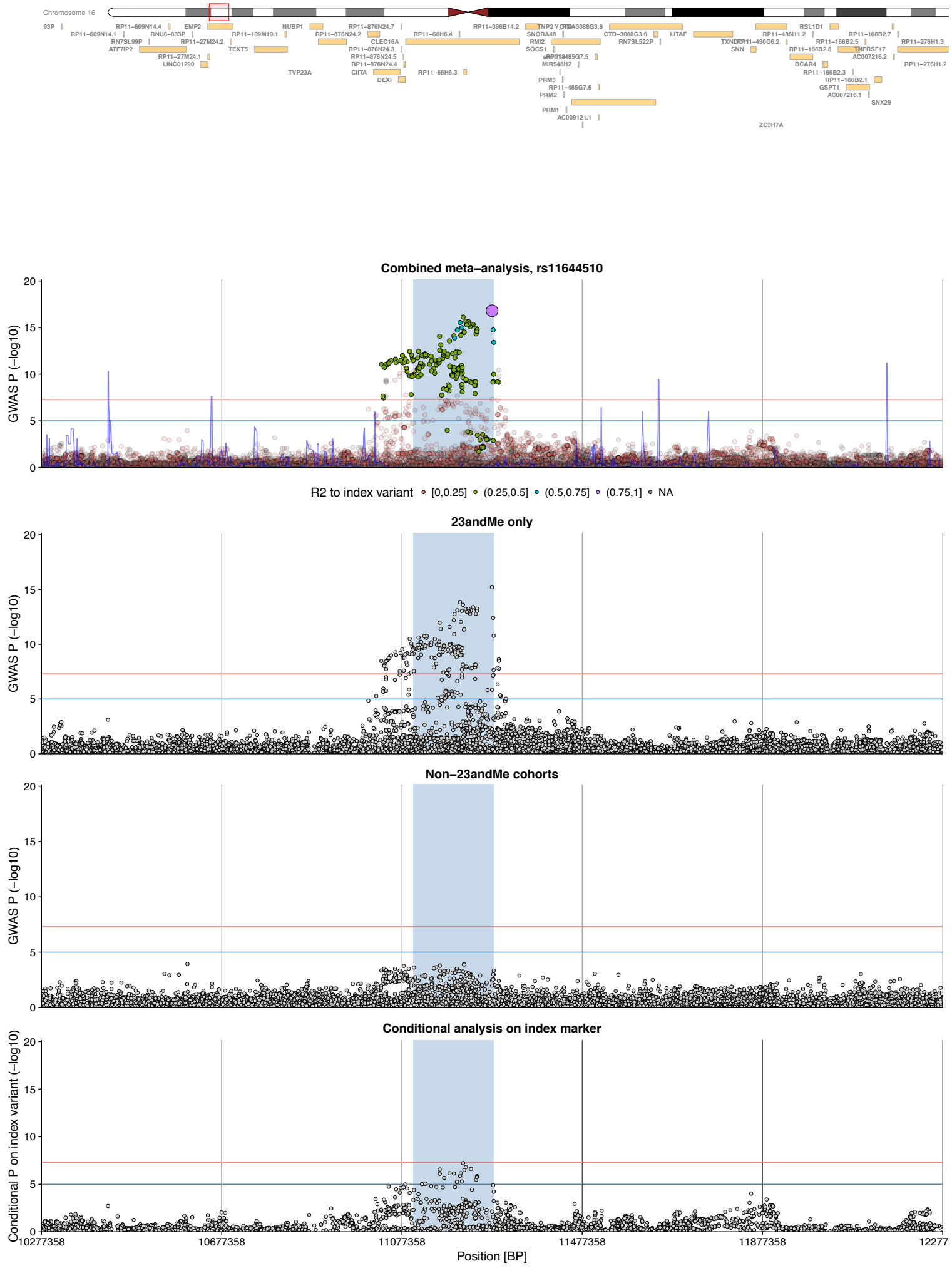

Chromosome 12
RP11−386G11.10
TROAP
RP11−133N21.10
TMBIM6
RP11−70F11.8
SMARCD1
LIMA1
LARP4
RNU6−769P
ATF1
LMBR1L
TUBA1C
SPATS2
FMNL3
RP11−70F11.7
RACGAP1
COX14
RNU6−1093P
DIP2B
TMPRSS12
DHH
TUBA1A
PRPH
KCNH3
BCDIN3D−AS1
AQP2
RP4−605O3.4
FAM186A
RNU6−238P
RN7SL519P
TUBA1B
RP11−161H23.9
RNU6−834P
NCKAP5L
AQP5
ASIC1
MIR1293
RHEBL1
RP11−977B10.2
MCRS1
BCDIN3D
AQP6
GPD1
AC140061.12
Y_RNA
RP11−161H23.5
FAM186B
RP11−70F11.11
RP3−405J10.3
DNAJC22
PRPF40B
FAIM2
CERS5
KAG1
C1QL4
RP11−469H8.6
RP3−405J10.4
RP11−386G11.8
RP11−469H8.8
DDN
KMT2D

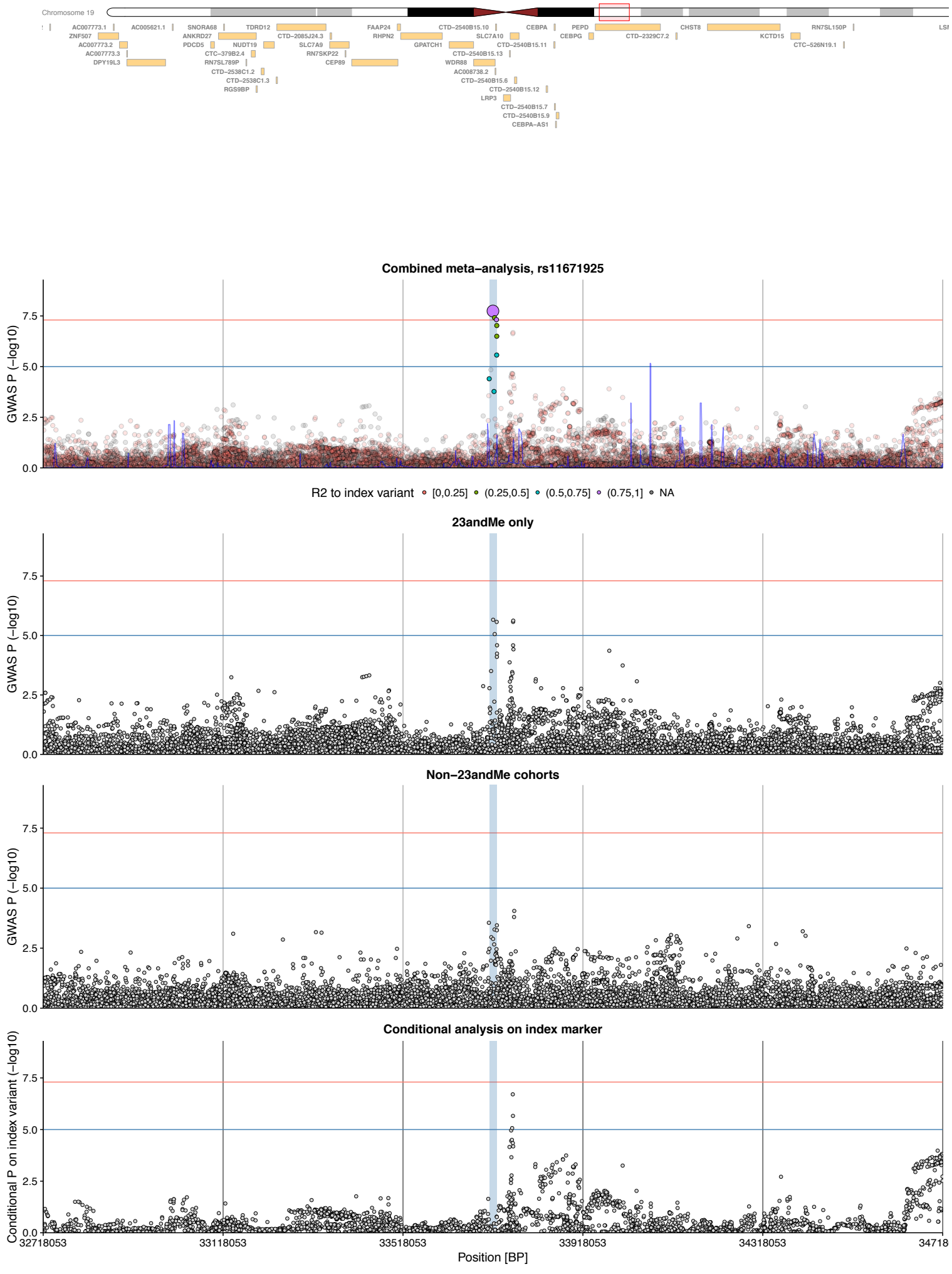

Combined meta−analysis, rs11169225
GWAS P (−log10)
10.0
7.5
5.0
2.5
0.0
R2 to index variant
[0,0.25]
(0.25,0.5]
(0.75,1]
NA
23andMe only
Non−23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (−log10)
49345671
49745671
50145671
50545671
50945671
51345
Position [BP]

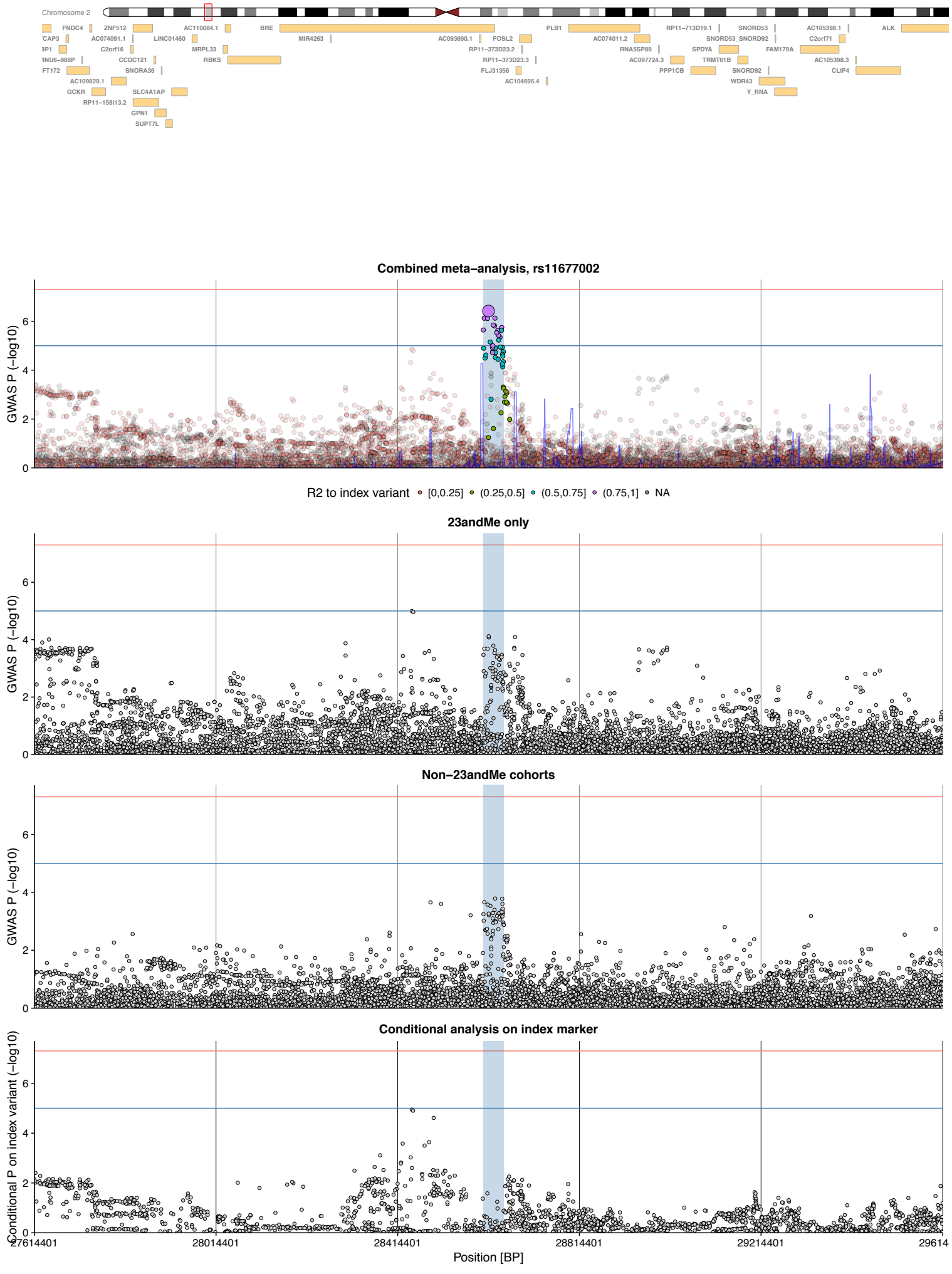

Chromosome 10
LINC00708
RP11−543F8.2
RNA5SP299
RP11−428L9.1
LINC00709
RP5−1051H14.2
RP5−1119O21.2
RP11−428L9.2
GATA3
Combined meta−analysis, rs11256017
GWAS P (−log10)
R2 to index variant [0,0.25] (0.25,0.5] (0.5,0.75] (0.75,1] NA
23andMe only
Non−23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (−log10)
8043919
8443919
8843919
9243919
9643919
10043
Position [BP]

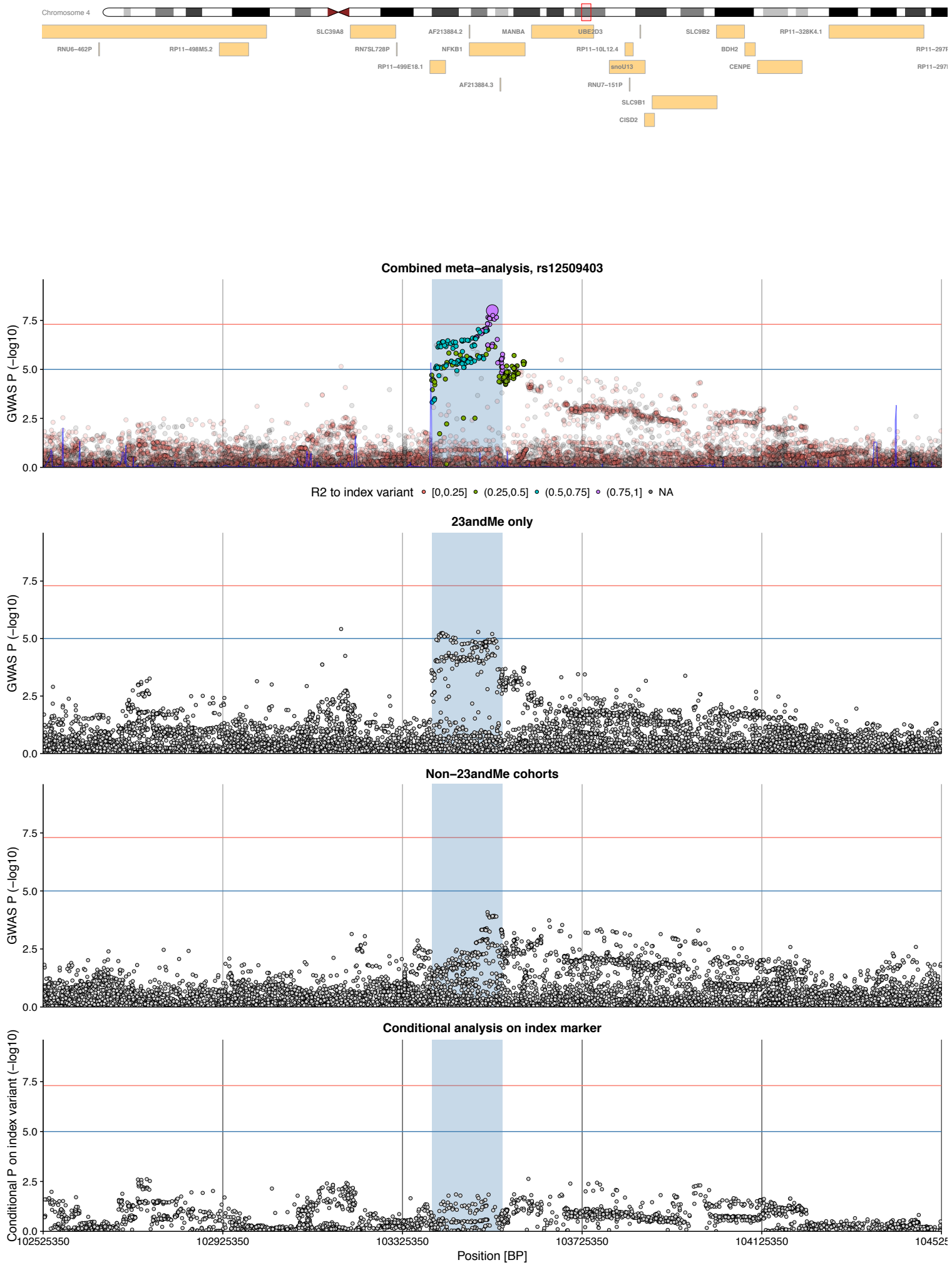

Chromosome 6
Combined meta–analysis, rs112779317
GWAS P (–log10)
R2 to index variant [0,0.25] (0.25,0.5] (0.5,0.75] (0.75,1] NA
23andMe only
Non–23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (–log10)
Position [BP]

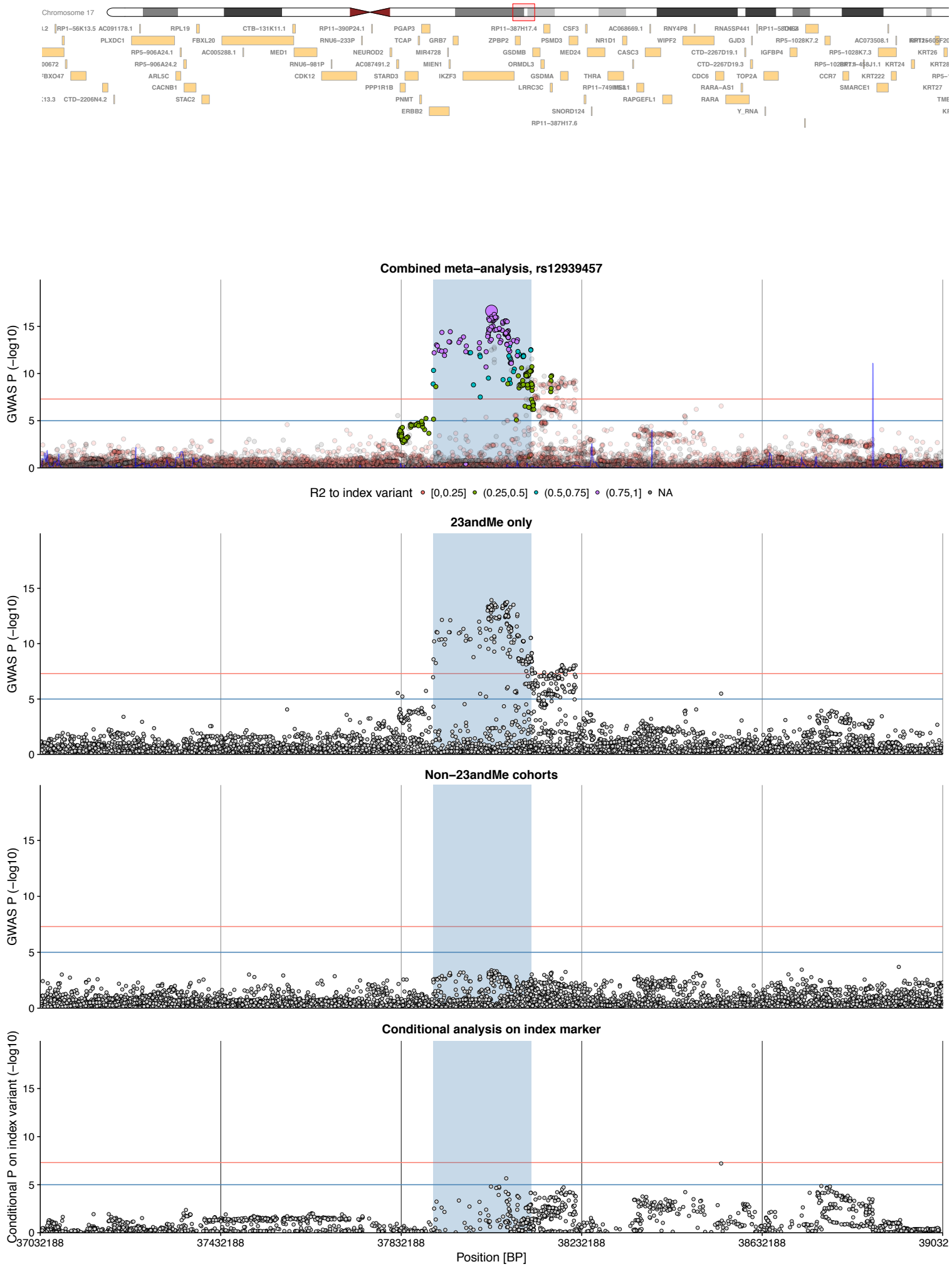

Chromosome 15
RP11−34F13.3
RP11−34F13.2
RP11−502I4.3
SKOR1
C15orf61
RNU6−1
MAP2K5
PIAS1
FEM1B
RP11−315D16.2
CALML4
ITGA11
AC107871.1
RP11−315D16.4
CLN6
CORO2B
ANP32A
MIR4312
RP11−809H16.2
SPESP1
EWSAT1
NOX5
RP11−809H16.4
RP11−809H16.5
AC026512.1
PAQR5
RP11−352D13.6
GLCE
RP11−352D13.5
AC026992.1
RN7SL438P
SNORA77
Combined meta−analysis, rs11637293
GWAS P (−log10)
7.5
5.0
2.5
0.0
R2 to index variant
[0,0.25]
(0.25,0.5]
(0.75,1]
NA
23andMe only
Non−23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (−log10)
67716567
68116567
68516567
68916567
69316567
Position [BP]

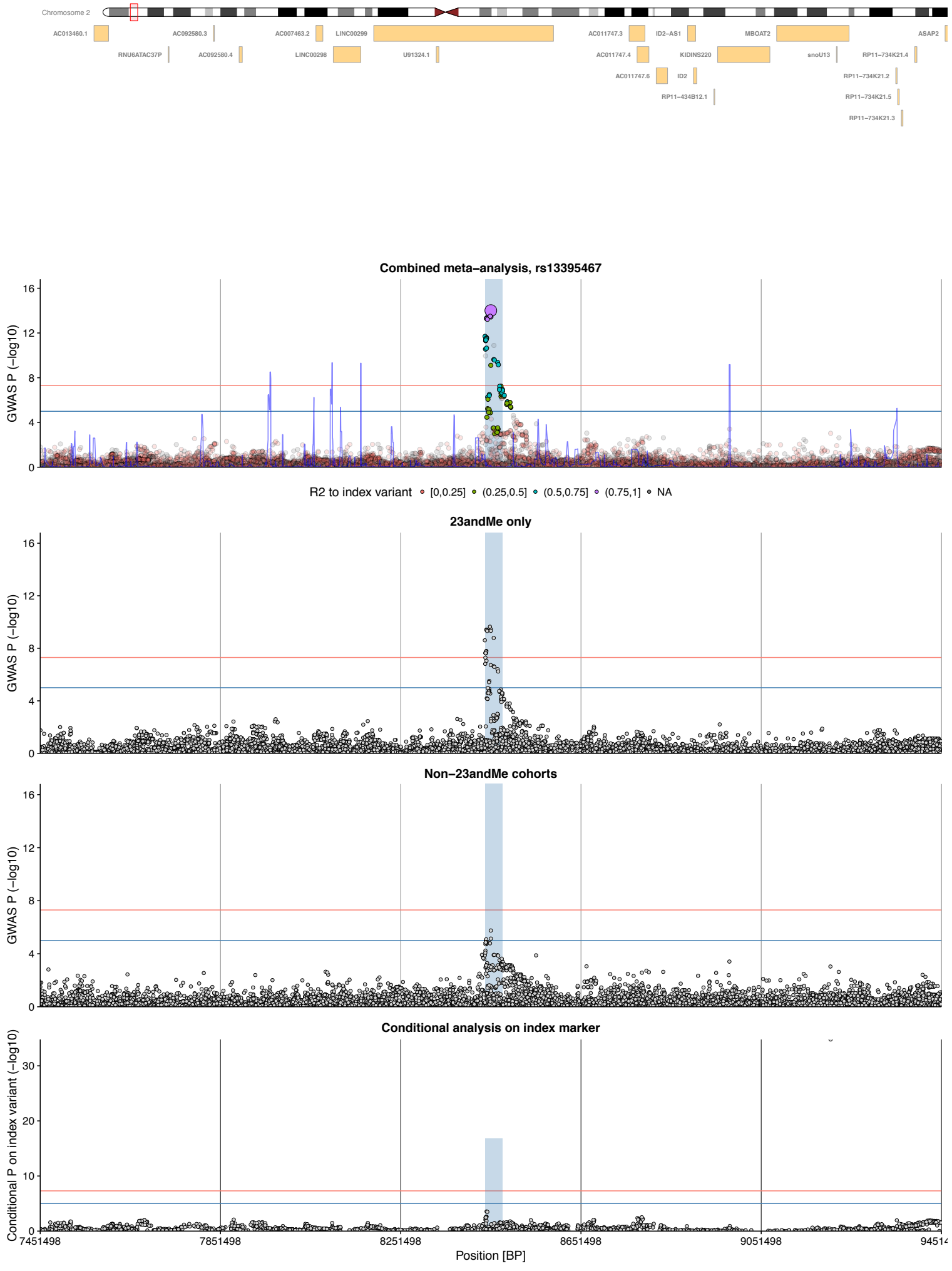

Chromosome 16
Combined meta–analysis, rs11644510
GWAS P (−log10)
R2 to index variant [0,0.25] (0.25,0.5] (0.5,0.75] (0.75,1] NA
23andMe only
Non−23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (−log10)
10277358
10677358
11077358
11477358
11877358
12277
Position [BP]

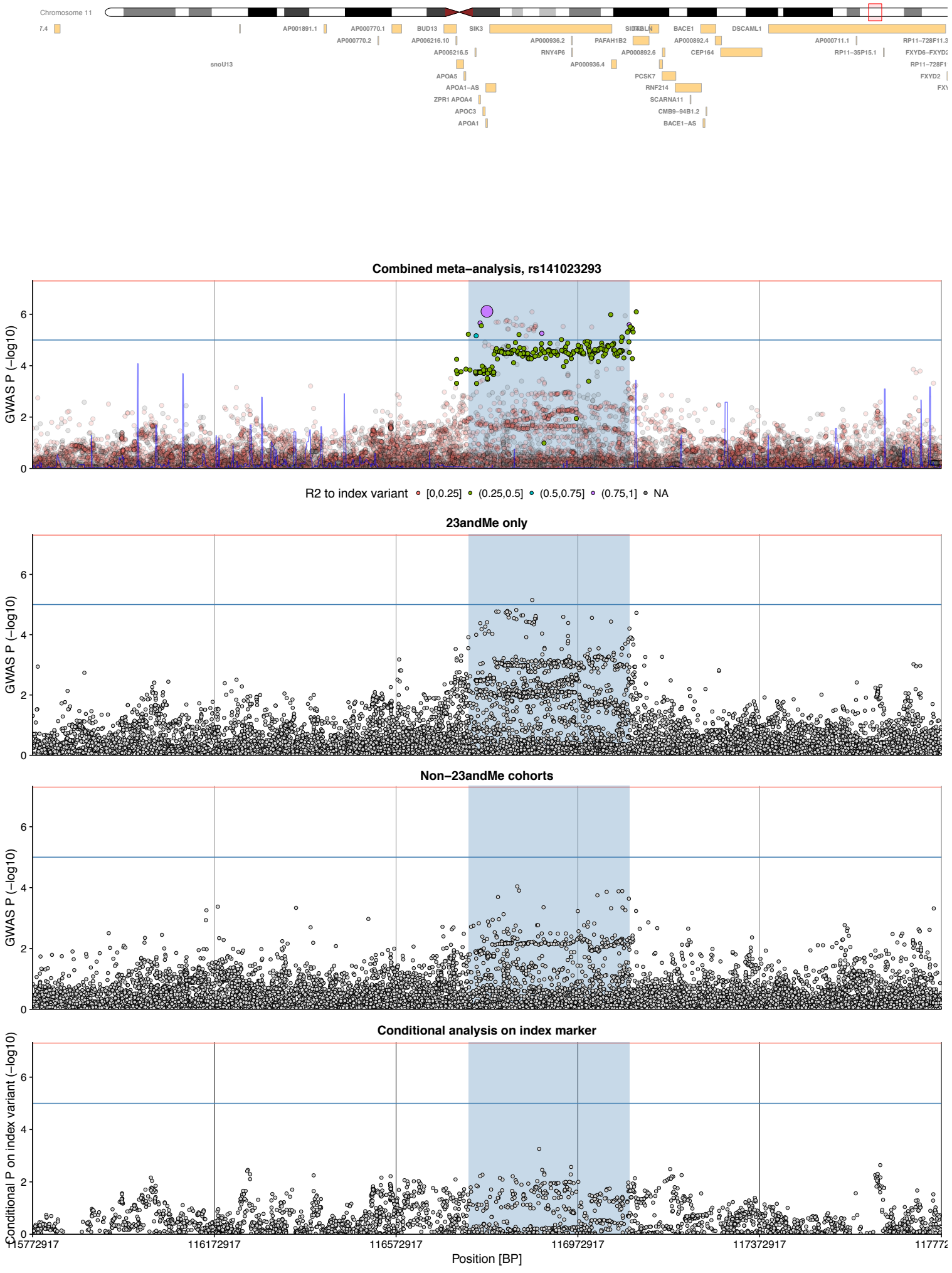

Chromosome 19
AC007773.1
AC005621.1
SNORA68
TDRD12
FAAP24
CTD−2540B15.10
CEBPA
PEPD
CHST8
RN7SL150P
ZNF507
ANKRD27
CTD−2085J24.3
RHPN2
SLC7A10
CEBPG
CTD−2329C7.2
KCTD15
AC007773.2
PDCD5
NUDT19
SLC7A9
GPATCH1
CTD−2540B15.11
CTC−526N19.1
AC007773.3
CTC−379B2.4
RN7SKP22
CTD−2540B15.13
DPY19L3
RN7SL789P
CEP89
WDR88
CTD−2538C1.2
AC008738.2
CTD−2538C1.3
CTD−2540B15.6
RGS9BP
CTD−2540B15.12
LRP3
CTD−2540B15.7
CTD−2540B15.9
CEBPA−AS1
Combined meta−analysis, rs11671925
GWAS P (−log10)
7.5
5.0
2.5
0.0
R2 to index variant
[0,0.25]
(0.25,0.5]
(0.5,0.75]
(0.75,1]
NA
23andMe only
Non−23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (−log10)
32718053
33118053
33518053
33918053
34318053
34718
Position [BP]

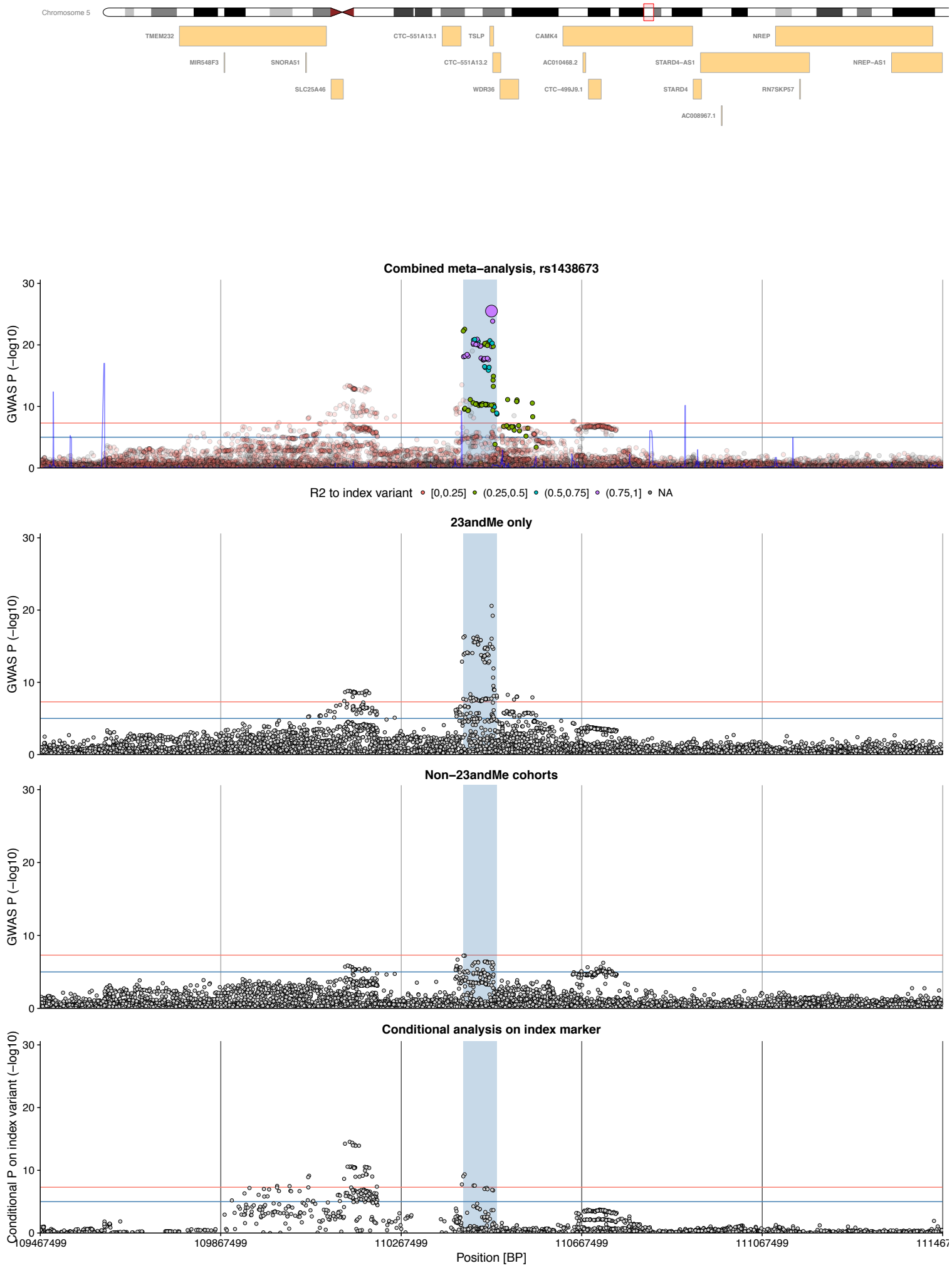

Chromosome 2
FNDC4
ZNF512
AC110084.1
BRE
PLB1
RP11−713D19.1
SNORD53
AC105398.1
ALK
AC074091.1
LINC01460
MIR4263
AC093690.1
FOSL2
AC074011.2
SNORD53_SNORD92
C2orf71
C2orf16
MRPL33
RP11−373D23.2
RNA5SP89
SPDYA
FAM179A
CCDC121
RBKS
RP11−373D23.3
AC097724.3
TRMT61B
AC105398.3
SNORA36
FLJ31356
PPP1CB
SNORD92
CLIP4
AC109829.1
AC104695.4
WDR43
GCKR
SLC4A1AP
Y_RNA
RP11−158I13.2
GPN1
SUPT7L
Combined meta−analysis, rs11677002
GWAS P (−log10)
R2 to index variant
[0,0.25]
(0.25,0.5]
(0.5,0.75]
(0.75,1]
NA
23andMe only
Non−23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (−log10)
27614401
28014401
28414401
28814401
29214401
29614
Position [BP]

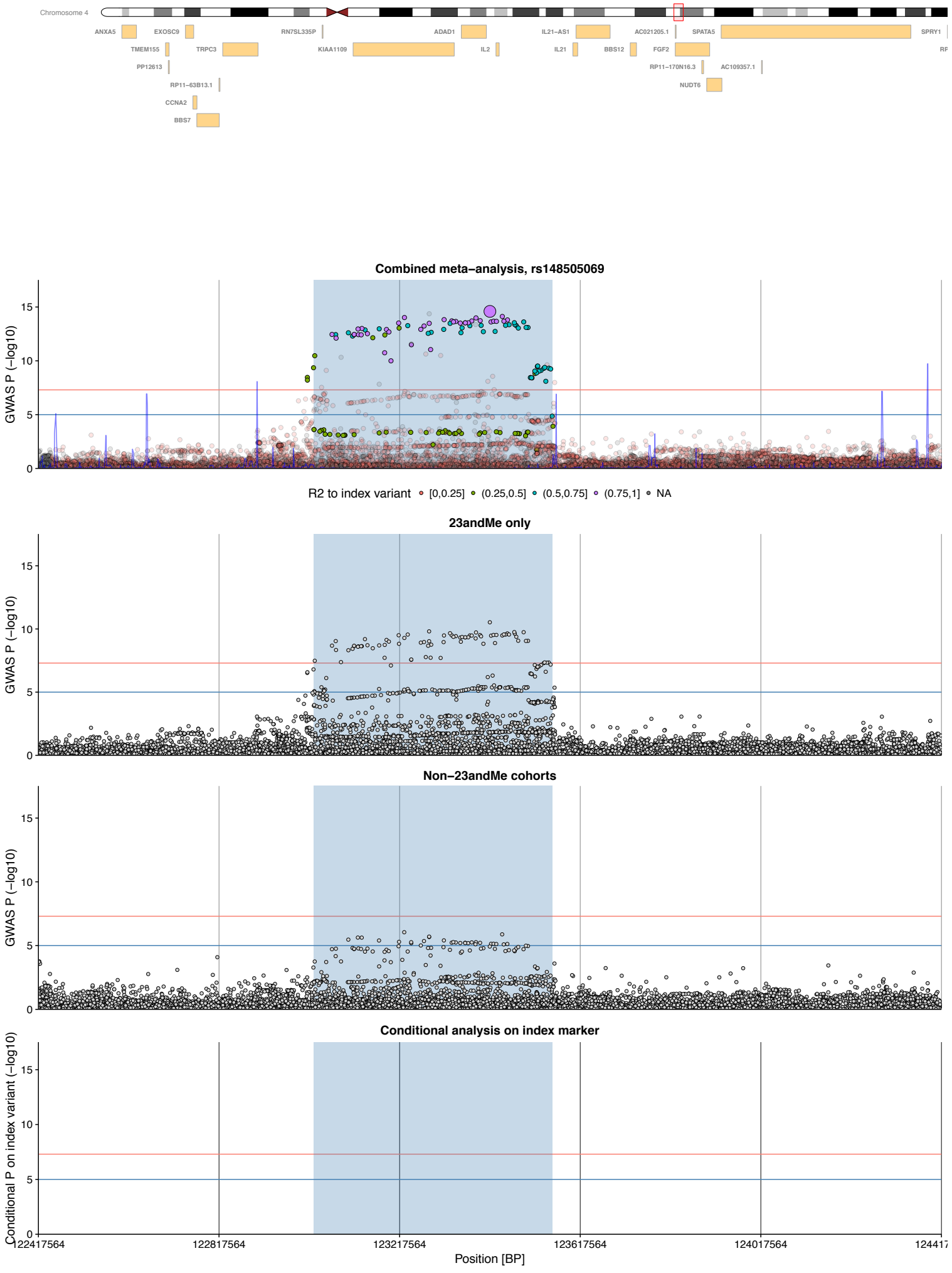

Chromosome 4
SLC39A8
AF213884.2
MANBA
UBE2D3
SLC9B2
RP11−328K4.1
RNU6−462P
RP11−498M5.2
RN7SL728P
NFKB1
RP11−10L12.4
BDH2
RP11−499E18.1
snoU13
CENPE
AF213884.3
RNU7−151P
SLC9B1
CISD2
Combined meta−analysis, rs12509403
GWAS P (−log10)
7.5
5.0
2.5
0.0
R2 to index variant
[0,0.25]
(0.25,0.5]
(0.5,0.75]
(0.75,1]
NA
23andMe only
Non−23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (−log10)
102525350
102925350
103325350
103725350
104125350
Position [BP]

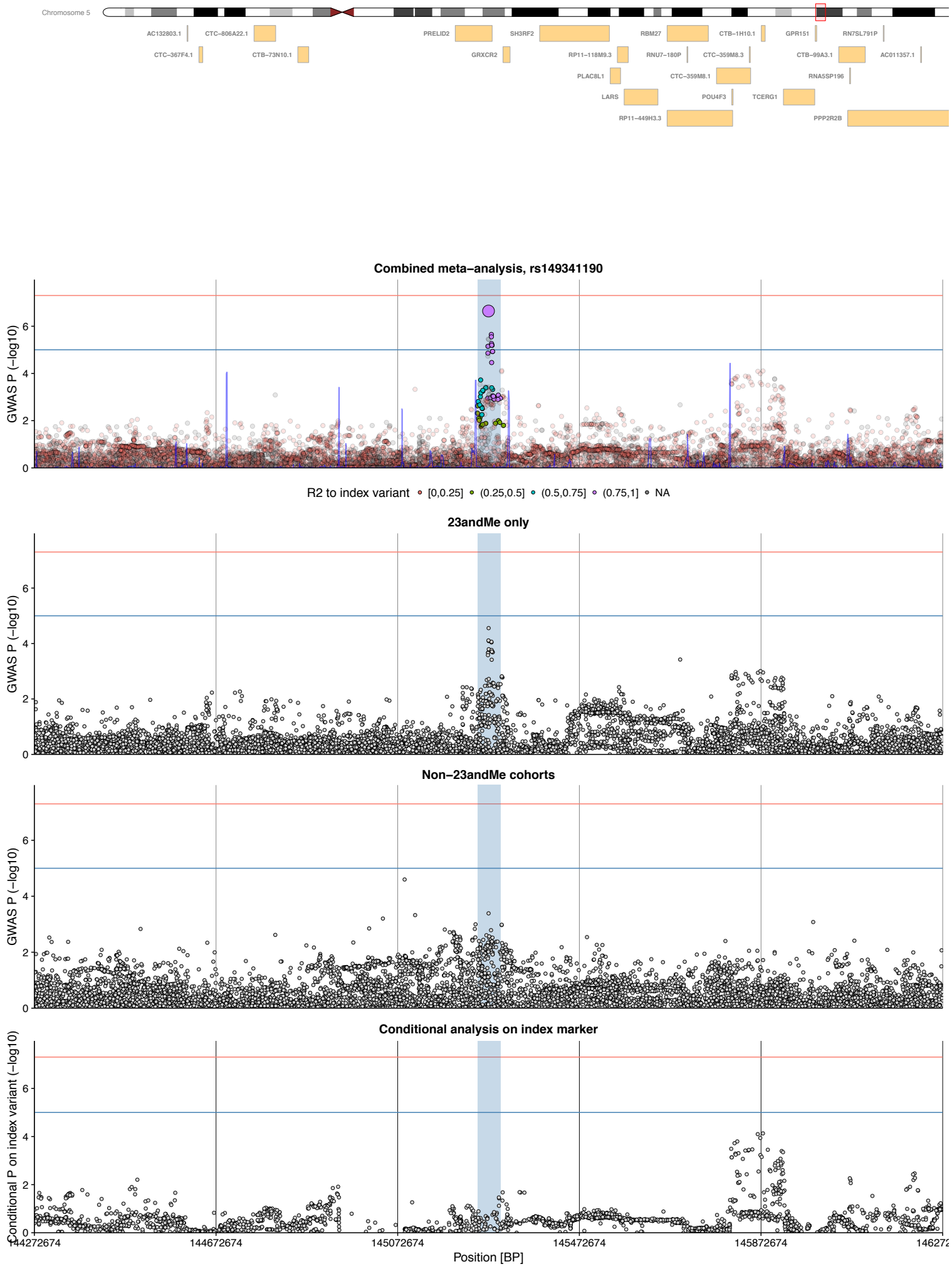

Chromosome 17
Combined meta–analysis, rs12939457
GWAS P (–log10)
R2 to index variant [0,0.25] (0.25,0.5] (0.5,0.75] (0.75,1] NA
23andMe only
Non–23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (–log10)
37032188
37432188
37832188
38232188
38632188
39032
Position [BP]

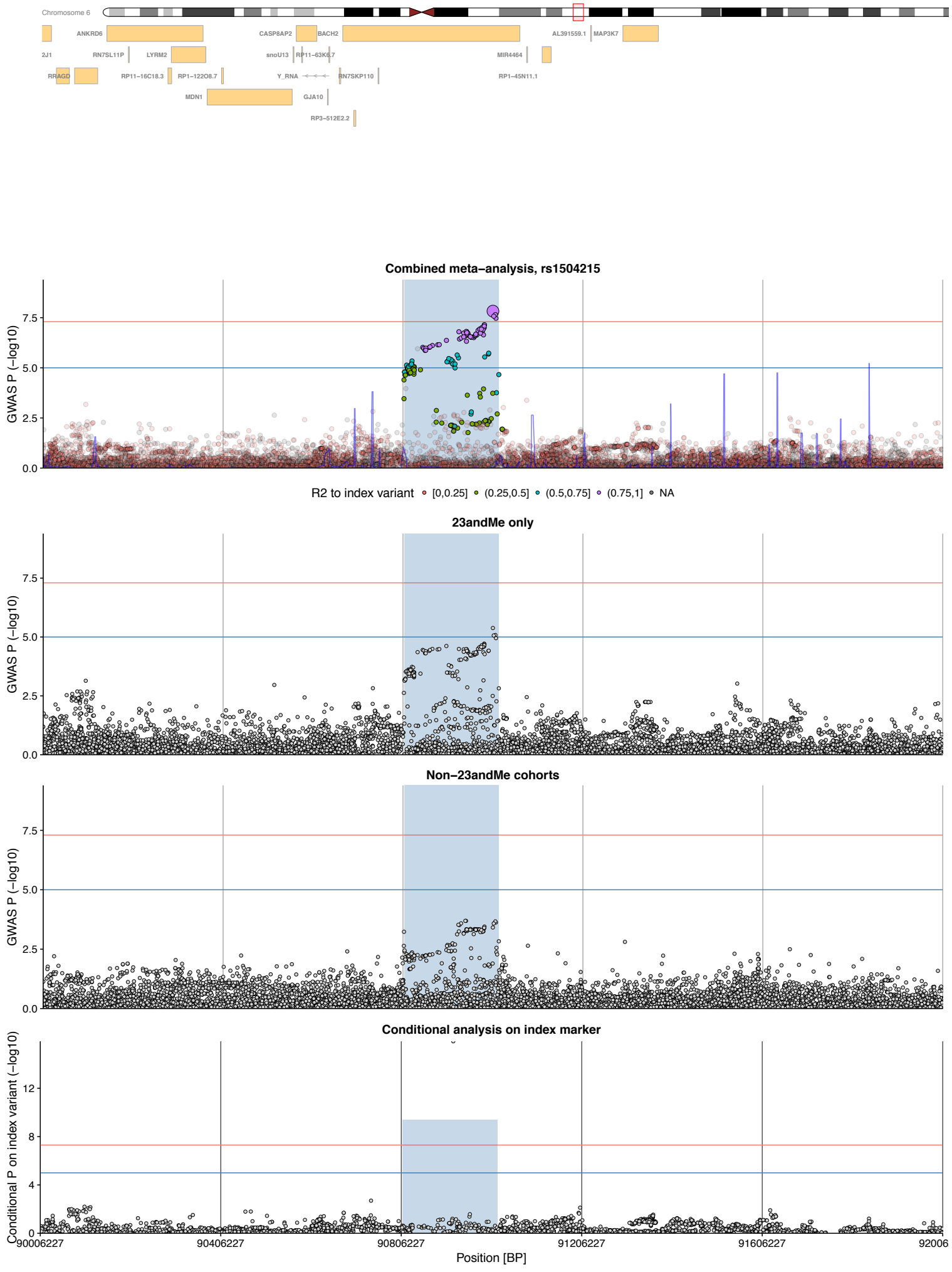

Chromosome 2
AC013460.1
AC092580.3
AC007463.2
LINC00299
AC011747.3
ID2−AS1
MBOAT2
ASAP2
RNU6ATAC37P
AC092580.4
LINC00298
U91324.1
AC011747.4
KIDINS220
snoU13
RP11−734K21.4
AC011747.6
ID2
RP11−734K21.2
RP11−434B12.1
RP11−734K21.5
RP11−734K21.3
Combined meta−analysis, rs13395467
GWAS P (−log10)
R2 to index variant
[0,0.25]
(0.25,0.5]
(0.5,0.75]
(0.75,1]
NA
23andMe only
Non−23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (−log10)
7451498
7851498
8251498
8651498
9051498
Position [BP]

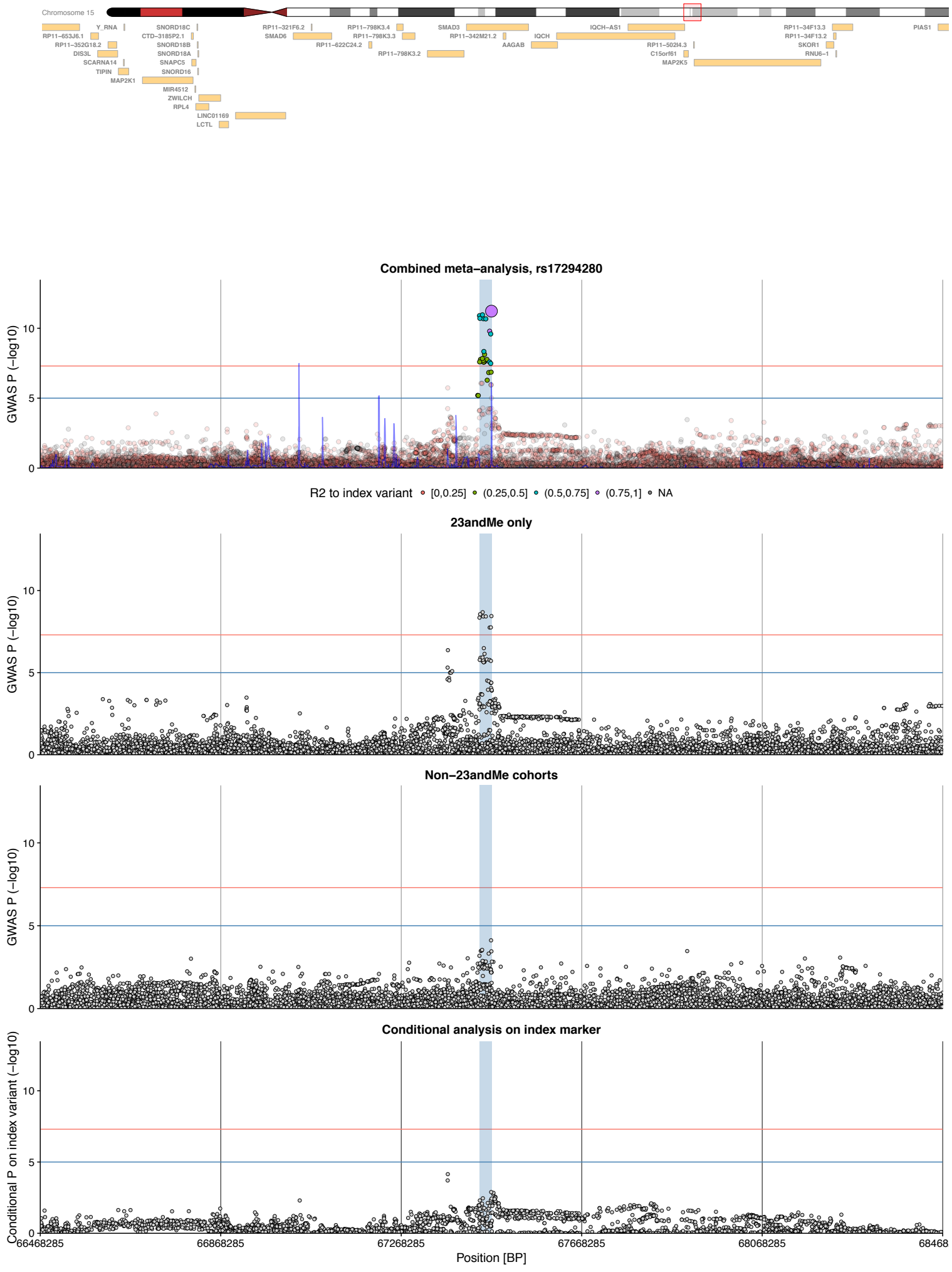

Chromosome 11
7.4
AP001891.1
AP000770.1
BUD13
SIK3
BACE1
DSCAML1
AP000770.2
AP006216.10
AP000936.2
PAFAH1B2
AP000892.4
AP000711.1
RP11−728F11.3
AP006216.5
RNY4P6
AP000892.6
CEP164
RP11−35P15.1
FXYD6−FXYD2
snoU13
AP000936.4
RP11−728F1
APOA5
PCSK7
FXYD2
APOA1−AS
RNF214
ZPR1 APOA4
SCARNA11
APOC3
CMB9−94B1.2
APOA1
BACE1−AS
Combined meta−analysis, rs141023293
GWAS P (−log10)
R2 to index variant
[0,0.25]
(0.25,0.5]
(0.5,0.75]
(0.75,1]
NA
23andMe only
Non−23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (−log10)
115772917
116172917
116572917
116972917
117372917
Position [BP]

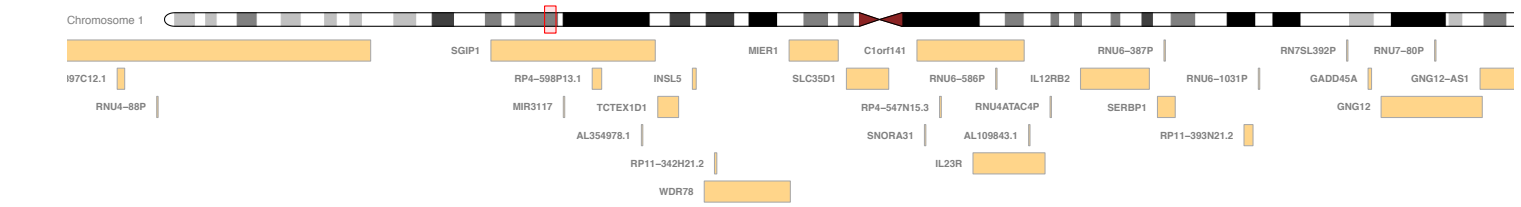

Chromosome 5
TMEM232
MIR548F3
SNORA51
SLC25A46
CTC−551A13.1
TSLP
CTC−551A13.2
WDR36
CAMK4
AC010468.2
CTC−499J9.1
NREP
STARD4−AS1
STARD4
AC008967.1
RN7SKP57
NREP−AS1
Combined meta−analysis, rs1438673
GWAS P (−log10)
R2 to index variant
[0,0.25]
(0.25,0.5]
(0.5,0.75]
(0.75,1]
NA
23andMe only
Non−23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (−log10)
109467499
109867499
110267499
110667499
111067499
Position [BP]

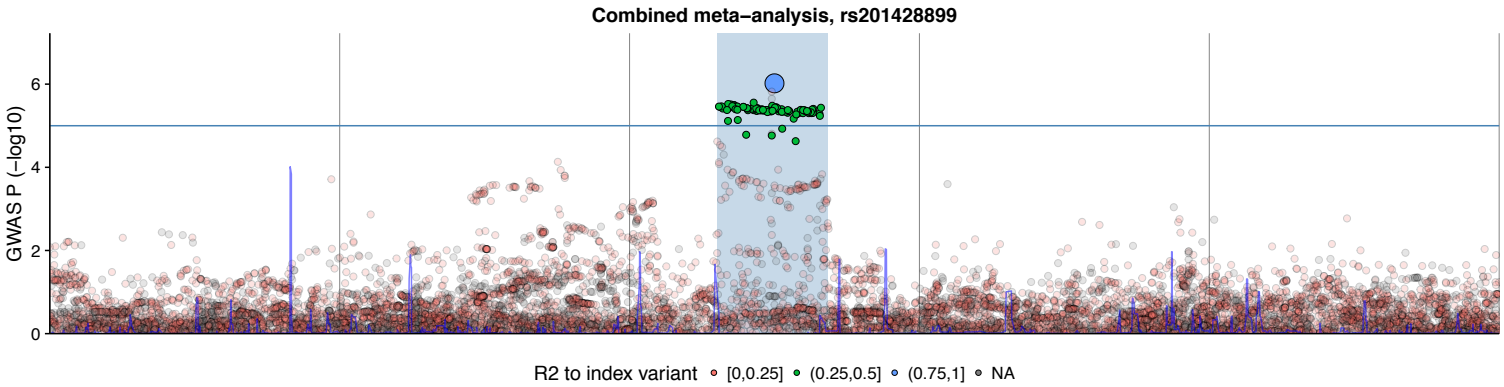

Chromosome 4
ANXA5
EXOSC9
RN7SL335P
ADAD1
IL21−AS1
AC021205.1
SPATA5
SPRY1
TMEM155
TRPC3
KIAA1109
IL2
IL21
BBS12
FGF2
PP12613
RP11−170N16.3
AC109357.1
RP11−63B13.1
NUDT6
CCNA2
BBS7
Combined meta−analysis, rs148505069
GWAS P (−log10)
R2 to index variant
[0,0.25]
(0.25,0.5]
(0.5,0.75]
(0.75,1]
NA
23andMe only
Non−23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (−log10)
122417564
122817564
123217564
123617564
124017564
Position [BP]


Chromosome 5
AC132803.1
CTC−806A22.1
CTC−367F4.1
CTB−73N10.1
PRELID2
SH3RF2
GRXCR2
RBM27
CTB−1H10.1
RP11−118M9.3
RNU7−180P
CTC−359M8.3
GPR151
RN7SL791P
CTB−99A3.1
AC011357.1
PLAC8L1
CTC−359M8.1
RNA5SP196
LARS
POU4F3
TCERG1
RP11−449H3.3
PPP2R2B
Combined meta−analysis, rs149341190
GWAS P (−log10)
R2 to index variant
[0,0.25]
(0.25,0.5]
(0.5,0.75]
(0.75,1]
NA
23andMe only
Non−23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (−log10)
144272674
144672674
145072674
145472674
145872674
Position [BP]

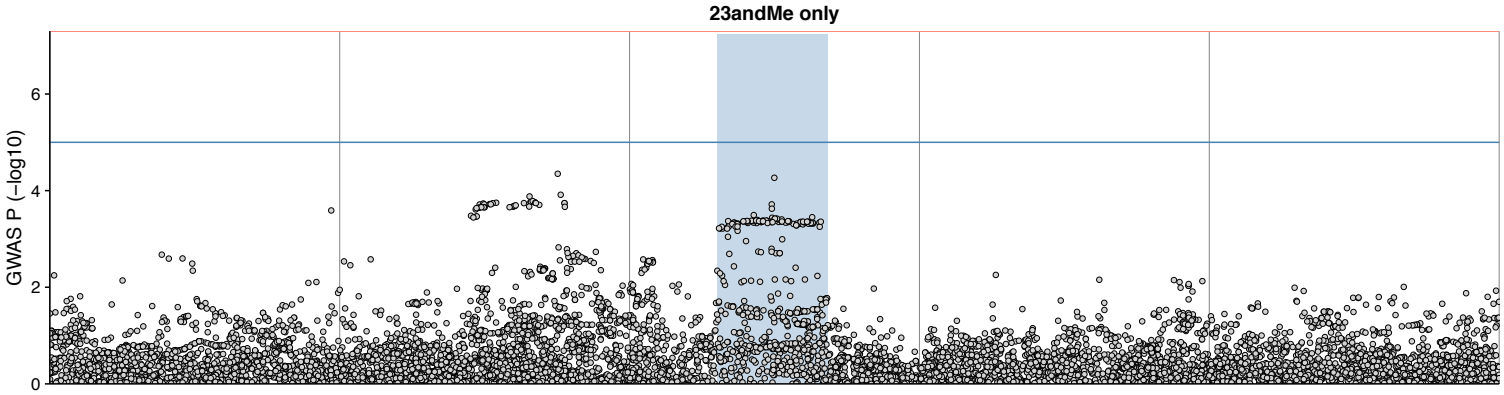

Chromosome 6
ANKRD6
CASP8AP2
BACH2
AL391559.1
MAP3K7
2J1
RN7SL11P
LYRM2
snoU13
RP11−63K6.7
MIR4464
RRAGD
RP11−16C18.3
RP1−122O8.7
Y_RNA
RN7SKP110
RP1−45N11.1
MDN1
GJA10
RP3−512E2.2
Combined meta−analysis, rs1504215
GWAS P (−log10)
7.5
5.0
2.5
0.0
R2 to index variant
[0,0.25]
(0.25,0.5]
(0.5,0.75]
(0.75,1]
NA
23andMe only
Non−23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (−log10)
12
8
4
0
90006227
90406227
90806227
91206227
91606227
92006
Position [BP]

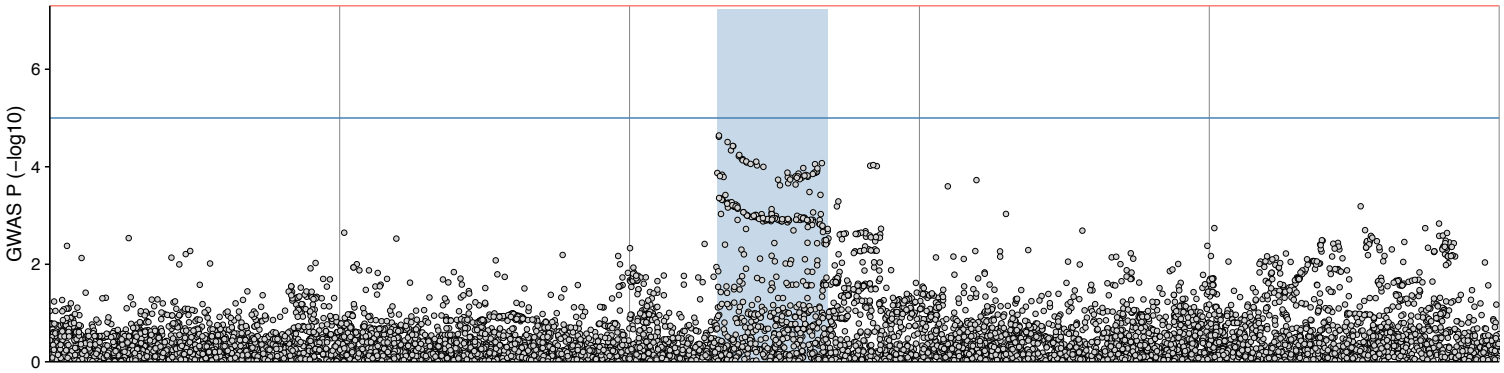

Chromosome 15
Y_RNA
SNORD18C
RP11−321F6.2
RP11−798K3.4
SMAD3
IQCH−AS1
RP11−34F13.3
PIAS1
RP11−653J6.1
CTD−3185P2.1
SMAD6
RP11−798K3.3
RP11−342M21.2
IQCH
RP11−34F13.2
RP11−352G18.2
SNORD18B
RP11−622C24.2
AAGAB
SKOR1
DIS3L
SNORD18A
RP11−798K3.2
RP11−502I4.3
RNU6−1
SCARNA14
SNAPC5
C15orf61
TIPIN
SNORD16
MAP2K5
MAP2K1
MIR4512
ZWILCH
RPL4
LINC01169
LCTL
Combined meta−analysis, rs17294280
GWAS P (−log10)
R2 to index variant
[0,0.25]
(0.25,0.5]
(0.5,0.75]
(0.75,1]
NA
23andMe only
Non−23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (−log10)
66468285
66868285
67268285
67668285
68068285
68468
Position [BP]

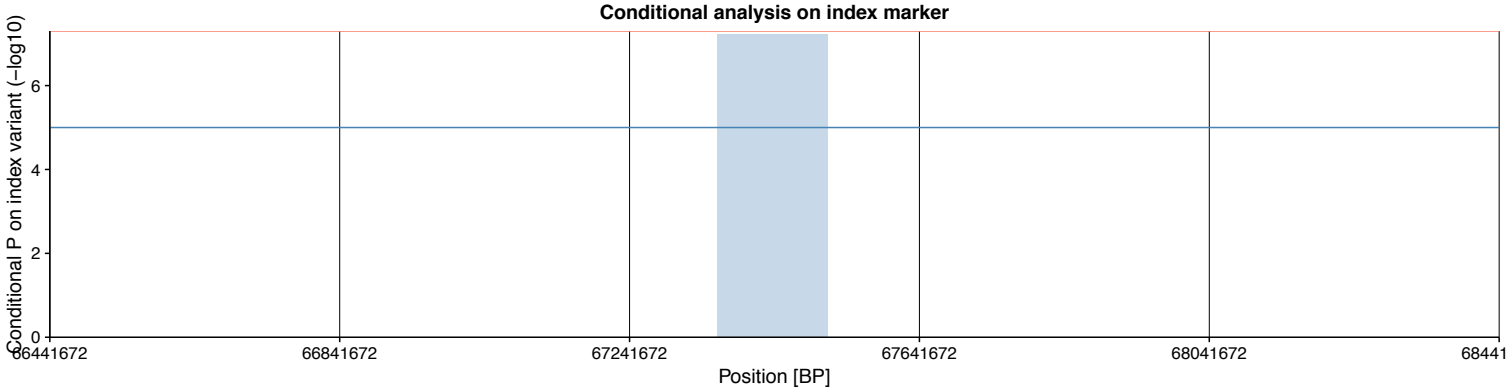


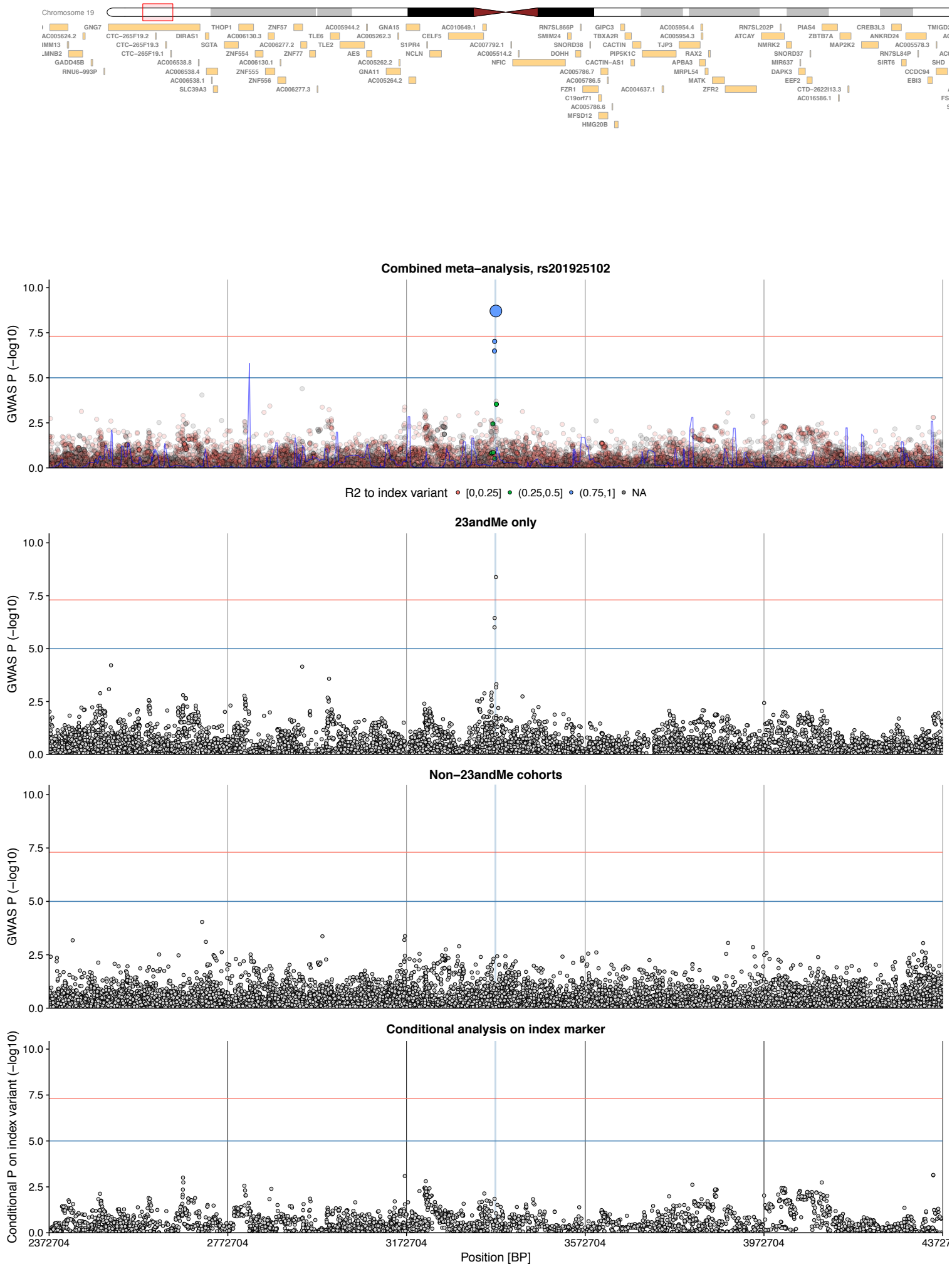


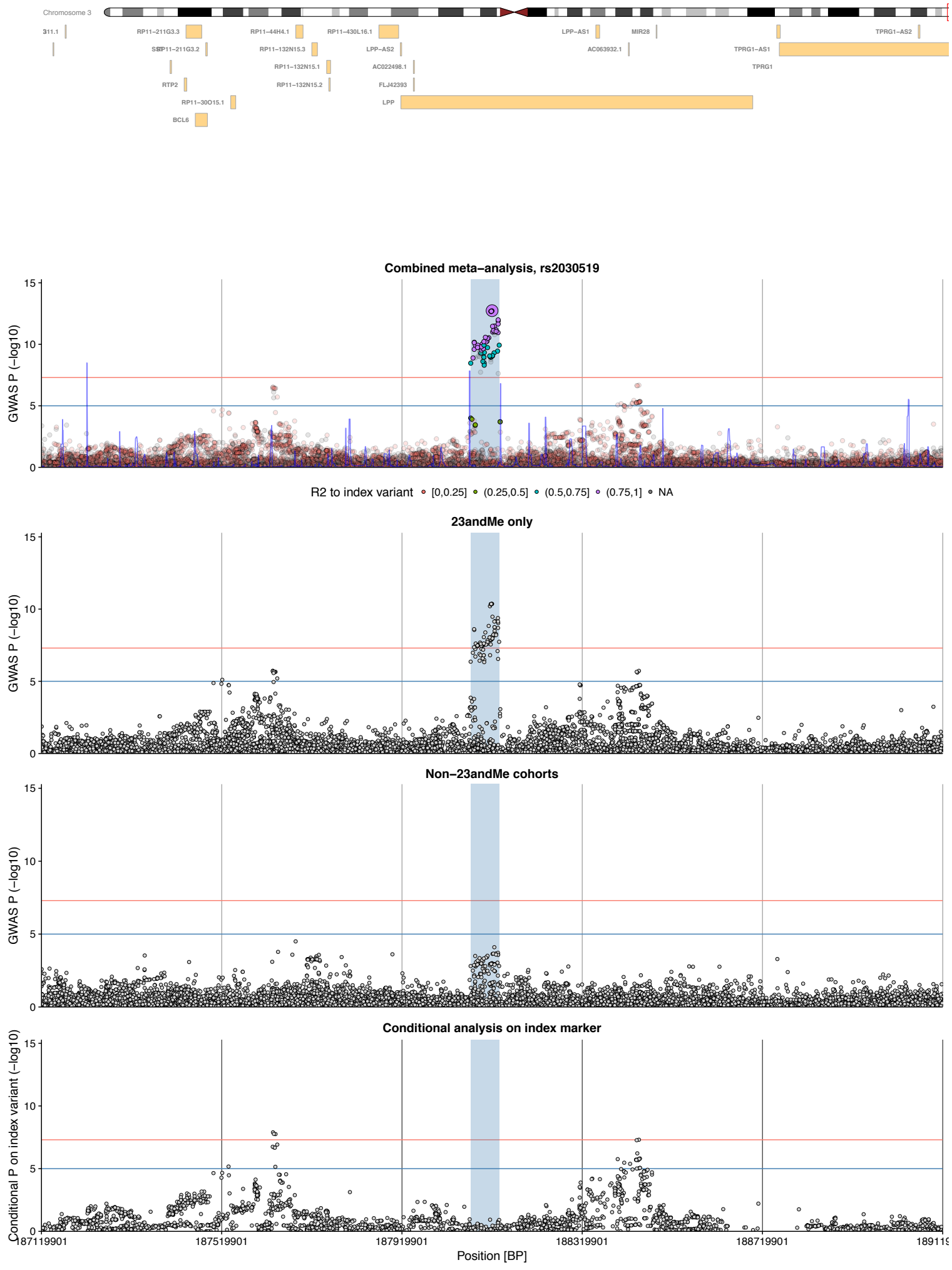
R2 to index variant [0,0.25] [0.25,0.5] (0.75,1] NA

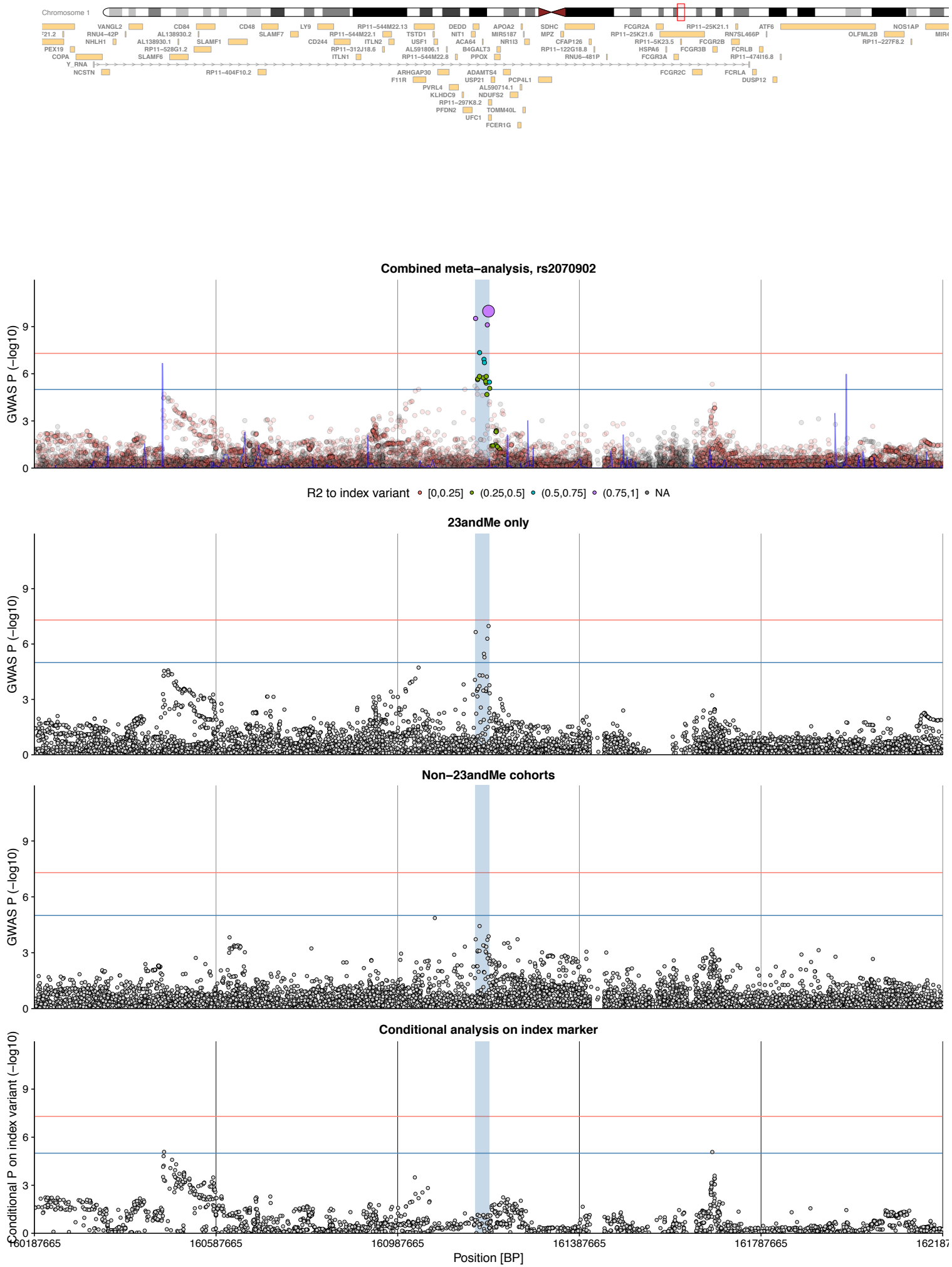


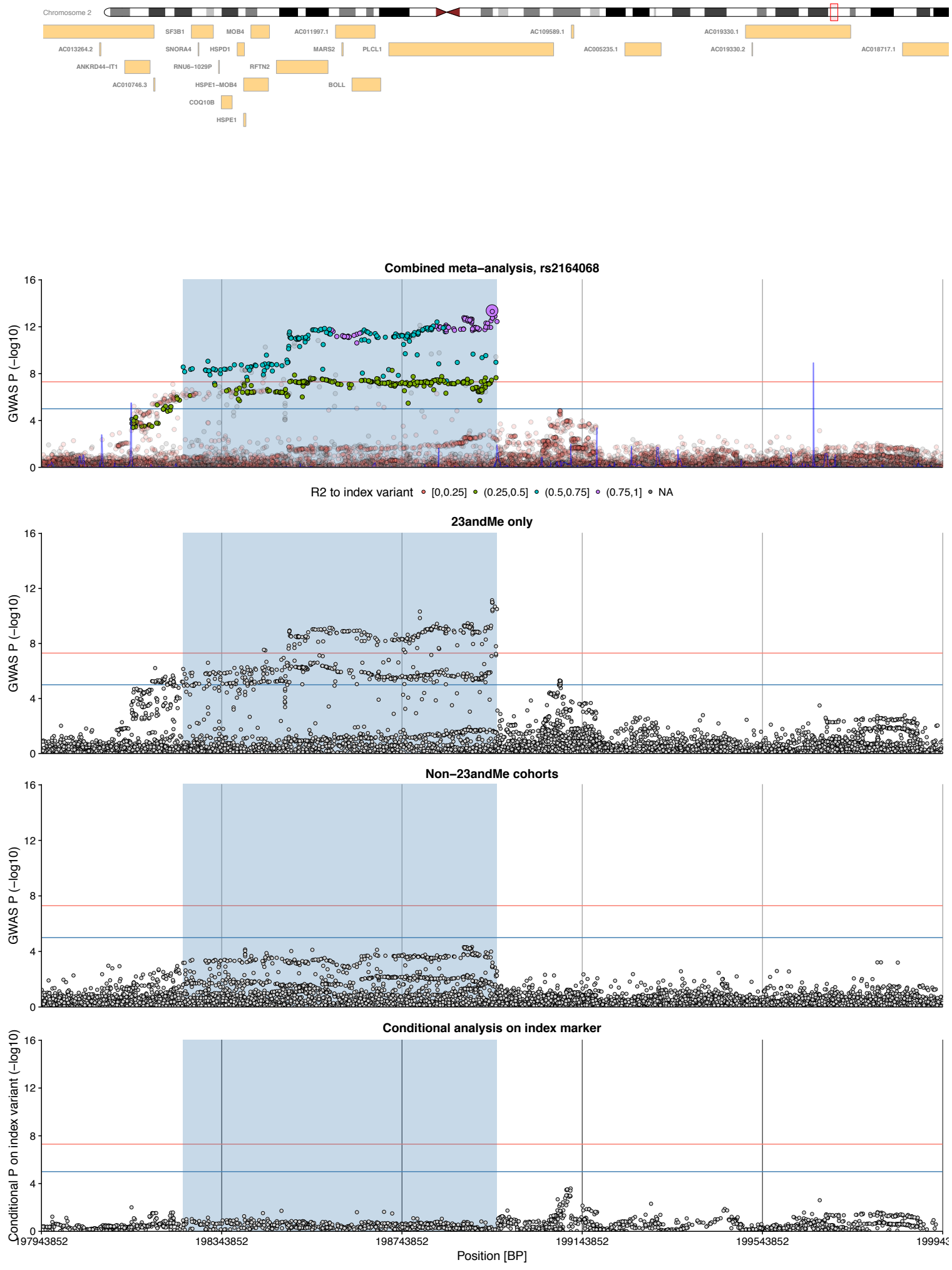


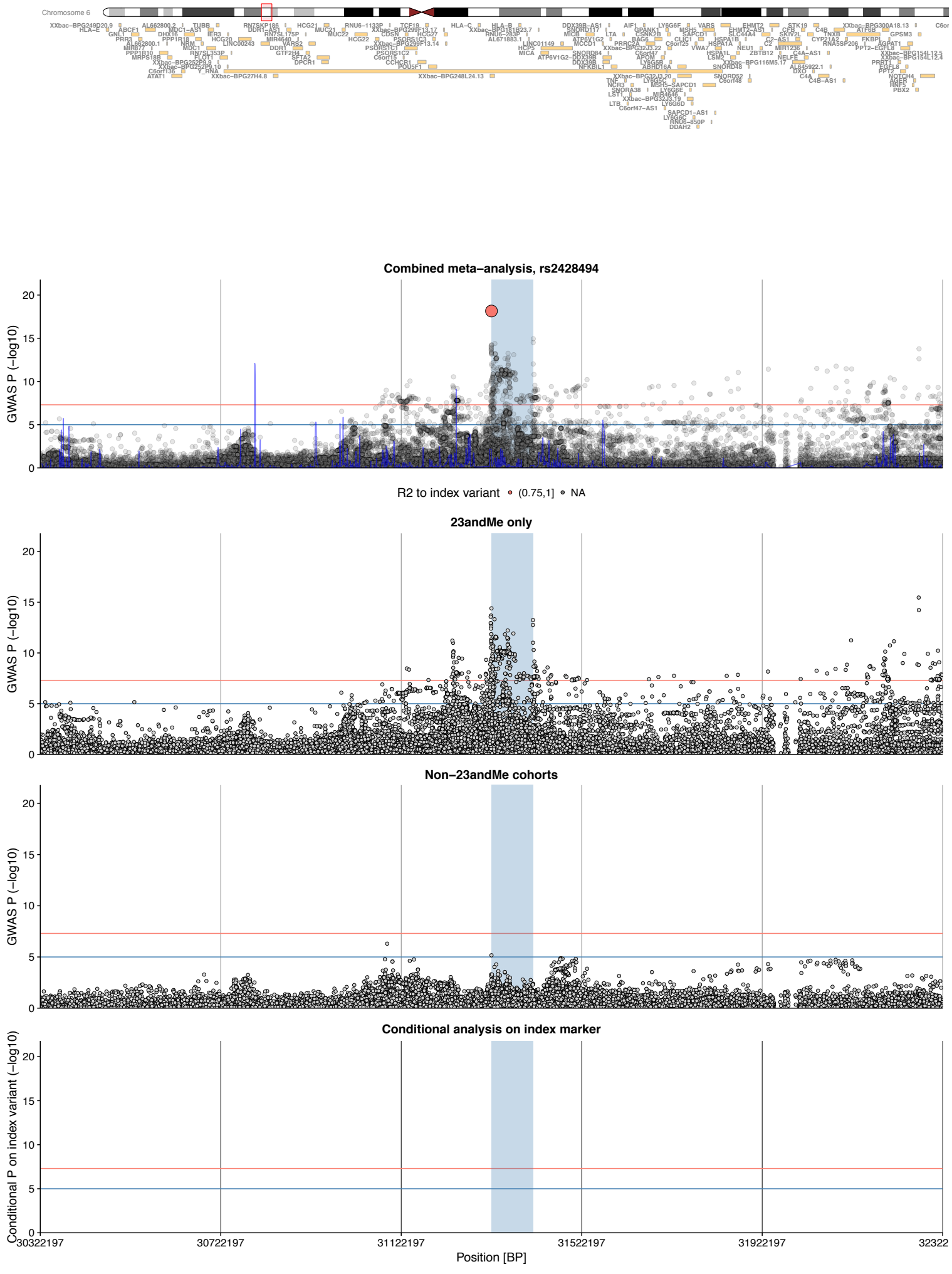


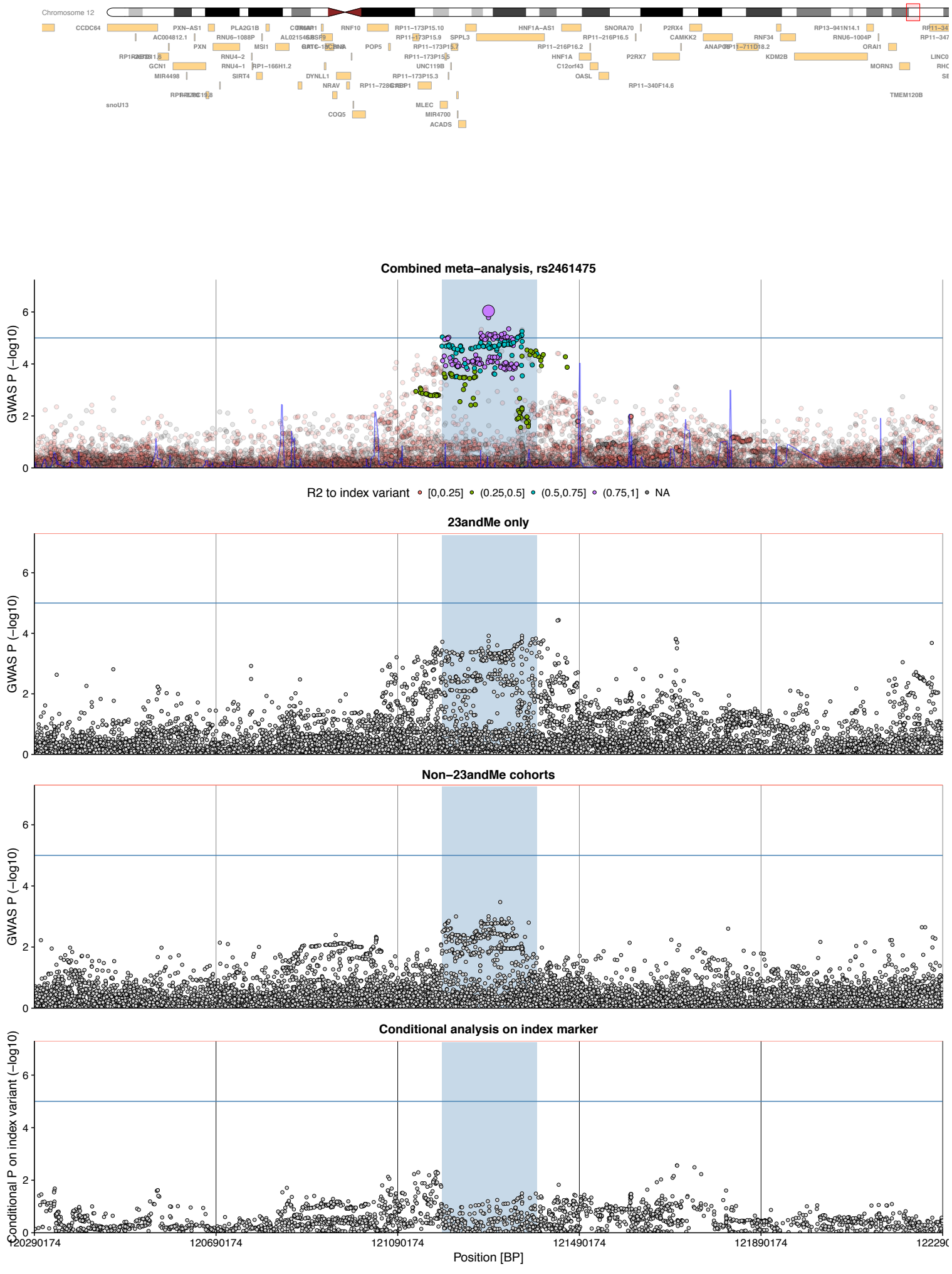

Chromosome 19
Combined meta−analysis, rs201925102
GWAS P (−log10)
R2 to index variant [0,0.25] (0.25,0.5] (0.75,1] NA
23andMe only
Non−23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (−log10)
2372704
2772704
3172704
3572704
3972704
Position [BP]

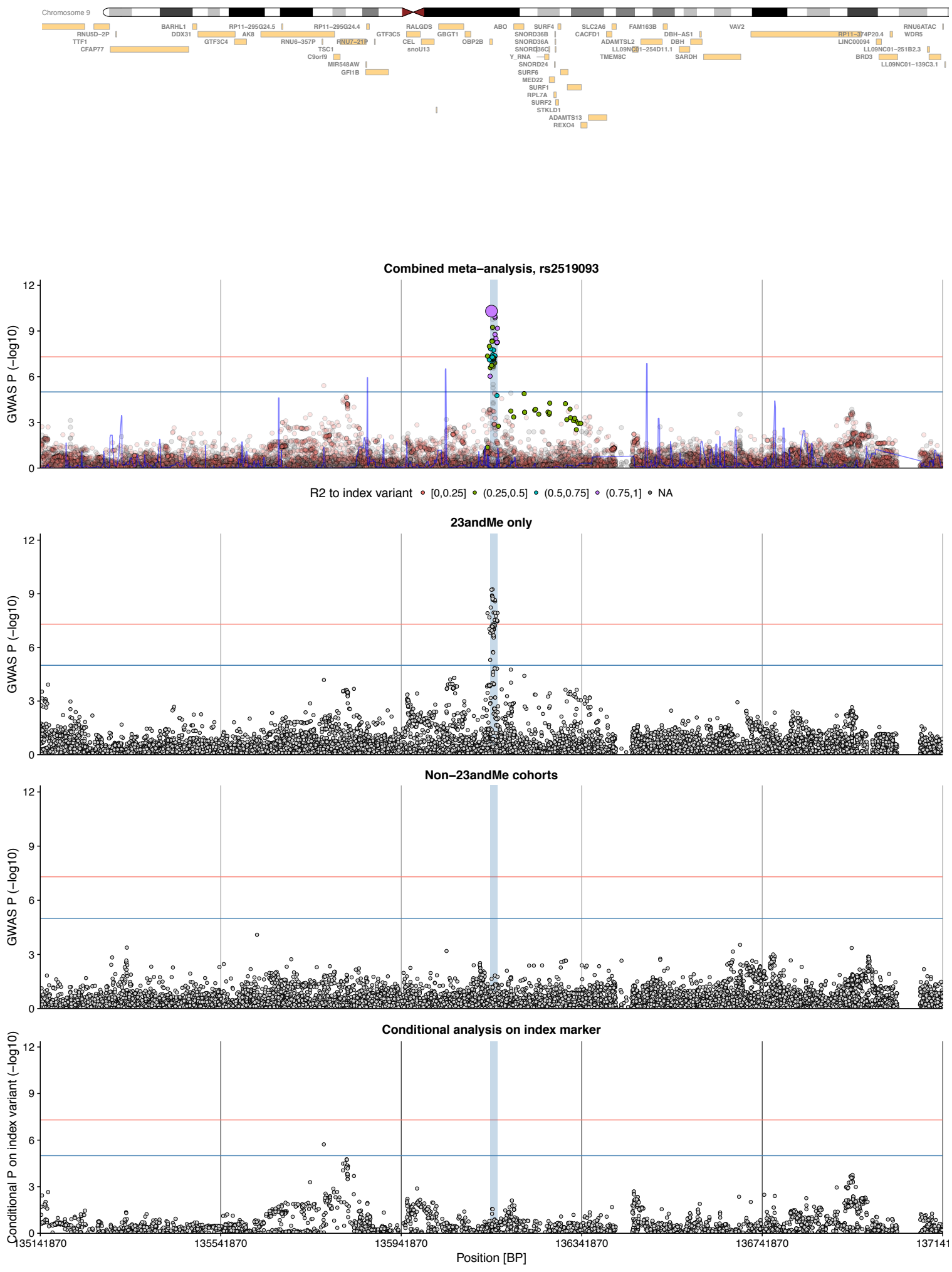

Chromosome 3
311.1
RP11−211G3.3
RP11−211G3.2
RP11−44H4.1
RP11−132N15.3
RP11−132N15.1
RP11−132N15.2
RP11−430L16.1
LPP−AS2
AC022498.1
FLJ42393
LPP
RTP2
RP11−30O15.1
BCL6
LPP−AS1
MIR28
AC063932.1
TPRG1−AS2
TPRG1−AS1
TPRG1
Combined meta−analysis, rs2030519
GWAS P (−log10)
R2 to index variant [0,0.25] (0.25,0.5] (0.5,0.75] (0.75,1] NA
23andMe only
Non−23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (−log10)
187119901
187519901
187919901
188319901
188719901
Position [BP]

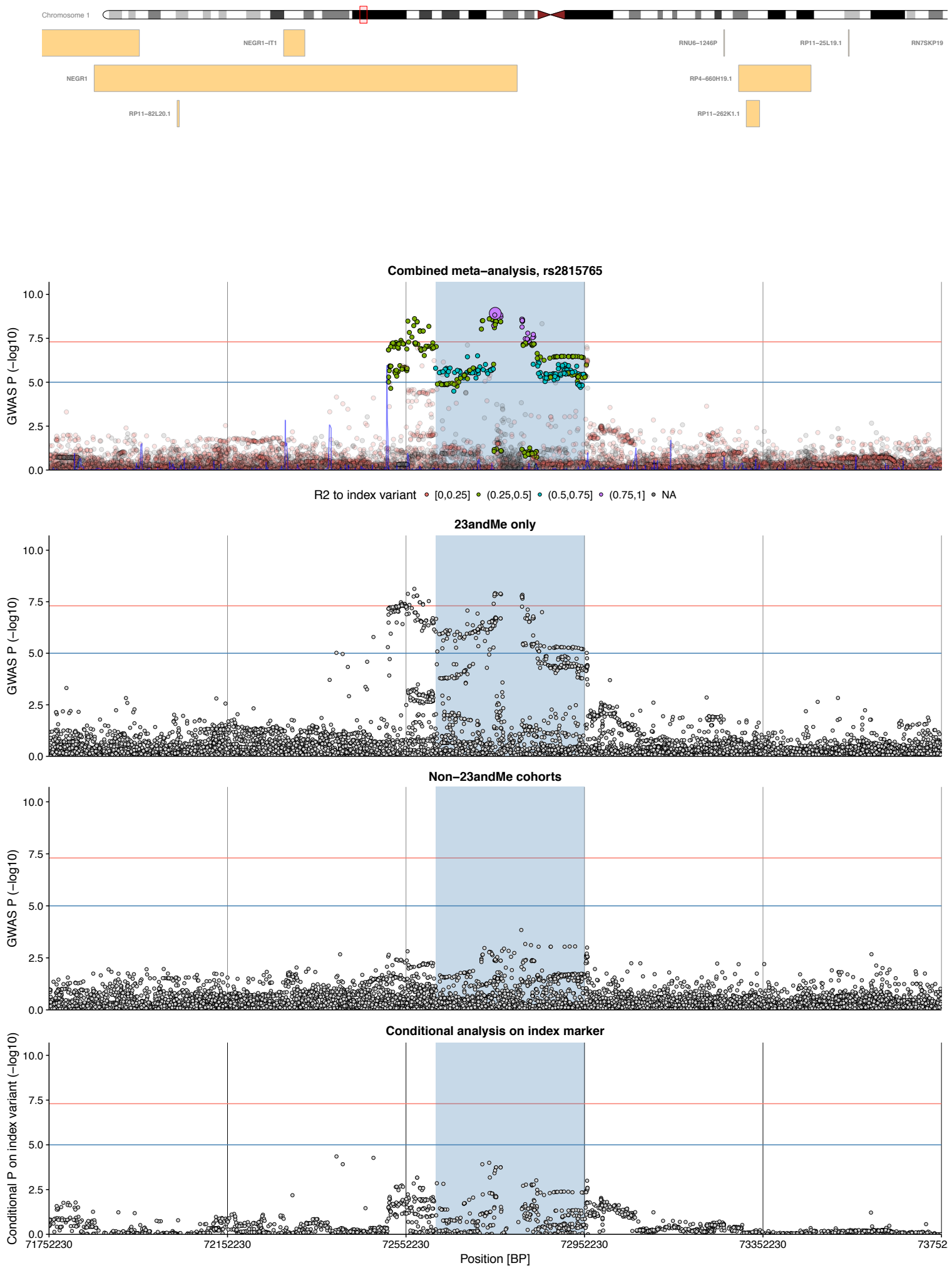

Chromosome 1
VANGL2
CD84
CD48
LY9
RP11−544M22.13
DEDD
APOA2
SDHC
FCGR2A
RP11−25K21.1
ATF6
NOS1AP
RNU4−42P
AL138930.2
SLAMF7
RP11−544M22.1
TSTD1
NIT1
MIR5187
MPZ
RP11−25K21.6
RN7SL466P
OLFML2B
NHLH1
AL138930.1
SLAMF1
CD244
ITLN2
USF1
ACA64
NR1I3
CFAP126
RP11−5K23.5
FCGR2B
RP11−227F8.2
PEX19
RP11−528G1.2
RP11−312J18.6
AL591806.1
B4GALT3
RP11−122G18.8
HSPA6
FCGR3B
FCRLB
COPA
SLAMF6
ITLN1
RP11−544M22.8
PPOX
RNU6−481P
FCGR3A
RP11−474H16.8
Y_RNA
NCSTN
RP11−404F10.2
ARHGAP30
ADAMTS4
FCGR2C
FCRLA
F11R
USP21
PCP4L1
DUSP12
PVRL4
AL590714.1
KLHDC9
NDUFS2
RP11−297K8.2
PFDN2
TOMM40L
UFC1
FCER1G
Combined meta−analysis, rs2070902
GWAS P (−log10)
R2 to index variant
[0,0.25]
(0.25,0.5]
(0.5,0.75]
(0.75,1]
NA
23andMe only
Non−23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (−log10)
160187665
160587665
160987665
161387665
161787665
Position [BP]

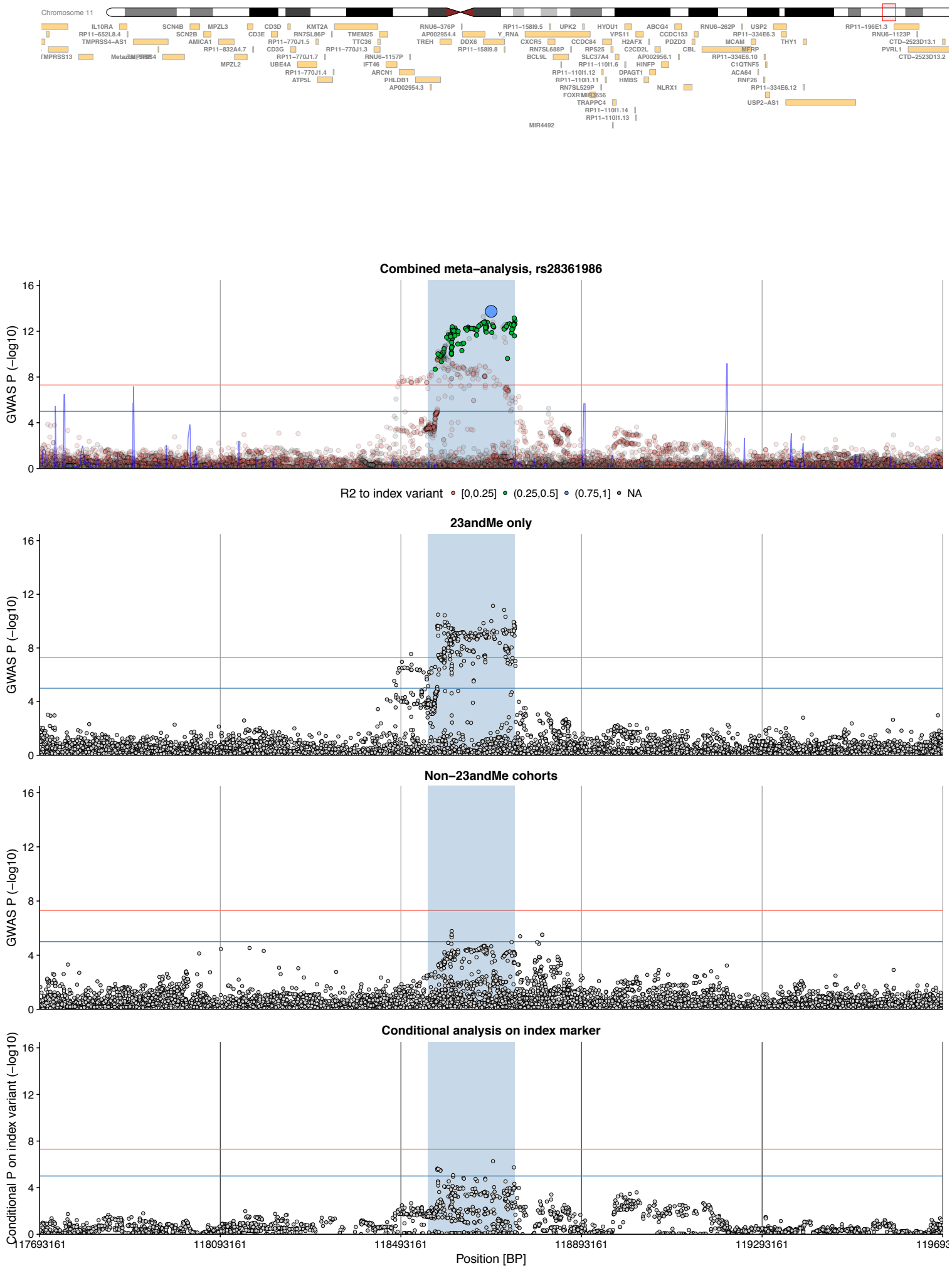

Chromosome 2
SF3B1
MOB4
AC011997.1
AC109589.1
AC019330.1
AC013264.2
SNORA4
HSPD1
MARS2
PLCL1
AC005235.1
AC019330.2
AC018717.1
ANKRD44−IT1
RNU6−1029P
RFTN2
AC010746.3
HSPE1−MOB4
BOLL
COQ10B
HSPE1
Combined meta−analysis, rs2164068
GWAS P (−log10)
R2 to index variant
[0,0.25]
(0.25,0.5]
(0.5,0.75]
(0.75,1]
NA
23andMe only
Non−23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (−log10)
197943852
198343852
198743852
199143852
199543852
Position [BP]

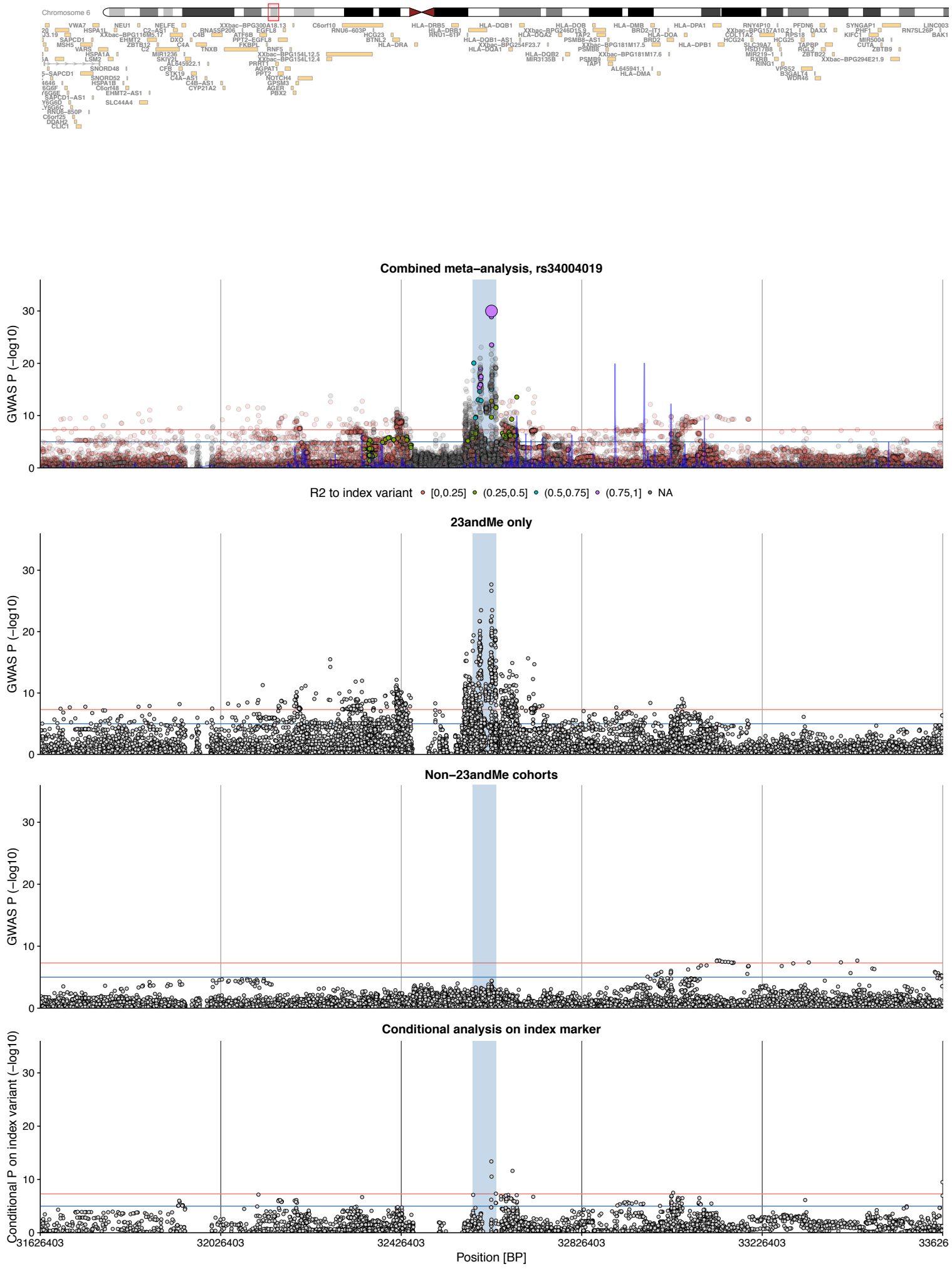

Chromosome 6
Combined meta−analysis, rs2428494
GWAS P (−log10)
R2 to index variant
(0.75,1]
NA
23andMe only
Non−23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (−log10)
30322197
30722197
31122197
31522197
31922197
32322
Position [BP]

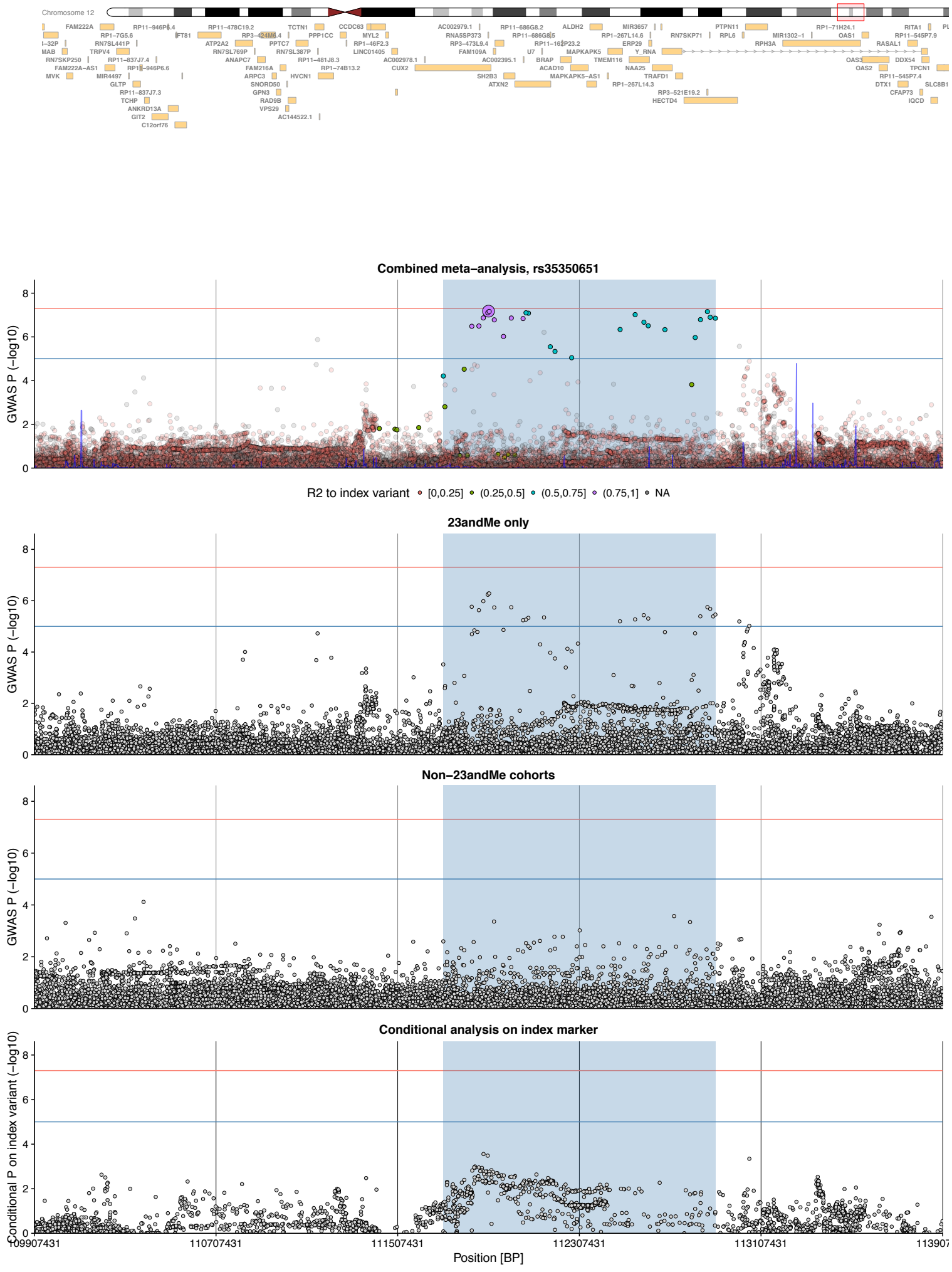

Chromosome 12
Combined meta−analysis, rs2461475
GWAS P (−log10)
R2 to index variant [0,0.25] (0.25,0.5] (0.5,0.75] (0.75,1] NA
23andMe only
Non−23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (−log10)
120290174
120690174
121090174
121490174
121890174
Position [BP]

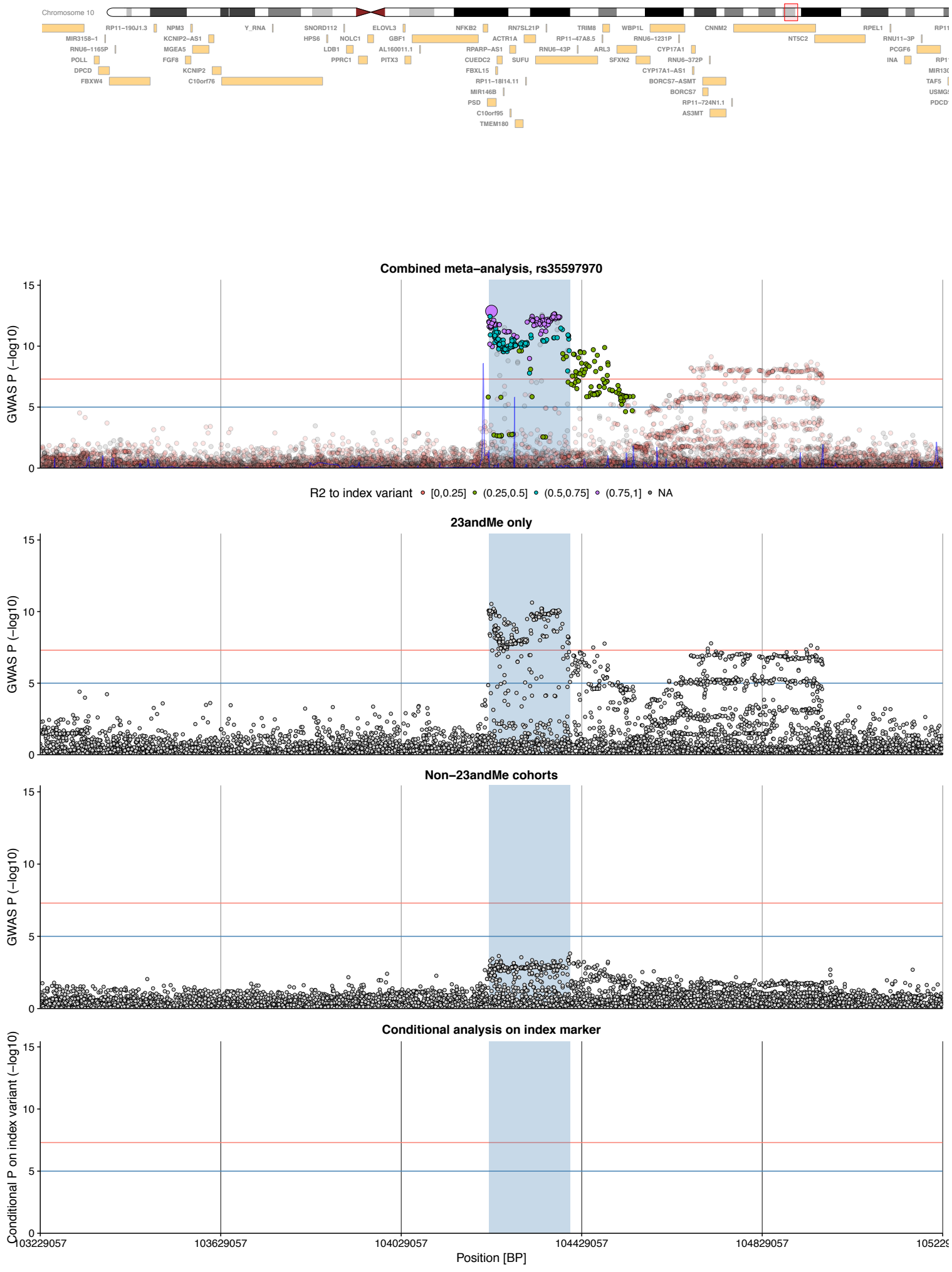

Chromosome 9
BARHL1
RP11−295G24.5
RP11−295G24.4
RALGDS
ABO
SURF4
SLC2A6
FAM163B
VAV2
RNU6ATAC
RNU5D−2P
DDX31
AK8
GTF3C5
GBGT1
SNORD36B
CACFD1
DBH−AS1
RP11−374P20.4
WDR5
TTF1
GTF3C4
RNU6−357P
RNU7−21P
CEL
OBP2B
SNORD36A
ADAMTSL2
DBH
LINC00094
CFAP77
TSC1
snoU13
SNORD36C
LL09NC01−254D11.1
LL09NC01−251B2.3
C9orf9
Y_RNA
TMEM8C
SARDH
BRD3
MIR548AW
SNORD24
LL09NC01−139C3.1
GFI1B
SURF6
MED22
SURF1
RPL7A
SURF2
STKLD1
ADAMTS13
REXO4
Combined meta−analysis, rs2519093
GWAS P (−log10)
R2 to index variant
[0,0.25]
(0.25,0.5]
(0.5,0.75]
(0.75,1]
NA
23andMe only
Non−23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (−log10)
135141870
135541870
135941870
136341870
136741870
Position [BP]

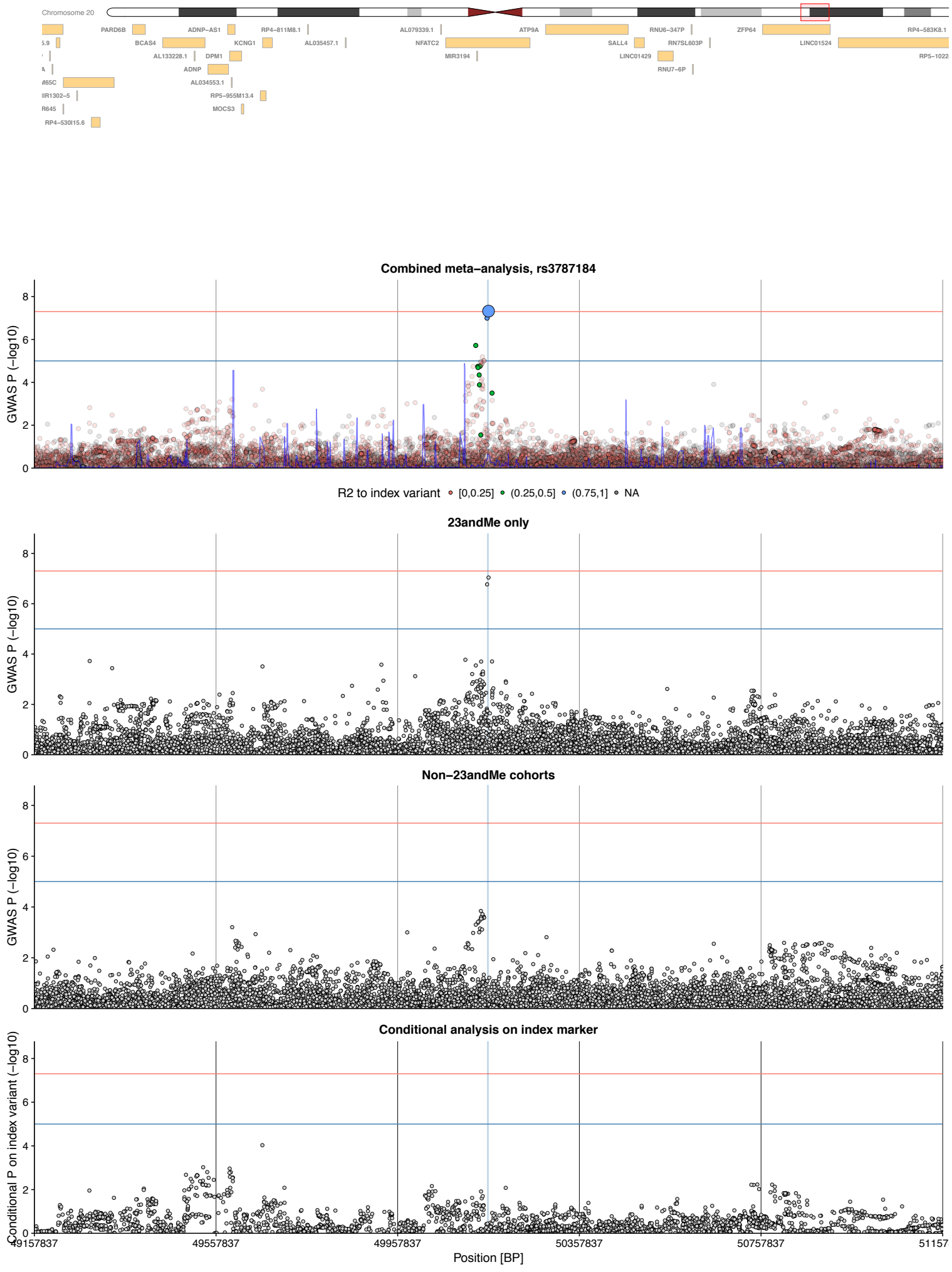

Chromosome 1
NEGR1–IT1
RNU6–1246P
RP11–25L19.1
RN7SKP19
NEGR1
RP4–660H19.1
RP11–82L20.1
RP11–262K1.1
Combined meta–analysis, rs2815765
GWAS P (–log10)
10.0
7.5
5.0
2.5
0.0
R2 to index variant [0,0.25] (0.25,0.5] (0.5,0.75] (0.75,1] NA
23andMe only
Non–23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (–log10)
71752230
72152230
72552230
72952230
73352230
73752
Position [BP]

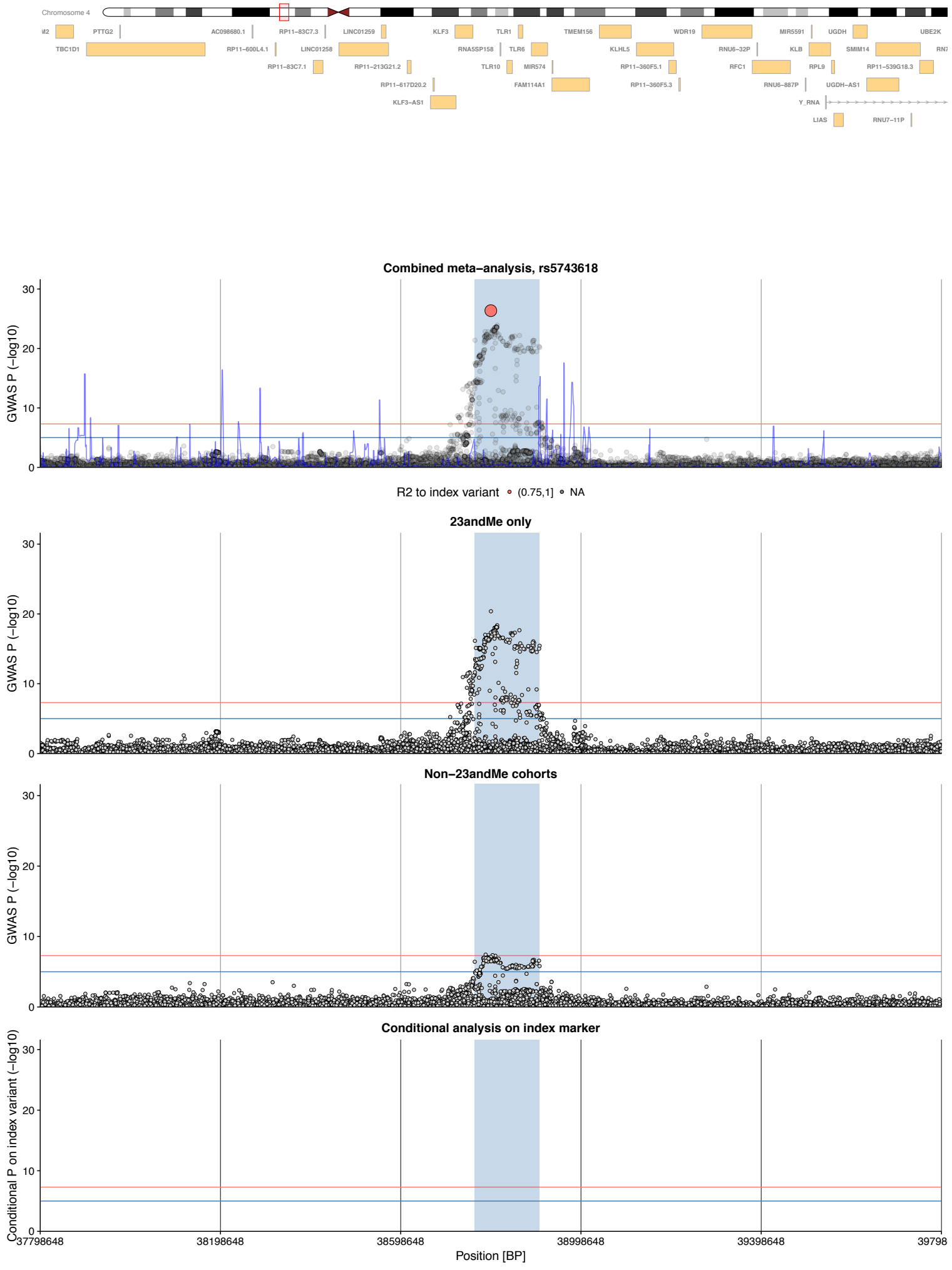

Chromosome 11
IL10RA
SCN4B
MPZL3
CD3D
KMT2A
RNU6−376P
RP11−158I9.5
UPK2
HYOU1
ABCG4
RNU6−262P
USP2
RP11−196E1.3
RP11−652L8.4
SCN2B
CD3E
RN7SL86P
TMEM25
AP002954.4
Y_RNA
VPS11
CCDC153
RP11−334E6.3
RNU6−1123P
TMPRSS4−AS1
AMICA1
RP11−770J1.5
TTC36
TREH
DDX6
CXCR5
CCDC84
H2AFX
PDZD3
MCAM
THY1
CTD−2523D13.1
RP11−832A4.7
CD3G
RP11−770J1.3
RP11−158I9.8
RN7SL688P
RPS25
C2CD2L
CBL
MFRP
PVRL1
TMPRSS13
RP11−770J1.7
RNU6−1157P
BCL9L
SLC37A4
AP002956.1
RP11−334E6.10
CTD−2523D13.2
MPZL2
UBE4A
IFT46
RP11−110I1.6
HINFP
C1QTNF5
RP11−770J1.4
ARCN1
RP11−110I1.12
DPAGT1
ACA64
ATP5L
PHLDB1
RP11−110I1.11
HMBS
RNF26
AP002954.3
RN7SL529P
NLRX1
RP11−334E6.12
TRAPPC4
USP2−AS1
RP11−110I1.14
RP11−110I1.13
MIR4492
Combined meta−analysis, rs28361986
GWAS P (−log10)
R2 to index variant
[0,0.25]
(0.25,0.5]
(0.75,1]
NA
23andMe only
Non−23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (−log10)
Position [BP]

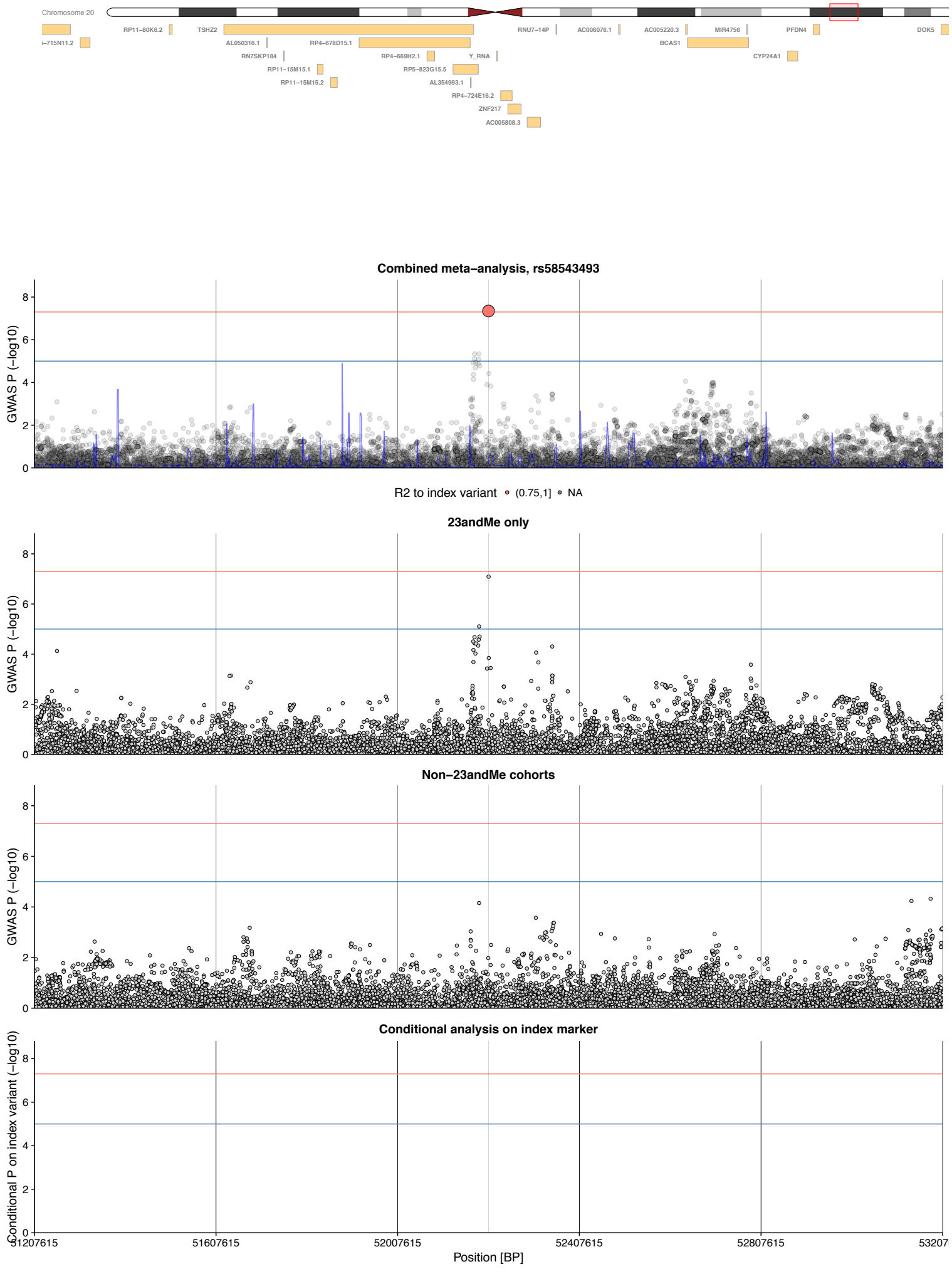

Chromosome 6
Combined meta−analysis, rs34004019
GWAS P (−log10)
R2 to index variant [0,0.25] (0.25,0.5] (0.5,0.75] (0.75,1] NA
23andMe only
Non−23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (−log10)
31626403
32026403
32426403
32826403
33226403
33626
Position [BP]

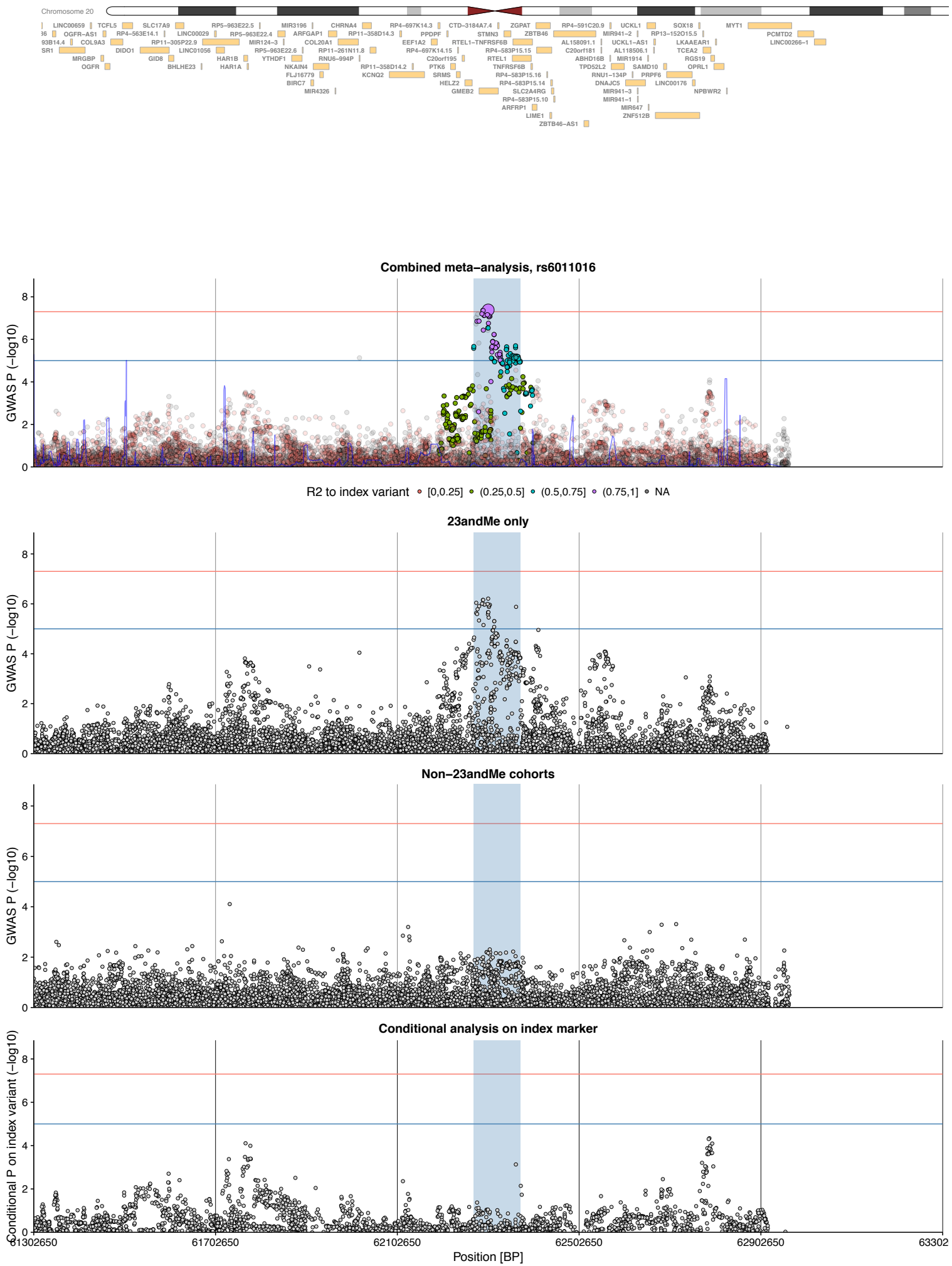

Chromosome 12
Combined meta−analysis, rs35350651
GWAS P (−log10)
R2 to index variant [0,0.25] (0.25,0.5] (0.5,0.75] (0.75,1] NA
23andMe only
Non−23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (−log10)
109907431
110707431
111507431
112307431
113107431
Position [BP]

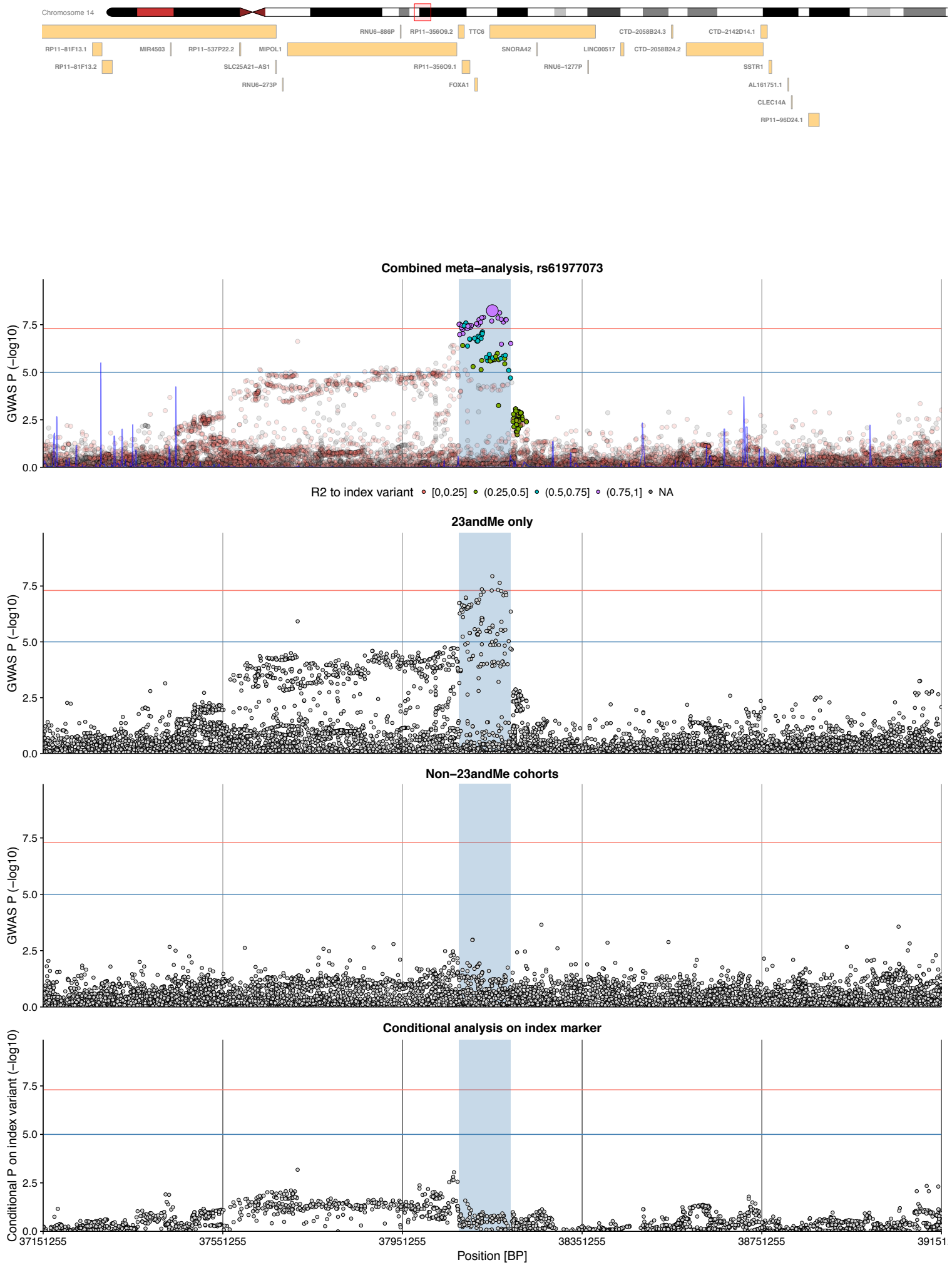

Chromosome 10
RP11−190J1.3
NPM3
Y_RNA
SNORD112
ELOVL3
NFKB2
RN7SL21P
TRIM8
WBP1L
CNNM2
RPEL1
MIR3158−1
KCNIP2−AS1
HPS6
NOLC1
GBF1
ACTR1A
RP11−47A8.5
RNU6−1231P
NT5C2
RNU11−3P
RNU6−1165P
MGEA5
LDB1
AL160011.1
RPARP−AS1
RNU6−43P
ARL3
CYP17A1
PCGF6
POLL
FGF8
PPRC1
PITX3
CUEDC2
SUFU
SFXN2
RNU6−372P
INA
DPCD
KCNIP2
FBXL15
CYP17A1−AS1
FBXW4
C10orf76
RP11−18I14.11
BORCS7−ASMT
TAF5
MIR146B
BORCS7
USMG5
PSD
RP11−724N1.1
PDCD7
C10orf95
AS3MT
TMEM180
Combined meta−analysis, rs35597970
GWAS P (−log10)
R2 to index variant
[0,0.25]
(0.25,0.5]
(0.5,0.75]
(0.75,1]
NA
23andMe only
Non−23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (−log10)
103229057
103629057
104029057
104429057
104829057
Position [BP]

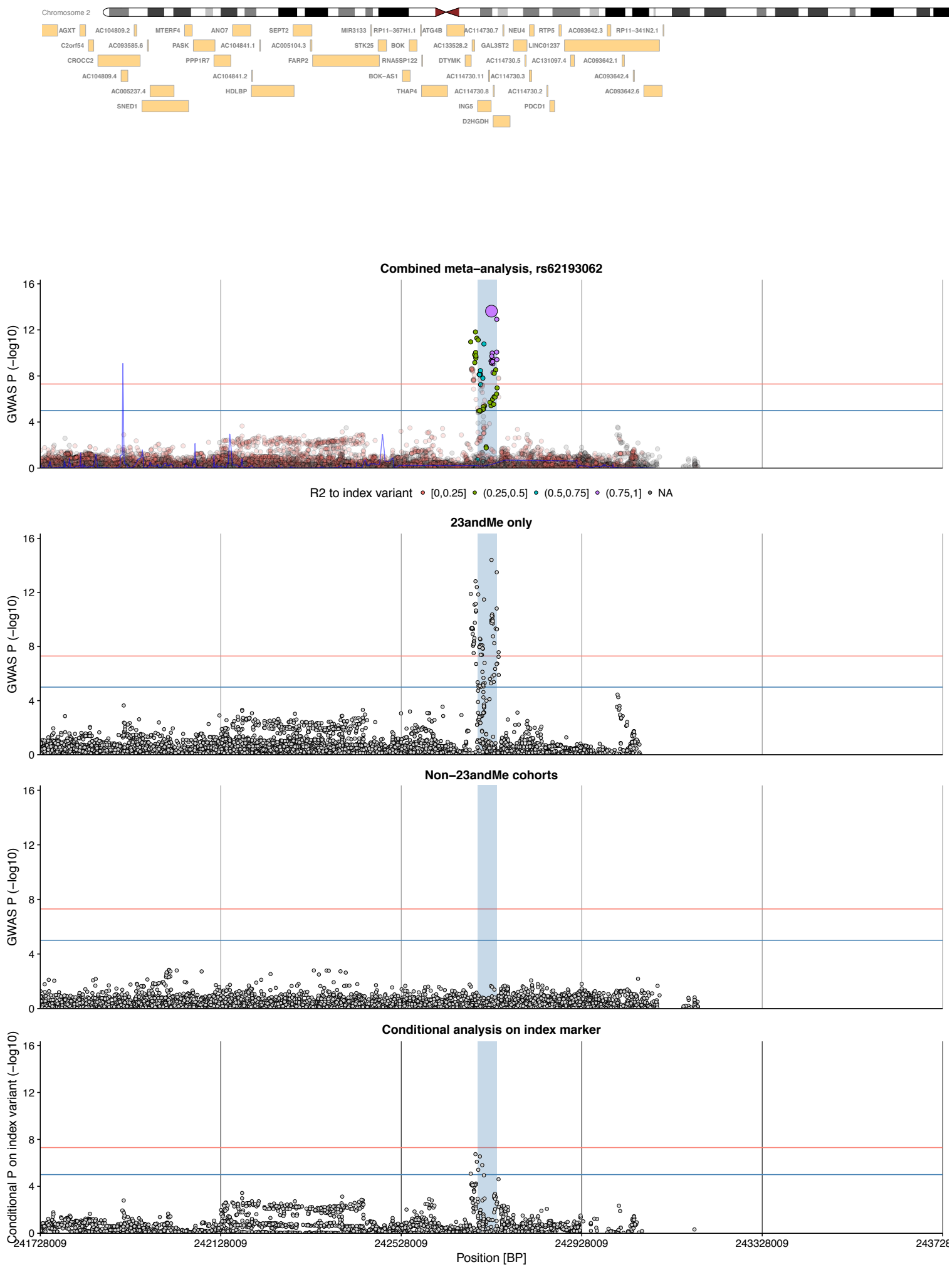

Chromosome 20
PARD6B
ADNP-AS1
RP4-811M8.1
AL079339.1
ATP9A
RNU6-347P
ZFP64
RP4-583K8.1
BCAS4
KCNG1
AL035457.1
NFATC2
SALL4
RN7SL603P
LINC01524
AL133228.1
DPM1
MIR3194
LINC01429
RP5-1022
ADNP
RNU7-6P
AL034553.1
RP5-955M13.4
MOCS3
RP4-530I15.6
Combined meta-analysis, rs3787184
GWAS P (-log10)
R2 to index variant
[0,0.25]
(0.25,0.5]
(0.75,1]
NA
23andMe only
Non-23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (-log10)
49157837
49557837
49957837
50357837
50757837
51157
Position [BP]

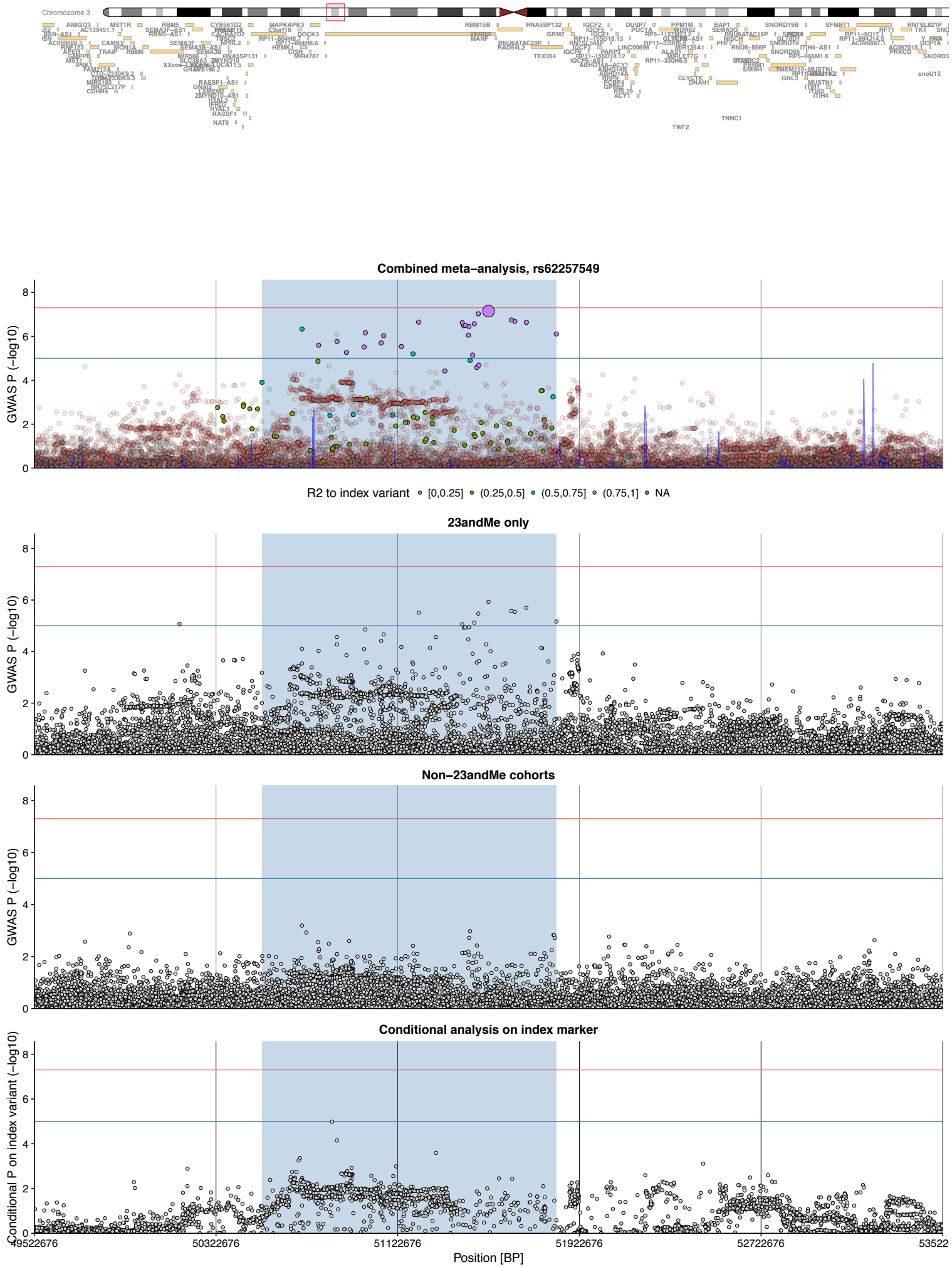

Chromosome 4
PTTG2
AC098680.1
RP11−83C7.3
LINC01259
KLF3
TLR1
TMEM156
WDR19
MIR5591
UGDH
UBE2K
TBC1D1
RP11−600L4.1
LINC01258
RNA5SP158
TLR6
KLHL5
RNU6−32P
KLB
SMIM14
RP11−83C7.1
RP11−213G21.2
TLR10
MIR574
RP11−360F5.1
RFC1
RPL9
RP11−539G18.3
RP11−617D20.2
FAM114A1
RP11−360F5.3
RNU6−887P
UGDH−AS1
KLF3−AS1
Y_RNA
LIAS
RNU7−11P
Combined meta−analysis, rs5743618
GWAS P (−log10)
R2 to index variant
(0.75,1]
NA
23andMe only
Non−23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (−log10)
37798648
38198648
38598648
38998648
39398648
39798
Position [BP]

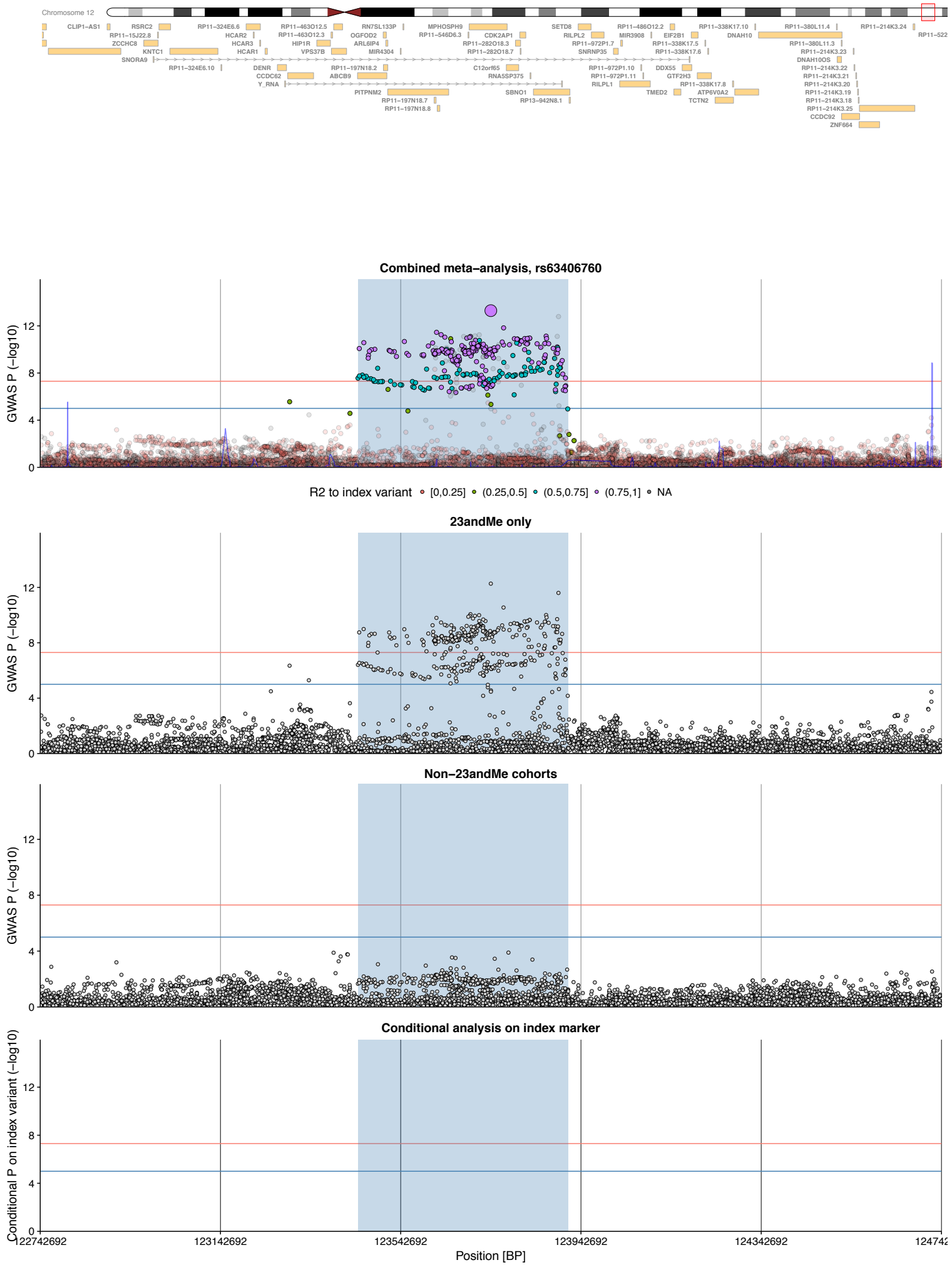

Chromosome 20
RP11−80K6.2
TSHZ2
RNU7−14P
AC006076.1
AC005220.3
MIR4756
PFDN4
DOK5
AL050316.1
RP4−678D15.1
BCAS1
RN7SKP184
RP4−669H2.1
Y_RNA
CYP24A1
RP11−15M15.1
RP5−823G15.5
RP11−15M15.2
AL354993.1
RP4−724E16.2
ZNF217
AC005808.3
Combined meta−analysis, rs58543493
GWAS P (−log10)
R2 to index variant
(0.75,1]
NA
23andMe only
Non−23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (−log10)
51207615
51607615
52007615
52407615
52807615
53207
Position [BP]

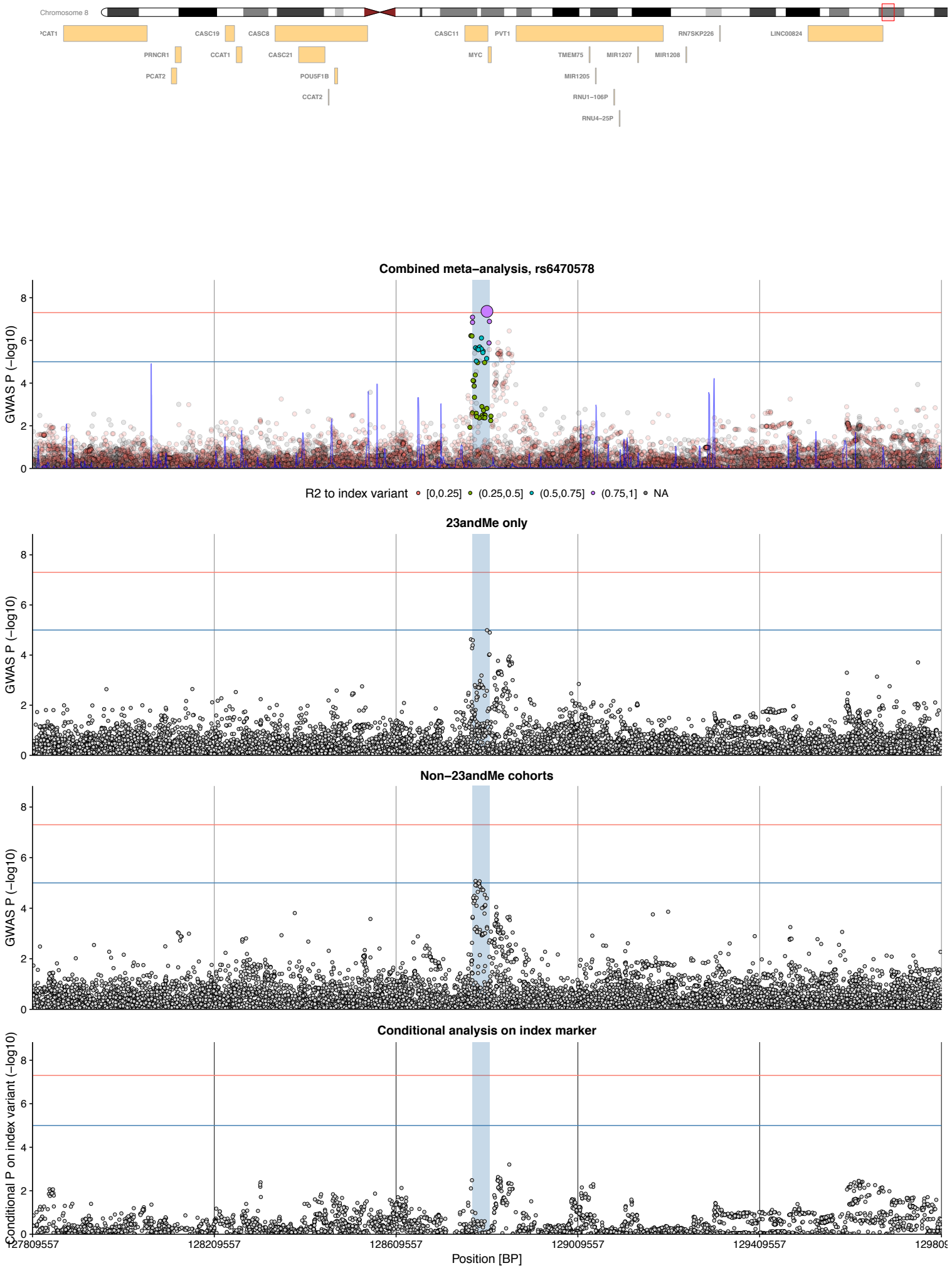

Chromosome 20
LINC00659 TCFL5 SLC17A9 RP5−963E22.5 MIR3196 CHRNA4 RP4−697K14.3 CTD−3184A7.4 ZGPAT RP4−591C20.9 UCKL1 SOX18 MYT1
OGFR−AS1 RP4−563E14.1 LINC00029 RP5−963E22.4 ARFGAP1 RP11−358D14.3 PPDPF STMN3 ZBTB46 MIR941−2 RP13−152O15.5 PCMTD2
93B14.4 COL9A3 RP11−305P22.9 MIR124−3 COL20A1 EEF1A2 RTEL1−TNFRSF6B AL158091.1 UCKL1−AS1 LKAAEAR1 LINC00266−1
SR1 DIDO1 LINC01056 RP5−963E22.6 RP11−261N11.8 RP4−697K14.15 RP4−583P15.15 C20orf181 AL118506.1 TCEA2
MRGBP GID8 HAR1B YTHDF1 RNU6−994P C20orf195 RTEL1 ABHD16B MIR1914 RGS19
OGFR BHLHE23 HAR1A NKAIN4 RP11−358D14.2 PTK6 TNFRSF6B TPD52L2 SAMD10 OPRL1
FLJ16779 KCNQ2 SRMS RP4−583P15.16 RNU1−134P PRPF6
BIRC7 HELZ2 RP4−583P15.14 DNAJC5 LINC00176
MIR4326 GMEB2 SLC2A4RG MIR941−3 NPBWR2
RP4−583P15.10 MIR941−1
ARFRP1 MIR647
LIME1 ZNF512B
ZBTB46−AS1
Combined meta−analysis, rs6011016
GWAS P (−log10)
R2 to index variant [0,0.25] (0.25,0.5] (0.5,0.75] (0.75,1] NA
23andMe only
GWAS P (−log10)
Non−23andMe cohorts
GWAS P (−log10)
Conditional analysis on index marker
Conditional P on index variant (−log10)
61302650
61702650
62102650
62502650
62902650
63302
Position [BP]

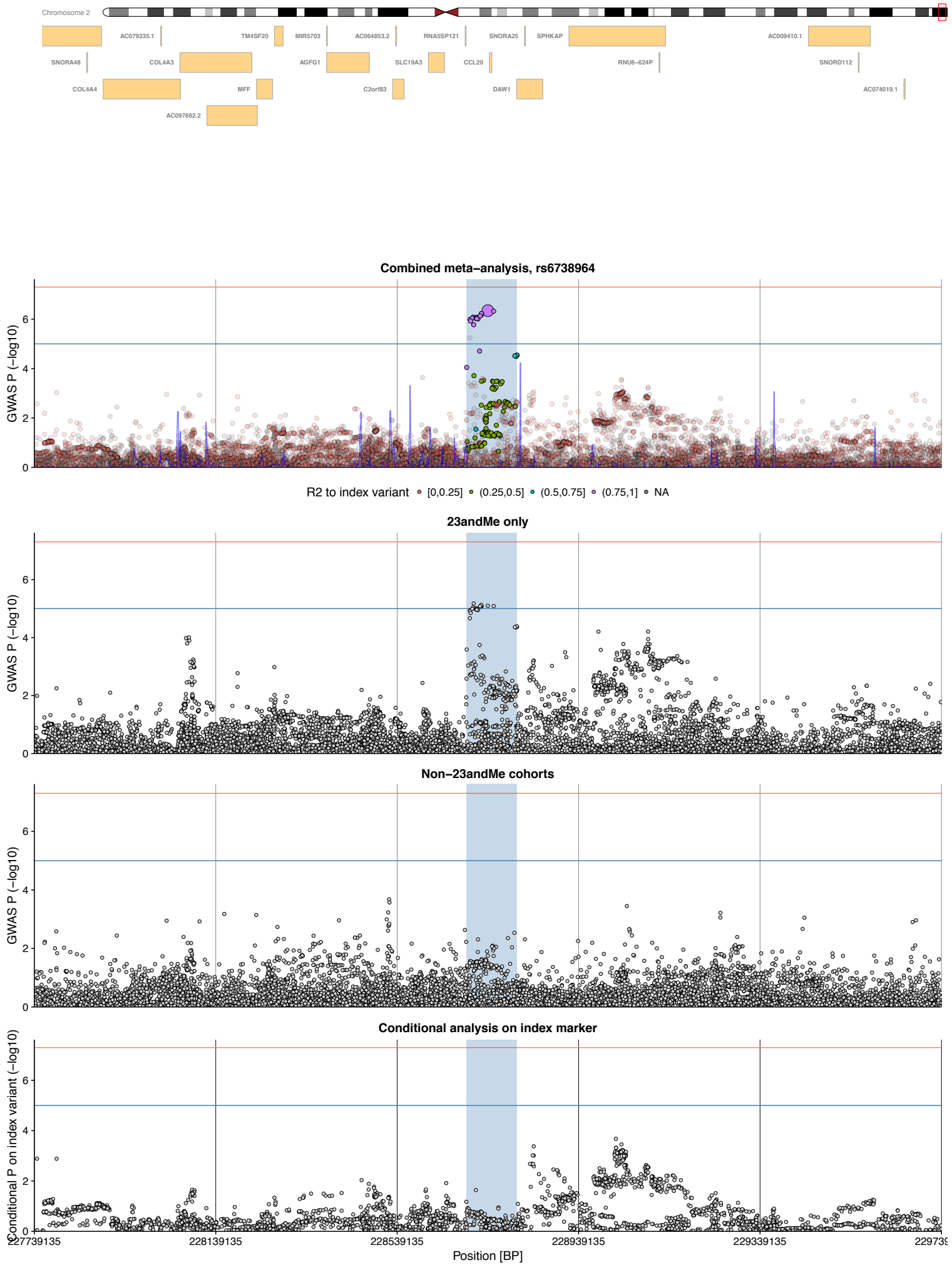

Chromosome 14
RNU6−886P
RP11−356O9.2
TTC6
CTD−2058B24.3
CTD−2142D14.1
RP11−81F13.1
MIR4503
RP11−537P22.2
MIPOL1
SNORA42
LINC00517
CTD−2058B24.2
RP11−81F13.2
SLC25A21−AS1
RP11−356O9.1
RNU6−1277P
SSTR1
RNU6−273P
FOXA1
AL161751.1
CLEC14A
RP11−96D24.1
Combined meta−analysis, rs61977073
GWAS P (−log10)
R2 to index variant
[0,0.25]
(0.25,0.5]
(0.5,0.75]
(0.75,1]
NA
23andMe only
Non−23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (−log10)
37151255
37551255
37951255
38351255
38751255
39151
Position [BP]

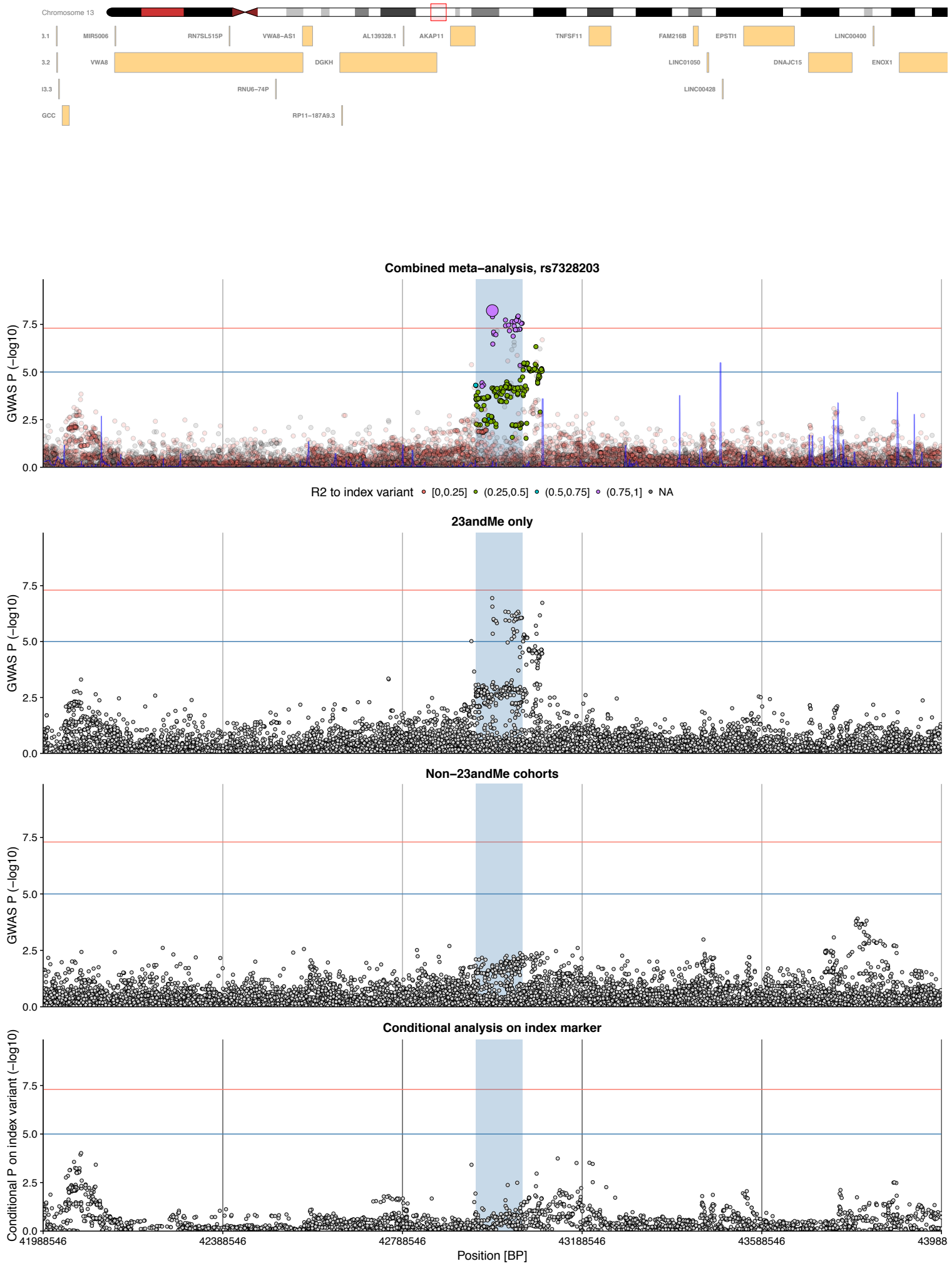

Chromosome 2
AGXT
AC104809.2
MTERF4
ANO7
SEPT2
MIR3133
RP11−367H1.1
ATG4B
AC114730.7
NEU4
RTP5
AC093642.3
RP11−341N2.1
C2orf54
AC093585.6
PASK
AC104841.1
AC005104.3
STK25
BOK
AC133528.2
GAL3ST2
LINC01237
CROCC2
PPP1R7
FARP2
RNA5SP122
DTYMK
AC114730.5
AC131097.4
AC093642.1
AC104809.4
AC104841.2
BOK−AS1
AC114730.11
AC114730.3
AC093642.4
AC005237.4
HDLBP
THAP4
AC114730.8
AC114730.2
AC093642.6
SNED1
ING5
PDCD1
D2HGDH
Combined meta−analysis, rs62193062
GWAS P (−log10)
R2 to index variant
[0,0.25]
(0.25,0.5]
(0.5,0.75]
(0.75,1]
NA
23andMe only
Non−23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (−log10)
241728009
242128009
242528009
242928009
243328009
Position [BP]

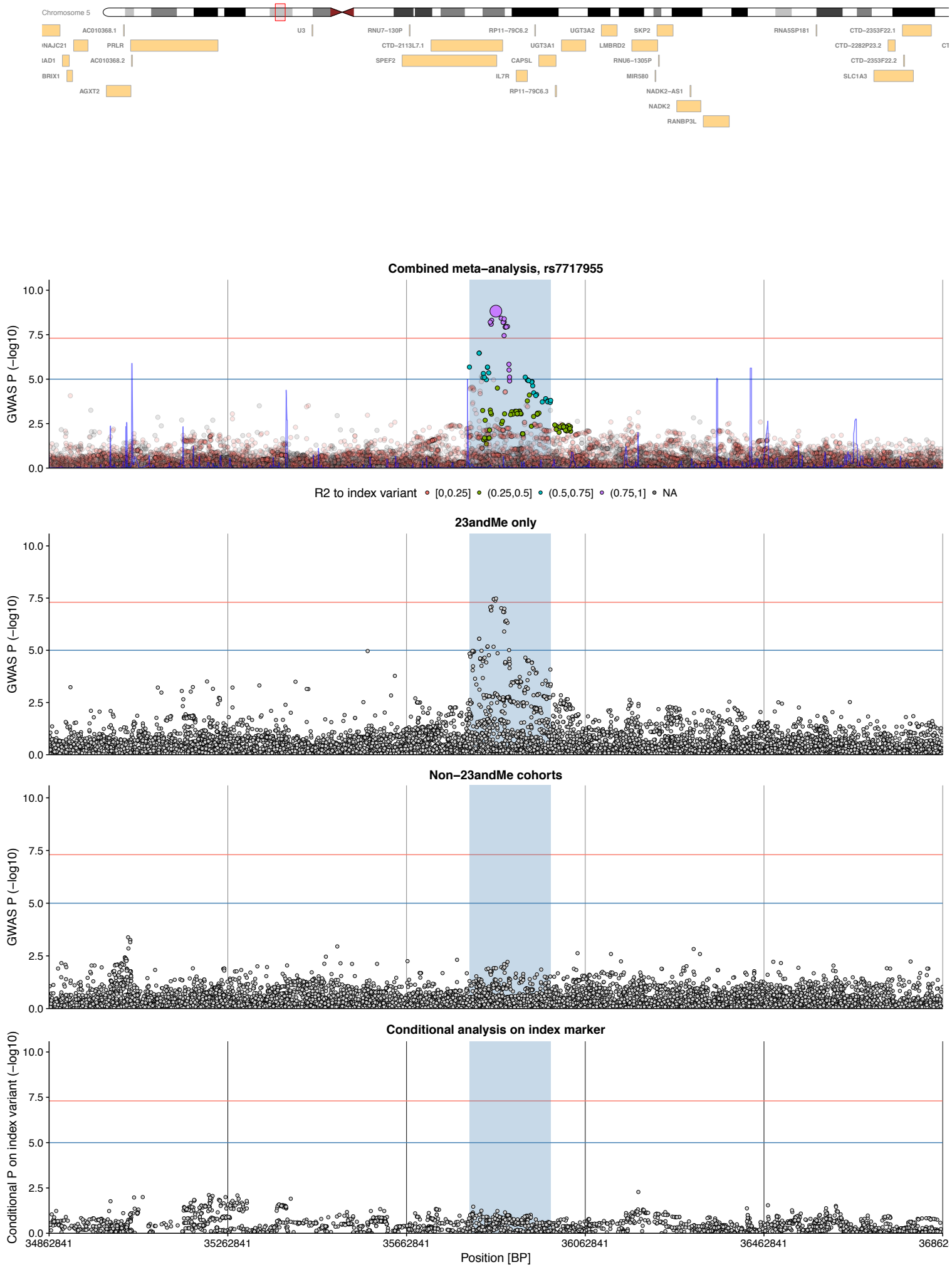

Chromosome 3
Combined meta−analysis, rs62257549
GWAS P (−log10)
R2 to index variant [0,0.25] (0.25,0.5] (0.5,0.75] (0.75,1] NA
23andMe only
Non−23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (−log10)
49522676
50322676
51122676
51922676
52722676
53522
Position [BP]

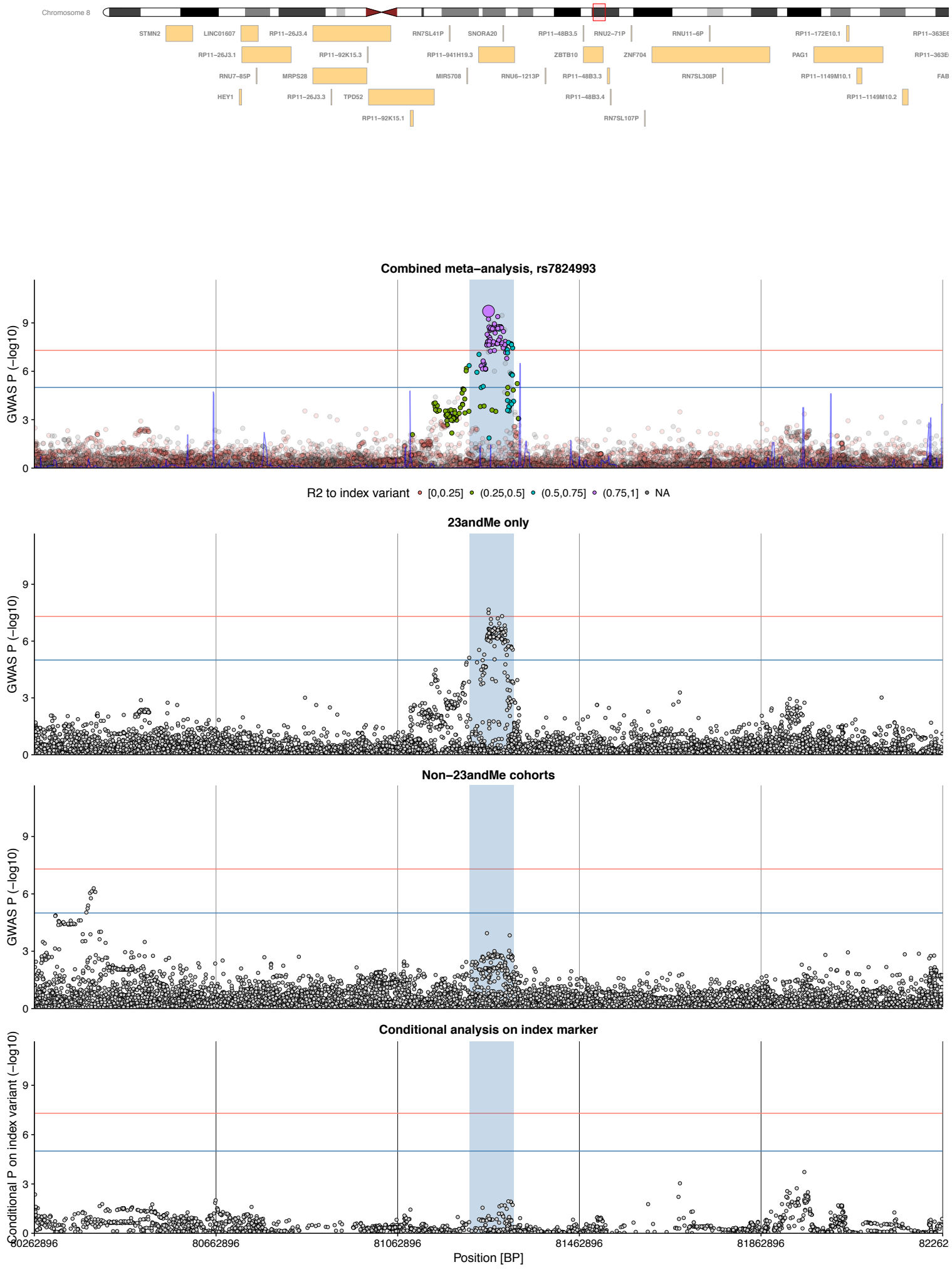

Chromosome 12
Combined meta−analysis, rs63406760
GWAS P (−log10)
R2 to index variant [0,0.25] (0.25,0.5] (0.5,0.75] (0.75,1] NA
23andMe only
Non−23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (−log10)
122742692
123142692
123542692
123942692
124342692
Position [BP]

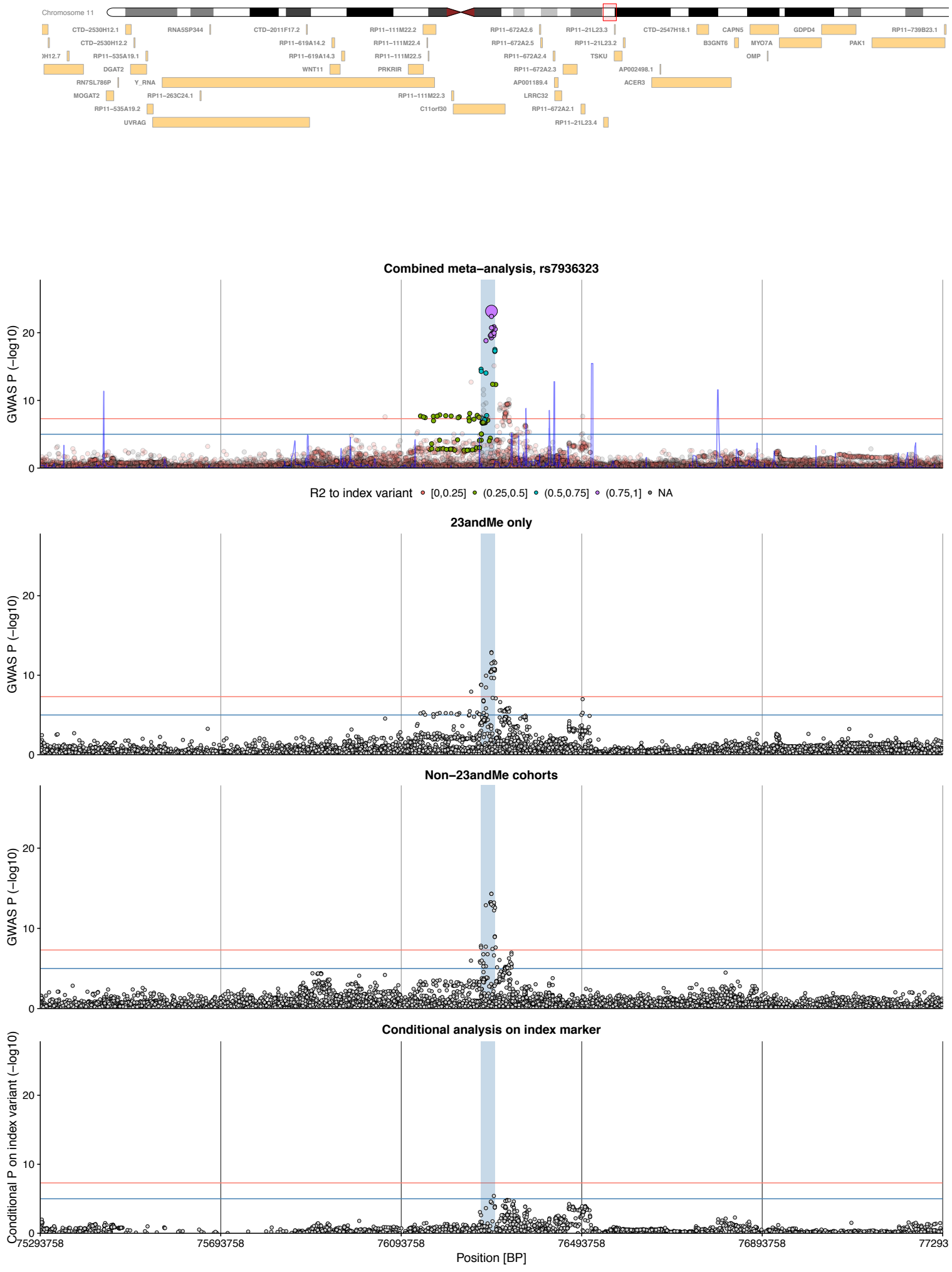

Chromosome 8
CASC19
CASC8
CASC11
PVT1
RN7SKP226
LINC00824
PRNCR1
CCAT1
CASC21
MYC
TMEM75
MIR1207
MIR1208
PCAT2
POU5F1B
MIR1205
CCAT2
RNU1–106P
RNU4–25P
Combined meta–analysis, rs6470578
GWAS P (–log10)
R2 to index variant
[0,0.25]
(0.25,0.5]
(0.5,0.75]
(0.75,1]
NA
23andMe only
Non–23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (–log10)
127809557
128209557
128609557
129009557
129409557
Position [BP]

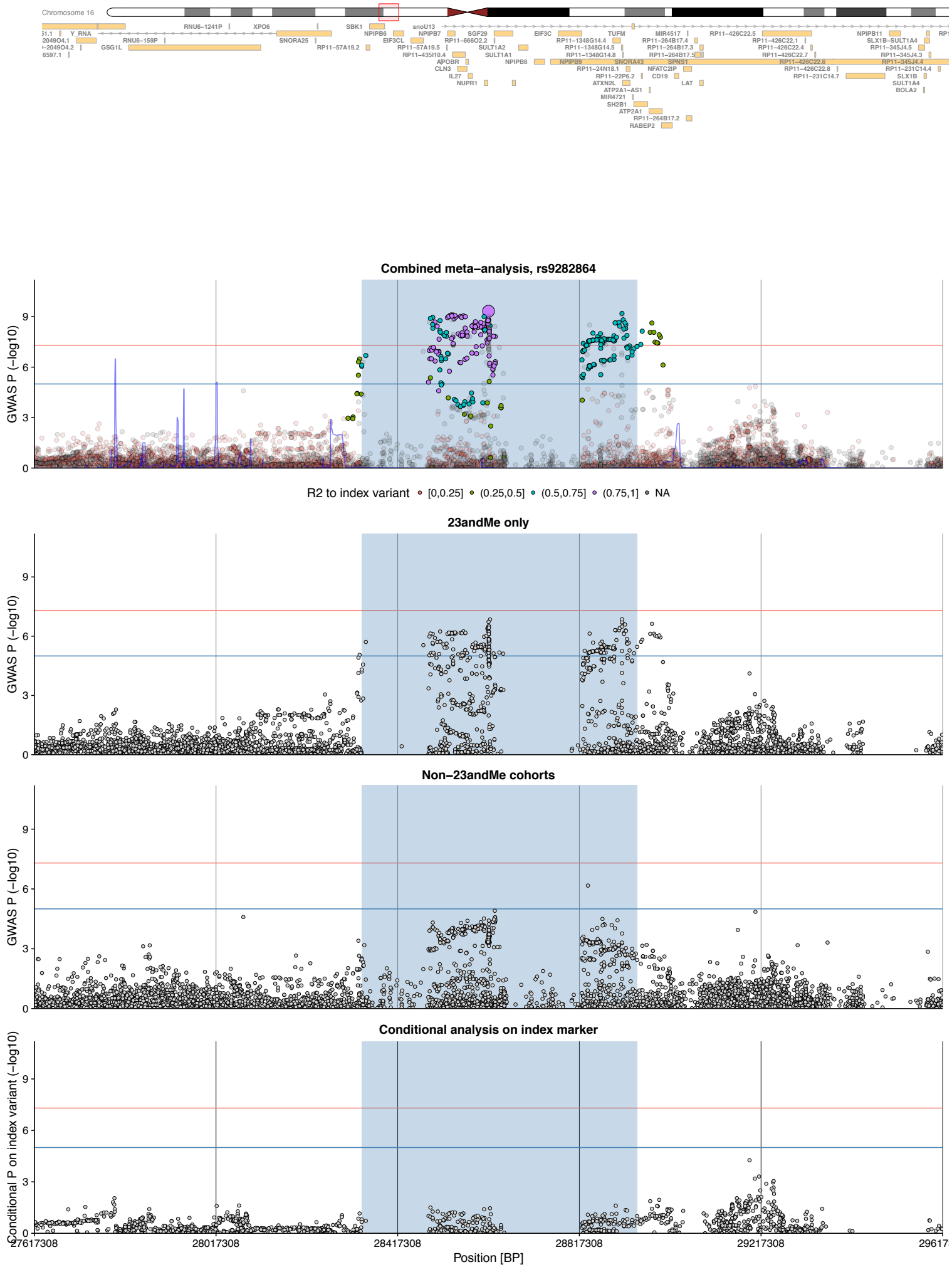

Chromosome 2
AC079235.1
TM4SF20
MIR5703
AC064853.2
RNA5SP121
SNORA25
SPHKAP
AC009410.1
SNORA48
COL4A3
AGFG1
SLC19A3
CCL20
RNU6−624P
SNORD112
COL4A4
MFF
C2orf83
DAW1
AC074019.1
AC097662.2
Combined meta−analysis, rs6738964
GWAS P (−log10)
R2 to index variant
[0,0.25]
(0.25,0.5]
(0.5,0.75]
(0.75,1]
NA
23andMe only
Non−23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (−log10)
227739135
228139135
228539135
228939135
229339135
Position [BP]

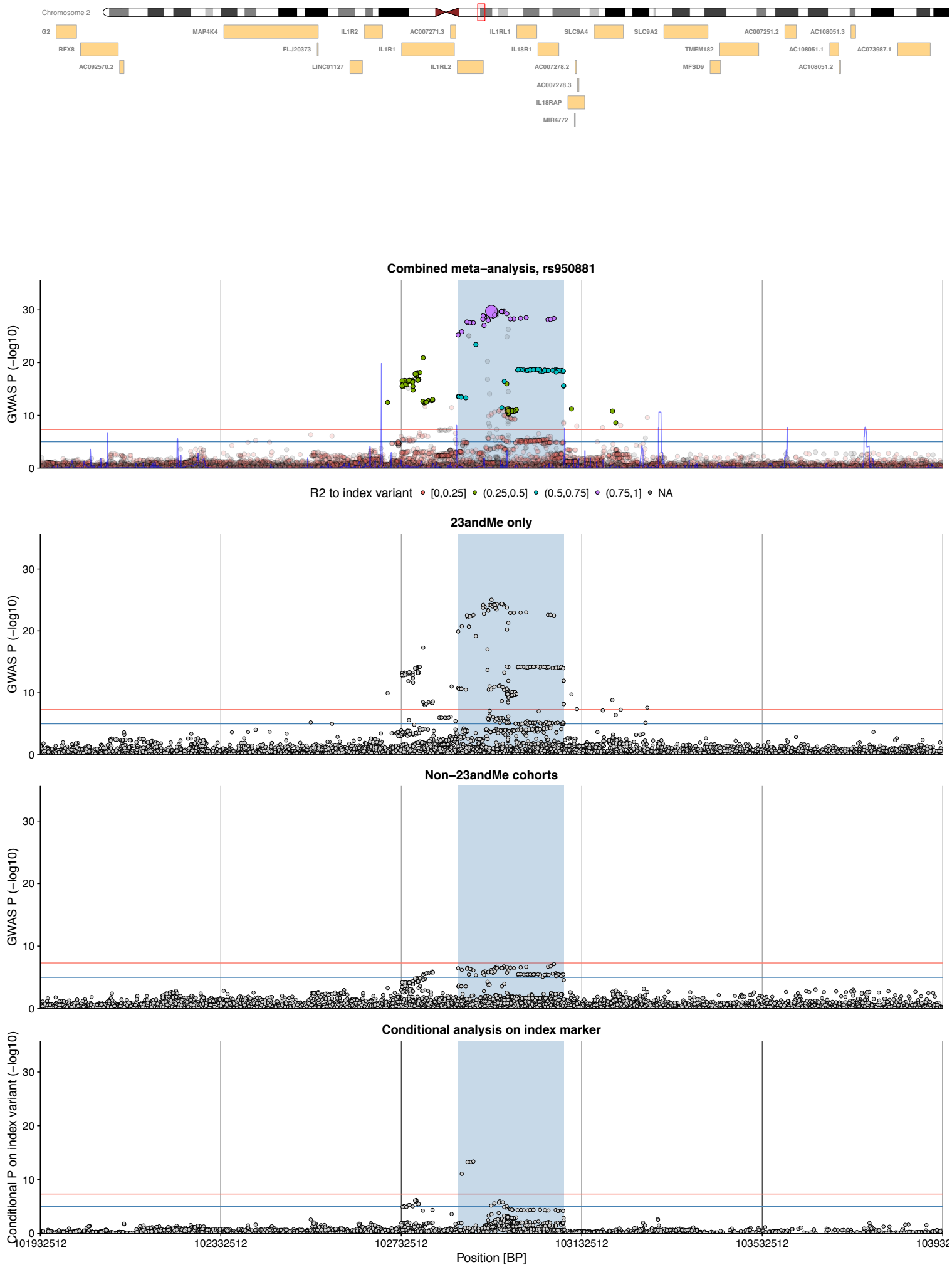

Chromosome 13
MIR5006
RN7SL515P
VWA8-AS1
AL139328.1
AKAP11
TNFSF11
FAM216B
EPSTI1
LINC00400
VWA8
DGKH
LINC01050
DNAJC15
ENOX1
RNU6-74P
LINC00428
RP11-187A9.3
Combined meta-analysis, rs7328203
GWAS P (-log10)
R2 to index variant [0,0.25] (0.25,0.5] (0.5,0.75] (0.75,1] NA
23andMe only
Non-23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (-log10)
41988546
42388546
42788546
43188546
43588546
Position [BP]

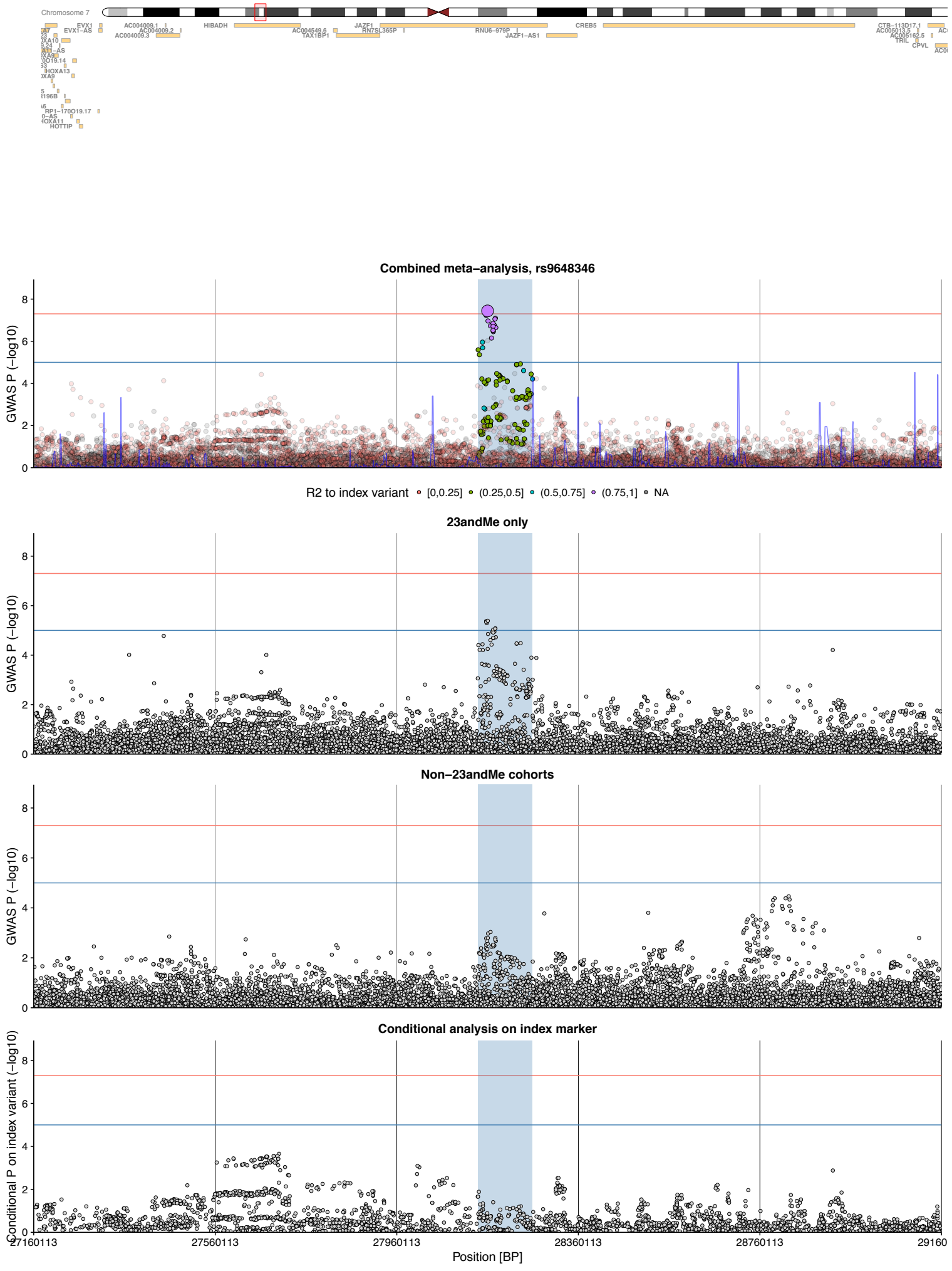

Chromosome 5
AC010368.1
U3
RNU7−130P
RP11−79C6.2
UGT3A2
SKP2
RNA5SP181
CTD−2353F22.1
PRLR
CTD−2113L7.1
UGT3A1
LMBRD2
CTD−2282P23.2
AC010368.2
SPEF2
CAPSL
RNU6−1305P
CTD−2353F22.2
BRIX1
IL7R
MIR580
SLC1A3
AGXT2
RP11−79C6.3
NADK2−AS1
NADK2
RANBP3L
Combined meta−analysis, rs7717955
GWAS P (−log10)
10.0
7.5
5.0
2.5
0.0
R2 to index variant
[0,0.25]
(0.25,0.5]
(0.5,0.75]
(0.75,1]
NA
23andMe only
Non−23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (−log10)
34862841
35262841
35662841
36062841
36462841
36862
Position [BP]

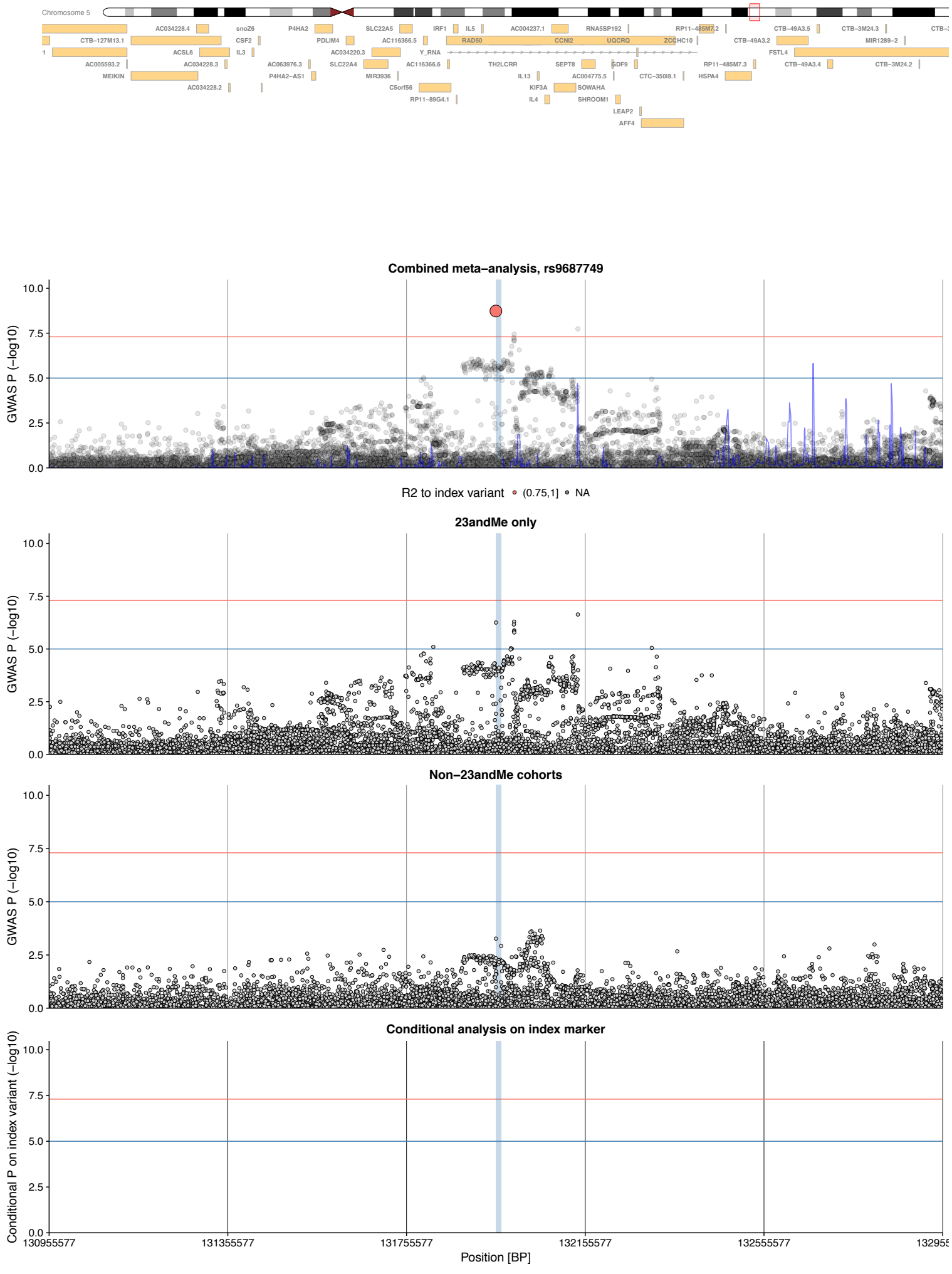

Chromosome 8
STMN2
LINC01607
RP11−26J3.4
RN7SL41P
SNORA20
RP11−48B3.5
RNU2−71P
RNU11−6P
RP11−172E10.1
RP11−26J3.1
RP11−92K15.3
RP11−941H19.3
ZBTB10
ZNF704
PAG1
RNU7−85P
MRPS28
MIR5708
RNU6−1213P
RP11−48B3.3
RN7SL308P
RP11−1149M10.1
HEY1
RP11−26J3.3
TPD52
RP11−48B3.4
RP11−1149M10.2
RP11−92K15.1
RN7SL107P
Combined meta−analysis, rs7824993
GWAS P (−log10)
R2 to index variant
[0,0.25]
(0.25,0.5]
(0.5,0.75]
(0.75,1]
NA
23andMe only
Non−23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (−log10)
80262896
80662896
81062896
81462896
81862896
82262
Position [BP]

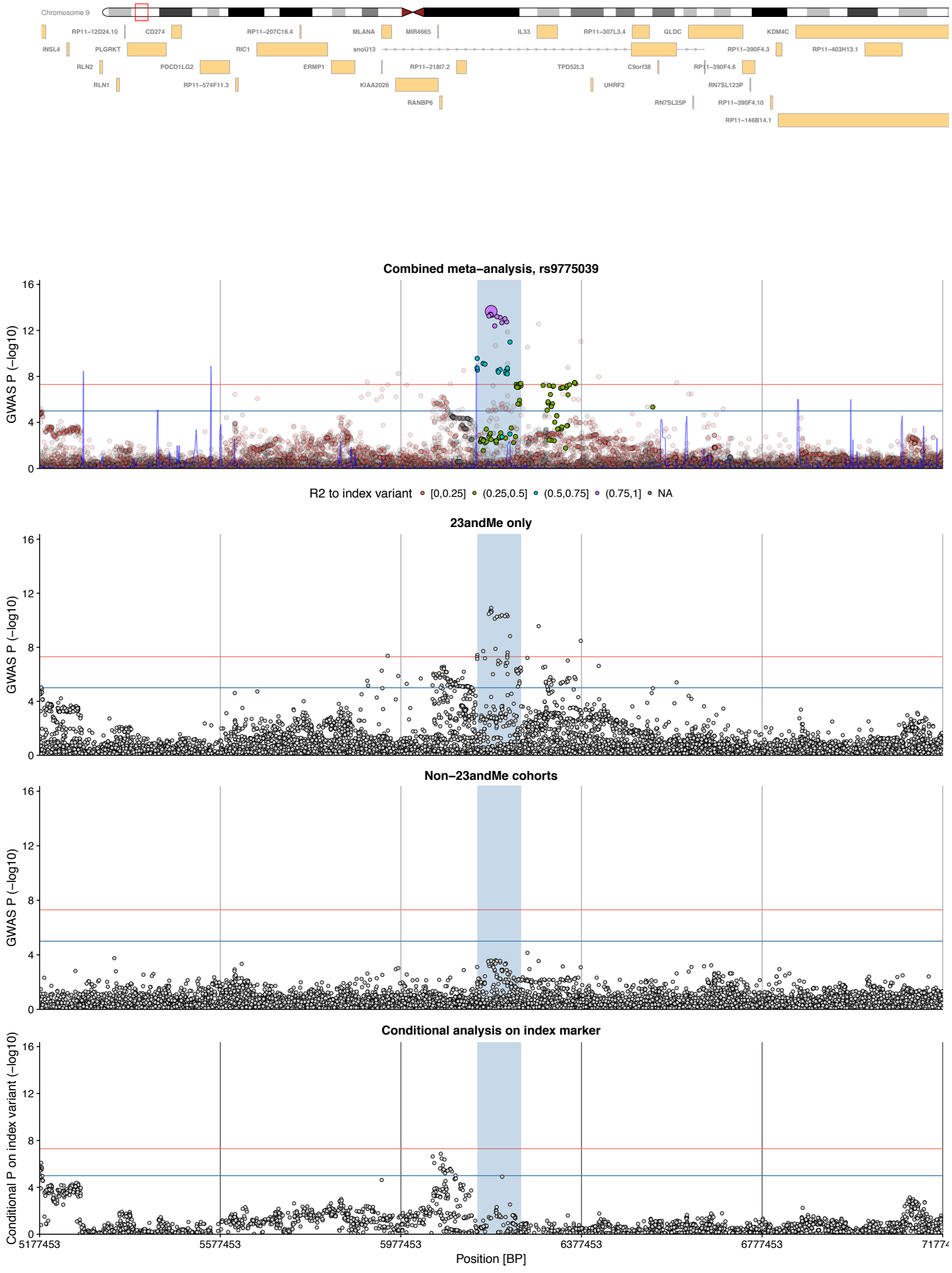

Chromosome 11
CTD−2530H12.1
RNA5SP344
CTD−2011F17.2
RP11−111M22.2
RP11−672A2.6
RP11−21L23.3
CTD−2547H18.1
CAPN5
GDPD4
RP11−739B23.1
CTD−2530H12.2
RP11−619A14.2
RP11−111M22.4
RP11−672A2.5
RP11−21L23.2
B3GNT6
MYO7A
PAK1
RP11−535A19.1
RP11−619A14.3
RP11−111M22.5
RP11−672A2.4
TSKU
OMP
DGAT2
WNT11
PRKRIR
RP11−672A2.3
AP002498.1
RN7SL786P
Y_RNA
AP001189.4
ACER3
MOGAT2
RP11−263C24.1
RP11−111M22.3
LRRC32
RP11−535A19.2
C11orf30
RP11−672A2.1
UVRAG
RP11−21L23.4
Combined meta−analysis, rs7936323
GWAS P (−log10)
R2 to index variant
[0,0.25]
(0.25,0.5]
(0.5,0.75]
(0.75,1]
NA
23andMe only
Non−23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (−log10)
75293758
75693758
76093758
76493758
76893758
77293
Position [BP]


Chromosome 16
Combined meta−analysis, rs9282864
GWAS P (−log10)
R2 to index variant [0,0.25] (0.25,0.5] (0.5,0.75] (0.75,1] NA
23andMe only
Non−23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (−log10)
27617308
28017308
28417308
28817308
29217308
Position [BP]


Chromosome 2
G2
RFX8
AC092570.2
MAP4K4
FLJ20373
LINC01127
IL1R2
IL1R1
IL1RL2
AC007271.3
AC007278.2
AC007278.3
IL18RAP
MIR4772
IL1RL1
IL18R1
SLC9A4
SLC9A2
TMEM182
MFSD9
AC007251.2
AC108051.3
AC108051.1
AC108051.2
AC073987.1
Combined meta−analysis, rs950881
GWAS P (−log10)
R2 to index variant
[0,0.25]
(0.25,0.5]
(0.5,0.75]
(0.75,1]
NA
23andMe only
Non−23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (−log10)
101932512
102332512
102732512
103132512
103532512
Position [BP]

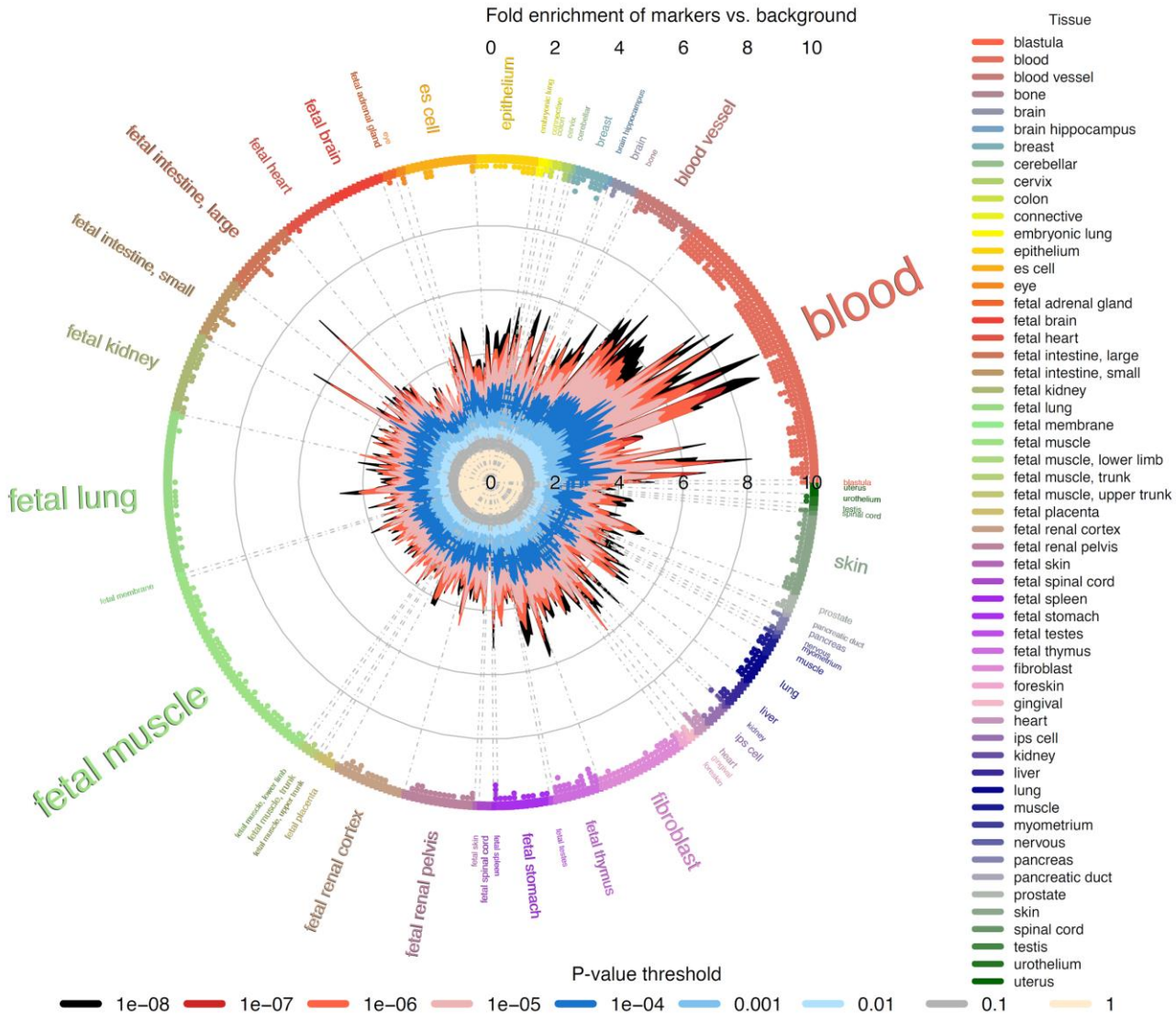

Chromosome 7
EVX1
EVX1−AS
AC004009.1
AC004009.2
AC004009.3
HIBADH
AC004549.6
TAX1BP1
JAZF1
RN7SL365P
RNU6−979P
JAZF1−AS1
CREB5
CTB−113D17.1
AC005013.5
AC005162.5
TRIL
CPVL
HOTTIP
Combined meta−analysis, rs9648346
GWAS P (−log10)
R2 to index variant
[0,0.25]
(0.25,0.5]
(0.5,0.75]
(0.75,1]
NA
23andMe only
Non−23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (−log10)
27160113
27560113
27960113
28360113
28760113
29160
Position [BP]


Chromosome 5
AC034228.4
snoZ6
P4HA2
SLC22A5
IRF1
IL5
AC004237.1
RNA5SP192
RP11−485M7.2
CTB−49A3.5
CTB−3M24.3
CTB−127M13.1
CSF2
PDLIM4
AC116366.5
RAD50
CCNI2
UQCRQ
ZCCHC10
CTB−49A3.2
MIR1289−2
1
ACSL6
IL3
AC034220.3
Y_RNA
FSTL4
AC005593.2
AC034228.3
AC063976.3
SLC22A4
AC116366.6
TH2LCRR
SEPT8
GDF9
RP11−485M7.3
CTB−49A3.4
CTB−3M24.2
MEIKIN
P4HA2−AS1
MIR3936
IL13
AC004775.5
CTC−350I8.1
HSPA4
AC034228.2
C5orf56
KIF3A
SOWAHA
RP11−89G4.1
IL4
SHROOM1
LEAP2
AFF4
Combined meta−analysis, rs9687749
GWAS P (−log10)
10.0
7.5
5.0
2.5
0.0
R2 to index variant
(0.75,1]
NA
23andMe only
Non−23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (−log10)
130955577
131355577
131755577
132155577
132555577
Position [BP]


Chromosome 9
RP11−12D24.10
CD274
RP11−207C16.4
MLANA
MIR4665
IL33
RP11−307L3.4
GLDC
KDM4C
INSL4
PLGRKT
RIC1
snoU13
RP11−390F4.3
RP11−403H13.1
RLN2
PDCD1LG2
ERMP1
RP11−218I7.2
TPD52L3
C9orf38
RP11−390F4.6
RLN1
RP11−574F11.3
KIAA2026
UHRF2
RN7SL123P
RANBP6
RN7SL25P
RP11−390F4.10
RP11−146B14.1
Combined meta−analysis, rs9775039
GWAS P (−log10)
R2 to index variant
[0,0.25]
(0.25,0.5]
(0.5,0.75]
(0.75,1]
NA
23andMe only
Non−23andMe cohorts
Conditional analysis on index marker
Conditional P on index variant (−log10)
5177453
5577453
5977453
6377453
6777453
Position [BP]

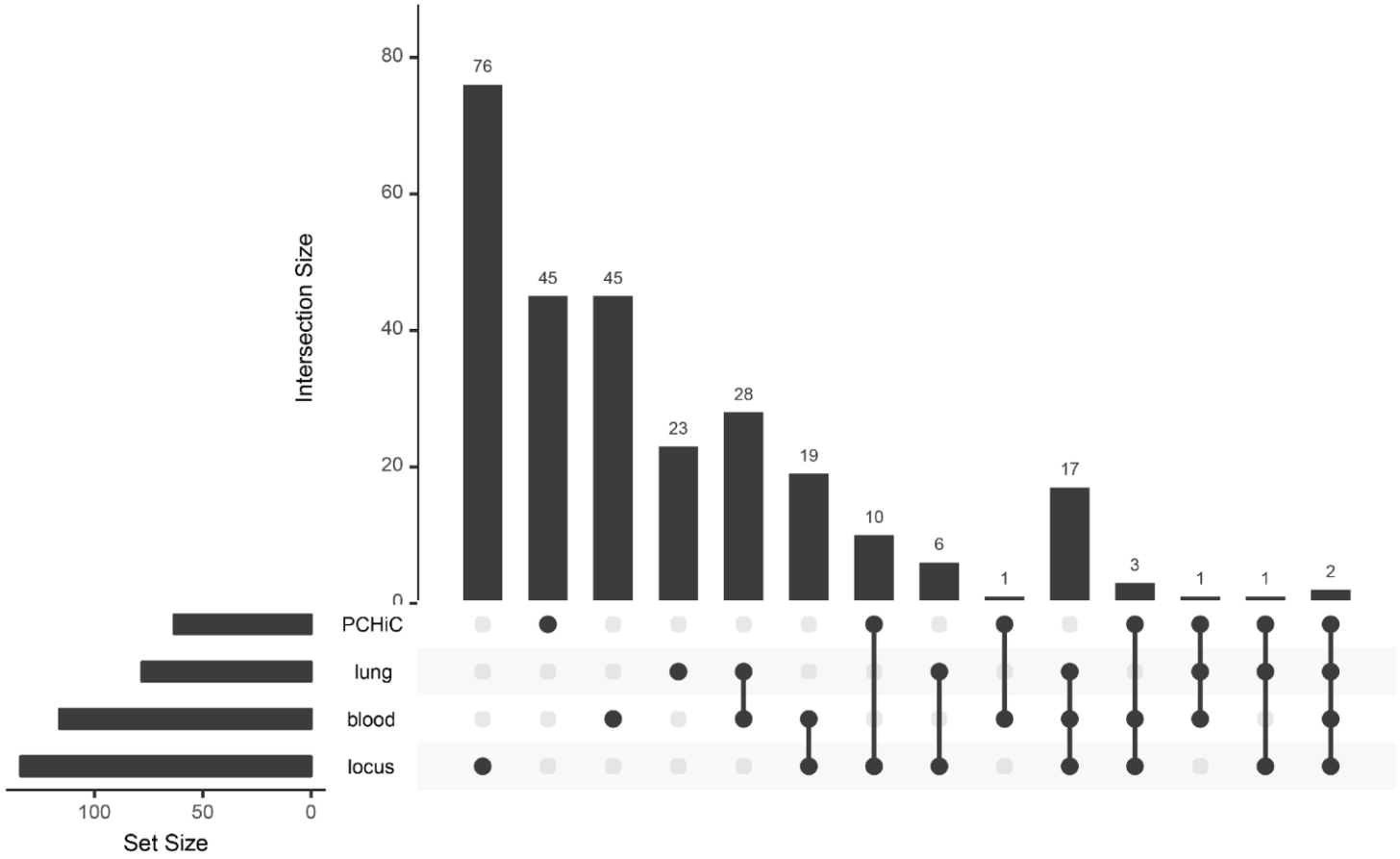
Supplementary Figure 6

Enrichment plot from the GARFIELD regulatory element enrichment pipeline, showing tissue specific enrichment of DNASE hypersensitivity hotspots. Each central layered densitogram color represents enrichment values for increasing marker p-value thresholds (1 through 1e-8). The GARFIELD analysis was run on p-values from genetic marker association of 16,531,985 genetic markers to allergic rhinitis from the discovery phase, including 212,120 individuals.



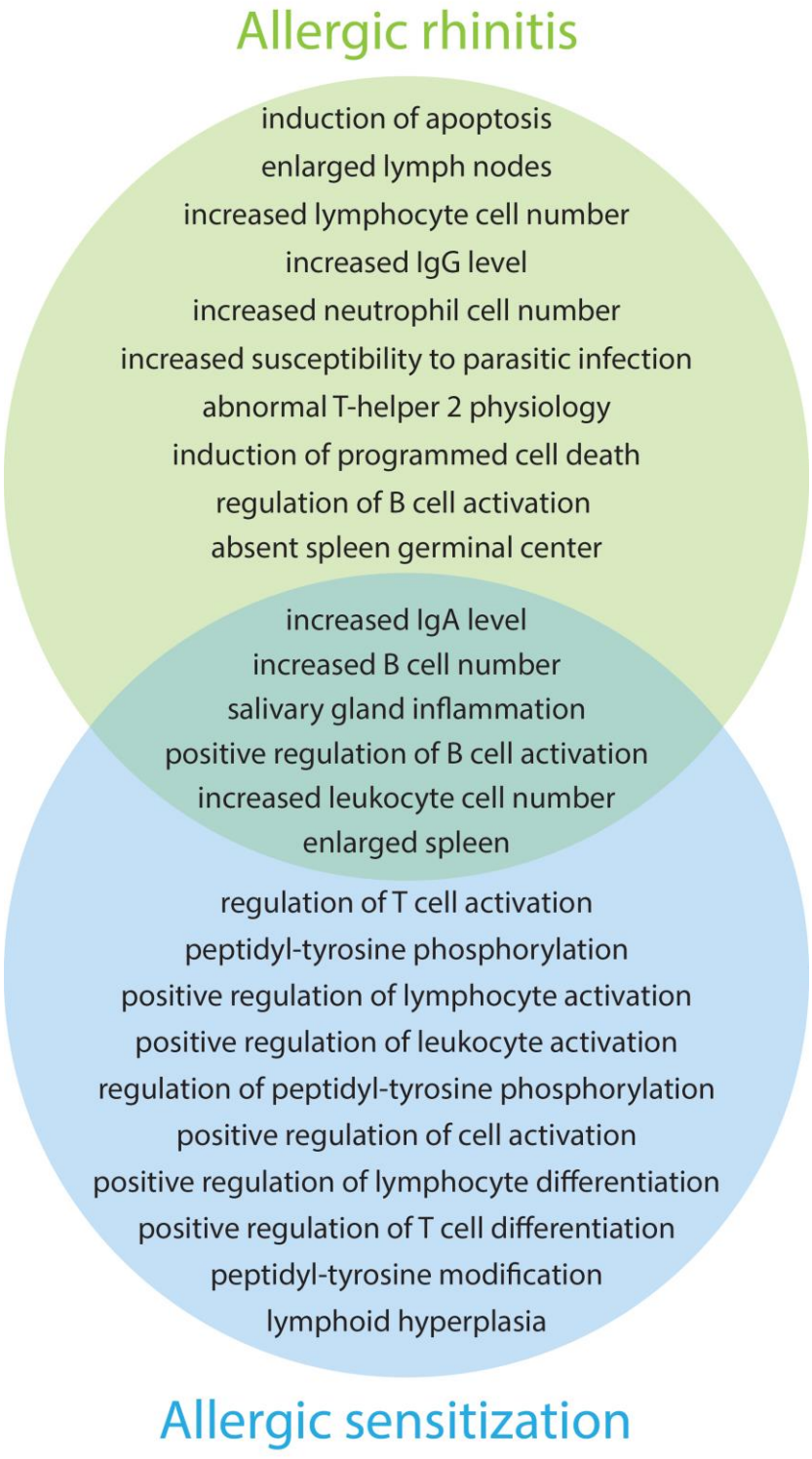
Supplementary Figure 7

"UpSet" set visualisation plot, indicating set intersections between e/meQTL blood, e/meQTL lung, PCHiC, and locus genes.



Supplementary Figure 8

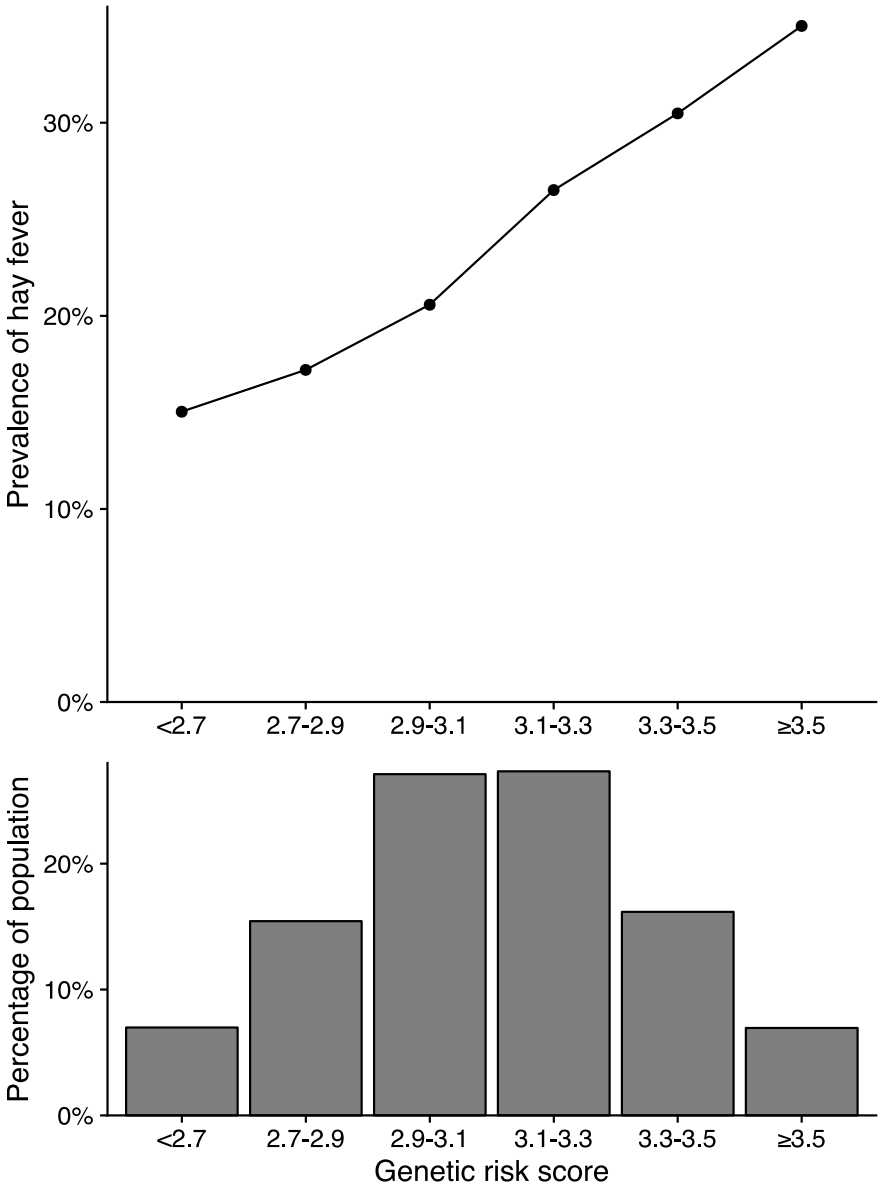
Overlap of enriched gene sets from the allergic rhinitis and allergic sensitization GWAS. All significant overlapping gene sets are shown together with the 10 gene sets with most statistically significant enrichment from each phenotype. Results for all gene sets are shown in Supplementary Tables 21 and 22. Enriched gene sets were calculated from an inverse variance weighted fixed-effect meta-analysis of genetic marker association of 16,531,985 genetic markers to allergic rhinitis from the discovery phase, including 212,120 individuals, and from inverse variance weighted fixed-effect meta-analysis of genetic marker association of 16,531,985 genetic markers to allergic sensitisation, including 24,481 individuals.



Supplementary Figure 9

Relationship between allergic rhinitis genetic risk score and disease prevalence.

Combined impact of risk alleles from the 41 genome-wide significant and replicating loci on prevalence of allergic rhinitis (hay fever) in the population-based B58C study. For each individual, we calculated a genetic risk score by applying per-allele risk estimates from the replication sets to the number of higher-risk alleles at the 41 genome-wide significant and replicating loci (one SNP per locus). The risk score thus represents an index of the number of weighted risk alleles. Along the x axis, individuals in each risk score interval are shown (with the lower bound included and the upper bound excluded in each interval). The prevalence of hay fever in each interval is plotted in the upper panel, and the histogram in the bottom panel shows the percentage of the B58C population in each risk score interval.



Supplementary Figure 10

Regional locus plot of association values from the allergic rhinitis GWAS for marker rs193243426 (N=203,356). The locus has an index marker with p < 1e5-8 (p-value from genetic marker association from the discovery phase), but lacks a credible locus LD structure, and was excluded from the study.