

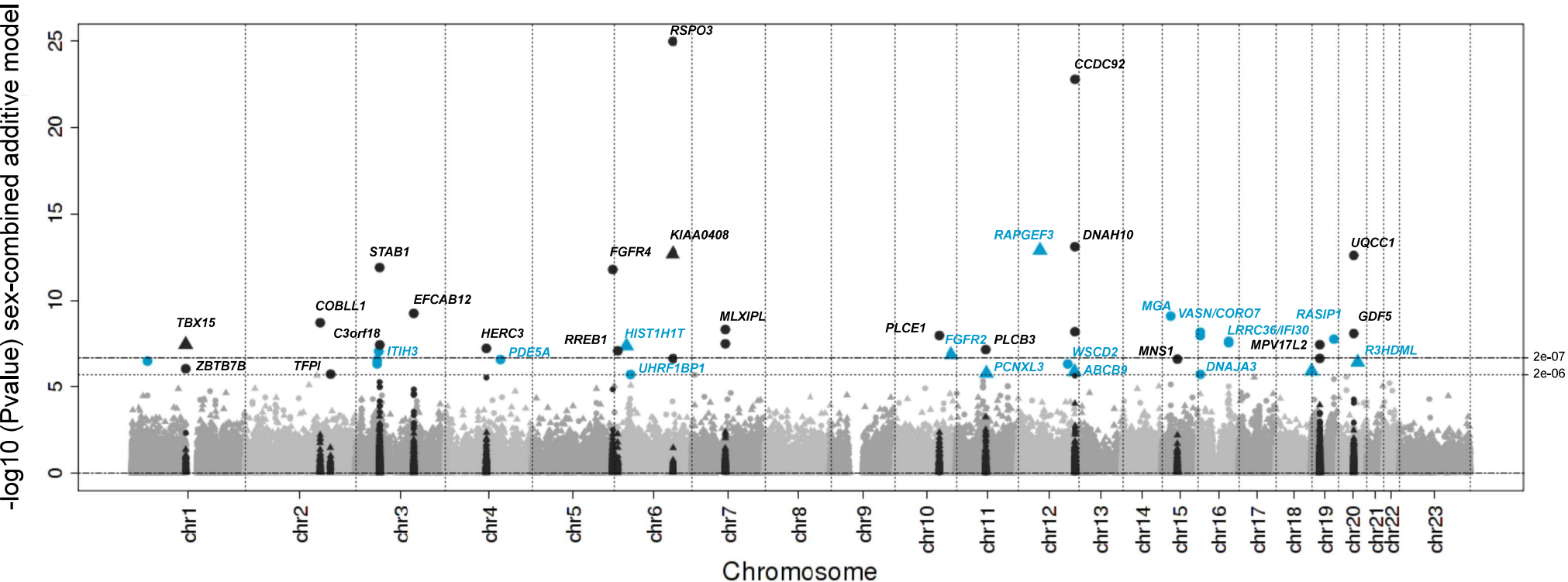
SUPPLEMENTARY ONLINE MATERIAL

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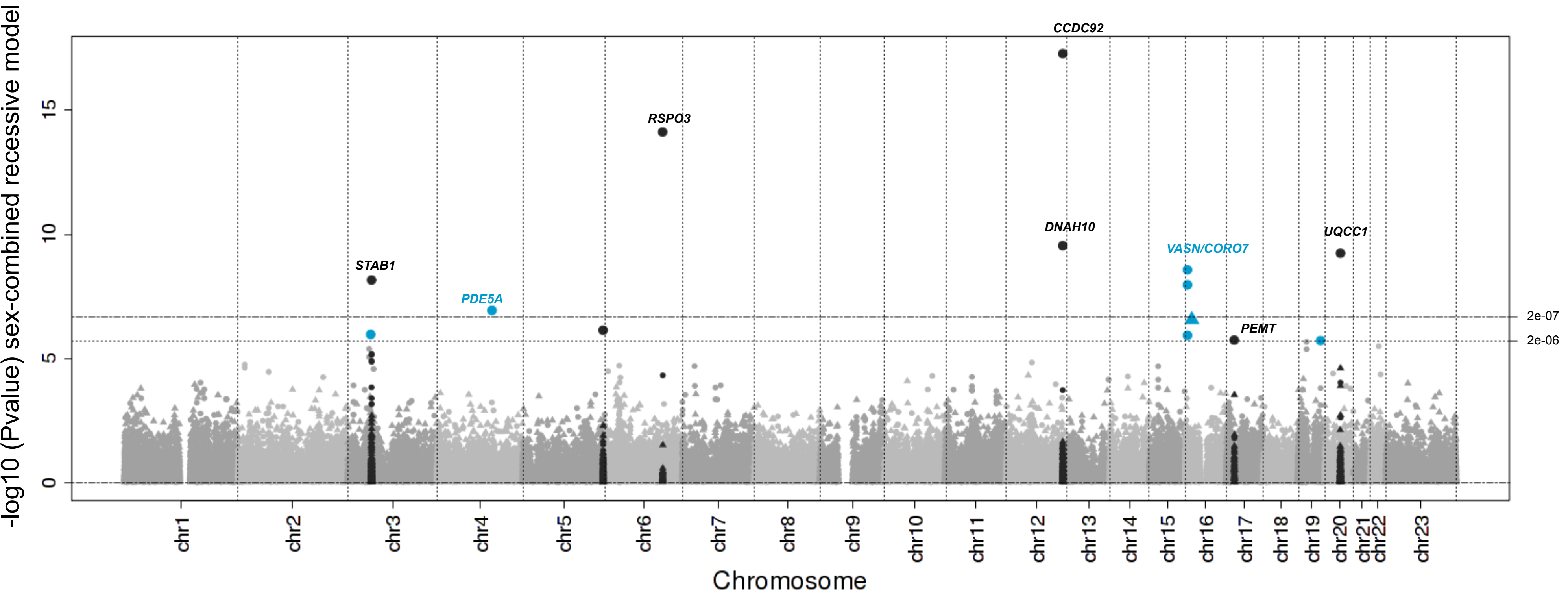
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Supplementary Figure 1. Manhattan plot. Manhattan plot of the all ancestry, sexes-combined, single variant, additive model analysis. Only splice site and coding variants are shown. key: Triangle- MAF <1%, Square- MAF 1% to 5%, Circle- >5%, black- known loci, blue- novel significant loci.



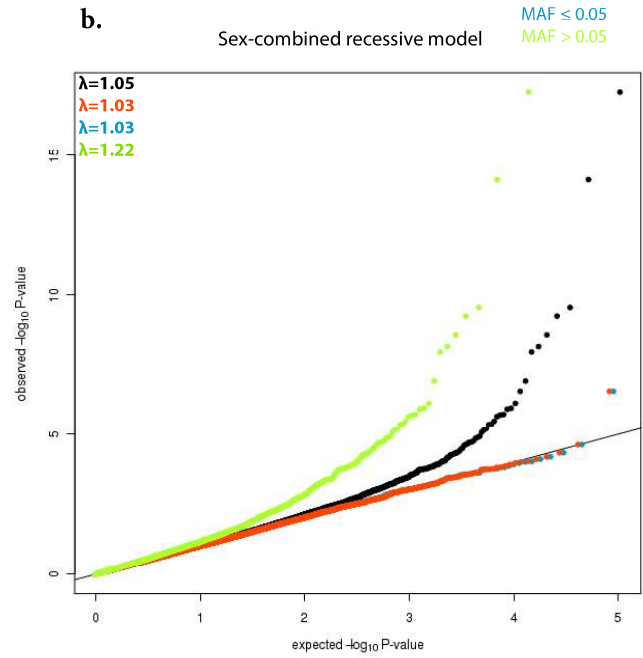
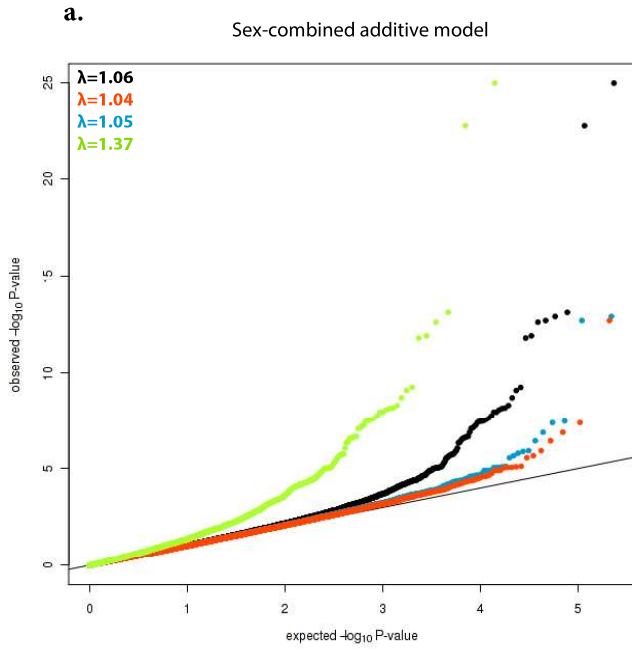
*rs55920843 in *ACVR1C*, rs2625973 in *PLXND1*, rs7657817 in *FAM13A*, rs2303361 in *DAGLB*, and rs2307019 in *IZUMO1* are not labeled because $P_{\text{Stage1}} < 2 \times 10^{-6}$

Supplementary Figure 2: Manhattan plot. Manhattan plot of the all ancestry sex-combined single variant recessive model analysis. Only splice site and coding variants are shown. key: Triangle- MAF <1%, Square- MAF 1% to 5%, Circle- > 5%, black- known loci, blue- novel significant loci.



Supplementary Figure 3. QQ Plots. QQ Plots for all ancestry, sexes-combined, single variant meta-analyses. Only splice site and coding variants are included: a) additive model; b) recessive model.

Legend:
All SNPs
MAF \leq 0.01
MAF \leq 0.05
MAF $>$ 0.05



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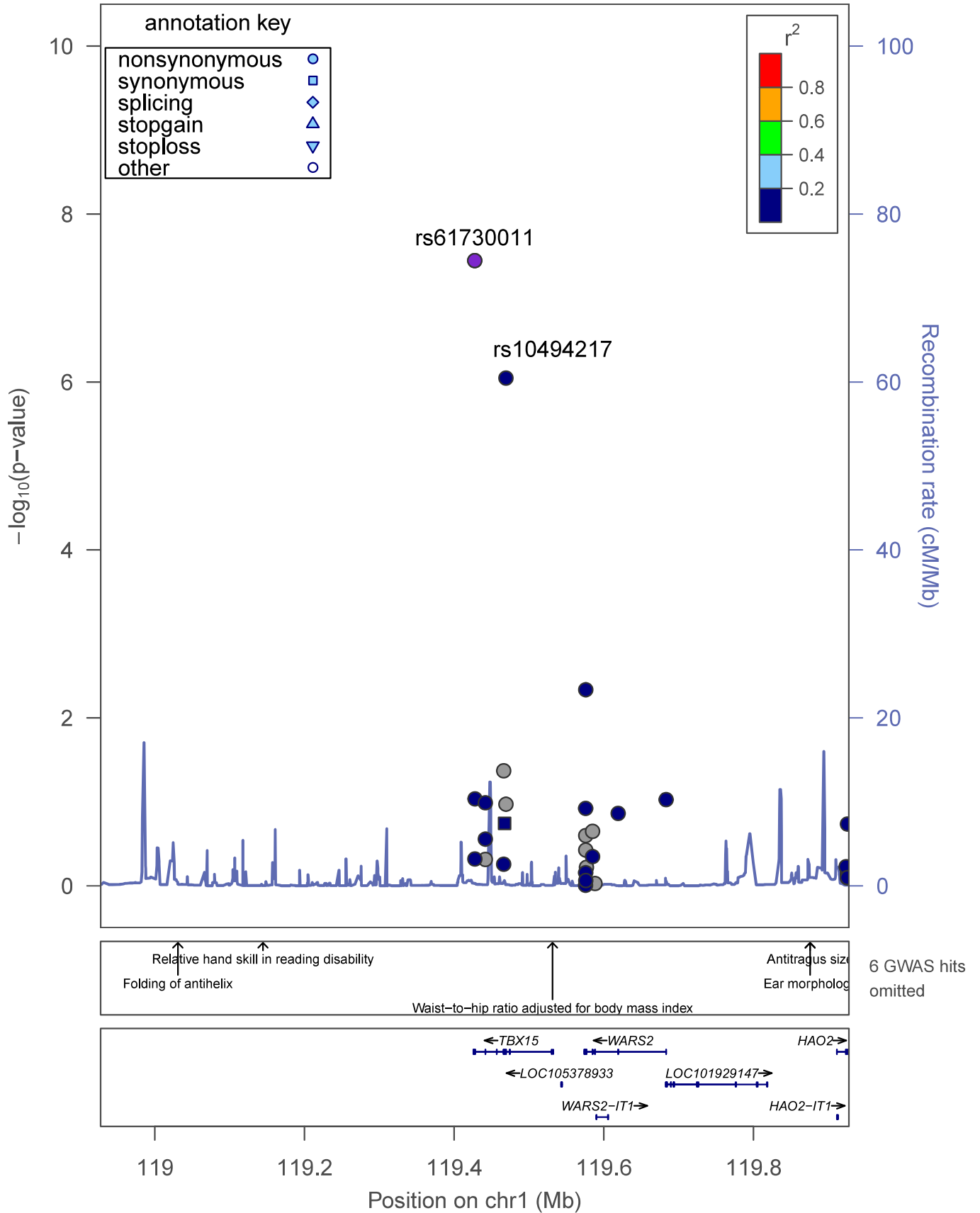
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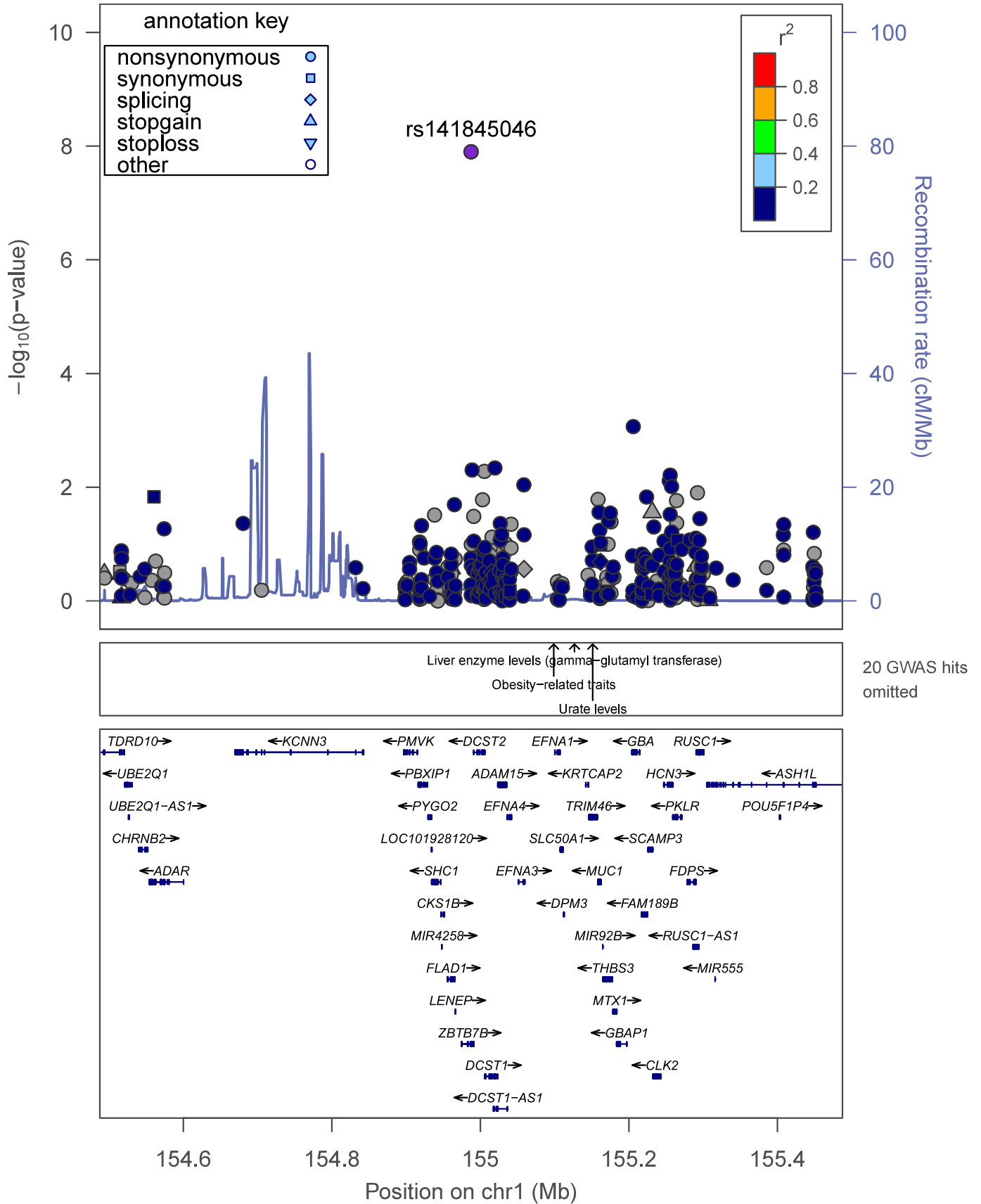
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k# h-U u in MPV17L2 and

rs11554159 in *IFI30*; ae) rs2287922 in *RASIP1* and rs2307019 in *IZUMO1*; af) rs4911494 in *UQCC1* and rs224331 in *GDF5*; ag) rs144098855, *R3HDML*.

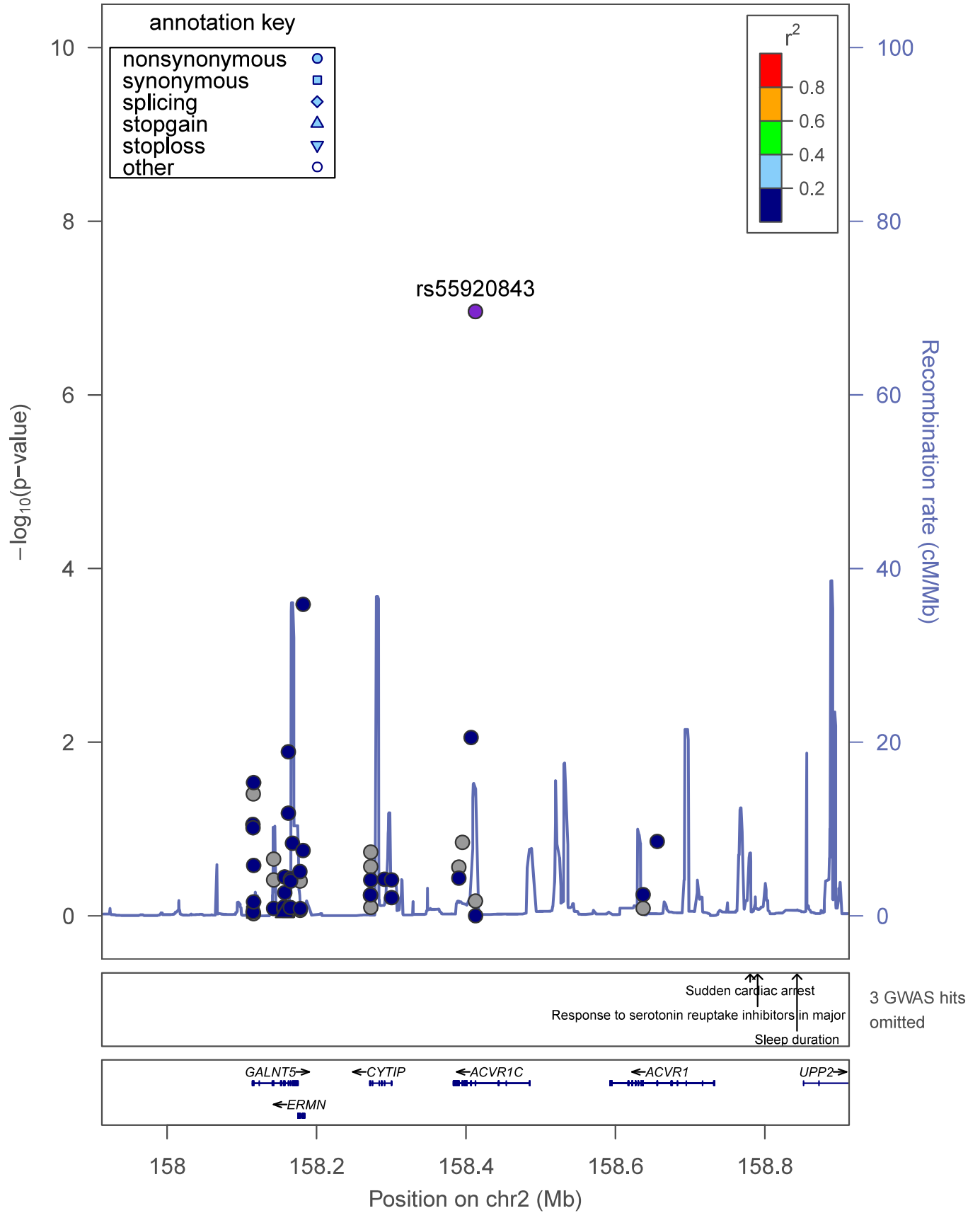
a) *TBX15* All Ancestry, Sexes-Combined



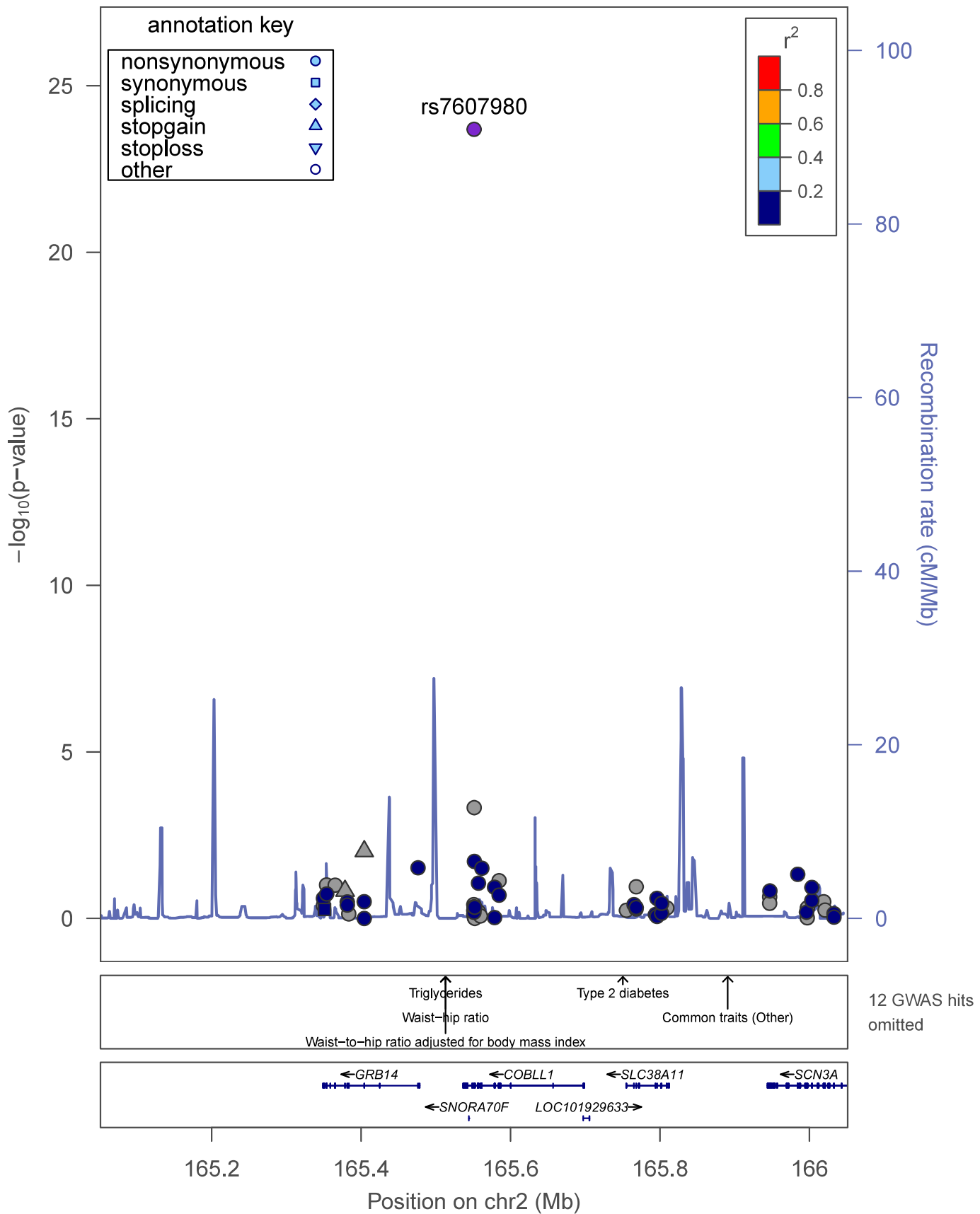
b) *ZBTB7B* All Ancestry, Women



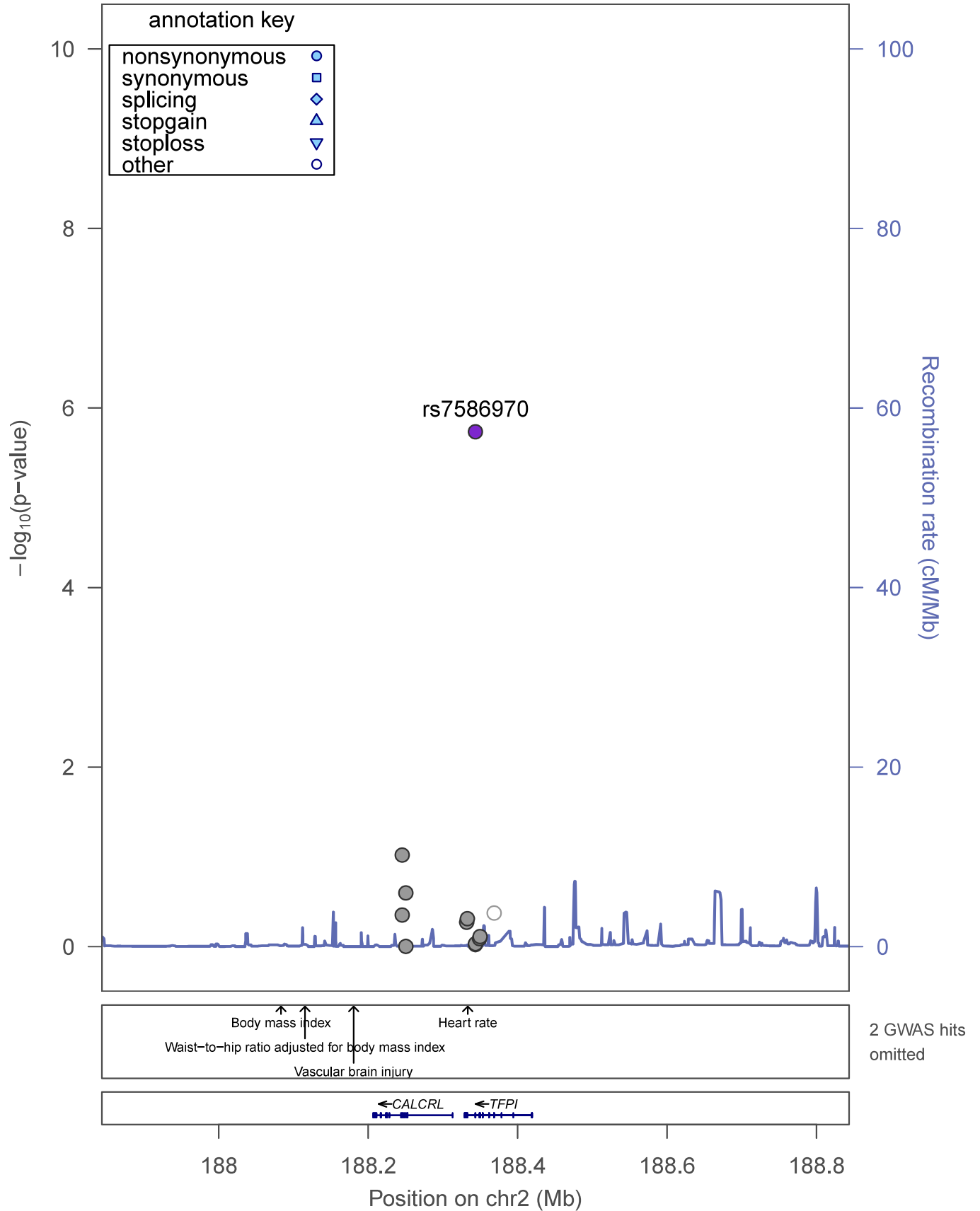
c) *ACVR1C* All Ancestry, Women



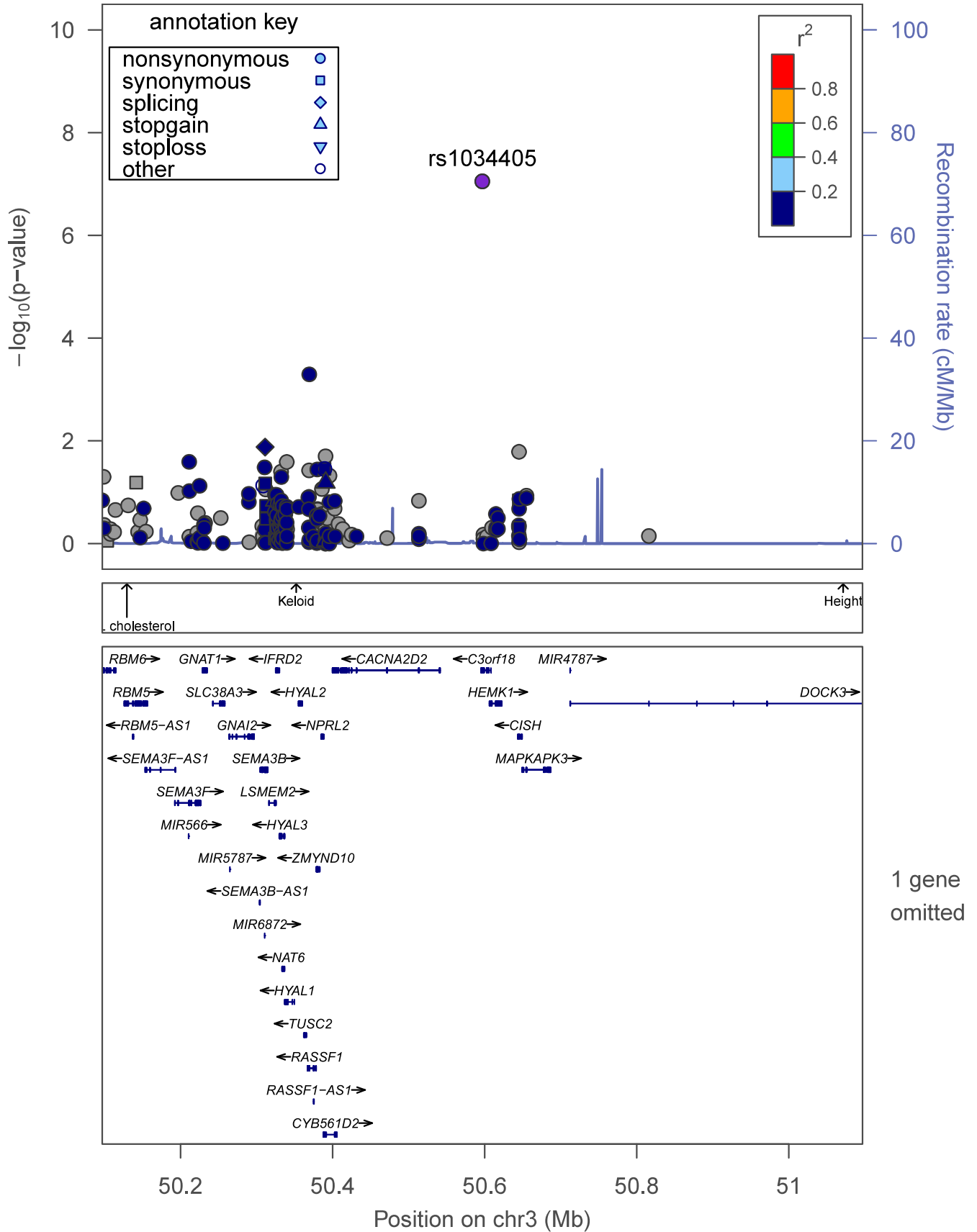
d) *COBLL1* All Ancestry, Women



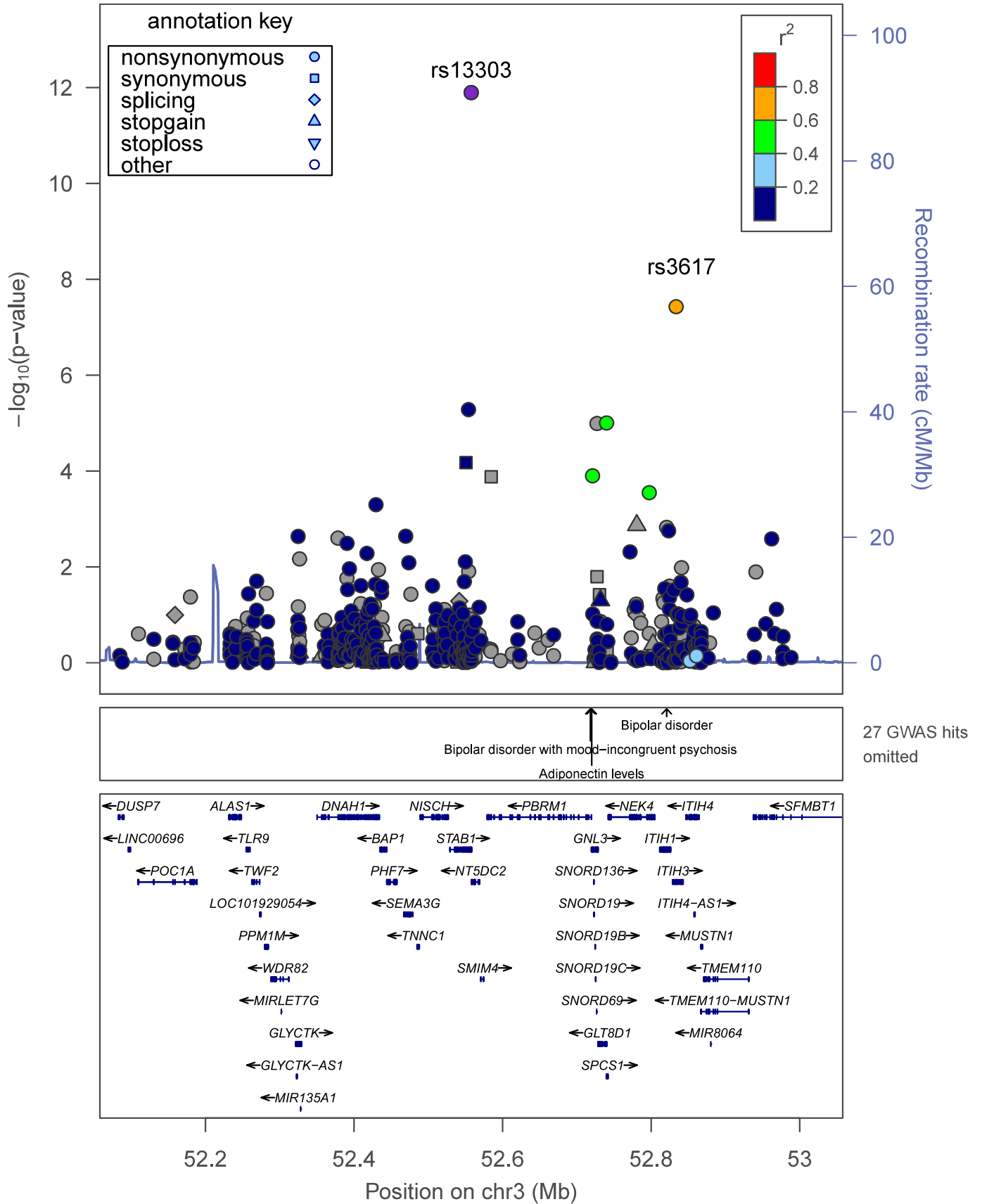
e) *TFPI* All Ancestry, Sexes-Combined



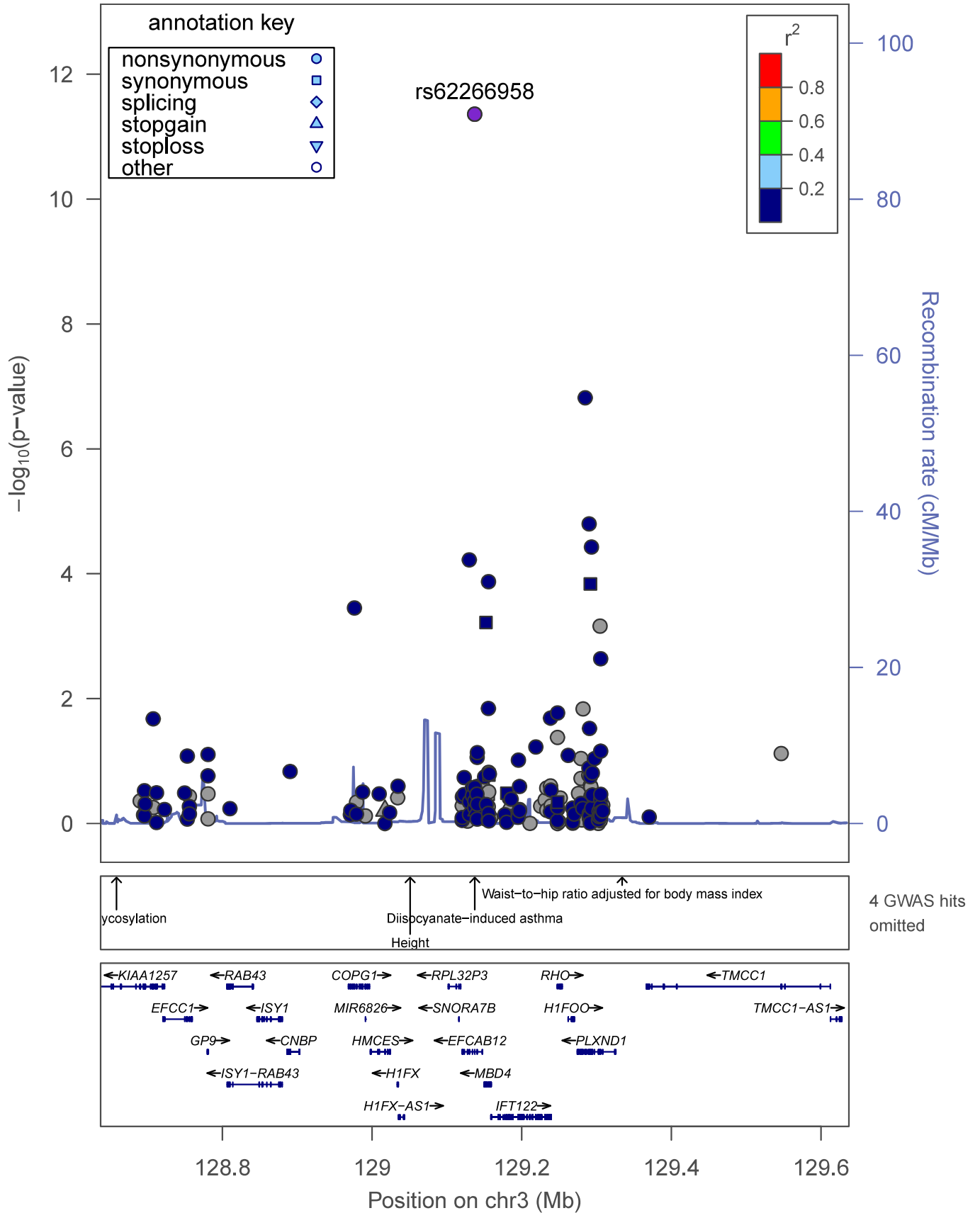
f) *C3orf18* All Ancestry, Sexes-Combined



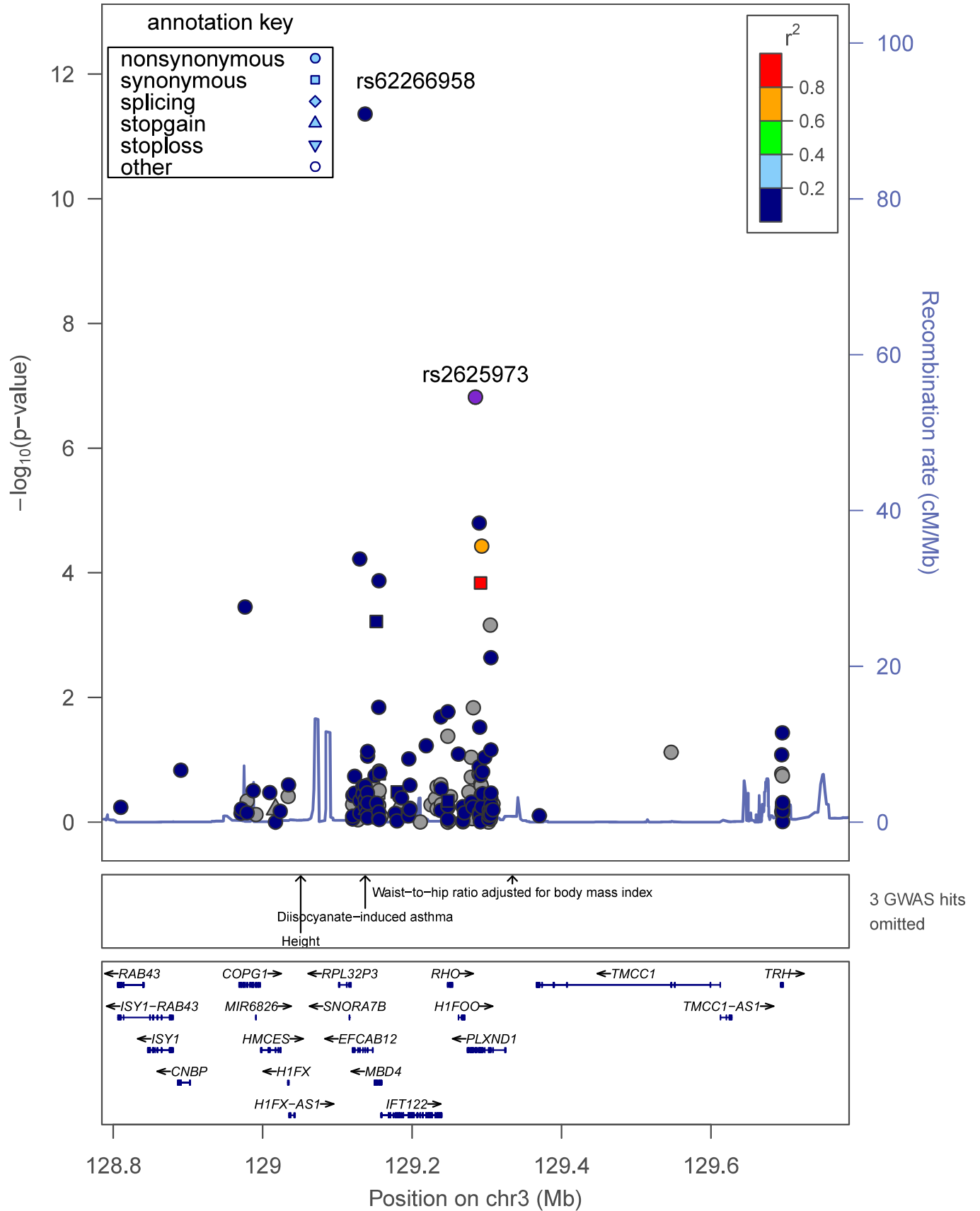
g) *STAB1* & *ITIH3* All Ancestry, Sexes-Combined



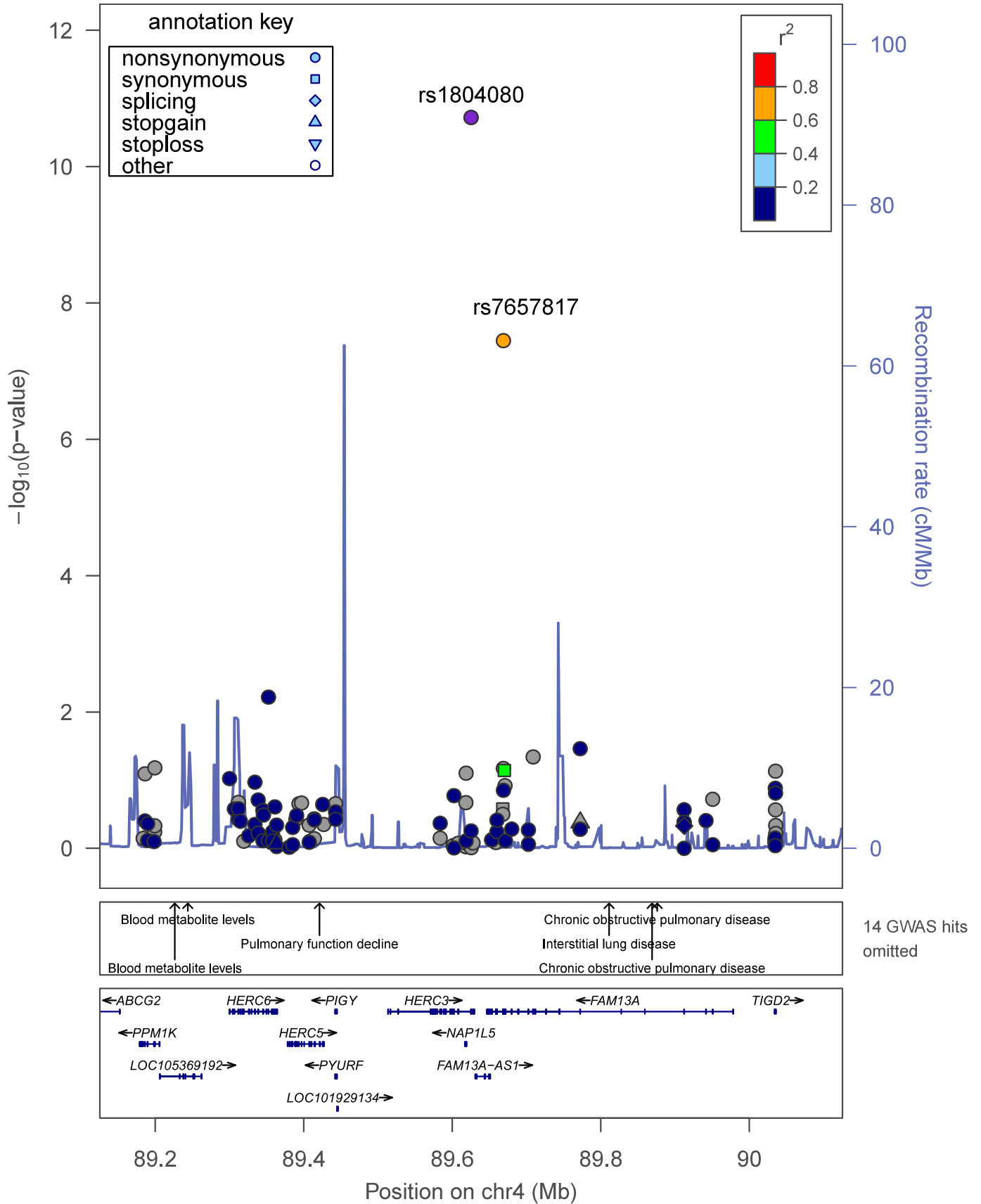
h) *EFCAB12* All Ancestry, Women



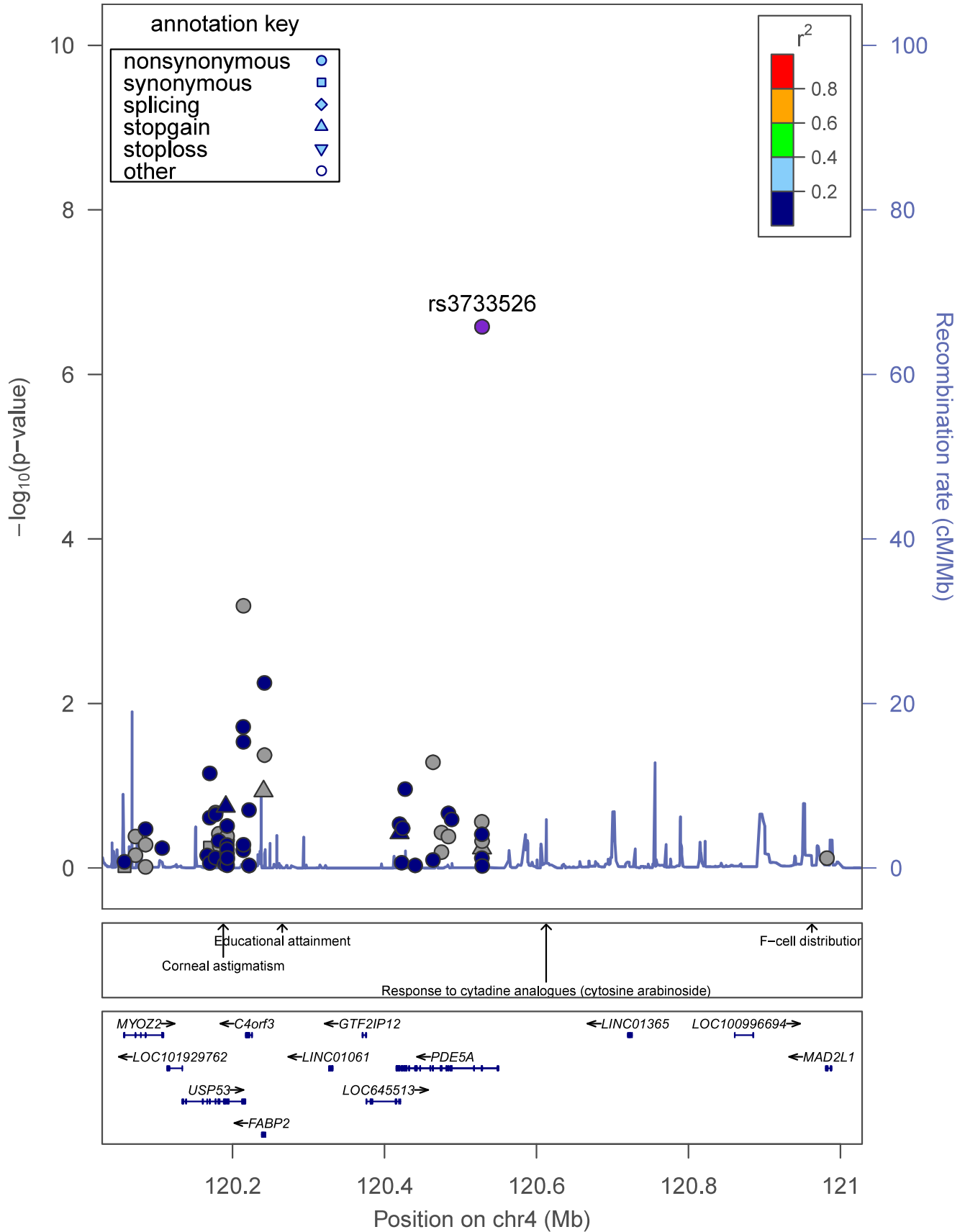
i) *PLXND1* All Ancestry, Women



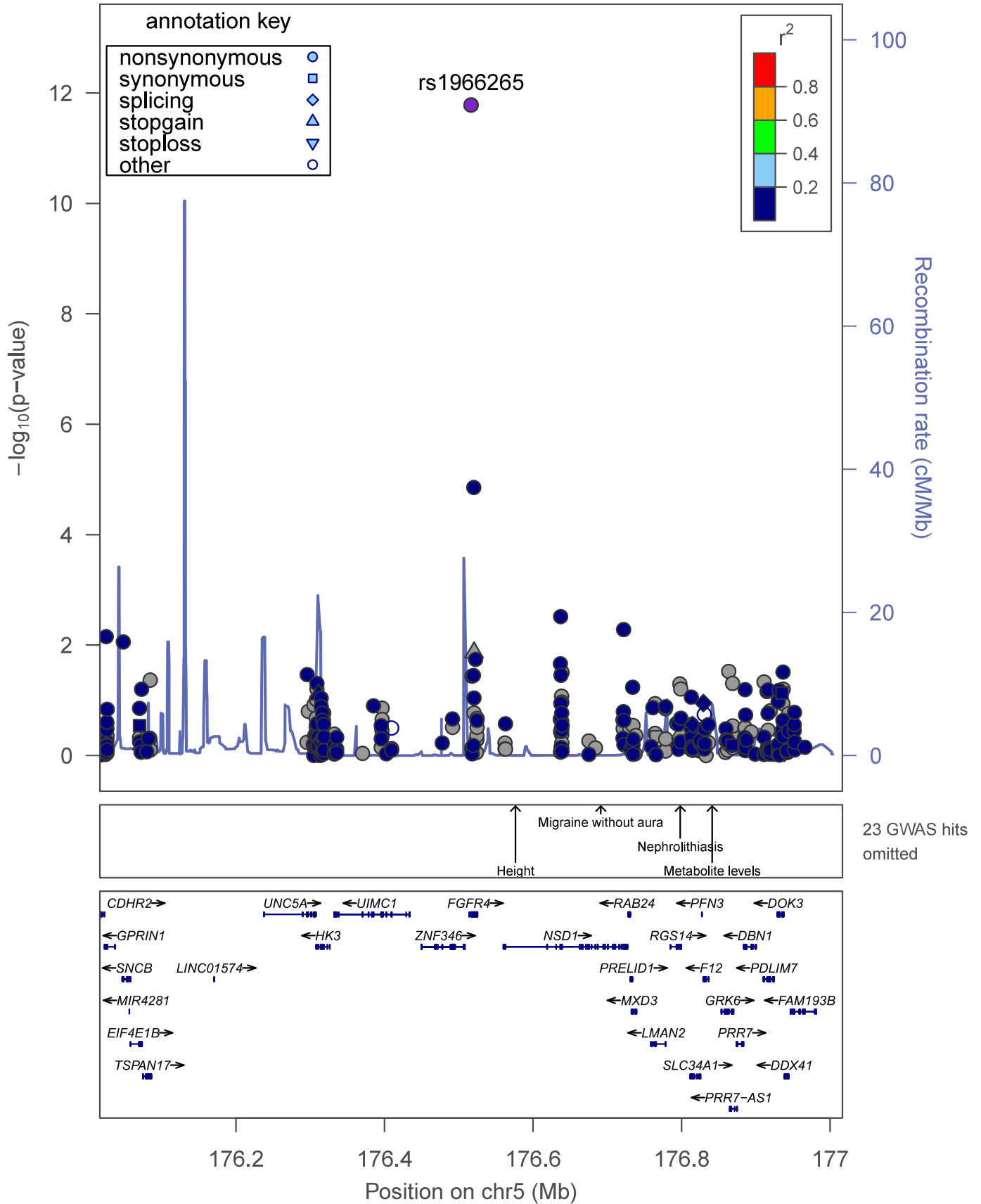
j) *HERC3* & *FAM13A* All Ancestry, Women



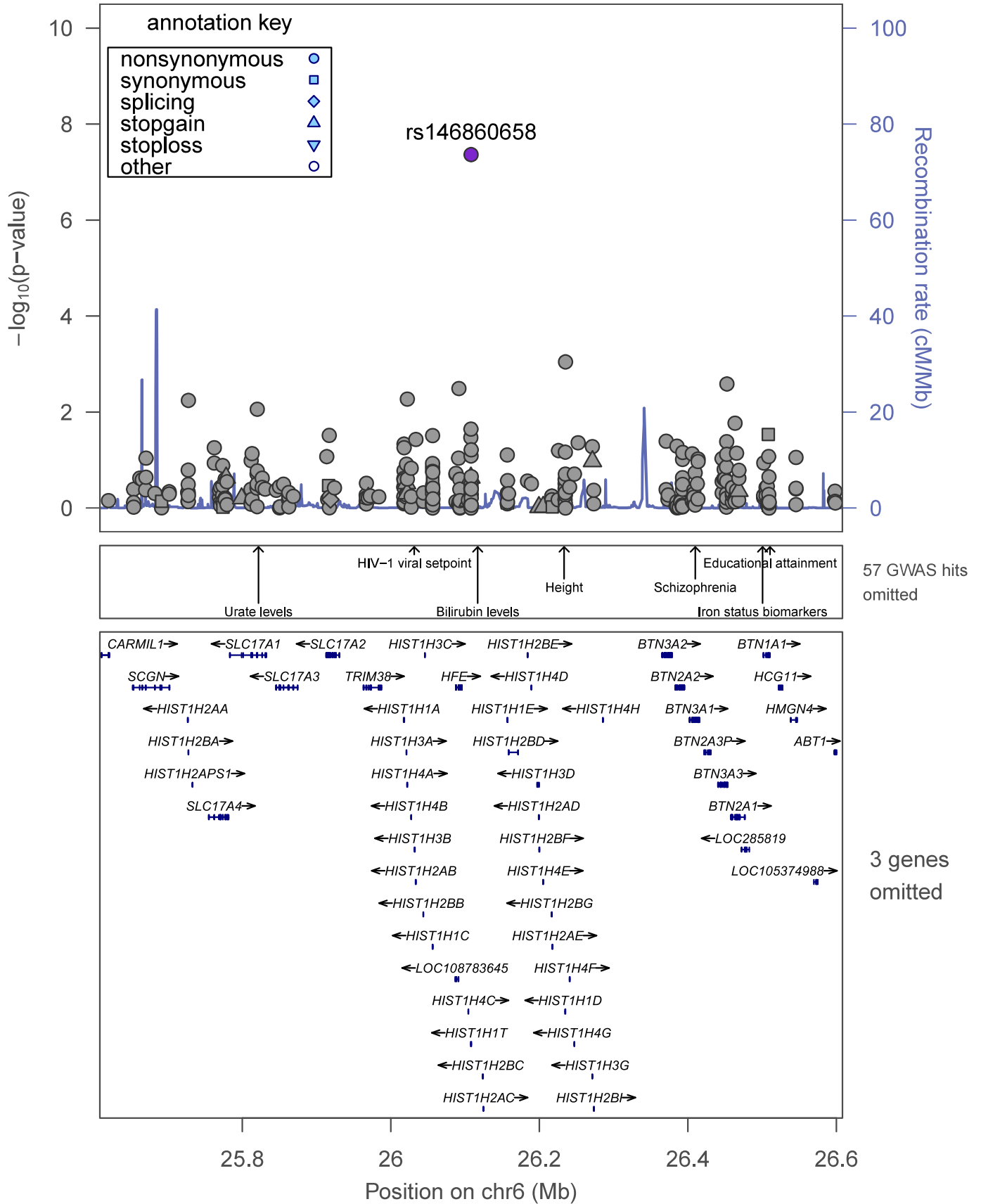
k) *PDE5A* All Ancestry, Sexes-Combined



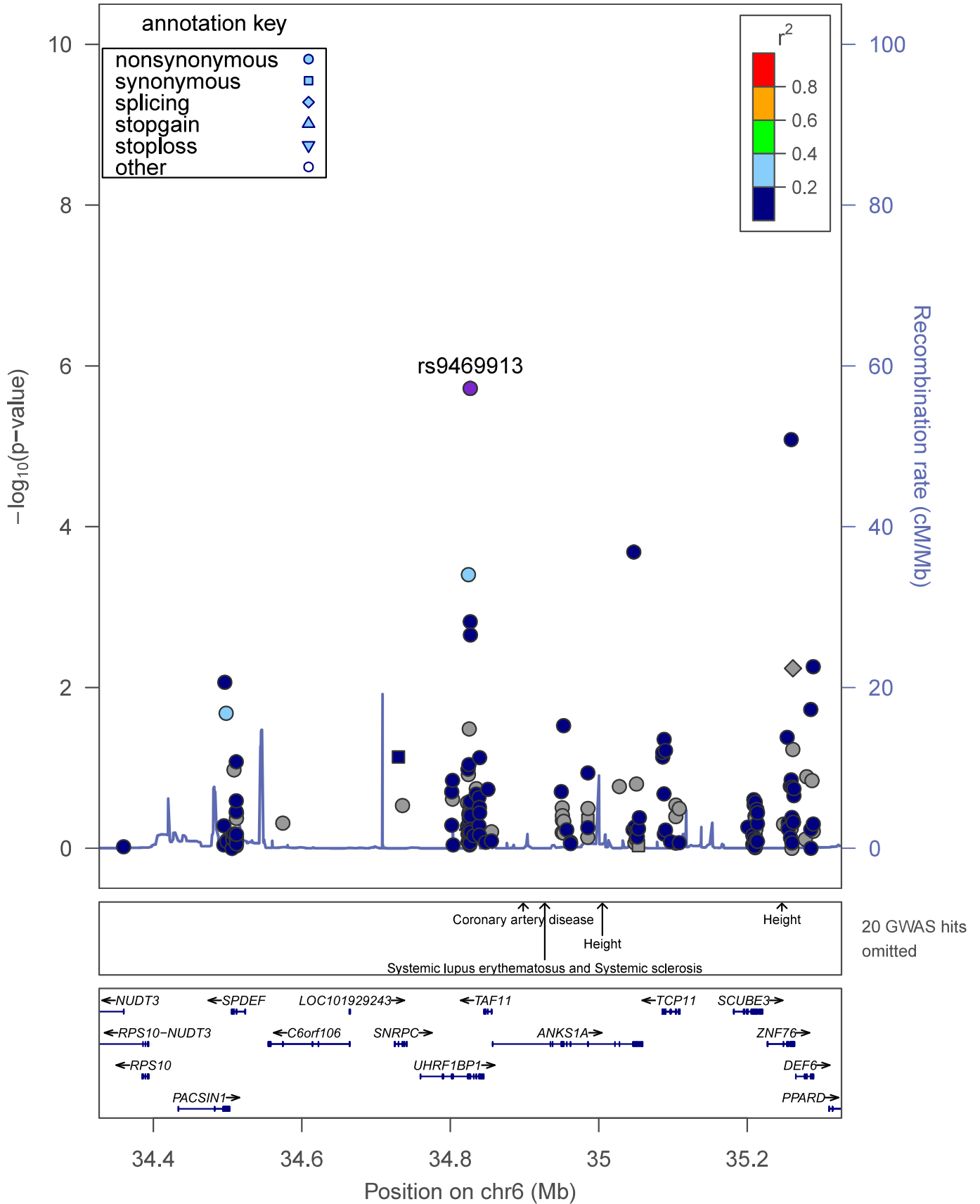
I) *FGFR4* All Ancestry, Sexes-Combined



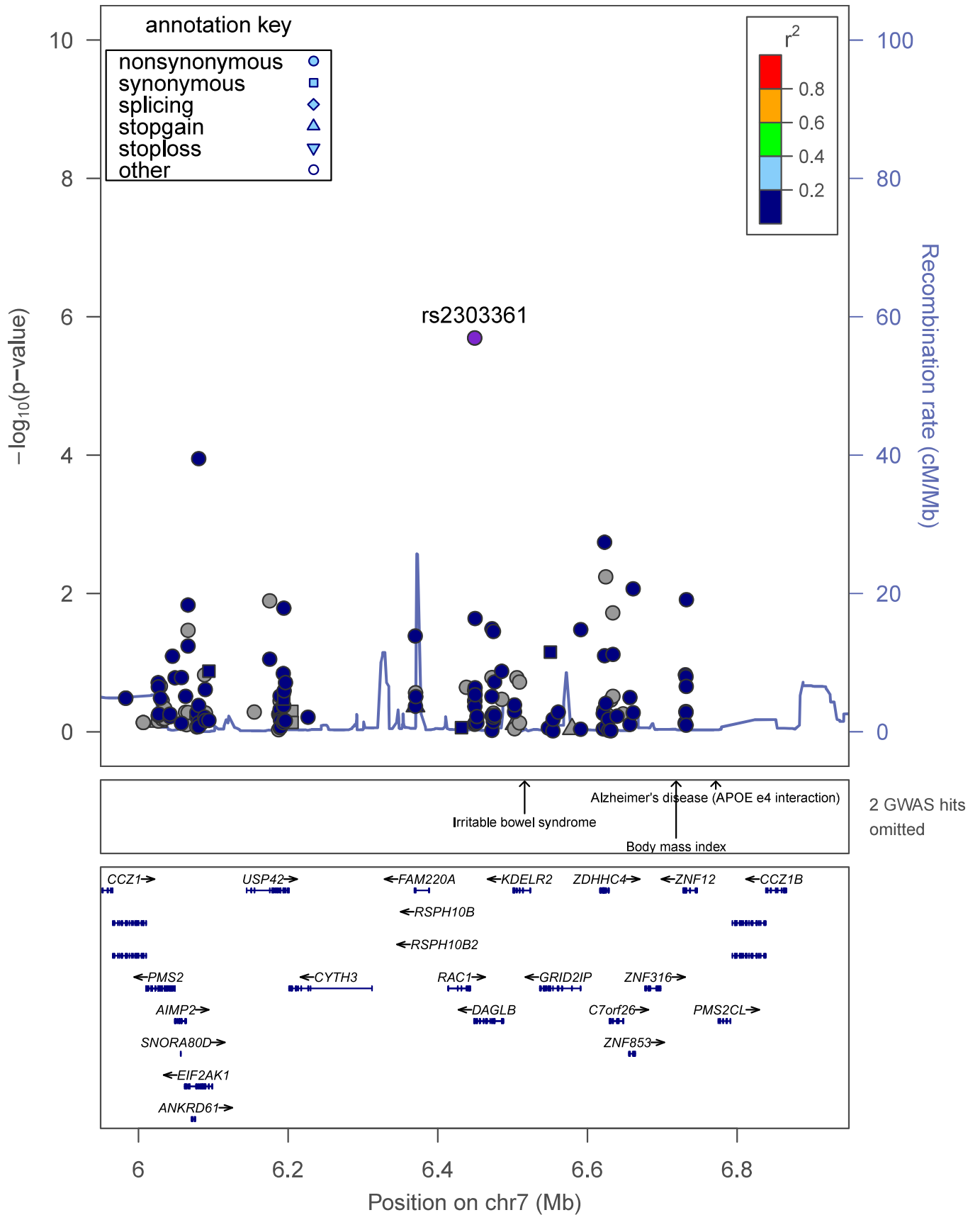
m) *HIST1H1T* All Ancestry, Sexes-Combined



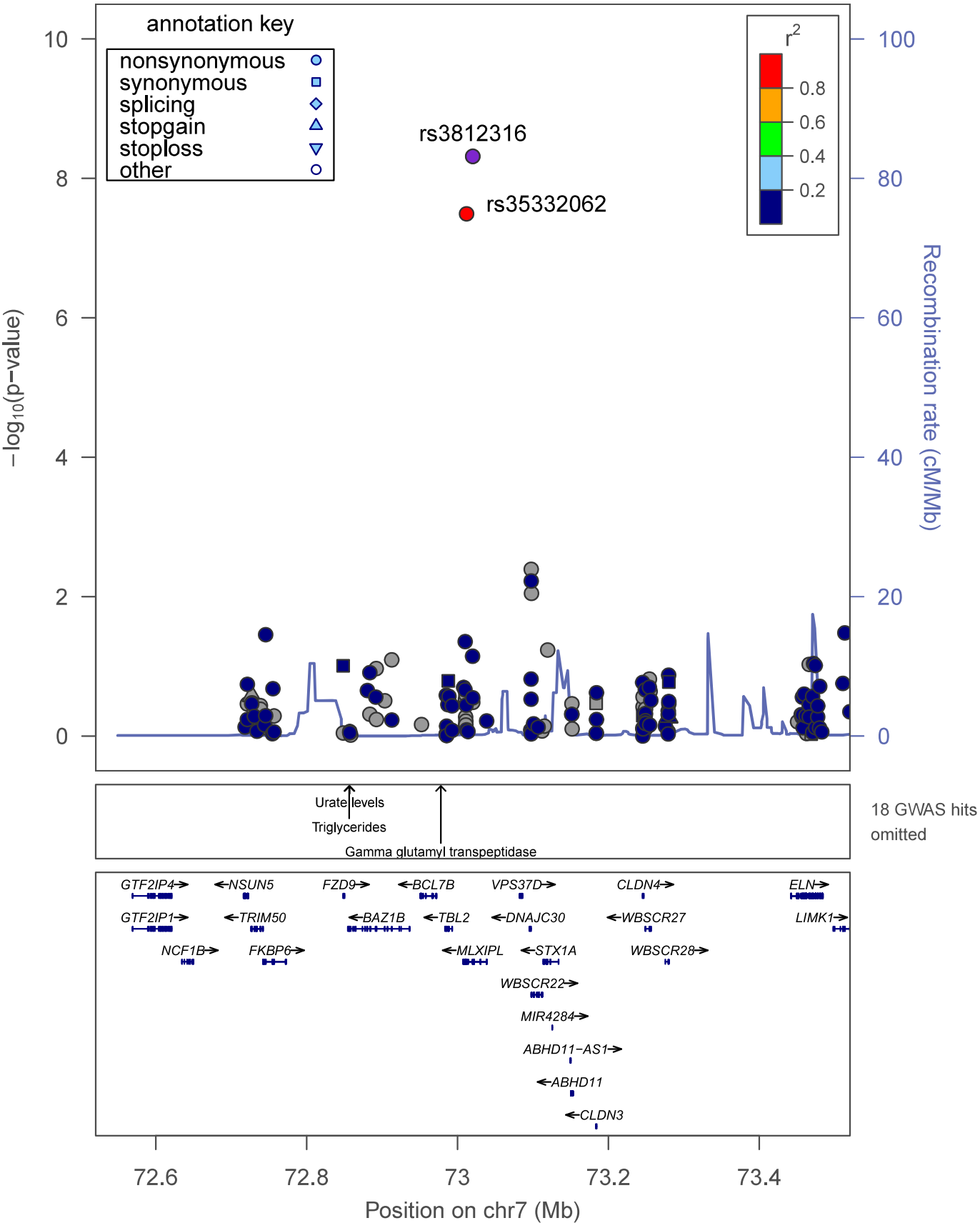
n) *UHRF1BP1* All Ancestry, Sexes-Combined



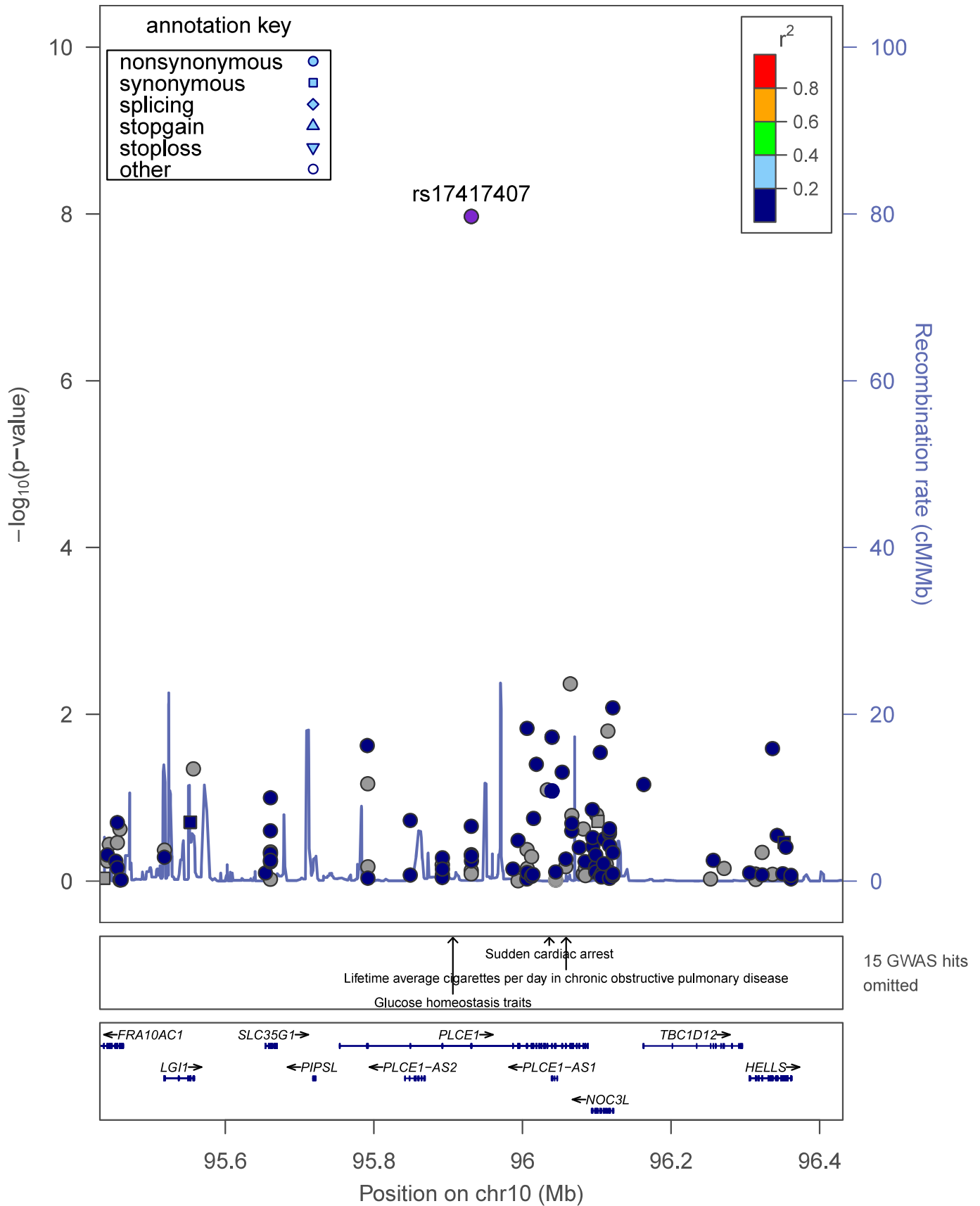
o) *DAGLB* All Ancestry, Sexes-Combined



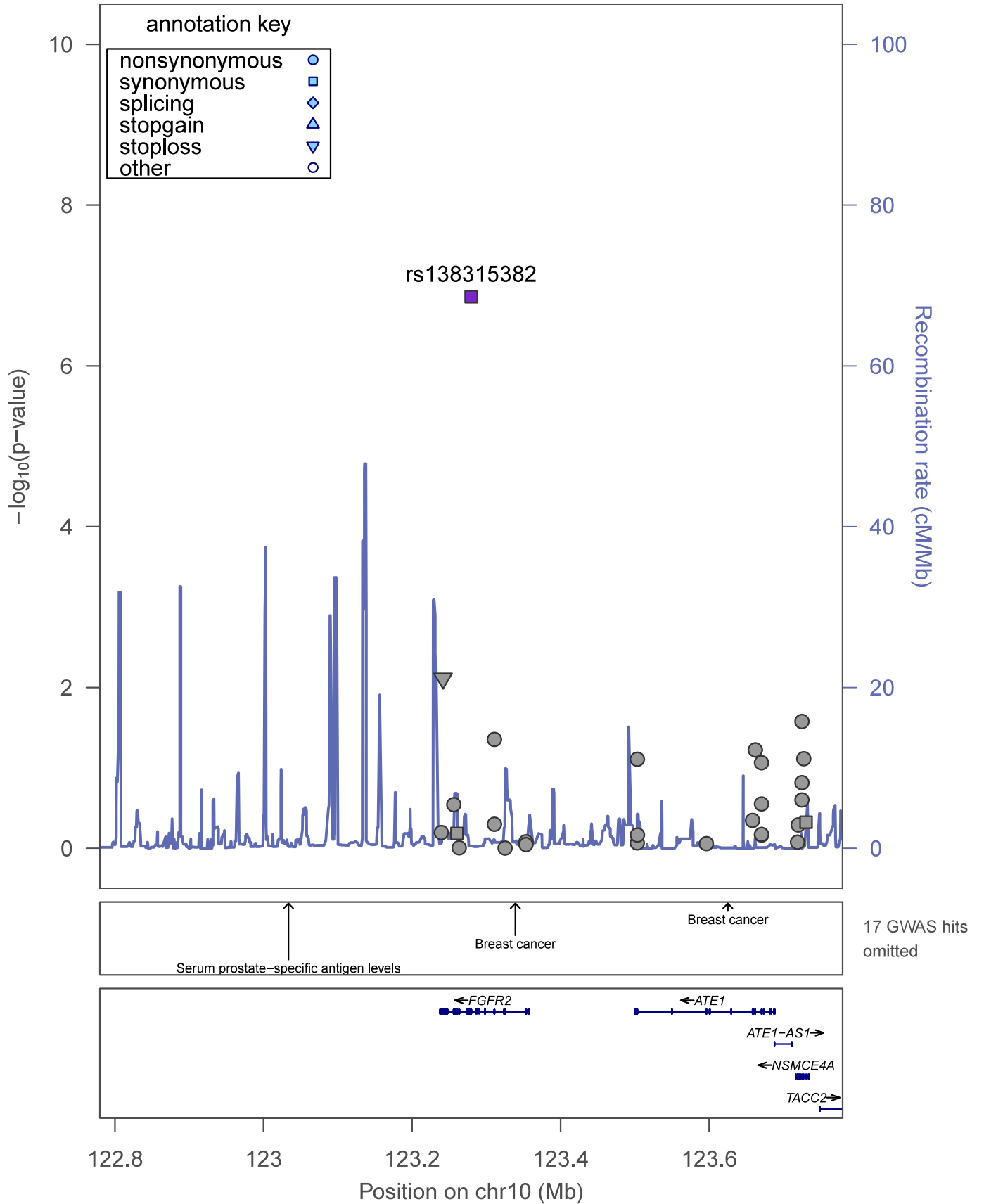
p) *MLXIPL* All Ancestry, Sexes-Combined



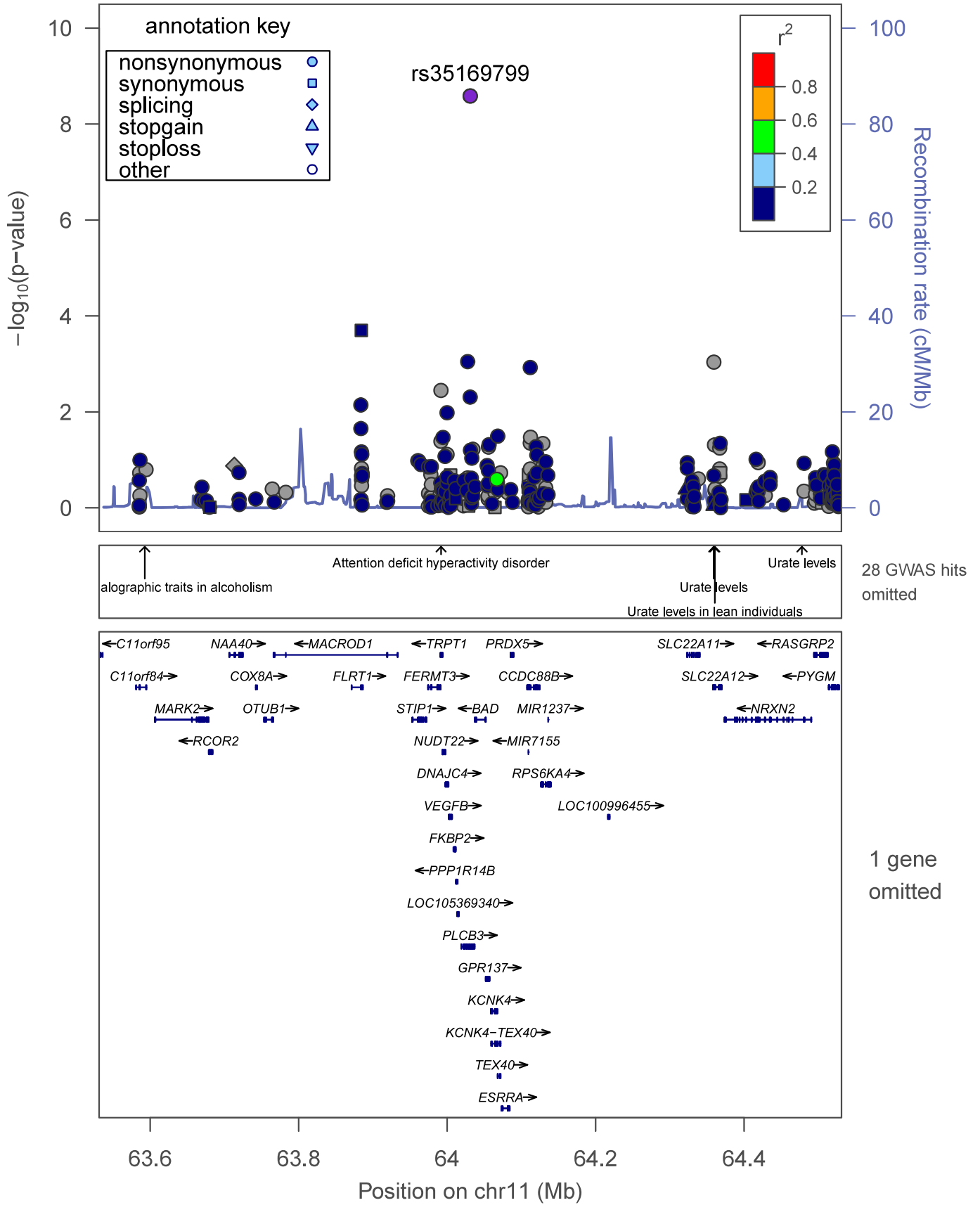
q) *PLCE1* All Ancestry, Sexes-Combined



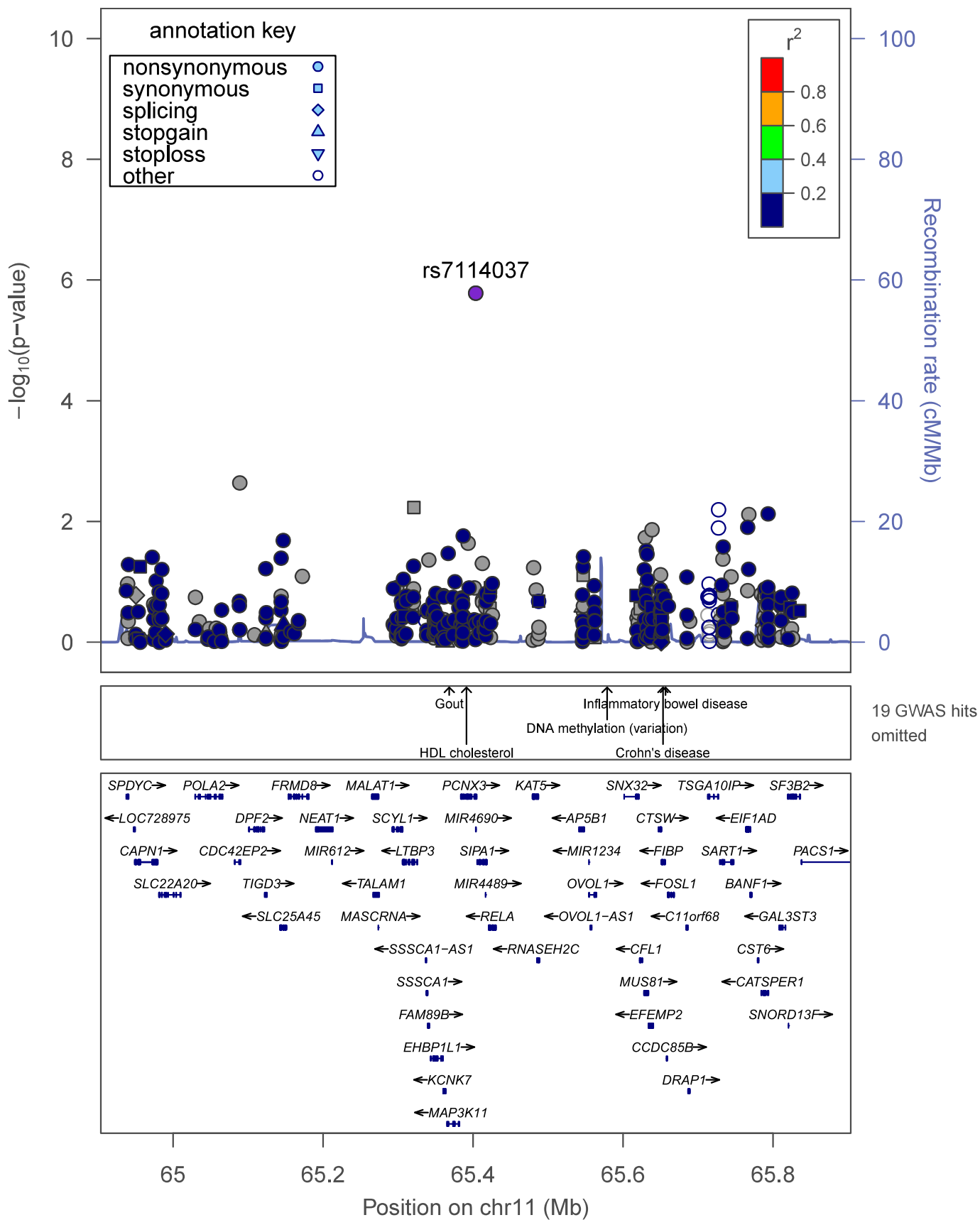
r) *FGFR2* All Ancestry, Sexes-Combined



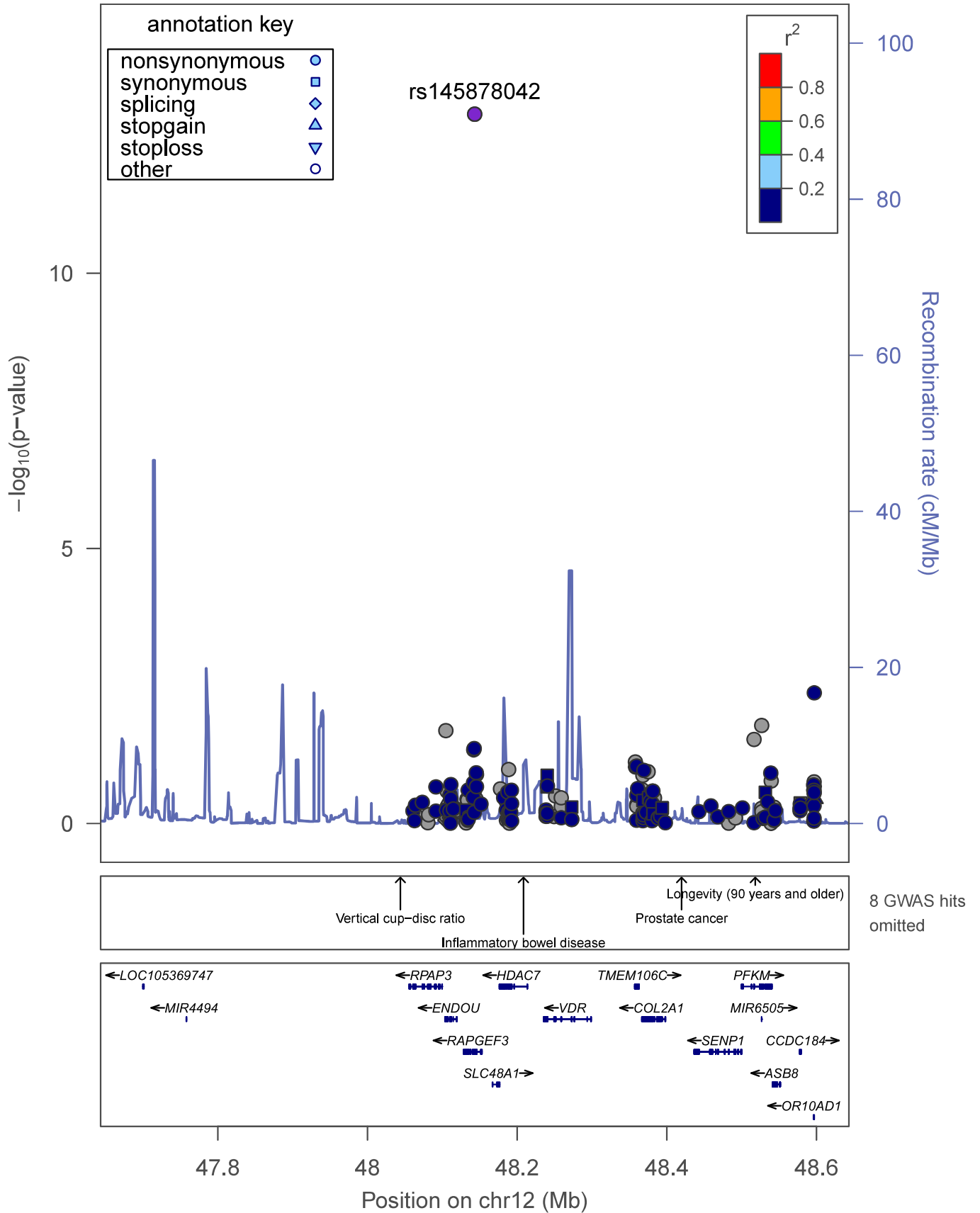
s) *PLCB3* All Ancestry, Women



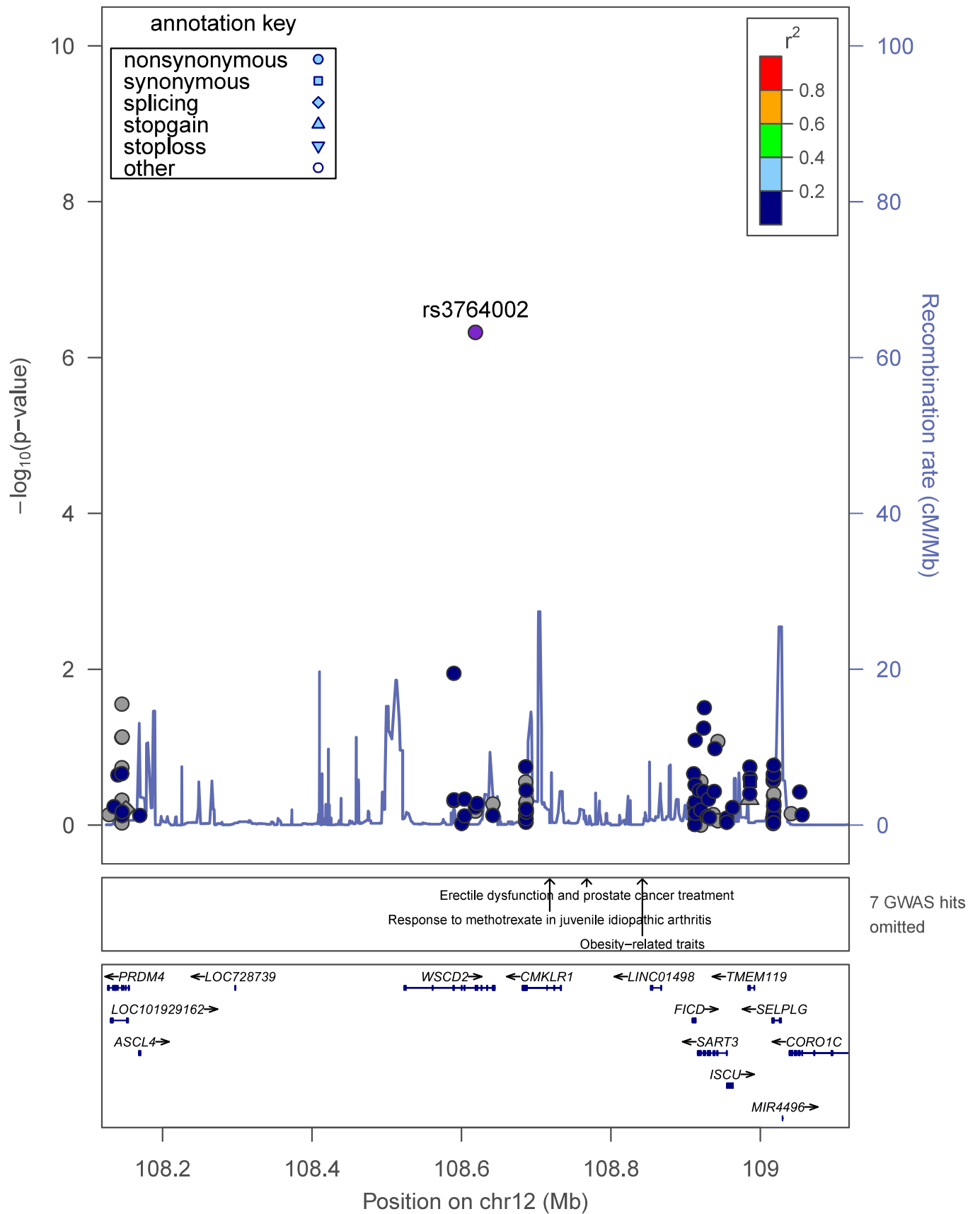
t) *PCNXL3* All Ancestry, Sexes-Combined



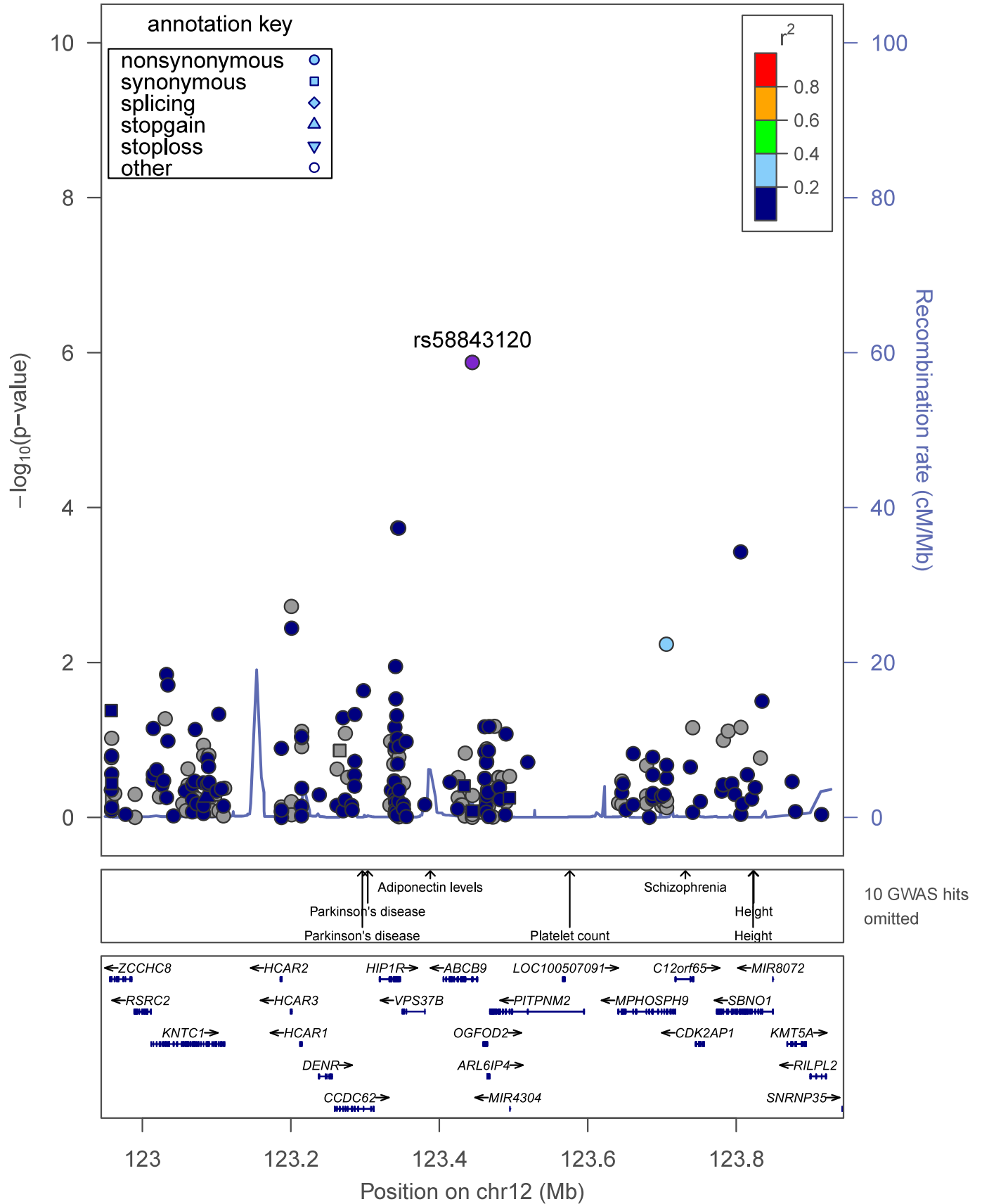
u) *RAPGEF3* All Ancestry, Sexes-Combined



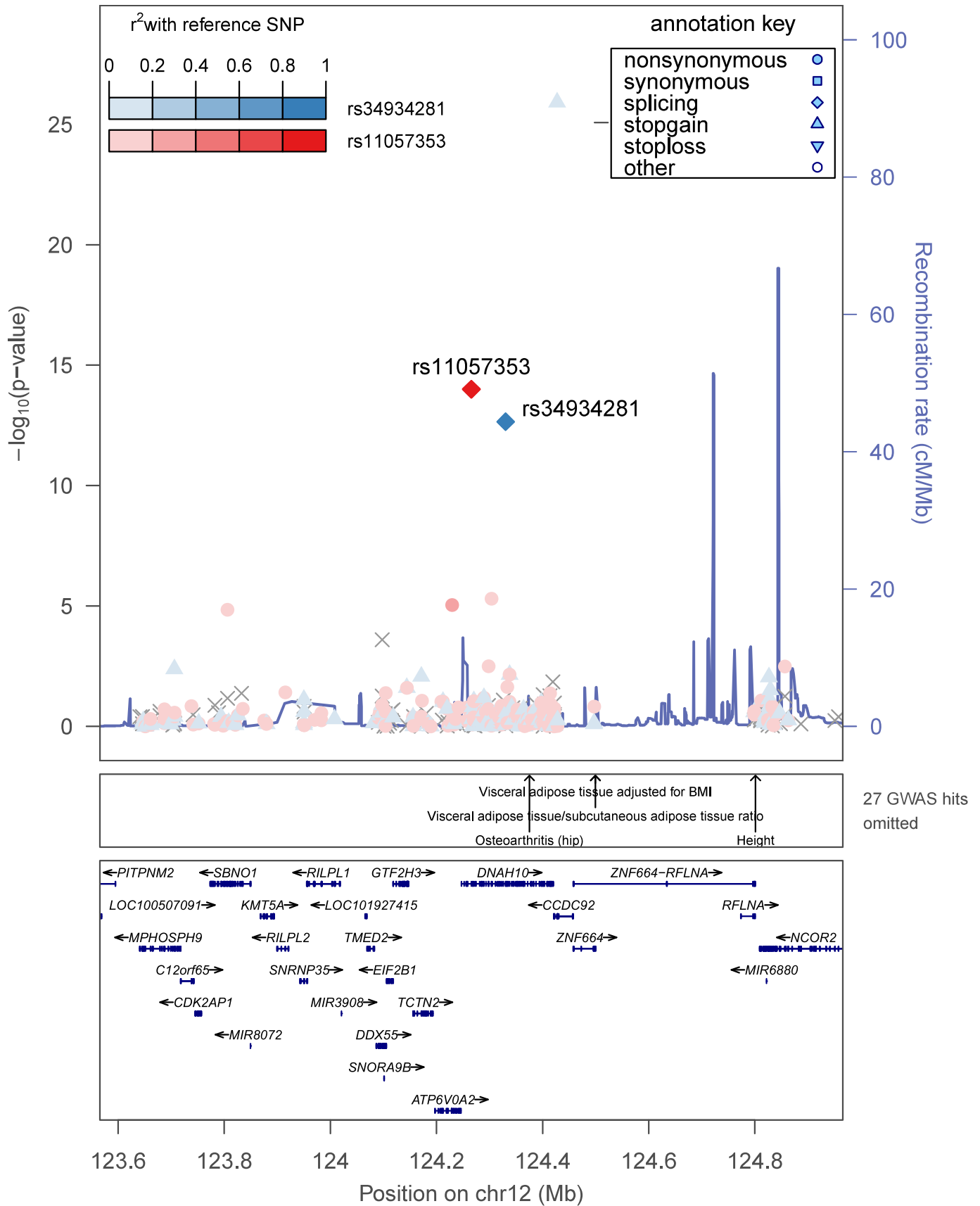
v) *WSCD2* All Ancestry, Sexes-Combined



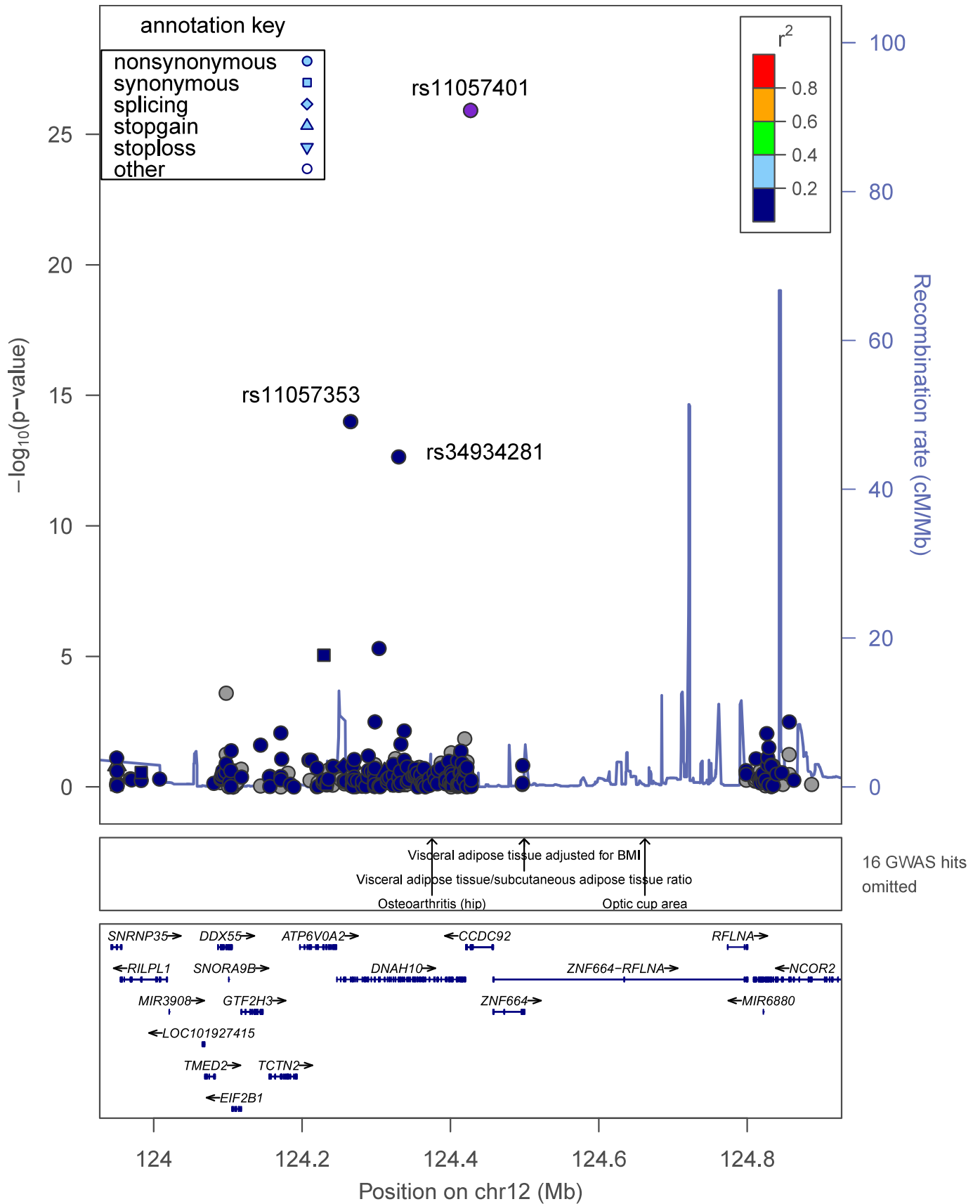
w) *ABCB9* All Ancestry, Sexes-Combined



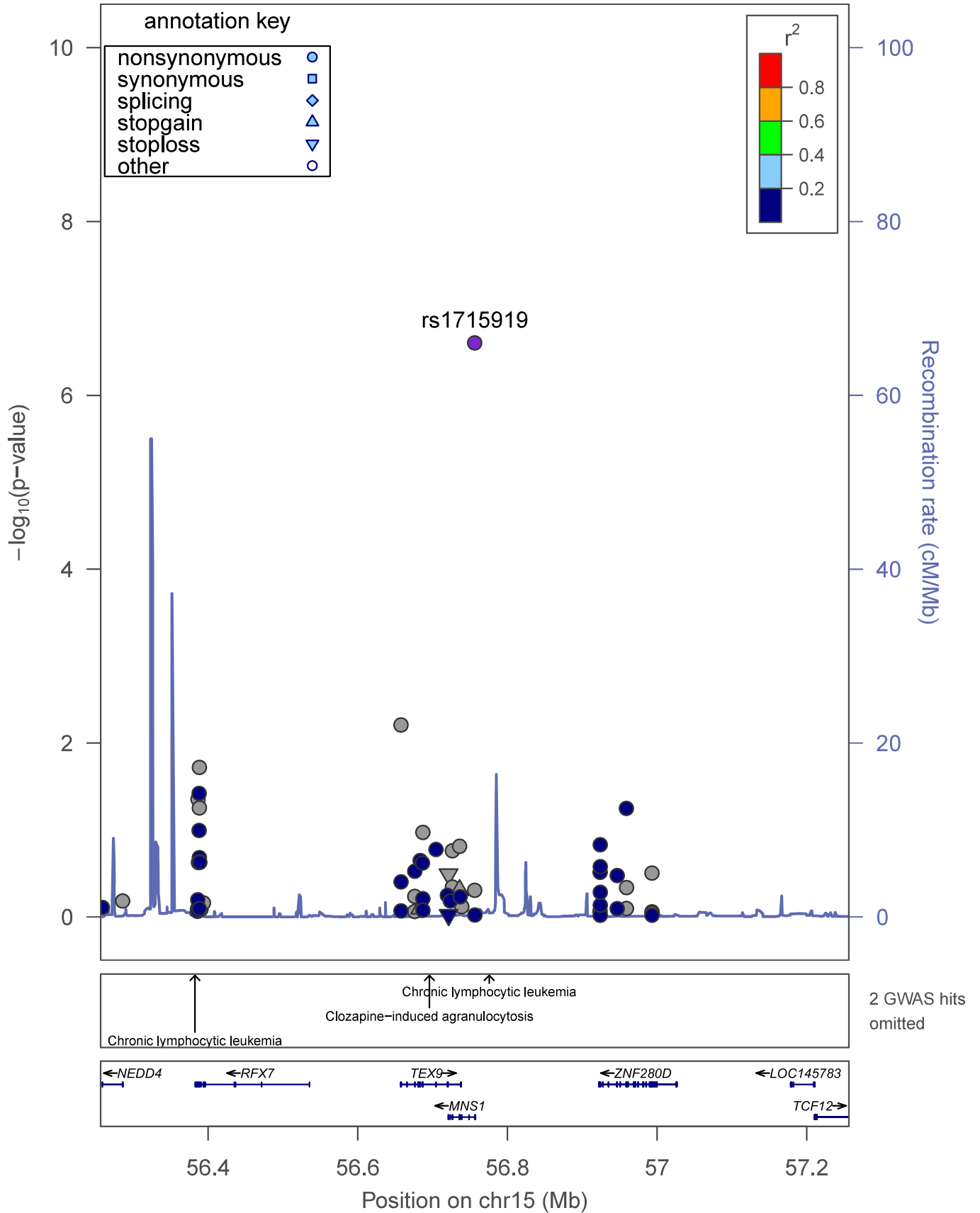
x) *DNAH10* All Ancestry, Women



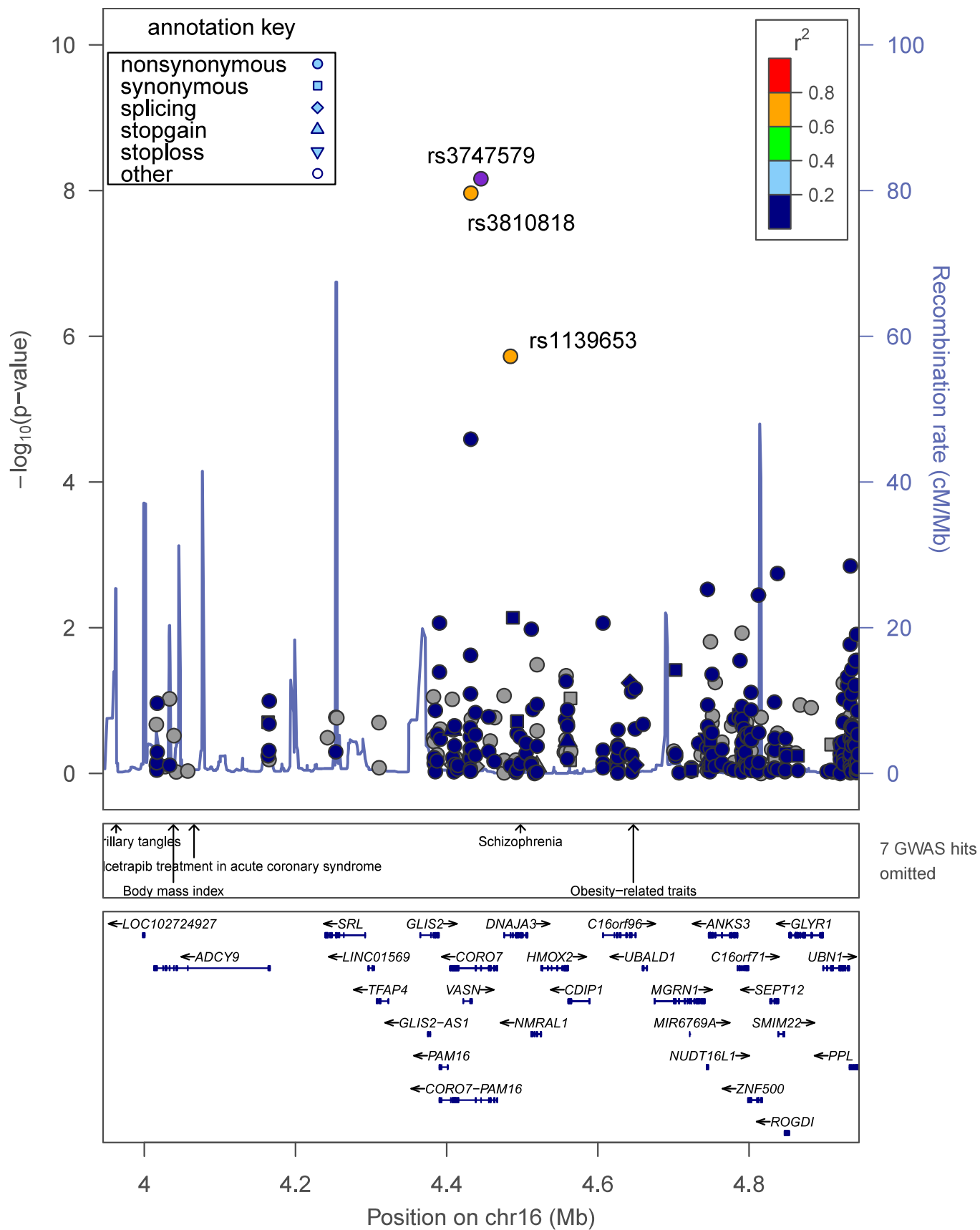
y) *CCDC92* All Ancestry, Women



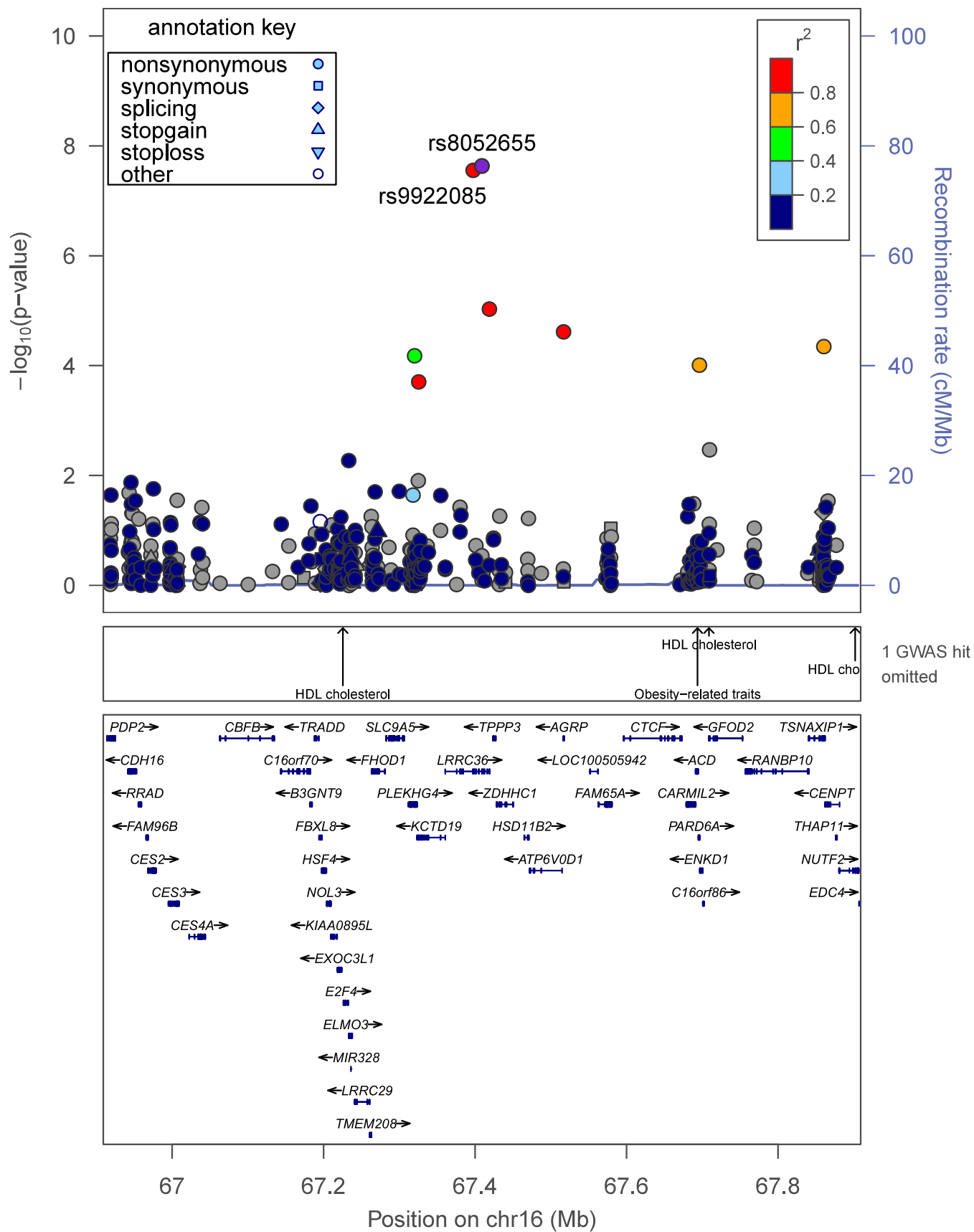
z) *MNS1* All Ancestry, Sexes-Combined



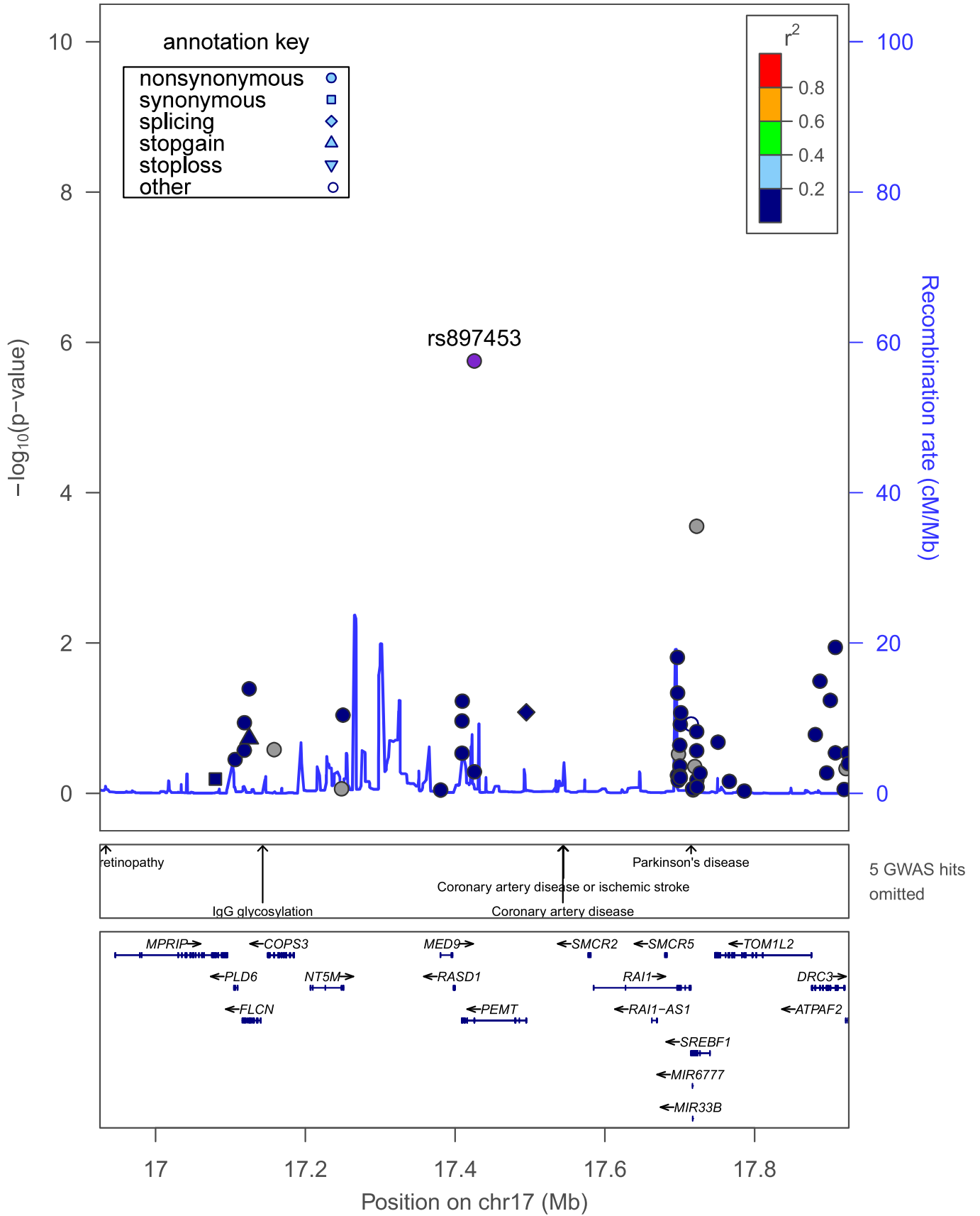
aa) *CORO7*, *DNAJA3*, & *VASN* All Ancestry, Sexes-Combined



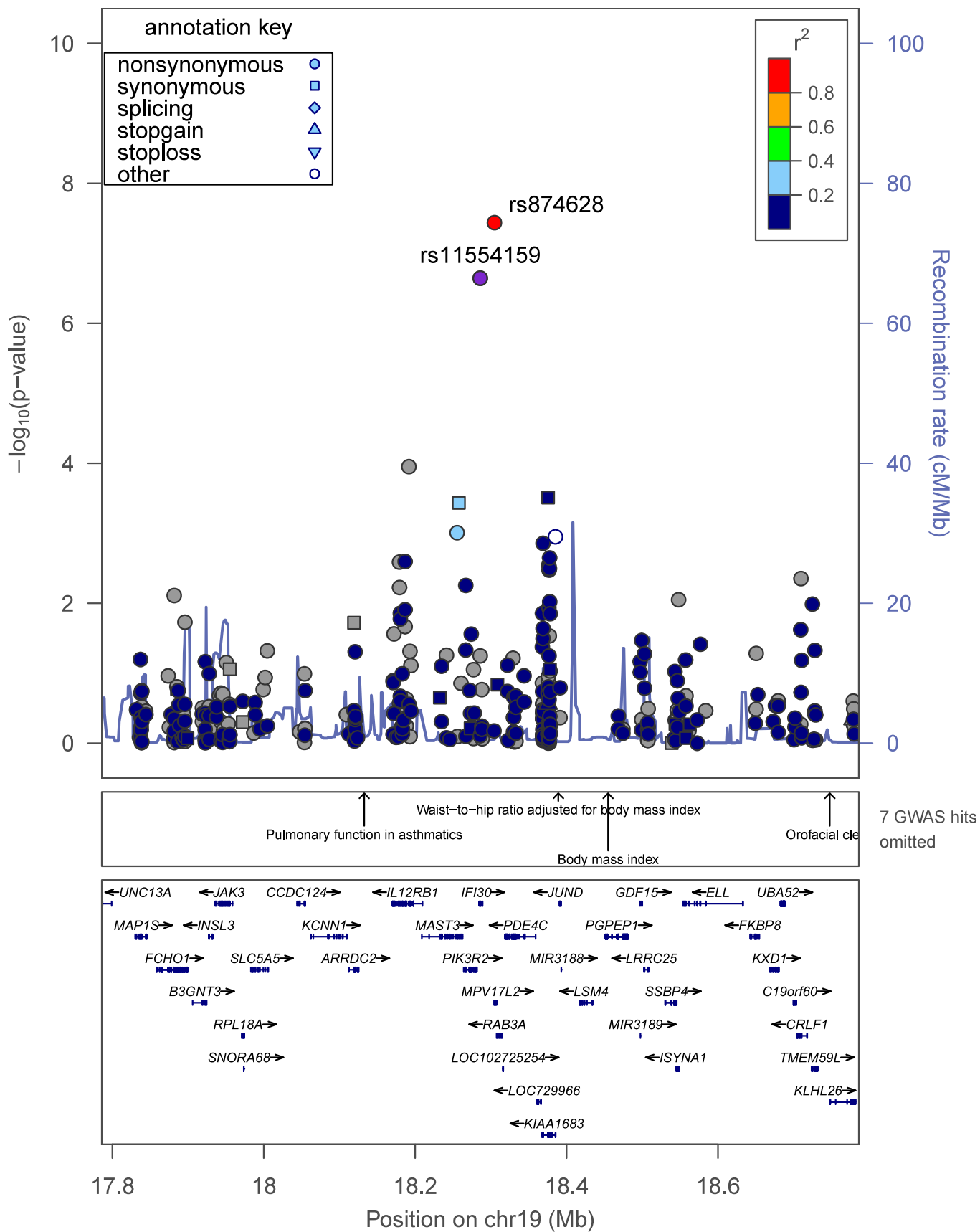
ab) *LRRC36* All Ancestry, Sexes-Combined



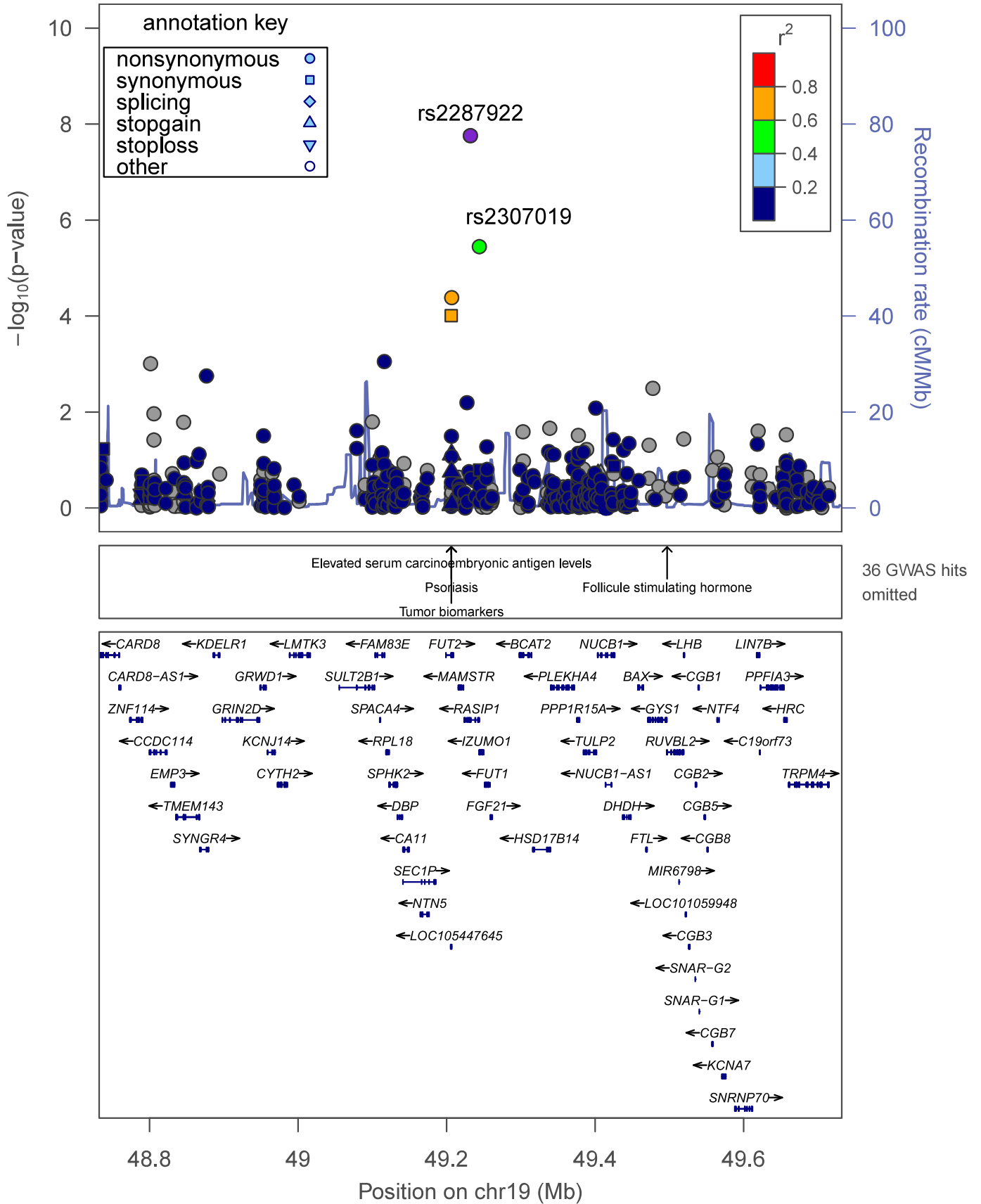
ac) *PEMT* All Ancestry, Sexes-Combined



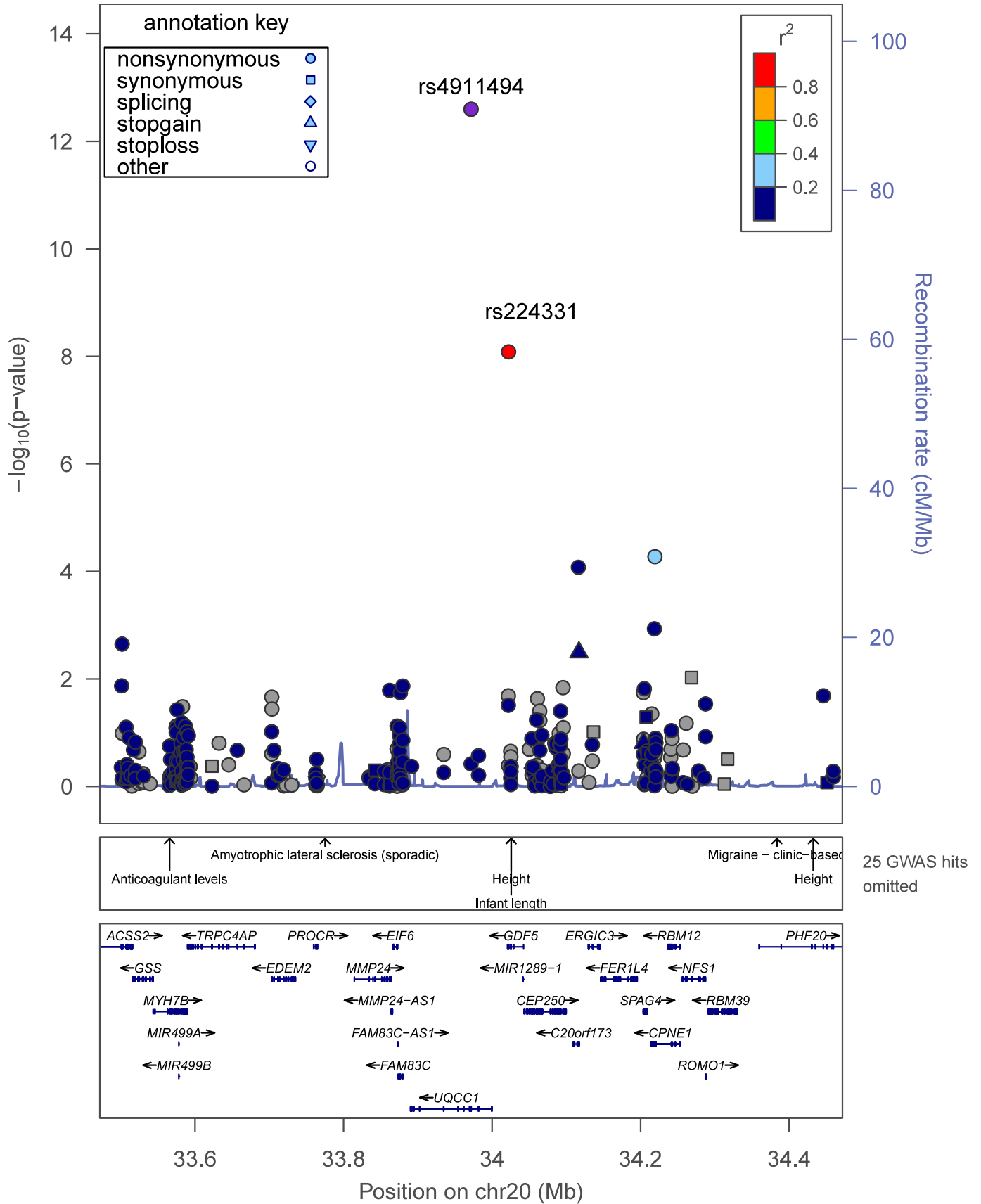
ad) *IFI30* & *MPV17L2* All Ancestry, Sexes-Combined



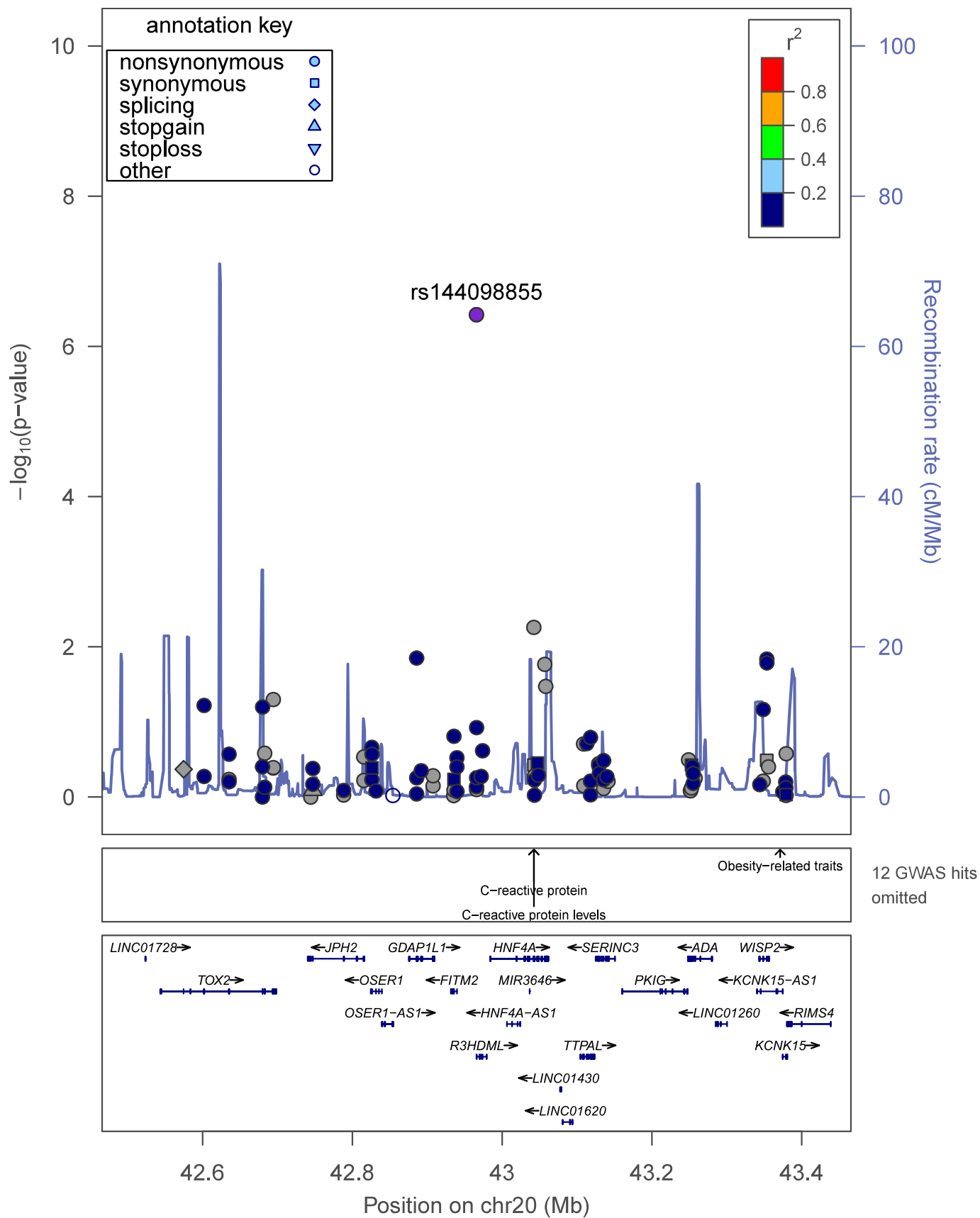
ae) *RASIP1* & *IZUMO1* All Ancestry, Sexes-Combined



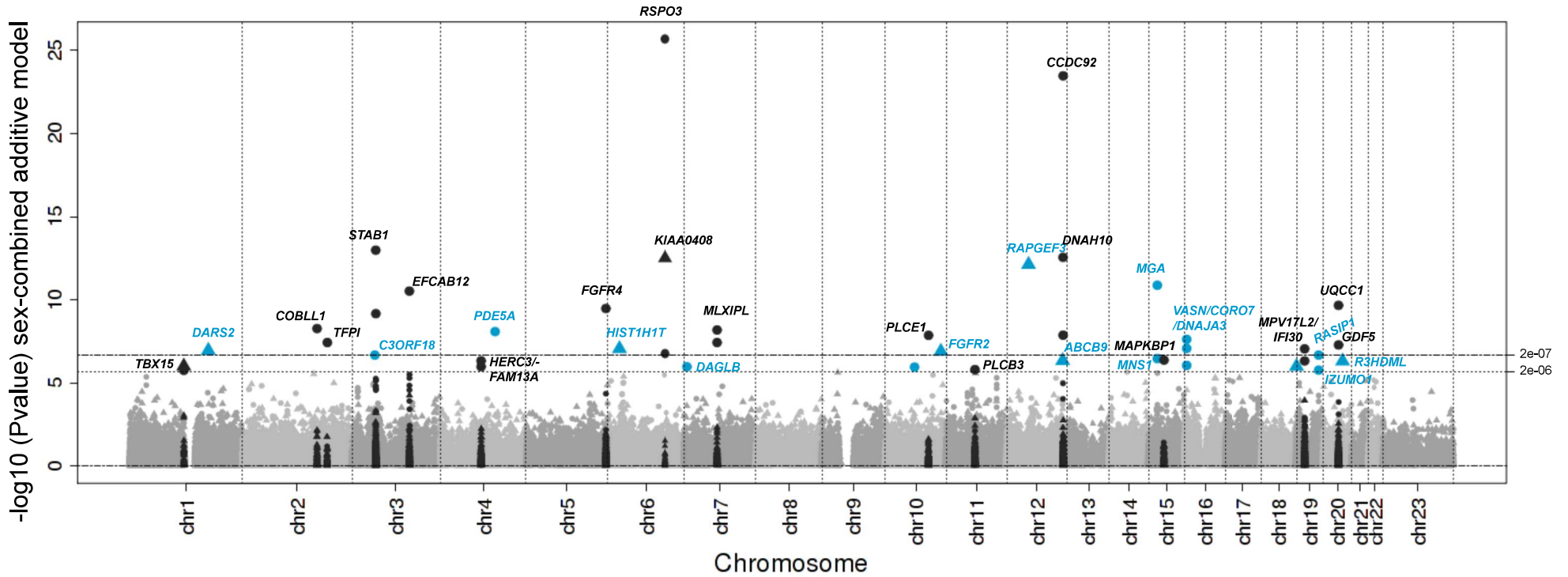
af) *UQCC1* & *GDF5* All Ancestry, Sexes-Combined



ag) *R3HDML* All Ancestry, Sexes-Combined

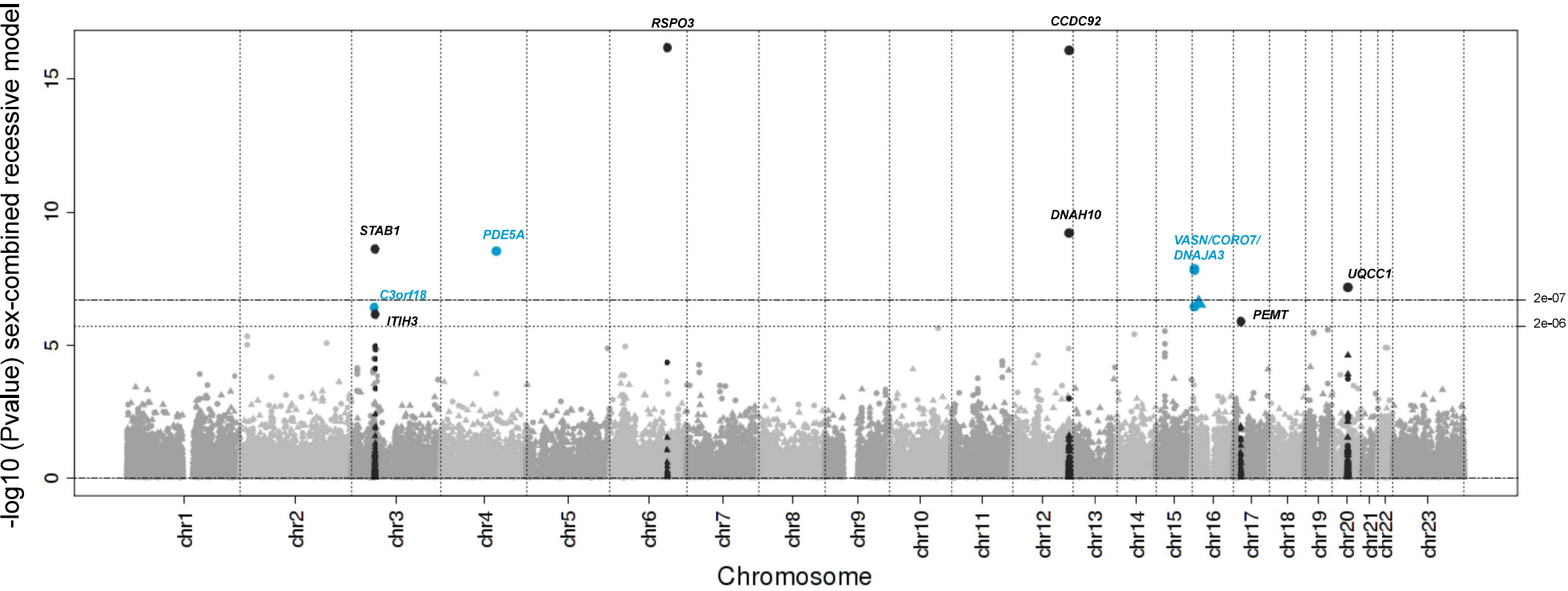


Supplementary Figure 5. Manhattan plot. Manhattan plot of the European, sexes-combined, single variant, additive model analysis. Only splice site and coding variants are shown. key: Triangle - MAF <1%, Square- MAF 1% to 5%, Circle- >5%, black - known loci, blue- novel loci.



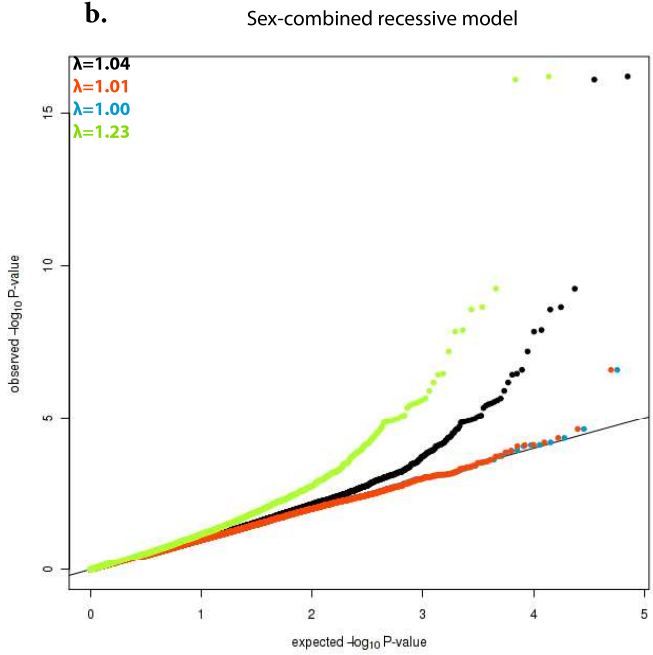
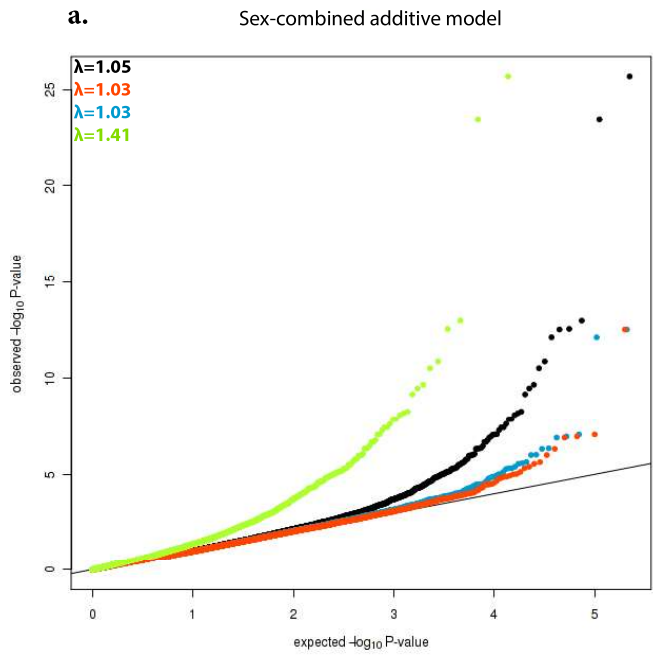
*rs2255703 in *PLXND1* and rs1051860 in *ARID4A* are not labeled because $P_{\text{stage1}} < 2 \times 10^{-6}$

Supplementary Figure 6. Manhattan plot. Manhattan plot of the European, sexes-combined, single variant, recessive model analysis. Only splice site and coding variants are shown. key: Triangle - MAF <1%, Square- MAF 1% to 5%, Circle- >5%, black - known loci, blue- novel loci.



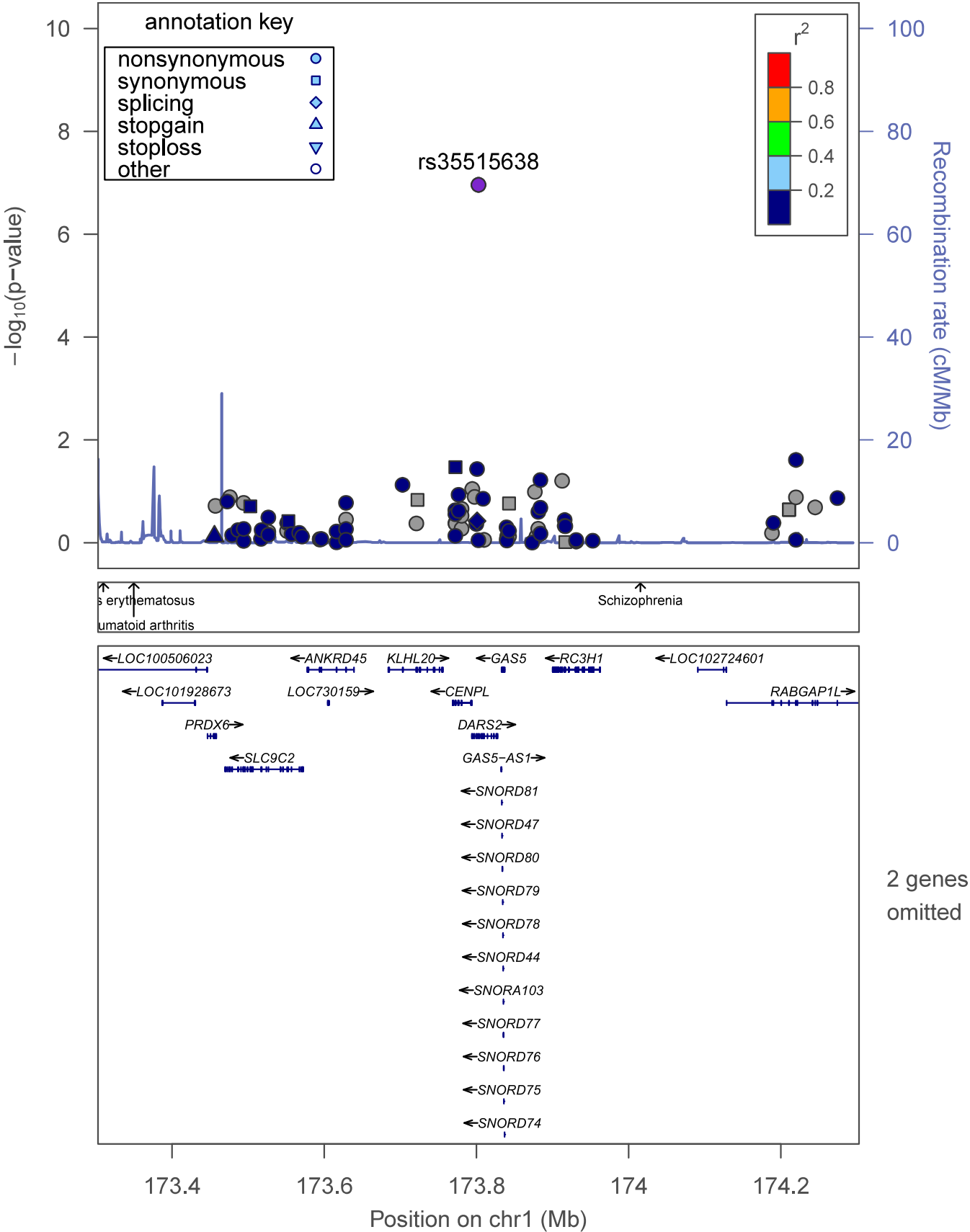
Supplementary Figure 7. QQ Plots. QQ Plots for European, sexes-combined, single variant meta-analyses. Only splice site and coding variants are included: a) additive model; b) recessive model.

Legend:
All SNPs
MAF \leq 0.01
MAF \leq 0.05
MAF $>$ 0.05

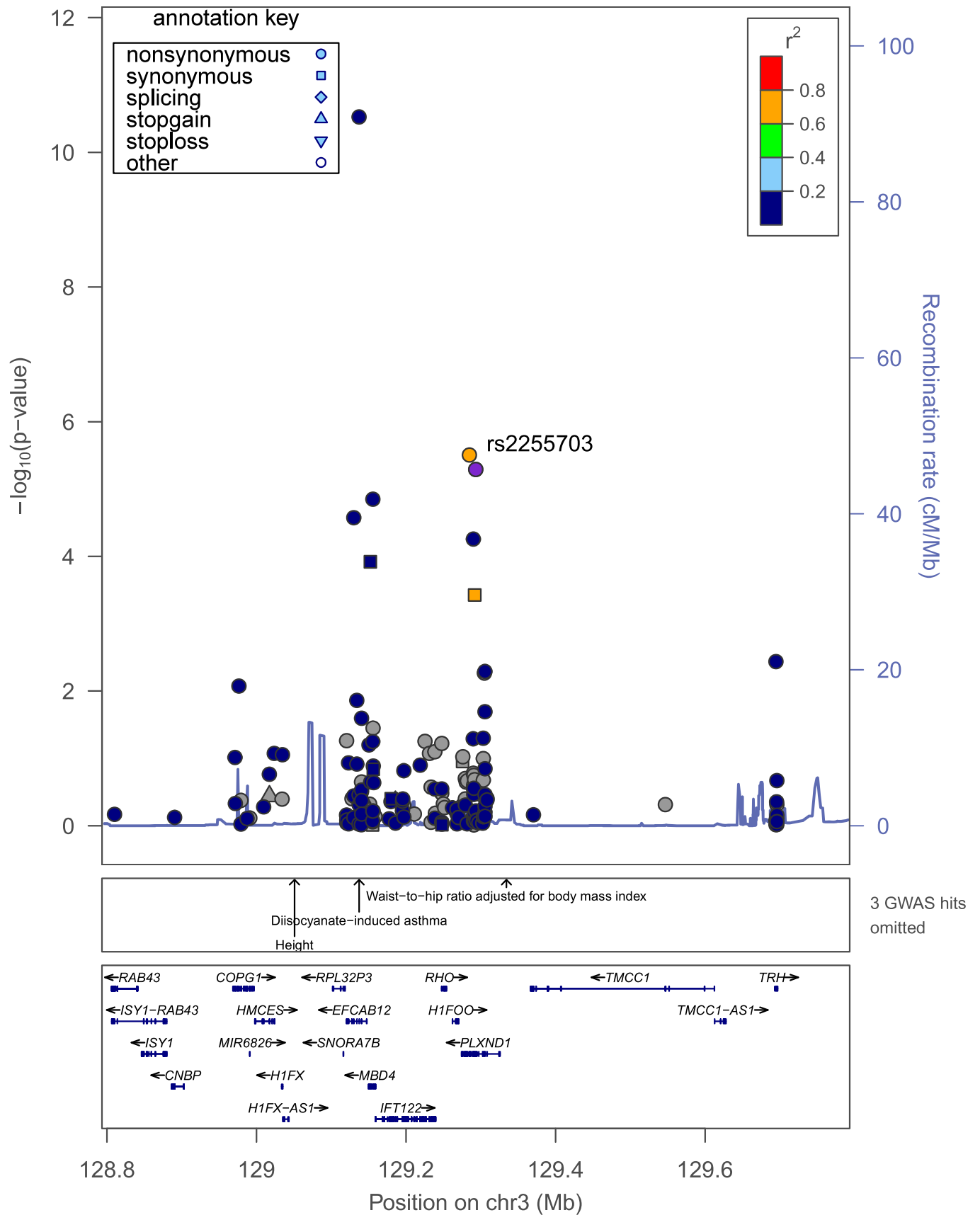


Supplementary Figure 8. Regional association plots. Regional association plots for each significant locus in the European, sexes-combined, meta-analysis. All results are shown for each significant region for the stratum (men, women, or sexes-combined) in which the association was most significant, as noted in the figure title. The plots appear in chromosome:position order. Dot color reflects r^2 calculated from the ARIC dataset. Point symbols represent variant functional classifications: a) rs35515638, *DARS2*; b) rs2255703, *PLXND1*; c) rs1051860, *ARID4A*; d) rs3959569, *MAPKBP1* and *MGA*.

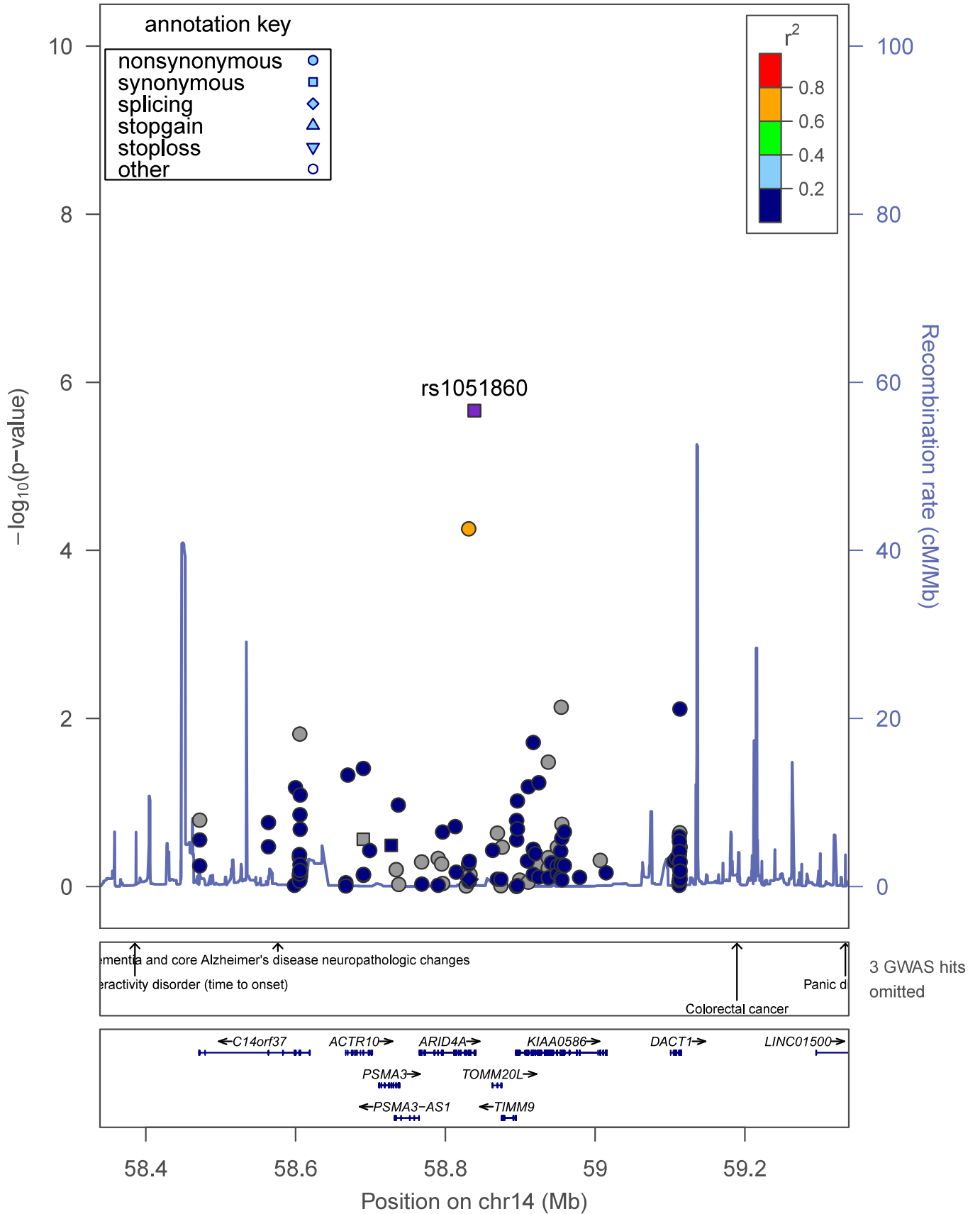
a) *DARS2* European, Sexes-Combined



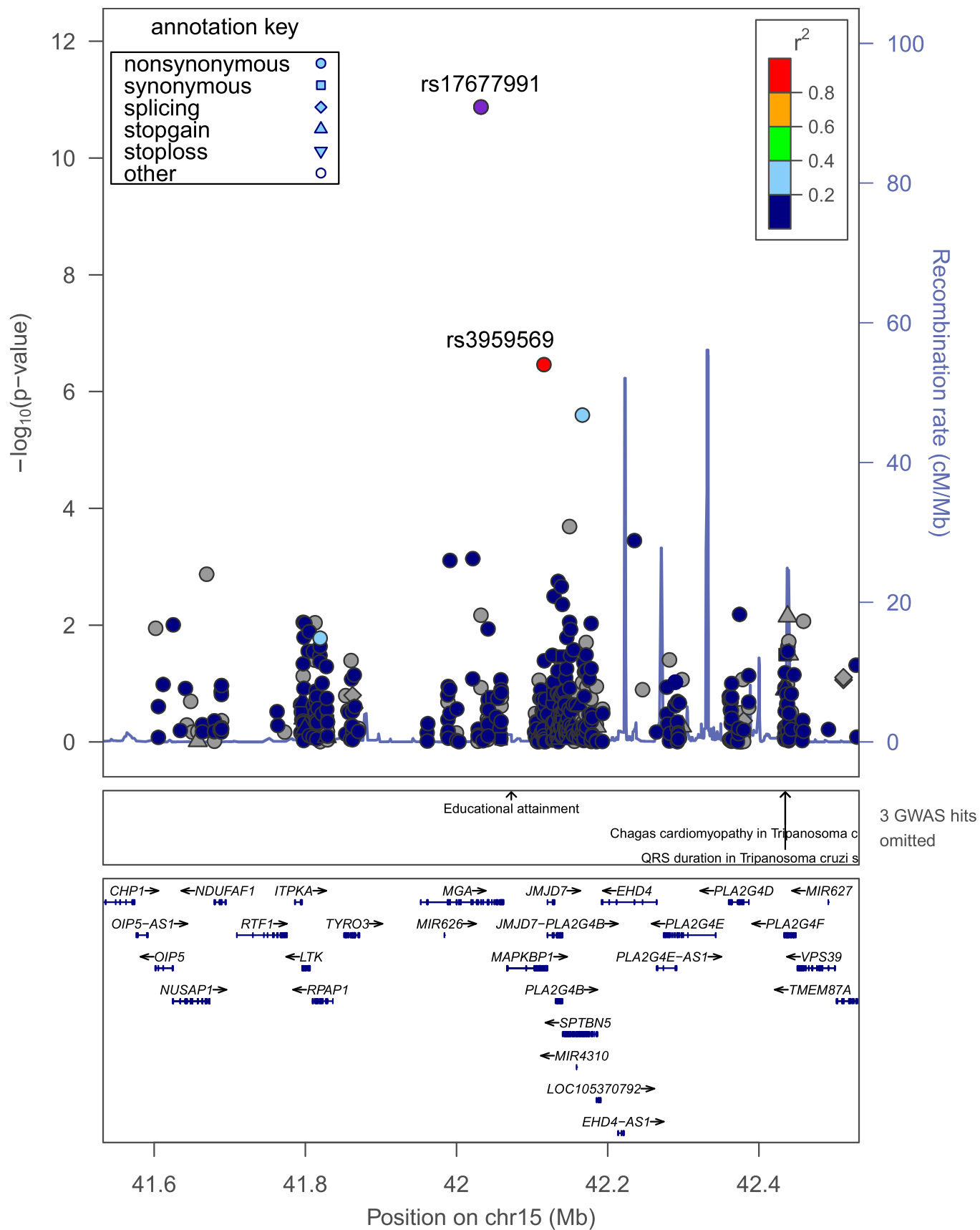
b) *PLXND1* European, Sexes-Combined



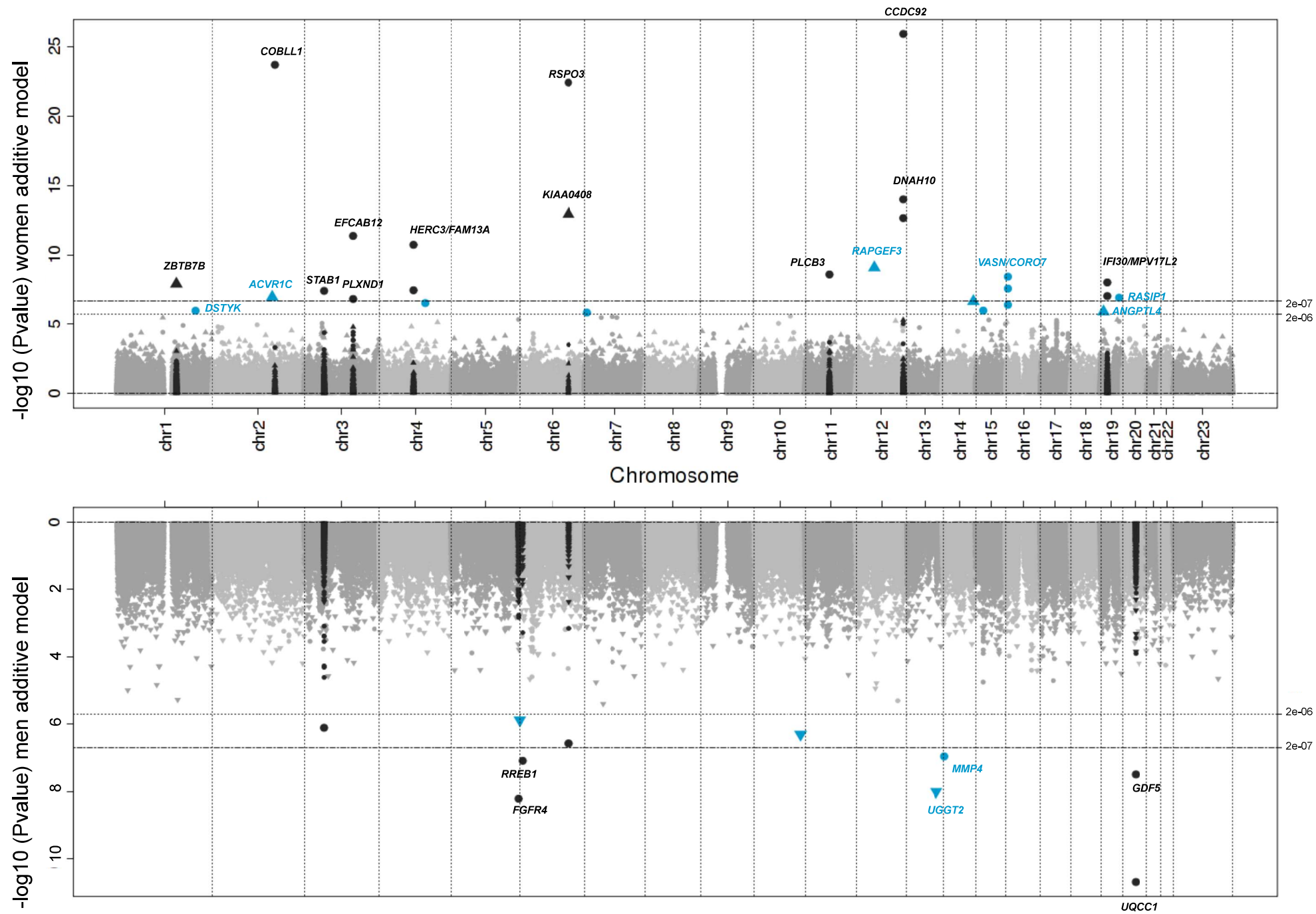
c) *ARID4A* European, Sexes-Combined



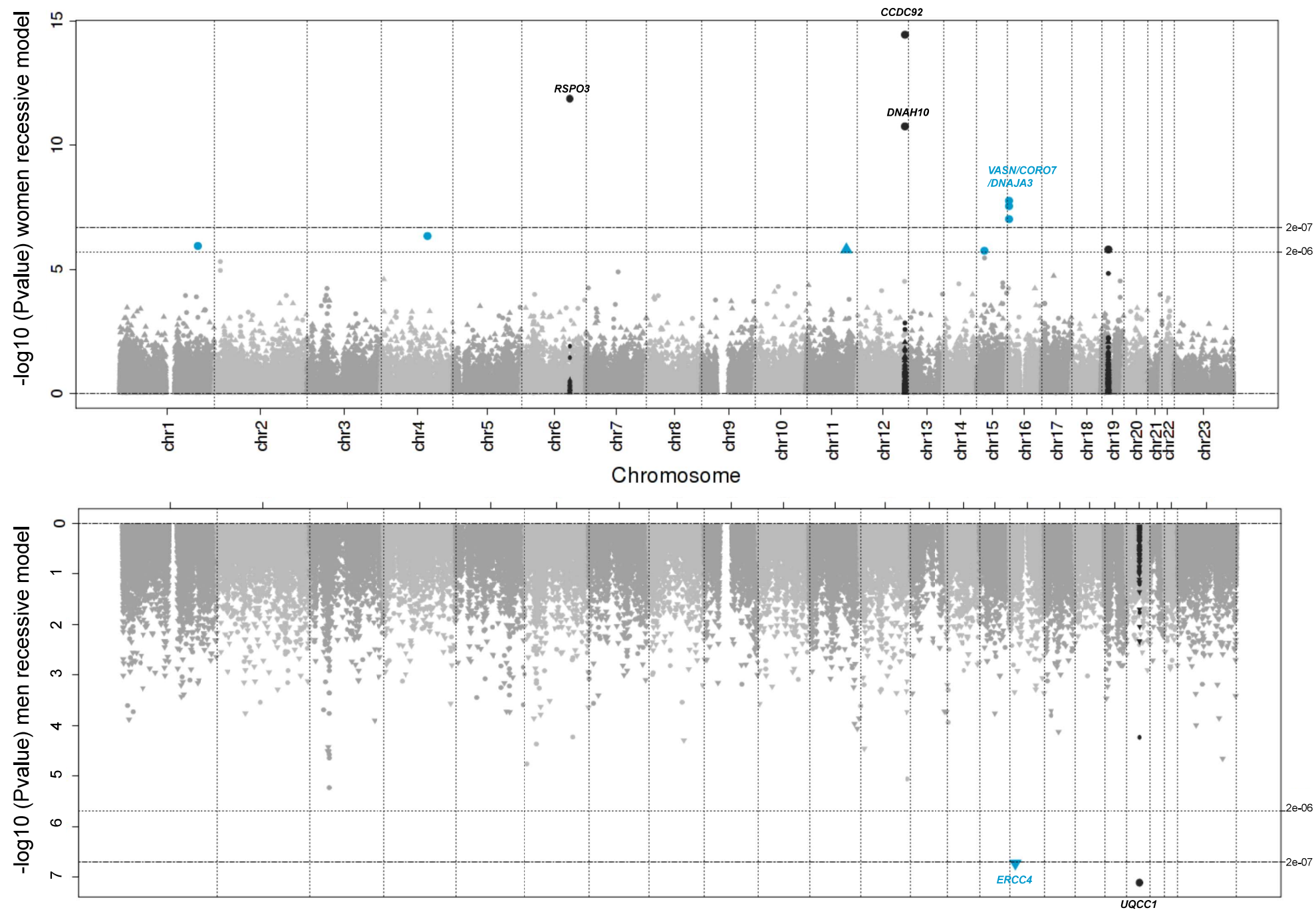
d) *MGA* & *MAPKBP1* European, Sexes-Combined



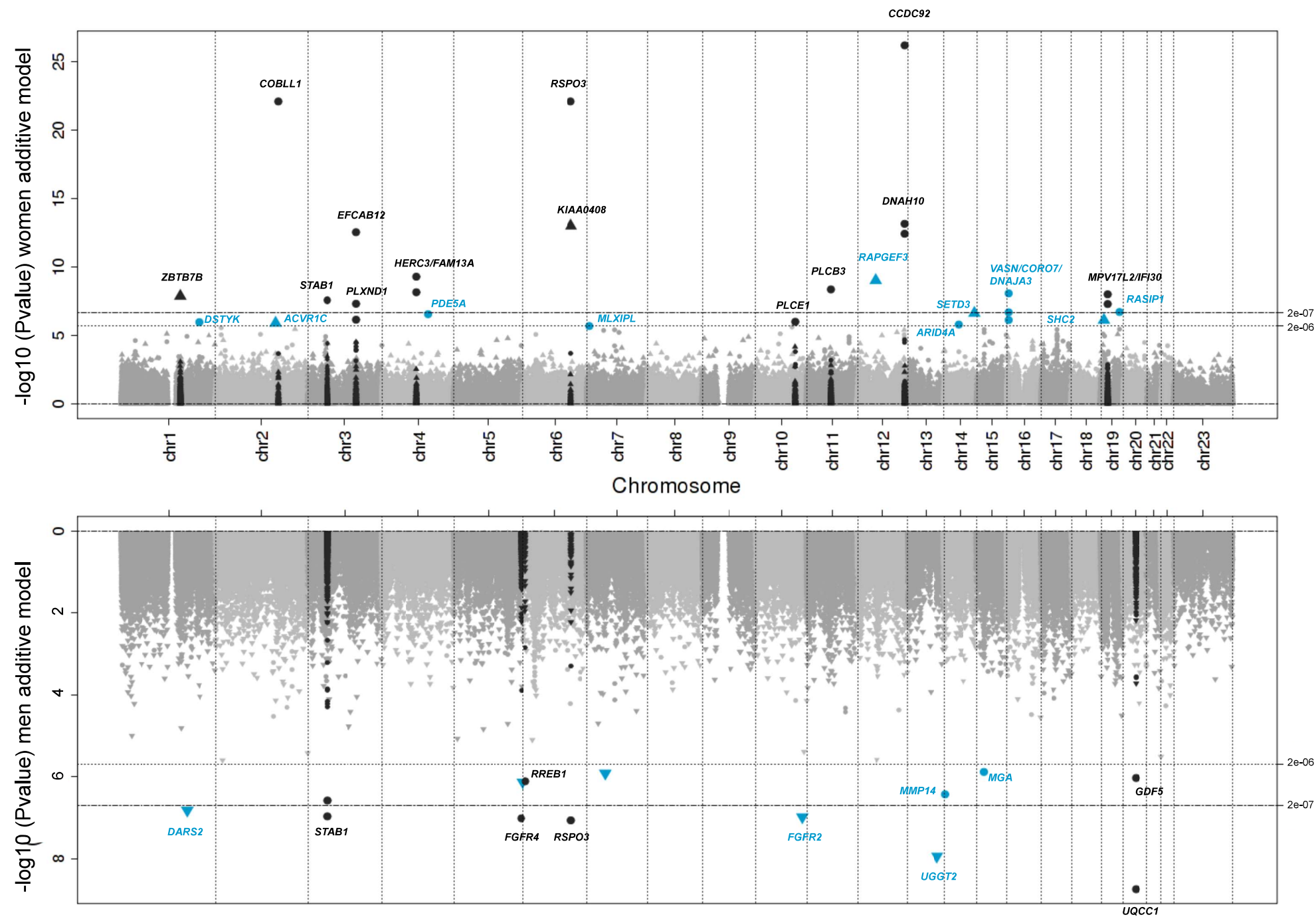
Supplementary Figure 9. Miami plot. Miami plot of the all ancestry, sex-stratified, single variant, additive model analysis. Only splice site and coding variants are shown. key: Triangle- MAF <1%, Square- MAF 1% to 5%, Circle- >5%, black- known loci, blue- novel significant loci.



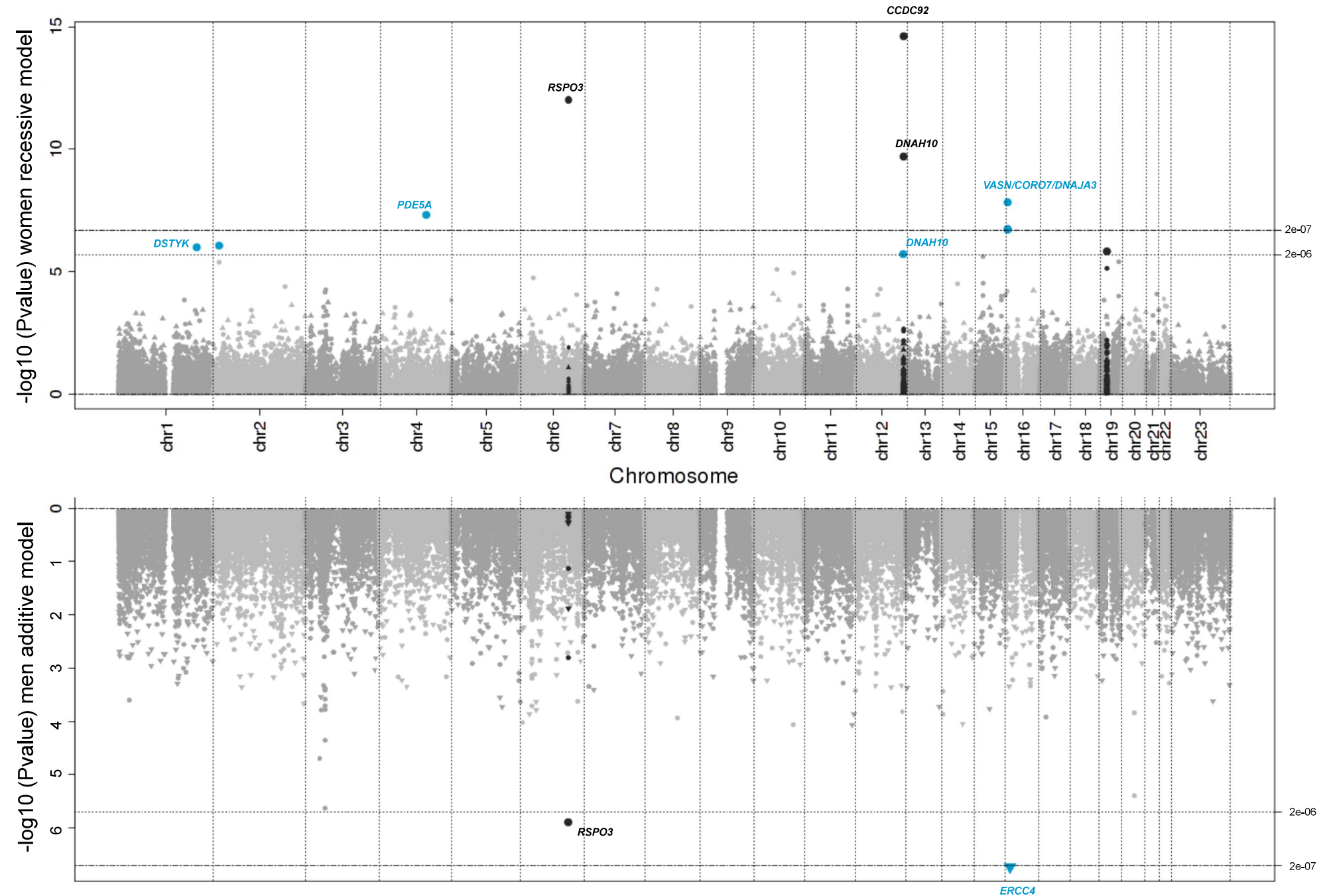
Supplementary Figure 10. Miami plot. Miami plot of the all ancestry, sex-stratified, single variant, recessive model analysis. Only splice site and coding variants are shown. key: Triangle- MAF <1%, Square- MAF 1% to 5%, Circle- > 5%, black- known loci, blue- novel significant loci.



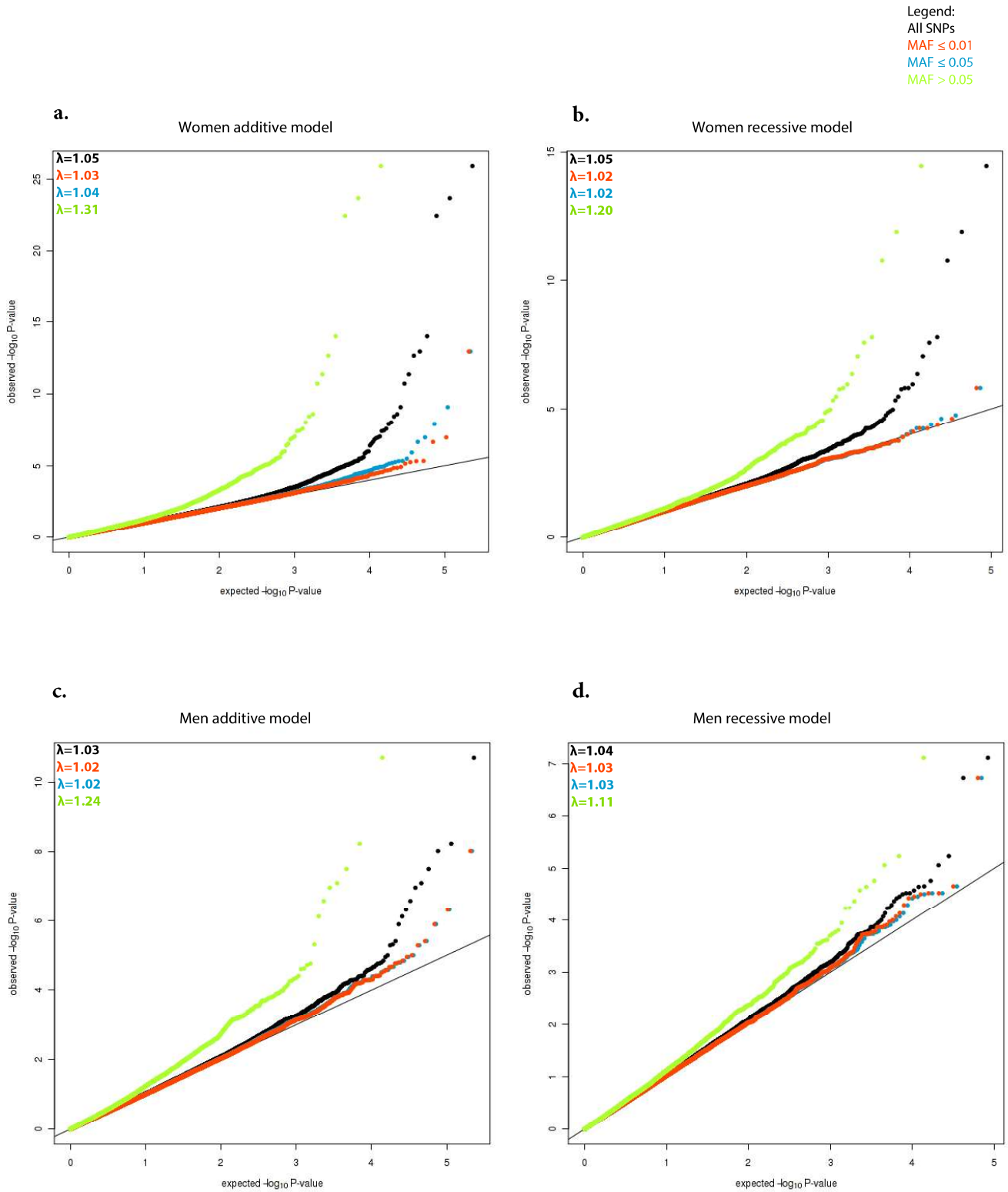
Supplementary Figure 11. Miami plot. Miami plot of the European sex-stratified single variant additive model analysis. Only splice site and coding variants are shown. key: Triangle- MAF <1%, Square- MAF 1% to 5%, Circle- > 5%, black- known loci, blue- novel significant loci.



Supplementary Figure 12. Miami plot. Miami plot of the European, sex-stratified, single variant, recessive model analysis. Only splice site and coding variants are shown. key: Triangle- MAF <1%, Square- MAF 1% to 5%, Circle- > 5%, black- known loci, blue- novel significant loci.

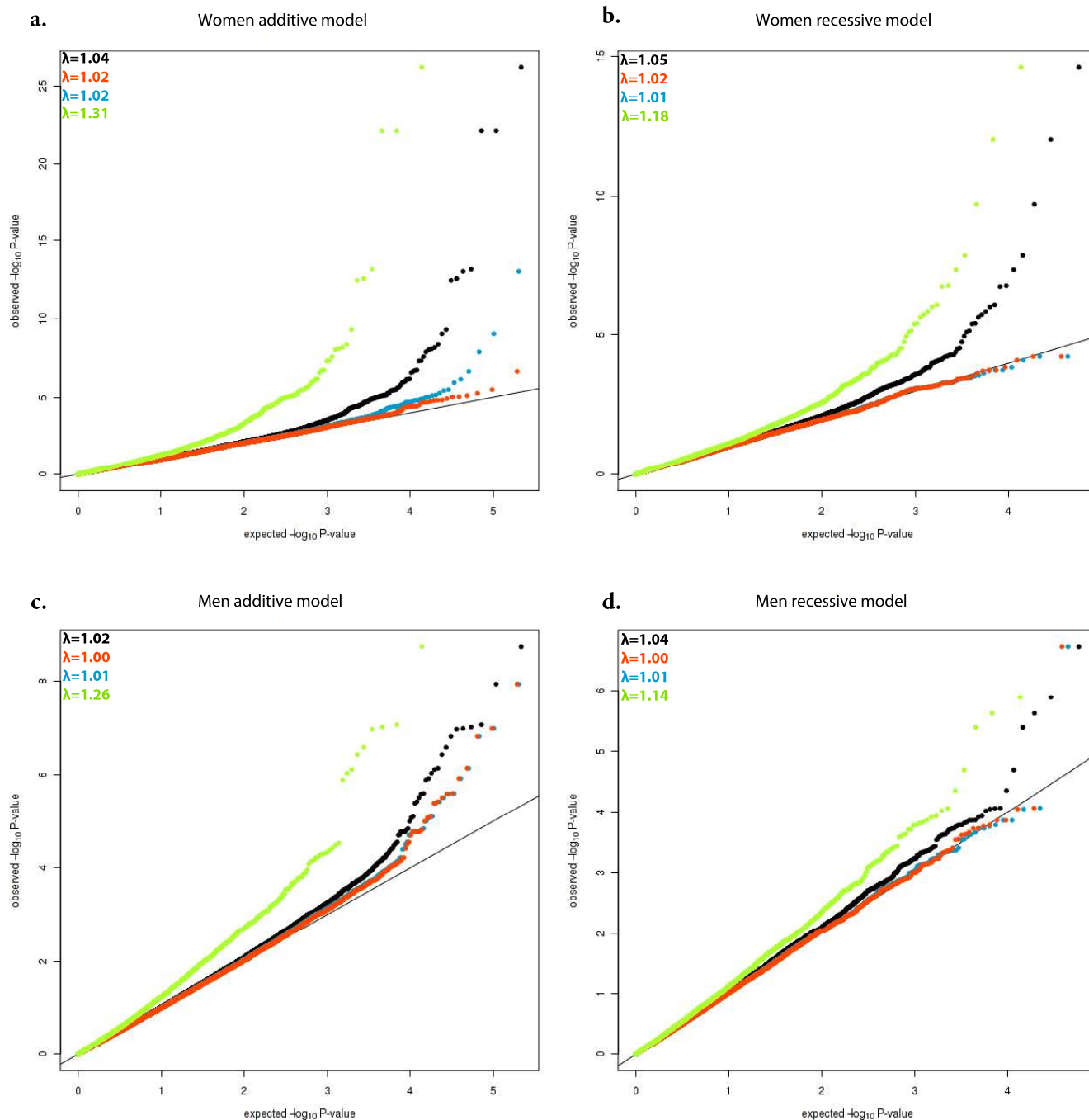


Supplementary Figure 13. QQ plots. QQ lots for all ancestry, sex-stratified, single-variant analyses. Only splice site and coding variants are included: a) women-only, additive model; b) women-only, recessive model; c) men-only, additive model; d) men-only, recessive model.



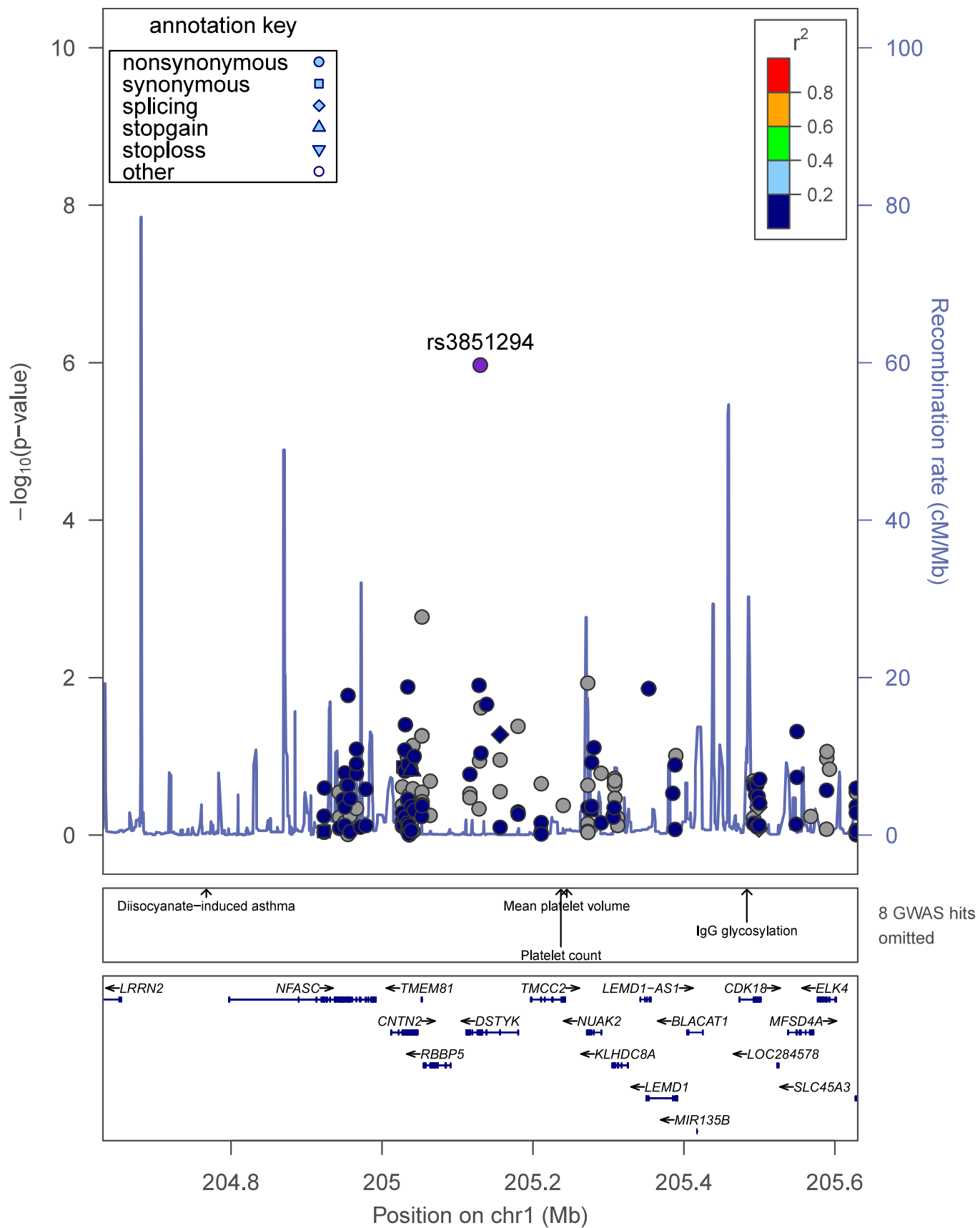
Supplementary Figure 14. QQ plots. QQ lots for European, sex-stratified, single-variant analyses. Only splice site and coding variants are included: a) women-only, additive model; b) women-only, recessive model; c) men-only, additive model; d) men-only, recessive model.

Legend:
 All SNPs
 MAF \leq 0.01
 MAF \leq 0.05
 MAF $>$ 0.05

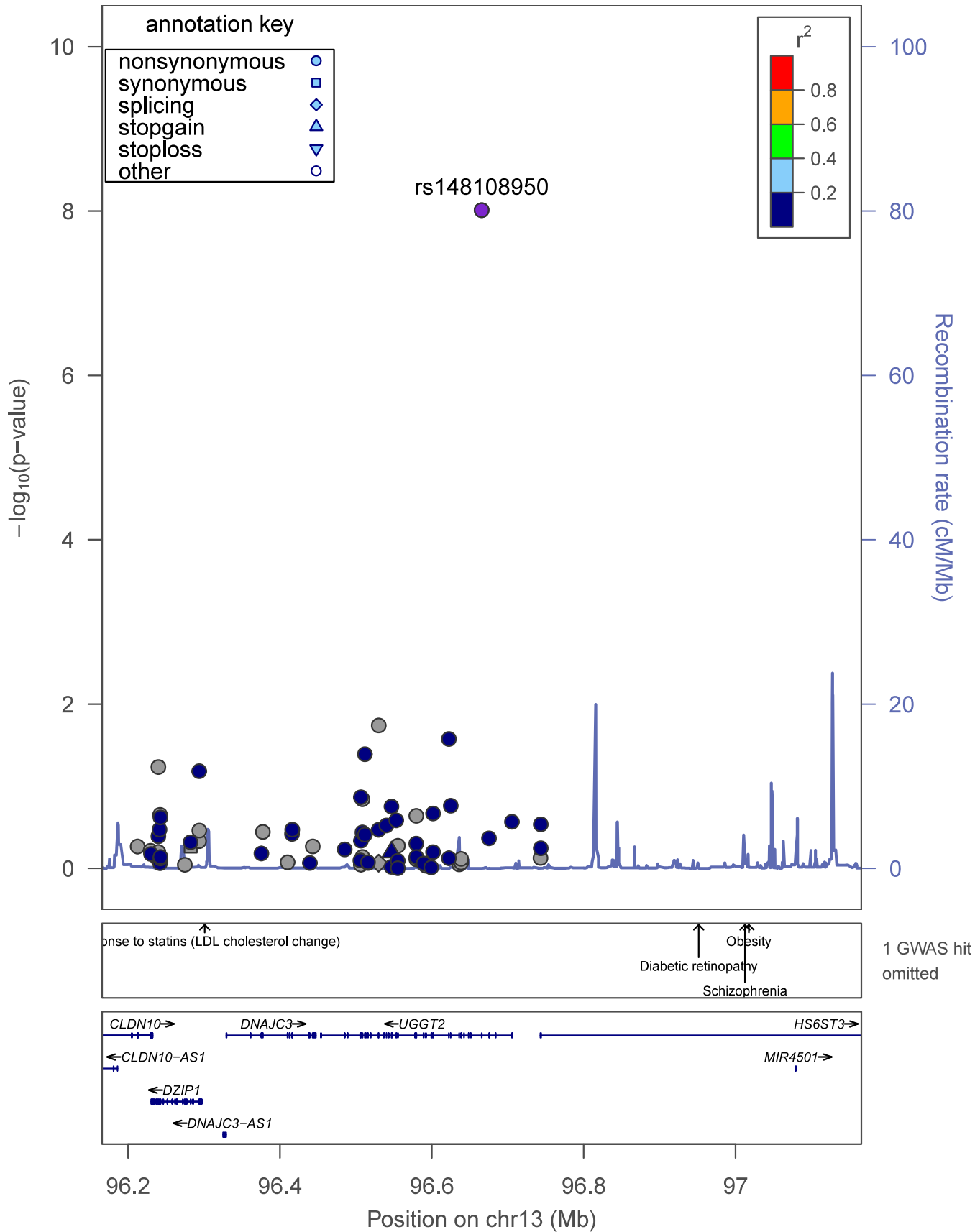


Supplementary Figure 15. Regional association plots. Regional association plots for each significant locus in the sex-stratified, meta-analysis, that was not significant in the sexes-combined results. All results are shown for each significant region for the stratum (men or women) in which the association was most significant, as noted in the figure title. The plots appear in chromosome:position order. Dot color reflects r^2 calculated from the ARIC dataset. Point symbols represent variant functional classifications: a) rs3851294, *DSTYK*; b) rs148108950, *UGGT2*; c) rs1042704, *MMP14*; d) rs116843064, *ANGPTL4*.

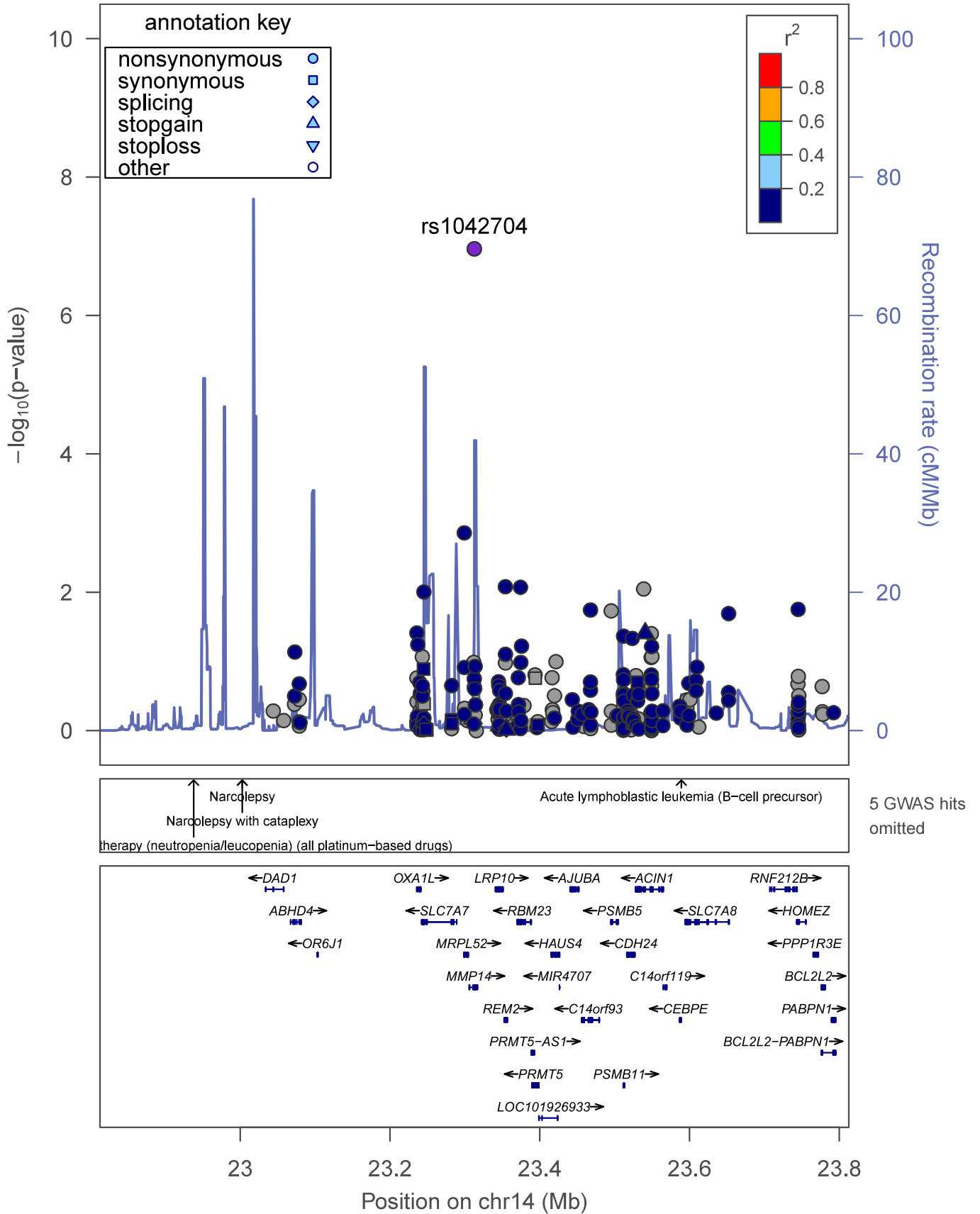
a) *DSTYK* All Ancestry, Women



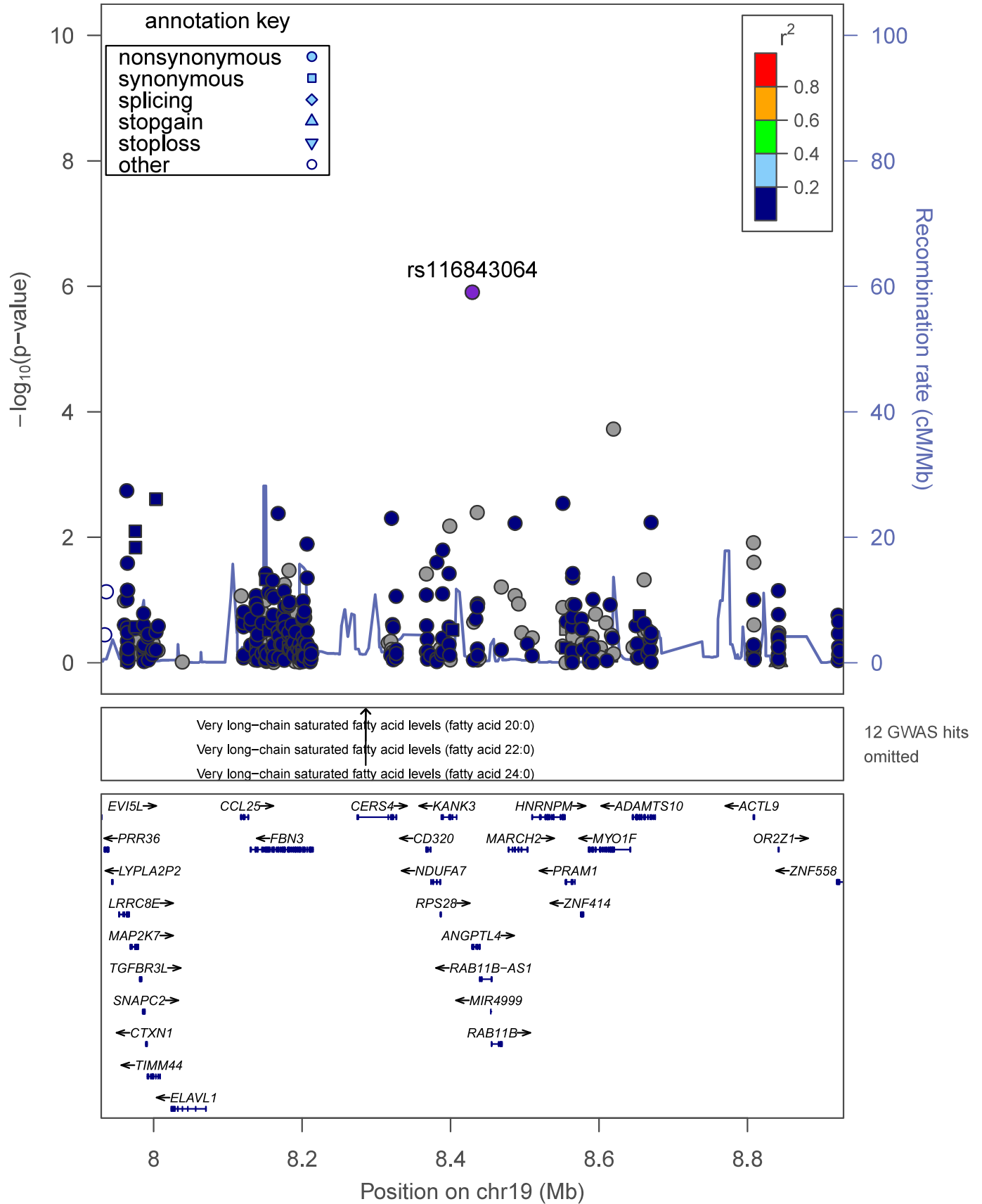
b) *UGGT2* All Ancestry, Men



c) *MMP14* All Ancestry, Men

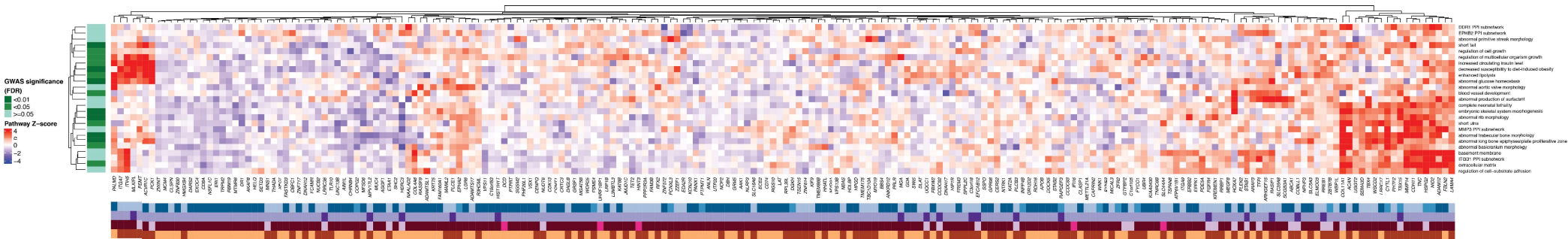


d) *ANGPTL4* All Ancestry, Women

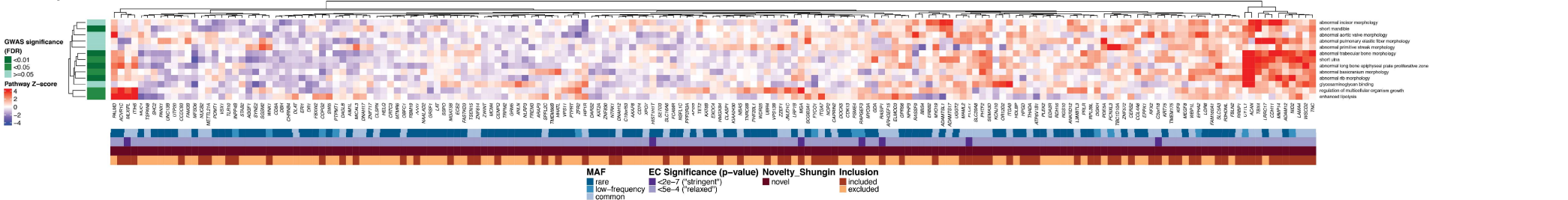


Supplementary Figure 16. Heatmaps showing full DEPICT gene set enrichment results. a) all coding variants and b) all coding variants excluding those mapping to a gene included in the Shungin et al. DEPICT analysis.¹⁰ For any given square, the color indicates how strongly the corresponding gene (shown on the x-axis) is predicted to belong to the reconstituted gene set (y-axis). This value is based on the gene's z-score for gene set inclusion in DEPICT's reconstituted gene sets, where red indicates a higher and blue a lower z-score. To visually reduce redundancy and increase clarity, we chose one representative "meta-gene set" for each group of highly correlated gene sets based on affinity propagation clustering (Online Methods, Supplementary Note 2). Heatmap intensity and DEPICT P-values (see P-values in Supplementary Data 4-5) correspond to the most significantly enriched gene set within the meta-gene set. Annotations for the genes indicate (1) the minor allele frequency of the significant ExomeChip (EC) variant (shades of blue; if multiple variants, the lowest-frequency variant was kept), (2) whether the variant's P-value reached array-wide significance ($<2 \times 10^{-7}$) or suggestive significance ($<5 \times 10^{-4}$) (shades of purple), (3) whether the variant was novel, overlapping "relaxed" GWAS signals from Shungin et al.¹⁰ (GWAS $P < 5 \times 10^{-4}$), or overlapping "stringent" GWAS signals (GWAS $P < 5 \times 10^{-8}$) (shades of pink), and (4) whether the gene was included in the gene set enrichment analysis or excluded by filters (shades of brown/orange) (Online Methods and Supplementary Note 2). Annotations for the gene sets indicate if the meta-gene set was found significant (shades of green; FDR < 0.01 , < 0.05 , or not significant) in the DEPICT analysis of GWAS results from Shungin et al.¹⁰

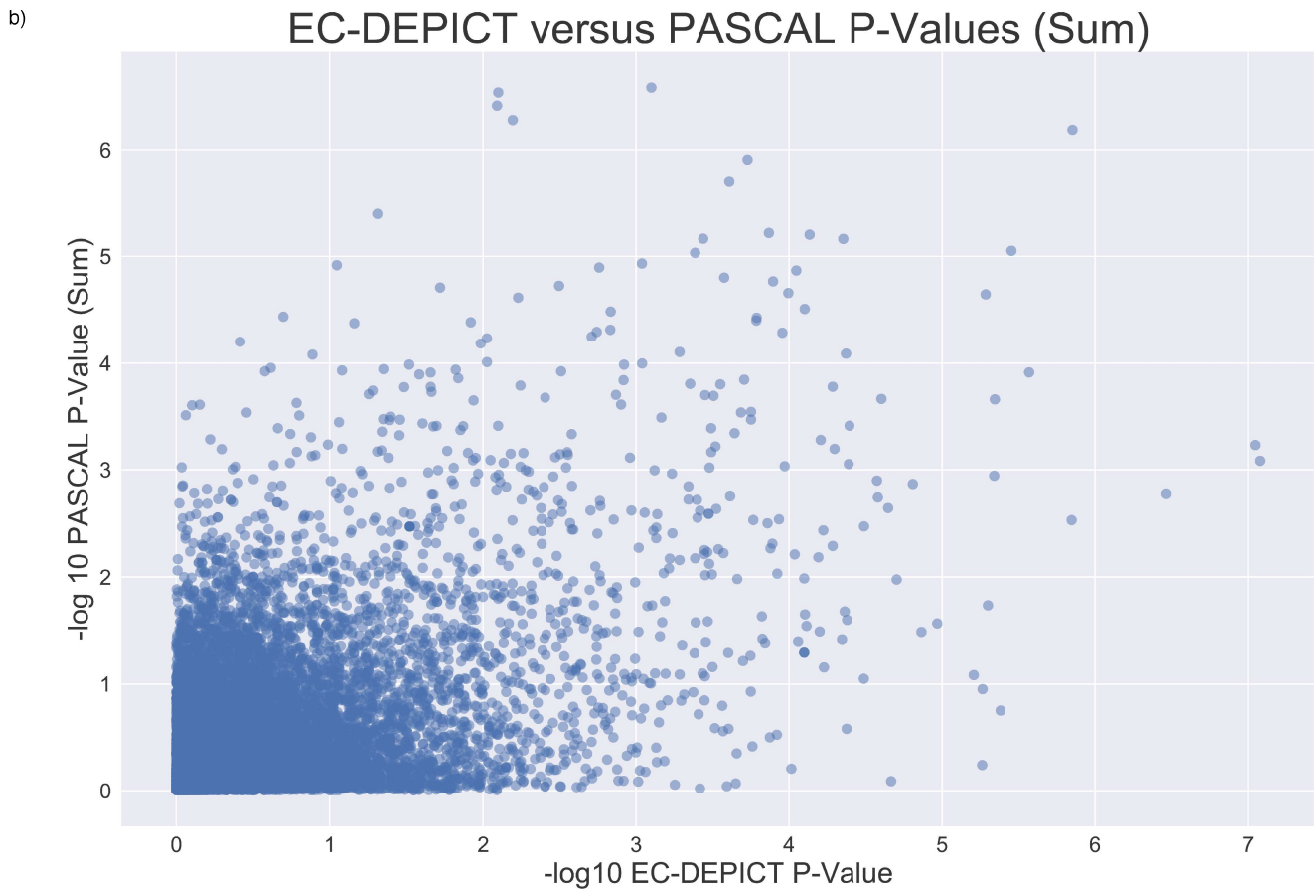
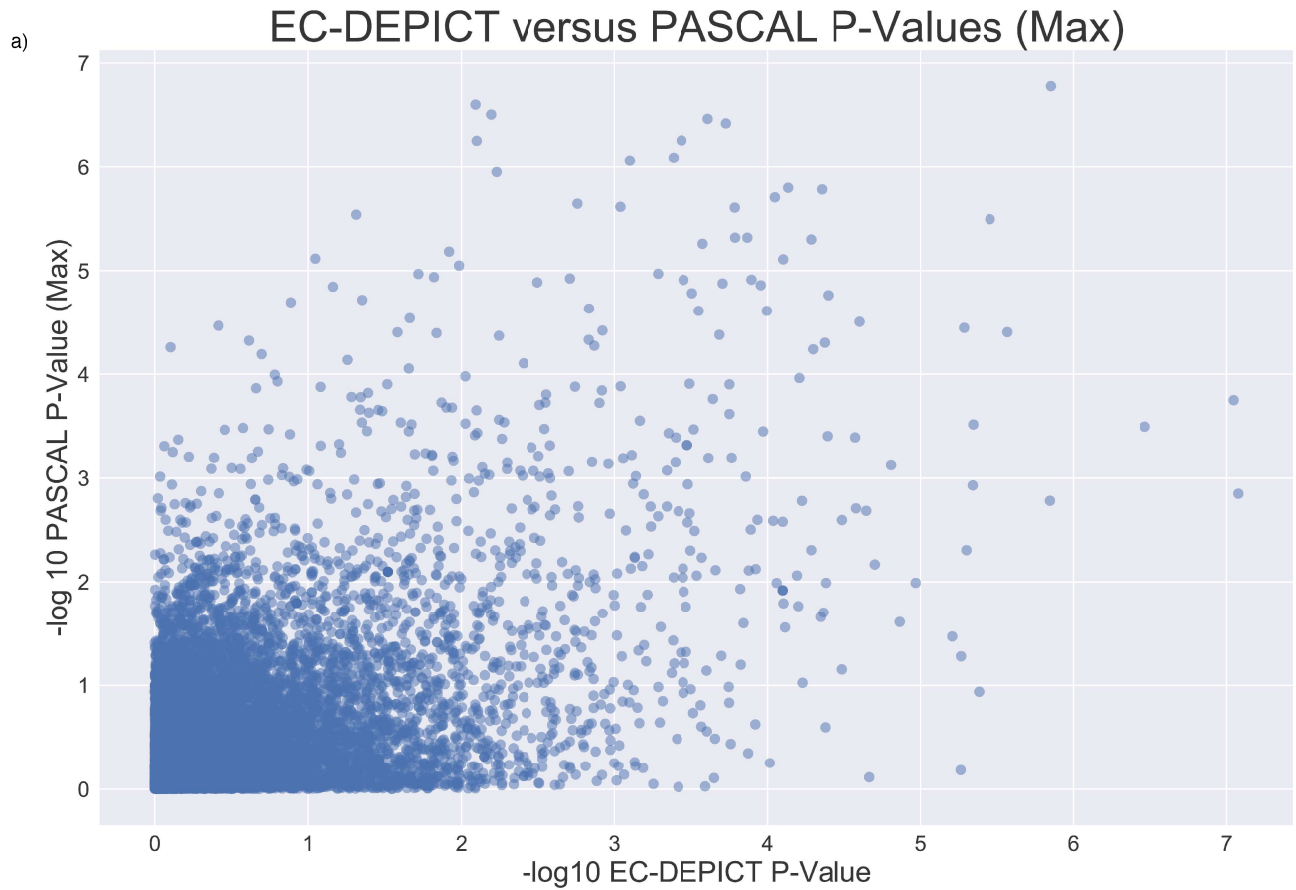
a)



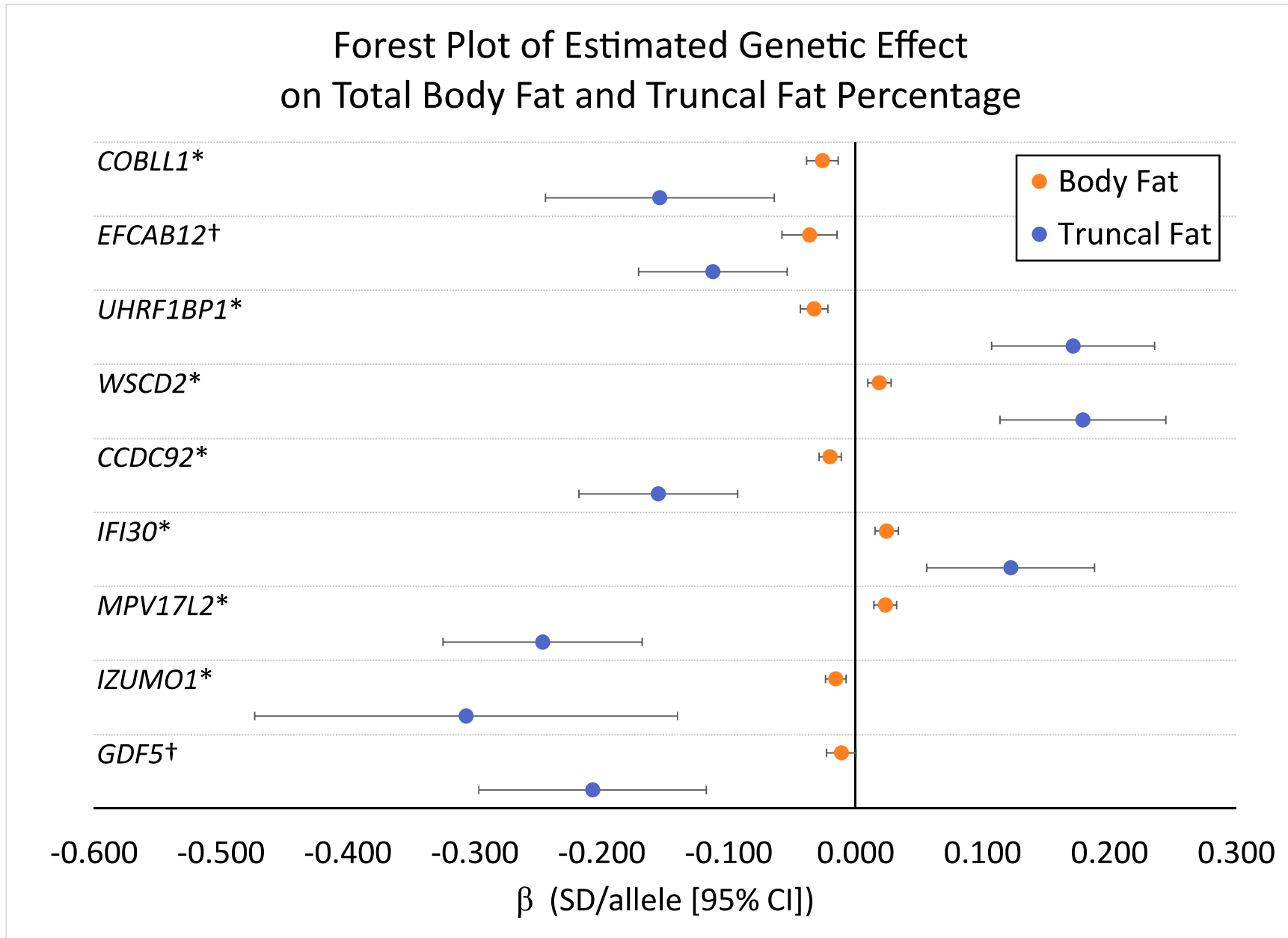
b)



Supplementary Figure 18. Comparison of $-\log_{10}(\text{p-values})$ for each gene set from EC-DEPICT and PASCAL. The PASCAL max statistic is shown in a) and the sum statistic in b). For the max statistic, $r = 0.277$ ($p = 9.8\text{e-}253$) and for the sum statistic, $r = 0.287$ ($p = 5.42\text{e-}272$).

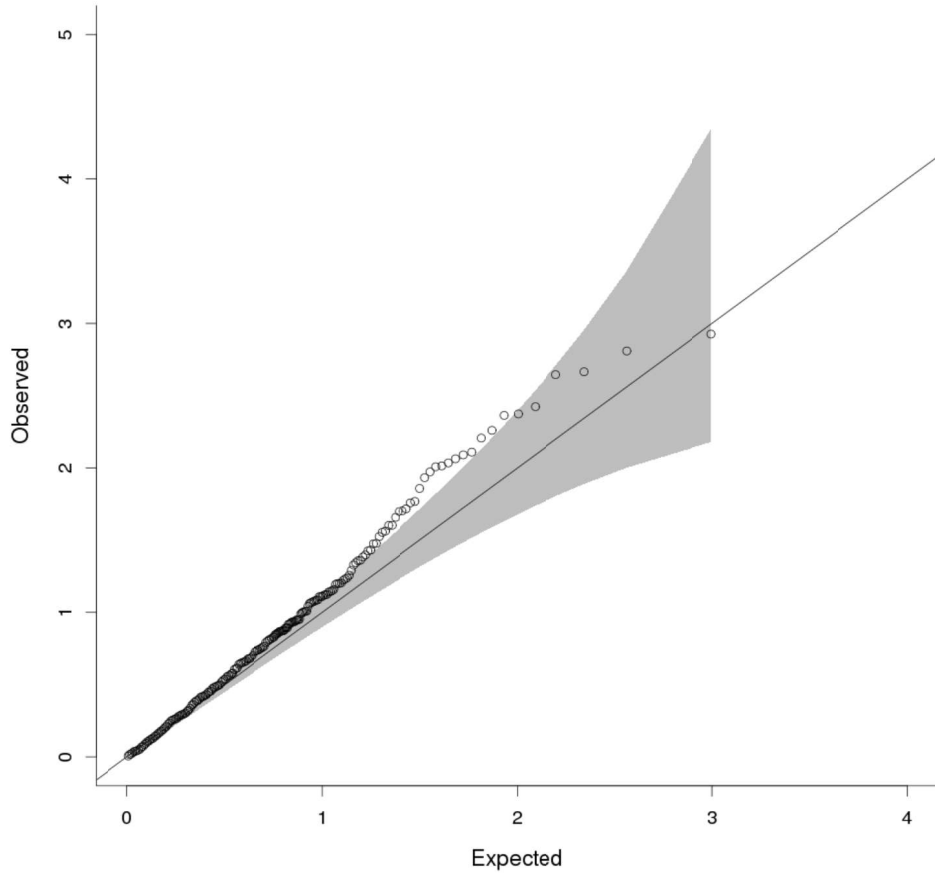


Supplementary Figure 20. Forest plot of WHRadjBMI loci associated with measures of body fat. All effect estimates (95% confidence interval) are oriented on the WHRadjBMI increasing allele and are provided as standard deviation per allele. Only variants that reach Bonferroni significance are provided ($P < 0.001$). *Effects are provided for the combined sexes analysis. †Effects are provided from the women-only analysis.

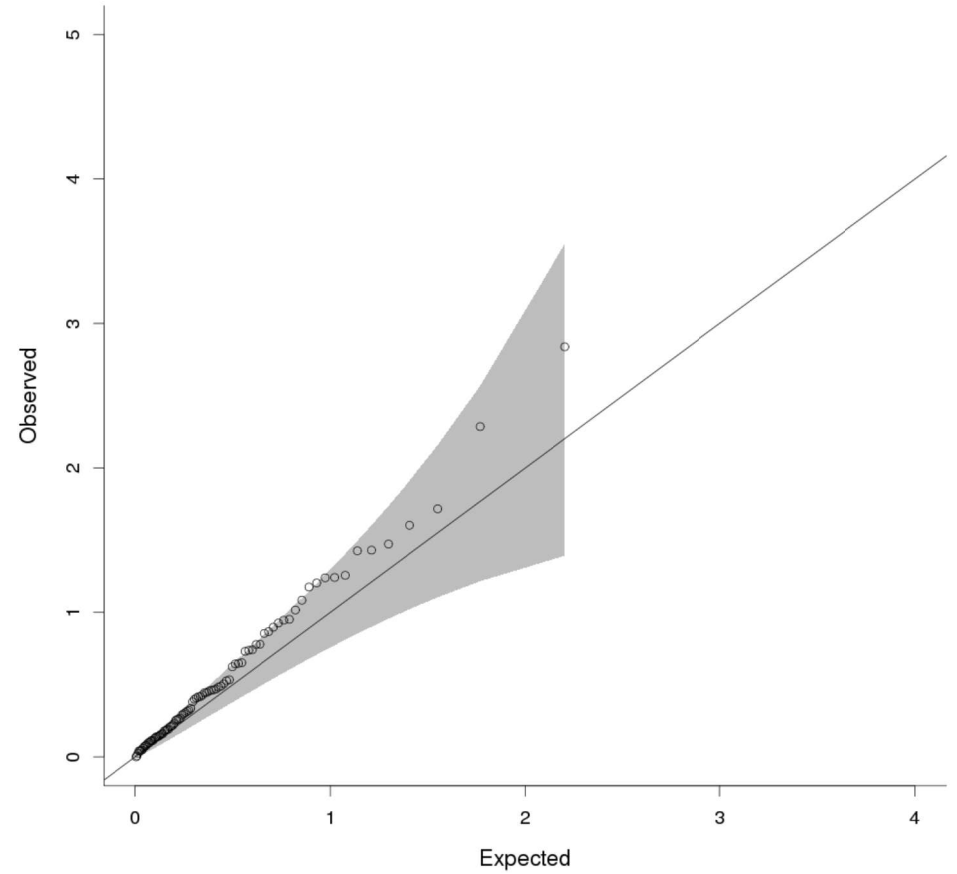


Supplementary Figure 21. Monogenic Enrichment QQ Plots. QQ plots of all-ancestry association results for single variants in established monogenic insulin resistance and lipodystrophy genes.

SNPs in monogenic insulin resistance genes

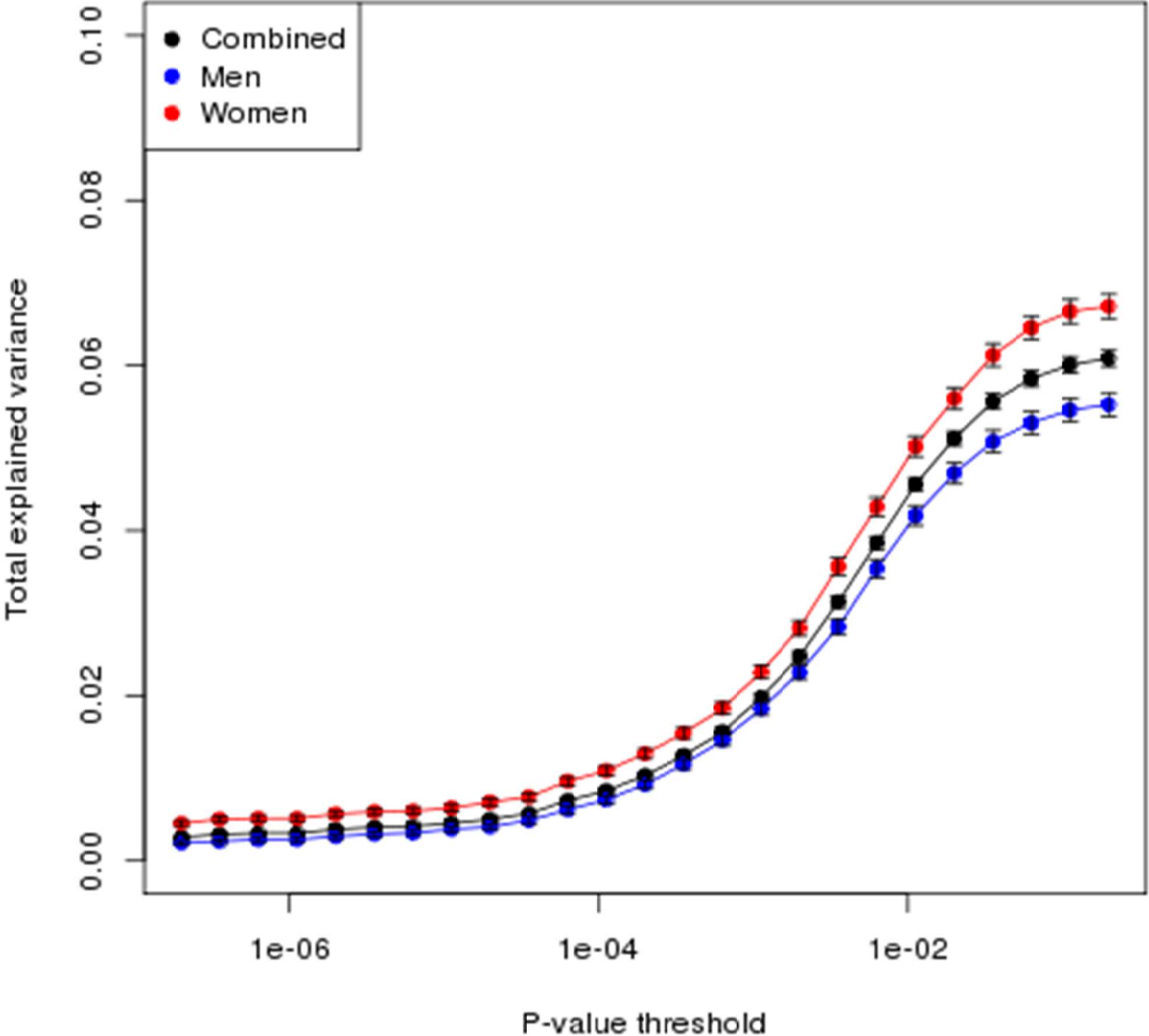


SNPs in monogenic lipodystrophy genes

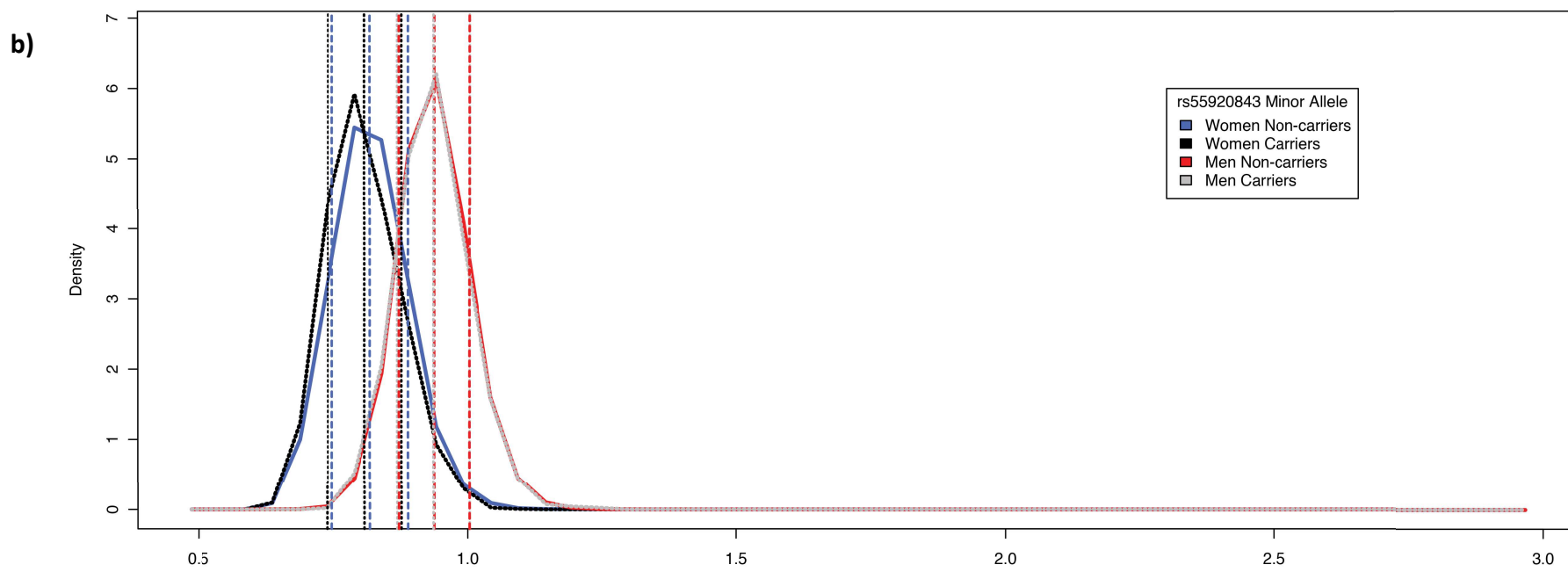
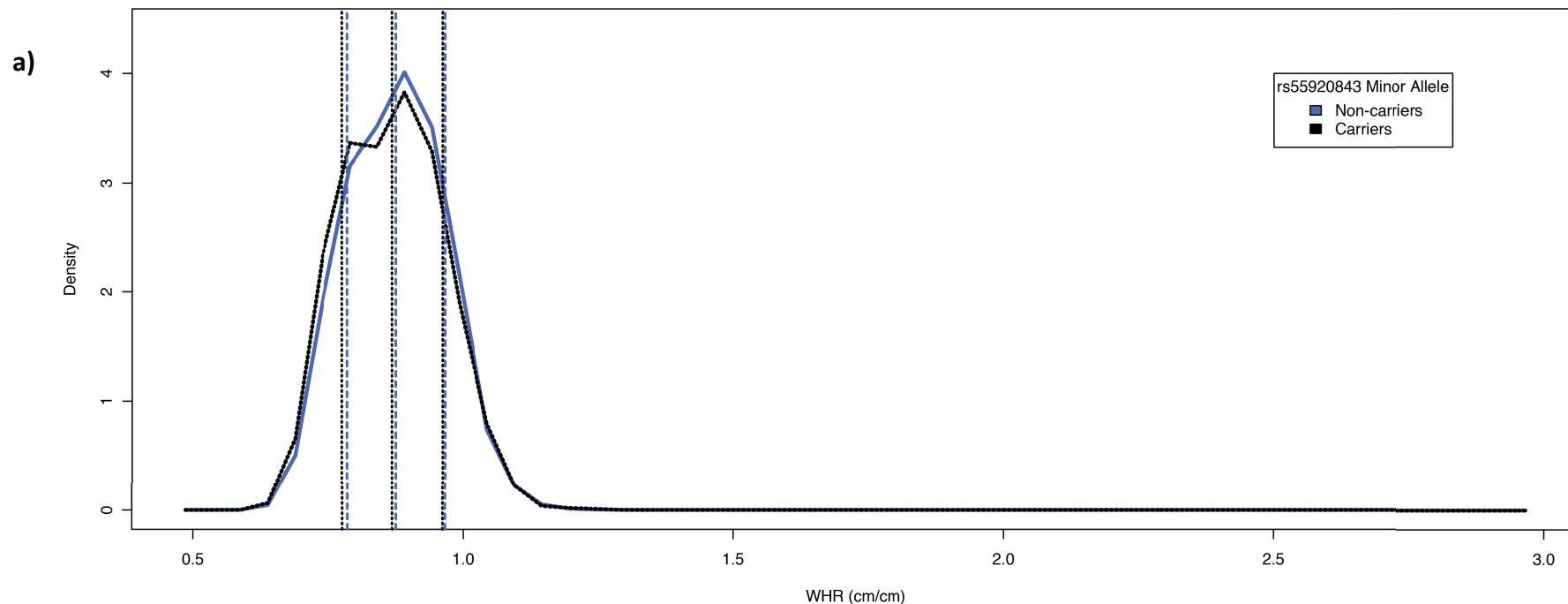


Supplementary Figure 22. Estimates of variance explained. Estimates of explained variance (+/- SE) in WHRadjBMI by SNPs meeting varying thresholds of overall associated in primary meta-analysis of all ancestry, sexes-combined.

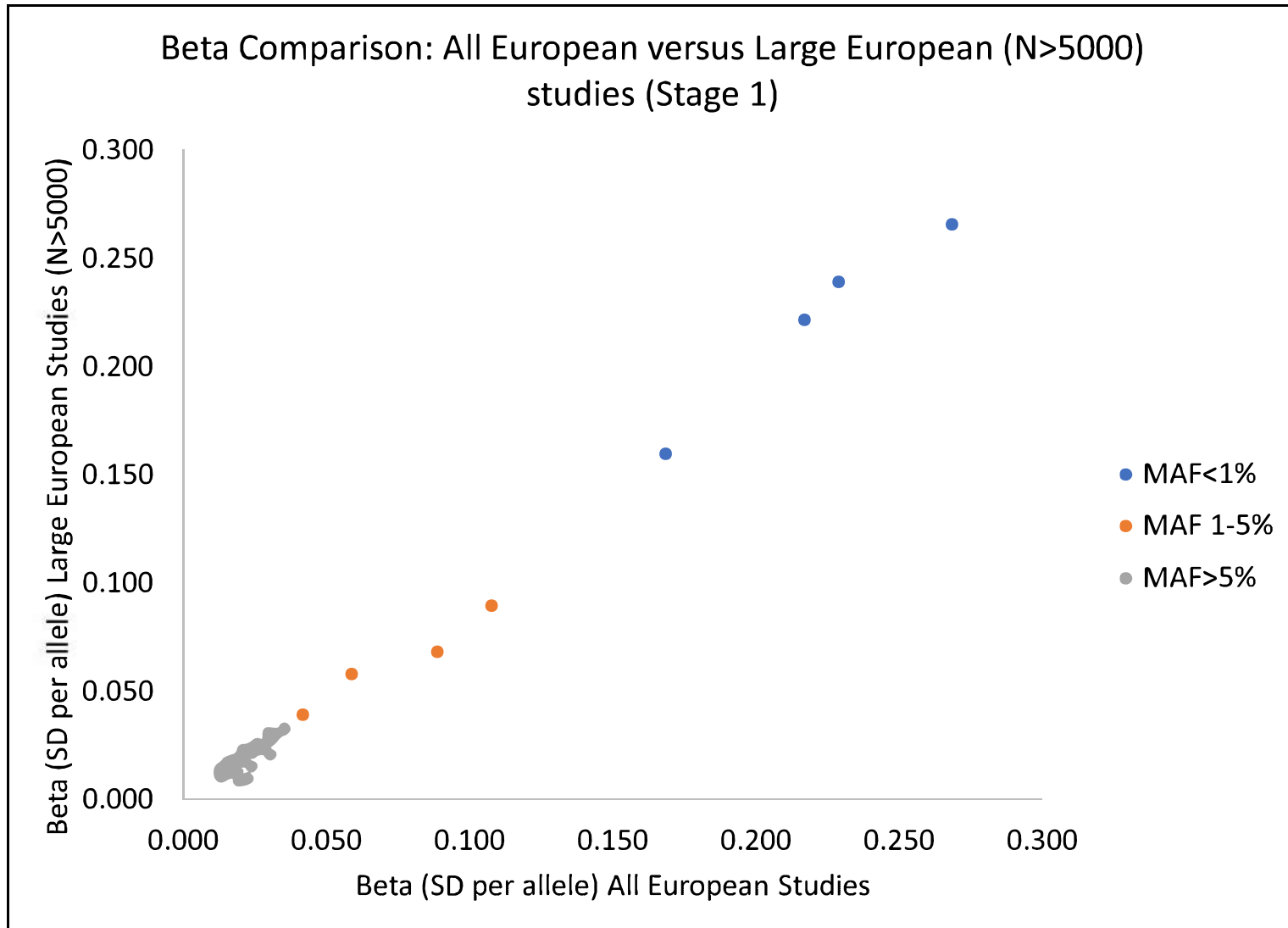
Variance explained for WHRadjBMI selected on Combined Sexes



Supplementary Figure 23. Penetrance Analysis for ACVR1C rs55920843 Variant in the UK Biobank. (a) Distribution of waist-to-hip ratio (WHR, cm/cm) in women-men combined sample. (b) Distribution of WHR in women and men separately. Carriers of the minor allele (G) show statistically significant difference in WHR compared to the non-carriers of the same allele (Supplementary Table 1). This difference is only significant in women-men combined ($p=9.25e-5$) and women only ($p=4.85e-5$) analyses but not in men only analysis ($p=0.177$). Color-coded vertical lines show mean WHR and one standard deviation from the mean. (Means; WHRCarriers=0.868, WHRNon-carriers=0.875, WHRWomen Carriers=0.809, WHRWomen Non-carriers=0.819, WHRMen Carriers=0.937, WHRMen Non-carriers=0.938)



Supplementary Figure 24. Scatterplot of Betas for Large vs. All Studies. Scatterplot for significant loci as estimated in all European studies combined in only large (N>5,000) European Studies.



Supplementary Table 1. Study design, number of individuals and sample quality control for ExomeChip study cohorts

Short name	Study Full name	Study design	Ethnicity	Total sample size (N)	Call rate ^a	Sample QC	Samples in analyses (N)	Anthropometric assessment method	References
						Other exclusions			
AIRWAVE	The Airwave Health Monitoring Study	Population-based	European	14904	≥ 95%	missing weight and height	14892	measured	[PMID: 25194498] Elliott P et al. The Airwave health Monitoring Study of police officers and staff in Great Britain: Rationale, design and methods. Environmental Research 2014; 134: 280-285
AMISH	Amish	Population-based	white European	1633	≥ 95%	1) MAF <1%. 2) HWE <1E-06	1613 (WHR)	measured	[PMID: 26374108] Bozzi, L.M. et al.: The Pharmacogenomics of Anti-Platelet Intervention (PAPI) Study: Variation in Platelet Response to Clopidogrel and Aspirin. Curr Vasc Pharmacol 14(1), 116-24 (2016). [PMID: 18440328] Mitchell, B.D. et al.: The genetic response to short-term interventions affecting cardiovascular function: rationale and design of the Heredity and Phenotype Intervention (HAPI) Heart Study. Am Heart J. 155(5), 823-8 (2008) [PMID: 17261661] Post, W. et al.: Determinants of coronary artery and aortic calcification in the Old Order Amish. Circulation 115(3), 717-24 (2007). [PMID: 15621217] Sorkin, J. et al.: Exploring the genetics of longevity in the Old Order Amish. Mech Ageing Dev. 126(2), 347-50 (2005).
ARIC	Atherosclerosis Risk in Communities	Population-based	European American (EA) African American (AA)	11,071 (EA) 3,364 (AA)	≥ 95%	1) call rate <95% 2) PCA outliers 3)sex mismatch 4) inbreeding coefficient +/-6SD from mean of ancestry distribution 5) first degree relatedness 6) comparison with GWAS data, exclude if >40% mismatch 7) (p10GC) genotype quality score, representing the 10th percentile of the distribution of GenCall scores across all SNPs 8) missing height, weight, or waist-hip measures (only exclude from analyses missing respective phenotype trait)	10,870 (EA) 3,354 (AA)	measured	[PMID: 2646917] The Atherosclerosis Risk in Communities (ARIC) Study: design and objectives. The ARIC investigators. Am J Epidemiol. 1989 ;129(4):687-702. [PMID: 2387450] Grove ML, Yu B, Cochran BJ, Haritunians T, Bis JC, et al. (2013) Best Practices and Joint Calling of the HumanExome BeadChip: The CHARGE Consortium. PLoS ONE 8(7): e68095. doi: 10.1371/journal.pone.0068095
BBMRI-NL	Biobanking and Biomolecular Resources Research Infrastructure	Compedium of 8 different studies	European	7140	≥ 99%	1) Missing body weight and height 2) Heterozygosity 3) duplicate samples	5242	measured	NA
BC1958	British 1958 Birth Cohort	Population-based, all collected at 44 years of age	European	5945	≥ 98%	Exomechip QC SOP v5 applied	5945	measured	[PMID 17554300] Nature. 2007 Jun 7;447(7145):661-78. Genome-wide association study of 14,000 cases of seven common diseases and 3,000 shared controls. Wellcome Trust Case Control Consortium.
BRAVE	Bangladeshi Risk of Acute Ventricular Events	Case-control	South-Asian (Bangladesh)	~6143	~≥ 97%	(1) Intensity Outliers (2) Gender mismatch (3) Non-concordance with previous genotyping (4) Duplicates or twins (5) Excess sample Heterozygosity (6) Ancestry outliers from PCA (7) Missing phenotype within each analysis	5756	measured	[PMID: 25930055] Chowdhury,R. et al. The Bangladesh Risk of Acute Vascular Events (BRAVE) Study: objectives and design. Eur J Epidemiol 30, 577-87 (2015).
BRIGHT	British Genetics of Hypertension	Hypertensive Cases	European	1452	≥ 98% from GenCall, then ≥ 99% post zCall	1) Missing age 2) Heterozygosity 3) Ancestry outliers 4) Gender mismatch 5) Duplicates & relateds	1361	measured	[PMID: 12826435] Caulfield, M.C. et al. Genome-wide mapping of human loci for essential hypertension. Lancet. 361(9375):2118-23 (2003).
CARDIA	The Coronary Artery Risk Development in Young Adults	Population-based	European American (EA) African-American (AA)	5115 total participants at CARDIA baseline examination; 4191 genotyped	≥ 95%	1) Missing body weight and height 2) sex-mismatch 3) high heterozygosity 4) Outlier in PCA	1,971 for black 2,180 for white (the above number is the overall samples in the analysis. samples in each analysis, please refer to table 3)	measured	[PMID: 23874508] Grove, Megan L., et al. "Best practices and joint calling of the HumanExome BeadChip: the CHARGE Consortium." PloS one 8.7 (2013): e68095. [PMID: 3204420] Friedman, Gary D., et al. "CARDIA: study design, recruitment, and some characteristics of the examined subjects." Journal of clinical epidemiology 41.11 (1988): 1105-1116.
CARL	INGI-Carlantino	Population-based	European	820	0.99	1) Missing phenotypes 2) Heterozygosity 3) ethnic outliers	573	measured	[PMID: 23249956] Mezzavilla,M. et al. Genetic characterization of northeastern Italian population isolates in the context of broader European genetic diversity. Eur J Hum Genet. 2013 Jun; 21(6): 659-665.

CHS	Cardiovascular Health Study	Population-based	European American (EA) African-American (AA)	5088	≥ 95%	Following the central QC and joint variant calling, additional QC steps were applied to the CHS data using PLINK. SNPs with a missingness rate of >95% were removed and individuals meeting the following criteria were excluded from analysis. We further excluded individuals with low P10GC call, a missing genotype rate of > 97%, gender mis-matches identified by X chromosome homozygosity rates. The sample was limited to those of self-described European-ancestry (EA) and African-American (AA) participants. Principal components analysis was performed using a subset of common LD-pruned variants from the Exome Chip both for the full sample as well as in EA and AA strata. Individuals whose full-sample first principal component suggested a different ancestry from their self-reported ancestry were excluded as were individuals who were outliers for the first 10 ancestry-specific principal components. Pair-wise IBD measures were calculated and outliers with high levels of IBD were removed.	5059	measured	[PMID: 23874508] Grove ML, Yu B, Cochran BJ, Haritunians T, Bis JC, Taylor KD, Hansen M, Borecki IB, Cupples LA, Fornage M <i>et al</i> : Best Practices and Joint Calling of the Human Exome BeadChip: The CHARGE Consortium. <i>PLoS One</i> 2013, 8(7):e68095. [PMID: 1669507] Fried, L. P., Borhani, N. O., Enright, P. et al. The Cardiovascular Health Study: design and rationale. <i>Ann.Epidemiol.</i> , Feb., 1991. Vol. 1, issue 3, pp.263-276. PM:1669507.
CLHNS	Cebu Longitudinal Health and Nutrition Survey	Population-based	Asian (Filipino)	1798	≥ 98%	gender; heterozygosity	1785	measured	[PMID: 20507864] Adair, L.S. et al. Cohort Profile: the Cebu Longitudinal health and nutrition survey. <i>Int J Epidemiol</i> 40, 619-625 (2011)
CROATIA-Korcula	CROATIA-Korcula	Population-based	European	855	>99%	1) Missing phenotype	~ 800	measured	[PMID:19260141] Zemunik, T., et al., Genome-wide association study of biochemical traits in Korcula Island, Croatia. <i>Croat Med J</i> , 2009. 50(1): p. 23-33.
deCODE	deCODE anthropometric study	Population-based	White European	150,657	≥ 98%	Non-Icelandic individual and individuals without antropometric measurements excluded.	12,605	Measured or self-reported	[PMID: 19079260] Thorleifsson G, et.al. Genome-wide association yields new sequence variants at seven loci that associate with measures of obesity. <i>Nat Genet.</i> 2009 Jan;41(1):18-24. doi: 10.1038/ng.274. Epub 2008 Dec 14. [PMID: 18391951] Gudbjartsson DF, et.al. Many sequence variants affecting diversity of adult human height. <i>Nat Genet.</i> 2008 May;40(5):609-15. doi: 10.1038/ng.122. Epub 2008 Apr 6.
DHS	Diabetes Heart Study	Family-based	European	1191	≥ 98%	1) Missing body weight and height 2) Gender discordant 3) Mendelian inconsistency 4) non-diabetics	1189	measured	[PMID: 18460048] Bowden,D.W. et al. Genetic epidemiology of subclinical cardiovascular disease in the diabetes heart study. <i>Ann Hum Genet</i> 72, 598-610 (2008). [PMID: 21409311] Bowden,D.W. et al. Review of the Diabetes Heart Study (DHS) family of studies: a comprehensively examined sample for genetic and epidemiological studies of type 2 diabetes and its complications. <i>Rev Diabet Stud</i> 7,188-201 (2010).
Diacore	DIAbetes COHoRTE	prospective cohort study of patients with diabetes mellitus type 2	European	1523	> 98%	1) Missing phenotype 2) Ancestry not European 3) Relatedness 2nd degree or closer 4) Genetic gender discordant with phenotypic gender 5) Gonosomal aberation 6) Excess of Heterozygosity 7) low callrate	WHR:1,505	measured	[PMID: 23409726] Dorhofer, L, Lammert, A., Krane, V., Gorski, M., Banas, B., Wanner, C., Kramer, B.K., Heid, I.M., and Boger, C.A. (2013). Study design of DIACORE (DIAbetes COHoRTE) - a cohort study of patients with diabetes mellitus type 2. <i>BMC Med Genet</i> 14, 25.
DPS	The Finnish Diabetes Prevention Study	Randomised controlled trial	European	486	≥ 99%	1) Heterozygosity >median + 3*IQR 2) Technical duplicates with lower call rate 3) Non-European population outliers 4) Sex discrepancy 5) Contamination score >10% 6) Exclusion of first-degree relateds across multiple Finnish studies (kinship > 0.177, KING software)	421	measured	[PMID: 11333990] Tuomilehto, J. et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. <i>N Engl J Med.</i> 2001 May 3;344(18):1343-50.
DR's EXTRA	The Dose Responses to Exercise Training Study	Randomised controlled trial	European	1243	≥ 99%	1) Heterozygosity >median + 3*IQR 2) Technical duplicates with lower call rate 3) Non-European population outliers 4) Sex discrepancy 5) Contamination score >10% 6) Exclusion of first-degree relateds across multiple Finnish studies (kinship > 0.177, KING software)	740	measured	[PMID: 21186108] Kouki, R. et al. Diet, fitness and metabolic syndrome--the DR's EXTRA study. <i>Nutr Metab Cardiovasc Dis.</i> 2012 Jul;22(7):553-60.
EFSOCH	The Exeter Family Study of Childhood Health	Family-based	European	1538	0.99	heterozygosity, duplicates, relatedness	1538	measured	[PMID:16466435] Knight B, Shields BM, Hattersley AT. The Exeter Family Study of Childhood Health (EFSOCH): study protocol and methodology. <i>Paediatr Perinat Epidemiol.</i> 2006 Mar;20(2):172-9.

EGCUT	Estonian Genome Center of University of Tartu	nested case-control	European	4788	≥ 99%	1) Missing phenotype 2) Heterozygosity 3) No duplicates 4) Gender mismatch 5) Population Outliers (Principal components obtained from MDS analysis)	3510	measured	[PMID: 24518929] Leitsalu et al, Cohort Profile: Estonian Biobank of the Estonian Genome Center, University of Tartu. Int J Epidemiol. 2014 Feb 11
EPIC-CVD	European Prospective Investigation into Cancer and Nutrition - Cardiovascular Disease Study	Case-cohort	European	~23749	~≥ 97%	(1) Intensity Outliers (2) Gender mismatch (3) Non-concordance with previous genotyping (4) Duplicates or twins (5) Excess sample Heterozygosity (6) Ancestry outliers from PCA (7) Missing phenotype within each analysis (8) Potsdam or Umea epic cohorts	22412	measured in >90% of participants, self-reported in the remainder	[PMID: 17295097] Danesh J, et al. EPIC-Heart: the cardiovascular component of a prospective study of nutritional, lifestyle and biological factors in 520,000 middle-aged participants from 10 European countries. Eur J Epidemiol 22, 129-41 (2007).
EPIC-Potsdam	European Prospective Investigation into Cancer and Nutrition - Potsdam Study	Population-based	European	2482	≥ 99%	Heterozygosity, sex mismatch, population outliers	2449	measured	[PMID: 10592368] Boeing H, Wahrendorf J, Becker N (1999) EPIC-Germany--A source for studies into diet and risk of chronic diseases. European Investigation into Cancer and Nutrition. Ann Nutr Metab 43: 195-204
EpiHealth	Epidemiology for Health	Population-based	European	2500	≥ 98%	1) Gender mismatch. 2) Ethnic outliers. 3) Heterozygosity > 5 s.d. 4) Cryptic relatedness. 5) Missing all anthropometric measures.	2373	Measured	[PMID: 23435790] Lind, L. et al. EpiHealth: a large population-based cohort study for investigation of gene-lifestyle interactions in the pathogenesis of common diseases. Eur J Epidemiol. 28(2):189-97 (2013).
EXTEND	Exeter 10,000	Population-based	European	1590	0.99	heterozygosity, duplicates, relatedness	1579	measured	http://www.exeter.crf.nihr.ac.uk/node/155
FamHS	Family Heart Study	Family-based	African American (AA) European American (EA)	608 (AA) 4135 (EA)	≥ 96% (AA) ≥99% (EA)	1) Missing body weight, height, waist and hip 2) Heterozygosity 3) Mendell errors	608 (AA) 3749 (EA)	measured	[PMID:8651220] Higgins M et al. NHLBI Family Heart Study: objectives and design. Am J Epidemiol 143, 1219-28 [PMID: 18200599] Zhang Q et al. Genome-wide admixture mapping for coronary artery calcification in African Americans: the NHLBI Family Heart Study. Genet Epidemiol 2008, 32: 264-72
Fenland	Fenland Study	Population-based	white European	1650	≥ 98%	1) heterozygosity outliers (>3.5 SDs) 2) ethnic outliers 3) sex discrepancy 4) unusually high number of singleton genotypes 5) related (IBD > 0.1875) 6) missing phenotypes required for the analyses	1341	measured	[PMID 20519560] Ede, L. et al. Association between birth weight and visceral fat in adults. Am J Clin Nutr 92(2), 347-352 (2010)
FIN-D2D 2007	National type 2 diabetes prevention programme in Finland: FIN-D2D	Population-based survey	European	2690	≥ 99%	1) Heterozygosity >median + 3*IQR 2) Technical duplicates with lower call rate 3) Non-European population outliers 4) Sex discrepancy 5) Contamination score >10% 6) Exclusion of first-degree relateds across multiple Finnish studies (kinship > 0.177, KING software)	2585	measured	[PMID: 20459722] Kotronen, A. et al. Non-alcoholic and alcoholic fatty liver disease - two diseases of affluence associated with the metabolic syndrome and type 2 diabetes: the FIN-D2D survey. BMC Public Health. 2010 May 10;10:237.
FINRISK 2007	National FINRISK 2007 Study	T2D case control study	European	1212	≥ 99%	1) Heterozygosity >median + 3*IQR 2) Technical duplicates with lower call rate 3) Non-European population outliers 4) Sex discrepancy 5) Contamination score >10% 6) Exclusion of first-degree relateds across multiple Finnish studies (kinship > 0.177, KING software)	1091	measured	[PMID: 19959603] Vartiainen, E. et al. Thirty-five-year trends in cardiovascular risk factors in Finland. Int J Epidemiol. 2010 Apr;39(2):504-18.
FINRISKEXTREMES	Samples are Height and BMI extremes from four Finrisk T2D Case Control cohorts: Finrisk 1992, Finrisk 1997, Finrisk 2002, Finrisk 2007.	T2D case control studies	European	29287	≥ 95%	1) Heterozygosity >median + 3*IQR 2) Duplicate samples 3) MDS outliers 6) Exclusion of first-degree relateds across multiple Finnish studies (kinship > 0.177, KING software)	774	measured	[PMID: 25422363] Borodulin K, Vartiainen E, Peltonen M, et al. Forty-year trends in cardiovascular risk factors in Finland. Eur J Public Health 2015;25:539-46. doi:10.1093/eurpub/cku174
FRAM	Framingham Heart Study	Population-based	European	8153	≥ 90%	1) GWAS discordance 2) heterozygosity 3)missingness 4) sex heterozygosity 5) missing trait and/or covariates	7715	measured	[PMID 14025561] Dawber TR, Kannel WB, Lyell LP. An approach to longitudinal studies in a community: the Framingham Study. Ann N Y Acad Sci. 1963;107:539-556. [PMID 1208363] Feinleib M, Kannel WB, Garrison RJ, McNamara PM, Castelli WP. The Framingham Offspring Study. Design and preliminary data. Prev Med. 1975;4:518-525. [PMID 17372189] Splansky GL, Corey D, Yang Q et al. The Third Generation Cohort of the National Heart, Lung, and Blood Institute's Framingham Heart Study: design, recruitment, and initial examination. Am J Epidemiol. 2007;165:1328-1335.

FUSION	Finland-United States Investigation of NIDDM Genetics Study	T2D case control study	European	4839	≥ 99%	1) Heterozygosity >median + 3*IQR 2) Technical duplicates with lower call rate 3) Non-European population outliers 4) Sex discrepancy 5) Contamination score >10% 6) Exclusion of first-degree relateds across multiple Finnish studies (kinship > 0.177, KING software)	4361	measured	[PMID: 9614613] Valle, T. et al. Mapping genes for NIDDM. Design of the Finland-United States Investigation of NIDDM Genetics (FUSION) Study. Diabetes Care. 1998 Jun;21(6):949-58. [PMID: 17463248] Scott, L.J., et al. A genome-wide association study of type 2 diabetes in Finns detects multiple susceptibility variants. Science. 2007 Jun 1;316(5829):1341-5.
FVG	INGI-FVG	Population-based	European	1581	0.99	1) Missing phenotypes 2) Heterozygosity 3) ethnic outliers	775	measured	[PMID: 23249956] Mezzavilla, M. et al. Genetic characterization of northeastern Italian population isolates in the context of broader European genetic diversity. Eur J Hum Genet. 2013 Jun; 21(6): 659-665.
GENOA	Genetic Epidemiology Network of Arteriopathy	Cohort of sibships enriched for hypertension	European American (EA) African American (AA)	1544 (EA) 1392 (AA)	≥ 95%	Gender inconsistency >6sd from mean of inbreeding coefficient >6sd from mean heterozygosity > 6sd from mean of singleton count >6sd from PCA	1512 (EA) 1126 (AA)	measured	[PMID: 11799070] FBPP Investigators. Multi-center genetic study of hypertension: The Family Blood Pressure Program (FBPP). Hypertension. 2002 Jan;39(1):3-9. [PMID: 15121494] Daniels PR, Kardia SL, Hanis CL, Brown CA, Hutchinson R, Boerwinkle E, Turner ST; Genetic Epidemiology Network of Arteriopathy study. Familial aggregation of hypertension treatment and control in the Genetic Epidemiology Network of Arteriopathy (GENOA) study. Am J Med. 2004 May 15;116(10):676-81. PubMed PMID:
GRAPHIC	Genetic Regulation of Arterial Pressure in Humans in the Community	Family-based	European	2037	≥ 98%	1) Missing Height, BMI or WHR 2) Heterozygosity 3) Ethnic outliers (using HapMap) 4) Duplicate checks 5) Identity checks 6) Gender checks 7) CR <95% in GenCall	1910	measured	[PMCID: PMC3035934] Tomaszewski M et al. Genetic architecture of ambulatory blood pressure in the general population: insights from cardiovascular gene-centric array. Hypertension. 2010;56:1069-76.
GS:SFHS	Generation Scotland: Scottish Family Health Study	Population-based	European	9947	>99%	1) Missing phenotype	WHR:9743	measured	[PMID:22786799] Smith, B.H. et al. Generation Scotland: Scottish family health study. A profile of the study, its participants, and their potential for genetic research on health and illness. Int J Epidemiol (2013).
Health	Health 2006 and 2008	Population-based	European	4037	≥ 98%	1) Missing body weight and height. 2) Heterozygosity were calculated separately for maf < 1% and maf > 1% and samples were dropped judged by plots 3) Cryptic relatedness (related to 20 or more individuals) 3) Technical duplicates 4) Non-European population outliers from PCA plot (based on AIM SNPs) 5) Sex discrepancy	3676	measured	[PMID: 23615486] Thuesen BH, et al. Cohort Profile: The Health2006 cohort, Research Centre for Prevention and Health. Int J Epidemiol. 2014, 568-75
HELIC MANOLIS	HELIC (Hellenic Isolated Cohorts) MANOLIS	Isolated population	European	1267	GenCall 98% and zCall 99%	Sex check, heterozygosity at MAF<1% and MAF≥1%, duplicates, ethnic outliers, GWAS concordance, phenotype missing	933 (WHR)	measured	NA
HELIC Pomak	HELIC (Hellenic Isolated Cohorts) Pomak	Isolated population	European	1012	GenCall 98% and zCall 99%	Sex check, heterozygosity at MAF<1% and MAF≥1%, duplicates, ethnic outliers, GWAS concordance, phenotype missing	841 (WHR)	measured	NA
HUNT	Nord-Trøndelag Health Study	MI cases and control, sepsis cases and control	European	Total N=17834: MI cases (N=2865), MI controls (N=12249), sepsis cases (N=1361), control (N=13753)	≥ 98%	1) Missing body weight and height. 2) Heterozygosity 3) Deviation from HWE P < 1e-06 4) Duplicate samples with lower call rate 5) Population PCA clustering outliers 6) Gender mismatches	15114	measured	[PMID: 22879362] Krokstad, S. et al. Cohort profile: the HUNT Study, Norway. Int. J. Epidemiol. 42, 968-977 (2013).
Inter99	Inter99	Population-based	European	6141	≥ 98%	1) Missing body weight and height. 2) Heterozygosity were calculated separately for maf < 1% and maf > 1% and samples were dropped judged by plots 3) Cryptic relatedness (related to 20 or more individuals) 3) Technical duplicates 4) Non-European population outliers from PCA plot (based on AIM SNPs) 5) Sex discrepancy	5991	measured	[PMID: 14663300] Jørgensen T, et al. (2003) A randomized non-pharmacological intervention study for prevention of ischaemic heart disease: Baseline results Inter99 (1). Eur J Cardiovasc Prev Rehab 10:377-386
InterAct	European Prospective Investigation into Cancer and Nutrition - InterAct	Case-cohort	white European	2,712 (non-subcohort cases)	≥ 98%	1) sex mismatch 2) het outlier 3) rare allele count outlier 4) IBD relatedness (0.1875) 5) missing phenotypes required for the analyses	2641	measured	[PMID: 21717116] Design and cohort description of the InterAct Project: an examination of the interaction of genetic and lifestyle factors on the incidence of type 2 diabetes in the EPIC Study. Diabetologia. 2011 Sep;54(9):2272-82

IRASFS	Insulin Resistance Atherosclerosis Family Study	Population-based	Hispanic American (HA) African American (AA)	2010 (HA) 596 (AA)	≥ 99%	1) Gender inconsistencies 2) Mendelian inconsistencies 3) Missing analysis variables	1260 (HA) 596 (AA)	measured	[PMID: 12684185] Henkin L. et al. Genetic epidemiology of insulin resistance and visceral adiposity. The IRAS Family Study design and methods. <i>Ann Epidemiol.</i> 2003 Apr;13(4):211-7. [PMID: 15534617] Norris et al. Quantitative trait loci for abdominal fat and BMI in Hispanic-Americans and African-Americans: the IRAS Family study. Norris JM, Langefeld CD, Scherzinger AL, Rich SS, Bookman E, Beck SR, Saad MF, Haffner SM, Bergman RN, Bowden DW, Wagenknecht LE.
JHS	Jackson Heart Study	Population-based	African American	2803	≥ 95%	1) Missing outcome or covariate 2) Heterozygosity 3) PC outlier 4) Half of overlap with ARIC African Americans (coordinated with ARIC)	2317	measured	[PMID: 16320381] Taylor, H.A., Jr. et al. Toward resolution of cardiovascular health disparities in African Americans: design and methods of the Jackson Heart Study. <i>Ethn Dis</i> 15, S6-4-17 (2005).
KORA-F4	Cooperative Health Research in the Region of Augsburg	Population-based	European	2921	≥ 98%	1) excess heterozygosity [i.e. het_rate > mean+/-5sd] 2) no German passport	2847	measured	[PMID: 16032514] Wichmann HE et al. KORA-gen--resource for population genetics, controls and a broad spectrum of disease phenotypes. <i>Gesundheitswesen</i> 67 Suppl 1, S26-30 (2005).
Leipzig-adults	LeipzigAdults	Populations-based	European	902	≥ 99%	1) Missing phenotype 2) Heterozygosity 3) Non-European population outliers 4) Technical duplicates with lower call rate 5) Sex discrepancy	902	measured	[PMID: 20935630] Speliotes, Elizabeth K., et al. Association analyses of 249,796 individuals reveal 18 new loci associated with body mass index. <i>Nature genetics</i> 42.11, 937-948 (2010)
LOLIPOP-Exome	London Life Sciences Prospective Population Study	Population-based	South Asian (Indian Asians)	1664	≥ 98%	Duplicates, gender discrepancy, ethnic outliers, contaminated samples, relatedness, extreme heterozygosity	1664	measured	[PMID:18193046] Kooner JS, Chambers JC, Aguilar-Salinas CA, et al. Genome-wide scan identifies variation in MLXIPL associated with plasma triglycerides. <i>Nat Genet.</i> 40:149-151 (2008). [PMID:18454146] Chambers JC, Elliott P, Zabaneh D, Zhang W, Li Yun, Froguel Philippe, Balding D, Scott J, Kooner JS. Common genetic variation near MC4R is associated with waist circumference and insulin resistance. <i>Nat Genet</i> 40, 716-718 (2008). [PMID:23222517] van der Harst P, et al. Seventy-five genetic loci influencing the human red blood cell. <i>Nature</i> 492:369-375 (2012).
LOLIPOP-OmniEE	London Life Sciences Prospective Population Study	Population-based	South Asian (Indian Asians)	977	≥ 98%	Duplicates, gender discrepancy, ethnic outliers, contaminated samples, relatedness, extreme heterozygosity	977	measured	[PMID:18193046] Kooner JS, Chambers JC, Aguilar-Salinas CA, et al. Genome-wide scan identifies variation in MLXIPL associated with plasma triglycerides. <i>Nat Genet.</i> 40:149-151 (2008). [PMID:18454146] Chambers JC, Elliott P, Zabaneh D, Zhang W, Li Yun, Froguel Philippe, Balding D, Scott J, Kooner JS. Common genetic variation near MC4R is associated with waist circumference and insulin resistance. <i>Nat Genet</i> 40, 716-718 (2008). [PMID:23222517] van der Harst P, et al. Seventy-five genetic loci influencing the human red blood cell. <i>Nature</i> 492:369-375 (2012).
MESA	Multi-Ethnic Study of Atherosclerosis (MESA) Cohort	Population-based	African American (AA), European American (EA), East Asian (Chinese EAS), Hispanic American (HA)	6375	≥ 95%	Ethnic outliers; duplicates; gender mismatch; Phenotypic outliers	EA 2497 EAS 769 AA 1655 HA 1435	measured	Bild DE, Bluemke DA, Burke GL, Detrano R, Diez Roux AV, Folsom AR, Greenland P, Jacob DR Jr, Kronmal R, Liu K, Nelson JC, O'Leary D, Saad MF, Shea S, Szklo M, Tracy RP. Multi-ethnic study of atherosclerosis: objectives and design. <i>Am J Epidemiol.</i> 2002 Nov 1;156(9):871-81. PubMed PMID: 12397006.
METSIM	Metabolic Syndrome in Men Study	Population-based cross-sectional study	European	9765	≥ 99%	1) Heterozygosity >median + 3*IQR 2) Technical duplicates with lower call rate 3) Non-European population outliers 4) Sex discrepancy 5) Contamination score >10% 6) Exclusion of first-degree relateds across multiple Finnish studies (kinship > 0.177, KING software)	8414	measured	[PMID: 19223598] Stancáková, A. et al. Changes in insulin sensitivity and insulin release in relation to glycemia and glucose tolerance in 6,414 Finnish men. <i>Diabetes.</i> 2009 May;58(5):1212-21.
MHIBB	Montreal Heart Institute Biobank	Population-based	European	10506	≥ 95%	1) For BMI and WHR: Pregnant women, Under medication to treat obesity (Orlistat or Rimonabant), History of bariatric surgery, Down Syndrome, Cushing Syndrome, Polycystic Ovary Syndrome 2) Missing body weight, height and waist-hip ratio. 3) Heterozygosity, gender discordance, relatedness 4) Not CEU based on 1000G CEU (PCA outliers)	9634	measured	[PMID: 24777453] Auer, P.L. et al. Rare and low-frequency coding variants in CXCR2 and other genes are associated with hematological traits. <i>Nature Genetics</i> (2014): doi:10.1038/ng.2962.

MORGAM	MOnica Risk, Genetics, Archiving and Monograph	Case-cohort	European	~6869	~≥ 97%	(1) Intensity Outliers (2) Gender mismatch (3) Non-concordance with previous genotyping (4) Duplicates or twins (5) Excess sample Heterozygosity (6) Ancestry outliers from PCA (7) Missing phenotype within each analysis	6128	measured	[PMID: 15561751] Evans A, Salomaa V, Kulathinal S, Asplund K, Cambien F, Ferrario M, Perola M, Peltonen L, Shields D, Tunstall-Pedoe H, Kuulasmaa K, for the MORGAM Project. MORGAM (an international pooling of cardiovascular cohorts). <i>Int J Epidemiol</i> 2005;34:21-27. Kulathinal S, Niemelä M, Niiranen T, Saarela O, Palosaari T, Tapanainen H, Kuulasmaa K, contributors from Participating Centres, for the MORGAM Project. Description of MORGAM Cohorts. MORGAM Project e-publications [Internet]. 2005-; (2). URN:NBN:fi-fe20051214. Available from URL: http://www.thl.fi/publications/morgam/cohorts/index.html Niemelä M, Kulathinal S and Kuulasmaa K, editors, for the MORGAM Project. Description and quality assessment of MORGAM data. MORGAM Project e-publications [Internet]. 2007; (3). URN:NBN:fi-fe20071495. Available from URL: http://www.thl.fi/publications/morgam/qa/contents.htm
NEO Study	The Netherlands Epidemiology of Obesity Study	Population-based	European	6604	≥ 98%	1) remove duplicate/swap samples 2) remove samples with gender mismatch 3) remove outliers in PCA	6127	measured	[PMID: 23576214] de Mutsert R, et al.(2013).The Netherlands Epidemiology of Obesity (NEO) study: study design and data collection. <i>Eur J Epidemiol</i> . 2013 Jun;28(6):513-23.
NHAPC	Nutrition and Health of Ageing Population in China	Population-based	East Asian (Chinese Han)	3161	≥ 98%	1) Heterozygosity 2) Duplications 3) Gender mismatches	3138	measured	[PMID:18633108] Wu Y, Li H, Loos R J F, et al. Common variants in CDKAL1, CDKN2A/B, IGF2BP2, SLC30A8, and HHEX/IDE genes are associated with type 2 diabetes and impaired fasting glucose in a Chinese Han population. <i>Diabetes</i> , 2008, 57(10): 2834-2842. [PMID:22961080] Li H, Gan W, Lu L, et al. A genome-wide association study identifies GRK5 and RASGRP1 as type 2 diabetes loci in Chinese Hans. <i>Diabetes</i> , 2013, 62(1): 291-298.
Nijmegen	Nijmegen Biomedical Study & Nijmegen Bladder Cancer Study	Case-Control	European	3509	≥ 99%	1) Missing body weight and height. 2) Heterozygosity 3) duplicate samples	3509	measured	[PMID: 21750109] Rafnar T, Vermeulen SH, Sulem P, Tet al. European genome-wide association study identifies SLC14A1 as a new urinary bladder cancer susceptibility gene. <i>Hum Mol Genet</i> . 2011 Nov 1;20(21):4268-81. doi: 10.1093/hmg/ddr303.
OMICS-EPICNorfolk	European Prospective Investigation into Cancer and Nutrition - Obesity Study	Population-based	European	21044	≥ 97%	1) Duplicates, 2) Sex discordance, 3) impossible IBDs	21044	measured	[PMID: 10466767] Day,N.E. et al. EPIC-Norfolk: study design and characteristics of the cohort. <i>European Prospective Investigation of Cancer. British Journal of Cancer</i> 80, 95-103 (1999).
OMICS-Fenland	Fenland Study	Population-based	European	8994	> 97%	Heterozygosity check; Ethnic outliers; sex discrepancy; unusually high number of singleton genotypes; impossible IBD values; phenotype missing; excluding overlap exomechip samples	7845	Measured	[PMID: 20519560] Rolfe Ede L, Loos RJ, Druet C, Stolk RP, Ekelund U, Griffin SJ, Forouhi NG, Wareham NJ, Ong KK. Association between birth weight and visceral fat in adults. <i>Am J Clin Nutr</i> . 2010 Aug;92(2):347-52. Epub 2010 Jun 2.
Oxford BioBank	The Oxford Biobank	Populations-based	European	4515	≥ 99%	1) Missing phenotype 2) Heterozygosity 3) Non-European population outliers 4) Technical duplicates with lower call rate 5) Sex discrepancy	4515	measured	http://www.oxfordbiobank.org.uk/
PCOS	Polycystic Ovary Syndrome	Population-based	European	667	≥ 99%	1) Missing phenotype 2) Heterozygosity 3) Non-European population outliers 4) technical duplicates with lower call rate 5) Sex discrepancy	582	measured	NA
PIVUS	Prospective Investigation of the Vasculature in Uppsala Seniors	Population-based	European	961	≥ 99%	1) Missing phenotype 2) Heterozygosity 3) Non-European population outliers 4) technical duplicates with lower call rate 5) Sex discrepancy	961	measured	Lind L, Fors N, Hall J, Marttala K, Stenborg A. A Comparison of Three Different Methods to Evaluate Endothelium-Dependent Vasodilation in the Elderly. The Prospective Investigation of the Vasculature in Uppsala Seniors (PIVUS) Study. <i>Arterioscler Thromb Vasc Biol</i> . 2005; 25:2368-75
PROMIS	Pakistani Risk of Myocardial Infarction Study	Case-control	South-Asian (Pakistan)	~24324	~≥ 97%	(1) Intensity Outliers (2) Gender mismatch (3) Non-concordance with previous genotyping (4) Duplicates or twins (5) Excess sample Heterozygosity (6) Ancestry outliers from PCA (7) Missing phenotype within each analysis	22094	measured	[PMID: 19404752] Saleheen,D. et al. The Pakistan Risk of Myocardial Infarction Study: a resource for the study of genetic, lifestyle and other determinants of myocardial infarction in South Asia. <i>Eur J Epidemiol</i> 24, 329-38 (2009).
RAINE	Western Australian Pregnancy Cohort (RAINE) Study	Population-based	European	1527	≥ 95%	1) Sample discordance with GWAS data 2) Heterozygosity 3) Missing body weight and height 4) Did not participant in DEXA scan	1078	self-reported	[PMID: 8105165] Newnham JP, Evans S., Michael CA, Stanley FJ, Landau LI. Effect of frequent ultrasound during pregnancy: A randomised controlled trial. <i>Lancet</i> 1993; 342: 887-891
RISC	Relationship between Insulin Sensitivity and Cardiovascular disease	Population-based	European	313	0.99	heterozygosity, duplicates, relatedness	313	measured	[PMID: 14968294] Hills SA et al. The EGIR-RISC STUDY (The European group for the study of insulin resistance: relationship between insulin sensitivity and cardiovascular disease risk): I. Methodology and objectives. <i>Diabetologia</i> . 2004 Mar;47(3):566-70. Epub 2004 Feb 14. http://www.egir.org/egirric/status.html
RSI	Rotterdam Study I	Population-based	European	3163	≥ 98%	Heterozygosity, gender-check	3163	measured	[PMID: 24258680] Hofman,E et al. The Rotterdam Study: 2014 objectives and design update. <i>European Journal of Epidemiology</i> 28, 889-926 (2013)

SDC	Steno Diabetes Center T2D Cases	Case study	European	1418	≥ 98%	1) Missing body weight and height. 2) Heterozygosity were calculated separately for maf < 1% and maf > 1% and samples were dropped judged by plots 3) Cryptic relatedness (related to 20 or more individuals) 3) Technical duplicates 4) Non-European population outliers from PCA plot (based on AIM SNPs) 5) Sex discrepancy	1390	measured	[PMID: 23160641] Albrechtsen A, et al. Exome sequencing-driven discovery of coding polymorphisms associated with common metabolic phenotypes. <i>Diabetologia</i> 56, 297-310 (2013)
SHIP	Study of Health in Pomerania	Population-based	European	3964	≥ 90%	1) missing data 2) duplicate samples (by estimated IBD) 3) reported and genotyped sex mismatch 4) Heterozygosity	3878	measured	[PMID: 20167617] Völzke H, et al. Cohort Profile: The Study of Health in Pomerania. <i>Int J Epidemiol.</i> 2011 Apr;40(2):294-307.
SHIP-TREND	Study of Health in Pomerania - TREND	Population-based	European	4331	≥ 90%	1) missing data 2) duplicate samples (by estimated IBD) 3) reported and genotyped sex mismatch 4) Heterozygosity	4251	measured	[PMID: 20167617] Völzke H, et al. Cohort Profile: The Study of Health in Pomerania. <i>Int J Epidemiol.</i> 2011 Apr;40(2):294-307.
SOLID-TIMI 52	The Stabilization of pLaques using Darapladib-Thrombolysis In Myocardial Infarction 52 Trial (SOLID-TIMI 52)	Interventional Clinical Trial	African American (AA), European American (EA), East Asian (EAS), South Asian (SA), Hispanic American (HA)	200 AA, 8102 EA, 255 EAS, 118 SA, 893 HA	≥ 94.5%	Sample call rate < 94.5% Heterozygosity; Cryptically related Not consented for genetic research; Only consented for genetic research of response to drug	200 AA, 8102 EA, 255 EAS, 118 SA, 893 HA	measured	[PMID: 25173516] O'Donoghue ML et al; SOLID-TIMI 52 Investigators. Effect of darapladib on major coronary events after an acute coronary syndrome: the SOLID-TIMI 52 randomized clinical trial. <i>JAMA.</i> 2014 Sep 10 [PMID: 21982651] O'Donoghue ML, et al. Study design and rationale for the Stabilization of pLaques using Darapladib-Thrombolysis in Myocardial Infarction (SOLID-TIMI 52) trial in patients after an acute coronary syndrome. <i>Am Heart J.</i> 2011 Oct
Sorbs	Sorbs	Populations-based	white European	1015	≥ 99%	1) Missing phenotype 2) Heterozygosity 3) Non-European population outliers 4) Technical duplicates with lower call rate 5) Sex discrepancy	1015	measured	NA
STABILITY	The Stabilization of Atherosclerotic Plaque by Initiation of Darapladib Therapy Trial (STABILITY)	Interventional Clinical Trial	African American (AA), European American (EA), East Asian (EAS), South Asian (SA), Hispanic American (HA)	123 AA, 8789 EA, 724 EAS, 380 SA, 518 HA	≥ 93.5%	Sample call rate < 94.5% Heterozygosity; Cryptically related Not consented for genetic research; Only consented for genetic research of response to drug	123 AA, 8789 EA, 724 EAS, 380 SA, 518 HA	measured	[PMID: 24678955] STABILITY Investigators, White HD, et al. Darapladib for preventing ischemic events in stable coronary heart disease. <i>N Engl J Med.</i> 2014 May 1;370(18):1702-11. doi: 10.1056/NEJMoa1315878. Epub 2014 Mar 30. [PMID: 22496275] Vedin O, Hagström E, Stewart R, Brown R, Krug-Gourley S, Davies R, Wallentin L, White H, Held C. Secondary prevention and risk factor target achievement in a global, high-risk population with established coronary heart disease: baseline results from the STABILITY study. <i>Eur J Prev Cardiol.</i> 2013 Aug;20(4):678-85. doi: 10.1177/2047487312444995. Epub 2012 Apr 10.
TUDR	Taiwan USA Diabetes Retinopathy	Population-based	East Asian	560	≥ 95%	1) Gender Mismatches 2) Heterozygosity 3) Missing body weight and height.	548	measured	[PMID: 23562823] Sheu, Wayne H-H., et al. "Genome-wide association study in a Chinese population with diabetic retinopathy." <i>Human molecular genetics</i> 22.15 (2013): 3165-3173.
TwinsUK	Twins UK	Populations-based	European	999	≥ 99%	1) Missing phenotype 2) Heterozygosity 3) Non-European population outliers 4) Technical duplicates with lower call rate 5) Sex discrepancy	999	measured	[PMID: 23088889] Moayyeri A, Hammond CJ, Hart DJ, Spector TD. The UK Adult Twin Registry (TwinsUK Resource). <i>Twin Res Hum</i>
UK Biobank	UK Biobank	Population-based	Caucasian (genetic)	120286	≥ 95%	See UK Biobank Documentation: http://www.ukbiobank.ac.uk/wp-content/uploads/2014/04/UKBiobank_genotyping_QC_documentation-web.pdf 1st, 2nd and 3rd degree relatives Non "white British" individuals	119572	measured	[PMID: 25826379] Sudlow C, Gallacher J, Allen N, et al., UK biobank: an open access resource for identifying the causes of a wide range of complex diseases of middle and old age. <i>PLoS Med</i> , 2015 12: e1001779
ULSAM	Uppsala Longitudinal Study of Adult Men	Population-based	European	1102	≥ 99%	1) Missing phenotype 2) Heterozygosity 3) Non-European population outliers 4) technical duplicates with lower call rate 5) Sex discrepancy	1102	measured	Hedstrand H. A study of middle-aged men with particular reference to risk factors for cardiovascular disease. <i>Ups J Med Sci Suppl</i> 1975; 19: 1-61.
Vejle	Vejle Biobank T2D Case-control study	Case-control	European	2076 cases 435 controls	≥ 98%	1) Missing body weight and height. 2) Heterozygosity were calculated separately for maf < 1% and maf > 1% and samples were dropped judged by plots 3) Cryptic relatedness (related to 20 or more individuals) 3) Technical duplicates 4) Non-European population outliers from PCA plot (based on AIM SNPs) 5) Sex discrepancy	2026 cases 435 controls	measured	[PMID: 23160641] Albrechtsen A, et al. Exome sequencing-driven discovery of coding polymorphisms associated with common metabolic phenotypes. <i>Diabetologia</i> 56, 297-310 (2013)
WGHS	Women's Genome Health Study	Population-based	European	22618	≥ 95%	missing outcome	22618	self-reported	[PMID: 18070814] Ridker PM et al. Women's Genome Health Study Working Group. Rationale, design, and methodology of the Women's Genome Health Study: a genome-wide association study of more than 25,000 initially healthy american women. <i>Clin Chem.</i> 2008 Feb;54(2):249-55. Epub 2007 Dec 10.

WHI	Women's Health Initiative	Population-based cohort	European American (EA) African American (AA)	21,858 (EA), 3519 (AA)	≥ 95%	1) Missing body weight, waist circumference, hip circumference, and height	21,858 (EA), 3519 (AA)	measured	[PMID: 22021425] Carty CL, Johnson NA, Hutter CM, Reiner AP, Peters U, Tang H, Kooperberg C. (2012) Genome-wide association study of body height in African Americans: the Women's Health Initiative SNP Health Association Resource (SHARe). Hum Mol Genet. 2012 Feb 1;21(3):711-20. doi: 10.1093/hmg/ddr489 [PMID: 26757982] Kan M, Auer PL, Wang GT, et al. (2016) Rare variant associations with waist-to-hip ratio in European-American and African-American women from the NHLBI-Exome Sequencing Project. Eur J Hum Genet. 2016 Jan 13. doi: 10.1038/ejhg.2015.272.
WTCCC/ UKT2D	Wellcome Trust Case Control Consortium/United Kingdom Type 2 Diabetes Genetics consortium	Populations-based	European	2016	≥ 99%	1) Missing phenotype 2) Heterozygosity 3) Non-European population outliers 4) Technical duplicates with lower call rate 5) Sex discrepancy	2016	measured	[PMID: 20581827] Voight BF et al. Twelve type 2 diabetes susceptibility loci identified through large-scale association analysis. Nat Genet. 2010 Jul;42(7):579-89.
YFS	The Young Finns Study	Population-based	European	1998	≥ 95%	1) Missing body height, weight or waist-hip ratio. Pregnancy 2) Heterozygosity 3) Gender mismatch	1893	measured	[PMID: 18263651] Raitakari, O.T. et al. Cohort profile: The cardiovascular risk in Young Finns Study. Int J Epidemiol 37(6): 1220-1226.

a. Call rate to exclude individuals for whom genotyping success rate is less than a certain percentage (to exclude 'bad' samples/DNA)

Supplementary Table 2. Information on genotyping methods, quality control of SNPs, imputation, and statistical analysis for ExomeChip study cohorts

Cohort	Genotyping Array	Genotype calling algorithm	Principal components					SNPs that met QC criteria	Association analyses	
			Software	SNPs used from GWAS/Exome Chip/AIMS/Other	MAF	Inclusion criteria			Polymorphic SNPs in meta-analysis	Analyses software
						Call rate ^a	Pvalue for HWE			
AIRWAVE	HumanExome 12v1-1/ HumanCoreExome-12v1-1_A	GeneCall + Zcall	PLINK-PCA	Exome Chip/GWAS	> 0%	≥ 95%	> 10 ⁻⁵	233013	153987	RareMetalWorker
AMISH	Illumina Exome Chip V1.0	Genome Studio	NONE	NONE	≥ 0%	≥ 95%	> 10 ⁻⁶	223290	40905	RareMetalWorker
ARIC	Illumina ExomeChip V1.0	GenTrain 2.0 clustering algorithm	Eigensoft v3.0	Exome Chip (MAF>5%)	≥ 0%	≥ 95%	> 10 ⁻⁶	237898	148699	RvTest
BBMRI-NL	Illumina ExomeChip V1.1	GeneCall + Zcall (Exome-chip QC SOP v5.pdf)	PLINK	AIMS	≥ 0%	≥ 95%	> 10 ⁻⁶	242474	133040	RvTest
BC1958	Illumina ExomeChip V1.0	GenCall + Zcall (Oxford Protocol)	PLINK	Exome Chip	no filter	≥ 98%	> 10 ⁻⁶	244669	139372	RareMetalWorker
BRAVE	Customized Illumina ExomeChip V1.1	Optical + Zcall	R	Other	≥ 0%	≥ 97%	10 ⁻⁶ for MAF ≥ 5% / 10 ⁻¹⁵ for MAF < 5%	236737	82824	RareMetalWorker
BRIGHT	Illumina Human Exome BeadChip v1.0	GeneCall + Zcall (Oxford Protocol)	PLINK	Exome Chip (1% MAF, LD pruned)	no filter	≥ 99%	> 10 ⁻⁴	245322	92641	RareMetalWorker
CARDIA	Illumina HumanExome BeadChip V1.0	GeneCall + Zcall	Eigensoft	Exome Chip SNPs (MAF > 1%)	> 0%	≥ 95%	> 10 ⁻⁶	237584 (AA) 237630 (EA)	139250 (AA) 122765 (EA)	RvTest
CARL	HumanExome-12v1-1_A.bpm	GenomeStudio + Zcall (Oxford Protocol)	GenABEL	Exome Chip	> 0%	> 99%	> 10 ⁻⁸	234995	64531	RareMetalWorker
CHS	Illumina ExomeChip V1.0	CHARGE joint calling	R	Exome Chip	> 0%	≥ 97%	no filter	227061	113606	RareMetalWorker
CLHNS	Asian_Vand_ExomeChip Consortium_15033784_A	GenomeStudio version 2011.1 + Genotyping Module version 1.9.4 + GenTrain Version 1.0	EigenSoft	GWAS	no filter	≥ 95%	> 10 ⁻⁶	239844	55138	RvTest
CROATIA-Korcula	Illumina ExomeChip V1.0	Used the GenomeStudio cluster files provided by the CHARGE consortium from their joint calling	GenABEL	Exome Chip (only variants with MAF>5%)	no filter	> 98%	> 10 ⁻⁶	234824	234824	RvTest
deCODE	Illumina HumanHap and OmniExpress arrays (followed by imputation)	BeadStudio	EIGENSTRAT	Use 120,732 uncorrelated SNPs on the Illumina chips	NA	NA	NA	Replication List	Replication List	In-house software at deCode
DHS	Illumina ExomeChip V1.0	GeneCall + Zcall	EIGENSOFT	GWAS	> 0%	≥ 95%	> 10 ⁻⁶	245370	89384	RvTest
Diacore	Axiom UK Biobank Array	Axiom GT1 in Genotyping Console 4.0	SNPRelate (R package)	Others:all pairwise independent (LD<0.5) variants on chip	no filter	≥ 95%	≥ 10 ⁻⁶	799756	752829	RvTest
DPS	HumanExome-12v1_A	Genotype calls generated on cluster boundaries trained on using study samples + manual review of clusterplots	PLINK	Exome Chip	> 0%	≥ 95%	> 10 ⁻⁵	241972	62015	RvTest (with empirical kinship)
DR's EXTRA	HumanExome-12v1-1_A	Illumina GenCall using standard Illumina cluster files + Zcall	PLINK	Exome Chip	> 0%	≥ 95%	> 10 ⁻⁵	101413	62002	RvTest (with empirical kinship)
EFSOCH	Illumina Human Exome Beadchip v1	GenCall followed by zCall	PLINK	Exome Chip	no filter	> 99%	> 10 ⁻⁴	234763	96644	RareMetalWorker
EGCUT	Illumina HumanExome-12v1-1	GeneCall + Zcall (Exome-chip QC SOP v5)	PLINK	Exome Chip	> 0%	≥ 90%	> 10 ⁻⁶	241834	102498	RareMetalWorker
EPIC	Customized Illumina ExomeChip V1.1	Optical + Zcall	R	Other	≥ 0%	≥ 97%	10 ⁻⁶ for MAF ≥ 5% / 10 ⁻¹⁵ for MAF < 5%	228846	173971	RareMetalWorker
EPIC-Potsdam	Illumina ExomeChip V1.1	GeneCall + Zcall (calling QC procedure according to Grove et al)	R version 3.0.3 / package SNPRelate 0.9.19 (PCs)	AIMs	no filter	≥ 99%	> 10 ⁻⁶	240027	107789	RareMetalWorker
EpiHealth	Illumina HumanCoreExome	GenCall + zCall (Oxford protocol)	PLINK	HumanCoreExome SNPs after minor allele frequency filtering and LD pruning.	> 0%	≥ 97% (GenCall), ≥ 99% (zCall)	≥ 10 ⁻⁴	233185	101355	RvTest
EXTEND	humanCore+exome	GenCall followed by zCall	PLINK	Human Core + Exome Chip	no filter	≥ 98%	> 10 ⁻⁴	236695	97733	RvTest

FamHS	Illumina ExomeChip V1.0	Charge Exomechip Joint calling	Eigensoft	GWAS	≥ 0%	> 90% (AA) ≥ 99% (EA)	no filter	237729 (AA) 237376 (EA)	100012 (AA) 96310 (EA)	RareMetalWorker
Fenland	Illumina ExomeChip V1.0	GeneCall + Zcall (Oxford Protocol)	PLINK	Exome Chip	>0%	≥ 97%	> 10 ⁻⁶	241,979	99,394	RareMetalWorker
FIN-D2D 2007	HumanExome-12v1-1_A	Illumina GenCall using standard Illumina cluster files + Zcall	PLINK	Exome Chip	> 0%	≥ 95%	> 10 ⁻⁵	238984	81883	RvTest (with empirical kinship)
FINRISK 2007	HumanExome-12v1-1_A	Illumina GenCall using standard Illumina cluster files + Zcall	PLINK	Exome Chip	> 0%	≥ 95%	> 10 ⁻⁵	238984	63310	RvTest (with empirical kinship)
FINRISKEXTRE MES	Illumina ExomeChip V1.2	GeneCall + Zcall (Oxford Protocol)	Eigensoft	Principal components	no filter	> 95%	no filter	219702	66303	RareMetalWorker
FRAM	Illumina ExomeChip V1.0	GenTrain 2.0 clustering algorithm	Eigensoft	GWAS	> 0%	≥ 90%	> 10 ⁻⁶	246673	133293	RareMetalWorker
FUSION	HumanExome-12v1-1_A	Illumina GenCall using standard Illumina cluster files + Zcall	PLINK	Exome Chip	> 0%	≥ 95%	> 10 ⁻⁵	238984	80155	RvTest (with empirical kinship)
FVG	HumanExome-12v1-1_A.bpm	GenomeStudio + Zcall (Oxford Protocol)	GenABEL	Exome Chip	> 0%	> 99%	> 10 ⁻⁸	239867	70386	RareMetalWorker
GENOA	Illumina ExomeChip 12v1.1 Beadchip	GeneCall	R	Autosome SNPs with MAF > 0.05 and complete data for the entire sample	no filter	≥ 95%	no filter	233507 (AA) 240121 (EA)	114091 (AA) 93284 (EA)	RareMetalWorker
GRAPHIC	Illumina HumanExomee 12v1.1	GenCall + zCall (Sanger/Oxford? protocol)	NA - empirical kinship matrix modelled instead	NA - empirical kinship matrix modelled instead	> 0%	≥ 99% (zCall)	> 10 ⁻⁶	245901	96963	RareMetalWorker
GS:SFHS	Illumina ExomeChip V1.0	Used the GenomeStudio cluster files provided by the CHARGE consortium from their joint calling	GenABEL	Exome Chip (only variants with MAF>5%)	no filter	> 98%	> 10 ⁻⁶	232931	136001	RvTest
Health	Illumina HumanExome-12v1	GenCall + Zcall	PLINK	AIM SNPs for outlier detection, Exome Chip for adjustment	> 0%	≥ 98%	> 10 ⁻⁴	227842	128036	RareMetalWorker (with empirical kinship)
HELIC MANOLIS	Illumina HumanExome-12v1_A	GenCall and Zcall (UK exomechip protocol SOPv5)	PLINK	Exome chip SNPs -MAF ≥ 1%, complex regions excluded and LD pruned using r-squared 0.2	≥ 0%	GenCall call rate 95% and zCall call rate 99%	> 10 ⁻⁶	239497	60488	RvTest
HELIC Pomak	Illumina HumanExome-12v1_A	GenCall and Zcall (UK exomechip protocol SOPv5)	PLINK	Exome chip SNPs -MAF ≥ 1%, complex regions excluded and LD pruned using r-squared 0.2	≥ 0%	GenCall call rate 95% and zCall call rate 99%	> 10 ⁻⁶	239506	54882	RvTest
HUNT	Illumina HumanExome-12v1-1	GeneCall + Zcall (Oxford Protocol)	smartpca	Exome Chip SNPs that are polymorphisms 1000G ALL	no filter	≥ 99.9%	> 10 ⁻⁴	231575	86581	RvTest
Inter99	Illumina HumanExome-12v1	GenCall + Zcall	PLINK	AIM SNPs for outlier detection, Exome Chip fo adjustment	> 0%	≥ 98%	> 10 ⁻⁴	227842	139181	RareMetalWorker (with empirical kinship)
InterAct	HumanCoreExome-12v1	GenCall + Zcall (Oxford Protocol)	PLINK	core exome chip	> 0%	≥ 95%	> 10 ⁻⁶	237,967	128,317	RareMetalWorker
IRASFS	Illumina ExomeChip V1.0 and V1.1	GeneCall + zCall	ADMIXTURE	Exome Chip	> 0%	≥ 99%	no filter	93966 (AA) 83337 (HA)	93168 (AA) 80791 (HA)	RareMetalWorker
JHS	Illumina ExomeChip V1.0	CHARGE joint calling (Illumina GenomeStudio v2011.1 software was utilized with the GenTrain 2.0 clustering algorithm)	Eigensoft	Bi-allelic Exome Chip SNPs with MAF > 0.05, HWE p > 0.000001, callrate > 99%, pruned to be pairwise independent with r = 0.3 in plink.	> 0%	≥ 95%	no filter	246669	136949	RareMetalWorker
KORA-F4	Illumina ExomeChip V1.0	GeneCall + Zcall (Oxford Protocol)	PLINK	AIMS	no filter	≥ 98%	> 10 ⁻⁷	245976	66896	RvTest
Leipzig-adults	Illumina HumanExome-12v1_A	GeneCall + Zcall (Oxford Protocol)	plink	Exome Chip	> 0%	≥ 99%	> 10 ⁻⁴	231460	82683	RareMetalWorker
LOLIPOP-Exome	Illumina Human Exome BeadChip	GeneCall + Zcall (Oxford Protocol)	Eigensoft	GWAS	≥ 0%	≥ 95%	> 10 ⁻⁴	240270	73936	RareMetalWorker
LOLIPOP-OmniEE	Illumina OmniExpressExome BeadChip	GeneCall + Zcall (Oxford Protocol)	Eigensoft	GWAS	≥ 0%	≥ 95%	> 10 ⁻⁴	240115	67834	RareMetalWorker

MESA	llumina Exome Chip v1.0	llumina GenomeStudio2011.1	Eigensoft	Exome Chip	> 0%	≥ 90%	> 10 ⁻⁶	238876	136368	RvTest
METSIM	HumanExome-12v1_A	Genotype calls generated on cluster boundaries trained on using study samples + manual review of clusterplots	PLINK	Exome Chip	> 0%	≥ 95%	> 10 ⁻⁵	241972	91099	RvTest (with empirical kinship)
MHIBB	llumina ExomeChip V1.0	GeneCall + Zcall (Oxford Protocol)	PLINK-MDS	AIMS	> 0%	≥ 90%	> 10 ⁻⁶	245241	136395	RvTest
MORGAM	Customized llumina ExomeChip V1.1	Opticall + Zcall	R	Other	≥ 0%	≥ 97%	10 ⁻⁶ for MAF ≥ 5% / 10 ⁻¹⁵ for MAF < 5%	233874	131212	RareMetalWorker
NEO Study	llumina HumanCoreExomeChip-24V1.0	GeneCall (SOP v5)	PLINK	Based on LD prune	> 0%	≥ 98%	> 10 ⁻⁶	209874	105552	RvTest
NHAPC	llumina ExomeChip+ v1.0 (Asian_Vand_ExomeChip Consortium)	central calling effort (Grove et al. PloS One 8(7):e68095)	EIGENSOFT	Exome Chip	> 0%	≥ 95%	> 10 ⁻⁶	208635	110204	RareMetalWorker
Nijmegen	llumina ExomeChip V1.1	GeneCall + Zcall (Exome-chip QC SOP v5.pdf)	PLINK	AIMS	≥ 0%	≥ 95%	> 10 ⁻⁶	242474	114532	RvTest
OMICS-EPICNorfolk	Affymetrix Axiom UKBiobank	Axiom GT1	PLINK v1.9beta	GWAS	> 0%	≥ 95%	> 10 ⁻⁶	728244	57836	RareMetalWorker
OMICS-Fenland	Affymetrix Axiom UKBiobank	Axiom GT1	PLINK v1.9beta	GWAS	> 0%	≥ 95%	> 10 ⁻⁶	719871	57988	RareMetalWorker
Oxford BioBank	llumina HumanExome-12v1_A	GeneCall + Zcall (Oxford Protocol)	PLINK	Exome Chip	> 0%	≥ 99%	> 10 ⁻⁴	233233	126490	RareMetalWorker
PCOS	llumina Human Core Exome	GeneCall + Zcall (Oxford Protocol)	PLINK-MDS	GWAS	> 0%	≥ 99%	> 10 ⁻⁴	524527	80909	RareMetalWorker
PIVUS	llumina HumanExome-12v1_A	GeneCall + Zcall (Oxford Protocol)	PLINK-MDS	AIMS	> 0%	≥ 99%	> 10 ⁻⁴	233149	79997	RareMetalWorker
PROMIS	Customized llumina ExomeChip V1.1	Opticall + Zcall	R	Other	≥ 0%	≥ 97%	10 ⁻⁶ for MAF ≥ 5% / 10 ⁻¹⁵ for MAF < 5%	233828	121848	RareMetalWorker
RAINE	lluminia HumanExome-12v1_A	llumina GenomeStudio GenTrain Clustering algorithm + zCall	Eigensoft	AIMS	> 0%	≥ 95%	> 10 ⁻⁴	240806	90819	RvTest
RISC	llumina Human Exome Beadchip v1	GenCall followed by zCall	PLINK	Exome Chip	no filter	> 99%	> 10 ⁻⁴	236875	69642	RareMetalWorker
RSI	llumina ExomeChip V1.1	GeneCall + Zcall (CHARGE Protocol)	PLINK	GWAS	> 0%	≥ 90%	> 10 ⁻⁶	237766	108330	RvTest
SDC	llumina HumanExome-12v1	GenCall + Zcall	PLINK	AIM SNPs for outlier detection, Exome Chip for adjustment	> 0%	≥ 98%	> 10 ⁻⁴	227842	98470	RareMetalWorker (with empirical kinship)
SHIP	llumina ExomeChip V1.0	GenCall + Zcall (Oxford Protocol)	Eigensoft	Exome Chip	≥ 0%	≥ 95%	≥ 10 ⁻⁴	247021	156503	RvTest
SHIP-TREND	llumina ExomeChip V1.0	GenCall + Zcall (Oxford Protocol)	Eigensoft	Exome Chip	≥ 0%	≥ 95%	≥ 10 ⁻⁴	247021	156503	RvTest
SOLID-TIMI 52	Affymetrix Axiom Biobank Plus GSKBB1	AxiomGT1	GCTA	GWAS	> 0%	≥ 95%	> 10 ⁻⁶	555033	56159	RareMetalWorker
Sorbs	llumina HumanExome-12v1_A	GeneCall + Zcall (Oxford Protocol)	PLINK	Exome Chip	> 0%	≥ 99%	> 10 ⁻⁴	231460	59808	RareMetalWorker
STABILITY	llumina HumanOmniExpressExome-8 V1.0	llumina pre-defined EGT clusters (version A) + zCall	SNPRelate (R package)	GWAS	> 0%	≥ 95%	> 10 ⁻²⁰	919271	79734	RareMetalWorker
TUDR	llumina Human ExomeChip V1.2	GenomeStudio with extensive manual review	SmartPCA	Exome Chip	> 1%	≥ 90%	> 10 ⁻⁶	237654	47497	RareMetalWorker
TwinsUK	llumina HumanExome-12v1_A	GeneCall + Zcall (Oxford Protocol)	PLINK	Exome Chip	> 0%	≥ 99%	> 10 ⁻⁴	233233	87603	RareMetalWorker

UK Biobank	Affymetrix UK Biobank Axiom Affymetrix UK BiLEVE Axiom	Algorithms implemented in Affymetrix Power Tools + Customised Algorithms by Affymetrix specifically for UK Biobank See UK Biobank Documentation: http://www.ukbiobank.ac.uk/wp-content/uploads/2014/04/UKBiobank_genotyping_QC_documentation-web.pdf	flashPCA See UK Biobank Documentation: http://www.ukbiobank.ac.uk/wp-content/uploads/2014/04/UKBiobank_genotyping_QC_documentation-web.pdf	-	-	-	-	-	Replication List	BOLT-LMM
ULSAM	Illumina HumanExome-12v1_A	GeneCall + Zcall (Oxford Protocol)	PLINK	AIMS	> 0%	≥ 99%	> 10 ⁻⁴	233149	81810	RareMetalWorker
Vejle	Illumina HumanExome-12v1	GenCall + Zcall	PLINK	AIM SNPs for outlier detection, Exome Chip for adjustment	> 0%	≥ 98%	> 10 ⁻⁴	227842	107395 (case) 73630 (control)	RareMetalWorker (with empirical kinship)
WGHS	Illumina Exome Chip v1.1	CHARGE Best Practices (PMID 23874508), GenomeStudio v 2011.1, Zcall, in-house manually validated statistical model	Eigensoft	SNPs used from GWAS	> 0%	≥ 95%	> 10 ⁻⁶	235667	176817	RareMetalWorker
WHI	Illumina ExomeChip V1.0	GenomeStudio v2010.3	PLINK-MDS	AIMS	> 0%	≥ 90%	> 10 ⁻⁶	246470	158669	RvTest
WTCCC/ UKT2D	Illumina HumanExome-12v1_A	GeneCall + Zcall (Oxford Protocol)	PLINK	Exome Chip	> 0%	≥ 99%	> 10 ⁻⁴	233233	103735	RareMetalWorker
YFS	Illumina CoreExome v1.0b	GenCall	PLINK	Exome Chip	> 0%	≥ 95%	> 10 ⁻⁶	238194	75794	RvTest

a. Call rate to exclude individuals for whom genotyping success rate is less than a certain percentage (to exclude poorly genotyped samples)

Vejle (cases)	BMI (kg/m ²)	1249	30.18	4.89	29.65	17.64	52.62	772	31.01	6.21	30.26	17.75	65.40
	Weight (kg)	1249	92.44	16.92	90.10	55.30	168.20	772	81.84	17.54	80.00	42.10	186.80
	Height (cm)	1249	174.83	6.31	175.00	148.00	203.00	772	162.34	6.35	162.00	140.00	182.00
	WC (cm)	1249	106.27	12.45	105.00	73.00	159.00	772	101.30	14.12	101.00	65.00	157.00
	Hip (cm)	1249	106.77	9.16	105.00	85.00	155.00	772	110.63	13.22	109.00	65.00	189.00
	WHR (cm/cm)	1249	0.99	0.06	0.99	0.82	1.25	772	0.92	0.06	0.92	0.68	1.20
Vejle (controls)	Age (yrs)	146	62.35	10.24	64.34	31.03	77.89	288	55.13	12.52	55.64	26.93	77.83
	BMI (kg/m ²)	146	23.05	1.47	23.33	16.53	25.00	288	21.75	1.93	21.77	15.74	24.99
	Weight (kg)	146	72.01	7.56	72.10	47.20	90.60	288	59.47	6.17	59.40	42.40	74.10
	Height (cm)	146	176.56	6.65	177.00	160.00	191.00	288	165.34	5.73	165.00	148.00	180.00
	WC (cm)	146	87.31	6.29	87.00	64.00	103.00	288	77.12	6.57	77.00	59.00	99.00
	Hip (cm)	146	95.07	5.29	95.75	80.00	108.00	288	91.87	6.25	92.00	71.00	113.00
	WHR (cm/cm)	146	0.92	0.05	0.92	0.74	1.04	288	0.84	0.06	0.84	0.63	1.03
WGHS	Age (yrs)	-	-	-	-	-	-	19930	54.74	7.05	53.04	38.71	89.89
	BMI (kg/m ²)	-	-	-	-	-	-	19578	25.71	4.82	24.70	14.23	59.58
	Weight (kg)	-	-	-	-	-	-	19708	69.45	13.77	67.13	38.56	158.80
	Height (cm)	-	-	-	-	-	-	19766	164.40	6.26	165.10	129.50	200.70
	WC (cm)	-	-	-	-	-	-	19930	88.85	14.31	86.36	38.10	167.60
	Hip (cm)	-	-	-	-	-	-	19930	106.30	12.06	104.10	50.80	193.00
	WHR (cm/cm)	-	-	-	-	-	-	19930	0.83	0.08	0.83	0.33	1.93
WHI (AA)	Age (yrs)	-	-	-	-	-	-	3519	64.90	6.60	65.00	50.00	79.00
	BMI (kg/m ²)	-	-	-	-	-	-	3519	30.60	6.20	29.80	15.80	141.00
	Weight (kg)	-	-	-	-	-	-	3515	80.60	17.10	78.20	42.60	171.50
	Height (cm)	-	-	-	-	-	-	3502	162.00	6.60	162.00	101.20	194.10
	WC (cm)	-	-	-	-	-	-	3513	90.90	13.00	90.00	35.50	161.70
	Hip (cm)	-	-	-	-	-	-	3512	110.20	12.50	109.00	43.50	170.50
	WHR (cm/cm)	-	-	-	-	-	-	3510	0.82	0.08	0.82	0.28	1.44
WHI (EA)	Age (yrs)	-	-	-	-	-	-	21858	66.20	6.70	67.00	50.00	81.00
	BMI (kg/m ²)	-	-	-	-	-	-	21857	28.20	5.90	27.30	13.80	159.70
	Weight (kg)	-	-	-	-	-	-	21820	73.90	16.20	71.20	32.00	197.50
	Height (cm)	-	-	-	-	-	-	21777	161.50	6.40	161.50	96.00	193.70
	WC (cm)	-	-	-	-	-	-	21791	87.90	13.90	86.00	35.50	191.80
	Hip (cm)	-	-	-	-	-	-	21780	107.00	12.20	105.00	42.00	196.50
	WHR (cm/cm)	-	-	-	-	-	-	21773	0.82	0.08	0.81	0.31	2.49
WTCCC/UKT2D	Age (yrs)	1165	52.46	10.12	53.00	20.90	87.00	851	52.99	11.02	54.00	23.38	83.35
	BMI (kg/m ²)	1165	30.46	5.55	29.70	16.80	60.30	850	32.90	7.21	31.95	17.90	65.16
	Weight (kg)	1165	94.16	18.71	92.08	47.63	190.51	850	85.84	20.45	82.56	43.00	171.00
	Height (cm)	1165	175.67	7.23	175.26	150.00	220.00	851	161.34	6.64	161.00	139.00	180.34
	WC (cm)	1144	106.83	14.06	105.00	71.12	200.66	835	102.54	15.67	101.00	66.04	172.00
	Hip (cm)	1144	109.17	11.49	108.00	78.70	215.90	835	115.15	15.31	114.00	71.00	177.00
	WHR (cm/cm)	1144	0.98	0.07	1.00	0.78	1.28	835	0.89	0.07	0.90	0.70	1.22
YFS	Age (yrs)	851	41.90	5.02	43.00	34.00	49.00	1042	42.06	4.94	43.00	34.00	49.00
	BMI (kg/m ²)	851	26.98	4.34	26.26	16.21	50.99	1042	26.10	5.49	25.04	16.49	58.47
	Weight (kg)	851	87.28	15.81	85.00	54.00	186.00	1042	71.96	15.34	69.00	43.00	167.00
	Height (cm)	851	179.70	6.70	180.00	156.00	203.00	1042	166.09	6.00	166.00	148.00	191.00
	WC (cm)	851	96.76	12.46	95.30	68.95	160.40	1042	87.58	14.02	85.30	61.10	145.70
	Hip (cm)	851	101.12	7.53	100.50	85.00	149.70	1042	102.04	10.20	100.45	79.40	167.25
	WHR (cm/cm)	851	0.95	0.07	0.95	0.73	1.20	1042	0.86	0.07	0.85	0.66	1.11

a. Studies that included more than one ancestry are indicated with abbreviations next to the study name including: EA-European Ancestry; AA-African Ancestry; HA-Hispanic Ancestry; EAS-East Asian Ancestry; SAS-South Asian Ancestry.

Supplementary Table 4. Approximate conditional analysis for multiple signals at a given locus (1Mb region) in the GIANT discovery set for array-wide significant coding variants^a (P-value<2e-7) in the all ancestry and European only analyses.

Locus (+/- 1 Mb of a given variant) ^b	rsID	Chr	Position (GRCh37) ^b	Effect/Other Alleles	Gene	Effect Allele Frequency	Unconditioned results				Lead Tag SNP (LTS) unconditioned by locus ^d	Secondary signals, Most significant SNP after conditioning on LTS by locus ^f						If applicable, additional significant SNPs after conditioning on secondary signal
							Effect size ^c (SD/allele)	SE	P-value	rsID		Distance From LTS	r ² with LTS	Effect Allele Frequency	Effect size ^c (SD/allele)	SE	P-value	
All Ancestry Additive model Sex-combined analyses																		
1	rs61730011	1	119427467	C/A	TBX15	0.042	-0.035	0.006	3.57E-08	Yes	None							
2	rs7607980	2	165551201	C/T	COBLL1	0.121	-0.026	0.004	1.94E-09	Yes	None							
3	rs1034405	3	50597092	A/G	C3orf18	0.137	-0.020	0.004	8.85E-08	Yes	None							
4	rs13303	3	52558008	C/T	STAB1	0.448	-0.018	0.003	1.26E-12	Yes	None							
	rs3617	3	52833805	A/C	ITIH3	0.463	-0.015	0.003	3.72E-08	No (rs13303)	None							
5	rs62266958	3	129137188	T/C	EFCAB12	0.060	-0.032	0.005	5.62E-10	Yes	None							
6	rs1804080	4	89625427	C/G	HERC3	0.160	-0.019	0.004	5.93E-08	Yes	None							
7	rs1966265	5	176516631	G/A	FGFR4	0.231	0.021	0.003	1.64E-12	Yes	None							
8	rs146860658	6	26108117	C/T	HIST1H1T	0.001	0.229	0.042	4.30E-08	Yes	None							
9	rs1892172	6	127476516	G/A	RSPO3	0.461	0.026	0.002	1.06E-25	Yes	rs139745911	291438	0.000	0.009	0.097	0.015	3.68E-11	None
	rs139745911	6	127767954	G/A	KIAA0408	0.009	0.107	0.015	2.07E-13	No (rs1892172)	rs1892172	291438	0.000	0.539	0.024	0.002	4.37E-23	None
10	rs1334576	6	7211818	A/G	RREB1	0.438	-0.014	0.003	8.23E-08	Yes	None							
11	rs35332062	7	73012042	A/G	MLXIPL	0.116	-0.022	0.004	3.21E-08	No (rs3812316)	None							
	rs3812316	7	73020337	G/C		0.114	-0.024	0.004	4.82E-09	Yes	None							
12	rs17417407	10	95931087	G/T	PLCE1	0.175	0.019	0.003	1.07E-08	Yes	None							
13	rs138315382	10	123279643	C/T	FGFR2	0.001	0.258	0.049	1.38E-07	Yes	None							
14	rs35169799	11	64031241	C/T	PLCB3	0.060	0.028	0.005	6.97E-08	Yes	None							
15	rs145878042	12	48143315	G/A	RAPGEF3	0.010	-0.090	0.012	1.28E-13	Yes	None							
16 ^f	rs11057353	12	124265687	C/T	DNAH10	0.364	-0.019	0.003	7.85E-14	No (rs11057401)	rs11057401	161619	0.005	0.303	-0.023	0.003	3.14E-16	None
	rs34934281	12	124330311	T/C		0.106	-0.023	0.004	6.46E-09	No (rs11057401)	rs11057401	96995	0.085	0.303	-0.025	0.003	4.54E-17	None
	rs11057401	12	124427306	A/T		CCDC92	0.303	-0.027	0.003	1.67E-23	Yes	None						
17	rs17677991	15	42032383	C/G	MGA	0.345	0.016	0.003	8.08E-10	Yes	None							
18	rs3810818	16	4432029	C/A	VASN	0.234	-0.018	0.003	1.08E-08	No (rs3810818)	None							
	rs3747579	16	4445327	T/C	CORO7	0.308	-0.017	0.003	6.85E-09	Yes	None							
19	rs9922085	16	67397580	C/G	LRRC36	0.068	-0.030	0.005	2.78E-08	No (rs8052655)	None							
	rs8052655	16	67409180	A/G		0.067	-0.030	0.005	2.32E-08	Yes	None							
20	rs874628	19	18304700	A/G	MPV17L2	0.266	0.016	0.003	3.64E-08	Yes	None							
21	rs2287922	19	49232226	G/A	RASIP1	0.470	0.016	0.003	1.74E-08	Yes	None							
22	rs4911494	20	33971914	C/T	UQCC1	0.414	0.020	0.003	2.51E-13	Yes	None							
	rs224331	20	34022387	C/A	GDF5	0.368	-0.019	0.003	8.19E-09	No (rs4911494)	None							
All Ancestry Additive model Women only analyses																		
1	rs141845046	1	154987704	T/C	ZBTB7B	0.023	-0.064	0.011	1.25E-08	Yes	None							
2	rs55920843	2	158412701	G/T	ACVR1C	0.010	-0.094	0.018	1.09E-07	Yes	None							
3	rs7607980	2	165551201	C/T	COBLL1	0.122	-0.060	0.006	2.02E-24	Yes	None							
4	rs13303	3	52558008	C/T	STAB1	0.565	-0.020	0.004	3.94E-08	Yes	None							
5	rs62266958	3	129137188	T/C	EFCAB12	0.061	-0.050	0.007	4.34E-12	Yes	None							
	rs2625973	3	129284818	C/A	PLXND1	0.262	-0.021	0.004	1.51E-07	No (rs62266958)	rs73202271 ^g	154800	0.002	0.082	0.046	0.007	3.18E-11	None
6	rs1804080	4	89625427	C/G	HERC3	0.161	-0.034	0.005	1.89E-11	Yes	None							
	rs7657817	4	89668859	T/C	FAM13A	0.189	-0.025	0.004	3.56E-08	No (rs1804080)	None							
7	rs1892172	6	127476516	G/A	RSPO3	0.542	0.035	0.003	3.83E-23	Yes	rs139745911	291438	0.000	0.009	0.137	0.020	1.46E-11	None
	rs139745911	6	127767954	G/A	KIAA0408	0.009	0.150	0.020	1.15E-13	No (rs1892172)	rs1892172	291438	0.000	0.542	0.032	0.003	2.40E-20	None
8	rs35169799	11	64031241	C/T	PLCB3	0.060	0.043	0.007	2.59E-09	Yes	None							
9	rs145878042	12	48143315	G/A	RAPGEF3	0.010	-0.102	0.017	8.29E-10	Yes	None							
10 ^h	rs11057353	12	124265687	C/T	DNAH10	0.632	-0.028	0.004	1.00E-14	No (rs11057401)	rs11057401	161619	0.005	0.311	-0.034	0.004	1.39E-18	None
	rs34934281	12	124330311	T/C		0.108	-0.041	0.006	2.25E-13	No (rs11057401)	rs11057401	96995	0.085	0.311	-0.034	0.004	2.77E-17	None
	rs11057401	12	124427306	A/T		CCDC92	0.311	-0.040	0.004	1.21E-26	Yes	None						
11	rs3810818	16	4432029	C/A	VASN	0.769	-0.025	0.005	2.69E-08	No (rs3747579)	None							
	rs3747579	16	4445327	T/C	CORO7	0.690	-0.023	0.004	3.75E-09	Yes	None							
12	rs11554159	19	18285944	G/A	IFI30	0.256	0.021	0.004	9.33E-08	No (rs874628)	None							
	rs874628	19	18304700	A/G	MPV17L2	0.269	0.023	0.004	9.76E-09	Yes	None							
13	rs2287922	19	49232226	G/A	RASIP1	0.477	0.020	0.004	1.22E-07	Yes	None							

All Ancestry Additive model Men only analyses

1	rs1966265	5	176516631	G/A	<i>FGFR4</i>	0.234	0.025	0.004	6.02E-09	Yes	None							
2	rs1334576	6	7211818	A/G	<i>RREB1</i>	0.448	-0.019	0.004	8.06E-08	Yes	None							
3	rs148108950	13	96665697	G/A	<i>UGGT2</i>	0.006	0.142	0.025	9.71E-09	Yes	None							
4	rs1042704	14	23312594	G/A	<i>MMP14</i>	0.197	0.023	0.004	1.09E-07	Yes	None							
5	rs4911494	20	33971914	C/T	<i>UQCC1</i>	0.579	0.024	0.004	2.02E-11	Yes	None							
	rs224331	20	34022387	C/A	<i>GDF5</i>	0.371	-0.025	0.005	3.17E-08	Yes	None							

European Additive model Sex-combined analyses

1	rs35515638	1	173802608	A/G	<i>DARS2</i>	0.001	0.217	0.041	1.09E-07	Yes	None							
2	rs62266958	3	129137188	T/C	<i>EFCAB12</i>	0.069	-0.035	0.005	2.97E-11	Yes	None							

European Additive model Men only analyses

1	rs4911494	20	33971914	C/T	<i>UQCC1</i>	0.609	0.019	0.003	2.14E-10	Yes	None							
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Abbreviations: GRCh37=human genome assembly build 37;rsID=based on dbSNP;SD=standard deviation; SE=standard error

a Coding variants refer to variants located in the exons and splicing junction regions.

b Variant positions are reported according to Human assembly build 37 and their alleles are coded based on the positive strand.

c Effect size is based on standard deviation (SD) per effect allele

d Lead Tag SNP is the most significant SNP in the locus (defined by a +/-1Mb region)

e Secondary signal , Pvalue cut-off at <2e-7

f rs11057353 conditional p=7.56e-07, beta=-0.013; rs34934281 conditional p=0.0415, beta=-0.0088

g rs73202271 Unconditioned results: Effect size=0.026; SE=0.006; P-value=5.96E-05

h rs11057353 conditional p=5.86e-07, beta=-0.018; rs34934281 conditional p=0.00077, beta=-0.019

Supplementary Table 5. Conditional analysis and reciprocal conditional analysis in the UK-Biobank data of coding variants^a that reach array-wide significance ($P < 2e-7$) in the sex-combined results with all known variants within a locus (1Mb region) identified from Genome-wide association studies (GWAS) for WHR adjusted for BMI.^b

Locus (+/- 1 Mb of a given variant) ^c	<i>gene</i>	ExomeChip Coding Variant			ExomeChip variant unconditioned		ExomeChip variant conditioned on GWAS variant		GWAS variant (all are non-coding)	GWAS variant unconditioned		GWAS variant conditioned on ExomeChip variant		CONCLUSION ^g									
		Chr	Position (GRCh37) ^d	rsID	Effect Allele	Frequency ^e	Effect size ^f (SD/allele)	P-value	Effect size ^f (SD/allele)	P-value	rsID	Effect size ^f (SD/allele)	P-value		Effect size ^f (SD/allele)	P-value							
Additive model Sex-combined analyses																							
1	<i>TBX15</i>	1	119427467	rs61730011	0.957	-0.053	7.54E-08	-0.037	2.56E-04	rs2645294	0.037	1.76E-19	0.034	4.64E-16	Inconclusive								
								-0.047	2.04E-06	rs12731372	-0.022	4.71E-06	-0.019	1.34E-04	Inconclusive								
								-0.050	4.28E-07	rs12143789	0.020	2.38E-04	0.017	1.45E-03	Inconclusive								
								-0.031	2.56E-03	rs1106529	0.038	4.20E-16	0.034	1.01E-11	Inconclusive								
								0.018	7.83E-04	rs2645294	0.037	1.76E-19	0.037	5.89E-19	Inconclusive								
								0.021	8.72E-05	rs12731372	-0.022	4.71E-06	-0.023	1.92E-06	Inconclusive								
								0.057	5.88E-01	rs12143789	0.020	2.38E-04	-0.037	7.23E-01	Inconclusive								
					0.008	1.31E-01	rs1106529	0.038	4.20E-16	0.036	1.37E-13	Inconclusive											
2	<i>ZBTB7B</i>	1	154987704	rs141845046	0.976	-0.069	9.91E-07	-0.052	3.83E-04	rs905938	-0.027	4.25E-09	-0.023	1.48E-06	Inconclusive - suggestive not independent								
3	<i>COBLL1</i>	2	165528624	rs7607980	0.879	-0.030	3.07E-06	-0.013	7.71E-02	rs1128249	-0.029	6.69E-12	-0.025	9.53E-08	Not independent								
								-0.012	9.12E-02	rs10195252	-0.030	5.06E-13	-0.027	8.06E-09	Not independent								
								-0.016	2.81E-02	rs12692737	-0.024	1.98E-08	-0.019	1.36E-04	Inconclusive								
								-0.015	6.56E-02	rs12692738	-0.025	5.64E-07	-0.017	9.92E-03	Not independent								
							-0.031	1.52E-06	rs17185198	-0.003	5.60E-01	-0.008	1.93E-01	Inconclusive									
4	<i>TFPI</i>	2	188343497	rs7586970	0.697	-0.024	1.50E-07	-0.007	2.45E-01	rs1569135	-0.027	1.40E-10	-0.022	1.12E-04	Not independent								
5	<i>STAB1</i> <i>ITIH3</i>	3	52558008	rs13303	0.445	-0.021	3.19E-07	-0.008	1.92E-01	rs2276824	-0.023	1.92E-08	-0.017	7.54E-03	Not independent								
															3	52833805	rs3617	0.541	-0.019	5.48E-06	-0.001	8.70E-01	-0.022
6	<i>EFCAB12</i> <i>PLXND1</i>	3	129137188	rs62266958	0.936	-0.041	2.71E-07	-0.020	2.24E-02	rs10804591	0.035	2.62E-12	0.029	1.40E-07	Inconclusive - suggestive not independent								
													3	129284818	rs2625973	0.733	-0.023	5.38E-07	-0.005	4.09E-01	0.032	7.38E-07	Not independent
													3	129293256	rs2255703	0.620	-0.014	7.17E-04	0.002	7.01E-01	0.036	8.43E-10	Inconclusive - suggestive not independent
7	<i>HERC3</i> <i>FAM13A</i>	4	89625427	rs1804080	0.838	-0.025	5.90E-06	-0.012	4.48E-02	rs9991328	0.033	1.68E-15	0.030	7.43E-12	Not independent								
													4	89668859	rs7657817	0.815	-0.021	1.35E-04	-0.010	6.39E-02	0.031	4.83E-13	Inconclusive - suggestive not independent
8	<i>FGFR4</i>	5	176516631	rs1966265	0.236	0.027	1.31E-08	0.013	4.92E-02	rs6556301	0.027	2.26E-10	0.020	6.01E-04	Not independent								
9	<i>RREB1</i>	6	7211818	rs1334576	0.565	-0.025	3.60E-09	-0.024	1.24E-08	rs1294410	0.029	1.17E-11	0.028	4.02E-11	Independent								
10	<i>UHRF1BP1</i>	6	34827085	rs9469913	0.847	-0.019	6.54E-04	-0.021	1.71E-04	rs1776897	-0.044	1.16E-09	-0.046	3.20E-10	Inconclusive								
<i>RSPO3</i>	6	127476516	rs1892172	0.543	0.040	3.08E-22	0.052	1.76E-26	rs11961815	0.006	2.02E-01	-0.025	4.63E-06	Colinearity									
							0.026	1.09E-09	rs72959041	0.168	1.94E-70	0.155	4.85E-58	Not independent - LD with another GWAS locus									
							0.013	2.18E-01	rs1936805	0.041	1.37E-23	0.029	5.60E-03	Not independent									

11							0.087	8.67E-06		rs1936805	0.041	1.37E-23	0.040	5.86E-22	Not independent - LD with another GWAS locus
	KIAA0408	6	127767954	rs139745911	0.010	0.101	1.82E-07								
							0.103	1.26E-07		rs11961815	0.006	2.02E-01	0.007	1.25E-01	Not independent - LD with another GWAS locus
							-0.024	2.51E-01		rs72959041	0.168	1.94E-70	0.172	8.49E-65	Not independent
12	MLXIPL	7	73012042	rs35332062	0.880	-0.018	3.93E-03	0.001	9.01E-01	rs6976930	-0.021	6.26E-05	-0.021	5.46E-03	Inconclusive
			73020337	rs3812316	0.881	-0.017	5.19E-03	0.002	8.29E-01				-0.022	4.06E-03	Inconclusive
13	PLCE1	10	95931087	rs17417407	0.173	0.020	2.05E-04	0.016	6.11E-03	rs10786152	-0.012	2.55E-03	-0.008	9.21E-02	Inconclusive
14	PLCB3	11	64031241	rs35169799	0.061	0.046	3.70E-08	0.035	2.18E-03	rs11231693	0.044	1.71E-06	0.018	1.59E-01	Not independent
	ABC9	12	123444507	rs58843120	0.987	-0.051	2.76E-03	-0.040	1.81E-02	rs4765219	-0.039	3.61E-19	-0.038	1.99E-18	Inconclusive
								-0.044	1.04E-02	rs863750	0.039	1.70E-20	0.039	5.72E-20	Inconclusive
								-0.002	5.88E-01	rs4765219	-0.039	3.61E-19	-0.038	1.27E-16	Inconclusive - suggestive not independent
	DNAH10	12	124265687	rs11057353	0.373	-0.015	5.69E-04								Inconclusive - suggestive not independent
								-0.007	1.29E-01	rs863750	0.039	1.70E-20	0.038	2.16E-18	Inconclusive - suggestive not independent
15								-0.010	1.53E-01	rs4765219	-0.039	3.61E-19	-0.036	1.30E-14	Not independent
		12	124330311	rs34934281	0.889	-0.030	1.86E-06	-0.016	1.46E-02	rs863750	0.039	1.70E-20	0.036	8.27E-17	Inconclusive - suggestive not independent
								0.016	2.50E-01	rs4765219	-0.039	3.61E-19	-0.054	8.55E-05	Not independent
	CCDC92	12	124427306	rs11057401	0.695	-0.036	4.59E-16	-0.031	7.94E-12	rs863750	0.039	1.70E-20	0.035	2.82E-16	Not independent - LD with another GWAS locus
16	MNS1	15	56756285	rs1715919	0.096	0.024	3.44E-04	0.019	1.89E-01	rs8030605	0.021	8.05E-04	0.005	7.06E-01	Inconclusive
		16	67397580	rs9922085	0.938	-0.045	6.76E-06	-0.047	3.81E-04				0.001	8.85E-01	Inconclusive
17	LRRC36	16	67409180	rs8052655	0.939	-0.044	1.03E-05	-0.045	5.92E-04	rs6499129	-0.019	5.66E-03	0.001	9.40E-01	Inconclusive
18	PEMT	17	17425631	rs897453	0.569	-0.023	3.69E-08	-0.017	9.18E-03	rs4646404	-0.022	6.37E-07	-0.008	2.59E-01	Not independent
		19	18285944	rs11554159	0.257	0.015	1.31E-03	0.005	3.78E-01				-0.022	5.94E-06	Inconclusive
19	MPV17L2	19	18304700	rs874628	0.271	0.013	3.44E-03	0.002	7.02E-01	rs12608504	-0.023	4.20E-08	-0.023	3.28E-06	Inconclusive
	UQCC1	20	33971914	rs4911494	0.602	0.016	2.11E-04	0.003	8.79E-01	rs224333	-0.016	1.65E-04	-0.013	4.85E-01	Inconclusive - suggestive not independent
	GDF5	20	34022387	rs224331	0.644	-0.015	4.96E-04	0.005	7.34E-01				-0.021	1.40E-01	Inconclusive
Additive model Women only analyses															
2	ZBTB7B	1	154987704	rs141845046	0.976	-0.102	1.40E-07	-0.084	2.51E-05	rs905938	-0.031	1.33E-06	-0.024	2.51E-04	Inconclusive - suggestive not independent
								-0.036	2.48E-04	rs1128249	-0.068	4.41E-32	-0.057	8.27E-19	Inconclusive - suggestive not independent
								-0.038	1.17E-04	rs10195252	-0.068	8.18E-32	-0.057	7.54E-19	Inconclusive - suggestive not independent

3	<i>COBLL1</i>	2	165528624	rs7607980	0.879	-0.076	7.85E-18	-0.045	7.64E-06	rs12692737	-0.057	9.24E-22	-0.042	7.41E-10	Inconclusive - suggestive not independent
								-0.044	1.41E-04	rs12692738	-0.060	2.11E-18	-0.037	3.58E-05	Inconclusive - suggestive not independent
								-0.080	2.53E-19	rs17185198	-0.016	4.98E-02	-0.026	1.11E-03	Colinearity
6	<i>EFCAB12</i>	3	129137188	rs62266958	0.936	-0.051	4.11E-06	-0.011	3.56E-01				0.056	5.78E-13	Not independent
	<i>PLXND1</i>	3	129284818	rs2625973	0.733	-0.035	2.77E-08	-0.002	7.62E-01	rs10804591	0.059	1.87E-17	0.057	1.17E-10	Not independent
		3	129293256	rs2255703	0.620	-0.027	4.66E-06	-0.001	9.36E-01				0.058	7.87E-13	Not independent
7	<i>HERC3</i>	4	89625427	rs1804080	0.838	-0.038	6.04E-07	-0.018	2.38E-02				0.045	1.66E-13	Inconclusive - suggestive not independent
	<i>FAM13A</i>	4	89668859	rs7657817	0.815	-0.032	1.33E-05	-0.017	2.62E-02	rs9991328	0.049	7.18E-18			Inconclusive - suggestive not independent
													0.046	8.80E-15	Inconclusive - suggestive not independent
								0.074	4.96E-28	rs11961815	0.012	5.67E-02	-0.032	2.46E-05	Colinearity
	<i>RSPO3</i>	6	127476516	rs1892172	0.543	0.059	6.28E-25	0.040	8.10E-12	rs72959041	0.229	2.70E-69	0.210	2.60E-56	Not independent - LD with another GWAS locus
								-0.001	9.28E-01	rs1936805	0.064	2.61E-29	0.065	7.68E-06	Not independent
11								0.116	1.30E-05	rs1936805	0.064	2.61E-29	0.062	1.43E-27	Not independent - LD with another GWAS
	<i>KIAA0408</i>	6	127767954	rs139745911	0.010	0.138	2.08E-07								
								0.141	1.19E-07	rs11961815	0.012	5.67E-02	0.014	2.98E-02	Not independent - LD with another GWAS
								-0.030	2.92E-01	rs72959041	0.229	2.70E-69	0.234	1.16E-63	Not independent
14	<i>PLCB3</i>	11	64031241	rs35169799	0.061	0.059	2.42E-07	0.046	3.77E-03	rs11231693	0.056	8.08E-06	0.022	2.00E-01	Not independent
	<i>ABCB9</i>	12	123444507	rs58843120	0.987	-0.048	3.86E-02	-0.033	1.60E-01	rs4765219	-0.057	3.27E-21	-0.056	1.05E-20	Inconclusive
								-0.037	1.10E-01	rs863750	0.059	4.42E-24	0.058	1.06E-23	Inconclusive
								-0.017	6.82E-03	rs4765219	-0.057	3.27E-21	-0.051	1.05E-15	Inconclusive - suggestive not independent
	<i>DNAH10</i>	12	124265687	rs11057353	0.373	-0.033	1.28E-08	-0.022	2.91E-04	rs863750	0.059	4.42E-24	0.054	7.36E-20	Inconclusive - suggestive not independent
15								-0.025	8.15E-03	rs4765219	-0.057	3.27E-21	-0.050	1.20E-14	Inconclusive - suggestive not independent
		12	124330311	rs34934281	0.889	-0.052	1.28E-09	-0.032	3.19E-04	rs863750	0.059	4.42E-24	0.053	7.73E-19	Inconclusive - suggestive not independent
								0.003	8.76E-01	rs4765219	-0.057	3.27E-21	-0.059	1.57E-03	Not independent
	<i>CCDC92</i>	12	124427306	rs11057401	0.695	-0.054	5.08E-19	-0.047	4.38E-14	rs863750	0.059	4.42E-24	0.052	3.67E-19	Not independent - LD with another GWAS locus

Additive model Men only analyses

20	<i>UQCC1</i>	20	33971914	rs4911494	0.602	0.028	4.39E-06	0.048	7.93E-02	rs224333	-0.027	1.66E-05	0.020	4.63E-01	Inconclusive - suggestive not independent
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a Coding variants refer to variants located in the exons and splicing junction regions.

b All the conditional analyses were performed in the UK Biobank dataset as all GWAS variants were available. Analyses performed in the ExomeChip discovery dataset if the GWAS variant or a proxy (at $r^2 \geq 0.8$) was available on the ExomeChip (see ST8-B).

c Loci 1-20 ExomeChip variant-known GWAS loci reciprocal conditional analyses.

d Variant positions are reported according to Human assembly build 37 and their alleles are coded based on the positive strand.

e Rare and low frequency variants in italics.

f Effect size is based on standard deviation (SD) per effect allele

g Only 1 variant in *RREB1* can be determined as independent (13 are not independent and for the rest the results is inconclusive)

Supplementary Table 6. Conditional analysis of coding variants^a that reach array-wide significance ($P < 2e-7$) on lead known variants within a locus (1Mb region) identified from Genome-wide association studies (GWAS) for WHR adjusted for BMI. Analyses were performed using the all ancestries ExomeChip discovery dataset when the variant or a proxy (at $R^2 \geq 0.8$) was available^{b,c}.

Locus (+/- 1 Mb of a given variant) ^b	ExomeChip Coding Variant						ExomeChip Variant:				GWAS Variant (all are non-coding)	Distance of Proxy variant from GWAS variant	R ² , D' of Proxy variant with GWAS Variant	GWAS/proxy Variant:		GWAS/proxy Variant:		Result of the coding ExomeChip variant when conditioned on the GWAS variant and vice versa	
	Gene	rsID	Chr	Position (GRCh37) ^d	Effect/Other Alleles	Effect Allele Frequency	Effect size ^e (SD/allele)	P-value	Effect size ^e (SD/allele)	P-value				Effect size ^e (SD/allele)	P-value	Effect size ^e (SD/allele)	P-value		
All Ancestry Additive model Sex-combined analyses																			
1	TBX15	rs61730011	1	119427467	C/A	0.04	-0.035	3.57E-08	-0.023	4.35E-04	rs2645294	1:119503843 (rs984222)	70744	0.775, 0.926	0.026	5.04E-22	0.024	2.77E-18	not independent
3	COBLL1	rs7607980	2	165551201	C/T	0.12	-0.026	1.94E-09	-0.011	2.62E-02	rs10195252	2:165528876 (rs13389219)	15785	0.933, 1.00	-0.029	3.33E-24	-0.026	5.97E-17	not independent
4	ITIH3	rs3617	3	52833805	A/C	0.46	-0.015	3.72E-08	-0.001	8.59E-01	rs2276824	3:52558008 (rs133303)	79478	0.871, 0.965	-0.018	1.26E-12	-0.015	2.16E-05	not independent
7	HERC3	rs1804080	4	89625427	C/G	0.16	-0.019	5.93E-08	-0.012	1.04E-03	rs9991328	4:89740128 (rs13133548)	27007	0.935, 1.00	0.020	9.15E-16	0.017	1.66E-11	not independent
9	RREB1	rs1334576	6	7211818	A/G	0.44	-0.014	8.23E-08	-0.013	3.06E-07	rs1294410	6:6743149 (rs1294421)	4397	0.833, 0.962	0.029	2.43E-31	0.029	3.67E-30	suggestive INDEPENDENT OF GWAS (also independent in UKBB)
11	RSPO3	rs1892172	6	127476516	G/A	0.54	0.026	1.06E-25	0.013	9.00E-03	rs1936805	6:127452639 (rs9491696)	523	0.967, 1.00	0.026	9.71E-26	0.015	2.69E-03	not independent
11	KIAA0408	rs139745911	6	127767954	G/A	0.01	0.107	2.07E-13	0.096	6.33E-11	rs1936805	6:127452639 (rs9491696)	523	0.967, 1.00	0.026	9.71E-26	0.024	8.29E-23	INDEPENDENT OF GWAS, but not independent of rs72959041 in UKBB
12	MLXIPL	rs35332062	7	73012042	A/G	0.88	0.020	1.78E-09	0.003	6.13E-01	rs6976930	7:72856430 (rs1178979)	155612	1.00, 1.00	-0.026	1.71E-15	-0.025	2.40E-08	suggestive INDEPENDENT OF GWAS, but suggestive not independent of rs863750 in the UKBB
15	DNAH10	rs3812316	7	73020337	G/C	0.88	0.021	1.98E-10	-0.003	6.52E-01	rs6976930	7:72856430 (rs1178979)	163907	1.00, 1.00	-0.026	1.71E-15	-0.024	1.06E-07	not independent
15	DNAH10	rs11057353	12	124265687	C/T	0.64	-0.019	7.85E-14	-0.013	7.56E-07	rs4765219	12:124427306 (rs11057401)	12804	0.931, 1.00	-0.027	1.67E-23	-0.023	3.14E-16	not independent
15	DNAH10	rs34934281	12	124330311	T/C	0.11	-0.023	6.46E-09	-0.009	4.15E-02	rs4765219	12:124427306 (rs11057401)	12804	0.931, 1.00	-0.027	1.67E-23	-0.025	4.54E-17	not independent
20	UQCC1	rs4911494	20	33971914	C/T	0.59	0.020	2.51E-13	-0.007	2.84E-01	rs224333	20:34025756 (rs143384)	1794	0.961, 1.00	-0.022	8.76E-18	-0.020	5.58E-05	not independent
20	GDF5	rs224331	20	34022387	C/A	0.37	-0.019	8.19E-09	0.013	5.68E-02	rs224333	20:34025756 (rs143384)	1794	0.961, 1.00	-0.022	8.76E-18	-0.020	4.19E-09	not independent
All Ancestry Additive model Women only analyses																			
3	COBLL1	rs7607980	2	165551201	C/T	0.12	-0.060	2.02E-24	-0.035	4.46E-08	rs10195252	2:165528876 (rs13389219)	15785	0.933, 1.00	-0.049	8.59E-38	-0.039	9.45E-21	INDEPENDENT, but not independent of other GWAS signals at the same locus
7	HERC3	rs1804080	4	89625427	C/G	0.16	-0.034	1.89E-11	-0.021	7.57E-05	rs9991328	4:89740128 (rs13133548)	27007	0.935, 1.00	0.033	3.64E-22	0.029	6.59E-16	not independent
7	FAM13A	rs7657817	4	89668859	T/C	0.19	-0.025	3.56E-08	-0.015	1.32E-03	rs9991328	4:89740128 (rs13133548)	27007	0.935, 1.00	0.033	3.64E-22	0.030	1.94E-17	not independent
11	RSPO3	rs1892172	6	127476516	G/A	0.54	0.035	3.83E-23	0.021	1.41E-03	rs1936805	6:127452639 (rs9491696)	523	0.967, 1.00	0.034	1.74E-21	0.015	2.62E-02	not independent
11	KIAA0408	rs139745911	6	127767954	G/A	0.01	0.150	1.15E-13	0.136	1.83E-11	rs1936805	6:127452639 (rs9491696)	523	0.967, 1.00	0.034	1.74E-21	0.030	1.29E-18	INDEPENDENT OF GWAS, but not independent of rs72959041 in UKBB
15	DNAH10	rs11057353	12	124265687	C/T	0.63	-0.028	1.00E-14	-0.018	5.86E-07	rs4765219	12:124427306 (rs11057401)	12804	0.931, 1.00	-0.040	1.21E-26	-0.034	1.39E-18	suggestive INDEPENDENT, but suggestive not independent of rs863750 in the UKBB
15	DNAH10	rs34934281	12	124330311	T/C	0.11	-0.041	2.25E-13	-0.020	7.73E-04	rs4765219	12:124427306 (rs11057401)	12804	0.931, 1.00	-0.040	1.21E-26	-0.034	2.77E-17	not independent
All Ancestry Additive model Men only analyses																			
20	UQCC1	rs4911494	20	33971914	C/T	0.58	0.024	2.02E-11	-0.012	1.40E-01	rs224333	20:34025756 (rs143384)	1794	0.961, 1.00	-0.030	1.03E-16	-0.038	1.79E-06	not independent
20	GDF5	rs224331	20	34022387	C/A	0.37	-0.025	3.17E-08	0.001	9.27E-01	rs224333	20:34025756 (rs143384)	1794	0.961, 1.00	-0.030	1.03E-16	-0.031	4.10E-10	not independent

a Coding variants refer to variants located in the exons and splicing junction regions.

b Analyses performed in the ExomeChip discovery dataset if the GWAS variant or a proxy (at $r^2 \geq 0.8$) was available on the ExomeChip. All the analyses were performed in the UK Biobank dataset (see ST8-A).

c The full list of conditional analyses performed in the UK Biobank are in Supplementary Tables 8(B) and 8(C). Only the UK Biobank analysis results related and informative with regards to the loci analysed in the ExomeChip discovery dataset are presented in this table.

d Variant positions are reported according to Human assembly build 37 and their alleles are coded based on the positive strand.

e Effect size is based on standard deviation (SD) per effect allele

12	124265687	T	C	rs11057353	<i>DNAH10</i>	-0.0036	0.0029	2.10E-01		0.029	0.003	3.08E-22	0.0273	0.0033	6.90E-16
12	124330311	C	T	rs34934281	<i>DNAH10</i>	-0.0105	0.0045	1.94E-02	Y	0.043	0.005	1.38E-20	0.0377	0.0051	5.66E-13
12	124427306	T	A	rs11057401	<i>CCDC92</i>	-0.0114	0.0031	2.23E-04	Y	0.043	0.003	1.02E-41	0.0377	0.0035	7.78E-26
19	8429323	G	A	rs116843064	<i>ANGPTL4</i>	-0.0082	0.0101	4.15E-01		0.064	0.011	1.20E-09	0.0603	0.0117	6.91E-07
Men															
13	96665697	A	G	rs148108950	<i>UGGT2</i>	-0.0192	0.0217	3.77E-01		0.1299	0.0240	6.14E-08	0.1205	0.0263	1.06E-05
14	23312594	A	G	rs1042704	<i>MMP14</i>	-0.0080	0.0036	2.66E-02	Y	0.0206	0.0037	2.60E-08	0.0167	0.0041	1.00E-04
European Additive model Men only analyses															
20	33971914	T	C	rs4911494	<i>UQC1</i>	-0.0026	0.0033	4.34E-01		0.025	0.003	2.6E-14	0.0240	0.0037	2.07E-10

Abbreviations: GRCh37=human genome assembly build 37;SD=standard deviation; SE=standard error;N=sample size

a Equation used: Corrected WHRadjBMI Standard error = $\sqrt{\text{WHRadjBMI Standard Error}^2 + \text{BMI Standard Error}^2 * 0.49^2}$, where 0.49 is the correlation between BMI and WHR.

b Variant positions are reported according to Human assembly build 37 and their alleles are coded based on the positive strand.

c Effect size is based on standard deviation (SD) per effect allele

d The direction of effect is opposite for BMI compared to WHRadjBMI and the P-value is <0.05. Y=Yes

Supplementary Table 8. Gene-based analyses that reached multiple correction threshold (Unconditioned P-value<2.5x10⁻⁶) in the sex-combined, men and women analyses using SKAT and/or VT test of association with conditional results on the most significant single variant.

Strata	GENE	Gene definition for variants included ^a	N	Top variant ^b	Top variant P-value ^c	SKAT			VT			
						Number of variants ^d	Unconditioned P-value	Conditioned on top variant P-value	Number of variants ^d	Unconditioned P-value	Conditioned on top variant P-value	
All Ancestries												
Sex-Combined	<i>RAPGEF3</i>	BROAD	344369	12:48143315	1.28E-13	19	2.71E-14	3.63E-01	18	9.92E-09	7.73E-01	
	<i>RAPGEF3</i>	STRICT	344369	12:48143315		7	6.89E-14	2.17E-01	7	2.16E-12	8.86E-01	
Women only	<i>RAPGEF3</i>	BROAD	180131	12:48143315	8.29E-10	18	4.51E-10	7.30E-01	17	4.44E-07	8.35E-01	
	<i>RAPGEF3</i>	STRICT	180131	12:48143315		6	5.90E-10	3.30E-01	6	2.88E-08	7.73E-01	
	<i>ACVR1C</i>	BROAD	180131	2:158412701		1.09E-07	5	3.62E-08	9.46E-03	5	5.83E-08	1.40E-01
	<i>ANGPTL4</i>	BROAD	180131	19:8429323		1.24E-06	8	8.87E-07	3.89E-01	Not significant ^e		
European only												
Sex-Combined	<i>DNAI1</i>	BROAD	288492	9:34500796	4.64E-05	Not significant ^e			4	7.93E-07	5.70E-01	
Women only	<i>NOP2</i>	BROAD	157516	12:6672587	3.69E-05	15	1.62E-06	6.87E-02	Not significant ^e			

Abbreviations: SKAT=SNP-set sequence kernel association test; VT=variable threshold burden test;GRCh37=human genome assembly build 37;N=sample size

a We created two lists (masks) of variant (minor allele frequency <5%) for gene-based analyses. The “broad” mask includes nonsense, stop-loss, splice site variants, and missense defined as damaging by at least one of prediction algorithms (PolyPhen2 HumDiv and HumVar, LRT, MutationTaster and SIFT). The “strict” mask included the same variants as the “broad” mask, except for missense variants. Only missense variants predicted to be damaging by all five algorithms were included in the “strict” list.

b Top variant is the most significant variant in the gene-based test. Chromosome:position is shown; positions are reported according to Human genome assembly build 37.

c P-value based on Stage 1 only.

d Number of variants included in the gene-based test

e Gene-based tests did not reach multiple testing correction threshold (unconditioned P-value<2.5x10⁻⁶) in any stratum.

Supplementary Table 9. Results from PASCAL (Pathway scoring algorithm) for Exomechip coding variants and genome-wide coding and regulatory variants associated with WHRadjBMI. ^a Only significant results are shown (FDR< 0.05). Bolded values are P-values that pass Bonferroni significance (P<0.05/14,000).

Pathway Name ^b	Exomechip ^c		Genome-wide variants ^d	
	P-MAX	P-SUM	P-MAX	P-SUM
abnormal skeleton morphology	1.67E-07	6.53E-07	NA	NA
REACTOME_NCAM1_INTERACTIONS	2.51E-07	3.87E-07	NA	NA
short ribs	3.13E-07	5.29E-07	NA	NA
abnormal tracheal cartilage morphology	3.45E-07	1.97E-06	3.03E-06	6.34E-08
abnormal vertebrae morphology	3.82E-07	1.24E-06	NA	4.55E-04
proteinaceous extracellular matrix	5.57E-07	6.86E-06	NA	2.34E-04
short radius	5.61E-07	2.91E-07	NA	NA
extracellular matrix	8.18E-07	9.28E-06	NA	7.35E-05
NID2 PPI subnetwork	8.71E-07	2.62E-07	5.14E-05	4.54E-06
FN1 PPI subnetwork	1.12E-06	2.42E-05	NA	NA
extracellular matrix part	1.59E-06	6.29E-06	NA	NA
abnormal rib morphology	1.64E-06	6.89E-06	7.87E-05	1.28E-06
abnormal long bone morphology	1.96E-06	1.36E-05	NA	NA
TGFBI PPI subnetwork	2.26E-06	1.27E-05	NA	NA
FGF7 PPI subnetwork	2.42E-06	1.17E-05	NA	NA
extracellular matrix structural constituent	2.47E-06	3.96E-05	NA	1.92E-04
incomplete somite formation	2.88E-06	4.03E-06	NA	NA
decreased susceptibility to diet-induced obesity	3.19E-06	8.87E-06	5.21E-05	3.47E-05
abnormal femur morphology	4.80E-06	3.73E-05	NA	NA
COL4A2 PPI subnetwork	4.80E-06	6.05E-06	NA	NA
COL2A1 PPI subnetwork	5.00E-06	1.66E-04	NA	3.04E-06
abnormal joint morphology	5.49E-06	1.58E-05	NA	NA
abnormal limb bone morphology	6.54E-06	4.12E-05	NA	2.49E-06
abnormal sternum ossification	7.65E-06	1.21E-05	NA	NA
abnormal blood vessel morphology	7.77E-06	3.09E-05	NA	1.63E-05
platelet-derived growth factor binding	8.92E-06	6.52E-05	NA	NA
collagen	1.07E-05	7.85E-05	NA	NA
REACTOME_NCAM_SIGNALING_FOR_NEURITE_OUT:GROWTH	1.07E-05	1.95E-05	NA	NA
CD36 PPI subnetwork	1.15E-05	1.15E-04	NA	NA
abnormal cutaneous collagen fibril morphology	1.19E-05	5.62E-05	NA	NA
cartilage development	1.22E-05	1.71E-05	1.64E-04	5.32E-06
collagen binding	1.23E-05	2.00E-04	NA	NA
COL4A1 PPI subnetwork	1.30E-05	1.88E-05	NA	4.43E-04
extracellular matrix binding	1.33E-05	1.43E-04	NA	1.58E-04
basement membrane	1.38E-05	5.15E-05	NA	NA
COL6A1 PPI subnetwork	1.43E-05	4.20E-05	NA	NA
growth factor binding	1.65E-05	2.03E-04	1.46E-04	2.94E-06
fibrillar collagen	1.72E-05	NA	NA	NA
LTBP1 PPI subnetwork	1.91E-05	1.14E-04	NA	NA
costamere	2.02E-05	8.31E-05	NA	NA
abnormal heart valve morphology	2.32E-05	3.27E-05	NA	NA
decreased subcutaneous adipose tissue amount	2.45E-05	2.20E-05	1.56E-04	1.54E-05
REACTOME_SIGNALING_BY_PDGF	2.45E-05	1.58E-04	NA	NA
cartilage development involved in endochondral bone morphogenesis	2.88E-05	1.86E-04	NA	NA
KEGG_ECM_RECEPTOR_INTERACTION	3.12E-05	2.17E-04	NA	NA
histone acetyltransferase activity	3.42E-05	6.28E-05	NA	NA

ITGB1 PPI subnetwork	3.58E-05	2.26E-05	4.74E-05	3.31E-05
hemorrhage	3.80E-05	1.03E-04	NA	2.97E-04
abnormal white adipose tissue physiology	3.94E-05	1.22E-04	NA	NA
abnormal compact bone morphology	3.95E-05	1.28E-04	NA	NA
abnormal Meckel's cartilage morphology	4.02E-05	1.38E-04	4.46E-05	2.48E-05
decreased retroperitoneal fat pad weight	4.17E-05	NA	2.77E-04	1.43E-04
SPARC PPI subnetwork	4.27E-05	1.62E-04	NA	NA
complete embryonic lethality during organogenesis	4.67E-05	4.83E-05	4.71E-05	NA
abnormal scapula morphology	4.76E-05	1.11E-04	NA	1.22E-04
delayed bone ossification	4.98E-05	8.15E-05	NA	1.20E-04
abnormal basement membrane morphology	5.32E-05	1.98E-04	2.12E-04	6.59E-06
ZMYND11 PPI subnetwork	5.51E-05	2.49E-04	NA	NA
abnormal bone ossification	5.75E-05	NA	NA	2.86E-04
abnormal cervical axis morphology	6.43E-05	3.66E-05	NA	NA
embryonic skeletal joint development	7.29E-05	1.95E-04	NA	NA
FGF2 PPI subnetwork	7.87E-05	2.11E-04	NA	NA
abnormal tendon morphology	8.83E-05	1.67E-04	NA	4.13E-05
abnormal posterior eye segment morphology	1.01E-04	2.37E-04	NA	NA
abnormal vertebral arch morphology	1.05E-04	5.82E-05	NA	NA
abnormal cartilage development	1.09E-04	NA	NA	6.42E-05
MED1 PPI subnetwork	1.17E-04	NA	NA	NA
abnormal cartilage morphology	1.24E-04	NA	NA	4.52E-05
thin diaphragm muscle	1.25E-04	1.03E-04	NA	NA
collagen fibril organization	1.25E-04	NA	NA	NA
blood vessel development	1.31E-04	1.01E-04	NA	7.18E-05
abnormal sternum morphology	1.32E-04	5.07E-05	NA	NA
abnormal cervical atlas morphology	1.33E-04	1.17E-04	NA	NA
ostium primum atrial septal defect	1.37E-04	NA	NA	NA
chondrocyte differentiation	1.43E-04	1.45E-04	NA	NA
COL1A2 PPI subnetwork	1.52E-04	NA	NA	NA
short snout	1.57E-04	NA	NA	NA
increased urine glucose level	1.66E-04	1.81E-04	NA	NA
shortened head	1.67E-04	NA	NA	9.57E-05
delayed endochondral bone ossification	1.73E-04	NA	NA	8.56E-05
abnormal long bone epiphyseal plate morphology	1.78E-04	NA	NA	NA
small basisphenoid bone	1.88E-04	NA	NA	NA
THBS2 PPI subnetwork	1.88E-04	NA	NA	NA
ITGB5 PPI subnetwork	1.89E-04	2.45E-04	NA	NA
asymmetric rib-sternum attachment	1.98E-04	1.19E-04	3.60E-05	1.20E-06
MAG PPI subnetwork	2.10E-04	NA	NA	NA
abnormal carpal bone morphology	2.10E-04	2.24E-04	2.23E-05	1.32E-06
COL4A4 PPI subnetwork	2.20E-04	NA	NA	NA
abnormal vertebrae development	2.21E-04	NA	NA	NA
abnormal artery morphology	2.23E-04	NA	NA	3.48E-04
increased fat cell size	2.27E-04	1.68E-04	NA	NA
abnormal forelimb morphology	2.35E-04	NA	NA	NA
decreased circulating leptin level	2.42E-04	NA	NA	NA
increased eating behavior	2.75E-04	NA	1.97E-04	5.58E-05
abnormal glucose homeostasis	2.81E-04	NA	NA	NA
decreased circulating triglyceride level	2.91E-04	NA	NA	NA
abnormal humerus morphology	2.93E-04	NA	1.53E-04	3.42E-04

abnormal dermal layer morphology	2.93E-04	NA	NA	NA
perimembraneous ventricular septal defect	2.99E-04	9.77E-05	NA	NA
abnormal patella morphology	3.05E-04	NA	NA	2.62E-04
short limbs	3.06E-04	2.19E-04	NA	NA
short femur	3.21E-04	NA	NA	3.51E-04
abnormal vestibulocochlear ganglion morphology	3.30E-04	1.19E-04	6.72E-05	2.50E-04
increased circulating insulin level	3.37E-04	NA	NA	NA
heart right ventricle hypertrophy	3.40E-04	NA	NA	NA
decreased brown adipose tissue amount	3.41E-04	NA	NA	NA
CTBP1 PPI subnetwork	3.43E-04	NA	7.30E-05	NA
AP1S2 PPI subnetwork	3.54E-04	NA	NA	NA
abnormal muscle morphology	3.55E-04	1.23E-04	NA	NA
abnormal bronchiole morphology	3.57E-04	NA	NA	NA
abnormal aorta elastic tissue morphology	3.69E-04	NA	NA	NA
abnormal cricoid cartilage morphology	3.71E-04	1.56E-04	1.07E-05	1.34E-04
BMP1 PPI subnetwork	3.80E-04	NA	NA	NA
REACTOME_TRANSCRIPTIONAL_REGULATION_OF_WHITE_ADIPOCYTE	3.88E-04	NA	5.62E-07	8.22E-06
abnormal long bone epiphysis morphology	3.96E-04	NA	NA	NA
SERTAD3 PPI subnetwork	NA	2.45E-04	NA	NA
abnormal brown adipose tissue morphology	NA	NA	1.14E-04	1.74E-04
LAMA1 PPI subnetwork	NA	NA	NA	8.21E-05
LAMB1 PPI subnetwork	NA	NA	NA	1.60E-04
impaired lipolysis	NA	NA	7.31E-05	1.85E-05
abnormal cervical vertebrae morphology	NA	NA	3.54E-06	7.95E-06
abnormal xiphoid process morphology	NA	NA	NA	4.41E-04
enlarged pancreatic islets	NA	NA	NA	1.12E-04
short mandible	NA	NA	4.82E-05	1.35E-05
intracranial hemorrhage	NA	NA	9.55E-05	1.09E-05
centrally nucleated skeletal muscle fibers	NA	NA	NA	4.35E-04
abnormal snout morphology	NA	NA	NA	1.71E-04
abnormal extraembryonic tissue morphology	NA	NA	1.11E-04	3.17E-04
cleft secondary palate	NA	NA	NA	7.04E-05
abnormal fat cell morphology	NA	NA	1.44E-04	3.40E-04
lumbar vertebral transformation	NA	NA	6.54E-05	1.04E-04
decreased epididymal fat pad weight	NA	NA	NA	4.22E-04
small kidney	NA	NA	NA	1.00E-04
short ulna	NA	NA	5.54E-06	1.19E-05
NOV PPI subnetwork	NA	NA	NA	3.50E-05
abnormal occipital bone morphology	NA	NA	7.71E-05	2.54E-05
bone morphogenesis	NA	NA	NA	3.93E-04
abnormal pulmonary elastic fiber morphology	NA	NA	NA	3.20E-04
abnormal angiogenesis	NA	NA	1.78E-04	3.48E-05
abnormal anterior-posterior polarity of the somites	NA	NA	NA	3.71E-04
MAML1 PPI subnetwork	NA	NA	2.38E-04	NA
abnormal intestine morphology	NA	NA	NA	1.44E-04
ARF GTPase activator activity	NA	NA	7.17E-05	NA
decreased circulating free fatty acid level	NA	NA	NA	3.39E-04
impaired lung alveolus development	NA	NA	2.84E-05	4.40E-05
abnormal glossopharyngeal nerve morphology	NA	NA	1.87E-04	NA
HOXA5 PPI subnetwork	NA	NA	1.02E-05	2.05E-05
abnormal axial skeleton morphology	NA	NA	8.27E-05	6.91E-05

abnormal branching involved in lung morphogenesis	NA	NA	2.36E-04	3.10E-05
abnormal tympanic ring morphology	NA	NA	2.47E-04	1.85E-04
vasculature development	NA	NA	NA	6.52E-05
ITM2C PPI subnetwork	NA	NA	1.02E-04	NA
regulation of cartilage development	NA	NA	2.59E-04	NA
SKIL PPI subnetwork	NA	NA	NA	2.78E-04
abnormal lung morphology	NA	NA	1.07E-04	4.91E-05
delayed embryo turning	NA	NA	7.42E-05	2.88E-04
partial postnatal lethality	NA	NA	NA	1.09E-04
decreased tongue size	NA	NA	NA	2.59E-05
abnormal craniofacial bone morphology	NA	NA	5.77E-05	8.55E-06
decreased total body fat amount	NA	NA	NA	1.64E-04
abnormal vascular smooth muscle morphology	NA	NA	NA	3.09E-04
abnormal rib-sternum attachment	NA	NA	1.18E-04	1.14E-05
RUNX1 PPI subnetwork	NA	NA	9.03E-05	7.36E-05
histone methyltransferase activity	NA	NA	4.07E-05	1.21E-04
abnormal renal/urinary system morphology	NA	NA	7.55E-07	2.02E-05
increased circulating free fatty acid level	NA	NA	1.41E-04	NA
PBX1 PPI subnetwork	NA	NA	2.73E-04	1.42E-04
TWIST1 PPI subnetwork	NA	NA	NA	2.20E-04
laminin binding	NA	NA	NA	7.66E-05
PDGFRA PPI subnetwork	NA	NA	3.54E-05	1.86E-04
thoracic vertebral transformation	NA	NA	1.09E-04	1.81E-04
lung hemorrhage	NA	NA	NA	3.96E-04
abnormal pterygoid process morphology	NA	NA	NA	9.00E-05
transmembrane receptor protein kinase activity	NA	NA	NA	2.69E-04
abnormal placenta vasculature	NA	NA	NA	2.31E-04
IGF1 PPI subnetwork	NA	NA	NA	2.65E-05
NR3C1 PPI subnetwork	NA	NA	NA	7.70E-05
P4HA2 PPI subnetwork	NA	NA	2.15E-04	NA
sacral vertebral transformation	NA	NA	NA	1.23E-04
REACTOME_CIRCADIAN_CLOCK	NA	NA	1.88E-04	NA
KEGG_CITRATE_CYCLE_TCA_CYCLE	NA	NA	NA	4.19E-04
decreased rib number	NA	NA	NA	5.87E-05
ITGA9 PPI subnetwork	NA	NA	NA	1.34E-04
ETS2 PPI subnetwork	NA	NA	1.82E-06	5.62E-06
abnormal cranium morphology	NA	NA	NA	1.21E-04
APP PPI subnetwork	NA	NA	1.97E-04	NA
HSP90B1 PPI subnetwork	NA	NA	2.62E-04	NA
lysine N-methyltransferase activity	NA	NA	2.29E-04	NA
protein-lysine N-methyltransferase activity	NA	NA	2.29E-04	NA
pale yolk sac	NA	NA	1.25E-04	NA
abnormal squamosal bone morphology	NA	NA	NA	2.22E-04
renal hypoplasia	NA	NA	1.47E-04	6.72E-05
abnormal fibula morphology	NA	NA	NA	2.53E-04
NCOA2 PPI subnetwork	NA	NA	NA	3.16E-04
chromatin modification	NA	NA	2.22E-04	NA
abnormal limb bud morphology	NA	NA	2.55E-04	6.32E-05
cleft palate	NA	NA	NA	1.93E-04
abnormal dorsal aorta morphology	NA	NA	NA	4.55E-04
herniated diaphragm	NA	NA	NA	1.68E-04

VDR PPI subnetwork	NA	NA	6.18E-05	1.49E-04
REACTOME_ACTIVATION_OF_CHAPERONES_BY_ATF6:ALPHA	NA	NA	2.42E-04	NA
abnormal middle ear morphology	NA	NA	NA	2.56E-04
short maxilla	NA	NA	2.62E-04	NA
vesicle transport along microtubule	NA	NA	NA	1.24E-04
abnormal lung development	NA	NA	NA	1.26E-04
SMAD7 PPI subnetwork	NA	NA	4.46E-05	NA
abnormal adipose tissue physiology	NA	NA	3.72E-05	3.69E-04
abnormal alisphenoid bone morphology	NA	NA	NA	3.94E-04
decreased chondrocyte cell number	NA	NA	NA	1.72E-04
SOX9 PPI subnetwork	NA	NA	1.28E-04	NA
abnormal thyroid cartilage morphology	NA	NA	1.74E-04	NA
abnormal kidney morphology	NA	NA	1.52E-04	9.04E-05
protein serine/threonine phosphatase complex	NA	NA	NA	3.94E-04
ribonucleoprotein complex binding	NA	NA	3.50E-05	NA
RUNX1T1 PPI subnetwork	NA	NA	5.01E-05	3.71E-04
transcription regulatory region DNA binding	NA	NA	1.52E-04	3.67E-05
decreased tympanic ring size	NA	NA	NA	2.22E-04
middle ear morphogenesis	NA	NA	1.10E-05	4.51E-05
regulatory region nucleic acid binding	NA	NA	1.64E-04	1.42E-05
regulatory region DNA binding	NA	NA	1.64E-04	1.42E-05
absent stapes	NA	NA	7.50E-05	2.75E-04
SNCG PPI subnetwork	NA	NA	NA	4.58E-04
overexpanded pulmonary alveoli	NA	NA	NA	2.11E-04
KDM6A PPI subnetwork	NA	NA	4.38E-05	NA
transcription factor binding	NA	NA	NA	1.30E-04
abnormal supraoccipital bone morphology	NA	NA	NA	4.18E-04
abnormal frequency of paradoxical sleep	NA	NA	NA	3.86E-04
SP1 PPI subnetwork	NA	NA	2.39E-04	1.08E-04
NR2C1 PPI subnetwork	NA	NA	NA	2.30E-04
VLDLR PPI subnetwork	NA	NA	NA	4.62E-04
JUN PPI subnetwork	NA	NA	NA	4.32E-04
ANKRD12 PPI subnetwork	NA	NA	2.70E-04	NA
ANKRD12 PPI subnetwork	NA	NA	2.70E-04	NA

a Pascal (Pathway scoring algorithm) details and software are available at <https://www2.unil.ch/cbg/index.php?title=Pascal>

b Pathway library from KEGG, REACTOME and BIOCARTA

c Coding variants from the exomechip were used to define the gene sets. Using chi-squared statistics, P-values were calculated from the sum or average association signals per gene (P-SUM) and maximum association signals per gene (P-MAX).

d Both coding and regulatory variants genom-wide were used to define the gene sets. Using chi-squared statistics, P-values were calculated from the sum or average association signals per gene (P-SUM) and maximum association signals per gene (P-MAX).

Supplementary Table 10. Association results in the UK BioBank for body fat percent in men and women combined, women only, and men only for variants of interest that were array wide significant for WHRadjBMI.

Alleles ^b							Men and Women (N=118,153)				Women only (N=62,356)				Men only (N=55,797)			
rsID	Chr	Position (GRCh37) ^a	Effect	Other	Gene ^c	Amino Acid change ^c	Effect Allele	Effect size ^d	SE	P-value ^c	Effect Allele	Effect size ^d	SE	P-value ^c	Effect Allele	Effect size ^d	SE	P-value ^c
							Frequency	(SD/allele)			Frequency	(SD/allele)			Frequency	(SD/allele)		
rs61730011	1	119427467	A	C	TBX15	M566R	0.955	-0.008	0.010	4.40E-01	0.954	0.002	0.014	9.11E-01	0.955	-0.018	0.014	2.11E-01
rs10494217	1	119469188	T	G	TBX15	H156N	0.180	0.002	0.005	7.33E-01	0.181	0.004	0.007	5.64E-01	0.180	-0.001	0.008	9.09E-01
rs141845046	1	154987704	C	T	ZBTB7B	P190S	0.978	0.000	0.014	9.76E-01	0.978	-0.018	0.019	3.61E-01	0.978	0.020	0.020	3.16E-01
rs55920843	2	158412701	T	G	ACVR1C	N150H	0.988	0.005	0.019	7.83E-01	0.988	0.024	0.026	3.50E-01	0.988	-0.017	0.028	5.50E-01
rs7607980	2	165551201	T	C	COBLL1	N941D	0.881	-0.026	0.006	4.04E-05	0.883	-0.029	0.009	1.18E-03	0.880	-0.023	0.009	1.08E-02
rs7586970	2	188343497	T	C	TFPI	N221S	0.706	0.011	0.005	1.90E-02	0.706	0.013	0.006	3.97E-02	0.706	0.008	0.007	2.16E-01
rs1034405	3	50597092	G	A	C3orf18	A162V	0.130	-0.001	0.006	8.33E-01	0.131	-0.002	0.008	7.79E-01	0.129	0.000	0.009	9.93E-01
rs13303	3	52558008	T	C	STAB1	M113T	0.442	-0.001	0.004	8.52E-01	0.443	0.000	0.006	9.97E-01	0.441	-0.002	0.006	7.90E-01
rs3617	3	52833805	C	A	ITIH3	Q315K	0.550	-0.007	0.004	8.18E-02	0.551	-0.007	0.006	2.05E-01	0.550	-0.007	0.006	2.33E-01
rs62266958	3	129137188	C	T	EFCAB12	R197H	0.929	-0.018	0.008	2.42E-02	0.929	-0.036	0.011	1.05E-03	0.928	0.002	0.012	8.64E-01
rs2625973	3	129284818	A	C	PLXND1	L1412V	0.712	-0.002	0.005	7.39E-01	0.713	-0.010	0.006	1.25E-01	0.711	0.007	0.007	2.58E-01
rs2255703	3	129293256	T	C	PLXND1	M870V	0.615	-0.003	0.004	4.84E-01	0.617	-0.009	0.006	1.08E-01	0.614	0.004	0.006	4.99E-01
rs1804080	4	89625427	G	C	HERC3	E946Q	0.837	-0.008	0.006	1.54E-01	0.837	-0.011	0.008	1.55E-01	0.838	-0.005	0.008	5.67E-01
rs7657817	4	89668859	C	T	FAM13A	V443I	0.824	-0.006	0.005	2.77E-01	0.823	-0.003	0.007	6.88E-01	0.824	-0.009	0.008	2.46E-01
rs3733526	4	120528327	G	A	PDE5A	A41V	0.180	0.009	0.005	9.54E-02	0.181	0.005	0.007	4.77E-01	0.180	0.013	0.008	9.36E-02
rs1966265	5	176516631	A	G	FGFR4	V10I	0.248	-0.001	0.005	7.65E-01	0.248	0.005	0.007	4.89E-01	0.248	-0.008	0.007	2.44E-01
rs1334576	6	7211818	G	A	RREB1	G195R	0.572	0.000	0.004	9.26E-01	0.571	0.004	0.006	4.59E-01	0.573	-0.004	0.006	5.18E-01
rs9469913	6	34827085	A	T	UHRF1BP1	Q984H	0.837	-0.033	0.006	4.82E-09	0.838	-0.037	0.008	1.18E-06	0.837	-0.027	0.008	7.14E-04
rs1892172	6	127476516	A	G	RSP03	synonymous	0.547	0.002	0.004	5.86E-01	0.547	0.007	0.006	2.50E-01	0.547	-0.003	0.006	6.75E-01
rs139745911	6	127767954	A	G	KIAA0408	P504S	0.011	-0.051	0.019	9.04E-03	0.012	-0.043	0.027	1.02E-01	0.011	-0.059	0.029	3.79E-02
rs2303361	7	6449496	C	T	DAGLB	Q664R	0.243	-0.001	0.005	9.02E-01	0.244	-0.003	0.007	6.87E-01	0.242	0.002	0.007	8.04E-01
rs35332062	7	73012042	G	A	MLXIPL	A358V	0.871	0.010	0.006	1.18E-01	0.871	0.004	0.008	5.98E-01	0.872	0.015	0.009	8.56E-02
rs3812316	7	73020337	C	G	MLXIPL	Q241H	0.871	0.009	0.006	1.63E-01	0.871	0.003	0.008	6.99E-01	0.871	0.014	0.009	1.06E-01
rs17417407	10	95931087	T	G	PLCE1	R240L	0.171	0.012	0.005	3.47E-02	0.172	0.003	0.008	7.38E-01	0.170	0.022	0.008	6.41E-03
rs35169799	11	64031241	T	C	PLCB3	S778L	0.063	0.015	0.008	7.90E-02	0.065	0.029	0.011	1.16E-02	0.062	-0.002	0.012	8.85E-01
rs7114037	11	65403651	C	A	PCNXL3	H1822Q	0.945	0.004	0.009	6.27E-01	0.945	0.005	0.012	6.80E-01	0.945	0.004	0.013	7.87E-01
rs145878042	12	48143315	A	G	RAPGEF3	L300P	0.989	0.010	0.020	6.21E-01	0.989	0.009	0.027	7.43E-01	0.989	0.011	0.029	7.08E-01
rs3764002	12	108618630	C	T	WSCD2	T266I	0.739	0.019	0.005	5.54E-05	0.739	0.018	0.006	4.16E-03	0.739	0.019	0.007	4.56E-03
rs58843120	12	123444507	G	T	ABC89	F92L	0.985	-0.010	0.017	5.67E-01	0.985	-0.018	0.023	4.36E-01	0.985	0.000	0.025	9.94E-01
rs11057353	12	124265687	T	C	DNAH10	S228P	0.393	-0.009	0.004	2.65E-02	0.393	-0.009	0.006	1.21E-01	0.394	-0.010	0.006	1.12E-01
rs34934281	12	124330311	C	T	DNAH10	T1785M	0.877	-0.020	0.006	1.71E-03	0.878	-0.013	0.009	1.44E-01	0.877	-0.027	0.009	2.54E-03
rs11057401	12	124427306	T	A	CCDC92	S53C	0.689	-0.020	0.004	6.86E-06	0.690	-0.013	0.006	2.77E-02	0.688	-0.027	0.006	2.45E-05
rs1051860	14	58838668	A	G	ARID4A	synonymous	0.414	0.008	0.004	4.86E-02	0.414	0.005	0.006	3.68E-01	0.415	0.012	0.006	5.49E-02
rs17677991	15	42032383	G	C	MGA	P1523A	0.345	-0.005	0.004	2.61E-01	0.344	0.001	0.006	8.78E-01	0.345	-0.011	0.006	7.23E-02
rs3959569	15	42115747	C	G	MAPKBP1	R1240H	0.334	-0.004	0.004	3.78E-01	0.334	0.002	0.006	7.95E-01	0.334	-0.010	0.006	1.19E-01
rs1715919	15	56756285	G	T	MNS1	Q55P	0.105	0.005	0.007	4.18E-01	0.106	0.011	0.009	2.20E-01	0.103	-0.001	0.010	9.03E-01
rs3810818	16	4432029	A	C	VASN	E384A	0.227	-0.006	0.005	2.53E-01	0.228	-0.003	0.007	6.89E-01	0.226	-0.009	0.007	2.14E-01
rs3747579	16	4445327	C	T	CORO7	R193Q	0.281	-0.001	0.005	7.71E-01	0.282	-0.008	0.006	2.17E-01	0.280	0.006	0.007	3.76E-01
rs1139653	16	4484396	A	T	DNAJA3	N75Y	0.279	0.003	0.005	5.06E-01	0.280	-0.002	0.006	7.77E-01	0.278	0.008	0.007	2.05E-01
rs9922085	16	67397580	G	C	LRR36	R101P	0.956	0.013	0.010	1.88E-01	0.956	0.006	0.014	6.59E-01	0.956	0.021	0.015	1.48E-01
rs8052655	16	67409180	G	A	LRR36	G388S	0.956	0.012	0.010	2.36E-01	0.957	0.005	0.014	6.99E-01	0.956	0.019	0.015	1.88E-01
rs897453	17	17425631	C	T	PEMT	V58L	0.523	-0.008	0.004	5.60E-02	0.523	-0.005	0.006	3.36E-01	0.524	-0.011	0.006	7.77E-02
rs11554159	19	18285944	A	G	IFI30	R76Q	0.269	0.025	0.005	1.17E-07	0.270	0.025	0.006	9.38E-05	0.268	0.024	0.007	3.44E-04
rs874628	19	18304700	G	A	MPV17L2	M72V	0.286	0.023	0.005	2.69E-07	0.286	0.024	0.006	1.11E-04	0.285	0.023	0.007	6.72E-04

rs2287922	19	49232226	A	G	<i>RASIP1</i>	R601C	0.536	-0.009	0.004	2.95E-02	0.538	-0.009	0.006	1.25E-01	0.534	-0.009	0.006	1.22E-01
rs2307019	19	49244220	G	A	<i>IZUMO1</i>	A333V	0.572	-0.016	0.004	1.85E-04	0.574	-0.014	0.006	1.27E-02	0.570	-0.017	0.006	5.00E-03
rs4911494	20	33971914	T	C	<i>UQCC1</i>	R51Q	0.633	0.004	0.004	3.26E-01	0.635	-0.008	0.006	1.79E-01	0.630	0.017	0.006	4.61E-03
rs224331	20	34022387	A	C	<i>GDF5</i>	S276A	0.659	0.001	0.004	7.41E-01	0.661	-0.011	0.006	6.17E-02	0.656	0.015	0.006	1.46E-02

Abbreviations: GRCh37=human genome assembly build 37;rsID=based on dbSNP; VEP=Ensembl Variant Effect Predictor toolset; GTEx=Genotype-Tissue Expression project;SD=standard deviation; SE=standard error;N=sample size
a Variant positions are reported according to Human assembly build 37 and their alleles are coded based on the positive strand.

b Effect allele is oriented on the WHRadjBMI increasing allele see Supplementary Tables 4,5,6.

c The gene the variant falls in and amino acid change from the most abundant coding transcript is shown (protein annotation is based on VEP toolset and transcript abundance from GTEx database).

d Effect size is based on standard deviation (SD) per effect allele

e Bolded P-values are variants that met bonferonni significance (P-value< 1.0E-03; i.e. 0.05/48 variants).

Supplementary Table 11. Association results in the UK BioBank for body trunk fat percent in men and women combined, women only, and men only for variants of interest that were array wide significant for WHRadjBMI.

Alleles ^b							Men and Women (N=118,160)				Women only (N=62,318)				Men only (N=55,842)			
rsID	Chr	Position (GRCh37) ^a	Effect		Gene ^c	Amino Acid change ^c	Effect Allele Frequency	Effect size ^d (SD/ allele)	SE	P-value ^c	Effect Allele Frequency	Effect size ^d (SD/ allele)	SE	P-value ^c	Effect Allele Frequency	Effect size ^d (SD/ allele)	SE	P-value ^c
			Effect	Other														
rs61730011	1	119427467	A	C	<i>TBX15</i>	M566R	0.955	-0.035	0.071	6.21E-01	0.954	0.045	0.104	6.66E-01	0.955	-0.126	0.095	1.84E-01
rs10494217	1	119469188	T	G	<i>TBX15</i>	H156N	0.180	0.017	0.039	6.62E-01	0.181	0.032	0.057	5.72E-01	0.180	0.000	0.051	9.98E-01
rs141845046	1	154987704	C	T	<i>ZBTB7B</i>	P190S	0.978	-0.036	0.101	7.24E-01	0.978	-0.116	0.149	4.38E-01	0.978	0.052	0.134	6.97E-01
rs55920843	2	158412701	T	G	<i>ACVR1C</i>	N150H	0.988	-0.021	0.136	8.79E-01	0.988	0.119	0.199	5.51E-01	0.988	-0.181	0.182	3.22E-01
rs7607980	2	165551201	T	C	<i>COBLL1</i>	N941D	0.881	-0.207	0.046	5.96E-06	0.883	-0.264	0.068	9.84E-05	0.880	-0.145	0.061	1.64E-02
rs7586970	2	188343497	T	C	<i>TFPI</i>	N221S	0.706	0.064	0.033	4.74E-02	0.706	0.097	0.048	4.34E-02	0.706	0.028	0.043	5.12E-01
rs1034405	3	50597092	G	A	<i>C3orf18</i>	A162V	0.130	0.018	0.044	6.75E-01	0.131	0.048	0.065	4.58E-01	0.129	-0.015	0.059	8.02E-01
rs13303	3	52558008	T	C	<i>STAB1</i>	M113T	0.442	0.006	0.030	8.35E-01	0.443	-0.002	0.044	9.69E-01	0.441	0.015	0.040	7.05E-01
rs3617	3	52833805	C	A	<i>ITIH3</i>	Q315K	0.550	-0.032	0.030	2.76E-01	0.551	-0.045	0.044	3.01E-01	0.550	-0.018	0.040	6.48E-01
rs62266958	3	129137188	C	T	<i>EFCAB12</i>	R197H	0.929	-0.149	0.058	9.77E-03	0.929	-0.307	0.085	3.06E-04	0.928	0.025	0.076	7.42E-01
rs2625973	3	129284818	A	C	<i>PLXND1</i>	L1412V	0.712	-0.028	0.033	3.88E-01	0.713	-0.099	0.048	4.07E-02	0.711	0.050	0.044	2.53E-01
rs2255703	3	129293256	T	C	<i>PLXND1</i>	M870V	0.615	-0.043	0.030	1.57E-01	0.617	-0.093	0.045	3.74E-02	0.614	0.012	0.040	7.58E-01
rs1804080	4	89625427	G	C	<i>HERC3</i>	E946Q	0.838	-0.078	0.040	5.13E-02	0.837	-0.103	0.059	8.18E-02	0.838	-0.051	0.054	3.44E-01
rs7657817	4	89668859	C	T	<i>FAM13A</i>	V443I	0.824	-0.062	0.039	1.08E-01	0.823	-0.044	0.057	4.36E-01	0.824	-0.083	0.052	1.11E-01
rs3733526	4	120528327	G	A	<i>PDE5A</i>	A41V	0.180	0.071	0.038	6.59E-02	0.181	0.059	0.056	2.97E-01	0.180	0.084	0.051	1.02E-01
rs1966265	5	176516631	A	G	<i>FGFR4</i>	V10I	0.248	0.014	0.034	6.77E-01	0.248	0.085	0.050	9.32E-02	0.248	-0.064	0.046	1.60E-01
rs1334576	6	7211818	G	A	<i>RREB1</i>	G195R	0.572	0.017	0.030	5.72E-01	0.571	0.043	0.044	3.26E-01	0.573	-0.013	0.040	7.53E-01
rs9469913	6	34827085	A	T	<i>UHRF1BP1</i>	Q984H	0.837	-0.247	0.040	7.19E-10	0.838	-0.299	0.059	4.03E-07	0.837	-0.188	0.053	4.03E-04
rs1892172	6	127476516	A	G	<i>RSPO3</i>	synonymous	0.547	0.022	0.030	4.68E-01	0.547	0.054	0.044	2.15E-01	0.547	-0.015	0.040	7.09E-01
rs139745911	6	127767954	A	G	<i>KIAA0408</i>	P504S	0.011	-0.328	0.140	1.88E-02	0.012	-0.243	0.204	2.35E-01	0.011	-0.427	0.188	2.31E-02
rs2303361	7	6449496	C	T	<i>DAGLB</i>	Q664R	0.243	-0.013	0.035	7.10E-01	0.244	-0.039	0.051	4.44E-01	0.242	0.016	0.046	7.22E-01
rs35332062	7	73012042	G	A	<i>MLXIPL</i>	A358V	0.871	0.077	0.044	7.99E-02	0.871	0.043	0.065	5.09E-01	0.872	0.116	0.059	4.93E-02
rs3812316	7	73020337	C	G	<i>MLXIPL</i>	Q241H	0.871	0.067	0.044	1.28E-01	0.870	0.031	0.065	6.38E-01	0.871	0.108	0.059	6.66E-02
rs17417407	10	95931087	T	G	<i>PLCE1</i>	R240L	0.171	0.091	0.039	2.14E-02	0.172	0.030	0.058	6.05E-01	0.170	0.159	0.053	2.52E-03
rs35169799	11	64031241	T	C	<i>PLCB3</i>	S778L	0.063	0.094	0.061	1.22E-01	0.065	0.195	0.088	2.71E-02	0.062	-0.025	0.082	7.62E-01
rs7114037	11	65403651	C	A	<i>PCNXL3</i>	H1822Q	0.945	0.016	0.065	8.04E-01	0.945	0.034	0.095	7.21E-01	0.945	-0.004	0.086	9.63E-01
rs145878042	12	48143315	A	G	<i>RAPGEF3</i>	L300P	0.989	0.127	0.140	3.67E-01	0.989	0.157	0.205	4.43E-01	0.989	0.091	0.189	6.28E-01
rs3764002	12	108618630	C	T	<i>WSCD2</i>	T266I	0.739	0.122	0.034	2.87E-04	0.739	0.128	0.050	9.94E-03	0.739	0.116	0.045	9.91E-03
rs58843120	12	123444507	G	T	<i>ABC9</i>	F92L	0.985	-0.051	0.123	6.77E-01	0.985	-0.061	0.180	7.35E-01	0.985	-0.040	0.164	8.08E-01
rs11057353	12	124265687	T	C	<i>DNAH10</i>	S228P	0.393	-0.069	0.030	2.24E-02	0.393	-0.075	0.045	9.39E-02	0.394	-0.063	0.040	1.19E-01
rs34934281	12	124330311	C	T	<i>DNAH10</i>	T1785M	0.877	-0.141	0.045	1.78E-03	0.878	-0.103	0.066	1.20E-01	0.877	-0.183	0.060	2.34E-03
rs11057401	12	124427306	T	A	<i>CCDC92</i>	S53C	0.689	-0.155	0.032	1.11E-06	0.690	-0.126	0.047	7.16E-03	0.688	-0.188	0.043	9.97E-06
rs1051860	14	58838668	A	G	<i>ARID4A</i>	synonymous	0.414	0.053	0.030	7.65E-02	0.414	0.036	0.044	4.14E-01	0.415	0.072	0.040	7.10E-02
rs17677991	15	42032383	G	C	<i>MGA</i>	P1523A	0.345	-0.026	0.031	3.96E-01	0.344	0.007	0.046	8.75E-01	0.345	-0.064	0.041	1.23E-01
rs3959569	15	42115747	C	G	<i>MAPKBP1</i>	R1240H	0.334	-0.016	0.031	6.02E-01	0.334	0.014	0.046	7.55E-01	0.334	-0.051	0.042	2.25E-01
rs1715919	15	56756285	G	T	<i>MNS1</i>	Q55P	0.105	0.046	0.048	3.42E-01	0.106	0.094	0.071	1.83E-01	0.103	-0.009	0.065	8.90E-01

rs3810818	16	4432029	A	C	VASN	E384A	0.227	-0.022	0.035	5.39E-01	0.228	-0.022	0.052	6.67E-01	0.226	-0.021	0.047	6.56E-01
rs3747579	16	4445327	C	T	CORO7	R193Q	0.281	0.003	0.033	9.37E-01	0.282	-0.060	0.048	2.16E-01	0.280	0.073	0.044	9.81E-02
rs1139653	16	4484396	A	T	DNAJA3	N75Y	0.279	0.039	0.033	2.38E-01	0.280	-0.010	0.049	8.30E-01	0.278	0.094	0.044	3.26E-02
rs9922085	16	67397580	G	C	LRR36	R101P	0.956	0.115	0.072	1.12E-01	0.956	0.100	0.107	3.47E-01	0.956	0.131	0.096	1.74E-01
rs8052655	16	67409180	G	A	LRR36	G388S	0.956	0.107	0.073	1.41E-01	0.957	0.096	0.107	3.68E-01	0.956	0.119	0.097	2.19E-01
rs897453	17	17425631	C	T	PEMT	V58L	0.523	-0.053	0.030	7.46E-02	0.523	-0.022	0.044	6.17E-01	0.524	-0.088	0.040	2.68E-02
rs11554159	19	18285944	A	G	IFI30	R76Q	0.269	0.179	0.033	7.43E-08	0.270	0.211	0.049	1.66E-05	0.268	0.144	0.044	1.23E-03
rs874628	19	18304700	G	A	MPV17L2	M72V	0.286	0.171	0.033	1.64E-07	0.286	0.207	0.048	1.83E-05	0.285	0.132	0.044	2.44E-03
rs2287922	19	49232226	A	G	RASIP1	R601C	0.537	-0.057	0.030	5.49E-02	0.538	-0.042	0.044	3.33E-01	0.534	-0.073	0.040	6.40E-02
rs2307019	19	49244220	G	A	IZUMO1	A333V	0.572	-0.112	0.030	1.67E-04	0.574	-0.100	0.044	2.34E-02	0.570	-0.126	0.040	1.48E-03
rs4911494	20	33971914	T	C	UQCC1	R51Q	0.632	-0.025	0.031	4.09E-01	0.635	-0.128	0.045	4.60E-03	0.630	0.088	0.041	3.08E-02
rs224331	20	34022387	A	C	GDF5	S276A	0.659	-0.045	0.031	1.51E-01	0.661	-0.154	0.046	8.12E-04	0.656	0.076	0.041	6.73E-02

Abbreviations: GRCh37=human genome assembly build 37;rsID=based on dbSNP; VEP=Ensembl Variant Effect Predictor toolset; GTEx=Genotype-Tissue Expression project;SD=standard deviation; SE=standard error;N=sample size

a Variant positions are reported according to Human assembly build 37 and their alleles are coded based on the positive strand.

b Effect allele is oriented on the WHRadjBMI increasing allele see Supplementary Tables 4,5,6.

c The gene the variant falls in and amino acid change from the most abundant coding transcript is shown (protein annotation is based on VEP toolset and transcript abundance from GTEx database).

d Effect size is based on standard deviation (SD) per effect allele

e Bolded P-values are variants that met bonferonni significance (P-value< 1.0E-03; i.e. 0.05/48 variants).

a The variance explained was estimated using a method previously reported by Kutalik et al. We selected subsets of SNPs that were based on varying thresholds of the P-value from 2×10^{-7} to 0.02 or minor allele frequency (MAF) thresholds from 0.0025 to 0.05. Each subset of SNPs was used together or clumped into independent regions using a physical distance criterion $< 500\text{kb}$ and the most significant lead SNP within the respective region was selected. Results are based on the All Ancestry analyses.

Kutalik, Z., et al., *Novel method to estimate the phenotypic variation explained by genome-wide association studies reveals large fraction of the missing heritability*. Genet Epidemiol, 2011. **35**(5): p. 341-9.

b The number of SNPs that meet the P-value or MAF threshold used to estimate the variance explained.

c P-value for the difference in the variance explained by the SNPs for men versus women.

Supplementary Table 13. Penetrance analysis for rare coding variants in KIAA0408, ABCB9, RAGGF3, ACVR1C, and ANGPTL4, using European ancestry data from the UKBiobank

Gene ^a	Chr	Pos (GRCh37) ^b	rsID	Minor/Major allele	Amino acid change ^a	Gender	Discovery GIANT meta-analysis - All Ancestries ^c			Results from the UKBB dataset ^c			Obesity and central adiposity class ^e			Observed Values by class				Expected Values by class				TOTAL	ChiSquare P-value ^f		
							MAF	Effect size ^d (SD/allele)	SE	P-value	MAF	Effect size ^d (SD/allele)	SE	P-value	Obesity class	WHR threshold	MAF by class	Carrier count	Carrier proportions	Non-carrier count	Non-carrier proportions	Carrier count	Carrier proportions			Non-carrier count	Non-carrier proportions
KIAA0408	6	127767954	rs139745911	A/G	P504S	ALL	0.009	0.107	0.015	2.07E-13	0.011	0.103	0.020	2.08E-07	non-obese	<=0.85 Women, <=0.90 Men, >0.85 Women,	0.011	1230	0.48	54533	0.49	1256	0.49	54507	0.49	55763	2.93E-01
						WOMEN	obese	>0.90 Men,	0.012	1315	0.52	55894	0.51	1289	0.51	55920	0.51	57209	3.83E-02								
							non-obese	<=0.85	0.011	899	0.66	39828	0.69	934	0.69	39793	0.69	40727									
						MEN	obese	>0.85	0.012	461	0.34	18113	0.31	426	0.31	18148	0.31	18574	9.49E-01								
							non-obese	<=0.90	0.011	331	0.28	14705	0.28	332	0.28	14704	0.28	15036									
						obese	>0.90	0.011	854	0.72	37781	0.72	853	0.72	37782	0.72	38635										
RAGGF3	12	48143315	rs145878042	G/A	L300P	ALL	0.010	-0.090	0.012	1.28E-13	0.011	-0.069	0.020	4.27E-04	non-obese	<=0.85 Women, <=0.90 Men, >0.85 Women,	0.015	1792	0.51	57637	0.49	1740	0.50	57689	0.50	59429	7.22E-02
						WOMEN	obese	>0.90 Men,	0.014	1719	0.49	58802	0.51	1771	0.50	58750	0.50	60521	2.33E-01								
							non-obese	<=0.85	0.015	1297	0.70	42122	0.69	1274	0.69	42145	0.69	43419									
						MEN	obese	>0.85	0.014	555	0.30	19165	0.31	578	0.31	19142	0.31	19720	1.28E-01								
							non-obese	<=0.90	0.016	495	0.30	15515	0.28	468	0.28	15542	0.28	16010									
						obese	>0.90	0.014	1164	0.70	39637	0.72	1191	0.72	39610	0.72	40801										
ACVR1C	2	158412701	rs55920843	G/T	N150H	ALL	0.009	-0.046	0.013	5.62E-04	0.012	-0.107	0.019	1.01E-08	non-obese	<=0.85 Women, <=0.90 Men, >0.85 Women,	0.013	1533	0.53	57881	0.49	1429	0.50	57985	0.50	59414	9.25E-05
						WOMEN	obese	>0.90 Men,	0.011	1352	0.47	59161	0.51	1456	0.50	59057	0.50	60513	4.85E-05								
							non-obese	<=0.85	0.013	1132	0.74	42276	0.69	1059	0.69	42349	0.69	43408									
						MEN	obese	>0.85	0.010	408	0.26	19307	0.31	481	0.31	19234	0.31	19715	1.77E-01								
							non-obese	<=0.90	0.013	401	0.30	15605	0.28	379	0.28	15627	0.28	16006									
						obese	>0.90	0.012	944	0.70	39854	0.72	966	0.72	39832	0.72	40798										

Abbreviations: GRCh37=human genome assembly build 37;rsID=based on dbSNP;SD=standard deviation; SE=standard error;N=sample size; MAF=minor allele frequency

a The gene the variant falls in and amino acid change from the most abundant coding transcript is shown (protein annotation is based on VEP toolset and transcript abundance from GTEx database).

b Variant positions are reported according to Human assembly build 37 and their alleles are coded based on the positive strand.

c Association results per minor allele from the discovery GIANT all ancestries sample in the sex-combined and sex stratified models. Similarly the association results are also shown for the UKBB European sample, which was used for the penetrance analysis, in the sex-combined and sex stratified model

d Effect size is based on standard deviation (SD) per minor allele

e The UKBB sample was divided by obesity classification (BMI<30:non-obese or BMI>=30:obese) and central adiposity (WHR<=0.85 for women and <=0.90 for men: no central adiposity or WHR>0.85 for women and >0.90 for men: has central adiposity)

f Bonferroni correction for 15 tests (5 SNPs x 3 gender groups) is Pvalue<0.0033; significant Pvalues are bolded.

Supplementary Table 14. Triglyceride change in transgenic RNAi *Drosophila* as compared to control for the genes having array-wide significant coding variants identified in the final combined meta-analysis and available fly orthologs

Human GeneID	Fly GeneID	Fly CG number ^a	mean TG/weight	P value	# Replicates ^b
ELAV Driver					
<i>PLXND1</i>	PlexB	CG17245	1.7365	0.0055	6
<i>DNAH10</i>	Dhc98D	CG1842	2.0364	0.0024	5
CG driver					
<i>PLXND1</i>	PlexB	CG17245	1.2997	0.4463	5
<i>DNAH10</i>	Dhc98D	CG1842	2.0058	0.0012	5

a *Drosophila* annotation IDs for protein-coding genes.

b Additional knockdown experiments with ≥ 5 replicates and using tissue-specific drivers (body fat, CG driver [cg-Gal4] and neuronal, ELAV driver [elav-Gal4] specific RNAi-knockdown) were

16:4484396	rs1139653	<i>DNAJA3</i>	A/T	<i>DNAJA3</i>	0.17815	4.36E-06	4.00E-05	Muscle_Skeletal	rs1139652	16:4476089	T/C	0.23	1.1E-09	0.69	0.92
16:4484396	rs1139653	<i>DNAJA3</i>	A/T	<i>NMRAL1</i>	-0.807375	9.54E-41	4.24E-05	Muscle_Skeletal	rs62039231	16:4519548	A/G	-0.93	1.5E-53	0.73	0.89
16:4484396	rs1139653	<i>DNAJA3</i>	A/T	<i>NMRAL1</i>	-0.424802	3.38E-06	3.41E-05	Pancreas	rs11643057	16:4544505	C/T	-0.6	7.4E-13	0.54	0.76
16:67397580	rs9922085	<i>LRRC36</i>	G/C	<i>RANBP10</i>	-0.417213	2.44E-06	1.98E-04	Adipose_Subcutaneous	rs8052687	16:67446037	T/G	-0.39	1.1E-08	0.36	1
16:67397580	rs9922085	<i>LRRC36</i>	G/C	<i>LRRC36</i>	0.585883	3.90E-06	2.00E-04	Adipose_Subcutaneous	rs28526086	16:67366809	A/T	0.58	1.2E-06	0.97	1
16:67397580	rs9922085	<i>LRRC36</i>	G/C	<i>LRRC36</i>	0.64795	4.90E-09	1.32E-04	Adipose_Visceral_Omentum	rs1559323	16:67447255	C/G	0.65	4.8E-09	1.00	1
16:67397580	rs9922085	<i>LRRC36</i>	G/C	<i>LRRC36</i>	1.05425	1.40E-17	1.43E-04	Muscle_Skeletal	rs1559323	16:67447255	C/G	1.1	1.3E-17	1.00	1
16:67397580	rs9922085	<i>LRRC36</i>	G/C	<i>LRRC36</i>	-1.48782	3.17E-15	1.46E-04	Pancreas	rs9922119	16:67411530	T/C	-1.5	3.1E-15	0.98	1
16:67409180	rs8052655	<i>LRRC36</i>	G/A	<i>RANBP10</i>	-0.41702	2.45E-06	1.98E-04	Adipose_Subcutaneous	rs8052687	16:67446037	T/G	-0.39	1.1E-08	0.36	1
16:67409180	rs8052655	<i>LRRC36</i>	G/A	<i>LRRC36</i>	0.585576	3.93E-06	2.00E-04	Adipose_Subcutaneous	rs28526086	16:67366809	A/T	0.58	1.2E-06	0.98	1
16:67409180	rs8052655	<i>LRRC36</i>	G/A	<i>LRRC36</i>	0.64795	4.90E-09	1.32E-04	Adipose_Visceral_Omentum	rs1559323	16:67447255	C/G	0.65	4.8E-09	1.00	1
16:67409180	rs8052655	<i>LRRC36</i>	G/A	<i>LRRC36</i>	1.05391	1.41E-17	1.43E-04	Muscle_Skeletal	rs1559323	16:67447255	C/G	1.1	1.3E-17	1.00	1
16:67409180	rs8052655	<i>LRRC36</i>	G/A	<i>LRRC36</i>	-1.48782	3.17E-15	1.46E-04	Pancreas	rs9922119	16:67411530	T/C	-1.5	3.1E-15	0.98	1
17:17425631	rs897453	<i>PEMT</i>	C/T	<i>PEMT</i>	-0.268982	5.87E-08	9.82E-05	Adipose_Subcutaneous	rs4646385	17:17448691	A/G	-0.37	5.9E-16	0.61	0.94
19:18285944	rs11554159	<i>IFI30</i>	G/A	<i>PDE4C</i>	-0.288488	9.07E-07	3.79E-05	Muscle_Skeletal	rs2384986	19:18356983	A/G	-0.3	1.1E-08	0.12	0.79
19:18285944	rs11554159	<i>IFI30</i>	G/A	<i>MPV17L2</i>	0.202855	1.75E-05	3.86E-05	Muscle_Skeletal	rs4808121	19:18358107	T/C	0.26	4.1E-09	0.40	0.66
19:18304700	rs874628	<i>MPV17L2</i>	A/G	<i>PDE4C</i>	-0.287308	8.85E-07	3.79E-05	Muscle_Skeletal	rs2384986	19:18356983	A/G	-0.3	1.1E-08	0.12	0.79
19:18304700	rs874628	<i>MPV17L2</i>	A/G	<i>MPV17L2</i>	0.246368	1.28E-07	3.86E-05	Muscle_Skeletal	rs4808121	19:18358107	T/C	0.26	4.1E-09	0.40	0.66
19:49232226	rs2287922	<i>RASIP1</i>	G/A	<i>MAMSTR</i>	0.131787	5.82E-07	3.93E-05	Muscle_Skeletal	rs519757	19:49224966	A/C	0.17	1.4E-11	0.74	0.98
19:49232226	rs2287922	<i>RASIP1</i>	G/A	<i>FUT2</i>	-0.743038	8.92E-15	3.39E-05	Pancreas	rs492602	19:49206417	A/G	-0.94	3.3E-25	0.66	0.87
19:49244220	rs2307019	<i>IZUMO1</i>	G/A	<i>IZUMO1</i>	-0.552316	3.26E-16	5.04E-05	Adipose_Subcutaneous	rs838143	19:49251755	G/A	0.92	5.2E-18	0.08	1
19:49244220	rs2307019	<i>IZUMO1</i>	G/A	<i>IZUMO1</i>	-0.499964	4.02E-10	2.41E-05	Adipose_Visceral_Omentum	rs838143	19:49251755	G/A	0.86	9.7E-14	0.08	1
19:49244220	rs2307019	<i>IZUMO1</i>	G/A	<i>IZUMO1</i>	-0.39286	1.06E-08	4.18E-05	Muscle_Skeletal	rs12327653	19:49252679	T/C	-0.46	6.0E-09	0.42	0.99
19:49244220	rs2307019	<i>IZUMO1</i>	G/A	<i>RASIP1</i>	-0.377204	8.04E-06	2.96E-05	Pancreas	rs838143	19:49251755	G/A	0.8	5.4E-14	0.08	1
19:49244220	rs2307019	<i>IZUMO1</i>	G/A	<i>FUT2</i>	0.723088	5.22E-14	3.39E-05	Pancreas	rs492602	19:49206417	A/G	-0.94	3.3E-25	0.36	0.75
19:49244220	rs2307019	<i>IZUMO1</i>	G/A	<i>IZUMO1</i>	-0.406701	2.52E-06	2.80E-05	Pancreas	rs838143	19:49251755	G/A	0.89	4.2E-17	0.08	1
20:33971914	rs4911494	<i>UQCC1</i>	C/T	<i>UQCC1</i>	0.32329	4.82E-10	1.65E-04	Adipose_Subcutaneous	rs6142373	20:33983314	T/A	0.35	2.3E-12	1.00	1
20:33971914	rs4911494	<i>UQCC1</i>	C/T	<i>UQCC1</i>	0.258781	1.89E-07	1.21E-04	Adipose_Visceral_Omentum	rs1406947	20:33969530	C/T	0.27	5.5E-08	0.95	1
20:33971914	rs4911494	<i>UQCC1</i>	C/T	<i>UQCC1</i>	0.200981	1.17E-10	1.70E-04	Muscle_Skeletal	rs6060402	20:34005240	T/C	0.22	7.6E-13	0.99	1
20:33971914	rs4911494	<i>UQCC1</i>	C/T	<i>CEP250</i>	0.277519	1.00E-07	1.33E-04	Muscle_Skeletal	rs10359	20:34099789	A/G	-0.42	2.2E-13	0.40	0.86
20:33971914	rs4911494	<i>UQCC1</i>	C/T	<i>UQCC1</i>	0.2713	4.70E-05	1.50E-04	Pancreas	rs6087705	20:34001250	G/A	0.29	5.1E-06	1.00	1
20:34022387	rs224331	<i>GDF5</i>	A/C	<i>UQCC1</i>	-0.329442	2.52E-10	1.65E-04	Adipose_Subcutaneous	rs6142373	20:33983314	T/A	0.35	2.3E-12	0.89	1
20:34022387	rs224331	<i>GDF5</i>	A/C	<i>UQCC1</i>	-0.199363	1.14E-04	1.21E-04	Adipose_Visceral_Omentum	rs1406947	20:33969530	C/T	0.27	5.5E-08	0.84	1
20:34022387	rs224331	<i>GDF5</i>	A/C	<i>UQCC1</i>	-0.216058	1.76E-12	1.70E-04	Muscle_Skeletal	rs6060402	20:34005240	T/C	0.22	7.6E-13	0.90	1
20:34022387	rs224331	<i>GDF5</i>	A/C	<i>CEP250</i>	-0.267842	2.04E-07	1.33E-04	Muscle_Skeletal	rs10359	20:34099789	A/G	-0.42	2.2E-13	0.36	0.77

a The results were extracted from the GTEx project (V6): <https://www.gtexportal.org/home/>; Bold lines represent the LD r^2 between exome variant and eSNP > 0.8.

b Alleles are presented as non-effect/effect with regard to cis-eQTL dataset.

c Inverse normalized individual tissue quantile normalized RPKM.

d The most significantly associated variants for each eQTL gene or eGene (excluding INDEL and multiple allelic variants).

e The linkage disequilibrium information is based on the European population included in 1000 Genome Phase 3 project.

Supplementary Table 16. Inflation factors (λ_{GC}) for BMI single-variant meta-analyses in the Discovery phase based on the different categories of variants present on the ExomeChip.

Type of variants	All Ancestries sex-combined additive		European ancestry sex-combined additive	
	Number of variants	λ_{GC}	Number of variants	λ_{GC}
All variants	244,618	1.08	236,804	1.07
All minor allele frequency >5%	28,089	1.43	27,228	1.45
All minor allele frequency \leq 5%	216,529	1.05	209,576	1.03
GWAS sentinel SNPs ^a	4,781	1.76	4,781	1.78
Ancestry informative markers	3,772	1.18	3,772	1.19
Grid SNPs ^b	4,676	1.34	4,676	1.33
All coding variants ^c	231,214	1.06	223,334	1.05
Coding minor allele frequency >5%	13,953	1.37	13,758	1.41
Coding minor allele frequency \leq 5%	217,261	1.05	209,576	1.03
Coding minor allele frequency \leq 1%	207,783	1.04	200,517	1.03

a GWAS sentinel SNPs include markers reported in the NHGRI GWAS catalog (for all phenotypes).

b Grid SNPs were selected to provide a scaffold across the genome for identity-by-descent analyses.

c Coding variants refer to variants located in the exons and splicing junction regions.

Supplementary Table 17. Detailed acknowledgements by study and/or contributing author(s).

Cohorts		
Abbreviations	Full Name(s)	Acknowledgements (funding, personal, groups, ...), include funding identification numbers/codes
Airwave	The Airwave Study	Funding: The Airwave Study is funded by the Home Office (grant number 780-TETRA) with additional support from the National Institute for Health Research (NIHR) Imperial College Healthcare NHS Trust (ICHNT) and Imperial College Biomedical Research Centre (BRC). PE is a UK Dementia Research Institute (DRI) Professor, UK DRI at Imperial College London. The UK DRI is funded by the Medical Research Council, Alzheimer's Society and Alzheimer's Research UK. This work used computing resources of the UK MEDical BIOinformatics partnership - aggregation, integration, visualisation and analysis of large, complex data (UK MED-BIO) which is supported by the Medical Research Council [grant number MR/L01632X/1]. Acknowledgements: We thank all participants in the Airwave Health Monitoring Study. We also thank Louisa Cavaliero who assisted in data collection and management as well as Peter McFarlane and the Glasgow CARE, Patricia Munroe at Queen Mary University of London, Joanna Sarnecka and Ania Zawodniak at Northwick Park for their contributions to the study.
AMISH	Amish	We gratefully acknowledge our Amish liaisons, field workers and clinic staff and the extraordinary cooperation and support of the Amish community without which these studies would not have been possible. The Amish studies are supported by grants and contracts from the NIH, including K01HL116770, U01 HL072515-06, U01 HL84756, U01HL105198, U01 GM074518, . We thank our Amish research volunteers for their long-standing partnership in research, and the research staff at the Amish Research Clinic for their hard work and dedication.
ARIC	The Atherosclerosis Risk in Communities	The Atherosclerosis Risk in Communities (ARIC) study is carried out as a collaborative study supported by the National Heart, Lung, and Blood Institute (NHLBI) contracts (HHSN268201100005C, HHSN268201100006C, HHSN268201100007C, HHSN268201100008C, HHSN268201100009C, HHSN268201100010C, HHSN268201100011C, and HHSN268201100012C). The authors thank the staff and participants of the ARIC study for their important contributions. Funding support for "Building on GWAS for NHLBI-diseases: the U.S. CHARGE consortium" was provided by the NIH through the American Recovery and Reinvestment Act of 2009 (ARRA) (5RC2HL102419).
BBMRI	BBMRI-NL	The BBMRI-NL embodies the Dutch Biobanking and Biomolecular Research Infrastructure project, including large population cohorts and clinical collections. All studies were financially supported by a Research Infrastructure financed by the Dutch government (NWO 184.021.007). The Hoorn Diabetes Care System Cohort study likes to acknowledge the Netherlands Organisation for Health Research and Development (ZonMW) for funding (grant number 113102006) and is supported by the Diabetes Care System West-Friesland. Contributing members of the DCS study are: G Nijpels, J Beulens, AMW van der Heijden, F Rutters, S Rauh, JM Dekker, all VU University Medical Center Amsterdam and LM 't Hart, N van Leeuwen, Leiden University Medical Center, Leiden, The Netherlands. NESCOG received funding from NWO/MaGW VIDI-016-065-318; NWO VICI 453-14-005, and this research was part of Science Live, the innovative research program of science center NEMO that enables scientists to carry out real, publishable, peer-reviewed research using NEMO visitors as volunteers. BOSOM received funding from the Dutch Cancer Society: NKI2009-4363 and would like to thank all their collaborators. HEBON will like to thank all their collaborators. The Longitudinal Aging Study Amsterdam is supported by a grant from the Netherlands Ministry of Health Welfare and Sports, Directorate of Long-Term Care. The authors would like to acknowledge DJH Deeg, M den Heijer, MA Huisman, NM van Schoor, and KMA Swart*. UCP would like to acknowledge Prof. Dr. Olaf H. Klungel and Dr. Anke-Hilse Maitland-Van der Zee for granting access to the UCP study data
BC1958	1958 Birth Cohort	We are grateful for being able to use the British 1958 Birth Cohort DNA collection. Sample collection funded by the Medical Research Council grant G0000934 and the Wellcome Trust grant 068545/Z/02. Genotyping was funded by the Wellcome Trust.
BRAVE	Bangladeshi Risk of Acute Ventricular Events	The BRAVE study genetic epidemiology working group is a collaboration between the Cardiovascular Epidemiology Unit, Department of Public Health and Primary Care, University of Cambridge, UK, the Centre for Control of Chronic Diseases, icddr,b, Dhaka, Bangladesh and the National Institute of Cardiovascular Diseases, Dhaka, Bangladesh.
BRIGHT	British Genetics of Hypertension	This work was funded by the Medical Research Council of Great Britain (grant number: G9521010D) and the Wellcome Trust Strategic Award (grant number: 083948). The BRIGHT study is extremely grateful to all the patients who participated in the study and the BRIGHT nursing team. The funders had no role in study design, data collection and analysis. The BRIGHT study genotyping of the Exome chip was funded by Wellcome Trust Strategic Awards 083948 and 085475.

CAMCANCER	Cambridge Cancer Studies (SEARCH, SIBS, UKO and UKGPCS)	CRUK ref: A490/A10124; CRUK ref: C8197/A16565; UKGPCS would also like to thank the following for funding support: The Institute of Cancer Research and The Everyman Campaign, The Prostate Cancer Research Foundation, Prostate Research Campaign UK (now Prostate Action), The Orchid Cancer Appeal, The National Cancer Research Network UK, The National Cancer Research Institute (NCRI) UK. We are grateful for support of NIHR funding to the NIHR Biomedical Research Centre at The Institute of Cancer Research and The Royal Marsden NHS Foundation Trust. UKGPCS should also like to acknowledge the NCRN nurses, data managers and Consultants for their work in the UKGPCS study. A list of UKGPCS collaborators can be found at: http://www.icr.ac.uk/our-research/research-divisions/division-of-genetics-and-epidemiology/oncogenetics/research-projects/ukgpcs/ukgpcs-collaborators
CARDIA	The Coronary Artery Risk Development in Young Adults	The CARDIA Study is conducted and supported by the National Heart, Lung, and Blood Institute in collaboration with the University of Alabama at Birmingham (HHSN268201300025C & HHSN268201300026C), Northwestern University (HHSN268201300027C), University of Minnesota (HHSN268201300028C), Kaiser Foundation Research Institute (HHSN268201300029C), and Johns Hopkins University School of Medicine (HHSN268200900041C). CARDIA is also partially supported by the Intramural Research Program of the National Institute on Aging. Exome Chip genotyping was supported from grants R01-HL093029 and U01-HG004729 to MF. This manuscript has been reviewed and approved by CARDIA for scientific content.
CARL	INGI-Carlantino	
CHES	The Chinese American Eye Disease Study	This study was analyzed as part of TUDR. This work was supported by grant EY-017337 from the National Eye Institute, National Institutes of Health, Bethesda, Maryland, and an unrestricted Departmental grant from Research to Prevent Blindness, New York, NY 10022.
CHS	Cardiovascular Health Study	
CLHNS	Cebu Longitudinal Health and Nutrition Survey	The Cebu Longitudinal Health and Nutrition Survey (CLHNS) was supported by National Institutes of Health grants DK078150, TW005596, HL085144 and TW008288 and pilot funds from RR020649, ES010126, and DK056350. We thank the USC-Office of Population Studies Foundation research and data collection teams and the study participants who generously provided their time for this study.
CROATIA_Korcula	CROATIA-Korcula	The CROATIA-Korcula study was funded by grants from the Medical Research Council (UK), European Commission Framework 6 project EUROSPAN (Contract No. LSHG-CT-2006-018947), European Commission Framework 7 project BBMR-LPC (grant 313010), Republic of Croatia Ministry of Science, Education and Sports research grant (216-1080315-0302) and Croatian Science Foundation (grant 8875). We would like to acknowledge the invaluable contributions of the recruitment team in Korcula, the administrative teams in Croatia and Edinburgh and the people of Korcula. The SNP genotyping for the CROATIA-Korcula cohort was performed in Helmholtz Zentrum München, Neuherberg, Germany
D2D2007	FIN-D2D 2007	The FIN-D2D 2007 study was supported by funds from the hospital districts of Pirkanmaa; Southern Ostrobothnia; North Ostrobothnia; Central Finland and Northern Savo; the Finnish National Public Health Institute; the Finnish Diabetes Association; the Ministry of Social Affairs and Health in Finland; Finland's Slottery Machine Association; the Academy of Finland [grant number 129293] and Commission of the European Communities, Directorate C-Public Health [grant agreement no. 2004310]. The Broad Genomics Platform performed the genotyping.
deCODE	deCODE	We thank participants in deCODE cardiovascular- and obesity studies and collaborators for their cooperation. The research performed at deCODE Genetics was part funded through the European Community's Seventh Framework Programme (FP7/2007-2013), ENGAGE project, grant agreement HEALTH-F4-2007- 201413.
DHS	Diabetes Heart Study	This study was supported in part by R01 HL67348, R01 HL092301, R01 NS058700 (to DWB) and the General Clinical Research Centre of the Wake Forest School of Medicine (M01 RR07122, F32 HL085989). The authors thank the other investigators, the staff, and the participants of the DHS study for their valuable contributions.

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DPS	The Finnish Diabetes Prevention Study	The DPS has been financially supported by grants from the Academy of Finland (117844 and 40758, 211497, and 118590 (MU); The EVO funding of the Kuopio University Hospital from Ministry of Health and Social Affairs (5254), Finnish Funding Agency for Technology and Innovation (40058/07), Nordic Centre of Excellence on ÖSystems biology in controlled dietary interventions and cohort studies, SYSDIET (070014), The Finnish Diabetes Research Foundation, Yrjö Jahnsson Foundation (56358), Sigrid Juselius Foundation and TEKES grants 70103/06 and 40058/07.
DR's EXTRA Study	The Dose Responses to Exercise Training Study	The DR's EXTRA Study was supported by grants to Rainer Rauramaa by the Ministry of Education and Culture of Finland (627;2004-2011), Academy of Finland (102318; 123885), Kuopio University Hospital, Finnish Diabetes Association, Finnish Heart Association, Päivikki and Sakari Sohlberg Foundation and by grants from European Commission FP6 Integrated Project (EXGENESIS); LSHM-CT-2004-005272, City of Kuopio and Social Insurance Institution of Finland (4/26/2010).
EFSOCH	The Exeter Family Study of Childhood Health	
EGCUT	Estonian Genome Center of University of Tartu	EGCUT work was supported by IUT20-60 from the Estonian Research Council;by the European Regional Development Fund to the Centre of Excellence in Genomics and Translational Medicine (GenTransMed); EGCUT were further supported by the US National Institute of Health [R01DK075787].
eMerge	eMERGE-Seattle	NIH UO1HG008657, UO1HG06375 and UO1AG006781; and a State of Washington Life Sciences Discovery Award (265508) to the Northwest Institute of Genetic Medicine and UO1 AG 06781 grant.
EPIC	EPIC-CVD Consortium	CHD case ascertainment and validation and genotyping in EPIC-CVD were principally supported by grants awarded to the University of Cambridge from the EU Framework Programme 7 (HEALTH-F2-2012-279233), the UK Medical Research Council (G0800270) and British Heart Foundation (SP/09/002), and the European Research Council (268834). We thank all EPIC participants and staff for their contribution to the study, the laboratory teams at the Medical Research Council Epidemiology Unit for sample management and Cambridge Genomic Services for genotyping, Sarah Spackman for data management, and the team at the EPIC-CVD Coordinating Centre for study coordination and administration.
EPIC	EPIC-InterAct	We thank all EPIC participants and staff for their contribution to the EPIC-InterAct study. Funding for the EPIC-InterAct project was provided by the EU FP6 programme (LSHM_CT_2006_037197).
EPIC	EPIC-Norfolk	EPIC-Norfolk is supported by programme grants from the Medical Research Council UK (G1000143) and Cancer Research UK (C864/A14136) and with additional support from the European Union, Stroke Association, British Heart Foundation, Research into Ageing, Department of Health, The Wellcome Trust and the Food Standards Agency. NJW, CL and RAS also acknowledge support from the Medical Research Council, UK (MC_UU_12015/1; MC_PC_13048). We thank all EPIC participants and staff for their contribution to the study, and the laboratory teams at the MRC Epidemiology Unit for sample management.
EPIC	EPIC-Potsdam	The study was supported in part by a grant from the German Federal Ministry of Education and Research (BMBF) to the German Center for Diabetes Research (DZD e.V.). The recruitment phase of the EPIC-Potsdam study was supported by the Federal Ministry of Science, Germany (01 EA 9401) and the European Union (SOC 95201408 05 F02). The follow-up of the EPIC-Potsdam study was supported by German Cancer Aid (70-2488-Ha I) and the European Community (SOC 98200769 05 F02). Exome chip genotyping of EPIC-Potsdam samples was carried out under supervision of Per Hoffmann and Stefan Herms at Life & Brain GmbH, Bonn. We thank all EPIC-Potsdam participants for their invaluable contribution to the study.

EpiHealth	Epidemiology for Health	EpiHealth was supported by the Swedish Research Council strategic research network Epidemiology for Health, Uppsala University and Lund University. Genotyping in EpiHealth was supported by Swedish Heart-Lung Foundation (grant no. 20120197 and 20140422), Knut och Alice Wallenberg Foundation (grant no. 2013.0126), and Swedish Research Council (grant no. 2012-1397). Genotyping was performed by the SNP&SEQ Technology Platform in Uppsala. We thank the EpiHealth participants for their <u>dedication and commitment</u> .
EXTEND	Exeter 10,000	EXTEND data were provided by the Peninsula Research Bank, part of the NIHR Exeter Clinical Research Facility
Fenland	Fenland	We thank the Fenland Study volunteers for their time and help, the General Practitioners and practice staff for assistance with recruitment, the Investigators, Co-ordination team and the Epidemiology Field, Data and Laboratory teams. The Fenland Study is funded by the MRC (MC_U106179471) and Wellcome Trust. NJW, CL and RAS also acknowledge support from the Medical Research Council, UK (MC_UU_12015/1; MC_PC_13046).
FHS	Family Heart Study	The Family Heart Study (FamHS) research was supported by NIH grants: R01-HL-117078 from NHLBI, and R01-DK-089256 from NIDDK.
FINRISK 2007	National FINRISK 2007 Study	VS was supported by the Academy of Finland, grant #139635, and the Finnish Foundation for Cardiovascular Research. PJ was supported by [TBA]. The Broad Genomics Platform performed the genotyping.
FramHS	Framingham Heart Study	This research was conducted in part using data and resources from the Framingham Heart Study of the National Heart Lung and Blood Institute of the National Institutes of Health and Boston University School of Medicine. The analyses reflect intellectual input and resource development from the Framingham Heart Study investigators participating in the SNP Health Association Resource (SHARe) project. This work was partially supported by the National Heart, Lung and Blood Institute's Framingham Heart Study (Contract No. HHSN268201500001) and its contract with Affymetrix, Inc for genotyping services (Contract No. N02-HL-6-4278). This research was partially supported by grant NIDDK 1R01DK8925601. A portion of this research utilized the Linux Cluster for Genetic Analysis (LinGA-II) funded by the Robert Dawson Evans Endowment of the Department of Medicine at Boston University School of Medicine and Boston Medical Center.
FUSION	Finland-United States Investigation of NIDDM Genetics Study	The FUSION study was supported by DK093757, DK072193, DK062370, and ZIA-HG000024. The Center for Inherited Disease Research (CIDR) and the Broad Genomics Platform performed the genotyping.
FVG	INGI-FVG	This study was partially supported by Regione FVG (L.26.2008) and Italian Ministry of Health (GR-2011-02349604).
GENOA	Genetic Epidemiology Network of Arteriopathy	Support for GENOA was provided by the National Heart, Lung and Blood Institute (HL119443, HL054464, HL054457, HL054481, HL087660, and HL086694) of the National Institutes of Health. Genotyping was performed at the Mayo Clinic (Stephan T. Turner, MD, Mariza de Andrade PhD, Julie Cunningham, PhD). Genotyping for GENOA whites was performed by Eric Boerwinkle, PhD and Megan L. Grove from the Human Genetics Center and Institute of Molecular Medicine and Division of Epidemiology, University of Texas Health Science Center, Houston, Texas, USA. Genotyping for GENOA African Americans was performed at the Center for Inherited Disease Research (CIDR) at Johns Hopkins University. We would also like to thank the families that participated in the GENOA study.
GRAPHIC	Genetic Regulation of Arterial Pressure in Humans in the Community	The GRAPHIC Study was funded by the British Heart Foundation (BHF) (RG/200004). Exome array genotyping was funded by the NIHR and the Wellcome Trust (083948/B/07/Z). NM is funded by the NIHR Leicester Cardiovascular Biomedical Research Unit. CPN is funded by the BHF (CH/03/001). NJS holds a Chair funded by the BHF (CH/03/001) and is a NIHR Senior Investigator.
GS	Generation Scotland	Generation Scotland received core funding from the Chief Scientist Office of the Scottish Government Health Directorate CZD/16/6 and the Scottish Funding Council HR03006. Genotyping of the GS:SFHS samples was carried out by staff at the Genetics Core Laboratory at the Wellcome Trust Clinical Research Facility, Edinburgh, Scotland and was funded by the UK's Medical Research Council. We are grateful to the families who took part in GS:SFHS, the GPs and Scottish School of Primary Care for their help in recruiting them, and the whole GS team, which includes academic researchers, clinic staff, laboratory technicians, clerical workers, statisticians and research managers. We are grateful to the families who took part in GS:SFHS, the GPs and Scottish School of Primary Care for their help in recruiting them, and the whole GS team, which includes academic researchers, clinic staff, laboratory technicians, clerical workers, statisticians and research managers
Health	Health2006	Establishment of the Health2006 cohort was financially supported by The Velux Foundation; The Danish Medical Research Council, Danish Agency for Science, Technology and Innovation; The Aase and Ejner Danielsens Foundation; ALK-Abelló A/S (Hørsholm, Denmark), Timber Merchant Vilhelm Bangs Foundation, MEKOS Laboratories (Denmark), and Research Centre for Prevention and Health, the Capital Region of Denmark.

HELIC	Hellenic Isolated Cohorts: MANOLIS and POMAK	This work was funded by the Wellcome Trust (098051) and the European Research Council (ERC-2011-StG 280559-SEPI). The MANOLIS cohort is named in honour of Manolis Giannakakis, 1978-2010. We thank the residents of the Mylopotamos villages, and of the Pomak villages, for taking part. The HELIC study has been supported by many individuals who have contributed to sample collection (including A. Athanasiadis, O. Balafouti, C. Batzaki, G. Daskalakis, E. Emmanouil, C. Giannakaki, M. Giannakopoulou, A. Kaparou, V. Kariakli, S. Koinaki, D. Kokori, M. Konidari, H. Koundouraki, D. Koutoukidis, V. Mamakou, E. Mamelaki, E. Mpamiaki, M. Tsoukana, D. Tzakou, K. Vosdogianni, N. Xenaki, E. Zenginini), data entry (T. Antonos, D. Papagrigroriou, B. Spiliopoulou), sample logistics (S. Edkins, E. Gray), genotyping (R. Andrews, H. Blackburn, D. Simpkin, S. Whitehead), research administration (A. Kolb-Kokocinski, S. Smee, D. Walker) and informatics (M. Pollard, J. Randall).
HRS	Health and Retirement Study	HRS is supported by the National Institute on Aging (NIA U01AG009740). The genotyping was funded separately by the National Institute on Aging (RC2 AG036495, RC4 AG039029) and was conducted by the NIH Center for Inherited Disease Research (CIDR) at Johns Hopkins University. Genotyping quality control and final preparation of the data were performed by the University of Michigan School of Public Health. A portion of this work was also supported by R03 AG046398.
HUNT	Nord-Trøndelag Health Study	The Nord-Trøndelag Health Study (The HUNT Study) is a collaboration between the HUNT Research Centre (Faculty of Medicine, Norwegian University of Science and Technology NTNU), the Nord-Trøndelag County Council, the Central Norway Health Authority and the Norwegian Institute of Public Health. The HUNT-MI study is a collaboration between investigators from the HUNT study and the University of Michigan. Genotyping services for 3992 samples were provided by the Northwest Genomics Center at the University of Washington, Department of Genome Sciences, under US Federal Government contract number HHSN268201100037C from the National Heart, Lung, and Blood Institute. We thank the HUNT study participants for their contributions to scientific research.
Inter99	Inter99	Data collection in the Inter99 study was supported economically by The Danish Medical Research Council, The Danish Centre for Evaluation and Health Technology Assessment, Novo Nordisk, Copenhagen County, The Danish Heart Foundation, The Danish Pharmaceutical Association, Augustinus foundation, Ib Henriksen foundation and Becket foundation. LLNH was supported by the Health Insurance Foundation (grant No. 2010 B 131).
IRASFS	Insulin Resistance Atherosclerosis Family Study	This research was supported by funding from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK): DK097524, DK085175, and DK087914; the National Institute for Heart, Lung, and Blood Disorders (NHLBI): HL060944, HL061019, HL060919, HL060944, HL061019, and the National Human Genome Research Institute (NHGRI): HG007112. The provision of genotyping data was supported in part by funds from the Department of Internal Medicine at the University of Michigan.
JHS	Jackson Heart Study	We thank the Jackson Heart Study (JHS) participants and staff for their contributions to this work. The JHS is supported by contracts HHSN268201300046C, HHSN268201300047C, HHSN268201300048C, HHSN268201300049C, HHSN268201300050C from the National Heart, Lung, and Blood Institute and the National Institute on Minority Health and Health Disparities.
KORA	Cooperative Health Research in the Region of Augsburg	The KORA study was initiated and financed by the Helmholtz Zentrum München – German Research Center for Environmental Health, which is funded by the German Federal Ministry of Education and Research (BMBF) and by the State of Bavaria. Furthermore, KORA research was supported within the Munich Center of Health Sciences (MC-Health), Ludwig-Maximilians-Universität, as part of LMUinnovativ.
KORA S4	Cooperative Health Research in the Region of Augsburg	The KORA study was initiated and financed by the Helmholtz Zentrum München – German Research Center for Environmental Health, which is funded by the German Federal Ministry of Education and Research (BMBF) and by the State of Bavaria. Furthermore, KORA research was supported within the Munich Center of Health Sciences (MC-Health), Ludwig-Maximilians-Universität, as part of LMUinnovativ. I.M.H. received funding from the Bundesministerium für Bildung und Forschung (BMBF 01ER1206, 01ER1507) and from the National Institutes of Health (NIH R01DK075787).
Leipzig	Leipzig-adults	This work was supported by the Kompetenznetz Adipositas (Competence network for Obesity) funded by the Federal Ministry of Education and Research (German Obesity Biomaterial Bank; FKZ 01GI1128), and by grants from the Collaborative Research Center funded by the German Research Foundation (CRC 1052 "Obesity mechanisms"; C01, B01, B03).

LOLIPOP-Exome, LOLIPOP-OmniEE	London Life Sciences Prospective Population Study	The LOLIPOP study is supported by the National Institute for Health Research (NIHR) Comprehensive Biomedical Research Centre Imperial College Healthcare NHS Trust, the British Heart Foundation (SP/04/002), the Medical Research Council (G0601966, G0700931), the Wellcome Trust (084723/Z/08/Z, 090532 & 098381) the NIHR (RP-PG-0407-10371), the NIHR Official Development Assistance (ODA, award 16/136/68), the European Union FP7 (EpiMigrant, 279143) and H2020 programs (iHealth-T2D, 643774). We acknowledge support of the MRC-PHE Centre for Environment and Health, and the NIHR Health Protection Research Unit on Health Impact of Environmental Hazards. The work was carried out in part at the NIHR/Wellcome Trust Imperial Clinical Research Facility. The views expressed are those of the author(s) and not necessarily those of the Imperial College Healthcare NHS Trust, the NHS, the NIHR or the Department of Health. We thank the participants and research staff who made the study possible. JC is supported by the Singapore Ministry of Health's National Medical Research Council under its Singapore Translational Research Investigator (STaR) Award (NMRC/STaR/0028/2017).
MESA	Multi-Ethnic Study of Atherosclerosis (MESA) Cohort	This research was supported by the Multi-Ethnic Study of Atherosclerosis (MESA) contracts N01-HC-95159, N01-HC-95160, N01-HC-95161, N01-HC-95162, N01-HC-95163, N01-HC-95164, N01-HC-95165, N01-HC-95166, N01-HC-95167, N01-HC-95168, N01-HC-95169 and by grants UL1-TR-000040 and UL1-RR-025005 from NCRRT. Funding for MESA Family was provided by grants R01-HL-071205, R01-HL-071051, R01-HL-071250, R01-HL-071251, R01-HL-071252, R01-HL-071258, R01-HL-071259, and UL1-RR-025005. Funding for MESA SHARe genotyping was provided by NHLBI Contract N02-HL-6-4278. The provision of genotyping data was supported in part by the National Center for Advancing Translational Sciences, CTSI grant UL1TR001881, and the National Institute of Diabetes and Digestive and Kidney Disease Diabetes Research Center (DRC) grant DK063491 to the Southern California Diabetes Endocrinology Research Center.
METSIM	Metabolic Syndrome in Men Study	Academy of Finland (137,544 and 272,741), the Finnish Cardiovascular Research Foundation. Genotyping was conducted at the Genetic Resources Core Facility (GRCF) at the Johns Hopkins Institute of Genetic Medicine.
MHIBB	Montreal Heart Institute Biobank	We thank all participants and staff of the André and France Desmarais Montreal Heart Institute's (MHI) Biobank. The genotyping of the MHI Biobank was done at the MHI Pharmacogenomic Centre and funded by the MHI Foundation.
MORGAM	MONica Risk, Genetics, Archiving and Monograph	The MORGAM Project received funding during the work from European Union FP 7 projects CHANCES (HEALTH-F3-2010-242244) and BiomarCaRE (278913). This has supported central coordination and part of the activities of the The MORGAM Data Centre, at THL in Helsinki, Finland. MORGAM Participating Centres are funded by regional and national governments, research councils, charities, and other local sources
NEO	The Netherlands Epidemiology of Obesity Study	The authors of the NEO study thank all individuals who participated in the Netherlands Epidemiology in Obesity study, all participating general practitioners for inviting eligible participants and all research nurses for collection of the data. We thank the NEO study group, Pat van Beelen, Petra Noordijk and Ingeborg de Jonge for the coordination, lab and data management of the NEO study. The genotyping in the NEO study was supported by the Centre National de Génotypage (Paris, France), headed by Jean-Francois Deleuze. The NEO study is supported by the participating Departments, the Division and the Board of Directors of the Leiden University Medical Center, and by the Leiden University, Research Profile Area Vascular and Regenerative Medicine. Dennis Mook-Kanamori is supported by Dutch Science Organization (ZonMW-VENI Grant 916.14.023).
NHPAC and GBTDS	The Nutrition and Health of Ageing Population in China study and the Guizhou-Bijie Type 2 Diabetes Study study	The NHPAC study and the GBTDS study are supported by the National Basic Research Program of China (973 Program 2012CB524900), and the National Natural Science Foundation of China (30930081, 81170734, 81321062, and 81471013). We are grateful to all participants of the NHPAC and the GBTDS studies, and also thank our colleagues at the laboratory and local CDC staffs of Beijing and Shanghai, as well as local staffs of the Bijie People's Hospital for their assistance with data collection.
Nijmegen	Nijmegen	The Nijmegen Biomedical Study is a population-based survey conducted at the Department for Health Evidence and the Department of Laboratory Medicine of the Radboud university medical center. Principal investigators of the Nijmegen Biomedical Study are L.A.L.M. Kiemeny, A.L.M. Verbeek, D.W. Swinkels en B. Franke. The NBS exome chip data were generated in a research project that was financially supported by BBMRI-NL, a Research Infrastructure financed by the Dutch government (NWO 184.021.007). The Nijmegen Bladder Cancer Study, NBS exome chip data were generated in a research project that was financially supported by BBMRI-NL, a Research Infrastructure financed by the Dutch government (NWO 184.021.007).
OBB	Oxford Biobank	The Oxford Biobank is supported by the Oxford Biomedical Research Centre and part of the National NIHR Bioresource.
PCOS	ENDO and PCOS	Genotyping was funded by the Wellcome Trust under awards WT064890 and WT086596. Analysis of genetic data was funded by the Wellcome Trust under awards WT098017, WT086596 and WT090532.

PIVUS and ULSAM	Prospective Investigation of the Vasculature in Uppsala	These projects were supported by Knut and Alice Wallenberg Foundation (Wallenberg Academy Fellow), European Research Council (ERC Starting Grant), Swedish Diabetes Foundation (2013-024), Swedish Research Council (2012-1397, 2012-1727, and 2012-2215), Marianne and Marcus Wallenberg Foundation, County Council of Dalarna, Dalarna University, and Swedish Heart-Lung Foundation (20120197). The computations were performed on resources provided by SNIC through Uppsala Multidisciplinary Center for Advanced Computational Science (UPPMAX) under Project b2011036. Genotyping was funded by the Wellcome Trust under awards WT064890 and WT086596. Analysis of genetic data was funded by the Wellcome Trust under awards WT098017 and WT090532. We thank the SNP&SEQ Technology Platform in Uppsala (www.genotyping.se) for excellent genotyping.
PROMIS	Pakistani Risk of Myocardial Infarction Study	We are thankful to all the study participants in Pakistan. Recruitment in PROMIS was funded through grants available to investigators at the Center for Non-Communicable Diseases, Pakistan (Danish Saleheen and Philippe Frossard) and investigators at the University of Cambridge, UK (Danish Saleheen and John Danesh). Field-work, genotyping, and standard clinical chemistry assays in PROMIS were principally supported by grants awarded to the University of Cambridge from the British Heart Foundation, UK Medical Research Council, Wellcome Trust, EU Framework 6-funded Bloodomics Integrated Project, Pfizer, Novartis, and Merck.
RAINE	The Western Australian Pregnancy Cohort (Raine) Study	This study was supported by the National Health and Medical Research Council of Australia [grant numbers 403981, 1021105 and 572613] and the Canadian Institutes of Health Research [grant number MOP-82893]. The authors are grateful to the Raine Study participants and their families, and to the Raine Study Team for cohort co-ordination and data collection. The authors gratefully acknowledge the following institutes for providing funding for Core Management of the Raine Study: The University of Western Australia (UWA), Curtin University of Technology, the Raine Medical Research Foundation, the Telethon Kids Institute, the Women and Infants Research Foundation (King Edward Memorial Hospital) Edith Cowan University, Murdoch University, and The University of Notre Dame Australia. The authors gratefully acknowledge the assistance of the Western Australian DNA Bank (National Health and Medical Research Council of Australia National Enabling Facility). This work was supported by resources provided by the Pawsey Supercomputing Centre with funding from the Australian Government and Government of Western Australia.
RISC	Relationship between Insulin Sensitivity and Cardiovascular disease	The RISC study was supported by European Union grant QLGI-CT-2001-01252 and AstraZeneca. The initial genotyping of the RISC samples was funded by Merck & Co Inc.
RSI	Rotterdam Study I	The generation and management of the Illumina exome chip v1.0 array data for the Rotterdam Study (RS-I) was executed by the Human Genotyping Facility of the Genetic Laboratory of the Department of Internal Medicine, Erasmus MC, Rotterdam, The Netherlands. The Exome chip array data set was funded by the Genetic Laboratory of the Department of Internal Medicine, Erasmus MC, from the Netherlands Genomics Initiative (NGI)/Netherlands Organisation for Scientific Research (NWO)-sponsored Netherlands Consortium for Healthy Aging (NCHA; project nr. 050-060-810); the Netherlands Organization for Scientific Research (NWO; project number 184021007) and by the Rainbow Project (RP10; Netherlands Exome Chip Project) of the Biobanking and Biomolecular Research Infrastructure Netherlands (BBMRI-NL; www.bbmi.nl). We thank Ms. Mila Jhamai, Ms. Sarah Higgins, and Mr. Marijn Verkerk for their help in creating the exome chip database, and Carolina Medina-Gomez, MSc, Lennard Karsten, MSc, and Linda Broer PhD for QC and variant calling. Variants were called using the best practice protocol developed by Grove et al. as part of the CHARGE consortium exome chip central calling effort. The Rotterdam Study is funded by Erasmus Medical Center and Erasmus University, Rotterdam, Netherlands Organization for the Health Research and Development (ZonMw), the Research Institute for Diseases in the Elderly (RIDE), the Ministry of Education, Culture and Science, the Ministry for Health, Welfare and Sports, the European Commission (DG XII), and the Municipality of Rotterdam. The authors are grateful to the study participants, the staff from the Rotterdam Study and the participating general practitioners and pharmacists.
SDC	Steno Diabetes Center T2D Cases	
SHIP-TREND	Study of Health in Pomerania - TREND	SHIP is part of the Community Medicine Research net of the University of Greifswald, Germany, which is funded by the Federal Ministry of Education and Research (grants no. 01ZZ9603, 01ZZ0103, and 01ZZ0403), the Ministry of Cultural Affairs as well as the Social Ministry of the Federal State of Mecklenburg-West Pomerania, and the network 'Greifswald Approach to Individualized Medicine (GANI_MED)' funded by the Federal Ministry of Education and Research (grant 03IS2061A). ExomeChip data have been supported by the Federal Ministry of Education and Research (grant no. 03Z1CN22) and the Federal State of Mecklenburg-West Pomerania. The University of Greifswald is a member of the Caché Campus program of the InterSystems GmbH.

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SORBS	SORBS	This work was supported by the Federal Ministry of Education and Research (BMBF), Germany, FKZ: 01EO1501 (AD2-060E). This project was further supported by grants from the Collaborative Research Center funded by the German Research Foundation (CRC 1052; C01, B01, B03), from the German Diabetes Association, from the DHFD (Diabetes Hilfs- und Forschungsfonds Deutschland) and from Boehringer Ingelheim Foundation . We thank all those who participated in the study. Sincere thanks are given to Knut Krohn (Microarray Core Facility of the Interdisciplinary Centre for Clinical Research, University of Leipzig) for the genotyping support.
STABILITY	The Stabilization of Atherosclerotic Plaque by Initiation of Darapladib Therapy Trial	
TUDR	TUDR	This study was supported by the National Eye Institute of the National Institutes of Health (EY014684 to J.I.R. and Y.-D.I.C.) and ARRA Supplement (EY014684-03S1, -04S1), the National Institute of Diabetes and Digestive and Kidney Disease grant DK063491 to the Southern California Diabetes Endocrinology Research Center, the Eye Birth Defects Foundation Inc., the National Science Council, Taiwan (NSC 102-2314-B-075A-002 to W.H.S.) and the Taichung Veterans General Hospital, Taichung, Taiwan (TCVGH-1047319D; TCVGH-1047311C to W.H.S.), the Ministry of Science and Technology, Taiwan (MOST 104-2314-B-075A-006 -MY3 to W.H.S.) and the Taichung Veterans General Hospital, Taichung, Taiwan (TCVGH-1030101C to W.H.S.).
TwinsUK	TwinsUK	TwinsUK study was funded by the Wellcome Trust; European Community's Seventh Framework Programme (FP7/2007-2013). The study also receives support from the National Institute for Health Research (NIHR) BioResource Clinical Research Facility and Biomedical Research Centre based at Guy's and St Thomas' NHS Foundation Trust and King's College London.
Veijle	Veijle Biobank T2D Case-control study	The Veijle Diabetes Biobank was supported by The Danish Research Council for Independent Research
WGHS	Women's Genome Health Study	The WGHS is supported by the National Heart, Lung, and Blood Institute (HL043851 and HL080467) and the National Cancer Institute (CA047988 and UM1CA182913), with collaborative scientific support and funding for genotyping provided by Amgen.
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SUPPLEMENTARY NOTE 1.

Collider bias

For all SNPs that reached array-wide significance in the stage 1+2 ADD meta-analysis ($P < 2 \times 10^{-7}$), we examined potential collider bias^{1,2} that could occur from adjustment of BMI and create artificial associations with WHRadjBMI (**Online Methods**). To obtain association estimates for BMI, we looked up the results for BMI in a concurrent GIANT ExomeChip Stage 1 investigation³ for the identified SNPs. If the beta estimate was in the opposite direction and reached a $P < 0.05$, these variants are highlighted in **Supplementary Table 7 (Online Methods)**. The observed associations for all 55 variants associated with WHRadjBMI were corrected in relevant stratum (e.g. All Ancestry, European-only, Women-only, Men-only) using the following equation¹,

$$\beta_{corrected} = \beta_{BMI} + \beta_{WHRadjBMI} \times \rho_{BMI \times WHR}$$

and,

$$SE_{corrected} = \sqrt{SE_{WHRadjBMI}^2 + SE_{BMI}^2 \times \rho_{BMI \times WHR}^2}$$

, where $\rho_{BMI \times WHR} = 0.49$, as observed in our previous work⁴ and,

$$\frac{\beta_{corrected}}{SE_{corrected}} \sim N(0,1) \rightarrow P_{corrected}$$

Of these 55, 51 variants remained significant at the Bonferroni-corrected significance threshold ($P < 9.09 \times 10^{-4}$, $0.05/55$). The remaining 4 variants, all from the primary meta-analyses in All Ancestries, sexes combined, should be interpreted with caution, including variants in *C3orf18*, *ZBTB7B*, *ITIH3*, and *UHRF1BP1*. While some SNPs no longer remained significant after the correction, in general they were nearly significant ($P < 0.05$, except for rs141845046) indicating that a true association may exist, although the effect may be slightly overestimated. Further, since it is biologically plausible for a variant to have pleiotropic effects both a positive effect on body mass while decreasing WHR (e.g. increase fat deposition in the hip and thighs), functional follow-up may be required to determine which associations are true and which are the result of collider bias.

SUPPLEMENTARY NOTE 2.

The EC-DEPICT method used here is identical to that described in the companion manuscript³.

EC-DEPICT

DEPICT is a method for gene set enrichment analysis and gene prioritization of GWAS data⁵. Briefly, 14,462 gene sets from KEGG⁶, REACTOME⁷, Gene Ontology⁸, InWeb⁹ (protein-protein networks) and Mouse Phenotype¹⁰ databases were obtained and “reconstituted” using large-scale microarray data, based on the logic of guilt-by-association (genes with similar patterns of expression are more likely to be members of the same gene sets). We have adapted the gene set enrichment functionality of DEPICT for the ExomeChip (EC-DEPICT), with a few alterations: (1) instead of including all genes within a specified amount of linkage disequilibrium to each index SNP, we include only the gene containing the index SNV, (2) we include only nonsynonymous and splicing (coding) SNVs, discarding noncoding associations, and

(3) we use null ExomeChip data for p-value calculation (rather than null GWAS data). In this supplement, we provide a brief overview of the method and more detailed explanations of each analysis.

Method

The EC-DEPICT method has been described elsewhere¹¹. We generated null ExomeChip data from the Malmö Diet and Cancer (MDC), All New Diabetics in Scania (ANDIS), and Scania Diabetes Registry (SDR) cohorts (a total of 11,899 samples with Swedish ancestry). After generating simulated normally-distributed phenotypes, we conducted 2,200 null ExomeChip association studies, filtering out all variants not present in the WHR association study. The variants in each null study were then sorted by ascending p-value and clumped (\pm 1 Mb on each side). Annotations from the CHARGE consortium were used to assign variants to genes (see URLs).

The method for gene set enrichment is as follows. A list of significant input variants from the ExomeChip is obtained (index nonsynonymous/splice-site SNVs for each locus) and filtered to remove (1) variants not present in the null backgrounds and (2) variants that are not marked as nonsynonymous/splice-site in the CHARGE consortium annotations. Then, we map the variants to genes. For each gene set, we then calculate a test statistic: the sum of gene set membership z-scores from the reconstituted gene sets¹ for the input genes. We then take 2000 nulls and compute the average (null) test statistic and standard deviation for the given gene set (where the number of top genes we take from each null as “input genes” is matched to the observed number of input genes). A z-score for the gene set is then computed as the observed test statistic minus the null test statistic divided by the null standard deviation, which is converted to a p-value based on the normal distribution. False discovery rates (FDRs) are calculated using an additional 50 null permutations to generate a distribution of null p-values. The FDR is calculated as the average number of null p-values less than a given threshold divided by the number of observed p-values less than that threshold.

We have noted that before performing the gene set enrichment analysis of WHR-associated variants, we removed variants absent in the null ExomeChip data (as we did in the height ExomeChip analysis, in which we used that same null data¹¹). This resulted in exclusion of about 50% of the WHR-associated variants at suggestive or array-wide significance. Most of the excluded variants were in the very rarest allele frequency bins, and mostly reached suggestive rather than array-wide significance. The exclusion of the rarest variants is expected due to the much smaller sample size of the null cohorts relative to the WHR data. To try to include more variants in the analysis, we also generated null ExomeChip data based on the UK Biobank, which resulted in the exclusion of fewer WHR-associated variants (due to the much larger sample size of the UK Biobank data). However, we observed that use of these null data, despite including more of the rarest WHR-associated variants in the gene set enrichment analysis, dampened the signal and resulted in fewer significantly enriched gene sets. This result suggests that 1) the rarest variants are more likely to have a lower true positive rate and/or 2) the heterogeneity of the underlying biology increases with the inclusion of very rare variants.

Although some variants were excluded from the EC-DEPICT analysis, we have included them in the heatmap figures (Figure 3, Supplementary Figure 13). This is because we assume that if the genes containing those variants have strong predicted membership in gene sets found to be significantly enriched, they are still good candidates for prioritization (and one of the main purposes of the heatmap strategy is to visually prioritize the best candidate genes). In fact, this is arguably even stronger evidence for prioritization of these genes, because they had no opportunity to influence the gene sets that are identified as enriched and, as such, independently support the biology implicated by these gene sets.

We have observed that extreme non-normality of gene set membership z-scores can, in certain situations, cause minor inflation of Type I error. To address this issue, we repeated the original EC-DEPICT analysis with an inverse-normal-transformed version of the reconstituted gene sets, in which every gene set is forced to have a normal z-score distribution for pathway membership. We then compared the rank of each significant gene set in the original results with the rank in the inverse normal transform and flagged “outliers” with respect to the change in rank ($>1.5 * \text{the interquartile range}$). In visualizing the results with heat maps, outlier gene sets were excluded. In supplementary tables, they are noted with an asterisk.

Affinity propagation clustering

To collapse the most highly correlated gene sets, affinity propagation clustering was performed as described in Marouli et al¹¹. Briefly, “meta-gene sets” were generated by affinity propagation clustering¹² of all pairs of 14,462 gene sets, using SciKit-Learn.clustering.AffinityPropagation version 0.17¹³, with a maximum iteration of 10,000 and a convergence iteration of 1,000. For each meta-gene set, P-values were assigned based on the most significant member gene set (considered the “best representative gene set”). In heat maps, z-scores for meta-gene set membership represent the z-score of the best representative gene set. Heat maps were generated with the ComplexHeatmap package in R¹⁴.

Analyses

We performed two analyses of WHR-associated variants. In the first analysis, we included all variants with $p < 5e-4$ (the best nonsynonymous variant per locus, where loci were clumped +/- 1 Mb). After filtering, this left 101 variants in 101 genes. There were 57 significant gene sets at $FDR < 0.05$ (27 meta-gene sets); after removal of inverse normal transform outliers, we were left with 49 significant gene sets in 25 meta-gene sets. In the second analysis, we used the same p-value threshold but removed all loci within 1 Mb of a known GWAS signal from Shungin et al. (2015)¹⁵. (“Known GWAS signals” included all GWAS hits at $p < 1e-5$, all of which were included in the original DEPICT analysis of those results.) After filtering, this gave an input of 75 variants in 75 genes. There were 29 significant gene sets in 14 significant meta-gene sets ($FDR < 0.05$); after removing inverse normal transform outliers, this left 26 significant gene sets in 13 meta-gene sets.

URLs

CHARGE Consortium ExomeChip annotation file: <http://www.chargeconsortium.com/main/exomechip/>
EC-DEPICT: <https://github.com/RebeccaFine/obesity-ec-depict>

EC-DEPICT meta-gene sets: https://github.com/RebeccaFine/obesity-ec-depict/blob/master/data/metacluster_labels.txt

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