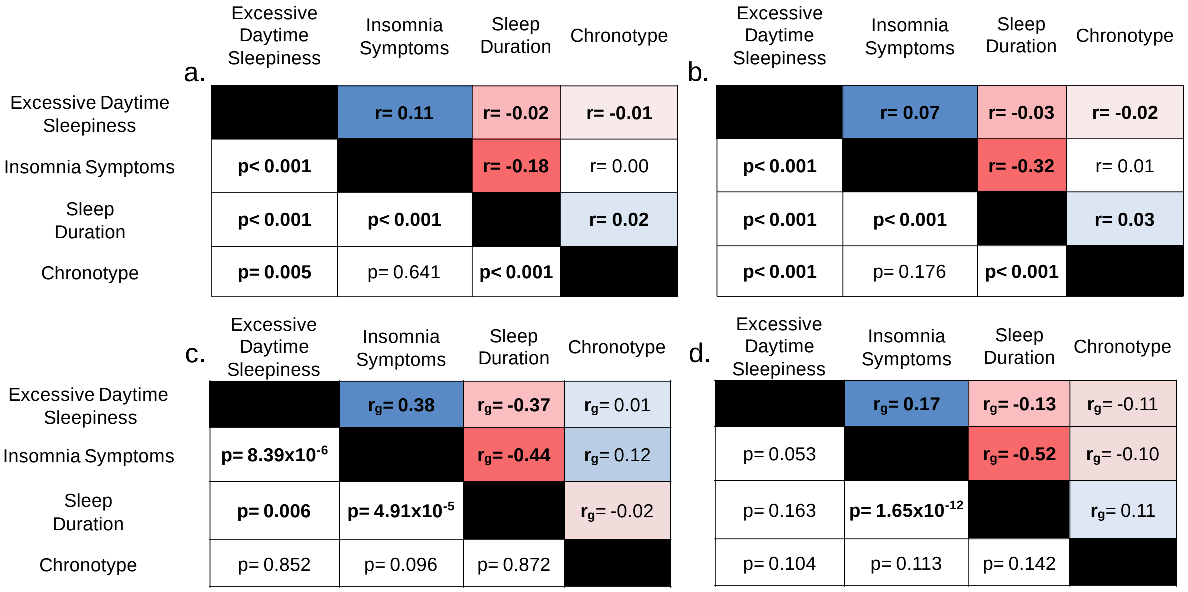


a.

	Excessive Daytime Sleepiness	Insomnia Symptoms	Sleep Duration	Chronotype
Excessive Daytime Sleepiness		**r= 0.11**	**r= -0.02**	**r= -0.01**
Insomnia Symptoms	**p< 0.001**		**r= -0.18**	r= 0.00
Sleep Duration	**p< 0.001**	**p< 0.001**		**r= 0.02**
Chronotype	**p= 0.005**	p= 0.641	**p< 0.001**	

b.

	Excessive Daytime Sleepiness	Insomnia Symptoms	Sleep Duration	Chronotype
Excessive Daytime Sleepiness		**r= 0.07**	**r= -0.03**	**r= -0.02**
Insomnia Symptoms	**p< 0.001**		**r= -0.32**	r= 0.01
Sleep Duration	**p< 0.001**	**p< 0.001**		**r= 0.03**
Chronotype	**p< 0.001**	p= 0.176	**p< 0.001**	

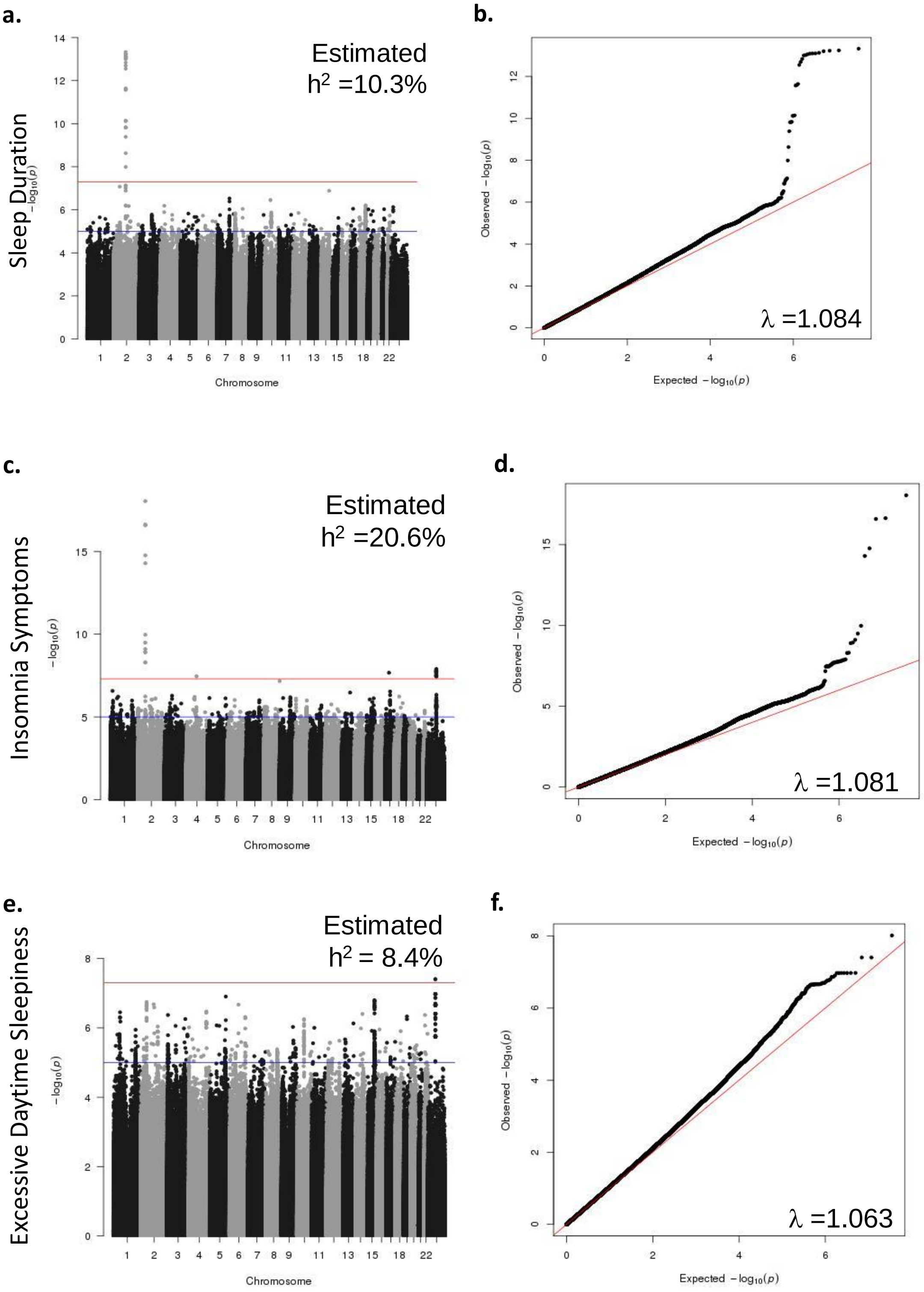
c.

	Excessive Daytime Sleepiness	Insomnia Symptoms	Sleep Duration	Chronotype
Excessive Daytime Sleepiness		**r_g= 0.38**	**r_g= -0.37**	r_g= 0.01
Insomnia Symptoms	**p= 8.39x10^{-6}**		**r_g= -0.44**	r_g= 0.12
Sleep Duration	**p= 0.006**	**p= 4.91x10^{-5}**		r_g= -0.02
Chronotype	p= 0.852	p= 0.096	p= 0.872	

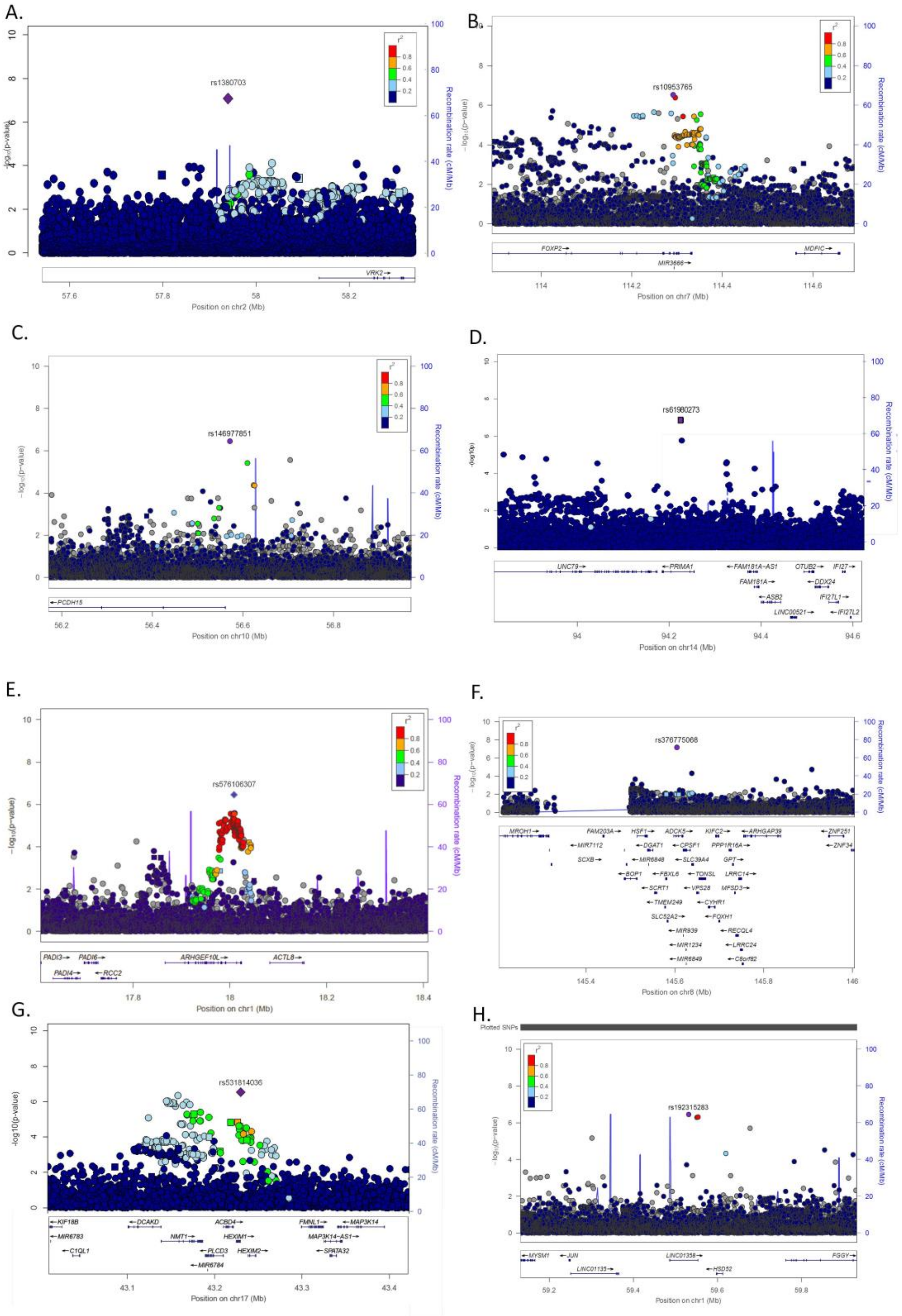
d.

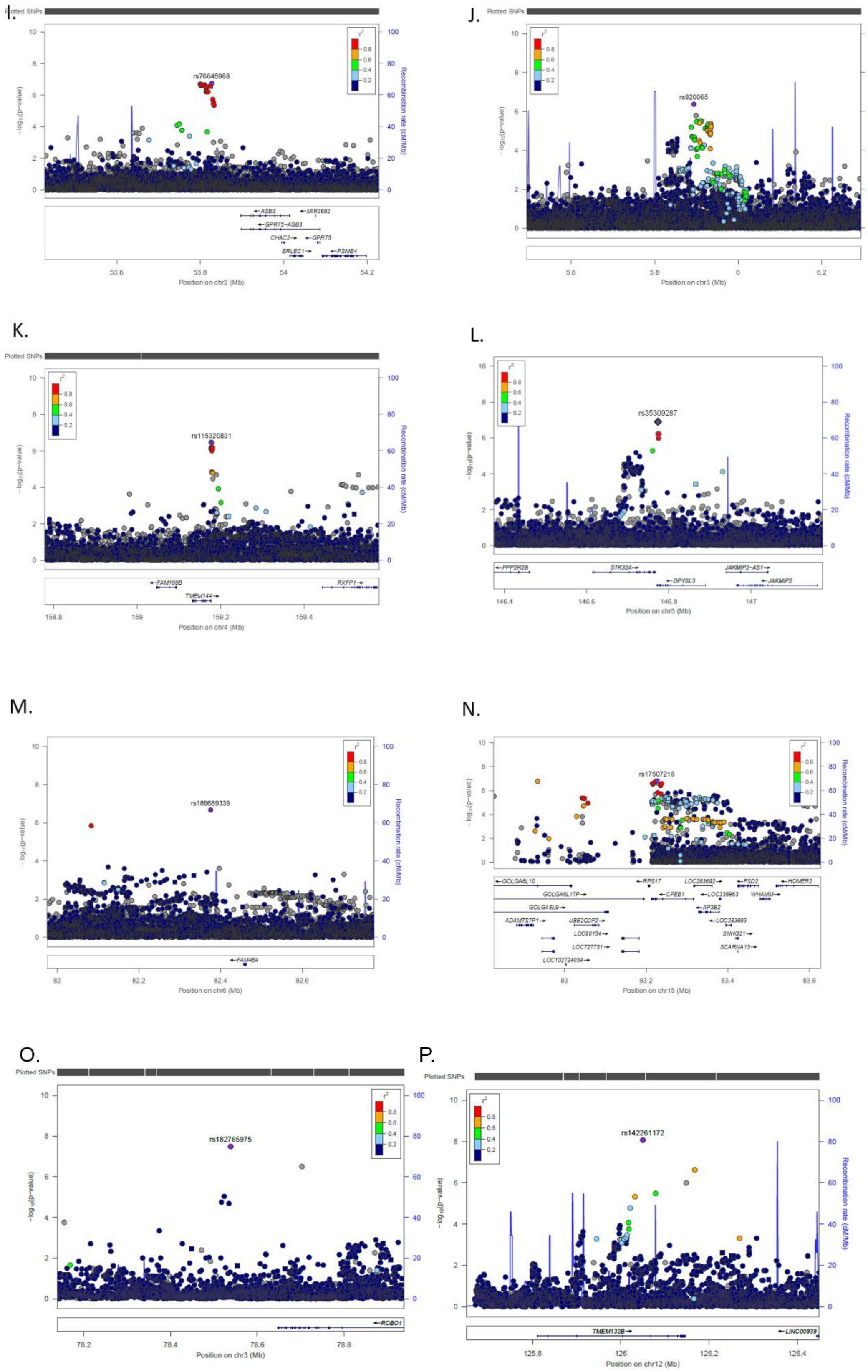
	Excessive Daytime Sleepiness	Insomnia Symptoms	Sleep Duration	Chronotype
Excessive Daytime Sleepiness		**r_g= 0.17**	**r_g= -0.13**	r_g= -0.11
Insomnia Symptoms	p= 0.053		**r_g= -0.52**	r_g= -0.10
Sleep Duration	p= 0.163	**p= 1.65x10^{-12}**		r_g= 0.11
Chronotype	p= 0.104	p= 0.113	p= 0.142	

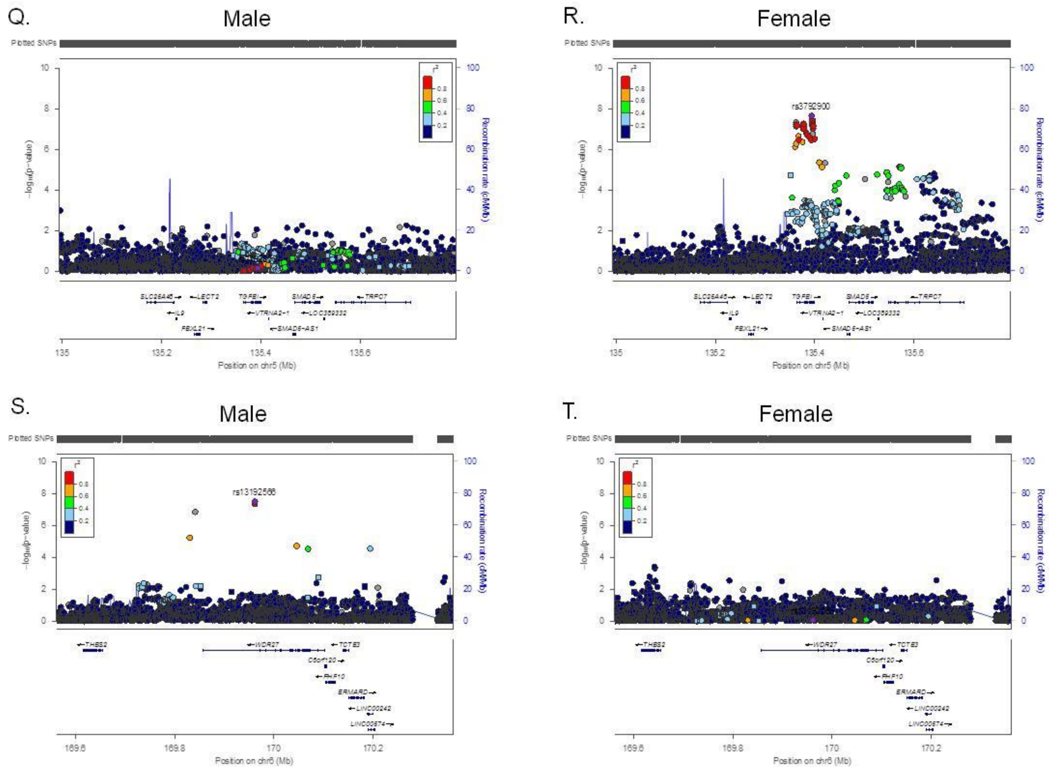
Supplementary Figure 1. Sleep traits are phenotypically and genetically correlated in men and women. Phenotypic correlation between the reported sleep traits, using Spearman correlation are shown stratified by sex (a. men, b. women). Color scale represents the strength of the correlation. Genetic correlation between the reported sleep traits shown stratified by sex, as measured by LDSC (c. men, d. women). Color scale represents the strength of the correlation. Blue indicates positive correlation, red indicates negative correlation.


a.
Sleep Duration
$-\log_{10}(p)$
Estimated h^2 =10.3%
Chromosome
b.
Observed $-\log_{10}(p)$
Expected $-\log_{10}(p)$
λ =1.084
c.
Insomnia Symptoms
$-\log_{10}(p)$
Estimated h^2 =20.6%
Chromosome
d.
Observed $-\log_{10}(p)$
Expected $-\log_{10}(p)$
λ =1.081
e.
Excessive Daytime Sleepiness
$-\log_{10}(p)$
Estimated h^2 = 8.4%
Chromosome
f.
Observed $-\log_{10}(p)$
Expected $-\log_{10}(p)$
λ =1.063

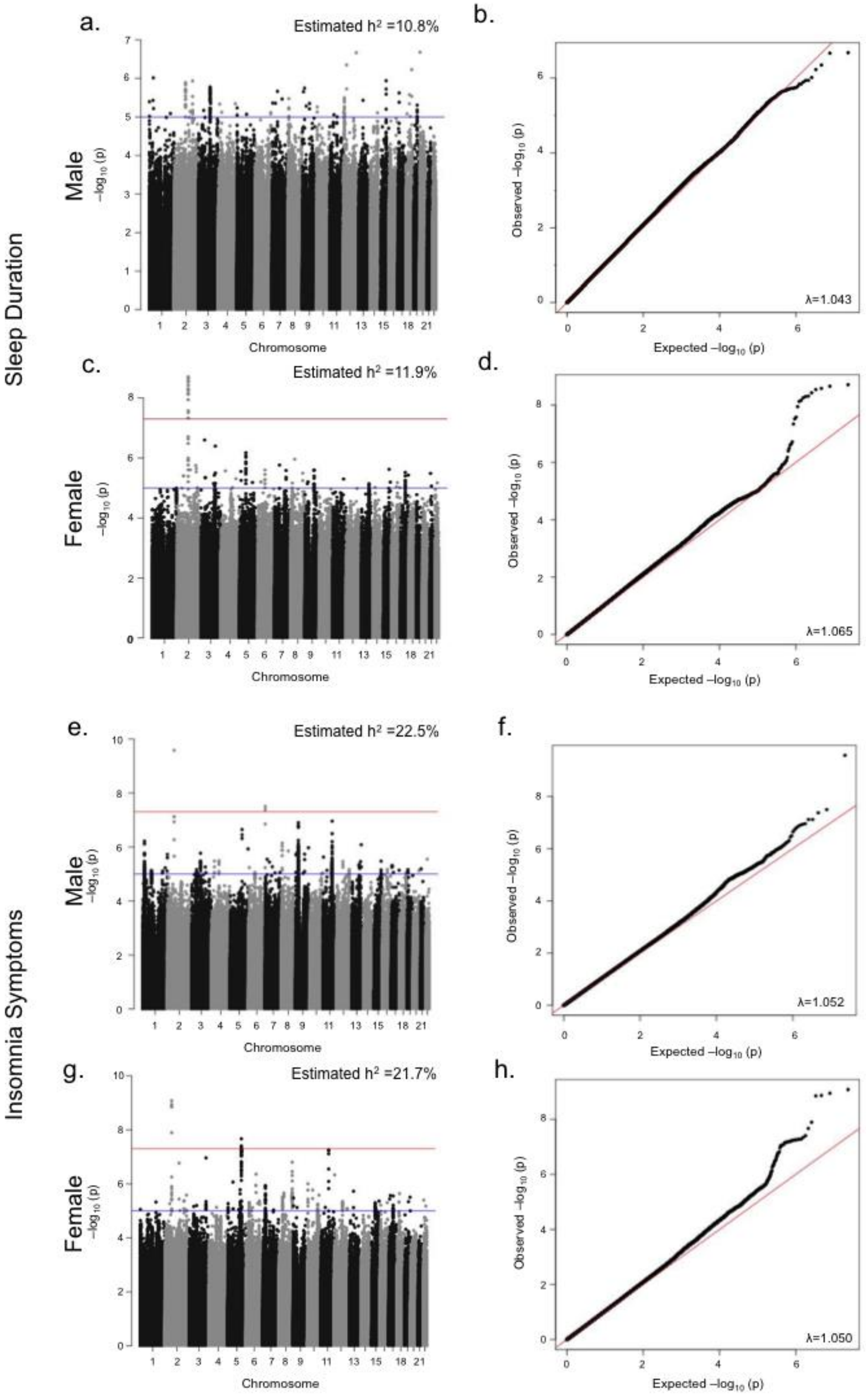
Supplementary Figure 2. Manhattan and Q-Q plots for genome-wide association analysis of sleep duration, insomnia symptoms, and excessive daytime sleepiness. GWAS results for sleep duration (a-b), insomnia symptoms (c-d), and excessive daytime sleepiness (e-f). Manhattan plots a, c, and e show the $-\log_{10}$ *p*-values (y-axis) for all genotyped and imputed SNPs passing quality control in each GWAS, plotted by chromosome (x-axis). Red line is genome-wide significant (5×10^{-8}) and blue line is 1×10^{-6}. Q-Q plots b, d, and f show the expected verses observed *p*-values from our association analysis. Heritability estimates were calculated using BOLT-REML and lambda inflation values using GenABEL in R.

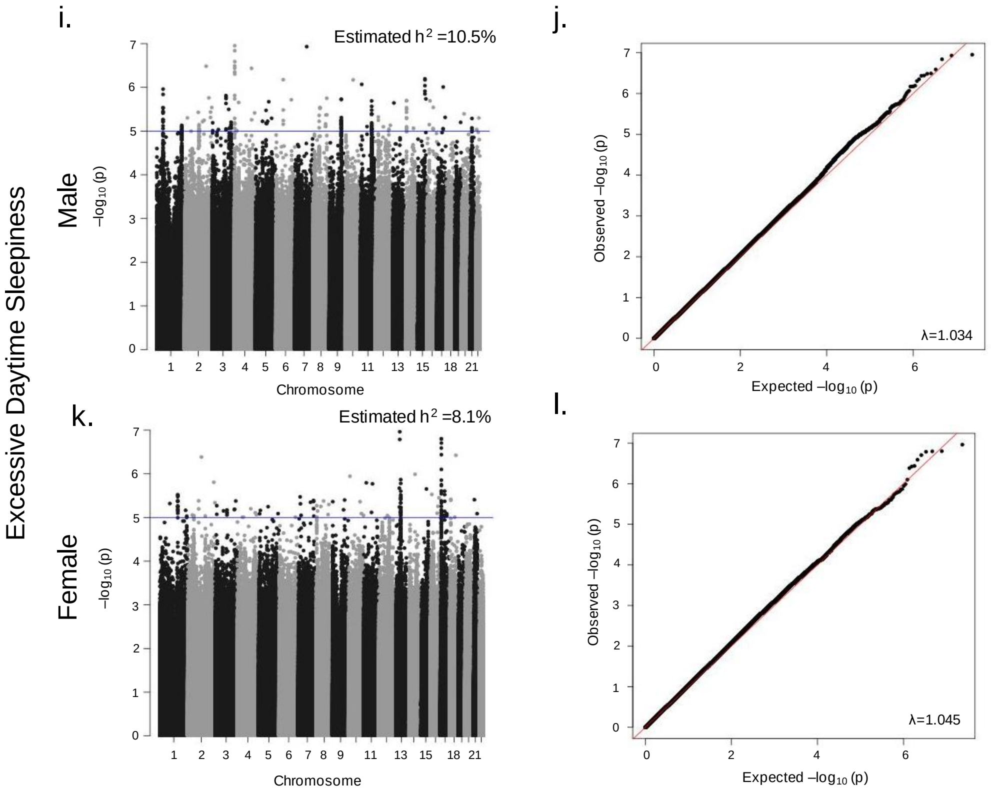

A.
rs1380703
-log10(p-value)
Recombination rate (cM/Mb)
VRK2
Position on chr2 (Mb)
B.
rs10953765
FOXP2
MIR3666
MDFIC
Position on chr7 (Mb)
C.
rs146977851
PCDH15
Position on chr10 (Mb)
D.
rs61980273
UNC79
PRIMA1
FAM181A-AS1
FAM181A
ASB2
LINC00521
OTUB2
DDX24
IFI27
IFI27L1
IFI27L2
Position on chr14 (Mb)
E.
rs576106307
PADI3
PADI6
PADI4
RCC2
ARHGEF10L
ACTL8
Position on chr1 (Mb)
F.
rs376775068
MROH1
FAM203A
MIR7112
SCXB
HSF1
DGAT1
MIR6848
BOP1
SCRT1
TMEM249
SLC52A2
ADCK5
CPSF1
SLC39A4
FBXL6
TONSL
VPS28
CYHR1
MIR939
MIR1234
MIR6849
FOXH1
KIFC2
PPP1R16A
GPT
LRRC14
MFSD3
RECQL4
LRRC24
C8orf82
ARHGAP39
ZNF251
ZNF34
Position on chr8 (Mb)
G.
rs531814036
KIF18B
MIR6783
C1QL1
DCAKD
NMT1
PLCD3
MIR6784
ACBD4
HEXIM1
HEXIM2
FMNL1
MAP3K14
MAP3K14-AS1
SPATA32
Position on chr17 (Mb)
H.
Plotted SNPs
rs192315283
MYSM1
JUN
LINC01135
LINC01358
HSD52
FGGY
Position on chr1 (Mb)


I.
Plotted SNPs
rs76645968
r²
0.8
0.6
0.4
0.2
−log₁₀(p-value)
Recombination rate (cM/Mb)
ASB3
MIR3682
GPR75-ASB3
CHAC2
GPR75
ERLEC1
PSME4
53.6
53.8
54
54.2
Position on chr2 (Mb)
J.
Plotted SNPs
rs920065
5.6
5.8
6
6.2
Position on chr3 (Mb)
K.
Plotted SNPs
rs115320831
FAM198B
TMEM144
RXFP1
158.8
159
159.2
159.4
Position on chr4 (Mb)
L.
rs35309287
PPP2R2B
STK32A
DPYSL3
JAKMIP2-AS1
JAKMIP2
146.4
146.6
146.8
147
Position on chr5 (Mb)
M.
rs189689339
FAM46A
82
82.2
82.4
82.6
Position on chr6 (Mb)
N.
rs17507216
GOLGA6L10
RPS17
LOC283692
FSD2
HOMER2
GOLGA6L17P
CPEB1
LOC338963
WHAMM
GOLGA6L9
AP3B2
ADAMTS7P1
UBE2Q2P2
LOC283693
LOC80154
SNHG21
LOC727751
SCARNA15
LOC102724034
83
83.2
83.4
83.6
Position on chr15 (Mb)
O.
Plotted SNPs
rs182765975
ROBO1
78.2
78.4
78.6
78.8
Position on chr3 (Mb)
P.
Plotted SNPs
rs142261172
TMEM132B
LINC00939
125.8
126
126.2
126.4
Position on chr12 (Mb)



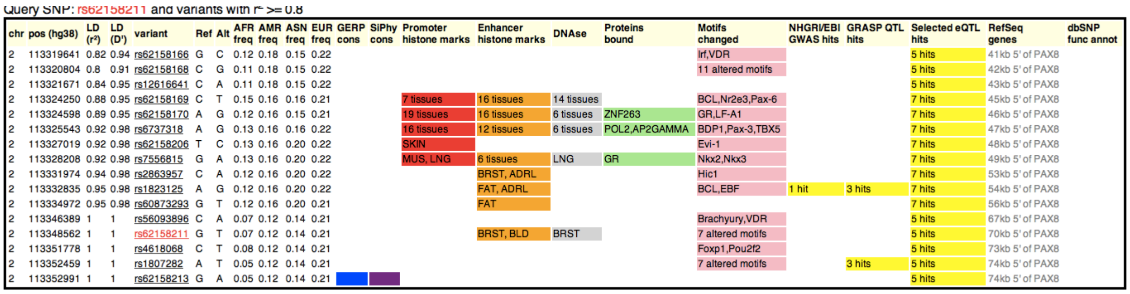
Supplementary Figure 3. Regional association plots for genome-wide significant and suggestive loci. Panel **a-d** sleep duration, **e-g** insomnia symptoms, **h-n** excessive daytime sleepiness, **o** excessive daytime sleepiness adjusted for depression, **p** excessive daytime sleepiness adjusted for BMI, **q-t** sex specific loci for insomnia symptoms. Chromosomal position is indicated on the x-axis and $-\log_{10}$ *p*-values for each SNP (filled circles and squares) is indicated on the y-axis, with the lead SNP shown in purple (400kb window around lead SNP shown). Genes within the region are shown in the lower panel. The blue line indicates the recombination rate. Additional SNPs in the locus are colored according to linkage disequilibrium (r^2) with the lead SNP (estimated by LocusZoom based on the CEU HapMap haplotypes). Squares represent genotyped SNPs and circles represent imputed SNPs.


Sleep Duration
Insomnia Symptoms
a.
Estimated h² =10.8%
Male
$-\log_{10}(p)$
Chromosome
1 2 3 4 5 6 7 8 9 11 13 15 18 21
b.
Observed $-\log_{10}(p)$
Expected $-\log_{10}(p)$
λ=1.043
c.
Estimated h² =11.9%
Female
d.
λ=1.065
e.
Estimated h² =22.5%
Male
f.
λ=1.052
g.
Estimated h² =21.7%
Female
h.
λ=1.050



Supplementary Figure 4. **Manhattan and QQ plot for sex stratified genome-wide association analysis of sleep duration (a-d), sleep disruption (e-h), and daytime sleepiness (i-l).** Manhattan plots a,c,e,g,i, and k show the –log$_{10}$ *p*-values (y-axis) for all genotyped and imputed SNPs passing quality control in each GWAS, plotted by chromosome (x-axis). Red line is genome-wide significant ($5\mathrm{x}10^{\wedge-8}$) and blue line is $1\times10^{\wedge-6}$. Plots b,d,f,h,j, and l show the expected verses observed P values from our association analysis. Heritability estimates were calculated using BOLT-REML and lambda inflation values using GenABEL in R.

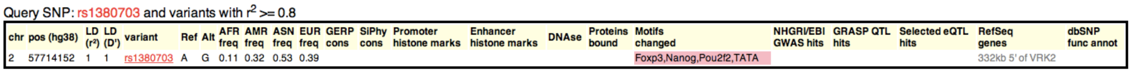
A. Sleep Duration: chr2: rs62158211 (*PAX-8* region)



Query SNP: rs62158211 and variants with r^2 >= 0.8

chr	pos (hg38)	LD (r^2)	LD (D')	variant	Ref	Alt	AFR freq	AMR freq	ASN freq	EUR freq	GERP cons	SiPhy cons	Promoter histone marks	Enhancer histone marks	DNAse	Proteins bound	Motifs changed	NHGRI/EBI GWAS hits	GRASP QTL hits	Selected eQTL hits	RefSeq genes	dbSNP func annot
2	113319641	0.82	0.94	rs62158166	G	C	0.12	0.18	0.15	0.22							Irf,VDR			5 hits	41kb 5' of PAX8	
2	113320804	0.8	0.91	rs62158168	C	G	0.11	0.18	0.15	0.22							11 altered motifs			5 hits	42kb 5' of PAX8	
2	113321671	0.84	0.95	rs12616641	C	A	0.11	0.18	0.15	0.22										5 hits	43kb 5' of PAX8	
2	113324250	0.88	0.95	rs62158169	C	T	0.15	0.16	0.16	0.21			7 tissues	16 tissues	14 tissues		BCL,Nr2e3,Pax-6			7 hits	45kb 5' of PAX8	
2	113324598	0.89	0.95	rs62158170	A	G	0.12	0.16	0.15	0.21			19 tissues	16 tissues	6 tissues	ZNF263	GR,LF-A1			7 hits	46kb 5' of PAX8	
2	113325543	0.92	0.98	rs6737318	A	G	0.13	0.16	0.16	0.22			16 tissues	12 tissues	6 tissues	POL2,AP2GAMMA	BDP1,Pax-3,TBX5			7 hits	47kb 5' of PAX8	
2	113327019	0.92	0.98	rs62158206	T	C	0.13	0.16	0.20	0.22			SKIN				Evi-1			7 hits	48kb 5' of PAX8	
2	113328208	0.92	0.98	rs7556815	G	A	0.13	0.16	0.20	0.22			MUS, LNG	6 tissues	LNG	GR	Nkx2,Nkx3			7 hits	49kb 5' of PAX8	
2	113331974	0.94	0.98	rs2863957	C	A	0.12	0.16	0.20	0.22				BRST, ADRL			Hic1			7 hits	53kb 5' of PAX8	
2	113332835	0.95	0.98	rs1823125	A	G	0.12	0.16	0.20	0.22				FAT, ADRL			BCL,EBF	1 hit	3 hits	7 hits	54kb 5' of PAX8	
2	113334972	0.95	0.98	rs60873293	G	T	0.12	0.16	0.20	0.21				FAT						7 hits	56kb 5' of PAX8	
2	113346389	1	1	rs56093896	C	A	0.07	0.12	0.14	0.21							Brachyury,VDR			5 hits	67kb 5' of PAX8	
2	113348562	1	1	rs62158211	G	T	0.07	0.12	0.14	0.21				BRST, BLD	BRST		7 altered motifs			5 hits	70kb 5' of PAX8	
2	113351778	1	1	rs4618068	C	T	0.08	0.12	0.14	0.21							Foxp1,Pou2f2			5 hits	73kb 5' of PAX8	
2	113352459	1	1	rs1807282	A	T	0.05	0.12	0.14	0.21							7 altered motifs		3 hits	5 hits	74kb 5' of PAX8	
2	113352991	1	1	rs62158213	G	A	0.05	0.12	0.14	0.21	🟦	🟪								5 hits	74kb 5' of PAX8	

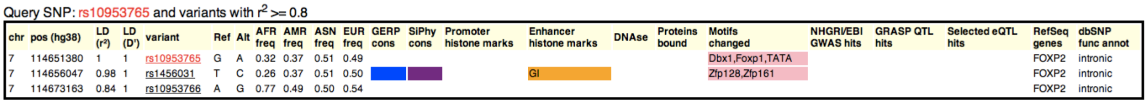
B. Sleep Duration: chr2: rs1380703 (*VRK2* region)



Query SNP: rs1380703 and variants with r^2 >= 0.8

chr	pos (hg38)	LD (r^2)	LD (D')	variant	Ref	Alt	AFR freq	AMR freq	ASN freq	EUR freq	GERP cons	SiPhy cons	Promoter histone marks	Enhancer histone marks	DNAse	Proteins bound	Motifs changed	NHGRI/EBI GWAS hits	GRASP QTL hits	Selected eQTL hits	RefSeq genes	dbSNP func annot
2	57714152	1	1	rs1380703	A	G	0.11	0.32	0.53	0.39							Foxp3,Nanog,Pou2f2,TATA				332kb 5' of VRK2	

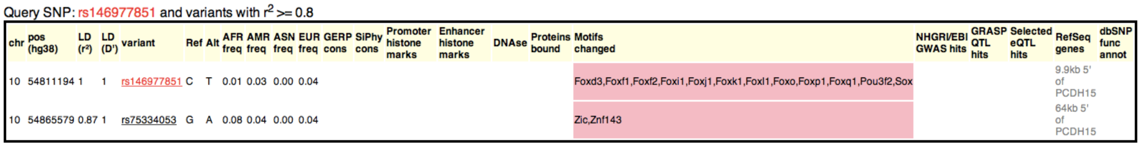
C. Sleep Duration: chr7: rs10953765 (*FOXP2* region)



Query SNP: rs10953765 and variants with r^2 >= 0.8

chr	pos (hg38)	LD (r^2)	LD (D')	variant	Ref	Alt	AFR freq	AMR freq	ASN freq	EUR freq	GERP cons	SiPhy cons	Promoter histone marks	Enhancer histone marks	DNAse	Proteins bound	Motifs changed	NHGRI/EBI GWAS hits	GRASP QTL hits	Selected eQTL hits	RefSeq genes	dbSNP func annot
7	114651380	1	1	rs10953765	G	A	0.32	0.37	0.51	0.49							Dbx1,Foxp1,TATA				FOXP2	intronic
7	114656047	0.98	1	rs1456031	T	C	0.26	0.37	0.51	0.50	🟦	🟪		GI			Zfp128,Zfp161				FOXP2	intronic
7	114673163	0.84	1	rs10953766	A	G	0.77	0.49	0.50	0.54											FOXP2	intronic

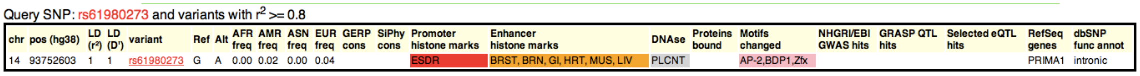
D. Sleep Duration: chr10: rs146977851 (*PCDH15* region)



Query SNP: rs146977851 and variants with r^2 >= 0.8

chr	pos (hg38)	LD (r^2)	LD (D')	variant	Ref	Alt	AFR freq	AMR freq	ASN freq	EUR freq	GERP cons	SiPhy cons	Promoter histone marks	Enhancer histone marks	DNAse	Proteins bound	Motifs changed	NHGRI/EBI GWAS hits	GRASP QTL hits	Selected eQTL hits	RefSeq genes	dbSNP func annot
10	54811194	1	1	rs146977851	C	T	0.01	0.03	0.00	0.04							Foxd3,Foxf1,Foxf2,Foxi1,Foxj1,Foxk1,Foxl1,Foxo,Foxp1,Foxq1,Pou3f2,Sox				9.9kb 5' of PCDH15	
10	54865579	0.87	1	rs75334053	G	A	0.08	0.04	0.00	0.04							Zic,Znf143				64kb 5' of PCDH15	

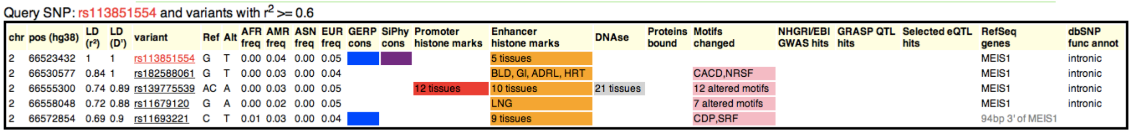
E. Sleep Duration: chr 14: rs61980273 (*PRIMA1* region)



Query SNP: rs61980273 and variants with r^2 >= 0.8

chr	pos (hg38)	LD (r^2)	LD (D')	variant	Ref	Alt	AFR freq	AMR freq	ASN freq	EUR freq	GERP cons	SiPhy cons	Promoter histone marks	Enhancer histone marks	DNAse	Proteins bound	Motifs changed	NHGRI/EBI GWAS hits	GRASP QTL hits	Selected eQTL hits	RefSeq genes	dbSNP func annot
14	93752603	1	1	rs61980273	G	A	0.00	0.02	0.00	0.04			ESDR	BRST, BRN, GI, HRT, MUS, LIV	PLCNT		AP-2,BDP1,Zfx				PRIMA1	intronic

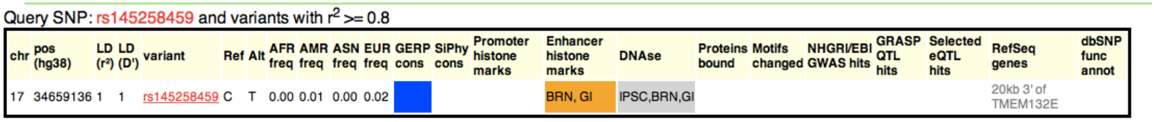
F. Insomnia Symptoms: chr 2: (*MEIS1* region; variants with r^2>0.6 shown)



Query SNP: rs113851554 and variants with r^2 >= 0.6

chr	pos (hg38)	LD (r^2)	LD (D')	variant	Ref	Alt	AFR freq	AMR freq	ASN freq	EUR freq	GERP cons	SiPhy cons	Promoter histone marks	Enhancer histone marks	DNAse	Proteins bound	Motifs changed	NHGRI/EBI GWAS hits	GRASP QTL hits	Selected eQTL hits	RefSeq genes	dbSNP func annot
2	66523432	1	1	rs113851554	G	T	0.00	0.04	0.00	0.05	🟦	🟪		5 tissues							MEIS1	intronic
2	66530577	0.84	1	rs182588061	G	T	0.00	0.03	0.00	0.04				BLD, GI, ADRL, HRT			CACD,NRSF				MEIS1	intronic
2	66555300	0.74	0.89	rs139775539	AC	A	0.00	0.03	0.00	0.05			12 tissues	10 tissues	21 tissues		12 altered motifs				MEIS1	intronic
2	66558048	0.72	0.88	rs11679120	G	A	0.00	0.02	0.00	0.05				LNG			7 altered motifs				MEIS1	intronic
2	66572854	0.69	0.9	rs11693221	C	T	0.01	0.03	0.00	0.04	🟦			9 tissues			CDP,SRF				94bp 3' of MEIS1	

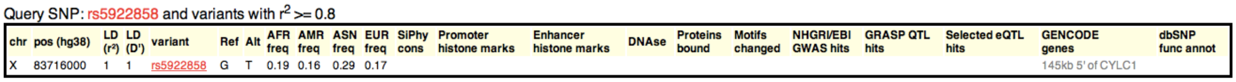
G. Insomnia Symptoms: chr 17: rs145258459 (*TMEM132E* region)



Query SNP: rs145258459 and variants with r^2 >= 0.8

chr	pos (hg38)	LD (r^2)	LD (D')	variant	Ref	Alt	AFR freq	AMR freq	ASN freq	EUR freq	GERP cons	SiPhy cons	Promoter histone marks	Enhancer histone marks	DNAse	Proteins bound	Motifs changed	NHGRI/EBI GWAS hits	GRASP QTL hits	Selected eQTL hits	RefSeq genes	dbSNP func annot
17	34659136	1	1	rs145258459	C	T	0.00	0.01	0.00	0.02	🟦			BRN, GI	IPSC,BRN,GI						20kb 3' of TMEM132E	

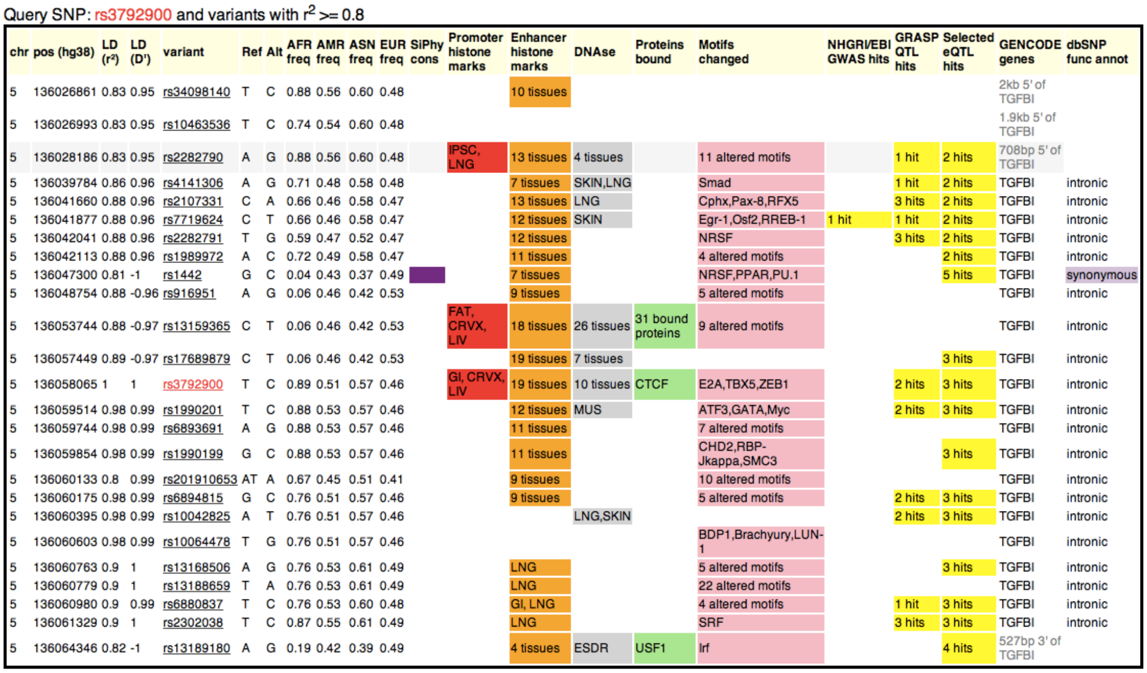
H. Insomnia Symptoms: chr X: *rs5922858* (*CYCL1* region)



Query SNP: rs5922858 and variants with r^2 >= 0.8

chr	pos (hg38)	LD (r^2)	LD (D')	variant	Ref	Alt	AFR freq	AMR freq	ASN freq	EUR freq	SiPhy cons	Promoter histone marks	Enhancer histone marks	DNAse	Proteins bound	Motifs changed	NHGRI/EBI GWAS hits	GRASP QTL hits	Selected eQTL hits	GENCODE genes	dbSNP func annot
X	83716000	1	1	rs5922858	G	T	0.19	0.16	0.29	0.17										145kb 5' of CYLC1	

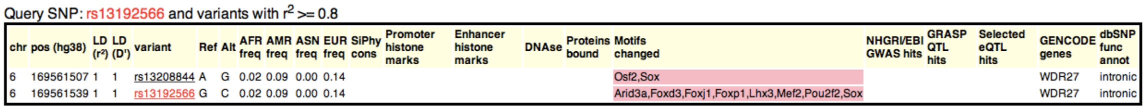
I. Insomnia Symptoms: chr 5: *rs3792900* (*TGFBI* region: females only)



Query SNP: rs3792900 and variants with r^2 >= 0.8

chr	pos (hg38)	LD (r^2)	LD (D')	variant	Ref	Alt	AFR freq	AMR freq	ASN freq	EUR freq	SiPhy cons	Promoter histone marks	Enhancer histone marks	DNAse	Proteins bound	Motifs changed	NHGRI/EBI GWAS hits	GRASP QTL hits	Selected eQTL hits	GENCODE genes	dbSNP func annot
5	136026861	0.83	0.95	rs34098140	T	C	0.88	0.56	0.60	0.48			10 tissues							2kb 5' of TGFBI	
5	136026993	0.83	0.95	rs10463536	T	C	0.74	0.54	0.60	0.48										1.9kb 5' of TGFBI	
5	136028186	0.83	0.95	rs2282790	A	G	0.88	0.56	0.60	0.48		IPSC, LNG	13 tissues	4 tissues		11 altered motifs		1 hit	2 hits	708bp 5' of TGFBI	
5	136039784	0.86	0.96	rs4141306	A	G	0.71	0.48	0.58	0.48			7 tissues	SKIN,LNG		Smad		1 hit	2 hits	TGFBI	intronic
5	136041660	0.88	0.96	rs2107331	C	A	0.66	0.46	0.58	0.47			13 tissues	LNG		Cphx,Pax-8,RFX5		3 hits	2 hits	TGFBI	intronic
5	136041877	0.88	0.96	rs7719624	C	T	0.66	0.46	0.58	0.47			12 tissues	SKIN		Egr-1,Osf2,RREB-1	1 hit	1 hit	2 hits	TGFBI	intronic
5	136042041	0.88	0.96	rs2282791	T	G	0.59	0.47	0.52	0.47			12 tissues			NRSF		3 hits	2 hits	TGFBI	intronic
5	136042113	0.88	0.96	rs1989972	A	C	0.72	0.49	0.58	0.47			11 tissues			4 altered motifs			2 hits	TGFBI	intronic
5	136047300	0.81	-1	rs1442	G	C	0.04	0.43	0.37	0.49	🟪		7 tissues			NRSF,PPAR,PU.1			5 hits	TGFBI	synonymous
5	136048754	0.88	-0.96	rs916951	A	G	0.06	0.46	0.42	0.53			9 tissues			5 altered motifs				TGFBI	intronic
5	136053744	0.88	-0.97	rs13159365	C	T	0.06	0.46	0.42	0.53		FAT, CRVX, LIV	18 tissues	26 tissues	31 bound proteins	9 altered motifs				TGFBI	intronic
5	136057449	0.89	-0.97	rs17689879	C	T	0.06	0.46	0.42	0.53			19 tissues	7 tissues					3 hits	TGFBI	intronic
5	136058065	1	1	rs3792900	T	C	0.89	0.51	0.57	0.46		GI, CRVX, LIV	19 tissues	10 tissues	CTCF	E2A,TBX5,ZEB1		2 hits	3 hits	TGFBI	intronic
5	136059514	0.98	0.99	rs1990201	T	C	0.88	0.53	0.57	0.46			12 tissues	MUS		ATF3,GATA,Myc		2 hits	3 hits	TGFBI	intronic
5	136059744	0.98	0.99	rs6893691	A	G	0.88	0.53	0.57	0.46			11 tissues			7 altered motifs				TGFBI	intronic
5	136059854	0.98	0.99	rs1990199	G	C	0.88	0.53	0.57	0.46			11 tissues			CHD2,RBP-Jkappa,SMC3			3 hits	TGFBI	intronic
5	136060133	0.8	0.99	rs201910653	AT	A	0.67	0.45	0.51	0.41			9 tissues			10 altered motifs				TGFBI	intronic
5	136060175	0.98	0.99	rs6894815	G	C	0.76	0.51	0.57	0.46			9 tissues			5 altered motifs		2 hits	3 hits	TGFBI	intronic
5	136060395	0.98	0.99	rs10042825	A	T	0.76	0.51	0.57	0.46				LNG,SKIN				2 hits	3 hits	TGFBI	intronic
5	136060603	0.98	0.99	rs10064478	T	G	0.76	0.51	0.57	0.46						BDP1,Brachyury,LUN-1				TGFBI	intronic
5	136060763	0.9	1	rs13168506	A	G	0.76	0.53	0.61	0.49			LNG			5 altered motifs			3 hits	TGFBI	intronic
5	136060779	0.9	1	rs13188659	T	A	0.76	0.53	0.61	0.49			LNG			22 altered motifs				TGFBI	intronic
5	136060980	0.9	0.99	rs6880837	T	C	0.76	0.53	0.60	0.48			GI, LNG			4 altered motifs		1 hit	3 hits	TGFBI	intronic
5	136061329	0.9	1	rs2302038	T	C	0.87	0.55	0.61	0.49			LNG			SRF		3 hits	3 hits	TGFBI	intronic
5	136064346	0.82	-1	rs13189180	A	G	0.19	0.42	0.39	0.49			4 tissues	ESDR	USF1	Irf			4 hits	527bp 3' of TGFBI	

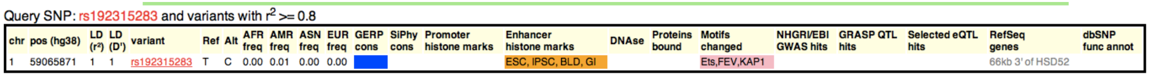
J. Insomnia Symptoms: chr 5: rs13192566 (*WDR27* region: males only)



Query SNP: rs13192566 and variants with r^2 >= 0.8

chr	pos (hg38)	LD (r^2)	LD (D')	variant	Ref	Alt	AFR freq	AMR freq	ASN freq	EUR freq	SiPhy cons	Promoter histone marks	Enhancer histone marks	DNAse	Proteins bound	Motifs changed	NHGRI/EBI GWAS hits	GRASP QTL hits	Selected eQTL hits	GENCODE genes	dbSNP func annot
6	169561507	1	1	rs13208844	A	G	0.02	0.09	0.00	0.14						Osf2,Sox				WDR27	intronic
6	169561539	1	1	rs13192566	G	C	0.02	0.09	0.00	0.14						Arid3a,Foxd3,Foxj1,Foxp1,Lhx3,Mef2,Pou2f2,Sox				WDR27	intronic

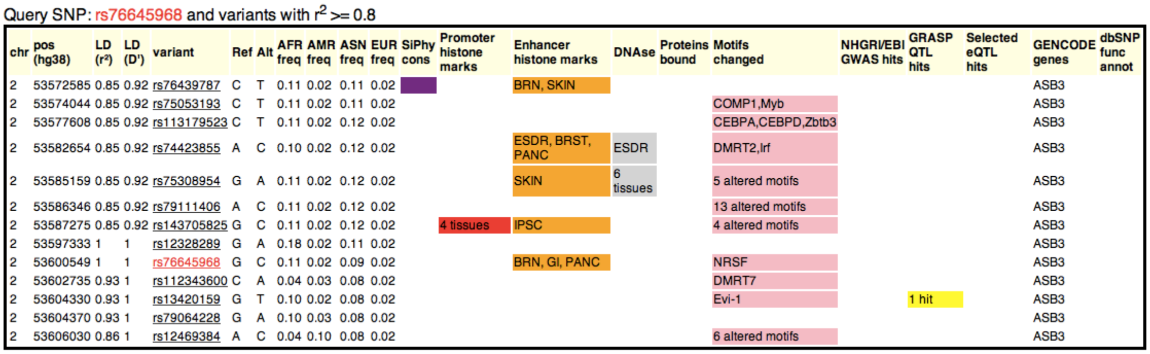
K. Daytime Sleepiness: chr 1: rs192315283 (*HSD52* region)



Query SNP: rs192315283 and variants with r^2 >= 0.8

chr	pos (hg38)	LD (r^2)	LD (D')	variant	Ref	Alt	AFR freq	AMR freq	ASN freq	EUR freq	GERP cons	SiPhy cons	Promoter histone marks	Enhancer histone marks	DNAse	Proteins bound	Motifs changed	NHGRI/EBI GWAS hits	GRASP QTL hits	Selected eQTL hits	RefSeq genes	dbSNP func annot
1	59065871	1	1	rs192315283	T	C	0.00	0.01	0.00	0.00	🟦			ESC, IPSC, BLD, GI			Ets,FEV,KAP1				66kb 3' of HSD52	

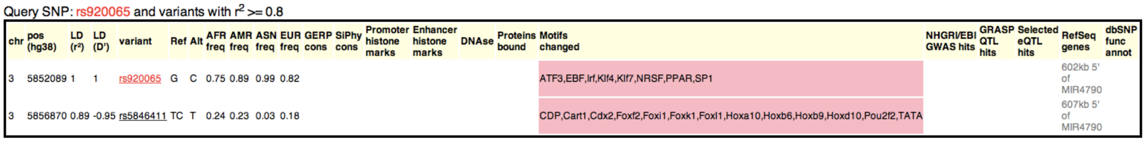
L. Daytime Sleepiness: chr 2: *rs76645968* (*ASB3* region)



Query SNP: rs76645968 and variants with r^2 >= 0.8

chr	pos (hg38)	LD (r^2)	LD (D')	variant	Ref	Alt	AFR freq	AMR freq	ASN freq	EUR freq	SiPhy cons	Promoter histone marks	Enhancer histone marks	DNAse	Proteins bound	Motifs changed	NHGRI/EBI GWAS hits	GRASP QTL hits	Selected eQTL hits	GENCODE genes	dbSNP func annot
2	53572585	0.85	0.92	rs76439787	C	T	0.11	0.02	0.11	0.02	🟪		BRN, SKIN							ASB3	
2	53574044	0.85	0.92	rs75053193	C	T	0.11	0.02	0.11	0.02						COMP1,Myb				ASB3	
2	53577608	0.85	0.92	rs113179523	C	T	0.11	0.02	0.12	0.02						CEBPA,CEBPD,Zbtb3				ASB3	
2	53582654	0.85	0.92	rs74423855	A	C	0.10	0.02	0.12	0.02			ESDR, BRST, PANC	ESDR		DMRT2,Irf				ASB3	
2	53585159	0.85	0.92	rs75308954	G	A	0.11	0.02	0.12	0.02			SKIN	6 tissues		5 altered motifs				ASB3	
2	53586346	0.85	0.92	rs79111406	A	C	0.11	0.02	0.12	0.02						13 altered motifs				ASB3	
2	53587275	0.85	0.92	rs143705825	G	C	0.11	0.02	0.12	0.02		4 tissues	IPSC			4 altered motifs				ASB3	
2	53597333	1	1	rs12328289	G	A	0.18	0.02	0.11	0.02										ASB3	
2	53600549	1	1	rs76645968	G	C	0.11	0.02	0.09	0.02			BRN, GI, PANC			NRSF				ASB3	
2	53602735	0.93	1	rs112343600	C	A	0.04	0.03	0.08	0.02						DMRT7				ASB3	
2	53604330	0.93	1	rs13420159	G	T	0.10	0.02	0.08	0.02						Evi-1		1 hit		ASB3	
2	53604370	0.93	1	rs79064228	G	A	0.10	0.03	0.08	0.02										ASB3	
2	53606030	0.86	1	rs12469384	A	C	0.04	0.10	0.08	0.02						6 altered motifs				ASB3	

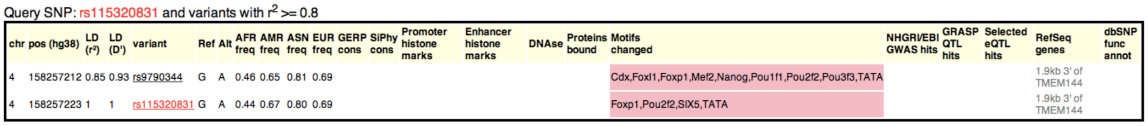
M. Daytime Sleepiness: chr 3: *rs920065* (*MRPS35P1/ MRPS36P1* region)



Query SNP: rs920065 and variants with r^2 >= 0.8

chr	pos (hg38)	LD (r^2)	LD (D')	variant	Ref	Alt	AFR freq	AMR freq	ASN freq	EUR freq	GERP cons	SiPhy cons	Promoter histone marks	Enhancer histone marks	DNAse	Proteins bound	Motifs changed	NHGRI/EBI GWAS hits	GRASP QTL hits	Selected eQTL hits	RefSeq genes	dbSNP func annot
3	5852089	1	1	rs920065	G	C	0.75	0.89	0.99	0.82							ATF3,EBF,Irf,Klf4,Klf7,NRSF,PPAR,SP1				602kb 5' of MIR4790	
3	5856870	0.89	-0.95	rs5846411	TC	T	0.24	0.23	0.03	0.18							CDP,Cart1,Cdx2,Foxf2,Foxi1,Foxk1,Foxl1,Hoxa10,Hoxb6,Hoxb9,Hoxd10,Pou2f2,TATA				607kb 5' of MIR4790	

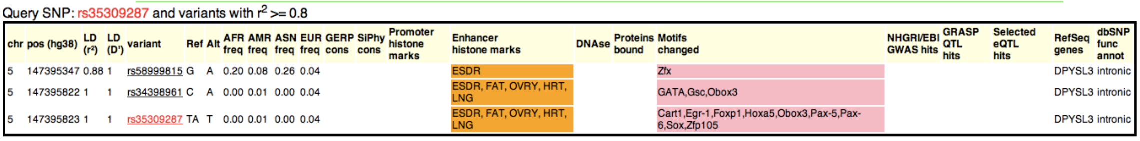
N. Daytime Sleepiness: chr 4: *rs115320831* (*TMEM144* region)



Query SNP: rs115320831 and variants with r^2 >= 0.8

chr	pos (hg38)	LD (r^2)	LD (D')	variant	Ref	Alt	AFR freq	AMR freq	ASN freq	EUR freq	GERP cons	SiPhy cons	Promoter histone marks	Enhancer histone marks	DNAse	Proteins bound	Motifs changed	NHGRI/EBI GWAS hits	GRASP QTL hits	Selected eQTL hits	RefSeq genes	dbSNP func annot
4	158257212	0.85	0.93	rs9790344	G	A	0.46	0.65	0.81	0.69							Cdx,Foxl1,Foxp1,Mef2,Nanog,Pou1f1,Pou2f2,Pou3f3,TATA				1.9kb 3' of TMEM144	
4	158257223	1	1	rs115320831	G	A	0.44	0.67	0.80	0.69							Foxp1,Pou2f2,SIX5,TATA				1.9kb 3' of TMEM144	

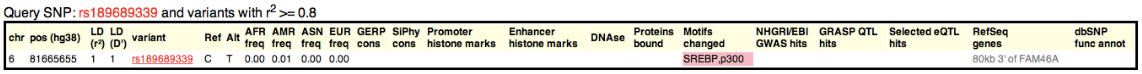
O. Daytime Sleepiness: chr 5: *rs35309287* (*DPYSL3* region)



Query SNP: rs35309287 and variants with r^2 >= 0.8

chr	pos (hg38)	LD (r^2)	LD (D')	variant	Ref	Alt	AFR freq	AMR freq	ASN freq	EUR freq	GERP cons	SiPhy cons	Promoter histone marks	Enhancer histone marks	DNAse	Proteins bound	Motifs changed	NHGRI/EBI GWAS hits	GRASP QTL hits	Selected eQTL hits	RefSeq genes	dbSNP func annot
5	147395347	0.88	1	rs58999815	G	A	0.20	0.08	0.26	0.04				ESDR			Zfx				DPYSL3	intronic
5	147395822	1	1	rs34398961	C	A	0.00	0.01	0.00	0.04				ESDR, FAT, OVRY, HRT, LNG			GATA,Gsc,Obox3				DPYSL3	intronic
5	147395823	1	1	rs35309287	TA	T	0.00	0.01	0.00	0.04				ESDR, FAT, OVRY, HRT, LNG			Cart1,Egr-1,Foxp1,Hoxa5,Obox3,Pax-5,Pax-6,Sox,Zfp105				DPYSL3	intronic

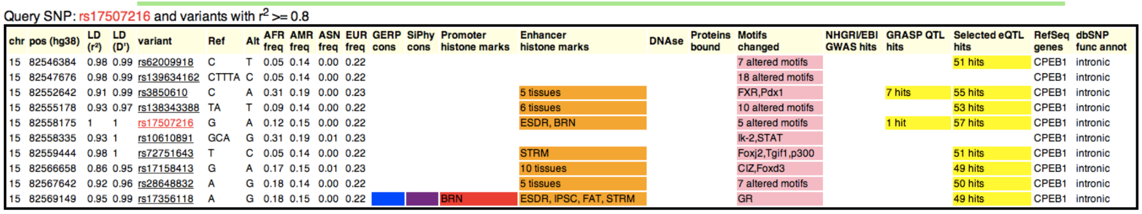
P. Daytime Sleepiness: chr 6: *rs189689339* (*FAM46A* region)



Query SNP: rs189689339 and variants with r^2 >= 0.8

chr	pos (hg38)	LD (r^2)	LD (D')	variant	Ref	Alt	AFR freq	AMR freq	ASN freq	EUR freq	GERP cons	SiPhy cons	Promoter histone marks	Enhancer histone marks	DNAse	Proteins bound	Motifs changed	NHGRI/EBI GWAS hits	GRASP QTL hits	Selected eQTL hits	RefSeq genes	dbSNP func annot
6	81665655	1	1	rs189689339	C	T	0.00	0.01	0.00	0.00							SREBP,p300				80kb 3' of FAM46A	

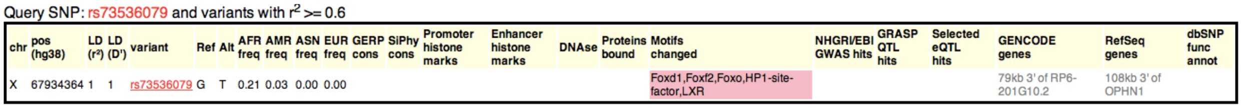
Q. Daytime Sleepiness: chr 15: *rs17507216* (*CPEB1* region)



Query SNP: rs17507216 and variants with r^2 >= 0.8

chr	pos (hg38)	LD (r^2)	LD (D')	variant	Ref	Alt	AFR freq	AMR freq	ASN freq	EUR freq	GERP cons	SiPhy cons	Promoter histone marks	Enhancer histone marks	DNAse	Proteins bound	Motifs changed	NHGRI/EBI GWAS hits	GRASP QTL hits	Selected eQTL hits	RefSeq genes	dbSNP func annot
15	82546384	0.98	0.99	rs62009918	C	T	0.05	0.14	0.00	0.22							7 altered motifs			51 hits	CPEB1	intronic
15	82547676	0.98	0.99	rs139634162	CTTTA	C	0.05	0.14	0.00	0.22							18 altered motifs				CPEB1	intronic
15	82552642	0.91	0.99	rs3850610	C	A	0.31	0.19	0.00	0.23				5 tissues			FXR,Pdx1		7 hits	55 hits	CPEB1	intronic
15	82555178	0.93	0.97	rs138343388	TA	T	0.09	0.14	0.00	0.22				6 tissues			10 altered motifs			53 hits	CPEB1	intronic
15	82558175	1	1	rs17507216	G	A	0.12	0.15	0.00	0.22				ESDR, BRN			5 altered motifs		1 hit	57 hits	CPEB1	intronic
15	82558335	0.93	1	rs10610891	GCA	G	0.31	0.19	0.01	0.23							Ik-2,STAT				CPEB1	intronic
15	82559444	0.98	1	rs72751643	T	C	0.05	0.14	0.00	0.22				STRM			Foxj2,Tgif1,p300			51 hits	CPEB1	intronic
15	82566658	0.86	0.95	rs17158413	G	A	0.17	0.15	0.01	0.23				10 tissues			CIZ,Foxd3			49 hits	CPEB1	intronic
15	82567642	0.92	0.96	rs28648832	A	G	0.18	0.14	0.00	0.22				5 tissues			7 altered motifs			50 hits	CPEB1	intronic
15	82569149	0.95	0.99	rs17356118	A	G	0.18	0.15	0.00	0.22	🟦	🟪	BRN	ESDR, IPSC, FAT, STRM			GR			49 hits	CPEB1	intronic

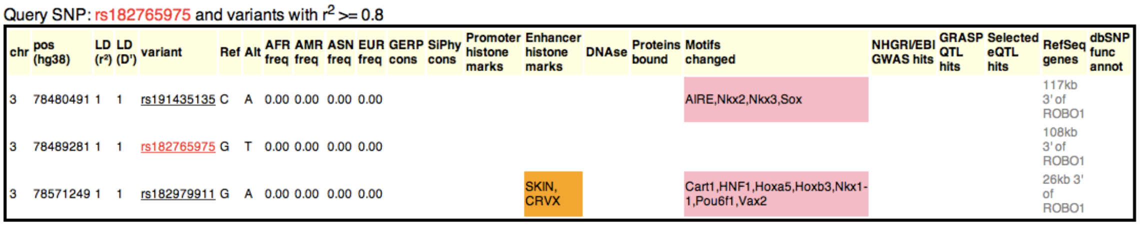
R. Daytime Sleepiness: chr X: *rs73536079* (*AR, OPHN1* region)



Query SNP: rs73536079 and variants with r^2 >= 0.6

chr	pos (hg38)	LD (r^2)	LD (D')	variant	Ref	Alt	AFR freq	AMR freq	ASN freq	EUR freq	GERP cons	SiPhy cons	Promoter histone marks	Enhancer histone marks	DNAse	Proteins bound	Motifs changed	NHGRI/EBI GWAS hits	GRASP QTL hits	Selected eQTL hits	GENCODE genes	RefSeq genes	dbSNP func annot
X	67934364	1	1	rs73536079	G	T	0.21	0.03	0.00	0.00							Foxd1,Foxf2,Foxo,HP1-site-factor,LXR				79kb 3' of RP6-201G10.2	108kb 3' of OPHN1	

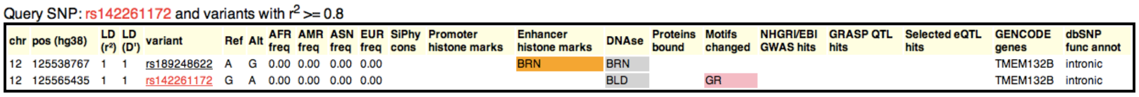
S. Daytime Sleepiness: chr 3: *rs182765975* (*ROBO1* region)



Query SNP: rs182765975 and variants with r^2 >= 0.8

chr	pos (hg38)	LD (r^2)	LD (D')	variant	Ref	Alt	AFR freq	AMR freq	ASN freq	EUR freq	GERP cons	SiPhy cons	Promoter histone marks	Enhancer histone marks	DNAse	Proteins bound	Motifs changed	NHGRI/EBI GWAS hits	GRASP QTL hits	Selected eQTL hits	RefSeq genes	dbSNP func annot
3	78480491	1	1	rs191435135	C	A	0.00	0.00	0.00	0.00							AIRE,Nkx2,Nkx3,Sox				117kb 3' of ROBO1	
3	78489281	1	1	rs182765975	G	T	0.00	0.00	0.00	0.00											108kb 3' of ROBO1	
3	78571249	1	1	rs182979911	G	A	0.00	0.00	0.00	0.00				SKIN, CRVX			Cart1,HNF1,Hoxa5,Hoxb3,Nkx1-1,Pou6f1,Vax2				26kb 3' of ROBO1	

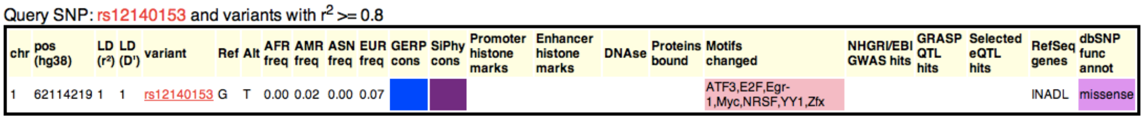
T. Daytime Sleepiness: chr 12: *rs142261172* (*TMEM132B* region)



Query SNP: rs142261172 and variants with r^2 >= 0.8

chr	pos (hg38)	LD (r^2)	LD (D')	variant	Ref	Alt	AFR freq	AMR freq	ASN freq	EUR freq	SiPhy cons	Promoter histone marks	Enhancer histone marks	DNAse	Proteins bound	Motifs changed	NHGRI/EBI GWAS hits	GRASP QTL hits	Selected eQTL hits	GENCODE genes	dbSNP func annot
12	125538767	1	1	rs189248622	A	G	0.00	0.00	0.00	0.00			BRN	BRN						TMEM132B	intronic
12	125565435	1	1	rs142261172	G	A	0.00	0.00	0.00	0.00				BLD		GR				TMEM132B	intronic

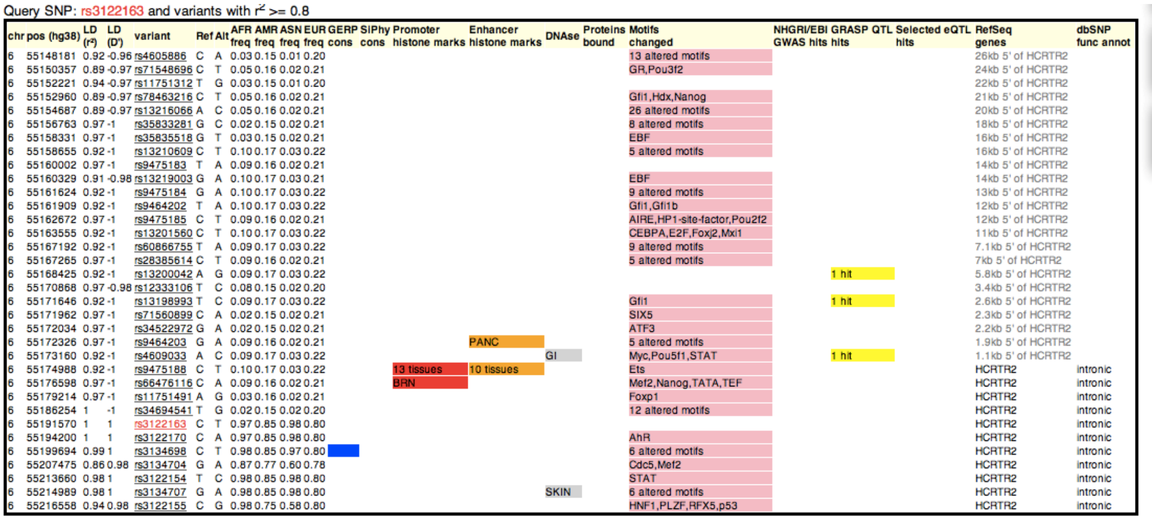
U. Multi-sleep Trait: chr 1: *rs12140153* (*INADL* region)



Query SNP: rs12140153 and variants with r^2 >= 0.8

chr	pos (hg38)	LD (r^2)	LD (D')	variant	Ref	Alt	AFR freq	AMR freq	ASN freq	EUR freq	GERP cons	SiPhy cons	Promoter histone marks	Enhancer histone marks	DNAse	Proteins bound	Motifs changed	NHGRI/EBI GWAS hits	GRASP QTL hits	Selected eQTL hits	RefSeq genes	dbSNP func annot
1	62114219	1	1	rs12140153	G	T	0.00	0.02	0.00	0.07	🟦	🟪					ATF3,E2F,Egr-1,Myc,NRSF,YY1,Zfx				INADL	missense

V. Multi-sleep Trait: chr 6: *rs3122163* (*HCRTR2* region)

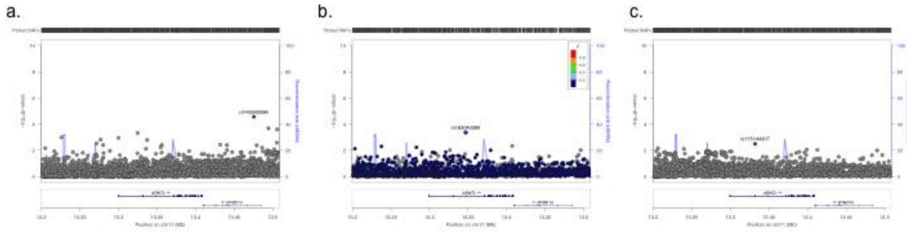


Query SNP: rs3122163 and variants with r^2 >= 0.8

chr	pos (hg38)	LD (r^2)	LD (D')	variant	Ref	Alt	AFR freq	AMR freq	ASN freq	EUR freq	GERP cons	SiPhy cons	Promoter histone marks	Enhancer histone marks	DNAse	Proteins bound	Motifs changed	NHGRI/EBI GWAS hits	GRASP QTL hits	Selected eQTL hits	RefSeq genes	dbSNP func annot
6	55148181	0.92	-0.96	rs4605886	C	A	0.03	0.15	0.01	0.20							13 altered motifs				26kb 5' of HCRTR2	
6	55150357	0.89	-0.97	rs71548696	C	T	0.05	0.16	0.02	0.21							GR,Pou3f2				24kb 5' of HCRTR2	
6	55152221	0.94	-0.97	rs11751312	T	G	0.03	0.15	0.01	0.20											22kb 5' of HCRTR2	
6	55152960	0.89	-0.97	rs78463216	C	T	0.05	0.16	0.02	0.21							Gfi1,Hdx,Nanog				21kb 5' of HCRTR2	
6	55154687	0.89	-0.97	rs13216066	A	C	0.05	0.16	0.02	0.21							26 altered motifs				20kb 5' of HCRTR2	
6	55156763	0.97	-1	rs35833281	G	C	0.02	0.15	0.02	0.21							8 altered motifs				18kb 5' of HCRTR2	
6	55158331	0.97	-1	rs35835518	G	T	0.03	0.15	0.02	0.21							EBF				16kb 5' of HCRTR2	
6	55158655	0.92	-1	rs13210609	C	T	0.10	0.17	0.03	0.22							5 altered motifs				16kb 5' of HCRTR2	
6	55160002	0.97	-1	rs9475183	T	A	0.09	0.16	0.02	0.21											14kb 5' of HCRTR2	
6	55160329	0.91	-0.98	rs13219003	G	A	0.10	0.17	0.03	0.21							EBF				14kb 5' of HCRTR2	
6	55161624	0.92	-1	rs9475184	G	A	0.10	0.17	0.03	0.22							9 altered motifs				13kb 5' of HCRTR2	
6	55161909	0.92	-1	rs9464202	T	A	0.10	0.17	0.03	0.22							Gfi1,Gfi1b				12kb 5' of HCRTR2	
6	55162672	0.97	-1	rs9475185	C	T	0.09	0.16	0.02	0.21							AIRE,HP1-site-factor,Pou2f2				12kb 5' of HCRTR2	
6	55163555	0.92	-1	rs13201560	C	T	0.10	0.17	0.03	0.22							CEBPA,E2F,Foxj2,Mxi1				11kb 5' of HCRTR2	
6	55167192	0.92	-1	rs60866755	T	A	0.09	0.17	0.03	0.22							9 altered motifs				7.1kb 5' of HCRTR2	
6	55167265	0.97	-1	rs28385614	C	T	0.09	0.16	0.02	0.21							5 altered motifs				7kb 5' of HCRTR2	
6	55168425	0.92	-1	rs13200042	A	G	0.09	0.17	0.03	0.22									1 hit		5.8kb 5' of HCRTR2	
6	55170868	0.97	-0.98	rs12333106	T	C	0.08	0.15	0.02	0.20											3.4kb 5' of HCRTR2	
6	55171646	0.92	-1	rs13198993	T	C	0.09	0.17	0.03	0.22							Gfi1		1 hit		2.6kb 5' of HCRTR2	
6	55171962	0.97	-1	rs71560899	C	A	0.02	0.15	0.02	0.21							SIX5				2.3kb 5' of HCRTR2	
6	55172034	0.97	-1	rs34522972	G	A	0.02	0.15	0.02	0.21							ATF3				2.2kb 5' of HCRTR2	
6	55172326	0.97	-1	rs9464203	G	A	0.09	0.16	0.02	0.21				PANC			5 altered motifs				1.9kb 5' of HCRTR2	
6	55173160	0.92	-1	rs4609033	A	C	0.09	0.17	0.03	0.22					GI		Myc,Pou5f1,STAT		1 hit		1.1kb 5' of HCRTR2	
6	55174988	0.92	-1	rs9475188	C	T	0.10	0.17	0.03	0.22			13 tissues	10 tissues			Ets				HCRTR2	intronic
6	55176598	0.97	-1	rs66476116	C	A	0.09	0.16	0.02	0.21			BRN				Mef2,Nanog,TATA,TEF				HCRTR2	intronic
6	55179214	0.97	-1	rs11751491	A	G	0.03	0.16	0.02	0.21							Foxp1				HCRTR2	intronic
6	55186254	1	-1	rs34694541	T	G	0.02	0.15	0.02	0.20							12 altered motifs				HCRTR2	intronic
6	55191570	1	1	rs3122163	C	T	0.97	0.85	0.98	0.80											HCRTR2	intronic
6	55194200	1	1	rs3122170	C	A	0.97	0.85	0.98	0.80							AhR				HCRTR2	intronic
6	55199694	0.99	1	rs3134698	C	T	0.98	0.85	0.97	0.80	🟦						6 altered motifs				HCRTR2	intronic
6	55207475	0.86	0.98	rs3134704	G	A	0.87	0.77	0.60	0.78							Cdc5,Mef2				HCRTR2	intronic
6	55213660	0.98	1	rs3122154	T	C	0.98	0.85	0.98	0.80							STAT				HCRTR2	intronic
6	55214989	0.98	1	rs3134707	G	A	0.98	0.85	0.98	0.80					SKIN		6 altered motifs				HCRTR2	intronic
6	55216558	0.94	0.98	rs3122155	C	G	0.98	0.75	0.58	0.80							HNF1,PLZF,RFX5,p53				HCRTR2	intronic

Supplementary Figure 5. Functional annotations of associated variants from Haploreg 4.1. Annotations of lead SNPs and correlated variants (r^2>0.8 to lead SNP except as indicated) are derived based on documentation available at http://www.broadinstitute.org/mammals/haploreg/haploreg.php and include human genome hg38 positions, LD (r^2 and D') to lead SNP shown in red in the 1KG EUR population, allele frequency in 1KG continental populations, conserved regions by GERP and Siphy annotation, tissue-specific chromatin state methylation marks (promoter, enhancer marks) based on the core-HMM 15 state model, tissue-specific DNAse1 hypersensitivity sites, bound proteins from Chip-seq experiments (ENCODE), predicted effect of regulatory SNP on transcription factor binding using position-weighted matrices, GWAS catalog hits (accessed October 31, 2015 by Haploreg 4.1), and GRASP build 2.0.0 QTLs complemented by 10 other eQTL studies including gTEX v6 and GEUVADIS analysis, as well as gene annotation by RefSeq and dbSNP annotation of variant function.

BMAL1

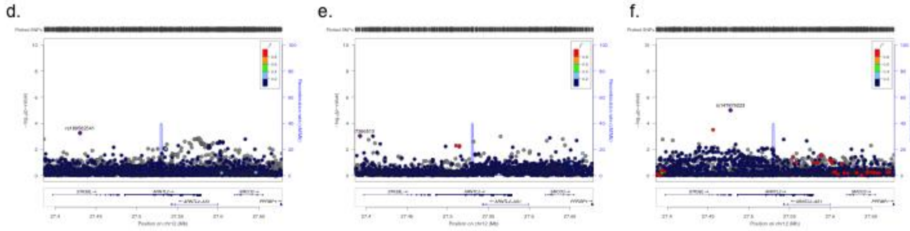


Sleep Duration

Insomnia Symptoms

Excessive Daytime Sleepiness

BMAL2

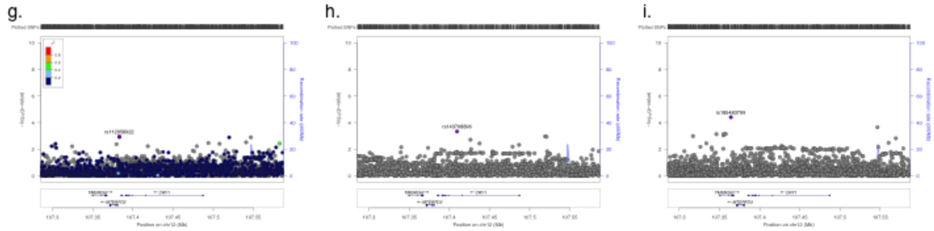


Sleep Duration

Insomnia Symptoms

Excessive Daytime Sleepiness

CRY1

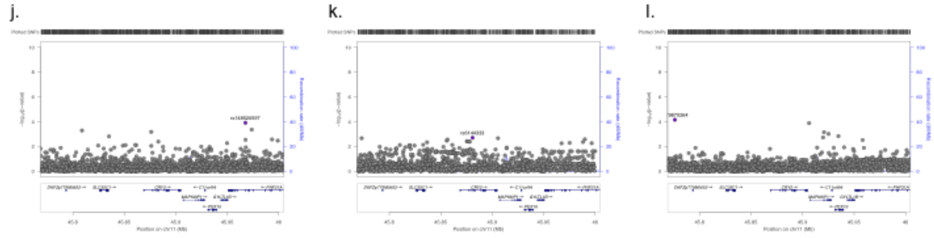


Sleep Duration

Insomnia Symptoms

Excessive Daytime Sleepiness

CRY2

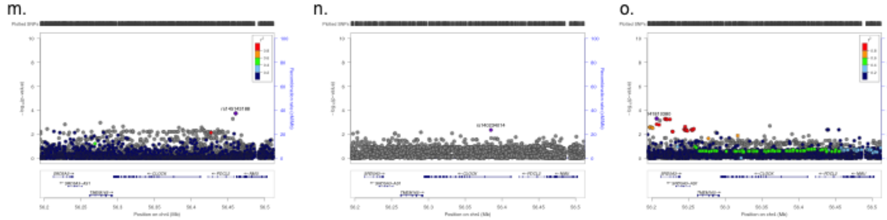


Sleep Duration

Insomnia Symptoms

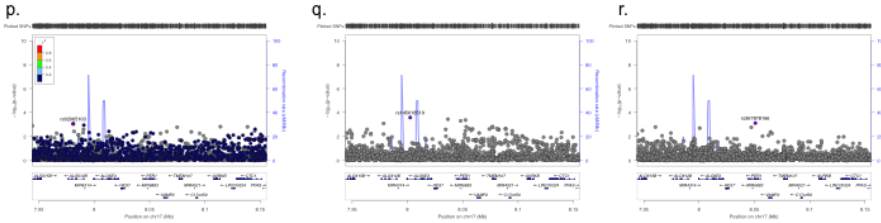
Excessive Daytime Sleepiness

CLOCK



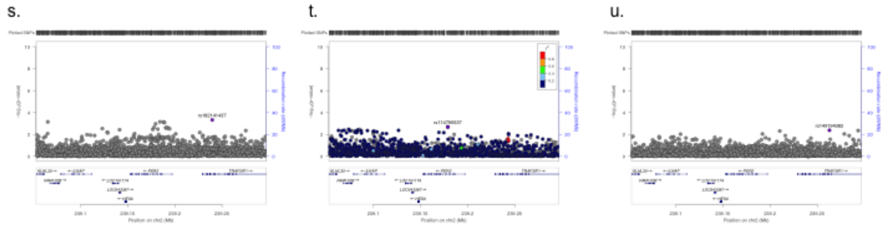
Sleep Duration Insomnia Symptoms Excessive Daytime Sleepiness

PER1



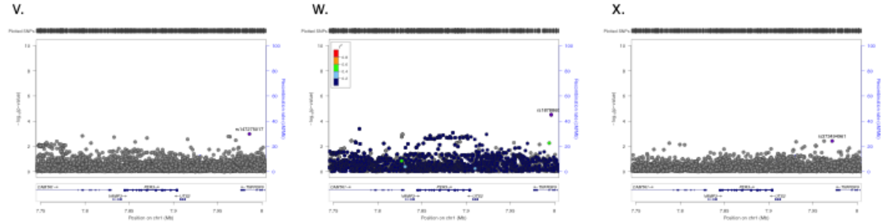
Sleep Duration Insomnia Symptoms Excessive Daytime Sleepiness

PER2



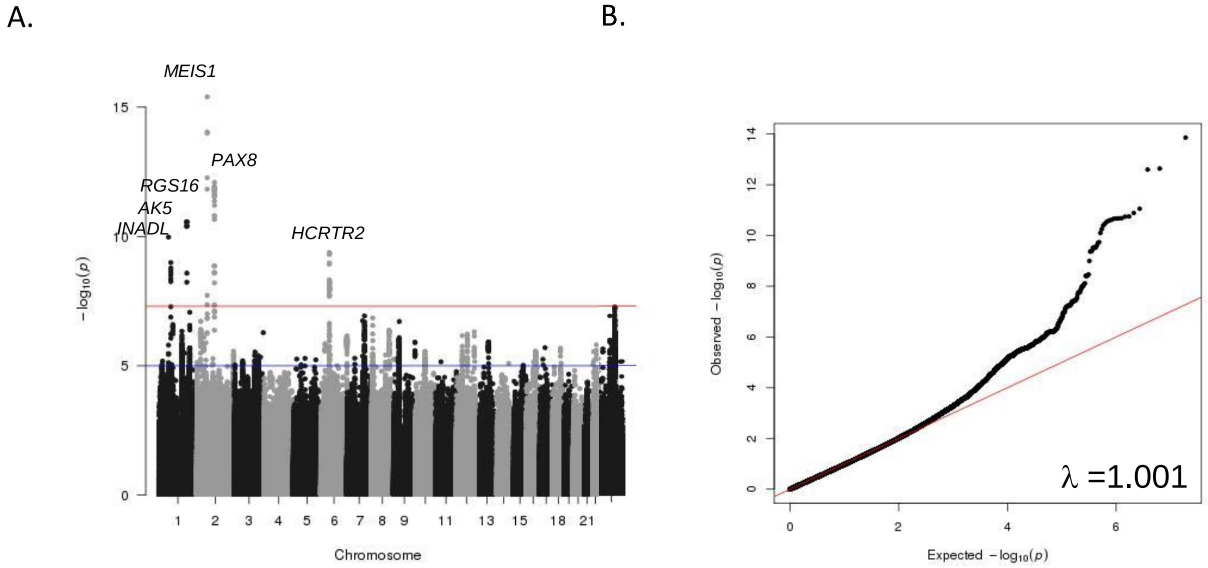
Sleep Duration Insomnia Symptoms Excessive Daytime Sleepiness

PER3

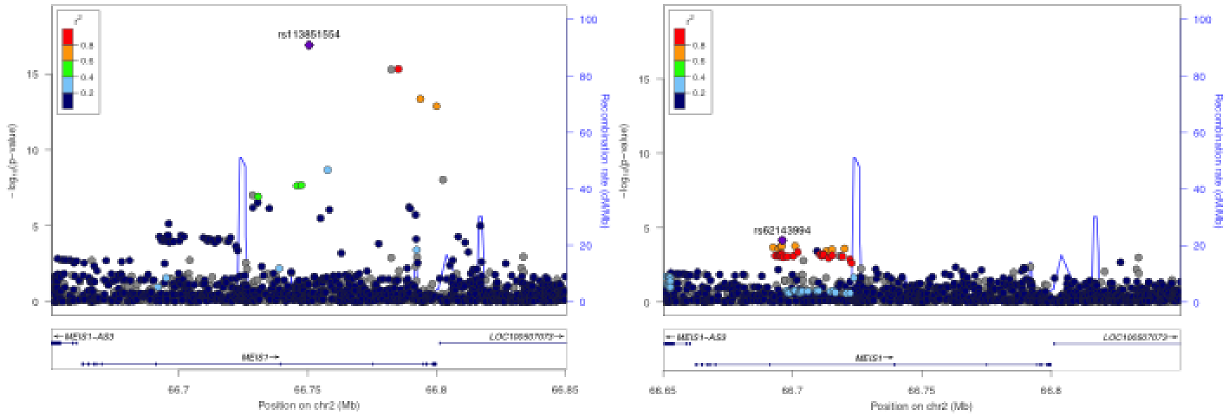


Sleep Duration Insomnia Symptoms Excessive Daytime Sleepiness

Supplementary Figure 6. Association of core circadian clock gene regions with sleep traits. Regional association plots for core circadian clock genes (*BMAL1* (a-c), *BMAL2* (d-f), *CRY1* (g-i), *CRY2* (j-l), *CLOCK* (m-o), *PER1* (p-r), *PER2* (s-u), *PER3* (v-x)) across sleep traits. Genes within the region are shown in the lower panel. The blue line indicates the recombination rate. Filled circles show the -$\log_{10}$ *p*-value for each SNP, with the lead SNP shown in purple. Additional SNPs in the locus are colored according to correlation (r^2) with the lead SNP (estimated by LocusZoom based on the CEU HapMap haplotypes).

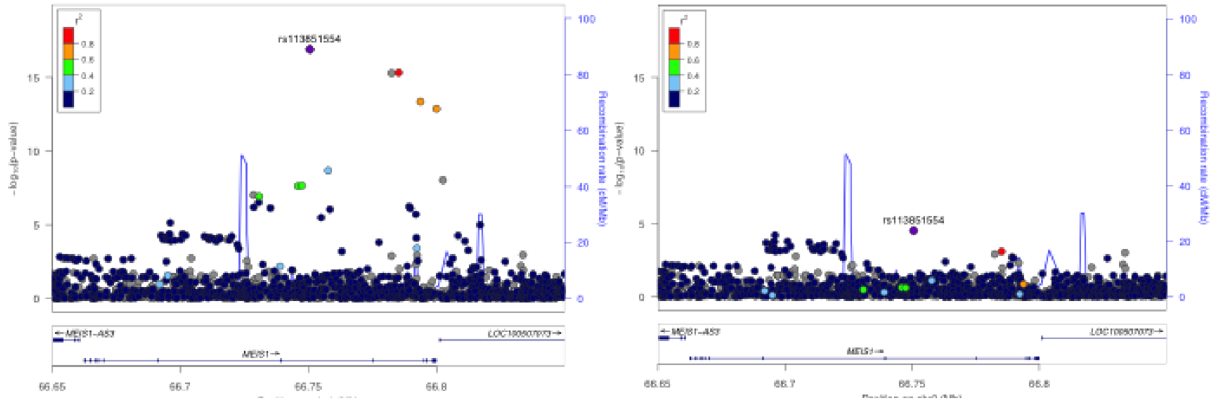


Supplementary Figure 7. Manhattan and Q-Q plot for genome-wide association multi-trait analysis of sleep duration, insomnia symptoms, excessive daytime sleepiness, and chronotype. Plot A shows the genome-wide association signals associated with the composite sleep phenotype. The Manhattan plot shows the $–\log_{10}$ *p*-values (y-axis) for all genotyped and imputed SNPs passing quality control in each GWAS, plotted by chromosome (x-axis). Red line is genome-wide significant ($5\text{x}10^{-8}$) and blue line is 1×10^{-6}. Q-Q plot (B) shows the expected verses observed P values from our association analysis. Signals are annotated with nearest gene symbol. Plot B shows the expected verses observed *p*-values from the multi-trait association analysis. Heritability estimates were calculated using BOLT-REML and lambda inflation values were calculated using GenABEL in R.



A. unadjusted

B. adjusted for lead SNP rs113851554



C. adjusted for RLS GWAS SNP rs2300478

D. adjusted for RLS SNP rs11693221

Supplementary Figure 8. *MEIS1* region association with insomnia symptoms. Regional association plot with lead association signal represented by SNP rs113851554 ($p_{unadj}=10^{-19}$; plot A). Conditioning on the lead SNP abolishes the lead regional association signal and shows no strong secondary association signals (best SNP rs62143994, $p=10^{-4}$; plot B). Analysis conditional on previously reported RLS GWAS SNP rs2300478 ($p_{unadj}=0.01$; plot C) does not alter insomnia symptoms association signals. Analysis conditional on rs11693221, a rare MEIS1 3' UTR SNP discovered by sequence analysis and also associated with RLS, abolishes the lead association signal ($p_{unadj}=10^{-14}$; plot D). Chromosomal position is indicated on the x-axis and $-\log_{10}$ *p*-values for each SNP (filled circles) is indicated on the y-axis, with the lead SNP shown in purple (200kb window around lead SNP shown). Genes within the region are shown in the lower panel. The blue line indicates the recombination rate. Additional SNPs in the locus are colored according to linkage disequilibrium (r^2) with the lead SNP (estimated by LocusZoom based on the CEU HapMap haplotypes).

Supplementary Table 1. Descriptive Characteristics of UKBiobank subjects of European ancestry used for GWAS (N=112,586).

Characteristic	**Mean (SD) N cases (%)**			**Pair-wise Phenotype Correlation**					
				Sleep Duration		**Insomnia Symptoms**		**Excessive Daytime Sleepiness**	
	Males	**Females**	**All**	**r**	***p*-val**	**r**	***p*-val**	**r**	***p*-val**
Sex (M)	52,817 (47%)	59,868 (53%)	112,586	-0.01	0.002	-0.14	<0.001	0.04	<0.001
Age, y	58.12 (7.96)	57.3 (7.83)	57.69 (7.90)	0.06	<0.001	0.09	<0.001	0.13	<0.001
Sleep duration, hrs	7.19 (1.07)	7.19 (1.09)	7.19 (1.08)	-	-	-0.25	<0.001	-0.03	<0.001
Insomnia Symptoms				-0.25	<0.001	-	-	0.08	<0.001
Never/Rarely	16,009 (55.8%)	10,964 (36.0%)	26,973 (46%)						
Usually	12,674 (44.2.0%)	19,481 (64.0%)	32,155 (54%)						
Excessive Daytime Sleepiness				-0.03	<0.001	0.08	<0.001	-	-
Never/Rarely	39,613 (75.0%)	46,762 (78.1%)	86,375 (76.7%)						
Sometimes	11,496 (21.8%)	11,365 (19.0%)	22,861 (20.3%)						
Often	1,524 (2.9%)	1,446 (2.4%)	2,970 (2.6%)						
All of the time	5 (0%)	3 (0%)	8 (0%)						
Depression (n=96,409)	1,913 (3.6%)	2,829 (4.7%)	4,242 (4.4%)	-0.07	<0.001	0.18	<0.001	0.11	<0.001
Psychiatric Medication (n=112,867)	503 (1%)	1,190 (2.0%)	1,693 (1.5%)	0.02	<0.001	0.03	<0.001	0.01	<0.001
Self-reported Sleep Apnea (n=99,500)	301 (0.6%)	97 (0.2%)	398 (0.4%)	-0.01	0.058	0.01	0.013	0.03	<0.001
BMI, kg/m2 (n=75,640)	29.66 (1.26)	27.66 (1.22)	29.23 (6.82)	-0.01	0.016	0.02	<0.001	0.07	<0.001
Townsend Deprivation Index (SES) (n=112,376)	-1.51 (3.02)	-1.55 (2.92)	-1.53 (2.97)	-0.04	<0.001	0.05	<0.001	0.05	<0.001
Smoking Status (n=112,225)				-0.02	<0.001	0.05	<0.001	0.02	<0.001
Never	26,236 (49.6%)	34,489 (57.9%)	60,625 (54.0%)						
Former	19,834 (37.7%)	18,704 (31.4%)	38,538 (34.3%)						
Current	6,670 (12.7%)	6,392 (10.7%)	13,062 (11.6%)						
Employment Status, retired (n=102,416)	18,754 (38.6%)	22,799 (42.3%)	41,553 (40.6%)	0.13	<0.001	0.10	<0.001	0.13	<0.001
Marital Status, spouse/partner (n=103,565)	40,899 (82.2%)	42,027 (78.1%)	82,926 (80.0%)	0.05	<0.001	-0.05	<0.001	-0.03	<0.001
Snoring (n=104,945)	24,119 (48.3%)	15,790 (28.7%)	39,909 (38.0%)	-0.02	<0.001	0.04	<0.001	-0.09	<0.001

Self-reported measures of sleep duration, insomnia symptoms, and excessive daytime sleepiness, as well as covariates.Our sample size for each phenotype-specific GWAS is a subset of the 112,586. The smaller sample size for each GWAS is attributable to subjects with either missing, “prefer not to answer”, or “don’t know” responses. Phenotype correlation was calculated using the Spearman correlation.

Supplementary Table 2. Genome-wide significant results from sex stratified analyses for sleep traits in the UK Biobank.

							Males			**Females**			
Trait	SNP	Chr:position NCBI 37	Nearest Gene(s)	Alleles (E/A)	EAF	Imputation Quality	n	OR [95% CI]	*p-val*	n	OR [95% CI]	*p-val*	interaction *p-val*
Insomnia Symptoms	rs3792900	5:135393754	*TGFBI*	C/T	0.47	0.99	28,511	1.007 [0.974-1.041]	0.70	**30,287**	**1.102 [1.065-1.14]**	**2.16x10^{-8}**	2.55x10^{-4}
	rs13192566	6:169961635	*WDR27*	G/C	0.86	0.99	**28,664**	**1.144 [1.091-1.200]**	**3.17x10^{-8}**	30,420	1.000 [0.957-1.053]	0.8781	8.89x10^{-5}

E=effect allele, A=alternative allele, Chr=chromosome, OR=Odds Ratio, CI=confidence interval, imputation quality from Impute2. EAF=effect allele frequency. Note, increasing odds ratio indicates increased insomnia symptoms. Analyses are adjusted for age, genetic ancestry and genotyping array and performed stratified by sex. Bold denotes genome-wide significant signals ($p<5x10^{-8}$).

Supplementary Table 3. Conditional Analysis. Secondary signal is the lead SNP after conditioning on lead GWAS SNP.

SNP	Nearest Gene(s)	Chr:position NCBI 37	Secondary SNP	Chr:position NCBI 37	Alleles (E/A)	Beta (SE)	*p-val*
Sleep Duration							
rs62158211	*PAX8*	2:114106139	rs183854670	2:115284353	G/T	-0.75 (0.18)	4.63E-05
rs1380703	*LOC647016/ LOC100131953*	2:57941287	rs375652393	2:58089047	T/C	0.48 (0.13)	2.64E-04
rs10953765	*FOXP2*	7:114291435	rs144294405	7:114368853	T/TTC	-0.10 (0.03)	5.98E-04
rs146977851	*PCDH15*	10:56570954	rs191835902	10:56511106	A/G	0.59 (0.15)	8.59E-05
rs61980273	*PRIMA1*	14:94218949	rs184953371	14:94221477	T/C	-0.53 (0.11)	2.07E-06
Insomnia Symptoms						OR (95%CI)	
rs576106307	*ARHGEF10L*	1:18007282	rs185896278	1:17807007	T/C	3.52 (1.46 - 8.47)	7.33E-05
rs113851554	*MEIS1*	2:66750564	rs62143994	2:66696080	T/C	0.93 (0.90 - 0.96)	7.10E-05
rs376775068	*ADCK5*	8:145604659	8:145651625_C_T	8:145651625	T/C	0.33 (0.18 - 0.61)	1.04E-05
rs145258459	*TMEM132E*	17:32986155	rs546643659	17:32812400	A/G	1.35 (1.09 - 1.65)	6.87E-04
rs531814036	*ACBD4*	17:43219921	rs186141052	17:43101593	C/T	0.50 (0.21 - 1.21)	6.01E-04
rs182765975	*ROBO1*	3:78538431	rs557285265	3:78706604	A/G	0.55 (0.35 - 0.85)	1.47E-04
rs142261172	*TMEM132B*	12:126049981	rs540711617	12:126033341	T/A	1.29 (1.06 - 1.58)	1.14E-04
rs5922858	*CYCL1*	X:82971008	rs147330274	X:82957216	C/T	1.14 (1.04 - 1.25)	4.67E-03
Daytime Sleepiness							
rs192315283	*HSD52*	1:59531543	rs371398972	1:59677576	C/A	0.76(0.16)	2.40E-06
rs76645968	*ASB3*	2:53827686	rs570953237	2:54059985	T/C	0.60 (0.14)	1.10E-05
rs920065	*MRPS35P1/ MRPS36P1*	3:5893776	rs148404446	3:6138051	T/A	0.31 (0.08)	1.37E-04
rs115320831	*TMEM144*	4:159178375	rs7663422	4:159185860	A/C	0.39 (0.12)	7.74E-04
rs35309287	*DPYSL3*	5:146775386	5:146997228_C_T	5:146997228	T/C	1.00 (0.27)	2.51E-04
rs189689339	*FAM46A*	6:82375372	rs562379407	6:82303450	G/A	0.82 (0.21)	9.16E-05
rs17507216	*CPEB1*	15:83226925	rs189218438	15:83362909	A/C	0.13 (0.04)	4.82E-04
rs73536079	*AR/OPHN1*	X:67154206	rs4827412	X:67288207	A/G	0.01 (0.01)	2.13E-02

Conditional association results include a ±500kb window around the lead SNP. Chr=chromosome, E=effect allele, A=alternate allele, SE=standard error, OR=Odds ratio, 95%CI= 95% confidence interval.

Supplementary Table 4. Sensitivity analyses adjusting for factors known to associate with sleep duration, insomnia symptoms, or excessive daytime sleepiness.

	SNP	CHR	POS	Alleles (E/A)	INFO	MAF	N	Aditional adjustment beyond baseline	Beta (SE)	P
Sleep Duration										
	rs10953765	7	114,291,435	A/G	0.977	0.446	74,025	-	-0.02 (0.006)	$9.34x10^{-5}$
							74,025	Sleep Apnea	-0.02 (0.006)	$9.30x10^{-5}$
							74,025	BMI	-0.02 (0.006)	$1.01x10^{-4}$
							71,091	Depression	-0.02 (0.006)	$9.86x10^{-5}$
							74,025	Psychiatric Medication	-0.02 (0.006)	$9.52x10^{-5}$
							73,931	SES	-0.02 (0.006)	$1.41x10^{-4}$
							73,840	Smoking	-0.02 (0.006)	$1.43x10^{-4}$
							73,476	Employment Status	-0.02 (0.006)	$7.71x10^{-5}$
							68,261	Marital Status	-0.02 (0.006)	$4.63x10^{-5}$
							69,190	Snoring	-0.02 (0.006)	$6.76x10^{-5}$
	rs1380703	2	57,941,287	G/A	0.893	0.382	59,469	-	-0.02 (0.006)	$7.63x10^{-4}$
							59,469	Sleep Apnea	-0.02 (0.006)	$7.65x10^{-4}$
							59,469	BMI	-0.02 (0.006)	$7.51x10^{-4}$
							57,073	Depression	-0.02 (0.007)	$1.39x10^{-3}$
							59,469	Psychiatric Medication	-0.02 (0.006)	$8.13x10^{-4}$
							59,395	SES	-0.02 (0.006)	$8.00x10^{-4}$
							59,309	Smoking	-0.02 (0.006)	$6.07x10^{-4}$
							59,021	Employment Status	-0.02 (0.006)	$1.06x10^{-3}$
							54,837	Marital Status	-0.02 (0.007)	$1.16x10^{-3}$
							55,524	Snoring	-0.03 (0.007)	$1.23x10^{-4}$
	rs146977851	10	56,570,954	T/C	0.965	0.029	74,893	-	-0.05 (0.017)	$4.85x10^{-3}$
							74,893	Sleep Apnea	-0.05 (0.017)	$4.85x10^{-3}$
							74,893	BMI	-0.05 (0.017)	$4.80x10^{-3}$
							71,922	Depression	-0.05 (0.017)	$4.53x10^{-3}$
							74,893	Psychiatric Medication	-0.05 (0.017)	$5.39x10^{-3}$
							74,798	SES	-0.05 (0.017)	$3.96x10^{-3}$
							74,710	Smoking	-0.05 (0.017)	$6.39x10^{-3}$
							74,337	Employment Status	-0.05 (0.017)	$2.72x10^{-3}$
							69,082	Marital Status	-0.05 (0.018)	$5.00x10^{-3}$
							70,000	Snoring	-0.05 (0.018)	$9.95x10^{-3}$
	rs61980273	14	94,218,949	A/G	1.000	0.039	75,476	-	0.06 (0.014)	$9.85x10^{-6}$
							75,476	Sleep Apnea	0.06 (0.014)	$1.00x10^{-5}$
							75,476	BMI	0.06 (0.014)	$9.96x10^{-6}$
							72,481	Depression	0.06 (0.014)	$4.03x10^{-5}$
							75,476	Psychiatric Medication	0.06 (0.014)	$1.01x10^{-5}$
							75,381	SES	0.06 (0.014)	$1.05x10^{-5}$
							75,291	Smoking	0.06 (0.014)	$1.37x10^{-5}$
							74,917	Employment Status	0.06 (0.014)	$2.86x10^{-5}$
							69,617	Marital Status	0.07 (0.015)	$3.94x10^{-6}$
							70,549	Snoring	0.06 (0.015)	$4.91x10^{-5}$
	rs62158211	2	114,106,139	T/G	0.992	0.214	74,729	-	0.04 (0.007)	$2.89x10^{-10}$
							74,729	Sleep Apnea	0.04 (0.007)	$2.91x10^{-10}$
							74,729	BMI	0.04 (0.007)	$2.73x10^{-10}$
							71,761	Depression	0.04 (0.007)	$1.65x10^{-10}$
							74,729	Psychiatric Medication	0.04 (0.007)	$2.66x10^{-10}$
							74,635	SES	0.04 (0.007)	$4.06x10^{-10}$
							74,548	Smoking	0.04 (0.007)	$3.70x10^{-10}$
							74,179	Employment Status	0.04 (0.007)	$2.07x10^{-10}$
							68,927	Marital Status	0.04 (0.007)	$4.03x10^{-10}$
							69,852	Snoring	0.04 (0.007)	$1.15x10^{-9}$
Insomnia Symptoms									**OR [95%CI]**	**P**
	rs113851554	2	66,750,564	T/G	1.000	0.056	39,812	-	1.27 [1.19-1.35]	$1.39x10^{-13}$
							39,812	Sleep Apnea	1.27 [1.19-1.35]	$1.47x10^{-13}$
							39,812	BMI	1.27 [1.19-1.35]	$1.50x10^{-13}$
							38,278	Depression	1.29 [1.21-1.38]	$4.73x10^{-14}$
							39,812	Psychiatric Medication	1.27 [1.19-1.35]	$1.55x10^{-13}$
							39,759	SES	1.27 [1.20-1.36]	$8.49x10^{-14}$
							39,704	Smoking	1.27 [1.19-1.35]	$1.87x10^{-13}$
							39,527	Employment Status	1.27 [1.19-1.35]	$1.88x10^{-13}$
							36,595	Marital Status	1.26 [1.18-1.35]	$7.14x10^{-12}$
							37,180	Snoring	1.27 [1.19-1.36]	$6.33x10^{-13}$

	rs145258459	17	32,986,155	T/C	0.695	0.017	38,305	-	0.71 [0.60-0.82]	1.17×10^{-5}
							38,305	Sleep Apnea	0.70 [0.60-0.82]	1.13×10^{-5}
							38,305	BMI	0.70 [0.60-0.82]	1.08×10^{-5}
							36,825	Depression	0.72 [0.62-0.85]	1.20×10^{-4}
							38,305	Psychiatric Medication	0.70 [0.60-0.82]	9.58×10^{-6}
							38,254	SES	0.70 [0.60-0.82]	9.43×10^{-6}
							38,202	Smoking	0.71 [0.60-0.83]	1.54×10^{-5}
							38,030	Employment Status	0.70 [0.60-0.82]	8.94×10^{-6}
							35,200	Marital Status	0.69 [0.59-0.81]	8.74×10^{-6}
							35,764	Snoring	0.74 [0.63-0.87]	3.01×10^{-4}
	rs376775068	8	145,604,659	C/G	0.672	0.066	32,923	-	0.85 [0.77-0.92]	2.05×10^{-4}
							32,923	Sleep Apnea	0.85 [0.77-0.92]	2.27×10^{-4}
							32,923	BMI	0.85 [0.78-0.93]	2.61×10^{-4}
							31,660	Depression	0.84 [0.77-0.92]	2.75×10^{-4}
							32,923	Psychiatric Medication	0.85 [0.77-0.92]	2.23×10^{-4}
							32,880	SES	0.85 [0.78-0.93]	4.01×10^{-4}
							32,824	Smoking	0.85 [0.78-0.93]	2.77×10^{-4}
							32,684	Employment Status	0.85 [0.78-0.93]	2.92×10^{-4}
							30,256	Marital Status	0.85 [0.78-0.93]	6.22×10^{-4}
							30,751	Snoring	0.85 [0.77-0.93]	3.83×10^{-4}
	rs531814036	17	43,219,921	C/CT	0.911	0.420	32,086	-	1.08 [1.04-1.11]	6.86×10^{-6}
							32,086	Sleep Apnea	1.08 [1.04-1.11]	6.51×10^{-6}
							32,086	BMI	1.08 [1.04-1.11]	8.42×10^{-6}
							30,839	Depression	1.08 [1.04-1.12]	2.47×10^{-5}
							32,086	Psychiatric Medication	1.08 [1.04-1.11]	7.58×10^{-6}
							32,043	SES	1.08 [1.04-1.12]	5.43×10^{-6}
							32,002	Smoking	1.08 [1.04-1.11]	1.81×10^{-5}
							31,868	Employment Status	1.08 [1.04-1.11]	8.59×10^{-6}
							29,491	Marital Status	1.08 [1.04-1.12]	2.08×10^{-5}
							29,976	Snoring	1.07 [1.03-1.11]	1.08×10^{-4}
	rs576106307	1	18,007,282	CT/C	0.893	0.212	33,570	-	0.91 [0.87-0.95]	2.30×10^{-6}
							33,570	Sleep Apnea	0.91 [0.87-0.95]	2.35×10^{-6}
							33,570	BMI	0.91 [0.87-0.95]	2.89×10^{-6}
							32,266	Depression	0.92 [0.88-0.96]	4.72×10^{-5}
							33,570	Psychiatric Medication	0.91 [0.87-0.95]	2.37×10^{-6}
							33,526	SES	0.91 [0.88-0.95]	8.30×10^{-6}
							33,477	Smoking	0.91 [0.87-0.95]	3.40×10^{-6}
							33,330	Employment Status	0.91 [0.87-0.95]	4.06×10^{-6}
							30,887	Marital Status	0.92 [0.87-0.96]	6.37×10^{-6}
							31,325	Snoring	0.91 [0.87-0.95]	3.37×10^{-6}
	rs5922858	X	82,971,008	G/T	0.992	0.849	39,512	-	0.88 [0.84-0.92]	1.29×10^{-7}
							39,512	Sleep Apnea	0.88 [0.84-0.92]	1.34×10^{-7}
							39,512	BMI	0.88 [0.84-0.92]	1.17×10^{-7}
							37,990	Depression	0.88 [0.84-0.92]	1.84×10^{-7}
							39,512	Psychiatric Medication	0.88 [0.84-0.92]	1.07×10^{-7}
							39,459	SES	0.88 [0.84-0.92]	1.84×10^{-7}
							39,406	Smoking	0.88 [0.84-0.93]	1.88×10^{-7}
							39,233	Employment Status	0.88 [0.84-0.92]	4.70×10^{-8}
							36,325	Marital Status	0.88 [0.84-0.93]	5.46×10^{-7}
							36,899	Snoring	0.87 [0.83-0.92]	4.57×10^{-8}
									Beta (SE)	**P**
Excessive Daytime Sleepiness										
	rs115320831	4	159,178,375	A/G	0.981	0.298	73,280	-	-0.01 (0.003)	1.96×10^{-5}
							73,280	Sleep Apnea	-0.01 (0.003)	2.41×10^{-5}
							73,280	BMI	-0.01 (0.003)	1.90×10^{-5}
							70,364	Depression	-0.01 (0.003)	3.39×10^{-5}
							73,280	Psychiatric Medication	-0.01 (0.003)	2.13×10^{-5}
							73,186	SES	-0.01 (0.003)	2.88×10^{-5}
							73,102	Smoking	-0.01 (0.003)	2.54×10^{-5}
							72,739	Employment Status	-0.01 (0.003)	1.01×10^{-5}
							67,586	Marital Status	-0.01 (0.003)	3.07×10^{-5}
							68,526	Snoring	-0.01 (0.003)	5.24×10^{-5}

rs17507216	15	83,226,925	A/G	1.000	0.232	75,639	-	0.01 (0.003)	4.87x10^{-6}
						75,639	Sleep Apnea	0.01 (0.003)	4.58x10^{-6}
						75,639	BMI	0.01 (0.003)	4.00x10^{-6}
						72,624	Depression	0.01 (0.003)	5.38x10^{-5}
						75,639	Psychiatric Medication	0.01 (0.003)	5.27x10^{-6}
						75,544	SES	0.01 (0.003)	3.68x10^{-6}
						75,451	Smoking	0.01 (0.003)	4.08x10^{-6}
						75,079	Employment Status	0.01 (0.003)	1.54x10^{-6}
						69,749	Marital Status	0.02 (0.003)	1.86x10^{-6}
						70,711	Snoring	0.02 (0.003)	1.56x10^{-6}
rs189689339	6	82,375,372	T/C	0.664	0.004	74,733	-	0.06 (0.032)	4.71x10^{-2}
						74,733	Sleep Apnea	0.06 (0.032)	4.80x10^{-2}
						74,733	BMI	0.06 (0.032)	4.36x10^{-2}
						71,756	Depression	0.06 (0.033)	8.69x10^{-2}
						74,733	Psychiatric Medication	0.06 (0.032)	4.59x10^{-2}
						74,640	SES	0.07 (0.032)	3.28x10^{-2}
						74,549	Smoking	0.06 (0.032)	4.68x10^{-2}
						74,180	Employment Status	0.07 (0.032)	4.21x10^{-2}
						68,927	Marital Status	0.06 (0.033)	5.33x10^{-2}
						69,864	Snoring	0.07 (0.033)	3.26x10^{-2}
rs192315283	1	59,531,543	C/T	0.757	0.010	74,322	-	0.06 (0.016)	7.77x10^{-5}
						74,322	Sleep Apnea	0.07 (0.016)	6.10x10^{-5}
						74,322	BMI	0.07 (0.016)	6.24x10^{-5}
						71,360	Depression	0.07 (0.017)	2.65x10^{-5}
						74,322	Psychiatric Medication	0.07 (0.016)	7.04x10^{-5}
						74,229	SES	0.06 (0.016)	9.01x10^{-5}
						74,140	Smoking	0.07 (0.016)	5.17x10^{-5}
						73,775	Employment Status	0.07 (0.016)	5.10x10^{-5}
						68,530	Marital Status	0.06 (0.017)	1.53x10^{-4}
						69,478	Snoring	0.05 (0.017)	2.14x10^{-3}
rs35309287	5	146,775,386	T/TA	0.937	0.030	74,463	-	-0.03 (0.008)	8.14x10^{-5}
						74,463	Sleep Apnea	-0.03 (0.008)	7.20x10^{-5}
						74,463	BMI	-0.03 (0.008)	8.03x10^{-5}
						71,491	Depression	-0.03 (0.008)	2.89x10^{-4}
						74,463	Psychiatric Medication	-0.03 (0.008)	8.64x10^{-5}
						74,368	SES	-0.03 (0.008)	1.31x10^{-4}
						74,277	Smoking	-0.03 (0.008)	5.67x10^{-5}
						73,912	Employment Status	-0.03 (0.008)	1.35x10^{-4}
						68,658	Marital Status	-0.03 (0.008)	9.41x10^{-4}
						69,614	Snoring	-0.03 (0.008)	6.32x10^{-4}
rs76645968	2	53,827,686	C/G	0.990	0.023	75,463	-	-0.03 (0.008)	1.87x10^{-4}
						75,463	Sleep Apnea	-0.03 (0.008)	2.18x10^{-4}
						75,463	BMI	-0.03 (0.008)	1.72x10^{-4}
						72,456	Depression	-0.03 (0.008)	2.90x10^{-4}
						75,463	Psychiatric Medication	-0.03 (0.008)	1.74x10^{-4}
						75,368	SES	-0.03 (0.008)	2.08x10^{-4}
						75,277	Smoking	-0.03 (0.008)	1.56x10^{-4}
						74,905	Employment Status	-0.03 (0.008)	1.56x10^{-4}
						69,586	Marital Status	-0.03 (0.009)	2.63x10^{-4}
						70,550	Snoring	-0.03 (0.009)	4.09x10^{-4}
rs920065	3	5,893,776	C/G	0.957	0.176	71,634	-	-0.02 (0.003)	3.47x10^{-6}
						71,634	Sleep Apnea	-0.02 (0.003)	3.04x10^{-6}
						71,634	BMI	-0.02 (0.003)	2.53x10^{-6}
						68,787	Depression	-0.02 (0.003)	5.25x10^{-6}
						71,634	Psychiatric Medication	-0.02 (0.003)	3.37x10^{-6}
						71,546	SES	-0.02 (0.003)	1.75x10^{-6}
						71,455	Smoking	-0.02 (0.003)	3.21x10^{-6}
						71,111	Employment Status	-0.02 (0.003)	1.55x10^{-6}
						66,056	Marital Status	-0.01 (0.004)	2.46x10^{-4}
						66,941	Snoring	-0.02 (0.004)	4.00x10^{-6}

rs182765975	3	78,538,431	T/G	0.855	0.003	75,312	-	0.08 (0.022)	3.34×10^{-4}
						75,312	Sleep Apnea	0.08 (0.022)	3.46×10^{-4}
						75,312	BMI	0.08 (0.022)	3.00×10^{-4}
						72,310	Depression	0.08 (0.022)	2.18×10^{-4}
						75,312	Psychiatric Medication	0.08 (0.022)	3.38×10^{-4}
						75,217	SES	0.08 (0.022)	4.79×10^{-4}
						75,124	Smoking	0.08 (0.022)	3.08×10^{-4}
						74,754	Employment Status	0.08 (0.022)	2.13×10^{-4}
						69,453	Marital Status	0.07 (0.023)	1.35×10^{-3}
						70,409	Snoring	0.08 (0.022)	2.85×10^{-4}
rs142261172	12	126,049,981	A/G	0.915	0.004	75,355	-	0.11 (0.019)	6.05×10^{-9}
						75,355	Sleep Apnea	0.11 (0.019)	7.79×10^{-9}
						75,355	BMI	0.11 (0.019)	7.05×10^{-9}
						72,353	Depression	0.12 (0.019)	1.65×10^{-9}
						75,355	Psychiatric Medication	0.11 (0.019)	6.15×10^{-9}
						75,261	SES	0.11 (0.019)	1.09×10^{-8}
						75,167	Smoking	0.11 (0.019)	3.25×10^{-9}
						74,796	Employment Status	0.11 (0.019)	7.51×10^{-9}
						69,483	Marital Status	0.11 (0.020)	1.13×10^{-8}
						70,449	Snoring	0.11 (0.020)	4.38×10^{-8}
rs73536079	X	67,154,206	T/G	0.903	0.003	75,583	-	0.74 (0.147)	4.88×10^{-7}
						75,583	Sleep Apnea	0.74 (0.146)	4.71×10^{-7}
						75,583	BMI	0.75 (0.146)	3.34×10^{-7}
						72,572	Depression	0.73 (0.145)	4.51×10^{-7}
						75,583	Psychiatric Medication	0.74 (0.146)	4.67×10^{-7}
						75,488	SES	0.74 (0.146)	3.87×10^{-7}
						75,395	Smoking	0.74 (0.146)	4.62×10^{-7}
						75,026	Employment Status	0.74 (0.146)	4.71×10^{-7}
						69,697	Marital Status	0.75 (0.153)	9.54×10^{-7}
						70,659	Snoring	0.73 (0.145)	4.50×10^{-7}

Sleep trait GWAS results are adjusted for age, sex, genetic ancestry, and genotyping array as baseline and additional covariates as indicated for each analysis. All analyses performed in subjects with non-missing covariates, therefore unadjusted results may differ from table 1. E=effect allele, A=alternative allele, MAF=minor allele frequency, SE=standard error.

Supplementary Table 5. Description of candidate genes within association signals and *In silico* functional interpretation using variant annotations (Haploreg 4.1)

	SNP	Chr:position NCBI 37	Nearest Gene(s)	Candidate genes	In silico functional assessment (Haploreg 4.1)
Sleep duration					
	rs62158211	2:114106139	*PAX8*	This lead SNP is in strong LD with the CHARGE multi-ethnic sleep duration signal (rs1823125 r2=0.95, D'=0.98 in 1KG CEU). The locus contains 6 genes under the peak *(IL1RN, PSD4, PAX8, PAX8-AS1, IGKV1OR2-108, AC016745.3, CBWD2, FOXD4L1*). *IL1RN* encodes interleukin 1 Receptor antagonist, and is upregulated in sleep-deprived mice. *PSD4* , Pleckstrin And Sec7 Domain Containing 4, is a guanine exchange factor for the RAS superfamily protein Arf6 that helps to assemble and stabilize tight junctions. *PAX-8* , paired-box 8 is a thyroid and kidney specific nuclear paired box homeodomain transcription factor involved in thyroid development. *IGKV1OR2-108* is an immunoglobulin kappa variable gene segment. CBWD2 is a family member of the cobalamin synthetase W domain proteins, FOXD4L1 is a neural forkhead box transcription factor that expands neural ectoderm by repressing genes that promote onset of neural differentiation, and upregulating genes that maintain immature proliferative neural precursors. AC016745.3 is a poorly characterized lincRNA with increased expression in recurrent glioma.	This region is adjacent to the head to head fusion site at chr 2q13-q14.1 that formed chromosome 2 during human evolution from hominids. Eqtls peaks are observed at the lead GWAS SNP for widely expressed gene AC016745.3 (thyroid, adrenal gland and skin), widely expressed CBWD2 (thyroid), IGKV1OR2108 (thyroid and skin) and FOXD4L1 (thyroid; gTEX consortium) with lower gene expression for the sleep duration increasing allele. Eqtls of lead SNPs for PAX-8 were also reported by the CHARGE Consortium. The lead SNPs are also associated with ratios of metabolites C3:1/C16-0H acylcarnitine to hydroxyacylcarnitine ratio (p=10-8), C3:1 involved in energy metabolism, and serum ratio of (linoleamide (18:2n6))/(stearidonate (18:4n3)p=1.5x10-6).
	rs1380703	2:57941287	*VRK2*	This locus is between annotated genes SNORD78 (169kb) and VRK2 (332kb). SNORD78 codes for a small nucleolar RNA upregulated in lung and prostate cancer. VRK2 encodes the protein vaccinia related kinase 2, a serine/threonine kinase and modulator or ERK/MAPK and CREB-regulated pathways.Independent variants at the VRK2 locus have previously been associated with schizophrena and epilepsy (rs13026414 r2=0.34, D'=0.89; rs11682175 r2=0.40, D'=0.82) and conditional analysis suggests that they are not associated with sleep duration. Rare variants have been identified in a family with bipolar disorder (PMID: 24348429).Pseudogenes in the locus include LOC100131953.	VRK2 is widely expressed, with greatest expression in gTEX in EBV-tranformed lymphocytes. The lead SNP is common but has no known SNPs in LD; the alternate allele is predicted to abolish Tregulatory cell specifying FoxP3 binding, enhance binding of the important pluripotency transcription factor Nanog and reduce binding of POU2F2 (OCT2) and TATA. No enhancer or promoter elements are predicted.
	rs10953765	7:114291435	*FOXP2*	This locus contains 3 genes, *FOXP2* , *MIR3666* and *MDFIC* . *FOXP2* encodes the forkhead box P2 protein and mutations cause developmental speech and language disorders in humans.MIR3666 lies within an intron of FOXP2. MDFIC encodes for the MyoD family inhibitor protein that has a cysteine rich C terminal domain important for transcriptional regulation of viral gene expression. Notably, an intronic SNP in MDFIC was associated with clozapine induced cell death in lymphoblastoid cell lines (rs2709505 r2=0.009, D'=0.36 to our lead SNP).	The lead SNP lies within an intron of *FOXP2* and alters binding of TATA-binding protein, with the sleep duration reducing allele showing enhanced binding. Notably, a corelated variant is highly conserved and the alternate allele decreases binding of zinc finger protein Zfp128 and enhances binding of Zfp161.
	rs146977851	10:56570954	*PCDH15*	There is one gene at the locus, *PCDH15* which encodes for protocadherin-related 15, a member of the cadherin superfamily involved in generating neural diversity for neuronal differentiation and synapse formation. It has previously been linked to hearing loss (Usher syndrome) and may be disrupted in neuropsychiatric disorders such as autism and schizophrenia.	The lead SNP alters bindng sites for 12 proteins, with most dramatic differential effects by allele for binding of FOXP1, FOXQ1, POU3f2_2 and Sox6 transcription factors.
	rs61980273	14:94218949	*PRIMA1*	This locus contains the genes *UNC79 (unc-79 homolog (C. elegans)), PRIMA1 (proline rich membrane anchor 1), FAM181A and FAM181A-AS1 and ASB2 (ankyrin repeat and SOCS box containing 2)* . Unc79 is a calcium channel previously implicated in circadian rhythms and sleep-wake regulation in Drosophila. PRIMA1 encodes for proline rich membrane anchor 1, organizes acetylcholinesterase into tetramers to tether it to neuronal membranes. A previously reported SNP in the gene has been implicated in a GWAS study of caffeine related sleep disturbance (rs6575353 r2=0.003, D'=1 to our lead SNP; P>10-6) unadjusted for insomnia.	The SNP lies within PRIMA1 and demonstrates a promoter mark in mesenchymal stem cells, enhancer marks in multiple brain regions, muscle and instestines, and the alternate allele is predicted to reduce binding of AP-2, a transcription factor expressed in neural crest celles, and slightly enhance binding of BDP1.
Insomnia Symptoms					
	rs576106307	1:18007282	*ARHGEF10L*	*ARHGEF10L* encodes Rho guanine nucleotide exchange factor 10 like and may be involved in cerebral visual impairment. *ACTL8* encodes actin-like 8, *RCC2* encodes Regulator of chromosome condensation-2 that may be involved in directional cell signaling	This variant is not present in the 1KG reference database.
	rs113851554	2:66750564	*MEIS1*	ME1S1 is a homeodomain protein important for stem cell self-renewal, and plays important roles in the development of the brain and heart. It has a role in motor neuron connectivity in Drosophila, retinal and lens development in mouse, and Substance P expression in the amygdala.	This variant is highly conserved, and acts as an enhancer in multiple cell lines including hematopoeitic cells, smooth muscle, lung, pancreas and liver. The most highly correlated variant is an enhancer in stem cells, fetal heart, adrenal gland and the rare allele is predicted to dramatically reduce binding of REST. In zebrafish, the enhancer element encompassing this variant has an enhancer role.
	rs376775068	8:145604659	*ADCK5*	*ADCK5* encodes AarF Domain Containing Kinase 5 on chr 1q24.3.	This variant is not present in the 1KG reference database.

	rs145258459	17:32986155	*TMEM132E*	TMEM132 family members are important in neuronal development, this gene has been implicated in autosomal-recessive nonsyndromic hearing loss. The gene family has roles in panic/anxiety disorder, and bipolar disorder.	This variant is 20kb downstream of the gene, conserved (GERP), has enhancer marks in the brain and GI tissues, has DNA hypersensitivity sites in induced pluripotent stem cells, brain and GI.
	rs531814036	17:43219921	*ACBD4*	This region harbors the genes *DCAKD, NMT1, PLCD3, ACBD4, HEXIM1, HEXIM2, FMNL1, MAP3K14, MAP3K14-AS1, SPATA32* . ACBD4 encodes an acyl-CoA binding domain containing protein involved in maintenance of Golgi structure and transport.	This variant is not present in the 1KG reference database.
Males	rs13192566	6:169961635	*WDR27*	This region comprises the genes *THBS2, WDR27, C6orf120, PHF10, TCTE3, ERMARD, LINC00242 and LINC00574* . WDR27 encodes a WD repeat containing protein, the family of which can act as a scaffold for protein-protein interactions important for cell signaling. Variants around this gene have been implicated in multiple human diseases including type 1 diabetes.	The lead SNP and correlated variant are in WDR27 and are predicted to alter binding sites for multiple transcription factors, but little else is known.
Females	rs3792900	5:135393754	*TGFBI*	This region harbors the genes *SLC25A48 (solute carrier family 25 member 48)* , IL9 (interleukin 9), FBXL21 (F-box and leucine rich repeat protein 21 (gene/pseudogene) , LECT2 (leukocyte cell derived chemotaxin 2), TGFBI (transforming growth factor beta induced), VTRNA2-1, SMAD5 (SMAD family member 5), SMAD5-AS1, LOC389332, TRPC7 (transient receptor potential cation channel subfamily C member 7). TGBI encodes the TGF-beta induced gene, an extracellular matrix protein responsible for human corneal dystrophy and that may act as a tumor suppressor gene.	There are many SNPs in this region that might be causal, with slightly greater probability for the lead SNP using PICS. The lead SNP is in an enhancer and binds CTCF in many cell types, is an expression-qtl for SMAD5 in monocytes (p=10-9) and for SMAD5 (p=10-30) and TGFBI (p=10-6) in whole blood and alters transcription factor binding sites for E2A, TBX5 and ZEB1.
Daytime Sleepiness					
	rs192315283	1:59531543	*HSD52*	This region contains genes for non-coding RNAs LINC01135, LINC01358, uncharacterized predicted protein HSD52, JUN proto-oncogene, AP-1 transcription factor subunit, MYSM1, Myb like, SWIRM and MPN domains 1 protein, and FGGY, a carbohydrate kinase domain containing protein, that phosphorylates carbohydrates. Variants in FGGY have been irreproducibly associated with ALS.	The lead SNP is predicted to be the likely causal variant, and is downstream of HSD52. It is highly conserved and is within an enhancer element in ES cells, blood and GI tissues, altering transcription factor binding sites for Ets.
	rs76645968	2:53827686	*ASB3*	This region harbors genes *ASB3, GPR75-ASB3, CHAC2, GPR75, ERLEC1, MIR3682 and PSME4* . ASB3 encodes an ankyrin repeat and SOCS box containing protein. The SOCs box may couple suppressor of cytokine signaling proteins to elongin complexes for degradation. This region has been previously implicated in responsiveness to short-acting beta-2 agonists in asthma and is associated with smooth muscle proliferation. GPR75-ASB3 is the product of a read-through transcript and the encoded protein is identical to ASB3 with a novel N-terminus from GPR75. GPR75 is a G-protein coupled receptor. CHAC2 encodes a cation transport regulator homolog and the familymay act as γ-glutamyl cyclotransferases that degrade glutathione. ERLEC1 encodes an endoplasmic reticulum lectin that functions in N-glycan recognition, and may function as a regulator of protein degradation and multiple cellular stress response pathways. MIR3682 is a microRNA of unknown function. PSME4 encodes the proteasome activator subunit 4 involved in DNA repair.	The lead SNP is within ASB3, and has 25% probability to be the causal SNP based on PICS analysis. It is in a region of enhancer histone marks in the brain, gastrointestinal tissues and in the pancrease. The SNP is predicted to alter a binding site for NRSF/REST, a neuron-restrictive silencing factor important for the establishing of neuronal specificity, by being expressed in non-neuronal and neuronal lineages. A correlated SNP is a trans-eqtl SNP, associated with gene expression of LRP5L, located on chr22, in peripheral blood monocytes.
	rs920065	3:5893776	*MRPS35P1/ MRPS36P1*	MRPS35P1 and MRPS36P1 are mitochondrial ribosomal protein S35 and S36 pseudogenes.	There are two SNPs in strong LD, both lead SNPs alter transcription factor binding sites for multiple transcription factors, most predominantly interferon regulatory factor for rs920065 and forkhead transcription factor Foxf2 for rs5846411, that is expressed predominantly in the lung and placenta.
	rs115320831	4:159178375	*TMEM144*	This region harbors poorly characterized genes FAM198B and transmembrane domain protein TMEM144, as well as relaxin/insulin like peptide receptor 1 (RXFP1), a G-protein coupled receptor. RXFP1 has been dysregulated in multiple diseases including bipolar disorder, stroke and cancer, is implicated in stress response, and also plays critical roles in spermatogenesis, pregnancy and birth as a receptor for relaxin. In zebrafish, it plays an important role in neurophysiology during early development	The lead SNP lies 1.8kb 3' of the gene TMEM144, and is predicted to most strongly alter binding of FOXP1 and SIX5 transcription factors. A correlated variant is also predicted to alter FOXP1 and Pou3f3 binding.
	rs35309287	5:146775386	*DPYSL3*	This region contains genes STK32A, DPYSL3, JAKMIP2-AS1, JAKMIP2. DPYSL3 encodes a dihydropyrimidinase like protein implicated as a tumor suppressor and ALS gene, and regulates the inflammatory response of activated microglia. STK32A encodes a serine/threonine kinase. JAKMIP2 is janus kinase and microtubule interacting protein 2, component of the Golgi matrix, and may be a scaffold or repress secretory processes.	Two variants could be causal by PICS credible set analysis, and are 1bp apart, suggesting that they might reflect the same insertion-deletion polymorphism. Both variants are predicted to lie in an enhancer site active in ES cell derived ectodermal cells, fat, ovary, heart and lung and alter binding sites for multiple transcription factors, most strongly for PAX-6, lead variant, and GATA for the correlated variant.
	rs189689339	6:82375372	*FAM46A*	This region contains the Fam46a gene that has been implicated in retinal diseases, is thought to be a poly-A polymerase, is enriched in Hcrt cells, with variants associated with posterior cortical atrophy variant of Alzheimer's disease. Mutations in mice cause skeletal dysplasia.	The lead variant is predicted to be causal and significantly alter binding of SREBP1 and p300.

	rs17507216	15:83226925	*CPEB1*	This region harbors multiple genes including *GOLGA6L10* (golgin A6 family-like 10), *ADAMTS7P1* (*ADAMTS7* pseudogene 1), *UBE2O2P2* , *RPS17* (ribosomal protein S17), *CPEB1* (cytoplasmic polyadenylation element binding protein 1), *AP3B2* (adaptor related protein complex 3 beta 2 subunit), *SNHG21* (small nucleolar RNA host gene 21), SCARNA15 (small Cajal body-specific RNA 15), FSD2 (fibronectin type III and SPRY domain containing 2), *WHAMM* (WAS protein homolog associated with actin, golgi membranes and microtubules), *HOMER2* (homer homolog 2 (Drosophila). CPEB1 regulates subcellular trafficking and translation of synaptic plasticity-related mRNAs, and may play a role in diurnal trafficking of mRNAs in astrocytes.	There are multiple SNPs that might be causal, and lie in the genes RP11-152F13.10 or CPEB1. The lead SNP is predicted to be an enhancer in ES cell derived endoderm and brain regions including the angular gyrus and it and associated SNPs form an eqtl peak for multiple genes (most strongly AP3B2, but also genes RP13-608F4.1,RP11-152F13.10, RP11-152F13.7, AC105339.1 and EFTUD1) in adipose tissue, aorta, cerebellum, breast, fibroblasts, colon, esophagus, heart, lung, muscle, skin, stomach, thyroid and whole blood. The SNP rs17356118 in strong LD is conserved, predicted to be a strong enhancer in multiple tissues and alters the glucocorticoid response element.
adj for depression	rs182765975	3:78538431	*ROBO1*	*ROBO1* encodes the roundabout guidance receptor 1 and is a neuronal axon guidance receptor previously implicated in dyslexia.	Little functional annotation is available for the three variants predicted to have highest probability for causality. While the lead variant is not predicted to alter transcription factor binding sites, the other two SNPs may alter multiple transcription factor binding sites including most strongly for NKX2.2 and NKX2.3 for variant rs191435135.
adj for BMI	rs142261172	12:126049981	*TMEM132B*	*TMEM132B* is a *TMEM132* family member involved in brain development that is differentially expressed in intracranial aneurysm.	Both correlated SNPs have equal probability of being causal. The lead SNP activates a glucocorticoid response element, and has DNAase hypersensitivity sites in the blood, while the correlated SNP is predicted to be an enhancer in the brain and has DNA hypersensitivity sites in the brain.
Multi-sleep trait					
	rs12140153	1:62352479	*INADL*	This region harbors *TM2D1* (TM2 domain containing 1), *L1TD1* (LINE1 type transposase domain containing 1), *KANK4* (KN motif and ankyrin repeat domains 4), *USP1* (ubiquitin specific peptidase 1), *DOCK7* (dedicator of cytokinesis 7) and INADL. *INADL* encodes PATJ, a crumbs cell polarity complex component, with multiple PDZ domains. It organizes multimeric complexes at the plamsa membrane and localizes to tight junctions. Variants in *INADL* have previously been associated with obesity.	The lead SNP is predicted to be causal and is a conserved missense SNP, that is predicted to be probably damaging by Polyphen and deleterious by SIFT. It is predicted to be a missense variant in all four transcripts (Transcript ENST00000316485 p.G1573V, ENST00000371158 G1543V, ENST00000543708 p.G357V, and ENST00000545929, p.G188V). Further, it might slightly alter transcription-factor binding and have a regulatory role.
	rs3122163	6:55164327	*HCRTR2*	This region harbors the orexin receptor, *HCRTR2* , a G-protein coupled receptor involved in sleep-wake regulation and regulation of feeding behavior.	Multiple SNPs in this region may be causal, and while the lead SNP is not well annotated, a correlated SNP rs9475186 is predicted to be within a strong bivalent promoter and alter transcription factor binding of ETS transcription factor which has roles in immune system and cancer.

Supplementary Table 6. Disease associated gene sets enriched in candidate genes from sleep duration, insomnia symptons, and excessive daytime sleepiness genes loci.

Trait	**Disease Gene Set**	**Genes**	**Fold Enrichment**	P_{Adjusted}
Sleep Duration	Nelson syndrome	*IL36B,RABL2A,FOXD4L1,PSD4,IL36G,IL36A*	12.02	6.04E-05
	Communication Disorders	*FOXP2,PCDH15*	23.24	6.80E-03
	Williams Syndrome	*RABL2A,FOXD4L1,PSD4*	8.77	8.70E-03
Insomnia Sympton	Virus Diseases	*CCL7,NMT1,VPS28,PLCD3,GPT,HEXIM1,CCL8,CCL1*	10.88	2.91E-05
	Bronchitis	*CCL13,CCL7,CCDC103,CCL11,CCL8,CCL1*	16.8	2.91E-05
	Sexually Transmitted Diseases	*CCL7,NMT1,VPS28,GFAP,PLCD3,HEXIM1,CCL11*	12.32	2.91E-05
	Brenner tumour of ovary	*CCL13,CCL7,GFAP,CCL11,CCL8,CCL1*	17.93	2.91E-05
	Immunologic Deficiency Syndror	*CCL7,NMT1,VPS28,GFAP,PLCD3,HEXIM1*	15.29	2.00E-04
	HIV Infections	*CCL7,NMT1,VPS28,GFAP,PLCD3,HEXIM1*	9.33	2.00E-04
	Retroviridae Infections	*CCL7,NMT1,VPS28,GFAP,PLCD3,HEXIM1*	7.65	2.00E-04
	HIV	*CCL7,NMT1,VPS28,GFAP,PLCD3,HEXIM1,CCL8,CCL1*	7.03	2.00E-04
	Lentivirus Infections	*CCL7,NMT1,VPS28,GFAP,PLCD3,HEXIM1*	10.62	2.00E-04
	Inflammation	*CCL13,CCL7,MAP3K14,CCL11,CCL8,CCL1*	9.15	3.00E-04
	Sclerosis	*PADI3,GFAP,PADI4,PADI6*	13.82	9.00E-04
	Multiple Sclerosis	*PADI3,GFAP,PADI4,PADI6*	12.06	1.30E-03
	Rheumatoid Arthritis	*PADI3,GFAP,PADI4,PADI6*	10.05	2.90E-03
	Osteosarcoma	*CCL7,RECQL4,CCL8*	15.55	3.70E-03
	Werner Syndrome	*RECQL4, CCDC103*	41.47	3.90E-03
	Myoclonus	*GFAP, MEIS1*	27.65	8.00E-03
Excessive Daytime Sleepiness	Diamond-Blackfan Anemia	*HOMER2, RPS17*	103.05	1.60E-03

Enrichment was tested using WebGestalt[66] from a list of genes in each association signal for the primary analysis for each trait, boundaries of the association signal are defined by 400kb windows around each SNP. Categories containing at least two different loci were included.

Supplementary Table 7. Transcription factor binding site enrichment in candidate sleep duration, insomnia symptoms, and excessive daytime sleepiness genes from significant loci.

Trait	**Transcription Factor**	**Fold Enrichment**	**Adjusted P-value**	**Genes**
Sleep Duration	*HSF1*	12.22	1.00E-02	*FOXP2,MDFIC, UNC79, IL36RN*
Insomnia Symptom	*MIF1 (HERPUD1)*	31.59	9.00E-04	*CCDC103, BOP1, EFTUD2, HSF1*
Excessive Daytime Sleepiness	*MEF2 (V$AMEF2_Q6)*	16.37	2.64E-02	*JUN, PPP2R2B, FAM46A*

Enrichment was tested using WebGestalt[66] from a list of genes in each association signal, boundaries of the association signal are defined by SNPs with pairwise linkage disequilibrium (r^2) >= 0.20.

Supplementary Table 8. Replication in UK Biobank of genetic variants previously reported to be associated with sleep duration, insomnia symptoms, or excessive daytime. sleepiness

Trait	**SNP**	**Gene**	**Chr:position NCBI 37**	**Alleles (E/A)**	**Imputation Quality**	**MAF**	**Beta (SE)**	***p*-val**	***Bonferroni corrected p*-val**	**Meta Analysis *p-val***	**First author, Year**	**PMID**	**Original Trait**
Sleep Duration													
	rs11932595	*CLOCK*	4:56323597	G/A	1.00	0.399	-0.001 (0.004)	0.822	1	0.952	Allebrandt, 2010	20149345	Sleep Duration
	rs12649507	*CLOCK*	4:56380484	A/G	1.00	0.305	0.00 (0.005)	0.982	1	0.747			Sleep Duration
	rs11046205	*ABCC9*	12:21992326	A/G	0.99	0.184	-0.001 (0.005)	0.801	1	0.422	Allebrandt, 2013	22105623	Sleep Duration
	rs4780805	*TMC5*	16:19404645	G/A	0.98	0.144	0.003 (0.006)	0.591	1	0.219	Byrne, 2013	23728906	Sleep Duration
	rs11214607	*DRD2*	11:113312139	G/T	0.97	0.159	0.013 (0.006)	0.025	0.48	8.451E-05	Cade, 2015	26464489	Sleep Duration
	rs17601612	*DRD2*	11:113317745	C/G	0.99	0.383	-0.014 (0.004)	1.406E-03	**0.027**	5.435E-07			Sleep Duration
	rs6599077	*MYRIP*	3:40096618	A/G	1.00	0.279	-0.001 (0.005)	0.809	1	-	Gottlieb, 2007*	17903308	Sleep Duration
	rs1823125	*PAX-8*	2:114090412	G/A	1.00	0.219	0.038 (0.005)	9.953E-14	**1.89E-12**	1.852E-22	Gottlieb, 2014	25469926	Sleep Duration
	rs1191685	*PAX-8*	2:114094984	G/C	1.00	0.410	-0.020 (0.004)	2.508E-06	**4.77E-05**	4.616E-13			Sleep Duration
	rs4587207	*IER3/DDR1*	6:30766945	G/A	1.00	0.140	-0.006 (0.006)	0.320	1	1.040E-04			Sleep Duration
	rs10914351	*PTPRU*	1:30234031	T/G	1.00	0.021	0.029 (0.015)	0.047	1	0.012	Oillila, 2014	25109461	Sleep Duration
	rs1037079	*PCDH7/CENTD1*	4:32590048	T/C	0.98	0.044	-0.024 (0.010)	0.021	0.40	0.079			Sleep Duration
	rs2031573	*KLF6*	10:4001897	T/C	0.98	0.190	0.001 (0.005)	0.798	1	0.755			Sleep Duration
	rs17043459	*DPP10*	2:115493714	A/G	0.75	0.000	0.342 (0.378)	0.365	1	0.599	Scheinfeldt, 2015	26333835	Sleep Duration
	rs16900727	*CDH6*	5:31150659	C/A	0.27	0.000	-0.401 (0.408)	0.326	1	0.546			Sleep Duration
	rs41463746	*ELOVL*	6:10983568	T/C	0.13	0.000	1.098 (0.989)	0.267	1	0.135			Sleep Duration
	rs17122013	*SORCS1*	10:108820205	C/A	0.61	0.000	0.098 (0.244)	0.688	1	0.459			Sleep Duration
	rs7096948	*FAM204A/ PRLHR*	10:120187299	G/C	0.74	0.000	0.392 (0.393)	0.318	1	0.566			Sleep Duration
	rs41348446	*ARNTL*	11:13259561	A/G	0.56	0.000	0.036 (0.143)	0.802	1	0.562			Sleep Duration
Insomnia Symptoms							OR (95%CI)						
	rs521704	*GBP1*	1:89680554	A/C	1.00	0.488	0.995 [0.973-1.018]	0.648	1	0.208	Byrne, 2012	22754043	Caffeine induced insomnia adj for IFS
	rs4822498	*ADORA2A*	22:24876800	C/T	0.99	0.399	0.982 [0.959-1.005]	0.142	1	0.050		22754043	Caffeine induced insomnia
	rs11174478	*SLC2A13*	12:40354244	A/G	0.98	0.390	1.001 [0.977-1.024]	0.963	1	0.330	Byrne, 2013	23728906	Insomnia Factor Score
	rs7304986	*CACNA1C*	12:2438105	C/T	1.00	0.016	0.989 [0.902-1.084]	0.912	1	0.405		23728906	Sleep Latency
	rs2302729	*CACNA1C*	12:2783972	C/T	0.99	0.168	1.012 [0.981-1.043]	0.484	1	0.834		23728906	Insomnia
	rs1986116	*WNCG*	14:77513844	C/T	0.99	0.240	0.989 [0.963-1.016]	0.315	1	0.052		23728906	Sleep quality
	rs1823068	*PDE4D*	5:58676049	G/A	0.97	0.141	1.033 [0.999-1.067]	0.057	1	-	Gottlieb, 2007*	17903308	Sleepiness
	rs1154155	*TRA*	14:23002684	G/T	1.00	0.151	1.014 [0.982-1.047]	0.399	1	0.001	Hallmayer, 2009	19412176	Narcolepsy
	rs2858884	*HLA-DQ2*	6:32700083	C/A	1.00	0.223	1.001 [0.974-1.029]	0.936	1	0.481	Hor, 2010	20711174	Narcolepsy
	rs16826005	*NCKAP1*	2:134266001	G/A	1.00	0.040	1.017 [0.959-1.078]	0.430	1	0.173	Peer , 2013	23646285	HLA negative essential hypersomnia
	rs10988217	*CRAT*	9:131888116	G/A	1.00	0.394	0.998 [0.975-1.022]	0.579	1	0.811		23646285	HLA negative essential hypersomnia
	rs11854769	*SPRED1*	15:38502243	T/C	0.99	0.250	0.987 [0.961-1.013]	0.696	1	0.880		23646285	HLA negative essential hypersomnia
Excessive Daytime Sleepiness							Beta (SE)						
	rs1986116	*WNCG*	14:77513844	C/T	0.99	0.240	-0.006 (0.005)	0.247	1	0.065	Byrne, 2013	23728906	Sleep quality
	rs1823068	*PDE4D*	5:58676049	G/A	0.97	0.141	0.007 (0.006)	0.269	1	-	Gottlieb, 2007*	17903308	Sleepiness
	rs1154155	*TRA*	14:23002684	G/T	1.00	0.150	-0.005 (0.006)	0.354	1	0.994	Hallmayer, 2009	19412176	Narcolepsy
	rs2858884	*HLA-DQ2*	6:32700083	C/A	1.00	0.223	-0.001 (0.005)	0.790	1	0.408	Hor, 2010	20711174	Narcolepsy
	rs12425451	*TEAD4*	12:3164923	T/C	0.95	0.277	-0.003 (0.005)	0.504	1	0.880	Luca, 2013	23496005	Age at onset of cataplexy in narcolepsy
	rs16966122	*THEG5*	19:32158464	G/A	1.00	0.170	0.005 (0.006)	0.360	1	0.168		23496005	ESS
	rs2859998	*UBXN2B*	8:59324162	A/G	1.00	0.299	-0.005 (0.005)	0.240	1	0.091		23496005	Age at onset of EDS in narcolepsy
	rs5770917	*CPT1B*	22:51017353	C/T	1.00	0.048	-0.002 (0.01)	0.831	1	0.811	Miyagawa, 2008	18820697	Narcolepsy
	rs11854769	*SPRED1*	15:38502243	T/C	0.99	0.249	0.002 (0.005)	0.649	1	0.398	Peer, 2013	23646285	HLA negative essential hypersomnia
	rs10988217	*CRAT*	9:131888116	G/A	1.00	0.394	-0.002 (0.004)	0.653	1	0.825		23646285	HLA negative essential hypersomnia
	rs16826005	*NCKAP1*	2:134266001	G/A	1.00	0.040	0.018 (0.011)	0.097	1	0.044		23646285	HLA negative essential hypersomnia

Sleep trait GWAS results are adjusted for age, sex, genetic ancestry, and genotyping array. E=effect allele, A=alternative allele, MAF=minor allele frequency, SE=standard error, PMID=pubmed ID. **Bold indicates Bonferroni corrected p<0.0**5.
Meta-analysis performed using a sample size weighted approach in METAL. * indicated the original effect allele was unavailable, therefore Meta analysis was not performed.

Supplementary Table 9. Heritability of sleep duration, insomnia symptoms, and excessive daytime sleepiness partitioned across functional annotation class using LDSC.

	Sleep Duration			Insomnia Symptoms			Excessive Daytime Sleepiness		
Category	Fold Enrichment	SE	*p*-value	Fold Enrichment	SE	*p*-value	Fold Enrichment	SE	*p*-value
29 mammals conserved	14.160	4.700	**5.11E-03**	15.052	4.189	**7.96E-04**	18.037	4.975	**6.15E-04**
29 mammals conserved, extended	1.761	0.306	1.27E-02	2.023	0.309	**9.22E-04**	1.523	0.355	1.41E-01
3-PrimeUTR	-2.261	3.751	3.85E-01	3.368	3.545	5.04E-01	-0.177	4.339	7.86E-01
3-PrimeUTR, extended	-1.216	1.954	2.57E-01	1.643	1.645	6.96E-01	0.620	1.928	8.44E-01
5-PrimeUTR	-2.651	6.903	5.97E-01	2.428	4.887	7.70E-01	9.022	7.606	2.92E-01
5-PrimeUTR, extended	-0.687	1.662	3.10E-01	0.415	1.558	7.07E-01	0.578	2.141	8.44E-01
Coding	1.433	3.943	9.12E-01	1.076	3.601	9.83E-01	1.880	4.315	8.38E-01
Coding, extended	-1.497	1.019	1.43E-02	0.643	0.926	7.00E-01	0.207	1.116	4.77E-01
CTCF	-6.797	3.688	3.45E-02	-1.885	3.389	3.95E-01	-1.526	4.718	5.92E-01
CTCF, extended	1.011	1.274	9.93E-01	0.524	1.118	6.71E-01	1.081	1.589	9.59E-01
DGF	-1.199	1.641	1.80E-01	0.357	1.290	6.18E-01	-1.509	1.890	1.84E-01
DGF, extended	1.001	0.277	9.98E-01	1.245	0.232	2.91E-01	1.607	0.328	6.44E-02
DHS	0.820	1.453	9.01E-01	1.958	1.262	4.48E-01	-2.099	1.761	7.84E-02
DHS peaks	-0.619	1.769	3.60E-01	1.028	1.653	9.87E-01	-2.881	2.162	7.27E-02
DHS, extended	1.117	0.335	7.28E-01	2.053	0.315	**8.39E-04**	1.305	0.406	4.52E-01
Enhancer	4.409	1.644	3.81E-02	4.408	1.741	5.03E-02	1.456	2.195	8.36E-01
Enhancer, extended	2.125	0.631	7.44E-02	2.957	0.665	3.24E-03	0.328	0.936	4.73E-01
FetalDHS	-2.488	2.229	1.18E-01	3.854	1.899	1.33E-01	-0.318	2.545	6.04E-01
FetalDHS, extended	1.471	0.541	3.84E-01	2.852	0.549	**7.37E-04**	1.666	0.699	3.41E-01
H3K27ac	1.494	0.206	1.65E-02	1.358	0.175	4.05E-02	0.880	0.232	6.04E-01
H3K27ac, extended	1.060	0.303	8.42E-01	1.658	0.305	3.08E-02	0.660	0.411	4.08E-01
H3K4me1	1.667	0.358	6.27E-02	1.995	0.395	1.18E-02	0.377	0.471	1.86E-01
H3K4me1 peaks	3.223	1.090	4.14E-02	3.626	1.004	8.94E-03	0.525	1.355	7.26E-01
H3K4me1, extended	1.243	0.150	1.06E-01	1.402	0.144	5.13E-03	1.278	0.204	1.73E-01
H3K4me3	1.058	0.756	9.39E-01	2.996	0.842	1.77E-02	2.159	1.009	2.51E-01
H3K4me3 peaks	0.498	2.641	8.49E-01	5.872	2.726	7.39E-02	4.109	3.243	3.38E-01
H3K4me3, extended	1.261	0.449	5.62E-01	1.992	0.420	1.82E-02	0.083	0.625	1.42E-01
H3K9ac	1.506	0.910	5.78E-01	3.951	0.907	**1.15E-03**	1.250	1.191	8.33E-01
H3K9ac peaks	0.014	2.776	7.22E-01	3.982	2.856	2.96E-01	5.782	4.013	2.33E-01
H3K9ac, extended	1.516	0.466	2.68E-01	1.947	0.409	2.05E-02	0.710	0.529	5.83E-01
Intron	1.062	0.142	6.64E-01	1.189	0.154	2.20E-01	1.109	0.184	5.53E-01
Intron, extended	1.126	0.128	3.24E-01	1.019	0.115	8.70E-01	1.273	0.161	9.02E-02
Promoter	0.197	2.121	7.05E-01	5.554	2.211	3.94E-02	3.822	2.813	3.16E-01
Promoter Flanking	3.365	6.817	7.29E-01	9.261	5.879	1.60E-01	3.390	7.954	7.64E-01
Promoter Flanking, extended	3.433	1.933	2.08E-01	3.538	1.859	1.72E-01	1.043	2.525	9.86E-01
Promoter, extended	2.388	1.298	2.85E-01	2.875	1.186	1.14E-01	1.337	1.540	8.27E-01
Repressed	0.905	0.350	7.86E-01	0.879	0.339	7.21E-01	0.442	0.507	2.71E-01
Repressed, extended	0.931	0.091	4.44E-01	0.770	0.078	**3.28E-03**	0.898	0.119	3.90E-01
SuperEnhancer	1.148	0.263	5.73E-01	1.780	0.274	**4.38E-03**	1.524	0.338	1.21E-01
SuperEnhancer, extended	1.285	0.238	2.30E-01	1.433	0.255	9.03E-02	1.582	0.335	8.20E-02
TFBS	2.492	1.864	4.24E-01	3.450	1.211	4.31E-02	0.792	1.579	8.95E-01
TFBS, extended	1.420	0.479	3.81E-01	1.898	0.422	3.33E-02	1.335	0.576	5.61E-01
Transcribed	1.101	0.423	8.12E-01	0.952	0.362	8.94E-01	1.684	0.580	2.38E-01
Transcribed, extended	0.891	0.156	4.84E-01	1.041	0.147	7.78E-01	1.007	0.158	9.64E-01
TSS	-5.445	3.438	6.09E-02	4.300	3.198	3.02E-01	7.675	4.255	1.17E-01
TSS, extended	3.446	1.699	1.50E-01	5.427	1.668	7.93E-03	2.037	2.206	6.38E-01
Weak Enhancer	9.976	4.425	4.25E-02	10.814	3.747	8.81E-03	5.142	4.841	3.92E-01
Weak Enhancer, extended	3.236	1.036	3.09E-02	3.017	0.909	2.65E-02	0.898	1.300	9.37E-01

Bold=significant after multiple testing correction. SE=standard error.

Supplementary Table 10. Conditional analysis of the *MEIS1* locus association signal with insomnia symptoms.

				Baseline		Adj rs113851554		Adj rs11693221		Adj rs2300478	
		Chr	Position hg19	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
MEIS1 lead insomnia symptoms SNP	rs113851554	2	66750564	1.26 (1.20 - 1.33)	9.10×10^{-19}	-	-	1.23 (1.12 - 1.36)	3.01×10^{-5}	1.28 (1.21 - 1.35)	1.27×10^{-17}
MEIS1 lead RLS GWAS SNP	rs2300478	2	66781453	1.04 (1.01 - 1.06)	1.04×10^{-2}	0.98 (0.95 - 1.01)	0.24	0.99 (0.97 - 1.02)	0.71	-	-
MEIS1 3'UTR RLS associated SNP	rs11693221	2	66799986	1.26 (1.19 - 1.33)	5.14×10^{-15}	1.03 (0.93 - 1.15)	0.54	-	-	1.26 (1.19 - 1.34)	1.35×10^{-13}

Conditioning on the lead SNP abolishes the lead regional association signal and shows no strong secondary association signals. Analysis conditional on previously reported RLS GWAS SNP rs2300478 does not alter insomnia symptoms association signals. Analysis conditional on rs11693221, a rare MEIS1 3' UTR SNP discovered by sequence analysis and also associated with RLS, attenuates the lead association signal. Associations are additionally adjusted for age, sex, ancestry PCs, and genotyping array.

Supplementary Table 11. Common genetic variants for restless legs syndrome (RLS) associate with increased insomnia symptoms in the UK Biobank.

							Restless Legs Syndrome*	**Periodic Limb Movements***	**Insomnia Symptoms (n=58,702)**	
SNP	**CHR**	**BP**	**Gene region**	**Alleles (E/A)**	**Imputation quality**	**MAF**	**OR**	**OR**	**OR(95%CI)**	***p*-val**
rs113851554#	2	66,750,564	*MEIS1*	T/G	1	0.057	4.42	n/a	1.26 (1.20 - 1.33)	9.10 x10^{-19}
rs2300478#	2	66,781,453	*MEIS1*	G/T	1	0.252	1.68	1.28	1.04 (1.01 - 1.06)	1.04x10^{-2}
rs6747972	2	68,070,225	*intergenic (MEIS1)*	A/G	1	0.424	1.23	1.04	1.02 (1.00 - 1.05)	9.67x10^{-2}
rs9357271	6	38,365,873	*BTBD9*	T/C	1	0.209	1.47	1.45	1.02 (0.99 - 1.04)	0.498
rs1975197	9	8,846,955	*PTPRD*	A/G	0.98	0.179	1.29	1.3	1.03 (1.00 - 1.06)	8.69x10^{-2}
rs12593813	15	68,036,852	*MAP2K5/ LBXCOR1*	G/A	0.98	0.322	1.41	1.24	1.04 (1.01 - 1.06)	4.92x10^{-3}
rs3104767	16	52,624,738	*TOX3/BC034767*	G/T	1	0.411	1.33	1.29	1.03 (1.01 - 1.05)	6.57x10^{-3}
Weighted Genetic Risk Score RLS									**1.06 (1.05 - 1.07)**	**1.17x10^{-21}**
Weighted Genetic Risk Score RLS without rs113851554									**1.03 (1.02 - 1.03)**	**8.03x10^{-7}**
Weighted Genetic Risk Score PLM									**1.02 (1.01 - 1.03)**	**5.99x10^{-6}**

Insomnia symptom GWAS results are adjusted for age, sex, genetic ancestry, and genotyping array. E=effect allele, A=alternative allele, MAF=minor allele frequency, OR=Odds Ratio, CI=confidence interval, * single SNP effect estimates for Restless leg syndrome and periodic limb movements are from Winkelmann et a;, PLoS Genet 2011 and Moore et al.Sleep 2014. #these SNPs represent the same underlying MEIS1 association signal

Supplementary Table 12. Genetic correlation between sleep traits and 20 traits using LD-score regression

			Sleep Duration		Insomnia Symptoms		Excessive Daytime Sleepiness	
Phenotype	First author, Year	PMID	r_g	p-value	r_g	p-value	r_g	p-value
Birth Weight	Horikoshi, M. *et al*., 2013	23202124	**-0.270**	**7.51E-04**	-0.114	1.20E-01	0.042	6.25E-01
Height	Wood, A.R.*et al.* 2014	25282103	0.053	1.28E-01	-0.037	2.45E-01	0.008	7.87E-01
BMI	Locke, A.E. *et al.,* 2015	25673413	-0.092	1.51E-02	**0.147**	**5.11E-05**	**0.199**	**3.12E-09**
Waist Circumference	Shungin, D. *et al.,* 2015	25673412	-0.046	2.57E-01	**0.165**	**2.96E-05**	**0.199**	**2.12E-07**
Waist-Hip Ratio	Shungin, D. *et al.,* 2015	25673412	-0.001	9.86E-01	0.127	3.83E-03	0.101	1.09E-02
T2D	Morris, A.P. *et al*., 2012	22885922	0.140	3.98E-02	0.113	1.27E-01	0.049	5.01E-01
HOMA-IR	Scott, R.A. *et al.,* 2012	22885924	0.090	4.29E-01	**0.354**	**4.42E-04**	0.253	5.52E-03
Fasting Insulin	Scott, R.A. *et al.,* 2012	22885924	0.040	6.09E-01	**0.367**	**1.85E-07**	0.231	4.24E-03
Fasting Glucose	Scott, R.A. *et al.,* 2012	22885924	0.000	9.97E-01	**0.237**	**3.35E-04**	0.036	5.99E-01
Coronary Artery Disease	Nikpay, M. *et al.*, 2015	26343387	-0.044	5.45E-01	0.168	1.30E-02	0.111	1.29E-01
Crohn's Disease	Franke, A., et al., 2010	21102463	**0.183**	**1.87E-03**	-0.067	1.42E-01	0.008	8.84E-01
Rheumatoid Arthritis	Stahl, E.A., *et al.* 2010	20453842	0.011	8.71E-01	-0.041	5.27E-01	-0.037	5.81E-01
Neck BMD	Rivadeneira, F. *et al*, 2009	19801982	0.120	1.78E-02	-0.113	8.53E-03	0.030	5.73E-01
Schizophrenia	PGC *et al.* 2014	25056061	**0.290**	**1.90E-13**	-0.052	2.73E-01	0.065	8.90E-02
Bipolar	PGC *et al.* 2011	21926972	0.213	3.29E-03	-0.066	2.49E-01	0.052	4.47E-01
Depression	PGC *et al.* 2013	22472876	0.088	3.96E-01	**0.344**	**5.58E-04**	0.130	1.59E-01
Alzheimer's	Lambert, J. *et al.*, 2013	24162737	0.091	4.39E-01	-0.135	1.65E-01	-0.026	8.07E-01
Autism Spectrum	Robinson, E.B., *et al.,* 2016	26998691	-0.015	8.76E-01	0.056	4.77E-01	0.019	7.95E-01
Cigarettes per Day	TAG consortium, *et al.*, 2010	20418890	-0.176	9.84E-02	0.313	3.29E-03	0.146	2.17E-01
Years of Education	Rietveld, C.A. *et al.*, 2013	23722424	0.026	6.57E-01	**-0.278**	**3.22E-08**	-0.028	6.25E-01

After Bonferroni correction, p-value cut-off is 0.0025. T2D=type 2 diabetes, BMI=body mass index, BMD=bone mineral density.