

Supplemental Information

Supplemental Methods & Materials

Sample recruitment

The primary sources for the analyses presented here are three studies, all recruited from families ascertained through the Australian Twin Panel (twin cohorts 1 and 2, plus spouses of cohort 1), which used a coordinated assessment protocol and coordinated ascertainment of informative families, and sought interviews and blood from identified index cases selected from these families, their cotwins (if dizygotic), and their full siblings and available biological parents. Although a volunteer panel, the Australian Twin Panel closely approximates the socioeconomic diversity of Australia, with little evidence for sampling biases with respect to alcohol use/dependence phenotypes (1,2). The three studies were: (i) the NAG (Nicotine Addiction Genetics) study whose goal was gene-discovery for heaviness of smoking and nicotine dependence (3), which ascertained families with a heavy smoking index case (smoked 20 or more cigarettes per day regularly, or 40 or more cigarettes per day on one or more occasions) and one or more additional full siblings who were regular smokers; (ii) the OZALC-EDAC study, which ascertained index cases with a history of DSM-IV alcohol dependence or scoring above the 85th percentile for heaviness of drinking (the latter operationalized by a quantitative factor score that we have previously shown to have high genetic correlation with alcohol dependence: (4)), and with one or more full siblings who were alcohol users, in order to identify sibships that were extreme concordant or extreme discordant for heaviness of alcohol use; and (iii) the OZALC-BIGSIB study, which targeted index cases and their full siblings from large sibships comprised of 4 or more full siblings (range 4-14), to take advantage of the power of large sibships (5) for genetic linkage and association analysis of quantitative traits. In a few cases

BIGSIB sibships were extended to cousinships, through either the maternal or paternal side or both, with the largest cousinship having 32 individuals including linking parents. Since sibship size shows minimal correlation with alcohol and tobacco outcomes in ever users, BIGSIB-eligible families approximate a random sample, while the remaining NAG and EDAC families are high-risk families selected respectively for heaviness of tobacco or alcohol use. *Additional AD case and control series:* Additional alcohol dependent cases and controls were added who had previously been identified through interview surveys of twin cohorts 1 and 2 that targeted all members of each cohort. *Population control series:* Finally, SNP genotype data from an additional unscreened population control series, comprising 3393 individuals from an Australian adolescent twin-family study (6), were used for confirmatory case-population control comparisons. For population control families where GWAS data were available from both biological parents, only parental data were used. For families missing data for one or both parents, data from all available family members were used. In total, family-based analyses of alcohol dependence diagnosis were based on a total of 2062 cases with a diagnosis of alcohol dependence, 6692 controls (see Table S10). Since not all consumption measures were available for all respondents, smaller sample sizes are available for these latter measures. Confirmatory case-population control (CPC) comparisons were based on the same case series, and 3393 unassessed population controls.

Table S1 summarizes numbers of index cases screened, by cohort of origin and study eligibility; numbers of families entered into the research program (one or more members interviewed); and numbers of individuals interviewed, providing blood sample (95%) or buccal sample with consent for genotyping, and having GWAS genotyping. Although the OZALC/NAG studies targeted full siblings, checks on genetic relatedness identified a small

number of paternal or maternal half-sibling relationships (N=34 families, 1.4%), for which genetic relatedness was corrected before analysis. In all cases, the half-sibling relationship was either unknown to, or not reported at interview by, one or more family members. Table S2 summarizes the distribution of sibship size for individuals with GWAS genotyping. Because of assessment instrument differences in the previous surveys of twin cohorts 1 and 2, for some outcome variables data were not available for individuals from either or both of these cohorts who did not complete the NAG-OZALC interview (Table S3).

Assessments

The major diagnostic sections that were the primary focus of the study were (i) alcohol use and alcohol abuse/dependence – which included extensive characterization of current (past 12-months) and heaviest drinking period alcohol consumption patterns to supplement the diagnostic questions, where heaviest drinking period was required to be of at least 12 months duration; (ii) tobacco use and tobacco dependence – adapted from the Composite International Diagnostic Interview (CIDI) (7), with inclusion of the full Fagerström Test for Nicotine Dependence (FTND) (8) to supplement DSM-based dependence items; and (iii) major depression. Tobacco use and dependence were not assessed in the original interview survey of twin cohort 1. Additional diagnostic variables assessed for use as control variables which were selected for their established comorbidity with alcohol use disorder included conduct disorder, antisocial personality disorder (NAG-OZALC only), and anxiety disorders (social phobia, panic disorder). A non-diagnostic screen for history of bipolar disorder was included to permit exclusion of probable bipolar cases in post-hoc analyses. While additional quantitative measures of maximum alcohol tolerance (drinks before getting drunk or before feeling any effect of the

alcohol) were obtained in the cohort 2 and NAG-OZALC assessments, a subset of respondents found these items impossible to answer, and so they are not used here. An assessment of history of suicidal ideation and attempt from the Semi-Structured Assessment for the Genetics of Alcoholism (SSAGA), which was not limited to suicidality occurring in the context of an episode of major depression, which we have previously found to document important heritable influences (9), was also included.

Since the three coordinated studies were originally conceptualized with a narrow focus on gene-discovery, and to maximize response rate by family members by maintaining a relatively brief interview, there was minimal assessment of environmental exposures. However, an assessment of family history of alcoholism was included (assessed using items about parent history of excessive drinking and of alcohol-related problems with health, family, job or police or other problems). This was supplemented by questions about maternal and paternal educational levels (used to index rearing family socioeconomic status), history of parental separation during childhood, and self-report ancestry of grandparents.

Supplemental Results

Sample characteristics

Table S4 summarizes sample characteristics for the BIGSIB series, and for non-overlapping families from the OZALC-EDAC and NAG samples and additional cohort 1 and 2 participants, stratified by respondent DSM-IV alcohol dependence history. In general, there is consistency of heaviest period drinking patterns, by alcohol dependence history, regardless of study of origin, supporting the decision to conduct a joint analysis of data from the constituent samples. Not unexpectedly, the subsample selected solely because of index case eligibility for the NAG sample had the highest rate of nicotine dependence, as well as an elevated rate of parental heavy smoking. Several other important sample characteristics may be noted from Table S4: (i) Consistent with the age of the sample, relatively few report a history of comorbid marijuana dependence. Reports of history of conduct disorder, and especially antisocial personality disorder, are also relatively rare. (ii) Rates of major depression are approximately doubled in those with a history of alcohol dependence, but further elevated in NAG families selected through a heavy smoking proband. (iii) Within studies, there are not marked case-control differences in family-of-origin socioeconomic background, as indexed by maternal and paternal educational levels, but greater socioeconomic disadvantage in those from heavy smoking families. (iv) Rates of parental marital separation before offspring age 16 are very low, not only for the BIGSIB sample, but also for the OZALC-EDAC and NAG series, reflecting the restrictive Australian divorce laws through 1974. (v) Report of parental history of alcoholism was especially common in alcohol dependent individuals from the OZALC-EDAC study and alcohol dependent women from the BIGSIB study.

GWAS results in detail

SNPs showing nominal association at $p < .0001$ are tabulated in Tables S5 (HOD-FS), S6 (AUD-FS), S7 (AD-FS), S8 (weekly alcohol consumption) and S10 (alcohol dependence diagnosis). Corresponding Q-Q plots (Figures S1-S5) and Manhattan plots (Figures S6-S10) are also included. Table S9 summarizes SNPs with convergent evidence for association, operationalized as a nominal association at $p < .0001$ for a primary phenotype, and at $p < .005$ for a confirmatory phenotype.

Power calculations

Power of our study design, for a range of true effect sizes, is summarized in Table S11.

Table S1. Numbers of participants completing the core OZALC/NAG protocol, and additional twins from Cohort 1 and Cohort 2^a.

	OZALC/NAG	Additional Cohort 1	Additional Cohort 2
Index cases/twins			
- screened	3297 ^b	-	-
- interviewed	2774	4103	3127
- blood/buccal sample	2450	3184	733
- with Illumina GWAS data	2408	1842	401
Siblings			
- interviewed	6025	-	-
- blood/buccal sample	5283	-	-
- with Illumina GWAS data	4115	-	-
Biological parents ^c			
- interviewed	889	-	-
- blood/buccal sample	2320	-	-
- with Illumina GWAS data	929	-	-

^a Not included here are unassessed population controls with Illumina GWAS data comprising 1552 parents, and an additional 1478 adolescent twins from families with either or both parents not having genotyping data.

^b An additional 29 siblings completed a screening interview in families where the index case was unavailable for screening.

^c Parental interview did not assess alcohol consumption/dependence history. GWAS, genome-wide association study.

Table S2. Distribution of sibship size for individuals with alcohol-related interview data and Illumina GWAS data.

Number of sibships	All Projects	
	Families	Individuals
1	1276	1276
2	1330	2660
3	481	1443
4	304	1216
5	207	1035
6	89	534
7	44	308
8	13	104
9	10	90
10 or more	9	100
Total	3763	8766

Table S3. Availability of alcohol symptom/factor measures as a function of sample-of-origin. Individual respondents will have missing data for additional variables because of item-level non-response.

	OZALC/NAG	Additional Cohort 1	Additional Cohort 2
Symptoms			
AD factor score	√	√	- ^a
AUD factor score	√	√	- ^a
Heaviest period consumption			
Max drinks	√	√	√
Frequency of any use	√	-	√
Drinks per drinking day	√	-	√
Drinks per week	√	-	√
Frequency drunk	√	-	√
Frequency 5+ drinks	√	-	√
HOD factor score	√	-	√
Past 12 –month consumption			
Max drinks	√	√	√
Frequency of any use	√	√	√
Drinks per drinking day	√	√	√
Drinks per week	√	√	√
Frequency drunk ^b	√	-	-
Frequency 5+ drinks ^b	√	-	-

^a Not used because of small numbers with GWAS and variant factor loadings.

^b Not reported in this paper, since not available in most datasets collected by other investigators with current consumption data.

AD, alcohol dependence; AUD, alcohol use disorder; GWAS, genome-wide association study; HOD, heaviness of drinking.

Table S4. Sample characteristics, stratified by study-of-origin, DSM-IV alcohol dependence history and gender. Study-of-origin is defined hierarchically, so that families who were eligible for both BIGSIB and OZALC-EDAC or NAG studies were assigned to BIGSIB, and families who were eligible for ALC-EDAC and NAG samples were assigned to OZALC-EDAC; remaining individuals are subdivided by twin cohort. Not included here are data from parents, who did not complete an alcohol assessment. Only individuals with GWAS data are included.^a

	BIGSIB				OZALC-EDAC				NAG			
	Unaffected		Affected		Unaffected		Affected		Unaffected		Affected	
	F	M	F	M	F	M	F	M	F	M	F	M
<i>N</i> =	2095	1359	310	517	455	381	320	500	169	172	28	71
Age (\bar{x})	46.4	46.7	40.9	42.4	42.2	45.0	37.5	40.9	47.2	49.5	46.2	47.8
Alcohol Use Variables												
Initiation < age 15 (%)	3.3	8.1	13.9	20.9	7.9	10.5	17.5	21.8	6.5	4.1	10.7	14.1
Max drinks (median)	7	18	15	30	10	22	15	30	8	20	14.5	30
Heaviest 12-Month Period												
Weekly intoxication (%)	13.9	24.9	61.3	70.0	29.5	36.8	70.0	71.0	16.0	30.0	50.0	59.2
Weekly heavy use (%)	30.8	58.9	89.7	94.4	57.1	72.2	88.8	94.0	43.2	63.4	82.1	94.4
Drinks per drinking day (\bar{x})	3.2	4.6	6.2	7.4	4.1	5.5	5.7	7.2	4.1	4.8	5.7	9.6
Number of symptoms (\bar{x})	0.7	1.1	4.0	4.1	1.1	1.4	4.0	4.1	0.8	1.3	3.8	4.2
Past 12 Months												
Max drinks (median)	4	6	5.5	12	5	8	8	12	4	8	6.5	12
Weekly intoxication (%)	1.1	3.3	14.8	22.1	4.0	6.6	15.3	25.8	4.1	4.7	10.7	19.7
Weekly heavy use (%)	6.6	24.1	35.8	53.2	14.5	34.1	35.9	57.4	17.2	32.0	42.9	62.0
Drinks per drinking day (\bar{x})	2.2	3.0	3.4	4.4	2.4	3.2	3.4	4.5	2.8	3.2	3.4	5.4
Psychiatric Comorbidity												
Nicotine dependence (%)	28.7	28.1	57.1	54.1	41.4	38.4	62.7	51.3	69.2	71.4	81.5	81.4
Major depression (%)	27.0	18.1	51.8	34.9	27.0	15.8	49.2	33.3	34.9	20.7	61.5	32.4
Conduct disorder (%)	0.8	2.3	4.6	10.5	1.3	2.7	6.9	9.0	2.5	1.2	0	8.5
Antisocial personality disorder (%)	0.2	0.8	2.3	5.4	0.2	1.1	2.5	5.8	0.6	0.6	0	1.4
Marijuana dependence (%)	1.5	2.7	11.6	11.8	1.5	3.7	13.5	13.0	3.6	1.2	7.4	2.9

Table S4 (continued)

	BIGSIB				OZALC-EDAC				NAG			
	Unaffected		Affected		Unaffected		Affected		Unaffected		Affected	
	F	M	F	M	F	M	F	M	F	M	F	M
<i>N</i> =	2095	1359	310	517	455	381	320	500	169	172	28	71
Family Background Variables												
Maternal education <=10 years (%)	52.7	47.8	48.4	42.6	47.5	43.6	40.0	42.8	54.4	47.7	57.1	47.9
Paternal education <=10 years (%)	47.2	43.0	44.2	41.2	38.7	37.8	37.5	37.2	45.6	37.8	60.7	39.4
Maternal alcoholism history (%)	5.5	3.5	10.0	6.0	10.3	5.3	15.3	8.2	6.5	7.0	14.3	12.7
Paternal alcoholism history (%)	27.7	20.1	45.5	34.2	31.0	25.2	41.6	40.4	25.4	18.6	17.9	31.0
Maternal heavy smoking history (%)	14.1	14.3	22.6	21.5	27.3	21.8	33.8	27.4	36.7	32.0	35.7	32.4
Paternal heavy smoking history (%)	39.8	45.7	57.4	58.6	55.2	52.8	53.4	60.4	59.2	65.7	57.1	62.0
Paternal separation before respondent age 16 (%)	2.8	1.7	4.5	2.9	6.2	3.9	6.6	5.0	4.1	7.0	14.3	7.0

Table S4 (continued)

	Additional Cohort 1				Additional Cohort 2			
	Unaffected		Affected		Unaffected		Affected	
	F	M	F	M	F	M	F	M
<i>N</i> =	1369	374	45	54	236	108	29	28
Age (\bar{x})	45.6	41.4	41.6	39.1	30.1	29.8	29.9	29.3
Alcohol Use Variables								
Initiation < age 15 (%)	15.1	24.5	25.7	33.3	14.0	25.0	24.1	46.4
Max drinks (median)	6	15	14	26	9	18	15	38
Heaviest 12-Month Period								
Weekly intoxication (%)	-	-	-	-	20.1	34.6	34.5	57.1
Weekly heavy use (%)	-	-	-	-	37.2	63.5	93.1	92.9
Drinks per drinking day (\bar{x})	-	-	-	-	3.8	4.9	6.7	5.6
Number of symptoms (\bar{x})	0.5	1.0	3.7	3.8	0.8	1.3	3.9	4.5

Table S4 (continued)

	Additional Cohort 1				Additional Cohort 2			
	Unaffected		Affected		Unaffected		Affected	
	F	M	F	M	F	M	F	M
<i>N</i> =	1369	374	45	54	236	108	29	28
Past 12 Months								
Max drinks (median)	4	7	7	12	-	-	-	-
Weekly intoxication (%)	-	-	-	-	-	-	-	-
Weekly heavy use (%)	-	-	-	-	-	-	-	-
Drinks per drinking day (\bar{x})	1.9	3.0	2.8	4.5	2.3	3.3	3.6	9.1
Psychiatric Comorbidity								
Nicotine dependence (%)	-	-	-	-	18.6	19.4	41.4	46.4
Major depression (%)	21.3	14.4	53.3	37.0	25.0	18.5	55.2	25.0
Conduct disorder (%)	1.8	12.1	17.8	35.2	0.9	0.0	0.0	17.9
Antisocial personality disorder (%)	-	-	-	-	-	-	-	-
Marijuana dependence (%)	-	-	-	-	4.2	6.5	13.8	28.6
Family Background Variables								
Maternal education <=10 years (%)	66.5	55.3	75.0	65.8	37.6	30.7	46.4	25.9
Paternal education <=10 years (%)	54.6	49.5	47.2	57.9	37.8	18.0	32.1	50.0
Maternal alcoholism history (%)	4.0	1.4	13.6	3.9	6.9	9.4	27.6	18.5
Paternal alcoholism history (%)	16.9	14.2	38.1	25.0	20.9	16.2	33.3	25.9
Maternal heavy smoking history (%)	6.2	5.3	17.2	10.0	-	-	-	-
Paternal heavy smoking history (%)	40.6	19.4	33.3	42.5	-	-	-	-
Paternal separation before respondent age 16 (%)	1.0	3.0	4.6	0.0	12.7	12.0	13.8	7.1

^a Excludes a small number of unrelated individuals who were ascertained for an alcohol dependent case – unrelated control series because of low cell frequencies.

F, female; M, male.

Table S5. SNPs showing nominal association ($p < .0001$) with heaviness of drinking factor score (HOD-FS) (Ns = 6194-6300).

SNP	Chr	Pos(bp)	p-value	Allele	Effect	h2	Gene	Class	MAF
rs760943	1	12521021	6.2E-05	T	-0.149	0.30%		nongenic	0.09
rs10889272	1	62175137	1.0E-04	T	0.078	0.28%	INADL	intron	0.36
rs195207	1	115529471	8.5E-05	C	0.099	0.28%		nongenic	0.16
rs195204	1	115535614	9E-06	T	0.1	0.36%		nongenic	0.24
rs844656	1	171502458	7.9E-05	T	-0.173	0.28%		nongenic	0.07
rs3753563	1	173189969	7.7E-05	C	-0.082	0.29%	RABGAP1L	intron	0.35
rs884895	2	19048477	7.4E-05	G	0.106	0.28%	FLJ41481	intron	0.12
rs6746923	2	113269897	1.8E-05	G	0.084	0.34%		nongenic	0.4
rs16834223	2	136910906	4.2E-05	A	0.158	0.30%		nongenic	0.08
rs10496746	2	136923552	2.6E-05	T	0.088	0.32%		nongenic	0.28
rs2033172	2	136956774	6.2E-05	G	0.085	0.29%		nongenic	0.24
rs6766181	3	27075294	2.4E-05	C	0.082	0.33%		nongenic	0.46
rs2369955	3	134176278	1.5E-06	A	-0.136	0.42%		nongenic	0.16
rs10935045	3	134282836	1.7E-06	C	-0.131	0.42%	TMEM108	intron	0.17
rs3961460	3	154798914	1.2E-05	T	0.109	0.35%		nongenic	0.13
rs1563749	4	17681598	7.7E-05	C	-0.091	0.29%		nongenic	0.22
rs9291662	4	17688615	1.0E-04	G	-0.089	0.28%		nongenic	0.22
rs2320289	4	17771202	4.9E-05	A	-0.097	0.31%		nongenic	0.23
rs1004064	4	38135015	8.5E-05	G	-0.153	0.29%		nongenic	0.1
rs1109501	4	71364079	5.2E-06	G	0.1	0.38%		nongenic	0.24
rs6600832	4	71388097	3.6E-05	T	-0.08	0.32%		nongenic	0.42
rs2867709	4	81469465	9.1E-05	A	0.083	0.28%		nongenic	0.28
rs2582662	5	16325637	2.6E-05	A	0.083	0.31%		nongenic	0.38
rs7727185	5	86213347	1.4E-05	A	0.115	0.35%		nongenic	0.13
rs2410729	5	86375643	4.7E-05	A	0.113	0.30%		nongenic	0.14
rs7715840	5	86386634	4.3E-05	C	0.093	0.31%	LOC645261	intron	0.23
rs2544689	5	86410514	6.3E-05	T	0.093	0.29%		nongenic	0.22
rs1004988	5	86446754	3.6E-05	G	0.112	0.30%		nongenic	0.13
rs2032793	5	86486061	7.9E-05	G	0.111	0.28%		nongenic	0.13
rs1737727	6	35012466	5.5E-05	T	0.101	0.31%	ANKS1	intron	0.22
rs2140418	6	35083393	4.4E-05	C	0.102	0.31%	ANKS1	intron	0.22
rs7775895	6	107993215	5.6E-05	G	0.111	0.29%	FLJ10159	intron	0.14
rs728260	7	9869882	2.0E-05	A	0.082	0.33%	LOC340268	intron	0.44
rs2915125	7	9873235	2.5E-05	C	0.081	0.32%	LOC340268	intron	0.09
rs2915131	7	9892555	2.0E-05	C	0.082	0.33%	LOC340268	intron	0.45
rs1557978	7	9932437	7.1E-05	C	-0.079	0.28%	LOC340268	intron	0.39
rs4961216	8	87830123	2.8E-05	A	0.18	0.29%		nongenic	0.05
rs971258	9	81919662	6.0E-05	T	0.086	0.30%		nongenic	0.27
rs10512096	9	81920153	5.6E-05	C	0.088	0.30%		nongenic	0.27
rs1328433	9	81933640	5.0E-05	G	0.088	0.31%		nongenic	0.27
rs10908907	9	91439404	6.3E-06	G	0.099	0.37%		nongenic	0.25
rs7867889	9	114934061	3.5E-05	G	-0.082	0.32%		nongenic	0.41
rs4979215	9	114943950	5.3E-05	T	-0.081	0.30%		nongenic	0.4
rs12247601	10	7651504	8.1E-05	T	-0.111	0.28%	ITIH5	intron	0.15
rs2247977	10	56642818	6.5E-05	A	0.175	0.30%		nongenic	0.05
rs10509177	10	64338054	9.6E-05	C	-0.144	0.28%		nongenic	0.05
rs977749	11	7340987	7.5E-05	T	-0.08	0.29%	SYT9	intron	0.32
rs4757574	11	17682950	1.0E-04	G	-0.085	0.28%		nongenic	0.26
rs755016	11	69630210	2.2E-05	G	0.083	0.33%	TMEM16A	intron	0.42
rs7940843	11	70203993	4.1E-05	C	-0.081	0.31%		nongenic	0.32
rs670821	13	21202216	9.0E-05	C	0.085	0.28%		nongenic	0.27
rs2094497	13	26808122	1.1E-05	C	-0.085	0.35%		nongenic	0.37

rs9512637	13	26818611	1.2E-07	C	-0.105	0.51%		nongenic	0.32
rs1380131	14	53142608	9E-06	C	0.147	0.36%		nongenic	0.07
rs8040009	15	90845343	3.1E-07	T	-0.123	0.48%	C15orf32	mRNA-utr	0.21
rs8060235	16	52823266	5.8E-05	G	0.078	0.30%		nongenic	0.42
rs363175	16	65413148	7.1E-05	C	0.08	0.29%	APPBP1	intron	0.38
rs422945	16	65424134	7.0E-05	T	0.08	0.29%		nongenic	0.38
rs8044334	16	79806436	8.9E-05	T	-0.079	0.29%	PKD1L2	intron	0.31
rs6117232	20	637537	9.5E-05	C	0.101	0.28%		nongenic	
rs6044991	20	17674623	9.6E-05	G					
rs1387616	21	19749070	5.6E-05	G	0.143	0.29%		nongenic	0.11
rs2827312	21	22553547	7.8E-06	G	0.089	0.36%		nongenic	0.32

Bp, base pair; Chr, chromosome; MAF, minor allele frequency; Pos, position; SNP, single nucleotide polymorphism.

Table S6. SNPs showing nominal association ($p < .0001$) with alcohol use disorder factor score (AUD-FS) (Ns = 7490-8209)^a.

SNP	Chr	Pos(bp)	p-value	Allele	Effect	h2	Gene	Class	MAF
rs1229430	1	165780042	0.00008	T	0.068	0.23%	CREG1	intron	0.37
rs11120594	1	213905713	0.00001	G	-0.078	0.27%	USH2A	intron	0.41
rs4329572*	1	233357545	0.0001	A	-0.071	0.22%	TOMM20	intron	
rs6716455	2	150834649	7.2E-07	G	0.123	0.35%		nongenic	0.13
rs7563911	2	201284529	6.6E-05	G	0.116	0.22%		nongenic	0.12
rs7566288*	2	202637185	8.9E-05	G	0.078	0.23%		nongenic	0.26
rs11710107	3	43448918	7.5E-05	A	0.078	0.23%	TMEM16K	intron	0.29
rs2888312	3	43459971	7.7E-05	G	0.078	0.22%	TMEM16K	intron	0.29
rs3930234	3	185698824	8.4E-06	C	0.104	0.28%		nongenic	0.15
rs2582662	5	16325637	5.5E-05	A	0.07	0.23%		nongenic	0.38
rs1389221	5	24920017	6.3E-05	T	0.092	0.23%		nongenic	0.21
rs2216712	5	37954460	7.9E-06	C	0.111	0.29%		nongenic	0.13
rs2548145	5	40170534	1.8E-06	G	-0.081	0.33%		nongenic	0.47
rs4273649	5	153100241	8.5E-05	G	-0.066	0.22%	GRIA1	intron	0.48
rs2963998	5	153157246	7.1E-05	T	-0.066	0.22%	GRIA1	intron	0.47
rs2273006	6	34959112	3.2E-05	T	0.1	0.25%	TAF11	intron	0.14
rs1737727	6	35012466	7.4E-06	T	0.098	0.29%	ANKS1	intron	0.22
rs847851	6	35012562	9.3E-06	G	0.087	0.29%	ANKS1	intron	0.27
rs847848	6	35014146	1.8E-05	T	0.104	0.27%	ANKS1	intron	0.14
rs2140418	6	35083393	4.3E-06	C	0.101	0.31%	ANKS1	intron	0.22
rs2436728	6	40473579	3.2E-05	G	-0.07	0.24%	LRFN2	intron	0.38
rs7768059*	6	103881999	8.6E-05	T	-0.124	0.23%		nongenic	0.07
rs11534045*	7	110723215	5.9E-05	G	0.074	0.24%	IMMP2L	intron	0.32
rs6962665*	7	110736802	6.5E-05	C	0.075	0.24%	IMMP2L	intron	0.32
rs7806781	7	112207308	6.6E-05	C	0.085	0.22%	FLJ13576	intron	0.16
rs10253361	7	121062465	3.1E-05	T	-0.071	0.25%		nongenic	0.38
rs7796556	7	141899504	5.5E-05	G	0.091	0.23%		nongenic	0.16
rs9299372	9	105344074	9.4E-05	C	0.068	0.22%		nongenic	0.38
rs1396554	9	105385131	9.8E-05	G	-0.066	0.22%		nongenic	0.41
rs7867889	9	114934061	7.1E-05	G	-0.068	0.23%		nongenic	0.41
rs4979215	9	114943950	2.1E-05	T	-0.074	0.26%		nongenic	0.4
rs11238042	11	70466648	5.2E-05	G	-0.074	0.24%		nongenic	0.32
rs17149719	11	86473581	1.1E-05	T	-0.13	0.28%	FLJ22104	intron	0.06
rs33153	12	30875105	6.5E-05	C	-0.074	0.23%		nongenic	0.26
rs203339	12	118721137	8.2E-05	T	-0.082	0.22%	CIT	intron	0.26
rs1556086	13	96776486	2.3E-05	A	-0.134	0.25%	MBNL2	intron	0.07
rs9556711	13	96814417	1.5E-06	G	-0.163	0.32%	MBNL2	intron	0.08
rs941612	14	51691418	7.4E-05	A	0.096	0.23%	LOC645417	locus	0.17
rs2414433	15	53831481	1.7E-05	C	-0.091	0.26%		nongenic	0.14
rs12443381	15	83115058	0.00005	G	-0.144	0.24%	ZNF592	intron	0.08
rs933769	15	93853746	1.5E-05	T	-0.094	0.27%		nongenic	0.19
rs10083941	18	48536120	1.2E-05	C	0.108	0.27%	DCC	intron	0.1
rs768048	18	48539396	8.1E-06	C	0.11	0.28%	DCC	intron	0.12
rs6508159	18	48542018	1.2E-05	C	0.108	0.27%	DCC	intron	0.12
rs10515956	18	48562430	4.9E-05	G	0.09	0.24%	DCC	intron	0.13
rs10469016	18	48580883	2.7E-05	G	0.095	0.25%	DCC	intron	0.14
rs4293630	21	46270219	8.1E-05	A	0.095	0.22%		nongenic	0.14

^a SNPs marked with an asterisk failed QC in at least one project, and have Ns = 7386 – 7427. For the remaining SNPs Ns = 7972 – 8105.

Bp, base pair; Chr, chromosome; MAF, minor allele frequency; Pos, position; QC, quality control; SNP, single nucleotide polymorphism.

Table S7. SNPs showing nominal association ($p < .0001$) with alcohol dependence factor score (AD-FS) ($N_s = 7386-8105$)^a.

SNP	Chr	Pos(bp)	p-value	Allele	Effect	h2	Gene	Class	MAF
rs1229430	1	165780042	5.6E-05	T	0.07	0.23%	CREG1	intron	0.37
rs11120594	1	213905713	7.6E-05	G	-0.07	0.22%	USH2A	intron	0.41
rs2033316	2	55994035	7.3E-05	A	-0.079	0.22%	EFEMP1	intron	0.17
rs10864971	2	118717122	8.6E-05	C	-0.068	0.22%		nongenic	0.31
rs6716455	2	150834649	9.2E-06	G	0.109	0.27%		nongenic	0.13
rs7563911	2	201284529	5.8E-05	G	0.116	0.23%		nongenic	0.12
rs7566288*	2	202637185	8.4E-05	G	0.078	0.23%		nongenic	0.26
rs750379	3	54086917	3.6E-05	C	-0.081	0.25%		nongenic	0.24
rs2369955	3	134176278	7.3E-05	A	-0.098	0.23%		nongenic	0.16
rs3930234	3	185698824	2.6E-05	C	0.098	0.25%		nongenic	0.15
rs2216712	5	37954460	1.2E-05	C	0.108	0.28%		nongenic	0.13
rs2548145	5	40170534	2.3E-05	G	-0.071	0.26%		nongenic	0.47
rs4273649	5	153100241	2.9E-05	G	-0.069	0.24%	GRIA1	intron	0.48
rs6889794	5	153103648	5.3E-05	G	-0.067	0.23%	GRIA1	intron	0.47
rs4128572*	5	153108908	7.9E-05	G	-0.068	0.23%	GRIA1	intron	0.47
rs7445323	5	153116978	9.8E-05	G	-0.065	0.21%	GRIA1	intron	0.47
rs2963998	5	153157246	1.8E-05	T	-0.071	0.26%	GRIA1	intron	0.47
rs888936	5	169856481	5.6E-05	T	-0.077	0.23%	KCNIP1	intron	0.22
rs2273006	6	34959112	4.5E-05	T	0.098	0.24%	TAF11	intron	0.14
rs1737727	6	35012466	6.6E-06	T	0.098	0.30%	ANKS1	intron	0.22
rs847851	6	35012562	2.3E-05	G	0.083	0.26%	ANKS1	intron	0.27
rs847848	6	35014146	2.7E-05	T	0.101	0.25%	ANKS1	intron	0.14
rs2140418	6	35083393	4.1E-06	C	0.1	0.31%	ANKS1	intron	0.22
rs9458121*	6	161442468	2.7E-05	A	-0.156	0.27%	MAP3K4	intron	0.08
rs11534045*	7	110723215	2.5E-05	G	0.077	0.27%	IMMP2L	intron	0.32
rs6962665*	7	110736802	2.3E-05	C	0.079	0.27%	IMMP2L	intron	0.32
rs7806781	7	112207308	4.5E-05	C	0.086	0.23%	FLJ13576	intron	0.16
rs10253361	7	121062465	5.9E-06	T	-0.076	0.29%		nongenic	0.38
rs10227063	7	121062713	5.2E-05	A	0.07	0.23%		nongenic	0.36
rs7796556	7	141899504	9.6E-05	G	0.088	0.22%		nongenic	0.16
rs11777086	8	8421889	8.9E-05	G	0.075	0.22%		nongenic	0.24
rs10956525	8	131512033	2.4E-05	T	0.092	0.25%		nongenic	0.17
rs7030400	9	19004645	6.8E-05	C	-0.11	0.22%	C9orf138	intron	0.13
rs7867889	9	114934061	4.8E-05	G	-0.07	0.24%		nongenic	0.41
rs4979215	9	114943950	1.3E-05	T	-0.075	0.27%		nongenic	0.4
rs1372325	10	90683549	7.6E-05	C	0.087	0.22%	ACTA2	locus	0.2
rs11238042	11	70466648	2.6E-05	G	-0.077	0.26%		nongenic	0.32
rs7925049	11	121957403	0.00003	A	-0.121	0.24%		nongenic	0.09
rs33153	12	30875105	0.0001	C	-0.072	0.22%		nongenic	0.26
rs1623319	12	74557023	9.3E-05	G	-0.074	0.22%		nongenic	0.28
rs2293050	12	116203205	8.7E-05	C	0.066	0.22%	NOS1	intron	0.48
rs1556086	13	96776486	9.6E-06	A	-0.139	0.27%	MBNL2	intron	0.07
rs9556711	13	96814417	8.2E-07	G	-0.167	0.33%	MBNL2	intron	0.08
rs1266294	14	45302604	7.6E-05	A	-0.068	0.23%		nongenic	0.4
rs1686312	14	45311247	9.5E-05	G	-0.067	0.22%		nongenic	0.4
rs4900680	14	45337935	8.9E-05	A	0.066	0.22%		nongenic	0.42
rs442555	14	58365937	9.8E-05	T	-0.097	0.21%		nongenic	0.2
rs933769	15	93853746	7.3E-06	T	-0.097	0.29%		nongenic	0.19
rs10083941	18	48536120	4.7E-05	C	0.1	0.23%	DCC	intron	0.1
rs768048	18	48539396	2.6E-05	C	0.103	0.25%	DCC	intron	0.12
rs6508159	18	48542018	3.9E-05	C	0.101	0.24%	DCC	intron	0.12
rs10469016	18	48580883	7.1E-05	G	0.089	0.22%	DCC	intron	0.14

rs7247916*	19	45508370	6.2E-05	A	-0.098	0.25%	nongenetic	
rs2827312	21	22553547	5.8E-05	G	0.07	0.23%	nongenetic	0.32
rs4293630	21	46270219	7.3E-06	A	0.108	0.28%	nongenetic	0.14

^a SNPs marked with an asterisk failed QC in at least one project, and have Ns = 7386 – 7423. For the remaining SNPs Ns = 8043 – 8105.

Bp, base pair; Chr, chromosome; MAF, minor allele frequency; Pos, position; QC, quality control; SNP, single nucleotide polymorphism.

Table S8. SNPs showing nominal association with 12-month weekly alcohol consumption (Ns = 7818-7907).

SNP	Chr	Pos(bp)	p-value	Allele	Effect	h2	Gene	Class	MAF
rs2275863	1	199595447	7.4E-05	G	0.118	0.24%	TNNT2	intron	0.08
rs2799686	1	199613938	1.6E-05	G	0.131	0.28%		nongenic	0.08
rs9808416	2	56417326	0.00002	C	0.114	0.27%	KIAA1912	intron	0.17
rs10197202	2	197231211	1.3E-05	A	0.086	0.28%	FLJ39660	intron	0.24
rs1248820	3	85014013	5.8E-05	T	0.073	0.24%		nongenic	0.33
rs10935342	3	140888032	6.7E-05	C	-0.077	0.23%		nongenic	0.38
rs10935348	3	140930190	2.8E-05	A	-0.074	0.26%		nongenic	0.45
rs11916446	3	166319066	9.1E-05	G	-0.072	0.23%		nongenic	0.23
rs4862932	4	32121171	7.4E-05	C	-0.069	0.23%		nongenic	0.48
rs2867709	4	81469465	4.9E-05	A	0.078	0.24%		nongenic	0.28
rs10516812	4	89697124	7.2E-05	C	0.165	0.23%		nongenic	0.07
rs979537	6	124024765	6.8E-05	T	-0.071	0.24%		nongenic	0.42
rs9322108	6	148086874	6.1E-05	G	0.07	0.24%		nongenic	0.5
rs395843	6	164398906	6.9E-05	C	-0.08	0.24%		intron	0.27
rs1111644	7	10419101	2.8E-05	G	-0.084	0.26%		nongenic	0.25
rs765805	7	10436059	6.4E-05	C	-0.084	0.24%		nongenic	0.17
rs2877260	7	55139123	4.7E-05	A	0.082	0.25%	EGFR	intron	0.24
rs237240	7	75048595	2.9E-05	C	0.144	0.26%	HIP1	intron	0.07
rs237238	7	75049350	7.2E-06	A	0.156	0.30%	HIP1	synon	0.07
rs10954654	7	139009627	8.4E-05	C	0.077	0.22%		nongenic	0.26
rs10113582	8	118878074	4.3E-05	T	0.139	0.24%		nongenic	0.06
rs2376397	9	76880569	1.1E-05	C	0.096	0.28%	C9orf95	intron	0.15
rs4748949	10	24843063	7.7E-05	G	-0.104	0.23%	KIAA1217	intron	0.12
rs4074967	12	5470727	5.6E-05	T	-0.098	0.24%		nongenic	0.14
rs1623319	12	74557023	2.9E-05	G	-0.081	0.26%		nongenic	0.28
rs7314267	12	74578155	4.1E-05	G	-0.116	0.25%		nongenic	0.1
rs4761378	12	76330817	3.3E-05	C	0.072	0.25%		nongenic	0.44
rs1347222	12	80918285	3.4E-05	C	-0.074	0.25%		nongenic	0.37
rs7961308	12	80928631	4.1E-05	T	0.074	0.24%		nongenic	0.33
rs898078	12	112947970	2.5E-05	G	-0.078	0.26%		nongenic	0.25
rs11620406	13	41458772	7.9E-05	C	0.089	0.23%		nongenic	0.13
rs1684716	14	41567781	6.8E-06	G	-0.077	0.29%		nongenic	0.47
rs1632694	14	41581597	6.5E-05	T	-0.069	0.23%		nongenic	
rs1684693	14	41618007	4.2E-05	G	-0.078	0.24%		nongenic	0.3
rs1542668	14	41618662	2.7E-05	G	-0.078	0.26%		nongenic	0.33
rs8006978	14	41703822	2.1E-05	G	-0.073	0.26%		nongenic	0.46
rs10135407	14	41714367	2.9E-05	A	-0.072	0.25%		nongenic	0.46
rs2154294	14	41725025	3.1E-06	G	0.08	0.32%		nongenic	0.44
rs1356410	15	40222129	3.5E-05	C	-0.076	0.25%	PLA2G4F	nonsynon	0.32
rs183008	16	12109192	2.8E-05	C	-0.073	0.26%	LOC92017	intron	0.42
rs350255	16	12113043	1.6E-05	G	-0.076	0.27%	LOC92017	intron	0.42
rs6501422	17	63901241	6.5E-05	T	0.173	0.24%	KIAA1001	intron	0.06
rs1221872	18	48384335	5.8E-05	G	-0.103	0.23%	DCC	intron	0.07
rs1221874	18	48385108	6.4E-05	G	-0.103	0.23%	DCC	intron	0.07
rs1221877	18	48387824	5.7E-05	G	-0.103	0.23%	DCC	intron	0.07
rs1221884	18	48389344	7.1E-05	G	-0.102	0.23%	DCC	intron	0.07
rs1944550	18	73144551	7.6E-05	A	0.09	0.23%		nongenic	0.16
rs30461	19	44480955	3.3E-05	A	-0.117	0.25%	IL29	nonsynon	0.12
rs3786949	19	44518319	2.5E-05	G	-0.144	0.26%	GMFG	intron	0.12
rs30454	19	44536016	7.1E-05	G	-0.112	0.23%	FLJ10211	intron	0.15
rs2827312	21	22553547	6.7E-05	G	0.071	0.23%		nongenic	0.32

Bp, base pair; Chr, chromosome; MAF, minor allele frequency; Pos, position; SNP, single nucleotide polymorphism.

Table S9. SNPs showing convergent evidence of association with heaviness of drinking and dependence measures (**primary measure significant at $p = 1E-4$** , highlighted in bold; secondary measure significant at $p = 5E-3$).

SNP	Chr	Pos(bp)	p Values				Nearest gene(s) [#]	r ² [#]
			HOD-FS	AUD-FS	AD (DSM-IV)	CPC		
rs195204 ^a	1	115535614	9.1E-6	2.0E-3				
rs844656 ^b	1	171502458	7.3E-5	6.6E-4			TNFSF4 .35	
rs11120594 ^c	1	213905713	3.6E-3	1.0E-5			USH2A	
rs6746923 ^d	2	113269897	1.7E-5	2.5E-3			IL1A, 1.0	
							CKAP2L, .67	
							NT5DC4 .65	
rs10496746 ^e	2	136923552	2.7E-5	2.9E-3		4.0E-3		
rs2033172 ^f	2	136956774	6.5E-5	3.0E-3				
rs2369955 ^g	3	134176278	1.6E-6	1.3E-4	1.5E-03		TMEM108, .58	
							ACAD11, .32	
							NPHP3 .32	
							TMEM108	
rs10935045 ^h	3	134282836	1.7E-6	6.4E-4				
rs3930234 ⁱ	3	185698824	1.9E-3	8.4E-6				
rs1004064 ^j	4	38135015	8.7E-5	2.0E-3				
rs2867709 ^k	4	81469465	9.3E-5	2.9E-3			FGF5, C4orf22 .92, .87	
rs2582662 ^l	5	16325637	2.6E-5	5.5E-5				
rs1389221	5	24920017	3.8E-3	6.3E-5				
rs2548145	5	40170534	4.1E-3	1.8E-6				
rs2544689 ^m	5	86410514	6.2E-5	2.1E-3				
rs1541918	5	171904091			1.1E-5	7.0E-3		
rs2273006	6	34959112	1.7E-3	3.2E-5			TAF11, 1.0	
							C6orf107, 1.0	
							ANKS1A 1.0	
rs1737727 ⁿ	6	35012466	5.5E-5	7.4E-6		3.4E-4	ANKS1A, 1.0	
							C6orf107, .64	
							TAF11 .64	
rs847851 ^o	6	35012562	5.4E-4	9.3E-6			TAF11, 1.0	
							C6orf107, 1.0	
							ANKS1A 1.0	
rs847848	6	35014146	1.3E-3	1.8E-5			ANKS1A, 1.0	
							C6orf107, 1.0	
							ANKS1A 1.0	
rs2140418 ^p	6	35083393	4.4E-5	4.3E-6		1.6E-4	ANKS1A, 1.0	
							TAF11, .80	
							C6orf107 .80	
rs2436728 ^q	6	40473579	3.4E-4	3.2E-5			LRFN2	
rs728260 ^r	7	9869882	2.0E-5	1.6E-3				
rs2915131 ^s	7	9892555	2.0E-5	3.5E-4				
rs1557978 ^t	7	9932437	6.9E-5	2.2E-3				
rs10089021	8	20683774			8.1E-5	3.0E-3		
rs4961216 ^u	8	87830123	2.8E-5	2.4E-4		1.3E-4	CN9B3, CNBD1 .41, .24	
rs9299372 ^v	9	105344074	3.4E-3	9.4E-5				
rs7867889 ^w	9	114934061	3.4E-5	7.1E-5				
rs4979215 ^x	9	114943950	5.4E-5	2.1E-5				

rs12247601 ^y	10	7651504	7.8E-5	3.9E-3			ITIH5	
rs786870 ^z	10	26814700			8.0E-5	1.0E-3	APBB1IP	
rs2789686 ^{aa}	10	81905116			1.4E-5	1.0E-3	ANXA11,	1.0
							MAT1A,	.71
							TSPAN14,	.57
							PLAC9	.43
rs7940843 ^{bb}	11	70203993	4.2E-5	2.5E-3			SHANK2	
rs11238042 ^{cc}	11	70466648	1.6E-3	5.2E-5			SHANK2	
rs2463107 ^{dd}	12	78617448	1.5E-4		5.3E-5		PAWR, SYT1	.84, .79
rs9556711 ^{ee}	13	96814417	1.0E-3	1.1E-6	4.6E-3		MBNL2, RAP2A	1.0, .28
rs8040009 ^{ff}	15	90845343	3.1E-7	1.0E-3			C15orf32,	1.0
							ST851A2	.38
rs9993769 ^{gg}	15	93853746	2.8E-3	1.6E-5				
rs16977135 ^{hh}	17	67704950	4.5E-4	5.4E-5				
rs10515956 ⁱⁱ	18	48562430	3.3E-3	5.0E-5			DCC	
rs4293630 ^{jj}	21	46270219	3.7E-3	7.2E-5			COL6A1	.72

AUD-FS, alcohol use disorder factor score; AD (DSM-IV), binary alcohol dependence diagnosis; CPC, AD (DSM-IV) vs. population control comparison; HOD-FS, heaviness of drinking factor score; Bp, base pair; Chr, chromosome; MAF, minor allele frequency; Pos, position; SNP, single nucleotide polymorphism.

Linkage disequilibrium (r^2) is listed if SNP is intergenic but in at least moderate LD with an intronic SNP in specified gene.

^a Also heaviest period frequency of heavy use ($p = 6.2E-6$), frequency drunk ($p = 2.0E-3$), drinks per drinking day ($p = 2.1E-4$) and max drinks ($p = 3.3E-3$).

^b Also heaviest period weekly alcohol consumption ($p = 3.2E-4$) and frequency of any use ($p = 9.9E-4$).

^c Also heaviest period frequency of heavy use ($p = 2.4E-3$) and 12-month max drinks ($p = 3.5E-3$).

^d Also heaviest period frequency of heavy use ($p = 3.6E-4$), drinks per drinking day ($p = 2.9E-3$), drinks per week ($p = 3.3E-3$) and max drinks ($p = 4.8E-3$), and 12-month drinks per week ($p = 3.0E-3$).

^e Also heaviest period weekly alcohol consumption ($p = 1.8E-5$), frequency ($p = 5.3E-4$), frequency of heavy drinking ($p = 1.0E-3$), and max drinks ($p = 1.4E-3$).

^f Also heaviest period weekly alcohol consumption ($p = 1.4E-4$), frequency ($p = 4.6E-3$), frequency of heavy drinking ($p = 1.4E-3$), frequency drunk ($p = 2.8E-3$) and max drinks ($p = 3.8E-3$).

^g Also heaviest period weekly alcohol consumption ($p = 2.7E-5$), frequency ($p = 4.9E-5$), frequency of heavy drinking ($p = 4.7E-6$) and frequency drunk ($p = 3.9E-5$).

^h Also heaviest period weekly alcohol consumption ($p = 4.2E-5$), frequency ($p = 1.9E-4$), frequency of heavy drinking ($p = 1.8E-5$), and frequency drunk ($p = 2.6E-4$).

ⁱ Also 12-month weekly consumption ($p = 3.2E-3$), drinks per drinking day ($p = 1.2E-3$), frequency drunk ($p = 5.7E-4$) and 12-month max drinks ($p = 2.2E-4$), and heaviest period frequency drunk ($p = 1.2E-3$) and max drinks ($p = 3.7E-3$).

^j Also heaviest period frequency drunk ($p = 6.8E-5$), frequency of heavy drinking ($p = 2.6E-3$) and weekly alcohol consumption ($p = 4.6E-3$).

^k Also heaviest period weekly alcohol consumption ($p = 3.8E-5$), frequency of heavy drinking ($p = 2.8E-4$) and drinks per drinking day ($p = 3.9E-3$), and 12-month weekly consumption ($p = 4.9E-5$), frequency drunk ($p = 5.1E-4$) and max drinks ($p = 3.7E-3$).

^l Also heaviest period weekly alcohol consumption ($p = 6.5E-4$), frequency ($p = 9.0E-4$), frequency drunk ($p = 6.3E-4$), frequency of heavy drinking ($p = 1.7E-5$) and max drinks ($p = 2.9E-3$).

^m Also heaviest period weekly alcohol consumption ($p = 2.0E-4$), frequency drunk ($p = 3.1E-3$), frequency of any use ($p = 3.1E-3$) and drinks per drinking day ($p = 5.0E-3$).

ⁿ Also heaviest period weekly alcohol consumption ($p = 6.3E-4$), frequency ($p = 4.1E-3$), frequency of heavy drinking ($p = 3.2E-4$) and max drinks ($p = 4.6E-3$).

^o Also heaviest period frequency heavy drinking ($p = 1.0E-3$).

- ^p Also heaviest period weekly alcohol consumption ($p = 6.7E-4$), frequency of heavy drinking ($p = 2.8E-4$), frequency ($p = 3.7E-3$), and max drinks ($p = 2.9E-3$).
- ^q Also heaviest period frequency of heavy drinking ($p = 4.8E-4$), weekly alcohol consumption ($p = 3.0E-3$), and frequency drunk ($p = 1.5E-3$).
- ^r Also heaviest period weekly alcohol consumption ($p = 2.0E-3$), frequency of heavy drinking ($p = 2.7E-4$), frequency drunk ($p = 2.5E-3$), max drinks ($p = 4.9E-3$) and drinks per drinking day ($p = 3.3E-3$).
- ^s Also heaviest period drinks per drinking day ($p = 2.6E-4$), frequency of heavy drinking ($p = 3.8E-4$), weekly alcohol consumption ($p = 1.8E-3$), max drinks ($p = 1.1E-3$) and 12-month frequency heavy drinking ($p = 4.6E-3$).
- ^t Also heaviest period max drinks ($p = 8.3E-5$), frequency of heavy drinking ($p = 5.5E-4$), and drinks per drinking day ($p = 1.9E-3$) and 12-month max drinks ($p = 3.1E-4$).
- ^u Also heaviest period frequency of use ($p = 3.8E-4$), frequency of heavy use ($p = 1.4E-3$) and weekly alcohol consumption ($p = 1.5E-3$).
- ^v Also heaviest period frequency of heavy use ($p = 1.8E-3$) and weekly consumption ($p = 4.9E-3$).
- ^w Also heaviest period frequency of heavy drinking ($p = 1.0E-5$), weekly consumption ($p = 8.3E-5$), frequency of any use ($p = 1.6E-4$), frequency drunk ($p = 1.2E-3$), max drinks ($p = 3.0E-3$) and current frequency of heavy drinking ($p = 2.3E-3$).
- ^x Also heaviest period frequency of heavy drinking ($p = 5.4E-6$), weekly alcohol consumption ($p = 2.9E-5$), frequency of any use ($p = 8.8E-5$), max drinks ($p = 4.3E-4$), drinks per drinking day ($p = 3.7E-3$), current frequency of heavy drinking ($p = 2.8E-4$) and drinks per drinking day ($p = 4.5E-3$).
- ^y Also max drinks ($p = 5.0E-3$).
- ^z Also current weekly consumption ($p = 1.9E-4$) and frequency of use ($p = 1.5E-3$).
- ^{aa} Also current frequency of heavy use ($p = 1.9E-3$).
- ^{bb} Also max drinks ($p = 5.1E-7$), heaviest period frequency of heavy drinking ($p = 2.5E-4$), weekly alcohol consumption ($p = 3.1E-4$), drinks per drinking day ($p = 1.5E-3$) and frequency drunk ($p = 3.4E-3$).
- ^{cc} Also heaviest period weekly alcohol consumption ($p = 7.4E-4$) and frequency of any use ($p = 2.6E-3$).
- ^{dd} Also heaviest period drinks per week ($p = 2.9E-4$), frequency of any use ($p = 3.7E-4$), frequency of heavy use ($p = 4.1E-3$) and max drinks ($p = 4.1E-3$).
- ^{ee} Also heaviest period drinks per week ($p = 2.1E-3$), frequency of heavy use ($p = 2.3E-3$) and frequency drunk ($p = 4.8E-3$).
- ^{ff} Also heaviest period frequency of heavy use ($p = 8.0E-6$), drinks per week ($p = 2.4E-5$), drinks per drinking day ($p = 4.7E-5$), frequency drunk ($p = 2.7E-3$) and max drinks ($p = 6.9E-4$).
- ^{gg} Also heaviest period drinks per week ($p = 4.0E-3$) and max drinks ($p = 1.1E-3$).
- ^{hh} Also heaviest period frequency of any use ($p = 5.2E-4$), drinks per drinking week ($p = 7.6E-4$) and frequency of heavy drinking ($p = 3.4E-3$).
- ⁱⁱ Also heaviest period frequency of heavy drinking ($p = 9.1E-4$), current frequency of any use ($p = 1.4E-4$), frequency of heavy use ($p = 1.6E-4$), drinks per week ($p = 2.9E-4$), drinks per drinking day ($p = 3.8E-3$) and 12-month max drinks ($p = 1.5E-3$).
- ^{jj} Also heaviest period frequency drunk ($p = 1.3E-3$), current weekly alcohol consumption ($p = 3.7E-3$) and 12-month max drinks ($p = 4.0E-3$).

Table S10. SNPs showing nominal association ($p < .0001$) with DSM-IV alcohol dependence diagnosis in family-based analyses (Ns = 1927-2062 cases, Ns = 4998-6692 controls^a).

SNP	Chr	Pos(bp)	p-value	Gene	Class	MAF
rs2001270	1	18276507	1.0E-04	C1orf21	intron	0.35
rs6731289	2	82746305	7.4E-05		nongenic	0.24
rs3769769	2	170384011	9.8E-06	METTL5	intron	0.24
rs1381471	2	170662652	3.8E-05		nongenic	0.27
rs788160	2	172654561	5.9E-05		nongenic	0.15
rs1882331	4	185360760	1.4E-05	ENPP6	intron	0.21
rs7717860	5	134218124	9.7E-05	FLJ37562	intron	0.12
rs1541918	5	171904091	1.1E-06		nongenic	0.13
rs7766862	6	32140985	3.4E-05	TNXB	intron	0.28
rs2071293	6	32170665	5.2E-05	TNXB	intron	0.27
rs1800624	6	32260365	5.4E-05	AGER	locus	0.15
rs4236064	6	39522005	4.1E-05	KIF6	intron	0.27
rs1321075	6	45499921	9.2E-05	RUNX2	intron	0.11
rs7775575	6	74915176	3.9E-05		nongenic	0.21
rs4724793	7	6281291	6.0E-05		nongenic	0.22
rs10089021	8	20683774	8.1E-05		nongenic	0.22
rs3911770	8	76974263	6.6E-05		nongenic	0.49
rs657152	9	135129086	4.1E-05	ABO	intron	0.38
rs786870	10	26814700	804E-05	APBB1IP	intron	0.19
rs2789686	10	81905116	1.4E-05	ANXA11	mRNA-utr	0.08
rs874651	11	11735950	7.9E-05		nongenic	0.16
rs656948	11	81430391	3.7E-05		nongenic	0.32
rs1785039	11	127405789	6.1E-05		nongenic	0.16
rs2463107	12	78617448	7.3E-05		nongenic	0.26
rs1344791	12	85988405	3.4E-05		nongenic	0.06
rs990324	13	32285246	2.0E-05		nongenic	0.09
rs679210	17	72557578	1.1E-06		nongenic	0.28

^a Ns = 2029-2062 cases, Ns = 5982-6692 controls excluding two SNPs (rs788160, rs1381471) which failed QC on one or more projects.

Bp, base pair; Chr, chromosome; MAF, minor allele frequency; Pos, position; QC, quality control; SNP, single nucleotide polymorphism.

Table S11. Study power. Assumes an additive genetic model with equal marker and trait allele frequencies and a residual full-sibling correlation of 0.30, with hypothesis-testing at $p = 5E-8$.

Effect size (QTL heritability)	Linkage Disequilibrium		
	D = 1	D = .9	D = .8
.01	99.9	99.3	94.0
.005	77.3	55.1	33.1
.0034	33.9	17.9	7.7
.0025	14.2	6.6	2.6
.0020	6.3	2.7	1.0
.0015	2.0	0.8	0.3
.0010	0.4	0.15	0.06

QTL, quantitative trait loci.

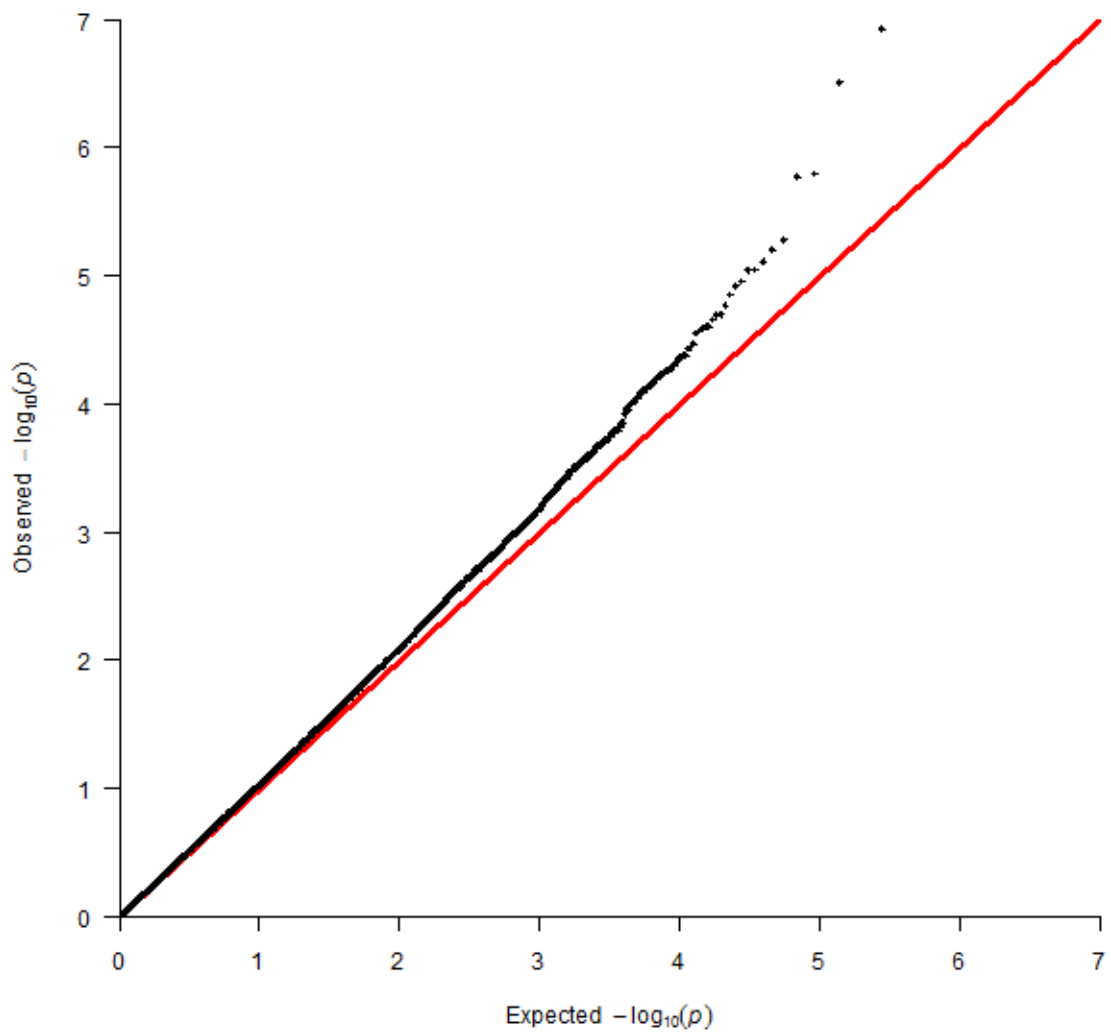


Figure S1. Q-Q plot for heaviness of drinking factor score (HOD-FS).

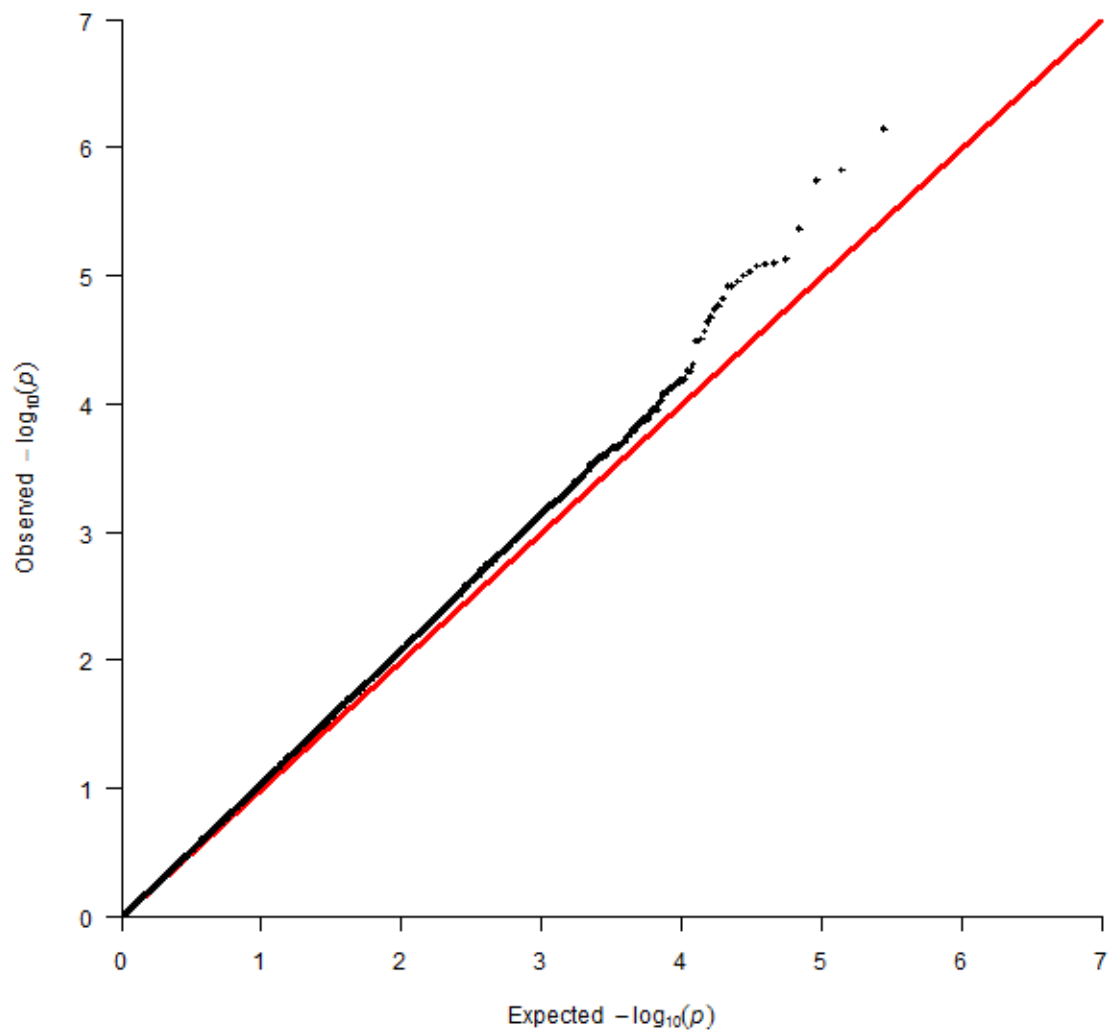


Figure S2. Q-Q plot for alcohol use disorder factor score (AUD-FS).

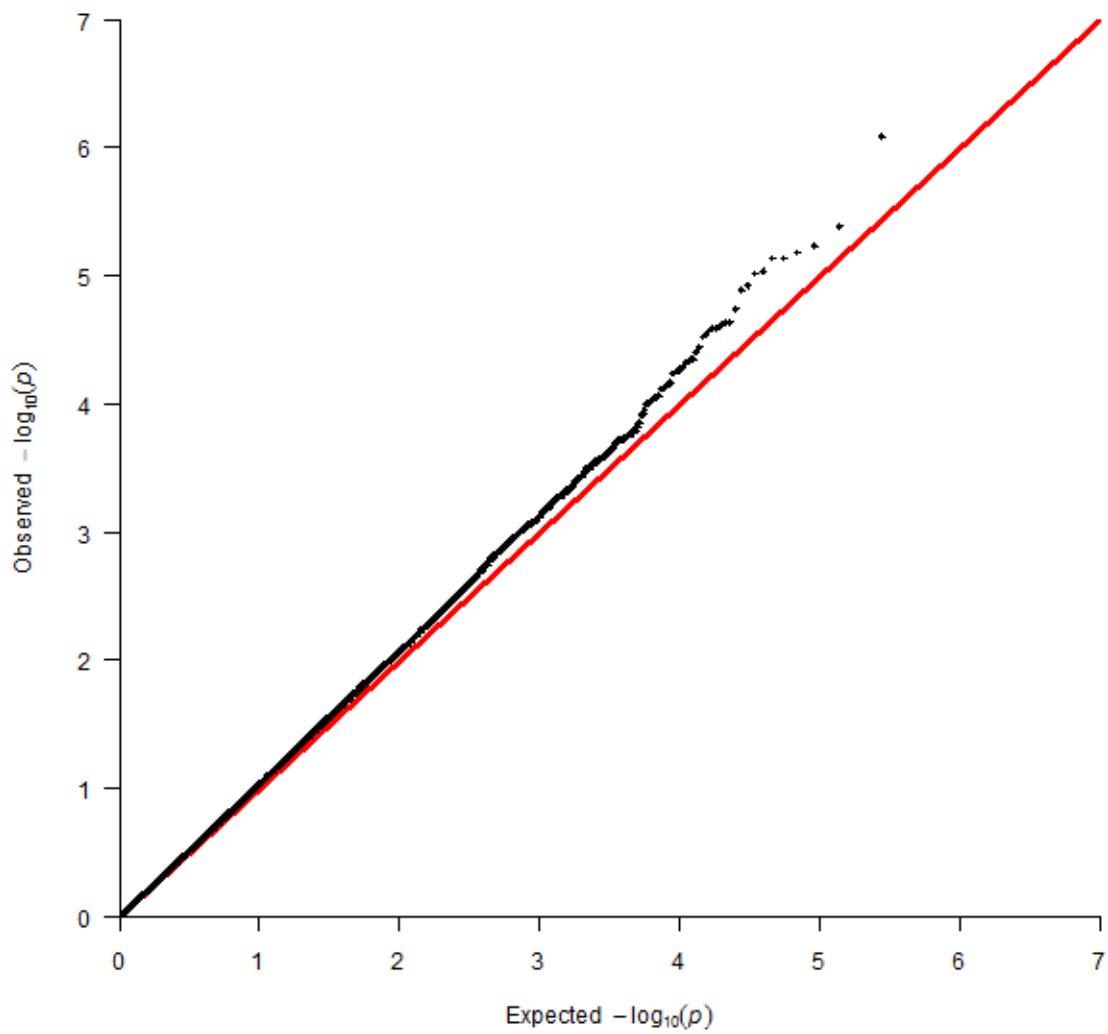


Figure S3. Q-Q plot for alcohol dependence factor score (AD-FS).

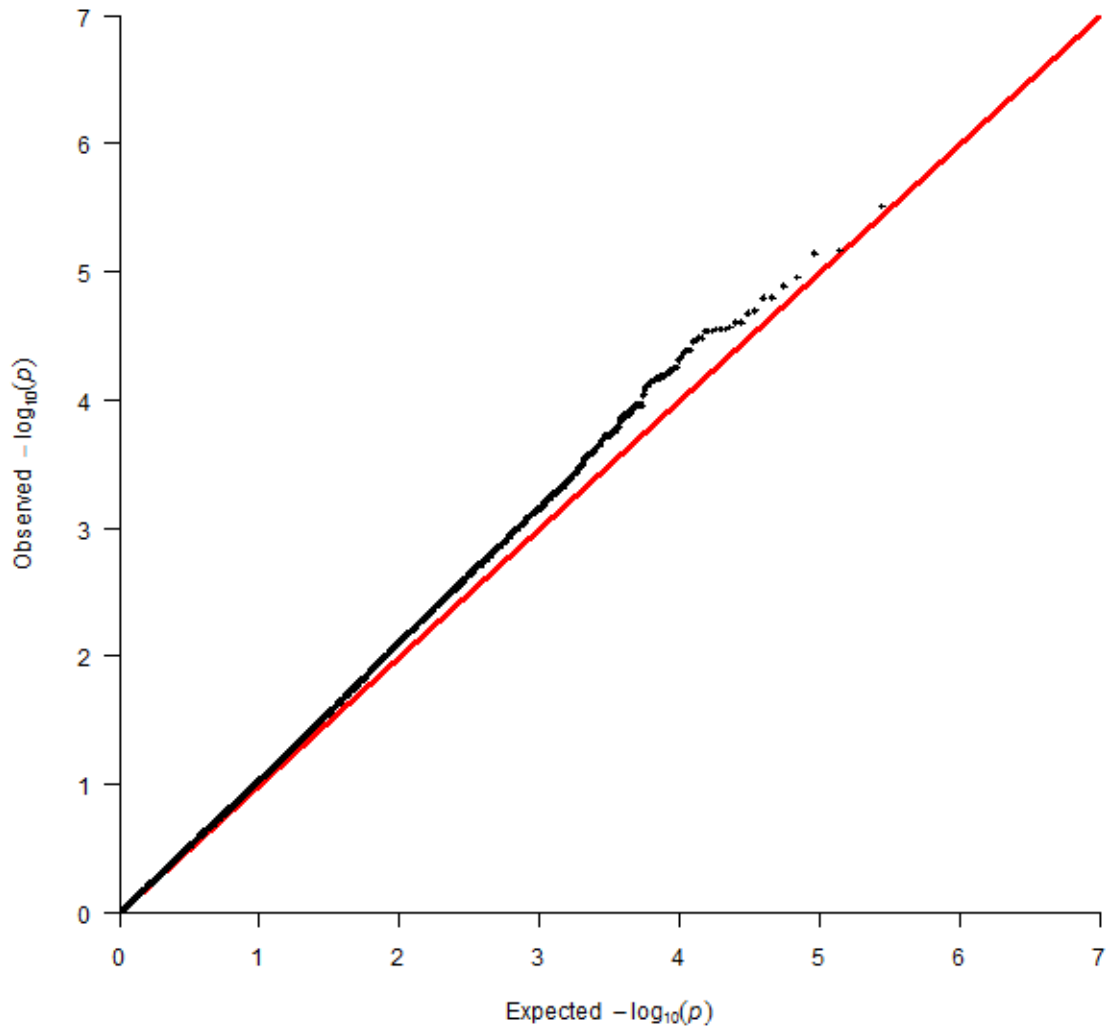


Figure S4. Q-Q plot for past 12-month weekly alcohol consumption.

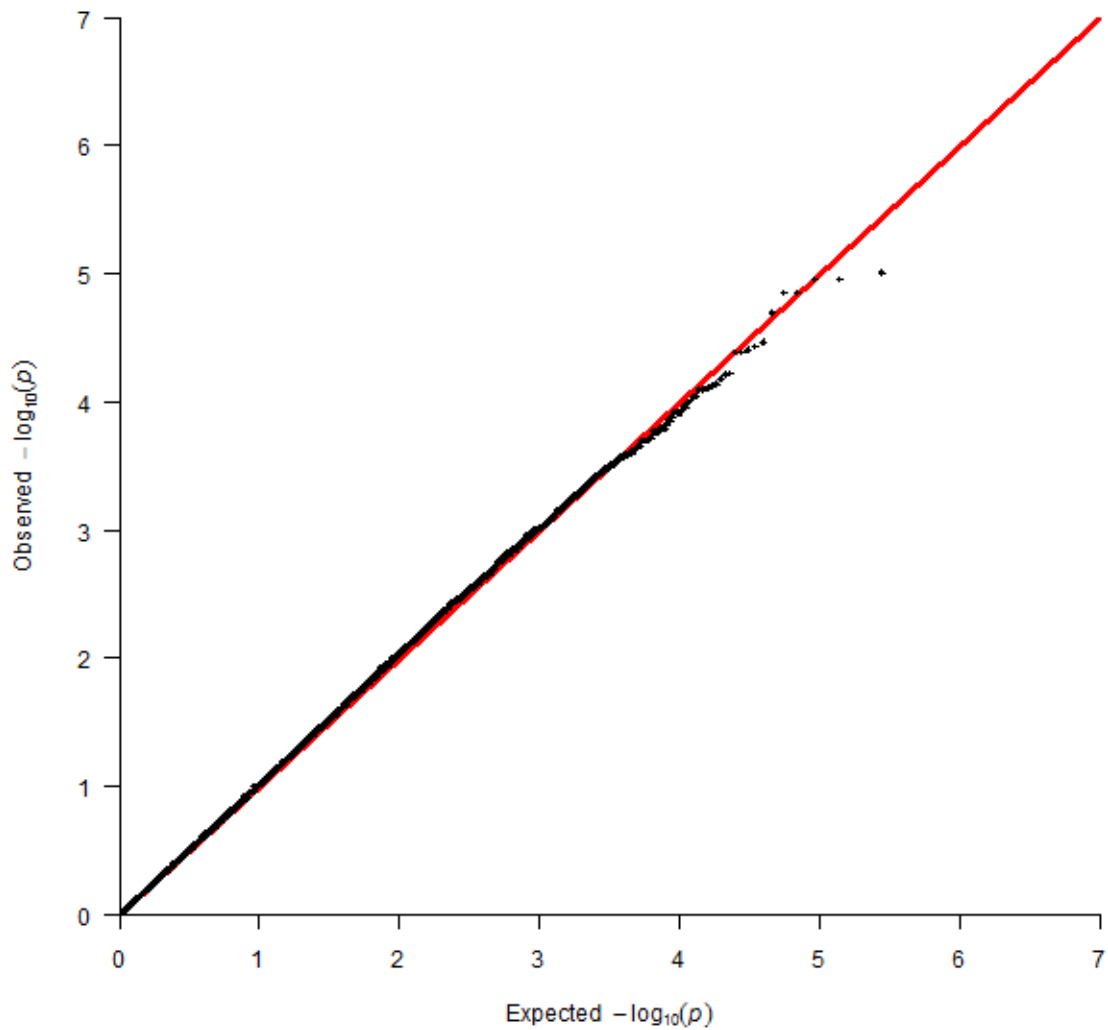


Figure S5. Q-Q plot for alcohol dependence diagnosis.

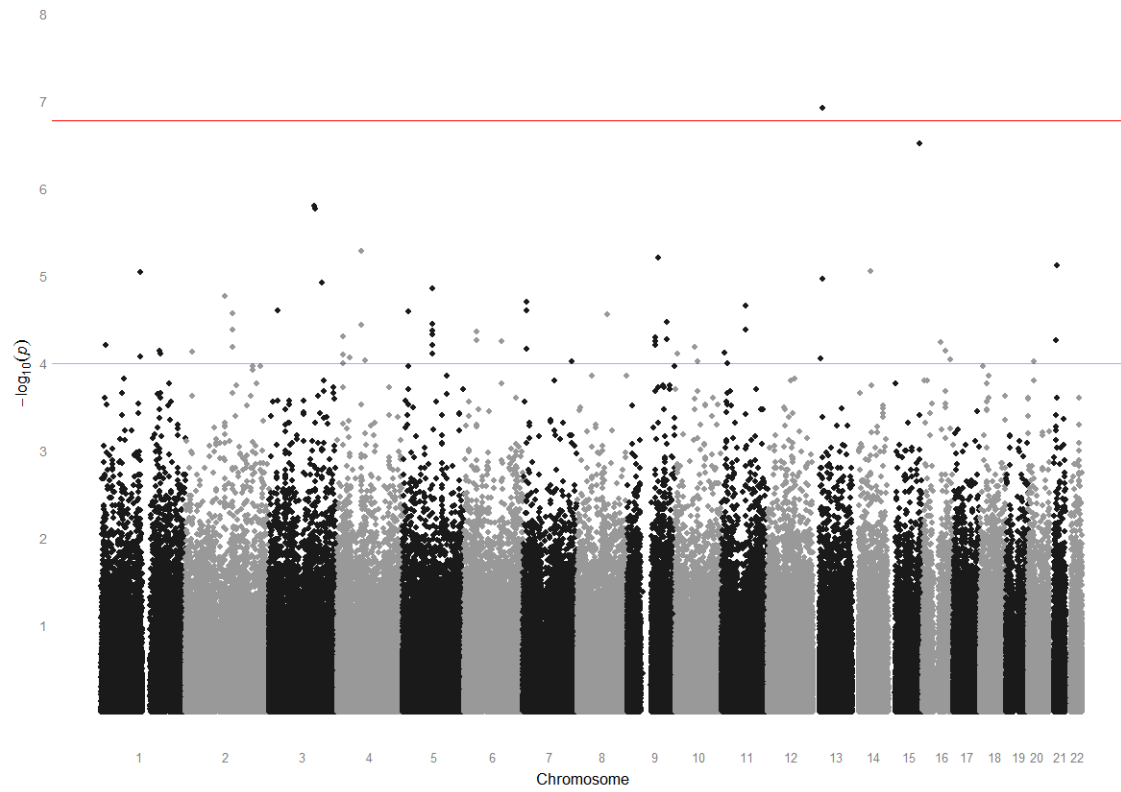


Figure S6. Manhattan plot for heaviness of drinking factor score (HOD-FS).

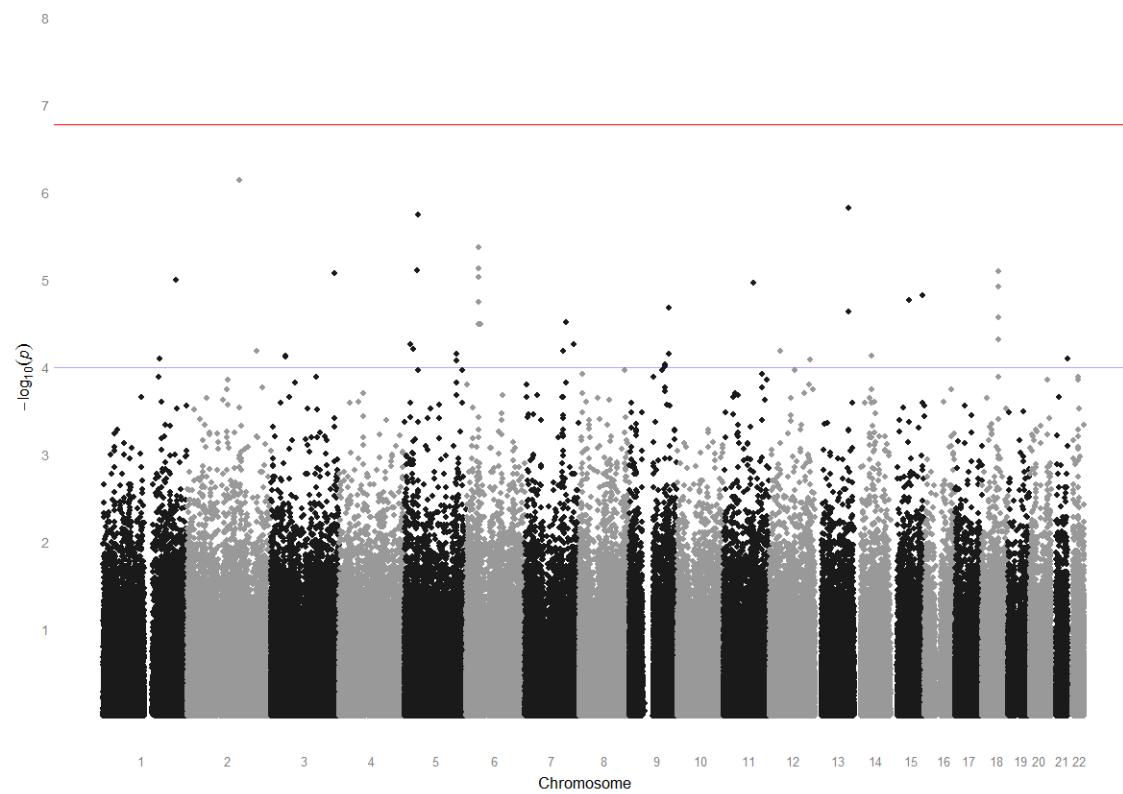


Figure S7. Manhattan plot for alcohol use disorder factor score (AUD-FS).

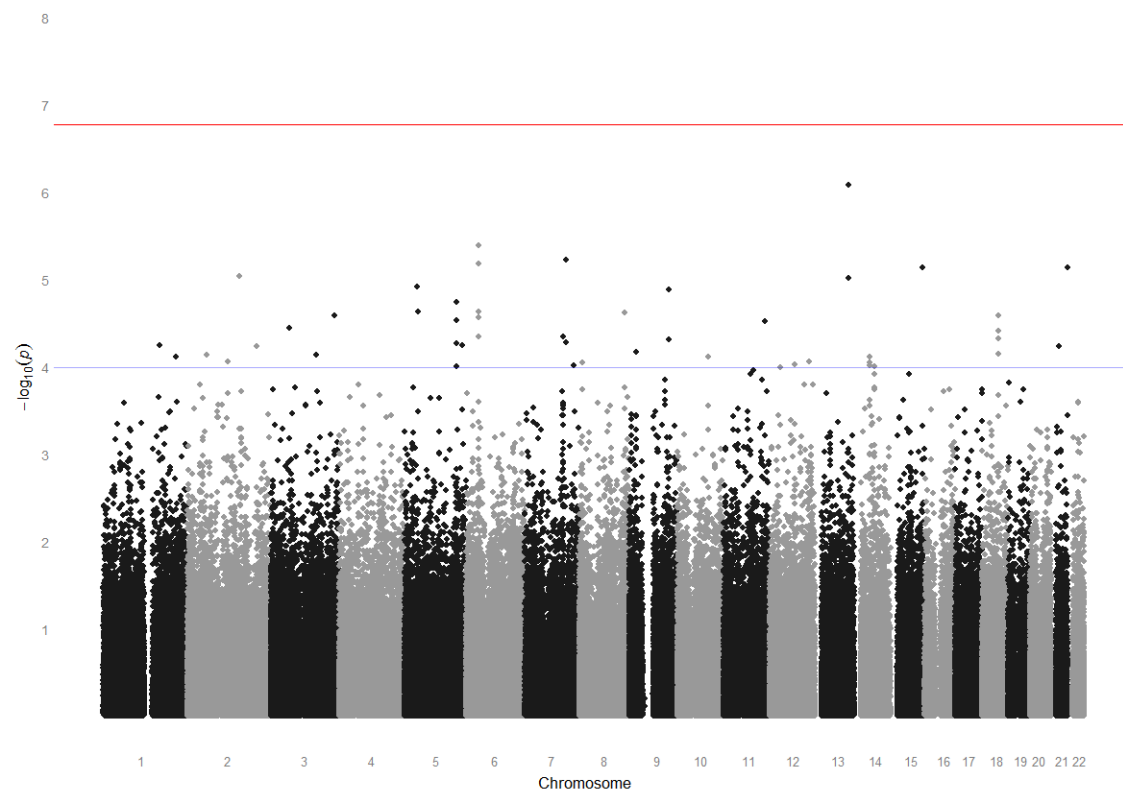


Figure S8. Manhattan plot for alcohol dependence factor score (AD-FS).

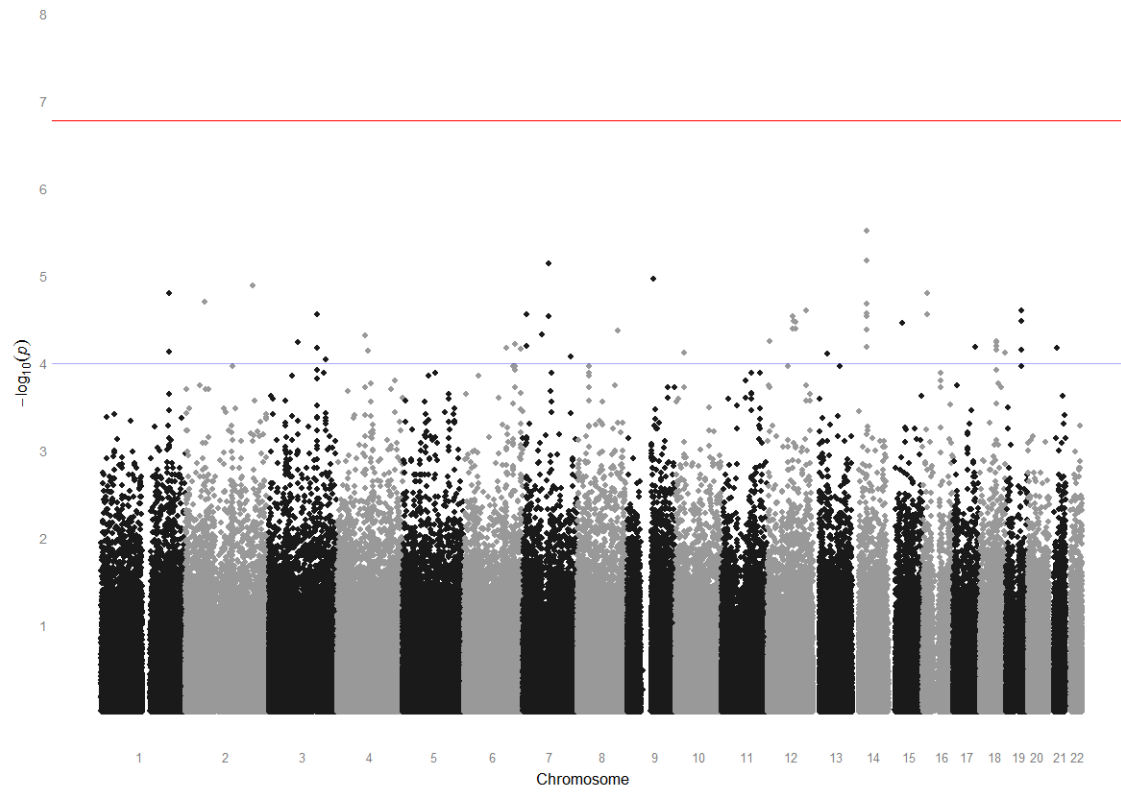


Figure S9. Manhattan plot for past 12-month weekly alcohol consumption.

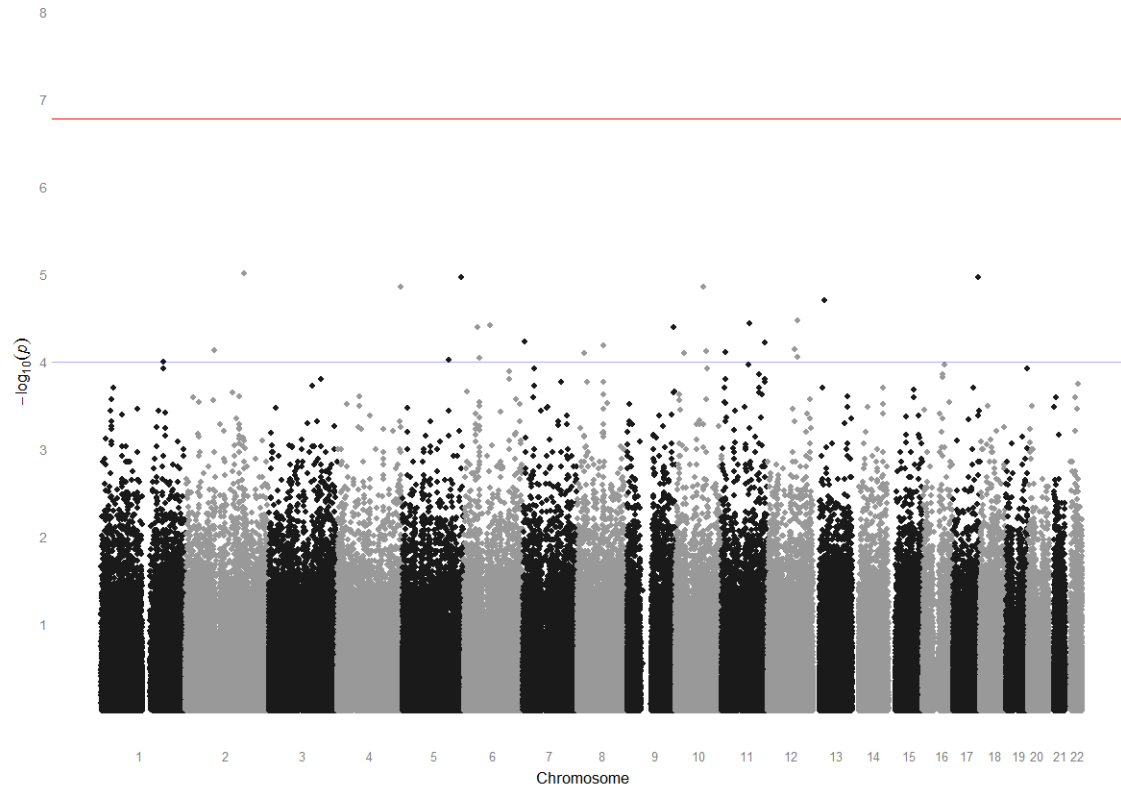


Figure S10. Manhattan plot for alcohol dependence diagnosis.

Supplemental References

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