ATTACHMENT 23

SAMPLE SIZE REQUIREMENTS FOR GENETIC ANALYSES

Numerous genetic variants (primarily SNP or related variants) previously identified as being related to alcohol use disorders and their associated disabilities appear in Figure A. These gene frequencies will form the basis of sample size calculations we can expect for any newly discovered or other genetic variants examined in the NESARC-III (such as CNVs). As can be seen in Table 1, these markers vary greatly in terms of their frequency, and the same marker may differ substantially in frequency within populations of different ancestry (Table 2). Second, sample size requirements for determining gene-environment or gene-gene interactions are substantially greater than those for detecting environmental or genetic effects alone. Finally, many phenotypes (outcomes) of interest have low lifetime prevalences, and a large sample size is required to ascertain a main genetic effect of large magnitude, i.e., a large odds ratio (OR). Typically, gene-disease associations between these variants have been empirically shown in the range of OR = 1.2 to 2.0. However, the current and major focus of gene-disease association studies is to identify CNVs and related variants (beyond SNPs) that relate to alcohol use disorders and their associated disabilities, and these variants are anticipated to be much more penetrant than SNPs, that is, have greater associations (OR >5.0) with the disease outcomes of the NESARC-III. To be conservative, we have retained the lower and more modest levels of associations previously found for SNP and related variants (OR = 1.2 to 2.0) in our sample size calculations. Accordingly, the required sample sizes shown in our calculations are very likely to be overestimates.

As illustrated in Figure B, for a condition such as alcohol dependence, depression or drug use disorders, all of which have a lifetime prevalence of approximately 13%, the sample size required to determine an OR of 1.2 ($p<.05$) in association with a given genetic variant (absent gene-environment or gene-gene interactions) varies from more than 40,000 for genetic variants with frequencies of only 5% to approximately 8,000 for

genetic variants with frequencies of 50%. Associations of greater magnitude, e.g. an OR of 1.5, can be established with far fewer cases, less than 10,000 for even rare genetic variants. However, the sample size requirements to ascertain an OR of 1.5 for a genetic variant for alcohol dependence are far greater when the intent is to examine gene-environment interactions, as illustrated in Figure C. For a relatively rare environmental factor with a prevalence of only 10%, a sample size of approximately 18,000 is required if the OR for the gene-environment interaction is assumed to be 2.0. For more common environmental factors whose prevalence is 25% or greater, the sample size requirement for an interaction OR of 2.0 drops to less than 10,000. The sample size calculations in Figure C also pertain to gene-gene interactions. The sample size of the NESARC III is thus sufficient for all of these purposes.

Sample size requirements are greater for outcomes with lower lifetime prevalence rates, such as most mood, anxiety and personality conditions. Figure D illustrates sample size requirements for conditions with a lifetime prevalence of 5%, which include, for example, generalized anxiety and specific and social phobias. The NESARC III sample will be adequate to determine fairly robust genetic associations (OR ≥ 1.5) for even rare genetic markers, and to determine more modest associations (e.g., OR = 1.2) with genetic markers whose prevalence is in excess of 12%, in the absence of gene-environment interactions. As illustrated in Figure E, for gene-environment interactions with OR=2.0, it will also be able to determine a genetic OR of 1.5 for almost all gene frequencies where the prevalence of the environmental factor is ≥10%.

Importantly, it should be noted again that CNVs and other unexplored gene variants are expected to be more penetrant and thus more strongly related to alcohol use disorders and their associated disabilities than are most of the

currently identified genetic variants. Thus, the higher OR expected from these new gene variants will result in much smaller sample size requirements than those illustrated in Figures B to E.

Table 1. Selected allele frequencies for genetic markers of various conditions and behaviors				
Gene	Marker	Allele	Frequency/ Prevalence*	Associated condition/behavior
ADH1B	rs1229984	[A/G]	0.322	Alcohol metabolism
ADH1C	rs698	[A/G]	0.39	Alcohol metabolism
ADH4	rs1042364	[A/G]	0.098	Alcohol metabolism
ADH7	rs1573496	[C/G]	0.026	Alcohol metabolism
ALDH2	rs671	[A/G]	0.082	Alcohol metabolism
NPY	rs16139	[A/C]	0.067	Stress regulation
SLC6A4	rs1042173	[A/G]	0.478	Stress regulation, obsessive-compulsive disorder
COMT	rs4680	[A/G]	0.337	Stress regulation and behavioral dyscontrol, impulsivity, attention-deficit/ hyperactivity disorder, mood disorders
BDNF	rs6265	[A/G]	0.251	Stress regulation, attention-deficit /hyperactivity disorder, mood disorders
HTR2C	rs6318	[C/G]	0.199	Stress regulation, behavioral dyscontrol, borderline PD, suicidality, anorexia
OPRM1	rs1799971	[A/G]	0.167	Stress regulation
HTTLPR	Vntr	L_G	0.09-0.15	Behavioral dyscontrol, impulsivity, suicidality, mood disorders
MAOA	Vntr	3.5 and 5 repeats	0.006-0.016	Behavioral dyscontrol, impulsivity, antisocial personality disorder, attention-deficit/hyperactivity disorder, stress regulation
DRD4	rs1800443	[G/T]	0.029	Behavioral dyscontrol, impulsivity, attention deficit/hyperactivity disorder
DBH	rs1611115	[C/T]	0.175	Behavioral dyscontrol, mood and anxiety disorders, impulsivity
SLC6A3	Vntr	10 repeats	0.71	Behavioral dyscontrol, attention deficit/hyperactivity disorder
CHRNA5	rs16969968	[A/G]	0.424	Nicotine dependence, alcohol abuse and dependence (cholinergic system)
*Allele frequencies have been documented for various populations. Those shown are for Caucasians of European ancestry.				

Table 2. Full listing of minor allele frequencies (MAF) for selected genetic markers, for individuals of various ethnic origins

SNP_Name	Chr	Coordinate	MAF Caucasian	MAF African	MAF African Amer.	MAF Japanese	MAF Chinese	Gene_ID	Gene_symbol	Accession
rs2376805	1	1946222	-99	-99	-99	-99	-99	2563	GABRD	NM_000815.2
rs204076	1	29062977	0.358	0.133	0.2333	0.057	0.078	4985	OPRD1	NM_000911.3
rs913168	1	46631163	0.424	0.408	-99	0.25	0.389	2166	FAAH	NM_001441.1
rs4845652	1	152804829	0.093	0.192	-99	0.125	0.1	1141	CHRNB2	NM_000748.1
rs3891068	1	204398689	-99	-99	-99	-99	-99	553	AVPR1B	NM_000707.2
rs6432224	2	11718851	0	0.158	-99	0	0	23620	NTSR2	NM_012344.2
rs6719226	2	25249516	0.058	0.383	-99	0.239	0.078	5443	POMC	NM_001035256.1
rs6709781	2	27384369	-99	-99	-99	-99	-99	7349	UCN	NM_003353.2
rs4538251	2	45739306	-99	-99	-99	-99	-99	5581	PRKCE	NM_005400.2
rs2111375	2	75281386	-99	-99	-99	-99	-99	6869	TACR1	NM_001058.2
rs2312955	2	96140895	0.292	0.1	-99	0.307	0.489	151	ADRA2B	NM_000682.4
rs11898177	2	119851961	0.317	0.467	-99	0.364	0.444	1622	DBI	NM_020548.4
rs13402440	2	138475664	0	0.017	-99	0	0	3176	HNMT	NM_006895.2
rs1978340	2	171378367	0.308	0.067	-99	0.182	0.222	2571	GAD1	NM_000817.2
rs769399	2	171425646	0	0.042	-99	0	0	2571	GAD1	NM_000817.2
rs2709376	2	208098633	0.05	0.35	-99	0	0	1385	CREB1	NM_004379.2
rs3806545	2	231698344	0.0625	0.442	-99	-99	0.2917	3357	HTR2B	NM_000867.2
rs2600072	3	10832067	0.224	0.153	-99	0.489	0.478	6538	SLC6A11	NM_014229.1
rs13069836	3	42282913	0.45	0.381	-99	0.422	0.444	885	CCK	NM_000729.3
rs13319651	3	48574845	0.017	0.093	-99	-99	0.081	90226	UCN2	NM_033199.3
rs3732791	3	115330379	0	0	-99	-99	0.011	1814	DRD3	NM_000796.3
rs7678463	4	3740750	0.167	0.195	-99	0.477	0.467	152	ADRA2C	NM_000683.3
rs4516717	4	9385751	-99	0.183	-99	0	0	1816	DRD5	NM_000798.3
rs4349588	4	26101460	0	0.083	-99	0	0	886	CCKAR	NM_000730.2
rs1504497	4	45643201	0.308	0.042	0.15	0.182	0.311	2565	GABRG1	NM_173536.3
rs11503014	4	46085622	0.1944	0.3158	-99	-99	0.0238	2555	GABRA2	NM_000807.1
rs1159396	4	46631579	0.483	0.408	-99	0.352	0.3	2557	GABRA4	NM_000809.2
rs10028945	4	47123062	0.25	0.3261	-99	-99	0.0833	2560	GABRB1	NM_000812.2
rs1126671	4	100267437	0.333	0.1	-99	0	0	127	ADH4	NM_000670.3
rs1229984	4	100458342	0	0	-99	0.261	0.233	125	ADH1B	NM_000668.3
rs1693482	4	100482988	0.484	0.0625	-99	-99	-99	126	ADH1C	NM_000669.3
rs1573496	4	100568692	0.092	0	0	0	0	131	ADH7	NM_000673.3
rs10213647	4	156346608	0.406	0.148	-99	0.444	0.466	4887	NPY2R	NM_000910.2
rs10517662	4	158312511	0.058	0.133	-99	0	0.022	2743	GLRB	NM_000824.2

rs4057797	4	164464503	0.308	0.2	-99	-99	0.4348	4886	NPY1R	NM_000909.4
rs6536721	4	164496347	0.358	0.308	-99	0.341	0.311	4889	NPY5R	NM_006174.2
rs27072	5	1447522	0.183	0.133	-99	0.133	0.378	6531	SLC6A3	NM_001044.2
rs1364043	5	63286607	0.217	0.183	0.2	0.3	0.378	3350	HTR1A	NM_000524.2
rs7731997	5	71052324	0	0.075	-99	0	0	9607	CARTPT	NM_004291.2
rs3792738	5	76283540	0.058	0.085	-99	0.133	0.178	1393	CRHBP	NM_001882.3
rs10482605	5	142763714	-99	-99	-99	-99	-99	2908	NR3C1	NM_001020825.1
rs12654778	5	148185934	0.336	0.203	-99	0.333	0.356	154	ADRB2	NM_000024.3
rs2240795	5	149569840	0.483	0.058	-99	0.344	0.367	6534	SLC6A7	NM_014228.2
rs2915885	5	151187261	0.408	0.449	-99	0.261	0.244	2741	GLRA1	NM_000171.1
rs4426954	5	160885609	0.407	0.175	-99	0.378	0.456	2561	GABRB2	NM_000813.1
rs3811991	5	161060987	0.3043	0.4565	-99	-99	0.1875	2559	GABRA6	NM_000811.1
rs209345	5	161423965	0.026	0.183	-99	0	0.011	2566	GABRG2	NM_198904.1
rs10078866	5	174804926	0	0	-99	0	0	1812	DRD1	NM_000794.3
rs3800373	6	35650454	0.3125	0.4783	-99	-99	0.2917	2289	FKBP5	NM_004117.2
rs851027	6	36098853	0.292	0.217	-99	0.443	0.344	116369	SLC26A8	NM_138718.1
rs7761118	6	36176281	0.108	0.241	-99	0.105	0.178	1432	MAPK14	NM_001315.1
rs507964	6	44294368	0	-99	-99	-99	-99	2030	SLC29A1	NM_004955.1
rs1213366	6	78233589	0.39	0.042	-99	0.068	0.111	3351	HTR1B	NM_000863.1
rs6911472	6	88909862	0	0.042	-99	0	0	1268	CNR1	NM_033181.2
rs7770466	6	146800958	0.025	0.242	-99	0	0	2911	GRM1	NM_000838.2
rs1799972	6	154402389	0.016	0.2085	-99	-99	-99	4988	OPRM1	NM_001008504.1
rs4314511	6	154607027	0.158	0.05	-99	0.364	0.307	26034	PIP3-E	NM_015553.1
rs10370	6	160021522	0.47	-99	-99	-99	-99	6648	SOD2	NM_001024466.1
rs16475	7	24298011	0.045	0	-99	-99	0.011	4852	NPY	NM_000905.2
rs8192492	7	30659687	0	0	-99	-99	0	1395	CRHR2	NM_001883.2
rs7804365	7	50604642	0.442	0.119	-99	0.302	0.33	1644	DDC	NM_000790.2
rs6465606	7	97192511	0.258	0.35	-99	0.08	0.1	6863	TAC1	NM_003182.1
rs3828942	7	127681541	0.492	0.108	-99	0.227	0.278	3952	LEP	NM_000230.1
rs10266026	7	136201512	0.008	0.075	-99	0	0.011	1129	CHRM2	NM_001006630.1
rs7820517	8	20088916	0.127	0.25	-99	0.318	0.344	6570	SLC18A1	NM_003053.1
rs2291776	8	26667553	0.068	0.158	-99	0.341	0.311	148	ADRA1A	NM_033302.1
rs7823854	8	27393424	0	0.188	-99	-99	0	1135	CHRNA2	NM_000742.1
rs2722897	8	28229116	0.125	0.492	-99	0.256	0.133	5368	PNOC	NM_006228.3
rs6989250	8	54328948	0	0.125	-99	0	0	4986	OPRK1	NM_000912.3
rs11998459	8	57516941	0	0.033	-99	0	0	5179	PENK	NM_006211.2
rs5030875	8	67256620	0.042	0.275	-99	0	0	1392	CRH	NM_000756.1
rs1187321	9	86472851	0.192	0.433	-99	0.239	0.233	4915	NTRK2	NM_006180.3

rs77905	9	135507918	0.458	0.383	-99	0.182	0.067	1621	DBH	NM_000787.2
rs2071644	9	139178730	0	0	-99	0.011	0.011	2902	GRIN1	NM_000832.4
rs10904478	10	5394347	0.475	0.192	-99	0.389	0.467	114131	UCN3	NM_053049.2
rs4747550	10	26625608	0.167	0.408	-99	0.43	0.389	2572	GAD2	NM_000818.1
rs638019	10	112821819	0.3542	0.067	-99	0.318	0.322	150	ADRA2A	NM_000681.2
rs363276	10	119023799	0.117	0.333	-99	0.318	0.422	6571	SLC18A2	NM_003054.2
rs3813865	10	135189234	0.025	0.1053	-99	-99	0.3478	1571	CYP2E1	NM_000773.3
rs11246226	11	631191	0.408	0.379	-99	0.244	0.239	1815	DRD4	NM_000797.2
rs2070762	11	2142911	0.483	0.161	-99	0.456	0.455	7054	TH	NM_000360.3
rs1805002	11	6247696	0.042	0.092	-99	0.068	0.011	887	CCKBR	NM_176875.2
rs10741734	11	18001224	0.4	0.142	-99	0.489	0.443	7166	TPH1	NM_004179.1
rs908867	11	27702340	0.117	0.1	-99	0.078	0.011	627	BDNF	NM_170731.3
rs4930241	11	68205159	-99	-99	-99	-99	-99	51083	GAL	NM_015973.3
rs12364283	11	112852165	0.075	0.008	-99	0	0.011	1813	DRD2	NM_000795.2
rs3758987	11	113280485	0.219	0.466	-99	0.35	0.151	9177	HTR3B	NM_006028.3
rs1176713	11	113365635	0.302	0.314	-99	0.273	0.211	3359	HTR3A	NM_000869.2
rs570680	12	200576	-99	-99	-99	-99	-99	6540	SLC6A13	NM_016615.2
rs1895056	12	14029302	0.258	0	-99	0	0.011	2904	GRIN2B	NM_000834.2
rs3803107	12	61827101	0.142	0.325	-99	0.193	0.144	552	AVPR1A	NM_000706.3
rs11179085	12	70824696	0.017	0.119	-99	0.102	0.133	121278	TPH2	NM_173353.2
rs6314	13	46307035	0.075	0.158	-99	0	0	3356	HTR2A	NM_000621.2
rs2273836	14	66716010	0.0208	0.0217	-99	-99	0	10243	GPHN	NM_001024218.1
rs11853694	15	24347672	0	0.4	-99	0	0	2562	GABRB3	NM_000814.4
rs2376481	15	24803459	0.45	0.325	-99	0.489	0.456	2558	GABRA5	NM_000810.2
rs140672	15	25154938	0	0.3478	-99	-99	0.0417	2567	GABRG3	NM_033223.1
rs6494223	15	30183749	0.433	0.492	-99	0.344	0.433	1139	CHRNA7	NM_000746.3
rs684513	15	76645455	0.217	0.158	-99	0.239	0.278	1138	CHRNA5	NM_000745.2
rs1878399	15	76699058	0.375	0.225	-99	0.159	0.178	1136	CHRNA3	NM_000743.2
rs6495309	15	76702300	0.2	0.25	-99	-99	-99	1143	CHRNB4	NM_000750.2
rs1071504	16	10187517	0.358	0.408	-99	0.1	0.1	2903	GRIN2A	NM_000833.2
rs7698	16	30033301	0.125	-99	-99	-99	-99	5595	MAPK3	NM_002746.2
rs1064448	16	48908384	0.492	0.058	-99	0.2	0.1	113	ADCY7	NM_001114.2
rs1532703	16	54243985	0.017	0.017	-99	0	0	6530	SLC6A2	NM_001043.2
rs4522461	17	4568522	0.217	0.117	-99	0	0	409	ARRB2	NM_004313.3
rs3813034	17	25548930	-99	-99	-99	-99	-99	6532	SLC6A4	NM_001045.2
rs734645	17	35045819	0.0417	0.25	-99	-99	0	84152	PPP1R1B	NM_032192.2
rs2293153	17	37581569	0	0.458	-99	0.034	0.011	23415	KCNH4	NM_012285.1
rs7226205	17	37594481	0	0.008	-99	0	0	84514	GHDC	NM_032484.3

rs9900679	17	41223923	0	0.1	-99	0	0	1394	CRHR1	NM_004382.2
rs2683267	17	70366578	0.225	0.492	-99	0.398	0.467	2905	GRIN2C	NM_000835.3
rs9916013	17	71583394	0	0.033	-99	0	0	8811	GALR2	NM_003857.2
rs949060	18	73087926	0.442	0.1	-99	0.205	0.2	2587	GALR1	NM_001480.2
rs6136667	20	1926301	0.127	0	-99	0.463	0.317	5173	PDYN	NM_024411.2
rs4813625	20	2997720	0.467	0.491	-99	0.455	0.444	5020	OXT	NM_000915.2
rs1321099	20	36792059	0.058	0.4	-99	0.455	0.467	140679	SLC32A1	NM_080552.2
rs2427400	20	60806120	0.125	0.1	-99	0.163	0.133	4923	NTSR1	NM_002531.1
rs755203	20	61464708	0.383	0.033	0.0909	0.442	0.344	1137	CHRNA4	NM_000744.3
rs6090041	20	62183120	0.3	0.442	-99	0.093	0.067	4987	OPRL1	NM_182647.1
rs2832489	21	30221341	0.233	0.4	-99	0.148	0.144	2897	GRIK1	NM_175611.2
rs737866	22	18310109	0.317	0.142	-99	0.352	0.322	10587	TXNRD2	NM_006440.3
rs9332377	22	18335692	0.167	0.375	-99	0	0	1312	COMT	NM_007310.1
rs5751862	22	23132564	0.5	0.117	-99	0.432	0.478	23384	SPECC1L	NM_015330.1
rs4822492	22	23173594	0.4	0.175	-99	0.42	0.467	135	ADORA2A	NM_000675.3
rs4821717	22	36546704	0.367	0.058	-99	0.216	0.078	8484	GALR3	NM_003614.1
rs3091367	22	36557767	0.175	0.3261	-99	-99	0.0833	129138	ANKRD54	NM_138797.1
rs6001728	22	38764703	0.233	0.067	-99	0.034	0.033	23112	TNRC6B	NM_001024843.1
rs1033372	22	48249853	0.008	0.133	-99	0.395	0.456	728652	LOC728652	XM_001128024.1
rs6526714	X	14485073	0.4444	0.2111	-99	0.1642	0.2647	2742	GLRA2	NM_002063.2
rs2239448	X	43487623	0.2333	0.4	-99	0.3788	0.3333	4128	MAOA	NM_000240.2
rs1799836	X	43512943	0.3833	0.2333	-99	0.1591	0.1304	4129	MAOB	NM_000898.3
rs508865	X	113720371	0.4	0.3833	-99	0.2045	0.1304	3358	HTR2C	NM_000868.1
rs1061421	X	150873252	0.0833	0.45	-99	0	0.0217	2564	GABRE	NM_004961.3
rs5970292	X	151311524	0.4	0.2889	-99	0.2424	0.2424	2556	GABRA3	NM_000808.2
rs3810651	X	151571933	0.4111	0.314	-99	0.2537	0.3824	55879	GABRQ	NM_018558.1
rs6670693	1	1095975	0	0.025	-99	0	0	254173	TTLL10	NM_153254.1
rs3100865	1	2795967	0.267	0.008	-99	0.409	0.278	728702	LOC728702	XM_001128239.1
rs4653130	1	35576728	0.067	0.392	-99	0.284	0.144	9202	ZMYM4	NM_005095.2
rs655590	1	35894634	0.058	0.325	-99	0.295	0.111	5690	PSMB2	NM_002794.3
rs6687440	1	106571633	0.3	0.083	-99	0.011	0.022	126987	LOC126987	XR_016153.1
rs11184898	1	106755851	0.442	0	-99	0.045	0.044	126987	LOC126987	XR_016153.1
rs10802184	1	116680864	0.1	0.017	-99	0.068	0.022	476	ATP1A1	NM_000701.6
rs1446959	1	157873428	0.433	0.042	-99	0.068	0.078	325	APCS	NM_001639.2
rs4265409	1	161681183	0.392	0.133	-99	0.023	0.044	83540	NUF2	NM_145697.1
rs6424922	1	182240761	0.158	0.05	-99	0.33	0.333	23127	GLT25D2	NM_015101.2
rs2220128	1	184002536	0.267	0.075	-99	0	0.022	83872	HMCN1	NM_031935.1
rs2759281	1	203132988	0.15	0.017	-99	0.2	0.122	23114	NFASC	NM_015090.2

rs6718709	2	5257953	0.45	0.175	-99	0.102	0.022	6664	SOX11	NM_003108.3
rs1368928	2	8668914	0.342	0.042	-99	0.034	0.056	3398	ID2	NM_002166.4
rs11126303	2	26027007	0.008	0.192	-99	0.091	0.078	3797	KIF3C	NM_002254.5
rs12618959	2	33017154	0.308	0.092	-99	0.023	0.044	4052	LTBP1	NM_206943.1
rs1811510	3	5750231	0.026	0.05	-99	0.205	0.167	9695	EDEM1	NM_014674.1
rs6785846	3	25714245	0.208	0.042	-99	0.159	0.067	55768	NGLY1	NM_018297.2
rs1028040	3	57215650	0.392	0.1	-99	0.114	0.078	8820	HESX1	NM_003865.1
rs1563382	3	79319581	0.05	0.075	-99	0	0.011	6091	ROBO1	NM_002941.2
rs6790692	3	98695905	0.183	0.042	-99	0.216	0.067	285220	EPHA6	XM_114973.6
rs1503079	3	106241722	0.492	0.133	-99	0.08	0.067	214	ALCAM	NM_001627.2
rs10933921	3	109082643	0.483	0.017	-99	0.341	0.089	285205	LOC285205	XM_001128618.1
rs4241398	3	110299018	0.475	0.042	-99	0.068	0.056	27136	MORC1	NM_014429.2
rs11713100	3	111513795	0.05	0.208	-99	0.307	0.478	389141	LOC389141	XR_016945.1
rs6414248	3	112365016	0.167	0.008	-99	0.17	0.322	25945	PVRL3	NM_015480.1
rs1698042	3	118667838	0.058	0.2	-99	0.489	0.478	728873	LOC728873	XR_015679.1
rs2626018	3	124774156	0.208	0.05	-99	0.352	0.3	201562	PTPLB	NM_198402.2
rs2625956	3	130747960	0.142	0.033	-99	0.409	0.389	132243	H1FOO	NM_153833.1
rs36110	3	136182877	0.45	0.058	-99	0.034	0.111	2047	EPHB1	NM_004441.3
rs1519260	3	137062756	0.425	0.017	-99	0.216	0.122	5523	PPP2R3A	NM_002718.3
rs7618370	3	169391997	0.167	0.042	-99	0.011	0.067	389174	LOC389174	XM_371678.4
rs3796285	3	189735795	0.467	0.108	-99	0.102	0.067	4026	LPP	NM_005578.2
rs4687002	3	190104562	0.317	0.058	-99	0.023	0.056	4026	LPP	NM_005578.2
rs733370	4	6010036	0.342	0.075	-99	0.216	0.111	389197	FLJ46481	NM_207405.1
rs16877243	4	25177016	0.183	0.033	-99	0.375	0.378	645433	LOC645433	XR_017242.1
rs1488299	4	26870541	0.483	0.15	-99	0.034	0.033	401123	FLJ45721	NM_207490.1
rs1507086	4	41651170	0.3	0	-99	0.023	0.022	55161	TMEM33	NM_018126.1
rs11098964	4	81106993	0.483	0.1	-99	0.023	0.044	118429	ANTXR2	NM_058172.3
rs1444893	4	82602473	0.208	0.067	-99	0.023	0.022	153020	RASGEF1B	NM_152545.1
rs1494962	4	84555307	0.117	0.092	-99	0	0.011	113510	HEL308	NM_133636.1
rs2231164	4	89234881	-99	-99	-99	-99	-99	9429	ABCG2	NM_004827.2
rs13134663	4	110060008	0.492	0.108	-99	0.068	0.067	84570	COL25A1	NM_032518.2
rs1827950	4	117317931	0.083	0.033	-99	0.08	0.078	645368	LOC645368	XR_017440.1
rs4863731	4	141184618	0.433	0.05	-99	0.034	0.056	55534	MAML3	NM_018717.3
rs1397529	4	144611612	0.367	0.042	-99	0.045	0.044	2549	GAB1	NM_207123.1
rs7692206	4	155326143	0.083	0.033	-99	0.341	0.256	54798	DCHS2	NM_017639.2
rs2345275	4	158944273	0.483	0.083	-99	0.089	0.111	729937	LOC729937	XM_001131838.1
rs12644851	4	159827612	0.383	0.008	-99	0.216	0.078	2110	ETFDH	NM_004453.1
rs6552216	4	178348998	0.192	0.358	-99	0.125	0.078	55247	NEIL3	NM_018248.1

rs26880	5	4958892	0.425	0.075	-99	0.189	0.122	340094	LOC340094	XM_295155.5
rs246760	5	5633216	0.325	0.05	-99	0.278	0.156	23379	KIAA0947	XM_029101.11
rs2937067	5	116167937	0.425	0.05	-99	0.078	0.133	57556	SEMA6A	NM_020796.2
rs2220858	5	116660106	0.367	0.05	-99	0.068	0.067	728342	LOC728342	XM_001129097.1
rs267071	5	116976402	0.319	0.025	-99	0.034	0.022	728342	LOC728342	XM_001129097.1
rs2416504	5	117436991	0.405	0.008	-99	0.023	0.022	728342	LOC728342	XM_001129097.1
rs6595142	5	117895090	0.367	0.033	-99	0.122	0.144	285605	DTWD2	NM_173666.1
rs2036565	5	118560770	0.442	0.175	-99	0.045	0.033	1657	DMXL1	NM_005509.3
rs326626	5	133639706	0.042	0.275	-99	0.056	0.067	51265	CDKL3	NM_016508.2
rs4958667	5	152940571	0.383	0.042	-99	0.244	0.067	2890	GRIA1	NM_000827.2
rs815608	5	153496967	0.367	0.046	-99	0.027	0.056	55568	GALNT10	NM_198321.2
rs692713	5	176186041	0.042	0.042	-99	0.08	0.122	90249	UNC5A	NM_133369.2
rs6869589	5	178559215	0	0.017	-99	0	0	9509	ADAMTS2	NM_021599.1
rs6926774	6	5677819	0.417	0.042	-99	0.102	0.078	10667	FARS2	NM_006567.2
rs1206920	6	9867494	0.308	0.167	-99	0.08	0.044	266553	OFCC1	NM_153003.1
rs2842063	6	71295098	0.183	0.05	-99	0.17	0.056	57579	FAM135A	NM_020819.2
rs1538956	6	127005719	0.425	0.15	-99	0	0.011	728666	LOC728666	XR_015645.1
rs9388989	6	132739275	0.117	0.017	-99	0.267	0.244	26002	MOXD1	NM_001031699.1
rs1052502	6	135648258	0.05	0.058	-99	0.136	0.144	54806	AHI1	NM_017651.3
rs1554817	6	154608113	0.158	0.058	-99	0.364	0.311	26034	PIP3-E	NM_015553.1
rs9639213	7	14707372	0.467	0.05	-99	0.114	0.067	1607	DGKB	NM_145695.1
rs4721415	7	15202657	0.058	0.358	-99	0	0.011	392636	TMEM195	NM_001004320.1
rs6955490	7	98812524	0.133	0.067	-99	0.023	0.022	10095	ARPC1B	NM_005720.2
rs10249419	7	117169042	0.383	0.083	-99	0.011	0	83992	CTTNBP2	NM_033427.2
rs10488401	7	135476064	0.433	0.008	-99	0.193	0.056	730221	LOC730221	XM_001133013.1
rs10488619	7	135824107	0.408	-99	-99	0.182	0.056	392100	LOC392100	XR_017485.1
rs315280	7	142552081	0.242	0.017	0.1446	0.091	0.167	5304	PIP	NM_002652.2
rs11136793	8	4767247	0.45	0.075	-99	0.193	0.078	64478	CSMD1	NM_033225.3
rs4841401	8	10527002	0.358	0	-99	0.102	0.089	94137	RP1L1	NM_178857.4
rs10107384	8	10890860	0.35	0.008	-99	0.057	0.033	286046	XKR6	NM_173683.3
rs2409710	8	11017231	0.475	0.042	-99	0.068	0.056	439940	C8orf15	NM_001033662.1
rs1347201	8	16581855	0.458	0.125	-99	0.057	0.033	26281	FGF20	NM_019851.1
rs12678324	8	16833064	0.058	0.067	-99	0.466	0.5	26281	FGF20	NM_019851.1
rs2927385	8	20744320	0.45	0.042	-99	0.227	0.111	646608	LOC646608	XM_929545.1
rs2102727	8	53063166	0.158	0.008	-99	0.341	0.344	9705	ST18	NM_014682.1
rs4737761	8	54867106	0.083	0.008	-99	0.466	0.4	51606	ATP6V1H	NM_213619.1
rs3912537	8	62354583	0.108	0.475	-99	0.189	0.089	157807	RLBP1L1	NM_173519.1
rs6991838	8	66633516	0.442	0.05	-99	0.102	0.1	55156	ARMC1	NM_018120.3

rs6472362	8	68994970	0.225	0.067	-99	0.068	0.022	80243	DEPDC2		NM_025170.4
rs1227647	8	80291691	0.25	0.033	-99	0.182	0.333	11075	STMN2		NM_007029.2
rs1402851	8	84417952	0.058	0.142	-99	0.284	0.5	389674	HNRPA1P4		XM_372050.5
rs1552314	8	93173981	0.308	0.05	-99	0	0.044	862	RUNX1T1		NM_175635.1
rs4484738	8	121772608	0.25	0.017	-99	0.318	0.278	6641	SNTB1		NM_021021.2
rs1514626	8	132834923	0.2	0.058	-99	0.273	0.367	23167	EFR3A		NM_015137.1
rs10113320	8	134925795	0.292	0.008	-99	0.136	0.167	6482	ST3GAL1		NM_173344.1
rs4907376	8	142602383	0.017	0.125	-99	0.465	0.489	389690	FLJ43860		NM_207414.1
rs1871534	8	145610489	0	0.017	-99	0	0	55630	SLC39A4		NM_130849.1
rs2225979	9	9720381	0.475	0.05	-99	0.125	0.067	5789	PTPRD		NM_002839.1
rs1885167	9	17504515	0.217	0.008	-99	0.045	0.033	54875	C9orf39		NM_017738.1
rs541805	9	25924932	0.108	0.075	-99	0.489	0.478	441390		-99	NM_001004352.1
rs2486448	9	71028805	0.342	0.017	-99	0.193	0.078	9414	TJP2		NM_004817.2
rs10868793	9	90352033	0.117	0.008	-99	0.17	0.2	158046	NXNL2		NM_145283.1
rs556399	9	109995109	0.475	0.125	-99	0.091	0.078	392382	LOC392382		XR_016755.1
rs2004426	9	111651570	0	0.417	-99	0.136	0.089	445815	PALM2-AKAP2		NM_147150.1
rs2241083	9	124854714	0.167	0.025	-99	0.159	0.233	23637	RABGAP1		NM_012197.2
rs3814134	9	126307510	0.017	0.033	-99	0.182	0.311	2516	NR5A1		NM_004959.3
rs590614	9	135625230	0.392	0.033	-99	0.023	0.033	7410	VAV2		NM_003371.2
rs2388511	10	3038498	0.092	0.05	-99	0.091	0.044	441546	LOC441546		XM_499190.2
rs10795588	10	8126176	0.475	0.167	-99	0.105	0.044	399717	FLJ45983		NM_207423.1
rs2008592	10	30542827	0.083	0.167	-99	0.5	0.422	57608	KIAA1462		XM_166132.7
rs1869237	10	33876047	0.375	0.167	-99	0	0.011	8829	NRP1		NM_003873.3
rs6593430	10	44422502	0.075	0	-99	0	0	728374	LOC728374		XR_015274.1
rs10745288	10	49801403	0.375	0.1	-99	0.023	0.022	474354	LRRC18		NM_001006939.2
rs10763013	10	55283129	0.233	0.2	-99	0	0.033	65217	PCDH15		NM_033056.2
rs11203006	10	90906065	0.15	0.483	-99	0.216	0.056	728303	LOC728303		XM_001127130.1
rs10785952	10	92038772	0.358	0.05	-99	0.011	0.033	119358	LOC119358		XM_061427.3
rs10883533	10	102462646	0.325	0.15	-99	0.034	0.033	5076	PAX2		NM_003987.2
rs10884188	10	107333364	0.392	0.008	-99	0.25	0.089	22986	SORCS3		NM_014978.1
rs1336978	10	108849094	0.408	0.025	-99	0.227	0.167	114815	SORCS1		NM_001013031.1
rs2082380	10	118144749	-99	-99	-99	-99	-99	374355	C10orf96		NM_198515.1
rs1986420	10	119746836	0.017	0.083	-99	0.193	0.211	22841	RAB11FIP2		NM_014904.1
rs2930125	10	127879147	0.15	0.058	-99	0.182	0.222	8038	ADAM12		NM_021641.2
rs10750836	11	68572099	0.008	0.217	-99	0.42	0.456	219931	TPCN2		NM_139075.1
rs2027760	11	72714129	0.1	0.333	-99	0.023	0.056	9828	ARHGEF17		NM_014786.2
rs7932809	11	121171910	0.433	0.033	-99	0.216	0.056	6653	SORL1		NM_003105.3
rs2416791	12	11592755	0.083	0.025	-99	0.284	0.278	2120	ETV6		NM_001987.3

rs2730891	12	37270952	0.042	0.075	-99	0.455	0.478	144402	CPNE8	NM_153634.2
rs1532052	12	53647581	0.233	0.342	-99	0.047	0.033	9840	KIAA0748	XM_374983.4
rs10879311	12	70352255	0.208	0.058	-99	0.125	0.211	83591	THAP2	NM_031435.1
rs711159	12	78632547	0.008	0.067	-99	0.136	0.222	5074	PAWR	NM_002583.2
rs12313915	12	83786783	0.308	0.05	-99	0.023	0.022	55117	SLC6A15	NM_182767.3
rs1001484	12	110021205	0.183	0.008	-99	0.33	0.333	23316	CUX2	NM_015267.1
rs628825	12	110436233	0.225	0.2	0.15	0.182	0.044	6311	ATXN2	NM_002973.2
rs1716167	12	122217115	0.2	0.05	-99	0.023	0.033	10198	MPHOSPH9	NM_022782.2
rs10847171	12	125546608	0.267	0.042	-99	0.102	0.033	728173	LOC728173	XM_001129061.1
rs9318026	13	71204246	0.083	0.092	-99	0.205	0.2	1602	DACH1	NM_080760.3
rs4981115	14	31240826	0.125	0.092	-99	0	0.011	80224	NUBPL	NM_025152.1
rs7158302	14	56720501	0.083	0.1	-99	0.011	0	10640	EXOC5	NM_006544.3
rs2193595	14	76914874	0.483	0.092	-99	0.091	0.067	161394	C14orf174	NM_001010860.1
rs1003229	14	97241370	0.183	0.067	-99	0.178	0.056	730217	LOC730217	XM_001132986.1
rs1375164	15	25965407	0.175	0.008	-99	0.102	0.067	4948	OCA2	NM_000275.1
rs1828774	15	26812205	0.367	0.05	-99	0.156	0.133	440253	WHDC1L2	XM_926785.2
rs2948905	15	42933056	0.052	0.025	-99	0.455	0.378	653381	LOC653381	XR_017364.1
rs10152524	15	44027656	0.196	0.086	-99	0.011	0.013	58472	SQRDL	NM_021199.2
rs2934193	15	46047011	0.092	0.025	-99	0.133	0.222	283652	SLC24A5	NM_205850.2
rs12595448	15	53691382	0.25	0	-99	0.057	0.022	283659	PRTG	NM_173814.3
rs289816	15	61582014	0.05	0.125	-99	0.1	0.067	9960	USP3	NM_006537.2
rs10152453	15	61885666	0.058	0.192	-99	0.1	0.067	8925	HERC1	NM_003922.2
rs4511483	15	69925644	0.198	0.042	-99	0.364	0.411	4649	MYO9A	NM_006901.1
rs6496858	15	90062853	0.15	0.017	-99	0.5	0.411	28232	SLCO3A1	NM_013272.2
rs1002587	16	13813024	0.2273	0.1136	-99	-99	0.1591	2072	ERCC4	NM_005236.1
rs4783432	16	21858916	0.183	0.025	-99	0.25	0.244	342293	LOC342293	XM_292468.4
rs4787645	16	30364851	0.358	0	-99	0.111	0.089	22928	SEPHS2	NM_012248.2
rs4889490	16	30730548	0.431	0	-99	0.091	0.067	647086	LOC647086	XR_017567.1
rs889548	16	31045213	0.392	0.042	-99	0.111	0.056	84148	MYST1	NM_032188.1
rs4240793	16	85946457	0.442	0.192	-99	0	0.011	79791	FBXO31	NM_024735.2
rs333113	17	4347105	0.183	0.075	-99	0.034	0	201305	SPNS3	NM_182538.3
rs4968382	17	54947497	0.208	0.067	-99	0.398	0.389	79665	DHX40	NM_024612.3
rs1719982	18	5598808	0.492	0.167	-99	0.034	0.022	388459	LOC388459	XM_373772.3
rs643272	18	38442319	0.175	0.033	-99	0.273	0.156	6014	RIT2	NM_002930.1
rs679832	18	39208685	0	0.183	-99	0	0.011	6860	SYT4	NM_020783.2
rs3786467	18	53289804	0.025	0	-99	0.352	0.444	9480	ONECUT2	NM_004852.1
rs1823778	18	65752616	0.058	0.058	0	0.068	0.067	10666	CD226	NM_006566.1
rs10420077	19	35338458	0.167	0.083	-99	0.5	0.367	728091	LOC728091	XM_001126514.1

rs6510332	19	38222770	0.242	0.025	-99	0.455	0.333	85415	RHPN2	NM_033103.3
rs7253691	19	47095447	0.008	0.083	-99	0.151	0.267	9138	ARHGEF1	NM_199002.1
rs8110904	19	47723209	-99	-99	-99	-99	-99	634	CEACAM1	NM_001712.3
rs344816	19	50517466	0.417	0.05	0.25	0.093	0.067	1158	CKM	NM_001824.2
rs2387137	19	55829472	0.158	0.042	-99	0.344	0.167	84258	SYT3	NM_032298.1
rs6074585	20	13223202	0.043	0.025	-99	0	0	140862	C20orf82	XM_097736.7
rs6141319	20	30608468	0.233	0.033	-99	0	0.011	149950	RP11-410N8.4	NM_001010976.1
rs6023367	20	52625318	0.283	0.083	-99	0	0	55816	DOK5	NM_018431.3
rs12481662	20	57451501	0.225	0.042	-99	0.102	0.056	645605	LOC645605	XM_001129785.1
rs6061779	20	59414462	0.217	0.1	-99	0	0	1002	CDH4	NM_001794.2
rs310644	20	61629948	0.117	0.075	-99	0	0.044	5753	PTK6	NM_005975.2
rs2823662	21	16514932	0.333	0.033	-99	0.08	0.044	388815	C21orf34	NM_001005734.1
rs2039248	21	17998320	0.258	0.017	-99	0.443	0.322	378826	C21orf114	NM_001012707.1
rs650276	22	25122236	0.225	0.017	-99	0.33	0.311	23544	SEZ6L	NM_021115.3
rs5753625	22	30184846	0.342	0.117	-99	0.114	0.078	56478	EIF4ENIF1	NM_019843.2
rs1894450	22	31237721	0.333	0	-99	0.148	0.078	8224	SYN3	NM_003490.2
rs4824001	22	47703910	0.017	0.167	-99	0.488	0.456	25817	FAM19A5	NM_015381.3
rs5988072	X	113797159	0.4111	0.0333	-99	0.3939	0.3382	677816	SNORA35	NR_002993.1
rs12125484	1	92584784	0.35	0.092	-99	0	0.011	79871	RPAP2	NM_024813.1
rs4768928	12	49070623	0.042	0.125	-99	0.384	0.467	121006	LOC121006	XM_926818.2

Figure A

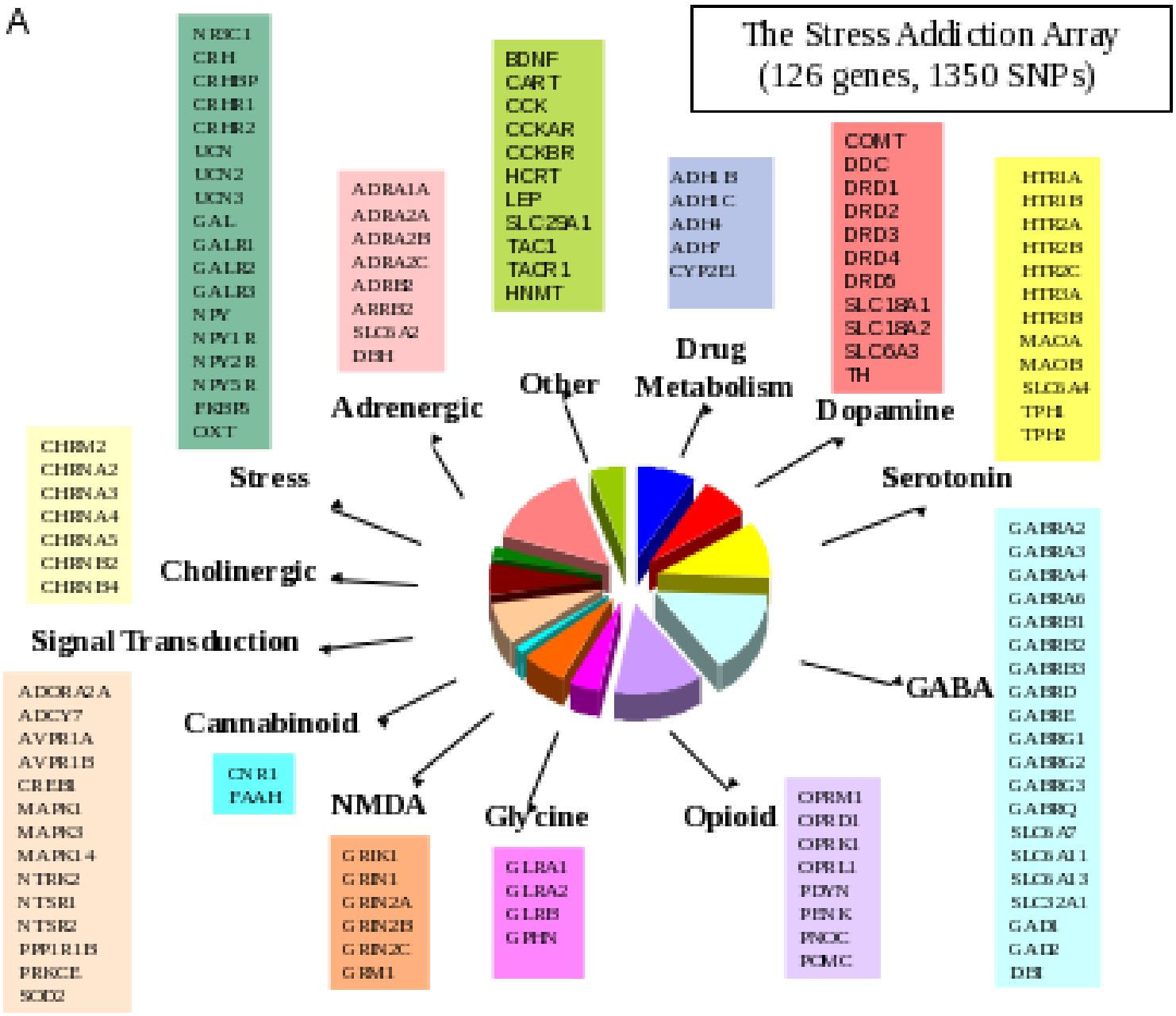
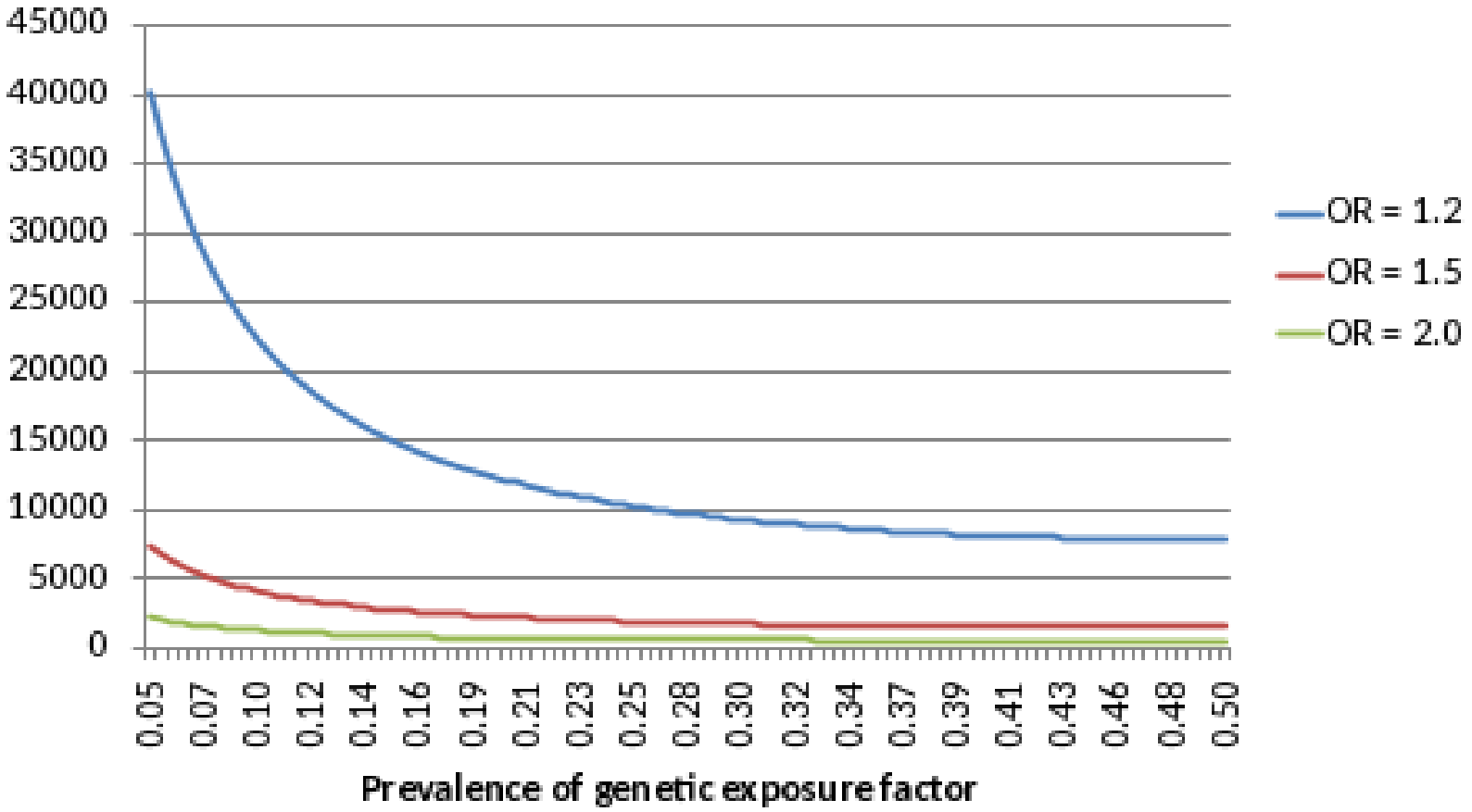
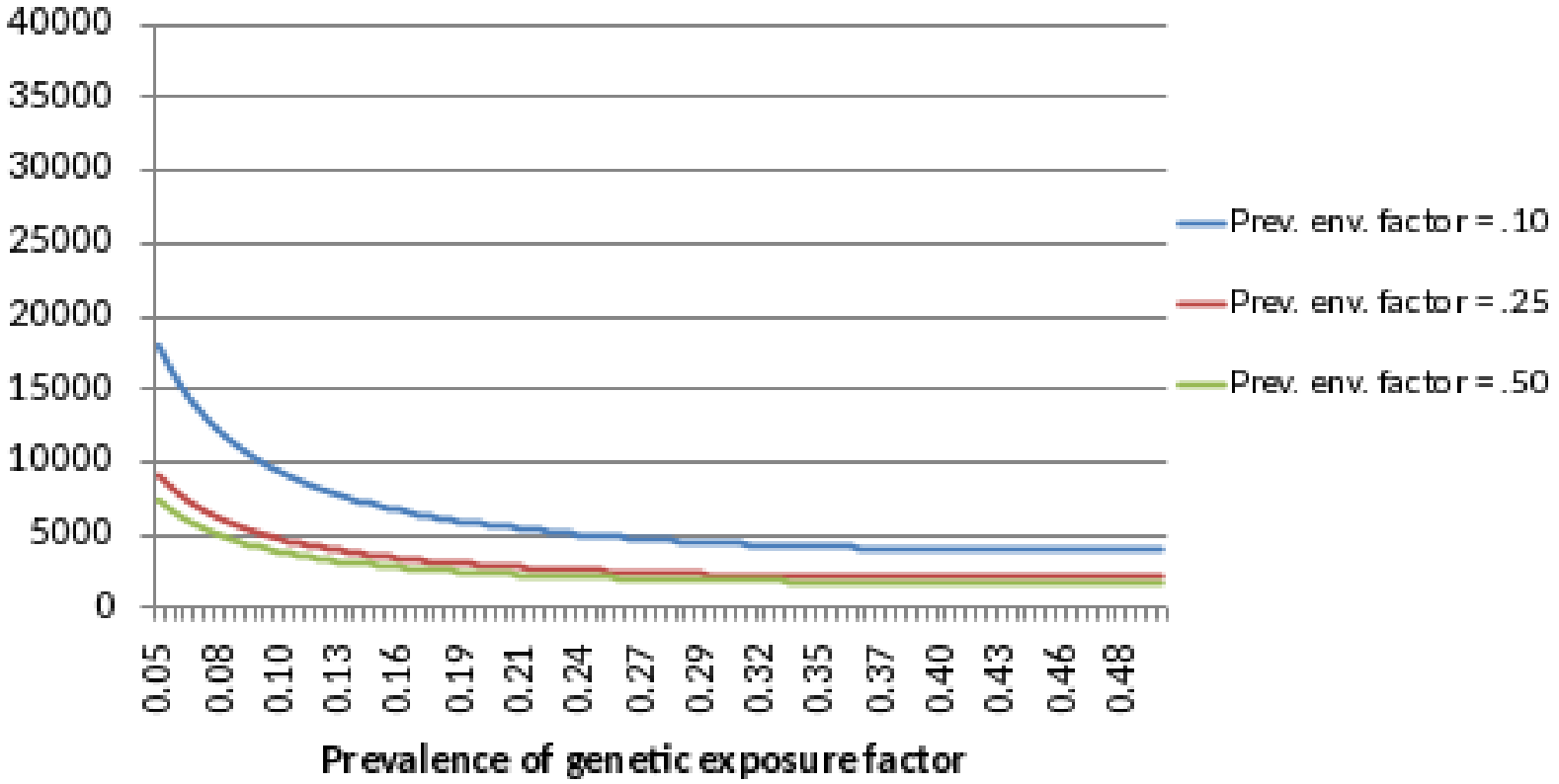

The Stress Addiction Array
(126 genes, 1350 SNPs)
NR3C1
CRH
CRHBP
CRHR1
CRHR2
UCN
UCN2
UCN3
GAL
GALR1
GALR2
GALR3
NPY
NPY1R
NPY2R
NPY5R
PRSS5
OXT
BDNF
CART
CCK
CCKAR
CCKBR
HCRT
LEP
SLC29A1
TAC1
TACR1
HNMT
ADRA1A
ADRA2A
ADRA2B
ADRA2C
ADRB2
ARRB2
SLC6A2
DBH
ADH1B
ADH1C
ADH4
ADH7
CYP2E1
COMT
DDC
DRD1
DRD2
DRD3
DRD4
DRD5
SLC18A1
SLC18A2
SLC6A3
TH
HTR1A
HTR1B
HTR2A
HTR2B
HTR2C
HTR3A
HTR3B
MAOA
MAOB
SLC6A4
TPH1
TPH2
Drug Metabolism
Other
Adrenergic
Dopamine
Serotonin
Stress
Cholinergic
Signal Transduction
Cannabinoid
NMDA
Glycine
Opioid
GABA
CHRM2
CHRNA2
CHRNA3
CHRNA4
CHRNA5
CHRNB2
CHRNB4
ADCRA2A
ADCY7
AVPR1A
AVPR1B
CREB1
MAPK1
MAPK3
MAPK14
NTRK2
NTSR1
NTSR2
PPP1R1B
PRKCE
SCD2
CNR1
FAAH
GRIK1
GRIN1
GRIN2A
GRIN2B
GRIN2C
GRM1
GLRA1
GLRA2
GLRB
GPHN
OPRM1
OPRD1
OPRK1
OPRL1
PDYN
PENK
PNOC
POMC
GABRA2
GABRA3
GABRA4
GABRA6
GABRB1
GABRB2
GABRB3
GABRD
GABRE
GABBG1
GABBG2
GABBG3
GABBQ
SLC6A7
SLC6A11
SLC6A13
SLC32A1
GAD1
GAD2
DBI

Figure B. Sample size requirements to detect OR of varying magnitudes ($p < .05$) for lifetime alcohol dependence (lifetime prevalence≈. 13) at various levels of prevalence for genetic exposure factor, assuming power = 0.80



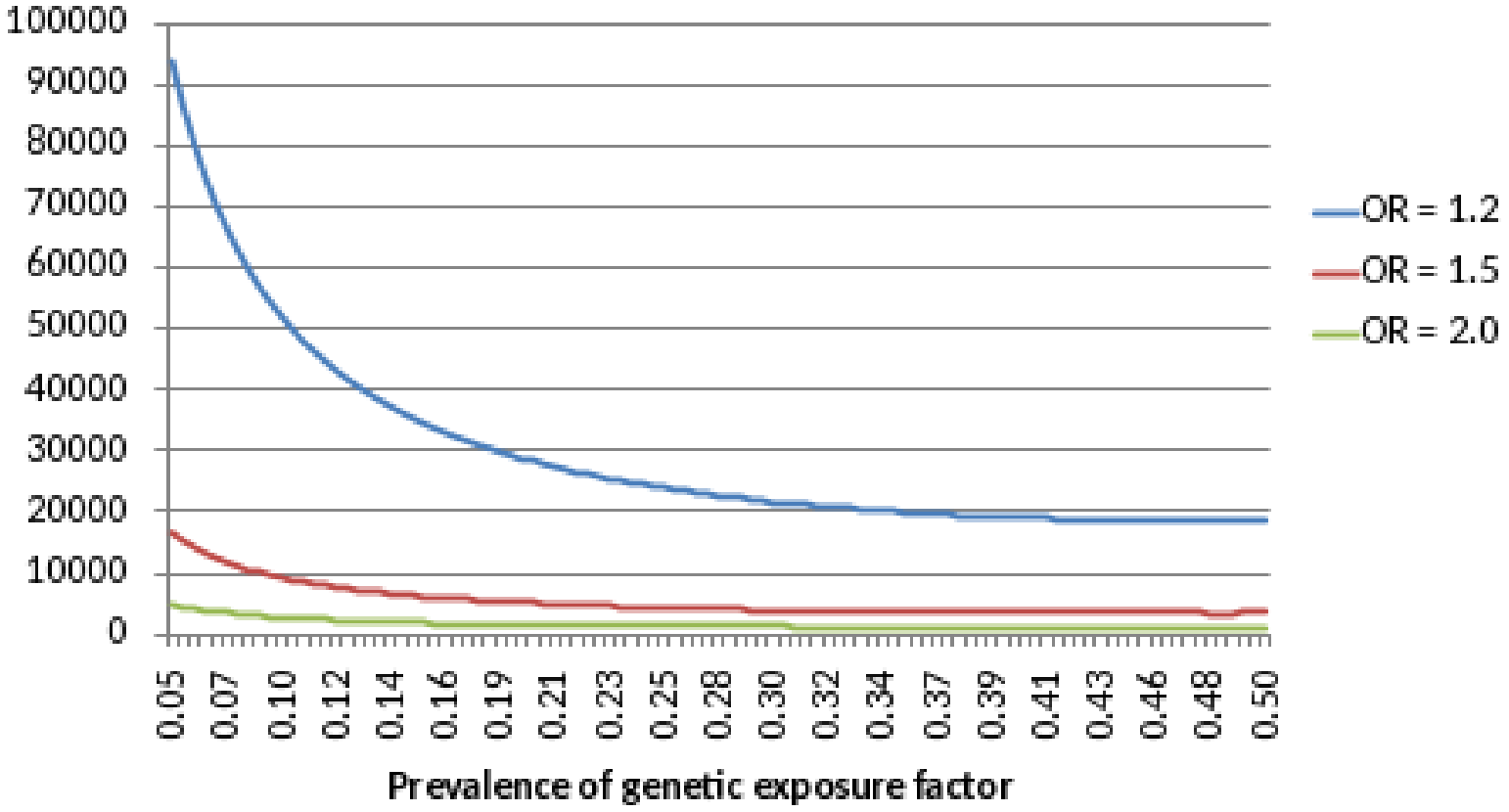
*Or lifetime depression or drug use disorders, with similar lifetime prevalences

Figure C. Sample size requirements to detect genetic and environmental OR of 1.5 ($p<.06$) for lifetime alcohol dependence (lifetime prevalence≈.13)* at various levels of prevalence for genetic and environmental exposure factors, assuming power = 0.80 and OR = 2.0 for interaction of genetic and environmental factors



*Or lifetime depression or drug use disorders, with similar lifetime prevalences

Figure D. Sample size requirements to detect OR of varying magnitudes (p<.05) for conditions with a lifetime prevalence of ≈.05*, at various levels of prevalence for genetic exposure factor, assuming power = 0.80



*Including generalized anxiety and specific and social phobias