Supplementary material

Latent subtypes of manic and/or irritable episode symptoms in the two population-based cohorts $% \left({{{\rm{cohor}}} \right)_{\rm{cohorts}}} \right)$

Arathimos et al.

Contents

1	Supplementary Methods	2
2	Supplementary Results	4
	2.1 Results section A	4
3	Supplementary Figures	5
4	Supplementary Tables	53

1 Supplementary Methods

1.0.1 UK Biobank

Phenotype data

In order to characterise probable history of bipolar disorder, questions based on the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) were included in the baseline questionnaire of UK Biobank. The questions included two stem questions on ever having experienced a manic/hyper/high episode, and ever having experienced an irritable episode; "Have you ever had a period of time lasting at least two days when you were feeling so good, "high", excited or "hyper" that other people thought you were not your normal self or you were so "hyper" that you got into trouble?"; "Have you ever had a period of time lasting at least two days when you were so irritable that you found yourself shouting at people or starting fights or arguments?" The question on symptoms present during these episodes contained 4 possible responses, in addition to fields "All of the above" and "None of the above"; "Please try to remember a period when you were in a "high" or "irritable" state and select which of the following apply: I was more active than usual, I was more talkative than usual, I needed less sleep than usual, I was more creative or had more ideas than usual." Follow-up questions asked participants to report on episode duration and episode disruptiveness; "What is the longest time period that these "high" or "irritable" periods have lasted?" with responses "At least two days but less than a week", "Less than a week", "A week or more"; and "How much of a problem have these "high" or "irritable" periods caused you?" with responses "No problems" and "Needed treatment or caused problems with work, relationships, finances, the law or other aspects of life". Both the question of episode duration and episode disruptiveness included response options for "Do not know" or "Prefer not to answer".

Sociodemographic data on participant sex, age, smoking status, alcohol intake frequency, Townsend deprivation index (TDI – as a measure of socioeconomic status) and education level were extracted from participant responses to the baseline questionnaire. Smoking status was defined as either "Never", "Past" or "Current". Alcohol intake frequency was defined as either "Never", "Occasionally", "Weekly" or "Daily". The rank-based inverse normal transformation was applied to the TDI scores to transform a skewed distribution. Education level was defined as either "University degree", "A-level, NVQ, HNC or HND", "O-levels or CSE" or "None".

In the MHQ, participants reported past diagnoses by a professional (field #20544) of several disorders. From the reports, six broad classes of disorders were defined; attention deficit hyperactivity disorder (ADHD), autism spectrum disorder (ASD), generalised anxiety disorder (GAD), depression, schizophrenia/psychosis, and mania/bipolar disorder. Cases of 'schizophrenia/psychosis' were defined by combining positive responses to reports of schizophrenia with reports of "any other type of psychosis or psychotic illness". Cases of 'generalised anxiety disorder' (GAD) were defined by positive responses to "anxiety, nerves or generalised anxiety disorder". Cases of 'mania/bipolar disorder' were defined by positive responses to "Mania, hypomania, bipolar or manic-depression". Cases of 'ASD' were defined by positive responses to "Autism, Asperger's or autistic spectrum disorder". Cases of personality disorder were also derived from responses to the same question in the MHQ. Due to the low number of cases, self-reported personality disorder was examined separately under the category of personality traits, which also included derived neuroticism score which was based on 12 neurotic behaviour domains reported in the baseline questionnaire, previously described by Smith et al.

Linked electronic health records to Hospital Episode Statistics (HES) which contain diagnoses recorded with the International Classification of Diseases, 10th Revision (ICD-10) beginning in 1997 in England and from 1999 in Wales, up until June 2020, were used to derive cases status for 3 broad disorder definitions (termed "ICD diagnoses" or "ICD cases"). Individuals that had been assigned a primary or secondary diagnosis for a) depressive episode or recurrent depressive disorder (F32; F33), b) schizophrenia, schizotypal disorder, schizoaffective disorder and delusional/psychotic disorders (F20-F29), c) mood disorders including bipolar, cyclothymia, dysthymia, hypomania or mania (F30; F31; F34; F38; F39), d) dementia in Alzheimer's disease, vascular dementia, dementia unspecified/of other diseases (F00; F01; F02; F03), were considered ICD cases for depression, schizophrenia/psychotic disorder, mania/bipolar disorder, and dementia respectively. Psychiatric data from Scotland was not available (as it was currently not linked), so some cases of the above disorders may have been missed.

Genetic data

Genotypes in UK Biobank were assayed using two different arrays (chips), the Affymetrix UK BiLEVE Axiom or Affymetrix UK Biobank Axiom array. Preliminary QC on genetic data was performed internally by UK Biobank for all participants. Using genetic principal components (PCs) provided by the UKB, 4-means clustering on the first two PCs was performed to identify individuals of European ancestry. QC was then performed using PLINK v1.9 to remove: variants with missingness > 0.02 (before individual QC), individuals with missingness > 0.02, individuals whose self-reported sex was discordant from their genetic sex, variants with missingness > 0.02 (after individual QC), variants departing from Hardy-Weinberg Equilibrium (p < 10e-8), and variants with minor allele frequency (MAF) < 0.01. Relatedness kinship estimates provided by the UK Biobank were used to identify pairs of related individuals using KING (r2 > 0.044) and the GreedyRelated algorithm was used to remove one individual from each pair, preferentially retaining individuals that survived previous QC. FlashPCA was used to generate PCs for the sub-set of individuals of European ancestry that survived QC.

1.0.2 PROTECT

The PROTECT study is a UK-based online participant registry with continuous, ongoing recruitment. The PROTECT study acts as a registry as well as a study with its own aims and outcomes. The PROTECT study aims are primarily to establish risk factors for cognitive ageing and dementia. Recruitment in to the study was on the basis of local and national publicity with the majority of participants joining on the launch of the study in November 2015.

Genetic data

In PROTECT, genotypes were assayed in two batches using a variant of the Illumina Infinium Global Screening Array. The total numbers of participants in the combined genotyped data was 9146. Iterative filtering for call rate at 98% completeness (for individuals and SNPs) resulted in the exclusion of 84 samples. Relatedness was estimated using KING 2.2.3, followed by extraction of a list of individuals that contained no pairs of individuals with a 1st-, 2nd- or 3rd-degree relationships. Variants with Hardy-Weinberg Equilibrium p-value < 0.00001 were excluded. Individuals whose gender estimated from the genetic data did not match that reported by the study participants were excluded. Principal components (PCs) were calculated for the unrelated subset of the data using EIGENSOFT 6.1.4 after pruning. K-means clustering (assuming 4 distinct clusters) was used on the first two derived principal components to define a cluster of European ancestry individuals. Principal components were then recalculated for the cluster of individuals of European ancestry, with outlier individuals removed by EIGENSOFT if exceeding a sigma threshold of 30. Finally, individuals with excess heterozygosity (unusual patterns of genome-wide heterogeneity) calculated using the ibc function in plink v1.90 were excluded. The total number of individuals excluded was 790, resulting in a sample size of 8272.

2 Supplementary Results

2.1 Results section A

2.1.1 Comparisons with definitions of probable bipolar disorder

We compared the overlap of each class with cases of probable bipolar disorder type I and type II, as defined by Davis et al.from responses in the MHQ, and Smith et al. from responses to similar questions at baseline (Figures S25-26). The majority of cases of probable bipolar disorder type I defined by Davis et al. (N=931) were members of either the active restless (36.3%), or the extensively affected class (31.8%) class. For probable bipolar disorder type II (N=455), the majority of cases were members of the focused creative class (49%). For the definition of probable bipolar disorder type I by Smith et al (N=248 MHQ responders), the majority of cases were members of the extensively affected class (42.7%) or the active restless class (17.7%). For probable bipolar disorder type II (N=252 MHQ responders), the majority were members of the focused creative class (21.8%) or the minimally affected class (12.7%). Notably a large proportion of cases of probable bipolar disorder type II were missing class assignment, indicating that despite reporting symptoms in the baseline questionnaire that conferred them probable case status, they did not report a manic or irritable episode in the follow-up MHQ or did not answer the specific question.

3 Supplementary Figures

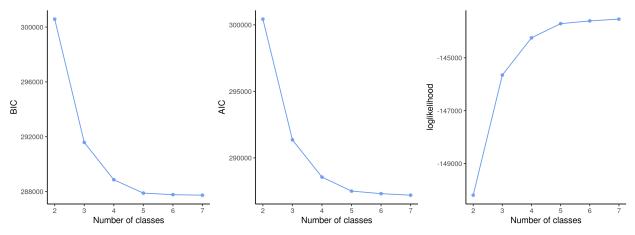


Figure S1 Elbow plots of fit statistics Bayesian Information Criterion (BIC) and Akaike Information Criterion (AIC), with log likelihood, from models with increasing number of classes (2:7 classes).

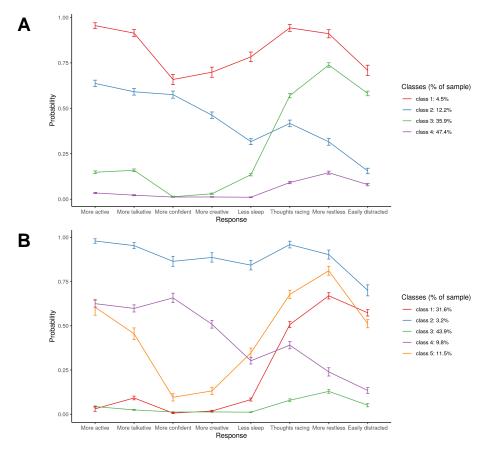


Figure S2 Comparison of conditional probabilities for each indicator symptom in the latent models with (A) 4 classes and (B) 5 classes. Note classes are unordered based on the default output from the LCA model.

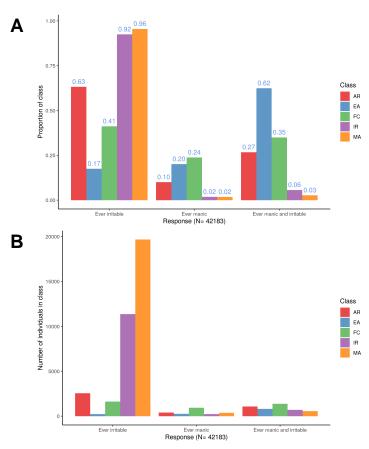


Figure S3 Distribution of responses to manic or irritable stem question by most likely class membership in the optimum 5-class model, where A) the proportion of responses in each class, and B) the absolute number of responses in each class.

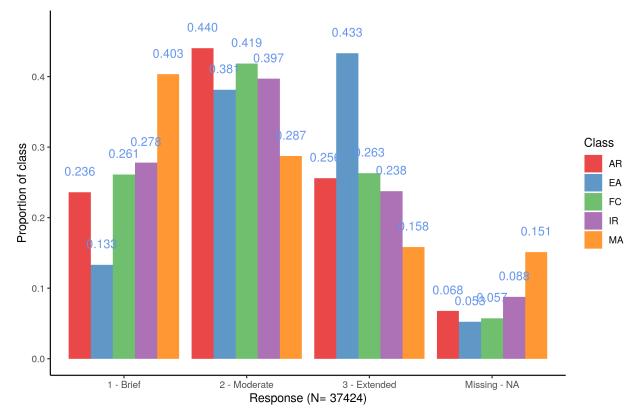


Figure S4 Distributions of responses to episode duration by most likely class membership, where "1 - Brief" <24 hours, "2 - Moderate"; duration >24 hours and <1 week, and "3 - Extended"; duration >1 week.

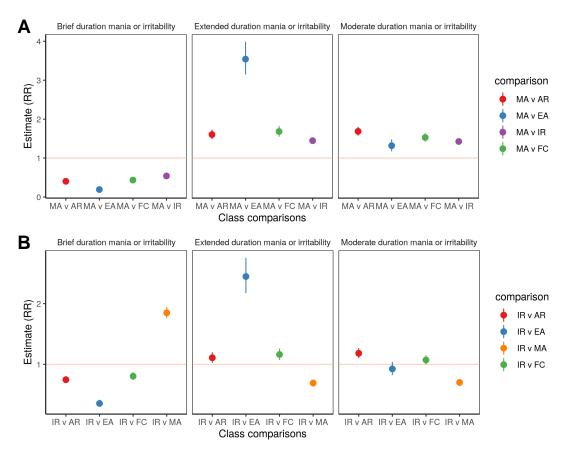


Figure S5 Associations of responses to episode duration question by most likely class membership in the optimum 5-class model.

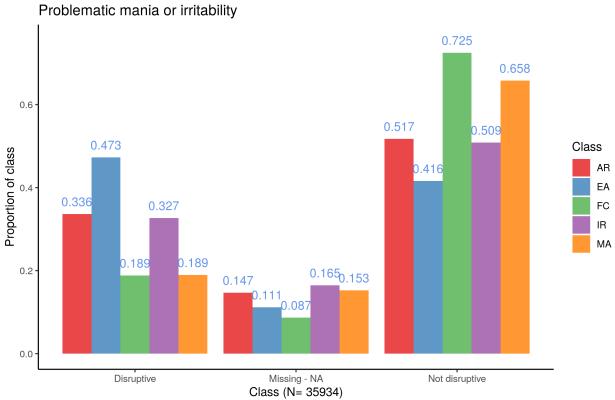


Figure S6 Distributions of responses to episode disruptiveness by most likely class membership.

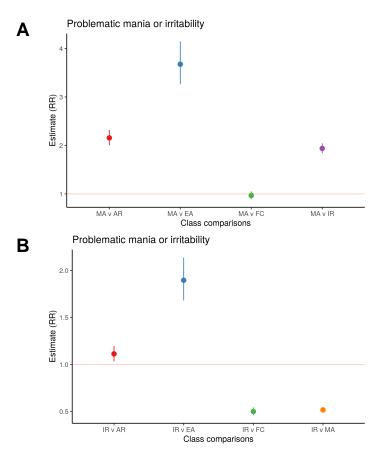
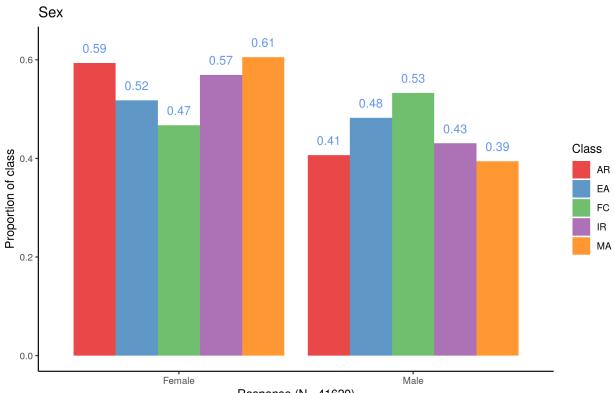


Figure S7 Associations of responses to episode disruptiveness question with most likely class membership in the optimum 5-class model.



Response (N= 41620)

Figure S8 Distributions of sex by most likely class membership.

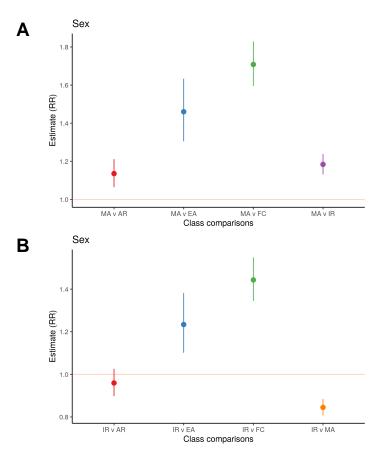


Figure S9 Associations of sex with most likely class membership in the optimum 5-class model.

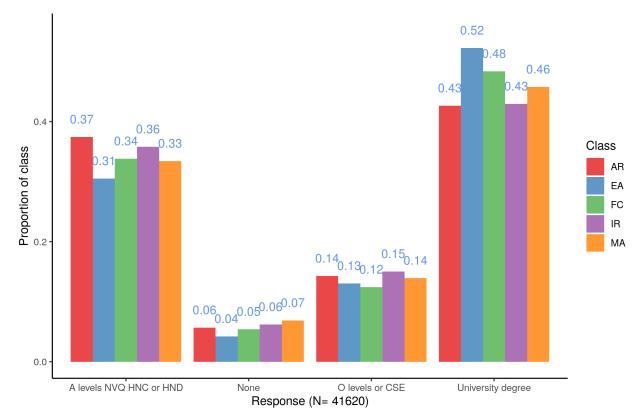


Figure S10 Distributions of educational attainment by most likely class membership.

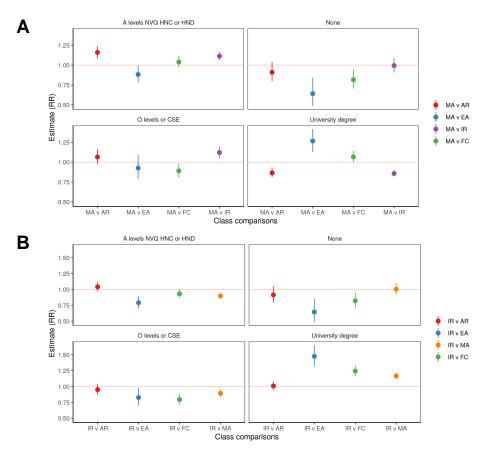


Figure S11 Associations of educational attainment with most likely class membership in the optimum 5-class model.

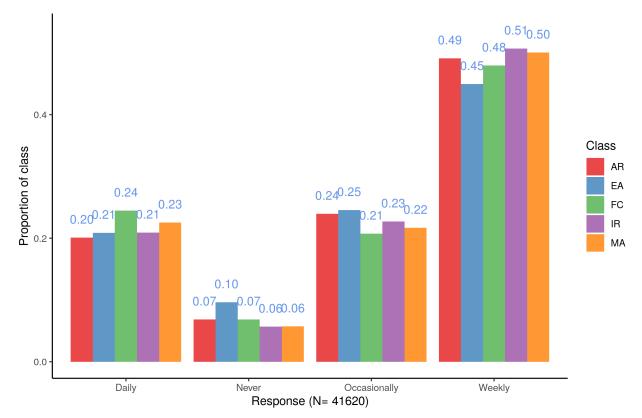


Figure S12 Distributions of alcohol consumption frequency by most likely class membership.

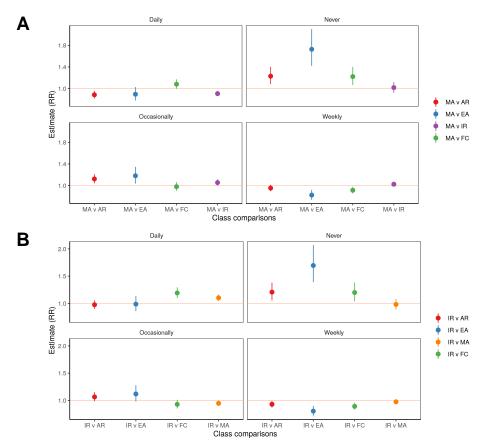


Figure S13 Associations of alcohol consumption frequency with most likely class membership in the optimum 5-class model.

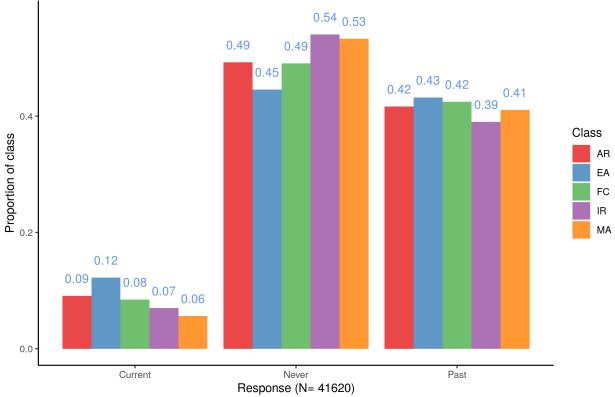


Figure S14 Distributions of smoking by most likely class membership.

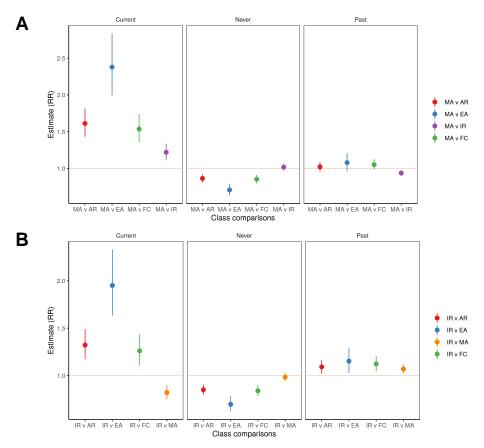


Figure S15 Associations of smoking with most likely class membership in the optimum 5-class model.

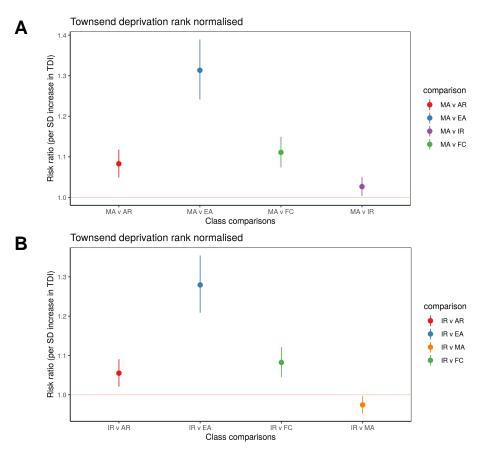


Figure S16 Associations of rank normalised Townsend deprivation index (TDI) with most likely class membership in the optimum 5-class model.

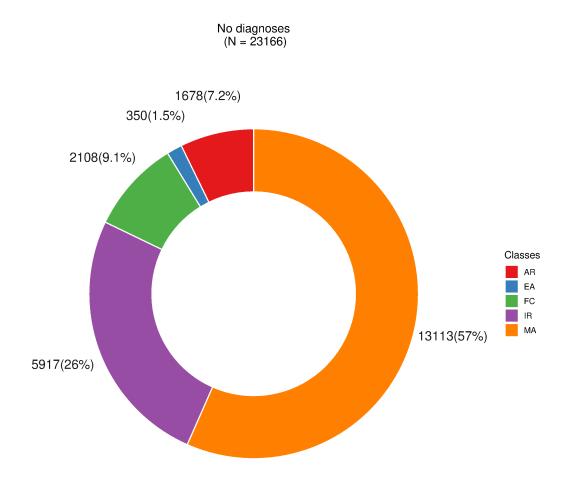


Figure S17 Distributions of individuals without a self-reported diagnosis of any of the six psychiatric disorders (54.9% of total) by most likely class assignment.

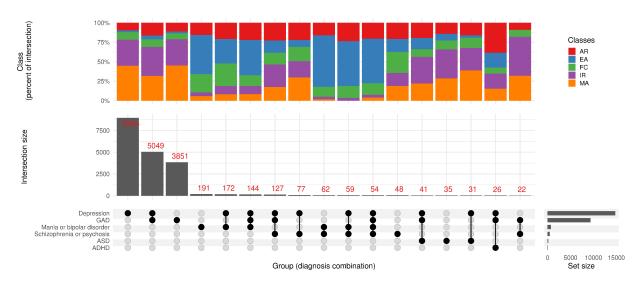


Figure S18 Distributions of different combinations of self-reported diagnoses of six psychiatric disorders (one or more diagnoses; N=19,017, 45.1% of analytical sample) by most likely class assignment. The lower panel indicates the intersection size (number of individuals reporting that combination of diagnoses). The upper panel indicates the percent of that intersection comprised by each class. Note that diagnosis combinations with fewer than 20 individuals are excluded (N=84 individuals). Classes are AR = active restless class, EA = extensively affected class, FC = focused creative class, IR = inactive restless class, MA = minimally affected class.

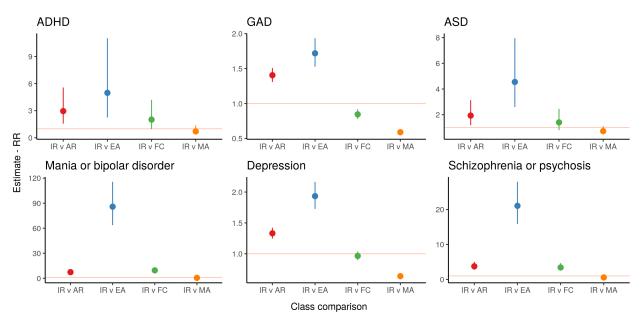


Figure S19 Associations of self-reported diagnoses of six disorders with most likely class membership in the optimum 5-class model.

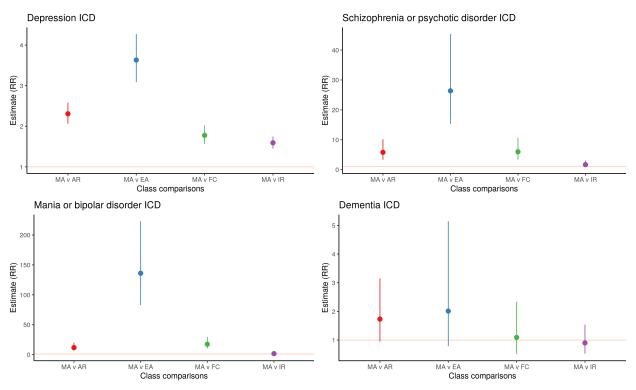


Figure S20 Associations of ICD diagnoses from hospital records of four disorders with most likely class membership in the optimum 5-class model.

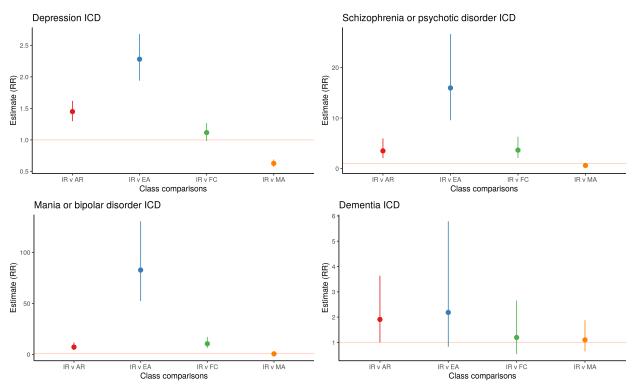


Figure S21 Associations of ICD diagnoses from hospital records of four disorders with most likely class membership in the optimum 5-class model.

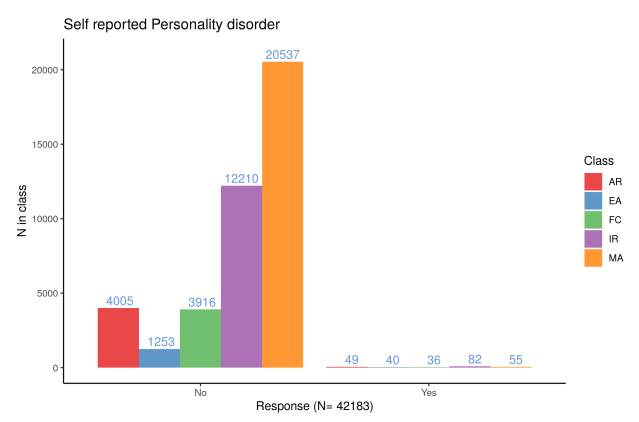


Figure S22 Distributions of self-reported diagnosis of personality disorder by most likely class membership.

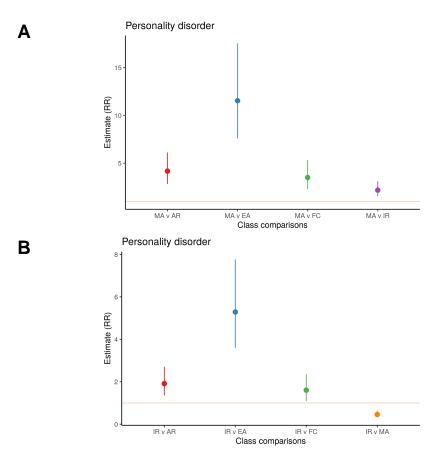


Figure S23 Associations of self-reported diagnosis of personality disorder with most likely class membership in the optimum 5-class model.

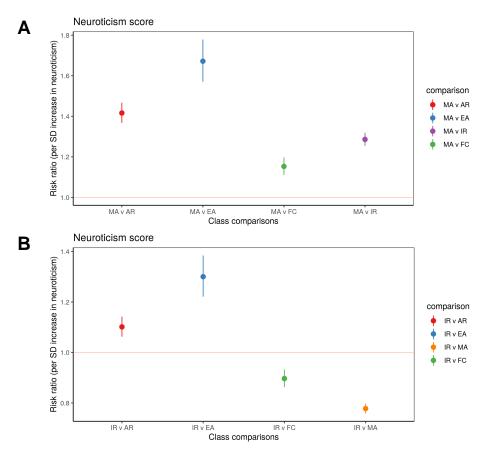


Figure S24 Associations of standardised neuroticism score with most likely class membership in the optimum 5-class model.

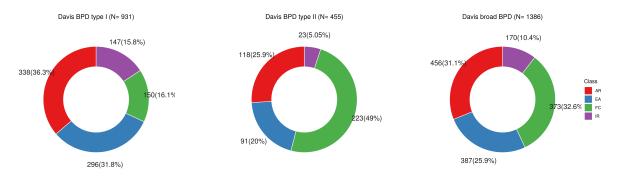


Figure S25 Comparison of the overlap of cases of probable bipolar disorder type I, bipolar disorder type II and broad bipolar disorder (combined type I and type II), as defined by Davis et al. with most likely latent class assignent.

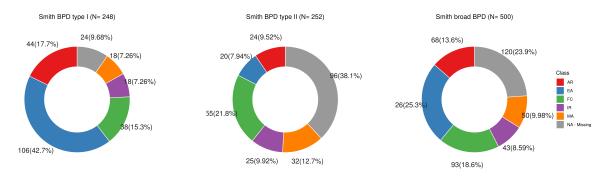


Figure S26 Comparison of the overlap of cases of probable bipolar disorder type I, bipolar disorder type II and broad bipolar disorder (combined type I and type II), as defined by Smith et al. with most likely latent class assignent.

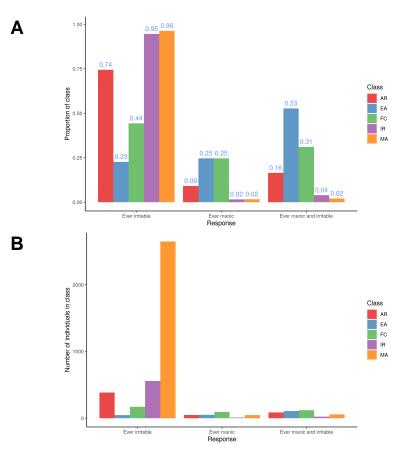


Figure S27 Distribution of responses to manic or irritable stem question by most likely class membership in the optimum 5-class model in PROTECT, where A) the proportion of responses in each class, and B) the absolute number of responses in each class.

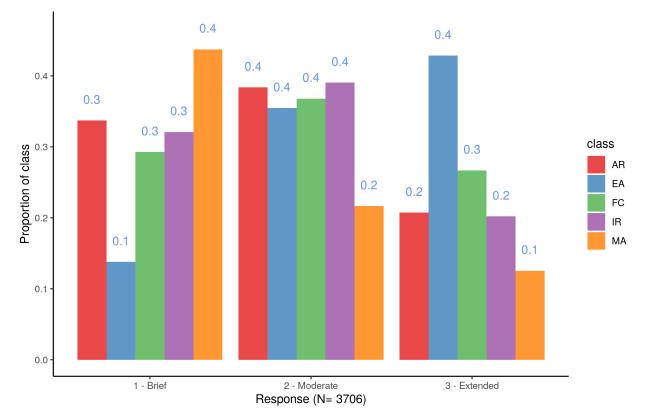


Figure S28 Distributions of responses to episode duration by most likely class membership, where "1 - Brief" <24 hours, "2 - Moderate"; duration >24 hours and < 1 week, and "3 - Extended"; duration > 1 week in PROTECT.

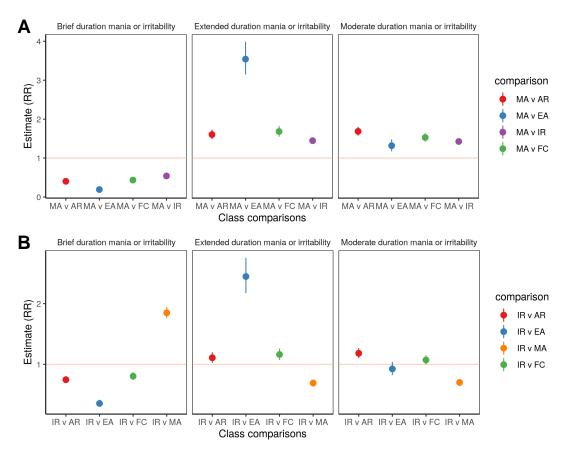


Figure S29 Associations of responses to episode duration question by most likely class membership in the optimum 5-class model in PROTECT.

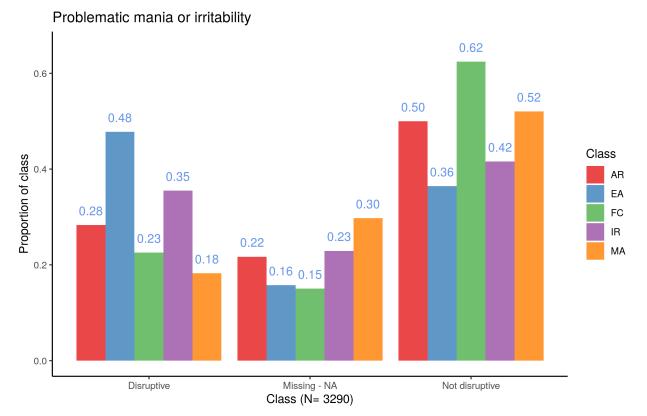


Figure S30 Distributions of responses to episode disruptiveness by most likely class membership in PRO-TECT.

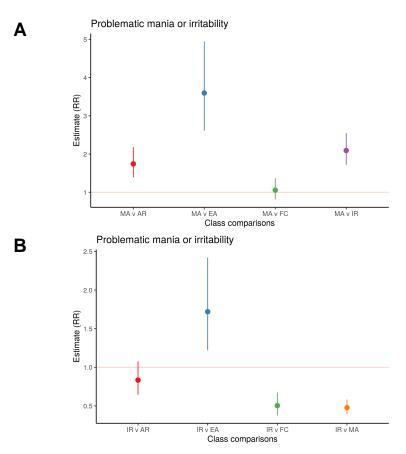


Figure S31 Associations of responses to episode disruptiveness question with most likely class membership in the optimum 5-class model in PROTECT.

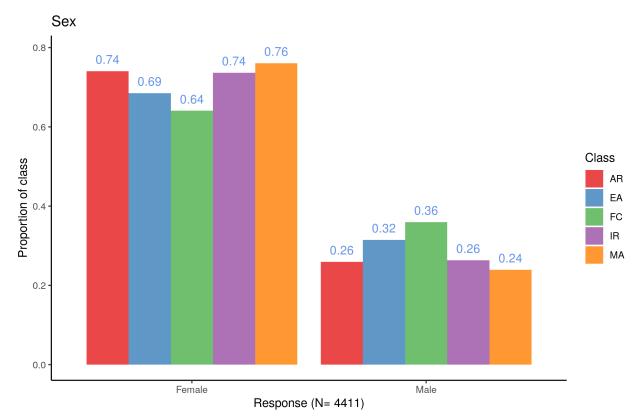


Figure S32 Distributions of sex by most likely class membership in PROTECT.

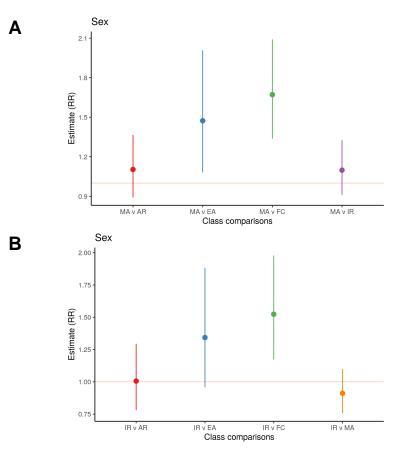


Figure S33 Associations of sex with most likely class membership in the optimum 5-class model in PROTECT.

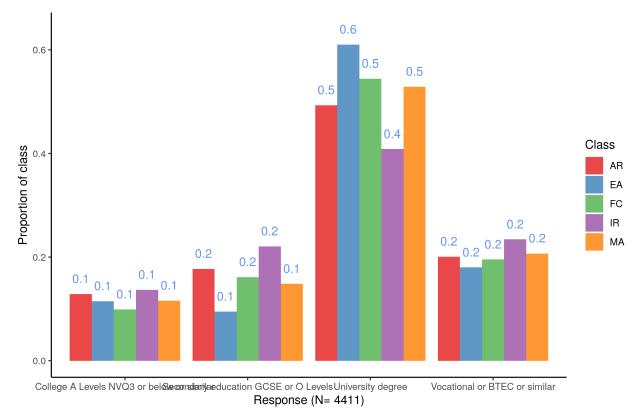


Figure S34 Distributions of educational attainment by most likely class membership in PROTECT.

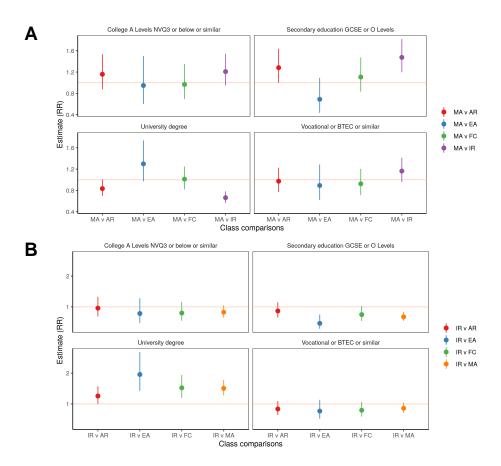


Figure S35 Associations of educational attainment with most likely class membership in the optimum 5-class model in PROTECT.

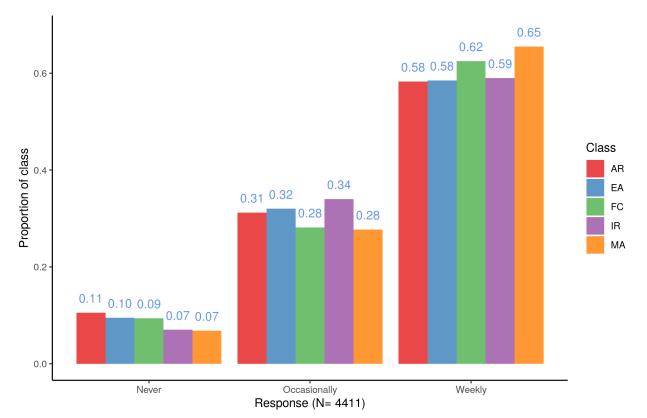


Figure S36 Distributions of alcohol consumption frequency by most likely class membership in PROTECT.

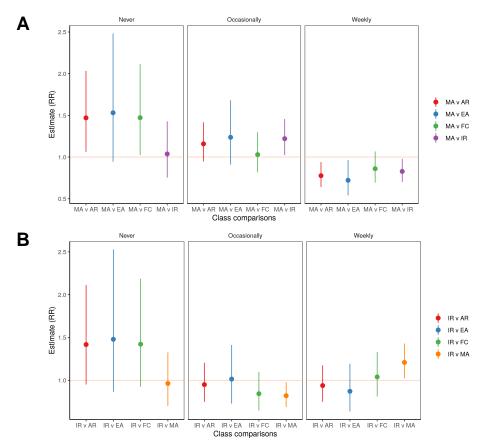


Figure S37 Associations of alcohol consumption frequency with most likely class membership in the optimum 5-class model in PROTECT.

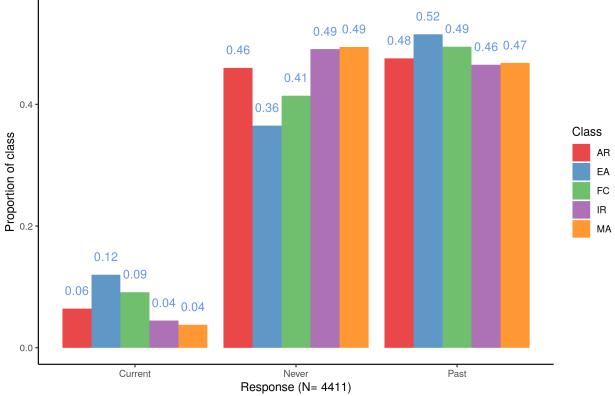


Figure S38 Distributions of smoking by most likely class membership.

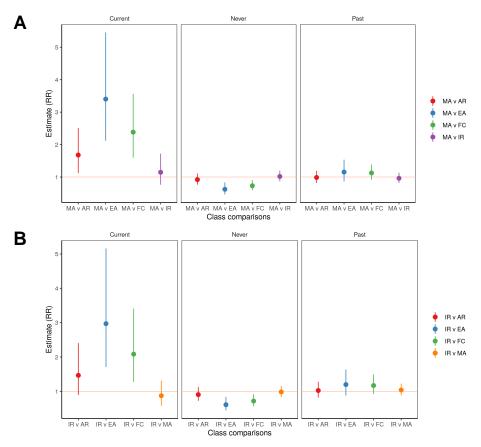


Figure S39 Associations of smoking with most likely class membership in the optimum 5-class model in PROTECT.

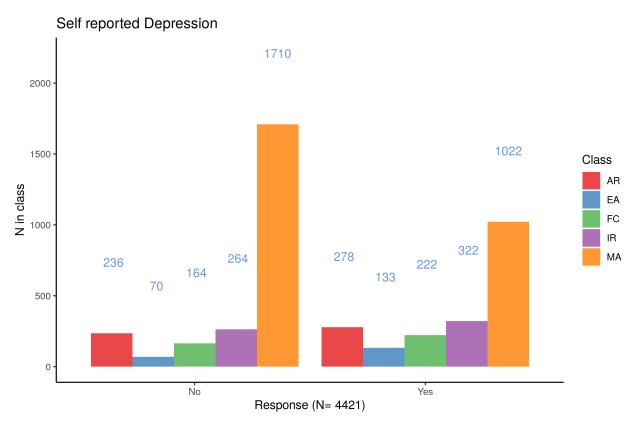


Figure S40 Distributions of self-reported diagnosis of depression by most likely class membership.

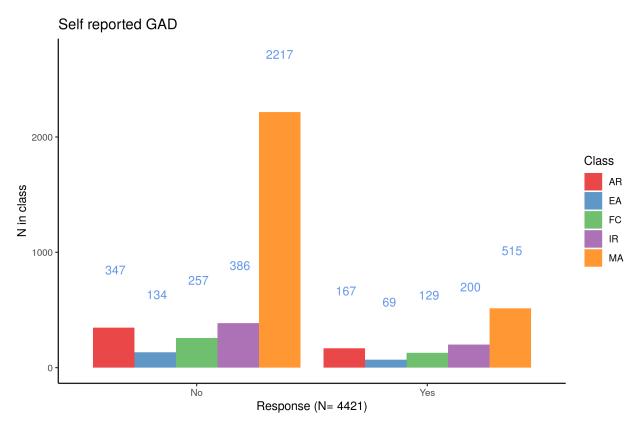


Figure S41 Distributions of self-reported GAD by most likely class membership.

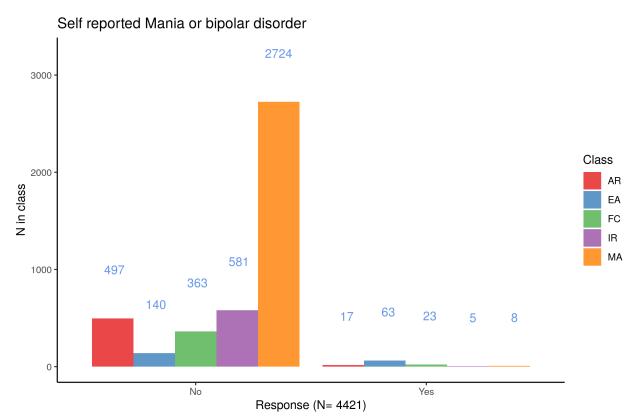
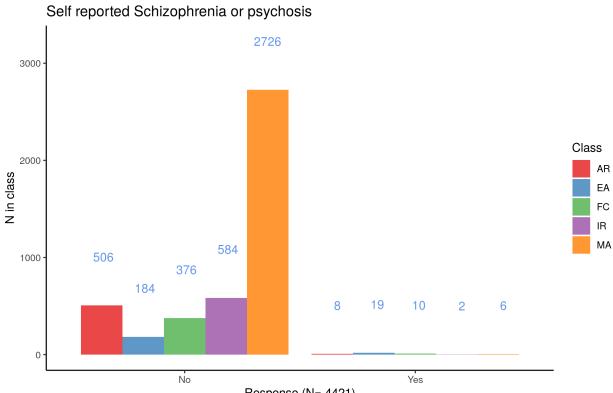


Figure S42 Distributions of self-reported mania or bipolar disorder by most likely class membership.



Response (N= 4421)

Figure S43 Distributions of self-reported diagnosis of schizophrenia or psychosis by most likely class membership.

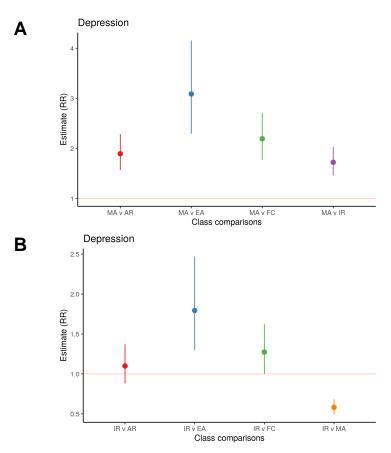


Figure S44 Associations of self-reported dignosis of depression with most likely class membership in the optimum 5-class model in PROTECT.

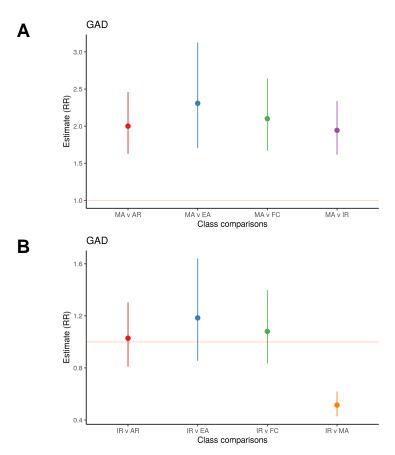


Figure S45 Associations of self-reported diagnosis of GAD with most likely class membership in the optimum 5-class model in PROTECT.

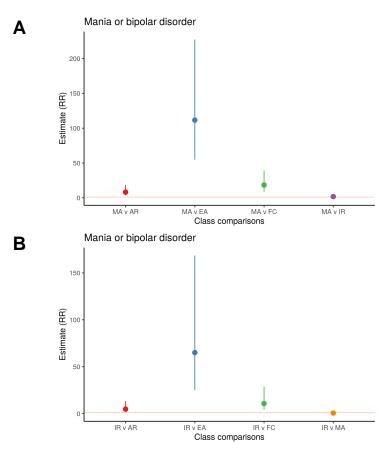


Figure S46 Associations of self-reported diagnosis of mania or bipolar disorder with most likely class membership in the optimum 5-class model in PROTECT.

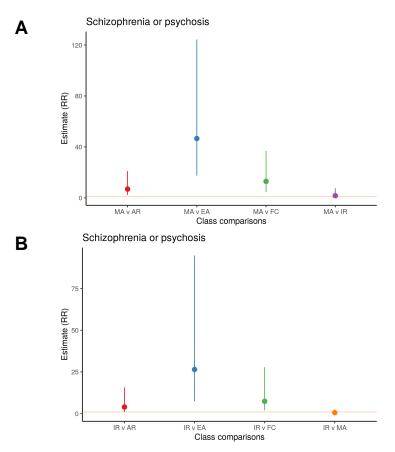


Figure S47 Associations of self-reported diagnosis of schizophrenia or psychosis with most likely class membership in the optimum 5-class model in PROTECT.

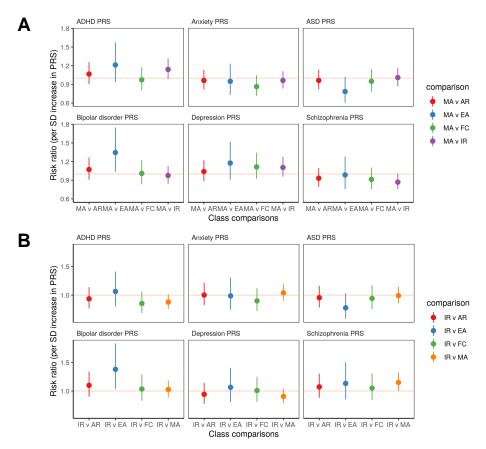


Figure S48 Associations of PRS of six disorders with most likely class membership in the optimum 5-class model in PROTECT.

4 Supplementary Tables

Trait	Publication year	Study population ancestry	Trait data type	N cases	N controls	Sample size (discovery)	PMID
ADHD	2017	European	binary	19099	34194	53293	30478444
Anxiety disorders	2016	European	binary	NULL	NULL	17310	26754954
Autism spectrum disorder	2017	European	binary	6197	7377	13574	28540026
Bipolar disorder	2011	European	binary	7481	9250	16731	21926972
Major depressive disorder	2018	European	binary	45591	97674	143265	29700475
Schizophrenia	2014	European	binary	33640	43456	77096	25056061

Table 1: Details of published genome-wide association studies from which summary results were used for calculating polygenic risk scores (PRS)

Where sample size for cases and controls is NULL the sample size was not reported or was not available for the subset of the data that was analysed in the original study.

Response	Value	N (percent)
More active	No	34148 (0.81)
More active	Yes	8035 (0.19)
More confident	No	37526(0.89)
More confident	Yes	4657 (0.11)
Easily distracted	No	29620(0.7)
Easily distracted	Yes	12563(0.3)
More creative	No	37770(0.9)
More creative	Yes	4413 (0.1)
Less sleep	No	36801(0.87)
Less sleep	Yes	5382(0.13)
Thoughts racing	No	27772(0.66)
Thoughts racing	Yes	14411(0.34)
More restless	No	24729(0.59)
More restless	Yes	17454(0.41)
More talkative	No	34547(0.82)
More talkative	Yes	7636 (0.18)

Table 2: Numbers of responses to individual symptoms questions out of a total sample of N=42183

Number of classes	2	3	4	5	6	7
BIC	300578.9	291581.9	288859.6	287883.9	287770.8	287732.7
AIC	300431.9	291357	288556.9	287503.4	287312.4	287196.4
loglikelihood	-150198.947	-145652.482	-144243.426	-143707.676	-143603.199	-143536.199
N iterations	86	198	187	686	5140	1892
Entropy	3.58	3.46	3.43	3.41	3.41	3.4
Relative entropy	0.761	0.665	0.665	0.626	0.629	0.592
Ν	42183	42183	42183	42183	42183	42183

Table 3: Fit statistics for latent class models with 2:7 classes

Class	Response	N (percent)
IR	Ever manic	229 (1.86)
IR	Ever irritable	11366 (92.47)
IR	Ever manic and irritable	697 (5.67)
EA	Ever manic	260(20.11)
EA	Ever irritable	226(17.48)
EA	Ever manic and irritable	807 (62.41)
MA	Ever manic	366(1.78)
MA	Ever irritable	$19670 \ (95.52)$
MA	Ever manic and irritable	556(2.7)
\mathbf{FC}	Ever manic	940(23.79)
\mathbf{FC}	Ever irritable	1629(41.22)
\mathbf{FC}	Ever manic and irritable	1383 (34.99)
AR	Ever manic	408(10.06)
AR	Ever irritable	$2562 \ (63.2)$
AR	Ever manic and irritable	1084 (26.74)

Table 4: Distribution of responses to manic or irritable stem question by most likely class membership in the optimum 5-class model

Class	Response	N (percent)
IR	1 - Brief	3417 (27.8)
IR	2 - Moderate	4878(39.68)
IR	3 - Extended	2920(23.76)
IR	Missing - NA	1077 (8.76)
\mathbf{EA}	1 - Brief	172 (13.3)
$\mathbf{E}\mathbf{A}$	2 - Moderate	493(38.13)
$\mathbf{E}\mathbf{A}$	3 - Extended	560(43.31)
$\mathbf{E}\mathbf{A}$	Missing - NA	68(5.26)
MA	1 - Brief	8303 (40.32)
MA	2 - Moderate	5915(28.72)
MA	3 - Extended	3261(15.84)
MA	Missing - NA	3113(15.12)
\mathbf{FC}	1 - Brief	1032 (26.11)
\mathbf{FC}	2 - Moderate	1654 (41.85)
\mathbf{FC}	3 - Extended	1040(26.32)
\mathbf{FC}	Missing - NA	226 (5.72)
AR	1 - Brief	957 (23.61)
AR	2 - Moderate	1784 (44.01)
AR	3 - Extended	1038(25.6)
AR	Missing - NA	275 (6.78)

Table 5: Distribution of responses to the episode duration question by most likely class membership in the optimum 5-class model

Response	Class comparison	Effect	95% CI	SE	P-value
	-				
Brief duration mania or irritability	MA v IR	0.541	0.515, 0.568	0.025	4.56e-132
Brief duration mania or irritability	MA v EA	0.192	0.164, 0.225	0.081	3.62e-92
Brief duration mania or irritability	MA v FC	0.435	0.403, 0.47	0.039	1.49e-100
Brief duration mania or irritability	MA v AR	0.404	0.375, 0.434	0.037	7.58e-131
Moderate duration mania or irritability	MA v IR	1.427	1.358, 1.498	0.025	6.35e-46
Moderate duration mania or irritability	MA v EA	1.319	1.173, 1.483	0.060	3.82e-06
Moderate duration mania or irritability	MA v FC	1.529	1.423, 1.642	0.036	2.78e-31
Moderate duration mania or irritability	MA v AR	1.686	1.576, 1.803	0.034	2.01e-52
Extended duration mania or irritability	MA v IR	1.447	1.366, 1.533	0.029	2.03e-36
Extended duration mania or irritability	MA v EA	3.542	3.148, 3.986	0.060	7.83e-98
Extended duration mania or irritability	MA v FC	1.682	1.551, 1.824	0.041	1.91e-36
Extended duration mania or irritability	MA v AR	1.604	1.485, 1.732	0.039	2.74e-33
Brief duration mania or irritability	IR v EA	0.355	0.303, 0.417	0.082	9.72e-37
Brief duration mania or irritability	IR v MA	1.848	1.759, 1.941	0.025	4.89e-132
Brief duration mania or irritability	IR v FC	0.804	0.742, 0.87	0.041	7.61e-08
Brief duration mania or irritability	IR v AR	0.746	0.692, 0.805	0.039	4.83e-14
Moderate duration mania or irritability	IR v EA	0.924	0.821, 1.04	0.060	1.93e-01
Moderate duration mania or irritability	IR v MA	0.701	0.668, 0.736	0.025	6.49e-46
Moderate duration mania or irritability	IR v FC	1.072	0.996, 1.153	0.037	6.27 e- 02
Moderate duration mania or irritability	IR v AR	1.182	1.103, 1.266	0.035	1.87e-06
Extended duration mania or irritability	IR v EA	2.447	2.174, 2.755	0.060	1.22e-49
Extended duration mania or irritability	IR v MA	0.691	0.652, 0.732	0.029	2.00e-36
Extended duration mania or irritability	IR v FC	1.162	1.071, 1.261	0.041	2.95e-04
Extended duration mania or irritability	IR v AR	1.108	1.025, 1.197	0.040	9.48e-03

Table 6: Associations of episode duration with most likely class membership weighted for the probability of inclusion in each class.

Class	Response	N (percent)
IR	Disruptive	4018 (39.13)
IR	Not disruptive	6251(60.87)
IR	Missing - NA	2023 (NA)
EA	Disruptive	611 (53.18)
$\mathbf{E}\mathbf{A}$	Not disruptive	538(46.82)
$\mathbf{E}\mathbf{A}$	Missing - NA	144 (NA)
MA	Disruptive	3898(22.34)
MA	Not disruptive	$13549\ (77.66)$
MA	Missing - NA	3145 (NA)
\mathbf{FC}	Disruptive	745 (20.64)
\mathbf{FC}	Not disruptive	$2865\ (79.36)$
\mathbf{FC}	Missing - NA	342 (NA)
AR	Disruptive	1362(39.38)
AR	Not disruptive	$2097 \ (60.62)$
AR	Missing - NA	595 (NA)

Table 7: Distribution of responses to episode disruptiveness question by most likely class membership in the optimum 5-class model

Response	Class comparison	Effect	95% CI	SE	P-value
Problematic mania or irritability	MA v IR	1.938	1.837,2.045	0.027	1.01e-128
Problematic mania or irritability	MA v EA	3.675	3.259, 4.144	0.061	3.19e-100
Problematic mania or irritability	MA v FC	0.967	0.887, 1.053	0.044	4.40e-01
Problematic mania or irritability	MA v AR	2.156	2.004, 2.319	0.037	8.85e-95
Problematic mania or irritability	IR v EA	1.895	1.68, 2.138	0.061	2.28e-25
Problematic mania or irritability	IR v MA	0.516	0.489, 0.544	0.027	1.06e-128
Problematic mania or irritability	IR v FC	0.499	0.458, 0.544	0.044	3.23e-56
Problematic mania or irritability	IR v AR	1.112	1.033, 1.197	0.037	4.53e-03

Table 8: Associations of episode disruptiveness with most likely class membership weighted for the probability of inclusion in each class.

Class	Response	N (percent)
IR	Female	6916 (56.95)
IR	Male	5229(43.05)
EA	Female	660(51.76)
EA	Male	615(48.24)
MA	Female	$12293 \ (60.55)$
MA	Male	8009(39.45)
\mathbf{FC}	Female	1819 (46.72)
\mathbf{FC}	Male	2074 (53.28)
AR	Female	2377 (59.35)
AR	Male	1628 (40.65)

Table 9: Distribution of sex by most likely class membership in the optimum 5-class model

Response	Class comparison	Effect	95% CI	SE	P-value
Sex	MA v IR	1.184	1.131,1.239	0.023	4.01e-13
Sex	MA v EA	1.460	1.305, 1.634	0.057	3.87e-11
Sex	MA v FC	1.708	1.595, 1.829	0.035	2.95e-53
Sex	MA v AR	1.135	1.064, 1.211	0.033	1.16e-04
Sex	IR v EA	1.234	1.101, 1.382	0.058	2.91e-04
Sex	IR v MA	0.845	0.807, 0.884	0.023	4.01e-13
Sex	IR v FC	1.443	1.345, 1.549	0.036	2.12e-24
Sex	IR v AR	0.959	0.897, 1.026	0.034	2.24e-01

Table 10: Associations of sex with most likely class membership weighted for the probability of inclusion in each class.

Class	Response	N (percent)
IR	A levels NVQ HNC or HND	4350 (35.82)
IR	None	752 (6.19)
IR	O levels or CSE	1826 (15.03)
IR	University degree	5217 (42.96)
EA	A levels NVQ HNC or HND	389(30.51)
EA	None	54(4.24)
EA	O levels or CSE	166(13.02)
EA	University degree	666 (52.24)
MA	A levels NVQ HNC or HND	6786(33.43)
MA	None	1393 (6.86)
MA	O levels or CSE	2829(13.93)
MA	University degree	9294 (45.78)
\mathbf{FC}	A levels NVQ HNC or HND	1317(33.83)
\mathbf{FC}	None	210(5.39)
\mathbf{FC}	O levels or CSE	483(12.41)
\mathbf{FC}	University degree	1883 (48.37)
AR	A levels NVQ HNC or HND	1499(37.43)
AR	None	227(5.67)
AR	O levels or CSE	571(14.26)
AR	University degree	1708(42.65)

Table 11: Distribution of educational attainment by most likely class membership in the optimum 5-class model

Response	Class comparison	Effect	95% CI	SE	P-value
A levels NVQ HNC or HND	MA v IR	1.113	1.062,1.167	0.024	7.80e-06
A levels NVQ HNC or HND	MA v EA	0.883	0.782, 0.997	0.062	4.37e-02
A levels NVQ HNC or HND	MA v FC	1.039	0.967, 1.116	0.037	2.98e-01
A levels NVQ HNC or HND	MA v AR	1.159	1.085, 1.239	0.034	1.24e-05
None	MA v IR	0.994	0.908, 1.088	0.046	9.02e-01
None	MA v EA	0.642	0.489, 0.843	0.139	1.41e-03
None	MA v FC	0.817	0.705, 0.947	0.075	7.13e-03
None	MA v AR	0.910	0.797, 1.039	0.068	1.62e-01
O levels or CSE	MA v IR	1.120	1.051, 1.194	0.032	4.66e-04
O levels or CSE	MA v EA	0.926	0.784, 1.094	0.085	3.66e-01
O levels or CSE	MA v FC	0.891	0.805, 0.987	0.052	2.73e-02
O levels or CSE	MA v AR	1.065	0.973, 1.167	0.046	1.72e-01
University degree	MA v IR	0.858	0.82, 0.897	0.023	2.52e-11
University degree	MA v EA	1.265	1.131, 1.415	0.057	3.97 e-05
University degree	MA v FC	1.066	0.996, 1.141	0.035	6.41e-02
University degree	MA v AR	0.865	0.812, 0.923	0.033	1.02e-05
A levels NVQ HNC or HND	IR v EA	0.793	0.701, 0.896	0.063	2.08e-04
A levels NVQ HNC or HND	IR v MA	0.898	0.857, 0.941	0.024	7.82e-06
A levels NVQ HNC or HND	IR v FC	0.933	0.866, 1.005	0.038	6.60e-02
A levels NVQ HNC or HND	IR v AR	1.041	0.972, 1.115	0.035	2.47e-01
None	IR v EA	0.646	0.491, 0.849	0.140	1.78e-03
None	IR v MA	1.006	0.919, 1.101	0.046	9.02e-01
None	IR v FC	0.821	0.706, 0.956	0.078	1.11e-02
None	IR v AR	0.915	0.797, 1.05	0.070	2.05e-01
O levels or CSE	IR v EA	0.827	0.698, 0.978	0.086	2.68e-02
O levels or CSE	IR v MA	0.893	0.838, 0.951	0.032	4.65e-04
O levels or CSE	IR v FC	0.795	0.716, 0.883	0.053	1.79e-05
O levels or CSE	IR v AR	0.951	0.866, 1.044	0.048	2.91e-01
University degree	IR v EA	1.475	1.316, 1.652	0.058	2.07e-11
University degree	IR v MA	1.166	1.115, 1.22	0.023	2.51e-11
University degree	IR v FC	1.244	1.159, 1.334	0.036	1.40e-09
University degree	IR v AR	1.009	0.944, 1.079	0.034	7.88e-01

Table 12: Associations of educational attainment with most likely class membership weighted for the probability of inclusion in each class.

Class	Response	N (percent)
IR	Daily	2538 (20.9)
IR	Never	693(5.71)
IR	Occasionally	2758(22.71)
IR	Weekly	6156 (50.69)
$\mathbf{E}\mathbf{A}$	Daily	266 (20.86)
$\mathbf{E}\mathbf{A}$	Never	123(9.65)
$\mathbf{E}\mathbf{A}$	Occasionally	313(24.55)
EA	Weekly	573(44.94)
MA	Daily	4577(22.54)
MA	Never	1165(5.74)
MA	Occasionally	4400 (21.67)
MA	Weekly	10160(50.04)
\mathbf{FC}	Daily	953~(24.48)
\mathbf{FC}	Never	266 (6.83)
\mathbf{FC}	Occasionally	807(20.73)
\mathbf{FC}	Weekly	1867 (47.96)
AR	Daily	804(20.07)
AR	Never	274(6.84)
AR	Occasionally	959(23.95)
AR	Weekly	1968 (49.14)

Table 13: Distribution of alcohol consumption frequency by most likely class membership in the optimum 5-class model

Degnonge	Class comparison	Effect	95% CI	SE	P-value
Response	-				
Daily	MA v IR	0.907	0.859, 0.958	0.028	4.46e-04
Daily	MA v EA	0.896	0.78, 1.028	0.070	1.17e-01
Daily	MA v FC	1.081	0.998, 1.171	0.041	5.59e-02
Daily	MA v AR	0.885	0.819, 0.957	0.040	2.23e-03
Never	MA v IR	1.019	0.925, 1.122	0.049	7.07e-01
Never	MA v EA	1.726	1.419, 2.1	0.100	4.66e-08
Never	MA v FC	1.222	1.065, 1.401	0.070	4.15e-03
Never	MA v AR	1.230	1.081, 1.398	0.065	1.61e-03
Occasionally	MA v IR	1.056	1,1.114	0.028	4.91e-02
Occasionally	MA v EA	1.182	1.037, 1.346	0.067	1.22e-02
Occasionally	MA v FC	0.980	0.902, 1.065	0.042	6.39e-01
Occasionally	MA v AR	1.124	1.042, 1.212	0.038	2.40e-03
Weekly	MA v IR	1.026	0.981, 1.073	0.023	2.69e-01
Weekly	MA v EA	0.825	0.737, 0.923	0.057	7.78e-04
Weekly	MA v FC	0.915	0.855, 0.979	0.035	1.02e-02
Weekly	MA v AR	0.954	0.895, 1.016	0.032	1.44e-01
Daily	IR v EA	0.987	0.858, 1.135	0.071	8.57 e-01
Daily	IR v MA	1.102	1.044, 1.164	0.028	4.42e-04
Daily	IR v FC	1.192	1.096, 1.295	0.042	3.66e-05
Daily	IR v AR	0.976	0.899, 1.059	0.042	5.57 e-01
Never	IR v EA	1.695	1.389, 2.07	0.102	2.16e-07
Never	IR v MA	0.982	0.891, 1.081	0.049	7.09e-01
Never	IR v FC	1.200	1.041, 1.383	0.073	1.22e-02
Never	IR v AR	1.207	1.056, 1.38	0.068	5.86e-03
Occasionally	IR v EA	1.119	0.98, 1.277	0.067	9.54 e- 02
Occasionally	IR v MA	0.947	0.897,1	0.028	4.90e-02
Occasionally	IR v FC	0.929	0.853, 1.012	0.044	8.98e-02
Occasionally	IR v AR	1.065	0.985, 1.151	0.040	1.16e-01
Weekly	IR v EA	0.804	0.718,0.901	0.058	1.76e-04
Weekly	IR v MA	0.975	0.932, 1.02	0.023	2.69e-01
Weekly	IR v FC	0.892	0.831, 0.957	0.036	1.44e-03
Weekly	IR v AR	0.930	0.87,0.994	0.034	3.13e-02

Table 14: Associations of alcohol consumption frequency with most likely class membership weighted for the probability of inclusion in each class.

Class	Response	N (percent)
IR	Current	847 (6.97)
IR	Never	6561 (54.02)
IR	Past	4737 (39)
\mathbf{EA}	Current	156(12.24)
\mathbf{EA}	Never	568 (44.55)
\mathbf{EA}	Past	551 (43.22)
MA	Current	1140(5.62)
MA	Never	10823(53.31)
MA	Past	8339 (41.07)
\mathbf{FC}	Current	329(8.45)
\mathbf{FC}	Never	1910 (49.06)
\mathbf{FC}	Past	1654 (42.49)
AR	Current	364 (9.09)
AR	Never	1973 (49.26)
AR	Past	1668 (41.65)

Table 15: Distribution of smoking by most likely class membership in the optimum 5-class model

Response	Class comparison	Effect	95% CI	SE	P-value
Current	MA v IR	1.219	1.111,1.338	0.047	2.75e-05
Current	MA v EA	2.379	1.995, 2.837	0.090	4.52e-22
Current	MA v FC	1.536	1.352, 1.746	0.065	4.22e-11
Current	MA v AR	1.612	1.432, 1.814	0.060	2.78e-15
Never	MA v IR	1.017	0.973, 1.064	0.023	4.52e-01
Never	MA v EA	0.708	0.632, 0.792	0.057	1.75e-09
Never	MA v FC	0.853	0.797, 0.913	0.035	4.28e-06
Never	MA v AR	0.864	0.811, 0.921	0.032	6.83e-06
Past	MA v IR	0.936	0.895, 0.98	0.023	4.91e-03
Past	MA v EA	1.079	0.963, 1.208	0.058	1.89e-01
Past	MA v FC	1.052	0.982, 1.127	0.035	1.51e-01
Past	MA v AR	1.022	0.958, 1.09	0.033	5.17e-01
Current	IR v EA	1.951	1.634, 2.331	0.091	1.69e-13
Current	IR v MA	0.820	0.747, 0.9	0.047	2.76e-05
Current	IR v FC	1.260	1.106, 1.435	0.066	4.99e-04
Current	IR v AR	1.322	1.171, 1.492	0.062	6.49e-06
Never	IR v EA	0.696	0.621, 0.78	0.058	4.37e-10
Never	IR v MA	0.983	0.94, 1.028	0.023	4.51e-01
Never	IR v FC	0.838	0.781, 0.899	0.036	8.53e-07
Never	IR v AR	0.849	0.795, 0.907	0.034	1.32e-06
Past	IR v EA	1.152	1.027, 1.293	0.059	1.54e-02
Past	IR v MA	1.068	1.02, 1.118	0.023	4.91e-03
Past	IR v FC	1.123	1.046, 1.206	0.036	1.44e-03
Past	IR v AR	1.091	1.02, 1.167	0.034	1.13e-02

Table 16: Associations of smoking with most likely class membership weighted for the probability of inclusion in each class.

Response	Class comparison	Effect	95% CI	SE	P-value
Townsend deprivation rank normalised	MA v IR	1.027	1.004,1.05	0.011	2.23e-02
Townsend deprivation rank normalised	MA v EA	1.313	1.242, 1.389	0.029	2.02e-21
Townsend deprivation rank normalised	MA v FC	1.111	1.074, 1.149	0.017	1.39e-09
Townsend deprivation rank normalised	MA v AR	1.083	1.049, 1.118	0.016	9.75e-07
Townsend deprivation rank normalised	IR v EA	1.279	1.209, 1.354	0.029	2.16e-17
Townsend deprivation rank normalised	IR v MA	0.974	0.953, 0.996	0.011	2.22e-02
Townsend deprivation rank normalised	IR v FC	1.082	1.045, 1.121	0.018	1.08e-05
Townsend deprivation rank normalised	IR v AR	1.055	1.021, 1.09	0.017	1.56e-03

Table 17: Associations of Townsend deprivation index (TDI) with most likely class membership weighted for the probability of inclusion in each class.

Class	Outcome	Response	N (percent)
IR	ADHD	Case	18(0.15)
$\mathbf{E}\mathbf{A}$	ADHD	Case	8(0.62)
MA	ADHD	Case	19 (0.09)
\mathbf{FC}	ADHD	Case	11(0.28)
\mathbf{AR}	ADHD	Case	$21 \ (0.52)$
IR	GAD	Case	3282 (26.7)
$\mathbf{E}\mathbf{A}$	GAD	Case	478(36.97)
MA	GAD	Case	3398(16.5)
\mathbf{FC}	GAD	Case	851 (21.53)
AR	GAD	Case	1362(33.6)
IR	ASD	Case	43 (0.35)
$\mathbf{E}\mathbf{A}$	ASD	Case	18(1.39)
MA	ASD	Case	41 (0.2)
\mathbf{FC}	ASD	Case	16(0.4)
\mathbf{AR}	ASD	Case	26(0.64)
IR	Mania or bipolar	Case	51(0.41)
$\mathbf{E}\mathbf{A}$	Mania or bipolar	Case	339(26.22)
MA	Mania or bipolar	Case	44 (0.21)
\mathbf{FC}	Mania or bipolar	Case	145(3.67)
\mathbf{AR}	Mania or bipolar	Case	139(3.43)
IR	Depression	Case	5020(40.84)
\mathbf{EA}	Depression	Case	698 (53.98)
MA	Depression	Case	5698(27.67)
\mathbf{FC}	Depression	Case	1468(37.15)
\mathbf{AR}	Depression	Case	1877 (46.3)
IR	Schizophrenia or psychosis	Case	80 (0.65)
\mathbf{EA}	Schizophrenia or psychosis	Case	146 (11.29)
MA	Schizophrenia or psychosis	Case	67(0.33)
\mathbf{FC}	Schizophrenia or psychosis	Case	75(1.9)
AR	Schizophrenia or psychosis	Case	98(2.42)

Table 18: Numbers of cases of self-reported diagnoses of six disorders by most likely class membership.

Response	Class comparison	Effect	95% CI	SE	P-value
Self reported ADHD	MA v IR	1.411	0.738, 2.697	0.331	2.98e-01
Self reported ADHD	MA v EA	6.973	$3.135,\!15.511$	0.408	1.93e-06
Self reported ADHD	MA v FC	2.852	1.363, 5.968	0.377	5.41e-03
Self reported ADHD	MA v AR	4.172	2.206, 7.892	0.325	1.12e-05
Self reported GAD	MA v IR	1.698	1.607, 1.795	0.028	3.01e-79
Self reported GAD	MA v EA	2.918	2.593, 3.284	0.060	1.23e-70
Self reported GAD	MA v FC	1.434	1.32, 1.558	0.042	1.86e-17
Self reported GAD	MA v AR	2.385	2.22, 2.562	0.037	7.24e-125
Self reported ASD	MA v IR	1.398	0.903, 2.163	0.223	1.33e-01
Self reported ASD	MA v EA	6.279	3.59, 10.982	0.285	1.18e-10
Self reported ASD	MA v FC	1.928	1.097, 3.391	0.288	2.26e-02
Self reported ASD	MA v AR	2.660	1.641, 4.314	0.247	7.27e-05
Self reported Mania or bipolar disorder	MA v IR	1.793	1.191, 2.7	0.209	5.19e-03
Self reported Mania or bipolar disorder	MA v EA	153.661	110.369, 213.934	0.169	2.17e-195
Self reported Mania or bipolar disorder	MA v FC	17.048	12.043, 24.135	0.177	1.46e-57
Self reported Mania or bipolar disorder	MA v AR	13.219	9.309, 18.771	0.179	3.32e-47
Self reported Depression	MA v IR	1.571	1.498, 1.647	0.024	7.65e-78
Self reported Depression	MA v EA	3.037	2.714, 3.399	0.057	2.25e-83
Self reported Depression	MA v FC	1.516	1.412, 1.627	0.036	9.08e-31
Self reported Depression	MA v AR	2.091	1.96, 2.232	0.033	9.28e-110
Self reported Schizophrenia or psychosis	MA v IR	1.792	1.278, 2.513	0.173	7.24e-04
Self reported Schizophrenia or psychosis	MA v EA	37.778	27.805, 51.329	0.156	2.68e-119
Self reported Schizophrenia or psychosis	MA v FC	6.111	4.366, 8.552	0.172	4.93e-26
Self reported Schizophrenia or psychosis	MA v AR	6.701	4.867,9.227	0.163	2.03e-31

Table 19: Associations of self-reported diagnoses of six disorders with most likely class membership weighted for the probability of inclusion in each class.

Response	Class comparison	Effect	95% CI	SE	P-value
Self reported ADHD	IR v EA	4.972	2.244, 11.015	0.406	7.78e-05
Self reported ADHD	IR v MA	0.707	0.37, 1.351	0.331	2.93e-01
Self reported ADHD	IR v FC	2.008	0.961, 4.199	0.376	6.38e-02
Self reported ADHD	IR v AR	2.951	1.564, 5.568	0.324	8.38e-04
Self reported GAD	IR v EA	1.718	1.526, 1.934	0.060	2.98e-19
Self reported GAD	IR v MA	0.589	0.557, 0.622	0.028	3.12e-79
Self reported GAD	IR v FC	0.844	0.777, 0.918	0.042	6.78e-05
Self reported GAD	IR v AR	1.404	1.307, 1.509	0.037	1.99e-20
Self reported ASD	IR v EA	4.549	2.602, 7.953	0.285	1.06e-07
Self reported ASD	IR v MA	0.720	0.465, 1.115	0.223	1.41e-01
Self reported ASD	IR v FC	1.402	0.798, 2.463	0.287	2.40e-01
Self reported ASD	IR v AR	1.933	1.193, 3.133	0.246	7.46e-03
Self reported Mania or bipolar disorder	IR v EA	85.812	$63.709,\!115.582$	0.152	1.07e-188
Self reported Mania or bipolar disorder	IR v MA	0.559	0.371, 0.842	0.209	5.33e-03
Self reported Mania or bipolar disorder	IR v FC	9.521	6.94, 13.062	0.161	2.51e-44
Self reported Mania or bipolar disorder	IR v AR	7.382	5.363, 10.162	0.163	1.50e-34
Self reported Depression	IR v EA	1.934	1.727, 2.166	0.058	4.37e-30
Self reported Depression	IR v MA	0.637	0.607, 0.668	0.024	7.39e-78
Self reported Depression	IR v FC	0.965	0.898, 1.037	0.037	3.34e-01
Self reported Depression	IR v AR	1.331	1.246, 1.423	0.034	3.13e-17
Self reported Schizophrenia or psychosis	IR v EA	21.055	15.873, 27.927	0.144	3.32e-99
Self reported Schizophrenia or psychosis	IR v MA	0.558	0.398, 0.783	0.172	7.29e-04
Self reported Schizophrenia or psychosis	IR v FC	3.411	2.491, 4.671	0.160	1.99e-14
Self reported Schizophrenia or psychosis	IR v AR	3.735	2.775, 5.025	0.151	3.31e-18

Table 20: Associations of self-reported diagnoses of six disorders with most likely class membership weighted for the probability of inclusion in each class.

Class	Outcome	Response	N (percent)
IR	Mania or bipolar disorder ICD	Case	22 (0.21)
$\mathbf{E}\mathbf{A}$	Mania or bipolar disorder ICD	Case	156(13.74)
MA	Mania or bipolar disorder ICD	Case	19 (0.11)
\mathbf{FC}	Mania or bipolar disorder ICD	Case	66(1.95)
AR	Mania or bipolar disorder ICD	Case	57(1.6)
IR	Depression ICD	Case	1032 (9.67)
EA	Depression ICD	Case	205(18.06)
MA	Depression ICD	Case	998(5.7)
\mathbf{FC}	Depression ICD	Case	347(10.26)
AR	Depression ICD	Case	455(12.76)
IR	Dementia ICD	Case	18(0.17)
$\mathbf{E}\mathbf{A}$	Dementia ICD	Case	5(0.44)
MA	Dementia ICD	Case	39(0.22)
\mathbf{FC}	Dementia ICD	Case	7(0.21)
\mathbf{AR}	Dementia ICD	Case	16(0.45)
IR	Schizophrenia or psychotic disorder ICD	Case	28 (0.26)
$\mathbf{E}\mathbf{A}$	Schizophrenia or psychotic disorder ICD	Case	39(3.44)
MA	Schizophrenia or psychotic disorder ICD	Case	$21 \ (0.12)$
\mathbf{FC}	Schizophrenia or psychotic disorder ICD	Case	24(0.71)
AR	Schizophrenia or psychotic disorder ICD	Case	29 (0.81)

Table 21: Numbers of cases of ICD hospital diagnoses of three disorders by most likely class membership.

Response	Class comparison	Effect	95% CI	SE	P-value
Mania or bipolar disorder ICD	MA v IR	1.654	0.882,3.099	0.320	1.16e-01
Mania or bipolar disorder ICD	MA v EA	136.051	83.01,222.982	0.252	1.33e-84
Mania or bipolar disorder ICD	MA v FC	17.448	10.35,29.412	0.266	7.24e-27
Mania or bipolar disorder ICD	MA v AR	11.784	6.907, 20.105	0.273	1.43e-19
Depression ICD	MA v IR	1.592	1.452, 1.747	0.047	6.26e-23
Depression ICD	MA v EA	3.631	3.086, 4.272	0.083	1.74e-54
Depression ICD	MA v FC	1.776	1.561, 2.021	0.066	2.47e-18
Depression ICD	MA v AR	2.308	2.061, 2.584	0.058	1.08e-47
Schizophrenia or psychotic disorder ICD	MA v IR	1.671	0.927, 3.012	0.301	8.79e-02
Schizophrenia or psychotic disorder ICD	MA v EA	26.354	15.312, 45.357	0.277	3.47e-32
Schizophrenia or psychotic disorder ICD	MA v FC	5.968	3.347, 10.642	0.295	1.42e-09
Schizophrenia or psychotic disorder ICD	MA v AR	5.784	3.3, 10.137	0.286	8.81e-10

Table 22: Associations of ICD hospital diagnoses of three disorders with most likely class membership weighted for the probability of inclusion in each class.

Response	Class comparison	Effect	95% CI	SE	P-value
Mania or bipolar disorder ICD	IR v EA	82.752	52.451,130.556	0.233	2.42e-80
Mania or bipolar disorder ICD	IR v MA	0.610	0.325, 1.143	0.320	1.23e-01
Mania or bipolar disorder ICD	IR v FC	10.509	6.459, 17.099	0.248	2.78e-21
Mania or bipolar disorder ICD	IR v AR	7.194	4.369, 11.848	0.255	9.00e-15
Depression ICD	IR v EA	2.280	1.94, 2.68	0.082	1.45e-23
Depression ICD	IR v MA	0.628	0.573, 0.689	0.047	6.39e-23
Depression ICD	IR v FC	1.116	0.982, 1.267	0.065	9.28e-02
Depression ICD	IR v AR	1.449	1.296, 1.62	0.057	6.65e-11
Schizophrenia or psychotic disorder ICD	IR v EA	15.962	9.564, 26.638	0.261	2.93e-26
Schizophrenia or psychotic disorder ICD	IR v MA	0.605	0.335, 1.093	0.301	9.58e-02
Schizophrenia or psychotic disorder ICD	IR v FC	3.643	2.105, 6.306	0.280	3.86e-06
Schizophrenia or psychotic disorder ICD	IR v AR	3.501	2.058, 5.957	0.271	3.81e-06

Table 23: Associations of ICD hospital diagnoses of three disorders with most likely class membership weighted for the probability of inclusion in each class.

Response	Class comparison	Effect	95% CI	SE	P-value
Self reported Personality disorder	MA v IR	2.175	1.525,3.103	0.181	1.80e-05
Self reported Personality disorder	MA v EA	11.538	7.595, 17.527	0.213	2.00e-30
Self reported Personality disorder	MA v FC	3.503	2.302, 5.331	0.214	4.92e-09
Self reported Personality disorder	MA v AR	4.165	2.833, 6.122	0.197	3.89e-13
Self reported Personality disorder	IR v EA	5.286	3.6, 7.761	0.196	1.95e-17
Self reported Personality disorder	IR v MA	0.458	0.321, 0.653	0.181	1.63e-05
Self reported Personality disorder	IR v FC	1.604	1.09, 2.36	0.197	1.65e-02
Self reported Personality disorder	IR v AR	1.913	1.352, 2.709	0.177	2.53e-04

Table 24: Associations of self-reported personality disorder with most likely class membership weighted for the probability of inclusion in each class.

Response	Class comparison	Effect	95% CI	SE	P-value
Neuroticism score	MA v IR	1.286	1.254,1.318	0.013	3.05e-87
Neuroticism score	MA v EA	1.672	1.571, 1.779	0.032	4.09e-59
Neuroticism score	MA v FC	1.153	1.11, 1.197	0.019	9.91e-14
Neuroticism score	MA v AR	1.416	1.367, 1.467	0.018	3.86e-84
Neuroticism score	IR v EA	1.300	1.221, 1.384	0.032	2.10e-16
Neuroticism score	IR v MA	0.778	0.759, 0.797	0.013	3.04e-87
Neuroticism score	IR v FC	0.896	0.863, 0.932	0.020	2.69e-08
Neuroticism score	IR v AR	1.101	1.062, 1.142	0.018	1.61e-07

Table 25: Associations of neuroticism score with most likely class membership weighted for the probability of inclusion in each class.

Response	Class comparison	Effect	95% CI	SE	P-value
Bipolar disorder PRS	MA v IR	1.000	0.975, 1.025	0.013	9.89e-01
Bipolar disorder PRS	MA v EA	1.172	1.101, 1.247	0.032	5.74 e-07
Bipolar disorder PRS	MA v FC	1.078	1.038, 1.12	0.019	1.06e-04
Bipolar disorder PRS	MA v AR	1.014	0.979, 1.051	0.018	4.35e-01
Schizophrenia PRS	MA v IR	0.992	0.967, 1.017	0.013	5.18e-01
Schizophrenia PRS	MA v EA	1.246	1.17, 1.327	0.032	7.04e-12
Schizophrenia PRS	MA v FC	1.109	1.068, 1.153	0.020	1.14e-07
Schizophrenia PRS	MA v AR	1.065	1.027, 1.103	0.018	5.88e-04
Depression PRS	MA v IR	1.022	0.997, 1.048	0.013	8.69e-02
Depression PRS	MA v EA	1.144	1.075, 1.217	0.032	2.10e-05
Depression PRS	MA v FC	1.053	1.014, 1.093	0.019	7.73e-03
Depression PRS	MA v AR	1.045	1.009, 1.083	0.018	1.46e-02
ADHD PRS	MA v IR	1.028	1.002, 1.054	0.013	3.21e-02
ADHD PRS	MA v EA	1.064	1,1.132	0.032	5.06e-02
ADHD PRS	MA v FC	1.010	0.972, 1.049	0.019	6.21 e- 01
ADHD PRS	MA v AR	1.051	1.014, 1.089	0.018	6.21e-03
ASD PRS	MA v IR	0.987	0.963, 1.013	0.013	3.26e-01
ASD PRS	MA v EA	1.001	0.94, 1.065	0.032	9.80e-01
ASD PRS	MA v FC	1.015	0.977, 1.055	0.019	4.33e-01
ASD PRS	MA v AR	0.991	0.956, 1.027	0.018	6.21e-01
Anxiety PRS	MA v IR	1.002	0.978, 1.028	0.013	8.53e-01
Anxiety PRS	MA v EA	0.978	0.919, 1.04	0.032	4.79e-01
Anxiety PRS	MA v FC	1.000	0.963, 1.038	0.019	9.91e-01
Anxiety PRS	MA v AR	1.014	0.978, 1.05	0.018	4.55e-01

Table 26: Associations of polygenic risk scores (PRS) of six disorders with most likely class membership weighted for the probability of inclusion in each class.

Response	Class comparison	Effect	95% CI	SE	P-value
Bipolar disorder PRS	IR v EA	1.172	1.101,1.248	0.032	7.86e-07
Bipolar disorder PRS	IR v MA	1.000	0.975, 1.026	0.013	9.90e-01
Bipolar disorder PRS	IR v FC	1.078	1.037, 1.122	0.020	1.75e-04
Bipolar disorder PRS	IR v AR	1.014	0.978, 1.053	0.019	4.47e-01
Schizophrenia PRS	IR v EA	1.256	1.179, 1.339	0.032	2.16e-12
Schizophrenia PRS	IR v MA	1.008	0.983, 1.034	0.013	5.17e-01
Schizophrenia PRS	IR v FC	1.118	1.075, 1.164	0.020	3.12e-08
Schizophrenia PRS	IR v AR	1.074	1.034, 1.114	0.019	1.82e-04
Depression PRS	IR v EA	1.119	1.051, 1.192	0.032	4.30e-04
Depression PRS	IR v MA	0.978	0.954, 1.003	0.013	8.69e-02
Depression PRS	IR v FC	1.030	0.991, 1.071	0.020	1.37e-01
Depression PRS	IR v AR	1.022	0.986, 1.061	0.019	2.36e-01
ADHD PRS	IR v EA	1.035	0.972, 1.102	0.032	2.81e-01
ADHD PRS	IR v MA	0.973	0.949, 0.998	0.013	3.21e-02
ADHD PRS	IR v FC	0.982	0.945, 1.022	0.020	3.76e-01
ADHD PRS	IR v AR	1.022	0.985, 1.061	0.019	2.39e-01
ASD PRS	IR v EA	1.013	0.951, 1.079	0.032	6.95e-01
ASD PRS	IR v MA	1.013	0.988, 1.038	0.013	3.25e-01
ASD PRS	IR v FC	1.028	0.988, 1.07	0.020	1.66e-01
ASD PRS	IR v AR	1.004	0.967, 1.041	0.019	8.47e-01
Anxiety PRS	IR v EA	0.976	0.916, 1.039	0.032	4.39e-01
Anxiety PRS	IR v MA	0.998	0.973, 1.023	0.013	8.51e-01
Anxiety PRS	IR v FC	0.997	0.959, 1.037	0.020	8.97 e-01
Anxiety PRS	IR v AR	1.011	0.975, 1.049	0.019	5.53e-01

Table 27: Associations of polygenic risk scores (PRS) of six disorders with most likely class membership weighted for the probability of inclusion in each class.

		LCA subset		Full MHQ	
		Ν	percent	Ν	percent
Total		4445		21475	
Sex	Female	3282	74	15803	74
	Male	1147	26	5643	26
	NA/Missing	16	0.36	29	0.14
Education	University degree	2272	51	11205	52
	College, A Levels NVQ3 or similar	527	12	2475	12
	Secondary education, GCSE or O Levels	708	16	3462	16
	Vocational, BTEC or similar	922	21	4304	20
	NA/ Missing	16	0.36	29	0.14
Alcohol consumption	Weekly	2789	63	14130	66
	Occasionally	1292	29	5809	27
	Never	336	7.6	1451	6.8
	NA/Missing	28	0.63	85	0.4
Smoking	Current	221	5	807	3.8
	Past	2087	47	9356	44
	Never	2109	47	11227	52
	NA/Missing	28	0.63	85	0.4
		Mean	SD	Mean	SD
Age		60.9	7.1	62.2	7.3
	NA/ Missing	16		29	

Table 28: Comparison of sociodemographic characteristics in the subset of participants in the latent class analysis (LCA subset) with responses to the stem question on ever having experienced a period of manic or irritable mood as well as the subsequent questions of symptoms, and the MHQ cohort responders (Full MHQ), in the PROTECT replication study.

Response	Value	N (percent)
More active	No	3664 (0.82)
More active	Yes	781 (0.18)
More confident	No	$3934 \ (0.89)$
More confident	Yes	511 (0.11)
Easily distracted	No	$3384 \ (0.76)$
Easily distracted	Yes	$1061 \ (0.24)$
More creative	No	$3901 \ (0.88)$
More creative	Yes	$544 \ (0.12)$
Less sleep	No	$3938\ (0.89)$
Less sleep	Yes	507 (0.11)
Thoughts racing	No	3139(0.71)
Thoughts racing	Yes	$1306 \ (0.29)$
More restless	No	$3076 \ (0.69)$
More restless	Yes	$1369\ (0.31)$
More talkative	No	$3653 \ (0.82)$
More talkative	Yes	$792 \ (0.18)$

Table 29: Numbers of responses to individual symptoms questions out of a total sample of N=4445 in PROTECT

Number of classes	2	3	4	5	6	7
BIC	29026.1	28121.7	27871.6	27853.9	27905.4	27964.2
AIC	28917.3	27955.3	27647.6	27572.3	27566.2	27567.4
loglikelihood	-14441.639	-13951.652	-13788.8	-13742.16	-13730.123	-13721.694
N iterations	62	129	234	1272	7770	1556
Entropy	3.27	3.15	3.11	3.1	3.09	3.09
Relative entropy	0.82	0.709	0.708	0.67	0.669	0.649

Table 30: Fit statistics for latent class models with 2:7 classes in PROTECT $\,$

Class	Response	N (percent)
IR	Ever manic	9(1.53)
IR	Ever irritable	557 (94.57)
IR	Ever manic and irritable	23(3.9)
EA	Ever manic	50(24.63)
EA	Ever irritable	46(22.66)
EA	Ever manic and irritable	107(52.71)
MA	Ever manic	46(1.67)
MA	Ever irritable	2649 (96.29)
MA	Ever manic and irritable	56(2.04)
\mathbf{FC}	Ever manic	95(24.61)
\mathbf{FC}	Ever irritable	171(44.3)
\mathbf{FC}	Ever manic and irritable	120(31.09)
AR	Ever manic	47 (9.11)
AR	Ever irritable	384(74.42)
AR	Ever manic and irritable	85(16.47)

Table 31: Distribution of responses to manic or irritable stem question by most likely class membership in the optimum 5-class model in PROTECT $\,$

Class	Response	N (percent)
IR	1 - Brief	189(32.088)
IR	2 - Moderate	230(39.049)
IR	3 - Extended	119(20.204)
EA	1 - Brief	28(13.793)
EA	2 - Moderate	72 (35.468)
EA	3 - Extended	87 (42.857)
MA	1 - Brief	1203(43.73)
MA	2 - Moderate	596(21.665)
MA	3 - Extended	345(12.541)
\mathbf{FC}	1 - Brief	113(29.275)
\mathbf{FC}	2 - Moderate	142 (36.788)
\mathbf{FC}	3 - Extended	103(26.684)
AR	1 - Brief	174 (33.721)
AR	2 - Moderate	198(38.372)
AR	3 - Extended	107 (20.736)

Table 32: Distribution of responses to the episode duration question by most likely class membership in the optimum 5-class model in PROTECT $\,$

Class	Response	N (percent)
IR	Disruptive	209 (46.04)
IR	Not disruptive	245(53.96)
IR	Missing - NA	135 (NA)
EA	Disruptive	97(56.73)
EA	Not disruptive	74(43.27)
EA	Missing - NA	32 (NA)
MA	Disruptive	502(25.97)
MA	Not disruptive	1431 (74.03)
MA	Missing - NA	818 (NA)
\mathbf{FC}	Disruptive	87(26.52)
\mathbf{FC}	Not disruptive	241 (73.48)
\mathbf{FC}	Missing - NA	58 (NA)
AR	Disruptive	146(36.14)
AR	Not disruptive	258(63.86)
AR	Missing - NA	112 (NA)

Table 33: Distribution of responses to the episode disruptiveness question by most likely class membership in the optimum 5-class model in PROTECT $\,$

Response	Class comparison	Effect	95% CI	SE	P-value
Brief duration mania or irritability	MA v IR	0.525	0.44,0.627	0.091	1.16e-12
Brief duration mania or irritability	MA v EA	0.140	0.093, 0.211	0.207	2.43e-21
Brief duration mania or irritability	MA v FC	0.389	0.308, 0.489	0.118	1.00e-15
Brief duration mania or irritability	MA v AR	0.456	0.372, 0.559	0.104	3.57e-14
Moderate duration mania or irritability	MA v IR	1.291	1.178,1.415	0.047	4.46e-08
Moderate duration mania or irritability	MA v EA	1.264	1.083, 1.474	0.079	2.94e-03
Moderate duration mania or irritability	MA v FC	1.300	1.161, 1.457	0.058	6.03e-06
Moderate duration mania or irritability	MA v AR	1.326	1.197, 1.469	0.052	6.30e-08
Extended duration mania or irritability	MA v IR	1.109	1.03, 1.194	0.038	6.08e-03
Extended duration mania or irritability	MA v EA	1.659	1.496, 1.839	0.053	6.19e-22
Extended duration mania or irritability	MA v FC	1.252	1.15, 1.364	0.043	2.14e-07
Extended duration mania or irritability	MA v AR	1.154	1.065, 1.251	0.041	4.99e-04
Brief duration mania or irritability	IR v EA	0.267	0.175, 0.408	0.217	1.08e-09
Brief duration mania or irritability	IR v MA	1.903	1.594, 2.273	0.091	1.20e-12
Brief duration mania or irritability	IR v FC	0.739	0.569, 0.961	0.134	2.41e-02
Brief duration mania or irritability	IR v AR	0.868	0.684, 1.102	0.122	2.46e-01
Moderate duration mania or irritability	IR v EA	0.979	0.83, 1.155	0.084	8.01e-01
Moderate duration mania or irritability	IR v MA	0.775	0.707, 0.849	0.047	4.46e-08
Moderate duration mania or irritability	IR v FC	1.007	0.886, 1.145	0.065	9.12e-01
Moderate duration mania or irritability	IR v AR	1.027	0.913, 1.156	0.060	6.56e-01
Extended duration mania or irritability	IR v EA	1.496	1.336, 1.676	0.058	3.13e-12
Extended duration mania or irritability	IR v MA	0.902	0.838, 0.971	0.038	6.07 e- 03
Extended duration mania or irritability	IR v FC	1.130	1.025, 1.245	0.050	1.41e-02
Extended duration mania or irritability	IR v AR	1.041	0.948, 1.143	0.048	4.01e-01

Table 34: Associations of episode duration with most likely class membership weighted for the probability of inclusion in each class in PROTECT.

Response	Class comparison	Effect	95% CI	SE	P-value
Problematic mania or irritability	MA v IR	2.092	1.718,2.547	0.100	1.97e-13
Problematic mania or irritability	MA v EA	3.596	2.615, 4.944	0.162	3.32e-15
Problematic mania or irritability	MA v FC	1.055	0.813, 1.368	0.133	6.89e-01
Problematic mania or irritability	MA v AR	1.743	1.394, 2.18	0.114	1.11e-06
Problematic mania or irritability	IR v EA	1.719	1.221, 2.421	0.175	1.92e-03
Problematic mania or irritability	IR v MA	0.478	0.393, 0.582	0.100	1.97e-13
Problematic mania or irritability	IR v FC	0.504	0.378, 0.673	0.148	3.47e-06
Problematic mania or irritability	IR v AR	0.833	0.645, 1.077	0.131	1.63e-01

Table 35: Associations of episode disruptiveness with most likely class membership weighted for the probability of inclusion in each class in PROTECT.

Response	Class comparison	Effect	95% CI	SE	P-value
Sex	MA v IR	1.098	0.91, 1.325	0.096	3.27e-01
Sex	MA v EA	1.473	1.081, 2.007	0.158	1.41e-02
Sex	MA v FC	1.671	1.337, 2.09	0.114	6.64 e- 06
Sex	MA v AR	1.103	0.892, 1.366	0.109	3.66e-01
Sex	IR v EA	1.343	0.958, 1.882	0.172	0.0874
Sex	IR v MA	0.911	0.755, 1.099	0.096	0.3309
Sex	IR v FC	1.523	1.173, 1.978	0.133	0.0016
Sex	IR v AR	1.006	0.781, 1.295	0.129	0.9651

Table 36: Associations of sex with most likely class membership weighted for the probability of inclusion in each class in PROTECT.

Response	Class comparison	Effect	95% CI	SE	P-value
College A Levels NVQ3 or below or similar	MA v IR	1.209	0.948,1.542	0.124	1.27e-01
College A Levels NVQ3 or below or similar	MA v EA	0.948	0.599, 1.502	0.234	8.21e-01
College A Levels NVQ3 or below or similar	MA v FC	0.968	0.694, 1.35	0.170	8.48e-01
College A Levels NVQ3 or below or similar	MA v AR	1.159	0.876, 1.534	0.143	3.00e-01
Secondary education GCSE or O Levels	MA v IR	1.475	1.196, 1.819	0.107	2.75e-04
Secondary education GCSE or O Levels	MA v EA	0.690	0.435, 1.093	0.235	1.13e-01
Secondary education GCSE or O Levels	MA v FC	1.107	0.832, 1.475	0.146	4.85e-01
Secondary education GCSE or O Levels	MA v AR	1.282	1.003, 1.639	0.125	4.68e-02
University degree	MA v IR	0.664	0.563, 0.782	0.084	1.02e-06
University degree	MA v EA	1.299	0.97, 1.738	0.149	7.88e-02
University degree	MA v FC	1.011	0.82, 1.247	0.107	9.19e-01
University degree	MA v AR	0.834	0.693, 1.005	0.095	5.62 e- 02
Vocational or BTEC or similar	MA v IR	1.163	0.957, 1.414	0.100	1.30e-01
Vocational or BTEC or similar	MA v EA	0.892	0.619, 1.286	0.186	5.42e-01
Vocational or BTEC or similar	MA v FC	0.924	0.71, 1.203	0.135	5.57 e-01
Vocational or BTEC or similar	MA v AR	0.973	0.772, 1.226	0.118	8.15e-01
College A Levels NVQ3 or below or similar	IR v EA	0.785	0.481, 1.282	0.250	3.34e-01
College A Levels NVQ3 or below or similar	IR v MA	0.827	0.649, 1.056	0.124	1.27e-01
College A Levels NVQ3 or below or similar	IR v FC	0.801	0.551, 1.164	0.191	2.44e-01
College A Levels NVQ3 or below or similar	IR v AR	0.959	0.692, 1.331	0.167	8.04e-01
Secondary education GCSE or O Levels	IR v EA	0.467	0.289, 0.755	0.245	1.91e-03
Secondary education GCSE or O Levels	IR v MA	0.678	0.55, 0.836	0.107	2.75e-04
Secondary education GCSE or O Levels	IR v FC	0.750	0.546, 1.032	0.163	7.72e-02
Secondary education GCSE or O Levels	IR v AR	0.868	0.655, 1.152	0.144	3.27e-01
University degree	IR v EA	1.957	1.427, 2.683	0.161	3.08e-05
University degree	IR v MA	1.507	1.278, 1.776	0.084	1.03e-06
University degree	IR v FC	1.523	1.196, 1.941	0.124	6.59e-04
University degree	IR v AR	1.257	1.007, 1.57	0.113	4.34e-02
Vocational or BTEC or similar	IR v EA	0.767	0.519, 1.134	0.200	1.84e-01
Vocational or BTEC or similar	IR v MA	0.860	0.707, 1.045	0.100	1.30e-01
Vocational or BTEC or similar	IR v FC	0.795	0.59, 1.071	0.152	1.31e-01
Vocational or BTEC or similar	IR v AR	0.836	0.638, 1.096	0.138	1.95e-01

Table 37: Associations of education levels with most likely class membership weighted for the probability of inclusion in each class in PROTECT.

Response	Class comparison	Effect	95% CI	SE	P-value
Never	MA v IR	1.037	0.753, 1.428	0.163	0.82539
Never	MA v EA	1.531	0.944, 2.482	0.247	0.08430
Never	MA v FC	1.472	1.024, 2.114	0.185	0.03665
Never	MA v AR	1.470	1.062, 2.033	0.166	0.02005
Occasionally	MA v IR	1.220	1.023, 1.456	0.090	0.02719
Occasionally	MA v EA	1.237	0.91, 1.681	0.157	0.17521
Occasionally	MA v FC	1.029	0.816, 1.298	0.118	0.80945
Occasionally	MA v AR	1.158	0.946, 1.417	0.103	0.15579
Weekly	MA v IR	0.827	0.699, 0.979	0.086	0.02701
Weekly	MA v EA	0.721	0.539, 0.964	0.148	0.02709
Weekly	MA v FC	0.860	0.693, 1.067	0.110	0.17026
Weekly	MA v AR	0.776	0.642, 0.939	0.097	0.00909
Never	IR v EA	1.479	0.865, 2.528	0.273	0.1523
Never	IR v MA	0.963	0.699, 1.326	0.163	0.8170
Never	IR v FC	1.422	0.924, 2.186	0.220	0.1092
Never	IR v AR	1.418	0.951, 2.113	0.204	0.0867
Occasionally	IR v EA	1.014	0.727, 1.413	0.169	0.9359
Occasionally	IR v MA	0.820	0.687, 0.978	0.090	0.0274
Occasionally	IR v FC	0.843	0.648, 1.098	0.135	0.2059
Occasionally	IR v AR	0.949	0.748, 1.205	0.122	0.6700
Weekly	IR v EA	0.871	0.636, 1.194	0.161	0.3916
Weekly	IR v MA	1.209	1.022, 1.43	0.086	0.0270
Weekly	IR v FC	1.040	0.811, 1.332	0.126	0.7589
Weekly	IR v AR	0.938	0.749, 1.176	0.115	0.5811

Table 38: Associations of alcohol consumption frequency with most likely class membership weighted for the probability of inclusion in each class in PROTECT.

Response	Class comparison	Effect	95% CI	SE	P-value
Current	MA v IR	1.145	0.763, 1.72	0.207	5.13e-01
Current	MA v EA	3.403	2.122, 5.456	0.241	3.70e-07
Current	MA v FC	2.383	1.595, 3.56	0.205	2.23e-05
Current	MA v AR	1.679	1.12, 2.515	0.206	1.20e-02
Never	MA v IR	1.017	0.864, 1.198	0.083	8.36e-01
Never	MA v EA	0.622	0.463, 0.835	0.150	1.58e-03
Never	MA v FC	0.731	0.591, 0.903	0.108	3.70e-03
Never	MA v AR	0.921	0.764, 1.109	0.095	3.85e-01
Past	MA v IR	0.962	0.817, 1.133	0.083	6.44 e- 01
Past	MA v EA	1.153	0.866, 1.535	0.146	3.30e-01
Past	MA v FC	1.125	0.912, 1.386	0.107	2.71e-01
Past	MA v AR	0.986	0.818, 1.188	0.095	8.80e-01
Current	IR v EA	2.971	1.711, 5.159	0.282	0.000111
Current	IR v MA	0.874	0.582, 1.312	0.207	0.514611
Current	IR v FC	2.084	1.273, 3.41	0.251	0.003495
Current	IR v AR	1.466	0.893, 2.405	0.253	0.130199
Never	IR v EA	0.611	0.445, 0.84	0.162	0.002421
Never	IR v MA	0.983	0.835, 1.157	0.083	0.835101
Never	IR v FC	0.718	0.563, 0.916	0.124	0.007692
Never	IR v AR	0.905	0.725, 1.129	0.113	0.376405
Past	IR v EA	1.198	0.878, 1.634	0.158	0.253981
Past	IR v MA	1.039	0.882,1.224	0.083	0.644564
Past	IR v FC	1.169	0.918, 1.488	0.123	0.205004
Past	IR v AR	1.024	0.821, 1.279	0.113	0.830648

Table 39: Associations of smoking with most likely class membership weighted for the probability of inclusion in each class in PROTECT.

Class	Outcome	Response	Ν
IR	GAD	Case	200
\mathbf{EA}	GAD	Case	69
MA	GAD	Case	515
\mathbf{FC}	GAD	Case	129
AR	GAD	Case	167
IR	Depression	Case	322
\mathbf{EA}	Depression	Case	133
MA	Depression	Case	1022
\mathbf{FC}	Depression	Case	222
AR	Depression	Case	278
IR	Mania or bipolar	Case	5
$\mathbf{E}\mathbf{A}$	Mania or bipolar	Case	63
MA	Mania or bipolar	Case	8
\mathbf{FC}	Mania or bipolar	Case	23
\mathbf{AR}	Mania or bipolar	Case	17
IR	Schizophrenia or psychosis	Case	2
\mathbf{EA}	Schizophrenia or psychosis	Case	19
MA	Schizophrenia or psychosis	Case	6
\mathbf{FC}	Schizophrenia or psychosis	Case	10
\mathbf{AR}	Schizophrenia or psychosis	Case	8

Table 40: Numbers of cases of self-reported diagnoses of six disorders by most likely class membership in PROTECT.

Response	Class comparison	Effect	95% CI	SE	P-value
Self reported GAD	MA v IR	1.944	1.616,2.337	0.094	1.59e-12
Self reported GAD	MA v EA	2.308	1.703, 3.127	0.155	6.80e-08
Self reported GAD	MA v FC	2.101	1.67, 2.642	0.117	2.18e-10
Self reported GAD	MA v AR	2.000	1.626, 2.46	0.106	$5.37e{-}11$
Self reported Schizophrenia or psychosis	MA v IR	1.760	0.409, 7.575	0.745	4.48e-01
Self reported Schizophrenia or psychosis	MA v EA	46.605	17.466, 124.356	0.501	1.69e-14
Self reported Schizophrenia or psychosis	MA v FC	12.984	4.559, 36.978	0.534	1.58e-06
Self reported Schizophrenia or psychosis	MA v AR	6.954	2.289, 21.123	0.567	6.24 e- 04
Self reported Depression	MA v IR	1.721	1.46, 2.028	0.084	9.48e-11
Self reported Depression	MA v EA	3.087	2.293, 4.156	0.152	1.09e-13
Self reported Depression	MA v FC	2.191	1.774, 2.707	0.108	3.27e-13
Self reported Depression	MA v AR	1.892	1.569, 2.282	0.095	2.40e-11
Self reported Mania or bipolar disorder	MA v IR	1.715	0.565, 5.21	0.567	3.41e-01
Self reported Mania or bipolar disorder	MA v EA	111.555	$54.728,\!227.39$	0.363	1.69e-38
Self reported Mania or bipolar disorder	MA v FC	18.352	8.603,39.146	0.387	5.15e-14
Self reported Mania or bipolar disorder	MA v AR	8.114	3.583, 18.373	0.417	5.15e-07

Table 41: Associations of self-reported diagnoses of three disorders with most likely class membership weighted for the probability of inclusion in each class in PROTECT.

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Response	Class comparison	Effect	95% CI	SE	P-value
Bipolar disorder PRS	MA v IR	0.976	0.844, 1.129	0.074	0.7417
Bipolar disorder PRS	MA v EA	1.346	1.035, 1.749	0.134	0.0264
Bipolar disorder PRS	MA v FC	1.010	0.834, 1.222	0.098	0.9227
Bipolar disorder PRS	MA v AR	1.072	0.909, 1.264	0.084	0.4072
Schizophrenia PRS	MA v IR	0.870	0.753, 1.004	0.073	0.0567
Schizophrenia PRS	MA v EA	0.985	0.758, 1.28	0.134	0.9098
Schizophrenia PRS	MA v FC	0.913	0.755, 1.103	0.097	0.3460
Schizophrenia PRS	MA v AR	0.932	0.791, 1.098	0.083	0.4007
Depression PRS	MA v IR	1.105	0.959, 1.274	0.072	0.1676
Depression PRS	MA v EA	1.176	0.91, 1.521	0.131	0.2157
Depression PRS	MA v FC	1.114	0.924, 1.343	0.095	0.2567
Depression PRS	MA v AR	1.040	0.886, 1.222	0.082	0.6302
ADHD PRS	MA v IR	1.140	0.986, 1.318	0.074	0.0764
ADHD PRS	MA v EA	1.212	0.933, 1.575	0.134	0.1502
ADHD PRS	MA v FC	0.973	0.804, 1.177	0.097	0.7759
ADHD PRS	MA v AR	1.066	0.904, 1.256	0.084	0.4478
ASD PRS	MA v IR	1.009	0.872, 1.166	0.074	0.9078
ASD PRS	MA v EA	0.784	0.603, 1.02	0.134	0.0700
ASD PRS	MA v FC	0.949	0.784, 1.149	0.098	0.5909
ASD PRS	MA v AR	0.963	0.816, 1.135	0.084	0.6514
Anxiety PRS	MA v IR	0.962	0.833, 1.111	0.074	0.5952
Anxiety PRS	MA v EA	0.948	0.73, 1.231	0.133	0.6902
Anxiety PRS	MA v FC	0.864	0.714, 1.045	0.097	0.1326
Anxiety PRS	MA v AR	0.963	0.818, 1.134	0.083	0.6505

Table 42: Associations of PRS of six disorders with most likely class membership weighted for the probability of inclusion in each class in PROTECT.