

Investigating the genetic architecture of general and specific psychopathology in adolescence -- Supplementary Material

Supplementary Methods

Genetic data

Genetic data were acquired using the Illumina HumanHap550 quad genome-wide single nucleotide polymorphism (SNP) genotyping platform from 9912 participants. Individuals were excluded from further analysis based on gender mismatches, minimal or excessive heterozygosity, disproportionate levels of individual missingness (>3%), evidence of cryptic relatedness (>10% of alleles identical by descent), and being of non-European ancestry (assessed by multidimensional scaling analysis including HapMap 2 individuals). SNPs with a minor allele frequency (MAF) of < 1%, Impute2 information quality metric of < 0.8, a call rate of < 95% or evidence for violations of Hardy-Weinberg equilibrium (P -value < $5e^{-7}$) were removed. Imputation of the target data was performed using Impute V2.2.2 against the 1000 genomes reference panel (Phase 1, Version 3; all polymorphic SNPs excluding singletons), using 2186 reference haplotypes (including non-Europeans). Following quality control assessment and imputation and restricting to 1 young person per family, genetic data was available for 8252 ALSPAC individuals.

Polygenic risk scores

Polygenic risk scores (PRSs) for schizophrenia, major depressive disorder (MDD), neuroticism and bipolar disorder were constructed, as described previously,^{1,2} using GWAS summary statistics from discovery studies.³⁻⁶

SNPs were excluded from the analysis if they had a minor allele frequency less than 0.01, imputation quality less than 0.8, or if there was allelic mismatch between samples (alleles reported by the discovery study not matching alleles in the ALSPAC sample). Due to the high linkage disequilibrium (LD) within the extended major histocompatibility complex (MHC; chromosome 6: 25-34Mb) only a single SNP was included to represent this region. Remaining SNPs were then further pruned for LD using the PLINK (v1.90)⁷ 'clump' command to retain SNPs with a trait association P -value ≤ 0.5 and $r^2 < 0.25$ within 500kb windows.

Polygenic scores were calculated for each ALSPAC individual using PLINK (v1.07)⁷ by summing the number of risk alleles for each SNP (0, 1 or 2) weighted by the logarithm of its discovery sample odds ratio (OR) for binary traits (schizophrenia, MDD, bipolar disorder) or by the beta for continuous traits

(neuroticism). Our primary analysis used scores generated from a list of SNPs with a GWAS training-set P -value threshold (P_T) ≤ 0.05 . As a secondary analysis, PRSs were also generated using SNPs meeting 0.5, $1e^{-5}$, and genome-wide level P -value thresholds. For all discovery studies, genome-wide significant was defined as $P \leq 5e^{-8}$, with the exception of the MDD discovery study⁴ where $P \leq 1e^{-8}$ was considered genome-wide significant due to the 15 million SNPs in the data used within the study from 23andMe, Inc., a personal genetics company.

Model fit

Absolute model fit was evaluated using the Root Mean Square Error of Approximation (RMSEA)⁸ index, the comparative fit index (CFI)⁹ and the Tucker-Lewis Index (TLI).¹⁰ Reasonably good fit between the target model and observed data is considered when RMSEA values are close to or below 0.06, and CFI and TLI values are close to or greater than 0.95.^{11, 12}

All candidate models were also re-estimated using full information maximum likelihood (FIML) to obtain Akaike Information Criterion (AIC),¹³ Bayesian Information Criterion (BIC)¹⁴ and sample size adjusted Bayesian Information Criterion (ssaBIC) measures. These measures allow for direct comparison of plausibility of each four candidate models with lower values indicating better model fit.

Model reliability

For the bifactor model, omega reliability coefficients were calculated to assess the share of the score variance as a result of all factors (omega; ω), the specific factors (omega subscale; ω_S), the general factor (omega hierarchical; ω_H) and the specific factors when the general factor is partialled out (omega hierarchical subscale; ω_{HS}).¹⁵

Inverse probability weighting

Inverse probability weighting (IPW) was used to investigate the potential of bias within our analyses due to systematic differences between our analysis sample (2863 individuals with genetic and phenotypic data) and individuals not included in our analyses (5389 individuals with genetic data but no phenotypic data).

We firstly generated a missingness model using potential predictors of whether an individual was in the final analysis or not (missingness). These predictors were strongly associated with missingness ($OR > 1.2$) and had minimal missing data (> 7000 data points). Modal imputation was used to replace

missing data within each predictor and a multivariable logistic regression was used to indicate which imputed predictors showed the strongest evidence of an association with missingness ($P < 0.1$). The final predictors used were maternal early parenthood/pregnancy, maternal partner status during pregnancy, parental lack of educational qualifications during pregnancy, maternal social network practical support during pregnancy, maternal parity, maternal financial difficulties during pregnancy, sex, whether the individual was part of the ALSPAC Phase I core sample,¹⁶ maternal partner affection during pregnancy, and maternal psychopathology during pregnancy. The genetic risk scores for schizophrenia, MDD, neuroticism and bipolar disorder were also included in the missingness model.

As the effect of an observed predictor on missingness may depend on which other predictors are observed,¹⁷ interaction terms were created between each predictor and a missingness flag deemed representative of the amount of missing data within each moderately incomplete predictor. This missingness flag was based on the missingness pattern of the “parental lack of educational qualifications during pregnancy” variable. Ordinary interactions between pairs of predictors were also generated. Forward stepwise selection was used, with threshold $P < 0.1$, to select which of the interaction terms to add to the existing missingness model and both the Hosmer-Lemeshow test¹⁸ ($P = 0.93$) and Hinkley’s test^{19, 20} ($P = 0.56$) indicated that the final model fit the data well.

Weights were generated by inverting the predicted probabilities estimated by the missingness model. Weights of the 2863 individuals within the final analysis models ranged from 1.27 to 58.22. To assess the effect of large weights on the analysis, additional weight sets were generated after truncation at the 50th percentile (2.48), 75th percentile (3.02), 90th percentile (3.95), 95th percentile (5.33) and 99th percentile (8.94).

Each weight set was used to perform IPW analyses between psychopathology factors within the correlated factor and bifactor models and psychiatric disorder PRSs. IPW results are shown in Supplementary Tables 6 and 7.

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Supplementary Table 1. Standardized factor loadings for the correlated factors and bifactor measurement models tested (n = 3650)

Item	Item question	Correlated				Bifactor				
		PE	NEG	DEP	ANX	PE	NEG	DEP	ANX	GEN
PE1	Young person believes someone else has read their thoughts	0.600**				0.545**				0.357**
PE2	Young person believes they have received special messages via TV/radio or program	0.703**				0.600**				0.422**
PE3	Young person believes they have been followed or spied on	0.748**				0.490**				0.481**
PE4	Young person has heard voices other people couldn't hear	0.748**				0.607**				0.461**
PE5	Young person has ever felt they were under the control of a special power	0.641**				0.626**				0.361**
PE6	Young person has ever seen something/someone other people could not see	0.738**				0.575**				0.461**
PE7	Young person has ever felt their thoughts were being taken out of their head against their will	0.784**				0.568**				0.508**
PE8	Young person has ever felt someone else's thoughts were inserted into their head against their will	0.770**				0.534**				0.502**
PE9	Young person has ever felt their thoughts were so loud people could hear what they were thinking	0.736**				0.479**				0.486**
PE10	Young person has ever felt they were someone really special or had special powers	0.635**				0.602**				0.367**
NEG1	Young person has felt lacking in energy		0.675**				0.244**			0.596**
NEG2	Young person has felt like they are not much of a talker		0.561**				0.414**			0.420**
NEG3	Young person has felt they experience few or no emotions at important events		0.637**				0.328**			0.527**
NEG4	Young person has felt lacking in motivation		0.790**				0.543**			0.601**
NEG5	Young person has felt that they are spending their days doing nothing		0.760**				0.530**			0.575**
NEG6	Young person has felt lacking in get up and go		0.835**				0.605**			0.624**
NEG7	Young person has felt they only have a few hobbies or interests		0.678**				0.385**			0.548**
NEG8	Young person has felt they have no interest in being with other people		0.746**				0.423**			0.604**

Supplementary Table 1 continued.

NEG9	Young person has felt they are not a very lively person		0.736**				0.510**			0.562**
NEG10	Young person has felt they are neglecting their appearance/personal hygiene		0.614**				0.289**			0.518**
NEG11	Young person has felt they can never get things done		0.793**				0.355**			0.677**
DEP1	Young person has felt unhappy/miserable			0.783**				0.377**		0.698**
DEP2	Young person hasn't enjoyed anything at all			0.751**				0.197**		0.718**
DEP3	Young person has felt so tired they sat around and did nothing			0.609**				-0.135**		0.653**
DEP4	Young person has felt very restless			0.577**				0.020		0.582**
DEP5	Young person has felt they were no good anymore			0.907**				0.444**		0.797**
DEP6	Young person has cried a lot			0.690**				0.433**		0.583**
DEP7	Young person has found it hard to think properly/concentrate			0.675**				-0.100		0.715**
DEP8	Young person has hated themselves			0.873**				0.475**		0.751**
DEP9	Young person has felt they were a bad person			0.816**				0.444**		0.704**
DEP10	Young person has felt lonely			0.824**				0.347**		0.747**
DEP11	Young person has thought nobody really loved them			0.845**				0.520**		0.707**
DEP12	Young person has thought they could never be as good as other kids			0.840**				0.410**		0.741**
DEP13	Young person has felt they did everything wrong			0.880**				0.461**		0.764**
ANX1	Compared to others of their age, amount young person has worried about own past behaviour				0.671**				0.555**	0.359**
ANX2	Compared to others of their age, amount young person has worried about school work/exams				0.499**				0.429**	0.260**
ANX3	Compared to others of their age, amount young person has worried about burglaries/muggings/bombs				0.569**				0.566**	0.254**
ANX4	Compared to others of their age, amount young person has worried about own health				0.642**				0.608**	0.305**
ANX5	Compared to others of their age, amount young person has worried about bad things happening to others				0.626**				0.597**	0.295**
ANX6	Compared to others of their age, amount young person has worried about the future – new school/house/job				0.641**				0.549**	0.334**

Supplementary Table 1 continued.

ANX7	Compared to others of their age, amount young person has worried about making and keeping friends				0.683**				0.573**	0.364**
ANX8	Compared to others of their age, amount young person has worried about death and dying				0.647**				0.621**	0.300**
ANX9	Compared to others of their age, amount young person has worried about being bullied or teased				0.654**				0.648**	0.290**
ANX10	Compared to others of their age, amount young person has worried about own appearance or weight				0.704**				0.562**	0.388**
ANX11	Young person has had panic attack for no reason				0.549**				0.329**	0.355**
ANX12	Young person has felt afraid of or tried to avoid crowds				0.725**				0.502**	0.445**
ANX13	Young person has felt afraid of or tried to avoid public places				0.774**				0.630**	0.429**
ANX14	Young person has felt afraid of or tried to avoid travelling alone				0.668**				0.509**	0.380**
ANX15	Young person has felt afraid of or tried to avoid being far from home				0.548**				0.497**	0.271**
ANX16 ¹	Young person fears/avoids situations that involve a lot of people or meeting new people AND young person avoids social situations because of their fear				0.547**				0.429**	0.305**
ANX17 ¹	Young person is worried in general AND young person has worried so much it has upset or interfered with their life				0.746**				0.595**	0.411**
					ω	-	-	-	-	0.970
					ω_S	0.913	0.919	0.955	0.922	-
					ω_H	-	-	-	-	0.786
					ω_{HS}	0.566	0.325	0.146	0.664	-

Note: Development and Well Being Assessment (DAWBA) items related to specific phobias and post-traumatic stress disorder were not included in the analysis due to low correlations with other anxiety items. PE, psychotic experience; NEG, negative dimension; DEP, depression; ANX, anxiety; GEN, general psychopathology; ω, omega; ω_S, omega subscale; ω_H, omega hierarchical; ω_{HS}, omega hierarchical subscale.

¹ Gated item pairs, where answering “yes” to an initial question lead onto an additional question, collapsed into single items, ** $P < 0.0001$

Supplementary Table 2. Correlations between polygenic risk scores for psychiatric disorders generated using lists of SNPs meeting *P*-value threshold of 0.05 (n = 2863)

	SCZ	MDD	NEU
MDD	0.110		
NEU	-0.031	0.087	
BIP	0.195	0.043	0.050

Note: SCZ, schizophrenia; MDD, major depressive disorder; NEU, neuroticism; BIP, bipolar disorder

Supplementary Table 3. Sociodemographic differences between individuals who had taken part in all psychopathology measures and the remainder of the ALSPAC sample

Measure			Taken part in all psychopathology measures?		P
			No	Yes	
Sex	male	N (%)	6092 (54.36)	1543 (42.31)	<0.001
	female	N (%)	5115 (45.64)	2104 (57.69)	
Highest parental social class	professional/managerial	N (%)	4131 (50.48)	2197 (66.52)	<0.001
	non-professional/managerial	N (%)	4052 (49.52)	1106 (33.48)	
Household income (quintiles; lowest income = 1, highest income = 5)	1	N (%)	1597 (23.75)	392 (12.23)	<0.001
	2	N (%)	1417 (21.08)	551 (17.19)	
	3	N (%)	1345 (20.01)	631 (19.69)	
	4	N (%)	1225 (18.22)	761 (23.74)	
	5	N (%)	1139 (16.94)	870 (27.15)	
Crowding index	≤ 1 individual per room	N (%)	9069 (91.66)	3270 (97.12)	<0.001
	> 1 individual per room	N (%)	825 (8.34)	97 (2.88)	
Parity	0	N (%)	4157 (42.76)	1716 (50.44)	<0.001
	1	N (%)	3413 (35.11)	1175 (34.54)	
	2	N (%)	1489 (15.32)	392 (11.52)	
	3+	N (%)	663 (6.82)	119 (3.5)	
Highest maternal education qualification	CSE	N (%)	2204 (24.29)	323 (9.45)	<0.001
	Vocational	N (%)	1008 (11.11)	221 (6.46)	
	O level	N (%)	3185 (35.1)	1142 (33.4)	
	A level	N (%)	1796 (19.79)	1005 (29.39)	
	Degree	N (%)	881 (9.71)	728 (21.29)	
Ethnicity	non-white	N (%)	263 (2.92)	63 (1.85)	0.001
	white	N (%)	8729 (97.08)	3346 (98.15)	
Birthweight (g)		N	10 459	3436	<0.001
		Mean	3371.57	3411.14	
		SD	594.26	537.06	

Note: CSE, Certificate of Secondary Education; SD, standard deviation; P, P-value for chi-squared test (categorical measures) or t-test (birthweight) of differences between individuals who had taken part in all psychopathology measures and the remainder of the ALSPAC sample

Supplementary Table 4. Permutation adjusted associations between exported latent trait factor scores, estimated using a correlated factors and bifactor model, and polygenic risk scores (PRSs) for psychiatric disorders generated using lists of SNPs meeting *P*-value threshold of 0.05

PRS trait	Outcome	Correlated factors model		Bifactor model	
		Beta ¹	<i>P</i> ²	Beta ¹	<i>P</i> ²
SCZ	PE	0.058	0.0006	0.021	0.7515
	NEG	0.071	0.0006	0.040	0.0848
	DEP	0.046	0.0895	-0.011	0.9997
	ANX	0.051	0.0132	0.021	0.9423
	GENERAL	-	-	0.058	0.0124
MDD	PE	0.018	0.8875	-0.004	1.0000
	NEG	0.020	0.9429	-0.013	0.9997
	DEP	0.036	0.3413	0.011	0.9997
	ANX	0.033	0.2902	0.018	0.9860
	GENERAL	-	-	0.033	0.5840
NEU	PE	0.030	0.2894	-0.005	1.0000
	NEG	0.046	0.0718	0.005	1.0000
	DEP	0.046	0.0667	-0.005	1.0000
	ANX	0.053	0.0049	0.031	0.3693
	GENERAL	-	-	0.053	0.0230
BIP	PE	-0.031	0.2852	-0.022	0.7118
	NEG	-0.006	1.0000	0.020	0.9605
	DEP	-0.018	0.9733	0.005	1.0000
	ANX	-0.025	0.7122	-0.014	0.9996
	GENERAL	-	-	-0.022	0.9825

Note: SCZ, schizophrenia; MDD, major depressive disorder; NEU, neuroticism; BIP, bipolar disorder; PE, psychotic experiences; NEG, negative dimension; DEP, depression; ANX, anxiety; GENERAL, general psychopathology; LCI, lower 95% confidence interval; UCI, upper 95% confidence interval; *P*, *P*-value for association between latent trait factor scores and PRS.

¹ Note that the estimates will differ from the latent factor estimates as the relationship between the factor scores may differ slightly from the latent factors. The estimated factor scores better approximate true factors the more highly correlated the two are.

² Empirical adjusted *P*-value calculated from 10 000 permutations to correct for multiple testing.

Supplementary Table 5. Correlations between 4 specific psychopathology factors as measured within the correlated factors model (n = 3650)

	PE	NEG	DEP
NEG	0.505		
DEP	0.523	0.723	
ANX	0.456	0.410	0.461

Note: PE, psychotic experience; NEG, negative dimension; DEP, depression; ANX, anxiety

Supplementary Table 6. Standardised effect sizes and standard errors from associations between latent traits, generated using a correlated factors model, and polygenic risk scores (PRSs) for psychiatric disorders following inverse probability weighting

PRS trait	Outcome	Unweighted Beta ¹ (SE)	Inverse Probability Weighted (% truncated)					Untruncated
			50%	75%	90%	95%	99%	
SCZ	PE	0.087 (0.027)	0.090 (0.028)	0.089 (0.028)	0.093 (0.029)	0.098 (0.029)	0.102 (0.03)	0.099 (0.031)
	NEG	0.085 (0.021)	0.089 (0.021)	0.083 (0.021)	0.078 (0.022)	0.075 (0.022)	0.075 (0.024)	0.064 (0.025)
	DEP	0.043 (0.021)	0.049 (0.021)	0.042 (0.021)	0.040 (0.022)	0.043 (0.023)	0.048 (0.024)	0.045 (0.024)
	ANX	0.055 (0.023)	0.065 (0.023)	0.064 (0.023)	0.067 (0.024)	0.072 (0.024)	0.071 (0.025)	0.071 (0.025)
MDD	PE	-0.002 (0.027)	-0.001 (0.027)	-0.001 (0.027)	-0.004 (0.028)	-0.007 (0.029)	-0.006 (0.030)	-0.005 (0.030)
	NEG	0.019 (0.020)	0.020 (0.020)	0.019 (0.021)	0.019 (0.021)	0.020 (0.022)	0.025 (0.023)	0.025 (0.024)
	DEP	0.037 (0.021)	0.040 (0.021)	0.040 (0.022)	0.040 (0.022)	0.041 (0.023)	0.041 (0.024)	0.042 (0.024)
	ANX	0.029 (0.024)	0.035 (0.024)	0.036 (0.025)	0.036 (0.025)	0.038 (0.026)	0.046 (0.027)	0.048 (0.027)
NEU	PE	-0.001 (0.027)	0.006 (0.027)	0.006 (0.027)	0.005 (0.027)	0.005 (0.028)	0.002 (0.028)	0.008 (0.029)
	NEG	0.059 (0.020)	0.061 (0.020)	0.058 (0.020)	0.059 (0.021)	0.062 (0.021)	0.067 (0.023)	0.073 (0.025)
	DEP	0.055 (0.020)	0.060 (0.020)	0.059 (0.021)	0.061 (0.021)	0.064 (0.021)	0.067 (0.022)	0.072 (0.023)
	ANX	0.082 (0.022)	0.086 (0.022)	0.084 (0.022)	0.084 (0.023)	0.087 (0.023)	0.095 (0.024)	0.101 (0.024)
BIP	PE	-0.039 (0.027)	-0.044 (0.027)	-0.045 (0.027)	-0.045 (0.028)	-0.045 (0.028)	-0.043 (0.028)	-0.036 (0.029)
	NEG	-0.004 (0.021)	-0.004 (0.021)	-0.001 (0.021)	0.005 (0.022)	0.005 (0.023)	0.004 (0.024)	0.005 (0.025)
	DEP	-0.024 (0.021)	-0.024 (0.022)	-0.022 (0.022)	-0.017 (0.022)	-0.018 (0.023)	-0.019 (0.023)	-0.018 (0.024)
	ANX	-0.028 (0.024)	-0.032 (0.024)	-0.032 (0.024)	-0.030 (0.025)	-0.032 (0.025)	-0.035 (0.026)	-0.033 (0.026)

Note: SCZ, schizophrenia; MDD, major depressive disorder; NEU, neuroticism; BIP, bipolar disorder; PE, psychotic experience; NEG, negative dimension; DEP, depression; ANX, anxiety; SE, standard error. Inverse probability weighted refers to analyses including sampling weights for non-response, where the “% truncated” indicates whether the weights were truncated based on the 50th percentile (2.48), 75th percentile (3.02), 90th percentile (3.95), 95th percentile (5.33) and 99th percentile (8.94).

¹ Standardized estimate

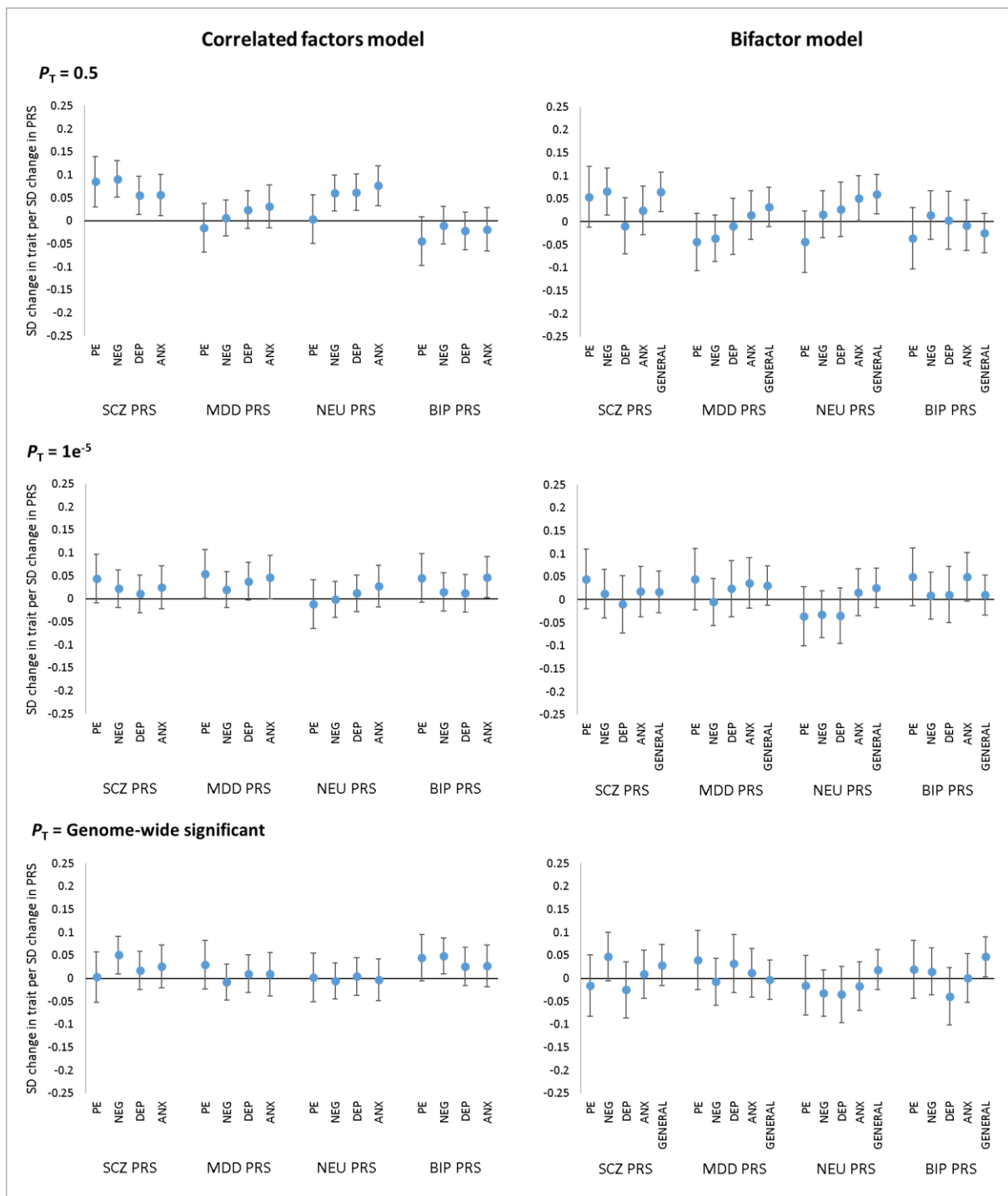
Supplementary Table 7. Effect sizes and standard errors from associations between latent traits, generated using a bifactor model, and polygenic risk scores (PRSs) for psychiatric disorders following inverse probability weighting

PRS trait	Outcome	Unweighted Beta (SE)	Inverse Probability Weighted (% truncated)					Untruncated
			50%	75%	90%	95%	99%	
SCZ	PE	0.062 (0.034)	0.060 (0.034)	0.063 (0.035)	0.070 (0.036)	0.074 (0.036)	0.074 (0.036)	0.072 (0.038)
	NEG	0.066 (0.027)	0.065 (0.026)	0.062 (0.026)	0.055 (0.027)	0.048 (0.027)	0.041 (0.028)	0.022 (0.031)
	DEP	-0.013 (0.031)	-0.013 (0.032)	-0.022 (0.032)	-0.027 (0.032)	-0.028 (0.032)	-0.033 (0.033)	-0.045 (0.034)
	ANX	0.029 (0.027)	0.037 (0.027)	0.039 (0.027)	0.044 (0.027)	0.047 (0.028)	0.043 (0.029)	0.042 (0.029)
	GENERAL	0.055 (0.023)	0.061 (0.022)	0.056 (0.023)	0.055 (0.023)	0.057 (0.024)	0.063 (0.025)	0.062 (0.025)
MDD	PE	-0.034 (0.033)	-0.034 (0.033)	-0.035 (0.033)	-0.039 (0.034)	-0.044 (0.034)	-0.043 (0.035)	-0.043 (0.036)
	NEG	-0.026 (0.026)	-0.027 (0.026)	-0.029 (0.026)	-0.029 (0.026)	-0.029 (0.026)	-0.022 (0.026)	-0.028 (0.028)
	DEP	-0.006 (0.032)	-0.002 (0.032)	0.000 (0.032)	-0.004 (0.032)	-0.008 (0.033)	-0.013 (0.034)	-0.024 (0.035)
	ANX	0.008 (0.028)	0.014 (0.028)	0.015 (0.028)	0.015 (0.029)	0.016 (0.030)	0.025 (0.031)	0.027 (0.031)
	GENERAL	0.043 (0.023)	0.044 (0.022)	0.044 (0.023)	0.045 (0.023)	0.046 (0.023)	0.047 (0.024)	0.050 (0.025)
NEU	PE	-0.058 (0.033)	-0.052 (0.033)	-0.050 (0.034)	-0.052 (0.034)	-0.054 (0.034)	-0.060 (0.035)	-0.060 (0.038)
	NEG	0.001 (0.025)	0.001 (0.025)	-0.001 (0.025)	0.000 (0.025)	0.003 (0.026)	0.007 (0.028)	0.009 (0.031)
	DEP	-0.024 (0.030)	-0.017 (0.030)	-0.014 (0.031)	-0.010 (0.031)	-0.006 (0.031)	-0.002 (0.033)	-0.009 (0.036)
	ANX	0.052 (0.026)	0.055 (0.026)	0.054 (0.026)	0.054 (0.026)	0.057 (0.027)	0.065 (0.028)	0.067 (0.028)
	GENERAL	0.071 (0.022)	0.073 (0.022)	0.071 (0.022)	0.071 (0.022)	0.073 (0.022)	0.075 (0.023)	0.082 (0.024)
BIP	PE	-0.023 (0.033)	-0.031 (0.033)	-0.034 (0.034)	-0.038 (0.034)	-0.039 (0.034)	-0.036 (0.035)	-0.028 (0.038)
	NEG	0.033 (0.027)	0.033 (0.027)	0.035 (0.027)	0.038 (0.028)	0.039 (0.028)	0.038 (0.029)	0.038 (0.030)
	DEP	0.013 (0.033)	0.013 (0.033)	0.017 (0.033)	0.019 (0.033)	0.021 (0.034)	0.025 (0.036)	0.019 (0.038)
	ANX	-0.015 (0.027)	-0.019 (0.027)	-0.021 (0.028)	-0.021 (0.028)	-0.023 (0.028)	-0.026 (0.029)	-0.024 (0.030)
	GENERAL	-0.030 (0.023)	-0.030 (0.023)	-0.028 (0.023)	-0.024 (0.023)	-0.024 (0.023)	-0.026 (0.024)	-0.023 (0.025)

Note: SCZ, schizophrenia; MDD, major depressive disorder; NEU, neuroticism; BIP, bipolar disorder; PE, psychotic experience; NEG, negative dimension; DEP, depression; ANX, anxiety; GENERAL, general psychopathology; SE, standard error. Inverse probability weighted refers to analyses including sampling weights for non-response, where the “% truncated” indicates whether the weights were truncated based on the 50th percentile (2.48), 75th percentile (3.02), 90th percentile (3.95), 95th percentile (5.33) and 99th percentile (8.94).

¹ Standardized estimate

Supplementary figure 1. Associations between psychopathology latent traits and polygenic risk scores (PRS) for psychiatric disorders



Associations are shown between latent traits for psychotic experiences (PE), negative dimension (NEG), depression (DEP), anxiety (ANX) and general psychopathology (GENERAL) generated using a correlated factors model (left-hand figures) and a bifactor model (right-hand figures) and polygenic risk scores (PRS) for schizophrenia (SCZ), major depressive disorder (MDD), neuroticism (NEU) and bipolar disorder (BIP) generated using lists of SNPs meeting 4 P-value thresholds (P_T). Standard deviation (SD) changes in latent trait per SD change in PRS are shown with upper and lower 95% confidence intervals. Genome-wide significant P_T = polygenic score created from independent genome-wide significant SNPs as reported by discovery studies. N = 2863.