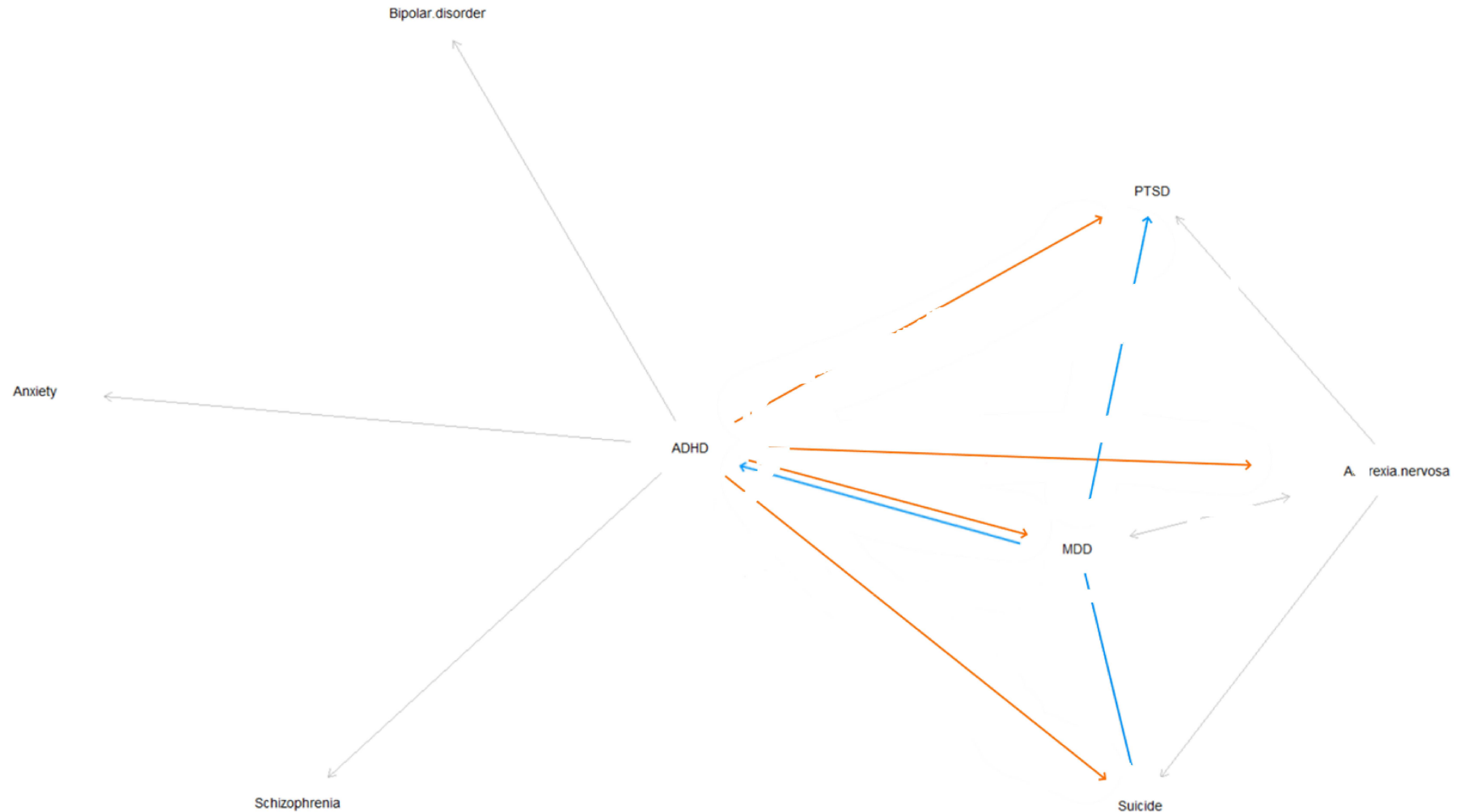**Understanding the causal relationships of Attention-Deficit/Hyperactivity Disorder with mental disorders and suicide attempt: a network Mendelian randomization study**

First author: Christa Meisinger

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Supplementary Method 1 Conceptualization of the step-wise network Mendelian randomization (MR) design. Each arrow represents at least one MR analysis. In the first step, the effects of ADHD on further mental disorders were modelled. In the second step, the ADHD related mental disorders on each other were modeled, if possible, to identify potential mediators or confounding factors. Notable associations are presented as orange colored arrows (step 1) and blue colored arrows (step 2)

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Supplementary Method 2 Description of datasets and cohorts

ADHD summary level data were derived from the iPSYCH project, based on a meta-analysis across 12 cohorts conducted by the Psychiatric Genomics Consortium[12]. The 19,099 cases (34,194 controls) were diagnosed by psychiatrists according to the ICD10 code.

The anxiety-GWAS consisted of 4,584 cases and 19,225 controls with no anxiety, stress-related or mood diagnoses[14]. Lifetime diagnoses of anxiety and stress-related disorders were obtained from the national Danish registers[14].

MDD data consisted of a meta-analysis of 33 cohorts (excluding 23andMe data) of the PGC and compared 170,756 cases with 329,443 controls[15].

PTSD data based on a meta-analysis on up to 42 studies comparing 23,185 cases with 151,309 controls[16]. Diagnosis was established using various instruments and different versions of the DSM (DSM-III-R, DSM IV, DSM-5)[16].

GWAS summary statistics for bipolar disorder (BD) met the criteria for DSM-IV, ICD-9, or ICD-10 codes and included 41,917 cases and 371,549 controls including 5 cohorts from iPSYCH, deCODE, Estonian Biobank, HUNT study, and UK Biobank[17].

The anorexia nervosa GWAS contained 16,992 diagnosed individuals and 55,525 controls from 33 cohorts[18]. The majority of samples came from the Anorexia Nervosa Genetics Initiative study, a multi-site recruitment effort in the USA, Sweden, Denmark, and Australia, with assistance from New Zealand. All cases either met the DSM or ICD criteria (DSM-III-R, DSM-IV, ICD-8, ICD-9, or ICD-10) or were based on self-reported diagnosis in the UK Biobank cohort. Note: This dataset was the only one containing genetic variants with an imputation quality score ≥ 0.7.

The schizophrenia GWAS were taken from the 3rd meta-analysis-wave conducted by PGC, which compared 39,910 diagnosed cases with 60,558 controls in a total of 36 cohorts[19].

In the suicide attempt GWAS overall 6,024 individuals with at least one recorded suicide attempt were compared to 44,240 persons from Denmark aged 15 years and older.

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Supplementary Method 3 Description of mediation analysis in presence of bidirectional effects

Aim: To assess the proportion mediated, which can be calculated as the ratio of the indirect effect and the total effect, in case of a bidirectional association between two exposures. Consider the following associations.
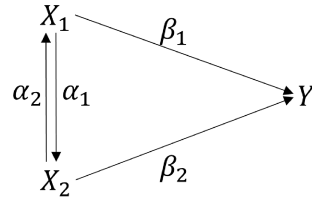
where X_1 and X_2 denote two exposures and Y the outcome. The bidirectional association of X_1 and X_2 is characterized by paths α_1 and α_2. The total effect β_1^* of X_1 on Y can be calculated as $\beta_1^* = \beta_1 + \alpha_1\beta_2$, where β_1 is the direct effect and $\alpha_1\beta_2$ the indirect effect. The same states for the effect of X_2 on Y, where $\beta_2^* = \beta_2 + \alpha_2\beta_1$. Usually, the total effect of X_1 on Y is estimated using univariable MR. To consider the bidirectional relationship between X_1 and X_2 and calculate the "unconfounded" total effects for mediation analysis, the effects β_1, α_1, and β_2 were estimated separately. α_1 was estimated using univariable MR. The direct effects β_1 and β_2 were estimated using mutually adjusted MVMR (i.e. conditioning X_1 and X_2 on each other) and in this way accounting for the X_1-X_2-association. The resulted estimates were also used, to calculate the indirect effect of X_1 on Y applying the product of coefficients method (i.e. $\alpha_1 \cdot \beta_2$).

Finally, the estimated indirect and total effects were used to calculate the proportion of the X_1-Y-association mediated by X_2 in the following way

$$\text{proportion mediated} = \frac{\alpha_1\beta_2}{\beta_1^*}$$

All calculations were done on the log scale.

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Supplementary Table 1 Genetic variants used as potential instruments in the univariable Mendelian randomization analyses investigating the effects of ADHD on psychiatric outcomes

Exposure	Outcome	SNP	CHR	POS	EA	OA	b_exp	se_exp	pval_exp	b_otcm	se_otcm	pval_otcm
							Main analyses					
ADHD	anorexia nervosa	rs10262192	7	114091753	A	G	0,07409583	0,0135	3,655E-08	0,033805	0,0137	0,01352
ADHD	anorexia nervosa	rs11591402	10	106747354	A	T	-0,09240042	0,0164	1,76E-08	-0,05399564	0,0164	0,0009615
ADHD	anorexia nervosa	rs1222063	1	96602440	A	G	0,09620069	0,0174	3,068E-08	0,01740051	0,0152	0,253
ADHD	anorexia nervosa	rs1427829	12	89760744	A	G	0,08219731	0,0136	1,349E-09	0,02430229	0,0135	0,0721
ADHD	anorexia nervosa	rs17531412	1	44182244	A	G	0,10539552	0,0148	1,072E-12	0,0145043	0,0147	0,3213
ADHD	anorexia nervosa	rs28411770	4	31151456	T	C	0,0861043	0,0151	1,152E-08	0,03859552	0,0146	0,008107
ADHD	anorexia nervosa	rs4858241	3	20669071	T	G	0,08219731	0,0143	8,172E-09	-0,01059594	0,014	0,4509
ADHD	anorexia nervosa	rs4916723	5	87854395	A	C	-0,07779939	0,0138	1,807E-08	0,01419872	0,0141	0,3145
ADHD	anorexia nervosa	rs74760947	8	34352610	A	G	-0,17960525	0,0317	1,393E-08	-0,0797036	0,0331	0,016
ADHD	anorexia nervosa	rs8039398	15	47730870	T	C	-0,07999604	0,0135	2,986E-09	-0,03770187	0,0134	0,004942
ADHD	anxiety	rs10262192	7	114091753	A	G	0,07409583	0,0135	3,655E-08	0,00169856	0,0243	0,9456
ADHD	anxiety	rs11591402	10	106747354	A	T	-0,09240042	0,0164	1,76E-08	-0,07239866	0,0295	0,01419
ADHD	anxiety	rs1427829	12	89760744	A	G	0,08219731	0,0136	1,349E-09	0,07160413	0,0245	0,0034
ADHD	anxiety	rs17531412	1	44182244	A	G	0,10539552	0,0148	1,072E-12	0,00159872	0,0266	0,9531
ADHD	anxiety	rs212178	16	72578131	A	G	-0,11709577	0,0205	1,198E-08	-0,02979963	0,0374	0,425
ADHD	anxiety	rs4858241	3	20669071	T	G	0,08219731	0,0143	8,172E-09	0,02740114	0,0253	0,2778
ADHD	anxiety	rs4916723	5	87854395	A	C	-0,07779939	0,0138	1,807E-08	0,02759571	0,0255	0,2791
ADHD	anxiety	rs74760947	8	34352610	A	G	-0,17960525	0,0317	1,393E-08	-0,12360369	0,0573	0,03111
ADHD	anxiety	rs8039398	15	47730870	T	C	-0,07999604	0,0135	2,986E-09	-0,00130085	0,0244	0,9575
ADHD	bipolar disorder	rs10262192	7	114091753	A	G	0,07409583	0,0135	3,655E-08	0,01630216	0,0094	0,0825
ADHD	bipolar disorder	rs11591402	10	106747354	A	T	-0,09240042	0,0164	1,76E-08	-0,02649586	0,0113	0,01896
ADHD	bipolar disorder	rs1427829	12	89760744	A	G	0,08219731	0,0136	1,349E-09	0,00229736	0,0094	0,8084
ADHD	bipolar disorder	rs17531412	1	44182244	A	G	0,10539552	0,0148	1,072E-12	0,0246048	0,0102	0,01526
ADHD	bipolar disorder	rs212178	16	72578131	A	G	-0,11709577	0,0205	1,198E-08	0,00439966	0,0151	0,773
ADHD	bipolar disorder	rs4858241	3	20669071	T	G	0,08219731	0,0143	8,172E-09	-0,00220242	0,0097	0,8218
ADHD	bipolar disorder	rs4916723	5	87854395	A	C	-0,07779939	0,0138	1,807E-08	-0,00010001	0,0096	0,9949
ADHD	bipolar disorder	rs8039398	15	47730870	T	C	-0,07999604	0,0135	2,986E-09	0,00560427	0,0093	0,5496

ADHD	MDD	rs10262192	7	114091753	A	G	0,07409583	0,0135	3,655E-08	0,0147	0,0043	0,0006712
ADHD	MDD	rs1427829	12	89760744	A	G	0,08219731	0,0136	1,349E-09	0,0087	0,0043	0,0446
ADHD	MDD	rs17531412	1	44182244	A	G	0,10539552	0,0148	1,072E-12	0,0116	0,0047	0,01328
ADHD	MDD	rs212178	16	72578131	A	G	-0,11709577	0,0205	1,198E-08	-0,001	0,0068	0,8788
ADHD	MDD	rs4858241	3	20669071	T	G	0,08219731	0,0143	8,172E-09	0,0133	0,0045	0,002808
ADHD	MDD	rs74760947	8	34352610	A	G	-0,17960525	0,0317	1,393E-08	0,0029	0,0103	0,775
ADHD	MDD	rs8039398	15	47730870	T	C	-0,07999604	0,0135	2,986E-09	-0,0018	0,0043	0,669
ADHD	PTSD	rs10262192	7	114091753	A	G	0,07409583	0,0135	3,655E-08	0,04469608	0,0147	0,002404
ADHD	PTSD	rs11591402	10	106747354	A	T	-0,09240042	0,0164	1,76E-08	-0,01139973	0,018	0,5275
ADHD	PTSD	rs1222063	1	96602440	A	G	0,09620069	0,0174	3,068E-08	0,02580419	0,0178	0,1471
ADHD	PTSD	rs1427829	12	89760744	A	G	0,08219731	0,0136	1,349E-09	0,02819865	0,0147	0,05561
ADHD	PTSD	rs17531412	1	44182244	A	G	0,10539552	0,0148	1,072E-12	-0,0010005	0,0161	0,9494
ADHD	PTSD	rs212178	16	72578131	A	G	-0,11709577	0,0205	1,198E-08	-0,02420048	0,0236	0,3054
ADHD	PTSD	rs28411770	4	31151456	T	C	0,0861043	0,0151	1,152E-08	-0,00989984	0,0171	0,5622
ADHD	PTSD	rs4858241	3	20669071	T	G	0,08219731	0,0143	8,172E-09	0,01580445	0,0154	0,3036
ADHD	PTSD	rs4916723	5	87854395	A	C	-0,07779939	0,0138	1,807E-08	-0,0154995	0,0151	0,3052
ADHD	PTSD	rs74760947	8	34352610	A	G	-0,17960525	0,0317	1,393E-08	-0,03779948	0,0361	0,2945
ADHD	PTSD	rs8039398	15	47730870	T	C	-0,07999604	0,0135	2,986E-09	0,0009995	0,0147	0,9436
ADHD	schizophrenia	rs10262192	7	114091753	A	G	0,07409583	0,0135	3,655E-08	0,02089683	0,0087	0,01613
ADHD	schizophrenia	rs1427829	12	89760744	A	G	0,08219731	0,0136	1,349E-09	-0,01089918	0,0087	0,2083
ADHD	schizophrenia	rs212178	16	72578131	A	G	-0,11709577	0,0205	1,198E-08	0,01290289	0,0141	0,3606
ADHD	schizophrenia	rs4858241	3	20669071	T	G	0,08219731	0,0143	8,172E-09	0,00219758	0,009	0,8058
ADHD	schizophrenia	rs4916723	5	87854395	A	C	-0,07779939	0,0138	1,807E-08	0,00029996	0,0088	0,9721
ADHD	schizophrenia	rs8039398	15	47730870	T	C	-0,07999604	0,0135	2,986E-09	-0,00470103	0,0086	0,5885
ADHD	suicide attempt	rs10262192	7	114091753	A	G	0,07409583	0,0135	3,655E-08	0,05145	0,0197	0,00903
ADHD	suicide attempt	rs1427829	12	89760744	A	G	0,08219731	0,0136	1,349E-09	0,04751	0,0199	0,01714
ADHD	suicide attempt	rs17531412	1	44182244	A	G	0,10539552	0,0148	1,072E-12	0,03263	0,0215	0,1292
ADHD	suicide attempt	rs212178	16	72578131	A	G	-0,11709577	0,0205	1,198E-08	0,003892	0,0307	0,8987
ADHD	suicide attempt	rs28411770	4	31151456	T	C	0,0861043	0,0151	1,152E-08	0,03211	0,0212	0,1308
ADHD	suicide attempt	rs4858241	3	20669071	T	G	0,08219731	0,0143	8,172E-09	0,01339	0,0205	0,515
ADHD	suicide attempt	rs4916723	5	87854395	A	C	-0,07779939	0,0138	1,807E-08	-0,009455	0,0204	0,641
ADHD	suicide attempt	rs74760947	8	34352610	A	G	-0,17960525	0,0317	1,393E-08	-0,02372	0,0468	0,6129

ADHD	suicide attempt	rs8039398	15	47730870	T	C	-0,07999604	0,0135	2,986E-09	-0,0199	0,0198	0,314
Secondary analyses												
ADHD	anorexia nervosa	rs11591402	10	106747354	A	T	-0,09240042	0,0164	1,76E-08	0,02935	0,04709	0,533
ADHD	anorexia nervosa	rs1427829	12	89760744	A	G	0,08219731	0,0136	1,349E-09	0,04074	0,04199	0,332
ADHD	anorexia nervosa	rs17531412	1	44182244	A	G	0,10539552	0,0148	1,072E-12	0,01301	0,04281	0,761
ADHD	anorexia nervosa	rs212178	16	72578131	A	G	-0,11709577	0,0205	1,198E-08	0,04833	0,08497	0,57
ADHD	anorexia nervosa	rs4858241	3	20669071	T	G	0,08219731	0,0143	8,172E-09	0,00163	0,0436	0,97
ADHD	anorexia nervosa	rs74760947	8	34352610	A	G	-0,17960525	0,0317	1,393E-08	-0,13763	0,07824	0,0785
ADHD	anorexia nervosa	rs8039398	15	47730870	T	C	-0,07999604	0,0135	2,986E-09	-0,01412	0,04143	0,733
ADHD	anxiety	rs10262192	7	114091753	A	G	0,07409583	0,0135	3,655E-08	-0,00601	0,02907	0,836
ADHD	anxiety	rs11591402	10	106747354	A	T	-0,09240042	0,0164	1,76E-08	-0,02185	0,03312	0,509
ADHD	anxiety	rs1427829	12	89760744	A	G	0,08219731	0,0136	1,349E-09	0,01482	0,02951	0,616
ADHD	anxiety	rs17531412	1	44182244	A	G	0,10539552	0,0148	1,072E-12	-0,01324	0,03017	0,661
ADHD	anxiety	rs212178	16	72578131	A	G	-0,11709577	0,0205	1,198E-08	-0,00774	0,05915	0,896
ADHD	anxiety	rs4858241	3	20669071	T	G	0,08219731	0,0143	8,172E-09	-0,02125	0,0305	0,486
ADHD	anxiety	rs4916723	5	87854395	A	C	-0,07779939	0,0138	1,807E-08	0,01144	0,02868	0,69
ADHD	anxiety	rs74760947	8	34352610	A	G	-0,17960525	0,0317	1,393E-08	-0,00771	0,05606	0,891
ADHD	anxiety	rs8039398	15	47730870	T	C	-0,07999604	0,0135	2,986E-09	-0,00763	0,02913	0,793
ADHD	bipolar disorder	rs10262192	7	114091753	A	G	0,07409583	0,0135	3,655E-08	0,01262	0,02301	0,583
ADHD	bipolar disorder	rs11591402	10	106747354	A	T	-0,09240042	0,0164	1,76E-08	-0,04315	0,02614	0,0988
ADHD	bipolar disorder	rs1427829	12	89760744	A	G	0,08219731	0,0136	1,349E-09	0,0525	0,02337	0,0247
ADHD	bipolar disorder	rs17531412	1	44182244	A	G	0,10539552	0,0148	1,072E-12	0,01305	0,02393	0,585
ADHD	bipolar disorder	rs212178	16	72578131	A	G	-0,11709577	0,0205	1,198E-08	-0,02987	0,04711	0,526
ADHD	bipolar disorder	rs4858241	3	20669071	T	G	0,08219731	0,0143	8,172E-09	-0,00944	0,02403	0,695
ADHD	bipolar disorder	rs4916723	5	87854395	A	C	-0,07779939	0,0138	1,807E-08	-0,01268	0,02269	0,576
ADHD	bipolar disorder	rs74760947	8	34352610	A	G	-0,17960525	0,0317	1,393E-08	-0,08398	0,04384	0,0554
ADHD	bipolar disorder	rs8039398	15	47730870	T	C	-0,07999604	0,0135	2,986E-09	0,00923	0,02301	0,688
ADHD	PTSD	rs10262192	7	114091753	A	G	0,07409583	0,0135	3,655E-08	-0,00526	0,04066	0,897
ADHD	PTSD	rs11591402	10	106747354	A	T	-0,09240042	0,0164	1,76E-08	-0,13685	0,0463	0,00312
ADHD	PTSD	rs1427829	12	89760744	A	G	0,08219731	0,0136	1,349E-09	-0,0117	0,04139	0,777
ADHD	PTSD	rs17531412	1	44182244	A	G	0,10539552	0,0148	1,072E-12	-0,00812	0,04199	0,847
ADHD	PTSD	rs212178	16	72578131	A	G	-0,11709577	0,0205	1,198E-08	0,04712	0,0828	0,569

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ADHD	PTSD	rs4858241	3	20669071	T	G	0,08219731	0,0143	8,172E-09	0,03833	0,04278	0,37
ADHD	PTSD	rs4916723	5	87854395	A	C	-0,07779939	0,0138	1,807E-08	0,01707	0,04002	0,67
ADHD	PTSD	rs74760947	8	34352610	A	G	-0,17960525	0,0317	1,393E-08	-0,08588	0,07696	0,264
ADHD	PTSD	rs8039398	15	47730870	T	C	-0,07999604	0,0135	2,986E-09	-0,04614	0,0408	0,258
ADHD	schizophrenia	rs10262192	7	114091753	A	G	0,07409583	0,0135	3,655E-08	-0,08293	0,03047	0,00649
ADHD	schizophrenia	rs11591402	10	106747354	A	T	-0,09240042	0,0164	1,76E-08	-0,02082	0,03439	0,545
ADHD	schizophrenia	rs1427829	12	89760744	A	G	0,08219731	0,0136	1,349E-09	0,00895	0,03082	0,772
ADHD	schizophrenia	rs17531412	1	44182244	A	G	0,10539552	0,0148	1,072E-12	0,00663	0,03149	0,833
ADHD	schizophrenia	rs212178	16	72578131	A	G	-0,11709577	0,0205	1,198E-08	-0,03677	0,06244	0,556
ADHD	schizophrenia	rs4858241	3	20669071	T	G	0,08219731	0,0143	8,172E-09	0,00342	0,03162	0,914
ADHD	schizophrenia	rs4916723	5	87854395	A	C	-0,07779939	0,0138	1,807E-08	0,0272	0,02983	0,362
ADHD	schizophrenia	rs74760947	8	34352610	A	G	-0,17960525	0,0317	1,393E-08	-0,07138	0,05746	0,214
ADHD	schizophrenia	rs8039398	15	47730870	T	C	-0,07999604	0,0135	2,986E-09	0,05646	0,03028	0,0623

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Supplementary Table 2 Identified pleiotropic SNPs by the iterative univariable Mendelian randomization approach regarding a significance threshold 0.01

Exposure	Outcome	Iteration	SNP	Q statistic	P value
Main analyses					
ADHD	anorexia nervosa	1	rs212178	9,249	2,4E-03
ADHD	bipolar disorder	1	rs74760947	15,134	1,0E-04
ADHD	MDD	1	rs11591402	12,003	5,3E-04
ADHD	MDD	1	rs4916723	17,687	2,6E-05
ADHD	schizophrenia	1	rs1427829	7,902	4,9E-03
ADHD	schizophrenia	1	rs74760947	11,269	7,9E-04
ADHD	schizophrenia	2	rs17531412	10,634	1,1E-03
ADHD	suicide attempt	1	rs11591402	10,203	1,4E-03
Secondary analyses					
ADHD	anorexia nervosa	1	rs10262192	8,099	4,4E-03
ADHD	anorexia nervosa	1	rs4916723	8,741	3,1E-03

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Supplementary Table 3 Results of the MR-PRESSO global and MR-Egger-intercept tests for detecting horizontal and directional pleiotropy and between SNP-heterogeneity based on the radial regression framework in the univariable network Mendelian randomization setting

| Exposure	Outcome	PRESSO RSSobs	P_{RSSobs}	Egger intercept	$P_{intercept}$	Cochrans Q	df	P_Q	Rueckers Q'	$P_{Q'}$	Q-Q'	$P_{Q-Q'}$	Q'/Q
ADHD	Anorexia nervosa (PGC)	24,999	0,034	3,783	0,517	19,210	9	0,023	16,551	0,056	2,659	0,103	0,862
ADHD	Anxiety (iPSYCH)	18,071	0,102	1,808	0,762	13,955	8	0,083	13,810	0,087	0,145	0,703	0,990
ADHD	Bipolar disorder (PGC)	13,938	0,179	-3,396	0,418	10,333	7	0,170	5,356	0,617	4,977	0,026	0,518
ADHD	MDD (PGC)	16,417	0,101	-1,896	0,739	11,602	6	0,071	7,851	0,249	3,751	0,053	0,677
ADHD	PTSD (PGC)	12,831	0,421	4,049	0,264	10,318	10	0,413	7,075	0,718	3,243	0,072	0,686
ADHD	Schizophrenia (PGC)	11,901	0,170	10,354	0,320	8,395	5	0,136	2,546	0,770	5,849	0,016	0,303
ADHD	Suicide attempt (iPSYCH)	7,984	0,640	-1,194	0,751	6,194	8	0,626	5,343	0,720	0,851	0,356	0,863
ADHD	Anorexia nervosa (FinnGen)	5,427	0,704	-2,358	0,251	3,902	6	0,690	2,335	0,886	1,567	0,211	0,598
ADHD	Anxiety (FinnGen)	2,130	0,989	0,445	0,709	1,670	8	0,990	1,625	0,990	0,045	0,832	0,973
ADHD	Bipolar disorder (FinnGen)	8,765	0,570	-0,454	0,850	6,721	8	0,567	6,475	0,594	0,246	0,620	0,963
ADHD	PTSD (FinnGen)	12,885	0,288	-0,977	0,735	10,122	8	0,257	9,363	0,313	0,759	0,384	0,925
ADHD	Schizophrenia (FinnGen)	17,092	0,113	-2,065	0,530	13,620	8	0,092	11,553	0,172	2,067	0,151	0,848
MDD	AN	44,566	0,632	-1,447	0,185	41,133	45,000	0,636	34,463	0,873	6,671	0,010	0,838
MDD	PTSD (PGC)	60,938	0,048	-2,042	0,118	58,076	42,000	0,050	49,160	0,208	8,916	0,003	0,846
MDD	PTSD (FinnGen)	72,358	0,006	-2,022	0,167	66,587	41,000	0,007	49,853	0,162	16,734	0,000	0,749
MDD	AN (PGC)	43,947	0,478	-0,071	0,948	41,962	42,000	0,473	41,939	0,474	0,022	0,881	0,999
MDD	AN (FinnGen)	47,243	0,219	-1,628	0,342	44,448	38,000	0,219	38,050	0,467	6,399	0,011	0,856
MDD	Suicide attempt	42,777	0,490	-0,020	0,989	39,598	40,000	0,488	39,512	0,492	0,087	0,769	0,998
MDD	ADHD	5,947	0,551	-4,026	0,042	3,977	5,000	0,553	0,678	0,984	3,298	0,069	0,171
AN (PGC)	ADHD	44,566	0,632	-1,447	0,185	41,133	45,000	0,636	34,463	0,873	6,671	0,010	0,838

Supplementary Table 4 Results of MR-Steiger tests from network Mendelian randomization analyses investigating possible reverse causation

Exposure	Outcome	Consortia	snp_r2.exposure	snp_r2.outcome	correct_causal_direction	steiger_pval
ADHD	Schizophrenia	PGC	0,002685	0,000049	TRUE	6,20E-17
ADHD	Schizophrenia	FinnGen	0,004397	0,000955	TRUE	1,11E-13
ADHD	Anorexia nervosa	PGC	0,005196	0,000665	TRUE	4,51E-16
ADHD	Anorexia nervosa	FinnGen	0,003541	0,000608	TRUE	7,41E-04
ADHD	PTSD	PGC	0,005583	0,000344	TRUE	6,79E-30
ADHD	PTSD	FinnGen	0,003830	0,000259	TRUE	2,10E-23
ADHD	Anxiety	iPSYCH	0,004397	0,001059	TRUE	3,11E-05
ADHD	Anxiety	FinnGen	0,004397	0,000094	TRUE	3,45E-32
ADHD	Bipolar disorder	PGC	0,003830	0,000099	TRUE	1,25E-29
ADHD	Bipolar disorder	FinnGen	0,003830	0,000259	TRUE	2,10E-23
ADHD	MDD	PGC	0,003496	0,000044	TRUE	1,23E-30
ADHD	Suicide attempt	iPSYCH	0,004469	0,000566	TRUE	4,47E-12
MDD	PTSD	PGC	0,002537	0,001701	TRUE	1,01E-03
MDD	PTSD	FinnGen	0,002388	0,007656	FALSE	1,29E-54
MDD	Anorexia nervosa	PGC	0,002283	0,001718	TRUE	1,11E-01
MDD	Anorexia nervosa	FinnGen	0,002376	0,005352	FALSE	9,69E-03
MDD	Suicide attempt	iPSYCH	0,002104	0,001824	TRUE	4,99E-01
MDD	ADHD	PGC	0,002185	0,001221	TRUE	9,43E-03
Anorexia nervosa	ADHD	PGC	0,003314	0,000064	TRUE	3,36E-18

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Supplementary Table 5 Results of the MR-Egger intercept tests for detecting directional pleiotropy and between SNP-heterogeneity based on the multivariable Mendelian randomization setting

Exposure	Outcome	heter_stat	heter_pval	intercept	interc_pval
ADHD	PTSD	55,823	0,298	0,001	0,764
MDD	PTSD	55,823	0,298	0,001	0,764
ADHD	Suicidce	58,446	0,071	0,002	0,785
MDD	Suicidce	58,446	0,071	0,002	0,785

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Supplementary Figure 1 Meta-analyses of main and secondary univariable Mendelian randomization studies investigating the effects of ADHD on psychiatric outcomes

Supplementary Figure 2 Sensitivity analyses of main and secondary univariable Mendelian randomization studies investigating the effects of ADHD on psychiatric outcomes

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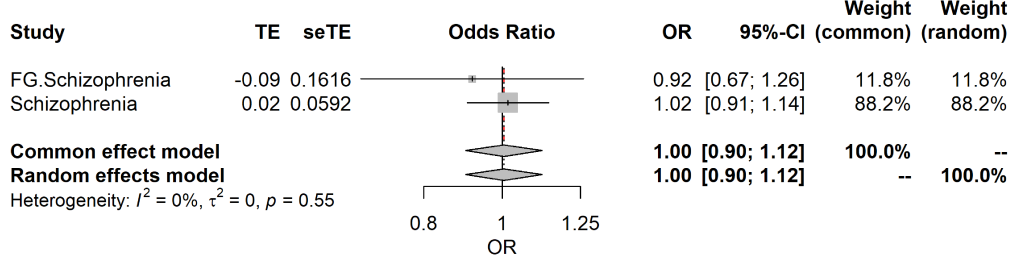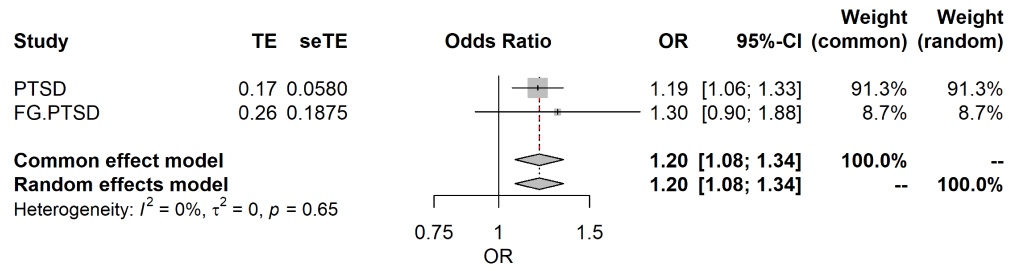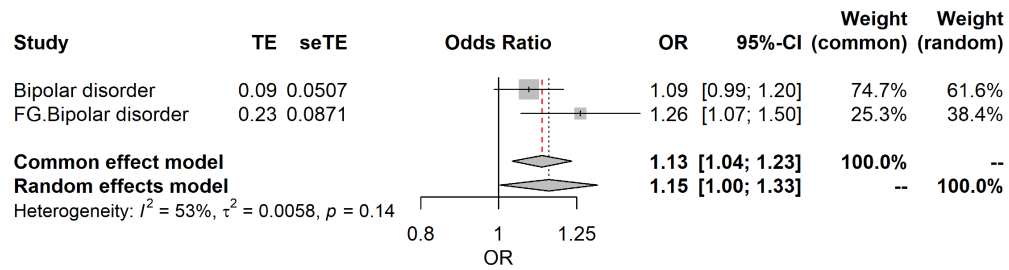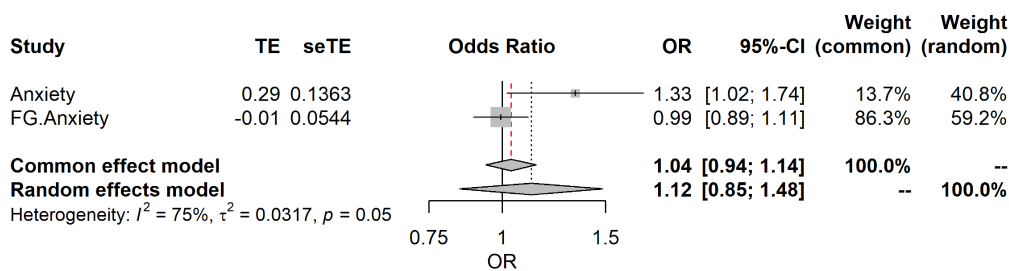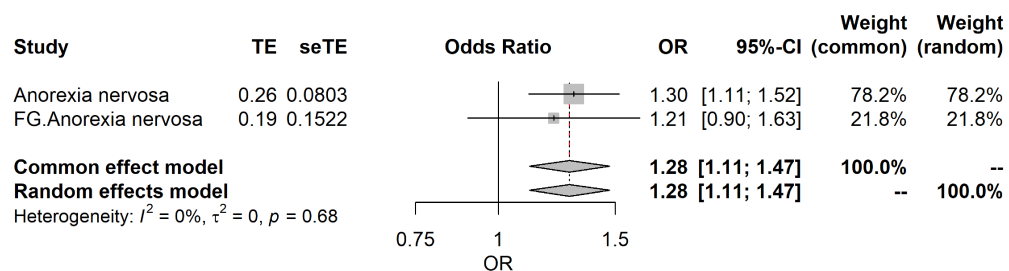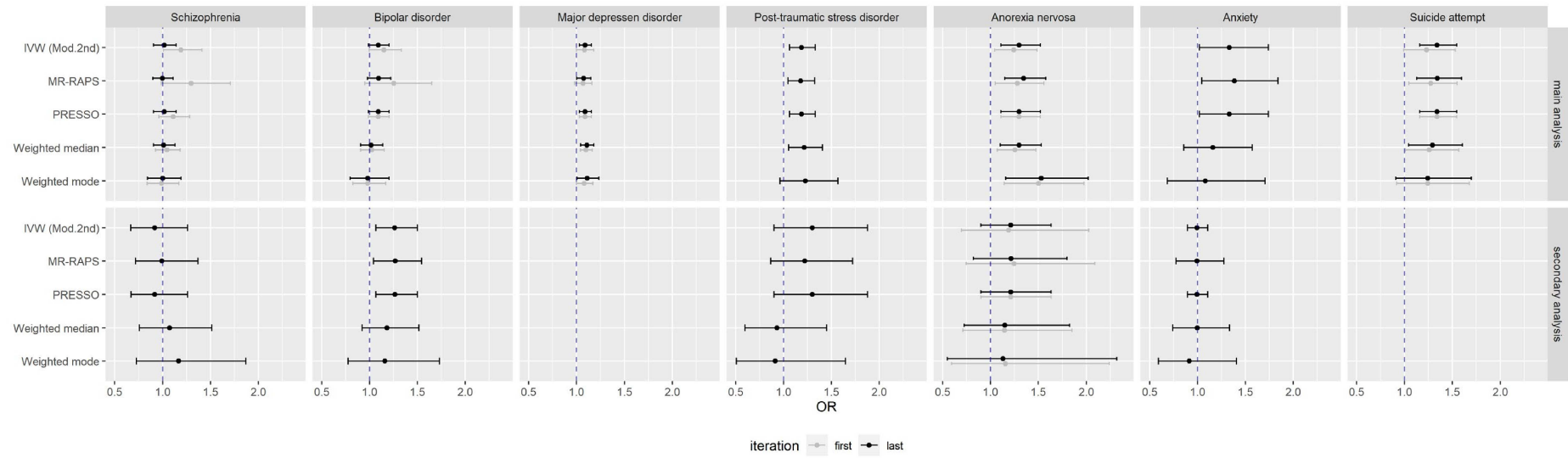
Supplementary Figure 3 Meta-analyses of network Mendelian randomization studies investigating the effects of major depression disorder and anorexia nervosa on psychiatric outcomes

Exposure: Major depression disorder

Study	TE	seTE	Odds Ratio	OR	95%-CI	Weight (common)	Weight (random)
PTSD	0.62	0.0792		1.87	[1.60; 2.18]	92.2%	92.2%
FG.PTSD	0.47	0.2717		1.59	[0.93; 2.71]	7.8%	7.8%
Common effect model				1.84	[1.59; 2.14]	100.0%	--
Random effects model				1.84	[1.59; 2.14]	--	100.0%
Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$, $p = 0.57$							

Study	TE	seTE	Odds Ratio	OR	95%-CI	Weight (common)	Weight (random)
Anorexia nervosa	0.59	0.1024		1.80	[1.47; 2.20]	84.1%	60.6%
FG.Anorexia nervosa	0.12	0.2353		1.13	[0.71; 1.80]	15.9%	39.4%
Common effect model				1.67	[1.39; 2.01]	100.0%	--
Random effects model				1.50	[0.96; 2.33]	--	100.0%
Heterogeneity: $I^2 = 69\%$, $\tau^2 = 0.0733$, $p = 0.07$							

Exposure: Anorexia nervosa

Study	TE	seTE	Odds Ratio	OR	95%-CI	Weight (common)	Weight (random)
PTSD	0.08	0.0823		1.09	[0.92; 1.28]	85.2%	76.1%
FG.PTSD	-0.17	0.1973		0.85	[0.58; 1.25]	14.8%	23.9%
Common effect model				1.05	[0.90; 1.21]	100.0%	--
Random effects model				1.02	[0.83; 1.26]	--	100.0%
Heterogeneity: $I^2 = 26\%$, $\tau^2 = 0.0079$, $p = 0.25$							

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Supplementary Figure 4 Sensitivity analyses of network Mendelian randomization studies investigating the effects of major depression disorder on psychiatric outcomes
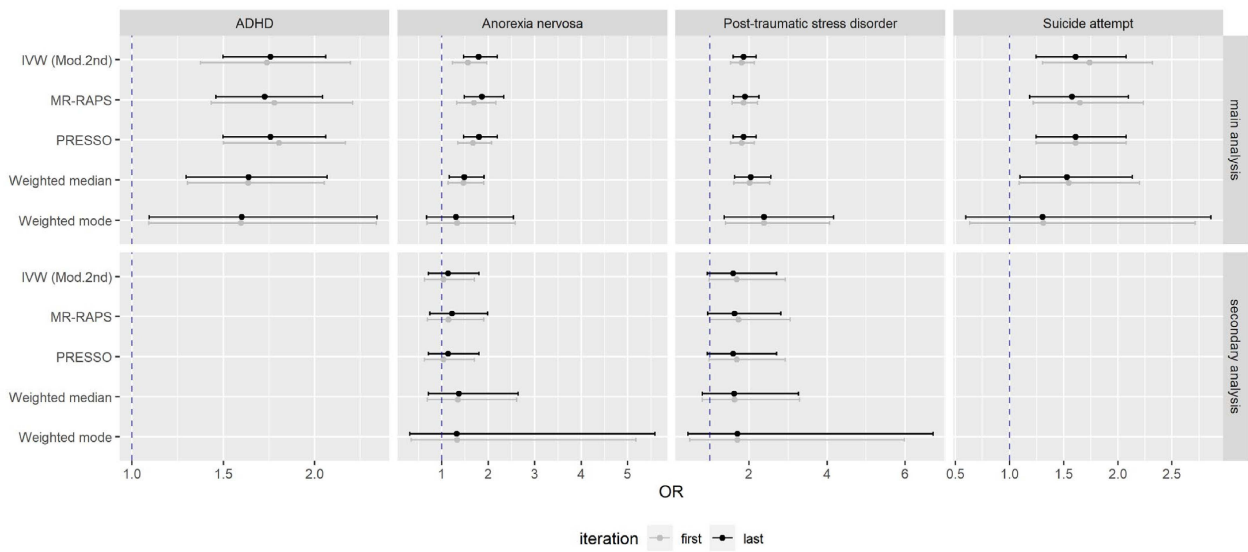
Supplementary Figure 5 Sensitivity analyses of network Mendelian randomization studies investigating the effects of anorexia nervosa on psychiatric outcomes

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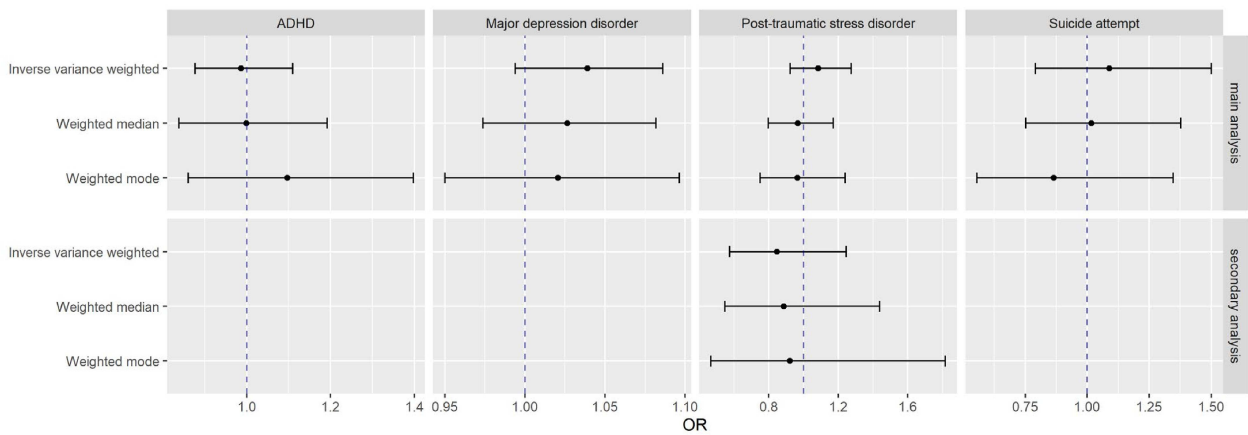
Supplementary Figure 6 Multivariable Mendelian randomization sensitivity analyses investigating the direct effects of ADHD and major depression disorder on both PTSD and suicide attempt