

APPENDIX

Table 1 - Description of Registers

Multi-Generation Register

The Multi-Generation Register is a register made up of persons who have been registered in Sweden at some time since 1961 and those who were born in 1932 or later. These are called index persons. The register contains connections between index persons and their biological parents. There are about 11 million index persons in the register. The Multi-Generation Register is a part of the register system for Total Population Register, where information comes from the National Tax Board. Every year, a new version of the register is created, including new index persons who immigrated or were born during the year. Information from the Multi-Generation Register may be disclosed for research and statistical purposes. For more information, see *Statistics Sweden, Background Facts, Population and Welfare Statistics 2017:2, Multi-generation register 2016. A description of contents and quality*

National Patient Register

In the 1960's the National Board of Health and Welfare started to collect information regarding in-patients at public hospitals, the National Patient Register (NPR). Initially it contained information about all patients treated in psychiatric care and approximately 16 percent of patients in somatic care. The register at that time covered six of the 26 county councils in Sweden. In 1984, the Ministry of Health and Welfare together with the Federation of County Councils decided a mandatory participation for all county councils. From 1987, NPR includes all in-patient care in Sweden. Since 2001, the register also covers outpatient doctor visits including day surgery and psychiatric care from both private and public caregivers. For more information, see <https://www.socialstyrelsen.se/en/statistics-and-data/register/register-information/the-national-patient-register/>

Primary Care Data

We also used information from our new Primary Care research dataset including individual-level information on clinical diagnoses from primary health care centers from the following Swedish counties: Blekinge (2009-2018), Dalarna (2005-2018), Gotland (2011-2018), Gävleborg (2010-2018), Halland (2007-2018), Jönköping (2008-2018), Kalmar (2007-2018), Kronoberg (2006-2018), Norrbotten (2001-2018), Skåne (1989-2018), Stockholm (2003-2018), Södermanland (1992-2018), Uppsala (2005-2018), Västra Götaland (2000-2018), Värmland (2005-2018), Västerbotten (1991-2018), Västernorrland (2008-2018), Västmanland (2014-2018), Östergötland (1990-2018), and Örebro (2006-2018). The retrieval of data differs due to timing of digitalization of patient records. In 2018, 99% of the Swedish population lived in these 20 counties. For more information see *Sundquist, J., Ohlsson, H., Sundquist, K. et al. Common adult psychiatric disorders in Swedish primary care where most mental health patients are treated. BMC Psychiatry 17, 235 (2017).*

The Population and Housing Censuses

Every fifth year between 1960 and 1990 Sweden conducted censuses. These registers include among other things, the population's employment, the composition of households and housing. For more information, see <https://www.scb.se/hitta-statistik/statistik-efter-amne/befolkning/befolkningens-storlek-och-forandringar/hushalls-och-bostadsrakning-census/>

Table 2 - Definition of Major Depression, Anxiety Disorders, Anxiety Disorder Subtypes, Bipolar Disorder and Schizophrenia by ICD Codes Utilized in the Swedish Hospital Discharge Register; Outpatient Care Register; Primary Care Registry

	Definition
Major Depression (MD)	and ICD-8 codes 296.0, 296.2, 298.0 and 300.4; ICD-9 codes 296B, 298A and 300E; and ICD-10 codes F32 and F33
Anxiety Disorder (AD)	ICD-8 codes 300.0 and 300.2, ICD-9 codes 300A and 300C and ICD-10 codes F40 and F41 (except F41.2)
Phobia	ICD-10 F40
Panic Disorder (PD)	ICD-10 F41.0
Generalized Anxiety Disorder (GAD)	ICD-10 F41.1
Anxiety Disorder-not otherwise specified (NOS),	ICD-10 F41.3, F41.8 and F41.9
Bipolar Disorder (BD)	ICD-8 codes 296.1, 296.3, 296.8 and 296.9; ICD-9 codes 296A, 296C, 296D, 296E, 296W and 296X; and ICD-10 codes F30 and F31.
Schizophrenia (SZ)	ICD-8 and ICD-9 codes 295; ICD-10 codes F20.

Table 3 - Calculation of the genetic and rearing correlations

We calculated the genetic correlation, r_g , and the rearing correlation, r_r , between AD and MD, using this formula (and the assumption of $-1 \leq r \leq 1$):

$$r = \frac{Cov(AD, MD)}{\sqrt{V(AD), V(MD)}} = \frac{r(AD, MD)}{\sqrt{r(AD, AD), r(MD, MD)}}$$

For the correlation $r(AD, MD)$ we made use of a weighted tetrachoric correlation explaining parent-offspring cross-transmissions from AD to MD as well as from MD to AD. For the correlations $r(AD, AD)$ and $r(MD, MD)$ we used the weighted tetrachoric correlations explaining parent-offspring transmissions from AD to AD and MD to MD, respectively. For the genetic correlation we made use of 129 538 parent-offspring pairs (based on 120 213 offspring) reflecting a genes-only relationship. These pairs were found in the following families: NLW father (biological father), NLW mother (biological mother) and adoptive (biological fathers and biological mothers). For the rearing correlation we made use of 127 555 parent-offspring pairs (based on 109 612 offspring) reflecting a rearing only relationship. These pairs were found in the following families: stepfather (stepfather), stepmother (stepmother) and adoptive (adoptive fathers and adoptive mothers). For the 95% confidence intervals, we used non-parametric bootstrap sampling along with the percentile method. We produced 10 000

samples of the same size as used for the calculation of the point estimates, by resampling from the individuals in the offspring population who were contributing to the genes only/rearing only data (n=120 213 for the genetic correlation and n=109 612 for the rearing correlation).

Table 4 – Algorithm used to decide whether an individual with both AD and MD diagnoses should be counted as a case of either AD or MD

		Number of lifetime MD diagnoses				
		1	2	3-5	6-10	>10
Number of lifetime AD diagnoses	1	Last diagnosis	Last diagnosis	Most common diagnosis	Most common diagnosis	Most common diagnosis
	2	Last diagnosis	Majority of last 3 diagnoses	Majority of last 3 diagnoses	Most common diagnosis	Most common diagnosis
	3-5	Most common diagnosis	Majority of last 3 diagnoses	Majority of last 3 diagnoses	Majority of last 3 diagnoses	Majority of last 5 diagnoses
	6-10	Most common diagnosis	Most common diagnosis	Majority of last 3 diagnoses	Majority of last 5 diagnoses	Majority of last 5 diagnoses
	>10	Most common diagnosis	Most common diagnosis	Majority of last 5 diagnoses	Majority of last 5 diagnoses	Majority of last 5 diagnoses

Table 5 – Details on R-packages used in statistical analyses

1. Fox J. polycor: Polychoric and Polyserial Correlations. R package. 2019.
2. Viechtbauer W. Conducting meta-analyses in R with the metafor package. J Stat Softw. 2010;36(3):1-48.
3. Wickham H. ggplot2: Elegant Graphics for Data Analysis. New York, NY: Springer-Verlag; 2016.
4. Neuwirth E. RColorBrewer: ColorBrewer Palettes. R package. 2014.
5. Wickham H, Miller E. haven: Import and Export 'SPSS', 'Stata' and 'SAS' Files. R package. 2021.
6. Wickham H, François R, Henry L, Müller K. dplyr: A Grammar of Data Manipulation. R package. 2021.
7. Dowle M, Srinivasan A. data.table: Extension of `data.frame`. R package. 2021.

Table 6
Prevalences of Phobia (%), PD (%), GAD (%), AD_NoS (%) and MD (%), using ICD-10 codes only

	Disorder	Intact	NLW Father	NLW Mother	Stepfather	Stepmother	Adoptive
All offspring	Phobia	1.6	2.9	2.8	2.4	2.6	1.7
	PD	3.4	5.9	4.8	5.6	6.1	4.5
	GAD	2.1	3.5	3.1	3.1	3.4	3.0
	AD_NoS	10.7	16.8	15.7	15.6	17.0	13.8
	MD	14.0	22.0	20.6	21.1	22.5	19.1
Female offspring	Phobia	1.9	3.3	3.4	2.7	3.1	1.9
	PD	4.4	7.5	6.8	7.1	8.2	5.6
	GAD	2.9	4.6	4.3	4.1	4.8	3.6
	AD_NoS	14.2	21.2	20.8	19.7	22.7	17.1
	MD	18.5	28.1	27.2	27.1	30.2	24.8
Male offspring	Phobia	1.3	2.5	2.3	2.0	2.2	1.6
	PD	2.5	4.4	3.2	4.1	4.4	3.4
	GAD	1.4	2.4	2.0	2.1	2.3	2.5
	AD_NoS	7.6	12.6	11.3	11.0	12.4	11.0
	MD	9.9	16.2	15.1	15.2	16.3	14.1
Biological mothers	Phobia	0.5	1.5	0.8	1.0	NA	0.6
	PD	1.8	4.3	2.9	3.4		1.9
	GAD	1.7	3.4	2.9	2.5		2.2
	AD_NoS	9.3	15.7	13.1	13.0		11.2
	MD	14.7	23.2	15.9	20.1		14.8
Biological fathers	Phobia	0.3	0.7	0.2	NA	0.5	0.2
	PD	0.9	1.5	1.3		1.1	0.9
	GAD	0.8	1.3	0.9		0.6	0.9
	AD_NoS	4.6	6.9	5.4		5.4	4.9
	MD	8.2	10.4	9.2		9.3	7.4
Stepmother or adoptive mother	Phobia	NA	NA	NA	NA	0.4	0.1
	PD					1.7	0.6
	GAD					1.9	1.5
	AD_NoS					10.0	9.3
	MD					16.3	14.7
Stepfather or adoptive father	Phobia	NA	NA	NA	0.4	NA	0.1
	PD				1.2		0.3
	GAD				0.9		0.3
	AD_NoS				5.3		3.5
	MD				9.3		6.7

Table 7

Parent-offspring tetrachoric correlations and 95% CI, Weighted Estimates and Heterogeneity Tests for Four Extended Adoption Designs for Panic Disorders

	Intact		NLW Father		NLW Mother		Step-Father		Step-Mother		Adoptive		Weighted Estimate		Het Test ^a
PD→PD															
<i>Mother-offspring</i>															
Genes + rearing	0.16	(0.15-0.17)	0.18	(0.15-0.21)	NA	NA	0.15	(0.12-0.19)	NA	NA	NA	NA	0.16	(0.15-0.17)	0.31
Genes only	NA	NA	NA	NA	0.09	(-0.04-0.23)	NA	NA	NA	NA	0.09	(-0.02-0.19)	0.09	(0.01-0.17)	0.94
Rearing only	NA	NA	NA	NA	NA	NA	NA	NA	0.05	(-0.04-0.15)	-0.04	(-0.21-0.14)	0.03	(-0.05-0.12)	0.81
<i>Father-offspring</i>															
Genes + rearing	0.16	(0.15-0.17)	NA	NA	0.19	(-0.23-0.60)	NA	NA	0.15	(-0.05-0.36)	NA	NA	0.16	(0.15-0.17)	0.96
Genes only	NA	NA	0.13	(0.10-0.17)	NA	NA	NA	NA	NA	NA	-0.07	(-0.29-0.14)	0.13	(0.09-0.16)	0.06
Rearing only	NA	NA	NA	NA	NA	NA	0.07	(0.02-0.11)	NA	NA	-0.10	(-0.35-0.16)	0.06	(0.02-0.11)	0.21
PD→MD															
<i>Mother-offspring</i>															
Genes + rearing	0.10	(0.09-0.11)	0.11	(0.09-0.14)	NA	NA	0.10	(0.08-0.13)	NA	NA	NA	NA	0.10	(0.10-0.11)	0.63
Genes only	NA	NA	NA	NA	0.04	(-0.06-0.13)	NA	NA	NA	NA	0.05	(-0.03-0.12)	0.04	(-0.01-0.10)	0.88
Rearing only	NA	NA	NA	NA	NA	NA	NA	NA	0.04	(-0.03-0.11)	0.01	(-0.09-0.12)	0.03	(-0.03-0.09)	0.70
<i>Father-offspring</i>															
Genes + rearing	0.10	(0.09-0.11)	NA	NA	0.28	(0.02-0.54)	NA	NA	0.11	(-0.05-0.26)	NA	NA	0.10	(0.09-0.11)	0.49
Genes only	NA	NA	0.07	(0.05-0.10)	NA	NA	NA	NA	NA	NA	0.02	(-0.11-0.14)	0.07	(0.05-0.10)	0.37
Rearing only	NA	NA	NA	NA	NA	NA	0.06	(0.03-0.09)	NA	NA	0.04	(-0.09-0.18)	0.06	(0.03-0.09)	0.82
MD→PD															
<i>Mother-offspring</i>															
Genes + rearing	0.12	(0.12-0.13)	0.13	(0.11-0.15)	NA	NA	0.13	(0.11-0.16)	NA	NA	NA	NA	0.13	(0.12-0.13)	0.63
Genes only	NA	NA	NA	NA	0.09	(0.01-0.18)	NA	NA	NA	NA	0.05	(-0.00-0.11)	0.07	(0.02-0.11)	0.43
Rearing only	NA	NA	NA	NA	NA	NA	NA	NA	0.03	(-0.02-0.08)	0.02	(-0.04-0.07)	0.02	(-0.01-0.06)	0.69
<i>Father-offspring</i>															
Genes + rearing	0.11	(0.10-0.11)	NA	NA	0.16	(-0.08-0.41)	NA	NA	0.09	(-0.03-0.20)	NA	NA	0.11	(0.10-0.11)	0.65
Genes only	NA	NA	0.06	(0.04-0.08)	NA	NA	NA	NA	NA	NA	0.04	(-0.04-0.13)	0.06	(0.04-0.08)	0.67
Rearing only	NA	NA	NA	NA	NA	NA	0.04	(0.02-0.07)	NA	NA	0.03	(-0.05-0.10)	0.04	(0.02-0.06)	0.64
MD→MD															
<i>Mother-offspring</i>															
Genes + rearing	0.17	(0.16-0.17)	0.18	(0.17-0.20)	NA	NA	0.18	(0.17-0.20)	NA	NA	NA	NA	0.17	(0.16-0.17)	0.02
Genes only	NA	NA	NA	NA	0.12	(0.06-0.18)	NA	NA	NA	NA	0.01	(-0.03-0.05)	0.05	(0.02-0.08)	<.01
Rearing only	NA	NA	NA	NA	NA	NA	NA	NA	0.05	(0.02-0.09)	0.04	(-0.00-0.07)	0.05	(0.02-0.07)	0.50
<i>Father-offspring</i>															
Genes + rearing	0.14	(0.14-0.14)	NA	NA	0.18	(0.03-0.33)	NA	NA	0.19	(0.11-0.26)	NA	NA	0.14	(0.14-0.14)	0.11
Genes only	NA	NA	0.07	(0.05-0.08)	NA	NA	NA	NA	NA	NA	0.02	(-0.04-0.08)	0.07	(0.05-0.08)	0.16
Rearing only	NA	NA	NA	NA	NA	NA	0.08	(0.06-0.09)	NA	NA	0.03	(-0.02-0.08)	0.07	(0.06-0.09)	0.06

a) Significance threshold after Bonferroni correction for 24 tests was $P < 0.002$. Significant tests are marked with *. Het test – Heterogeneity test with nominal p value. NLW – Not-lived-with. PD - Panic Disorder; MD – Major Depression.

Table 8

Tests of Transmission from Mothers and Fathers using Weighted Estimates across all Family Types for Panic Disorder

	Mothers		Fathers		Weighted estimate		Nominal P value for test of heterogeneity ^a
PD → PD							
Genes + rearing	0.16	(0.15-0.17)	0.16	(0.15-0.17)	0.16	(0.15-0.17)	0.64
Genes only	0.09	(0.01-0.17)	0.13	(0.09-0.16)	0.12	(0.09-0.15)	0.42
Rearing only	0.03	(-0.05-0.12)	0.06	(0.02-0.11)	0.06	(0.02-0.10)	0.68
PD → MD							
Genes + rearing	0.10	(0.10-0.11)	0.10	(0.09-0.11)	0.10	(0.10-0.11)	0.11
Genes only	0.04	(-0.01-0.10)	0.07	(0.05-0.10)	0.07	(0.04-0.09)	0.42
Rearing only	0.03	(-0.03-0.09)	0.06	(0.03-0.09)	0.05	(0.03-0.08)	0.62
MD → PD							
Genes + rearing	0.13	(0.12-0.13)	0.11	(0.10-0.11)	0.12	(0.11-0.12)	<.001*
Genes only	0.07	(0.02-0.11)	0.06	(0.04-0.08)	0.06	(0.05-0.08)	0.06
Rearing only	0.02	(-0.01-0.06)	0.04	(0.02-0.06)	0.04	(0.02-0.06)	0.43
MD → MD							
Genes + rearing	0.17	(0.16-0.17)	0.14	(0.14-0.14)	0.16	(0.15-0.16)	<.001*
Genes only	0.05	(0.02-0.08)	0.07	(0.05-0.08)	0.06	(0.05-0.08)	0.27
Rearing only	0.05	(0.02-0.07)	0.07	(0.06-0.09)	0.07	(0.05-0.08)	0.08

a) Significance threshold after Bonferroni correction for 12 tests was $P < 0.004$. Significant tests are marked with *. PD - Panic Disorder; MD – Major Depression.

Table 9

Parent-offspring tetrachoric correlations and 95% CI, Weighted Estimates and Heterogeneity Tests for Four Extended Adoption Designs for Generalized Anxiety Disorder

	Intact		NLW Father		NLW Mother		Step-Father		Step-Mother		Adoptive		Weighted Estimate		Het Test ^a
GAD→GAD															
<i>Mother-offspring</i>															
Genes + rearing	0.15	(0.14-0.16)	0.18	(0.15-0.21)	NA	NA	0.14	(0.09-0.18)	NA	NA	NA	NA	0.15	(0.14-0.16)	0.28
Genes only	NA	NA	NA	NA	0.09	(-0.07-0.25)	NA	NA	NA	NA	0.14	(0.03-0.24)	0.12	(0.03-0.21)	0.63
Rearing only	NA	NA	NA	NA	NA	NA	NA	NA	0.08	(-0.02-0.19)	0.01	(-0.13-0.15)	0.06	(-0.03-0.14)	0.40
<i>Father-offspring</i>															
Genes + rearing	0.13	(0.11-0.14)	NA	NA	0.33	(-0.11-0.76)	NA	NA	0.09	(-0.24-0.42)	NA	NA	0.13	(0.11-0.14)	0.52
Genes only	NA	NA	0.09	(0.05-0.14)	NA	NA	NA	NA	NA	NA	0.11	(-0.07-0.30)	0.10	(0.05-0.14)	0.85
Rearing only	NA	NA	NA	NA	NA	NA	0.06	(0.00-0.12)	NA	NA	-0.03	(-0.30-0.24)	0.06	(-0.00-0.11)	0.52
GAD→MD															
<i>Mother-offspring</i>															
Genes + rearing	0.11	(0.11-0.12)	0.14	(0.11-0.16)	NA	NA	0.12	(0.10-0.15)	NA	NA	NA	NA	0.12	(0.11-0.12)	0.20
Genes only	NA	NA	NA	NA	0.05	(-0.04-0.15)	NA	NA	NA	NA	0.10	(0.03-0.16)	0.08	(0.03-0.14)	0.46
Rearing only	NA	NA	NA	NA	NA	NA	NA	NA	0.01	(-0.05-0.08)	0.04	(-0.04-0.12)	0.02	(-0.03-0.07)	0.66
<i>Father-offspring</i>															
Genes + rearing	0.10	(0.09-0.11)	NA	NA	0.21	(-0.10-0.53)	NA	NA	0.07	(-0.12-0.27)	NA	NA	0.10	(0.09-0.11)	0.67
Genes only	NA	NA	0.09	(0.06-0.11)	NA	NA	NA	NA	NA	NA	0.01	(-0.11-0.14)	0.08	(0.06-0.11)	0.25
Rearing only	NA	NA	NA	NA	NA	NA	0.05	(0.02-0.09)	NA	NA	0.01	(-0.14-0.15)	0.05	(0.02-0.08)	0.53
MD→GAD															
<i>Mother-offspring</i>															
Genes + rearing	0.13	(0.12-0.13)	0.14	(0.12-0.17)	NA	NA	0.11	(0.09-0.14)	NA	NA	NA	NA	0.13	(0.12-0.13)	0.42
Genes only	NA	NA	NA	NA	0.12	(0.02-0.21)	NA	NA	NA	NA	0.08	(0.01-0.14)	0.09	(0.04-0.14)	0.51
Rearing only	NA	NA	NA	NA	NA	NA	NA	NA	0.00	(-0.05-0.06)	0.01	(-0.06-0.07)	0.01	(-0.04-0.05)	0.95
<i>Father-offspring</i>															
Genes + rearing	0.11	(0.10-0.11)	NA	NA	0.11	(-0.17-0.39)	NA	NA	0.08	(-0.06-0.22)	NA	NA	0.11	(0.10-0.11)	0.82
Genes only	NA	NA	0.06	(0.04-0.09)	NA	NA	NA	NA	NA	NA	0.03	(-0.07-0.13)	0.06	(0.04-0.08)	0.57
Rearing only	NA	NA	NA	NA	NA	NA	0.03	(0.01-0.06)	NA	NA	0.07	(-0.01-0.15)	0.04	(0.01-0.07)	0.38
MD→MD															
<i>Mother-offspring</i>															
Genes + rearing	0.17	(0.16-0.17)	0.18	(0.17-0.20)	NA	NA	0.18	(0.17-0.20)	NA	NA	NA	NA	0.17	(0.16-0.17)	0.02
Genes only	NA	NA	NA	NA	0.12	(0.06-0.18)	NA	NA	NA	NA	0.01	(-0.03-0.05)	0.05	(0.02-0.08)	<.01
Rearing only	NA	NA	NA	NA	NA	NA	NA	NA	0.05	(0.02-0.09)	0.04	(-0.00-0.07)	0.05	(0.02-0.07)	0.50
<i>Father-offspring</i>															
Genes + rearing	0.14	(0.14-0.14)	NA	NA	0.18	(0.03-0.33)	NA	NA	0.19	(0.11-0.26)	NA	NA	0.14	(0.14-0.14)	0.11
Genes only	NA	NA	0.07	(0.05-0.08)	NA	NA	NA	NA	NA	NA	0.02	(-0.04-0.08)	0.07	(0.05-0.08)	0.16
Rearing only	NA	NA	NA	NA	NA	NA	0.08	(0.06-0.09)	NA	NA	0.03	(-0.02-0.08)	0.07	(0.06-0.09)	0.06

a) Significance threshold after Bonferroni correction for 24 tests was $P < 0.002$. Significant tests are marked with *. Het test – Heterogeneity test with nominal p value. NLW – Not-lived-with. GAD – Generalized Anxiety Disorder; MD – Major Depression.

Table 10

Tests of Transmission from Mothers and Fathers using Weighted Estimates across all Family Types for Generalized Anxiety Disorder

	Mothers		Fathers		Weighted estimate		Nominal P value for test of heterogeneity ^a
GAD →GAD							
Genes + rearing	0.15	(0.14-0.16)	0.13	(0.11-0.14)	0.14	(0.14-0.15)	<.01*
Genes only	0.12	(0.03-0.21)	0.10	(0.05-0.14)	0.10	(0.06-0.14)	0.60
Rearing only	0.06	(-0.03-0.14)	0.06	(-0.00-0.11)	0.06	(0.01-0.10)	0.96
GAD →MD							
Genes + rearing	0.12	(0.11-0.12)	0.10	(0.09-0.11)	0.11	(0.11-0.12)	<.001*
Genes only	0.08	(0.03-0.14)	0.08	(0.06-0.11)	0.08	(0.06-0.11)	0.97
Rearing only	0.02	(-0.03-0.07)	0.05	(0.02-0.08)	0.04	(0.01-0.07)	0.40
MD→ GAD							
Genes + rearing	0.13	(0.12-0.13)	0.11	(0.10-0.11)	0.12	(0.11-0.12)	<.001*
Genes only	0.09	(0.04-0.14)	0.06	(0.04-0.08)	0.07	(0.04-0.09)	0.35
Rearing only	0.01	(-0.04-0.05)	0.04	(0.01-0.07)	0.03	(0.01-0.05)	0.22
MD→MD							
Genes + rearing	0.17	(0.16-0.17)	0.14	(0.14-0.14)	0.16	(0.15-0.16)	<.001*
Genes only	0.05	(0.02-0.08)	0.07	(0.05-0.08)	0.06	(0.05-0.08)	0.27
Rearing only	0.05	(0.02-0.07)	0.07	(0.06-0.09)	0.07	(0.05-0.08)	0.08

a) Significance threshold after Bonferroni correction for 12 tests was $P < 0.004$. Significant tests are marked with *. GAD – Generalized Anxiety Disorder; MD – Major Depression.

Table 11

Parent-offspring tetrachoric correlations and 95% CI, Weighted Estimates and Heterogeneity Tests for Four Extended Adoption Designs for Anxiety Disorder Not Otherwise Specified

	Intact		NLW Father		NLW Mother		Step-Father		Step-Mother		Adoptive		Weighted Estimate		Het Test ^a
AD_NoS → AD_NoS															
<i>Mother-offspring</i>															
Genes + rearing	0.16	(0.15-0.16)	0.20	(0.18-0.21)	NA	NA	0.17	(0.15-0.19)	NA	NA	NA	NA	0.18	(0.15-0.20)	<.001*
Genes only	NA	NA	NA	NA	0.15	(0.09-0.21)	NA	NA	NA	NA	0.09	(0.05-0.14)	0.11	(0.08-0.15)	0.13
Rearing only	NA	NA	NA	NA	NA	NA	NA	NA	0.04	(-0.00-0.08)	0.05	(0.01-0.10)	0.05	(0.02-0.08)	0.70
<i>Father-offspring</i>															
Genes + rearing	0.14	(0.14-0.15)	NA	NA	0.07	(-0.12-0.27)	NA	NA	0.19	(0.10-0.29)	NA	NA	0.15	(0.14-0.15)	0.50
Genes only	NA	NA	0.09	(0.08-0.11)	NA	NA	NA	NA	NA	NA	0.10	(0.03-0.17)	0.10	(0.08-0.11)	0.74
Rearing only	NA	NA	NA	NA	NA	NA	0.06	(0.04-0.08)	NA	NA	0.10	(0.04-0.16)	0.07	(0.05-0.09)	0.31
AD_NoS → MD															
<i>Mother-offspring</i>															
Genes + rearing	0.13	(0.12-0.13)	0.15	(0.14-0.17)	NA	NA	0.13	(0.12-0.15)	NA	NA	NA	NA	0.13	(0.13-0.13)	<.01
Genes only	NA	NA	NA	NA	0.08	(0.02-0.14)	NA	NA	NA	NA	0.06	(0.02-0.10)	0.07	(0.04-0.10)	0.59
Rearing only	NA	NA	NA	NA	NA	NA	NA	NA	0.03	(-0.01-0.07)	0.05	(0.00-0.09)	0.04	(0.01-0.06)	0.50
<i>Father-offspring</i>															
Genes + rearing	0.11	(0.11-0.12)	NA	NA	0.08	(-0.10-0.27)	NA	NA	0.12	(0.03-0.21)	NA	NA	0.11	(0.11-0.12)	0.80
Genes only	NA	NA	0.06	(0.04-0.08)	NA	NA	NA	NA	NA	NA	0.11	(0.04-0.17)	0.06	(0.05-0.08)	0.17
Rearing only	NA	NA	NA	NA	NA	NA	0.06	(0.04-0.07)	NA	NA	0.05	(-0.00-0.11)	0.06	(0.04-0.07)	0.99
MD → AD_NoS															
<i>Mother-offspring</i>															
Genes + rearing	0.15	(0.15-0.15)	0.19	(0.17-0.20)	NA	NA	0.16	(0.15-0.18)	NA	NA	NA	NA	0.15	(0.15-0.15)	<.001*
Genes only	NA	NA	NA	NA	0.07	(0.01-0.13)	NA	NA	NA	NA	0.02	(-0.02-0.06)	0.04	(0.00-0.07)	0.17
Rearing only	NA	NA	NA	NA	NA	NA	NA	NA	0.05	(0.01-0.09)	0.02	(-0.02-0.06)	0.04	(0.01-0.06)	0.24
<i>Father-offspring</i>															
Genes + rearing	0.13	(0.13-0.13)	NA	NA	0.17	(0.01-0.33)	NA	NA	0.07	(-0.01-0.15)	NA	NA	0.13	(0.13-0.13)	0.16
Genes only	NA	NA	0.08	(0.07-0.09)	NA	NA	NA	NA	NA	NA	-0.01	(-0.07-0.06)	0.08	(0.06-0.09)	0.01
Rearing only	NA	NA	NA	NA	NA	NA	0.07	(0.05-0.08)	NA	NA	0.06	(0.01-0.11)	0.07	(0.05-0.08)	0.88
MD → MD															
<i>Mother-offspring</i>															
Genes + rearing	0.17	(0.16-0.17)	0.18	(0.17-0.20)	NA	NA	0.18	(0.17-0.20)	NA	NA	NA	NA	0.17	(0.16-0.17)	0.02
Genes only	NA	NA	NA	NA	0.12	(0.06-0.18)	NA	NA	NA	NA	0.01	(-0.03-0.05)	0.05	(0.02-0.08)	<.01
Rearing only	NA	NA	NA	NA	NA	NA	NA	NA	0.05	(0.02-0.09)	0.04	(-0.00-0.07)	0.05	(0.02-0.07)	0.50
<i>Father-offspring</i>															
Genes + rearing	0.14	(0.14-0.14)	NA	NA	0.18	(0.03-0.33)	NA	NA	0.19	(0.11-0.26)	NA	NA	0.14	(0.14-0.14)	0.11
Genes only	NA	NA	0.07	(0.05-0.08)	NA	NA	NA	NA	NA	NA	0.02	(-0.04-0.08)	0.07	(0.05-0.08)	0.16
Rearing only	NA	NA	NA	NA	NA	NA	0.08	(0.06-0.09)	NA	NA	0.03	(-0.02-0.08)	0.07	(0.06-0.09)	0.06

a) Significance threshold after Bonferroni correction for 24 tests was $P < 0.002$. Significant tests are marked with *. Het test – Heterogeneity test with nominal p value. NLW – Not-lived-with. AD_NoS - Anxiety Disorder Not Otherwise Specified; MD – Major Depression.

Table 12

Tests of Transmission from Mothers and Fathers using Weighted Estimates across all Family Types for Anxiety Disorder Not Otherwise Specified

	Mothers		Fathers		Weighted estimate		Nominal P value for test of heterogeneity ^a
AD_NoS →AD_NoS							
Genes + rearing	0.18	(0.15-0.20)	0.15	(0.14-0.15)	0.16	(0.15-0.16)	<.001*
Genes only	0.11	(0.08-0.15)	0.10	(0.08-0.11)	0.10	(0.08-0.11)	0.29
Rearing only	0.05	(0.02-0.08)	0.07	(0.05-0.09)	0.06	(0.05-0.08)	0.25
AD_NoS →MD							
Genes + rearing	0.13	(0.13-0.13)	0.11	(0.11-0.12)	0.12	(0.12-0.13)	<.001*
Genes only	0.07	(0.04-0.10)	0.06	(0.05-0.08)	0.06	(0.05-0.08)	0.66
Rearing only	0.04	(0.01-0.06)	0.06	(0.04-0.07)	0.05	(0.03-0.06)	0.26
MD →AD NoS							
Genes + rearing	0.15	(0.15-0.15)	0.13	(0.13-0.13)	0.14	(0.14-0.14)	<.001*
Genes only	0.04	(0.00-0.07)	0.08	(0.06-0.09)	0.07	(0.06-0.08)	0.04
Rearing only	0.04	(0.01-0.06)	0.07	(0.05-0.08)	0.06	(0.04-0.07)	0.08
MD →MD							
Genes + rearing	0.17	(0.16-0.17)	0.14	(0.14-0.14)	0.16	(0.15-0.16)	<.001*
Genes only	0.05	(0.02-0.08)	0.07	(0.05-0.08)	0.06	(0.05-0.08)	0.27
Rearing only	0.05	(0.02-0.07)	0.07	(0.06-0.09)	0.07	(0.05-0.08)	0.08

a) Significance threshold after Bonferroni correction for 12 tests was $P < 0.004$. Significant tests are marked with *. AD_NoS - Anxiety Disorder Not Otherwise Specified; MD – Major Depression.

Figure 1

Figure of number of diagnoses of AD and MD for the 158,386 offspring having both diagnoses

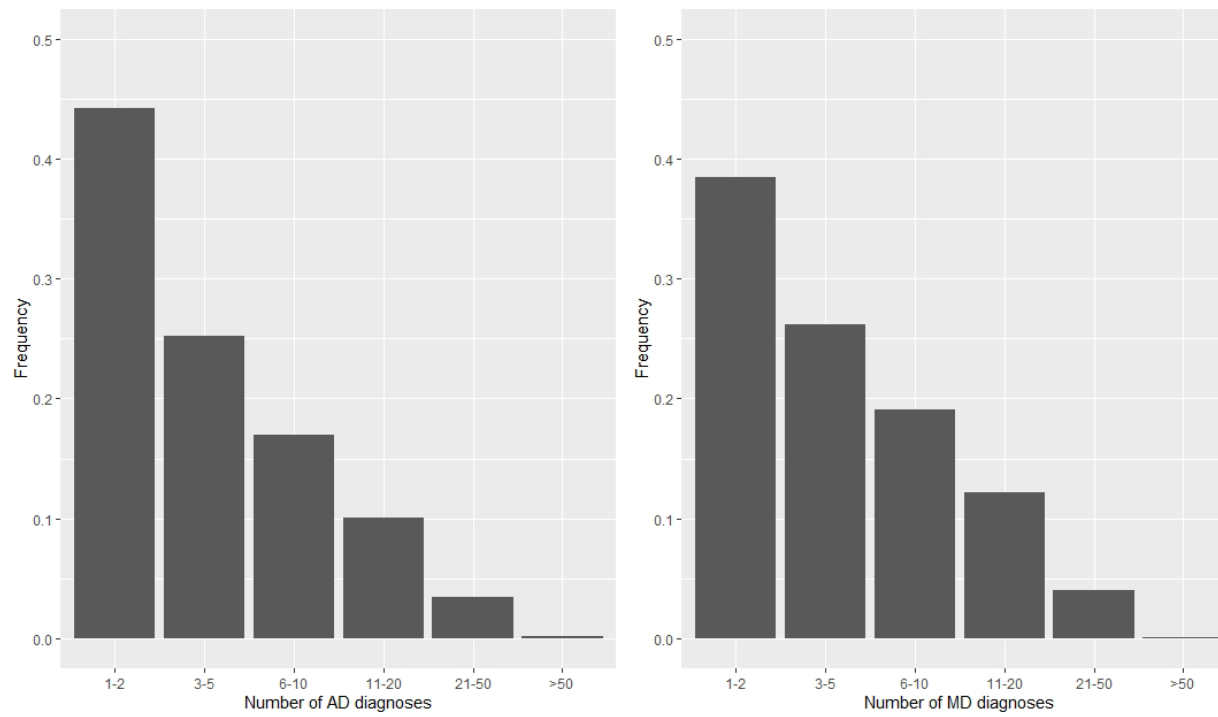


Table13

Prevalences of Anxiety disorder only (%), Major Depression only (%) and both Anxiety Disorder and Major Depression (%) in the Relatives from the Six Family Types Included in this Study

	Disorder	Intact	NLW Father	NLW Mother	Stepfather	Stepmother	Adoptive
All offspring	AD only	6.5	8.7	8.2	8.2	8.7	7.6
	MD only	7.4	10.5	10.6	10.4	11.2	10.4
	AD+MD	6.9	12.2	11.4	11.4	12.5	10.0
Female offspring	AD only	8.0	10.0	9.6	9.4	10.0	8.2
	MD only	9.3	12.6	12.4	12.8	13.7	13.1
	AD+MD	9.5	16.2	15.9	15.0	17.6	13.2
Male offspring	AD only	5.2	7.5	7.1	6.9	7.7	7.1
	MD only	5.6	8.4	9.0	8.1	9.1	8.1
	AD+MD	4.6	8.5	7.5	7.7	8.3	7.1
Biological mothers	AD only	5.5	7.8	7.4	6.9	NA	6.5
	MD only	9.9	13.8	12.3	13.0		11.9
	AD+MD	5.9	12.0	10.4	9.5		8.2
Biological fathers	AD only	3.1	4.7	4.1	NA	3.8	3.7
	MD only	6.5	9.1	8.6		7.8	8.2
	AD+MD	2.7	4.7	3.1		3.2	3.3
Stepmother or adoptive mother	AD only	NA	NA	NA	NA	5.8	5.6
	MD only					11.6	12.1
	AD+MD					6.8	5.6
Stepfather or adoptive father	AD only	NA	NA	NA	3.6	NA	2.5
	MD only				7.6		6.8
	AD+MD				3.4		1.7

Table 14

Prevalences of Anxiety disorder (%) and Major Depression (%) in the Relatives from the Six Family Types Included in this Study After Imposition of a Diagnostic Hierarchy

	Disorder	Intact	NLW Father	NLW Mother	Stepfather	Stepmother	Adoptive
All offspring	AD MD	9.8 10.8	14.7 16.4	14.1 15.9	13.6 16.0	14.9 17.2	12.4 15.3
Female offspring	AD MD	12.5 14.1	17.8 20.7	17.8 20.0	17.1 20.7	18.8 22.2	14.6 19.6
Male offspring	AD MD	7.3 7.8	11.7 12.4	11.0 12.4	10.9 12.2	11.7 13.1	10.5 11.6
Biological mothers	AD MD	8.2 12.9	13.7 19.7	13.2 16.8	11.3 17.8	NA	10.9 15.5
Biological fathers	AD MD	4.3 7.9	7.0 11.4	5.9 9.9	NA	5.5 9.3	5.4 9.8
Stepmother or adoptive mother	AD MD	NA	NA	NA	NA	9.1 14.9	8.2 15.0
Stepfather or adoptive father	AD MD	NA	NA	NA	5.1 9.4	NA	3.3 7.7

Table 15

Parent-offspring tetrachoric correlations and 95% CI, Weighted Estimates and Heterogeneity Tests for Four Extended Adoption Designs After Imposition of a Diagnostic Hierarchy

	Intact		NLW Father		NLW Mother		Step-Father		Step-Mother		Adoptive		Weighted Estimate		Het Test ^a
AD → AD															
<i>Mother-offspring</i>															
Genes + rearing	0.13	(0.13-0.14)	0.17	(0.16-0.19)	NA	NA	0.15	(0.13-0.17)	NA	NA	NA	NA	0.14	(0.13-0.14)	<.001*
Genes only	NA	NA	NA	NA	0.10	(0.04-0.17)	NA	NA	NA	NA	0.10	(0.05-0.14)	0.10	(0.06-0.14)	0.92
Rearing only	NA	NA	NA	NA	NA	NA	NA	NA	0.06	(0.01-0.10)	0.01	(-0.04-0.06)	0.04	(0.00-0.07)	0.15
<i>Father-offspring</i>															
Genes + rearing	0.12	(0.12-0.13)	NA	NA	-0.04	(-0.25-0.16)	NA	NA	0.16	(0.06-0.25)	NA	NA	0.12	(0.12-0.13)	0.18
Genes only	NA	NA	0.11	(0.09-0.13)	NA	NA	NA	NA	NA	NA	0.09	(0.02-0.16)	0.11	(0.09-0.12)	0.60
Rearing only	NA	NA	NA	NA	NA	NA	0.06	(0.03-0.08)	NA	NA	0.07	(0.01-0.14)	0.06	(0.04-0.08)	0.63
AD → MD															
<i>Mother-offspring</i>															
Genes + rearing	0.07	(0.06-0.07)	0.04	(0.03-0.06)	NA	NA	0.05	(0.03-0.07)	NA	NA	NA	NA	0.07	(0.06-0.07)	<.01
Genes only	NA	NA	NA	NA	0.04	(-0.02-0.11)	NA	NA	NA	NA	0.05	(0.01-0.09)	0.05	(0.01-0.08)	0.85
Rearing only	NA	NA	NA	NA	NA	NA	NA	NA	0.00	(-0.04-0.05)	0.04	(-0.00-0.09)	0.02	(-0.01-0.05)	0.21
<i>Father-offspring</i>															
Genes + rearing	0.07	(0.06-0.07)	NA	NA	0.06	(-0.13-0.25)	NA	NA	0.06	(-0.04-0.16)	NA	NA	0.07	(0.06-0.07)	0.99
Genes only	NA	NA	0.03	(0.02-0.05)	NA	NA	NA	NA	NA	NA	0.04	(-0.03-0.11)	0.03	(0.02-0.05)	0.81
Rearing only	NA	NA	NA	NA	NA	NA	0.02	(0.00-0.04)	NA	NA	0.07	(0.01-0.14)	0.03	(0.01-0.05)	0.13
MD → AD															
<i>Mother-offspring</i>															
Genes + rearing	0.09	(0.09-0.09)	0.09	(0.07-0.10)	NA	NA	0.08	(0.06-0.10)	NA	NA	NA	NA	0.09	(0.09-0.09)	0.61
Genes only	NA	NA	NA	NA	0.00	(-0.06-0.06)	NA	NA	NA	NA	0.03	(-0.02-0.07)	0.02	(-0.02-0.05)	0.53
Rearing only	NA	NA	NA	NA	NA	NA	NA	NA	0.04	(0.00-0.08)	0.02	(-0.02-0.06)	0.03	(0.00-0.06)	0.51
<i>Father-offspring</i>															
Genes + rearing	0.08	(0.08-0.09)	NA	NA	0.16	(0.00-0.32)	NA	NA	0.01	(-0.08-0.10)	NA	NA	0.08	(0.08-0.09)	0.18
Genes only	NA	NA	0.04	(0.03-0.06)	NA	NA	NA	NA	NA	NA	-0.02	(-0.08-0.04)	0.04	(0.02-0.05)	0.06
Rearing only	NA	NA	NA	NA	NA	NA	0.03	(0.01-0.05)	NA	NA	0.03	(-0.02-0.08)	0.03	(0.01-0.05)	0.99
MD → MD															
<i>Mother-offspring</i>															
Genes + rearing	0.13	(0.13-0.14)	0.13	(0.11-0.14)	NA	NA	0.14	(0.13-0.16)	NA	NA	NA	NA	0.13	(0.13-0.14)	0.27
Genes only	NA	NA	NA	NA	0.12	(0.06-0.18)	NA	NA	NA	NA	0.01	(-0.03-0.05)	0.05	(0.01-0.08)	<.01
Rearing only	NA	NA	NA	NA	NA	NA	NA	NA	0.02	(-0.02-0.05)	0.00	(-0.04-0.04)	0.01	(-0.02-0.04)	0.64
<i>Father-offspring</i>															
Genes + rearing	0.11	(0.11-0.12)	NA	NA	0.06	(-0.10-0.23)	NA	NA	0.19	(0.11-0.27)	NA	NA	0.11	(0.11-0.12)	0.15
Genes only	NA	NA	0.06	(0.05-0.08)	NA	NA	NA	NA	NA	NA	0.07	(0.01-0.12)	0.06	(0.05-0.08)	0.86
Rearing only	NA	NA	NA	NA	NA	NA	0.06	(0.04-0.07)	NA	NA	0.01	(-0.04-0.06)	0.05	(0.04-0.07)	0.09

a) Significance threshold after Bonferroni correction for 24 tests was $P < 0.002$. Significant tests are marked with *. Het test – Heterogeneity test with nominal p value. NLW – Not-lived-with. AD- Anxiety Disorder; MD – Major Depression.

Table 16

Tests of Transmission from Mothers and Fathers using Weighted Estimates across all Family Types After Imposition of a Diagnostic Hierarchy

	Mothers		Fathers		Weighted estimate		Nominal P value for test of heterogeneity ^a
AD→AD							
Genes + rearing	0.14	(0.13-0.14)	0.12	(0.12-0.13)	0.13	(0.13-0.13)	<.001*
Genes only	0.10	(0.06-0.14)	0.11	(0.09-0.12)	0.11	(0.09-0.12)	0.66
Rearing only	0.04	(0.00-0.07)	0.06	(0.04-0.08)	0.05	(0.03-0.07)	0.31
AD→MD							
Genes + rearing	0.07	(0.06-0.07)	0.07	(0.06-0.07)	0.07	(0.06-0.07)	0.33
Genes only	0.05	(0.01-0.08)	0.03	(0.02-0.05)	0.04	(0.02-0.05)	0.49
Rearing only	0.02	(-0.01-0.05)	0.03	(0.01-0.05)	0.03	(0.01-0.04)	0.72
MD→AD							
Genes + rearing	0.09	(0.09-0.09)	0.08	(0.08-0.09)	0.09	(0.08-0.09)	<.001*
Genes only	0.02	(-0.02-0.05)	0.04	(0.02-0.05)	0.04	(0.02-0.05)	0.29
Rearing only	0.03	(0.00-0.06)	0.03	(0.01-0.05)	0.03	(0.02-0.05)	0.92
MD→MD							
Genes + rearing	0.13	(0.13-0.14)	0.11	(0.11-0.12)	0.13	(0.12-0.13)	<.001*
Genes only	0.05	(0.01-0.08)	0.06	(0.05-0.08)	0.06	(0.05-0.07)	0.43
Rearing only	0.01	(-0.02-0.04)	0.05	(0.04-0.07)	0.04	(0.03-0.05)	0.01

a) Significance threshold after Bonferroni correction for 12 tests was $P < 0.004$. Significant tests are marked with *. AD- Anxiety Disorder; MD – Major Depression.

Table 17

Sample Size, Birth Year, Age and Sex Distributions Across the Six Family Types Included in the Study Including offspring born 1960-1975 (for the adoptive sample, offspring born 1955-1970).

	Intact	NLW Father	NLW Mother	Stepfather	Stepmother	Adoptive
Sample size offspring	1006921	65777	4348	51726	9066	11197
Sample size biological mother	1006921	44402	4348	35714	NA	10700
Sample size biological father	1006921	65777	815	NA	2255	6443
Offspring						
Year of birth, mean (sd)	1967.5 (4.5)	1967.7 (4.3)	1966.2 (4.2)	1967.6 (4.3)	1966.9 (4.5)	1961.4 (4.2)
Age, mean (sd)	49.0 (7.0)	48.7 (7.0)	49.9 (7.4)	48.8 (6.9)	49.0 (7.6)	54.7 (7.7)
Male, %	53.1	50.9	54.7	50.5	55.0	53.1

Table 18

Prevalences of Anxiety disorder (%) and Major Depression (%) in the Relatives from the Six Family Types Included in this Study Including offspring born 1960-1975 (for the adoptive sample, offspring born 1955-1970).

	Disorder	Intact	NLW Father	NLW Mother	Stepfather	Stepmother	Adoptive
All offspring	AD MD	11.4 13.7	17.9 21.0	18.2 21.2	17.0 20.3	18.8 22.3	16.8 20.0
Female offspring	AD MD	14.7 18.0	22.5 27.0	23.8 27.8	21.6 26.2	24.4 29.5	20.4 25.7
Male offspring	AD MD	8.5 9.9	13.4 15.1	13.5 15.8	12.6 14.5	14.3 16.4	13.6 15.0
Biological mothers	AD MD	11.3 15.9	16.2 22.2	17.9 23.3	14.6 20.3	NA	13.9 19.4
Biological fathers	AD MD	5.5 9.5	7.7 12.7	5.6 11.0	NA	6.0 9.9	6.4 11.1
Stepmother or adoptive mother	AD MD	NA	NA	NA	NA	11.8 17.1	11.0 17.8
Stepfather or adoptive father	AD MD	NA	NA	NA	6.2 10.5	NA	3.9 8.5

Table 19

Parent-offspring tetrachoric correlations and 95% CI, Weighted Estimates and Heterogeneity Tests for Four Extended Adoption Designs - Including offspring born 1960-1975 (for the adoptive sample, offspring born 1955-1970).

	Intact		NLW Father		NLW Mother		Step-Father		Step-Mother		Adoptive		Weighted Estimate		Het Test ^a
AD → AD															
<i>Mother-offspring</i>															
Genes + rearing	0.15	(0.15-0.16)	0.18	(0.16-0.20)	NA	NA	0.17	(0.14-0.19)	NA	NA	NA	NA	0.15	(0.15-0.16)	0.09
Genes only	NA	NA	NA	NA	0.15	(0.09-0.21)	NA	NA	NA	NA	0.10	(0.06-0.14)	0.12	(0.08-0.15)	0.19
Rearing only	NA	NA	NA	NA	NA	NA	NA	NA	0.03	(-0.01-0.08)	0.02	(-0.02-0.07)	0.03	(-0.00-0.06)	0.79
<i>Father-offspring</i>															
Genes + rearing	0.13	(0.13-0.14)	NA	NA	0.04	(-0.18-0.25)	NA	NA	0.12	(-0.00-0.25)	NA	NA	0.13	(0.13-0.14)	0.98
Genes only	NA	NA	0.10	(0.08-0.12)	NA	NA	NA	NA	NA	NA	0.07	(-0.00-0.14)	0.10	(0.08-0.11)	0.41
Rearing only	NA	NA	NA	NA	NA	NA	0.07	(0.04-0.09)	NA	NA	0.08	(0.02-0.14)	0.07	(0.05-0.09)	0.82
AD → MD															
<i>Mother-offspring</i>															
Genes + rearing	0.12	(0.11-0.12)	0.14	(0.12-0.15)	NA	NA	0.12	(0.10-0.14)	NA	NA	NA	NA	0.12	(0.11-0.12)	0.17
Genes only	NA	NA	NA	NA	0.12	(0.06-0.18)	NA	NA	NA	NA	0.07	(0.03-0.11)	0.08	(0.05-0.12)	0.15
Rearing only	NA	NA	NA	NA	NA	NA	NA	NA	0.05	(0.00-0.10)	0.05	(0.01-0.09)	0.05	(0.02-0.08)	0.99
<i>Father-offspring</i>															
Genes + rearing	0.11	(0.10-0.11)	NA	NA	0.08	(-0.13-0.28)	NA	NA	0.09	(-0.03-0.21)	NA	NA	0.11	(0.10-0.11)	0.95
Genes only	NA	NA	0.06	(0.04-0.08)	NA	NA	NA	NA	NA	NA	0.10	(0.04-0.17)	0.07	(0.05-0.08)	0.28
Rearing only	NA	NA	NA	NA	NA	NA	0.05	(0.03-0.08)	NA	NA	0.04	(-0.02-0.10)	0.05	(0.03-0.07)	0.71
MD → AD															
<i>Mother-offspring</i>															
Genes + rearing	0.13	(0.13-0.13)	0.15	(0.13-0.17)	NA	NA	0.14	(0.12-0.16)	NA	NA	NA	NA	0.13	(0.13-0.14)	0.21
Genes only	NA	NA	NA	NA	0.06	(0.00-0.12)	NA	NA	NA	NA	0.05	(0.01-0.09)	0.05	(0.02-0.09)	0.77
Rearing only	NA	NA	NA	NA	NA	NA	NA	NA	0.03	(-0.01-0.08)	0.01	(-0.03-0.05)	0.02	(-0.01-0.05)	0.44
<i>Father-offspring</i>															
Genes + rearing	0.11	(0.11-0.12)	NA	NA	0.20	(0.04-0.37)	NA	NA	0.09	(0.02-0.20)	NA	NA	0.11	(0.11-0.12)	0.51
Genes only	NA	NA	0.07	(0.05-0.08)	NA	NA	NA	NA	NA	NA	0.01	(-0.05-0.07)	0.06	(0.05-0.08)	0.08
Rearing only	NA	NA	NA	NA	NA	NA	0.05	(0.03-0.07)	NA	NA	0.05	(0.01-0.10)	0.05	(0.03-0.07)	0.93
MD → MD															
<i>Mother-offspring</i>															
Genes + rearing	0.15	(0.14-0.15)	0.16	(0.14-0.18)	NA	NA	0.16	(0.14-0.18)	NA	NA	NA	NA	0.15	(0.14-0.15)	0.28
Genes only	NA	NA	NA	NA	0.12	(0.06-0.18)	NA	NA	NA	NA	0.03	(-0.01-0.07)	0.06	(0.03-0.09)	0.01
Rearing only	NA	NA	NA	NA	NA	NA	NA	NA	0.03	(-0.01-0.07)	0.04	(-0.00-0.08)	0.03	(0.01-0.06)	0.78
<i>Father-offspring</i>															
Genes + rearing	0.12	(0.12-0.13)	NA	NA	0.22	(0.06-0.37)	NA	NA	0.24	(0.15-0.34)	NA	NA	0.12	(0.12-0.13)	0.03
Genes only	NA	NA	0.08	(0.06-0.09)	NA	NA	NA	NA	NA	NA	0.05	(-0.01-0.10)	0.08	(0.06-0.09)	0.31
Rearing only	NA	NA	NA	NA	NA	NA	0.06	(0.04-0.09)	NA	NA	0.03	(-0.02-0.08)	0.06	(0.04-0.08)	0.19

a) Significance threshold after Bonferroni correction for 24 tests was $P < 0.002$. Significant tests are marked with *. Het test – Heterogeneity test with nominal p value. NLW – Not-lived-with. AD- Anxiety Disorder; MD – Major Depression.

Table 20

Tests of Transmission from Mothers and Fathers using Weighted Estimates across all Family Types Including offspring born 1960-1975 (for the adoptive sample, offspring born 1955-1970).

	Mothers		Fathers		Weighted estimate		Nominal P value for test of heterogeneity ^a
AD→AD							
Genes + rearing	0.15	(0.15-0.16)	0.13	(0.13-0.14)	0.15	(0.14-0.15)	<.001*
Genes only	0.12	(0.08-0.15)	0.10	(0.08-0.11)	0.10	(0.08-0.12)	0.24
Rearing only	0.03	(-0.00-0.06)	0.07	(0.05-0.09)	0.06	(0.04-0.08)	0.05
AD→MD							
Genes + rearing	0.12	(0.11-0.12)	0.11	(0.10-0.11)	0.11	(0.11-0.12)	<.001*
Genes only	0.08	(0.05-0.12)	0.07	(0.05-0.08)	0.07	(0.05-0.09)	0.31
Rearing only	0.05	(0.02-0.08)	0.05	(0.03-0.07)	0.05	(0.03-0.07)	0.95
MD→AD							
Genes + rearing	0.13	(0.13-0.14)	0.11	(0.11-0.12)	0.12	(0.12-0.13)	<.001*
Genes only	0.05	(0.02-0.09)	0.06	(0.05-0.08)	0.06	(0.05-0.08)	0.70
Rearing only	0.02	(-0.01-0.05)	0.05	(0.03-0.07)	0.04	(0.03-0.06)	0.09
MD→MD							
Genes + rearing	0.15	(0.14-0.15)	0.12	(0.12-0.13)	0.14	(0.13-0.14)	<.001*
Genes only	0.06	(0.03-0.09)	0.08	(0.06-0.09)	0.07	(0.06-0.09)	0.49
Rearing only	0.03	(0.01-0.06)	0.06	(0.04-0.08)	0.05	(0.04-0.07)	0.13

a) Significance threshold after Bonferroni correction for 12 tests was $P < 0.004$. Significant tests are marked with *. AD- Anxiety Disorder; MD – Major Depression.

Figure 2

Parent-Offspring Resemblance for MD and AD in the Older Half of our Cohort - Offspring born 1960-1975 (for the adoptive sample, offspring born 1955-1970)

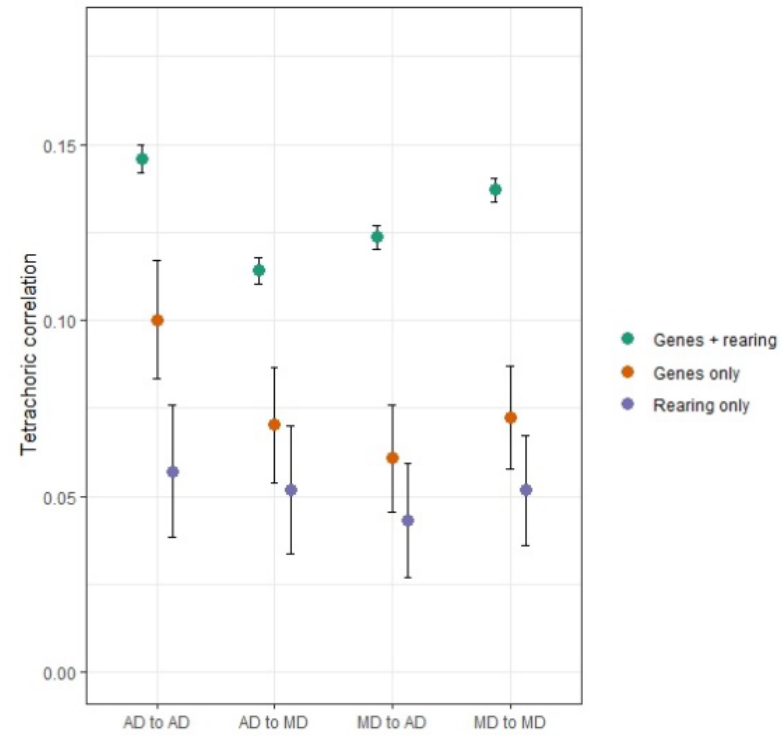


Table 21

Sample Size, Birth Year, Age and Sex Distributions Across the Six Family Types Included in the Study Including offspring born 1976-1992 (for the adoptive sample, offspring born 1971-1992)

	Intact	NLW Father	NLW Mother	Stepfather	Stepmother	Adoptive
Sample size offspring	961431	38466	796	35747	4962	1830
Sample size biological mother	961431	33048	796	29744	NA	1789
Sample size biological father	961431	38466	211	NA	1787	1219
Offspring						
Year of birth, mean (sd)	1984.1 (5.0)	1984.9 (5.0)	1984.2 (5.0)	1982.2 (4.6)	1981.9 (4.7)	1977.8 (6.1)
Age, mean (sd)	33.3 (5.3)	32.5 (5.3)	32.8 (5.8)	35.0 (5.3)	35.3 (5.3)	39.3 (6.8)
Male, %	51.8	51.4	52.9	49.7	55.1	53.7

Table 22

Prevalences of Anxiety disorder (%) and Major Depression (%) in the Relatives from the Six Family Types Included in this Study Including offspring born 1976-1992 (for the adoptive sample, offspring born 1971-1992)

	Disorder	Intact	NLW Father	NLW Mother	Stepfather	Stepmother	Adoptive
All offspring	AD MD	15.6 15.0	26.3 25.7	27.4 26.0	23.1 23.9	25.7 26.2	22.3 23.0
Female offspring	AD MD	20.5 19.7	32.6 31.9	34.4 31.7	28.6 30.0	33.6 34.7	27.7 30.5
Male offspring	AD MD	11.2 10.5	20.5 19.9	21.1 20.9	17.6 17.8	19.2 19.3	17.6 16.5
Biological mothers	AD MD	11.5 15.7	24.6 30.7	17.2 19.2	18.4 25.2	NA	19.6 24.1
Biological fathers	AD MD	6.2 8.9	12.4 15.7	13.3 14.2	NA	8.2 12.5	10.0 14.1
Stepmother or adoptive mother	AD MD	NA	NA	NA	NA	14.1 20.7	12.7 17.4
Stepfather or adoptive father	AD MD	NA	NA	NA	8.1 11.8	NA	6.2 8.6

Table 23

Parent-offspring tetrachoric correlations and 95% CI, Weighted Estimates and Heterogeneity Tests for Four Extended Adoption Designs Included in the Study Including offspring born 1976-1992 (for the adoptive sample, offspring born 1971-1992)

	Intact		NLW Father		NLW Mother		Step-Father		Step-Mother		Adoptive		Weighted Estimate		Het Test ^a
AD → AD															
<i>Mother-offspring</i>															
Genes + rearing	0.18	(0.17-0.18)	0.20	(0.18-0.22)	NA	NA	0.18	(0.16-0.20)	NA	NA	NA	NA	0.18	(0.17-0.18)	0.10
Genes only	NA	NA	NA	NA	0.19	(0.06-0.32)	NA	NA	NA	NA	0.18	(0.09-0.26)	0.18	(0.11-0.25)	0.87
Rearing only	NA	NA	NA	NA	NA	NA	NA	NA	0.03	(-0.03-0.08)	0.08	(-0.02-0.18)	0.04	(-0.01-0.09)	0.37
<i>Father-offspring</i>															
Genes + rearing	0.16	(0.15-0.16)	NA	NA	0.04	(-0.26-0.33)	NA	NA	0.24	(0.13-0.35)	NA	NA	0.16	(0.15-0.16)	0.27
Genes only	NA	NA	0.10	(0.08-0.12)	NA	NA	NA	NA	NA	NA	0.10	(-0.03-0.23)	0.10	(0.08-0.12)	0.94
Rearing only	NA	NA	NA	NA	NA	NA	0.04	(0.02-0.07)	NA	NA	-0.00	(-0.13-0.12)	0.04	(0.02-0.07)	0.47
AD → MD															
<i>Mother-offspring</i>															
Genes + rearing	0.15	(0.14-0.15)	0.15	(0.13-0.17)	NA	NA	0.14	(0.12-0.17)	NA	NA	NA	NA	0.15	(0.14-0.15)	0.90
Genes only	NA	NA	NA	NA	0.12	(-0.01-0.26)	NA	NA	NA	NA	0.07	(-0.02-0.16)	0.09	(0.01-0.16)	0.53
Rearing only	NA	NA	NA	NA	NA	NA	NA	NA	-0.03	(-0.09-0.03)	0.01	(-0.10-0.11)	-0.02	(-0.07-0.03)	0.55
<i>Father-offspring</i>															
Genes + rearing	0.13	(0.12-0.13)	NA	NA	0.06	(-0.24-0.35)	NA	NA	0.15	(0.04-0.26)	NA	NA	0.13	(0.12-0.13)	0.92
Genes only	NA	NA	0.08	(0.05-0.10)	NA	NA	NA	NA	NA	NA	-0.04	(-0.18-0.09)	0.07	(0.05-0.09)	0.08
Rearing only	NA	NA	NA	NA	NA	NA	0.04	(0.01-0.07)	NA	NA	0.04	(-0.08-0.17)	0.04	(0.02-0.07)	0.95
MD → AD															
<i>Mother-offspring</i>															
Genes + rearing	0.17	(0.16-0.17)	0.17	(0.15-0.19)	NA	NA	0.17	(0.15-0.19)	NA	NA	NA	NA	0.17	(0.17-0.17)	0.93
Genes only	NA	NA	NA	NA	0.17	(0.04-0.30)	NA	NA	NA	NA	0.10	(0.01-0.19)	0.12	(0.05-0.20)	0.37
Rearing only	NA	NA	NA	NA	NA	NA	NA	NA	0.04	(-0.02-0.09)	0.00	(-0.09-0.10)	0.03	(-0.02-0.07)	0.51
<i>Father-offspring</i>															
Genes + rearing	0.15	(0.14-0.15)	NA	NA	0.00	(-0.29-0.29)	NA	NA	0.06	(-0.05-0.16)	NA	NA	0.15	(0.14-0.15)	0.23
Genes only	NA	NA	0.09	(0.07-0.11)	NA	NA	NA	NA	NA	NA	0.06	(-0.06-0.18)	0.09	(0.07-0.11)	0.61
Rearing only	NA	NA	NA	NA	NA	NA	0.06	(0.04-0.08)	NA	NA	-0.04	(-0.15-0.08)	0.06	(0.03-0.08)	0.11
MD → MD															
<i>Mother-offspring</i>															
Genes + rearing	0.19	(0.19-0.19)	0.19	(0.17-0.21)	NA	NA	0.19	(0.17-0.21)	NA	NA	NA	NA	0.19	(0.19-0.19)	0.99
Genes only	NA	NA	NA	NA	0.25	(0.13-0.38)	NA	NA	NA	NA	0.07	(-0.02-0.16)	0.13	(0.06-0.20)	0.02
Rearing only	NA	NA	NA	NA	NA	NA	NA	NA	0.04	(-0.01-0.09)	0.04	(-0.05-0.13)	0.04	(-0.01-0.09)	0.96
<i>Father-offspring</i>															
Genes + rearing	0.16	(0.15-0.16)	NA	NA	0.02	(-0.27-0.31)	NA	NA	0.14	(0.04-0.24)	NA	NA	0.16	(0.15-0.16)	0.79
Genes only	NA	NA	0.08	(0.06-0.10)	NA	NA	NA	NA	NA	NA	0.08	(-0.04-0.20)	0.08	(0.06-0.10)	0.98
Rearing only	NA	NA	NA	NA	NA	NA	0.08	(0.05-0.10)	NA	NA	-0.02	(-0.14-0.09)	0.07	(0.05-0.08)	0.09

a) Significance threshold after Bonferroni correction for 24 tests was $P < 0.002$. Significant tests are marked with *. Het test – Heterogeneity test with nominal p value. NLW – Not-lived-with. AD- Anxiety Disorder; MD – Major Depression.

Table 24

Tests of Transmission from Mothers and Fathers using Weighted Estimates across all Family Types Included in the Study Including offspring born 1976-1992
(for the adoptive sample, offspring born 1971-1992)

	Mothers		Fathers		Weighted estimate		Nominal P value for test of heterogeneity ^a
AD→AD							
Genes + rearing	0.18	(0.17-0.18)	0.16	(0.15-0.16)	0.17	(0.17-0.17)	<.001*
Genes only	0.18	(0.11-0.25)	0.10	(0.08-0.12)	0.11	(0.09-0.13)	0.05
Rearing only	0.04	(-0.01-0.09)	0.04	(0.02-0.07)	0.04	(0.02-0.06)	0.93
AD→MD							
Genes + rearing	0.15	(0.14-0.15)	0.13	(0.12-0.13)	0.14	(0.14-0.14)	<.001*
Genes only	0.09	(0.01-0.16)	0.07	(0.05-0.09)	0.07	(0.05-0.09)	0.78
Rearing only	-0.02	(-0.07-0.03)	0.04	(0.02-0.07)	0.03	(0.01-0.05)	0.04
MD→AD							
Genes + rearing	0.17	(0.17-0.17)	0.15	(0.14-0.15)	0.16	(0.16-0.16)	<.001*
Genes only	0.12	(0.05-0.20)	0.09	(0.07-0.11)	0.09	(0.07-0.11)	0.46
Rearing only	0.03	(-0.02-0.07)	0.06	(0.03-0.08)	0.05	(0.03-0.07)	0.33
MD→MD							
Genes + rearing	0.19	(0.19-0.19)	0.16	(0.15-0.16)	0.18	(0.17-0.18)	<.001*
Genes only	0.13	(0.06-0.20)	0.08	(0.06-0.10)	0.08	(0.06-0.10)	0.24
Rearing only	0.04	(-0.01-0.09)	0.07	(0.05-0.10)	0.07	(0.05-0.09)	0.23

a) Significance threshold after Bonferroni correction for 12 tests was $P < 0.004$. Significant tests are marked with *. AD- Anxiety Disorder; MD – Major Depression.

Figure 3

Parent-Offspring Resemblance for MD and AD in the Younger Half of our Cohort - Offspring born 1971-1992

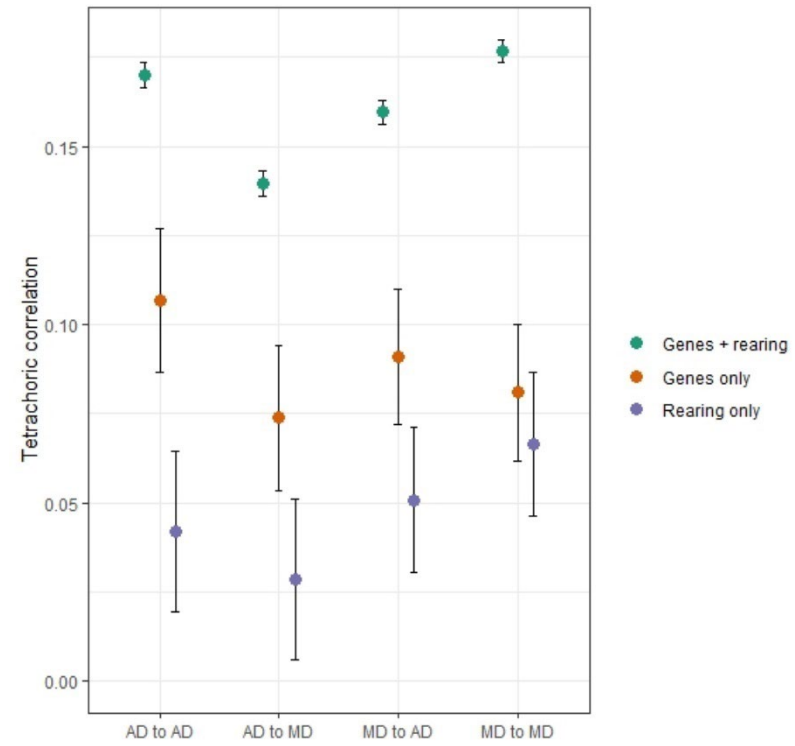


Table 25

Weighted Estimates across all Family Types and Tests of Transmission from Old and Young Cohort

	Weighted estimate older cohort		Weighted estimate younger cohort		Nominal P value for test of heterogeneity ^a
AD→AD					
Genes + rearing	0.15	(0.14-0.15)	0.17	(0.17-0.17)	<.001*
Genes only	0.10	(0.08-0.12)	0.11	(0.09-0.13)	0.60
Rearing only	0.06	(0.04-0.08)	0.04	(0.02-0.06)	0.38
AD→MD					
Genes + rearing	0.11	(0.11-0.12)	0.14	(0.14-0.14)	<.001*
Genes only	0.07	(0.05-0.09)	0.07	(0.05-0.09)	0.76
Rearing only	0.05	(0.03-0.07)	0.03	(0.01-0.05)	0.11
MD→AD					
Genes + rearing	0.12	(0.12-0.13)	0.16	(0.16-0.16)	<.001*
Genes only	0.06	(0.05-0.08)	0.09	(0.07-0.11)	0.02
Rearing only	0.04	(0.03-0.06)	0.05	(0.03-0.07)	0.47
MD→MD					
Genes + rearing	0.14	(0.13-0.14)	0.18	(0.17-0.18)	<.001*
Genes only	0.07	(0.06-0.09)	0.08	(0.06-0.10)	0.49
Rearing only	0.05	(0.04-0.07)	0.07	(0.05-0.09)	0.07

a) Significance threshold after Bonferroni correction for 12 tests was $P < 0.004$. Significant tests are marked with *. AD – Anxiety Disorder; MD – Major Depression.