Rai et al. **Parental depression, maternal antidepressant use during pregnancy, and the risk of autism spectrum disorders: population based case-control study**

SUPPLEMENTARY TABLES

Table S1. International classification of diseases diagnostic codes used to identify a history of depression and other psychiatric disorders in parents before the birth of the index child.

Diagnosis group	ICD10 (1997-)	Nordic version of ICD9 (1987-1996)	Nordic version of ICD8 (1969-1986)
Alcohol/drugs misuse	F10-F19	291A-292X, 303A-305X	291.00-291.99, 294.30, 303.00-304.99
Schizophrenia	F20-29	295,297,298 [C-Z]	295,297,29820-29899, 29999
Bipolar disorder	F30-31	296 [A,C,D,E]	2961, 2963
Depression	F32-39	300E, 298A, 296B, 311	2962, 3004
Anxiety disorders	F40-43	300[A,C,D], 308, 309	300 [0,2,3]
Somatoform disorders	F44-48	300 [B,F,G,H]; 306, 307W	300 [1,5,6,7]; 305
Personality disorder	F60-F69	301	301
Neurodevelopment disorder	F70-F82, F84, F889, F90, F95, F98 [5,6]	299, 307 [A,C], 314-315, 317-319	306 [0,1,2,3], 308, 310-315

Table S2 Individual antidepressant drugs according to the Anatomical Therapeutic Chemical Classification system by the World Health Organization.	
ATC category N06AB: Selective Serotonin Reuptake Inhibitors	*ATC category N06AA:* Non-selective monoamine reuptake inhibitors
Fluoxetine Citalopram Paroxetine Sertraline	Clomipramine Amitryptiline Nortryptiline
Note: the list includes the drugs used in the sample	

Table S3 Parental History of Depression before birth of child and risk of offspring ASD in children BORN BEFORE 1990					
	N cases/ controls	Crude OR	Model 1	Model 2	Model 3
Mothers					
ASD	14/46	3.03 (1.64-5.59)	2.56 (1.36-4.79)	2.66 (1.42-4.99)	2.61 (1.39-4.91)
ASD+ID	3/16	2.02 (0.57-7.09)	1.80 (0.49-6.58)	1.97 (0.54-7.19)	1.88 (0.51-6.88)
ASD-ID	11/30	3.52 (1.74-7.13)	2.63 (1.27-5.47)	2.68 (1.29-5.56)	2.65 (1.27-5.51)
Fathers					
ASD	2/24	0.75 (0.18-3.17)	0.78 (0.18-3.34)	0.78 (0.18-3.37)	0.79 (0.18-3.40)
ASD+ID	2/7	2.67 (0.54-13.27)	2.43 (0.47-12.53)	2.44 (0.47-12.60)	2.47 (0.48-12.82)
ASD-ID	0/17	-	-	-	-
Numbers in study: ASD cases n=1113, controls n=10599; ASD+ID cases n=442, controls n=4319; ASD-ID cases n=671, controls n=6280 Model 1 adjusted for parental ages, income, education, occupation, migration status, parity Model 2= model 1+ any other psychiatric condition (including psychosis, bipolar, neurodevelopmental, personality or drug and alcohol misuse disorders) Model 3= model 2+ both parents depression, both parents other psych condition					

Table S4 Parental History of Depression before birth of child and risk of offspring ASD- PRIMIPARAS					
	N cases/ controls	Crude OR	Model 1	Model 2	Model 3
Mothers					
ASD	25/109	2.20 (1.32-3.68)	1.97 (1.17-3.30)	2.01 (1.20-3.38)	1.92 (1.14-3.24)
ASD+ID	5/40	1.41 (0.50-4.02)	1.47 (0.49-4.36)	1.51 (0.51-4.51)	1.36 (0.44-4.19)
ASD-ID	20/69	2.59 (1.43-4.69)	2.15 (1.17-3.94)	2.19 (1.19-4.01)	2.18 (1.19-4.02)
Fathers					
ASD	6/72	0.81 (0.34-1.97)	0.68 (0.28-1.65)	0.70 (0.29-1.70)	0.70 (0.29-1.70)
ASD+ID	3/31	1.45 (0.38-5.57)	1.02 (0.26-3.98)	1.03 (0.26-4.01)	1.05 (0.27-4.12)
ASD-ID	3/41	0.57 (0.17-1.91)	0.49 (0.14-1.67)	0.50 (0.15-1.70)	0.50 (0.15-1.70)

Numbers in study: ASD cases n=2104, controls n=19163;
ASD+ID cases n=773, controls n=8139;
ASD-ID cases n=1331, controls n=11024

Model 1 adjusted for parental ages, income, education, occupation, migration status, parity

Model 2= model 1+ any other psychiatric condition (including psychosis, bipolar, neurodevelopmental, personality or drug and alcohol misuse disorders)

Model 3= model 2+ both parents depression, both parents other psych condition

DEPRESSION	N cases/ controls	Crude OR	Model 1	Model 2	Model 3
Table S5 Parental History of Depression before birth of child and risk of offspring ASD- IN SWEDISH PARENTS ONLY					
Mothers					
ASD	39/223	1.82 (1.27-2.60)	1.67 (1.16-2.39)	1.71 (1.19-2.46)	1.66 (1.15-2.39)
ASD+ID	12/99	1.48 (0.79-2.80)	1.33 (0.70-2.53)	1.37 (0.72-2.60)	1.32 (0.69-2.53)
ASD-ID	27/124	2.02 (1.31-3.11)	1.82 (1.17-2.83)	1.87 (1.20-2.90)	1.83 (1.18-2.85)
Fathers					
ASD	14/106	1.44 (0.81-2.56)	1.27 (0.71-2.27)	1.30 (0.72-2.32)	1.32 (0.74-2.37)
ASD+ID	7/44	2.18 (0.93-5.11)	1.92 (0.81-4.56)	1.97 (0.83-4.68)	2.01 (0.85-4.78)
ASD-ID	7/62	1.07 (0.48-2.38)	0.95 (0.42-2.12)	0.97 (0.43-2.17)	0.98 (0.44-2.19)

Numbers in study: ASD cases n=3434, controls n=33939;
ASD+ID cases n=1286, controls n=14400;
ASD-ID cases n=2148, controls n=19539

Model 1 adjusted for parental ages, income, education, occupation, migration status, parity

Model 2= model 1+ any other psychiatric condition (including psychosis, bipolar, neurodevelopmental, personality or drug and alcohol misuse disorders)

Model 3= model 2+ both parents depression, both parents other psych condition

Table S6 Parental History of Depression before birth of child and risk of offspring ASD using a non-hierarchical coding of psychiatric disorders (multiple diagnoses in each parent were allowed)					
Relationship with prenatal Depression	N cases/ controls	Crude OR	Model 1	Model 2	Model 3
Mothers	4429/43277				
ASD	61/340	1.79 (1.36-2.37)	1.65 (1.25-2.19)	1.34 (1.00-1.80)	1.32 (0.98-1.77)
ASD+ID	20/154	1.35 (0.84-2.17)	1.24 (0.77-2.01)	1.01 (0.61-1.68)	0.98 (0.59-1.63)
ASD-ID	41/186	2.14 (1.51-3.03)	1.91 (1.34-2.71)	1.57 (1.09-2.26)	1.55 (1.07-2.23)
Fathers					
ASD	33/192	1.72 (1.19-2.51)	1.53 (1.05-2.23)	1.31 (0.89-1.94)	1.29 (0.88-1.92)
ASD+ID	17/77	2.29 (1.35-3.91)	2.03 (1.18-3.50)	1.72 (0.98-3.02)	1.67 (0.95-2.93)
ASD-ID	16/115	1.36 (0.80-2.31)	1.19 (0.70-2.04)	1.01 (0.58-1.76)	1.01 (0.58-1.76)
Model 1 adjusted for parental ages, income, education, occupation, migration status, parity Model 2= model 1+ any other psychiatric condition (including psychosis, bipolar, neurodevelopmental, personality or drug and alcohol misuse disorders) Model 3= model 2+ both parents depression, both parents other psych condition					

	N (exposed) cases/ controls	Crude OR	Model 1	Model 2	Model 3
Table S7 Odds ratios depicting the relationship between parental depression before birth of child and offspring ASD, ASD with and without ID in at least 8 YEAR OLD children					
Maternal depression					
ASD	30/151	1.97 (1.32-2.94)	1.77 (1.18-2.65)	1.81 (1.21-2.71)	1.75 (1.17-2.62)
ASD+ID	7/66	1.11 (0.50-2.44)	1.05 (0.48-2.32)	1.08 (0.49-2.40)	1.04 (0.47-2.32)
ASD-ID	23/85	2.59 (1.62-4.14)	2.21 (1.37-3.56)	2.24 (1.39-3.62)	2.19 (1.35-3.54)
Paternal depression					
ASD	11/99	1.06 (0.56-1.98)	0.99 (0.53-1.86)	1.00 (0.53-1.88)	1.01 (0.54-1.89)
ASD+ID	4/38	0.98 (0.35-2.76)	0.93 (0.33-2.64)	0.94 (0.33-2.68)	0.93 (0.33-2.63)
ASD-ID	7/61	1.10 (0.50-2.43)	1.00 (0.45-2.22)	1.02 (0.46-2.26)	1.03 (0.46-2.28)

Numbers in study (maximum): ASD cases n=3877, controls n=37500;
ASD+ID cases n=1612, controls n=15967;
ASD-ID cases n=2265, controls n=21533

Model 1 adjusted for parental ages, income, education, occupation, migration status, parity

Model 2= model 1+ any other psychiatric condition (including psychosis, bipolar, neurodevelopmental, personality or drug and alcohol misuse disorders)

Model 3= model 2+ both parents depression, both parents other psych condition

Table S8 Parental History of Depression before birth of child and risk of offspring ASD- MODEL 4 for each analysis (includes mediators)						
	For main analysis (Table 2)	**Born before 1990 (Table S3)**	**Primiparous (Table S4)**	**Swedish parents (Table S5)**	**Non hierarchical coding (Table S6)**	**At least 8 year olds (Table S7)**
Mothers						
ASD	1.50 (1.06-2.13)	2.30 (1.11-4.76)	1.93 (1.09-3.42)	1.69 (1.14-2.50)	1.23 (0.90-1.70)	1.71 (1.11-2.64)
ASD+ID	1.17 (0.62-2.19)	2.03 (0.50-8.14)	1.91 (0.57-6.38)	1.78 (0.90-3.52)	0.89 (0.50-1.59)	1.18 (0.52-2.67)
ASD-ID	1.72 (1.13-2.64)	2.22 (0.93-5.31)	2.04 (1.04-3.97)	1.70 (1.05-2.75)	1.46 (0.98-2.17)	2.09 (1.24-3.54)
Fathers						
ASD	1.04 (0.61-1.77)	0.92 (0.21-4.04)	0.56 (0.19-1.63)	1.12 (0.58-2.17)	1.23 (0.80-1.90)	0.83 (0.40-1.74)
ASD+ID	1.28 (0.59-2.77)	3.19 (0.56-18.08)	0.79 (0.14-4.46)	1.90 (0.71-5.06)	1.58 (0.85-2.94)	0.75 (0.22-2.50)
ASD-ID	0.82 (0.39-1.74)	-	0.37 (0.08-1.64)	0.73 (0.28-1.87)	0.88 (0.47-1.64)	0.81 (0.32-2.06)
Model 4 = model 3 in tables 2, S3, S4, S5, S6 and S7 further adjusted for gestational age at birth, birth weight for gestational age, maternal smoking, diabetes, hypertension.						

	N (max exposed) cases/ controls	Crude OR	Model 1	Model 2	Model 3	Model 4
Table S9 Odds ratios depicting the relationship between parental depression before birth of child and offspring ASD, ASD with and without ID in children born between 1984-2003 with ALL AVAILABLE DATA						
Maternal depression						
ASD	47/284	1.67 (1.22-2.28)	1.50 (1.08-2.08)	1.54 (1.11-2.13)	1.49 (1.08-2.08)	1.50 (1.06-2.13)
ASD+ID	13/124	1.05 (0.59-1.86)	0.96 (0.52-1.76)	0.98 (0.53-1.80)	0.96 (0.52-1.77)	1.17 (0.62-2.19)
ASD-ID	34/160	2.15 (1.48-3.12)	1.85 (1.24-2.74)	1.90 (1.28-2.82)	1.86 (1.25-2.77)	1.72 (1.13-2.64)
Paternal depression						
ASD	19/159	1.18 (0.73-1.90)	1.11 (0.68-1.79)	1.13 (0.70-1.83)	1.12 (0.69-1.82)	1.04 (0.61-1.77)
ASD+ID	9/64	1.38 (0.69-2.78)	1.33 (0.65-2.72)	1.36 (0.67-2.78)	1.35 (0.66-2.77)	1.28 (0.59-2.77)
ASD-ID	10/95	1.04 (0.54-2.00)	0.96 (0.50-1.87)	0.98 (0.51-1.91)	0.97 (0.50-1.89)	0.82 (0.39-1.73)

Numbers in study (maximum): ASD cases n=4952, controls n=49520;
ASD+ID cases n=2097, controls n=20970;
ASD-ID cases n=2855, controls n=28550
Model 1 adjusted for parental ages, income, education, occupation, migration status, parity
Model 2= model 1+ any other psychiatric condition (including anxiety disorder, psychotic and bipolar disorders, neurodevelopmental, personality or drug and alcohol misuse disorders)
Model 3= model 2+ both parents depression, both parents other psych condition
Model 4= adjusted for maternal report of smoking, record of diabetes, hypertension, birth weight for gestational age, gestational age at birth and Apgar score at 5 minutes

	N (exposed) cases/ controls	Crude OR	Model 1	Model 2	Model 3
Table S10 Odds ratios depicting the relationship between maternal depression before birth of child and offspring ASD adjusting for antidepressant use during pregnancy in children born 1995-2003 USING ALL AVAILABLE DATA					
Maternal depression					
ASD	25/181	1.39 (0.91-2.12)	1.25 (0.81-1.93)	1.34 (0.87-2.08)	1.19 (0.76-1.87)
ASD+ID	9/87	1.04 (0.52-2.07)	1.03 (0.51-2.09)	1.06 (0.52-2.16)	1.04 (0.50-2.13)
ASD-ID	16/94	1.72 (1.01-2.94)	1.43 (0.82-2.51)	1.58 (0.90-2.79)	1.30 (0.72-2.34)

Numbers in study (maximum): ASD cases n=1918, controls n=19180;
ASD+ID cases n=743, controls n=7584;
ASD-ID cases n=936, controls n=9261
Model 1 adjusted for antidepressant use during pregnancy only
Model 2= adjusted for parental ages, income, education, occupation, migration status, parity
Model 3= model 2 adjusted for antidepressant use during pregnancy

Table S11 Odds ratios depicting the relationship between maternal depression, antidepressant use during pregnancy, and offspring ASD (with and without ID) in children born between 1995-2003 USING ALL AVAILABLE DATA								
	ASD			ASD + ID			ASD-ID		
	N case/ control	Crude OR	Adjusted OR	N case/ control	Crude OR	Adjusted OR	N case/ control	Crude OR	Adjusted OR
No depression, no antidepressant use	1872/ 18877	1.00 (Ref)	1.00 (Ref)	849/ 8508	1.00 (Ref)	1.00 (Ref)	1023/ 10369	1.00 (Ref)	1.00 (Ref)
Depression but no antidepressant use	25/198	1.28 (0.84-1.95)	1.06 (0.68-1.66)	11/93	1.19 (0.63-2.23)	1.06 (0.54-2.07)	14/105	1.36 (0.77-2.38)	1.04 (0.57-1.92)
Depression with antidepressant use	9/28	3.31 (1.54-7.08)	3.34 (1.50-7.47)	2/13	1.54 (0.35-6.84)	1.81 (0.39-8.56)	7/15	4.99 (1.98-12.61)	4.94 (1.85-13.23)
Antidepressant use but no depression	12/77	1.58 (0.86-2.91)	1.61 (0.85-3.06)	3/36	0.84 (0.26-2.73)	0.93 (0.27-3.21)	9/41	2.24 (1.08-4.63)	2.10 (0.97-4.57)

Max n ASD=1918, controls=19180, ASD+ID=865, controls 8650; ASD-ID=1053 controls=10530

Note: Depression refers to any outpatient (secondary care) or inpatient record of depression before the birth of the child. Antidepressant use refers to any antidepressant use recorded at the first antenatal interview.

Adjusted OR= adjusted for history of psychiatric disorders other than depression, parental ages, income, education, occupation, migration status, parity

Table S12 Odds ratios depicting the relationship between antidepressant use during pregnancy and offspring ASD, and ASD with and without ID in children born 1995-2003 USING ALL AVAILABLE DATA									
	ASD			**ASD + ID**			**ASD-ID**		
	N case/ control	Crude OR	Adjusted OR	N case/ control	Crude OR	Adjusted OR	N case/ control	Crude OR	Adjusted OR
Any antidepressant	21/105	2.02 (1.26-3.25)	1.90 (1.15-3.14)	5/49	1.02 (0.40-2.57)	1.09 (0.41-2.88)	16/56	2.92 (1.66-5.14)	2.54 (1.37-4.68)
SSRI	14/75	1.88 (1.06-3.35)	1.65 (0.90-3.03)	4/39	1.03 (0.37-2.88)	1.01 (0.34-2.98)	10/36	2.86 (1.40-5.84)	2.34 (1.09-5.06)
Non-selective MRI	6/22	2.73 (1.11-6.73)	2.69 (1.04-6.96)	1/8	1.25 (0.16-9.99)	1.72 (0.20-15.03)	5/14	3.57 (1.29-9.92)	2.93 (0.98-8.82)

Max n= ASD 1918, control 19180

SSRI=selective serotonin reuptake inhibitors; Non-selective MRI=non selective monoamine reuptake inhibitors

Adjusted OR=adjusted for any maternal psychiatric disorder, maternal age, paternal age, parental income, education and occupation, and maternal country of birth and birth parity.