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This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix A: Descriptive Statistics Based on Maternal Self-reported Antidepressant Use

In the main paper, we presented the distribution of covariates and outcomes stratified by maternal self-reported use of any antidepressant (Table 1). We have also provided the distribution of outcomes and covariates stratified by maternal self-reported use of any antidepressant in a subsample of differentially exposed siblings (eTable 1), as well as the distribution of outcomes and covariates stratified by maternal self-reported use of SSRIs specifically in all offspring in the sample and in a subsample of differentially exposed siblings (eTables 2 and 3, respectively). Because families in which all siblings are concordant on the outcomes cannot contribute to sibling comparison analyses, we have also provided information about subsamples of offspring from families with outcome-discordant siblings (eTable 4).

eTable 1. Descriptive statistics stratified by maternal self-reported first-trimester use of any antidepressant in a subsample of differentially exposed siblings

	Exposed offspring	Unexposed offspring
	(n=10,975)	(n=13,994)
	No. (%)	No. (%)
Offspring outcomes		
Preterm birth	685 (6.24)	710 (5.07)
Small for gestational age	205 (1.87)	277 (1.98)
Autism spectrum disorder ^a	136 (5.52)	274 (4.55)
Attention-deficit/hyperactivity disorder ^a	280 (12.38)	699 (12.73)
Pregnancy covariates		
First born	2942 (26.81)	5803 (41.47)
Second born	4279 (38.99)	5346 (38.20)
Third born	2506 (22.83)	1803 (12.88)
Fourth born or higher	1248 (11.37)	1042 (7.45)
Born 1996 to 1999 ^b	534 (4.87)	2648 (18.92)
Born 2000 to 2003 ^b	1592 (14.51)	3653 (26.10)
Born 2004 to 2007 ^b	3658 (33.33)	3882 (27.74)
Born 2008 to 2012 ^b	5191 (47.30)	3811 (27.23)
Maternal covariates		
Age at birth		
< 20 years	111 (1.01)	509 (3.64)
20 to 24 years	1203 (10.96)	3158 (22.57)
25 to 29 years	3061 (27.89)	4720 (33.73)
30 to 34 years	3853 (35.11)	3800 (27.15)
35 to 39 years	2290 (20.87)	1543 (11.03)
≥ 40 years	457 (4.16)	264 (1.89)
Education		
Primary and lower secondary, < 9 years	99 (0.90)	141 (1.01)
Primary and lower secondary, 9 years	1375 (12.53)	1892 (13.52)
Upper secondary, 1-2 years	1951 (17.78)	2607 (18.63)
Upper secondary, 3 years	3022 (27.54)	3850 (27.51)
Post-secondary, < 3 years	1363 (12.42)	1670 (11.93)
Post-secondary, ≥ 3 years	3077 (28.04)	3737 (26.70)
Postgraduate	88 (0.80)	97 (0.69)
Nationality (Swedish)	9856 (89.80)	12469 (89.10)
Criminal convictions (any)	2007 (18.29)	2722 (19.45)
Severe psychiatric illness ^c	812 (7.40)	991 (7.08)
Suicide attempt (definite or uncertain)	1552 (14.14)	2018 (14.42)
Paternal covariates		
Age at birth		
< 20 years	50 (0.46)	191 (1.36)
20 to 24 years	706 (6.43)	1760 (12.58)
25 to 29 years	2358 (21.49)	4192 (29.96)
30 to 34 years	3571 (32.54)	4241 (30.31)
35 to 39 years	2666 (24.29)	2374 (16.96)
≥ 40 years	1624 (14.80)	1236 (8.83)
Education		
Primary and lower secondary, < 9 years	137 (1.25)	180 (1.29)

	Exposed offspring	Unexposed offspring
	(n=10,975)	(n=13,994)
	No. (%)	No. (%)
Primary and lower secondary, 9 years	1290 (11.75)	1769 (12.64)
Upper secondary, 1-2 years	2810 (25.60)	3748 (26.78)
Upper secondary, 3 years	3076 (28.03)	3872 (27.67)
Post-secondary, < 3 years	1422 (12.96)	1788 (12.78)
Post-secondary, ≥ 3 years	2061 (18.78)	2420 (17.29)
Postgraduate	179 (1.63)	217 (1.55)
Nationality (Swedish)	9533 (86.86)	12023 (85.92)
Criminal convictions (any)	4603 (41.94)	6206 (44.35)
Severe psychiatric illness ^c	152 (1.38)	175 (1.25)
Suicide attempt (definite or uncertain)	621 (5.66)	802 (5.73)

All percentages are based on the number of offspring. ^aAge 15 Kaplan Meier estimates. ^bYear of birth is presented in bins in eTable 1 but was not binned when used as a covariate in models. ^cSevere psychiatric illness was defined as an inpatient or outpatient diagnosis of schizophrenia, bipolar disorder, or other non-drug induced psychosis.

eTable 2. Descriptive statistics stratified by maternal self-reported first-trimester SSRI use

	Exposed offspring	Unexposed offspring
	(n=18,470)	(n=1,562,159)
	No. (%)	No. (%)
Offspring outcomes		
Preterm birth	1214 (6.57)	74847 (4.79)
Small for gestational age	453 (2.45)	34275 (2.19)
Autism spectrum disorder ^a	236 (5.21)	14381 (2.14)
Attention-deficit/hyperactivity disorder ^a	476 (13.29)	32448 (5.47)
Pregnancy covariates		
First born	8658 (46.88)	684412 (43.81)
Second born	5717 (30.95)	579902 (37.12)
Third born	2777 (15.04)	210605 (13.48)
Fourth born or higher	1318 (7.14)	87240 (5.58)
Born 1996 to 1999 ^b	1063 (5.76)	332728 (21.30)
Born 2000 to 2003 ^b	2340 (12.67)	346803 (22.20)
Born 2004 to 2007 ^b	5230 (28.32)	381281 (24.41)
Born 2008 to 2012 ^b	9837 (53.26)	501347 (32.09)
Maternal covariates		
Age at birth		
< 20 years	290 (1.57)	25347 (1.62)
20 to 24 years	2224 (12.04)	208328 (13.34)
25 to 29 years	5123 (27.74)	489927 (31.36)
30 to 34 years	6146 (33.28)	538600 (34.48)
35 to 39 years	3794 (20.54)	250977 (16.07)
≥ 40 years	893 (4.83)	48980 (3.14)
Education		
Primary and lower secondary, < 9 years	133 (0.72)	33515 (2.15)
Primary and lower secondary, 9 years	2115 (11.45)	105838 (6.78)
Upper secondary, 1-2 years	3009 (16.29)	243406 (15.58)
Upper secondary, 3 years	5043 (27.30)	409906 (26.24)
Post-secondary, < 3 years	2450 (13.26)	222256 (14.23)
Post-secondary, ≥ 3 years	5588 (30.25)	528122 (33.81)
Postgraduate	132 (0.71)	19116 (1.22)
Nationality (Swedish)	16719 (90.52)	1264423 (80.94)
Criminal convictions (any)	3158 (17.10)	170473 (10.91)
Severe psychiatric illness ^c	1350 (7.31)	15386 (0.98)
Suicide attempt (definite or uncertain)	2530 (13.70)	64125 (4.10)
Paternal covariates		
Age at birth		
< 20 years	116 (0.63)	7673 (0.49)
20 to 24 years	1287 (6.97)	99052 (6.34)
25 to 29 years	3973 (21.51)	361019 (23.11)
30 to 34 years	5890 (31.89)	541773 (34.68)
35 to 39 years	4371 (23.67)	350929 (22.46)
≥ 40 years	2833 (15.34)	201713 (12.91)
Education		
Primary and lower secondary, < 9 years	194 (1.05)	29175 (1.87)

	Exposed offspring (n=18,470)	Unexposed offspring (n=1,562,159)
	No. (%)	No. (%)
Primary and lower secondary, 9 years	2141 (11.59)	151436 (9.69)
Upper secondary, 1-2 years	4460 (24.15)	399459 (25.57)
Upper secondary, 3 years	5261 (28.48)	376485 (24.10)
Post-secondary, < 3 years	2408 (13.04)	231152 (14.80)
Post-secondary, ≥ 3 years	3697 (20.02)	344700 (22.07)
Postgraduate	309 (1.67)	29752 (1.90)
Nationality (Swedish)	16195 (87.68)	1257778 (80.52)
Criminal convictions (any)	7538 (40.81)	574464 (36.77)
Severe psychiatric illness ^c	247 (1.34)	10126 (0.65)
Suicide attempt (definite or uncertain)	1082 (5.86)	63797 (4.08)

All percentages are based on the number of offspring. ^aAge 15 Kaplan Meier estimates. ^bYear of birth is presented in bins in eTable 2 but was not binned when used as a covariate in models. ^cSevere psychiatric illness was defined as an inpatient or outpatient diagnosis of schizophrenia, bipolar disorder, or other non-drug induced psychosis.

eTable 3. Descriptive statistics stratified by maternal self-reported first-trimester use of SSRIs in a subsample of differentially exposed siblings

	Exposed offspring	Unexposed offspring
	(n=9,063)	(n=15,906)
	No. (%)	No. (%)
Offspring outcomes		
Preterm birth	544 (6.00)	851 (5.35)
Small for gestational age	162 (1.79)	320 (2.01)
Autism spectrum disorder ^a	108 (5.59)	229 (4.64)
Attention-deficit/hyperactivity disorder ^a	229 (13.61)	585 (13.00)
Pregnancy covariates		
First born	2377 (26.23)	6368 (40.04)
Second born	3639 (40.15)	5986 (37.63)
Third born	2072 (22.86)	2237 (14.06)
Fourth born or higher	975 (10.76)	1315 (8.27)
Born 1996 to 1999 ^b	369 (4.07)	2813 (17.69)
Born 2000 to 2003 ^b	1256 (13.86)	3989 (25.08)
Born 2004 to 2007 ^b	3027 (33.40)	4513 (28.37)
Born 2008 to 2012 ^b	4411 (48.67)	4591 (28.86)
Maternal covariates		
Age at birth		
< 20 years	96 (1.06)	524 (3.29)
20 to 24 years	1003 (11.07)	3358 (21.11)
25 to 29 years	2554 (28.18)	5227 (32.86)
30 to 34 years	3146 (34.71)	4507 (28.34)
35 to 39 years	1888 (20.83)	1945 (12.23)
≥ 40 years	376 (4.15)	345 (2.17)
Education		
Primary and lower secondary, < 9 years	83 (0.92)	157 (0.99)
Primary and lower secondary, 9 years	1075 (11.86)	2192 (13.78)
Upper secondary, 1-2 years	1555 (17.16)	3003 (18.88)
Upper secondary, 3 years	2548 (28.11)	4324 (27.18)
Post-secondary, < 3 years	1118 (12.34)	1915 (12.04)
Post-secondary, ≥ 3 years	2614 (28.84)	4200 (26.41)
Postgraduate	70 (0.77)	115 (0.72)
Nationality (Swedish)	8157 (90.00)	14168 (89.07)
Criminal convictions (any)	1607 (17.73)	3122 (19.63)
Severe psychiatric illness ^c	630 (6.95)	1173 (7.37)
Suicide attempt (definite or uncertain)	1203 (13.27)	2367 (14.88)
Paternal covariates		
Age at birth		
< 20 years	42 (0.46)	199 (1.25)
20 to 24 years	580 (6.40)	1886 (11.86)
25 to 29 years	1933 (21.33)	4617 (29.03)
30 to 34 years	2989 (32.98)	4823 (30.32)
35 to 39 years	2189 (24.15)	2851 (17.92)
≥ 40 years	1330 (14.68)	1530 (9.62)
Education		
Primary and lower secondary, < 9 years	108 (1.19)	209 (1.31)

	Exposed offspring	Unexposed offspring
	(n=9,063)	(n=15,906)
	No. (%)	No. (%)
Primary and lower secondary, 9 years	1054 (11.63)	2005 (12.61)
Upper secondary, 1-2 years	2283 (25.19)	4275 (26.88)
Upper secondary, 3 years	2557 (28.21)	4391 (27.61)
Post-secondary, < 3 years	1180 (13.02)	2030 (12.76)
Post-secondary, ≥ 3 years	1727 (19.06)	2754 (17.31)
Postgraduate	154 (1.70)	242 (1.52)
Nationality (Swedish)	7898 (87.15)	13658 (85.87)
Criminal convictions (any)	3771 (41.61)	7038 (44.25)
Severe psychiatric illness ^c	122 (1.35)	205 (1.29)
Suicide attempt (definite or uncertain)	499 (5.51)	924 (5.81)

All percentages are based on the number of offspring. ^aAge 15 Kaplan Meier estimates. ^bYear of birth is presented in bins in eTable 3 but was not binned when used as a covariate in models. ^cSevere psychiatric illness was defined as an inpatient or outpatient diagnosis of schizophrenia, bipolar disorder, or other non-drug induced psychosis.

eTable 4. Information on families with outcome discordant siblings in the cohort born 1996 to 2012

	Number of distinct outcome discordant siblings	Number of distinct mothers with outcome discordant offspring	Number of siblings with outcomes
Preterm birth	96866	40416	42557
Small for gestational age	45155	18926	19581
Autism spectrum disorder	24969	10105	10371
Attention-deficit/hyperactivity disorder	55526	22301	23522

eAppendix B: Descriptive Statistics and Analyses Based on Antidepressant Dispensation Records

Exposure status was based on dispensation data for the timing of exposure comparisons and paternal comparisons. Dispensation windows used in main analyses were: (1) only before pregnancy, (2) during the first trimester of pregnancy, (3) only during the second and/or third trimester, and (4) only after pregnancy (see eFigure 1 for a diagram of the dispensation windows). We have presented the distribution of outcomes and covariates stratified by maternal dispensation windows for any antidepressants and for SSRIs specifically (eTables 5 and 6, respectively). In addition, we have presented the distribution of outcomes and covariates for offspring of fathers with first-trimester dispensations and offspring of fathers without dispensations before, during, or after pregnancy (see eTable 7 for any antidepressant dispensations and eTable 8 for SSRI dispensations).

Timing of exposure analyses compared associations with dispensations before pregnancy to associations with first-trimester dispensations. We evaluated whether these associations differed statistically using Wald χ^2 tests. We also compared the fit of two models using the Akaike information criterion (AIC). The first model included four parameters that compared the following groups to offspring unexposed to any antidepressants: (1) dispensations only before pregnancy, (2) dispensations for the first trimester of pregnancy, (3) dispensations only for the second and/or third trimester of pregnancy, and (4) dispensations only after pregnancy. The second model constrained the first two parameters to be equal so that the model included the following three parameters: (1) dispensations before and/or during the first trimester of pregnancy, (2) dispensations for the second and/or third trimester of pregnancy, and (3) dispensations after pregnancy. Thus, the four-parameter model included separate parameters for dispensations before pregnancy and first-trimester dispensations, whereas the three-parameter model included one parameter for dispensations before pregnancy and first-trimester dispensations. If associations with dispensations before pregnancy differed from associations with dispensations during the first trimester of pregnancy, the model that included separate parameters for those two time periods would fit better.

For preterm birth, the association between dispensations before pregnancy and preterm birth was significantly smaller than the association between first-trimester dispensations and preterm birth ($p = 0.0007$ for any antidepressant, $p = 0.001$ for SSRIs specifically), and the four-parameter model fit better than the three-parameter model. However, for small for gestational age, autism spectrum disorder, and attention-deficit/hyperactivity disorder the associations with dispensations before pregnancy did not significantly differ from associations with first-trimester dispensations (small for gestational age: $p = 0.64$ for any antidepressant, $p = 0.74$ for SSRIs specifically; autism spectrum disorder: $p = 0.21$ for any antidepressant, $p = 0.46$ for SSRIs specifically; attention-deficit/hyperactivity disorder: $p = 0.49$ for any antidepressant, $p = 0.76$ for SSRIs specifically). The three-parameter model also fit better than the four-parameter model for these outcomes. The four-parameter model estimates and the model fit for both models are presented in eTable 9.

eTable 5. Descriptive statistics stratified by maternal dispensation windows for any antidepressants

	Before pregnancy dispensations only (n=8203 [1.16%])	1 st -trimester dispensations (n=26477 [3.74%])	2 nd and/or 3 rd trimester dispensations only (n=746 [0.11%])	After pregnancy dispensations only (n=6574 [0.93%])	No dispensations before, during, or after pregnancy (n=666450)
	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)
Offspring outcomes					
Preterm birth	484 (5.90)	1842 (6.96)	42 (5.63)	419 (6.37)	30945 (4.64)
Small for gestational age	205 (2.50)	660 (2.49)	20 (2.68)	148 (2.25)	14348 (2.15)
Autism spectrum disorder ^a	35 (0.96)	143 (1.14)	6 (2.00)	29 (0.90)	2044 (0.59)
Attention-deficit/hyperactivity disorder ^a	27 (1.03)	80 (0.83)	0 (0.00)	24 (0.88)	931 (0.34)
Pregnancy covariates					
First born	4097 (49.95)	12244 (46.24)	281 (37.67)	2666 (40.55)	296400 (44.47)
Second born	2298 (28.01)	8224 (31.06)	261 (34.99)	2586 (39.34)	250549 (37.59)
Third born	1219 (14.86)	4031 (15.22)	130 (17.43)	898 (13.66)	85821 (12.88)
Fourth born or higher	589 (7.18)	1978 (7.47)	74 (9.92)	424 (6.45)	33680 (5.05)
Born 2006 to 2009 ^b	4316 (52.61)	13570 (51.25)	364 (48.79)	3514 (53.45)	377773 (56.68)
Born 2010 to 2012 ^b	3887 (47.39)	12907 (48.75)	382 (51.21)	3060 (46.55)	288677 (43.32)
Maternal covariates					
Age at birth					
< 20 years	152 (1.85)	439 (1.66)	20 (2.68)	172 (2.62)	9470 (1.42)
20 to 24 years	1244 (15.17)	3345 (12.63)	134 (17.96)	1080 (16.43)	84356 (12.66)
25 to 29 years	2257 (27.51)	7030 (26.55)	211 (28.28)	1871 (28.46)	193442 (29.03)
30 to 34 years	2660 (32.43)	8710 (32.90)	203 (27.21)	2080 (31.64)	234498 (35.19)
35 to 39 years	1522 (18.55)	5549 (20.96)	133 (17.83)	1088 (16.55)	120041 (18.01)
≥ 40 years	368 (4.49)	1404 (5.30)	45 (6.03)	283 (4.30)	24643 (3.70)
Education					
Primary and lower secondary, < 9 years	152 (1.85)	346 (1.31)	28 (3.75)	108 (1.64)	17093 (2.56)
Primary and lower secondary, 9 years	1077 (13.13)	3482 (13.15)	138 (18.58)	941 (14.31)	44637 (6.70)
Upper secondary, 1-2 years	1103 (13.45)	3513 (13.27)	97 (13.00)	820 (12.47)	61107 (9.17)
Upper secondary, 3 years	2363 (28.81)	7534 (28.45)	186 (24.93)	1922 (29.24)	189191 (28.39)
Post-secondary, < 3 years	1030 (12.56)	3358 (12.68)	104 (13.94)	789 (12.00)	84692 (12.71)
Post-secondary, ≥ 3 years	2408 (29.36)	8045 (30.38)	189 (25.34)	1956 (29.75)	261200 (39.19)
Postgraduate	70 (0.85)	199 (0.75)	4 (0.54)	38 (0.58)	8530 (1.28)

	Before pregnancy dispensations only (n=8203 [1.16%])	1st-trimester dispensations (n=26477 [3.74%])	2nd and/or 3rd trimester dispensations only (n=746 [0.11%])	After pregnancy dispensations only (n=6574 [0.93%])	No dispensations before, during, or after pregnancy (n=66450)
	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)
Nationality (Swedish)	6839 (83.37)	23220 (87.70)	543 (72.79)	5481 (83.37)	523334 (78.53)
Criminal convictions (any)	1417 (17.27)	4676 (17.66)	158 (21.18)	1058 (16.09)	62678 (9.40)
Severe psychiatric illness ^c	336 (4.10)	1736 (6.56)	37 (4.96)	370 (5.63)	3604 (0.54)
Suicide attempt (definite or uncertain)	1003 (12.23)	3685 (13.92)	101 (13.54)	676 (10.28)	23861 (3.58)
Paternal covariates					
Age at birth					
< 20 years	55 (0.67)	185 (0.70)	11 (1.47)	50 (0.76)	3033 (0.46)
20 to 24 years	708 (8.63)	2006 (7.58)	73 (9.79)	599 (9.11)	39498 (5.93)
25 to 29 years	1801 (21.96)	5543 (20.94)	165 (22.12)	1461 (22.22)	139335 (20.91)
30 to 34 years	2464 (30.04)	8096 (30.58)	200 (26.81)	2101 (31.96)	226642 (34.01)
35 to 39 years	1897 (23.13)	6260 (23.64)	176 (23.59)	1472 (22.39)	161388 (24.22)
≥ 40 years	1278 (15.58)	4387 (16.57)	121 (16.22)	891 (13.55)	96554 (14.49)
Education					
Primary and lower secondary, < 9 years	165 (2.01)	398 (1.50)	21 (2.82)	131 (1.99)	14251 (2.14)
Primary and lower secondary, 9 years	1027 (12.52)	3200 (12.09)	96 (12.87)	799 (12.15)	59882 (8.99)
Upper secondary, 1-2 years	1569 (19.13)	5345 (20.19)	150 (20.11)	1234 (18.77)	111799 (16.78)
Upper secondary, 3 years	2569 (31.32)	8243 (31.13)	224 (30.03)	2189 (33.30)	200790 (30.13)
Post-secondary, < 3 years	1052 (12.82)	3394 (12.82)	101 (13.54)	827 (12.58)	94032 (14.11)
Post-secondary, ≥ 3 years	1740 (21.21)	5536 (20.91)	143 (19.17)	1315 (20.00)	173513 (26.04)
Postgraduate	81 (0.99)	361 (1.36)	11 (1.47)	79 (1.20)	12183 (1.83)
Nationality (Swedish)	6704 (81.73)	22443 (84.76)	535 (71.72)	5415 (82.37)	522698 (78.43)
Criminal convictions (any)	3263 (39.78)	10434 (39.41)	309 (41.42)	2516 (38.27)	213431 (32.03)
Severe psychiatric illness ^c	78 (0.95)	351 (1.33)	8 (1.07)	88 (1.34)	3177 (0.48)
Suicide attempt (definite or uncertain)	488 (5.95)	1560 (5.89)	46 (6.17)	343 (5.22)	25464 (3.82)

All percentages are based on the number of offspring. ^aAge 6 Kaplan Meier estimates. ^bYear of birth is presented in bins in eTable 5 but was not binned when used as a covariate in models. ^cSevere psychiatric illness was defined as an inpatient or outpatient diagnosis of schizophrenia, bipolar disorder, or other non-drug induced psychosis.

eTable 6. Descriptive statistics stratified by maternal dispensation windows for SSRIs

	Before pregnancy dispensations (n=6674 [0.94%])	1 st -trimester dispensations (n=22125 [3.12%])	2 nd /3 rd trimester dispensations (n=775 [0.11%])	After pregnancy dispensations (n=6007 [0.85%])	No dispensations before, during, or after pregnancy (n=672869)
	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)
Offspring outcomes					
Preterm birth	381 (5.71)	1512 (6.83)	41 (5.29)	378 (6.29)	31420 (4.67)
Small for gestational age	167 (2.50)	550 (2.49)	21 (2.71)	130 (2.16)	14513 (2.16)
Autism spectrum disorder ^a	30 (1.05)	115 (1.10)	6 (1.89)	31 (1.04)	2075 (0.59)
Attention-deficit/hyperactivity disorder ^a	21 (0.98)	64 (0.79)	1 (0.38)	24 (0.96)	952 (0.35)
Pregnancy covariates					
First born	3294 (49.36)	10220 (46.19)	293 (37.81)	2471 (41.14)	299410 (44.50)
Second born	1928 (28.89)	7022 (31.74)	274 (35.25)	2370 (39.45)	252324 (37.50)
Third born	997 (14.94)	3325 (15.03)	130 (16.77)	803 (13.37)	86844 (12.91)
Fourth born or higher	455 (6.82)	1558 (7.04)	78 (10.06)	363 (6.04)	34291 (5.10)
Born 2006 to 2009 ^b	3550 (53.19)	11212 (50.68)	374 (48.26)	3192 (53.14)	381209 (56.65)
Born 2010 to 2012 ^b	3124 (46.81)	10913 (49.32)	401 (51.74)	2815 (46.86)	291660 (43.35)
Maternal covariates					
Age at birth					
< 20 years	141 (2.11)	387 (1.75)	20 (2.58)	153 (2.55)	9552 (1.42)
20 to 24 years	1021 (15.30)	2826 (12.77)	140 (18.06)	1000 (16.65)	85172 (12.66)
25 to 29 years	1855 (27.79)	5926 (26.78)	218 (28.13)	1694 (28.20)	195118 (29.00)
30 to 34 years	2158 (32.33)	7269 (32.85)	216 (27.87)	1889 (31.45)	236619 (35.17)
35 to 39 years	1214 (18.19)	4580 (20.70)	137 (17.68)	1019 (16.96)	121383 (18.04)
≥ 40 years	285 (4.27)	1137 (5.14)	44 (5.68)	252 (4.20)	25025 (3.72)
Education					
Primary and lower secondary, < 9 years	108 (1.62)	254 (1.15)	29 (3.74)	90 (1.50)	17246 (2.56)
Primary and lower secondary, 9 years	880 (13.19)	2795 (12.63)	149 (19.23)	831 (13.83)	45620 (6.78)
Upper secondary, 1-2 years	857 (12.84)	2802 (12.66)	104 (13.42)	740 (12.32)	62137 (9.23)
Upper secondary, 3 years	1901 (28.48)	6303 (28.49)	194 (25.03)	1756 (29.23)	191042 (28.39)
Post-secondary, < 3 years	861 (12.90)	2831 (12.80)	109 (14.06)	730 (12.15)	85442 (12.70)
Post-secondary, ≥ 3 years	2012 (30.15)	6973 (31.52)	185 (23.87)	1824 (30.36)	262804 (39.06)
Postgraduate	55 (0.82)	167 (0.75)	5 (0.65)	36 (0.60)	8578 (1.27)

	Before pregnancy dispensations (n=6674 [0.94%])	1 st -trimester dispensations (n=22125 [3.12%])	2 nd /3 rd trimester dispensations (n=775 [0.11%])	After pregnancy dispensations (n=6007 [0.85%])	No dispensations before, during, or after pregnancy (n=672869)
	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)
Nationality (Swedish)	5616 (84.15)	19486 (88.07)	570 (73.55)	5036 (83.84)	528709 (78.58)
Criminal convictions (any)	1160 (17.38)	3750 (16.95)	165 (21.29)	974 (16.21)	63938 (9.50)
Severe psychiatric illness ^c	278 (4.17)	1418 (6.41)	49 (6.32)	358 (5.96)	3980 (0.59)
Suicide attempt (definite or uncertain)	817 (12.24)	2927 (13.23)	112 (14.45)	625 (10.40)	24845 (3.69)
Paternal covariates					
Age at birth					
< 20 years	46 (0.69)	154 (0.70)	12 (1.55)	47 (0.78)	3075 (0.46)
20 to 24 years	608 (9.11)	1682 (7.60)	76 (9.81)	551 (9.17)	39967 (5.94)
25 to 29 years	1441 (21.59)	4662 (21.07)	169 (21.81)	1341 (22.32)	140692 (20.91)
30 to 34 years	2054 (30.78)	6823 (30.84)	216 (27.87)	1889 (31.45)	228521 (33.96)
35 to 39 years	1522 (22.80)	5248 (23.72)	175 (22.58)	1353 (22.52)	162895 (24.21)
≥ 40 years	1003 (15.03)	3556 (16.07)	127 (16.39)	826 (13.75)	97719 (14.52)
Education					
Primary and lower secondary, < 9 years	126 (1.89)	305 (1.38)	22 (2.84)	115 (1.91)	14398 (2.14)
Primary and lower secondary, 9 years	847 (12.69)	2612 (11.81)	108 (13.94)	724 (12.05)	60713 (9.02)
Upper secondary, 1-2 years	1241 (18.59)	4347 (19.65)	158 (20.39)	1110 (18.48)	113241 (16.83)
Upper secondary, 3 years	2076 (31.11)	6938 (31.36)	236 (30.45)	1996 (33.23)	202769 (30.13)
Post-secondary, < 3 years	864 (12.95)	2880 (13.02)	100 (12.90)	759 (12.64)	94803 (14.09)
Post-secondary, ≥ 3 years	1452 (21.76)	4731 (21.38)	139 (17.94)	1227 (20.43)	174698 (25.96)
Postgraduate	68 (1.02)	312 (1.41)	12 (1.55)	76 (1.27)	12247 (1.82)
Nationality (Swedish)	5491 (82.27)	18855 (85.22)	559 (72.13)	4960 (82.57)	527930 (78.46)
Criminal convictions (any)	2614 (39.17)	8608 (38.91)	333 (42.97)	2285 (38.04)	216113 (32.12)
Severe psychiatric illness ^c	74 (1.11)	289 (1.31)	8 (1.03)	87 (1.45)	3244 (0.48)
Suicide attempt (definite or uncertain)	416 (6.23)	1282 (5.79)	56 (7.23)	312 (5.19)	25835 (3.84)

All percentages are based on the number of offspring. ^aAge 6 Kaplan Meier estimates. ^bYear of birth is presented in bins in eTable 6 but was not binned when used as a covariate in models. ^cSevere psychiatric illness was defined as an inpatient or outpatient diagnosis of schizophrenia, bipolar disorder, or other non-drug induced psychosis.

eTable 7. Descriptive statistics stratified by paternal first-trimester dispensations of any antidepressants

	1 st -trimester dispensations (n=18,727)	No dispensations before, during, or after pregnancy (n= 675,620)
	No. (%)	No. (%)
Offspring outcomes		
Preterm birth	992 (5.30)	32024 (4.74)
Small for gestational age	423 (2.26)	14623 (2.16)
Autism spectrum disorder ^a	77 (0.81)	2125 (0.61)
Attention-deficit/hyperactivity disorder ^a	49 (0.68)	972 (0.36)
Pregnancy covariates		
First born	7893 (42.15)	301793 (44.67)
Second born	6554 (35.00)	252447 (37.37)
Third born	2833 (15.13)	87218 (12.91)
Fourth born or higher	1447 (7.73)	34162 (5.06)
Born 2006 to 2009 ^b	10064 (53.74)	381620 (56.48)
Born 2010 to 2012 ^b	8663 (46.26)	294000 (43.52)
Maternal covariates		
Age at birth		
< 20 years	309 (1.65)	9583 (1.42)
20 to 24 years	2195 (11.72)	85688 (12.68)
25 to 29 years	4955 (26.46)	195867 (28.99)
30 to 34 years	6373 (34.03)	237503 (35.15)
35 to 39 years	3971 (21.20)	121792 (18.03)
≥ 40 years	924 (4.93)	25187 (3.73)
Education		
Primary and lower secondary, < 9 years	600 (3.20)	16585 (2.45)
Primary and lower secondary, 9 years	1838 (9.81)	46592 (6.90)
Upper secondary, 1-2 years	2140 (11.43)	62703 (9.28)
Upper secondary, 3 years	5271 (28.15)	191879 (28.40)
Post-secondary, < 3 years	2305 (12.31)	85920 (12.72)
Post-secondary, ≥ 3 years	6374 (34.04)	263433 (38.99)
Postgraduate	199 (1.06)	8508 (1.26)
Nationality (Swedish)	14604 (77.98)	534445 (79.10)
Criminal convictions (any)	2586 (13.81)	65127 (9.64)
Severe psychiatric illness ^c	379 (2.02)	5393 (0.80)
Suicide attempt (definite or uncertain)	1192 (6.37)	27118 (4.01)
Paternal covariates		
Age at birth		
< 20 years	83 (0.44)	3158 (0.47)
20 to 24 years	844 (4.51)	40960 (6.06)
25 to 29 years	3099 (16.55)	142359 (21.07)
30 to 34 years	5746 (30.68)	229720 (34.00)
35 to 39 years	4980 (26.59)	162975 (24.12)
≥ 40 years	3975 (21.23)	96448 (14.28)
Education		
Primary and lower secondary, < 9 years	474 (2.53)	13993 (2.07)
Primary and lower secondary, 9 years	2640 (14.10)	59944 (8.87)

	1st-trimester dispensations (n=18,727)	No dispensations before, during, or after pregnancy (n= 675,620)
	No. (%)	No. (%)
Upper secondary, 1-2 years	3871 (20.67)	113159 (16.75)
Upper secondary, 3 years	4931 (26.33)	205399 (30.40)
Post-secondary, < 3 years	2347 (12.53)	95382 (14.12)
Post-secondary, ≥ 3 years	4156 (22.19)	175515 (25.98)
Postgraduate	308 (1.64)	12228 (1.81)
Nationality (Swedish)	14870 (79.40)	532719 (78.85)
Criminal convictions (any)	8514 (45.46)	214354 (31.73)
Severe psychiatric illness ^c	978 (5.22)	2142 (0.32)
Suicide attempt (definite or uncertain)	1808 (9.65)	24632 (3.65)

All percentages are based on the number of offspring. ^aAge 6 Kaplan Meier estimates. ^bYear of birth is presented in bins in eTable 7 but was not binned when used as a covariate in models. ^cSevere psychiatric illness was defined as an inpatient or outpatient diagnosis of schizophrenia, bipolar disorder, or other non-drug induced psychosis.

eTable 8. Descriptive statistics stratified by paternal first-trimester dispensations of SSRIs

	1 st -trimester dispensations (n=13,521)	No dispensations before, during, or after pregnancy (n=684,714)
	No. (%)	No. (%)
Offspring outcomes		
Preterm birth	720 (5.33)	32486 (4.74)
Small for gestational age	291 (2.15)	14851 (2.17)
Autism spectrum disorder ^a	55 (0.75)	2157 (0.61)
Attention-deficit/hyperactivity disorder ^a	37 (0.67)	994 (0.36)
Pregnancy covariates		
First born	5754 (42.56)	305525 (44.62)
Second born	4776 (35.32)	255557 (37.32)
Third born	2032 (15.03)	88602 (12.94)
Fourth born or higher	959 (7.09)	35030 (5.12)
Born 2006 to 2009 ^b	7252 (53.64)	386666 (56.47)
Born 2010 to 2012 ^b	6269 (46.36)	298048 (43.53)
Maternal covariates		
Age at birth		
< 20 years	222 (1.64)	9756 (1.42)
20 to 24 years	1496 (11.06)	87065 (12.72)
25 to 29 years	3616 (26.74)	198353 (28.97)
30 to 34 years	4675 (34.58)	240266 (35.09)
35 to 39 years	2859 (21.14)	123621 (18.05)
≥ 40 years	653 (4.83)	25653 (3.75)
Education		
Primary and lower secondary, < 9 years	347 (2.57)	17032 (2.49)
Primary and lower secondary, 9 years	1216 (8.99)	47800 (6.98)
Upper secondary, 1-2 years	1471 (10.88)	63936 (9.34)
Upper secondary, 3 years	3816 (28.22)	194470 (28.40)
Post-secondary, < 3 years	1656 (12.25)	86992 (12.70)
Post-secondary, ≥ 3 years	4873 (36.04)	265887 (38.83)
Postgraduate	142 (1.05)	8597 (1.26)
Nationality (Swedish)	10890 (80.54)	540855 (78.99)
Criminal convictions (any)	1756 (12.99)	66667 (9.74)
Severe psychiatric illness ^c	248 (1.83)	5608 (0.82)
Suicide attempt (definite or uncertain)	839 (6.21)	27761 (4.05)
Paternal covariates		
Age at birth		
< 20 years	67 (0.50)	3201 (0.47)
20 to 24 years	608 (4.50)	41491 (6.06)
25 to 29 years	2300 (17.01)	143887 (21.01)
30 to 34 years	4284 (31.68)	232237 (33.92)
35 to 39 years	3649 (26.99)	165167 (24.12)
≥ 40 years	2613 (19.33)	98731 (14.42)
Education		
Primary and lower secondary, < 9 years	270 (2.00)	14374 (2.10)
Primary and lower secondary, 9 years	1764 (13.05)	61624 (9.00)
Upper secondary, 1-2 years	2705 (20.01)	115293 (16.84)

	1st-trimester dispensations (n=13,521)	No dispensations before, during, or after pregnancy (n=684,714)
	No. (%)	No. (%)
Upper secondary, 3 years	3658 (27.05)	207594 (30.32)
Post-secondary, < 3 years	1692 (12.51)	96471 (14.09)
Post-secondary, ≥ 3 years	3199 (23.66)	177024 (25.85)
Postgraduate	233 (1.72)	12334 (1.80)
Nationality (Swedish)	11062 (81.81)	539150 (78.74)
Criminal convictions (any)	5885 (43.52)	219182 (32.01)
Severe psychiatric illness ^c	620 (4.59)	2634 (0.38)
Suicide attempt (definite or uncertain)	1126 (8.33)	25773 (3.76)

All percentages are based on the number of offspring. ^aAge 6 Kaplan Meier estimates. ^bYear of birth is presented in bins in eTable 8 but was not binned when used as a covariate in models. ^cSevere psychiatric illness was defined as an inpatient or outpatient diagnosis of schizophrenia, bipolar disorder, or other non-drug induced psychosis.

eTable 9. Adjusted associations between maternal antidepressant dispensations before pregnancy, during the first trimester of pregnancy, during the second and/or third trimester of pregnancy, and after pregnancy and offspring birth and neurodevelopmental outcomes

	Four parameter model estimates								Model fit	
	1. Before pregnancy		2. 1 st trimester		3. 2 nd and/or 3 rd trimester		4. After pregnancy		Four Parameter model	Parameters 1 and 2 constrained to equality
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	AIC	AIC
Any antidepressant										
Preterm birth	1.17	1.07-1.28	1.40	1.33-1.47	1.15	0.84-1.57	1.34	1.21-1.48	268512.64	268522.38
Small for gestational age	1.07	0.93-1.24	1.12	1.03-1.21	1.17	0.75-1.84	1.05	0.89-1.24	143724.04	143722.26
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	AIC	AIC
Autism spectrum disorder	1.40	1.02-1.93	1.75	1.49-2.07	2.18	0.98-4.85	1.45	1.03-2.04	65876.69	65876.32
Attention deficit/hyperactivity disorder	2.09	1.53-2.86	1.85	1.55-2.20	0.24	0.06-1.01	1.86	1.39-2.48	46856.51	46854.97
SSRIs										
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	AIC	AIC
Preterm birth	1.13	1.02-1.25	1.37	1.30-1.45	1.06	0.77-1.45	1.31	1.18-1.46	268561.62	268570.72
Small for gestational age	1.09	0.94-1.28	1.13	1.03-1.23	1.17	0.76-1.82	1.01	0.85-1.21	143723.97	143722.08
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	AIC	AIC
Autism spectrum disorder	1.49	1.06-2.10	1.72	1.43-2.06	2.13	0.96-4.76	1.64	1.17-2.29	65881.61	65880.16
Attention deficit/hyperactivity disorder	1.93	1.35-2.74	1.81	1.50-2.19	0.50	0.17-1.42	1.86	1.37-2.52	46876.16	46874.25

OR = odds ratio. HR = hazard ratio. CI = confidence interval. Models were fit in a sample of 708,450 offspring. The four parameter model included the following four parameters that compared the following groups to offspring unexposed to any antidepressants: (1) dispensations only before pregnancy, (2) dispensations for the first trimester of pregnancy, (3) dispensations only for the second and/or third trimester of pregnancy, and (4) dispensations only after pregnancy. Models also controlled for parity and year of birth and maternal and paternal country of birth, age at childbearing, highest level of completed education, history of any criminal convictions, history of severe psychiatric illness, and history of any suicide attempts. Models were compared using the Akaike information criterion (AIC).

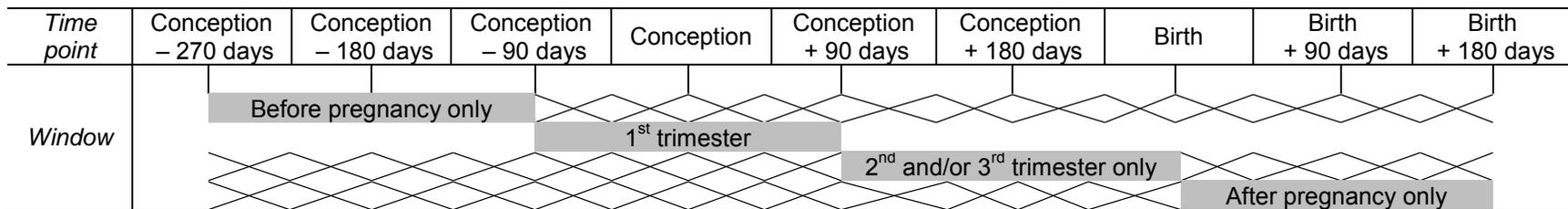


Figure legend:

 At least one dispensation occurred during this period
 No dispensations occurred during this period

eFigure 1. Dispensation windows. The before-pregnancy-only window included offspring of women who were dispensed antidepressants in the period 270 days before conception to 90 days before conception but were not dispensed antidepressants in the period 90 days before conception to 180 days after birth. The 1st-trimester window included offspring of women who were dispensed antidepressants in the period 90 days before conception to 90 days after conception. Offspring of women who were also dispensed antidepressants before or after the defined exposure window were considered exposed in the 1st-trimester window. The 2nd- and/or 3rd-trimester only window included offspring of women who were dispensed antidepressants in the period 90 days after conception to birth but were not dispensed antidepressants in the period 270 days before conception to 90 days after conception and were not dispensed antidepressants in the period 180 days after birth. The after pregnancy only window included offspring of women who were dispensed antidepressants in the period 180 days after birth but were not dispensed antidepressants in the period 270 days before conception through birth.

eAppendix C: Test of Exposure Misclassification

In the sample of 708,450 offspring born between 2006 and 2012, maternal self-report data on antidepressant use was used in combination with maternal antidepressant dispensation data to evaluate whether exposure misclassification may have biased the results.

The main analyses used two different definitions for first-trimester antidepressant exposure. First-trimester exposure was defined (a) according to maternal self-reports and (b) according to dispensation data. Women self-reported antidepressant use at the first antenatal visit, which typically occur between the 10th and 12th week of pregnancy. First-trimester exposure based on dispensation records was defined as having at least one dispensation between 90 days before estimated conception and 90 days after estimated conception. (eFigure 1 shows a diagram of exposure windows.)

To test for biases from exposure misclassification, we first calculated kappa estimates to assess agreement between the two exposures definitions used in the main analyses.

Then, four additional exposure definitions were created.

The first definition classified cases as exposed if *either* exposure definition used in the main analyses indicated exposure. According to this definition, 28,158 (4.0% of the 2006-2012 cohort) offspring were exposed to any antidepressant, and 23,422 (3.3%) offspring were exposed to SSRIs specifically.

The second definition classified cases as exposed if *both* exposure definitions used in the main analyses indicated exposure. According to this definition, 13,435 (1.9%) offspring were exposed to any antidepressant, and 11,516 (1.6%) offspring were exposed to SSRIs specifically.

The third definition used a narrower window than the main analyses' first-trimester dispensation definition. Specifically, it defined exposure as having at least one dispensation between 30 days before estimated conception and 90 days after estimated conception. According to this definition, 7,455 (1.1%) offspring were exposed to any antidepressant, and 5,593 (0.8%) offspring were exposed to SSRIs specifically.

The fourth definition required at least *two* dispensations in the dispensation window used in the main analyses (between 90 days before estimated conception and 90 days after estimated conception). According to this definition, 14,288 (2.0%) offspring were exposed to any antidepressant, and 11,333 (1.6%) offspring were exposed to SSRIs specifically.

Models assessing associations between the four additional definitions of exposure and offspring problems included pregnancy-related, maternal, and paternal covariates.

In general, the results from the sensitivity analyses suggest that exposure misclassification and self-report biases did not influence the results.

Maternal reports and dispensation records showed substantial agreement (kappa = 0.64, 95% CI [0.63-0.64] for any antidepressant, and kappa = 0.65, 95% CI [0.65-0.66] for SSRIs). Additionally, commensurate associations were found across the two exposure definitions used in the main paper and the four additional definitions described here (Table 2, Table 3, eTable 10).

eTable 10. Adjusted associations between four definitions of first-trimester antidepressant use and offspring birth and neurodevelopmental outcomes

	Exposure according to self-reported use <i>OR</i> dispensation data		Exposure according to self-report use <i>AND</i> dispensation data		Narrower first-trimester exposure dispensation window		Two dispensations during 1 st trimester	
Any antidepressant	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Preterm birth	1.38	1.31-1.45	1.40	1.31-1.50	1.44	1.36-1.52	1.54	1.41-1.68
Small for gestational age	1.12	1.03-1.21	1.13	1.01-1.26	1.14	1.04-1.25	1.13	0.98-1.31
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
Autism spectrum disorder	1.71	1.46-2.01	1.83	1.46-2.28	1.85	1.54-2.22	1.72	1.28-2.31
Attention deficit/hyperactivity disorder	1.70	1.44-2.00	1.75	1.38-2.22	1.83	1.50-2.22	1.81	1.34-2.44
SSRIs	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Preterm birth	1.34	1.27-1.42	1.34	1.24-1.44	1.42	1.34-1.51	1.45	1.31-1.61
Small for gestational age	1.12	1.03-1.22	1.13	1.01-1.28	1.17	1.06-1.29	1.17	0.99-1.38
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
Autism spectrum disorder	1.71	1.44-2.04	1.75	1.37-2.24	1.83	1.50-2.24	1.71	1.21-2.41
Attention deficit/hyperactivity disorder	1.62	1.35-1.95	1.76	1.36-2.28	1.87	1.51-2.31	1.83	1.29-2.58

OR = odds ratio. HR = hazard ratio. CI = confidence interval. Models were fit in a sample of 708,450 offspring. Models controlled for parity and year of birth and maternal and paternal country of birth, age at childbearing, highest level of completed education, history of any criminal convictions, history of severe psychiatric illness, and history of any suicide attempts.

eAppendix D: Test of Generalizability of Sibling Comparisons

An assumption of sibling comparisons is that results will generalize to other samples (e.g., families with only one child, families without variability in the outcome). An additional analysis was conducted to test this assumption. Specifically, given that families with single included offspring were excluded from sibling comparison analyses (because they cannot provide information), we assessed baseline and adjusted associations in a subsample of 1,139,753 offspring who had at least one sibling in the dataset in order to assess the generalizability of the sibling comparison results. Although associations with small for gestational age were not statistically significant, the general pattern of results were consistent with findings from the main analyses (eTable 11), suggesting that reduction in the effect sizes in the sibling-comparison models, particularly for the neurodevelopmental outcomes, was not due to the exclusion of single-offspring families.

eTable 11. Baseline and adjusted associations between maternal self-reported first-trimester antidepressant use and offspring birth and neurodevelopmental outcomes in multiple-offspring families

	Baseline Model		Adjusted Model	
	OR	95% CI	OR	95% CI
Any antidepressant				
Preterm birth	1.48	1.38-1.58	1.37	1.28-1.47
Small for gestational age	1.06	0.94-1.20	1.06	0.94-1.19
SSRIs				
Preterm birth	1.39	1.29-1.50	1.29	1.20-1.39
Small for gestational age	1.03	0.90-1.18	1.03	0.90-1.18
HRs				
Autism spectrum disorder	2.08	1.80-2.39	1.70	1.47-1.96
Attention deficit/hyperactivity disorder	2.09	1.89-2.31	1.48	1.34-1.64
Autism spectrum disorder	2.06	1.75-2.42	1.69	1.44-1.99
Attention deficit/hyperactivity disorder	2.18	1.94-2.44	1.54	1.37-1.73

OR = odds ratio. HR = hazard ratio. CI = confidence interval. All models were fit in a sample of 1,139,753 offspring who had at least one sibling in the dataset. Baseline models controlled for parity and year of birth. Adjusted models controlled for parity and year of birth and maternal and paternal country of birth, age at childbearing, highest level of completed education, history of any criminal convictions, history of severe psychiatric illness, and history of any suicide attempts.

eAppendix E: Test of Confounding from Exposure to Other Psychotropic Medications

Offspring with maternal self-reported first-trimester exposure to other psychotropic medications, defined as antiepileptic medications, antipsychotic medications, medications used to treat addictive disorders, anxiolytics, attention-deficit/hyperactivity disorder medication, and opioid analgesics, were identified (eTable 12 lists specific drug names and Anatomical Therapeutic Chemical Classification [ATC] codes). Given that 9.8% (2,204) of offspring exposed to antidepressants were also exposed to other psychotropic medications, associations between maternal self-reported first-trimester antidepressant use and offspring outcomes were assessed in a subsample of 1,563,250 offspring who were not exposed to the other psychotropic medications. These associations were commensurate to associations observed in the main analyses (eTable 13), suggesting that exposure to other psychotropic medications did not bias the results.

eTable 12. Drug names and Anatomical Therapeutic Chemical Classification codes for other psychotropic medications

ATC code	Medication name
Antiepileptic medications	
N03AA01	methylphenobarbital
N03AA02	phenobarbital
N03AA03	primidone
N03AA04	barbexaclone
N03AA30	metharbital
N03AB01	ethotoin
N03AB02	phenytoin
N03AB03	amino(diphenylhydantoin) valeric acid
N03AB04	mephenytoin
N03AB05	fosphenytoin
N03AB52	phenytoin, combinations
N03AB54	mephenytoin, combinations
N03AC01	paramethadione
N03AC02	trimethadione
N03AC03	ethadione
N03AD01	ethosuximide
N03AD02	phensuximide
N03AD03	mesuximide
N03AD51	ethosuximide, combinations
N03AF01	carbamazepine
N03AF02	oxcarbazepine
N03AF03	rufinamide
N03AF04	eslicarbazepine
N03AG01	valproic acid
N03AG02	valpromide
N03AG03	aminobutyric acid
N03AG04	vigabatrin
N03AG05	progabide
N03AG06	tiagabine
N03AX03	sultiame
N03AX07	phenacemide
N03AX09	lamotrigine
N03AX10	felbamate
N03AX11	topiramate
N03AX12	gabapentin
N03AX13	pheneturide
N03AX14	levetiracetam
N03AX15	zonisamide
N03AX16	pregabalin

ATC code	Medication name
Antiepileptic medications	
N03AX17	stiripentol
N03AX18	lacosamide
N03AX19	carisbamate
N03AX21	retigabine
N03AX22	perampanel
N03AX30	beclamide
N05AN01	lithium
Antipsychotic medications	
N05AA01	chlorpromazine
N05AA02	levomepromazine
N05AA03	promazine
N05AA04	acepromazine
N05AA05	triflupromazine
N05AA06	cyamemazine
N05AA07	chlorproethazine
N05AB01	dixyrazine
N05AB02	fluphenazine
N05AB03	perphenazine
N05AB04	prochlorperazine
N05AB05	thiopropazate
N05AB06	trifluoperazine
N05AB07	acetophenazine
N05AB08	thiopropazine
N05AB09	butaperazine
N05AB10	perazine
N05AC01	periciazine
N05AC02	thioridazine
N05AC03	mesoridazine
N05AD01	haloperidol
N05AD02	trifluoperidol
N05AD03	melperone
N05AD04	moperone
N05AD05	pipamperone
N05AD06	bromperidol
N05AD07	benperidol
N05AD08	droperidol
N05AD09	fluanisone
N05AE01	oxypertine
N05AE02	molindone
N05AE03	sertindole
N05AE04	ziprasidone

ATC code	Medication name
Antipsychotic medications	
N05AE05	lurasidone
N05AF01	flupentixol
N05AF02	clopenthixol
N05AF03	chlorprothixene
N05AF04	tiotixene
N05AF05	zuclopenthixol
N05AG01	fluspirilene
N05AG02	pimozide
N05AG03	penfluridol
N05AH01	loxapine
N05AH02	clozapine
N05AH03	olanzapine
N05AH04	quetiapine
N05AH05	asenapine
N05AH06	clotiapine
N05AL01	sulpiride
N05AL02	sultopride
N05AL03	tiapride
N05AL04	remoxipride
N05AL05	amisulpride
N05AL06	veralipride
N05AL07	levosulpiride
N05AX07	prothipendyl
N05AX08	risperidone
N05AX10	mosapramine
N05AX11	zotepine
N05AX12	aripiprazole
N05AX13	paliperidone
N05AX14	iloperidone
Medications for addictive disorders	
N07BA01	nicotine
N07BA03	varenicline
N07BB01	disulfiram
N07BB02	calcium carbimide
N07BB03	acamprosate
N07BB04	naltrexone
N07BC01	buprenorphine
N07BC02	methadone
N07BC03	levacetylmethadol
N07BC04	lofexidine
N07BC05	levomethadone

ATC code	Medication name
Medications for addictive disorders	
N07BC06	diamorphine
N07BC51	buprenorphine, combinations
Anxiolytics	
N03AE01	clonazepam
N05BA01	diazepam
N05BA02	chlordiazepoxide
N05BA04	oxazepam
N05BA05	clorazepate
N05BA06	lorazepam
N05BA12	alprazolam
N05CD01	flurazepam
N05CD04	estazolam
N05CD05	triazolam
N05CD07	temazepam
N05CD08	midazolam
N05CD110	quazepam
N05BE01	bupirone
N05BB01	atarax
N05BB01	vistaril
Attention-deficit/hyperactivity disorder medications	
N06BA01	amfetamine
N06BA02	dexamfetamine
N06BA04	methylphenidate
N06BA09	atomoxetine
Opioids	
N02AA01	Morphine
N02AA03	Hydromorphone
N02AA05	Oxycodone
N02AA55	Oxycodone/nalaxone
N02AA59	Codeine excl. psychotropics
N02AB01	Ketobemidone
N02AB02	Pethidine
N02AB03	Fentanyl
N02AC04	Dextropropoxyphene
N02AC54	Dextropropoxyphene excl psycholeptics
N02AD01	Pentazocine
N02AE01	Buprenorphine
N02AG01	Morphine & antispasmodics
N02AG02	Ketobemidone/ dimethylaminophenylbutene
N02AG04	Hydromorphone & antispasmodics

ATC code	Medication name
Opioids	
N02AX02	Tramadol

ATC = Anatomical Therapeutic Chemical Classification

eTable 13. Baseline, adjusted, and sibling comparison associations between maternal self-reported first-trimester antidepressant use and offspring birth and neurodevelopmental outcomes in a subsample of offspring *not exposed to other psychotropic medications*

	Baseline Model		Adjusted Model		Sibling Comparison	
	OR	95% CI	OR	95% CI	OR	95% CI
Any antidepressant						
Preterm birth	1.40	1.32-1.48	1.30	1.22-1.37	1.30	1.13-1.49
Small for gestational age	1.12	1.03-1.23	1.11	1.02-1.22	0.92	0.73-1.17
SSRIs						
	OR	95% CI	OR	95% CI	OR	95% CI
Preterm birth	1.31	1.23-1.40	1.22	1.15-1.30	1.27	1.10-1.48
Small for gestational age	1.08	0.98-1.20	1.08	0.98-1.20	0.82	0.63-1.06
	HR	95% CI	HR	95% CI	HR	95% CI
Autism spectrum disorder	1.85	1.64-2.10	1.53	1.35-1.74	0.67	0.48-0.94
Attention deficit/hyperactivity disorder	2.16	1.99-2.35	1.58	1.46-1.72	1.02	0.79-1.30
	HR	95% CI	HR	95% CI	HR	95% CI
Autism spectrum disorder	1.85	1.61-2.13	1.53	1.33-1.76	0.67	0.46-0.97
Attention deficit/hyperactivity disorder	2.17	1.98-2.39	1.58	1.44-1.74	0.96	0.73-1.27

OR = odds ratio. HR = hazard ratio. CI = confidence interval. Baseline and adjusted models were fit in a sample of 1,563,250 offspring. Baseline models controlled for parity and year of birth. Adjusted models controlled for parity and year of birth and maternal and paternal country of birth, age at childbearing, highest level of completed education, history of any criminal convictions, history of severe psychiatric illness, and history of any suicide attempts. Sibling comparisons controlled for parity and year of birth, paternal country of birth, age at childbearing, highest level of completed education, history of any criminal convictions, history of severe psychiatric illness, and history of any suicide attempts, and maternal age at childbearing.

eAppendix F: Test of Bias from Left Censoring

Given that, prior to 2001, outpatient psychiatric diagnoses were not included in the National Patient Register, we conducted analyses in a sample of 1,162,873 offspring born in 2001 or later to assess whether left censoring of the neurodevelopmental outcomes may have biased the results. The analyses also enabled us to examine whether cohort effects influenced the results. These analyses assessed associations between maternal self-reported first-trimester antidepressant use and offspring autism spectrum disorder and attention-deficit/hyperactivity disorder in baseline, adjusted, and sibling comparison models. The results were commensurate to the main analyses (eTable 14), suggesting that left censoring of the outcomes and cohort effects did not influence the results.

eTable 14. Baseline, adjusted, and sibling comparison associations between maternal self-reported first-trimester antidepressant use and offspring neurodevelopmental outcomes in a subsample born in 2001 or after

	Baseline Model		Adjusted Model		Sibling Comparison	
	HR	95% CI	HR	95% CI	HR	95% CI
Any antidepressant						
Autism spectrum disorder	2.04	1.79-2.32	1.71	1.49-1.95	0.88	0.59-1.33
Attention-deficit/hyperactivity disorder	2.29	2.09-2.52	1.63	1.48-1.80	1.05	0.73-1.50
SSRIs						
Autism spectrum disorder	2.06	1.78-2.38	1.75	1.51-2.02	0.90	0.58-1.40
Attention-deficit/hyperactivity disorder	2.28	2.05-2.53	1.63	1.46-1.81	0.92	0.62-1.35

HR = hazard ratio. CI = confidence interval. Baseline and adjusted models were fit in a sample of 1,162,873 offspring. Baseline models controlled for parity and year of birth. Adjusted models controlled for parity and year of birth and maternal and paternal country of birth, age at childbearing, highest level of completed education, history of any criminal convictions, history of severe psychiatric illness, and history of any suicide attempts. Sibling comparisons controlled for parity and year of birth, paternal country of birth, age at childbearing, highest level of completed education, history of any criminal convictions, history of severe psychiatric illness, and history of any suicide attempts, and maternal age at childbearing.

eAppendix G: Test of Validity of Early Autism Spectrum Disorder and Attention-Deficit/Hyperactivity Disorder Diagnoses

There is uncertainty about the stability over time of early neurodevelopmental disorder diagnoses.^{e.g.,1} Thus, we conducted a sensitivity analyses to test the validity of early autism spectrum disorder and attention-deficit/hyperactivity disorder diagnoses. Offspring diagnosed before the age of 2 were excluded from the sample and baseline, adjusted, and sibling comparison associations were re-examined. Associations with autism spectrum disorder were assessed in a sample of 1,580,430 offspring. Associations with attention-deficit/hyperactivity disorder were assessed in a sample of 1,580,509 offspring. Associations were commensurate to main analyses associations (eTable 15), suggesting that early neurodevelopmental diagnoses of potentially questionable validity did not bias the results.

eTable 15. Baseline, adjusted, and sibling comparison associations between maternal self-reported first-trimester antidepressant use and offspring neurodevelopmental outcomes in a sample excluding offspring diagnosed before age 2 years

	Baseline Model		Adjusted Model		Sibling Comparison	
	HR	95% CI	HR	95% CI	HR	95% CI
Any antidepressant						
Autism spectrum disorder	2.01	1.80-2.26	1.63	1.45-1.83	0.83	0.61-1.13
Attention-deficit/hyperactivity disorder	2.21	2.04-2.38	1.58	1.46-1.71	1.00	0.79-1.26
SSRIs						
Autism spectrum disorder	2.03	1.79-2.31	1.65	1.45-1.88	0.81	0.57-1.14
Attention-deficit/hyperactivity disorder	2.25	2.06-2.46	1.60	1.46-1.75	0.95	0.73-1.23

HR = hazard ratio. CI = confidence interval. Baseline and adjusted associations with autism spectrum disorder were assessed in a sample of 1,580,430 offspring. Baseline and adjusted associations with attention-deficit/hyperactivity disorder were assessed in a sample of 1,580,509 offspring. Adjusted models controlled for parity and year of birth and maternal and paternal country of birth, age at childbearing, highest level of completed education, history of any criminal convictions, history of severe psychiatric illness, and history of any suicide attempts. Sibling comparisons controlled for parity and year of birth, paternal country of birth, age at childbearing, highest level of completed education, history of any criminal convictions, history of severe psychiatric illness, and history of any suicide attempts, and maternal age at childbearing.

eAppendix H: Examining Associations Between Dispensations During Later Pregnancy and Offspring Outcomes Among Those with a First-trimester Dispensation

Given that the main analyses focused on first-trimester antidepressant exposure, we conducted a sensitivity analysis to explore whether continued dispensations in the second and/or third trimester was associated with the birth and neurodevelopmental outcomes compared to dispensations only during the first trimester. We defined a group of offspring, labeled Continuers, as those whose mothers had a first-trimester dispensation *and* a second- or third-trimester dispensation. We defined a second group, labeled Discontinuers, as offspring whose mothers had a first-trimester dispensation but not a second- or third-trimester dispensation. Of the 26,477 offspring in the cohort with first-trimester dispensations, 12,291 (46%) were Continuers and 14,186 (54%) were Discontinuers. Of the 22,125 offspring with first-trimester dispensations of SSRI specifically, 10,757 (49%) were continuers and 11,368 (51%) were discontinuers.

We examined adjusted associations between continuation of use late in pregnancy and the birth and neurodevelopmental outcomes (eTable 16). The association between continued dispensations of antidepressants and preterm birth (OR = 1.4, 95% CI [1.3, 1.6]) and small for gestational age (OR = 1.2, 95% CI [1.0, 1.4]) were statistically significant. The association with autism spectrum disorder was moderate in magnitude (HR = 1.3, 95% CI [1.0, 1.8]), though not statistically significant. Continuation of dispensations was associated with a moderate decrease in the risk for attention-deficit/hyperactivity disorder (HR = 0.8, 95% CI [0.5, 1.1]), but the association was not statistically significant.

These analyses cannot differentiate whether the associations were due to the intrauterine exposure to antidepressants later in pregnancy, increased severity of depression (i.e., confounding by indication severity), or other unmeasured confounding.

eTable 16. Adjusted associations between continuation of antidepressant dispensations late in pregnancy and offspring birth and neurodevelopmental outcomes among those with a first-trimester dispensation

Adjusted Model		
Any antidepressant		
	OR	95% CI
Preterm birth	1.44	1.30-1.59
Small for gestational age	1.18	1.01-1.39
	HR	95% CI
Autism spectrum disorder	1.32	0.96-1.81
Attention deficit/hyperactivity disorder	0.76	0.53-1.08
SSRIs		
	OR	95% CI
Preterm birth	1.39	1.24-1.54
Small for gestational age	1.21	1.01-1.44
	HR	95% CI
Autism spectrum disorder	1.22	0.86-1.74
Attention deficit/hyperactivity disorder	0.71	0.47-1.06

OR = odds ratio. HR = hazard ratio. CI = confidence interval. Models predicting outcomes from any antidepressant dispensation were fit in a sample of 26,477 offspring. Models predicting outcomes from SSRIs dispensation were fit in a sample of 22,125 offspring. Models controlled for parity and year of birth and maternal and paternal country of birth, age at childbearing, highest level of completed education, history of any criminal convictions, history of severe psychiatric illness, and history of any suicide attempts.

eReferences

1. Turner LM, Stone WL. Variability in outcome for children with an ASD diagnosis at age 2. *J Child Psychol Psychiatry*. 2007;48(8):793-802.