

Maternal Psychiatric Conditions, Treatment with Selective Serotonin Reuptake Inhibitors, and Neurodevelopmental Disorders

Supplementary Information

Supplementary Table S1 - Sample Selection from Full Study to Explore Early Development (SEED)

	Total N	Index Child Only	Final Classification	Complete Data ^a	Complete Covariates ^b (Final Analytic Sample)
SEED 1+2	7271	7116	6099	5013	4788

N=Number

^a Caregiver interview, maternal medical history form, and prenatal medical records available for analysis

^b Sample including non-missing values for maternal race, maternal education, household income, and maternal smoking

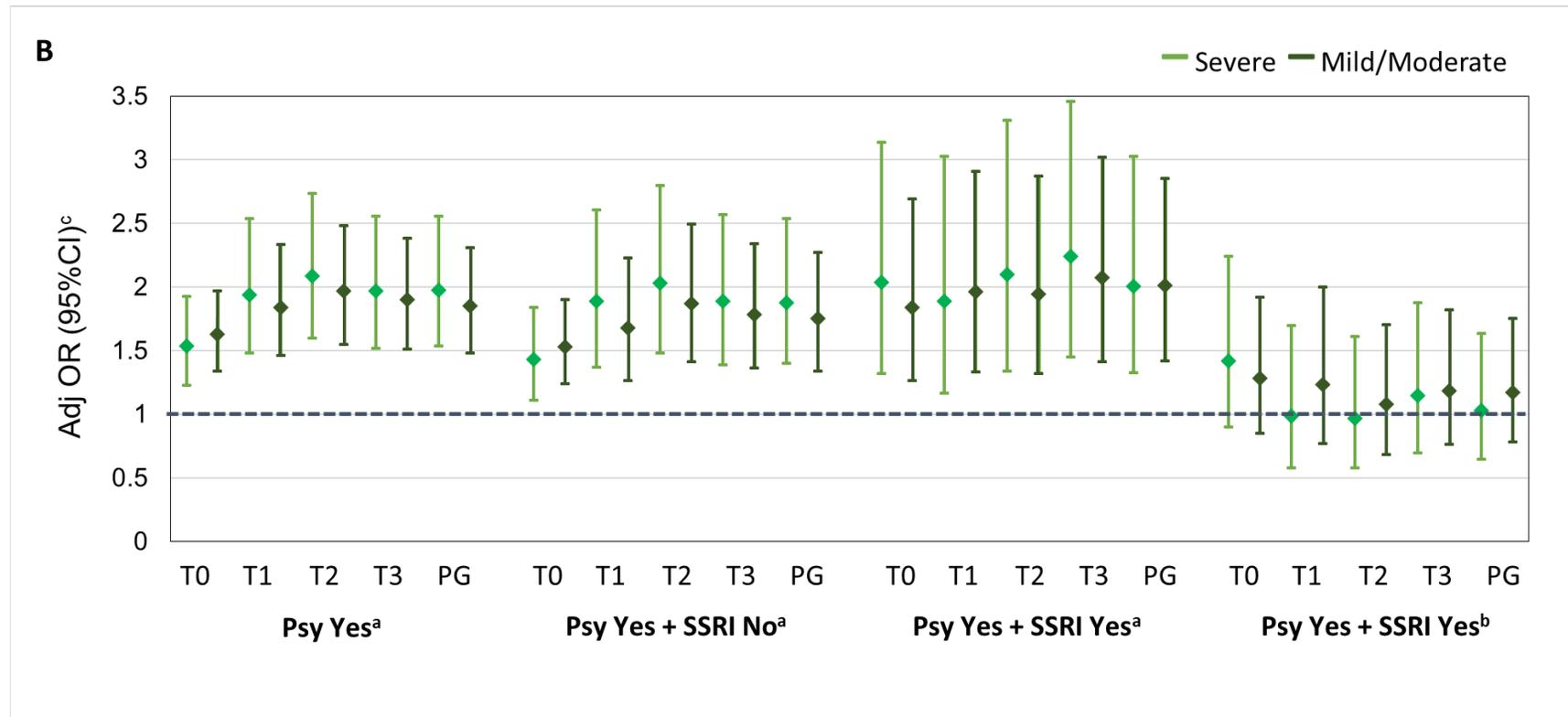
Supplementary Table S2 - Distribution of Psychiatric Types by SSRI Use Status Among Women with Any Psychiatric Disorder (T0+PG)

Psychiatric Condition	SSRI Use		p-value
	Yes (n=389)	No (n=1159)	
	n (%)	n (%)	
ADHD	26 (6.68)	116 (10.01)	0.05
Anxiety	247 (63.50)	416 (35.89)	<0.001
Bipolar Disorder	56 (14.40)	90 (7.77)	<0.001
Depression	353 (90.75)	758 (65.40)	<0.001
Eating Disorder	26 (6.68)	98 (8.46)	0.27
Obsessive-Compulsive Disorder	21 (5.40)	48 (4.14)	0.30
Personality Disorder	9 (2.31)	20 (1.73)	0.46
Schizophrenia	8 (2.06)	6 (0.52)	0.006
Sleep Disorder	66 (16.97)	227 (19.59)	0.25
Self-Injury	19 (4.88)	43 (3.71)	0.31
Suicide Attempt	42 (10.80)	94 (8.11)	0.11
One psychiatric condition	119 (30.59)	698 (60.22)	<0.001
2+ psychiatric conditions	270 (69.41)	461 (39.78)	<0.001

ADHD=Attention-deficit/hyperactivity disorder; n=Number; PG=Anytime during pregnancy; SSRI=Selective serotonin reuptake inhibitor; T0=3 months before conception

Supplementary Figure S1– A) Sample Distribution and B) Plotted Odds of ASD Severity (Defined by ADOS Calibrated Symptom Severity Score) Associated with Maternal Psychiatric Conditions and SSRI Use During Pre-conception and Pregnancy, Study to Explore Early Development, 2002-2006 and 2008-2011 Births

A	ASD Severity Sub-group		
	Severe	Mild/Moderate	POP
	n_{exposed} (%)	n_{exposed} (%)	n_{exposed} (%)
All Mothers^a			
Maternal Psychiatric Condition (Psy Yes vs. Psy No)			
T0	172 (32.76)	276 (34.94)	416 (25.49)
T1	117 (24.89)	176 (25.51)	225 (15.61)
T2	122 (25.68)	182 (2.15)	218 (15.20)
T3	129 (26.76)	194 (27.40)	241 (16.54)
PG	140 (28.40)	208 (28.81)	264 (17.84)
Maternal Psychiatric Condition and No Maternal SSRI Use (Psy Yes + SSRI No vs. Psy No)			
T0	127 (26.46)	202 (28.21)	328 (21.31)
T1	76 (17.72)	103 (16.69)	144 (10.63)
T2	79 (18.29)	111 (17.76)	140 (10.36)
T3	85 (19.41)	121 (19.06)	160 (11.67)
PG	92 (20.67)	131 (20.31)	177 (12.75)
Maternal Psychiatric Condition and Maternal SSRI Use (Psy Yes + SSRI Yes vs. Psy No)			
T0	38 (9.72)	57 (9.98)	70 (5.46)
T1	30 (7.83)	56 (9.82)	63 (4.95)
T2	34 (8.79)	58 (10.14)	64 (5.02)
T3	38 (9.72)	60 (10.45)	67 (5.24)
PG	42 (10.63)	73 (12.44)	81 (6.27)
Restricted to Mothers with Psychiatric Condition^b			
Maternal SSRI Use (Psy Yes + SSRI Yes vs. Psy Yes + SSRI No)			
T0	38 (23.03)	57 (22.01)	70 (17.59)
T1	30 (28.30)	56 (35.22)	63 (30.43)
T2	34 (30.09)	58 (34.32)	64 (31.37)
T3	38 (30.89)	60 (33.15)	67 (29.52)
PG	42 (31.34)	73 (35.78)	81 (31.40)



Adj-OR=Adjusted odds ratio; ASD=Autism spectrum disorder; CI=confidence interval; Multiplex=One or more siblings with ASD; n=Number; PG=Anytime during pregnancy; POP=Population controls; SSRI=Selective serotonin reuptake inhibitor; T0=3 months before conception; T1=Trimester one; T2=Trimester two; T3=Trimester three. ASD Severity was determined ADOS Calibrated Symptom Severity Score (Mild/Moderate, Severe)

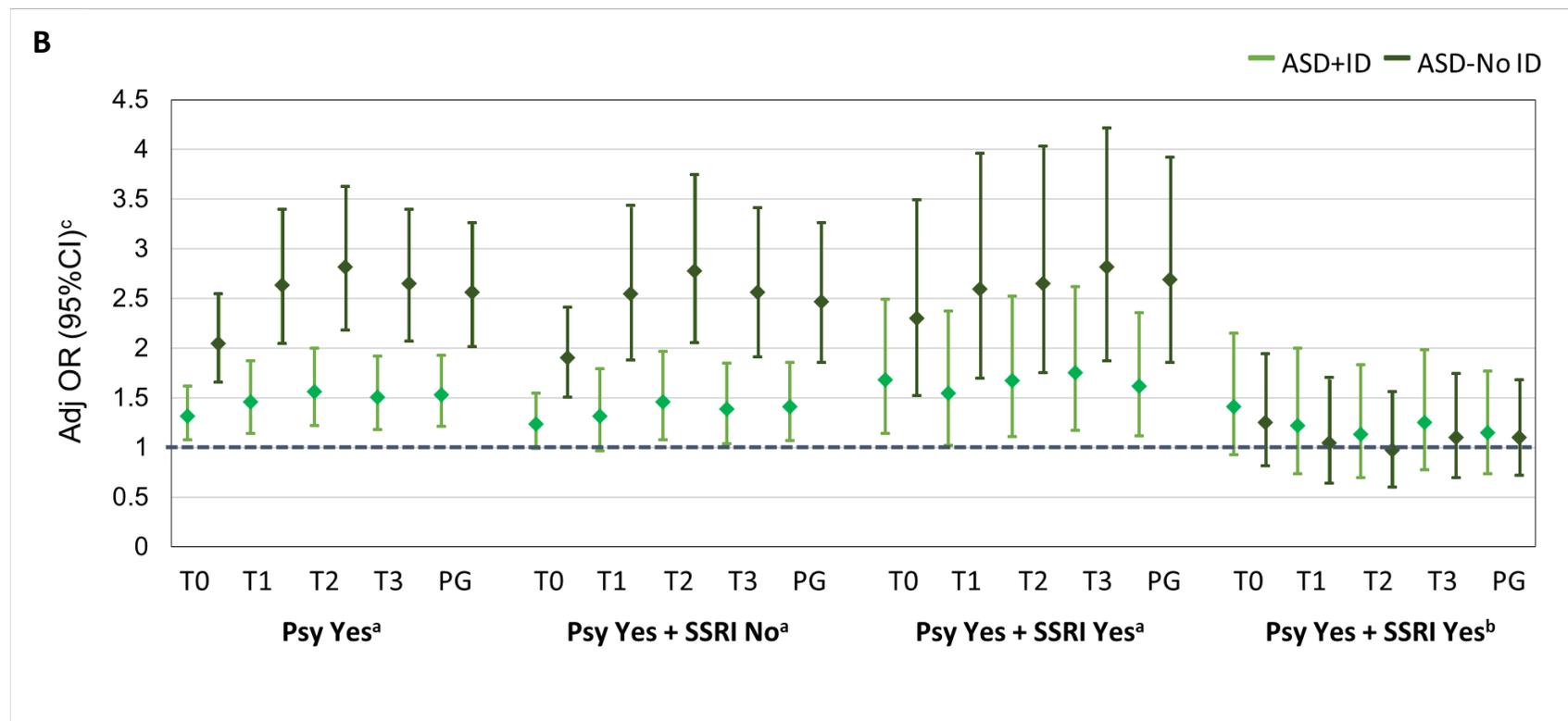
^a Reference group only includes children who were unexposed to both maternal psychiatric condition and SSRIs throughout pre-conception and pregnancy.

^b Reference group only includes children of mothers with an active maternal psychiatric condition during the specific time period and no SSRI exposure throughout pre-conception and pregnancy. Mothers in the reference group included those who used other forms of psychiatric treatment, including non-SSRI medications and therapy.

^c Adjusted ORs were adjusted by the following variables: maternal age (continuous), maternal race, maternal education, family income, and smoking history.

Supplementary Figure S2 – A) Sample Distribution and B) Plotted Odds of ASD with Co-occurring ID Associated with Maternal Psychiatric Conditions and SSRI Use During Pre-conception and Pregnancy, Study to Explore Early Development, 2002-2006 and 2008-2011 Births

A	ASD Sub-group		
	ASD+ID	ASD -No ID	POP
	n_{exposed} (%)	n_{exposed} (%)	n_{exposed} (%)
All Mothers^a			
Maternal Psychiatric Condition (Psy Yes vs. Psy No)			
T0	241 (29.46)	207 (41.65)	416 (25.49)
T1	148 (20.41)	145 (33.33)	225 (15.61)
T2	155 (21.17)	149 (33.94)	218 (15.20)
T3	166 (22.34)	157 (35.12)	241 (16.54)
PG	182 (23.98)	166 (36.40)	264 (17.84)
Maternal Psychiatric Condition and No Maternal SSRI Use (Psy Yes + SSRI No vs. Psy No)			
T0	177 (23.47)	152 (34.39)	328 (21.31)
T1	88 (13.23)	91 (23.88)	144 (10.63)
T2	95 (14.14)	95 (24.68)	140 (10.36)
T3	104 (15.27)	102 (26.02)	160 (11.67)
PG	115 (16.62)	108 (27.14)	177 (12.75)
Maternal Psychiatric Condition and Maternal SSRI Use (Psy Yes + SSRI Yes vs. Psy No)			
T0	54 (8.56)	41 (12.39)	70 (5.46)
T1	45 (7.23)	41 (12.39)	63 (4.95)
T2	49 (7.83)	43 (12.91)	64 (5.02)
T3	52 (8.27)	46 (13.69)	67 (5.24)
PG	60 (9.42)	55 (15.94)	81 (6.27)
Restricted to Mothers with Psychiatric Condition^b			
Maternal SSRI Use (Psy Yes + SSRI Yes vs. Psy Yes + SSRI No)			
T0	54 (23.38)	41 (21.24)	70 (17.59)
T1	45 (33.83)	41 (31.06)	63 (30.43)
T2	49 (34.03)	43 (31.16)	64 (31.37)
T3	52 (33.33)	46 (31.08)	67 (29.52)
PG	60 (34.29)	55 (33.74)	81 (31.40)



Adj-OR=Adjusted odds ratio; ASD=Autism spectrum disorder; CI=confidence interval; n=Number; ID=Intellectual disability; PG=Anytime during pregnancy; POP=Population controls; SSRI=Selective serotonin reuptake inhibitor; T0=3 months before conception; T1=Trimester one; T2=Trimester two; T3=Trimester three

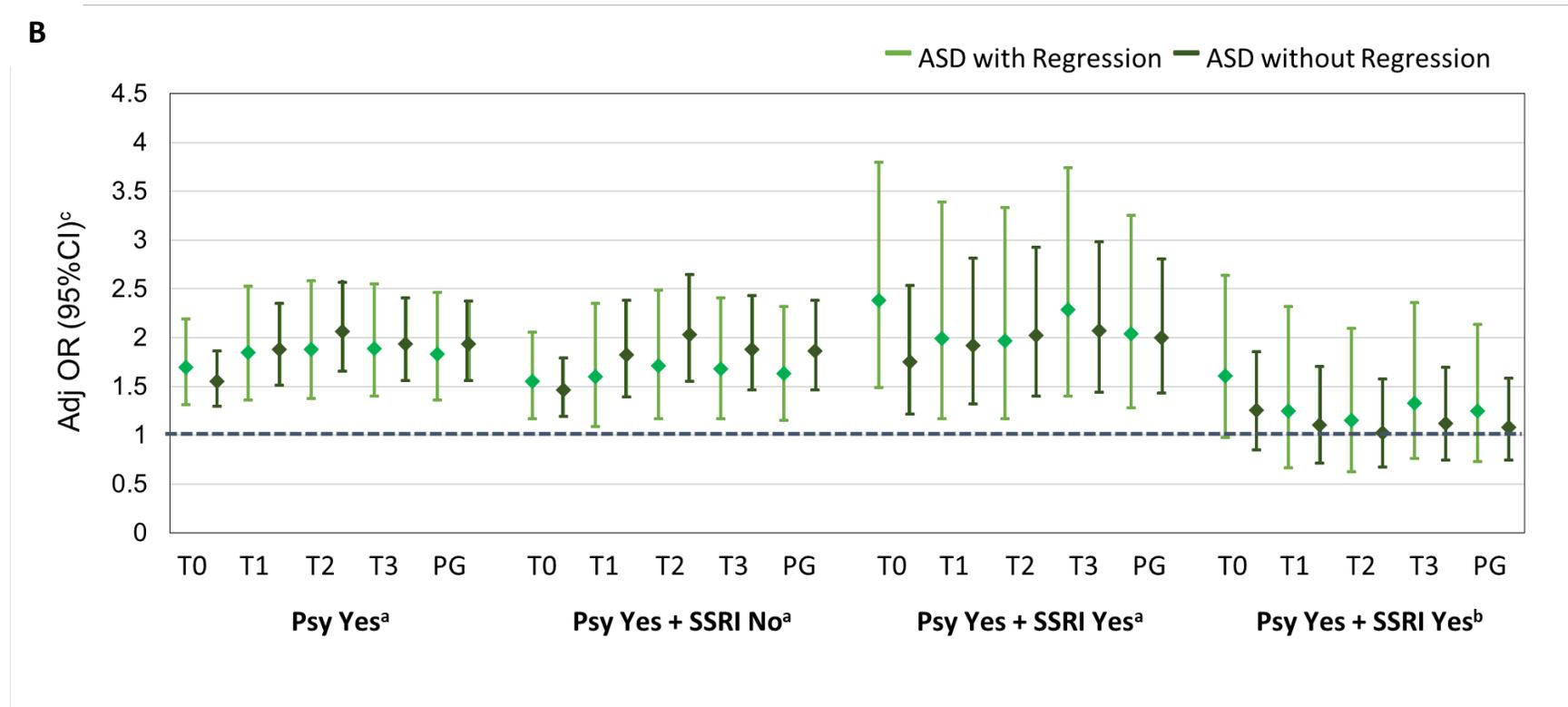
^a Reference group only includes children who were unexposed to both maternal psychiatric condition and SSRIs throughout pre-conception and pregnancy.

^b Reference group only includes children of mothers with an active maternal psychiatric condition during the specific time period and no SSRI exposure throughout pre-conception and pregnancy. Mothers in the reference group included those who used other forms of psychiatric treatment, including non-SSRI medications and therapy.

^c Adjusted ORs were adjusted by the following variables: maternal age (continuous), maternal race, maternal education, family income, and smoking history.

Supplementary Figure S3 – A) Sample Distribution and B) Plotted Odds of ASD with Developmental Regression Associated with Maternal Psychiatric Conditions and SSRI Use During Pre-conception and Pregnancy, Study to Explore Early Development, 2002-2006 and 2008-2011 Births

A	ASD Sub-group		
	Any Regression	No Regression	POP
	n_{exposed} (%)	n_{exposed} (%)	n_{exposed} (%)
All Mothers^a			
Maternal Psychiatric Condition (Psy Yes vs. Psy No)			
T0	134 (36.31)	314 (33.19)	416 (25.49)
T1	82 (25.87)	211 (25.03)	225 (15.61)
T2	81 (25.63)	223 (26.08)	218 (15.20)
T3	89 (27.47)	234 (27.02)	241 (16.54)
PG	94 (28.57)	254 (28.67)	264 (17.84)
Maternal Psychiatric Condition and No Maternal SSRI Use (Psy Yes + SSRI No vs. Psy No)			
T0	97 (29.22)	232 (26.85)	328 (21.31)
T1	48 (16.96)	131 (17.17)	144 (10.63)
T2	50 (17.54)	140 (18.13)	140 (10.36)
T3	55 (18.97)	151 (19.28)	160 (11.67)
PG	59 (20.07)	164 (20.60)	177 (12.75)
Maternal Psychiatric Condition and Maternal SSRI Use (Psy Yes + SSRI Yes vs. Psy No)			
T0	31 (11.65)	64 (9.20)	70 (5.46)
T1	22 (8.56)	64 (9.20)	63 (4.95)
T2	23 (8.91)	69 (9.84)	64 (5.02)
T3	27 (10.31)	71 (10.10)	67 (5.24)
PG	30 (11.32)	85 (11.85)	81 (6.27)
Restricted to Mothers with Psychiatric Condition^b			
Maternal SSRI Use (Psy Yes + SSRI Yes vs. Psy Yes + SSRI No)			
T0	31 (24.22)	64 (21.62)	70 (17.59)
T1	22 (31.43)	64 (32.82)	63 (30.43)
T2	23 (31.51)	69 (33.01)	64 (31.37)
T3	27 (32.93)	71 (31.98)	67 (29.52)
PG	30 (33.71)	85 (34.14)	81 (31.40)



Adj-OR=Adjusted odds ratio; ASD=Autism spectrum disorder; CI=confidence interval; Multiplex=One or more siblings with ASD; n=Number; PG=Anytime during pregnancy; POP=Population controls; Regression = history of developmental regression based on caregiver report of language or social regression on the ADI-R; SSRI=Selective serotonin reuptake inhibitor; T0=3 months before conception; T1=Trimester one; T2=Trimester two; T3=Trimester three

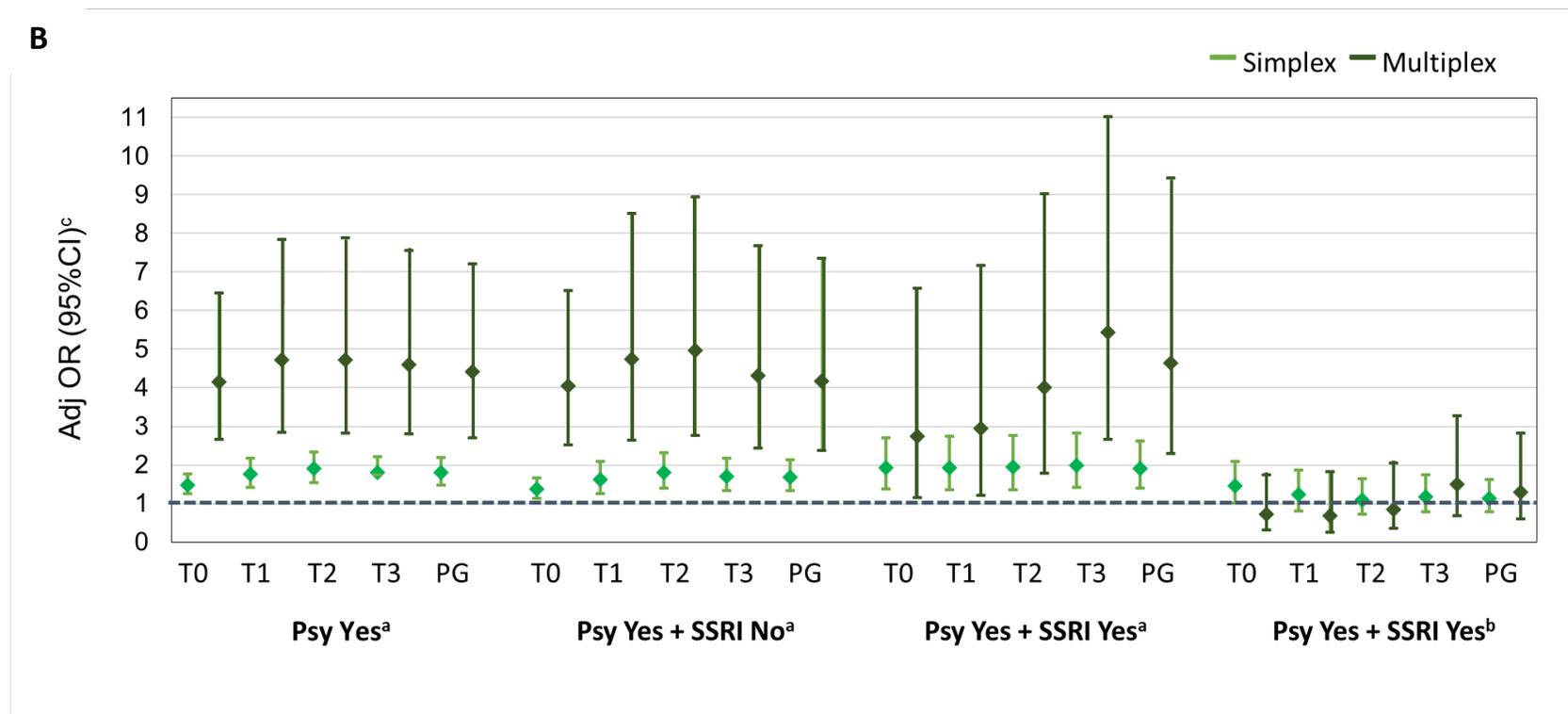
^a Reference group only includes children who were unexposed to both maternal psychiatric condition and SSRIs throughout pre-conception and pregnancy.

^b Reference group only includes children of mothers with an active maternal psychiatric condition during the specific time period and no SSRI exposure throughout pre-conception and pregnancy. Mothers in the reference group included those who used other forms of psychiatric treatment, including non-SSRI medications and therapy.

^c Adjusted ORs were adjusted by the following variables: maternal age (continuous), maternal race, maternal education, family income, and smoking history.

Supplementary Figure S4 – A) Sample Distribution and B) Plotted Odds of ASD by Simplex/Multiplex Subgroups Associated with Maternal Psychiatric Conditions and SSRI Use During Pre-conception and Pregnancy, Study to Explore Early Development, 2002-2006 and 2008-2011 Births

A	ASD Sub-group		
	Any Regression	No Regression	POP
	n_{exposed} (%)	n_{exposed} (%)	n_{exposed} (%)
All Mothers^a			
Maternal Psychiatric Condition (Psy Yes vs. Psy No)			
T0	393 (32.27)	55 (56.70)	416 (25.49)
T1	258 (23.82)	35 (45.45)	225 (15.61)
T2	270 (24.66)	34 (44.74)	218 (15.20)
T3	285 (25.68)	38 (47.50)	241 (16.54)
PG	309 (27.25)	39 (48.15)	264 (17.84)
Maternal Psychiatric Condition and No Maternal SSRI Use (Psy Yes + SSRI No vs. Psy No)			
T0	287 (25.81)	42 (50.00)	328 (21.31)
T1	156 (15.90)	23 (35.38)	144 (10.63)
T2	167 (16.83)	23 (35.38)	140 (10.36)
T3	182 (18.07)	24 (36.36)	160 (11.67)
PG	198 (19.35)	25 (37.31)	177 (12.75)
Maternal Psychiatric Condition and Maternal SSRI Use (Psy Yes + SSRI Yes vs. Psy No)			
T0	88 (9.64)	7 (14.29)	70 (5.46)
T1	79 (8.74)	7 (14.29)	63 (4.95)
T2	83 (9.14)	9 (17.65)	64 (5.02)
T3	85 (9.34)	13 (23.64)	67 (5.24)
PG	102 (11.00)	13 (23.64)	81 (6.27)
Restricted to Mothers with Psychiatric Condition^b			
Maternal SSRI Use (Psy Yes + SSRI Yes vs. Psy Yes + SSRI No)			
T0	88 (23.47)	7 (14.29)	70 (17.59)
T1	79 (33.62)	7 (23.33)	63 (30.43)
T2	83 (33.20)	9 (28.13)	64 (31.37)
T3	85 (31.84)	13 (35.14)	67 (29.52)
PG	102 (34.00)	13 (34.21)	81 (31.40)



Adj-OR=Adjusted odds ratio; ASD=Autism spectrum disorder; CI=confidence interval; Multiplex=One or more siblings with ASD; n=Number; PG=Anytime during pregnancy; POP=Population controls; Simplex=No sibling with ASD; SSRI=Selective serotonin reuptake inhibitor; T0=3 months before conception; T1=Trimester one; T2=Trimester two; T3=Trimester three

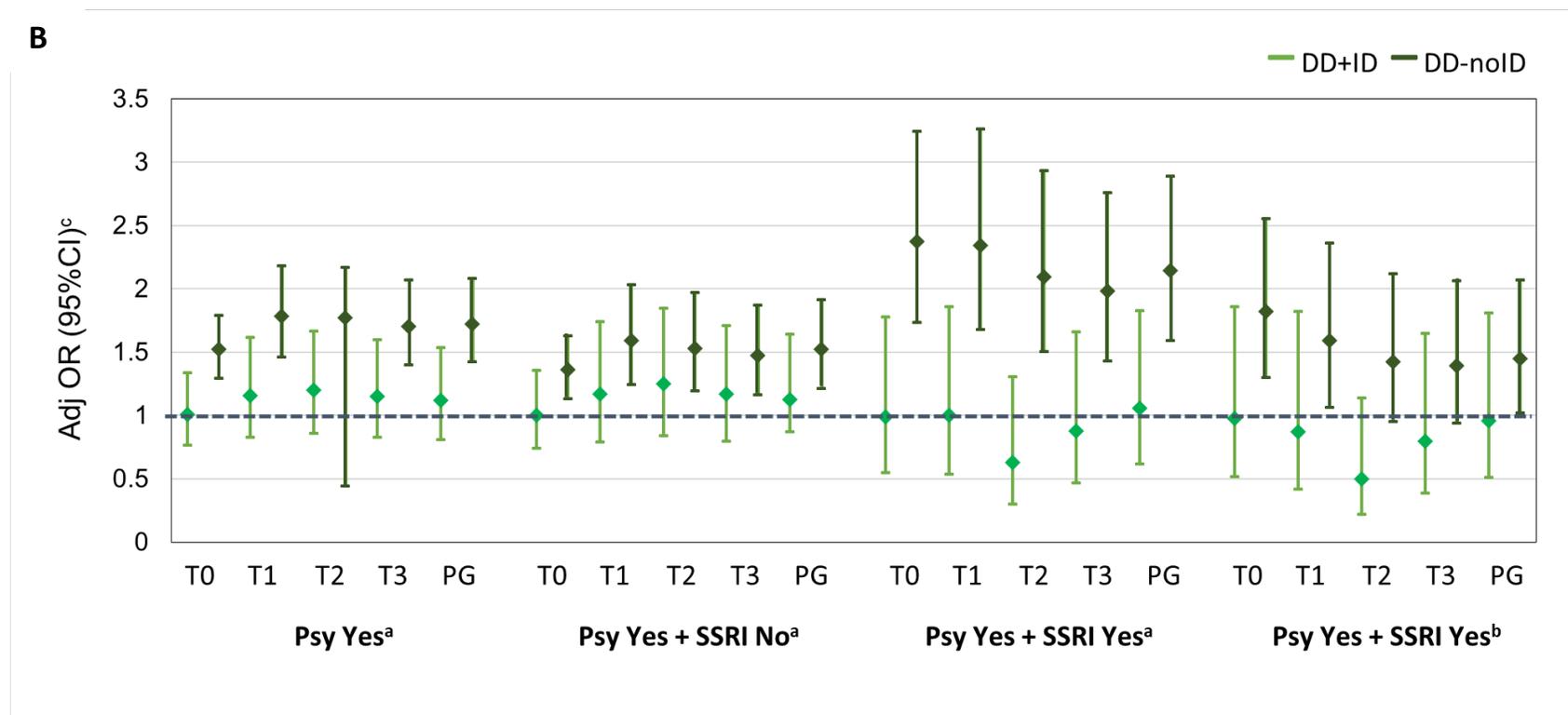
^a Reference group only includes children who were unexposed to both maternal psychiatric condition and SSRIs throughout pre-conception and pregnancy.

^b Reference group only includes children of mothers with an active maternal psychiatric condition during the specific time period and no SSRI exposure throughout pre-conception and pregnancy. Mothers in the reference group included those who used other forms of psychiatric treatment, including non-SSRI medications and therapy.

^c Adjusted ORs were adjusted by the following variables: maternal age (continuous), maternal race, maternal education, family income, and smoking history.

Supplementary Figure S5 – A) Sample Distribution and B) Plotted Odds of DD with Co-occurring ID Associated with Maternal Psychiatric Conditions and SSRI Use During Pre-conception and Pregnancy, Study to Explore Early Development, 2002-2006 and 2008-2011 Births

A	DD Sub-group		
	DD+ID n_{exposed} (%)	DD-No ID n_{exposed} (%)	POP n_{exposed} (%)
All Mothers^a			
Maternal Psychiatric Condition (Psy Yes vs. Psy No)			
T0	95 (26.10)	455 (33.88)	416 (25.49)
T1	63 (18.98)	293 (24.81)	225 (15.61)
T2	64 (19.22)	284 (24.23)	218 (15.20)
T3	67 (19.94)	301 (25.32)	241 (16.54)
PG	71 (20.88)	333 (27.27)	264 (17.84)
Maternal Psychiatric Condition and No Maternal SSRI Use (Psy Yes + SSRI No vs. Psy No)			
T0	74 (21.70)	318 (26.41)	328 (21.31)
T1	43 (13.87)	169 (16.02)	144 (10.63)
T2	45 (14.42)	161 (15.38)	140 (10.36)
T3	47 (14.97)	174 (16.42)	160 (11.67)
PG	50 (15.77)	198 (18.27)	177 (12.75)
Maternal Psychiatric Condition and Maternal SSRI Use (Psy Yes + SSRI Yes vs. Psy No)			
T0	16 (5.65)	121 (12.02)	70 (5.46)
T1	14 (4.98)	106 (10.69)	63 (4.95)
T2	9 (3.26)	95 (9.68)	64 (5.02)
T3	13 (4.64)	96 (9.78)	67 (5.24)
PG	19 (6.64)	126 (12.45)	81 (6.27)
Restricted to Mothers with Psychiatric Condition^b			
Maternal SSRI Use (Psy Yes + SSRI Yes vs. Psy Yes + SSRI No)			
T0	16 (17.78)	121 (27.56)	70 (17.59)
T1	14 (24.56)	106 (38.55)	63 (30.43)
T2	9 (16.67)	95 (37.11)	64 (31.37)
T3	13 (21.67)	96 (35.56)	67 (29.52)
PG	19 (27.54)	126 (38.89)	81 (31.40)



Adj-OR=Adjusted odds ratio; ASD=Autism spectrum disorder; CI=confidence interval; DD=Developmental disorder; ID=Intellectual disability; n=Number; PG=Anytime during pregnancy; POP=Population controls; SSRI=Selective serotonin reuptake inhibitor; T0=3 months before conception; T1=Trimester one; T2=Trimester two; T3=Trimester three

^a Reference group only includes children who were unexposed to both maternal psychiatric condition and SSRIs throughout pre-conception and pregnancy.

^b Reference group only includes children of mothers with an active maternal psychiatric condition during the specific time period and no SSRI exposure throughout pre-conception and pregnancy. Mothers in the reference group included those who used other forms of psychiatric treatment, including non-SSRI medications and therapy.

^c Adjusted ORs were adjusted by the following variables: maternal age (continuous), maternal race, maternal education, family income, and smoking history.