

Supplementary Online Content

Quinn PD, Rickert ME, Weibull CE, et al. Association between maternal smoking during pregnancy and severe mental illness in offspring. *JAMA Psychiatry*. Published online May 3, 2017. doi:10.1001/jamapsychiatry.2017.0456

eTable 1. *International Classification of Diseases (ICD) Codes*

eTable 2. Discordant Cousin and Sibling Samples

eTable 3. Sensitivity Analyses: First-Born Cousins, Additional Outcomes, and Missing Data

eTable 4. Sensitivity Analyses: Population Associations

eFigure. Kaplan-Meier Plots for Bipolar Disorder, Schizophrenia Spectrum Disorders, Severe Mental Illness and Substance Use Disorder, and Any Substance Use Disorder

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

eTable 1. International Classification of Diseases (ICD) Codes

Disorder	ICD-10	ICD-9	ICD-8
Bipolar disorder	F30-F31	296A, 296C-296E, 296W	296.1, 296.3, 296.8
Schizophrenia spectrum disorders	F20-F29	295, 297, 298	295, 297, 298, 299
Substance use disorder	F10-F19, except F17 (tobacco)	291, 292, 303, 304, 305, except 305.1 (tobacco)	291, 303, 304

eTable 2. Discordant Cousin and Sibling Samples

Outcome	Cousins		Siblings	
	Extended Families	Cousin Pairs	Families	Individual Siblings
Any severe mental illness (SMI)	1799	3140	1501	3615
Bipolar disorder	1171	1998	990	2381
Schizophrenia spectrum disorders	786	1393	630	1513
SMI and substance use disorder	795	1456	676	1679

Cousin pairs and siblings discordant on severe mental illness and exposure to maternal smoking during pregnancy.

eTable 3. Sensitivity Analyses: First-Born Cousins, Additional Outcomes, and Missing Data

Sensitivity Analysis	Included n	1. Population HR/OR (95% CI)	2. Adjusted HR/OR (95% CI)	3. Cousin HR/OR (95% CI)	4. Sibling HR/OR (95% CI)
First-born cousins	638 056				
Moderate SDP		1.33 (1.25-1.42)	1.17 (1.09-1.25)	1.11 (0.87-1.40)	--
High SDP		1.66 (1.54-1.79)	1.35 (1.25-1.47)	1.16 (0.85-1.58)	--
Additional Outcomes					
Any substance use disorder	1 680 219				
Moderate SDP		1.69 (1.66-1.73)	1.36 (1.33-1.39)	1.19 (1.15-1.24)	1.03 (0.97-1.09)
High SDP		2.08 (2.03-2.12)	1.50 (1.46-1.53)	1.29 (1.24-1.35)	1.01 (0.94-1.09)
Small for gestational age^{a,b}	1 680 219				
Moderate SDP		2.10 (2.05-2.16)	2.04 (1.98-2.09)	2.11 (1.89-2.34)	1.63 (1.50-1.77)
High SDP		2.78 (2.70-2.86)	2.58 (2.51-2.66)	2.62 (2.29-3.00)	1.83 (1.66-2.02)
Preterm birth^{a,c}	1 679 346				
Moderate SDP		1.25 (1.23-1.28)	1.17 (1.14-1.19)	1.16 (1.07-1.26)	1.13 (1.06-1.20)
High SDP		1.50 (1.47-1.54)	1.36 (1.32-1.39)	1.29 (1.17-1.42)	1.22 (1.13-1.32)
Missing Data					
Missing assumed high SDP	1 789 475				
Moderate SDP		1.25 (1.19-1.30)	1.12 (1.07-1.17)	1.11 (1.02-1.21)	1.03 (0.91-1.17)
High SDP		1.38 (1.33-1.44)	1.19 (1.14-1.24)	1.22 (1.13-1.33)	1.05 (0.94-1.18)
Missing assumed no SDP	1 789 475				
Moderate SDP		1.23 (1.17-1.28)	1.11 (1.06-1.16)	1.08 (1.00-1.18)	1.04 (0.92-1.18)
High SDP		1.49 (1.42-1.56)	1.25 (1.19-1.31)	1.20 (1.09-1.33)	1.09 (0.94-1.26)

“Assumed high SDP” indicates that all missing SDP values were set to high SDP (i.e., the worst case). “Assumed no SDP” indicates all missing values set to no SDP (i.e., the best case). Unless otherwise noted, outcome is any severe mental illness, and estimates are hazard ratios (HRs). CI = confidence interval. SDP = maternal smoking during pregnancy.

^a Estimates are odds ratios (ORs).

^b 41 614 cases (2.48%).

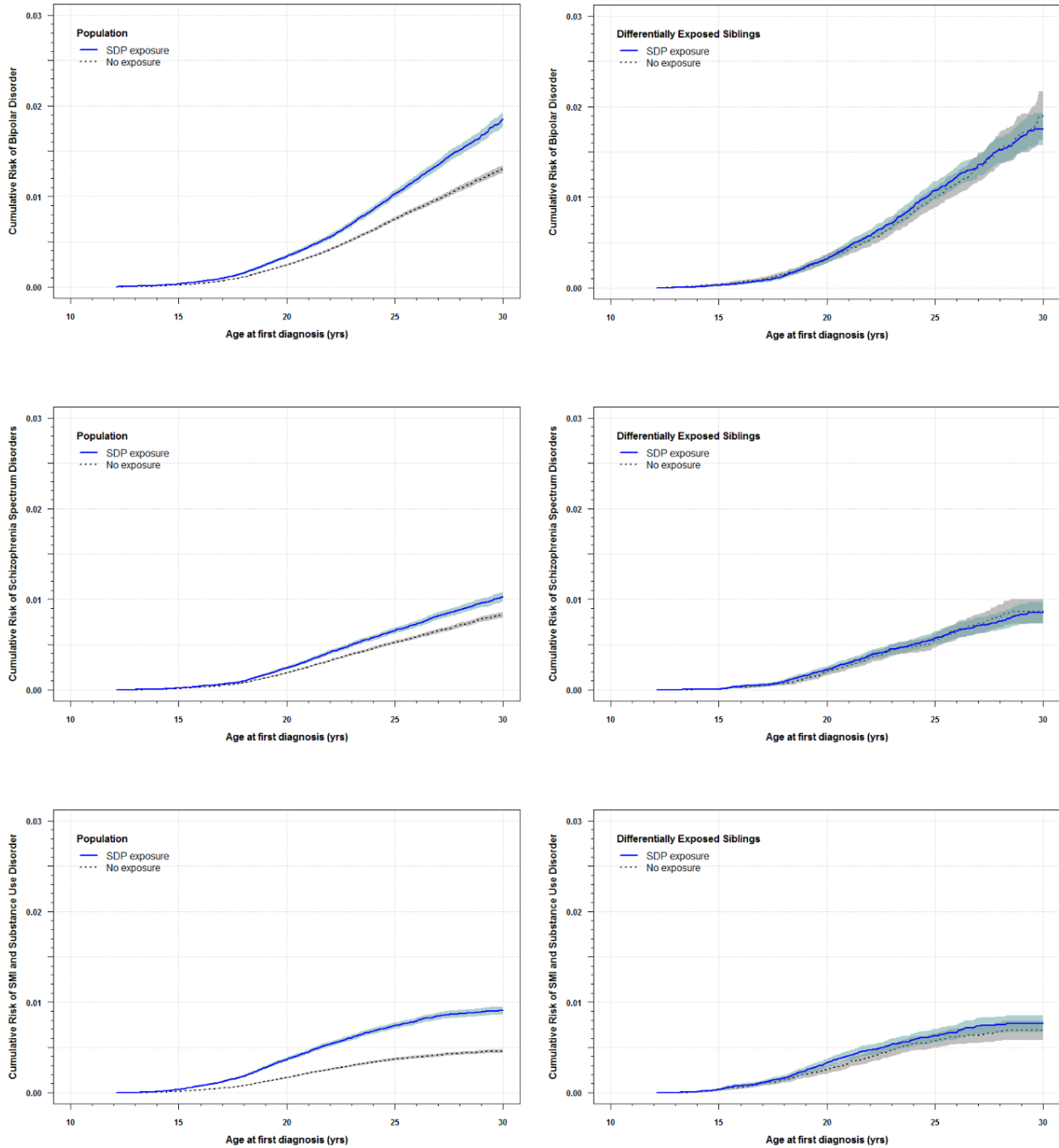
^c 80 712 cases (4.81%).

eTable 4. Sensitivity Analyses: Population Associations

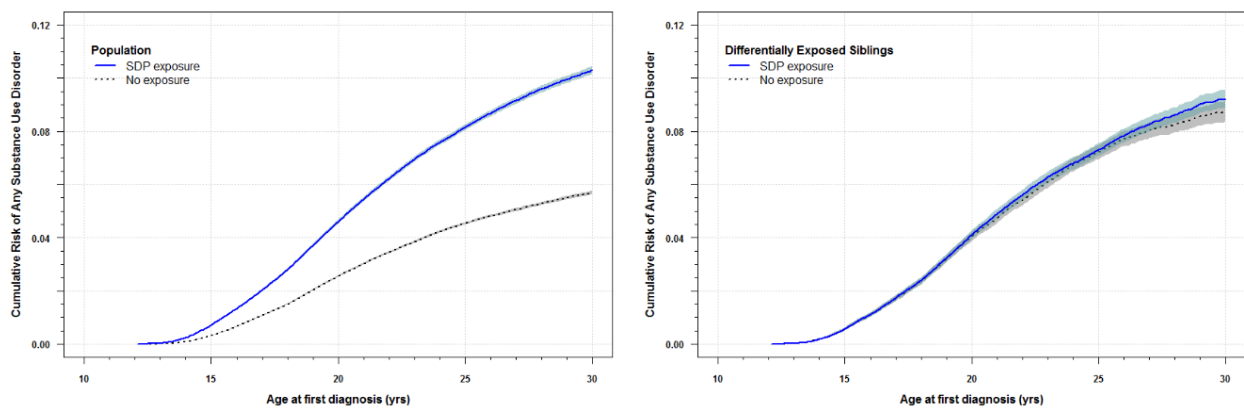
Population	Included n	Moderate SDP HR (95% CI)	High SDP HR (95% CI)
Family size			
Single offspring	434 920	1.17 (1.09-1.27)	1.42 (1.30-1.54)
Multiple offspring	1 245 299	1.27 (1.20-1.34)	1.53 (1.45-1.63)
Birth year			
1983-1991	825 671	1.23 (1.18-1.29)	1.50 (1.43-1.59)
1992-2001	854 548	1.50 (1.36-1.66)	1.82 (1.63-2.05)

Associations are between maternal smoking during pregnancy (SDP) and any offspring severe mental illness. HR = hazard ratio. CI = confidence interval.

eFigure. Kaplan-Meier Plots for Bipolar Disorder, Schizophrenia Spectrum Disorders, Severe Mental Illness and Substance Use Disorder, and Any Substance Use Disorder



eFigure (continued)



Kaplan-Meier estimates of cumulative risk (i.e., proportion diagnosed) by age among those with and without any smoking during pregnancy (SDP) exposure. Left panels include full cohort; right panels include siblings discordant for SDP exposure only. Shaded areas are pointwise 95% confidence intervals. SMI = severe mental illness.