

Electronic Supplementary Material for the Article ‘Antidepressant use during pregnancy and risk of congenital heart defects: a case-time-control

Yuelian Sun <sup>a,b\*</sup>, Lars Henning Pedersen <sup>c</sup>, Chun Sen Wu <sup>d,e</sup>, Irene Petersen <sup>a,f</sup>, Henrik Toft Sørensen <sup>a</sup>, Jørn Olsen <sup>a,g</sup>

<sup>a</sup> Department of Clinical Epidemiology, Department of Clinical Medicine, Aarhus University Hospital, Aarhus, Denmark

<sup>b</sup> Department of Neurology, Department of Clinical Medicine, Aarhus University Hospital, Aarhus, Denmark

<sup>c</sup> Department of Obstetrics and Gynecology, Department of Clinical Medicine, Aarhus University Hospital, Aarhus, Denmark

<sup>d</sup> Research Unit of Gynecology and Obstetrics, Institute of Clinical Research, University of Southern Denmark, Odense, Denmark

<sup>e</sup> Department of Obstetrics & Gynecology, Odense University Hospital, Odense, Denmark

<sup>f</sup> Department of Primary Care and Population Health, University College London, London, UK

<sup>g</sup> Department of Epidemiology, Fielding School of Public Health, University of California, Los Angeles (UCLA), Los Angeles, California, USA

\* Correspondence to:

Yuelian Sun

Email: [ys@clin.au.dk](mailto:ys@clin.au.dk)

Address: Olof Palmes Allé 43-45, DK-8200 Aarhus N, Denmark (where the work was done);  
current address: Fuglesangs Allé 4, DK-8210 Aarhus V, Denmark

Table 1. Anatomical Therapeutical Chemical (ATC) codes used to identify antidepressants

Antidepressants	ATC codes
Antidepressants	N06A
Selective serotonin reuptake inhibitors (SSRIs)	N06AB03-10
Fluoxetine	N06AB03
Citalopram	N06AB04
Paroxetine	N06AB05
Sertraline	N06AB06
Escitalopram	N06AB10
Serotonin-norepinephrine reuptake inhibitors (SNRIs)	N06AX16 and N06AX21
Venlafaxine	N06AX16
Tricyclic antidepressants	N06AA02-7, N06AA09-12, N06AA16-17, and N06AA21
Others	N06AF01, N06AG02, N06AX03, N06AX06, N06AX11-12, and N06AX18

Table 2. International Classification of Diseases, tenth revision (ICD10) codes used to identify heart defects according to the categories used in the paper by Louik C (24)

Heart defects	ICD10 codes
Any heart defect	Q20-Q26 (Q2111, Q250, Q2541, Q256 if gestational age <37 weeks, and Q261 were excluded)
Looping defects	DQ204, DQ205
Conotruncal and major arch defects	DQ200, DQ201, DQ203, and DQ213, DQ254
Atrioventricular canal and septal defects	DQ212
Right ventricular outflow tract obstruction	DQ220-226, DQ229, DQ243, DQ255-257
Left ventricular outflow tract obstruction	DQ230-234, DQ238-239, DQ242, DQ258, DQ251, DQ253, DQ254
Septal defects	DQ210, DQ211, DQ219
Ventricular septal defects	DQ210
Atrial septal defects	DQ211
Anomalous pulmonary venous return	DQ262-263

Table 3. Characteristics of cases and controls in the study population of the case-time-control and the cohort design

	Case-time-control design								Cohort design			
	Participants with discordant information on maternal use of AD in the risk and reference periods <sup>a</sup>				Participants with accordant information on maternal use of AD in the risk and reference periods <sup>a</sup>				Cases		Controls	
	Cases		Controls		Cases		Controls		No.	%	No.	%
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Sex of the child												
Boys	47	53.4	2,677	52.5	34	42.0	1,912	51.7	5,480	52.0	401,277	51.3
Girls	41	46.6	2,424	47.5	47	58.0	1,787	48.3	5,052	48.0	380,876	48.7
Gestational age												
Preterm	15	17.0	372	7.3	13	16.0	367	9.9	1,208	11.5	37,772	4.8
Term	68	77.3	4,427	86.8	68	84.0	3,243	87.7	8,597	81.6	685,179	87.6
Postterm	5	5.7	302	5.9	0 <sup>b</sup>	0	89	2.4	727	6.9	59,202	7.6
Maternal age at the birth (years)												
<25	20	22.7	832	16.3	9	11.1	380	10.3	1,538	14.6	108,133	13.8
25-29	28	31.8	1,564	30.7	13	16.0	1,057	28.6	3,618	34.4	274,015	35.0
30-35	22	25.0	1,617	31.7	37	45.7	1,384	37.4	3,681	35.0	275,008	35.2
35-39	15	17.0	889	17.4	16	19.8	747	20.2	1,454	13.8	107,669	13.8
40+	3	3.4	199	3.9	6	7.4	131	3.5	241	2.3	17,328	2.2
Parity												
1 child	40	45.5	2,147	42.1	29	35.8	1,639	44.3	4,750	45.1	336,195	43.0
2 children	28	31.8	1,612	31.6	32	39.5	1,277	34.5	3,657	34.7	293,372	37.5
3+ children	20	22.7	1,342	26.3	20	24.7	783	21.2	2,125	20.2	152,553	19.5
Maternal education at the birth												
Primary	32	36.4	1,757	34.4	23	28.4	968	26.2	2,371	22.5	157,025	20.1
Medium	40	45.5	2,035	39.9	38	46.9	1,460	39.5	4,450	42.3	334,158	42.7

High	16	18.2	1,198	23.5	20	24.7	1,220	33.0	3,529	33.5	275,600	35.2
Missing	0	0	111	2.2	0 <sup>b</sup>	0	51	1.4	182	1.7	15,370	2.0
Maternal civil status												
Married	34	38.6	2,315	45.4	43	53.1	1,805	48.8	5,879	55.8	449,693	57.5
Cohabitant	45	51.1	2,370	46.5	30	37.0	1,623	43.9	4,162	39.5	300,788	38.5
Others	9	10.2	404	7.9	8	9.9	262	7.1	468	4.4	29,516	3.8
Family income (quantiles)												
Low	32	36.4	1,839	36.1	18	22.2	977	26.4	2,774	26.3	195,399	25.0
Low-medium	23	26.1	1,300	25.5	26	32.1	859	23.2	2,648	25.1	195,523	25.0
Medium-high	24	27.3	1,082	21.2	16	19.8	953	25.8	2,591	24.6	195,579	25.0
High	9	10.2	880	17.3	21	25.9	910	24.6	2,519	23.9	195,652	25.0
Maternal depression												
No	71	80.7	4,153	81.4	49	60.5	2,636	71.3	10,345	98.2	773,025	98.8
Yes	17	19.3	948	18.6	32	39.5	1,063	28.7	187	1.8	9,128	1.2
Maternal antiepileptic medication use in the first three months of pregnancy												
No	88	100	5,012	98.3	81	100	3,615	97.7	10,465	99.4	779,553	99.7
Yes	0 <sup>b</sup>	0	89	1.7	0 <sup>b</sup>	0	84	2.3	67	0.6	2,600	0.3
Calendar year												
1995-1999	6	6.8	703	13.8	5	6.2	235	6.4	2,893	27.5	235,205	30.1
2000-2004	35	39.8	1,898	37.2	30	37.0	1,258	34.0	4,297	40.8	304,491	38.9
2005-2009	47	53.4	2,500	49	46	56.8	2,206	59.6	3,342	31.7	242,457	31.0

a: Risk period: gestational months 1-3; Reference period: gestational months 5-7; AD: antidepressant

b: The number of participants in the cell is less than 3. We categorized them in the group next to the cell to protect privacy of participants.