

Supplementary Online Content

Razaz N, Tedroff K, Villamor E, Cnattingius S. Maternal body mass index in early pregnancy and risk of epilepsy in offspring. *JAMA Neurol*. Published online April 3, 2017. doi:10.1001/jamaneurol.2016.6130

eTable 1. ICD-10 Codes for Maternal, Neonatal, and Childhood Diseases

eTable 2. Incidence Rates and Hazard Ratios of Epilepsy in Children According to Maternal Characteristics

eTable 3. Incidence Rates and Hazard Ratios of Epilepsy According to Maternal and Neonatal Complications

eTable 4. Early Pregnancy Body-Mass Index and Rates of Epilepsy in Children Without Cerebral Palsy

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

eTable 1. ICD-10 Codes for Maternal, Neonatal, and Childhood Diseases.

Diseases	ICD-10 codes
Epilepsy*	G40, G41
Maternal complications**	
Pre-gestational hypertension [†]	I10 to I15, O10 and O11
Preeclampsia and eclampsia	O14 and O15
Pregestational diabetes	E10 to E14, O24.0 to O24.3
Gestational diabetes	O24.4
Maternal infection	A00-B99, G00-G07; I00-I02; I32.0; I33, I38; I40.0; J00-J06; J10-J18; J20-J22; J36; J39.0; J85.1; J86; K35-K37; K57.0; K57.2; K57.4; K57.8; K61; K63.0; K65.0; K65.9; K67; K75.0; K75.1; K80.0; K80.3; K80.4; K81.0; K81.9; K83.0; L00-L03; L05-L08; M00; M01; M86; N10; N12; N15.1; N30; N39.0; N41; N45; N70-N77; O23
Chorioamnionitis	O411, O4110, O411A, O411B, O411C, O411X
Neonatal complications[‡]	
Neonatal infections [¶]	P77.9, P35 to P39
Asphyxia-related neonatal complications	
Meconium aspiration	P24.0
Hypoxic ischemic encephalopathy and related conditions	P91.0, P91.3 to P91.6, P91.8 to P91.9
Convulsions/seizures	P90
Hypoglycemia	P70
Jaundice	P55-P59
Respiratory distress	P20, P22, P24-P28
Birth asphyxia	P21
Birth Trauma	P10-P15
Congenital malformations	
Any malformation	Q00 to Q99, excluding minor malformations as defined by the Swedish National Board of Health and Welfare [‡] : Q17.0, Q17.5, Q18.0, Q18.1, Q25.0, Q27.0, Q31.5, Q32.0, Q52.3, Q53.0 to Q53.9, Q66.5 to Q66.9, Q69.0 to Q69.9, Q70.0 to Q70.9, Q76.0, Q79.9, Q82.5, and Q82.9
Chromosomal abnormalities	Q90 to Q93, Q95 to Q99
Circulatory system malformations	Q20 to Q28, excluding Q25.0 and Q27.0
Nervous system malformations	Q00 to Q07

Diseases were defined using the Swedish version of the International classification of Diseases, tenth revision (ICD-10).

*A case of epilepsy was identified if it met any of the following conditions between 1997 and 2012: A) An occurrence of ≥ 2 ICD-10 codes G40 and/or G41 (epilepsy and status epilepticus, respectively) on separate dates; *or* B) An occurrence of ≥ 1 ICD-10 code R56 (convulsions not elsewhere classified) *and* ≥ 1 ICD-10 codes G40 and/or G41 on separate dates; diagnosis of R56 had to precede that of G40 and/or G41.^{25,26}

** Maternal diseases, other than maternal epilepsy, were identified from ICD-10 codes from the Medical Birth Register.

† Definition of pre-gestational hypertension also included self-reported information at the first antenatal visit.

‡ Neonatal diseases were identified from ICD-10 codes from the Medical Birth Register and the National Patient Register.

§ Information on infections was restricted to the first 28 days of life.

¶ ICD-10 codes of minor malformations are available at

<http://www.socialstyrelsen.se/register/halsodataregister/medicinskafodelsregistret/Documents/diagnoser-som-inte-ska-rapporteras.pdf>

eTable 2. Incidence Rates and Hazard Ratios of Epilepsy in Children According to Maternal Characteristics. Live-born singleton children in Sweden 1997-2011.

Characteristic	Number of children	Child-years of follow-up	Epilepsy		Adjusted hazard ratio (95% CI)*
			n	Rate per 10,000 child-yr	
Total	1,421,551	11,176,386	7592	6.79	
Maternal age (years)					
≤19	24,611	200166	128	6.39	0.77 (0.63 to 0.93)
20-24	18357	1,519965	1101	7.24	1.00
25-29	440836	3,617805	2441	6.75	0.97 (0.90 to 1.05)
30-34	491274	3820511	2502	6.55	0.96 (0.88 to 1.04)
≥35	276473	2,017939	1420	7.04	0.98 (0.89 to 1.07)
P, trend†					0.82
Country of birth					
Nordic	1,167513	9391891	6434	6.85	1.00
Non-Nordic	253267	1775760	1154	6.50	1.15 (1.07 to 1.24)
Data missing	771	8735	4	4.58	
P†					<0.001
Education (years)					
≤9	136691	1037194	845	8.15	1.28 (1.17 to 1.41)
10-11	222905	2143013	1605	7.49	1.25 (1.16 to 1.34)
12	365852	2769496	1851	6.68	1.06 (0.99 to 1.14)
13-14	197955	1662957	1080	6.49	1.07 (1.00 to 1.16)
≥15	479194	3496421	2153	6.18	1.00
Data missing	18954	77305	58	7.50	
P, trend†					<0.001
Mother cohabits with partner					
Yes	1,274479	10003942	6671	6.67	1.00
No	74,661	548319	495	9.03	1.27 (1.15 to 1.40)
Data missing	72,411	624125	426	6.83	
P					<0.001
Parity					
1	627772	4876638	3363	6.90	1.00
2	523127	4123730	2692	6.53	0.95 (0.90 to 1.01)

3	190068	1527441	1018	6.66	0.96 (0.89 to 1.04)
≥4	80584	648577	519	8.00	1.11 (1.00 to 1.24)
P, trend					0.66
Maternal height (cm)					
≤159	184470	1423080	998	7.01	1.02 (0.94 to 1.10)
160-164	357202	2811783	1925	6.84	1.02 (0.95 to 1.09)
165-169	409787	3241051	2191	6.79	0.98 (0.92 to 1.04)
≥170	444300	3486784	2310	6.63	1.00
Data missing	25792	213689	169	7.91	
P, trend					0.27
Year of delivery					
1997-1999	248949	3495773	2101	6.01	0.94 (0.88 to 0.99)
2000-2004	541273	4575776	3173	6.93	1.00
2005-2008	400694	2331142	1706	7.32	1.01 (0.95 to 1.08)
2009-2011	320635	773695	612	7.91	0.89 (0.81 to 0.98)
P					0.80
Smoking					
No	1220555	9406877	6253	6.65	1.00
Yes	133622	1188011	927	7.80	1.07 (0.99 to 1.16)
Data missing	67374	581498	412	7.09	
P					0.08

Footnotes to eTable 2

*Hazard ratios and 95% confidence intervals from Cox proportional hazards models with robust estimates of variance. Covariates included adjusted for maternal age, country of origin, education level, cohabitation with a partner, parity, height, smoking during pregnancy, maternal epilepsy and year of delivery. N denotes sample size for complete case analyses including only women with non-missing values in all covariates.

Complete case analyses including 6422 cases among 1,228,641 children.

† Wald test when a variable representing ordinal categories of the predictor was introduced into the regression model as a continuous covariate.

eTable 3. Incidence Rates and Hazard Ratios of Epilepsy According to Maternal and Neonatal Complications. Live-born singleton children born at term in Sweden 1997-2011.

Characteristic	Epilepsy		Unadjusted hazard ratio (95% CI)*	Adjusted hazard ratio (95% CI)**
	n	Rate per 10,000 child-years		
Maternal diseases and pregnancy complications				
Maternal epilepsy				
No	6720	6.36	1.00	1.00
Yes	82	28.2	4.30 (3.44 to 5.38)	4.21 (3.35 to 5.30)
P†			<0.001	<0.001
Diabetic disease				
No	6700	6.41	1.00	1.00
Gestational diabetes	71	7.66	1.18 (0.94 to 1.50)	1.25 (0.98 to 1.58)
Pregestational diabetes	31	8.24	1.28 (0.90 to 1.82)	1.28 (0.88 to 1.85)
P			0.14	0.09
Hypertensive disease				
No	6586	6.40	1.00	1.00
Pregestational hypertension	31	5.97	0.91 (0.64 to 1.30)	0.86 (0.59 to 1.25)
Preeclampsia	185	7.49	1.17 (1.01 to 1.36)	1.11 (0.95 to 1.30)
P			0.09	0.31
Chorioamnionitis				
No	6793	6.42	1.00	1.00
Yes	9	7.25	1.30 (0.59 to 2.16)	1.19 (0.62 to 2.29)
P			0.71	0.60
Maternal infections				
No	6752	6.41	1.00	1.00
Yes	50	8.33	1.30 (0.98 to 1.71)	1.30 (0.98 to 1.74)
P			0.07	0.07
Birth characteristics and neonatal complications				
Mode of delivery				
Vaginal non-instrumental	4995	6.01	1.00	1.00
Vaginal instrumental	547	6.72	1.11 (1.02 to 1.22)	1.11 (1.01 to 1.22)
Elective cesarean section	563	8.23	1.35 (1.40 to 1.48)	1.33 (1.21 to 1.46)
Emergency cesarean section	644	8.81	1.45 (1.34 to 1.58)	1.43 (1.31 to 1.56)
P, trend†			<0.001	<0.001
Newborn's sex				
Male	3626	6.67	1.00	1.00
Female	3176	6.16	0.92 (0.88 to 0.97)	0.92 (0.87 to 0.96)
P			0.001	0.0005

Characteristic	Epilepsy		Unadjusted hazard ratio (95% CI)*	Adjusted hazard ratio (95% CI)**
	n	Rate per 10,000 child-years		
Birth weight for gestational age (percentiles)				
<3	210	15.7	2.55 (2.22 to 2.93)	2.46 (2.13 to 2.58)
3 to <10	399	8.38	1.36 (1.22 to 1.50)	1.25 (1.12 to 1.40)
10 to 90	5327	6.17	1.00	1.00
>90 to 97	572	6.01	0.98 (0.90 to 1.06)	0.99 (0.91 to 1.08)
>97	294	7.36	1.20 (1.06 to 1.35)	1.17 (1.03 to 1.32)
P, trend			<0.001	<0.001
Birth Trauma				
No	6620	6.38	1.00	1.00
Yes	182	8.44	1.34 (1.16 to 1.55)	1.28 (1.10 to 1.50)
P			<0.001	0.002
Congenital malformations				
Any malformations				
No	5442	5.44	1.00	1.00
Yes	1360	23.0	4.23 (3.98 to 4.49)	4.18 (3.92 to 4.44)
P			<0.001	<0.001
Chromosomal abnormalities				
No	6528	6.18	1.00	1.00
Yes	2941	124.7	20.1 (17.1 to 22.8)	20.2 (17.8 to 23.1)
P			<0.001	<0.001
Circulatory malformations				
No	6445	6.19	1.00	1.00
Yes	357	20.3	3.24 (2.91 to 3.61)	3.20 (2.86 to 3.58)
P			<0.001	<0.001
Nervous system malformations				
No	6303	5.96	1.00	1.00
Yes	499	298.0	49.8 (45.2 to 54.8)	48.3 (43.6 to 53.5)
P			<0.001	<0.001
Asphyxia-related neonatal complications				
Meconium aspiration				
No	6764	6.39	1.00	1.00
Yes	38	29.5	4.61 (3.35 to 6.35)	4.16 (2.93 to 5.90)
P			<0.001	<0.001
Hypoxic ischemic encephalopathy and related conditions				
No	6568	6.21	1.00	1.00
Yes	234	165.8	26.5 (23.2 to 30.3)	26.3 (22.8 to 30.3)
P			<0.001	<0.001

Characteristic	Epilepsy		Unadjusted hazard ratio (95% CI)*	Adjusted hazard ratio (95% CI)**
	n	Rate per 10,000 child-years		
Neonatal convulsions/seizures				
No	6434	6.08	1.00	1.00
Yes	368	228.0	33.4 (33.4 to 41.5)	35.7 (31.7 to 40.1)
P			<0.001	<0.001
Birth Asphyxia				
No	6494	6.19	1.00	1.00
Yes	308	31.8	5.17 (4.61 to 5.80)	5.03 (4.45 to 5.69)
P			<0.001	<0.001
Apgar score at 5 minutes				
7 – 10	6434	6.16	1.00	1.00
4 – 6	186	30.2	4.89 (4.22 to 5.66)	4.89 (4.20 to 5.70)
0 – 3	110	83.1	13.6 (11.3 to 16.5)	13.1 (10.6 to 16.0)
Data missing	72	11.5		
P, trend			<0.001	<0.001
Other neonatal complications				
Neonatal infections				
No	6613	6.32	1.00	1.00
Yes	189	14.2	2.26 (1.95 to 2.62)	2.21 (1.90 to 2.58)
P			<0.001	<0.001
Neonatal hypoglycemia				
No	6486	6.26	1.00	1.00
Yes	316	14.2	2.27 (2.02 to 2.54)	2.22 (1.97 to 2.50)
P			<0.001	<0.001
Neonatal Jaundice				
No	6600	6.39	1.00	1.00
Yes	202	7.96	1.24 (1.08 to 1.43)	1.23 (1.06 to 1.42)
P			0.003	0.007
Respiratory distress				
No	6483	6.25	1.00	1.00
Yes	319	14.9	2.38 (2.13 to 2.66)	2.34 (2.08 to 2.63)
P			<0.001	<0.001

Footnotes to eTable 3

* From unadjusted Cox proportional hazards models. Robust estimates of the variance were calculated to account for women who delivered more than once during the study period.

**Hazard ratios and 95% confidence intervals from Cox proportional hazards models with robust estimates of variance. Covariates included adjusted for maternal age, country of origin, education level, cohabitation with a partner, parity, height, smoking during pregnancy, maternal epilepsy and year of delivery.

† Wald test when a variable representing ordinal categories of the predictor was introduced into the regression model as a continuous covariate.

‡ Wald χ^2 test

eTable 4. Early Pregnancy Body-Mass Index and Rates of Epilepsy in Children Without Cerebral Palsy.

Maternal BMI (kg/m ²)	Children without cerebral palsy		
	n	Rate per 10,000 child-yr	Adjusted HR (95% CI)* n = 1,226,085
Total			
<18.5	134	5.59	1.00 (0.84 to 1.20)
18.5 to <25	3387	5.50	1.00
25 to <30	1499	6.18	1.09 (1.02 to 1.16)
30 to <35	510	6.90	1.18 (1.07 to 1.30)
35 to <40	161	7.51	1.27 (1.08 to 1.50)
≥40	72	10.1	1.68 (1.31 to 2.14)
Missing	820	6.25	
P, trend [†]			<0.001

*Hazard ratios and 95% confidence intervals from Cox proportional hazards models with robust estimates of variance. Covariates included adjusted for maternal age, country of origin, education level, cohabitation with a partner, parity, height, smoking during pregnancy, maternal epilepsy and year of delivery. N denotes sample size for complete case analyses including only women with non-missing values in all covariates.

[†] Wald test when a variable representing ordinal categories of BMI was introduced into the model as a continuous covariate.