

Supplementary Online Content

Qiu C, Lin JC, Shi JM, et al. Association between epidural analgesia during labor and risk of autism spectrum disorders in offspring. *JAMA Pediatr*. Published online October 12, 2020. doi:10.1001/jamapediatrics.2020.3231

eTable 1. Characteristics of the Cohort at the Time of the Index Pregnancy

eTable 2. Associations Between Labor Epidural Analgesia (LEA) Use at Delivery and Risk of Autism Spectrum Disorders (ASD) in Offspring (Randomly Select One Child per Family)

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

eTable 1. Characteristics of the Cohort at the Time of the Index Pregnancy

	Before Weighting			After Weighting		
	LEA unexposed	LEA Exposed	SMD*	LEA unexposed	LEA Exposed	SMD*
Characteristics:	N=38176	N= 109719		N=38311	N=109664	
Mean (SD) or N (%)						
Maternal Characteristics						
Age at delivery	30.6 (5.5)	29.8 (5.6)	0.132	30.1 (5.5%)	30.0 (5.6%)	0.014
Race/Ethnicity (%)			0.155			0.018
Non-Hispanic white	8292 (21.7%)	29149 (26.6%)		10003 (26.1%)	27869 (25.4%)	
Non-Hispanic black	2749 (7.2%)	8231 (7.5%)		2860 (7.5%)	8167 (7.4%)	
Hispanic	21591 (56.6%)	53878 (49.1%)		19185 (50.1%)	55801 (50.9%)	
Asian/Pacific Islanders	4679 (12.3%)	15546 (14.2%)		993 (2.6%)	2813 (2.6%)	
Others	865 (2.3%)	2915 (2.7%)		5270 (13.8%)	15014 (13.7%)	
Parity (%)			0.406			0.012
0	8821 (23.1%)	39362 (35.9%)		12254 (32.0%)	35679 (32.5%)	
1	13293 (34.8%)	33891 (30.9%)		12359 (32.3%)	35011 (31.9%)	
≥2	13349 (35%)	22962 (20.9%)		9466 (24.7%)	26948 (24.6%)	
Unknown	2713 (7.1%)	13504 (12.3%)		4232 (11.0%)	12026 (11.0%)	
Education (%)			0.115			0.023
≤High school	13152 (34.5%)	31995 (29.2%)		11341 (29.6%)	33326 (30.4%)	
Some College	10988 (28.8%)	34343 (31.3%)		14875 (38.8%)	41418 (37.8%)	
College and Post grade	13547 (35.5%)	42108 (38.4%)		11648 (30.4%)	33612 (30.6%)	
Unknown	489 (1.3%)	1273 (1.2%)		447 (1.2%)	1308 (1.2%)	
Household income (%)			0.144			0.017
< \$30,000	1116 (2.9%)	2457 (2.2%)		916 (2.4%)	2645 (2.4%)	
\$30,000 - \$49,999	10453 (27.4%)	25233 (23%)		9066 (23.7%)	26407 (24.1%)	
\$50,000 - \$69,999	12787 (33.5%)	35652 (32.5%)		12379 (32.3%)	35862 (32.7%)	
\$70,000 - \$89,999	7835 (20.5%)	24884 (22.7%)		8623 (22.5%)	24304 (22.2%)	
≥ \$90,000	5985 (15.7%)	21493 (19.6%)		7327 (19.1%)	20446 (18.6%)	
History of comorbidity (%)	5498 (14.4%)	19056 (17.4%)	0.081	6324 (16.5%)	18220 (16.6%)	0.003
Diabetes during pregnancy (%)			0.053			0.004
Gestational diabetes	3172 (8.3%)	8663 (7.9%)		34348 (89.7%)	98200 (89.5%)	

Pre-gestational diabetes	726 (1.9%)	2934 (2.6%)		3012 (7.9%)	8749 (8.0%)	
Smoking during pregnancy (%)	188 (0.5%)	939 (0.9%)	0.044	951 (2.5%)	2715 (2.5%)	
Pre-eclampsia/eclampsia (%)	823 (2.2%)	3777 (3.4%)	0.078	279 (0.7%)	833 (0.8%)	0.004
Pre-pregnancy BMI (kg/m ²)	26.1 (5.7)	26.4 (5.9)	0.042	1171 (3.1%)	3412 (3.1%)	0.003
Gestational weight gain (lbs)	25.9 (13.6)	27.8 (13.9)	0.136	26.3 (5.9)	26.3 (5.8)	0.012
				27.3 (13.9)	27.3 (13.8)	0.001
Child Characteristics				3344 (484.8)	3344 (480.0)	<0.001
Birthweight (g)	3316.2 (495.3)	3354.5 (475.7)	0.079	38.9 (1.5)	38.9 (1.5)	0.004
Gestational age at delivery (wks)	38.7 (1.6)	38.9 (1.5)	0.126	4827 (12.6%)	13840 (12.6%)	0.001
Presence of any birth defect (%)	4447 (11.6%)	14159 (12.9%)	0.038	30.1 (5.5%)	30.0 (5.6%)	0.014
Medical Center (%)			0.268			0.029
Baldwin Park	3021 (7.9%)	9605 (8.8%)		3235 (8.4%)	9356 (8.5%)	
Bellflower	4750 (12.4%)	10628 (9.7%)		3945 (10.3%)	11373 (10.4%)	
Fontana	4589 (12.0%)	11488 (10.5%)		3985 (10.4%)	11830 (10.8%)	
Irvine	2162 (5.7%)	7861 (7.2%)		2724 (7.1%)	7473 (6.8%)	
Los Angeles	2593 (6.8%)	7262 (6.6%)		2560 (6.7%)	7319 (6.7%)	
Moreno Valley	898 (2.4%)	1996 (1.8%)		728 (1.9%)	2142 (2.0%)	
Ontario	1020 (2.7%)	3806 (3.5%)		1228 (3.2%)	3578 (3.3%)	
Orange County	2808 (7.4%)	9553 (8.7%)		3297 (8.6%)	9201 (8.4%)	
Panorama City	2202 (5.8%)	7232 (6.6%)		2320 (6.1%)	6972 (6.4%)	
Riverside	4789 (12.5%)	8484 (7.7%)		3412 (8.9%)	9845 (9.0%)	
San Diego	3061 (8.0%)	14599 (13.3%)		4826 (12.6%)	13142 (12.0%)	
South Bay	2383 (6.2%)	6778 (6.2%)		2396 (6.3%)	6809 (6.2%)	
West LA	2134 (5.6%)	5186 (4.7%)		1899 (5.0%)	5444 (5.0%)	
Woodland Hills	1766 (4.6%)	5241 (4.8%)		1756 (4.6%)	5180 (4.7%)	

*SMD: standardized mean difference

eTable 2. Associations Between Labor Epidural Analgesia (LEA) Use at Delivery and Risk of Autism Spectrum Disorders (ASD) in Offspring (Randomly Select One Child per Family)

	No. with ASD/Total	Bivariable^a	Adjusting for Covariates^b
		HR (95% CI)	HR (95% CI)
Epidural			
No	386/30529	1.0 (Reference)	1.0 (Reference)
Yes	1669/89444	1.45 (1.19-1.77)	1.42 (1.23-1.64)
Epidural Duration			
No Epidural	386/30529	1.0 (Reference)	1.0 (Reference)
<4 hrs	407/25257	1.25 (1.09-1.44)	1.37 (1.15-1.63)
4-8 hrs	752/41019	1.43 (1.27-1.62)	1.42 (1.22-1.66)
>8 hrs	510/23168	1.70 (1.49-1.95)	1.49 (1.25-1.78)
Linear trend (per 4 hour) ^c	1669/89444	1.10 (1.06-1.14)	1.05 (1.00-1.11)

^a LEA was analyzed individually where only birth year was adjusted in the model.

^b Covariates included birth year, maternal age at delivery, parity, race/ethnicity, education, household income, history of comorbidity, diabetes during pregnancy, smoking during pregnancy, pre-eclampsia/eclampsia, pre-pregnancy BMI, gestational weight gain, gestational age at delivery, birth weight, and medical center.

^c Linear trend is defined as LEA duration as a continuous variable within LEA group