Supplementary Online Content

Zerbo O, Qian Y, Yoshida C, Fireman BH, Klein NP, Croen LA. Association between influenza infection and vaccination during pregnancy and risk of autism spectrum disorder. *JAMA Pediatr*. Published online November 28, 2016. doi:10.1001/jamapediatrics.2016.3609

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

eTable 1: Characteristics of Pregnant Women With and Without Influenza Infection Who Delivered a Live Born at Kaiser Permanente Northern California, 2000–2010

	Women with Influenza N= 1400 N (%)	Women without Influenza N= 195529 N (%)	P values
Mean age in year (standard deviation)	29.36 (5.73)	30.66 (5.51)	<0.0001
Education			<0.0001
≤High school	428 (30.6)	54124 (27.7)	
Some college	435 (31.1)	55628 (28.5)	
College graduate	310 (22.1)	47562 (24.3)	
Post-graduate	186 (13.3)	33889 (17.3)	
Unknown	41 (2.9)	4326 (2.2)	
Race			0.001
White	902 (64.4)	127500 (65.2)	
Black	116 (8.3)	13674 (7.0)	
Asian	306 (21.9)	46981 (24.0)	
Other	76 (5.4)	7374 (3.8)	
Gestational age			<0.0001
< 37 Weeks	103 (7.4)	12734 (6.5)	
≥ 37 Weeks	1297 (92.6)	182795 (93.5)	
Mean Pre-pregnancy BMI (standard deviation)	27.42 (5.96)	26.67 (5.54)	<0.0001
Gestational diabetes	142 (10.1)	16621 (8.5)	0.0423
Maternal pre-pregnancy asthma	34 (2.4))	2500 (1.3)	<0.0001
Maternal pre-pregnancy autoimmune diseases	48 (3.4)	3716 (1.9)	<0.0001
Maternal pre-pregnancy allergies	74 (5.3)	7693 (3.9)	0.009
Maternal pre-pregnancy hypertension	17 (1.2)	1367 (0.7)	0.0215

eMethods: Sensitivity Analysis, Effect of Unmeasured Confounders

We used the method developed by Ding and VanderWeele to perform a sensitivity analysis to determine the effect of an unmeasured confounder on the association between maternal influenza vaccination in the first trimester and risk of ASD. Ding and VanderWeele defined a bounding factor (BF) based on the association between the

exposure- confounder (RR_EU) and the association between outcome- confounder (RR_UD) as follows: *BF= (RR_EU x RR_UD)/ RR_EU + RR_UD -1).(Ding and VanderWeele 2016)* This bounding factor is then used to correct the observed measure of association between the exposure and the outcome along with the 95% confidence values.

From our multivariate cox model and logistic regression model we obtained a hazard ratio= relative risk= 1.20, 95% CI (1.04 – 1.39). The following eTable 2 presents different scenarios of the effect of an unmeasured confounder on our observed adjusted measure of association between maternal influenza vaccination during the first trimester and risk of ASD. For example, if an unmeasured confounder increased both the propensity of maternal influenza vaccination during the first trimester and the risk of ASD by 30%, then our observed hazard ratio of 1.20 associated with maternal vaccination in the first trimester could be attributed to a combination of bias and chance. If such a confounder increases by 70% both ASD risk and the propensity for vaccination in the first trimester, then appropriate adjustment would reduce the measured estimate from 1.20 to a null value of 1.00.

eTable 2: Different Scenarios of the Effect of an Unmeasured Confounder on an Adjusted Measure of Association Between Maternal Influenza Vaccination During the First Trimester and Risk of ASD

RR_EU	RR_UD	Bounding factor (BF)	Corrected relative risk	Lower 95% confidence limit	Upper 95% confidence limit
1.1	1.1	1.01	1.19	1.03	1.38
1.2	1.2	1.03	1.17	1.01	1.35
1.2	1.3	1.04	1.15	1.00	1.34
1.3	1.1	1.02	1.17	1.02	1.36
1.3	1.3	1.06	1.14	0.98	1.32
1.4	1.1	1.03	1.17	1.01	1.35
1.4	1.2	1.05	1.14	1.00	1.32
1.4	1.3	1.07	1.12	0.97	1.30
1.7	1.7	1.20	1.00	0.86	1.15
2.0	1.1	1.05	1.15	1.00	1.33
2.0	1.2	1.09	1.10	0.95	1.27

Ding, P. and T. J. VanderWeele (2016). "Sensitivity Analysis Without Assumptions." Epidemiology **27**(3): 368-377.