

## Supplementary Online Content

Surén P, Roth C, Bresnahan M, et al. Association between maternal use of folic acid supplements and risk of autism spectrum disorders in children. *JAMA*. doi:10.1001/jama.2012.155925

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

**eTable 1. ASD Cases by Year of Birth**

Cohort		ASD		Autistic Disorder		Asperger's Syndrome		PDD-NOS	
Year of Birth	n	n	%	n	%	n	%	n	%
2002	7,377	49	0.66 %	19	0.26 %	15	0.20 %	15	0.20 %
2003	10,858	72	0.66 %	26	0.24 %	24	0.22 %	22	0.20 %
2004	11,882	42	0.35 %	13	0.11 %	9	0.08 %	20	0.17 %
2005	13,711	40	0.29 %	16	0.12 %	5	0.04 %	19	0.14 %
2006	15,364	31	0.20 %	14	0.09 %	2	0.01 %	15	0.10 %
2007	14,140	19	0.13 %	12	0.08 %	1	0.01 %	6	0.04 %
2008	11,844	17	0.14 %	14	0.12 %	0	0.00 %	3	0.03 %
<b>Total</b>	<b>85,176</b>	<b>270</b>	<b>0.32 %</b>	<b>114</b>	<b>0.13 %</b>	<b>56</b>	<b>0.07 %</b>	<b>100</b>	<b>0.12 %</b>

Includes ASD cases identified in the study sample (n=85,176: 43,759 boys and 41,417 girls) by March 31<sup>st</sup>, 2012. Of the 270 ASD cases, 135 (50%) have participated in the clinical assessments of the ABC study: 63 (55%) of autistic disorder cases, 16 (29%) of Asperger's syndrome cases, and 56 (56%) of PDD-NOS cases. For those who have not participated, diagnoses were derived from the Norwegian Patient Registry.

**eTable 2.** Parent and Child Characteristics by Maternal Fish Oil Use

			Fish Oil Use Week (-4) to 8			
	Total Study Sample (n=85,176)		No Fish Oil (n=46,314)		Use of Fish Oil (n=38,862)	
	n	%	n	%	n	%
<b>Maternal education, y</b>						
< 12	6,264	7.4 %	4,580	9.9 %	1,684	4.3 %
12	22,616	26.6 %	14,364	31.0 %	8,252	21.2 %
13 - 16	34,641	40.7 %	17,819	38.5 %	16,822	43.3 %
>= 17	19,910	23.4 %	8,520	18.4 %	11,390	29.3 %
Missing data	1,745	2.0 %	1,031	2.2 %	714	1.8 %
<b>Paternal education, y</b>						
< 12	9,067	10.6 %	6,079	13.1 %	2,988	7.7 %
12	32,161	37.8 %	19,216	41.5 %	12,945	33.3 %
13 - 16	22,476	26.4 %	11,121	24.0 %	11,355	29.2 %
>= 17	18,835	22.1 %	8,307	17.9 %	10,528	27.1 %
Missing data	2,637	3.1 %	1,591	3.4 %	1,046	2.7 %
<b>Maternal age, y</b>						
< 25	9,384	11.0 %	6,220	13.4 %	3,164	8.1 %
25 - 29	28,107	33.0 %	15,305	33.0 %	12,802	32.9 %
30 - 34	32,975	38.7 %	17,134	37.0 %	15,841	40.8 %
>= 35	14,710	17.3 %	7,655	16.5 %	7,055	18.2 %
<b>Paternal age, y</b>						
< 25	4,041	4.7 %	2,734	5.9 %	1,307	3.4 %
25 - 29	19,167	22.5 %	10,650	23.0 %	8,517	21.9 %
30 - 34	33,101	38.9 %	17,446	37.7 %	15,655	40.3 %
35 - 39	20,231	23.8 %	10,749	23.2 %	9,482	24.4 %
>= 40	8,411	9.9 %	4,608	9.9 %	3,803	9.8 %
Missing data	225	0.3 %	127	0.3 %	98	0.3 %
<b>Planned pregnancy</b>						
Yes	68,094	79.9 %	35,966	77.7 %	32,128	82.7 %
No	16,061	18.9 %	9,737	21.0 %	6,324	16.3 %
Missing data	1,021	1.2 %	611	1.3 %	410	1.1 %
<b>Maternal smoking</b>						
No	77,845	91.4 %	41,140	88.8 %	36,705	94.4 %
Yes	6,740	7.9 %	4,798	10.4 %	1,942	5.0 %
Missing data	591	0.7 %	376	0.8 %	215	0.6 %
<b>Maternal pre-pregnancy BMI</b>						
< 25	56,614	66.5 %	29,241	63.1 %	27,373	70.4 %
25 - 29	18,332	21.5 %	10,633	23.0 %	7,699	19.8 %
30 - 34	5,830	6.8 %	3,639	7.9 %	2,191	5.6 %
>= 35	2,158	2.5 %	1,403	3.0 %	755	1.9 %
Missing data	2,242	2.6 %	1,398	3.0 %	844	2.2 %
<b>Parity</b>						
0	37,946	44.6 %	18,948	40.9 %	18,998	48.9 %
1	30,674	36.0 %	17,000	36.7 %	13,674	35.2 %
>= 2	16,556	19.4 %	10,366	22.4 %	6,190	15.9 %

**eTable 2 (continued)**

	<b>Fish Oil Use Week (-4) to 8</b>					
	<b>Total Study Sample (n=85,176)</b>		<b>No Fish Oil (n=46,314)</b>		<b>Use of Fish Oil (n=38,862)</b>	
	<b>n</b>	<b>Column %</b>	<b>n</b>	<b>Row %</b>	<b>n</b>	<b>Row %</b>
<b>Year of birth</b>						
2002	7,377	8.7 %	5,706	77.3 %	1,671	22.7 %
2003	10,858	12.7 %	7,389	68.1 %	3,469	31.9 %
2004	11,882	13.9 %	6,954	58.5 %	4,928	41.5 %
2005	13,711	16.1 %	7,600	55.4 %	6,111	44.6 %
2006	15,364	18.0 %	7,339	47.8 %	8,025	52.2 %
2007	14,140	16.6 %	6,326	44.7 %	7,814	55.3 %
2008	11,844	13.9 %	5,000	42.2 %	6,844	57.8 %

<sup>a</sup> p<0.001 for all variables, 2-sided chi-square test for independence.

<sup>b</sup> Maternal smoking, daily or occasionally, during pregnancy.

<sup>c</sup> Parity including previous miscarriage or abortion after week 22 of gestation.

**eTable 3A.** Maternal Illness and Medication Use in Pregnancy Across Categories of Folic Acid Use

			Folic Acid Use Week (-4) to 8			
	Total Study Sample (n=85,176)		No Folic Acid (n=24,134)		Use of Folic Acid (n=61,042)	
	n	%	n	%	n	%
<b>Anxiety</b>						
No	84,840	99.6 %	23,996	99.4 %	60,844	99.7 %
Yes	336	0.4 %	138	0.6 %	198	0.3 %
<b>Anti-anxiety medications</b>						
No	85,034	99.8 %	24,074	99.8 %	60,960	99.9 %
Yes	142	0.2 %	60	0.2 %	82	0.1 %
<b>Depression</b>						
No	84,541	99.3 %	23,852	98.8 %	60,689	99.4 %
Yes	635	0.7 %	282	1.2 %	353	0.6 %
<b>Antidepressant use</b>						
No	84,856	99.6 %	24,001	99.4 %	60,855	99.7 %
Yes	320	0.4 %	133	0.6 %	187	0.3 %
<b>Epilepsy</b>						
No	85,094	99.9 %	24,110	99.9 %	60,984	99.9 %
Yes	82	0.1 %	24	0.1 %	58	0.1 %
<b>Use of anti-epileptics</b>						
No	85,103	99.9 %	24,112	99.9 %	60,991	99.9 %
Yes	73	0.1 %	22	0.1 %	51	0.1 %
<b>Preeclampsia<sup>a</sup></b>						
No	82,493	96.9 %	23,365	96.8 %	59,128	96.9 %
Yes	2,683	3.1 %	769	3.2 %	1,914	3.1 %
<b>Diabetes<sup>b</sup></b>						
No	83,917	98.5 %	23,787	98.6 %	60,130	98.5 %
Yes	1,259	1.5 %	347	1.4 %	912	1.5 %
<b>Hormone treatment</b>						
No	82,978	97.4 %	23,716	98.3 %	59,262	97.1 %
Yes	2,198	2.6 %	418	1.7 %	1,780	2.9 %
<b>In vitro fertilization</b>						
No	83,315	97.8 %	23,828	98.7 %	59,487	97.5 %
Yes	1,861	2.2 %	306	1.3 %	1,555	2.5 %

<sup>a</sup> Includes eclampsia and HELLP syndrome

<sup>b</sup> All types of diabetes

**eTable 3B.** Adjustments for Maternal Illness and Medication Use During Pregnancy

	<b>OR</b>	<b>95% CI</b>
Unadjusted model	0.51	0.35 - 0.73
Adjusted model <sup>a</sup>	0.61	0.41 - 0.90
<i>Additional adjustments<sup>b</sup></i>		
Anxiety	0.60	0.41 - 0.89
Use of medications against anxiety	0.60	0.41 - 0.89
Depression	0.60	0.41 - 0.90
Use of antidepressants	0.60	0.41 - 0.90
Epilepsy	0.60	0.40 - 0.89
Use of anti-epileptics	0.60	0.41 - 0.89
Preeclampsia <sup>c</sup>	0.61	0.41 - 0.90
Diabetes <sup>d</sup>	0.61	0.41 - 0.90
Hormone treatment	0.60	0.41 - 0.89
In vitro fertilization	0.60	0.40 - 0.88

<sup>a</sup> Adjusted for maternal education level, parity, and child's year of birth

<sup>b</sup> Adjustments in addition to maternal education level, parity, and child's year of birth

<sup>c</sup> Includes eclampsia and HELLP syndrome

<sup>d</sup> All types of diabetes

**eFigure.** Fish Oil Supplement Use by Pregnancy Interval

