

Supplementary Online Content

Schmidt RJ, Iosif A-M, Guerrero Angel E, Ozonoff S. Association of maternal prenatal vitamin use with risk for autism spectrum disorder recurrence in young siblings. *JAMA Psychiatry*. Published online February 27, 2019. doi:10.1001/jamapsychiatry.2018.3901

eMethods. MARBLES Interview Questions on Vitamins and Supplements

eFigure 1. Unadjusted Relative Risk for Associations of Maternal Prenatal Vitamin Use (Yes versus No) For Each Month From 6 Months Before Pregnancy Through the End of Pregnancy With Child 36-month Outcomes of Autism Spectrum Disorder (ASD) and Nontypical Development (Non-TD) Versus Typical Development.

eFigure 2. Adjusted Relative Risk for Associations of Maternal Prenatal Vitamin Use (Yes versus No) For Each Month From 6 Months Before Pregnancy Through the End of Pregnancy With Child 36-month Outcomes of Autism Spectrum Disorder (ASD) and Nontypical Development (Non-TD) Versus Typical Development.

eTable 1. Results of the Sensitivity Analyses Using MLE and TMLE Approaches for the 233 Participants With Complete Covariate Data

eTable 2. Stratified Unadjusted and Adjusted Associations of Maternal Prenatal Vitamin Use in the First Month of Pregnancy and Child 36-month Outcomes

eTable 3. Results of the Sensitivity Analyses Examining Associations of Maternal Mean Daily Intake of Folic Acid and Iron Supplements in the First Month of Pregnancy With Child 36-month Outcomes Using MLE and TMLE Approaches for the 233 Participants With Complete Covariate Data

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

eMethods. MARBLES Interview Questions on Vitamins and Supplements.

Interview 1: Environmental Exposures Questionnaire, First Trimester

The next questions are about prenatal vitamins and other supplements you may have taken.

34a. Since 6 months before this pregnancy until now have you taken any....	34b. What was the brand name you took?	34c. During which months did you take (VITAMIN/ Supp)?	34d. How often/number of capsules
Prenatal vitamins	Y N RF DK	-6 -5 -4 -3 -2 -1 1 2 3 4 5 6 7 8 9 RF DK	____ tablets/capsules per day, for ____ days ____ tablets/capsules per week ____ tablets/capsules per month ____ tablets/capsules everyday Other, specify _____ ____ RF ____ DK
Multivitamins	Y N RF DK	-6 -5 -4 -3 -2 -1 1 2 3 4 5 6 7 8 9 RF DK	____ tablets/capsules per day, for ____ days ____ tablets/capsules per week ____ tablets/capsules per month ____ tablets/capsules everyday Other, specify _____ ____ RF ____ DK
Vitamin A	Y N RF DK	-6 -5 -4 -3 -2 -1 1 2 3 4 5 6 7 8 9 RF DK	____ tablets/capsules per day, for ____ days ____ tablets/capsules per week ____ tablets/capsules per month ____ tablets/capsules everyday Other, specify _____ ____ RF ____ DK
Vitamin B6	Y N RF DK	-6 -5 -4 -3 -2 -1 1 2 3 4 5 6 7 8 9 RF DK	____ tablets/capsules per day, for ____ days ____ tablets/capsules per week ____ tablets/capsules per month ____ tablets/capsules everyday Other, specify _____ ____ RF ____ DK
Vitamin B12	Y N RF DK	-6 -5 -4 -3 -2 -1 1 2 3 4 5 6 7 8 9 RF DK	____ tablets/capsules per day, for ____ days ____ tablets/capsules per week ____ tablets/capsules per month ____ tablets/capsules everyday Other, specify _____ ____ RF ____ DK
Folic acid	Y N RF DK	-6 -5 -4 -3 -2 -1 1 2 3 4 5 6 7 8 9 RF DK	____ tablets/capsules per day, for ____ days ____ tablets/capsules per week ____ tablets/capsules per month ____ tablets/capsules everyday Other, specify _____ ____ RF ____ DK

Vitamin C	Y N RF DK		-6 -5 -4 -3 -2 -1 1 2 3 4 5 6 7 8 9 RF DK	____ tablets/capsules per day, for ____ days ____ tablets/capsules per week ____ tablets/capsules per month ____ tablets/capsules everyday Other, specify _____ ____ RF ____ DK
Vitamin D	Y N RF DK		-6 -5 -4 -3 -2 -1 1 2 3 4 5 6 7 8 9 RF DK	____ tablets/capsules per day, for ____ days ____ tablets/capsules per week ____ tablets/capsules per month ____ tablets/capsules everyday Other, specify _____ ____ RF ____ DK
Vitamin E	Y N RF DK		-6 -5 -4 -3 -2 -1 1 2 3 4 5 6 7 8 9 RF DK	____ tablets/capsules per day, for ____ days ____ tablets/capsules per week ____ tablets/capsules per month ____ tablets/capsules everyday Other, specify _____ ____ RF ____ DK
Iron	Y N RF DK		-6 -5 -4 -3 -2 -1 1 2 3 4 5 6 7 8 9 RF DK	____ tablets/capsules per day, for ____ days ____ tablets/capsules per week ____ tablets/capsules per month ____ tablets/capsules everyday Other, specify _____ ____ RF ____ DK
Calcium	Y N RF DK		-6 -5 -4 -3 -2 -1 1 2 3 4 5 6 7 8 9 RF DK	____ tablets/capsules per day, for ____ days ____ tablets/capsules per week ____ tablets/capsules per month ____ tablets/capsules everyday Other, specify _____ ____ RF ____ DK
Zinc	Y N RF DK		-6 -5 -4 -3 -2 -1 1 2 3 4 5 6 7 8 9 RF DK	____ tablets/capsules per day, for ____ days ____ tablets/capsules per week ____ tablets/capsules per month ____ tablets/capsules everyday Other, specify _____ ____ RF ____ DK
Cereals	Y N RF DK	_____ _____ _____	-6 -5 -4 -3 -2 -1 1 2 3 4 5 6 7 8 9 RF DK	____ cups per day ____ cups per week ____ cups per month ____ RF ____ DK
Other supplements e.g. Slim Fast, Instant Breakfast, protein	Y N RF DK		-6 -5 -4 -3 -2 -1 1 2 3 4 5 6 7 8 9 RF DK	____ tablets/capsules per day, for ____ days ____ tablets/capsules per week ____ tablets/capsules per month ____ tablets/capsules everyday Other, specify _____

powder, brewer's yeast				____RF ____DK
St. John's worts	Y N RF DK		-6 -5 -4 -3 -2 -1 1 2 3 4 5 6 7 8 9 RF DK	____ tablets/capsules per day, for ____ days ____ tablets/capsules per week ____ tablets/capsules per month ____ tablets/capsules everyday Other, specify _____ ____RF ____DK
Ginseng	Y N RF DK		-6 -5 -4 -3 -2 -1 1 2 3 4 5 6 7 8 9 RF DK	____ tablets/capsules per day, for ____ days ____ tablets/capsules per week ____ tablets/capsules per month ____ tablets/capsules everyday Other, specify _____ ____RF ____DK
Omega-3 Fatty Acids	Y N RF DK		-6 -5 -4 -3 -2 -1 1 2 3 4 5 6 7 8 9 RF DK	____ tablets/capsules per day, for ____ days ____ tablets/capsules per week ____ tablets/capsules per month ____ tablets/capsules everyday Other, specify _____ ____RF ____DK
Fish oil	Y N RF DK		-6 -5 -4 -3 -2 -1 1 2 3 4 5 6 7 8 9 RF DK	____ tablets/capsules per day, for ____ days ____ tablets/capsules per week ____ tablets/capsules per month ____ tablets/capsules everyday Other, specify _____ ____RF ____DK
Other supplements or vitamins	Y N RF DK		-6 -5 -4 -3 -2 -1 1 2 3 4 5 6 7 8 9 RF DK	____ tablets/capsules per day, for ____ days ____ tablets/capsules per week ____ tablets/capsules per month ____ tablets/capsules everyday Other, specify _____ ____RF ____DK

Interview 2: Environmental Exposures Questionnaire, Third Trimester

The next questions are about prenatal vitamins and other supplements you may have taken.

35a. Since the last time we spoke have you taken any....	b. What was the brand name you took?	c. During which months did you take (VITAMIN/Supp)?	d. How often/number of capsules
Prenatal vitamins Y N RF DK		3 4 5 6 7 8 9 RF DK	_____ tablets/capsules per day, for _____ days _____ tablets/capsules per week _____ tablets/capsules per month _____ tablets/capsules everyday Other, specify _____ _____DK _____RF
Multivitamins Y N RF DK		3 4 5 6 7 8 9 RF DK	_____ tablets/capsules per day, for _____ days _____ tablets/capsules per week _____ tablets/capsules per month _____ tablets/capsules everyday Other, specify _____ _____DK _____RF
Vitamin A Y N RF DK		3 4 5 6 7 8 9 RF DK	_____ tablets/capsules per day, for _____ days _____ tablets/capsules per week _____ tablets/capsules per month _____ tablets/capsules everyday Other, specify _____ _____DK _____RF
Vitamin B6 Y N RF DK		3 4 5 6 7 8 9 RF DK	_____ tablets/capsules per day, for _____ days _____ tablets/capsules per week _____ tablets/capsules per month _____ tablets/capsules everyday Other, specify _____

			____DK ____RF
Vitamin B12	Y N RF DK		3 4 5 6 7 8 9 RF DK ____tablets/capsules per day, for ____ days ____tablets/capsules per week ____tablets/capsules per month ____tablets/capsules everyday Other, specify _____ ____DK ____RF
Folic acid	Y N RF DK		3 4 5 6 7 8 9 RF DK ____tablets/capsules per day, for ____ days ____tablets/capsules per week ____tablets/capsules per month ____tablets/capsules everyday Other, specify _____ ____DK ____RF
Vitamin C	Y N RF DK		3 4 5 6 7 8 9 RF DK ____tablets/capsules per day, for ____ days ____tablets/capsules per week ____tablets/capsules per month ____tablets/capsules everyday Other, specify _____ ____DK ____RF
Vitamin D	Y N RF DK		3 4 5 6 7 8 9 RF DK ____tablets/capsules per day, for ____ days ____tablets/capsules per week ____tablets/capsules per month ____tablets/capsules everyday Other, specify _____ ____DK ____RF
Vitamin E	Y N RF DK		3 4 5 6 7 ____tablets/capsules per day, for ____ days ____tablets/capsules per week

			8 9 RF DK	_____tablets/capsules per month _____tablets/capsules everyday Other, specify _____ _____DK _____RF
Iron	Y N RF DK		3 4 5 6 7 8 9 RF DK	_____tablets/capsules per day, for _____ days _____tablets/capsules per week _____tablets/capsules per month _____tablets/capsules everyday Other, specify _____ _____DK _____RF
Calcium	Y N RF DK		3 4 5 6 7 8 9 RF DK	_____tablets/capsules per day, for _____ days _____tablets/capsules per week _____tablets/capsules per month _____tablets/capsules everyday Other, specify _____ _____DK _____RF
Zinc	Y N RF DK		3 4 5 6 7 8 9 RF DK	_____tablets/capsules per day, for _____ days _____tablets/capsules per week _____tablets/capsules per month _____tablets/capsules everyday Other, specify _____ _____DK _____RF
Cereals	Y N RF DK	_____ _____ _____	3 4 5 6 7 8 9 RF DK	_____ cups per day _____ cups per week _____ cups per month _____DK _____RF

Other supplements e.g. Slim Fast, Instant Breakfast, protein powder, brewer's yeast	Y N RF DK	3 4 5 6 7 8 9 RF DK	____ tablets/capsules per day, for ____ days ____ tablets/capsules per week ____ tablets/capsules per month ____ tablets/capsules everyday Other, specify _____ ____ DK _____ RF
St. John's worts	Y N RF DK	3 4 5 6 7 8 9 RF DK	____ tablets/capsules per day, for ____ days ____ tablets/capsules per week ____ tablets/capsules per month ____ tablets/capsules everyday Other, specify _____ ____ DK _____ RF
Ginseng	Y N RF DK	3 4 5 6 7 8 9 RF DK	____ tablets/capsules per day, for ____ days ____ tablets/capsules per week ____ tablets/capsules per month ____ tablets/capsules everyday Other, specify _____ ____ DK _____ RF
Omega-3 Fatty Acids	Y N RF DK	3 4 5 6 7 8 9 RF DK	____ tablets/capsules per day, for ____ days ____ tablets/capsules per week ____ tablets/capsules per month ____ tablets/capsules everyday Other, specify _____ ____ DK _____ RF
Fish oil	Y N RF DK	3 4 5 6 7 8 9 RF DK	____ tablets/capsules per day, for ____ days ____ tablets/capsules per week ____ tablets/capsules per month

			_____ tablets/capsules everyday Other, specify _____ _____ DK _____ RF
Other vitamins or supplements	Y N RF DK	3 4 5 6 7 8 9 RF DK	_____ tablets/capsules per day, for _____ days _____ tablets/capsules per week _____ tablets/capsules per month _____ tablets/capsules everyday Other, specify _____ _____ DK _____ RF

Interview 3: Environmental Exposure Questionnaire, 6 months postnatal

The next questions are about prenatal vitamins and other supplements you may have taken.

36a. Since the last time we spoke through 6 months post-partum (or the end of BF) have you taken any....	36b. What was the brand name you took?	36c. During which months did you take (VITAMIN/Supp)?	36d. How often/number of capsules
Prenatal vitamins		4 5 6 7 8 9 BF RF DK	_____ tablets/capsules per day, for _____ days _____ tablets/capsules per week _____ tablets/capsules per month _____ tablets/capsules everyday Other, specify _____ _____ RF _____ DK
Multivitamins (not prenatal)	Y N RF DK	4 5 6 7 8 9 BF RF DK	_____ tablets/capsules per day, for _____ days _____ tablets/capsules per week _____ tablets/capsules per month

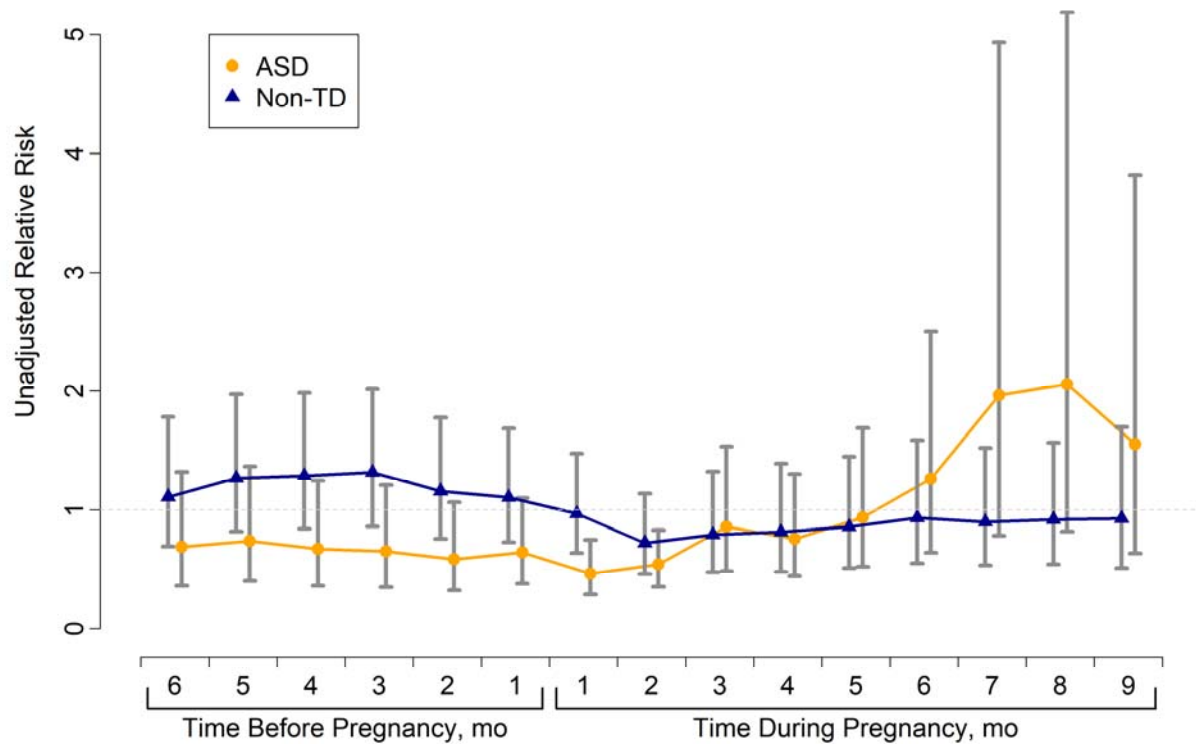
			_____ tablets/capsules everyday Other, specify _____ _____ RF _____ DK
Vitamin A	Y N RF DK		4 5 6 7 8 9 BF RF DK _____ tablets/capsules per day, for _____ days _____ tablets/capsules per week _____ tablets/capsules per month _____ tablets/capsules everyday Other, specify _____ _____ RF _____ DK
Vitamin B6	Y N RF DK		4 5 6 7 8 9 BF RF DK _____ tablets/capsules per day, for _____ days _____ tablets/capsules per week _____ tablets/capsules per month _____ tablets/capsules everyday Other, specify _____ _____ RF _____ DK
Vitamin B12	Y N RF DK		4 5 6 7 8 9 BF RF DK _____ tablets/capsules per day, for _____ days _____ tablets/capsules per week _____ tablets/capsules per month _____ tablets/capsules everyday Other, specify _____ _____ RF _____ DK

Folic acid	Y N RF DK	4 5 6 7 8 9 BF RF DK	____ tablets/capsules per day, for ____ days ____ tablets/capsules per week ____ tablets/capsules per month ____ tablets/capsules everyday Other, specify _____ ____ RF ____ DK
Vitamin C	Y N RF DK	4 5 6 7 8 9 BF RF DK	____ tablets/capsules per day, for ____ days ____ tablets/capsules per week ____ tablets/capsules per month ____ tablets/capsules everyday Other, specify _____ ____ RF ____ DK
Vitamin D	Y N RF DK	4 5 6 7 8 9 BF RF DK	____ tablets/capsules per day, for ____ days ____ tablets/capsules per week ____ tablets/capsules per month ____ tablets/capsules everyday Other, specify _____ ____ RF ____ DK
Vitamin E	Y N RF DK	4 5 6 7 8 9 BF RF DK	____ tablets/capsules per day, for ____ days ____ tablets/capsules per week ____ tablets/capsules per month

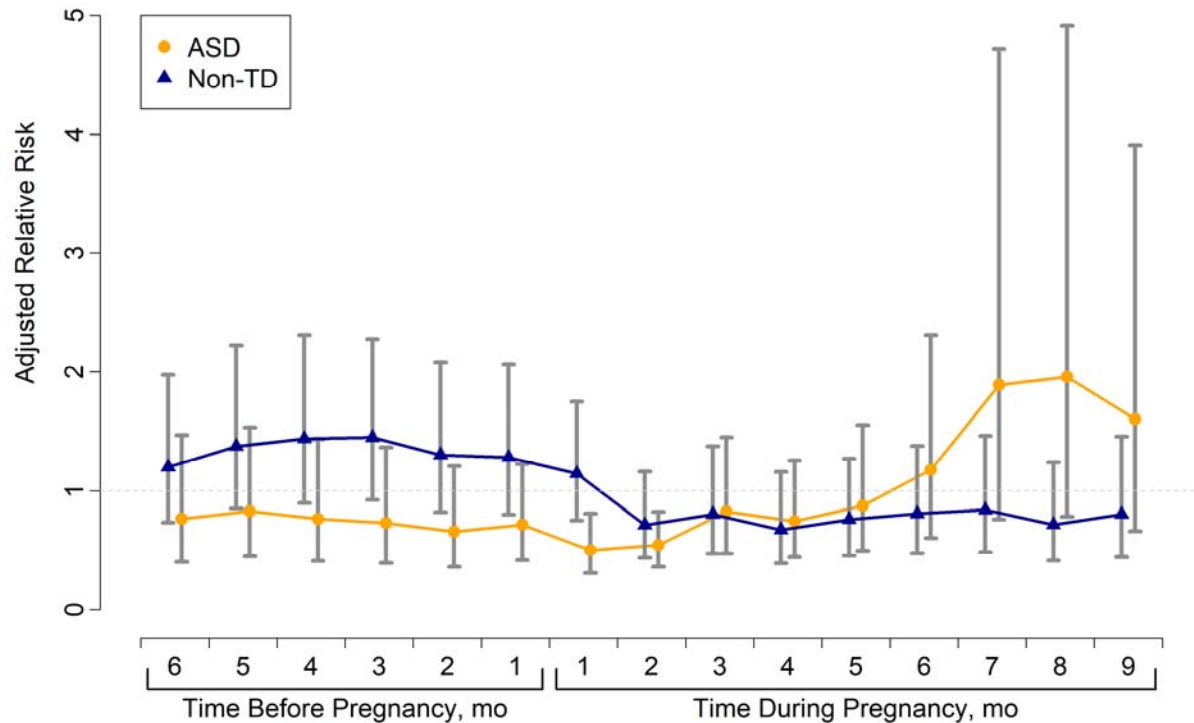
			_____ tablets/capsules everyday Other, specify _____ _____ RF _____ DK
Iron	Y N RF DK		4 5 6 7 8 9 BF RF DK _____ tablets/capsules per day, for _____ days _____ tablets/capsules per week _____ tablets/capsules per month _____ tablets/capsules everyday Other, specify _____ _____ RF _____ DK
Calcium	Y N RF DK		4 5 6 7 8 9 BF RF DK _____ tablets/capsules per day, for _____ days _____ tablets/capsules per week _____ tablets/capsules per month _____ tablets/capsules everyday Other, specify _____ _____ RF _____ DK
Zinc	Y N RF DK		4 5 6 7 8 9 BF RF DK _____ tablets/capsules per day, for _____ days _____ tablets/capsules per week _____ tablets/capsules per month _____ tablets/capsules everyday Other, specify _____ _____ RF _____ DK

Cereals	Y N RF DK	_____ _____ _____	4 5 6 7 8 9 BF RF DK	____ cups per day ____ cups per week ____ cups per month ____ RF ____ DK
Other supplements e.g. Slim Fast, Instant Breakfast, protein powder, brewer's yeast	Y N RF DK		4 5 6 7 8 9 BF RF DK	____ tablets/capsules per day, for ____ days ____ tablets/capsules per week ____ tablets/capsules per month ____ tablets/capsules everyday Other, specify _____ ____ RF ____ DK
St. John's worts	Y N RF DK		4 5 6 7 8 9 BF RF DK	____ tablets/capsules per day, for ____ days ____ tablets/capsules per week ____ tablets/capsules per month ____ tablets/capsules everyday Other, specify _____ ____ RF ____ DK
Ginseng	Y N RF DK		4 5 6 7 8 9 BF RF DK	____ tablets/capsules per day, for ____ days ____ tablets/capsules per week ____ tablets/capsules per month ____ tablets/capsules everyday Other, specify _____ ____ RF ____ DK

Omega-3 Fatty Acids	Y N RF DK		4 5 6 7 8 9 BF RF DK ____ tablets/capsules per day, for ____ days ____ tablets/capsules per week ____ tablets/capsules per month ____ tablets/capsules everyday Other, specify _____ ____ RF ____ DK
Fish oil	Y N RF DK		4 5 6 7 8 9 BF RF DK ____ tablets/capsules per day, for ____ days ____ tablets/capsules per week ____ tablets/capsules per month ____ tablets/capsules everyday Other, specify _____ ____ RF ____ DK
Other vitamins or supplements	Y N RF DK		4 5 6 7 8 9 BF RF DK ____ tablets/capsules per day, for ____ days ____ tablets/capsules per week ____ tablets/capsules per month ____ tablets/capsules everyday Other, specify _____ ____ RF ____ DK



eFigure 1. Unadjusted Relative Risk for Associations of Maternal Prenatal Vitamin Use (Yes versus No) For Each Month From 6 Months Before Pregnancy Through the End of Pregnancy With Child 36-month Outcomes of Autism Spectrum Disorder (ASD) and Nontypical Development (Non-TD) Versus Typical Development. Vertical bars represent 95% confidence intervals.



eFigure 2. Adjusted Relative Risk for Associations of Maternal Prenatal Vitamin Use (Yes versus No) For Each Month From 6 Months Before Pregnancy Through the End of Pregnancy With Child 36-month Outcomes of Autism Spectrum Disorder (ASD) and Nontypical Development (Non-TD) Versus Typical Development.

Relative risks were adjusted for maternal education in the ASD models and for child white or non-white race, maternal age and education, insurance delivery type, and maternal intention to become pregnant in the Non-TD models. Vertical bars represent 95% confidence intervals.

eTable 1. Results of the Sensitivity Analyses Using MLE and TMLE Approaches for the 233 Participants With Complete Covariate Data

Model	Child 36-mo Outcome	
	ASD RR (95% CI)	Non-TD RR (95% CI)
MLE (unadjusted)	0.48 (0.29, 0.78)	0.96 (0.62, 1.47)
MLE (adjusted) ^a	0.51 (0.31, 0.83)	1.07 (0.71, 1.61)
TMLE - Model 1	0.45 (0.27, 0.75)	1.10 (0.68, 1.80)
TMLE - Model 2	0.50 (0.29, 0.87)	1.18 (0.72, 1.92)
TMLE - Model 3	0.42 (0.26, 0.70)	1.10 (0.68, 1.77)
TMLE - Model 4	0.50 (0.31, 0.82)	1.22 (0.93, 1.61)

Abbreviations: MLE, maximum likelihood estimation; TMLE, targeted maximum likelihood estimation; RR, Relative Risk; ASD, autism spectrum disorder; Non-TD, nontypical development.

^aAdjusted for maternal education in the ASD model and for child white or non-white race, maternal age and education, insurance delivery type, and maternal intention to become pregnant (yes or no) in the Non-TD model.

TMLE - Model 1: Algorithm estimated using R-package `tmle` and default Super-Learner (SL) library (`SL.glm`, `SL.step`, and `SL.glm.interaction`) with a set of set of covariates similar to primary analyses (child white or non-white race, maternal age and education, insurance delivery type, and maternal intention to become pregnant).

TMLE - Model 2: Algorithm estimated using R-package `tmle` and default SL library (`SL.glm`, `SL.step`, and `SL.glm.interaction`) with a full set of covariates (all covariates in TMLE - Model 1 and child gender and ethnicity, paternal age, maternal pre-pregnancy BMI and place of birth, and home ownership).

TMLE - Model 3: Algorithm computed using R-package `tmle`, user-supplied SL library (`SL.gam`, `SL.randomForest`, and `SL.rpart`) with a set of set of covariates similar to primary analyses (child white or non-white race, maternal age and education, insurance delivery type, and maternal intention to become pregnant).

TMLE - Model 4: Algorithm computed using R-package `tmle`, user-supplied SL library (`SL.gam`, `SL.randomForest`, and `SL.rpart`) with a full set of covariates (all covariates in TMLE - Model 3 and child gender and ethnicity, paternal age, maternal pre-pregnancy BMI and place of birth, and home ownership).

eTable 2. Stratified Unadjusted and Adjusted Associations of Maternal Prenatal Vitamin Use in the First Month of Pregnancy and Child 36-month Outcomes

Variable	Frequency taking vitamin (%)			ASD vs. TD		Non-TD vs. TD	
	ASD (n = 55)	Non-TD (n = 60)	TD (n = 126)	RR (95% CI)	Interaction P-Value	RR (95% CI)	Interaction P-Value
Child Sex							
No. Male Sex	38	37	65				
Male (crude)	16 (42%)	23 (62%)	34 (52%)	0.77 (0.46, 1.29)		1.30 (0.76, 2.22)	
No. Female Sex	17	23	61				
Female (crude)	2 (12%)	12 (52%)	41 (67%)	0.11 (0.03, 0.44)	0.01	0.64 (0.32, 1.27)	0.11
Male (adjusted ^a)				0.86 (0.51, 1.42)		1.80 (0.99, 3.28) [#]	
Female (adjusted ^a)				0.11 (0.03, 0.46)	0.01	0.75 (0.32, 1.74)	0.13
Child Race							
No. White	36	34	89				
White (crude)	11 (31%)	22 (65%)	54 (61%)	0.41 (0.22, 0.75) [*]		1.13 (0.62, 2.07)	
No. Non-White	19	26	37				
Non-White (crude)	7 (37%)	13 (50%)	21 (57%)	0.58 (0.27, 1.26)	0.47	0.85 (0.47, 1.54)	0.51
White (adjusted ^a)				0.44 (0.24, 0.83) [*]		1.32 (0.66, 2.62)	
Non-White (adjusted ^a)				0.61 (0.28, 1.31)	0.53	1.07 (0.57, 2.00)	0.48
Child Ethnicity							
No. Hispanic	21	19	37				
Hispanic (crude)	7 (33%)	8 (42%)	22 (59%)	0.50 (0.24, 1.06) [#]		0.63 (0.30, 1.33)	
No. Non-Hispanic	34	41	89				
Non-Hispanic (crude)	11 (32%)	27 (66%)	53 (60%)	0.44 (0.24, 0.82) [*]	0.80	1.21 (0.70, 2.07)	0.17
Hispanic (adjusted ^a)				0.57 (0.26, 1.23)		0.81 (0.32, 2.07)	
Non-Hispanic (adjusted ^a)				0.46 (0.25, 0.86) [*]	0.73	1.29 (0.69, 2.43)	0.29

Supplement eTable 2. (continued) Stratified Unadjusted and Adjusted Associations of Maternal Prenatal Vitamin Use in the First Month of Pregnancy and Child 36-Month Outcomes

Variable	Frequency taking vitamin (%)			ASD vs. TD		Non-TD vs. TD	
	ASD (n = 55)	Non-TD (n = 60)	TD (n = 126)	RR (95% CI)	Interaction P-Value	RR (95% CI)	Interaction P-Value
Child Mullen Composite Score ^b							
No. 70 or higher	25	52	126				
70 or higher (crude)	7 (28%)	30 (58%)	75 (60%)	0.33 (0.15, 0.74)*		0.95 (0.60, 1.50)	
No. < 70	22	6	0				
< 70 (crude) ^d	7 (32%)	3 (50%)	–	0.38 (0.16, 0.87)*	NA ^c	0.69 (0.15, 3.30)	NA ^c
70 or higher (adjusted ^a)				0.33 (0.15, 0.76)*		1.13 (0.71, 1.80)	
< 70 (adjusted ^a) ^d				0.44 (0.19, 1.01) [#]	NA ^c	–	NA ^c
Maternal Age (Years)							
No. 35 or older	27	29	48				
35 or older (crude)	10 (37%)	15 (52%)	30 (63%)	0.51 (0.27, 0.97)*		0.76 (0.43, 1.35)	
35 or older	28	31	78				
No. < 35	8 (29%)	20 (65%)	45 (58%)	0.40 (0.19, 0.83)*	0.61	1.23 (0.66, 2.31)	0.27
35 or older (adjusted ^a)				0.53 (0.28, 1.02) [#]		0.95 (0.45, 1.97)	
< 35 (adjusted ^a)				0.47 (0.23, 0.94)*	0.43	1.39 (0.75, 2.57)	0.47

Abbreviations: ASD, autism spectrum disorder; Non-TD, nontypical development; TD, typical development.

^aAdjusted for maternal education in the ASD model and for child white or non-white race, maternal age and education, insurance delivery type, and maternal intention to become pregnant (yes or no) in the Non-TD model.

^bFrequency data missing for 8 children in ASD group and 2 in Non-TD.

^cEstimates were not reported and interaction *p*-values were not calculated when expected cell sizes (based on the margin totals) were less than 5 and due to quasi-complete separation in the logistic models.

^dThe reference group for this models is the TD group; **p* < .05; #*p* < .10.

eTable 3. Results of the Sensitivity Analyses Examining Associations of Maternal Mean Daily Intake of Folic Acid and Iron Supplements in the First Month of Pregnancy With Child 36-month Outcome Using MLE and TMLE Approaches for the 233 Participants With Complete Covariate Data

	ASD		Non-TD	
	RR (95% CI)		RR (95% CI)	
	Tertile 2 vs. Tertile 1 ^a	Tertile 3 vs. Tertile 1 ^a	Tertile 2 vs. Tertile 1 ^a	Tertile 3 vs. Tertile 1 ^a
Folic Acid				
MLE (unadjusted)	0.66 (0.41, 1.05)	0.41 (0.17, 0.97)	0.94 (0.57, 1.55)	1.05 (0.58, 1.89)
MLE (adjusted) ^b	0.68 (0.43, 1.08)	0.46 (0.19, 1.10)	1.04 (0.65, 1.66)	1.26 (0.67, 2.35)
TMLE - Model 1	0.68 (0.43, 1.08)	0.24 (0.10, 0.60)	1.02 (0.63, 1.65)	1.78 (1.01, 3.14)
TMLE - Model 2	0.67 (0.44, 1.01)	0.22 (0.09, 0.52)	1.10 (0.73, 1.66)	1.77 (1.16, 2.70)
TMLE - Model 3	0.65 (0.43, 0.98)	0.26 (0.11, 0.59)	1.03 (0.65, 1.63)	1.76 (1.06, 2.92)
TMLE - Model 4	0.63 (0.47, 0.85)	0.44 (0.31, 0.61)	1.16 (0.84, 1.61)	1.59 (1.13, 2.23)
Iron				
MLE (unadjusted)	0.58 (0.33, 1.01)	0.54 (0.31, 0.97)	0.79 (0.48, 1.30)	0.72 (0.43, 1.22)
MLE (adjusted) ^b	0.61 (0.35, 1.05)	0.57 (0.32, 1.01)	0.85 (0.52, 1.38)	0.78 (0.47, 1.28)
TMLE - Model 1	0.54 (0.31, 0.95)	0.57 (0.32, 1.03)	0.89 (0.54, 1.47)	0.74 (0.40, 1.34)
TMLE - Model 2	0.59 (0.36, 0.97)	0.59 (0.35, 1.00)	0.79 (0.50, 1.25)	0.69 (0.44, 1.08)
TMLE - Model 3	0.56 (0.33, 0.96)	0.56 (0.32, 0.98)	0.89 (0.55, 1.45)	0.80 (0.49, 1.31)
TMLE - Model 4	0.60 (0.39, 0.92)	0.61 (0.37, 1.02)	0.74 (0.56, 0.98)	0.77 (0.59, 1.02)

Abbreviations: MLE, maximum likelihood estimation; TMLE, targeted maximum likelihood estimation; RR, Relative Risk; ASD, autism spectrum disorder; Non-TD, nontypical development.

^aTMLE algorithms were implemented separately for Tertile 2 vs. Tertile 1 and Tertile 3 vs. Tertile 1 comparisons.

^bAdjusted for maternal education in the ASD model and for child white or non-white race, maternal age and education, insurance delivery type, and maternal intention to become pregnant (yes or no) in the Non-TD model.

TMLE - Model 1: Algorithm estimated using R-package tmle and default Super-Learner (SL) library (SL.glm, SL.step, and SL.glm.interaction) with a set of set of covariates similar to primary analyses (child white or non-white race, maternal age and education, insurance delivery type, and maternal intention to become pregnant).

TMLE - Model 2: Algorithm estimated using R-package tmle and default SL library (SL.glm, SL.step, and SL.glm.interaction) with a full set of covariates (all covariates in TMLE - Model 1

and child gender and ethnicity, paternal age, maternal pre-pregnancy BMI and place of birth, and home ownership).

TMLE - Model 3: Algorithm computed using R-package tmle, user-supplied SL library (SL.gam, SL.randomForest, and SL.rpart) with a set of set of covariates similar to primary analyses (child white or non-white race, maternal age and education, insurance delivery type, and maternal intention to become pregnant).

TMLE - Model 4: Algorithm computed using R-package tmle, user-supplied SL library (SL.gam, SL.randomForest, and SL.rpart) with a full set of covariates (all covariates in TMLE - Model 3 and child gender and ethnicity, paternal age, maternal pre-pregnancy BMI and place of birth, and home ownership).