

Supplementary Online Content

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

eAppendix. Methods

Healthcare provision in the study population

Since 1995, public healthcare has been mandatory for *all* de-jure residents of Israel. Public healthcare is provided to the population by one of four non-profit national insurance agencies (Clalit, Maccabi, Meuchedet, Leumit).¹ The agencies have equivalent fees and services. By law, these agencies are not permitted to deny healthcare to any ethnic or social group (e.g., Druze, Muslim Arabs, Christian Arabs, ultra-orthodox Jews, Ethiopian Jews etc.), decreasing the likelihood of selection bias. Benefits are determined by the Ministry of Health and include vitamins and ASD care, the key variables in this study.

In 2007, 13.2% of the Israeli population was insured by the agency Meuchedet.^{1,2} Our sample consisted of all persons who remained insured by Meuchedet through the end of follow-up (this is a minority since, across the four agencies, approximately 100,000 persons switched to another insurance provider during data collection). The data was linked through the unique identification number all Israeli citizens receive at birth or immigration by Meuchedet. Encrypted unique identification numbers were received by the researchers, so participant identification was not possible.

Diagnostic codes

ICD codes - broad psychiatric disorder definitions

ICD-9 295*-315* not including: 302, 302.*, 305, 305.*, 307, 307.*, 309, 309.*; and ICD-8 295*-315*, not including: 302, 302.*, 305, 305.*, 307, 307.*, 309, 309.*

ICD codes - Intellectual disability

Available diagnoses: 317, 317.9, 318, 318.1, 318.2, 319, 319.9, F70, F71, F72, F73, F78, F79

ICD codes - vitamin deficiency

173.9, 200.0, 200.2, 201, 201.4, 201.40, 201.5, 201.9, 202.0, 202.00, 202.02, 202.05, 202.2, 202.4, 202.47, 202.8, 202.87, 202.88, 202.9, 203.1, 204, 204.0, 204.1, 204.2, 204.8, 205, 205.0, 205.1, 205.2, 206, 206.0, 206.1, 207, 207.0, 208, 208.0, 208.1, 208.9, 238.7, 267.9, 268.0, 268.1, 268.2, 269, 269.2, 280, 280.0, 280.1, 280.9, 281, 281.0, 281.2, 281.3, 281.8, 281.9, 282, 282.2, 282.4, 282.6, 282.7, 282.9, 283, 283.0, 283.1, 283.9, 284, 284.0, 284.8, 285, 285.0, 285.1, 285.9, 288.8, 648.2, 709.0, 713.2, 773.5, 776.5, 776.6, 790.0.

ATC codes

ATC codes consist of five levels. Level 1 of the ATC consists of one letter that indicates the anatomical main group. Level 2 is comprised of 2 digits and indicates the therapeutic main group. Level 3 consists of 1 letter that indicates the therapeutic/pharmacological subgroup. Level 4 consists of one letter that indicates the therapeutic subgroup. Level 5 is comprised of 2 digits and indicates the chemical substance. A level 5 values of 00 indicate codes that are Israel specific (and not included in the ATC that is produced and approved by the WHO in Norway).

It is important to note that ATC codes cannot discriminate multivitamins with and without folic acid.

To classify maternal multivitamin exposure, we used the following ATC codes: A11AA03, A11CB00, A11CC03, A11CC05, A11CC20, A11DA01, A11DB00, A11GA01, A11GB01, A11HA02, A11HA03, and A11JB00. In addition, we used the following ATC codes to classify maternal folic acid exposure: B03BB01, and B03BB51.

eTable 1. Descriptive Characteristics of Autism Spectrum Disorder (ASD) Cases and Controls

Covariate	Covariate category	Control N (%)	ASD N (%)
Birth year	2003	9353 (20.91)	132 (23.08)
	2004	9187 (20.54)	127 (22.20)
	2005	8934 (19.97)	102 (17.83)
	2006	8529 (19.07)	110 (19.23)
	2007	8725 (19.51)	101 (17.66)
Offspring sex	Female	21988 (49.16)	102 (17.83)
	Male	22740 (50.84)	470 (82.17)
SES	Low	27140 (60.68)	243 (42.48)
	High	17588 (39.32)	329 (57.52)
Paternal psychiatric diagnosis	Absent	29809 (66.65)	314 (54.90)
	Present	14919 (33.35)	258 (45.10)
Paternal age at childbirth	< 40 years of age	39091 (87.40)	502 (87.76)
	≥ 40 years of age	5637 (12.60)	70 (12.24)
Maternal psychiatric diagnosis	Absent	29859 (66.76)	343 (59.97)
	Present	14869 (33.24)	229 (40.03)
Maternal age at childbirth	< 35 years of age	35753 (79.93)	454 (79.37)
	≥ 35 years of age	8975 (20.07)	118 (20.63)
Parity	1 child	11150 (24.93)	269 (47.03)
	> 1 child	33578 (75.07)	303 (52.97)
Folic acid and/or multivitamins supplement before pregnancy	Not before pregnancy ^a	32873 (73.50)	510 (89.16)
	Before pregnancy ^a	11855 (26.50)	62 (10.84)
Folic acid and/or multivitamins supplement during pregnancy	Not during pregnancy ^b	22952 (51.31)	464 (81.12)
	During pregnancy ^b	21776 (48.69)	108 (18.88)
Folic acid supplement before pregnancy	Not before pregnancy ^a	37549 (83.95)	524 (91.61)
	Before pregnancy ^a	7179 (16.05)	48 (8.39)
Folic acid supplement during pregnancy	Not during pregnancy ^b	28929 (64.68)	488 (85.31)
	During pregnancy ^b	15799 (35.32)	84 (14.69)
Multivitamin supplement before pregnancy	Not before pregnancy ^a	38029 (85.02)	545 (95.28)
	Before pregnancy ^a	6699 (14.98)	27 (4.72)
Multivitamin supplement during pregnancy	Not during pregnancy ^b	29049 (64.95)	486 (84.97)
	During pregnancy ^b	15679 (35.05)	86 (15.03)

Note. Abbreviations: ASD, Autism Spectrum Disorder, SES, Socioeconomic status.

^a 'Before pregnancy' refers to the interval from 271 to 540 days before childbirth

^b 'During pregnancy' refers to the interval from 270 days before childbirth to childbirth

The covariates ^a 'Before pregnancy' and ^b 'During pregnancy' are not mutually exclusive.

eTable 2. Descriptive Characteristics of Autism Spectrum Disorder (ASD) Cases and Controls: Exposures in Sensitivity Analyses

Sensitivity analysis	Exposure interval	Exposure groups: Dispensed vitamin supplement classification					
		Folic acid and/or Multivitamin		Folic Acid		Multivitamin	
		Control N(%)	ASD N(%)	Control N(%)	ASD N(%)	Control N(%)	ASD N(%)
Model 1. Comparing maternal exposure to vitamin supplements in mutually exclusive exposure intervals	Not exposed	18198 (40.69)	434 (75.87)	25863 (57.82)	469 (81.99)	25766 (57.61)	472 (82.52)
	Before pregnancy ^a only	4754 (10.63)	30 (5.24)	3066 (6.85)	19 (3.32)	3283 (7.34)	14 (2.45)
	During pregnancy ^b only	14675 (32.81)	76 (13.29)	11686 (26.13)	55 (9.62)	12263 (27.42)	73 (12.76)
	Before ^a and during ^b pregnancy	7101 (15.88)	32 (5.59)	4113 (9.20)	29 (5.07)	3416 (7.64)	13 (2.27)
Model 2. Comparing maternal exposure to vitamin supplements <u>before pregnancy</u> to maternal exposure to vitamin supplements <u>during pregnancy</u>	Before pregnancy ^a only	4754 (24.47)	30 (28.30)	3066 (20.78)	19 (25.68)	3283 (21.12)	14 (16.09)
	During pregnancy ^b only	14675 (75.53)	76 (71.70)	11686 (79.22)	55 (74.32)	12263 (78.88)	73 (83.91)
Model 3. Comparing maternal exposure to vitamin supplements from 4 weeks before up to 8 weeks into pregnancy to no maternal vitamin supplements exposure in the same interval	No exposure from four weeks before to eight weeks into pregnancy	33542 (74.99)	502 (87.76)	36617 (81.87)	522 (91.26)	37589 (84.04)	535 (93.53)

Sensitivity analysis	Exposure interval	Exposure groups: Dispensed vitamin supplement classification					
		Folic acid and/or Multivitamin		Folic Acid		Multivitamin	
		Control N(%)	ASD N(%)	Control N(%)	ASD N(%)	Control N(%)	ASD N(%)
	Exposure from four weeks before to eight weeks into pregnancy	11186 (25.01)	70 (12.24)	8111 (18.13)	50 (8.74)	7139 (15.96)	37 (6.47)
Model 4. Comparing maternal exposure to vitamin supplements two years before pregnancy to maternal exposure to vitamin supplements during pregnancy in mutually exclusive exposure intervals	Never exposed, or not exposed during the two-year-period before pregnancy or not exposed during pregnancy ^b	12073 (34.13)	333 (75.68)	17457 (49.35)	350 (79.55)	17646 (49.88)	350 (79.55)
	During the second year before pregnancy only	4927 (13.93)	14 (3.18)	4080 (11.53)	17 (3.86)	4413 (12.47)	12 (2.73)
	During pregnancy ^b only	11289 (31.91)	70 (15.91)	9758 (27.58)	63 (14.32)	9137 (25.83)	67 (15.23)
	During pregnancy ^b and during the second year before pregnancy only	7086 (20.03)	23 (5.23)	4080 (11.53)	10 (2.27)	4179 (11.81)	11 (2.50)

Sensitivity analysis	Exposure interval	Exposure groups: Dispensed vitamin supplement classification					
		Folic acid and/or Multivitamin		Folic Acid		Multivitamin	
		Control N(%)	ASD N(%)	Control N(%)	ASD N(%)	Control N(%)	ASD N(%)
Model 5. Comparing maternal exposure to vitamin supplements before pregnancy and maternal exposure to vitamin supplements during pregnancy <i>in singletons only</i>	Not before pregnancy ^a	8564 (76.81)	239 (88.85)	9285 (83.27)	245 (91.08)	9995 (89.64)	262 (97.40)
	Before pregnancy ^a	2586 (23.19)	30 (11.15)	1865 (16.73)	24 (8.92)	1155 (10.36)	7 (2.60)
	Not during pregnancy ^b	5821 (52.21)	219 (81.41)	7068 (63.39)	223 (82.90)	7291 (65.39)	225 (83.64)
	During pregnancy ^b	5329 (47.79)	50 (18.59)	4082 (36.61)	46 (17.10)	3859 (34.61)	44 (16.36)
Model 6. Comparing maternal exposure to vitamin supplements before pregnancy and maternal exposure to vitamin supplements during pregnancy <i>in male offspring only</i>	Not before pregnancy ^a	16754 (73.68)	420 (89.36)	19098 (83.98)	430 (91.49)	19320 (84.96)	450 (95.74)
	Before pregnancy ^a	5986 (26.32)	50 (10.64)	3642 (16.02)	40 (8.51)	3420 (15.04)	20 (4.26)
	Not during pregnancy ^b	11703 (51.46)	374 (79.57)	14743 (64.83)	400 (85.11)	14753 (64.88)	396 (84.26)
	During pregnancy ^b	11037 (48.54)	96 (20.43)	7997 (35.17)	70 (14.89)	7987 (35.12)	74 (15.74)

Sensitivity analysis	Exposure interval	Exposure groups: Dispensed vitamin supplement classification					
		Folic acid and/or Multivitamin		Folic Acid		Multivitamin	
		Control N(%)	ASD N(%)	Control N(%)	ASD N(%)	Control N(%)	ASD N(%)
Model 7. Comparing maternal exposure to vitamin supplements before pregnancy and maternal exposure to vitamin supplements during pregnancy <i>in female offspring only</i>	Not before pregnancy ^a	16119 (73.31)	90 (88.24)	18451 (83.91)	94 (92.16)	18709 (85.09)	95 (93.14)
	Before pregnancy ^a	5869 (26.69)	12 (11.76)	3537 (16.09)	8 (7.84)	3279 (14.91)	7 (6.86)
	Not during pregnancy ^b	11249 (51.16)	90 (88.24)	14186 (64.52)	88 (86.27)	14296 (65.02)	90 (88.24)
	During pregnancy ^b	10739 (48.84)	12 (11.76)	7802 (35.48)	14 (13.73)	7692 (34.98)	12 (11.76)
Model 8. Comparing maternal exposure to vitamin supplements before pregnancy and maternal exposure to vitamin supplements during pregnancy <i>in offspring of low SES parents</i>	Not before pregnancy ^a	20252 (74.62)	224 (92.18)	23241 (85.63)	230 (94.65)	22985 (84.69)	232 (95.47)
	Before pregnancy ^a	6888 (25.38)	19 (7.82)	3899 (14.37)	13 (5.35)	4155 (15.31)	11 (4.53)
	Not during pregnancy ^b	14031 (51.70)	208 (85.60)	17808 (65.62)	218 (89.71)	17703 (65.23)	216 (88.89)
	During pregnancy ^b	13109 (48.30)	35 (14.40)	9332 (34.38)	25 (10.29)	9437 (34.77)	27 (11.11)

Sensitivity analysis	Exposure interval	Exposure groups: Dispensed vitamin supplement classification					
		Folic acid and/or Multivitamin		Folic Acid		Multivitamin	
		Control N(%)	ASD N(%)	Control N(%)	ASD N(%)	Control N(%)	ASD N(%)
Model 9. Comparing maternal exposure to vitamin supplements before pregnancy and maternal exposure to vitamin supplements during pregnancy <i>in offspring of parents with a psychiatric diagnosis at time of childbirth (present in both parents)</i>	Not before pregnancy ^a	4450 (72.32)	109 (86.51)	5063 (82.29)	111 (88.10)	5237 (85.11)	120 (95.24)
	Before pregnancy ^a	1703 (27.68)	17 (13.49)	1090 (17.71)	15 (11.90)	916 (14.89)	6 (4.76)
	Not during pregnancy ^b	3071 (49.91)	100 (79.37)	3819 (62.07)	107 (84.92)	3982 (64.72)	106 (84.13)
	During pregnancy ^b	3082 (50.09)	26 (20.63)	2334 (37.93)	19 (15.08)	2171 (35.28)	20 (15.87)
Model 10. Comparing maternal exposure to vitamin supplements before pregnancy and maternal exposure to vitamin supplements during pregnancy <i>in offspring of parents without a psychiatric diagnosis at time of childbirth (absent in both parents)</i>	Not before pregnancy ^a	15734 (74.59)	191 (90.52)	17901 (84.87)	197 (93.36)	17999 (85.33)	203 (96.21)
	Before pregnancy ^a	5359 (25.41)	20 (9.48)	3192 (15.13)	14 (6.64)	3094 (14.67)	8 (3.79)
	Not during pregnancy ^b	11070 (52.48)	174 (82.46)	14008 (66.41)	182 (86.26)	13726 (65.07)	179 (84.83)

Sensitivity analysis	Exposure interval	Exposure groups: Dispensed vitamin supplement classification					
		Folic acid and/or Multivitamin		Folic Acid		Multivitamin	
		Control N(%)	ASD N(%)	Control N(%)	ASD N(%)	Control N(%)	ASD N(%)
	During pregnancy ^b	10023 (47.52)	37 (17.54)	7085 (33.59)	29 (13.74)	7367 (34.93)	32 (15.17)
Model 11. Comparing maternal exposure to vitamin supplements before pregnancy and maternal exposure to vitamin supplements during pregnancy <i>in offspring of mothers with a documented vitamin deficiency at time of childbirth</i>	Not before pregnancy ^a	3489 (61.66)	30 (62.50)	4274 (75.54)	32 (66.67)	4413 (78.00)	43 (89.58)
	Before pregnancy ^a	2169 (38.34)	18 (37.50)	1384 (24.46)	16 (33.33)	1245 (22.00)	5 (10.42)
	Not during pregnancy ^b	2415 (42.68)	37 (77.08)	3151 (55.69)	34 (70.83)	3322 (58.71)	39 (81.25)
	During pregnancy ^b	3243 (57.32)	11 (22.92)	2507 (44.31)	14 (29.17)	2336 (41.29)	9 (18.75)

Sensitivity analysis	Exposure interval	Exposure groups: Dispensed vitamin supplement classification					
		Folic acid and/or Multivitamin		Folic Acid		Multivitamin	
		Control N(%)	ASD N(%)	Control N(%)	ASD N(%)	Control N(%)	ASD N(%)
Model 12. Comparing maternal exposure to vitamin supplements before pregnancy and maternal exposure to vitamin supplements during pregnancy <i>in offspring of mothers without a documented vitamin deficiency at time of childbirth</i>	Not before pregnancy ^a	29384 (75.21)	480 (91.60)	33275 (85.17)	492 (93.89)	33616 (86.04)	502 (95.80)
	Before pregnancy ^a	9686 (24.79)	44 (8.40)	5795 (14.83)	32 (6.11)	5454 (13.96)	22 (4.20)
	Not during pregnancy ^b	20537 (52.56)	427 (81.49)	25778 (65.98)	454 (86.64)	25727 (65.85)	447 (85.31)
	During pregnancy ^b	18533 (47.44)	97 (18.51)	13292 (34.02)	70 (13.36)	13343 (34.15)	77 (14.69)
Model 13. Comparing maternal exposure to vitamin supplements before pregnancy and maternal exposure to vitamin supplements during pregnancy Outcome: ASD with ID	Not before pregnancy ^a	32921 (73.51)	462 (89.19)	37599 (83.96)	474 (91.51)	38081 (85.04)	493 (95.17)
	Before pregnancy ^a	11861 (26.49)	56 (10.81)	7183 (16.04)	44 (8.49)	6701 (14.96)	25 (4.83)
	Not during pregnancy ^b	22997 (51.35)	419 (80.89)	28980 (64.71)	437 (84.36)	29095 (64.97)	440 (84.94)

Sensitivity analysis	Exposure interval	Exposure groups: Dispensed vitamin supplement classification					
		Folic acid and/or Multivitamin		Folic Acid		Multivitamin	
		Control N(%)	ASD N(%)	Control N(%)	ASD N(%)	Control N(%)	ASD N(%)
	During pregnancy ^b	21785 (48.65)	99 (19.11)	15802 (35.29)	81 (15.64)	15687 (35.03)	78 (15.06)
Model 14. Comparing maternal exposure to vitamin supplements before pregnancy and maternal exposure to vitamin supplements during pregnancy Outcome: ASD without ID	Not before pregnancy ^a	33335 (73.68)	48 (88.89)	38023 (84.04)	50 (92.59)	38522 (85.14)	52 (96.30)
	Before pregnancy ^a	11911 (26.32)	6 (11.11)	7223 (15.96)	4 (7.41)	6724 (14.86)	2 (3.70)
	Not during pregnancy ^b	23371 (51.65)	45 (83.33)	29366 (64.90)	51 (94.44)	29489 (65.17)	46 (85.19)
	During pregnancy ^b	21875 (48.35)	9 (16.67)	15880 (35.10)	3 (5.56)	15757 (34.83)	8 (14.81)

Note: Abbreviations: ASD, Autism Spectrum Disorder. ID., Intellectual disability, SES., Socioeconomic Status.

^a 'Before pregnancy' refers to the interval of 271 to 540 days before childbirth

^b 'During pregnancy' refers to the interval of 270 days before childbirth to childbirth

Exposure intervals are not mutually exclusive except Models 1-4

eTable 3. Unadjusted Relative Risk (RR) Estimates and 95% Confidence Intervals From Sensitivity Analysis

Sensitivity analysis	Exposure interval	Exposure groups: Dispensed vitamin supplement classification					
		Folic acid and/or Multivitamin		Folic Acid		Multivitamin supplements	
		RR (95% CI)	p-value	RR (95% CI)	p-value	RR (95% CI)	p-value
Model 1. Comparing maternal exposure to vitamin supplements in mutually exclusive exposure intervals	Before pregnancy only ^a	0.27 (0.19, 0.39)	<.001	0.35 (0.22, 0.55)	<.001	0.24 (0.14, 0.40)	<.001
	During pregnancy only ^a	0.22 (0.17, 0.28)	<.001	0.26 (0.20, 0.35)	<.001	0.33 (0.26, 0.42)	<.001
	Before and during pregnancy ^a	0.19 (0.14, 0.28)	<.001	0.39 (0.27, 0.57)	<.001	0.21 (0.12, 0.37)	<.001
Model 2. Comparing maternal exposure to vitamin supplements <u>before pregnancy</u> to maternal exposure to vitamin supplements <u>during pregnancy</u>	During pregnancy only ^b	0.82 (0.54, 1.25)	0.36	0.76 (0.45, 1.28)	0.30	1.40 (0.79, 2.45)	0.25
Model 3. Comparing maternal exposure to vitamin supplements from 4 weeks before up to 8 weeks into pregnancy to no maternal vitamin supplements exposure in the same interval	Exposure from 4 weeks before to 8 weeks into pregnancy ^c	0.42 (0.33, 0.54)	<.001	0.43 (0.32, 0.58)	<.001	0.37 (0.26, 0.51)	<.001

Sensitivity analysis	Exposure interval	Exposure groups: Dispensed vitamin supplement classification					
		Folic acid and/or Multivitamin		Folic Acid		Multivitamin supplements	
		RR (95% CI)	p-value	RR (95% CI)	p-value	RR (95% CI)	p-value
Model 4. Comparing maternal exposure to vitamin supplements two years before pregnancy to maternal exposure to vitamin supplements during pregnancy in mutually exclusive exposure intervals	During the second year before pregnancy only ^d	0.11 (0.06, 0.18)	<.001	0.21 (0.13, 0.35)	<.001	0.14 (0.08, 0.25)	<.001
	During pregnancy only ^d	0.23 (0.18, 0.30)	<.001	0.33 (0.25, 0.43)	<.001	0.38 (0.29, 0.49)	<.001
	During the second year before pregnancy and during pregnancy only ^d	0.12 (0.08, 0.19)	<.001	0.13 (0.07, 0.24)	<.001	0.14 (0.07, 0.25)	<.001
Model 5. Comparing maternal exposure to vitamin supplements before pregnancy and maternal exposure to vitamin supplements during pregnancy <i>in singletons only</i>	Before pregnancy ^e	0.50 (0.35, 0.72)	<.001	0.62 (0.41, 0.93)	0.02	0.27 (0.13, 0.57)	<.001
	During pregnancy ^f	0.28 (0.20, 0.37)	<.001	0.39 (0.29, 0.53)	<.001	0.40 (0.29, 0.55)	<.001
Model 6. Comparing maternal exposure to vitamin supplements before pregnancy and	Before pregnancy ^e	0.40 (0.30, 0.54)	<.001	0.64 (0.46, 0.87)	0.005	0.30 (0.19, 0.47)	<.001

Sensitivity analysis	Exposure interval	Exposure groups: Dispensed vitamin supplement classification					
		Folic acid and/or Multivitamin		Folic Acid		Multivitamin supplements	
		RR (95% CI)	p-value	RR (95% CI)	p-value	RR (95% CI)	p-value
maternal exposure to vitamin supplements during pregnancy <i>in male offspring only</i>	During pregnancy ^f	0.31 (0.25, 0.38)	<.001	0.35 (0.28, 0.45)	<.001	0.38 (0.30, 0.49)	<.001
Model 7. Comparing maternal exposure to vitamin supplements before pregnancy and maternal exposure to vitamin supplements during pregnancy <i>in female offspring only</i>	Before pregnancy ^e	0.47 (0.26, 0.85)	0.01	0.58 (0.29, 1.15)	0.12	0.52 (0.24, 1.09)	0.08
	During pregnancy ^f	0.15 (0.08, 0.28)	<.001	0.31 (0.18, 0.54)	<.001	0.26 (0.15, 0.48)	<.0001
Model 8. Comparing maternal exposure to vitamin supplements before pregnancy and maternal exposure to vitamin supplements during pregnancy <i>in offspring of low SES parents</i>	Before pregnancy ^e	0.32 (0.20, 0.51)	<.001	0.47 (0.27, 0.81)	0.007	0.33 (0.18, 0.61)	<.001
	During pregnancy ^f	0.20 (0.14, 0.29)	<.001	0.24 (0.16, 0.36)	<.001	0.26 (0.17, 0.39)	<.001

Sensitivity analysis	Exposure interval	Exposure groups: Dispensed vitamin supplement classification					
		Folic acid and/or Multivitamin		Folic Acid		Multivitamin supplements	
		RR (95% CI)	p-value	RR (95% CI)	p-value	RR (95% CI)	p-value
Model 9. Comparing maternal exposure to vitamin supplements before pregnancy and maternal exposure to vitamin supplements during pregnancy <i>in offspring of parents with a psychiatric diagnosis at time of childbirth (present in both parents)</i>	Before pregnancy ^e	0.50 (0.30, 0.82)	0.006	0.81 (0.49, 1.36)	0.43	0.34 (0.15, 0.75)	0.008
	During pregnancy ^f	0.29 (0.19, 0.44)	<.001	0.31 (0.19, 0.49)	<.001	0.38 (0.24, 0.61)	<.001
Model 10. Comparing maternal exposure to vitamin supplements before pregnancy and maternal exposure to vitamin supplements during pregnancy <i>in offspring of parents without a psychiatric diagnosis at time of childbirth (absent in both parents)</i>	Before pregnancy ^e	0.38 (0.24, 0.59)	<.001	0.52 (0.31, 0.87)	0.01	0.28 (0.14, 0.56)	<.001
	During pregnancy ^f	0.26 (0.19, 0.37)	<.001	0.35 (0.24, 0.50)	<.001	0.37 (0.26, 0.54)	<.001

Sensitivity analysis	Exposure interval	Exposure groups: Dispensed vitamin supplement classification					
		Folic acid and/or Multivitamin		Folic Acid		Multivitamin supplements	
		RR (95% CI)	p-value	RR (95% CI)	p-value	RR (95% CI)	p-value
Model 11. Comparing maternal exposure to vitamin supplements before pregnancy and maternal exposure to vitamin supplements during pregnancy <i>in offspring of mothers with a documented vitamin deficiency at time of childbirth</i>	Before pregnancy ^e	1.10 (0.62, 1.94)	0.75	1.80 (1.00, 3.21)	0.05	0.46 (0.18, 1.13)	0.09
	During pregnancy ^f	0.22 (0.12, 0.43)	<.001	0.47 (0.26, 0.85)	0.01	0.35 (0.17, 0.71)	0.004
Model 12. Comparing maternal exposure to vitamin supplements before pregnancy and maternal exposure to vitamin supplements during pregnancy <i>in offspring of mothers without a documented vitamin deficiency at time of childbirth</i>	Before pregnancy ^e	0.34 (0.25, 0.46)	<.001	0.49 (0.35, 0.69)	<.001	0.33 (0.21, 0.50)	<.001
	During pregnancy ^f	0.28 (0.23, 0.35)	<.001	0.33 (0.26, 0.42)	<.001	0.37 (0.29, 0.47)	<.001

Sensitivity analysis	Exposure interval	Exposure groups: Dispensed vitamin supplement classification					
		Folic acid and/or Multivitamin		Folic Acid		Multivitamin supplements	
		RR (95% CI)	p-value	RR (95% CI)	p-value	RR (95% CI)	p-value
Model 13. Comparing maternal exposure to vitamin supplements before pregnancy and maternal exposure to vitamin supplements during pregnancy Outcome: ASD with ID	Before pregnancy ^e	0.43 (0.19, 0.98)	0.04	0.63 (0.24, 1.66)	0.35	0.26 (0.06, 1.06)	0.06
	During pregnancy ^f	0.23 (0.12, 0.47)	<.001	0.12 (0.04, 0.36)	<.001	0.36 (0.17, 0.76)	0.007
Model 14. Comparing maternal exposure to vitamin supplements before pregnancy and maternal exposure to vitamin supplements during pregnancy Outcome: ASD without ID	Before pregnancy ^e	0.41 (0.31, 0.54)	<.001	0.62 (0.46, 0.84)	0.002	0.34 (0.23, 0.51)	<.001
	During pregnancy ^f	0.28 (0.22, 0.34)	<.001	0.37 (0.29, 0.46)	<.001	0.36 (0.28, 0.46)	<.001

Note: Abbreviations, ASD, Autism Spectrum Disorder, ID, Intellectual Disability, RR, Relative Risk, CI, Confidence Intervals, SES: Socioeconomic status, P, P-value that tests the hypothesis RR=0 vs RR ≠ 0.

Each numbered model (1-14) consists of unadjusted models, one for each vitamin supplement classification.

^a Reference group: Not exposed

^b Reference group: Before pregnancy

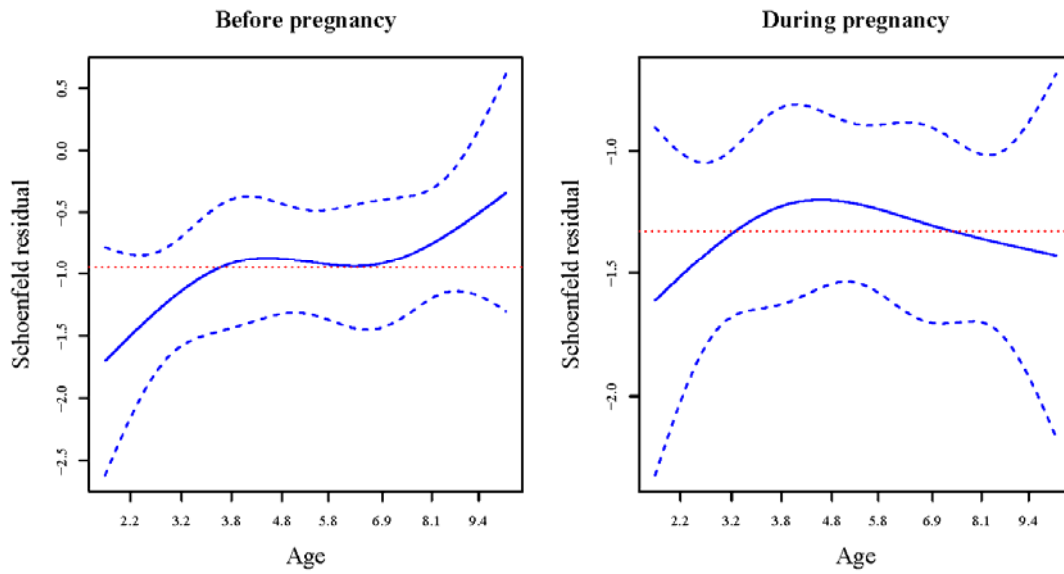
^c Reference group: No exposure from 4 weeks before to 8 weeks into pregnancy

^d Reference group: Never exposed, or not exposed during the two-year-period before pregnancy or not exposed during pregnancy

^e Reference group: Before pregnancy refers to exposure to vitamin supplement intake during the interval 271 to 540 days before childbirth, compared to the reference category of exposure not before pregnancy

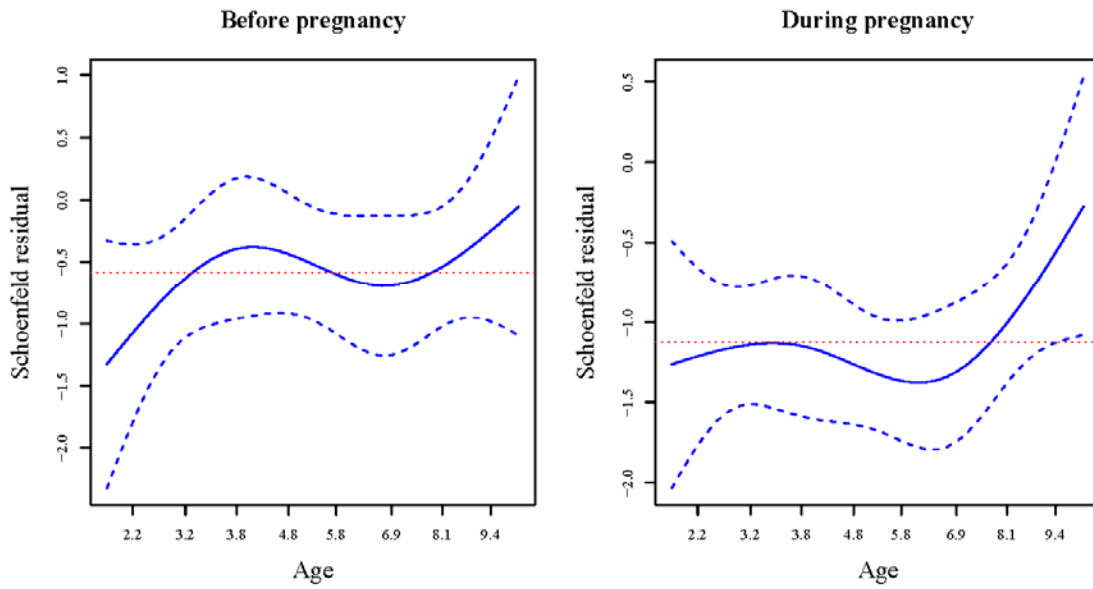
^f Reference group: During pregnancy refers to vitamin supplement intake during the interval from 270 days before childbirth to childbirth, compared to the reference category of exposure not during pregnancy

eFigure 1. Schoenfeld Residual Plots to Assess Proportional Hazards for the Primary Exposures to Folic Acid and/or Multivitamin Before and During Pregnancy



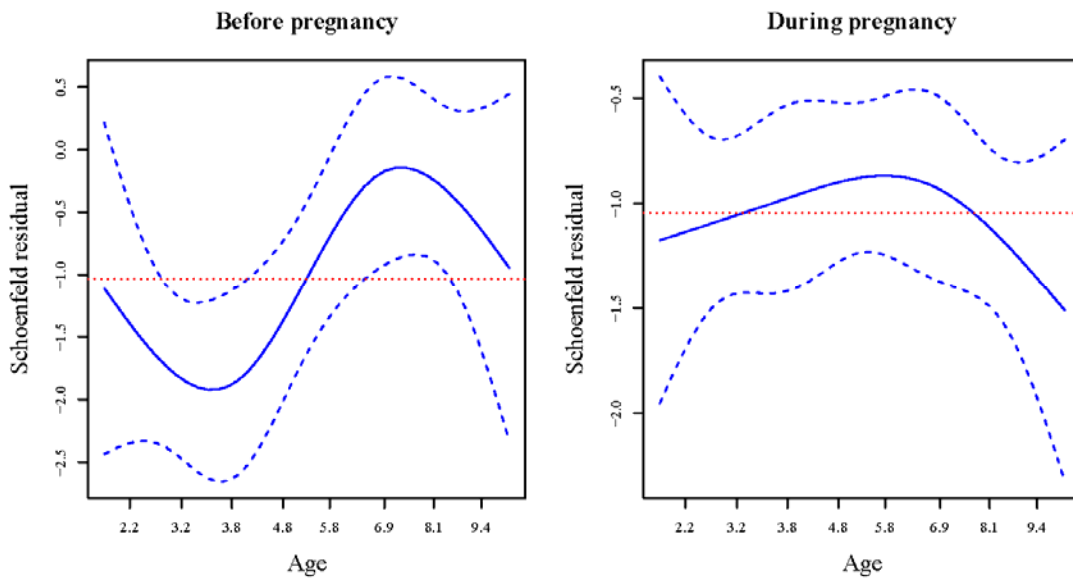
Note. Natural cubic splines and pointwise 95% two-sided confidence intervals estimating the mean residuals vs time (age). The red dotted line is the log of the Relative Risk.

eFigure 2. Schoenfeld Residual Plots to Assess Proportional Hazards for the Primary Exposures to Folic Acid Before and During Pregnancy



Note. Natural cubic splines and pointwise 95% two-sided confidence intervals estimating the mean residuals vs time (age). The red dotted line is the log of the Relative Risk.

eFigure 3. Schoenfeld Residual Plots to Assess Proportional Hazards for the Primary Exposures to Multivitamin Supplement Before and During Pregnancy



Note. Natural cubic splines and pointwise 95% two-sided confidence intervals estimating the mean residuals vs time (age). The red dotted line is the log of the Relative Risk.

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