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Association of prenatal vitamin E levels with child asthma and wheeze

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Abstract

Background: We investigated the individual and interaction effects of maternal plasma α- and γ-tocopherol levels (vitamin E isomers) on child asthma and wheeze at age 8–9.

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Methods: Mother-child dyads were enrolled between 2006–2011 into the Conditions Affecting Neurocognitive Development and Learning in Early Childhood (CANDLE) prenatal cohort. Maternal 2nd trimester samples were analyzed for tocopherol and lipid concentrations. We assessed child asthma/wheeze using the International Study of Asthma and Allergies in Childhood (ISAAC) and other self-reported questionnaires and derived four outcome variables: (1) ever, (2) current, and (3) strict current asthma, (4) current wheeze. In multivariable logistic regression analyses we assessed associations of vitamin E isomers and child asthma/wheeze outcomes (n=847 mother-child dyads) and tested for pre-specified interaction terms.

Results: Median cholesterol-corrected tocopherol levels [interquartile range (IQR)] were 5.0 (4.3–5.7) and 0.8 (0.7–0.9) (umol/mmol) for α- and γ-tocopherol, respectively. Associations between α-tocopherol and asthma outcome variables were inverse but not statistically significant. In contrast, for γ-tocopherol associations were in the positive direction, but also non-significant. Interactions analysis between tocopherols did not reach statistical significance for any outcome. Among children of women with a history of asthma, the likelihood of ever asthma in the child appears to be decreasing with increasing maternal α-tocopherol levels whereas this trend was not observed among those without a history of asthma (p-interaction=0.05).

Conclusion: We observed no associations for prenatal α- or γ-tocopherol concentrations with child asthma/wheeze. We detected some evidence of effect modification by maternal asthma history in associations between α-tocopherol and child asthma.

Keywords

Prenatal; vitamin E; alpha-tocopherol; gamma-tocopherol; asthma; wheezing

Introduction

Asthma is a common chronic condition which affects an estimated 7 million US children.[1] Recent research has focused on the hypothesis that inflammation and oxidative stress initiated *in utero* and during early life may play important roles in asthma development. Maternal prenatal dietary intake could impact childhood respiratory health through effects on inflammation and oxidative stress and by influencing early immune system development and predisposition to asthma-related disorders.[2, 3]

Vitamin E is a potent lipid soluble antioxidant which plays a role in mitigating oxidative stress and inflammation and in protecting cell membranes from free radical damage.[4] Vitamin E exists as eight isomers, alpha- (α-), beta-, gamma- (γ-), and delta-tocopherols and tocotrienols. Although α-tocopherol is thought to have the highest biological activity and is usually included in supplements, γ-tocopherol is the predominant form in the US diet[5] with higher levels found in nuts, seeds, whole grains, and vegetable oils.[3] Supplement users generally have higher blood α- and lower γ-tocopherol concentrations; in part, because blood lipid concentrations influence levels of vitamin E and these two isomers compete for hepatic lipoprotein transport.[6,7] This has led to recommendations that when vitamin E concentrations are used as an indicator of dietary intake, they should be adjusted for blood cholesterol.[8]

Animal models have demonstrated protective effects of vitamin E on allergic lung inflammation,[7] with some studies suggesting differential, possibly antagonistic effects, for α- and γ-tocopherol. In mice, allergic inflammation decreased with α-tocopherol but increased with γ-tocopherol supplementation and the anti-inflammatory actions of α-tocopherol declined with higher γ-tocopherol levels,[3] highlighting that these isomers should be considered concomitantly.

Two epidemiological studies of early life Vitamin E and child asthma have adopted this approach.[9, 10] Project Viva[9] measured tocopherols in 2nd trimester maternal and child plasma samples (n=622 mother-child dyads) and observed that higher α-tocopherol levels in childhood were positively associated with lung function but only when γ-tocopherol levels were low. Maternal concentrations of tocopherols (i.e. *in utero* child exposure) were not consistently associated with child spirometry parameters.[9] The Infant Susceptibility to Pulmonary Infections and Asthma Following RSV Exposure (INSPIRE)[11] examined the association between maternal postpartum α- and γ-tocopherol blood levels with child wheeze. Among 652 mother-child dyads higher postpartum maternal α-tocopherol concentrations were associated with a lower likelihood of wheezing in children. In contrast, γ-tocopherol concentrations were not associated with wheezing, and the protective association for α-tocopherol was attenuated among those with higher γ-tocopherol levels.[10] While these results are intriguing, neither study corrected tocopherols for blood cholesterol concentrations or assessed whether the association between prenatal vitamin E status and child asthma was modified by biological factors such as child sex or maternal asthma/atopic disease, a marker of a familial predisposition to atopy.

This research investigated the individual and interactive effects of maternal 2nd trimester plasma α- and γ-tocopherol levels corrected for cholesterol status on child asthma and wheeze at 8–9 years in mother-child dyads enrolled in the CANDLE prenatal prospective cohort study. *A priori*, we planned to assess potential effect modification by maternal asthma history and child sex. This research will contribute to efforts aimed at the primary prevention of childhood asthma, while providing greater insight into the mechanisms surrounding atopic disease pathogenesis.

Methods

Study Population

CANDLE is a prospective pregnancy cohort that enrolled approximately 1500 mother-child pairs between 2006 to 2011 in Shelby County, Tennessee (Memphis area).[12] Pregnant women were recruited during the 2nd trimester from community obstetric practices and an obstetric clinic and reflected the demographics of the County, which is roughly 2/3 African American and 1/3 White with a high proportion of low-income families.[13] To be eligible, women had to be County residents between 16–40 years of age, at 16–27 weeks of gestation with a singleton and low medical risk pregnancyand able to speak and understand English.[12, 14] For this investigation, dyads with infant estimated gestational age (EGA) <32 weeks were excluded to limit potential confounding from prematurity-associated lung disease. CANDLE child participants have been followed prospectively through ages 8–9 years. Study procedures were approved by the Institutional Review Boards of the University of Tennessee

Health Sciences Center (UTHSC), Vanderbilt University and the Icahn School of Medicine at Mount Sinai. Women 18 years of age and older provided informed consent while those under 18 years of age provided assent with consent provided by their legally authorized representative. Children participating in this investigation provided assent.

Child Asthma and Wheeze Assessment

We defined asthma/wheeze outcomes using the International Study of Asthma and Allergies in Childhood (ISAAC)[15] and other self-reported questionnaires administered at 8–9 years. E*ver asthma* was defined as an affirmative response to "Has a physician or other health care provider ever told your family that your child had asthma or reactive airway disease?" C*urrent asthma* was defined as an affirmative response to 2 out of 3 of the following questions: "Has a physician or other health care provider ever told your family that your child had asthma or reactive airway disease?" "Has your child ever had wheezing or whistling in the chest in the last 12 months?" and/or "In the past 12 months, has your child used any type of medicines, liquids, puffers or other medication for wheezing or asthma?" *Strict current asthma* was defined as an affirmative response to "Has a physician or other health care provider ever told your family that your child had asthma or reactive airway disease?" and either a) report of current wheezing, or b) asthma medication use in the past 12 months. *Current wheeze* was defined as affirmative response to "Had wheezing or whistling in the chest in the last 12 months."[14, 16]

Vitamin E Assessment

Our primary predictor variables were prenatal plasma tocopherol concentrations corrected for blood lipid (i.e., cholesterol) concentrations, expressed as umol tocopherol / mmol cholesterol, or umol/mmol.[17] Plasma α- and γ-tocopherol levels were measured in 2nd trimester maternal blood specimens. Tocopherols were assayed via HPLC and total cholesterol via an enzymatic method in the Molecular Epidemiology and Biomarker Research at the University of Minnesota (Dr. Myron Gross, Director; Hannah Carlson, Project Manager).[18, 19] We ran two control samples for each type of analysis. Inter-assay CVs for γ-tocopherol were 4.7% at 0.151 mg/dL, and 7.0% at 0.171 mg/dL and 8.5% at 0.797 mg/dL, and 8.8% at .741 mg/dL for α-tocopherol. Total cholesterol was measured on a Roche COBAS 8000 chemistry analyzer. For cholesterol, the inter-assay CVs were 4% at 168 mg/dL and 1.1% at 258 mg/dL. We defined adequacy of plasma α-tocopherol as ≥ 30 umol/L; McBurney and colleagues[6] derived a cutoff for adequacy for cholesterol-corrected α-tocopherol of 5.8 (umol/mmol) from the National Health and Nutrition Examination Survey data. Criteria for adequacy for γ-tocopherol have not been established.

Covariates

At enrollment, information on maternal age, race (self-reported Black/African American, White, other), educational attainment (<high school, high school/GED, colloge degree / technical school, >college degree), self-reported asthma history (yes/no), parity (primiparous/multiparous), smoking during pregnancy (yes/no) and pre-pregnancy body mass index (BMI (weight (kg)/ height (m^2)) were collected. Data collected at birth included gestational weight gain (kg), delivery type (vaginal, cesarean), sex (male, female), and estimated gestational age (weeks). Duration of any (none, <6 months, ≥6 months) and

exclusive breastfeeding (none, < 6 months, ≥6 months) and presence of pets in the home were assessed by questionnaire at 4–6 years of age.

Statistical Analysis

A total of 912 dyads had primary outcome variables available. Of these, 18 were excluded due to birth < 32 weeks. Exposure (levels of tocopherols and cholesterol) data were available for 847 women yielding a final analytic dataset of 847 dyads. Univariate and bivariate descriptive analysis of exposure, outcome and covariate data were conducted and we evaluated the distributions of potential confounders across quintiles of plasma α- and γ-tocopherol. Our primary models were adjusted for *a priori* selected covariates[14,16], similar to what we have reported previously: maternal age, race, educational status, parity and pre-pregnancy BMI and child sex and age (years) at the 8–9 year visit.

In separate multivariable logistic regression models, we investigated the association of α- and γ-tocopherol as log transformed continuous and categorical predictors (quintiles) with asthma/wheeze outcomes. We also evaluated non-linear associations using restricted cubic splines. Wald tests (P=overall) were used to test overall effects of tocopherols in the models. We tested for pre-specified interaction between α- and Y-tocopherol by including cross-product terms first using quintiles and then using continuous measures expanded with non-linear terms using restricted cubic splines. In separate multivariable regression models, we tested for potential effect modification by (1) maternal atopy (ever; yes/no), and (2) child sex, on the relationship between α- or Y-tocopherol exposure variables and child wheeze/asthma outcomes by including the relevant interaction term.

In sensitivity analyses, we included weight gain during pregnancy and duration of exclusive breastfeeding as covariates in our fully-adjusted models. Additionally, we modeled associations between α- and γ-tocopherol with asthma outcomes without correction for cholesterol to allow for direct comparisons to previously reported results by others and analyzed the associations of interest using the α- and γ-tocopherol ratio as a measure of exposure. Analyses were performed in R Version 4.2.1 (Vienna, Austria) with statistical significance at the 2-sided level alpha level of 0.05.

Results

In our sample of 847 mother-child dyads, parents reported ever asthma in 18.3%, current asthma in 13.5%, strict asthma in 11.3% and current wheeze in 12.9% of children. Approximately 65% of women were African American and 12% reported a history of asthma. About 37% and 28% of mothers met criteria for adequacy of plasma α-tocopherol and cholesterol-corrected α-tocopherol concentrations, respectively. The Spearman non-parametric correlation coefficient between α- and γ-tocopherol concentrations was ρ=0.15 for raw levels and ρ=0.11 (both P<0.001) for cholesterol-corrected tocopherol levels. Compared with women who had higher concentrations of α-tocopherol, those with lower levels tended to be younger and more likely to be African American; however, for γ-tocopherol, women with lower levels tended to be older and less likely to be African American (Table 1).

The associations between quintiles of α-tocopherol and our four asthma outcome variables (Table 2) were in the protective direction (inverse) but none reached statistical significance and 95% CIs were wide. In contrast, for quintiles of γ-tocopherol, the associations were trending in the positive direction and non-significant. Sensitivity analyses which additionally adjusted models for gestational weight gain and duration of exclusive breast feeding generated similar results. In sensitivity analyses conducted with expanded nonlinear terms, with low levels of γ-tocopherol (but not high), we observed the suggestion of a curvilinear protective effect for α-tocopherol with strict asthma (Supplemental Figure 1); however, the 95% CI bands for risk estimates overlapped. In covariate adjusted models, interactions for α- and γ-tocopherol did not reach statistical significance for any asthma outcome variables. Additional analyes using the ratio of α-tocopherol:γ-tocopherol as the measure of exposure yielded consistent results (Supplemental Table 1).

There were no significant interactions observed by sex with either tocopherol for any asthma/wheeze outcomes. For maternal atopy, we observed a significant interaction for the ever asthma outcome with α-tocopherol in the adjusted model (p interaction=0.05). For children of women with an asthma history, the likelihood of ever asthma appeared to decrease with increasing α-tocopherol; this trend was not observed among women without an asthma history (Figure 1A). We did not observe significant interactions between maternal atopy history and α-tocopherol for the other three outcomes.

Lastly, we conducted sensitivity analyses to assess associations between α- and γ-tocopherol with asthma/wheeze outcome variables utilizing tocopherol variables with raw value measures (without cholesterol correction) to allow for comparisons with results of previous investigations. Overall, these demonstrated a similar pattern (not presented) to our reported results.

Discussion

In this large diverse prospective prenatal cohort study, we did not find evidence for robust associations for either maternal 2nd trimester α- or γ-tocopherol concentrations with child asthma/wheeze at eight years of age. Among women with a history of asthma, the likelihood of child ever asthma, but not other outcomes, was lower with higher α-tocopherol concentrations, but there was no association among women without asthma. This finding, in particular, requires examination in other populations as it suggests that α-tocopherol could have a role in buffering risk of intergenerational transmission of risk.

Previous research examining pregnancy vitamin E measures in relation to child respiratory outcomes has produced mixed results. Prior studies did not correct tocopherol levels for cholesterol concentrations and one study collected blood specimens at a postpartum visit via finger stick. In a Massachusetts cohort, Kumar et al.[9] evaluated associations between maternal 2nd trimester plasma tocopherols in relation to spirometry measures in children at ages 6–10 years (n=622). Maternal tocopherol levels were not consistently associated with child spirometry parameters in multivariable models.[9] In another prospective birth cohort in Tennessee, Stone et al.[11] analyzed the association between maternal postpartum finger stick blood samples analyzed for α- and γ-tocopherol with child wheeze or asthma medication

receipt in the past 12 months or parent reported child asthma diagnosis (n=652). Higher α-tocopherol concentrations were associated with a lower likelihood of wheezing (OR for interquartile range increase = 0.70 (95% CI: 0.53, 0.92)); γ-tocopherol concentrations were not associated with wheezing (OR=0.79; 95% CI: 0.56, 1.10). Further, the protective association for α-tocopherol was attenuated among those with higher γ-tocopherol levels (p-interaction=0.05).[10]

Vitamin E levels in this population were similar to those observed in previous research and in US nationally representative data. Recommended intakes for vitamin E for pregnant women are 15 mg/day (as α-tocopherol) and are set to result in serum α-tocopherol levels of approximately 27.9 umol/L (1.2017 mg/dL).[20] Although national surveys have reported that most adults do not meet the recommendations for vitamin E intakes, deficiency (defined as serum < 12 umol/L or 0.5169 mg/dL) symptoms are rare.[6] No women in the current study had vitamin E levels < 12 umol/L.

Possible interpretations for our interaction results suggesting that the potential protective effect of higher α-tocopherol concentrations related to childhood asthma development is limited to women with asthma history could be that the potential for protective effects is more likely to be observed among those at higher risk. Previous research has shown that childhood asthma may be more common among children of women with uncontrolled asthma during pregnancy.[18, 21, 22] Another possibility is that maternal atopy or the medications to treat this condition may affect the bioavailability or metabolism of α-tocopherol thereby contributing to protective effects. In this study, women in the lowest quintile of α-tocopherol were the least likely to report a history of asthma (8% in the lowest v. 13% in the highest quintile). Lastly, we cannot rule out the possibility that the observed differences could be due to chance; however, in previous analyses in the CANDLE cohort we observed related results. Maternal n-6 PUFA concentrations were positively associated with child respiratory outcomes in main effects models, and in interaction models, increasing n-6 PUFAS were associated with higher risk of respiratory outcomes only among children of women with asthma history.[14]

This study has a number of strengths and some potential limitations. Our analyses were conducted in a well-characterized, large, ethnically diverse prospective cohort and utilized objectively measured exposures. Samples measured for tocopherols were all collected at a similar time during pregnancy and adjusted for blood lipid concentrations. Limitations of this study include that tocopherol measures were analyzed at only one time during pregnancy. We used parent-reported questionnaire data to derive our child asthma/wheeze variables; however, these questions have been previously validated.[23] Nevertheless, although we include one measure of a familial predisposition to develop asthma, maternal asthma, there are likely some children in the group of dyads without maternal asthma who have a first degree relative with asthma. While we controlled for a number of potential confounders and assessed several possible effect modifiers, the possibility of unmeasured confounding or effect modifying variables that may have influenced our results cannot be ruled out.

This study adds to the research assessing prenatal diet as an important consideration in the development of child respiratory diseases. Future research should include investigations of

these biomarkers across multiple time points in pregnancy and address the role of prenatal vitamin E status in child respiratory disease development at other ages and using objective outcomes and/or physician diagnosed asthma/wheeze.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations:

α-tocopherol	alpha-tocopherol
γ- tocopherol	gamma-tocopherol
CI	95% confidence interval
IQR	interquartile range
OR	odds ratio

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Key messages

This study did not find evidence for robust associations for either maternal α- or γ-tocopherol concentrations with child asthma/wheeze overall. Among women with a history of asthma, the likelihood of children ever having asthma was lower with higher α-tocopherol concentrations, but there was no association among women without asthma. Future research to investigate the potential role for α-tocopherol in buffering risk of intergenerational transmission of risk is warranted.

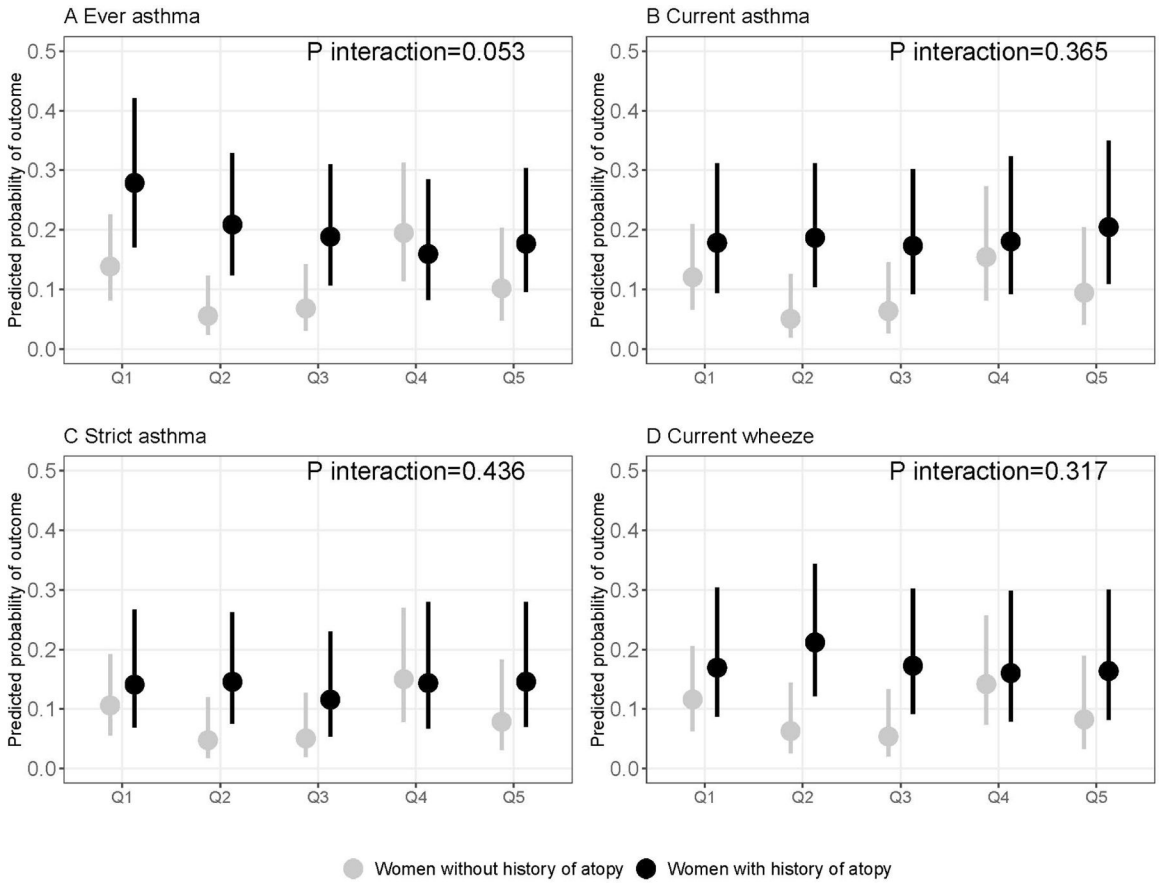

FIGURE 1.

Interaction analysis of the association between mother's atopy status and α- tocopherol with asthma outcomes. Model covariates included mother's age, educational status, parity and prepregnancy BMI, and child's age and sex. Alpha-tocopherol quintiles are on the X-axes and each panel presents an asthma outcome.

Table 1:

Characteristics of mother-child dyads enrolled in CANDLE by maternal 2nd trimester plasma vitamin E status

Characteristics	α-tocopherol (umol/mmol)					γ-tocopherol (umol/mmol)				
	Q1	Q2	Q3	Q4	Q5	Q1	Q2	Q3	Q4	Q5
	<4.17	4.17–4.74	4.75–5.26	5.27–5.89	≥5.90	<0.67	0.67–0.74	0.75–0.83	0.84–0.97	≥0.98
	n=170	n=169	n=170	n=169	n=169	n=170	n=169	n=170	n=169	n=169
Maternal race; n (%)										
White	26 (15)	35 (21)	59 (35)	73 (43)	95 (56)	72 (43)	108 (64)	106 (62)	118 (70)	142 (85)
African-American	143 (84)	133 (79)	109 (64)	89 (53)	72 (43)	95 (56)	58 (34)	62 (36)	48 (28)	25 (15)
Other	1 (1)	1 (1)	1 (1)	7 (4)	2 (2)	2 (1)	3 (2)	2 (1)	3 (2)	1 (1)
Maternal age (y); median (IQR)	25 (21–28)	24 (24–29)	27 (22–31)	28 (24–32)	29 (25–33)	28 (23–33)	26 (23–31)	26 (23–30)	25 (21–30)	26 (21–30)
Maternal education; n (%)										
< than high school	24 (14)	35 (21)	6 (4)	13 (8)	6 (3)	9 (5)	17 (10)	20 (12)	18 (11)	20 (12)
High school / GED	94 (56)	85 (50)	84 (49)	66 (39)	57 (34)	61 (36)	71 (41)	76 (45)	94 (56)	85 (51)
> College / Tech School	44 (26)	37 (22)	56 (33)	60 (36)	70 (41)	60 (35)	57 (34)	57 (34)	40 (24)	53 (32)
College+	7 (4)	12 (7)	24 (14)	30 (18)	36 (21)	40 (24)	25 (15)	17 (10)	17 (10)	10 (6)
Maternal insurance; n (%)										
Private	48 (28)	60 (36)	32 (48)	85 (50)	109 (64)	66 (39)	100 (59)	89 (52)	99 (59)	109 (64)
Medicaid	122 (72)	109 (64)	88 (52)	84 (50)	60 (36)	104 (61)	69 (41)	81 (40)	70 (41)	60 (36)
Marital status; n (%)										
Single, separated, divorced	89 (53)	87 (52)	63 (37)	69 (40)	45 (26)	41 (24)	65 (39)	76 (45)	8 (46)	91 (54)
Married or with partner	30 (47)	82 (49)	107 (63)	102 (60)	124 (74)	129 (75)	104 (61)	94 (55)	91 (54)	77 (46)
Maternal asthma ever in life; n (%)										
Yes	13 (8)	31 (18)	23 (14)	14 (8)	22 (13)	25 (15)	20 (12)	16 (9)	22 (13)	20 (12)
No	154 (92)	138 (82)	147 (86)	155 (92)	144 (87)	145 (85)	145 (88)	153 (91)	146 (87)	149 (88)
Maternal smoking during pregnancy; n (%)										
Yes	14 (8)	19 (11)	11 (6)	15 (9)	11 (7)	15 (9)	17 (10)	9 (5)	20 (12)	9 (5)
No	155 (92)	150 (94)	159 (94)	154 (91)	158 (93)	155 (91)	151 (90)	161 (95)	149 (88)	160 (95)

Characteristics	α-tocopherol (umol/mmol)					γ-tocopherol (umol/mmol)				
	Q1	Q2	Q3	Q4	Q5	Q1	Q2	Q3	Q4	Q5
	<4.17	4.17–4.74	4.75–5.26	5.27–5.89	≥5.90	<0.67	0.67–0.74	0.75–0.83	0.84–0.97	≥0.98
	n=170	n=169	n=170	n=169	n=169	n=170	n=169	n=170	n=169	n=169
Maternal pre-pregnancy BMI (kg/m^2); median (IQR)	28 (22–33)	27 (23–32)	25 (22–32)	26 (22–33)	25 (23–31)	24 (21–28)	26 (22–30)	26 (22–32)	27 (23–33)	30 (25–37)
Maternal gestational wt. gain (kg); median (IQR)	14 (9–19)	15 (11–19)	15 (11–19)	14 (10–17)	14 (10–18)	14 (10–17)	14 (10–20)	14 (10–18)	15 (11–20)	14 (9–18)
Maternal parity; n (%)										
Yes	118 (69)	101 (60)	97 (57)	99 (59)	99 (59)	92 (54)	109 (64)	100 (59)	101 (60)	112 (66)
No	32 (31)	68 (40)	73 (45)	70 (41)	70 (41)	78 (46)	60 (36)	70 (41)	68 (40)	37 (34)
Maternal delivery; n (%)										
Vaginal	111 (65)	108 (64)	113 (66)	106 (63)	97 (57)	110 (65)	112 (66)	109 (64)	107 (63)	97 (57)
C-section	59 (35)	61 (36)	57 (34)	63 (37)	72 (43)	60 (35)	57 (34)	61 (36)	62 (37)	72 (43)
Maternal plasma cholesterol (mg/dL); median (IQR)	222 201–245	211 185–241	206 186–232	202 178–224	212 179–232	244 221–268	222 204–240	205 185–224	198 177–221	181 156–203
Birth weight (g); median (IQR)	3236 2940–3489	3166 2891–3500	3260 3025–3618	3348 2984–3666	3360 3090–3690	3280 3029–3620	3233 2955–3535	3295 2999–3638	3280 2980–3670	3230 2950–3480
Infant EGA (weeks); median (IQR)	38 39–40	38 39–40	38 39–40	38 39–40	38 39–40	38 39–40	38 39–40	38 39–40	38 39–40	38 39–40
Child BMI (%); median IQR)	70 (41–90)	74 (44–91)	69 (49–88)	73 (47–91)	63 (38–86)	68 (39–86)	66 (41–89)	65 (44–88)	71 (40–90)	70 (50–93)
Child sex; n (%)										
Male	75 (44)	89 (53)	88 (52)	81 (48)	87 (51)	83 (49)	88 (52)	82 (48)	92 (54)	75 (44)
Female	95 (56)	80 (47)	82 (48)	88 (52)	82 (49)	87 (51)	81 (48)	88 (52)	77 (46)	94 (56)
Secondhand smoke exposure; n (%)										
Yes	111 (65)	108 (64)	113 (66)	106 (63)	97 (57)	110 (65)	112 (66)	109 (64)	107 (63)	97 (57)
No	59 (35)	61 (36)	57 (34)	63 (37)	72 (43)	60 (35)	57 (34)	61 (36)	62 (37)	72 (43)
Breastfeeding; n (%)										
No breastfeeding	72 (43)	63 (37)	47 (28)	50 (30)	36 (22)	40 (24)	45 (27)	52 (31)	60 (36)	71 (43)
≤6 mos. exclusive	83 (50)	88 (53)	99 (59)	92 (55)	102 (61)	98 (59)	98 (59)	92 (55)	95 (56)	81 (49)

Characteristics	α-tocopherol (umol/mmol)					γ-tocopherol (umol/mmol)				
	Q1	Q2	Q3	Q4	Q5	Q1	Q2	Q3	Q4	Q5
	<4.17	4.17–4.74	4.75–5.26	5.27–5.89	≥5.90	<0.67	0.67–0.74	0.75–0.83	0.84–0.97	≥0.98
	n=170	n=169	n=170	n=169	n=169	n=170	n=169	n=170	n=169	n=169
>6mos. exclusive	12 (7)	14 (8)	22 (13)	25 (15)	28 (17)	29 (17)	23 (14)	23 (14)	13 (8)	13 (8)
Pets in home; n (% yes)										
Cat	13 (8)	18 (11)	22 (13)	26 (15)	30 (18)	38 (22)	22 (13)	18 (11)	17 (10)	14 (8)
Dog	57 (34)	52 (31)	67 (39)	65 (38)	79 (47)	70 (41)	64 (38)	71 (42)	68 (40)	47 (28)

*Some percentages may not add to 100% due to rounding. Pets in home variables only include yes responses; categories are not mutually exclusive.

Table 2:

Association between maternal 2nd trimester plasma α- and γ-tocopherol concentrations[1] with asthma and wheeze in children ages 8–9 years

Cases (n)	Ever Asthma[2] (n=155)		Current Asthma[2] (n=114)		Strict Current Asthma[2] (n=96)		Current Wheeze[2] (n=108)	
	OR (95% CI)	aOR (95% CI)	OR (95% CI)	aOR (95% CI)	OR (95% CI)	aOR (95% CI)	OR (95% CI)	aOR (95% CI)
α-tocopherol								
Q1	Referent	Referent	Referent	Referent	Referent	Referent	Referent	Referent
Q2	0.72 (0.43–1.23)	0.65 (0.37–1.19)	0.83 (0.45–1.53)	0.80 (0.43–1.50)	0.81 (0.42–1.55)	0.78 (0.40–1.51)	1.05 (0.57–1.92)	1.00 (0.54–1.86)
Q3	0.56 (0.32–0.97)	0.60 (0.34–1.07)	0.70 (0.37–1.31)	0.77 (0.40–1.48)	0.57 (0.28–1.16)	0.64 (0.31–1.32)	0.73 (0.38–1.39)	0.76 (0.39–1.50)
Q4	0.81 (0.48–1.36)	0.97 (0.56–1.69)	0.96 (0.53–1.74)	1.20 (0.64–2.25)	1.01 (0.54–1.88)	1.29 (0.67–2.49)	0.96 (0.52–1.78)	1.12 (0.59–2.14)
Q5	0.56 (0.32–0.97)	0.72 (0.40–1.30)	0.83 (0.45–1.53)	1.07 (0.56–2.07)	0.72 (0.37–1.39)	0.95 (0.46–1.93)	0.74 (0.38–1.41)	0.90 (0.45–1.80)
p-overall	0.18	0.26	0.82	0.63	0.47	0.37	0.70	0.84
γ-tocopherol								
Q1	Referent	Referent	Referent	Referent	Referent	Referent	Referent	Referent
Q2	1.16 (0.65–2.06)	0.98 (0.53–2.04)	1.67 (0.86–3.26)	1.41 (0.71–2.79)	1.87 (0.89–3.93)	1.54 (0.72–3.29)	1.49 (0.78–2.84)	1.28 (0.66–2.50)
Q3	1.33 (0.76–2.35)	1.13 (0.62–2.04)	1.58 (0.81–3.10)	1.34 (0.67–2.69)	1.96 (0.94–4.10)	1.60 (0.75–3.43)	1.14 (0.58–2.24)	0.95 (0.47–1.91)
Q4	1.40 (0.80–2.45)	1.04 (0.57–1.89)	2.08 (1.09–3.98)	1.61 (0.82–3.16)	2.18 (1.05–4.52)	1.62 (0.76–3.45)	1.63 (0.86–3.09)	1.22 (0.62–2.37)
Q5	1.35 (0.77–2.38)	1.00 (0.54–1.85)	1.22 (0.60–2.46)	0.91 (0.43–1.92)	1.47 (0.68–3.19)	1.07 (0.47–2.42)	1.01 (0.51–2.02)	0.74 (0.35–1.56)
p-overall	0.76	0.99	0.20	0.38	0.26	0.52	0.42	0.51

[1] Tocopherol concentrations are all cholesterol-corrected.

[2] Unadjusted OR (OR) and with adjustment (aOR) for covariates (mother's age, educational status, parity and prepregnancy BMI, child's age and sex), each with 95% Confidence Intervals (95% CI).