

“Online Data Supplement”

Vitamin C to Pregnant Smokers Persistently Improves Infant Airway Function to 12 Months of Age: A Randomized Trial

Cindy T. McEvoy, MD, MCR, Lyndsey E. Shorey-Kendrick, PhD, Kristin Milner BA, Diane Schilling, RRT, Christina Tiller, RRT, Brittany Vuylsteke, MPH, Ashley Scherman RN, PhD, Keith Jackson, RRT, David M. Haas MD, MS, Julia Harris,BS, Byung S.Park, PhD, Annette Vu, MPH, Dale F. Kraemer, PhD, David Gonzales, PhD, Carol Bunten, MD, Eliot R. Spindel, MD, PhD, Cynthia D. Morris, PhD, MPH, Robert S. Tepper, MD, PhD

Supplement Table S1A. Reasons for Missing Data of Delivered Patients

Supplement Table S1B. Details of Missingness of Delivered Patients

Supplement Table S2. Demographics of Patients at 3 and 12 Month Airway Function Testing

Supplement Table S3A. Mixed-model, Repeated Measures Analysis of Covariance

Results for Airway Function Test Parameters

Supplement Table S3B. Sample Sizes for Airway Function Test Analyses

Supplemental Table S4. Infant Airway Function Tests at 12 Months of Age

Supplement Table S1A **Reasons for Missing Data of Delivered Patients**

Population: Delivered (n=241)^a

	3 month test		12 month test	
	Vitamin		Vitamin	
	C	Placebo	C	Placebo
Withdrew consent	1	3	4	3
Airway Function Test not performed	4	7	8	13
Technically Unacceptable Airway Function Test	1	2	5	5
Airway Function Test performed outside of window	0	1	1	0

^a Delivered 243, excluding 2 infant deaths prior to the 3 month airway function test=241

AFT= Airway Function Test

Supplement Table S1B
Details of Missingness of Delivered Patients

Population: Delivered (n=241)^a

	3 Month Airway Function Test				12 Month Airway Function Test			
	Placebo		Vitamin C		Placebo		Vitamin C	
	Missing (n=13)	Present (n=109)	Missing (n=6)	Present (n=113)	Missing (n=21)	Present (n=101)	Missing (n=18)	Present (n=101)
Race, n (%)								
White	12 (92.3)	86 (78.9)	5 (83.3)	88 (77.9)	17 (80.9)	81 (80.2)	11 (61.1)	82 (81.2)
Non-white	1 (7.7)	23 (21.1)	1 (16.7)	25 (22.1)	4 (19.1)	20 (19.8)	7 (38.9)	19 (18.8)
Ethnicity, n (%)								
Hispanic or Latino	0 (0)	7 (6.4)	0 (0)	2 (1.8)	0 (0)	7 (6.9)	1 (5.6)	1 (0.9)
Non-Hispanic or Latino	13 (100)	102 (93.6)	6	110 (97.3)	21 (100)	94 (93.1)	17 (94.4)	99 (98.0)
Unknown or not reported	0 (0)	0 (0)	0 (0)	1 (0.9)	0 (0)	0 (0)	0 (0)	1 (0.9)
Maternal age at enrollment (years)								
n	13	109	6	113	21	101	18	101
Mean(SD)	24.1 (5.3)	26.6 (5.9)	28.5 (5.3)	26.5 (5.2)	25.3 (6.4)	26.6 (5.8)	26.9 (4.5)	26.5 (5.4)
Median	22	26	31	26	24	26	27.5	26
Min, Max	18, 33	17, 42	20, 33	17, 38	17, 41	17, 42	19, 33	17, 38
GA at randomization (weeks)								
n	13	109	6	113	21	101	18	101
Mean(SD)	18.6 (2.6)	18.2 (2.8)	17.0 (3.2)	18.6 (3.0)	18.5 (2.5)	18.3 (2.8)	18.7 (2.9)	18.4 (3.0)
Median	18.7	18.3	15.6	19.3	18.6	18.1	20.3	19.3
Min, Max	14.7, 22.6	12.9, 22.9	13.7, 21.3	13.0, 22.9	17, 41	12.9, 22.9	13.9, 22.4	13.0, 22.9
GA at birth (weeks)								
n	13	109	6	113	21	101	18	101
Mean(SD)	38.5 (1.2)	38.6 (1.9)	39.0 (0.7)	38.7 (1.9)	38.5 (1.1)	38.6 (1.8)	38.1 (2.3)	38.8 (1.7)
Median	39	39	39	39	38.6	39	38.8	39
Min, Max	35.7, 39.7	31.3, 41.3	37.7, 39.6	30.6, 42.4	35.7, 40.1	31.3, 41.3	30.6, 40.7	30.6, 42.4
Infant birthweight (grams)								
n	11	108	6	113	19	100	18	101
Mean(SD)	3182 (550)	3063 (554)	3312 (283)	3118 (524)	3200 (590)	3050 (545)	2932 (536)	3162 (506)
Median	3266	3135	3285	3070	3266	3135	3005	3170

Min, Max	2241, 3920	1280, 4125	2860, 3620	1540, 4295	2241, 4125	1280, 3990	1540, 3620	1580, 4295
Center, n (%)								
IU	10 (77)	37 (33.9)	5 (83.3)	40 (35.4)	10 (47.6)	37 (36.6)	10 (55.6)	35 (34.6)
OHSU	0 (0)	20 (18.3)	0 (0)	20 (17.7)	2 (9.5)	18 (17.8)	1 (5.6)	19 (18.8)
SWW	3 (23)	52 (47.7)	1 (16.7)	53 (46.9)	9 (42.9)	46 (45.5)	7 (38.9)	47 (46.5)
Health Insurance Type, n (%)								
Government Assistance	13 (100)	89 (81.6)	6 (100)	100 (88.5)	19 (90.5)	83 (82.2)	16 (88.9)	90 (89.1)
Private Insurance	0 (0)	18 (16.5)	0 (0)	13 (11.5)	2 (9.5)	16 (15.8)	2 (11.1)	11 (10.9)
None of Self Pay	0 (0)	2 (1.83)	0 (0)	0 (0)	0 (0)	2 (2)	0 (0)	0 (0)
Highest Education Level, n (%)								
Less than high school	4 (30.8)	27 (24.8)	1 (16.7)	19 (16.8)	5 (23.8)	26 (25.7)	2 (11.1)	18 (17.8)
High School or GED	5 (38.5)	32 (29.4)	1 (16.7)	53 (46.9)	7 (33.3)	30 (29.7)	7 (38.9)	47 (46.5)
Some College	4 (30.8)	44 (40.4)	4 (66.7)	38 (33.6)	8 (38.1)	40 (39.6)	9 (50)	33 (32.7)
Bachelor's Degree	0 (0)	6 (5.5)	0 (0)	3 (2.6)	1 (4.7)	5 (5.0)	0 (0)	3 (3.0)
Maternal asthma, n (%)								
Yes	3 (23.1)	35 (32.1)	3 (50)	37 (32.7)	7 (33.3)	31 (30.7)	4 (22.2)	36 (35.6)
No	10 (76.9)	74 (67.9)	3 (50)	76 (67.2)	14 (66.7)	70 (69.3)	14 (77.8)	65 (64.4)
Average # cigarettes/day at delivery								
N	13	109	6	113	21	101	18	101
Mean(SD)	4.7 (4.6)	6.0 (5.8)	5.2 (3.3)	6.8 (5.4)	6.0 (5.7)	5.9 (5.7)	7.2 (7.0)	6.6 (5.0)
Median	5	5	4.5	6	5	5	5.5	6
Min, Max	0, 13	0, 20	2, 10	0, 20	0, 20	0, 20	0, 20	0, 20

^a Delivered 243, excluding 2 infant deaths prior to the 3 month airway function test=241

Supplement Table S2. Demographics of Patients at 3 and 12 Month Airway Function Testing

	Vitamin C treated at 3 month test (n=113)	Vitamin C treated at 12 month test (n=101)	Placebo treated at 3 month test (n=109)	Placebo treated at 12 month test (n=101)
Length (cm), mean (SD)	60.2 (3.2)	74.4 (3.2)	60.2 (2.9)	73.9 (3.3)
Length z-score, mean (SD)	-0.897 (0.913)	-0.307 (0.883)	-0.917 (0.972)	-0.389 (1.007)
Weight (kg), mean (SD)	6.39 (0.96)	10.06 (1.23)	6.27 (0.96)	9.66 (1.26)
Weight z-score, mean (SD)	0.28 (0.96)	0.05 (1.00)	0.10 (1.17)	-0.28 (1.19)
Female infants, n (%)	54 (48%)	49 (49%)	54 (50%)	50 (50%)
White infants, n (%)	88 (79%)	82 (81%)	86 (79%)	81 (80%)

Supplement Table S3A
Mixed-model, Repeated Measures Analysis of Covariance Results for Airway Function Test Parameters

Population: Delivered (n=241)^a

AFT Parameter	Treatment Group Effect			Visit Effect			ANCOVA Model p-values		
	Vitamin C Group Mean	Placebo Group Mean	Mean Difference	3-Month Visit Mean	12-Month Visit Mean	Mean Difference	Treatment Group Effect	Visit Effect	Treatment by Visit Interaction
FEF ₇₅	290.4 (260.6, 320.3)	250.2 (234.1, 266.4)	40.2 (6.6, 73.8)	198.2 (178.9, 217.6)	342.4 (322.2, 362.7)	-144.2 (-163.9, -124.5)	0.0248	<0.0001	0.0565
FEF ₅₀	562.3 (520.1, 604.5)	504.0 (481.1, 526.9)	58.3 (10.9, 105.8)	423.4 (395.0, 451.7)	642.9 (612.9, 672.9)	-219.6 (-251.8, -187.3)	0.0081	<0.0001	0.168
FEF ₂₅₋₇₅	531.1 (472.7, 553.5)	458.0 (436.1, 479.9)	55.1 (9.6, 100.5)	377.2 (350.3, 404.1)	593.9 (565.6, 622.2)	-216.7 (-246.5, -187.0)	0.0130	<0.0001	0.1195
FEV	256.0 (242.3, 269.6)	239.6 (232.4, 246.9)	16.3 (1.0, 31.6)	182.5 (173.6, 191.4)	313.1 (303.8, 322.4)	-130.5 (-140.0, -121.1)	0.0174	<0.0001	0.2685
FVC	315.1 (296.3, 334.0)	302.2 (292.0, 312.4)	13.0 (-8.2, 34.2)	220.8 (208.1, 233.4)	396.6 (383.2, 409.9)	-175.8 (-190.1, -161.4)	0.1350	<0.0001	0.7967
FEV 0.5/FVC	.8295 (.8018, .8572)	.8054 (.7906, .8202)	0.024 (-0.007, 0.055)	.8365 (.8183, .8547)	.7984 (.7793, 8174)	0.038 (0.019, 0.058)	0.1198	0.0029	0.3776

^a Delivered 243, excluding 2 infant deaths prior to the 3 month airway function test=241

AFT= Airway Function Test

Supplement Table S3B
Sample Sizes for Airway Function Test Analyses

Population: Delivered (n=241)^a

Variable	Months 3 and 12	Month 3 only	Month 12 only	Total
FEF ₇₅	198	24	4	226
FEF ₅₀	198	24	4	226
FEF ₂₅₋₇₅	198	24	4	226
FEV	198	23	4	225
FVC	198	24	4	226
FEV 0.5/FVC	198	23	4	225

^a Delivered 243, excluding 2 infant deaths prior to the 3 month airway function test=241

Supplemental Table S4
Infant Airway Function Tests at 12 Months of Age

	Infants of Vitamin C Treated Smokers n=101	Infant of Placebo Treated Smokers n=101	P-Value ¹	Infants of Vitamin C Treated Smokers n=101	Infant of Placebo Treated Smokers n=101	P-Value ²
FEF ₇₅ (mL/sec)	352 ± 7	324 ± 8	0.013	350 ± 10	323 ± 10	0.026
FEF ₅₀ (mL/sec)	654 ± 13	616 ± 12	0.031	657 ± 16	620 ± 15	0.051
FEF ₂₅₋₇₅ (mL/sec)	609 ± 11	567± 12	0.011	612 ± 14	570 ± 14	0.011
FEV _{0.5} (mL)	317 ± 5	308± 4	0.13	316 ± 5	310± 5	0.29
FVC (mL)	397 ±7	394± 7	0.76	395 ±7	398 ± 7	0.70
FEV _{0.5} /FVC	0.806 ± 0.007	0.787 ± 0.007	0.055	0.808 ± 0.009	0.784 ± 0.009	0.032

Values are Mean ± SEM;

1. The unadjusted analysis compares groups using a two-independent t-test of means.

2. The adjusted analysis compare groups using an analysis of covariance model that includes design factors (site stratum, gestational age at randomization, and treatment group (and all interactions of these) and infant gender, white/non-white, and PFT length (without higher order interactions).