

Supplementary Appendix

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Online Supplementary Appendix
for
Effect of Inhaled Corticosteroid Use in Childhood on Adult Height

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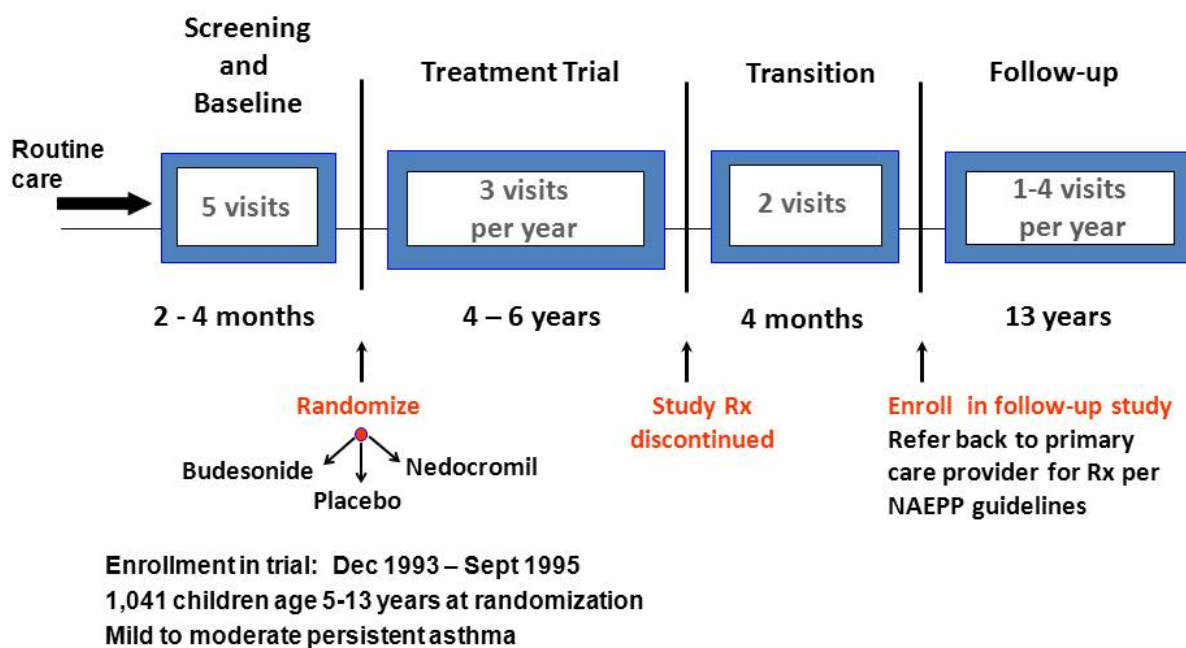
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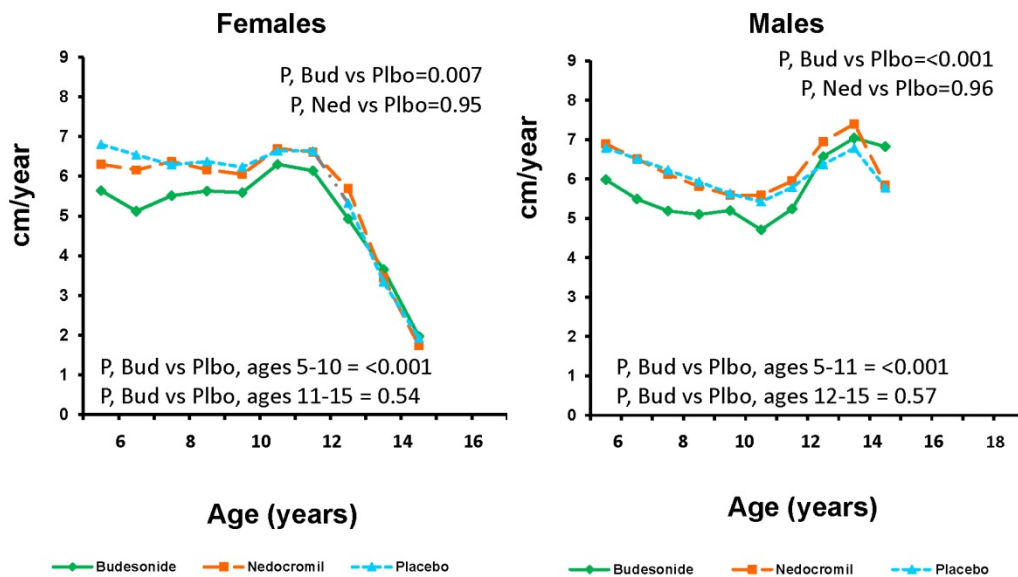
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Supplementary Appendix Figure S1. CAMP trial and follow-up design and features



Supplementary Appendix Figure S2. Growth velocity by sex and age during the first 2 years of randomized treatment for 1041 participants in the CAMP trial



*Velocities are adjusted for age, race/ethnicity, sex, clinic, duration of asthma, asthma severity, skin test reactivity, and height at trial entry. Bud = budesonide, Ned = nedocromil, Plbo = placebo.

Supplementary Appendix Table S1. Adjusted mean* adult height (cm)† by treatment group for 943 participants with adult height known, overall and by subgroup

	Bud	Ned	Plbo	Bud vs Plbo		Ned vs Plbo	
				Difference (95% CI)	P	Difference (95% CI)	P
Overall	171.1	172.1	172.3	-1.2	0.001	-0.2	0.61
(N[total N=943])	(281)	(285)	(377)	(-1.9 to -0.5)		(-0.9 to 0.5)	
By subgroup							
Sex							
Females	162.8	163.9	164.6	-1.8	0.001	-0.7	0.26
(N[total N=385])	(120)	(100)	(165)	(-2.9 to -0.7)		(-1.8 to 0.5)	
Males	176.8	177.6	177.6	-0.8	0.10	-0.0	0.98
(N [total N=558])	(161)	(185)	(212)	(-1.8 to 0.2)		(-0.9 to 0.9)	
P (interaction, by sex)					0.10		0.49
Age at randomization (years)							
5-8	170.7	171.8	172.6	-1.9	0.004	-0.8	0.22
(N[total N=489])	(145)	(150)	(194)	(-3.2 to -0.6)		(-2.1 to 0.5)	
9-13	171.4	172.4	171.9	-0.5	0.37	0.5	0.48
(N[total N=454])	(136)	(135)	(183)	(-1.7 to 0.6)		(-0.8 to 1.6)	
P (interaction, by age)					0.12		0.15
Race/ethnicity							
White or other	171.3	172.4	172.7	-1.4	0.001	-0.3	0.51
(N [total N=725])	(209)	(225)	(291)	(-2.3 to -0.6)		(-1.1 to 0.5)	
Black	169.9	172.4	171.2	-1.3	0.27	1.2	0.31
(N [total N=131])	(42)	(35)	(54)	(-3.5 to 1.0)		(-1.1 to 3.5)	
Hispanic	171.4	168.4	170.3	1.1	0.35	-1.9	0.11
(N [total N=87])	(30)	(25)	(32)	(-1.2 to 3.4)		(-4.2 to 0.4)	
P (interaction, by race/ethnicity)					0.50		0.07

	Bud	Ned	Plbo	Bud vs Plbo		Ned vs Plbo	
				Difference (95% CI)	P	Difference (95% CI)	P
Duration of asthma							
Less than 3 years (N [total N = 249])	169.5 (61)	171.2 (83)	171.4 (105)	-1.9 (-3.5 to -0.4)	0.02	-0.2 (-1.6 to 1.3)	0.84
At least 3 but < 7 years (N [total N = 486])	171.4 (153)	172.1 (138)	172.1 (195)	-0.7 (-1.9 to 0.2)	0.13	-0.0 (-1.1 to 1.1)	0.86
At least 7 years (N [total N = 208])	172.1 (67)	173.2 (64)	173.7 (77)	-1.6 (-3.4 to -0.2)	0.05	-0.5 (-2.1 to 1.1)	0.59
P (interaction by duration)					0.35		0.89

Bud = budesonide, Ned=nedocromil, Plbo=placebo, CI=confidence interval

*Means are adjusted for age, race/ethnicity, sex, clinic, duration of asthma, asthma severity, skin test reactivity, and height at trial entry.

†Adult height is the mean of all height measures at age ≥ 18 (female) or age ≥ 20 (male) if there is at least 1 measure at age ≥ 18 (females) or age ≥ 20 (males) and is the chronologically later height in the most recent pair of height measurements obtained at least 1 year apart and differing by < 1 cm otherwise. Of the 943 participants with adult height known, adult height is calculated from heights at age ≥ 18 (females) or age ≥ 20 (males) for 913 (96.8%) participants and from heights obtained ≥ 1 year apart and differing by < 1 cm for 30 (3.2%) participants. Adult height is not known for 98 (9.4%) participants (35 females with median age at last height measurement = 12 years (range 8-17) and 63 males with median age at last height measurement = 14 years (range 7-19)).

Supplementary Appendix Table S2. Comparison of those with adult height missing* to those with adult height known, as of entry into the CAMP trial

	N	Adult height missing* (N=98)	Adult height known (N=943)	P†	P‡	P§
Total	1041	9.4%	90.6%			
Treatment group in CAMP trial				0.86		
Budesonide	311	30.6%	29.8%			
Nedocromil	312	27.6%	30.2%			
Placebo	418	41.8%	40.0%			
Clinic				0.002	0.18	0.59
Albuquerque	121	16.3%	11.1%			
Baltimore	128	11.2%	12.4%			
Boston	124	7.1%	12.4%			
Denver	144	22.4%	12.9%			
San Diego	122	12.2%	11.7%			
Seattle	144	16.3%	13.6%			
St Louis	133	1.0%	14.0%			
Toronto	125	13.3%	11.9%			
Age (years)				0.67	0.57	0.53
5-8	542	54.1%	51.9%			
9-13	499	45.9%	48.1%			

	N	Adult height missing* (N=98)	Adult height known (N=943)	P†	P‡	P§
Race or ethnic group				0.16	0.59	0.51
White or other	805	81.6%	76.9%			
Black	138	7.1%	13.9%			
Hispanic	98	11.2%	9.2%			
Sex				0.33	0.34	0.20
Female	420	35.7%	40.8%			
Male	621	64.3%	59.2%			
Duration of since doctor diagnosis of asthma (years)				0.96	0.74	0.21
Less than 3	276	27.6%	26.4%			
At least 3 but less than 7	535	50.0%	51.5%			
At least 7	230	22.4%	22.1%			
Severity of asthma				0.85	0.53	0.80
Mild	498	46.9%	47.9%			
Moderate	543	53.1%	52.1%			
Any skin test reactivity				0.10	0.47	0.40
Yes	914	82.7%	88.3%			
No	127	17.3%	11.7%			
Linear height						
cm	--	131.1 ± 13.5	133.7 ± 13.9	0.08	0.94	0.50

*Adult height missing: no height measurement at age ≥ 18 (females) or age ≥ 20 (males) and no pair of height measurements ≥ 1 year apart and differing by < 1 cm.

†Chi squared test or t test P-value for homogeneity among groups.

‡P-value for interaction of budesonide treatment with covariate in logistic regression model with adult height status (known vs. missing) as the outcome and budesonide treatment (yes vs. no), the covariate, and the budesonide by covariate interaction as the regressors.

§ P-value for interaction of nedocromil treatment with covariate in logistic regression model with adult height status (known vs. missing) as the outcome and nedocromil treatment (yes vs. no), the covariate, and the nedocromil by covariate interaction as the regressors.

Supplementary Appendix Table S3: Measures of treatment and other characteristics related to adult height in mild/moderate asthma for 914 participants with adult height and all covariates known

		Multiple linear regression on adult height:		
		% with feature or mean	Diff in height (cm) (95% CI)	P
Mean daily weight-adjusted ICS dose during 1 st 2 years of follow-up (mcg/kg)	0.005	-0.1 (-0.2 to -0.0)	0.007	
Total prednisone dose over follow-up to adult height (mg)	992.0	-0.0 (-0.0 to 0.0)	0.76	
Demographics				
Race/ethnicity				<0.001
Black (vs. White or other)	13.8%	-0.1 (-1.3 to 1.1)	0.88	
Hispanic (vs. White or other)	9.5%	-3.0 (-4.4 to -1.6)	<0.001	
Female (vs. male)	40.8%	-13.7 (-14.4 to -12.9)	<0.001	
Physical development at trial entry and parental height				
≥Tanner Stage 2 in ≥ 1 category (vs. Stage 1 in all)†	30.5%	-3.9 (-4.9 to -2.9)	<0.001	
Height, cm (per unit change)	133.8	0.3 (0.3 to 0.4)	<0.001	

		Multiple linear regression on adult height:		
	% with feature or mean	Diff in height (cm) (95% CI)	P	P*
Body mass index, kg/m ² (per unit change)	18.2	-0.3 (-0.4 to -0.2)	<0.001	
Asthma severity and atopy at trial entry				
Moderate severity (vs. mild)	52.5%	0.5 (-0.3 to 1.4)	0.22	
Duration since diagnosis				<0.001
Medium (≥3 years and <7 years; vs. short duration)	51.9%	-0.4 (-1.3 to 0.6)	0.45	
Long (≥7 years; vs. short duration)	21.9%	-2.6 (-3.8 to -1.4)	<0.001	
Any prednisone in 6 months prior to screening (vs. none)	35.5%	0.8 (-0.1 to 1.7)	0.07	
Any ICS in 6 months prior to screening (vs. none)	38.0%	0.2 (-0.6 to 1.1)	0.59	
Any positive skin tests (vs. none)§	88.2%	-2.3 (-3.5 to -1.0)	<0.001	
Vitamin D level at trial entry				
30 ng/mL or less (vs. > 30 ng/mL)	35.9%	-1.2 (-2.1 to -0.4)	0.004	
<i>In utero</i> smoke exposure				
Any (vs. none)	14.0%	-0.8 (-1.9 to 0.3)	0.14	

Notes: ICS = inhaled corticosteroid. Outcome is also adjusted for clinic.

*P-value for indicated combination of factors.

††Tanner stage categories: females: breast, pubic hair, and menarche status; males: genital and pubic hair.

§Each participant was tested with 10 core allergens and up to 10 additional allergens considered to be relevant to the location of the CAMP clinical center.