

**Defining the normal range of fractional exhaled nitric oxide in children and adolescents –  
one size does not fit all**

**Online supplement**

*Figure E1. Population selection*

*Figure E2: Inclusion and exclusion of FeNO measurements*

*Figure E3. Distribution of FeNO in MAAS cohort: A) box plot of log (FeNO) in healthy, atopic and asthmatic children at 4 clinical follow up at different age. Log FeNO is present for visual clarity. B) Scatterplot for FeNO in ppb stratified by atopic status and asthma.*

*Figure E4. When asthma was stratified by atopic status, FeNO levels were markedly different in MAAS cohort.*

*Figure E5. The sex disparity in FeNO in non-asthmatic children beyond the age 13-16 years, coinciding with disparity in height (MAAS cohort).*

Table E1. Definitions of variables and populations in MAAS and SEATON birth cohorts

	MAAS	SEATON
<b>Definitions of variables:</b>		
<b>Current wheeze</b>	<p><u>Age 8, 11 and 13-16 years:</u> A positive answer to the question “Has your child had wheezing or whistling in the chest in the past 12 months?”</p> <p><u>Age 18 years:</u> A positive answer to the question “Have you had wheezing or whistling in the chest in the past 12 months?”</p>	<p><u>Age 10 years:</u> A positive answer to the question “Has your child had wheezing or whistling in the chest in the past 12 months (but not from the nose or throat)?”</p> <p><u>Age 15 years:</u> A positive answer to the question “Have you had wheezing or whistling in the chest in the last 12 months (but not from the nose or throat)?”</p>
<b>History of physician diagnosed asthma</b>	<p><u>Age 8, 11 and 13-16 years:</u> A positive answer to the question “Has the doctor ever told you that your child had asthma?”</p> <p><u>Age 18 years:</u> A positive answer to the question “Has the doctor ever told you had asthma?”</p>	<p><u>Age 10 years:</u> Positive answers to the question “Has your child ever suffered from asthma?” <b>and</b> “Confirmed by a doctor?”</p> <p><u>Age 15 years:</u> Positive answers to the question “Have you ever suffered from asthma?” <b>and</b> “Has this been confirmed by a doctor?”</p>
<b>Definition of populations:</b>		
<b>Non-asthmatic children*</b>	<u>Absence</u> of all of the following: current wheeze, history of physician diagnosed asthma and current asthma medication use	<u>Absence</u> of all of the following: current wheeze <b>and</b> history of physician diagnosed asthma
<b>Healthy non-atopic children*</b>	<u>Absence</u> of all of the following: current wheeze, history of physician diagnosed asthma, current asthma medication use <b>and</b> evidence of SPT sensitisation to common inhaled allergens	<u>Absence</u> of all of the following: current wheeze, history of physician diagnosed asthma, <b>and</b> evidence of SPT sensitisation to common inhaled allergens.
<b>Asymptomatic non-asthmatic but atopic children*</b>	Children with SPT sensitisation to at least one of eight common inhalant allergens but no current wheeze, current asthma medications or history of physician diagnosed asthma.	Children with SPT sensitisation to at least one common inhalant allergens (cat, dog, grass or house dust mite at age 10 years, and dog, grass and house dust mite at 15 years), but no current wheeze or history of physician diagnosed asthma.

Table E2 RADicA study visits and diagnostic procedures. [1]

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<b>Current asthma</b>	Children with current wheeze <b>and</b> history of physician-diagnosed asthma.	Children with current wheeze <b>and</b> history of physician-diagnosed asthma.
SPT: Skin prick test *Populations that were included in the model development and external validation		

	Visit 1	Visit 2	Optional Visit	Visit 3	Visit 4
<b>Diagnostic procedures</b>	Screening/ baseline/ dispense treatment	Methacholine challenge	Mannitol challenge	1-3week ICS response	6-14 week ICS response
Clinical history	✓				
Symptoms (Asthma Control Questionnaire)	✓	✓	✓	✓	✓
Examination	✓				✓
FeNO	✓	✓		✓	✓
Skin Prick test*	✓				
Blood Eosinophils	✓				✓
Spirometry	✓	✓	✓	✓	✓
Bronchodilator Reversibility	✓				
Mannitol challenge			✓		
Methacholine challenge		✓			✓

8 weeks of ICS (fluticortide 100mcg twice a day)

**The expert panel objective evidence review outcome definitions:**

**Asthma:** panel agrees asthma diagnosis based on clinical information and all available objective evidence before and after treatment.

**Not asthma:** panel agrees asthma is confidently ruled out following review of clinical information and objective evidence before and after treatment.

**Possible asthma:** panel cannot confirm diagnosis despite all tests being completed

**Insufficient evidence:** panel unable to confirm or refute diagnosis due to incomplete tests.

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\*SPT to cat, dog, birch, grass mix, Aspergillus fumigatus, Alternaria alternata, Cladosporium spp., house dust mite

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**Table E3. Baseline characteristics in patient who had FeNO measurements and those without**

*populations in MAAS cohort.*

	<b>With FeNO measurements (n=840)</b>	<b>Without FeNO measurements (n=344)</b>	<b>P-value</b>
<b>Sex (male) n(%)</b>	443 (52.7%)	199 (57.8%)	0.12
<b>Ethnicity (White) n(%)</b>	786 (96.0%)	272 (92.2%)	0.02
<b><u>Socioeconomic status</u></b>			
<b>Managerial n(%)</b>	373/586 (63.6%)	91/168 (54.2%)	<0.001
<b>Intermediate n(%)</b>	137/586 (23.4%)	28 /168 (16.7%)	
<b>Routine n(%)</b>	57/586 (9.7%)	37/168 (22.0%)	
<b>Not working n(%)</b>	14/586 (2.4%)	12/168 (7.1%)	
<b>unclassified n(%)</b>	5 /586 (0.9%)	-	
<b><u>SPT sensitisation at</u></b>			
<b>8 years n(%)</b>	254/771 (32.9%)	60/156 (38.5%)	0.22
<b>11 years n(%)</b>	247/713 (34.6%)	25/70 (35.7%)	0.96
<b>13-16 years n(%)</b>	316 /601 (52.6%)	15/31 (48.4%)	0.79
<b>18 years n(%)</b>	275/ 491 (56%)	10/16 (62.5%)	0.80
<b><u>Current wheeze at</u></b>			
<b>8 years n(%)</b>	148 /828 (17.8%)	37/197 (18.8%)	0.85
<b>11 years n(%)</b>	149/794 (18.8%)	26/133 (19.5%)	0.93
<b>13-16 years n(%)</b>	114/661 (17.2%)	13/79 (16.5%)	0.98
<b>18 years n(%)</b>	137/550 (24.9%)	9/43 (20.9%)	0.69
<b><u>History of doctor-diagnosed asthma at</u></b>			
<b>8 years n(%)</b>	191/807 (23.7%)	56 /186 (30.1%)	0.08
<b>11 years n(%)</b>	212/779 (27.2%)	41/131 (31.3%)	0.39
<b>13-16 years n(%)</b>	200/ 663 (30.2%)	29/81 (35.8%)	0.36
<b>18 years n(%)</b>	140/505 (27.7%)	16/39 (41.0%)	0.11

Table E4. Proportion of healthy, atopic and asthma children at each follow-up within MAAS cohort.

<b>MAAS Follow-up</b>	<b>Healthy n (%)</b>	<b>Atopic n (%)</b>	<b>Asthmatic n (%)</b>	<b>Total n (%)</b>
<b>Year 8</b>	470 (63.6%)	147 (19.9%)	122 (16.5%)	739
<b>Year 11</b>	379 (61.2%)	128 (20.7%)	125 (18.1%)	632
<b>Year 13-16</b>	227 (45.9%)	150 (30.3%)	118 (23.8%)	495
<b>Year 18</b>	160 (41.5%)	134 (34.7%)	92 (23.8%)	386

Table E5. Differences in FeNO across age groups in all children in MAAS cohort.

Variables	Median (IQR) FeNO When condition present	Median (IQR) FeNO When condition absent	P-value
<b>Age 8 years</b>			
Current asthma medication	23.9 (10.5-50.3) n=62	9 (6.9-13.4) n=355	<0.001
Current wheeze	23.1 (10.0-46.3) N=71	9.1 (6.8-13.2) N=346	<0.001
Physician diagnosed asthma ever	11.8 (7.7-34.2) N=94	9.2 (6.9-13.5) N=311	<0.001
Current hayfever	16.4 (8.6-34.1) N=62	9.2 (6.8-13.4) N=332	<0.001
SPT sensitisation	20.7 (10.5-40.0) N=128	8.5 (6.6-11.4) N=275	<0.001
<b>Age 11 years</b>			
Current asthma medication	26.0 (11.0-51.1) N=116	9.3 (7-14.2) N=484	<0.001
Current wheeze	27 (14.1-53.6) N=107	9.4 (7.0-13.8) N=493	<0.001
Physician diagnosed asthma ever	16.8 (8.7-40.2) N=152	9 (6.9-14.0) N=434	<0.001
Current hayfever	19.6 (10.6-39.8) N=140	9 (6.9-14.0) N=441	<0.001
SPT sensitisation	25.3 (11.8-48.2) N=191	8.5 (6.6-11.3) N=383	<0.001
<b>Age 13-16 years</b>			
Current asthma medication	33 (15.0- 64.5) N=416	16 (11-28) N=74	<0.001
Current wheeze	26 (13.8-63.2) N=83	16 (11-29) N=396	<0.001
Physician diagnosed asthma ever	25.6 (13.0 -48.4) N=143	15 (11-26) N=337	<0.001
Current hayfever	24.5 (15.2-40.0) N=187	14 (10.5-25) N=281	<0.001
SPT sensitisation	26(15.2-46) N=258	12.8 (10-18) N=220	<0.001
<b>Age 18 years</b>			
Current asthma medication	25 (11.5-43.5) N=83	15 (10-24) N=340	<0.001
Current wheeze	24 (11.5-43.5) N=107	14 (9.8-23.0) N=316	<0.001
Physician diagnosed asthma ever	24.5 (11.38-41.5) N=112	14 (10-22) N=279	<0.001
Current hayfever	20 (12-36) N=203	13 (9-19) N=220	<0.001
SPT sensitisation	21.5 (13-36) N=238	12 (8-17) N=181	<0.001

Table E6. Longitudinal correlations between FeNO and height, weight, age, and BMI in healthy non-atopic and atopic children without asthma using repeated measure correlation-MAAS cohort.

Variables	Correlation coefficient r	Bootstrapped 95%CI	p-value
<b>Healthy non-atopic</b>			
<i>Height</i>	0.42	0.33-0.50	<0.001
<i>Age</i>	0.39	0.29-0.47	<0.001
<i>Weight</i>	0.41	0.32-0.49	<0.001
<i>BMI</i>	0.33	0.24-0.42	<0.001
<b>Atopic non-asthmatic</b>			
<i>Height</i>	0.26	0.10-0.40	0.001
<i>Age</i>	0.22	0.06-0.36	0.006
<i>Weight</i>	0.26	0.11-0.40	0.001
<i>BMI</i>	0.26	0.11-0.10	0.001



Table E7. The sex differences of FeNO in children without asthma in MAAS Cohort.

Age groups (n, male:female)	FeNO in boys (ppb) Median (IQR)	FeNO in girls (ppb) Median (IQR)	p-value
All children without asthma			
8 years (n=135:140)	8.7 (6.3-12.4)	9.3 (7-13.1)	0.192
11 years (n=175:212)	9 (6.9-13.7)	9.4 (7.1-12.8)	0.853
13-16 years (n=147:162)	18.2 (13-30)	13 (10.1-20)	<b>&lt;0.001</b>
18 years (n=109:140)	17 (12-25)	11.5 (9-18)	<b>&lt;0.001</b>
Healthy non-atopic children			
8 years (n=101:110)	8.1 (6.2-10.4)	9 (7-11.4)	0.104
11 years (n=123:171)	8.4 (6.6-10.6)	8.6 (6.8-11.3)	0.489
13-16 years (n=67:101)	15 (11.2-19)	12 (10-16)	<b>0.017</b>
18 years (n=49:86)	15 (10-20)	10 (8-14)	<b>&lt;0.001</b>
Atopic children without asthma			
8 years (n=34:30)	12.8 (7.5-25.4)	15.1 (8.0-29.5)	0.493
11 years (n=52:41)	14.8 (8.3-29.4)	17.3 (9.9-33.7)	0.388
13-16 years (n=80:61)	27.4 (17-41.8)	17 (11-35)	<b>0.017</b>
18 years (n=60:54)	19(13-29)	17 (10-31.8)	0.534

Table E8. Difference in height between non-asthmatic boys and girls at each follow up in MAAS Cohort.

Clinical follow up	Boys height (cm)	Girls height (cm)	p-value
	Mean (SD)	Mean (SD)	
Year 8 follow-up	129 (5.0)	128 (5.0)	0.115
Year 11 follow-up	148 (7.2)	149 (7.3)	0.175
Year 13-16 follow-up	176.0 (6.7)	165 (6.2)	<0.001
Year 18 follow-up	180 (7.0)	166 (6.0)	<0.001

Table E9. Characteristics of Tanner Scale at age 11 and 13-16 years follow-up in non-asthmatic children in MAAS cohort.

Tanner Scale	Age 11 years follow up, Median (IQR) score	Age 13-16 years follow up, Median (IQR) score	P-value
Pubic hair scale (male)	1 (1-2) N=189	5 (4-5) N=186	<0.001
Male external genitalia scale	2 (2-3) N=179	4 (4-5) N=179	<0.001
Pubic hair scale (female)	1 (1-3) N=241	4(4-5) N=199	<0.001
Female breast development scale	2 (1-3) N=241	4 (4-5) N=199	<0.001

Table E10. Mixed effect quantile regression for 50<sup>th</sup>, 75<sup>th</sup>, 90<sup>th</sup> and 98<sup>th</sup> percentiles for Tanner scale and FeNO in 11 and 13-16 year old non-asthmatic children. Following adjustment for height (multivariate analysis), the pubertal stages no longer remained significantly associated with FeNO.

Pubertal stages	Univariate analysis			Multivariate analysis <u>adjusted by height</u> in predicting FeNO	
	Regression coefficient (RC)	Lower and upper bound for RC	P-value	P-value for pubertal stage variables (after adjustment for height)	P-value for height
<i>50<sup>th</sup> percentile</i>					
Male external genitalia scale	2.44	1.66, 3.22	<b>&lt;0.001</b>	0.672	p<0.001
Breast development scale (female)	0.63	0.05, 1.22	0.077	0.245	p=0.205
Pubic hair scale (male and female)	1.70	1.28, 2.12	<b>&lt;0.001</b>	0.212	p=0.016
<i>75<sup>th</sup> percentile</i>					
Male external genitalia scale	4.81	2.78, 6.84	<b>&lt;0.001</b>	0.668	p<0.001
Breast development scale (female)	1.53	0.56, 2.51	<b>&lt;0.001</b>	0.971	p=0.160
Pubic hair scale (male and female)	2.25	1.14, 3.35	<b>&lt;0.001</b>	0.059	p=0.005
<i>90<sup>th</sup> percentile</i>					
Male external genitalia scale	6.59	3.92, 9.26	<b>&lt;0.001</b>	0.665	p<0.001
Breast development scale (female)	2.16	0.42, 3.90	<b>0.033</b>	0.969	p=0.055
Pubic hair scale (male and female)	2.90	2.07, 3.73	<b>&lt;0.001</b>	0.06	p<0.001
<i>98<sup>th</sup> percentile</i>					
Male external genitalia scale	6.88	-0.76, 14.52	<b>0.020</b>	0.667	p<0.001
Breast development scale (female)	4.31	-2.67, 11.28	0.328	0.965	p=0.005
Pubic hair scale (male and female)	3.68	-1.63, 9.00	0.179	0.059	p<0.001

Table E11. Mixed-effect **univariate** quantile regression for the 50<sup>th</sup>, 75<sup>th</sup>, 90<sup>th</sup> and 98<sup>th</sup> percentiles in non-asthmatic children (both atopic and non-atopic) from MAAS cohort.

Predictors	Regression Coefficient	bootstrap 95%CI	P-value
<b>50<sup>th</sup> percentile</b>			
Height	0.18	(0.12, 0.23)	<0.001
Weight	0.09	(0.08, 0.11)	0.004
Age	0.51	(0.36, 0.67)	<0.001
Sex (girls compared to boys)	-1.95	(-4.84, -1.00)	0.031
<b>75<sup>th</sup> percentile</b>			
Height	0.22	(0.16, 0.27)	<0.001
Weight	0.28	(0.23, 0.32)	<0.001
Age	0.85	(0.68, 0.97)	<0.001
Sex (girls compared to boys)	0.19	(-6.18, 2.33)	0.936
<b>90<sup>th</sup> percentile</b>			
Height	0.32	(0.25, 0.38)	<0.001
Weight	0.46	(0.38, 0.49)	<0.001
Age	1.22	(1.05, 1.46)	<0.001
Sex (girls compared to boys)	1.48	(-5.04, 3.96)	0.427
<b>98<sup>th</sup> percentile</b>			
Height	0.57	(0.49, 0.66)	<0.001
Weight	0.31	(0.24, 0.45)	<0.001
Age	2.39	(1.65, 2.89)	<0.001
Sex (girls compared to boys)	-5.53	(-13.31, 16.50)	0.534

### **Chart development in healthy non-atopic children and atopic children separately**

To establish percentiles ranges in non-asthma children (defined as no current wheeze, no history of physician-diagnosed asthma *and* not on asthma medications), stratified by atopy, univariate analysis for the 50<sup>th</sup>, 75<sup>th</sup>, 90<sup>th</sup> and 98<sup>th</sup> percentiles FeNO were performed within children with and without atopy separately (non-atopic children: Tables E11-E12, Figures E9; atopic children: Tables E13-14, Figure E10). Variables with  $p < 0.10$  in the univariate analysis (Tables E11 and E13) were included in the multivariate backwards regression model and only height remained significant. The final equations and chart are presented in Tables E12 and E14 and Figures E9-10.

#### In healthy non-atopic children

<i>Table E12. Mixed-effect univariate quantile regression for the 50<sup>th</sup>, 75<sup>th</sup>, 90<sup>th</sup> and 98<sup>th</sup> percentiles in healthy non-atopic children from MAAS cohort.</i>			
<b>Predictors</b>	<b>Regression Coefficient</b>	<b>Bootstrapped 95%CI</b>	<b>P-value</b>
<b>50<sup>th</sup> percentile</b>			
Height	0.10	0.07, 0.12	<0.001
Weight	0.06	0.05, 0.07	0.001
Exact age	0.37	0.33, 0.41	<0.001
Sex (girls compared to boys)	0.05	-0.17, 0.36	0.916
<b>75<sup>th</sup> percentile</b>			
Height	0.12	0.09, 0.15	<0.001
Weight	0.13	0.11-0.14	<0.001
Exact age	0.59	0.54, 0.65	<0.001
Sex (girls compared to boys)	-0.60	-1.29, 0.07	0.453
<b>90<sup>th</sup> percentile</b>			
Height	0.15	0.12, 0.18	<0.001
Weight	0.20	0.16, 0.25	<0.001
Exact age	0.84	0.71, 0.98	<0.001
Sex (girls compared to boys)	1.57	0.68, 2.23	0.204
<b>98<sup>th</sup> percentile</b>			
Height	0.19	0.14, 0.24	<0.001
Weight	0.35	0.17, 0.42	<0.001
Exact age	1.38	0.71, 1.48	<0.001
Sex (girls compared to boys)	-2.49	-3.23, 0.46	0.442

*Table E13, Intercepts and regression coefficient for healthy non-atopic children for 50<sup>th</sup>, 75<sup>th</sup>, 90<sup>th</sup> and 98<sup>th</sup> percentile.*

Percentiles	RC	Bootstrapped 95% CI	Intercept	Equations
50th	0.10	0.07, 0.12	-4.4	0.10xheight (cm) -4.4
75 <sup>th</sup>	0.12	0.09, 0.15	-4.4	0.12xheight (cm) -4.4
90 <sup>th</sup>	0.15	0.12 0.18	-4.4	0.15xheight (cm) -4.4
98 <sup>th</sup>	0.19	0.14, 0.24	-4.3	0.19xheight (cm) -4.3

*Figure E6. A) FeNO percentile chart for healthy non-atopic children; B) FeNO percentile chart for atopic but non-asthmatic children.*

*In asymptomatic atopic children without asthma*

*Table E14. Mixed-effect univariate quantile regression for the 50<sup>th</sup>, 75<sup>th</sup>, 90<sup>th</sup> and 98<sup>th</sup> percentiles in asymptomatic atopic children without asthma from MAAS cohort.*

Predictors	Regression Coefficient	Bootstrap 95%CI	P-value
<b>50<sup>th</sup> percentile</b>			
Height	0.11	-0.03, 0.22	0.072
Weight	0.02	-0.11, 0.15	0.822
Exact age	0.62	0.43, 0.73	0.06
Sex (girls compared to boys)	-1.31	-6.85, 2.86	0.598
<b>75<sup>th</sup> percentile</b>			
Height	0.21	0.07, 0.34	0.004
Weight	0.30	0.14, 0.46	0.002
Exact age	0.96	0.86, 1.24	0.002
Sex (girls compared to boys)	0.98	-4.40, 6.60	0.604
<b>90<sup>th</sup> percentile</b>			
Height	0.39	0.22, 0.51	<0.001
Weight	0.41	0.39, 1.00	0.006
Exact age	1.42	1.18, 1.76	0.043
Sex (girls compared to boys)	-0.0001	-4.92, 16.02	1.0
<b>98<sup>th</sup> percentile</b>			
Height	0.62	0.46, 0.75	<0.001
Weight	1.42	0.89, 1.60	<0.001
Exact age	2.69	-0.50, 5.89	0.10
Sex (girls compared to boys)	-2.01	-31.28, 38.99	0.80

*Table E15. Intercepts and regression coefficient for asymptomatic non-asthmatic but atopic children for 50<sup>th</sup>, 75<sup>th</sup>, 90<sup>th</sup> and 98<sup>th</sup> percentile.*

Percentiles*	RC	Bootstrap 95%CI	Intercept	Equations
75 <sup>th</sup>	0.21	0.07, 0.34	0.48	0.21x height (cm)+0.48
90 <sup>th</sup>	0.39	0.22, 0.51	0.48	0.39x height (cm)+0.48
98 <sup>th</sup>	0.62	0.46, 0.75	0.48	0.62x height (cm)+0.48

*\*Height was not significant in univariate analysis for predicting the 50<sup>th</sup> percentile of FeNO in atopic children without asthma*



## SEATON external validation of non-atopic and atopic children separately

Table E16, Baseline characteristics of SEATON validation cohort (asymptomatic non-asthmatic children).

	Age 10 years follow up	Age 15 years follow up
<b>Total number with FeNO measurements (n)</b>	N=332	N=328
<b>SPT sensitised<sup>‡</sup> n(%)</b>	91/324 (28.1%)	97/326 (29.8%)
<b>Height (cm), mean (SD) [range]</b>	142.2 (6.7) [114-159.9]	169.7 (9.0) [144-198]
<b>FeNO (ppb), median (IQ)</b>	9 (6.7-13.3)	13 (9-21)

<sup>‡</sup> SPT sensitisation at age 10 years were defined as positive test to one of the aeroallergens (grass, house dust mite, dog and cat); SPT sensitisation at age 15 years were defined as positive test to one of the aeroallergens (grass, house dust mite and dog).

Table E17. Proposed FeNO percentile developed from MAAS correlated well with percentile within non-asthmatic children within SEATON cohort, stratified by atopic status.

MAAS FeNO percentiles	Number of SEATON participants had FeNO above MAAS-defined percentile, N (%)	Equivalent percentile in non-asthmatic children from SEATON (95%CI)
Healthy non-atopic (n=462 measurements from SEATON)		
<b>50<sup>th</sup></b>	162 (35%)	65 <sup>th</sup> (60-69 <sup>th</sup> )
<b>75<sup>th</sup></b>	91 (20%)	80 <sup>th</sup> (76-84 <sup>th</sup> )
<b>90<sup>th</sup></b>	39 (8%)	92 <sup>nd</sup> (89-94 <sup>th</sup> )
<b>98<sup>th</sup></b>	16 (3%)	97 <sup>th</sup> (94-98 <sup>th</sup> )
Atopic children without asthma (n=188 measurements from SEATON)*		
<b>75<sup>th</sup></b>	60 (32%)	68 <sup>th</sup> (61-75 <sup>th</sup> )
<b>90<sup>th</sup></b>	17 (9%)	91 <sup>st</sup> (86-94 <sup>th</sup> )
<b>98<sup>th</sup></b>	5 (3%)	97 <sup>th</sup> (94-99 <sup>th</sup> )

\*Height was not significant in univariate analysis for predicting the 50<sup>th</sup> percentile of FeNO in atopic children without asthma

## RADICA study

Table E18. Baseline characteristics of included children and adolescents in RADICA study

	<b>Asthma (n=51)</b>	<b>Non asthma (n=22)</b>	<b>p-value</b>
Age (years), median (IQR) [range]	11 (7.5-16) [5-22]	10 (8.3-11.8) [5-22]	0.515
Sex (male), n (%)	25 (49.0%)	10 (45.5%)	0.981
Ethnicity (White), n (%)	27 (52.9%)	13 (59.1%)	0.953
Height (cm) [range]	147 (22.5)	146.0 (18.2)	0.710
SPT sensitisation, n (%)	37 (72.5%)	12 (54.5 %)	0.218
FeNO (ppb), median (IQR)	42 (13.5-77.5)	12 (8-16.5)	<b>&lt;0.001</b>

Figure E7. Scattered plot of FeNO vs. height in RADICA patients

Table E19. Validation in RADICA study stratified by atopic status.

<b>Percentiles</b>	<b>Sensitivity</b>	<b>Specificity</b>	<b>PPV</b>	<b>NPV</b>	<b>+LR</b>	<b>-LR</b>
Symptomatic non-atopic children (n=24, 14 [58.3%] asthmatics) using non-atopic percentile chart						
<b>&gt;50<sup>th</sup> percentile</b>	42.9% 6/14	50% 5/10	54.5% 6/11	38.5% 5/13	0.9	1.1
<b>&gt;75<sup>th</sup> percentile</b>	42.9% 6/14	70% 7/10	66.7% 6/9	46.7% 7/15	1.4	0.8
<b>&gt;90<sup>th</sup> percentile</b>	28.6% 4/14	90% 9/10	80% 4/5	47.4% 9/19	2.9	0.8
<b>&gt;98<sup>th</sup> percentile</b>	21.4% 3/14	100% 10/10	100% 3/3	47.6% 10/21	∞	0.8
Symptomatic atopic children (n=49, 37 [75.5%] asthmatics) using atopic percentile chart						
<b>Percentiles<sup>Ⓜ</sup></b>	<b>Sensitivity</b>	<b>Specificity</b>	<b>PPV</b>	<b>NPV</b>	<b>+LR</b>	<b>-LR</b>
<b>&gt;75<sup>th</sup> percentile</b>	75.7% 28/37	91.7% 11/12	96.6% 28/29	55% 11/20	9.1	0.3
<b>&gt;90<sup>th</sup> percentile</b>	45.9% 17/37	100% 12/12	100% 17/17	37.5% 12/32	∞	0.5
<b>&gt;98<sup>th</sup> percentile</b>	21.6%	100%	100%	29.3%	∞	0.8

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\*+LR: sensitivity/(1-specificity);  $\square$  -LR: (1-sensitivity)/specificity.  $\square$  Height was not significant in univariate analysis for predicting the 50<sup>th</sup> percentile of FeNO in atopic children without asthma

**References:**

1. Drake S, Wang R., Healy L et al. Diagnosing asthma with and without aerosol generating procedures. J Allergy Clin Immunol Pract 2021;9(12):4243-4251.