

## **Supplement**

Childhood factors associated with complete and clinical asthma remission at 25 and 49 years.

Carpaij & Nieuwenhuis et al.

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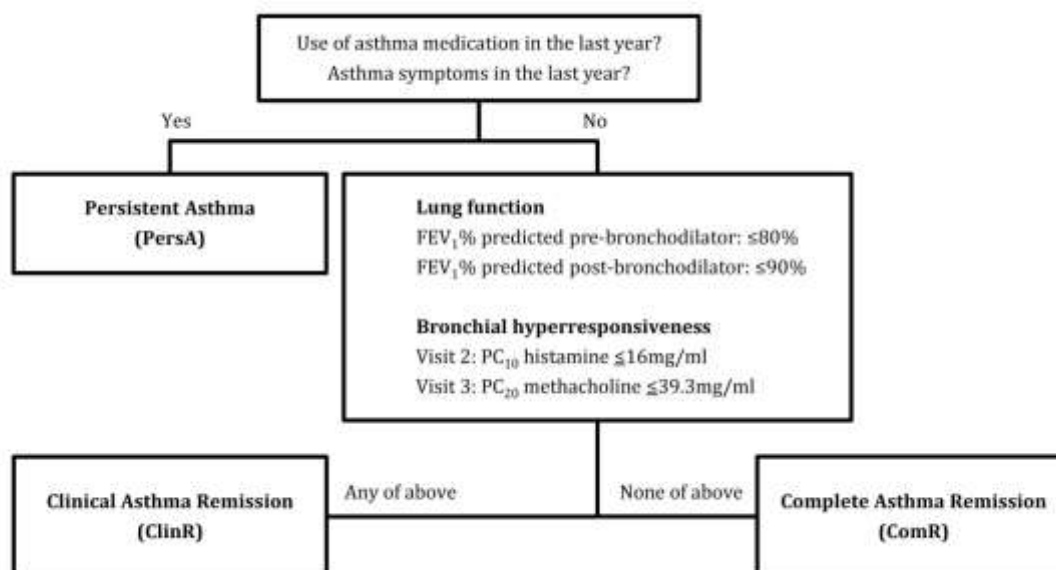
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**Spirometry measurements**

Predicted spirometry values at all visits were those of Quanjer (2012). At visit 1 and 2, the histamine concentration (range 0.5 to 32 mg/ml) with a decrease in FEV<sub>1</sub>  $\geq$ 10% from pre-challenge FEV<sub>1</sub> was taken as the threshold for BHR. At visit 3, the BHR-test was discontinued if the FEV<sub>1</sub> decreased  $\geq$ 20% from pre-challenge FEV<sub>1</sub> or if the highest dose of methacholine bromide (range 0.038 – 39.3 mg/ml) had been given. The skin prick test (SPT) was regarded positive if the mean of the perpendicular diameters of the wheal was > 0.7 times the mean diameter of histamine as positive control.

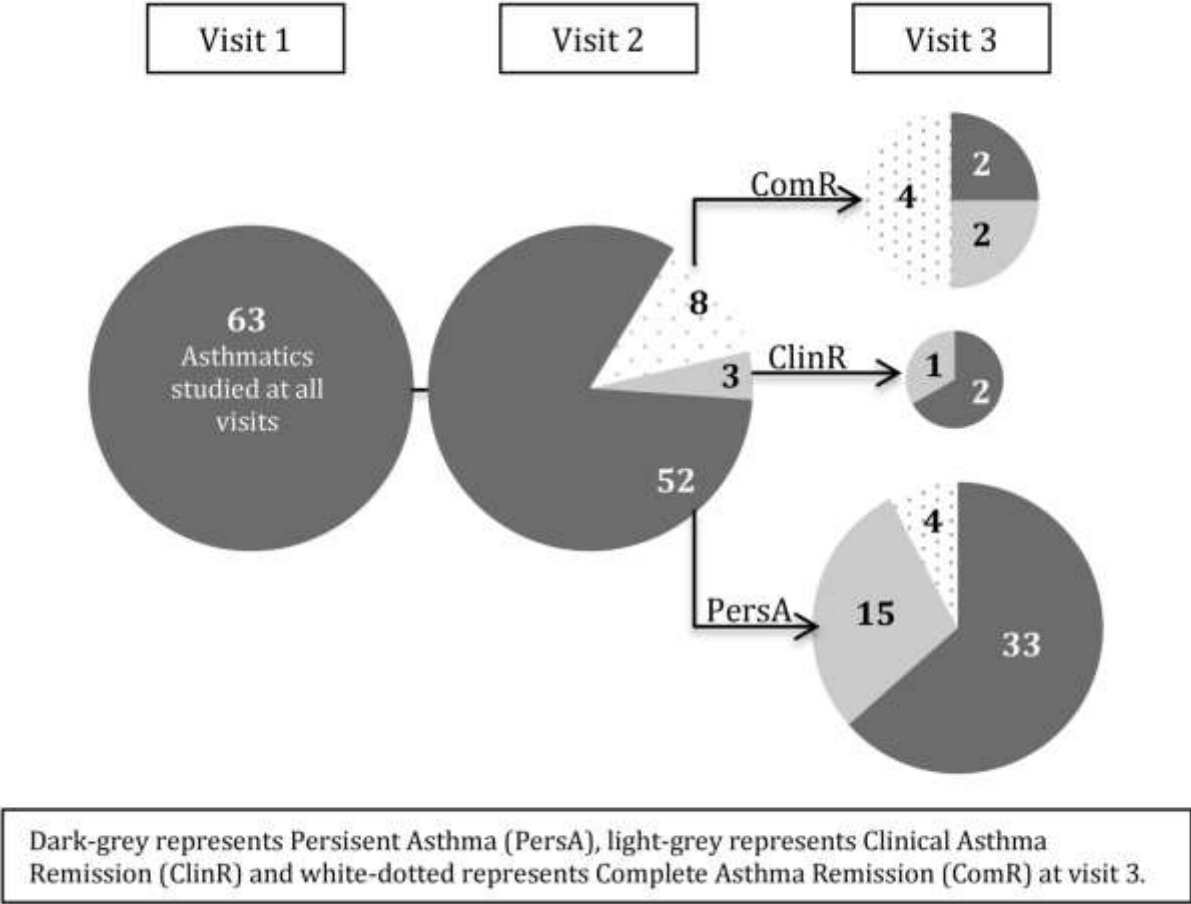
Supplemental Figure 1: Flow chart to define persistent asthma, clinical asthma remission and complete asthma remission



Supplemental Figure 2: Subject recruitment

Visit 1 (1972-76) 406 subjects			Visit 2 (1987-89) 209 subjects			Visit 3 (2013-14) 209 subjects	
Excluded			Excluded			Excluded	
	187 No BHR 10 Incomplete childhood data	➡		21 Lost to follow-up	➡	65 No response 31 Untraceable 6 Not cooperative 5 Deceased	
Included	209 subjects		Included	188 subjects		Included	102 subjects
Asthma outcome	-		154 PersA (81.9%) 20 ClinR (10.6%) 14 ComR (7.5%)			61 PersA (59.8%) 31 ClinR (30.4%) 10 ComR (9.8%)	

Supplemental Figure 3: Course of asthma status



**Supplemental table 1: Characteristics of subjects who were fully examined versus only filled in a questionnaire**

	Visit 2 (n=188)			Visit 3 (n=102)		
			P			P
Baseline characteristics	FE (n=163)	Q (n=25)		FE (n=68)	OQ (n=34)	
Age at visit 1, years	9.7 (1.4)	9.2 (1.4)	.16	9.6 (1.6)	9.8 (1.4)	.64
Male sex, %	69.9	80.0	.35	76.5	63.2	.26
Height, cm	143 (10)	140 (9)	.15	143 (10)	144 (10)	.47
FEV <sub>1</sub> predicted, %	77 (68-85)	73 (63-83)	.18	77 (65-84)	76 (68-80)	.60
FEV <sub>1</sub> /IVC ratio, %	<b>74 (67-78)</b>	<b>67 (60-77)</b>	<b>.02</b>	74 (66-79)	71 (67-77)	.30
Histamine threshold, mg/ml	8 (4-16)	8 (4-16)	.18	12 (8-16)	8 (4-16)	.27
Eosinophil count x 10 <sup>6</sup> /L *	451 (231-715)	440 (336-605)	.53	462 (264-710)	402 (237-677)	.55

Data are presented as mean (standard deviation), median (25th-75th percentile), or percentage, P: p-value calculated with Fisher's exact test, Independent t-test and Mann-Whitney U test, FE: subjects who were fully examined during the visit, Q: subjects who only filled in a questionnaire during the visit, \*: for visits 1 and 2 eosinophils from a counting chamber.

**Supplemental table 2: complete list of childhood factors ComR versus PersA at visit 2**

	(n=168)				
	ComR (n=14)	PersA (n=154)	Total (n)	Multivariate analysis	
				OR (95% CI)	P
<b>Characteristics</b>					
Age at first visit, years	10.1 (1.2)	9.6 (1.5)	168	1.3 (0.9-1.9)	.20
Period between visit 1 and 2, years	16.1 (14.4-17.4)	15.1 (14.4-16.4)	168	1.3 (0.9-1.9)	.18
Male seks	11 (78.6)	105 (68.5)	168	1.7 (0.4-6.3)	.45
Weight at first visit, kg	34.7 (6.3)	32.8 (6.7)	166	1.0 (0.9-1.1)	.84
Height at first visit, cm	146.6 (10.1)	142.8 (9.6)	168	1.0 (0.9-1.1)	.56
Cough	12 (85.7)	118 (77.6)	166	1.8 (0.4-8.6)	.46
Age at development of cough, years	2 (0-4)	4 (1-6)	124	0.9 (0.7-1.1)	.20
Cough accompanied by fever	5 (38.5)	55 (41.0)	147	0.9 (0.3-3.1)	.93
Cough ≥ 3 months	2 (16.7)	52 (40.3)	141	0.3 (0.1-1.6)	.16
Sputum	5 (38.5)	71 (48.0)	161	0.6 (0.2-2.0)	.41
Shortness of breath at rest	3 (21.4)	42 (29.4)	157	0.7 (0.2-2.5)	.53
Shortness of breath during walking stairs/playing	2 (14.3)	34 (25.8)	146	0.5 (0.1-2.2)	.33
Shortness of breath during cycling against the wind	8 (57.1)	109 (75.2)	159	0.4 (0.1-1.3)	.13
Age at development of shortness of breath, years	5 (1-8)	4 (1-7)	112	1.0 (0.8-1.2)	.85
Attack of dyspnea at rest with wheezing	10 (71.4)	125 (82.8)	165	0.5 (0.2-1.8)	.31
Wheeze ever	10 (76.9)	132 (93.0)	155	0.3 (0.1-1.1)	.07
Wheeze during a cold	<b>4 (30.8)</b>	<b>82 (66.1)</b>	<b>137</b>	<b>0.2 (0.1-0.8)</b>	<b>.02</b>
Wheeze without a cold	4 (30.8)	51 (43.6)	130	0.5 (0.2-1.9)	.32
Runny or stuffed nose	10 (71.4)	84 (58.3)	158	1.7 (0.5-5.8)	.39
Age at development of runny/stuffed nose, years	5 (2-9)	4 (2-7)	86	1.0 (0.8-1.2)	.68
Eczema	6 (42.9)	65 (43.9)	162	1.0 (0.3-3.1)	.98
Urticaria	2 (14.3)	14 (10.2)	151	1.4 (0.3-6.9)	.71

≥3 symptoms: cough, sputum, shortness of breath at rest, attack of dyspnea at rest with wheezing, wheeze ever	9 (75.0)	100 (75.2)	145	1.0 (0.2-3.8)	.97
Physical signs of pulmonary rhonchi	4 (40.0)	64 (64.0)	110	0.4 (0.1-1.5)	.16
Physical signs of thorax deformation	4 (40.0)	22 (22.0)	110	1.5 (0.4-6.4)	.56
<b>Peripheral blood measurements</b>					
LN Leukocyte count, cells x 10 <sup>6</sup> /L	8.9 (0.2)	9.0 (0.3)	164	0.6 (0.1-5.4)	.67
Leukocyte count level 75 <sup>th</sup> percentile (>9.600 x 10 <sup>6</sup> /L )	4 (28.6)	38 (25.3)	164	1.2 (0.4-4.2)	.73
Leukocyte count level 90 <sup>th</sup> percentile (>10.880 x 10 <sup>6</sup> /L)	0 (0.0)	14 (9.3)	164	Fisher's	.61
Haemoglobin, g/dL	13.2 (1.0)	13.6 (1.0)	163	0.6 (0.4-1.2)	.16
Haemoglobin level 75 <sup>th</sup> percentile (>14.2g/dL)	3 (21.4)	33 (22.1)	163	0.9 (0.2-3.4)	.87
Haemoglobin level 90 <sup>th</sup> percentile (>14.8g/dL)	0 (0.0)	13 (8.7)	163	Fisher's	.61
LN eosinophil count, cells x 10 <sup>6</sup> /L	5.8 (0.8)	5.9 (1.0)	164	0.9 (0.5-1.5)	.69
Eosinophil count level 75 <sup>th</sup> percentile (>699 10 <sup>6</sup> /L )	3 (21.4)	40 (26.7)	164	0.8 (0.2-3.0)	.74
Eosinophil count level 90 <sup>th</sup> percentile (>961 10 <sup>6</sup> /L)	2 (14.3)	12 (8.0)	164	2.3 (0.4-11.9)	.32
Electrophoresis total protein, g/dL	7.1 (6.9-7.5)	7.0 (6.7-7.4)	165	1.1 (0.6-2.2)	.74
Total protein level 25 <sup>th</sup> percentile (<6.8g/dL)	1 (7.1)	42 (27.8)	165	0.2 (0.03-1.8)	.16
Total protein level 10 <sup>th</sup> percentile (<6.5g/dL)	0 (0.0)	19 (12.6)	165	Fisher's	.37
Electrophoresis albumin, % of total protein	61.6 (10.4)	65.2 (7.8)	168	0.9 (0.9-1.01)	.10
Albumin level 25 <sup>th</sup> percentile (<60.2g/dL)	4 (28.6)	40 (26.0)	168	1.2 (0.3-4.3)	.76
Albumin level 10 <sup>th</sup> percentile (<55.6g/dL )	3 (21.4)	16 (10.4)	168	2.8 (0.7-11.7)	.17
<b>Perinatal factors</b>					

Gestational age, weeks	40.0 (40.0-40.0)	40.0 (40.0-40.0)	148	0.9 (0.6-1.3)	.59
Premature birth ( $\leq 37$ weeks)	0 (0.0)	5 (3.7)	148	Fisher's	1.0
Use of caesarean section at birth	0 (0.0)	5 (5.4)	101	Fisher's	1.0
Use of forceps at birth	1 (10.0)	3 (3.3)	101	3.6 (0.3-43.9)	.31
Birth weight, kg	4.0 (3.4-4.0)	3.5 (3.2-4.0)	110	1.2 (0.5-3.0)	.75
Weight $< 2.5$ kg at birth	0 (0.0)	4 (4.0)	110	Fisher's	1.0
Hospital childbirth	4 (30.8)	28 (21.5)	143	1.5 (0.4-5.3)	.53
Cyanosis at birth	1 (7.7)	15 (10.6)	155	0.5 (0.1-4.7)	.58
Shortness of breath at birth	0 (0.0)	7 (4.9)	156	Fisher's	1.0
Icterus at birth	2 (14.3)	19 (13.2)	158	1.2 (0.2-6.1)	.80
<b>Postnatal factors</b>					
Breastfeeding	5 (71.4)	64 (72.7)	95	1.1 (0.2-6.0)	.96
Duration of breastfeeding, months	4.0 (0.9-7.5)	3.0 (1.5-6.0)	62	1.1 (0.7-1.6)	.67
Duration of breastfeeding $> 6$ months	1 (20.0)	7 (12.3)	62	2.4 (0.2-28.1)	.50
History of variola vaccination	7 (63.6)	103 (72.0)	154	0.7 (0.2-2.7)	.63
History of DKTP vaccination	13 (100.0)	146 (98.6)	161	Fisher's	1.0
History of morbilli vaccination	1 (11.1)	12 (10.4)	124	1.1 (0.1-9.6)	.94
History of otitis	5 (35.7)	43 (29.3)	161	1.4 (0.4-4.3)	.60
History of pseudo croup	0 (0.0)	15 (11.0)	150	Fisher's	.36
History of surgery for acute tonsillitis	9 (64.3)	97 (64.3)	167	1.1 (0.3-3.3)	.93
Age at surgery for acute tonsillitis, years	5 (2-6)	4 (4-5)	94	0.9 (0.6-1.3)	.51
History of pneumonia	1 (7.7)	30 (23.3)	142	0.2 (0.03-1.8)	.16
History of scarlet fever	1 (7.1)	11 (7.3)	164	0.9 (0.1-7.4)	.89
History of morbilli	11 (78.6)	127 (84.7)	164	0.7 (0.2-2.8)	.61
History of rubella	4 (30.8)	72 (50.0)	157	0.5 (0.1-1.6)	.22
History of varicella	9 (64.3)	110 (72.8)	165	0.6 (0.2-2.1)	.46
History of smallpox	0 (0.0)	1 (0.7)	156	Fisher's	1.0
History of parotitis epidemica	8 (61.5)	86 (57.7)	162	1.2 (0.4-3.8)	.79
$\geq 1$ of scarlet fever, morbilli, rubella, varicella, smallpox, parotitis epidemica	13 (92.9)	147 (97.4)	165	0.3 (0.03-3.3)	.33



≥1 of scarlet fever, rubella, varicella, smallpox, parotitis epidemica	12 (85.7)	137 (91.9)	163	0.5 (0.1-2.8)	.47
<b>Exposure</b>					
Contact with animals	2 (15.4)	43 (31.9)	148	0.4 (0.1-1.9)	.25
Pets	9 (64.3)	87 (58.8)	162	1.3 (0.4-4.1)	.65
Firstborn child	7 (50.0)	56 (38.4)	160	1.5 (0.5-4.4)	.52
Rented house	4 (28.6)	68 (54.0)	140	0.3 (0.1-1.2)	.09
Dusty or damp vs. dry house	0 (0.0)	10 (8.1)	135	Fisher's	1.0
Rotten floor in house	2 (14.3)	4 (3.1)	144	5.3 (0.8-33.6)	.08
Mould in house	2 (14.3)	7 (5.4)	143	3.0 (0.5-17.0)	.21
≥1 of dusty/damp house, rotten floor, mould in house	4 (33.3)	16 (13.9)	127	2.9 (0.8-11.0)	.12
Old state of house	2 (15.4)	54 (40.6)	146	0.2 (0.04-1.04)	.06
Kapok/feather mattress	2 (15.4)	12 (8.3)	158	2.4 (0.4-12.8)	.31
Kapok/feather pillow	5 (41.7)	41 (29.3)	152	1.8 (0.5-6.2)	.34
Use of gas heater	8 (57.1)	69 (52.7)	145	1.1 (0.3-3.4)	.92
<b>Family history</b>					
Age of father, years	39 (35-45)	40 (36-44)	146	1.0 (0.9-1.1)	.79
Age father at birth of child, years	29 (26-34)	30 (27-34)	146	1.0 (0.9-1.1)	.79
Age of mother, years	36 (34-45)	37 (34-42)	147	1.0 (0.9-1.1)	.99
Age mother at birth of child, years	27 (23-34)	27 (25-32)	147	1.0 (0.9-1.1)	.99
Father with asthma	2 (15.4)	17 (12.5)	149	1.6 (0.3-8.3)	.57
Father with bronchitis	2 (15.4)	24 (18.0)	146	1.0 (0.2-4.8)	.97
Father with eczema	1 (7.7)	15 (11.4)	145	0.8 (0.1-6.5)	.81
Father with hayfever	1 (7.7)	13 (9.8)	146	0.9 (0.1-8.5)	.96
Father with atopic symptoms (asthma, eczema, hay fever)	3 (23.1)	38 (27.9)	149	0.9 (0.2-3.6)	.88
Mother with asthma	0 (0.0)	17 (12.6)	148	Fisher's	.36
Mother with bronchitis	1 (7.7)	25 (18.7)	147	0.4 (0.05-3.0)	.35
Mother with eczema	0 (0.0)	15 (11.3)	146	Fisher's	.36

Mother with hayfever	0 (0.0)	12 (9.0)	146	Fisher's	.60
Mother with atopic symptoms (asthma, eczema, hay fever)	<b>0 (0.0)</b>	<b>39 (28.9)</b>	<b>148</b>	<b>Fisher's</b>	<b>.02</b>
Rest of the family with asthma	8 (61.5)	67 (48.6)	151	1.8 (0.5-5.7)	.35
Rest of the family with bronchitis	5 (41.7)	69 (51.5)	146	0.7 (0.2-2.3)	.52
Rest of the family with eczema	4 (33.3)	43 (32.8)	143	1.2 (0.3-4.4)	.77
Rest of the family with hay fever	1 (7.7)	18 (14.0)	142	0.6 (0.1-5.0)	.63
Family with atopic symptoms (asthma, eczema, hay fever)	11 (84.6)	91 (66.4)	150	3.3 (0.7-16.1)	.14
Family members with rheumatoid arthritis	1 (7.7)	24 (17.6)	149	0.4 (0.04-2.9)	.34
Family members with heart disease	5 (38.6)	21 (15.6)	148	3.2 (0.9-10.9)	.06
Family members with mental retardation	0 (0.0)	8 (5.9)	148	Fisher's	1.0
Family members with diabetes mellitus	5 (38.5)	39 (28.5)	150	1.8 (0.5-6.2)	.33
Family members with leukaemia	<b>3 (23.1)</b>	<b>2 (1.5)</b>	<b>149</b>	<b>18.0 (2.6-124)</b>	<b>.003</b>
<b>Lung function (Quanjer-adjusted)</b>					
FEV <sub>1</sub> % predicted	84.8 (72.4-90.8)	76.7 (67.3-83.5)	168	1.0 (0.99-1.1)	.08
FEV <sub>1</sub> % predicted < 80	6 (42.9)	102 (66.2)	168	0.4 (0.1-1.1)	.07
FEV <sub>1</sub> % predicted <70	3 (21.4)	47 (30.5)	168	0.6 (0.2-2.3)	.46
IVC % predicted	89.7 (6.6)	89.2 (12.7)	168	1.0 (0.96-1.1)	.74
FEV <sub>1</sub> %IVC ratio	<b>79.0 (69.3-84.3)</b>	<b>73.0 (67.0-78.0)</b>	<b>168</b>	<b>1.1 (1.01-1.2)</b>	<b>.02</b>
FEV <sub>1</sub> %IVC < 70	3 (21.4)	52 (33.8)	168	0.5 (0.1-1.8)	.28
FEF <sub>25-75</sub> %IVC	82.8 (24.4)	70.4 (22.6)	133	1.0 (0.99-1.05)	.06
FEF <sub>25-75</sub> %IVC < 70	4 (30.8)	57 (47.5)	133	0.5 (0.1-1.6)	.23
FEF <sub>25-75</sub> %IVC < 50	1 (7.7)	24 (20.0)	133	0.3 (0.04-2.6)	.28
RV%TLC	21.9 (7.4)	21.3 (6.8)	167	1.0 (0.9-1.1)	.80
<b>Skin prick test (histamine-adjusted)</b>					
House dust mite positive	5 (35.7)	66 (45.5)	159	0.7 (0.2-2.4)	.62
Hairs and feathers positive	5 (35.7)	42 (29.4)	157	1.4 (0.4-4.6)	.54
Moulds positive	<b>3 (23.1)</b>	<b>8 (5.6)</b>	<b>156</b>	<b>8.8 (1.7-46.1)</b>	<b>.01</b>

Grass pollen positive	4 (28.6)	24 (16.8)	157	2.1 (0.6-7.5)	.26
Any SPT positive	6 (42.9)	74 (51.4)	158	0.8 (0.2-2.3)	.63
<b>BHR provocation test</b>					
2log (Histamine threshold), mg/ml	4 (3-4)	3 (2-4)	168	1.1 (0.7-1.6)	.80
Histamine threshold < 8 mg/ml	6 (42.9)	79 (51.3)	168	0.6 (0.2-2.0)	.43
Histamine threshold < 4 mg/ml	3 (21.4)	42 (27.3)	168	0.7 (0.2-2.8)	.67
Data are presented as mean (SD), median (25 <sup>th</sup> -75 <sup>th</sup> percentile), or n (%). Odds Ratios (OR) with 95% Confidence Intervals (CI) are given for a logistic regression model adjusted for age at visit 1 and sex. If one of the groups contains 0 cases the p-value for the Fisher's exact test is given.					

**Supplemental table 3: All investigated childhood factors for ComR/ClinR versus PersA at visit 2**

	(n=188)				
	ComR/ClinR (n=34)	PersA (n=154)	Total (n)	Multivariate analysis	
				OR (95% CI)	P
<b>Characteristics</b>					
Age at first visit, years	9.6 (1.3)	9.6 (1.5)	188	1.0 (0.8-1.3)	.99
Period between visit 1 and 2, years	15.0 (14.5-16.9)	15.1 (14.4-16.4)	188	1.1 (0.9-1.4)	.40
Male sex	29 (85.3)	105 (68.3)	188	2.7 (0.99-7.4)	.05
Weight at first visit, kg	32.7 (5.6)	32.8 (6.7)	186	1.0 (0.9-1.1)	.70
Height at first visit, cm	143.2 (9.5)	142.8 (9.6)	188	1.0 (0.9-1.1)	.94
Cough	25 (73.5)	118 (77.6)	186	0.8 (0.3-1.8)	.53
Age at development of cough, years	2 (0-5)	4 (1-6)	138	0.9 (0.8-1.05)	.19
Cough accompanied by fever	12 (37.5)	55 (41.0)	166	0.9 (0.4-1.9)	.73
Cough ≥ 3 months	8 (26.7)	52 (40.3)	159	0.5 (0.2-1.3)	.15
Sputum	14 (43.8)	71 (48.0)	180	0.8 (0.4-1.8)	.65
Shortness of breath at rest	10 (31.3)	42 (29.4)	175	1.1 (0.5-2.6)	.79
Shortness of breath during walking stairs/playing	8 (25.8)	34 (25.8)	163	0.9 (0.4-2.3)	.84
Shortness of breath during cycling against the wind	22 (64.7)	109 (75.2)	179	0.5 (0.2-1.2)	.15
Age at development of shortness of breath, years	6 (2-8)	4 (1-7)	125	1.1 (0.9-1.3)	.25
Attack of dyspnea at rest with wheezing	28 (82.4)	125 (82.8)	185	1.0 (0.4-2.6)	.96
Wheeze ever	29 (87.9)	132 (93.0)	175	0.6 (0.2-2.0)	.38
Wheeze during a cold	<b>11 (36.7)</b>	<b>82 (66.1)</b>	<b>154</b>	<b>0.3 (0.1-0.7)</b>	<b>.004</b>
Wheeze without a cold	12 (41.4)	51 (43.6)	146	0.9 (0.4-2.0)	.76
Runny or stuffed nose	23 (69.7)	84 (58.3)	177	1.7 (0.8-4.0)	.19
Age at development of runny/stuffed nose, years	6 (2-8)	4 (2-8)	93	1.0 (0.9-1.2)	.80
Eczema	17 (50.0)	65 (43.9)	182	1.4 (0.6-2.9)	.42
Urticaria	3 (9.7)	14 (10.2)	168	1.0 (0.3-3.9)	.99

≥3 symptoms: cough, sputum, shortness of breath at rest, attack of dyspnea at rest with wheezing, wheeze ever	23 (79.3)	100 (75.2)	162	1.3 (0.5-3.4)	.65
Physical signs of pulmonary rhonchi	10 (45.5)	64 (64.0)	122	0.4 (0.1-1.1)	.07
Physical signs of thorax deformation	7 (31.8)	22 (22.0)	122	1.3 (0.4-3.8)	.64
<b>Peripheral blood measurements</b>					
LN Leukocyte count, cells x 10 <sup>6</sup> /L	9.0 (0.2)	9.0 (0.3)	184	1.1 (0.2-4.7)	.93
Leukocyte count level 75 <sup>th</sup> percentile (>9.600 x10 <sup>6</sup> /L)	8 (23.5)	38 (25.3)	184	0.9 (0.4-2.2)	.86
Leukocyte count level 90 <sup>th</sup> percentile (>10.880 10 <sup>6</sup> /L)	1 (2.9)	14 (9.3)	184	0.3 (0.04-2.4)	.26
Haemoglobin, g/dL	13.6 (1.2)	13.6 (1.0)	182	1.0 (0.7-1.5)	.92
Haemoglobin level 75 <sup>th</sup> percentile (>14.2 g/dL)	9 (27.3)	33 (22.1)	182	1.3 (0.5-3.1)	.58
Haemoglobin level 90 <sup>th</sup> percentile (>14.8 g/dL)	4 (12.1)	13 (8.7)	182	1.6 (0.5-5.4)	.47
LN eosinophil count, cells x 10 <sup>6</sup> /L	5.8 (0.9)	5.9 (1.0)	184	0.8 (0.6-1.2)	.36
Eosinophil count level 75 <sup>th</sup> percentile (>699 x 10 <sup>6</sup> /L)	5 (14.7)	40 (26.7)	184	0.5 (0.2-1.4)	.19
Eosinophil count level 90 <sup>th</sup> percentile (>961 x 10 <sup>6</sup> /L)	4 (11.8)	12 (8.0)	184	1.7 (0.5-5.8)	.40
Electrophoresis total protein, g/dL	7.1 (7.0-7.4)	7.0 (6.7-7.4)	184	1.1 (0.7-1.9)	.64
Total protein level 25 <sup>th</sup> percentile (<6.8 g/dL)	<b>3 (9.1)</b>	<b>42 (27.8)</b>	<b>184</b>	<b>0.2 (0.1-0.8)</b>	<b>.03</b>
Total protein level 10 <sup>th</sup> percentile (<6.5 g/dL)	<b>0 (0.0)</b>	<b>19 (12.6)</b>	<b>184</b>	<b>Fisher's</b>	<b>.03</b>
Electrophoresis albumin, % of total protein	64.0 (8.2)	65.2 (7.8)	188	1.0 (0.9-1.02)	.24
Albumin level 25 <sup>th</sup> percentile (<60.2g/dL)	9 (26.5)	40 (26.0)	188	1.3 (0.5-3.0)	.61
Albumin level 10 <sup>th</sup> percentile (<55.6g/dL )	3 (8.8)	16 (10.4)	188	1.1 (0.3-4.0)	.93
<b>Perinatal factors</b>					

Gestational age, weeks	40.0 (40.0-40.0)	40.0 (40.0-40.0)	164	0.9 (0.7-1.1)	.34
Premature birth ( $\leq 37$ weeks)	2 (6.7)	5 (3.7)	164	1.9 (0.3-10.7)	.48
Use of caesarean section at birth	1 (5.3)	5 (5.4)	111	1.4 (0.1-13.6)	.79
Use of forceps at birth	1 (4.8)	3 (3.3)	112	1.5 (0.1-16.4)	.73
Birth weight, kg	3.8 (3.3-4.0)	3.5 (3.2-4.0)	121	0.9 (0.5-1.9)	.89
Weight <2.5kg at birth	0 (0.0)	4 (4.0)	121	Fisher's	1.0
Hospital childbirth	8 (29.6)	28 (21.5)	157	1.4 (0.6-3.7)	.44
Cyanosis at birth	2 (6.5)	15 (10.6)	173	0.5 (0.1-2.3)	.36
Shortness of breath at birth	1 (3.1)	7 (4.9)	174	0.6 (0.1-5.0)	.62
Icterus at birth	4 (12.5)	19 (13.2)	176	1.0 (0.3-3.1)	.94
<b>Postnatal factors</b>					
Breastfeeding	12 (75.0)	64 (72.7)	104	1.2 (0.3-4.1)	.81
Duration of breastfeeding, months	6.0 (2.5-7.0)	3.0 (1.5-6.0)	68	1.3 (0.98-1.7)	.07
Duration of breastfeeding >6 months	<b>4 (36.4)</b>	<b>7 (12.3)</b>	<b>68</b>	<b>5.5 (1.1-27.1)</b>	<b>.04</b>
History of variola vaccination	24 (77.4)	103 (72.0)	174	1.3 (0.5-3.3)	.59
History of DKTP vaccination	33 (100.0)	146 (98.6)	181	Fisher's	1.0
History of morbilli vaccination	4 (15.4)	12 (10.4)	141	1.5 (0.4-5.2)	.52
History of otitis	12 (37.5)	43 (29.3)	179	1.5 (0.7-3.4)	.32
History of pseudo croup	2 (6.5)	15 (11.0)	167	0.5 (0.1-2.3)	.37
History of surgery for acute tonsillitis	18 (52.9)	97 (63.4)	187	0.6 (0.3-1.3)	.22
Age at surgery for acute tonsillitis, years	4 (2-5)	4 (4-5)	100	0.9 (0.6-1.2)	.37
History of pneumonia	<b>1 (3.6)</b>	<b>30 (23.3)</b>	<b>157</b>	<b>0.1 (0.01-0.9)</b>	<b>.04</b>
History of scarlet fever	3 (9.1)	11 (7.3)	183	1.2 (0.3-4.6)	.81
History of morbilli	28 (82.4)	127 (84.7)	184	0.9 (0.3-2.4)	.82
History of rubella	12 (40.0)	72 (50.0)	174	0.7 (0.3-1.6)	.37
History of varicella	23 (69.7)	110 (72.8)	184	0.9 (0.4-2.0)	.73
History of smallpox	1 (3.1)	1 (0.7)	175	6.6 (0.3-125)	.21
History of parotitis epidemica	20 (60.6)	86 (57.7)	182	1.0 (0.5-2.3)	.90
$\geq 1$ of scarlet fever, morbilli, rubella, varicella, smallpox, parotitis	32 (94.1)	147 (97.4)	185	0.5 (0.1-2.8)	.41

epidemica					
≥1 of scarlet fever, rubella, varicella, smallpox, parotitis epidemica	30 (88.2)	137 (91.9)	183	0.7 (0.2-2.4)	.58
<b>Exposure</b>					
Contact with animals	7 (23.3)	43 (31.9)	165	0.7 (0.3-1.7)	.42
Pets	20 (60.6)	87 (58.8)	181	1.1 (0.5-2.5)	.74
Firstborn child	11 (32.4)	45 (38.4)	180	0.7 (0.3-1.6)	.42
Rented house	10 (34.5)	68 (54.0)	155	0.4 (0.2-1.03)	.06
Dusty or damp vs. dry house	3 (11.5)	10 (8.1)	150	1.4 (0.3-5.5)	.65
Rotten floor in house	3 (9.7)	4 (3.1)	161	3.6 (0.7-17.7)	.12
Mould in house	4 (12.9)	7 (5.4)	160	3.0 (0.8-11.5)	.11
≥1 of dusty/damp house, rotten floor, mould in house	<b>9 (33.3)</b>	<b>16 (13.9)</b>	<b>142</b>	<b>3.1 (1.2-8.2)</b>	<b>.02</b>
Old state of house	7 (24.1)	54 (40.6)	162	0.4 (0.2-1.1)	.09
Kapok/feather mattress	6 (18.8)	12 (8.3)	177	2.3 (0.8-6.7)	.13
Kapok/feather pillow	10 (32.3)	41 (29.3)	171	1.1 (0.5-2.6)	.81
Use of gas heater	15 (53.6)	69 (52.7)	159	1.0 (0.4-2.4)	.94
<b>Family history</b>					
Age of father, years	40 (38-44)	40 (36-44)	161	1.0 (0.98-1.1)	.19
Age father at birth of child, years	31 (28-35)	30 (27-34)	161	1.0 (0.98-1.1)	.19
Age of mother, years	38 (34-40)	37 (34-42)	162	1.0 (0.95-1.1)	.73
Age mother at birth of child, years	28 (24-31)	27 (25-32)	162	1.0 (0.9-1.1)	.73
Father with asthma	7 (25.0)	17 (12.5)	164	2.6 (0.9-7.2)	.07
Father with bronchitis	7 (25.0)	24 (18.0)	161	1.5 (0.5-4.0)	.44
Father with eczema	3 (10.7)	15 (11.4)	160	1.0 (0.3-3.8)	.99
Father with hayfever	1 (3.6)	13 (9.8)	161	0.5 (0.1-4.0)	.50
Father with atopic symptoms (asthma, eczema, hay fever)	9 (32.1)	38 (27.9)	164	1.4 (0.6-3.5)	.44
Mother with asthma	<b>0 (0.0)</b>	<b>17 (12.6)</b>	<b>163</b>	<b>Fisher's</b>	<b>.046</b>
Mother with bronchitis	3 (10.7)	25 (18.7)	162	0.6 (0.2-2.0)	.37

Mother with eczema	0 (0.0)	15 (11.3)	160	Fisher's	.08
Mother with hayfever	1 (3.6)	12 (9.0)	161	0.4 (0.05-3.1)	.37
Mother with atopic symptoms (asthma, eczema, hay fever)	<b>1 (3.7)</b>	<b>39 (28.9)</b>	<b>162</b>	<b>0.1 (0.01-0.7)</b>	<b>.02</b>
Rest of the family with asthma	12 (41.4)	67 (48.6)	167	0.8 (0.4-1.8)	.59
Rest of the family with bronchitis	12 (44.4)	69 (51.5)	161	0.8 (0.3-1.8)	.54
Rest of the family with eczema	9 (34.6)	43 (32.8)	157	1.2 (0.5-3.0)	.68
Rest of the family with hay fever	3 (10.7)	18 (14.0)	157	0.8 (0.2-3.1)	.77
Family with atopic symptoms (asthma, eczema, hay fever)	19 (65.5)	91 (66.4)	166	1.1 (0.5-2.6)	.83
Family members with rheumatoid arthritis	4 (13.3)	24 (17.6)	166	0.7 (0.2-2.1)	.50
Family members with heart disease	<b>10 (33.3)</b>	<b>21 (15.6)</b>	<b>165</b>	<b>2.8 (1.1-6.8)</b>	<b>.03</b>
Family members with mental retardation	0 (0.0)	8 (5.9)	165	Fisher's	.35
Family members with diabetes mellitus	9 (30.0)	39 (28.5)	167	1.1 (0.4-2.6)	.88
Family members with leukaemia	<b>3 (10.0)</b>	<b>2 (1.5)</b>	<b>166</b>	<b>7.6 (1.2-49.0)</b>	<b>.03</b>
<b>Lung function (Quanjer-adjusted)</b>					
FEV <sub>1</sub> % predicted	82.7 (71.4-89.4)	76.7 (67.3-83.5)	188	1.0 (0.99-1.1)	.12
FEV <sub>1</sub> % predicted < 80	<b>16 (47.1)</b>	<b>102 (66.2)</b>	<b>188</b>	<b>0.5 (0.2-0.97)</b>	<b>.04</b>
FEV <sub>1</sub> % predicted <70	7 (20.6)	47 (30.5)	188	0.7 (0.3-1.6)	.36
IVC % predicted	93.8 (10.2)	89.2 (12.7)	188	1.0 (0.99-1.1)	.07
FEV <sub>1</sub> %IVC ratio	74.5 (65.8-80.0)	73.0 (67-78)	188	1.01 (0.97-1.1)	.53
FEV <sub>1</sub> %IVC < 70	10 (29.4)	52 (33.8)	188	0.8 (0.4-1.9)	.70
FEF <sub>25-75</sub> %IVC	74.8 (22.9)	70.4 (22.6)	148	1.0 (0.99-1.03)	.36
FEF <sub>25-75</sub> %IVC < 70	13 (46.4)	57 (47.5)	148	1.0 (0.4-2.3)	.99
FEF <sub>25-75</sub> %IVC < 50	4 (14.3)	24 (20.0)	148	0.7 (0.2-2.4)	.62
RV%TLC	20.5 (5.9)	21.3 (6.8)	187	1.0 (0.9-1.05)	.69
<b>Skin prick test (histamine-adjusted)</b>					
House dust mite positive	11 (35.5)	66 (45.5)	176	0.7 (0.3-1.6)	.44



Hairs and feathers positive	9 (29.0)	42 (29.4)	174	1.1 (0.4-2.5)	.91
Moulds positive	4 (13.3)	8 (5.6)	173	3.6 (0.9-14.1)	.07
Grass pollen positive	8 (25.8)	24 (16.8)	174	2.0 (0.8-5.1)	.15
Any SPT positive	14 (45.2)	74 (51.4)	175	0.9 (0.4-1.9)	.69
<b>BHR provocation test</b>					
2log (Histamine threshold), mg/ml	3 (2-4)	3 (2-4)	188	1.0 (0.8-1.3)	.92
Histamine threshold < 8 mg/ml	19 (55.9)	79 (51.3)	188	1.3 (0.6-2.8)	.53
Histamine threshold < 4 mg/ml	10 (29.4)	42 (27.3)	188	1.1 (0.5-2.6)	.75
Data are presented as mean (SD), median (25 <sup>th</sup> -75 <sup>th</sup> percentile), or n (%). Odds Ratios (OR) with 95% Confidence Intervals (CI) are given for a logistic regression model adjusted for age at visit 1 and sex. If one of the groups contains 0 cases the p-value for the Fisher's exact test is given.					

**Supplemental table 4: complete list of childhood factors ComR versus PersA at visit 3**

	(n=71)				
	ComR (n=10)	PersA (n=61)	Total (n)	Multivariate analysis	
				OR (95% CI)	P
<b>Characteristics</b>					
Age at first visit, years	9.7 (1.5)	9.8 (1.5)	71	1.0 (0.6-1.5)	.94
Period between visit 1 and 2, years	39.0 (37.0-40.0)	39.0 (38.0-41.0)	71	1.0 (0.9-1.1)	.82
Male sex	7 (70.0)	38 (62.3)	71	1.4 (0.3-6.0)	.64
Weight at first visit, kg	33.0 (5.7)	33.0 (6.5)	71	1.0 (0.9-1.2)	.95
Height at first visit, cm	145.9 (10.4)	143.4 (10.3)	71	1.1 (0.96-1.2)	.22
Cough	8 (80.0)	50 (82.0)	71	0.9 (0.2-4.7)	.87
Age at development of cough, years	3 (1 – 5)	2 (1 – 7)	51	1.0 (0.8-1.3)	.98
Cough accompanied by fever	2 (25.0)	28 (51.9)	62	0.3 (0.1-1.7)	.17
Cough ≥ 3 months	3 (37.5)	26 (48.1)	62	0.6 (0.1-2.9)	.54
Sputum	4 (40.0)	36 (60.0)	70	0.4 (0.1-1.7)	.21
Shortness of breath at rest	2 (22.2)	23 (39.0)	68	0.4 (0.1-2.3)	.33
Shortness of breath during walking stairs/playing	1 (12.5)	16 (30.2)	61	0.3 (0.03-2.7)	.29
Shortness of breath during cycling against the wind	6 (60.0)	45 (77.6)	68	0.4 (0.1-1.8)	.24
Age at development of shortness of breath, years	8 (0 – 11)	4 (1 – 7)	50	1.1 (0.8-1.4)	.59
Attack of dyspnea at rest with wheezing	7 (70.0)	51 (83.6)	71	0.4 (0.1-2.0)	.29
Wheeze ever	9 (90.0)	52 (94.5)	65	0.5 (0.05-6.1)	.62
Wheeze during a cold	7 (77.8)	23 (50.0)	55	3.7 (0.7-20.0)	.13
Wheeze without a cold	5 (55.6)	23 (50.0)	55	1.3 (0.3-5.9)	.72
Runny or stuffed nose	9 (90.0)	37 (63.8)	68	5.9 (0.7-52.8)	.11
Age at development of runny/stuffed nose, years	6 (1 – 10)	6 (2 – 8)	40	1.0 (0.8-1.3)	.94
Eczema	4 (44.4)	24 (39.3)	70	1.3 (0.3-5.3)	.75
Urticaria	2 (25.0)	7(12.1)	66	2.6 (0.4-16.3)	.30

≥3 symptoms: cough, sputum, shortness of breath at rest, attack of dyspnea at rest with wheezing, wheeze ever	7 (77.8)	43 (79.6)	63	0.9 (0.2-5.2)	.91
Physical signs of pulmo ronchi	3 (60.0)	25 (62.5)	45	0.7 (0.1-6.5)	.79
Physical signs of thorax deformation	1 (20.0)	2 (30.0)	45	0.4 (0.04-5.3)	.51
<b>Peripheral blood measurements</b>					
LN Leukocyte count, cells x 10 <sup>6</sup> /L	9.0 (0.3)	9.0 (0.3)	69	2.3 (0.2-26.4)	.52
Leukocyte count level 75 <sup>th</sup> percentile (>9.600 x 10 <sup>6</sup> /L)	5 (50.0)	14 (23.7)	69	3.2 (0.8-12.6)	.10
Leukocyte count level 90 <sup>th</sup> percentile (>10.880 x 10 <sup>6</sup> /L )	1 (10.0)	4 (6.8)	69	1.7 (0.2-18.1)	.65
Haemoglobin, g/dL	13.4 (1.2)	13.5 (1.0)	69	0.8 (0.4-1.6)	.58
Haemoglobin level 75 <sup>th</sup> percentile (>14.2g/dL)	3 (30.0)	13 (22.0)	69	1.4 (0.3-6.5)	.64
Haemoglobin level 90 <sup>th</sup> percentile (>14.8g/dL)	1 (10.0)	6 (10.2)	69	1.0 (0.1-9.4)	.99
LN eosinophil count, cells x 10 <sup>6</sup> /L	5.8 (0.9)	5.8 (1.2)	69	1.0 (0.6-1.9)	.96
Eosinophil count level 75 <sup>th</sup> percentile (>699 x 10 <sup>6</sup> /L)	1 (10.0)	17 (28.8)	69	0.3 (0.03-2.5)	.25
Eosinophil count level 90 <sup>th</sup> percentile (>961 x 10 <sup>6</sup> /L)	1 (10.0)	7 (11.9)	69	0.9 (0.1-8.7)	.92
Electrophoresis total protein, g/dL	7.1 (6.5 – 7.4)	7.3 (6.8 – 7.5)	70	0.3 (0.1-1.5)	.17
Total protein level 25 <sup>th</sup> percentile (<6.8g/dL)	3 (30.0)	12 (20.0)	70	1.8 (0.4-8.2)	.46
Total protein level 10 <sup>th</sup> percentile (<6.5g/dL)	2 (20.0)	4 (6.7)	70	3.6 (0.5-23.3)	.19
Electrophoresis albumin, % of total protein	62.3 (6.6)	65.6 (7.5)	71	0.9 (0.9-1.02)	.14
Albumin level 25 <sup>th</sup> percentile (<60.2g/dL)	4 (40.0)	13 (21.3)	71	2.8 (0.6-12.1)	.17
Albumin level 10 <sup>th</sup> percentile (<55.6g/dL)	2 (20.0)	5 (8.2)	71	3.1 (0.5-20.1)	.23
<b>Perinatal factors</b>					
Gestational age, weeks	40.0 (39.0-40.0)	40.0 (40.0-40.0)	66	0.8 (0.5-1.1)	.20

Premature birth ( $\leq 37$ weeks)	1 (11.1)	1 (1.8)	66	7.7 (0.4-138)	.17
Use of caesarean section at birth	0 (0.0)	3 (8.8)	40	Fisher's	1.0
Use of forceps at birth	0 (0.0)	0 (0.0)	37	NA	NA
Birth weight, kg	3.5 (3.3-3.9)	3.5 (3.0-4.0)	47	1.1 (0.3-4.7)	.88
Weight <2.5kg at birth	0 (0.0)	3 (7.7)	47	Fisher's	1.0
Hospital childbirth	2 (28.6)	12 (22.2)	61	1.4 (0.2-8.3)	.73
Cyanosis at birth	0 (0.0)	6 (10.3)	68	Fisher's	.58
Shortness of breath at birth	0 (0.0)	2 (3.5)	67	Fisher's	1.0
Icterus at birth	1 (10.0)	7 (11.9)	69	0.9 (0.1-8.3)	.89
<b>Postnatal factors</b>					
Breastfeeding	2 (50.0)	22 (64.7)	38	0.5 (0.1-4.4)	.56
Duration of breastfeeding, months	5.0 (4.0 – 5.0)	4.0 (1.8 – 7.0)	19	1.2 (0.6-2.5)	.55
Duration of breastfeeding >6 months	0 (0.0)	5 (29.4)	19	Fisher's	1.0
History of variola vaccination	8 (88.9)	42 (70.0)	69	3.5 (0.4-30.5)	.25
History of DKTP vaccination	10 (100)	60 (100)	70	NA	NA
History of morbilli vaccination	1 (14.3)	4 (8.5)	54	1.7 (0.2-18.2)	.66
History of otitis	4 (44.4)	16 (26.7)	69	2.3 (0.5-10.4)	.26
History of pseudo croup	0 (0.0)	5 (8.5)	67	Fisher's	1.0
History of surgery for acute tonsillitis	7 (70.0)	38 (62.3)	71	1.4 (0.3-5.9)	.67
Age at surgery for acute tonsillitis, years	5 (2 – 8)	4 (3 – 5)	43	1.1 (0.8-1.7)	.52
History of pneumonia	1 (11.1)	10 (18.9)	62	0.5 (0.1-4.8)	.57
History of scarlet fever	0 (0.0)	5 (8.3)	70	Fisher's	1.0
History of morbilli	8 (80.0)	48 (81.4)	69	1.0 (0.2-5.2)	.95
History of rubella	3 (33.3)	29 (51.8)	65	0.4 (0.1-2.0)	.28
History of varicella	8 (80.0)	39 (65.0)	70	2.2 (0.4-11.4)	.35
History of smallpox	0 (0.0)	1 (1.8)	66	Fisher's	1.0
History of parotitis epidemica	5 (55.6)	34 (57.6)	68	1.0 (0.2-4.3)	.99
$\geq 1$ of scarlet fever, morbilli, rubella, varicella, smallpox, parotitis epidemica	10 (100.0)	57 (95.0)	70	Fisher's	1.0
$\geq 1$ of scarlet fever, rubella, varicella, smallpox, parotitis epidemica	9 (90.0)	53 (89.8)	69	1.1 (0.1-10.6)	.94

<b>Exposure</b>					
Contact with animals	4 (50.0)	17 (30.9)	63	2.3 (0.5-10.5)	.28
Pets	7 (77.8)	36 (59.0)	70	2.4 (0.4-12.5)	.31
Firstborn child	2 (20.0)	20 (33.3)	70	0.5 (0.1-2.7)	.42
Rented house	2 (28.6)	30 (55.6)	61	0.3 (0.1-1.7)	.17
Dusty or damp vs. dry house	0 (0.0)	5 (10.2)	63	Fisher's	1.0
Rotten floor in house	1 (12.5)	4 (7.5)	66	1.9 (0.2-21.3)	.59
Mould in house	1 (12.5)	3 (5.5)	63	2.6 (0.2-31.6)	.45
≥1 of dusty/damp house, rotten floor, mould in house	2 (33.3)	9 (20.0)	51	1.7 (0.3-11.6)	.57
Old state of house	4 (44.4)	19 (35.2)	63	1.6 (0.4-6.6)	.55
Kapok/feather mattress	2 (20.0)	6 (10.0)	70	2.2 (0.4-12.8)	.39
Kapok/feather pillow	2 (20.0)	14 (24.6)	67	0.8 (0.1-4.0)	.74
Use of gas heater	4 (44.4)	32 (59.3)	63	0.6 (0.1-2.4)	.45
<b>Family history</b>					
Age of father, years	38 (36 – 45)	40 (37 – 44)	61	1.0 (0.9-1.2)	.71
Age father at birth of child, years	29 (26 – 34)	30 (27 – 34)	61	1.0 (0.9-1.2)	.71
Age of mother, years	37 (34 – 47)	39 (36 – 42)	61	1.0 (0.9-1.2)	.64
Age mother at birth of child, years	28 (24 – 36)	28 (26 – 32)	61	1.0 (0.9-1.2)	.64
Father with asthma	1 (12.5)	9 (15.5)	66	0.7 (0.1-6.9)	.75
Father with bronchitis	0 (0.0)	12 (21.1)	65	Fisher's	.33
Father with eczema	1 (12.5)	8 (14.0)	65	0.8 (0.1-7.7)	.87
Father with hayfever	1 (12.5)	9 (15.5)	66	0.8 (0.1-7.5)	.81
Father with atopic symptoms (asthma, eczema, hay fever)	2 (25.0)	22 (37.9)	66	0.5 (0.1-3.0)	.45
Mother with asthma	0 (0.0)	7 (11.9)	67	Fisher's	.59
Mother with bronchitis	2 (25.0)	10 (17.2)	66	1.5 (0.3-9.1)	.65
Mother with eczema	0 (0.0)	5 (8.6)	66	Fisher's	1.0
Mother with hayfever	0 (0.0)	4 (6.9)	66	Fisher's	1.0
Mother with atopic symptoms (asthma,	0 (0.0)	15 (25.4)	67	Fisher's	.18

eczema, hay fever)					
Rest of the family with asthma	4 (50.0)	30 (50.8)	67	0.9 (0.2-4.1)	.92
Rest of the family with bronchitis	2 (28.6)	32 (55.2)	65	0.3 (0.1-1.8)	.21
Rest of the family with eczema	3 (42.9)	20 (35.1)	64	1.4 (0.3-6.9)	.71
Rest of the family with hay fever	1 (12.5)	9 (15.8)	65	0.8 (0.1-7.4)	.84
Family with atopic symptoms (asthma, eczema, hay fever)	7 (87.5)	40 (67.8)	67	3.2 (0.4-28.5)	.29
Family members with rheumatoid arthritis	3 (33.3)	10 (17.9)	65	2.5 (0.5-11.9)	.26
Family members with heart disease	2 (22.2)	7 (12.5)	65	2.0 (0.3-11.5)	.45
Family members with mental retardation	0 (0.0)	3 (5.3)	66	Fisher's	1.0
Family members with diabetes mellitus	3 (33.3)	15 (26.3)	66	1.4 (0.3-7.0)	.65
Family members with leukaemia	0 (0.0)	2 (3.5)	66	Fisher's	1.0
<b>Lung function (Quanjer-adjusted)</b>					
FEV <sub>1</sub> % predicted	79 (68 – 86)	77 (67 – 84)	71	1.0 (0.97-1.1)	.48
FEV <sub>1</sub> % predicted < 80	6 (60.0)	39 (63.9)	71	0.8 (0.2-3.2)	.78
FEV <sub>1</sub> % predicted <70	2 (20.0)	19 (31.1)	71	0.6 (0.1-3.0)	.52
IVC % predicted	88.7 (13.5)	88.0 (12.4)	71	1.0 (0.9-1.1)	.97
FEV <sub>1</sub> %IVC ratio	79 (67 – 84)	73 (67 – 78)	71	1.1 (0.97-1.2)	.21
FEV <sub>1</sub> %IVC < 70	3 (30.0)	19 (31.1)	71	0.9 (0.2-4.1)	.94
FEF <sub>25-75</sub> %IVC	86.7 (22.1)	72.2 (24.8)	57	1.0 (0.99-1.1)	.11
FEF <sub>25-75</sub> %IVC < 70	2 (22.2)	23 (47.9)	57	0.3 (0.1-1.7)	.17
FEF <sub>25-75</sub> %IVC < 50	1 (11.1)	10 (20.8)	57	0.5 (0.1-4.3)	.51
RV%TLC	21.4 (9.1)	21.3 (6.1)	71	1.0 (0.9-1.1)	.99
<b>Skin prick test (histamine-adjusted)</b>					
House dust mite positive	7 (70.0)	24 (42.9)	66	3.3 (0.8-14.2)	.11
Hairs and feathers positive	5 (50.0)	15 (27.3)	65	2.9 (0.7-11.7)	.15
Moulds positive	2 (22.2)	2 (3.6)	64	9.4 (0.99-89.5)	.05
Grass pollen positive	3 (30.0)	11 (20.0)	65	1.9 (0.4-8.9)	.42
Any SPT positive	7 (70.0)	28 (50.0)	66	2.5 (0.6-11.0)	.22

<b>BHR provocation test</b>					
2log (Histamine threshold), mg/ml	4 (3 – 4)	4 (3 – 4)	71	1.9 (0.8-4.7)	.17
Histamine threshold < 8 mg/ml	4 (40.0)	28 (45.9)	71	0.8 (0.2-3.3)	.78
Histamine threshold < 4 mg/ml	0 (0.0)	15 (24.6)	71	Fisher's	.11
<p>Data are presented as mean (SD), median (25<sup>th</sup>-75<sup>th</sup> percentile), or n (%). Odds Ratios (OR) with 95% Confidence Intervals (CI) are given for a logistic regression model adjusted for age at visit 1 and sex. If one of the groups contains 0 cases the p-value for the Fisher's exact test is given.</p>					

**Supplemental table 5: complete list of childhood factors ComR/ClinR versus PersA at visit 3**

	(n=102)				
	ComR/ClinR (n=41)	PersA (n=61)	Total (n)	Multivariate analysis	
				OR (95% CI)	P
<b>Characteristics</b>					
Age at first visit, years	9.7 (1.4)	9.8 (1.5)	102	1.0 (0.7-1.3)	.88
Period between visit 1 and 2, years	39.0 (38.0-41.0)	39.0 (38.0-41.0)	102	1.0 (0.9-1.1)	.70
Male sex	31 (75.6)	38 (62.3)	102	1.9 (0.8-4.5)	.17
Weight at first visit, kg	34.0 (7.7)	33.0 (6.5)	102	1.0 (0.96-1.1)	.41
Height at first visit, cm	144.2 (9.9)	143.4 (10.3)	102	1.0 (0.96-1.1)	.57
Cough	32 (80.0)	50 (82.0)	101	0.8 (0.3-2.4)	.75
Age at development of cough, years	3 (1 – 7)	2 (1 – 7)	76	1.0 (0.9-1.2)	.71
Cough accompanied by fever	15 (40.5)	28 (51.9)	91	0.7 (0.3-1.6)	.36
Cough ≥ 3 months	12 (35.3)	26 (48.1)	88	0.6 (0.2-1.4)	.24
Sputum	<b>14 (35.9)</b>	<b>36 (60.0)</b>	<b>99</b>	<b>0.4 (0.1-0.8)</b>	<b>.02</b>
Shortness of breath at rest	9 (24.3)	23 (39.0)	96	0.5 (0.2-1.2)	.12
Shortness of breath during walking stairs/playing	8 (21.6)	16 (30.2)	90	0.6 (0.2-1.6)	.31
Shortness of breath during cycling against the wind	27 (69.2)	45 (77.6)	97	0.6 (0.2-1.5)	.29
Age at development of shortness of breath, years	4 (1 – 7)	4 (1 – 7)	71	1.0 (0.9-1.1)	.85
Attack of dyspnea at rest with wheezing	30 (75.0)	51 (83.6)	101	0.5 (0.2-1.5)	.24
Wheeze ever	35 (87.5)	52 (94.5)	95	0.4 (0.1-1.9)	.26
Wheeze during a cold	24 (66.7)	23 (50.0)	82	2.0 (0.8-5.0)	.13
Wheeze without a cold	14 (40.0)	23 (50.0)	81	0.6 (0.3-1.6)	.32
Runny or stuffed nose	27 (67.5)	37 (63.8)	98	1.2 (0.5-2.9)	.67
Age at development of runny/stuffed nose, years	6 (1 – 8)	6 (2 – 8)	57	1.0 (0.8-1.2)	.81
Eczema	18 (47.4)	24 (39.3)	99	1.4 (0.6-3.2)	.41



Urticaria	3 (8.1)	7 (12.1)	95	0.7 (0.2-2.8)	.59
≥3 symptoms: cough, sputum, shortness of breath at rest, attack of dyspnea at rest with wheezing, wheeze ever	27 (75.0)	43 (79.6)	90	0.7 (0.3-2.1)	.57
Physical signs of pulmo ronchi	13 (54.2)	25 (62.5)	64	0.7 (0.2-2.1)	.52
Physical signs of thorax deformation	5 (20.8)	12 (30.0)	64	0.5 (0.1-1.8)	.28
<b>Peripheral blood measurements</b>					
LN Leukocyte count, cells x 10 <sup>6</sup> /L	9.0 (0.3)	9.0 (0.3)	99	0.8 (0.2-3.7)	.80
Leukocyte count level 75 <sup>th</sup> percentile (>9.600 x 10 <sup>6</sup> /L)	14 (35.0)	14 (23.7)	99	1.7 (0.7-4.3)	.22
Leukocyte count level 90 <sup>th</sup> percentile (>10.880 x 10 <sup>6</sup> /L)	4 (10.0)	4 (6.8)	99	1.8 (0.4-7.9)	.45
Haemoglobin, g/dL	13.6 (0.9)	13.5 (1.0)	99	1.0 (0.7-1.6)	.85
Haemoglobin level 75 <sup>th</sup> percentile (>14.2g/dL)	9 (22.5)	13 (22.0)	99	0.9 (0.3-2.4)	.83
Haemoglobin level 90 <sup>th</sup> percentile (>14.8g/dL)	3 (7.5)	6 (10.2)	99	0.7 (0.2-3.1)	.66
LN eosinophil count, cells x 10 <sup>6</sup> /L	6.0 (0.7)	5.8 (1.2)	99	1.2 (0.8-1.9)	.33
Eosinophil count level 75 <sup>th</sup> percentile (>699 x 10 <sup>6</sup> /L)	8 (20.0)	17 (28.8)	99	0.7 (0.3-1.8)	.41
Eosinophil count level 90 <sup>th</sup> percentile (>961 x 10 <sup>6</sup> /L)	2 (5.0)	7 (11.9)	99	0.4 (0.1-2.2)	.31
Electrophoresis total protein, g/dL	7.1 (6.7 – 7.4)	7.3 (6.8 – 7.5)	101	0.6 (0.3-1.2)	.19
Total protein level 25 <sup>th</sup> percentile (<6.8g/dL)	11 (26.8)	12 (20.0)	101	1.4 (0.5-3.8)	.48
Total protein level 10 <sup>th</sup> percentile (<6.5g/dL)	6 (14.6)	4 (6.7)	101	2.3 (0.6-8.9)	.24
Electrophoresis albumin, % of total protein	63.6 (8.2)	65.6 (7.5)	102	1.0 (0.9-1.02)	.17
Albumin level 25 <sup>th</sup> percentile (<60.2g/dL)	10 (24.4)	13 (21.3)	102	1.3 (0.5-3.4)	.58
Albumin level 10 <sup>th</sup> percentile (<55.6g/dL)	6 (14.6)	5 (8.2)	102	2.2 (0.6-7.9)	.24

<b>Perinatal factors</b>					
Gestational age, weeks	40.0 (39.0-40.0)	40.0 (40.0-40.0)	96	0.8 (0.6-1.1)	.11
Premature birth ( $\leq 37$ weeks)	4 (10.3)	1 (1.8)	96	6.0 (0.6-56.5)	.12
Use of caesarean section at birth	1 (3.8)	3 (8.8)	60	0.4 (0.04-4.6)	.49
Use of forceps at birth	1 (3.7)	0 (0.0)	58	Fisher's	.47
Birth weight, kg	3.5 (3.1-4.0)	3.5 (3.0-4.0)	58	1.1 (0.5-2.2)	.85
Weight <2.5kg at birth	0 (0.0)	3 (7.7)	68	Fisher's	.26
Hospital childbirth	11 (33.3)	12 (22.2)	87	1.8 (0.7-4.7)	.25
Cyanosis at birth	3 (7.9)	6 (10.3)	96	0.7 (0.2-3.1)	.64
Shortness of breath at birth	2 (5.0)	2 (3.5)	97	1.7 (0.2-12.9)	.63
Icterus at birth	6 (15.0)	7 (11.9)	99	1.3 (0.4-4.4)	.65
<b>Postnatal factors</b>					
Breastfeeding	19 (79.2)	22 (64.7)	58	2.1 (0.6-7.3)	.23
Duration of breastfeeding, months	5.0 (2.3 – 6.0)	4.0 (1.8 – 7.0)	33	1.0 (0.8-1.4)	.74
Duration of breastfeeding >6 months	2 (12.5)	5 (29.4)	33	0.3 (0.1-2.1)	.24
History of variola vaccination	30 (83.3)	42 (70.0)	96	2.2 (0.8-6.2)	.15
History of DKTP vaccination	38 (97.4)	60 (100)	99	Fisher's	.39
History of morbilli vaccination	7 (23.3)	4 (8.5)	77	3.2 (0.8-12.2)	.09
History of otitis	14 (35.9)	16 (26.7)	99	1.6 (0.7-4.0)	.28
History of pseudo croup	4 (10.8)	5 (8.5)	96	1.3 (0.3-5.2)	.73
History of surgery for acute tonsillitis	25 (61.0)	38 (62.3)	102	0.9 (0.4-2.1)	.83
Age at surgery for acute tonsillitis, years	5 (4 – 6)	4 (3 – 5)	60	1.2 (0.9-1.5)	.24
History of pneumonia	5 (13.9)	10 (18.9)	89	0.7 (0.2-2.2)	.52
History of scarlet fever	3 (7.5)	5 (8.3)	100	0.8 (0.2-3.8)	.83
History of morbilli	34 (85.0)	48 (81.4)	99	1.3 (0.4-4.0)	.60
History of rubella	13 (36.1)	29 (51.8)	92	0.5 (0.2-1.2)	.14
History of varicella	31 (77.5)	39 (65.0)	100	1.9 (0.8-4.9)	.16
History of smallpox	1 (2.7)	1 (1.8)	94	1.8 (0.1-32.2)	.68
History of parotitis epidemica	22 (56.4)	34 (57.6)	98	1.0 (0.4-2.3)	.97

≥1 of scarlet fever, morbili, rubella, varicella, smallpox, parotitis epidemica	39 (97.5)	57 (95.0)	100	2.2 (0.2-22.2)	.51
≥1 of scarlet fever, rubella, varicella, smallpox, parotitis epidemica	36 (90.0)	53 (89.8)	99	1.1 (0.3-4.2)	.89
<b>Exposure</b>					
Contact with animals	12 (33.3)	17 (30.9)	91	1.2 (0.5-3.1)	.67
Pets	<b>31 (81.6)</b>	<b>36 (59.0)</b>	<b>99</b>	<b>3.1 (1.2-8.2)</b>	<b>.02</b>
Firstborn child	11 (29.7)	20 (33.3)	97	0.9 (0.3-2.1)	.75
Rented house	16 (48.5)	30 (55.6)	87	0.7 (0.3-1.8)	.48
Dusty or damp vs. dry house	3 (8.8)	5 (10.2)	83	0.8 (0.2-3.6)	.75
Rotten floor in house	2 (5.6)	4 (7.5)	89	0.8 (0.1-4.7)	.80
Mould in house	5 (13.9)	3 (5.5)	91	3.2 (0.7-15.0)	.14
≥1 of dusty/damp house, rotten floor, mould in house	9 (27.3)	9 (20.0)	78	1.6 (0.5-4.6)	.41
Old state of house	14 (38.9)	19 (35.2)	90	1.3 (0.5-3.1)	.60
Kapok/feather mattress	2 (5.4)	6 (10.0)	97	0.5 (0.1-2.6)	.40
Kapok/feather pillow	15 (40.5)	14 (24.6)	94	2.1 (0.8-5.2)	.11
Use of gas heater	17 (48.6)	32 (59.3)	89	0.7 (0.3-1.7)	.41
<b>Family history</b>					
Age of father, years	39 (36 – 44)	40 (37 – 44)	88	1.0 (0.9-1.1)	.62
Age father at birth of child, years	29 (26 – 35)	30 (27 – 34)	88	1.0 (0.9-1.1)	.62
Age of mother, years	37 (34 – 40)	39 (36 – 42)	88	1.0 (0.9-1.1)	.64
Age mother at birth of child, years	27 (24 – 30)	28 (26 – 32)	88	1.0 (0.9-1.1)	.64
Father with asthma	6 (16.7)	9 (15.5)	94	1.1 (0.4-3.6)	.84
Father with bronchitis	<b>2 (5.9)</b>	<b>12 (21.1)</b>	<b>91</b>	<b>0.2 (0.04-0.9)</b>	<b>.04</b>
Father with eczema	3 (8.8)	8 (14.0)	91	0.6 (0.1-2.4)	.45
Father with hayfever	3 (8.8)	9 (15.5)	92	0.6 (0.1-2.6)	.51
Father with atopic symptoms (asthma, eczema, hay fever)	9 (25.0)	22 (37.9)	94	0.6 (0.2-1.5)	.27
Mother with asthma	1 (2.9)	7 (11.9)	94	0.2 (0.03-1.9)	.17

Mother with bronchitis	3 (8.8)	10 (17.2)	92	0.5 (0.1-1.9)	.29
Mother with eczema	2 (5.9)	5 (8.6)	92	0.7 (0.2-3.8)	.67
Mother with hayfever	0 (0.0)	4 (6.9)	92	Fisher's	.29
Mother with atopic symptoms (asthma, eczema, hay fever)	3 (8.6)	15 (25.4)	94	0.3 (0.1-1.1)	.06
Rest of the family with asthma	23 (63.9)	30 (50.8)	95	1.8 (0.7-4.1)	.20
Rest of the family with bronchitis	15 (45.5)	32 (55.2)	91	0.7 (0.3-1.6)	.37
Rest of the family with eczema	11 (33.3)	20 (35.1)	90	0.9 (0.4-2.3)	.85
Rest of the family with hay fever	4 (12.1)	9 (15.8)	90	0.7 (0.2-2.7)	.65
Family with atopic symptoms (asthma, eczema, hay fever)	28 (77.8)	40 (67.8)	95	1.7 (0.7-4.6)	.26
Family members with rheumatoid arthritis	8 (22.2)	10 (17.9)	92	1.4 (0.5-4.2)	.52
Family members with heart disease	8 (22.9)	7 (12.5)	91	2.0 (0.6-6.2)	.24
Family members with mental retardation	2 (5.9)	3 (5.3)	91	1.0 (0.2-6.4)	.99
Family members with diabetes mellitus	11 (30.6)	15 (26.3)	93	1.4 (0.5-3.6)	.55
Family members with leukaemia	2 (5.7)	2 (3.5)	92	1.2 (0.2-9.8)	.84
<b>Lung function (Quanjer-adjusted)</b>					
FEV <sub>1</sub> % predicted	77 (66 – 85)	77 (67 – 84)	102	1.0 (0.97- 1.03)	.85
FEV <sub>1</sub> % predicted < 80	29 (70.7)	39 (63.9)	102	1.4 (0.6-3.2)	.47
FEV <sub>1</sub> % predicted <70	12 (29.3)	19 (31.3)	102	1.0 (0.4-2.5)	.95
IVC % predicted	89.5 (10.8)	88.0 (12.4)	102	1.0 (0.97- 1.04)	.79
FEV <sub>1</sub> %IVC ratio	74 (67 – 79)	73 (67 – 78)	102	1.0 (0.96-1.1)	.92
FEV <sub>1</sub> %IVC < 70	15 (36.6)	19 (31.1)	102	1.3 (0.5-3.0)	.57
FEF <sub>25-75</sub> %IVC	75.1 (22.3)	72.2 (24.8)	80	1.0 (0.98- 1.02)	.50
FEF <sub>25-75</sub> %IVC < 70	15 (46.9)	23 (47.9)	80	0.9 (0.4-2.3)	.88
FEF <sub>25-75</sub> %IVC < 50	4 (12.5)	10 (20.8)	80	0.6 (0.2-2.0)	.38
RV%TLC	20.3 (8.0)	21.3 (6.1)	102	1.0 (0.9-1.04)	.53

<b>Skin prick test (histamine-adjusted)</b>					
House dust mite positive	16 (41.0)	24 (42.9)	95	1.0 (0.4-2.2)	.91
Hairs and feathers positive	13 (33.3)	15 (27.3)	94	1.3 (0.5-3.2)	.56
Moulds positive	4 (10.5)	2 (3.6)	93	3.1 (0.5-18.7)	.21
Grass pollen positive	7 (17.9)	11 (20.0)	94	0.9 (0.3-2.6)	.83
Any SPT positive	17 (43.6)	28 (50.0)	95	0.8 (0.3-1.8)	.61
<b>BHR provocation test</b>					
2log (Histamine threshold), mg/ml	3 (2 – 4)	4 (3 – 4)	102	0.9 (0.6-1.2)	.34
Histamine threshold < 8 mg/ml	26 (63.4)	28 (45.9)	102	2.2 (0.96-5.1)	.06
Histamine threshold < 4 mg/ml	13 (31.7)	15 (24.6)	102	1.5 (0.6-3.6)	.39
Data are presented as mean (SD), median (25 <sup>th</sup> -75 <sup>th</sup> percentile), or n (%). Odds Ratios (OR) with 95% Confidence Intervals (CI) are given for a logistic regression model adjusted for age at visit 1 and sex. If one of the groups contains 0 cases the p-value for the Fisher's exact test is given.					