

Supplementary material to the manuscript:

**Virus, allergic sensitisation and cortisol in infant bronchiolitis and risk of early asthma**

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A study performed within ORAACLE (the Oslo Research Group of Asthma and Allergy in Childhood; the Lung and Environment).

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## **SUBJECTS AND METHODS**

### **Methods**

Educational level was categorized into 1- no school completed, 2- primary school completed, 3- secondary school completed, 4- higher education, up to three years and 5 higher education, more than three years.

Nasopharyngeal aspirates were collected using standardized procedure performed by trained paediatric nurses at study inclusion, using a tracheal suction set, and immediately frozen at -20°C.

**Table S1** The Clinical Score used in the study (1), Kristjansson et.al.

	<b>Score 0</b>	<b>Score 1</b>	<b>Score 2</b>
Respiratory rate (breaths/min)	<40	40-60	>60
Respiratory Chest recessions	none	Moderate Costodiaphragmatic	Severe. As 1+ rib and jugular retractions
Auscultatory breath sounds	Vesicular	Wheeze, rales/ronchi	Faint ± severe wheeze ± pronounced rales and rhonci
Skin colour	Normal	Pallor	Cyanosis
General Condition	Not affected	Moderately affected	Severely affected

The clinical score was completed by doctors at inclusion and daily during hospital stay. A clinical score  $\geq$ four of ten was required for study inclusion. The score is identical to that used in a study of acute bronchiolitis by Kristjansson et al (1).

**Table S2** Background Characteristics of the 404 infants hospitalised with acute bronchiolitis, comparing those attending two- years follow-up and those who did not.

	Attending two- years follow-up n= 294 (72.8)	No two- years follow-up n= 110 (27.2)	p
<b>At birth</b>			
<i>Male sex n (%)</i>	181/294 (61.6)	59/110 (53.6)	0.15
Gestational age (GA) weeks (SD)	38.6 (3.3)	38.8 (2.8)	0.54
Born at GA<37 weeks, n (%)	46/294 (15.6)	14/110 (12.7)	0.46
<i>Birth weight, grams (SD)</i>	3424 (641)	3450 (615)	0.74
<b>At enrolment</b>			
Age, days (range)	124.6 (7,363)	134.6 (10, 364)	0.31
Weight, grams (SD)	6442 (1847)	6692 (1942)	0.23
Eczema n (%)	29/271 (10.7)	11/103 (10.7)	1
One previous episode of wheeze	69/ 260 (26.5)	29/ 102 (28.4)	0.72
Length of hospital stay, hours (SD)	80.3 (66.0)	80.0 (70.9)	0.97
Need of supportive treatment, n (%)	152/294 (51.7)	52/110 (47.3)	0.43
<b>Virus detected during acute bronchiolitis</b>			
RSV, n (%)	219/266 (82.3)	81/97 (83.5)	0.79
HRV, n (%)	93/266 (35.0)	29/97 (29.9)	0.37
HRV A or B, n (%)	28/266 (10.5)	7/97 (7.2)	0.34
HRV C, n (%)	65/266 (24.4)	22/97 (22.7)	0.73
RSV, high genomic load, n (%)	145/266 (54.5)	55/97 (56.7)	0.71
HRV, high genomic load, n (%)	16/266 (6.0)	7/97 (7.2)	0.68
More than 1 virus, n (%)	170/ 266 (63.9)	54/97 (55.7)	0.15
<b>Allergic sensitisation, IgE ≥ 0.35</b>			
Any sensitisation, n (%)	22/271 (8.1)	9/97 (9.3)	0.72
Any food sensitisation, n (%)	20/271 (7.4)	8/97 (8.2)	0.78
Any inhalant sensitisation, n (%)	5/267 (1.9)	2/97 (2.1)	0.91
Egg sensitisation, n (%)	8/271 (3.0)	4/97 (4.1)	0.58
Cow's milk sensitisation, n (%)	13/271 (4.8)	4/97 (4.1)	0.79
Peanut sensitisation, n (%)	3/271 (1.1)	1/97 (1.0)	0.95
Polysensitisation, n (%)	6/268 (2.2)	1/97 (1.0)	0.46
Cortisol geometric mean, mmol/l (95% CI)	42.0 (32.9, 53.7)	35.2 (30.9, 10.0)	
<b>Parental education</b>			
<i>Maternal Education<sup>a</sup> (SD)</i>	3.99 (0.98)	3.47 (0.98)	<b>&lt;0.001</b>
<i>Paternal Education<sup>a</sup> (SD)</i>	3.85 (1.0)	3.57 (0.92)	<b>0.019</b>
<b>Parental allergic diseases</b>			
Any n (%)	128/258 (49.6)	46/99 (46.5)	0.59
<i>Maternal Asthma, n (%)</i>	36/ 235 (15.3)	12/90 (13.3)	0.65
<i>Paternal Asthma, n (%)</i>	31/235 (13.2)	12/90 (13.3)	0.97
Maternal Rhinoconjunctivitis, n (%)	42/258 (16.3)	20/98 (20.4)	0.36
<i>Paternal Rhinoconjunctivitis, n (%)</i>	56/258 (21.7)	14/98 (14.3)	0.12
Maternal eczema, n (%)	31/263 (11.8)	9/98 (9.2)	0.48
<i>Paternal eczema, n (%)</i>	25/263 (9.5)	4/ 98 (4.1)	0.092
<b>Environment</b>			
Smoking at home n (%)	38/253 (15.0)	20/88 (22.7)	0.097

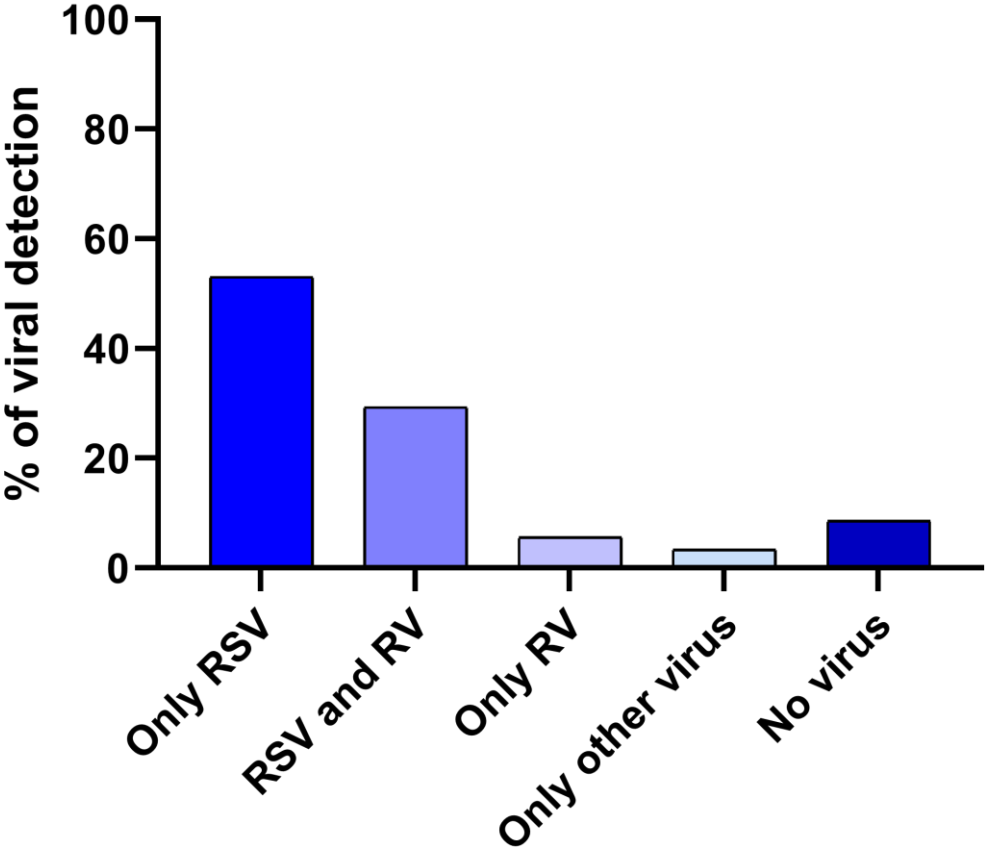
<sup>a</sup> Education was categorised from 1 (no school completed) to 5 (higher education, more than three years)

**Table S3** The distribution of low sensitisation defined by IgE 0.10- 0.34 kU/l before one year of age, of the 294 infants hospitalised with bronchiolitis and attending two- year follow up, shown for those with and without recurrent wheeze.

	Recurrent wheeze n= 143 (48.6)	No recurrent wheeze n= 151 (51.4)	p
<b>Low Allergic sensitisation</b>			
Any sensitisation, n (%)	18/130 (13.8)	17/141 (12.1)	0.66
Any food sensitisation, n (%)	18/130 (13.8)	17/141 (12.1)	0.66
Any inhalant sensitisation, n (%)	15/129 (11.6)	14/138 (10.1)	0.70
Egg sensitisation, n (%)	18/130 (13.8)	17/141 (12.1)	0.66
Cow's milk sensitisation, n (%)	15/130 (11.5)	16/141 (11.3)	0.96
Peanut sensitisation, n (%)	15/130 (11.5)	15/141 (10.6)	0.81

Fig S1

The figure shows the distribution of the viruses analysed in 266 infants hospitalized with bronchiolitis disease (RSV 53%, HRV and RSV 29.3%, HRV 5.6%, other viruses 3.4%, no virus detected 8.6%)



## REFERENCES

1. Kristjansson S, Lodrup Carlsen KC, Wennergren G, Strannegard IL, Carlsen KH. Nebulised racemic adrenaline in the treatment of acute bronchiolitis in infants and toddlers. *Archives of disease in childhood*. 1993;69(6):650-4.