

SUPPLEMENTARY TABLES

Table S1: Baseline characteristics of the EuroPrevall cohort by centre

	All centres (n=12049)	Reykjavik (n=1341)	Southampton (n=1140)	Amsterdam (n=976)	Berlin (n=1570)	Lodz (n=1513)	Vilnius (n=1556)	Madrid (n=1387)	Milan (n=1486)	Athens (n=1080)
BASIC DEMOGRAPHICS AND BIRTH DETAILS										
Male sex % *	51.4	51.2	51.2	52.7	51.7	51.7	51.2	50.7	50.1	52.6
Gestation, weeks median (range) #	39 (34-44)	40 (34-44)	40 (34-43)	40 (34-43)	39 (34-43)	39 (34-42)	39 (34-42)	39 (34-43)	39 (34-43)	40 (34-44)
Birth weight, kg mean (SD) §	3.40 (0.51)	3.76 (0.51)	3.46 (0.52)	3.48 (0.51)	3.41 (0.49)	3.28 (0.50)	3.52 (0.44)	3.25 (0.43)	3.27 (0.51)	3.20 (0.46)
Birth length, cm mean (SD) §	51.5 (3.02)	51.7 (2.21)	52.8 (3.09)	50.9 (2.34)	51.3 (2.54)	54.2 (3.14)	52.7 (2.23)	49.3 (2.08)	49.3 (2.41)	50.5 (2.70)
Apgar score at 5 mins median (range) #	10 (7-10)	9 (7-10)	10 (7-10)	10 (7-10)	10 (7-10)	9 (7-10)	10 (8-10)	10 (7-10)	9 (7-10)	10 (7-10)
Single birth % *	97.9	98.7	97.7	98.4	96.4	96.1	99.2	99.6	98.2	96.7
Caesarean section % *	24.0	12.8	30.8	11.0	31.1	37.5	15.6	2.5	30.8	44.2
Caucasian mother % *	93.3	99.2	95.9	72.2	93.4	99.9	99.9	84.5	89.9	99.2
Caucasian father % *	92.7	98.4	97.0	69.7	90.0	99.3	99.5	84.8	90.4	99.4
Maternal age, years mean (SD) §	30.7 (5.21)	30.1 (4.81)	31.8 (5.18)	29.9 (4.82)	31.4 (5.41)	28.8 (4.43)	28.2 (5.20)	31.4 (5.10)	33.6 (4.66)	30.9 (4.86)
Paternal age, years mean (SD) §	33.3 (6.10)	32.2 (5.50)	34.1 (5.67)	33.0 (6.07)	34.6 (6.61)	31.1 (5.40)	30.9 (6.25)	33.7 (5.65)	36.1 (5.75)	34.8 (5.47)

	All centres (n=12049)	Reykjavik (n=1341)	Southampton (n=1140)	Amsterdam (n=976)	Berlin (n=1570)	Lodz (n=1513)	Vilnius (n=1556)	Madrid (n=1387)	Milan (n=1486)	Athens (n=1080)
FAMILIAL ALLERGIC DISEASE										
Maternal self-reported, doctor-diagnosed allergic disease %										
-Any *	26.3	44.5	51.4	36.5	35.3	9.7	5.9	24.8	23.7	14.0
-Asthma *	9.4	17.2	22.8	13.3	10.8	3.2	1.5	6.2	8.7	5.2
-Allergic rhinitis *	15.3	15.9	26.3	24.1	24.6	7.2	3.5	16.2	14.9	9.5
-Eczema *	11.7	28.0	28.1	14.5	13.4	1.7	2.6	10.1	9.6	2.0
Paternal self-reported, doctor-diagnosed allergic disease %										
-Any *	21.0	32.1	41.0	30.8	29.3	8,7	2.8	19.4	21.4	11.7
-Asthma *	7.2	9.9	19.4	9.8	8.7	2.1	0.8	5.2	8.7	3.7
-Allergic rhinitis *	14.1	15.4	22.8	20.2	23.6	7.2	2.1	15.1	15.7	8.8
-Eczema *	6.2	16.1	15.7	9.3	7.1	1.1	0.3	2.5	5.4	0.5
LIVING ENVIRONMENT										
Rural housing % *	16.1	7.2	76.1	0.6	2.2	22.4	13.6	12.3	8.6	7.9
Mould in house % *	9.9	7.6	10.7	17.5	11.4	2.0	10.2	4.6	9.3	21.5
Pets %										
-Any *	35.5	28.0	50.2	54.5	33.1	46.3	43.8	23.5	24.4	19.5
-Cat *	15.1	11.3	28.8	26.8	15.0	15.1	22.0	5.4	10.5	3.7
-Dog *	16.0	9.3	18.1	14.1	9.0	34.8	21.7	13.5	10.8	10.2
MATERNAL EDUCATION										
Basic not completed % *	5.9	0.8	0.9	1.1	11.2	6.2	6.9	12.3	0.5	11.1
Basic completed % *	18.2	15.1	10.8	11.8	10.8	27.2	19.1	24.9	12.8	31.0
Junior College/ vocational % *	34.0	30.7	30.2	45.6	37.7	15.7	21.6	62.8	40.3	23.3
College/ university % *	42.0	53.5	58.1	41.4	40.2	50.9	52.5	0.0	46.4	34.6

Study centre (n) = total number of infants recruited.

Any allergic disease was defined as asthma, allergic rhinitis or eczema.

Rural housing was defined as living in a village or the countryside and urban living was defined as living in a town or city.

Basic education was defined as completing 10 years in school.

**p <0.05 using Chi-squared to test differences between centres.*

p<0.05 using Kruskal-Wallis to test differences between centres.

\$ p<0.05 using one-way ANOVA to test differences between centres.

Table S2: Number of participants followed up in each centre

	All centres	Reykjavik	Southampton	Amsterdam	Berlin	Lodz	Vilnius	Madrid	Milan	Athens
Total number recruited	12049	1341	1140	976	1570	1513	1556	1387	1486	1080
Number with one-year follow up data n (%)	8174 (67.8)	1017 (75.8)	621 (54.5)	845 (86.6)	1406 (90.0)	1210 (80.0)	1168 (75.1)	1015 (73.2)	30 (2.0)	862 (79.8)
Number with two-year follow up data n (%)	8805 (73.1)	1078 (80.4)	766 (67.2)	624 (63.9)	1296 (82.6)	1263 (83.5)	1166 (75.0)	911 (65.7)	904 (60.8)	797 (73.8)
Number with one-year data, two-year data or both n (%)	9963 (82.7)	1245 (92.8)	882 (77.4)	887 (90.9)	1447 (92.2)	1339 (88.5)	1299 (83.5)	1387 (76.6)	912 (61.4)	890 (82.4)
Number with one-year and two-year data n (%)	7016 (58.2)	850 (63.4)	505 (44.3)	582 (59.6)	1255 (80.0)	1134 (75.0)	1035 (66.5)	864 (62.3)	22 (1.5)	769 (71.2)

One-year data= data collected between 6 and less than 18 months of age.

Two-year data= data collected between 18 and 30 months of age.

Table S3: Comparison of the key baseline characteristics of participants with and without two-year follow up data

	Participants with two-year follow up data (n=8805)	Participants without two-year follow up data (n=3244)
BASIC DEMOGRAPHICS AND BIRTH DETAILS		
Male gender %	51.4	51.2
Gestation, weeks median, range	39 (34-44)	39 (34-44)
Birth weight, kg mean (SD)	3.42 (0.51)	3.37 (0.51)
Caesarean section %	24.6	22.4
Caucasian mother %	95.4	87.6
Caucasian father %	94.8	86.8
Maternal age, years mean (SD)	31.0 (5.00)	29.8 (5.64)
Paternal age, years mean (SD)	33.5 (5.89)	32.8 (6.59)
FAMILIAL ALLERGIC DISEASE		
Maternal self-reported, doctor diagnosed allergic disease %		
-Any	26.3	26.4
-Asthma	9.2	9.8
-Allergic rhinitis	15.2	15.6
-Eczema	11.9	11.3
Paternal self-reported, doctor diagnosed allergic disease %		
-Any	21.3	20.1
-Asthma	7.1	7.5
-Allergic rhinitis	14.4	13.5
-Eczema	6.2	6.2
LIVING ENVIRONMENT		
Rural housing %	16.2	15.8
Mould in house %	9.8	10.2
Pets %		
-Any	36.1	34.1
-Cat	15.5	14.0
-Dog	16.1	15.8
MATERNAL EDUCATION		
Basic not completed %	4.4	10.0
Basic completed %	16.6	22.5
Junior College/ vocational %	33.2	36.1
University/ college %	45.9	31.4

Any allergic disease was defined as asthma, allergic rhinitis and/or eczema.

Rural housing was defined as living in a village or the countryside and urban living was defined as living in a town or city.

Basic education was defined as completing 10 years in school.

Table S4: Alternative multivariate models to evaluate factors associated with wheeze in the second year of life

	Unadjusted IRR [95% CI] (p-value)	Sensitivity model 2 - Adjusted IRR [95% CI] (p-value) (n=3612)	Sensitivity model 3- Adjusted IRR [95% CI] (p-value) (n=4172)
FOOD ALLERGY			
Food allergy diagnosed in first two years of life (yes vs no)	2.84 (<0.001) [1.92-4.20]	1.29 [0.56-2.99] (0.547)	
FEEDING			
Ever breast fed (yes vs no)	1.30 (0.089) [0.96-1.77]	0.72 [0.15-3.39] (0.673)	
Duration of breastfeeding (per month increase)	1.00 (0.918) [0.98-1.02]	1.01 [0.92-1.12] (0.760)	
Age at introduction of solids (per month increase)	0.98 (0.384) [0.93-1.03]	0.95 [0.83-1.08] (0.447)	
Overlap of breast feeding/solids (per month increase)	0.99 (0.709) [0.96-1.03]	0.94 [0.83-1.07] (0.361)	
SMOKE EXPOSURE			
Mother ever smoked (yes vs no)	1.29 (0.001) [1.11-1.50]	1.15 [0.87-1.51] (0.322)	
Smoking at any time during pregnancy (yes vs no)	1.25 (0.086) [0.97-1.61]	0.66 [0.40-1.09] (0.105)	
Mother smoking at one year follow up (yes vs no)	1.15 (0.237) [0.91-1.45]	1.56 [1.05-2.30] (0.026)	1.41 [1.07-1.87] (0.015)
Other smokers in household (yes vs no)	0.81 (0.033) [0.66-0.98]	1.05 [0.72-1.53] (0.814)	
BASIC DEMOGRAPHICS AND BIRTH DETAILS			
Male gender (vs female)	1.35 [1.16-1.58] (<0.001)	1.31 [1.02-1.68] (0.032)	1.31 [1.05-1.63] (0.017)
Gestation (per week increase)	1.04 [0.99-1.10] (0.105)	1.02 [0.93-1.12] (0.680)	
Birth weight (per kg increase)	1.24 [1.07-1.44] (0.004)	1.02 [0.71-1.43] (0.955)	
Birth length (per cm increase)	0.96 [0.94-0.99] (0.004)	0.97 [0.91-1.03] (0.346)	
Apgar score at 5 minutes (per 1 point increase)	0.94 [0.84-1.05] (0.282)		
Multiple birth (vs single birth)	1.13 [0.69-1.86] (0.626)		
Caesarean delivery (vs vaginal delivery)	1.05 [0.88-1.25] (0.577)		
Non-Caucasian mother (vs Caucasian mother)	1.29 [0.94-1.77] (0.120)		
Non-Caucasian father (vs Caucasian father)	1.58 [1.20-2.09] (0.001)	1.37 [0.82-2.29] (0.232)	1.50 [1.01-2.21] (0.043)
Maternal age (per 1 year increase)	1.00 [0.98-1.01] (0.691)		
Paternal age (per 1 year increase)	1.00 [0.99-1.01] (0.918)		

	Unadjusted IRR [95% CI] (p-value)	Sensitivity model 2 - Adjusted IRR [95% CI] (p-value) (n=3612)	Sensitivity model 3 - Adjusted IRR [95% CI] (p-value) (n=4172)
FAMILIAL ALLERGIC DISEASE			
Maternal self-reported, doctor-diagnosed allergic disease			
-Any (yes vs no)	2.11 [1.81-2.45] (<0.001)	1.28 [0.95-1.71] (0.105)	
-Asthma (yes vs no)	2.44 [2.02-2.95] (<0.001)	1.36 [0.94-1.94] (0.104)	1.71 [1.30-2.24] (<0.001)
-Allergic rhinitis (yes vs no)	1.81 [1.52-2.16] (<0.001)		
-Eczema (yes vs no)	1.93 [1.60-2.32] (<0.001)		
Paternal self-reported, doctor-diagnosed allergic disease			
-Any (yes vs no)	2.03 [1.73-2.38] (<0.001)	1.36 [1.01-1.83] (0.044)	1.40 [1.11-1.60] (0.004)
-Asthma (yes vs no)	2.18 [1.76-2.71] (<0.001)	0.76 [0.48-1.20] (0.244)	
-Allergic rhinitis (yes vs no)	1.572 [1.304-1.895] (<0.001)		
-Eczema (yes vs no)	2.051 [1.622-2.594] (<0.001)		
LIVING ENVIRONMENT			
Rural housing (vs urban housing)	0.90 [0.73-1.11] (0.330)		
Mould in house (yes vs no)	1.26 [1.00-1.60] (0.051)	1.01 [0.68-1.51] (0.954)	
Pets			
-Any (yes vs no)	0.98 [0.83-1.14] (0.752)		
-Cat (yes vs no)	1.09 [0.89-1.34] (0.395)		
-Dog (yes vs no)	0.63 [0.49-0.80] (<0.001)	0.82 [0.55-1.22] (0.322)	
DAY CARE ATTENDANCE			
Day care in first year of life (yes vs no)	2.31 [1.93-2.76] (<0.001)		
Day care in second year of life (yes vs no)	2.74 [2.29-3.28] (<0.001)		
Day care at any time in first two years of life (yes vs no)	3.51 [2.82-4.38] (<0.001)	2.32 [1.58-3.40] (<0.001)	2.52 [1.81-3.53] (<0.001)
RESPIRATORY TRACT INFECTIONS			
URTIs in first year of life (≥ quarterly vs ≤ one)	3.13 [2.52-3.90] (<0.001)	1.55 [1.09-2.19] (0.014)	1.65 [1.21-2.26] (0.002)
URTIs in second year of life (≥ quarterly vs ≤ one)	2.88 [2.38-3.47] (<0.001)	1.62 [1.11-2.36] (0.012)	1.41 [1.02-1.93] (0.036)
LRTIs in first year of life (≥ quarterly vs ≤ one)	3.60 [2.84-4.56] (<0.001)	1.77 [1.27-2.46] (0.001)	1.69 [1.24-2.30] (0.001)
LRTIs in second year of life (≥ quarterly vs ≤ one)	3.77 [3.17-4.48] (<0.001)	2.51 [1.85-3.41] (<0.001)	2.45 [1.84-3.26] (<0.001)
ALLERGIC DISEASE			
Eczema in first two years of life (yes vs no)	2.41 [2.03-2.85] (<0.001)	1.21 [0.94-1.55] (0.147)	1.36 [1.09-1.70] (0.007)

IRR= Incidence rate ratio

LRTIs= Lower respiratory tract infections, URTIs= Upper respiratory tract infections

Sensitivity model 2: Includes all variables with $p < 0.1$ in univariate analysis (gender, gestation, birth weight, birth length, ethnicity of father, maternal allergy, maternal asthma, paternal allergy, paternal asthma, mould in house, dog ownership, day care attendance, respiratory tract infections and eczema) plus food allergy and variables related to feeding and smoke exposure.

Sensitivity model 3: This was generated by applying backward deletion to sensitivity model 2. It includes mother smoking at one-year follow up, gender, ethnicity of father, maternal asthma, paternal allergy, day care attendance, respiratory tract infections and eczema.

Table S5: Association of risk factors with recurrent wheeze (wheeze in the first and second years of life)

	Unadjusted IRR [95% CI] (p-value)	Primary model- Adjusted IRR [95% CI] (p-value) (n=3177)	Sensitivity model 1- Adjusted IRR [95% CI] (p-value) (n=5044)	Sensitivity model 2- Adjusted IRR [95% CI] (p-value) (n=3177)	Sensitivity model 3- Adjusted IRR [95% CI] (p-value) (n=4688)
FOOD ALLERGY					
Food allergy diagnosed in first two years of life (yes vs no)	5.50 [3.30-9.14] (<0.001)	2.20 [0.77-6.23] (0.140)		2.61 [0.92-7.42] (0.071)	2.38 [1.22-4.63] (0.011)
FEEDING					
Ever breast fed (yes vs no)	1.24 [0.74-2.06] (0.416)	3.39 [0.34-33.28] (0.295)		3.81 [0.39-37.60] (0.252)	2.09 [1.00-4.35] (0.049)
Duration of breastfeeding (per month increase)	1.01 [0.98-1.05] (0.481)	0.98 [0.85-1.13] (0.799)		0.96 [0.83-1.23] (0.627)	
Age at introduction of solids (per month increase)	0.93 [0.84-1.03] (0.163)	0.90 [0.74-1.11] (0.329)		0.90 [0.74-1.10] (0.300)	0.82 [0.72-0.92] (0.001)
Overlap of breastfeeding/solids (per month increase)	1.02 [0.99-1.07] (0.211)	0.97 [0.80-1.18] (0.764)		1.01 [0.83-1.12] (0.903)	
SMOKE EXPOSURE					
Mother ever smoked (yes vs no)	1.20 [0.92-1.57] (0.177)	1.38 [0.93-2.07] (0.112)		1.39 [0.94-2.06] (0.102)	
Smoking at any time during pregnancy	1.16 [0.74-1.82] (0.519)	0.74 [0.34-1.59] (0.435)		0.78 [0.37-1.65] (0.510)	
Mother smoking at one year follow up (yes vs no)	1.05 [0.73-1.51] (0.795)	1.28 [0.66-2.48] (0.470)		1.16 [0.61-2.19] (0.654)	1.41 [1.07-1.87] (0.015)
Other smokers in household (yes vs no)	0.60 [0.41-0.88] (0.009)	1.64 [0.92-2.91] (0.094)		1.29 [0.73-2.25] (0.378)	

	Unadjusted IRR [95% CI] (p-value)	Primary model- Adjusted IRR [95% CI] (p-value) (n=3177)	Sensitivity model 1- Adjusted IRR [95% CI] (p-value) (n=5044)	Sensitivity model 2- Adjusted IRR [95% CI] (p-value) (n=3177)	Sensitivity model 3- Adjusted IRR [95% CI] (p-value) (n=4688)
BASIC DEMOGRAPHIC AND BIRTH DETAILS					
Male gender (vs female)	2.13 [1.60-2.85] (<0.001)	1.92 [1.29-2.84] (0.001)	2.04 [1.49-2.78] (<0.001)	1.84 [1.35-2.72] (0.002)	1.77 [1.26-2.49] (0.001)
Gestation (per week increase)	1.08 [0.99-1.18] (0.097)	0.93 [0.81-1.07] (0.325)	0.88 [0.81-0.97] (0.010)	0.98 [0.85-1.13] (0.827)	
Birth weight (per kg increase)	1.73 [1.32-2.26] (<0.001)	1.16 [0.67-1.99] (0.600)		1.62 [0.97-2.70] (0.064)	1.84 [1.23-2.75] (0.003)
Birth length (per cm increase)	0.96 [0.92-1.01] (0.128)	0.97 [0.88-1.08] (0.622)		0.91 [0.83-1.00] (0.047)	0.88 [0.81-0.95] (0.001)
Apgar score at 5 mins (per 1 point increase)	0.83 [0.68-1.01] (0.061)	0.85 [0.66-1.09] (0.194)		0.82 [0.65-1.05] (0.116)	
Multiple birth (vs single birth)	0.61 [0.20-1.91] (0.396)				
Caesarean delivery (vs vaginal delivery)	0.70 [0.49-0.99] (0.043)	0.88 [0.52-1.50] (0.651)		0.75 [0.45-1.26] (0.277)	
Non-Caucasian mother (vs Caucasian mother)	1.33 [0.76-2.33] (0.315)				
Non-Caucasian father (vs Caucasian father)	1.86 [1.18-2.95] (0.008)	1.76 [0.81-3.82] (0.154)		1.60 [0.76-3.38] (0.216)	
Maternal age (per 1 year increase)	0.98 [0.96-1.01] (0.171)				
Paternal age (per 1 year increase)	0.99 [0.97-1.01] (0.403)				

	Unadjusted IRR [95% CI] (p-value)	Primary model- Adjusted IRR [95% CI] (p-value) (n=3177)	Sensitivity model 1- Adjusted IRR [95% CI] (p-value) (n=5044)	Sensitivity model 2- Adjusted IRR [95% CI] (p-value) (n=3177)	Sensitivity model 3- Adjusted IRR [95% CI] (p-value) (n=4688)
FAMILIAL ALLERGIC DISEASE					
Maternal self-reported, doctor-diagnosed allergic disease					
-Any (yes vs no)	3.35 [2.57-4.39] (<0.001)	1.11 [0.70-1.75] (0.656)		1.27 [0.80-2.01] (0.304)	
-Asthma (yes vs no)	4.29 [3.18-5.80] (<0.001)	1.81 [1.09-3.01] (0.022)	1.85 [1.32-2.59] (<0.001)	2.13 [1.29-3.51] (0.003)	2.31 [1.60-3.34] (<0.001)
-Allergic rhinitis (yes vs no)	2.39 [1.77-3.22] (<0.001)				
-Eczema (yes vs no)	3.12 [2.30-4.23] (<0.001)				
Paternal self-reported, doctor-diagnosed allergic disease					
-Any (yes vs no)	2.63 [1.99-3.48] (<0.001)	1.57 [1.02-2.41] (0.039)	1.42 [1.06-1.92] (0.019)	1.67 [1.09-2.57] (0.019)	1.42 [1.02-1.98] (0.036)
-Asthma (yes vs no)	2.94 [2.03-4.26] (<0.001)	0.79 [0.42-1.48] (0.461)		0.78 [0.42-1.45] (0.431)	
-Allergic rhinitis (yes vs no)	1.99 [1.44-2.74] (<0.001)				
-Eczema (yes vs no)	2.57 [1.71-3.88] (<0.001)				
LIVING ENVIRONMENT					
Rural housing (vs urban housing)	1.35 [0.96-1.89] (0.083)	0.84 [0.43-1.65] (0.611)		1.60 [0.96-2.65] (0.071)	
Mould in house (yes vs no)	1.09 [0.705-1.676] (0.706)				
Pets					
-Any (yes vs no)	0.97 [0.74-1.28] (0.841)				
-Cat (yes vs no)	1.15 [0.80-1.63] (0.453)				
-Dog (yes vs no)	0.66 [0.44-1.00] (0.051)	0.73 [0.40-1.33] (0.300)		0.72 [0.39-1.32] (0.289)	

		Primary model- Adjusted IRR [95% CI] (p-value) (n=3177)	Sensitivity model 1- Adjusted IRR [95% CI] (p-value) (n=5044)	Sensitivity model 2- Adjusted IRR [95% CI] (p-value) (n=3177)	Sensitivity model 3- Adjusted IRR [95% CI] (p-value) (n=4688)
DAY CARE ATTENDANCE					
Day care in first year of life (yes vs no)	4.03 [3.07-5.30] (<0.001)				
Day care in second year of life (yes vs no)	3.92 [2.80-5.49] (<0.001)				
Day care at any time in first two years of life (yes vs no)	3.90 [2.77-5.50] (<0.001)	1.17 [0.64-2.14] (0.621)		1.72 [0.98-2.99] (0.057)	
RESPIRATORY TRACT INFECTIONS					
URTIs in first year of life (≥ quarterly vs ≤ one)	6.23 [4.21-9.21] (<0.001)	1.52 [0.80-2.87] (0.202)	1.92 [1.17-3.13] (0.009)	2.45 [1.34-4.48] (0.004)	3.11 [1.95-4.90] (<0.001)
URTIs in second year of life (≥ quarterly vs ≤ one)	3.64 [2.60-5.08] (<0.001)	1.26 [0.70-2.29] (0.446)		1.45 [0.81-2.60] (0.206)	
LRTIs in first year of life (≥ quarterly vs ≤ one)	9.48 [7.05-12.76] (<0.001)	3.34 [2.17-5.14] (<0.001)	3.36 [2.30-4.93] (<0.001)	3.70 [2.42-5.66] (<0.001)	3.97 [2.73-5.77] (<0.001)
LRTIs in second year of life (≥ quarterly vs ≤ one)	7.20 [5.31-9.77] (<0.001)	2.57 [1.66-3.96] (<0.001)	2.42 [1.63-3.59] (<0.001)	2.82 [1.85-4.30] (<0.001)	2.45 [1.67-3.60] (<0.001)
ALLERGIC DISEASE					
Eczema in first two years of life (yes vs no)	3.52 [2.68-4.63] (<0.001)	1.36 [0.94-1.97] (0.105)	1.77 [1.32-2.38] (<0.001)	1.39 [0.95-2.01] (0.086)	1.90 [1.22-4.63] (<0.001)

	IRR [95% CI] (p-value)	Primary model- Adjusted IRR [95% CI] (p-value) (n=3177)	Sensitivity model 1- Adjusted IRR [95% CI] (p-value) (n=5044)	Sensitivity model 2- Adjusted IRR [95% CI] (p-value) (n=3177)	Sensitivity model 3- Adjusted IRR [95% CI] (p-value) (n=4688)
STUDY CENTRE					
Reykjavik	Baseline comparator	Baseline comparator	Baseline comparator		
Southampton	0.79 [0.54-1.15] (0.221)	1.34 [0.60-3.00] (0.481)	1.27 [0.81-2.00] (0.303)		
Amsterdam	0.59 (0.008) [0.40-0.88]	0.87 [0.36-2.11] (0.752)	1.19 [0.75-1.89] (0.451)		
Berlin	0.16 [0.10-0.25] (<0.001)	0.28 [0.15-0.53] (<0.001)	0.29 [0.18-0.48] (<0.001)		
Lodz	0.06 [0.03-0.13] (<0.001)	0.16 [0.05-0.53] (0.003)	0.19 [0.09-0.39] (<0.001)		
Vilnius	0.02 [0.01-0.07] (<0.001)	0.09 [0.02-0.49] (0.005)	0.12 [0.03-0.41] (0.001)		
Madrid	0.15 [0.09-0.25] (<0.001)	0.29 [0.12-0.71] (0.007)	0.42 [0.23-0.78] (0.005)		
Milan	0.51 [0.07-3.67] (0.505)	-	2.35 [0.32-17.35] (0.401)		
Athens	0.03 [0.01-0.09] (<0.001)	-	-		

IRR- Incidence rate ratio.

URTIs= Upper respiratory tract infections, LRTIs= Lower respiratory tract infections.

Primary model: Includes all variables with $p < 0.1$ in univariate analysis (gender, gestation, birth weight, birth length, Apgar score at 5 minutes, type of delivery, maternal allergy, maternal asthma, paternal allergy, paternal asthma, rural vs urban housing, dog ownership, day care attendance, respiratory tract infections and eczema) plus food allergy, variables related to feeding and smoke exposure and study centre.

Sensitivity model 1: This was generated by applying backward deletion to the primary model. It includes gender, gestation, maternal asthma, paternal allergy, URTIs in the first year of life, LRTIs in the first and second years of life, eczema and study centre.

Sensitivity model 2: Includes all variables with $p < 0.1$ in univariate analysis (gender, gestation, birth weight, birth length, Apgar score at 5 minutes, type of delivery, maternal allergy, maternal asthma, paternal allergy, paternal asthma, rural vs urban housing, dog ownership, day care attendance, respiratory tract infections and eczema) plus food allergy and variables related to feeding and smoke exposure.

Sensitivity model 3: This generated by applying backward deletion to sensitivity model 2. It includes food allergy, breastfeeding, age at introduction of solids, mother smoking at one-year follow up, gender, birth weight, birth length, maternal asthma, paternal allergy, URTIs the first year of life, LRTIs in the first and second years of life and eczema.

Table S6: Association of risk factors with wheeze in the second year of life by centre (unadjusted)

	All centres (n=12049)	Reykjavik (n=1341)	Southampton (n=1140)	Amsterdam (n=976)	Berlin (n=1570)	Lodz (n=1513)	Vilnius (n=1556)	Madrid (n=1387)	Milan (n=1486)	Athens (n=1080)
FOOD ALLERGY										
Food allergy diagnosed in first two years of life (yes vs no)	2.84 [1.92-4.20] (<0.001)	2.07 [1.02-4.20] (0.045)	3.34 [1.68-6.62] (0.001)	0.98 [0.24-3.99] (0.974)	1.22 [0.30-4.92] (0.782)	3.87 [0.52-28.85] (0.186)	-	8.63 [2.60-28.64] (<0.001)	1.51 [0.21-10.87] (0.680)	-
FEEDING										
Ever breast fed (yes vs no)	1.30 [0.96-1.77] (0.089)	0.41 [0.19-0.86] (0.019)	1.20 [0.55-2.60] (0.643)	1.32 [0.65-2.68] (0.437)	1.97 [0.63-6.18] (0.246)	0.33 [0.12-0.89] (0.028)	-	1.27 [0.38-4.22] (0.695)	0.87 [0.43-1.73] (0.685)	3.86 [0.52-28.80] (0.187)
Duration of breastfeeding (per month increase)	1.00 [0.98-1.02] (0.918)	0.95 [0.91-0.99] (0.022)	0.93 [0.87-0.98] (0.014)	0.97 [0.89-1.05] (0.421)	0.98 [0.93-1.03] (0.453)	0.90 [0.77-1.04] (0.148)	0.97 [0.85-1.11] (0.653)	1.01 [0.87-1.18] (0.879)	0.96 [0.89-1.03] (0.253)	1.03 [0.89-1.20] (0.658)
Age at introduction of solids (per month increase)	0.98 [0.93-1.03] (0.384)	0.95 [0.85-1.07] (0.409)	1.05 [0.92-1.20] (0.489)	0.99 [0.85-1.16] (0.903)	0.91 [0.82-1.01] (0.065)	0.50 [0.35-0.73] (<0.001)	1.02 [0.88-1.19] (0.785)	1.10 [0.93-1.31] (0.279)	1.02 [0.89-1.17] (0.770)	1.26 [0.90-1.77] (0.173)
Overlap of breast feeding/solids (per month increase)	0.99 [0.96-1.03] (0.709)	0.92 [0.87-0.98] (0.014)	0.87 [0.78-0.98] (0.020)	0.97 [0.84-1.12] (0.654)	0.98 [0.90-1.07] (0.666)	0.89 [0.71-1.11] (0.290)	0.93 [0.74-1.16] (0.515)	1.06 [0.87-1.29] (0.574)	0.92 [0.82-1.03] (0.162)	1.05 [0.85-1.28] (0.670)
SMOKE EXPOSURE										
Mother ever smoked (yes vs no)	1.29 [1.11-1.49] (0.001)	1.00 [0.74-1.35] (0.995)	1.06 [0.71-1.59] (0.767)	1.36 [0.84-2.20] (0.207)	1.41 [1.02-1.95] (0.038)	0.68 [0.25-1.86] (0.457)	1.55 [0.67-3.58] (0.302)	1.86 [0.87-3.97] (0.110)	1.52 [0.99-2.33] (0.054)	1.41 [0.61-3.27] (0.419)
Smoking at any time during pregnancy (yes vs no)	1.25 [0.97-1.61] (0.086)	1.53 [0.96-2.44] (0.071)	2.28 [1.00 - 5.20] (0.051)	1.62 [0.85-3.10] (0.142)	0.68 [0.35-1.33] (0.262)	2.30 [0.68-7.80] (0.182)	1.68 [0.39-7.21] (0.482)	0.81 [0.19-3.48] (0.781)	1.76 [0.88-3.52] (0.109)	1.48 [0.54-4.05] (0.441)
Mother smoking at one year follow up (yes vs no)	1.15 [0.91-1.45] (0.237)	1.22 [0.72-2.05] (0.464)	2.60 [1.21-5.44] (0.011)	1.49 [0.71-2.87] (0.236)	1.20 [0.79-1.82] (0.390)	2.16 [0.70-6.69] (0.183)	0.67 [0.09-5.01] (0.695)	1.45 [0.63-3.34] (0.379)	3.17 [0.33-30.44] (0.318)	1.62 [0.67-3.19] (0.283)
Other smokers in household (yes vs no)	0.81 [0.66-0.98] (0.033)	1.13 [0.50-2.55] (0.770)	1.83 [1.14-2.94] (0.012)	1.20 [0.67-2.17] (0.539)	1.20 [0.70-2.05] (0.502)	2.11 [0.90-4.97] (0.088)	1.73 [0.75-4.01] (0.198)	0.98 [0.40-2.58] (0.960)	1.48 [0.94-2.33] (0.094)	1.56 [0.67-3.66] (0.303)

	All centres (n=12049)	Reykjavik (n=1341)	Southampton (n=1140)	Amsterdam (n=976)	Berlin (n=1570)	Lodz (n=1513)	Vilnius (n=1556)	Madrid (n=1387)	Milan (n=1486)	Athens (n=1080)
BASIC DEMOGRAPHICS AND BIRTH DETAILS										
Male gender (vs female)	1.35 [1.16-1.58] (<0.001)	1.28 [0.95-1.71] (0.101)	1.39 [0.93-2.08] (0.104)	2.36 [1.38-4.05] (0.002)	1.21 [0.86-1.66] (0.253)	1.53 [0.63-3.68] (0.346)	1.70 [0.71-4.03] (0.236)	1.07 [0.50-2.28] (0.856)	1.32 [0.86-2.03] (0.200)	0.89 [0.39-2.05] (0.781)
Gestation (per week increase)	1.04 [0.99-1.10] (0.105)	0.89 [0.81-0.98] (0.012)	1.02 [0.89-1.16] (0.783)	0.88 [0.75-1.03] (0.105)	1.04 [0.93-1.16] (0.516)	1.05 [0.80-1.37] (0.752)	0.82 [0.60-1.12] (0.200)	1.08 [0.83-1.41] (0.583)	0.93 [0.82-1.05] (0.225)	1.05 [0.78-1.42] (0.758)
Birth weight (per kg increase)	1.24 [1.07-1.44] (0.004)	0.85 [0.64-1.13] (0.257)	1.15 [0.78-1.69] (0.482)	0.72 [0.45-1.13] (0.152)	1.08 [0.78-1.49] (0.654)	0.70 [0.30-1.62] (0.402)	0.60 [0.24-1.56] (0.296)	2.07 [0.86-5.00] (0.106)	0.83 [0.55-1.25] (0.376)	0.53 [0.21-1.32] (0.170)
Birth length (per cm increase)	0.96 [0.94-0.99] (0.004)	0.97 [0.91-1.03] (0.326)	0.94 [0.87-1.00] (0.052)	0.89 [0.72-1.10] (0.276)	1.02 [0.96-1.09] (0.493)	0.93 [0.82-1.05] (0.235)	0.94 [0.79-1.13] (0.511)	1.15 [0.95-1.40] (0.145)	0.99 [0.91-1.08] (0.845)	0.95 [0.84-1.07] (0.390)
Apgar score at 5 mins (per 1 point increase)	0.94 [0.84-1.05] (0.282)	1.01 [0.84-1.22] (0.907)	1.07 [0.727-1.57] (0.741)	0.81 [0.54-1.22] (0.310)	0.95 [0.76-1.12] (0.675)	0.67 [0.35-1.27] (0.218)	1.19 [0.44-3.21] (0.739)	0.49 [0.26-0.93] (0.028)	0.98 [0.66-1.45] (0.922)	0.84 [0.28-2.52] (0.751)
Multiple birth (vs single birth)	1.13 [0.69-1.86] (0.626)	1.59 [0.51-4.99] (0.423)	1.09 [0.27-4.25] (0.902)	0.93 [0.13-6.68] (0.940)	0.61 [0.20-1.93] (0.403)	2.29 [0.53-9.84] (0.264)	-	-	3.65 [1.40-8.56] (0.007)	-
Caesarean delivery (vs vaginal delivery)	1.05 [0.88-1.25] (0.577)	1.34 [0.91-1.98] (0.133)	1.11 [0.73-1.69] (0.640)	0.56 [0.23-1.39] (0.213)	0.99 [0.70-1.39] (0.931)	1.02 [0.42-2.46] (0.969)	1.22 [0.41-3.61] (0.716)	1.55 [0.21-11.40] (0.668)	1.45 [0.94-2.25] (0.093)	1.47 [0.64-3.41] (0.365)
Non-Caucasian mother (vs Caucasian mother)	1.29 [0.94-1.77] (0.120)	-	0.73 [0.23-2.30] (0.587)	1.27 [0.74-2.19] (0.384)	0.75 [0.33-1.70] (0.490)	-	-	2.53 [1.07-5.99] (0.034)	1.53 [0.67-3.50] (0.317)	-
Non-Caucasian father (vs Caucasian father)	1.58 [1.20-2.09] (0.001)	1.37 [0.51-3.69] (0.533)	0.34 [0.052-4.5] (0.285)	1.37 [0.84-2.34] (0.245)	1.11 [0.63-1.95] (0.731)	-	-	2.98 [1.1-6.81] (0.010)	2.37 [1.19-4.74] (0.014)	-
Maternal age (per 1 year increase)	1.00 [0.98-1.01] (0.691)	0.96 [0.93-0.99] (0.008)	0.99 [0.94-1.03] (0.480)	0.99 [0.94-1.04] (0.624)	0.98 [0.95-1.01] (0.224)	0.96 [0.86-1.06] (0.413)	1.08 [1.00-1.17] (0.057)	0.90 [0.84-0.96] (0.003)	0.99 [0.94-1.04] (0.710)	0.96 [0.88-1.06] (0.431)
Paternal age (per 1 year increase)	1.00 [0.99-1.01] (0.918)	0.98 [0.96-1.01] (0.186)	0.97 [0.93-1.01] (0.095)	0.99 [0.95-1.03] (0.564)	0.99 [0.96-1.02] (0.420)	0.95 [0.87-1.05] (0.327)	1.05 [0.99-1.12] (0.121)	0.94 [0.87-1.01] (0.087)	1.01 [0.97-1.05] (0.697)	1.01 [0.93-1.09] (0.872)

	All centres (n=12049)	Reykjavik (n=1341)	Southampton (n=1140)	Amsterdam (n=976)	Berlin (n=1570)	Lodz (n=1513)	Vilnius (n=1556)	Madrid (n=1387)	Milan (n=1486)	Athens (n=1080)
FAMILIAL ALLERGIC DISEASE										
Maternal self-reported, doctor diagnosed allergic disease										
-Any (yes vs no)	2.11 [1.81-2.45] (<0.001)	1.55 [1.56 - 2.07] (0.003)	1.55 [1.04-2.32] (0.033)	1.32 [0.81-2.15] (0.264)	1.18 [0.85-1.64] (0.323)	1.65 [0.45-1.64] (0.423)	2.76 [0.82-9.33] (0.102)	0.50 [0.17-1.46] (0.206)	1.18 [0.73-1.89] (0.500)	1.69 [0.62-4.57] (0.304)
-Asthma (yes vs no)	2.44 [2.02-2.95] (<0.001)	1.85 [1.34- 2.56] (<0.001)	1.70 [1.12- 2.59] (0.014)	1.33 [0.69-2.53] (0.393)	1.26 [0.79-2.01] (0.343)	-	3.21 [0.43- 23.89] (0.254)	1.91 [0.57-6.33] (0.292)	1.95 [1.01-3.46] (0.022)	2.70 [0.80- 9.11] (0.111)
-Allergic rhinitis (yes vs no)	1.81 [1.52-2.16] (<0.001)	1.91 [1.38- 2.65] (0.001)	1.17 [0.77-1.80] (0.463)	1.54 [0.919- 2.590] (0.101)	1.18 [0.83-1.69] (0.359)	2.28 [0.67-7.79] (0.188)	4.33 [1.28- 14.61] (0.018)	0.65 [0.20-2.16] (0.480)	1.16 [0.67-2.00] (0.597)	-
-Eczema (yes vs no)	1.93 [1.60-2.32] (<0.001)	1.11 [0.81- 1.52] (0.515)	1.51 [1.01-2.27] (0.045)	1.24 [0.66-2.31] (0.502)	1.10 [0.70-1.73] (0.6760)	-	-	-	1.29 [0.68- 2.42] (0.438)	4.58 [1.07- 19.58] (0.040)
Paternal self-reported, doctor diagnosed allergic disease										
-Any (yes vs no)	2.03 [1.73-2.38] (<0.001)	1.37 [1.01- 1.85] (0.041)	1.66 [1.11-2.49] (0.013)	2.06 [1.26-3.37] (0.004)	0.97 [0.69-1.38] (0.880)	1.65 [0.49-5.60] (0.422)	5.08 [1.51- 17.18] (0.009)	0.93 [0.35-2.46] (0.882)	1.46 [0.92-2.34] (0.112)	1.06 [0.31-3.57] (0.928)
-Asthma (yes vs no)	2.18 [1.76-2.71] (<0.001)	1.12 [0.70- 1.78] (0.638)	1.39 [0.87-2.22] (0.172)	2.39 [1.30-4.39] (0.005)	1.47 [0.91-2.38] (0.118)	2.27 [0.31- 16.94] (0.423)	10.48 [2.45- 44.84] (0.002)	2.09 [0.63-6.98] (0.228)	2.00 [1.11-3.62] (0.021)	1.13 [0.15-8.42] (0.903)
-Allergic rhinitis (yes vs no)	1.57 [1.30-1.90] (<0.001)	1.07 [0.72- 1.60] (0.740)	1.24 [0.79-1.94] (0.348)	1.99 [1.18-3.35] (0.010)	0.88 [0.60-1.29] (0.510)	2.05 [0.61-6.97] (0.249)	4.37 [1.02- 18.71] (0.047)	0.93 [0.32-2.71] (0.898)	1.55 [0.9-2.56] (0.101)	0.95 [0.22-4.05] (0.940)
-Eczema (yes vs no)	2.05 [1.62-2.59] (<0.001)	1.44 [1.01- 2.06] (0.047)	0.78 [0.42-1.42] (0.411)	1.47 [0.70-3.09] (0.307)	0.86 [0.45-1.63] (0.637)	-	-	-	2.31 [1.23-4.36] (0.010)	-
LIVING ENVIRONMENT										
Rural housing (yes vs no)	0.90 [0.73-1.11] (0.330)	0.98 [0.56- 1.72] (0.943)	0.61 [0.40-0.93] (0.023)	-	1.14 [0.42- 3.07] (0.800)	0.35 [0.08-1.50] (0.158)	0.62 [0.15-2.65] (0.517)	1.19 [0.41-3.44] (0.748)	0.56 [0.20-1.52] (0.254)	1.16 [0.27-4.97] (0.840)
Mould in house (yes vs no)	1.26 [1.00-1.60] (0.051)	0.46 [0.91- 2.35] (0.117)	1.08 [0.58-2.02] (0.815)	1.34 [0.75-2.38] (0.318)	0.79 [0.44- 1.39] (0.406)	6.17 [1.44- 26.50] (0.014)	0.45 [0.06-3.33] (0.431)	1.80 [0.42- 7.58] (0.428)	1.76 [0.95-3.24] (0.073)	0.80 [0.27-2.38] (0.693)

	All centres (n=12049)	Reykjavik (n=1341)	Southampton (n=1140)	Amsterdam (n=976)	Berlin (n=1570)	Lodz (n=1513)	Vilnius (n=1556)	Madrid (n=1387)	Milan (n=1486)	Athens (n=1080)
Pets										
-Any (yes vs no)	0.98 [0.83-1.14] (0.752)	0.94 [0.68-1.30] (0.705)	0.84 [0.56-1.24] (0.373)	0.78 [0.48-1.25] (0.300)	1.29 [0.93-1.79] (0.121)	0.72 [0.30-1.73] (0.458)	1.27 [0.55-2.92] (0.579)	1.24 [0.54-2.83] (0.613)	0.99 [0.60-1.63] (0.964)	1.48 [0.59-3.77] (0.415)
-Cat (yes vs no)	1.09 [0.89-1.34] (0.395)	1.21 [0.79-1.86] (0.386)	0.83 [0.53-1.30] (0.419)	0.60 [0.33-1.08] (0.090)	1.38 [0.93-2.06] (0.111)	0.56 [0.13-2.42] (0.441)	0.81 [0.27-2.37] (0.699)	1.13 [0.27-4.76] (0.870)	1.22 [0.63-2.36] (0.559)	1.35 [0.18-10.07] (0.767)
- Dog (yes vs no)	0.63 [0.49-0.80] (<0.001)	0.73 [0.43-1.26] (0.264)	0.87 [0.50-1.54] (0.641)	0.54 [0.22-1.33] (0.179)	0.87 [0.47-1.61] (0.664)	0.59 [0.22-1.60] (0.296)	2.05 [0.86-4.88] (0.106)	1.72 [0.70-4.26] (0.241)	0.85 [0.39-1.85] (0.683)	1.27 [0.38-4.29] (0.702)
Maternal education: Only basic education completed vs:										
Basic education not completed	1.16 [0.77-1.74] (0.483)	1.86 [0.29-4.93] (0.815)	-	2.39 [0.29-19.45] (0.414)	1.89 [0.92-3.91] (0.082)	2.79 [0.56-13.81] (0.209)	1.73 [0.16-19.10] (0.654)	0.88 [0.22-3.35] (0.860)	-	2.79 [0.75-10.40] (0.126)
Junior College/vocational	1.15 [0.91-1.45] (0.255)	0.77 [0.50-1.18] (0.223)	0.58 [0.30-1.10] (0.094)	1.04 [0.46-2.38] (0.918)	1.24 [0.68-2.26] (0.480)	1.35 [0.41-4.41] (0.625)	1.53 [0.28-8.34] (0.625)	0.99 [0.39-2.48] (0.974)	0.50 [0.24-1.04] (0.064)	1.17 [0.34-4.04] (0.804)
College/university	1.20 [0.96-1.50] (0.114)	0.79 [0.53-1.16] (0.223)	0.52 [0.29-0.93] (0.028)	1.02 [0.45-2.32] (0.969)	1.15 [0.63-2.08] (0.656)	0.64 [0.22-1.83] (0.403)	2.27 [0.52-9.94] (0.275)	-	0.73 [0.37-1.43] (0.353)	1.20 [0.39-3.66] (0.751)
DAY CARE ATTENDANCE										
Day care in first year of life (yes vs no)	2.31 [1.93-2.76] (<0.001)	1.15 [0.80-1.64] (0.445)	1.28 [0.78-2.07] (0.327)	1.12 [0.61-2.05] (0.709)	1.45 [1.05-2.01] (0.024)	2.05 [0.47-9.01] (0.343)	-	0.63 [0.28-1.45] (0.280)	0.96 [0.16-5.76] (0.967)	-
Day care in second year of life (yes vs no)	2.74 [2.29-3.28] (<0.001)	1.29 [0.66-2.51] (0.464)	1.10 [0.74-1.65] (0.630)	1.44 [0.69-3.01] (0.335)	1.53 [0.95-2.44] (0.078)	1.46 [0.53-4.02] (0.463)	3.22 [1.39-7.45] (0.006)	0.78 [0.36-1.70] (0.535)	1.49 [0.93-2.39] (0.100)	0.79 [0.23-2.67] (0.702)
Day care at any time in first two years of life (yes vs no)	3.51 [2.82-4.38] (<0.001)	1.96 [0.63-6.14] (0.247)	1.12 [0.69-1.82] (0.649)	1.62 [0.65-4.03] (0.301)	1.70 [1.02-2.81] (0.040)	1.73 [0.59-5.05] (0.319)	3.44 [1.41-8.43] (0.007)	0.70 [0.32-1.52] (0.361)	0.53 [0.07-3.85] (0.534)	0.83 [0.24-2.84] (0.762)

	All centres (n=12049)	Reykjavik (n=1341)	Southampton (n=1140)	Amsterdam (n=976)	Berlin (n=1570)	Lodz (n=1513)	Vilnius (n=1556)	Madrid (n=1387)	Milan (n=1486)	Athens (n=1080)
RESPIRATORY TRACT INFECTIONS										
URTIs in first year of life (≥ quarterly vs ≤ one)	3.13 [2.52-3.90] (<0.001)	1.32 [0.67-2.60] (0.418)	1.11 [0.60-2.03] (0.744)	3.07 [1.11-8.47] (0.031)	1.08 [0.71-1.66] (0.708)	0.66 [0.25-1.77] (0.405)	8.83 [3.18-24.52] (<0.001)	3.70 [1.71-8.00] (0.001)	0.67 [0.11-3.99] (0.657)	1.20 [0.50-2.87] (0.690)
URTIs in second year of life (≥ quarterly vs ≤ one)	2.88 [2.38-3.47] (<0.001)	1.41 [0.77-2.60] (0.267)	0.66 [0.44-0.97] (0.036)	1.49 [0.74-3.01] (0.267)	1.72 [0.88-3.38] (0.114)	0.68 [0.28-1.63] (0.384)	1.37 [0.18-10.19] (0.758)	5.12 [2.38-11.03] (<0.001)	3.71 [1.86-7.41] (<0.001)	0.95 [0.38-2.37] (0.915)
LRTIs in first year of life (≥ quarterly vs ≤ one)	3.60 [2.83-4.56] (<0.001)	2.47 [1.74-3.50] (<0.001)	1.83 [0.84-4.01] (0.130)	2.60 [0.63-10.64] (0.185)	1.30 [0.64-2.65] (0.472)	4.54 [1.03-19.97] (0.045)	19.02 [2.54-142.46] (0.004)	9.51 [4.31-20.94] (<0.001)	-	
LRTIs in second year of life (≥ quarterly vs ≤ one)	3.77 [3.17-4.48] (<0.001)	2.92 [2.19-3.90] (<0.001)	2.04 [1.09-3.82] (0.026)	2.70 [0.66-11.02] (0.167)	1.25 [0.68-2.31] (0.473)	24.24 [8.16-72.02] (<0.001)	4.21 [0.57-31.32] (0.160)	15.11 [7.10-32.14] (<0.001)	3.33 [2.15-5.16] (<0.001)	6.60 [0.60-72.79] (0.123)
ALLERGIC DISEASE										
Eczema in first two years of life (yes vs no)	2.41 [2.03-2.85] (<0.001)	1.63 [1.17-2.28] (0.004)	1.54 [0.95-2.48] (0.078)	2.48 [1.48-4.16] (0.001)	1.36 [0.98-1.89] (0.063)	2.62 [1.03-6.63] (0.043)	1.18 [0.16-8.85] (0.871)	2.23 [1.02-4.86] (0.043)		1.49 [0.55-4.07] (0.437)

Values represent: Incidence rate ratio, IRR [95% confidence intervals] (p-value)

URTIs= Upper respiratory tract infections, LRTIs= Lower respiratory tract infections.

Where no figures are entered, Poisson estimation was not possible.

APPENDICES

Appendix A: Description of dichotomous variables generated using questionnaire data

Variable	Source of data	Question/questions asked	Classification
Allergic disease in parents	Baseline questionnaire	<p>For each parent:</p> <ul style="list-style-type: none"> • Do you or did you ever suffer from pollen-related rhinitis (hay fever)? <ul style="list-style-type: none"> ○ Was it medically diagnosed? • Do you or did you ever suffer from eczema? <ul style="list-style-type: none"> ○ Was it medically diagnosed? • Do you or did you ever suffer from asthma? <ul style="list-style-type: none"> ○ Was it medically diagnosed? 	Parents were defined as having self-reported, doctor diagnosed allergic disease if they reported medically diagnosed hay fever, eczema or asthma.
Any maternal smoking	Baseline questionnaire	<ul style="list-style-type: none"> • Do you smoke? <ul style="list-style-type: none"> ○ Yes ○ No, ex-smoker ○ No, never smoked 	Current smokers and ex-smokers were grouped together to create a dichotomous variable for ever versus never smoked.
Smoking during pregnancy	Baseline questionnaire	<ul style="list-style-type: none"> • Do you smoke? <ul style="list-style-type: none"> ○ Yes ○ No, ex-smoker ○ No, never smoked • Did you stop smoking or reduce the number of cigarettes you smoked when you were pregnant? <ul style="list-style-type: none"> ○ Yes, stopped completely ○ Yes, reduced the number of cigarettes smoked ○ No, continued to smoke at the same level ○ I had already stopped before becoming pregnant 	Mothers were classified as having smoked during pregnancy if they answered yes or no, ex-smoker to 'Do you smoke?' and reported that they had reduced the number of cigarettes smoked or continued smoking at the same level when they were pregnant.
Mother smoking at one-year follow up	One-year data	<ul style="list-style-type: none"> • Do you smoke? <ul style="list-style-type: none"> ○ No ○ Yes, daily ○ Yes, occasionally 	Daily and occasional smokers were grouped together to differentiate smokers from non-smokers.

Day care at any time in first two years of life	One and two-year data	<ul style="list-style-type: none"> • Does your child attend day care or a nursery? <ul style="list-style-type: none"> ○ Yes ○ No 	If parents replied yes to this question in the time frame for one-year data, two-year or data both children were classified as having attended day care in the first two years of life.
Upper respiratory tract infections	One and two-year data	<ul style="list-style-type: none"> • How often has your child had an upper respiratory tract infection in the last 12 months? <ul style="list-style-type: none"> ○ None/once ○ Occasionally (once every 3 months) ○ Often (once a month or more) 	Frequent upper respiratory tract infections were defined as one every 3 months (quarterly) or more.
Lower respiratory tract infections	One and two-year data	<ul style="list-style-type: none"> • How often has your child had a lower respiratory tract infection in the last 12 months? <ul style="list-style-type: none"> ○ None/once ○ Occasionally (once every 3 months) ○ Once a month or more 	Frequent lower respiratory tract infections were defined as one every 3 months (quarterly) or more.
Eczema in the first two years of life	One and two-year data	<ul style="list-style-type: none"> • Has your child had a rash or eczema that has lasted for at least 7 days or more? (Do not count regular nappy rash) <ul style="list-style-type: none"> ○ Yes ○ No 	If parents replied yes to this question in the time frame for one-year data, two-year data or both, children were classified as having eczema in the first two years of life.