

TABLE S1 Prevalence of respiratory symptoms at ages 1, 4, 6, and 9 years

A) All children who participated at the respective survey[#] (main analysis)									
Symptoms	Age (years) 1		4		6		9		
	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	
	N=4,101		N=2,854		N=2,369		N=1,688		
Any wheeze (with or without night cough)	1,420	35 (33-36)	476	17 (15-18)	325	14 (12-15)	224	13 (12-15)	
Any night cough (with or without wheeze)	938	23 (22-24)	762	27 (25-28)	583	25 (23-26)	409	24 (22-26)	
Isolated night cough (without wheeze)	427	10 (9-12)	520	18 (17-20)	423	18 (16-19)	296	18 (16-19)	
B) Only children who participated in all 4 surveys (N=1,318) (sensitivity analysis)									
	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	
Any wheeze (with or without night cough)	377	29 (27-31)	182	14 (12-16)	149	11 (10-13)	170	13 (11-15)	
Any night cough (with or without wheeze)	278	21 (19-23)	304	23 (21-25)	307	23 (21-26)	301	23 (21-25)	
Isolated night cough (without wheeze)	146	11 (10-13)	220	17 (15-19)	238	18 (16-20)	220	17 (15-19)	

CI, confidence interval.

[#]: Children who were 1 year old at baseline survey (in 1998) and replied to the following respective surveys (in 2001, 2003, or 2006).

TABLE S2 Risk factors for prevalent isolated night cough and wheeze in 4-year-old children (N=2,854)

Association of different factors with cough and wheeze, compared to asymptomatic children, in an unadjusted and adjusted model presented as relative risk ratio estimates with confidence intervals. Cough was defined as isolated night cough (without wheeze).

Risk factors at age 4	Unadjusted model			Adjusted model [#]		
	Night cough [¶]	Wheeze	Similarity p-value ⁺	Night cough [¶]	Wheeze	Similarity p-value ⁺
	RRR (95% CI)	RRR (95% CI)		RRR (95% CI)	RRR (95% CI)	
South Asian ethnicity	1.3 (1.0-1.6)	1.1 (0.8-1.4)	0.279	1.2 (0.9-1.7)	1.3 (0.9-1.8)	0.900
Male sex	1.0 (0.8-1.2)	1.4 (1.1-1.7)	0.014	1.0 (0.8-1.2)	1.4 (1.1-1.8)	0.008
Family history of:						
Asthma	0.9 (0.7-1.2)	2.2 (1.8-2.8)	<0.001	0.9 (0.7-1.2)	2.0 (1.5-2.5)	<0.001
Bronchitis	1.1 (0.8-1.4)	1.7 (1.4-2.2)	0.002	1.1 (0.8-1.4)	1.5 (1.1-1.9)	0.095
Hay fever	1.0 (0.8-1.2)	1.3 (1.1-1.6)	0.033	1.0 (0.8-1.3)	1.0 (0.8-1.3)	0.828
Eczema	1.0 (0.8-1.2)	1.2 (1.0-1.5)	0.072	0.9 (0.7-1.2)	1.1 (0.8-1.4)	0.320
Exposure to infections						
Crowding	1.0 (0.8-1.3)	1.3 (1.0-1.6)	0.109	0.9 (0.7-1.1)	1.0 (0.8-1.3)	0.403
Day care at age 1	1.0 (0.8-1.2)	0.7 (0.5-0.9)	0.010	1.0 (0.8-1.3)	0.7 (0.6-1.0)	0.079
Older siblings	0.8 (0.7-1.0)	1.0 (0.8-1.2)	0.208	-	-	-
Air pollution						
Cooking with gas	1.4 (1.1-1.8)	1.0 (0.8-1.3)	0.071	1.4 (1.1-1.8)	1.0 (0.7-1.3)	0.042
Mother smoking	1.1 (0.8-1.4)	1.7 (1.3-2.2)	0.003	0.8 (0.6-1.1)	1.3 (0.9-1.7)	0.030
Father smoking	1.4 (1.1-1.8)	1.2 (1.0-1.6)	0.394	1.5 (1.1-1.9)	0.9 (0.7-1.2)	0.012
Allergens						
Pets	0.9 (0.8-1.1)	0.9 (0.7-1.1)	0.925	-	-	-
Socioeconomic factors						
Low maternal education [§]	1.1 (0.9-1.3)	1.3 (1.1-1.6)	0.143	1.0 (0.8-1.3)	1.1 (0.8-1.3)	0.906
Deprivation(Townsend)	1.1 (0.9-1.4)	1.7 (1.3-2.1)	0.007	1.0 (0.8-1.3)	1.5 (1.1-1.9)	0.017
Perinatal and early life						
Preterm (GA<37 weeks)	0.9 (0.6-1.4)	1.3 (0.9-1.9)	0.178	-	-	-
Low birthweight(<2500g)	1.0 (0.7-1.5)	1.5 (1.1-2.2)	0.071	1.0 (0.6-1.5)	1.7 (1.1-2.5)	0.042
Young mother (<25 yrs) ^f	1.4 (1.1-1.8)	1.7 (1.3-2.2)	0.180	1.4 (1.1-1.8)	1.3 (1.0-1.7)	0.697
Breastfeeding	0.9 (0.7-1.1)	0.6 (0.5-0.8)	0.016	0.9 (0.7-1.1)	0.7 (0.6-0.9)	0.264
Reflux in infancy	1.2 (1.0-1.5)	1.3 (1.0-1.7)	0.621	1.2 (0.9-1.5)	1.3 (1.0-1.7)	0.661

RRR, relative risk ratio; CI, confidence interval; GA, gestational age.

[#]: Adjusted model includes all covariates with p-values <0.10 for either cough or wheeze in univariable models; baseline for multinomial regression: asymptomatic children.

[¶]: Defined as night cough without wheeze (ISAAC questions).

⁺: p-value from test for difference between associations of risk factors with cough and those with wheeze (Wald test).

[§]: End of education of mother at age <16 years.

^f: When the child was born.

TABLE S3 Risk factors for prevalent isolated night cough and wheeze in 6-year-old children (N=2,369)
 Association of different factors with cough and wheeze, compared to asymptomatic children, in unadjusted and adjusted models presented as relative risk ratio estimates with confidence intervals. Cough was defined as isolated night cough (without wheeze).

Risk factors at age 6	Unadjusted model			Adjusted model [#]		
	Night cough [¶]	Wheeze	Similarity p-value ⁺	Night cough [¶]	Wheeze	Similarity p-value ⁺
	RRR (95% CI)	RRR (95% CI)		RRR (95% CI)	RRR (95% CI)	
South Asian ethnicity	1.3 (1.0-1.7)	1.1 (0.8-1.6)	0.577	1.3 (0.9-1.9)	1.3 (0.9-1.9)	0.906
Male sex	0.8 (0.6-0.9)	1.3 (1.0-1.6)	0.001	0.8 (0.6-1.0)	1.3 (1.0-1.6)	0.002
<i>Family history of:</i>						
Asthma	1.0 (0.8-1.3)	2.0 (1.6-2.6)	<0.001	0.9 (0.7-1.2)	1.8 (1.3-2.4)	<0.001
Bronchitis	1.3 (1.0-1.7)	1.7 (1.3-2.2)	0.166	1.4 (1.1-1.9)	1.4 (1.0-1.9)	0.791
Hay fever	1.2 (0.9-1.4)	1.5 (1.2-1.9)	0.089	1.1 (0.9-1.4)	1.3 (1.0-1.7)	0.495
Eczema	1.2 (1.0-1.5)	1.2 (1.0-1.6)	0.873	1.1 (0.9-1.4)	1.0 (0.8-1.4)	0.782
<i>Exposure to infections</i>						
Crowding	1.2 (0.9-1.5)	1.4 (1.1-1.7)	0.354	1.0 (0.8-1.3)	1.1 (0.9-1.5)	0.365
Older siblings	0.9 (0.7-1.1)	0.8 (0.7-1.1)	0.733	-	-	-
<i>Air pollution</i>						
Cooking with gas	1.1 (0.9-1.4)	0.9 (0.7-1.2)	0.242	-	-	-
Mother smoking	1.4 (1.1-1.9)	1.4 (1.0-2.0)	0.978	1.2 (0.9-1.7)	1.4 (1.0-1.9)	0.540
Father smoking	1.2 (0.9-1.6)	0.9 (0.6-1.2)	0.095	-	-	-
<i>Allergens</i>						
Pets	0.8 (0.7-1.0)	0.9 (0.7-1.1)	0.868	-	-	-
<i>Socioeconomic factors</i>						
Low maternal education [§]	1.3 (1.0-1.6)	1.1 (0.9-1.4)	0.318	1.2 (1.0-1.5)	1.0 (0.8-1.4)	0.350
Deprivation(Townsend)	1.5 (1.2-1.9)	1.5 (1.2-1.9)	0.918	1.3 (1.0-1.7)	1.5 (1.1-2.0)	0.384
<i>Perinatal and early life</i>						
Preterm (GA<37 weeks)	1.0 (0.6-1.5)	2.1 (1.4-3.1)	0.006	0.9 (0.5-1.6)	1.8 (1.0-3.1)	0.052
Low birthweight(<2500g)	1.4 (0.9-2.1)	1.8 (1.2-2.7)	0.313	1.3 (0.7-2.2)	1.2 (0.7-2.1)	0.920
Young mother (<25 yrs) ^f	1.6 (1.2-2.1)	1.4 (1.0-1.9)	0.510	1.4 (1.1-1.9)	1.2 (0.9-1.7)	0.452
Breastfeeding	0.9 (0.7-1.1)	0.8 (0.6-1.1)	0.606	-	-	-
Reflux in infancy	1.3 (1.0-1.6)	1.2 (0.9-1.6)	0.778	1.2 (1.0-1.6)	1.2 (0.9-1.6)	0.843

RRR, relative risk ratio; CI, confidence interval; GA, gestational age.

[#]: Adjusted model includes all covariates with p-values <0.10 for either cough or wheeze in univariable models; baseline for multinomial regression: asymptomatic children.

[¶]: Defined as night cough without wheeze (ISAAC questions).

⁺: p-value from test for difference between associations of risk factors with cough and those with wheeze (Wald test).

[§]: End of education of mother at age <16 years.

^f: When the child was born.

TABLE S4 Risk factors for prevalent isolated night cough and wheeze in 9-year-old children (N=1,688)
Association of different factors with cough and wheeze, compared to asymptomatic children, in unadjusted and adjusted models presented as relative risk ratio estimates with confidence intervals. Cough was defined as isolated night cough (without wheeze).

Risk factors at age 9	Unadjusted model			Adjusted model [#]		
	Night cough [¶]	Wheeze	Similarity p-value ⁺	Night cough [¶]	Wheeze	Similarity p-value ⁺
	RRR (95% CI)	RRR (95% CI)		RRR (95% CI)	RRR (95% CI)	
South Asian ethnicity	1.7 (1.2-2.3)	1.0 (0.7-1.5)	0.029	1.6 (1.0-2.4)	1.5 (0.9-2.5)	0.873
Male sex	0.9 (0.7-1.1)	2.0 (1.4-2.6)	<0.001	0.8 (0.6-1.1)	2.1 (1.6-2.9)	<0.001
Family history of:						
Asthma	0.9 (0.7-1.2)	2.7 (2.0-3.6)	<0.001	0.9 (0.7-1.3)	2.5 (1.8-3.4)	<0.001
Bronchitis	1.3 (0.9-1.8)	1.5 (1.1-2.1)	0.444	1.5 (1.0-2.1)	1.2 (0.8-1.8)	0.446
Hay fever	1.1 (0.9-1.4)	1.7 (1.3-2.3)	0.019	1.2 (0.9-1.6)	1.4 (1.0-1.9)	0.428
Eczema	0.9 (0.7-1.1)	1.1 (0.8-1.5)	0.162	-	-	-
Exposure to infections						
Older siblings	1.0 (0.8-1.3)	0.9 (0.7-1.2)	0.671	-	-	-
Air pollution						
Cooking with gas	1.4 (1.0-1.9)	1.1 (0.8-1.5)	0.185	1.3 (0.9-1.8)	1.1 (0.8-1.6)	0.617
Mother smoking	1.2 (0.8-1.7)	1.1 (0.7-1.6)	0.725	-	-	-
Father smoking	1.3 (1.0-1.9)	0.9 (0.6-1.4)	0.124	1.3 (0.9-1.8)	0.9 (0.6-1.4)	0.185
Allergens						
Pets	0.7 (0.6-1.0)	1.0 (0.8-1.4)	0.065	0.8 (0.6-1.1)	1.0 (0.7-1.4)	0.334
Socioeconomic factors						
Low maternal education [§]	1.3 (1.0-1.7)	1.3 (1.0-1.7)	0.942	1.3 (1.0-1.7)	1.4 (1.0-1.9)	0.750
Deprivation(Townsend)	1.4 (1.1-1.9)	0.9 (0.6-1.3)	0.024	1.1 (0.7-1.5)	0.7 (0.5-1.1)	0.171
Perinatal and early life						
Preterm (GA<37 weeks)	1.0 (0.6-1.8)	1.8 (1.1-3.0)	0.117	1.2 (0.6-2.4)	1.2 (0.6-2.6)	0.919
Low birthweight(<2500g)	1.0 (0.6-1.7)	1.8 (1.1-3.0)	0.077	0.9 (0.4-1.8)	1.9 (0.9-3.7)	0.091
Young mother (<25 yrs) ^f	1.6 (1.1-2.2)	1.5 (1.0-2.2)	0.929	1.3 (0.9-2.0)	1.6 (1.0-2.4)	0.530
Breastfeeding	0.8 (0.6-1.0)	0.8 (0.6-1.1)	0.824	0.8 (0.6-1.1)	0.8 (0.6-1.1)	0.901
Reflux in infancy	1.1 (0.8-1.5)	0.8 (0.6-1.1)	0.067	-	-	-

RRR, relative risk ratio; CI, confidence interval; GA, gestational age.

[#]: Adjusted model includes all covariates with p-values <0.10 for either cough or wheeze in univariable models; baseline for multinomial regression: asymptomatic children.

[¶]: Defined as night cough without wheeze (ISAAC questions).

⁺: p-value from test for difference between associations of risk factors with cough and those with wheeze (Wald test).

[§]: End of education of mother at age <16 years.

^f: When the child was born.

FIGURE S1 Risk factors for prevalent isolated night cough and wheeze at age 1 year (N=4,101)

Association of different factors with cough and with wheeze, compared to asymptomatic children, in a fully adjusted model (adjusted for all covariates with p-values <0.10 for either cough or wheeze in univariable models), presented as relative risk ratio estimates with confidence intervals. Cough was defined as night cough without wheeze.

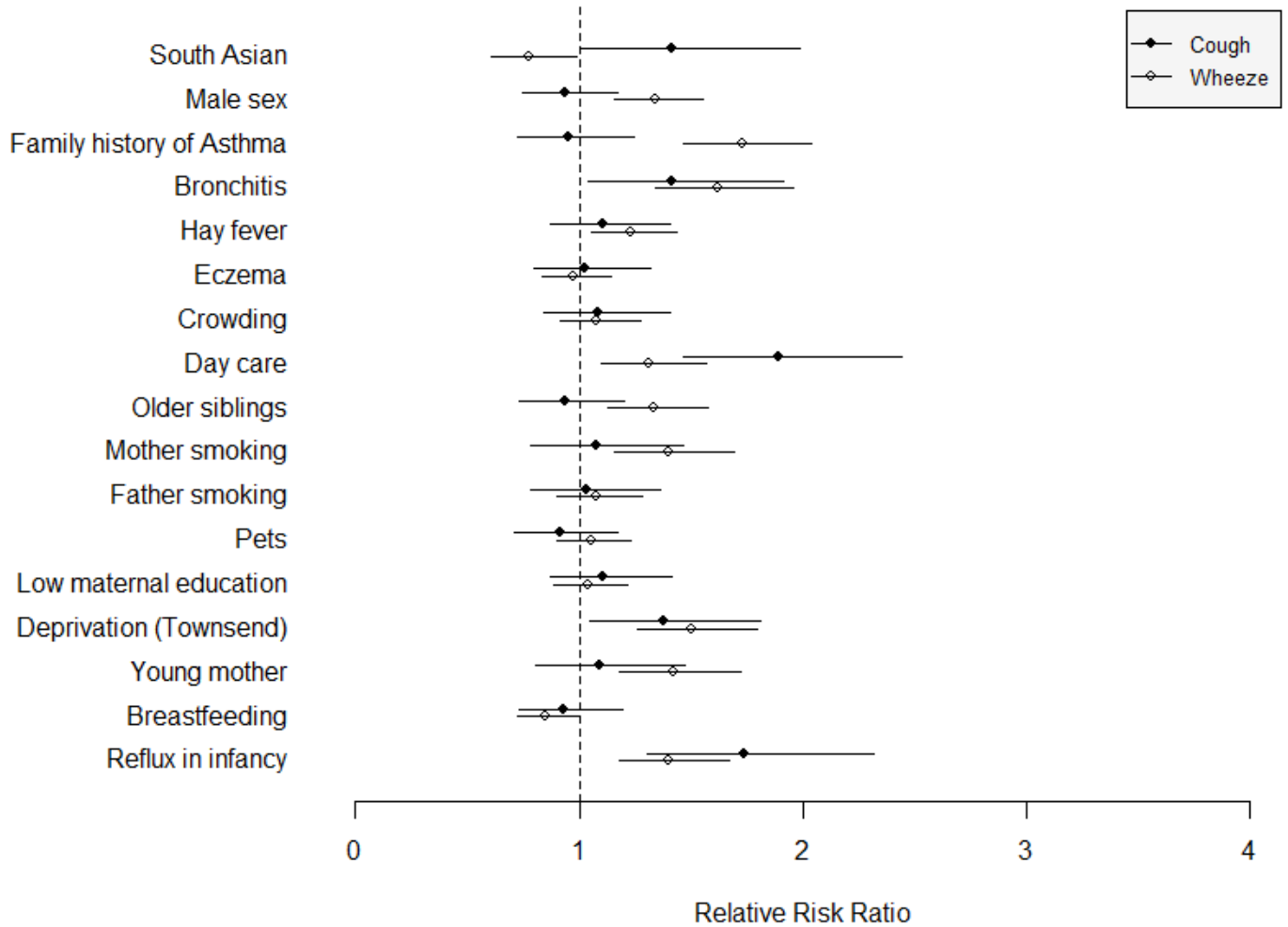


TABLE S5 Prognosis of isolated night cough and wheeze from age 1-4 years, 4-6 years, 6-9 years

Prognosis shown for all children who were aged 1 in 1998, and who replied to the questionnaires in the respective surveys.

Cough was defined as night cough without wheeze.

			Night cough [#] at follow up			Asymptomatic at follow up		Wheeze at follow up	
Prognosis from age 1 to 4 years (N=2,854)									
Age at baseline (years)	Age at follow-up (years)	Symptoms at baseline	N (100%)	n	(%)	n	(%)	n	(%)
1	4	Night cough ^a	305	99	(32)	155	(51)	51	(17)
		Asymptomatic	1,628	240	(15)	1,246	(76)	142	(9)
		Wheeze	921	181	(20)	457	(50)	283	(31)
Prognosis from age 4 to 6 years (N=2,062)									
4	6	Night cough	381	160	(42)	189	(50)	32	(8)
		Asymptomatic	1,366	168	(12)	1,113	(81)	85	(6)
		Wheeze	315	56	(18)	108	(34)	151	(48)
Prognosis from age 6 to 9 years (N=1,413)									
6	9	Night cough	249	97	(39)	128	(51)	24	(10)
		Asymptomatic	999	124	(13)	812	(81)	63	(6)
		Wheeze	165	21	(13)	46	(28)	98	(59)

Overall chi-square test p-values for each age interval <0.001.

Subgroup analysis comparing children with cough and asymptomatic children regarding probability to have future incident wheeze. Fisher's exact test showed for the age interval from 1 to 4 years the p-value of <0.001, from age 4 to 6 years the p-value of 0.133 and from age 6 to 9 years the p-value of 0.071.

[#]: Defined as night cough without wheeze (ISAAC questions).

TABLE S6 Predictors of future wheeze in the total population of children with isolated night cough and asymptomatic children at baseline for different age intervals (from age 1 to 4 years, from age 4 to 6 years, and from age 6 to 9). Multivariable analysis.

Risk factors at baseline	From age 1 to 4 years (N=1,933)		From age 4 to 6 years (N=1,747)		From age 6 to 9 years (N=1,248)	
	Wheeze at follow up		Wheeze at follow up		Wheeze at follow up	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Isolated night cough	2.2 (1.5-3.1)	0.001	1.2 (0.7-2.1)	0.471	1.4 (0.8-2.5)	0.228
Male sex	1.4 (1.0-2.0)	0.025	1.4 (0.9-2.3)	0.148	2.0 (1.2-3.3)	0.009
Family history of asthma	2.0 (1.4-2.8)	0.001	1.4 (0.9-2.3)	0.165	2.0 (1.2-3.3)	0.006
Day care at age 1	0.5 (0.4-0.8)	0.003	-	-	-	-
Cooking with gas	-	-	-	-	2.2 (1.1-4.1)	0.020
Mother smoking	1.5 (1.0-2.1)	0.051	-	-	-	-
Pets	-	-	0.6 (0.3-0.9)	0.020	-	-
Low maternal education [#]	-	-	-	-	1.6 (1.0-2.7)	0.046
Deprivation (Townsend)	1.5 (1.1-2.1)	0.012	-	-	0.5 (0.3-1.1)	0.080
Reflux in infancy	-	-	-	-	0.5 (0.3-0.9)	0.012
Rhinitis	-	-	-	-	2.2 (1.2-3.8)	0.007
Hay fever [¶]	-	-	-	-	1.8 (0.9-3.6)	0.093
Current eczema	-	-	2.4 (1.5-3.9)	0.001	-	-
Frequent colds [†]	-	-	2.7 (1.2-6.0)	0.012	-	-
Snoring	1.5 (1.2-2.1)	0.012	1.8 (1.1-3.0)	0.024	2.3 (1.3-3.9)	0.003

OR, odds ratio; CI, confidence interval. Independent variables in the multivariable analysis are selected via backward selection approach, leaving in the model isolated night cough, sex and parental asthma.

[#]: End of education of mother at age <16 years.

[¶]: Not inquired about in 1998 survey.

[†]: >6 episodes of colds in the past year.