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

A) All children who participated at the re	espective s	survey <sup>#</sup> (main a	nalysis)					
Age (years)	1		4		6		9	
	N=4,101	l	N=2,8	54	N=2,3	69	N=1,6	88
Symptoms	n	% (95%CI)	n	% (95%CI)	n	% (95%CI)	n	% (95%CI)
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	4 surveys	(N=1,318) (sens	sitivity a	nalysis)				
	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.

<sup>#</sup>: 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).

	Un	adjusted model		Adjusted model <sup>#</sup>			
Risk factors at age 4	Night cough <sup>¶</sup>	Wheeze		Night cough <sup>¶</sup>	Wheeze		
	RRR (95% CI)	RRR (95% CI)	Similarity p-value <sup>+</sup>	RRR (95% CI)	RRR (95% CI)	Similarity p-value <sup>+</sup>	
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) <sup>f</sup>	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.

<sup>#</sup>: 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).

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

<sup>§</sup>: 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).

	Un	adjusted model		Adjusted model <sup>#</sup>			
Risk factors at age 6	Night cough <sup>¶</sup>	Wheeze		Night cough <sup>¶</sup>	Wheeze		
	RRR (95% CI)	RRR (95% CI)	Similarity p-value <sup>+</sup>	RRR (95% CI)	RRR (95% CI)	Similarity p-value <sup>+</sup>	
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	
Family history of:							
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	
Exposure to infections							
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	-	-	-	
Air pollution							
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	-	-	-	
Allergens							
Pets	0.8 (0.7-1.0)	0.9 (0.7-1.1)	0.868	-	-	-	
Socioeconomic factors							
Low maternal education <sup>§</sup>	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	
Perinatal and early life							
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) <sup>f</sup>	1.6 (1.2-2.1)	1.4 (1.0-1.9)	0.510	<b>1.4</b> (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.

<sup>#</sup>: 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).

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

<sup>§</sup>: End of education of mother at age <16 years.

*<sup>f</sup>*: 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).

	Un	adjusted model		Adjusted model <sup>#</sup>			
Risk factors at age 9	Night cough <sup>¶</sup> Wheeze			Night cough <sup>¶</sup>	Wheeze		
	RRR (95% CI)	RRR (95% CI)	Similarity p-value+	RRR (95% CI)	RRR (95% CI)	Similarity p-value+	
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 <sup>§</sup>	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) <sup>f</sup>	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.

<sup>#</sup>: 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).

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

<sup>§</sup>: End of education of mother at age <16 years.

<sup>*f*</sup>: 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.



**Relative Risk Ratio** 

## 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.

				Nig at f	ht cough <sup>#</sup> collow up	Asymptomatic at follow up		Wheeze at follow up	
Prognosis from age	e 1 to 4 years (N=2,85	54)							
Age at baseline (years)	Age at follow-up (years)	Symptoms at baseline	N (100%)	n	(%)	n	(%)	n	(%)
1	4	Night cough <sup>a</sup>	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	e 4 to 6 years (N=2,06	62)							
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	e 6 to 9 years (N=1,41	3)							
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.

<sup>#</sup>: Defined as night cough without wheeze (ISAAC questions).

	From age 1 to	From age 1 to 4 years (N=1,933) Wheeze at follow up		to 6 years (N=1,747)	From age 6 to 9 years (N=1,248)		
	Wheeze			ze at follow up	Wheeze at follow up		
Risk factors at baseline	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 <sup>¶</sup>	-	-	-	-	1.8 (0.9-3.6)	0.093	
Current eczema	-	-	2.4 (1.5-3.9)	0.001	-	-	
Frequent colds <sup>+</sup>	-	-	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	

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.

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.

<sup>#</sup>: End of education of mother at age <16 years.

<sup>¶</sup>: Not inquired about in 1998 survey.

<sup>+</sup>: >6 episodes of colds in the past year.