



LETTER TO THE EDITOR



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High prevalence of wheeze and atopy in rural Malagasy children

To the Editor,

Asthma and allergies in children are not only a matter of concern in affluent countries, but also increasingly so in developing countries.¹⁻³ Madagascar is one of the least developed countries, not only of Africa but worldwide and lower respiratory tract infections are the second most frequent cause of death in Madagascar.⁴ Data from the VAVANY study were the first to suggest that in Madagascar's urban capital schoolchildren have a high prevalence of wheeze.^{5,6} In order to assess the prevalence of asthma and allergies in a comparable rural setting, the Malagasy Kids with Asthma and Allergies (MAKI) Study was conducted. We hypothesized that atopic diseases are less prevalent than in an urban setting, as seen not only in more developed countries⁷ but also in other sub-Saharan African countries.⁸

We conducted a cross-sectional study on 212 Malagasy children aged 8-15 years in the highlands north of the capital Antananarivo without any industry and with most of the children living in remote villages (for description of the study population see Tables S1 and S2, Supporting Information Methods). The main income source in this sparsely populated area is farming along with some limited livestock breeding. The regional mode of transportation is the oxcart, and the water supply for households is restricted to wells. At the time of our study, there was neither electricity nor mobile networks available in most of the villages. In general, asthma is unknown to people in Madagascar. Accordingly, only one child had ever had therapy with an oral salbutamol, and at the time of study, none of the children were undertaking any type of therapy. The examinations were performed in schools and healthcare centers by the same group of researchers. The questionnaire was based on items from the ISAAC questionnaire, and the core questions on wheeze were identical to the urban VAVANY study. Main outcome measures were *wheeze ever* and *current wheeze* (past 12 months). We performed skin prick tests (SPTs) with seven inhalant allergens, and atopy was defined as an average wheal diameter ≥ 3 mm to any allergen. Atopic and nonatopic wheeze were defined as current wheeze with or without atopy. Furthermore, spirometry and bronchodilator reversibility were tested.

In our study population, current wheeze was reported in 59 children (28.2%) and wheeze ever in 76 children (36.0%). This was significantly higher than in the urban VAVANY study, with a lifetime prevalence of wheeze of 25.2% ($P < .001$). A fairly high proportion of

children was sensitized, with almost a third (27.5%) being sensitized to at least one allergen, cockroach being the allergen the children were sensitized to most frequently (20.8%), followed by *B tropicalis* (8.1%) and *D pter.* (4.3%). A total of 134 children (64.1%) reported to ever have had rhinitis symptoms without a cold, and 34.0% had current rhinitis symptoms in combination with itching or watering eyes. In contrast, skin symptoms, that is an itchy rash, were fairly rare, with only 16 children (7.9%) reporting to ever have had an itchy rash and only 11 children (5.3%) with a current itchy rash.

Wheeze was significantly associated with inhalant sensitization (OR = 2.19, 95% CI 1.13-4.23, $P = .020$ for current wheeze), the strongest effect being observed for sensitization to *D pter.* (OR = 4.77, 95% CI 1.10-20.68, $P = .037$). In total, 39% of currently wheezing children were atopic. On a population basis, atopic wheeze was almost as prevalent (13.3%) as nonatopic wheeze (19.3%). In contrast, no association with atopy was observed for rhinitis or eczema (data not shown). Nevertheless, current rhinoconjunctivitis symptoms were significantly associated with current wheeze (OR = 2.04, 95% CI 1.08-3.84, $P = .028$) and a current itchy rash with wheezing ever (OR = 8.25, 95% CI 1.70-40.00, $P = .009$). With respect to spirometry, MEF_{25-75} was significantly reduced in current wheezers (93.4 ± 29.6 vs 103.3 ± 25.2 , $P = .016$), although no other lung function parameter showed similar decrements. Inhalant sensitization showed no association with any of the assessed lung function measures (data not shown).

In multivariate models with stepwise variable selection of all variables with a P -value < 0.1 in univariate analysis (Tables S3 and S4), only a few independent factors remained in the final models (Table 1). A major factor associated with wheeze both ever and current was reduced flow in small airways as assessed by the MEF_{25-75} . Ever having had a pneumonia increased the risk of wheeze, both ever and current and a higher BMI was associated with current wheezing. When trying to disentangle risk factors for atopic and nonatopic wheeze, a different pattern of risk factors was observed. The only relevant factors for atopic wheeze were BMI, with heavier children having a higher risk, and current eczema symptoms, even though not being associated with atopic sensitization themselves. Relevant factors for nonatopic wheeze were reduced MEF_{25-75} , having had a pneumonia and, in line with the hygiene hypothesis, having older siblings. Other factors potentially indicating a more hygienic, affluent

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TABLE 1 Study characteristics and wheeze: adjusted odds ratios from stepwise multivariate logistic regression

	Risk for wheeze ever N = 180			Risk for current wheeze N = 187			Risk for nonatopic wheeze N = 170			Risk for atopic wheeze N = 150		
	aOR	95% CI	P	aOR	95% CI	P	aOR	95% CI	P	aOR	95% CI	P
MEF ₂₅₋₇₅ (in % predicted)	0.98	0.97-1.00	.011	0.98	0.96-0.99	.002	0.97	0.96-0.99	.002	–	–	–
Pneumonia	5.19	1.72-15.70	.004	4.90	1.55-15.50	.007	5.08	1.55-16.69	.007	–	–	–
BMI (in kg/m ²)	–	–	–	1.32	1.05-1.67	.019	–	–	–	1.58	1.14-2.21	.007
≥1 older sibling	0.40	0.18-0.88	.024	–	–	–	0.38	0.16-0.94	.036	–	–	–
Skin prick test												
Cockroach	–	–	–	2.82	1.22-6.50	.015	–	–	–	–	–	–
<i>D pter.</i>	6.52	1.09-39.02	.040	–	–	–	–	–	–	–	–	–
Current symptoms												
Nasal	–	–	–	2.25	1.03-4.89	.041	–	–	–	–	–	–
Skin	7.01	1.38-35.50	.019	–	–	–	–	–	–	5.42	1.03-28.62	.047

Abbreviations: 95% CI, 95% confidence interval; aOR, adjusted odds ratio.

or modern household, such as owning a means of transportation or wearing shoes at study date were neither associated with the wheezing outcomes, nor with any other outcomes.

In conclusion, the prevalence of wheeze was surprisingly high for a developing country.¹⁻³ An overview over the large span of wheezing prevalences in children aged 13-14 years in sub-Saharan African countries is best depicted by data from ISAAC centers revealing numbers as low as 5.7% in Cameroun to 13.0% in Nigeria and as high as 19.3% in Urban Cote d'Ivoire and 20.4% in Cape Town, South Africa.^{1,2} Furthermore, objective assessment of atopic sensitization revealed a surprisingly high prevalence of cockroach sensitization, while house dust mite sensitization was associated with wheeze, an association so far mostly observed in the developed world.⁹ However, among atopic wheezers no association with FEV₁/FVC and bronchodilator response was seen, indicators for reversible airway obstruction which would be typical for asthma. This may argue against an atopic asthma phenotype as seen in developed countries and is in line with the observation from ISAAC that the link between atopic sensitization and asthma symptoms in children increases with economic development and would thus be low in our nonaffluent population.⁹ In contrast, nonatopic wheeze was strongly associated with a past history of pneumonia and showed decreased flow rates in the smaller airways suggesting that these wheezing symptoms may not be interpreted as variable airway obstruction, that is asthma, but rather as a sequelae of lower respiratory tract infections in children living in poverty and exposed to indoor air pollution. This is in line with results from a recent study in rural Bolivia, in that asthma symptoms may be more related to respiratory infections than to allergy.¹⁰ Hence, the prevention of airway infections by means of improving living conditions is crucial for the reduction of the prevalence of wheeze in the developing world. Surprisingly, wheeze was clearly more prevalent in rural as compared to urban regions within Madagascar, as observed in the VAVANY study.⁵ However, no factors associated with lifestyle or rural living showed an effect,

potentially due to little variation within this poor rural environment and a sample size that might not suffice to detect effects in such a homogeneous population. Unfortunately, we have no information on a family history of allergic diseases and thus cannot disentangle the issue of heritability. Further limitations are given by the fact that difficulties may arise when working in a rural region, especially in one with such a limited set of resources. Because of these practical constraints and their impact on this study, we cannot rule out possible selection bias, misclassification, or residual confounding. Nevertheless, these findings underline that wheezing illnesses are not only an issue in industrialized countries, but also in nonaffluent countries and regions with low socioeconomic conditions, though the determinants and the underlying pathomechanisms may differ significantly.

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CONFLICT OF INTEREST

P. T. Wolff, M. Götschke, A. Rakotozanany, A. L. Robinson, and L. K. Wolff have nothing to disclose; E. von Mutius reports grants from German Research Foundation, during the conduct of the study; personal fees from OM Pharma S. A., Böhringer Ingelheim International GmbH, Peptinnovent Ltd., PharmaVentures Ltd., and Nestlé Deutschland AG, outside the submitted work; in addition, Dr von Mutius has a patent Application number LU101064, Barn dust extract for the prevention and treatment of diseases pending, a patent Publication number EP2361632: Specific environmental bacteria for the protection from and/or the treatment of allergic, chronic

inflammatory and/or autoimmune disorders. With royalties paid to Protectimmun GmbH, a patent Publication number EP 1411977: Composition containing bacterial antigens used for the prophylaxis and the treatment of allergic diseases. Licensed to Protectimmun GmbH, a patent Publication number EP1637147: Stable dust extract for allergy protection licensed to Protectimmun GmbH, and a patent Publication number EP 1964570: Pharmaceutical compound to protect against allergies and inflammatory diseases licensed to Protectimmun GmbH. S. Illi has nothing to disclose.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

Supporting Information

High prevalence of wheeze and atopy in rural Malagasy children

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METHODS

Population

We conducted a cross-sectional study on 212 Malagasy children aged 8-15 years in the highlands of Analamanga, 85 km north of the capital Antananarivo, situated at 1,300 m above sea level with a temperate climate. The population is from the Merina tribe with Polynesian heritage. Study area was the district of Fihaonana without any industry and with most of the children living in remote villages. The main income source in this sparsely populated area is farming along with some limited livestock breeding. The regional mode of transportation is the oxcart, and the water supply for households is restricted to wells. At the time of our study, there was neither electricity nor mobile networks available in most of the villages. People generally live in two-story adobe-houses – most of them with thatched and some with ribbed roofs – with the living room and kitchen on the first floor, while the ground floor is used for storage of the harvest. Kitchens usually have a fireplace in one corner, the fumes outlet being a small window on the opposite side of the room.

Data collection

Before starting the study, the first author and the study nurse visited the village of Fihaonana. The purpose of the study was discussed with the mayor of the village, his deputy and some of the Fokotany, which are official delegates from the surrounding villages who have considerable influence on public opinion in the area. The assembly of each rural community then discussed participating in the study, ultimately 8 out of 18 villages took part in the study. After obtaining their consent, the study nurse revisited the community to explain the purpose of and the steps involved in the study to interested parents from the different villages and also to provide flyers setting out the details. Based on power calculations using data from our prior study on asthma in

children in the capitol of Madagascar (VAVANY) the authors had planned a sample size of N=200 children. At time of study, children were included on a first-come-first-served basis up to our planned sample size. We collected data in eight villages in May 2013. The examinations were performed in schools and health care centers by the same group of researchers. All children attended with their legal guardian and provided a signed consent. The study was approved by the ethical committees of the Malagasy Ministère de la Santé Publique and the German Landesärztekammer Baden-Württemberg.

Questionnaire

The questionnaire was based on items from the ISAAC (French version) questionnaire, the core questions on wheeze were thus identical to the previous VAVANY study in urban Madagascar. These core questions were supplemented by questions of regional importance related to socio-economic status, vaccinations and school attendance. Main outcome measures were *wheeze ever* and wheeze in the last 12 months (*current wheeze*), furthermore, atopic wheeze and non-atopic wheeze was defined as current wheeze with or without any inhalant sensitization, with children without wheeze as reference group. A French/Malagasy bilingual pediatrician translated the questions into the Malagasy language according to the ISAAC guidelines.¹ Some of the older children completed the questionnaires themselves, but most were completed by the parents and/or legal guardians with the assistance of our Malagasy staff, as the illiteracy rate is still high in Madagascar. To evaluate the occurrence of eczema, several pictures of atopic dermatitis in African and Caucasian children were presented to each child and parent (or guardian).

Skin Prick Test

We performed skin prick tests (SPTs) with 7 inhalant allergens: *Dermatophagoides pteronyssinus* (*D.pter*), *Blomia tropicalis* (*B.tropicalis*), cockroach, *Alternaria alternata*, rat, dog, cat and grass pollen (*Phleum pratense*) (ALK-Abelló, Hørsholm, Denmark and Madrid, Spain). SPT was performed by three trained individuals on the skin of the inner side of the forearm with a 1-mm-metal-lancet (ALK Lancet) according to AAAAI/ACAAI² and EAACI³ with a positive (10 mg/mL histamine) and a negative control (saline). Wheal size was measured 15 minutes after application. Sensitization to a specific allergen was defined as an average wheal diameter of 3mm or greater, and atopy was defined as sensitization to any inhalant allergen.

Lung function test

Prior to spirometry, height and weight were measured and the BMI was calculated: standing height was measured without shoes, with the child standing on the scale (SecaTM 217, Hamburg, Germany) with an accuracy of 0.1 cm. Weight was taken with light clothes and without shoes (SecaTM 899, Hamburg, Germany) to the nearest 0.1 kg. To define underweight, we took the BMI-for-age-cut-off points as defined by the WHO.⁴

Lung function testing was completed using a spirometer (KokoTM Legend, nSpire Health Inc., Longmont, CO) meeting all requirements of the ATS/ERS Task Force⁵ with a viral and bacterial filter for each patient (*Pulmosafe*©, Lemon Medical GmbH, Hammelburg, Germany). BTPS correction and calibration (3-L syringe) was done twice daily due to regional temperature differences. The mean temperature was 23° Celsius (Minimum 13.8°, Maximum 29.7°), the mean atmospheric pressure was 878 hPa, the mean humidity being at 51.5% (Minimum 34%, Maximum 76%). All lung function tests were supervised by the same person. After an instruction provided by a

Malagasy team member, three maneuvers were obtained from each child.⁶ The spirometry was taken in a standing position, the nose occluded by a nose clip. Results were defined as evaluable according to the ATS/ERS Task Force criteria.⁵ Spirometric measurements included forced vital capacity (FVC), forced expiratory flow at 1 second (FEV₁) and midexpiratory flow at 25% to 75% of FVC (MEF₂₅₋₇₅). For statistical analyses, we calculated the FEV₁ to FVC ratio, as well as MEF₂₅₋₇₅ in % predicted, based on height-adjusted gender-specific reference equations resulting from non-wheezing controls within our population. All spirometry testing was done by the same principle investigator (PTW).

After the baseline lung function was established, we tested bronchodilator reversibility about 15 minutes after administration of 2 puffs of a short-acting β -agonist (Salbutamol, 2 puffs á 100 μ g) with a holding chamber (*Vortex*©, PARI GmbH, Starnberg, Germany). Bronchodilator reversibility testing was not performed in children (34%), whose patient's history (i.e. no wheeze ever), curve's shape or FVC-value suggested no bronchial obstruction. This classification was always done by the same principle investigator (PTW). Bronchodilator response (BDR) was defined as the difference between post- and pre-bronchodilator FEV₁, in percent of pre-bronchodilator FEV₁. A positive bronchodilator response was defined as having a 12% or greater increase in FEV₁ and was set to zero in children with no suspected bronchial obstruction.

Statistics

Continuous variables are given as mean $\pm$ standard deviation (SD), differences of lung function parameters between groups are assessed by the t-test. The association of the outcome variables with various characteristics of the study population was assessed by means of unadjusted logistic regression models, results are expressed as odds ratios (OR) and 95% confidence intervals (95%-CI). All variables with a p-value of less than 0.1 were then included in a multivariate logistic regression model with stepwise variable selection procedure. Statistical analyses were performed with SAS 9.4 (The SAS Institute, Cary, NC, USA); a p-value of 0.05 or less was considered significant.

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Table S1. Study characteristics.

			Total N	Mean	SD
Anthropometrics	Age (in years)		212	10.8	1.8
	Height (in cm)		212	131.2	11.6
	Weight (in kg)		212	26.9	6.5
	BMI (in kg/m ²)		212	15.4	1.6
			Total N	n	%
	BMI (WHO)	severe thin	212	8	3.8
		thin	212	23	10.8
		normal	212	177	83.5
		overweight	212	4	1.9
Gender	Female		212	110	51.9
	Male		212	102	48.1
Major diseases ever	Malaria		203	60	29.6
	Tuberculosis		200	1	0.5
	High fever >5 days		209	63	30.1
	Pneumonia		201	20	9.9
Vaccinations	BCG		211	208	98.6
	BCG scar		208	127	61.1
	Tetanus		210	133	63.3
	Measles		210	194	92.4
Family	Older siblings	0	209	45	21.5
		1	209	53	25.4
		2-3	209	62	29.7
		4-9	209	49	23.4
	Breastfeeding ≥3 months		207	202	97.6
Living environment	Cat in the house past 12 months		211	49	23.2
	Dog in the house past 12 months		210	75	35.7
	Maternal smoking		210	31	14.8
	Paternal smoking		210	65	30.9
	Parental smoking		210	73	34.8
	Enrolled in school		212	203	95.7
	Wearing shoes at study date		212	66	31.1
	Daily TV watching ≥1 hour		208	22	10.6
	Physically strenuous work ≥1x/week		210	95	45.2
Household characteristics	Household size	3-5	211	83	39.3
		6-7	211	80	37.9
		8-12	211	48	22.7
	# rooms	1-2	209	85	40.7
		3	209	55	26.3
		≥4	209	69	33.0
	Cooking with wood/coal		209	209	100.0
	Bicycle available		210	83	39.5
	Motor scooter available		211	10	4.7
	Car available		211	1	0.5

Table S2. Study outcomes.

		Total N	Mean	SD
Spirometry	FEV ₁ / FVC	207	89.6	9.8
	MEF ₂₅₋₇₅ (in % predicted)	206	100.3	26.8
	BDR (in %)	139	3.0	11.1
		Total N	n	%
Asthmatic outcomes	Positive BDR	207	15	7.2
	Wheeze ever	211	76	36.0
	Current wheeze	209	59	28.2
	Non-atopic wheeze	186	36	19.3
	Atopic wheeze	173	23	13.3
	Current wheeze after exercise	210	43	20.5
	Current nocturnal cough	211	96	45.5
	Asthma attack ever	209	19	9.1
Other outcomes	Rhinitis symptoms w/o cold ever	209	134	64.1
	Current rhinitis symptoms w/o cold	208	135	64.9
	Current rhinoconjunctivitis symptoms	206	70	34.0
	Itchy rash ever	202	16	7.9
	Current itchy rash	207	11	5.3
Inhalant sensitization	Cockroach	211	44	20.8
	<i>Blomia tropicalis</i>	211	17	8.1
	<i>Dermatophagoides pteronyssinus</i>	211	9	4.3
	<i>Alternaria alternata</i>	211	4	1.9
	Cat	211	3	1.4
	Dog	211	2	0.9
	Rat	211	1	0.5
	Grass	211	1	0.5
	Any inhalant	211	58	27.5

Table S3. Study characteristics and wheeze ever / current: odds ratios from univariate logistic regression.

		Risk for wheeze ever			Risk for current wheeze		
		OR	95%-CI	p	OR	95%-CI	p
Spirometry	FEV ₁ / FVC	0.96	0.92-1.00	0.071	0.96	0.91-1.00	0.068
	MEF ₂₅₋₇₅ (in % predicted)	0.99	0.98-1.00	0.019	0.99	0.97-1.00	0.031
	BDR (in %)	1.00	0.96-1.03	0.774	0.99	0.95-1.02	0.437
	Positive BDR	0.88	0.29-2.69	0.826	0.94	0.29-3.08	0.915
Other outcomes	Rhinitis symptoms w/o cold ever	1.85	0.99-3.46	0.056	2.16	1.07-4.35	0.032
	Current rhinitis symptoms w/o cold	1.76	0.93-3.30	0.080	2.62	1.25-5.48	0.011
	Current rhinoconjunctivitis symptoms	1.57	0.86-2.87	0.141	2.04	1.08-3.84	0.028
	Itchy rash ever	5.82	1.78-19.05	0.004	1.92	0.65-5.67	0.240
	Current itchy rash	8.25	1.70-40.00	0.009	2.82	0.78-10.15	0.113
	Eczema ever	2.37	0.62-9.12	0.209	1.34	0.32-5.55	0.687
Inhalant sensitization	Cockroach	1.82	0.92-3.60	0.085	2.67	1.32-5.41	0.006
	<i>Blomia tropicalis</i>	1.71	0.63-4.64	0.293	1.99	0.72-5.51	0.187
	<i>Derm. pteronyssinus</i>	7.00	1.41-34.64	0.017	4.77	1.10-20.68	0.037
	Any inhalant	1.84	0.98-3.43	0.056	2.19	1.13-4.23	0.020
Anthropometrics	Age (in years)	1.10	0.94-1.29	0.249	1.21	1.02-1.45	0.028
	Height (in cm)	1.01	0.98-1.03	0.582	1.01	0.99-1.04	0.318
	Weight (in kg)	1.02	0.98-1.07	0.297	1.04	0.99-1.09	0.115
	BMI (in kg/m ²)	1.13	0.94-1.35	0.192	1.18	0.98-1.43	0.080
	BMI (WHO): severe/thin vs. normal	0.87	0.39-1.95	0.738	0.65	0.28-1.50	0.314
Gender	Male	1.16	0.65-2.05	0.614	0.93	0.50-1.72	0.809
Major diseases ever	Malaria	1.79	0.95-3.36	0.072	1.98	1.01-3.90	0.048
	High fever >5 days	1.96	1.07-3.62	0.030	1.74	0.91-3.33	0.094
	Pneumonia	5.46	1.99-14.97	<0.001	4.26	1.65-11.02	0.003
Vaccinations	BCG scar	0.74	0.41-1.33	0.314	0.83	0.44-1.55	0.558
	Tetanus	2.47	1.30-4.70	0.006	2.19	1.09-4.43	0.028
	Measles	1.71	0.53-5.51	0.369	1.70	0.47-6.21	0.421
Family	≥1 older sibling	0.46	0.23-0.90	0.023	0.63	0.31-1.30	0.212
	Breastfeeding ≥3mths	0.34	0.06-2.09	0.245	0.23	0.04-1.44	0.118
Living environment	Cat in the house 12mths	0.79	0.40-1.58	0.507	0.98	0.48-2.04	0.967
	Dog in the house 12mths	1.36	0.76-2.46	0.301	1.63	0.87-3.05	0.128
	Maternal smoking	1.42	0.65-3.10	0.378	2.25	1.02-4.98	0.045
	Paternal smoking	0.96	0.52-1.79	0.907	1.36	0.71-2.62	0.351
	Parental smoking	1.08	0.59-1.97	0.798	1.63	0.86-3.07	0.131
	Enrolled in school	0.90	0.21-3.90	0.893	0.61	0.14-2.66	0.513
	Wearing shoes at study date	1.08	0.58-2.00	0.805	1.01	0.52-1.97	0.983
	Daily TV watching ≥1 hour	0.62	0.23-1.66	0.343	0.52	0.17-1.61	0.258
	Physically strenuous work ≥1x/week	1.14	0.64-2.01	0.662	1.82	0.98-3.39	0.059
Household characteristics	Household size: 3-5	1.00	—	—	1.00	—	—
	6-7	1.16	0.60-2.24	0.655	1.41	0.69-2.89	0.342
	8-12	1.44	0.68-3.03	0.342	1.67	0.74-3.74	0.216
	≥3 rooms	0.81	0.46-1.45	0.482	1.10	0.59-2.06	0.763
	Bicycle available	1.09	0.61-1.94	0.779	1.20	0.64-2.24	0.572
	Any means of transport available	1.02	0.57-1.82	0.945	1.13	0.61-2.11	0.698

Statistically significant results are given in **bold**

OR = odds ratio; 95%-CI = 95% confidence interval

Table S4. Study characteristics and non-atopic / atopic wheeze: odds ratios from univariate logistic regression.

		Risk for non-atopic wheeze			Risk for atopic wheeze		
		OR	95%-CI	p	OR	95%-CI	p
Spirometry	FEV ₁ / FVC	0.97	0.92-1.02	0.250	0.95	0.90-1.01	0.090
	MEF ₂₅₋₇₅ (in % predicted)	0.98	0.96-0.99	0.007	1.00	0.98-1.01	0.676
	BDR (in %)	0.99	0.95-1.03	0.687	0.97	0.91-1.04	0.381
	Positive BDR	1.18	0.31-4.48	0.809	0.58	0.07-4.73	0.611
Other outcomes	Rhinitis symptoms w/o cold ever	1.81	0.79-4.15	0.161	2.93	0.94-9.10	0.063
	Current rhinitis symptoms w/o cold	2.08	0.88-4.92	0.095	4.06	1.15-14.33	0.030
	Current rhinoconjunctivitis symptoms	1.85	0.86-3.99	0.114	2.35	0.95-5.83	0.066
	Itchy rash ever	1.55	0.40-6.09	0.529	2.50	0.62-10.10	0.198
	Current itchy rash	1.82	0.34-9.81	0.486	4.45	0.98-20.15	0.052
	Eczema ever	1.48	0.29-7.67	0.641	1.13	0.13-9.83	0.914
Anthropometrics	Age (in years)	1.14	0.92-1.40	0.234	1.37	1.06-1.77	0.018
	Height (in cm)	1.00	0.97-1.03	0.922	1.03	0.99-1.08	0.095
	Weight (in kg)	1.01	0.95-1.07	0.747	1.09	1.02-1.17	0.014
	BMI (in kg/m ²)	1.01	0.80-1.29	0.907	1.60	1.18-2.16	0.002
	BMI (WHO): severe/thin vs. normal	0.41	0.17-1.02	0.054	2.79	0.35-22.05	0.331
Gender	Male	1.07	0.51-2.25	0.860	0.74	0.30-1.84	0.517
Major diseases ever	Malaria	1.56	0.69-3.53	0.289	2.97	1.10-8.05	0.032
	High fever >5 days	1.83	0.84-3.95	0.126	1.61	0.62-4.16	0.329
	Pneumonia	4.23	1.44-12.41	0.009	4.32	1.18-15.84	0.027
Vaccinations	BCG scar	0.79	0.37-1.68	0.536	0.90	0.36-2.24	0.819
	Tetanus	2.15	0.91-5.08	0.080	2.25	0.79-6.44	0.129
	Measles	3.18	0.40-25.13	0.274	0.96	0.20-4.58	0.962
Family	≥1 older sibling	0.48	0.21-1.11	0.086	1.04	0.33-3.32	0.946
	Breastfeeding ≥3mths	0.43	0.04-4.86	0.493	0.14	0.02-1.03	0.054
Living environment	Cat in the house 12mths	1.17	0.50-2.75	0.714	0.72	0.23-2.28	0.581
	Dog in the house 12mths	1.60	0.75-3.41	0.228	1.68	0.68-4.17	0.260
	Maternal smoking	1.96	0.74-5.16	0.174	2.73	0.95-7.88	0.063
	Paternal smoking	1.04	0.46-2.36	0.930	1.99	0.80-4.94	0.139
	Parental smoking	1.20	0.55-2.64	0.647	2.53	1.02-6.25	0.045
	Enrolled in school	0.56	0.10-2.99	0.494	0.73	0.08-6.55	0.778
	Wearing shoes at study date	1.26	0.57-2.77	0.563	0.68	0.24-1.96	0.474
	Daily TV watching ≥1 hour	0.20	0.03-1.59	0.129	1.07	0.29-3.98	0.914
	Physically strenuous work ≥1x/week	1.73	0.82-3.66	0.153	1.97	0.79-4.90	0.144
Household characteristics	Household size: 3-5	1.00	—	—	1.00	—	—
	6-7	1.21	0.49-2.95	0.679	1.74	0.63-4.80	0.285
	8-12	2.00	0.78-5.12	0.149	1.14	0.31-4.20	0.841
	≥3 rooms	1.49	0.68-3.28	0.322	0.71	0.29-1.75	0.459
	Bicycle available	1.42	0.67-3.01	0.361	0.91	0.36-2.31	0.847
	Any means of transport available	1.34	0.63-2.84	0.443	0.86	0.34-2.18	0.754

Statistically significant results are given in **bold**

OR = odds ratio; 95%-CI = 95% confidence interval