OPEN ACCESS

ORIGINAL ARTICLE

Hygiene, atopy and wheeze–eczema–rhinitis symptoms in schoolchildren from urban and rural Ecuador

Philip J Cooper,[1,2,3] Maritza Vaca,[1] Alejandro Rodriguez,[1] Martha E Chico,[1] Darci N Santos,[4] Laura C Rodrigues,[5] Mauricio L Barreto[4]

▶ Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/thoraxjnl-2013-203818).

[1]Laboratorio de Investigaciones FEPIS, Quinindé, Esmeraldas Province, Ecuador
[2]Clinical Sciences, Liverpool School of Tropical Medicine, Liverpool, UK
[3]Escuela de Biología, Pontificia Universidad Católica del Ecuador, Quito, Ecuador
[4]Instituto de Saude Coletiva, Universidade Federal da Bahia, Salvador, Brazil
[5]Department of Epidemiology, London School of Hygiene and Tropical Medicine, London, UK

Correspondence to
Dr P J Cooper, Casilla 17-22-20418, Quito, Ecuador; P.J.Cooper@liv.ac.uk

Received 30 April 2013
Revised 20 August 2013
Accepted 16 September 2013
Published Online First 8 October 2013

ABSTRACT

Background Rural residence is protective against atopy and wheeze–rhinitis–eczema symptoms in developed countries, an effect attributed to farming and poor hygiene exposures. There are few data from developing countries addressing this question. We compared atopy and wheeze–rhinitis–eczema symptoms between urban and rural Ecuador, and explored the effects of farming and poor hygiene exposures.

Methods We performed cross sectional studies of schoolchildren living in rural and urban Ecuador. Data on symptoms and farming/hygiene exposures were collected by parental questionnaire, atopy by allergen skin prick test reactivity and geohelminth infections by stool examinations.

Results Among 2526 urban and 4295 rural schoolchildren, prevalence was: atopy (10.0% vs 12.5%, p=0.06), wheeze (9.4% vs 10.1%, p=0.05), rhinitis (8.1% vs 6.4%, p=0.02) and eczema (5.9% vs 4.7%, p=0.06). A small proportion of symptoms were attributable to atopy (range 3.9–10.7%) with greater attributable fractions for respiratory symptoms observed in urban schoolchildren. Respiratory symptoms were associated with poor hygiene/farming exposures: wheeze with lack of access to potable water; and rhinitis with household pets, no bathroom facilities and contact with large farm animals. Birth order was inversely associated with respiratory symptoms. Area of residence and atopy had few effects on these associations.

Conclusions Urban schoolchildren living in Ecuador have a similar prevalence of atopy, eczema and wheeze but a higher prevalence of rhinitis compared with rural children. Some farming and poor hygiene exposures were associated with an increase in the prevalence of wheeze or rhinitis while birth order was inversely associated with these symptoms.

Key messages

What is the key question?

- Do poor hygiene and farming exposures explain the prevalence of atopy and wheeze–rhinitis–eczema symptoms in urban and rural children in a developing country?

What is the bottom line?

- The prevalence of rhinitis symptoms but not atopy and wheeze–eczema symptoms was greater in urban compared with rural schoolchildren in tropical Ecuador. Some poor hygiene exposures were associated with an increase in the prevalence of respiratory symptoms while others were associated with less atopy and respiratory symptoms, effects that were largely independent of area of residence.

Why read on?

- There are few data from developing countries investigating the effect of poor hygiene and farming exposures on the prevalence of atopy and symptoms of wheeze–rhinitis–eczema. Our data show that environmental exposures indicative of poor hygiene or farming have variable effects on atopy and the risk of respiratory symptoms.

INTRODUCTION

Asthma, rhinitis and eczema are the commonest chronic diseases of childhood in developed countries. A high prevalence of these diseases has been reported in urban centres in Latin America, and the prevalence has been suggested to be lower in rural areas.[1–3]

Several epidemiological studies in developed countries have shown a greater prevalence of asthma in urban compared with rural, essentially farming, populations, and a few studies have shown a similar trend in developing countries.[4] The protective effects of rural residence have been attributed to farming and hygiene related exposures in developed countries,[4 5] while in developing countries protective effects have in addition been attributed to the presence of chronic childhood infections, such as geohelminth parasites.[6] Such protection may be strongest when exposures occur during pregnancy[7] or early childhood[5 8] and be mediated through effects on the developing immune response.[5]

There are limited data from developing countries exploring the effects of hygiene and farming exposures on the prevalence of atopy and symptoms of wheeze–rhinitis–eczema in urban and rural populations.[9] In the present study, we hypothesised that the prevalence of atopy and wheeze–rhinitis–eczema symptoms would be lower in rural compared with urban schoolchildren in Ecuador, and that greater exposure to environmental factors associated with farming and poor hygiene would explain such an effect. We therefore examined the prevalence of atopy and wheeze–rhinitis–eczema symptoms in

Open Access
Scan to access more free content

To cite: Cooper PJ, Vaca M, Rodriguez A, *et al*. *Thorax* 2014;**69**:232–239.

Thorax: first published as 10.1136/thoraxjnl-2013-203818 on 8 October 2013. Downloaded from http://thorax.bmj.com/ on April 20, 2024 by guest. Protected by copyright.

comparable populations of schoolchildren living in urban and rural areas of the same province in Ecuador, and examined the effects on prevalence of farming and hygiene related factors.

METHODS

Study area and population

The study was performed in the coastal Province of Esmeraldas, Ecuador, one of the poorest regions of Ecuador with limited public services and infrastructure. The study area was tropical rain forest. The rural area comprised a convenience sample of 59 traditional Afro-Ecuadorian communities along the tributaries of the Santiago river basin in the districts of San Lorenzo and Eloy Alfaro. Economic activities in these communities are logging, subsistence agriculture and African palm oil extraction. The urban study area was the provincial capital of Esmeraldas, the city of Esmeraldas, a city of ~190 000 inhabitants[10] whose main economic activities are tourism, services and the oil industry. In the urban area we chose a convenience sample of 11 urban schools in neighbourhoods that contained significant proportions of Afro-Ecuadorian migrants from the same two rural districts who had settled in these neighbourhoods.

Study design

We did a cross sectional survey of children attending the schools that served the rural communities and the urban neighbourhoods. All children attending the schools at the time of the survey were eligible for inclusion. Based on annually updated school lists, we were able to evaluate 91.3% of children in rural schools and 90.8% of those attending urban schools. Data collection for the rural study was done between March 2005 and August 2008, and for the urban study between September 2008 and January 2010.

Data collection

Questionnaires

The questionnaire was modified from the International Study of Asthma and Allergies in Childhood (ISAAC) phase II questionnaire translated into Spanish, and has been extensively field tested. The questionnaire collected information on symptoms of wheeze, rhinitis and eczema, and risk factors, as described elsewhere,[11] and is provided as an online archive. The questionnaire was administered to a parent in the presence of the child.

Allergen skin prick test reactivity

Allergic sensitisation was measured by skin prick testing with *Dermatophagoides pteronyssinus/farina*e mix, American cockroach (*Periplaneta americana*), *Alternaria tenuis*, cat, dog, '9 southern grass mix' and 'New stock fungi mix', and positive histamine and negative saline controls (Greer Laboratories, Lenoir, North Carolina, USA), as described previously.[11] A positive reaction was defined as a mean wheal diameter of at least 3 mm greater than the saline control at 15 min. The same observer performed all skin prick testing (MV).

Stool examinations

Single stool samples were collected and analysed for geohelminth eggs and larvae using the modified Kato Katz and formol–ether concentration methods.[12]

Definition of outcomes

Outcomes were defined as: atopy—the presence of at least one positive allergen skin test; recent wheeze—reported wheezing during the previous 12 months; recent eczema—having a reported itchy rash with a flexural distribution in the previous 12 months; and recent rhinitis—nasal stuffiness or sneezing without a cold accompanied by itchy eyes in the previous 12 months.

Statistical analysis

Sample sizes of 2500 for the urban and 4000 for the rural studies were estimated to yield approximately 200 asthma cases for nested case control studies in each area. Associations between poor hygiene/farming exposures and study outcomes were explored using univariate and multivariate random effects logistic regression adjusted for clustering by community or neighbourhood. Exposures in multivariate models were selected using a backwards stepwise procedure in which exposures were included if $p<0.2$ or OR ≥10%. Interactions by area of residence or atopy were assessed using the Wald test. Because of multiple comparisons, we used a p value ≤0.01 as evidence for effect modification or of a variable being statistically significant in multivariate models. Population attributable fractions (PAF) were calculated by: $P_{ew}\times(OR-1)/OR$, where P_{ew} is the prevalence of allergen skin test reactivity among children with the specific symptom of interest. Analyses were done using STATA (V.10).

Written informed consent was obtained from a parent, and signed minor assent from the child. Appropriate antiparasitic treatment was offered where necessary.

RESULTS

Characteristics of urban and rural schoolchildren

We studied a total of 6821 schoolchildren in urban (2526) and rural (4295) areas. Recruitment of the study subjects is shown in figure 1 and the distributions of risk factors between urban and rural schoolchildren in table 1. Rural compared with urban children were slightly older ($p<0.001$), more likely to be Afro-Ecuadorian ($p<0.001$), have less educated mothers ($p<0.001$) and a lower household income ($p<0.001$), be underweight ($p<0.001$) and higher in the birth order ($p<0.001$), not have access to a bathroom for defecation ($p<0.001$) or access to potable drinking water ($p<0.001$), to have attended daycare ($p=0.008$), to have a father engaged in agriculture ($p<0.001$) and have contact with large farm animals ($p<0.001$), to consume unpasteurised milk ($p<0.001$) and have a higher prevalence of *Ascaris lumbricoides* ($p<0.001$) and *Trichuris trichiura* ($p<0.001$).

Prevalence of atopy and symptoms of wheeze–rhinitis–eczema

The prevalence of atopy and recent symptoms of wheeze–rhinitis–eczema symptoms in the urban and rural samples is shown in table 2. The prevalence of wheeze was slightly greater in rural (10.1%) compared with urban (9.4%) schoolchildren ($p=0.05$). There were no differences in the prevalence of other wheeze related symptoms and markers of wheeze severity between urban and rural schoolchildren (data not shown). The prevalence of rhinitis symptoms (with itchy eyes) was significantly higher in urban schoolchildren ($p=0.02$). There was some evidence for a higher prevalence of eczema symptoms (itchy flexural rash) in the urban sample ($p=0.06$). The prevalence of allergen skin prick test reactivity (SPT) tended to be greater in rural children (urban 10.0% vs rural 12.5%, $p=0.06$), a difference largely explained by a higher prevalence of SPT to American cockroach ($p<0.001$) and dog ($p<0.001$) in rural children.

Thorax: first published as 10.1136/thoraxjnl-2013-203818 on 8 October 2013. Downloaded from http://thorax.bmj.com/ on April 20, 2024 by guest. Protected by copyright.

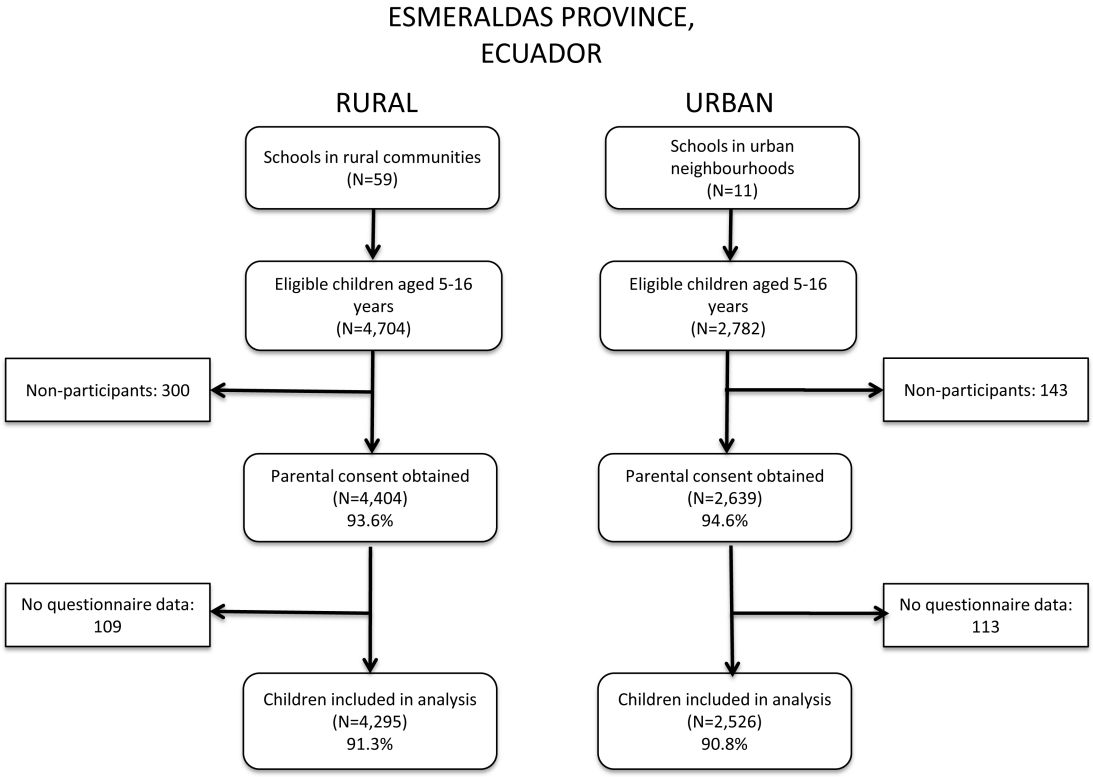

Figure 1 Flow diagram showing recruitment of schoolchildren in urban and rural areas.

Associations between atopy and symptoms of wheeze–rhinitis–eczema

The associations between recent symptoms and SPT in urban and rural schoolchildren are shown in table 3. Wheeze ($p<0.001$) and rhinitis ($p=0.004$) were significantly associated with SPT in urban children while among rural children a significant association was seen for wheeze only ($p=0.04$). The associations between atopy and wheeze or rhinitis were significantly stronger in urban than rural children (interaction $p=0.01$). Recent eczema (itchy flexural rash) was weakly associated with SPT (urban, $p=0.06$; rural, $p=0.05$). A small fraction of symptoms were attributable to SPT (table 3): population attributable fractions for wheeze in urban and rural children were 10.7% and 3.9%, respectively, and for rhinitis and eczema were <10% in both areas.

Associations between hygiene/farming exposures and atopy and wheeze–rhinitis–eczema symptoms

We explored the effects of poor hygiene and farming exposures on study outcomes (table 4; frequencies are provided in the online supplementary table S1). Multivariate analyses controlled simultaneously for the effects of these exposures: SPT was inversely associated with *A lumbricoides* ($p=0.002$) and *T trichiura* ($p<0.001$) infections; wheeze was positively associated with lack of potable drinking water ($p=0.001$) and inversely associated with being higher in the birth order ($p=0.005$); rhinitis was positively associated with household pets ($p=0.004$), lack of household bathroom facilities ($p=0.003$) and contact with farm animals ($p=0.001$) but inversely with birth order ($p<0.001$); eczema was not associated with any of the exposures.

Effect modification by area or residence and atopy on associations between poor hygiene/farming exposures and wheeze–rhinitis–eczema symptoms

We explored the effects of area of residence or atopy on the associations between study exposures and wheeze–rhinitis–eczema symptoms. Complete results are provided in online supplementary tables S2 and S3. Area of residence modified the association between birth order and wheeze, with an inverse association seen only in rural schoolchildren (urban, adjusted OR 1.13 (95% CI 0.79 to 1.81, $p=0.497$) vs rural, adjusted OR 0.63 (95% CI 0.50 to 0.80, $p<0.001$), interaction $p=0.007$). For atopy, there was evidence of a significantly greater prevalence of wheeze among non-atopic children without access to potable drinking water (SPT–, adjusted OR 1.42, 95% CI 1.13 to 1.79, $p=0.002$; SPT+, adjusted OR 0.74, 95% CI 0.47 to 1.14, $p=0.172$; interaction $p=0.01$). Non-atopic children living in traditionally built houses had a greater prevalence of rhinitis compared with atopics (SPT–, adjusted OR 1.37, 95% CI 1.09 to 1.72, $p=0.008$; SPT+, adjusted OR 0.66, 95% CI 0.36 to 1.21, $p=0.179$; interaction $p=0.005$) while atopic children without access to potable drinking water had a reduced risk of rhinitis compared with non-atopics (SPT+, adjusted OR 0.48, 95% CI 0.26 to 0.88, $p=0.019$; SPT–, adjusted OR 1.05, 95% CI 0.79 to 1.40, $p=0.741$; interaction $p=0.003$). No effect modification by atopy was observed for eczema.

DISCUSSION

In the present study of schoolchildren living in urban and rural areas of a tropical region in Latin America, we did not observe a significantly greater prevalence of atopy, wheeze and eczema symptoms in urban compared with rural samples although there was a greater prevalence of rhinitis symptoms in urban

Thorax: first published as 10.1136/thoraxjnl-2013-203818 on 8 October 2013. Downloaded from http://thorax.bmj.com/ on April 20, 2024 by guest. Protected by copyright.

Table 1 Characteristics of schoolchildren in urban and rural areas

Risk factor	Urban (n=2526) n	Urban (n=2526) %	Rural (n=4295) n	Rural (n=4295) %	p Value for rural vs urban
Demographics					
Age (years)					
5–8	856	33.9	1197	27.9	<0.001
9–11	1252	49.6	1511	35.2	
12–16	418	16.5	1587	36.9	
Sex					
Female	1196	47.4	2089	48.6	0.303
Male	1330	52.6	2206	51.4	
Ethnicity*					
Afro-Ecuadorian	2116	83.9	3957	92.5	<0.001
Other	405	16.1	323	7.5	
Maternal educational level					
Illiterate	546	22.0	2434	56.8	<0.001
Completed primary	1257	50.0	1498	35.0	
Completed secondary	720	28.0	353	8.2	
Monthly income (US$)					
≤150	968	39.2	3370	79.9	<0.001
>150	1499	60.8	845	20.1	
Nutritional status					
Underweight	341	13.5	703	16.4	<0.001
Normal	1718	68.0	2976	69.3	
Overweight	467	18.5	616	14.3	
General hygiene factors					
Pets inside the house					
No	1004	39.7	1650	38.5	0.293
Yes	1522	60.3	2640	61.5	
Crowding (persons/sleeping room)					
<Median	1298	51.5	2141	49.9	0.202
>Median	1222	48.5	2149	50.1	
Birth order					
≥5th	1367	54.2	1726	40.2	<0.001
3rd–4th	727	28.8	1119	26.1	
1st–2nd	426	17.0	1450	33.7	
Bathroom (%)					
Field	178	7.1	1553	36.1	<0.001
Latrine	595	23.5	2617	61.0	
WC	1752	69.4	123	2.9	
Potable drinking water					
No	199	7.9	4028	93.8	<0.001
Yes	2320	92.1	266	6.2	
Daycare attendance					
No	1431	57.4	2291	54.1	0.008
Yes	1061	42.6	1944	45.9	
Household construction					
Wood/bamboo	218	8.7	2443	57.2	<0.001
Mixed cement/wood	1139	45.2	1151	26.9	
Cement	1163	46.1	678	15.9	
Farming exposures					
Father with agricultural occupation					
No	2306	93.8	2213	52.4	<0.001
Yes	152	6.2	2007	47.5	
Contact with large farm animals*					
No	2306	91.4	2979	69.5	<0.001
Yes	218	8.6	1310	30.5	
Unpasteurised milk†					
No	1594	63.2	2455	57.3	<0.001
Yes	927	36.8	1831	42.7	
Infections					
Geohelminth infections					
Any geohelminth	1036	42.9	2849	69.0	<0.001
Ascaris lumbricoides	479	19.9	1752	42.4	<0.001
Trichuris trichiura	853	35.4	2234	54.1	<0.001
Hookworm	111	4.6	228	5.5	0.106

Median crowding was 3.
Numbers of missing values (rural/urban) are given in parentheses: ethnicity (15/5); maternal educational level (10/3); monthly income (80/59); pets inside the house (5/0); crowding (5/6); birth order (0/6); bathroom (2/1); potable drinking water (1/7); daycare attendance (60/34); household construction (23/6); father with agricultural occupation (75/68); contact with large farm animals (6/2); unpasteurised milk (9/5); any geohelminth (163/113); *Ascaris lumbricoides* (163/113); *Trichuris trichiura* (163/113); Hookworm (163/113).
*Pigs, cows, horses, mules, donkeys.
†Consumption of unpasteurised milk at least once weekly.

schoolchildren. The strength of the association between atopy and respiratory symptoms was greater in urban children. Some poor hygiene/farming exposures were associated with an increased risk of respiratory symptoms, while being higher in the birth order was inversely associated. There was limited evidence for modification of these effects by urban versus rural residence or atopy. Our data emphasise the fact that rural children do not necessarily have a reduced prevalence of atopy and wheeze–rhinitis–eczema symptoms compared with urban children, and that some exposures indicative of poorer hygiene may increase the risk of respiratory symptoms.

A previous study comparing population samples of individuals living in rural subsistence communities with those in a non-industrial urban environment showed a higher prevalence of atopy to house dust mite in the rural but more wheeze symptoms in the urban population.[13] Since then, other studies have reported an elevated prevalence of asthma and atopy in urban compared with rural populations in both developing and developed countries.[4 14] An urban–rural effect on risk of eczema is less consistent although a systematic review suggested that the prevalence of eczema may be increased in some urban populations.[15]

So why did we not observe such differences in the present study? We have shown previously that there is significant heterogeneity in the level of urbanisation between rural communities in the rural area where we conducted the study and that a higher level of urbanisation, particularly the adoption of a more urban lifestyle, was associated with the prevalence of wheeze at the community level.[16] Thus there is considerable heterogeneity in asthma risk between rural communities, and considering all as a single entity will mask these differences. Urban residence in the present study, although associated with changes in the living environment and presumably other factors such as exposure to air pollution, was still associated with significant rural exposures, such as farming. Such exposures likely reflect the lifestyle of more recent rural migrants who maintain rural lifestyles and contacts with their origins. Our urban study population can, therefore, be considered at a relatively early stage in the transition to an urban way of life, and such changes as do occur did not translate into significant changes in the prevalence of atopy, wheeze and eczema. Perhaps the first changes to occur in allergy during this early stage of urban transition are an increase in the

Thorax: first published as 10.1136/thoraxjnl-2013-203818 on 8 October 2013. Downloaded from http://thorax.bmj.com/ on April 20, 2024 by guest. Protected by copyright.

Table 2 Frequencies of symptoms and atopy in 6821 schoolchildren living in urban and rural areas of Esmeraldas Province

	Urban (n=2526)		Rural (n=4295)			
Variable	**n**	**%**	**n**	**%**	**OR (95% CI)**	**p Value**
Wheeze						
Wheeze ever	801	32.7	1362	32.7	0.97 (0.87 to 1.09)	0.64
Recent wheeze	231	9.4	421	10.1	0.84 (0.71 to 1.00)	0.05
Rhinitis						
Rhinitis ever	489	19.5	553	13.1	**1.57 (1.37 to 1.80)**	<0.001
Recent rhinitis	203	8.1	270	6.4	**1.25 (1.03 to 1.52)**	0.02
Eczema						
Eczema ever	323	12.9	358	8.4	**1.57 (1.33 to 1.84)**	<0.001
Recent eczema	146	5.9	199	4.7	1.24 (1.00 to 1.56)	0.06
Skin prick test reactivity						
Any allergen	246	10.0	515	12.5	0.85 (0.72 to 1.01)	0.06
House dust mite	185	7.6	281	6.8	1.19 (0.97 to 1.44)	0.09
Mixed grass	27	1.1	76	1.8	0.68 (0.43 to 1.07)	0.10
American cockroach	55	2.2	185	4.5	**0.54 (0.40 to 0.74)**	<0.001
Mixed fungi	10	0.4	18	0.4	1.31 (0.58 to 2.94)	0.52
Alternaria tenuis	3	0.1	8	0.2	0.67 (0.17 to 2.60)	0.456
Cat	8	0.3	17	0.4	0.84 (0.36 to 1.98)	0.69
Dog	6	0.2	68	1.7	**0.15 (0.07 to 0.35)**	<0.001

ORs and 95% CIs show urban and rural comparisons adjusted for age and sex.
Numbers in bold represent p<0.05.
Recent represents symptoms within the previous 12 months.
Eczema was defined by an itchy rash with a flexural distribution and rhinitis by nasal stuffiness/sneezing with itchy eyes.

prevalence of rhinitis and a strengthening of the association between atopy and respiratory symptoms, as observed here.

The rural area where we conducted this study represents traditional rural communities that have just started the transition to a more modern way of living. Many were accessible only by river, were not connected to the national electricity grid and used traditional materials for housing. But no community was truly isolated from urban influences—many rural residents had travelled to urban centres and the economies of all communities were money based. Most agriculture in these rural communities was subsistence. The urban study population was chosen to be representative ethnically and socially of the rural population, and urban study neighbourhoods were located at the periphery of the city of Esmeraldas where some but limited basic services were present. Such marginal populations living at the periphery of small to medium sized cities is expected to fuel much of the growth of the world population in the 21st century.

The hygiene hypothesis developed from the observation of an inverse association between sibling number and rhinitis that was explained by unhygienic contacts with older siblings.[17] Since then, this hypothesis has been extended to include the effects of a wide variety of infectious and other microbial exposures (eg, farming and pets in affluent countries and parasites in non-affluent countries) on a wide range of inflammatory diseases, extending from allergic to autoimmune diseases.[18] A plausible underlying mechanism to explain such wide ranging effects is the induction of immune regulation through the production of regulatory cytokines, such as interleukin 10 that serves to modulate Th1 and Th2 mediated inflammation.[18] Several environmental exposures associated with poor hygiene, including geohelminths, have been associated with increased interleukin 10,[19 20] providing a biologically plausible link between chronic microbial exposures and reduction in tissue inflammation. Consistent with such a paradigm, we observed a reduced prevalence of SPT among children with geohelminths. Being higher in the birth order was inversely associated with respiratory symptoms, in agreement with previous studies,[17 21] but other exposures representative of farming, poor hygiene or increased risk

Table 3 Associations between recent symptoms and allergen skin prick test reactivity and population fractions of symptoms attributable to skin prick test reactivity (PAF%) in urban and rural schoolchildren

	SPT						
	Urban			Rural			
Recent symptoms	**OR (95% CI)**	**p Value**	**PAF%**	**OR (95% CI)**	**p Value**	**PAF%**	**Interaction p value**
Wheeze	**2.35 (1.63 to 3.40)**	**<0.001**	10.7	**1.36 (1.01 to 1.83)**	**0.04**	3.9	0.01
Rhinitis	**1.82 (1.22 to 2.73)**	**0.004**	7.3	0.94 (0.63 to 1.40)	0.75	–	0.01
Eczema	1.60 (0.99 to 2.60)	0.06	5.7	1.47 (1.00 to 2.16)	0.05	5.3	0.74

Shown also are p values for the interaction effect of the area of residence.
Numbers in bold represent p<0.05.
ORs are adjusted for age, sex and maternal educational level (eczema only).
PAF%, population attributable fraction; SPT, skin prick test reactivity.

Thorax: first published as 10.1136/thoraxjnl-2013-203818 on 8 October 2013. Downloaded from http://thorax.bmj.com/ on April 20, 2024 by guest. Protected by copyright.

Table 4 Univariate and multivariate associations between outcomes and hygiene exposures in 6821 schoolchildren

	SPT OR (95% CI) p Value		Wheeze OR (95% CI) p Value		Rhinitis OR (95% CI) p Value		Eczema OR (95% CI) p Value	
Hygiene exposure	**Univariate**	**Multivariate**	**Univariate**	**Multivariate**	**Univariate**	**Multivariate**	**Univariate**	**Multivariate**
Pets inside home Yes vs no	0.91 (0.78 to 1.06) 0.215		1.09 (0.93 to 1.29) 0.296		1.34 (1.09 to 1.62) 0.005	**1.34 (1.09 to 1.63)** **0.004**	1.28 (1.03 to **1**.60) 0.031	1.19 (0.94 to 1.51) 0.151
Crowding ≥3 vs <3	0.79 (0.67 to 0.92) 0.004		0.97 (0.82 to 1.16) 0.733		0.86 (0.70 to 1.05) 0.133	0.81 (0.66 to 1.0) 0.053	0.88 (0.71 to 1.11) 0.276	
Birth order ≥5th vs ≤4th	1.58 (0.98 to 1.37) 0.084		0.75 (0.62 to 0.91) 0.003	**0.75 (0.61 to 0.91)** **0.005**	0.62 (0.49 to 0.78) <0.001	**0.62 (0.49 to 0.79)** **<0.001**	0.79 (0.62 to 1.02) 0.069	0.78 (0.60 to 1.02) 0.070
Bathroom Field vs others	0.91 (0.76 to 1.09) 0.299		1.19 (0.99 to 1.43) 0.054		1.32 (1.08 to 1.62) 0.008	**1.44 (1.13 to 1.83)** **0.003**	0.80 (0.62 to 1.04) 0.097	
Potable drinking water No vs yes	1.05 (0.81 to 1.34) 0.700		1.21 (1.02 to 1.43) 0.028	**1.44 (1.16 to 1.78)** **0.001**	0.92 (0.72 to 1.20) 0.562	0.79 (0.59 to 1.06) 0.123	0.96 (0.78 to 1.20) 0.771	
Attended daycare Yes vs no	0.96 (0.82 to 1.12) 0.642		0.99 (0.84 to 1.16) 0.889		1.11 (0.92 to 1.33) 0.296		1.28 (1.4 to 1.59) 0.023	1.28 (1.02 to 1.60) 0.037
House construction Wood/bamboo vs others	1.14 (0.98 to 1.33) 0.087		0.95 (0.81 to 1.12) 0.508		1.12 (0.93 to 1.35) 0.242	1.28 (1.03 to 1.61) 0.027	1.02 (0.83 to 1.26) 0.854	
Father engaged in agriculture Yes vs no	1.55 (1.32 to 1.81) <0.001	1.24 (1.01 to 1.51) 0.036	0.89 (0.74 to 1.06) 0.176	0.86 (0.70 to 1.05) 0.144	0.82 (0.66 to 1.01) 0.062	0.89 (0.69 to 1.15) 0.386	1.24 (0.99 to 1.56) 0.055	
Contact with farm animals* Yes vs no	1.40 (1.18 to 1.66) <0.001	1.15 (0.95 to 1.41) 0.146	1.03 (0.85 to 1.25) 0.781		1.28 (1.04 to 1.59) 0.021	**1.50 (1.19 to 1.91)** **0.001**	1.38 (1.09 to 1.75) 0.008	1.41 (1.07 to 1.84) 0.014
Unpasteurised milk† Yes vs no	1.13 (0.97 to 1.32) 0.109		1.05 (0.89 to 1.24) 0.557		1.02 (0.85 to 1.24) 0.810		1.34 (1.08 to 1.65) 0.008	1.13 (0.89 to 1.43) 0.321
Any geohelminth Yes vs no	0.66 (0.56 to 0.77) <0.001		1.12 (0.95 to 1.34) 0.165		0.94 (0.78 to 1.14) 0.550		0.97 (0.78 to 1.21) 0.810	1.31 (0.93 to 1.85) 0.125
Ascaris lumbricoides Yes vs no	0.71 (0.59 to 0.84) <0.001	**0.73 (0.60 to 0.89)** **0.002**	1.01 (0.84 to 1.20) 0.924		0.83 (0.68 to 1.02) 0.079		1.03 (0.82 to 1.29) 0.810	
Trichuris trichiura Yes vs no	0.63 (0.53 to 0.73) <0.001	**0.71 (0.59 to 0.85)** **<0.001**	1.16 (0.98 to 1.36) 0.084		1.07 (0.88 to 1.29) 0.505		0.78 (0.63 to 0.97) 0.025	0.72 (0.51 to 1.02) 0.061
Hookworm Yes vs no	1.38 (1.01 to 1.88) 0.047	1.37 (0.95 to 1.97) 0.088	1.10 (0.77 to 1.58) 0.591		0.74 (0.46 to 1.20) 0.221		1.37 (0.90 to 2.12) 0.143	

Variables in multivariate analyses with p≤0.01 were considered statistically significant and are shown in bold type.
Median crowding was 3.
*Pigs, cows, horses, mules, donkeys.
†Consumption of unpasteurised milk at least once weekly.
SPT, skin prick test reactivity.

Thorax: first published as 10.1136/thoraxjnl-2013-203818 on 8 October 2013. Downloaded from http://thorax.bmj.com/ on April 20, 2024 by guest. Protected by copyright.

of infections (ie, lack of potable drinking water) were associated with an increased risk of these symptoms.

Previous observations from urban Brazil showed strong associations between non-atopic wheeze and indicators of dirt, increased urban poverty and respiratory infections.[22] Although such observations are not consistent with the hygiene hypothesis, increased exposure to chronic parasitic, bacterial and viral infections were strongly inversely associated with atopy.[23] In our study, only a minority of wheeze–rhinitis–eczema symptoms were attributable to atopy (<11%), in agreement with previous studies from Latin America.[2 24–26] A study of European children indicated that the effects of hygiene exposures on non-atopic symptoms were distinct from those on atopic symptoms.[27] In the present study, there was some evidence to suggest that poor hygiene exposures might increase the prevalence of respiratory symptoms in non-atopic compared with atopic schoolchildren.

Being born and raised on a livestock farm in Europe provides the strongest protection against atopy and allergic symptoms.[5] Such protection may require an intimate relationship between herd animals and their owners, particularly during the winter months when the animals may be kept in barns close to the farmer's living space and where exposures to the animals and their microbes is intense, perhaps leading to immune tolerance and reduced inflammation. Clearly not all farm exposures are protective, and significant heterogeneity of effects has been reported across Europe,[28] while an increased risk has been reported in Australasian[29 30] and Iowan children.[31] The relationship between farming families and their animals is different in the tropical lowlands of Ecuador and a less intimate association could explain why childhood contact with large farm animals, through exposures to farming related irritants or proinflammatory substances, might be associated with an increase in rhinitis and perhaps also eczema symptoms.

The strengths of the present study were: evaluation of a large population of urban and rural schoolchildren within the same geographic region in Ecuador with sufficient power to detect relevant effects of exposures on atopy and allergic symptoms; very high rates of participation in both study areas (>90%) ensuring the relevance of our findings to the largely Afro-Ecuadorian population we studied; and use of simple and widely used measurements of parentally reported symptoms. The use of symptoms to estimate the prevalence of wheeze–rhinitis–eczema is probably subject to less bias than a doctor diagnosis in a population with limited access to healthcare and where such access differs between urban and rural populations. The term wheeze–rhinitis–eczema was used as a substitute for 'allergic' because few such symptoms in our study population appear to be explained by atopy. Weaknesses were a lack of data on the intensity and age of initial exposures to these factors, and the questionnaire data may have been subject to recall bias and misclassification. We used SPT rather than allergen specific IgE to measure atopy and cannot comment on the effects of the study exposures on this latter marker. However, SPT, a measure of allergic effector responses rather than allergic sensitisation per se, may be more appropriate for the exploration of such effects in a population in which the two atopic markers are dissociated.[23 26]

In summary, the present study, performed in rural and urban schoolchildren in Ecuador, showed a greater risk of rhinitis symptoms in urban compared with rural children but no such effects on the prevalence of wheeze and eczema. There was evidence that some poor hygiene/farming exposures were associated with an increased risk of respiratory symptoms, while being higher in the birth order was protective. Our observations provide further insights into the determinants of the prevalence of atopy and wheeze–rhinitis–eczema symptoms in a population in Latin America undergoing development and at an early stage in the evolution of the so-called allergy epidemic that has emerged over recent years in more advanced Latin American countries and in other developing regions.

Acknowledgements The Ecuadorian Elimination Programme for Onchocerciasis (Dr Eduardo Gomez, Lcda Raquel Lovato, Lcda Sra Margarita Padilla, Lcda Anabel Ponce, Ing Sandra Barreno, Sra Magdalena Cortez), CECOMET (Dr Gregorio Montalvo and Lcda Monica Marquez) and SNEM (Dr César Diaz) are thanked for support in visiting rural communities and urban neighbourhoods in the city of Esmeraldas. Silvia Erazo and Gisela Oviedo are thanked for their technical support. The health promoters, teachers, parents and children are thanked for their enthusiastic cooperation.

Contributors Study idea and design: PJC, LCR and MLB. Data collection: MEC and MV. Data analysis: AR, PJC, MV and DNS. Drafting the manuscript: PJC and MV. Critical review of the manuscript: AR, MEC, DNS, LCR and MLB. Final approval: all authors.

Funding The study forms part of the SCAALA (Social Changes, Asthma and Allergies in Latin America) programme of research. The research was supported by grants from the Wellcome Trust (072405/Z/03/Z and 088862/Z/09/Z). The funders had no role in the study design, data collection and analysis, decision to publish or preparation of the manuscript.

Competing interests None.

Ethics approval The ethics committee of the Hospital Pedro Vicente Maldonado, Ecuador, approved the study protocol.

Provenance and peer review Not commissioned; externally peer reviewed.

Open Access This is an Open Access article distributed in accordance with the terms of the Creative Commons Attribution (CC BY 3.0) license, which permits others to distribute, remix, adapt and build upon this work, for commercial use, provided the original work is properly cited. See: http://creativecommons.org/licenses/by/3.0/

REFERENCES

1 The International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee. Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC. *Lancet* 1998;351:1225–32.
2 Cooper PJ, Chico ME, Griffin GE, *et al*. Allergy symptoms, atopy, and geohelminth infections in a rural area of Ecuador. *Am J Resp Crit Care Med* 2003;168:313–17.
3 Weinmayr G, Weiland SK, Bjorksten B, *et al*. Atopic sensitization and the international variation of asthma symptom prevalence in children. *Am J Respir Crit Care Med* 2007;166:565–74.
4 Wong GW, Chow CM. Childhood asthma epidemiology: insights from comparative studies of rural and urban populations. *Pediatr Pulmonol* 2008;43:107–16.
5 von Mutius E. 99th Dahlem Conference on Infection, Inflammation and Chronic Inflammatory Disorders: farm lifestyles and the hygiene hypothesis. *Clin Exp Immunol* 2010;160:130–5.
6 Cooper PJ. Interactions of parasites with allergy. *Curr Opin Allergy Clin Immunol* 2009;9:29–37.
7 Douwes J, Cheng S, Travier N, *et al*. Farm exposure in utero may protect against asthma, hay fever and eczema. *Eur Respir J* 2008;32:603–11.
8 Rodrigues LC, Newland P, Cunha SS, *et al*. Early infections with intestinal helminths reduce the risk of atopy later in childhood. *Clin Exp Allergy* 2008;38:1769–77.
9 Viinanen A, Munhbayarlah S, Zevgee T, *et al*. Prevalence of asthma, allergic rhinoconjunctivitis and allergic sensitization in Mongolia. *Allergy* 2005;60:1370–7.
10 Instituto Nacional De Estadística Y Censos—INEC. Informacion Censal Cantonal. INEC, 2010. http://www.inec.gob.ec/estadisticas/?option=com_content&view=article&id=91&Itemid=56&TB_iframe=true&height=512&width=1242 (accessed 15 Mar 2013).
11 Cooper PJ, Chico ME, Vaca MG, *et al*. Risk factors for asthma and allergy associated with urban migration: background and methodology of a cross-sectional study in Afro-Ecuadorian school children in Northeastern Ecuador (Esmeraldas-SCAALA Study). *BMC Pulm Med* 2006;6:24.
12 WHO. *Diagnostic techniques for intestinal parasitic infections (IPI) applicable to primary health care (PHC) services*. WHO/PDP, 1985:85.
13 Yemaneberhan H, Bekele Z, Venn A, *et al*. Prevalence of wheeze and asthma and relation to atopy in urban and rural Ethiopia. *Lancet* 1997;350:85–90.
14 Nicolaou N, Siddique N, Custovic A. Allergic disease in urban and rural populations: increasing prevalence with increasing urbanization. *Allergy* 2005;60:1357–60.
15 Schram ME, Tedja AM, Spijker R, *et al*. Is there a rural/urban gradient in the prevalence of eczema? A systematic review. *Br J Dermatol* 2010;162:964–73.

Thorax: first published as 10.1136/thoraxjnl-2013-203818 on 8 October 2013. Downloaded from http://thorax.bmj.com/ on April 20, 2024 by guest. Protected by copyright.

16 Rodriguez A, Vaca M, Teles C, *et al*. Urbanisation is associated with prevalence of childhood asthma in diverse, small rural communities in Ecuador. *Thorax* 2011;66:1043–50.
17 Strachan DP. Hay fever, hygiene, and household size. *BMJ* 1989;299:1259–60.
18 Rook GA. Hygiene and other early childhood influences on the subsequent function of the immune system. *Dig Dis* 2011;29:144–53.
19 Figueiredo CA, Alcantara-Neves NM, Amorim LD, *et al*. Evidence for a modulatory effect of IL-10 on both Th1 and Th2 cytokine production: the role of the environment. *Clin Immunol* 2011;139:57–64.
20 Figueiredo CA, Barreto ML, Rodrigues LC, *et al*. Chronic intestinal helminth infections are associated with immune hyporesponsiveness and induction of a regulatory network. *Infect Immun* 2010;78:3160–7.
21 Karmaus W, Botezan C. Does a higher number of siblings protect against the development of allergy and asthma? A review. *J Epidemiol Community Health* 2002;56:209–17.
22 Barreto ML, Cunha SS, Fiaccone R, *et al*. Poverty, dirt, infections and non-atopic wheezing in children from a Brazilian urban center. *Respir Res* 2010;11:67.
23 Alcantara-Neves NM, Veiga RV, Dattoli VCC, *et al*. The effect of single and multiple infections on atopy and wheezing in children. *J Allergy Clin Immunol* 2012;129:359–67.
24 Penny ME, Murad S, Madrid SS, *et al*. Respiratory symptoms, asthma, exercise test spirometry, and atopy in schoolchildren from a Lima shanty town. *Thorax* 2001;56:607–12.
25 Cunha S, Barreto ML, Fiaccone RL, *et al*. Population attributable fraction of asthma due to atopy among Brazilian children. *Rev Panam Salud Publica* 2010;28:405–10.
26 Moncayo AM, Vaca M, Oviedo G, *et al*. Effects of geohelminth infection and age on the associations between allergen-specific IgE, skin test reactivity and wheeze: a case-control study. *Clin Exp Allergy* 2013;43:60–72.
27 Braun-Fahrländer C, Riedler J, Herz U, *et al*. Environmental exposure to endotoxin and its relation to asthma in school-age children. *N Engl J Med* 2002;347:869–77.
28 Ege MJ, Frei R, Bieli C, *et al*. Not all farming environments protect against the development of asthma and wheeze in children. *J Allergy Clin Immunol* 2007;119:1140–7.
29 Downs SH, Marks GB, Mitakakis TZ, *et al*. Having lived on a farm and protection against allergic diseases in Australia. *Clin Exp Allergy* 2001;31:570–5.
30 Wickens K, Lane JM, Fitzharris P, *et al*. Farm residence and exposures and the risk of allergic diseases in New Zealand children. *Allergy* 2002;57:1171–9.
31 Merchant JA, Naleway AL, Svendsen ER, *et al*. Asthma and farm exposures in a cohort of rural Iowa children. *Environ Health Perspect* 2005;113:350–6.

Thorax: first published as 10.1136/thoraxjnl-2013-203818 on 8 October 2013. Downloaded from http://thorax.bmj.com/ on April 20, 2024 by guest. Protected by copyright.

1. NUMERO……

CUESTIONARIO

FACTORES DE RIESGO PARA ALERGIAS Y ASMA

2. Fecha...../...../200

3.Apellidos/Nombres delJefedela casa.....

4. Número de casa por Censo de Oncocercosis.....

5. Apellidos y Nombres del entrevistador.....

A. Datos personales

6. Apellidos y Nombres (del niño)……..

7. **Edad**.....años **8. Fecha de nacimiento**...../...../.....

9. Raza: Afro-ecuatoriana ❒ **1** Mestiza ❒ **2** Indígena ❒ **3**

10.**Localidad donde vive el niño**…….. **11**. **Provincia**.....

12. **Escuela**..... No estudia ❒

13. Paralelo: .....de EB No sabe ❒

14. Sexo: F ❒ **2** M ❒ **1**

B. Datos Socio-Económicos

19. La relación entre el niñ(a) y el JEFE de la casa es: Ausente ❒ **0**

Padre ❒ **1** Padrastro ❒ **2** Abuelo ❒ **3** Tío ❒ **4** Otro **5**.....

20. Ocupación del JEFE de la casa (especificar):

Jornalero	❒ **1**	Comerciante	❒ **6**	Chofer	❒ **11**
Agricultor	❒ **2**	Profesor	❒ **7**	Desempleado	❒ **12**
Ganadero	❒ **3**	Carpintero	❒ **8**	No sabe	❒ **99**
Motorista	❒ **4**	Albañil	❒ **9**		
Maderero	❒ **5**	Mecánico	❒ **10**	Otros (especifique) **13**	_____

Firma……. **Fecha…../……./200**

1. NUMERO……

21. Instrucción del JEFE de la casa:

primaria completa	❒ **1**	primaria incompleta	❒ **5**
secundaria completa	❒ **2**	secundaria incompleta	❒ **6**
superior completa	❒ **3**	superior incompleta	❒ **7**
analfabeto	❒ **4**	No sabe	❒ **99**

22. Lugar de nacimiento del jefe de la casa:

.....(localidad/ ciudad/ provincia)

23. El jefe de la casa se crió en zona: urbana ❒ **1** rural ❒ **2** No sabe ❒ **99**

24. ¿Actualmente el jefe de la casa vive en una zona (rural o urbana) distinta a la que se crió?

Si ❒ **1** No ❒ **0** No sabe ❒ **99**

☛ **Si la respuesta a la pregunta 24 es <u>SI,</u> indique si el jefe de la casa ha migrado de:**

25. Zona rural a urbana Si ❒ **1** No ❒ **0**

26. Zona urbana a rural Si ❒ **2** No ❒ **0**

☛ **Si el jefe de la casa ha migrado especificar la ocupación que tuvo antes de migrar:**

27. (De zona rural a urbana) _____

28. (De zona urbana a rural) _____

29. La relación entre el niño(a y la SEÑORA de la casa es: Ausente ❒ **0**

Madre ❒ **1** Madrastra ❒ **2** Abuela ❒ **3** Tía ❒ Otro **5**.....

30. **Ocupación de la SEÑORA de la casa (especificar):**

Quehaceres domésticos	❒ **1**	Profesora	❒ **6**	Desempleada	❒ **11**
Empleada doméstica	❒ **2**	Comerciante	❒ **7**	No sabe	❒ **99**
Jornalera	❒ **3**	Cocinera	❒ **8**		
Agricultora	❒ **4**	Partera	❒ **9**		
Lavandera	❒ **5**	Costurera	❒ **10**		

Otros (especifique) **12** _____

Firma……. **Fecha…../……./200**

1. NUMERO……

31. Instrucción de la SEÑORA de la casa:

primaria completa	❒ **1**	primaria incompleta	❒ **5**
secundaria completa	❒ **2**	secundaria incompleta	❒ **6**
superior completa	❒ **3**	superior incompleta	❒ **7**
analfabeta	❒ **4**	No sabe	❒ **99**

32. Lugar de nacimiento de la señora de la casa?

.....(localidad/ ciudad/ provincia)

33. La señora de la casa se crió en zona: urbana ❒ **1** rural ❒ **2** No sabe ❒**99**

34. ¿Actualmente si la señora de la casa vive en una zona (rural o urbana) distinta a la que se crió?

Si ❒ **1** No ❒ **0** No sabe ❒ **99**

☛ **Si la respuesta a la pregunta 34 es <u>SI</u>, indique si la señora de la casa ha migrado de:**

35. Zona rural a urbana Si ❒ **1** **36. Zona urbana a rural** Si ❒ **1**

No ❒ **0** No ❒ **0**

☛ **Si la señora de la casa ha migrado especificar la ocupación que tuvo antes de migrar:**

37. (De zona rural a urbana) _____

38. (De zona urbana a rural) _____

39. ¿Cuánto es el ingreso mensual familiar? **$**.....
(suma total del dinero que aportan todas las personas que viven en la casa**)**

40. Vive en casa: propia ❒ **1** arrendada ❒ **2** prestada ❒ **3**

Firma……. **Fecha…../……./200**

1. NUMERO……

41. ¿Qué tipo de construcción tienen las paredes de la casa en la que vive el Niño(a)?

Madera ❒ **1** Ladrillo/ bloque/ cemento ❒ **4**

Mixta (madera/ caña) ❒ **2** Mixta (madera /cemento) ❒ **5**

Caña ❒ **3** Otro (especifique) ❒ **6** _____

42. ¿Cuántos cuartos (no se incluye los baños) existen en la casa? .....

43. ¿Cuántos dormitorios existen en la casa? .....

44. ¿Cuántas personas viven/ duermen permanentemente en la casa? .....

45. Usted utiliza:

Letrina ❒ **1** Servicio higiénico ❒ **2** Campo ❒ **3** Otro (especifique) **4** _____

46. ¿El baño lo comparte con otras familias? : Si ❒ **1** No ❒ **0**

47. ¿**Usted tiene Luz?** Si ❒ **1** No ❒ **0**

☛ **¿Qué artefactos eléctricos hay en la casa?**

48. Refrigeradora Si ❒ **1** No ❒ **0** **49.** Televisión Si ❒ **1** No ❒ **0**

50. Equipo de sonido Si ❒ **1** No ❒ **0** **51.** Radio Si ❒ **1** No ❒ **0**

☛ **¿Qué material utiliza para cocinar?**

52. Gas Si ❒ **1** No ❒ **0**

53. Carbón Si ❒ **1** No ❒ **0**

54. Leña Si ❒ **1** No ❒ **0**

55. Otro (especifique) _____

☛ **¿En su casa tiene?**

56. Carro **Si** ❒ **1** **No** ❒ **0**

57. Canoa a motor **Si** ❒ **1** **No** ❒ **0**

Firma……. **Fecha…../……./200**

1. NUMERO……

☛ **¿Cuáles son las fuentes principales de recolección de agua?**

58. Potable **Si** ❒ **1** **No** ❒ **0**

59. Entubada **Si** ❒ **1** **No** ❒ **0**

60. Pozo **Si** ❒ **1** **No** ❒ **0**

61. Río **Si** ❒ **1** **No** ❒ **0**

62. Lluvia **Si** ❒ **1** **No** ❒ **0**

63. Estero **Si** ❒ **1** **No** ❒ **0**

64. Otras (especifique).....

65. ¿Uno de los padres /representantes/ familiares, se dedica a la agricultura o cría de animales domésticos para consumo de la casa?

Si ❒ **1** No ❒ **0**

☛ **Si la respuesta a la pregunta 65 fue <u>SI</u> indicar el lugar en que se lo hace:**

66. En la casa donde vive el niño(a) o sus alrededores **Si** ❒ **1** **No** ❒ **0**

67. En una finca o terreno alejado de la casa en la que vive el niño(a) **Si** ❒ **1** **No** ❒ **0**

C. <u>Datos</u> <u>Generales</u>

68. ¿**Cuántos hijos son en la familia?** .....

69. ¿**Cuántos hermanos mayores tiene el niño?** …….

70. ¿Cuántos hermanos menores tiene el niño(a)? ……..

71. ¿Qué lugar ocupa el niño(a)? .....
(llena el entrevistador, en relación a todos los hijos nacidos vivos de la madre)

72. ¿Cuántos niños (r. nacidos -15 años**) viven permanentemente en la casa?** .....

73. ¿Cuántos de los niños que viven en la casa permanentemente, son mayores que el niño(a)?

…….

Firma……. **Fecha…../……./200**

1. NUMERO……

74. ¿Cuántos de los niños que viven permanentemente en la casa, son menores que el niño(a)?

…….

75. ¿Qué lugar ocupa el niño(a) en relación a los niños que vive permanen - Te mente en la casa?

…….

76. **¿El niño(a) recibió lactancia materna?** Si ❒ **1** No ❒ **0** No sabe ❒ **99**

77. **Si la respuesta anterior fue <u>SI,</u> hasta qué edad lo hizo?**

menos de 6 meses	❒ **1**	mas de 24 meses	❒ **4**
De los 6 a los 12 meses	❒ **2**	No sabe	❒ **99**
De los 13 a los 24 meses	❒ **3**		

78. ¿Trajo el niño(a) o su representante el CARNET DE VACUNACIÓN?

Si ❒ **1** **No** ❒ **0**

☛ **Si la respuesta anterior fue <u>SI</u>, señale las dosis que se indica en el carnet:**

Vacunas que ha recibido el niño	Número de dosis de vacunas
79. **BCG**:	❒ **0** ❒ **1** ❒ **2**
80. **DTP**:	❒ **0** ❒ **1** ❒ **2** ❒ **3** ❒ **4**
81. **SARAMPION**:	❒ **0** ❒ **1**
82. **POLIO**:	❒ **0** ❒ **1** ❒ **2** ❒ **3** ❒ **4**

☛ **Si la respuesta anterior fue <u>NO</u>, señale las vacunas (cualquier número de dosis) que indica la madre o su representante:**

83. BCG: **Si** ❒ **1** **No** ❒ **0** **No sabe** ❒ **99**

84. DTP: **Si** ❒ **1** **No** ❒ **0** **No sabe** ❒ **99**

85. SARAMPION: **Si** ❒ **1** **No** ❒ **0** **No sabe** ❒ **99**

86. POLIO: **Si** ❒ **1** **No** ❒ **0** **No sabe** ❒ **99**

87. Tiene el niño(a) la cicatriz de la vacuna BCG? Si ❒ **1** No ❒ **0**

Firma……. **Fecha…../……./200**

1. NUMERO……

88. **¿Su niño(a) fue a la guardería?:** **Si** ❒ **1** **No** ❒ **0** **No sabe** ❒ **99**

89. A qué edad fue su niño a la guardería por primera vez.....meses

90. **Si la respuesta anterior fue <u>SI</u>, por cuánto tiempo?**.....meses

☛**Vamos a hablar sobre la frecuencia con que el niño(a) come o bebe los siguientes productos:**

Productos	Nunca **0**	A veces **1**	**1** vez al mes **2**	**1-4** veces por semana **3**	mas de **4** veces por semana (diario) **4**
91. CARNES (res, cerdo, pollo)					
92. PESCADO					
93. CAMARONES					

94. FRUTAS					
95. ENSALADAS					
96.ARROZ					
97. PLATANO					
98. YUCA					
99. PAN					
100. MANI					
101. PAPAS					
102. HUEVOS					
103. LECHE					
104. COLAS					
105. HAMBURGUESAS					

106. ¿El niño(a) consume leche cruda / ordeñada por lo menos 1 vez a la semana?

Si ❒ **1** No ❒ **0**

107. ¿**Durante el día cuántas horas mira la televisión el niño?**

Nunca❒ **0** A veces ❒ **1** 1-3 h ❒ **2** 4-5 h ❒ **3** más de 5 h ❒ **4**

Firma……. **Fecha…../……./200**

1. NUMERO……

108. ¿Con que frecuencia el niño(a) hace ejercicios para que le falte el aire o la respiración?

a diario	❒ **1**	cada 15 días	❒ **4**
3 veces por semana	❒ **2**	1 vez al mes	❒ **5**
1 vez a la semana	❒ **3**		

☛ ¿**Alguno de estos animales pasa dentro de la casa en la que vive el niño(a) ?**
(anotar si el animal pasa durante el día y/o la noche dentro de la casa en la que vive el niño)

109 Perro Si ❒ **1** No ❒ **0**

110. Gato: Si ❒ **1** No ❒ **0**

☛ **¿Alguno de estos animales pasa alrededor de la casa en la que vive el niño(a)?**
(anotar si los animales están la mayor parte del tiempo en el patio o jardín, así estos animales ingresen a la casa en forma esporádica).

111. Perro Si ❒ **1** No ❒ **0**
112. Gato: Si ❒ **1** No ❒ **0**
113. Cerdos Si ❒ **1** No ❒ **0**
114. Gallinas Si ❒ **1** No ❒ **0**
115. Otro Si ❒ **1** No ❒ **0**

116. ¿El niño(a) tiene contacto con animales en fincas por lo menos una vez por semana?

Si ❒ **1** No ❒ **0**

☛ **¿Alguna vez en la vida del niño(a), alguno de estos animales pasó /vivió dentro de la casa?**

117. Perro Si ❒ **1** No ❒ **0**
118. Gato Si ❒ **1** No ❒ **0**

Firma……. **Fecha…../……./200**

1. NUMERO……

☛ **¿La madre del niño(a) ha presentado?**

119. Asma **Si** ❒ **1** **No** ❒ **0** **No Sabe** ❒ **99**

(algún médico le diagnosticó de ASMA o tuvo ataques de silbido al pecho 3 o más veces y por un lapso de 3 días)

120. Rinitis **Si** ❒ **1** **No** ❒ **0** **No Sabe** ❒ **99**

(algún médico le diagnosticó de rinitis alérgica, o tuvo estornudos, moqueo, picazón de la nariz o lagrimeo/ picazón de los ojos, sin estar con gripe, más de una vez)

121. Eczema **Si ❒ 1** **No ❒ 0** **No Sabe ❒ 99**

(algún médico le diagnosticó de eczema o tuvo granos o ronchas que piquen, localizados en cuello, parte anterior del codo, posterior de la rodilla, tobillos y /o nalgas que aparecen y desaparecen y que duren por lo menos 6 meses)

☛ **¿El padre del niño(a) ha presentado?**

122. Asma **Si ❒ 1** **No ❒ 0** **No Sabe ❒ 99**

(algún médico le diagnosticó de ASMA o tuvo ataques de silbido al pecho 3 o más veces y por un lapso de 3 días)

123. Rinitis **Si ❒ 1** **No ❒ 0** **No Sabe ❒ 99**

(algún médico le diagnosticó de rinitis alérgica, o tuvo estornudos, moqueo, picazón de la nariz o lagrimeo/picazón de los ojos, sin estar con gripe, más de una vez)

124. Eczema **Si ❒ 1** **No ❒ 0** **No Sabe ❒ 99**

(algún médico le diagnosticó de eczema o tuvo granos o ronchas que piquen, localizados en cuello, parte anterior del codo, posterior de la rodilla, tobillos y/o nalgas que aparecen y desaparecen y que duren por lo menos 6 meses)

Firma……. **Fecha…../……./200**

1. NUMERO……

☛ **¿Fuma o fumaba la madre del niño(a)?**

125. En la actualidad	Si	❒ **1**	No	❒ **0**	No sabe	❒ **99**
126. Durante el embarazo	Si	❒ **1**	No	❒ **0**	No sabe	❒ **99**
127. En el primer año de vida del niño	Si	❒ **1**	No	❒ **0**	No sabe	❒ **99**

128. ¿Actualmente fuma alguien en la casa? Si ❒ **1** No ❒ **0**

D. <u>Migración</u>

129. ¿Su niño(a) ha vivido en este lugar toda su vida? Si ❒ **1** No ❒ **0**

☛ **Si la respuesta anterior fue <u>NO</u> conteste la siguiente.**
(Para contestar esta pregunta el niño tiene que haber pasado en el lugar 3 o más meses de su vida)

	SITIOS (localidad/ciudad/ provincia)	**TIEMPO (meses o años)**	**Rural**	**Urbano**
130. Primer año de vida	**130**	**174**	**175** **1❐**	**2❐**
131. Primer año de vida	**131**	**176**	**177** **1❐**	**2❐**
132. De los 2 a los 5 años	**132**	**178**	**179** **1❐**	**2❐**
133. De los 2 a los 5 años	**133**	**180**	**180** **1❐**	**2❐**
134. Mayor que 5 años	**134**	**182**	**183** **1❐**	**2❐**
135. Mayor que 5 años	**135**	**184**	**185** **1❐**	**2❐**

136 ¿El niño(a) tiene familiares viviendo en Guayaquil? Si **❐1** No **❐0**

137. Si la respuesta anterior fue <u>SI,</u> sabe la dirección (localidad/ barrio)?

Relación Familiar	**Dirección (localidad/ barrio)**

Firma……. **Fecha…../……./200**

1. NUMERO……

138. ¿El niño(a) tiene familiares viviendo en la ciudad de Esmeraldas?

Si ❒ **1** No ❒ **0**

139. Si la respuesta es <u>SI,</u> sabe la dirección (localidad/ barrio)?

Relación Familiar	**Dirección (localidad/ barrio)**

E. <u>Tratamiento</u> <u>antiparasitario</u>

140. **¿Cuándo fue la última vez que el niño(a) tomó purgante?** .....meses

141. ¿Sabe el nombre del medicamento?_____

F. <u>Silbido</u>

142. **¿Alguna vez en la vida, el niño(a) tuvo silbido al pecho, (en cualquier época del pasado)?**

Si ❒ 1 No ❒ 0 No Sabe ❒ 99

143. **¿El niño(a) ha tenido silbido al pecho en los últimos 12 meses (último año)?**

Si ❒ 1 No ❒ 0 No Sabe ❒ 99

144. ¿Cuántos ataques o crisis de silbido al pecho, ha tenido el niño(a) en estos últimos 12 meses (último año)?

Ninguno ❒ **0** 1 a 3 ❒ **1** 4 a 12 ❒ **2** más de 12 ❒ **3**

145. ¿En estos últimos 12 meses (último año) cuántas veces el niño(a) se ha despertado en la noche debido al silbido al pecho?

Nunca ha despertado con silbido ❒ 0

Menos de una noche por semana ❒ 1

Una o más noches por semana ❒ 2

Firma……. **Fecha…../……./200**

1. NUMERO……

146. ¿En estos últimos 12 meses (último año) ha sido el silbido al pecho tan severo (o tan fuerte) como para no dejarlo hablar más de una o dos palabras entre cada respiración?

Si ❒ 1 No ❒ 0 No Sabe ❒ 99

147. ¿En estos últimos 12 meses (último año), el niño(a) ha tenido silbido al pecho durante o después de hacer ejercicio (correr, trabajar, etc.)?

Si ❒ 1 No ❒ 0 No Sabe ❒ 99

148. ¿Alguna vez en la vida el niño(a) fue diagnosticado de asma o bronquitis por un médico?

Si ❒ 1 No ❒ 0 No Sabe ❒ 99

149. ¿En estos últimos 12 meses (último año), el niño(a), ha tenido tos seca en la noche? (aparte de la asociada con resfríos, gripes, o a infecciones respiratorias)

Si ❒ 1 No ❒ 0 No Sabe ❒ 99

G. <u>Rinitis</u>

150. ¿Alguna vez en su vida, el niño(a), ha tenido problemas de estornudo, goteo de la nariz (moqueo), o que se le tape la nariz? (cuando no tenía resfrío común ni gripe)

Si ❒ 1 No ❒ 0 No Sabe ❒ 99

151. ¿En los últimos 12 meses, el niño, tuvo problemas de estornudo, goteo de la nariz (moqueo), o que se le tape la nariz? (cuando no tenía resfrío común ni gripe)

Si ❒ 1 No ❒ 0 No Sabe ❒ 99

152. ¿En los últimos 12 meses, al niño(a), junto con el problema de la nariz ¿le picaban y lloraban los ojos?

Si ❒ 1 No ❒ 0 No Sabe ❒ 99

Firma……. Fecha…../……./200

1. NUMERO……

153. ¿En los últimos 12 meses (último año) en que cantidad interfirieron estos problemas nasales con las actividades diarias del niño(a)?

En nada ❒ **0** Un poco ❒ **1** Moderadamente ❒ **2** Mucho ❒ **3**

154. ¿Alguna vez en la vida el niño(a) fue diagnosticado por un médico de rinitis alérgica?

Si ❒ 1 No ❒ 0 No Sabe ❒ 99

H. <u>Eczema</u>

155. ¿El niño(a) ha tenido alguna vez en la vida granos o ronchas acompañados de picazón, que aparezcan y desaparezcan durante por lo menos 6 meses?

Si ❒ 1 No ❒ 0 No Sabe ❒ 99

156. ¿El niño(a) ha atenido éstas ronchas o granos con picazón en algún momento de estos últimos 12 meses ?

Si ❒ 1 No ❒ 0 No Sabe ❒ 99

☛¿Los granos o ronchas con picazón le han salido en alguno de los siguientes lugares?

	SI	NO
157. Alrededor de los ojos.....	❒ **1**	❒ **0**
158. Alrededor o parte frontal del cuello.....	❒ **1**	❒ **0**
159. En las orejas.....	❒ **1**	❒ **0**

160. Parte frontal de los codos..... ❒ **1** ❒ **0**

161. Detrás de las rodillas..... ❒ **1** ❒ **0**

162. Parte frontal de los tobillos..... ❒ **1** ❒ **0**

163. Nalgas..... ❒ **1** ❒ **0**

164. ¿A qué edad aparecieron los granos o ronchas por primera vez en el niño(a)?

_____

Firma……. **Fecha…../……./200**

1. NUMERO……

165. ¿Ha estado completamente sano de este problema de la piel (granos o ronchas con picazón) en algún momento en los últimos 12 meses (último año)?

Si ❒ **1** **No** ❒ **0**

166. ¿Cuántas veces en los últimos 12 meses (último año) (en promedio) se ha mantenido despierto el niño durante la noche debido a la picazón con granos o ronchas?

Ninguna vez en los últimos 12 meses ❒ **0**

Menos de una noche por semana ❒ **1**

Una o más noches por semana ❒ **2**

167. ¿Alguna vez un médico le ha diagnosticado al niño(a) de eczema o dermatitis atópica?

Si ❒ **1** **No** ❒ **0** **No Sabe** ❒ **99**

I. <u>Fuente</u> <u>de</u> <u>información</u>:

168. Niño **Si**❒ **1** **No**❒ **0** **169.** Tía (o) **Si**❒ **1** **No**❒ **0**

170. Hermana (o) **Si❐ 1 No❐ 0**

171. Padre **Si❐ 1 No❐ 0**

172. Madre **Si❐ 1 No❐ 0**

173. Representante **Si❐ 1 No❐ 0**

		SPT				Wheeze				Rhinitis				Eczema			
		No		Yes		No		Yes		No		Yes		No		Yes	
		N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Pets inside	No	2240	38.6%	311	40.9%	2355	39.3%	242	37.2%	2460	39.4%	155	32.8%	2513	39.3%	121	33.6%
home	Yes	3565	61.4%	449	59.1%	3641	60.7%	409	62.8%	3791	60.6%	318	67.2%	3878	60.7%	239	66.4%
Crowding	< 3	1768	30.5%	271	35.6%	1845	30.8%	204	31.4%	1928	30.9%	161	34.2%	1972	30.9%	121	33.6%
	>=3	4031	69.5%	490	64.4%	4149	69.2%	445	68.6%	4320	69.1%	310	65.8%	4414	69.1%	239	66.4%
Birth order	<5th	4234	72.9%	531	70.0%	4311	71.9%	503	77.4%	4496	71.9%	380	80.5%	4614	72.2%	275	76.6%
	>=5th	1571	27.1%	228	30.0%	1686	28.1%	147	22.6%	1756	28.1%	92	19.5%	1778	27.8%	84	23.4%
Bathroom	Field	1482	25.5%	181	23.8%	1497	25.0%	185	28.4%	1557	24.9%	144	30.4%	1636	25.6%	78	21.7%
	Others	4324	74.5%	580	76.2%	4501	75.0%	466	71.6%	4696	75.1%	329	69.6%	4757	74.4%	282	78.3%
Potable	No	3580	61.6%	504	66.2%	3711	61.9%	432	66.3%	3907	62.5%	279	59.0%	3993	62.4%	222	61.7%
drinking water	Yes	2229	38.4%	257	33.8%	2289	38.2%	220	33.7%	2349	37.5%	194	41.0%	2403	37.6%	138	38.3%
Attended	No	3155	55.0%	419	55.9%	3270	55.1%	356	55.4%	3419	55.4%	249	52.9%	3505	55.5%	176	49.3%
daycare	Yes	2577	45.0%	330	44.1%	2667	44.9%	287	44.6%	2758	44.6%	222	47.1%	2812	44.5%	181	50.7%
House	others	2825	48.6%	345	45.3%	2863	47.7%	320	49.1%	3018	48.2%	215	45.5%	3070	48.0%	171	47.5%
construction	bamboo/wood	2984	51.4%	416	54.7%	3137	52.3%	332	50.9%	3238	51.8%	258	54.5%	3326	52.0%	189	52.5%
Father engaged	No	3907	68.7%	434	58.6%	3947	67.1%	445	69.7%	4120	67.3%	334	71.5%	4252	67.9%	221	63.0%
in agriculture	Yes	1783	31.3%	307	41.4%	1935	32.9%	193	30.3%	2000	32.7%	133	28.5%	2011	32.1%	130	37.0%
Contact with	No	4545	78.3%	548	72.1%	4650	77.6%	502	77.1%	4871	78.0%	347	73.4%	4982	78.0%	259	71.9%
farm animals*	Yes	1257	21.7%	212	27.9%	1343	22.4%	149	22.9%	1377	22.0%	126	26.6%	1406	22.0%	101	28.1%
Unpasteurized	No	3478	60.0%	431	56.9%	3580	59.8%	382	58.6%	3717	59.5%	279	59.0%	3821	59.9%	190	52.8%
milk†	Yes	2321	40.0%	326	43.1%	2409	40.2%	270	41.4%	2525	40.5%	194	41.0%	2561	40.1%	170	47.2%
Any	No	2221	39.4%	363	49.7%	2361	41.0%	238	38.1%	2432	40.5%	192	41.9%	2493	40.6%	144	41.3%
geohelminth	Yes	3410	60.6%	367	50.3%	3404	59.0%	387	61.9%	3573	59.5%	266	58.1%	3646	59.4%	205	58.7%
A. lumbricoides	No	3670	65.2%	530	72.6%	3802	65.9%	411	65.8%	3940	65.6%	319	69.7%	4049	66.0%	228	65.3%
	Yes	1961	34.8%	200	27.4%	1963	34.1%	214	34.2%	2065	34.4%	139	30.3%	2090	34.0%	121	34.7%

T. trichiura	No	2897	51.4%	459	62.9%	3078	53.4%	311	49.8%	3178	52.9%	235	51.3%	3228	52.6%	205	58.7%
	Yes	2734	48.6%	271	37.1%	2687	46.6%	314	50.2%	2827	47.1%	223	48.7%	2911	47.4%	144	41.3%
Hookworm	No	5351	95.0%	681	93.3%	5471	94.9%	590	94.4%	5690	94.8%	440	96.1%	5827	94.9%	325	93.1%
	Yes	280	5.0%	49	6.7%	294	5.1%	35	5.6%	315	5.2%	18	3.9%	312	5.1%	24	6.9%

Supplementary Table 1. Frequencies of poor hygiene and farming exposures according to the presence and absence of allergen skin test reactivity (SPT), and recent symptoms of wheeze, rhinitis, and eczema in urban and rural schoolchildren combined. *Pigs, cows, horses, mules, donkeys. † - Consumption of unpasteurized milk at least once weekly. Median crowding was 3 persons per sleeping room.

	SPT OR (95% CI) p value		Inter. P value	Wheeze OR (95% CI) p value		Inter. P value	Rhinitis OR (95% CI) p value		Inter. P value	Eczema OR (95% CI) p value		Inter. P value
Hygiene exposure	Urban	Rural		Urban	Rural		Urban	Rural		Urban	Rural	
Pets inside home	0.75(0.57-0.98)	1.08(0.88-1.32)	0.036	1.16(0.88-1.55)	1.07(0.86-1.32)	0.616	1.53(1.12-2.10)	1.22(0.93-1.60)	0.245	1.05(0.75-1.47)	1.37(1-1.87)	0.229
Yes vs. No	0.035	0.451		0.291	0.560		0.007	0.143		0.779	0.053	
Crowding	0.73(0.55-0.96)	0.89(0.72-1.09)	0.297	1.03(0.77-1.39)	0.88(0.70-1.10)	0.421	1.02(0.74-1.40)	0.77(0.59-1.01)	0.290	1.01(0.71-1.44)	0.84(0.62-1.15)	0.620
≥3 vs. <3	0.025	0.261		0.829	0.254		0.901	0.063		0.942	0.285	
Birth order	0.83(0.57-1.20)	1.16(0.95-1.41)	0.105	**1.13(0.79-1.61)**	**0.63(0.50-0.80)**	**0.007**	0.80(0.53-1.22)	0.59(0.44-0.79)	0.292	0.97(0.62-1.52)	0.75(0.55-1.03)	0.413
≥5th vs. ≤4th	0.317	0.145		**0.497**	**<0.001**		0.304	<0.001		0.894	0.079	
Bathroom	0.67(0.37-1.24)	0.92(0.74-1.14)	0.368	0.77(0.43-1.38)	1.17(0.93-1.47)	0.187	0.86(0.47-1.58)	1.78(1.35-2.35)	0.032	0.53(0.23-1.21)	1.06(0.76-1.48)	0.095
Field vs. others	0.202	0.443		0.382	0.179		0.630	<0.001		0.131	0.722	
Potable drinking water	0.87(0.48-1.57)	0.80(0.45-1.45)	0.896	1.25(0.71-2.20)	2.10(1.13-3.90)	0.167	1.29(0.75-2.22)	2.66(1.24-5.72)	0.288	1.25(0.73-2.14)	2.78(0.92-8.39)	0.146
No vs. Yes	0.648	0.477		0.446	0.019		0.363	0.012		0.420	0.069	
Attended daycare	1.17(0.89-1.53)	0.83(0.67-1.02)	0.046	0.91(0.69-1.21)	0.97(0.78-1.19)	0.689	1.50(1.12-2.0)	0.95(0.73-1.24)	0.030	1.40(1-1.96)	1.19(0.88-1.61)	0.522
Yes vs. No	0.263	0.073		0.530	0.767		0.007	0.716		0.047	0.247	
House construction	1(0.74-1.37)	1.07(0.86-1.32)	0.846	0.93(0.68-1.28)	0.86(0.68-1.07)	0.690	1.14(0.83-1.59)	1.52(1.13-2.05)	0.254	0.87(0.59-1.27)	1.28(0.91-1.80)	0.080
Wood/bamboo vs. others	0.954	0.565		0.669	0.179		0.412	0.006		0.468	0.150	
Father engaged in agriculture	0.94(0.53-1.68)	1.25(0.99-1.57)	0.367	0.96(0.53-1.74)	0.85(0.68-1.05)	0.672	1.21(0.68-2.15)	1(0.75-1.34)	0.479	1.20(0.61-2.33)	1.11(0.79-1.55)	0.972
Yes vs. No	0.844	0.057		0.899	0.144		0.514	0.980		0.600	0.546	
Contact with farm animals*	0.89(0.54-1.46)	1.25(1-1.55)	0.203	1.02(0.63-1.66)	1.06(0.85-1.34)	0.908	1.86(1.21-2.85)	1.42(1.07-1.87)	0.194	2.14(1.34-3.41)	1.29(0.94-1.78)	0.063
Yes vs. No	0.644	0.042		0.931	0.599		0.005	0.015		0.002	0.118	
Unpasteurized milk†	1.16(0.88-1.53)	0.96(0.77-1.19)	0.257	0.88(0.66-1.18)	1.18(0.96-1.48)	0.107	0.85(0.63-1.16)	1.23(0.93-1.61)	0.081	0.89(0.62-1.25)	1.46(1.05-2)	0.029
Yes vs. No	0.283	0.683		0.394	0.118		0.312	0.143		0.494	0.021	
Any geohelminth	0.78(0.59-1.05)	0.58(0.47-0.72)	0.099	1.24(0.93-1.64)	0.97(0.76-1.22)	0.216	0.86(0.63-1.16)	1.19(0.88-1.61)	0.135	0.95(0.67-1.34)	1.30(0.92-1.84)	0.118
Yes vs. No	0.109	<0.001		0.136	0.770		0.327	0.246		0.765	0.132	
A. lumbricoides	0.60(0.40-0.91)	0.69(0.56-0.87)	0.556	0.74(0.51-1.09)	1.06(0.86-1.32)	0.101	0.62(0.40-0.94)	1.09(0.84-1.44)	0.033	0.93(0.60-1.43)	1.20(0.88-1.65)	0.206
Yes vs. No	0.015	0.001		0.130	0.571		0.027	0.502		0.738	0.252	
T. trichiura	0.81(0.60-1.10)	0.59(0.48-0.73)	0.091	1.40(1.05-1.87)	0.95(0.76-1.19)	0.044	0.98(0.72-1.34)	1.17(0.88-1.54)	0.351	1.01(0.71-1.44)	0.89(0.65-1.23)	0.868
Yes vs. No	0.181	<0.001		0.020	0.651		0.892	0.282		0.938	0.504	
Hookworm	1.18(0.57-2.45)	1.14(0.76-1.70)	0.975	1.69(0.84-3.41)	0.90(0.54-1.48)	0.216	0.91(0.43-1.90)	0.80(0.41-1.58)	0.813	0.50(0.16-1.58)	1.76(1.02-3.03)	0.011
Yes vs. No	0.658	0.526		0.138	0.683		0.803	0.520		0.238	0.042	

Supplementary Table 2. Associations between study outcomes and poor hygiene/farming exposures stratified by área of residence. Odds ratios (ORs) and 95% confidence intervals (95% CI) were calculated using random effects logistic regression in which clustering by rural community or urban neighbourhood was adjusted. Age and sex were included as *a priori* confounders and ethnicity, maternal educational level, household income and body mass index were considered as potential confounders and adjusted for where they had a significant effect on study outcomes. Interactions (inter.) with P≤0.01 were considered relevant.

*Pigs, cows, horses, mules, donkeys. † - Consumption of unpasteurized milk at least once weekly. Median crowding was 3 persons per sleeping room.

Hygiene exposure	Wheeze OR (95% CI) P value		Inter. P value	Rhinitis OR (95% CI) P value		Inter. P value	Eczema OR (95% CI) P value		Inter. P value
	SPT-	SPT+		SPT-	SPT+		SPT-	SPT+	
Pets inside home	1.08 (0.89-1.30)	1.30 (0.84-2.01)	0.470	1.54 (1.23-1.93)	0.80 (0.46-1.37)	0.019	1.27 (0.98-1.64)	1.22 (0.67-2.24)	0.724
Yes vs. No	0.449	0.245		0.001	0.410		0.071	0.516	
Crowding	0.94 (0.77-1.15)	1.07 (0.69-1.67)	0.618	0.89 (0.71-1.11)	0.98 (0.55-1.74)	0.786	0.86 (0.67-1.12)	0.85 (0.46-1.59)	0.989
≥3 vs. <3	0.573	0.760		0.301	0.941		0.259	0.629	
Birth order	0.75 (0.60-0.93)	0.75 (0.47-1.23)	0.987	0.65 (0.50-0.84)	0.64 (0.32-1.25)	0.675	0.81 (0.61-1.08)	0.64 (0.32-1.27)	0.716
≥5th vs. ≤4th	0.010	0.261		0.001	0.191		0.157	0.201	
Bathroom	1.18 (0.94-1.47)	0.97 (0.59-1.69)	0.355	1.53 (1.19-1.95)	0.80 (0.38-1.68)	0.027	0.92 (0.68-1.26)	0.90 (0.44-1.86)	0.768
Field vs. others	0.147	0.899		0.001	0.550		0.616	0.778	
Potable drinking water	**1.42 (1.13-1.79)**	**0.74 (0.47-1.14)**	**0.010**	**1.05 (0.79-1.40)**	**0.48 (0.26-0.88)**	**0.010**	0.99 (0.70-1.39)	0.87 (0.39-1.94)	0.623
No vs. Yes	**0.002**	**0.172**		**0.741**	**0.019**		0.949	0.726	
Attended daycare	0.99 (0.82-1.19)	0.87 (0.56-1.33)	0.588	1.15 (0.93-1.42)	1.48 (0.85-2.57)	0.471	1.33 (1.04-1.70)	1.12 (0.62-2.02)	0.455
Yes vs. No	0.888	0.510		0.202	0.163		0.025	0.712	
House construction	1.01 (0.84-1.23)	0.59 (0.38-0.90)	0.018	**1.37 (1.09-1.72)**	**0.66 (0.36-1.21)**	**0.005**	1.03 (0.77-1.38)	0.79 (0.41-1.50)	0.462
Wood/bamboo vs. others	0.904	0.014		**0.008**	**0.179**		0.858	0.466	
Father engaged in agriculture	0.95 (0.77-1.18)	0.77 (0.49-1.20)	0.465	0.87 (0.67-1.13)	1.04 (0.53-2.04)	0.775	1.03 (0.77-1.38)	1.55 (0.77-3.12)	0.484
Yes vs. No	0.663	0.247		0.285	0.920		0.858	0.220	
Contact with farm animals*	1.07 (0.85-1.34)	0.93 (0.57-1.51)	0.658	1.36 (1.05-1.75)	1.73 (0.92-3.26)	0.789	1.48 (1.11-1.97)	1.18 (0.61-2.32)	0.703
Yes vs. No	0.561	0.770		0.018	0.087		0.008	0.615	
Unpasteurized milk†	1.05 (0.87-1.28)	1.08 (0.71-1.65)	0.892	1.02 (0.82-1.27)	1.18 (0.68-2.07)	0.666	1.12 (0.86-1.44)	1.47 (0.80-2.70)	0.663
Yes vs. No	0.584	0.718		0.856	0.560		0.396	0.218	
Any geohelminth	1.22 (1.00-1.49)	0.87 (0.57-1.35)	0.130	1.02 (0.81-1.28)	0.95 (0.54-1.67)	0.675	1.01 (0.78-1.31)	1.32 (0.71-2.47)	0.376
Yes vs. No	0.055	0.543		0.877	0.860		0.919	0.384	
A. lumbricoides	1.00 (0.82-1.23)	1.25 (0.77-2.02)	0.487	0.83 (0.65-1.05)	1.50 (0.79-2.82)	0.202	0.94 (0.72-1.24)	1.88 (0.98-3.63)	0.062
Yes vs. No	0.971	0.362		0.116	0.212		0.679	0.058	
T. trichiura	1.23 (1.01-1.49)	0.85 (0.54-1.34)	0.094	1.14 (0.92-1.43)	0.78 (0.43-1.43)	0.194	0.86 (0.66-1.12)	0.96 (0.51-1.82)	0.690
Yes vs. No	0.037	0.472		0.235	0.431		0.257	0.907	
Hookworm	1.09 (0.70-1.69)	1.21 (0.52-2.80)	0.854	0.64 (0.34-1.19)	2.00 (0.74-5.46)	0.057	1.21 (0.70-2.09)	0.96 (0.33-3.04)	0.884
Yes vs. No	0.700	0.658		0.156	0.174		0.490	0.991	

Supplementary Table 3. Associations between study outcomes and poor hygiene/farming exposures stratified by allergen skin prick test reactivity (SPT). Odds ratios (ORs) and 95% confidence intervals (95% CI) were calculated using random effects logistic regression in which clustering by rural community or urban neighbourhood was adjusted. Age and sex were included as *a priori* confounders and ethnicity, maternal educational level, household income and body mass index were considered as potential confounders and adjusted for where they had a significant effect on study outcomes. Interactions (inter.) with P≤0.01 were considered relevant.

*Pigs, cows, horses, mules, donkeys. † - Consumption of unpasteurized milk at least once weekly. Median crowding was 3 persons per sleeping room.