

Original article

Allergic diseases and atopic sensitization in children related to farming and anthroposophic lifestyle – the PARSIFAL study

Background: The prevalence of allergic diseases has increased rapidly in recent decades, particularly in children. For adequate prevention it is important not only to identify risk factors, but also possible protective factors. The aim of this study was to compare the prevalence of allergic diseases and sensitization between farm children, children in anthroposophic families, and reference children, with the aim to identify factors that may protect against allergic disease.

Methods: The study was of cross-sectional design and included 14 893 children, aged 5–13 years, from farm families, anthroposophic families (recruited from Steiner schools) and reference children in Austria, Germany, the Netherlands, Sweden and Switzerland. A detailed questionnaire was completed and allergen-specific IgE was measured in blood.

Results: Growing up on a farm was found to have a protective effect against all outcomes studied, both self-reported, such as rhinoconjunctivitis, wheezing, atopic eczema and asthma and sensitization (allergen specific IgE ≥ 0.35 kU/l). The adjusted odds ratio (OR) for current rhinoconjunctivitis symptoms was 0.50 (95% confidence interval (CI) 0.38–0.65) and for atopic sensitization 0.53 (95% CI 0.42–0.67) for the farm children compared to their references. The prevalence of allergic symptoms and sensitization was also lower among Steiner school children compared to reference children, but the difference was less pronounced and not as consistent between countries, adjusted OR for current rhinoconjunctivitis symptoms was 0.69 (95% CI 0.56–0.86) and for atopic sensitization 0.73 (95% CI 0.58–0.92).

Conclusions: This study indicates that growing up on a farm, and to a lesser extent leading an anthroposophic life style may confer protection from both sensitization and allergic diseases in childhood.

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*The PARSIFAL study group is given in Appendix.

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The prevalence of allergic asthma, allergic rhinoconjunctivitis and atopic eczema has increased markedly in recent decades, particularly among children (1, 2), although there is some recent evidence that the prevalence rates are stabilizing (3–5). The total costs for the major allergic diseases are estimated to 10 billion Euros for direct costs and 19 billion Euros for indirect costs in Europe (6). For

adequate prevention it is important not only to identify risk factors, but also possible protective factors.

The PARSIFAL (Prevention of Allergy Risk factors for Sensitization In children related to Farming and Anthroposophic Lifestyle) project focuses on two groups of children who have shown a lower prevalence of atopic diseases and sensitization: farm children (7–11) and

children in families with an anthroposophic lifestyle (12). Contact with farm animals, especially in early childhood, has been associated with a decrease in the risk of atopic disease (8, 9, 13, 14). This protective effect might partly arise through exposure to microbial compounds (15–18).

The anthroposophic way of life involves several characteristics that were more common in the general population some decades ago, such as restrictive use of antibiotics, antipyretics and vaccinations, as well as certain dietary habits. In a previous Swedish study it was not possible to identify any single lifestyle factor as primarily responsible for the lower prevalence of atopy, because the behavioural characteristics of the anthroposophic lifestyle were strongly correlated (12).

In this article we compared the prevalence of allergic diseases and sensitization in children from farm or anthroposophic families and their respective reference group in five European countries (Austria, Germany, the Netherlands, Sweden and Switzerland). The study is larger than most previous studies; moreover farming practices and the lifestyle of the anthroposophic communities differ between the countries, enhancing the resolution power of identifying important determinants of the lower disease rates.

Methods

Study design

Children, aged 5–13 years, from farm families or attending Steiner schools were compared with children from appropriate reference groups in Austria, Germany, the Netherlands, Sweden and Switzerland. Children in Steiner schools often come from families with an anthroposophic lifestyle. Farm children were defined as children currently living on a farm and whose family runs the farm. In Austria, children of farmers and reference children not designated as farm children were selected from schools in rural areas by their teachers, who had a good knowledge of the pupils and their parents. In Germany, the Netherlands and Switzerland children were selected from schools in rural areas known to have a high percentage of farmers. All farm children in the selected schools were included in these countries and all of the farm reference children were included in Germany and the Netherlands, whereas in Switzerland only a random sample of the farm reference children were included. In Sweden, farmers with children, in selected areas, were identified from the Farming Registry at the National Bureau of Statistics and farm reference children were randomly selected from the population registry among children living in the same area. In all countries, children with an anthroposophic lifestyle were recruited from classes in Steiner schools. All children in the selected Steiner schools were invited to participate. Corresponding reference children were selected from other schools in the vicinity. After a first sampling seven Steiner schools and one reference school, all located in Germany, were excluded because of low participation rate, which appeared to be due to lack of interest on the part of the school rather than refusal by individuals.

Questionnaire and clinical examination

The parents completed a detailed questionnaire, which included questions on environmental exposures, lifestyle, socio-economic

conditions, history of infections, diet, contact with animals, and on symptoms of bronchial asthma, rhinoconjunctivitis and atopic eczema. Most of the questions were based on the internationally validated and translated ISAAC phase-II questions (19) and the Swedish BAMSE study (20). Questions on exposures and lifestyle factors related to living on a farm were largely from the earlier ALEX study in Switzerland, Germany and Austria (13) and questions regarding factors associated with anthroposophic lifestyle were based on a Swedish study (12). The questionnaires were distributed and collected from October 2000 to May 2002, during largely overlapping time periods in the five countries.

In Austria, the Netherlands and Sweden all children whose parents had consented to blood sampling were invited to a clinical examination. In Germany and Switzerland only a random sample of those who consented were invited, because of the comparatively large number of children included in these countries. In Germany there was also a selection among the Steiner school children, only children whose parents had reported an anthroposophic lifestyle were included. The clinical examination was performed by specially trained nurses and included blood samples, measurement of weight and height as well as collection of information about the child's immunizations.

Allergen-specific IgE was measured against a mix of common inhalant allergens (Phadiatop®; allergens included are *Dermatophagoides pteronyssinus*, *D. farinae*, birch, timothy, mugwort, cat, dog, horse and *Cladosporium herbarum*) and a mix of common food allergens (fx5®; allergens included are hen's egg white, codfish, cow's milk, peanut, soy bean and wheat flour) (Pharmacia CAP System, Pharmacia Diagnostics AB, Uppsala, Sweden). All analyses were performed at the Department of Clinical Immunology, Karolinska University Hospital, Stockholm, Sweden.

Endpoint definitions and statistical analyses

All health endpoints were self-reported by the parents of the children except atopic sensitization which was assessed by blood samples. Children were considered to have current rhinoconjunctivitis symptoms if sneezing, runny nose, stuffy nose and itchy eyes were reported in the last 12 months without the child having a cold at the same time. Current wheezing was defined as at least one episode of wheezing during the last 12 months. Current atopic eczema symptoms was considered present if the child had ever had an itchy rash intermittently for at least 6 months and, in addition, reported an itchy rash in defined locations (bend of the arm/knee, backside of thighs, neck and around eyes/ears) at any time during the last 12 months. Children reported to ever have had symptoms of seasonal rhinoconjunctivitis and been diagnosed with seasonal rhinoconjunctivitis, were considered to have a doctor's diagnosis of rhinoconjunctivitis. Children with an intermittent itchy rash lasting at least 6 months and who had been diagnosed with atopic/allergic eczema were considered to have a doctor's diagnosis of atopic eczema and children who had ever been diagnosed with asthma, or with obstructive bronchitis more than once, were considered to have a doctor's diagnosis of asthma. IgE values ≥ 0.35 kU/l in either Phadiatop® and/or the mix of common food allergens (fx5®) defined atopic sensitization.

Statistical analyses were performed using Stata (Version 8.0, Stata Corp LP, College Station, TX, USA) and SAS (Version 8.1, SAS Institute Inc., SAS Software). Statistical significance was defined as a two-sided $P < 0.05$, using chi-square analyses. Odds ratios (OR) with 95% confidence intervals (CI) were computed using logistic regression analysis. In the logistic regression analyses adjustments were made for country, sex, age (five categories), mother's reported asthma and/or rhinoconjunctivitis, father's reported asthma and/or

rhinoconjunctivitis, parental education (three categories), maternal smoking during pregnancy, current smoking in the household and older siblings (four categories).

The study was approved by local research ethics committees in each country and informed consent was obtained from the parents of each child.

Results

Of the 21 905 children invited to take part in the study 15 137 (69%) provided questionnaire data (Table 1). The combined participation rate for farm children and farm reference children was 70%. The corresponding figure for Steiner school children was 67% and for Steiner school reference children 70%. The participation rate ranged from 50% in the Netherlands to 82% in Switzerland (Table 1), and did not differ to any major extent between the subgroups within each country (data not shown). A total of 237 children were excluded because they were outside the age limits (5–13-year old) and seven children because of missing information regarding sex or which

group they belonged to, leaving 14 893 children for the analyses.

In all 8788 children gave consent for blood sampling and of these 4854 were invited for blood sampling and 4049 gave a blood sample. Overall there were no consistent differences in the prevalence of various allergic symptoms between those who provided blood samples and those who did not (data not shown). However, while the prevalence of any allergic symptoms or Dr diagnosed disease was similar among those with and without blood samples from the Steiner school children, 30 and 29%, respectively, it appeared higher for those with blood samples (36%) than those without (31%) in the Steiner reference group. These differences in symptoms/disease rates related to blood samples between Steiner and Steiner reference children tended to be most pronounced in Sweden, Switzerland and the Netherlands.

There were clear differences between the four groups of children in terms of heredity (Table 2). Both maternal and paternal reported asthma or rhinoconjunctivitis was significantly more common in the Steiner school and

Table 1. Participation rates in the PARSIFAL study, subdivided by country

Country	No. of selected children	No. of obtained questionnaires	Participation rate questionnaires (%)	Consent for blood sample	Blood samples	Participation rate blood samples (%)
Austria	1589	1282	80.7	806	759	47.8
Germany	9240	6963	75.4	5045*	1159	40.9†
Netherlands	6403	3230	50.4	691	552	8.6
Sweden	1550	1109	71.5	944	836	53.9
Switzerland	3123	2553	81.7	1302*	743	35.8†
Total	21 905	15 137	69.1	8788	4049	33.5

*In Germany and Switzerland only a random sample of the children who had consented to give a blood sample was selected (1548 and 865, respectively).

†Calculated as (no of blood samples/selected for blood samples) × (consent for blood samples/No. of selected children).

Table 2. Characteristics of children in the PARSIFAL study subdivided by study group

	Farm children	Farm reference children	Steiner school children	Steiner school reference children	All children
Number of children (n)	2823	5440	4606	2024	14 893
Sex (% males)*	51.5	51.4	48.0	49.2	50.0
Age (years)*	9.0	8.7	9.1	8.8	8.9
Older siblings (n)*	1.3	0.8	1.1	0.8	1
Height (cm)*	139.3	137.1	139.2	137.7	138.3
Weight (kg)*	34.2	32	32.2	32.5	32.5
Mother's reported asthma or rhinoconjunctivitis† (% yes)*	12.4	18.6	26.9	24	20.7
Father's reported asthma or rhinoconjunctivitis† (% yes)*	9.3	15.8	26	23.8	18.8
Parental education‡, *					
Gymnasium (%)	53.7	51.9	31.2	47.4	45.2
University (%)	11.1	18.3	66.4	39.2	34.7
Maternal smoking during pregnancy (%)*	6.4	12.4	8.1	13	10.2
Current smoking in the household§ (%)*	15.6	24.6	13.8	19.3	19.9

*Computed among those answering a specific question. Internal nonresponse/missing rate was for height and weight approximately 11% and for all other characteristics less than 3%.

†Defined as having or having had asthma and/or rhinoconjunctivitis.

‡Three groups according to the highest level of education of the mother and father: elementary school or lower, gymnasium/secondary school and university education.

§Mother, father or someone else smokes regularly in the child's home.

Table 3. Prevalence of allergic diseases and atopic sensitisation*, for all the PARSIFAL children subdivided by study group

	Farm children		Farm reference children		Steiner school children		Steiner school reference children	
	%	n/N	%	n/N	%	n/N	%	n/N
Current rhinoconjunctivitis symptoms	3.3	91/2801	7.7	416/5373	8.0	363/4558	10.6	212/1998
Dr's diagnosis of rhinoconjunctivitis	1.3	37/2789	4.4	236/5347	4.8	216/4532	6.1	121/1987
Current wheezing	5.0	140/2795	7.7	412/5374	8.8	398/4548	8.4	168/2002
Dr's diagnosis of asthma	6.3	172/2750	9.1	484/5330	9.3	421/4551	11.0	217/1979
Current atopic eczema symptoms	8.6	239/2791	9.7	526/5399	11.6	525/4540	14.6	294/2011
Dr's diagnosis of atopic eczema	7.1	198/2790	9.9	535/4848	11.5	521/4004	12.3	246/2001
Atopic sensitisation*	22.7	314/1386	34.7	243/701	32.2	387/1201	39.1	248/634

n, number of children with actual outcome; N, total number of responses to the question/analyses.

*IgE ≥ 0.35 kU/l in Phadiatop® and/or mix of common food allergens (fx5®).

Steiner school reference group than in the farm reference group and was most rare in the farm group. University education was most common among the parents of the Steiner school children. Both maternal smoking and current smoking in the household were more common in the reference groups than in the farm and Steiner school group. The country-specific results regarding differences between the four groups in relation to the characteristics described in Table 2 were largely consistent (not shown in table).

The prevalence of various symptoms of allergy and doctor's diagnosis of allergic disease as well as atopic sensitization is illustrated in Table 3. The prevalence for all outcomes was significantly lower in the farm group than in the reference group, except for current atopic eczema symptoms where the difference was of borderline significance. Similarly, the Steiner school children showed significantly lower prevalence of all outcomes, except current wheezing and doctor's diagnosis of atopic eczema, as compared to their reference children.

Substantial differences in prevalence of allergic diseases and sensitization were evident between countries and exposure groups (Fig. 1A–G). However, in all countries the lowest prevalence rates tended to be found among the farm children, with the most consistent differences between the farm children and the farm reference children for rhinoconjunctivitis and atopic sensitization (Fig. 1A, B, G). The effects of group belonging on doctor's diagnosis of asthma prevalence varied with the most pronounced differences in Germany (Fig. 1D). The effects of the differences between the Steiner children and the Steiner reference children also varied from country to country. The most consistent differences in prevalence between the Steiner school children and their references across several outcomes were seen in Germany, the Netherlands and Sweden.

The OR for the studied health outcomes, comparing the farm group and the Steiner school group with their respective reference group, are shown in Table 4. For the farm group, the adjusted ORs were significantly lower than in the reference group for all the studied health

outcomes, except current atopic eczema symptoms and doctor's diagnosis of eczema, where the results were of borderline significance. For instance, the adjusted OR for current rhinoconjunctivitis symptoms was 0.50 (95% CI 0.38–0.65) and for atopic sensitization 0.53 (95% CI 0.42–0.67). Among the Steiner school children the adjusted ORs were significantly lower for current rhinoconjunctivitis symptoms, doctor's diagnosis of rhinoconjunctivitis, current atopic eczema symptoms and atopic sensitization, and of borderline significance for doctor's diagnosis of asthma and doctor's diagnosis of atopic eczema. In this group the adjusted OR for current rhinoconjunctivitis symptoms was 0.69 (95% CI 0.56–0.86) and for atopic sensitization 0.73 (95% CI 0.58–0.92). When adjustment was made for prevalence of allergic symptoms or Dr diagnosed disease, to minimize potential selection bias in blood sampling, the OR for atopic sensitization was 0.79 (95% CI 0.62–1.01). Additional adjustment for height and weight did not result in any notable changes in the OR estimates.

Discussion

This large cross-sectional study among children aged 5–13 years in Austria, Germany, the Netherlands, Sweden and Switzerland indicated that growing up on a farm, and to a lesser extent leading an anthroposophic life-style is protective against both atopic sensitization and childhood allergic diseases.

The beneficial influence of growing up on a farm against sensitization and development of allergic diseases in childhood has earlier been reported in studies from Austria, Canada, Finland, Germany, Sweden and Switzerland (7–10, 13, 21, 22). The farming environment appeared to provide more consistent protection against rhinoconjunctivitis and sensitization than against asthma and other atopic diseases (7–10, 13, 21, 22), and this was confirmed by our study. Farm children are more exposed to micro-organisms related to livestock animals, which has been proposed to protect against developing

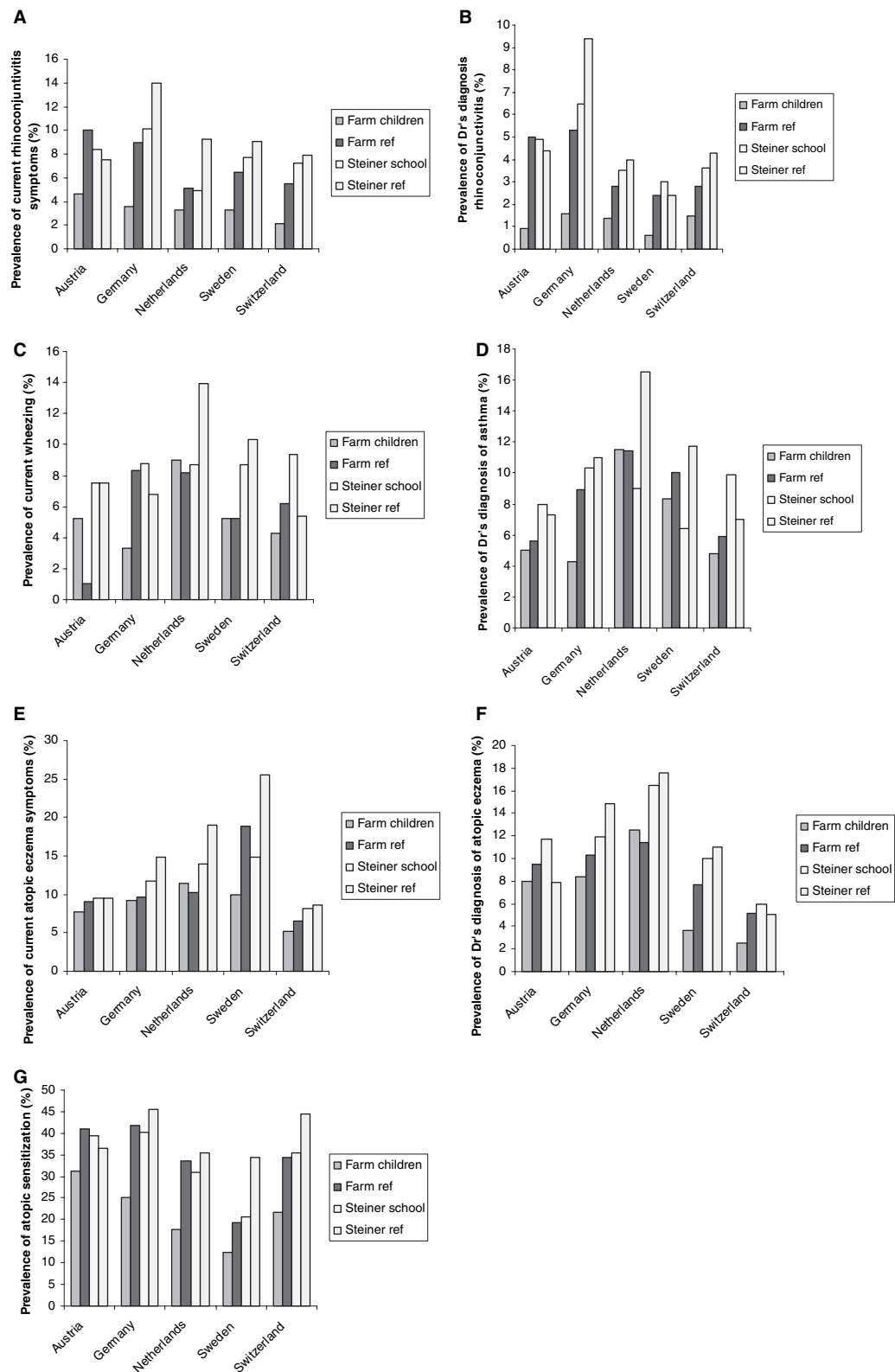


Figure 1. (A) Prevalence of current rhinoconjunctivitis symptoms, (B) Dr's diagnosis of current rhinoconjunctivitis, (C) current wheezing, (D) Dr's diagnosis of asthma, (E) current atopic eczema symptoms, (F) Dr's diagnosis of current atopic eczema and (G) atopic sensitization (IgE, ≥ 0.35 kU/l in Phadiatop[®] and/or mix of common food allergens (fx5[®])), subdivided by country and study group.

Table 4. Odds ratios for allergic diseases and sensitisation among farm children and Steiner school children compared to their respective reference groups

	Unadjusted OR*				Adjusted OR†			
	Farm children vs reference		Steiner school children vs reference		Farm children vs reference		Steiner school children vs reference	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Current rhinoconjunctivitis symptoms	0.43	0.33–0.54	0.73	0.61–0.87	0.50	0.38–0.65	0.69	0.56–0.86
Dr's diagnosis of rhinoconjunctivitis	0.33	0.23–0.48	0.78	0.62–0.98	0.39	0.26–0.58	0.72	0.55–0.94
Current wheezing	0.70	0.57–0.86	1.03	0.86–1.26	0.78	0.62–0.99	1.10	0.89–1.36
Dr's diagnosis of asthma	0.70	0.58–0.85	0.83	0.70–0.99	0.74	0.60–0.92	0.85	0.69–1.03
Current atopic eczema symptoms	0.90	0.76–1.07	0.75	0.64–0.87	0.89	0.74–1.07	0.68	0.57–0.81
Dr's diagnosis of eczema	0.82	0.69–0.98	0.92	0.78–1.08	0.83	0.68–1.01	0.88	0.73–1.06
Atopic sensitisation	0.53	0.42–0.65	0.77	0.63–0.95	0.53	0.42–0.67	0.73	0.58–0.92

OR, odds ratio; CI, confidence interval.

*Only adjusted for country.

†Adjusted for country, sex, age, mother's reported asthma and/or rhinoconjunctivitis, father's reported asthma and/or rhinoconjunctivitis, parental education, maternal smoking during pregnancy, current smoking in the household and older siblings.

sensitization and allergic diseases (13, 15, 16). In addition, long-term and early life exposure to stables and farm milk has been shown to protect against the development of asthma, rhinoconjunctivitis and atopic sensitisation (13).

We also report lower prevalence overall of all studied outcomes, with the exception of current wheezing, among children attending Steiner schools (as a proxy for leading an anthroposophic lifestyle). However, these results tended to vary more between the countries, possibly because the anthroposophic lifestyle to some extent differs between the countries and that the families who have their children in Steiner schools are more or less anthroposophic. Nevertheless, our results confirm previous findings from Sweden (12). The lifestyle of children in anthroposophic families differs with respect to several characteristics that may be of importance for allergy, e.g. restrictive use of antibiotics, antipyretics and certain vaccinations, as well as dietary habits including intake of fermented vegetables and biodynamic food. The prevalence of allergic diseases, but not atopic sensitization, was slightly lower in the farm reference group than in the Steiner children group. This could possibly be explained by the fact that most of the Steiner schools were in urban/suburban areas and the farm reference group in a rural setting, as earlier studies have shown a lower prevalence of allergic diseases in rural than in urban areas (23). However, the study was not designed test, this hypothesis, so no further comparisons between these groups have been made.

It is important to consider the possibilities of bias. The questions regarding symptoms and diagnosis of asthma, rhinoconjunctivitis and atopic eczema were based on the internationally validated and translated ISAAC phase-II questions (19). We used the overall denotation 'allergic diseases' to characterize these conditions, primarily based on questionnaire responses regarding symptoms and/or Doctor's diagnosis (24). The response rate for the questionnaire was high in all countries except the

Netherlands, where it was 50%. The participation rate in blood sampling was also low there, which may partly be related to outbreaks of Foot and Mouth Disease during the recruitment phase, as well as recently changed Institutional Review Board requirements. However, our data on the prevalence of the studied outcomes in the Netherlands were comparable with the results from the Dutch part of the ISAAC-II study (25) where the participation rate was higher (65%), speaking against important selection bias. In the assessment of results based on the blood samples among the Steiner and Steiner reference groups, e.g. atopic sensitization, there is additional concern for possible selection bias since participation seemed to be related to allergic symptoms/Dr diagnosed disease. However, adjustment for symptoms/disease prevalence, to minimize disease related selection bias, resulted in a small effect on OR's. Considering also that this represents an overadjustment it speaks against a major effect by selection bias. The 'healthy farmer effect', i.e. a selective avoidance of farming by atopic families may be a problem. The reported prevalence of asthma and/or rhinoconjunctivitis was lower among parents in the farm group than in the other studied groups. This might in part be explained by families with atopic diseases leaving their farms, although we do not have supporting evidence. Another possibility is that farming protects against atopy not only among children but also among adults, or that the childhood protection once similarly afforded to the parent generation extends into their adulthood.

An ultimate aim of epidemiological research on allergic diseases is to better understand and identify which factors in the environment and lifestyle are responsible for the increase in prevalence of these diseases over the recent decades. There is most probably no single factor in the farm and/or anthroposophic environment that prevents children from developing allergic diseases; but rather that the effects result from a complex interplay between

various environmental and life style factors. The rich database and the differences between the countries in the present study will permit further studies into specific possible protective factors.

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Appendix: The PARSIFAL study group

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Corrigendum

In (1), the following sentence was published on page 415:

Current atopic eczema symptoms was considered present if the child had ever had an itchy rash intermittently for at least 6 months and, in addition, reported an itchy rash in defined locations (bend of the arm/knee, backside of thighs, neck and around eyes/ears) at any time during the last 12 months.

The authors wish to change this sentence to read:

Current atopic eczema symptoms were present if the child ever had had an itchy rash intermittently for at least 6 months, and if the child had had this rash at any time during the last 12 months.

The authors would also like to change the values in Table 3 for the line Dr's diagnosis of atopic eczema, the correct table is published below.

Table 3. Prevalence of allergic diseases and atopic sensitisation*, for all the PARSIFAL children subdivided by study group

	Farm children		Farm reference children		Steiner school children		Steiner school reference children	
	%	n/N	%	n/N	%	n/N	%	n/N
Current rhinoconjunctivitis symptoms	3.3	91/2801	7.7	416/5373	8.0	363/4558	10.6	212/1998
Dr's diagnosis of rhinoconjunctivitis	1.3	37/2789	4.4	236/5347	4.8	216/4532	6.1	121/1987
Current wheezing	5.0	140/2795	7.7	412/5374	8.8	398/4548	8.4	168/2002
Dr's diagnosis of asthma	6.3	172/2750	9.1	484/5330	9.3	421/4551	11.0	217/1979
Current atopic eczema symptoms	8.6	239/2791	9.7	526/5399	11.6	525/4540	14.6	294/2011
Dr's diagnosis of atopic eczema	7.1	198/2790	9.9	535/5383	11.5	521/4525	12.3	246/2001
Atopic sensitisation*	22.7	314/1386	34.7	243/701	32.2	387/1201	39.1	248/634

n, number of children with actual outcome; N, total number of responses to the question/analyses.

*IgE ≥ 0.35 kU/l in Phadiatop® and/or mix of common food allergens (fx5®).

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