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Allergy gap between Finnish and Russian Karelia on increase

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Abstract

Background: Multinational time-trend analyses of atopic disease have shown that the East–West gradients in prevalence are shrinking. We set out to clarify whether the disparities in the occurrence of atopy and atopic diseases in Finnish and Russian Karelia during the past 10 years have diminished and how the prevalence of atopy has evolved with successive years of birth.

Methods: Two surveys with identical methodology were performed in 1997/1998 and 2007. The study population comprised randomly selected adults, aged 25–54 years, from Finnish and Russian Karelia. Serum samples were collected for total and specific IgE measurements. Clinical data were obtained by questionnaires.

Results: Sensitization rates to birch pollen increased from 7.8% to 14.8% ($P < 0.001$) and to cat from 6.1% to 10.8% ($P < 0.001$) in Finland. In Russia, no significant increase was found. Contrary to this, total IgE remained stable in Finland but decreased significantly ($P < 0.001$) in Russia. Analyses based on years of birth revealed that the prevalence of sensitization to allergens increased with successive birth years in Finland, but remained stable in Russia. Over the 10 years, self-reported physician-diagnosed asthma increased from 5.5% to 8.1% ($P = 0.05$) and hay fever from 8.1% to 13.2% ($P < 0.001$) in Finland.

Conclusions: Disparities in the prevalence of atopy and atopic disease between Finnish and Russian Karelia have further grown. The 'allergy epidemic' continues in Finland and is mainly attributable to the years of birth effect shown in atopy prevalence. In Russia, no signs of the epidemic are discernible, although the decrease in total IgE may indicate a change in environmental exposure.

Two large multinational studies, the International Study of Asthma and Allergies in Childhood (ISAAC), launched in 1991, and the European Community Respiratory Health Survey (ECRHS), in 1991–1992, were designed to enable reliable comparisons of the prevalence of allergic diseases between different populations and their trends over time, as earlier studies lacked standardisation in methodology and case definition (1, 2). The former focused on schoolchildren and the latter on adults.

Time-trend analyses of the ECRHS data showed that asthma incidence has progressively increased by years of birth in European adults born between 1946 and 1971; each new generation had more incident asthma than the previous (2). The emerging picture based on the ISAAC data is that although the global burden of asthma and allergic rhinitis is continuing to rise, the global differences in prevalence are shrinking. In many English-speaking countries, the rising trends in occurrence of allergic diseases appear to have levelled off, or even reversed, while in many developing countries, the increase in prevalence has only recently started (1, 3). Thus far, no definite and overarching explanation has been given either for the rise or particularly for the decline in prevalence (4).

In an earlier generational analysis of schoolchildren and their mothers, we found that in Russian Karelia, an economically depressed area next to the Finnish eastern border, the

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younger generation was no more allergic than the older; rather, the opposite was true. In Finland, by contrast, a substantial increase in the prevalence of atopy and atopic disease in children emerged when compared to their mothers. Based on these results, there had been no signs of westernisation, using atopy as a proxy, in Russian Karelia by the year 2003 (5). No systematic time-trend data on allergies are available from Russian Karelia. The last decade is interesting, as the transition crisis in Russia during the 1990s following the collapse of the Soviet Union in 1991 may have to some extent cooled down, and the first early signs of an economic upturn are to be expected (6).

The aim of this survey was to clarify whether the disparities in allergy prevalence between Finnish and Russian Karelia have shrunk, in line with the ISAAC results, by analysing time trends in the prevalence of atopy and atopic diseases between 1997 and 2007, and to compare the possible years of birth effects in time trends of atopy prevalence (determined by specific IgE) among adults in Finnish and Russian Karelia to assess the evolution of sensitization in adults in two contrasting environments over time.

Irrespective of the proximity of these areas and the similarity of their climatic and geo-vegetative conditions, the occurrence of atopy and atopic diseases is many times lower in Russian Karelia than on the Finnish side of the border (5). Owing to the huge economic gap between the areas – one of the deepest in the world – the living conditions in Russian Karelia are simple and still largely resemble those seen in Finland 50 years ago (7). The area was part of Finland until the Second World War, but is now governed by the Russian Federation, and the border, which is also the eastern external border of the European Union, is still strictly guarded. Most of the Finns were moved from the area during the war, and the area was later populated by people from different parts of the Soviet Union. Nonetheless, for historical reasons, the Finnish and Russian Karelians share partly the same ancestry.

Methods

Asthma and allergy studies in North Karelia, in Finland, and in the Republic of Karelia, in Russia, were carried out at regular intervals to monitor changes in the prevalence and risk factors of chronic diseases as part of the National FINRISK Studies in 1997/1998 and 2007 (8) using identical methodology in both survey years. The target population, aged 25–54 years (1500 Finns and 750 Russians in 1997, and 1200 Finns and 750 Russians in 2007), was drawn from population registers and stratified by 10-year age groups and sex as described earlier in detail (9). All the participants in the FINRISK study were included in the asthma and allergy substudy. Owing to the high mortality and economic crisis in Russia during the study period, a large proportion of the sample (n = 105) had died or moved out from the survey area, and thus, the purified sample size in 2007 in Russia was 645. The number of participants in the FINRISK survey in 1997 was 1070 (71%) Finns and 560 (75%) Russians. They were further invited to take part in this asthma and allergy study. Of these, 790 Finns (74%) and 387 (69%) Russians participated. In 2007, the corresponding figures in the FINRISK study were 783 (65%) Finns and 333 (52%) Russians. Of these, 722 Finns (92%) and 311 Russians (93%) also participated in the asthma and allergy study.

Surveys included self-administered questionnaires and health checks that were organised in local health centres and carried out by trained survey nurses. Questionnaires included items on background characteristics and allergic diseases and related symptoms. Serum samples were collected for total and specific IgE (birch, timothy, cat, *Dermatophagoides pteronyssinus* and *Cladosporium herbarum*) measurements using a radioallergosorbent test (UniCAP 1000v2; Pharmacia Upjohn, Uppsala, Sweden). Concentrations of ≥110 IU/l for total IgE and ≥0.35 IU/l for specific IgE were considered as a positive test result. Atopy was defined as one or more positive specific IgE results.

Statistical analyses

Statistical analyses were performed using the SAS program, version 6.12 (SAS Institute Inc., Cary, NC, USA). Categorical data between areas and survey years were compared using the chi-square test. Age and sex adjustments were made using the survey population. Relative risks for atopic diseases and trends between areas and survey years were estimated using log-binomial regression. If the log-binomial model failed to converge, Poisson regression with robust variance was used to estimate RR. Relative risks in Table 3 were adjusted with age and sex and also further with smoking, years of education, living place (urban/rural) and visible

Table 1 Characteristics of the survey samples in Finland (FIN) and in Russia (RUS) in 1997/1998 and 2007

	FIN		RUS	
	1997	2007	1997	2007
N	781	680	386	312
Age (years)				
Mean	40.8	40.2	39.7	41.5
SD	8.3	8.7	8.3	8.8
Sex (%)				
Men	43.5	46.1	35.9	39.3
Women	56.6	53.9	64.1	60.7
Years of education				
Mean	12.0	13.9	11.9	12.2
SD	3.4	3.3	2.5	2.7
Living place (%)				
City/town	40.7	47.7	59.8	54.8
Countryside	59.3	52.3	40.2	45.2
Smoking (%)				
Smoker	26.2	27.2	43.3	43.6
Nonsmoker	74.0	72.8	56.7	56.4

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Table 2 Occurrence of positive total (total IgE ≥ 110 IU/l) and specific IgE (specific IgE ≥ 0.35 IU/l) responses (%) among Finnish and Russian adults and relative risks of positive responses for living in Finland when compared with living in Russia in 1997/1998 and 2007

	FIN			RUS			RR (95% CI) for FIN *vs* RUS	
Allergen	1997	2007	*P*-value	1997	2007	*P*-value	1997	2007
N	772	722		385	305			
Birch	7.8	14.8	<0.001	2.1	3.3	0.33	3.7 (1.81–7.74)	4.5 (2.40–8.53)
Timothy	8.6	14.5	<0.001	3.9	3.6	0.84	2.2 (1.27–3.79)	4.0 (2.20–7.41)
Cat	6.1	10.8	<0.001	2.1	3.9	0.15	2.9 (1.40–6.14)	2.8 (1.52–4.97)
*D. pteronyssinus**	10.4	9.6	0.60	11.7	14.4	0.29	0.9 (0.63–1.25)	0.7 (0.47–0.94)
C. herbarum†	1.9	0.7	0.04	0.5	1.3	0.27	3.7 (0.86–16.27)	0.5 (0.14–1.96)
Any positive‡	21.5	27.1	0.01	15.8	16.7	0.76	1.4 (1.04–1.77)	1.6 (1.23–2.15)
Two or more positive	7.8	15.0	<0.001	3.1	5.6	0.11	2.5 (1.36–4.58)	2.7 (1.66–4.44)
None	78.5	72.9	0.01	84.2	83.3	0.76	0.9 (0.88–0.99)	0.9 (0.82–0.94)
Total IgE	21.8	24.3	0.24	41.6	29.4	<0.001	0.5 (0.44–0.63)	0.8 (0.67–1.03)

**Dermatophagoides pteronyssinus* = House dust mite.

†*Cladosporium herbarum*.

‡Any positive specific IgE response to birch, timothy, cat, house dust mite or *C. herbarum* allergens.

Table 3 The effect of birth year and age on positive specific and total IgE prevalence in Finnish (FIN) and Russian Karelia (RUS)

	FIN				RUS			
	Birth year		Age		Birth year		Age	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Total IgE*								
Unadjusted†	1.04 (0.93, 1.17)	0.473	1.01 (0.98, 1.04)	0.564	0.79 (0.68, 0.92)	0.002	0.97 (0.94, 1.00)	0.056
Adjusted for sex‡	1.04 (0.92, 1.17)	0.532	1.01 (0.98, 1.03)	0.679	0.77 (0.66, 0.90)	0.001	0.96 (0.93, 1.00)	0.032
Birch§								
Unadjusted†	1.35 (1.14, 1.59)	<0.001	0.99 (0.95, 1.03)	0.647	1.05 (0.67, 1.65)	0.817	1.00 (0.91, 1.11)	0.924
Adjusted for sex‡	1.35 (1.14, 1.59)	<0.001	0.99 (0.95, 1.03)	0.664	1.05 (0.67, 1.65)	0.821	1.00 (0.91, 1.11)	0.929
Timothy§								
Unadjusted†	1.30 (1.11, 1.53)	0.001	0.98 (0.94, 1.02)	0.247	0.94 (0.64, 1.38)	0.760	0.96 (0.89, 1.05)	0.379
Adjusted for sex‡	1.30 (1.11, 1.53)	0.002	0.98 (0.94, 1.01)	0.226	0.92 (0.63, 1.35)	0.677	0.96 (0.88, 1.04)	0.309
Cat§								
Unadjusted†	1.27 (1.06, 1.53)	0.010	1.00 (0.95, 1.04)	0.861	1.22 (0.80, 1.87)	0.363	1.03 (0.94, 1.14)	0.475
Adjusted for sex‡	1.27 (1.06, 1.53)	0.010	1.00 (0.95, 1.04)	0.850	1.21 (0.79, 1.85)	0.380	1.03 (0.94, 1.13)	0.499
One positive IgE except *Dermatophagoides pteronyssinus*§								
Unadjusted†	1.24 (1.09, 1.42)	0.001	0.99 (0.96, 1.02)	0.422	1.02 (0.76, 1.35)	0.912	0.99 (0.93, 1.06)	0.853
Adjusted for sex‡	1.24 (1.09, 1.42)	0.001	0.99 (0.96, 1.02)	0.398	1.00 (0.75, 1.33)	0.991	0.99 (0.93, 1.05)	0.758
D. pteronyssinus§								
Unadjusted†	0.96 (0.81, 1.13)	0.604	0.97 (0.94, 1.01)	0.201	1.16 (0.93, 1.43)	0.183	0.99 (0.94, 1.04)	0.664
Adjusted for sex‡	0.95 (0.80, 1.12)	0.556	0.97 (0.94, 1.01)	0.162	1.14 (0.92, 1.41)	0.242	0.98 (0.94, 1.03)	0.515

*Positive response if total IgE ≥ 110 IU/l.

†Birth year groups and age simultaneously in model.

‡Birth year groups and age simultaneously in model, adjusted additionally with sex.

§Positive response if specific IgE ≥ 0.35 IU/l.

mould in the house. None of these adjustments made a difference in the RRs, and thus, only results adjusted with age and sex are shown. For the analysis of the years of birth effect, the population born between 1944 and 1983 was stratified into groups by birth year (5 years). The effect of years of birth and age on total and specific IgE prevalence was assessed by logistic regression models. Odds ratios were adjusted with sex and further with smoking, years of education, living place (urban/rural) and visible mould in the house. None of these adjustments made a difference in the results, and thus, only the unadjusted model and model adjusted with sex are shown.

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Results

The characteristics of the survey samples in Finland and in Russia in 1997/1998 and 2007 are presented in Table 1. In Finland, the sensitization rate to birch pollen increased from 7.8% to 14.8% ($P < 0.001$), to timothy from 8.6% to 14.5% ($P < 0.001$) and to cat from 6.1% to 10.8% ($P < 0.001$) (Table 2). On the Russian side, no significant changes in these sensitization rates occurred. In addition, sensitization rates to house dust mite (*D. pteronyssinus*) did not change significantly on either the Finnish or Russian side. Sensitization to *Cladosporium* was low in both countries in both surveys.

Overall, the occurrence of atopy (any positive specific IgE result) increased significantly only in Finland (from 21.5% to 27%, $P = 0.01$) and the occurrence of polysensitization (two or more positive IgE results) even doubled in Finland (from 7.8% to 15%, $P < 0.001$), whereas the changes in Russia did not reach significance (Table 2).

Compared with the general pattern found for most inhalant allergens, total IgE behaved differently; the prevalence of IgE ≥ 110 IU/l remained stable in Finland over the 10 years, whereas in Russian Karelia, a significant decrease of 30% emerged ($P < 0.001$) (Table 2).

The analysis of the effect of birth years on sensitization rates revealed that every new generation in Finland was more atopic than the previous. The progressive increase in sensitization rates with successive years of birth was similar for birch, timothy and cat (P for the effect of birth years = <0.001, 0.001 and 0.01, respectively) (Fig. 1, Table 3). Again, no increase in the prevalence of sensitization by birth years in Russia could be observed, whereas for total IgE, a significant downward trend by later birth years emerged (Fig. 1, Table 3). Adjustment with sex, years of education, smoking, living in an urban or rural setting and visible mould in the house did not change the results.

Trends in the prevalence of self-reported, physician-diagnosed diseases were in line with the trends in specific IgE results. Over the 10 years, the increase in Finland for asthma was from 5.5% to 8.1% ($P = 0.05$), for hay fever from 8.1% to 13.2% ($P < 0.001$) and for allergic rhinoconjunctivitis from 7.4% to 10.8% ($P = 0.03$). In Russia, the prevalence remained unchanged or even declined 2007 when compared with 1997/1998 (Table 4). The relative risk for physician-diagnosed asthma in Finland *vs* Russia increased from 3.5 to 8.4, for hay fever from 5.2 to 13.6 and for allergic rhinoconjunctivitis from 5.7 to 11.2 (Table 4). Adjustment with age, sex, years of education, smoking, living in an urban or rural

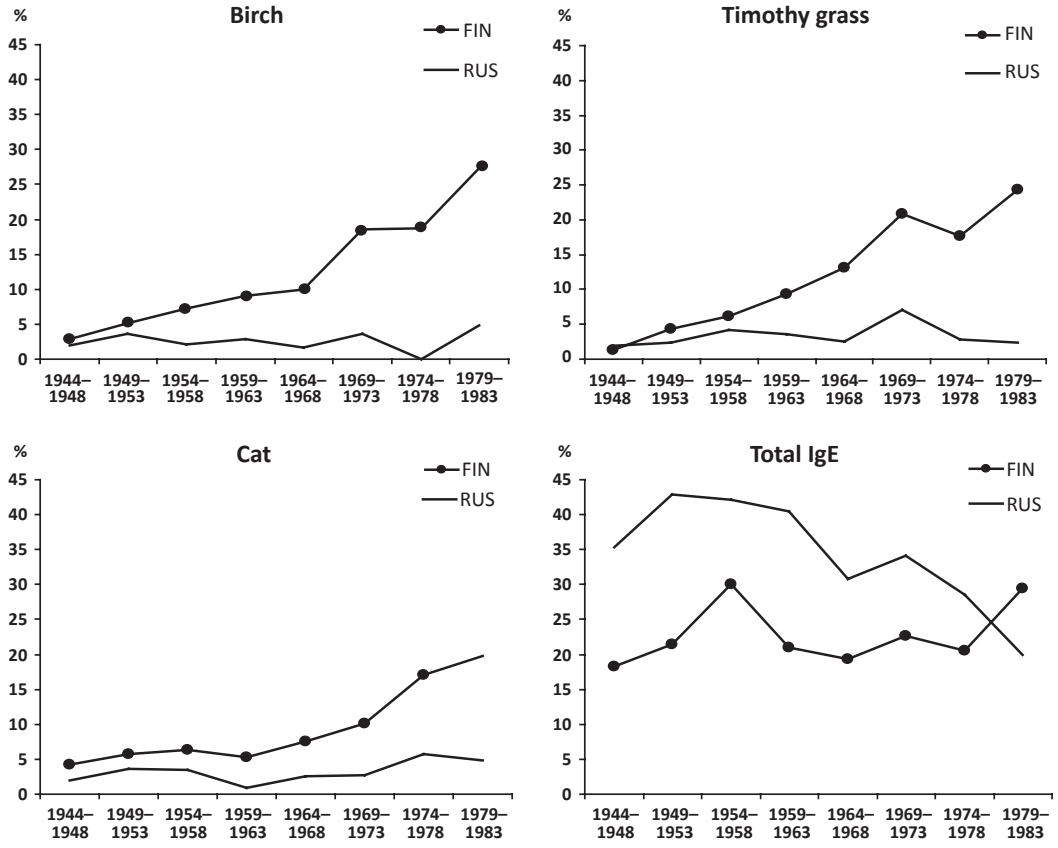

Figure 1 The prevalence of positive IgE response in total IgE (≥110 IU/l), birch (≥0.35 IU/l), timothy grass (≥0.35 IU/l) and cat (≥0.35 IU/l) according to birth year in Russian (RUS) and Finnish Karelia (FIN). Odds ratios (OR) for birth year and age effect are found in Table 3, both unadjusted and adjusted with sex.

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Table 4 Occurrence (%) of self-reported atopic diseases among Finnish (FIN) and Russian (RUS) adults and relative risks of atopic diseases for living in Finland when compared with living in Russia in 1997/1998 and 2007

	FIN			RUS			RR (95% CI) for FIN *vs* RUS	
Disease/symptoms	1997	2007	*P*-value	1997	2007	*P*-value	1997	2007
N	773	679		383	310			
Hay fever, ever*								
Unadjusted	21.9	30.5	<0.001	4.2	5.8	0.32	5.29 (3.2–8.7)	5.28 (3.3–8.4)
Adjusted†	22.1	30.8	<0.001	3.9	5.3	0.19	5.50 (3.4–9.1)	5.27 (3.3–8.4)
Hay fever, phys-dg‡								
Unadjusted	8.1	13.2	<0.001	1.6	1.0	0.49	5.23 (2.3–12.0)	13.63 (4.3–42.7)
Adjusted†	8.3	13.4	0.001	1.4	0.9	0.71	5.63 (2.5–12.9)	13.66 (4.4–42.8)
Rhinoconjunctivitis, ever								
Unadjusted	23.7	32.1	<0.001	3.9	3.9	0.98	6.07 (3.6–10.1)	8.32 (4.7–14.6)
Adjusted†	23.9	32.6	<0.001	3.7	3.6	0.52	6.31 (3.8–10.5)	8.39 (4.8–14.8)
Rhinoconjunctivitis, phys-dg								
Unadjusted	7.4	10.8	0.03	1.3	1.0	0.68	5.73 (2.3–14.2)	11.15 (3.5–35.1)
Adjusted†	7.5	11.2	0.01	1.2	0.8	0.67	6.33 (2.6–15.6)	11.45 (3.6–36.0)
Atopic eczema, ever								
Unadjusted	28.1	30.4	0.33	11.6	18.4	0.11	2.43 (1.8–3.3)	1.65 (1.3–2.1)
Adjusted†	28.1	30.8	0.17	11.5	17.6	0.02	2.51 (1.9–3.4)	1.63 (1.3–2.1)
Atopic eczema, phys-dg								
Unadjusted	17.7	18.7	0.60	7.8	8.7	0.67	2.25 (1.5–3.3)	2.14 (1.4–3.2)
Adjusted†	17.7	19.2	0.25	7.7	8.6	0.33	2.36 (1.6–3.4)	2.19 (1.5–3.2)
Asthma, ever								
Unadjusted	5.8	9.0	0.02	2.1	1.0	0.24	2.78 (1.3–5.8)	9.33 (2.9–29.5)
Adjusted†	5.9	9.1	0.01	2.1	0.7	0.93	2.79 (1.3–5.9)	9.48 (3.0–30.0)
Asthma, phys-dg								
Unadjusted	5.5	8.1	0.05	1.6	1.0	0.48	3.53 (1.5–8.2)	8.40 (2.6–26.6)
Adjusted†	5.6	8.3	0.03	1.5	0.7	0.81	3.56 (1.5–8.3)	8.60 (2.7–27.3)

*Ever occurred, self-reported symptoms/disease.
†Adjusted for age and sex.
‡Self-reported physician-diagnosed disease.

setting and visible mould in the house did not change the results.

Discussion

Repeated studies in Finnish and Russian Karelia provide a unique means of studying allergy trends in two contrasting environments. We found here that the 'allergy epidemic' still continues in Finland, contrary to Russia, where there was no increase in allergy prevalence. This finding was consistently shown by all the indicators/measures used, specific and total IgE measurements, the occurrence of self-reported diseases and years of birth analyses.

Over 10 years, sensitization rates for birch/timothy/cat allergens have nearly doubled in Finnish adults and the prevalence of asthma and allergic rhinitis increased by 46–63%. In Russia, by contrast, the changes in sensitization rates or the prevalence of atopic disease have been negligible.

Our finding is in contrast to the results of the ISAAC showing that, in general, disparities in asthma and allergy prevalence worldwide are shrinking (1). Our results differ even from those of von Mutius et al. (10), who showed that only a couple of years after the fall of the Iron Curtain, children from the former East Germany began to resemble their western counterparts with respect to hay fever prevalence and sensitization rates. This was most likely due to the tremendous improvement in living conditions in the East German population after the fall of the Iron Curtain; such development has not as yet been seen in Russian Karelia. Several reports have further shown that in many former socialist countries, the allergy trends are now on the increase (11, 12).

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All participants in this study were born during the Soviet Era. Allergy, and asthma in particular, is considered to have its origin very early in life (13, 14). An analysis of the effect of birth year among adults from the former East and West Germany revealed that in subjects born before the division of Germany in 1949, no East–West differences in allergy prevalence were found. However, divergent trends in atopy emerged among those born during the era of the Iron Curtain and these trends had not begun to converge several years after reunification (15). Immigration studies, on the other hand, have provided compelling evidence that even in adults, the new environment can readily modulate the immigrant's immunological tolerance; the longer the immigrant has lived in the new environment, the more his/her atopy status resembles that of the original population (16).

Nonetheless, during the 18 postcommunist years in Russian Karelia, apparently no major change for the better has occurred in living conditions. Improvement in socioeconomic indicators has been slow because of the transition crisis in the 1990s and the fact that the old power blocks and new oligarchic structures have hindered the privatisation of the economy and the creation of democratic institutions (6).

Increase in the prevalence of sensitization does not necessarily mean an increase in clinical relevant allergy, as shown recently in a time-trend analysis of Swedish children (17). In the present study, however, the occurrence of both clinical diseases and sensitization among Finnish adults increased progressively over the 10 years, providing convincing evidence that changes in labelling or improved recognition of cases are not the cause of the 'allergy epidemic'. The prevalence of total IgE ≥ 110 IU/l remained unchanged in Finland, but, interestingly, showed a downward trend in Russia. Whether this may implicate a decreasing parasite load, an early indicator of improving living conditions in Russia, remains to be seen. A small nonsignificant increase in house dust mite sensitization, particularly monosensitization, is not necessarily associated with atopic diseases, but may be a marker of exposure only (18).

These studies were carried out following the same methodology in both survey years and areas. Self-reported diseases and symptoms are always likely to cause either under- or overreporting. We have earlier found that subjects in Russia seem to report more asthma- and atopy-related symptoms without having as IgE component or positive prick tests than subjects in Finland (19). This most likely is due to higher prevalence of other conditions in the area that cause similar symptoms (smoking, infectious diseases and other lung diseases). Thus, analyses in this study have concentrated on allergy estimates based on more objective measures such as specific IgE response. The samples of these studies are random population samples, but the nonresponse has increased slightly between the two survey years. In population surveys, the most usual health reasons for nonresponse are excessive alcohol use and diseases that substantially decrease functional capacity. Prevalent allergy and asthma and their symptoms as the reason for nonresponse would have had a diluting effect on the results.

The analysis of sensitization rates by years of birth corroborated further that the 'allergy epidemic' in Finland does exist and is mostly explained by the birth year effect, i.e. each new generation is more atopic than the previous. A similar finding has earlier been shown among adult Greenlanders (20) and Finns (21). Data on sensitization rates from Middle-European children have in turn shown opposite or plateaued trends (11–17, 22–24). When compared with the two earlier studies including adults (20, 21), we went further here and analysed the effect of birth year for each common inhalant allergen separately. We also found that adults do not become more atopic as they age. The sharp increase in atopy prevalence among Finns born from the 1960s onwards coincides with mass movements from rural to urban areas that occurred particularly in the 1960s and 1970s in Finland. The substantial rise in sensitization rates irrespective of unchanged exposure (e.g. birch and timothy) over 10 years points to impaired tolerance mechanisms in groups with successive years of birth. In this study, the adjustment of data by living conditions after the end of the 1990s did not affect the results as the effect of urbanisation most likely originates in early childhood, which in the case of this segment of the Finnish population was 20–30 years before the data were collected.

In conclusion, divergent trends in atopy and atopic diseases during 1997–2007 emerged between Finnish and Russian Karelia. The allergy gap between these two geographically adjacent areas has further widened.

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Conflict of interest

None of the authors have any conflict of interest.

Ethics committee approval

The study protocol has in both survey years been approved by the Coordinating Ethics Committee of the Helsinki University Hospital District. All participants have given their informed consent.

Contribution of authors

All the authors have been involved in planning the study protocol and analysing the data. TV, TL, PJ and MA were involved in and responsible for the practical implementation of data collection under the supervision of TH and EV. TL and J-PK performed the data analyses. The major responsibility for writing was assumed by TL, LvH and J-PK. MM, TUK, PJ, EV, TV and MA critically reviewed and commented on the manuscript.

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References

1. Pearce N, Ait-Khaled N, Beasley R, Mallol J, Keil U, Mitchell E et al. Worldwide trends in the prevalence of asthma symptoms: phase III of the International Study of Asthma and Allergies in Childhood (ISAAC). *Thorax* 2007;**62**:758–766.
2. Sunyer J, Anto JM, Tobias A, Burney P for the European Community Respiratory Health Study (ECRHS). Generational increase of self-reported first attack of asthma in fifteen industrialized countries. *Eur Respir J* 1999;**14**:885–891.
3. Björksten B, Clayton T, Ellwood P, Steward A, Strachan D; ISAAC Phase III Study Group. Worldwide time trends for symptoms of rhinitis and conjunctivitis: Phase III of the International Study of Asthma and Allergies in Childhood. *Pediatr Allergy Immunol* 2008;**19**:110–124.
4. Partridge MR. Has ISAAC told us as much as it can? Where now? *Thorax* 2009;**64**:482–483.
5. von Hertzen L, Mäkelä MJ, Petäys T, Jousilahti P, Kosunen TU, Laatikainen T et al. Growing disparities in atopy between the Finns and the Russians – a comparison of 2 generations. *J Allergy Clin Immunol* 2006;**117**:151–157.
6. Liikanen I, Zimin D, Ruusuvuori J, Eskelinen H. Karelia – a cross-border region? The EU and cross-border region-building on the Finnish-Russian border. Publications of the Karelian Institute no. 146. University Press, Joensuu, 2007.
7. Laatikainen T, Vartiainen E, Puska P, Pokusajeva S, Uhanov M. Pitkäranta-project. Risk factors and health behaviour in Pitkäranta, the Republic of Karelia in 1992 and 1994 (in Finnish, English summary). Publications of the National Public Health Institute B5/1996. Helsinki, 2006.
8. Vartiainen E, Laatikainen T, Peltonen M, Juolevi A, Männistö S, Sundvall J et al. Thirty-five-year trends in cardiovascular risk factors in Finland. *Int J Epidemiol* 2009; **39**:504–518.
9. Vartiainen E, Petäys T, Haahtela T, Jousilahti P, Pekkanen J. Allergic diseases, skin prick test responses, and IgE levels in North Karelia, Finland, and the Republic of Karelia, Russia. *J Allergy Clin Immunol* 2002;**109**:643–648.
10. von Mutius E, Weiland SK, Fritzsch C, Duhme H, Keil U. Increasing prevalence of hay fever and atopy among children in Leipzig, East Germany. *Lancet* 1998;**351**: 862–866.
11. Annus T, Riikjärv MA, Rahu K, Björksten B. Modest increase in seasonal allergic rhinitis and eczema over 8 years among Estonian schoolchildren. *Pediatr Allergy Immunol* 2005;**16**:315–320.
12. Kudzyte J, Griska E, Bojarskas J. Time trends in the prevalence of asthma and allergy among 6-7 year-old children. Results from ISAAC phase I and III studies in Kaunas, Lithuania. *Medicina* 2008;**44**:944–952.
13. Schaub B, Campo M, He H, Perkins D, Gillman MW, Gold DR et al. Neonatal immune responses to TLR2 stimulation: influence of maternal atopy on Foxp3 and IL-10 expression. *Respir Res* 2006;**7**:40.
14. Roponen M, Hyvärinen A, Hirvonen MR, Keski-Nisula L, Pekkanen J. Change in IFN-γ-producing capacity in early life and exposure to environmental microbes. *J Allergy Clin Imminol* 2005;**116**:1048–1052.
15. Heinrich J, Nowak D, Wassmer G, Jörres R, Wjst M, Berger J et al. Age-dependent differences in the prevalence of allergic rhinitis and atopic sensitization between an eastern and western German city. *Allergy* 1998; **53**:89–93.
16. Kalyoncu AF, Stålenheim G. Serum IgE levels and allergic spectra in immigrants to Sweden. *Allergy* 1992;**47**:277–280.
17. Rönmark E, Bjerg A, Perzanowski M, Platts-Mills T, Lundbäck B. Major increase in allergic sensitization in schoolchildren from 1996 to 2006 in northern Sweden. *J Allergy Clin Immunol* 2009;**124**:357–363.
18. Hertzen L, Laatikainen T, Pennanen S, Mäkelä MJ, Haahtela T; Karelia Allergy Study Group. Is house dust mite monosensitization associated with clinical disease? *Allergy* 2008;**63**:379–381.
19. Pekkarinen P, von Herzen L, Laatikainen T, Mäkelä M, Jousilahti P, Kosunen T et al. A disparity in the association of asthma, rhinitis and eczema with allergen specific IgE between Finnish and Russian Karelia. *Allergy* 2007;**62**:281–287.
20. Krause T, Koch A, Friborg J, Poulsen LK, Kristensen B, Melbye M. Frequency of atopy in the Arctic in 1987 and 1998. *Lancet* 2002;**360**:691–692.
21. Isolauri E, Huurre A, Salminen S, Impivaara O. The allergy epidemic extends beyond the past few decades. *Clin Exp Allergy* 2004;**34**:1007–1010.
22. Zöllner IK, Weiland SK, Piechotowski I, Gabrio T, von Mutius E, Link B et al. No increase in the prevalence of asthma, allergies and atopic sensitisation among children in Germany: 1992–2001. *Thorax* 2005;**60**: 545–548.
23. Braun-Fahrländer C, Gassner M, Grize L, Takken-Sahli K, Neu U, Stricker T et al.; the Swiss Study on Childhood Allergy and Respiratory symptoms with respect to SCARPOL team. No further increase in asthma, hay fever and atopic sensitisation in adolescents living in Switzerland. *Eur Respir J* 2004;**23**:407–413.
24. Thomsen SF, Ulrik CS, Forsbjerg C, Backer V. Skin test reactivity among Danish children measured 15 years apart. *J Asthma* 2006;**43**:151–153.

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