

ORIGINAL ARTICLE

Trends of allergic symptoms in school children: large-scale long-term consecutive cross-sectional studies in Osaka Prefecture, Japan

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Abstract

Background: Trends in the prevalence rates of allergic symptoms in children have been discussed extensively, but it remains uncertain which symptoms increase or decrease over time owing to the lack of large-scale long-term consecutive cross-sectional studies performed on a representative population of children.

Objective: To clarify the trends in the prevalence rates of allergic symptoms in Japanese children.

Methods: Total population questionnaire surveys were conducted 15 times from 1975 to 2006 for all children attending public elementary schools in Osaka Prefecture, Japan, with the number of subjects ranging from 460,000 to 900,000. Parents of the children completed the questionnaire about allergic symptoms and other symptoms, including wheeze, physician-diagnosed atopic dermatitis, rhinitis, and itching eyes.

Results: Response rates were consistently over 90%. The prevalence of wheezing was constant until 1983, then increased from 1983 until 1993, then stabilized at about 4.4%. The lifetime prevalence of atopic dermatitis increased to 24% by 1993, and then decreased. The prevalence of rhinitis increased to 25% by 2003, whereas the prevalence of non-seasonal symptoms plateaued from 1993 on at 11% and vernal symptoms increased. The prevalence of itching eyes continued to increase to 21% in 2006, and vernal symptoms increased sharply.

Conclusions: In Osaka Prefecture, Japan, the turning point when the prevalence of wheezing in schoolchildren had begun to increase was 1983. And the turning point when the increase in the prevalence of wheezing, atopic dermatitis, and non-seasonal allergic rhinitis turned to decrease or constant was 1993. The prevalence of rhinitis and itching eyes in spring was still increasing in 2006.

The prevalence of pediatric allergic diseases has increased throughout the world in the past 50 yr, Japan being no exception (1–6). However, the scope of allergic diseases includes asthma, atopic dermatitis, and allergic rhinitis, and these conditions often follow one after the other as an atopic child grows in the ‘allergic march’ (7–9). Therefore, it is no easy matter to elucidate how the different allergic conditions have increased over the years, and how their characteristics have changed over the years. A large number of studies have examined the changes in the prevalence of individual conditions (10–14). A number of surveys have addressed changes in the main allergic conditions over the same time period, but most of these are cross-sectional

surveys with only a limited number of time points (15–20). It has until now been unclear how allergic conditions overall have increased over time.

In Osaka Prefecture, Japan, questionnaire surveys have investigated various symptoms targeting all public primary schoolchildren over many years, with the aim of monitoring the health of children (21). A total of 15 surveys were conducted at two to three yearly intervals between 1975 and 2006, using the same survey format, providing data about changes in childhood subjective symptoms over a 30-yr period. The number of children surveyed each time was of the order of 460,000 to 900,000, and responses were consistently received from approximately 90% of all primary schoolchildren in this

region, corresponding to a complete survey of the target population. Such a large-scale complete survey of uniform age populations in the same region over a long period is unprecedented. In this study, we present an overview of changes over the last 30 yr in allergic conditions (wheezing, atopic dermatitis, allergic rhinitis, and pollinosis symptoms) in Japanese children, identified in detail by our large-scale long-term consecutive cross-sectional surveys.

Methods

Survey

The Osaka Children's Health Study has conducted a total of 17 surveys, including a survey every 2 yr from 1971 to 1997 and thereafter a survey every 3 yr until 2006, jointly with the Osaka Medical Association and the Osaka Prefectural Board of Education. We investigated 15 sets of available survey results from 1975 to 2006. Each survey was a questionnaire about symptoms that targeted all the children at public elementary schools (7–12 yr old) in Osaka Prefecture, which has a total population of about 8.8 million and contains Osaka City, the third largest city in Japan, in the central area.

Subjects

Table 1 shows the number of elementary schools and the number of children surveyed each time. In 2006, there were a total of 1041 elementary schools, of which 1022 were public schools. Three state-run schools and 16 private schools were excluded because the living area of the children could not be determined. A total of 1015 public schools (99.3%) participated in the survey. Of the 490,505 children enrolled therein, responses were received for 452,213 children

(response rate: 92.2%). The response rate as a proportion of the number of eligible children (the total number of children attending all public elementary schools in Osaka Prefecture: 493,025) was 91.7%. The proportion of the number of the respondents to the total number of children attending elementary schools located in Osaka Prefecture was 90.8%. The response rate was approximately 90% for every survey. Changes in the number of children surveyed were because of population fluctuations in the relevant age range (Table 1).

School totalization tables

School personnel in charge of the survey distributed the questionnaire to the children in mid-October each time and asked the parents to answer questions about subjective symptoms. The questionnaires were recovered by each school, and the number of responses was totaled for each grade. We collected these school totalization tables and used them to perform overall totalization and statistical analysis.

Individual questionnaires

Osaka Prefecture was classified into five areas, which were a mainly industrial area, a mainly commercial area, an urban residential area, a suburban residential area, and a rural area. Several schools from each area, 30 in total, were randomly selected to investigate relationships among individual symptoms. For the schools thus selected, we collected the individual questionnaire forms and 24–27 of them participated in the survey. As the number of children in each survey gradually decreased because of the declining birth rate, an additional 16 schools were selected in 2003 and 41–44 of them participated thereafter. The number of collected individual

Table 1 Number of elementary schools, number of pupils, and response rate for each survey

	Total number of schools in Osaka Prefecture*	Number of schools surveyed	Total number of pupils in Osaka Prefecture (a)*	Total number of pupils in the schools surveyed (b)	Number of pupils responding (c)	Response rate (%) (c/b)	Response rate (%) (c/a)
1975	874	848	802,399	770,602	729,048	94.6	90.9
1977	920	882	861,417	822,356	788,859	96.0	91.6
1979	964	940	913,952	891,947	858,679	96.3	94.0
1981	1007	985	919,423	900,767	871,008	96.7	94.7
1983	1033	1009	868,263	853,461	828,252	97.0	95.4
1985	1040	1001	791,034	764,106	741,823	97.1	93.8
1987	1041	1000	702,763	677,367	657,542	97.1	93.6
1989	1047	1008	642,170	619,270	598,893	96.7	93.3
1991	1049	1002	595,996	568,119	539,683	95.0	90.6
1993	1050	1007	564,944	541,726	514,656	95.0	91.1
1995	1049	1012	541,307	520,476	496,158	95.3	91.7
1997	1050	1016	508,490	489,725	458,284	93.6	90.1
2000	1050	1014	490,815	468,083	437,589	93.5	89.2
2003	1049	1022	483,288	475,639	443,503	93.2	91.8
2006	1041	1015	498,170	490,505	452,213	92.2	90.8

*Including some state schools and private schools that were excluded from the surveys.

questionnaires ranged from 8295 to 16,767 with the response rate of 91.7–95.1%.

Survey questions

The questionnaire was a single-page document, with 11–13 questions regarding common subjective symptoms. Of these, we analyzed eight questions concerning allergic symptoms in this study (Table 2). We considered a positive response to question 1 to denote a child with wheezing; a positive response to question 2, with a doctor diagnosing atopic dermatitis, to denote a child with a history of atopic dermatitis; and a positive response to question 3, with a doctor diagnosing atopic dermatitis within the previous 1-yr period, to denote a child with a atopic dermatitis within the previous year. We considered a positive response to question 4 to denote a sneezing child, a positive response to question 5 to denote a child with rhinitis, and a positive response to question 7 to denote a child with itching eyes. We further asked the child with rhinitis and itching eyes which season/s (possibly two or more) they experienced the symptoms from question 6 or 8, asking them to choose from: (1) spring, (2) summer, (3) autumn, (4) winter, or (5) year round (no particular season). Questions about sneezing and rhinitis were added to the survey form in 1983, although the sneezing question was cut out in 1993. The question about a history of atopic dermatitis was added in 1985, and the questions regarding atopic dermatitis within the previous year, itching eyes, and the seasonal breakdown were added in 1993.

Prevalence of symptoms

The prevalence of each symptom was determined by dividing the number of symptomatic persons by the total number of

respondents. To examine the trends of prevalence rates during the study period, differences of age composition were adjusted by using the respondents in 2000 as the reference group. With respect to itching eyes, the wording of the question was modified for the 1997 survey, so the prevalence in 1997 was excluded from analysis.

Results

The trends in the overall prevalence of each allergic symptom in Osaka Prefecture are shown in Fig. 1. The prevalence of wheezing was constant at $3.0 \pm 0.1\%$ between 1975 and 1983, then increased to 4.7% in 1993. It again stabilized at $4.4 \pm 0.3\%$ between 1993 and 2006. The lifetime prevalence of atopic dermatitis (a history of this condition), a question added to the survey in 1985, increased sharply from 15.3% in that year to 24.2% in 1993, then decreased to 16.5% in 2006. The prevalence of atopic dermatitis within the previous year decreased gradually from 6.8% in 1993 to 4.6% in 2006. The prevalence of sneezing increased from 11.6% in 1983 to 15.1% in 1991 and that of rhinitis increased from 12.3% to 16.7% over the same period. The prevalence of rhinitis increased further to 25.4% in 2003, then leveled out to 24.7% in 2006. The prevalence of itching eyes increased from 13.9% in 1993 to 21.0% in 2006, with most of the increase occurring after 2000 (Table S1).

Fig. 2 shows the trends in the seasonal prevalence of rhinitis and itching eyes. Rhinitis patients with non-seasonal symptoms were in the majority, followed by those with symptoms in spring or autumn. There were few rhinitis patients with symptoms in winter or summer. The prevalence of non-seasonal rhinitis remained almost constant (at around 11%) from 1993 to 2006, but the prevalence of rhinitis during spring increased from 5.1% to 8.9% over the course of this 13-yr period. The prevalence of rhinitis during autumn also increased slightly. The symptom of itching eyes was most

Table 2 Questions

Please circle the number next to any of the following statements that apply to your child

1. Even when my child does not have a cold, he/she is often wheezy
2. We have been told by a doctor at some time in the past that my child has atopic dermatitis
3. We have been told by a doctor within the previous year that my child has atopic dermatitis
4. Even when my child does not have a cold, he/she often sneezes
5. Even when my child does not have a cold, after sneezing he/she often gets a runny nose or stuffy nose
6. (only if you circled no. 5) During which season(s) does this happen (can circle two or more)?
(1) Spring (2) Summer (3) Autumn (4) Winter (5) Year round (no particular season)
7. At the same time each year, my child gets itchy eyes
8. (only if you circled no. 7) During which season(s) does this happen (can circle two or more)?
(1) Spring (2) Summer (3) Autumn (4) Winter (5) Year round (no particular season)

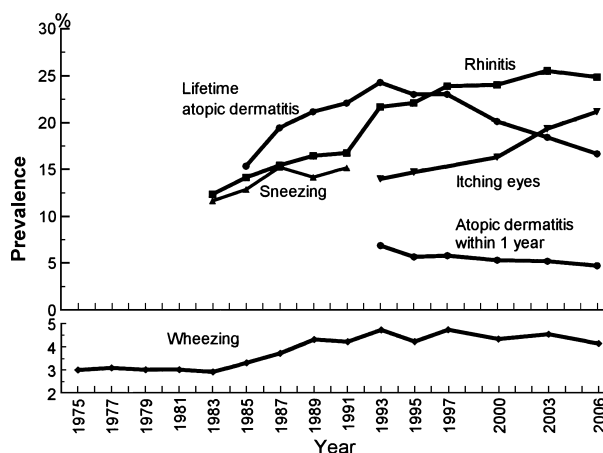


Figure 1 Trends in the age-adjusted prevalence rates* of allergic symptoms. *The age composition of pupils in each survey was adjusted by using the respondents in 2000 as the reference population.

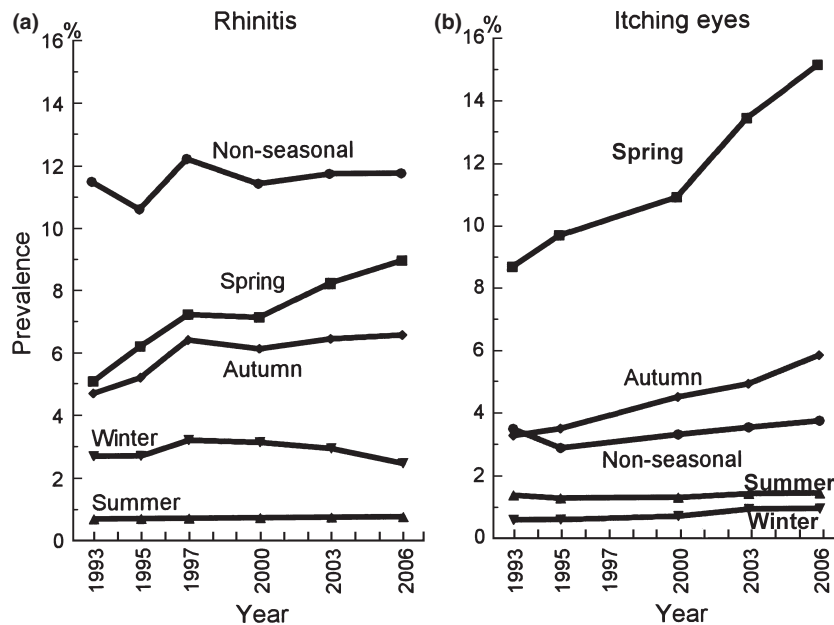


Figure 2 Trends in the age-adjusted prevalence rates* of allergic symptoms by season. *The age composition of pupils in each survey was adjusted by using the respondents in 2000 as the reference population.

common in spring and its prevalence during spring increased sharply from 8.7% to 15.1% over the same 13-yr period. The prevalence during autumn also increased somewhat from 3.3% to 5.8%, while the prevalence of non-seasonal symptoms was constant at about 3.5% (Table S2).

Surveys were conducted at 2-yr intervals until 1997, so students in first to fourth grade at one survey would be in third to sixth grade at the next. Approximately two of three students participating in a given survey also participated in the next survey and approximately half of those in the following one. After 1997, surveys were conducted at 3-yr intervals, so students in first to third grade at one survey would be in fourth to sixth grade at the next, and so half of students participating in a given survey also participated in the next

survey. Fig. 3 plots prevalence of non-seasonal and vernal rhinitis and itching eyes according to school grade, showing changes in prevalence within birth cohorts as straight lines. The prevalence of non-seasonal rhinitis and itching eyes were lowest among first-grade children and highest in fifth-grade and sixth-grade children, showing a steady increase with age. The prevalence in each school grade was mostly stable over the 13-yr survey period. The prevalence of vernal rhinitis and itching eyes was higher as the school grade advanced, as for non-seasonal symptoms, but a significant increase in vernal symptoms was seen in every grade over the 13 yr of survey, particularly marked in sixth-grade children (Table S3).

Fig. 4 shows the trends in the prevalence of children with at least one allergic symptom that were determined by

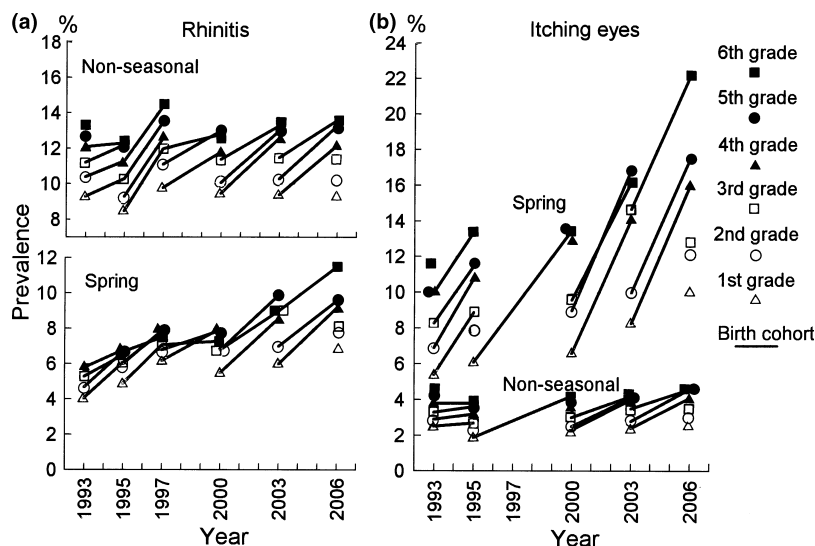


Figure 3 Trends in the prevalence of allergic symptoms by birth cohort analysis.

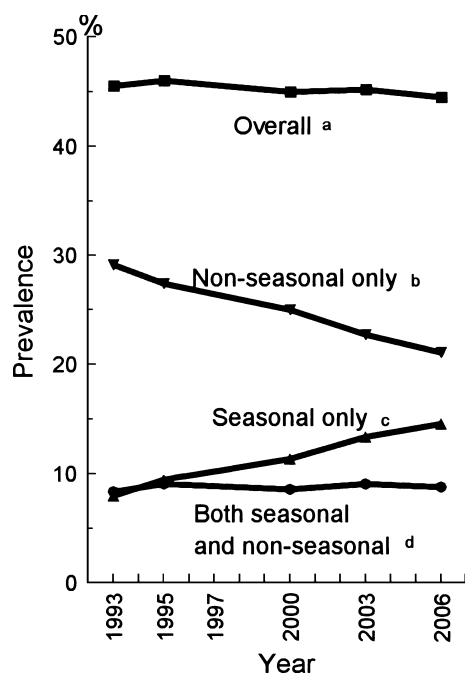


Figure 4 Trends in the rate of those who had at least one allergic symptom. ^aChildren with at least one allergic symptom from among wheezing, lifetime atopic dermatitis, atopic dermatitis within the past year, rhinitis, and itching eyes. ^bChildren with at least one symptom regardless of the season, from among wheezing, lifetime atopic dermatitis, atopic dermatitis within the past year, and non-seasonal rhinitis or itching eyes. ^cChildren with at least one seasonal symptom from among rhinitis or itching eyes in spring, summer, autumn, or winter. ^dChildren who had both seasonal and non-seasonal symptoms.

reviewing individual questionnaires from a set of schools selected by consideration of regional characteristics. The percentage of children with at least one positive allergic symptom among wheezing, lifetime atopic dermatitis, atopic dermatitis within the past year, rhinitis, and itching eyes was about 45% from 1993 to 2006, i.e., the rate was almost constant. However, the percentage of children who had at least one symptom regardless of season (that is, wheezing, lifetime atopic dermatitis, atopic dermatitis within the past year, and non-seasonal rhinitis or itching eyes) decreased from 29% to 21% over the course of this 13-yr period. On the other hand, the percentage of children who had at least one seasonal symptom (rhinitis or itching eyes during spring, summer, autumn, or winter) increased from 8% to 15% during the same period. Children who had both seasonal and non-seasonal symptoms accounted for around 9% of the survey population and remained constant throughout the 13-yr period (Table. S4).

Discussion

In this study, we present the long-term trends in the prevalence of allergic conditions in Japanese children, taken from

the results of surveys conducted every 2 or 3 yr over a 30-yr period with the aim of monitoring the health of children in the area. A number of studies have been published concerning changes in pediatric allergic conditions (1–6, 10–14). However, most of these have conducted only a small number of surveys over at most from 5- to 10-yr period (15–20), and they have been unable to identify turning points in prevalence trends that might occur between surveys. In this study, we showed that the prevalence of wheezing in Osaka children, stable since 1975, began to increase in 1983, and then entered another period of stability in 1993. The lifetime prevalence of atopic dermatitis increased sharply at the same time as the period of rising wheezing prevalence and began to decrease in 1993. The prevalence of rhinitis also increased between 1983 and 1993 as did that of wheezing. The prevalence of rhinitis then increased sharply to 21.6% in 1993, possibly because the sneezing question was cut out that year, and a number of respondents with mild disease and sneezing as their main symptom answered the rhinitis question in the affirmative. The prevalence of non-seasonal rhinitis subsequently remained fairly constant, whereas the prevalence of rhinitis and itching eyes during spring continued to rise.

Japan enjoyed a period of rapid economic growth between 1956 and 1973, with an average yearly economic growth of 9%, followed by a period of consistent economic growth between 1974 and 1990 averaging 4% (Japanese Government Cabinet Office: 'Annual Report on National Accounts'). The proportion of Japanese households with an electric refrigerator was only 10% in 1960, rising to 51% in 1965, and exceeding 96% in 1975 (Japanese Government Cabinet Office: 'Annual Consumer Confidence Survey Report'). The standard of living of the Japanese people and the standard of public health and medical services improved as the economy grew. This was also associated with a decrease in infectious diseases [incidence rate per 100,000 population: dysentery 100.6 (1960), 1.3 (1975), 0.7 (2000); tuberculosis 524.2 (1960), 96.6 (1975), 31.0 (2000); Ministry of Health, Labour and Welfare: 'Statistics on Communicable Diseases']. As the nutritional status of the Japanese people improved, their diet became increasingly Westernized, and their consumption of meat and fat increased [proportion of energy intake from fat: 8.7% (1955), 22.3% (1975), 26.5% (2000); Ministry of Health, Labour and Welfare: 'The National Nutrition Survey in Japan']. On the other hand, the number of children per household has decreased over the same period [total fertility rate: 3.65 (1950), 1.91 (1975), 1.36 (2000)]. In the previous study, we reported that the lifetime prevalence of atopic dermatitis was more common in areas with a higher income level, although a similar rate of increase in the prevalence of this condition was seen up until 1993 in all income groups, and the differences in prevalence between income levels have become smaller (21). As espoused in the 'hygiene hypothesis' (8), pediatric allergic conditions increased until 1993 as a modern urban lifestyle became more common in this country. Subsequently, the lifetime prevalence of atopic dermatitis has become less common, and the prevalence of wheezing, atopic dermatitis within the previous year, and non-seasonal rhinitis has been stable.

Over the same period, however, rhinitis and itching eyes in spring and autumn, of the pollinosis type, continued to increase. In Japan, pollen of the Japanese cedar (*Cryptomeria japonica*) and the Japanese cypress (*Chamaecyparis obtusa*), which shares common antigenicity with the Japanese cedar, spreads ubiquitously through the air at high levels from February to May, and the number of pollinosis patients has increased over the past 40 yr to become a major concern (22–24). Some 70% of the land surface of Japan is covered in forest, and 28% of those forests are made up of plantations of the Japanese cedar and the Japanese cypress (Japanese Forestry Agency: 'State of Forestry Resources' 2007). These Japanese cedar and Japanese cypress plantations are little utilized at present, as imported timber is much cheaper. We can therefore expect large amounts of Japanese cedar and Japanese cypress pollen for the foreseeable future. It is possible to reduce exposure to house dust mite, the major allergen associated with pediatric allergic conditions (25–27), through room cleaning and other measures, but it is difficult to avoid exposure to airborne pollens. It is therefore possible that the number of spring pollinosis sufferers will continue to rise in the future.

As shown in Fig. 4, the proportion of children with at least one allergic symptom of some sort has been stable over the last 13 yr. It is unclear, however, whether this is the upper limit of children with allergies or whether the decrease in the prevalence of non-seasonal symptoms and the increase in seasonal symptoms have just happened to be about the same. This will be the subject of future studies. The decrease in non-seasonal allergic symptoms appears mainly to be as a result of a decrease in the proportion of children with a history of atopic dermatitis. We need to determine whether or not children with only seasonal allergic symptoms had a history of asthma as infants, but it is possible that more children are developing pollinosis alone without experiencing the 'allergic march', the traditional pattern of development of allergic diseases.

Because of the extremely large number of subjects for this survey, we made the questionnaire just one page long and the questions as simple and easy to understand as possible. This could conceivably affect the accuracy of the survey. The question from which we derived the prevalence of atopic dermatitis refers to diagnoses made by medical practitioners. We did not confirm the diagnosis through any dermatological testing. Furthermore, during the early years of this survey, there were no standard diagnostic criteria for allergic condi-

tions. The increased prevalence of allergic conditions has become a matter of public concern, and the reported prevalence may have been further inflated by an increased rate of presentation for treatment, overdiagnosis, or parental misreporting. The increased prevalence of allergic conditions seen in this study cannot be fully explained by changes in public awareness, however, because the prevalence of atopic dermatitis has fallen over the last 10 yr, a period of heightened public awareness.

As described previously, rapid postwar economic growth in Japan brought about considerable changes in the social environment and lifestyle of the populace. The Japanese economy then entered a period of stable growth and has now entered a period of low growth. We can expect that developing countries will follow a similar pattern. Our survey results, showing the trends in pediatric allergic conditions over the survey period, may be of use to developing countries. Factors relating to allergies differ from country to country and region to region, and some form of epidemiological surveillance is needed to assist in developing policy in the area. The survey methods we have employed are useful in terms of reliability of results, cost-effectiveness, and continuity.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. Supplementary data for Figure 1.

Table S2. Supplementary data for Figure 2.

Table S3. Supplementary data for Figure 3.

Table S4. Supplementary data for Figure 4.

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Supporting Information

Table S1 The age-adjusted prevalence rates* of allergic symptoms

	Wheezing	Sneezing	Rhinitis	Lifetime atopic dermatitis	Atopic dermatitis within 1 year	Itching eyes
1975	3.0					
1977	3.1					
1979	3.0					
1981	3.0					
1983	2.9	11.6	12.3			
1985	3.3	12.8	14.1	15.3		
1987	3.7	15.2	15.4	19.4		
1989	4.3	14.1	16.4	21.1		
1991	4.2	15.1	16.7	22.0		
1993	4.7		21.6	24.2	6.8	13.9
1995	4.2		22.0	22.9	5.6	14.6
1997	4.7		23.8	22.9	5.7	-
2000	4.3		23.9	20.0	5.2	16.2
2003	4.5		25.4	18.3	5.1	19.2
2006	4.1		24.7	16.5	4.6	21.0

* The age composition of pupils in each survey was adjusted by using the respondents in 2000 as the reference population.

6 **Table S2** The age-adjusted prevalence rates* of allergic symptoms by season

	Rhinitis					Itching eyes				
	Spring	Summer	Autumn	Winter	Non-seasonal	Spring	Summer	Autumn	Winter	Non-seasonal
1993	5.1	0.7	4.7	2.7	11.5	8.7	1.4	3.3	0.6	3.5
1995	6.2	0.7	5.2	2.7	10.6	9.7	1.3	3.5	0.6	2.9
1997	7.2	0.7	6.4	3.2	12.2	-	-	-	-	-
2000	7.1	0.7	6.1	3.1	11.4	10.9	1.3	4.5	0.7	3.3
2003	8.2	0.7	6.4	2.9	11.7	13.4	1.4	4.9	0.9	3.5
2006	8.9	0.7	6.5	2.4	11.7	15.1	1.4	5.8	0.9	3.7

7 * The age composition of pupils in each survey was adjusted by using the respondents in
8 2000 as the reference population.

9 **Table S3** The prevalence of allergic symptoms by school grade

	Rhinitis											
	Spring						Non-seasonal					
	1st	2nd	3rd	4th	5th	6th	1st	2nd	3rd	4th	5th	6th
1993	4.1	4.7	5.3	5.8	5.4	5.5	9.3	10.4	11.2	12.1	12.7	13.2
1995	4.9	6.0	6.1	6.7	6.5	6.8	8.5	9.3	10.3	11.3	12.2	12.3
1997	6.2	6.8	7.1	7.9	7.8	7.5	9.8	11.1	12.0	12.6	13.5	14.4
2000	5.5	6.8	6.8	8.0	7.9	7.3	9.5	10.1	11.4	11.8	13.0	12.8
2003	6.0	7.0	9.0	8.6	9.9	9.0	9.4	10.3	11.5	12.6	13.0	13.3
2006	6.8	7.9	8.1	9.2	9.6	11.5	9.4	10.3	11.3	12.2	13.3	13.6
	Itching eyes											
	Spring						Non-seasonal					
	1st	2nd	3rd	4th	5th	6th	1st	2nd	3rd	4th	5th	6th
1993	5.4	6.9	8.3	10.0	10.0	11.5	2.5	2.9	3.3	3.8	4.1	4.3
1995	6.1	7.9	8.9	10.8	11.5	13.4	1.9	2.2	2.7	3.2	3.6	3.8
1997	-	-	-	-	-	-	-	-	-	-	-	-
2000	6.6	9.0	9.6	13.1	13.6	13.5	2.3	2.5	3.0	3.6	4.1	4.2
2003	8.3	10.0	14.7	14.1	16.9	16.2	2.4	2.8	3.5	4.0	4.1	4.2
2006	10.0	12.2	13.0	16.0	17.5	22.2	2.6	3.0	3.6	4.1	4.6	4.6

10 **Table S4** The rate of those who had at least one allergic symptom

	Overall ^a	Non-seasonal only ^b	Seasonal only ^c	Both seasonal and non-seasonal ^d
1993	45.5	29.1	8.0	8.4
1995	46.0	27.4	9.5	9.1
1997	-	-	-	-
2000	45.0	25.0	11.4	8.6
2003	45.2	22.7	13.4	9.1
2006	44.5	21.1	14.6	8.8

11 ^a: Children with at least one allergic symptom from among wheezing, lifetime atopic
12 dermatitis, atopic dermatitis within the past year, rhinitis, and itching eyes.

13 ^b: Children with at least one symptom regardless of the season, from among wheezing,
14 lifetime atopic dermatitis, atopic dermatitis within the past year, and non-seasonal rhinitis or
15 itching eyes.

16 ^c: Children with at least one seasonal symptom from among rhinitis or itching eyes in spring,
17 summer, autumn, or winter.

18 ^d: Children who had both seasonal and non-seasonal symptoms.