

Changing Trends in Sex Specific Prevalence Rates for Childhood Asthma, Eczema, and Hay Fever

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Summary. Numerous surveys of school-aged children have shown increasing asthma prevalence with a less publicized but noticeable change in the male to female ratio. We sought to confirm this change in the sex ratio in four questionnaire-based surveys and investigate possible explanations. Identical questionnaire surveys were performed in 1989 ($n = 3,390$), 1994 ($n = 4,047$), 1999 ($n = 3,540$) and 2004 ($n = 1,920$) in school-children aged 9–11 years. Over these 15 years the male to female ratio (M:F) significantly narrowed for wheeze (1.34 to 0.98:1 $P < 0.0002$), for asthma (1.74 to 1.02:1 $P < 0.0001$), for eczema (1.42:1 to 0.81:1 $P < 0.0001$) and for hay fever (1.46 to 0.93:1 $P < 0.0001$). The diagnosis of asthma in children with wheeze was more commonly made in boys in 1989 relative risk RR 1.32 (1.12, 1.56), even in those with accompanying eczema and/or hay fever RR 1.20 (0.99, 1.45). By 2004 this sex bias in diagnosis was no longer present, RR 1.01 (0.91, 1.12) for wheeze and 1.02 (0.85, 1.21) for those with wheeze and eczema and/or hay fever. From 1989 to 2004 no significant difference in sex distribution changes between older and younger children occurred, making secular trends in the onset of puberty in females an unlikely contributory factor. The disappearance of the bias to diagnose asthma in symptomatic males but not in females may be partly responsible for the narrowing of the sex ratio, but other factors such as those enhancing the expression of asthma and atopy in females may also be implicated. *Pediatr Pulmonol.* 2007; 42:60–65. © 2006 Wiley-Liss, Inc.

Key words: asthma; survey; trends; epidemiology; sex ratio; sex; hay fever; eczema; wheeze.

INTRODUCTION

Childhood asthma has become more common in Western societies¹ although recent reports have suggested that its prevalence may have stabilized^{2,3} or even begun to decline.⁴ The precise extent of the increased prevalence is debated, reflecting the lack of agreed definitions and objective tests for asthma and the possibility of systematic errors and information biases in surveys.⁵ The reason for the rise is not known though changes in diet,⁶ decreased exposure to infection⁷ and increased allergic exposure⁸ have all been implicated.

One potential risk factor for the expression of asthma and the associated atopic diseases eczema and allergic rhinitis (hay fever) that has received scant attention in the context of changing prevalence is sex. During childhood, most earlier studies showed that asthma was about twice as common in boys as in girls,^{9–11} a situation that reverses after puberty.¹² However, we have previously reported that the increased prevalence of wheezing illness has not occurred equally among the sexes. In a series of four surveys of school children in Aberdeen, Scotland, covering the period from 1964 to 1999, we found that the male:female (M:F) ratio for asthma had decreased from

greater than 2:1 to nearly equalize, with apparent stabilization at the 1999 survey.¹³

This fall in M:F ratio may be artefactual, may reflect biological differences between the sexes, or may reflect environmental factors that differ in their effects between boys and girls. In seeking to explain these changes a number of factors need to be considered.

Reports of the under-diagnosis and under-management of childhood asthma¹⁴ and of rising asthma-related

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medical activity¹⁵ have received a great deal of professional and public attention. It is therefore possible that increased awareness of asthma, reflected in an increase in the number of wheezing children offered a diagnosis of asthma,^{13,16} might have differed in timing and magnitude between the sexes.

Alternatively, the M:F ratio for diagnosed asthma might have fallen due to a real increase in the prevalence of asthma in girls, which would be reflected in an increased proportion of girls with symptoms, in addition to an increase in the diagnosis of asthma. Because asthma in childhood is commonly associated with atopy,^{17,18} and because it is known that the prevalence of both eczema and allergic rhinitis has also been increasing,¹⁹ the narrowing of the M:F ratio for asthma might also reflect a greater increase in the prevalence of atopic disorders in girls relative to boys.

Because the incidence of asthma has been found to be greater in boys before puberty and in girls after puberty,¹² changes in the time-course of puberty in girls could also have influenced the prevalence of asthma.

We therefore sought to confirm the secular trend in sex ratio by including data from the most recent Aberdeen survey of 2004 and if confirmed to explore possible reasons for the changing sex ratio.

METHODS

The methods have been described in previous publications.^{13,20,21} Four surveys have been carried out on children attending all the publicly maintained elementary schools that lay within the same Aberdeen City boundaries over the 15-year-period. The population studied was based on class attended. We studied children in classes 5–7, and therefore aged mainly 9–11 years with outliers' aged 8, 12, and 13 years. Cross-sectional surveys were performed in the same schools in 1989 ($n = 3,390$ valid response rate 86.0%), 1994 ($n = 4,047$ valid response rate 96.4%), 1999 ($n = 3,540$ valid response rate 84.0%) and most recently in 2004 ($n = 1,920$ valid response rate 57.2%). After receiving an explanatory letter, the parents completed printed questionnaires that focused on respiratory symptoms and diagnosed atopic disorders. A period prevalence for wheeze was estimated with the following wording on the questionnaire "Has your child wheezed or had a 'whistle' in the chest in the past three years?". For asthma and atopic conditions life time prevalence was surveyed with the questions "Has your child ever had: Asthma? Eczema? Hay fever?". Eighty-five parents in 1999 declined to provide identifying data, which included sex, leaving 3,540 for inclusion in the present analysis. The data from the surveys were entered into an SPSS (Windows version, release 11.0, 2001) database. The sex ratios were calculated using the percentages of males and females for each category of symptoms. Analysis was

carried out with chi-squared and chi-squared test for trend to evaluate statistical significance and estimate the relative risk.

RESULTS

Although the population prevalence of reported asthma in girls continued to rise the prevalence in boys stabilized with no apparent increase from 1999 to 2004 (Fig. 1).

The M:F ratio for asthma and its principal symptom wheeze, and for eczema and hay fever narrowed consistently and significantly between 1989 and 2004. Atopic wheeze, defined as wheeze accompanied by report of ever having either eczema or hay fever, and non-atopic wheeze also showed a consistent fall in M:F ratio across the four studies (Table 1). Reported eczema and/or hay fever also showed the same downward trend in male predominance over the 15-year-period. The only category for which there was no significant trend for a declining male predominance in the series of surveys was for wheeze in the absence of either ever eczema or ever hay fever, even though a steep reduction occurred early on between 1989 and 1994.

In 1989 and 1994 boys with wheeze were more likely than girls with wheeze to report a diagnosis of asthma, whether or not the wheeze was accompanied by eczema or hay fever (Table 2). This difference disappeared over the next decade, and in 1999 and 2004 sex differences in the proportion of symptomatic children with a reported diagnosis of asthma had disappeared. As might be anticipated the diagnosis of asthma was more frequently reported in children whose wheeze was accompanied by ever eczema or hay fever, but even in this group boys were more likely than girls to report a diagnosis of asthma in 1989 and 1994, and with a reducing M:F ratio over the

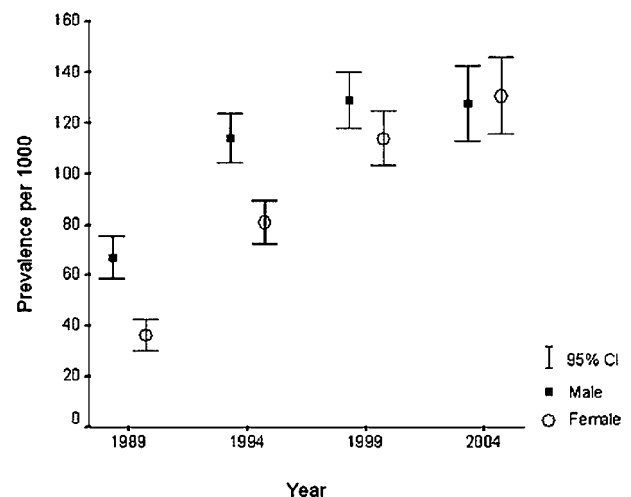


Fig. 1. Sex specific prevalence rate for reported asthma by year of survey.

TABLE 1—Sex Distribution and Sex Ratio for Wheeze, Asthma, Eczema and Hay Fever From 1989 to 2004

	1989	1994	1999	2004	Trend χ^2 (P)
Total study population	3,942	4,197	4,209	3,358	
Valid responses	3,390	4,047	3,540	1,920	
Response rate (%)	86.0	96.4	84.0	57.2	
Male:female (n)	1,746:1,644	2,021:2,026	1,752:1,788	935:980	
Wheeze in past 3 years					
Male:female (n)	396:279	562:463	516:472	233: 249	13.51 (<0.0002)
Male:female (%)	22.7:17.0	27.8:22.9	29.5:26.4	24.9:25.4	
Ratio	1.34:1	1.22:1	1.12:1	0.98:1	
Ever asthma					
Male:female (n)	227:123	461:328	456:404	245:251	24.30 (<0.0001)
Male:female (%)	13.0:7.5	22.8:16.2	26.0:22.6	26.2:25.6	
Ratio	1.74:1	1.41:1	1.15:1	1.02:1	
Atopic wheeze ¹					
Male:female (n)	166:110	249:202	225:218	118:145	14.38(<0.0001)
Male:female (%)	9.5:6.7	12.3:10.0	12.8:12.2	12.6:14.8	
Ratio	1.42:1	1.24:1	1.05:1	0.81:1	
Non-atopic wheeze ²					
Male:female (n)	230:169	313:261	291:254	115:104	1.94 (0.16)
Male:female (%)	7.0:3.2	15.5:12.9	16.6:14.2	12.3:10.6	
Ratio	2.21:1	1.20:1	1.17:1	1.11:1	
Ever eczema					
Male:female (n)	245:163	360:354	373:384	221:283	21.12 (<0.0001)
Male:female (%)	14.0:9.9	17.9:17.5	21.3:21.5	23.6:28.9	
Ratio	1.42:1	1.02:1	0.99:1	0.82:1	
Ever hay fever					
Male:female (n)	246:159	288:223	289:255	171:192	15.21 (<0.0001)
Male:female (%)	14.1:9.7	14.3:11.0	16.5:14.3	18.3:19.6	
Ratio	1.46:1	1.29:1	1.16:1	0.93:1	
Ever eczema or hay fever					
Male:female (n)	418:288	567:506	556:543	323:399	29.80 (<0.0001)
Male:female (%)	23.9:17.5	28.1:25.0	31.7:30.4	34.5:40.7	
Ratio	1.37:1	1.12:1	1.04:1	0.85:1	

¹Atopic wheeze defined as wheeze in a child who had ever had either eczema and/or hay fever.²Non-atopic wheeze defined as wheeze in a child who had neither asthma nor hay fever.**TABLE 2—The Proportion of Boys and Girls With Wheeze, Atopic Wheeze and Non-Atopic Wheeze, in Whom a Diagnosis of Asthma was Made**

	1989 n (%)	1994 n (%)	1999 n (%)	2004 n (%)
Wheeze with diagnosis of asthma				
Boys	216/396 (52.5)	383/562 (68.1)	347/516 (67.2)	176/233 (75.5)
Girls	115/279 (41.2)	271/463 (58.5)	317/472 (67.2)	186/249 (74.7)
RR (boys/girls)	1.32 (1.12, 1.56)***	1.16 (1.06, 1.28)**	1.00 (0.92, 1.09)	1.01 (0.91, 1.12)
Atopic wheeze ¹ with diagnosis of asthma				
Boys	114/166 (68.7)	184/249 (73.9)	165/225(73.3)	95/118 (80.5)
Girls	63/110 (57.3)	132/202 (65.3)	157/218 (72.0)	114/145 (78.6)
RR (boys/girls)	1.20 (0.99, 1.45)	1.13 (1.00, 1.28)*	1.02 (0.91, 1.14)	1.02 (0.91, 1.16)
Non-atopic wheeze ² with diagnosis of asthma				
Boys	102/230 (44.3)	199/313 (63.6)	182/291 (62.5)	81/115 (70.4)
Girls	52/169 (30.8)	139/261 (53.3)	160/254 (63.0)	72/104 (69.2)
RR (boys/girls)	1.44 (1.10, 1.89)**	1.19 (1.04, 1.38)*	0.99 (0.87, 1.13)	1.02 (0.85, 1.21)

RR, relative risk.

¹Atopic wheeze was defined as wheeze in a child who had ever had either eczema or hay fever.

*P values from chi-squared tests of proportions of boys to girls by survey year <0.05.

**P values from chi-squared tests of proportions of boys to girls by survey year <0.01.

***P values from chi-squared tests of proportions of boys to girls by survey year <0.001.

15-year-period. A similar pattern was observed in children whose wheeze was not accompanied by other atopic disorders.

When the median age was used to divide the population into two age groups, there was no evidence that the decline in M:F ratio was occurring selectively in either older or younger children (Table 3).

DISCUSSION

In this series of four cross-sectional studies from 1989 to 2004 examining a defined population of elementary school children aged 9–11 years, we noted a continuing fall in the earlier male predominance for wheeze, diagnosed asthma, atopic wheeze, and hay fever, and in the case of eczema a clear reversal so that this latter condition was now more commonly reported in girls.

Earlier epidemiological studies of asthma invariably reported a M:F ratio of 2:1 or greater.^{9,10,22} Between 1973 and 1988 the M:F ratio for asthma decreased from 1.75:1 to 1.5:1 in cross-sectional surveys of Cardiff school children aged 12 years.²³ Further evidence of the differential increase in asthma in females comes from cross-sectional surveys of children and adolescents carried out in Copenhagen, Denmark in 1986 (n = 580), and repeated in 2001 (n = 480),²⁴ which documented a

two fold increase in the overall prevalence of current asthma from 5.3% in 1986 to 11.7% in 2001 but with a reversal of the M:F ratio from 1.6:1 in 1986 to 0.9:1 in 2001.

Sex differences in asthma prevalence have been attributed to bias by health professions in the diagnosis of asthma according to sex.²⁵ In one group of children with similar levels of reported symptoms to those in the current report, boys were more likely than girls to be diagnosed with asthma, despite more girls having bronchial hyper-responsiveness.²⁶ Similarly, a study in Cardiff, UK, showed significant male bias in the diagnosis of asthma in symptomatic children.²⁷ In the present report the trend to disappearance of the M:F ratio was evident for wheeze whether or not it was accompanied by ever eczema or hay fever. Similar trends were also seen for reported asthma, eczema or hay fever. Even in those children in whom wheeze was accompanied by eczema or hay fever, and in whom it would seem reasonable to consider that the diagnosis of asthma would be more likely to be made, the clear male preponderance in 1989 had subsequently disappeared (Table 1). The increased likelihood of a diagnosis of asthma in symptomatic girls and the fact that it is now at the same level as boys points to a move away from an earlier diagnostic male bias (Table 2).

TABLE 3—No Relationship Between Age and Sex Ratio

	1989		1994		1999		2004	
Valid responses for each survey	3,390		4,047		3,540		1,920	
Age groups ¹	Older	Younger	Older	Younger	Older	Younger	Older	Younger
Wheeze								
M:F (n)	191:127	203:150	273:242	289:221	250:239	266:231	118:133	115:115
M:F (ratio)	1.42:1	1.27:1	1.13:1	1.31:1	1.07:1	1.17:1	0.92:1	1.05:1
RR older vs. younger males (95%CI)	1.04 (0.92, 1.19)		0.94 (0.84, 1.05)		0.96 (0.85, 1.08)		0.94 (0.78, 1.13)	
Atopic wheeze ²								
M:F (n)	84:56	122:97	117:113	132:89	100:110	125:107	60:73	58:72
M:F (ratio)	1.41:1	1.19:1	1.04:1	1.49:1	0.92:1	1.19:1	0.86:1	0.84:1
RR for older vs. younger males (95%CI)	1.08 (0.90, 1.29)		0.85 (0.72, 1.01)		0.88 (0.73, 1.06)		1.01 (0.77, 1.32)	
Eczema								
M:F (n)	117:73	127:89	165:174	195:180	170:190	202:193	111:142	110:140
M:F (ratio)	1.51:1	1.35:1	0.95:1	1.08:1	0.91:1	1.07:1	0.81:1	0.82:1
RR for older vs. younger males (95%CI)	1.05 (0.89, 1.23)		0.94 (0.81, 1.08)		0.92 (0.80, 1.07)		1.00 (0.82, 1.22)	
Hay fever								
M:F (n)	135:96	110:63	146:134	142:89	157:140	132:113	89:116	82:76
M:F (ratio)	1.32:1	1.65:1	1.09:1	1.60:1	1.14:1	1.19:1	0.80:1	1.13:1
RR for older vs. younger males (95%CI)	0.92 (0.79, 1.08)		0.85 (0.73, 0.99)*		0.98 (0.84, 1.15)		0.84 (0.67, 1.04)	

RR relative risk.

¹The median age was used to divide the population into older and younger halves.

²Atopic wheeze was defined as wheeze in the presence of eczema or hay fever.

*P values from chi-squared tests of boys to girls by survey year <0.05.

However, there were also increases in the prevalence of wheeze, the cardinal symptom of asthma, and of other allergic conditions, all of which have been more rapid in girls than in boys (Table 1), so that there is now no longer a significant male preponderance in the prevalence of asthma and allergic conditions in children. Diagnostic drift is therefore unlikely to be the only explanation for the narrowing M:F ratio.

There is a well-characterized relationship between age and the incidence of asthma, which is higher in boys before puberty and in girls after puberty.¹² There has been an earlier onset of puberty in females in most European countries during recent decades,²⁸ partly related to nutritional factors including obesity. Although the age of the menarche has not changed,²⁹ the duration of puberty has increased due to its earlier onset.²⁸ Changes in the age of onset of puberty might therefore have played a part in determining the M:F ratio in childhood asthma, a hypothesis supported by the Copenhagen study²⁴ which found a much greater increase in asthma in younger (mainly pre-menarchal) than in older (mainly post-menarchal) girls, whereas the rate of increase was similar in boys in both age-groups. As can be seen from Table 3 we could find no evidence in support of this concept as there were no systematic differences in the secular trend of the M:F ratio between younger and older children.

We can only speculate on other environmental and constitutional factors that might have narrowed the M:F ratio by altering the relative vulnerability of the two sexes. Various physiological differences between the sexes may be important.

During childhood boys have lower maximal airflow rates than girls after adjustment for lung volumes,^{30,31} and this apparent narrowness of the male airways during childhood may explain why in the past wheezing illnesses were more common in boys.

Another potential male disadvantage during childhood is that boys have higher IgE concentrations and more atopy than girls,^{18,32} predisposing them to allergic airways disease.

The narrowing of the M:F ratio could be explained by lessening of these male disadvantages, thus allowing the adverse environmental influences responsible for the general increase in asthma to have an equal effect on girls and boys. One factor that might be responsible for such an alteration is exposure to estrogens. The total amount of estrogen ingested from environmental sources has increased, and is considered to have the potential to produce biological effects.³³ Such estrogens come from estrogen-like substances in the diet, and from the rise in the use of the oral contraceptive pill (OCP) and its appearance in ground water.³⁴ The introduction of the OCP has already led to the suspicion that it might be related to the increase in asthma,³⁵ presumably by accelerating the changes that lead to the increased

incidence of asthma in adult females, thereby serving to reduce the relative male disadvantage.

Another identifiable factor with sex specific effects is obesity. In longitudinal studies an association has been shown between asthma and obesity, but only in females.³⁶ Huang has reported an association between body mass index (BMI) and positive skin prick test to at least one of several allergens in teenage females living in Taiwan.³⁷ Although in the European Respiratory Health Survey an association between obesity and asthma was confirmed, no such association was evident between obesity and atopy.³⁸ In UK, the National Growth Study found a secular trend towards obesity but no relationship between the trends for asthma and obesity in either boys or girls.³⁹ The Copenhagen study did not observe an effect of BMI on asthma prevalence between 1986 and 2001.²⁴ Even if there is an association between obesity and asthma it is certainly insufficient to explain the very large increases we have reported in the prevalence in girls of wheeze, asthma and other atopic disorders.

In conclusion, the rise in asthma and allergic conditions has been accompanied by changes in the sex distribution of these disorders. The changing sex ratio is due partly to changes in diagnostic labeling, but also reflects a real increase in wheeze and other allergic conditions, all of which have been greater in girls than in boys, so that there is now no longer a significant male preponderance in the prevalence of asthma and allergic conditions in children around the ages of 9–11 years. Changing sex ratios for asthma and atopic disease are likely to be contributed to by changing diagnostic fashion but may also allow us to identify other as yet unidentified environmental factors contributing to the expression of this common group of diseases.

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