

Original article

Strategies for preventing wheezing and asthma in small children

Objective: To assess the effects of living in agreement with allergy preventive guidelines on wheezing and asthma at 2 years of age.

Design: Prospective birth cohort study (BAMSE). Questionnaires on heredity and environmental factors were answered when the child was 2 months, and detailed questionnaires on symptoms at 1 and 2 years of age.

Participants: 4089 children, born during 1994–1996.

Setting: Child Health Centres in central and north-western parts of Stockholm, Sweden.

Main outcome measures: Wheezing and asthma up to the age of 2.

Results: The effects of preventive guidelines regarding breastfeeding, maternal tobacco smoke and home dampness on wheezing and asthma were assessed in multiple logistic regression models. The cumulative incidence of recurrent wheezing at 2 years of age was 12.6% and of asthma 6.8% among those with a lifestyle in agreement with all guidelines and 24.1 and 17.9%, respectively, in families exposed to at least two of the three risk factors. Among children with no heredity, family lifestyle according to the guidelines gave a twofold reduction of asthma (5.3 vs. 10.5%), while the group with heredity had a threefold reduction (9.1 vs. 27.3%). The attributable fraction for asthma associated with the guidelines was 23% in total and 33% among those with heredity.

Conclusion: In this observational study, family lifestyle according to preventive guidelines is associated with an important reduction of recurrent wheezing and asthma at 2 years of age, especially among children with allergic heredity.

A follow-up will determine whether there still a risk reduction of both symptoms and disease.

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Allergic diseases are major causes of morbidity in developed countries and their incidence is increasing steadily. Asthma, in particular, has increased rapidly in children throughout the world in the last 30 years and confers a major cause of hospitalization (1). To counter this trend preventive strategies have been proposed, in particular for children in early life. Since more than a decade, strategies in Sweden have focused on influencing risk factors such as parental smoking, short period of breastfeeding, home dampness, high-risk families, the keeping of pets (2, 3). Apart from exposure to environmental tobacco smoke (ETS), the scientific evidence on the effect of environmental exposure factors on the development of asthmatic disease is still contradictory, effective primary preventive methods have been difficult to establish and those suggested today are questioned (4).

The optimal approach to study the effects of primary prevention would be a randomized intervention study starting at early pregnancy. For obvious ethical reasons such a study is impossible. However, with regard to dust mites, different intervention studies have been undertaken (5–7). Multifaceted intervention programmes may be

used for high-risk infants and evidence of decreased asthma incidence up to the age of 1 is reported from a Canadian intervention study (8). BAMSE is a Swedish prospective birth cohort study aiming at identifying early risk factors for the development of allergic disease in children. An evaluation of the effects of primary prevention of wheezing and asthma in small children has been performed, based on what parents have chosen to expose their children to.

Material and methods

Study subjects

From February 1994 until November 1996, 4089 newborn infants (2065 boys and 2024 girls) were included in a prospective study. They comprised 75% of all eligible children born in predefined areas of central and north-western parts of Stockholm who fulfilled our inclusion criteria. Study design, enrolment, criteria for inclusion and the procedures for data collection are described in detail elsewhere (9, 10). The study was approved by the ethical committee of Karolinska Institutet, Stockholm, Sweden.

Questionnaire

Data on detailed residential characteristics, environmental factors, and allergic heredity were obtained from questionnaires to parents when the child's median age was 2 months. At one and 2 years of age similar questionnaires were mailed to the parents, the main focus now was on symptoms related to asthma and other allergic diseases, including information on breastfeeding and other key exposure factors. The response rate for the questionnaires at 1 and 2 years of age was 96 and 94%, respectively. For the present report it was required that the parents had answered all three questionnaires including key variables used in this presentation. This left 3692 children for analysis (90%).

Heredity for allergic disease was defined as at least one of the two factors: doctor's diagnosed asthma or allergic rhinitis in combination with allergy to furred pets or pollens in one (single heredity) or both parents (double heredity). Asthma was defined as at least three episodes of wheezing after 3 months and up to 2 years of age, combined with treatment with inhaled glucocorticoids, or signs of suspected hyperreactivity (cough or wheeze at excitement or emotional stress) without concurrent upper respiratory infection. Episodes of wheezing during the first 3 months were not included. Any episode of wheezing and recurrent wheezing, i.e. wheezing more than three times, was also used as primary outcome.

Preventive guidelines

Primary preventive guidelines for allergic disease in childhood have been available at all Swedish Health Care centres and are promoted by the authorities. Since the mid-1990s the following general recommendations were given to all families:

- breastfeeding encouraged;
- exposure of the child to tobacco smoke to be avoided;
- good ventilation and normal dampness in the home environment to be aimed at.

Statistical analysis

Cumulative incidence is presented as percentage with 95% confidence intervals. Multiple logistic regression models were used to determine the association between outcome variables (wheezing ever, wheezing more than three times and asthma per definition) and a number of explanatory variables. The models contained gender, heredity for allergic disease, socio-economic status, mother's age, exclusive breastfeeding, maternal smoking, pet ownership and signs of dampness and age of the building. The results of the logistic regression analyses are presented as odds ratios (OR) with 95% confidence intervals. Adjusted population attributable fractions were calculated for a subset of the independent variables in the regression model (11). All statistical analyses were performed with Stata, Statistical Software, release 7.0 (College Station, TX, USA).

Results

The cumulative incidence of wheezing, recurrent wheezing and asthma per definition up to the age of 2 was 25.7, 14.6 and 8.5%, respectively. In Table 1, the cumulative incidence of wheezing and asthma is shown by background variables. Adjusted ORs from a logistic regression model including all presented variables are shown in

Table 1. Cumulative incidence wheezing and asthma at age 2, by background and environmental factors in the Swedish prospective birth cohort BAMSE

	<i>n</i>	Wheezing ever, % (95% CI)	Recurrent wheezing, % (95% CI)	Asthma*, % (95% CI)
Total	3692	25.7 (24.3–27.1)	14.6 (13.5–15.8)	8.5 (7.6–9.5)
Sex				
Girl	1817	21.7 (19.9–23.7)	11.9 (10.5–13.5)	6.6 (5.5–7.8)
Boy	1875	29.5 (27.4–31.6)	17.2 (15.5–19.0)	10.3 (9.0–11.8)
Heredity†				
None	2181	21.8 (20.1–23.6)	11.7 (10.4–13.2)	6.3 (5.3–7.4)
Single	1286	29.9 (27.4–32.5)	17.8 (15.8–20.0)	10.6 (8.9–12.4)
Double	225	38.7 (32.3–45.4)	24.4 (19.0–30.6)	17.8 (13.0–23.4)
Mother's age				
<25 years	440	31.8 (27.5–36.4)	20.0 (16.4–24.0)	14.5 (11.4–18.2)
26–30 years	1430	25.7 (23.4–28.0)	13.6 (11.9–15.5)	8.2 (6.8–9.7)
>31 years	1822	24.2 (22.3–26.2)	14.1 (12.5–15.8)	7.3 (6.1–8.6)
Socio-economic status‡				
Manual workers	1668	27.3 (25.2–29.5)	16.1 (14.3–17.9)	10.3 (8.8–11.8)
Non-manual workers	1837	24.9 (22.9–26.9)	13.8 (12.3–15.5)	7.5 (6.3–8.8)
Academic profession	187	18.7 (13.4–25.1)	9.6 (5.8–14.8)	2.7 (0.9–6.1)
Exclusive breastfeeding				
<3 months	744	28.8 (25.5–32.2)	18.7 (15.9–21.7)	11.8 (9.6–14.4)
4–5 months	1175	25.1 (22.6–27.7)	13.8 (11.9–15.9)	8.2 (6.7–9.9)
>6 months	1773	24.8 (22.8–26.8)	13.5 (11.9–15.2)	7.3 (6.2–8.6)
Smoking mother§				
No	3212	24.7 (23.2–26.2)	13.7 (12.5–14.9)	7.8 (6.9–8.8)
Yes	480	32.1 (27.9–36.5)	21.0 (17.5–25.0)	13.3 (10.4–16.7)
Ownership of furred pets				
No	3122	26.0 (24.5–27.6)	14.6 (13.4–15.9)	8.5 (7.5–9.5)
Yes	570	23.7 (20.3–27.4)	14.7 (11.9–17.9)	8.8 (6.6–11.4)
Damp home environment¶				
No	3228	24.7 (23.2–26.2)	14.1 (12.9–15.3)	7.8 (6.9–8.8)
Yes	464	32.5 (28.3–37.0)	18.3 (14.9–22.1)	13.1 (10.2–16.6)
Year of construction of building				
Before 1940	1165	25.2 (22.7–27.7)	12.4 (10.6–14.5)	6.0 (4.7–7.5)
1941–1975	1532	25.5 (23.4–27.8)	14.6 (12.9–16.5)	8.9 (7.5–10.4)
1976 and after	995	26.5 (23.8–29.4)	17.2 (14.9–19.7)	10.9 (9.0–13.0)

* Asthma defined as at least three episodes of wheezing between 3 months and 2 years of age, in combination with treatment of inhaled glucocorticoids or signs of hyperactivity without concurrent upper-respiratory infection; episodes of wheezing during the first 3 months were not included.

† Heredity defined as doctor's diagnosis of asthma and/or rhinitis with pet and/or pollen allergy.

‡ Socio-economic status classified as manual workers if at least one parent was manual worker (including students, unemployed and homemakers), academic profession only if both parents had a university degree.

§ Reported maternal smoking during pregnancy and/or at the time of enrolment.

¶ At least one of: smell and visible signs of mould, water damage inside construction, and persistent windowpane condensation in dwellings with double-glazing.

Table 2. Male sex, allergic heredity, home dampness and maternal smoking during pregnancy and/or at the time of enrolment were associated with an increase in all three outcomes. High socio-economic status, i.e. academic profession, mother's age above 25, and exclusive breastfeeding for at least 4 months were associated with a reduction in all three outcomes. Living in a building

Table 2. Adjusted odds ratios from a logistic regression analysis for the association between wheezing and asthma at age 2, and background and environmental factors in the Swedish prospective birth cohort BAMSE

	Wheezing ever, OR (95% CI)	Recurrent wheezing, OR (95% CI)	Asthma*, OR (95% CI)
Sex			
Girl	1.0	1.0	1.0
Boy	1.52 (1.31–1.77)	1.56 (1.29–1.89)	1.66 (1.31–2.12)
Heredity†			
None	1.0	1.0	1.0
Single	1.51 (1.28–1.77)	1.62 (1.33–1.97)	1.72 (1.34–2.21)
Double	2.22 (1.66–2.97)	2.48 (1.76–3.47)	3.24 (2.18–4.82)
Mother's age			
<25 years	1.0	1.0	1.0
26–30 years	0.79 (0.59–1.05)	0.74 (0.53–1.04)	0.60 (0.41–0.89)
>31 years	0.73 (0.54–0.98)	0.77 (0.55–1.09)	0.55 (0.37–0.82)
Socio-economic status‡			
Manual workers	1.0	1.0	1.0
Non-manual workers	0.94 (0.79–1.10)	0.93 (0.76–1.14)	0.87 (0.68–1.13)
Academic profession	0.66 (0.44–0.98)	0.66 (0.39–1.12)	0.34 (0.13–0.84)
Exclusive breastfeeding			
<3 months	1.0	1.0	1.0
4–5 months	0.86 (0.70–1.06)	0.75 (0.58–0.97)	0.74 (0.54–1.02)
>6 months	0.85 (0.70–1.04)	0.74 (0.58–0.93)	0.67 (0.50–0.91)
Smoking mother§			
No	1.0	1.0	1.0
Yes	1.42 (1.14–1.76)	1.59 (1.23–2.05)	1.65 (1.21–2.25)
Ownership of furred pets			
No	1.0	1.0	1.0
Yes	0.84 (0.67–1.04)	0.93 (0.72–1.21)	0.91 (0.66–1.27)
Damp home environment¶			
No	1.0	1.0	1.0
Yes	1.45 (1.17–1.80)	1.34 (1.03–1.75)	1.74 (1.28–2.39)
Year of building construction			
Before 1940	1.0	1.0	1.0
1941–1975	0.91 (0.76–1.10)	1.08 (0.86–1.37)	1.24 (0.91–1.70)
After 1976	1.04 (0.85–1.27)	1.42 (1.10–1.82)	1.75 (1.26–2.43)

* Asthma defined as at least three episodes of wheezing between 3 months and 2 years of age, in combination with treatment of inhaled glucocorticoids or signs of hyperactivity without concurrent upper-respiratory infection; episodes of wheezing during the first 3 were not included.

† Heredity defined as doctor's diagnosis of asthma and/or rhinitis with pet and/or pollen allergy.

‡ Socio-economic status classified as manual workers if at least one parent was manual worker (including students, unemployed and homemakers), academic profession only if both parents had a university degree.

§ Reported maternal smoking during pregnancy and/or at the time of enrolment.

¶ At least one of: smell and visible signs of mould, water damage inside construction, and persistent windowpane condensation in dwellings with double-glazing.

erected after 1975 was associated with recurrent wheezing and asthma. No association was found between pet ownership and the outcomes, or for the number of older siblings or older children within the household (data not shown).

Compliance with the Swedish national allergy preventive guidelines, deliberate or not, was associated with recurrent wheezing in 12.6% of the children, as compared

Table 3. Cumulative incidence of wheezing and asthma at age 2 by number of preventable exposures* in the Swedish National Guidelines

Atopic heredity†	Number of exposures	n	Wheezing ever, % (95% CI)	Recurrent wheezing, % (95% CI)	Asthma‡, % (95% CI)
Total	0 of 3	2316	22.9 (21.2–24.7)	12.6 (11.2–14.0)	6.8 (5.8–7.9)
	1 of 3	1130	29.8 (27.2–32.6)	16.5 (14.4–18.9)	9.6 (8.0–11.5)
	2–3 of 3	274	31.8 (26.3–37.6)	24.1 (19.1–29.6)	17.9 (13.5–22.9)
None	0 of 3	1378	20.5 (18.4–22.8)	10.7 (9.1–12.4)	5.3 (4.2–6.6)
	1 of 3	670	24.0 (20.8–27.5)	12.8 (10.4–15.6)	7.3 (5.5–9.6)
	2–3 of 3	153	23.5 (17.1–31.1)	16.3 (10.9–23.2)	10.5 (6.1–16.4)
Any	0 of 3	938	26.3 (23.5–29.3)	15.4 (13.1–17.8)	9.1 (7.3–11.1)
	1 of 3	460	38.3 (33.8–42.9)	22.0 (18.3–26.0)	13.0 (10.1–16.5)
	2–3 of 3	121	42.1 (33.2–51.5)	33.9 (25.5–43.0)	27.3 (19.6–36.1)
Single	0 of 3	800	25.5 (22.5–28.7)	14.6 (12.2–17.3)	8.1 (6.3–10.2)
	1 of 3	390	36.2 (31.4–41.1)	20.8 (16.9–25.1)	11.8 (8.8–15.4)
	2–3 of 3	104	40.4 (30.9–50.5)	31.7 (22.9–41.6)	26.0 (17.9–35.5)
Double	0 of 3	138	31.2 (23.6–39.6)	19.6 (13.3–27.2)	14.5 (9.1–21.5)
	1 of 3	70	50.0 (37.8–62.2)	28.6 (18.4–40.6)	20.0 (11.4–31.3)
	2–3 of 3	17	52.9 (27.8–77.0)	47.1 (23.0–72.2)	35.3 (14.2–61.7)

* Exposure to maternal tobacco smoke, being raised in damp home, breastfeeding less than 4 months. In families with double heredity of allergic disease.

† Heredity defined as doctor's diagnosis of asthma and/or rhinitis with pet and/or pollen allergy.

‡ Asthma defined as at least three episodes of wheezing between 3 months and 2 years of age, in combination with treatment of inhaled glucocorticoids or signs of hyperactivity without concurrent upper-respiratory infection; episodes of wheezing during the first 3 months were not included.

to 24.1% of the children exposed to at least two of these three factors (maternal tobacco smoke, being raised in a damp home and breastfeeding less than 4 months, Table 3). The corresponding figures for asthma were 6.8 and 17.9%, respectively. A protective effect, as a result of lifestyle factors in accordance with these guidelines, was found in all subgroups of children independent of allergic heredity. There was a 1.5–2-fold reduction of recurrent wheezing and asthma in children with no heredity (10.7 vs. 16.3% and 5.3 vs. 10.5%, respectively) and a 2–3-fold reduction in children with any heredity (15.4 vs. 33.9% and 9.1 vs. 27.3%). The relative reduction in recurrent wheezing and asthma was about the same in the groups with single and double heredity. Similar results, but not equally pronounced, were also seen for wheezing ever.

Adjusted population-attributable fractions (AF) were calculated for the variables included in the guidelines in the full logistic regression model for recurrent wheezing and asthma per definition (Table 2). The AF is interpreted as the fraction of the disease in the population that would be avoided if the three studied exposures were to be eliminated, adjusted for all other explanatory variables in the logistic regression model. The AF was estimated to 14.5 and 23.1% overall for recurrent wheezing and asthma, respectively, with the largest effect in children with heredity, AF = 25.4 and 36.6%. However, a moderate effect was also seen in children with no heredity, AF = 4.0 and 10.0% (Table 4). The calculated propor-

Table 4. Adjusted population attributable fraction (AF*) and calculated reduction of recurrent wheezing and asthma as a result of primary preventive strategies comment

	Recurrent wheezing		Asthma‡	
	Attributable fraction, % (95 CI)	Preventable cases of population (%)	Attributable fraction, % (95 CI)	Preventable cases of population (%)
Atopic heredity†				
None	3.8 (–9.9, 15.9)	0.45	9.8 (–9.9, 26.0)	0.62
Any	24.1 (12.0, 34.5)	4.53	33.2 (17.8, 45.7)	3.87
Single	25.4 (11.5, 37.2)	4.53	36.6 (18.6, 50.7)	3.88
Double	22.9 (–3.7, 42.7)	5.60	27.6 (–4.3, 49.8)	4.91
Total	14.5 (5.6, 22.6)	2.12	23.1 (11.2, 33.4)	1.96

* AF = Adjusted Population Attributable Fraction, calculated for the three preventable exposures (maternal tobacco smoke, being raised in damp home, breastfeeding less than 4 months) in the full logistic regression model presented in Table 2.

† Heredity defined as doctor's diagnosis of asthma and/or rhinitis with pet and/or pollen allergy.

‡ AF multiplied by cumulative incidence in the respective groups.

tion of children in the study who could have been prevented from developing asthma in early life was estimated to 2.12% of the population for recurrent wheezing and 1.96% for that of asthma.

Discussion

The effect of restricting some environmental exposures including short period of human milk and onset of early childhood wheezing and asthma has been elucidated in this longitudinal birth cohort study. The data indicate that it may be possible to reduce the incidence of wheezing and early childhood asthma with preventive advice such as encouragement of breastfeeding, to emphasize the importance of refraining from parental tobacco smoking and to keep suitable housing conditions.

As wheezing during the first 2 years of life is one of the most common causes both of disease and hospitalization in early childhood, the social and economic impact of such prevention should not be overlooked (1). At present, we do not know whether these measures only postpone the onset of wheezing and early childhood asthma or if the effect is long-lasting.

In earlier, and mainly cross-sectional or retrospective studies, unsuitable housing conditions (e.g. home dampness), maternal tobacco smoke, keeping of pets and/or breastfeeding during a short period were found to be associated with allergic disease in small children (12–16). The present study is prospective in design, uses a population-based birth cohort, an inclusion period of more than 2 years and families living in suburban/urban areas representative of Stockholm. Further, all exposure data, except for breastfeeding, was collected when the children were on average 2 months old, thus prior to onset of disease. The exposure questionnaire was in 86%

of the cases completed by both parents together. Still, there is always a risk for methodological problems, such as underreporting of exposure, particularly in families with heredity, or denial of symptoms that could be related to exposure. However, this would most likely lead to an underestimation of the importance of prevention. An intervention study focusing on our identified risk factors would have been desirable, but that is for ethical and practical reasons not possible. Procedures of enrolment and a high participation rate as well as the prospective design contribute to the possibility to generalize the results. One limitation so far is that conclusions can only be drawn for the first 2 years of life. A 4-year follow-up study, with objective outcome measurements, is under way and will probably elucidate the relationships between early exposure and asthma.

Two randomized intervention studies starting in early pregnancy indicate that a risk reduction for respiratory diseases may be obtained up to the age of 12 months (5, 17). Follow-up examinations in the study by Arshad and co-workers (18) revealed no protective effect for asthma at 2 and 4 years, but significantly lower risk of sensitization to common allergens. Our study showed that the reduced cumulative incidence for asthmatic disease during the first 2 years of life was not restricted only to those with parental heredity. For children without such heredity, and no preventable exposure, the cumulative incidence of asthma was half that of those who were exposed to at least two exposure factors. On the other hand, the attributable fraction for this group was only 9.8% as compared to 36.6% among children with single heredity, a group that constituted more than one-third of all children. The cumulative incidence was also substantially reduced for wheezing children, in particular among those with heredity for allergic diseases. This indicates that the preventive measures both for wheezing and asthma are likely to have an effect in particular among those with heredity. Even if we do not know the direct cause of onset of respiratory allergic disease in early childhood, primary preventive efforts seem to increase the likelihood to postpone disease in a large number of children. Follow-up of the BAMSE children is planned to investigate further the effect of early environmental factors and later onset of allergic disease. When preventive measures are being recommended it is important to consider whether they apply to the whole population, whether costs for both the individual and for the community are acceptable, and whether there are any negative effects. Recent review articles on primary prevention of asthma point out the complexities of preventive strategies and conclude that better understanding of an individual's genetic set-up and the interaction between genetic and environmental factors is required before any successful prevention will be accomplished (19, 20). Nevertheless, the present results suggest that the risk of wheezing and asthma may be substantially reduced. We believe there is a widespread consensus on

the negative health effects of exposure to tobacco smoke in early childhood, as well as of the overall beneficial effects of breastfeeding (21, 22). However, damp and humid homes as risk environments are a rather complex issue. In the Stockholm region, as in most parts of Sweden, exposure to mites is considered to be very low and the reason for this is the cold winter climate. Thus, exposure to mites in these homes with reported signs of home dampness does not explain the increased risk of early onset of asthma in our study. Instead, such dampness is believed more to be associated with indoor combustion and trapping of indoor pollution because of inefficient ventilation (23). The solution might be amendment of building construction regulations.

Still, many causes of the epidemic of allergic diseases in the western world are unknown and our understanding of the natural process of allergic disease in childhood is very limited. We are certainly more susceptible and tend to develop allergic diseases easier than 50 years ago. Thus, the prevention or postponement of the onset of wheezing and asthma by simple preventive strategies seems desirable, not only for the individual and the family, but also for the community. Our results indicate that, in families

with heredity, having a lifestyle in accordance with the Swedish allergy preventive guidelines may reduce the cumulative incidence of wheezing and early childhood asthma down to the level of that for subjects exposed but with no heredity. Nevertheless, the preventive measures also have an effect on subjects with no heredity, which is important from a public health perspective. Of the around 100 000 children born per year in Sweden, and based on the estimations from findings in this study nearly 2000 of 8500 can be prevented from developing asthma up to the age of 2 if the family's lifestyle is consonant with the national guidelines. This is likely to have an impact not only for the child and its family, but also for the community.

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