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Study on the Prevention of Allergy in Children in Europe (SPACE): Allergic sensitization in children at 1 year of age in a controlled trial of allergen avoidance from birth

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Several studies have demonstrated that early intervention may modulate the natural course of atopic disease. Our objective was to prevent sensitization to house-dust mite and food allergens, as well as the development of atopic symptoms during infancy, by the combination of an educational package and the use of mite allergen-impermeable mattress encasings. A multicentre European, population-based, randomized, controlled study of children at increased atopic risk [Study on the Prevention of Allergy in Children in Europe (SPACE)] was performed in five countries (Austria, Germany, Greece, the UK, and Lithuania), and included three cohorts – schoolchildren, toddlers, and newborns. We report on the newborn cohort. A total of 696 newborns were included from Austria, the UK, and Germany. Inclusion criteria were: a positive history of parental allergy; and a positive skin-prick test or specific immunoglobulin E (IgE) (IgE $\geq$ 1.43 kU/L) against at least one out of a panel of common aeroallergens in one or both parents. At 1 year of age, the overall sensitization rate against the tested allergens [dust-mite allergens: *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae* (*Der* p and *Der* f)] and food allergens (egg, milk) in the prophylactic group was 6.21% vs. 10.67% in the control group. The prevalence of sensitization against *Der* p was 1.86% in the prophylactic group vs. 5% in the control group. In conclusion, we were able to demonstrate, in a group of newborns at risk for atopic diseases, that the sensitization rate to a panel of aero- and food allergens could be effectively decreased through the use of impermeable mattress encasings and the implementation of easy-to-perform preventive measures.

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It is commonly accepted that the expression of atopic diseases is dependent upon an interaction of genetic factors and allergen exposure (1,2). Allergic diseases are most often preceded by sensitization to various allergens (2,3). It has been demonstrated that exposure to house-dust mite allergens in early childhood is an important determinant of the subsequent development of bronchial asthma (4–6). Recent findings in T-cell immunology suggest that early childhood is a unique period during which the immune responses that trigger atopic disorders can potentially be

manipulated prophylactically (7). During the last year it has become clear that early intervention may modulate the natural course of atopic disease (8–11). It has been shown by Arshad et al. that reduction in the exposure of high-risk infants to food and house-dust mite allergens substantially lowered the frequency of allergic manifestations in infancy (8). However, a very high-risk group was included and prevention measures were used that are not easy to perform for the average family (i.e. use of acaracides, diet for the mother during lactation).

There is a diversity of opinion about the usefulness of mattress covers in reducing the exposure to mite allergens (12–15). They have been proposed as a simple way of mite-allergen prevention that is uncomplicated and inexpensive to perform. Hill and co-workers demonstrated that concentrations of *Dermatophagoides pteronyssinus* (*Der* p) can be reduced below the reported threshold for sensitization (2 μg) by the use of impermeable mattress encasings (15).

In a recently published meta-analysis of mite-preventive measures in mite-sensitive asthmatics, it has been suggested that current chemical and physical methods aimed at reducing exposure to allergens from house-dust mites seem to be ineffective in the tertiary prophylaxis of asthmatic patients (16). Our objective was to show if simple preventive measures – mite-impermeable mattress covers combined with an educational package of other mite- and food allergen-preventive measures that are easy to perform – are able to reduce the sensitization rate and, as a secondary outcome, the incidence and symptoms of atopic diseases. A study was set up to test this hypothesis in a multinational cohort of newborns with a positive parental history of allergy.

Methods

Informed consent was obtained from the parents prior to all measurements, and the study protocol was approved by local Ethical Committees in each centre. The study was prospective, randomized and controlled, and followed the intention-to-treat principle. The inclusion criteria were single or dual heredity (allergic disease in one or both parents), which was confirmed by allergy testing. Exclusion criteria were birthweight below 2500 g and admission to a neonatal intensive care unit for longer than 7 days.

Study design and subjects

All children participated in an international multicentre study [Study on the Prevention of Allergy in Children in Europe (SPACE, Biomed II programme of the EC; grant no. PL95-1211)] that included three cohorts of different age (newborns, toddlers, and schoolchildren) from Austria, Germany, the UK, Greece, and Lithuania (data on toddlers and schoolchildren are not discussed in the present article). We report here on the newborn cohort that was recruited in Austria (Vienna), Germany (Freiburg), and the UK (Newport) only.

Mothers were identified either at routine visits to obstetric wards during pregnancy [Vienna, Austria: Allgemeines Krankenhaus der Stadt Wien (AKH), Sozialmedizinisches Zentrum Ost (SMZ-Ost); Freiburg, Germany: St. Josefskrankenhaus and Diakoniekrankenhaus; Newport, UK: St. Mary's Hospital in Newport] or shortly after birth at the children's departments of the respective clinics (Austria 50%, Germany, 5%, UK, 0%).

Screening questionnaires for symptoms associated with allergic diseases were distributed and filled in together with the parents (Austria, UK), or distributed and returned by mail (Germany). In Austria, screening questionnaires were distributed by students who talked to the mothers and, some days later, contacted them by telephone at home. In the UK, research nurses explained the study to the parents, carried out the allergy testing with the parents, and included them on the same day into the study. If a history of allergic rhinitis, hayfever, bronchial asthma or atopic eczema was reported by any parent or a sibling, skin-prick testing (ALK Scherax, Hamburg, Germany) or measurement of serum immunoglobulin E (IgE) (CAP system; Upjohn & Pharmacia, Uppsala, Sweden) was performed in parents. The newborn was included in the event of a positive history in a parent of allergy and positivity to at least one allergen out of a panel of five aeroallergens (*Der* p, *Der* f, birch pollen, grass pollen, cat dander). In Austria, ragweed, and in the UK, dog and tree pollen mix, were tested in addition.

This report covers the time-period from April 1997 to June 1999. All participating families were visited at home during the first 4 weeks after birth of the infant to implement allergy-preventive measures. Randomization was performed according to the expected or actual date of birth, depending on whether the child was included pre- or postnatally in the study. Two-week periods were assigned to either control or intervention, according to standard randomization tables. Once the child was randomized, the field workers gave the parents verbal and written explanation of these measures. The parents of participants were informed of the rationale behind the study. They

were also informed that there would be two groups taking part in the study – equally at high risk, but following different advice. However, as control parents did not receive a placebo mattress cover, owing to the possibility of a small protective effect against allergens, they might have suspected that their children belonged to the control arm. At 6 months of age, all children were revisited in Austria. In the UK, only the families of the prophylactic group were visited, and families of the control group were contacted by telephone. In Germany, questionnaires were sent to the families of both groups by mail. At 12 months of age, children in Austria and the UK were seen in the clinic, and a physician, unaware of group allocation, performed the allergy testing. In Germany, children were visited and allergy-tested at home by a study worker not involved with statistical analyses. The parents completed a standardized questionnaire without the help of observers; this questionnaire was similar to the one completed at the beginning of the study, which sought information on the presence of allergic symptoms/disorders during the last 12 months. Detailed information on pet ownership, smoking in the home, and ventilation and heating of rooms was obtained. The prophylactic group also completed questions on the use of mattress encasing and other intervention measures. Development of sensitization to house-dust mite was evaluated by using skin-prick testing or IgE analysis performed by personnel blinded to the group allocation.

At all visits parents were given background information on allergic diseases and the higher-than-average risk of their children becoming allergic.

Prophylactic group

Exclusive breast-feeding was recommended for as long as possible and at least for 3 months following birth. Introduction of solid foods and soy milk formula was delayed until at least 6 months of age. If supplementation was required, a hypoallergenic formula was preferred before 6 months of age (except in the UK). Solid foods were introduced gradually, with 1–2 weeks allowed between the introduction of each new food. Cow's milk, egg and fish were not introduced into the child's diet before 12 months, and peanut or tree nuts not before the age of 3 years. Environmental measures focused primarily on anti-dust-mite procedures. All beds in the child's room had the mattress covered with special dust-mite protection covers. The infant's cot mattress was covered with special dust-mite protection covers, provided by the centres (Acb® Original covers; Dr Beckmann GmbH, Seefelden, Germany), unless it had a vinyl mattress (the UK only). Other mattresses where the infant might sleep, such as other beds in the infant's room or the mattress on the mother's bed, were also covered. Parents were advised not to place the infant on an uncovered bed or upholstery. Advice was also given to remove the carpet from the infant's room and to select curtains that could be hot washed. Curtains, bedding, pillow and soft toys were washed weekly at a temperature of $>55^{\circ}$C to kill the mites. Alternatively, soft toys were frozen once a week. The infant's room was ventilated at least once a day and cleaned with a damp cloth. Vacuum cleaning was advised once a week in the absence of the child. It was recommended that toys, books and clothes should be stored in cupboards so that they did not collect dust. Smoking was discouraged in the house, as was the keeping of pets. If pets were present they were not allowed into the child's bedroom. Further advice given was to discourage the child from sleeping in, or playing on, beds that were not covered, and to discourage sleeping on the bottom bed of a bunk bed.

Control group

Standard recommendation from the relevant authorities in each country was briefly reiterated for children in the control group. These were therefore slightly different in each of the participating centres. Exclusive breast-feeding was encouraged for at least 3 months following birth, with a delay in the introduction of solid food until at least 6 months of age and cow's milk until 12 months of age. Other general environmental measures were also recommended, such as avoidance of exposure to pets and cigarette smoke, and keeping rooms well ventilated.

Outcome measurement

Allergy testing was performed at 12 months of age by specific IgE testing (MagicLite™; Ciba Corning, Fernwald, Germany) or skin-prick test (SPT). A child was considered sensitized to mite allergens (*Der* p and *Der* f) at a specific IgE of $\geq$1.43 kU/L if the mean weal diameter was 2 mm larger than the negative control and at least 50% the size of the histamine weal (17). To account for different attitudes of parents towards allergen testing between countries, different allergen-testing procedures were used. In Austria and Germany, solely specific IgE analysis was performed, and in the UK skin-prick testing.

Table 1. Intention-to-treat analyses via logistic regression in 1-year-old children in the UK, Germany, and Austria

	All missings positive			All missings negative		
	OR	95% CI	p-value	OR	95% CI	p-value
Definite allergy*	0.55	(0.36–0.85)	0.007	0.51	(0.23–1.15)	0.105
Sensitization†	0.54	(0.38–0.78)	0.001	0.61	(0.39–0.98)	0.040
Der p	0.50	(0.31–0.79)	0.003	0.41	(0.15–1.08)	0.073
Egg	0.58	(0.39–0.85)	0.005	0.68	(0.40–1.15)	0.157
Milk	0.63	(0.41–0.96)	0.032	0.87	(0.43–1.75)	0.690
Food intolerance	0.67	(0.49–0.92)	0.014	0.70	(0.50–0.96)	0.027

*Defined as sensitization to one of the four tested allergens [*Dermatophagoides pteronyssinus* (*Der* p), *Dermatophagoides farinae* (*Der* f), milk, egg].
†Defined as sensitized to one of the four tested allergens plus doctor-diagnosed asthma or more than three episodes of wheeze, doctor-diagnosed eczema or doctor-diagnosed food allergy.
CI, confidence interval; OR, odds ratio.

SPT

The SPT was carried out by trained members of staff under the supervision of a physician who used the same equipment and technique each time. To achieve standardization, a videotape was made to show the different steps of the procedure, giving detailed instructions for the field workers. The allergens [*Der* p, *Der* f, grass pollens, cat dander, ragweed (Austria only) and dog and tree pollen mix (the UK only)] (ALK Scherax; concentration: 10 histamine equivalents in skin-prick testing), and the negative (sodium chloride 9 g/L) and positive (histamine hydrochloride 10 mg/mL) controls, were applied to the forearm with the aid of an ALK prick needle (ALK Scherax). The weal reactions were marked with a pen and the circle was transferred to paper using a transparent strip. Then, the largest and perpendicular diameters of each weal reaction were measured by means of a transparent ruler and the arithmetic mean was calculated. A positive test required a weal diameter of at least 2 mm larger than the negative control and an allergen weal : histamine weal ratio of ≥ 0.5. Sensitization to a mite allergen required a positive test to *Der* p or *Der* f.

Specific IgE

Specific IgE concentrations against the same allergens were determined by using the MagicLite™ test (Ciba Corning). The test results were regarded positive when values of ≥ 1.43 kU/L were obtained.

Statistical analysis

The data were entered at each centre, and then sent to the data centre to be checked for consistency. EPI-INFO was used for data entry, as this tool was available in all centres, and SAS (version 8.0) was used for data analyses (18). Differences between the groups were examined by using the one-sided Fisher's Exact Test. In an additional logistic regression approach, following the intention-to-treat principle (19,20), we included all randomized children in the arms in which they were randomly assigned, regardless of their compliance and subsequent loss in follow-up. Confounding factors, such as centre, gender, and pets in the household, were included (Table 1). We further considered potential covariates for house-dust mite, such as parental and maternal asthma, gender of the child, socio-economic status, smoking during pregnancy, smoking in the household, birthweight and pets in the household. However, they did not change our results. To compensate for the loss of follow-up we applied two approaches: first, we assumed that all lost to follow-up acquired an allergic sensitization, developed any symptoms, etc.; or, second, that all lost to follow-up did not develop an allergic sensitization or any symptoms, etc. The level of significance was considered at a level of alpha of $<5\%$. In order to verify whether the randomization was effective, we also compared household conditions and the prevalence of symptoms in the intervention and control arms.

Results

Detailed figures of the number of participants in each step of the recruitment procedure are shown in Table 2. Approximately eight families had to be screened for the inclusion of one newborn. A total of 696 children entered the study; 349 were randomly assigned to the prophylactic group and 347 to the control group. The average birthweight of the children was 3.4 ± 0.45 kg (mean $\pm$ SD).

Prevention measures were carried out satisfactorily by the study families (Table 3). However, the questionnaires were not completed properly by all the study members. The compliance regarding the use of mattress covers was high and the

Table 2. Recruitment of a cohort of newborn children in the UK, Germany, and Austria

Study centres with newborns	A: Screening questionnaires distributed	B: Screening questionnaires returned	C: Positive screening and SPT of parents performed	D: SPT of parents positive	E: Infants included (PR/CO)	F: Follow-up after 12 months (%)*	G: Infants tested after 12 months (%)*
Freiburg (Germany)	862	245	167	146	145 (84/61)	142 (97.9%)	132 (93.0%)
Vienna (Austria)	4309	4159	1227	553	402 (186/216)	382 (95.0%)	347 (86.3%)
Newport (UK)	430	430	176	153	149 (79/70)	146 (97.9%)	143 (96.0%)
Total	5601	4834	1570	852	696 (349/347)	670 (96.3%)	622 (89.4%)

CO, control group; PR, prophylactic group; SPT, skin-prick test.
*Percentage of children included.

average time of mattress cover use was >85% of the children's sleeping time in all countries. For various reasons, 26 newborns (12 in the prophylactic and 14 in the control group) were not seen at 1 year of age. Hence, after 1 year of age, 670 (96.3%) children of the initial study population were seen again (Table 2). Of these, 622 (89.4%) were tested for at least one out of four different

Table 3. Intervention measures in children of the prophylactic group at 1 year of age in the UK, Germany, and Austria

	Total (349)*		UK (79)*		Germany (84)*		Austria (186)*	
	n	%	n	%	n	%	n	%
Mattress cover use								
Sometimes	9	2.6	1	1.3	5	6.2	3	1.6
Most of the time	42	12.3	9	11.4	13	16.0	20	11.0
Always	291	85.1	69	87.3	63	77.8	159	87.4
Time of use on a daily average		88.4		92.9		89.3		86
Bed linen washed								
Never	8	2.3	4	5.1	1	1.2	3	1.6
>4 week intervals	13	3.7	1	1.3	5	6.0	7	3.8
2–4 week intervals	98	28.2	4	5.1	49	59.0	45	26.2
<2 week intervals	132	37.9	33	41.8	17	20.5	82	44.1
Every week	97	27.9	37	46.8	11	13.3	49	26.3
Soft toys washed	225	68.6	49	67.1	55	67.1	121	69.9
Ventilation of the house								
Daily	300	89.3	58	73.4	78	95.1	164	93.7
Several times a week	33	9.8	19	24.1	4	4.9	10	5.7
Never	3	0.9	2	2.5	–	–	1	0.6
Ventilation of the child's bedroom								
Several times a day	209	62.4	14	17.7	58	70.7	137	78.7
Once a day	96	28.7	39	49.4	23	28.0	34	19.6
About every 2 days	16	4.8	13	16.5	–	–	3	1.7
Less than every 2 days	14	4.2	13	16.5	1	1.2	–	–
External contact to pets	101	30.2	28	35.4	16	19.5	57	32.8
Heating off during the night								
Never	50	20.4	–	–	8	10.0	42	25.5
Sometimes	32	13.1	–	–	7	8.8	25	15.2
Ever	163	66.5	–	–	65	81.3	98	59.4
Carpet								
No carpet	70	21.1	1	1.3	18	22.0	51	29.8
Carpet	247	74.4	76	97.4	60	73.2	111	64.9
Carpet removed	18	5.4	1	1.3	4	4.9	13	7.6
Smoking in the household	83	24.6	18	22.8	14	17.1	51	29.0
Passive smoking elsewhere								
Often	9	2.7	3	3.8	1	1.2	5	2.9
Sometimes	193	57.8	26	32.9	51	62.2	116	67.1
Never	132	39.5	50	63.3	30	36.6	52	30.0
Food prevention								
No egg during year 1	336	96.3	79	100.0	82	97.6	175	94.1
No milk during year 1	337	100.0	79	100.0	81	100.0	177	100.0

*Children included (prophylactic).

Table 4. Positive skin-prick test (SPT) or specific immunoglobulin E (IgE) analysis in 1-year-old children in the UK, Germany and Austria

	Total (696: 349/347)*				UK (149: 79/70)*				Germany (145: 84/61)*				Austria (402: 186/216)*			
	Prophylactic		Control		Prophylactic		Control		Prophylactic		Control		Prophylactic		Control	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Definite allergy†	10	3.12	18	6	4	5.12	10	15.38	3	3.75	2	3.84	3	1.84	6	3.27
Allergic sensitization‡	20	6.21	32	10.67	6	7.69	10	15.38	4	5	5	9.61	10	6.09	17	9.28
Der p	6	1.86	15	5	1	1.28	2	3.07	0	0	2	3.84	5	3.04	11	6.01
Der f	2	0.62	2	0.66	1	1.28	0	0	1	1.25	1	1.92	0	0	1	0.54
Egg	15	4.67	16	5.35	6	7.69	8	12.3	4	5	3	5.76	5	3.04	5	2.74
Milk	4	1.24	8	2.67	2	2.56	3	4.6	2	2.5	3	5.76	0	0	2	1.09

*Children included: prophylactic/control.
†Defined as sensitized to one of the four tested allergens plus doctor diagnosed asthma or more than 3 episodes of wheeze, doctor diagnosed eczema or doctor diagnosed food allergy.
‡Defined as sensitization to one of the four tested allergens [*Dermatophagoides pteronyssinus* (*Der* p), *Dermatophagoides farinae* (*Der* f), milk, egg].

allergens (*Der* p, *Der* f, milk and egg). Forty-eight could not be tested because the parents did not give consent.

Regarding sensitization to any allergen tested (against *Der* p, *Der* f, egg, milk) there was a significant difference between the groups (20 vs. 32; $p < 0.03$, Fisher's Exact Test). Assuming that all lost to follow-up did not acquire any allergic sensitization to one of the tested allergens, there is a clear reduction in risk [odds ratio (OR) = 0.54, 95% confidence interval (CI): 0.38–0.78]; in addition, under the condition that all children who were lost in follow-up did develop any sensitization, there is also a clear reduction in risk (OR = 0.61, 95% CI: 0.39–0.98). The incidence of sensitization after 1 year of age in newborns against one out of four tested allergens was 6.21% in the prophylactic group (322 infants tested) vs. 10.67% in the control group (300 infants tested).

More than twice the number of children in the control group developed sensitization against *Der* p compared with children in the prophylactic group (15 vs. 6; $p < 0.03$, Fisher's Exact Test). The incidence of sensitization against *Der* p after 1 year of age was 1.86% (322 infants tested) in the prophylactic group vs. 5% (300 infants tested) in the control group (Table 4). Assuming that all lost to follow-up did not acquire an allergic sensitization to *Der* p, there is a clear reduction in risk (OR = 0.5, 95% CI: 0.31–0.79). Under the condition that all children who were lost in follow-up did develop any sensitization to *Der* p, the association remains unchanged (OR = 0.41, 95% CI: 0.15–1.08), but the 95% CI includes 1 (Table 1). The incidence of sensitization against *Der* f after 1 year was low, with only two children seen in each group. Taken together, the sensitization rate to mite allergens (*Der* p and *Der* f) tended to be lower in the prophylactic group (2.48% and 5.33%).

There was a tendency towards a reduction in definite allergy (defined as sensitization against one of the four tested allergens plus doctor-diagnosed asthma, or more than three episodes of wheeze, doctor-diagnosed eczema or doctor-diagnosed food allergy) in the prophylactic group vs. the control group (3.12% and 6%; Table 1).

Table 5. Clinical manifestations of allergy in 1-year-old children in the UK, Germany, and Austria

	Total (696: 349/347)*				UK (149: 79/70)*				Germany (145: 84/61)*				Austria (402: 186/216)*			
	Prophylactic		Control		Prophylactic		Control		Prophylactic		Control		Prophylactic		Control	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Wheezy bronchitis*	63	18.1	61	17.8	7	8.9	7	10.0	10	12.0	9	15.2	46	24.7	45	21.1
Eczema*	40	11.6	46	13.5	18	22.3	19	27.1	8	9.8	8	13.3	14	7.6	19	9.0
Food allergy*	18	5.2	14	4.1	8	10.1	4	5.7	1	1.2	4	6.8	9	4.8	6	2.9
Wheezing episodes																
Never	260	78.8	254	78.4	53	67.1	38	59.4	66	80.5	49	83.1	141	83.4	167	83.1
1–2	45	13.6	47	14.5	13	16.5	16	25.0	12	14.6	7	11.9	20	11.8	24	11.9
3–12	18	5.5	19	5.9	8	10.1	8	12.5	3	3.7	2	3.4	7	4.1	9	4.5
12†	7	2.1	4	1.2	5	6.3	2	3.1	1	1.2	1	1.7	1	0.6	1	0.5
Food intolerance‡	99	28.5	125	36.5	28	35.4	24	34.3	24	29.3	21	35.0	47	25.3	80	37.7

*Children included: prophylactic/control.
†Doctor diagnosis.
‡As reported by the parents.

One-hundred and twenty five (36.5%) children in the control group vs. 99 (28.5%) children in the prophylactic group showed symptoms of food intolerance, defined as vomiting, prolonged crying, diarrhoea or swollen lips after eating (Table 5). Assuming that all lost in follow-up did not acquire food intolerance, there is a clear reduction in risk (OR = 0.67, 95% CI: 0.49–0.92), as well as under the condition that all children who were lost in follow-up developed food intolerance (OR = 0.7, 95% CI: 0.5–0.96; Table 1).

Discussion

In our study, the incidence of sensitization to *Der* p was lower in the prophylactic than in the control group. Under the condition that all children who were lost in follow-up did not develop sensitization to *Der* p there is a clear reduction in risk (OR = 0.5, 95% CI: 0.31–0.79). However, under the condition that all children who were lost in follow-up did develop any sensitization to *Der* p, the association remains unchanged (OR = 0.41, 95% CI: 0.15–1.08) but the 95% CI includes 1. Thus, the data support a reduction of sensitization to *Der* p as a result of the preventive measures undertaken. Mite-preventive measures are recommended for the treatment of mite-sensitive asthmatics. However, a meta-analysis by Gôetsche et al. suggested that current chemical and physical methods aimed at reducing exposure to allergens from house-dust mites might be ineffective (16). The authors stated that one important potential explanation for this finding is that the methods studied did not adequately reduce levels of mite antigens. However, studies that employed effective encasings, as used in our study, were able to demonstrate a substantial reduction in mite-allergen concentrations (13,14). Hence, we assume that by the measures recommended in our study, mite allergens were substantially reduced.

Some previous prevention studies have shown a reduced incidence of symptoms of allergic diseases (8,12,21), but recently doubts were also raised about the effect of primary prevention on the development of atopic diseases (22,23). Our data show that in children with definite allergy there was a trend towards a reduction in the prophylactic group vs. the control group. One reason for this trend could have been low compliance by the parents in the prophylactic group and 'wild' intervention in the control group. However, the compliance regarding the use of mattress covers was high (Table 3) and the average time of mattress cover use was >85% (86–92%) of the children's sleeping time in all countries. It is possible that some of our outcome measures (bronchial asthma, cough, wheezing) had a viral or non-allergic aetiology at this age (24). However, in later childhood, allergic asthma as a result of mite-allergen exposure becomes more frequent. Therefore, it can be speculated that the clinical effects of preventing sensitization to mite allergens might occur much later. Seasonal factors may have affected the development of allergic disorders (25); however, as we studied mothers and their infants throughout the year, this could not have influenced the outcome of our investigation. A study on the effect of intervention measures should ideally be performed in a double-blind manner. As placebo mattress covers might themselves have mite-protective effects, we decided not to provide a control group with mattress encasings. As a consequence, we let the parents fill in the questionnaires on their own without help from observers. Furthermore, the single-blinded design could not have affected the objective SPT/specific IgE outcome. Differences occurred in how the study was conducted within the participating countries. In particular, children on the Isle of Wight were allergy tested by using skin-prick testing, whereas in Freiburg and Vienna radioallergosorbent test (RAST) analyses were performed. However, according to current literature (26) it seems unlikely that this may have resulted in a different outcome.

It has been demonstrated that food-allergen avoidance lowers the incidence of food allergy and eczema (10,11). We did not identify any difference between the groups regarding food allergy. As we only asked for this diagnosis in the questionnaire and did not perform food-challenge tests with the children, the prevalence might have been overestimated. However, the proportion of children with symptoms of food intolerance in the prophylactic group was significantly lower than in the control group (Table 1). The incidence of eczema in the prophylactic group was not significantly reduced compared with the control group (11.6% in the prophylactic group vs. 13.5% in the control group).

The use of mattress covers can easily be recommended to families, as they have no detrimental side-effects and are not expensive. Furthermore, all other educational measures that were part of our prevention programme are affordable by the average family and can be implemented without great effort. We conclude that a reduction in the exposure of high-risk infants to mite allergens, combined with dietary advice, substantially lowered the incidence of sensitizations in the first year of life. As it has been demonstrated that mite-sensitive children have a several-fold increased risk of asthma in later life (2), further observation

of the cohort will show whether mattress covers and other measures can also be recommended as a tool to lower the incidence of allergic symptoms and diseases.

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