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Atopic dermatitis at preschool age and contact allergy in adolescence: a population-based cohort study

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Running head: Preschool atopic dermatitis and adolescent contact allergy

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Author contributions: CFW and IK were involved since the start of the dermatology part of the study. IK coordinated the data collection during the entire 16-year follow-up. CL was responsible for data on contact allergy and hand eczema. CL, CFW, ML and MM made final assessments of the patch test results. ML analysed the data together with CL, AB, CFW and IK. All authors participated in the interpretation of the findings. ML wrote the initial draft. All authors had full access to all of the data, participated in critical revision of the manuscript, provided intellectual input and approved the final version. CL is the guarantor.

Bulleted statements:

What is known about this topic?

- Atopic dermatitis (AD) is characterized by an impaired skin barrier that can allow penetration of allergens.
- Children with AD in early childhood may be frequently exposed to contact allergens through topical treatments, such as moisturizers and topical medicaments.

What does this study add?

- AD at preschool age was not associated with contact allergy to nickel in adolescence.
- Our results indicate that AD at preschool age may be associated with contact allergy to fragrances in adolescence.
- Avoidance of skin exposure to scented products containing fragrance substances seems warranted in children with AD in early childhood.

Abstract

Background

Atopic dermatitis (AD) is characterized by an impaired skin barrier that can allow enhanced penetration of allergens. It is not clear whether AD influences the risk of developing contact allergy.

Objectives

To examine the association between AD at preschool age and contact allergy at 16 years of age.

Methods

At 16 years of age, 2215 adolescents from the population-based cohort BAMSE were included. These adolescents had been followed with repeated questionnaires regarding AD throughout childhood, and contact allergy was assessed by skin patch test at 16 years.

Results

AD at preschool age was associated with contact allergy to at least one of the tested substances at 16 years of age among boys (adjusted odds ratio [OR] 1.51, 95% confidence interval 1.03-2.20), but not among girls (adjusted OR 0.77, 95% CI 0.54-1.10). AD at preschool age was not associated with contact allergy to nickel in either boys or girls. In contrast, AD at preschool age was associated with contact allergy to fragrance mix I (adjusted OR 3.10, 95% CI 1.66-5.80). This association was observed especially for AD at preschool age in combination with immunoglobulin E (IgE) sensitization to airborne or food allergens (adjusted OR 3.80, 95% CI 1.67-8.61).

Conclusions

The results suggest that AD in early childhood may be associated with contact allergy to fragrances, but not to nickel, in adolescence.

Introduction

Atopic dermatitis (AD) is characterized by an impaired skin barrier and this can potentially facilitate penetration of different types of allergens. AD in early childhood is associated with immunoglobulin E (IgE) sensitization to food and airborne allergens.¹ The role of AD in development of contact allergy is less well-known. Since the immune profile in individuals with AD is directed towards a Th2 response, it has been hypothesized that these individuals may have a decreased risk of developing contact allergy, which is characterized mainly by a Th1 response.^{2,3} In contrast, it has also been suggested that the impaired skin barrier function in AD could increase the risk of sensitization to contact allergens. Frequent skin exposure to chemical substances in topical treatments, for example moisturizers and topical medicaments, at an early age and for long periods may also contribute to a heightened risk for skin sensitization among individuals with AD.^{4,5} Moisturizers often contain contact allergens such as preservatives and fragrances.⁵⁻⁸ This is true also for products labelled as hypoallergenic.⁹ A recent large study among paediatric dermatology patients shows that patients with AD have increased frequency of contact allergy to substances common in skin care products compared with patients without AD.⁵

Most published studies on AD as a risk factor for developing contact allergy have been performed among adult patients with AD in dermatological specialist care, few have been performed among the general population. These studies show diverging results.^{10,11} A recent systematic review and meta-analysis of studies performed mainly among adult AD patients, could not conclude any association between AD and contact allergy. However, an association was indicated in the general population, although based on few studies.¹⁰

We have previously shown that contact allergy is frequent already in adolescence, affecting around 15% of the population. The most common causes of contact allergy in adolescence are nickel and substances included in fragrance mix I.¹²

Population-based studies among children are scarce and those published also show diverging results concerning associations between AD and contact allergy.¹³⁻¹⁵ Some studies of contact allergy in children under dermatological specialist care indicate that children with AD are sensitized to contact allergens as frequently as children with skin diseases other than AD.¹⁶⁻¹⁸

Patch-tested paediatric patients, however, generally represent a highly selected population: they have usually been patch-tested owing to symptoms strongly suggestive of contact allergy.¹⁶ Moreover, there is a lack of prospective studies on the association between AD in early childhood and subsequent occurrence of contact allergy.

Prospective birth cohort studies provide an opportunity to study the association between AD in early childhood and subsequent contact allergy. In the present study, we aimed to investigate the association between AD at preschool age and contact allergy according to patch test at 16 years of age in a population-based birth cohort, where information on AD had been collected repeatedly from infancy to adolescence.

Materials and Methods

Original cohort

In the BAMSE population-based cohort (BAMSE is the Swedish acronym for Children, Allergy, Milieu, Stockholm, Epidemiological survey), children were consecutively recruited in infancy and prospectively followed up to 16 years of age. Children born between 1994 and

1996 in predefined areas of Stockholm were invited to participate. The cohort (n = 4089) represents 75% of the eligible children.¹⁹ At inclusion, the parents answered a baseline questionnaire enquiring about sociodemographic characteristics and parental atopic disease. The children were followed up at ages 1, 2, 4, 8, 12 and 16 years with parental questionnaires including questions on symptoms of AD, asthma and rhinitis. At ages 4, 8 and 16 years, children with completed questionnaire were also invited to participate in a clinical examination.

Assessment of contact allergy

The clinical examination at age 16 years included testing for contact allergy by skin patch test with an array of substances used routinely by dermatologists to diagnose contact allergy. TRUE test® (Mekos Laboratories AS, Hillerød, Denmark) was used, containing ready to use test material (panels 1 and 2 were regular panels and panel 3 was specially prepared for this study, totally 30 substances) including common contact allergens like metals, fragrance substances, preservatives, plastic chemicals, rubber chemicals, *p*-phenylenediamine and glucocorticoids. The test was applied at home according to written instructions of the study. Two days later, the test sites were assessed and photographed at the clinical examination facility of the study by our specially trained research nurses. The photographs were assessed by two dermatologists under coded conditions to assure proper assessment of the patch test results in the population-based setting. This procedure and the results have previously been described in detail.¹²

The present study used three categorizing variables for contact allergy in separate analyses:

(i) *any contact allergy* (contact allergy to one or more of the 30 tested substances), (ii) *contact allergy to nickel* (the most common contact allergy), and (iii) *contact allergy to fragrance mix I* (the second most common contact allergy).

Assessment of IgE antibodies at preschool age

At the clinical examinations at age 4, blood was collected for analysis of IgE antibodies. Airborne allergens and common food allergens were analysed using ImmunoCAP System (Thermo Fischer Scientific, Uppsala, Sweden) with Phadiatop® [cat, dog, horse, birch, timothy, mugwort, *Dermatophagoides pteronyssinus* (house dust mite) and *Cladosporium* (mould)] and fx5 (cow's milk, wheat, soy, cod, egg and peanut). Results were considered positive at $\geq 0.35 \text{ kU}_A/\text{L}$ and negative at $< 0.35 \text{ kU}_A/\text{L}$. To be classified as IgE sensitized a child had to have a positive result to either Phadiatop® or fx5 or both.

Atopic dermatitis variables

The exposure variables related to AD are defined in Table 1. AD was categorized according to age of onset and persistence, and was assessed based on parental reporting of symptoms of AD at different ages. IgE sensitization was assessed based on blood tests at 4 years.

Study population

The study population (Fig. 1) consisted of all participants whose parents had completed questions regarding symptoms of AD in the questionnaires at 1, 2 and 4 years, and who were patch tested at the clinical examination at the 16-year follow-up ($n = 2215$).

Ethical approval

This study was approved by the Regional Ethical Review Board in Stockholm, Sweden. The Declaration of Helsinki principles were followed. All parents gave written informed consent for their children to participate in the clinical examinations.

Statistical analysis

The study population was compared with the original cohort on a number of background characteristics and calculated 95% confidence intervals. Differences in the distribution of background characteristics in relation to AD at preschool age were assessed using chi-square test. Differences were considered statistically significant at $P < 0.05$.

To assess the association between AD at preschool age and contact allergy at 16 years we used logistic regression analysis. AD was exposure and contact allergy was outcome. Crude analysis was performed and adjustment was made for the following potential confounders suggested for AD (see Table 2 for details): gender, parental atopic disease, parental smoking, breastfeeding, parental migration status and socioeconomic status, after testing with exploratory stepwise logistic regression. Final models were then made based on all these variables. Data for boys and girls were analysed separately and interaction with gender was tested. Results are presented as odds ratios and 95% confidence intervals. Analyses were performed with STATA 13.

Results

Study population

The study population (n = 2215) was comparable with the study base (original BAMSE birth cohort, n = 4089) for most of the examined background characteristics (Table S1). Small but significant differences were observed for socioeconomic status (84.9% versus 82.7% white-collar workers) and gender (47.6% versus 50.5% boys). The present study population comprised 54.2% of the original cohort.

The prevalence of AD at preschool age was 34% (n = 753). Participants with AD at preschool age more often had parents with reported atopic disease compared to participants without AD at preschool age (54.0% versus 40.2%, $P < 0.01$). No other significant differences in background characteristics were observed (Table 2).

AD at preschool age and contact allergy at 16 years of age

At age 16 years, 15.3% (n = 338) had contact allergy to at least one of the 30 tested substances. Among the participants with AD at preschool age, 15.8% (n = 119) had *any contact allergy* at 16 years compared to 15.0% (n = 219) among adolescents without AD at preschool age ($P = 0.612$, Table 2).

In a logistic regression analysis, the association between AD at preschool age and contact allergy at 16 years of age was investigated. The results are shown in Table 3. AD at preschool age was not associated with *any contact allergy* (adjusted OR 1.04, 95% CI 0.81-1.35).

However, when investigated for boys and girls separately, AD at preschool age was significantly associated with *any contact allergy* among boys, but not among girls (adjusted OR 1.51, 95% CI 1.03-2.20 and adjusted OR 0.77, 95% CI 0.54-1.10, respectively; P for interaction with gender = 0.012). AD at preschool age was not associated with contact allergy to nickel in either boys or girls. A statistically significant association was found between AD at preschool age and fragrance mix I allergy (adjusted OR 3.10, 95% CI 1.66-5.80). When boys and girls were analysed separately in the crude model, the associations between AD at preschool age and fragrance mix I allergy were significant among both boys and girls. After adjustment for potential confounders (parental atopic disease, parental smoking, breastfeeding, parental migration status and socioeconomic status), the association remained statistically significant among boys (adjusted OR 3.66, 95% CI 1.58-8.46), but not among girls (adjusted OR 2.54, 95% CI 0.98-6.56), P for interaction with gender = 0.69.

Association between persistency of AD in childhood and contact allergy at 16 years

Analyses of associations between persistency of AD at preschool age and contact allergy showed no associations for *any contact allergy* or nickel allergy. In contrast, children with AD at preschool age who also had AD at ages 8, 12 and/or 16 years (persistent AD) had increased odds ratio of contact allergy to fragrance mix I at 16 years of age (adjusted OR 3.82, 95% CI 1.77-8.22). The odds ratio was also higher (albeit not significantly so) for children with AD at preschool age but not thereafter (transient AD) (adjusted OR 2.29, 95% CI 0.98-5.36) (Fig. 2).

Association between AD at preschool age with or without IgE sensitization and contact allergy

In total, 37% (n = 218) of participants with AD at preschool age had IgE sensitization at 4 years of age compared to 18% (n = 213) of participants without AD at preschool age. No association was found between AD at preschool age with concurrent IgE sensitization and *any contact allergy* or nickel allergy. Having both AD at preschool age and IgE sensitization at 4 years of age was associated with contact allergy to fragrance mix I at 16 years of age (adjusted OR 3.80, 95% CI 1.67-8.61), while no association was observed for AD at preschool age without concurrent IgE sensitization (adjusted OR 1.19, 95% CI 0.45-3.17) (Table 4).

Discussion

The results from our population-based cohort indicate that AD at preschool age was associated with increased odds of *any contact allergy* (i.e. to at least one of 30 patch tested substances) at 16 years of age in boys, but not in girls. AD at preschool age was not associated with increased odds of contact allergy to nickel; in contrast, there was an association with contact allergy to fragrance mix I. In particular, this association was observed for AD at preschool age in combination with IgE sensitization to airborne or food allergens, while no association was observed for AD at preschool age without concurrent IgE sensitization. Analyses of persistence of AD through childhood indicated that both transient and persistent AD is associated with increased odds of contact allergy to fragrance mix I.

The BAMSE cohort is a large, well-characterized, prospective cohort with population-based design, and high participation rate. Information on AD had been collected repeatedly by parental questionnaires, from infancy to adolescence, and was collected before assessment of contact allergy at age 16 years. Population-based patch test studies in children and adolescents are rare, and the use of patch test to assess contact allergy in over 2200 adolescents is a major strength of our study.

Some limitations are worth mentioning. Patch test readings were done on day 2 only, to ensure a high participation rate. Although readings done solely on day 2 are known to underestimate contact allergy somewhat, potentially resulting in underestimation of the association between AD and contact allergy, fragrance mix I reactions are usually positive already on day 2.^{20,21} Moreover, associations might have been stronger if fragrance mix II had been tested as well, but this mix was not available in TRUE test® at the time.

Not all adolescents for whom we had data on AD at preschool age were patch tested, mostly because they did not participate in the clinical examination at age 16 years. Although this could potentially result in selection bias, the study population was comparable to the original cohort. There were no statistically significant differences in parental atopic disease between the study population and the original cohort. A survey performed 2002 of the non-responders shows that parental atopic disease did not differ between non-responder families and families in the original cohort, although parental smoking was more common among non-responders.¹⁹

The association between AD at preschool age and *any contact allergy* among boys, but not among girls, may be explained by the fact that *any contact allergy* among girls is numerically dominated by contact allergy to nickel.¹² Previous results from our cohort show that 69% of the cases of contact allergy to nickel at age 16 years occurred among girls, where the prevalence was 9.8% compared to 4.9% among boys.¹² One can speculate that since there is no association between AD at preschool age and nickel allergy, this can possibly ‘hide’ an association to other specific contact allergens of the totally 30 tested. In addition, an association between AD and contact allergy has been described in a cross-sectional study of adults when nickel was excluded from the analysis based on the assumption that the high frequency of piercing among women might result in bias.²²

Results from previous studies on the association between AD and nickel allergy have diverged, but since one cause of sensitization to nickel is piercing, it has been suggested that the exposure to nickel by piercing may be more important than exposure via the impaired skin barrier in AD for sensitization to nickel.^{13,23,24} However, nickel exposure is complex since there are numerous sources of exposure to nickel beyond piercing and jewellery²⁵.

Contact allergy to fragrance mix I is one of the most frequent contact allergies from an early age among children and adolescents.²⁶ Our previous studies of the same cohort estimated the prevalence of contact allergy to fragrance mix I at 2.1%, and observed an association between self-reported eczema or itchy rash after use of personal hygiene products or makeup and contact allergy to fragrance mix I.^{12 27}

Our results on association between AD and fragrance allergy correspond with a Dutch study reporting that patch tested paediatric patients with AD reacted significantly more often to fragrances than those without AD.²⁸ Fragrance allergy has previously been found to be more common among adults with than without AD – both in general populations and among patients.^{22,29} Nonetheless, our results describing an association between AD in early childhood and fragrance mix I are based on relatively few individuals with a positive patch test to fragrance mix I (n = 47), and should be interpreted in context.

Products such as soaps, moisturizers and wipes intended for young children often contain fragrances, and children with AD may be exposed frequently and for prolonged periods.^{30,31}

This may explain or contribute to the association with fragrance allergy. Sensitization to a contact allergen is dependent on skin exposure to that specific substance. This may be one reason why studies focusing mainly on contact allergy to any substance have seen no or weak associations with AD.

The association between AD at preschool age with IgE sensitization early in life and contact allergy to fragrances at 16 years indicates that the impaired skin barrier may facilitate penetration not only of airborne and food allergens, but also of contact allergens. It is also possible that these individuals have had a more severe AD during childhood.³² Whether the association is caused by the severe impairment of the skin barrier (which facilitates penetration of contact allergens) or increased skin exposure to locally applied fragrances (due to the more chronic and severe dermatitis) or a combination of the two, cannot be determined from our results.

Contact allergy to fragrances can result in persistent dermatitis that may be incorrectly interpreted as AD. Children with allergic contact dermatitis may meet the criteria for AD, and it can be difficult to distinguish allergic contact dermatitis from AD.³³ This can create diagnostic challenges in clinical practice as well as in epidemiological studies. A recent study of dermatology patients with difficult-to-treat AD showed a high prevalence of contact allergy among both children and adults.³⁴

Due to the population-based design of our study, and its limited loss to follow-up, the external generalization ought to be valid for general populations in north-western Europe.

In conclusion, the results from our population-based cohort indicate that AD at preschool age may be associated with increased odds of contact allergy in adolescence to fragrance mix I, but not to nickel. Our results speak in favour of preventive measures aiming to reduce the use of scented products (including natural extracts/essential oils) in children with AD, to avoid sensitization to fragrances.

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Supporting information

Additional supporting information:

Table S1.

Background characteristics of children in the study base (original BAMSE cohort) and the study population (adolescents patch tested at age 16 years, with prospective data on atopic dermatitis at preschool age)

Table 1 Definitions of exposure variables related to atopic dermatitis (AD) in this study, based on parental questionnaires and blood tests

Variable	Definition
AD at preschool age	Dry skin and itchy rash for ≥ 2 weeks with rash on specific locations (face or arm/leg extension surfaces or arm/leg flexures or wrist/ankles or neck) in the last 12 months and/or doctor's diagnosis of atopic dermatitis since the last follow-up on at least one of the follow-ups at age 1, 2 and 4 years.
Persistent AD	AD at preschool age and AD at 1 or more follow-ups after 4 years to 16 years.
Transient AD	AD at preschool age but no AD at follow-ups after 4 years to 16 years.
School onset AD	AD at follow-ups at the age of 8, 12 and/or 16 years, but no AD at preschool age.
IgE sensitization	IgE value for Phadiatop [®] ≥ 0.35 kU _A L ⁻¹ and/or for food mix ≥ 0.35 kU _A L ⁻¹ at 4 years of age.

Table 2 Selected background factors and main exposure show the comparability of the patch tested adolescents who did versus did not have atopic dermatitis at preschool age.

Background factors	AD at preschool age (n = 753)		No AD at preschool age (n = 1462)		P-value
	n	%	n	%	
Any contact allergy	119	15.8	219	15.0	0.612
Male gender	353	46.9	702	48.0	0.609
Parental atopic disease ^a	404	54.0	582	40.2	< 0.01
Parental smoking ^b	159	21.3	276	19.0	0.188
Socioeconomic status ^c : white-collar worker	610	82.8	1247	85.9	0.050
Parental migration status ^d	122	17.1	210	14.9	0.198
Exclusive breastfeeding ^e	596	80.3	1180	80.8	0.804

AD, atopic dermatitis.

P-values obtained from chi-square test.

^a Self-reported doctor's diagnosis of asthma and asthma medication and/or doctor's diagnosis of hay fever in combination with furred pets and/or pollen allergy and/or doctor's diagnosis of atopic dermatitis at baseline in any parent.

^b Mother or father smoked at least 1 cigarette daily.

^c White-collar worker in household; socioeconomic groups according to Statistics Sweden.

^d Any parent from outside Scandinavia.

^e Exclusive breastfeeding for ≥ 4 months.

Table 3 Association between AD at preschool age and contact allergy based on patch test at 16 years. Results obtained by logistic regression analyses (n = 2215).

	Any contact allergy			Nickel allergy			Fragrance allergy		
	n	Crude OR (95% CI)	Adjusted OR (95% CI) ^b	n	Crude OR (95% CI)	Adjusted OR (95% CI) ^b	n	Crude OR (95% CI)	Adjusted OR (95% CI) ^b
AD at preschool age									
All (N = 2215)									
No (N = 1462)	219	1.00 (ref.)	1.00 (ref.)	112	1.00 (ref.)	1.00 (ref.)	19	1.00 (ref.)	1.00 (ref.)
Yes (N = 753)	119	1.07 (0.84-1.36)	1.04 (0.81-1.35)	51	0.88 (0.62-1.23)	0.81 (0.56-1.17)	28	2.93 (1.63-5.29)	3.10 (1.66-5.80)
Boys (N = 1055)									
No (N = 702)	84	1.00 (ref.)	1.00 (ref.)	31	1.00 (ref.)	1.00 (ref.)	10	1.00 (ref.)	1.00 (ref.)
Yes (N = 353)	60	1.51 (1.05-2.16)	1.51 (1.03-2.20)	21	1.37 (0.77-2.42)	1.33 (0.73-2.46)	16	3.29 (1.48-7.32)	3.66 (1.58-8.46)
Girls (N = 1160)									
No (N = 760)	135	1.00 (ref.)	1.00 (ref.)	81	1.00 (ref.)	1.00 (ref.)	9	1.00 (ref.)	1.00 (ref.)
Yes (N = 400)	59	0.80 (0.57-1.12)	0.77 (0.54-1.10)	30	0.68 (0.44-1.05)	0.63 (0.40-1.01)	12	2.58 (1.08-6.18)	2.54 (0.98-6.56)

Significant ORs are in bold. AD, atopic dermatitis; CI, confidence interval; OR, odds ratio; n, number of adolescents patch tested positive and having data on AD at preschool age; N, number of adolescents patch tested and having data on AD at preschool age. ^aAdjusted for gender, parental atopic disease, parental smoking, breastfeeding, parental migration status, socioeconomic status. ^bPositive patch test reaction to fragrance mix I.

Table 4 Association between presence or absence of atopic dermatitis at preschool age and presence or absence of IgE sensitization at 4 years of age, in relation to contact allergy, based on patch test at 16 years. Results obtained by logistic regression analysis (n = 1739)

	Any contact allergy			Nickel allergy			Fragrance allergy ^a		
	n	Crude OR (95% CI)	Adjusted OR (95% CI) ^b	n	Crude OR (95% CI)	Adjusted OR (95% CI) ^b	n	Crude OR (95% CI)	Adjusted OR (95% CI) ^b
No AD at preschool age, no IgE sensitization (N = 934)	143	1.00 (ref.)	1.00 (ref.)	66	1.00 (ref.)	1.00 (ref.)	13	1.00 (ref.)	1.00 (ref.)
No AD at preschool age, IgE sensitization (N = 213)	34	1.06 (0.71-1.60)	1.05 (0.69-1.59)	21	1.45(0.87-2.43)	1.51(0.89-2.54)	3	1.02 (0.29-3.62)	0.64 (0.14-2.89)
AD at preschool age, no IgE sensitization (N = 365)	56	1.01 (0.72-1.42)	0.97 (0.68-1.37)	24	0.94 (0.58-1.52)	0.89 (0.54-1.48)	6	1.20 (0.45-3.17)	1.19 (0.45-3.17)
AD at preschool age and IgE sensitization (N = 218)	36	1.11 (0.74-1.65)	1.13 (0.75-1.71)	15	0.98 (0.55-1.76)	1.07 (0.59-1.94)	12	4.17 (1.87-9.27)	3.80 (1.67-8.61)

Significant ORs are in bold. AD, atopic dermatitis; CI, confidence interval; OR, odds ratio; N, number of adolescents patch tested and having data on AD at preschool age and IgE sensitization at 4 years; n, number of adolescents with AD at preschool age or not and with or without IgE sensitization at 4 years of age and contact allergy according to patch test. ^a Positive patch test reaction to fragrance mix I. ^b Adjusted for gender, parental atopic disease, parental smoking, breastfeeding, parental migration status, socioeconomic status.

Figure legends

Fig 1

Flow-chart showing the original cohort and the way to the final study population.

Fig 2

Results of logistic regression analysis of the association between persistency of atopic dermatitis in childhood (transient atopic dermatitis, school age onset atopic dermatitis and persistent atopic dermatitis) and contact allergy to any contact allergen (n = 317), nickel (n = 157) and fragrance mix I (n = 41) based on patch test at 16 years. OR adjusted for gender, parental atopic disease, parental smoking, breastfeeding, parental migration and socioeconomic status. AD, atopic dermatitis, OR, odds ratio

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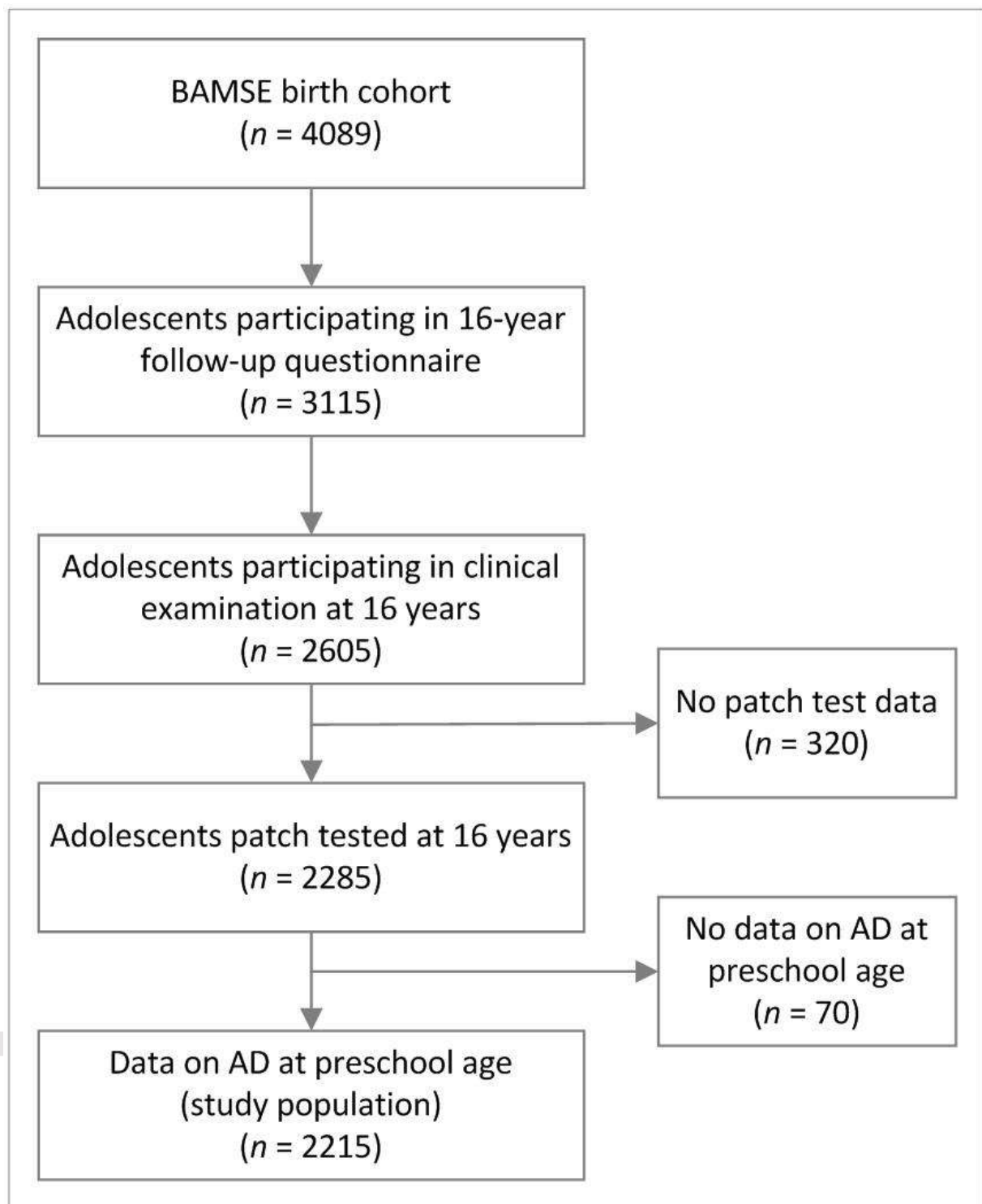


Fig 1.

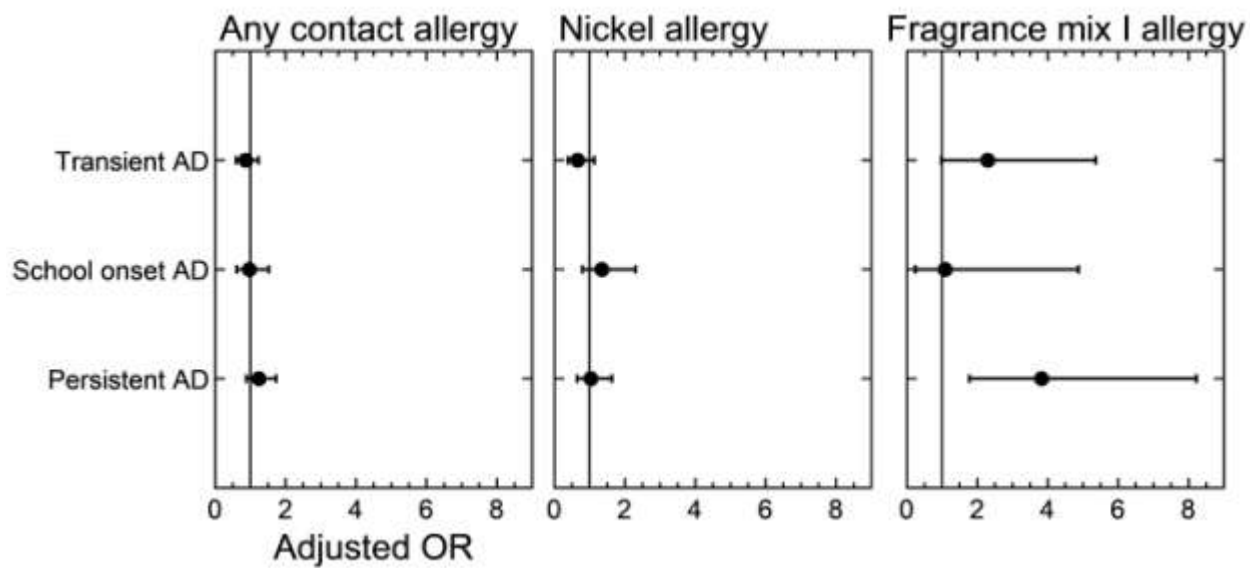


Table S1

Background characteristics of children in the study base (original BAMSE cohort) and the study population (adolescents patch tested at age 16 years, with prospective data on atopic dermatitis at preschool age)

Background factors	Study base (n = 4089)	Study population (n = 2215)	
	%	%	95% CI
Male gender	50.5	47.6	45.5-49.7
Parental atopic disease ^a	43.2	44.9	42.8-47.0
Parental smoking ^b	21.0	19.8	18.1-21.4
Socioeconomic status ^c : white-collar worker	82.7	84.9	83.4-86.4
Young mother ^d	7.8	7.2	6.1-8.3
Parental migration status ^e	16.0	15.6	14.1-17.2
Exclusive breastfeeding ^f	79.5	80.6	79.0-82.3

Significant differences are in bold.

AD, atopic dermatitis; CI, confidence interval.

^a Self-reported doctor's diagnosis of asthma and asthma medication and/or doctor's diagnosis of hay fever in combination with furred pets and/or pollen allergy and/or doctor's diagnosis of AD at baseline in any parent.

^b Mother or father smoked at least 1 cigarette daily.

^c White-collar worker in household , Socioeconomic groups according to Statistics Sweden.

^d Mother's age below 25 years at birth of the child.

^e Any parent from outside Scandinavia.

^f Exclusive breastfeeding $\geq$ 4 months.