ORIGINAL ARTICLE

# Prevalence and characteristics of atopic dermatitis among young adult females and males—report from the Swedish population-based study BAMSE

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## Abstract

**Background** There is limited knowledge regarding prevalence and characteristics of atopic dermatitis (AD) among young adults in the general population.

**Objectives** To study AD among young adults in a Swedish population-based birth cohort, with a particular focus on prevalence, sex differences including risk for AD at different ages, disease course and characteristics of AD at 24 years.

**Methods** The BAMSE cohort includes 4089 individuals who have been followed regularly from birth to age 24 years regarding AD and atopic diseases. For this study 3055 individuals who answered questions regarding AD at the 24-year follow-up were included. All were invited to a clinical examination including skin examination, evaluation by William's criteria and collection of blood for analysis of specific IgE, and 2264 individuals chose to participate.

**Results** At 24 years, the 12-month prevalence of AD was 17.8% and more females than males had AD (20.5% vs. 14.8%), $P < 0.0001$. The point prevalence of ongoing AD at clinical examination was 8.0%. AD severity as assessed by Patient-Oriented Eczema Measure (POEM) did not differ between sexes. The proportion of adult onset of AD was 16.9% (92 of 543), females 17.3% vs. males 16.4%. More females than males with AD at 24 years reported disturbed sleep due to itch (26.1% vs. 15.5%, $P < 0.003$). IgE sensitization was less common among females with AD than males with AD (61.3% vs. 79.6%, $P < 0.0001$). In addition, male sex (female sex being the reference) was associated with increased odds for AD the first year of life (OR: 1.31, 95% CI; 1.10–1.56), and decreased odds of AD in adolescence and young adulthood (OR: 0.66, 95% CI; 0.55–0.80).

**Conclusions** Atopic dermatitis is a common disease among young adults, and even though more females than males have AD at 24 years, adult onset of AD seems to be equally prevalent among both sexes in young adulthood.

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## Conflict of interest

EJ received lecture fees from LEO Pharma, Sanofi Genzyme, Novartis and AbbVie and consultancy fees from Sanofi Genzyme and LEO Pharma. SL received consultancy fee from Sanofi Genzyme. NB received lecture fees from Sanofi AB and consultancy fees from Galenica AB and Sanofi Genzyme. CFW has participated as unpaid expert in meetings with Sanofi Genzyme and AbbVie. EM, AB, IK and MJ reported no conflict of interest.

## Funding information

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## Introduction

Atopic dermatitis (AD) is an inflammatory skin disease characterized by recurrent itchy eczematous lesions and dry skin. People of all ages are affected by AD although the disease can start at any age the usual age of onset is in early childhood. AD is very common in childhood, affecting up to at least 20% of children.[1] However, AD is also common at older ages and in high-income countries around 10% of the adult population is affected by AD.[2,3] A recent systematic review reported the 12-month prevalence of AD in adults, based on symptoms, to range between 1.3% and 22.7%.[4] Despite this, there is limited knowledge regarding AD in young adults and the course of AD beyond childhood.[5]

Males and females are not equally affected by AD, and studies have shown that AD is more common among males during infancy and childhood.[6,7] However, around puberty, there is a shift towards more females than males having AD and this female predominance continues into adulthood.[2,3,6,8,9] Even though AD does not affect males and females equally, relatively little is known regarding differences between females and males concerning the course and characteristics of AD.

We therefore aimed to study the prevalence and characteristics of AD among young adults in a Swedish population-based birth cohort followed up to age 24 years, with a particular focus on sex differences including treatment of AD, disease course, IgE-sensitization, sleep disturbance and severity of AD. In addition, we wanted to validate the questionnaire-based BAMSE AD definition at 24 years against William's criteria.

## Participants and methods

### Study design and setting

The BAMSE project is a population-based cohort from Stockholm, Sweden. Newborn children were recruited from 1994 to 1996 and followed up to 24 years of age. The BAMSE cohort comprised 4089 infants, corresponding to 75% of the eligible subjects.[10] When the boys ($n$ = 2065) and girls ($n$ = 2024) were 2 months (baseline), parents completed questionnaires on background factors and follow-up questionnaires including questions regarding manifestations of AD, asthma, and rhinitis were sent out and answered by parents and/or participants at 1, 2, 4, 8, 12 and 16 years of age. At the 24-year follow-up, participants answered a questionnaire including questions about dry skin, itchy skin rash, affected localizations and nocturnal sleep disturbance due to itch. There were also questions regarding the use of moisturizers, topical glucocorticoids and other treatments for AD. Individuals who had answered the questionnaire were invited to a clinical examination including blood samples. Participants with visible AD at the clinical examination were asked to complete Patient-Oriented Eczema Measure (POEM), a validated scale for self-evaluation of AD severity the last week.[11] Sera were analysed for IgE antibodies to inhalant and food allergens by the use of Phadiatop®, Thermo Fisher, Uppsala, Sweden (timothy, birch, cat, dog, house dust mites, mugwort, horse and mould) and Fx5 (peanut, soy, wheat, milk, egg and cod) ImmunoCAP system®, Thermo Fisher, Uppsala, Sweden. A positive test result was defined as ≥0.35 kUA/l.

### Study population

The 24-year follow-up of the BAMSE cohort was finalized in 2019 and included 3069 individuals corresponding to 75% of the original cohort,[12] Fig. 1. For the current study, we included individuals who had answered the questions regarding AD ($n$ = 3055). Among these, 2264 (74%) had participated in the clinical examination and data on IgE sensitization were available for 2229 (73%) individuals. Fig. 1 shows a flow chart of the study.

### Definitions

AD definitions based on questionnaire data at the 24-year follow-up and at previous follow-ups are shown in Table 1.

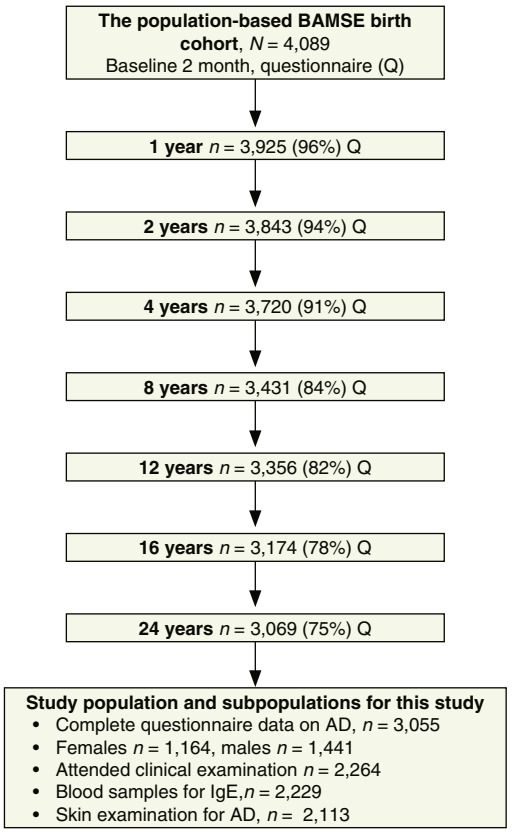


**Figure 1** Flow chart of the study.

**Table 1** Definition of atopic dermatitis at different ages based on questionnaire data in the BAMSE cohort

| Variable | Definition of atopic dermatitis (AD) |
|---|---|
| **AD at age 1, 2 and 4 years** | Dry skin and itchy skin rash for ≥2 weeks on specific locations (face or arm/leg extension surfaces or arm/leg flexures or wrist/ankle flexures) over the last 12 months and/or doctor's diagnosis of AD since last follow-up. Reported by parent |
| **AD at age 8 years** | Dry skin and itchy skin rash for ≥2 weeks on specific locations (face or arm/leg flexures or wrists/ankles or neck) over the last 12 months and/or doctor's diagnosis of AD after 4 years of age up to 8 years of age. Reported by parent |
| **AD at age 12 years** | Dry skin and itchy skin rash on specific locations (arm/leg flexures or wrists/ankles or neck) over the last 12 months and/or doctor's diagnosis of AD after 10 years of age up to 12 years of age. Reported by parent |
| **AD at age 16 years** | Dry skin and itchy skin rash on specific locations (arm/leg flexures or wrists/ankles or neck) over the last 12 months. Reported by adolescent |
| **AD at age 24 years** | Itchy skin rash the last 12 months in combination with three of the following four criteria:<br>1 dry skin the last 12 months<br>2 history of AD at age 1 and/or 2 years based on questionnaire data (onset below age 2)<br>3 history of flexural dermatitis at any BAMSE follow-up<br>4 personal history of asthma or hay fever defined as reported asthma and/or rhinitis at any BAMSE follow-up from age 4 years |

*AD at the 24-year follow-up based on clinical examination* Fulfilling UK Working Party criteria,[13,14] also called William's criteria, (itchy skin condition the last 12 months and three minor criteria). The minor criterion assessed at the clinical examination was visible flexural dermatitis. Questionnaire data were used for assessment of the other four minor criteria: (i) report of dry skin the last 12 months at the 24-year follow-up, (ii) history of AD at age 1 and/or 2 years based on prospectively collected questionnaire data, (iii) history of flexural dermatitis at any previous BAMSE follow-up and (iv) personal history of asthma or hay fever defined as reported asthma and/or rhinitis at one or more BAMSE follow-ups from age 4 years.

*AD with IgE association* Individuals classified with AD that displayed any IgE sensitization defined as positive Phadiatop and/or Fx5 at the 24-year follow-up.

### Statistics

The prevalence of AD based on questionnaire data was assessed during a 12-month period and expressed as percentage of the total number of study subjects with complete questionnaire data on AD. The point prevalence of AD was assessed at the clinical examination and expressed as percentage of the total number of study subjects that participated at the clinical examination. For dichotomous variables, chi-squared tests were used for evaluation of differences between males and females. For POEM scores, mean and median values as well as interquartile range were used. The Mann–Whitney *U*-test was used to calculate *P*-values for evaluation of differences between males and females regarding POEM. *P*-values <0.05 were considered statistically significant.

Generalized estimating equations (GEEs)[15] with an unstructured correlation matrix were used to assess the impact of sex over time for AD. Potential confounders were tested using exploratory backward stepwise logistic regression. None of the tested factors, parental allergy, low birthweight (<2500 g), exclusive breast-feeding ≥4 months, maternal smoking during pregnancy and at enrolment, parental low socioeconomic status and young mother (<26 years), confounded the association between sex and AD, and unadjusted odds ratios are therefore presented. All statistical calculations were performed with STATA Statistical Software (release 16:1; Stata-Corp, College Station, TX, USA).

### Ethics

The study was approved by the regional ethics committee in Stockholm (2016/1380-31/2), and participants provided written informed consent.

## Results

### AD prevalence at the 24-year follow-up

In the study-population, 543 of 3055 individuals (17.8%, 95% CI: 16.4%−19.1%) fulfilled the criteria to be classified as having had AD the past year. AD was significantly more prevalent among females compared with males (20.5% vs. 14.8%, $P < 0.0001$). Among those who participated at the clinical examination, 8.0% (95% CI: 6.8%–9.2%) had ongoing AD (females 8.5%, males 7.3%, $P = 0.33$).

### History of AD among the 543 individuals with AD at the 24-year follow-up

A majority (63.7%, 95% CI: 59.7%–67.8%) of individuals with AD at the 24-year follow-up debuted in early childhood with AD before the age of 2 years, Fig. 2. A history of onset of AD in this age was more common among males compared with females (69.5% vs. 60.0%, $P < 0.02$). More males than females with AD at the 24-year follow-up had a history of persistent AD defined as AD at four or more of the six previous follow-ups, (30.5% vs. 21.2%, $P < 0.01$). Among those with AD at the 24-year follow-up, 16.9% (92 of 543) presented with AD for the first time and

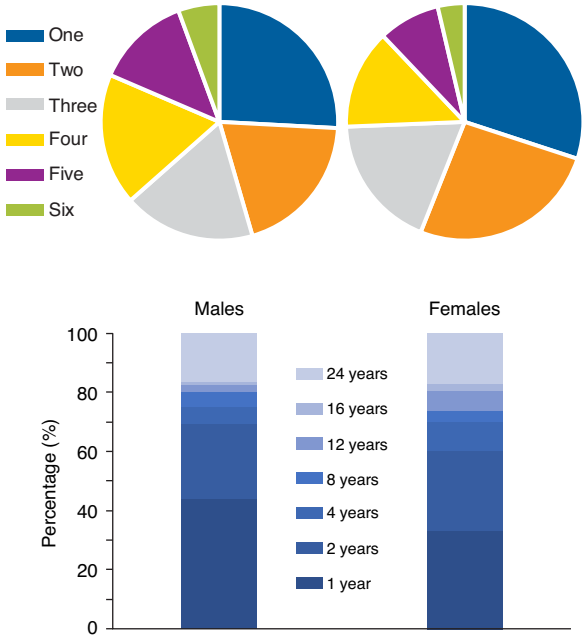


**Figure 2** History of AD among males and females with AD at age 24 years. Bar sections represent the proportions of males and females with onset of AD at different ages. Sections in the above circles show the number of previous follow-ups with AD. Missing data at previous follow-ups ranged between 2% and 13% and were counted as not having AD. Somewhat, more males than females lacked data regarding AD at previous follow-ups.

had no history of AD at previous follow-ups. The proportion with such adult onset did not differ significantly between males and females (16.4% vs. 17.3%), Fig. 2.

### Location of AD at the 24-year follow-up

Extremities and hands were the most common sites affected by AD among both sexes, followed by the trunk and scalp, Table 2. In general, reports from males and females regarding body sites affected by AD were similar. The exception was AD affecting the groin and pubic area that was reported by 14.1% of males compared with 7.9% of females ($P = 0.02$). A majority of both males and females reported that AD had affected up to three of the body sites in Table 2 the last year. Widespread AD affecting seven or more body sites the last year was reported by 14.5% of males and 11.8% of females with AD, $P = 0.35$.

### Sleep disturbance due to itch at the 24-year follow-up

Most individuals with AD reported no sleep disturbance or seldomly disturbed sleep due to itch. Yet, significantly, more females than males reported sleep disturbance due to itch sometimes, often, or always during the past year (26.1% vs. 15.5%, $P < 0.003$). The distribution of answer alternatives was as follows for females vs. males: never (47.7% vs. 58.7%), seldom (26.1% vs. 25.8%), sometimes (19.8% vs. 9.9%), often (5.5% vs. 3.8%) and always (0.9% vs. 1.9%).

**Table 2** Location of atopic dermatitis (AD) among young adults at age 24 years in the population-based cohort BAMSE

| Location of AD | *n* | % |
|---|---|---|
| Extensor surface of extremities | 226/543 | 41.6 |
| Flexural surface of extremities | 218/543 | 40.2 |
| Hands | 216/543 | 39.8 |
| Trunk | 175/543 | 32.2 |
| Neck or throat | 163/543 | 30.0 |
| Wrist or ankles | 162/543 | 29.8 |
| Scalp | 161/543 | 29.7 |
| Face | 157/543 | 28.9 |
| Inside of the thighs | 144/543 | 26.5 |
| Buttocks | 97/543 | 17.9 |
| Feet | 76/543 | 14.0 |
| Armpits | 59/543 | 10.9 |
| Groin or pubic area | 56/543 | 10.3 |
| Ears | 42/543 | 7.7 |
| Elsewhere | 27/543 | 5.0 |

### AD treatment at the 24-year follow-up

More than 90% of individuals with AD reported having used emollients, and 64.6% reported the use of topical glucocorticoids the last year. The use of oral glucocorticoids due to skin disorder was reported by 9.3%, and phototherapy treatment during the past year was reported by 3.7% of individuals with AD. We also asked for the use of alternative supplements/drugs for AD, such as herbal medicines, and 30.6% of individuals with AD reported the use of alternative treatments. More females than males used emollients; otherwise, there were only minor differences between sexes regarding AD treatments, Table 3.

**Table 3** Reported treatments for atopic dermatitis the past year among young females and males in the population-based cohort BAMSE

| Reported treatments for AD the past year | Females | | Males | | *P*-value† |
|---|---|---|---|---|---|
| | *n* | % | *n* | % | |
| Emollients | 312/322 | 96.9 | 183/198 | 92.4 | 0.02 |
| Topical glucocorticoids | 215/322 | 66.8 | 121/198 | 61.1 | 0.19 |
| Phototherapy | 13/317 | 4.1 | 6/196 | 3.1 | 0.54 |
| Oral glucocorticoids | 32/317 | 10.1 | 16/196 | 8.2 | 0.46 |
| Other alternative AD treatments | 99/317 | 31.2 | 58/196 | 29.6 | 0.69 |

AD, atopic dermatitis.
†*P*-values calculated by chi-squared tests.

### Self-assessed severity of ongoing AD at the 24-year follow-up

The mean value for POEM scores for all individuals with ongoing AD was 8.4, SD 5.5 and the median 7 (IQR: 4–12). POEM scores were similar for males (mean: 8.3, SD: 5.8) and females (mean: 8.4, SD: 5.2). Classification of AD severity based on POEM[11] resulted in 52.1% with mild disease (POEM score 1–7), 37.7% with moderate AD (POEM score 8–16) and 10.2% with severe AD (POEM score 17–28). Severity based on POEM for females vs. males: mild (49.5% vs. 55.9%), moderate (40.4% vs. 33.8%) and severe (10.1% vs. 10.3%), $P = 0.62$.

### IgE sensitization among males and females with AD at the 24-year follow-up

Of individuals with AD that provided blood, 67.8% (282 of 416) had specific IgE to one or more of the tested allergens and the corresponding proportion among individuals without AD was 39.0% (707 of 1813), $P < 0.0001$. IgE sensitization among individuals with AD was significantly more common among males compared with females (79.6% vs. 61.3%), $P < 0.0001$.

### Validation of the BAMSE AD definition at the 24-year follow-up

Among those who had been clinically examined for AD at the 24-year follow-up, 384 individuals were defined as having AD by the questionnaire-based BAMSE AD definition, Table 1. When the original William's criteria including visual flexural AD (gold standard) was used, 407 individuals were classified as having AD. A validation of the questionnaire-based BAMSE AD definition at age 24 years against gold standard resulted in a sensitivity of 94.3% (384 of 407), 95% CI: 91.6%–96.4%, and a specificity of 100% (1706 of 1706), one-sided 97.5% CI: 99.8%.

### Impact of sex on the odds of having AD from birth to young adulthood

We finally explored the impact of sex for having AD at 24 years as well as for having AD at previous follow-ups in BAMSE by the use of generalized estimating equations allowing for adjustment for potential confounders. The overall odds ratio for male sex, using female sex as the reference, was 0.90, 95% CI; 0.81–1.02 for the whole follow-up period. However, as shown in Fig. 3, the impact of male sex for having AD changed over time with significantly increased odds for AD the first year of life, OR: 1.31, 95% CI; 1.10–1.56. There was no significant difference between males and females at the ages 2, 4 and 8 years for the odds of having AD. In contrast, male sex was associated with decreased odds of having AD at 12 years (OR: 0.64, 95% CI; 0.52–0.79), 16 years (OR: 0.68, 95% CI; 0.52–0.87) and 24 years (OR: 0.66, 95% CI; 0.55–0.80), Fig. 3.

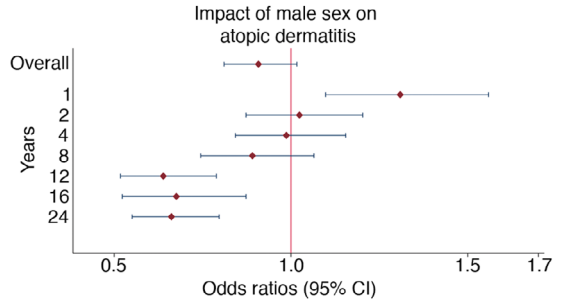


**Figure 3** Impact of male sex for having AD up to age 24 years in the population-based BAMSE birth cohort including 2065 males and 2024 females (reference). ORs calculated by generalized estimating equations.

## Discussion

In this large population-based birth cohort, the questionnaire-based 12-month prevalence of AD at age 24 years was 17.8%, and more females than males had AD. The point prevalence of AD at clinical examination was 8.0% in the whole population, and no significant difference was found in relation to sex. Extremities and hands were the most commonly affected sites in both sexes. More females than males with AD at 24 years reported disturbed sleep due to itch, while IgE sensitization was less common among females compared with males. Sex did not seem to influence self-rated severity of AD evaluated by POEM. Adult onset of AD was similar for females and males. In addition, we found that male sex was associated with increased odds for AD the first year of life but decreased odds of AD in adolescence and young adulthood.

Comparisons between prevalence studies are difficult since there is a large heterogenicity regarding, for example how AD is defined[4,16] and also since AD prevalence has changed over time. However, a Japanese study from a community-based sample found that 9.8% of individuals aged 20–30 years had AD based on clinical examination,[7] which is comparable with the point prevalence of AD in our study. The 12-month prevalence of AD at 24 years in our study is higher than the most other studies. A Swedish cross-sectional study used the Global Allergy and Asthma European Network[17] definition of AD ('Have you ever had an itchy rash which was coming and going for at least 6 months?' and 'Have you had this itchy rash in the last 12 months?') and found the prevalence of AD to be 12.1% among adults. Another large population-based birth cohort study, initiated in 1970 in the UK followed up the participants at 26 years of age and 12%, reported having had AD in the past year.[5] In all these studies,[3,5,7] AD was significantly more prevalent among adult females, which is consistent with our findings. Adult onset of AD has been shown to be more common among females in two large studies from the UK.[5] In contrast, we found no sex differences regarding adult onset of AD. However, the follow-up time in our study was considerably shorter and our definition of adult onset AD included individuals with AD at 24 years that could have debuted at any time between 16 and 24 years.

The finding that IgE sensitization is significantly more common among males with AD compared with females with AD is not surprising since the same pattern is seen also among individuals without AD.[12–18] Nevertheless, it is an important finding to consider when studying AD, especially since AD prevalence differs with sex, and also with age. Thus, it is important to stratify for sex when comparing groups of AD to avoid bias. Even though sleep disturbance due to itch was more common among females in our study, severity of AD evaluated by POEM did not differ significantly between females and males, a finding that is consistent with reports from previous BAMSE follow-ups.[8,19] A weakness of our study is that no investigator-based assessment of AD severity was included. However, the low proportion of severe AD cases based on self-assessment by POEM in our study is comparable with findings from other European countries.[20]

A clinician's assessment is considered the gold standard for diagnosis of AD and a strength of our study is that a majority of the participants underwent skin examination and that William's criteria were used for diagnosing AD. Moreover, for epidemiological studies, William's criteria have been widely used.[21] These criteria have been thoroughly validated for diagnosing AD in childhood[14,16,22–24] and have also been shown to have a sensitivity of 68.8% and specificity of 93.5% for diagnosing AD in adults as compared to clinical diagnosis by a dermatologist.[25] In the BAMSE birth cohort, AD up to 16 years has been defined as reports of itchy skin rash on age-specific locations in combination with dry skin the previous year. The BAMSE AD definition used up to 4 years has previously been validated in relation to clinical diagnosis by a dermatologist showing high sensitivity (92%) and specificity (100%).[26] However, the AD definitions used in BAMSE have not been validated in older children or adolescents. AD in adults is often located on face and hands with many possible differential diagnoses,[27] and for the latest follow-up at 24 years, we therefore used a modified questionnaire-based version of William's criteria. For this definition, both new and previously collected data regarding age of onset, atopic comorbidities, history of dry skin the past year and typical location of AD were used, which minimizes recall bias. We found that the BAMSE AD definition at age 24 years had a sensitivity of 94.3% and a specificity of 100% compared with the original Williams criteria. Thus, some AD cases at the 24-year follow-up in our study are misclassified as not having AD and this could lead to an underestimation of the AD prevalence. In addition, it has been pointed out that the use of William's criteria among adults might underestimate the AD prevalence.[28] As in most longitudinal cohort studies, potential selection bias needs to be taken into account, especially since more males than females were lost to follow-up at 24 years. In a recent publication, we found that the willingness to participate at the 24-year follow-up was somewhat higher among individuals with IgE-sensitization, AD and rhinitis at previous follow-ups. This could lead to an overestimation of AD prevalence at 24 years. However, difference between females and males was minor.[12] In addition, in the same study, we explored differences regarding background factors between males and females participating at the 24-year follow-up and the original cohort and found only minor differences.[12] Thus, selection bias is unlikely to explain the sex differences found in this study.

In conclusion, AD is a common disease among young adults, and even though more females than males have AD, adult onset of AD seems to be equally prevalent among sexes in young adulthood. Our findings demonstrate that in some aspects, AD differs between males and females and this is important to consider for clinicians that treat patients with AD, and for future studies of AD.

## Acknowledgement

We thank all participants in the BAMSE project.

## Author contributions

CFW, NB and EJ were responsible for AD questions and AD definitions. IK, EM and AB managed the Data collection. NB and EJ conducted the statistical analysis. CFW, NB and EJ conducted the analysis and drafting of the manuscript. All authors participated in critical revision of the manuscript, provided important intellectual input and approved the final version.

## Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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