Accepted Manuscript

Incidence and sociodemographic characteristics of eczema diagnosis in children: a cohort study

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PII: S0091-6749(18)30128-3

DOI: 10.1016/j.jaci.2017.12.997

Reference: YMAI 13253

To appear in: Journal of Allergy and Clinical Immunology

Received Date: 26 May 2017

Revised Date: 23 November 2017

Accepted Date: 20 December 2017

Please cite this article as: Ban L, Langan SM, Abuabara K, Thomas KS, Sultan AA, Sach T, McManus E, Santer M, Ratib S, Incidence and sociodemographic characteristics of eczema diagnosis in children: a cohort study, *Journal of Allergy and Clinical Immunology* (2018), doi: 10.1016/j.jaci.2017.12.997.

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- 1 Incidence and sociodemographic characteristics of eczema diagnosis in children: a cohort
- 2 study
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- 20 Word count: 1,016
- 21 Keywords: Eczema; Incidence; Infant and Child; Socioeconomic Factors; Ethnic Groups
- 22 Summary conflict of interest statements: All authors declare no conflicts of interest.
- 23 Funding information: This work has been internally funded by the University of
- 24 Nottingham. THS holds a Career Development Fellowship (CDF-2014-07-006) supported
- 25 by the National Institute for Health Research (NIHR). SML was funded by a National

- 26 Institute for Health Research Clinician Scientist award (NIHR/CS/010/014) and is
- 27 currently funded by a Wellcome Trust Senior Clinical Fellowship in Science
- 28 (205039/Z/16/Z). The views and opinions expressed therein are those of the authors
- and do not necessarily reflect those of the NIHR, NHS or the Department of Health.

30 Capsule Summary:

- 31 The incidence of childhood eczema is approximately 14% in the first year of life and
- 32 decreases substantially in later childhood; early onset is significantly associated with
- 33 gender, ethnicity and socioeconomic status.

34 To the Editor:

We report the results of a large population-based cohort study examining the incidence
of clinically diagnosed eczema in children and the variations by sociodemographic
characteristics. Eczema (also known as atopic eczema/dermatitis¹) affects up to 1 in 5
children² and is associated with high morbidity.³

39 There are limited estimates on the incidence of eczema and how the incidence varies by sociodemographic factors, which is important for generating hypotheses regarding the 40 disease aetiology and for health service planning. To address this issue, we examined 41 42 the incidence of eczema diagnosis in children aged 0-17 years between 1st April 1997 and 31st March 2015 using the Clinical Practice Research Datalink (CPRD).⁴ CPRD is a 43 44 routinely collected primary care database in the United Kingdom (UK) covering 45 approximately 7% of the UK population.⁴ CPRD has been linked to the Hospital Episode 46 Statistics (HES), a secondary healthcare administrative database in England, and is 47 broadly representative of the general UK population regarding age, gender and life-style related factors.4,5 48

49 We defined a child as having eczema if he/she had one diagnostic code for eczema with at least two eczema-related treatment codes on separate days within three months 50 51 before or one year after the eczema diagnosis (see Online Repository, for additional 52 details). The earliest date of an eczema diagnosis was defined as the incidence date. Previous research⁶ has shown that the combination of one eczema diagnostic code with 53 54 two eczema-related treatment codes on separate days at any time gives a 90% (95% 55 confidence interval (95%CI) 83-96%) positive predictive value for identifying prevalent eczema in children. We excluded children registered with their current primary care 56 57 practice after three months of birth or children with a history of eczema before the start 58 of the study to minimise the risk of misclassifying recurrent eczema events as first 59 events (see Figure E1, Online Repository, for additional details).

60 We calculated incidence rates per 100 person-years and adjusted rate ratios (aRR) for 61 age (< 1 year old, 1-4 years old, 5-17 years old), gender, socioeconomic status (defined as guintiles of the patient-level English Index of Multiple Deprivation⁷), and ethnicity 62 63 (when available) using Poisson regression modelling with mutual adjustment (see Table 64 1). Since people with different socio-demographic characteristics could have different 65 health seeking behaviours, we also adjusted for the number of annual consultations in 66 the study follow-up period to minimise potential ascertainment bias. We also examined 67 the incidence rate and aRR for calendar year adjusted for age, gender and socioeconomic status. We examined whether there was evidence of statistical interaction between age 68 69 and gender, socioeconomic status and ethnicity using the likelihood ratio test (p < 0.05). 70 Since the quality of ethnicity recording in the HES-linked CPRD population is only 71 comparable to the UK population for people registered after 2006⁸, for any analysis using 72 ethnicity data we excluded children registered before 1st April 2006 and conducted a 73 complete case analysis. To test the robustness of our results, we conducted four 74 sensitivity analyses (Online Repository). The study protocol was approved by the 75 Independent Scientific Advisory Committee (Protocol No: 16_056) and published here: https://www.cprd.com/isac/Protocol_16_056.asp. 76

The study population consisted of 675,087 children of which 98,082 (14.5%) had a first
clinical diagnosis of eczema. Compared to children without eczema, children with eczema
had a slightly longer follow-up period and a higher annual consultation rate (Table E1,
Online Repository).

The incidence rate by calendar year remained stable in 1997-2015 (Figure E2, Online Repository) and the aRR for each additional calendar year was 1.0 (95%CI 1.0-1.0). The incidence rate of eczema was highest in the first year of life (13.8 per 100 person-years, 95%CI 13.7-13.9) and decreased substantially afterwards (Figure 1). We found statistically significant interaction between age and other sociodemographic factors (p<0.001). There was a 30% higher incidence rate in boys than in girls in children <1 year old (aRR=1.3, 95%CI 1.3-1.4) and a 20% lower rate in boys than in girls for

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88 children \geq 5 years old (aRR=0.8, 95%CI 0.7-0.8) (Table 1). Comparing the incidence 89 rate in children of the lowest socioeconomic status, children of the highest socioeconomic 90 status had a 20% higher incidence rate in the younger age groups (aRR=1.2, 95%CI 91 1.2-1.3 in <1 year old and 1.2, 1.1-1.3 in 1-4 years old); such difference however was 92 not observed in children \ge 5 years old (Table 1). Moreover, the incidence of clinically 93 diagnosed eczema in the first year of life was 2 to 3-fold higher in Chinese children (aRR=3.4, 95%CI 3.0-3.8), Bangladeshi children (aRR=2.5, 95%CI 2.3-2.8) and Black 94 95 Caribbean children (aRR=2.5, 95%CI 2.3-2.9) compared to white children (Table 1). The 96 incidence decreased by age for all ethnic groups but generally remained higher in non-97 white children than white children (Table E2, Online Repository). Results from the sensitivity analyses were all similar compared to the main analysis (see Tables E3, E4 98 99 and E5, Online Repository).

100 Our study shows that the incidence of eczema varies substantially by age and is highest 101 in the first year of life, especially in boys, Chinese, Bangladeshi and Black Caribbean 102 children and children of high socioeconomic status. The study confirms the previously reported link between high socioeconomic status and the occurrence of eczema,⁹ and 103 104 also reports novel findings on ethnic group and gender differences. The former could be 105 due to different environmental risk factors such as diet, living conditions at home or decreased exposure to ultraviolet light.^{E1-E3} The latter may be potentially due to different 106 immune responses of boys and girls in early childhood,^{E4} but different environment 107 exposures such as differing exposures to soap/shampoo products^{E5} at older age . 108

109 The main strength of our study is the large sample size, which has allowed us to 110 examine interactions with age. A potential limitation is ascertainment bias but we have 111 tried to minimise this by adjusting for the number of annual consultations during the 112 study follow-up period in all the analyses.

In conclusion, our findings highlight the early onset of eczema in children, with higherincidence found in boys, Chinese, Bangladeshi and Black Caribbean children, and those

6

- 115 with high socio-economic status. With new prevention approaches potentially available^{E6}
- and early intervention trials currently underway,^{E7} our study may help policy makers
- 117 identify high risk children and better allocate limited healthcare resources.

118 **References**

119 Johansson SGO, Bieber T, Dahl R, Friedmann PS, Lanier BQ, Lockey RF, et al. 1. 120 Revised nomenclature for allergy for global use: Report of the Nomenclature Review 121 Committee of the World Allergy Organization, October 2003. J Allergy Clin Immunol. 2004;113:832-6. 122 123 2. Odhiambo JA, Williams HC, Clayton TO, Robertson CF, Asher MI. Global variations 124 in prevalence of eczema symptoms in children from ISAAC Phase Three. J Allergy Clin 125 Immunol. 2009;124:1251-1258.e23.

Zuberbier T, Orlow SJ, Paller AS, Taïeb A, Allen R, Hernanz-Hermosa JM, et al.
 Patient perspectives on the management of atopic dermatitis. J Allergy Clin Immunol.

128 2006;118:226-32.

Herrett E, Gallagher AM, Bhaskaran K, Forbes H, Mathur R, Staa T van, et al.
 Data Resource Profile: Clinical Practice Research Datalink (CPRD). Int J Epidemiol.
 2015;44:827–36.

132 5. Crooks CJ. The epidemiology of upper gastrointestinal bleeding [Internet]. 2013

133 [cited 2016 Jul 5]. Available from: http://eprints.nottingham.ac.uk/13394/

134 6. Abuabara K, Magyari A, Hoffstad O, Jabbar-Lopez Z, Smeeth L, Williams HC, et al.

135 Development and validation of an algorithm to accurately identify eczema patients in

136 primary care electronic health records from the UK. J Invest Dermatol.

137 7. Noble M, Wright G, Smith G, Dibben C. Measuring multiple deprivation at the
138 small-area level. Environ Plan A. 2006;38:169 – 185.

Mathur R, Bhaskaran K, Chaturvedi N, Leon DA, vanStaa T, Grundy E, et al.
 Completeness and usability of ethnicity data in UK-based primary care and hospital
 databases. J Public Health Oxf Engl. 2014;36:684–92.

142 9. Taylor-Robinson D c., Williams H, Pearce A, Law C, Hope S. Do early-life

143 exposures explain why more advantaged children get eczema? Findings from the U.K.

144 Millennium Cohort Study. Br J Dermatol. 2016;174:569–78.

Figure Legends

Figure 1 Incidence rate (per 100 person-years) of eczema by age and sex, N=675,087 (dotted lines showing 95% confidence intervals)

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	< 1 year old		1-4 years old	~	5-17 years		
	n of eczema=55,5	25	n of eczema=34,	n of eczema=34,729		n of eczema=7,828	
	Rate* (95% CI)	aRR ^{\$} (95% CI)	Rate* (95% CI)	aRR ^{\$} (95% CI)	Rate* (95% CI)	aRR ^{\$} (95% CI)	
Sex							
Male	15.9 (15.7-16.1)	1.3 (1.3-1.4) [£]	2.9 (2.9-3.0)	0.9 (0.9-1.0)	0.4 (0.3-0.4)	0.8 (0.7-0.8) [£]	
Female	11.7 (11.5-11.8)	Reference	3.0 (2.9-3.0)	Reference	0.5 (0.5-0.5)	Reference	
Index of Multiple Deprivation							
1 (least deprived)	15.5 (15.3-15.8)	1.2 (1.2-1.3) [£]	3.2 (3.2-3.3)	$1.2 (1.1-1.3)^{\pounds}$	0.4 (0.4-0.4)	1.0 (0.9-1.1)	
2	13.7 (13.5-14.0)	1.1 (1.0-1.1)	3.0 (2.9-3.1)	1.1 (1.0-1.1)	0.4 (0.4-0.4)	1.0 (0.9-1.1)	
3	13.5 (13.3-13.8)	1.0 (1.0-1.1)	2.9 (2.8-3.0)	1.0 (0.9-1.1)	0.4 (0.4-0.4)	1.0 (0.9-1.1)	
4	13.1 (12.8-13.3)	1.0 (1.0-1.1)	2.8 (2.8-2.9)	1.0 (0.9-1.1)	0.4 (0.4-0.5)	1.0 (1.0-1.1)	
5 (most deprived)	12.9 (12.6-13.2)	Reference	2.8 (2.7-2.9)	Reference	0.4 (0.4-0.5)	Reference	
Ethnicity**	n of eczema=25,5	93	n of eczema=12,862		n of eczema=391		
White	12.4 (12.2-12.6)	Reference	3.3 (3.2-3.3)	Reference	0.5 (0.4-0.5)	Reference	
Black Caribbean	28.8 (25.6-32.4)	2.5 (2.3-2.9) [£]	5.4 (4.5-6.6)	2.0 (1.6-2.4) [£]	1.5 (0.6-4.0)	3.5 (1.3-9.3) [£]	
Bangladeshi	30.4 (27.2-34.1)	2.5 (2.3-2.8) [£]	5.3 (4.3-6.5)	$1.4 (1.1-1.7)^{\pounds}$	1.0 (0.3-3.0)	1.6 (0.5-5.1)	
Chinese	41.7 (36.9-47.2)	3.4 (3.0-3.8) [£]	4.6 (3.4-6.2)	1.6 (1.2-2.2) [£]	0.7 (0.1-5.1)	1.9 (0.3-13.3)	
All other ethnic groups combined ^{&}	20.8 (20.2-21.4)	$1.7 (1.6 - 1.8)^{\pounds}$	3.9 (3.8-4.1)	1.1 (1.0-1.2)	1.0 (0.8-1.2)	1.9 (1.5-2.5) [£]	

Table 1 Incidence rates and rate ratios of eczema by different sociodemographic factors stratified by age (N=675,087)

aRR=adjusted rate ratio

95% CI=95% confidence interval

*Rate per 100 person-years

**Restricted to children with current registration dates on or after April 1st 2006 (N=303,327 of which 48,301 with eczema) and a complete case analysis was conducted first by excluding 55,529 (18.3%) children with missing ethnicity (N=247,798)

\$For sex, model adjusted for Index of Multiple Deprivation and the number of annual consultations during the study follow-up period; for Index of Multiple Deprivation, model adjusted for sex and the number of annual consultations during the study follow-up period; for ethnicity (only available for children registered after 2006), model adjusted for sex, Index of Multiple Deprivation and the number of annual consultations during the study follow-up period

£p<0.05

&including mixed, black African, black other, Indian, Pakistani, Asian other and other children (e.g. Egyptian)



1 Supplementary Methods

2 Defining eczema

3 Diagnoses in the CPRD are coded using the Read code system, which is based on a 4 hierarchal clinical classification system and can be cross referenced to the International 5 Classification of Disease (ICD).^{E8} We defined a child as having eczema if he/she had one 6 diagnostic code for eczema (Read codes M111.00 Atopic dermatitis/eczema, M112.00 7 Infantile eczema, M113.00 Flexural eczema, M114.00 Allergic intrinsic eczema, M12z100 8 Eczema NOS) with at least two eczema-related treatment codes on separate days within 9 three months before or one year after the diagnosis. The following eczema-related treatments were used: prescriptions of emollients, topical steroids, topical calcineurin 10 11 inhibitors (including pimecrolimus and tacrolimus), systemic steroids, systemic 12 immunomodulatory agents (including methotrexate, cyclosporine, azathioprine and 13 mycophenolate mofetil) and ultraviolet light therapy. Drug prescriptions were identified 14 from the CPRD using drug codes based on the British National Formulary chapters. 15 Ultraviolet light therapy treatments were identified from both the CPRD and HES using 16 Read and OPCS4 codes, respectively.)

17 Sensitivity analyses

To test the robustness of our results, we conducted four sensitivity analyses andcompared the results to the main analysis.

Missing ethnicity data: Since 18.3% children had missing information on ethnicity, we
 used multiple imputation to replace missing values for ethnicity by using multinomial
 logistic regression and created 10 imputed datasets. We combined estimates using
 Rubin's rule to obtain final estimates and compared the results to the complete case
 analysis.

25 2. More inclusive eczema definition: We defined a child as having eczema if he/she had
26 one diagnostic code for eczema with at least one eczema-related treatment within three
27 months before or after the eczema diagnosis.

28 3. More restrictive eczema definition for the first year of life: To minimise the potential 29 misclassification of eczema diagnosis in the first year of life, we defined a child as having eczema in the first year if he/she had eczema in the first year and prescribed any 30 31 eczema-related treatment in the second year of life also. 32 4. Alternative study population: As we excluded a large proportion of children, i.e. those registered with their current primary care physician after the first three months of birth 33 34 (1,097,638 out of 1,838,877; 59.7%), our study population could be less representative 35 of the general paediatric population. Therefore we re-ran our analysis on the total 36 population identified from the HES-linked CPRD. For this sensitivity analysis, to ensure 37 we only included incident diagnoses and not prevalent ones in children registered after 38 the first year of life, we excluded the first 12 months after the current registration date 39 and children whose first eczema diagnosis was within this first 12 months period were 40 also excluded.

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Supplementary References

E1. Flohr C, Mann J. New insights into the epidemiology of childhood atopic dermatitis. Allergy. 2014;69:3–16.

E2. Ellwood P, Asher MI, Björkstén B, Burr M, Pearce N, Robertson CF. Diet and asthma, allergic rhinoconjunctivitis and atopic eczema symptom prevalence: an ecological analysis of the International Study of Asthma and Allergies in Childhood (ISAAC) data. Eur Respir J. 2001;17:436–43.

E3. Thyssen JP, Zirwas MJ, Elias PM. Potential role of reduced environmental UV exposure as a driver of the current epidemic of atopic dermatitis. J Allergy Clin Immunol. 2015;136:1163–9.

E4. Muenchhoff M, Goulder PJR. Sex differences in pediatric infectious diseases. J Infect Dis. 2014;209:S120–6.

E5. Clough, S. Gender and the hygiene hypothesis. Social Science & Medicine.2011;72(4),486-93.

E6. Cipriani F, Dondi A, Ricci G. Recent advances in epidemiology and prevention of atopic eczema. Pediatr Allergy Immunol. 2014;25:630–8.

E7. ISRCTN Registry. Barrier Enhancement for Eczema Prevention [Internet]. [cited2016 Oct 19]. Available from:

http://www.isrctn.com/ISRCTN21528841?q=beep&filters=&sort=&offset=2&totalResults =10&page=1&pageSize=10&searchType=basic-search

E8. Green LA. Read Codes: a tool for automated medical records. *J Fam Pract* 1992;34: 633-

	Children without eczema	Children with eczema
	n =577,005	n =98,082
	n (%)	n (%)
Age at registration with current GP	0.77 (0.20-1.40)	0.80 (0.37-1.33)
months, median (IQR)		
Age at start of prospective follow-up	1.30 (0.63-16.67)	0.90 (0.47-1.57)
months, median (IQR)		
Average length of prospective follow-up	54.73 (20.22-112.00)	74.27 (37.53-125.93)
months, median (IQR)		
Sex, male	293,828 (50.92)	53,124 (54.16) [£]
Index of Multiple Deprivation		
1 (Least deprived)	123,060 (21.33)	24,334 (24.81) [£]
2	120,913 (20.96)	20,646 (21.05)
3	110,121 (19.08)	18,019 (18.37)
4	117,033 (20.28)	18,442 (18.80)
5 (most deprived)	105,878 (18.35)	16,641 (16.97)
Ethnicity*	n= 255,026	n= 48,301
White	176,964 (84.69)	30,761 (79.19) [£]
Mixed	7,824 (3.74)	1,604 (4.13)
Black Caribbean	1,094 (0.52)	378 (0.97)
Black African	4,779 (2.29)	1,172 (3.02)
Black Other	1,030 (0.49)	323 (0.83)
Indian	4,560 (2.18)	1,319 (3.40)
Bangladeshi	1,084 (0.52)	396 (1.02)
Pakistani	4,265 (2.04)	1,114 (2.87)
Chinese	704 (0.34)	294 (0.76)
Asian Other	2,961 (1.42)	790 (2.03)
Other	3,687 (1.76)	695 (1.79)
Missing	46,074	9,455
Annual consultation rate ^{\$} , median (IQR)	3.50 (1.84-6.36)	10.29 (5.92-16.23) [£]

Table E1 Characteristic of children without and with eczema (N=675,087)

IQR=interquartile range

*Restricted to children with current registration dates on or after April 1^{st} 2006 (N=303,327 of which 48,301 with eczema) and a complete case analysis was conducted first by excluding 55,529 (18.3%) children with missing ethnicity (N=247,798)

\$Number of consultations per year during the study follow-up period p < 0.05

Ethnicity	< 1 year old		1-4 years old		5-17 years old	
	n of eczema=25,593		n of eczema=12,	862	n of eczema=391	1
	Rate* (95% CI)	aRR ^{\$} (95% CI)	Rate* (95% CI)	aRR ^{\$} (95% CI)	Rate* (95% CI)	aRR ^{\$} (95% CI)
White	12.4 (12.2-12.6)	Reference	3.3 (3.2-3.3)	Reference	0.5 (0.4-0.5)	Reference
Mixed	17.7 (16.7-18.8)	1.5 (1.4-1.6)	3.7 (3.3-4.0)	1.1 (1.0-1.3)	0.6 (0.3-1.0)	1.2 (0.7-2.3)
Black Caribbean	28.8 (25.6-32.4)	2.6 (2.3-2.9) ^{&}	5.4 (4.5-6.6)	2.0 (1.6-2.4)	1.5 (0.6-4.0)	3.5 (1.3-9.4) ^{&}
Black African	22.3 (20.8-23.8)	2.0 (1.8-2.1)	3.9 (3.5-4.4)	1.3 (1.2-1.5)	1.1 (0.6-1.9)	2.6 (1.5-4.5)
Black Other	29.6 (26.1-33.5)	2.6 (2.3-3.0)	4.0 (3.1-5.1)	1.4 (1.1-1.8)	2.4 (1.2-4.8)	5.8 (2.8-11.8)
Indian	24.3 (22.9-25.9)	1.8 (1.6-2.0)	4.2 (3.7-4.6)	1.2 (1.1-1.4)	0.9 (0.6-1.6)	1.8 (1.1-3.1)
Bangladeshi	30.4 (27.2-34.1)	2.5 (2.3-2.8)	5.3 (4.3-6.5)	1.4 (1.1-1.7)	1.0 (0.3-3.0)	1.6 (0.5-5.1)
Pakistani	20.6 (19.2-22.1)	1.7 (1.5-1.9)	4.1 (3.7-4.6)	0.7 (0.5-1.2)	0.8 (0.5-1.4)	1.4 (0.8-2.5)
Chinese	41.7 (36.9-47.2)	3.4 (3.0-3.8)	4.6 (3.4-6.2)	1.6 (1.2-2.2)	0.7 (0.1-5.1)	1.9 (0.3-13.3)
Asian Other	23.6 (21.8-25.6)	2.0 (1.8-2.1)	4.4 (3.8-5.1)	1.2 (1.1-1.4)	1.8 (1.0-3.3)	3.3 (1.8-6.1)
Other (e.g. Egyptian)	16.4 (15.0-17.9)	1.3 (1.1-1.5)	3.6 (3.1-4.2)	1.2 (1.0-1.4)	0.7 (0.3-1.8)	1.6 (0.6-3.8)

Table E2 Incidence rates and rate ratios of eczema by ethnicity stratified by age (N=247,798 with complete data on ethnicity)

aRR=adjusted rate ratio

95% CI=95% confidence interval

*Rate per 100 person-years

\$Model adjusted for sex, Index of Multiple Deprivation and the number of annual consultations during the study follow-up period & compared to Table 1 these estimates changed slightly due to a different number of covariates included in the regression model

Table E3 Results after using a more inclusive eczema definition: Incidence rates and rate ratios of eczema by sociodemographic factors stratified by age (N=675,087 for analysis on sex and Index of Multiple Deprivation and N=247,798 for analysis on ethnicity)

	< 1 year old		1-4 years old	1-4 years old		
	n of eczema=70,4	25	n of eczema=57,	809	n of eczema=18,247	
	Rate* (95% CI)	aRR ^{\$} (95% CI)	Rate* (95% CI)	aRR ^{\$} (95% CI)	Rate* (95% CI)	aRR ^{\$} (95% CI)
Sex						
Male	20.3 (20.1-20.5)	1.3 (1.3-1.3)	5.3 (5.2-5.3)	1.0 (0.9-1.0)	0.9 (0.9-0.9)	0.7 (0.7-0.8)
Female	15.3 (15.1-15.5)	Reference	5.4 (5.4-5.4)	Reference	1.2 (1.2-1.3)	Reference
Index of Multiple Deprivation			$\overline{}$			
1 (least deprived)	20.0 (19.7-20.3)	1.2 (1.2-1.2)	5.9 (5.8-6.0)	1.1 (1.1-1.2)	1.1 (1.1-1.1)	1.0 (1.0-1.1)
2	17.8 (17.5-18.1)	1.1 (1.1-1.1)	5.4 (5.3-5.5)	1.1 (1.1-1.1)	1.1 (1.0-1.1)	1.0 (1.0-1.1)
3	17.5 (17.2-17.8)	1.1 (1.0-1.1)	5.2 (5.1-5.3)	1.1 (1.0-1.1)	1.1 (1.0-1.1)	1.0 (1.0-1.1)
4	16.9 (16.6-17.2)	1.0 (1.0-1.1)	5.0 (4.9-5.1)	1.0 (1.0-1.1)	1.0 (1.0-1.1)	1.0 (0.9-1.0)
5 (most deprived)	16.5 (16.2-16.8)	Reference	4.9 (4.8-5.0)	Reference	1.1 (1.0-1.1)	Reference
Ethnicity	n of eczema=32,2	15	n of eczema=20,476		n of eczema=893	
White	16.2 (16.0-16.4)	Reference	5.7 (5.6-5.8)	Reference	1.3 (1.2-1.3)	Reference
Mixed	22.1 (21.0-23.3)	1.4 (1.3-1.5)	6.0 (5.6-6.5)	1.1 (1.0-1.2)	1.5 (1.0-2.2)	1.2 (0.8-1.8)
Black Caribbean	33.6 (30.1-37.5)	2.3 (2.0-2.5)	7.1 (6.0-8.5)	1.3 (1.1-1.6)	2.4 (1.1-5.3)	2.0 (0.9-4.6)
Black African	26.2 (24.6-27.9)	1.8 (1.7-1.9)	5.5 (5.0-6.1)	1.0 (0.9-1.1)	1.8 (1.2-2.8)	1.4 (0.9-2.3)
Black Other	33.1 (29.5-37.3)	2.2 (2.0-2.5)	5.7 (4.6-7.0)	1.1 (0.9-1.3)	3.9 (2.2-6.9)	3.5 (2.0-6.3)
Indian	28.8 (27.1-30.5)	1.7 (1.5-1.8)	6.4 (5.9-7.0)	1.1 (1.0-1.2)	1.5 (1.0-2.4)	1.1 (0.7-1.8)
Bangladeshi	34.1 (30.6-38.0)	2.2 (1.9-2.4)	7.8 (6.5-9.2)	1.3 (1.1-1.6)	3.4 (1.7-6.4)	2.3 (1.2-4.5)
Pakistani	23.5 (22.0-25.1)	1.5 (1.4-1.6)	5.9 (5.4-6.5)	1.0 (0.9-1.1)	1.8 (1.2-2.7)	1.3 (0.9-2.0)

Chinese	51.0 (45.5-57.1)	3.1 (2.8-3.5)	7.6 (5.9-9.7)	1.4 (1.1-1.8)	0.8 (0.1-6.0)	0.8 (0.1-5.5)
Asian Other	28.0 (26.0-30.2)	1.8 (1.6-1.9)	6.2 (5.5-7.1)	1.1 (1.0-1.2)	2.5 (1.5-4.2)	1.9 (1.1-3.2)
Other	21.2 (19.6-22.9)	1.3 (1.1-1.4)	5.7 (5.1-6.4)	1.0 (0.9-1.2)	1.8 (1.0-3.2)	1.5 (0.8-2.6)

aRR=adjusted rate ratio

95% CI=95% confidence interval

*Rate per 100 person-years

\$Model adjusted for sex, Index of Multiple Deprivation and the number of annual consultations during the study follow-up period

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Table E4 Results after using a more strict eczema definition for the first year of life: Incidence rates and rate ratios of eczema by sociodemographic factors stratified by age (N=675,087 for analysis on sex and Index of Multiple Deprivation and N=247,798 for analysis on ethnicity)

	< 1 year old		1-4 years old		5-17 years old	
	n of eczema=39,5	79	n of eczema=34,	729	n of eczema=7,828	
	Rate* (95% CI)	aRR ^{\$} (95% CI)	Rate* (95% CI)	aRR ^{\$} (95% CI)	Rate* (95% CI)	aRR ^{\$} (95% CI)
Sex						
Male	11.0 (10.9-11.2)	1.3 (1.3-1.3)	2.9 (2.8-2.9)	1.0 (0.9-1.0)	0.4 (0.3-0.4)	0.7 (0.7-0.9)
Female	8.2 (8.1-8.3)	Reference	2.9 (2.9-3.0)	Reference	0.5 (0.5-0.5)	Reference
Index of Multiple Deprivation			Y .			
1 (least deprived)	11.2 (11.0-11.4)	1.3 (1.2-1.4)	3.1 (3.1-3.2)	1.2 (1.1-1.2)	0.4 (0.4-0.4)	0.9 (0.9-1.0)
2	9.7 (9.5-9.9)	1.1 (1.1-1.2)	2.9 (2.9-3.0)	1.1 (1.0-1.1)	0.4 (0.4-0.4)	0.9 (0.9-1.0)
3	9.4 (9.2-9.6)	1.0 (0.9-1.1)	2.8 (2.7-2.9)	1.0 (1.0-1.0)	0.4 (0.4-0.4)	0.9 (0.9-1.0)
4	8.9 (8.7-9.1)	1.1 (1.0-1.1)	2.8 (2.7-2.8)	1.0 (1.0-1.1)	0.4 (0.4-0.4)	1.0 (0.9-1.1)
5 (most deprived)	8.7 (8.5-8.9)	Reference	2.7 (2.6-2.8)	Reference	0.4 (0.4-0.5)	Reference
Ethnicity	n of eczema=18,5	83	n of eczema=12,862		n of eczema=391	
White	8.6 (8.4-8.7)	Reference	3.2 (3.1-3.2)	Reference	0.4 (0.4-0.5)	Reference
Mixed	11.9 (11.2-12.8)	1.4 (1.3-1.5)	3.5 (3.2-3.9)	1.1 (1.0-1.2)	0.5 (0.3-1.0)	1.2 (0.6-2.3)
Black Caribbean	20.6 (18.0-23.6)	2.7 (2.4-3.1)	5.3 (4.3-6.4)	1.8 (1.4-2.2)	1.5 (0.6-3.9)	3.2 (1.2-8.7)
Black African	15.3 (14.1-16.6)	2.0 (1.8-2.2)	3.8 (3.4-4.3)	1.3 (1.1-1.4)	1.1 (0.6-1.8)	2.3 (1.3-4.1)
Black Other	18.6 (16.0-21.7)	2.4 (2.1-2.8)	3.8 (3.0-4.9)	1.3 (1.0-1.6)	2.4 (1.2-4.7)	5.2 (2.5-10.5)
Indian	17.3 (16.0-18.6)	1.7 (1.3-2.3)	4.0 (3.6-4.4)	1.3 (1.1-1.4)	0.9 (0.5-1.5)	2.0 (1.2-3.4)

Bangladeshi	23.4 (20.6-26.5)	2.9 (2.6-3.3)	5.1 (4.1-6.2)	1.6 (1.3-2.0)	0.9 (0.3-2.9)	2.0 (0.6-6.1)
Pakistani	14.1 (13.0-15.3)	1.8 (1.6-1.9)	4.0 (3.5-4.4)	1.3 (1.1-1.4)	0.8 (0.4-1.4)	1.7 (0.9-3.0)
Chinese	24.4 (20.9-28.5)	2.8 (2.4-3.3)	4.2 (3.1-5.7)	1.3 (1.0-1.8)	0.7 (0.1-4.6)	1.5 (0.2-10.5)
Asian Other	15.1 (13.7-16.7)	1.8 (1.6-2.0)	4.2 (3.6-4.8)	1.3 (1.1-1.5)	1.7 (0.9-3.1)	3.7 (2.0-6.8)
Other	9.9 (8.8-11.0)	1.2 (1.1-1.4)	3.4 (3.0-4.0)	1.1 (1.0-1.3)	0.7 (0.3-1.7)	1.5 (0.6-3.7)

aRR=adjusted rate ratio

95% CI=95% confidence interval

*Rate per 100 person-years

\$Model adjusted for sex, Index of Multiple Deprivation and the number of annual consultations during the study follow-up period

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Table E5 Results in the overall child population regardless of the GP registration date related to birth: Incidence rates and rate ratios of eczema by sociodemographic factors stratified by age (N=1,472,337 for analysis on sex and Index of Multiple Deprivation and N=392,830 for analysis on ethnicity)

	< 1 year old		1-4 years old		5-17 years old	
	n of eczema=59,8	40	n of eczema=44,	.111	n of eczema=22,527	
	Rate* (95% CI)	aRR ^{\$} (95% CI)	Rate* (95% CI)	aRR ^{\$} (95% CI)	Rate* (95% CI)	aRR ^{\$} (95% CI)
Sex						
Male	15.9 (15.7-16.1)	1.3 (1.3-1.4)	2.8 (2.8-2.9)	1.0 (1.0-1.0)	0.4 (0.4-0.4)	0.7 (0.7-0.7)
Female	11.7 (11.6-11.8)	Reference	2.9 (2.8-2.9)	Reference	0.5 (0.5-0.5)	Reference
Index of Multiple Deprivation			V.			
1 (least deprived)	15.6 (15.4-15.9)	1.2 (1.2-1.3)	3.1 (3.1-3.2)	1.3 (1.2-1.3)	0.4 (0.4-0.4)	0.9 (0.9-1.0)
2	13.8 (13.5-14.0)	1.1 (1.0-1.1)	2.9 (2.8-2.9)	1.2 (1.1-1.2)	0.4 (0.4-0.4)	0.9 (0.9-0.9)
3	13.6 (13.3-13.8)	1.1 (1.0-1.1)	2.8 (2.7-2.9)	1.1 (1.1-1.2)	0.4 (0.4-0.5)	0.9 (0.9-1.0)
4	13.1 (12.9-13.3)	1.0 (1.0-1.1)	2.7 (2.7-2.8)	1.1 (1.1-1.1)	0.5 (0.5-0.5)	1.0 (1.0-1.0)
5 (most deprived)	12.9 (12.6-13.1)	Reference	2.7 (2.6-2.7)	Reference	0.5 (0.5-0.5)	Reference
Ethnicity	n of eczema=26,9	58	n of eczema=15,269		n of eczema=1,824	
White	12.4 (12.2-12.5)	Reference	3.1 (3.1-3.2)	Reference	0.5 (0.5-0.5)	Reference
Mixed	17.8 (16.8-18.8)	1.5 (1.4-1.6)	3.6 (3.3-3.9)	1.2 (1.1-1.4)	0.7 (0.5-0.9)	1.4 (1.0-1.9)
Black Caribbean	28.6 (25.5-32.0)	2.5 (2.3-2.8)	5.3 (4.4-6.4)	2.1 (1.7-2.5)	1.7 (1.1-2.5)	3.5 (2.4-5.2)
Black African	21.9 (20.6-23.4)	1.9 (1.8-2.1)	3.9 (3.5-4.3)	1.5 (1.3-1.6)	1.0 (0.8-1.2)	2.1 (1.7-2.6)
Black Other	28.5 (25.2-32.2)	2.5 (2.2-2.8)	3.9 (3.2-4.9)	1.4 (1.1-1.8)	1.8 (1.3-2.5)	3.7 (2.6-5.3)
Indian	24.1 (22.7-25.6)	1.9 (1.7-2.0)	4.0 (3.7-4.4)	1.3 (1.2-1.4)	1.0 (0.9-1.3)	2.2 (1.8-2.7)

Bangladeshi	31.2 (28.0-34.8)	2.4 (2.1-2.9)	5.3 (4.4-6.3)	1.6 (1.3-1.9)	1.2 (0.7-2.1)	2.3 (1.3-4.0)
Pakistani	20.1 (18.7-21.5)	1.6 (1.5-1.8)	3.8 (3.5-4.2)	1.1 (0.9-1.3)	1.0 (0.8-1.2)	1.8 (1.5-2.3)
Chinese	41.8 (37.1-41.1)	3.4 (3.0-3.8)	4.6 (3.5-5.9)	1.7 (1.3-2.2)	0.5 (0.2-1.6)	1.1 (0.3-3.3)
Asian Other	23.6 (21.8-25.5)	2.0 (1.8-2.1)	4.3 (3.8-4.9)	1.3 (1.2-1.5)	1.2 (0.8-1.6)	2.3 (1.6-3.2)
Other	16.7 (15.4-18.2)	1.3 (1.2-1.5)	3.2 (2.8-3.6)	1.1 (1.0-1.3)	0.9 (0.7-1.2)	1.9 (1.4-2.6)

aRR=adjusted rate ratio

95% CI=95% confidence interval

*Rate per 100 person-years

\$Model adjusted for sex, Index of Multiple Deprivation and the number of annual consultations during the study follow-up period

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Figure E1 Constructing the final study population (N=675,087)



Figure E2 Incidence rate (per 100 person-years) of eczema by calendar year, N=675,087