Supplementary Methods

Defining eczema

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

Sensitivity analyses

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

1. 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.

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

3. More restrictive eczema definition for the first year of life: To minimise the potential 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 eczema-related treatment in the second year of life also.

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 (1,097,638 out of 1,838,877; 59.7%), our study population could be less representative of the general paediatric population. Therefore we re-ran our analysis on the total population identified from the HES-linked CPRD. For this sensitivity analysis, to ensure we only included incident diagnoses and not prevalent ones in children registered after the first year of life, we excluded the first 12 months after the current registration date and children whose first eczema diagnosis was within this first 12 months period were also excluded.

Supplementary References

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

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

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

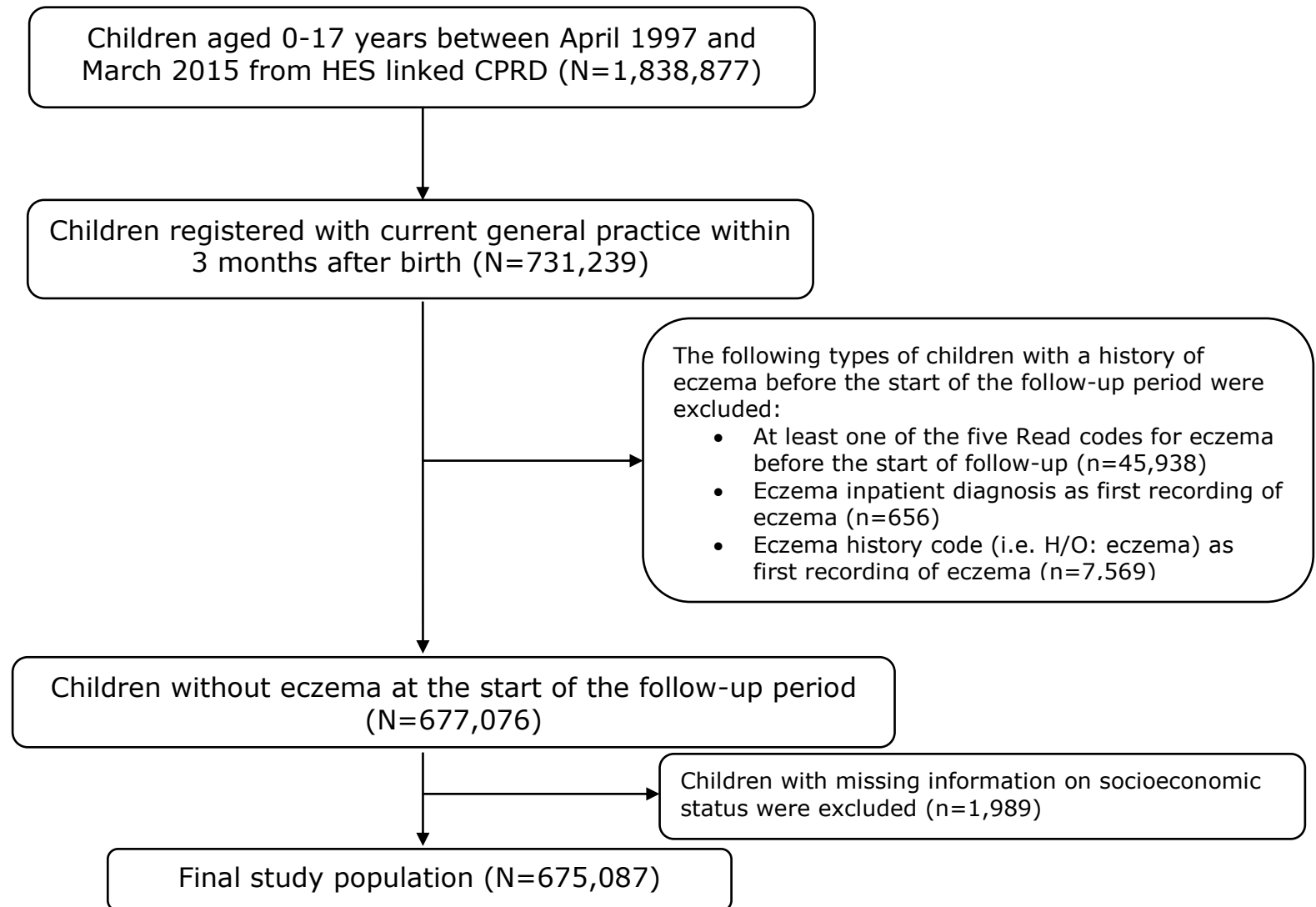E8. Green LA. Read Codes: a tool for automated medical records. *J Fam Pract* 1992; **34**: 633–4.

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

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

	Children without eczema	Children with eczema
	n=577,005	**n**=98,082
	n (%)	n (%)
Age at registration with current GP months, median (IQR)	0.77 (0.20-1.40)	0.80 (0.37-1.33)
Age at start of prospective follow-up months, median (IQR)	1.30 (0.63-16.67)	0.90 (0.47-1.57)
Average length of prospective follow-up months, median (IQR)	54.73 (20.22-112.00)	74.27 (37.53-125.93)
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)[£]

IQR=interquartile range

*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)

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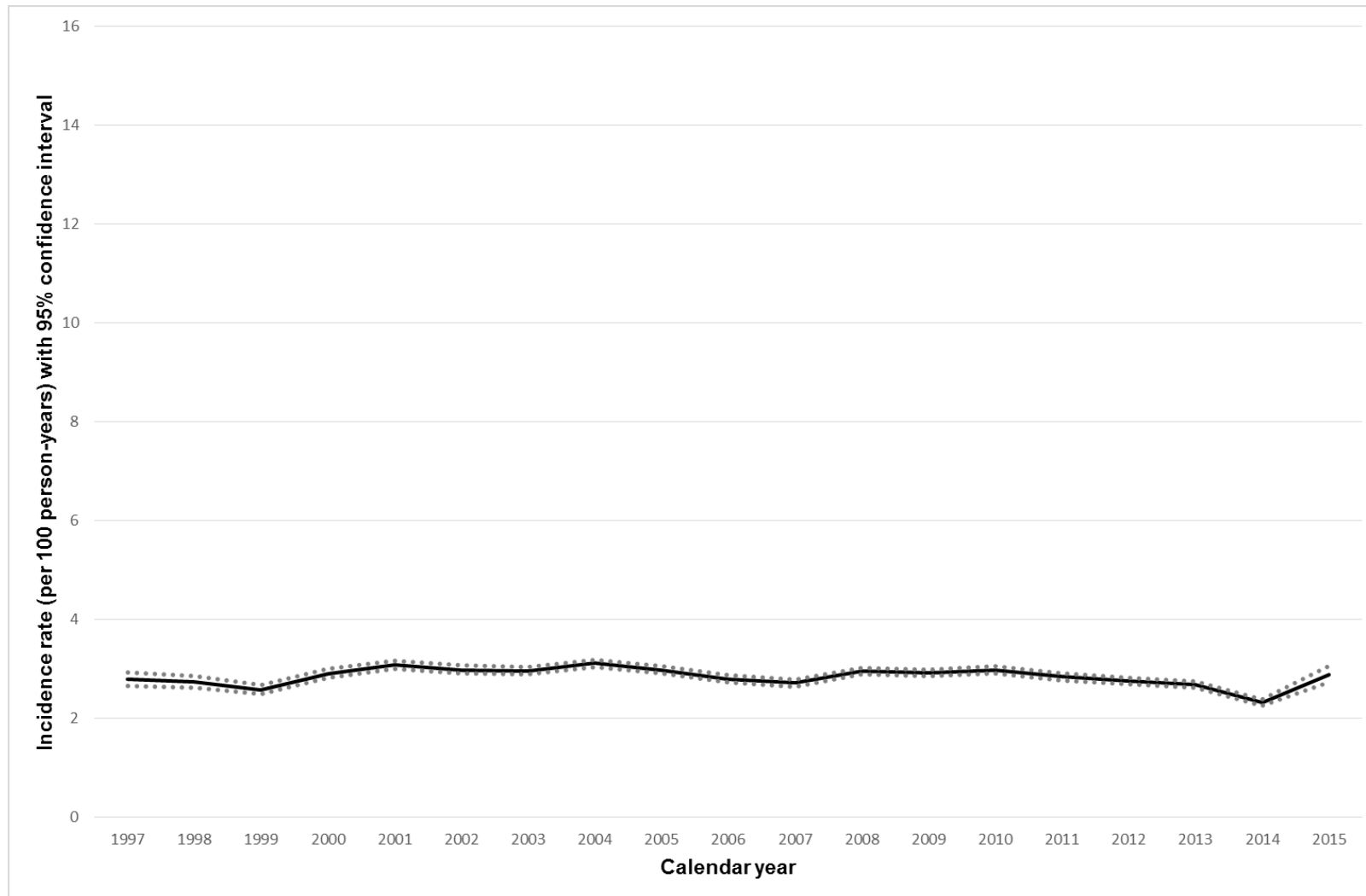
£p<0.05

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

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

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	
	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)

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		5-17 years old	
	n of eczema=70,425		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						
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=32,215		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

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=39,579		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						
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=18,583		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

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=59,840		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						
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=26,958		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