

PROFESSOR CARSTEN FLOHR (Orcid ID : 0000-0003-4884-6286)

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Patterns and trends in eczema management in UK primary care (2009-2018): a population-based cohort study

Author list

S. de Lusignan^{1,2}, H. Alexander³, C. Broderick³, J. Dennis⁴, A. McGovern⁴, C. Feeney⁵, C. Flohr^{3*}

¹ Nuffield Department of Primary Care health Sciences, University of Oxford, UK

² Royal College of General Practitioners, Research and Surveillance Centre, London, UK

³ Unit for Population-Based Dermatology Research, St John's Institute of Dermatology, Guy's & St Thomas' NHS Foundation Trust and King's College London, UK

⁴ Momentum Data, Pendragon House, St. Albans, Hertfordshire, UK

⁵ Pfizer Ltd, Walton Oaks, Walton on the Hill, Tadworth, Surrey, UK

*Corresponding author

Correspondence to: Professor Carsten Flohr, Unit for Population-Based Dermatology Research, St John's Institute of Dermatology, Guy's & St Thomas' NHS Foundation Trust and King's College London, UK, WC2R 2LS. Email: carsten.flohr@kcl.ac.uk. Phone: +44 20 7188 6399.

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30 Dennis and A. McGovern conducted and are responsible for the data analysis. All authors
31 critically reviewed the manuscript. S. de Lusignan had full access to all the data in the study
32 and takes responsibility for the integrity of the data and the accuracy of the data analysis.

38 Abstract

39 Background

40 Despite the high disease burden of eczema, a contemporary overview of the patterns and
41 trends in UK primary care healthcare utilisation and treatment is lacking.

42 Objective

43 To quantify primary care consultations, specialist referrals, prescribing, and treatment
44 escalation, in children and adults with eczema in England.

45 Methods

46 A large primary care research database was used to examine healthcare and treatment
47 utilisation in people with active eczema (n=411,931). Management trends and variations by
48 age, sex, socioeconomic status, and ethnicity were described from 2009-2018 inclusive.

49 Results

50 Primary care consultation rates increased from 87.8 (95% confidence interval [95%CI] 87.3-
51 88.3) to 112.0 (95%CI 111.5-112.6) per 100 person-years over 2009 to 2018. Specialist
52 referral rates also increased from 3.8 (95%CI 3.7-3.9) to 5.0 (95%CI 4.9-5.1). Consultation
53 rates were highest in infants. Specialist referrals were greatest in the over 50s and lowest in
54 people of lower socioeconomic status, despite the highest rates of primary care
55 consultations. There were small changes in prescribing over time; emollients increased
56 (prescribed to 48.5% of people with active eczema in 2009 compared to 51.4% in 2018) and
57 topical corticosteroids decreased (57.3% to 52.0%). Prescribing disparities were observed,
58 including less prescribing of potent and very potent topical corticosteroids in non-white
59 ethnicities and people of lower socioeconomic status. Treatment escalation was more
60 common with increasing age and in children of non-white ethnicity.

61 Conclusion and clinical relevance

62 The management of eczema varies by sociodemographic status in England, with lower rates
63 of specialist referral in people from more deprived backgrounds. There are different
64 patterns of healthcare utilisation, treatment, and treatment escalation in people of non-white
65 ethnicity and of more deprived backgrounds.

66 **Registration information:** The study protocol was pre-registered as an observational study
67 on [clinicaltrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT03823794) (NCT03823794).

69 Introduction

70 Eczema (syn. 'atopic dermatitis', 'atopic eczema') is the most common inflammatory skin
71 condition worldwide in children(1) and persistence of chronic disease into adulthood is
72 common.(2, 3) Eczema can be extremely disabling and has a significant psychological impact
73 in both children and adults.(4-6)

74
75 In the UK, the burden of eczema management falls on primary care. Attendance rates are
76 high, with 96% of children with eczema reported to have had a primary care attendance
77 within the preceding year.(7) Whilst contemporary UK population-based estimates of
78 eczema disease severity are lacking, a 1998 cross-sectional analysis in a UK general practice
79 setting estimated 16% of eczema in children aged 1-5 to be moderate or severe.(7) Recent
80 studies of children with eczema actively recruited from UK primary care suggest this figure
81 may be even higher.(8, 9) US population-based studies have reported 7% of children and
82 11% of adults with eczema have severe disease.(10, 11) Whilst those with more severe
83 disease are more likely to be referred for specialist care, the majority of these cases are
84 managed without secondary care referral.(7) As a result, the principal costs for eczema are
85 those of primary care attendances and prescribing.(12)

86
87 Standard topical eczema care includes regular emollient application. Escalation to topical
88 corticosteroids (TCS), or, as an alternative, topical calcineurin inhibitors (TCI), is common
89 for maintenance and flare management,(13, 14) and topical antimicrobials can be used to
90 address secondary skin infections, or pruritis.(14) Antihistamines are also commonly used
91 to treat pruritus associated with eczema, although evidence for their effectiveness is
92 limited.(15) In more severe disease, systemic immuno-modulatory treatment may be
93 required.(16, 17) Recently, the first biologic therapy for eczema, dupilumab, was approved,
94 and this can now be prescribed for adults and adolescents with moderate or severe eczema
95 who have not responded or have contraindications to conventional systemic therapies.(18)

96
97 Despite the high disease burden and multiple treatments available, a contemporary
98 overview of UK primary care healthcare and treatment utilisation patterns and trends in

99 children and adults with eczema is lacking. We set out to describe healthcare utilisation in
100 people with eczema across the lifespan, including primary care attendances, specialist
101 referrals, prescribing and, as a surrogate marker of moderate and severe eczema, treatment
102 escalation patterns.(19)

103 **Methods**

104 **Data source and setting**

105 We used the Oxford-Royal College of General Practitioners (RCGP) Research and
106 Surveillance Centre (RSC) network database. The RCGP RSC comprises the pseudonymised
107 primary care records of all individuals registered with a large network of general practices,
108 providing a broadly representative sample of the English primary care population.(20) Over
109 the entire study period, the RCGP RSC database contained data from 3.85 million people
110 registered with 293 general practitioner (GP) practices across England.

111
112 RCGP RSC primary care records include information on demographics, clinical diagnoses,
113 laboratory tests, prescriptions, and care processes (e.g. patient referrals). Data are captured
114 using the Read coding system (a thesaurus of clinical terms).(21) Key strengths of the
115 English primary care system include: it is a registration-based system (each patient registers
116 with a single GP), has been computerised since the 1990s, laboratory results are
117 electronically uploaded, and, since 2004, a pay-for-performance scheme has resulted in high-
118 quality chronic disease clinical data entry.(22, 23) Additionally, RCGP RSC practices have
119 practice visits and receive feedback via a dashboard to improve data quality.(24)

120
121 All children and adults registered with an RCGP RSC contributing practice between January
122 1, 2009 and January 1, 2019 were eligible for inclusion in this study. Individuals required at
123 least one year of follow-up in RCGP RSC, unless under one year old. The full protocol for the
124 study was pre-specified and has been previously published.(25)

125

126 Eczema definitions

127 People with eczema were identified using Read diagnostic codes and prescription records,
128 applying a validated algorithm recently developed in a random sample of children and adults
129 in UK primary care, and previously applied in several UK primary care studies.(19, 26, 27)
130 The positive predictive value of this algorithm for a physician-confirmed diagnosis of eczema
131 is 90% (95% confidence interval (CI) 80-91%) in children and 82% (95% CI 73- 89%) in
132 adults.(27)

133
134 Active eczema was defined, as in a recent UK primary care study,(19) as two eczema records
135 (either diagnoses or treatment) appearing within any one year period. Active eczema was
136 then assumed to last for one year, unless another eczema record appeared, in which case its
137 duration was prolonged for a further one year.(19) We utilised this approach but used the
138 first of two codes (rather than the latter) within one year to signify the onset of active
139 eczema, as this has been shown to have good agreement to physician confirmed onset,(27)
140 and has been used elsewhere.(26)

141
142 Eczema treatments are also prescribed for other conditions and the indication for treatment
143 is not readily available in primary care data. We therefore excluded people with potential
144 confounding comorbidities from our eczema cohort. We excluded people who had other skin
145 conditions (psoriasis, contact dermatitis, photodermatitis, and ichthyosis) as these are
146 managed with similar topical treatments to eczema.(27) In addition we excluded people
147 with inflammatory bowel disease (IBD), rheumatoid arthritis, and a history of organ
148 transplantation, as these are commonly managed with treatments also used in eczema (e.g.
149 methotrexate and azathioprine); topical treatments for dermatological conditions and oral
150 immuno-modulating drugs for the other conditions listed. IBD and rheumatoid arthritis were
151 identified using validated approaches.(28-30) Organ transplantation was identified using a
152 Read code list generated in accordance with publicly available guidance.(31, 32)

153

154 **Definition of sociodemographic factors**

155 Ethnicity was categorised in accordance with the major UK census categories: white, Asian,
156 black African/Caribbean, mixed, other, and not recorded. Deprivation was defined using the
157 official national measure of socioeconomic status, the Index of Multiple Deprivation
158 (IMD).(33) Scores, based on postcode, were stratified by deprivation quintile according to
159 the national distribution.

160

161 **Primary care visits and specialist referrals**

162 The reason for primary care attendances are not always coded in the primary care record.
163 To define primary care attendances specifically for eczema, we matched primary care
164 appointment dates to the dates of prescriptions issued for eczema treatment (as defined
165 below). A primary care attendance for eczema was defined as either a visit where an eczema
166 diagnosis code was recorded or a prescription for eczema treatment was issued. Specialist
167 referrals were identified by the presence of a Read code for referral to either a
168 dermatologist, a GP with a specialty interest in dermatology, or a dermatology specialist
169 nurse.

170

171 **Treatment and treatment escalation**

172 We extracted prescription records for therapy classes commonly used to manage eczema in
173 the UK: emollients and soap substitutes (combined into a single therapy class for the
174 purposes of analysis), TCS, TCI, systemic immuno-modulatory therapy (ciclosporin,
175 azathioprine, methotrexate, mycophenolate and oral corticosteroids), oral antihistamines,
176 and topical antimicrobial treatments.

177

178 In line with published work, we used treatment escalation as a surrogate marker to define
179 moderate and severe eczema.(19) We analysed three elements of treatment escalation: 1)
180 time to a prescription of a second potent topical corticosteroid treatment within one year or
181 a first topical calcineurin inhibitor (moderate eczema); 2) time to a systemic immuno-

modulatory therapy or a dermatology referral (severe eczema); 3) time to a first systemic immuno-modulatory therapy (as an important component of [2]).

Statistical Analyses

Definition of the prevalent cohort

Prevalent individuals were those fulfilling the diagnostic criteria for active eczema at the 31st December of each calendar year of the study.

Primary care visits and specialist referrals

Within the prevalent cohort we described annual rates of primary care attendances and specialist referrals for eczema. In the prevalent cohort in 2018, we calculated stratified rates of attendances and referrals by age category, sex, ethnicity, and deprivation quintile.

Treatment patterns

We described the patterns of eczema treatment in the prevalent cohort. Results were stratified by the same sociodemographic factors and calendar year. The proportion of the prevalent cohort receiving each medication class was calculated as the number of the prevalent cohort receiving at least one prescription for a particular medication class during a year divided by the total number in the prevalent cohort for that year. As a sensitivity analysis we repeated the analysis for antihistamine prescriptions in the subset of people with active eczema without a clinical diagnosis of allergic rhinitis, as antihistamines are commonly prescribed for this condition.

Definition of the incident cohort

To evaluate treatment escalation, a subset of people with incident eczema were identified as those diagnosed with new onset eczema over the study period. Patients with an eczema diagnosis recorded in their primary care record prior to the study period were excluded from this incident cohort.

210

211 Treatment escalation

212 In the incident cohort we examined each of the three treatment escalation outcomes using
213 time to event analysis, separately analysing children and adults. First, we compared the
214 cumulative incidence of each outcome by age at diagnosis category (age groups: 0-1, 2-11,
215 12-17, 18-49, 50+) using the Kaplan-Meier estimator. Second, we examined the non-linear
216 effect of continuous age (modelled as a restricted cubic spline with 3 knots) using
217 multivariable Cox proportional hazards models, with adjustment for sex, ethnicity and
218 deprivation quintile. The impact of age category was also evaluated using adjusted Cox
219 regression. Follow-up began on the date of diagnosis and extended to the earliest of the
220 study end-date (January 1, 2019), the date of patient transfer from an included practice, date
221 of death, or the date an individual developed an outcome of interest.

222

223 Statistical analyses were performed using R version 3.4.1 (R Core Team, Vienna, Austria,
224 2017).

225

226 Ethics approval

227 Study approval was granted by the Research Committee of the RCGP RSC. The study did not
228 meet the requirements for formal ethics board review as defined using the NHS Health
229 Research Authority research decision tool ([http://www.hra-](http://www.hra-decisiontools.org.uk/research/)
230 [decisiontools.org.uk/research/](http://www.hra-decisiontools.org.uk/research/)).

231

232 The study was conducted following RECORD (REporting of studies Conducted using
233 Observational Routinely-collected Data) guidelines.(34)

234 Results

235 411,931 individuals in the RCGP RCS database met the definition of active eczema for at least
236 one year over 2009 to 2018 inclusive (Supplementary Flowchart 1). Annual rates of primary
237 care consultations for eczema increased over the study period, from 87.8 (95% CI 87.3;88.3)

consultations per 100 person-years in 2009 to 112.0 (95% CI 111.5;112.6) per 100 person-years in 2018 (Figure 1A). Specialist dermatology referral rates increased from 3.8 (95% CI 3.7;3.9) per 100 person years in 2009 to 5.0 (95% CI 4.9;5.1) per 100 person-years in 2018 (Figure 1B).

242

Rates of eczema consultations and specialist referrals differ by age and sociodemographic factors

In people with active eczema in 2018 (n=148,166), rates of eczema consultations were markedly higher in children under 2 than in other age groups, but rates of specialist referrals were highest in adults aged 50 or over (Table 1). Rates of eczema consultations were similar by sex, but were higher in all non-white ethnicity categories. There was little difference in the rates of specialist referrals by sex or ethnicity. Primary care eczema consultation rates were highest for those in the most deprived quintile. However, rates of specialist referrals were highest in the least deprived quintile. Whilst there was no difference in rates of specialist referral between rural and urban areas, GP consultation rates were higher in urban settings.

254

Prescribing for eczema has changed little but varies markedly by age and sociodemographic characteristics

Over 2009-2018 (n=411,931 with active eczema), the most common therapy classes prescribed were emollients and TCS (Figure 2), and there was a slight increase in prescribing of emollients (prescribed to 51.4% of people in 2018 compared to 48.5% in 2009) and a decrease in prescribing of TCS (52.0% 2018, 57.3% in 2009) over the 10 year study period. There were also increases in prescribing of TCI therapy (1.8% in 2018, 0.8% in 2009), systemic immuno-modulatory therapy (1.9% in 2018, 1.2% in 2009), and oral corticosteroids (8.2% in 2018, 6.6% in 2009), but little change in antihistamine prescribing (19.6% in 2018, 19.4% in 2009) and a reduction in prescribing of topical antimicrobials (13.1% in 2018, 14.8% in 2009).

266

267 In people with active eczema in 2018 (n=148,166), emollients were the most commonly
268 prescribed treatment in children, whilst TCS were the most common treatment in adults
269 (Table 2 and Figure 3). Mild TCS were commonly prescribed in children under 2, whilst use
270 of very potent TCS was mainly restricted to adults. Antihistamines and oral corticosteroids
271 were the most common systemic therapies prescribed, with oral corticosteroids more
272 frequently prescribed in adults than children.

273

274 Fewer people of non-white ethnicities and people from the two most deprived IMD quintiles
275 were prescribed potent and very potent TCS (Table 2). People of non-white ethnicities were
276 also more likely to be prescribed emollients, TCI or antihistamines, and less likely to be
277 prescribed oral corticosteroids. People from less deprived IMD quintiles were less likely to
278 be prescribed emollients or antihistamines. Antihistamine prescribing was lower in people
279 with active eczema without a clinical diagnosis of allergic rhinitis (overall prescribing
280 prevalence 15.1% versus 19.6% in all people with active eczema, but prescribing time trends
281 and differences in antihistamine prescribing by sociodemographic factors were consistent in
282 this subgroup were consistent with the whole active eczema population (Supplementary
283 Figure 1, Supplementary Table 1).

284

285 Treatment escalation

286 167,311 people with incident eczema were included in the analysis of treatment escalation.
287 Incidence of moderate and severe eczema was higher in adolescents than younger children
288 (Figure 4A and Figure 4B, Table 3A), with both peaking at age 18 when age was analysed as a
289 continuous measure (Supplementary Figure 2). In adults, incidence of moderate and severe
290 eczema increased with a higher age at diagnosis, although the difference in incidence by age
291 was more marked in moderate than severe eczema (Figure 4A and Figure 4B, Table 3B,
292 Supplementary Figure 2). Initiation of systemic immuno-modulatory therapy was low and
293 higher in adults than children (Figure 4C), and in adults was highest in those aged 50 to 68,
294 before declining at older ages (Supplementary Figure 2). 10-year absolute risks of
295 progressing to each endpoint are reported, by age category, in Supplementary Table 2.

296

297 In children there was a greater risk of treatment escalation in people of non-white ethnicity.
298 In adults, only in people of Asian ethnicity was there evidence of a greater risk of
299 progression to moderate but not severe eczema (Table 3). Males were more likely to
300 progress to moderate eczema than females (Table 3). Children and adults from the least
301 deprived category were more likely to progress to severe eczema. Conversely, children from
302 the least deprived category were less likely to progress to moderate eczema. For adults,
303 there was no evidence of a difference in progression to moderate eczema by deprivation
304 quintile. As initiation of systemic immuno-modulatory therapy was uncommon, stratification
305 by deprivation and quintile was not possible for this endpoint.

306 **Discussion**

307 Our study provides important insight into the primary care management and disease course
308 of eczema across the lifespan. Both primary care consultation and specialist referral rates for
309 eczema increased over the last decade, and we observed substantial differences in
310 consultation rates by age, ethnicity and deprivation category. Notable findings include that,
311 although primary care consultation rates for eczema were highest in the people of lower
312 socioeconomic status, people of higher socioeconomic status were more likely to have a
313 specialist referral for eczema. We also observed higher primary care consultation rates in
314 non-white ethnicities, with the highest rates seen in people from an Asian background.
315 Whilst over the study period we observed little change in overall treatment patterns,
316 treatment escalation varied by socioeconomic status and ethnicity, and in particular was
317 more common in children of non-white ethnicity.

319 **Strengths and Limitations**

320 Strengths of this study include the use of contemporary data from a large representative
321 cohort with high quality ethnicity and deprivation data. Accurate prescribing data is ensured
322 through automatic entry when prescriptions are generated. A limitation of our study is the
323 likelihood that some patients included in the incident eczema cohort did not have true new
324 onset eczema, as they had a historical onset of eczema prior to our study period that was not
325 captured in the primary care record. Although diagnoses dates can be retrospectively coded,

326 this may not always be done correctly. This limitation will be most applicable to older
327 patients, for example if they had childhood eczema at a time before the introduction of
328 electronic health records which has not been subsequently retrospectively coded. This
329 limitation is common to all studies using primary care databases to define incident disease
330 cohorts. A further limitation is that prescriptions issued in secondary care are not available
331 in UK electronic health record data, and as a result our study will have systematically
332 undercaptured prescribing of systemic immuno-modulatory therapies. We are also likely to
333 have underestimated specialist dermatology referral rates in this study, as it is likely that
334 some dermatology referrals will have been coded as unspecified referrals without mention
335 of clinical speciality and were therefore not included in our estimates. In addition, we found
336 that phototherapy data captured in RCGP RCS was not complete enough to be used for
337 analysis, and this data was therefore not included in this paper.

338
339 Our definitions of active, moderate and severe eczema are concordant with recently
340 published work exploring outcomes for people with eczema,(19) but the accuracy of this
341 approach to classify eczema has not been validated against physician-assessed disease
342 severity. Similarly, although the algorithm used to identify eczema has been demonstrated to
343 have high positive predictive value, the negative predictive value, sensitivity and specificity
344 has not been assessed.(27) It is likely that some patients self-managing with very mild
345 eczema will have been missed using the algorithm, and so the healthcare utilisation
346 measures in this study should be interpreted as estimates applicable for patients in contact
347 with primary care physicians to manage their eczema. Future studies incorporating our
348 findings must acknowledge this limitation and be cautious if they seek to generalise to the
349 population of all patients with eczema, including the very mildest, self-managed forms. This
350 could be especially relevant for health economics analysis, as to neglect to do so could
351 exaggerate the healthcare resources required by patients with eczema. The definitions for
352 treatment escalation are in-line with a previous systematic review which proposed that an
353 eczema flare should be defined as an episode requiring treatment escalation or seeking
354 additional medical advice.(35) Nonetheless, as the reason underlying prescribing decisions
355 is not captured, our data cannot elucidate why treatment was escalated. Performance of the
356 diagnostic algorithm has also not been assessed as yet in socio-demographic subgroups, and

357 a potential explanation of the differences in treatment escalation is variation in algorithm
358 performance across such different population groups. A more comprehensive evaluation of
359 the diagnostic algorithm performance, as well as evaluation of definitions of eczema severity,
360 progression and escalation in primary care would be a useful area for further work.

361

362 **Context of previous work**

363 The increase in primary and secondary care consultations concur with a large retrospective
364 analysis of overall GP clinical workload in the UK, which found that annual consultation rates
365 increased by 10.5% between 2007 and 2014.(36) A rising elderly population and a doubling
366 of telephone consultations were amongst possible explanations.

367

368 To our knowledge there have been no large-scale studies of overall GP clinical workload
369 from 2014 onwards. We observed a plateau in consultation rates. This may have resulted
370 from an emphasis placed on self-management of chronic conditions in recent years, leading
371 to a reduced requirement for doctor-patient interactions.(37) Written action plans have
372 been demonstrated to be an effective means of patient education in eczema, improving
373 understanding of both the condition and its treatment.(38).

374

375 We found specialist referrals for eczema were highest in the over 50s age group. A
376 qualitative study of GP's experiences of eczema stated that while most GPs feel confident in
377 diagnosing uncomplicated eczema, many report uncertainty in diagnosing and managing
378 more complex cases, particularly where potent steroids are required.(39) This may explain
379 the increase in referral rates for eczema among the elderly, who are often resistant to
380 standard treatments.(40)

381

382 Our observation of disparities in referral to secondary care by socioeconomic status fits with
383 the inverse care law (that those who most need medical care are least likely to receive it
384 (41)), and has been observed in studies examining GP referral patterns for other conditions.
385 McBride et al observed people of higher socioeconomic status had higher rates of specialist
386 referral for hip pain and dyspepsia, postulating that this might reflect higher workloads for

387 practitioners in socially disadvantaged communities (42). In addition, patients from more-
388 deprived areas have a greater burden of multi-morbidity and present to GP consultations
389 with more problems to discuss (43); potentially diverting the focus of the encounter away
390 from eczema.

391
392 The relatively stable prescribing patterns we observed for eczema are in contrast to the vast
393 changes seen in prescribing for other conditions in recent years, such as type 2 diabetes.(44)
394 This likely reflects the fact that UK National Institute for Health and Care Excellence (NICE)
395 treatment guidelines for eczema,(14) in contrast to those for type 2 diabetes,(45) have not
396 been updated since 2007. A potential explanation for the decline in prescribing of emollients
397 in recent years are recently updated UK prescribing recommendations,, which for dry skin
398 conditions (although not eczema itself) encourage over the counter purchases of emollients
399 instead of the provision of routine prescriptions.(46)

400
401 Differences in prescribing patterns by age found in this study are broadly in-line with
402 treatment guidelines and previous studies. US Population-based studies have estimated that
403 7% of children and 11% of adults with eczema have severe disease.(10, 11) Our finding of 8-
404 10% of under 12s prescribed potent TCS is therefore likely in-line with national guidelines,
405 which recommend potent TCS are to be used in moderate to severe eczema.(14, 47)

406
407 Our study shows important differences in prescribing by socioeconomic status, with a
408 greater rate of topical antimicrobial, antihistamine and oral steroid prescribing in more
409 deprived groups and lower rates of potent TCS and systemic immuno-modulatory treatment
410 use. This may be related in part to higher levels of specialty referral with increasing
411 socioeconomic status, as seen in our study and others.(48) GPs are very unlikely or unable to
412 prescribe oral immuno-suppressive agents without secondary care initiation and shared
413 care agreements.

414
415 Differences in prescribing by ethnicity was also observed; emollient use was higher in those
416 from non-white ethnicities, whereas oral steroid and other systemic therapies were more
417 frequently prescribed to those from a white background. Important nuances in the visual

418 appearance of eczema in non-white skin may lead to under-estimation of its severity and
419 hence under treatment.(49, 50) Higher rates of antihistamine prescriptions in black and
420 Asian populations fits with previous studies showing higher rates of pruritus, scratching and
421 subsequent lichenification in these groups.(50)

422

423 **Clinical implications**

424 Our study highlights important health disparities in the management of eczema in England
425 that warrant further study. Of particular note are the lower rates of referral to secondary
426 care and prescription of topical and systemic immuno-modulatory treatments in those from
427 more deprived backgrounds, and the greater risk of progression to moderate and severe
428 eczema in children of non-white ethnicity. It is unlikely that individual GPs are aware of the
429 disparities in referral, and feedback of practice-level data to GPs via dashboards and
430 observatories may be able to raise awareness of such disparities.(51)

431

432

433 Although prescribing trends were consistent over the study period, it will be important to
434 monitor prescribing behaviour in primary and secondary care over the coming years due to
435 likely changes in prescribing guidelines and the availability of new systemic treatments.

436

437

438

439

440

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449 Conflict of Interest Statement

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451 Surveillance Centre as part of his academic post; he has also received funding for projects
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468 College London.

469 **Data availability statement**

470 The RCGP RSC dataset is held securely at University of Oxford and the University of Surrey
471 and can be accessed by bona fide researchers. Approval is on a project-by-project basis
472 (www.rcgp.org.uk/rsc). Ethical approval by an NHS Research Ethics Committee may be
473 needed before any data release/other appropriate approval. Researchers wishing to directly
474 analyse the patient-level pseudonymised data will be required to complete information
475 governance training and work on the data from university secure servers. Patient-level data
476 cannot be taken out of the secure network.

477

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- 628

632 **Table 1.** Primary care attendance rates and specialist referral rates for eczema by
 633 sociodemographic factors, in people with active eczema in 2018 (n=148,166)

	Number of individuals with eczema	Eczema consultation rates (per 100 person-years)	Specialist referral rates (per 100 person- years)
Overall	148,166	112.0 (111.5, 112.6)	5.0 (4.9, 5.1)
Age group			
<2	7,230	213.3 (211.7, 215.2)	5.8 (5.2, 6.4)
2-11	34,074	95.6 (94.6, 96.7)	2.4 (2.3, 2.6)
12-17	12,476	84.3 (82.7, 86.0)	3.8 (3.4, 4.1)
18-49	37,995	106.2 (105.2, 107.3)	5.8 (5.5, 6.0)
≥50	56,391	119.8 (118.8, 120.7)	6.3 (6.1, 6.5)
Sex			
Female	81,357	113.8 (113.0, 114.5)	5.1 (4.9, 5.3)
Male	66,809	109.9 (109.1, 110.7)	4.9 (4.7, 5.1)
IMD quintile*			
1 (most deprived)	26,454	131.2 (129.8, 132.6)	4.5 (4.2, 4.8)
2	25,520	118.6 (117.3, 120.0)	4.8 (4.6, 5.1)
3	26,445	110.0 (108.7, 111.2)	5.0 (4.8, 5.3)
4	31,426	105.3 (104.1, 106.4)	5.1 (4.9, 5.4)
5 (least deprived)	36,467	101.2 (100.1, 102.2)	5.4 (5.1, 5.6)
Ethnicity †			
White	87,717	108.6 (107.9, 109.3)	5.0 (4.8, 5.2)
Asian	14,980	138.3 (136.4, 140.2)	5.3 (4.9, 5.7)
Black	5,799	116.7 (113.9, 119.6)	4.4 (3.9, 5.0)
Mixed	2,808	116.0 (112.0, 120.1)	4.6 (3.8, 5.5)
Other	1,234	124.5 (118.3, 131.0)	6.2 (4.9, 7.8)
Rural-Urban Classification ††			
Urban	117,466	103.1 (101.9, 104.3)	5.1 (4.8, 5.3)
Rural	29,005	114.3 (113.7, 115.0)	5.0 (4.9, 5.1)

635 * IMD = index of multiple deprivation. IMD data was not available for n=1,854. † Ethnicity data was not
 636 available for n=35,628. †† Rural-Urban classification was not available for n=1,695

Table 2. Prescribing of therapy by sociodemographic factors for people with active eczema in 2018 (n=148,166).

Therapy class											
	N	Emollients and soap substitutes	Mild TCS	Moderate TCS	Potent TCS	Very potent TCS	TCI	Topical antimicrobial s	Antihistamin es	Systemic immuno- modulatory therapy	Oral corticosteroi ds
		N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Overall	148,166	76095 (51.4%)	40478 (27.3%)	19575 (13.2%)	34997 (23.6%)	6478 (4.4%)	2683 (1.8%)	19378 (13.1%)	29041 (19.6)	2785 (1.9)	12087 (8.2)
Age group											
<2	7,230	5368 (74.2)	4384 (60.6)	1135 (15.7)	635 (8.8)	18 (0.2)	73 (1.0)	1614 (22.3)	1315 (18.2)	0 (0)	291 (4.0)
2-11	34,074	19431 (57.0)	11256 (33.0)	3967 (11.6)	3431 (10.1)	176 (0.5)	530 (1.6)	4508 (13.2)	6811 (20.0)	31 (0.1)	1353 (4.0)
12-17	12,476	6777 (54.3)	3425 (27.5)	1686 (13.5)	2260 (18.1)	208 (1.7)	326 (2.6)	1307 (10.5)	3022 (24.2)	73 (0.6)	455 (3.6)
18-49	37,995	15016 (39.5)	8529 (22.4)	5520 (14.5)	11568 (30.4)	2127 (5.6)	1096 (2.9)	4333 (11.4)	6932 (18.2)	860 (2.3)	2629 (6.9)
≥50	56,391	29503 (52.3)	12884 (22.8)	7267 (12.9)	17103 (30.3)	3949 (7)	658 (1.2)	7616 (13.5)	10961 (19.4)	1821 (3.2)	7359 (13)
Sex											
Male	81,357	41139 (50.6)	22237 (27.3)	10692 (13.1)	18658 (22.9)	3832 (4.7)	1489 (1.8)	10960 (13.5)	16394 (20.2)	1704 (2.1)	6905 (8.5)
Female	66,809	34956 (52.3)	18241 (27.3)	8883 (13.3)	16339 (24.5)	2646 (4.0)	1194 (1.8)	8418 (12.6)	12647 (18.9)	1081 (1.6)	5182 (7.8)
IMD quintile*											
1 (most deprived)	26,454	14785 (55.9)	7761 (29.3)	3425 (12.9)	5834 (22.1)	1029 (3.9)	499 (1.9)	3765 (14.2)	6413 (24.2)	404 (1.5)	2270 (8.6)
2	25,520	13784 (54)	7182 (28.1)	3380 (13.2)	5832 (22.9)	1048 (4.1)	469 (1.8)	3393 (13.3)	5480 (21.5)	378 (1.5)	2002 (7.8)
3	26,445	13273 (50.2)	6977 (26.4)	3540 (13.4)	6410 (24.2)	1197 (4.5)	454 (1.7)	3440 (13)	4944 (18.7)	541 (2)	2212 (8.4)
4	31,426	15538 (49.4)	8350 (26.6)	4039 (12.9)	7691 (24.5)	1472 (4.7)	532 (1.7)	3986 (12.7)	5563 (17.7)	684 (2.2)	2581 (8.2)
5 (least deprived)	36,467	17738 (48.6)	9648 (26.5)	4921 (13.5)	8761 (24)	1659 (4.5)	690 (1.9)	4554 (12.5)	6259 (17.2)	745 (2)	2853 (7.8)
Ethnicity†											

White	87,717	42490 (48.4)	22791 (26)	11437 (13)	21859 (24.9)	4227 (4.8)	1353 (1.5)	11496 (13.1)	16214 (18.5)	1913 (2.2)	8311 (9.5)
Asian	14,980	8900 (59.4)	4188 (28)	2133 (14.2)	3502 (23.4)	671 (4.5)	513 (3.4)	2005 (13.4)	4064 (27.1)	211 (1.4)	975 (6.5)
Black	5,799	3659 (63.1)	1409 (24.3)	683 (11.8)	1154 (19.9)	196 (3.4)	122 (2.1)	660 (11.4)	1486 (25.6)	50 (0.9)	241 (4.2)
Mixed	2,808	1660 (59.1)	836 (29.8)	385 (13.7)	561 (20)	92 (3.3)	73 (2.6)	344 (12.3)	637 (22.7)	30 (1.1)	129 (4.6)
Other	1,234	638 (51.7)	340 (27.6)	166 (13.5)	265 (21.5)	46 (3.7)	34 (2.8)	192 (15.6)	301 (24.4)	12 (1)	56 (4.5)

* IMD = index of multiple deprivation. IMD data was not available for n=1,854. † Ethnicity data was not available for n=35,628.

Table 3: Hazard ratios (95% confidence intervals) for time to moderate eczema and severe eczema in eligible populations with incident eczema over 2009-2018, by sociodemographic characteristics. Individuals with each outcome at baseline excluded from analysis of each outcome.

A) Children

		Moderate eczema (n=84,819)	Severe eczema (n=84,819)
Sex	Female	1.00 (ref)	1.00 (ref)
	Male	1.10 (1.04, 1.16)	1.01 (0.96, 1.07)
Age category	<2	1.00 (ref)	1.00 (ref)
	2-11	0.92 (0.87, 0.98)	0.65 (0.61, 0.69)
	12-17	2.85 (2.78, 3.07)	1.31 (1.20, 1.43)
IMD quintile ^x	1 (most deprived)	1.00 (ref)	1.00 (ref)
	2	1.02 (0.95, 1.11)	1.14 (1.05, 1.25)
	3	0.87 (0.79, 0.94)	1.15 (1.05, 1.26)
	4	0.92 (0.85, 1.01)	1.13 (1.03, 1.23)
	5 (least deprived)	0.90 (0.83, 0.98)	1.22 (1.12, 1.32)
Ethnicity ^x	White	1.00 (ref)	1.00 (ref)
	Asian	1.71 (1.58, 1.86)	1.82 (1.67, 1.98)
	Black	1.54 (1.37, 1.73)	1.49 (1.31, 1.69)
	Mixed	1.41 (1.21, 1.65)	1.59 (1.36, 1.85)
	Other	1.57 (1.25, 1.97)	1.47 (1.15, 1.89)

^xHazard ratios for IMD not recorded 1.02 (95% CI 0.81, 1.29) for moderate eczema and 1.02 (0.78, 1.32) for severe eczema; Hazard ratios for Ethnicity not recorded category 1.08 (1.01, 1.15) for moderate eczema and 1.29 (1.21, 1.37) for severe eczema.

B) Adults

		Moderate eczema (n=55,417)	Severe eczema (n=55,417)
Sex	Female	1.00 (ref)	1.00 (ref)
	Male	1.31 (1.27, 1.36)	0.96 (0.91, 1.01)
Age category	18-49	1.00 (ref)	1.00 (ref)
	50+	1.40 (1.35, 1.45)	1.24 (1.18, 1.31)
IMD quintile ^x	1 (most deprived)	1.00 (ref)	1.00 (ref)
	2	1.00 (0.95, 1.07)	1.05 (0.96, 1.14)
	3	1.04 (0.99, 1.11)	1.11 (1.01, 1.21)
	4	0.99 (0.94, 1.05)	1.18 (1.09, 1.29)
	5 (least deprived)	0.97 (0.92, 1.03)	1.26 (1.16, 1.37)
Ethnicity ^x	White	1.00 (ref)	1.00 (ref)
	Asian	1.12 (1.06, 1.19)	0.97 (0.88, 1.07)
	Black	0.89 (0.79, 0.99)	0.86 (0.73, 1.02)
	Mixed	1.05 (0.88, 1.25)	1.16 (0.91, 1.49)
	Other	0.88 (0.72, 1.07)	0.89 (0.66, 1.19)

^xHazard ratios for IMD not recorded 1.03 (0.87, 1.21) for moderate eczema, 1.26 (1.00, 1.59) for severe eczema; Hazard ratios for Ethnicity not recorded category 0.97 (0.93, 1.01) for moderate eczema, 0.96 (0.90, 1.02) for severe eczema.

Figure legends

Figure 1. The annual rates of eczema primary care consultations and specialist referrals for eczema between 2009-2018 (n=411,931)

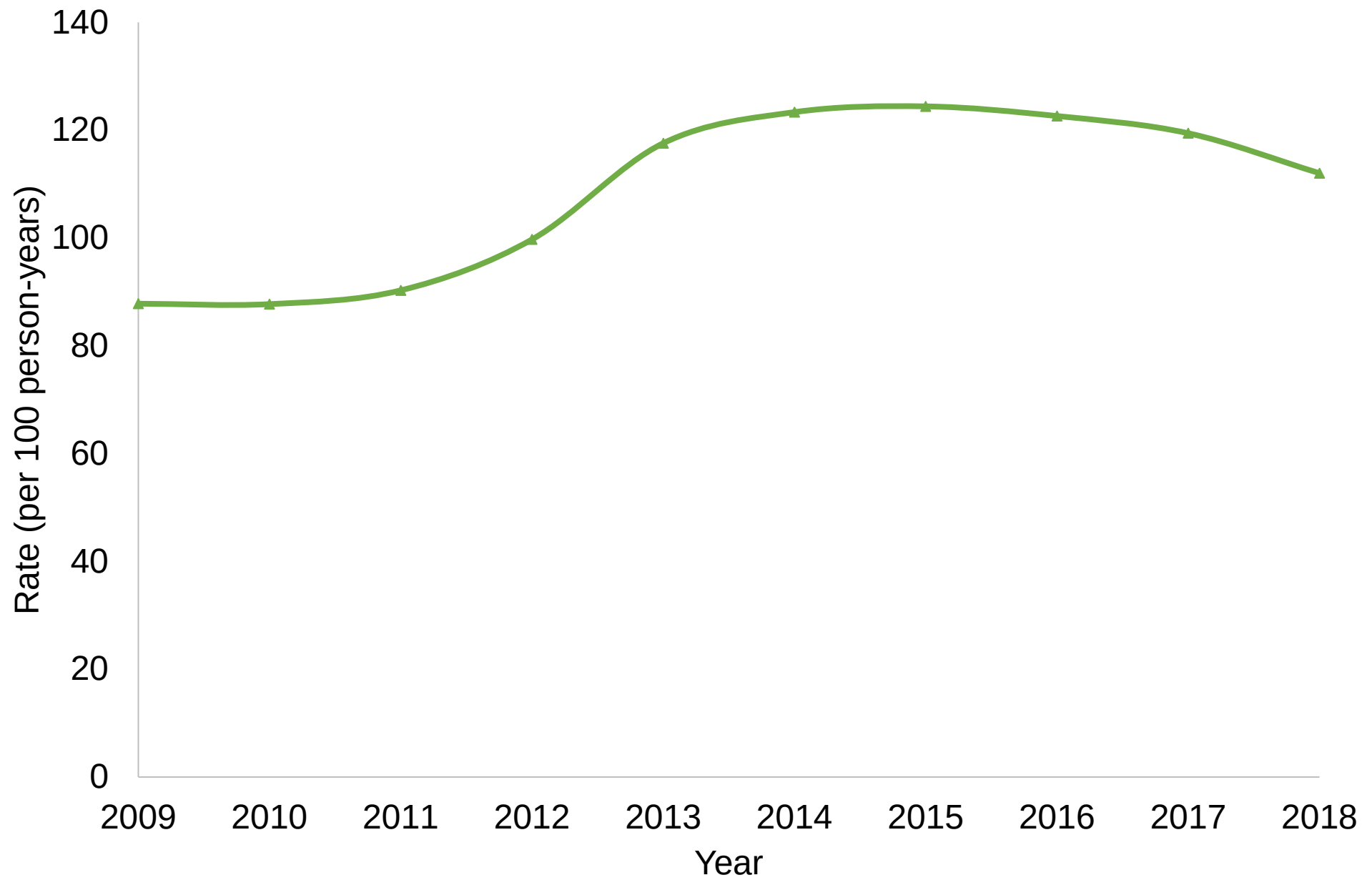
- A) Primary care consultations
- B) Specialist referrals for eczema

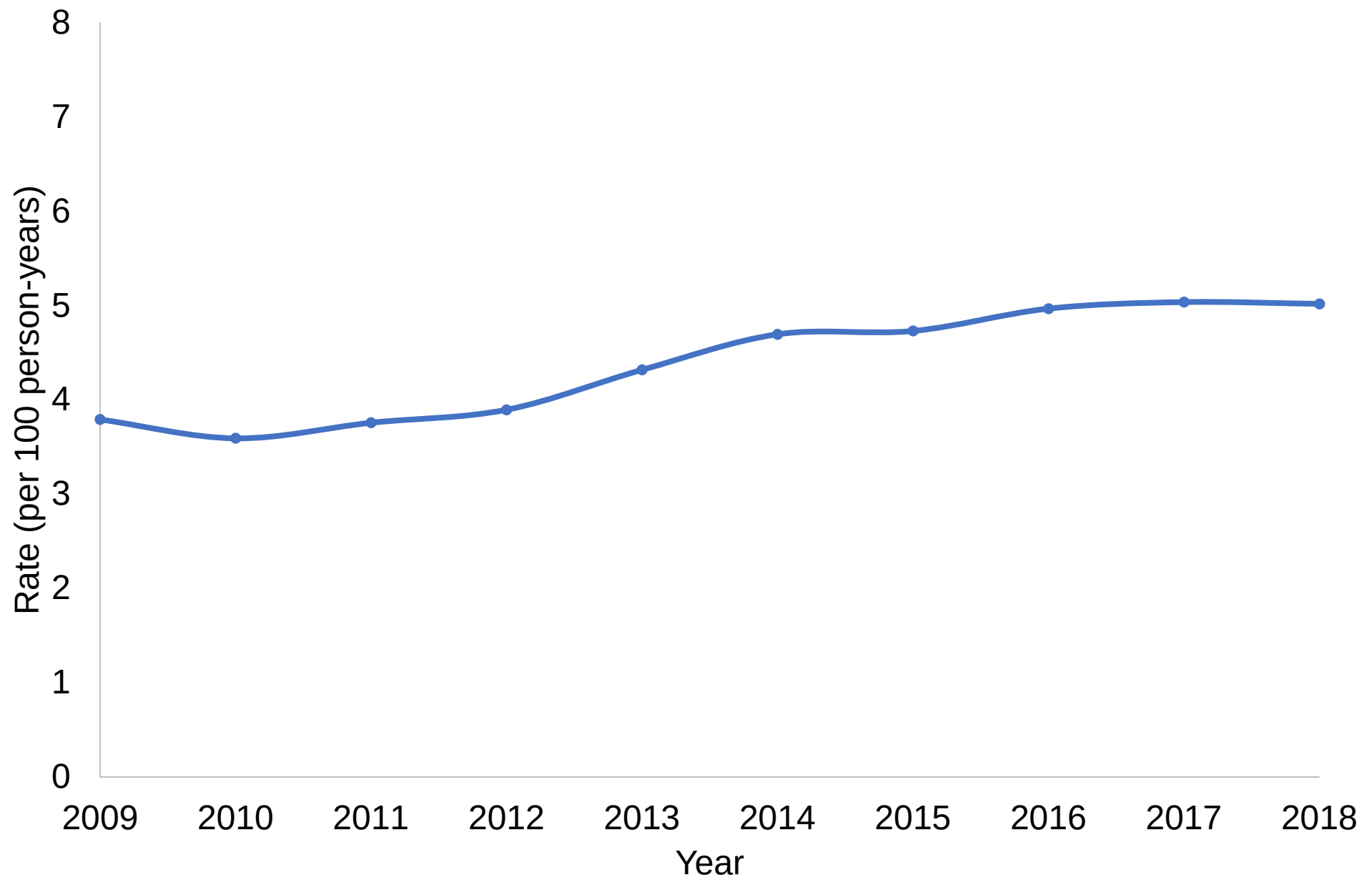
Figure 2. The annual prevalence of prescribing for eczema by therapy class between 2009-2018 (n=411,931)

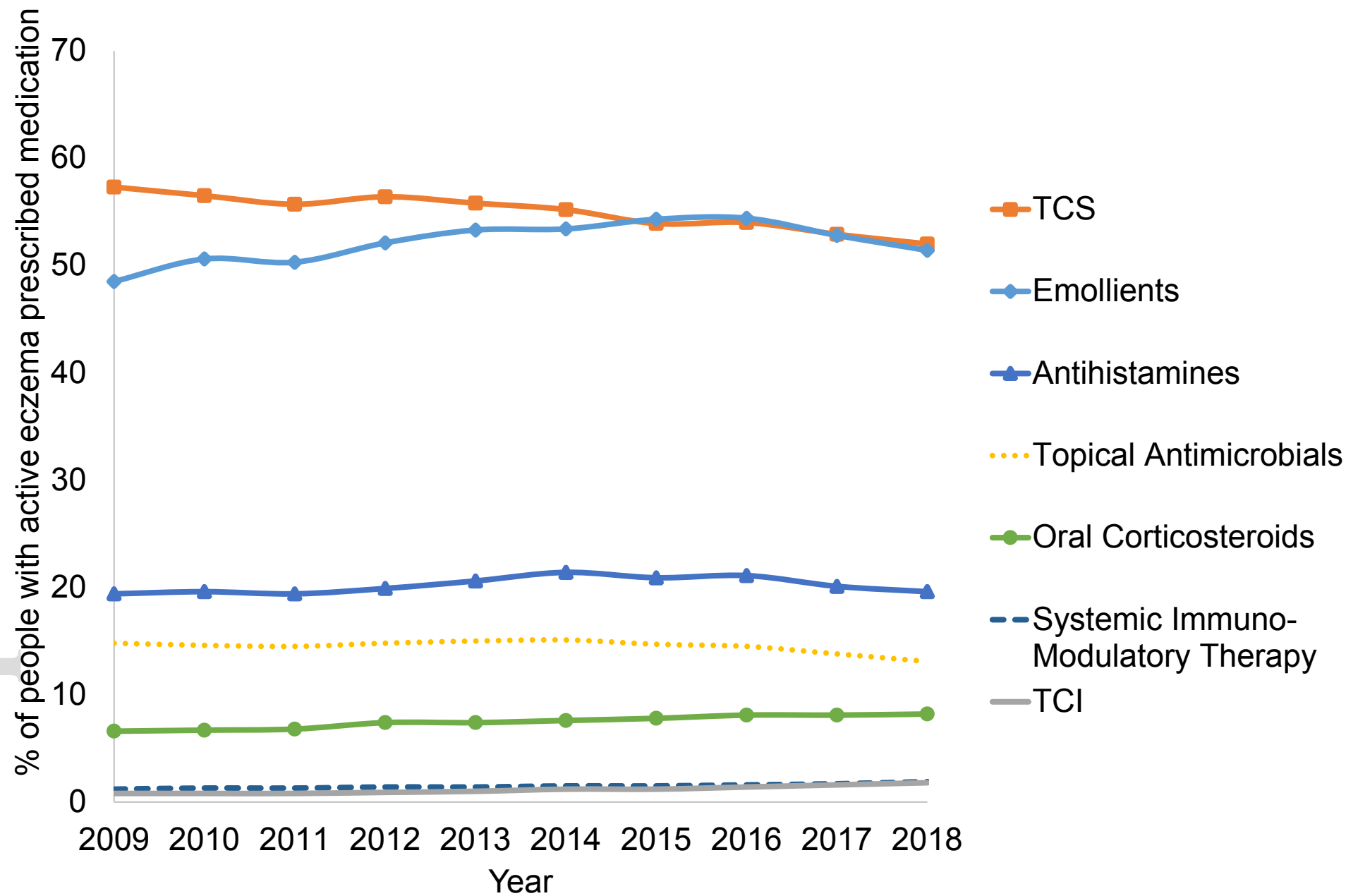
Figure 3. The prevalence of prescribing for eczema by age group and by therapy class for people with active eczema in 2018 (n=148,166)

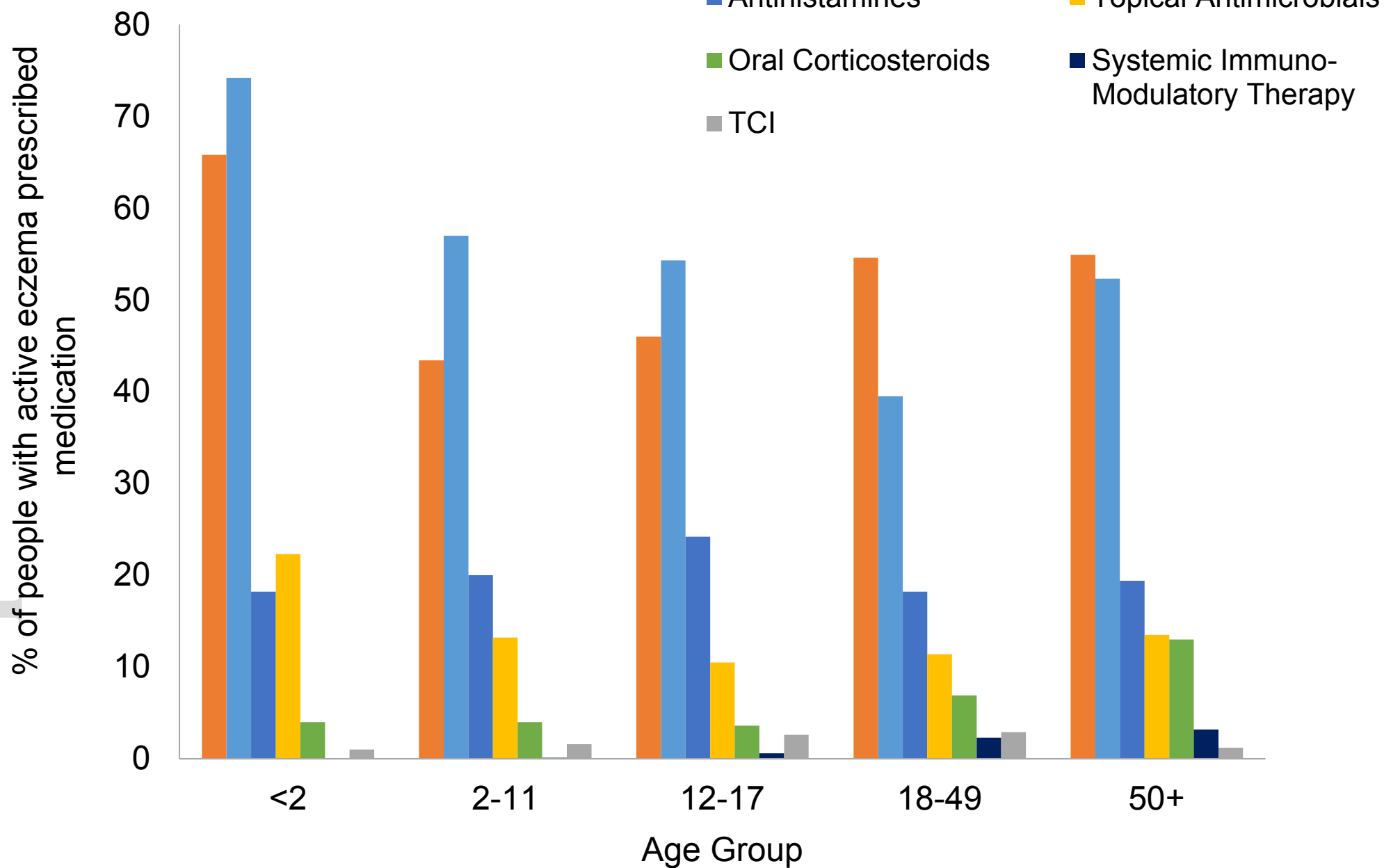
Figure 4: Cumulative incidence of treatment escalation by age at diagnosis category in people with incident eczema over 2009-2018

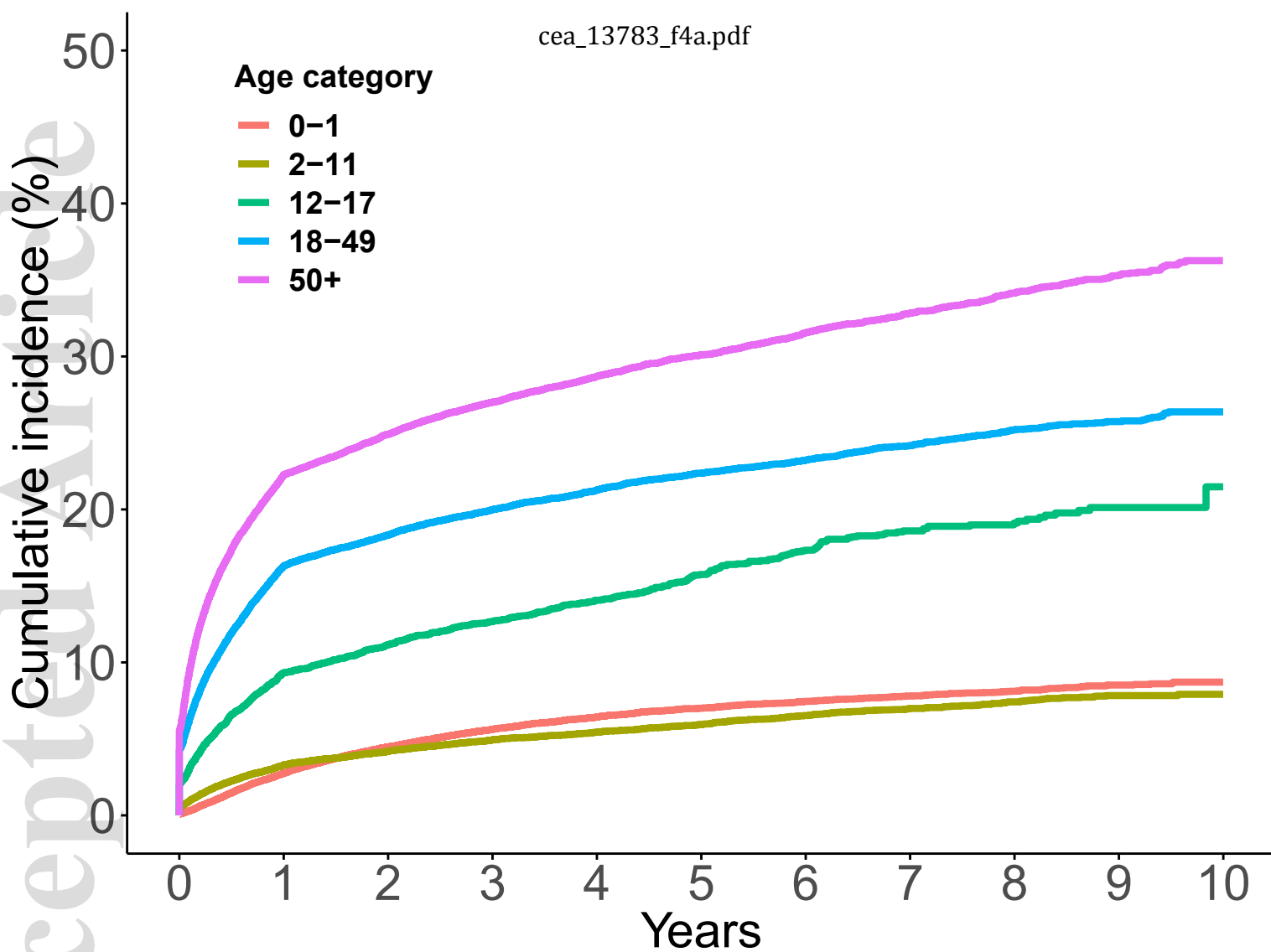
- A) Cumulative incidence of the prescription of a second potent topical corticosteroid treatment within one year or a first topical calcineurin inhibitor (TCI) (moderate eczema) in 140,236 people without moderate or severe eczema at diagnosis.
- B) Cumulative incidence of the first of systemic immuno-modulatory therapy or a dermatology referral (severe eczema) in 140,236 people without moderate or severe eczema at diagnosis.
- C) Cumulative incidence of initiation of systemic immuno-modulatory therapy (Ciclosporin, Azathioprine, Methotrexate & Mycophenolate mofetil) in 167,311 people with incident eczema.





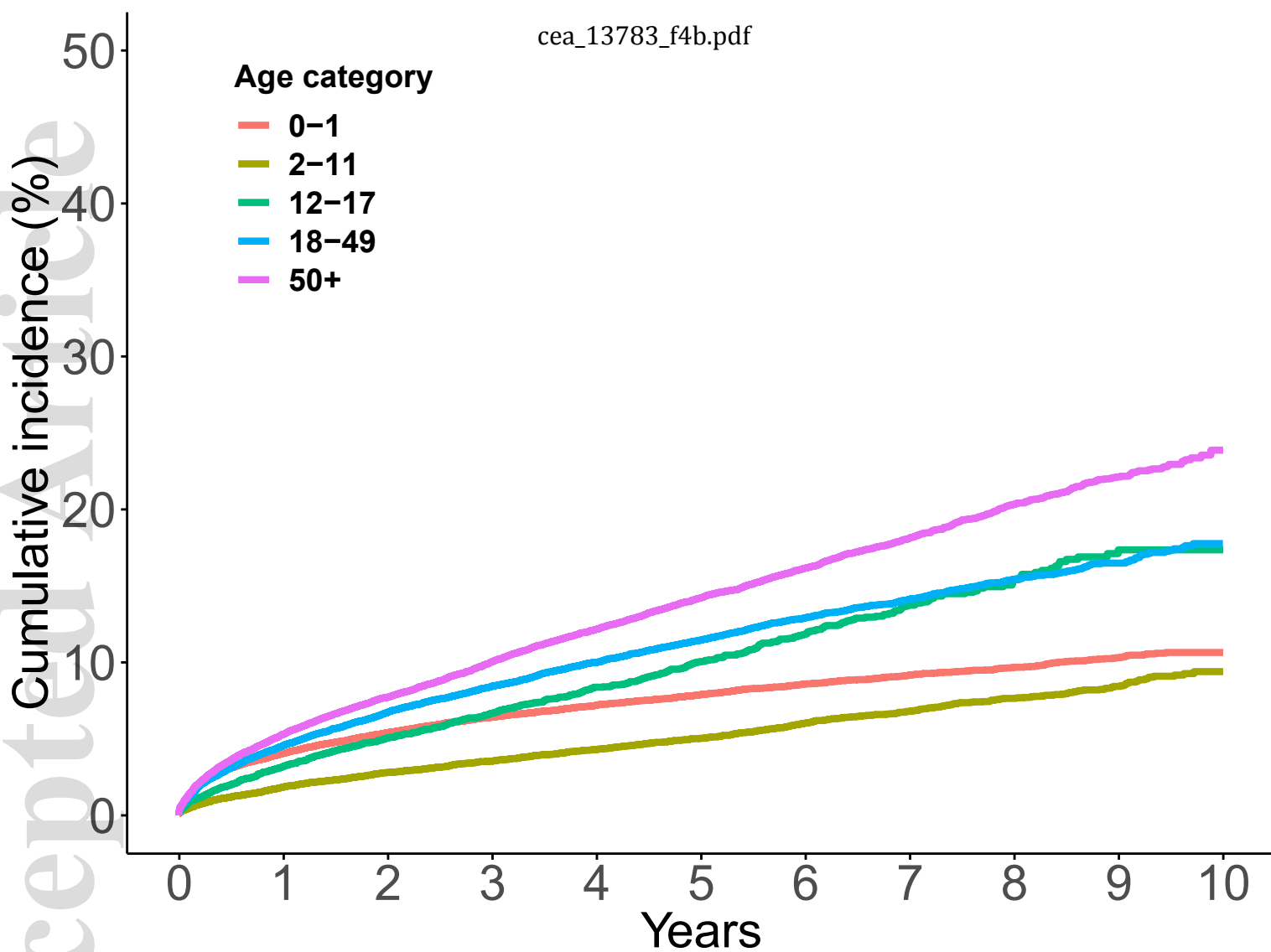






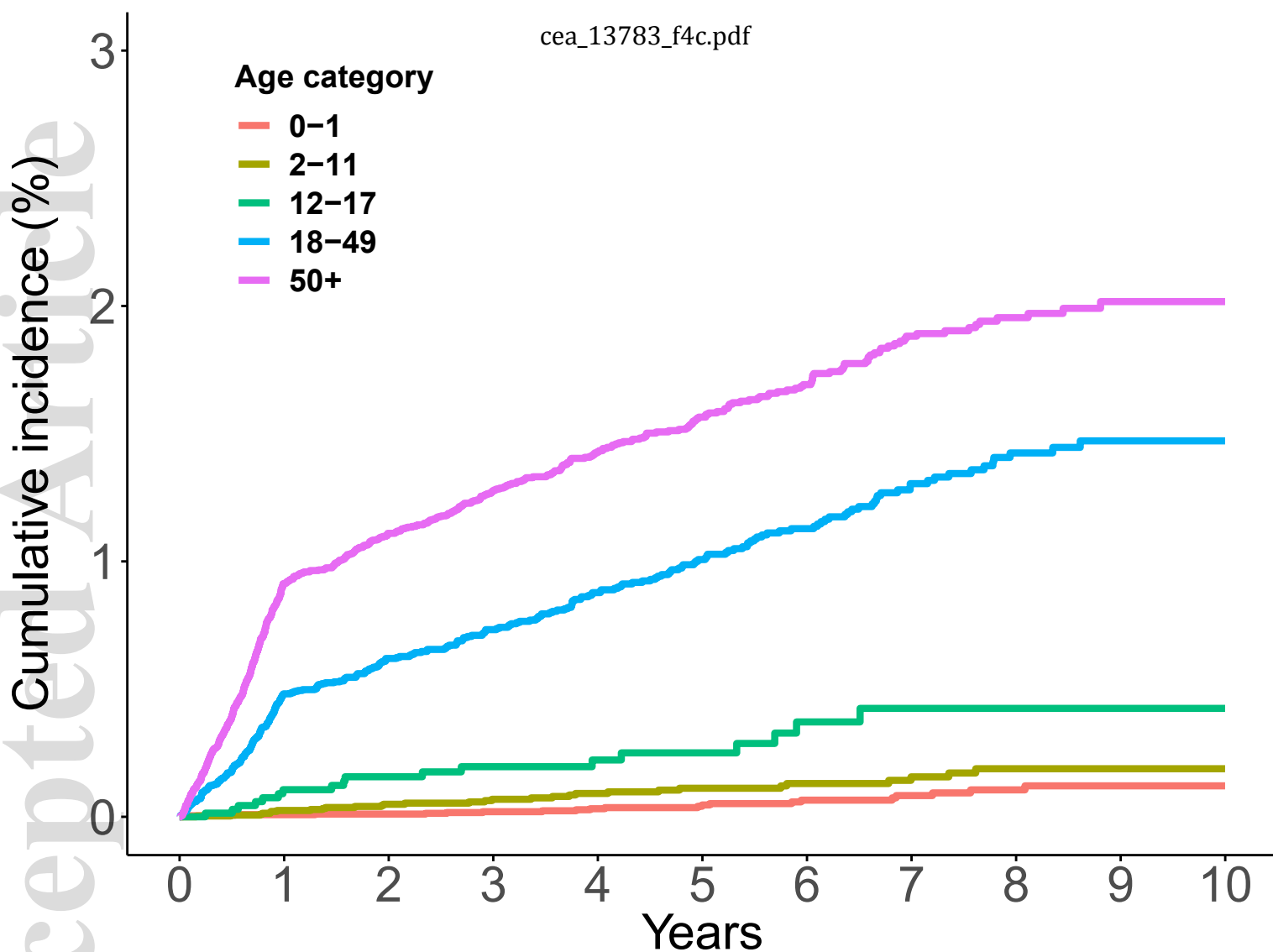
Number at risk

0-1	47966	41895	34297	27987	22224	17503	13273	9484	6044	2837	184
2-11	29510	25067	21332	17831	14709	11844	9082	6623	4377	2103	123
12-17	6349	5162	4411	3665	2942	2265	1681	1141	681	315	14
18-49	27889	20471	17092	14069	11534	9118	7023	5119	3413	1671	88
50+	28522	19740	16592	13735	11284	9065	6872	4948	3175	1460	72



Number at risk

0-1	47966	41349	34054	27832	22194	17485	13270	9478	6030	2833	182
2-11	29510	25446	21677	18144	14945	12019	9199	6653	4366	2106	124
12-17	6349	5507	4687	3914	3141	2431	1805	1234	729	335	14
18-49	27889	23303	19429	16020	13136	10359	7910	5738	3821	1856	89
50+	28522	23969	20235	16764	13672	10807	8164	5822	3738	1732	82



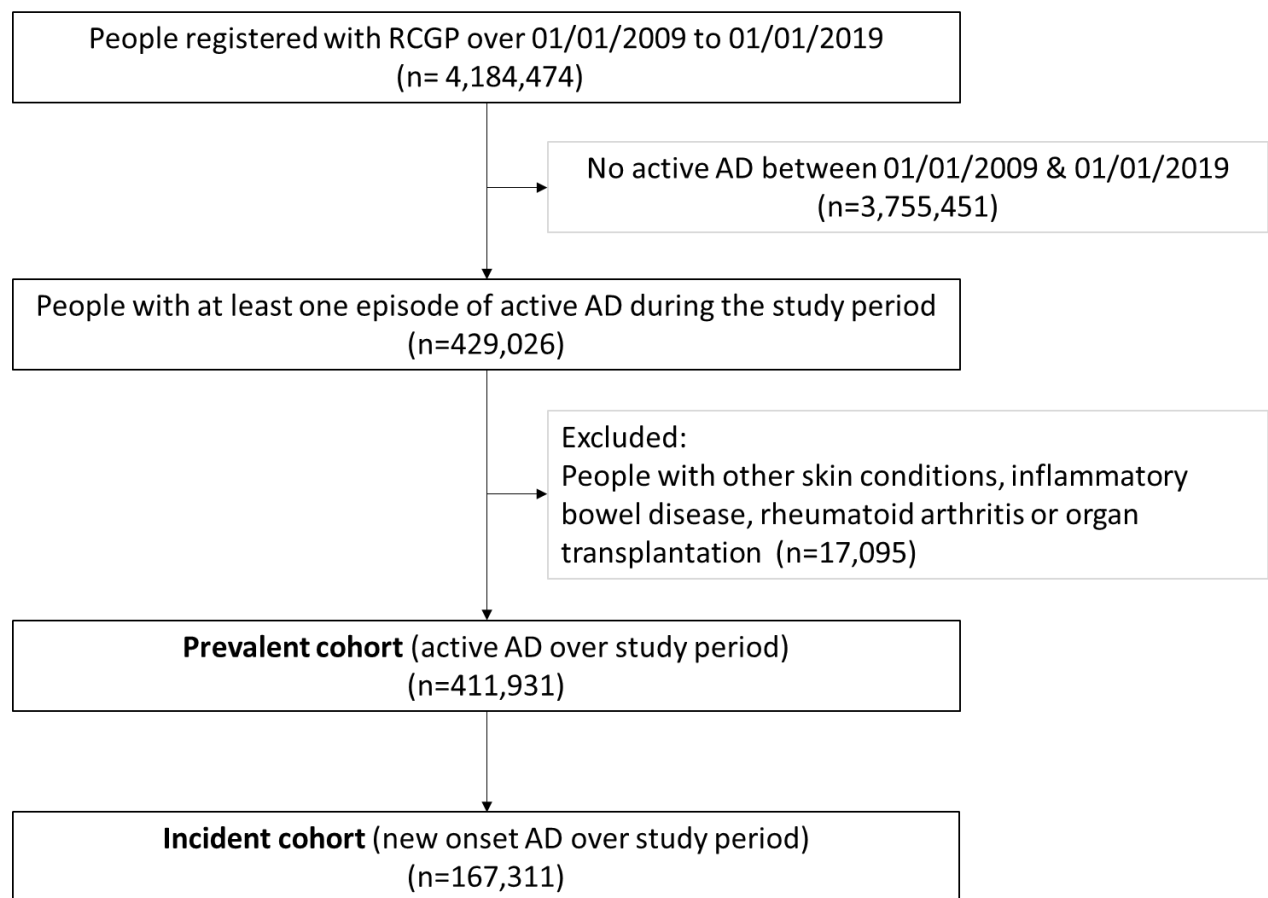
Number at risk

0-1	48525	43524	36258	29882	23908	18923	14391	10301	6590	3114	202
2-11	30688	26899	23085	19427	16095	13000	10037	7342	4838	2348	133
12-17	7070	6308	5472	4613	3736	2924	2201	1511	922	425	17
18-49	35653	30859	26187	21873	18049	14384	11056	8114	5444	2701	141
50+	45375	39215	33301	27753	22704	18104	13739	9845	6364	2954	142

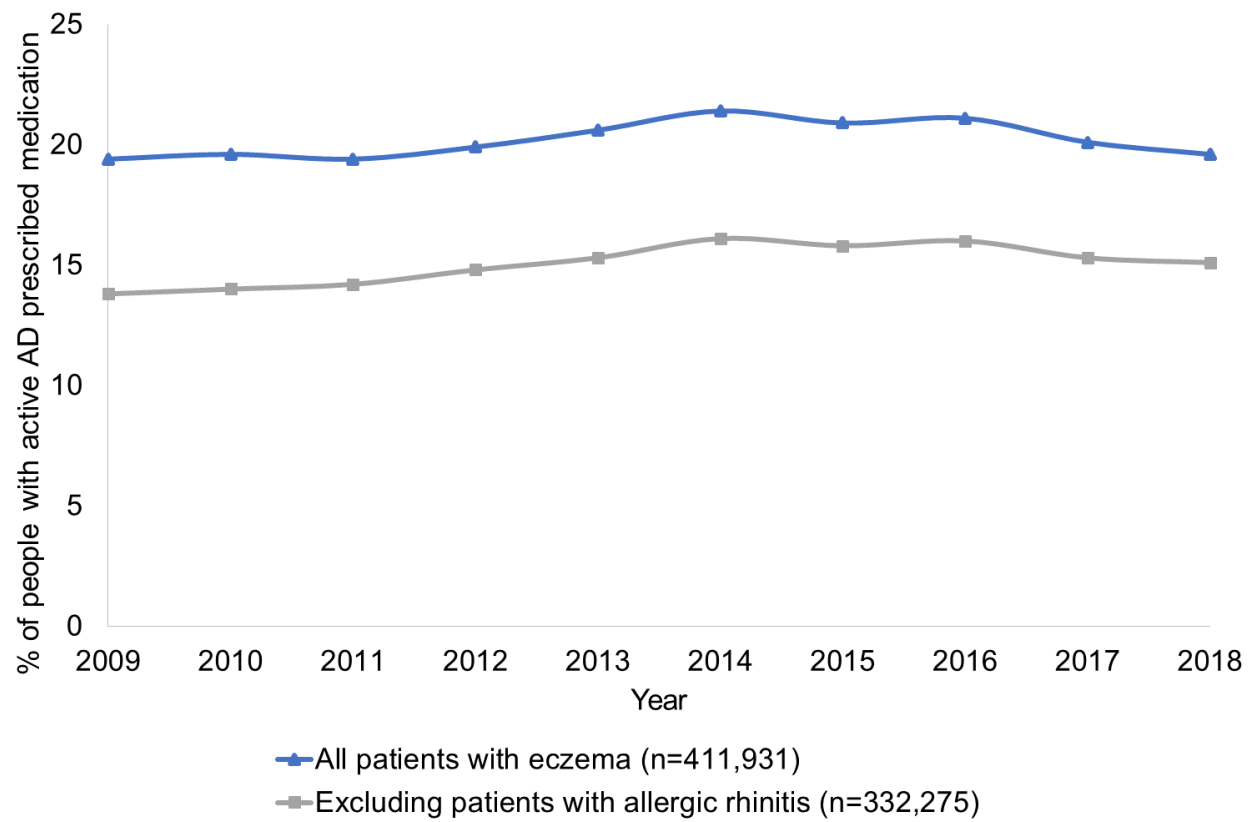
Supplementary material for: Patterns and trends in eczema management in UK primary care (2009-2018): a population-based cohort study

Authors: S. de Lusignan, H. Alexander, C. Broderick, J. Dennis, A. McGovern, C. Feeney, C. Flohr

Supplementary Flowchart 1: Flowcharts for construction of study population



Supplementary Figure 1: The annual prevalence of antihistamine prescribing for eczema between 2009-2018, in all patients with eczema (n=411,931) and the subset of patients with active eczema and no clinical diagnosis of allergic rhinitis (n=332,275)



Supplementary Table 1: Prescribing of antihistamine therapy by sociodemographic factors for people with active eczema in 2018, in all patients with eczema (n=148,166) and the subset of patients with active eczema and no clinical diagnosis of allergic rhinitis (n=117,375)

	All patients with active eczema (n=148,166)		Patients with active eczema and no clinical diagnosis of allergic rhinitis (n=117,375)	
	N (%)	N prescribed antihistamine (%)	N (%)	N prescribed antihistamine (%)
Overall	148,166	29041 (19.6)	117,375	17697 (15.1)
Age group				
<2	7,230	1315 (18.2)	7,140	1263 (17.7)
2-11	34,074	6811 (20.0)	30,520	4921 (16.1)
12-17	12,476	3022 (24.2)	9,026	1371 (15.2)
18-49	37,995	6932 (18.2)	25,967	3,188 (12.3)
≥50	56,391	10961 (19.4)	44,722	6,954 (15.5)
Sex				
Male	81,357	16394 (20.2)	63,953	9,913 (15.5)
Female	66,809	12647 (18.9)	53,422	7,784 (14.6)
IMD quintile*				
1 (most deprived)	26,454	6413 (24.2)	20,643	4,036 (19.6)
2	25,520	5480 (21.5)	20,206	3,397 (16.8)
3	26,445	4944 (18.7)	21,053	2,967 (14.1)
4	31,426	5563 (17.7)	25,057	3,376 (13.5)
5 (least deprived)	36,467	6259 (17.2)	28,915	3,667 (12.7)
Ethnicity†				
White	87,717	16214 (18.5)	69,610	9,904 (14.2)
Asian	14,980	4064 (27.1)	10,870	2,288 (21.0)
Black	5,799	1486 (25.6)	4,133	779 (18.8)
Mixed	2,808	637 (22.7)	2,172	366 (16.9)
Other	1,234	301 (24.4)	962	181 (18.8)

Supplementary Table 2: 10 year absolute risk of the three treatment escalation endpoints in people with incident AD, by age category. Values are percentages (95% confidence intervals)

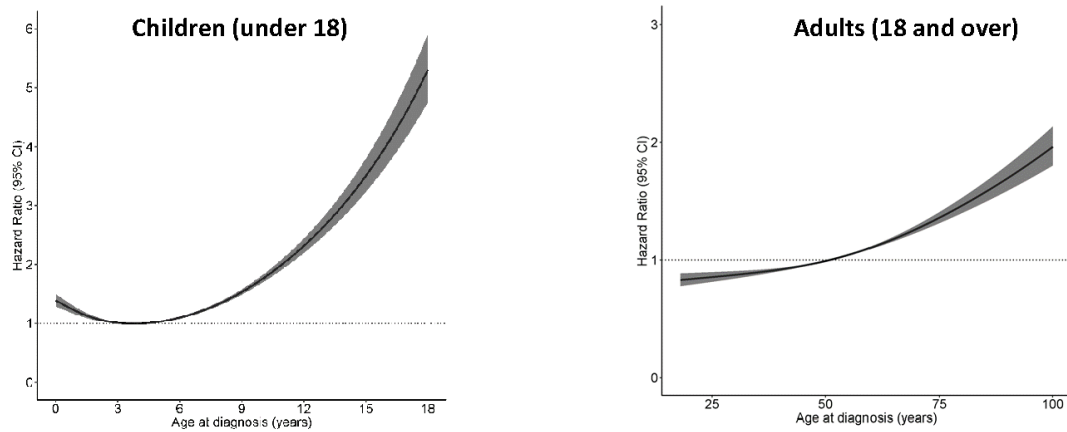
	Moderate AD (n=140,236)*	Severe AD (n=140,236)*	First systemic therapy (n=167,311)**
Age category			
<2	8.7 (8.3, 9.1)	10.6 (10.2, 11.1)	0.12 (0.06, 0.18)
2-11	7.9 (7.4, 8.4)	9.4 (8.7, 10.1)	0.19 (0.11, 0.27)
12-17	21.5 (18.4, 24.4)	17.4 (15.6, 19.1)	0.42 (0.21, 0.64)
18-49	26.4 (25.6, 27.2)	17.8 (16.9, 18.7)	1.47 (1.28, 1.66)
50+	36.3 (35.3, 37.2)	23.9 (22.6, 25.1)	2.02 (1.83, 2.20)

*Individuals without moderate or severe AD at diagnosis

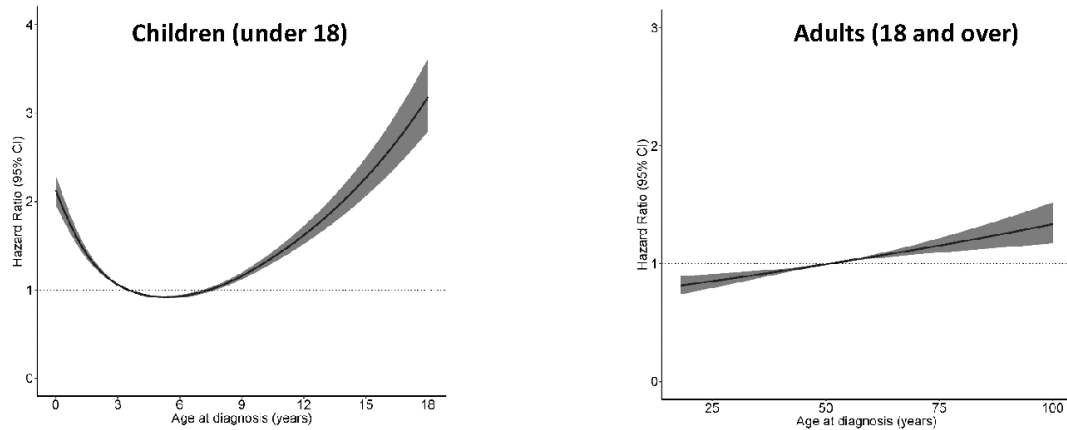
**All individuals with incident AD

Supplementary Figure 2: Risk of treatment escalation by age in children and adults. Hazard ratio estimates are relative to average age at diagnosis (3.5 for children and 53 for adults) and are adjusted for sex, ethnicity and index of multiple deprivation. Grey shading represents 95% confidence intervals.

A) Hazard ratio for moderate AD (the prescription of a second potent topical corticosteroid treatment within one year or a first topical calcineurin inhibitor (TCI)) in 140,236 individuals without moderate or severe AD at diagnosis.



B) Hazard ratio for severe AD (the first of a systemic immuno-modulatory therapy, phototherapy, or a dermatology referral) in 140,236 individuals without moderate or severe AD at diagnosis.



C) Hazard ratio for initiation of systemic immuno-modulatory treatment* (n=167,311) *Ciclosporin, Azathioprine, Methotrexate & Mycophenolate

