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A study on the epidemiology of rosacea in the U.K.

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Summary

Background Rosacea is a chronic facial skin disease of unclear origin. Epidemiological data are scarce and controversial, with reported prevalences ranging from 0·09% to 22%. To our knowledge, incidence rates have not been quantified before.

Objectives In this observational study we quantified incidence rates of diagnosed rosacea in the U.K. and described demographic characteristics and the prevalence of ocular symptoms in patients with rosacea. We compared lifestyle factors such as smoking and alcohol consumption between patients with rosacea and controls.

Methods Using the U.K.-based General Practice Research Database, we identified patients with an incident diagnosis of rosacea between 1995 and 2009 and matched them (1 : 1) to rosacea-free control patients. We assessed person-time of all patients at risk and assessed incidence rates of rosacea, stratified by age, sex, year of diagnosis and region.

Results We identified 60 042 rosacea cases and 60 042 controls (61·5% women). The overall incidence rate for diagnosed rosacea in the U.K. was 1·65 per 1000 person-years. Rosacea was diagnosed in some 80% of cases after the age of 30 years. Ocular symptoms were recorded in 20·8% of cases at the index date. We observed a significantly reduced relative risk of developing rosacea among current smokers (odds ratio 0·64, 95% confidence interval 0·62–0·67). Alcohol consumption was associated with a marginal risk increase.

Conclusions We quantified incidence rates and characteristics of patients with rosacea diagnosed in clinical practice in a large epidemiological study using primary care data from the U.K. Smoking was associated with a substantially reduced risk of developing rosacea.

Rosacea is a chronic inflammatory facial skin disease characterised by flushing episodes, erythema, papules, pustules and telangiectasia. Phymatous changes mostly of the nose, the rhinophyma, as well as inflammation of the eye and the eyelid can also be manifestations of the disease.[1–4] Rosacea is not life-threatening, but affects quality of life.[1,2,4–6] Official diagnostic guidelines do not exist, due to lacking measurable parameters and an official clinical definition of rosacea.[1,2,4,7,8,9] In 2002, the American National Rosacea Society Expert Committee introduced a classification system which divides the disease into four subtypes: 'erythematotelangiectatic', 'papulopustular', 'phymatous' and 'ocular' rosacea.[2]

The pathogenesis of rosacea remains unclear. Among various other factors, an altered innate immune response, neurogenic inflammation, neurovascular dysregulation or sun damage have been hypothesised as possible causes.[1,2,7,9,10–16]

Epidemiological data on rosacea are scarce, with reported prevalences between 0·09% and 22%.[11,17–23] A study from Sweden screened 809 office employees and revealed a rosacea prevalence of 10%,[11] while a German and an Estonian study reported prevalences of 2·2% and 22%, respectively.[20,24] Incidence rates (IRs) of rosacea, to our knowledge, have not been studied before. Rosacea is usually diagnosed after the third decade of life. Most studies reported the disease to be more common in women, but to develop into phymatous stages more frequently in men.[1,10,11,18–20,24–26] Rosacea seems to be diagnosed more often in fair-skinned people of Celtic origin. However, it is unclear whether pigmentation simply obscures detection of typical skin symptoms in darker skin.[1,2,4,8,10,11,21,23,24]

Ocular rosacea is most likely to be of inflammatory nature, but the exact aetiology remains unclear. Blepharitis,

conjunctivitis, hordeola/chalazia, tear film insufficiency and foreign body sensation have been described as frequent ophthalmic symptoms, while sight-threatening corneal involvement may occur in rare cases.[1,4,27–30] Ophthalmic involvement in patients with rosacea has been observed in 6–72% of cases, depending on diagnostic methods and the population under study.[2–4,27–32]

The association between cigarette smoking and the risk of developing rosacea has been explored in three studies: while one study found patients with rosacea to smoke less frequently than the general population,[33] two other studies associated cessation of smoking with an increased risk of developing this skin disease.[14,34] Despite sparse evidence, rosacea and in particular rhinophyma have been linked to excessive alcohol consumption.[1,7,10,35] Alcohol can trigger flushing episodes, but previous studies did not find evidence for a materially altered rosacea risk associated with alcohol consumption.[7,14,35–37]

We conducted a large observational study to establish IRs of diagnosed rosacea in the U.K., to characterise demographics of patients with rosacea, to quantify the prevalence of diagnosed ocular involvement, and to explore the impact of various lifestyle factors on the risk of developing the disease.

Materials and methods

Study design and data source

We conducted a retrospective case–control study using the U.K.-based General Practice Research Database (GPRD). This database is a large source of anonymised primary care data comprising approximately 7 million active patients who are enrolled with selected general practitioners (GPs). Those GPs have been trained to provide clinical data in a standardised format. Participating practices provide information on patient demographics and characteristics (e.g. age, sex, height, weight, smoking status), symptoms or medical diagnoses, laboratory test results, referrals to secondary care and drug prescriptions, which are directly generated by the computer. The Medicines and Healthcare Products Regulatory Agency (MHRA) anonymises the raw data before release and performs quality control checks, to ensure that the standards are followed. The patients enrolled in the GPRD are representative of the U.K. population with regard to age, sex, geographical distribution and annual turnover rate. Extensive validation of the GPRD[38,39] has documented high case validity, especially for chronic conditions.[38] The database has been the source for numerous pharmacoepidemiological studies and for public health and disease epidemiology studies.[40] The study protocol was approved by the Independent Scientific Advisory Committee for MHRA database research.

Study population

The study population consisted of all patients in the GPRD with a first-time recorded READ-code for rosacea[38] at a date between January 1995 and September 2009 [subsequently referred to as index date (ID)]. We excluded patients with < 3 years of recorded active history on the database prior to their first-time rosacea diagnosis to increase the likelihood of including only incident cases. Patients with a diagnosis for rhinophyma only or ocular rosacea only were not included.

For the case–control analysis we randomly identified a rosacea-free control group of the same size and applied the same exclusion criteria as to cases. In addition, control patients were not eligible for inclusion if they had rhinophyma (without facial rosacea) or flushing symptoms recorded at any time. Controls were matched 1 : 1 to case patients on age (year of birth), sex, general practice, calendar time (ID), and number of years of recorded history in the database prior to the ID.

We assessed ocular symptoms in cases and controls within 1 year prior to and within 90 days after the ID. We further evaluated whether differential diagnoses of rosacea were recorded in cases and controls, in particular acne, perioral dermatitis, lupus erythematosus, atopic dermatitis and seborrhoeic dermatitis.

We assessed the smoking status (non, current, ex, unknown), body mass index (BMI; < 18·5, 18·5–24·9, 25·0–29·9 or 30+ kg m^{-2}) and alcohol consumption (0, 1–4, 5–9, 10–14, 15–24 or 25+ units per week, or unknown) for cases and controls, as well as the number of GP visits over a 1-year period prior to the ID as a marker for medical attention. Furthermore, we assessed the number of rosacea cases who had been referred to a dermatologist or an ophthalmologist within 1 year prior to or after the ID.

Statistical analysis

We estimated IRs of diagnosed rosacea for all patients in the GPRD between 1995 and 2008, overall and stratified by age, sex and index year. Rates were calculated as the number of new cases divided by the total number of person-years (py) at risk. For rosacea-free patients, the number of py at risk was calculated by adding up person-time of all patients at risk in the GPRD between 1 January 1995 and the end of follow-up, which was the earliest of the following: a rosacea diagnosis, death, leaving the practice, or the end of the study period. In an additional analysis, we established IRs stratified into three geographical regions, i.e. the North (Scotland, Northern Ireland, North East England, North West England, and Yorkshire and the Humber), the Centre (Wales, East Midlands, West Midlands, East of England), or the South (South West, South Central, London, South East Coast) of the U.K. We age-standardised IRs stratified by geographical regions and by index year applying the direct method, using the European standard population as reference.

For the case–control analysis, we conducted conditional logistic regression analyses using SAS statistical software (version 9.2; SAS Institute, Inc., Cary, NC, U.S.A.). Relative risk estimates were calculated as odds ratios (ORs) with 95% confidence intervals (CIs).

Results

The study population encompassed 60 042 rosacea cases and 60 042 controls, of whom 61·5% were female. The vast majority (80%) of patients with rosacea were at or above the age of 30 years at the ID (Table 1). Only 7·3% of the rosacea cases were referred to a dermatologist, and 4·1% saw an ophthalmologist within 1 year before or after the ID. A rhinophyma diagnosis was recorded in 422 (0·7%) of the cases, of whom 80·3% were male.

Incidence rates

The overall IR of diagnosed rosacea in the GPRD population was 1·65 per 1000 py (95% CI 1·63–1·66). It was higher in women (IR 1·92 per 1000 py, 95% CI 1·90–1·94) than in men (IR 1·34 per 1000 py, 95% CI 1·32–1·36), and peaked between the age of 40 and 59 years (Fig. 1). The crude rate increased between 1995 and 2002 and then levelled off; the same was the case for the European-standardised rates over time, although slightly lower (Table 1). The crude IR was higher in the North with an IR of 1·93 per 1000 py (95% CI 1·90–1·95) than in the South of the U.K. (IR 1·46 per 1000 py, 95% CI 1·44–1·48). The age-standardised IR was 1·71 per 1000 py (95% CI 1·69–1·73) in the North and 1·29 per 1000 py (95% CI 1·27–1·31) in the South of the U.K.

Demographics and lifestyle characteristics

Current smokers had a significantly reduced relative risk of developing rosacea when compared with nonsmokers, yielding an OR of 0·64 (95% CI 0·62–0·67). The OR for ex-smokers, when compared with nonsmokers, was slightly increased (OR 1·14, 95% CI 1·10–1·18). The OR for rosacea increased slightly with increasing number of alcohol units consumed per week, with the highest OR of 1·51 (95% CI 1·41–1·63) for patients consuming more than 25 units per week, as compared with those not drinking alcohol. Neither high nor low BMI was associated with an altered risk.

Rosacea cases had more GP visits in the year prior to the ID than controls, with the highest OR of 2·33 (95% CI 2·25–2·41) for those with 10 or more GP visits when compared with patients with 0–2 GP visits (Table 2).

Ocular symptoms and differential diagnoses

In total, 12 480 (20·8%) of 60 042 rosacea cases had at least one ocular symptom recorded within a 1-year period prior to

Table 1 Incidence rates of rosacea diagnosed in the U.K. between 1995 and 2008

	Person-years at risk	Rosacea cases	IR per 1000 person-years (95% CI)	IR per 1000 person-years (95% CI)	IR per 1000 person-years (95% CI)
Overall	34 136 657	56 253	1·65 (1·63–1·66)		
By sex					
Men	16 141 632	21 645	1·34 (1·32–1·36)		
Women	17 995 025	34 608	1·92 (1·90–1·94)		
By age (years)			Men and women	Men	Women
< 20	7 179 962	6367	0·89 (0·87–0·91)	0·83 (0·80–0·86)	0·95 (0·92–0·98)
20–29	3 948 312	5147	1·30 (1·27–1·34)	0·91 (0·87–0·95)	1·68 (1·63–1·74)
30–39	4 776 305	8657	1·81 (1·77–1·85)	1·05 (1·01–1·10)	2·47 (2·41–2·53)
40–49	5 020 453	11 734	2·34 (2·30–2·38)	1·54 (1·49–1·59)	3·06 (3·00–3·13)
50–59	4 685 054	10 164	2·17 (2·13–2·21)	1·86 (1·81–1·92)	2·46 (2·39–2·52)
60–69	3 747 948	7608	2·03 (1·98–2·08)	2·03 (1·97–2·10)	2·03 (1·96–2·09)
70+	4 778 621	6576	1·38 (1·34–1·41)	1·59 (1·54–1·65)	1·23 (1·19–1·27)
By year of diagnosis				Age-standardised rates[a]	
1995	1 734 936	2428	1·40 (1·34–1·46)	1·29 (1·24–1·34)	
1996	1 934 725	2929	1·51 (1·46–1·57)	1·42 (1·37–1·47)	
1997	2 081 764	3123	1·50 (1·45–1·55)	1·41 (1·36–1·46)	
1998	2 200 167	3467	1·58 (1·52–1·63)	1·48 (1·43–1·53)	
1999	2 315 649	3504	1·51 (1·46–1·56)	1·41 (1·36–1·46)	
2000	2 429 796	4139	1·70 (1·65–1·76)	1·58 (1·53–1·63)	
2001	2 502 051	4408	1·76 (1·71–1·81)	1·61 (1·56–1·66)	
2002	2 564 020	4591	1·79 (1·74–1·84)	1·63 (1·58–1·68)	
2003	2 622 215	4276	1·63 (1·58–1·68)	1·48 (1·44–1·52)	
2004	2 686 549	4716	1·76 (1·71–1·81)	1·58 (1·54–1·62)	
2005	2 722 527	4581	1·68 (1·63–1·73)	1·50 (1·46–1·54)	
2006	2 760 846	4568	1·65 (1·61–1·70)	1·46 (1·42–1·50)	
2007	2 779 225	4625	1·66 (1·62–1·71)	1·46 (1·42–1·50)	
2008	2 802 186	4898	1·75 (1·70–1·80)	1·54 (1·50–1·58)	

IR, incidence rate; CI, confidence interval. [a]Rates were age-standardised using the European standard population as reference.

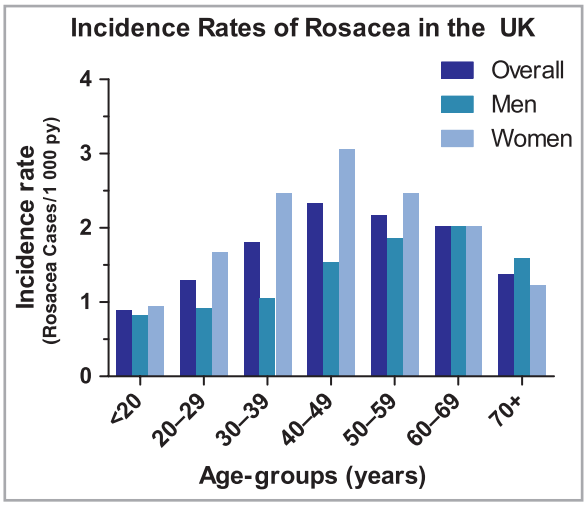

Fig 1. Incidence rates of rosacea diagnosed in the U.K. between 1995 and 2008. py, person-years.

or up to 90 days after the ID, compared with 7737 (12·9%) controls. Thus, the relative risk for cases to be diagnosed with ocular symptoms was 1·82 (95% CI 1·76–1·88). The prevalence of ocular symptoms was similar in men (19·8%) and women (21·4%). The most frequent ocular symptoms were hordeola/chalazia, followed by conjunctivitis and dry or watery eyes. The largest difference between cases and controls was seen for blepharitis, where the OR was 3·57 (95% CI 3·17–4·02).

We identified 23·2% of cases and 6·3% of controls with a recorded acne diagnosis prior to or up to 90 days after the ID, with most co-diagnoses in the age group of < 20 years. Seborrhoeic dermatitis was found in 10·9% of the cases and in 3·7% of the controls. The distribution of differential diagnoses of rosacea in cases and controls is displayed in Table 3.

Discussion

In this large observational study we quantified IRs and assessed the demographic distribution of patients with rosacea in a primary care setting in the U.K. Overall, the IR of GP-diagnosed rosacea in the U.K. was 1·65 per 1000 py (95% CI 1·63–1·66), with higher IRs in females. Rosacea also tended to be diagnosed earlier in women than in men, a finding consistent with other studies, and usually developed after the age of 30 years.[1,2,9–11,18,25,26] We further observed a slight increase in the crude and age-standardised IRs over the course of the study period until 2002, as was reported by the authors of a U.S.-based publication from 2002.[12] A possible explanation for this rise is increased awareness of rosacea among GPs. In our study population, IRs were higher in the North than in the South of the U.K. This observation was not changed after age standardisation. The Irish population has been reported to be predominantly fair-skinned,[41] so our findings may reflect an increased risk of rosacea with more fair-skinned populations.[2,10,11,21,23,24]

We observed a significantly decreased OR for current smokers when compared with nonsmokers. Ex-smokers, on the other hand, yielded a slightly increased OR. It has been suggested that there is an immunosuppressive effect of cigarette smoking leading to potential beneficial effects in certain inflammatory diseases, such as ulcerative colitis and sarcoidosis.[42,43] However, a negative impact on other inflammatory diseases, such as Crohn disease or rheumatoid arthritis, has also been reported.[42] Further, neurovascular dysfunction causing vasodilatation has been implicated in the pathogenesis of rosacea.[15,16] Cigarette smoking impairs peripheral microvascular relaxation and might thus decrease the risk of incident rosacea.[44] Three small studies of no more than 172 rosacea cases previously addressed the association between cigarette smoking and rosacea. One study found patients with rosacea to smoke less frequently than the general population,[33] and the other two found that cessation of smoking was associated with an increased risk of developing rosacea when compared with current or nonsmokers. The latter two hypothesised an immunosuppressive effect of cigarette smoking on rosacea, exerting a triggering or aggravating effect upon withdrawal, as has been described for ulcerative colitis.[14,33,34,43] All three studies were based on self-reported smoking status. Current smoking status has been shown to be more reliably recorded than former smoking in the GPRD, with about 30% of 'ex-smokers' actually being current smokers.[45] Thus, the risk of developing rosacea for ex-smokers may be somewhat higher than observed due to misclassification of smoking status. Regardless of some possible misclassification, our data suggest that cigarette smoking reduces the risk of developing rosacea.

A potential causal role of alcohol in the pathogenesis of rosacea has been discussed controversially for decades.[7,36] However, most previous studies found a nonsignificant association between alcohol and the skin disease.[14,35–37] In our study, ORs increased marginally with increasing number of alcohol units consumed per week, yielding an OR of 1·51 for patients drinking more than 25 units per week (4·4% of cases and 3·4% of controls). These data do not suggest that alcohol consumption plays a major role in the pathophysiology of rosacea.

We observed ocular symptoms in 20·8% of the cases within a year prior to or up to 90 days after the ID, implying an almost two-fold increased likelihood that patients with rosacea would be affected by ocular disorders when compared with controls. A study from 1953 reported that ocular symptoms preceded dermatological findings in up to 20% of patients with rosacea, whereas 27% of patients were diagnosed concomitantly.[1,3,46] We observed men and women to be similarly at risk, while previously reported male/female ratios were not consistent.[28,29,31,46] Hordeola/chalazia were the most prevalent ocular symptoms in our study population, followed by conjunctivitis and dry or watery eyes. Although the reported frequencies of ocular symptoms of rosacea varied in the literature[27–29] the overall distribution of observed symptoms in our study was consistent with most publications.[1,4,27,28] However, blepharitis was recorded in only 2·1% of rosacea cases in this

Table 2 Distribution of patient characteristics and lifestyle factors in patients with rosacea and controls in the U.K.

	Rosacea cases (n = 60 042), n (%)	Rosacea-free controls (n = 60 042), n (%)	OR crude (95% CI)	OR adjusted[a] (95% CI)
Age (years)				
< 20	6673 (11·1)	6680 (11·1)	NA	NA
20–29	5425 (9·0)	5420 (9·0)	NA	NA
30–39	9172 (15·3)	9184 (15·3)	NA	NA
40–49	12 576 (21·0)	12 550 (20·9)	NA	NA
50–59	10 851 (18·1)	10 855 (18·1)	NA	NA
60–69	8246 (13·7)	8250 (13·7)	NA	NA
70+	7099 (11·8)	7103 (11·8)	NA	NA
Sex				
Male	23 118 (38·5)	23 118 (38·5)	NA	NA
Female	36 924 (61·5)	36 924 (61·5)	NA	NA
Alcohol consumption (units per week)				
None/ex	7622 (12·7)	7874 (13·1)	1·00 (ref.)	1·00 (ref.)
Current (units?)	10 929 (18·2)	10 957 (18·3)	1·04 (0·99–1·08)	1·03 (0·99–1·08)
1–4	10 455 (17·4)	10 150 (16·9)	1·09 (1·04–1·13)	1·06 (1·02–1·11)
5–9	5764 (9·6)	5462 (9·1)	1·12 (1·06–1·18)	1·10 (1·05–1·16)
10–14	5087 (8·5)	4516 (7·5)	1·20 (1·14–1·27)	1·20 (1·14–1·26)
15–24	3299 (5·5)	2859 (4·8)	1·25 (1·17–1·33)	1·26 (1·19–1·35)
25+	2668 (4·4)	2032 (3·4)	1·43 (1·33–1·53)	1·51 (1·41–1·63)
Unknown	14 218 (23·7)	16 192 (27·0)	0·81 (0·78–0·85)	0·95 (0·90–1·00)
Smoking status				
Non	30 105 (50·1)	27 681 (46·1)	1·00 (ref.)	1·00 (ref.)
Current	8972 (14·9)	12 274 (20·4)	0·66 (0·64–0·68)	0·64 (0·62–0·67)
Ex	11 863 (19·8)	9657 (16·1)	1·17 (1·13–1·21)	1·14 (1·10–1·18)
Unknown	9102 (15·2)	10 430 (17·4)	0·68 (0·65–0·71)	0·82 (0·77–0·86)
BMI (kg m^{-2})				
12·0–18·4	995 (1·7)	1070 (1·8)	0·85 (0·77–0·92)	0·90 (0·82–0·98)
18·5–24·9	21 038 (35·0)	19 556 (32·6)	1·00 (ref.)	1·00 (ref.)
25·0–29·9	15 116 (25·2)	14 233 (23·7)	0·99 (0·96–1·02)	0·97 (0·94–1·00)
30·0–60·0	8020 (13·4)	8235 (13·7)	0·91 (0·88–0·94)	0·89 (0·86–0·93)
Unknown	14 873 (24·8)	16 948 (28·2)	0·72 (0·70–0·75)	0·82 (0·78–0·86)
GP visits (1 year prior to ID)				
0–2	10 290 (17·1)	16 888 (28·1)	1·00 (ref.)	NA
3–4	7332 (12·2)	7440 (12·4)	1·67 (1·60–1·74)	NA
5–9	14 834 (24·7)	12 922 (21·5)	2·03 (1·96–2·10)	NA
10+	27 586 (45·9)	22 792 (38·0)	2·33 (2·25–2·41)	NA

OR, odds ratio; CI, confidence interval; NA, not applicable; BMI, body mass index; GP, general practitioner; ID, index date. [a]Adjusted for BMI, smoking, alcohol consumption.

study, while it has previously been among the most frequently reported ocular symptoms.[27,30] It is possible that blepharitis usually occurs at a later stage of the disease and was therefore not yet present at the time of the diagnosis in our study population. Most ocular findings in our study were GP diagnosed, with only 4·1% of cases referred to an ophthalmologist within the year prior to or after the ID. Diagnostic bias has been implicated before, suggesting that ocular rosacea may often go undetected in clinical practice.[2–4,27–31]

As there are no strict guidelines for diagnosing rosacea, differential diagnostic criteria may have led to some misdiagnoses. Of all rosacea cases, 23·2% also had an acne diagnosis recorded before or up to 90 days after the ID, most of them in the age group of < 20 years. Rosacea is a common disease and can, just by coincidence, coexist with acne vulgaris.[25,47] However, as rosacea does not typically manifest before the age of 20 years,[10,11,18,26] it is unclear whether these results represent diagnostic uncertainty by the GP, or whether these two diseases actually coexisted in our sample. A study from the 1950s found acne to be present in about 7% of rosacea cases and controls.[37] On the other hand, young patients with rosacea were mentioned often to have a history of acne, although statistical evidence to back up this hypothesis was not found.[10,47] The magnitude of the increase of co-diagnoses, however, suggests that diagnostic bias may play a certain role which needs to be considered when interpreting our results.

Seborrhoeic dermatitis has been referred to as a common feature of rosacea,[10,25,37,48] although an increased sebum excretion in rosacea-affected skin was not observed.[49] We observed a three-fold increased OR of seborrhoeic dermatitis

Table 3 Distribution of ocular symptoms and differential diagnoses in rosacea cases and controls in the U.K.

	Rosacea cases (n = 60 042), (n [%])	Rosacea-free controls (n = 60 042), (n [%])	OR crude (95% CI)
Ocular symptoms (1 year prior to and up to 90 days after the ID)			
Blepharitis	1250 (2·1)	360 (0·6)	3·57 (3·17–4·02)
Hordeolum/chalazion	4573 (7·6)	2240 (3·7)	2·15 (2·04–2·26)
Conjunctivitis	2471 (4·1)	1443 (2·4)	1·75 (1·64–1·87)
Other inflammation	262 (0·4)	130 (0·2)	2·02 (1·63–2·49)
Other conjunctival disorders	193 (0·3)	144 (0·2)	1·34 (1·08–1·66)
Corneal disorders	416 (0·7)	308 (0·5)	1·35 (1·17–1·57)
Red eyes	1358 (2·3)	958 (1·6)	1·43 (1·32–1·56)
Watery or dry eye	2149 (3·6)	1259 (2·1)	1·78 (1·66–1·92)
Itchy eye	1157 (1·9)	709 (1·2)	1·67 (1·51–1·83)
Eye irritation/pain	1928 (3·2)	1320 (2·2)	1·49 (1·39–1·60)
Blurred vision	620 (1·0)	512 (0·9)	1·21 (1·08–1·37)
Eye involvement total	12 480 (20·8)	7737 (12·9)	1·82 (1·76–1·88)
Men	4585 (19·8)	2630 (11·4)	1·97 (1·87–2·08)
Women	7895 (21·4)	5107 (13·8)	1·74 (1·67–1·81)
Differential diagnoses (prior to or up to 90 days after the ID)			
Acne	13 921 (23·2)	3772 (6·3)	6·13 (5·85–6·43)
< 20 years	3842 (6·4)	834 (1·4)	11·88 (10·50–13·44)
20–29 years	3052 (5·1)	1141 (1·9)	5·27 (4·76–5·83)
30–39 years	3065 (5·1)	879 (1·5)	5·20 (4·73–5·71)
40–49 years	2411 (4·0)	606 (1·0)	5·03 (4·54–5·57)
50–59 years	1013 (1·7)	219 (0·4)	4·94 (4·24–5·76)
60–69 years	367 (0·6)	71 (0·1)	5·68 (4·35–7·42)
70+ years	171 (0·3)	22 (0·0)	7·68 (4·93–11·98)
Seborrhoea/seborrhoeic dermatitis	6528 (10·9)	2199 (3·7)	3·25 (3·09–3·42)
Perioral dermatitis	974 (1·6)	172 (0·3)	5·92 (5·01–6·99)
Lupus erythematosus	173 (0·3)	85 (0·1)	2·04 (1·57–2·64)
Atopic dermatitis	4125 (6·9)	2922 (4·9)	1·48 (1·40–1·55)

OR, odds ratio; CI, confidence interval; ID, index date.

in patients with rosacea compared with controls. Again, we cannot establish whether these patients had seborrhoeic dermatitis as a feature of their rosacea, or whether they had been misdiagnosed. The results on atopic dermatitis (marginally elevated OR) as well as on lupus erythematosus or perioral dermatitis (low prevalence) do not imply major diagnostic bias within our study.

This study has several limitations that should be considered in interpreting our findings. First, mild rosacea may not necessarily cause patients to seek medical help; thus, a certain portion of cases may remain undetected, and our rates may be lower than the true rates in the U.K. population. Also, there is possible detection bias present as women might seek medical care more often than men.[8] Second, the likelihood of being diagnosed with rosacea may increase with increasing medical attention. To address this issue, we quantified the number of GP visits, and observed that patients with rosacea tended to see the GP more often prior to the diagnosis than controls. Thus, a certain degree of diagnostic bias cannot be ruled out. Third, due to lacking diagnostic guidelines or clinically measurable parameters, rosacea is diagnosed based on visible symptoms and by exclusion of other diseases. Such GP-diagnosed diseases are difficult to validate because most usual options for a case validation are not available, such as sending for referral letters, hospital discharge letters, or questionnaires. The observed overlap of rosacea and acne diagnoses around the ID might represent some degree of diagnostic uncertainty or misclassification of disease. However, a cross-sectional study analysing dermatology patient data from South-East Scotland revealed a concordance of rosacea diagnoses of dermatologists and the referring GPs of 74%.[50] The fact that only 7·3% of all patients with rosacea were referred to a dermatologist, most probably those with an uncertain or more complicated diagnosis, allows us to assume an overall high validity of rosacea diagnoses in the GPRD. Finally, we could not control for ethnic background, skin pigmentation, socioeconomic status (e.g. income, education), or lifestyle factors such as sun exposure, profession or nutrition, as these parameters are not recorded in the GPRD.[1,2,7,10–12,14] We were also not in a position to distinguish between erythematotelangiectatic and papulopustular rosacea, which may cause overdiagnosis of the disease because chronic actinic damage such as heliodermatitis is not always distinguishable from erythematotelangiectatic rosacea, in the absence of inflammatory lesions.[7,23] Despite these limitations, this is – to our knowledge – the first epidemiological study on rosacea using U.K.-based primary care

data, and by far the largest study to focus on the characteristics of patients with rosacea, including an analysis on the impact of alcohol consumption and cigarette smoking on the risk of incident rosacea.

In summary, this large observational study describes the epidemiology of rosacea in a large sample of the U.K. population and quantifies the presence of ocular involvement in this skin disease. Our findings suggest that smoking may substantially reduce the risk of developing rosacea, whereas alcohol consumption is associated with only a small increase in risk.

What's already known about this topic?

- Rosacea is a common skin disease, but epidemiological data are scarce and controversial.
- Data on the incidence of rosacea are lacking so far.
- Despite scarce evidence, rosacea has been linked to excessive alcohol consumption.
- Studies on the association between cigarette smoking and rosacea have produced inconsistent findings.

What does this study add?

- This large primary care-based observational study provides data on the epidemiology of rosacea in the U.K., including incidence rates over time.
- Alcohol consumption was associated with only a marginal risk increase for rosacea.
- Current smokers were at a significantly decreased risk of developing an incident rosacea diagnosis in our study population.

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