Report on the incidence of squamous cell carcinomas affecting the eyelids in England over a 15-year period (2000–2014)

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ABSTRACT

Aims The authors report on trends in the incidence of squamous cell carcinoma (SCC) affecting the eyelids in England over a 15-year period and identify associations between demographic factors and SCC risk.

Methods The National Cancer Registration and Analysis Service identified all cases of eyelid SCC in England between 2000 and 2014. The crude and age-standardised rates of eyelid SCCs in England were calculated. The association of SCC with several known demographic risk factors was then examined to assess their importance in periocular cases.

Results Over the 15 years studied, there were 4022 patients in England diagnosed with a first episode of SCC affecting the eyelids. The age-standardised number of reported cases rose between 2000 and 2014 by a mean of 0.0137 cases per 100 000 population per year (equivalent to a rise in SCC incidence of approximately 2% per year). The mean age-standardised incidence rate of SCC during the study period was 0.63 cases per 100 000 population per year. Age was exponentially correlated with incidence, with an approximate doubling of the risk for every decade over the age of 60. The relative risk of eyelid SCC in men compared with women was 1.9. Social deprivation quintile by income was not found to be associated with risk of SCC.

Conclusion The incidence of eyelid SCC in England is rising. In addition, the age-standardised and population-standardised rate of SCC is also rising. A higher risk of SCC is strongly correlated with age and male sex but not with deprivation.

INTRODUCTION

At least one-quarter of all malignancy diagnosed in humans originates from skin cells and squamous cell carcinoma (SCC) is the second most common skin malignancy. Over the past 20 years, there has been a rise in the global incidence of SCC of the skin.[1] However, there has been no recent comprehensive review of how this trend applies to SCC of the eyelids in England.

There is known to be an association between SCC incidence and male sex, age and sun exposure (SCC incidence halves with each 10° displacement in latitude away from the equator),[1] with the latter two thought to be the predominant factors underlying the continuing rise in global incidence. There is also known to be a strong correlation between higher socioeconomic status and an increased incidence of both cutaneous melanoma and, to a lesser extent, non-melanoma skin cancer.[2] This is in contrast to many other cancers, which are more likely in the more deprived. Once again, there is no recent and comprehensive analysis on how sex, age and socioeconomic status influence the incidence of eyelid SCC in England.

SCC arises in keratin-producing epidermal cells as a result of oncogenic mutations and can affect any part of the skin. In most of the body, it is not considered to be a high-risk cancer due to a low rate of local invasion to other non-skin structures, a relatively low rate of metastasis and a low recurrence rate if excised with clear margins. In addition, excision can often be performed with minimal cosmetic or functional sequelae. However, SCC affecting the head and neck has a different phenotype with a higher risk of metastasis to the local, nervous and lymphatic system.[3] In addition, periocular SCC has a particularly high risk of causing severe morbidity and occasional mortality through local invasion to the orbit and other adjacent structures, including the brain, eye, nose, facial bones and sinuses.[4] Excision of periocular SCC can cause further cosmetic and functional morbidity if a significant amount of the periocular skin or eyelids are removed.[5]

In this study, we aim to characterise how the aforementioned demographic trends apply to SCC of the eyelids in England.

MATERIALS AND METHODS

The recording and monitoring of SCC incidence is very variable among different countries in Europe.[1] The UK has a comprehensive system for registration of new cases of cancer through the National Cancer Registration and Analysis Service (NCRAS). There are four registries, one each for England, Scotland, Wales and Northern Ireland. For the present study, data from the English registry relating to SCC of the skin of the eyelid (including the canthus) diagnosed from 2000 to 2014 were identified by NCRAS (ICD-10 code C44.1, morphology codes beginning '807', behaviour code '3').

All diagnoses were made after histological examination of specimens from excisional or punch biopsies. By convention, only the first report of SCC anywhere on the skin is registered for each patient. Therefore patients previously diagnosed with SCC affecting any part of the skin other than the eyelid were not captured in our data, however, this strategy also prevented the double counting

of patients with recurrences of eyelid SCC or multiple eyelid SCC's, thus capturing new cases and providing a measure of incidence. Previous diagnosis with a different type of skin malignancy, whether on the eyelids or elsewhere, did not exclude patients from our analysis.

Using population-based national data, we report the incidence of eyelid SCC for the period 2000–2014. We also report on the patients' age, sex and social deprivation quintile by income.

Statistical analysis

Statistical analysis conformed to methods used by NCRAS. The annual absolute number of eyelid SCCs in England was reported for the period 2000–2014. Age-standardised incidence rates (ASRs) per 100 000 population per year were calculated using the 2013 European Standard population. The rate of change in the ASR was calculated using linear regression analysis and a Spearman's rank order correlation test was performed to determine whether the trend was statistically significant. The relationship between eyelid SCC incidence and several demographic risk factors (that are known to be relevant to SCC of the skin) was examined in order to assess their importance in periocular cases. The demographic factors selected were age group, sex and social deprivation quintile by income. Further analysis was undertaken to examine whether there has been any change in the effect of sex on eyelid SCC risk over the 15-year period of the study. This was examined by comparing the 3-year age-standardised eyelid SCC incidence among men to that for women.

The effect of age on the relative risk of male or female sex was further evaluated by examining the ratio of SCC incidence in males versus females within 10-year age bands.

RESULTS

Number of newly registered cases of eyelid SCC

Over the 15-year period studied (2000–2014), there were a total of 4022 patients in England diagnosed with an eyelid SCC as their first SCC (figure 1 and online supplementary table).

Trends in the incidence of eyelid SCC in England between 2000 and 2014

There has been a gradual rise in the ASR of SCC in England between 2000 and 2014 (Spearman's rank order correlation 0.952, P<0.05). Linear regression analysis revealed a rate of increase of 0.0137 cases per 100 000 population per year (equivalent to a rise in SCC risk of approximately 2% per year). The rise in ASR affected men and women equally (table 1). The mean ASR of SCC during the study period was 0.63 cases per 100 000 population per year.

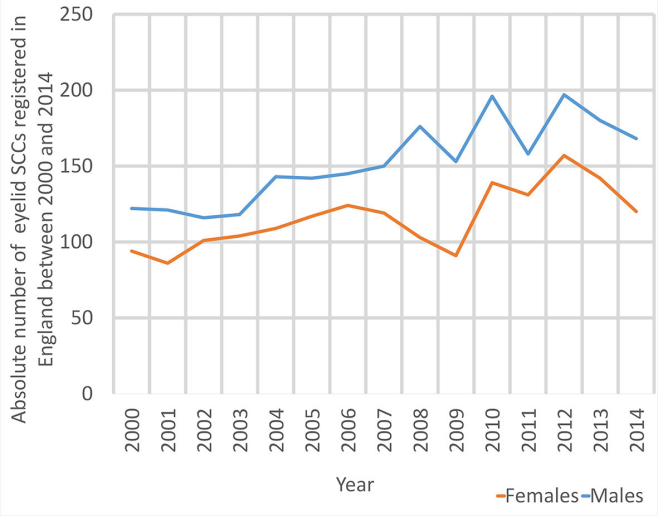

Figure 1 Absolute number of eyelid squamous cell carcinomas (SCCs) registered in England between 2000 and 2014.

Table 1 Age-standardised incidence of eyelid squamous cell carcinomas per 100 000 people by gender for 3-year intervals 2000–2014

Years	Males	Females	Combined males/females
2000–2002	0.72 (0.64 to 0.80)	0.39 (0.34 to 0.43)	0.55 (0.51 to 0.60)
2003–2005	0.79 (0.71 to 0.87)	0.44 (0.39 to 0.49)	0.61 (0.57 to 0.66)
2006–2008	0.86 (0.78 to 0.94)	0.45 (0.40 to 0.50)	0.65 (0.61 to 0.70)
2009–2011	0.88 (0.80 to 0.96)	0.46 (0.41 to 0.51)	0.67 (0.62 to 0.72)
2012–2014	0.88 (0.81 to 0.96)	0.50 (0.45 to 0.55)	0.69 (0.65 to 0.74)

ASR values are followed by 95% CIs in brackets.
ARS, age-standardised incidence rate.

Factors affecting relative risk for eyelid SCC

Effect of sex

The relative risk of being diagnosed with eyelid SCC is 1.9 (95% CI 1.5 to 2.3) times greater in men than in women, a ratio that has remained quite stable over the course of the study period (table 2). The increased relative risk of eyelid SCC in men is present across all age bands above 50 (figure 2, table 2).

Effect of age

Incidence of SCC increased exponentially with age in both men and women with the rate approximately doubling with every decade of life over the age of 60 (figure 2, table 3).

Effect of social deprivation by income

The age-standardised incidence of SCC was similar across all quintiles of deprivation. The age-standardised rate of eyelid SCC per 100 000 people over the study period was divided among the five quintiles of deprivation by income as follows: quintile 1 (least deprived): 0.65 (0.61–0.70); quintile 2: 0.62 (0.58–0.66); quintile 3: 0.67 (0.63–0.72); quintile 4: 0.67 (0.62–0.72); quintile 5 (most deprived): 0.57 (0.52–0.62).

DISCUSSION

We present the previously unreported incidence of eyelid SCC for the population of England over a 15-year period, highlighting trends over this time and investigating demographic risk

Table 2 Relative risk of eyelid squamous cell carcinoma in males versus females sex over the study period (left) and then with respect to age (right), followed by 95% CIs in brackets

Years	Relative risk of male versus female sex	Age band	Relative risk of male versus female sex
2000–2002	1.9 (1.5 to 2.4)	0–49	0.9 (0.6 to 1.5)
2003–2005	1.8 (1.4 to 2.2)	50–59	1.5 (1.1 to 2.1)
2006–2008	1.9 (1.6 to 2.4)	60–69	1.9 (1.5 to 2.4)
2009–2011	1.9 (1.6 to 2.3)	70–79	2.3 (2.0 to 2.7)
2012–2014	1.8 (1.5 to 2.1)	80–89	1.7 (1.5 to 2.0)
Mean value across all years	1.9 (1.5 to 2.3)	90+	1.6 (1.2 to 2.2)

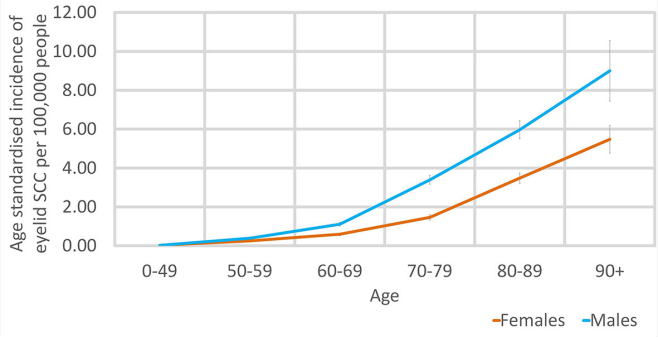

Figure 2 Fifteen-year age-standardised incidence of eyelid squamous cell carcinoma (SCC) by age and sex over the total study period (2000–2014).

factors. The data also form a contemporaneous baseline that can be used to inform service planning.

The data presented here show an increase in the number of patients newly diagnosed with eyelid SCC of approximately 4% per year over the 15-year study period. There has been an increase in the age-standardised rate of eyelid SCC from 0.55 per 100 000 people in 2000–2002 to 0.69 per 100 000 people in 2012–2014, an increase of approximately 2% per year.

As is the case for many other cancers, age was found to be a significant risk factor for the development of eyelid SCC. The incidence of SCC increases exponentially (approximately doubling with every decade of life) in patients aged 60 and over. Patients under 60 have a much lower incidence of SCC. This was the case for both men and women and was a consistent finding across all quintiles of deprivation by income.

Male sex was also a risk factor for eyelid SCC in patients over the age of 50. However, we found an equal rate of SCC in men and women under the age of 50. Overall men carried a relative risk of acquiring an SCC of 1.9 compared with women. This was the case over the entire period studied.

No association was found between deprivation quintile (by income) and the age-standardised incidence of SCC.

Our results relating to SCCs of the eyelids were broadly consistent with previously published data for SCC of the skin in general. The continuous rise in the age-standardised incidence of eyelid SCC over the past 15 years in England appears to be part of an ongoing rise in the rate of skin SCC across predominantly Caucasian populations globally. Reports from the Netherlands, Ireland, Denmark, Sweden, Australia and the USA spanning the past four decades all report such a progressive rise.[6–12]

The effects of age and sex of the incidence of eyelid SCC were also found to be very similar to those on skin SCC in general. Our study's finding of an exponential rise in the rate of SCC over the age of 60 was also reported in a study in the Netherlands of very similar methodology focusing on all skin SCCs reported to the cancer registry in the Netherlands between 1989 and 2008.[6] Our report of an increased relative risk for SCC in males at 1.9 was also comparable to the relative risk of male sex found by the Dutch study at 1.7[6] and has previously been found to apply to another Caucasian population in Australia between 1992 and 2001, which found a relative risk ratio of 2.0.[5]

Our finding that the increased risk associated with male sex is only present in patients aged 50 and over has not been reported in other studies of skin SCC and should be interpreted with caution because our data included only 147 patients below the age of 50. However, it is interesting to draw a parallel with a recent study of basal cell carcinoma (BCC) incidence in England,[13] which found that men were at increased risk aged over 50 but women were at increased risk in the 0–49 age group.

The reason for the strong association between eyelid SCC and age is likely to be due to cumulative exposure to environmental risk factors including UV radiation and iatrogenic causes such the use of systemic immunosuppression to treat autoimmune disease and prevent rejection of solid organ transplants.[8] Furthermore secular increases in the aforementioned risk factors due to behavioural changes and medical advances might underlie the increasing age-standardised incidence in eyelid SCC over the study period.[8]

The reasons for the disparity between men and women are much less clear. Behavioural factors, in particular an increased UV exposure in men as well as increased likelihood of presenting to a doctor with a skin lesion have been implicated.[14] However, there is no strong association between sex and cutaneous melanoma, suggesting intrinsic factors may also be implicated.[15] One theory that has been proposed is a protective effect of oestrogen on keratinocytes.[16] By contrast, no protective effect of oestrogen has been found on melanocytes.[17] Alternatively, the behavioural factors relevant to cutaneous melanoma incidence may simply be different to those relevant to SCC of the eyelids, as demonstrated by the strong association between higher socioeconomic status and cutaneous melanoma while this effect was found to be weaker for non-melanoma skin cancer[2] and in the present study to be completely absent for eyelid SCC.

Limitations of our study include that only the first SCC that each patient has biopsied (anywhere on the body) is recorded by NCRAS, therefore our data omit patients who had previously had SCCs reported elsewhere in the body and later had an eyelid SCC. For the same reason, the data presented here omit patients who have recurrences of SCC affecting the eyelids. In addition, only SCC's that were biopsied were included in our data as it relies on histological diagnosis in order to ensure accuracy. The authors make the assumption that in the vast majority of cases, first episodes of eyelid SCC are biopsied to confirm the diagnosis as this is the standard management.

Table 3 Age-standardised incidence of eyelid squamous cell carcinoma per 100 000 by age group in 3-year intervals (followed by 95% CIs in brackets)

Age group	2000–2002	2003–2005	2006–2008	2009–2011	2012–2014
0–49	0.03 (0.02 to 0.04)	0.02 (0.01 to 0.03)	0.04 (0.03 to 0.05)	0.03 (0.02 to 0.04)	0.03 (0.02 to 0.04)
50–59	0.35 (0.27 to 0.44)	0.30 (0.23 to 0.39)	0.35 (0.27 to 0.45)	0.30 (0.22 to 0.39)	0.31 (0.24 to 0.40)
60–69	0.67 (0.54 to 0.83)	0.82 (0.67 to 0.97)	0.95 (0.79 to 1.10)	0.92 (0.77 to 1.07)	0.87 (0.73 to 1.01)
70–79	2.30 (2.00 to 2.59)	2.24 (1.95 to 2.53)	2.21 (1.92 to 2.50)	2.62 (2.31 to 2.93)	2.74 (2.43 to 3.04)
80–89	3.93 (3.33 to 4.53)	4.77 (4.13 to 5.40)	4.78 (4.18 to 5.38)	5.02 (4.42 to 5.62)	5.04 (4.47 to 5.62)
90+	4.69 (3.33 to 6.41)	7.20 (5.62 to 9.08)	8.51 (6.74 to 10.59)	6.95 (5.38 to 8.84)	8.18 (6.61 to 9.75)

Another limitation is that the lack of an association with deprivation should be interpreted with caution. The measure of deprivation used was income as this information was linked to our dataset and therefore available to use. However, a more detailed study encompassing further measures of deprivation beyond income alone is warranted before drawing firm conclusions.

Finally, the study did not analyse subgroups of patients by race and therefore the conclusions drawn should be applied with caution to parts of England with a different racial makeup from the country's average. The predominant racial group in England is Caucasian and therefore the study's findings would be most applicable to the Caucasian population.

CONCLUSION

The data presented in this study reveal that the incidence of eyelid SCC in England is rising with an increased risk among the elderly and men. We show that the epidemiology of eyelid SCC has strong similarities with SCC of the skin and with eyelid BCC but less so with cutaneous melanoma. The data presented here represent the only recent comprehensive evaluation of the demographics of eyelid SCC in England over more than a decade.

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Competing interests None declared.

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