



National incidence of eyelid cancer in Ireland (2005–2015)

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Abstract

Aims We report on the incidence of cutaneous eyelid tumours in Ireland over the 11-year-period from 2005 to 2015, we identify associations between demographic factors and cutaneous eyelid tumour risk.

Methods Skin cancers, including basal cell carcinoma (BCC), squamous cell carcinoma (SCC), melanoma, and other cancers, located on the eyelid or canthus according to ICD-10 coding, as registered by the National Cancer Registry of Ireland (NCRI), were captured from the period 2005 to 2015. Age standardised rates (ASR) were calculated according to the European Standard Population (2013). Longitudinal data analysis using linear regression, and associations with age and sex were evaluated with the statistics program R.

Results There were 4824 patients diagnosed with eyelid BCC during the study period, the ASR in men and women was mean 15.87 and 13.49 per 100,00, respectively. The relative risk for eyelid BCC in men compared with women was 1.18, age was associated with incidence. There were 528 patients diagnosed with SCC; the ASR of eyelid SCC in men and women was 2.10 and 1.39 per 100,000, respectively, and increased in women annually ($\beta = 0.07$, $p = 0.0005$). The relative risk for eyelid SCC in men compared with women was 1.51, and age was exponentially associated with SCC. Melanoma and other eyelid tumours were uncommon—50 and 55 cases, respectively.

Conclusion Incidence of both BCC and SCC increases with age and male sex. The incidence of eyelid SCC is increasing in women, and under age 50, eyelid BCC is more common in women than men.

Synopsis We describe the recent incidence of eyelid cancers in Ireland, from National Cancer Registry Data. We find eyelid BCC, and also SCC, are associated with increased age. Rate of eyelid SCC is increasing in women.

Introduction

Skin cancer is the most common type of cancer in humans [1]. Basal cell carcinoma (BCC) is the most common skin cancer, of which 10% are estimated to occur in the periocular skin [2, 3]. Squamous cell carcinoma (SCC) is the second most common skin cancer [4]. Skin cancers affecting the periocular skin are more detrimental than elsewhere, due to both the morbidity or uncommonly mortality, which may arise from local invasion [5], and also the morbidity associated with

treatment, as excision can involve removal of the eyelids, or a significant amount of periocular skin [6]. Compared to other skin regions periocular BCCs grow more rapidly [7].

UV radiation, especially for fair-skinned persons, is the primary aetiology for development of keratinocyte carcinoma [8] and melanoma [9]. As with most cancers, skin cancer is more common in older people [4]. There is predicted to be a substantial increase in the older population over the age 65 in Ireland, which is projected to more than double from a population of 532,000 older persons in 2011, to 1.4 million in 2046 [10]. The National Cancer Registry of Ireland (NCRI) predicts a commensurate increase in the incidence of skin cancer [11].

The incidence of skin cancer worldwide, including keratinocyte carcinoma and melanoma, is indeed reported to be increasing; the rate, however, varies significantly, with highest rates of BCC reported in Australia (>1000 per 100,000) and lowest rates reported in parts of Africa (<1 per 100,000) [12, 13]. The UK National Institute for Health and Clinical Excellence has recommended that the epidemiology of skin cancer is studied further [14]. We aimed to estimate the current burden of eyelid skin cancer in Ireland, to inform

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service provision. We sought national data, from the NCRI, a publicly funded body, which has recorded information on all cancers occurring in Ireland since 1994 [15].

Materials and methods

Data from the NCRI were accessed to determine the incidence of eyelid tumours from annual registration data. Data from the period 2005–2015 were retrieved, during which period the population nationally increased from 4.13 million in 2005, to 4.64 million in 2015 [16]. All eyelid tumours were detected according to specification of ICD-03 topography codes [17], which include the tumour site “eyelid”, coded as C44.1. This tumour site also incorporates the medial and lateral canthus.

By convention, the site of only the first BCC and first SCC in any individual patient is registered. Consequently, patients who first developed a BCC or SCC elsewhere prior to biopsy of an eyelid tumour of the same type, were not captured by our data. This removed the possibility of duplication in patients who may have had multiple biopsies carried out of an eyelid tumour, e.g. incision biopsy followed by excision biopsy, and prevented the ‘double counting’ of patients with multiple eyelid cancers of the same type or recurrences of tumour, thus capturing only new cases and providing a measure of incidence. Eyelid melanoma was an exception to this— the site of each melanoma is recorded, resulting in capture of all cases.

Tumour histology data, and demographic data including patient age and sex, were also collected, according to data release policy of the NCRI.

Statistical analysis

The incidence rate of eyelid cancers per year was determined. Age-standardised incidence rates (ASRs) per 100,000 population per year were calculated according to the European Standard population (2013). Linear regression was carried out to analyse for significant change in the ASR of eyelid BCC and SCC. The year was used as a continuous variable in the model to test for a longitudinal trend in incidence, with significance level set as $p < 0.05$. Relative risk for men compared with women was calculated. Data analysis was carried out using the statistics program R [18].

Results

Eyelid basal cell carcinoma

Over the 11-year-period studied (2005–2015), there were 4824 cases of eyelid basal cell carcinoma (BCC) being the

first BCC diagnosed—2408 in men (annual range 178–256) and 2416 in women (annual range 185–271), see Table 1. The ASR for BCC was, in men, 15.87 per 100,000 (95% confidence interval (CI) 15.54–16.21), and in women, 13.49 per 100,000 (95% CI 13.22–13.76), see Fig. 1. The annual BCC ASR did not change significantly over time in men or women.

Overall there was a higher risk in men compared with women for eyelid BCC, relative risk was 1.18 (95% CI 1.06–1.29), though under age 60, the sex association was reversed, see Table 2. The incidence of eyelid BCC rose with age, in both men and women, see Fig. 2a, with the rate in men and women approximately doubling per decade between the age of 50 and 80, and reducing after age 90.

Eyelid squamous cell carcinoma

There were 528 cases of eyelid SCC being their first skin SCC diagnosed—290 in men (annual range 19–39), and 238 in women (annual range 13–29), see Table 1. The ASR for SCC was, in men, 2.10 per 100,000 (95% CI 1.98 to 2.23), and in women, 1.39 per 100,000 (95% CI 1.30 to 1.48), see Fig. 3. The ASR increased significantly in women, at a rate of 0.07 cases per 100,000 annually ($\beta = 0.07$, $p = 0.0005$), with a non-significant increase in men ($\beta = 0.6$, $p = 0.18$).

There was increased risk of SCC in men; relative risk for men compared to women was 1.51 (95% CI 1.32–1.71), see Table 2. The incidence of eyelid SCC rose exponentially with age, shown in Fig. 2b, with approximate doubling of rate of SCC per decade from age 50 to 90, followed by a reduction in both men and women after age 90.

Table 1 New cases of eyelid BCC and eyelid SCC in males and females 2005–2015 reported by the national cancer registry of Ireland (NCRI)

Year	Eyelid BCC			Eyelid SCC		
	Males	Females	Combined	Males	Females	Combined
2005	187	192	379	19	13	32
2006	208	185	393	26	15	41
2007	178	203	381	22	18	40
2008	203	199	402	24	20	44
2009	210	205	415	20	18	38
2010	199	207	406	26	23	49
2011	238	271	509	34	24	58
2012	239	243	482	19	28	47
2013	256	218	474	26	24	50
2014	246	253	499	39	26	65
2015	244	240	484	35	29	64
Total	2408	2416	4824	290	238	528

Other eyelid tumours

There were 50 eyelid malignant melanomas diagnosed during the study period—29 in women, and 21 in men, approximating an annual incidence of 0.1 per 100,000 overall. There were 55 cases of other eyelid tumours, including sebaceous adenocarcinoma, Merkel cell carcinoma, unspecified carcinomas and other tumours—29 in women and 26 in men.

Discussion

We present heretofore unreported data on eyelid cancer registrations in Ireland, which establishes a baseline esti-

mate of rate of eyelid skin cancer, and highlights new trends in demographic risk factors in the population. We demonstrate that periocular BCC and SCC are associated with older age and male sex, and SCC is increasing nationally in women, whereas the rate of eyelid BCC is not changing significantly. Eyelid BCC was more common in women than men under age 60. Our data is especially important as there are skin cancer prevention initiatives which have been found to be highly cost-effective [19].

In both men and women the development of BCC and more particularly SCC was associated with increased age, in keeping with previous reports from cancer registries in England [20, 21]. This differential age profile may be due to the aetiology of the keratinocyte carcinomas, whereby cumulative UV exposure, and also immunosuppression are implicated in SCC, whereas development of BCC is related to intermittent high-dose sun exposure [22].

Overall periocular BCC was more common in men, with a relative risk of 1.2 for men compared with women. In the under 60-year-old cohort, the sex association was reversed, with BCC more common in women. This differential sex association with eyelid BCC according to age cohort has also been described in England [20], and increased keratinocyte carcinoma has been described recently in younger women; this may be secondary to greater UV exposure, including from tanning beds, and may also be contributed to by greater self-surveillance and seeking of medical attention amongst women versus men, in this age group [23]. There are reports of a rapid and disproportionate increase in BCC in young women in Denmark, the Netherlands, and the US [22, 24, 25], and in the UK, a loss of an association of BCC

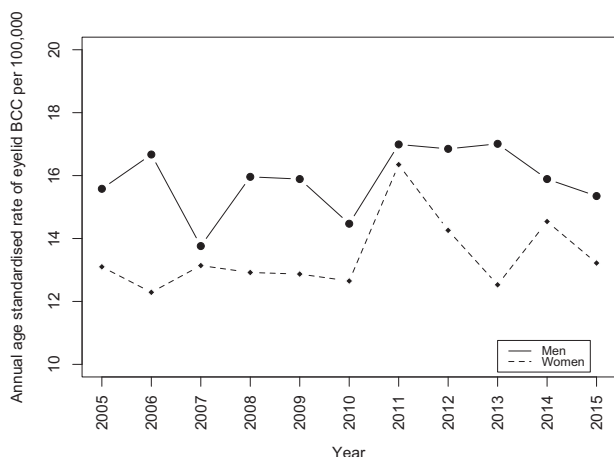


Fig. 1 Annual age standardised rate of eyelid basal cell carcinoma in men and women per 100,000, 2005–2015, Ireland

Table 2 Relative risk in men compared with women of eyelid basal cell carcinoma (left) and squamous cell carcinoma (right) with respect to age and overall during the study period

	Age band	Eyelid BCC relative risk of men compared with women	Eyelid SCC relative risk of men compared with women
Age band	<50	0.97 (0.96–0.99)	1.21 (1.16–1.26)
	50–59	0.91 (0.87–0.96)	1.17 (1.13–1.21)
	60–69	1.07 (1.04–1.11)	1.48 (1.37–1.59)
	70–79	1.19 (1.09–1.28)	1.75 (1.54–1.95)
	80–89	1.55 (1.28–1.83)	1.43 (1.17–1.68)
	≥90	2.10 (1.55–2.65)	1.40 (0.93–1.86)
Years	2005–2006	1.27 (1.12–1.42)	1.86 (1.61–2.10)
	2007–2008	1.14 (1.03–1.25)	1.55 (1.33–1.77)
	2009–2010	1.19 (1.07–1.31)	1.42 (1.22–1.63)
	2011–2012	1.11 (1.01–1.21)	1.31 (1.15–1.46)
	2013–2015	1.20 (1.10–1.31)	1.54 (1.35–1.74)
	Mean value across all years	1.18 (1.06–1.29)	1.51 (1.32–1.71)

Relative risk values are followed by 95% CIs in brackets

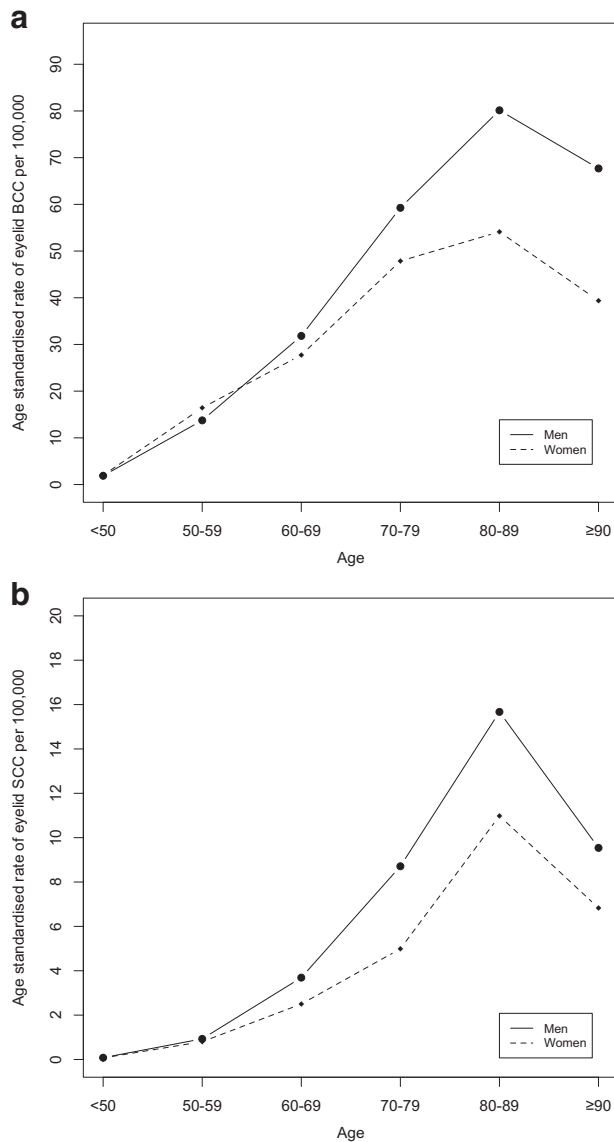


Fig. 2 **a.** Age standardised rate of eyelid basal cell carcinoma in men and women by age, per 100,000, 2005–2015, Ireland, **b.** Age standardised rate of eyelid squamous cell carcinoma in men and women by age, per 100,000, 2005–2015, Ireland

with male sex in the younger population [26]. Longitudinal studies are required to determine whether the association with women compared to men we observe in this age cohort carries forward in older age.

Eyelid SCC was more common in men, in all age groups, with an overall relative risk of 1.5. This finding has been reported in other populations, though with a greater sex association, including a relative risk for men compared to women of 1.9 in England [21], and 2.0 in Australia [6], for eyelid SCC.

The ASR of eyelid BCC was found to be constant in both men and women over the study period. In comparison, there was an increase in rate of eyelid SCC in women by a mean rate of 3% annually, though no change in men. An increase in

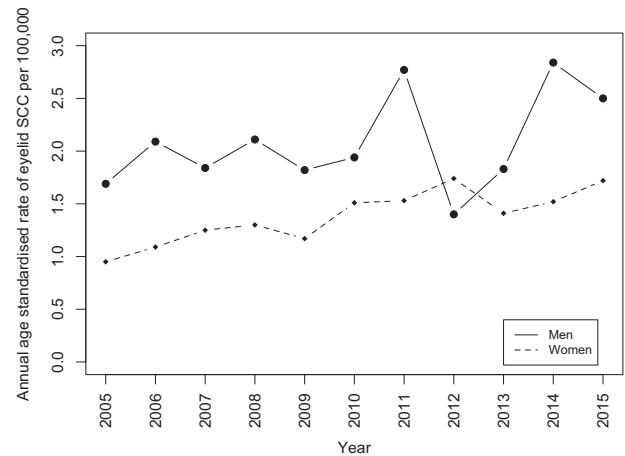


Fig. 3 Annual age standardised rate of eyelid squamous cell carcinoma in men and women per 100,000, 2005–2015, Ireland

skin SCC in other Caucasian populations has been described, in Northern Ireland, England, Canada, the Netherlands, and Australia [21, 27–30]. There are a variety of possible contributing factors to our finding of increasing SCC in women—increased awareness and surveillance for skin cancer, with subsequent increased detection may be relevant. Greater incidence due to increased sun seeking behaviour, and also due to population ageing may also be important.

The annual ASR we report, 15.87 and 13.49 per 100,000 in men and women, respectively, for eyelid BCC, and 2.10 and 1.39 in men and women, respectively, for eyelid SCC, is over twice that was described in recent reports from England, which described an annual overall ASR of 0.63 for eyelid SCC, and rates of 4.51 and 4.53 per 100,000 in men and women, respectively, for eyelid BCC [20, 21]. The accuracy of the reporting of BCC in the UK has been previously examined; a 2013 report compared the reporting of BCC rate from cancer registry data, versus histopathology data in a representative area in England, and showed that the true BCC rate may be over twice that reported by local cancer registry data [31]. Another analysis has shown discrepancies between skin cancer registration, and under-detection effecting especially BCC, in the cancer registries in the UK [32]. This may contribute to the higher rate of eyelid BCC and SCC we observe, although similar limitations may apply to the Irish Cancer Registry data on keratinocyte skin cancers. Further complicating comparisons, the rate of BCC and SCC varies according to a population's skin pigment, and also latitude, among other factors [33, 34]. The reported rate of BCC varies substantially even within England—in a report of eyelid BCC, the largest Cancer Registry in England, the Thames Cancer Registry, which covers over 13 million people, reported less eyelid BCC than any other Cancer Registry in England, over the period 2000–2010 [20].

We found that eyelid malignant melanoma and other eyelid cancers were uncommon, with the rate of eyelid

melanoma approximating 1 per million annually. Malignant melanoma however accounts for most deaths from skin cancer [35], increasing the importance of monitoring its rate.

Limitations of our study include a likelihood of underestimation of the true rate of cutaneous eyelid cancers, as only the body site of the first BCC or SCC diagnosed in a given patient is recorded. Therefore, subsequent eyelid cancers of the same type, in the same patient, are not captured. For the same reason the data presented here omits patients with tumour recurrence. The study did not analyse subgroups of patients according to race, limiting the application of our conclusions in other populations. The role of socio-economic status was not assessed in this study, however, it may be important, as keratinocyte carcinoma in Ireland has been found to be positively associated with socio-economic status [36].

Conclusion

We show that there is increased risk of eyelid cancer in the elderly, and in men. Eyelid SCC is increasing in women, and younger women are at greater risk of eyelid BCC.

Summary

What was known before

- Eyelid cancers, including BCC and SCC, are more common in older people, and more common in men.

What this study adds

- Eyelid SCC is increasing in women, and in younger cohorts, eyelid BCC is more common in women than in men.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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