Trends in Basal Cell Carcinoma Incidence Rates: A 37-Year Dutch Observational Study

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Basal cell carcinoma (BCC) incidence rates are increasing. From 1973 to 2009, data on all first histologically confirmed BCCs were gained from the Eindhoven Cancer Registry to estimate trends in patient-based BCC incidence rates by sex, age group, and site in the southeast Netherlands. Trends in European age-standardized rates and age- and site-specific incidence rates were assessed by calculating the estimated annual percentage change (EAPC). Between 1973 and 2009, the European standardized rate quadrupled from 40 to 165 per 100,000 person-years for men and from 34 to 157 for women, significantly increasing since 1973 in both sexes, but accelerating from 2002 until 2009 with an EAPC of 6.8% (95% confidence interval (CI), 5.3–8.3) for men and 7.9% (95% CI, 6.2–9.7) for women. Women below the age of 40 years exhibited a constant linear increase of 6.3% since 1973. The head and neck region was most often affected in both sexes, but the steepest increase was seen for the trunk (EAPC men 13%, women 15%). In the absence of reliable tumor-based rates, these alarming patient-based rates are probably an interesting indicator for the impact of more intensive UV exposure in a prosperous European population.

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INTRODUCTION

The incidence rates of UV-induced skin cancers, including basal cell carcinoma (BCC), are increasing worldwide and are becoming a major public health concern (Bath-Hextall *et al.*, 2007; Birch-Johansen *et al.*, 2010; Holterhues *et al.*, 2010; Flohil *et al.*, 2011a). Mortality rates associated with BCC are low (<0.1%), but localized tissue invasion may induce considerable functional and cosmetic morbidity, especially because the majority of the lesions are located on the face (Hannuksela-Svahn *et al.*, 1999; Lewis and Weinstock, 2007; Jensen *et al.*, 2008). Only few cancer registries record BCC, and in most cases only the first histologically confirmed BCC per patient is included (Bath-Hextall *et al.*, 2007; Birch-Johansen *et al.*, 2010; Flohil *et al.*, 2011a). This is mainly because of the large number of tumors involved and its associated costs.

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Abbreviations: BCC, basal cell carcinoma; CI, confidence interval EAPC, estimated annual percentage change; ECR, Eindhoven Cancer Registry; SCC, squamous cell carcinoma

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In general, BCCs are considered a disease of the elderly (Karagas *et al.*, 1999; Bath-Hextall *et al.*, 2007; Flohil *et al.*, 2011a). However, a recent large Danish population-based study between 1978 and 2007 showed that the average percentage change in BCC incidence was significantly higher among those younger than 40 years than in older persons, especially in women (Birch-Johansen *et al.*, 2010; Flohil *et al.*, 2011a). This was in accordance with most other studies reporting a trend toward higher increase in BCC incidence in younger persons (de Vries *et al.*, 2004; Christenson *et al.*, 2005; Bivens *et al.*, 2006). For squamous cell carcinoma (SCC) and melanoma, similar increases in rates have been observed for younger persons (Purdue *et al.*, 2008). An increase in the number of BCC patients, especially in younger age groups, may lead to an exponential rise in the overall occurrence of BCC over time, particularly because the population ages and most likely around 30% will develop subsequent BCCs within 5 years (Flohil *et al.*, 2011b).

A previous study of the BCCs registered in the Dutch Eindhoven Cancer Registry (ECR) from 1973 until 2000 observed significant and consistent increases in BCC rates for both sexes (Coebergh *et al.*, 1991; de Vries *et al.*, 2004). The objective of this study was to investigate potential changes in trends in the increasing BCC incidence rates by age and site in the southeast Netherlands (latitude 51° north), using up-to-date ECR data until 2009.

RESULTS

Age-standardized incidence rates

Between 1973 and 2009, first histologically confirmed 52,831 BCCs were registered in 52,831 patients recorded in the ECR,

corresponding to 26,155 (49.5%) men and 26,676 (50.5%) women. During this 37-year period, the age-standardized incidence rates increased approximately fourfold for both men and women, respectively, from 40 to 165 and 34 to 157 per 100,000 person-years (Figure 1 and Table 1).

The highest relative increase in rates (12-fold) was found in women below the age of 40 years, with an increase from 1.82 to 22.2 per 100,000 persons-years, followed by women aged between 40 and 64 years (Table 1). For men, this was observed within the oldest age group (4.4-fold), whereas women in this age group had the lowest increase (3-fold) over time.

For all body sites, the age-standardized BCC incidence rates increased significantly between 1973 and 2009. In 2009, the head and neck region was most often affected in both men and women (99.2 and 85.5 per 100,000 persons-years, respectively). More than 58% of the total number of newly diagnosed BCCs ($n = 4\ 511$) in 2009 was located within the head and neck region. However, during the 37 years of observation, the highest relative increase in rates was found on trunk in men (77-fold), followed by legs (32-fold) and trunk (25-fold) in women (Table 1).

Trends by age

Since 1973, a significant increase in patient-based incidence rates was observed with joinpoint analyses for men and women, 2.3% and 3.9%, respectively (Table 2). Around the years 2002 to 2003 until 2009, this trend accelerated, which resulted in a more-than-doubled annual percentage change (EAPC) of 6.8% for men and 7.9% for women. Men within the youngest age group had no significant increase in BCC incidence from 1973 to 1985, whereas after that period the EAPC rose to 4.5% (95% confidence interval (CI), 3.3–5.8). For women below the age of 40 years, no joinpoint was observed between 1973 and 2009, resulting in an annual linear increase of BCC incidence of 6.3% from 1973 to 2009 (Figure 2). From 1973 onward, the BCC incidence of men and women in the age groups 40–64 and ⩾65 years increased steadily over time, with EAPCs ranging from 2.3 to 4.6% (Figure 2). Around the years 2002–2004, this pattern significantly altered according to the joinpoint analysis and trends in BCC incidence accelerated, with the highest EAPC of 7.9% (95% CI, 5.2–10.6) found in women aged between 40 and 64 years (Table 2).

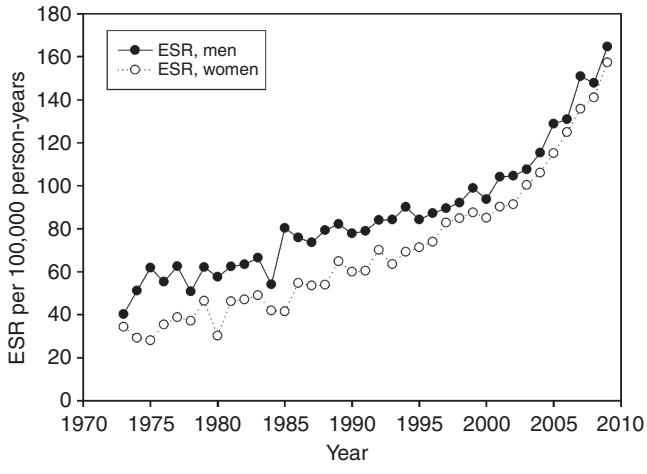

Figure 1. Age-standardized incidence rates (European standardized rates (ESR)) from 1973 to 2009 of the first, histologically confirmed basal cell carcinoma in the southeast Netherlands by men and women.

Trends by site

All body sites exhibited significant increases in BCC rates, except for the lip in men (Table 2). The head and neck region was the most commonly affected site for BCC during the whole study period, but showed the lowest annual increase in rates per year (4.7% in men and 5.8% in women). In the last 4–6 years before 2009, steep increases were especially seen for BCC on the trunk in men (EAPC 12.8%) and women (EAPC 14.8%). From 1998 onward, a similar acceleration in rates was observed for BCCs on arms in men. For BCC located on the legs, there was a constant linear increase in rates (Table 2).

BCC cumulative risk

In 2009, the cumulative risk for developing a first histologically confirmed BCC before the age of 40 years was higher in women (0.9%) than in men (0.4%), corresponding to 1 in 112 and 1 in 250, respectively. When expanding the risk set to 65 years, again women were more often affected by BCC than men (7.0% (1 in 14) vs. 5.5% (1 in 18)). However, the lifetime BCC risk for men was approximately 1 in 5 (21%) and for women it was 1 in 6 (18%).

DISCUSSION

In 2009, more Dutch citizens were newly diagnosed with BCC than with any other cancer (http://cijfersoverkanker.nl/,

Table 1. Age-standardized incidence rates (ESR) by age and site from 1973 to 2009 of first, histologically confirmed BCC in the southeast Netherlands

	ESR, men		ESR, women	
	1973	2009	1973	2009
Age (years)				
All	40.2	164.7	34.4	157.3
<40	2.4	9.9	1.8	22.2
40–64	53.9	203.1	35.4	242.8
⩾65	196.6	854.6	199.6	608.8
Site				
Head/neck	37.7	99.2	28.5	85.5
Trunk	0.5	38.7	1.7	41.7
Arms	1.4	15.0	1.8	12.5
Legs	0.5	8.5	0.4	12.8
Lip	0.0	2.4	1.4	4.2

Abbreviations: BCC, basal cell carcinoma; ESR, European standardized rates.
ESR expressed per 100,000 persons-years.

Table 2. Time trends in age- and site-specific incidence rates of BCC among men and women in the southeast Netherlands from 1973 to 2009

	Men				Women			
	Trend 1		Trend 2		Trend 1		Trend 2	
	Years[1]	EAPC (95% CI)	Years	EAPC (95% CI)	Years	EAPC (95% CI)	Years	EAPC (95% CI)
Age (years)								
All	1973–2002	2.3 (2.0–2.7)	2002–2009	6.8 (5.3–8.3)	1973–2003	3.9 (3.5–4.2)	2003–2009	7.9 (6.2–9.7)
<40	1973–1985	−2.4 (−9.6–5.5)	1985–2009	4.5 (3.3–5.8)	1973–2009	6.3 (5.6–7.0)		
40–64	1973–2003	2.4 (1.9–2.7)	2003–2009	6.4 (4.4–8.5)	1973–2004	4.6 (4.2–5.1)	2004–2009	7.9 (5.2–11)
⩾65	1973–2002	2.3 (1.9–2.8)	2002–2009	7.5 (5.8–9.3)	1973–2002	2.6 (2.1–3.1)	2002–2009	7.8 (6.1–9.6)
Site								
Head/neck	1973–2003	1.6 (1.2–1.9)	2003–2009	4.7 (2.3–7.1)	1973–2004	2.8 (2.4–3.1)	2004–2009	5.8 (2.8–8.8)
Trunk	1973–2003	5.6 (4.6–6.5)	2003–2009	12.8 (8.8–17)	1973–2005	7.8 (7.0–8.5)	2005–2009	15 (9.4–21)
Arms	1973–1998	4.2 (2.5–6.0)	1998–2009	11.2 (9.0–13)	1973–2009	8.7 (8.0–9.5)		
Legs	1973–2009	8.1 (6.9–9.4)			1973–2009	7.8 (7.0–8.6)		
Lip	1973–2009	0.5 (−0.8–1.9)			1973–2009	3.2 (2.3–4.1)		

Abbreviations: BCC, basal cell carcinoma; CI, confidence interval; EAPC, estimated annual percentage change within joinpoint segment.
[1]Period in years within joinpoint segment.

accessed 15 March 2012). Elderly people were most often affected by BCC, but increases in BCC occurrence were steepest among young women, which is in line with other observational studies (Christenson *et al.*, 2005; Birch-Johansen *et al.*, 2010). Between 1973 and 2009, women aged 40 years or less showed the most rapid increase in BCC rates compared with other age groups. Young women were also the only subgroup with a high constant linear increase in BCC rates over the past 37 years. Since 2002, accelerations in the speed of increase of incidence were also noted among older women and in men.

The continuous increment was not restricted to BCC incidence. The melanoma and SCC incidence increased significantly in young people, but this is even more pronounced in the elderly (Purdue *et al.*, 2008; Jemal *et al.*, 2011). In accordance with previous studies, BCCs were predominantly located in the chronically UV-exposed head and neck region (Scrivener *et al.*, 2002; Flohil *et al.*, 2011b). However, the steepest acceleration in site-specific BCC rates was detected on the trunk, most likely due to more frequent intermittent UV exposure (e.g., more people traveling, wearing a bikini, and practicing outdoor activities) of otherwise covered body parts (Randle, 1997).

Accelerating increase in BCC rates

From 2002 onward, we observe an acceleration in the increase in BCC rates. Interestingly, we also observed a joinpoint for SCC trends in the same year with an EAPC of 9.2% for women and 6.9% for men (Hollestein *et al.*, 2012), but not in trends of melanoma incidence using nationwide cancer registry data (Holterhues *et al.*, 2010). This deviation from the trend in incidence of keratinocyte carcinomas (BCC and SCC) may be due to several factors. An increased awareness of cutaneous malignancies in the general population due to skin cancer prevention campaigns may have led to more skin checks and diagnoses of previously undiagnosed keratinocyte carcinomas. In addition, the number of practicing dermatologists in the ECR region may have increased. This, together with the fact that clinicians are more aware of skin cancer and more often perform full body skin examinations, increases the likelihood of keratinocyte carcinomas being diagnosed (Bastiaens *et al.*, 1998; Valery *et al.*, 2004). The fact that the most marked increase in incidence is on the trunk is also consistent with increased surveillance as suggested previously (Valery *et al.*, 2004). Although the rise in melanoma incidence can partly be explained by overdiagnosis through improvement of histological diagnostic criteria, this is probably not the case for BCC (Weyers, 2012). An increased detection rate of BCC in cancer registries based on pathology reports may also be induced by changes in health-care organization and/or reimbursement of care. The joinpoint for BCC was observed in 2002; however, market forces were introduced much later in the Netherlands, namely in 2006, stimulating Dutch clinicians to treat non-life-threatening BCCs more rigorously than before (e.g., surgical excision instead of cryotherapy, curettage, electro-dissection, or a wait-and-see policy in elderly with multiple comorbidities). This resulted in more histopathologically confirmed BCCs. It is unlikely that improved processes within the registry resulted in a higher capture rate and explain the changes in BCC and SCC incidence, as there is substantial continuity in the registration staff (personal communication ECR). The demographic changes in the Dutch population (i.e., gender and age) were adjusted for in the analyses and, therefore, cannot explain the increase in BCC either. In fact, the proportion of people with dark skin, protective of skin cancer, increased during the study

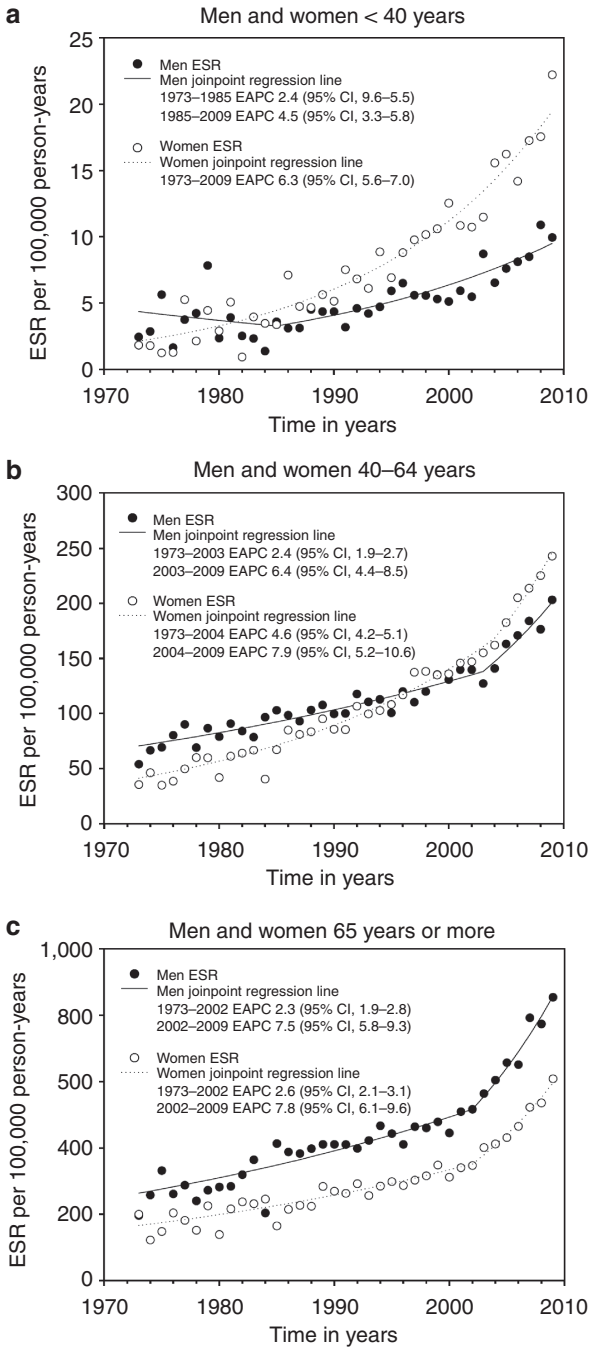

Figure 2. Joinpoint regression lines based on basal cell carcinoma age-standardized incidence rates (European standardized rates) from 1973 to 2009 in the southeast Netherlands. (**a**) Men and women aged <40 years. (**b**) Men and women aged 40–64 years. (**c**) Men and women aged ⩾65 years. CI, confidence interval; EAPC, estimated annual percentage change (within joinpoint time segment); ESR, European standardized rate.

period, which would, in theory, lead to dilution of risk (Rubin *et al.*, 2005; Kiiski *et al.*, 2010; http://www.cbs.nl/, accessed 15 March 2012). The most plausible explanation is increased UV exposure due to outdoor leisure activities and sports since the 1950s when weekly working hours were reduced and the number of holidays were increased (Randle, 1997). In the early 1980s, air travel became less expensive and more accessible to the general Dutch population, encouraging people to travel to sunny destinations (http://www.cbs.nl/, accessed 2 July 2012). Furthermore, in the past decade, sunbed use has increased markedly, particularly in younger populations (Levine *et al.*, 2005). In the Netherlands, the popularity of sunbed use started around 1990, but regulatory changes have only been introduced recently.

Implications

Knowledge about sun protective behavior is considered to be relatively good among the European population, but informing people about adverse effects (of the sun) does not necessarily induce changes in risk behavior (Peacey *et al.*, 2006; Paul *et al.*, 2008; Suppa *et al.*, 2012), because despite multiple prevention campaigns the ''knowledge-behavior gap'' remains (Garbe and Buettner, 2000; Devos *et al.*, 2003; Schneider *et al.*, 2009; Flohil *et al.*, 2011a; Jones *et al.*, 2012; Suppa *et al.*, 2012). Therefore, more effective interventions focused on specific subgroups of the populations to influence skin cancer risk behavior should be explored. More strict legislations should be considered, for example, restricting sunbed use to persons aged 18 years or older (http://www.vwa.nl/, accessed 15 March 2012). The growing number of skin cancers will place increasing demands on health-care providers, i.e., more dermatologists, nurse practitioners, and physician assistants specialized in skin cancer may be required. In addition, general physicians and (plastic) surgeons might wish to be more informed about the diagnosis and treatment of cutaneous (pre)malignancies.

Moreover, the fast-growing number of (young) BCC patients emphasizes the need to increase skin cancer awareness among all clinicians to improve the case-finding strategy among those involved in skin cancer care (e.g., general practitioners, dermatologists, and (plastic) surgeons). BCCs should be part of the differential diagnosis in persistent solitary skin lesion even in younger persons.

Strengths and limitations

The ECR reports the first histologically confirmed BCC per patient, ignoring BCCs that were clinically diagnosed and treated without histological confirmation. Therefore, the incidence rates provided within this study are probably an underestimation of the true BCC incidence. The degree of underestimation is likely to be small, as a previous Dutch study observed that 7% of all subsequent BCCs in patients with prior BCC were not histologically diagnosed (Flohil *et al.*, 2012a,b). Unfortunately, there is no information available on the proportion of nonhistologically diagnosed BCC before this study of 2012.

It was assumed that the age-standardized BCC rates calculated with population-based data from the ECR were representative for the Netherlands as a whole (Flohil *et al.*, 2011a), although other demographic factors such as socio-economic status and ethnicity that affect BCC risk may vary across the country. However, age-standardized incidence rates of melanoma, based on nationwide data from 2009, differed only slightly from the rates calculated with data from ECR

(22.8 vs. 19.6, respectively), indicating a minor underestimation when extrapolating our BCC estimates (http://cijfersoverkanker.nl/, accessed 15 March 2012).

The nonsignificant trend in rates observed among men aged below 40 years from 1973 to 1985 is probably because of the small number of men with BCC in this age category during that period.

Conclusion

In addition to the continuous increase in BCC incidence rates, an alarming acceleration in BCC rates was observed after 2002 in the southeast Netherlands. Besides emphasizing the need for effective primary preventative skin cancer strategies, these results are a warning to our society. Governments, together with health professionals, need to respond more actively and differently to this ''BCC epidemic'' to stabilize and ultimately decrease BCC rates in the future.

MATERIALS AND METHODS

Data collection

For BCC incidence, we used patient-based data from ECR, which is part of the Netherlands Cancer Registry and located at the Comprehensive Cancer Centre South. ECR is the only population-based cancer registry in the Netherlands that routinely registers the first, histologically confirmed BCC per patient using PALGA, the nationwide network and registry of histopathology and cytopathology, as a signaling source (Casparie *et al.*, 2007; Flohil *et al.*, 2011a). PALGA contains all excerpts of pathology reports and has nationwide coverage since 1991, based on all Dutch laboratories, which gave their excerpts to the cancer registry (Casparie *et al.*, 2007). In this study, all individuals with a first, histologically confirmed BCC diagnosed between 1973 and 2009 were obtained from ECR (Fritz *et al.*, 2000). During this period (1 January 1973 to 1 January 2010), primarily because of expansion of the registry area, the number of inhabitants within the ECR catchment area increased from 591,916 to 2,261,967 (Coebergh *et al.*, 1991).

Statistical analysis

First, the crude incidence of the first histologically confirmed BCC per patient was calculated. Numbers of BCC cases, subdivided by sex and eighteen 5-year age groups (0–4, 5–9, 10–15, and so on), were divided by the number of inhabitants in the ECR catchment area in these same categories. Furthermore, age-standardized incidence rates were calculated for sex by age group and site by direct standardization to the European Standard Population (European standardized rates), expressed per 100,000 person-years (Flohil *et al.*, 2011a).

The BCC site was coded according to the International Classification of Diseases for Oncology-3 and categorized into head and neck, trunk, arms, legs, lips, and other (Fritz *et al.*, 2000). Given the small number of BCC cases within the category ''other'', these data have not been reported in this study. ''Age'' at the date of first histologically confirmed BCC was (*a priori*) subdivided into three groups: <40 years, 40–64 years, and $\geqslant 65$ years.

Trends in BCC incidence rates were assessed by calculating the EAPC and the corresponding 95% CI, with the joinpoint regression model. The latter identifies the year in which a significant change in rates occurred (Kim *et al.*, 2000; Purdue *et al.*, 2008). To calculate this, a regression line was fitted to the natural logarithm of the rates, using the calendar year as a regressor variable (i.e., $y = ax + b$, where $y = \ln(\text{rate})$ and $x =$ calendar year, then $\text{EAPC} = 100 \times (e^a - 1)$). Trends in incidence rates were described for site and age group by sex. Statistical analyses were performed with Joinpoint version 3.5.2 obtained from the National Cancer Institute (http://surveillance.cancer.gov/joinpoint).

The cumulative risk of developing a BCC before ages 40, 65, and 85 years (the latter considered as BCC lifetime risk) was calculated for the year 2009. First, the cumulative incidence rates of BCC occurrence before ages 40, 65, and 85 years were calculated as the sum of the sex- and age-specific incidence rates for ages 0–39, 0–64, and 0–84 years, respectively, and multiplied by the width of the age groups (5 years). Thereafter, cumulative risks were calculated from the cumulative incidence rates using the following formula: cumulative risk $= 100 \times (1 - \exp$ (cumulative rate/100); Flohil *et al.*, 2011a).

CONFLICT OF INTEREST

The authors state no conflict of interest.

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