INVESTIGATIVE REPORT

Incidence, Prevalence and Future Trends of Primary Basal Cell Carcinoma in the Netherlands

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Basal cell carcinoma (BCC) incidence rates are increasing worldwide. This study's objective was to estimate the occurrence of BCC in the Netherlands in terms of incidence and prevalence. Data on first primary carcinomas were retrieved from the Eindhoven Cancer Registry and extrapolated to the Dutch population. Extrapolated data showed a total of 444,131, histologically confirmed cases in the Netherlands between 1973 and 2008. During this period, age-adjusted incidence rates (European Standard Population) increased approximately three-fold from 40 to 148 per 100,000 in males and from 34 to 141 in females. Lifetime risk of BCC was 1 in 5–6 for Dutch citizens. Disease prevalence in the Netherlands was 1.4% and almost four times higher than this (5.4%) in the oldest age group (age 65 years or more). Predictions of future trends showed no signs of a plateau in the number of cases. These estimates should urge Dutch policymakers to provide solutions for the growing group of patients with BCC. *Key words: basal cell carcinoma; epidemiology; incidence; prevalence.*

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Non-melanoma skin cancer (NMSC) is by far the most common cancer in Caucasians and numerous studies have shown that incidence rates, especially for basal cell carcinomas (BCC), are increasing worldwide (1–5). The burden of BCC is becoming an increasingly important public health issue, because of the rapidly increasing numbers of patients with a history of BCC, the total number of BCC patients and the costs of their treatment and follow-up (4, 6, 7).

A Dutch population-based survey revealed increases in European Standardized BCC incidence rates between 1973 and 2000, from 40 to 92 per 100,000 in men and 34 to 79 per 100,000 in women (6). Forecasts of BCC incidence in the Netherlands, based on data from the Eindhoven Cancer Registry (ECR) for the years 1989–2000, estimated annual incidence rates of 122 and 119 per 100,000 for males and females, respectively, in 2015 (7).

The main causes of this continuous rise in BCC incidence are the effects of altered UV exposure patterns, population aging, the increasing number of people with a prior skin cancer diagnosis, who are at high risk of developing subsequent skin cancers, and an increased awareness of skin cancer among patients and physicians (i.e., detection bias). An estimated 40% of patients with a first BCC will develop subsequent tumours in the next 5 years (8, 9).

Whilst BCC causes very low mortality, it is associated with considerable functional and cosmetic morbidity as most lesions are located on the face and are typically treated surgically. There is currently a shortage of dermatologists in the Netherlands (about 475 full- and part-time specialists for a population of 16.4 million) and the rising incidence of BCC is putting a heavy burden on the already limited healthcare system in terms of diagnosis, treatment and especially follow-up, which represents a substantial proportion of dermatologists' workload (10). Earlier predictions for 2015 (made in 2004), warned Dutch policy makers about the need to provide solutions in order to continue to be able to provide sufficient management for the already large and continuously growing group of BCC patients (7). Direct treatment-related costs depend on the number of treated lesions and selected therapies. In order to make correct workload and cost estimates, we need recent, accurate estimates of the scale of the problem with BCC in the Netherlands (which are currently not up-to-date), including estimates of the prevalence of BCC (which are lacking).

The objective of this study was to reliably estimate the occurrence of BCC in the Netherlands, in terms of incidence and prevalence, using up-to-date data from the ECR. Using BCC data from the period 1973 to 2008, we were the first to estimate the 19-year prevalence of first, histologically proven BCC in the Netherlands. Additionally, new predictions were made for incidence rates and patient numbers in the Netherlands for the years 2010, 2015 and 2020.

METHODS

Data

Data were obtained from the ECR, which is part of the Netherlands Cancer Registry, located at the only population-based

cancer registry in the Netherlands that routinely registers the first, histologically proven BCC cases, using the national pathology laboratories network (PALGA) as a signalling source (6). All individuals with a histologically proven first primary BCC, diagnosed between 1973 and 2008, were included. The ECR also registers data concerning BCC body location. During the study period (January 1, 1973 to January 1, 2009) the population size of the ECR catchment region increased from 591,916 to 2,252,757, mainly due to expansion of the registry area (11). Age-adjustment was performed by direct standardisation according to European Standardized Rates (ESR) and World Standardized Rates (WSR), respectively. Annual incidence rates were computed per 100,000 person-years for each sex and calculated as 5-year moving means, except for annual incidence by site (3-year moving means) (6).

Statistical analysis

The incidence of the first primary, histologically confirmed BCC was calculated. Numbers of BCC cases, subdivided by sex and into eighteen 5-year age groups (0–4, 5–9, 10–14, etc.), were divided by the number of inhabitants in the ECR catchment area in these same categories. Sex- and age-specific incidence rates were multiplied by the population size of these specific categories in the Netherlands in the year concerned to provide an estimate of the number of first primary BCC patients in the country as a whole. Population sizes were obtained from Statistics Netherlands and estimated on the first of January of the relevant year (12).

The cumulative incidence rates at age 84 were calculated as the sum of the age-specific incidence rates for ages 0–84, multiplied by the width of the age groups (5 years). Cumulative risks were calculated from the cumulative incidence rates using the following formula:

Cumulative risk = $100 \times (1-\exp$ (cumulative rate/100)).

To calculate the prevalence of BCC in the ECR catchment area between 1990 and 2008, we retrieved data of the vital status of all patients diagnosed with a BCC since 1990 and still alive on the first of January 2009, a method that was previously used in reports of cancer prevalence in the Netherlands (13).

Predicted numbers of BCC cases in the Netherlands in 2010, 2015 and 2020 were estimated by first predicting the incidence rates on the basis of observed rates for the period 2000–2008, and then multiplying these rates by the population forecasts for these periods, derived from Statistics Netherlands. The statistical models used have been described before (7, 14). The following best-fitted model was employed:

$E_{mit} = \alpha_i + \beta_i \times t$.

Analyses were performed using SPSS for Windows version 15.0 (SPSS inc., Chicago, IL, USA) and STATA statistical software version 10.0 (College Station, TX, USA). *p*-values were calculated in two-sided tests and were considered statistically significant if less than 0.05.

Table I. *First primary, histologically confirmed basal cell carcinoma (BCC) cases extrapolated to the population of the Netherlands*

	Men		Women	
	1973	2008	1973	2008
ESR	40	148	34	141
WSR	27	101	22	101
Cumulative risk*, %	5.0	19.3	5.2	16.3
Total number of BCC cases	1,946	13,891	2,233	15,094

*Calculated at age 84 years.
ESR: European Standard Rate; WSR: World Standard Rate; both expressed per 100,000 inhabitants.

RESULTS

Incidence data from the Eindhoven Cancer Registry

A total of 48,221 first primary BCC cases were diagnosed in the ECR catchment area between January 1, 1973 and December 31 2008. Of these, 23,918 (49.6%) were men and 24,303 (50.4%) women. The age-adjusted ESR for BCC increased from 40 to 148 per 100,000 for males and from 34 to 141 per 100,000 for females (Table I and Fig. 1A). The age-adjusted incidence rates calculated using the WSR rose from 27 to 101 per 100,000 for males and from 22 to 101 per 100,000 for females (Table I). During this 25-year period, the cumulative incidence rate for BCC development at age 84 increased from 5.0% to 19.3% in males and from 5.2% to 16.3% in females (Table I). This implies that, in 2008, 1 in 5 men and 1 in 6 women had developed a BCC before the age of 85.

We plotted BCC incidence rates stratified by age and sex for the most recent year (2008) (Fig. 1B). The results showed that, up to the age of 60, women had higher BCC incidence rates than men, with this trend being reversed in subjects over the age of 60.

Incidence data extrapolated to the Netherlands

We assumed the age-specific ESR of the ECR region to be representative of the Netherlands as a whole. Extrapolating the age-specific incidence rates to the entire Dutch population estimated the diagnosis of a total of 444,131 primary BCC cases between 1973 and 2008. Of these cases, 220,758 were men and 223,373
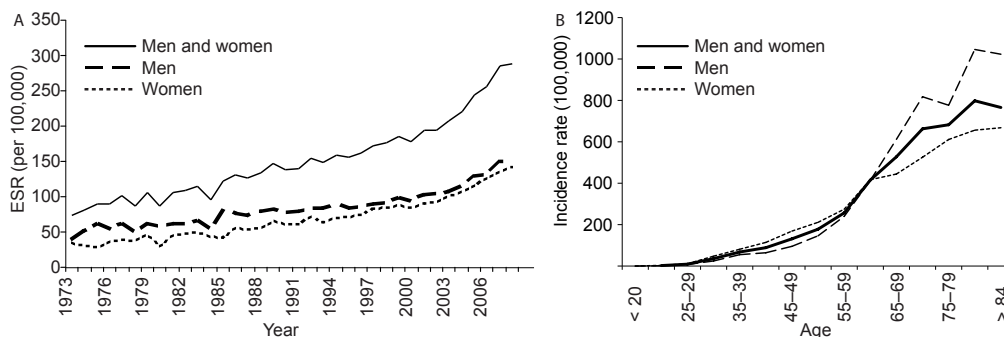

Fig. 1. Incidence of first primary basal cell carcinomas diagnosed in the Netherlands. (A) Age-standardized period 1973 to 2008 (B) by age for 2008. ESR: European Standardized Rates.
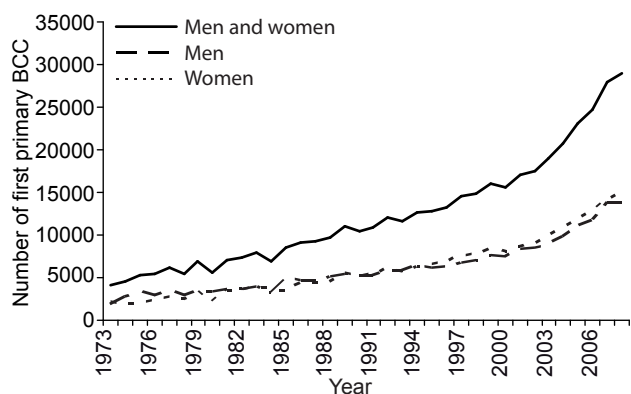
Fig. 2. Estimated absolute numbers of first primary basal cell carcinomas (BCC) diagnosed between 1973 and 2008 in the Netherlands.

women. During the study period, the total annual number of newly diagnosed BCC patients rose from 4,179 to 28,985 (from 1,946 to 13,891 in men and from 2,233 to 15,094 in women) (Table I and Fig. 2).

Incidence data by site

In both sexes, BCC occurred approximately ten-fold more often in the head and neck region than in other regions, such as the trunk and limbs. Men had higher BCC rates in the head and neck than women (Fig. 3). All body sites displayed increases in incidence rates, with the most prominent increase relating to the trunk, and the smallest to the lips, whose incidence remained close to 1/100,000 person-years. Extrapolating these estimates to the Netherlands, between 2000 and 2008, yielded estimated increases in incident cases of women of 2.8-fold for first BCC on arms, 2.7 for legs and 2.3 for trunk. For men, the largest increase (3.0) also occurred on the arms, followed by the trunk (2.6) and legs (2.4).

BCC prevalence

Of the 39,595 patients with a first primary BCC diagnosed between 1990 and 2008, 31,414 (79.3%) were confirmed to be alive on January 1 2009. Of the remaining 8,181 patients, 7,916 (20.0%) had died and 265 (0.7%) had been lost to follow-up. Of the 31,414 BCC patients known to be alive on the January 1, 2009, 14,904 (47.4%) were men and 16,510 (52.6%) women. Based on these figures, the overall prevalence in the ECR catchment area was estimated to be 1.4% (1.3% and 1.5% for men and women, respectively). The overall 19-year prevalence for the 65+ age group was 5.4% (6.1% for men and 4.9% women). The overall 5-year prevalence for this same age group was 2.7% (3.1% and 2.3% for men and women, respectively) (Table II).

BCC trend predictions

Trends in BCC incidence for 2010, 2015 and 2020 (estimations based on available data for the time period 2000–2008) showed continuous increases among all age groups in both sexes. The predicted rates and absolute numbers of BCC cases showed no signs of plateauing up to 2020 (Table III). Compared to the observed incidence rates and numbers of cases in 2005, the steepest increases by 2020 occurred in the 65+ age group, with the exception of the incidence rate in women, which increased most steeply in the 35–64 age group.

Trends in BCC incidence by sub-site, calculated for the four most common BCC locations based on data from the years 2000–2008, showed continuous increases (Table IV). The head and neck area was predicted to be the most common site for first primary BCCs for 2010, 2015 and 2020. By 2020, incidence rates for first primary BCCs on the arm in men, are expected to have increased more than 2.5-fold from those in 2005. In women, the steepest increase in incidence rate is predicted for first primary BCCs located on the trunk (2.3-fold). The highest increases in predicted BCC numbers by 2020 are predicted for the arms in men (3.5-fold) and legs in women (2.9-fold).

DISCUSSION

In the last 25 years, the absolute numbers of patients in the Netherlands with first, histologically confirmed BCC
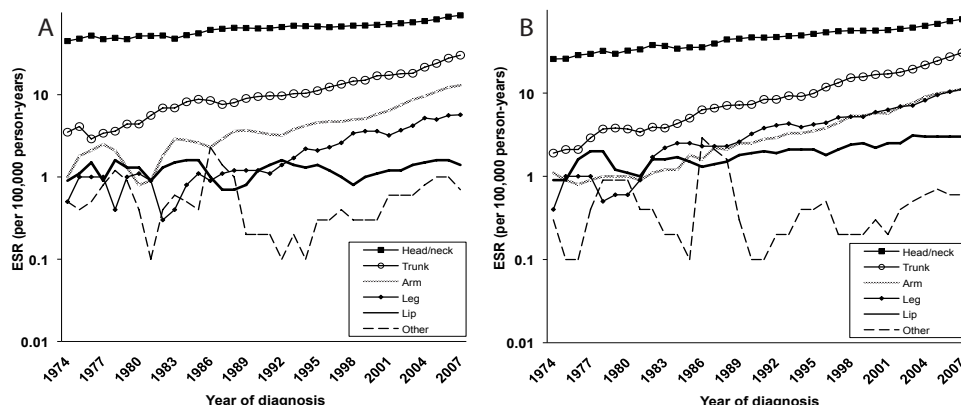

Fig. 3. Incidence of basal cell carcinoma by body site in men (A) and women (B) as 3-year moving average European Standardized Rates (ESR).

Table II. *Five- and 19-year prevalence of basal cell carcinoma (BCC) in the Netherlands*

Prevalence	BCC cases	Population	Prevalence (%)
5 years			
Total	16,356	2,252,757	0.7
15–34 years	224	535,445	0.04
35–64 years	6,954	979,963	0.7
>65 years	9,178	342,381	2.7
Men	7,896	1,125,315	0.7
15–34 years	85	274,553	0.03
35–64 years	3,112	497,898	0.6
>65 years	4,699	151,004	3.1
Women	8,460	1,127,442	0.8
15–34 years	139	260,892	0.05
35–64 years	3,842	482,065	0.8
>65 years	4,479	191,377	2.3
19 years			
Total	31,414	2,252,757	1.4
15–34 years	299	535,445	0.06
35–64 years	12,474	979,963	1.3
>65 years	18,641	342,381	5.4
Men	14,904	1,125,315	1.3
15–34 years	114	274,553	0.04
35–64 years	5,527	497,898	1.1
>65 years	9,263	151,004	6.1
Women	16,510	1,127,442	1.5
15–34 years	185	260,892	0.07
35–64 years	6,947	482,065	1.4
>65 years	9,378	191,377	4.9

increased with about 7-fold in both men and women. Furthermore, 1 in 5 men and 1 in 6 women will have developed BCC before the age of 85 years. The 19-year BCC prevalence in the ECR region was 1.4% and was assumed to be representative of the Netherlands as a whole. Although the epidemiology of BCC varies geographically, it is difficult to compare these observations with the results of international studies because very few cancer registries document BCC and its prevalence has not been studied extensively. Nevertheless, other studies confirm a trend toward increased incidence of BCC (5, 15). A recent study in the United States based on a mathematical model found a 31-year prevalence of NMSC of nearly 5% (16). Although this reported prevalence was about 3 times higher than that in the present study, we calculated the prevalence of first primary, histologically confirmed BCC cases alone. Moreover, our prevalence was not calculated using a statistical model, but with data from a population-based cancer registry.

The ECR does not have reliable data on multiple BCCs. A recent Dutch prospective population-based cohort study involving subjects aged > 55 showed that approximately one-third of BCC patients developed multiple BCCs during an average follow-up period of almost 10 years, of whom 18.1% developed two and 12.9% three or more BCCs (9). Taking these figures into consideration, the absolute number of BCC tumours in the Netherlands since 1990 may be as high as 300,000 or more. Moreover, the high risk of developing subsequent BCC tumours places a heavy burden on the dermatologists' restricted time, since, besides diagnosis and treatment, follow-up is extremely time-consuming. Although recent revisions of the BCC guidelines recommend that only high-risk patients and/or those with multiple BCCs should be followed, this in practice means that almost all BCC patients are examined at least once a year for 5 or more years after diagnosis (17).

Table III. *Predicted basal cell carcinoma (BCC) incidence rates (European Standardized Rates per 100,000 person years) and number of newly diagnosed tumours in the Netherlands*

	2005 Observed	2010 Expected (95% PI)	2015 Expected (95% PI)	2020 Expected (95% PI)
BCC incidence rate				
Men				
15–34 years	7.8	9.8 (6.5–12.9)	12.2 (7.1–17.3)	14.6 (7.5–21.7)
35–64 years	136.5	167.6 (155.8–179.3)	198.2 (178.9–217.5)	228.8 (201.5–256.1)
>65 years	658.1	859.9 (813.6–906.3)	1,067.5 (992.4–1,142.6)	1,275.0 (1,169.7–2,168.8)
All	139.5	162.7 (155.8–169.5)	198.1 (186.9–209.3)	233.5 (217.7–249.2)
Women				
15–34 years	14.2	16.1 (11.9–20.3)	18.7 (12.0–25.4)	21.3 (12.0–30.6)
35–64 years	160.7	216.0 (202.9–229.6)	267.4 (246.0–288.8)	318.7 (288.7–348.8)
>65 years	458.8	587.3 (556.0–618.7)	727.6 (677.5–777.8)	867.9 (797.9–938.0)
All	143.7	153.4 (147.2–159.6)	189.5 (179.4–199.6)	225.6 (211.5–239.8)
Number of cases				
Men				
15–34 years	163	195 (131–259)	251 (146–357)	306 (157–456)
35–64 years	4,741	6,235 (5,798–6,672)	7,335 (6,616–8,054)	8,604 (7,565–9,642)
>65 years	6,347	9,584 (9,067–10,101)	14,308 (13,300–15,316)	20,019 (18,350–21,689)
All	11,250	16,011 (15,335–16,687)	21,884 (20,646–23,123)	28,913 (26,943–30,883)
Women				
15–34 years	304	320 (237–403)	377 (242–512)	418 (238–598)
35–64 years	5,463	7,846 (7,369–8,323)	9,670 (8,892–10,448)	11,627 (10,514–12,741)
>65 years	6,074	8,750 (8,301–9,199)	12,252 (11,433–13,072)	16,282 (15,010–17,555)
All	11,841	16,913 (16,248–17,579)	22,288 (21,130–23,447)	28,338 (26,596–30,080)

PI: prediction interval.

Table IV. Predicted basal cell carcinoma (BCC) incidence rates (European Standardized Rates per 100,000 person years) and number of newly diagnosed tumours by body site in the Netherlands

	2005 Observed	2010 Expected (95% PI)	2015 Expected (95% PI)	2020 Expected (95% PI)
BCC incidence rate				
Men				
Head/Neck	83.1	100.6 (95.7–105.5)	117.2 (109.3–125.1)	133.8 (122.7–145.0)
Trunk	26.2	36.0 (33.0–39.0)	46.8 (42.0–51.5)	57.5 (50.9–64.2)
Arm	10.3	16.2 (14.6–17.9)	21.7 (19.2–24.3)	27.2 (23.7–30.7)
Leg	5.8	7.3 (6.0–8.5)	9.4 (7.4–11.4)	11.5 (8.7–14.3)
Women				
Head/Neck	67.2	85.1 (80.9–89.4)	101.0 (94.1–107.8)	116.8 (107.2–126.3)
Trunk	24.6	36.0 (33.3–38.7)	46.8 (42.6–51.0)	57.6 (51.7–63.4)
Arm	9.7	13.9 (12.1–15.7)	24.7 (15.3–21.1)	22.6 (18.6–26.6)
Leg	9.7	13.5 (12.0–15.0)	17.5 (15.1–20.0)	21.5 (18.2–24.9)
Number of cases				
Men				
Head/Neck	7,188	9,972 (9,487–10,456)	13,221 (12,331–14,111)	17,190 (15,764–18,616)
Trunk	2,350	3,477 (3,189–3,765)	4,945 (4,438–5,451)	6,651 (5,876–7,427)
Arm	907	1,579 (1,419–1,738)	2,339 (2,064–2,614)	3,200 (2,780–3,620)
Leg	500	721 (597–845)	1,048 (824–1,272)	1,454 (1,099–1,809)
Women				
Head/Neck	7,131	9,856 (9,388–10,324)	12,576 (11,762–13,390)	15,785 (14,552–17,018)
Trunk	2,273	3,537 (3,279–3,796)	4,797 (4,371–5,222)	6,083 (5,472–6,694)
Arm	974	1,466 (1,280–1,652)	2,083 (1,762–2,403)	2,750 (2,275–3,225)
Leg	989	1,491 (1,327–1,655)	2,113 (1,832–2,394)	2,827 (2,405–3,249)

PI: prediction interval.

Incidence predictions for the future showed no signs of plateauing. Therefore, policymakers and the dermatologic community should work together to find a solution to the ever-growing burden of BCC. Raised public awareness may have contributed to the increase in BCC detection, but the main causes of the "BCC epidemic" are probably ageing and lifestyle changes, such as altered patterns of UV exposure. Although earlier skin cancer and sun tanning campaigns have increased general awareness, they have failed to greatly influence our behaviour (because of the so called "knowledge-behaviour gap") (18–20). Regulation of the use of commercial sunbeds has recently been introduced in the Netherlands. Users must now be >18 years of age and limits have been placed on UV exposure per visit, depending on skin type. However, the use of sunbeds, or at least their purchase for home use, could be banned completely, because indoor tanning represents an avoidable risk factor for NMSC (21). Strategies, besides prevention that have to be addressed to deal with the worsening BCC epidemic, include increasing the dermatologist workforce and re-evaluating its organisational structure. Investment in supporting professionals, with specialised nurses and nurse practitioners, could release pressure on dermatologists' already restricted time. Furthermore, technical advances in the management of BCC patients may alleviate the pressure on specialised care. BCC treatments other than surgery could contribute to a more efficient strategy for dealing with the large group of BCC patients. Although new therapies, such as photodynamic therapy and treatment with imiquimod, have been developed over the past decade, they may not be very effective at reducing the BCC burden. Currently, no new technological perspectives exist that could make BCC care more efficient in the future, although promising studies reported the early diagnosis of NMSC by fluorescence detection (19, 22).

Strengths and limitations

Extrapolating data from the ECR gave us an impression of the annual number of newly diagnosed BCC patients in the Netherlands. Nevertheless, demographic factors such as socio-economic status, (work-related) UV exposure and ethnicity, which can influence BCC development (23–25), vary across the country. Indeed, nationwide age-specific incidence rates of melanoma standardised to the European Standard Population do differ slightly from melanoma incidence rates calculated using ECR data. However, this difference is relatively small (20.0 versus 18.8, respectively), although it indicates slight underestimation in our extrapolated BCC estimates (26).

In practice, BCCs may be treated without histological verification. BCCs diagnosed non-histologically do not appear in the cancer registry. Thus, the absolute numbers of first, histologically proven BCCs in the ECR data likely underestimates the overall number of cases when extrapolated to the Netherlands as a whole.

Our estimated first primary BCC numbers affecting different body sub-sites, are in concordance with the results of a large Dutch population-based study involving more than 11,000 people aged 55 years or more, which showed the head and neck area to be the predominant site for BCCs, followed by trunk (9). Therefore, body

sub-site seems to be adequately registered by the ECR with PALGA as a signalling source. To validate the prediction methods used, we compared predicted and observed BCC incidence rates and numbers of cases in the Netherlands for the year 2005 (Table III) (7). The rates and numbers of cases of predicted BCC for 2005 have been re-calculated from those published by de Vries et al. (7), because of corrections to the registry database, but using the same methodology and based on the corrected data for 1989–2000. The observed BCC incidence in 2005 was higher than predicted, suggesting it increased faster than was estimated based on data from 1989–2000 (data not shown). The total number of patients diagnosed with a first BCC in 2005 was 23,091, 21% higher than the predicted total of 19,023 (95% PI 17,913–20,132). This 21% underestimation of the predicted number of cases is likely due to apparent acceleration in the estimated absolute numbers of first primary BCCs, starting around the year 2000, as shown in Fig. 2. The most probable explanation for this relatively steep acceleration in the first primary BCC incidence rate and number of cases is changes in medical practice, i.e. increased (early) detection and more BCCs being diagnosed histologically. Other causes may include a genuine increase in the incidence of BCCs or methodological problems in the prediction models (27). The time period on which the predictions were based was probably correct, as the increases in incidence have been steady over time since 1989. However, our future predictions should be interpreted with caution when used as guidelines by healthcare organisations, since actual BCC rates and numbers of cases will probably be much higher than we have estimated.

The advantage of using prevalence data is that the "multiple" BCCs are of less importance. Patients who have been diagnosed with one or multiple tumours are still only one person. Hence the number of cases is informative. Moreover, since we know from previous studies that within 5 years after diagnosis about 40% of BCC patients develop multiple tumours, we can apply these numbers to the prevalence data to get a grasp of the problem of multiple BCCs (8, 9).

In conclusion, this observational study shows that BCC is a significant healthcare issue and that its burden is likely to increase further over time. The incidence and prevalence estimates of BCC should urge policymakers to provide solutions, since this growing group of BCC patients is, and will remain, a serious healthcare problem in terms of numbers of patients treated and monitored and related healthcare costs.

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