Population-Based Estimates of the Occurrence of Multiple vs First Primary Basal Cell Carcinomas in 4 European Regions

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Objective: To estimate the population-based incidence of first and multiple basal cell carcinomas (BCCs) throughout Europe.

Design: The registry practices of 4 population-based cancer registries that routinely register BCC incidence were evaluated for inclusion of first and subsequent histologically confirmed BCCs. Where multiple BCCs were not routinely registered, comparisons with hospital databases were made.

Data Sources: Cancer registry databases from Finland, Malta, the Netherlands (Eindhoven), and Scotland were inspected for registry of first and multiple BCCs in recent years. Cross-checks with hospital and pathology databases were made to check for completeness.

Results: Age-standardized first BCC incidence rates varied between 77 (Malta) and 158 (Eindhoven) per 100,000 person-years. Generally, rates were higher in males than in females, and incidences increased steeply with increasing age. There were approximately 30% more patients with a BCC and 40% to 100% more BCC tumors diagnosed in a given calendar year than were routinely reported for patients with a first primary BCC. The difference between the number of first primary BCCs and the total number of BCCs in a calendar year was generally slightly higher for males than for females and increased substantially with increasing age.

Conclusion: Currently, routinely reported first BCC incidence rates of the included countries should be multiplied by a factor of 1.3 for an estimate of total number of patients diagnosed as having a BCC in a given year.


Basal cell carcinoma (BCC) is the most common cancer in white people by far, and incidence rates are increasing worldwide.1-6 Multiple primary tumors in patients with a BCC history on the one hand and the large total number of patients with a BCC on the other hand translate into substantial costs related to diagnosis, treatment, and follow-up and transform these cancers into an important public health burden.1,7,8

However, the precise magnitude of BCC incidence and prevalence is largely unknown. Only a few population-based cancer registries collect BCC information, and those that do usually collect or publish only the first primary histologically confirmed BCC per patient because of practical problems in coding multiple BCCs (eg, difficulty in defining separate unrelated tumors based on BCC pathology reports). However, a large proportion of patients with a BCC develop multiple BCCs over time,9 and a proportion of patients present with multiple BCCs on the day of diagnosis. Moreover, physicians sometimes treat clinically diagnosed BCC without histologic confirmation, especially when a patient presents simultaneously with multiple BCCs, of which only 1, or perhaps 2, will receive a skin biopsy. These characteristics complicate BCC registration and cause an unknown proportion of unregistered BCCs in population-based cancer registries every year.10

The aim of this study was to get a better estimate of the BCC “epidemic” by ascertaining the degree of underregistration of histologically confirmed BCCs due to registry rules and practices on reporting only first-ever primary BCCs or only 1 BCC per year in 4 different population-based European cancer registries (Finland, Malta, the southeast Netherlands, and Scotland). This estimate is of particular relevance for public health as reported numbers of first primary BCCs only do not correctly reflect the financial impact of these cancers on the European economy.11

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Group Information: A list of the members of the EPIDERM Group appears on page 353.
Four countries or regions with a population-based cancer registry collecting information on BCC were selected from different regions in Europe: Finland (Finnish Cancer Registry [FCR]), Malta (Maltese Cancer Registry [MCR]), Eindhoven—the southeast Netherlands (Eindhoven Cancer Registry [ECR]), and Scotland (Scottish Cancer Registry [SCR]).

These registries routinely collect information on BCC. Details of the registries are described elsewhere.6,7,12-14 According to the guidelines of the European Network of Cancer Registries, registries that record information on BCC are advised to use the International Agency for Research on Cancer/International Association of Cancer Registries rules for multiple tumors, implying that only a first tumor of a defined histologic type (in this case BCC) is registered as a new primary tumor. Notification of second or subsequent BCCs in the same individual may be recognized by updating the recorded morphologic code to 8091 (multifocal BCC).15 No human subjects committee approval was needed for this study.

SPECIFIC CANCER REGISTRY RULES

The few population-based cancer registries that collect information on BCC generally follow this guideline and register (or report) only the first BCC occurring in a patient. The registries included in this study all rely principally on histopathologic findings for BCC diagnoses and have the following specific registry rules:

In Finland, all histologically confirmed BCCs are reported to the FCR, regardless of being the first or subsequent BCCs. The FCR also receives some notifications on clinically diagnosed–only BCCs. In the MCR, all histologically confirmed BCCs are reported, regardless of being first or subsequent BCCs. The ECR routinely reports only the first primary histologically verified BCC per patient.1 However, because the ECR collects more information, more than 1 primary BCC can be registered per patient, according to the following rules: (1) when simultaneous multiple BCCs (ie, with incidence dates ≤3 months apart) occur on the same subsite, 1 primary tumor is registered using the morphologic code 8091 (multifocal BCC); (2) when simultaneous multiple BCCs occur on different subsites, 1 tumor per subsite is registered; (3) when a “new” BCC occurs on the same subsite as a previous BCC, this is considered a recurrence, and only date and origin are registered; and (4) when a “new” BCC occurs on a different subsite from the previous BCC, it is registered as a new primary tumor.

In the SCR, due to resource constraints, only the first occurrence of BCC in any individual is recorded according to the European Network of Cancer Registries rules using the date of first contact with the hospital as the date of diagnosis unless the patient is managed entirely by a general practitioner.6

MONITORING UNDERREPORTING OR UNDERREGISTRATION OF HISTOPATHOLOGICALLY VERIFIED BCCs BECAUSE OF THE OCCURRENCE OF MULTIPLE BCCs IN THE DIFFERENT REGISTRIES

Finland

The FCR routinely reports the first BCC and subsequent BCCs in different skin areas as defined by the topographic codes of the International Classification of Diseases for Oncology, Third Revision, with coding criteria as those in Eindhoven. Owing to coding of repeated subsequent BCCs in the same topographic areas of skin simply as “multiple,” only the first tumor in the skin area is reported. Only new tumors in new skin areas are reported during any year. These practices result in approximately half of the annually registered BCCs in the FCR being reported in their annual statistics. An audit of the cancer registry and hospital database was performed to estimate completeness of histopathologically verified BCC. All BCCs (n=787) diagnosed between November 1, 2009, and March 31, 2010, at the Skin and Allergy Hospital of the Helsinki University Hospital, the regional center for dermatology, were checked for inclusion in the FCR. Only 14 patients were missing from the FCR files, which had no histopathology report, causing them to be missed by the FCR as the information usually reaches the FCR through pathology laboratories, showing that information from pathology laboratories is well transferred to the FCR, and only the exclusion criteria and treating BCC without histopathologic confirmation affect the registered and reported numbers. Because data for the complete year of 2009 are available, those numbers are presented herein.

Malta and Eindhoven

Data from the MCR and the ECR were obtained for 2009 to investigate the occurrence of first and subsequent BCCs. Routine reports include only first primary BCCs, but all information on histopathologically confirmed BCCs is available from the registries, as described in the “Specific Cancer Registry Rules” subsection.

Scotland

From the SCR, all patients registered as having a first-ever BCC in 2006 (the most recent year for which the cancer registration data were essentially complete at the time the study was initiated) and living in the Dundee and Perth regions (postal codes beginning with DD and PH) were identified with their unique patient number, resulting in 578 unique patient numbers. Since a proportion of the patients were living outside of the hospital serving areas, the corresponding population sizes (age and sex specific) were corrected by the same proportion when calculating rates.

The pathology database of Ninewells Hospital records all pathology reports for NHS Tayside (the cities of Perth and Dundee, the districts of Perth and Kinross, Angus, and parts of North East Fife). From this database, all pathology reports for BCC (n=1025) in the DD and PH postal codes were analyzed for 2006. Of these 1025 pathology reports, there were 1017 unique reports (7 had supplementary reports issued) corresponding to 887 unique patients; the other 130 reports (12.8%) had duplicate patient numbers because patients presented with multiple BCCs in the same year or had subsequent surgery on the same BCC. The 578 patient records from the SCR were compared with those of the pathology database.

RESULTS

Tables 1, 2, 3, and 4 show the numbers of patients and the (age-standardized) incidence rates of BCC for the cancer registries included in this study. Incidence rates for first primary BCC were highest in the ECR area (the Netherlands), with a European standardized incidence rate of 158 per 100,000 person-years. The incidence was lowest for Malta, with a European standard-
ized incidence rate of 77, and Finland and Scotland had intermediate rates of 95 and 99. Overall, rates were higher in males than in females except for age groups younger than 70 years in the ECR and the FCR and in the youngest age group in the SCR. The incidence increased steeply with increasing age in all the registries (Figure 1), as did the difference between first and total BCC incidence rates.

It is apparent in Tables 1 through 4 that there were approximately 30% more patients with BCC and 40% to 100% more BCC tumors diagnosed in a given calendar year than patients with a first primary BCC, as routinely reported. The difference between the number of first primary BCCs and the total number of BCCs in a calendar year was generally slightly higher for males than for females and increased substantially with increasing age.

### FINLAND

In 2009, the FCR received 14,943 notifications of individual tumors with a diagnosis of BCC from all 67 pathology laboratories in Finland, which is the best available estimate of the total numbers of actual tumors removed. The 14,943 BCCs were diagnosed in 10,085 persons, translating to 1.48 BCCs per person (ie, many patients had several BCCs diagnosed in 2009). Of the 10,085 patients, 272 had a clinical notification only. Many of these 10,085 individuals had 1 or more BCCs diagnosed in previous years or on different body sites. Because only new BCCs arising in a new skin area are reported in the annual statistics, the 2009 annual statistics of the FCR reflect the new BCCs, including the number of patients with a first BCC should...
be multiplied by approximately 1.3 to achieve the total number of patients diagnosed as having a BCC in Finland in 2009; this multiplication factor depends on age (1.2 for those <45 years old at diagnosis and 1.4 for those ≥70 years) (Table 1). The number of patients with BCCs as routinely reported by the FCR was approximately half the actual number of BCC tumors diagnosed in 2009.

### MALTA

In Malta in 2009, 334 patients were diagnosed as having a first-ever primary, histologically confirmed BCC, of whom 57% were males and 43% were females. Seventeen persons developed 2 or more BCCs in 2009. However, in total, 420 patients received 1 or more diagnoses of BCC in 2009, including those who had a previously histologically proved BCC. In total, these 420 patients accounted for at least 447 BCC lesions diagnosed.

Based on these data, more than a quarter of the 420 patients diagnosed as having a BCC in Malta in 2009 had a previous BCC diagnosis (pre-2009); therefore, the MCR captures 34% more BCCs than registries that report statistics only. Among women, the highest percentage of additional BCC cases captured by the cancer registry was the highest in the oldest age group for males, with 42% additional cases compared with first primary statistics only. Among women, the highest percentage of additional cases was 26% found in the middle age group.

### SOUTHEAST NETHERLANDS: THE ECR

During 2009 in the ECR area, 4513 patients were diagnosed as having a first primary BCC, of whom 49% were...
men and 51% were women. However, in total, 5884 patients were diagnosed as having a BCC in 2009 and appeared in the ECR, who together had at least 6420 BCCs diagnosed in 2009. Thus, of all patients with BCCs diagnosed in 2009, 30% had not been reported in the incidence statistics because they had a previously diagnosed BCC lesion (pre-2009) (Table 3).

Thus, in the Netherlands, the annual number of patients diagnosed as having 1 or more BCCs in a year should be multiplied by a factor of approximately 1.3 to estimate the total number of patients diagnosed as having a BCC in a given year. This multiplication factor is at least 1.3 to 1.4 for the number of tumors. Stratifying for sex and age, reported numbers of first primary BCCs should be multiplied by 1.12 (young females) to 1.43 (elderly males) to obtain total numbers of patients diagnosed as having BCC in 2009 (Table 3).

**SCOTLAND**

In Scotland, comparing the 577 patient records in the SCR with the 887 patient records in the pathology database for 2006, 487 patients were present in both databases (Figure 2). Of the 90 patients who appeared in the SCR data set but not in the pathology data set, 53, despite having postal codes beginning with DD or PH, lived outside the hospital catchment area; 1 did not get a histopathologic confirmation; and 36 did not undergo surgery for BCC until 2007. The latter caused these patients to be registered for 2007 in the pathology database and for 2006 in the SCR database.

An additional 400 patients were registered in the pathology database but were not found in the SCR. Of these patients, 305 (76.3%) had a previous histologically proven BCC lesion (pre-2006) diagnosed at Ninewells Hospital, explaining their absence in the SCR records. Of the remaining 95 patients, 91 (95.8%) were allocated a 2005 incidence date in the SCR since their first contact with the medical profession was in 2005, but the date of the final pathology report was in 2006. Three cases were first diagnosed before 2006 while living in England and were considered ineligible for registration as they had their first BCC diagnosed while residing outside of Scotland, and 1 was a late supplementary pathology report that never appeared in the SCR.

In total, in Scotland, an estimated 34.5% of patients with a BCC (306 of 887) had been omitted on an annual basis because only the first-ever BCC is recorded (Figure 2). Age-specific incidence rates for first-ever BCCs in Scotland were lower than those reported in Finland and Eindhoven but higher than those in Malta. However, estimates on multiple BCCs show high incidence rates, particularly in the older age categories (Figure 1 and Table 4).

**COMMENT**

The results of this study confirm and update available information on BCC incidence in Europe, where age-standardized incidence rates of first primary BCCs are now estimated to be 77 to 158 per 100,000 person-years. It also shows that the total number of BCCs continues to be markedly underreported by cancer registries with a good record for registering other malignancies. The main reason for this occurrence is that most cancer registries that collect information on...
BCCs collected or report information on first primary BCCs only. The present data suggest that in the included registries, the total annual incidence rates and numbers are approximately 1.3 times higher compared with the incidence rates of first primary BCCs. The reported total number of BCCs diagnosed per year is a conservative estimation as multiple BCCs occurring on the same body site are counted as only 1 BCC, and some patients are marked as having “multifocal” BCCs without information on the exact number. In these multifocal cases, 2 BCCs were counted, but in many other cases, patients will have had more than 2 BCCs diagnosed.

In terms of first histologically verified primary BCCs, the registries are assumed to be almost complete, which was confirmed in this study for the Scottish and Finnish cancer registries: all but 1 diagnosed, first primary, histologically confirmed case from the hospitals were encountered in the SCR (99.8%) and the FCR (100%).

The problems of underregistration of the total number of BCCs arise because of lack of histologic verification and the occurrence of multiple primaries, both on the day of diagnosis and subsequent to the primary diagnosis. The present results indicate that the number of histologically verified patients who develop a BCC in a given year is approximately 20% to 35% lower than the total number of patients diagnosed as having a BCC. A previous study from Scotland compared the number of BCCs diagnosed during 2001 in a defined area served by a single pathology laboratory between the cancer registry data (first-ever BCC per individual) and the pathology laboratory records (all new incident cases, including multiple tumors in an individual but excluding rebiopsies, reexcisions, and recurrences). It was then estimated that the policy of registering only the first BCC per person is underestimating the true incidence by approximately one-third.6 The present values are similar to those previously recorded in Glasgow,10 Bristol,16 and South Wales.17

In Australia, a survey was performed to identify people treated for BCC in the previous year, showing high age-specific incidence and age-standardized incidence rates (world standard) of 1041 per 100 000 men and 745 for women. These age-standardized rates cannot be directly compared with the European standardized rates because of the lower average age distribution in the world standard population. Overall, self-reported incidence rates were higher in Australia than in the included European countries, as expected.

The extent of “underestimation” was higher in the elderly as they are more likely to have been affected by multiple tumors and seem to be at increased risk for multiple tumors compared with younger patients.10

Previous analyses suggest that the 3-year cumulative risk of a subsequent BCC after a first BCC is approximately 44%.9 Previous studies focused primarily on numbers of persons developing subsequent BCC lesions after their first primary BCC, ignoring the total numbers of BCC lesions occurring in these patients.

The numbers of cases and rates reported herein reflect the histologically confirmed BCCs in the cancer registry regions. Besides underregistration due to lack of information on subsequent BCCs, it is likely that further underregistration will result from medical or cryotherapy treatment of BCC without obtaining a tissue diagnosis. Moreover, the indolent nature of some BCCs makes it likely that a proportion of patients never present with them in a clinical setting during their lifetime and that they, therefore, remain undiagnosed.

If, indeed, many BCCs are diagnosed only clinically and are treated without histopathologic confirmation, the real numbers of BCCs diagnosed and treated annually will be even higher. The extent of “underregistration” due to the lack of a tissue diagnosis will depend on local practices of physicians treating BCCs, which are probably affected by the anatomical site of the BCC, reimbursement schemes, and local logistics regarding pathology confirmation. A previous study in Scotland found that most BCCs were confirmed by a tissue diagnosis. However, practices may vary within and across countries and may have changed with the advent of nonsurgical treatments, such as photodynamic therapy, cryosurgery, and imiquimod cream. It seems probable that tissue diagnosis may be lacking particularly in people who had multiple BCCs diagnosed previously and in elderly people with heavily sun-damaged skin. Some private (laser) clinics may also treat without performing biopsies.

Inclusion of clinically diagnosed cases would lead to an inflation of incidence rates that could be false depending on the positive predictive value of the clinical diagnosis of BCC. Little information is available on this, but one study from the United States suggests that the positive predictive value of a clinical diagnosis of BCC is 68% to 83%20-22 and 80% when the dermatologist is reasonably confident about the diagnosis.20 The only solution for this would be to encourage physicians who treat BCCs to always confirm their clinical diagnosis by collecting biopsy specimens in order for the lesions to be included in histopathology or cancer registry databases, which can be examined more easily than clinical records only. However, it may simply not be feasible or appropriate to pursue histologic confirmation in every case.

The results of this study confirm that studies of BCC incidence based on first incident BCC result in 30% to 50% lower numbers compared with the absolute number of histopathologically confirmed BCCs diagnosed per year, as patients often present with multiple tumors at the time of diagnosis and also often develop multiple tumors over time.

Estimates of the absolute numbers of BCC tumors diagnosed per year would provide more insights into the time needed for diagnosis, treatment, and follow-up of these lesions within the already limited time of dermatologists, plastic surgeons, and other health professionals involved in the care of patients with BCC. Accurate estimates of numbers are vital for optimal manpower-planning strategies to cope with the continuously growing group of patients with skin cancer, of whom patients with BCC constitute the largest proportion.3 In relation to manpower planning, the numbers of primary BCCs, biopsies, reexcisions and recurrences of a primary BCC, and specialized treatments (such as Mohs micrographic surgery) place a relatively large burden on
physicians' time, which is becoming increasingly scarce. Had health care planners reacted to the rising trends during the 1980s, there might be more manpower available to deal with this ever-increasing problem.

For cancer registries, it is almost impossible to collect information on every BCC as it is difficult for registry clerks to distinguish between rebiopsies, reexcisions, recurrences, and genuine new independent primary tumors occurring in the same location. One improvement that could be made is to include more detailed codes for body site location (topography), as was already advised in the European Network of Cancer Registries recommendation for nonmelanoma skin cancer, applied by the ECR and used to describe melanoma incidence by body site.

Exercises such as ours, performed occasionally, provide an estimate of the degree of underestimation that a report on first incident BCC provides compared with the absolute number of BCCs diagnosed in a certain population during a given period. These estimates should be made for each region and period specifically, as medical practice, age distributions, and risk profiles may differ considerably between populations and over time. It would be worthwhile to know whether the discrepancy between first and multiple BCCs differs between countries; in the 4 registries included in this study, findings were surprisingly similar, suggesting that it might be a consistent finding. Such exercises, repeated at regular intervals, would not only give insight into the burden of BCC in societies in terms of total numbers rather than of first primary BCCs only but would also add to our knowledge regarding the time trends of BCC.

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The Best of the Best

Top-Accessed Article: Handheld Dermatoscope as Capillaroscopic Instrument


Nail-fold capillaroscopy is a technique that aids in the early diagnosis of connective tissue diseases and in distinguishing primary from secondary Raynaud phenomenon. Its use was largely prompted by the 1973 work of Maricq and LeRoy,

1 who described the different capillaroscopic patterns in connective tissue disease, including dilation of capillary loops and focal loss of capillaries, using wide-field stereomicroscopy.

In their article, Bergman and colleagues demonstrate that the handheld dermatoscope, an instrument typically used by dermatologists for the diagnosis of pigmented lesions, is able to provide results comparable to those of traditionally used capillaroscopic devices in identifying patterns in the nail folds. Using an unmodified dermatoscope, they found a statistically significant increase in the frequency of the scleroderma-dermatomyositis capillaroscopic pattern in patients with scleroderma, dermatomyositis, and mixed connective tissue disease compared with that in their control group of healthy subjects.

The authors show that the dermatoscope provides a simple and effective means to perform capillaroscopy. Their work has helped to expand the applications of the standard dermatoscope and to make capillaroscopy more widely accessible to dermatologists.

From August 2009 through August of 2010, this article was viewed 2795 times on the Archives of Dermatology Web site.

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