



Incidence, Mortality, and Trends of Nonmelanoma Skin Cancer in Germany

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Increasing incidence rates (IRs) of nonmelanoma skin cancer (NMSC) in white populations have been described worldwide. Cancer registry data from the Saarland and Schleswig-Holstein federal states were used to analyze incidence and mortality trends in Germany. Age-standardized rates were compared with crude rates to assess disease burden. Joinpoint regression models were used to estimate annual percentage changes and 95% confidence intervals, allowing us to assess temporal trends between 1970 and 2012. Incidence predictions until 2030 were based on age-period-cohort models and linear extrapolation techniques. In the Saarland federal state, between 1970 and 2012, NMSC age-standardized and crude IRs increased 10- to 22-fold, respectively. In Schleswig-Holstein, between 1999 and 2012, NMSC age-standardized and crude IRs increased 250 cases/100,000 persons per year in 2012, with age-standardized IRs increasing 1.5-fold. During this period, NMSC mortality remained stable or decreased. For 2030, the predicted age-standardized IRs are as follows: males, 230 cases; females, 180–200 cases. The predicted crude IRs for the same year are males, 450–500 cases; females, 380–430 cases. There is a continuous long-term increase of NMSC incidence with no tendency for leveling off. By 2030, the current NMSC IR in Germany is expected to double.

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INTRODUCTION

Presently, skin cancer is the most frequent malignant neoplasm in white populations (Garbe and Leiter, 2009; Leiter et al., 2014; Nikolaou and Stratigos, 2014). Over the last four decades, nonmelanoma skin cancer (NMSC), mainly consisting of basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), has risen dramatically, and a steep increase of incidence has been described (Eisemann et al., 2014; Rudolph et al., 2015). The expression *skin cancer epidemic* has been coined to illustrate this phenomenon (Donaldson and Coldiron, 2011).

Accurate data on NMSC incidence and mortality evolution are difficult to obtain. Many cancer registries do not register NMSC or record only the first tumor (Katalinic et al., 2003; Rogers et al., 2015; Rudolph et al., 2015). Therefore, the true disease burden of skin cancer remains unclear and is often underestimated.

Increasing incidence rates of BCC and SCC have been reported in several European countries. A study from the Scottish cancer registry over a period of 12 years showed an annual increase of 1.4–3.5% (Brewster et al., 2007). The Danish cancer registry also evaluated the incidence rates of BCC and SCC, and over a period of 30 years the incidence rates have raised between 3.1% and 4.6% per year (Birch-Johansen et al., 2010). Finally, a German study including data from 11 cancer registries over a period of 13 years reported an annual increase of 3.3–11.6% for BCC and SCC (Rudolph et al., 2015).

NMSC is diagnosed mainly in older age groups. Because these groups are not appropriately represented when using age standardization for the European Standard Population (ESP), incidence and mortality rates (MRs) are artificially diminished. Therefore, the evolution of NMSC disease burden may be better characterized through crude incidence rates (CIRs) (Revenga Arranz et al., 2004; Tejera-Vaquero et al., 2016).

This study evaluated a time period of 43 years and extrapolated trends over a 60-year period from 1970 to 2030. To characterize the NMSC disease burden, CIRs have also been calculated. Registry data from the Schleswig-Holstein federal state (~2.8 million inhabitants) between 1999 and 2012 and from the Saarland federal state (~1.0 million inhabitants) between 1970 and 2012 were included in this analysis. The Schleswig-Holstein registry reports the highest incidence rates for NMSC, and the Saarland registry has the longest period of cancer registration in Germany.

RESULTS

NMSC incidence and mortality

Schleswig-Holstein federal state. Between 1999 and 2012, the NMSC age-standardized incidence rate (ASIR) in the male

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Abbreviations: AAPC, average annual percentage change; ASIR, age-standardized incidence rate; ASMR, age-standardized mortality rate; BCC, basal cell carcinoma; CI, confidence interval; CIR, crude incidence rate; CMR, crude mortality rate; MR, mortality rate; NMSC, nonmelanoma skin cancer; SCC, squamous cell carcinoma

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population increased from 125 to 170 (average annual percentage of change [AAPC] = +2.3%, 95% confidence interval [CI] = 1.6–3.0) and in the female population from 92 to 134 cases per 100,000 persons per year (AAPC = +3.3%, 95% CI = 2.5–4.1) (Figure 1a). A steeper rise has been observed for CIRs. Between 1999 and 2012 the CIRs increased from 147 to 278 in men (AAPC = +5.0%, 95% CI = 4.4–5.7) and from 143 to 241 in women (AAPC = +4.4%, 95% CI = 3.6–5.1) (Figure 1b and Table 1).

Between 1999–2001 and 2010–2012, the age-standardized MRs (ASMRs) decreased from 0.45 to 0.31 in men, and in women they were rather stable at 0.16 in 1999–2001 and 0.19 in 2010–2012 (Figure 1c). The corresponding crude MRs (CMRs) in men showed a slight decrease from 0.51 in 1999–2001 to 0.46 in 2010–2012, whereas in women a small increase from 0.40 to 0.46 was observed (Figure 1d and Table 2).

A trend toward decreasing MRs could also be observed for the age-specific MRs, with the greatest decline being reported among persons 75 years or older. In this subgroup, the MRs declined from 8.25 in 1999–2001 to 2.3 in 2010–2012 in males and from 3.42 to 3.23 in females. Over time, the lowest MRs were observed in patients 50 years or younger: MRs decreased from 0.07 in 1999–2001 to 0.04 in 2010–2012 in males and were stable in females at 0.08 for both time periods (data not shown).

The predicted ASIRs for 2030 are 232 for males and 204 for females (Figure 1e). For the same year, the predicted CIRs are 459 for males and 386 for females (Figure 1f).

Predicted age-specific incidence rates were also calculated until 2030. In the age groups of 60–79 years and greater than 80 years a dramatic increase to 1,250–2,000 in males and 900–1,100 in females is expected (Figure 1g and 1h).

Saarland federal state. Between 1970–1972 and 2010–2012, the NMSC ASIRs increased from 10.5 to 117.7 cases in males (AAPC = +6.0%, 95% CI = 4.8–7.1) and from 8.1 to 93.1 cases in females (AAPC = +6.3%, 95% CI = 5.4–7.2) per 100,000 persons per year (Figure 2a and Table 1).

In the same period, the CIRs increased from 8.4 to 186.1 in males (AAPC = +7.7%, 95% CI = 6.4–9.0) and from 9.1 to 163.1 in females (AAPC = +7.4%, 95% CI = 6.4–8.5) (Figure 2b and Table 1).

The NMSC ASMRs in males decreased from an average of 1.3 cases in the decade 1970–1979 to 0.6 cases in the decade 2003–2012. In females the corresponding rates were 0.8 and 0.3, respectively (Figure 2c and Table 2). The CMRs remained rather stable when comparing the two decades: 0.96 and 0.8 for males and 0.86 and 0.8 for females (Figure 2d and Table 2).

Age-specific MRs continuously decreased between 1970–1979 and 2003–2012. Throughout the entire observation period, the highest MRs were observed in persons 75 years and older. In this age group, MRs declined from 18.7 in the first decade to 6.3 in the last decade in males and from 13.9 to 5.4 in females.

In the same period, considerably lower MRs were observed in the youngest age group (50 years and younger). The MRs dropped from 0.02 to less than 0.01 in males and from 0.05 to 0.04 in females (data not shown).

For 2030, the predicted ASIRs are 230 for males and 180 for females (Figure 2e). The predicted CIRs for the same year are 510 for males and 440 for females (Figure 2f).

The predicted ASIRs were calculated for both sexes until 2030 (Figure 2g and h). In age groups of 60–79 years and older than 80 years, an increase to 1,115 and 1,900 in males and to 800–1,290 in females is expected.

DISCUSSION

The continuously increasing incidence rates of NMSC are the most striking observation in skin cancer epidemiology in Germany. This is better illustrated using data of the Saarland Cancer Registry (Figure 2), which documented incidence and mortality of NMSC over a period of more than four decades.

Because for most German federal states a complete cancer registration over a chronological period is not yet available, our analysis refers to two registries that have a stable registration with a completeness of more than 90%. Approximately 70% of the NMSCs are classified histologically as BCC and 27–28% as SCC (Rudolph et al., 2015). However, a histological subclassification is not routinely performed. Therefore, we did not consider histologic subtypes.

To evaluate NMSC incidence and mortality, we performed ASIR and CIR trend analyses for two different geographical regions. The European Standard Population underrepresents elderly patients with the highest disease burden. To account for the current age distribution in the German population, we have also analyzed CRIs and CMRs in addition to age-standardized rates. This may help to make reasonable decisions regarding allocation of limited resources toward effective disease control.

An analysis of cancer registry data from 1998 through 2010 from 14 federal states in Germany shows a continuous 2.4-fold increase of NMSC incidence rates (Eisemann et al., 2015), which corresponds to an increase of 10.5% per year until 2003 and 6.7% thenceforward. Similar observations were made for a screening pilot project in Schleswig-Holstein in the years 2003 and 2004 (Eisemann et al., 2014; Waldmann et al., 2012a, 2012b).

The introduction of skin cancer screening examinations, reimbursed by health insurances from July 2008 onwards probably has led to higher detection rates and a further increase of observed incidence rates in the Saarland Cancer registry (Figure 2a and b). However, as the result of a pilot project for skin cancer screening, which was performed in 2003, an earlier increase of CIR was observed in Schleswig-Holstein (Figure 1a and b). Therefore, overdiagnosis has to be discussed as a limitation of this analysis. Because many NMSCs never cause symptoms or death during a patient's lifetime, they are often not detected until the patients attend screening programs. Early forms of skin cancer that would never have harmed patients are diagnosed and subsequently treated. This is true for patients older than 60 years who attended skin cancer screening programs most frequently (36%) compared with other age groups. (Augustin et al., 2012).

Another reason for the rapid increase could be the improvement in the NMSC registration process in Germany, where estimations are gradually becoming more close to reality. However, it should be mentioned that

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