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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 crude IRs doubled, reaching 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.

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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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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-Vaquerizo 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

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

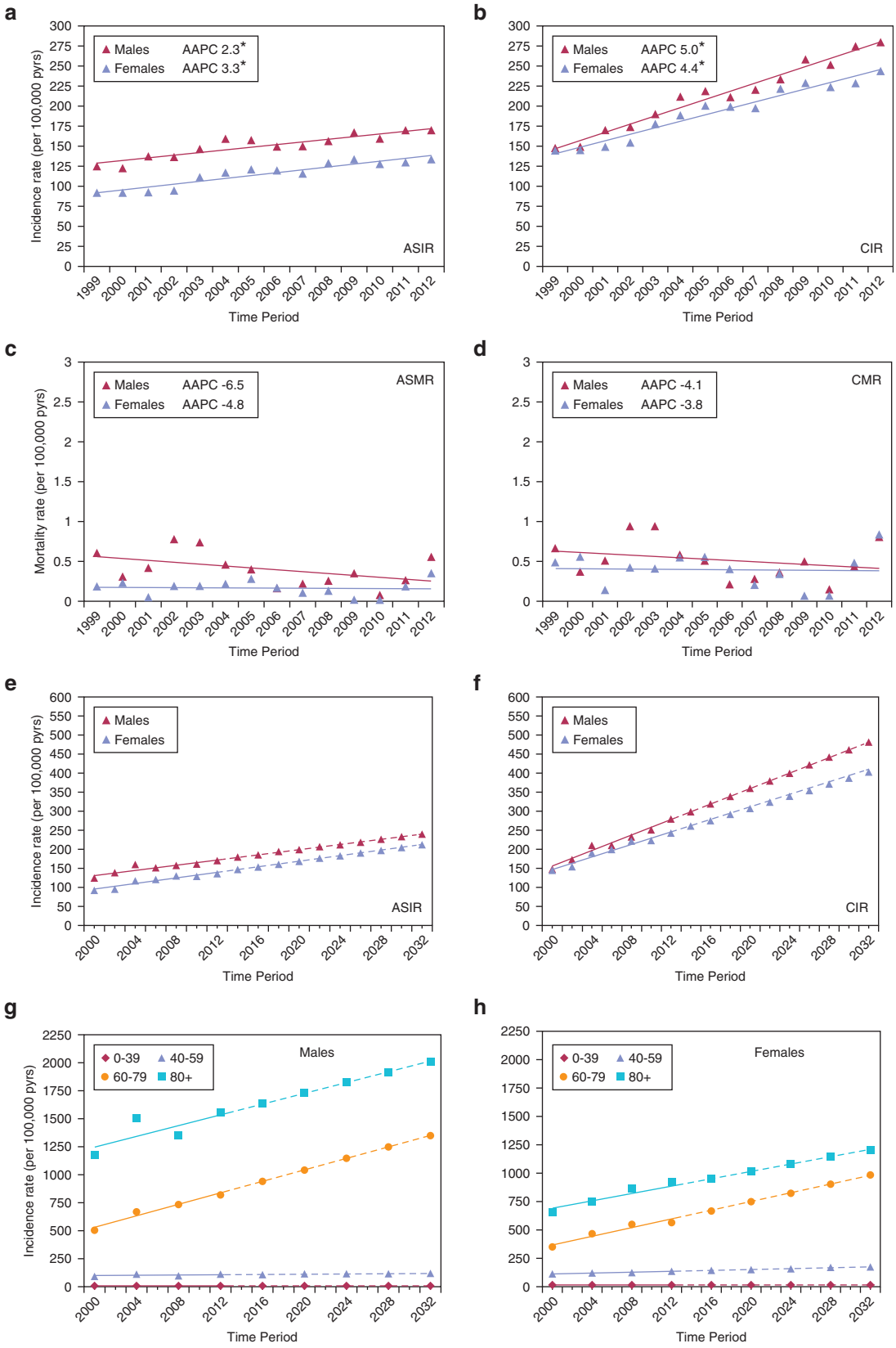

Figure 1. Incidence and mortality rates of nonmelanoma skin cancer per 100,000 persons per year for the Schleswig-Holstein federal state. (**a**) Age-standardized incidence rates according to the European standard population, (**b**) crude incidence rates, (**c**) age-standardized mortality rates according to the European standard population, (**d**) crude mortality rates, (**e**) prediction of age-standardized incidence rates according to the European standard population until 2030, (**f**) prediction of crude incidence rates until 2030, (**g**) prediction of age-specific incidence rates for males until 2030, and (**h**) prediction of age-specific incidence rates for females until 2030. *AAPC is significantly different from zero at $\alpha = 0.05$. AAPC, average annual percentage change; pyrs, per year.

Table 1. Age-standardized and crude incidence rates per 100,000 persons and year by sex[1]

	Age-Standardized Incidence Rates					Crude Incidence Rates				
Region	Time Period		% Change	EAPC[2] (95% CI)	AAPC[2] (95% CI)	Time Period		% Change	EAPC[2] (95% CI)	AAPC[2] (95% CI)
Schleswig-Holstein	**1999**	**2012**				**1999**	**2012**			
Males	125.3	169.6	+35.4	1999–2012:	2.3[2] (1.6–3.0)	146.6	277.5	+89.3	1999–2012:	5.0[2] (4.4–5.7)
Females	91.5	133.8	+46.2	1999–2012:	3.3[2] (2.5–4.1)	143.1	240.6	+68.1	1999–2012:	4.4[2] (3.6–4.1)
Saarland	**1970–1972**	**2010–2012**				**1970–1972**	**2010–2012**			
Males	10.5	117.7	+1,021	1970–1989: 11.1[2] (10.5–13.0) 1989–2003: -2.1[2] (−4.0 to −0.1) 2003–2012: 7.1[2] (3.5–10.8)	6.0[2] (4.8–7.1)	8.4	186.1	+2,115	1970–1989: 13.1[2] (11.7–14.5) 1989–2002: −0.6 (−3.0 to 1.9) 2002–2012: 8.9[2] (5.4–12.6)	7.7[2] (6.4–9.0)
Females	8.1	93.1	+1,049	1970-1989: 10.9[2] (9.9–11.8) 1989-2002: −1.4 (-3.1–0.4) 2002-2012: 8.0[2] (5.5–10.5)	6.3[2] (5.4–7.2)	9.1	163.1	+1,692	1970–1989: 12.8[2] (11.6–13.9) 1989–2001: −0.8 (−2.8 to 1.1) 2001–2012: 8.8[2] (6:0–11.6)	7.4[2] (6.4–8.5)

Abbreviations: AAPC, average annual percentage change; CI, confidence interval; EAPC, estimated annual percentage change.
[1]Trends in percentages for nonmelanoma skin cancer in the federal states of Schleswig-Holstein and Saarland.
[2]EAPC or AAPC is significantly different from zero at $\alpha = 0.05$; age standardization based on the European standard population.

population-based cancer registries record only the first tumor for a particular localization and consider all subsequent NMSCs as recurrences. Therefore, because recurrences and multiple NMSCs are common, NMSC ASIRs and CIRs do not reflect the actual disease burden (Stang, 2007). An Australian publication shows that up to 50% of patients with NMSC develop additional tumors (Keim et al., 2015).

Increasing ASIRs were also recorded in other European countries, the United States, and Australia (Lomas et al., 2012; Trakatelli et al., 2007). NMSCs show higher ASIRs in men compared with women (Brewster et al., 2007; Kim and Armstrong, 2012; Trakatelli et al., 2007). However, in The Netherlands and in Denmark, steeper increases in female ASIRs were observed (Birch-Johansen et al., 2010; de Vries et al., 2005; Hollestein et al., 2012; Jensen et al., 2012). An analysis of the Danish cancer registry data found increasing ASIRs in both sexes, yet the rise with respect to BCC and SCC was significantly higher among women than men (Birch-Johansen et al., 2010). Increased incidence of BCC could be caused by increased outdoor activities that increase sun exposure or by the use of tanning beds.

NMSC MRs developed differently in Schleswig-Holstein and in Saarland. In Schleswig-Holstein, a clear decrease in MRs (until 2010) was observed for both sexes. This was likewise true for ASMRs and for CMRs. The CMRs dropped to 0.2 cases per 100,000 person years in 2010, whereas they ranged between 0.5 and 0.7 in 1999. In Saarland, ASMRs also showed a trend toward lower rates, whereas CMRs showed a more stable situation: from 1970 through 2012, no clear trend was visible. A possible explanation could be the fact that in Schleswig-Holstein, NMSCs were detected in an earlier stage because of the implementation of skin cancer screening (Eisemann et al., 2015). Similar results were found in The Netherlands, where NMSC mortality had an annual decrease of −1.9% between 1989 and 2008 (Hollestein

Table 2. Age-standardized and crude mortality rates per 100,000 persons and year by sex[1]

	Age-Standardized Mortality Rates				Crude Mortality Rates			
Region	Time Period		% Change	AAPC[2] (95% CI)	Time Period		% Change	AAPC[2] (95% CI)
Schleswig-Holstein	1999 −2001	2010 −2012			1999 −2001	2010 −2012		
Males	0.45	0.31	−31.1	1999–2012: −6.5 (−13.6 to 1.2)	0.51	0.46	−9.8	1999–2012: −4.1 (−11.3–3.6)
Females	0.16	0.19	+18.8	1999–2012: −4.8 (−16.8 to 8.9)	0.40	0.46	+15.0	1999–2012: −3.8 (−14.2 to 7.9)
Saarland	1970 −1979	2003 −2012			1970 −1979	2003 −2012		
Males	1.3	0.6	−53.8	1970-2012: −4.3 (−10.9 to 2.9)	0.96	0.8	−16.7	1970–2012: −2.0 (−7.7 to 4.2)
Females	0.8	0.3	−62.5	1970-–2012: −2.5 (−6.6 to 1.9)	0.86	0.8	−7.0	1970–2012: 0.3 (−4.1 to 4.8)

Abbreviations: AAPC, average annual percentage change; CI, confidence interval.
[1]Trends in percentages for nonmelanoma skin cancer in the federal states of Schleswig-Holstein and Saarland.
[2]AAPC is significantly different from zero at $\alpha = 0.05$; age standardization based on the European standard population.

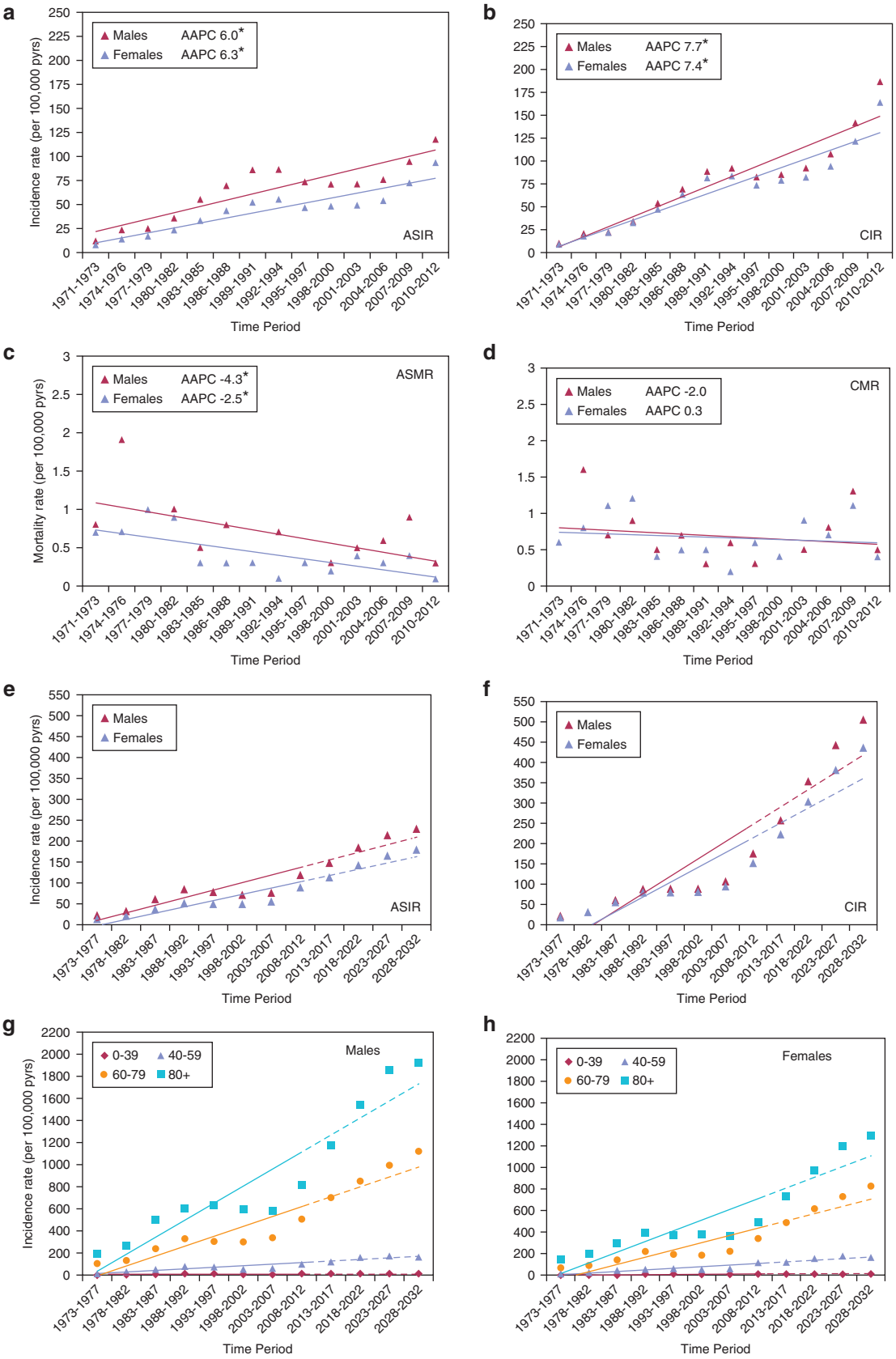

Figure 2. Incidence and mortality rates of nonmelanoma skin cancer per 100,000 persons per year for the Saarland federal state. (**a**) Age-standardized incidence rates according to the European standard population, (**b**) crude incidence rates, (**c**) age-standardized mortality rates according to the European standard population, (**d**) crude mortality rates, (**e**) prediction of age-standardized incidence rates according to the European standard population until 2030, (**f**) prediction of crude incidence rates until 2030, (**g**) prediction of age-specific crude incidence rates for males until 2030, and (**h**) prediction of age-specific crude incidence rates for females until 2030. *AAPC is significantly different from zero at $\alpha = 0.05$. AAPC, average annual percentage change; pyrs, per year.

et al., 2012). This is also in line with studies from the United States (Lewis and Weinstock, 2007).

The decreasing MRs cannot be explained by a more rapid increase of BCC than SCC incidence. For the period between 1998 and 2010, data from 11 cancer registries in Germany showed an increase of 141% for BCC ASIRs and of 187% for SCC ASIRs (Rudolph et al., 2015). Likewise, in Scotland a higher increase of ASIRs was reported for SCC compared with BCC (Brewster et al., 2007). The decline in disease-specific MRs may be caused by earlier detection and treatment. Skin cancer screening and increased awareness about the disease has certainly contributed to early detection, which has been noticeable in Germany since the 1990s. A further reason might be that the increasing incidence rates are especially seen in the oldest age groups. These patients often have other comorbidities and predominantly die of reasons other than NMSC. Other publications also show a low rate of disease-specific deaths and a decrease of MRs over time (Lewis and Weinstock, 2004, 2007; Stang and Jockel, 2004).

BCC may barely contribute to the NMSC MR. In Denmark, the incidence of metastatic BCC was estimated to be 1 case per 14,000,000 (Nguyen-Nielsen et al., 2015), and assuming there are 2 more patients per 14,000000 dying from locally advanced BCC (Sekulic et al., 2012), then a MR of approximately 0.02 per 100,000 is to be expected. A Danish analysis showed stable MRs for BCC but increasing rates for SCC and discussed the confounding factors associated with differences in immunosuppression and chronic diseases that influenced the all-cause mortality (Jensen et al., 2008). Therefore, these registry analyses discuss an overestimation of SCC-specific mortality (Hollestein et al., 2012; Jensen et al., 2008).

Unfortunately, in the cancer registries, there are no documented data on comorbidities like immunosuppressive conditions. Data from both registries showed that MRs are strongly associated with sex and age. NMSC mortality was higher among men than women throughout the studied period. This was particularly true for the ASMRs (Table 2 and Figures 1c and d and 2c and d). Mortality from NMSC increased with age and was highest among persons 75 years and older, which is concordant with other publications (Lewis and Weinstock, 2004, 2007; Stang and Jockel, 2004).

We extrapolated current trends of the NMSC development incidences until 2030 to give a possible prediction of the skin cancer disease burden in the future. Two different methods (linear extrapolation and age period cohort model) were applied to project future incidence rates. Sensitivity analyses have shown that there are only minor differences between the methods: predicted CIRs estimated through linear extrapolation were slightly lower than those based on the age period cohort model. This suggests the presence of age-related cohort effects, which may be more accurately represented by models that take into account any cohort effects. Especially in the age groups of 60 years and older, a steep 2-fold increase of the IR may be expected for both cancer registries, predominantly in men. Similar findings from The Netherlands extrapolate ASIRs of 49.7 for men and 29.8 for women in 2020 (Hollestein et al., 2012), showing a 1.5-fold increase. Predictions based on different databases showed similar trends, and we expect at least a doubling of incidence rates during the next 15 years. Our assumption is based on the fact that a latency period of around 20–30 years exists between exposure to causative carcinogens and development of skin cancer. Thus, people developing skin cancer during the next 15 years have seemingly already accumulated their UV exposure-induced mutations. Future successes in preventive behavior may not influence this development to a large extent. Moreover, in 2025, 25% of the German society will be older than 65 years and thus will have a high risk for NMSC (Statistisches Bundesamt, 2016).

We do not expect a leveling off of CIRs before 2050. Skin cancer prevention campaigns have not yet altered UV protective behavior in a sustainable fashion.

The trend for sunny holidays seems still to be unbroken, and people still desire a suntan to feel attractive. Furthermore, the protective potential of sunscreens is largely overestimated in the setting of intentional sun exposure. So far, to the best of our knowledge, there are no study results showing any cancer protective effects of sunscreens for sunbathing (Autier et al., 2007).

We will have to face a tremendous increase in NMSC CIRs in the next decades. It is unlikely that dermatologists alone will be able to manage all the NMSC cases in future. Therefore, general practitioners may play a greater role in the management of skin cancer, and they must be trained and prepared for this challenge.

There are a number of limitations for such predictions: (i) ongoing increase of life expectancy, which may lead to a higher overall disease burden, was not considered; (ii) immigration of younger people of non-white ethnicities with decreased NMSC burden, which may further affect future incidence rates, was not considered; (iii) implications of early detection activities in the future, which may result in additional removal of preinvasive tumors, and subsequently, reduced incidence rates of NMSC, were not considered; however, the experience of the last decades favors the hypothesis of the continuous increase of incidence rates and (iv) a limitation of cancer registries in general is the fact that the disease-specific mortality is documented on the basis of death certificates. Therefore, an underestimation of mortality caused by NMSC should be taken into account; however, this may be applied for all cancer entities. Lewis and Weinstock (2004) showed that for NMSC, there is a significant proportion of misclassified deaths, especially for mucosal NMSC (which accounted for 50% of all NMSC deaths but which were not a topic of this analysis).

In addition to these issues, the further points require careful consideration: (i) possible under-ascertainment of NMSC because of underreporting, because in many federal states only one notification of an NMSC tumor is accepted and reimbursed by the population-based cancer registries, and (ii) the less frequent use of invasive diagnostics in the elderly, which diminishes the number of correctly diagnosed skin cancers. The estimates of NMSC incidence reported in this study may therefore actually underestimate the real burden of NMSC to some extent (Muir and Percy, 1991).

In conclusion, there was a continuous long-term increase of the NMSC incidence in Germany in the past decades, with no tendency for leveling off in recent years. Furthermore, both the NMSC risk and disease burden will most probably continue to substantially increase in the future because of

increased UV exposure and an aging population. However, there is evidence that NMSC mortality at the same time will remain stable or even decrease.

MATERIALS AND METHODS

Cancer registry and population data

Data on incidence and mortality were used from the two German federal states of Schleswig-Holstein and Saarland. Both registries provide high-quality cancer data with a high level of case ascertainment (>90%) (Robert Koch Institute et al., 2015). The registries obtain notifications from hospitals, outpatient clinics, general practitioners, and pathology laboratories, as well as death certificates. Based on record linkage methods, these data are combined to derive data representing disease cases rather than tumors, and to estimate the cancer risk and disease burden on a population level. The proportion of patients with a death certificate-only notification is a good indicator for the completeness of case ascertainment.

The Saarland Cancer Registry has a long period of registration and has provided data on NMSC since 1970 (Saarland Cancer Registry, 2016). In 2012, 1,017 NMSCs were reported in men and 997 in women. These account for about 30.4% of all malignancies. In the same year, the proportion of death certificate-only–notified cases for all invasive cancers combined was 5.4%. The Schleswig-Holstein registry provided data on NMSC for the period 1999–2012 based on the same inclusion criteria (Schleswig Holstein Cancer Registry, 2016). Schleswig-Holstein had 2.8 million inhabitants in 2014. In 2012, the number of NMSCs was 4,756 for men and 4,254 for women. These account for 26.2% of all malignancies. Also in 2012, the proportion of death certificate-only cases for all invasive cancers in Schleswig-Holstein was 13.0%. The completeness of registration in both registries was greater than 90% (Schleswig Holstein Cancer Registry, 2016).

Historic and forecast population sizes and age distribution for the Saarland federal state (1973–2035) and Schleswig-Holstein Federal State (1999–2035) were retrieved from the Federal Statistical Office (Statistisches Bundesamt, 2016).

Population figures for 1970–2012 (Saarland Cancer Registry, 2016) and for 1999–2014 (Schleswig Holstein Cancer Registry, 2016) and forecasts of population size and structure in 2015–2030 were used to estimate the possible evolution of the population by 2030. Population data were retrieved from the Online Database "Genesis" of the Federal Statistical Office. Calculations are given for sex and age groups.

Frequently, ASIRs and ASMRs, based on the European Standard Population, are used to compare incidence and mortality over time with other populations and to evaluate changes in the prevalence of risk factors. However, the European Standard Population no longer matches with the age structure of the present population in Germany (see Supplementary Figure S1 online). Therefore, we also evaluated CIRs and CMRs to more appropriately characterize the NMSC disease burden.

Time trends and incidence predictions

The time trends analyses were performed with the Joinpoint Regression Program, using linear regression to model the logarithm of incidence and MRs (Kim et al., 2000). Estimated annual percentage changes and 95% CIs were estimated for NMSC incidence and disease-specific mortality stratified by sex and age.

Two different methods were used to predict incidence rates up to 2030:

Incidence predictions for Saarland were based on modified age-period-cohort models with a power link function. ASIRs and CIRs were modeled as a function of age, calendar period, and birth cohort using the R statistical software package NORDPRED (Moller et al., 2002).

A simple linear extrapolation technique was used to predict incidence rates for Schleswig-Holstein (where data since 1999 are available) (Dyba and Hakulinen, 2000; Hakulinen and Dyba, 1994). Predictions of ASIRs were based on linear regression models with common slope parameters for all age groups together. To predict age-specific incidence rates and CIRs, each age group had to be modeled separately.

In sensitivity analyses, we checked the performance of the linear model by applying both methods (the modified age-period-cohort model and the linear regression model) to the Saarland data (see Supplementary Table S1 online).

Methodological details are available in the Supplementary Material online.

CONFLICT OF INTEREST

The authors state no conflict of interest.

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SUPPLEMENTARY MATERIAL

Supplementary material is linked to the online version of the paper at www.jidonline.org, and at http://dx.doi.org/10.1016/j.jid.2017.04.020.

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