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INVESTIGATIVE REPORT

Non-melanoma Skin Cancer and Ten-year All-cause Mortality: A Population-based Cohort Study

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Confounding from comorbidity and socioeconomic status may have biased earlier findings of all-cause mortality among patients with basal cell carcinoma (BCC) and squamous cell carcinoma (SCC). We therefore examined all-cause mortality among 72,295 Danish patients with BCC, 11,601 with SCC, and 383,714 age- and gender-matched population control cohort subjects with extensive control for comorbidity and socioeconomic status. Data on cancer, death, and socioeconomic status were obtained from medical databases and Statistics Denmark. We analysed data using Cox regression analysis, with estimation of 10-year mortality rate ratios (MRRs) and 95% confidence intervals (CI). Mortality was reduced among patients with BCC (10-year MRR = 0.91 (95% CI: 0.89–0.92) and did not vary by age, comorbidity, or socioeconomic status. Mortality among patients with SCC was increased and varied by age, selected chronic diseases, but not socioeconomic status. The reduced mortality observed among patients with BCC and the increased mortality among patients with SCC persisted even after extensive control for comorbidity and socioeconomic status. ***Key words: all-cause mortality; basal cell carcinoma; squamous cell carcinoma; registry study; epidemiology.***

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Intermittent exposure to ultraviolet light (UV) is the main risk factor for basal cell carcinoma (BCC) (1), whereas risk factors for squamous cell carcinoma (SCC) include cumulative UV exposure (2), immunosuppressive treatments, cutaneous viral carcinogens, chemical carcinogens, ionizing radiation, phototherapy, and associated comorbidities (3–7). An earlier Danish study reported differential mortality patterns among patients with BCC and those with SCC (8); all-cause mortality was reduced among Danish patients with BCC (standardized mortality ratio (SMR) = 0.97; 95% confidence interval (CI): 0.96–0.98), but increased among patients with SCC (SMR = 1.30; 95% CI: 1.26–1.33), compared with expected mortality rates in the general population. In contrast, the US Cancer Prevention Study II study, which included 35,062 non-melanoma skin cancer (NMSC) patients and 1,061,844 controls, reported slightly increased all-cause mortality among patients with NMSC, with a mean length of follow-up of 12 years (9). This study did not separate NMSCs into BCC and SCC.

The differential mortality pattern among patients with BCC and those with SCC can probably be explained by the different aetiologies underlying these two common cancers. Alternatively, the discrepancy in results may stem from differences in setting, adjustments for covariates, and type of NMSC. Also, the studies might be subject to potential uncontrolled confounding from comorbidity and socioeconomic status (SES). Sun-exposure may be associated with SES, which in turn affects morbidity and mortality (10, 11). Similarly, the risk of SCC is strongly associated with a number of chronic diseases, and comorbidity itself is a strong predictor of mortality. We therefore examined 10-year all-cause mortality in a large cohort of Danish patients with BCC and SCC registered in the Danish Cancer Registry (DCR) from 1990 to 2005, compared with mortality among age- and gender-matched population control cohort subjects. SES and detailed information on comorbidity were included in the analysis.

MATERIALS AND METHODS

We conducted this nationwide population-based cohort study in Denmark, which has a population of approximately 5.3 million inhabitants (12). The entire Danish population receives tax-supported healthcare from the National Health Service, including free access to hospital care. We were able to perform unambiguous record linkage using the unique 10-digit civil registry number (CPR number) assigned to all Danish residents, which encompasses date of birth and gender (12).

Study cohorts

We identified all patients with a diagnosis of BCC or SCC recorded in the DCR from 1990 to 2005. The DCR has collected information on primary cases of cancer on a nationwide basis since 1943, and its data has been shown to be 95% complete with a validity of 98% (13). However, regarding NMSC registration the DCR is less complete. In 1995, we estimated the incompleteness of BCC registration to 33% and the incompleteness of SCC registration to 25%. The incomplete registration was, however, non-differential regarding NMSC mortality (14). DCR files include information on cancer type, site, morphology, and cancer history. The DCR has coded tumours according to the

10th revision of the International Classification of Diseases (ICD-10) since 1978, and, in addition, according to the third version of the International Classification of Diseases for Oncology (ICD-O-3) (15), which includes a four-digit code for tumour morphology. Throughout the study period, ICD-10 codes were generated by uniform conversion of the two ICD-O-3 codes (topography and morphology) for each case.

We first identified patients with NMSC using ICD-10 codes C44.x, covering all non-melanoma skin cancer diagnoses. We then identified patients with BCC with the following ICD-O-3 morphology codes: 80903 (BCC), 80913 (multicentric BCC), 80923 (BCC, morphea type), 80933 (BCC, fibroepithelial type), 80943 (BCC, basosquamous carcinoma), and 80953 (BCC, metatypical carcinoma). We identified patients with SCC using ICD-O-3 codes 80513 (verrucous carcinoma), 80523 (SCC, papillary), 80703 (SCC), 80713 (keratinized SCC), 80743 (SCC, spindle cell type), 80753 (SCC, adenoid), and 80763 (micro-invasive SCC). Patients with BCC who developed a SCC after/or on the date of their primary BCC were grouped with patients with SCC.

Population control cohort subjects and mortality data

The Civil Registration System (CRS) contains information on vital status, date of death, and residence of all residents of Denmark, and is updated daily. For each NMSC patient, approximately five population control cohort subjects were chosen from the CRS, matched on age, gender and calendar year, and selected on the date of their corresponding patient's NMSC diagnosis (index date). Follow-up data on all-cause mortality and migration for patients and population control cohort subjects were obtained from the CRS.

Data on comorbidity

We controlled for the impact of comorbidity on BCC and SCC mortality by classifying diagnoses of chronic diseases into 23 categories, based on a modified version of the Charlson Comorbidity Index (CCI) (16). The CCI is a validated index developed to predict 1-year patient mortality on the basis of comorbidity data obtained from hospital chart review (17, 18). In our study, comorbid diseases were categorized based on diagnosis codes in the Danish National Patient Registry (DNPR) and coded using the International Classification of Disease (ICD)-8 version through 1993 and the ICD-10 version thereafter. Data on comorbidities were collected until the BCC or SCC diagnosis date of each patient and index date of the population control cohort. The DNPR contains 99.4% of all discharge records from Danish non-psychiatric hospitals, and since 1994 outpatient specialist and emergency room visits also have been included (19). The relevant ICD-8 and ICD-10 codes associated with the comorbidities under study, which we broadly divided into diseases associated with immunosuppression, obesity, smoking, alcohol, and others, are shown in Appendix I (available from http://adv.medicaljournals.se/article/abstract/10.2340.00015555-0899/app1).

Data on socioeconomic status

Databases maintained by Statistics Denmark since 1980 (updated annually on December 31) provide detailed data on SES for the entire Danish population. We used four variables to classify SES among patients with BCC and those with SCC and their population control cohorts: occupational level, education attainment, income, and marital status (20, 21). Information on marital status and education was obtained as of the diagnosis/index date. For occupational level and income, information was obtained for the time-point 10 years prior to the diagnosis/index date, because occupational group and income variables are based on employment status, and NMSC patients tend to be elderly and retired when they are diagnosed. It was assumed that occupational group and income 10 years prior to diagnosis would give a more accurate picture of overall occupational and income status (20).

We used four occupational levels to classify SES: persons with high SES were defined as directors and those with a high-level or executive position; the second highest SES level included all occupations below an executive position; the next level was comprised of the unemployed; disability pensioners made up the lowest level (20). Education-based SES was comprised of three levels: high SES was defined as higher education >4 years in duration, medium SES was defined as higher education 1–4 years in duration, and low SES was defined as no higher education (or high-school diploma only). However, many patients and population control cohort subjects had missing educational information (32% of patients with BCC and their population control cohort subjects, and 52% of patients with SCC and their population control cohort subjects). The reason is that the cohorts of patients with BCC and with SCC were mainly above 50 years of age on their diagnosis date, and information on educational level was unavailable until 1980 (i.e. the year the database was established in Statistics Denmark). We carried out the analyses both with and without highest educational attainment and found that this variable did not change our estimates. For this reason we excluded education in the final analyses.

Income-based SES was divided into four groups according to quartiles of national average income for a given year. Marital status was categorized as married/cohabiting, divorced/widowed, and never married as of the diagnosis or index date.

Statistical analyses

We estimated 10-year cumulative mortality for NMSC patients and population control cohort subjects using the Kaplan-Meier technique (22). The follow-up period began on the diagnosis/index date of NMSC patients and population control cohort subjects and ended 10 years after this date, the date of emigration, the date of death, or on 31 December 2008, whichever occurred first.

Cox's proportional regression analyses were used to compute the hazard ratio as an estimate of the 10-year mortality rate ratio (MRR) among patients with NMSC compared with their age- and gender-matched population control cohort subjects, with associated 95% confidence intervals (CI). All analyses were mutually adjusted by age group, gender, each of the 23 comorbid disease categories, and each SES group.

To evaluate the effect on BCC and SCC patients' mortality, presence of comorbidities (using the 23 disease categories), and SES level, we stratified analyses among sub-cohorts of patients with BCC and with SCC and their population control cohort subjects based on the following variables: lack of history of recorded comorbidities, presence of the same comorbidity history, and presence of the same SES levels. As age and comorbidity are associated, we further stratified our analyses by age (e.g. according to three age-groups: < 60, 60–70, > 70 years for patients with BCC and their population control cohort subjects, and < 70, 70–80, and > 80 years for patients with SCC and their population control cohort subjects. We choose different age-group categories for patients with BCC and SCC, because patients with BCC on average are 10 years younger than patients with SCC at diagnosis).

In analyses disaggregated by age group (< 70, 70–80, and > 80 years) for SCC, the assumption of proportional hazards was found appropriate in all models. Statistical analyses were performed using Stata 10.1 software (StataCorp., College Station, Texas, USA; copyright: 1984–2009). The study was approved by the Danish Data Protection Agency.

RESULTS

Descriptive data

Our study included a total of 72,295 patients with BCC and 327,859 population control cohort subjects and 11,601 patients with SCC and 55,855 population control cohort subjects. Of the 11,601 patients with SCC, a total of 2058 (18%) developed SCC on or after the date of their primary BCC. The median age of patients with BCC was 68 years (quartiles: 56–77; range: 8–104 years), and 53% were females. Patients with BCC had the same level of comorbidity and a slightly higher SES according to all SES groups than their population control cohort subjects (Tables I and II).

The median age of patients with SCC was 78 years (quartiles: 69–84; range: 17–106 years), and 35% were females. Patients with SCC and their population control cohort subjects had a similar SES level (Table I). A higher proportion of patients with SCC had a history of comorbidities as of their diagnosis date, compared with their population control cohort. Notably, the prevalence of diseases associated with immunosuppression, obesity, smoking and alcohol was particularly elevated among patients with SCC (Table II).

All-cause mortality among patients with BCC compared with their population control cohort subjects

The crude 10-year MRR was 0.93 (95% CI: 0.91–0.94) and the adjusted 10-year MRR was 0.91 (95% CI: 0.89–0.92) for patients with BCC compared with their population control cohort subjects. Ten-year MRRs did not change when we restricted the analyses to patients and population control cohort subjects who had no recorded hospitalizations as of their diagnosis/index date, or when we disaggregated the analyses by age group (Table III). Ten-year MRRs also did not change in stratified analyses focusing on patients with BCC and population control cohort subjects in each of the 23 comorbid disease categories, those with a history of hospitalizations, or those with the same SES level (data not shown).

All-cause mortality among patients with SCC compared with their population control cohort subjects

Analyses of patients with SCC and their population control cohort subjects encompassed three age groups: < 70, 70–80, and > 80 years. For patients with SCC aged < 70 years as of their diagnosis/index date,

Table I. *Characteristics of non-melanoma skin cancer patients and their population control cohort subjects*

	Patients with BCC *n* = 72,295 *n* (%)	Population cohort subjects (for patients with BCC) *n* = 327,859 *n* (%)	Patients with SCC *n* = 11,601 *n* (%)	Population cohort subjects (for patients with SCC) *n* = 55,855 *n* (%)
Age, median (range)	68 (8–104)	67 (8–104)	78 (17–106)	78 (17–106)
< 60 years (< 70 years)	24,342 (34)	115,670 (35)	3267 (28)	16,143 (29)
60–70 (70–80)	16,901 (23)	76,407 (23)	3706 (32)	17,869 (32)
> 70 (> 80 years)	31,052 (43)	135,782 (42)	4628 (40)	21,843 (39)
Gender				
Male	33,900 (47)	152,443 (47)	7133 (61)	34,034 (61)
Female	38,395 (53)	175,416 (53)	4468 (39)	21,821 (39)
Socioeconomic status				
Occupational level				
Missing information	4671 (6)	20,782 (6)	814 (7)	3879 (7)
Pensioners (lowest SES)	28,037 (39)	129,914 (40)	244 (2)	1180 (2)
Unemployed	2332 (3)	12,557 (4)	6738 (58)	32,075 (58)
Below an executive position	18,445 (26)	89,069 (27)	1646 (14)	8036 (14)
Superior or executive position (highest SES)	18,810 (26)	75,537 (23)	2159 (19)	10,685 (19)
Educational level				
Missing information	22,126 (31)	101,169 (31)	6088 (52)	29,132 (52)
No higher education (low SES)	20,230 (28)	111,675 (34)	2829 (25)	14,034 (25)
Short to medium academic education	17,836 (25)	74,283 (23)	1743 (15)	8361 (15)
Long academic education (High SES)	12,103 (17)	40,732 (12)	941 (8)	4328 (8)
Income				
Missing information	5272 (7)	26,120 (8)	871 (8)	4357 (8)
Lowest quartile	14,809 (20)	76,396 (23)	2511 (22)	13,016 (23)
Second lowest quartile	15,769 (22)	76,013 (23)	2590 (22)	12,846 (23)
Second highest quartile	16,383 (23)	76,582 (23)	2693 (23)	12,889 (23)
Highest quartile	20,062 (28)	72,748 (23)	2936 (25)	12,747 (23)
Marital status				
Missing information	4943 (7)	24,767 (8)	1438 (12)	7045 (13)
Divorced/widower	20,759 (29)	97,589 (30)	4058 (35)	19,874 (36)
Never married	5449 (8)	28,466 (8)	694 (6)	3741 (7)
Married/cohabiting	41,144 (57)	177,037 (54)	5411 (47)	25,195 (45)

BCC: basal cell carcinoma; SCC: squamous cell carcinoma

Table II. *The prevalence of selected comorbidities among non-melanoma skin cancer patients and their population control cohort subjects*

	Basal cell carcinoma (BCC), all age groups		Squamous cell carcinoma (SCC), all age groups	
	Patients with BCC *n* = 72,295 *n* (%)	Population cohort subjects (for patients with BCC) *n* = 327,859 *n* (%)	Patients with SCC *n* = 11,601 *n* (%)	Population cohort subjects (for patients with SCC) *n* = 55,855 *n* (%)
Diseases associated with immunosuppression				
Connective tissue disease	1933 (3)	7509 (2)	477 (4)	1615 (3)
Moderate to severe renal disease	783 (1)	2630 (1)	348 (3)	638 (1)
Any solid tumour except skin cancer	4848 (7)	18,583 (6)	1059 (9)	3856 (7)
Leukaemia	240 (<1)	442 (<1)	157 (1)	121 (<1)
Lymphoma	453 (1)	1063 (<1)	176 (2)	161 (<1)
Metastatic solid tumour	414 (1)	1650 (1)	145 (1)	355 (<1)
HIV/AIDS	22 (<1)	47 (<1)	10 (<1)	6 (<1)
Severe skin disease	1263 (2)	4662 (1)	428 (4)	865 (2)
Organ transplantation	137 (<1)	192 (<1)	157 (1)	36 (<1)
Diseases associated with obesity				
Diabetes I or II	1950 (3)	10,756 (3)	526 (5)	2290 (4)
Diabetes with end organ disease	688 (1)	3762 (1)	194 (2)	801 (1)
Diseases associated with smoking				
Myocardial infarction	2921 (4)	13,860 (4)	764 (7)	3684 (7)
Congestive heart failure	2191 (3)	10,497 (3)	812 (7)	3231 (6)
Peripheral vascular disease	1987 (3)	9384 (3)	601 (5)	2289 (4)
Cerebrovascular disease	4117 (6)	19,648 (6)	1184 (10)	5499 (10)
Chronic pulmonary disease	3371 (5)	15,901 (5)	804 (7)	3513 (6)
Diseases associated with alcohol				
Moderate to severe liver disease	91 (<1)	456 (<1)	21 (<1)	70 (<1)
Ulcer disease	2461 (3)	11,787 (4)	723 (6)	2889 (5)
Mild liver disease	428 (1)	2189 (1)	106 (1)	349 (1)
Alcohol-related disease	917 (1)	5707 (2)	177 (2)	793 (1)
Others				
Dementia	540 (1)	3416 (1)	215 (2)	1111 (2)
Hemiplegia	122 (<1)	566 (<1)	32 (<1)	126 (<1)
Malignant melanoma	714 (1)	1182 (<1)	119 (1)	235 (<1)

compared with their population control cohorts, the crude 10-year MRR was 1.85 (95% CI: 1.70–2.01) and the adjusted 10-year MRR was 1.54 (95% CI: 1.41–1.68). For patients with SCC aged 70–80 years as of their diagnosis/index date, compared with their population control cohort subjects, the crude 10-year MRR was 1.20 (95% CI: 1.14–1.27) and the adjusted 10-year MRR was 1.17 (95% CI: 1.10–1.23). Finally, for patients with SCC aged over 80 years as of their diagnosis/index date, compared with their population control cohort subjects, the crude 10-year MRR was 1.11 (95% CI: 1.07–1.16) and the adjusted 10-year MRR was 1.11 (95% CI: 1.07–1.15). The 10-year MRRs increased when we restricted the analyses to patients and population control cohort subjects who had no recorded hospitalizations as of their diagnosis/index date (Table III).

For patients with SCC and population control cohort subjects under 70 years of age, the adjusted 10-year MRR was increased among patients with SCC with a history of hospitalization prior to their diagnosis date for a cerebro-vascular disease (MRR = 1.62 (95% CI: 1.18–2.21)), connective tissue disease (MRR = 1.83 (95% CI: 1.13–2.98)), ulcer disease (MRR = 1.90 (95% CI: 1.31–2.76)), mild liver disease (MRR = 2.00 (95% CI: 1.13–3.52)), moderate to severe renal disease (MRR = 1.86 (95% CI: 1.18–2.93)), leukaemia (MRR = 32.0 (95% CI: 1.77–574)), and lymphoma (MRR = 4.00 (95% CI: 1.54–10.0)), based on comparisons with population control cohort subjects hospitalized for the same categories of disease (data not shown). For all other disease categories and age groups, mortality was the same among patients with SCC and population control cohort subjects with a history of a hospitalization for a given disease prior to the diagnosis/index date (data not shown). The 10-year MRRs did not change in analyses stratified by SES level (data not shown).

DISCUSSION

In this prospective study of patients with NMSC in Denmark, we found that patients with BCC had substantially reduced all-cause mortality, compared with population control cohort subjects, persisting even after extensive control for comorbidity and SES. We found that SCC is a marker of elevated all-cause mortality in an individual.

The mortality reduction among patients with BCC in our study is similar to results of a large meta-analysis

Table III. *Total mortality among patients with basal cell carcinoma (BCC) and patients with squamous cell carcinoma (SCC), respectively, compared with their population control cohort subjects*

		10-year cumulative mortality, % (95% CI)	10-year MRR, crude (95% CI)	10-year MRR, adjusted (95% CI)
Basal cell carcinomas				
Total mortality, all age groups	Patients	29.3 (28.9–29.6)	0.93 (0.91–0.94)	0.91[a] (0.89–0.92)
	Population cohort subjects	30.8 (30.6–30.9)	1.00 (ref.)	1.00 (ref.)
Total mortality, restricted to patients with BCC and population control cohort subjects without recorded hospitalizations or outpatient specialist visits visits as of the diagnosis/index date, all age-groups	Patients	21.4 (21.0–21.8)	0.93 (0.91–0.95)	0.91[b] (0.89–0.93)
	Population cohort subjects	22.7 (22.5–22.9)	1.00 (ref.)	1.00 (ref.)
Total mortality, restricted to patients with BCC and population control cohort subjects, aged < 60 years	Patients	5.6 (5.3–5.9)	0.94 (0.88–1.00)	0.96[a] (0.90–1.02)
	Population cohort subjects	5.9 (5.8–6.1)	1.00 (ref.)	1.00 (ref.)
Total mortality, restricted to patients with BCC and population control cohort subjects, aged 60–70 years	Patients	20.2 (19.5–21.0)	0.90 (0.86–0.93)	0.92[a] (0.88–0.96)
	Population cohort subjects	22.1 (21.8–22.5)	1.00 (ref.)	1.00 (ref.)
Total mortality, restricted to patients with BCC and population controls cohort subjects, aged > 70 years	Patients	53.5 (52.9–54.2)	0.87 (0.86–0.89)	0.90[a] (0.88–0.92)
	Population cohort subjects	57.6 (57.2–57.9)	1.00 (ref.)	1.00 (ref.)
Squamous cell carcinomas				
Total mortality, restricted to patients with SCC and population control cohort subjects, aged < 60 years	Patients	27.0 (25.3–28.9)	1.85 (1.70–2.01)	1.54[a] (1.41–1.68)
	Population cohort subjects	16.6 (15.9–17.3)	1.00 (ref.)	1.00 (ref.)
Total mortality, restricted to patients with SCC and population control cohort subjects without recorded hospitalizations or outpatient specialist visits as of the diagnosis/index date, aged < 60 years	Patients	18.5 (16.7–20.5)	1.67 (1.47–1.89)	1.70 (1.50–1.92)
	Population cohort subjects	12.2 (11.6–12.9)	1.00 (ref.)	1.00 (ref.)
Total mortality, restricted to patients with SCC and population control aged 60–70 years	Patients	54.5 (52.5–56.4)	1.20 (1.14–1.27)	1.17 (1.10–1.23)
	Population cohort subjects	49.2 (48.4–50.2)	1.00 (ref.)	1.00 (ref.)
Total mortality, restricted to patients with SCC and population control cohort subjects without recorded hospitalizations or outpatient specialist visits at index date, aged 60–70 years	Patients	44.3 (41.6–46.9)	1.17 (1.08–1.27)	1.21 (1.12–1.31)
	Population cohort subjects	40.7 (39.6–41.9)	1.00 (ref.)	1.00 (ref.)
Total mortality, restricted to patients with SCC and population control cohort subjects, aged > 70 years	Patients	80.5 (79.0–82.1)	1.11 (1.07–1.16)	1.11 (1.07–1.15)
	Population cohort subjects	78.6 (77.8–79.3)	1.00 (ref.)	1.00 (ref.)
Total mortality, restricted to patients with SCC and population control cohort subjects without recorded hospitalizations or outpatient specialist visits as of the diagnosis/index date, aged > 70 years	Patients	76.5 (74.3–78.8)	1.13 (1.07–1.20)	1.16 (1.10–1.23)
	Population cohort subjects	73.7 (72.6–74.7)	1.00 (ref.)	1.00 (ref.)

[a]Adjusted for age, gender, socio-economic status, and all 23 comorbidity categories.
[b]Adjusted for age, gender, and socio-economic status.
MRR: mortality rate ratio; CI: confidence intervals.

of 18 randomized trials (encompassing 57,311 participants), which reported a relative risk of all-cause mortality of 0.93 among individuals randomized to vitamin D intake (23). Although speculative and non-proven, our data go beyond randomized trials to support the hypothesis that patients with BCC, through intermittent exposure to solar radiation, have had adequate vitamin D status with beneficial effects on their mortality – a finding not explained by confounding from comorbidity or SES. An earlier Danish analysis of cause-specific mortality showed reduced mortality from cardiovascular diseases, chronic pulmonary disease, and diabetes mellitus among patients with BCC, the diseases for which vitamin D is expected to be protective (8). On the other hand, SCC is associated with cumulative, prolonged UV-exposure, which causes substantial systemic immune suppression (24), as well as chronic diseases associated with a weakened immune system or immunosuppressive treatments (7). Thus, differences in sun-exposure patterns, immunosuppression and chronic diseases as risk factors between individuals developing BCC and SCC probably explain the differential mortality pattern and clinical course of the two diseases observed in our study.

Our true population-based design ensured complete data on migration, vital status and hospital care, precluding major sources of bias such as recall and selection bias. Misclassification on NMSC, mortality and confounding factors is likely to be slight given our study design. Thus, we controlled for each of 23 comorbidity categories and each of four SES levels, instead of collapsing comorbidity categories and SES groups. However, particularly for patients with SCC a relevant proportion of patients and population control cohort subjects may have been coded as low occupation SES ("pensioner" category), although they may in fact have been in occupations considered to represent a higher SES until they retired. This misclassification of the occupational SES category is expected to be non-differential regarding mortality and would thus bias the estimates towards unity. Despite our study's strengths, the results should be interpreted with some caution. A major limitation is lack of information

on potential health-related confounding factors, such as use of immunosuppressive medications, obesity, physical activity, smoking and alcohol use. Although we were able to control for hospitalizations due to diseases related to use of immunosuppressive medications, obesity, physical obesity, smoking, and alcohol use, we still expect some residual confounding, which may have caused underestimation of true BCC-related mortality and overestimation of true SCC-related mortality. Nevertheless, the almost identical comorbidity distribution among patients with BCC and their population control cohort subjects, as well as the almost identical comorbidity distribution of disease categories (other than those associated with immunosuppression) among patients with SCC and their population control cohort subjects, suggest that residual confounding from these factors was slight.

In conclusion, we found reduced all-cause mortality among patients with BCC, which cannot be explained by confounding from comorbidity or SES. We also found that SCC is a marker of elevated all-cause mortality in an individual.

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