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ORIGINAL PAPER

A cohort study of personal and family history of skin cancer in relation to future risk of non-cutaneous malignancies

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Abstract

Purpose Skin cancer has repeatedly been observed to be a marker of increased risk for developing an internal malignancy. The purpose of our study was to further investigate this association while also characterizing the potential role of family history of skin cancer in relation to risk for non-cutaneous malignancies.

Methods Our study used data from 8,408 participants from the NHANES I epidemiological follow-up study. Cox-proportional hazards models were used to estimate the risk for developing an internal cancer associated with a personal history and family history of skin cancer during follow-up.

Results A personal history of skin cancer was associated with significantly increased risk of developing an internal cancer in adjusted models [hazard ratio (HR) 1.33, 95% confidence interval (CI) 1.09–1.61] but a family history of skin cancer was not associated with increased risk (HR 0.80, 95% CI 0.58–1.11).

Conclusions Consistent with prior reports, a personal history of skin cancer was associated with increase of developing internal malignancies, but this did not hold true for a family history of skin cancer. Further research is needed to understand why a personal history of skin cancer acts as a marker for increased risk for internal cancer.

Keywords Skin neoplasms/epidemiology · Neoplasms, second primary/epidemiology · Family medical history · Cohort studies · Follow-up studies · Humans

Introduction

Keratinocyte carcinoma (KC) and melanoma are two of the most common forms of cancer in the United States with an estimated 2 million and 87,000 new cases annually and account for ~ 99% of all skin cancers [1–5], but these diseases are rarely fatal with an estimated 0.69 and 2.7 deaths per hundred thousand person years (PY) for KC and melanoma, respectively [3, 6]. The low overall mortality rates suggest that only advanced or metastatic cancers would contribute to patient death.

However, a strong body of evidence documents that a prior diagnosis of skin cancer is associated with subsequent increased risk for developing non-cutaneous cancers [7–11]. This association is not specific to a single tumor site but to a broad spectrum of malignancies. For example, in a large British cohort participants with a personal history of KC had significantly greater risk for developing 26 of the 29 types of internal cancer investigated [7]. Similarly, melanoma has been associated with overall increased risk of numerous types of internal cancer [8, 12].

Studies of KC in relation to the risk of developing an internal cancer have generated evidence to suggest that genetic variants in DNA repair pathways may be a mediating factor contributing to this link [13, 14]. This evidence implies that KC may be a marker for underlying cancer susceptibility that results in increased risk for both skin cancer

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and non-cutaneous malignancies. Integrating measurement of a family history of skin cancer into this line of inquiry holds promise for shedding light on this question, but this has only rarely been investigated in previous studies.

An earlier small-scale, clinic-based pilot study by our research team suggested family history of skin cancer may be relevant to this question [15]. To further explore this question, the purpose of the present study is to assess whether, within a large-scale nationally representative US cohort, a personal history of skin cancer along with a family history of skin cancer is associated with increased risk for non-cutaneous malignancies.

Methods

Study design and population

The source population of our study is the NHANES Epidemiological Follow-up Study (NHEFS). This prospective cohort followed participants for a maximum of 10 years, from 1982 to 1992. The NHEFS is a nationally representative U.S. cohort with a complex survey design. The NHEFS is well-suited to address this research topic because skin cancer is included in the questionnaire items for personal and family history of cancer. The sources of data are the initial interview and medical examination in 1982, the follow up interviews for the entire cohort in 1987 and 1992, and the mortality data set linked to the National Death Index.

The NHEFS cohort was composed of persons who completed the medical examination during NHANES I study (1971–1975) and were projected to be between the ages of 25 and 74 in 1982 ($N = 14{,}407$). These 14,407 patients include those who died between the NHANES I data collection and the NHEFS baseline interview in 1982 and had their death information recorded for the NHEFS. For the present study additional inclusion criteria were: (1) participant or a proxy (i.e., a spouse or sibling) was present for the 1982 medical examination and interview, (2) participant was alive in 1982, (3) Caucasian ancestry, (4) free of non-cutaneous cancers prior to 1982, (5) not have missing information for personal or family diagnoses of cancer. Participants with a prior internal cancer diagnosis were excluded due to the role of prior cancer diagnoses and treatments in influencing a patient's risk of developing another malignancy. As for race, the differences in skin cancer epidemiology between races, such as a 25-fold difference in melanoma incidence and a 3-fold difference in mortality [3], would introduce heterogeneity that would necessitate a subgroup analysis. However, the numbers of skin cancers in non-whites in this cohort were too few for meaningful subgroup analyses. After applying these inclusion criteria 8,408 cohort numbers were included in the present study (Fig. 1).

Measurement

Due to varying data collection practices at different time points, our study was unable to differentiate between skin cancer subtypes. At the 1982 interview, all cancer related questions had a single categorization for skin cancer: "skin cancer including melanoma." Later interviews used separate categorizations for melanoma, KC, and miscellaneous skin cancers. However; family history of cancer was only collected at baseline and the final follow-up, thus for the 1,579 participants that died during follow-up it was not possible to conclusively determine if they had a family history of specifically KC. To keep measurement consistent across the cohort and allow use of the full cohort, measurement of personal and family history of skin cancer was limited to the 1982 interview designation of "skin cancer including melanoma."

Personal histories of skin cancer and internal cancer were abstracted from all three interviews. In the 1982 interview, a positive response to having a diagnosis of skin cancer from the self-reported cancer or dermatological questionnaires resulted in being classified as positive for a personal history of skin cancer. Additionally, skin cancer reported at the 1987 or 1992 interview diagnosed before the participant developed an internal cancer also resulted in being classified as positive for a personal history of skin cancer.

For the study outcome, a personal history of internal cancer, a positive report at the 1987 or 1992 interviews for a specific internal cancer resulted in a positive classification for personal history of internal cancer. Table 1 summarizes the internal cancer classifications used in 1982, 1987, and 1992. For example a report of breast cancer would result in a positive personal history of internal cancer. However, if the specific type of cancer was not provided the respondent was classified as unknown because it was indeterminate if the cancer was a skin cancer or non-cutaneous malignancy. Cause of death data was also used; if a participant's cause of death was listed as a specific internal cancer then they were classified as outcome-positive, i.e., having developed an internal cancer during follow-up.

Family history of cancer was ascertained for up to five first-degree relatives in 1982 and up to nine first-degree relatives in 1992. Participants who reported ≥ 1 first-degree relatives were diagnosed with any type of skin cancer (KC, melanoma, or other skin cancer) at either time point were classified as positive for family history of skin cancer. Similarly, a participant who reported ≥ 1 first-degree relatives with a specific cancer other than KC, melanoma, or "other

skin cancer" at either time point were classified as positive for a family history of internal cancer. As expected, the majority of the non-cutaneous cancers reported in relatives were made up of prostate, breast, lung, and colon cancer with notable numbers of reports of familial cases of leukemia and cancers of the stomach, liver, female reproductive organs.

Statistical analyses

T tests and Cochran-Mantel–Haenszel tests were used to explore the distribution of common cancer risk factors among patients with a personal history of skin cancer and a family history of skin cancer. Cox proportional hazards models were fit to measure the associations between personal history of skin cancer, family history of skin cancer, and family history of internal cancer with risk of developing an internal malignancy during the follow-up period. To evaluate these associations several models were fit: unadjusted models, age-adjusted models, and fully adjusted models. Fully adjusted models accounted for age, gender, smoking history, regular aspirin use, highest completed level of education, personal history of cancer, and family history of cancer. These variables were selected a priori for their associations with overall cancer risk or associations with cancer at multiple sites. To investigate the possibility that a family history of skin cancer might interact with a personal history of skin cancer to increase the risk of internal malignancies, an interaction term was added to the fully adjusted model that included family history of skin cancer and personal history of skin cancer; analyses stratified by family history of skin cancer were used to estimate the hazard ratio for the association between personal history of skin cancer with risk of internal cancers among those with and without a family history of skin cancer.

The models were analyzed accounting for the complex survey design used in the NHEFS cohort. All analyses were performed in SAS 9.4.

Results

Of the 8,408 participants, 748 developed an internal cancer during the follow-up period. The average follow-up was 8.2 years. Compared to patients without a personal history of skin cancer, those with a personal history of skin cancer were on average more likely to be male, be older, have a family history of skin cancer, and have a family history of internal cancer (Table 1). Compared to those with no family history of skin cancer, participants with a family history of skin cancer at baseline were on average younger and were less likely to smoke cigarettes but more likely to be female, be of normal weight, have a family history of internal cancer, and have a personal history of skin cancer (Table 1). The incidence of internal cancer was similar between participants with and without a family history of skin cancer, 7.7% and 9.0% respectively (Table 2).

A personal history of skin cancer was significantly associated with increased risk for internal cancer in the unadjusted model (hazard ratio (HR) 1.72, 95% confidence interval (CI) 1.43–2.07) (Table 3). This association was attenuated after adjusting for age (HR 1.31. 95% CI 1.07–1.60) and changed only slightly after further adjusting for gender, smoking history, regular aspirin use, highest completed level of education, and family history of cancer (HR 1.33; 95% CI 1.09–1.61) (Table 3).

The unadjusted association between family history of skin cancer and risk of internal cancers was a statistically significant inverse association (HR 0.69, 95% CI 0.51–0.95). This association was attenuated and no longer statistically significant in the age-adjusted (HR 0.83, 95% CI 0.61–1.13) and fully adjusted models (HR 0.80; 95% CI 0.58–1.11) (Table 3). There was no evidence family history of skin cancer was associated with increased risk of non-cutaneous malignancies in subgroups defined by type of first-degree relative or number of affected first-degree relatives (Table 2). In analyses stratified by family history of skin cancer, the association between a personal history of skin cancer increased risk for non-cutaneous malignancies was slightly stronger among those with a positive family history of skin cancer (HR 1.81; 95% CI 0.79–4.16) than among those with a negative family history of skin cancer (HR 1.30; 95% CI 1.06–1.6) but the test for interaction was not statistically significant (*p* value for interaction 0.50) (Table 4).

Discussion

In our study, a personal history of skin cancer was associated with increased risk for developing an internal cancer. This finding is consistent with prior research on this topic and further deepens the overall body of evidence documenting this association with data from a nationally representative prospective cohort with adjustment for other cancer risk factors such as cigarette smoking [7, 8, 10, 11].

Patients with a personal history of skin cancer were also observed to be more likely to report a family history of internal cancer implying a greater burden of non-cutaneous malignancies on both the personal and familial level compared to participants without a personal history of skin cancer. Associations were in the expected direction for most of the study variables, suggesting the study had strong internal

validity. For example, compared with never smokers, risk for developing non-cutaneous malignancies was elevated in former smokers and further elevated in current smokers (Table 3). The exception among the associations was aspirin use which has previously been associated with decreased risk for colorectal and other internal cancers; it is unclear why in our study aspirin was associated with increased internal cancer risk [16, 17]. With further research the finding that a personal history of skin cancer increases a person's risk for developing an internal cancer can be of clinical use. One practical use would be to determine if including a personal history of skin cancer can improve internal cancer risk models. If that situation were the case then risk models for breast, lung, and 26 other cancers associated with skin cancer could be improved and used to detect high risk patients, increasing early detection and saving lives. Overall, the results bolster the existing evidence that a personal history of skin cancer is a robust marker of increased risk for non-cutaneous malignancies.

Conversely, the null or inverse results for family history of skin cancer provided evidence against the hypothesis that a family history of skin cancer is associated with increased risk of internal malignancies. Participants with a family history of skin cancer were more likely to be younger, better educated, less likely to smoke, and have a healthy BMI according to CDC guidelines. These traits are generally recognized to reduce overall cancer risk [18]. However despite this overall healthier profile, time to event analyses showed patients with a family history of skin cancer were not at increased risk. Additionally, when our time to event analyses were stratified by a family history of skin cancer, the risk estimates for having a personal history of skin cancer or a family history of internal cancer increased. However these increases were not statistically significant. In a prior study, there was a lack of a statistically significant association between a family history of KC and risk for developing an internal cancer, but family history of KC was not a focus of the study and no measure of association was reported [11]. A second study, a clinic-based case–control study, provided possible evidence in support of an association between a family history of skin cancer and increased risk for developing internal cancer. This case–control study observed three matched groups: KC plus another type of cancer ($n = 50$), KC only ($n = 50$), and cancer-free controls ($n = 50$) [19]. Compared to the control group with no history of any type of cancer, patients with a family history of both KC and internal cancer were at increased risk for developing both KC and another type of cancer (odds ratio (OR) 9.8, 95% CI 1.7–57.0) [19]. However, a similar association for family history was observed for the comparison of the group with KC only compared with the cancer-free controls (OR 9.9, 95% CI 1.7–59.7) [19], suggesting the observed associations may be more relevant to developing KC rather than KC plus another type of cancer. The paucity of prior research on this topic and equivocal findings to date highlights the need for further research to clarify this association.

The current study has limitations related to measurement and classification of skin cancer among participants. First, our study relied on self-reported data instead of pathologic confirmation for personal history of skin cancer and other cancers. With respect to self-reported KC history, studies have reported sensitivity ranging from 69 to 94% and specificity ranging from 87 to 99% [20, 21]. Furthermore, self-reported family history could be expected to be less accurate than personal history and impacted by socio-economic status. For reference, overall the sensitivity of self-reported cancer ranges from 79 to 93% with a specificity of 99% [22, 23]. The error from self-reported histories of KC and other cancers is anticipated to result in under-ascertainment and be non-differential, and therefore, likely resulting in bias towards the null. Second, our study did not distinguish between skin cancer subtypes, either for a personal history or family history of skin cancer. This limitation was due to a set of circumstances that for the example of family history of skin cancer included not distinguishing skin cancer types in the 1982 interview and even in 1992 when an attempt was made to collect type of skin cancer family history the majority of responses were "unknown." Thus, although examination the risk of future cancer risk by family history of cancer according to specific type of skin cancer is scientifically meaningful it was not feasible to do so in the present study due to limitations in the data. This may have contributed to the null association between family history of cancer and future cancer risk observed in the present study. This is less of a concern for a personal history of skin cancer, as both KC and melanoma have been associated with overall increased risk for internal cancer and collectively make up roughly 99% of all skin cancers [3, 7, 8, 24].

Despite these weaknesses, the study also has notable strengths. The NHEFS cohort is nationally representative of the U.S. adult population and included important covariate information. Additionally, few prior studies have integrated family history of skin cancer along with personal skin cancer history into studies looking at risk of developing internal malignancies.

To summarize, in a prospective US cohort study, the risk of internal malignancies was significantly increased with a personal history of skin cancer but this did not hold true for a family history of skin cancer. Further research is warranted to help understand why a personal history of skin cancer is a marker of increased risk for non-cutaneous malignancies, and to explore with more detailed data on skin cancer type the potential contribution of family history of skin cancer to this association.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

Appendix 1

See Fig. 1 and Tables 1, 2, 3, 4.

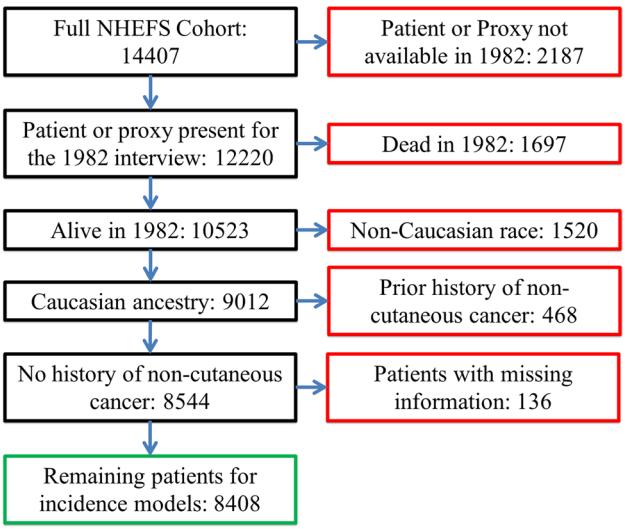

Fig. 1 Patient inclusion and exclusion from the NHEFS cohort

Table 1 Cancer history and risk factor distribution in the full NHEFS cohort and subdivided by personal and family history of skin cancer

	Entire cohort	Personal history of skin cancer		*p* value	Family history of skin cancer		*p* value
		No, *N* (%)	Yes, *N* (%)		No, *N* (%)	Yes, *N* (%)	
Number of participants	8408	7110	1298		7811	597	
Mean age (SD)	56.5 (14.8)	55.4 (14.7)	62.6 (13.7)	< 0.01	56.8 (14.8)	52.3 (14.2)	< 0.01
Mean time of follow-up (SD)	8.2 (2.4)	8.3 (2.4)	8.1 (2.4)	< 0.01	8.2 (2.4)	8.7 (1.8)	< 0.01
Gender				< 0.01			< 0.01
Men	3223	2627 (37.0)	596 (45.9)		3024 (40.0)	181 (30.3)	
Women	5185	4483 (63.0)	702 (54.1)		4769 (61.1)	416 (69.7)	
BMI				0.39			0.02
Underweight	213	179 (2.5)	34 (2.6)		193 (2.5)	20 (3.4)	
Normal weight	3715	3150 (44.3)	565 (43.5)		3417 (43.8)	298 (49.9)	
Over weight	3013	2512 (35.3)	501 (38.6)		2840 (36.4)	173 (30.0)	
Obese	1467	1296 (17.9)	198 (15.3)		1361 (17.4)	106 (17.8)	

Table 1 (Continued)

	Entire cohort	Personal history of skin cancer		*p* value	Family history of skin cancer		*p* value
		No, *N* (%)	Yes, *N* (%)		No, *N* (%)	Yes, *N* (%)	
Smoking behavior				0.06			0.06
Never smoked	3825	3246 (45.6)	579 (44.6)		3530 (45.2)	295 (49.4)	
Former smoker	2347	1909 (26.9)	438 (33.7)		2191 (28.1)	156 (26.1)	
Current smoker	2236	1955 (27.5)	281 (21.7)		2090 (26.8)	146 (24.5)	
How many years since patient quit smoking?				< 0.01			0.07
Less than 5	837	710 (37.2)	127 (29.0)		792 (36.2)	45 (28.8)	
More than 5	1510	1199 (62.8)	311 (71.0)		1399 (63.9)	111 (71.2)	
Regular aspirin use				0.74			0.38
No	6282	5317 (74.8)	965 (74.3)		5845 (74.8)	437 (73.2)	
Yes	2126	1793 (25.2)	333 (25.7)		1966 (25.2)	160 (26.8)	
Highest completed level of education				0.84			< 0.01
Less than high school	2981	2500 (35.2)	481 (37.1)		2833 (36.3)	148 (24.8)	
High school graduate	3198	2751 (38.7)	447 (34.4)		2963 (37.9)	235 (39.4)	
More than high school	2229	1859 (26.1)	370 (28.5)		2015 (25.8)	214 (35.9)	
Number of participants	8408	7110	1298		7811	597	
Personal history of skin cancer				NA			< 0.01
No	7110	7110 (100.0)	0 (0.0)		6638 (85.0)	472 (79.1)	
Yes	1298	0 (0.0)	1298 (100.0)		1173 (15.0)	125 (20.9)	
Family history of skin cancer				< 0.01			NA
No	7811	6638 (93.4)	1173 (90.4)		7811 (100.0)	0 (0.0)	
Yes	597	472 (6.6)	125 (9.6)		0 (0.0)	597 (100.0)	
Family history of internal cancer				< 0.01			< 0.01
No	4408	3807 (53.5)	601 (46.3)		4132 (53.0)	276 (46.2)	
Yes	4000	3303 (46.5)	697 (53.7)		3679 (47.1)	321 (53.8)	

Table 2 Number of incident internal cancers in 10-year NHEFS cohort subdivided by personal and family history of skin cancer

	Entire cohort	Personal history of skin cancer		*p* value
		No, *N* (%)	Yes, *N* (%)	
Number of participants	8408	7110	1298	
Developed cancer				< 0.01
No	7660	6539 (92.0)	1121 (86.4)	
Yes	748	571 (8.0)	177 (13.6)	
	Entire cohort	Family history of skin cancer		*p* value
		No, *N* (%)	Yes, *N* (%)	
Number of participants	8408	7811	597	
Developed cancer				0.29
No	7660	7109 (91.0)	551 (92.3)	
Yes	748	702 (9.0)	46 (7.7)	

Table 3 Hazards ratios (HRs) and 95% confidence intervals (CIs) for developing an internal cancer during 10-year follow-up of the NHEFS cohort, $N = 8408$

Variable	Unadjusted[a] results HR (95% CI)	Age-adjusted[b] results HR (95% CI)	Fully adjusted[c] results HR (95% CI)	Fully adjusted[c] *p* value
Age at 1982 interview	1.05 (1.05–1.06)	1.05 (1.05–1.06)	1.05 (1.04–1.06)	< 0.01
Gender				
Men ($N = 3223$)	1.00 (ref)	1.00 (ref)	1.00 (ref)	
Women ($N = 5185$)	1.05 (0.88–1.26)	0.93 (0.78–1.11)	1.02 (0.83–1.26)	0.86
Smoking habit in 82				
Never Smoked ($N = 3825$)	1.00 (ref)	1.00 (ref)	1.00 (ref)	
Previous smoker ($N = 2347$)	1.25 (0.99–1.56)	1.35 (1.08–1.69)	1.34 (1.04–1.72)	0.02
Current smoker ($N = 2236$)	1.14 (0.90–1.45)	1.65 (1.29–2.11)	1.63 (1.27–2.09)	< 0.01
Regular aspirin use				
No ($N = 6282$)	1.00 (ref)	1.00 (ref)	1.00 (ref)	
Yes ($N = 2126$)	1.50 (1.24–1.82)	1.36 (1.12–1.64)	1.36 (1.12–1.66)	< 0.01
Highest completed level of education				
Less than high school ($N = 2981$)	1.00 (ref)	1.00 (ref)	1.00 (ref)	
High school graduate ($N = 3198$)	0.60 (0.49–0.73)	0.86 (0.70–1.06)	0.86 (0.70–1.06)	0.16
More than high school ($N = 2229$)	0.51 (0.41–0.64)	0.77 (0.62–0.97)	0.77 (0.62–0.96)	0.02
Personal history of skin cancer				
No ($N = 7110$)	1.00 (ref)	1.00 (ref)	1.00 (ref)	
Yes ($N = 1298$)	1.72 (1.43–2.07)	1.31 (1.07–1.60)	1.33 (1.09–1.61)	< 0.01
Family history of skin cancer				
No ($N = 7811$)	1.00 (ref)	1.00 (ref)	1.00 (ref)	
Yes ($N = 597$)	0.69 (0.51–0.95)	0.83 (0.60–1.13)	0.80 (0.58–1.11)	0.18
Family history of internal cancer				
No ($N = 4408$)	1.00 (ref)	1.00 (ref)	1.00 (ref)	
Yes ($N = 4000$)	1.29 (1.10–1.52)	1.19 (1.00–1.40)	1.18 (0.99–1.40)	0.06

[a]Results are not adjusted for any other covariate

[b]Results are adjusted for age

[c]Results are adjusted for age, gender, BMI, smoking habit, regular aspirin use, highest completed level of education, personal history of skin cancer, family history of skin cancer, and family history of internal cancer

Table 4 Hazards ratios (HRs) and 95% confidence intervals (CIs) for developing an internal cancer during 10-year follow-up of the NHEFS cohort, $N = 8408$

Variable	Fully adjusted results HR (95% CI) ($N = 8408$, 748 internal cancer cases)	Participants without a family history of skin cancer ($N = 7811$, 702 internal cancer cases)	Participants with a family history of skin cancer ($N = 597$, 46 internal cancer cases)
Personal history of skin cancer			
No ($N = 7110$)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Yes ($N = 1298$)	1.33 (1.09–1.61)	1.30 (1.06–1.60)	1.81 (0.79–4.16)
Family history of internal cancer			
No ($N = 4408$)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Yes ($N = 4000$)	1.18 (0.99–1.40)	1.14 (0.95–1.36)	2.66 (0.95–7.47)

Results are adjusted for age, gender, BMI, smoking habit, regular aspirin use, highest completed level of education, personal history of skin cancer, family history of skin cancer, and family history of internal cancer

Appendix 2

Tables 5 and 6.

Table 5 Types of internal cancer considered for family history of internal cancer, exclusion from study due to a personal history of internal cancer, and the end point of incident internal cancer across the different study data collection time points

Categories use in all years: Bladder, Brain, Cervix, Larynx, Leukemia, Liver, Pancreas, Prostate, Stomach

Additional categories used in 1982: Bone or articular cartilage, Breast (female), Breast (male), Colon/Large Intestine, Connective or other soft tissue including diaphragm, Digestive organs NEC, Esophagus, Eye, Female genital organ or tract, female genitourinary tract NEC, Gallbladder, Gum, Heart/thymus gland, Hodgkin's disease/Hodgkin's lymphoma, Kidney, renal, urinary organ or system NEC, Lip, Lip/oral cavity/pharynx NEC, Lung/bronchus/trachea, Lymph gland/lymphoma/lymph node NEC/marrow (bone) NEC, Lymphosarcoma/reticulosarcoma, Male genital organ or tract/male genitourinary tract NEC, Mouth NEC, Nasopharynx/nasopharyngeal, Nervous system (central) NEC, Oropharynx/tonsil, Other and ill-defined sites, Ovary, Rectum/anus, Respiratory organs or systems/respiratory tract NEC, Small intestine, Thyroid gland, Tongue, Unspecified, Uterus/uterine

Additional categories used in 1987: Blood (lymphomas, multiple myeloma), Bone, Breast, Colon (rectum, anus, intestines), Female genital, Kidney, Lung, Head and neck, Other GI, Possible metastatic, Spine, Throat, Uterus

Additional categories used in 1992: Bone, Bone marrow, Breast, Cancer spread throughout body, Colon, Endometrium or corpus, Esophagus, Female cancer non-specified, Gastrointestinal, Hodgkin's Disease, Kidney, Lung, Lymph glands, Non-Hodgkin's lymphoma, Oral, Ovary, Rectum, Testicular, Throat, Thyroid

Table 6 Age and gender adjusted risk for developing an internal cancer according to which relative or the number of relatives with skin cancer

Relative	*N* (%)	Did not develop an internal cancer (%)	Developed an internal cancer (%)	HR (95% CI)
Parent	386 (4.59)	365 (94.56)	21 (5.44)	0.83 (0.50–1.37)
Sibling	234 (2.78)	208 (88.89)	26 (3.48)	0.97 (0.63–1.50)
Child	56 (0.67)	50 (89.29)	6 (10.71)	0.74 (0.33–1.69)
Number of relatives with skin cancer				
0	7811 (92.90)	7109 (92.81)	702 (93.85)	1.00 (ref)
1	534 (6.35)	493 (6.44)	41 (5.48)	0.84 (0.60–1.19)
≥2	63 (0.75)	58 (0.75)	5 (0.66)	0.75 (0.23–2.39)

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