



Original article

Scand J Work Environ Health [2007;33\(1\):66-73](#)

doi:10.5271/sjweh.1066

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Refers to the following texts of the Journal: [1998;24\(3\):175-182](#)
[1999;25 suppl 2:1-116](#)

The following articles refer to this text: [2008;34\(1\):5-22](#);
[2009;35\(6\):446-453](#); [2010;36\(2\):163-179](#)

Key terms: [breast cancer](#); [cancer risk](#); [cohort study](#); [health care](#);
[malignant melanoma](#); [Norway](#); [nurse](#); [occupational exposure](#);
[radiation](#); [record linkage](#)

This article in PubMed: www.ncbi.nlm.nih.gov/pubmed/17353967



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Cancer risk among 43 000 Norwegian nurses

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Lie J-AS, Andersen A, Kjærheim K. Cancer risk among 43 000 Norwegian nurses. *Scand J Work Environ Health* 2007;33(1):66–73.

Objectives This study evaluated the influence of occupational exposure on cancer risk among female Norwegian nurses.

Methods A historical prospective cohort study was performed. The cohort was established from the Norwegian Board of Health's registry of nurses and included women who graduated from a nursing school before 1985. The cohort (N=43 316) was linked to the Cancer Registry of Norway. The observed number of cases was compared with the expected number on the basis of national rates. Time since first employment, period of first employment, and duration of employment were used as indicators of exposure. Poisson regression analyses were used for internal comparisons, adjusting for age, period, and fertility.

Results The nurses were followed over 1 473 931 person-years. During the follow-up (1953–2002), 6193 cancer cases were observed. The standardized incidence ratio (SIR) for all cancers combined was close to unity. Significantly lower risks were found for cancers with a known association with alcohol and tobacco consumption and sexual activity. A significantly increased risk was found for breast cancer (SIR 1.14, 95% confidence interval (95% CI) 1.09–1.19), ovarian cancer (SIR 1.14, 95% CI 1.04–1.25), malignant melanoma (SIR 1.15, 95% CI 1.04–1.28), and borderline significant risk appeared for other skin cancer (SIR 1.12, 95% CI 0.98–1.29). A positive trend for increasing time since first exposure was found for breast cancer and malignant melanoma.

Conclusions The results indicate an association between working as a nurse and an increased risk of breast cancer and malignant melanoma. Decreased risks, found for several cancers, indicate favorable lifestyle habits among nurses.

Key terms breast cancer; cohort study; health care; malignant melanoma; occupational exposure; radiation; record linkage.

Nursing constitutes one of the oldest female occupations in modern society, providing work for a large number of women. Being a nurse implies the possibility of exposure to different established and suspected carcinogens such as ionizing radiation (1), antineoplastic drugs (2, 3), and sterilizing gases (4), as described in a recent review (5). The nature of the work performed by nurses also makes shift and night work inevitable. Exposure to light at night and a disruption of the circadian rhythm have been hypothesized to influence the risk of breast cancer (6, 7). This possibility has recently been investigated in a nested case-control study of Norwegian nurses (8). Up to recent decades, being a nurse has also defined central aspects of lifestyle, with possible influence on cancer risk.

In Norway a 3-year nursing education was established about a hundred years ago. Even though most of the schools were secular, the regulations for living were not very different from those of nuns. Theoretical

skills, good health, and high morals were required for admission to nursing schools. The nurses often had to work both morning and evening, with a short break only in the middle of the day. Accommodations were usually in a room at the hospital or in an apartment building nearby. Two nurses often shared a room. Before 1948 married women were not admitted to nursing schools, and nurses who married had to terminate their work as registered nurses (9).

On the basis of this description, it is to be expected that nurses have a low risk of cancers related to lifestyle factors (alcohol and tobacco consumption and sexual activity) such as cancers of the lung, pancreas, liver, bladder and esophagus, oral cancer, and cervical cancer. A high risk of breast and ovarian cancer would be expected, due to a large proportion of nullipara in the group. Breast cancer and hematological malignancies have been suggested as occupationally related cancers, on the basis of the recognized hazards that many nurses

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have been exposed to and the findings of an increased risk of one or both of these cancers in several studies (5).

In occupational cancer studies, time since first employment is often used as an indicator variable of the period between first exposure and cancer diagnosis, while duration of employment may be interpreted as an indicator of cumulative exposure. An occupationally related cancer risk is ideally seen as increasing with increasing values of the indicator variable. In the case of lifestyle-related cancer risks, such increases by duration and time since first employment are not necessarily found. When exposures have been introduced or stopped at certain periods of time during the observation period, an analysis by period of first employment may help distinguish between groups ever or never exposed to the specific agent or situation and may thus describe the effects of change.

In our present study, we investigated cancer risk in a cohort of Norwegian nurses. The aim was to analyze risk according to time since first employment, period of first employment, and duration of employment to evaluate the possible contribution of occupational exposures.

Study population and methods

A cohort of 49 402 women who graduated from a 3-year nursing school between 1914 and 1984 and were alive on 1 January 1953 or were born later was established. In addition to Norwegian nurses, it also included nurses who had received their nursing degree in another country but had Norwegian authorization. The information was based on the Norwegian Board of Health's register of nurses, which was established in 1949, of all nurses alive that year. A complete work history prior to 1949 was included, and further work experience was updated yearly until 1960. A last regular update was performed in 1968, and thereafter only sporadically. The following information was extracted from the file of nurses: name, date of birth, year of graduation from nursing school and year of authorization, year of start and end of each job. The year of graduation from nursing school determined the year of each individual's entry into the study. If it was unknown, year of entry was defined as year of first employment or year of authorization, whichever came first.

Twelve percent (N=6074) of the women had no information on employment in this register and were excluded. Of these, 85% graduated in 1970 or later. Excluded were also 12 nurses for whom time of entry seemingly succeeded date of death. The resulting cohort consisted of 43 316 women. An 11-digit personal identification number was assigned to all Norwegian

citizens alive in 1960 or born later. The nurse cohort was linked by this number or, for those diseased before 1960, by name and date of birth, to the Cancer Registry of Norway. Since 1953 the Cancer Registry of Norway has collected data on incident cases of cancer in the total population. The registration system is built on compulsory reporting from physicians, giving multiple reporting from pathology laboratories and hospital departments. The coding of cancer was based on a modified version of the 7th revision of the International Classification of Diseases (ICD-7). Basal cell carcinoma is not included in the group "other skin cancer", which thus comprised squamous-cell carcinoma. On the basis of the World Health Organization (WHO) classification (10), tumors of hematopoietic and lymphoid tissues were divided into two main groups (myeloproliferative and lymphoproliferative diseases), plus one group including histocytic and dendritic cell neoplasms, mastocytosis, and other unspecified nonsolid tumors.

Person-years were calculated for each person, commencing in the starting year or 1953, the first year of the Cancer Registry, whichever came later, and ending with the date of death or emigration, or on 31 December 2002, whichever occurred first. The total number of person-years of follow-up was 1 473 931. Due to new coding procedures at the Cancer Registry, follow-up for nonsolid tumors does not include 2002.

The dates of death and emigration were found by linkage to the Population Registry of Norway using the personal identification number. For the period before 1960 the linkage was made by name and date of birth. The birth dates of the children were obtained by linkage to files at Statistics Norway, according to the personal identification number. These files have been compiled with the use of information from censuses and annual population statistics and include children who were living with their parents in 1960 or were born after that year. In Norway married women were not admitted to nursing schools until 1948. This exclusion, combined with the strict rules that the nurses had to follow, implied that very few nurses had children before that year. For 393 women, we did not have information about childbirth, and these nurses were excluded from the analyses controlling for fertility. Ninety-nine percent of these women were either dead, had emigrated, or were otherwise lost to follow-up before 1960, with a last day of contact before that year. Among the nurses for whom we had information about childbirth, 26% had no children, and the average number of children was 1.83.

Exposure indicators

The following three indicators of occupational exposure were used: time since first employment, period of first employment, and duration of work. The variable

duration of work was based on the work history from the nurse register; it was counted from the entry into the study until the end of the last registered employment. For as many as 74% of the nurses, however, the ending time of the last registered job was unknown. Of the nurses with an unknown duration of last employment, 95% had a work history of <10 years, and half of them were educated in 1970 or later. To all such last registered jobs that lacked an ending time, we assigned 1 year's duration. Thus the total work duration represents the minimum total employment time. Although all of the nurses were working during their 3 years of education and thus potentially were exposed to different hazards, this period was not included in the duration of work. Work periods outside Norway were, however, included.

The following categories were used for period of first employment: before 1940, 1940–1959, and 1960–1984.

Table 1. Characteristics of female nurses in Norway with work history in the Norwegian Board of Health's registry of nurses.

Characteristic	Nurses (N=43 316)			
	N	%	Person-years	%
Year of birth				
Before 1925	9 797	22.6	.	.
1925–1934	5 731	13.2	.	.
1935–1944	8 734	20.2	.	.
1945–1954	12 813	29.6	.	.
1955–1963	6 241	14.4	.	.
Time since first employment				
0–14 years	.	.	537 910	36.5
15–29 years	.	.	524 716	35.6
30–44 years	.	.	298 829	20.3
≥45 years	.	.	112 476	7.6
Period of first employment				
Before 1940	4 139	9.6	.	.
1940–1949	4 890	11.3	.	.
1950–1959	7 282	16.8	.	.
1960–1969	10 503	24.2	.	.
1970–1984	16 502	38.1	.	.
Duration of work as nurse				
1–9 years	36 247	83.7	.	.
10–19 years	3 860	9.8	.	.
≥20 years	3 209	7.4	.	.
Age at first employment				
<25 years	28 547	65.9	.	.
25–29 years	11 702	27.0	.	.
≥30 years	3 067	7.1	.	.
Number of children				
0	11 104	25.6	.	.
1	4 547	10.5	.	.
2	13 303	30.7	.	.
3	9 853	22.8	.	.
≥4	4 116	9.5	.	.
Unknown	393	0.9	.	.
Age at first birth among parous women				
<25 years	7 826	24.6	.	.
25–29 years	14 178	44.6	.	.
≥30 years	9 815	31.0	.	.

For time since first employment the following were used: 0–14, 15–29, 30–44, and ≥45 years. Duration of work was categorized as 0–9, 10–19, and ≥20 years. Due to old age at the time of diagnosis of other skin cancer, we used the following categories for time since first employment in the internal analyses for this cancer site: 0–29, 30–44, 45–59, and ≥60 years. Categorizations were chosen partly to facilitate comparisons with previous studies and partly to provide groups of equal size. Descriptive characteristics of the cohort are provided in table 1.

Statistical analyses

Two analytical methods were applied. First, the cancer incidence of the cohort was compared with that of the female Norwegian population. The expected number of cases was computed by multiplying the person-years of follow-up by national rates in 5-year time periods and 5-year age groups. Standardized incidence ratios (SIR) were computed along with 95% confidence intervals (95% CI) on the assumption of a Poisson distribution of the observed cancer cases. Second, Poisson regression analyses were used to determine the internal exposure–response relations with adjustment for the effects of calendar period and age and to estimate the statistical significance of the trends.

Poisson regression analyses were made for cancers of the breast, ovary, malignant melanoma, and other skin cancer. Adjustment for age was made in narrow age groups to adjust for possible residual confounding by age. For breast and ovarian cancer and malignant melanoma we used the age categories of <33, 33–35, ..., 78–80, and >80 years, and the calendar periods used were before 1970, 1970–1989, and 1990–2002. Number of children and age at first birth were included in the models for breast and ovarian cancer. The categories for age at first birth were <25, 25–29, and ≥30 years, and for number of children 0, 1, 2–3, and ≥4 were used. Since very few cases of other skin cancer were diagnosed among women younger than 40 years, and after 1980, adjustment was made for this cancer site with the following age-groups: <45, 45–47, ..., 78–80, >80 years. Calendar periods were before 1985 and 1985–2002.

The DATAB and AMFIT modules in the EPICURE software package were used in the analyses (11). The study was approved by the Norwegian Data Inspectorate.

Results

During the follow-up, 6193 new cancer cases were identified, of which 30% were breast cancer. The standardized

incidence ratios are shown in table 2 for all major cancer sites. The standardized incidence ratio for total cancer was 0.97 (95% CI 0.95–1.00). Significantly increased standardized incidence ratios were observed for cancers of the breast and ovary and for malignant melanoma, and other skin cancer reached borderline significance. Significantly lower risks were found for cancers of the mouth, esophagus, stomach, liver, gallbladder, pancreas, lung, cervix, kidney, and “unspecified sites”. No significant excess of hematopoietic cancers was observed in the cohort.

Table 3 shows the standardized incidence ratios for cancers of the breast and ovary, malignant melanoma, and other skin cancer according to period of first employment and time since first employment. A 10–20% increased incidence of breast cancer was observed for all categories of time since first employment and for all periods of first employment. The highest significant standardized incidence ratio was found for nurses who began work before 1940, for whom 15–29 years had elapsed since first employment. When period of first employment was categorized in 10-year intervals, a significant elevation of breast cancer was found for all periods before 1970, but not after 1970 (not shown).

A significantly increased risk of ovarian cancer was found among the nurses who were first employed in 1960 or later and had ≥ 15 years since first employment. The standardized incidence ratio of malignant melanoma was highest for the nurses who were first employed before 1940 and had ≥ 45 years since first employment (SIR 1.7, 95% CI 1.2–2.5). The standardized incidence ratio for malignant melanoma decreased with a more recent period of first employment. For other skin cancer a significantly elevated risk was confined to nurses first employed before 1940.

Analyses of the standardized incidence ratio by duration of employment (not shown) showed a significantly increased risk of breast cancer among women with a work duration of ≥ 10 years, and borderline significance was shown for the women with < 10 years of employment. The standardized incidence ratios for ovarian cancer and malignant melanoma increased as the duration of employment increased. The highest risk of other skin cancer was found among the nurses with a work duration of ≥ 20 years.

Equivalent analyses were made for two of the cancer sites with decreased standardized incidence ratios, namely, cancers of the lung and cervix (results not shown). A significant deficit of cervical cancer was found for all of the periods of first employment, for all of the categories of time since first employment, and for all of the categories of work duration. Likewise, a decreased incidence of lung cancer was found for all of the periods of first employment (significant for nurses with first employment after 1940), for all of the categories of

time since first employment (significant in those with ≥ 15 years of employment), and for all of the categories of work duration (significant in those with < 20 years of employment).

The results of the internal analyses of risk according to time since first employment are shown in table 4. The rate ratio for breast cancer had a borderline significant increase among the nurses with ≥ 45 years since first employment, when compared with those with < 15 years since first employment, and a borderline significant trend was found for increasing time since first employment. A significant increase in the risk of malignant melanoma was shown for the nurses with > 30 years since first

Table 2. Observed and expected numbers of cancer cases, standardized incidence ratios (SIR), and 95% confidence intervals (95% CI) for 43 316 nurses (1 473 932 person-years) in a follow-up from 1953 to 2002.

Cancer site ^a	Observed (N)	Expected (N)	SIR	95% CI
All sites (140–204)	6193	6370	0.97	0.95–1.00
Lip (140)	9	10	0.94	0.43–1.78
Oral cavity, pharynx (141, 143–148)	35	54	0.65	0.45–0.90
Esophagus (150)	9	23	0.39	0.18–0.74
Stomach (151)	186	217	0.86	0.74–0.99
Colon (153)	588	581	1.01	0.93–1.10
Rectum (154)	234	256	0.92	0.81–1.04
Liver (155)	9	24	0.37	0.17–0.70
Gallbladder (156)	23	42	0.55	0.35–0.82
Pancreas (157)	127	163	0.78	0.66–0.93
Nose, sinuses (160)	6	10	0.60	0.22–1.30
Larynx (161)	5	10	0.49	0.16–1.15
Trachea, bronchus, lung (162)	199	328	0.61	0.53–0.70
Breast (170)	1900	1669	1.14	1.09–1.19
Cervix uteri (171)	190	380	0.50	0.43–0.58
Corpus uteri (172, 174)	357	349	1.02	0.92–1.13
Ovary (175)	432	379	1.14	1.04–1.25
Other female genital organs (176)	47	60	0.78	0.57–1.03
Kidney (180)	108	135	0.80	0.66–0.97
Bladder (181)	128	139	0.92	0.78–1.10
Melanoma of skin (190)	375	325	1.15	1.04–1.28
Other skin ^b (191)	201	179	1.12	0.98–1.29
Brain, nervous system (193)	204	212	0.96	0.84–1.10
Thyroid gland (194)	127	108	1.17	0.98–1.39
Myeloproliferative diseases ^c	64	63	1.01	0.78–1.29
Lymphoproliferative diseases ^c	315	299	1.05	0.94–1.18
Other hematopoietic diseases ^{c,d}	8	13	0.61	0.26–1.20
Unspecified sites (199)	162	208	0.78	0.67–0.91
Other specified sites	115	113	1.02	0.85–1.22

^a Code of the International Classification of Diseases (7th revision) in parentheses.

^b Basal cell carcinomas not included.

^c Follow-up 1953–2001.

^d Histocytic and dendritic cell neoplasms, mastocytosis, other unspecified nonsolid tumors.

Table 3. Observed number of cases, standardized incidence ratios (SIR), and 95% confidence interval (95% CI) for cancers of the breast and ovary, malignant melanoma, and other skin by period of first employment as a nurse and time since first employment for 43 316 nurses in a follow-up from 1953 to 2002.

Period of first employment	Time since first employment														
	0–14 years			15–29 years			30–44 years			≥45 years			Total		
	Observed (N)	SIR	95% CI	Observed (N)	SIR	95% CI	Observed (N)	SIR	95% CI	Observed (N)	SIR	95% CI	Observed (N)	SIR	95% CI
Breast cancer															
<1940	1	2.9	0.1–16	60	1.8	1.3–2.3	97	1.1	0.9–1.4	143	1.1	0.9–1.3	301	1.2	1.0–1.3
1940–1959	40	1.1	0.8–1.5	232	1.2	1.1–1.4	384	1.2	1.1–1.3	182	1.1	0.9–1.2	838	1.2	1.1–1.2
1960–1984	101	1.2	1.0–1.5	404	1.0	0.9–1.1	256	1.2	1.1–1.4	–	–	–	761	1.1	1.0–1.2
Total	142	1.2	1.0–1.4	696	1.1	1.0–1.2	737	1.2	1.1–1.3	325	1.1	1.0–1.2	1900	1.1	1.1–1.2
Ovarian cancer															
<1940	–	–	–	16	1.6	0.9–2.5	32	1.2	0.8–1.7	30	1.1	0.7–1.6	78	1.2	1.0–1.5
1940–1959	9	0.9	0.4–1.7	48	0.9	0.7–1.2	89	1.0	0.8–1.3	44	1.1	0.8–1.5	190	1.0	0.9–1.2
1960–1984	18	0.8	0.5–1.3	91	1.3	1.1–1.7	55	1.5	1.1–2.0	–	–	–	164	1.3	1.1–1.5
Total	27	0.8	0.5–1.2	155	1.2	1.0–1.4	176	1.2	1.0–1.4	74	1.1	0.9–1.4	432	1.1	1.0–1.3
Malignant melanoma															
<1940	–	–	–	1	0.6	0.0–3.4	5	0.8	0.2–1.9	29	1.7	1.2–2.5	35	1.4	1.0–2.0
1940–1959	10	1.4	0.7–2.6	29	1.0	0.7–1.4	75	1.3	1.0–1.6	43	1.3	1.0–1.8	157	1.2	1.1–1.4
1960–1984	55	1.1	0.8–1.4	94	1.1	0.9–1.3	34	1.0	0.7–1.4	–	–	–	183	1.1	0.9–1.2
Total	65	1.1	0.9–1.4	124	1.0	0.9–1.2	114	1.2	1.0–1.4	72	1.5	1.2–1.9	375	1.1	1.0–1.3
Other skin cancer															
<1940	–	–	–	–	–	–	6	1.4	0.5–3.1	69	1.6	1.2–2.0	75	1.5	1.2–1.9
1940–1959	1	1.3	0.0–7.1	1	0.2	0.0–1.1	34	1.0	0.7–1.4	54	1.0	0.8–1.3	90	1.0	0.8–1.2
1960–1984	4	1.0	0.3–2.7	24	1.4	0.9–2.1	8	0.6	0.2–1.1	–	–	–	36	1.0	0.7–1.4
Total	5	1.1	0.4–2.5	25	1.1	0.7–1.6	48	0.9	0.7–1.2	123	1.2	1.0–1.5	201	1.1	1.0–1.3

Table 4. Rate ratios (RR) from the Poisson regression analyses for cancer of the breast and ovary, malignant melanoma, and other skin by years since first employment for 43 316 nurses in a follow-up from 1953 to 2002. (95% CI = 95% confidence interval)

Cancer site	Years since first employment	Cases (N)	RR	95% CI
Breast cancer	<15	137	1.00 ^{a, b}	..
	15–29	685	1.03 ^{a, b}	0.77–1.38
	30–44	730	1.17 ^{a, b}	0.82–1.67
	≥45	325	1.47 ^{a, b}	0.95–2.29
			$P_{\text{trend}} 0.06$	
Ovary cancer	<15	25	1.00 ^{a, b}	..
	15–29	146	1.37 ^{a, b}	0.70–2.69
	30–44	171	1.19 ^{a, b}	0.55–2.60
	≥45	74	1.63 ^{a, b}	0.62–4.24
			$P_{\text{trend}} >0.5$	
Malignant melanoma	<15	65	1.00 ^a	..
	15–29	124	1.68 ^a	0.84–3.36
	30–44	114	2.64 ^a	1.12–6.26
	≥45	72	3.21 ^a	1.12–9.23
			$P_{\text{trend}} 0.03$	
Other skin cancer ^c	<30	30	1.00 ^d	..
	30–44	48	1.02 ^d	0.32–3.22
	45–59	102	1.33 ^d	0.37–4.77
	≥60	21	1.37 ^d	0.34–5.48
			$P_{\text{trend}} >0.5$	

^a Adjusted for age (<33, 33–35, ..., >80 years) and calendar period (<1970, 1970–1989, 1990–2002).

^b Adjusted for number of children (0, 1, 2–3, ≥4). Women without data on children excluded.

^c Basal cell carcinomas not included.

^d Adjusted for age (<45, 45–47, ..., ≥80 years) and calendar period (<1985, ≥1985).

employed, compared with the nurses with <15 years since first employment, and a significant trend was found for increasing time since first employment. For ovarian cancer and other skin cancer, no significant increase in risk was found, nor was there a trend for increasing time since first employment. Adjustment for the number of children had only a marginal effect on the rate ratios for breast and ovarian cancer. Age at first birth was not included in the final model, since it did not alter the risk estimates.

Discussion

This historical prospective study aimed at examining cancer risk among nurses and at evaluating the contribution of occupational exposure to cancer risk among nurses. It had a large cohort, consisting of female nurses in Norway educated during a period of 70 years and representing nearly 1.5 million person-years. The use of personal identification numbers facilitated the identification and the linkage to the cancer data of the Cancer Registry, and to data on mortality, emigration, and fertility, and thus ensured a complete ascertainment of relevant events.

Elevated risks of breast and ovarian cancer, malignant melanoma, and other skin cancer (squamous cell carcinoma) were found. For several cancer sites, of

which most can be related to lifestyle factors such as alcohol and tobacco consumption and sexual activity (12, 13), risks were decreased. The total cancer incidence was close to that of the general female population.

The standardized incidence ratio of breast cancer was elevated for the nurses with more than 10 years of employment. Internal analyses showed a borderline significant trend for increasing time since first employment. Results from a study among Icelandic nurses also showed a positive gradient for breast cancer incidence by increasing time since graduation (14). An association between working as a nurse and an excess of breast cancer is in agreement with results from some previous studies including nurses (1, 15–20), although not all of the results have been consistent (21, 22).

It has been estimated that less than 50% of breast cancer incidence can be explained by known risk factors related to reproduction and hormones (23). Few of the occupational studies demonstrating an excess of breast cancer among nurses have adjusted for such factors. In the present study, the number of children and age at first birth did not confound the estimates of the association between time since first employment and cancers of the breast and ovary. In a previous nested case–control study of Norwegian nurses, an association was found between longer duration of night work and breast cancer risk (8). Such an association has also been observed in a few other recent studies (24–26). The suggested biological mechanism for this occurrence includes disruption of the normal circadian rhythm and suppression of the normal nocturnal secretion of the hormone melatonin by exposure to light at night (6, 7).

Ionizing radiation is another occupational risk factor for breast cancer (27), and such exposure has been present in the work environment of many nurses, as X-rays, radioactive isotopes, and implants. Although some of the adverse effects of X-rays have been known for more than 100 years, protective measures have not always been taken, partly due to a neglect of the problem and partly due to a tight schedule in X-ray departments. Radiation exposure was higher in the first decades of the last century, when old apparatus was used and when the radiation doses given were more uncertain (28). In 1934, the International Commission on Radiological Protection established a radiation dose limit per day for X-ray workers. The dose limit established that year was, however, 30 times today's limit (28). Thus an association with breast cancer cannot be excluded.

In our study, we found an excess of breast cancer among the nurses first employed before 1970, but not for those employed later. One reason for this difference could be an occupational risk that was present before 1970, but not later. Another possible explanation is that nurses employed after this year had become more similar to women in the rest of the population concerning

lifestyle, parity, and the like. For other typical “lifestyle cancers”, such as cervical and lung cancer, a significant lower risk was, however, observed among nurses employed after 1970.

The standardized incidence ratio was elevated for ovarian cancer among the nurses with 10 or more years of work and with 15 or more years since first employment. The internal analyses did not show any trend with increasing time since first employment; thus there is little support for an association between work as a nurse and the risk of ovarian cancer. Among occupational risk factors that have been suspected to induce ovarian cancer are high doses of radiation, although the magnitude of the effect is assumed to be small (29). Most of the studies including ovarian cancer risk among nurses report no significant excess of this cancer (15, 17, 20, 30). As with breast cancer, the risk of ovarian cancer is influenced by hormones and reproductive factors (31). Confounding by reproductive factors has been suggested to explain earlier findings of an association (32–34). In our present study, the number of children and age at first birth explained very little of the observed excess of ovarian cancer, and the observed increase according to time since first employment (table 3) may have been due to different and nonoccupational causes.

The standardized incidence ratio was elevated for malignant melanoma among the nurses who started to work before 1960. The risk decreased with later periods of first employment and increased with the duration of work. Internal analysis showed a significantly increased risk for the women for whom 30 or more years had elapsed since first employment. In the general Norwegian population, the incidence of malignant melanoma increased between 1950 and 1990 (35).

According to estimates by the International Agency for Research on Cancer (IARC), at least 80% of all melanomas are caused by sun exposure to sensitive skin. Especially sporadic intense exposure and sunburn are assumed to be hazardous (31).

Few studies have investigated the relationship between medical occupational exposure to ionizing radiation and melanoma. However, a recent study of malignant melanoma among radiological technologists in the United States showed an increased risk among those who first worked before 1950 (RR 1.8, 95% CI 0.6–5.5), particularly among those who worked 5 or more years before 1950 (36). In a study of occupation and the risk of malignant melanoma in the United States (37), exposure to X-rays appeared to be the only occupational exposure that significantly raised the risk (odds ratio 1.37, 95% CI 1.12–1.67). As several of the workers occupationally exposed to X-rays in that study were dentists, the association could have been due to confounding factors related to high socioeconomic status. Groups with a high income may have traveled to the south and experienced

sunburn more frequently than workers with lower incomes. Excesses of malignant melanoma have also been observed among female physicians in Denmark and Finland and among female teachers in Denmark, Finland, Norway, and Sweden (20). In our present study, we had no information on radiation exposure or sunbathing habits. The dispersion of melanomas on the body was the same among the nurses as in the general female population. An internal analysis showed a significant positive trend for increasing time since first employment. An influence of occupational risk factors on the observed risk elevation cannot be excluded.

The standardized incidence ratio of other skin cancer was also elevated. Ultraviolet radiation from the sun is regarded as the main etiological factor also in the development of this cancer, and there seems to be a clear relationship between cumulative lifetime exposure to ultraviolet radiation and cancer risk (29, 38). In hospitals ultraviolet radiation has been used to treat skin diseases ever since the beginning of 1900; it has also been used for neonatal jaundice since around 1960 (the Norwegian Radiation Protection Authority, <http://uv.nropa.no/helseeffekter.htm>, 2005). The first radiation-induced skin cancers were recognized among radiologists in 1902 (29). Most of these cancers were squamous-cell carcinomas. In more recent studies, an increased risk of skin cancer has been reported among persons exposed to X-rays and among atomic bomb survivors; however the cancers included more basal cell carcinomas (39). A study from New Hampshire in the United States suggests an increased risk of both basal-cell and squamous-cell carcinomas due to exposure to X-rays (40).

In our study the highest standardized incidence ratio of other skin cancer was found among the nurses who first graduated, had the longest work duration, and for whom ≥ 30 years had elapsed since first employment. This finding could be due to a higher exposure level in earlier years. As for malignant melanoma, the dispersion of other skin cancer on the body resembled that of the general female population. However, the lack of trend with increasing time since first employment lends little support for an occupational association.

The significantly lower risks of some cancers are assumed to be due mainly to lifestyle factors. While smoking is a well documented risk factor for lung cancer, the most important cause of cervical cancer is sexually transmitted infection with human papillomavirus (41). A decreased risk of lung cancer has also been observed among other health care workers in some studies (17, 20), explained by a low prevalence of smoking. Until the last decades of the 20th century, the alcohol and tobacco consumption among women in Norway was very low (www.ssb.no/histstat/tabeller/7-7-13t.txt); thus the rates of relevant cancers in the general female population were also low. The significantly lower risks of cancers

of the mouth and pharynx, esophagus, liver, pancreas, and kidney among the nurses are therefore notable. A possible explanation is the strict regulations that the nurses had to follow well into the second half of the last century, with limited spare time and privacy.

Some potential limitations of our study should be addressed. A major limitation is the lack of information on the actual exposures of interest. Instead, we used the crude exposure indicator variables "time since first employment", "period of first employment" and "duration of work" (which covered the complete work history only for a subgroup of the nurses). We also used the conservative assumption of about 1 year for the duration of work in the last registered employment if the ending time of this employment was unknown.

The results of our study indicate an association between working as a nurse and an increased risk of breast cancer and malignant melanoma. The observed increase in ovarian cancer risk may have been due to factors not related to occupation. The elevated risk of malignant melanoma among the nurses first employed before 1940 could have been caused by higher exposure to ionizing radiation during the first part of the 20 century. We found no excess of hematological cancers in this study. The decreased risks found for several cancer sites indicate that nurses have had favorable habits with respect to many lifestyle factors.

Acknowledgments

The study was financially supported by a grant from the Norwegian Women's Public Health Association.

The authors thank the Norwegian Nurses' Association for its cooperation, Berit H Ingebrigtsen and Hege Supphellen for their assistance with the data collection, and Jan Ivar Martinsen for the data preparation and management.

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Received for publication: 23 February 2006