Cutaneous Melanoma in Swedish Women: Occupational Risks by Anatomic Site

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Background *Few occupational studies have addressed melanoma in women. Accordingly, our aim was to identify occupations with higher risk of cutaneous melanoma, overall and by site, in Swedish female workers.*
Methods *All gainfully employed Swedish women were followed-up from 1971 to 1989, using Death/Cancer Registers. Occupational risk ratios adjusted for age, period, town size, and geographic zone were computed for each site. Risk patterns for different sites were then compared.*
Results *High risks were observed among educators, bank tellers, dental nurses, librarians/archivists/curators, horticultural workers, and hatmakers/milliners. Telephone operators and textile workers had increased risk, mainly in the leg. Other occupation-specific site excesses were also found. Upper-limb risks were correlated with head/neck and thorax, though these two sites were not associated. Legs registered a special pattern, with a moderate correlation with upper limbs or thorax, and no correlation with head/neck.*
Conclusions *Some occupations with possible exposure to arsenic/mercury displayed increased risk. The generalized excess risk among hatmakers/milliners warrants further attention. The weak correlation between legs and other sites suggests site specificity in melanoma risk factors.* Am. J. Ind. Med. 48:270–281, 2005. *© 2005 Wiley-Liss, Inc.*

***KEY WORDS:* melanoma; occupation; women; site; cohort; milliner; arsenic; mercury**

INTRODUCTION

Over a 20-year period, melanoma has shown itself to be one of the most rapidly increasing malignant tumors, particularly in Caucasian populations. Sweden, with an average annual increase in incidence of 2.1% in men and 1.7% in women [Center for Epidemiology, 2004], can be regarded as a paradigm. This sharp rise is generally explained as being a consequence of changes in sun-exposure patterns in leisure-time activities and holiday travel to sunny countries, both of which have gradually become more common [Armstrong and Kricker, 1994]. However, these factors cannot account for the increased risk reported for professional categories such as lithographers [Nielsen et al., 1996; Bouchardy et al., 2002] and electrical workers [Fritschi and Siemiatycki, 1996], suggesting the influence of certain occupational factors. Most occupational studies on melanoma have focused only on men [Linet et al., 1995; Fritschi and Siemiatycki, 1996], since in previous decades the low number of female workers has acted as a bar to occupational studies in women. Nevertheless, extrapolation of male-results to women can be misleading for a number of reasons.

Abbreviations: CM, cutaneous melanoma; RR, risk ratio; UV, ultraviolet; EMF, electromagnetic field.

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First, there are notable sex-related differences in the epidemiologic characteristics of melanoma, with anatomic distribution being particularly noteworthy: while the trunk is the most common location in men, legs are the primary site in women, and these differences are found in countries with large variations in latitude [Armstrong and Kricker, 1994]. Some authors link such differences to gender-specific patterns of sun exposure [Elwood and Gallagher, 1998], yet MacLennan et al. [2003] have nevertheless reported the same gender differences in nevus density on the back and lower limbs in young children unrelated to sun exposure. It has also been suggested that melanocytes might have site-dependent susceptibility towards malignancy [Green, 1992] or even that different pathways related to anatomic site might possibly coexist [Maldonado et al., 2003; Rivers, 2004].

Second, men and women holding occupations with the same job title cannot automatically be assumed to be performing the same work, since exposure patterns and levels may be gender-specific due to gender-based job patterns, with different tasks being assigned or different approaches being taken to the same task [Blair et al., 1999]. Third, toxicokinetic differences between sexes might interact with exposure. Women's thinner skin (which might be relevant here) and higher percentage of fat could modify their susceptibility to certain toxic substances. In addition, there could be hormonal factors linked to melanoma. Estrogens seem to increase the number of melanocytes and to modify their melanin content [Jee et al., 1994]. Moreover, they can also cause skin hyperpigmentation [Jelinek, 1970]. Oral contraceptives have been suggested as another possible risk factor in the development of melanoma, although results have not been conclusive to date [Karagas et al., 2002].

Sweden can be regarded as the ideal candidate for conducting a study into melanoma and female occupation: the country has one of the highest incidences [Center for Epidemiology, 2004], a high percentage of working women that was approaching 50% in 1970 [Andersen et al., 1999], and its epidemiologic registers have been used to construct a huge historical cohort [Barlow and Eklund, 1995] numbering over 1,000,000 working women, followed from 1970 to 1989. Our main aim was to study the relationship between occupation and melanoma in women, by giving a comparative view of the occupational risk of this neoplasm by site, nationwide, using the same approach previously used in men [Perez-Gomez et al., 2004]. The large size of the cohort enabled us to estimate the risk of melanoma even for occupations that are relatively unusual in women.

The relationship between total melanoma and occupation has already been studied, using a related cohort in a different time frame (1960–1979) [Vagero et al., 1990] and the same material, but within a broader context that sought to link occupation to all types of cancer [Andersen et al., 1999; Pollán and Gustavsson, 1999]. Our study reports site-specific relative risks by job title, suitably adjusted for town size and geographic distribution, using the whole female cohort as a reference, as well as comparisons within occupational sectors to serve as a contrast with people having a more homogeneous socioeconomic status. As in a previous study [Perez-Gomez et al., 2004] that focused on men, we also compared site-risk distributions to assess disparities or similarities between locations that might possibly suggest etiologic relationships. Throughout the study, the terms ''site'' and ''location'' are used synonymously to denote anatomic distribution of melanomas.

MATERIALS AND METHODS

The base population for this historical cohort comprised Swedish women gainfully employed at the time of the 1970 census, present in the 1960 census, and still alive, and aged 25–64 years on January 1, 1971. The restriction imposed on all members of the cohort of being present in both the 1960 and 1970 censuses, ensured their residence in the country for at least 10 years. The cohort included 1,101,669 women followed-up until the end of 1989; and within it, a subcohort was also defined, including only those women who declared the same occupation in both the 1960 and 1970 censuses, comprising 2,45,921 women. Two-thirds of the cohort members were full-time workers, while 23% worked for 20–34 hr and 11% for under 20 hr per week.

Information was drawn from two linked data sets, namely: the Swedish Cancer-Environment register, including incident cases and some demographic variables from the 1960 and 1970 censuses, which were used to compute specific rate numerators; and a background population register comprising all individuals in the 1970 census, with information on occupation and residence in 1970, occupation in 1960, and where applicable, date of death that was used to calculate specific rate denominators. The record-linkage between these two registers has been described in detail elsewhere [Center for Epidemiology, 1994]. Melanoma was coded under rubric 190 of the International Classification of Diseases (7th revision); a fourth digit specifies anatomic site. All head and neck melanomas were jointly analyzed. It should be borne in mind that cutaneous melanomas with multiple sites or of non-specified location are included in the global melanoma data but not in the site analysis. They accounted for 0.4% and 9.8% of all registered melanomas, respectively.

Person-years in each of the 278 occupations were accumulated from 1971 until date of death or year-end 1989. The overall person-time that each worker contributed to the study was allocated to the corresponding cells of the stratification variables. These were occupation, county, and size of town of residence in 1970, which were taken as fixed variables, and 5-year age-groups and the calendar periods 1971–75, 1976–80, 1981–85, and 1986–89, which were time-dependent variables. Clayton's algorithm [Breslow and

Day, 1987] was used to calculate the exact number of person-years.

Occupation was coded as a three-digit number as per the Nordic Classification of Occupations [Center for Epidemiology, 1994]. The first digit refers to 1 of 10 major occupational sectors (0–9), where higher numbers indicate manual occupations and lower numbers non-manual occupations, often associated with a higher socio-economic status. Expected cases were computed for each occupation using the age-period specific rates for the whole cohort as the reference.

On the assumption that the observed number of cases were distributed in each stratum as a Poisson variable, log-linear Poisson models were fitted to estimate risk ratios (RRs). Swedish counties were classified into low, medium or high melanoma risk, using a Poisson model adjusted for sex, age, period, occupational sector, and town size, and taking the incidence for the whole country as the reference. This classification was also geographically meaningful, with low risks in the north, and all the high risks in the southern Swedish counties [Perez-Gomez et al., 2004].

For each occupation, site-specific RRs, adjusted for town size and geographic area, were then extracted from log-linear Poisson models; the number of expected cases that had been computed on the basis of the age- and period-specific reference rates, were introduced as an offset [Breslow and Day, 1987] to obtain RRs that were also adjusted for age and period.

Each occupation with at least three observed cases of total cutaneous melanoma was first compared against the whole working female population, and then only against others within the same occupational sector to serve as a contrast with people having a more homogeneous socio-economic status. Production sectors (Sector VII and VIII) were treated as a single category.

These analyses were also repeated for the subcohort reporting the same occupation in the 1970 and 1960 censuses, though only for all cutaneous melanoma due to the low number of cases. This subcohort represents a more specifically exposed group, which is mainly used to check the consistency of the results observed for the general cohort but nevertheless displays certain differences with it, these being: a) a lower number of cases by job title, due partly to the lower female participation in the labor force in 1960, which either reduces statistical power or even renders computation of the risk for some jobs impossible; b) an absence of subjects in terms of jobs that either did not exist or were uncommon among women in 1960 (i.e., mechanical engineers & technicians, or system analysts and programmers), or in terms of occupations with a lower stability (i.e., those implying promotion, such as clerical staff); and c) a slightly different composition of sectors as between subcohort and cohort.

Logarithms of occupational RRs obtained with the whole cohort were also used to compare risk patterns across different locations. The results are depicted on a graph, highlighting occupations with high RRs and those with discrepant RRs for different sites in Swedish women (Figure 1). Pairwise site agreement was tested using Spearman's correlation coefficient.

RESULTS

Across follow-up, 3,598 cases of cutaneous melanoma were detected in the whole cohort and 875 in the subcohort with a similar anatomic distribution in both cases. Lower limbs, the most frequent location, proved slightly more frequent in the subcohort (40% vs. 38%), as did thorax in the general cohort (23% vs. 20%), while head/neck and upper-limb melanomas accounted for 11% and 18% of the cases, respectively.

In general, RRs in the cohort showed a certain socioeconomic gradation, albeit clearly less evident than that previously reported for men [Perez-Gomez et al., 2004], with excess risk in sectors 0-III, which mainly contain professional and clerical workers, and reduced risks in the production (VII-VIII) and services sectors (IX). Sector V (Mining) registered only one case. In head/neck, this gradation was not in evidence. Sector VI (Transport and Communications) revealed excess risk in this anatomic location as well as in lower limbs.

Table I shows risk ratios (RR) by job title in the cohort and subcohort for all melanomas with the whole population as reference, as well as with the intrasectorial approach. Table II contains the results by site, though only for the whole cohort, due to the low number of cases in the subcohort. All these RR are adjusted by age, period, town-size, and geographic zone.

All occupations having a minimum of three cases and an $RR > 1.5$ for global cutaneous melanoma in any of the analyses, or a minimum of three cases and an $RR > 2$ for any site, regardless of its statistical significance, are reported. A higher cut-off was used for specific sites, since higher risks were also expected given the lower number of cases. For comparison purposes, all job titles fulfilling the established criteria were included in both tables. However, jobs with less than three cases in all the specific sites are only reported in Table I. Risks for job titles not shown in the tables are available and can be provided on request.

ALL CUTANEOUS MELANOMA

When all cases of cutaneous melanoma were taken into account, only 13 occupations displayed increased risk in any of the analyses (Table I). In general, the intrasectorial approach yielded results similar to those of the general approach, though its lower power resulted in wider confidence intervals. In Sectors 0–III, significant excesses were found for dental nurses, authors, bank tellers, and several types of teachers. Insofar as blue-collar workers were concerned, special mention should be made of the consistent

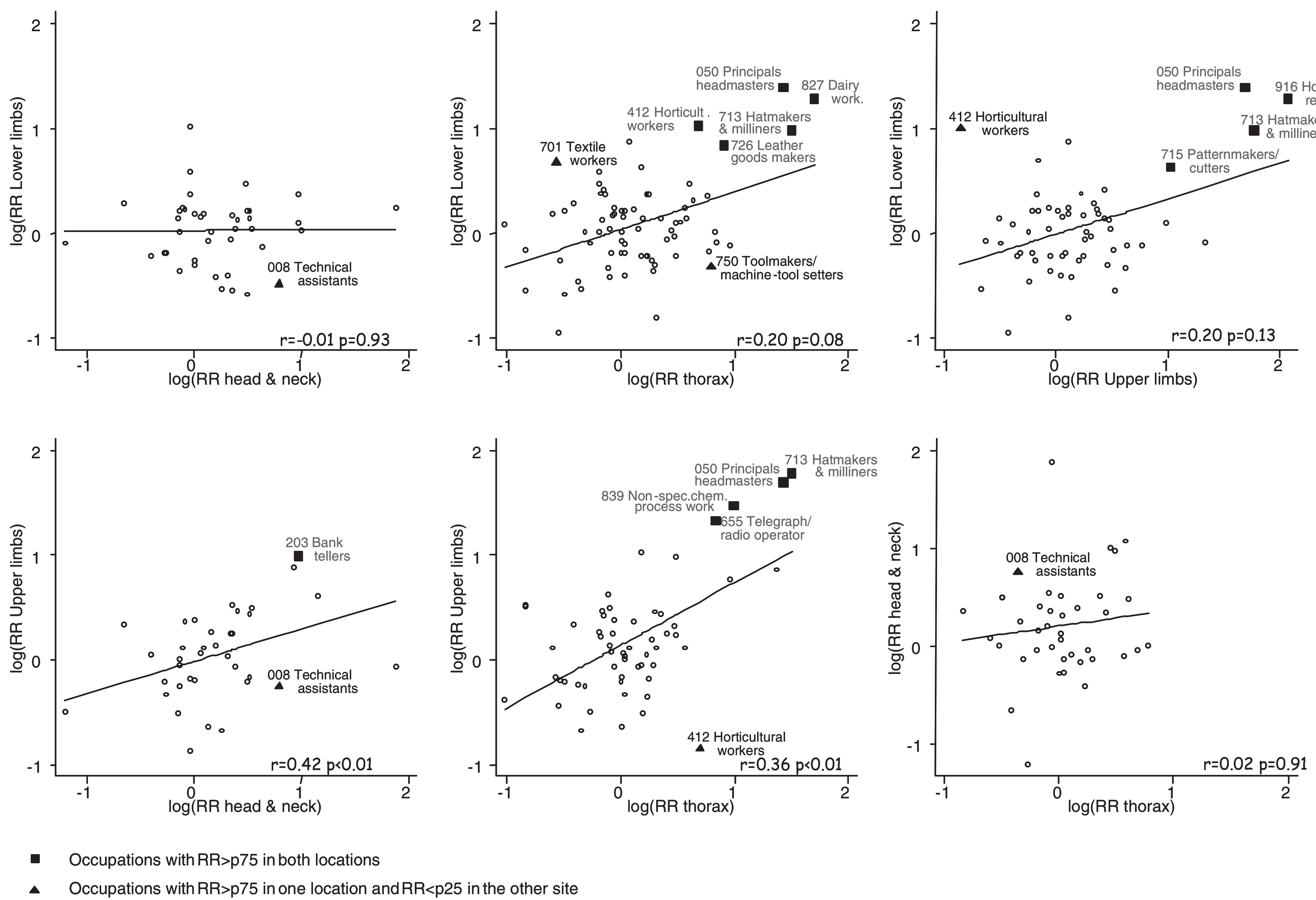

FIGURE 1. Linear regression and Spearman correlation coefficients between site risks in Swedish women. All occupations with two or more cases in both sites are considered.

TABLE I. All Cases: Age-, Period-, Townsize-, and Geographically-Adjusted RR of Cutaneous Melanoma in Swedish Women by Job Title (Cohort and Subcohort). General and Intrasectorial Risks Shown

	All cutaneous melanoma												
	Complete cohort						Subcohort with same occupation in the 1960 & 1970 censuses						
			General		Intrasectorial				General		Intrasectorial		
Occupational titles	Pop	C	RR	95% CI	RR	95% CI	Pop	C	RR	95% CI	RR	95% CI
SECTOR 0: Professional & technical work												
032 Dentists	1,571	7	1.40	0.67–2.94	1.28	0.61–2.69	842	2	0.63	0.16–2.53	0.59	0.15–2.36
041 Midwives	1,490	7	1.51	0.72–3.17	1.37	0.65–2.87	606	4	1.84	0.69–4.91	1.68	0.63–4.52
044 Dental nurses	5,670	32	1.71	1.21–2.42	1.57	1.10–2.23	2,592	10	1.15	0.62–2.15	1.07	0.57–2.01
045 Medical technicians	4,716	21	1.36	0.89–2.09	1.24	0.81–1.92	705	2	0.80	0.20–3.19	0.75	0.19–3.02
046 Pharmacists	2,601	10	1.27	0.68–2.36	1.15	0.62–2.15	951	4	1.18	0.44–3.15	1.10	0.41–2.94
047 Physiotherapists, occupational therapists	5,731	16	0.88	0.54–1.44	0.80	0.49–1.31	1,144	7	1.84	0.87–3.87	1.72	0.81–3.65
050 Principals, headmasters	555	7	3.77	1.79–7.91	3.44	1.63–7.24	83	**2**	**6.37**	**1.59–25.52**	**5.85**	**1.45–23.5**
051 University, higher education teachers	1,711	9	1.74	0.90–3.35	1.60	0.83–3.09	92	1				
052 Teachers in theoretical subjects	**14,009**	**63**	**1.49**	**1.16–1.91**	**1.37**	**1.06–1.77**	3,466	17	1.35	0.84–2.19	1.27	0.78–2.09
056 Pre-school teachers	6,805	28	1.33	0.91–1.92	1.21	0.83–1.76	1,185	8	1.88	0.94–3.78	1.80	0.89–3.66
057 Educational methods advisors	1,428	9	1.98	1.03–3.81	1.81	0.94–3.49	84	0				
061 Ministers, priests	819	5	2.00	0.83–4.81	1.81	0.75–4.35	331	3	2.61	0.84–8.10	2.33	0.74–7.27
084 Authors	163	3	6.28	2.02–19.49	5.73	1.84–17.8	34	0				
085 Journalists, editors	2,474	9	1.16	0.60–2.24	1.06	0.55–2.05	539	3	1.60	0.52–4.98	1.52	0.49–4.78
086 Performing artists	932	5	1.71	0.71–4.12	1.58	0.65–3.81	358	0				
091 Accountants & auditors	640	4	1.97	0.74–5.24	1.80	0.67–4.80	52	1				
093 Librarians, archivists, & curators	4,703	17	1.15	0.72–1.86	1.05	0.65–1.70	949	7	2.09	0.99–4.41	2.02	0.95–4.29
095 Psychologists	1,167	5	1.50	0.62–3.59	1.36	0.57–3.29	117	1				
SECTOR I: Administrative & managerial work[a]												
101 Government legislative & admin. work	4,306	16	1.14	0.70–1.87	1.17	0.62–2.24	453	0				
111 Managing directors	927	5	1.68	0.70–4.04	1.71	0.67–4.40	162	0				
118 Other business managers	6,321	18	0.87	0.55–1.38	0.71	0.38–1.33	493	2	1.06	0.27–4.26		
SECTOR II: Bookkeeping & clerical work												
203 Bank tellers	3,360	20	1.84	1.19–2.86	1.68	1.08–2.63	519	2	1.05	0.26–4.19	0.91	0.22–3.68
292 Bank employees (general bank work)	7,666	28	1.11	0.76–1.61	1.00	0.68–1.45	1,229	7	1.65	0.78–3.47	1.41	0.66–3.01
293 Travel agency employees	803	3	1.14	0.37–3.53	1.01	0.33–3.14	149	0				
296 Insurance raters, claims adjusters	3,764	13	1.04	0.60–1.80	0.92	0.53–1.60	1,189	5	1.15	0.48–2.79	0.94	0.38–2.29
SECTOR IV: Agriculture, forestry, fishing												
401 Working prop (agric, hortic., & forestry)	4,247	10	0.85	0.45–1.58	0.82	0.44–1.56	1,116	3	0.90	0.29–2.82	1.05	0.30–3.66
412 Horticultural workers	5,467	30	1.60	1.11–2.29	1.73	1.10–2.74	969	6	1.57	0.70–3.51	0.62	0.17–2.24
441 Forest workers & log-drivers	674	3	1.76	0.57–5.48	1.64	0.52–5.18		27	0			
SECTOR VI: Transport & communications												
633 Motor-vehicle drivers, tram drivers	2,871	6	0.68	0.30–1.50	0.61	0.27–1.38	182	0				
643 Railway station master/ train dispatchers	285	3	3.18	1.02–9.85	2.84	0.90–8.92	9	0				
653 Telephone operators	4,161	22	1.60	1.05–2.43	1.41	0.89–2.24	3,069	16	1.44	0.88–2.37	1.86	0.94–3.69
655 Telegraph & radio operators	1,193	7	1.77	0.84–3.72	1.57	0.73–3.36	433	2	1.26	0.32–5.06	1.41	0.34–5.92
SECTORS VII & VIII: Production												
701 Textile workers	7,208	26	1.00	0.68–1.47	1.13	0.76–1.69	3,258	15	1.13	0.68–1.89	1.19	0.69–2.06
713 Hatmakers & milliners	1,129	10	2.62	1.41–4.88	3.10	1.65–5.82	589	6	2.94	1.32–6.56	3.40	1.48–7.80
715 Patternmakers & cutters	2,184	11	1.34	0.74–2.43	1.52	0.83–2.77	783	4	1.22	0.46–3.26	1.26	0.46–3.43
718 Other sewing work	4,398	15	0.95	0.57–1.57	1.09	0.65–1.82	677	4	1.50	0.56–4.01	1.65	0.61–4.47
726 Leather goods makers	1,037	5	1.29	0.54–3.10	1.48	0.61–3.58	269	2	1.74	0.43–6.99	1.77	0.43–7.24
744 Dental technicians	604	3	1.53	0.49–4.74	1.81	0.58–5.63	368	0				
750 Toolmakers, machine-tool setters/operat.	5,833	17	0.91	0.56–1.46	1.08	0.66–1.76	327	0				
826 Butchers & meat preparers	1,584	9	1.66	0.86–3.20	1.93	1.00–3.74	201	1				
827 Dairy workers	561	4	2.16	0.81–5.77	2.52	0.94–6.76	109	0				
828 Other food-processing work	810	4	1.47	0.55–3.92	1.71	0.64–4.57	40	0				
831 Chemical process workers	341	3	2.65	0.85–8.22	3.14	1.00–9.81	35	0				
839 Non-spec. chemical & cellulose processes	1,214	6	1.51	0.68–3.37	1.85	0.82–4.16	153	0				
881 Packers	10,285	36	1.01	0.73–1.40	1.19	0.84–1.67	1316	9	1.84	0.95–3.55	2.19	1.10–4.35
SECTOR IX: Services & military work												
914 Nursemaids	28,864	87	0.94	0.76–1.16	1.14	0.91–1.42	5,207	23	1.38	0.91–2.09	1.81	1.15–2.86
916 Hotel receptionists	551	4	2.27	0.85–6.05	2.65	0.99–7.09	33	0				
942 Bath attendants	1,341	3	0.67	0.22–2.09	0.79	0.25–2.44	350	0				
946 Photographers	642	3	1.47	0.47–4.56	1.74	0.56–5.42	251	2	2.43	0.61–9.74	3.01	0.74–12.17

Pop, population; C, cases; RR, risk ratio; CI, confidence interval.
All occupations reported have a minimum of three cases and an RR $>$ 1.5 for global cutaneous melanoma in the whole cohort and/or 60–70 subcohort, or a minimum of three cases with RR $>$ 2 for any of the sites (whole cohort only) in the general or intrasectorial analyses, regardless of their statistical significance.
Shaded job titles have more than three cases, RRs over the established threshold for all cases (1.5) and $P < 0.05$. Bold text indicates only $P < 0.05$.
Sector V (Miners and quarrymen) is not shown, as there was only one case of melanoma.
[a]Intrasectorial analysis could not be performed in SECTOR I for the 60-70 subcohort, as only one job title had melanoma cases.

TABLE II. Sites: Age-, Period-, Townsize- and Geographically-Adjusted RR of Cutaneous Melanoma in Swedish Women by Job Title (Whole Cohort). General and Intrasectorial Analyses

	Head and Neck					Thorax					Upper limbs					Lower limbs				
		General		Intrasectorial			General		Intrasectorial			General		Intrasectorial			General		Intrasectorial	
Occupational titles	**C**	**RR**	**95% CI**	**RR**	**95% CI**	**C**	**RR**	**95% CI**	**RR**	**95% CI**	**C**	**RR**	**95% CI**	**RR**	**95% CI**	**C**	**RR**	**95% CI**	**RR**	**95% CI**
SECTOR 0: Professional & technical work																				
032 Dentists	0					3	2.51	0.81–7.79	2.14	0.69–6.70	0					3	1.57	0.51–4.87	1.43	0.46–4.45
041 Midwives	1					3	2.68	0.86–8.32	2.30	0.74–7.20	1					2	1.14	0.29–4.57	1.01	0.25–4.06
044 Dental nurses	1					6	1.27	0.57–2.83	1.08	0.48–2.44	4	1.24	0.47–3.33	1.12	0.41–3.02	19	2.60	1.65–4.09	2.40	1.51–3.82
045 Medical technicians	3	2.45	0.78–7.62	2.73	0.85–8.74	7	1.82	0.86–3.83	1.56	0.73–3.31	1					7	1.15	0.55–2.41	1.03	0.49–2.19
046 Pharmacists	0					1					1					7	2.28	1.09–4.80	2.04	0.97–4.33
047 Physiotherapists, occupational therapists	2	1.03	0.26–4.14	1.14	0.28–4.66	5	1.18	0.49–2.83	1.01	0.42–2.45	2	0.62	0.15–2.48	0.53	0.13–2.16	7	1.02	0.49–2.15	0.93	0.44–1.97
050 Principals, headmasters	0					**2**	**4.91**	**1.23–19.67**	**4.18**	**1.04–16.85**	**2**	**5.85**	**1.46–23.47**	**5.43**	**1.34–21.95**	3	4.39	1.41–13.64	3.99	1.28–12.44
051 University, higher education teachers	1					4	3.04	1.14–8.13	2.61	0.97–7.05	2	2.28	0.57–9.13	2.16	0.53–8.75	2	0.97	0.24–3.89	0.89	0.22–3.57
052 Teachers in theoretical subjects	3	0.80	0.26–2.50	0.90	0.28–2.87	21	2.00	1.30–3.08	**1.75**	**1.12–2.75**	9	1.24	0.64–2.40	1.12	0.57–2.20	23	1.42	0.94–2.14	1.27	0.83–1.94
056 Pre-school teachers	2	1.30	0.32–5.21	1.43	0.35–5.84	6	1.10	0.49–2.45	0.93	0.41–2.09	5	1.40	0.58–3.37	1.28	0.52–3.11	11	1.32	0.73–2.39	1.19	0.65–2.18
057 Educational methods advisors	0					5	4.56	1.89–11.00	3.91	1.61–9.50	2	2.51	0.63–10.05	2.37	0.59–9.58	1				
085 Journalists, editors	2	2.82	0.70–11.32	2.93	0.71–12.13	4	2.12	0.79–5.67	1.79	0.66–4.83	1					1				
086 Performing artists	0					1					0					4	3.46	1.30–9.24	3.27	1.21–8.81
093 Librarians, archivists, & curators	0					5	1.49	0.62–3.59	1.26	0.52–3.07	2	0.75	0.19–3.02	0.70	0.17–2.84	5	0.91	0.38–2.18	0.81	0.33–1.96
SECTOR I: Administrative & managerial work																				
101 Government legislative & admin. work	3	2.07	0.66–6.46	6.55	0.66–64.51	2	0.61	0.15–2.44	0.94	0.16–5.71	5	2.00	0.83–4.82	0.94	0.31–2.84	6	1.13	0.50–2.51	1.27	0.44–3.71
111 Managing directors	0					0					1					3	2.73	0.88–8.48	3.34	0.92–12.06
118 Other business managers	1					3	0.62	0.20–1.92	1.37	0.23–8.28	8	2.16	1.07–4.34	1.12	0.39–3.24	5	0.63	0.26–1.53	0.45	0.15–1.35
SECTOR II: Bookkeeping & clerical work																				
203 Bank tellers	2	2.12	0.53–8.49	2.66	0.64–10.97	5	1.83	0.76–4.41	1.63	0.67–3.97	6	3.23	1.45–7.22	2.68	1.18–6.10	5	1.19	0.49–2.86	1.10	0.45–2.66
292 Bank employees (general bank work)	2	0.94	0.23–3.78	1.10	0.27–4.49	4	0.63	0.24–1.70	0.55	0.21–1.49	6	1.37	0.61–3.06	1.12	0.49–2.53	13	1.32	0.77–2.28	1.20	0.69–2.09
293 Travel agency employees	0					0					0					3	2.82	0.91–8.77	2.45	0.78–7.63
296 Insurance raters, claims adjusters	0					3	1.00	0.32–3.10	0.89	0.28–2.79	5	2.26	0.94–5.48	1.86	0.76–4.57	4	0.83	0.31–2.20	0.72	0.27–1.93
SECTOR IV: Agriculture, forestry, & fishing																				
401 Working prop (agric, hortic., & forestry)	1					5	2.27	0.93–5.51	2.18	0.85–5.59	0					3	0.78	0.25–2.42	0.84	0.26–2.70
412 Horticultural workers	4	1.50	0.56–4.03	0.97	0.28–3.45	8	2.03	1.01–4.09	1.98	0.78–5.02	2	0.55	0.14–2.19	0.42	0.08–2.19	12	**1.79**	**1.01–3.16**	2.78	1.36–5.65
SECTOR VI: Transport & communications																				
633 Motor-vehicle drivers, tram drivers	3	3.86	1.24–12.05	3.18	0.90–11.25	0					2	1.28	0.32–5.13	1.84	0.42–8.15	1				
653 Telephone operators	3	2.36	0.76–7.35	1.62	0.46–5.75	5	1.44	0.60–3.48	1.82	0.67–4.90	1					12	2.23	1.26–3.94	1.60	0.84–3.02
SECTORS VII & VIII: Production																				
701 Textile workers	1					3	0.55	0.18–1.72	0.56	0.18–1.79	3	0.61	0.20–1.89	0.85	0.26–2.72	16	**1.68**	**1.02–2.75**	**2.00**	**1.18–3.38**
713 Hatmakers & milliners	1					3	3.81	1.22–11.83	4.51	1.42–14.34	3	4.25	1.37–13.23	5.90	1.83–19.03	3	2.12	0.68–6.58	2.66	0.84–8.38
715 Patternmakers & cutters	0					2	1.10	0.28–4.42	1.20	0.29–4.90	3	2.03	0.65–6.30	2.80	0.87–9.02	5	1.59	0.66–3.82	1.87	0.76–4.58
718 Other sewing work	2	0.98	0.24–3.94	1.00	0.24–4.12	3	0.89	0.29–2.76	0.94	0.30–2.97	3	1.02	0.33–3.17	1.46	0.46–4.67	6	1.02	0.46–2.28	1.21	0.53–2.74
726 Leather goods makers	0					2	2.29	0.57–9.20	2.49	0.61–10.20	0					3	2.02	0.65–6.27	2.31	0.73–7.32
750 Toolmakers, machine-tool setters/operat.	2	0.93	0.23–3.73	1.01	0.25–4.18	8	1.84	0.92–3.69	2.18	1.05–4.53	1					4	0.58	0.22–1.54	0.74	0.27–2.01
826 Butchers & meat preparers	1					3	2.45	0.79–7.60	2.75	0.87–8.71	1					1				
881 Packers	4	0.96	0.36–2.56	0.96	0.34–2.66	9	1.12	0.58–2.17	1.28	0.64–2.56	4	0.62	0.23–1.65	0.84	0.30–2.32	15	1.12	0.67–1.86	1.45	0.84–2.48
SECTOR IX: Services & military work																				
914 Nursemaids	15	1.50	0.90–2.52	1.50	0.87–2.59	14	0.64	0.38–1.09	0.85	0.49–1.47	20	1.22	0.78–1.91	1.60	0.99–2.57	32	0.92	0.65–1.31	1.13	0.78–1.64
942 Bath attendants	0					0					0					3	1.88	0.61–5.85	2.32	0.74–7.25

C, cases; RR, risk ratio; CI, confidence interval.

All jobs reported have a minimum of three cases and an RR > 1.5 for global cutaneous melanoma in the whole cohort and/or 60–70 subcohort, or a minimum of three cases with RR > 2 for any of the sites (whole cohort only) in the general or intrasectorial analyses, regardless of their statistical significance. Occupations with fewer than three cases in all sites are excluded.

Shaded job titles have more than three cases, RRs over the established threshold for the sites (2) and $P < 0.05$. Bold text indicates only $P < 0.05$.

increase in risk found among horticultural workers and hatmakers/milliners. Railway station masters/train dispatchers and telephone operators also registered a significant excess risk in the general analysis, which remained high, although not statistically significant, in the intrasectorial approach. The opposite was true of Butchers/meat preparers and chemical process workers, where the high, although not significant, excess risks found in the general analysis attained statistical significance in the intrasectorial approach.

Subcohort analysis confirmed the increased risk found for hatmakers/milliners, and highlighted two new occupations—packers and nursemaids, with marginally significant excess risks, which became clearly significant when compared solely with jobs within their own sector.

MELANOMA SUBSITES (Table II)

In the case of the head & neck, only motor-vehicle drivers/tram drivers presented a significant excess risk for this site. In the case of the thorax, both the general and intrasectorial analyses showed significant or marginally significant high risks for university and higher education teachers, teachers in theoretical subjects, and educational methods advisors, as well as for principals/headmasters, although based only on two cases in this last-mentioned occupation. In addition, excess risks were also found among horticultural workers, hatmakers/milliners, and toolmakers/machine-tool setters/operators.

Other business managers displayed increased risk of melanoma in the upper limbs but this disappeared in the intrasectorial analysis, unlike bank tellers and hatmakers/milliners who registered significant excesses in both approaches for this site. Principals and headmasters also had a very high significant risk, but again, based only on two cases.

Lastly, in the case of lower limbs, both the general and intrasectorial analyses showed a significant or marginally significant high risk for dental nurses, pharmacists, principals/headmasters, performing artists, horticultural workers, and textile workers. Telephone operators also had an increased risk, although this was only significant when the whole cohort was used as reference.

ESTIMATION OF ERROR DUE TO CHANCE

Table III shows an estimation of the expected number of significant associations with an $RR > 1$ assuming the null hypothesis, that is, attributable to chance, by site and analysis, assuming two-tailed $\alpha = 0.05$, as well as the observed number of significant associations and those over the established threshold (1.5 for all cases and 2 for sites). It is interesting to note that, except for head and neck, all sites registered a number of statistically significant excess risks that proved at least three times greater than the expected number. However, the importance of our findings should be judged in the light of available knowledge.

CORRELATIONS OF RESULTS BY SITE

In order to detect disparities or similarities between locations, we performed pairwise comparisons between occupational log(RR) by site. Figure 1 depicts occupations with discordant risks (logRR < percentile 25 in one site and logRR > percentile 75 in the other), and indicates jobs with increased risk (logRR > percentile 75) for both locations. Both Figure 1 and Table IV show that upper limb risks registered a significant correlation with head and neck estimates ($r = 0.42$) and thorax risks ($r = 0.36$), and a non-significant correlation of 0.20 with lower limbs. Thorax and lower limbs likewise showed a non-significant correlation ($r = 0.20$). The lack of correlation between head and neck and thorax ($r = 0.02$), or lower limbs ($r = -0.01$) is noteworthy. Horticultural workers revealed a big discrepancy between the relative risk observed for melanomas in thorax and in lower limbs, and a lack of excess risk in upper limbs. Textile workers displayed a similar pattern, with a high risk in lower limbs and a low risk in thorax. The contrary was observed for

TABLE III. Estimation of Observed and Expected Associations due to Chance, by Site and Analysis

		Total cases				Head & neck				Thorax				Upper limbs				Lower limbs			
		Total	ex	ob	thr	Total	ex	ob	thr	Total	ex	ob	thr	Total	ex	ob	thr	Total	ex	ob	thr
General	Cohort	112	2.8	13	9	30	0.8	2	1	62	1.6	7	5	43	1.1	5	3	74	1.9	8	5
	Subcoh.	49	1.2	3	1																
Intrasectorial	Cohort	112	2.8	11	8	30	0.8	1	0	62	1.6	5	3	43	1.1	3	2	74	1.9	5	5
	Subcoh.	49	1.2	3	3																

Total, number of occupations with more than three cases, that is, number of comparisons performed.
ex, number of expected significant RRs > 1 for two-tailed $\alpha = 0.05$.
ob, number of observed significant RRs > 1.
thr, number of observed significant RRs over the indicated threshold (1.5 for all cases and 2 for sites).

TABLE IV. Spearman Correlation Coefficients Between Site Risks in Swedish Women. All Occupations With Two or More Cases in Both Sites are Considered

		Head/neck	Thorax	Upper limbs
Thorax	r	0.02		
	p	0.91		
Upper limbs	r	0.42	0.36	
	p	<0.01	<0.01	
Lower limbs	r	0.01	0.20	0.20
	p	0.93	0.08	0.13

technical assistants, who had an excess risk for head and neck melanoma and lower risk in upper limbs and thorax.

DISCUSSION

Ultraviolet radiation from sunlight is generally acknowledged as playing a main role in the etiology of melanoma. However, a number of studies [Pion et al., 1995; Andersen et al., 1999; Perez-Gomez et al., 2004] have reported associations between certain jobs and this neoplasm, which cannot be explained by sunlight exposure alone, suggesting a role for occupational factors that may be gender specific. As in our earlier study [Perez-Gomez et al., 2004], we again studied the occupational risk distribution for this neoplasm, but this time with the focus on women in order to ascertain any possible occupational hazards that might be linked to female melanoma.

The lack of personal information in our data led us to adopt an indirect approach, aimed at trying to control those factors associated with non-occupational characteristics that could confound the results, adjusting our risk estimations: a) for town size, in view of the fact that an urban/rural gradient of risk has been described in Sweden, which, according to some authors [Eklund and Malec, 1978], can probably be considered a proxy of travel habits to sunny countries; and b) for geographical distribution [Westerdahl et al., 1992] that might reflect environmental UV exposure. Furthermore, there is a well-known relationship between socioeconomic class and melanoma risk [Pion et al., 1995], which is also thought to reflect lifestyle differences. It has been pointed out that women working outside the home can differ from homeworkers in many lifestyle-related factors [Blair et al., 1999], such as tobacco, drug or alcohol use, or reproductive history, all of which have been studied as possible modifiers of melanoma risk [Westerdahl et al., 1996]. Dietary fat and coffee consumption have also been associated with melanoma in women [Veierod et al., 1997]. Accordingly, the fact that our cohort, and thus our reference group, is solely made up of working women, should be seen as an additional strength of the study. Furthermore, we also calculated the risk for each occupation, taking into account only those women working within the same occupational sector as the job considered, an approach that enables comparison with subjects having a more homogeneous socioeconomic status. A general limitation of such cohort studies is the use of data, such as occupation, town size, and county of residence registered at one point in time, which might change across follow-up. As stated above, although the subcohort had a more specific definition of exposure, it had lower statistical power and fewer occupations.

In these types of studies that entail multiple comparisons, there is always a certain risk of obtaining some spuriously significant associations. Table III provides an estimation of expected associations due to chance, by site and analysis, together with the real number of associations obtained. These data show that the only significant result (Table III) for head and neck could also be explained by chance, suggesting that occupation-related factors do not play an important role in this site, despite its being the most exposed part of the body. To weight the plausibility of the associations found, several considerations have also been taken into account, namely: a) consistency between the results of the cohort and subcohort analyses; b) similar results being observed for jobs with quite similar occupational exposures; and c) the existence of comparable results in the literature that are specifically discussed.

According to our results, at least five education-related occupations were shown by both the general and intrasectorial approaches to have a significant or marginally significant excess risk of melanoma in the whole cohort. While the thorax was the most common location for this increased risk, there was no excess risk for the head and neck. Educational occupations have been repeatedly associated with excess of risk of melanoma in men [Goodman et al., 1995; Andersen et al., 1999; Bouchardy et al., 2002] and women alike [Gallagher et al., 1986; Vagero et al., 1990; Andersen et al., 1999], and it is noteworthy that this increased risk has been described throughout the whole range of teachers, from preschool to college. No clear explanation can be given, except perhaps their longer holidays (at least a month more de facto). The Association of Swiss Cancer Registries [Bouchardy et al., 2002] reported socioeconomically adjusted estimators for men, which did not confirm the excess risk yielded by their crude data. In addition, King et al. [1994] found that the high proportional mortality rate described for female teachers in British Columbia disappeared when housewives were excluded from the analysis. However, none of these reasons are capable of explaining our results, since our intrasectorial estimates, which are socioeconomically adjusted to a certain degree, continue to show excess risks in women in the same way as they did in men [Perez-Gomez et al., 2004], and yet only female workers were used as the reference.

Probably, the clearest and most consistent result in our study is the previously unreported significant risk observed for hatmakers and milliners. This occupational category showed significant excess incidence in all the analyses that reflected a generalized increase in all the anatomic sites covered. This increased risk was likewise found in the subcohort that declared the same job category in 1960, thereby reinforcing the possibility of an occupational association. Social confounding and sun-related lifestyles would not seem plausible explanations for these results.

The women engaged in this occupation are mainly milliners, some of whom probably handle fur hats. Swedish male fur tailors also registered a consistent excess risk [Perez-Gomez et al., 2004]. Therefore, both sexes in these categories may be exposed to tricloroethylene that was related to excess melanoma in a Canadian case-control study [Fritschi and Siemiatycki, 1996] and in a California community where drinking water was contaminated with ammonium perchlorate and trichloroethylene [Morgan and Cassady, 2002]. Nevertheless, no excess risk was found in a Danish cohort of workers exposed to this same chemical [Raaschou-Nielsen et al., 2003].

If female hatmakers were involved, mercury might be an alternative candidate to explain our findings. Bouchardy et al. [2002] also reported a non-significant increased risk for male tailors and hatters. The use of mercuric nitrate in the production of felt hats to hydrolyze rabbit fur has been classically described [ATSDR, 1999], with Lewis Carroll's Mad Hatter typically used as an example of its neurologic toxicity. On the other hand, Merler et al. [1994] did not describe higher mortality due to melanoma in a cohort of workers of both sexes that received compensation for mercury poisoning in a fur hat industry. Mercury is also used in dental offices, where both dentists and dental nurses may be exposed to it. Even after socioeconomic adjustment, dental nurses in our study also showed a clear excess risk of cutaneous melanoma in the general cohort, mainly affecting legs. Female dentists also had a certain degree of increased risk in the general analysis, though this failed to attain statistical significance. This excess, mainly due to thorax and leg cases, was reduced in the intrasectorial approach and disappeared entirely in the subcohort. Higher incidences than expected by chance for dentistry, in both men and women, have been found in pooled standardized incidence ratios (SIR) of Nordic countries [Andersen et al., 1999], in England and Wales [Vagero et al., 1990], and also in socioeconomically adjusted estimators for men [Goodman et al., 1995; Bouchardy et al., 2002], though these results could also be due to other occupational factors, such as artificial UV exposure. An English case-control study on males reported a significant RR of melanoma of 2.9 associated with occupational exposure to mercury [Magnani et al., 1987], but Boffeta et al. [1998] failed to find increased risk of death from melanoma in mercury miners from four European countries, compared with national reference rates. However, no socioeconomic adjustment was performed, the female population was made up of only 256 Ukrainian miners, and most workers belonged to Mediterranean countries, where melanoma incidence is lower, likely due to different skin pigmentation. Furthermore, no increase in melanoma has been reported in chloralkali workers, who are known to undergo exposure to mercury, although nearly all of the published studies have been confined to men. The International Agency for Research on Cancer (IARC) considers that there is inadequate evidence in humans to support the carcinogenicity of mercury and mercury compounds [IARC, 1997a].

Both the general and intrasectorial approaches showed an almost significant RR of 2 for female librarians, archivists and curators in the subcohort; and a similar increase was seen in men [Perez-Gomez et al., 2004]. Curators comprise the subgroup with more frequent exposure to toxic preservative agents, such as solvents or pesticides, and topical application of DDT, mercuric chloride or arsenic [National Parks Service, 2001]. This last-mentioned substance that is used for preserving animal specimens is known to be a skin carcinogen. Yet, while its role is clearly established in non-melanoma skin cancer, this is not the case in melanoma. Ecologic studies have yielded contradictory results [Philipp et al., 1983; Guo et al., 2001]. An increased risk of melanoma has been recently reported among farmers with high arsenic concentration in toenails [Beane Freeman et al., 2004], but more information is needed to assess this suggested association.

Mercury seed disinfectants and arsenic pesticides have been used by horticultural workers, who registered a significant excess risk in the thorax and legs. After socioeconomic adjustment, a significant excess risk has also been reported for Swiss male horticultural workers, mainly due to head and neck and thorax cases [Bouchardy et al., 2002]. According to Wiklund et al. [1988], mercury compounds were used in Swedish agriculture for over 60 years, although in the mid-1960s alkyl mercury compounds were forbidden and limitations placed on mercury disinfection. Zinc arsenate was also used by horticultural workers in Sweden until 1966 when it was replaced by DDT. Nevertheless, the subcohort results that should register higher risks than did the cohort results if arsenic or mercury enhanced the risk of melanoma, do not support this hypothesis. Despite the increased risk for horticultural workers, female farm workers as a whole did not show any excess risk of melanoma, which is in line with the results reported by Wiklund et al. for Swedish female farmers [Wiklund and Dich, 1994]. Notwithstanding this, these same authors described a high SIR for melanoma in elder farmers, a finding that would be congruent with a role for mercury or arsenic.

A further noteworthy result is the increased risk among bank tellers in the cohort, which reflected the excess risk found in upper limbs. The use of ultraviolet A radiation to verify signatures has been quite common, exposing hands to UVA, which is regarded as probably being carcinogenic to humans by the IARC (Group 2A) [IARC, 1997b]. This result could suggest a local effect of such radiation, though irradiation from these devices is quite low [Diffey, 1990]. Moreover, the excess risk previously reported for male bank tellers was mainly due to thorax cases [Perez-Gomez et al., 2004].

Within the transport and communication sector, railway station masters/train dispatchers showed significant excesses in the cohort analysis. Vagero et al. [1990] also reported high, though non-significant, proportional registration ratios in railway linesmen in England and Wales. In addition, motor-vehicle/tram drivers showed a high risk of melanoma though only in head and neck and due to just three cases. Chance could account for this result, as this is the only significant occupation in this anatomic location.

The telecommunications industry has been repeatedly associated with melanoma [Vagero et al., 1985; DeGuire et al., 1992]. In our study, telephone operators in both the cohort and subcohort registered a significant or marginally significant excess risk and an RR of over 1.4 for all sites, although this only attained significance in the legs. A high although non-significant risk was likewise observed for telegraph and radio operators. These occupations could entail EMF exposure.

We found an increased risk of melanoma in legs for textile workers. A similar result for men was described in Switzerland [Bouchardy et al., 2002], and our analysis of Swedish men [Perez-Gomez et al., 2004] also yielded marginally significant excesses, though in the thorax and upper limbs. Yet, other authors have failed to detect increased risks in the textile industry [Nelemans et al., 1993]. According to Deadman and Infante-Rivard [2002], sewing- and textile-machine operators rank among the female occupational categories most highly exposed to electromagnetic fields, which would lend some support to the theory of an association between melanoma and EMF exposure. Exposure to EMF might also affect precision toolmakers, who had a marginally significant risk in thorax that became significant in the intrasectorial approach. In general, results regarding EMF and melanoma have not been conclusive to date. Floderus et al. [1999] used a job exposure matrix to estimate EMF exposure among Swedish workers, and reported a high risk of melanoma in both sexes. However, another Swedish study showed no increased risk of malignant melanoma following exposure to EMF among a cohort of welders [Hakansson et al., 2002].

Chemical process workers had a relative risk of 3.14 in the intrasectorial analysis, although it is based on only three cases. More difficult to explain are the excesses found among butchers (only in the intrasectorial analysis for the whole cohort), packers (subcohort only), and nursemaids (subcohort and marginally significant in the head and neck and thorax).

Correlation coefficients (Figure 1 & Table IV) were higher between the upper limbs and head/neck. These two sites may well share occupational risks, as they are the most exposed parts of the body in occupational settings. A significant correlation was also found between the upper limbs and thorax. However, the lack of correlation between head/neck and thorax, or lower limbs was noteworthy. Legs seemed to show a special pattern, with only a moderate and non-significant correlation with upper limbs or thorax. Although such specificity could be due to differential sun exposure resulting from the use of stockings, it could also be explained by particular responses of the skin in this anatomic location. In this regard, Cress et al. [1995] found that risk ratios among women for major sun-related and phenotype risk factors, such as the number of large nevi or frequent sunburns in elementary school, were lower for leg melanomas than for other sites, suggesting that phenotypic factors might differ according to anatomic site. These results could support the possible existence, proposed by some authors [Maldonado et al., 2003; Rivers, 2004], of different pathways leading to site-specific melanoma.

To sum up, some occupations with possible exposure to arsenic or mercury display an increased risk of melanoma. Among these, the generalized excess risk among hatmakers/milliners warrants further attention. The weak correlation between legs and other sites suggests site-specificity in melanoma risk factors.

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