Cancer Causes and Conrrol **10**: 209–217, 1999.

Occupation and bladder cancer in European women

Andrea 't Mannetje', Manolis Kogevinas[1,]* Jenny Chang-Claude', Sylvaine Cordier[3], Carlos-Albert0 González[4], Martine Hours[5], Karl-Heinz Jöckel[6], Ulrich Bolm-Audorff[7], Elsebeth Lynge[8], Stefano Porru[9], Francesco Donato[10], Ulrich Ranft[11], Consol Serra", Anastasia Tzonou[13], Paolo Vineis[14], Jürgen Wahrendorf' & Paolo Boffetta''
'Respiratory and Environmental Health Research Unit, Insitut Municipal d'Investigació Mèdica(IMIM), 80 Doctor Aiguader Rd., Barcelona 08003, Spain (Tel: +34-93-2211009, Fax: +34-93-2216448, E-mail: kogevinas@imim.es); [2]Deutsches Krebsforschungszentrum, Abteilung Epidomiologie, Heidelberg, Germany; [3]Institut National de la Santé et de la Recherche Medicale-INSERM, Villejuif, France; [4]Institut de recerca epidemioldgica clìnica, Mataró, Spain; [5]Insitut d'Épidémiologie, Université Claude Bernard, Lyon, France: [6]Institut fur Medizinische Informatik, Biometrie und Epidemiologie, Essen, Germany; [7]Hessisches Ministerium fur Frauen, Arbeit and Sozialordnung, Wiesbaden, Germany; 'Danish Cancer Society, Kobenhavn, Denmark: 'Institute of Occupational Health, University of Brescia, Italy: "Institute of Hygiene, University of Brescia: "Medical Institute of Environmental Hygiene, Heinrich-Heine University, Düsseldorf, Germany: [12]Centre d'Estudis, Programes i Serveis Sanitaris, Sabadell, Spain: [13]Department of Hygiene and Epidemiology, Medical School of Athens, Athens, Greece: [14]Unit of Cancer Epidemiology, Turin, Italy; [15]Unit of Environemntal Cancer Epidemiology, International Agency for Research on Cancer, Lyon, France (*Author for correspondence)

Received 23 July 1998; accepted in revised form 12 December 1998

Key words: bladder neoplasms, occupation, risk factors, women.

Abstract

Objectives: We examined the importance of occupational exposures for bladder cancer in women.
Methods: We combined data from 11 case-control studies conducted between 1976 and 1996 in six European countries. The pooled data comprised 700 incident female cases and **2425** population or hospital controls, aged 30–79 years. Lifetime occupational and smoking history were examined using common coding.
Results: Excess risks were found in only a few of the occupations previously identified at high risk for bladder cancer. Statistically significant excess risks were observed for metal workers, particularly blacksmiths, toolmakers and machine tool operators (OR: 2.0, 95% CI: 1.1–3.6), tobacco workers (OR: 3.1, 95% CI: 1.1–9.3), field crop and vegetable farm workers (OR: 1.8, 95% CI: 1.0–3.1), tailors and dress makers (**OR:** 1.4, 95% CI: 1.0–2.1), saleswomen (OR: **2.6,** 95% CI: 1.0–6.9), and mail sorting clerks (OR: **4.4,** 95% CI: 1.0–19.5). About 8% (95% CI: 3.1–19.9) of all bladder cancers in women could be attributed to occupation after adjusting for smoking. The attributable risk was higher in women aged less than 65 years (12%), compared to older women (4%).
Conclusions: The calculation of the attributable risk on the basis of results from this analysis may have caused some overestimation of the proportion of occupational bladder cancer in women. **A** significant proportion, however, of bladder cancer cases among European women less than 65 years is likely to be attributed to occupation. This link between bladder cancer in women and occupational factors has received little recognition, probably because studies addressing these issues have predominantly been done in men.

Introduction

In most European countries, bladder cancer is at least three times less frequent in women than in men [1]. The higher incidence among men can be attributed, in part, to the differences in smoking habits. Occupational exposures have been identified as the second most important risk factor for bladder cancer in men. Whether they significantly contribute to the occurrence of bladder cancer in women has received less attention. In most studies on occupational bladder cancer, the study population has been too small to evaluate in detail high-risk occupations separately in women, although some studies did report these results [2–6]. Most well established occupational risks, such as employment in the rubber and dye industries, have been recognized on the basis of findings in exposed men. The largest study on occupational bladder cancer risks in women so far published included 652 cases and 1266 controls from 10 areas of the United States [7]. The authors concluded that patterns of bladder cancer risk among women are similar to those in men and that 11% of the bladder cancer cases in **US** white women could be attributed to occupational exposure.

To identify occupations at a high risk for bladder cancer in women we pooled the data of 11 case-control studies conducted in six European countries and estimated the percentage of bladder cancer cases that can be attributed to occupational exposure in European women.

Methods

We performed a pooled analysis of case-control studies on bladder cancer that were conducted in European countries between 1976 and 1996. A total of 11 studies were identified using as criteria the availability of detailed occupational and smoking information and the accessibility of the primary data. The pooled file comprises data from three studies from Germany, [8–10], two from France, [3, 11], Italy [12, 13] and Spain [14] (Serra, unpublished) and one each from Greece [15] and Denmark [16].

Primary data from these 11 studies were combined using common coding and classification schemes for all variables. Originally used occupational codes were recoded to 5-digit ISCO (International Standard Classification of Occupations) '68 codes [17] and industry codes, to ISIC (International Standard Industrial Classification of All Economic Activities) revision-2 codes [18]. All studies recorded the occupational and industry code of every job done more than 6 months and year of starting and end of each job, except for one study [15] for which only information for the longest held job was available. No information on industry was recorded in two studies [8, 15] and consequently they were excluded from analyses by industry. For these two studies, only 3-digit ISCO codes were available. We limited the analysis to cases and controls within the age range 30 years up to 79 years and excluded subjects outside this age range (n_{cases} = 161, n_{controls} = 357) and also prevalent cases (n_{cases} = 92), defined as those with more than 2 years time between diagnosis and interview. This final pooled data set comprised 700 cases and 2425 hospital or population controls. Controls were individually or frequency matched to cases on age (within 5 years) and geographic area (Table 1). The case-control ratio differed per study, ranging from 1:1 to 1:8, with Germany forming the largest national component for the cases as well as the controls. The mean age of cases was 66.2 years compared to 61.9 years controls. Of the cases, 44.9% had ever smoked compared to 31.8% in the controls.

An *a priori* list of high-risk occupations was constructed, on the basis of existing evidence on occupation and bladder cancer [19]. The list consisted of well established high-risk occupations (in men): chemical workers (ISCO 74); textile workers including spinners, weavers, knitters and dyers (ISCO 75); leather workers (ISCO 80); metal product workers including toolmakers, machine-tool setter-operators, metal grinders and machinery fitters (ISCO 832, 833, 834, 835, 841, 849); rubber and plastic workers (ISCO 90); painters (ISCO 93); motor vehicle drivers (ISCO 985) and hairdressers (ISCO 57).

Two job-exposure matrices (JEM) were applied to estimate the risk for specific agents and groups of agents. The MRC-JEM [20] includes 50 agents and the FINJEM which includes 38 agents [21]. For each JEM, subjects were classified into those non-exposed, and those with an estimated low, medium or high exposure, using the maximum overall job periods. This was done for all substances available in the JEMs, with cut-off points for low/medium/high exposure based on level of exposure as well as proportion of people within occupation exposed. When using the MRC-JEM, a subject was evaluated to be low exposed if proportion of exposed workers in this occupational group was low and level of exposure was low, according to the JEM. A subject was evaluated to have a medium exposure if the proportion exposed was high and level was low, or if proportion was low and level was high. Those working in occupations with a high proportion of workers being highly exposed according to the JEM were evaluated to be highly exposed. When using FINJEM, the quantitative evaluations of proportion exposed and level of exposure for every occupation were multiplied. A subject was evaluated to be highly exposed if this exposure estimate was higher than the upper quartile of all exposed subjects, low exposed if this exposure estimate was lower than the lower quartile, and having medium exposure if this exposure estimate was found to be between the higher and lower quartile of all exposed subjects.

Unconditional logistic regression was applied to calculate odds ratios (OR) and 95% confidence intervals (95% CI) for every occupation and industry with at least 10 subjects (cases and controls). In each comparison, those 'never' employed in the occupation or industry were used as the reference population. All odds ratios were adjusted for age (5-year age groups), smoking status

Table 1. Description of the studies included in the pooled bladder cancer analysis in women

Studies (Reference)	Country	Mean year of enrolment	Cases		Controls		
			n	%	*n*	$n_{(hospital)}/n_{(population)}$	%
All studies			700		2425	761/1664	
Jensen et al. 16	Denmark	1980	96	13.7	193	0/193	8.0
Claude et al. 8	Germany	1980	95	13.6	120	120/0	4.9
Rebelakos et al. 15	Greece	1982	47	6.7	44	44/0	1.8
Vineis et al. 12	Italy	1982	39	5.6	183	183/0	7.5
Cordier et al. 3	France	1985	83	11.9	101	101/0	4.2
Gonzalez et al. 14	Spain	1986	49	7.0	120	57/63	4.9
Hours et al. 11	France	1986	19	2.7	38	38/0	1.6
Bolm-Audorff et al. 9	Germany	1991	51	7.3	55	55/0	2.3
Porru et al. 13	Italy	1992	30	4.3	163	163/0	6.7
Greiser et al. 10	Germany	1993	176	25.1	1390	0/1390	57.3
Serra (unpublished)	Spain	1995	15	2.1	18	0/18	0.7
Age							
30–39 years			12	1.7	109	72/37	4.5
40–49 years			26	3.7	240	105/135	9.9
50–59 years			119	17.0	573	152/421	23.6
60–69 years			253	36.1	760	221/539	31.3
70–79 years			290	41.4	743	211/532	30.6
Smoking							
Non-smokers			383	55.1	1649	608/1041	68.2
Ex-smokers			111	16.0	322	49/273	13.3
Current smokers			201	28.9	446	103/343	18.5
Of which:							
1–10,000 packs			111	16.0	316	86/230	13.1
10,000–15,000			46	6.6	81	11/70	3.4
> 15,000			44	6.3	49	6/43	2.0

(categorical never, ex- and current smokers, broken down in three groups of cumulative consumption), study center and the interaction between center and age (continuous). Risks by duration of employment in selected occupations and industries were calculated using four categories of duration (1–4, 5–9, 10–24 and ≥25 years). If a subject occupied the same job over different job periods, the total duration of periods was used. Odds ratios by duration of employment are shown for those major occupations for which a duration–response relation was found. Adjusted estimates of the attributable risk were calculated [22] together with their 95% confidence interval [23], using the odds ratio and percentage of cases 'ever' employed in at least one high-risk occupation. Analysis was done using SAS an Stata packages.

Results

Analysis by occupation

Among all *a priori* high risk occupations, only the metal and rubber workers appeared to have a higher risk for bladder cancer, although this was not statistically significant (Table 2). Hairdressers, chemical processors, textile workers (spinners, weavers, knitters, dyers) and leather workers did not show an elevated risk (all ORs below 1). Textile workers appeared to have a higher risk if they worked longer than 25 years in this occupation. Only two cases and five controls had worked as textile dyers (OR: 1.9, p-value = 0.5). Excluding these seven textile dyers/bleachers did not lead to appreciable changes in the overall OR for textile workers, nor in the OR for subjects working longer than 25 years in a textile occupation. Fewer than 10 subjects had ever worked as a painter or motor vehicle driver and consequently ORs were not calculated for these occupations.

Occupations with statistically significant ($p < 0.05$) elevated risk irrespective of whether they were included in the *a priori* high risk list are shown in Table 3. A statistically significant excess risk was found for three metal working occupations. The major group of blacksmiths, toolmakers and machine-tool operators had an OR of 1.9 (95% CI: 1.1–3.6), with a higher risk found for those working in this occupation longer than 10 years. The highest risk for cancer within this group was

Table 2. Bladder cancer risk for European women employed in the *a* priori defined high-risk occupations

Job description (ISCO '68 code)	Duration (years)	$n_{(cases)}/n_{(control)}$	Odds ratio[a]	95% confidence interval
Hairdressers, barbers, beauticians and related workers (57)	–	11/56	0.8	(0.4–1.7)
Chemical processors and related workers (74)	–	3/40	0.6	(0.2–2.2)
Spinners, weavers, knitters, dyers and related workers (75)		44/139	0.9	(0.6–1.3)
	< 5	12/42	0.9	(0.5–1.9)
	5–9	7/33	0.5	(0.2–1.3)
	10–24	12/42	0.7	(0.4–1.5)
	≥25	8/15	1.8	(0.7–4.9)
Shoe makers and leather goods makers (80)	–	7/37	0.4	(0.2–1.1)
Metal working including toolmakers, machine-tool setter-operators, metal grinders and machinery fitters (832–835, 841, 849)	–	18/57	1.5	(0.8–2.7)
Rubber and plastics product makers (90)	–	7/28	1.2	(0.5–3.0)
Painters (93)	–	1/7	–	–
Motor-vehicle drivers (985)	–	2/6	–	–

[a] All odds ratios were adjusted for age (5-year age groups), smoking status (categorical in 5 groups: never-, ex-, and current smokers in three groups of cumulative consumption), study center and the interaction between center and age (continuous). In each comparison, those 'never' employed in the occupation were used as the reference population.

Table 3. Occupations showing a statistically significant excess risk for bladder cancer in European women

Occupations (ISCO '68 codes)	Duration (years)	$n_{(cases)}/n_{(controls)}$	Odds ratio[a]	95% confidence interval
Blacksmiths, toolmakers and machine-tool operators (83)		20/51	1.9	(1.1–3.6)
	< 5	10/26	1.9	(0.84.4)
	5–9	3/8	1.1	(0.2–4.8)
	10–24	4/11	3.2	(0.9–1 1.6)
	≥25	2/1	7.8	(0.5–132)
Lathe operator (83420)		3/8	4.6	(1.1–19.2)
Blacksmiths, toolmakers and machine-tool operators nec.[b] (839)		13/21	2.9	(1.3–6.3)
Field crop and vegetable farm workers (622)		33/41	1.8	(1.0–3.1)
	< 5	3/7	0.9	(0.2–4.1)
	5–9	2/6	1.2	(0.2–6.7)
	10–24	8/15	1.3	(0.5–3.6)
	225	8/9	2.1	(0.8–6.0)
Tobacco prepares and tobacco product makers (78)	–	8/8	3.1	(1.1–9.3)
Tailors and dressmakers (791)	–	61/147	1.4	(1.0–2.1)
Other saleswomen, shop assistants and demonstrators (45190)	–	7/21	2.6	(1.0–6.9)
Mail sorting clerk (37020)	–	4/6	4.4	(1.0–19.5)

[a] All odds ratios were adjusted for age (5-year age groups), smoking status (categorical in 5 groups; never-, ex- and current smokers in three groups of cumulative consumption). study center and the interaction between center and age (continuous). In each comparison, those 'never' employed in the occupation were used as the reference population.

[b] Not elsewhere classified.

found for lathe operators (OR: 4.6, 95% CI: 1.1–19.2) and other blacksmiths (OR: 2.9, 95% CI: 1.3–6.3). Other occupations at high risk were field crop and vegetable farm workers (OR: 1.8, 95% CI: 1.0–3.1), tobacco workers (OR: 3.1, 95% CI: 1.1–9.3), the subgroup of tailors and dressmakers (OR: 1.4, 95%

CI: 1.0–2.1), other saleswomen (OR: 2.6, 95% CI: 1.0–6.6) and mail sorting clerks (OR: 4.4, 95% CI: 1.0–19.5). Only among field crop/vegetable farm workers and blacksmiths, toolmakers and machine-tool operators, was there a duration–response relation observed.

Women ever occupied as a government executive official (ISCO code 31) had a decreased risk (OR: 0.7, 95% CI: 0.5–1.0, 45 cases, 414 controls). No other occupations with a statistically significant decreased risk were found.

If a subject was only considered exposed when working more than 10 years in the same occupation, a higher risk for bladder cancer was found for a few additional occupations. A statistically significant elevated risk (OR: 1.4, 95% CI: 1.1–1.9) was found for the major group of sale workers, including 94 cases employed longer than 10 years and particularly for sales supervisors and buyers (OR: 4.8, 95% CI: 1.2–18.7). An eight-fold higher risk was found for women working longer than 10 years as a telephone switchboard operator (OR: 8.1, 95% CI: 2.1–32.0).

Analyses were repeated excluding the largest individual study contribution to the pooled data [10] and also the Greek study [15], which used a more simple occupational classification. Results did not differ overall in any consistent pattern, with only minor changes observed in the ORs for most occupational groups.

Analysis by industry

An excess risk for bladder cancer was found in women in the manufacturing industry, particularly tobacco manufactures (OR: 3.0, 95% CI: 1.2–7.4 ISIC code 314), manufacture of wood products (OR: 3.5, 95% CI: 1.0–12.1, ISIC code 331) and manufacture of other non-metallic mineral products including clay, cement, plaster and other (OR: 3.6, 95% CI: 1.2–10.7, ISIC code 369). Significant lower risk was found for women ever having worked in agriculture (ISIC code 1) with an OR of 0.6 (95% CI: 0.4–0.9) and in community, social and personal services (ISIC code 9) with an OR of 0.7 (95% CI: 0.6–0.9). Twenty-seven percent of the cases and 50% of controls had been ever employed in the latter group.

Attributable risk

The attributable risk for bladder cancer in women due to occupational exposure was calculated using alternative definitions of high-risk occupations. The *a priori* defined high-risk occupations do not appear to be associated with an excess bladder cancer risk in women and this is reflected in the calculation of the attributable risk which is below zero (Table **4**). We also calculated the attributable risk for all occupations that showed a significant elevated risk in the pooled analysis (reported in Table **3**). Women employed in these occupations constituted 18% of all the cases and the attributable risk associated with employment in these occupations was 7.8% (95% CI: 3.1–19.9). When the large group of tailors and dressmakers for whom no dose response relation was found was excluded, the AR was calculated to be **4.9%**. A higher AR was found for those diagnosed with bladder cancer aged under 65 (AR: 12.5%, 95% CI: 6.7–23.3). For this group of women diagnosed with bladder cancer at a relatively young age (< 65 years), the risk estimate as well as the percentage of cases having worked in high risk occupations is higher than for those diagnosed with bladder cancer at an older age. This indicates that occupational exposures are relatively more important in younger than in older ages. The attributable risk ranged between 5% and 15% in 7 out of the 10 studies for which it was estimated was around 2% in one study and negative in the remaining two.

Table 4. Attributable risk (AR) for bladder cancer due to occupation in European women[a]

Group of high risk occupations	$n_{(cases)}/n_{(controls)}$	Odds ratio	95% confidence interval (OR)	Attributable risk	95% confidence interval (AR)
A priori group	82/343	0.8	(0.6–1.1)	–	–
A posteriori group[b]					
All	119/266	1.8	(1.3–2.3)	7.8	(3.1–20.0)
Age 30-64	53/145	2.4	(1.6–3.6)	12.5	(6.7–23.3)
Age 65–79	66/121	1.4	(1.0–2.0)	4.8	(0.5–39.5)
Never smoker	66/176	2.0	(1.4–2.9)	9.8	(4.5–21.4)
Ever smoker	53/90	1.4	(0.9–2.2)	5.1	(0.6–40.3)

[a] The study of Rebelakos [15] was excluded from calculations of AR.
[b] AR was calculated using ‘ever worked’ in any of the occupations showing statistically ($p < 0.05$) high-risk (blacksmiths, toolmakers and machine tool operators, fieldcrop and vegetable farm workers, tobacco prepares and tobacco product makers, tailors and dressmakers, other saleswomen, shop assistants and demonstrators, and mail sorting clerks).

***Table* 5. Agents and groups of agents showing a dose-response relation in the job-exposure matrix (JEM) analysis (women)**

	Level	$n_{(cases)}$	$n_{(controls)}$	OR	95% CI
FINJEM[a]					
Chromium	Low	8	51	0.8	(0.3–1.8)
	Medium	17	63	1.4	(0.8–2.6)
	High	18	50	1.8	(1.O-3.4)
Oil mist	Low/Medium	34	117	1.0	(0.7–1.6)
	High	18	47	1.9	(1.0–3.7)
Polycyclic aromatic	Low	17	46	1.5	(0.8–2.9)
hydrocarbons	Medium	4	22	1.1	(0.4–3.5)
PAHs	High	7	33	1.0	(0.4–2.5)
MRC-JEM[b]					
Polycyclic aromatic	Low	42	201	0.9	(0.6–1.4)
hydrocarbons	Medium	5	18	1.1	(0.4–3.4)
(PAHs)	High	5	22	1.2	(0.4–3.3)
Aromatic amines	Low	42	185	1.0	(0.6–1.4)
	Medium	21	94	1.0	(0.6–1.6)
	High	8	33	1.3	(0.6–3.0)
Chromium compounds	Low	63	299	1.1	(0.8–1.5)
	Medium	7	21	1.7	(0.7–4.5)
	High	2	4	1.3	(0.2–8.4)

[a] Aromatic amines are not included in FINJEM.
[b] Oil mist is not included in the MRC-JEM.

Application of JEMs

Two JEMs (Job-exposure matrices) including 50 (MRC JEM) and 38 (FINJEM) substances were used to calculate risk by level of exposure to specific agents. Table 5 shows the substances that showed a dose–response relation in women. Subjects evaluated by the FINJEM to be highly exposed to chromium had an OR of 1.8 (1.0–3.4) compared to those not exposed according to FINJEM. An OR of 1.9 (1.0–3.7) was found for women highly exposed to oil mist. In the MRC-JEM, the subjects evaluated to be exposed to Polycyclic Aromatic Hydrocarbons **(PAHs)** showed a slight exposure-response relation. In the FINJEM, a dose-response relation was not found for PAHs, although the low, medium and high level exposure groups all had an OR higher than 1. High exposure to aromatic amines (evaluated only in MRC-JEM) was associated with an elevated risk for bladder cancer, although the OR was low and not statistically significant. Pesticides, as a group, were not included in the FINJEM or the MRC-JEM. The MRC-JEM, however, included herbicides and the FINJEM included herbicides, fungicides, and insecticides. For none of these exposures was a dose–response relation found.

Smoking

Compared to never smokers, current smokers had more than a threefold risk for bladder cancer (OR: *3.6,* 95% CI: 2.8–4.7) and ex-smokers had an odds ratio of 2.5 (95% CI: 1.9–3.4). The attributable risk for women ever having smoked cigarettes was 30.5%. Occupational analyses were repeated limiting the data base to never smokers. Although there was a general tendency to observe higher ORs among non-smokers compared to smokers, differences were relatively small.

Discussion

Bladder cancer is less frequent in women than in men. Tobacco smoking and also occupational exposures, such as those of rubber workers, truck drivers or dye manufacturers have been more prevalent in men than in women and this may, in part, explain the higher incidence among the former group. Results from the **US** study indicated that much of the male excess of bladder cancer persisted after occupation and smoking were taken into account [24]. Although a number of case-control and cohort studies have examined occupational bladder cancer in women [2, 4–8, 14], most did not have the statistical power to evaluate occupational risks in detail. In this pooled analysis of case-control studies in six European countries we identified several occupations at a high risk including metal workers, tailors, field crop and vegetable workers. We estimated that about 8% of all bladder cancers were associated with occupation.

Pooling results of different studies conveys a considerable advantage by increasing the power of the study and also by verifying the presence of similar risks in different populations. There are, however, complexities concerning the methodology to be used and also the interpretation of the findings of pooled studies. The increased risks for the major occupations observed in the pooled analysis were identified in most individual studies. The differences between studies concerned mainly the magnitude of the risk rather than the pattern of the risk. The variation in results between studies could be due to chance, differences in study design, differences in exposure patterns or confounding by other exposures. Differences in exposure assessment were reduced in the pooled analysis by re-coding all occupational information and by using JEMs providing semi-quantitative estimates of exposure for specific agents. Re-coding, however, does not exclude coding errors in the original files, or differences in coding policy between countries.

All risk estimates for occupations/industries were adjusted by smoking. To minimize differences in the age distribution of subjects between centers, we only included subjects within the range of **30–79** years and included an interaction between age and center in each mode. Furthermore, differences in the case-control ratio between studies were handled by using a term for center in each model. Other differences, however, in the design of individual studies, such as control selection, matching, or potential study-specific confounding effects could only, in part, be taken into account in the pooled analysis.

Workers in the metal and clothing industry, and field crop and vegetable workers were the major (numerically) occupations identified at high risk. The most consistent results were those for blacksmiths, toolmakers and machine-tool operators who had a twofold risk for bladder cancer, which increased with duration of employment. Their main tasks are hammering, forging cutting and grinding metal (mainly by machine) and other metalworking machine tasks with which cutting and cooling lubricants are used. Excess risk in this group has been shown in studies in men and also in the largest study in American women **[7]**. The fact that **3%** of all cases were active in this job group implies that this occupation contributes substantially to the bladder cancer risk in women. Tailors and dressmakers form a bigger group in the study populations **(8.7%** of cases ever active). Their risk was not as high as for blacksmiths and no clear duration–response relation was found. While agricultural occupations in general form a low risk group, a twofold excess risk which increased with duration of exposure was found for the group of field crop and vegetable farm workers **(4.7%** of cases exposed). Field and crop vegetable workers are one of the subgroups of agricultural workers with heavy exposure to insecticides and pesticides. There is some evidence associating exposure to pesticides and bladder cancer **[25–27]**, but the findings are not consistent **[28]**.

An excess risk was found for some other smaller occupational groups including tobacco preparers, other saleswomen and mail sorting clerk. It was not possible to estimate risk by duration for these occupations because of small numbers. In the large group of sales workers, a statistically significant excess risk was found among women having been employed more than 10 years. Sales workers were also found to be at higher risk for bladder cancer in American women **[7]** and being a relative big group among female workers **(22.7%** of cases ever active as sales worker) can be an important risk occupation in women. It is difficult to identify specific occupational exposures associated with this elevated risk since sales workers do not form a homogeneous group in terms of tasks or contact with specific substances. High risk in these and other white-collar occupations such as telephone switchboard operators is more likely to be related to factors indirectly related to the job, for example environmental tobacco smoke, environmental exposure to air pollutants, sedentary type of work and frequency of urination, or to general lifestyle factors.

The results from the application of two job-exposure matrices were inconsistent. The results from the FIN-JEM **[21]** indicated that substances used in the metal industry, chromium and oil mist, were associated with risk for bladder cancer. Weak dose–response relations were found for PAHs and aromatic amines resulting from the MRC-JEM. Both JEMs, however, have been constructed mainly on the basis of occupational exposure data in men and may not apply well to the assessment of occupational exposures in women. Results from **the use** of general **JEMs** on **a** specific female population should therefore be interpreted with caution. Also the possibility of misclassification in exposure when applying a **JEM,** which is based on national experience, on an international population, cannot be ruled out, considering that occupation-specific exposure can vary from country to country. These misclassifications together with the probability that a certain proportion of misclassification is always present when using a general JEM, might explain the low estimates of risk associated with specific exposure as being a result of misclassification and not necessarily as a result of the absence of risk.

We calculated that about 8% of bladder cancers in European women can be attributed to employment in occupations found at increased risk. This overall result was not driven by any specific study included in this analysis, and the AR was above 5% in most individual studies. The AR estimates were higher in younger women than in women above 65 years, a pattern similar to men [29]. The calculations of AR estimates on the basis of result from this analysis is likely to have caused some overestimation of the proportion of occupational bladder cancer in women, since the AR was based on all occupations with a significant (p-value < 0.05) risk. An effect of chance, however, is more likely to occur in small occupational groups that do not contribute greatly to the overall AR. In addition, there are no recognized etiological occupational exposures in one of the major occupational groups identified, tailors and dressmakers. Excluding this group resulted to an attributable risk estimate of about 5%. On the other hand the calculation of AR risks on the basis of results from previous studies in men would have led to underestimation of the risk in women. Men and women have different employment patterns both concerning types of job and job mobility, and may also have different exposures within the same job. **As** a consequence, occupations and industries with a high bladder cancer risk in men may not be the same as those in women. The AR found in this study is slightly lower than that estimated in an earlier large study in the USA **[7]** and considerably higher than that proposed in a recent review on the causes of cancer in the population of the Nordic countries [30]. The study population examined in this analysis should not be considered as representative of the female European Union population, even though it was drawn from six European countries. The results from this study, however, indicate that occupational exposures may contribute considerably to bladder cancer risk among women particularly at younger ages, and are likely to cause around 1 in 10 to 1 in 20 bladder cancers in European women.

Acknowledgements

We thank Aureli Tobias for helping in data management and statistical analysis The study was partly supported by grant ***SOC*** 96-200742 05F02 of the Europe Against Cancer programme, European Commission; by a grant by the Generalitat (Government) of Catalunya (CIRIT/1995 **SGR** 00434); and by a grant of the Fondo de Investgacion Sanitaria, ministry of Education, Spain (97/1105E, 96/1998-01).

References

1. Parkin DM, Whelan SL, Ferlay J, Raymond L. Young J (1997) ***Cancer Incidence in Five Continents.*** Vol. VII. Lyon, France: **IARC** Scientific Publications Number 143.
2. Swanson GM, Bums PB (1995) Cancer incidence among women in the workplace: a study of the association between occupation and industry and 11 cancer sites. ***J Occup Environ Med*** 37: 282–287.
3. Cordier **S,** Clavel J, Limasset JC, Boccon-Gibod L, Moua NLE, Mandereau L, Hemon D (1993) Occupational risks of bladder cancer in France: a multicentric case-control study. ***Int J Epidemiol 22:*** 403–411.
4. Anton-Culver H, Lee-Peldstein **A,** Taylor TH (1992) Occupation and bladder cancer risk. ***Am J Epidemiol 136*** 89–94.
5. Piper JM, Matanoski GM, Tonascia J (1986) Bladder cancer in young women ***Am J Epidemiol* 123**: 1033–1042.
6. Maffi L, Vineis P (1986) Occupation and bladder cancer in females. ***Med Lav*** 7 7 511–514.
7. Silverman DT, Levin L, Hoover RN (1990) Occupational risks of bladder cancer among white women in the United States. ***Am J Epidemiol* 132**: 453–461.
8. Claude JC, Frentzel-Beyme RR, Kunze E (1988) Occupation and risk of cancer of the lower urinary tract among men. A case-control study. ***Int J Cancer* 41:** 371–379.
9. Bolm-Audorff U, Jöckel KH, Kilguss B, Pohlabeln H, Siepenkothen T (1993) Occupational risk factors for cancer of the lower urinary tract. Bremerhaven: Schriftenreihe der Bundesanstalt fur Arbeitsschutz, Wirtschaftsverlag NW, pp. 1–179 (in German).
10. Greiser E, Molzahn M, eds. (1997) Multizentrische Nieren- **und** Urothel-Carcinom-Studie [Multi-Center Urothelial and Renal Cancer Study]. Bremerhaven: Wirtschaftsveralg NW, Verlag fur Neue Wiss. (Schriftenreihe der Bundesanstalt fur Arbeitsschutz und Arbeitsmedizin: Forschung; Fb 780).
11. Hours M, Dananche B, Fevotte J, Bergeret A, Ayzac L, Cardis E, ***et al.*** (1994) Bladder cancer and occupational exposures. ***Scand J Work Environ Health 20:*** 322–330.
12. Vineis **P,** Magnani C (1985) Occupation and bladder cancer in males: a case-control study. ***Int J Cancer*** 3 5 599–606.
13. Porru **S,** Aultenti V, Donato F, Boffetta P, Fazioli R, Cosciani Cunico S, ***et al.*** (1996) Bladder cancer and occupation: a case-control study in northern Italy. ***Occup Environ Med 5 3*** 6–10.
14. Gonzalez CA, López-Abente G, Errezola M, Escolar **A,** Riboli **E,** Izarzugaza I, Nebot M (1989) Occupation and bladder cancer in Spain: a multi-centre case-control study ***Int J Epidemiol* 18**: 569–577.
15. Rebelakos A, Trichopoulos D, Tzonou **A,** Zavitsanos **X,** Velonakis E, Trichopoulos A (1985) Tobacco smoking, coffee drinking and occupation as risk factors for bladder cancer in Greece. *J* ***Natl Cancer Inst 75:*** 455–461.
16. Jensen OM, Wahrendorf J, Knudsen JB, Sorensen BL (1987) The Copenhagen case-referent study on bladder cancer. Risks among drivers, painters and certain other occupations. ***Scand J Work Environ Health*** **1 3** 129–134.
17. International Standard Classification of Occupations (ISCO. Revised 1968) Geneva: International Labour Organization (ILO): ILO Publications 2nd ed.
18. International Standard Classification of **All** Economic Activities (ISIC) (1971) United Nations Publication **ST/STAT/M.4/Rev.2/** Add.1, Sales No.: E.71.XVII.8). New York: Publishing Service United Nations.
19. Silverman D, Morrison A, Devesa S (1996) Bladder Cancer. **In:** Schottenfeld D, Fraumeni J, eds. ***Cancer Epidemiology and Prevention.*** New York: Oxford University Press, pp. 1156–1179.
20. Pannett B, Coggon D, Acheson ED (1985) **A** job-exposure matrix for use in population based studies in England and Wales. ***Br J Ind Med*** **4 2** 777–783.
21. Kauppinen T, Toikkanen J, Pukkala E (1998) From cross-tabulations to multipurpose exposure information systems: a newly job-exposure matrix. ***Am J Ind Med 33:*** 409–417.

22. Bruzzi P, Green SB, Byar DP, Brinton LA, Schairer C (1985) Estimating the population attributable risk for multiple risk factors using case-control data. *Am J Epidemiol* **122:** 904–914.
23. Greenland S, Drescher K (1993) Maximum likelihood estimation of the attributable fraction from logistic models. *Biometrics* **49:** 865–872.
24. Hartge P, Harvey EB, Linehan WM, Silverman DT, Sullivan JW, Hoover RN, Fraumeni JF Jr (1990) Unexplained excess risk of bladder cancer in men. *J Natl Cancer Inst 82:* 1636–1640.
25. Blair A, Grauman DJ, Lubin JH, Fraumeni JF Jr (1983) Lung cancer and other causes of death among licensed pesticide applicators. *J Natl Cancer Inst* **71:** 31–37.
26. Viel JF, Callier B (1995) Bladder cancer among French farmers: does exposure to pesticides in vineyards play a part? *Occup Environ Med 52* 587–592.
27. Akdas A, Kirkali Z, Bilir N (1990) Epidemiological case-control study on the etiology of bladder cancer in Turkey. *Eur Urol* **17:** *23–26.*
28. IARC (1991) ***Monographs on the Evaluation of Carcinogenic Risks to Humans.*** Vol. 53. ***Occupational Exposures in Insecticide Application and Some Pesticides.*** Lyon: International Agency for Research on Cancer.
29. Kogevinas M, Kauppinen T, Boffetta P, Saracci R (1998) Estimation of the burden of occupational cancer in Europe. Final Report, IMIM, Barcelona.
30. Dreyer L, Andersen A, Pukkala E (1997) Occupation. In: Olsen JH, Andersen A, Dreyer L, Pukkala E, Tryggvadottir L, Gerhardsson de Verdier M, Winther JF, eds. Avoidable cancers in the Nordic countries. *APMIS* **105** (Suppl 105): 68–79.