Int Arch Occup Environ Health (2005) 78: 387–393
DOI 10.1007/s00420-004-0599-x

ORIGINAL ARTICLE

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Cancer mortality among municipal pest-control workers

Received: 30 June 2004 / Accepted: 3 November 2004 / Published online: 22 April 2005

Abstract ***Objectives***: This epidemiological study was carried out in order to investigate the hypothesis of a relationship between cancer occurrence and occupational exposure in a population of municipal pest-control workers exposed to a wide range of pesticides and other chemicals. ***Methods***: The study was designed as a mortality historical cohort study. The cohort comprised all subjects ever employed in a municipal pest-control service between 1979 and 1994. The follow-up period lasted from 1979 to 2000. The mortality rates of pest-control workers were compared with those of a regional population. A job exposure matrix was developed, which took into account four types of chemicals: formaldehyde, ethylene oxide, insecticides and rodenticides. ***Results***: None of the 181 subjects of the cohort, leading to 3,107 person-years, was lost to follow-up. Thirty-nine of them died, and all the causes of deaths were ascertained. The standardized mortality ratios (SMRs) for all causes of deaths and for all cancer causes were significantly greater than unity: 1.61 (1.14–2.20) and 2.24 (1.39–3.43), respectively. Non-significant excesses were observed for most cancer sites, except for lung cancer, which had a low SMR. We obtained significant excesses for cancer in workers with more than 20 years of employment [SMR = 2.42 (1.43–3.82)]. Cancer mortality tended to increase insignificantly with formaldehyde and rodenticides exposures, whereas no clear patterns were observed for ethylene oxide and insecticides. However, significant excesses were observed for the highest exposure levels of formaldehyde, insecticides and rodenticides. ***Conclusions***: This study showed a statistically significant excess of cancer mortality in a population of municipal pest-control workers exposed to a wide variety of chemicals. These cancer sites might be related to occupational activities, since they tended to be more frequently observed when duration of employment increased.

Keywords Pest control · Cohort studies · Cancer · Pesticides · Occupational exposure

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Introduction

Urban pest-control workers handle pesticides and are exposed to a wide range of chemicals, mainly disinfectants, insecticides and rodenticides. Their activities often take place in unhealthy buildings, cellars or attics where simultaneous exposure to dust, moulds and humidity may occur. Scientific publications on their occupational health, however, remain rare, in particular for non-agricultural environments.

A few years ago, pest-control officers and unions from a large French city raised the question of a possible excess of cancer in active and retired workers, and they asked our institute whether an epidemiological study could be carried out. In order to check the hypothesis of a relationship between cancer occurrence and occupational exposure, a historical cohort study was set up, the mortality rates of this population being compared with those of a regional population.

The present paper gives the methods and the results of this study.

Materials and methods

Study design

The study was designed as a historical cohort study with mortality as the outcome. The cohort comprised all subjects ever employed in the department of pest control

("the department") between 1 August 1979, date of creation of the first exhaustive worker file, and 31 December 1994. Using number of persons employed by year of follow-up and interviews with present or retired employees, we assessed the exhaustiveness of the cohort.

The follow-up period for mortality lasted from 1 August 1979, or the date of first employment if later, up to 31 December 2000. Vital status was assessed through the registry offices of birthplaces for people born in France and through the national file of the Institut National de la Statistique et des Etudes Economiques (INSEE). Causes of death, coded according to the International Classification of Diseases (ICD), 9th revision (World Health Organisation 1977), were ascertained by matching places of death and birth and death dates in the national file of death certificates, managed by the Institut National de la Santé et de la Recherche Médicale (INSERM). In addition, for three subjects who died abroad, their vital status was ascertained by interviewing colleagues. Other data for individual subjects were collected from administrative records and comprised: year of employment, duration of employment, date and job type.

No data on smoking habits were available.

Exposure assessment

Because no regular airborne exposure measurements had been performed in the past, exposure parameter estimates were based on experts' subjective quantification. In so doing, a specific, retrospective, job exposure matrix (JEM) was developed by a panel of three experts comprising two epidemiologists and an industrial hygienist. The sources of information were: administrative records for job histories, interviews with former and present workers on workplaces, historical description of activities and relevant information on exposure and working conditions. The development of the JEM and the scoring of exposure levels were based on the consensus of the experts.

Historical description of activities

A meeting with former workers allowed the authors to collect information on the evolution of activities, in terms of frequency, respective importance in the working day and preventive measures used.

In order to take into account periods of employment of the oldest workers, we investigated the activities of the department since the 1940s. The first 20 years were focused on the fight against flea, lice or scabies infestation and tuberculosis transmission. Campaigns to get rid of insects or microorganisms took place both within dwelling houses, for premises and furniture, and in four pest-control workshops, for clothes or mattresses. These operations were conducted with steam sterilizers or a limited number of compounds such as formaldehyde or metallic salts, which were mostly applied by spraying. Rodents control measures appeared around 1950 and used pulverized anticoagulants.

During this period, the wearing of overalls and gloves were the only measures intermittently used to avoid exposure. Some former workers reported haemorrhagic episodes or gingivitis and teeth loss, which may have been clinical signs of intoxication, respectively, to warfarin and mercury dichloride.

The 1960s were marked by the diversification of the chemicals used, in relation to a wider commercial supply and the rise of new-targeted insects: mites and termites. The end of this decennium also showed the emergence of disinfection activities, which were developed for hospital materials and relied on formaldehyde or ethylene oxide sterilizers located in the workshops. This activity represented the most important part of work time during the 1970s and disappeared in 1994. For 20 years the importance of pest-control activities has decreased as private pest-control societies and the new activity of environmental sampling and analytical control increased. At the same time the degree of protection increased, with the use of personal protective equipment and new chemicals that have low exposure potential.

In the past few years the department limited its activities to environmental control, which is specifically dedicated to one of the workshops, and the fight against insects and rodents in dwelling houses. These later tasks represent now, respectively, 80% and 20% of pest-control workers' activities.

Job exposure matrix

During the oldest periods, each workshop chose and ordered its own products without keeping any records. It was thus impossible to trace all chemical compounds used by the workers over the years. In the 1970s, procurements were centralized, and lists of products were available, indicating that more than 60 chemicals belonging to all the existing pesticides families, including carbamates, chlorinated hydrocarbons and organophosphates, were used. However, no information was available to estimate exposure to insecticide or rodenticide compounds at an individual level. Formaldehyde and ethylene oxide were used mostly by sterilizers, so that it was possible to distinguish different periods according to dates of starting, improving and abandoning the use of sterilizers.

We developed a job exposure matrix, which consisted of assigning semi-quantitative exposure codes for four pollutants or groups of pollutants: formaldehyde, ethylene oxide, insecticides, and rodenticides, which were the columns of the matrix. The rows of the matrix were 'post-periods', defined according to job type, the workshop where they had been employed, dates of employment and protection used. Four categories of workers were identified: (1) applicators who had been in charge of disinfection in dwelling houses and had had the greatest potential exposure to insecticides and

rodenticides, (2) workers who used the sterilizers at the workshop and who were exposed to formaldehyde and/or ethylene oxide, (3) foremen who worked with the applicators and (4) supervisors who were very intermittently exposed. Of the four different workshops, three (workshops 1, 2 and 3) had sterilizers.

Exposure intensity was coded between 0 (no exposure) and 9 (highest exposure level), and exposure frequency was coded from 0% to 100% of working time.

Cumulative exposure doses were then calculated as the lifetime sum of the products of intensity × duration × frequency. The cumulative exposure scores were divided into four categories according to quartiles of the exposure distribution of the cases, meaning that each category contained 25% of the observed cases. Workers' exposure was also estimated by the duration of employment, i.e. the time between the beginning and the end of employment.

Statistical methods

Standard methods as described by Breslow and Day (1987) were used, to compute person-years at risk, expected numbers of causes of death and standardized mortality ratios (SMRs), with the program written by Coleman et al. (1986). Regional death rates, relevant for calendar year, gender and age-specific groups, were used for the calculation of expected numbers of deaths. In order to account for geographical factors, we considered regional rates to be more relevant than national rates. The 95% confidence intervals (CIs) of the SMRs were computed under the standard Poisson assumption (Breslow and Day 1987; Coleman et al. 1986).

Quality assurance

The Epidemiological Department of the Institut National de Recherche et de Sécurité (INRS) has developed a quality assurance system based on the recommendations for good epidemiology practices in occupational epidemiology laid down by the Chemical Manufacturers Association (The Chemical Manufacturers Associations Epidemiology Task Group, 1991). The French Association for Quality Assurance (AFAQ) formally certified that this quality system conformed to the requirements of the ISO 9002 standard from 1995 to 2000 and of the ISO 9001 standard since 2001. The standard operating procedures laid down in this quality system were applied in the present study.

Ethical and legal aspects

All searches were made respecting the French regulation on individual protection. Our research and files have been declared to, and approved by, the Commission National Informatique et Liberté.

Results

Follow-up

Table 1 shows the main characteristics of the cohort, which comprised 181 male subjects, leading to 3,107 person-years. Sixty-seven workers were still active in the service at the end of the follow-up period. The earliest employment dates were in the 1940s.

The mean duration of employment was 25.8 years (SD 10.7 years). None of the subjects was lost to follow-up. Thirty-nine died. The causes of the 39 registered deaths were ascertained from death certificates (36 causes) and from the personnel department (three causes).

Exposure

As shown in Table 2, which presents the distribution of the study population and person-years according to workshop, job type or groups of products ever encountered, most subjects had been exposed to all chemical groups. Only one subject, contributing 9 person-years, was not exposed to any compound, five (94 person-years) were exposed only to formaldehyde and 35 (666 person-years) were exposed to all pesticide categories but ethylene oxide. All the other 140 subjects of

Table 1 Cohort description

Parameter	Description
Follow-up period	01/08/1979–31/12/2000
Subjects (men)	181
Person-years	3,107
Still active at 31/12/2000	67
Leaving before 31/12/2000	114
Lost to follow-up	0
Deaths	39

Table 2 Distribution of subjects and person-years according to activities

Activities	Subjects	Percentage	Person-years[a]	Percentage
	181	(100)	3,107	(100)
Workshop 1	98	(54)	1,677	(54)
Workshop 2	77	(42)	1,382	(44)
Workshop 3	66	(36)	1,199	(39)
Workshop 4	75	(41)	1,353	(44)
Applicators	180	(99)	2,986	(99)
Sterilizers	6	(3)	183	(6)
Foremen	40	(22)	1,133	(36)
Supervisors	12	(7)	387	(12)
Formaldehyde	180	(99)	3,098	(99)
Ethylene oxide	140	(77)	2,441	(79)
Insecticides	175	(97)	2,995	(96)
Rodenticides	175	(97)	2,995	(96)

[a]Ever-exposed person-years, i.e. from first exposure to end of follow-up

the cohort (2,338 person-years) were exposed to all chemicals. Thus, people with three or more periods of exposure provided almost 97% of all the person-years of our study. This is because the workers of this department always began as workers in charge of disinfection in dwelling houses and then changed from workshop to workshop during their working history. It was, therefore, not possible to define an unexposed group that could be used as an internal reference. Moreover, large correlations between exposures were observed. Statistically significant associations existed between the cumulative doses of formaldehyde and insecticides ($r = 0.33$, $P < 10^{-4}$), formaldehyde and rodenticides ($r = 0.23$, $P < 10^{-2}$) and insecticides and rodenticides ($r = 0.92$, $P < 10^{-4}$).

Mortality rates

Table 3 shows SMRs and their 95% confidence intervals for selected causes of death. The observed SMRs for all causes of deaths 1.61 (1.14–2.20) and for all cancer 2.24 (1.39–3.43) were significantly higher than expected. As shown in Fig. 1, excesses in observed deaths particularly concerned subjects aged 40–60 years.

When the results were considered by cancer site, no statistically significant excess emerged, although most SMRs were greater than unity, with the notable exception of lung cancer.

It is worth noticing that the observed mortality from lung cancer (ICD 162) was not elevated [SMR = 0.39 (0.01–2.19)].

A statistically significant excess of arterial diseases (ICD 440–448) appeared [SMR = 7.78 (1.60–22.74)] but it is based on a small number of cases (3 observed vs 0.39 expected).

Non-significant trends were observed for all causes of death according to duration of employment ($P = 0.11$): SMR = 0.00 (0.00–1.84) among people with fewer than 10 years; 1.21 (0.44–2.63) for 10–20 years; 2.05 (1.31–3.04) for 20–30 years; 1.62 (0.74–3.07) for people employed for 30 years or more. The overall mortality tended to increase non-significantly ($P = 0.10$) with duration of employment as applicators. Workers employed for more than 20 years showed a significant excess [SMR = 1.91 (1.31–2.68)], which contrasted with that of workers having a shorter duration of employment [SMR = 0.86 (0.31–1.87)]. With regard to cancer, we obtained significant excesses for workers with more than 20 years of employment [SMR = 2.42 (1.43–3.82)], but the test for trend was non-significant.

No trend appeared for workers who had been in charge of the sterilizers, foremen or supervisors. We observed no differences in excess mortality between the

Table 3 Mortality by selected causes of death (Reference: Regional population, male gender-follow-up period 01.08.1979–31.12.2000)

Cause of death	ICD	Observed	Expected	SMR	95% CI
All causes	1–999	39	24.27	1.61	1.14–2.20
Circulatory system	390–459	6	4.75	1.26	0.46–2.75
Ischaemic heart diseases	410–414	1	2.01	0.50	0.01–2.77
Cerebrovascular diseases	430–438	1	0.96	1.04	0.03–5.77
Heart failure	428–429	1	0.50	2.02	0.05–11.25
Arterial diseases	440–448	3	0.39	7.78	1.60–22.74
Respiratory system	460–519	0	0.94	0.00	0.00–3.91
Digestive system	520–579	3	1.58	1.90	0.39–5.54
Liver cirrhosis	571–571	2	1.07	1.88	0.23–6.78
Endocrinous diseases	240–279	1	0.32	3.08	0.08–17.16
Infectious diseases	1–139	3	1.41	2.13	0.44–6.21
Mental diseases	290–319	1	0,31	3.19	0.08–17.79
Nervous system and sense organs	320–389	0	0.38	0.00	0.00–9.65
Accidents and violence	800–999	3	1.79	1.67	0.34–4.89
Suicide	950–959	1	0.46	2.15	0.05–11.98
Travel accidents	810–829/846–848	1	0.37	2.71	0.07–15.10
All malignant neoplasms	140–208	21	9.36	2.24	1.39–3.43
Oesophagus	150	1	0.52	1.91	0.05–10.62
Stomach	151	1	0.31	3.18	0.08–17.70
Colon–intestine	152–153	1	0.50	1.98	0.05–11.04
Rectum	154	1	0.18	5.57	0.14–31.06
Liver	155	1	0.51	1.96	0.05–10.93
Pancreas	157	0	0.34	0,00	0.00–10.77
All digestive cancers	150–159	5	2.53	1.97	0.64–4.61
Buccal cavity– pharynx	140–149	2	0.81	2.47	0.30–8.92
Larynx	161	0	0.40	0.00	0.00–9.29
All upper airways cancers	140–149, 161	2	1.21	1.66	0.20–5.98
Lung, bronchus	162	1	2.55	0.39	0.01–2.19
Pleura	163	1	0.09	11.19	0.28–62.36
Prostate	185	2	0.39	5.17	0.63–18.67
Bladder	188	2	0.30	6.67	0.81–24.10
Leukaemia	204–208	1	0.23	4.42	0.11–24.64

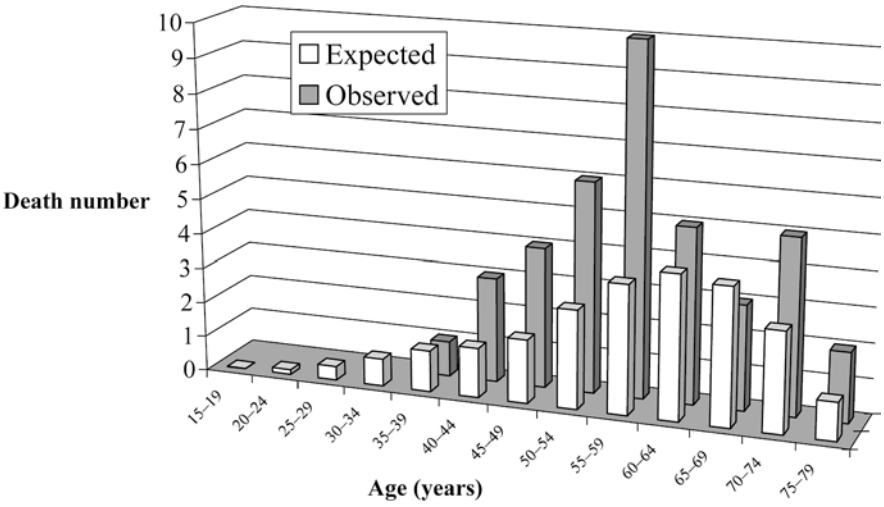

Fig. 1 Observed and expected numbers of deaths according to age group

four workshops according to year of employment, age at employment, reason for leaving and year of death.

Figure 2 shows SMRs for cancer and their 95% confidence intervals, by cumulative dose, for each of the study pollutants or groups of pollutants. Cancer mortality seems to increase, although non-significantly, with cumulative formaldehyde and rodenticides exposure, whereas no clear pattern was observed for ethylene oxide and insecticides. However, significant excesses were observed for the highest exposure levels of formaldehyde, insecticides and rodenticides.

Discussion

A weakness of our study may be the lack of validity of death certificates. It is actually well known that causes of death from death certificates are sometimes inexact.

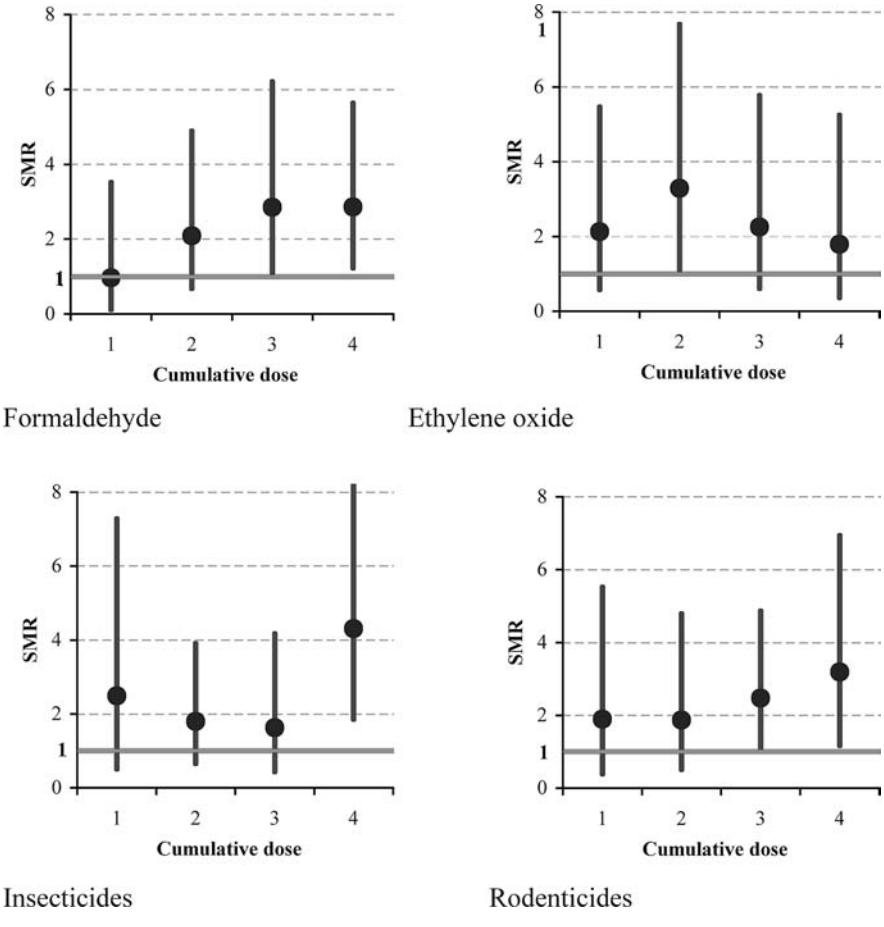

Fig. 2 SMRs and 95% confidence intervals by cumulative doses

This inaccuracy effects equally the exposed and the reference population. It may also be of interest to point out that our study focused on primary causes of death, omitting to explore underlying diseases at the time of death. The number of cancers may, therefore, be underestimated, both in the exposed and in the reference population. Despite the limited number of workers in the present cohort, and the limited number of deaths, our results are consistent and show a significant excess of cancer deaths in pest-control workers. Some arguments support the hypothesis of an occupational origin for these cancers. The observed versus expected death ratio is especially raised for the age group 50–59 years. Cancer mortality was higher for a duration of employment longer than 20 years and, although non-significantly, increased with the estimated cumulative exposure to formaldehyde and rodenticides. This lack of statistical significance may, however, be the result of the small study size. Although information on smoking habits was not available, positive confounding by smoking is unlikely to have occurred since SMRs were low for lung cancer, ischaemic heart diseases and non-malignant respiratory diseases.

The lack of differences in mortality rates between workshops could be explained by the fact that most of the subjects had worked in more than one workshop during their job history.

The absorption of pesticides by different pathways during their use has already been described (Krieger 1995). Some studies suggested the possibility of an excess of cancer in agricultural pesticides applicators or industrial workers, but conflicting results do not allow one to draw a firm conclusion. Conversely, there are very few epidemiological studies on pest-control officers in urban areas.

In a cohort of 1,214 pest-control workers employed for at least 5 years, Barthel (1986) observed significantly elevated SMRs for all malignant neoplasms (SMR = 1.33, 65 observed vs 48.5 expected), oesophagus cancer (SMR = 4.30, 4 observed vs 0.9 expected) and stomach cancer (SMR = 1.80, 14 observed vs 7.8 expected). The data suggested, also, an increasing trend for the risk of stomach cancer by number of years licensed as pesticide applicator. Wang and MacMahon (1979), in a cohort of pesticide workers from three pest-control companies, observed high SMRs for three cancer sites: lung, skin and bladder, only the latter reaching significance. The main limitation of that study was, however, that only 15% of person-years contributed to more than 5 years of employment and to more than 10 years since first employment. In an update of their study over a 10-year follow-up, lung cancer appeared as the single significantly increased risk (MacMahon et al. 1988).

A cohort of 3,827 men licensed to apply pesticides in Florida (USA) was followed up for mortality between 1965 and 1977 (Blair et al. 1983). The overall SMR was not significantly elevated in that population, but excess deaths were observed for leukaemia and cancers of the brain and lung. An update of that study, with an extended 5 year follow-up, confirmed these results: SMRs for all cancers [1.2 (1.0–1.4)] and lung cancer [1.4 (1.0–1.8)] were significantly elevated, whereas many other cancers, including leukaemia and cancers of the brain, showed a slight but non-significant excess (Pesatori et al. 1994). An increasing lung cancer risk with duration of licensure as pesticide applicator was also observed, but this trend was not significant ($P = 0.11$). In that study, mortality from other tobacco-related diseases was not in excess, suggesting that there was no positive confounding due to smoking.

On the other hand, Morgan et al. (1980), after a 7 year follow-up period, failed to observe any excess mortality from cancer in a population of workers exposed to pesticides. In the same way, Thomas et al. (1996), studying 200 deaths among a population of 1,485 pest-control workers from 290 local authority departments, observed no excess of cancer. SMRs were even significantly lower than 1.00 for all causes and lung cancer. This population was, however, exposed for fewer than 15 years to pesticides, and the mean age on entering employment was 37 years. Our subjects were thus exposed 10 years younger and for 10 years more than those of Thomas et al. The spectrum of the pesticides used in both populations might also have been different, and it is likely that at least part of our population had been exposed to previous and more dangerous products.

If one considers the broad spectrum of handled products, some of them being known as mutagenic or suspected to be carcinogenic, our results are not surprising. We observed excess mortality for most cancer sites but without any significant result, due to small cohort size. Another explanation could be that the joint effects of several chemicals may initiate malignancies with different target organs or may act as a global promoter on cancer cells from different origins. As 99% of the officers worked as pesticide applicators during their careers, most of them were exposed to several chemicals. For that reason a considerable overlap existed between the workers in terms of their exposure profile. As a result we were unable to discriminate specific exposure groups with a sufficient power. We had, therefore, no possibility to study the association of multiple or single exposure with cancer rates. In our JEM, exposure intensity was coded according to changes in the mode of application of chemicals or modification of the protective devices. The frequency of exposure was related to the evolution of workshop activities across time. As some of these evaluation criteria affected more than one exposure, our pollutant-related cumulative doses are highly correlated. The respective SMRs, therefore, probably reflected multiple exposures rather that single ones.

Observed numbers of cases of upper airways cancer and leukaemia, which might be related, respectively, to formaldehyde and ethylene oxide, which are known carcinogen, were higher than expected, but all confidence intervals included unity, so no conclusion could be drawn. We have no explanation for the excess deaths due to arterial diseases, and we have not found any

relevant argument in the scientific literature. Of the three observed deaths from pulmonary or peripheral embolism, two had occurred several years after the workers had retired. An occupational origin of these deaths therefore seems unlikely. Moreover, with regard to the intensive use of rodenticides, haemorrhagic accidents would have been expected rather than embolism (Svendsen 2002).

Conclusion

This study showed a statistically significant excess of cancer mortality in a population of municipal pest-control workers exposed to a wide variety of chemicals belonging to several disinfectants or pesticides categories, including, in particular, formaldehyde and ethylene oxide. These cancers might be related to occupational activities, as they occurred more often with a long duration of employment (>20 years).

Because of the small size of the cohort, no single cancer type could be identified as being specifically associated with these occupational activities. Non-significant excesses were observed for most cancer sites, except for lung cancer, suggesting that there was no positive confounding due to smoking.

Acknowledgments The authors thank Ms. Le Bozec and Mr. Even for technical assistance in collecting the data.

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