ORIGINAL ARTICLE

Cancer mortality in a synthetic spinning plant in Besancon, France

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M Hours, J Févotte, S Lafont, A Bergeret

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Objectives: To assess the mortality of a cohort of workers in a synthetic textile spinning plant and to evaluate the relationship between mortality from lung, liver and bladder cancer and the processes or the products used. Methods: The study population consisted of male workers present for at least 6 months in the plant from 1968 to 1984. The cohort was followed until 1999. Vital status and the causes of death were determined by consulting national registries. The population of the Franche-Comté region was used for comparison. In total, 17 groups of exposure were assessed by the industrial hygienist, based on the consensus of an expert group that determined the exposure levels of each job to selected occupational hazards. Each worker was assigned to one or several groups, according to his occupational history. Confounding factors could not be assessed. Standardised mortality ratios (SMR) and 95% bilateral confidence intervals were calculated based on an assumed Poisson distribution of the number of cases to compare the plant mortality and the population mortality. Internal analyses were performed with Cox models in order to assess the risks of death related to the various exposures.

Results: In the whole cohort, mortality from all malignant neoplasms was lower than expected, but this was not significant. All the estimated SMRs were lower than or close to 1. The "hot -line fitters" (RR = 2.13; n = 9; 1.06 to 4.29) and the "fibre-drawing workers" (RR = 1.83 ; n = $20;1.09$ to 3.07) experienced a statistically significant excess in mortality from lung cancer. A slightly elevated but not significant risk of death related to lung cancer (RR = 1.5; n = 41; 0.8 to 2.7) was observed in the groups with the highest exposure to mineral fibres. A statistically significant increase in cancer deaths was observed for workers with high exposure to dust (higher intensity: RR = 1.42; n = 79; 1.06 to 1.89).

See end of article for authors' affiliations

Correspondence to: M Hours, Epidemiological Research and Surveillance Unit in Transport Occupation and Environment, INRETS, UMR T9002, Bron, F-69500, France; martine.hours@ inrets.fr

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Conclusion: Some findings, mainly of lung cancer, justify further exploration in other plants in this industry,

S everal publications have suggested an increased cancer risk in the textile industry,¹⁻⁷ but there is no consensus on the type of cancer, processes or jobs at risk. An increased risk of bladder the textile industry, $1-7$ but there is no consensus on the type of cancer, processes or jobs at risk. An increased risk of bladder cancer has been observed in various workers such as dyers,³ spinners and winders.⁸ An excess of lung cancer has been described in weavers⁹ and an increase in non-Hodgkin lymphomas was reported in a cellulose acetate fibre plant.⁷ Similarly, various other exposures have been suspected: asbestos, cellulose triacetate,¹⁰ fabric dust,^{11 12} or formaldehyde.¹³ In 1995, occupational physicians in Besançon (Franche-Comté region, France) were concerned about the diagnosis of cancer among workers in their care. They noticed that these workers had all been employed in a synthetic spinning factory that had ceased production in Besançon 15 years previously. Upon enquiry, it appeared that heat-transfer fluids, textile lubricants, heated polyester polymers, heated polyamide polymers and mineral fibres including asbestos were the products in closest proximity to these workers when in the plant. No publication on cancer risk related to synthetic textile spinning was found, but we had reported previously 14 an increased risk of mortality for lung, bladder and liver cancer in a chemical plant, which synthesised nylon and polyester (Tergal) polymers used in Besançon. At the request of the local occupational physicians, a mortality cohort study was designed, which aimed to compare the mortality of workers from this plant with the mortality of the general population and to evaluate the possibility of an excess in mortality within the cohort in relation to the different processes and products, specifically lung, bladder and liver cancer mortality.

METHODS

Population

The study population consisted of all male workers employed in the factory from 1968 to 1984 for at least 6 months. Name, date

and place of birth, work history, start and finish dates of employment in specific jobs within the plant were collected through the legal registry of employees and individual occupational records. Vital status was ascertained by consulting the population registry for France, and the causes of death for deceased subjects were obtained from the French causes of death registration department. The matching process was probabilistic and used four keys (sex, date of birth, date and place of death) because registration of cause of death is anonymous in France. A small number of workers could not be traced for their vital status or for the cause of death. Personyears were calculated within the period of follow-up, which began on 1 January 1968 (start date of the death registration department in France) for workers already in service at this date and at the time of first employment for all others. In all cases, the beginning of follow-up was lagged by 6 months to account for the minimum duration. Follow-up ended at the date of death, at 31 December 1999 for surviving workers, or at the date of departure for workers who were lost to follow-up. No data were available for confounding factors such as tobacco and alcohol consumption, as at that time the doctors did not record this information in their files.

Plant

The plant started spinning polyester fibres and thread in 1955, then added polyamide spinning in 1958. The raw material (polyester and polyamide polymers) was received from another factory in granular form, and pumped directly to the fourth level of the factory to be dried before the start of a vertical

Abbreviations: RR, relative risk; SEG, similar exposure group; SMR, standardised mortality ratio; TWA, time-weighted average

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spinning process. Hoppers fed hot boxes (285 \degree C) at the third level, in which the granules were melted through a ''spinning position'' and dropped down to the second level, then the first level where the yarns were wound. This part of the process led to some exposures for the workers involved. Both polymers were processed without any possibility of distinguishing one exposure from another. Heat-transfer fluids were used to warm up the granules, mainly in the upper part of the factory, but owing to leaks in the heating system, respiratory exposure occurred at all steps of the process. Asbestos blankets were used to insulate hot boxes and spinning positions, leading to a higher exposure for the ''hot-line fitters'' responsible for this step on the third floor than for others. Textile lubricants were sprayed onto the yarn to help winding of coils, entailing an exposure to aerosols of these oils at all further steps.

The coils of polyamide or polyester fibres or thread were then processed in horizontal workshops to be drawn and finished (such as sizing of the yarn); all workshops but one (drawing of polyester fibre) processed both polymer yarns. During this horizontal process, textile lubricants were more or less extensively added (spray or bath), depending on the kind of work on the yarn and on its final use. Apart from very rare attempts, dyes were never used in that plant. In the production area, solvents were only used by workers in charge of certain types of maintenance, and people in the laboratories might use various oxygenated and chlorinated solvents. Industrial hygiene measurements were not available for any exposure in that plant.

Fabrication stopped in 1981, the industrial installations were taken apart and the plant was closed in 1984.

Exposure assessment

A group of experts led by the team's industrial hygienist and composed of former technicians and professionals of the plant was formed, as described in other publications.¹⁵ First, the team determined the exposures to be assessed.

Determination of exposure

Six exposure groups were defined: heat-transfer fluids, polyester, polyamide, textile lubricants, mineral fibres and solvents. Two other exposures were added in a second step to take into account some particularities of some tasks: degradation products (of hot polymers) and dust.

Heated polyamide and polyester polymers

Although the temperatures of the process were set to melt polymers without any degradation, we evaluated working with heated polyamide or polyester in the first part of the process, and concluded that overheating with mixed degradation fumes was likely to occur at two steps (hot-line fitting and continuous polymerisation).

Polymer dusts

These were present everywhere, either from the granular raw material or from mechanical work (such as winding) with fibre or thread. A general category of exposure to any dust (eg, polymer dust, dust from mineral fibres, or others, as described below) was created to take into account the global ambient dust.

Heat-transfer fluids

The fluids used in the plant as heat-transfer agents to some extent varied over the years, but were mainly comprised of biphenyl and biphenyl oxide, which are widely used in other similar factories because of their high thermal stability.

Mineral fibres

As in any plant involving a hot process, insulation material was present everywhere, either as asbestos or mineral wool. Although some typical positions necessarily involved asbestos (eg, hot-line fitters, insulators, laboratory workers), it was impossible to clearly distinguish workers exposed to asbestos from those exposed to other mineral fibres, therefore exposure to any insulation materials was classified as one group.

Textile lubricants

The formulation of textile lubricants had varied over time without any possibility of precisely identifying all components, but they were mainly soluble petroleum oils, with aliphatic amines as antioxidants and formaldehyde as biocide.

Solvents

Various solvents may have been used but we were unable to assign specific solvent exposure to specific workers, therefore exposure to any solvent was assessed as a single category.

Degradation products

For the exposure to ''degradation products of polymers'', "polyester polymers" and "nylon polymers", only two categories were considered: exposed or non-exposed.

Examination of records and assignment of groups

Personnel records were examined to identify all jobs held by the cohort members and to determine their tasks and location. Based on the expert consensus and using a plant internal comparative approach, three qualitative levels of exposure (high, medium and low) to each of the six main chemicals were assessed for different processes and occupational tasks. These qualitative levels were then combined with the time-weighted average (TWA) for each job, based on a typical working day in this factory. Then, 17 similar exposure groups (SEGs) were defined as combinations of job title and working environment leading to similar exposures. Each grouping was based on the fraction of working hours in a week spent in exposed areas and on the proportion of workers in a given job, with the constraint that at least 50% of these workers should be exposed. The SEGs were constructed using the following rules: level 3 exposure meant that $>90\%$ of workers in this SEG had high exposure to the product and formed the most exposed population of the factory; level 2 exposure meant that $>75\%$ of workers in this SEG were exposed to the product, with a medium TWA; and level 1 meant that >50% of workers in this SEG were exposed to the product, with a low TWA. For mineral fibres, level 1 was divided into two categories to distinguish the workers who had certainly had level 1 exposure from those for whom exposure was questionable $(<25\%$ probability), such as warehouse workers.

Finally, all the jobs were classified within the different SEGs. Each worker was assigned to one or several groups, according to his occupational history. Table 1 shows the description of the SEGs and the distribution of the level of exposure to the main products of interest within each of the SEGs.

Statistical analysis

Two complementary methods were used in the present study. First, the rates of death in the plant were compared with the rates of death in the general population. Standardised mortality ratios (SMRs) were calculated as the ratio between the observed and the expected number of deaths. The expected number of deaths was calculated using age-specific rates of death (5-year periods) for the Franche-Comté population which was estimated from the 1968, 1975, 1982, 1990 and 1999 population censuses. Linear interpolation for intermediate years was applied. The 95% CI of the SMR was computed with Table 1 Distribution of the exposure level to the main products of interest within each of the similar exposure groups

the assumption of a Poisson distribution of the causes of death.16 SMRs were calculated for the different causes of death according to the duration of service and the length of follow-up since first employment. For the duration of service, personyears were distributed into two groups $(\leq 10 \text{ years}$ and $>$ 10 years). For example, the total number of person-years of observation of a subject who joined the plant in 1957 was assigned to the duration group >10 years since 1 January 1968, whereas that of a person who joined the plant on 1 April 1962 was considered in the group ≤ 10 years from 1 January 1968 to 31 March 1971 and in the group >10 years until the end of follow-up. Time of follow-up since first employment was also distributed into two groups $(\leq 20 \text{ years}$ and $\geq 20 \text{ years})$ according to the same rules for the duration of service.

In the second method, relative risk (RR) was calculated within the cohort in order to detect a potential risk of death associated with a given exposure. Mortality from all causes, all cancers, lung, bladder and liver cancer was available. RR was estimated according to the duration of exposure, time between the first exposure and the end of follow-up, and intensity of the exposure. Three groups were constituted for the duration of exposure (not exposed, ≤ 10 years and > 10 years), for the time between first exposure and end of follow-up (not exposed, \leq 20 years and $>$ 20 years) and for intensity of exposure (no exposure, low exposure, high exposure). An algorithm was used to take into account the exposure level determined by the exposure assessment group and the number of years exposed to this level (see Appendix 1). The attribution of person-years for the three criteria (duration, time since the first exposure and intensity) was similar to that described above. RR was assessed with Cox models (proportional hazard regression analyses) with delayed entry. Using age as the time variable, each subject entered the regression at his age at the beginning of follow-up. The 95% CI was calculated for the RR.

We were unable to separate the different types of products in the analysis, owing to the extent of colinearity of these variables. For all analyses, the SAS statistical package V.8.2 was used.

RESULTS

Analysis of the whole cohort

The 2916 men included in the cohort during the period 1968– 1984 contributed 84 045 person-years. Demographic characteristics of the cohort are shown in table 2. Vital status was unknown for 1.1% of the entire cohort, and cause of death was determined for 92.2% of the deceased subjects (46 causes remained unknown, mainly workers born abroad). In total, 655 subjects had died during the follow-up period.

An analysis of some specific causes of death is presented in table 3. A significant decrease in mortality from all causes was observed in the whole cohort (SMR = 0.89 , 95% CI 0.83 to 0.96). Mortality from all malignant neoplasms was lower than expected. All the estimated SMRs were less than or close to 1 except for pleural, liver and bladder cancer, none of which reached significance. There was no excess of death for ''liver cirrhosis, alcoholic psychosis, alcoholism''. There was no significant excess when duration of employment was $>$ 10 years, or when time since first exposure was $>$ 20 years, for any of the causes of death (data not shown).

Table 2 Working characteristics and vital status of male workers present in the plant between 1 January 1968 and date of closure (1984) of the plant, $n = 2916$

*Status not obtained for 1997–1999.

Table 3 Observed deaths and SMRs for selected causes of death among the male Besancon workers, compared with the Franche-Comté population (84 045 person-years)

Analyses of SEGs

In the analysis by job group (table 4), the spinners had a limit significant excess of mortality from all causes, particularly from cancer. The hot-line fitters experienced a statistically significant increase for cancer mortality, mainly due to lung cancer. The fibre-drawing workers also had a significant increase in mortality from lung cancer $p<0.05$. The "finishing" workers had a non significant excess of mortality from lung cancer and liver cancer. Workers in the general maintenance group experienced a non-significantly higher risk of dying from lung cancer.

 $*p<0.01$.

Analyses by product

No excess of mortality was observed for bladder or liver cancer in any of the different exposure groups. Table 5 summarises the observed relation between the main exposures and mortality due to lung cancer.

Heat-transfer fluids

The group exposed to heat-transfer fluids experienced a high but non-significant risk of lung cancer death compared with the non-exposed group, with a trend towards increase in intensity and time since first exposure, but not duration.

Mineral fibres

A slightly raised but non-significant risk of death related to lung cancer was shown in the groups with the highest exposure or the longest duration to mineral fibres. When analysing duration or intensity of exposure by time since first exposure, we found a significant RR for exposure duration $>$ 10 years compared with <10 years ($RR_{>10ans} = 4.36$, n = 5, 95% CI 1.15 to 16.48) for time since first exposure of ≤ 20 years. When considering time since first exposure of >20 years, RR was higher in the high exposure group compared with the low exposure group ($RR_{high intensity} = 2.41$, n = 37, 1.07 to 5.41).

Of the three workers who died of mesothelioma, two (one insulator and one hot-line fitter) had high exposure to mineral fibres and one (warehouse worker) was possibly exposed to low levels.

Textile lubricants

A significant increase in mortality for lung cancer was observed in the group exposed to lubricants (only one lung cancer among non-exposed workers), whatever the indicator (intensity, duration or latency) used. When analysing mineral fibres concomitantly with textile lubricants, the excess was not observed in the group of workers exposed only to the textile lubricants but rather was restricted to the workers exposed concomitantly to the two products (data not shown).

Dust

A statistically significant increase in death from all cancers was observed for workers with high or former exposure to dust (higher intensity: $RR = 1.42$, $n = 79$, 95% CI 1.06 to 1.89; time since exposure >20 years: RR = 1.38, n = 105, 1.05 to 1.81). Highly significant increased RRs were observed for lung cancer mortality in the group exposed to dust, whatever the intensity, the duration or the time since first exposure.

Degradation products of hot polymers

There was a significant increase in risk of lung cancer with exposure to degradation products, but this increase affected only subjects having shorter duration of exposure and less time since first exposure.

Summary

We did not observe any significant excess of mortality in the groups exposed to polyamide or polyester. Subjects exposed to solvents for $>$ 20 years experienced a non-significant risk of death by lung cancer compared withs non-exposed subject $(RR = 2.33, n = 4, 95\% \text{ CI } 0.84 \text{ to } 6.52).$

DISCUSSION

The significant SMR of 0.89 for all causes of death is a clear demonstration of the well-known healthy worker effect, mainly due to a lower mortality risk for circulatory and respiratory diseases. Non-significant increases in mortality due to various cancers, mainly lung cancer, were seen in the hot-line fitters group and in workers with high exposure to heat-transfer fluids

RR, relative risk; SEG, similar exposure group.

*41 workers (8 deceased) were not taken into account in the analyses due to missing occupational information.

-Other jobs are not presented because of their small contribution to person-years. A worker could be employed in more than one job group.

`p,0.10, 1p,0.05, p,0.001.

and mineral fibres. A statistically significant increase in mortality from lung cancer was observed in groups of subjects exposed to textile lubricants, dust or the degradation products of hot polymer.

Increased lung cancer mortality was found in several exposure groups in this cohort. It is difficult to isolate the exposure responsible for the increase in lung cancer, because of the multiexposure pattern. In part, it might be related to asbestos, which was a concomitant exposure. Asbestos was certainly used in the early days of the existence of the plant, and afterwards in a few specific tasks, notably by the hot-line fitters group, who worked on the spinning-position insulation; one person in this group died from mesothelioma. However, it was difficult to separate exposure to asbestos from exposure to other mineral fibres because of their simultaneous presence during the intermediate working period. It seems unlikely that textile lubricants would be responsible for an increase in mortality; the wire-drawing group, for whom lubricants were the only exposure, did not experience an excess of mortality from lung cancer. Furthermore, the excess mortality was restricted to workers exposed concomitantly to textile lubricants and mineral fibres. The lubricants contained formaldehyde, which was suspected to be related to lung cancer in cohorts in the garment industry,¹³ but a new publication

reporting analyses for a longer follow-up of these cohorts concluded that formaldehyde could not be related to an excess of lung cancer.¹⁷ In the past, we have found an increase in lungcancer mortality in the textile industry in the Lyon area.¹⁸ Some cases in this study were former workers in another spinning plant in Lyon. Other researchers have published the same findings,¹⁹ sometimes attributed to asbestos,^{9 20} but never to spinning of nylon or polyester thread.

A further interesting result is the increased mortality in the group exposed to dust. Four of the five SEGs exposed to dust experienced an increased mortality from lung cancer. However, the observed excess was higher among those exposed to low intensity or short duration of work, which might possibly suggest a potential bias due to tobacco. Information on smoking was not available. Besides the increased mortality from lung cancer, we observed some slight excess mortality for laryngeal cancer (three observed cases) among hot-line fitters but not for oesophageal cancer or respiratory disease, therefore, these results on lung cancer could not be entirely due to tobacco.

Bladder cancer is the most usual cancer for which an increase has been reported in the textile industry.¹³⁸ This study did not show any risk of bladder cancer mortality in this synthetic spinning factory, in spite of a greater than expected number of Table 5 Relative risk of death from lung cancer for the main group of exposures by duration, intensity and latency (82 960 personyears, $n = 2875$

deaths compared with the general population (11 observed versus 8.2 expected). Apart from dyes containing aromatic amines, no specific chemical has been shown to be related to this increase in the textile industry. Dyes were not usually used in this plant. Nylon and polyester polymers, biphenyl or biphenyl oxide in the heat-transfer fluids, textile lubricants and mineral fibres were the main exposures in the plant. A recent publication reported that 2-year oral administration of a diet containing biphenyl induced bladder papillomas and carcinomas in male rats.²¹ We failed to find a relationship between this product and deaths from bladder cancer in Besancon, but it should be noted that mortality might not reflect the importance of bladder cancer, which is a cancer with long survival duration.

Similarly, non-significant increases of liver cancer mortality were observed for the finishing, spinning and maintenance groups but could not be related to any specific exposure. Recently, Umeda et al demonstrated that biphenyl could also induce benign and malignant tumours in the liver of female mice.22 23 The non-significant increase for liver cancer observed in several groups could be explained partly but not fully by alcohol consumption: the increase for liver cancer and an increase for non-cancerous diseases related to alcohol were not observed in the same groups of workers in our study. In a previous study, we observed an excess of bladder and liver cancers in the cohort of the chemical plant that synthesised the polymers used in Besançon, where heat transfer fluids were also used.14 Therefore, the question should be further explored in other factories, particularly taking into account potential confounding factors.

In spite of the existence of a cancer registry in this region, we were not able to undertake a cancer incidence study, owing to the large number of workers who have left the region at the closure of the plant. This mortality cohort study benefited from a long and complete follow-up. Some unknown causes of death, mainly for subjects born abroad, could have led to an underestimation by 8.5% on average of some SMRs for specific causes, notably lung cancer (five additional lung cancers, one bladder cancer and 1–2 liver cancers, if the proportion among

been closed for >15 years. Every attempt was made to ensure the quality of the cohort. Despite the absence of exposure measurements in the factory, the experts defined the exposure groups and the grouping of the jobs for several exposures, thanks to their considerable knowledge of the factory and of other plants of the same type still functioning today. Retrospective assessment of exposure is always difficult, especially when exposure measurements are lacking. Several authors have shown that an assessment performed by experienced hygienists helped by local specialists is reliable,^{24 25} albeit not very sensitive.26 Some misclassification of exposure may occur due to the lack of detail in some work histories. This

disease risk towards the null value.

difference observed between the different groups.

Some difficulties were encountered because the factory has

CONCLUSIONS

Some findings, mainly in relation to lung cancer justify further exploration in other plants in this industry, where the confounding factors could be taken into account and the exposure levels better determined.

will tend to bias any true associations between exposure and

unknown deaths is the same as among the known causes). This could explain part of the decrease in lung cancer mortality of the groups of administration and warehouse workers. Conversely, in the Cox model, the calculated risk could have been incorrectly estimated if the unknown deaths were restricted to a specific group. To explore this possibility, we evaluated the distribution of the unknown deaths among the different groups; there were only 13 unknown causes of death in the administration group, 13 in the thread drawing group (the largest group), and the 10 in the warehouse workers group. When the warehouse workers were excluded from the analysis of mineral fibres, the RR for lung cancer did not change significantly. This hypothesis could not explain the

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Main messages

- An increase of cancer mortality was found for workers engaged as hot-line fitters.
- A higher mortality from lung cancer was observed in several other groups of workers.
- \bullet It is difficult to determine precisely which exposure in that plant was related to the observed increase in cancer mortality.

Policy implications

- Exposure measurements should be conducted in spinning plants.
- Further surveys in other plants of synthetic textile spinning should be undertaken to explore more precisely the relationship between exposures and cancer.

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Authors' affiliations

M Hours, Epidemiological Research and Surveillance Unit in Transport Occupation and Environment, INRETS, UMR T9002, Bron, France J Févotte, InVS, UMR T9002, Lyon, France

S Lafont, A Bergeret, Université Lyon 1, UMR T9002, Lyon, France

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APPENDIX 1: ALGORITHM USED TO QUANTIFY THE INTENSITY OF THE EXPOSURES

For an exposure x :

High intensity group: workers who responded to one of the following criteria at least:

- $\frac{1}{\text{duration}_{x \text{ at level } 1}} + \frac{1}{\text{duration}_{x \text{ at level } 2}} + \frac{1}{\text{duration}_{x \text{ at level } 3}}$.75th percentile of the distribution of duration of workers ever exposed to exposure x; OR
- \bullet (duration_{x at level 2}+duration_{xat level 3}) > median of the distribution of duration of workers ever exposed to exposure x; OR
- (duration_{x at level 3} $>$ 25th percentile of the distribution of duration of workers ever exposed to exposure x).

Low intensity group: all other exposed workers.