The influence of occupational exposure to pesticides, polycyclic aromatic hydrocarbons, diesel exhaust, metal dust, metal fumes, and mineral oil on prostate cancer: a prospective cohort study

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The influence of occupational exposure to pesticides, polycyclic aromatic hydrocarbons, diesel exhaust, metal dust, metal fumes, and mineral oil on prostate cancer: a prospective cohort study

D Boers, M P A Zeegers, G M Swaen, IJ Kant, P A van den Brandt

Aims: To investigate the relation between exposure to pesticides, polycyclic aromatic hydrocarbons (PAHs), diesel exhaust, metal dust, metal fumes, and mineral oil in relation to prostate cancer incidence in a large prospective study.

Methods: This cohort study was conducted among 58 279 men in the Netherlands. In September 1986, cohort members (55–69 years) completed a self-administered questionnaire on potential cancer risk factors, including job history. Follow up for prostate cancer incidence was established by linkage to cancer registries until December 1995 (9.3 years of follow up). The analyses included 1386 cases of prostate cancer and 2335 subcohort members. A blinded case-by-case expert exposure assessment was carried out to assign cases and subcohort members a cumulative probability of exposure for each potential carcinogenic exposure.

Results: In multivariate analyses there was a significant negative association for pesticides (RR 0.60; 95% CI 0.37 to 0.95) when comparing the highest tertile of exposure to pesticides with no exposure. No association was found for occupational exposure to PAHs (RR 0.75; 95% CI 0.42 to 1.31), diesel exhaust (RR 0.81; 95% CI 0.62 to 1.06), metal dust (RR 1.01; 95% CI 0.72 to 1.40), metal fumes (RR 1.11; 95% CI 0.80 to 1.54), or mineral oil (RR 0.99; 95% CI 0.66 to 1.48) when comparing the highest tertile of exposure with no exposure. In subgroup analysis, with respect to tumour invasiveness and morphology, null results were found for occupational exposure to pesticides, PAH, diesel exhaust, metal dust, metal fumes, and mineral oil.

Conclusions: These results suggest a negative association between occupational exposure to pesticides and prostate cancer. For other carcinogenic exposures results suggest no association between occupational exposure to PAHs, diesel exhaust, metal dust, metal fumes, or mineral oil and prostate cancer.
Furthermore, very few studies have examined the association between some metals and prostate cancer. The few studies that analysed specific exposures, provided some evidence for associations with some specific metal dusts and metalworking fluids like mineral oil. And some studies, but not all reported excess risks for workers exposed to cadmium. In a review, investigating the association between metal workers and prostate cancer, most studies reported an excess risk. But the literature provides too little information for firm conclusions about the relation between exposure to specific metals or metallic compounds and prostate cancer risk. Few studies investigating the risk of prostate cancer in metal workers reported mineral oils as a risk factor. Some studies investigating the association between mineral oil and prostate cancer have reported an increased risk for prostate cancer; and some have not. In summary, there is still uncertainty about the possible association between the exposures mentioned above and the risk for prostate cancer.

In this study we will examine the association between occupational exposure to pesticides, polycyclic aromatic hydrocarbons (PAHs), diesel exhaust, metal dust, metal fumes, or mineral oil and prostate cancer within a large prospective cohort study in the Netherlands.

METHODS

Study population

The study design and data collection strategies have been described previously. In summary, the Netherlands Cohort Study (NLCS) is a prospective cohort study on diet, other lifestyle factors, sociodemographic characteristics, job history, and cancer risk, which started in 1986 among the general population in the Netherlands. The cohort includes 58 279 men aged 55–69 years at baseline. The study population originated from 204 municipal population registries throughout the Netherlands. The case-cohort approach was used for data processing and analysis. Cases were enumerated from the entire cohort, while the accumulated person-years in the cohort were estimated from a subcohort sample. Following this approach, a subcohort of 2335 men was randomly sampled from the cohort after baseline measurement. The subcohort has been biennially followed up for information on vital status. No subcohort members were lost to follow up. A subcohort has the advantage of being cost effective compared to follow up of an entire cohort of this size.

Case ascertainment and follow up

Follow up for incident cancer was established by record linkage to all nine regional cancer registries in the Netherlands and PALGA, the Dutch database for pathology reports, leading to at least a 96% ascertainment of all incident cancers. The presented analysis was restricted to 9.3 years of follow up, from September 1986 to December 1995.

Prevalent cases, other than skin cancer, were excluded. This led to a total of 2335 male subcohort members and 1386 cases with microscopically confirmed incident prostate cancer. Among the cases 526 men were diagnosed with localised prostate cancer, and 453 subjects were diagnosed with advanced prostate cancer; the remaining subjects had an unknown tumour grade.

Exposure assessment

From all occupational exposures reported to be associated with prostate cancer, those that were selected were thought to have a sufficient high prevalence to yield relevant information. This restriction with regard to the prevalence of occupational exposure resulted in six relevant exposures: pesticides, PAHs, diesel exhaust, metal dust, metal fumes, and mineral oils. At baseline, the cohort members completed a self-administered questionnaire on potential risk factors for cancer. In this questionnaire, job history was covered by questions on job title, name of the company, type of company, time period, and information on type of products produced at the company. Information on job title, type of company, and type of product were coded according to the Dutch Occupational Classification System of the Central Bureau of the Statistics (CBS). Experts in the fields of occupational epidemiology (GMHS) and occupational hygiene (UKJ) assessed separately the cumulative probability of carcinogenic exposures, blinded with respect to case or subcohort status.

Exposure assessment was conducted using information about company name, company type, product type, and employment period.

Four exposure categories were defined: no exposure to the specific agent, possible exposure (probability of exposure estimated to be lower than 30%), probable exposure (probability of exposure lies between 30% and 90%), and nearly certain exposure (probability of exposure over 90%). For a quantification of exposure a cumulative probability of exposure (CPE) was calculated, which combines information about the probability of exposure and the duration of exposure. A weight was assigned to each exposure category: no exposure, weight 0; possible exposure, weight 0.15; probable exposure, weight 0.6; and nearly certain exposure, weight 0.95. Each weight corresponds to the midpoint of each exposure category. The CPE was calculated by multiplication of the weight given to each exposure category by the number of years exposed. Subsequently, for each person all weighted exposures were summed, for every carcinogen separately, and the exposed subjects were categorised in tertiles of exposure index.

Statistical analysis

Based on earlier studies on prostate cancer risk factors, the following variables were considered as potential confounders: age (years), first degree family history of prostate cancer (yes/no), consumption of vegetables, fruit, meat, alcohol (g/day), smoking (ever/never), level of education (no education of primary school, lower vocational training, medium vocational training, high educational level (that is, university)), and physical activity (no, low, medium, or high). Men with incomplete or inconsistent dietary data were excluded from analysis with dietary variables.

Incidence rate ratios and corresponding 95% confidence intervals for prostate cancer were calculated in the age adjusted and multivariate case-cohort analysis with cumulative probability of exposure and dichotomous variables (exposed versus non-exposed), using the Cox proportional
hazards model, processed with the Stata statistical software package. The proportional hazards assumption was tested using the scaled Schoenfeld residuals. Two sided confidence limits are reported throughout the paper.

We have calculated subgroup analysis for occupational exposure to pesticides, PAHs, diesel exhaust, metal dust, metal fumes, or mineral oil, with respect to tumour invasiveness and morphology into localised prostate tumours (T0–2, M0: no evidence of primary tumour [T0], clinically unapparent tumour [T1], or tumour confined within the prostate [T2], and no distant metastasis) or advanced prostate tumours (T3–4, M0 or T1–4, M1: tumour extending through the capsule [T3], fixed tumour or tumour invading the capsule [T4], fixed tumour involving adjacent tissue [T4], or distant metastasis). The results are presented in Table 1 and Table 2.

| Table 1 | Association between potential confounders and occupational exposure to pesticides, polycyclic aromatic hydrocarbons, diesel exhaust, metal dust, metal fumes and mineral oil and prostate cancer among subcohort members: the Netherlands Cohort Study 1986–1995 |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| **Exposure**    | **Pesticides**  | **PAH**         | **Diesel exhaust** | **Metal dust**  | **Metal fumes** | **Mineral oil** |
| **Age (mean years)** | **Never** (n = 59) | **Ever** (n = 4) | **Never** (n = 60) | **Ever** (n = 2) | **Never** (n = 45) | **Ever** (n = 16) | **Never** (n = 53) | **Ever** (n = 9) | **Never** (n = 54) | **Ever** (n = 8) |
| **Vegetables** | 61.35 | 61.38 | 61.41 | 60.38 | 61.12 | 61.48 | 60.69 | 61.47 | 60.72 | 61.44 | 60.57 |
| **Fruit** | 190.2 | 182.9 | 188.1 | 206.4 | 187.9 | 29 | 588 | 197.1 | 188.0 | 199.0 |
| **Meat** | 150.6 | 157.1 | 150.6 | 159.4 | 151.2 | 152.8 | 16.42 | 15.1 | 16.57 | 19.01 | 16.57 |

*Polycyclic aromatic hydrocarbons.
†Consumption of these foods.

| Table 2 | Incidence rate ratios for prostate cancer (n = 1376) according to cumulative exposure to pesticides, polycyclic aromatic hydrocarbons, diesel exhaust, metal dust, metal fumes, and mineral oil in age adjusted and multivariate analysis: the Netherlands Cohort Study 1986–95 |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| **Exposure**    | **Cases (n)**   | **Person-years (subcohort)** | **RR (95% CI)** | **Cases (n)**   | **Person-years (subcohort)** | **RR (95% CI)** |
| **Pesticides** | 1285 | 17996 | 1.00 (reference) | 1196 | 17129 | 1.00 (reference) |
| **1 tertile (low)** | 29 | 572 | 0.81 (0.51 to 1.28) | 26 | 526 | 0.85 (0.53 to 1.36) |
| **2 tertile** | 30 | 620 | 0.66 (0.42 to 1.04) | 29 | 588 | 0.72 (0.45 to 1.14) |
| **3 tertile (high)** | 32 | 635 | 0.64 (0.41 to 0.99) | 27 | 570 | 0.60 (0.37 to 0.92) |
| **PAH** | 1305 | 18524 | 1.00 (reference) | 1213 | 17586 | 1.00 (reference) |
| **1 tertile (low)** | 25 | 448 | 1.02 (0.62 to 1.69) | 23 | 428 | 1.01 (0.60 to 1.71) |
| **2 tertile** | 26 | 452 | 0.91 (0.55 to 1.49) | 23 | 442 | 0.76 (0.44 to 1.32) |
| **3 tertile (high)** | 20 | 421 | 0.74 (0.43 to 1.28) | 19 | 387 | 0.75 (0.42 to 1.31) |
| **Diesel exhaust** | 1065 | 14757 | 1.00 (reference) | 991 | 14011 | 1.00 (reference) |
| **1 tertile (low)** | 102 | 1738 | 0.88 (0.68 to 1.14) | 93 | 1663 | 0.85 (0.64 to 1.11) |
| **2 tertile** | 98 | 1582 | 0.92 (0.70 to 1.21) | 90 | 1489 | 0.89 (0.67 to 1.20) |
| **3 tertile (high)** | 102 | 1659 | 0.82 (0.63 to 1.06) | 95 | 1582 | 0.81 (0.62 to 1.06) |
| **Metal dust** | 1168 | 16443 | 1.00 (reference) | 1082 | 15555 | 1.00 (reference) |
| **1 tertile (low)** | 66 | 1161 | 0.90 (0.66 to 1.24) | 64 | 1133 | 0.88 (0.64 to 1.22) |
| **2 tertile** | 70 | 1095 | 1.01 (0.74 to 1.38) | 64 | 1045 | 0.97 (0.70 to 1.36) |
| **3 tertile (high)** | 65 | 1081 | 0.98 (0.71 to 1.35) | 64 | 1062 | 1.01 (0.72 to 1.40) |
| **Metal fumes** | 1182 | 16659 | 1.00 (reference) | 1096 | 15777 | 1.00 (reference) |
| **1 tertile (low)** | 63 | 1124 | 0.88 (0.64 to 1.21) | 60 | 1083 | 0.84 (0.60 to 1.17) |
| **2 tertile** | 55 | 970 | 0.91 (0.65 to 1.29) | 50 | 935 | 0.87 (0.60 to 1.25) |
| **3 tertile (high)** | 69 | 1046 | 1.06 (0.77 to 1.47) | 68 | 1018 | 1.11 (0.80 to 1.54) |
| **Mineral oil** | 1242 | 17699 | 1.00 (reference) | 1151 | 16791 | 1.00 (reference) |
| **1 tertile (low)** | 45 | 729 | 1.02 (0.70 to 1.51) | 42 | 686 | 1.01 (0.68 to 1.50) |
| **2 tertile** | 43 | 723 | 1.02 (0.69 to 1.50) | 42 | 711 | 1.01 (0.68 to 1.51) |
| **3 tertile (high)** | 44 | 700 | 0.99 (0.67 to 1.47) | 42 | 663 | 0.99 (0.66 to 1.48) |

*Incidence rate ratio adjusted for age with corresponding 95% confidence intervals.
†Incidence rate ratio adjusted for age, family history of prostate cancer, vegetable, fruit, and meat consumption, with corresponding 95% confidence intervals.
‡Polycyclic aromatic hydrocarbons.
adjacent structures other than seminal vesicles [T4], and no distant metastasis [M0]; or any tumour [T0–4] with distant metastasis [M1]), based on the TNM classification system.

Results
The distribution of potential confounders was comparable between cases and subcohort members. In cases, a slightly higher consumption of vegetables (51.38% versus 49.14%) and fruit (51.52% versus 48.11%) was reported, compared to subcohort members. Furthermore, family history of prostate cancer was more frequently reported by cases (RR 1.26; 95% CI 0.89 to 1.77) compared to no consumption of fruit. A statistically significant increased risk has been found for men exposed to diesel exhaust with a high consumption of fruit (RR 0.81; 95% CI 0.62 to 1.06); 1.01 (95% CI 0.72 to 1.40); 1.11 (95% CI 0.80 to 1.54); and 0.99 (95% CI 0.66 to 1.48) for highest tertile of CPE compared to no exposure (see table 2).

Table 3 shows incidence rate ratios for the association between prostate cancer and occupational exposure stratified for low or high consumption of vegetables, fruit, and meat. A statistically significant increased risk has been found for men exposed to diesel exhaust with a high consumption of fruit (RR 0.81; 95% CI 0.62 to 1.06); 1.01 (95% CI 0.72 to 1.40); 1.11 (95% CI 0.80 to 1.54); and 0.99 (95% CI 0.66 to 1.48) for highest tertile of CPE compared to no exposure (see table 2).

Table 3 shows incidence rate ratios for the association between prostate cancer and occupational exposure stratified for low or high consumption of vegetables, fruit, and meat. A statistically significant increased risk has been found for men exposed to diesel exhaust with a high consumption of fruit (RR 0.81; 95% CI 0.62 to 1.06); 1.01 (95% CI 0.72 to 1.40); 1.11 (95% CI 0.80 to 1.54); and 0.99 (95% CI 0.66 to 1.48) for highest tertile of CPE compared to no exposure (see table 2).

DISCUSSION
In this study we have examined the association between six occupational exposures and the incidence of prostate cancer. The results suggest no association between exposure to occupational exposures and prostate cancer. Subgroup analyses showed null results for occupational exposure to pesticides, PAH, diesel exhaust, metal dust, metal fumes, and mineral oil.

For occupational exposure to PAHs, diesel exhaust, metal dust, metal fumes, and mineral oil non-significant null results were noted of respectively 0.75 (95% CI 0.42 to 1.31); 0.81 (95% CI 0.62 to 1.06); 1.01 (95% CI 0.72 to 1.40); 1.11 (95% CI 0.80 to 1.54); and 0.99 (95% CI 0.66 to 1.48) for highest tertile of CPE compared to no exposure (see table 2).
study by Elghany and colleagues, the researchers also made a distinction between all tumours and aggressive tumours. The results by Elghany et al support our reported null findings for exposure to metal dust or fumes and localised or advanced prostate cancer.

Excesses in risk have been found in most, but not all studies investigating the relation between exposure to pesticides and prostate cancer. However, there are many different pesticides and most studies, including ours, have not analysed specific compounds. Some other studies have reported excess risk among farmers or herbicide applicators. Yet, farmers perform a wide variety of tasks, and are therefore exposed to numerous potential carcinogenic substances like solvents, fuels and oils, pesticides, and more. Occupations with exposure to pesticides are (mostly) farmers, gardeners, and pesticide applicators. In this study we have reported a slight inverse association for weighted duration of exposure to pesticides and prostate cancer. Also, in our previous analyses, no association was found for farming and prostate cancer. Our results are consistent with these findings. Assuming there is an excess risk from certain pesticides, it is not surprising that results show inconsistency. Farming practices differ between countries or even regions, leading to differences in exposure. Furthermore, many studies have grouped farm owners and farm workers together. They should be treated as distinct groups, and additionally some studies have not sufficiently adjusted for potential confounders. Moreover, most studies, including our study, have not been able to take into account the use of protective equipment (for example, clothing, mask). This may influence the risk of prostate cancer for exposure for farmers, since not all farmers are actually exposed.

Additionally, the analysis of other occupational exposures like PAHs, diesel exhaust, metal dust, metal fumes, and mineral oil also suggested no association with prostate cancer in the multivariate analysis. All these occupational exposures are, like farmers, troubled with heterogeneity in exposure. Metalworkers are exposed to a wide variety of solvents, oils, lubricants, metal dust, or metal fumes. Excess risk among metalworkers might be contributed to several risk factors. Exposure to PAHs is usually in the form of exposure to particles with PAHs, which makes it difficult to investigate because subjects are exposed to mixtures of PAH compounds and other chemicals. The same applies to exposure to diesel exhaust. A limitation of our analysis is that we have not actually measured exposure to these carcinogens, but made an estimate of the exposure, based on job title, type of company, company name, type of product, and duration of employment. Furthermore, we had no information on types of pesticides or metals being used.

The quality of the exposure assessment strongly affects the outcome of the risk estimate and ideally includes both intensity and duration of the occupational exposure for each specific study subject. However, in large population based studies it is almost impossible to obtain this information. Moreover, in this type of study the range of jobs with potential exposures may be large and within given jobs there may be a great possible variation of exposures. This makes it even more difficult to identify a clear link between jobs and exposures, compared with industry based studies. Farmers in particular show extreme heterogeneity in occupational exposures. In our study the occupational history of the study participants was obtained through questionnaires, which did not allow an estimation of the actual exposure concentrations that were experienced in the past. The highest achievable was a retrospective exposure assessment in terms of probability of exposure. In general this can be obtained through a job exposure matrix (JEM) or a case-by-case expert assessment. We used the case-by-case expert assessment in this study. The main advantage of the method, compared with the use of a JEM, is that all the available information (job title, type and name of company, type of product, and time period) was used for the exposure assessment. Moreover, a JEM may produce greater non-differential misclassification than exposure assessment by experts, because information obtained from a JEM is mistakenly taken to relate to individual exposure. In case-by-case expert assessment different measures for exposures are applied; this allows more control of heterogeneity. However, a case-by-case expert assessment may not be sufficient to control for extreme heterogeneity as seen among farmers. It is possible that we have overestimated pesticide exposure in this study, and that our results for pesticide exposure are possibly biased.

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**Table 4** Adjusted incidence rate ratios of prostate cancer for any exposure compared with no exposure to pesticides, polycyclic aromatic hydrocarbons, diesel exhaust, metal dust, metal fumes, and mineral oil, in subgroups of localised versus advanced prostate tumours: the Netherlands Cohort Study 1986–95

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Cases (n)</th>
<th>PY*</th>
<th>Localised tumours† (n = 526)</th>
<th>Cases (n)</th>
<th>PY*</th>
<th>Advanced tumours‡ (n = 453)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pesticides</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No exposure</td>
<td>483</td>
<td>17996</td>
<td>1.00 (reference)</td>
<td>417</td>
<td>17996</td>
<td>1.00 (reference)</td>
</tr>
<tr>
<td>Any exposure</td>
<td>41</td>
<td>1879</td>
<td>0.83 (0.60 to 1.15)§</td>
<td>34</td>
<td>1879</td>
<td>0.81 (0.57 to 1.15)§</td>
</tr>
<tr>
<td><strong>PAH</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No exposure</td>
<td>495</td>
<td>18524</td>
<td>1.00 (reference)</td>
<td>431</td>
<td>18524</td>
<td>1.00 (reference)</td>
</tr>
<tr>
<td>Any exposure</td>
<td>29</td>
<td>1351</td>
<td>0.96 (0.66 to 1.40)§</td>
<td>20</td>
<td>1351</td>
<td>0.75 (0.47 to 1.18)§</td>
</tr>
<tr>
<td><strong>Diesel exhaust</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No exposure</td>
<td>408</td>
<td>14757</td>
<td>1.00 (reference)</td>
<td>346</td>
<td>14757</td>
<td>1.00 (reference)</td>
</tr>
<tr>
<td>Any exposure</td>
<td>116</td>
<td>5118</td>
<td>0.87 (0.71 to 1.07)§</td>
<td>105</td>
<td>5118</td>
<td>0.93 (0.75 to 1.16)§</td>
</tr>
<tr>
<td><strong>Metal dust</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No exposure</td>
<td>450</td>
<td>16443</td>
<td>1.00 (reference)</td>
<td>375</td>
<td>16443</td>
<td>1.00 (reference)</td>
</tr>
<tr>
<td>Any exposure</td>
<td>74</td>
<td>3432</td>
<td>0.91 (0.71 to 1.17)§</td>
<td>76</td>
<td>3432</td>
<td>1.09 (0.85 to 1.39)§</td>
</tr>
<tr>
<td><strong>Metal fumes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No exposure</td>
<td>451</td>
<td>16659</td>
<td>1.00 (reference)</td>
<td>382</td>
<td>16659</td>
<td>1.00 (reference)</td>
</tr>
<tr>
<td>Any exposure</td>
<td>73</td>
<td>3216</td>
<td>0.97 (0.75 to 1.24)§</td>
<td>69</td>
<td>3216</td>
<td>1.05 (0.81 to 1.36)§</td>
</tr>
<tr>
<td><strong>Mineral oil</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No exposure</td>
<td>471</td>
<td>17699</td>
<td>1.00 (reference)</td>
<td>411</td>
<td>17699</td>
<td>1.00 (reference)</td>
</tr>
<tr>
<td>Any exposure</td>
<td>53</td>
<td>2176</td>
<td>1.07 (0.80 to 1.43)§</td>
<td>40</td>
<td>2176</td>
<td>0.93 (0.67 to 1.29)§</td>
</tr>
</tbody>
</table>

*Person-years (subcohort).
†Localised tumours: T0–T2 and M0.
‡Advanced tumours: T3–T4 and M1.
§Incidence rate ratios adjusted for age [years] with corresponding 95% confidence intervals.
¢Polycyclic aromatic hydrocarbons.
To incorporate the effect of duration of exposure, which appeared to be essential in evaluation of exposures to carcinogenic agents, we calculated a cumulative probability of exposure, for the six carcinogens separately. However, there are no criteria for determination of exposure in a case-by-case expert assessment, and the exposure assessment is affected by the learning phenomenon of the expert(s). To improve reliability we used a two stage exposure assessment in which two experts, blinded with respect to disease status, assessed the exposure. Disagreements were solved through consensus meetings.20–22

Furthermore, the same experts have implicated the case-by-case expert exposure assessment before using data from the same cohort.23–26 In these investigations researchers have reported increased risks27–29 for exposure to chemical carcinogens and cancer. Therefore, our null associations could also indicate that there is no association between occupational exposures and prostate cancer.

Epidemiological evidence on occupational exposure and prostate cancer, mostly, has been derived from either job titles (through a JEM)25,26–28 or self-assessed exposures to certain occupational agents.29–32 Self-assessment of occupational exposure is considered inadequate since chemical knowledge of study subjects in general may not be sufficient to recall substance specific or duration specific occupational exposure. Only a few other studies have conducted an expert exposure assessment,33,34 as in our study. An important advantage of our study is that we were able to adjust for nutritional, physical activity, alcohol use, and smoking, and that these data were collected prior to the diagnosis of prostate cancer. This approach essentially eliminates the likelihood of recall bias and has the advantage that the effect of non-occupational risk factors could be eliminated. Furthermore, we carried out a cohort study, which is less vulnerable for bias than a case-control study, for instance.

Our results are not supportive of associations between the investigated occupational exposures and prostate cancer, outside of exposure to pesticides. We noted a significant negative association for exposure to pesticides in the multivariate analysis. However, these results are possibly biased. Both positive and negative results have been reported for occupational exposure and prostate cancer, therefore more specific data is needed. In these future studies more detailed information on exposure (or potential confounders) is needed, and also information on protective measures while working with the substances.

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