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**DRAFT**

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**CC/04/12**

**COMMITTEE ON CARCINOGENICITY OF CHEMICALS IN FOOD CONSUMER PRODUCTS AND THE ENVIRONMENT**

**Prostate Cancer: Review of occupational exposure to PAHs.**

1. The appended draft review from the DH Toxicology Unit was written in order to complete the review of relevant epidemiology papers which have investigated the potential association between occupational exposure to PAHs and risk of prostate cancer (Annex 1). The DH Toxicology Unit paper presents a tabular overview of all the retrieved studies. A number of the more significant papers have also been appended (Annex 2).
2. Members are asked to consider the review and appended papers and to comment on the draft overall conclusion prepared by the secretariat as given below:

**Draft conclusion**

3. The DH Toxicology review reports that there are several occupational groups where relatively high exposures to PAHs can be anticipated, e.g. truck drivers, foundry workers, chimney sweeps and to a lesser extent fire-fighters. There have been a number of epidemiological investigations of the potential association between exposure to PAHs in these occupational groups and risk of prostate cancer. This has included several cohort studies. The adequacy of exposure data documented is very limited in most of the reports. Where exposure data or information on the duration of occupational exposure are available, there is no consistent evidence for an increased risk of prostate cancer in any of the PAH occupational groups studied. Overall the available studies do not provide convincing evidence for an association between occupations with exposure to PAHs and an increased risk of prostate cancer.

**Secretariat May 2004**

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## **Introduction**

This report is a follow-up to the review entitled “Prostate cancer-trends and risk factors: an overview”, annex 1 to CC/04/12 - Prostate Cancer: Review of PAHs & Occupation. In the review, established risk factors for prostate cancer (PC) such as age, family history and ethnicity/ country of residence were discussed, as well as hormonal patterns and dietary factors. The review has suggested that polycyclic aromatic hydrocarbons (PAHs) may contribute to the aetiology of PC, as studies in the US had shown positive associations for several occupations involving potential exposure to PAHs (Krstev *et al.*, 1998a; Krstev *et al.*, 1998b). These groups include firefighters (Demers *et al.*, 1994; Grimes *et al.*, 1991; Krstev *et al.*, 1998a; Krstev *et al.*, 1998b; Ma *et al.*, 1998), power plant operators (Krstev *et al.*, 1998a; Krstev *et al.*, 1998b), foundry workers (Sharma-Wagner *et al.*, 2000), coke oven workers (Costantino *et al.*, 1995), furnace, kiln and oven operators (Krstev *et al.*, 1998b), chimney sweeps (Evanoff *et al.*, 1993), railway workers (Sharma-Wagner *et al.*, 2000), heavy equipment operators (Krstev *et al.*, 1998a), farm machine operators and paving and stone cutting workers (Sharma-Wagner *et al.*, 2000). These studies were not critically assessed for the overview on PC, hence this report further discusses whether occupational exposure to PAHs may be a possible risk factor for this disease.

Polycyclic aromatic hydrocarbons are compounds made up of three or more benzene interlinked rings. They are ubiquitously distributed in the environment in fossil fuels, or formed as a result of incomplete thermal decomposition of organic materials such as wood, diesel, coal, oil and coke (Shimada and Fujii-Kuriyama, 2004). Exposure to PAHs can occur via several routes including inhalation, skin contamination and oral ingestion (Brandt and Watson, 2003). Several studies have been carried out to investigate possible relationships between exposure to PAHs and PC. Aronson and colleagues found an excess risk of PC with exposure to PAHs from coal, although a weaker association with diesel engine emissions was presented (Aronson *et al.*, 1996). In contrast, Seidler found excess risk in relation to diesel fuel and fumes, soot, tar and pitch (Seidler *et al.*, 1998).

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#### **Recommended levels of PAHs**

Polycyclic aromatic hydrocarbons never exist as sole entities but as complex mixtures. Various approaches have been adopted to quantitate exposure to such mixtures, such as measuring benzene soluble fraction or total PAHs. Because various combinations of PAHs have been measured in different epidemiology studies and used to report occupational exposure, comparison between the different studies was difficult. The Expert Panel on Air Quality Standards (EPAQS) uses benzo[a]pyrene (B[a]P) as a marker for the total mixture of PAHs in the United Kingdom, and suggested an Air Quality Standard of 0.25 ng/m<sup>3</sup> B[a]P as an annual average (EPAQS, 1999), and the European Commission working group recommended a limit value of between 0.5-1 ng/m<sup>3</sup> B[a]P. Different standards have also been suggested by various bodies (Table 1). However, Brandt and Watson suggested that the use of B[a]P be treated with caution, depending on the occupation, as the total PAHs generally measured can represent different burdens of exposure. For example, total PAHs constitute only a small fraction (<1%) of bitumen fumes, but 40-90% of coal tar pitch volatiles (CTPV). Hence total PAH exposure may over represent the carcinogenic potential of bitumen fume exposure (Brandt and Watson, 2003).

Such measurements only give estimates of external concentrations. Biomarkers of internal exposure have not been taken into account in this report.

#### **Environmental air levels of PAHs**

Exposure to PAHs has been measured in a number of environmental and occupational settings (figure 1, table 1).

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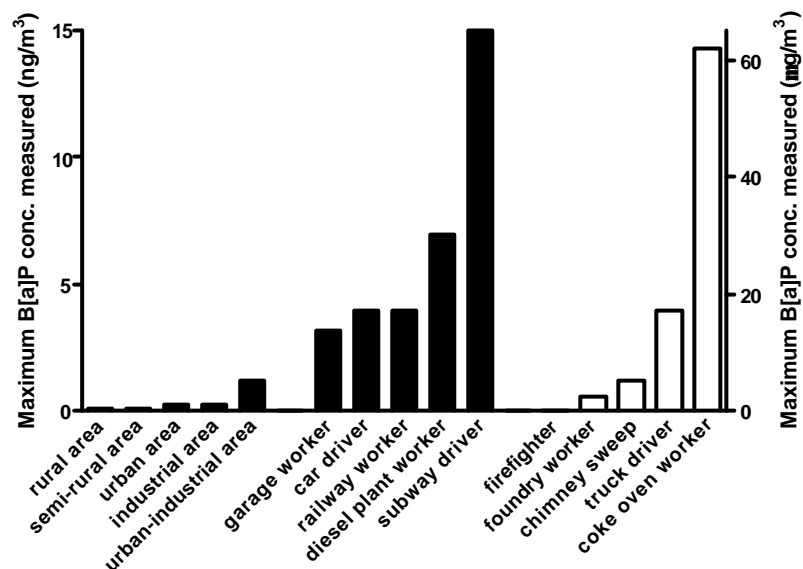


Figure 1. Maximum concentrations of B[a]P measured in environmental and occupational settings.

Black bars are expressed in ng/m<sup>3</sup> (left axis) and white bars are expressed in µg/m<sup>3</sup> (right axis)

Table 1. Recommended, environmental and occupational levels of B[a]P

B[a]P concentration	
<b>Recommended levels</b>	
Air quality standard (EPAQS)	0.25 ng/m <sup>3</sup> annual average
Occupational exposure limit (HSE)	Under review
Maximum permissible concentration (RIVM)	1 ng/m <sup>3</sup>
Threshold limit value (ACGIH)	0.2 mg/m <sup>3</sup> time-weighted

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	average
Permissible exposure limit (OSHA)	0.2 mg/m <sup>3</sup>
Recommended exposure limit (NIOSH)	0.1 mg/m <sup>3</sup> 8-hour weighted average
<b>Environmental levels (annual average)</b>	
<b>(DEFRA, 2001)</b>	
Rural	0.04-0.09 ng/m <sup>3</sup>
Semi rural	0.06 ng/m <sup>3</sup>
Urban	0.12-0.24 ng/m <sup>3</sup>
Urban industrial	0.28-1.17 ng/m <sup>3</sup>
Industrial	0.25 ng/m <sup>3</sup>
<b>Occupational levels</b>	
Coke oven workers	17000-50000 ng/m <sup>3</sup>
Workers exposed to diesel fuel	
Diesel plants	7 ng/m <sup>3</sup>
Garage workers	3.2 ng/m <sup>3</sup>
Car drivers	4 ng/m <sup>3</sup>
Subway drivers	<15 ng/m <sup>3</sup>
Truck drivers	17000 ng/m <sup>3</sup>
Railway workers	4 ng/m <sup>3</sup>
Foundry workers	60-2300 ng/m <sup>3</sup>
Fire fighters	160 ng/m <sup>3</sup> 8-hour weighted

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	average
Chimney sweeps	5080 ng/m <sup>3</sup>

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The concentration of PAHs deposited on the skin or inhaled is commonly measured by using skin wipes, or in air samples taken with a personal sampler near the breathing zone, respectively (Brandt and Watson, 2003). Air levels of PAHs are largely affected by seasonal changes, and tend to be higher in winter months due to the increased residential heating compared to the summer, during which time the main source is from exhaust fumes. Concentrations of PAHs also largely differ between different environmental settings (figure 1; table 1). In rural and semi-rural areas, average concentrations of 0.04-0.09 and 0.06 ng/m<sup>3</sup> of B[a]P were measured, respectively. In urban areas, average concentrations of 0.12-0.24 ng/m<sup>3</sup> of individual PAHs were measured and in urban-industrial area, levels as high as 0.28-1.17 ng/m<sup>3</sup> were reached, whereas near industrial sources, lower levels of 0.25 ng/m<sup>3</sup> were reported (DEFRA, 2001). Similar levels were measured by the Dutch RIVM (levels of 0.05-0.15 ng/m<sup>3</sup>, 0.2-0.5 ng/m<sup>3</sup> and 0.2-0.4 ng/m<sup>3</sup> B[a]P were measured in rural, industrial and urban areas, respectively) (RIVM, 1999) and in the US (0.3 and 0.6 ng/m<sup>3</sup> B[a]P were detected in rural and urban areas) (EPA, 1998).

In this report, studies have been subdivided into occupational category. Detailed exposure data were only available for coke oven workers. Semi-quantitative exposure was available for the case-control study carried out by Nadon and co-workers regarding a range of occupations including railway workers and mechanics. Difficulties were encountered in assessing case-control studies since it is difficult to be precise when making case-controls for PC risk factors. General problems also included case identification in cohort studies and data collection.

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### Exposure to diesel fuel

#### *Published exposure data*

Concentrations of total PAH and B[a]P have been measured in various occupational settings. Diesel/gasoline plant workers were exposed to 32-52 and 0.21-4.3 ng/m<sup>3</sup> total PAH and B[a]P, respectively over a 24-hour period (Adonis *et al.*, 2003), car drivers, 10.2-28.7 and 1-3.2 ng/m<sup>3</sup> (Fromme *et al.*, 1998), subway drivers, 30.2-67.5 and 0.7-4 ng/m<sup>3</sup> (Fromme *et al.*, 1998), garage workers, 150 and <15 ng/m<sup>3</sup> (Hemminki *et al.*, 1994), truck drivers, 170-1000 µg/m<sup>3</sup> and 4.7-17 µg/m<sup>3</sup> (IARC, 1984).

#### *Epidemiology studies presenting semi-quantitative data on exposure*

Two case-control studies were retrieved regarding PC and exposure to diesel fuel. Seidler and colleagues carried out a case-control study in two urologic practices in Germany. Subjects with a histological diagnosis of PC were considered as cases and those with negative biopsies were used as controls. These control patients exhibited either prostate hypertrophy or had the biopsy to eliminate suspected PC. From the 272 patients and 371 controls identified, 192 (71%) and 210 (55%) participated, respectively. A self-administrable questionnaire was used to gain information regarding occupation and the participant's own assessment of frequency of exposure to a number of substances, as well as confounding factors such as car driving, alcohol drinking and smoking. For each occupation or industry, the probability (none, small proportion of workers, high proportion of workers) and intensity (none, lightly exposed, heavily exposed) of exposure to each chemical was classified. Subjects were categorised as having no exposure, exposure < 25 dose-years or exposure > 25 dose-years, a dose-year being the exposure duration weighted by intensity and probability of exposure. A statistically significant association between exposure to diesel fuel and PC was observed that displayed a dose-related tendency (< 25 years odds ratio (OR)=1.1, 95% confidence interval (CI)=0.7-1.8; > 25 years OR=3.7, 95% CI=1.4-

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9.8). Although a slight increase in risk due to PAH was observed, the relationship was not dose-dependent (< 25 years OR=1.6, 95% CI=1-2.4; > 25 years OR=1.4, 95% CI=0.4-4.7). When only subjects with a high probability of exposure were regarded as exposed, PAHs were significantly related to the increased risk of PC (OR=2.1, 95% CI=1-4.2). However, this latter analysis did not reveal any significant association of PC with other substances tested, including diesel fuel. In this study, subjects exposed to diesel fuel for more than 25 years mainly worked as drivers, motor mechanics, auto engineers or boatmen. This job spectrum suggests that exposure to PAH as a component of inhalatory diesel exhaust may be a potential risk factor for PC, although the authors suggest further experimental research should be carried out (Seidler *et al.*, 1998).

In contrast, Krstev and colleagues presented conflicting data showing that risks were decreased for persons working in local- and long distance trucking (OR= 0.5, 95% CI=0.3-0.9)(Krstev *et al.*, 1998a). These data were collected from a large US population-base case control study of four cancer sites, including the prostate. 981 patients with histologically confirmed PC were identified from pathology and out patient records, and took part in the study, along with 1315 controls from the general population. All participants were interviewed by a trained interviewer who used a questionnaire to collect information on occupation, work history since the age of 16 and possible confounders.

#### *Epidemiology studies with no exposure data*

One case-control and one retrospective cohort study was retrieved. In an attempt to identify occupational risk factors for PC, a large population-based case control study was conducted in three areas of the US, using a two-tier approach (Krstev *et al.*, 1998b). 60878 cases whose death certificates listed PC as underlying cause of death were included in this study. Controls consisted of subjects, who died of all other causes except cancer, and were matched by age, and race. Following a detailed analysis of different occupational groups, although bus drivers were significantly associated with PC (mortality odds ratio (MOR)=1.4, 95% CI= 1.0-1.8), a statistically significant decreased risk was observed for taxi drivers

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(MOR=0.8, 95% CI=0.8-0.9), truck drivers (MOR=0.8, 95% CI=0.6-1.0), mechanics and repairers (MOR=0.8, 95% CI=0.7-0.9) and taxi drivers and chauffeurs (MOR=0.7, 95% CI=0.5-0.8). Although identifying some occupations and industries with an increased risk of mortality, the authors concluded that the study could not identify occupational risk factors that could account for the substantial proportion of PC occurring on the US (Krstev *et al.*, 1998b).

Sharma-Wagner and colleagues also linked PC incidence data in Sweden between 1960 and 1979 with employment information reported in the 1960 National Census (Sharma-Wagner *et al.*, 2000). All malignant tumours are reported to the Swedish National Cancer registry. 25000 new cases of PC are diagnosed every year and a total of 39422 men employed in 1960 developed PC during 19 years of follow-up. 36269 of these cases (92%) were microscopically confirmed, and hence were included into the study. Data from this retrospective cohort study showed a small but significant excess risk for PC in automotive repairers (standardised incidence ratio (SIR)=1.12, 95% CI=1.0-1.2), railroad traffic workers (SIR=1.1, 95% CI=1.0-1.2) and travelling salesmen (SIR=1.18, 95% CI=1.1-1.3). However, the authors concluded that these occupations were unlikely to play a central role in the aetiology of PC, as the excess risks observed in the study were relatively small (<10%) (Sharma-Wagner *et al.*, 2000).

#### *Conclusion*

There is no convincing evidence regarding an association between occupational exposure to diesel fuel and PC. In some studies, no data is presented regarding the exposure to PAHs or duration of exposure. Problems of interpretation included selection of controls with benign prostatic disease, poor response rate and the use of a self-administered questionnaire.

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### Coke oven workers

#### *Published exposure data*

Coke oven workers have been repeatedly shown to be exposed to PAHs (Hemminki *et al.*, 1990; Kalina *et al.*, 1998; Reuterwall *et al.*, 1991; Zhang *et al.*, 2000). The exposure among coke oven workers ranged from 2 to 62  $\mu\text{g}/\text{m}^3$  (Binkova *et al.*, 1998; Kalina *et al.*, 1998). In a Finnish cokery, the mean concentration of B[a]P measured during the work shift was 5.7  $\mu\text{g}/\text{m}^3$  (Kuljukka *et al.*, 1996) and in a plant making carbon anode for aluminium electrolysis, 0.17 to 4.88  $\mu\text{g}/\text{m}^3$  B[a]P was measured over five consecutive 8-hour shifts (Petry *et al.*, 1996). In a Swedish coke oven plants, exposure to levels of B[a]P sometimes exceeded 5  $\mu\text{g}/\text{m}^3$  (Reuterwall *et al.*, 1991). Similarly, van Schooten demonstrated that coke-oven workers were exposed to substantial concentrations of B[a]P (0.1-7.8  $\mu\text{g}/\text{m}^3$ ) over three consecutive shifts (van Schooten *et al.*, 1990). The Expert Panel on Air Quality Standards stated that studies in coke plants in USA, Scandinavia and Czechoslovakia identified concentrations of B[a]P of approximately 10-40  $\mu\text{g}/\text{m}^3$  on top ovens and 10-20 fold lower concentrations in the general work atmosphere (EPAQS, 1999). In addition, B[a]P concentrations of 4.7-17  $\mu\text{g}/\text{m}^3$  were measured in coke oven plants in Germany and Sweden (IARC, 1984).

#### *Epidemiology studies presenting exposure data*

Two cohort studies were retrieved regarding coke oven workers. Following an initial study of two cohorts of steel or coke oven workers, Costantino and colleagues carried out a follow-up cohort study, consisting of 15818 individuals from Allegheny County, US, that had work histories and vital status information spanning 30 years (Costantino *et al.*, 1995). The underlying cause of death was obtained from death certificates and was coded according to the international classification of disease. On average, this updated study contained 14.5 additional years of work experience data and 7 years more vital status information for each worker than the original investigation. The follow-up study investigated the

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mortality risk of coke oven workers compared to matched controls of non-coke oven workers, taking into account relative risk (RR) by years of employment, period of follow-up and cumulative exposure levels. Exposure to coke oven emissions was measured in terms of CTPV for various job categories and ranged between 0.88 and 3.15  $\mu\text{g}/\text{m}^3$  for side jobs and topside jobs, respectively. The study identified an overall significant excess mortality from PC (RR=1.57, 95% CI=1.1-2.3,  $p<0.01$ ), an increase of more than 25% over the original study. However, the existence of an exposure response was not clear. The RR of PC in employees in the middle exposure category (200-399  $\text{mg}/\text{m}^3$ ) was significantly increased (RR=1.93, 95% CI=1.1-3.1, no. at risk=1276, no. of deaths=20) and was higher than in the lower exposure category (1-199  $\text{mg}/\text{m}^3$ ; RR=1.43, 95% CI=0.8-2.4, no. at risk=2638, no. of deaths=21) or the highest exposure category (>400  $\text{mg}/\text{m}^3$ ; RR=1.4, 95% CI=0.8-2.4, no. at risk=1407, no. of deaths=17). The authors stated that the assessment of exposure-response relationships was restricted due to the relative infrequency of PC occurring (58 cases) (Costantino *et al.*, 1995).

Another cohort study carried out in Norwegian coke plant, operating from 1964 to 1988 investigated whether workers had a higher mortality rate and whether it could be linked to a specific exposure (Bye *et al.*, 1998). 888 employees were identified from the Norwegian Bureau of Statistics and their personal data were obtained from the plants archives. All participants had worked in the plant for at least one year. Causes of death were obtained from Norwegian Bureau of Statistics and cancer diagnoses from the Norwegian Cancer Registry. Specific exposures were estimated with records from actual measurements carried out at this plant and interviews with former workers. Values 2-300  $\mu\text{g}/\text{m}^3$  PAHs were measured. Dose-response relationships were investigated by stratified analysis of SIRs with the calculated cumulative exposure as an indicator of individual dose. Data show that the incidence of PC in the cohort was not significantly different (observed (O)=5, expected (E)=9.6, SIR=0.53, 95% CI=0.2-1.2) to expected values in the Norwegian general population. In addition, there was no association between cumulative exposure to PAHs and PC (unexposed, SIR=0.7; <50, SIR=0.6; 50-149, SIR=0; >150, SIR=0;  $p=0.3$ )(Bye *et al.*, 1998).

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#### *Conclusion*

Some statistical evidence has been presented to suggest coke oven workers may have an increased risk of PC, but no dose-response relationship has been demonstrated.

### **Fire fighters**

#### *Published exposure data*

Fire fighters are exposed to complex mixtures of toxic compounds due to the increasing use of synthetic materials in building and furnishing although benzene, PAHs (mainly B[a]P) and asbestos have been reported to be the most common carcinogens found (Krstev *et al.*, 1998b). Exposure levels of fire fighters to B[a]P were measured in one study by personal air sampling. Eight-hour time-weighted average concentrations of 0.029-0.16  $\mu\text{g}/\text{m}^3$  were reported, depending on the task involved (Feunekes *et al.*, 1997). Because of a high exposure to such complex mixtures, including PAHs, fire fighting has been suggested as being a potential risk factor for PC.

#### *Epidemiology studies presenting data on duration of exposure*

There were 2 cohort studies and 1 case-control study retrieved that investigated the association between PC and fire fighters and which presented data on the duration of exposure to PAHs.

Demers and co-workers carried out a cohort study of 2447 US male fire fighters that were employed for at least one year between 1944 and 1979, alive as of 1974. The follow-up period was from January 1974 to December 1989. Work history and vital status was obtained through pension boards, fire or police departments, state vital record offices and the National Death Index. Cancer cases were identified through the population-based registry of the Cancer-Surveillance

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System. Data obtained show that the overall risk of PC was elevated (SIR=1.4, 95% CI=1.1-1.7, observed cases=66) compared to 1878 police and population controls. However, mortality did not increase with the duration of employment. In addition, the RR was highest for fire fighters less than 30 years after first employment (< 30 years, SIR=7.4, 95% CI=0.2-41; >30 years, SIR=1.3, 95% CI=1-1.7). Because the majority of fire fighters began employment before the age of thirty, the results seen can be closely correlated with age rather than occupational exposure, as 25 cases under the age of 65 were diagnosed with PC (Demers *et al.*, 1994). Overall, although excess of PC was observed in fire fighters, similar excess were also seen in the control group of policemen, selected as controls due to their similar socio-economic backgrounds, healthcare and physical entry requirements and no gradient of PC occurrence with duration of employment was observed.

In a cohort study of 205 Honolulu fire fighters, mortality data of the cohort between 1969 and 1988 were collected from mortality records. On the basis of death certificates, deaths were compared between fire fighters and other males in Hawaii, older than 20 years of age. Data suggest a significantly elevated risk of PC mortality (E=1.68, O=4.39, RR=2.61, 95% CI=1.4-5.0) in the total cohort, as well as in Caucasian (E=2.25, O=8.33, RR=3.7, 95% CI=1.7-8.0) and Hawaiian (O=2.97, E=0.89, RR=3.35, 95% CI=1.1-10.5) fire fighters. No exposure relationship was observed due to the relatively small number in the firemen population and because comparable data in a control group was not available (Grimes *et al.*, 1991).

An excess risk of PC was observed amongst fire fighters in a case-control study carried out in the US that showed a significant trend with increasing duration of employment (OR=5.15, 95% CI=1.1-25.2,  $\chi^2_{\text{trend}} p=0.02$ )(Krstev *et al.*, 1998a).

#### *Epidemiology studies with no exposure data*

There were 3 cohort studies and 1 case-control study retrieved that investigated the association between PC and fire fighters and but did not present data on PAHs exposure.

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Ma and co-workers obtained data by using death certificates from a total of 6607 fire fighters. 1883 deaths from cancer were identified (1817 in white and 66 in black fire fighters) of which 189 and 16 cases, respectively, were diagnosed with PC. The study showed that the risk of PC was slightly elevated in both US white (MOR=1.2, 95% CI=1.0-1.3) and black (MOR=1.9, 95% CI=1.2-3.2) fire fighters (Ma *et al.*, 1998). In contrast, no significant increase of PC was recorded amongst Canadian (standardised mortality ratio (SMR)=146.1, 95% CI=63.1-287.9) (Guidotti, 1993) or Swedish fire fighters (SMR=114, 95% CI=76.0-165.0) (Tornling *et al.*, 1994). In US fire fighters, a significantly increased OR in fire fighting occupations (OR= 1.2, 95% CI=1.0-1.4) was observed that was increased in African American men (OR=2.2, 95% CI=1.2-3.9) (Krstev *et al.*, 1998b).

#### *Conclusion*

Some statistical evidence has been presented to suggest fire fighters may have an increased risk of PC, but no dose-response relationship has been demonstrated. Some of the studies summarised were limited to relatively small numbers. Problems of interpretation included the increased incidence of PC in police controls and that some of the studies do not present exposure data for PAHs or data regarding the duration of exposure.

### **Railway workers**

#### *Published exposure data*

In a German study, mean values of total PAHs (30.2 and 67.5 ng/m<sup>3</sup>) and B[a]P (0.7 and 4.0 ng/m<sup>3</sup>) were measured in an electric subway train during summer and winter periods, respectively (Fromme *et al.*, 1998). However, little data regarding railway workers occupational exposure to PAHs are available and none of the epidemiology studies under review present such data.

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*Epidemiology studies presenting data on duration of exposure*

Two case-control studies were retrieved that investigated the association between railway workers and PC. Despite the lack of exposure data, several studies have identified railway work as being a potential risk factor for PC.

The US population-based case control study carried out by Krstev and co-workers showed an elevated risk for PC in those carrying out railroad locomotive work, especially African American men. Authors suggest it may be due to high exposure to B[a]P or 1-nitropyrene (MOR=1.61, 95% CI=1.1-2.4) and showed a significant trend with increasing duration of employment ( $\chi^2_{\text{trend}} p=0.002$ ) (Krstev *et al.*, 1998a).

In contrast, a Canadian population-based case-control study found an elevated risk in railway workers (OR=4.47, 95% CI=1.3-15.8) although it was not significantly related to duration of employment (OR=1.81, 95% CI=0.7-4.6) (Aronson *et al.*, 1996). 3730 cancer patients (82%) of a possible 4576 participated in this study. Of these, 449 patients were diagnosed with PC and were eligible for inclusion as diagnosis was histologically proven. Two sets of controls were used. 740 population controls were selected and of these, 533 (72%) were interviewed. In addition, a cancer control group was made up of all other cancer patients, with the exception of lung cancer, and consisted of 1550 subjects.

*Conclusion*

There is evidence presented in these population based case-control studies that railway workers may be at an increased risk of PC. However, no dose-response relationship was seen and a duration-related response was only observed in one of the studies. The use of a low number of controls or controls with other forms of cancer made interpretation of data difficult.

**Water transport workers**

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*Published exposure data*

No studies have been retrieved that measured the occupational exposure of water transport workers to PAHs.

*Epidemiology studies presenting data on duration of exposure*

Only 1 case-control study was retrieved. This study, carried out by Aronson as described above, stated that the risk of PC was particularly high amongst water transport workers (OR=3.04, 95% CI=1.1-8.5) based on the magnitude of OR, statistical significance and significant duration-response trend. Moreover, water transport workers exhibited an increased risk when undergoing non-substantial<sup>1</sup> exposure to liquid fuel combustion products (OR=5.6, 95% CI=1.4-22.5) or substantial exposure<sup>2</sup> (OR=17.3, 95% CI=1.3-99.9). Given a set of risk factors, including exposure to different substances, occupations and industries, the authors calculated the fraction of PC that were attributable to occupational exposure to PAHs to be up to 20% and concluded that, although possibly over-estimated, the percentage of cases of PC attributed to occupational exposure to PAHs may represent an important public health issue (Aronson *et al.*, 1996).

*Conclusion*

No occupational exposure data for PAH were presented in this epidemiology study. There is some evidence to suggest that water transport workers may have an increased risk of PC, although only one case-control study has been carried out. Interpretation of data was made difficult particularly due to a low response rate (72%) of controls.

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<sup>1</sup> Authors classified non-substantial exposure as having probable or definite exposure, latency >5 years, duration <5 years, concentration x frequency <4

<sup>2</sup> Authors classified non-substantial exposure as having probable or definite exposure, latency >5 years, duration <5 years, concentration x frequency <4

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### **Power plant workers**

#### *Published exposure data*

No data regarding occupational exposure to PAH in power plants are available.

#### *Epidemiology studies presenting data on duration of exposure*

One population-based case-control study was retrieved. This study described above (Krstev *et al.*, 1998a) showed an excess risk for PC (MOR=4.04, 95% CI=0.4-39.8) among power plant operators, particularly stationary engineers usually exposed to B[a]P, and PAHs from coal and fuel oil, asbestos and soot. Data showed a significant trend with longer duration of employment ( $\chi^2_{\text{trend}} p=0.03$ ).

#### *Conclusion*

This case-control study does not present occupational data regarding PAH levels of exposure. However, the study indicates an increased risk of PC for power plant workers exposed to B[a]P and PAH from different sources, as duration of employment was associated with risk of PC.

### **Chimney sweeps**

#### *Published exposure data*

Many studies have investigated the association between cancer, primarily oesophageal and lung cancer, in chimney sweeps, and PAHs as a component of soot produced from the combustion of coal, coke, oil or wood. Knecht and co-workers measured total PAHs and B[a]P in different fuels. Levels of 2.27, 5.06 and 5.08  $\mu\text{g}/\text{m}^3$  total PAH in oil, solid fuel

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and combinations of both, respectively, were detected, and 0.36, 0.83 and 0.82  $\mu\text{g}/\text{m}^3$  B[a]P (Knecht *et al.*, 1989). In a German study of 115 samples, average values of 0.09  $\mu\text{g}/\text{m}^3$  B[a]P were measured (IARC, 1984).

#### *Epidemiology studies presenting data on duration of exposure*

One cohort study was retrieved regarding the risk of PC in chimney sweeps. In an epidemiological study, Evanoff and colleagues explored a cohort of 5242 Swedish chimney sweeps in a follow-up study. The initial study carried out examined mortality and incidence of cancer in chimney sweeps employed at any time between 1918 and 1980. This follow-up study extended mortality analysis by 7.5 years to cover the period 1951-1990 and cancer incidence analysis by 6 years to cover the period 1958-1987. The study population consisted of all chimney sweeps registered in the trade Union. Data regarding years of active employment were obtained from the union records as years of active work as a sweep was used as a measure of cumulative exposure. The mean employment time in this cohort was 12 years. The cause of death and incidence of cancer were obtained from the National Cause of Death Registry and from the National Cancer Registry. The data obtained showed an increased incidence and mortality of PC (SMR=169, 95% CI= 106-256). However, no significant relationship was observed between the cumulative exposure and incidence, although mortality by latency since first exposure was significantly increased (20-29 years, O/E=1/0.28, SMR=357; > 30 years, O/E=21/12.7, SMR=166). Due to chimney sweeps being exposed to a wide range of compounds, such as cadmium, which has also been suggested as a potential risk factor for PC, the authors concluded that this study could not show a link between combustion products and PC, but their findings should be further investigated (Evanoff *et al.*, 1993).

#### *Conclusion*

Despite being potentially exposed to relatively high concentrations of B[a]P, the available study does not provide convincing evidence to suggest that chimney sweeps have an increased risk of PC due to occupational exposure to PAHs.

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### Foundry workers

#### *Published exposure data*

Although not measured in the epidemiology studies considered in this report, other investigations have shown that foundry workers could be exposed to PAHs at concentrations of 10.4  $\mu\text{g}/\text{m}^3$  (Omland *et al.*, 1996), 9.6-11.2  $\mu\text{g}/\text{m}^3$  (Hansen *et al.*, 1994) for total PAHs or 36-60  $\text{ng}/\text{m}^3$  (Perera *et al.*, 1994) or <5-60  $\text{ng}/\text{m}^3$  B[a]P (Perera *et al.*, 1993). Concentrations of 2-60  $\text{ng}/\text{m}^3$ , 0.09-0.12  $\mu\text{g}/\text{m}^3$  and 3-2300  $\text{ng}/\text{m}^3$  B[a]P were measured in Finnish, Canadian and French foundries, respectively (IARC, 1984).

#### *Epidemiology studies with no exposure data*

There were 2 cohort studies and 2 retrospective cohort studies retrieved. Wingren and co-workers carried out a cohort study of 625 male art glass workers, employed for more than one month between 1964 and 1985 predominantly in context of glass refinement, such as grinding, etching and polishing. Vital statistics were traced from National Health Insurance and taxation authorities. Information on deaths within the cohort was obtained from the National Central Bureau of Statistics, and information on diagnosed cancers was obtained from the Swedish Cancer Registry. The definition of exposure was taken as employment in the glassworks for more than one month. Workers were also subdivided into six exposure categories; smelters and oven workers; glassblowers and manufacturers of heavy crystal glass; glassblowers and manufacturers of semi-crystal glass; refinement workers i.e. grinders, etchers and polishers; glass painters; and packers, transportation workers and storehouse workers. The overall data indicated a non-significant excess number of cases of PC (O=4, E=3 or 2.4, SMR=1.34 or 1.65 for national or county death rates respectively). When analysing data from the different categories, only refinement workers had a significantly increased mortality from PC (O=2, E=0.2, SMR=10) (Wingren and Englander, 1990). Similarly, the retrospective cohort mortality study carried out by Andjelkovich,

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consisting of 8147 males employed in a gray iron foundry for at least 6 months between 1950 and 1979, showed a moderate, but non-significant excess for PC among non-white males (O=22, E=14.9, SMR=147, 95% CI=92.0-223.0), whereas a deficit in PC was observed in white males (O=5, E=12, SMR=42, 95% CI=13.0-97.0) (Andjelkovich *et al.*, 1990).

In a retrospective follow-up study of 18770 male foundry and engine plant workers was carried out during a follow-up period of 1970-1987 (Rotimi *et al.*, 1993). 2235 members died during the follow-up period. A computerised work history file was used to obtain information on employees, including job held, start date, location and department. Death certificates of decedents were obtained and the cause of death coded according to the International Classification of Diseases. Mortality rates in the cohort were compared to those of the US general population. Data show that only black men working in the foundry had a significantly increased mortality of PC (SMR=234, 95% CI=112.0-430.0) (Rotimi *et al.*, 1993).

Sharma-Wagner and colleagues demonstrated a small but significant risk of PC in pig iron and steel foundries (SIR=1.23, 95% CI=1.0-1.4) and iron and steel plants (SIR=1.17, 95% CI= 1.0-1.01) in a retrospective cohort study carried out in Sweden, (Sharma-Wagner *et al.*, 2000).

#### *Conclusion*

These epidemiology studies do not present exposure data for PAHs or data regarding the duration of exposure. Foundry workers could be potentially exposed to relatively high concentrations of B[a]P. However, the studies do not present convincing evidence to suggest an excess risk of PC in foundry workers were identified in three follow-up studies.

#### **Multioccupational group case-control study**

A population based, case-control study, carried out by Nadon and co-workers in Montreal, examined the occupational exposure to PAHs from different sources (Nadon *et al.*, 1995). Out of 4576 patients with histologically confirmed cancer of

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any site, 3730 (82%) were interviewed, as well as 533 (71%) population controls. Information regarding potential confounders and a detailed description of employment was obtained via questionnaires. All cancer patients were also used as controls, with the exception of those with lung cancer, which was excluded from the reference pool. 452 cases of PC were observed and were matched with 1733 controls. Exposure to all chemicals was estimated taking into account the probability of exposure (possible, probable, definite), the frequency of exposure during the working week (<5%, 5-30%, >30%) and level of concentration of agent in the occupational environment (low, medium, high). Benzo[a]pyrene was used as an indicator of total PAHs. Exposure to other specific PAHs was characterised according to source materials i.e. coal, petroleum, wood, other sources (plastics, rubber). Benchmark occupations corresponding to low, medium or high concentrations of PAHs from different sources were identified and authors estimated that categories correspond to <1 µg/m<sup>3</sup>, 1-10 µg/m<sup>3</sup> and >10 µg/m<sup>3</sup>, respectively (table 2).

Table 2. Selected occupations corresponding to low, medium and high concentrations of exposure to PAHs from different sources

Category of PAHs	Occupation		
	Low exposure	Medium exposure	High exposure
Benzo[a]pyrene	Mechanics	Fire fighters	Aluminium refinery
	Gas pump operators	Rubber workers	workers Roofers
PAHs from coal	Other metal workers	Ferrous foundry	Aluminium refinery
	Railway brakemen	workers	workers
PAHs from	Printers	Cooks	Forgers
		Miners	Machinists

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petroleum	Plumbers	Truck drivers	Mechanics
PAHs from wood	Restaurant managers	Farmers	Fire fighters
	Roofers	Cooks	Industrial oven operators
PAHs from other sources	Sheet metal workers	Cranemen	Fire fighters
	Metal grinders	Plumbers	Janitors
PAHs for any sources	Agricultural workers	Commercial salesmen	Aluminium refinery workers
	Truck drivers	Roofers	workers
			Industrial oven operators

Data obtained from this study illustrated moderate statistical evidence of an association between PC and low exposure to B[a]P ( $<1 \mu\text{g}/\text{m}^3$  OR=1.3, 95% CI=1.0-1.6) and low exposure ( $<1 \mu\text{g}/\text{m}^3$ ; OR=1.7, 95% CI=1.2-2.5) to PAHs from coal. However, no statistically significant OR showing a dose-response was established for either (high exposure B[a]P, OR=1.2, 95% CI=0.8-1.8; high exposure PAHs from coal, OR=0.9, 95% CI=0.5-1.7). The authors identified mechanics and gas pump operators, and railway brakemen as having a low exposure to B[a]P and PAHs from coal, respectively (Nadon *et al.*, 1995).

## Discussion

Most of the data collected on the human health effects of PAH exposure arise from epidemiological studies conducted in different occupational settings. Target organs for PAHs include the respiratory system, skin, bladder and kidneys (NIOSH, 1997). There is a large body of evidence supporting an excess risk of lung cancer in workers exposed to mixtures of PAHs at coke ovens, petroleum refineries, aluminium smelters, iron and steel foundries and with bitumen, diesel and asphalt (DEH, 1999). However, little data are available regarding the excess risk of PC in such workers and the exact mechanism by which PAHs could potentially initiate its development has not been evaluated.

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Several studies have shown the induction of a number of enzymes in the prostate both *in vitro* and *in vivo*, which might play a role in the mechanism of action of PAH in the prostate (Carnell *et al.*, 2004; Finnstrom *et al.*, 2001; Ramesh *et al.*, 2000; Seidler *et al.*, 1998; Shimada and Fujii-Kuriyama, 2004; Shimada *et al.*, 2003).

Studies measuring concentrations of PAHs in different occupational settings demonstrated that coke oven workers, truck drivers, foundry workers, chimney sweeps, and to a lesser extent, fire fighters, were exposed to relatively higher levels than the published occupational exposure values. Despite this potential high exposure to B[a]P, a corresponding increase in the risk of PC was not reported in most occupational studies carried out. In contrast, a significantly decreased risk of PC was observed in truck drivers, although it is recognised that this is questionable, as PAH levels were not measured in the epidemiology study but taken from published sources. Water transport workers and employees in power plants did show an excess risk of PC. However, as little data regarding PAH exposure in these workers are available, interpretation of the epidemiology data is difficult. The lack of a dose-response relationship, either in terms of increased concentration of PAHs or increased duration of exposure in most studies suggests that PAHs from occupational sources are not associated with increased risk of PC. It is notable there was a slight excess of PC amongst cohort foundry workers in three follow-up studies. However, there was no evidence of an association with exposure or duration of exposure to PAHs. Several studies present data that show an increased risk of PC in workers not occupationally exposed to PAHs.

Several difficulties in data interpretation were encountered during this report. Problems with case-control matching arose, as risk factors for PC have not yet been fully established. Within cohort studies, cases of PC were not microscopically identified in all studies.

The comparison of the working population with the general public may introduce a conservative bias, due to the healthy worker effect. This might result in an underestimation of mortality due to PC that is attributable to occupational factors. However, a number of studies used workers with similar occupations but which were not occupationally exposed to PAH, or patients with other types of cancer as controls to reduce such bias.

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### **Final conclusion**

Overall, the available studies do not provide convincing evidence for an association between occupations with exposure to PAHs and an increased risk of PC.

### **Abbreviations**

ACGIH	American Conference of Governmental Industrial Hygienists
B[a]P	Benzo[a]pyrene
CI	Confidence interval
CTPV	Coal tar pitch volatiles
DEFRA	Department for Environment, Food and Rural Affairs
E	Expected
EPA	Environmental Protection Agency
EPAQS	Expert Panel on Air Quality Standards
HSE	Health and Safety Executive
MOR	Mortality odds ratio
NIOSH	National Institute for Occupational Safety and Health
O	Observed
OR	Odds ratio
OSHA	Occupational Safety and Health Administration
PAH	Polycyclic aromatic hydrocarbons
PC	Prostate cancer

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RIVM	Rijkinstituut voor Volksgezondheid en Milieu
RR	Relative risk
SIR	Standardised incidence ratio
SMR	Standardised mortality ratio

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## References

- ACGIH (1999): TLVs and BEIs: *Threshold limit values for chemical substances and physical agents, biological exposure indices.*, Cincinnati, OH.
- Adonis, M., Martinez, V., Riquelme, R., Ancic, P., Gonzalez, G., Tapia, R., Castro, M., Lucas, D., Berthou, F., and Gil, L. (2003): Susceptibility and exposure biomarkers in people exposed to PAHs from diesel exhaust. *Toxicol Lett* **144**, 3-15.
- Andjelkovich, D. A., Mathew, R. M., Richardson, R. B., and Levine, R. J. (1990): Mortality of iron foundry workers: I. Overall findings. *J Occup Med* **32**, 529-40.
- Aronson, K. J., Siemiatycki, J., Dewar, R., and Gerin, M. (1996): Occupational risk factors for prostate cancer: results from a case-control study in Montreal, Quebec, Canada. *Am J Epidemiol* **143**, 363-73.
- Binkova, B., Topinka, J., Mrackova, G., Gajdosova, D., Vidova, P., Stavkova, Z., Peterka, V., Pilcik, T., Rimar, V., Dobias, L., Farmer, P. B., and Sram, R. J. (1998): Coke oven workers study: the effect of exposure and GSTM1 and NAT2 genotypes on DNA adduct levels in white blood cells and lymphocytes as determined by 32P-postlabelling. *Mutat Res* **416**, 67-84.
- Brandt, H. C., and Watson, W. P. (2003): Monitoring human occupational and environmental exposures to polycyclic aromatic compounds. *Ann Occup Hyg* **47**, 349-78.
- Bye, T., Romundstad, P. R., Ronneberg, A., and Hilt, B. (1998): Health survey of former workers in a Norwegian coke plant: Part 2. Cancer incidence and cause specific mortality. *Occup Environ Med* **55**, 622-6.
- Carnell, D. M., Smith, R. E., Daley, F. M., Barber, P. R., Hoskin, P. J., Wilson, G. D., Murray, G. I., and Everett, S. A. (2004): Target validation of cytochrome P450 CYP1B1 in prostate carcinoma with protein expression in associated hyperplastic and premalignant tissue. *Int J Radiat Oncol Biol Phys* **58**, 500-9.
- Costantino, J. P., Redmond, C. K., and Bearden, A. (1995): Occupationally related cancer risk among coke oven workers: 30 years of follow-up. *J Occup Environ Med* **37**, 597-604.
- DEFRA (2001): Air quality strategy: Particles, benzene, carbon monoxide and polycyclic aromatic hydrocarbons, Department for environment, food and rural affairs.
- DEH (1999): Technical report No. 2. Polycyclic Aromatic Hydrocarbons (PAHs) in Australia: *Department of Environment and Heritage*.
- Demers, P. A., Checkoway, H., Vaughan, T. L., Weiss, N. S., Heyer, N. J., and Rosenstock, L. (1994): Cancer incidence among firefighters in Seattle and Tacoma, Washington (United States). *Cancer Causes Control* **5**, 129-35.
- EPA (1998): Locating and estimating air emissions from sources of polycyclic organic matter.: *Office of Air Quality Planning and Standards*, Research Triangle Park, NC.

This is a draft paper for discussion. It should not be quoted, cited or reproduced.

- EPAQS (1999): Polycyclic Aromatic Hydrocarbons: *Department of the environment, transport and the regions, National assembly for Wales, Scottish executive and department of the environment (Northern Ireland)*.
- Evanoff, B. A., Gustavsson, P., and Hogstedt, C. (1993): Mortality and incidence of cancer in a cohort of Swedish chimney sweeps: an extended follow up study. *Br J Ind Med* **50**, 450-9.
- Feunekes, F. D., Jongeneelen, F. J., vd Laan, H., and Schoonhof, F. H. (1997): Uptake of polycyclic aromatic hydrocarbons among trainers in a fire-fighting training facility. *Am Ind Hyg Assoc J* **58**, 23-8.
- Finnstrom, N., Bjelfman, C., Soderstrom, T. G., Smith, G., Egevad, L., Norlen, B. J., Wolf, C. R., and Rane, A. (2001): Detection of cytochrome P450 mRNA transcripts in prostate samples by RT-PCR. *Eur J Clin Invest* **31**, 880-6.
- Fromme, H., Oddoy, A., Piloty, M., Krause, M., and Lahrz, T. (1998): Polycyclic aromatic hydrocarbons (PAH) and diesel engine emission (elemental carbon) inside a car and a subway train. *Sci Total Environ* **217**, 165-73.
- Grimes, G., Hirsch, D., and Borgeson, D. (1991): Risk of death among Honolulu fire fighters. *Hawaii Med J* **50**, 82-5.
- Guidotti, T. L. (1993): Mortality of urban firefighters in Alberta, 1927-1987. *Am J Ind Med* **23**, 921-40.
- Hansen, A. M., Omland, O., Poulsen, O. M., Sherson, D., Sigsgaard, T., Christensen, J. M., and Overgaard, E. (1994): Correlation between work process-related exposure to polycyclic aromatic hydrocarbons and urinary levels of alpha-naphthol, beta-naphthylamine and 1-hydroxypyrene in iron foundry workers. *Int Arch Occup Environ Health* **65**, 385-94.
- Hemminki, K., Grzybowska, E., Chorazy, M., Twardowska-Sauchka, K., Sroczynski, J. W., Putman, K. L., Randerath, K., Phillips, D. H., Hewer, A., Santella, R. M., and et al. (1990): DNA adducts in human environmentally exposed to aromatic compounds in an industrial area of Poland. *Carcinogenesis* **11**, 1229-31.
- Hemminki, K., Soderling, J., Ericson, P., Norbeck, H. E., and Segerback, D. (1994): DNA adducts among personnel servicing and loading diesel vehicles. *Carcinogenesis* **15**, 767-9.
- IARC (1984): Polynuclear aromatic compounds. Part 3: Industrial exposures in aluminium production, coal gasification, coke production and iron and steel founding., pp. 219: *International Agency for Research on Cancer. IARC monographs on the evaluation of the carcinogenic risk of chemicals to humans.*, Lyon.
- Kalina, I., Brezani, P., Gajdosova, D., Binkova, B., Salagovic, J., Habalova, V., Mrackova, G., Dobias, L., and Sram, R. J. (1998): Cytogenetic monitoring in coke oven workers. *Mutat Res* **417**, 9-17.
- Knecht, U., Bolm-Audorff, U., and Weitowitz, H. J. (1989): Atmospheric concentrations of polycyclic aromatic hydrocarbons during chimney sweeping. *Br J Ind Med* **46**, 479-82.
- Krstev, S., Baris, D., Stewart, P., Dosemeci, M., Swanson, G. M., Greenberg, R. S., Schoenberg, J. B., Schwartz, A. G., Liff, J. M., and Hayes, R. B. (1998a): Occupational risk factors and prostate cancer in U.S. blacks and whites. *Am J Ind Med* **34**, 421-30.
- Krstev, S., Baris, D., Stewart, P., Hayes, R. B., Blair, A., and Dosemeci, M. (1998b): Risk for prostate cancer by occupation and industry: a 24-state death certificate study. *Am J Ind Med* **34**, 413-420.

This is a draft paper for discussion. It should not be quoted, cited or reproduced.

- Kuljukka, T., Vaaranrinta, R., Veidebaum, T., Sorsa, M., and Peltonen, K. (1996): Exposure to PAH compounds among cokery workers in the oil shale industry. *Environ Health Perspect* **104 Suppl 3**, 539-41.
- Ma, F., Lee, D. J., Fleming, L. E., and Dosemeci, M. (1998): Race-specific cancer mortality in US firefighters: 1984-1993. *J Occup Environ Med* **40**, 1134-8.
- Nadon, L., Siemiatycki, J., Dewar, R., Krewski, D., and Gerin, M. (1995): Cancer risk due to occupational exposure to polycyclic aromatic hydrocarbons. *Am J Ind Med* **28**, 303-24.
- NIOSH (1997): Pocket guide to chemical hazards. In P. H. S. U.S. Department of Health and Human Services, Centres for Disease Control and Prevention. (Ed.), Cincinnati, OH.
- Omland, O., Sherson, D., Hansen, A. M., Sigsgaard, T., Autrup, H., and Overgaard, E. (1996): Urinary 1-hydroxypyrene, a PAH biomarker in foundry workers. *Cancer Detect Prev* **20**, 57-62.
- OSHA (1998): Occupational safety and health standards, toxic and hazardous substances.: *Code of federal regulations*.
- Perera, F. P., Dickey, C., Santella, R., O'Neill, J. P., Albertini, R. J., Ottman, R., Tsai, W. Y., Mooney, L. A., Savelle, K., and Hemminki, K. (1994): Carcinogen-DNA adducts and gene mutation in foundry workers with low-level exposure to polycyclic aromatic hydrocarbons. *Carcinogenesis* **15**, 2905-10.
- Perera, F. P., Tang, D. L., O'Neill, J. P., Bigbee, W. L., Albertini, R. J., Santella, R., Ottman, R., Tsai, W. Y., Dickey, C., Mooney, L. A., and et al. (1993): HPRT and glycophorin A mutations in foundry workers: relationship to PAH exposure and to PAH-DNA adducts. *Carcinogenesis* **14**, 969-73.
- Petry, T., Schmid, P., and Schlatter, C. (1996): Airborne exposure to polycyclic aromatic hydrocarbons (PAHs) and urinary excretion of 1-hydroxypyrene of carbon anode plant workers. *Ann Occup Hyg* **40**, 345-57.
- Ramesh, A., Inyang, F., Hood, D. B., and Knuckles, M. E. (2000): Aryl hydrocarbon hydroxylase activity in F-344 rats subchronically exposed to benzo(a)pyrene and fluoranthene through diet. *J Biochem Mol Toxicol* **14**, 155-61.
- Reuterwall, C., Aringer, L., Elinder, C. G., Rannug, A., Levin, J. O., Juringe, L., and Onfelt, A. (1991): Assessment of genotoxic exposure in Swedish coke-oven work by different methods of biological monitoring. *Scand J Work Environ Health* **17**, 123-32.
- RIVM (1999): Assessment of air quality for Polycyclic Aromatic Hydrocarbons in the Netherlands.
- Rotimi, C., Austin, H., Delzell, E., Day, C., Macaluso, M., and Honda, Y. (1993): Retrospective follow-up study of foundry and engine plant workers. *Am J Ind Med* **24**, 485-98.
- Seidler, A., Heiskel, H., Bickeboller, R., and Elsner, G. (1998): Association between diesel exposure at work and prostate cancer. *Scand J Work Environ Health* **24**, 486-94.
- Sharma-Wagner, S., Chokkalingam, A. P., Malker, H. S., Stone, B. J., McLaughlin, J. K., and Hsing, A. W. (2000): Occupation and prostate cancer risk in Sweden. *J Occup Environ Med* **42**, 517-25.
- Shimada, T., and Fujii-Kuriyama, Y. (2004): Metabolic activation of polycyclic aromatic hydrocarbons to carcinogens by cytochromes P450 1A1 and 1B1. *Cancer Sci* **95**, 1-6.

This is a draft paper for discussion. It should not be quoted, cited or reproduced.

- Shimada, T., Sugie, A., Shindo, M., Nakajima, T., Azuma, E., Hashimoto, M., and Inoue, K. (2003): Tissue-specific induction of cytochromes P450 1A1 and 1B1 by polycyclic aromatic hydrocarbons and polychlorinated biphenyls in engineered C57BL/6J mice of arylhydrocarbon receptor gene. *Toxicol Appl Pharmacol* **187**, 1-10.
- Tornling, G., Gustavsson, P., and Hogstedt, C. (1994): Mortality and cancer incidence in Stockholm fire fighters. *Am J Ind Med* **25**, 219-28.
- van Schooten, F. J., van Leeuwen, F. E., Hillebrand, M. J., de Rijke, M. E., Hart, A. A., van Veen, H. G., Oosterink, S., and Kriek, E. (1990): Determination of benzo[a]pyrene diol epoxide-DNA adducts in white blood cell DNA from coke-oven workers: the impact of smoking. *J Natl Cancer Inst* **82**, 927-33.
- Wingren, G., and Englander, V. (1990): Mortality and cancer morbidity in a cohort of Swedish glassworkers. *Int Arch Occup Environ Health* **62**, 253-7.
- Zhang, J., Ichiba, M., Feng, Y., Pan, G., Hanaoka, T., Yamano, Y., Hara, K., Takahashi, K., and Tomokuni, K. (2000): Aromatic DNA adducts in coke-oven workers, in relation to exposure, lifestyle and genetic polymorphism of metabolic enzymes. *Int Arch Occup Environ Health* **73**, 127-35.

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Occupational exposure to PAHs-risk for prostate cancer

In order to summarise the table in an accessible form, studies were sub-divided, for purposes of the table, according to whether exposure levels of PAHs were measured.

	<i>Occupation</i>	<b>PAH measured</b>	<b>Exposure</b>		<i>Discussion</i>
<i>Defined occupational exposure to PAHs – concentration of PAH measured</i>					
Costantino <i>et al.</i> , 1995	Cohort study of US coke oven workers	Coal tar pitch volatiles (CTPV)	Top oven, full time - 3.15 mg/m <sup>3</sup> Top oven part time - 1.99 mg/m <sup>3</sup> Side oven - 0.88 mg/m <sup>3</sup>	Overall, significant excess mortality from PC (RR=1.57, 95% CI=1.1-2.3 p<0.05).	Occupational exposure to coke oven emissions may be associated with excess mortality from PC. However, due to the small number of cases, conclusions regarding exposure-response relationship cannot be made.
Bye <i>et al.</i> , 1998	Cohort study of Norwegian coke plant workers	PAHs	2-300 µg/m <sup>3</sup>	Incidence of PC was not significantly different to expected values (O=5, E=9.6, SMR=0.53, 95% CI=0.17-1.24) and no association between cumulative exposure to PAHs and PC was seen unexposed, SIR=0.7; <50, SIR=0.6; 50-149, SIR=0; >150, SIR=0; p=0.3.	No association between the dose variable and PC were observed. Authors suggest that results warrant further follow-studies to improve statistical power.

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Nadon <i>et al.</i> , 1995	Population-based case-control study of Canadian workers in various occupations	B[a]P PAH from coal PAH from petroleum PAH from wood PAH from other sources	B[a]P Low exposure < 1 µg/m <sup>3</sup> Medium exposure 1-10 1 µg/m <sup>3</sup> High exposure >10 µg/m <sup>3</sup>	An associations between PC and low exposure to B[a]P (OR=1.3, 95% CI=1-1.6) and low exposure to coal (1.7 , 95% CI=1.2-2.5) was seen although no significant dose-response was observed (low exposure, OR=1.3, 95% CI=1.0-1.6; high exposure, OR=1.2, 95% CI=0.8-1.8).	Gas pump operators, mechanics, metal workers, railway workers may have increased risk due to PAHs in soot and the widespread use of diesel engines. Authors suggest, the excess risk for PC in these occupations, although evidence is not that convincing.
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Possible occupational exposure to PAHs – semi-quantitative estimates of exposure (e.g. duration)					
Krstev <i>et al.</i> , 1998b	Population-based case-control study of US fire fighters, stationary power plant workers, railroad workers		< 5, 5-19, > 20 years in employment	Risk of PC was significantly elevated and showed a significant trend with increasing duration of employment among fire fighters (OR=5.15, 95% CI=1.05-25.20, $\chi^2$ trend, p = 0.02), power plant workers (OR=4.04, 95% CI=0.41-39.8, $\chi^2$ trend, p = 0.03) and railroad workers (OR=1.61, 95% CI=1.13-2.44, $\chi^2$ trend, p = 0.002).	Fire fighters, stationary power plant workers and railroad workers may be exposed to PAHs such as B[a]P and I-nitropyrene from combustion-related sources, such as diesel exhausts or coal and fuel. However, this study could not identify occupational risk factors that could account for the substantial proportion of PC occurring on the US.
Aronson <i>et al.</i> , 1996	Population-based case-control study of Canadian water transport	Diesel engine emissions, liquid fuel combustion products,	< 10, > 10 years in employment Concentration (low, medium/high)	Increased risk of PC showing a duration-response trend in water transport workers (10 years OR=1.51, 95% CI=0.65-3.48; > 10 year OR=3.04, 95% CI=1.09-8.46). Railway workers	Study gave moderate to strong support that occupations such as water transport workers and railway transport workers have an increased risk of

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	workers, railway workers	PAHs from coal	Frequency (low/ medium, high)	show an increased risk of PC (OR=4.47, 95% CI=1.26-15.83) but this was not duration-dependent (OR=1.81, 95% CI=0.71-4.58). Diesel engine emissions showed an increased risk with increased duration of exposure (>11 years OR=1.5, 95% CI=1.1-2.1). Liquid fuel combustion products caused the highest risk at the highest frequency of exposure (OR=1.6, 95% CI=1-2.6). Water transport workers exposed to liquid fuel combustion products showed an increased risk when undergoing non-substantial (OR=5.6, 95% CI=1.4-22.5) and substantial exposure (OR=17.3, 95% CI=1.3-99.9). Increasing risk was also observed for PAHs from coal when frequency of exposure was increased (OR=1.7, 95% CI=1-2.7).	PC. PAHs from coal pose a significant risk with diesel fuel being less of a risk factor. The authors calculated the population attributable risk to be ~20 %. Although possibly over-estimated, they concluded the percentage of PC cases attributed to occupation to represent an important public health issue.
Seidler <i>et al.</i> , 1998	Case-control study of German drivers, mechanic, boat workers	PAH Diesel fuel	0, <-25 years, >25 years, estimated exposure	Significant link between PC and exposure to diesel fuel (OR 3.7, 95% CI 1.4-9.8) and PAHs (OR 1.6, 95% CI 1-2.4) although PAH exposure was not dose dependent.	Exposure to PAH as a component of diesel fuel may be a risk factor for PC in the light of the elevated OR for high potential exposure.
Demers <i>et al.</i> ,	Cohort study		< 10, 10-19,	The overall risk of PC was	Authors suggested that

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1994	of US fire fighters		20-29, >30 years of employment  < 20, 20-29, >30 years since first employment	elevated (SIR 1.4, 95% CI 1.1-1.7). However, the RR did not vary in a systematic manner, as mortality did not increase with duration of employment (< 10 years, RR=1.4, 95% CI=0.6-2.8; 10-19 years, RR=1.2, 95% CI=0.4-2.6; 20-29 years, RR=1.5, 95% CI=1.1-2; >30 years, RR=0.9, 95% CI=1.9). In addition, SIR for fire fighters < 20 years after first employment (RR=7.4, 95% CI=0.2-41) was higher than after longer periods (20-29 years, RR=1.8, 95% CI=0.6-4.3; >30 years, RR=1.3, 95% CI=1-1.7).	although duration of employment was used as an index of exposure, it is a poor surrogate for dose to specific agents. Fire fighters are exposed to a great variety of building materials, the most commonly observed carcinogens in fire smoke being PAHs such as B[a]P. Although excess PC was observed and was highest under 65 years of age, this was similar to that seen among police and no gradient with duration of employment was seen.
Grimes <i>et al.</i> , 1991	Cohort study of Honolulu fire fighters		< 20, 20-27, >28 years in employment	Data showed an elevated risk of PC (RR=2.61, 95% CI=1.38-4.97). No significant differences were seen. Comparison between age adjusted employment showed no significant differences.	As the number of fire fighters was relatively small further studies should be executed
Guidotti 1993	Cohort study of Canadian fire fighters		Weighted employment history using an exposure opportunity index term. <20, 20-29, 30-39, 40-49, >50 years	No significant increase in PC was seen (SMR 146.1, 95% CI=63.1-287.9). No significant increased risk was observed with duration of employment of exposure index.	Although an increase risk of genitourinary disorders was observed, fire fighters showed no increased risk for PC.

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			after employment		
Wingren & Englander 1990	Cohort study of Swedish glass foundry workers		Exposure was defined as employment in the glassworks for more than one month. Workers were subdivided into exposure categories: smelters and oven workers; heavy crystal glassblowers; semi-crystal glassblowers; refinement workers; glass painters; and transportation workers	Overall data show a non-significant increased risk of PC (O=4, E=3, SMR=1.34). Refinement workers had a significantly increased mortality (O=2, E=0.2, SMR=10).	Authors suggest that the increase in PC seen in refinement workers could be a chance finding or reflects only a specific situation in the glassworks in question.
Evanoff <i>et al.</i> , 1993	Cohort study of Swedish chimney sweeps		1-9, 10-19, 20-29, > 30 years in employment  1-9, 10-19, 20-29, > 30 years since first exposure	Significant excess risk of mortality (SMR=197, 95% CI=90-375) with a significant increase > 30 years since first employment (SMR=166), although no correlation with cumulative exposure was observed.	Due to the sweeps exposure to combustion products, mortality from PC have been associated with exposure to exhaust fumes. However, due to the small numbers of cases of PC observed, there is no convincing evidence that

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					chimney sweeps are at an increased risk of PC
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<i>Possible occupational exposure PAHs – no measurement of exposure or duration</i>					
Sharma-Wagner <i>et al.</i> , 2000	Retrospective cohort study of Swedish car repair, travelling salesmen, railroad workers			Small but significant risk of PC in car repairers (SIR=1.12, 95% CI=1-1.24), travelling salesmen (SIR=1.18, 95% CI=1.05-1.31), railroad workers (SIR=1.12, 95% CI=1.02-1.22).	Results suggest that occupation is unlikely to play a central role in the aetiology of PC because the excess risks observed in this study are quite small (10%).
Krstev <i>et al.</i> , 1998a	Population-based case-control study of US bus drivers Trucking/taxi drivers			Bus drivers showed an increased risk of PC (MOR=1.4, 95% CI=1-1.8). Truck/taxi drivers had a decreased risk of PC (MOR=0.8, 95% CI=0.8-0.9).	Differences were observed in the risk factors for groups possibly exposed to PAHs from diesel exhausts. This population-based study did not identify occupational risk factors that could account for a substantial proportion of PC in US.
Ma <i>et al.</i> , 1998	Cohort study of US fire fighters			Risk for PC was elevated in both white (MOR=1.2, 95% CI=1-1.3) and black fire fighters (MOR=1.9, 95% CI=1.2-3.2). Dose-dependency was not assessed.	Both black and white fire fighters have excess risks for PC. However, results could be affected by lack of information on confounding factors as well as lack of exposure data.
Tornling <i>et al.</i> , 1994	Cohort study of Swedish fire fighters			SMR for mortality and incidence of PC were non-significant (mortality SMR=114,	The authors concluded that in general, Stockholm fire fighters exhibited lower total

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				95% CI=76-165; incidence SMR=114, 95% CI=76-165).	mortality than expected
Krstev <i>et al.</i> , 1998b	Population-based case-control study of US Fire fighters			Elevated risk of PC was observed (OR=2.2, 95% CI=1.2-3.9).	Fire fighters are exposed to complex mixtures of toxic compounds due to increasing use of synthetic building materials and furnishings. Most common carcinogens identified in smoke are PAHs (B[a]P). However, this population-based study of prostate cancer did not identify occupational risk factors that could account for a substantial proportion of PC in US.
Sharma-Wagner <i>et al.</i> , 2000	Retrospective cohort study of Swedish pig iron/steel foundry workers			Small but significant risk of PC (SIR=1.23, 95% CI=1-1.4) was shown.	The excess risk of PC amongst pig iron workers may be related to a variety of potential carcinogens, including PAHs. However, due to the small excess risks observed in the study, occupational exposure is unlikely to play a central role in the aetiology of PC.
Rotimi <i>et al.</i> , 1993	Retrospective follow-up study of US foundry and engine plant workers			Only black workers have a significantly increased mortality of PC (SMR=234, 95% CI=112-430).	Because the observed excess of PC mortality were only present for one racial group, and due to the lack of a duration-response relationship, it is unlikely

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					that the excess seen are related to occupational exposure.
Andjelkovich <i>et al.</i> , 1990	Retrospective cohort study of US gray iron foundry workers			Moderate, but non-significant excess of PC in non-white males (O=22, E=14.9, SMR=147, 95% CI=92-223) and a significant deficit in PC in white males (O=5, E=12, SMR=42, 95% CI=13-97).	Authors state that it is unlikely that only one racial group would be subjected to PAHs hence, the differences observed in black and white workers is unlikely to be caused by occupational exposure to PAH.

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## References

- Andjelkovich, D. A., R. M. Mathew, R. B. Richardson and R. J. Levine (1990). Mortality of iron foundry workers: I. Overall findings. *J Occup Med* **32**(6): 529-40.
- Aronson, K. J., J. Siemiatycki, R. Dewar and M. Gerin (1996). Occupational risk factors for prostate cancer: results from a case-control study in Montreal, Quebec, Canada. *Am J Epidemiol* **143**(4): 363-73.
- Bye, T., P. R. Romundstad, A. Ronneberg and B. Hilt (1998). Health survey of former workers in a Norwegian coke plant: Part 2. Cancer incidence and cause specific mortality. *Occup Environ Med* **55**(9): 622-6.
- Costantino, J. P., C. K. Redmond and A. Bearden (1995). Occupationally related cancer risk among coke oven workers: 30 years of follow-up. *J Occup Environ Med* **37**(5): 597-604.
- Demers, P. A., H. Checkoway, T. L. Vaughan, N. S. Weiss, N. J. Heyer and L. Rosenstock (1994). Cancer incidence among firefighters in Seattle and Tacoma, Washington (United States). *Cancer Causes Control* **5**(2): 129-35.
- Evanoff, B. A., P. Gustavsson and C. Hogstedt (1993). Mortality and incidence of cancer in a cohort of Swedish chimney sweeps: an extended follow up study. *Br J Ind Med* **50**(5): 450-9.
- Grimes, G., D. Hirsch and D. Borgeson (1991). Risk of death among Honolulu fire fighters. *Hawaii Med J* **50**(3): 82-5.
- Guidotti, T. L. (1993). Mortality of urban firefighters in Alberta, 1927-1987. *Am J Ind Med* **23**(6): 921-40.
- Krsteve, S., D. Baris, P. Stewart, M. Dosemeci, G. M. Swanson, R. S. Greenberg, J. B. Schoenberg, A. G. Schwartz, J. M. Liff and R. B. Hayes (1998a). Occupational risk factors and prostate cancer in U.S. blacks and whites. *Am J Ind Med* **34**(5): 421-30.
- Krsteve, S., D. Baris, P. Stewart, R. B. Hayes, A. Blair and M. Dosemeci (1998b). Risk for prostate cancer by occupation and industry: a 24-state death certificate study. *Am J Ind Med* **34**(5): 413-420.
- Ma, F., D. J. Lee, L. E. Fleming and M. Dosemeci (1998). Race-specific cancer mortality in US firefighters: 1984-1993. *J Occup Environ Med* **40**(12): 1134-8.
- Nadon, L., J. Siemiatycki, R. Dewar, D. Krewski and M. Gerin (1995). Cancer risk due to occupational exposure to polycyclic aromatic hydrocarbons. *Am J Ind Med* **28**(3): 303-24.
- Rotimi, C., H. Austin, E. Delzell, C. Day, M. Macaluso and Y. Honda (1993). Retrospective follow-up study of foundry and engine plant workers. *Am J Ind Med* **24**(4): 485-98.
- Seidler, A., H. Heiskel, R. Bickeboller and G. Elsner (1998). Association between diesel exposure at work and prostate cancer. *Scand J Work Environ Health* **24**(6): 486-94.
- Sharma-Wagner, S., A. P. Chokkalingam, H. S. Walker, B. J. Stone, J. K. McLaughlin and A. W. Hsing (2000). Occupation and prostate cancer risk in Sweden. *J Occup Environ Med* **42**(5): 517-25.

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Tornling, G., P. Gustavsson and C. Hogstedt (1994). Mortality and cancer incidence in Stockholm fire fighters. *Am J Ind Med* **25**(2): 219-28.  
Wingren, G. and V. Englander (1990). Mortality and cancer morbidity in a cohort of Swedish glassworkers. *Int Arch Occup Environ Health* **62**(3): 253-7.