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Lung Cancer and Occupational Exposure to Combustion Products

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ABSTRACT

Lung cancer, the most common cause of cancer death, is predominantly attributable to tobacco smoking. One of the many carcinogenic components of tobacco smoke are polycyclic aromatic hydrocarbons (PAH). Several occupational exposures containing high levels of PAHs are classified as carcinogenic to humans (Group 1) by the International Agency for Research on Cancer (IARC). Bitumen fumes and diesel motor exhaust (DME) which are complex mixtures of agents containing small quantities of PAHs, are classified as possibly (Group 2B) and probably carcinogenic (Group 2A) to humans, respectively.

The main goals of this thesis were to explore 1) the role of occupational exposures overall, and in particular combustion products in Central and Eastern Europe, a region with the world's highest lung cancer incidence rate in men; 2) whether occupational DME exposure in a population-based study and 3) exposure to bitumen fume among asphalt workers were associated with increased lung cancer risk.

The aims were addressed using three data sources; 1) the IARC multicenter case-control study on lung cancer conducted in six countries in Central and Eastern Europe (CEE) and the United Kingdom (2852 cases, 2923 controls); 2) the SYNERGY pooling project of eleven case-control studies of lung cancer from Europe and Canada (13479 cases, 16510 controls); and 3) a case-control study of lung cancer nested within a cohort of European asphalt workers (433 cases, 1253 controls). All three studies allowed careful adjustment for lifetime cumulative tobacco smoking.

The attributable fraction (AF) of lung cancer to occupational exposure overall in CEE was 7.9% (95% CI: 1.9 to 13.5%) in men. Silica and metals had the greatest AF contributions, and there was some suggestion that the AFs were higher among current- than among ex- or never-smokers. Among women, AFs were small or close to zero, except for small cell carcinoma lung cancers (AF 7.1%, 95% CI: 0 to 14.4%), an observation which needs further investigation and confirmation. We found no evidence of an association between occupational PAH exposure and lung cancer risk in CEE after adjusting for relevant occupational exposures and smoking.

Occupational DME exposure was associated with an increased lung cancer risk. Exposed subjects in the highest quartile of cumulative exposure had a 1.31-fold higher lung cancer risk (95% CI 1.19-1.43) than never exposed subjects. This association held in workers never employed in occupations known to have excess lung cancer risks, in women and in never-smokers. This result is in line with previous research, though most previous studies could not control for major potential confounders and have not had as large sample sizes as ours.

Amongst European asphalt workers, there was no evidence that lung cancer risk was related to indicators of inhalation or dermal exposure to bitumen fume, nor to other known or suspected occupational lung carcinogens present in this industry, with the exception of coal tar.

This thesis demonstrates (i) that both community-based and industry-based studies are important to identify and quantify risks in occupational cancer epidemiology; (ii) the significance of international collaborations to establish large-scale studies examining exposures and risks which cannot otherwise be adequately studied; and (iii) the necessity to consider the joint effect of exposures with each other and with smoking as agents commonly confer stronger effects when acting together.