

Corresponding values above the WHO threshold of 20 µg/m³ would be 51.73 attributable deaths (12.58 cardiovascular and 4.17 respiratory) 13.60 cardiac, 5.37 cerebrovascular and 49.13 respiratory hospital admissions.

Conclusions The expected exposure appears to have a limited impact on health. Future monitoring of the actual exposure levels during the progress of the works will allow evaluating the accuracy of those estimates.

0259 INTERACTION BETWEEN GENETIC AND OCCUPATIONAL FACTORS IN LUNG CANCER AETIOLOGY. A POPULATION-BASED CASE-CONTROL STUDY

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Objectives Genetic susceptibility in work-related lung cancer aetiology could have an important public health impact. Few studies have previously evaluated this issue, with inconsistent results. We aimed to investigate interactions between exposure to occupational carcinogens and genetic polymorphisms in lung cancer aetiology, adopting a systematic integrated approach.

Method EAGLE, a population-based case-control study, enrolled 2100 lung cancer cases and 2120 controls (Italy, 2002–2005). Lifetime work histories were collected for 4059 subjects and translated into exposure to six occupational carcinogens (asbestos, silica, polycyclic aromatic hydrocarbons, diesel exhausts, chromium, and nickel) using a job-exposure matrix. We selected 23 candidate genes among phase II metabolic genes reported in association with lung cancer susceptibility and/or metabolism of selected carcinogens. 298 tagging single nucleotide polymorphisms (SNPs) were genotyped on 4050 subjects. We tested for interaction within smoking-adjusted logistic regressions where SNPs were modelled individually, by gene group (using gene scores and haplotypes), and by pathways. False discovery rate (FDR) was used to account for multiple testing. Gene expression changes in lung tissues were studied for SNPs-carcinogens significant interactions.

Results As asbestos had the highest impact on lung cancer burden, we restricted interaction tests to this carcinogen. GSTM4 polymorphisms consistently showed positive interactions across different analysis levels, especially by SNP group score (FDR-adjusted p-value for interaction < 0.0001). No significant genetic “signal” by asbestos exposure was found at lung tissue level.

Conclusions GSTM4 polymorphisms may play a role in asbestos-related lung cancer aetiology. These findings are biologically plausible and have never previously been reported; they should therefore be validated in further studies.

0261 ESTIMATING THE BURDEN OF OCCUPATIONAL CANCER TAKING INTO ACCOUNT AGE

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Objectives Estimates of burden of disease are generally based on population attributable fractions (PAFs) calculated for a whole population. However, the age structure of an exposed group has an impact on these estimates, because disease rates vary by age and the exposed population may be younger than the national population in the estimation year.

Method To account for this, PAFs can be calculated by age, and applied separately by age to national incidence data. We have adapted our risk period methodology, which takes account of latency to estimate numbers exposed to a causative agent using Levin's formula for PAF, to estimate a workforce turnover factor by age group, which accounts for the age structure of an exposed population. To estimate age-specific RRs from unit relative risks per year of exposure, the link between age and duration of exposure can be modelled using Monte-Carlo methods.

Results We show the effect of estimating the burden of lung cancer due to occupational exposure to respirable crystalline silica for Britain using PAF estimates which do or do not take age into account. Taking account of age and assuming recruitment between ages 15–44, there were 1188 lung cancer registrations in males in 2010, or 798 without accounting for age, or 636 vs. 804 assuming recruitment between ages 15–24. The extension to using age-specific RRs is demonstrated for occupational asbestos-related lung cancers.

Conclusions Given the above results, and although highly dependent on assumptions made about workforce ages, there is clearly a case to be made to estimate PAFs by age.

0266 MORTALITY IN THE FRENCH COHORT OF NUCLEAR WORKERS MONITORED FOR EXTERNAL RADIATION EXPOSURE

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Objectives Understanding the effect of chronic low dose radiation exposure is crucial for radiation protection. This study analyses mortality of workers monitored for external radiation exposure while employed at three major French nuclear companies.

Method The cohort includes all workers employed at least one year by CEA, AREVA NC or EDF between 1950 and 1994, monitored for radiation exposure and alive on 1 January 1968. The mortality follow-up was to 2004. Vital status and causes of death were obtained from national registries. Standardised mortality ratios were assessed using national rates as the reference.

Results A total of 59 004 workers were followed-up for an average of 25 years. Mean age at end of follow-up was 56 years. Less than 1% of workers were lost to follow-up. 6310 deaths occurred between 1968 and 2004 including 2547 cancer deaths. A strong healthy worker effect was observed (all-cause SMR = 0.61, 95%-CI: 0.60–0.63). Significant excess mortality was observed for pleura cancer (SMR= 1.71, 95%-CI: 1.24–2.30) and for melanoma (SMR= 1.43, 95%-CI: 1.04–1.92), with no significant trend in SMRs for these outcomes across categories of cumulative radiation exposure.

Conclusions This analysis of French nuclear workers confirms a healthy worker effect but also an excess risk of death

from pleura cancer and melanoma. This cohort study is the most informative ever conducted in France among nuclear workers.

0278 THE PESTIMAT PROGRAM: DEVELOPMENT OF A CROP EXPOSURE MATRIX FOR PESTICIDE EXPOSURE ASSESSMENT IN AGRICULTURE

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Objectives Pesticides include ~1000 chemicals with various toxicological properties. Pesticide exposure assessment represents a crucial methodological issue for epidemiological studies. A reconstitution of pesticides used in entire professional careers based only on the memory is questionable. PESTIMAT is a crop exposure matrix, which intends to reconstitute parameters of pesticide exposure in France.

Method PESTIMAT is made of tables crossing crops and active ingredients (a.i.) by year from 1950 to 2010 and providing the following exposure parameters: 1) probability corresponding to the proportion of farmers having used the a.i. (in%), 2) frequency expressed as the number of treatment days, 3) intensity documented by the application rate of the a.i. (in kg/ha). Parameters were obtained by the combination of six complementary sources: i) registrations and withdrawals from the Agriculture Ministry, ii) information from ACTA* on products marketed iii) agricultural recommendations by the Plant Health Protection body, iv) treatment calendars provided by farmers, v) information from professional associations of farmers, vi) data from the industry

Results To date, 529 a.i. usable between 1950 and 2010 on 4 crops are included in PESTIMAT, corresponding to 160 fungicides (30%), 160 herbicides (30%) and 209 insecticides (40%). The total numbers were comparable on wheat/barley (N = 293), vineyards (N = 280), and apple-growing (N = 267) but lower on corn (N = 196). We will present an illustration with data obtained for dithiocarbamates fungicides, and examples of use in epidemiological studies, e.g. PHYTONER and AGRICAN cohorts.

Conclusions The multisource information available in the PESTIMAT matrix should enable to assess associations between pesticides and health at the a.i. level.

0282 A CROSS-SECTIONAL STUDY OF MARKERS OF EARLY IMMUNOLOGICAL AND CARDIOVASCULAR HEALTH EFFECTS AMONG A POPULATION EXPOSED TO CARBON NANOTUBES: THE CANTES STUDY

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Objectives To assess the association between occupational exposure to carbon nanotubes (CNTs) and early immunological and cardiovascular health effects.

Method We collected biological samples (blood, urine, buccal and nasal epithelium cells) from a group of workers in a CNT production factory and approximately age and sex matched unexposed individuals working in a different workplace. Based on an initial assessment of exposure data collected in the weeks before biological sampling we further classified CNT production workers as operators (high probability of exposure) and R&D workers (lower probability of exposure). We analysed blood samples for a panel of inflammatory markers.

Results We included 8 operators (median age 34.8), 16 R&D workers (median age 32.2), and 43 controls (median age 30.6). Preliminary analyses provide some evidence for an association between CNT exposure and selected cytokines. We observed a similar pattern when we restricted our analyses to non-smoking men. Concentrations of cytokines were exposure dependently upregulated with higher levels among operators than R&D workers; both higher than unexposed workers (p for trend <0.05).

Conclusions We observed some indications of early immunological health effects in a pilot study conducted among workers exposed to CNTs. Further analyses are planned, including assessment of lung function, heart rate variability, oxidative stress, and blood coagulation markers. Extensive exposure measurements were conducted in the CNT production factory as well and additional analyses will use these individual exposure measurements to more thoroughly explore exposure dependent effects.

0285 DEVELOPMENT OF A SOURCE-BASED APPROACH TO ASSESSING OCCUPATIONAL EXPOSURE TO ELECTROMAGNETIC FIELDS IN THE INTEROCC STUDY

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Objectives Exposure to electromagnetic fields (EMF) has become ubiquitous in modern life and concern has increased regarding possible associated health effects. To date, assessment of occupational exposure has relied on job-exposure matrices, with exposure estimates for very broad occupational categories. To move EMF research forward, a new approach was necessary. A source-based strategy, incorporating detailed information on tasks, equipment used and work organisation could allow a more individualised exposure assessment.

Method Information on occupational histories and sources of EMF was collected as part of the INTERPHONE-INTEROCC study, providing an opportunity to assess occupational EMF exposure by assigning exposure to each source used. A source-exposure matrix (SEM) was developed based on measurements identified in the literature and estimates obtained through experts' elicitation, for sources without available measurements. This paper focuses on the SEM development methodology to ensure the quality and representativeness of the estimates.