357 THE TWO-PHASE DESIGN MAKES EFFICIENT USE OF EXPERT-TIME IN ASSESSING EXPOSURE TO OCCUPATIONAL CARCINOGENS: A LUNG CANCER CASE-CONTROL STUDY

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Objectives To identify dose-response relationship between lung cancer incidence and cumulative exposure to the main occupational carcinogens as assessed by experts making use of an initial algorithmic exposure assessment within the two-phase design.
Methods A population-based case-control study including 246 cases and 531 controls was conducted in North-Eastern France. Detailed occupational and personal risk factors were obtained in face-to-face interviews based on a task-based questionnaire and a series of job-specific questionnaires. In the conceptual framework of a two-phase design, cumulative expert-based exposure scores were obtained in a subset of 215 cases and 269 controls stratified on smoking and a prior algorithmic exposure assessment. The cases and controls included in the expert assessment were chosen in order to over-sample rare exposure categories. The data were analysed using logistic regression models adapted to two-phase data. This analysis makes use of the subset of subjects with expert assessments but also of the initial data set from which the subset was sampled.
Results Expert based cumulative exposure scores were lower than the corresponding algorithmic scores. The correlation between algorithmic and expert-assessed cumulative exposure scores were high for asbestos (r = 0.80) but less so for crystalline silica (CS) (r = 0.60) and polycyclic aromatic hydrocarbons -PAH (r = 0.56). We identified significant dose-response relationships (DRR) for asbestos, CS and Diesel Motor Exhaust (DME) with significant ORs exceeding 2 in the respective highest tertiles of cumulative exposure. The dose-response relationship with PAH was borderline significant but the OR in the highest tertile was 1.96 (95%CI [1.11–3.46]). All DRRs were steeper when using expert-based scores than when using algorithmic scores.
Conclusion Dose-response relationships between lung cancer incidence and cumulative exposure scores could be identified based on expert-assessment in a subset of cases and controls chosen to be informative in the framework of a two-phase design.

358 UNDERSTANDING FACTORS RELATED TO BETWEEN- AND WITHIN-SUBJECT VARIATION IN AN EFFORT TO BETTER DEFINE SEGS

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Objectives One approach for characterising exposures of an occupational cohort when measurement data are limited is to divide the population into Similar Exposure Groups (SEGs), or clusters of workers believed to have the same general exposure profile for the agent (s) under study, from which individual levels are established. However, when the assumed homogeneity of an SEG is incorrect, researchers risk misclassifying exposures. Through analyses of formaldehyde exposures of veterinary students enrolled in a gross anatomy laboratory course, this research examines methods for improved understanding of variability sources within a dataset in an effort to better define SEGs.
Methods Initial analyses suggested classifying this cohort as one single SEG may be questionable and demonstrated the importance of an appropriate sampling strategy. A mixed-effects model was thus used to identify exposure determinants and assess sources of variation. Using formaldehyde exposure as the dependent variable, explanatory variables were partitioned into fixed effects (animal, animal part, lab location, sample collection date) and random effects (subject). Additional analyses were run separately for each animal type in an effort to examine variability by task.
Results Examination of the data identified several potential sources of variability. The model indicated that animal and animal part may have a significant effect on exposure, with a within-subject to between-subject variance ratio of 2:1. The proportion of total variability attributable to within-subject variation differed by animal type, with 46.4, 98.6, and 70.2% associated with dog, goat, and horse dissections, respectively.
Conclusions These results help identify and describe work characteristics influencing exposure levels within the cohort. Understanding factors related to between- and within-subject variability allows for refined sub-grouping of the population and identification of work conditions that influence day-to-day exposure variations. With on-going analyses, this work will attempt to create more informative SEGs as a way to reduce exposure misclassification.

359 AN EXPOSURE ASSESSMENT MODEL FOR INADVERTENT INGESTION EXPOSURE

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Inadvertent ingestion exposure (IIE) arises from contact between the mouth and contaminated hands and objects. It may be a significant route of occupational exposure for metals, pharmaceuticals, pesticides and infectious agents (Cherrie *et al*, 2006). We have developed a predictive model of IIE. The deterministic model structure was based on data collected in: (i) a literature review of the determinants of ingestion exposure; (ii) a database of published transfer efficiencies for dermal and oral transfer; (iii) laboratory experiments to determine the efficiency of transfer of materials between hands, glove, objects and the mouth in different scenarios; and (iv) real-time observations of workers to identify rates and determinants of hand-to-mouth behaviour. The model estimates exposure to the hands and the perioral area (the area around the mouth). It was validated against measurements of hand and perioral exposure taken from 65 exposure scenarios (exposure to metals, pesticides, and cytotoxic drugs) across 13 worksites. Using written descriptions of worksites and practices, three exposure assessors, blinded to the measurement data, generated model estimates that were compared to the measured data. The correlation coefficient between model estimates and measurements ranged from 0.69 - 0.81 for hands and from 0.74 - 0.84 for perioral. The model was relatively reliable between assessors with between-assessor correlation coefficients ranging from 0.75 - 0.98. The model was designed to be used to estimate exposure at the job group level and could be used to develop job exposure matrices. Because the model can be used with historical written descriptions of tasks it may also be used to create retrospective exposure estimates. Based on the validation that has been conducted, the model appears to be a promising

new exposure assessment tool that could be used to estimate IIE exposure for epidemiology.

Cherrie JW, Semple S, Christopher Y, *et al* (2006). Ann Occup Hyg 50(7): 693–704.

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360 DOSE-RESPONSE RELATIONSHIP BETWEEN A PARTICULAR FORM OF CRYPTOCRYSTALLINE SILICA AND THE INCIDENCE OF SILICOSIS

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Objectives It has been known for centuries that crystalline silica induces silicosis. However, there are different entities of crystalline silica. Siliceous earth is a worldwide unique blend of amorphous and cryptocrystalline silica and lamellar kaolinite. This retrospective cohort study is the first that investigated the silicosis risk of siliceous earth.

Methods The cohort consists of employees exposed to siliceous earth in one company in Bavaria, Germany. Their job activities were collected from personnel files. Workers were included, if they had worked at least one year from the date of recruitment to the end of the study in 2008. The disease data were collected from occupational disease records of the Raw Materials and Chemical Industry Employers' Liability Insurance Association (BG RCI). Two pneumologists reviewed the radiographic findings independently on the basis of reports of radiological findings according to ILO 2000. Workers with an ILO profusion ≥ 1/1 (p, q, r) were considered to have silicosis. Using the existing 709 measurement records of the years 1961–2008 exposure to silica was assessed for each subject with a job-exposure matrix. To determine the risk of silicosis Poisson regression was performed and to determine the dose-response relationship cubic splines were applied.

Results In total 675 persons were enumerated, including 84 women. Among women, there were no silicosis but 55 among men. The evaluation of the exposed men showed a silicosis risk at a cumulative exposure of more than 6 mg/m^{3}xyears (RR = 25; 95% CI 5.3–111.5) and especially in underground mining (RR = 12; 95% CI 4.9–28.6). In addition, a dose-response relationship with increasing cumulative exposure was found.

Conclusions We found a dose-response relationship between silicosis and cumulative exposure to siliceous earth. The silicosis risk of siliceous earth is according to these results not higher than that described in the literature for crystalline or cryptocrystalline silica.

361 SILICA DUST AND MORTALITY FROM NON-MALIGNANT RESPIRATORY DISEASES IN THE GERMAN WISMUT MINERS COHORT, 1946–2008

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Objectives To investigate possible associations between silica dust exposure and death from chronic obstructive pulmonary diseases (COPD) and silicosis in German uranium miners.

Methods The cohort consists of 58,672 miners comprising 2,167,600 person-years and 25,239 deaths in the follow-up period 1946–2008. A detailed job-exposure matrix was used to estimate the cumulative exposure to crystalline silica in mg/m^3-years. The total numbers of underlying causes of death from COPD (ICD-10 code: J40-J44) or silicosis (J62-J65) was determined based on certificates of death and autopsy files. Internal Poisson regression with baseline-stratification by age, calendar year and duration of employment was used to estimate the relative risk (RR) and 95% confidence limits (CI) in different categories of cumulative exposure to silica dust for mortality from COPD and silicosis.

Results Nearly all cohort members were exposed to silica dust at some stage with a wide exposure range (mean = 5.9, max = 56 mg/m^3-years). No increase in risk with increasing cumulative silica dust was found for COPD as underlying cause of death only (n = 719), whereas statistically significantly increased RR's in exposure categories above 10 mg/m^3-years were found when COPD was considered as underlying or contributing cause of death (n = 2,675). The corresponding RR in the highest exposure category of 30 or more compared to less than 0.5 mg/m^3-years was 2.2 (95% CI: 1.6–2.8). The RR for silicosis as underlying cause of death (n = 976) compared to the reference category 0–2 mg/m^3-years increased systematically with increasing exposure from RR = 2.8 (95% CI: 1.03–4.6) to 118.1 (95% CI: 50.3–188.0) in the exposure categories 2–5 and 30 or more mg/m^3-years, respectively.

Conclusions Mortality of silicosis is confirmed to be associated with cumulative silica dust exposure even at low levels. Results indicate that death from COPD is related to silica dust, when considering underlying and contributing causes of death.

362 UPDATED RESULTS ON THE RISK OF DEATH FROM LUNG CANCER BY SILICA DUST IN GERMAN WISMUT URANIUM MINERS, 1946–2008

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Objectives To investigate the exposure-response relationship between silica dust and lung cancer mortality within German uranium miners in the extended follow-up period from 1946 to 2008. The cohort consists of 58,672 miners including 2.2 Mio person-years and 3,477 lung cancer deaths.

Methods Individual information on occupational exposure to crystalline silica in mg/m^3-years and the potential confounders radon and arsenic is available for all cohort members based on a detailed job-exposure matrix. Internal Poisson regression with baseline-stratification by age and calendar year was used to estimate the excess relative risk (ERR) per mg/m^3-year. Several spline functions were applied to investigate the exposure-response relationship. Detailed adjustment for cumulative radon and arsenic exposure was conducted. Effect modification by age, time and exposure-rate was tested. Additionally detailed risk analyses with specific focus on the low dose range have been performed.

Results All miners were exposed to crystalline silica at any time. The mean cumulative silica exposure was 5,9 mg/m^3-years with a maximum of 56 mg/m^3-years. A piece-wise linear spline function with a knot at 10 mg/m^3-years provided the best model fit. After full adjustment for radon (continuous variable with