measured by intermediate markers into the modelling of the natural history of cancer. Together with its ability to elucidate temporal effects of exposure on disease risk, this suggests a large range of applications in chronic disease epidemiology.

Session: 20. Risk modelling

328 MODELLING COMPLEX MIXTURES IN EPIDEMIOLOGIC ANALYSIS: ADDITIVE VERSUS RELATIVE MEASURES FOR DIFFERENTIAL EFFECTIVENESS

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Mixed exposures are often combined into single exposure measures using weighting factors. An example of this arises in radiation epidemiology where doses of distinct forms of ionising radiation (such as alpha, beta, and gamma radiation) are combined based on knowledge of their biological effectiveness relative a reference form of radiation (most often gamma). Similar pooling of mixed exposures may occur with multiple congeners or air pollutants to develop more parsimonious models. The weights used for combining exposures are determined from experimental animal and cellular research, but not observational research. In this work, we show that these weights, which are the ratio of two normally distributed variables, cannot be reliably estimated from observational research. We propose an alterative approach for estimating differences in effectiveness of distinct exposures based on their excess effectiveness compared to a reference exposure. This alternative provides reliable estimates of differences in effectiveness of distinct exposures.

329 IMPROVING COUNTER-MATCHING DESIGN IN NESTED CASE-CONTROL STUDY TO ANALYSE THE EFFECT OF A CONTINUOUS OCCUPATIONAL EXPOSURE

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Introduction Nested case-control studies are classically used in epidemiology to reduce time and cost for data collection while minimising bias induced by sample size reduction. However, if the continuous exposure of interest have a highly skewed probability distribution, rare exposure values are less likely to be selected. Therefore, the sampling process can miss important information in the long tail of the exposure distribution. Counter-matching design attempt to maximise the information on known exposure of interest during sampling process by the selection of controls in several categories covering all the range of the exposure. This study attempt to assess the influence of the choice of the categorisation method on the risk estimation.

Method The categorisation of continuous exposure is provided by several classification or clustering Methods: a priori thresholds, quantiles and k-means. To investigate the robustness of these methods, a simulation study is realised with several shapes of the probability distribution of the exposure, addition of covariate and missing collected data. Theoretical results will be illustrated with the example of a case-control study of cardiovascular diseases mortality (440 cases, 5 controls per cases (1:5)) nested within the French cohort of uranium miners (including 5086 men followed-up between 1945 and 2007) where cases and controls are matched on age and birth cohort and counter-matched on cumulative radon exposure.

Results 5000 samples 1:5 have been generated from the French uranium miners cohort for each methods applied on the cumulated radiation exposure. Relatively to the risk estimated from the cohort, the bias was systematically lower by using the k-means method.

Perspectives Results of the simulation study and application to the case-control study nested within the French uranium miners cohort could confirm this trend and contribute to the improvement of the efficiency of nested case-control study for the assessment of risk of exposure.

330 A DYNAMIC POPULATION-BASED MODEL FOR THE DEVELOPMENT OF WORK-RELATED RESPIRATORY HEALTH EFFECTS AMONG MOTOR VEHICLE REPAIR WORKERS EXPOSED TO ISOCYANATES

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Objectives Spray painters, who are exposed to isocyanate mixtures, are among the occupational groups with the highest incidence of occupational asthma in industrialised countries. In the Netherlands the motor vehicle repair (MVR) industry comprises one of the largest occupational populations potentially exposed to isocyanates. We present a mathematical model which simulates a population of spray painters exposed to isocyanates longitudinally through time and tracks the development of symptoms in each worker.

Methods First, based on the literature a conceptual disease model was defined which differentiates between different severities of symptoms: healthy, upper airway symptoms only, lower airway symptoms only, both upper and lower airway symptoms, and work-disabling symptoms, where all states are stratified on sensitisation. A Weibull survival analysis of data from an epidemiological study of 424 workers in the Dutch MVR industry confirmed the relationships of respiratory symptoms with isocyanate exposure and atopy. Furthermore, the data provided us with the necessary task-based exposure distributions, patterns of work and use of respiratory equipment that served as inputs for the simulation model.

Results Individual workers had the highest chance of developing respiratory symptoms within the first five years of working in the MVR sector, after which their risks decrease. Furthermore, the risk of developing lower airway symptoms after 5 years doubled when a worker was atopic. The following example illustrates the application of the modelling approach: The prevalence of lower airway symptoms found in the epidemiological study was 5%. On average, 93% of spray painters used respiratory protection equipment. The dynamic population model predicted that when frequency of use increases to 98%, the prevalence of lower airway symptoms would decrease to 4%.

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328 Modelling complex mixtures in epidemiologic analysis: Additive versus relative measures for differential effectiveness

G B H Hamra, R F M MacLehose, D B R Richardson, et al.

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