Results The presentations will provide examples of how such models can offer a richer description of epidemiologic associations. Insights may be important when risk assessments are based on epidemiologic results that assess cumulative exposures without consideration of exposure patterns or age-related susceptibility.
Conclusions Models that encompass dynamic aspects of exposure should be encouraged in risk modelling. Such models may also provide information about biologic pathways of disease, leading to better understanding of (for instance) the impact of metabolic saturation on the observed exposure–response curve, or the natural progression of the disease.

0368 DISENTANGLING THE EFFECT OF EXPOSURE DURATION, INTENSITY, AND TIME SINCE EXPOSURE IN STUDIES OF CHRONIC HEALTH EFFECTS

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Objectives Due to their interrelatedness, modelling independent effects of intensity, duration, and time since exposure on disease risk is complex. The indiscriminate use of the cumulative exposure metric (product of intensity and duration of exposure) might bias reported associations between exposure to hazardous agents and disease risk. We explored the use of a general framework to flexibly model the effects of intensity, duration, and time since exposure on chronic disease.
Method We will provide examples of models falling within the flexible framework. One of such models is an excess relative risk model that is linear in cumulative exposure and exponential in the intensity (or duration) of exposure and time since cessation. This model has been applied successfully to explore effect modification of cumulative exposure by intensity (or duration) of exposure for a number of exposures. We will demonstrate the application of this model in two studies of smoking and chronic disease.
Results In our example the excess relative risk model generally fits the data best. In both studies we observed a strong effect of time since cessation. We observed effect modification by intensity of smoking in one study.
Conclusions Application of flexible models will provide insight into whether the use of cumulative exposure in an epidemiological analysis is justified or whether reducing complex exposure history to a metric such as cumulative exposure is overly restrictive. Combining information on observed patterns of effect modification with mechanistic insights might contribute to the incorporation of biological hypotheses in the development of more biologically relevant exposure metrics.

0376 PROTRACTING EXPOSURES

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Objectives When an exposure is protracted or repeated over time, questions arise regarding variation in the effect for different temporal patterns of exposure. We review approaches to describe variation in an exposure's effect as a function of age-at-exposure, time-since-exposure, and exposure rate. These models implicitly assume that the effect of an exposure increment on subsequent disease risk depends upon its intensity and time-since-exposure, but not upon the intensities of prior exposures. Then, we consider the possibility that the effect of an exposure is dependent upon earlier exposures. We use the term 'desensitisation' to refer to the scenario in which a person's response to an exposure diminishes if they have been previously exposed to it. We use the term 'sensitisation' to refer to the scenario in which a person becomes more susceptible to the effect of an exposure if they have been previously exposed to it.
Method We propose a general model for analysis of disease rates in a setting of protracted or repeated exposure that encompasses (de)sensitisation. We illustrate the model using empirical data from a cohort mortality study.
Results The presentation provide examples of how such models can offer a insights into a notion of interaction between an exposure at one point in time and later exposure to the same agent.
Conclusions The possibility that an exposure's effect may depend upon prior exposure to it is often considered in narrative descriptions of etiological processes, yet not readily accommodated by most standard approaches for analysis of protracted occupational and environmental data.

0377 REPRODUCTIVE EFFECTS OF WORKING NIGHT AND ROTATING SHIFTS

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Objectives Recent studies suggest that shift workers who experience exposure to light at night could be at increased risk for adverse reproductive outcomes.
Method Defined by cyclical patterns of circulating hormones, the reproductive system is vulnerable to shifts in circadian rhythms, either through sleep disturbances, altered melatonin production, exposure to light at night, or some other mechanism. Several occupational groups, including health care workers, law enforcement, firefighters, and manufacturing workers are required to work night shifts. Worldwide, millions work at least one night per month.
Results Research will be reviewed on shift work and reproductive outcomes, including menstrual cycle patterns, fertility, pregnancy loss, preterm delivery, and birth weight. The limitations of current research will also be discussed: is there a dose response effect from the number of years of shift work, or can the effects be reversed once shift work stops? Are there different effects from permanent night shift versus rotating shift involving nights?
Conclusions Future research needs will be identified, including the need for validation of self-reported shift work data and the mechanisms by which shift work affects reproductive health. Recommendations for shift workers and employers will be explored.

0380 DYNAMICS OF EXPOSURE AND DISEASE PROGRESSION: THE USE OF COMPARTMENTAL MODELS

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Objectives Chronic diseases are usually slow-developing condition and their risk may result from both long-term exposure and successive exposure increments, hence calling for models accounting for dynamics of exposure and disease progression.

Method Discrete compartmental models are defined by a set of ordered states (compartments) reflecting the health status, and can be fully characterised by the set of transition probabilities between each compartment. When defined at the individual level, each participant contributes to the likelihood of the model at each year from the time of entering the initial stage (e.g. birth) to the moment they reach an absorbing state (e.g. death or clinical onset). Model estimation aims at quantifying the transitions ensuring the best reconstruction of the pathological trajectories in each subject, hence adding to the classification problem (discriminating healthy and diseased subjects) a dynamic component (estimating the time of onset).

Individual exposure histories can be summarised through cumulative exposure functions and subsequently plugged into the compartmental framework as parameters of transition probabilities.

Results While these models were initially developed to accommodate data from longitudinal studies, we will illustrate, using lung cancer case control and smoking history data, the validity and utility of such approaches. We will assess the underlying assumptions yielded by this methodological drift and will exemplify the rich statistical inference these approaches are able to provide.

Conclusions We will finally introduce potential extensions over this framework that include omics biomarkers to model genetically-driven susceptibility and/or to identify the stage (s) at which exposure (s) are more likely to mediate their effects.

0410 LONG NIGHT SHIFTS AMONG HEALTH WORKERS AND PHYSICAL AND MENTAL HEALTH: THE INFLUENCE OF ON-SHIFT NAP AND DOMESTIC WORK

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Objectives This presentation during the Shift work Symposium aims to discuss data on physical and mental health among health workers, considering the relevance of on-shift naps and routine housework. In addition, the presentation aims also to analyse the cumulative exposure to night work.

Method Data to be presented are based on several epidemiological studies among nursing teams working at 18 Brazilian public hospitals. Databank includes information on socio-demographic and health. Data on work refers to the allowance (or not) to take naps during the night shift and nap regularity. Occupational history data considers (i) whether day workers have worked at night in the past and for how long and (ii) the reasons for quitting night work among former night workers.

Results The allowance for taking naps was observed in all studied hospitals. On-shift nap is a frequent practice among nursing workers. The analysis of occupational history revealed to be relevant as regards physical and mental health. Among former night workers, those who quitted night work for health reasons are at a higher risk of reporting mental suffering.

Conclusions Housework demands seem to aggravate sleep deprivation related to night work, despite evidences of beneficial effects of on-shift naps on workers' recovery. The specific study of former night workers has revealed to be a fruitful approach in studies on health, obesity included, lifestyle and habits, as well as sleep disturbances. Occupational history is an adequate approach for a comprehensive understanding of the impact of night work on health.

0422 CORONARY ARTERY DISEASE MORTALITY AMONG WORKERS EXPOSED TO CARBON DISULFIDE AND SHIFT WORK AT A CHEMICAL MANUFACTURING PLANT

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Objectives Previous studies at a New York State chemical manufacturing plant reported elevated risks of cardiovascular disease among workers. We updated the mortality experience of 1874 workers employed between 1949 and 2006 through December 31, 2007. We investigated exposures to carbon disulfide and shift work and their association with coronary artery disease.

Method Jobs with carbon disulfide and shift work exposure (≥1 day) were identified among departments and job titles in specific years. Standardised mortality ratios (SMR) compared mortality to the US population, adjusted for gender, race, age, and calendar year. Internal comparisons used directly standardised rate ratios (SRR).

Results Overall, excess deaths were observed for coroanary artery disease (SMR=1.24, 95% CI 1.04–1.48). Most workers exposed to carbon disulfide perfortmed shift work; we evaluated coronary artery disease mortality in groups defined by duration of exposure to these agents. Compared to the US population, statistically significant increases in mortality were observed among workers with both exposures for 90 days or more (SMR=1.36, 95% CI 1.03–1.76), and among workers with fewer than 90 days of both exposures (SMR=1.31, 95% CI 0.65–2.34). Using cutpoints of 4 years (median exposure duration among long-term cases), the results were no longer statistically significant. In internal comparisons, long-term workers exposed to carbon disulfide and shift work for 4 years or more had a near 3-fold increase in coronary artery disease mortality, compared to workers exposed less than 4 years.

Conclusions Excess coronary artery disease mortality confirms earlier results, but further investigation is needed to understand risk factors.

0430 INDIVIDUAL VARIABILITY, FROM CANDIDATE G*E TO GEWIS

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Objectives In the 1990s there were great expectations that the use of markers of genetic susceptibility would allow the identification of new occupational risks, a more complete characterisation of dose-response relationships and improved risk assessment. Several interaction studies were conducted examining candidate genes, for example on isocyanate exposure, genes in immune pathways (e.g. HLAII group) and occupational asthma, or studies on cancer, aromatic amines and the NAT2 gene.

Method Very few replicated in more than one population. Part of the problem was the small sample size and the selective