Objectives Standard data analysis procedures provide biassed answers to etiologic questions in occupational studies. G-estimation is an alternative that allows researchers to avoid healthy worker survivor bias, and its results can be expressed as estimates of the impacts of hypothetical policy interventions.

Method Rather than estimating the association between observed exposure and observed outcome, g-estimation models the counterfactual outcomes under no exposure as a function of observed outcomes and exposures. Adjustment for confounders is achieved by predicting exposure conditional on those confounders and on the counterfactual outcome. The method leverages the assumption that all confounders are measured: within strata of the measured confounders, observed exposure is "randomised"–that is, statistically independent of counterfactual outcome. This allows for correct adjustment for time-varying confounders affected by prior exposure and thus avoids healthy worker survivor bias.

Results Results can be expressed in terms of the impacts of hypothetical exposure limits. For example, after g-estimation of an accelerated failure time model, counterfactual survival times under a series of specified exposure limits can each be compared to observed survival time. This allows the researcher to report estimates of the total number of years of life that could have been saved by enforcing each limit.

Conclusions G-estimation is a valuable tool for occupational epidemiologists because it can both prevent bias due to the healthy worker survivor effect and estimate the impacts of hypothetical exposure limits.

0359 NIGHSHIFT WORK AND BREAST CANCER RISK – GOOD NEWS, BAD NEWS?

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Objectives Using two large prospective data sets, we explored associations between rotating nightshift work and breast cancer risk.

Method Among 193 396 women from the Nurses' Health Study (NHS and NHS2) cohorts, we documented 5575 (NHS) and 2869 (NHS2) incident invasive breast cancer cases as well as 696 (NHS) breast cancer deaths over 22 years of follow-up. Compared to our initial analysis within NHS, which was based only on 10 years of follow-up and showed that 30+ years of rotating nightshift work was associated with a 36% significant increase in breast cancer risk, we added 12 years of follow-up, which were accrued for the most part after nurses' retirement.

Results In these extended analyses, 30+ years of rotating night shift work was no longer associated with breast cancer risk (multivariable RR_{30+yrs}=0.95, 95% CI 0.77–1.17; p_{trend}=0.95), and only insignificantly associated with breast cancer mortality (multivariable HR_{30+yrs}=1.50, 95% CI, 0.95–2.36). By contrast, in the younger NHS2 cohort, baseline 20+ years of rotating nightshift work was associated with a significantly increased risk of breast cancer (RR_{20+yrs} =2.11, 95% CI 1.21–3.66; p_{trend}=0.22). Updated rotating night shift work exposure was also associated, albeit non-significantly, with a modest increase in risk of breast cancer (RR_{20+yrs}=1.33, 95% CI0.93–1.89; p_{trend}=0.68).

Conclusions Taken together, these results suggest that long-term rotating night shift work particularly early in career may be associated with an increased risk of breast cancer, which appears to diminish after nightshift work ceases. Future studies are needed to confirm these findings and should explore the potential for tailored risk factor counselling in nightshift workers.

0363 MARGINAL STRUCTURAL MODELS TO ACCOUNT FOR TIME-VARYING CONFOUNDING VARIABLE AND THE HEALTH WORKER SURVIVOR EFFECT (FOR A MINI-SYMPOSIUM ON 'DYNAMICS OF EXPOSURE AND DISEASE', ORGANISED BY VERMEULEN)

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Objectives Marginal structural models (MSMs) in longitudinal studies are needed when time-varying confounders are themselves predicted by previous exposure, and are intermediate variables on the pathway between exposure and disease. The epidemiologist is left with the unenviable choice of adjusting or not for the confounder/intermediate variable. An example would be whether aspirin decreases cardiovascular mortality, in which the confounder/intermediate variable is cardiovascular morbidity.

Method MSMs use inverse-probability weights based on an 'exposure' model which assesses the probability that each subject has received their own exposure and confounder history up to time t, with the follow-up period divided into T (t=1 to T) categories. These weights are then used in standard regression models (eg., pooled logistic regression models across T categories) relating exposure to disease. Their use creates a pseudo-population where time-varying confounding is eliminated.

Results Empirical results show that standard methods to control for time-varying confounders can result in bias towards the null, compared to MSMs. A recent simulation study showed MSMs lead to unbiased results under a variety of assumptions.

Conclusions Some studies have used somewhat different but related methods ("g-estimation") to account for the healthy worker survivor effect, where employment status is a time-varying confounder which predicts future exposure and may predict disease, but may also act as an intermediate variable because prior exposure may cause illness which results in leaving employment. Here we will present an overview of MSMs and the related g-estimation models.

0367 RATIONAL FOR CHOOSING EXPOSURE METRICS: A SHORT HISTORY

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Objectives Risk of chronic disease may be governed not only by cumulative levels of exposure but also by dynamic aspects of the exposure history. These dynamic aspects include characteristics of the exposure history itself (such as duration of exposure or time-varying intensities of exposure) as well as aspects of age-related susceptibility. This workshop will provide an overview of methods developed to better understand the dynamic aspects of exposure in epidemiological models.

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