Tuesday 9 August 2011
Parallel session 3
3.1 NOVEL APPROACHES TO REDUCING BIAS

Chair: Prof. Iain Crombie, UK

03-1.1 DOES DROP-OUT FROM COHORT STUDIES BIAS ESTIMATES OF SOCIOECONOMIC INEQUALITIES IN HEALTH?

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Introduction Scandinavian studies exploiting record-linkage have shown that although cohort members tend to be healthy and affluent compared to the whole population, this does not bias at least certain well-established exposure-outcome associations. It is unknown whether this holds when estimating health inequalities. Individuals of lower socioeconomic position (SEP) may be less likely to consent to participation in a cohort study and more likely to drop-out over time.

Methods We assess whether socially-patterned drop-out affects the estimation of health inequalities in the Avon Longitudinal Study of Parents and Children. In this UK cohort, children of higher SEP (measured by maternal education) are more likely to continue participating as they get older. We estimate SEP inequalities in maternal and infant outcomes for which we have data on almost the whole cohort (birthweight and length, breastfeeding, preterm birth, maternal obesity and smoking during pregnancy, N ~ 12 000). We then restrict analyses to individuals who participated in subsequent data collections when the child was aged 9 (N ~ 7000) and aged 15 (N ~ 5000).

Results Drop-out was related to SEP and outcomes, so under missing data theory analysis may be biased. For each outcome, inequality was greatest in the full sample; the more selected the sample became, the more the inequality was underestimated; for example, mean birthweight difference between highest and lowest SEP was 116 g (95% CI 78 to 153) in the full sample, but 93 g (95% CI 45 to 141) and 62 g (95% CI 5 to 119) in those attending at ages 9 and 15 respectively.

Conclusion Selection bias in cohorts may result in underestimation of health inequalities.

03-1.2 HOW TO PERFORM A SENSITIVITY ANALYSIS EXPLORING THE IMPACT OF MISSING NOT AT RANDOM DATA WITH THE R® SOFTWARE

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Introduction The impact of missing data (MD) on the validity of results, although often discussed, is not often investigated. Sensitivity analyses under different scenarios of non-ignorable MD are an attractive approach but they are rarely performed, probably due to lack of tools.

Methods We propose an R function to perform multiple imputation based on the principle of mixture modelling, assuming that the variable of interest has different distributions according to the status missing / non-missing. We propose a 3-step strategy:

Fit an imputation model assuming ignorable MD;

Modify the imputation model by adding a parameter (expressed as the OR comparing the odds of the modality of interest among subjects with MD with those without MD for categorical variables; as the difference in expected values for continuous variables);

Impute MD under the scenario thus specified.

A sensitivity analysis was performed on data from HIV+ patients, to assess the robustness of the OR between mental health and self-reported viral load, including MD. We assumed that non-responders were more likely to have high viral load.

Results Adjusted OR was reduced from 2.01 [1.21 to 3.35] to 1.75 [1.03 to 2.97]. Conclusions were robust to the explored scenarios reinforcing the confidence in results from the analysis assuming ignorable MD.

Conclusion A sensitivity analysis is easy to perform using the proposed package SensMice. The impact of imposed variations in the imputation model on the overall results helps to assess their robustness. This is particularly interesting for self-reported characteristics when MD are highly suspected to be non-ignorable.

03-1.3 SENSITIVITY ANALYSIS FOR AN APPARENT DIRECT EFFECT AFTER CONDITIONING ON AN INTERMEDIATE VARIABLE

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Introduction Determining factors in the causal pathway between an exposure and a disease is often the aim of etiologic research. For example, if a gene is associated with a certain disease, one would like to know if this relation can be explained by one or more intermediary variables. A naive approach to explore this is to condition on the intermediate factor and perform a stratified analysis. However, when an association remains, it is not always clear how this should be interpreted. It may be explained by a true direct effect of the exposure on the disease, or it may be explained by different types of error.

Methods We study different situations, using directed acyclic graphs, where despite absence of a direct effect, still a conditional relation between the exposure and the outcome remains. By quantifying the effect on the association parameter in each of the situations, we develop tools for sensitivity analysis of the completeness of adjusting for a mediator. The performance of the sensitivity tools is studied by simulation and by applying the tools on data of the LETS study. In this case-control study the question was whether the relation between blood group and venous thrombosis was mediated through coagulation factor VIII.

Results A remaining association can be caused by different types of measurement error, reverse causation or unmeasured confounding. In the LETS study intra-individual variation explained most of the remaining association.

Conclusion Sensitivity analyses should be performed before the conclusion is made that effects are not completely mediated.

03-1.4 MULTIPLE IMPUTATION: PANACEA OR PLACEBO, THE CASE OF MISSING CAROTID INTIMA-MEDIA THICKNESS MEASUREMENTS IN CLINICAL TRIALS

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Introduction We assessed the added value of multiple imputation (MI) of missing values in longitudinal datasets with carotid intima-