



Department of Epidemiology, Biostatistics & Occupational Health

Biostatistics Seminars

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*Estimating gene-gene and gene-environment interaction effects:
taking advantage of study design to maximize efficiency.*

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4:00 pm - 5:00 pm

Purvis Hall, 1020 Pine Ave. West, Room 24

ALL ARE WELCOME

Abstract:

It is well known that estimating interaction effects requires larger sample sizes than estimating main association effects. In that context, it is particularly important to maximize estimation efficiency when designing and analyzing an epidemiologic study. In this talk, I will present approaches to optimize efficiency in two situations.

The first is the study of interactions in samples drawn from large prospective cohorts. I have compared the efficiency of nested case-control and case-cohort sampling designs with and without stratification for estimating the effects of genetic and environmental risk factors and their interactions. Asymptotic calculations show that the relative efficiency of the case-cohort and nested case-control designs implementing the same sampling stratification are similar over a range of scenarios for the relationships among genes, environmental exposures and disease status. Sampling equal numbers of exposed and unexposed subjects improves efficiency when the exposure is rare. The case-cohort designs had a slight advantage in simulations of sampling designs within the Framingham Offspring Study, using the interaction between Apolipoprotein E and smoking on the risk of coronary heart disease as an example. It was possible to estimate the interaction effect with precision close to that of the full cohort when using case-cohort or nested case-control samples containing fewer than half the subjects of the cohort.

The second situation is the study of diseases early in life where the genotype of both the mother and child need to be considered. In the context of a case-mother – control-mother design, others have demonstrated how to take advantage of constraints in the genotype distribution of the mother-child pairs to improve efficiency in estimating main genetic effects. I am working on an extension to the estimation of gene-environment interaction effects, which can also take advantage of the gene-environment independence assumption. Preliminary results indicate important power gains.