HOW TO IDENTIFY STATISTICALLY SIGNIFICANT AMONG SEVERAL PUTATIVE, INTER-CORRELATED INTERACTIONS?

M. Abrahamowicz[†1,2], Y.L. Xiao[1,2]

[1] *McGill University, Montreal, Canada*
[2] *Montreal General Hospital, Montreal, Canada*

[†] E-mail: *michal@epimgh.mcgill.ca*

Increasing size and complexity of datasets collected in biomedical and epidemiological research opens new opportunities for investigating questions rarely addressed in previous studies. In particular, a traditional "excuse" for not investigating interactions between prognostic factors does not apply to administrative databases or large cohorts. Indeed, those few studies that did attempt to investigate, e.g. drug-drug interactions, yielded potentially exciting results [e.g. Hippisley-Cox, BMJ 2005]. However, the validity and/or efficiency of some popular procedures to test for interactions may be questionable. It is difficult to strike a balance between the opposing trends to (i) increase notoriously low power for interactions testing, and (ii) control overall 'experiment-wise′ type I error rate, and things get worse if e.g. many of the 'candidate′ X(j)*Z interactions involve the same exposure Z and/or inter-correlated covariates X(j). We propose a simple approach to identify statistically significant among a number of possibly intercorrelated interactions. The approach involves (a) stepwise selection among candidate interactions, and (b) bootstrap inference to adjust the critical test value for data-dependent choices in (a). In simulations, we evaluate the proposed approach with respect to overall type I error, power, and the ability to discriminate between "true" and "spurious" among several, possibly inter-correlated interactions, and compare it to conventional methods.