ESTIMATING AND TESTING INTERACTIONS IN LINEAR REGRESSION MODELS WHEN EXPLANATORY VARIABLES ARE SUBJECT TO NON-CLASSICAL MEASUREMENT ERROR

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Estimating and testing interactions in a linear regression model when normally distributed explanatory variables are subject to measurement error is complex, since the interaction term is a product of two or more covariates and involves errors of more complex structure.

Earlier work on this problem used a structural equations model framework but was applied under the assumption that errors in covariates are independent of each other, which is often unrealistic in epidemiology.

We have described in recent work [1] how to estimate and test for interactions when covariates are normally distributed and subject to classical measurement error, i.e. when the magnitude and direction of the error do not depend on the true value and the error has zero mean. We proposed a version of regression calibration (RC), which allows correlated errors and showed that it yields consistent estimators and standard errors, and that its test for interaction appears to have a Type I error rate close to the nominal level, irrespective of the number of interactions included in the model.

In many applications the classical measurement error model does not hold, particularly when measurements are based on self-report. In this paper, we generalize our RC approach for interaction models to a class of non-classical measurement error models and compare its performance to the naive uncorrected method. Motivated by an application that includes a sub-sample calibration, we account for the extra uncertainty involved in estimating the measurement error parameters, using the stacking equations method. We apply our method to data from the Observing Protein and Energy Nutrition (OPEN) study, where the level of errors is high, and find that RC does not work well for estimation, yielding inflated parameters and standard error estimates. Using simulations, based on the design of the OPEN study, we show that, to perform better, our method requires either much larger samples than were in OPEN (approximately 220 for each gender) or a much lower level of measurement error.

In another set of simulations, we investigate the Type I error rate of the interaction test and show that in this context large sub-sample sizes ($\geq$500) are needed for good performance of the RC-based test, and that otherwise the test is too conservative.

1. Murad, H. and Freedman, L. S. (2007). Estimating and testing interactions in linear regression models when explanatory variables are subject to classical measurement error. *Statistics in Medicine* **26**, 4293-4310.