Daniel Mork. **Estimating Perinatal Critical Windows to Environmental Mixtures via Structured Bayesian Regression Tree Pairs.**

Background. Maternal exposure to environmental chemicals during pregnancy can alter birth and children's health outcomes. Research seeks to identify critical windows, time periods when exposures can change future health outcomes, and estimate the exposure-response relationship. The majority of evidence regarding the effects of maternal exposure to air pollution on birth outcomes considers either a single pollutant or a mixture observed at one time point. Existing statistical approaches that allow for high temporal resolution (e.g. weekly throughout pregnancy) exposure measurements primarily account for a single environmental chemical. Extending to multiple chemicals observed at high temporal resolution poses a dimensionality problem and statistical methods are lacking.

Methods. We propose a regression tree-based model for mixtures of exposures observed at high temporal resolution. The proposed approach uses an additive ensemble of tree pairs that define structured main effects and interactions between time-resolved predictors and performs variable selection to select out of the model predictors not correlated with the outcome. In simulation, we show that the tree-based approach performs better than existing spline-based methods for a single exposure and can accurately estimate critical windows in the exposure-response relation for mixtures. Software is made available in the R package dlmtree.

Results. We apply our method to estimate the relationship between five exposures measured weekly throughout pregnancy and resulting birth weight in a Denver, Colorado birth cohort. We identified critical windows during which fine particulate matter (PM_(2.5)), sulfur dioxide (SO_2), and temperature are negatively associated with birth weight and an interaction between fine particulate matter and temperature. In addition, we develop an innovative post-analysis technique to adjust for correlation between co-occurring exposures. We find that an IQR increase in PM_(2.5) (6.12 to 8.67Î¼g/m^3) at each week of pregnancy, adjusting for expected changes in co-occurring exposures, is associated with a 27.7g decrease in birth weight. An IQR increase in SO_2 (0.94 to 1.90ppb) at each week of pregnancy, adjusting for expected changes in co-occurring exposures, is associated with a 20.7g decrease in birth weight.

Conclusions. In this work we proposed a method to estimate the association between mixtures of environmental exposures observed at high-temporal resolution on birth and children's health outcomes. Our analysis of five pollutants observed weekly throughout pregnancy and birth weight is the first analysis to identify critical windows to a mixture observed at high-temporal resolution within a distributed lag mixture model framework. As the size and resolution of the exposure data available continues to grow, our method fills a critical research gap in statistical methods for epidemiology and environmental health in being able to estimate the effects of time-resolved measures of a mixture on a continuous or binary health outcome.