

Kernel Machine and Distributed Lag Models for Assessing Windows of Susceptibility to Mixtures of Time-Varying Environmental Exposures in Children's Health Studies

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Abstract: Research has shown that early life exposures to environmental chemicals, starting as early as conception, can reprogram developmental trajectories to result in altered health status later in life. These principles likely apply to complex mixtures as well as individual chemicals. We thus consider statistical methods to estimate the association between mixtures of multiple time-varying exposures and a future health outcome, e.g. exposure to multiple air pollutants observed weekly throughout pregnancy and birth weight. First, we illustrate how to use traditional distributed lag models, distributed lag nonlinear models, and Bayesian kernel machine regression to estimate the association between multiple time-varying exposures and a health outcome. While none of these methods simultaneously accounts for exposure-timing, nonlinear association, and interactions, we highlight situations in which each model performs well. Second, we propose a new method to estimate the association between multiple time-varying exposures and a health outcome. The proposed approach is, to our knowledge, the first method to simultaneously account for exposure-timing, nonlinear associations, and interactions between time-varying exposures. The proposed approach is a Bayesian kernel machine regression method that accounts for exposure timing using a functional weight component within the kernel. The weight function identifies developmental periods with increased association between exposure and a future health outcome, often referred to as a window of susceptibility. We demonstrate the proposed methods in an analysis of exposure to four ambient pollutants and birth weight in a Boston-area perinatal cohort.