Case series analysis for dependent recurrent events

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The self-controlled case series method was developed to investigate the strength of association between a time-varying exposure and a potentially recurrent adverse event, using cases only. This method has two important features: it uses only cases and adjusts for fixed confounders, which minimizes selection or indication biases. It has been used widely in pharmaco-epidemiology, particularly in the study of vaccine safety.

To analyse recurrent events, we assume that the events are conditionally independent given fixed or random individual effects. A multivariate generalisation of the self-controlled case series method is proposed to handle the analysis of more general dependencies, such as those induced by unmeasured time-varying random individual effects, or causal mechanisms. In this approach, the standard model is augmented by an association parameter, which provides the focus for a test of independence.

Parametric and semi-parametric estimation methods are described, as well as some simpler techniques that do not require special programming. The methods are applied to two data sets, relating to a rare bleeding disorder in children and to myocardial infraction in adults.