Kolloquium „Statistische Methoden in der empirischen Forschung“

Wann: 11. Dezember 2012, 17:00 – 18:30 Uhr

Wo: Landwirtschaftlich-Gärtnerische Fakultät der HU, Hörsaal 2, 2. Etage, Invalidenstr. 42, 10115 Berlin

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Risk assessment based on case series: When and how?

Cohort or case-control studies are the standard set-ups for the evaluation of risk factors in epidemiology. However, these designs often reach their limitations: Cohort studies are hardly feasible when disease of interest is rare. Instead, a case-control design is often applied, but then control selection is a major challenge. When, in addition, the risk factor of interest is rare (or common), even this approach becomes impractical. Such situation arose, for example, when drugs as risk factors for Stevens-Johnson syndrome and toxic epidermal necrolysis that represent severe cutaneous adverse reactions were evaluated. Both, the reaction as well as some drugs of interest, are very rare. Past case-control studies (e.g. EuroSCAR [1]) were thus of limited success. Here, the analysis of a case series might be of advantage.

In the context of adverse reactions, different approaches for the analysis of a case series were published in order to assess the risk of time-varying risk factors such as drugs or vaccines. Maclure [1] introduced the case-crossover method that is, loosely speaking, a case-control study but without controls. Farrington [2], on the other hand, proposed the self-controlled case series method that can be viewed as a cohort study where only those individuals are included who experienced the disease of interest. The main idea of both methods is to compare different time periods within each individual to assess risk factors.

Since their introduction, both methods have been successfully applied in different areas. In general, the realisation of such a study has the advantage that they can be conducted rather quickly and with low budget in comparison to a corresponding cohort or case-control study, especially when data are already available (e.g. through an existing registry). Risk evaluation is valid as long as necessary requirements regarding the practical setting (e.g. acuteness of disease) and assumptions for risk estimation which depend on applied estimator are fulfilled. Moreover, the risk estimator is automatically adjusted for fixed patient-specific confounders because of the intra-individual comparisons.

For illustration, applicability and limitations of case series methods are discussed in the setting of severe cutaneous adverse reactions.

1 Mockenhaupt M, et al. Stevens-Johnson syndrome and toxic epidermal necrolysis: Assessment of medication risks with emphasis on recently marked drugs. The EuroSCAR-study. *J Invest Dermatol* 2008; 128(1):35-44.

2 Maclure, M. The case-crossover design: A method for studying transient effects on the risk of acute events. *Am J Epidemiol* 1991; 133(2):144-53.

3 Farrington, CP. Relative incidence estimation from case series for vaccine safety. *Biometrics* 1995; 51(1):228-35.