Nested case-control designs in a subsequent event setting

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Abstract

Antibiotic resistance is one of the most challenging problems in the healthcare sector worldwide. Most worrying is the emerge and rapid global spread of bacteria, which are resistant against an increasing amount of antibiotics. Therefore, the European prospective cohort study EURECA assesses risk factors for carbapenem-resistant enterobacteriaceae (CRE). By this, new opportunities are opened up regarding the best available treatment. Moreover, economical concerns, as length of hospital stay associated with a drug-resistant bacteria infection, are pursued.

In the context of this study, a highly interesting statistical challenge arises when it comes to analyzing the effect of infection due to CRE on the length of hospital stay within a subsequent event setting. As covariate information is hard to obtain, a nested case-control (NCC) design is applied. However, it remains unclear how to sample controls when only a small amount of patients experiences the incident event, but the outcome event is not rare at all. Therefore, a modified nested case-control design is suggested, where the basic idea of exposure density sampling is incorporated. On the way, limits of nested case-control designs are demonstrated and an approach is proposed, where controls for all individuals, that experience the incident event, are sampled at the time of the outcome event. Additionally, the analysis requires the sampling of controls for some non-exposed patients, which are randomly selected by a Bernoulli experiment. Counting process formulation is established and weights are calculated in order to develop a stratified, weighted partial likelihood function. Theoretical results are applied to a practical data set and corresponding confidence intervals by means of the observed information matrix are established.