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Tiivistelmä – Referat – Abstract <p>All pharmaceutical products, including vaccines, can increase the risk of some undesired medical occurrences (adverse events). Evaluating these risks post-licensure is essential for evaluating the safety of vaccines, since rare adverse events might go undetected in pre-licensure studies. This thesis introduces and applies a method for vaccine safety surveillance, suitable for monitoring the safety of vaccines in near real-time, utilizing electronic health care records. Adverse events are operationalized by diagnosis codes related to health care visits.</p> <p>Vaccine safety surveillance studies suspected, biologically plausible causal relationships between a vaccine and an adverse event. Information regarding such relationships are called safety signals. Safety surveillance can be seen as an observational study for which different study designs could be used. The popularity of vaccination, self-selection and changes in diagnosis coding practises, along with other possible sources of bias, present challenges for commonly used cohort designs. Self-controlled study designs such as the self-controlled case series (SCCS) eliminate time-invariant confounders and are therefore often more suitable for evaluating vaccine risks. This thesis introduces both a simple and a more general version of SCCS and explicitly describes the assumptions related to the method.</p> <p>A vaccine safety surveillance method involves a decision rule for generating safety signals. Natural goals of a safety surveillance method are to control the rates of false positive and false negative signals, as well as to generate a signal as soon as possible when an association between the vaccine and the adverse event exists. Statistical hypothesis testing can be used to derive the decision rules. This thesis describes the maximized sequential probability ratio test (maxSPRT), a hypothesis testing method designed for vaccine safety surveillance.</p> <p>Binomial maxSPRT (BmaxSPRT) is a variant of maxSPRT based on a self-controlled study design such as the SCCS. The BmaxSPRT method addresses hypotheses concerning the relative incidence of adverse events during specified risk and control periods. The derivation of the decision rules for BmaxSPRT, including the computation of critical values, is described in detail both mathematically and algorithmically in this work.</p> <p>As a proof-of-concept BmaxSPRT is retrospectively applied to Finnish register data. The relationships between the incidence of febrile seizures and three childhood vaccines, Measles-Mumps-Rubella (MMR), Pneumococcal (PCV) and the Rota virus vaccination (Rota) are studied. BmaxSPRT generated an expected safety signal related to MMR; the incidence rate of febrile seizures was higher during a period 0-13 days following MMR vaccination compared to a period 14-41 days following vaccination (relative rate RR = 1.59 at the time of signal). Results for PCV are inconclusive and the experiment highlights the need for more in depth analysis regarding PCV vaccinations and febrile seizures.</p> <p>The sensitivity of BmaxSPRT to the specifications of the risk and control periods is also studied in this thesis. The sensitivity analysis highlights the importance of careful consideration of the risk and control periods by quantifying the loss of power due to poor choices.</p>		
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