
Oral Presentations

O.06 Choice of the Comparator for Signal Generation in Pharmacovigilance Databases: Impact On Detection Thresholds

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Background: Many statistical methods are used for automated detection of signals in pharmacovigilance, mostly based on disproportionality measures. They compare the relative reporting of one event for one drug to reporting for all other drugs. This comparator seems appropriate when it does represent the baseline risk of reporting. This might not be the case when it includes drugs known to be involved in the occurrence of a specific event.

Objective: To study the effect of removing reports concerning drugs involved in particular events on the detection thresholds of signals for other drugs, newly marketed or older.

Methods: We used the case-non case approach to estimate detection thresholds for new or old drugs in the French Pharmacovigilance database. We studied reports notified between October 1, 2005 and September 30, 2006. We considered events of bleeding, headache, hepatitis, Lyell syndrome, myalgia, myocardial infarction and stroke.

Results: During the study period, 19,173 reports were registered in the database, among which were: 908 bleeding cases, 361 headache cases, 548 hepatitis cases, 49 TEN, 369 myalgia cases, 53 myocardial infarction cases and 321 stroke cases. For bleeding, the number of reports of interest (detection threshold) for new drugs with 50 reports all events considered, was estimated at 6 when compared to all other drugs and at 3 after excluding reports concerning the main drugs already associated with bleeding. These thresholds were decreased for all reporting frequencies studied for bleeding and stroke. They were not modified for headache, hepatitis, TEN, myalgia or myocardial infarction. Thresholds were similar whether they were evaluated for a new drug or for an existing one.

Conclusion: The choice of the comparator is of great importance for signal generation and has great influence on detection thresholds. The inability to define a specific comparator might limit the performance of data mining when it is used to generate signals without prior hypotheses. For orientated signal exploration, a specific comparator should be defined, especially for serious, specific and frequent adverse events.