# New and old strategies for the signal detection in pharmacovigilance

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As known, signal detection is the main objective of pharmacovigilance. A signal is information on an adverse event that is new or incompletely documented, that may have causal relationship to treatment and is recognized as being worthy of further exploration (according CIOMS Working Group VIII on points to consider in the application of signal detection and signal management in pharmacovigilance). In other words, signal is based on information from one or more sources (including observations and experiments), suggesting an association (either adverse or beneficial) between a drug or intervention and an event or set of related events (e.g., a syndrome); it represents an association that is new and important, or a new aspect of a known association, and has not been previously investigated and refuted; and It demands investigation, being judged to be of sufficient likelihood to justify verificatory and, when necessary, remedial actions (Hauben & Aronson, 2009). It is thus evident that a signal in pharmacovigilance may arise from various data sources, such as spontaneous reporting databases, case reports, observational studies, clinical trials, prescription event monitoring, longitudinal administrative or claim databases, electronic health data. Over time, different strategies have been developed to bring out a signal in pharmacovigilance. Data mining of adverse drug reactions (ADR) in spontaneous reporting databases is the older methodology. The statistical techniques used in this context are Bayesian, e.g. the Information Component system used to analyses the WHO database, or classical approaches, e.g. the Proportional Reporting Ratio or the Reporting Odds Ratio, based on the disproportion principle. Multivariate methods such as logistic regression (that may use propensity score-adjustment) have the theoretical capability to reduce masking and confounding by co-medication and underlying disease (Harpaz R. et al., 2013). However, it is necessary to highlight the variability of results obtained in different studies based on this method and the daunting computational task it requires; more work is needed on its value for pharmacovigilance in the real world. Many of the statistical techniques used in data mining are the same as conventional methods used in pharmacoepidemiology. Their use differs in that there is no prior hypothesis, and power calculations are not performed. Also qualitative analyses can reveal safety signals that are not otherwise detected by data mining methods. Therefore data mining should not be relied upon as a substitute for traditional methods, particularly considering designated medical events, e.g. adverse events which are rare, serious and which are more likely to be associated with a high drug-attributable risk. In the selection of signals are taken in account the so-called SNIPs criteria: Strength, Novelty, clinical Importance, and Preventability of the signal (Almenoff J. et al., 2009). The large observational databases such as claims and electronic medical records databases are potentially useful as part of a larger signal detection and refinement strategy (Norén & Edwards,2009). Newer strategies in the signal detection are represented by the search of narrative description of adverse event in internet, e.g. in social forum or twitter (White R.W. et al., 2014; Noren G.N., 2014; Freifeld C.C. et al., 2014).

Anyway, the data mining of spontaneous reporting databases currently remain the main evidence source contributing to drug safety labeling changes (Lester J. et al., 2013).

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