

The UMC Measures of Disproportionate Reporting

A brief guide to their interpretation

The information component (IC)

The information component (IC), originally introduced through the BCPNN (Bayesian Confidence Propagation Neural Network), is a measure of the disproportionality between the observed and the expected reporting of a drug-ADR pair. A positive IC value indicates that a particular drug-ADR pair is reported more often than expected, based on all the reports in the database. Conversely, a negative IC value means that the drug-ADR pair is reported less frequently than expected. The higher the value of the IC, the more the combination stands out from the background.

The IC value is solely calculated from:

- the total number of reports in the database (N_{tot})
- the total number of reports no the ADR term (N_{adr})
- the number of reports on the drug (N_{drug}), and
- the total number of reports on the specific drug-ADR pair (N_{comb})

New reports may cause the IC to either increase or decrease. When the IC is calculated from large numbers, a new report is less likely to cause major fluctuation in the IC value. The $IC_{0.95}$ value is the lower limit of a 95% credibility interval for the IC. The credibility interval provides information about the stability of a particular IC value: the narrower the interval, the higher the stability.

The IC does not imply causality of a potential adverse reaction caused by a drug. The IC shows the quantitative dependency between the ADR and the drug based on the reporting to VigiBase®, the WHO international database of suspected adverse drug reactions.

If the IC value increases over time, and the $IC_{0.95}$ value is positive, this is suggestive of a connection between the drug and the adverse reaction. However, as alternative explanations for the positive IC need to be considered, clinical assessment remains essential in the identification of a signal.

Omega (Ω)

Omega (Ω) is, just as with the IC, a measure of disproportionate reporting, however not for a drug-ADR pair but for a drug-drug-ADR triplet. The purpose of Ω is to detect potential signals of drug-drug interactions.

For Ω , the expected reporting on a drug-drug-ADR triplet is

based on a model where both drugs add to the baseline risk of the ADR, independently of each other. A positive Ω indicates that the two drugs, when taken together, increase the risk of the ADR more than the sum of the risks attributable to each drug in itself.

Ω is calculated based on the following information:

- the relative reporting rate of the ADR for reports listing neither of the drugs (f_{00})
- the relative reporting rate of the ADR for reports listing drug 1 but not drug 2 (f_{10})
- the relative reporting rate of the ADR for reports listing drug 2 but not drug 1 (f_{01})
- the relative reporting rate of the ADR for reports listing both drugs (f_{11}).

As with the IC, Ω may fluctuate over time as new reports enter the database. Similarly, each Ω comes with a 95% credibility interval, whose lower limit is denoted $\Omega_{0.95}$. Ω does not imply causality of a potential drug-drug interaction. It is a quantitative measure of the deviation in reporting on the drug-drug-ADR triplet relative to a baseline mode where the drugs are assumed to independently add to the baseline risk of the ADR.

If Ω increases over time and $\Omega_{0.95}$ is positive, this is suggestive of a drug-drug interaction, based on the reporting to VigiBase. However, as alternative explanations for the positive Ω need to be considered, clinical assessment of the case series is essential in the identification of an interaction signal.

References

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