Pre-symposium training: Introduction to disproportionality analysis

Andreas Brueckner

PROTECT Symposium February 19-20 2015
Disclaimer

The views expressed in this talk are those of the author.
They do not necessarily represent those of Novartis.
Introduction to disproportionality analysis
Measures of disproportionality

IC vs ROR

EBGM vs PRR
Obs = 3
Exp = ?
Exp

ROR
RR = \frac{3}{\left( \frac{(3+7)(3+7)}{(3+7+7+83)} \right)} = 3

PRR = \frac{3}{\left( \frac{(7*(3+7))}{(7+83)} \right)} = 3.86

ROR = \frac{3}{\left( \frac{7*7}{83} \right)} = 5.08
3

10000

1 m.
\[ \text{RR} = \frac{3}{ \text{(...)} } = 3 \]

\[ \text{PRR} = \frac{3}{ \text{(...)} } = 3.006 \]

\[ \text{ROR} = \frac{3}{ \text{(...)} } = 3.012 \]
The same proportion (of reports on the ADR)
Which measures of disproportionality?
Disproportionality and Reporting Rates

Disproportionality methods do not estimate reporting rates. No drug usage is involved in the calculation.

While reporting rates can increase for all drug-AE combinations, measures of disproportionality are interdependent:

- An increase in a measure of disproportionality for one combination causes a decrease for other related combinations.
Rubber Dinghy

Rather like a rubber dinghy floating on the sea:

• if pressure causes one side to rise this causes the other to go down.

• As reports for one combination rise, this makes the expected count increase for other combinations involving the drug or the AE.

How to protect against spurious associations?
1 vs 0.001
RR: \( \frac{1}{0.001} = 1000 \)
Simple shrinkage

\[ \frac{\text{Obs} + 1/2}{\text{Exp} + 1/2} \]
RR: \frac{1}{0.001} = 1000
\frac{1+1/2}{0.001+1/2} = 3

Norén et al
Bayesian analysis: start from prior distribution
Here: our baseline assumption (until we have looked at data) is that the RR is 1 (most likely between 0.2 and 3)
Bayesian shrinkage

From data it appears that the RR is around 3
Bayesian shrinkage

Posterior distribution provides a compromise between data (likelihood) and prior. Balance between prior and likelihood depends on strength of prior and amount of data.
Bayesian credibility intervals provide a ‘most likely’ range for RR. In practice used much the same way as confidence intervals.
PRR \quad X^2 \quad C \quad RR = 1
Knowledge discovery process

Pattern discovery

Clinical review

Communication

Safety Database

Medical triages

Disproportionality analysis


