Features of case reports that support putative causal relationships between medicinal products and suspected adverse drug reactions.
Preliminary results from a scoping review

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Background

Bradford Hill's viewpoints, as he called them, also called guidelines, can be used to help determine whether an adverse event can form the basis of a pharmaco-vigilance signal. Beside a few applications of the viewpoints, little has been done to study which features of reports most often support such assessments.
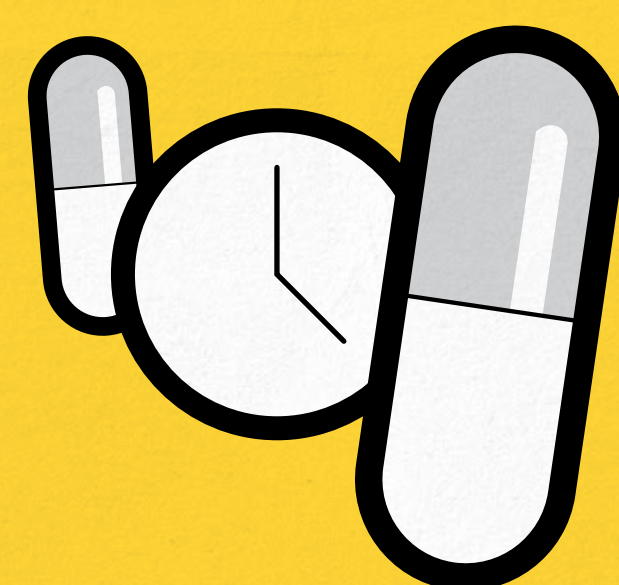
Objectives

To characterise the features of reports of adverse events used to support signals of suspected adverse drug reactions (ADRs).

When reports were screened these 3 features stood out as signs of a signal

Positive de/rechallenge
Withdrawal and re-administration of treatment results at first in an event's abatement and then in its reoccurrence.

TTO (Time to observation)
Occurrence of an event within a plausible, clinically compatible, time window, subsequent to drug administration.

One specific medicine
Within the reports: presence of a drug as the only "suspect" (as flagged by a reporter), or availability of sufficient medical history/free text information to rule out the role of e.g. underlying conditions as triggers of an event.

Signals

Methods

We retrieved electronic records (PubMed, EMBASE, Web of Science, PsycINFO) and grey literature records that described findings as signals of ADRs or signals of disproportionate reporting, without time or language restrictions; when necessary, we contacted regulatory agencies and authors to obtain other records or clarifications. We included previously undocumented signals and excluded records that did not explicitly describe findings as signals. We also charted the features of reports of suspected ADRs that authors advanced as supportive of signals and when possible coded them to mirror the Bradford Hill view-points, omitting biological plausibility and strength of association. One author performed title/abstract screening, eligibility assessment, and data charting; a second author independently cross-validated the findings. We analysed the data descriptively.

Results

We screened the titles/abstracts of 9525 electronic records and the full texts of 1509. We also reviewed the full texts of 2249 entries from websites/cited references/original authors, and included 1721 in the review. In all, we screened 11,774 unique records and included 2125. Of those, 1081 concerned clinical reviews of reports of ADRs (either alone or with other types of evidence); 136 of these mentioned at least one feature and concerned 228 distinct signals: 88 presented one feature, 80 two, 48 three, and 12 > three.
We recorded 440 instances of relevant features; the most frequent was positive dechallenge/positive rechallenge (217 occurrences), followed by temporality (130) and exclusion of competing causes/only one suspect drug in a report (53). Other signals depended on available information to ascertain the suspected ADRs (15), the report's consistency (12), and biological gradient (6).

Conclusions

In this scoping review positive dechallenge/rechallenge, temporality, and exclusion of competing causes were the most frequent factors supporting signals

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