

Supplementary materials

Suppl. 1 – Method for Table 1 (Exhaustivity of domains analysis)

This Part of the study was performed two reviewers (R2-ML and R3-PP) together. All the 21 tools in our study were listed in an MS word file. To be noted, all the tools have a specific set of questions. We investigated each set of questions to identify each domain covered. Please be advised that these domains are retrieved from different articles. Few examples of questions and domains (highlighted in bold) are listed below:

Are there previous conclusive reports on this reaction? – Domain noted “Previous reports”.

Did the adverse event appear after the suspected drug was administered? – Domain noted “Temporality”.

Did the adverse reaction improve when the drug was discontinued, or a specific antagonist was administered? – Domain noted “Dechallenge”.

Did the adverse reaction reappear when the drug was readministered? – Domain noted “Rechallenge”.

Are there alternative causes that could on their own have caused the reaction? – Domain noted “Alternative cause”.

Was the drug detected in the blood in concentrations known to be toxic? – Domain noted “Toxicity in fluid”.

Was the reaction more severe when the dose was increased, or less severe when the dose was decreased? – Domain noted “Dose response”.

Once all the domains covered by each tool were retrieved, the type of causality assessment tool, name of the author, year of publication, title of the article, and all the domains were listed in an excel sheet.

When a domain was covered by a tool, it was identified and marked with tick mark (☒) as shown in the table. Then, the percentage of domains covered by each tool was calculated to quantify the most exhaustive and comprehensive tool. Each question was considered the same weigh for this exercise as the goal was to assess exhaustivity of domains.

Suppl. 2 – Method for Table 2 (“Ease-of-use” in clinical setting)

This part of the study was performed by five reviewers (including four healthcare workers and one reviewer who has 3-year experience working in a pharmacovigilance center). These reviewers have respective experience in the Canadian (R1-JL and R2-ML), Indian (R3-PP), Hungarian (R4-SA), and Brazilian (R4-FREG) clinical context due to their respective origins. All the 21 tools were listed in an excel sheet with the name of author, year of publication and country of origin. Then all the reviewers were given all the 21 tools along with the excel sheet. All the reviewers were asked to go through all the tools and provide their inputs in 4 forms. All the 5 reviewers were also instructed of following.

1. Easy to use (well defined and simple set of questions).
2. Complex (difficult set of questions and not well defined).
3. Time consuming (more than one hour to answer all the questions).
4. Complex and Time consuming (difficult set of questions and not well defined and more than one hour to answer all the questions).

Each reviewer identified the easiest tools according to the clinical context of his/her country of origin.

All the communication was done in the form of email exchange. Once all the inputs were received, the scoring was done (Easy to use as 1, Complex as 2, Time consuming as 3, Complex and Time consuming as 4).

The mean value of the score assigned by the reviewers for each tool was calculated and rounded up to the nearest whole number.

Both reviewers from Canada agreed and counted as one single score; no weighted analysis was used to prevent over representativeness of Canada into the final score.