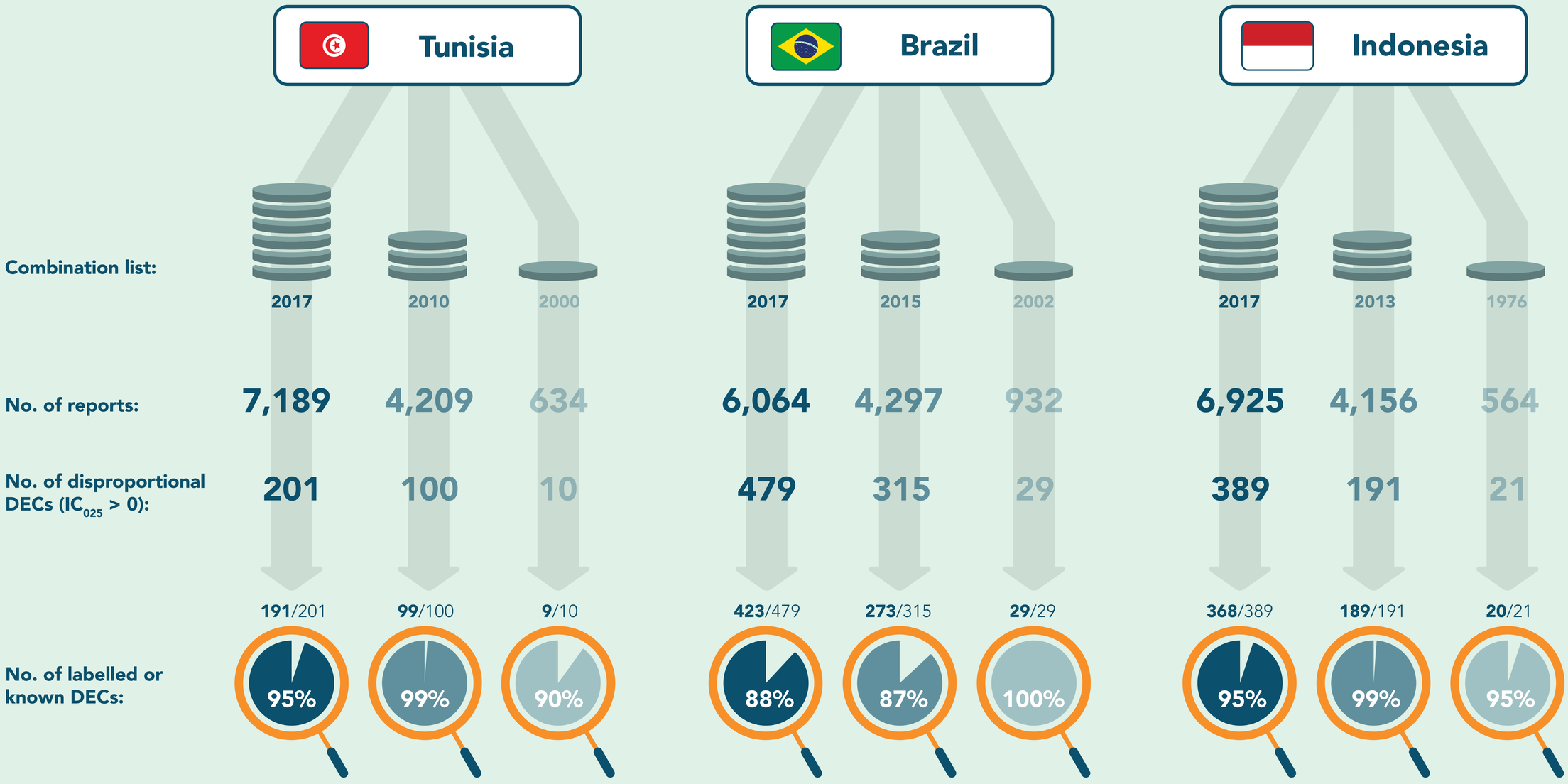
Disproportionality analysis in small national databases: **robust results but questionable utility**

Birgitta Grundmark[1], Yasunori Aoki[1,2], Lucie Gattepaille[1] and Ola Caster[1]. [1]Uppsala Monitoring Centre, Uppsala, Sweden; [2]National Institute of Informatics, Tokyo, Japan



Results from clinical assessment of small national subsets of VigiBase. DEC = drug-event combination; IC = Information Component

Background

Disproportionality analysis (DA) is the predominant quantitative approach to guide signal detection in collections of spontaneous reports.[1] Yet, there is little guidance for small national databases about the potential usefulness of DA in this setting. Preliminary results suggest statistical robustness of DA in national databases as small as 500 reports [2], but this does not ensure relevance for signal detection.

Objectives

To investigate the robustness of DA when used in small national databases of spontaneous reports.

Methods

Three countries (Tunisia, Brazil, and Indonesia) were selected from all countries with between 5,000 and 10,0000 reports submitted to VigiBase, the WHO global database of ICSRs, by end of 2017. For each country, one current (end of 2017) and two backdated lists of drug-event combinations (DECs) were generated. The latter were based on reports up to the respective years before the country surpassed 5,000 and 10,000 reports in VigiBase. These lists contained DECs statistically highlighted as disproportionately reported by IC (Information Component) analysis, defined as $IC_{025} > 0$.[3] Apart from drug and event names, basic reporting statistics and drug information (e.g. ATC groups) were provided. As an indicator of robustness, an experienced pharmacovigilance medical doctor (BG) identified combinations that were labelled or otherwise known.

Results

Six small (4,000-8,000 reports) and three very small (500-1,000 reports) national subsets of VigiBase were created (see above). In all nine resulting combination lists, the vast majority (87%-100%) of DECs were known. A slightly lower proportion was observed for Brazil, due to more reporting of lack of effect- and indication-related terms. The very small data sets resulted in only 10-30 disproportional DECs.

Conclusions

Because a substantial proportion of disproportionally reported DECs are already known, **DA in small and very small national data sets appears robust but may generate few signals. In addition, the total number of disproportional DECs is low, especially for the smallest data sets. Signal detection based on case-by-case assessment may therefore be more effective for national databases of the sizes studied.** Although some of the DECs may not have been known at the time of backdating the data, and therefore at the time would have been classified as unknown, this does not explain the results for the most recent combination lists. While these results were generated for only three countries, they agree well with previous results based on statistical properties for a large number of countries.

References

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Uppsala Monitoring Centre

Uppsala Monitoring Centre (UMC)
Box 1051, SE-751 40 Uppsala, Sweden
+46 18 65 60 60 www.who-umc.org