# Recommendations for **disproportionality analysis** in **small databases**

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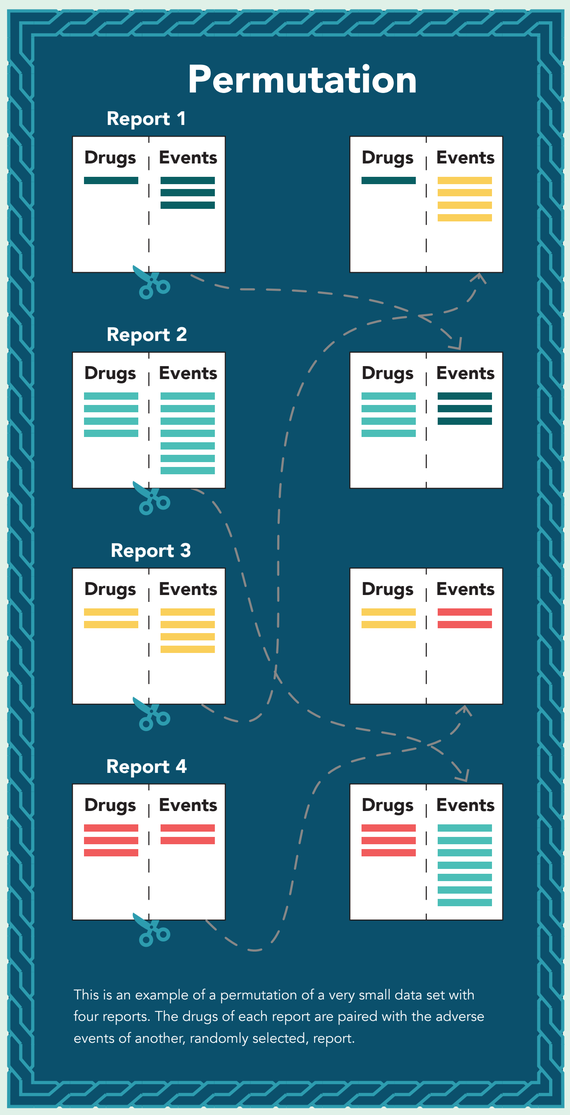
## Background

Detecting signals of hitherto unknown adverse reactions is of paramount importance to the ongoing monitoring of the safety of marketed medicines. Disproportionality analysis is the most common quantitative approach to guide signal detection in collections of spontaneous reports. Yet, little is known about when disproportionality analysis can be expected to be robust. Such knowledge would be useful for countries and other organizations with newly set up pharmacovigilance systems, and for signal detection software users.

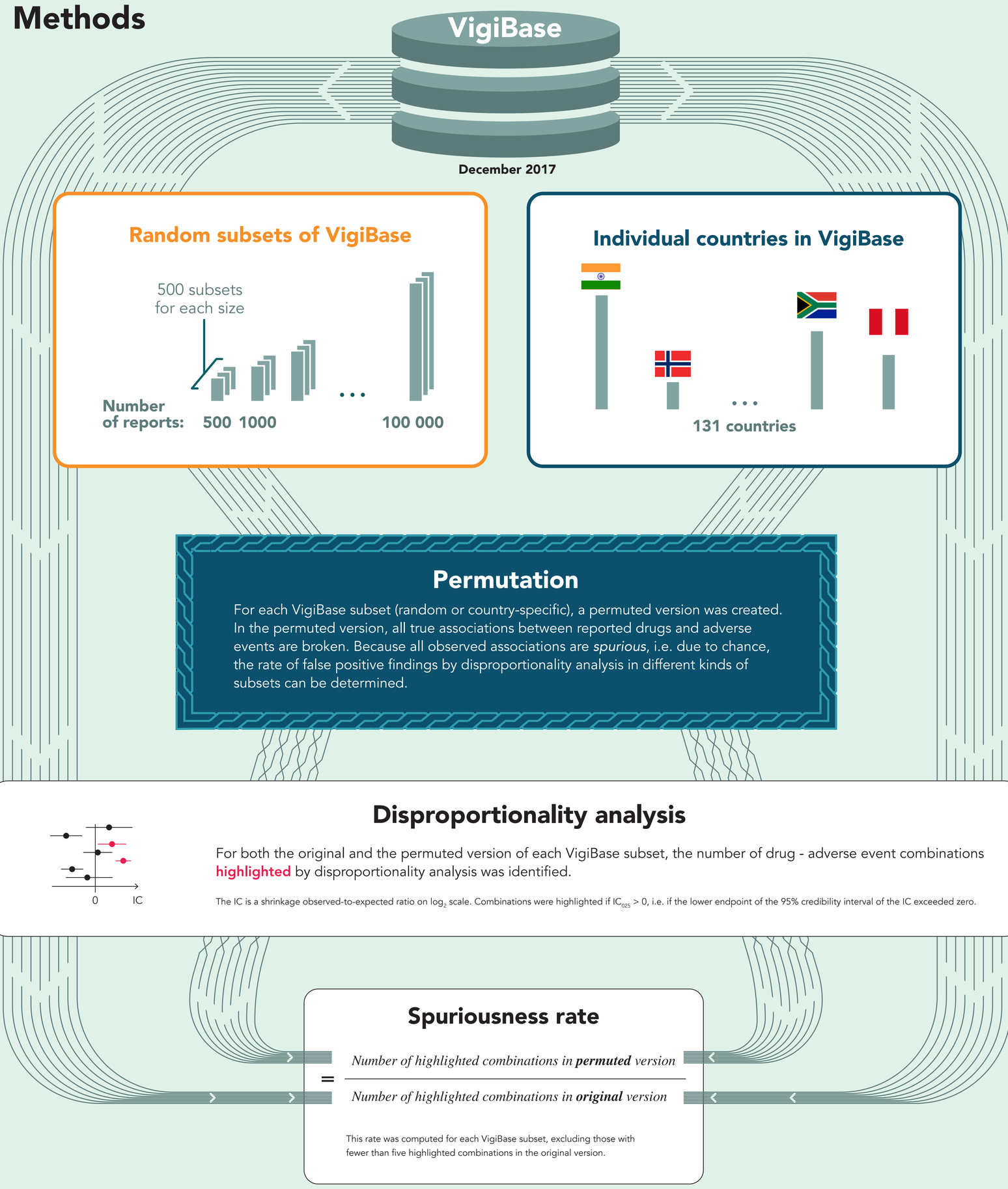
## Objectives

To determine safe lower limits on the number of reports for performing disproportionality analysis in (i) general subsets of larger databases, and (ii) country-specific databases.




This is an example of a permutation of a very small data set with four reports. The drugs of each report are paired with the adverse events of another, randomly selected, report.

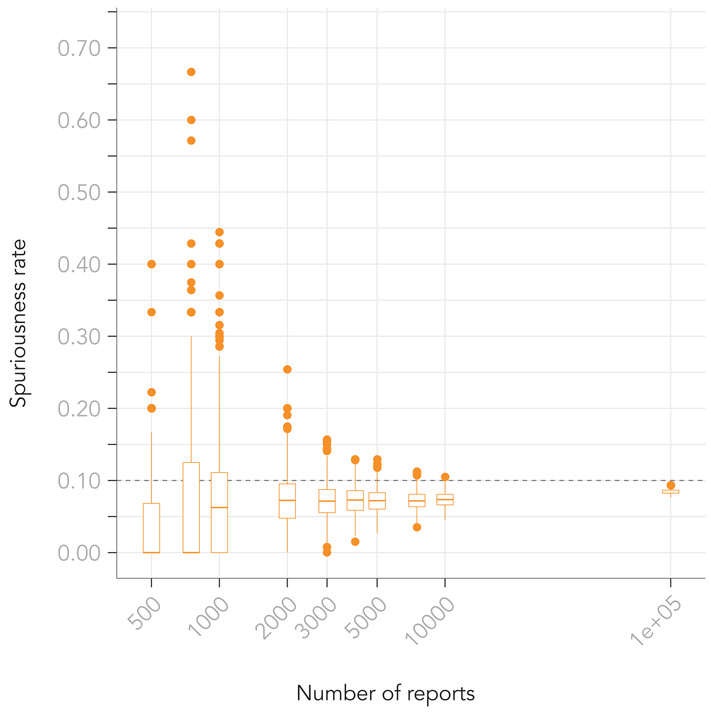
## Methods




## Results

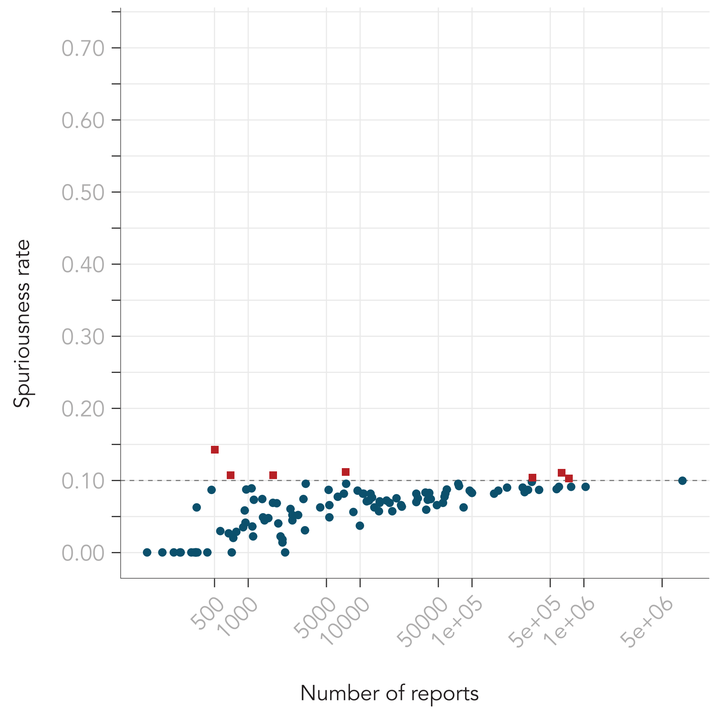
### Random subsets of VigiBase

- High or very high spuriousness rates common for subsets with 2,000 or fewer reports
- Consistently decreasing variability with increased subset size




### Individual countries in VigiBase

- Generally low spuriousness rates, and no increase for countries with few reports
- 21 countries were excluded because of too few associations; all of these had fewer than 500 reports




## Conclusions

For disproportionality analysis in generically constructed subsets of databases of spontaneous reports, we recommend a lower subset size of about 3,000-5,000 reports. For disproportionality analysis in country-specific databases, we recommend at least 500 reports. However, while disproportionality analysis may produce robust results in very small databases, its utility is likely to be minor as few associations will be generated. Signal detection based on case-by-case assessment is likely to be more effective in such cases.

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