

Case Study 1 – Identification of under-reported adverse events

In this case study, we consider a double blind randomized phase III study in infectious disease. More than 5000 patients were randomized across 150 sites from 18 countries. A total 400 variables were collected in the CRF. A run of CluePoints was performed at the beginning of the follow-up period to detect any atypical site behavior and associated patient data issues.

Approximately 11,000 p-values (a single p-value being the probability of an observed result arising by chance) were generated by the SMART™ engine. The CluePoints scoring algorithm identified one site as strikingly different from the other sites. **Figure 1** shows the distribution of the scores for all study sites. The center labeled INV204 had the smallest score as compared to the other centers and was clearly outside the normal distribution expected. An inspection of the individual tests that determined the statistical significance for this center revealed atypical distribution characteristics for the adverse events collected, as shown in **Figure 2**. On the one hand, the rate of adverse event was far below the average and on the other hand, most of the adverse events reported were serious. In other words, non-serious adverse events were reported less than expected. With this finding in mind, the sponsor triggered a monitoring visit of the site and the CRA ultimately confirmed a training issue for the site.

Conclusion

Thanks to the early discovery of the issue, the sponsor had the opportunity to take corrective actions and perform re-training of the site. In the subsequent runs of CluePoints, the site was ranked down which confirmed the effectiveness of the actions taken.

FIGURE 1 – Site scoring: histogram of score

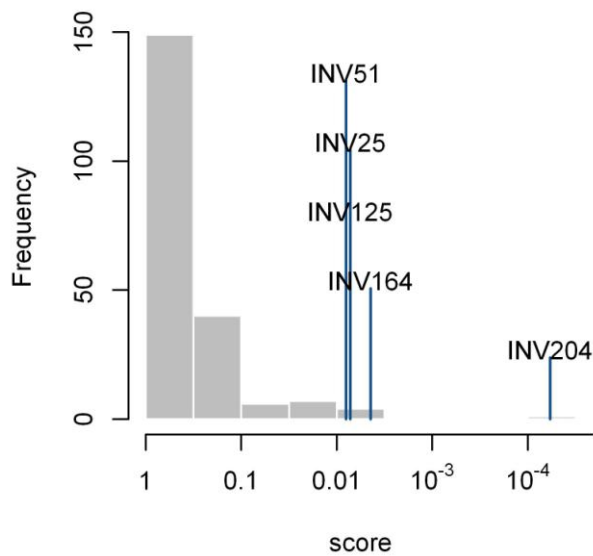


FIGURE 2 – Distribution characteristics of adverse events

