

## Oral Presentations

### O.07 Effect of Well Established Drug-Event Associations on the Generation of New Signals in Spontaneous Reporting Databases

A. Pariente,<sup>1,2,3</sup> P. Avillach,<sup>3</sup> F. Thiessard,<sup>2,3,4</sup> G. Miremont-Salamé,<sup>1,3</sup> A. Fourrier-Reglat,<sup>1,2,3</sup> F. Haramburu,<sup>1,3</sup> N. Moore<sup>1,2,3</sup>

1 INSERM U657, Bordeaux, France; 2 Université Bordeaux 2, Bordeaux, France; 3 CHU de Bordeaux, Bordeaux, France; 4 INSERM U593, Bordeaux, France

**Background:** Automated disproportionality analysis of spontaneous reporting is increasingly used routinely, but it may be influenced by the presence in the database of well-established drug-event associations which could hamper the generation of new signals.

**Objective:** To explore the influence of well-established drug-event associations on the generation of new safety signals in spontaneous reporting databases.

**Methods:** Within 16 years of spontaneous reporting in the French Pharmacovigilance database (January 1986 to December 2001), disproportionality of reporting was tested before and after removing reports concerning well-established drug-event associations for six events of interest (gastro-intestinal haemorrhage, headache, hepatitis, myalgia, myocardial infarction, and haemorrhagic stroke) using the case non-case approach.

**Results:** In the whole database, we initially identified 51 signals for gastrointestinal haemorrhage. After removing reports involving NSAIDs, thrombolytic, anticoagulant and antiplatelet agents, 3 new signals appeared (incriminating prednisone, rivastigmine and isotretinoïde) and 6 disappeared, concerning drugs frequently associated to the above-mentioned drugs in the removed reports. The same approach was applied to other events: after removing well-known drugs associated with each event of interest, for headache 5 signals appeared whereas 1 disappeared, for hepatitis NEC 30 appeared whereas 4 disappeared, for myocardial infarction 1 appeared whereas 1 disappeared and for haemorrhagic stroke 3 appeared whereas 33 disappeared.

**Conclusion:** These results suggest that using the whole database as a comparison group for disproportionality analysis does not provide a good estimation of the baseline risk of an event when it includes drugs known to be associated with the event. Excluding these drugs from the comparison group could greatly improve the efficiency of automated methods of signal generation.