Drug Safety 2007; 30 (10): 919-990
0114-5916/07/0010-0919/$44.95/0

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Oral Presentations

O.08 An Automated Method to Eliminate Bias Induced by Co-Prescription in Safety Signal Generation using Spontaneous Reporting Databases

P. Avillach,[3] *A. Pariente*,[1,2,3] *F. Thiessard*,[2,3,4] *G. Miremont-Salamé*,[1,3] *A. Fourrier-Réglat*,[1,2,3] *F. Haramburu*,[1,3] *N. Moore*[1,2,3]

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

Introduction: Automated disproportionality analysis of spontaneous reporting is increasingly used routinely. It can generate a huge amount of signals that require time-consuming expert assessment, most of which irrelevant. False positive signals may be generated by drug co-prescription. For instance, a signal for acetylsalicylic acid and gastro-intestinal (GI) bleeding could induce a second signal for ascorbic acid because of their frequent co-prescription.

Objective: To minimise the number of signals generated by confounding due to co-prescription.

Methods: We present here an automated method based on a backward stepwise removal of all reports involving the drug leading to the most important signal for an event in the database, until no signal remains. We tested this method for gastro-intestinal (GI) bleeding, headache, hepatitis NEC, myocardial infarction and haemorrhagic stroke over 16 years of spontaneous reporting in the French Pharmacovigilance database. Signals were identified using the case non-case approach, the most important being the one with the highest Reporting Odds Ratio (ROR) IC95% lower limit. When the most important signal for an event was identified in the whole database, all reports concerning the involved drug were deleted and a second database was generated, where another signal could be identified. The method ran until no signal remained.

Results: In the whole database, we initially identified 48 signals for GI bleeding, 55 for headache, 19 for hepatitis NEC, 38 for myocardial infarction and 48 for haemorrhagic stroke. After running the backward stepwise procedure, 17 of these initially identified signals disappeared for GI bleeding, 42 for headache, 14 for hepatitis NEC, 15 for myocardial infarction and 37 for haemorrhagic stroke. Most of these signals concerned drugs classically prescribed in association with those involved in the backward removed observations.

Conclusion: These results suggest that numerous false positive signals generated by automated methods could be eliminated by exploring biases such as channelling due to co-prescription. However, such an approach should be refined so that potential interactions between co-prescribed drugs may be detected.