

Reliability of Drug-Drug Interaction Measurement on Real-World Data: The ReMIAMes Project

Catherine DUCLOS^{a,1}, Nicolas GRIFFON^{a,b}, Christel DANIEL^{a,b},
Guillaume BOUZILLÉ^c, Denis DELAMARRE^c, Stefan DARMONI^{a,d},
Laurent TOUBIANA^a and Julien GROSJEAN^{a,d}

^a Sorbonne Université, Université Sorbonne Paris Nord, INSERM, Laboratoire d'Informatique Médicale et d'Ingénierie des connaissances en e-Santé, LIMICS, F-75006 Paris, France

^b Innovation and Data, IT Department, AP-HP, Paris, France

^cInserm, Laboratoire Traitement du Signal et de l'Image - UMR 1099, Centre Hospitalier Universitaire de Rennes, Université de Rennes 1, Rennes, France

^dDepartment of Digital Health, Rouen University Hospital, France

Abstract. The ReMIAMes project proposes a methodological framework to provide a reliable and reproducible measurement of the frequency of drug-drug interactions (DDI) when performed on real-world data. This framework relies on (i) a fine-grained and contextualized definition of DDIs, (ii) a shared minimum information model to select the appropriate data for the correct interpretation of potential DDIs, (iii) an ontology-based inference module able to handle missing data to classify prescription lines with potential DDIs, (iv) a report generator giving the value of the measurement and explanations when potential false positive are detected due to a lack of available data. All the tools developed are intended to be publicly shared under open license.

Keywords. Methodology, Quality, Data warehouse, drug drug interaction

1. Introduction

Drug-drug interactions (DDI) are a major source of adverse events and care consumption (1) that could be avoided if they were taken into account at the time of prescribing. Care data generated during hospitalization are now integrated in clinical data warehouses (CDW). Detection of DDIs present in CDWs is therefore a mean to control the quality of prescriptions and their pharmaceutical review process. To provide reliable and reproducible results, observational studies on real-world data have to rely on robust methodological basis (2). Many factors related to data source, DDI definition, drug attributes or patient should be taken into account to correctly analyze DDIs (3).

The objective of the project ReMIAMes is to propose a methodological framework to provide a reliable and reproducible measurement of DDIs frequency when performed on different CDWs.

¹ Corresponding Author, Catherine Duclos, LIMICS, Université Sorbonne Paris Nord, 74 rue Marcel Cachin, Bobigny, France; E-mail: catherine.duclos@inserm.fr

2. Methods

The French Thesaurus of DDIs (4) is the reference material for DDIs. These DDIs are analyzed to identify contextual attributes that may restrict their scope. It results in a conceptual model of DDI and requirements on minimum dataset to be provided by CDWs that are translated into a common model in a standard formalism (FHIR). Three University Hospital (APHP, Rouen, Rennes) participate. They have audited their data (drug administration data, lab data, clinical data) to identify their availability, their formalism. Several cycles of process of extraction, transfer, loading (ETL) are performed depending of the difficulty of providing certain requested data and according to a pattern of increasing complexity. A DDI ontology based on OWL formalism is modeled. Data received from CDWs are considered as instances and are used to classify pairs of prescription lines as potential DDI. According to the availability of information to decide, detected DDIs are classified as true positives, or potential false positives. Several rounds of data analysis are performed to identify the causes of false positives and let data providers to improve their ETL to reduce these false positive.

3. Results

The project will result in recommendations for ETL, open data to populate the ontology, ontology of DDIs and algorithms to analyze the data. A platform will integrate all these components.

4. Discussion Conclusion

The project ReMIAMes project is part of the production of methodological frameworks for the analysis of CDW data. It aims to improve the relevance and the quality of CDW data and to raise awareness of their impact in order to make analyses more reliable.

Acknowledgments

This study was granted by ReMIAMes (Ressources et méthodes libres pour la détection des interactions médicamenteuses dans les entrepôts de données de santé) ANR-19-CE19-0025-01

References

- [1] Dechanont S, Maphanta S, Butthum B, Kongkaew C. Hospital admissions/visits associated with drug-drug interactions: a systematic review and meta-analysis. *Pharmacoepidemiol Drug Saf.* mai 2014;23(5):489-97.
- [2] Agency for Healthcare Research and Quality. Developing a Protocol for Observational Comparative Effectiveness Research: A User's Guide.
- [3] Horn J, Ueng S. The Effect of Patient-Specific Drug-Drug Interaction Alerting on the Frequency of Alerts: A Pilot Study. *Ann Pharmacother.* nov 2019;53(11):1087-92.
- [4] Agence nationale de sécurité du médicament et des produits de santé. Thésaurus des interactions médicamenteuses [Internet]. Disponible sur: <https://ansm.sante.fr/documents/referance/thesaurus-des-interactions-medicamenteuses-1>