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Use of Real-World Data to Support Adverse Drug Reactions Prevention During ePrescription

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Abstract. Adverse Drug Reactions (ADRs) are a crucial public health issue due to the significant health and monetary burden that they can impose. Real-World Data (RWD), e.g., Electronic Health Records, claims data, etc., can support the identification of potentially unknown ADRs and thus, they could provide raw data to mine ADR prevention rules. The PrescIT project aims to create a Clinical Decision Support System (CDSS) for ADR prevention during ePrescription and uses OMOP-CDM as the main data model to mine ADR prevention rules, based on the software stack provided by the OHDSI initiative. This paper presents the deployment of OMOP-CDM infrastructure using the MIMIC-III as a testbed.

Keywords. Real-World Data, Adverse Drug Reactions, Drug Safety, ePrescription

1. Introduction

Drug safety is a crucial issue for public health, as adverse drug reactions (ADRs) can have significant and lasting consequences on the health and well-being of individuals. The prevention of ADRs or drug-drug interactions (DDI), promotes the effective treatment of illnesses and reduces healthcare costs [1]. “Intelligent” technical paradigms, including Machine Learning (ML) and Knowledge Engineering (KE), can assist

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healthcare providers (HCP) during the prescription process to ensure safe medications for their patients [2]. To this end, Artificial Intelligence (AI) can be used to analyze Real-World Data (RWD) i.e., patient medical history, allergies, and medication.

PrescIT is a nationally-funded project aiming to support safe e-Prescription focusing on ADRs and drug-disease interactions. PrescIT employs three components: a set of Knowledge Graphs employing expert knowledge, a dynamic workflow module using Business Process Management Notation (BPMN) to exploit clinically validated Therapeutic Prescription Protocols [3], and lastly, RWD analysis to identify potentially useful drug usage patterns and drug safety issues, based on the power of plain statistics or AI/ML [4]. Along these lines, the OMOP-CDM and open-source software provided by OHDSI (Observational Health Data Sciences and Informatics) are engaged. This paper outlines the PrescIT RWD infrastructure using MIMIC-III as a data testbed.

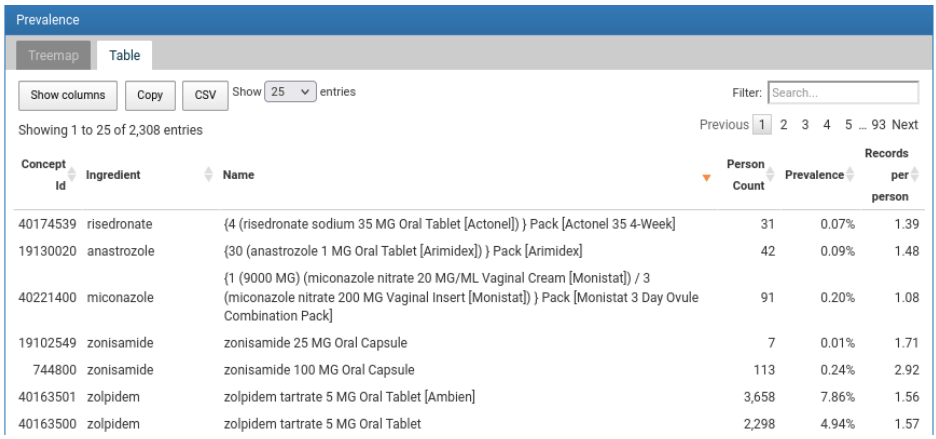
2. Methods

The OMOP-CDM is a standardized flexible and scalable data model, maintained by OHDSI to be used for observational studies [5]. The model is designed to harmonize data from diverse sources, including electronic health records, administrative claims, and registries, into a common structure that facilitates large-scale analyses. The model includes patient data (e.g., demographics, diagnosis, laboratory results, vital signs, etc.) but also interlinked reference vocabularies/terminologies, such as SNOMED-CT, WHO-ATC, and RxNorm, to ensure consistency and interoperability across different data sources. OMOP-CDM has been used for a wide range of analyses, including cohort studies, comparative effectiveness studies, and safety analyses across large datasets containing potentially millions of patient records. OMOP-CDM is also used as the main reference data model for the European Medicines Agency DARWIN infrastructure [6].

As part of the PrescIT project, an OMOP-CDM infrastructure is used to mine potentially unknown ADR prevention rules which could be used in the PrescIT CDSS. Due to legal and ethical issues preventing the use of real clinical data, MIMIC-III (Medical Information Mart for Intensive Care III) is used as the testbed dataset. MIMIC-III is a large, freely available -upon request- relational database that contains anonymized health data for over 40,000 patients [7]. MIMIC-III was chosen over the latest version available, i.e., MIMIC-IV since at the time of the selection version III contains additional data not present in version IV (free text elements to be used for Natural Language Processing - NLP). MIMIC-III's EHR data were transformed into OMOP-CDM format (v5.4) utilizing the openly available tools [8]. Moreover, to support the qualitative and quantitate evaluation of the EHR data, OHDSI community-based software (mainly Atlas) was also utilized to provide web-based interactive data analytics.

3. Results

This section outlines the use of these tools in the context of the PrescIT project. For example, **Figure 1** shows an overview of drug usage while **Figure 2** depicts a screen for creating a cohort comparison regarding drug exposure based on the available data.


Prevalence

Treemap | Table

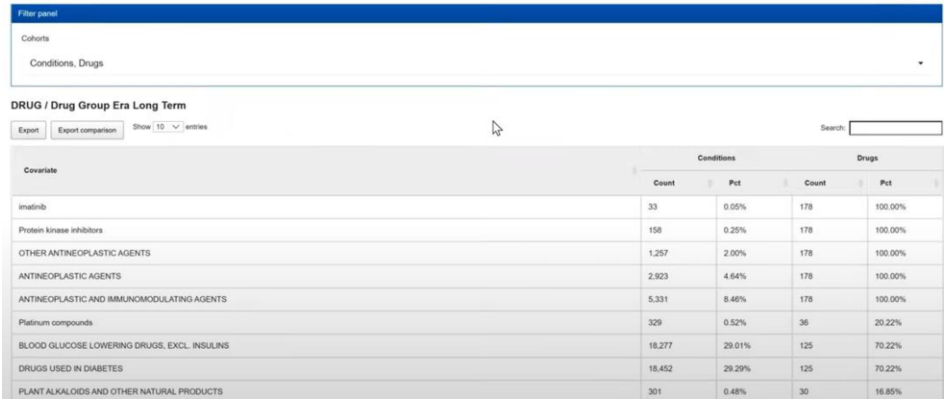
Show columns | Copy | CSV | Show 25 entries | Filter: Search...

Showing 1 to 25 of 2,308 entries | Previous 1 2 3 4 5 … 93 Next

Concept Id	Ingredient	Name	Person Count	Prevalence	Records per person
40174539	risedronate	{4 (risedronate sodium 35 MG Oral Tablet [Actonel]) } Pack [Actonel 35 4-Week]	31	0.07%	1.39
19130020	anastrozole	{30 (anastrozole 1 MG Oral Tablet [Arimidex]) } Pack [Arimidex]	42	0.09%	1.48
40221400	miconazole	{1 (9000 MG) (miconazole nitrate 20 MG/ML Vaginal Cream [Monistat]) / 3 (miconazole nitrate 200 MG Vaginal Insert [Monistat]) } Pack [Monistat 3 Day Ovule Combination Pack]	91	0.20%	1.08
19102549	zonisamide	zonisamide 25 MG Oral Capsule	7	0.01%	1.71
744800	zonisamide	zonisamide 100 MG Oral Capsule	113	0.24%	2.92
40163501	zolpidem	zolpidem tartrate 5 MG Oral Tablet [Ambien]	3,658	7.86%	1.56
40163500	zolpidem	zolpidem tartrate 5 MG Oral Tablet	2,298	4.94%	1.57

Figure 1. OMOP-CDM Drug Exposure Report

There are additional functionalities provided by Atlas, i.e., patient-level prediction, or population-level estimation which can be used to explore the causal effects of exposures (drug usage, medical procedure, etc.) on specific health outcomes by estimating an exposure's effect on the risk of an outcome, either as compared to no exposure or another exposure. Some of those tools use advanced statistics/ML techniques that could be further fine-tuned or adapted to fit a model supporting e-prescription needs. Lastly, OMOP-CDM can also support NLP on free-text elements.


Filter panel

Cohorts

Conditions, Drugs

DRUG / Drug Group Era Long Term

Export | Export comparison | Show 10 entries | Search:

Covariate	Conditions		Drugs	
	Count	Pct	Count	Pct
imatinib	33	0.05%	178	100.00%
Protein kinase inhibitors	158	0.25%	178	100.00%
OTHER ANTINEOPLASTIC AGENTS	1,257	2.00%	178	100.00%
ANTINEOPLASTIC AGENTS	2,923	4.64%	178	100.00%
ANTINEOPLASTIC AND IMMUNOMODULATING AGENTS	5,331	8.46%	178	100.00%
Platinum compounds	329	0.52%	36	20.22%
BLOOD GLUCOSE LOWERING DRUGS, EXCL. INSULINS	18,277	29.01%	125	70.22%
DRUGS USED IN DIABETES	18,452	29.29%	125	70.22%
PLANT ALKALOIDS AND OTHER NATURAL PRODUCTS	301	0.48%	30	16.85%

Figure 2. Cohort Comparison

4. Discussion

The functionalities provided by the Atlas tools can facilitate retrospective observational studies and even analyses which could be conducted as part of the PrescIT CDSS. A set of common analytics can be executed on that model's data, allowing already developed tools and analyses to be applied to a new dataset easily, after an initial effort to align the data from a third-party data provider. Additionally, independent data scientists can develop analytics that the data providers themselves can execute within their infrastructure, thus minimizing potential data safety and regulatory issues.

It should be noted that real clinical data have not been used due to legal and administrative issues. However, the data provided by MIMIC-III were sufficient for the testing and integration of OMOP-CDM with the project's platform, and the infrastructure already in place could work with real data when they become available. Another critical challenge worth to be noted is that while OMOP-CDM can support NLP, still, modules trained on English-language-based models cannot be directly applied to the Greek text.

5. Conclusion

RWD has huge potential in terms of drug safety but is often being underutilized due to a lack of interoperability and regulations. The PrescIT infrastructure supports RWD's use to mine potential ADR prevention rules but there are still issues to be tackled. Technical data modeling is a time-consuming procedure imposing unique challenges for each original data source. Data access, and privacy concerns will always be a blocking issue when dealing with hospitals and patients. All analytics used in the context of CDSS should be validated and moreover, they should be incorporated seamlessly into an existing clinic's workflow to maximize the system's adoption rates.

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