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| Presentation type (select one): | Poster |

International RxNorm Extension to support the expansion of the OHDSI research network beyond the US.

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Abstract

We are presenting an extension of the RxNorm Drug Naming and Interoperation System to include systematic drug terminologies from all over the world, as well as a Semi-automated System to create and maintain this RxNorm Extension to support the expansion of the OHDSI research network beyond the US. We present both the mechanism of adapting drug terminologies from Canada, the UK, Germany, France and Australia, the structural extensions necessary to make the extension possible for the OHDSI use cases, and the challenges arising from combining different local drug markets into a common system.

Introduction

The OHDSI network research started as a scientific collaborative out of Columbia University in New York, USA. However, international participation would greatly benefit this network for a number of reasons: First, it is our belief that clinical research is inherently global, as the similarities between populations in different parts of the world by far outweigh the differences. Secondly, the solution of many clinical research problems requires well sized samples in order to develop statistics of effects that might be weak, biased or happen in the shadow of a strong background. And finally, a network that spans different social and healthcare systems allows avoiding bias and understanding the effects introduced by those healthcare systems and distinguishing them from the biological effects on the outcomes of treatment interventions.

Such an expansion to international participants creates the needs to get the data into the OMOP Common Data Model. Part of it is the ability to define the semantic content of the data through the OMOP Standardized Vocabularies, which is commonly but somewhat imprecisely referred to as "Mapping". This Mapping consists of

1. Mapping of local coding scheme to a set of Standard Concepts, or
2. Creating new Standard Concepts and incorporating them into the existing hierarchy.

The amount and nature of the effort required for such an effort is very different for the different Domains. Conditions are inherently “international”, as people generally have the same diseases, and there is are international initiatives to define them: ICD10 and their modifications (ICD10CM for US, ICD10GM for Germany) and SNOMED-CT. However, in the Drug Domain captures Concepts describing the exposure of patients to drug products available on local markets, the knowledge of the content of these products, and their participation in classification systems. These local markets are governed by the authorities of the countries (even though there is some harmonization efforts going on), and as a result there are common products all over the world, but drugs distinct to a subset or a single market.

In the US, there are several organizations providing a comprehensive system of drugs sold in the country. Some of them are commercial vendors to EMR systems, such as First Databank, GPI or Multum. However, a very well curated system is also available for free by the National Library of Medicine, called RxNorm. It consists of:

1. Unique Concepts for each drug, with a Concept identifier (RxCui), defining it unambiguously through a set of attributes:
	1. Its ingredients
	2. The strengths of the ingredients
	3. The Dose Form
	4. The Brand Name (if there is one)
	5. The total volume or quantity.

Each of these components is also represented as a Concept, and so are combinations of attributes that don't represent full products, but semantic notions of exposure to patients, such as Clinical Drug Components (Ingredients and strength, but without a specified Dose Form or Brand Name). The latter proved very useful when dealing with partial clinical data.

1. A standardized naming convention for all Concepts.
2. A set of relationships between these Concepts. This set creates a graph, which connects Concepts of higher specificity to those of lower specificity, making hierarchical querying of data very elegant and reliable.

Such a system is not available internationally, preventing researchers with clinical data containing drugs to participate in the OHDSI research network. We therefore created RxNorm Extension, which contains drugs available on international markets in the RxNorm System: With Concepts constructed by the same principles and attributes, connected through the graph.

**Solution**

We created a system that can add any international systematic drug terminology to the existing RxNorm implementation in the Standardized Vocabularies. Note that this implementation differs in its format from the original provided by the NLM, but leaving its content or logic almost entirely intact.

* Active Ingredients not approved for marketing in the US are added
* Dose Forms not used in the US are added, which is not common
* Brand Names not used in the US are added.
* Additional attributes are added that are necessary to project foreign drug markets:
	+ Box Size: Prescription drugs are mostly pre-packed to standardized products, similar to the situation in the US Over-the-Counter market. Therefore, it is necessary to capture this attribute in the RxNorm Extension, as prescription orders generally don't contain a variable of drug amount.
	+ Supplier: RxNorm does not normalize Suppliers, even though that the NDC system does. In international markets, this attribute is also essential since coding systems explicitly state the supplier.
* All relationships between Concepts, which cross between RxNorm and RxNorm extension depending on whether or not attributes exist in RxNorm or not.
* Relationship to classification systems such as ATC.

All together, a new vocabulary "RxNorm Extension" is created containing all the additions as specified above. The RxNorm and RxNorm Extension vocabularies together form a comprehensive Drug Domain able to codify the local drug market of any country and therefore the patient data containing the drug exposure in these markets.

**Result**

We show that it is possible to create a RxNorm Extension and project international drug markets to it. We will provide details about specific international drug markets in Canada (DPD), UK (dm+d), France (BDPM), Germany (AMIS), Japan (JMDB), Australia (AMT). We will discuss the quality of incoming drug systems, as well as that of the RxNorm Extension derived from them. We also provide details about general trends of sizes, overlap with the US and with each other, national preferences of forms, branding, dosing etc. for each market.