Research Proposal

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Background:

One of IMEDS research agenda goals for 2015 is Enhancing Safety Surveillance. We hope to contribute novel methods to classify drugs by pregnancy risk. Many users of big data in healthcare may struggle with analyzing dispensed clinical drug by their drug class or individual ingredients. Within this project, we hope to link data in CDM format with APIs for RxNorm.

Eighty percent of the pregnant women in the United States have at least one drug prescription during pregnancy. The U.S. Food and Drug Administration (FDA) regulates the labeling of drug products and has established five risk categories for drug use during pregnancy. This classification was introduced in 1979. New FDA regulations (June 30, 2015) deeply revised the pregnancy and lactation labeling by eliminating these categories and replacing them with narrative summaries describing the risk of the drug and the data supporting this description. In a recent study on Medicaid data, 40% of pregnant women were dispensed at least one medication from categories D or X, for which there is positive evidence of human fetal risk.

Research Objectives and Aims:

To assess the potential risk in drug prescriptions during pregnancy, with respect to the new FDA standard.

Scope/Proposed Approach:

As a proxy for the FDA standard, we are planning to use the “pregnancy recommendations” from a reference textbook (Briggs, 10th ed. 2015). For each ingredient, it provides the level of risk (contraindicated, high risk, moderate risk, low risk, probably compatible and compatible with pregnancy), the source of evidence, if any (human or animal data), and other information as appropriate (trimester, dose, drug association restrictions). We will analyze drug prescription data (DRUG_EXPOSURE OMOP CDM table) from the most suitable IMEDS Cloud lab datasets . (Patient-level data is required in order to be able to count the number of pregnant women exposed to a risk. Data aggregated by prescription drug would not support this analysis.)

We will rely on procedure codes for delivery to identify pregnant women (13 CPT codes covering all vaginal deliveries and caesarean sections). We will analyze drugs dispensed up to 1 year prior to delivery or C-section to cover both pre-partum and pregnancy. We will consider dispensed during pregnancy those drugs dispensed during a period of 270 days prior to delivery. We will use the RxNorm API to relate drugs from the claims data to the reference. We will derive the risk and supporting evidence associated with each drug, taking the highest risk in case of multi-ingredient drugs. We will restrict our analysis to systemic drugs, because topical drugs generally pose a much lower risk.

Of note, this study will be greatly facilitated by the fact that the IMEDS Cloud lab datasets conform with the OMOP CDM, which already normalizes prescription drugs to RxNorm.

Impact:
There are a few published studies on potential risk in drug prescriptions during pregnancy, but these studies have been performed in reference to the old FDA categories (i.e., not systematically taking into account the existence of human data as evidence of human fetal risk). Moreover, these studies were limited in scale and performed on narrow populations (e.g., Medicaid patients). The proposed analysis on drug dispensing data with the Briggs reference addresses both these issues.

Experience:
Dr. Ferdinand Dhombres, MD, PhD, provides practicing clinician expertise as well as knowledge of informatics.
Dr. Vojtech Huser, MD, PhD, has experience with CDM data model and cloud lab environment and has R language experience. He also has experience with existing research lab environment.
Dr. Olivier Bodenreider, MD, PhD, is senior informatics expert in ontologies, terminologies, drug classifications and data analysis.

Timeline:
We expect the project to take 12 months. (March 2016 – February 2017). We plan to publish papers for the methodological framework and case studies.

References:

1. Analyzing U.S. prescription lists with RxNorm and the ATC/DDD Index. Bodenreider O, Rodriguez LM. AMIA Annu Symp Proc 2014:297-306.
2. Exploring adverse drug events at the class level. Winnenburg R, Sorbello A, Bodenreider O. J Biomed Semantics. 2015 May 1;6:18. doi: 10.1186/s13326-015-0017-1. eCollection 2015.