Observational Medical Outcomes Partnership and Mini-Sentinel Common Data Models and Analytics: A Systematic Data Driven Comparison

Xiaofeng Zhou, Xu Yihua, Brandon Suehs, Abraham Hartzema, Michael Kahn, Yola Moride, Brian Sauer, Qing Liu, Keran Moll, Margaret Pasquale, Vinit Nair, and Andrew Bate

Pfizer Inc, New York, NY, USA; Humana Inc, Louisville, KY, USA; College of Pharmacy, University of Florida, Gainesville, FL, USA; Department of Pediatrics, University of Colorado, CO, USA; Faculty of Pharmacy, Université de Montreal, Montreal, QC, Canada; University of Utah, UT, USA

OHSDI presentation 9/29/2015  Bram Hartzema &Brian Sauer
Disclosure

• Xiaofeng Zhou, Qing Liu, and Andrew Bate are employees and stockholders of Pfizer Inc.

• Yihua Xu, Brandon Suehs, Keran Moll, and Margaret Pasquale are employees of Comprehensive Health Insights, a wholly owned subsidiary of Humana. Brandon Suehs is a stockholder of Humana. Vinit Nair is an employee of Comprehensive Health Insights, and serves as the primary investigator from Humana for both the Observational Medical Outcomes Partnership and the Mini-Sentinel program.

• Abraham Hartzema, Michael Kahn, Brian Sauer, and Yola Moride received consulting fees and travel expenses in connection with providing input on the design of the study and interpretation of results.
A key component to coordinating surveillance activities across distributed networks is the design and implementation of a Common Data Model (CDM).

CDM supports implementation of standardized analytics across organizations with different database structures.

Observational Medical Outcome Partnership (OMOP) and FDA Mini-Sentinel (MS) CDMs have been proposed and widely used for Safety Surveillance activities, but no detailed comparison of the CDMs previously conducted.
Objective

- The overall objective of Humana-Pfizer CDM project is to evaluate OMOP and Mini-Sentinel CDMs from an ecosystem perspective to better understand how differences in CDMs and analytic tools affect usability and interpretation of results
  - Both CDMs have extensive purpose-built ecosystems of tools and programs for analytics capability and quality assurance
Method

- Data Source: Humana claims data (2007-2012)
- Data Mapping: Humana data to OMOP and MS CDMs
- Exposure and Outcome: six established positive drug-outcome pairs
- Analytic Methods:
  - High-dimensional propensity score (HDPS) based analytic procedure
  - Univariate self-controlled case series (SCCS) method
- Comparison:
  - Data at the patient level by source code and mapped concepts
  - Study cohort construction and effect estimates using two analytic methods
Key Conceptual Difference

- **OMOP**
  - Standardized vocabularies
  - Data aggregation tables
  - Additional data elements

- **Mini-Sentinel**
  - Reflects concepts and granularity of source data
  - No standardized vocabulary
  - No secondary data aggregation tables
Results: Differences in the Key Steps of the Dissection

- Define HOI cohort
- Define DOI cohort
- DOI-HOI cohort
- Analytic outputs

Humana source data

CDM Creation 7.7 m

Steps where further discordance was introduced

Step with no or minimal discordance
DOI – Drug of Interest
HOI – Health Outcome of Interest

Common Conditions/Diagnosis Codes – Source level

Data reported are unique patient counts

Unspecified essential hypertension
Other and unspecified hyperlipidemia
Essential hypertension, benign
Other malaise and fatigue
Pure hypercholesterolemia
Pain in soft tissues of limb
Chest pain, unspecified

Million Members

MS
OMOP
Results: Conceptual Differences in Mapping

- No information loss when mapping source codes into MS CDM
- There was minimal information loss when source data were transformed into OMOP standard vocabulary
- Most unmapped codes in this study had no or minimal impact on the active surveillance method testing.

Database heat map: overall mapping quality of the Humana database in OMOP CDM

Dark green, complete mapping; light green, incomplete mapping; yellow, not available to map; white, system generated.

Note: Selected Humana OMOP CDM data tables used for this study were included in this figure.
- Drug exposure table structure differs across two CDMs
- Large differences in three HOI and two DOI cohorts extracted from each CDM
Rx Frequency – Source Level

Impact of J-code and CPT inclusion in drug table

MS Rx

OMOP Rx

Thousands

0

1000

HYDROCODONE/APAP

AZITHROMYCIN

HYDROCODONE/APAP

SMZ/TMP

PROAIR HFA

Influenza vaccine

HYDROCODONE/APAP

Ondasetron Inj (J code)

Midazolam Inj (J code)

AZITHROMYCIN

MS Counts

OMOP
• Good agreement:
  – Indomethacin
  – Valproic acid
  – Carbamazepine
  – Amoxicillin

• Discordance:
  – Ketorolac
  – Benzodiazepine
HOI Cohorts

- Good agreement:
  - AMI, Hip Fracture

- Discordance:
  - GI bleed, ALI, Anaphylaxis
Potential Explanations for Findings

3 primary factors that may contribute to differences observed in HOI & DOI cohorts:

- Mapping
- CDM structure
- Definitional differences
Methods Testing

• Why methods testing?
• HDPS and USCCS methods
• “Community-developed” code
• Key differences in method implementation
  – Cohort identification
  – Analysis
Results: Testing SCCS Method

Key Finding: Conceptual differences at data model level had slight but not significant Impact on identifying the known safety associations

<table>
<thead>
<tr>
<th>DOI</th>
<th>HOI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indomethacin</td>
<td>AMI</td>
</tr>
<tr>
<td>Ketorolac</td>
<td>GI bleeding</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>Hip Fracture</td>
</tr>
<tr>
<td>Valproic acid</td>
<td>Acute Liver Injury</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>Acute Liver Injury</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>Anaphylactic Shock</td>
</tr>
</tbody>
</table>

Variable Risk Period

<table>
<thead>
<tr>
<th></th>
<th>OMOP method</th>
<th>SCCS method</th>
<th>MS Sentinel SCCS method</th>
</tr>
</thead>
<tbody>
<tr>
<td>DOI: Indomethacin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DOI: Ketorolac</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DOI: Benzodiazepines</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DOI: Valproic acid</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DOI: Carbamazepine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DOI: Amoxicillin</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Fixed Risk Period

<table>
<thead>
<tr>
<th></th>
<th>OMOP method</th>
<th>SCCS method</th>
<th>MS Sentinel SCCS method</th>
</tr>
</thead>
<tbody>
<tr>
<td>DOI: Indomethacin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DOI: Ketorolac</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DOI: Benzodiazepines</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DOI: Valproic acid</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DOI: Carbamazepine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DOI: Amoxicillin</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

RR: Relative Risk
Key Finding: Differences at ecosystem level can lead to strikingly different risk estimation (primarily due to choice of analytic approach and its implementation).

<table>
<thead>
<tr>
<th>DOI</th>
<th>HOI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indomethacin</td>
<td>AMI</td>
</tr>
<tr>
<td>Ketorolac</td>
<td>GI bleeding</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>Hip Fracture</td>
</tr>
<tr>
<td>Valproic acid</td>
<td>Acute Liver Injury</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>Acute Liver Injury</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>Anaphylactic Shock</td>
</tr>
</tbody>
</table>

Variable Risk Period

<table>
<thead>
<tr>
<th></th>
<th>OMOP HDPS</th>
<th>MS Sentinel HDPS</th>
</tr>
</thead>
<tbody>
<tr>
<td>OR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.1 - 10</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Fixed Risk Period

<table>
<thead>
<tr>
<th></th>
<th>OMOP HDPS</th>
<th>MS Sentinel HDPS</th>
</tr>
</thead>
<tbody>
<tr>
<td>OR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.1 - 10</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

[Graphs showing data for variable and fixed risk periods]
Conclusions

- The clear conceptual differences between OMOP and Mini-Sentinel CDMs had limited impact on identifying known safety associations in Humana data at the data model level.
- Strikingly different risk estimation can occur at an ecosystem level, but this is primarily attributed to the choices of analytic approach and their implementation in the community developed analytic tools.
- There is a need for ongoing efforts to ensure sustainable and transparent platforms to maintain and develop CDMs and associated tools for effective safety surveillance.
We would like to thank Dr. James Harnett, Mr. Daniel Wiederkehr, and Dr. Robert Reynolds at Pfizer Inc. for their support and advice to this study.
Thank you!