Pathways for advanced transformation of CDISC SDTM data sets into OMOP CDM

Eva-Maria Didden, Rose Ong, Patricia Biedermann, Graham Wetherill
Actelion (now Janssen Pharmaceutical Companies)

Alexander Davydov, Alexandra Orlova, Gregory Klebanov, Michael Kallfelz
Odysseus
CDISC SDTM

- Introduced and required for regulatory submission of clinical trial data to authorities
- Allows for harmonization of clinical trial and registry data
- Provides not only a data model but is also supported by a controlled terminology
- Meant for organizing raw data, not primarily for analysis purposes
<table>
<thead>
<tr>
<th>Source data: OPUS and OrPHeUS registries</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Trial identifier</strong></td>
</tr>
<tr>
<td><strong>Study location</strong></td>
</tr>
<tr>
<td><strong>Study type</strong></td>
</tr>
<tr>
<td><strong>Observation period</strong></td>
</tr>
<tr>
<td><strong>Latest data cut mapped</strong></td>
</tr>
<tr>
<td><strong>Patients, N</strong></td>
</tr>
<tr>
<td><strong>Primary objective</strong></td>
</tr>
<tr>
<td><strong>Original format</strong></td>
</tr>
<tr>
<td><strong>Exclusion criteria</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>
Problem statement
Challenge

- Convert rare-disease drug registry data to the OMOP Common Data Model
- Merge 2 Pulmonary Hypertension (PH) data sets
Challenges with SDTM to OMOP conversion

• Meet OMOP CDM constraints
  – Record dates must be complete and consistent (correct/logical sequence)

• Convert and combine information
  – Complex mapping, in particular for adverse events:
    • Extraction of information from multiple sources or source tables
    • Adverse event terms mapping
  – Relationship building, e.g. cause of (adverse) event, (adverse) event, outcome of (adverse) event
Challenges with SDTM to OMOP conversion (2)

• Specific structure of SDTM data
  – Complex and individual Case Report Forms
  – Code systems not widely used in observational health data (e.g. MedDRA, WHODrug)
  – Free text decoding
  – SDTM table content – potential dependencies and inconsistencies

• Uncharted territory
  – No guidelines and conventions for converting SDTM to OMOP
Challenges with SDTM to OMOP conversion (3)

• Access only to “non-curated” registry data (no prior exclusion of patients or records, no prior imputation work)

• Registry data collection may still be ongoing:
  → Case report form may change over time or be amended → Impact on SDTM database content → impact on conversion to OMOP CDM

• Regular feedback sessions between study team and mapping team are crucial to ensure high quality deliverables
Strategies
Methods for imputation rules

- Comparison of the year[, month] of a medical event with calculated 'reference time points':
  - Date of birth / death
  - Osumit initiation date / exposure end date
  - Date of last available information
  - Latest date of dataset
  - Date of last follow-up visit
- Usage of time points available in the SDTM such as
  - 'ongoing / before at last patient visit'
  - 'ongoing at Osumit initiation'
  - 'before patient discontinuation’
- For Osumit, in addition, imputation based on the previous interval of taking a drug
- Extraction of date from free text fields
Examples for imputation rules (1/3):

missing day of Adverse Events [AE]

• If the SDTM time point for study treatment [Opsumit] initiation had the same month and year as the AE date, then the incomplete date was imputed with the day after Opsumit initiation date.

• If the SDTM time point for Opsumit initiation is earlier than incomplete AE date and if the study enrolment date had the same month and year as the AE date, then the incomplete date was imputed with the day of the study enrolment date.

• If the SDTM time point for Opsumit initiation is later than incomplete AE date, then the incomplete date was imputed with the middle of the month.

• If the study enrolment date is earlier than the incomplete adverse AE date, then impute with the first day of the month.
Examples for imputation rules (2/3)

completely missing date of Clinical Management [CM] of an AE

If the start date of a concomitant medication to treat and AE is completely missing in CM table, then the adverse event start date is used for imputation.
Examples for imputation rules (3/3)

date of death

- Possible sources:
  - drug safety database
  - death form
  - date of an adverse event with a fatal outcome
  - flagged in the demographics table

- Search sequence for possible dates:
  - details from the study CRF → adverse events with a fatal outcome from the study CRF → details from the drug safety database → adverse events with a fatal outcome from the drug safety database → flags in the demographics table

- If date of death is still missing, it is imputed with the date of last available information
Complex ETL rules

• Comprehensive definitions of source concepts for PH WHO groups, etiologies, and sub-etiologies/groups:
  – 5 different attributes from 2 tables:
    – Medical History [MH]
    – Supplements to Medical History [SUPPMH]

• Extraction of historical context from the medical history free text.
Methods for information rescue

- Keep study name with enrolment consent / date
- Use enrolment date as observation start date
- Build custom concepts
- fact_relationship links
  - Additional characteristic of a medical event (e.g. severity)
  - Outcome of medical event (e.g. hospitalization)
  - Reason for ... (e.g. dose change)
  - Adverse event to symptom / treatment linkage
  - Measurements to method linkage
Examples for information rescue (1/2)

Relation to Opsumit

Adverse Events (AE)

<table>
<thead>
<tr>
<th>AE TERM</th>
<th>AESTDT</th>
<th>AEENDT</th>
<th>AEREL</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOW HEMATOCRIT AND HEMOGLOBIN</td>
<td>2015-05-06</td>
<td>2015-07-29</td>
<td>POSSIBLY RELATED</td>
</tr>
</tbody>
</table>

OMOP CDM MEASUREMENT

<table>
<thead>
<tr>
<th>measurement_id</th>
<th>measurement_concept_id</th>
<th>measurement_date</th>
<th>value_as_concept_id</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4151358 - Hematocrit determination</td>
<td>2015-05-06</td>
<td>4267416 - Low</td>
</tr>
<tr>
<td>2</td>
<td>4153000 - Hemoglobin level estimation</td>
<td>2015-05-06</td>
<td>4267416 - Low</td>
</tr>
</tbody>
</table>

OMOP CDM OBSERVATION

<table>
<thead>
<tr>
<th>observation_id</th>
<th>observation_concept_id</th>
<th>observation_date</th>
<th>value_as_concept_id</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2000000076 - Relationship to Opsumit</td>
<td>2015-05-06</td>
<td>4162850 - Possibly</td>
</tr>
</tbody>
</table>

OMOP CDM FACT_RELATIONSHIP

<table>
<thead>
<tr>
<th>domain_concept_id_1</th>
<th>fact_id_1</th>
<th>domain_concept_id_2</th>
<th>fact_id_2</th>
<th>relationship_concept_id</th>
</tr>
</thead>
<tbody>
<tr>
<td>1147330 - Measurement</td>
<td>1</td>
<td>1147304 - Observation</td>
<td>1</td>
<td>4165382 - Associated with</td>
</tr>
<tr>
<td>1147330 - Measurement</td>
<td>2</td>
<td>1147304 - Observation</td>
<td>1</td>
<td>4165382 - Associated with</td>
</tr>
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</table>

AE mapping

Relation to Opsumit mapping (new custom concept)

Link AE and its relation to Opsumit
Examples for information rescue (2/2)

Measurements to methods

<table>
<thead>
<tr>
<th>XP</th>
<th>XPTEST</th>
<th>XPDT</th>
<th>XPMETHOD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean Pulmonary Arterial Pressure (mPAP)</td>
<td>2015-02-19</td>
<td>THERMODILUTION METHOD</td>
</tr>
</tbody>
</table>

**OMOP CDM MEASUREMENT**

<table>
<thead>
<tr>
<th>measurement_id</th>
<th>measurement_concept_id</th>
<th>measurement_date</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>3028074 - Pulmonary artery Mean blood pressure</td>
<td>2015-02-19</td>
</tr>
</tbody>
</table>

<table>
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<tr>
<th>observation_id</th>
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<th>observation_date</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>4122989 - Thermodilution technique</td>
<td>2015-02-19</td>
</tr>
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<th>fact_id_2</th>
<th>relationship_concept_id</th>
</tr>
</thead>
<tbody>
<tr>
<td>1147304 - Observation</td>
<td>2</td>
<td>1147330 - Measurement</td>
<td>3</td>
<td>4152892 - Measurement method</td>
</tr>
</tbody>
</table>
Examples of data flow from „Event“ tables

(OPUS Registry)
Results
SDTM to OMOP - Proof of concept

• Facilitates combining Clinical Trial / Registry data with other Real World Data

• Enables use of the Standardized OHDSI Toolset

• Allows entering the OHDSI Network
Data rescue graph

- Selected tables that had a below than 90% coverage
Custom Vocabulary

- MedDRA is recognized as a source vocabulary.
- Concomitant and study medication data (WHODrug and free text in EX table).
- Free text in AE, MH, CM, XP, LB, VS, DD, etc. tables.
- Custom concepts created to reflect the highly-specific terms (PAH subtypes, study drugs, specific tests/assessments/scales).
- Relationships / hierarchy between custom and OMOP vocabulary.