

Mapping Clinical Trial Adverse Events in the OMOP CDM

Cynthia Sung¹, Ivona Anastasova², Qi Yang³, Mike Hamidi⁴, Rebecca Baker⁵, Ingeborg Holt⁶,
Vojtech Huser⁷, Melanie Philofsky⁷, Asieh Golozar⁸, and Christian Reich⁸

¹Duke-NUS Medical School, ²German Center for Diabetes Research, ³IQVIA, Inc., ⁴Walmart Healthcare Research Institute, ⁵CDISC, ⁶Orizaba Solutions, ⁷EPAM Services, Inc., ⁸Nemesis Health

Background

In observational data, an adverse reaction to a drug typically is inferred by a temporal relationship between drug exposure and an occurrence of a new condition or abnormal laboratory value. In clinical trials, however, investigators are required to record any adverse event (AE) that occurs during a patient's involvement in the trial, along with the seriousness, severity, and relationship to the intervention. When evaluating an application for marketing approval, regulators weigh the efficacy of the intervention against its safety profile, including the seriousness and frequency of AEs observed during clinical trials, especially Phase 3 trials. After approval, AEs continue to be monitored to detect new or worsening safety signals that may become evident when the intervention is used in larger and more diverse populations in comparison to the populations studied in clinical trials. Given the importance of safety data to benefit-risk assessments, consistent conventions for capturing AE attributes in the OMOP CDM are desirable.

Expected use cases for converting clinical trial data to the OMOP CDM are (1) to conduct meta-analyses of multiple trials for the same intervention and indication, (2) to compare outcomes obtained during well-controlled trials on a restricted population (multiple inclusion and exclusion criteria) with real world outcomes when an intervention is used in a much larger and more diverse patient population, and (3) to enable comparison to historical data or external control arms constructed using OHDSI tools, which is especially important for single arm studies when patient numbers are limited, effective standard treatments are lacking, or randomization is not ethically feasible.

Methods

Regulatory authorities such as the FDA, EMA, and PMDA require or highly recommend that submissions use the Clinical Data Interchange Standards Consortium (CDISC) Study Data Tabulation Model (SDTM)¹²; hence, a large volume of patient-level clinical trial data exists in this format. The OHDSI Clinical Trial Working Group (CTWG) is focused on expanding previous work³ to prepare a guideline for transforming clinical trial data from CDISC SDTM to the OMOP CDM.

The proposed conventions and best practices are mostly informed by the ongoing conversion of tuberculosis clinical trial data from SDTM to the OMOP CDM using data sets provided by C-PATH, in particular TB-1015 (NCT02193776) "A Phase 2 Open-Label, Partially Randomized Trial to Evaluate the Efficacy, Safety and Tolerability of Combinations of Bedaquiline, Moxifloxacin, PA-824 and Pyrazinamide in Adult Subjects with Newly Diagnosed, Drug-Sensitive or Multi Drug-Resistant Pulmonary Tuberculosis."

At multiple CTWG biweekly meetings, conventions were discussed for representing AEs and associated attributes such as seriousness, severity, toxicity grade, causality, and outcome for investigational drug trials. Also discussed were methods for linking individual AEs to the associated drug_exposure and condition_occurrence. The proposed conventions were then reviewed by members of the Vocabulary, Oncology, and THEMIS workgroups.

Results

The recommended conventions relate to the following tasks:

1. Link the record of an event in the SDTM AE domain to both the clinical finding and the drug exposure
 - Map SDTM AETERM, the clinical finding of the AE, to the CONDITION_OCCURRENCE table. This becomes the primary key for linkage to OBSERVATION records containing attributes of the AE.
 - Create two records in the OMOP CDM OBSERVATION domain with observation_concept_id 441207 (adverse reaction to drug). Link one record to the primary key of the above-mentioned CONDITION_OCCURRENCE record, the other record to the primary key of the DRUG_EXPOSURE record of the drug associated with the AE, mapped either from SDTM EXTRT (investigational drug) or CMTRT (concomitant drug).
 - Use domain_event_id in OBSERVATION records as the foreign key to the primary key of the above-mentioned CONDITION_OCCURRENCE record and domain_event_field_concept_id 11147663 (condition_occurrence.condition_occurrence_id) to indicate that the linked record is in the CONDITION_OCCURRENCE domain.
 - Similarly, use domain_event_id in the OBSERVATION record as the foreign key to the primary key of the associated DRUG_EXPOSURE record and domain_event_field_concept_id 1147707 (drug_exposure.drug_exposure_id) to indicate that the linked record is in the DRUG_EXPOSURE domain.
2. Use existing standard vocabulary terminology as much as possible and propose new concepts only when existing concepts do not have a close semantic meaning or can be confused with other definitions.
 - Standard vocabulary terms already exist in the August 2026 OHDSI Vocabulary release for seriousness, severity, toxicity grade, and AE outcome.
 - For example, SDTM terms for AESER (Severity of Adverse Event) are MILD, MODERATE, and SEVERE. We propose to use existing SNOMED concepts that have been mapped to OMOP standard_concepts as observation_concept_ids 4116992, 4285732, and 4087703, respectively.
 - New standard vocabulary terms are proposed to the Vocabulary Team for causality.
 - In the existing OHDSI Vocabulary, relatedness refers to familial relationships. We propose to create new concepts of “Causality–Related”, “Causality–Probably Related”, “Causality–Possibly Related”, “Causality–Unlikely Related” and “Causality–Not Related” to represent these commonly used terms in AEREL (Adverse Event Attribution to Product or Procedure).
 - We also propose non-standard to standard mappings when CDISC codes are missing those mappings in ATHENA.
 - For example, CDISC code C49495 (recovered from adverse event with sequelae) currently lacks a mapping to a standard concept. We propose mapping it to the OMOP standard_concept_id 1074130 from the SNOMED vocabulary.
3. Map multiple attributes of an AE from a clinical trial aligned with the conceptual framework of observational data.
 - OMOP CDM typically records positive clinical assertions and not explicit negations for event attributes, hence, only affirmative findings are represented.
 - SDTM AESER (Seriousness of Adverse Event) is coded as Y (Yes) for a serious AE and N (No) or blank when not serious; “unknown” is not an allowed value. Since all serious adverse events must be reported to the regulatory authority and ethics committee, map AESER=Y to observation_concept_id 41958959 serious

reportable event. Do not map N or blank values; non-serious AEs can be inferred by the presence of 441207 (adverse reaction to drug) and absence of 41958959.

- SDTM captures investigator assessments such as causality, whereas OMOP CDM may not, instead using statistical inference to infer causality. Cross comparisons of causality between trial and observational data will require a phenotyping algorithm applied to the observational data.

Conclusion

Conventions for mapping AEs occurring during clinical trials proposed by the Clinical Trial Working Group are described in a living document “Clinical Trial Wiki”, which may be found in OHDSI Teams/[Clinical Trials/Conventions](#). Several examples are also presented of AEs and the proposed mappings of different attributes from the CDISC SDTM AE table to the OMOP CDM condition_occurrence, drug_exposure and observation tables. A limitation of the proposed mappings is that they are mostly based on one tuberculosis drug trial. It may be necessary to propose alternative or additional mappings for other trials or indications. Bring your use case or clinical trial mapping issues to The Clinical Trial Workgroup, which meets the second and fourth Fridays of each month at 11 AM ET (8 AM PT, 10 AM CT, 4 PM UK, 5 PM CET).

The proposed conventions establish a consistent approach for representing adverse events observed in clinical trials and their associated attributes in the OMOP CDM. These recommendations leverage existing OMOP structures and standard vocabularies whenever possible while introducing new concepts only when necessary to preserve clinical meaning. Adoption of these conventions will improve consistency across SDTM-to-OMOP transformations, and facilitate clinical trial meta-analysis, external control arm generation, and comparative effectiveness and safety studies using the OHDSI ecosystem.

The next task for the CTWG is to complete the ETL of AE data in TB-1015 to the OMOP CDM to validate the proposed conventions.

References

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