

# Fitting Observational Studies to the SDTM

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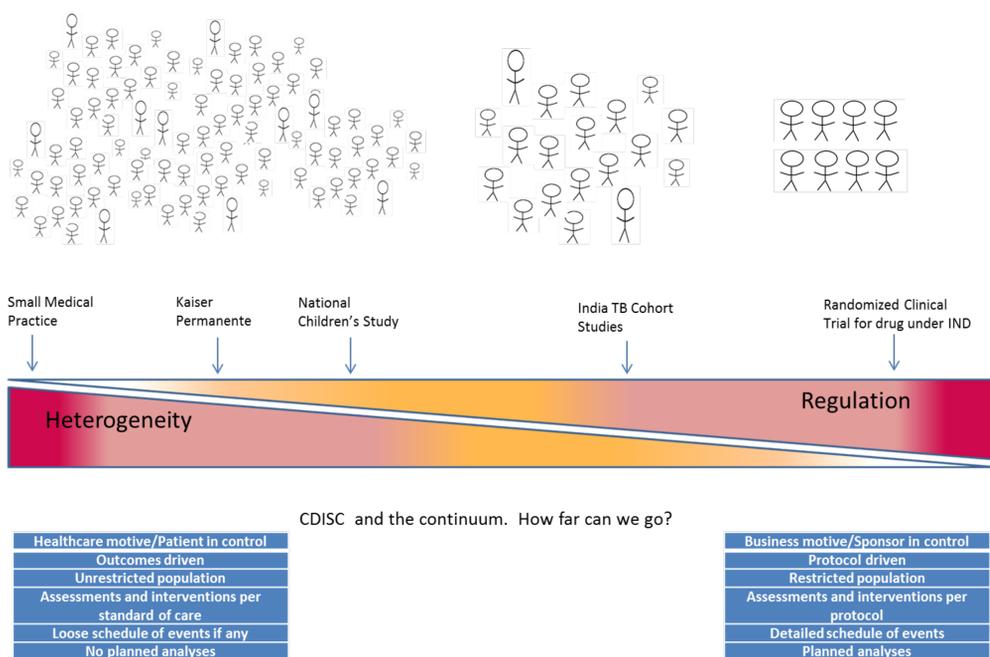
## Introduction



Observational studies are a less expensive way to gather information about the safety and efficacy of approved drugs than controlled clinical trials because they use information that is already collected for healthcare delivery. Observational Study databases can resemble clinical trial databases when the study is planned and executed with research endpoints in mind; however they have some fundamental differences. The CDISC Study Data Tabulation Model (SDTM) is designed to support the requirements of controlled clinical trials, but can it support observational studies data as well?

If we look at healthcare information as a continuum, going from that which is collected for healthcare delivery at one end of the spectrum, through that which is collected for a regulated trial at the other end of the spectrum, we see that Observational Studies fall in the middle, sharing some characteristics with the data from uses on either side.

## Gradients in Healthcare Information



## Technical Challenges

If users of regulated research data impose their expectations about data from controlled clinical trials on data from observational studies they will be disappointed. OpenCDISC checks are too rigorous, and other tests of reasonableness are not applicable, such as the expectation that a database will include certain domains. For example:

### Subject identification

- The concept of USUBJID does not apply outside of a drug/device development program.

### Missing domains

- IE (Inclusion/Exclusion Criteria Not Met), EX (Exposure), AE (Adverse Events), DV (Protocol Deviations) and other domains that we expect for clinical trial databases do not apply to most observational studies. DS (Disposition Events) will be used differently.

### Unplanned time points

- The visit concept may not apply. If it does, more visits will be unscheduled than planned. The concept of reference dates may not apply or may vary by subject; study days may not apply either.

### Incomplete and/or inconsistent data

- Dirty data is to be expected. Rigorous site training and monitoring may not be realistic.

## Abbreviations

- CDASH: Clinical Data Acquisition Standards Harmonization<sup>2</sup>
- SDTM: Study Data Tabulation Model<sup>2</sup>
- TDM: Trial Design Model<sup>2</sup>

## Case Study

Cohort studies are planned for several sites in India to gather information about subjects being treated for TB. The sponsors include Indian and U.S. research institutes.<sup>1</sup>

These observational studies will adhere to a common protocol that governs certain aspects of operations, including specimen acquisition, laboratory methods, and enrollment criteria. The common protocol will be the basis for cohort-specific protocols, which will be developed according to site requirements and the research objectives of the lead investigators.

An important goal of the India cohort studies is to develop a biobank of sputum and blood specimens, some of which will be used in prospective analyses, and others which will be used in retrospective analyses designed to identify biomarkers.

Work began on the common protocol in 2013 Q1. Design decisions about the data collection forms, operational databases, and publication format(s) will follow in Q2. No decisions have been made on how to apply the SDTM, however we plan to use much of it and we hope to engage others with similar use cases through PhUSE and CDISC.

So far we know that we will use the common protocol to define key time points and methods of assessment. We will use CDASH data elements for data collection wherever we can. And we will propose new Trial Design Model (TDM)<sup>2</sup> standards to identify this as an observational study.

## Conclusions

Standardized data is self-documenting; poolability is possible, inter-operability is enhanced. These benefits accrue as much (or more) to observational studies as to clinical trials.

The CDISC SDTM is a flexible reporting model that has been validated by its now ubiquitous use for regulated clinical trials. Much, but not all, of the CDISC SDTM applies to observational studies, and it would be difficult to argue against using it. Yet there are downsides.

### Erosion of CDISC standards with scope creep

- When exceptions overtake mainstream applications conformance suffers.
- The bigger a model gets the harder it is to teach and the more attention it calls to itself for its inadequacies.

### Overselling data that does not meet clinical trial standards

- Observational studies get less cleaning, have more variation. These traits will be even more noticeable when the data are in a standard format.
- CDISC is a recognized brand. When we receive a CDISC database we expect it to be complete and conforming. Do we need to change this perception? Do we want to change this perception?

### Mitigating the Risks

#### Protect the brand

- Leave the Controlled Clinical Trial use case alone.
- Sub-brand the SDTM for special uses, such as observational studies. Train users to recognize the difference.

#### Manage expectations

- Characterize observational databases so that they are identifiable in data repositories and data are fit to the SDTM in a uniform way.
- Use existing metadata models to document the special characteristics of the sub-brands; see the SDTM Trial Summary (TS) dataset and define.xml (CRT-DDS).

#### Collect better data in all studies!

- Use a common protocol for eligibility, assessments, and laboratory methods.
- Build standards into data collection -- see CDISC CDASH.

### Next Steps

**Users:** Take what you can from public standards but use them right.

**PhUSE:** Propose Trial Summary (TS) standards, metadata standards, and custom validation rules to support sub-branding.

**CDISC:** Recognize new use cases for CDISC models, support with new standards.

**FDA/CDC/NIH/CMC:** Achieving interoperability between clinical trial databases and observational study databases would be a big win. How can we ensure success?

**All:** Be aware of the risks of standards erosion but manage them and keep going.

## Links and References

- <http://www.crdglobal.org/grants-and-grantees/current-funding-opportunities/2012/04/17/indo-u.s.-vaccine-action-program-TB-competition>
- <http://www.cdisc.org/standards>
- <http://www.opencdisc.org/>