Digitizing Therapeutic Areas: Increasing Standardization and Reusability

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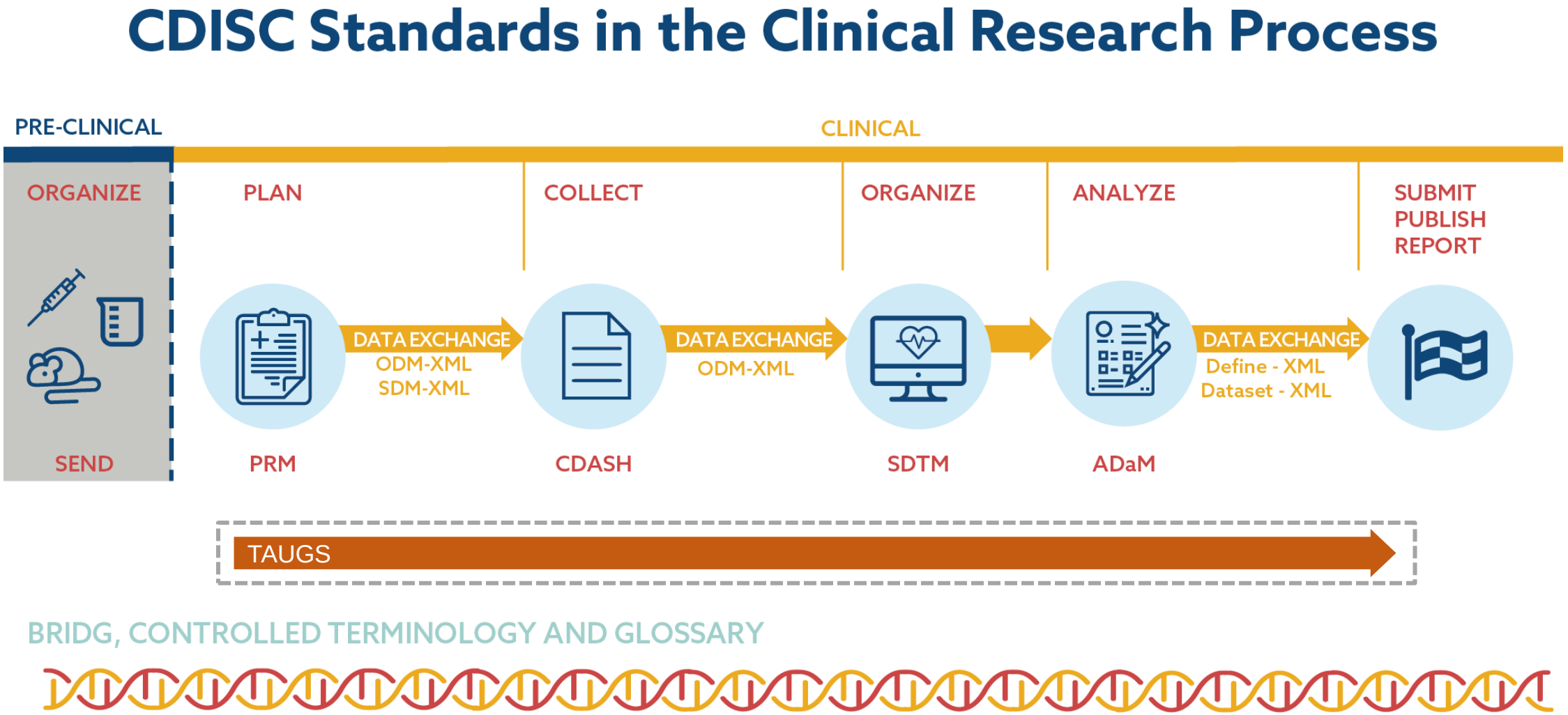
History of Therapeutic Area User Guides

- First one published in 2011 – Alzheimer's Therapeutic Area User Guide v1.0

- CFAST is Launched in 2012

- Original plan: 55 TA Standards in 5 years, today 44 TA Standards in 8 years

Today we are here



Current Therapeutic Area User Guide Overview

Therapeutic Area (TA) Standards extend the Foundational Standards to represent data that pertains to specific disease areas. TA Standards include disease-specific metadata, examples and guidance on implementing CDISC standards for a variety of uses, including global regulatory submission.

Autoimmune
- Psoriasis
- Rheumatoid Arthritis

Cardiovascular
- Cardiovascular
- Heart Failure
- QT Studies
- Traditional Chinese Medicine - Coronary Artery Disease-Angina

Endocrine
- Acute Kidney Injury
- Diabetes
- Diabetes - Type 1
- Diabetic Kidney Disease
- Dyslipidemia
- Kidney Transplant
- Polycystic Kidney Disease

Gastrointestinal
- CDAD
- Crohn's Disease

Infectious
- COVID-19
- Ebola
- Hepatitis C
- HIV
- Influenza
- Malaria
- Tuberculosis
- Virology

Mental Health
- Major Depressive Disorder
- Post Traumatic Stress Disorder
- Schizophrenia

Neurology
- Alzheimer's
- Huntington's Disease
- Multiple Sclerosis
- Parkinson's Disease
- Traumatic Brain Injury

Oncology
- Breast Cancer
- Colorectal Cancer
- Lung Cancer
- Pancreatic Cancer
- Prostate Cancer

Other
- Nutrition
- Traditional Chinese Medicine - Acupuncture

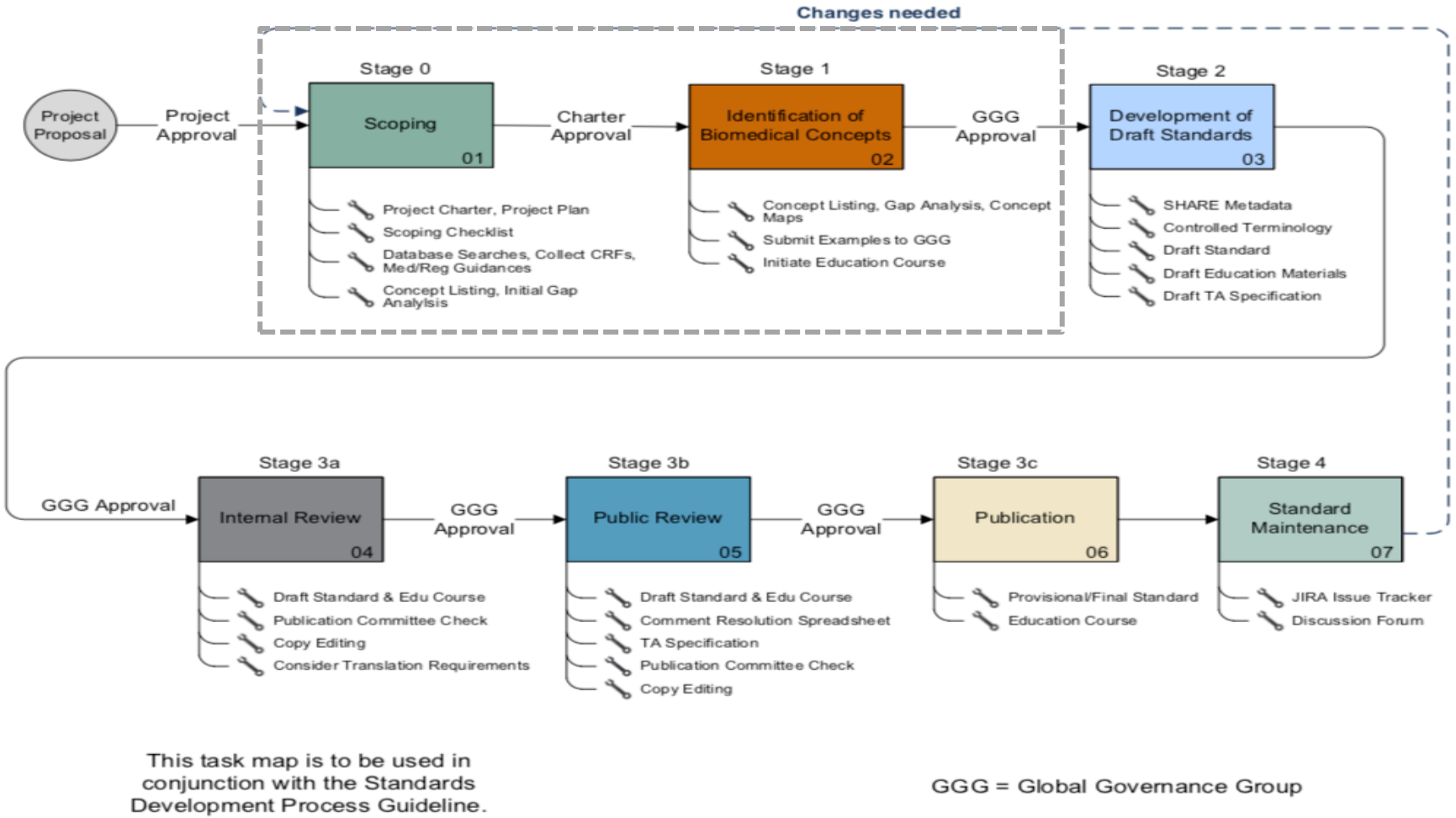
Rare Diseases
- Duchenne Muscular Dystrophy

Respiratory
- Asthma
- COPD
- COVID-19

Treatments
- Pain
- Vaccines

https://www.cdisc.org/standards/therapeutic-areas/disease-area

CDISC Standards Development Process

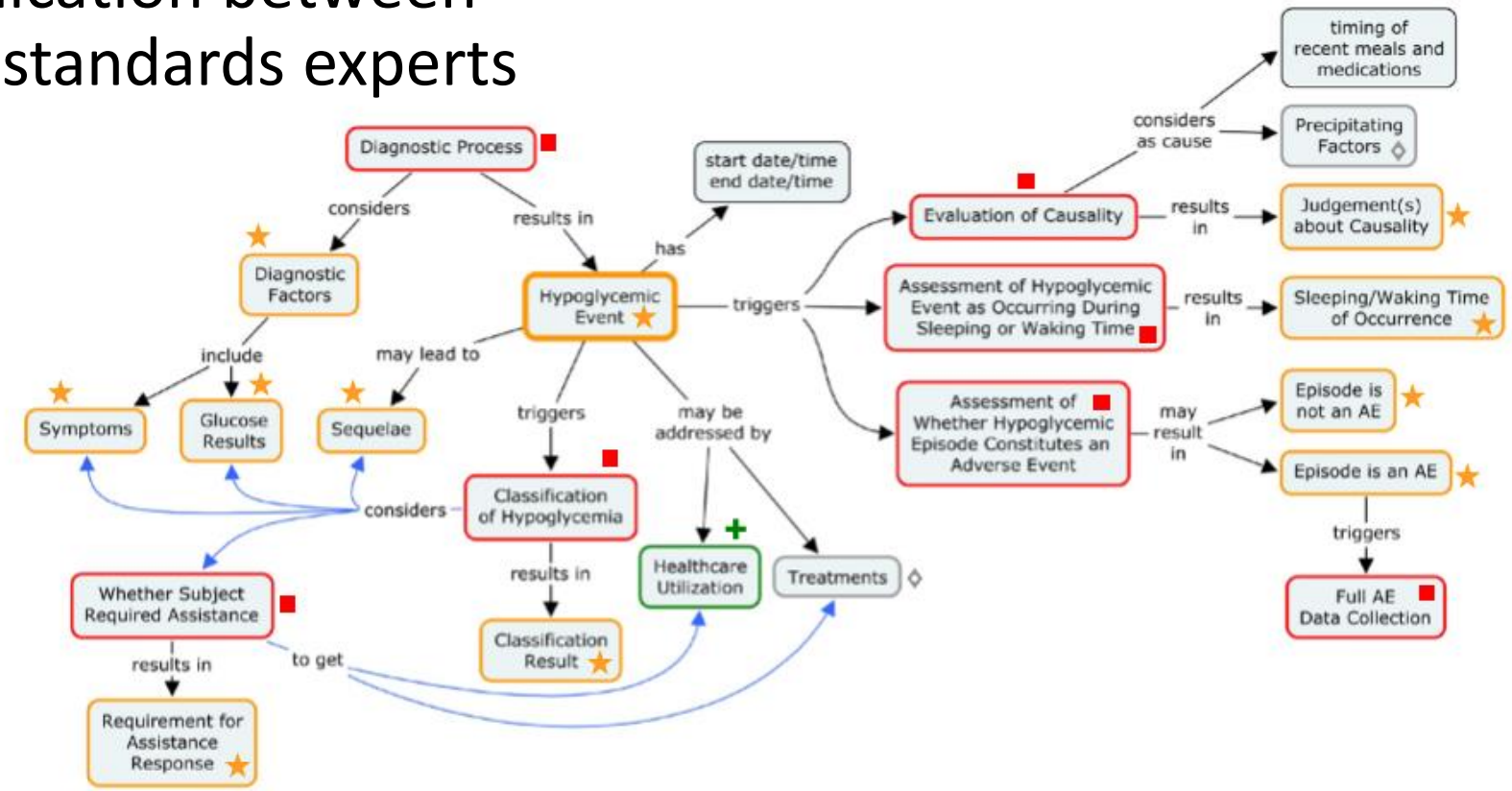


This task map is to be used in conjunction with the Standards Development Process Guideline.

GGG = Global Governance Group

Concept Map (scoping)

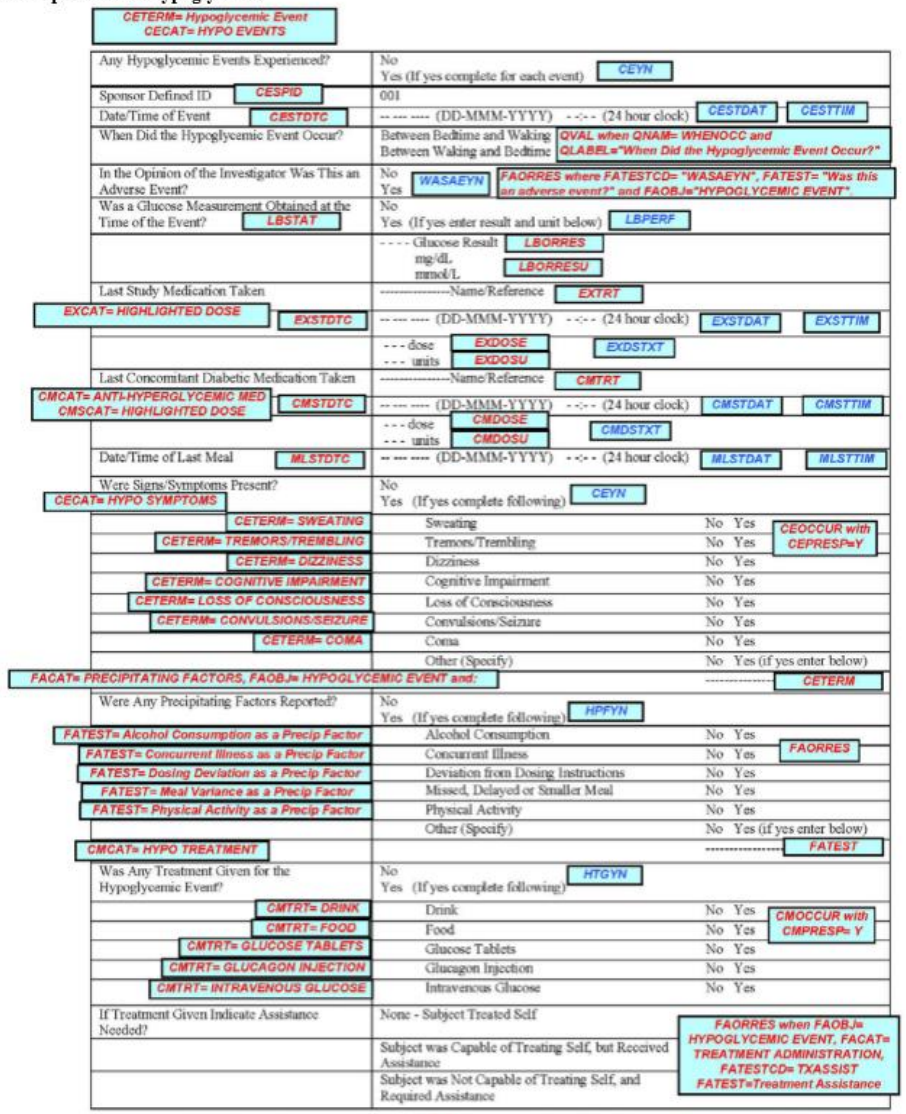
- Provides scope and extent of TA User Guide
- Facilitates communication between scientists and data standards experts



Concept Map 7: Hypoglycemic Event

Annotated Case Report Forms and Datasets

Example CRF 5: Hypoglycemia



CRF annotated to show mapping SDTM variables are in **Red**. If CDASH variable differs from SDTM the CDASH variable is in **Blue**.

Row	STUDYID	DOMAIN	USUBJID	CESEQ	CECAT	CETERM	CEDECOD	CEPRESP	CEOCCUR	CESTDTC	CESTDY
2	XYZ	CE	XYZ-001-001	2	HYPO SYMPTOMS	SWEATING	Hyperhidrosis	Y	N		
3	XYZ	CE	XYZ-001-001	3	HYPO SYMPTOMS	TREMORS/TREMBLING	Tremor	Y	N		
4	XYZ	CE	XYZ-001-001	4	HYPO SYMPTOMS	DIZZINESS	Dizziness	Y	N		
5	XYZ	CE	XYZ-001-001	5	HYPO SYMPTOMS	COGNITIVE IMPAIRMENT	Cognitive Disorder	Y	Y		
6	XYZ	CE	XYZ-001-001	6	HYPO SYMPTOMS	LOSS OF CONSCIOUSNESS	Loss of Consciousness	Y	Y		
7	XYZ	CE	XYZ-001-001	7	HYPO SYMPTOMS	CONVULSIONS/SEIZURES	Convulsion	Y	N		
8	XYZ	CE	XYZ-001-001	8	HYPO SYMPTOMS	COMA	Coma	Y	N		
9	XYZ	CE	XYZ-001-001	9	HYPO EVENTS	HYPOGLYCEMIC EVENT	Hypoglycaemia			2013-09-24T08:48	50

Row	RELMIDS	MIDS	MIDSDTC
1 (cont)		HYPO 1	
2 (cont)	DURING	HYPO 1	2013-09-01T11:00
3 (cont)	DURING	HYPO 1	2013-09-01T11:00
4 (cont)	DURING	HYPO 1	2013-09-01T11:00
5 (cont)	DURING	HYPO 1	2013-09-01T11:00
6 (cont)	DURING	HYPO 1	2013-09-01T11:00
7 (cont)	DURING	HYPO 1	2013-09-01T11:00
8 (cont)	DURING	HYPO 1	2013-09-01T11:00
9 (cont)		HYPO 2	

Analysis Datasets and Results (example)

3.3 Hypoglycemic Episodes Summary Dataset

The analysis dataset ADHYSUM is built from an ADHYPO data set and supports both the statistical analysis of the hypoglycemic events and the tabular summary of frequencies of hypoglycemic episodes (see Table 3.3.1). The dataset includes one observation per combination of subject, analysis parameter, time window and indicator (e.g., treatment emergent flag). Each record is a summary of the type of hypoglycemic episode described by the parameter, per subject. For each combination of parameter and the timing variable, AVISIT, records are created even if no hypoglycemic episodes occurred. The statistical model presented below is based on the actual treatment received (TRTA) and adjusted for subject-level values of country and sex. Therefore, these variables are included in ADHYSUM from ADSL to support analysis readiness. The duration of exposure (TRTDURD) is added to the dataset in order to facilitate exposure adjusted incidence rates. For overall summaries the records which have "cumulative frequency count" within the text of PARAM and AVISIT = "End of treatment" can be selected. In this example, parameters for each of the five ADA classification values are defined, along with a derived parameter that represents a grouping of two of the classification values (documented symptomatic or severe hypoglycemia). Mock data for this summary dataset is provided below in Table 3.3.1, yet this mock data shows only a subset of the possible values of analysis parameters. The examples below do not attempt to show all the data needed fully visualize the traceability between ADHYPO and ADHYSUM for a given subject since the volume of required mock data would be large,. In practice, however, the counts derived in ADHYSUM for a given subject would be completely traceable to the counts of individual rows for that subject found in the source ADHYPO dataset.

Table 3.3.1: ADHYSUM Analysis Dataset

Row	STUDYID	USUBJID	PARAMCD	PARAM	AVISIT	AVAL	TRTDURD	SEX	AGE	COUNTRY	TRTA
1	XYZ	000008	ASSYMP	Asymptomatic Hypoglycemia (frequency count)	Week 1	3	72	F	35	DZA	Drug B
2	XYZ	000008	ASSYMPC	Asymptomatic Hypoglycemia (cumulative frequency count)	Week 1	3	72	F	35	DZA	Drug B
3	XYZ	000008	ASSYMP	Asymptomatic Hypoglycemia (frequency count)	Week 2	1	72	F	35	DZA	Drug B
4	XYZ	000008	ASSYMPC	Asymptomatic Hypoglycemia (cumulative frequency count)	Week 2	4	72	F	35	DZA	Drug B
5	XYZ	000008	ASSYMP	Asymptomatic Hypoglycemia (frequency count)	Week 3	0	72	F	35	DZA	Drug B
6	XYZ	000008	ASSYMPC	Asymptomatic Hypoglycemia (cumulative frequency count)	Week 3	4	72	F	35	DZA	Drug B
7	XYZ	000008	ASSYMP	Asymptomatic Hypoglycemia (frequency count)	Week 4	1	72	F	35	DZA	Drug B
8	XYZ	000008	ASSYMPC	Asymptomatic Hypoglycemia (cumulative frequency count)	Week 4	5	72	F	35	DZA	Drug B
10	XYZ	000008	ASSYMPC	Asymptomatic Hypoglycemia (cumulative frequency count)	End of Treatment	7	72	F	35	DZA	Drug B

3.4 Hypoglycemic Episodes Summary Analysis Results

The summary statistics in Table 3.4.1 are presented for all hypoglycemic episodes as well as by ADA classification group. The statistics presented in the current example are number of subjects experiencing an event, the number of events, and the raw event rate. To estimate and present the event-rate information, exposure time is needed. Table 3.4.1 is based on the ADHYSUM dataset.

Table 3.4.1: Summary of Hypoglycemic Episodes by Classification – Table Shell

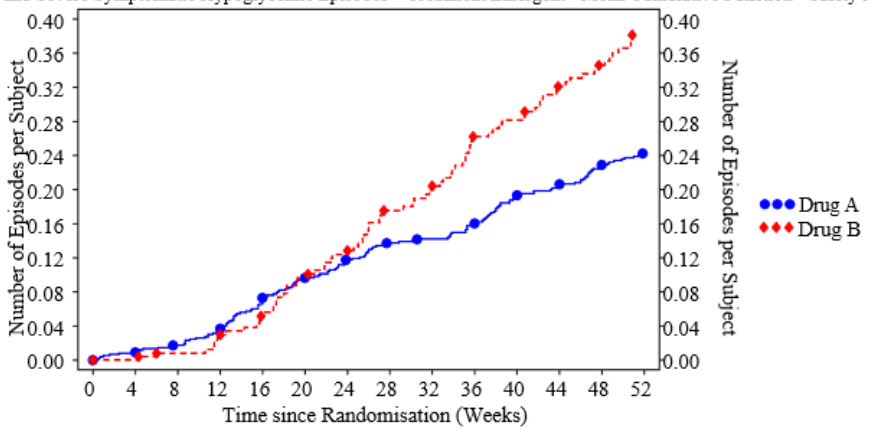
Hypoglycemic Episodes by Classification – Treatment Emergent – Summary – Safety Analysis Set

	Drug A				Drug B				Total			
	N	(%)	E	R	N	(%)	E	R	N	(%)	E	R
Number of subjects	xxx				xxx				xxx			
Total events	xx	(xx.x)	xx	xxx.x	xx	(xx.x)	xx	xxx.x	xx	(xx.x)	xxx	xxx.x
ADA												
Severe hypoglycemia	x	(x.x)	x	xx.x	x	(x.x)	x	x.x	x	(x.x)	x	x.x
Documented symptomatic hypoglycemia	xx	(xx.x)	xx	xxx.x	xx	(xx.x)	xx	xxx.x	xx	(xx.x)	xxx	xxx.x
Asymptomatic hypoglycemia	x	(x.x)	xx	xx.x	x	(x.x)	x	xx.x	xx	(x.x)	xx	xx.x
Probable symptomatic hypoglycemia	x	(x.x)	x	x.x	x	(x.x)	x	x.x	x	(x.x)	x	x.x
Pseudo-hypoglycemia	x				x				x			

N: Number of subjects; %: Percentage of subjects; E: Number of events; R: Event rate per 100 exposure years;
Severe: Subject unable to treat himself/herself and/or have a recorded PG < 3.1 mmol/L (56 mg/dL)
Treatment emergent episodes occur after trial product administration after randomization and no later than 1 day after last trial product administration.

Figure 3.4.1: Mean Cumulative Function Plot of Documented and Severe Symptomatic Hypoglycemic Episodes

Documented and Severe Symptomatic Hypoglycemic Episodes – Treatment Emergent - Mean Cumulative Function - Safety Analysis Set



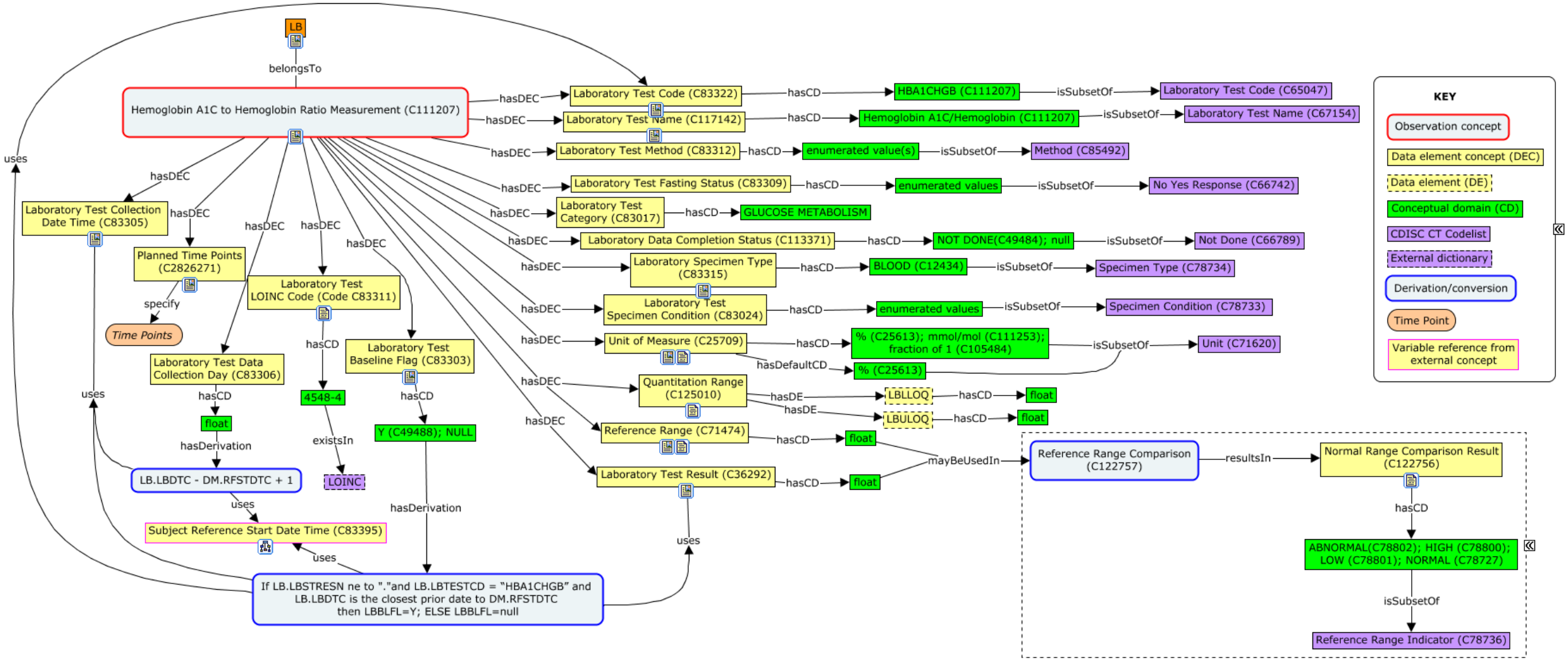
Biomedical Concepts

The CDISC 360 Project: Adding a conceptual layer to standards

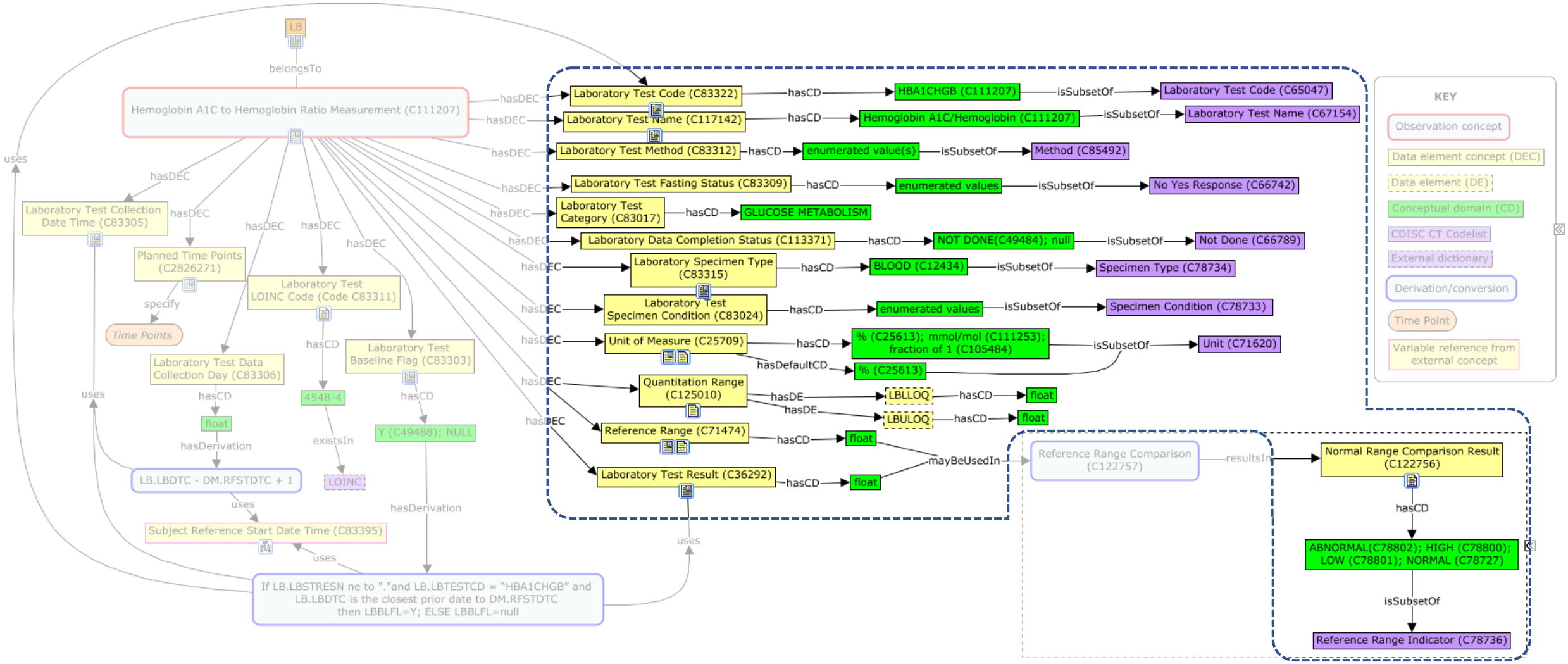
- Create and store standards as concepts which create meaning between data
- Electronically publish data standards as linked metadata
- Add derivation and transformation metadata to avoid unnecessary variability

→ CDISC 360 will develop concept-based standard definitions, and test and demonstrate end-to-end automation of study specification, data processing, and analysis

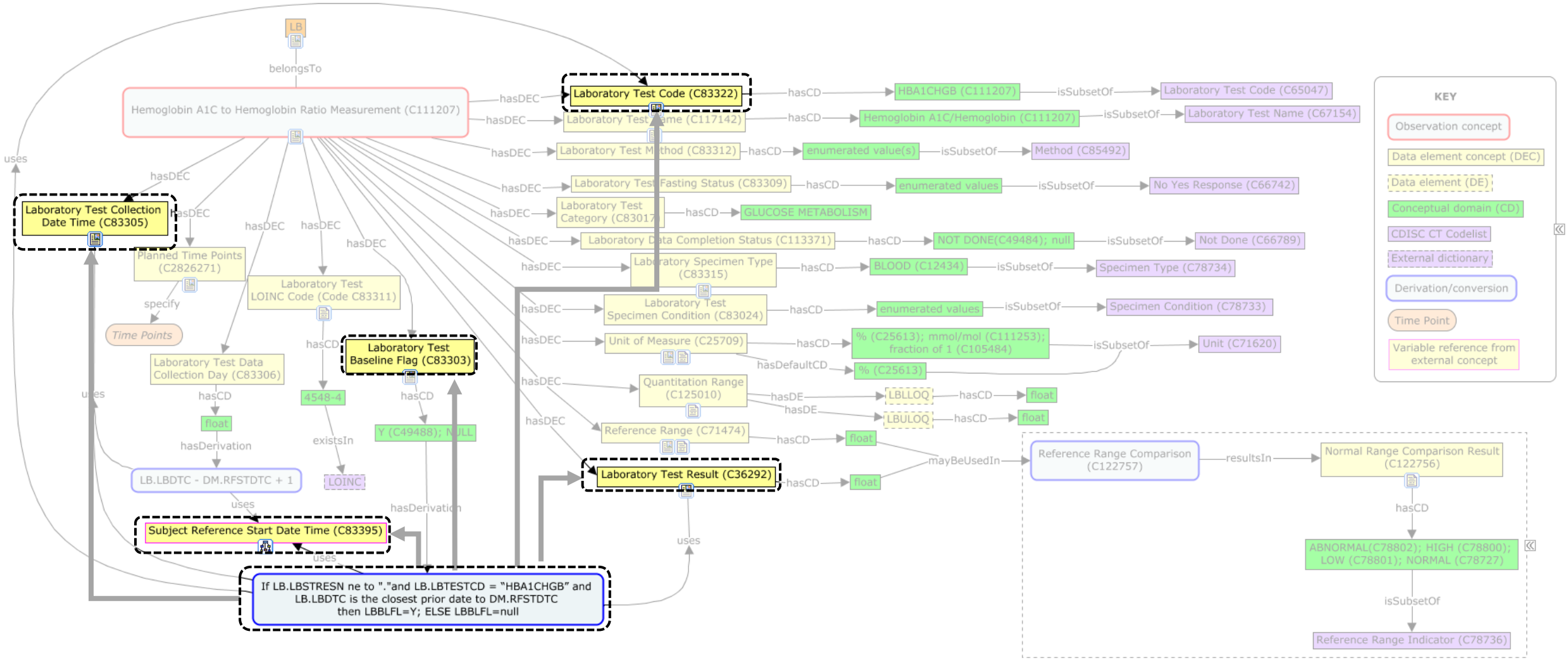
Biomedical Concept



Standardize implementation



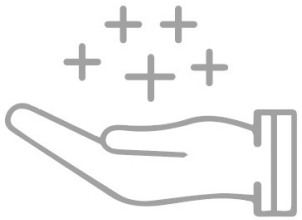
Linked derivations & transformations



What Follows?

- Create biomedical and analysis concepts
  - Establish semantic link between end to end implementation
  - Standardize derivation and transformation metadata

- Evolve Therapeutic Area standards
  - Analog documents to electronic metadata
  - End to End: from collection through analysis



- CDASH eCRF Library
  - Will cover Therapeutic Area content

- Analysis Results Metadata
  - Standardize most common analysis