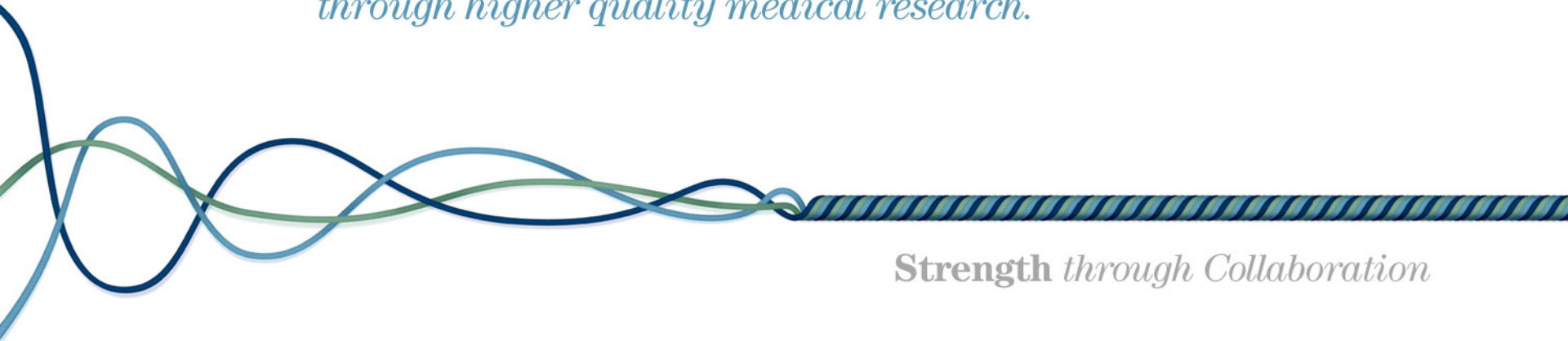




CLINICAL DATA INTERCHANGE STANDARDS CONSORTIUM

*The CDISC vision is to inform patient care & safety
through higher quality medical research.*

A decorative graphic consisting of three overlapping wavy lines in dark blue, teal, and light blue. These lines start on the left side of the slide and extend horizontally across the bottom. On the right side, the lines transition into a solid horizontal band with a diagonal hatched pattern in dark blue and teal.

Strength *through Collaboration*

What's going on here?

TA standards and SHARE

Diane Wold, PhD
PhUSE Single-Day Event
May 14, 2015



Strength *through Collaboration*

Overview

- TA projects
 - Drive standards development
 - Source of research concepts
- Concept modeling
 - Common patterns
 - Concept models and SDTM
- Examples from the TA projects
 - Pulmonary function tests
 - ECG devices
 - MELD score
- Research concepts in SHARE

TA projects and SHARE

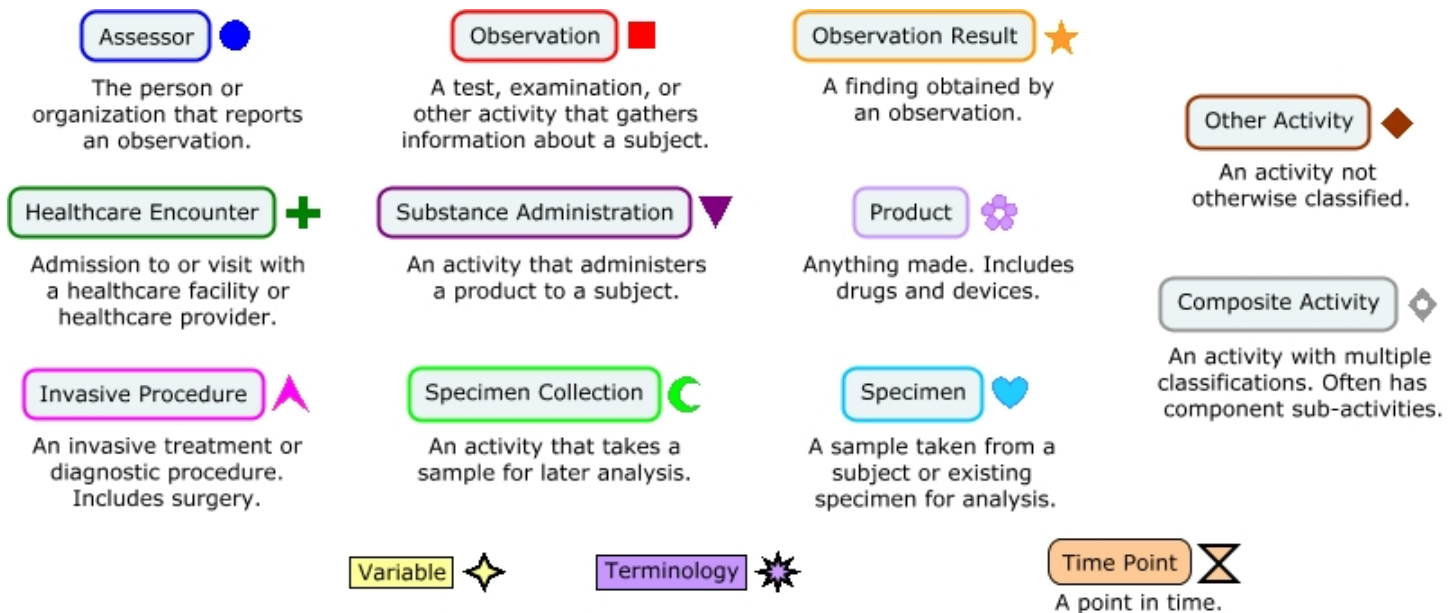
- TA Projects are driving standards development
 - Tend to focus on SDTM
 - New variables
 - New domains
 - Unresolved issues in existing SDTM domains
 - Ripple effects on CDASH
 - QS, FT and other supplements
 - Controlled terminology
- All of these come together in research concepts
- SHARE is (among other things) a repository for research concepts

TA projects expand content scope

- SDS (pre-SDTM model) dealt with the most familiar types of data
 - You've probably experienced most of these as a patient
- SDTM was intended to handle additional data of all types
- In the TA projects we encounter data beyond our own experience as patients
 - Trying to sort poorly understood data items into SDTM "boxes" results in confusing, inconsistent tabulations
 - We need to understand where the data came from and what it means before trying to map it to SDTM
 - TA projects do this work of understanding, share the results in examples and research concepts

Concept modeling

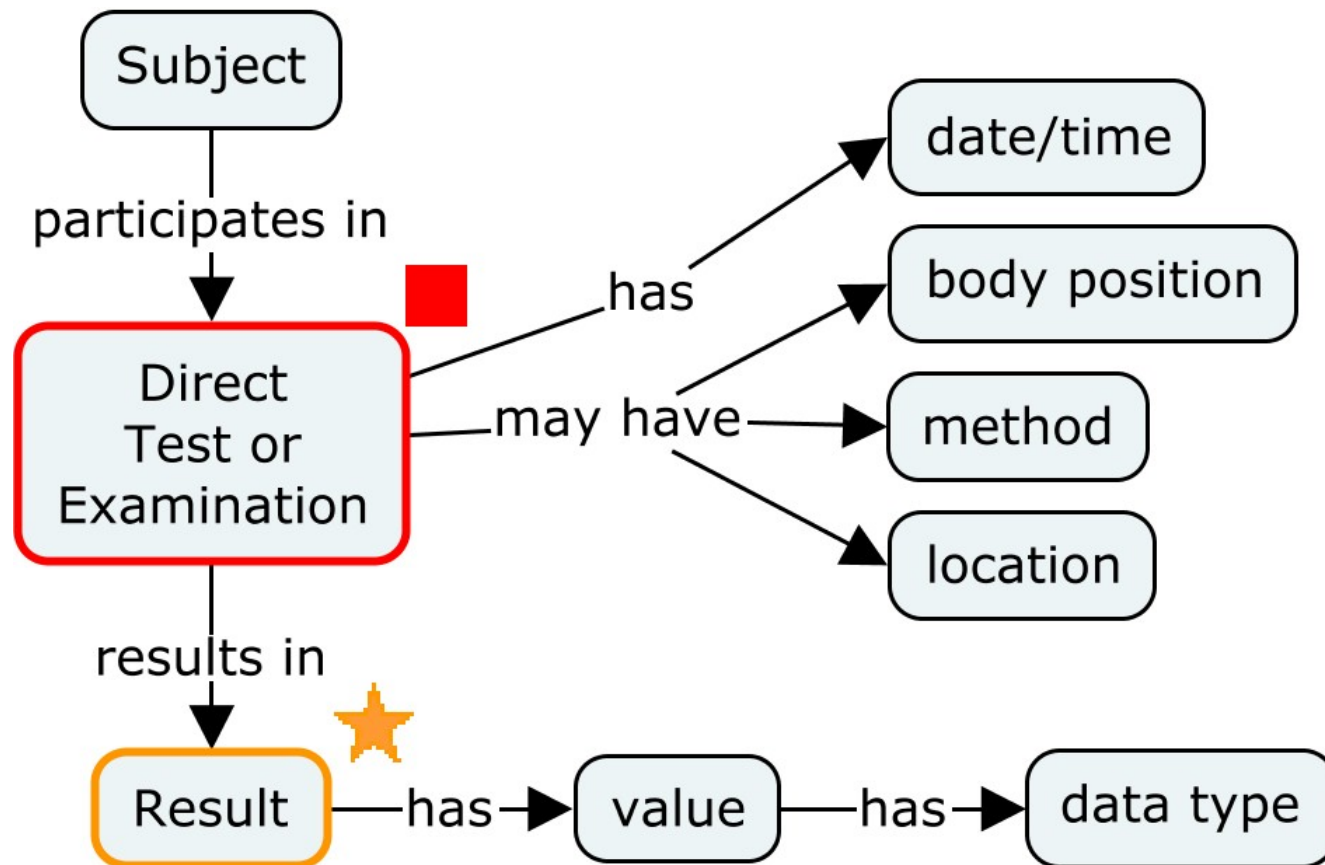
- We're using cmap tools, developed by IHMC (Florida Institute for Human and Machine Cognition)
 - Free, easy to use, can export to multiple formats
- We're also using conventions based on BRIDG



Common data patterns

– direct test

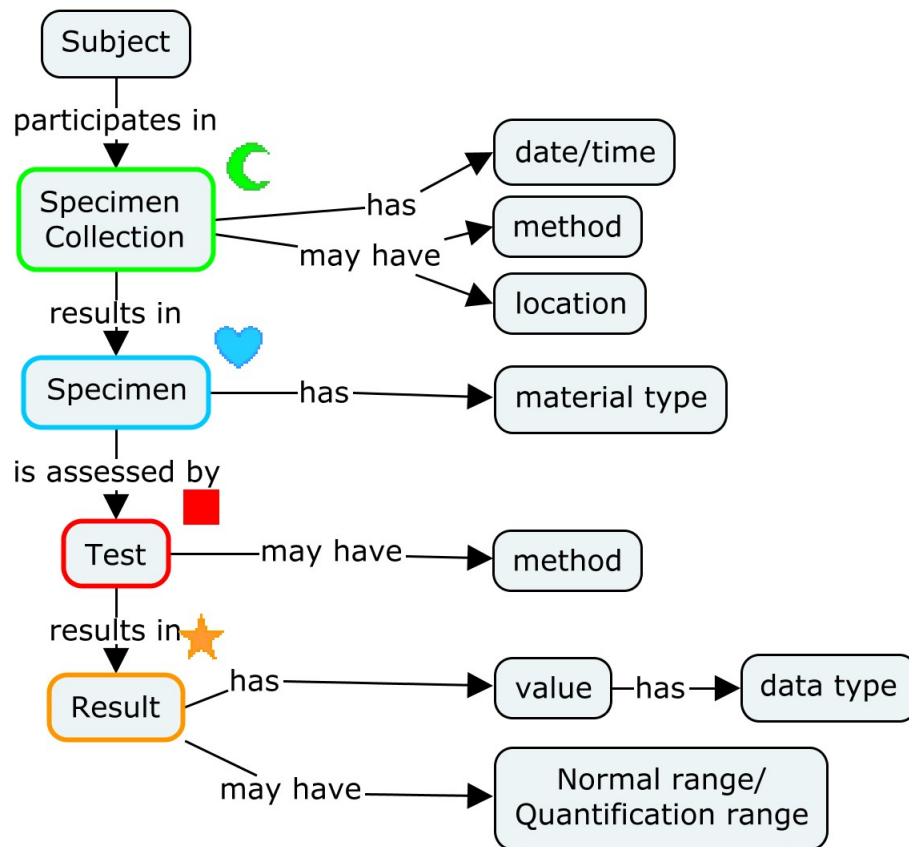
- Test performed directly on a subject
 - e.g., vital signs



Common data patterns

– test on a specimen

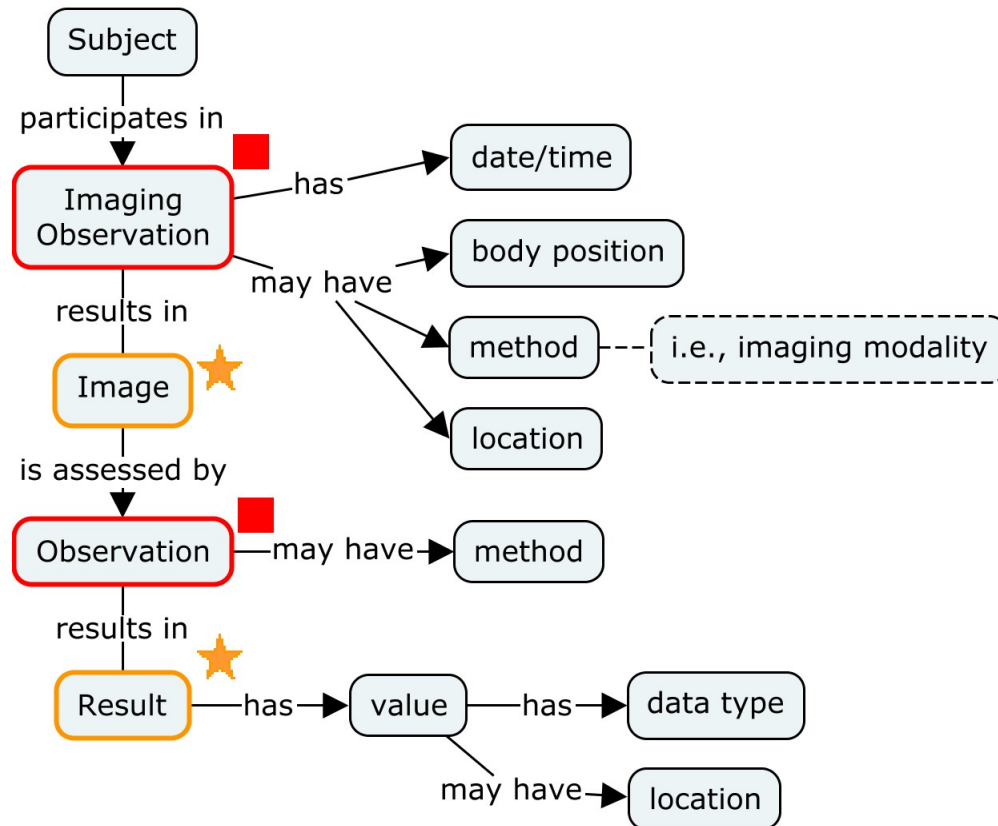
- Labs, Microbiology, PK
- Histopathology on tissue specimens



Common data patterns

-- test on an image

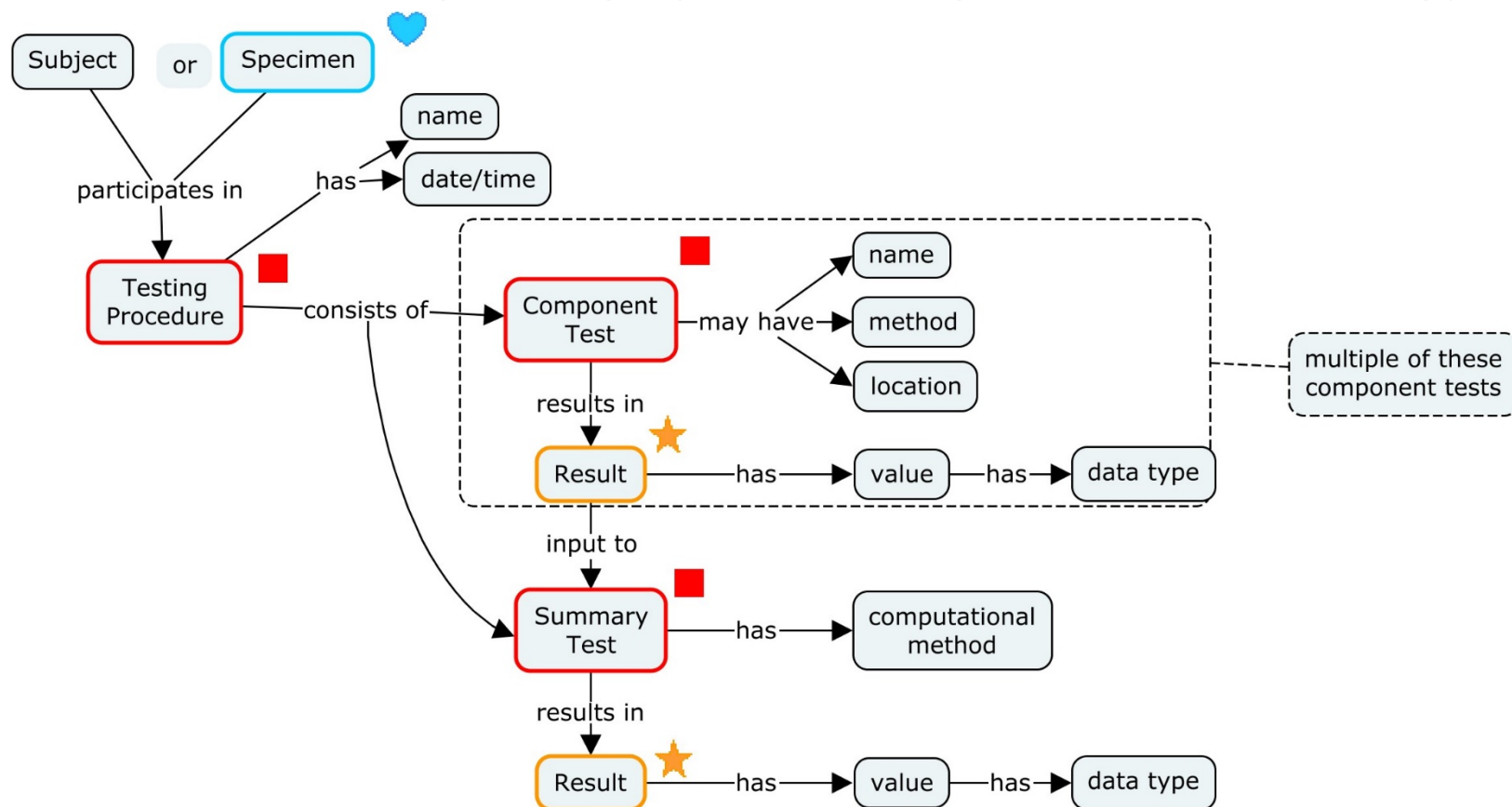
- Lesion assessments
- Some morphology and physiology



Common data patterns

-- compound test

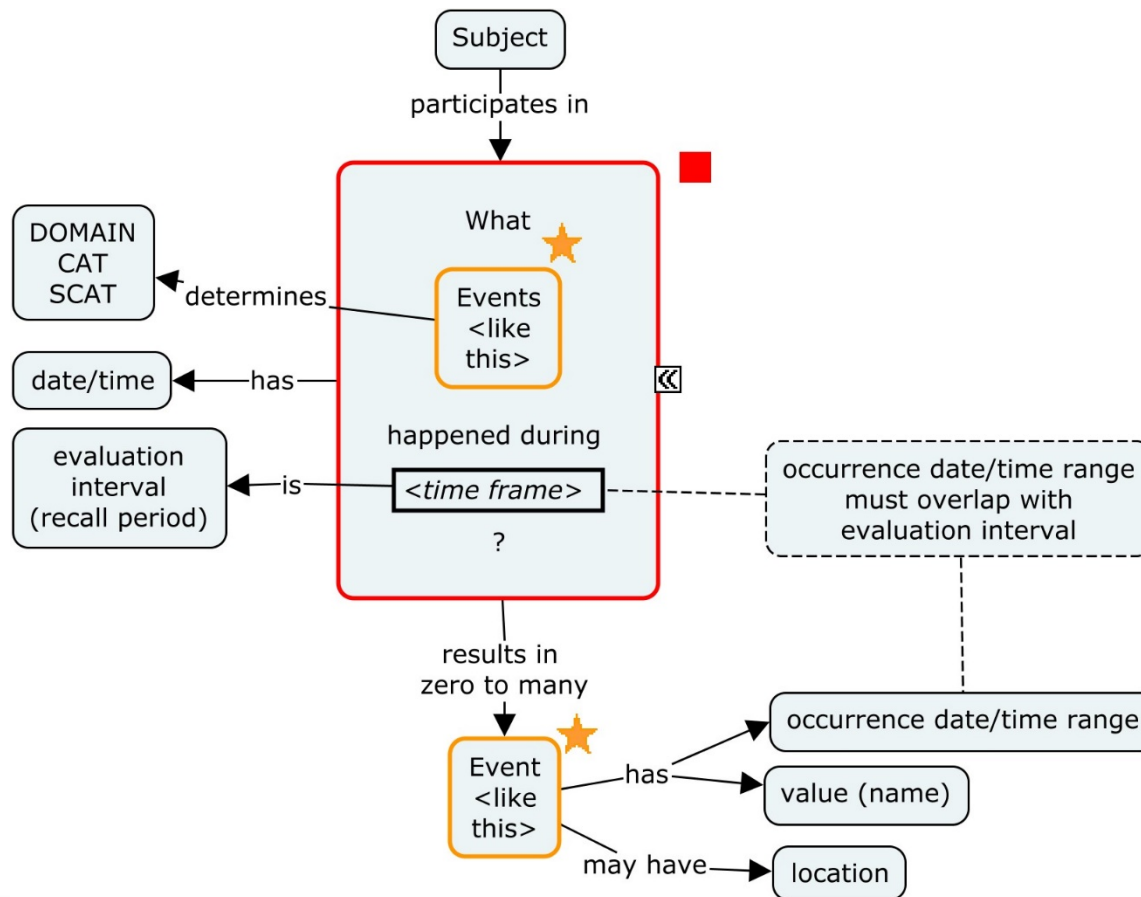
- Questionnaires and similar structured instruments
- Some grading systems, e.g., in histopathology



Common data patterns

-- events as observation results

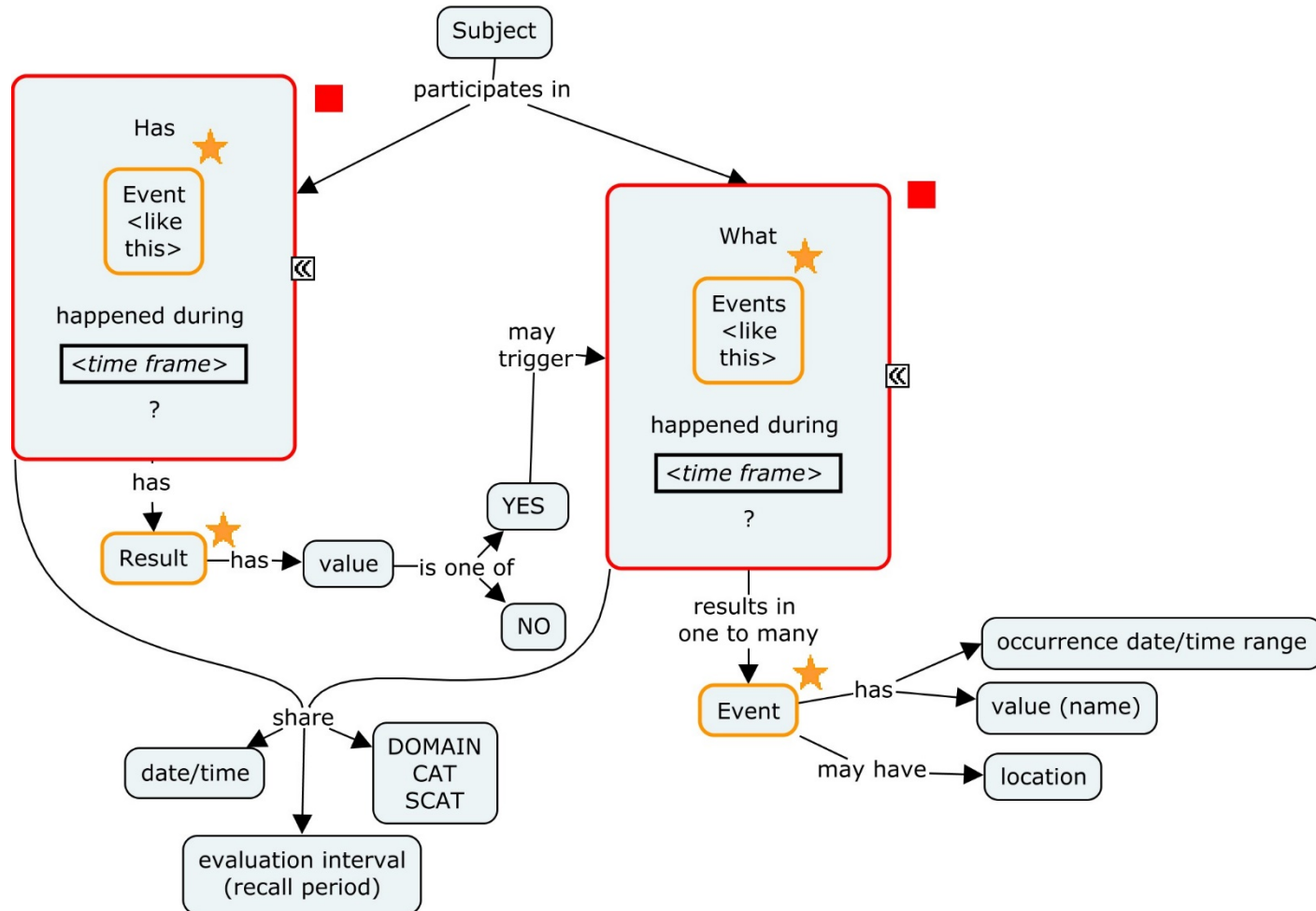
- For events which are medical conditions
 - Adverse events, medical history, etc.



Common data patterns

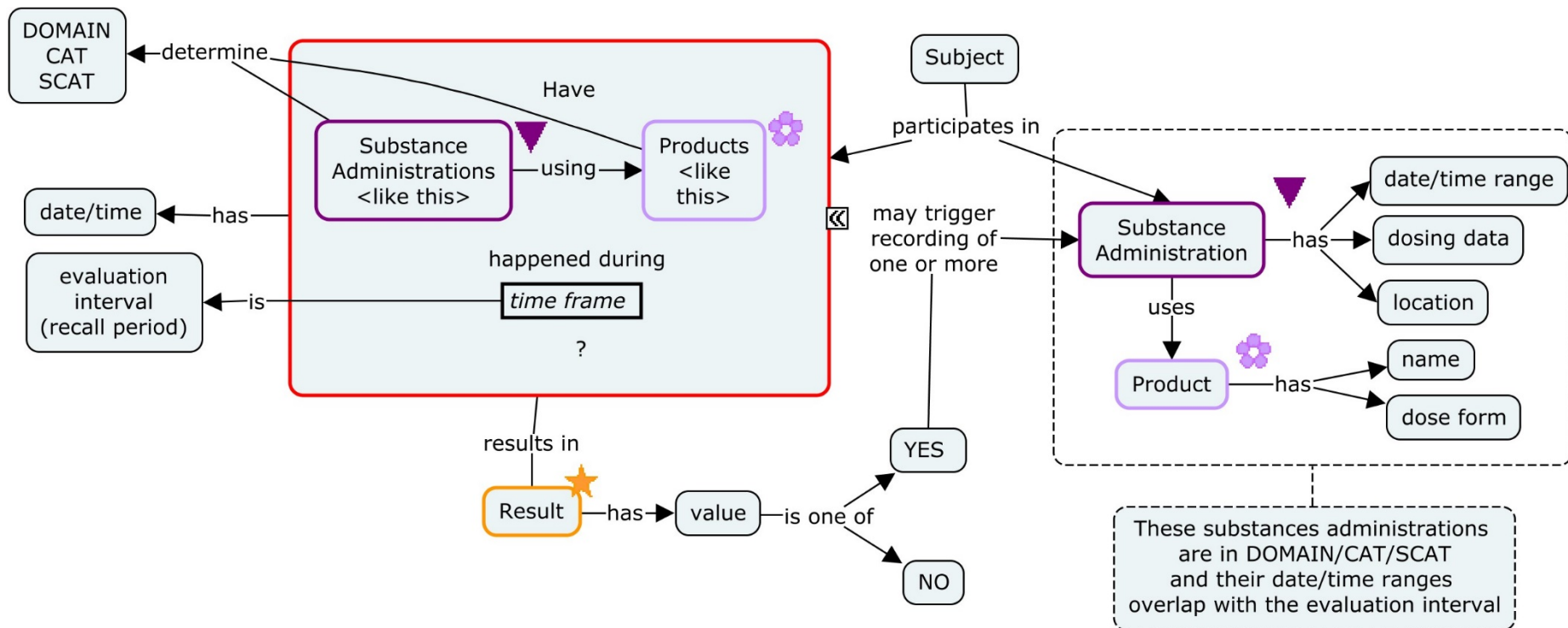
-- event occurrence and collection

- Adding “Any events” and SDTM OCCUR



Common data patterns

-- substance administrations



Each of these patterns is a “template” for research concepts

- This is not a complete set of templates
- Each of these templates is simplified, leaves some things out

All models are wrong;
some are useful.

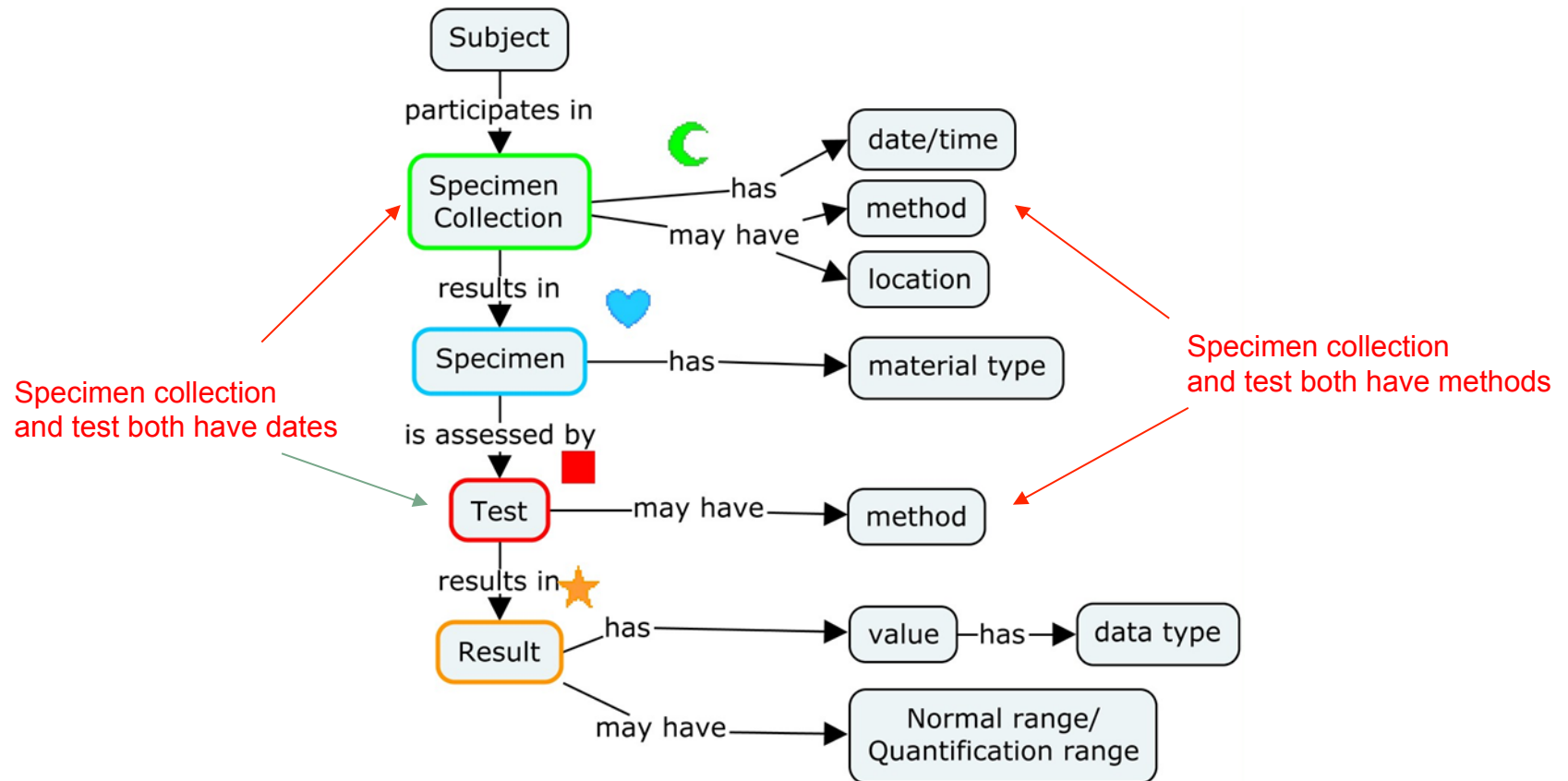
~ George Box

Uses for concept models

- Communicate with clinicians
 - TA projects provide access to clinicians often not routinely available
- Form the basis of tools for research concept metadata creation
- Highlight SDTM modeling issues

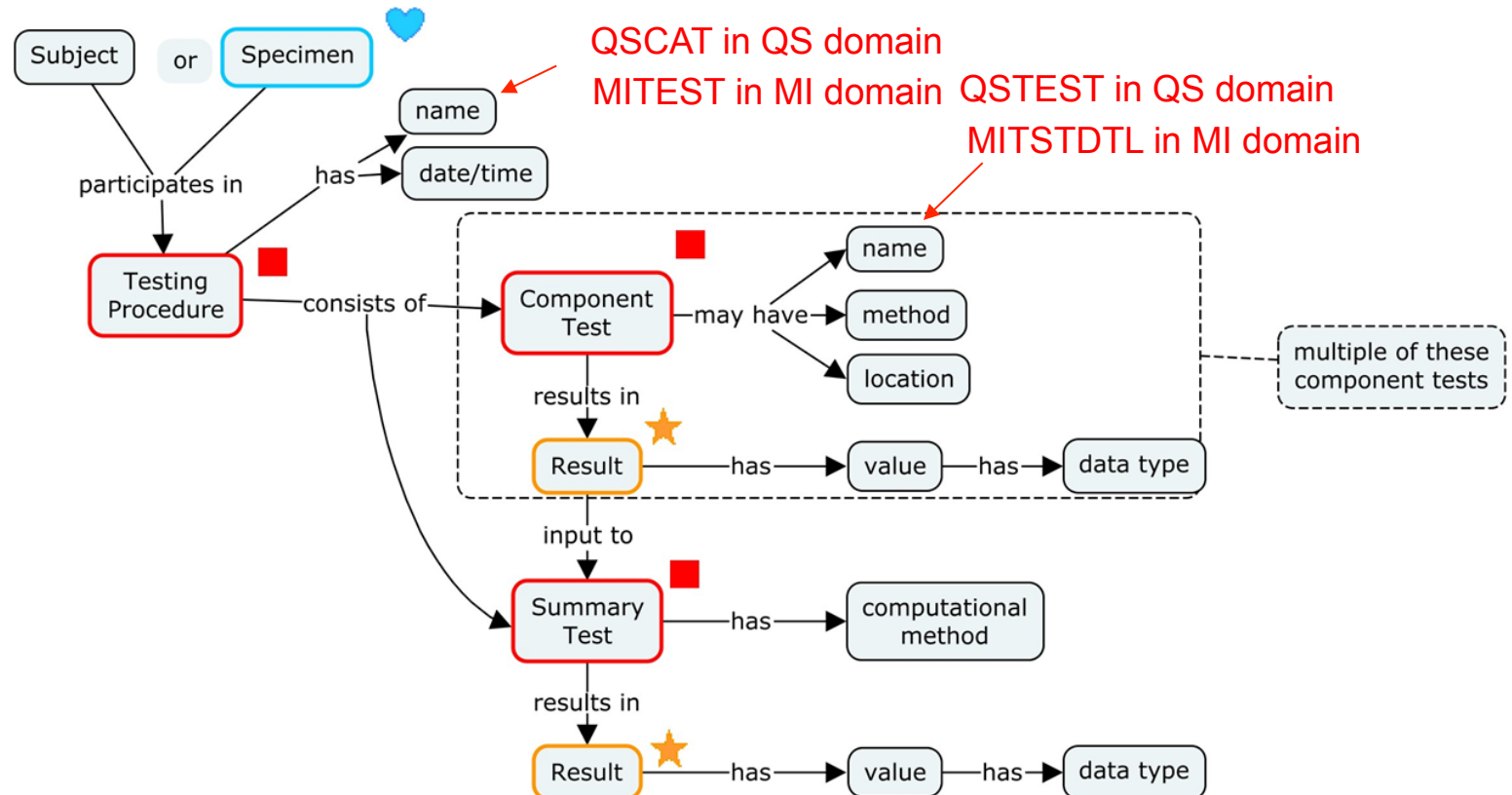
SDTM Issue

– which method? – which date?



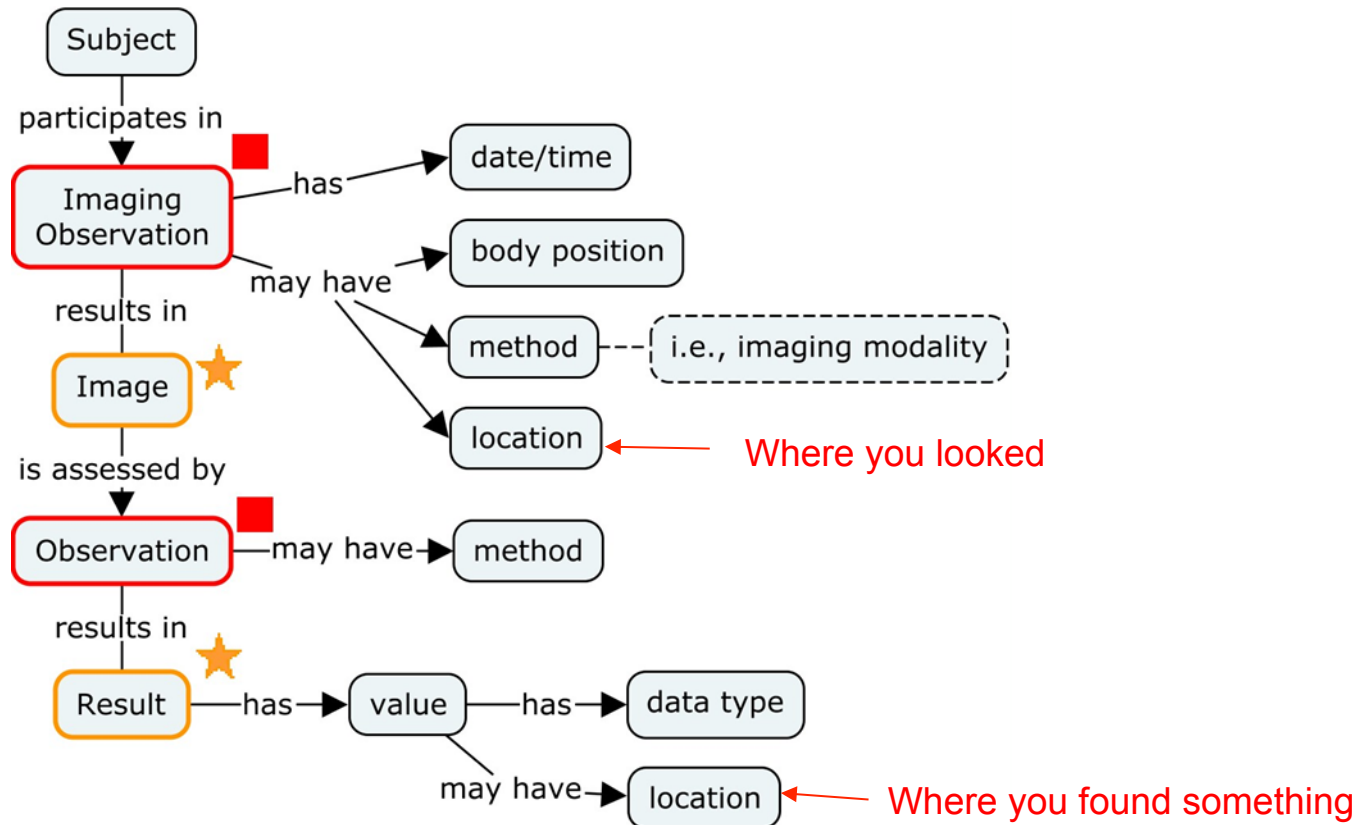
SDTM Issue

-- representing compound tests



SDTM Issue

-- which location?

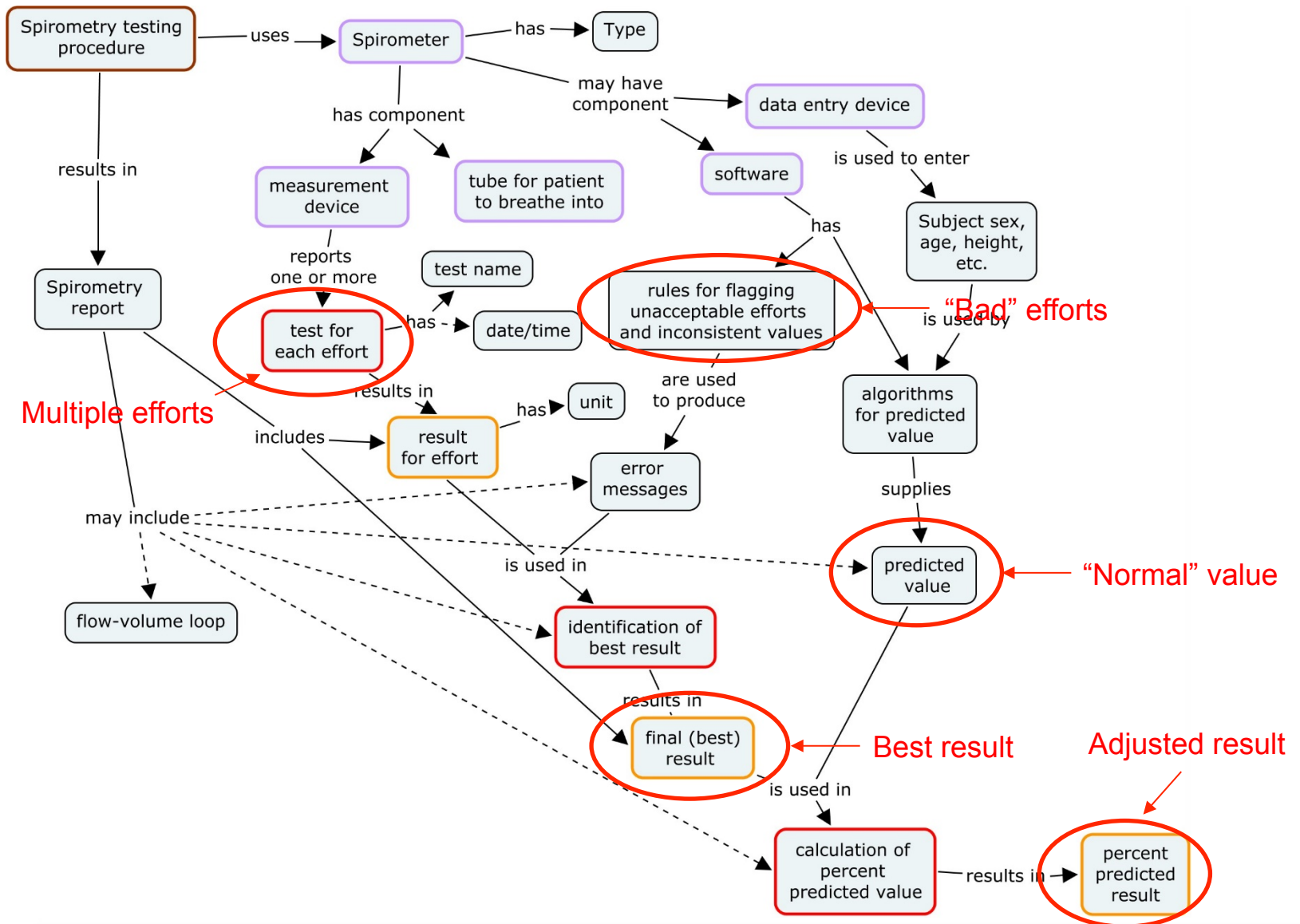


TA Example

Pulmonary Function Tests

- These are functional tests that require the subject to perform tasks: maximal inhalation and exhalation
- Results are variable
 - Use “best” of multiple repeats to reduce variability
 - Throw out “bad” efforts
- “Normal” isn’t expressed as a range, but as a predicted value
 - “Percent predicted” more meaningful than raw value
 - Somewhat analogous to “times ULN” for liver enzymes

Spirometry concept map



TA Example

Pulmonary Function Test solutions

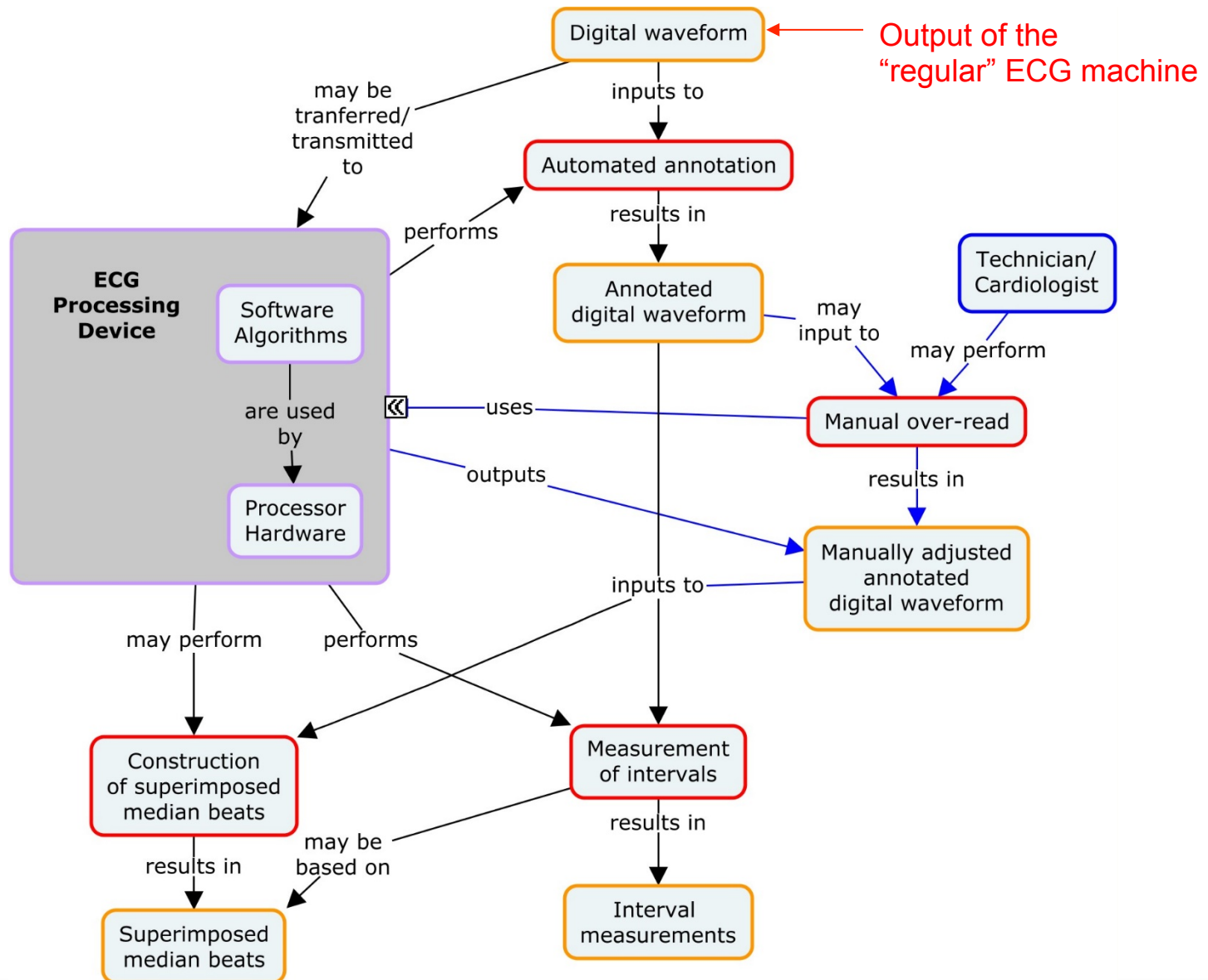
- Repeat number (we used time points in Asthma, but REPNO variable created for QT is better)
- Best result flag (handled as supplemental qualifier REBRESFL)
- A way to flag inadequate results and why they were inadequate (variable REIRESFL and supplemental qualifiers REIRREAn for reasons)
- REORREF and RESTREFN for reference results (as opposed to ranges)
- Used device domains for properties of devices, including algorithm used for predicted values

TA Example

ECG devices

- The usual kind of ECG is done using one device, a “regular” ECG machine
- For QT studies, the data from a “regular” ECG machine is fed into a workstation for further analysis, which can be done via automated algorithms or can involve manual override

ECG workstation concept map

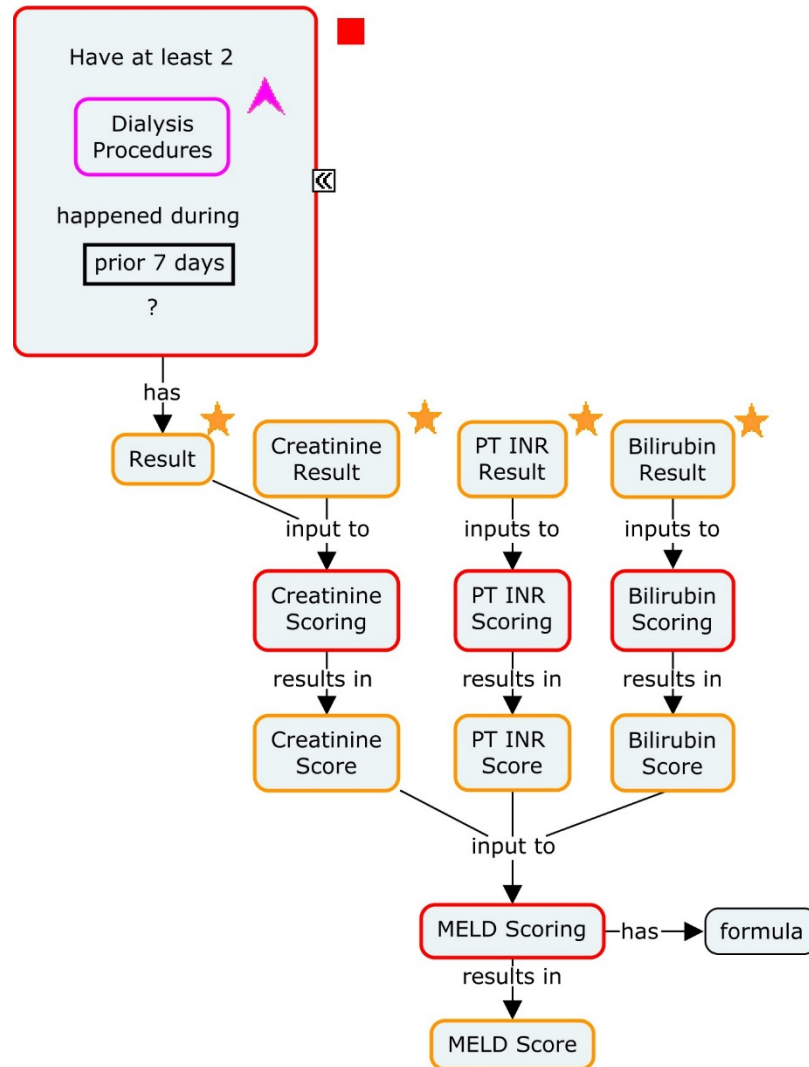


TA Example

ECG devices – compound device

- The variable SPDEVID introduced in the SDTMIG-MD allows one to link a device to a record in a findings domain.
 - For QT studies ECGs, the basic ECG machine and the ECG analysis workstation are used together
 - Proposed RELDEV domain allows one to define a group of devices and assign a value of SPDEVID to the group
- Device properties, including properties of software, in device domains

MELD concept map



TA Example

MELD (Model for End Stage Liver Disease)

- SDTM issues, some still unresolved:
 - When should this be in SDTM, when in ADaM?
 - If in SDTM, in CC (Clinical Classifications) domain?
 - If in SDTM, are the lab values represented in both the LB domain and the CC domain?
 - Where does the dialysis question go? Only in the CC domain?
 - Which variables do the scores go in?
- The computational formula is research concept metadata that will appear in define, not in an SDTM variable

Research Concepts and SHARE

- This talk has concentrated on modelling research concepts so that we can create their metadata
- Once a research concept has been created, it has
 - BRIDG metadata
 - Used to ensure consistency of modeling
 - Can be “hidden” from users who don’t care about it
 - SDTM metadata
 - Supplemented with CDASH metadata
 - Controlled terminology
 - Relevant subsets for large code lists like unit, location, method

Asthma Therapeutic Area Work

Concept: Forced Vital Capacity

Domain: RE
TEST: Forced Vital Capacity
TESTCD: FVC

value(s)	BRIDG-based concept variable	Attribute	SDTM variable(s)
C11468	PVC_OBS DefinedObservation.targetAnatomicSiteCode CD.code	Pre-specified target site	via DOMAIN/RE
LUNGS	PVC_OBS DefinedObservation.targetAnatomicSiteCode CD.displayname value	Pre-specified site of administration	RELOC
C12421	PVC_OBS DefinedObservation.approachAnatomicSiteCode CD.code		
ORAL CAVITY	PVC_OBS DefinedObservation.approachAnatomicSiteCode CD.displayname value		
SPIROMETRY	PVC_OBS DefinedObservation.methodCode CD.code	Method	REMETHOD
From code list C85492	PVC_OBS DefinedObservation.methodCode CD.displayname value		
Free text	PVC_OBS DefinedObservation.methodCode CD.originalText value		
datetime	PVC_OBS PerformedObservation.startDateRange VL<TS> low value	Date Range	REDTC
integer	PVC_OBS PerformedObservation.startDateRange VL<TS> low value	Study Day Range	REDY
TRUE, FALSE (SDTM NOT DONE, null)	PVC_RES PerformedObservation.negativeIndicator BL value	Negation Indicator	RESTAT
Free text	PVC_OBS PerformedObservation.negativeReason DSET<SC> item value	Negation Reason	RESEASND
Free text	PVC_RES PerformedClinicalResult.valueNullFlavorReason ST value	Value NullFlavor	
Free text	PVC_RES PerformedClinicalResult.value PQ originalText value	Result v	REDRES, REDTRES, REDTRESU
decimal	PVC_RES PerformedClinicalResult.value PQ value	Result unit	REDRESU, REDTRESU
C85492, C48505	PVC_RES PerformedClinicalResult.value PQ unit code	Baseline indicator	REBLI
ML, L	PVC_RES PerformedClinicalResult.value PQ unit displayname value	Referent result value	REDREFR, REDTREFR
TRUE, FALSE (SDTM Y, null)	PVC_RES PerformedClinicalResult.baselineIndicator BL value	Referent result unit	
Formula for predicted normal value	PVC_RES ReferenceResult.value PQ expression value		
decimal	PVC_RES ReferenceResult.value PQ value		
C85492, C48505	PVC_RES ReferenceResult.value PQ unit code		
ML, L	PVC_RES ReferenceResult.value PQ unit displayname value		

Possible associated concepts

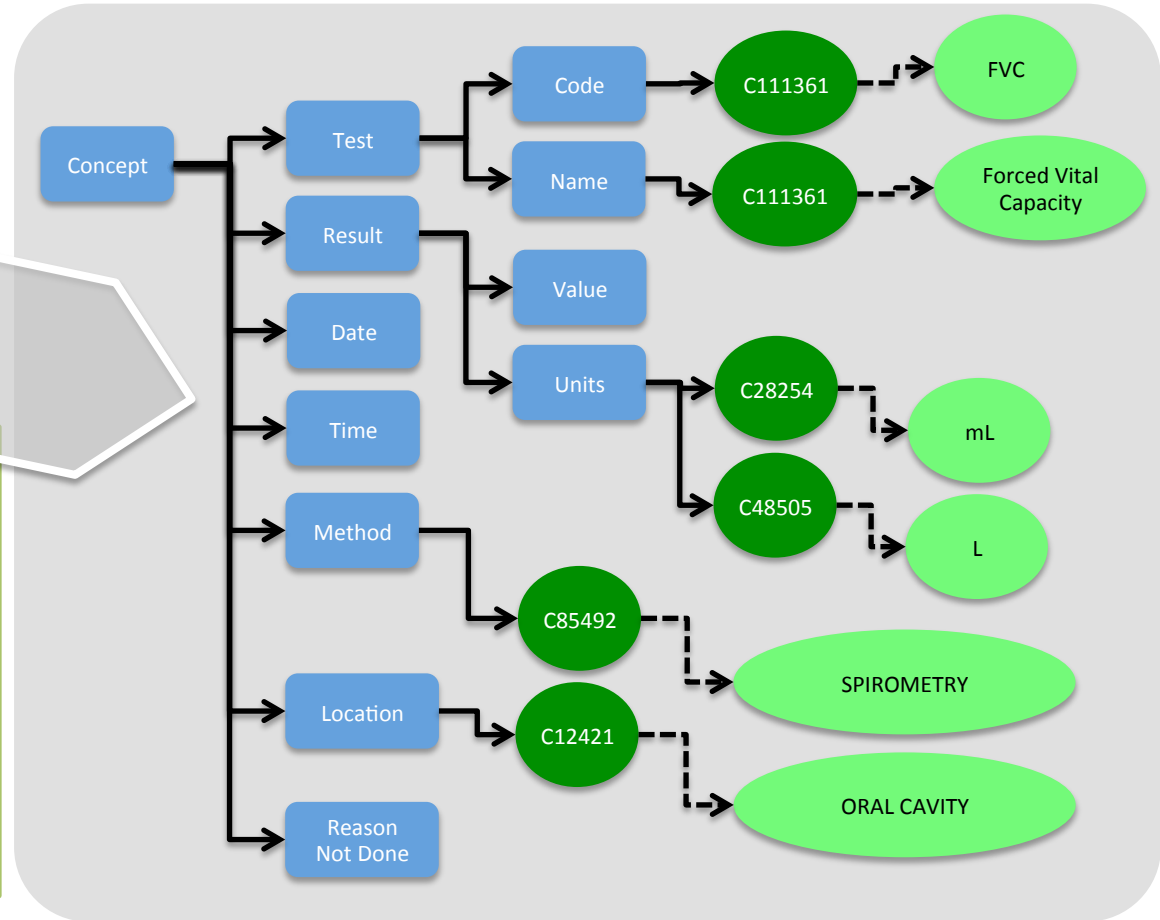
Device used in testing	SPOVED
Spirometer	
Percent Predicted FVC	

SDTM mapping

- Assumes RE domain
- What about use of test in another domain?

Note BRIDG mapping

- Want if for consistent and well structured concepts (Templates)
- Don't want to see it after that



Slide courtesy Dave Iberson-Hurst

Example research concept metadata

-- Liver elasticity

Natural
language
aliases for
BRIDG class
and attribute
information

	Attribute	value(s)	SDTM variable(s)
pre-specified properties of test	Location	C12392	MOLOC
		LIVER	
	Method	C106517	MOMETHOD
		ELASTOGRAPHY	
collected properties of test	Date Range	datetime	MODTC
	Study Day Range	integer	MODY
collected properties of response	Result Value (numeric)	decimal	MOORRES, MOSTRESC, MOSTRESN
		C67284	MOORRESU, MOSTRESU
	Result Unit	kPa	

Research Concepts in SHARE

Next steps

- Decisions about research concept representation
 - How big is a research concept?
 - Exactly what metadata is needed?
 - What CDASH metadata?
- Figuring out how to make full use of them
 - Protocol schedule of events
 - CRF setup
 - Database setup
 - SDTM creation
 - Define files
 - Value level metadata
 - Analysis