Towards Better Data

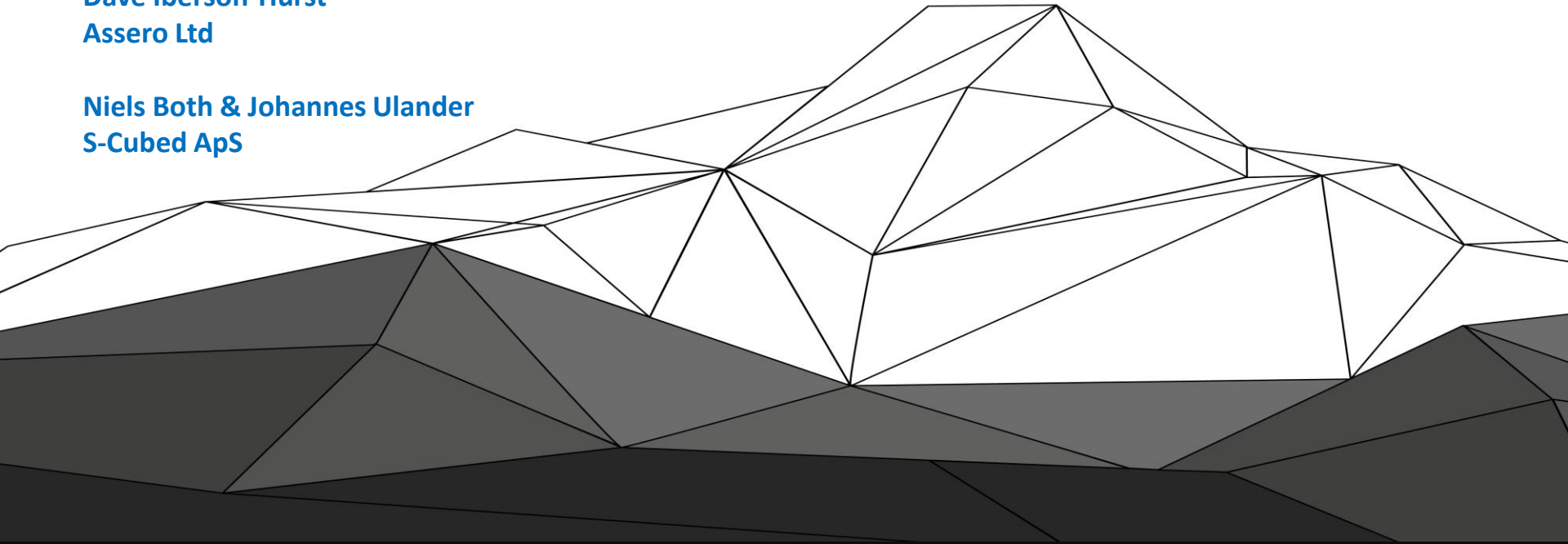
PhUSE SDE Copenhagen

1st June 2017

Dave Iberson-Hurst
Assero Ltd

Niels Both & Johannes Ulander
S-Cubed ApS

GLANDON
METADATA REPOSITORY



Agenda

- Abstract & Introduction
- Issues
- Vision & Theory
- Iterative Approach
- Reality
- Summary

Abstract & Introduction

Abstract

The industry has long talked about 'end-to-end' and 'metadata-driven approaches' as a way of improving processes within clinical research. Meanwhile the FDA talk about issues with the data quality and integrity of electronic submissions and have announced further rules and submission checks. Sponsors want to ensure their submissions are accepted. This presentation will describe significant tangible progress that has been made in moving towards the vision against this backdrop of increased data scrutiny.

The presentation will quickly outline the vision to align the audience, and describe experiences from the industry, when implementing MDR technology today.

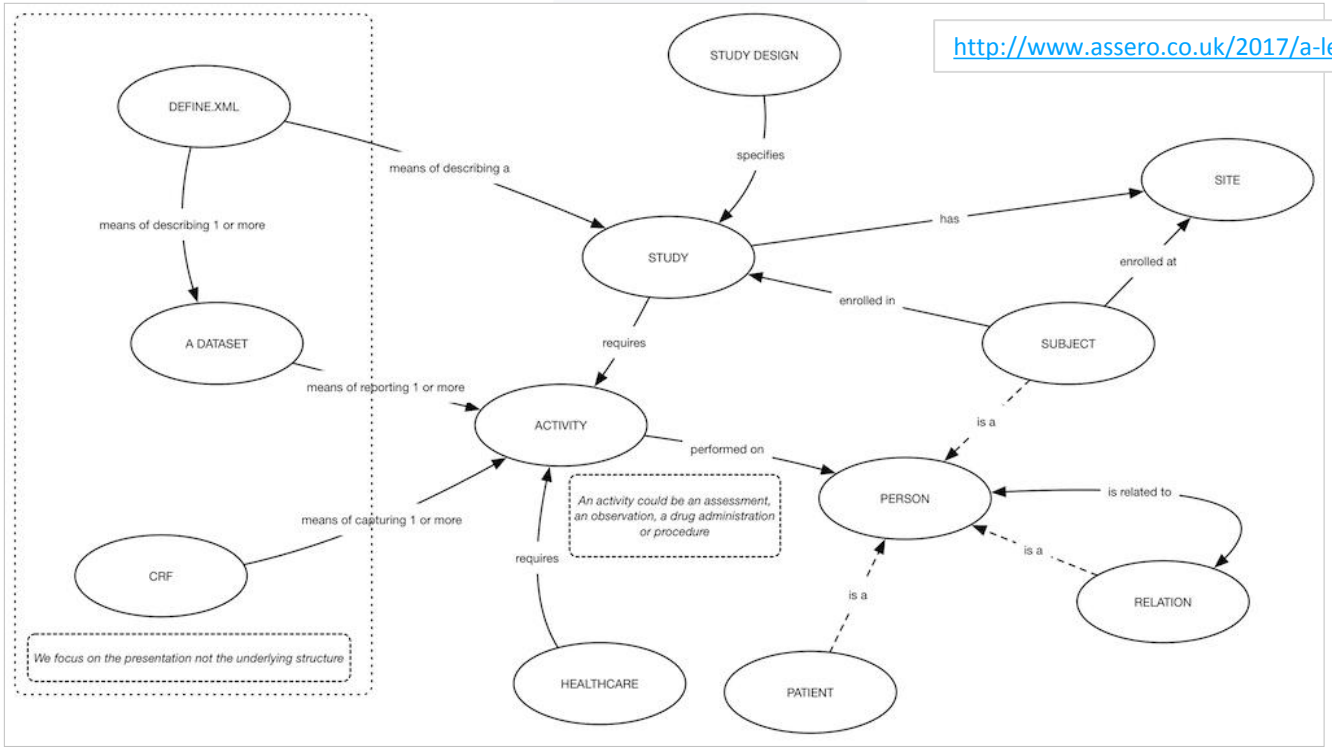
The main part of the talk will detail the current progress demonstrating improved version control and visibility of the impact of change including changes across CDISC terminology and SDTM releases. The creation of CRFs, the automated creation of annotated CRFs and the ability to build studies will also be discussed and demonstrated. The presentation will then discuss some immediate next steps including the automated creation of define.xml from a study build, the feasibility on the creation of SDTM domains from captured data and the potential to link back to the protocol.

The longer-term vision and next steps will then be discussed of including analysis, AdaM and TLFs into the picture as well as the link to EHRs as iterations in capability take us towards the end-to-end goal.

The summary will the review the presentation and discuss how this approach can help a sponsor meet their submission goals.

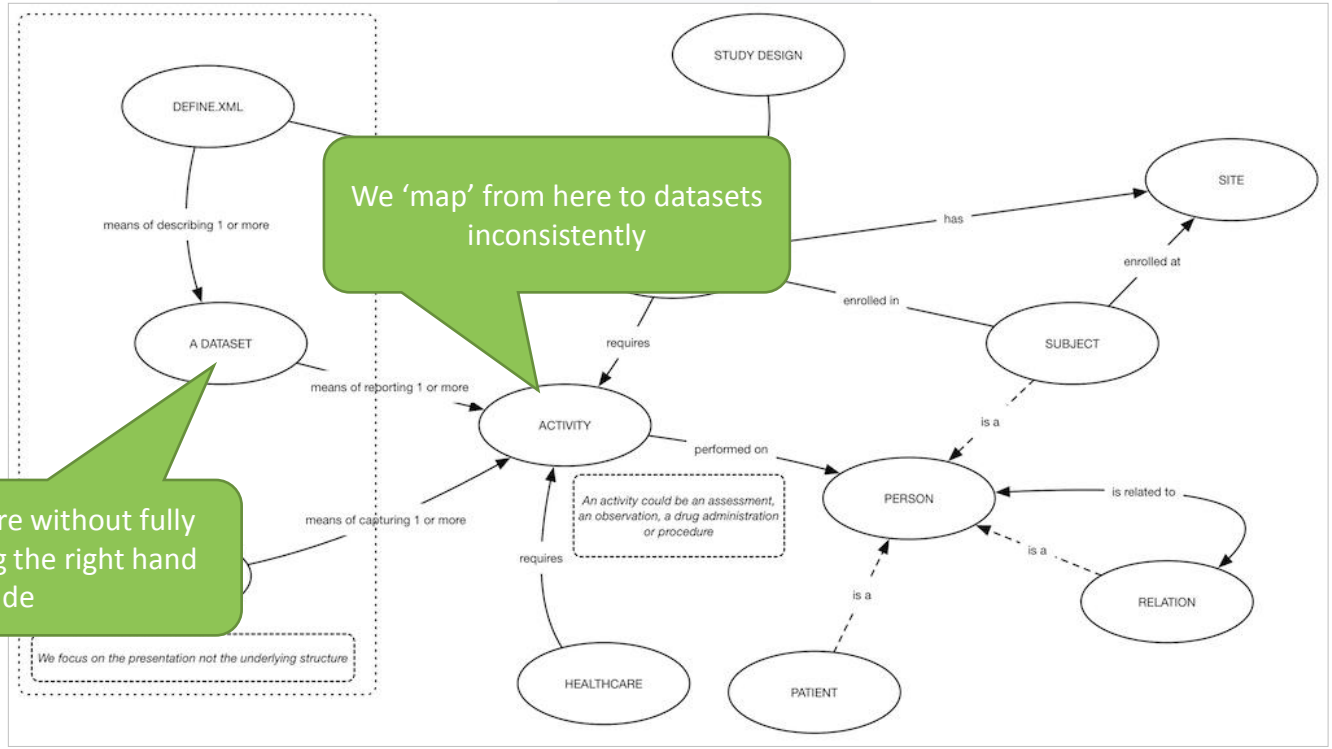
The Issues

Left and Right Sides

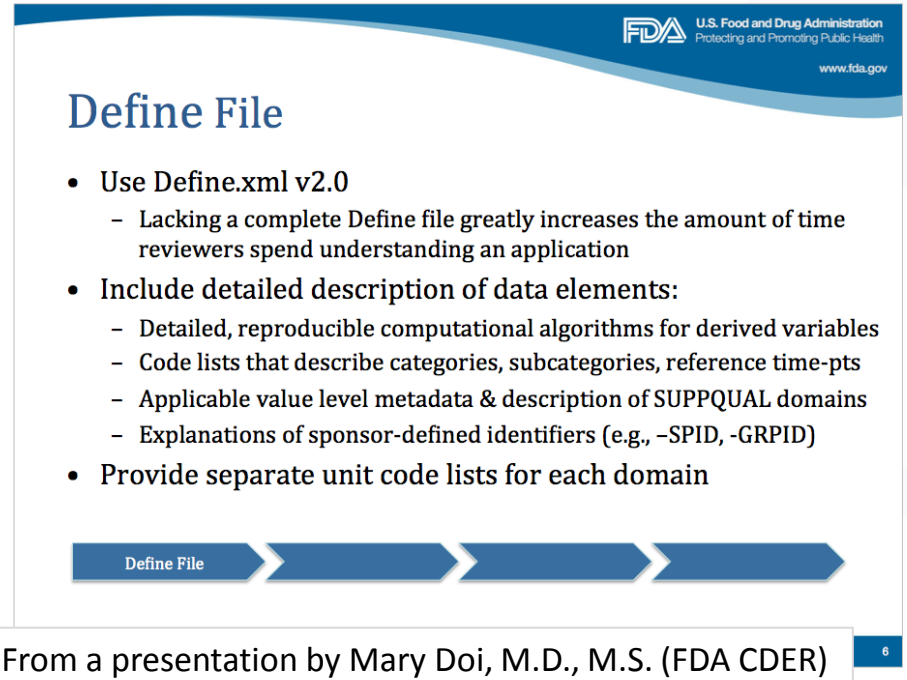


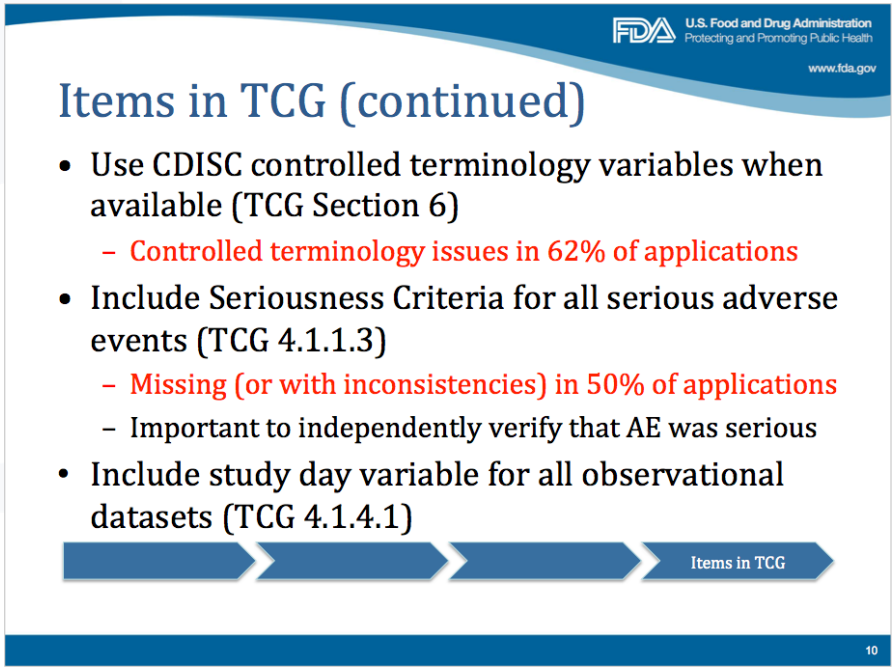
http://www.assero.co.uk/2017/a-left-side-and-a-right-side/

Left and Right Sides



FDA @ PhUSE CSS 2016





From a presentation by Mary Doi, M.D., M.S. (FDA CDER)

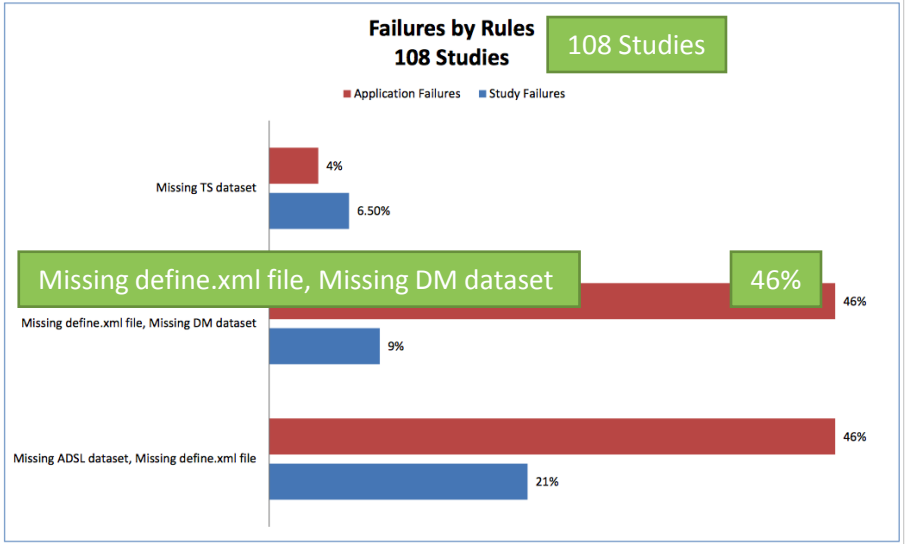
FDA @ PhUSE CSS 2017

eCTD Technical Validation of Study Data

High Level Rule #1	High Level Rule #2
Rule # 1734 : A Trial Summary (TS) dataset must be present for each study in module 4, sections 4.2.3.1, 4.2.3.2, 4.2.3.4 and in module 5, sections 5.3.1.1, 5.3.1.2, 5.3.3.1, 5.3.3.2, 5.3.3.3, 5.3.3.4, 5.3.4, 5.3.5.1, 5.3.5.2	Rule #1736: DM dataset and define.xml must be submitted in module 4, sections 4.2.3.1, 4.2.3.2, 4.2.3.4. DM dataset, ADSL dataset, define.xml must be submitted in module 5, sections 5.3.1.1, 5.3.1.2, 5.3.3.1, 5.3.3.2, 5.3.3.3, 5.3.3.4, 5.3.4, 5.3.5.1, 5.3.5.2

https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/UCM523539.pdf

11



13

From a presentation by Crystal Allard, Special Assistant to the Director Office of Computational Science

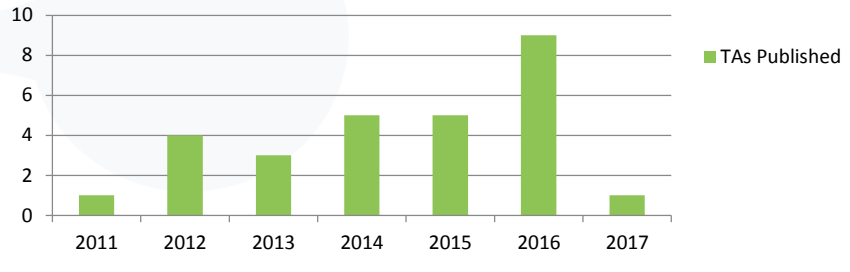
Rate of Change

Published TA User Guides

Project	Publication Date	Terminology	SDTM	CDASH	ADaM
Alzheimer's Disease v1	September 9, 2011	X	X		
Tuberculosis v1	June 29, 2012	X	X		
Pain v1	August 7, 2012	X	X		
Virology v1	December 6, 2012	X	X		
Parkinson's Disease v1	December 18, 2012	X	X		
Polycystic Kidney Disease v1	February 26, 2013	X	X		
Asthma v1	November 26, 2013	X	X		
Alzheimer's Disease v2	December 16, 2013	X	X		
Multiple Sclerosis v1	May 2, 2014	X	X		
Diabetes v1 (ADaM Supplement)	September 11, 2014 (December 18, 2015)	NA	X	X	X
Cardiovascular Endpoints v1	October 17, 2014	X	X		
Influenza v1	November 25, 2014	X	X		
QT Studies v1	December 12, 2014	X	X		
Chronic Hepatitis C Virus v1	May 8, 2015	X	X	X	
Schizophrenia v1	June 9, 2015	X	X		
Dyslipidemia v1	June 19, 2015	X	X	X	X
Virology v2	September 30, 2015	X	X		Partial
Traumatic Brain Injury v1	December 14, 2015	X	X	X	

Published TA User Guides

Project	Publication Date	Terminology	SDTM	CDASH	ADaM
COPD v1	January 26, 2016	X	X	X	X
Tuberculosis v2	February 26, 2016	X	X		
Breast Cancer v1	May 16, 2016	X	X	X	X
Rheumatoid Arthritis v1	November 14, 2016	X	X	X	X
Kidney Transplant	October 31, 2016	X	X	X	X
Major Depressive Disorder v1	December 5, 2016	X	X	X	X
Diabetic Kidney Disease v1	December 13, 2016	X	X	X	X
Pain v1.1 (update)	December 13, 2016	X	X		
Ebola v1	December 19, 2016	X	X	X	
Malaria v1	January 9, 2017	X	X	X	

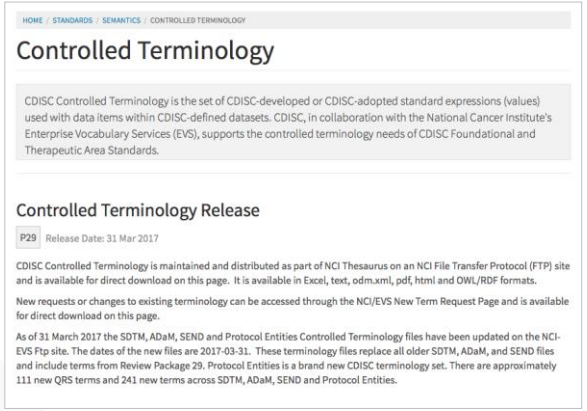


We Need …

Published TA User Guides

Project	Publication Date	Terminology	SDTM	CDASH	ADaM
Alzheimer's Disease v1	September 9, 2011	X	X		
Tuberculosis v1	June 29, 2012	X	X		
Pain v1	August 7, 2012	X	X		
Virology v1	December 6, 2012	X	X		
Parkinson's Disease v1	December 18, 2012	X	X		
Polycystic Kidney Disease v1	February 26, 2013	X	X		
Asthma v1	November 26, 2013	X	X		
Alzheimer's Disease v2	December 16, 2013	X	X		
Multiple Sclerosis v1	May 2, 2014	X	X		
Diabetes v1 (ADaM Supplement)	September 11, 2014 (December 18, 2015)	NA	X	X	X
Cardiovascular Endpoints v1	October 17, 2014	X	X		
Influenza v1	November 25, 2014	X	X		
QT Studies v1	December 12, 2014	X	X		
Chronic Hepatitis C Virus v1	May 8, 2015	X	X	X	
Schizophrenia v1	June 9, 2015	X	X		
Dyslipidemia v1	June 19, 2015	X	X	X	X
Virology v2	September 30, 2015	X	X		Partial
Traumatic Brain Injury v1	December 14, 2015	X	X	X	

- Control
  - Constant new versions
  - Rate-of-change of versions
- Precision
  - Which version am I using?
- Visibility
  - What changed?
  - When did it change
  - What is the impact of the change?
- Ease-of-use
  - Make it easier to use
  - Machine readable



HOME / STANDARDS / SEMANTICS / CONTROLLED TERMINOLOGY

Controlled Terminology

CDISC Controlled Terminology is the set of CDISC-developed or CDISC-adopted standard expressions (values) used with data items within CDISC-defined datasets. CDISC, in collaboration with the National Cancer Institute's Enterprise Vocabulary Services (EVS), supports the controlled terminology needs of CDISC Foundational and Therapeutic Area Standards.

Controlled Terminology Release

P29 Release Date: 31 Mar 2017

CDISC Controlled Terminology is maintained and distributed as part of NCI Thesaurus on an NCI File Transfer Protocol (FTP) site and is available for direct download on this page. It is available in Excel, text, odm.xml, pdf, html and OWL/RDF formats.

New requests or changes to existing terminology can be accessed through the NCI/EVS New Term Request Page and is available for direct download on this page.

As of 31 March 2017 the SDTM, ADaM, SEND and Protocol Entities Controlled Terminology files have been updated on the NCI-EVS Ftp site. The dates of the new files are 2017-03-31. These terminology files replace all older SDTM, ADaM, and SEND files and include terms from Review Package 29. Protocol Entities is a brand new CDISC terminology set. There are approximately 111 new QRS terms and 241 new terms across SDTM, ADaM, SEND and Protocol Entities.

Current State of Metadata Use

Where Are We Today With The Use Of MDR Tools?

- Few commercial MDR tools are available for actual practical use in the industry.
- Many commercial tools, which does a part of the job exist.
- Several companies use home-made MS Excel and/or SAS tools to work as source of metadata.

Issues on Current State I

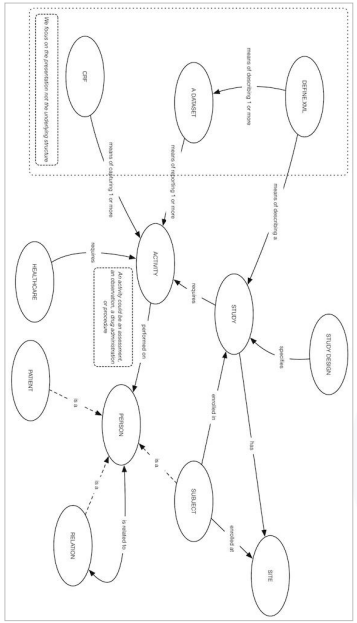
- True MDR Tools working with metadata to aid – starting from Protocol and CRF design, often turns out to struggle in implementation
- Because of the increased workload and complexity pushed upstream
- Because of lack of acceptance of standards internally in the organisations

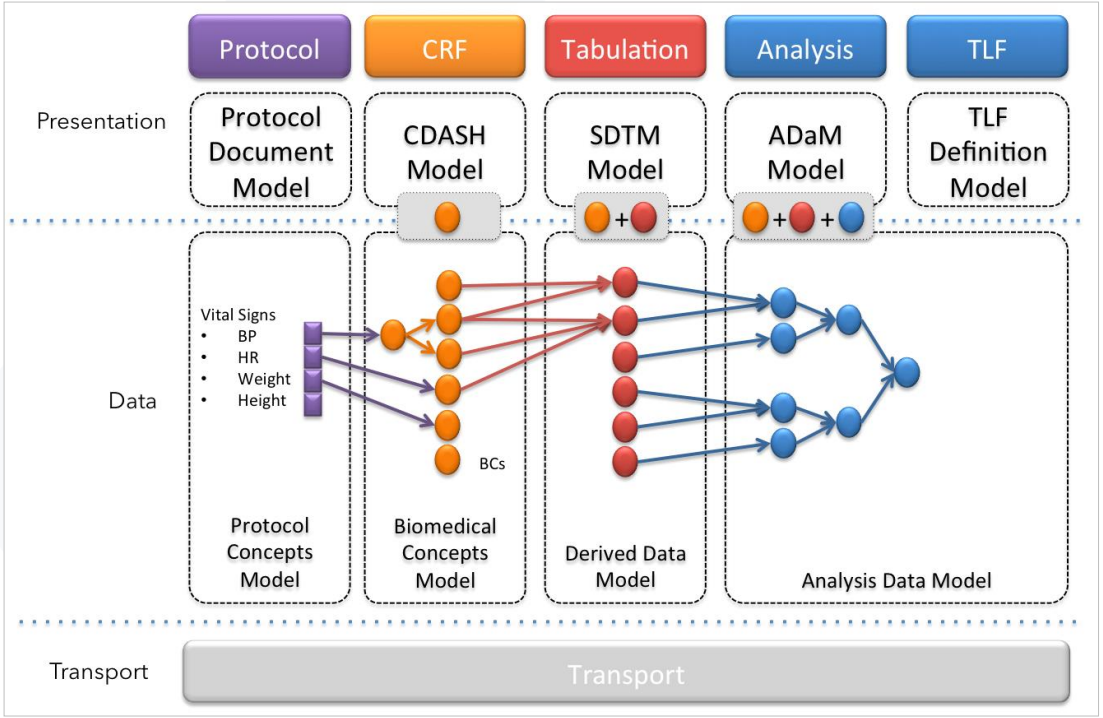
Issues on Current State II

- Homegrown Excel / SAS solutions, tends to be successful to some extent
- But they are rarely built in a way, that they are scalable
- And over the years might cause situations with “Islands of Metadata”

Vision & Theory

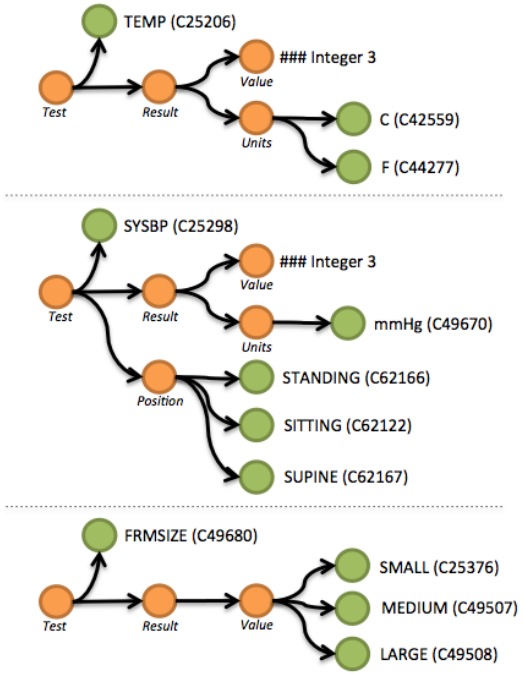
Vision



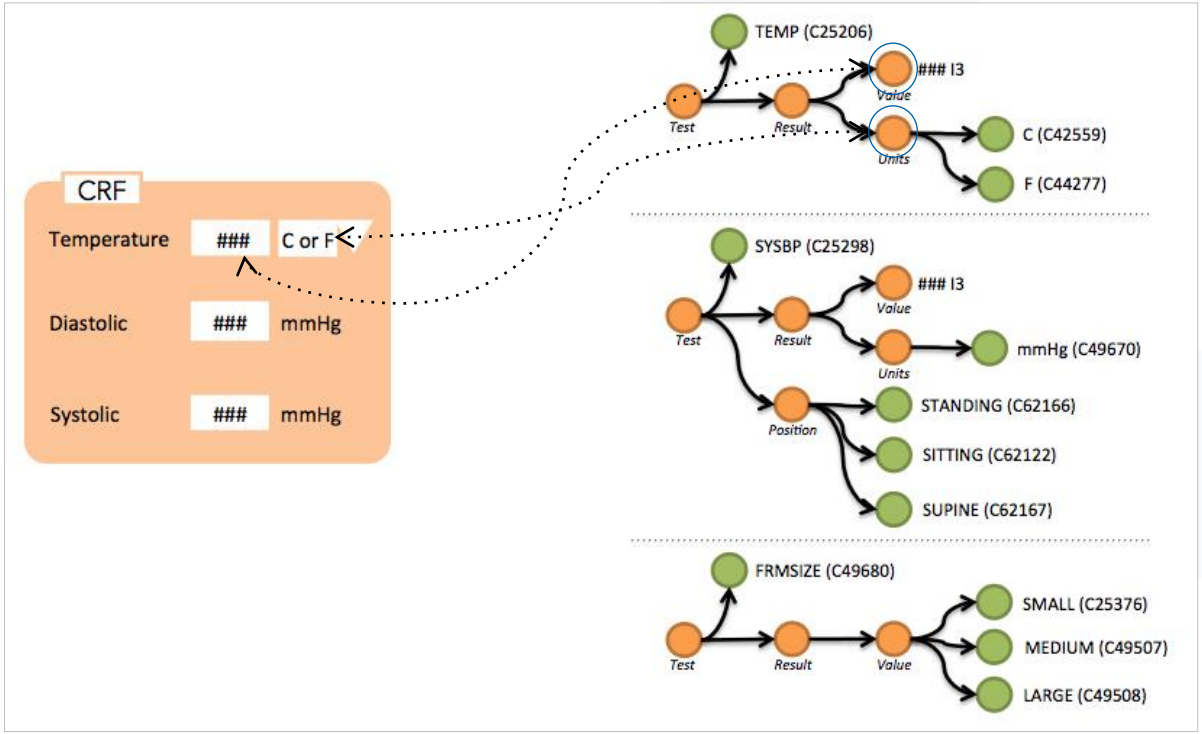


Biomedical Concepts

- Better structure and relationships, not just individual variables 'floating. A collection of variables with logical structure.
- Consistent structure
- Note the definition of value level metadata
- CDISC have just released an updated SHARE model for review/comment containing BCs
- BCs derived from concept maps as seen in TA User Guides
- Can exists independent of SDTM & CDASH

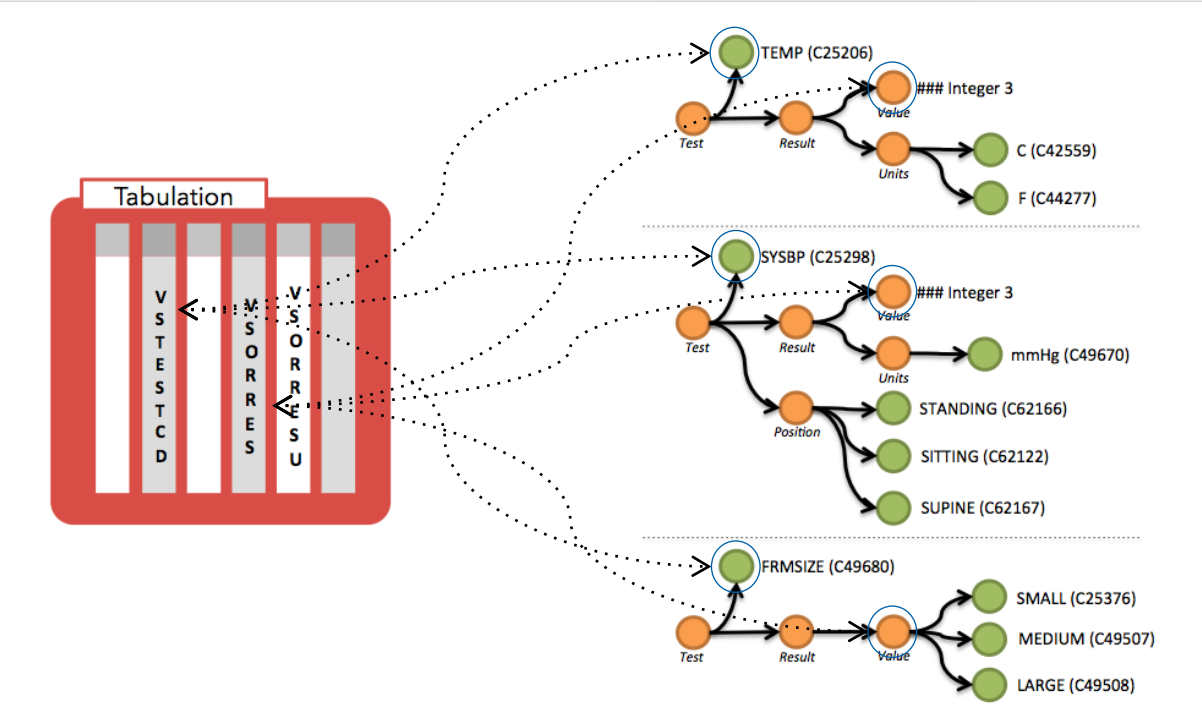


Biomedical Concepts & Forms



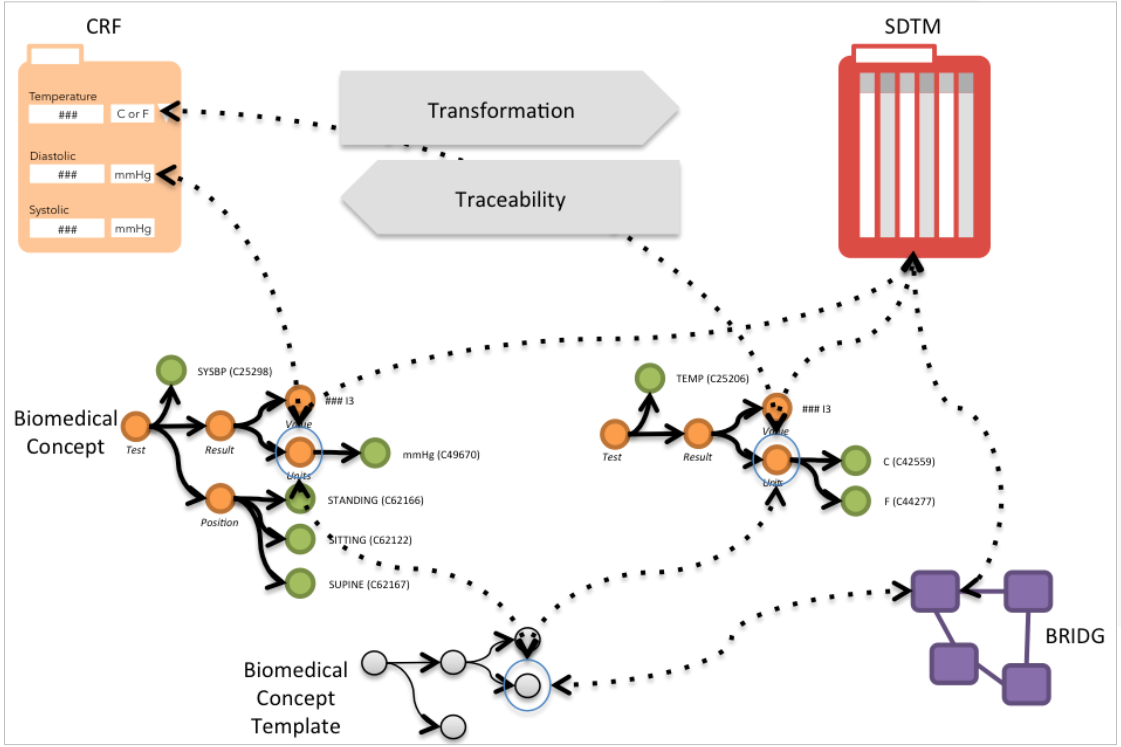
Note: Only a couple of relationships shown so as to convey the principle

Biomedical Concepts & Domains



Note: Only a couple of relationships shown so as to convey the principle

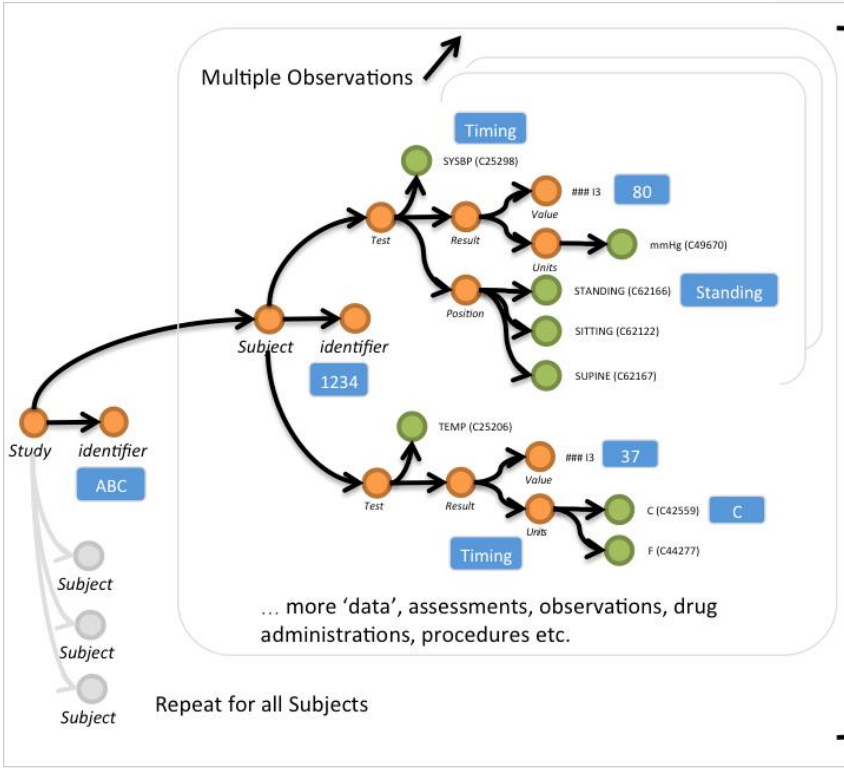
Using Biomedical Concepts



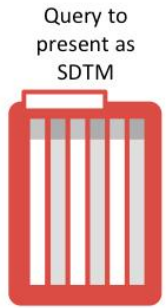
Notes:

1. A template is used to build BCs. There will be many templates.
2. The template is based on the BRIDG model.
3. BRIDG provides an invisible reference framework.
4. The dotted links provide machine capable automated processing and traceability.
5. Biomedical Concepts need only be associated with the target domain, the machine can link the individual pieces itself

SDTM Data I



1. The next step is to start generating domains automatically from data
2. Having a machine representation of the metadata (the study definition) allows for the data to be 'attached'
3. Then significant parts of a domain can be created via a query. SDTM is a view of the data
4. The data can be used for other purposes
5. Learn and iterate to allow for the other variables to be created automatically
6. **This is the subject of a FDA/PhUSE CSS Project**



Query would be something like:

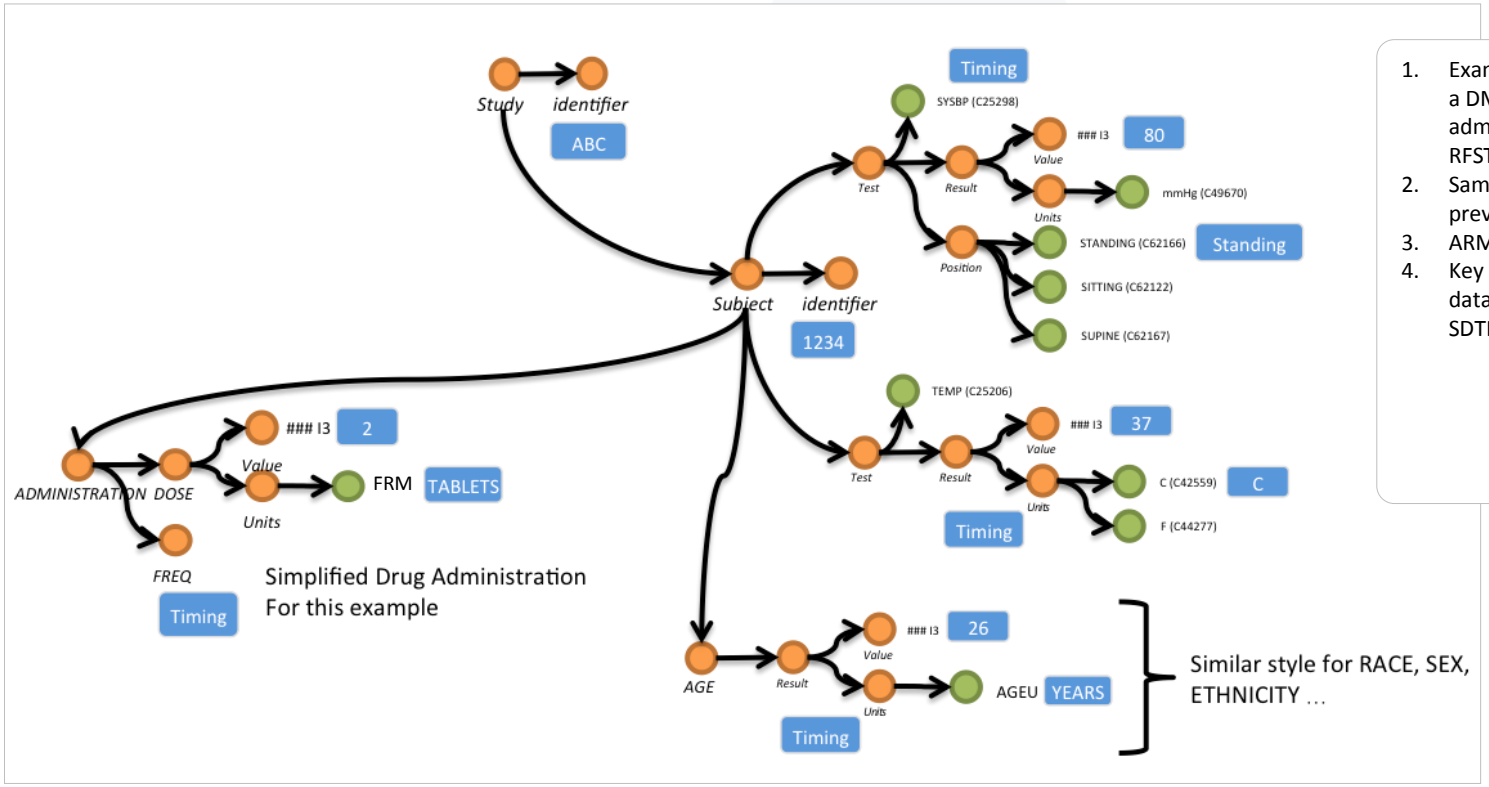
"For all VS tests start at study ABC, for all subjects get the identifier, get the test code, the result, additional properties and the date/time of the observation."

Query driven by the domain definition.

ABC	VS	ABC-1234	SYSBP	Standing	80	mmHg	…	Timing
ABC	VS	ABC-1234	TEMP		37	C	…	Timing

Standard Results & Units, Status, Baseline & Derived

SDTM Data II

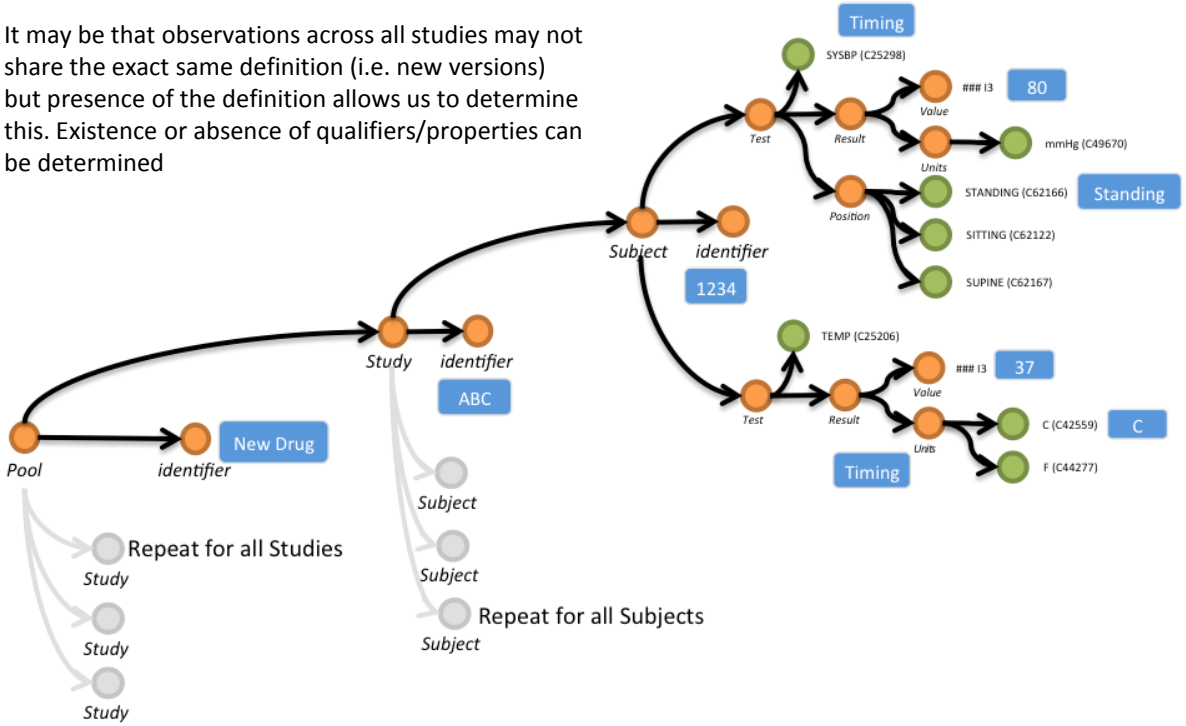


1. Example to give a flavour of generating a DM domain and the link to drug administration events to obtain RFSTDTC
2. Same query can be used for –DY for previous VS example.
3. ARM gets interesting!
4. Key high-level point is the raw captured data versus all of the 'derived' data in SDTM

Warning! ☺
Dangerous Thoughts

Pooled Data

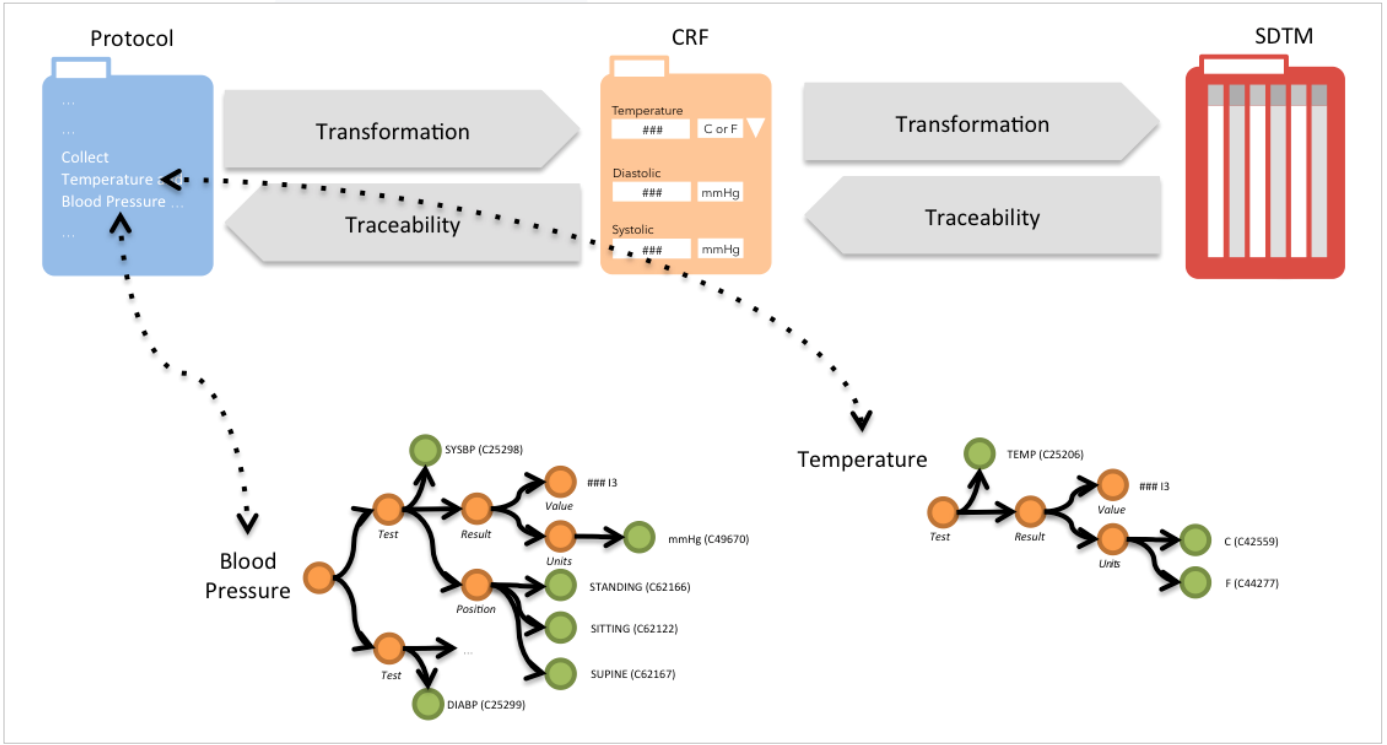
It may be that observations across all studies may not share the exact same definition (i.e. new versions) but presence of the definition allows us to determine this. Existence or absence of qualifiers/properties can be determined



1. Can get to larger pools of data
2. Query for a domain is the same, starting point is the Pool rather than the Study

Protocol

1. Link the names of the concepts back into the protocol document.
2. From a quick initial examination this looks possible with the TransCelerate protocol tool

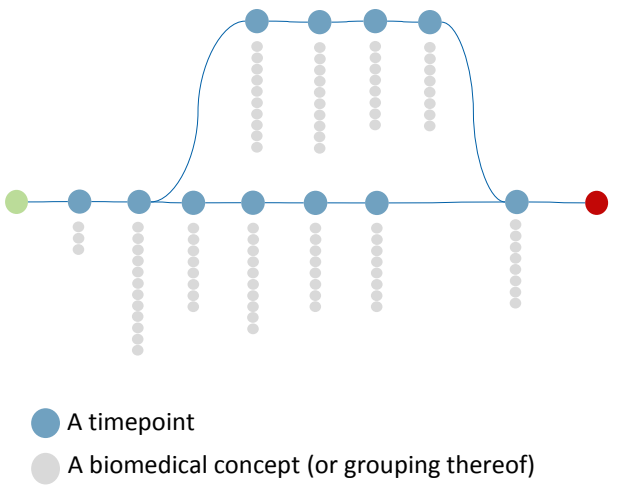


Protocol

Topic	Variable	Year						
		0	1		2	3	4	5/7	6/8
		Pre-V	V1a	V1b	V2	V3	V4	V5/V7	V6/V8
	Eligibility Form (Inclusion & Exclusion Criteria)	♦							
	Consent Form and Study Brochure	♦							
	Family Binder		♦	♦	♦	♦	♦	♦	♦
Kidney	Iohexol-based GFR		X		X		X		X
	Cystatin C		X		X	X	X	X	X
	Serum Creatinine		X		X	X	X	X	X
	Central Renal Panel[a]		X		X	X	X	X	X
	Central Uric Acid[b]		X		X	X	X	X	X
	Central Urine Creatinine and Protein		X		X	X	X	X	X
	Central Urine Albumin		X		X	X	X	X	X
	Local Complete Blood Count[c]		X		X	X	X	X	X
	Local Pregnancy Tests[d]		X		X	X	X	X	X
	Local Renal Panel[e]		X		X	X	X	X	X
	Local Urine Creatinine and Urine Protein[f]		X		X	X	X	X	X
Cardiovascular	Clinical Blood Pressure (centrally calibrated)		■	■	■	■	■	■	■
	Clinical Blood Pressure (locally measured)		■	■	■	■	■	■	■
	Lipid Profile				■		■		■
	Ambulatory Blood Pressure Monitoring				■		■		■
	Echocardiography				■		■		■
	Carotid Intima-Media Thickness[g]				■		■		■
	Pulse Wave Velocity[h]				■		■		■
	Cardiac Magnetic Resonance Imaging (MRI)[i]						■		
Neurocognitive	Pediatric Quality of Life			▲	▲	▲	▲	▲	▲
	Cognitive and Development Assessments			▲		▲		▲	
	Behavioral Assessments			▲		▲		▲	
Growth	Height/Length and Weight	●		●	●	●	●	●	●
	Head Circumference[j]	●		●	●	●	●	●	●
	Mid-Arm Circumference[j]	●		●	●	●	●	●	●
	Waist and Hip Circumferences[k]	●		●	●	●	●	●	●
	Tanner Stage	●			●	●	●	●	●
	Food Frequency Questionnaire (FFQ)			●	●	●	●	●	●
	Intact Parathyroid Hormone (iPTH)			●		●		●	
	High Sensitivity CRP (hsCRP)			●		●		●	
	Vitamin D			●		●		●	
	Fibroblast Growth Factor-23 (FGF-23)			●		●		●	
	6 Minute Walk Test (6MWT)					●		●	
	Grip Strength					●		●	

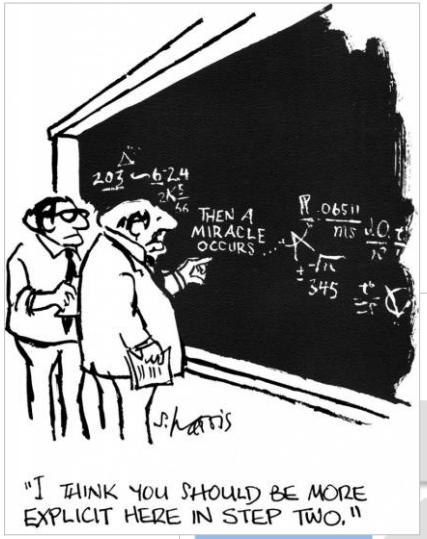
[a] **Central Renal Panel**: Blood drawn at each site and sent to Central Biochemistry Laboratory (CBL) where basic metabolic panel, phosphorous, and albumin are performed.
[b] **Cohort 2**: For Cohort 2, these tests will be measured at baseline and annual visits. For Cohort 1, the measurements of these tests were initiated at follow-up.
[c] **Local CBC**: The local laboratory at each clinical site will perform CBC tests.
[d] **Pregnancy Tests**: Pregnancy tests will be performed on females of child bearing potential. Childbearing potential occurs when the female has reached menarche.
[e] **Local Renal Panel**: Clinical sites will perform renal panel tests at their local laboratory for all participants in addition to the central renal panel tests that are sent to CBL.
[f] **Local Urine Creatinine and Urine Protein**: Clinical sites that require immediate results will perform urine creatinine and urine protein tests at their local laboratory in addition to the tests that are sent to CBL.
[g] **IMT**: At selected sites, sub-set of the entire cohort will have carotid IMT performed (N=100).
[h] **PWV**: At selected sites, sub-set of the entire cohort will have pulse wave velocity performed.
[i] **Cardiac MRI**: Sub-set of the entire cohort with a high probability of reaching ESRD will have cardiac MRI performed.
[j] **Head Circumference**: Head circumference will be measured at every study visit for children 3 years old and younger.
[k] **Mid-Arm Circumference**: Mid-arm circumference will be measured at every study visit for the entire cohort.
[l] **Waist and Hip Circumferences**: Waist and Hip circumference will be measured at every study visit for the entire cohort.

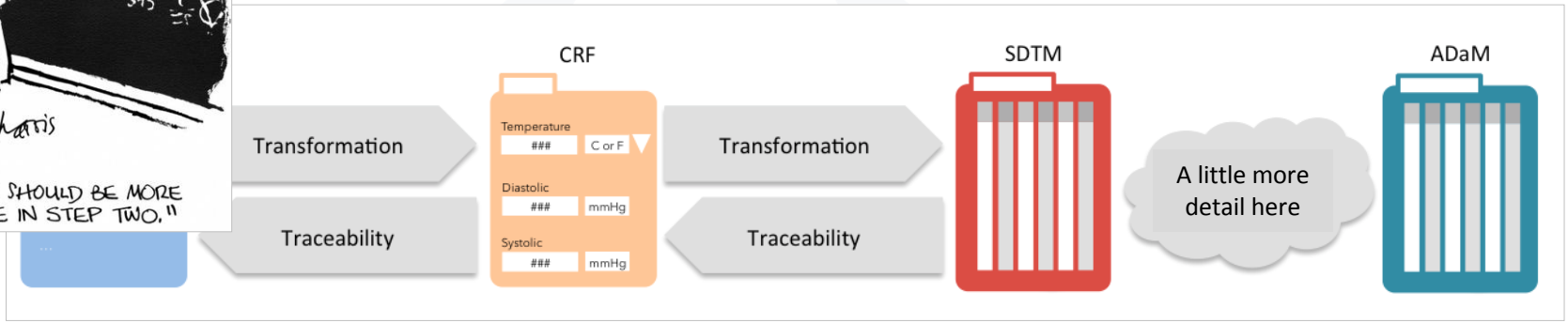
1. Is it possible to base protocols on the concepts to be collected rather than the form?
2. Create timelines rather than the rectangular ‘Schedule of Assessments’ we see today.
3. Link study designs in an explicit way to the data to be collected.



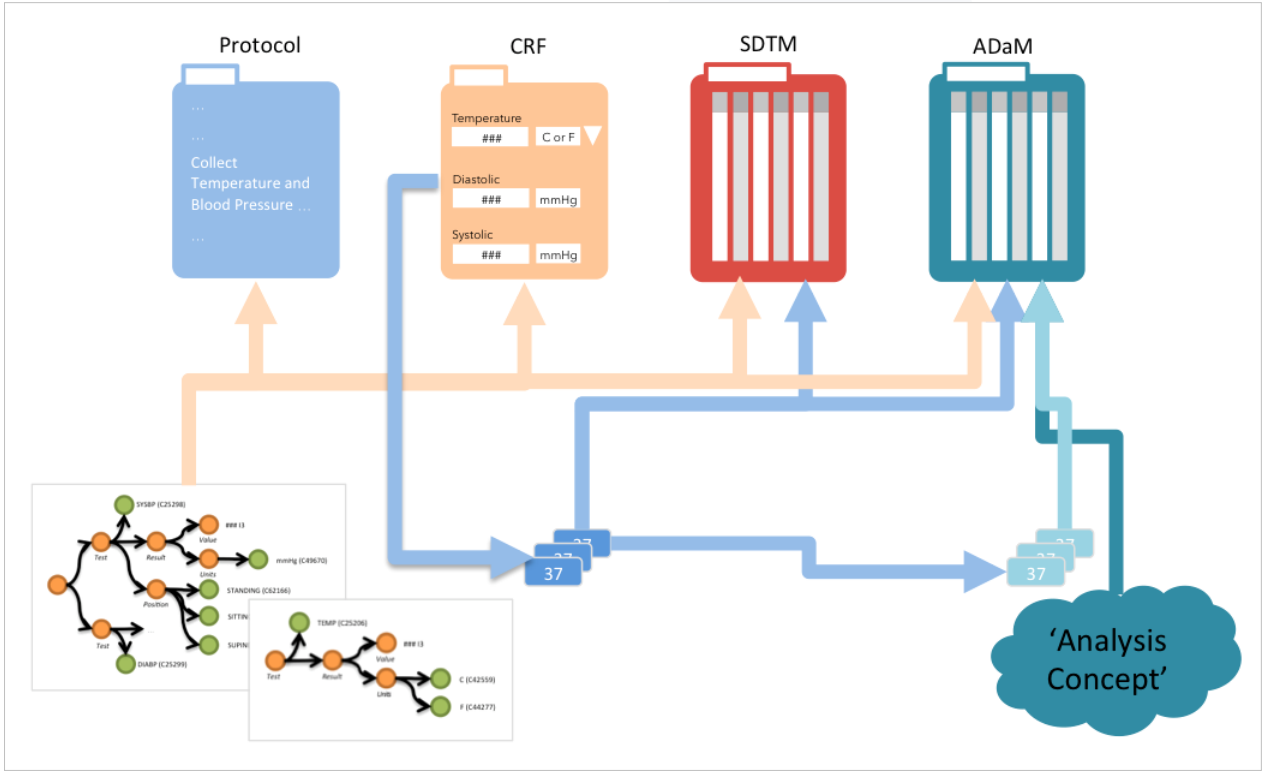
Warning! ☺
Dangerous Thoughts

Analysis



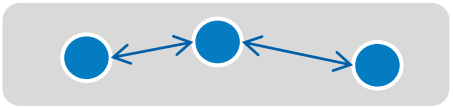


A Big Step



1. Results in an underlying model used across the life-cycle.
2. Requires 'analysis concepts', some thinking has been done in this area.
3. Large amount of work being done in sponsors re TLFs

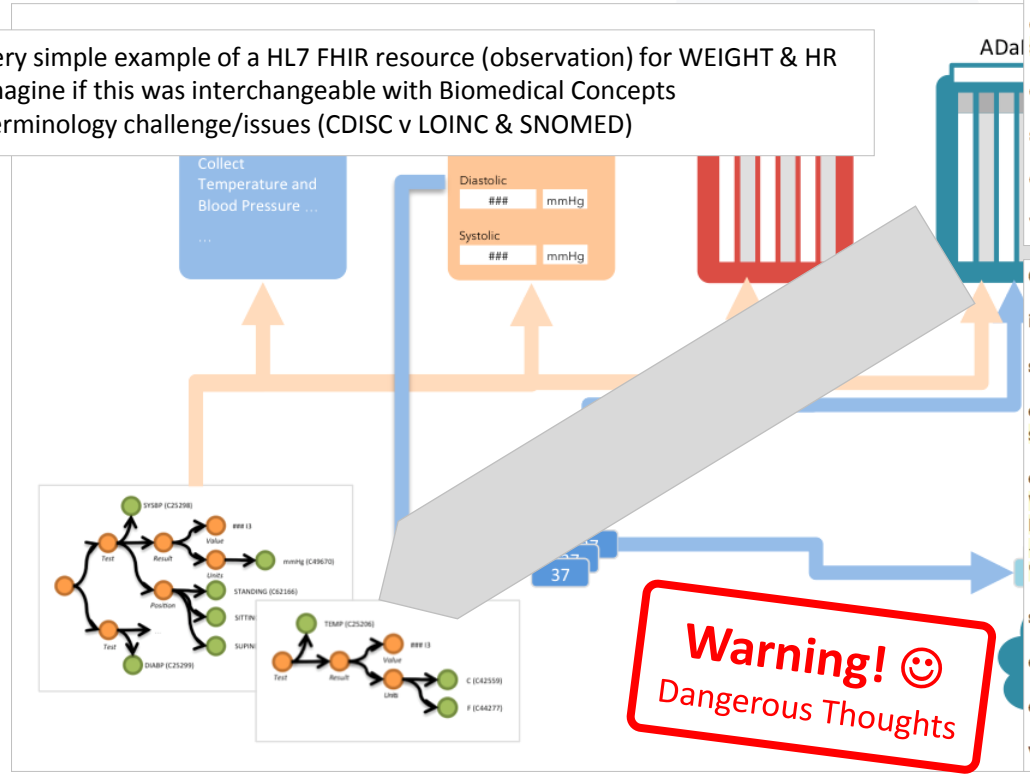
1. Forward and Reverse links through the entire lifecycle.
2. Traceability comes for free.



Warning! ☺
Dangerous Thoughts

Healthcare

1. Very simple example of a HL7 FHIR resource (observation) for WEIGHT & HR
2. Imagine if this was interchangeable with Biomedical Concepts
3. Terminology challenge/issues (CDISC v LOINC & SNOMED)



Generated Narrative with Details

id: heart-rate

meta:

status: final

category: Vital Signs (Details : {http://hl7.org/fhir/observation-category code 'vital-signs' = 'Vital Signs', given as 'Vital Signs'})

code: Heart rate (Details : {LOINC code '8867-4' = 'Heart rate', given as 'Heart rate'})

subject: Patient/example

effective: 02/07/1999

value: 44 beats/minute (Details: UCUM code /min = '/min')

Generated Narrative with Details

id: example

status: final

category: Vital Signs (Details : {http://hl7.org/fhir/observation-category code 'vital-signs' = 'Vital Signs', given as 'Vital Signs'})

code: Body Weight (Details : {LOINC code '29463-7' = 'Body weight', given as 'Body Weight'}; {LOINC code '3141-9' = 'Body weight Measured', given as 'Body weight Measured'}; {SNOMED CT code '27113001' = 'Body weight', given as 'Body weight'}; {http://acme.org/devices/clinical-codes code 'body-weight' = 'body-weight', given as 'Body Weight'})

subject: Patient/example

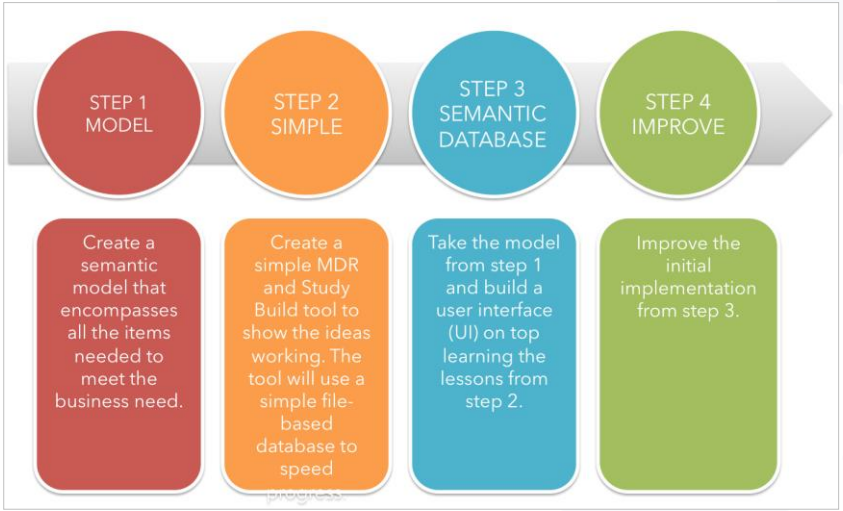
context: Encounter/example

effective: 28/03/2016

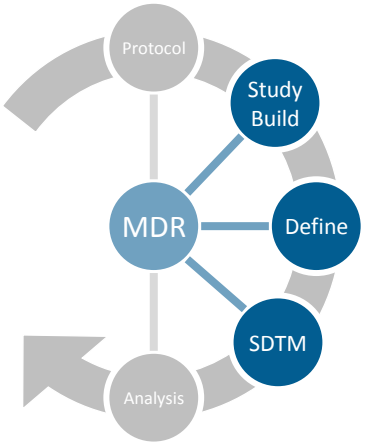
value: 185 lbs (Details: UCUM code [lb_av] = 'lb_av')

Iterative Approach

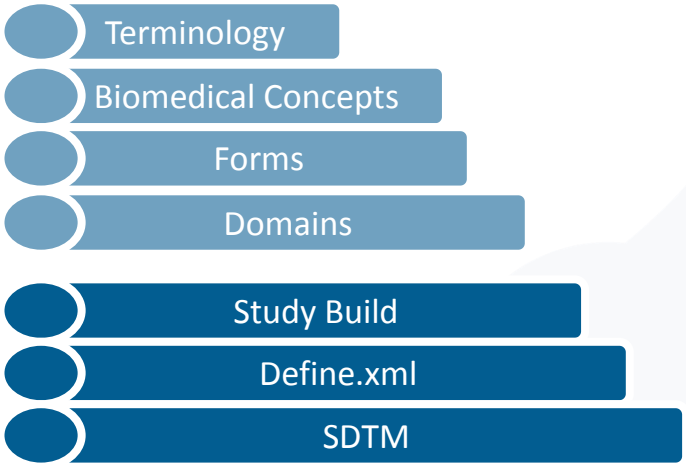
Iterative Approach



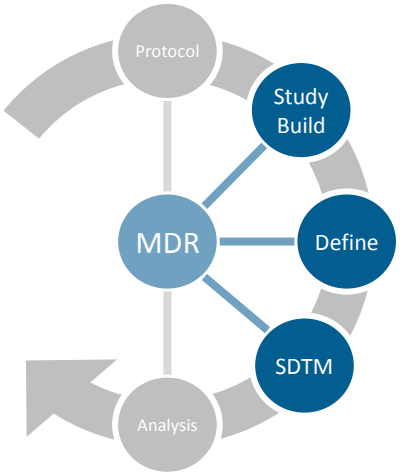
- Drivers
  - Control (new versions, rate-of-change)
  - Precision (which version)
  - Visibility (what changed)
  - Ease-of-use, make it easier
- Need a solid foundation, a model
- Implement in an MDR
- 'Hide' the new world underneath the user interface
- Present to the user in ways they currently understand
- **Utilize graph technologies**
- Then build tools to use the solid foundation accessed vi an API
- Iterate, learn, adjust, increase capability



Iterative Approach



- MDR
  - Handle terminologies including CDISC
  - Manage the new Biomedical Concepts
  - Major aim was to investigate BCs and their use
  - Manage Forms
  - Managed SDTM Domains
  - Expand as needed by tools
- Study Build using definitions held by the MDR
- Produce define.xml from the study build information
- Step into SDTM data
- Important that this is done in a manner that allows for new process to be introduced in parallel with current ones



Reality

Terminology

GLANDON
METADATA REPOSITORY

History: CDISC Terminology

Show 15 entries

Search:

Version	Label	Identifier	Version Label	Owner						Status		C		
35.0.0	CDISC Terminology 2014-03-28	CDISC Terminology	2014-03-28	CDISC	Show		Search			Standard	Status			T Gr- Gr+
36.0.0	CDISC Terminology 2014-06-27	CDISC Terminology	2014-06-27	CDISC	Show		Search			Standard	Status			T Gr- Gr+
37.0.0	CDISC Terminology 2014-09-24	CDISC Terminology	2014-09-24	CDISC	Show		Search			Standard	Status			T Gr- Gr+
38.0.0	CDISC Terminology 2014-10-06	CDISC Terminology	2014-10-06	CDISC	Show		Search			Standard	Status			T Gr- Gr+
39.0.0	CDISC Terminology 2014-12-16	CDISC Terminology	2014-12-16	CDISC	Show		Search			Standard	Status			T Gr- Gr+
40.0.0	CDISC Terminology 2015-03-27	CDISC Terminology	2015-03-27	CDISC	Show		Search			Standard	Status			T Gr- Gr+
41.0.0	CDISC Terminology 2015-06-26	CDISC Terminology	2015-06-26	CDISC	Show		Search			Standard	Status			T Gr- Gr+
42.0.0	CDISC Terminology 2015-09-25	CDISC Terminology	2015-09-25	CDISC	Show		Search			Standard	Status			T Gr- Gr+
43.0.0	CDISC Terminology 2015-12-18	CDISC Terminology	2015-12-18	CDISC	Show		Search			Standard	Status	✔		T Gr- Gr+
44.0.0	CDISC Terminology 2016-03-25	CDISC Terminology	2016-03-25	CDISC	Show		Search			Standard	Status			T Gr- Gr+
45.0.0	CDISC Terminology 2016-06-24	CDISC Terminology	2016-06-24	CDISC	Show		Search			Standard	Status			T Gr- Gr+
46.0.0	CDISC Terminology 2016-09-30	CDISC Terminology	2016-09-30	CDISC	Show		Search			Standard	Status			T Gr- Gr+
47.0.0	CDISC Terminology 2016-12-13	CDISC Terminology	2016-12-13	CDISC	Show		Search			Standard	Status			T Gr- Gr+
48.0.0	CDISC Terminology 2017-03-31	CDISC Terminology	2017-03-31	CDISC	Show		Search			Standard	Status			T Gr- Gr+

Showing 1 to 14 of 14 entries

Previous 1 Next

Import Changes Submission Files

Terminology Changes

GLANDON METADATA REPOSITORY

Changes: CDISC Terminology CDISC Terminology

Show 10 entries Search:

Identifier	Label	Submission Value	2015-06-26	2015-09-25	2015-12-18	2016-03-25	2016-06-24	2016-09-30	2016-12-13	2017-03-31	
C100129	CDISC Questionnaire Category Terminology	QSCAT	✎	✎	✎	✎	✎	✎	✎	✎	Changes
C100130	CDISC SDTM Relationship to Subject Terminology	RELSUB	–	–	–	–	✎	–	✎	✎	Changes
C100131	CDISC Questionnaire ADAS-Cog CDISC Version Test Name Terminology	ADCTN	–	–	✎	✎	–	–	–	–	Changes
C100132	CDISC Questionnaire ADAS-Cog CDISC Version Test Code Terminology	ADCTC	–	–	✎	✎	–	–	–	–	Changes
C100133	CDISC Questionnaire BPRS-A Test Name Terminology	BPR01TN	–	–	✎	✎	–	–	–	–	Changes
C100134	CDISC Questionnaire BPRS-A Test Code Terminology	BPR01TC	–	–	✎	✎	–	–	–	–	Changes
C100135	CDISC Questionnaire EQ-5D-3L Test Name Terminology	EQ5D01TN	–	–	✎	✎	–	–	–	–	Changes
C100136	CDISC Questionnaire EQ-5D-3L Test Code Terminology	EQ5D01TC	–	–	✎	✎	–	–	✎	–	Changes
C100137	CDISC Clinical Classification HAMD 17 Test Name Terminology	HAMD1TN	–	–	✎	✎	✎	–	–	–	Changes
C100138	CDISC Clinical Classification HAMD 17 Test Code Terminology	HAMD1TC	–	–	✎	✎	✎	–	–	–	Changes

Showing 1 to 10 of 616 entries

Previous 1 2 3 4 5 … 62 Next

Close Report

Code List Changes I

GLANDON
METADATA REPOSITORY

Changes: CDISC Questionnaire Category Terminology C100129

Code List Changes

Show 15 entries

Search:

Version	Date	Identifier	Submision Value	Preferred Term	Synonym	Extensible	Definition
35	2014-03-28	C100129	QSCAT	CDISC Questionnaire Category Terminology	Questionnaire Category	✔	A grouping of observations within the Questionnaire domain.
36	2014-06-27	↓	↓	↓	Questionnaire Category Category of Questionnaire	↓	↓
37	2014-09-24	↓	↓	↓	↓	↓	↓
38	2014-10-06	↓	↓	↓	↓	↓	↓
39	2014-12-16	↓	↓	↓	↓	↓	↓
40	2015-03-27	↓	↓	↓	↓	↓	↓
41	2015-06-26	↓	↓	↓	↓	↓	↓
42	2015-09-25	↓	↓	↓	↓	↓	↓
43	2015-12-18	↓	↓	↓	↓	↓	↓
44	2016-03-25	↓	↓	↓	↓	↓	↓
45	2016-06-24	↓	↓	↓	↓	↓	↓
46	2016-09-30	↓	↓	↓	↓	↓	↓
47	2016-12-13	↓	↓	↓	↓	↓	↓
48	2017-03-31	↓	↓	↓	↓	↓	↓

Showing 1 to 14 of 14 entries

Previous 1 Next

Code List Changes II

GLANDON
METADATA REPOSITORY

Code List Item Changes

Show 15 entries Search:

Identifier	Label	Submission Value	2015-06-26	2015-09-25	2015-12-18	2016-03-25	2016-06-24	2016-09-30	2016-12-13	2017-03-31	
C100759	Brief Pain Inventory Questionnaire	BPI	–	–	–	–	–	–	–	–	Changes
C100760	Brief Pain Inventory Short Form Questionnaire	BPI SHORT FORM	–	–	–	–	–	–	–	–	Changes
C100761	Brief Psychiatric Rating Scale A Questionnaire	BPRS-A	–	–	–	–	–	–	–	–	Changes
C100762	Alzheimer's Disease Assessment Scale-Cognitive CDISC Version Questionnaire	ADAS-COG	–	–	–	–	–	–	–	–	Changes
C100763	Clinical Global Impression Questionnaire	CGI	–	–	–	–	–	–	–	–	Changes
C100764	Current Opioid Misuse Measure Questionnaire	COMM	–	–	–	–	–	–	–	–	Changes
C100765	Columbia-Suicide Severity Rating Scale Baseline Questionnaire	C-SSRS BASELINE	–	☑	–	–	–	–	–	–	Changes
C100766	Faces Pain Scale Revised Questionnaire	FPSR	–	–	–	–	–	–	–	–	Changes
C100767	Hamilton Depression Rating Scale 17 Item Questionnaire	HAMD 17	–	–	–	–	✖				Changes
C100768	Karnofsky Performance Status Scale Questionnaire	KPS SCALE	–	–	–	–	–	–	–	–	Changes
C100769	Movement Disorder Society Unified Parkinson's Disease Rating Scale Questionnaire	MDS-UPDRS	–	–	–	–	–	–	–	–	Changes
C100771	Michigan Neuropathy Screening Instrument Questionnaire	MNSI	–	–	–	–	–	–	–	–	Changes
C100772	Neuropsychiatric Inventory Questionnaire	NPI	–	–	–	–	–	–	–	–	Changes
C100773	Parkinson's Disease Quality of Life Scale Questionnaire	PDQUALIF	–	–	–	–	–	–	–	–	Changes
C100774	Roland Morris Disability Questionnaire	RDQ	–	–	–	–	–	–	–	–	Changes

Showing 1 to 15 of 182 entries

Previous 1 2 3 4 5 … 13 Next

Close

Code List Item Changes

GLANDON METADATA REPOSITORY

Changes: Columbia-Suicide Severity Rating Scale Baseline Questionnaire C100765

Code List Item Full History

Show 15 entries Search:

Version	Date	Identifier	Submission Value	Preferred Term	Synonym	Definition
35	2014-03-28	C100765	C-SSRS BASELINE	Columbia-Suicidality Severity Rating Scale Baseline Questionnaire	CSS01	Columbia-Suicidality Severity Rating Scale (C-SSRS) Baseline Version 2009-01-14 (Posner, K.; Brent, D.; Lucas, C.; Gould, M.; Stanley, B.; Brown, G.; Fisher, P.; Zelazny, J.; Burke, A.; Oquendo, M.; Mann, J.; copyright 2008 The Research Foundation for Mental Hygiene, Inc.).
36	2014-06-27	↓	↓	↓	↓	↓
37	2014-09-24	↓	↓	↓	↓	↓
38	2014-10-06	↓	↓	↓	↓	↓
39	2014-12-16	↓	↓	↓	↓	↓
40	2015-03-27	↓	↓	↓	↓	↓
41	2015-06-26	↓	↓	↓	↓	↓
42	2015-09-25	↓	↓	Columbia-Suicidality Severity Rating Scale Baseline Questionnaire Columbia-Suicide Severity Rating Scale Baseline Questionnaire	↓	Columbia-Suicidality Severity Rating Scale (C-SSRS) Baseline Version 2009-01-14 (Posner, K.; Brent, D.; Lucas, C.; Gould, M.; Stanley, B.; Brown, G.; Fisher, P.; Zelazny, J.; Burke, A.; Oquendo, M.; Mann, J.; copyright 2008 The Research Foundation for Mental Hygiene, Inc.). Columbia-Suicide Severity Rating Scale (C-SSRS) Baseline Version 2009-01-14 (Posner, K.; Brent, D.; Lucas, C.; Gould, M.; Stanley, B.; Brown, G.; Fisher, P.; Zelazny, J.; Burke, A.; Oquendo, M.; Mann, J.; copyright 2008 The Research Foundation for Mental Hygiene, Inc.).
43	2015-12-18	↓	↓	↓	↓	↓
44	2016-03-25	↓	↓	↓	↓	↓
45	2016-06-24	↓	↓	↓	↓	↓
46	2016-09-30	↓	↓	↓	↓	↓
47	2016-12-13	↓	↓	↓	↓	↓
48	2017-03-31	↓	↓	↓	↓	↓

Showing 1 to 14 of 14 entries Previous 1 Next

Close

Submission Value Changes

GLANDON
METADATA REPOSITORY

Show 10 entries

Search: TIMI

Code List	Item	Label	Original Submission Value	2014-06-27	2014-09-24	2014-10-06	2014-12-16	2015-03-27	2015-06-26	2015-09-25	2015-12-18	2016-03-25	2016-06-24	2016-09-30	2016-12-13	
C101841	C100041	Thrombolysis in Myocardial Infarction Flow-1	TIMI-1	✎			✎									Changes
C101841	C100040	Thrombolysis in Myocardial Infarction Flow-0	TIMI-0	✎			✎									Changes
C101841	C100043	Thrombolysis in Myocardial Infarction Flow-3	TIMI-3	✎			✎									Changes
C101841	C100042	Thrombolysis in Myocardial Infarction Flow-2	TIMI-2	✎			✎									Changes
C118971	C119106	Stent Thrombosis Coronary ARC Timing Clinical Classification	STENT THROMBOSIS CORONARY ARC TIMING						✎							Changes
C118971	C119104	Coronary Thrombus TIMI Grade Clinical Classification	CORONARY THROMBUS TIMI GRADE								✎					Changes
C119077	C119197	ARC STC Timing - Stent Thrombosis Coronary ARC Timing	STCT01-STC ARC Timing						✎							Changes
C119078	C119197	ARC STC Timing - Stent Thrombosis Coronary ARC Timing	STCT0101						✎							Changes

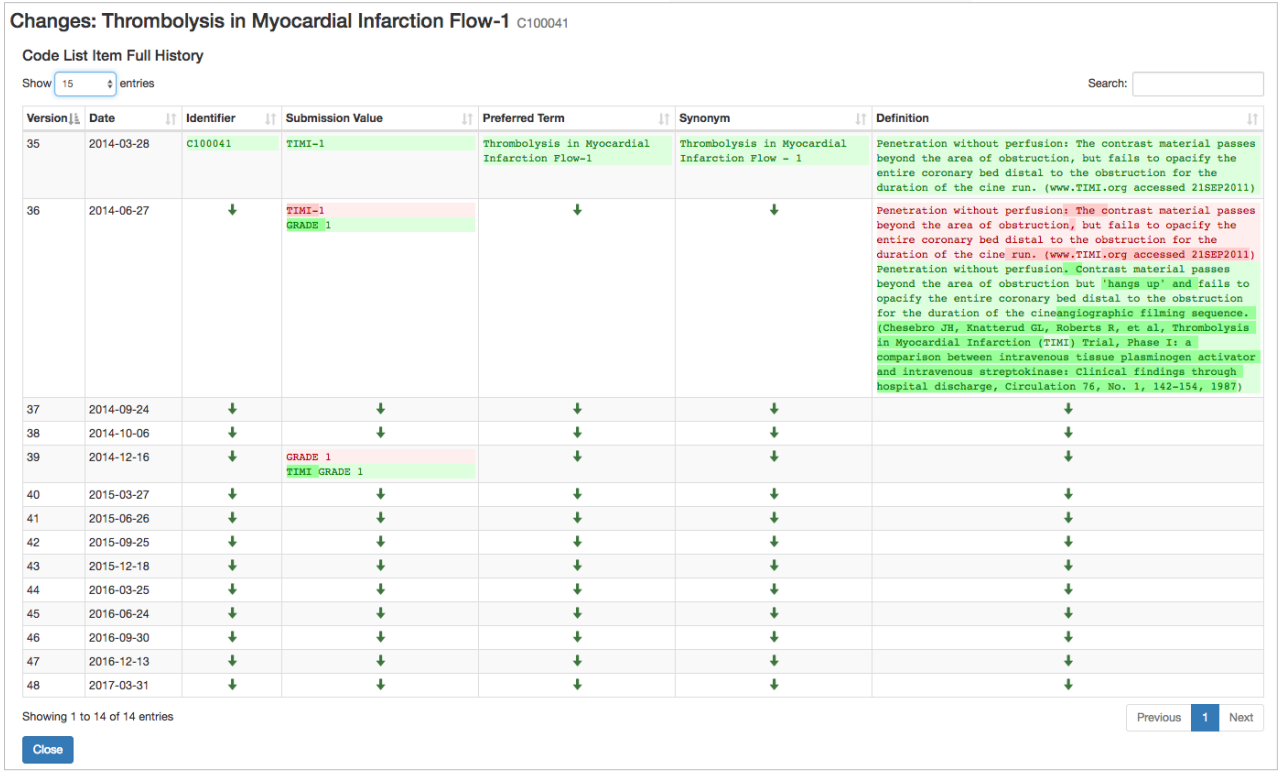
Showing 1 to 8 of 8 entries (filtered from 1,234 total entries)

Previous 1 Next

< > Close Report

Submission Value Changes

GLANDON
METADATA REPOSITORY



Changes: Thrombolysis in Myocardial Infarction Flow-1 C100041

Code List Item Full History

Show 15 entries

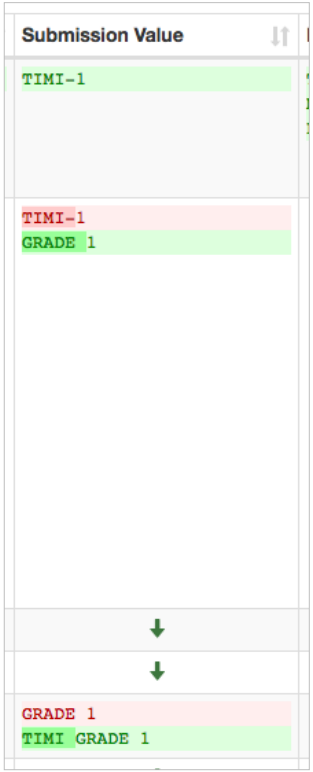
Search:

Version	Date	Identifier	Submission Value	Preferred Term	Synonym	Definition
35	2014-03-28	C100041	TIMI-1	Thrombolysis in Myocardial Infarction Flow-1	Thrombolysis in Myocardial Infarction Flow - 1	Penetration without perfusion: The contrast material passes beyond the area of obstruction, but fails to opacify the entire coronary bed distal to the obstruction for the duration of the cine run. (www.TIMI.org accessed 21SEP2011)
36	2014-06-27	↓	TIMI-1 GRADE 1	↓	↓	Penetration without perfusion: The contrast material passes beyond the area of obstruction, but fails to opacify the entire coronary bed distal to the obstruction for the duration of the cine run. (www.TIMI.org accessed 21SEP2011) Penetration without perfusion. Contrast material passes beyond the area of obstruction but 'hangs up' and fails to opacify the entire coronary bed distal to the obstruction for the duration of the cineangiographic filming sequence. (Chesebro JH, Knatterud GL, Roberts R, et al, Thrombolysis in Myocardial Infarction (TIMI) Trial, Phase I: a comparison between intravenous tissue plasminogen activator and intravenous streptokinase: Clinical findings through hospital discharge, Circulation 76, No. 1, 142-154, 1987)
37	2014-09-24	↓	↓	↓	↓	↓
38	2014-10-06	↓	↓	↓	↓	↓
39	2014-12-16	↓	GRADE 1 TIMI GRADE 1	↓	↓	↓
40	2015-03-27	↓	↓	↓	↓	↓
41	2015-06-26	↓	↓	↓	↓	↓
42	2015-09-25	↓	↓	↓	↓	↓
43	2015-12-18	↓	↓	↓	↓	↓
44	2016-03-25	↓	↓	↓	↓	↓
45	2016-06-24	↓	↓	↓	↓	↓
46	2016-09-30	↓	↓	↓	↓	↓
47	2016-12-13	↓	↓	↓	↓	↓
48	2017-03-31	↓	↓	↓	↓	↓

Showing 1 to 14 of 14 entries

Previous 1 Next

Close



Submission Value

TIMI-1

TIMI-1
GRADE 1

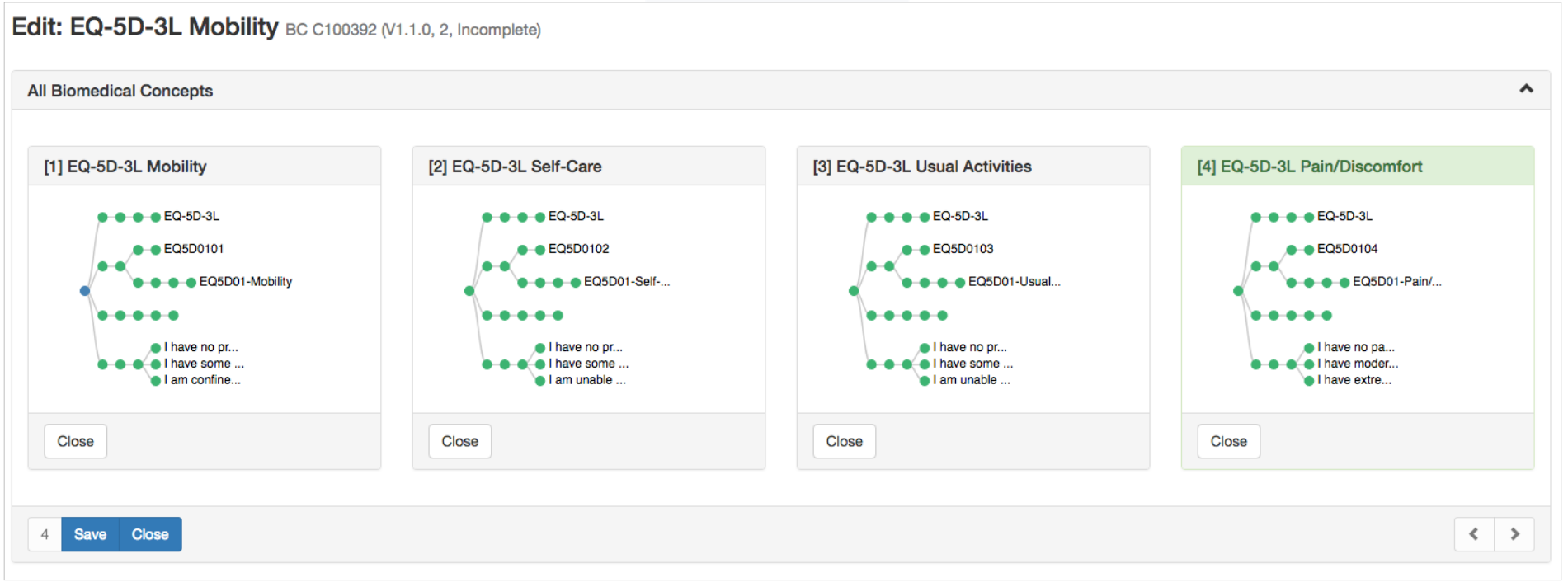
↓

↓

GRADE 1
TIMI GRADE 1

Biomedical Concepts

GLANDON
METADATA REPOSITORY



Biomedical Concepts

GLANDON METADATA REPOSITORY

Current Biomedical Concept

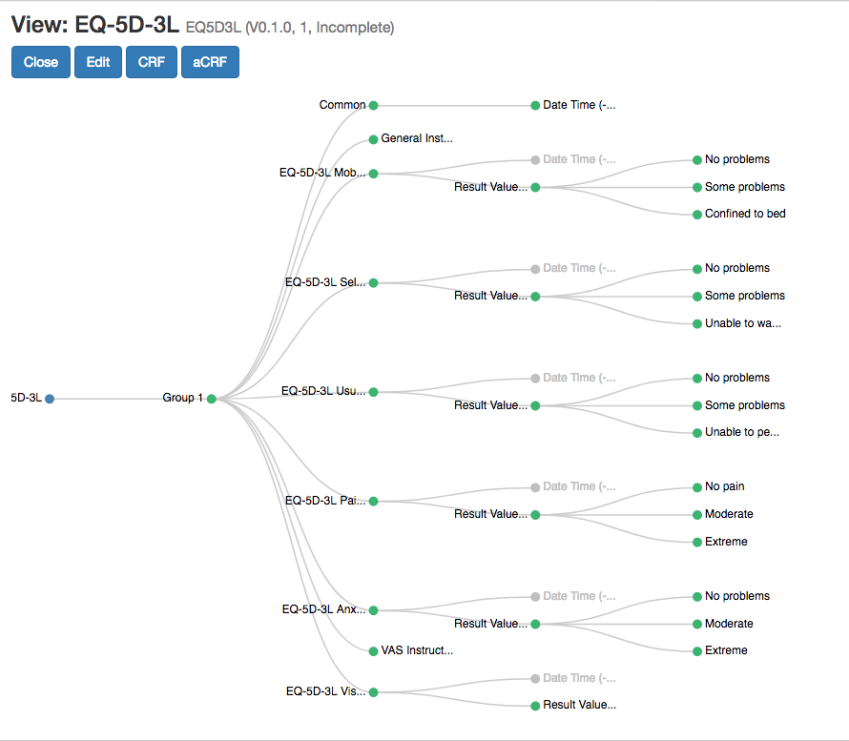
Show 15 entries Search:

Alias	Question Text	Prompt Text	Enabled	Collect	Datatype	Format	Terminology	
Baseline (--BLFL)			✗	✗	boolean			
Body Position (--POS)			✗	✗	string [coded]			
Category (--CAT)			✓	✗	string [coded]		EQ-5D-3L [C66957]	T
Date Time (--DTC)	Date & Time		✓	✓	dateTime			
Laterality (--LAT)			✗	✗	string [coded]			
Method (--METHOD)			✗	✗	string [coded]			
Reason Not Done (--REASND)			✗	✗	string [coded]			
Result Value (--ORRES)	Mobility		✓	✓	string [coded]		I have no problems in walking about [EQ5D3L.MOBILITY.NONE] I have some problems in walking about [EQ5D3L.MOBILITY.SOME] I am confined to bed [EQ5D3L.MOBILITY.CONFINED]	T
Site Of Administration (--LOC)			✗	✗	string [coded]			
Subcategory (--SCAT)			✗	✗	string [coded]			
Test Code (--TESTCD)			✓	✗	string [coded]		EQ5D0101 [C100392]	T
Test Name (--TEST)			✓	✗	string [coded]		EQ5D01-Mobility [C100392]	T

Showing 1 to 12 of 12 entries Previous 1 Next

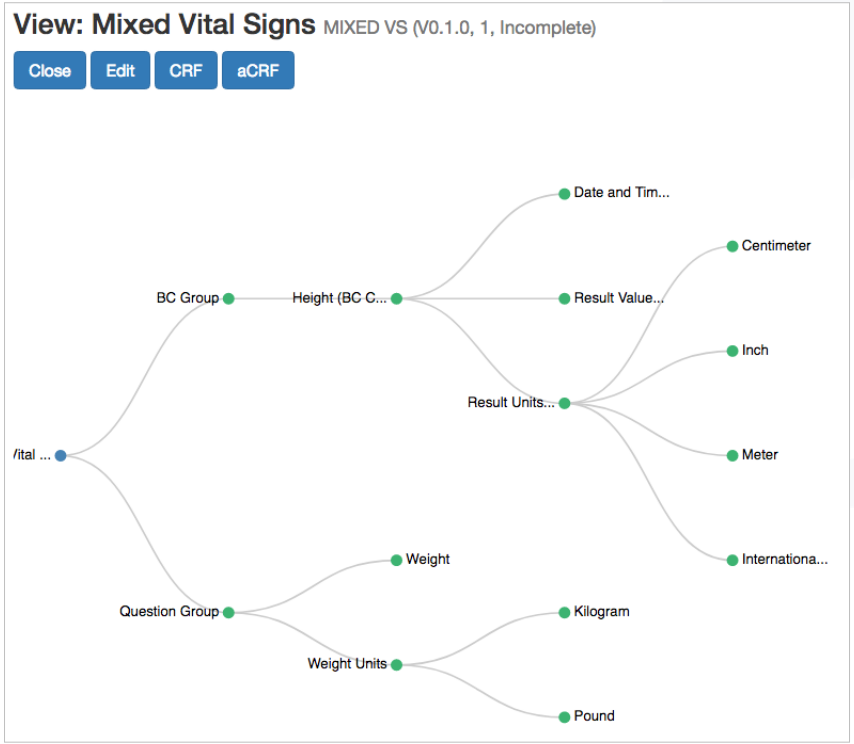
- Biomedical Concept shown as a ‘flattened structure’ with alias names to relate it to the current world
- Note that terminology is bound in and defined as part of BC.

Forms



1. Use the Biomedical Concepts to build forms
2. Example here is EQ-5D-3L using 6 concepts that each use a mix of CDISC and sponsor terminology
3. Makes it easy to build forms
4. When a Biomedical Concept is used on two or more forms then definitions will be consistent across those forms, including use of terminology
5. Results in less variation

Iterative Forms



1. Ability to mix Biomedical Concepts and 'traditional' individual questions and mappings
2. This is essential to allow for iterative development of Biomedical Concepts.
3. Need to be able to mix the old and the new
4. Not all Biomedical Concepts will be available immediately so we will require flexibility

1. We need to keep the lights on
2. One example where we can mix the 'old' world and the 'new world'
3. This will be required through the life-cycle
4. Take an 80-20 approach, do the easy stuff in new ways, learn, do the difficult using current methods
5. Work through domain by domain
6. Use existing information to build BCs

Annotated CRF

GLANDON
METADATA REPOSITORY

Annotated CRF: Mixed Vital Signs MIXED VS (V0.1.0, 1, Incomplete)

Mixed Vital Signs		VS=Vital Signs
BC Group		
Height (BC C25347)		
Question text	VSDTC where VSTESTCD=HEIGHT	D D / M M M / Y Y Y Y H H : M M
Result value?	VSORRES where VSTESTCD=HEIGHT	# # # . #
Result units?	VSORRESU where VSTESTCD=HEIGHT	○ Centimeter ○ Inch ○ Meter ○ International Foot
Question Group		
Weight?	VSORRES	# # # . # #
Units	VSORRESU	○ Kilogram ○ Pound

Report Close

1. Having the definitions allows for annotation of CRFs
2. Use of Biomedical Concepts allows for auto-annotation using the links shown in previous slides
3. Use of 'traditional' questions allows for the mapping information to be exposed

SDTM

GLANDON
METADATA REPOSITORY

Show: Demographics SDTM IG DM (V3.2.0, 3, Standard)

Details

Identifer	Label	Owner	Version	Version Label
SDTM IG DM	Demographics	CDISC	3.2.0	3.2

Variables

Show 5 entries Search:

Ordinal	Name	Label	Datatype	CT or Format	Role	Sub Role	Notes	Core
16	BRTHDTC	Date/Time of Birth	Char	ISO 8601	Qualifier	Record Qualifier	Date/time of birth of the subject.	Permissible
17	AGE	Age	Num		Qualifier	Record Qualifier	Age expressed in AGEU. May be derived from RFSTDTC and BRTHDTC, but BRTHDTC may not be available in all cases (due to subject privacy concerns).	Expected
18	AGEU	Age Units	Char	AGEU	Qualifier	Record Qualifier	Units associated with AGE.	Expected
19	SEX	Sex	Char	SEX	Qualifier	Record Qualifier	Sex of the subject.	Required
20	RACE	Race	Char	RACE	Qualifier	Record Qualifier	Race of the subject. Sponsors should refer to "Collection of Race and Ethnicity Data in Clinical Trials" (FDA, September 2005) for guidance regarding the collection of race (http://www.fda.gov/RegulatoryInformation/Guidances/ucm126340.htm) See Assumption below regarding RACE.	Expected

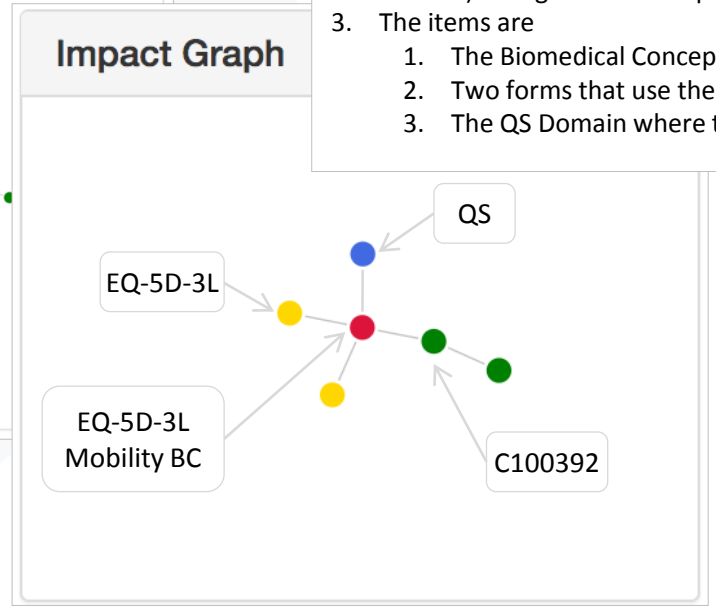
Showing 16 to 20 of 28 entries

Previous 1 2 3 4 5 6 Next

Clone Export JSON Export Turtle

1. SDTM Definitions held by the MDR
    1. SDTM Model
    2. SDTM IG
    3. SDTM IG Domains
2. Allows for sponsor domains to be created based on IG domains

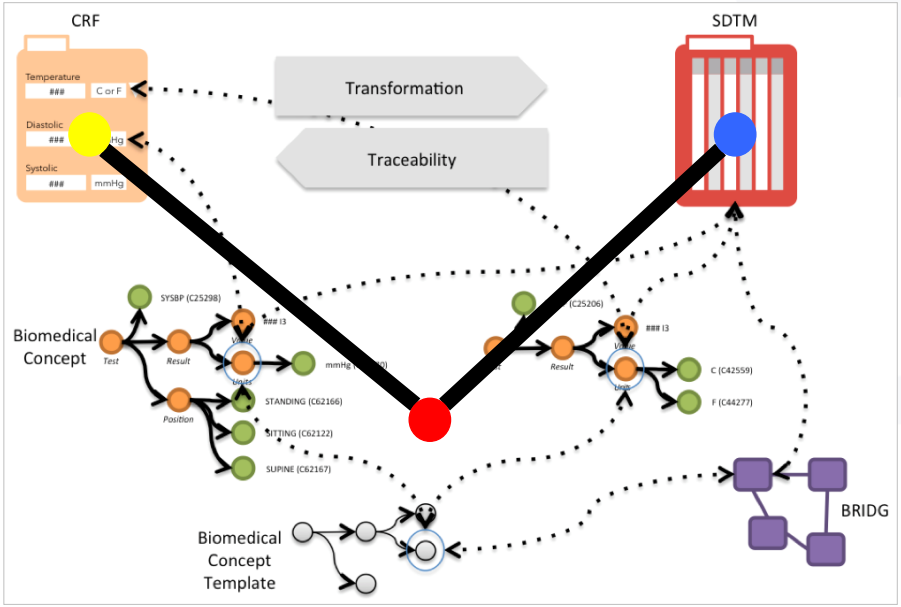
Impact Analysis

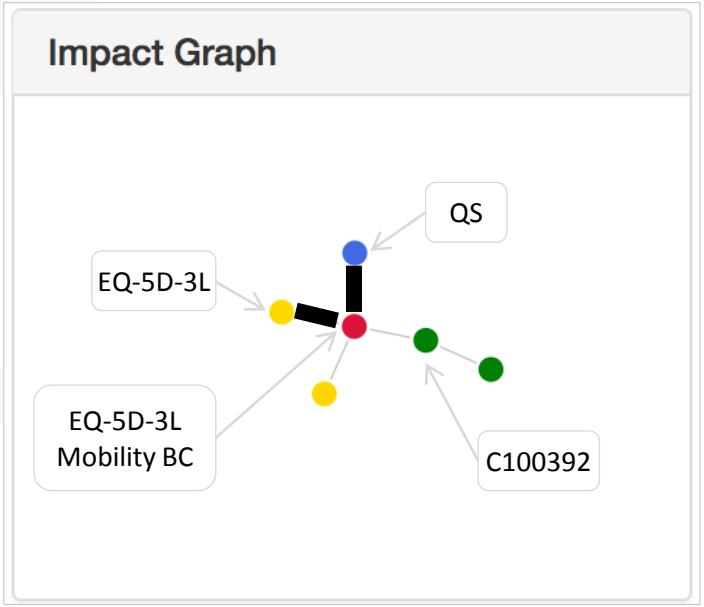


1. All of the definitions, and the linked nature of the definitions, allows impact analysis to be performed.
2. Simple example of terminology change. If C100392 (EQ-5D-3L TESTCD) changes what is impacted.
3. The items are
    1. The Biomedical Concept
    2. Two forms that use the concept
    3. The QS Domain where the captured data will go

Impact Analysis

GLANDON
METADATA REPOSITORY

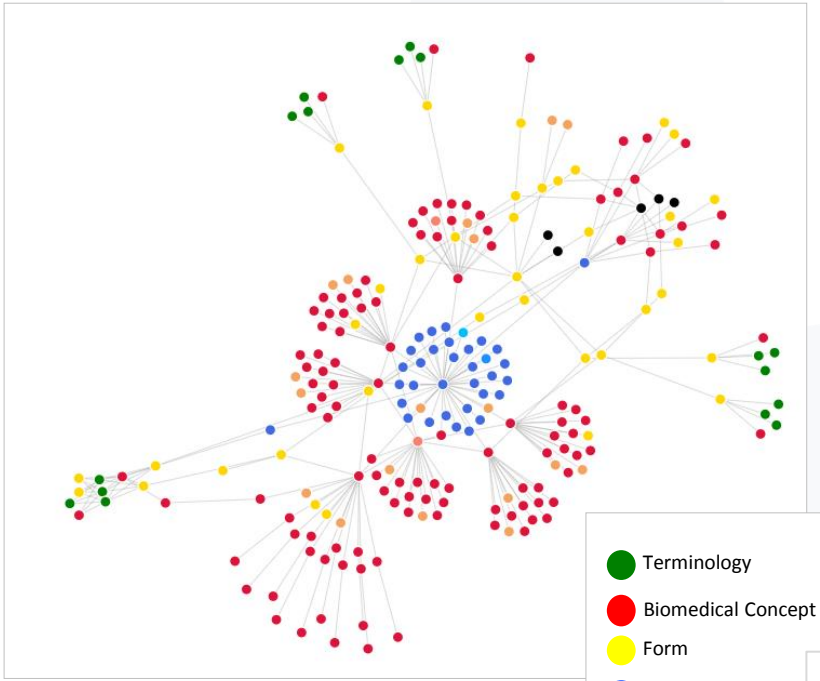


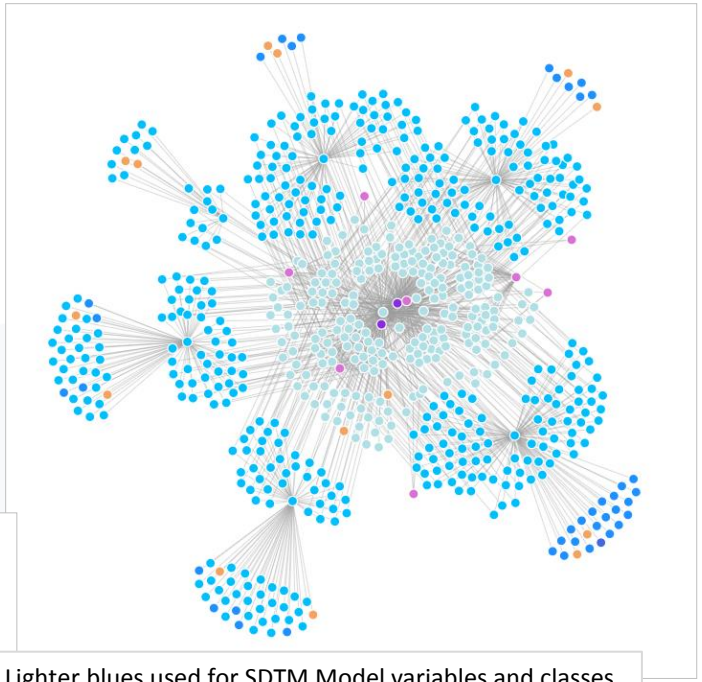


Everything is Linked

GLANDON
METADATA REPOSITORY

1. The metadata is one large graph
2. Some examples of partial views of the graph
3. A form built from BCs that are linked to terminology with Domains linked to the BCs
4. The second graph is of the SDTM Model with the core variables and the model domain classes

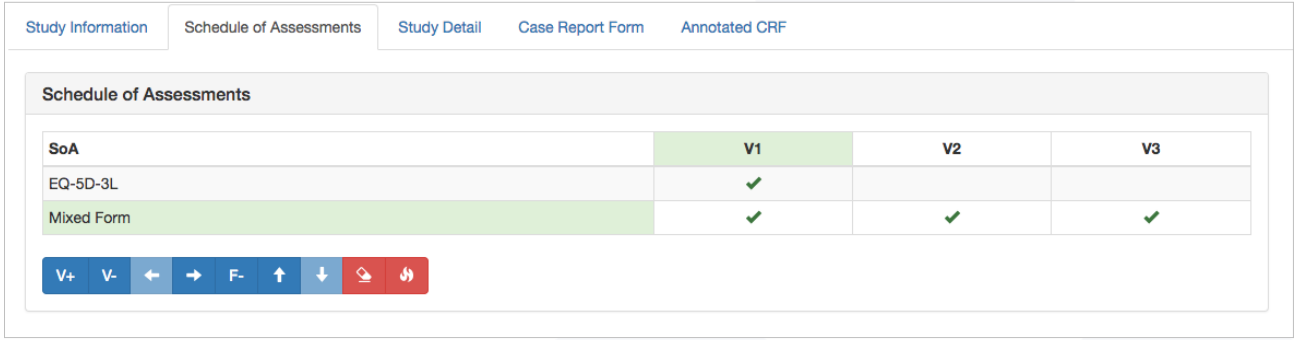




Lighter blues used for SDTM Model variables and classes

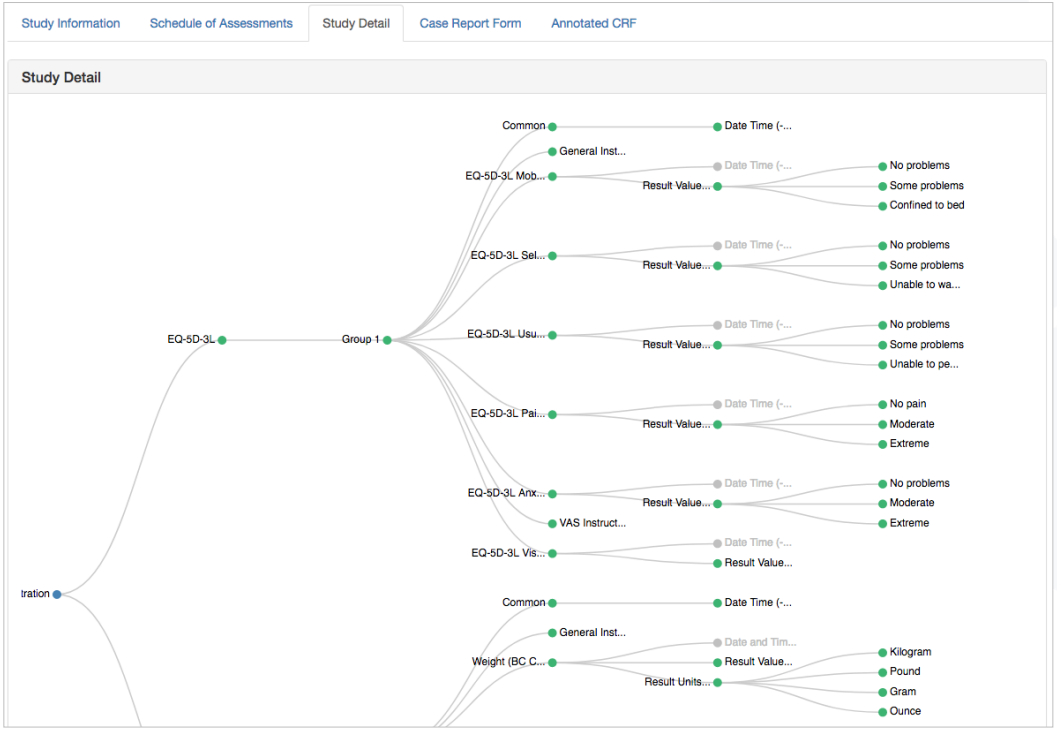
Iteration: Study Builds

GLANDON
METADATA REPOSITORY



1. With solid foundation of definitions we are now in a position to undertake the functions required by the business
2. Build studies, using the form definitions held within the MDR (accessed via the MDR API)
3. Build the Schedule of Assessments

Iteration: Study Builds

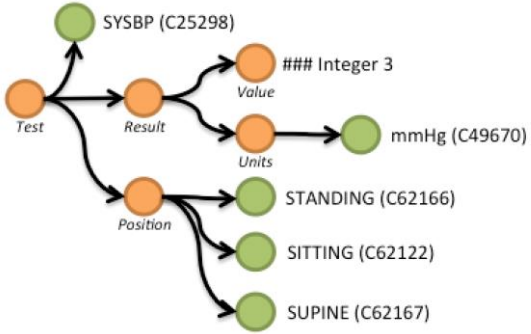


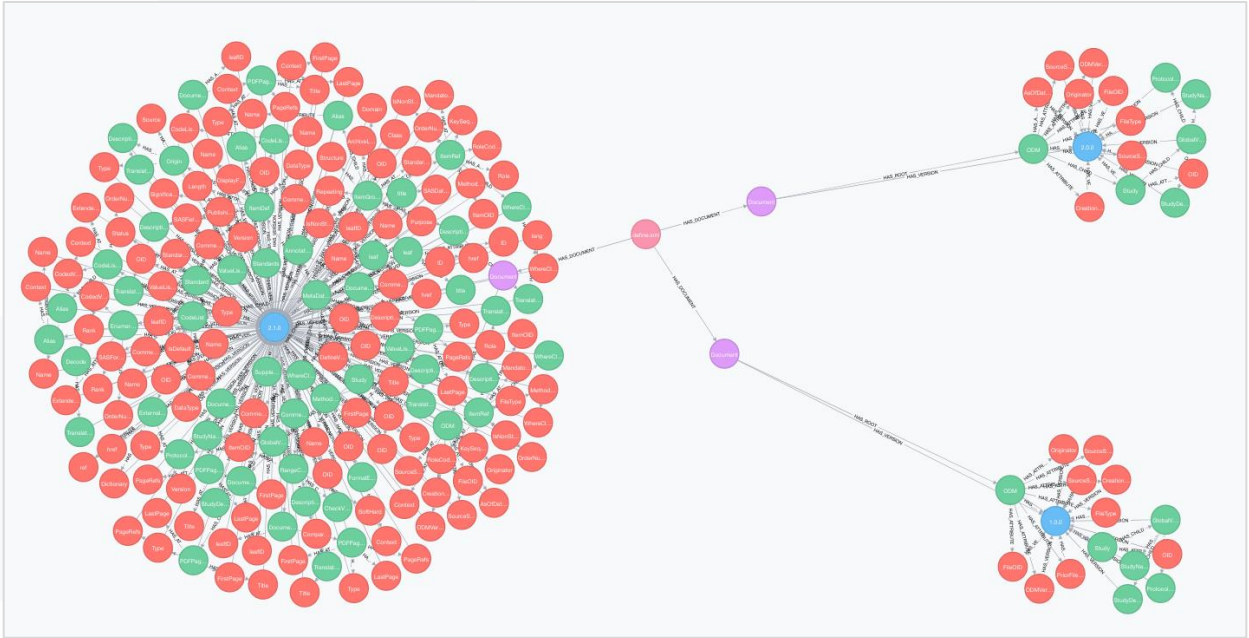
1. The tool can then turn that automatically into the detail
2. Can export it to EDC systems (ALS, ODM, JSON)
3. Allows for study-specific changes
4. Produce the aCRF automatically
5. The study build contains all the version information (forms, terminology etc)
6. Provides control, what's been used, impact analysis etc.

Iteration: Define.xml

GLANDON
METADATA REPOSITORY

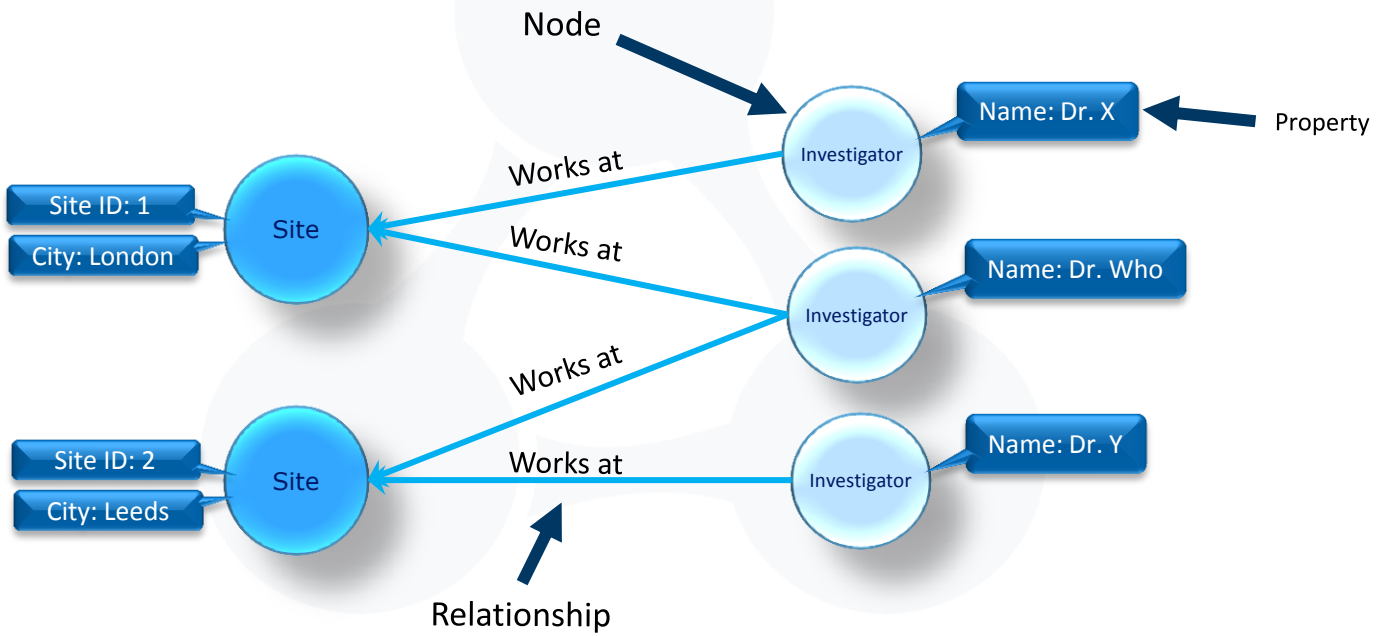
1. With a study build that contains a lot of detail we can move towards a full automation of the define.xml
2. We also are able to support manual creation of define.xml. By having all the definitions that the MDR holds the tooling can help build definitions (e.g. VLM from Biomedical Concepts).
3. This is the current work focus





SDTM, Data & Graphs

Journey into the Graph



Race / Ethnicity

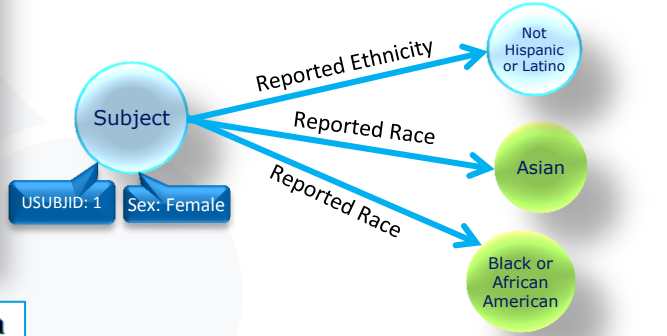
MULTIPLE

StudyDesign: Demographics (DM_1) [DM_UseCase1]		
Demographics [DM_UseCase1]		
1.*	Sex	X Female ○ Male
2.*	Ethnicity	○ Hispanic or Latino X Not Hispanic or Latino ○ Not reported ○ Unknown
3.*	Race	○ American Indian or Alaska Native X Asian X Black or African American ○ Native Hawaiian or Other Pacific Islander ○ White

Usubjid	Sex	Race	Ethnicity
1			

\+

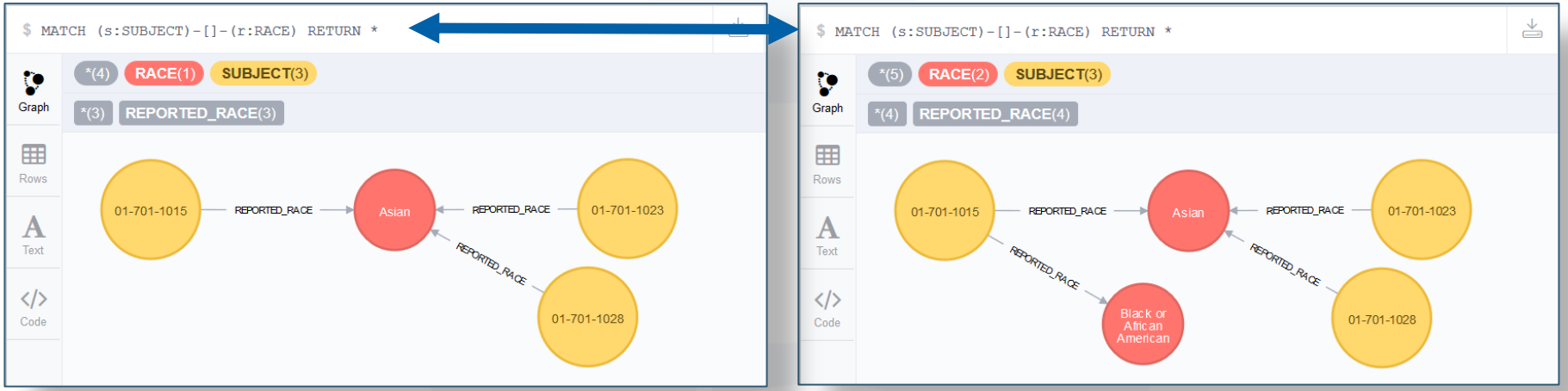
RACE1	ASIAN
RACE2	BLACK OR AFRICAN AMERICAN



Collection of Race and Ethnicity Data in Clinical Trials

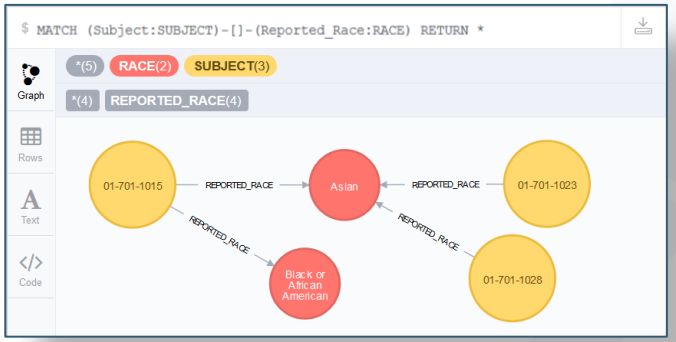
We recommend offering an option of selecting one or more racial designations or additional subgroup designations. Recommended forms for the instruction accompanying the multiple response questions are "Mark one or more" and "Select one or more."

The Graph can be Queried

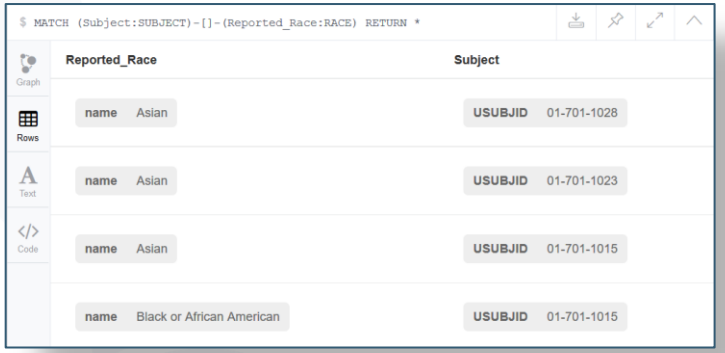


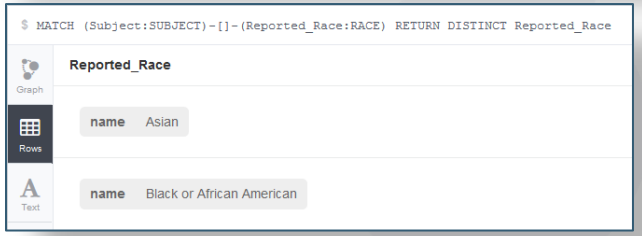
Don’t need to change the question

The Graph is for storing information

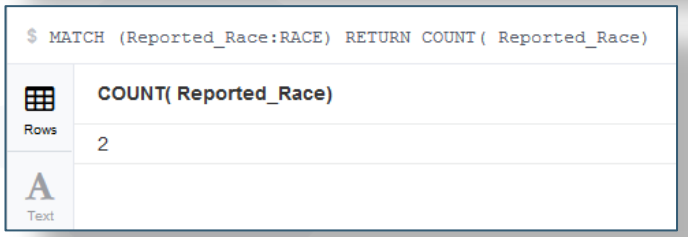


=





=



Visualization is something different

Medical History

TAUG Parkinson's Disease Diagnostic Criteria Example CRF

Date Medical History Taken (m m/dd/yyyy):

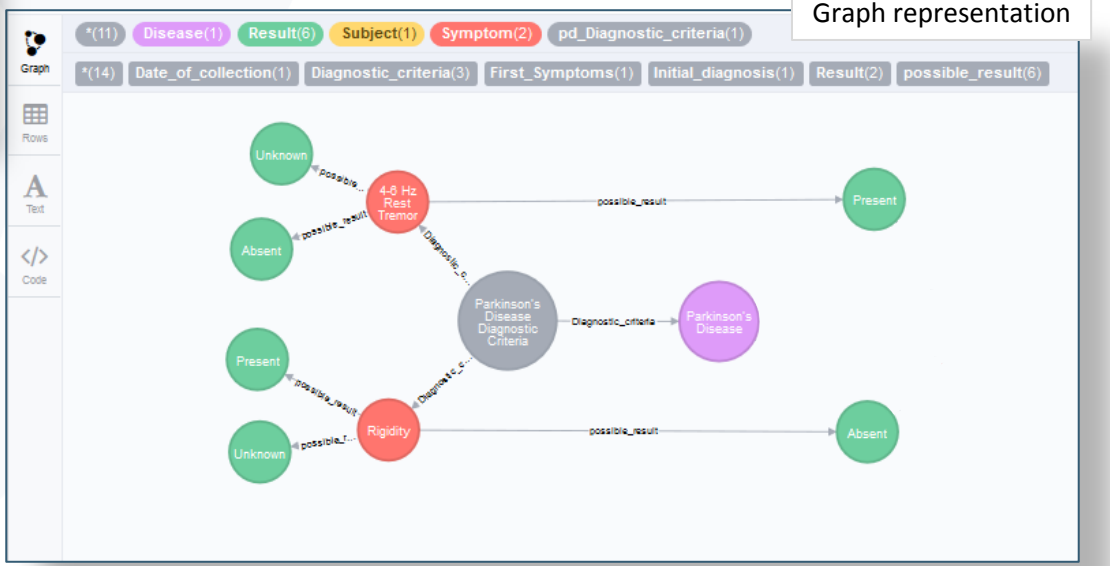
1. Year of first symptoms as confirmed by history obtained by the physician?
2. Year of Initial Diagnosis?
3. Diagnostic Features/Criteria (as evident on clinical assessment of the patient):
   a. 4-6 Hz Rest Tremor: ☒ Present ☐ Absent ☐ Unknown
   b. Bradykinesia: ☐ Present ☐ Absent ☐ Unknown
   c. Rigidity: ☐ Present ☒ Absent ☐ Unknown
   d. Asymmetric Onset: ☐ Present ☐ Absent ☐ Unknown
   e. Substantial Response to Dopaminergic Therapy: ☐ Present ☐ Absent ☐ Unknown

Tremor (including internal tremor) | Micrographia
Stiffness | Weakness
Change in facial expression | Dystonia (specify symptoms)
Disturbances of dexterity
a. Ambulatory/Axial Difficulties:
Freezing | Falls
Lack of arm swing | Slowness of gait
Leg Dragging | Other abnormality of posture or gait (other, specify)
Shuffling of gait
Postural imbalance (excluding falls)

6. Side of Body of Initial Symptoms:
Right ☐ Left ☐ Bilateral ☐ Midline ☐ Unknown

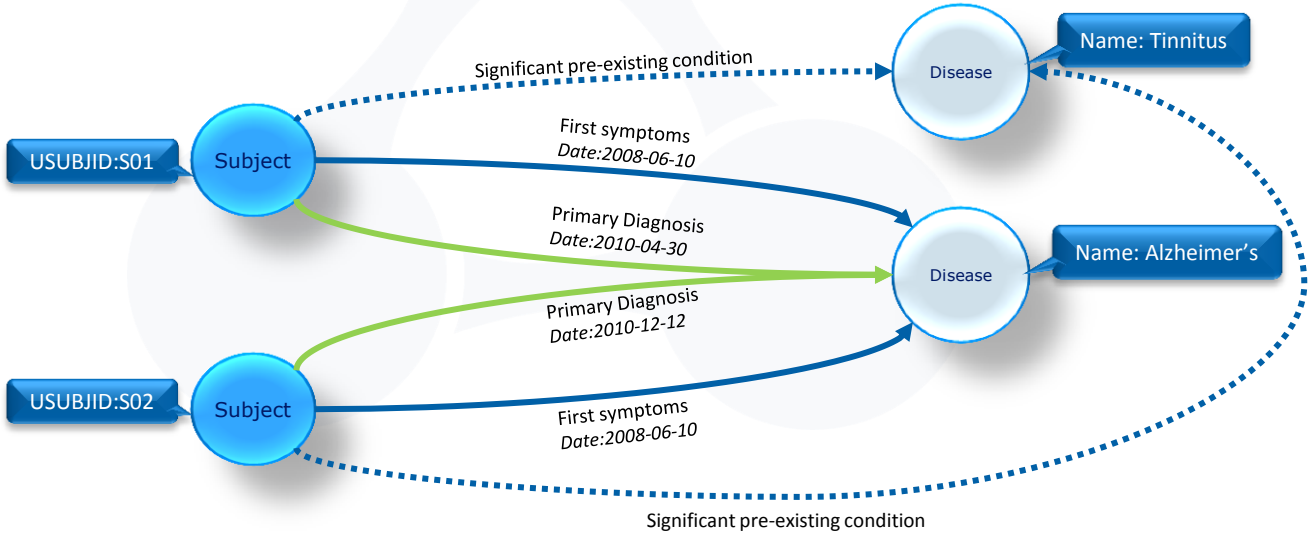
7. Motor symptoms developing over the course of illness (Please check all that applies):
Tremor (including internal tremor) - Approximate date of onset (m m/dd/yyyy): ☐ Unknown
Stiffness - Approximate date of onset (m m/dd/yyyy): ☐ Unknown
Micrographia - Approximate date of onset (m m/dd/yyyy): ☐ Unknown
Change in facial expression - Approximate date of onset (m m/dd/yyyy): ☐ Unknown
Disturbances of dexterity - Approximate date of onset (m m/dd/yyyy): ☐ Unknown
Weakness - Approximate date of onset (m m/dd/yyyy): ☐ Unknown
Dystonia - Approximate date of onset (m m/dd/yyyy): ☐ Unknown
a. Ambulatory/Axial Difficulties:
Freezing - Approximate date of onset (m m/dd/yyyy): ☐ Unknown
Lack of arm swing - Approximate date of onset (m m/dd/yyyy): ☐ Unknown
Leg Dragging - Approximate date of onset (m m/dd/yyyy): ☐ Unknown
Shuffling of gait - Approximate date of onset (m m/dd/yyyy): ☐ Unknown
Postural imbalance (excluding falls) - Approximate date of onset (m m/dd/yyyy): ☐ Unknown
Falls - Approximate date of onset (m m/dd/yyyy): ☐ Unknown
Slowness of gait - Approximate date of onset (m m/dd/yyyy): ☐ Unknown
Stooped posture - Approximate date of onset (m m/dd/yyyy): ☐ Unknown
Other abnormality of posture or gait (other, specify) – Approximate date of onset (m m/dd/yyyy): ☐ Unknown

Graph representation

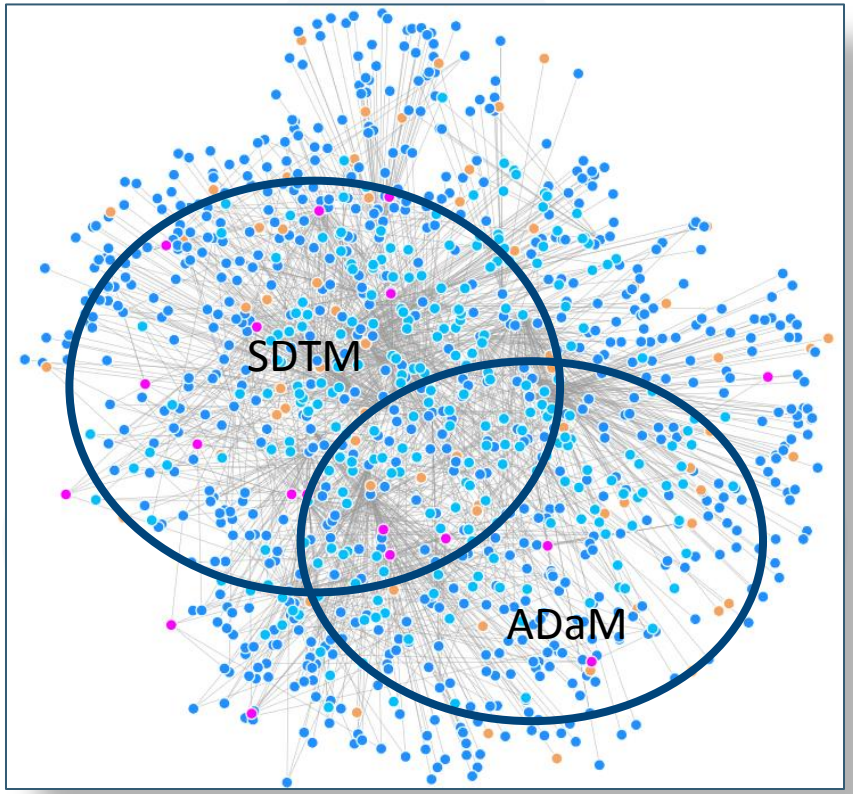


Medical History

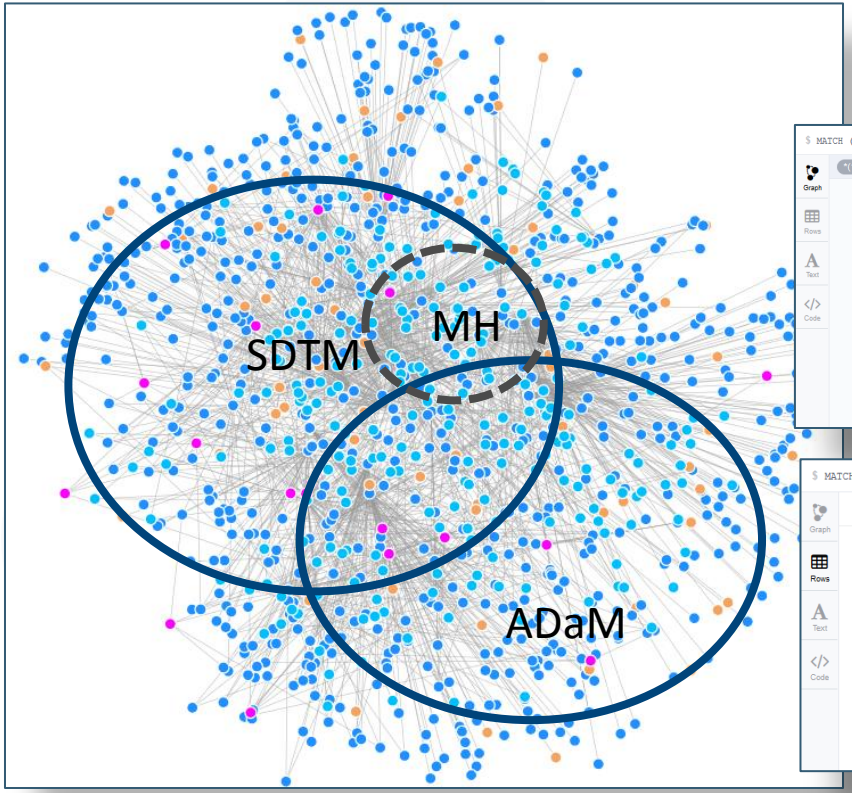
STUDYID	DOMAIN	USUBJID	MHTERM	MHLLT	MHDECOD	MHCAT	MHBODSYS	MHSTDTC
CDISCPILOT01	MH	01-701-1015	ALZHEIMER'S DISEASE			PRIMARY DIAGNOSIS		2010-04-30
CDISCPILOT01	MH	01-701-1015	ALZHEIMER'S DISEASE			FIRST SYMPTOMS		2008-06-10
CDISCPILOT01	MH	01-701-1015	VERBATIM_0825	TINNITUS	TINNITUS	SIGNIFICANT PRE-EXISTING CONDITION	EAR AND LABYRINTH DISORDERS	
CDISCPILOT01	MH	01-701-1148	ALZHEIMER'S DISEASE			PRIMARY DIAGNOSIS		2010-12-12
CDISCPILOT01	MH	01-701-1148	ALZHEIMER'S DISEASE			FIRST SYMPTOMS		2008-06-10
CDISCPILOT01	MH	01-701-1148	VERBATIM_0047	TINNITUS	TINNITUS	SIGNIFICANT PRE-EXISTING CONDITION	EAR AND LABYRINTH DISORDERS	



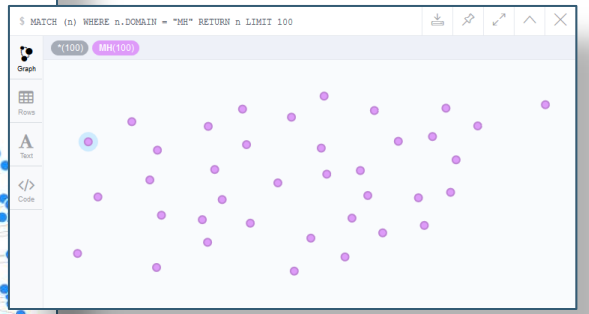
Where did my SDTM domain go?

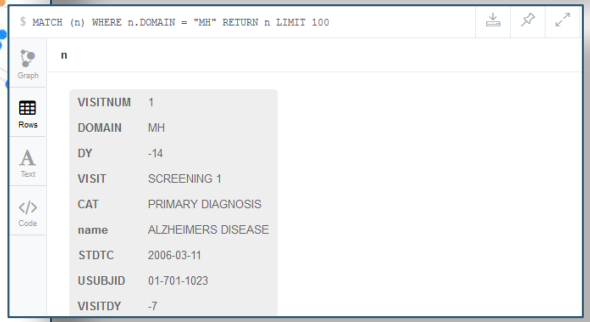


Where did my SDTM domain go?

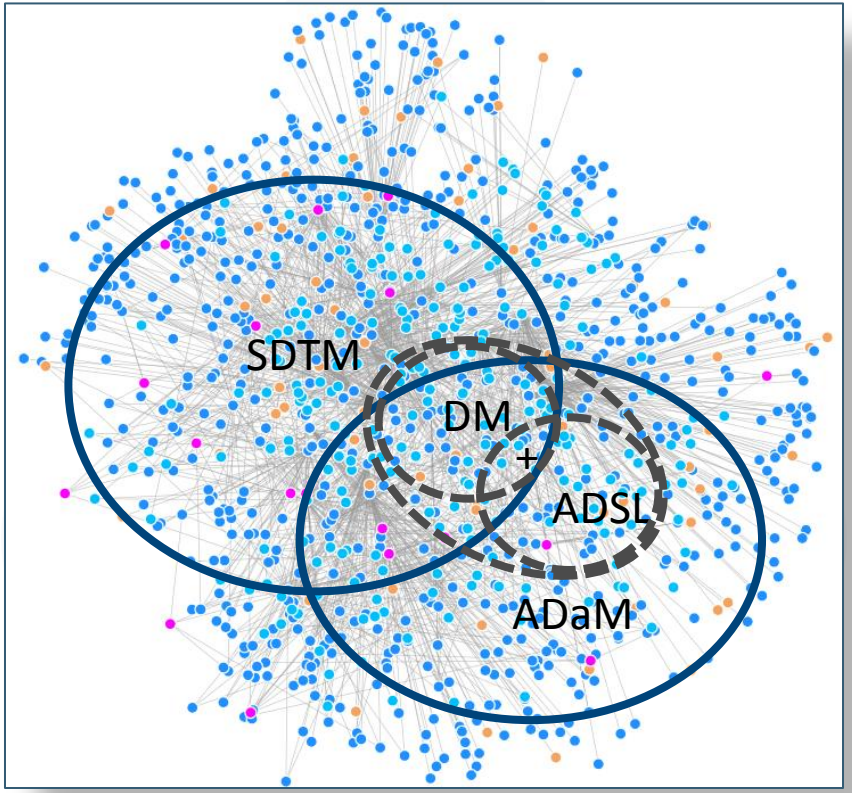


Pre-defined query



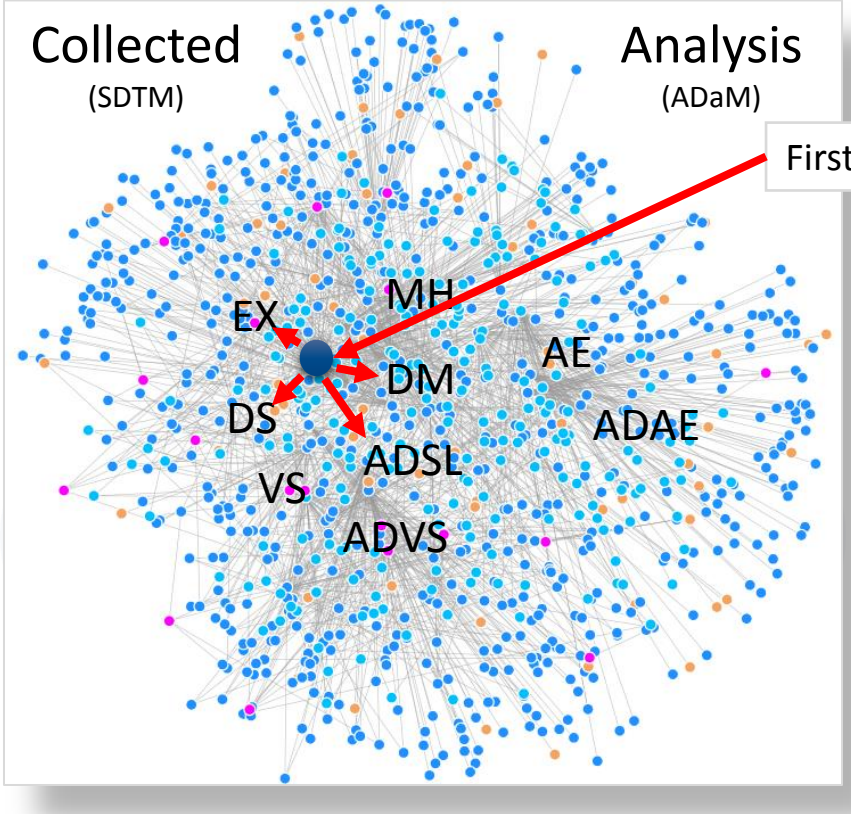


Where did my SDTM domain go?



Where did my SDTM domain go?

1. Part of the query
2. Not duplicated
3. Not mapped



Summary

Summary

GLANDON
METADATA REPOSITORY

- Build a linked view of the world and break the silos down.
- Consistent way to generate the existing views of that world.
- Do this in iterative fashion that allows the old and the new to co-exist.
- Solid foundation of linked high-quality definitions consistent across the life-cycle present opportunities for automation.

Contact Details

Dave Iberson-Hurst
dave.iberson-hurst@assero.co.uk
www.assero.co.uk

Contact Details

Niels Both & Johannes Ulander
nb@s-cubed.dk ju@s-cubed.dk
www.s-cubed.dk