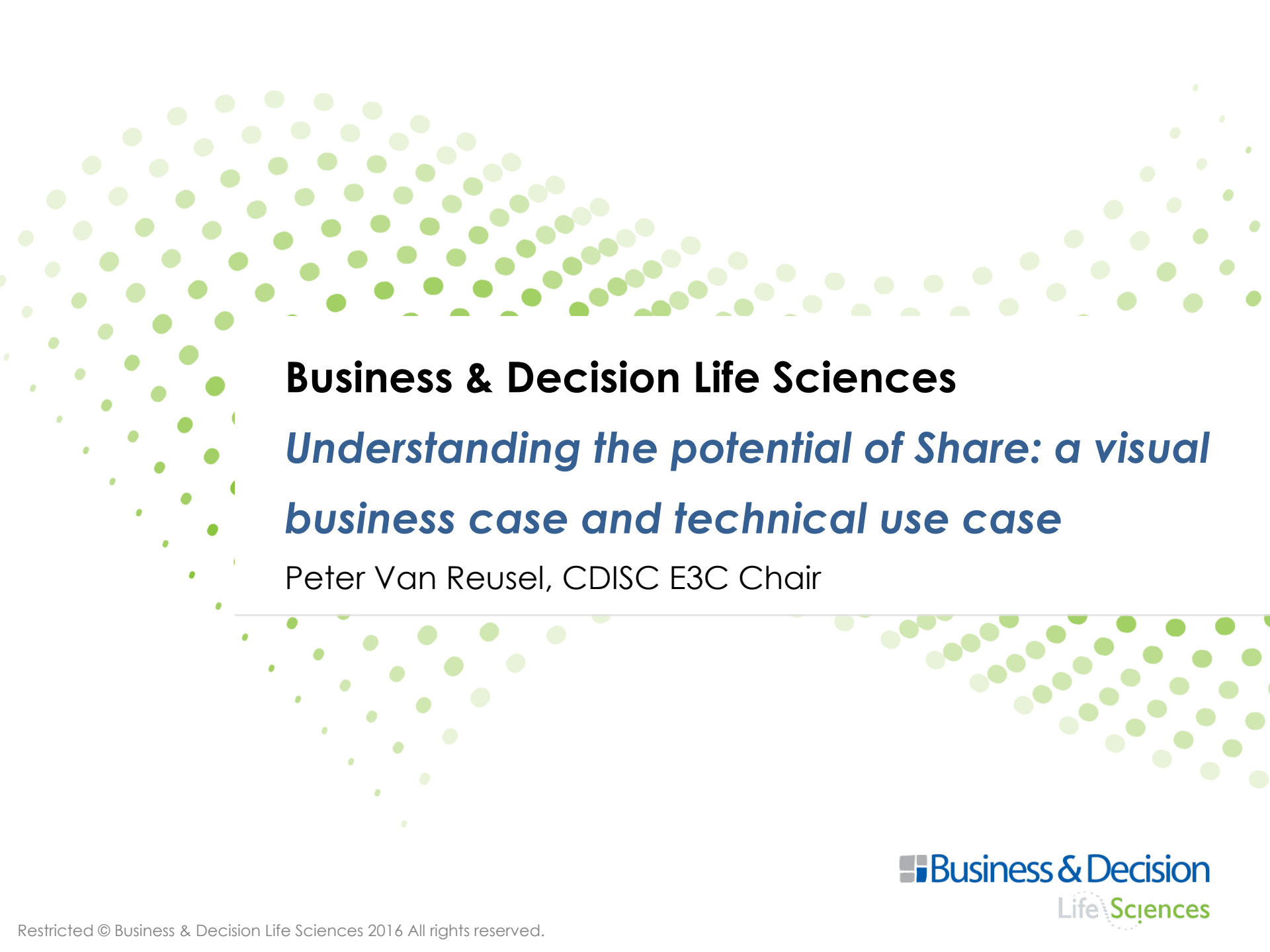


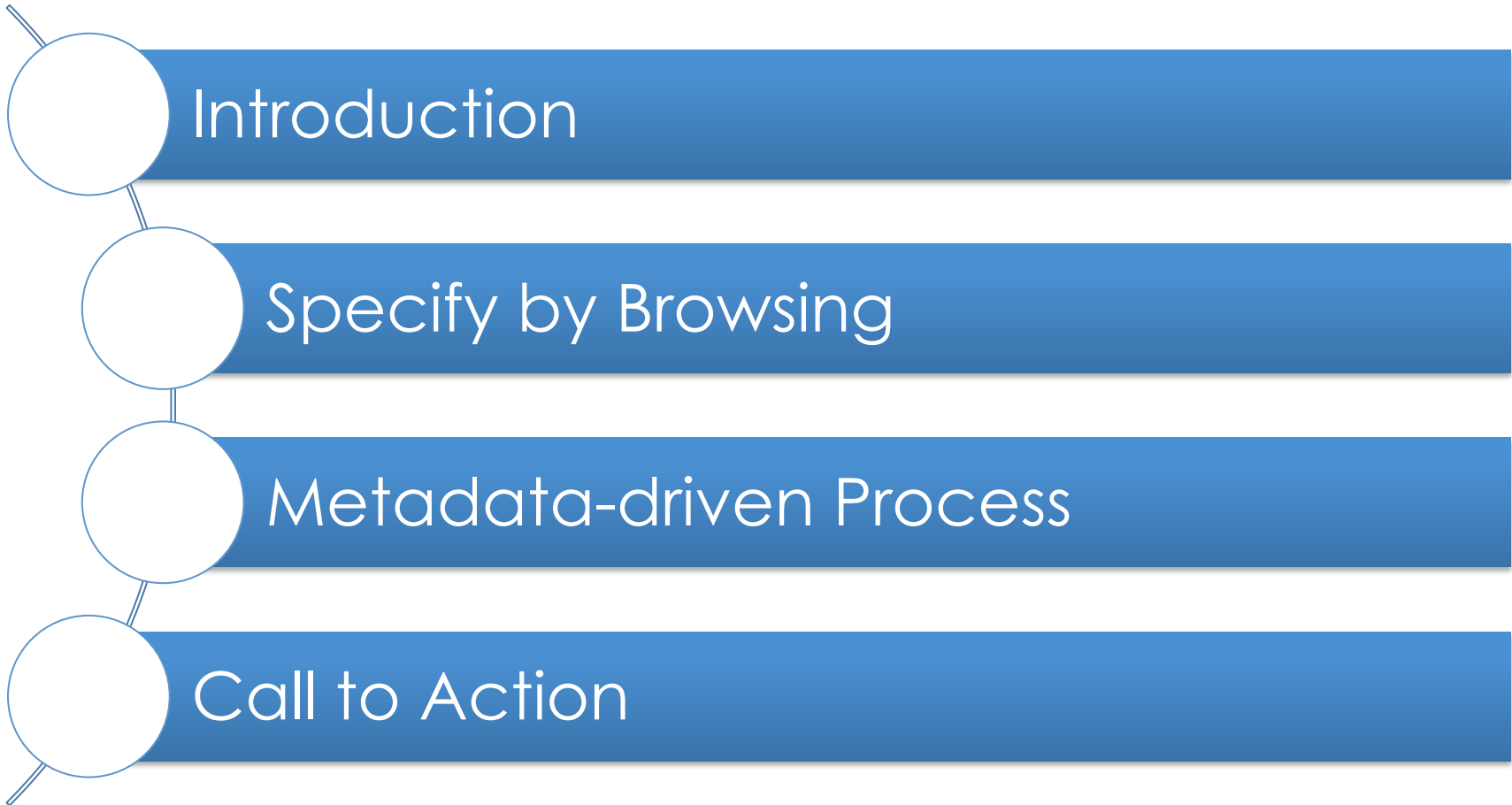


Business & Decision Life Sciences

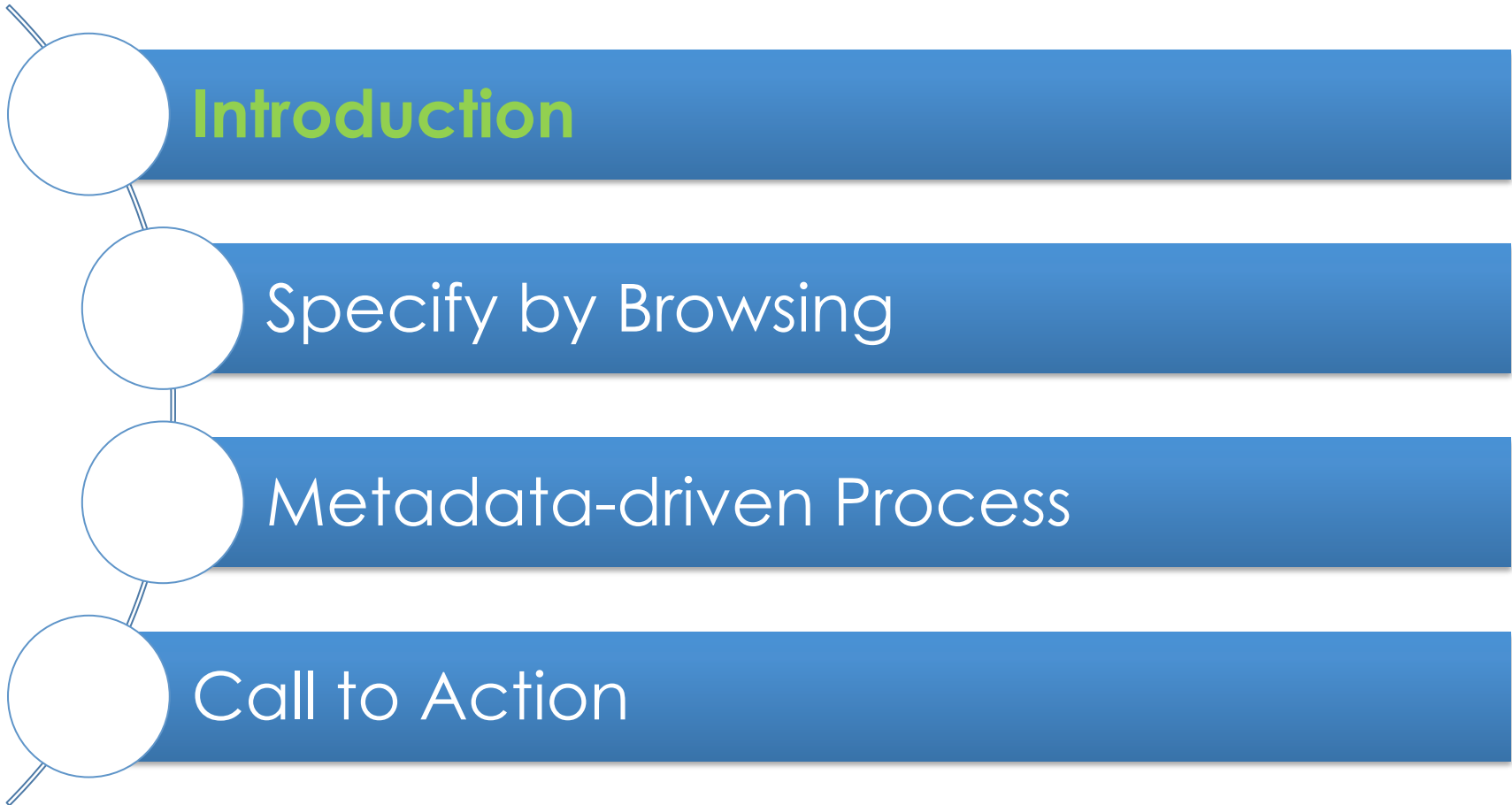
Understanding the potential of Share: a visual business case and technical use case

Peter Van Reusel, CDISC E3C Chair

Agenda



Agenda



The Responsibilities of Clinicians & Statisticians



Clinicians

Provides input to the **operational feasibility** of **clinical research studies**
Participates in **defining key components** of **clinical protocols**
Data review, analysis and interpretation
Analyze emerging **safety profile** of the **drug**
Ensure appropriate **subject population**
Assesses **performance of chosen endpoint measures**



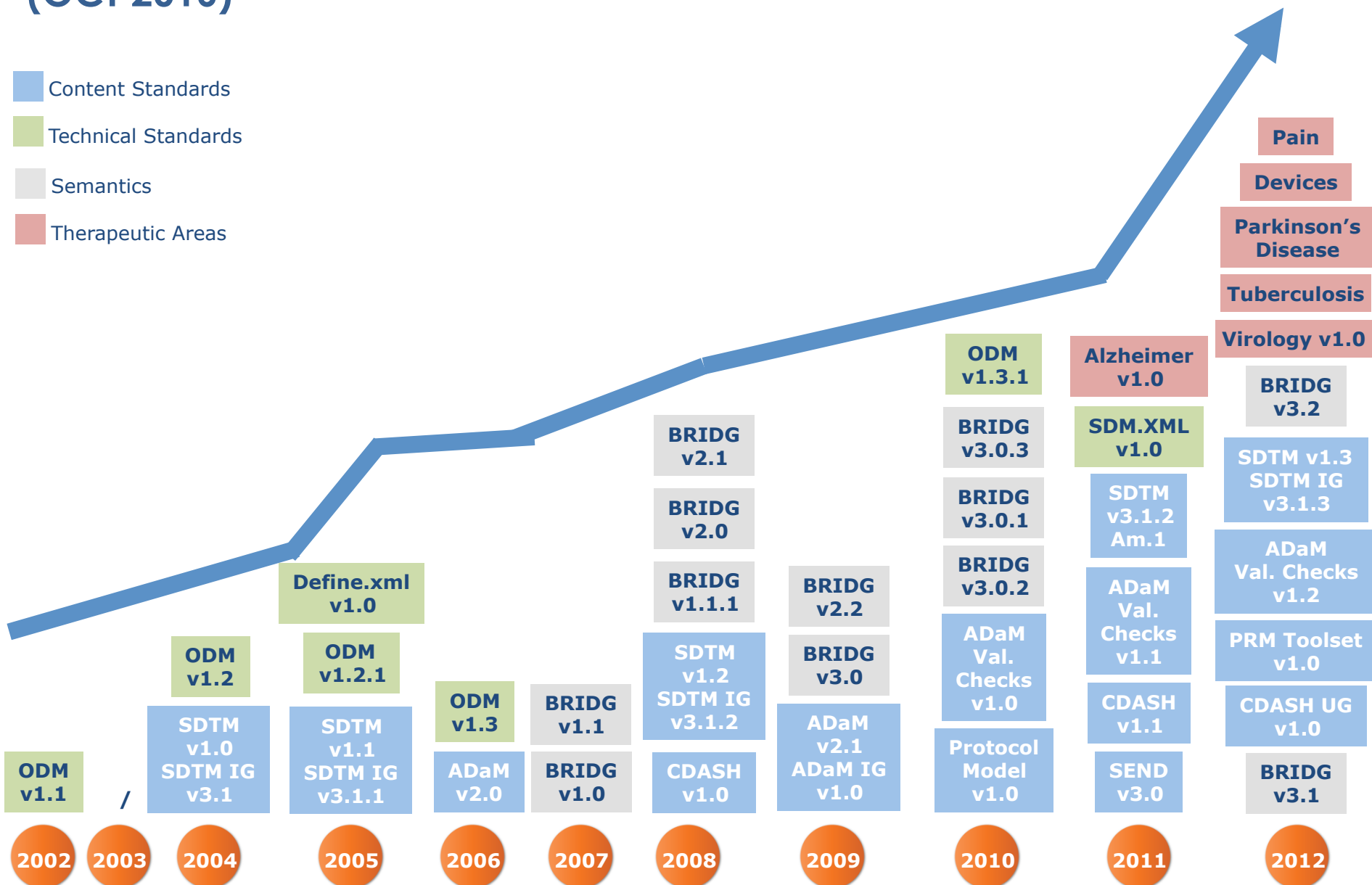
Statisticians

Establishing an **objective framework** for **conducting an investigation**
Placing **data and analysis** in **context**
Designing **data products** for **decision making**
Quantifying the influence of **chance**
Estimating systematic and random **effects**
Combining **the collected data** using formal methods

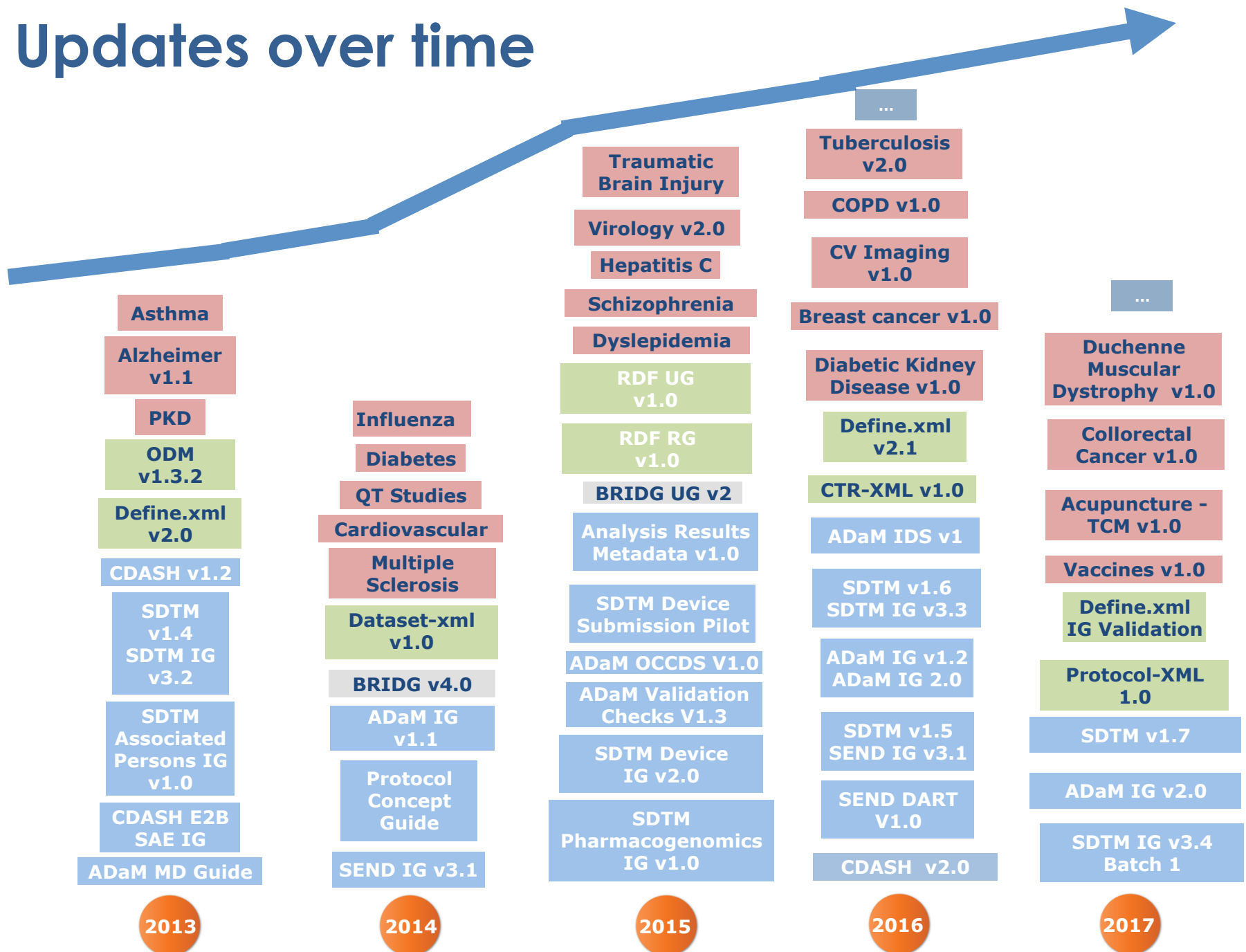
**Data
Standards
Experts**

Updates over time

(OCT 2016)



Updates over time



Overview of CDISC Models (OCT 2016)

PROTOCOL

PROTOCOL v1.0 (JAN 2010)
PRM TOOLSET v1.0 (APR 2012)
PROTOCOL CONCEPTS GUIDE
(AUG 2014)

CDASH

CDASH v1.0 (OCT 2008)
CDASH v1.1 (JAN 2011)
CDASH UG v1.0 (APR 2012)
CDASH E2B SAE IG (NOV 2013)
CDASH v2.0 (DEC 2016)

BRIDG

BRIDG v1.0 (JUN 2007)
BRIDG v1.1 (OCT 2007)
BRIDG v1.1.1 (FEB 2008)
BRIDG v2.0 (JUN 2008)
BRIDG v2.1 (OCT 2008)
BRIDG v2.2 (MAY 2009)
BRIDG v3.0 (OCT 2009)
BRIDG v3.0.1 (FEB 2010)
BRIDG v3.0.2 (AUG 2010)
BRIDG v3.0.3 (DEC 2010)
BRIDG v3.1 (FEB 2012)
BRIDG v3.2 (SEP 2012)
BRIDG v4.0 (NOV 2014)
BRIDG UG v2.0 (MAR 2015)

HEALTHCARE LINK

DEFINE.XML

DEFINE.XML v1.0 (FEB 2005)
DEFINE.XML v2.0 (MAR 2013)
DATASET-XML v1 (APR 2014)
CTR-XML v1.0 (MAR 2016)
DEFINE.XML IG VALIDATION
(NOV 2014)
DEFINE.XML v2.1 (2016)

SDTM

SDTM v1.0 + SDTM IG v3.1
(JUL 2004)
SDTM v1.1 + SDTM IG v3.1.1
(DEC 2014)
SDTM v1.2 + SDTM IG v3.1.2
(NOV 2008)
SDTM IG v3.1.2 + AMENDMENT 1
(DEC 2011)
SDTM MEDICAL DEVICES v1.0
(DEC 2012)
SDTM ASSOCIATED PERSONS
IG v1.0 (DEC 2013)
SDTM v1.4 + SDTM IG v3.2
(DEC 2013)
SDTM QRS SUPPLEMENTS
(PERIODIC)
SDTM PHARMACOGENOMICS
IG v1.0 (MAY 2015)
SDTM v1.6 + SDTM IG v3.3
(MAY 2014 – SEP 2016)
SDTM DEVICE IG v2.0
(DEC 2016)
SDTM IG v3.4 Batch 1 (Q1 2017)

XML TECH

SDM.XML v1.0 (SEP 2011)
RDF RG v1.0 (JUN 2015)
RDF UG v1.0 (JUL 2015)
PROTOCOL.XML (Q4 2016)

ODM

ODM v1.1 (APR 2002)
ODM v1.2 (JAN 2004)
ODM v1.2.1 (JAN 2005)
ODM v1.3 (DEC 2006)
ODM v1.3.1 (FEB 2012)
ODM v1.3.2 (MAR 2013)

ADaM

ADaM v2.0 (AUG 2006)
ADaM v2.21 + ADaM IG
(DEC 2009)
ADaM VALIDATION CHECKS
v1.0 (SEP 2010)
ADaM VALIDATION CHECKS
v1.1 (JUL 2011)
ADaM VALIDATION CHECKS
v1.2 (JUL 2012)
Analysis Results Metadata v1.0
(JAN 2015)
ADaM OCCDS v1.0 (JUL 2015)
ADaM VALIDATION CHECKS
v1.3 (MAR 2015)
ADaM IG v1.1 (FEB 2016)
ADaM IG v1.2 (Q1 2016)
ADaM IG v2.0 (Q4 2016)

SEND

SEND IG v3.0 (MAY 2011)
SDTM v1.5 + SEND IG v3.1
(Q1 2016)
SEND DART v1.0 (Q1 2016)

SHARE

CDISC SHARE
SHARE API PILOT (Q2 2016)

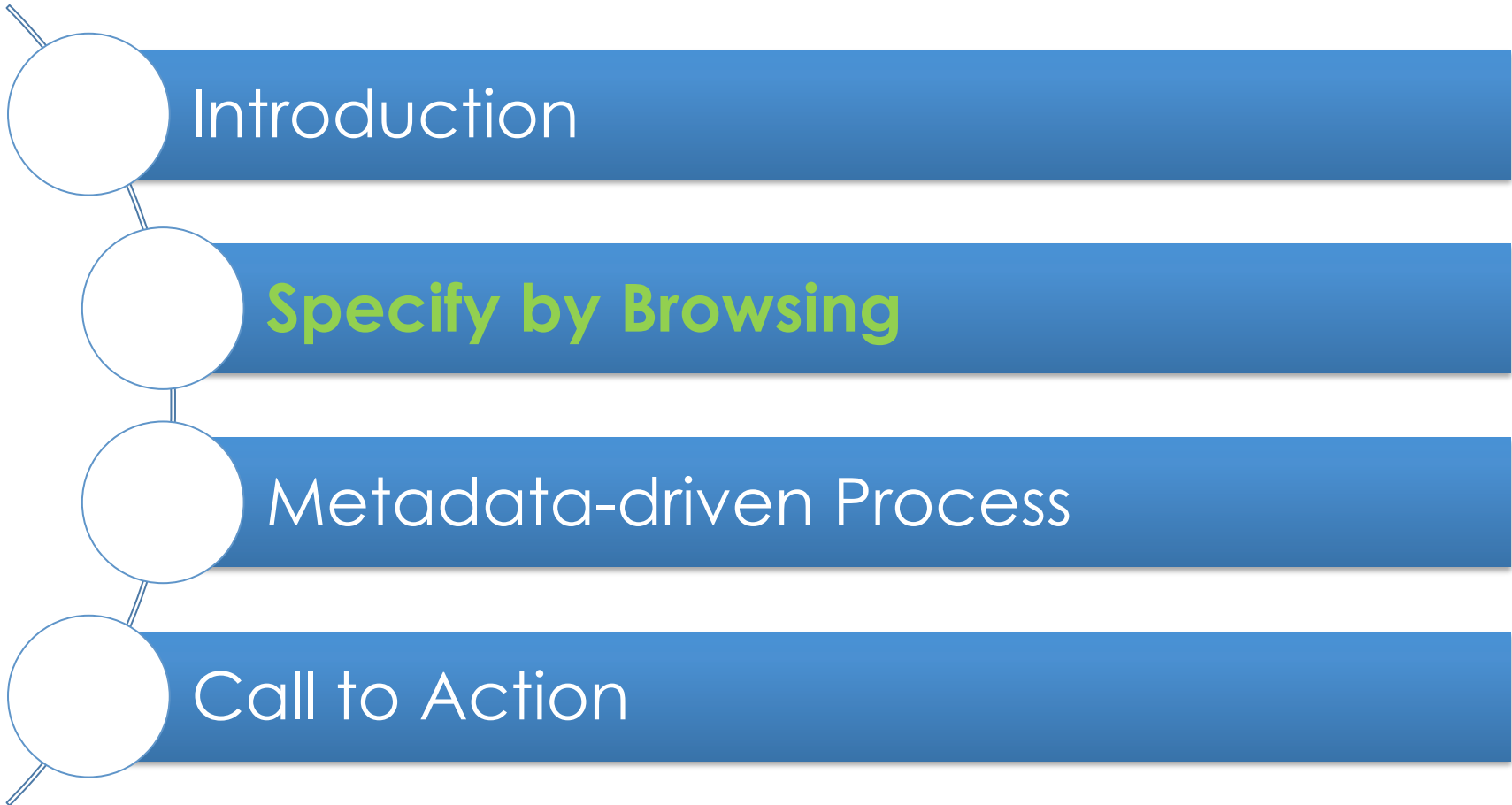
THERAPEUTIC AREAS

ALZHEIMER v1.0 (SEP 2011)
PAIN (JUN 2012)
TUBERCULOSIS (JUN 2012)
PARKINSON'S DISEASE
(OCT 2012)
VIROLOGY v1.0 (NOV 2012)
DEVICES (DEC 2012)
PKD (FEB 2013)
ALZHEIMER v2.0
ASTHMA v1.0
MULTIPLE SCLEROSIS
(MAY 2014)
DIABETES (AUG 2014)
CARDIOVASCULAR v1.0
(OCT 2014)
INFLUENZA v1.0 (NOV 2014)
QT STUDIES v1.0 (DEC 2014)
HEPATITIS C v1.0 (MAY 2015)
DISLIPIDEMIA v1.0 (JUN 2015)
SCHIZOPHRENIA v1.0 (JUN 2015)
VIROLOGY v2.0 (SEP 2015)
TRAUMATIC BRAIN INJURY v1.0
(DEC 2015)
ADaM SUPPLEMENT TO DIABETES
(DEC 2015)
COPD v1.0 (JAN 2016)
TUBERCULOSIS v2.0 (FEB 2016)
BREAST CANCER v1.0 (MAY 2016)
RHEUMATOID ARTHRITIS
(MAY 2016)
CV IMAGING v1.0 (MAY 2016)
SOLID ORGAN (KIDNEY)
TRANSPLANT (JUN 2016)
MAJOR DEPRESSIVE DISORDER
(JUL 2016)
DIABETIC KIDNEY DISEASE v1.0
(JUL 2016)

PROSTATE CANCER v1.0
(Q4 2016)
EBOLA v1.0 (Q4 2016)
MALARIA v1.0 (Q4 2016)
VACCINES (Q1 2017)
NUTRITIONAL STANDARDS
(Q4 2016)

-  Upcoming
-  Content Standards
-  Technical Standards
-  Semantics
-  Therapeutic Areas

Agenda



Visualizing Metadata Today

Table 1 Demographic Data - Per-Protocol

	Treatment 1	Treatment 2
Baseline body mass index (BMI) [kg/m**2]		
N	167	167
Mean	29.08	29.04
SD	4.84	4.80
Min	20.3	16.0
Median	28.69	28.47
Max	40.1	41.2
Baseline BMI (categorical) [N (%)]		
<25 kg/m**2	41 (24.6%)	71 (21.1%)
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Patient Demographics - Part I

Patient X5 Page 4 (Demo-V1a for Visit 1a) Page 1 of 1.

Visit Date 11-Dec-2007 Blank Comment

PATIENT DEMOGRAPHICS - Part I

Inform consent was obtained on **DSSTDC**

DSTERM / DSDECODE

Gender **SEX**

Date of birth **BRTHDTC**

Age **AGE** years **AGEU**

Height **VSORRES** / **VSORRESU** where **VSTESTCD** = "HEIGHT", "WEIGHT", "WAIST"

	STUDYID	USUBJID	SUBJID	BMI	BMIGR1	BMIGR1N	BMIGR2	BMIGR2N
2	9999-0001	9999-0001-000001	000001	27.77777778 <30 kg/m**2		1	25-<30 kg/m**2	2
3	9999-0001	9999-0001-000002	000002	25.50361502 <30 kg/m**2		1	25-<30 kg/m**2	2
4	9999-0001	9999-0001-000003	000003	26.175194521 <30 kg/m**2		1	25-<30 kg/m**2	2
5	9999-0001	9999-0001-000004	000004	35.15625 >=30 kg/m**2		2	>=30 kg/m**2	3
6	9999-0001	9999-0001-000005	000005	30.96889911 >=30 kg/m**2		2	>=30 kg/m**2	3
7	9999-0001	9999-0001-000006	000006	39.697163916 >=30 kg/m**2		2	>=30 kg/m**2	3
8	9999-0001	9999-0001-000007	000007	25.826446281 <30 kg/m**2		1	25-<30 kg/m**2	2
9	9999-0001	9999-0001-000008	000008	30.103806228 >=30 kg/m**2		2	>=30 kg/m**2	3
10	9999-0001	9999-0001-000009	000009	32.28962683 >=30 kg/m**2		2	>=30 kg/m**2	3
11	9999-0001	9999-0001-000010	000010	28.876133787 <30 kg/m**2		1	25-<30 kg/m**2	2
12	9999-0001	9999-0001-000011	000011	29.372397383 <30 kg/m**2		1	25-<30 kg/m**2	2
13	9999-0001	9999-0001-000012	000012	26.714852608 <30 kg/m**2		1	25-<30 kg/m**2	2
14	9999-0001	9999-0001-000013	000013	32.718619869 >=30 kg/m**2		2	>=30 kg/m**2	3
15	9999-0001	9999-0001-000014	000014	28.719723183 <30 kg/m**2		1	25-<30 kg/m**2	2
16	9999-0001	9999-0001-000015	000015	32.274020377 >=30 kg/m**2		2	>=30 kg/m**2	3

Variable	Label	Type	Controlled Terminology	Origin	Role	Comment
STUDYID	Study Identifier	text		Protocol, CRF Page 1	IDENTIFIER	The STUDYID variable has a fixed format: 'XXXX-YYYY', where 'XXXX' indicates the 4-digit compound code and the 'YYYY' the 4-digit study code
DOMAIN	Domain Abbreviation	text	DOMAIN	Assigned	IDENTIFIER	
USUBJID	Unique Subject Identifier	text		Protocol	IDENTIFIER	The USUBJID variable has a fixed format: 'XXXX-YYYY-ZZZZZ', where 'XXXX' indicates the 4-digit compound code, 'YYYY' the 4-digit study code and 'ZZZZZ' the 5-digit patient code
VSSQ	Sequence Number	integer		Derived	IDENTIFIER	Sequence number (automatically generated) to ensure uniqueness within a dataset for a subject
VSTESTCD	Vital Signs Test Short Name	text		Assigned	TOPIC	
VSTEST	Vital Signs Test Name	text		Derived	SYNONYM QUALIFIER	
VSPOS	Vital Signs Position of Subject	text	POSITION	CRF Page 11	RECORD QUALIFIER	
VSORRES	Result or Finding in Original Units	text		Derived, CRF Page 9, 11	RESULT QUALIFIER	
VSORRESU	Original Units	text	VSRESU	CRF Page 9, 11	VARIABLE QUALIFIER	
VSTRESRC	Character Result Finding in Std Format	text		Derived	RESULT QUALIFIER	
VSTRESN	Numeric Result Finding in Standard Units	float	1:1	Derived	RESULT QUALIFIER	

Variable	Label	Type	Controlled Terminology or Format	Computation or Method	Origin	Role	Comment
STUDYID	Study Identifier	text			DM	IDENTIFIER	The STUDYID variable has a fixed format: 'XXXX-YYYY', where 'XXXX' indicates the 4-digit compound code and the 'YYYY' the 4-digit study code
USUBJID	Unique Subject Identifier	text			DM	IDENTIFIER	The USUBJID variable has a fixed format: 'XXXX-YYYY-ZZZZZ', where 'XXXX' indicates the 4-digit compound code, 'YYYY' the 4-digit study code and 'ZZZZZ' the 5-digit patient code
SUBJID	Subject Identifier for the Study	text			DM	IDENTIFIER	
HEIGHT	Baseline Height (cm)	integer		ADSL HEIGHT	Derived	ANALYSIS	
WEIGHT	Baseline Weight (kg)	integer		ADSL WEIGHT	Derived	ANALYSIS	
BMI	Baseline BMI (kg/m**2)	integer		ADSL BMI	Derived	ANALYSIS	
BMIGR1	Category 1 of Baseline BMI	text	BMIGR1L	ADSL BMIGR1	Derived	ANALYSIS	
BMIGR1N	Category 1 of Baseline BMI (N)	integer	BMIGR1N	ADSL BMIGR1N	Derived	ANALYSIS	
BMIGR2	Category 2 of Baseline BMI	text	BMIGR2L	ADSL BMIGR2	Derived	ANALYSIS	
BMIGR2N	Category 2 of Baseline BMI (N)	integer	BMIGR2N	ADSL BMIGR2N	Derived	ANALYSIS	
BMIGR3	Category 3 of Baseline BMI	text	BMIGR3L	ADSL BMIGR3	Derived	ANALYSIS	
BMIGR3N	Category 3 of Baseline BMI (N)	integer	BMIGR3N	ADSL BMIGR3N	Derived	ANALYSIS	

Visualizing Metadata Today

■ Analysis Results

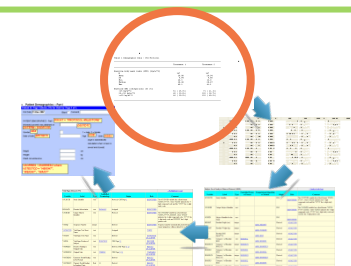
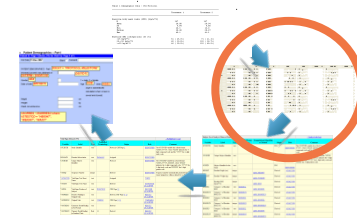


Table 1 Demographic Data - Per-Protocol

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Max	40.1	41.2
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Visualizing Metadata Today

■ Analysis Dataset

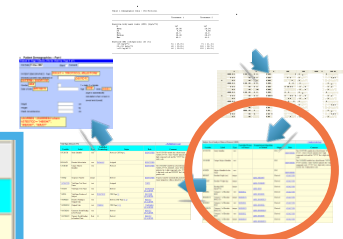


	STUDYID	USUBJID	SUBJID	BMI	BMIGR1	BMIGR1N	BMIGR2	BMIGR2N
2	9999-0001	9999-0001-000001	000001	27.777777778	<30 kg/m**2	1	25-<30 kg/m**2	2
3	9999-0001	9999-0001-000002	000002	25.503615702	<30 kg/m**2	1	25-<30 kg/m**2	2
4	9999-0001	9999-0001-000003	000003	26.175194521	<30 kg/m**2	1	25-<30 kg/m**2	2
5	9999-0001	9999-0001-000004	000004	35.15625	>=30 kg/m**2	2	>=30 kg/m**2	3
6	9999-0001	9999-0001-000005	000005	30.968858131	>=30 kg/m**2	2	>=30 kg/m**2	3
7	9999-0001	9999-0001-000006	000006	39.697163916	>=30 kg/m**2	2	>=30 kg/m**2	3
8	9999-0001	9999-0001-000007	000007	25.826446281	<30 kg/m**2	1	25-<30 kg/m**2	2
9	9999-0001	9999-0001-000008	000008	30.103806228	>=30 kg/m**2	2	>=30 kg/m**2	3
10	9999-0001	9999-0001-000009	000009	32.280962683	>=30 kg/m**2	2	>=30 kg/m**2	3
11	9999-0001	9999-0001-000010	000010	28.876133787	<30 kg/m**2	1	25-<30 kg/m**2	2
12	9999-0001	9999-0001-000011	000011	29.372397383	<30 kg/m**2	1	25-<30 kg/m**2	2
13	9999-0001	9999-0001-000012	000012	26.714852608	<30 kg/m**2	1	25-<30 kg/m**2	2
14	9999-0001	9999-0001-000013	000013	32.718619869	>=30 kg/m**2	2	>=30 kg/m**2	3
15	9999-0001	9999-0001-000014	000014	28.719723183	<30 kg/m**2	1	25-<30 kg/m**2	2
16	9999-0001	9999-0001-000015	000015	32.270420377	>=30 kg/m**2	2	>=30 kg/m**2	3

Visualizing Metadata Today

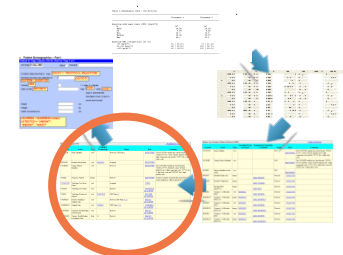
ADaM Define.xml

Computational Algorithms (ADSL.BMI)							
Reference Name		Computation Method					
ADSL BMI		Continuous variable, calculated using ADSL.WEIGHT/(ADSL.HEIGHT*0,01)**2 value at visit 3 if visit 3 data not available, the last data collected before randomisation					
Computational Algorithms (ADSL.HEIGHT)							
Reference Name		Computation Method					
ADSL HEIGHT		equal to VS.VSSTRESN when VS.VSTESTCD="HEIGHT"					
Computational Algorithms (ADSL.WEIGHT)							
Reference Name		Computation Method					
ADSL WEIGHT		equal to VS.VSSTRESN when VS.VSTESTCD="WEIGHT" and VS.VISITNUM=30 if visit 3 data not available, the last data collected before randomisation					
				ADSL HEIGHT			
WEIGHT	Baseline Weight (kg)	integer		ADSL WEIGHT	Derived	ANALYSIS	
BMI	Baseline BMI (kg/m**2)	integer		ADSL BMI	Derived	ANALYSIS	
BMIGR1	Category 1 of Baseline BMI	text	BMIGR1L	ADSL BMIGR1	Derived	ANALYSIS	
BMIGR1N	Category 1 of Baseline BMI, (N)	integer	BMIGR1N	ADSL BMIGR1N	Derived	ANALYSIS	
BMIGR2	Category 2 of Baseline BMI	text	BMIGR2L	ADSL BMIGR2	Derived	ANALYSIS	
BMIGR2N	Category 2 of Baseline BMI, (N)	integer	BMIGR2N	ADSL BMIGR2N	Derived	ANALYSIS	
BMIGR3	Category 3 of Baseline BMI	text	BMIGR3L	ADSL BMIGR3	Derived	ANALYSIS	
BMIGR3N	Category 3 of Baseline BMI, (N)	integer	BMIGR3N	ADSL BMIGR3N	Derived	ANALYSIS	



Visualizing Metadata Today

SDTM Define.xml and aCRF



Value Level Metadata (ValueList.VS.VSTESTCD)

Source Variable	Value	Label	Type	Controlled Terminology	Origin	Role	Comment
VSTESTCD	DIABP	DIASTOLIC BLOOD PRESSURE	text		CRF Page 13		
VSTESTCD	HEIGHT	HEIGHT	text		CRF Page 9		
VSTESTCD	PULSE	PULSE RATE	text		CRF Page 13		
VSTESTCD	SYSBP	SYSTOLIC BLOOD PRESSURE	text		CRF Page 13		
VSTESTCD	WAIST	WAIST CIRCUMFERENCE	text		CRF Page 9		
VSTESTCD	WEIGHT	WEIGHT	text		CRF Page 9		

VSTESTCD	Vital Signs Test Short Name
VSTEST	Vital Signs Test Name
VSTEST	Vital Signs Test Name
VSPOS	Vital Signs Position of Subject
VSORRES	Result or Finding in Original Units
VSORRESU	Original Units
VSSSTRESC	Character Result/Finding in Std Format
VSSSTRESN	Numeric Result/Finding in Standard Units

• Patient Demographics – Part I

Patient X5 Page 4 (Demo_V1a for Visit 1a) Page 1 of 1.

Visit Date 11-Dec-2007

Blank ☐ Comment

PATIENT DEMOGRAPHICS - Part I DSCAT = "PROTOCOL MILESTONE"

Informed consent was obtained on

DSTERM / DSDECOD

DSSTDTC

Gender SEX

1 = male, 2 = female

Date of birth BIRTHDTC

Age AGE

years AGEU

(Age is automatically calculated when screen is saved and closed)

Height

cm

Weight

kg

Waist circumference

cm

VSORRES / VSORRESU where VSTESTCD = "HEIGHT", "WEIGHT", "WAIST"

Current Metadata Repository

- Current MDRs represent metadata in a tabular format

The image displays two overlapping software interfaces for managing ADaM metadata. The top interface, titled 'ADaM Domain', shows a table of datasets. The bottom interface, titled 'ADaM Metadata', shows a table of parameters. Red circles and lines highlight the relationship between the 'ADVS' dataset and the 'PARAMCD' parameter across both tables.

ADaM Domain Table:

Locked	Invalid	Active from	Active to	Dataset	Description
		2016-01-16		ADVS	One record per subject, per parameter, per analysis visit, per date
		2016-01-16		ADTTE	One record per subject per parameter
				ADSU	One record per subject per parameter per analysis visit
				ADSL	One record per subject
				ADSC	One record per subject per parameter per analysis visit
				ADPE	One record per subject, per parameter, per analysis visit
				ADMH	One record per subject per medical history per start date
				ADLB	One record per subject per parameter per analysis visit
				ADIE	One record per subject per parameter per analysis visit
				ADEX	One record per subject per sequence number

ADaM Metadata Table:

ADaM Dataset	Name	Label
advs		
ADVS	VSTRESU	Standard Units
ADVS	PARAMCD	Parameter Code
ADVS	VSTRESU	Character Result/Finding in Std Format
ADVS	VSORRESU	Original Units
ADVS	USUBJID	Unique Subject ID
ADVS	PARAM	Parameter
ADVS	VSORRES	Result or Finding in Original Units

ADaM Parameter Name Table:

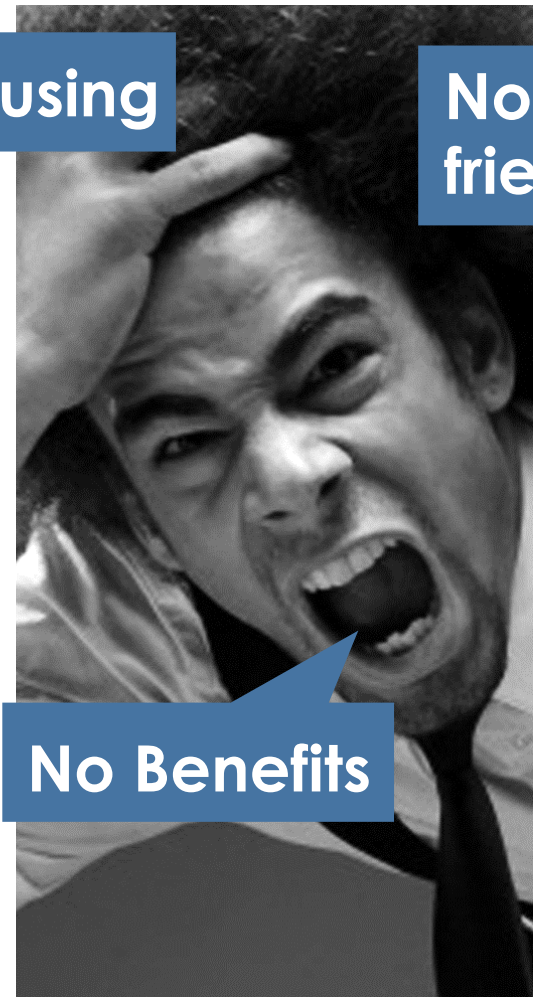
Locked	Invalid	Active from	Active to	ADaM Dataset	Name	VLM Values
		2016-01-16		ADVS	PARAMCD	

Current Metadata Repository

- Current MDRs represent metadata in a tabular format



Confusing



No Benefits

Not user friendly



Boring



DISCLAIMER NOTE

The following is not a software demonstration

Sole purpose is to illustrate

NeXtGenMdr

Welcome

Login:

Password:

[SIGN IN >>](#)





CDASH

DOMAIN
CDASH Variable
Value Level Metadata
Controlled Terminology

SDTM

DOMAIN
SDTM Variable
Value Level Metadata
Controlled Terminology
Computational algorithm

ADaM

DOMAIN
ADaM Variable
ADaM Parameters
Controlled Terminology
Computational algorithm



SHOPPING
CART



DATA
COLLECTION



ANALYSIS

AE

Adverse
Events

EX

Exposure

CM

Concomittant
Medication

MH

Medical
History

VS

Vital Signs

LB

Laboratory
Test Results



Tables



Figures



Listings



End Points

CDASH

DOMAIN
CDASH Variable
Value Level Metadata
Controlled Terminology

SDTM

DOMAIN
SDTM Variable
Value Level Metadata
Controlled Terminology
Computational algorithm

ADaM

DOMAIN
ADaM Variable
ADaM Parameters
Controlled Terminology
Computational algorithm

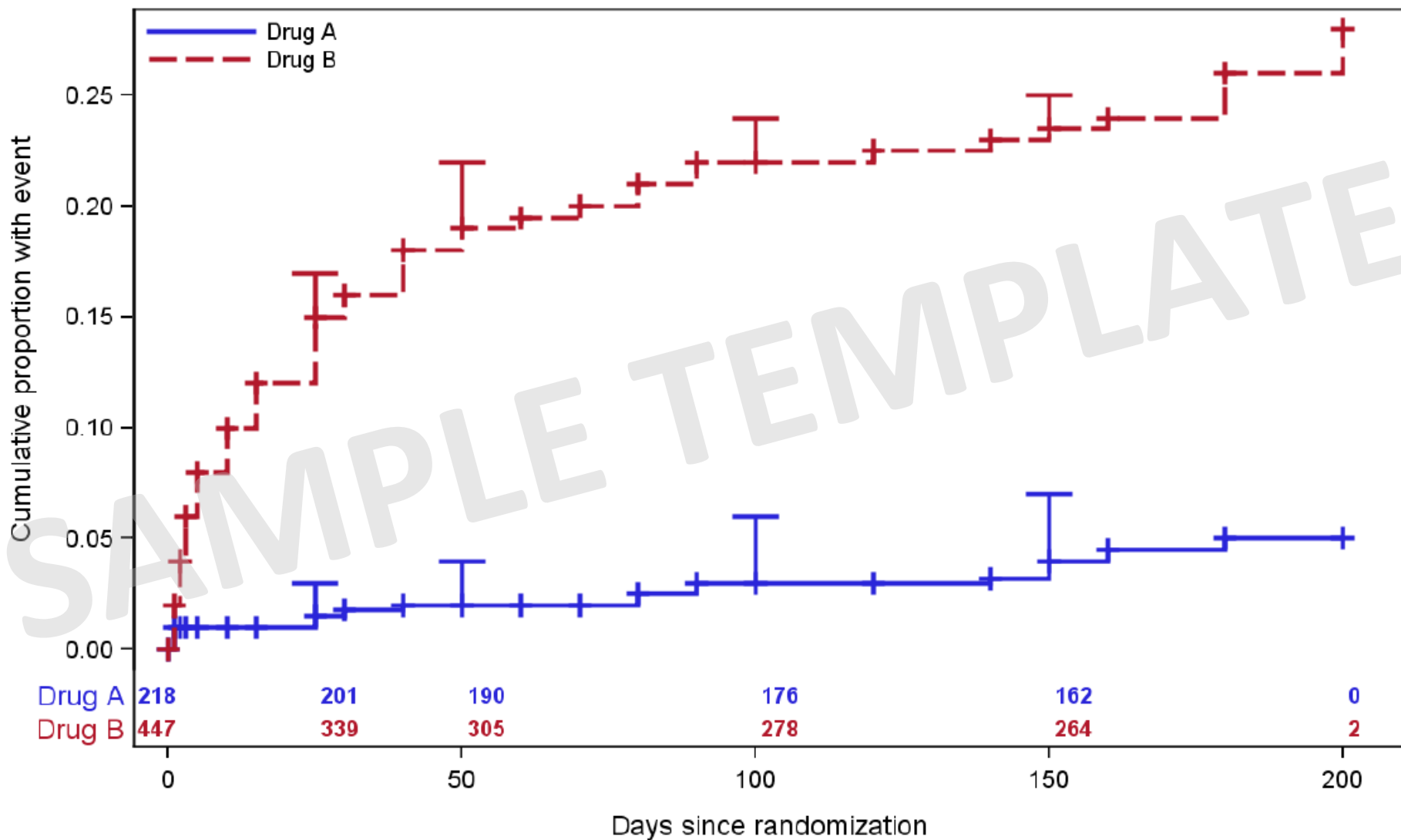


Figures

Graphical Approaches to the Analysis of Safety Data from Clinical Trials”. Amit, et. al.
From “Graphical Approaches to the Analysis of Safety Data from Clinical Trials”. Amit, et. al.
Mean Change from Baseline in QTc by time and treatment.
Distribution of ASAT by time and treatment
Distribution of maximum LFT values by treatment.
Panel of LFT shift from baseline to maximum by treatment
LFT Patient profiles
Most Frequent On Therapy Adverse Events
Cumulative distribution (with SEs) of time to first AE of special interest



Cumulative Distribution of Time to First AE



CDASH

DOMAIN
CDASH Variable
Value Level Metadata
Controlled Terminology

SDTM

DOMAIN
SDTM Variable
Value Level Metadata
Controlled Terminology
Computational algorithm

ADaM

DOMAIN
ADaM Variable
ADaM Parameters
Controlled Terminology
Computational algorithm

AE
Adverse
Events

EX
Exposure

CM
Concomittant
Medication

MH
Medical
History

VS
Vital Signs

LB
Laboratory
Test Results


Tables


Figures


Listings


End Points

CDASH

DOMAIN
CDASH Variable
Value Level Metadata
Controlled Terminology

SDTM

DOMAIN
SDTM Variable
Value Level Metadata
Controlled Terminology
Computational algorithm

ADaM

DOMAIN
ADaM Variable
ADaM Parameters
Controlled Terminology
Computational algorithm



Listings

Listing 2.4 Current Cancer History – All Treated Patients Experiencing Critical Events
Listing 2.5 Prior and Concomitant Medication – All Treated Patients Experiencing Critical Events
Listing 2.6 Physical Examination at Screening – All Treated Patients Experiencing Critical Events
Listing 3.1 Reference Chemotherapy and Concomitant Chemotherapies – All Treated Patients Experiencing ..
Listing 4.1 Adverse Event Listing. All Pre-Treatment Adverse Events – All Treated Patients Experiencing ...
Listing 4.2 Adverse Event Listing. Treatment Emergent Adverse Events – All Treated Patients Experiencing ...
Listing 4.3 Adverse Event Listing. Serious Treatment Emergent Adverse Events – All Treated Patients ..
Listing 4.4 Adverse Event Listing. Serious Treatment Emergent Adverse Events Related To Study Drug ...
Listing 4.5 Adverse Event Listing. Serious Treatment Emergent Adverse Events Related To Treatment



Listing 4.5 Adverse Event Listing. Serious Treatment Emergent Adverse Events Related To "Treatment" - All Treated Patients Experiencing Critical Events

Country	Site/ Patient ID	AE Verbatim Term MedDRA SOC Name MedDRA Preferred Term	Start Date/Time Stop Date/Time Duration (Days/Hours)	Day of onset	Occurrence	Intensity CTC grade	Relationship to Dexamethasone	Action Taken	Outcome
xxxxxxxx	xx/xxx	XXXXXXXXXXXXXXXXX XXXXXXXXXXXXXXXXXXXXX XXXXXXXXXXXXXXXXXXXXX	DDMMYYYY/HH:MM DDMMYYYY/HH:MM xxxxx/xxxxx	xx	Intermittent	Grade X	Possibly	None	Resolved

Analysis dataset: ADAE.SAS7BDAT ddmmmyyyy hh:mm

Note: Critical events are defined as: Serious Adverse Events (extracted from the clinical database reconciled with the safety database), Suspected Unexpected Serious Adverse Reactions (extracted from the safety database), wrong study medication used (patients who received a wrong medication kit by mistake in one cycle, resulting in the administration of drug from both treatment groups during the study).

Note: "Treatment" related adverse events are adverse events with a missing relationship to "Treatment" or assessed by the Investigator as definite, probable, possible or unassessable.

Program: <DIRECTORY PATH>\XXXXXX.sas; Date & Time program was run: ddmmmyyyy hh:mm; Date & Time analysis dataset was run: ddmmmyyyy hh:mm

CDASH

DOMAIN

CDASH Variable

Value Level Metadata

Controlled Terminology

SDTM

DOMAIN

SDTM Variable

Value Level Metadata

Controlled Terminology

Computational algorithm

ADaM

DOMAIN

ADaM Variable

ADaM Parameters

Controlled Terminology

Computational algorithm

ADaM

Domain

Variables

Computational Algorithm

 SHOPPING
CART

 DATA
COLLECTION

 ANALYSIS

Dataset	Description
ADAE	One record per subject per adverse event, per date

CDASH

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CDASH Variable
Value Level Metadata
Controlled Terminology

SDTM

DOMAIN
SDTM Variable
Value Level Metadata
Controlled Terminology
Computational algorithm

ADaM

DOMAIN
ADaM Variable
ADaM Parameters
Controlled Terminology
Computational algorithm

ADaM

Domain

Variables

Computational Algorithm

Domain	Name	Label	Computational Algorithm
ADAE	USUBJID	Unique Subject Identifier	
ADAE	SUBJID	subject identifier for the study	
ADAE	SITEID	Study Site identifier	
ADAE	DOSEAEONU	Study Drug Dose at AE Onset Units	ADAE.DOSEAEONU
ADAE	DOSEAEON	Study Drug Dose at AE Onset	ADAE.DOSEAEON
ADAE	COUNTRY	Country	
ADAE	ASTTM	Analysis Start Time	ADAE.ASTTM
ADAE	ASTDT	Analysis Start Time	ADAE.ASTD
ADAE	AETERM	Reported Term for the Adverse Events	

 SHOPPING CART

 DATA COLLECTION

 ANALYSIS

CDASH

DOMAIN
CDASH Variable
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Controlled Terminology

SDTM

DOMAIN
SDTM Variable
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Controlled Terminology
Computational algorithm

ADaM

DOMAIN
ADaM Variable
ADaM Parameters
Controlled Terminology
Computational algorithm

Reference

Description

ADAE.AENDT	Equals to % SDTM_DATE_VARIABLE % transformed into % DATE_NUMERIC_FORMAT% when length (%SDTM_DATE_VARIABLE%) > 9
ADAE.ADURN	Equals to ADAE.AENDT – ADAE.ASTDT + 1.
ADAE.DOSEAEON	Equals to EX.EXDOSE where the numeric version of EX.EXSTDTC <= ASTDT <= the Numeric version of EX.EXENDTC.
ADAE.DOSEAEONU	Equals to EX.EXDOSU where the numeric version of EX.EXSTDTC <= ASTDT <= the Numeric version of EX.EXENDTC.
ADAE.DOSEAEON	Equals to "DAYS"

CDASH

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CDASH Variable
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SDTM

DOMAIN
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Computational algorithm

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DOMAIN
ADaM Variable
ADaM Parameters
Controlled Terminology
Computational algorithm

ADaM

Domain

Variables

Computational Algorithm

Reference

Description

ADAE.DOSEAEON	Equals to EX.EXDOSE where the numeric version of EX.EXSTDTC <= ASTDT <= the Numeric version of EX.EXENDTC.
---------------	--

Name	Label	Origin	Role	Core
AESTDTC	Start date/Time of Adverse Event	CRF	Timing	Exp
EXDOSE	Dose per administration	Derived	Record Qualifier	Exp
EXTDTC	Start date/Time of treatment	CRF	Timing	Exp
EXENDTC	End date/Time of treatment	CRF	Timing	Perm

Domain	Name	Question
AE	AESTDAT	Start Date
AE	AESTIM	Start Time
EX	EXAMONT	Dose
EX	EXAMONTU	Units
EX	EXENDAT	End Date
EX	EXENTIM	End Time
EX	EXSTDAT	Start Date



CDASH

DOMAIN
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SDTM Variable
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Computational algorithm

ADaM

DOMAIN
ADaM Variable
ADaM Parameters
Controlled Terminology
Computational algorithm

ADaM

Domain

Variables

Computational Algorithm



DCM's



SHOPPING
CART



DATA
COLLECTION



ANALYSIS

EX - EXPOSURE

Study: Study
Site: Site
Subject: Subject
Visit Number: Visit Number
Visit Time Point: Visit Time Point

SCREEN ID: EX-01

Site Number: Site Number
Site Name: Site Name
Site Type: Site Type

Study Drug Administration - for Study Specific Drug Name

EXCAT - Treatment Type
EXCAT - Treatment Name
EXDOPRE - What was the prescribed dose level?
EXDOPRU - Prescribed dose level Units
EXDOPR - What is the treatment label identifier?
EXDOPR - Dose
EXDOPR - Units
EXDOPR - Frequency
EXDOPR - Frequency
EXDOPR - What was the anatomical location of the administration?
EXDOPR - Start Date
EXDOPR - Start Time

UNIT

LOC

ADVERSE EVENTS

Study: Study
Site: Site
Subject: Subject
Visit Number: Visit Number
Visit Time Point: Visit Time Point

SCREEN ID: AE-01

Site Number: Site Number
Site Name: Site Name
Site Type: Site Type

Study Drug Administration - for Study Specific Drug Name

AEVNT - Adverse Event
AEVNT - Adverse Event Name
AEVNT - Adverse Event Description
AEVNT - Adverse Event Severity
AEVNT - Adverse Event Onset Date
AEVNT - Adverse Event Onset Time
AEVNT - Adverse Event End Date
AEVNT - Adverse Event End Time
AEVNT - Adverse Event Outcome
AEVNT - Adverse Event Resolution
AEVNT - Adverse Event Action Taken
AEVNT - Adverse Event Action Taken Date
AEVNT - Adverse Event Action Taken Time
AEVNT - Adverse Event Action Taken Location
AEVNT - Adverse Event Action Taken Time Point

UNIT

LOC

EX - EXPOSURE

Study: Study
Site: Site
Subject: Subject
Visit Number: Visit Number
Visit Time Point: Visit Time Point

SCREEN ID: EX-01

Site Number: Site Number
Site Name: Site Name
Site Type: Site Type

Study Drug Administration - for Study Specific Drug Name

EXCAT - Treatment Type
EXCAT - Treatment Name
EXDOPRE - What was the prescribed dose level?
EXDOPRU - Prescribed dose level Units
EXDOPR - What is the treatment label identifier?
EXDOPR - Dose
EXDOPR - Units
EXDOPR - Frequency
EXDOPR - Frequency
EXDOPR - What was the anatomical location of the administration?
EXDOPR - Start Date
EXDOPR - Start Time

UNIT

LOC

ADVERSE EVENTS

Study: Study
Site: Site
Subject: Subject
Visit Number: Visit Number
Visit Time Point: Visit Time Point

SCREEN ID: AE-01

Site Number: Site Number
Site Name: Site Name
Site Type: Site Type

Study Drug Administration - for Study Specific Drug Name

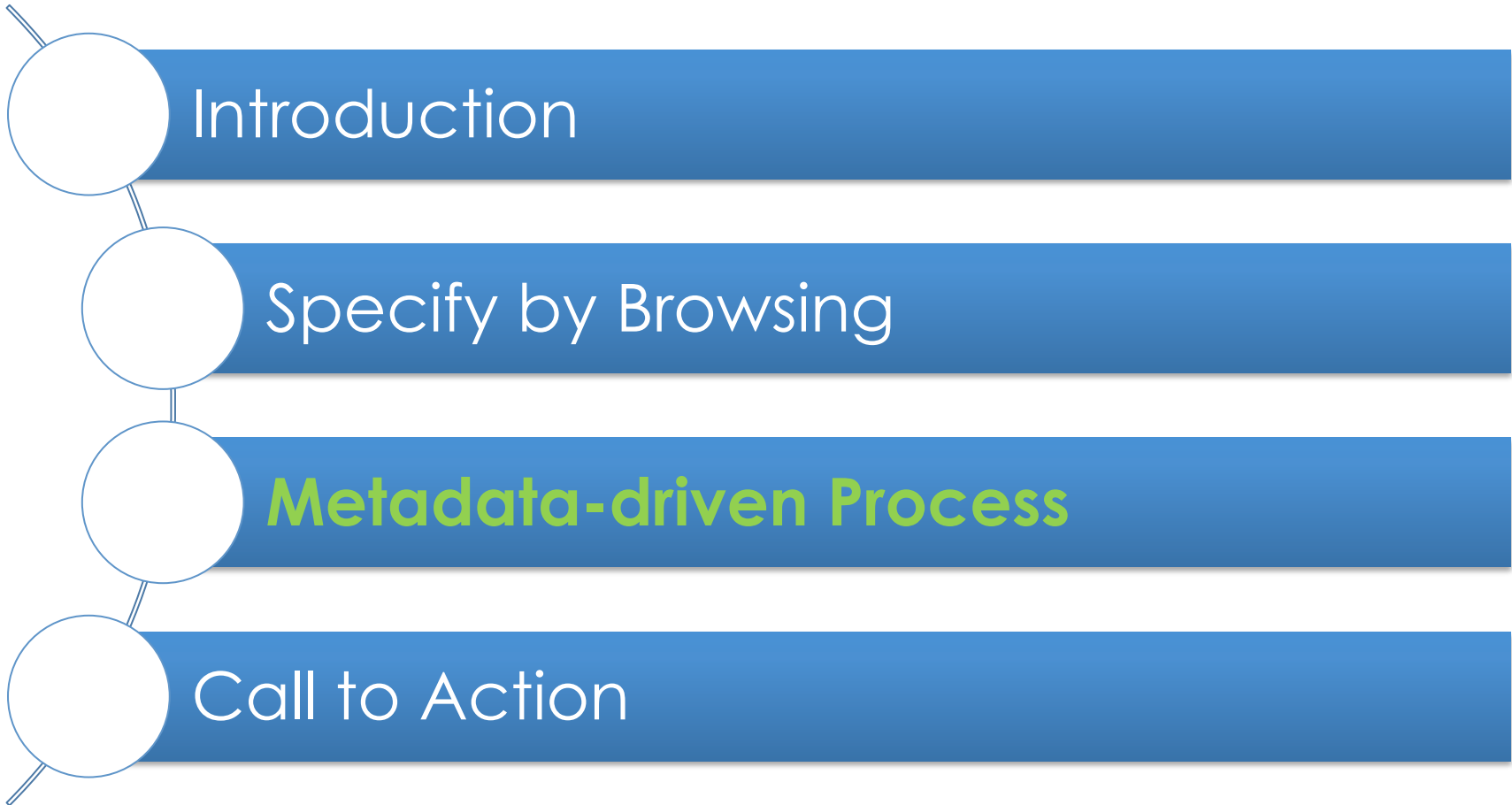
AEVNT - Adverse Event
AEVNT - Adverse Event Name
AEVNT - Adverse Event Description
AEVNT - Adverse Event Severity
AEVNT - Adverse Event Onset Date
AEVNT - Adverse Event Onset Time
AEVNT - Adverse Event End Date
AEVNT - Adverse Event End Time
AEVNT - Adverse Event Outcome
AEVNT - Adverse Event Resolution
AEVNT - Adverse Event Action Taken
AEVNT - Adverse Event Action Taken Date
AEVNT - Adverse Event Action Taken Time
AEVNT - Adverse Event Action Taken Location
AEVNT - Adverse Event Action Taken Time Point

UNIT

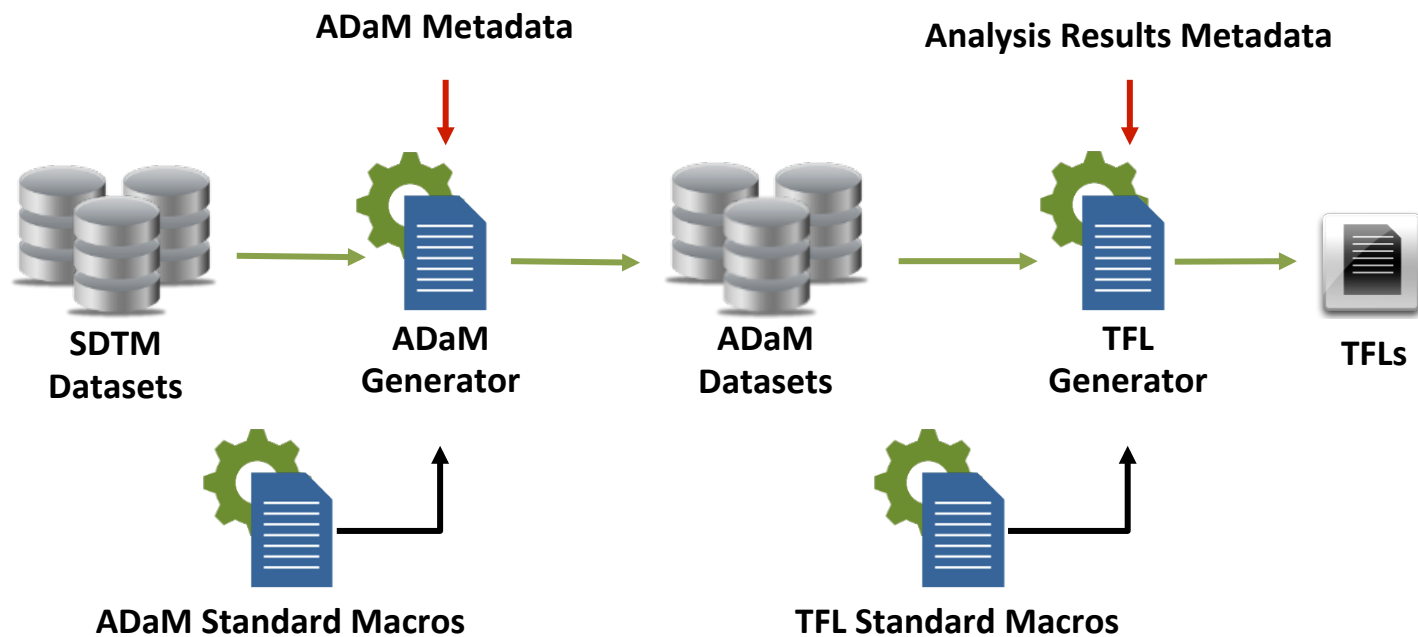
LOC



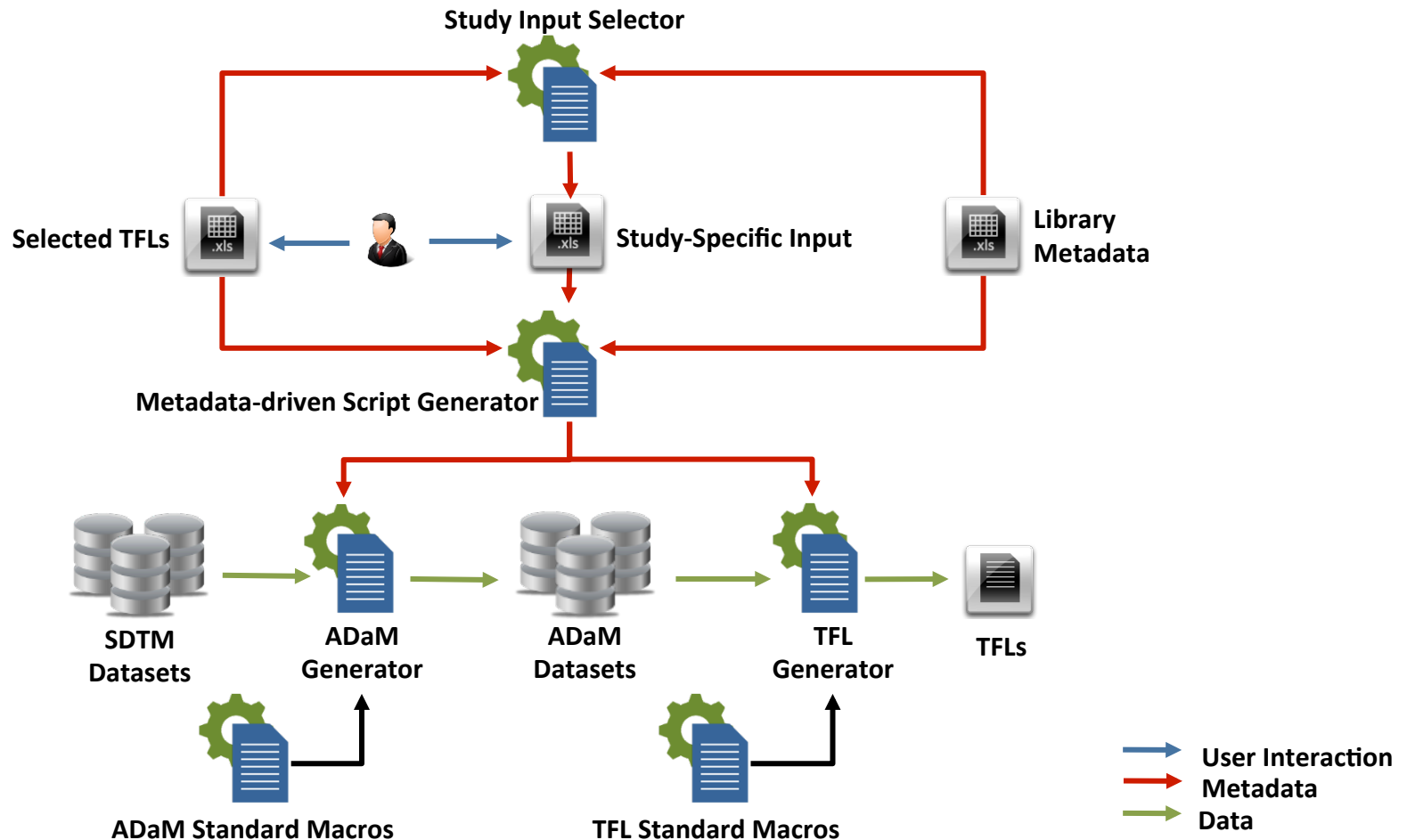
Agenda



Specification, Execution



Metadata-driven Process



What is a Concept Map

- **Concept maps = diagram which include “bubbles” representing concepts/ideas/things and labeled arrows that represent the relationships between the concepts/ideas/things.**
- **Advantage = easier to draw and more accessible than more formal modeling diagrams (e.g. UML diagrams)**

Concept Map Legend

Assessor



The person or organization that reports an observation.

Product



Anything made. Includes drugs and devices.

Specimen



A sample taken from a Subject or existing Specimen for analysis.

Healthcare Encounter



Administration to or visit with A healthcare facility or healthcare provider.

Observation



A test, examination, or other activity that gathers Information about a subject.

Substance Administration



An activity that administers A product to a subject

Specimen Collection



An activity that takes a Sample for later analysis

Initiative Procedure



An invasive treatment or Diagnostic procedure.

Observation Result



A finding obtained by an observation.

Other Activity



An activity not otherwise classified.

Composite Activity



An activity with multiple classifications. Often has component sub-activities.

Time Point



A defined point in time.

Terminology



Verbatim terms or vocabulary from a codelist or dictionary.

Variable



The name and/or label of an attribute when represented as a column in normalized dataset

CDISC Domain



A Specification for creating normalized datasets compliant with CDISC standards.

Study Context



Identifiers and relative timing used to describe a concept as it relates to the study.

Statistical Concept



Type of statistical analysis required for an endpoint

Computational Algorithm



Algorithm used to calculate some analysis variable or parameter

SAS Script



SAS script that implements a standard, re-usable, computational algorithm

TFL Definition



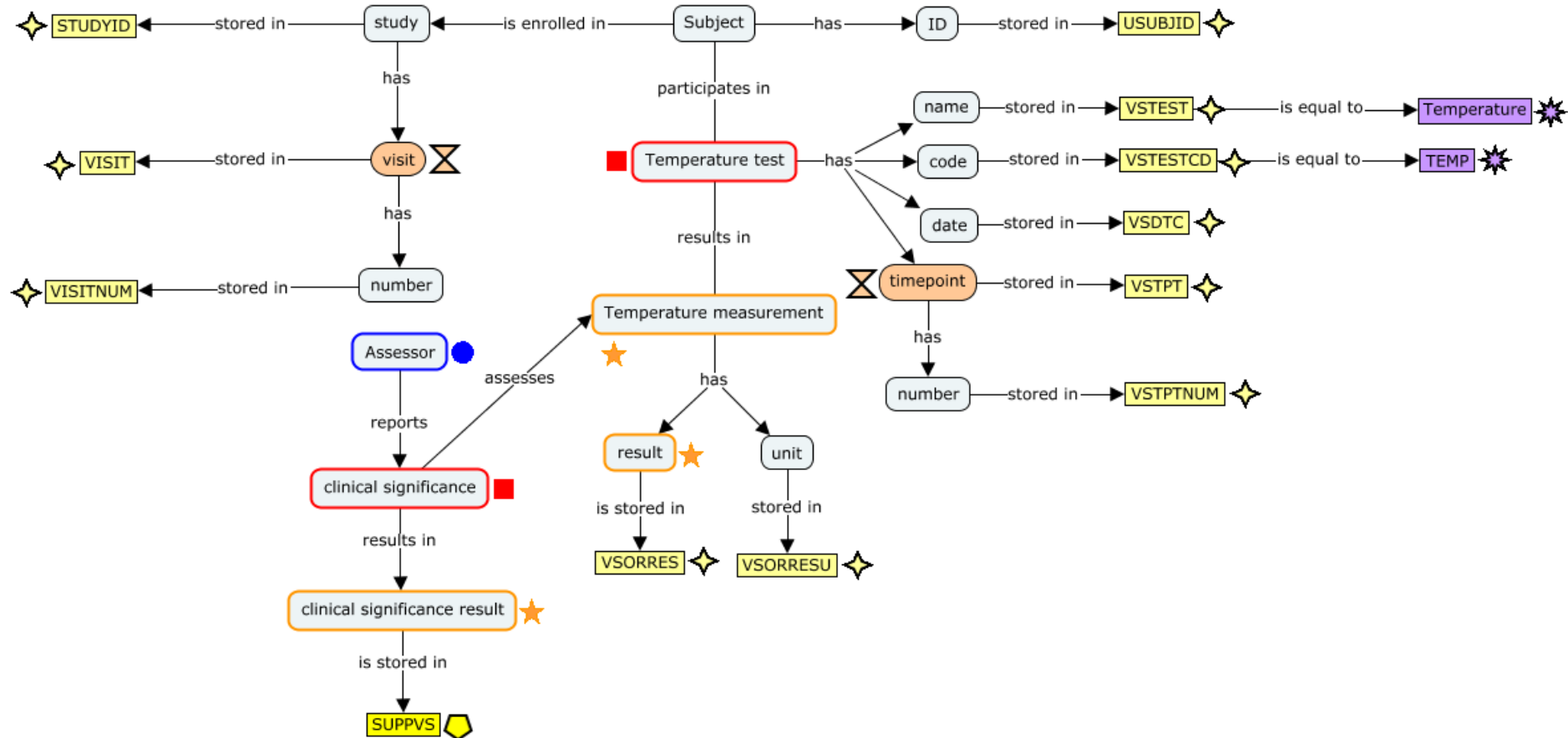
Type of TFL used to represent some data or analysis results

Document

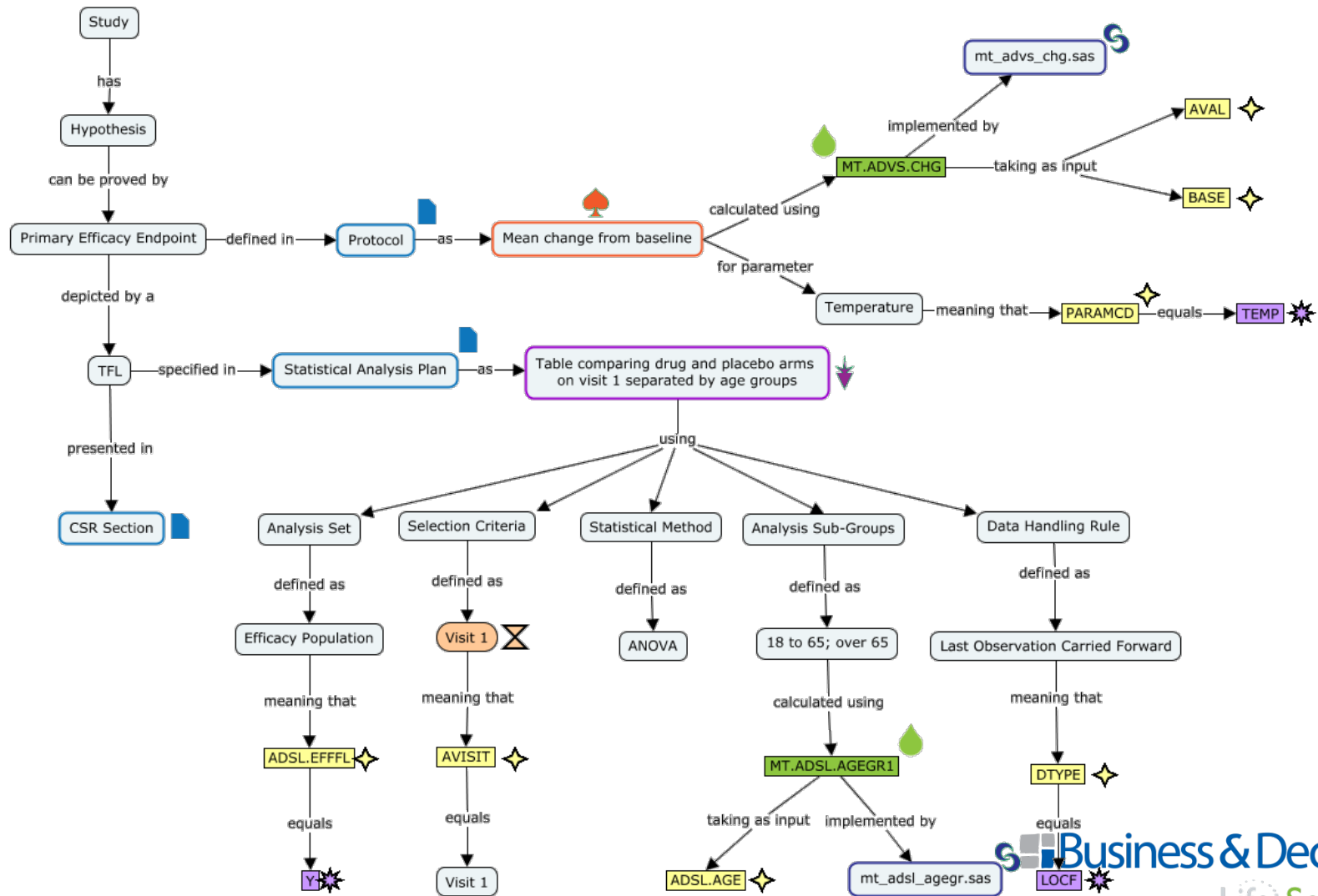


Document produced within the Clinical Trial

Tabulation concept map



Analysis Concept Map

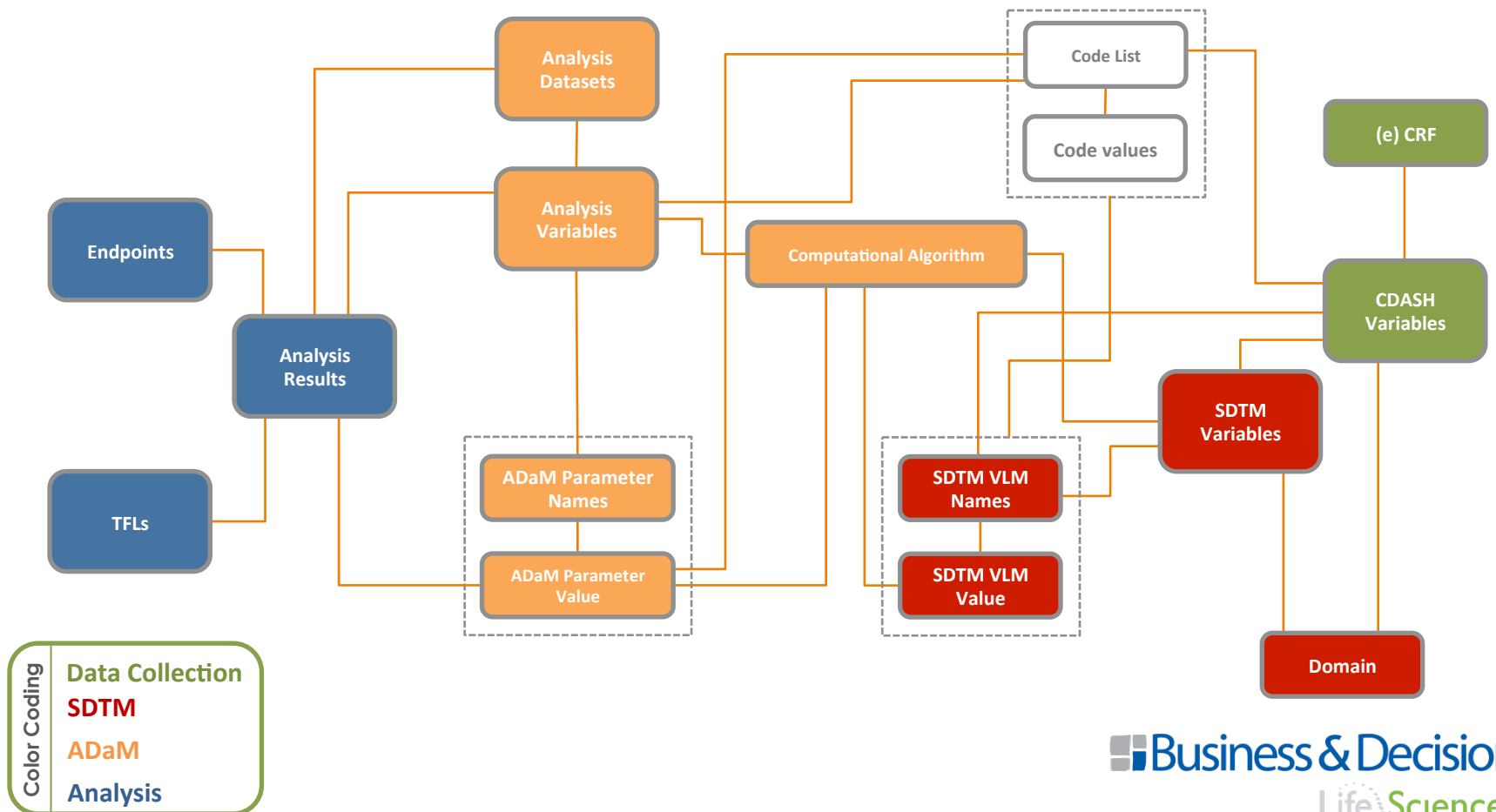


[illegible]

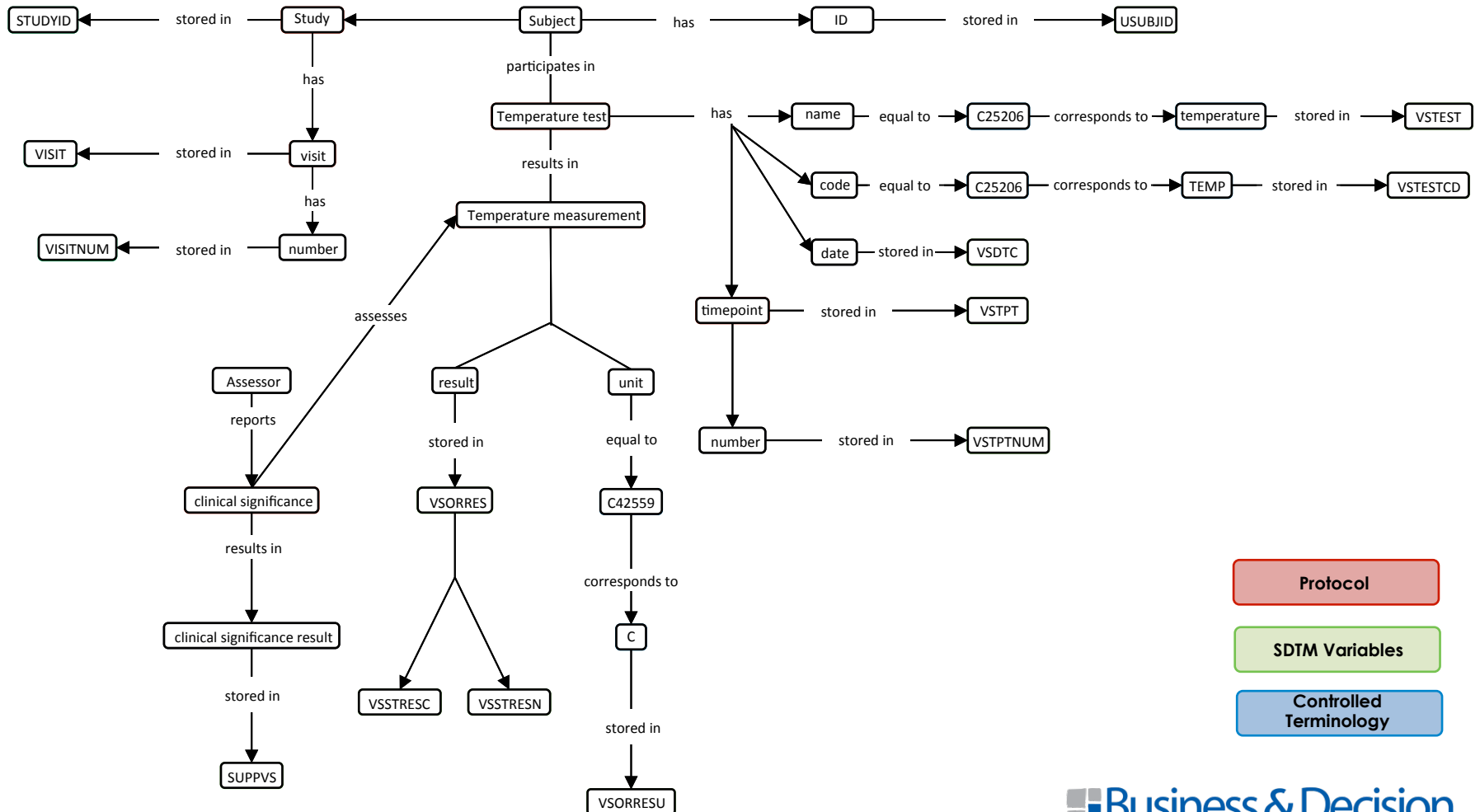
 **The Tabulation and Analysis**
Concept Map will link perfectly

Simplified view

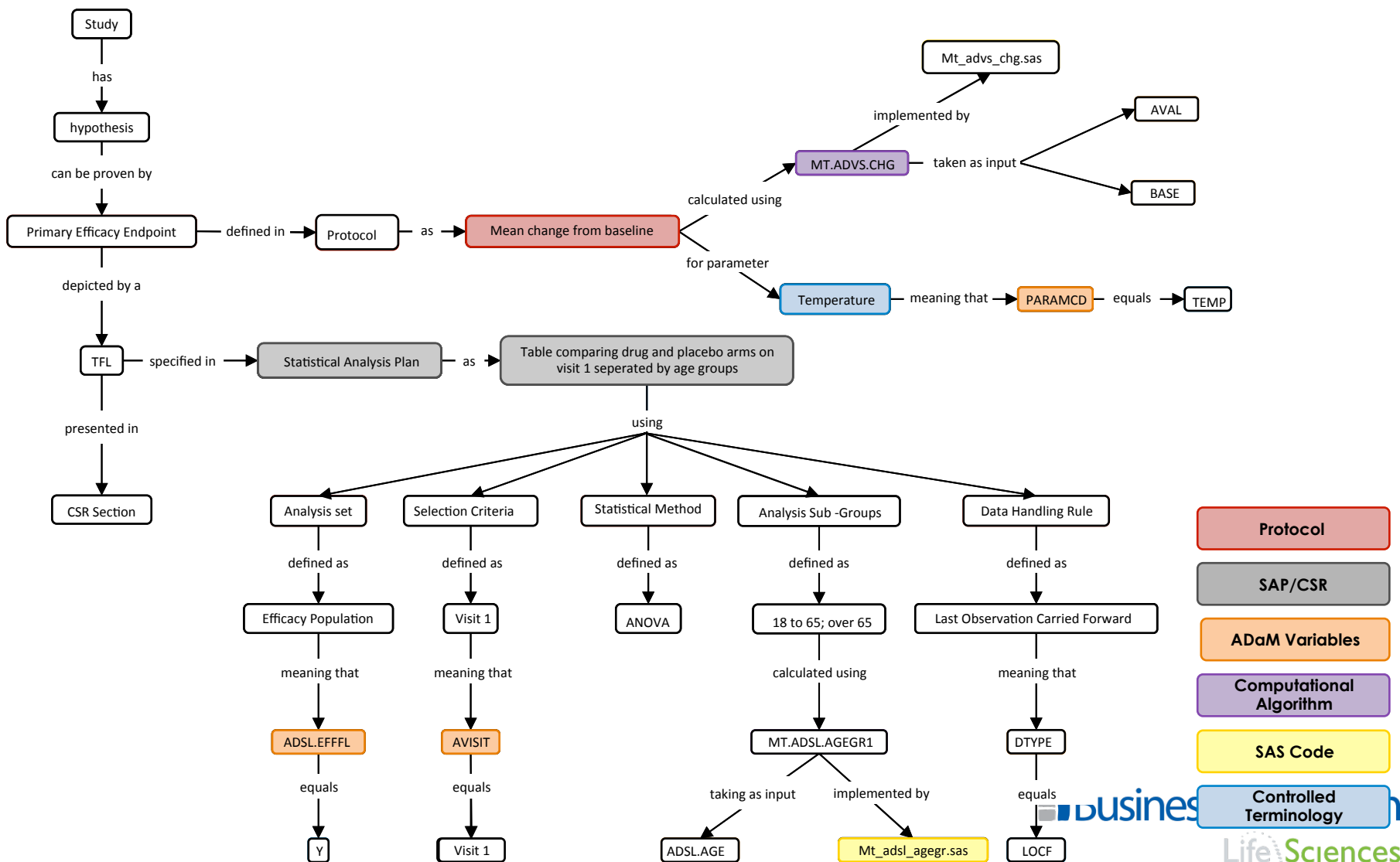
- Only Semantic Interoperability can achieve real benefits from clinical data standards.



Tabulation Implementation Layer



Analysis Implementation Layer



Implementation example: Analysis Results Metadata

Table comparing drug and placebo arms on visit 1 separated by age groups		Table 10-1.01 Primary Endpoint Analysis: ADVS-Temperature - Summary at Visit 1 - LOCF (Efficacy Population)
Temperature	Mean change from baseline	Dose Response Analysis for ADVS.TEMP changes from baseline
Analysis Parameter	PARAMCD	PARAMCD = "TEMP"
Analysis Variable	MT.ADVS.CHG	CHG (Change from Baseline)
Analysis Reason		SPECIFIED IN SAP
Analysis Purpose		PRIMARY OUTCOME MEASURE
Dataset Selection Criteria	ADSL.EFFFL AVISIT	ADVS [PARAMCD = "TEMP" and AVISIT = "Visit 1" and EFFFL = "Y"]
Statistical Analysis Plan		Linear model analysis of CHG for dose response using randomized dose (0mg for placebo; 10mg for low dose; 50mg for high dose) and site group in model. Used PROC GLM in SAS to produce p-value (from Type III SS for treatment dose). SAP Section 10.1.2
Programming Statements		[SAS version 9.2] proc glm data = ADVS; where EFFFL='Y' and AVISIT='Visit 1' and PARAMCD="TEMP"; class AGEGR1; model CHG = TRTPN AGEGR1; run;
	Mt_adsl_agegr.sas	

Agenda



Gap Analysis 1



Protocol
& SAP

Statistical Method
Clinical Study Protocol
Statistical Analysis Plan
Statistical Requirements



SDTM

Version
SDTM Domain
SDTM Variable
Code List
Value Level Metadata
Computational Algorithm
Data Handling Rules



Analysis
Results

Display
Display Layout
Footnote
Titles
Analysis Rule
Output Specification Rule
SAS Code



CDASH
Standard
CRF

Version
CDASH Dataset
CDASH Variable
Completion Guidelines
Implementation Guidelines
Data Validation Rule
Data Collection Module
CRF Template



ADaM

Version
ADaM Domain
ADaM Variable
Code List
Computational Algorithm
Analysis Sub Groups
SAS Code



Clinical Study
Report

Clinical Study Report
CSR Section

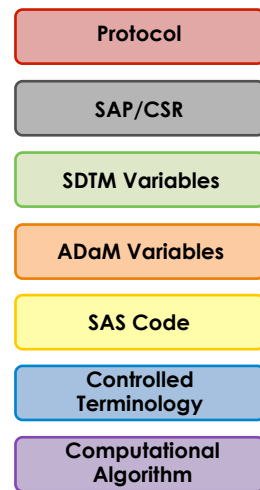
Color Coding

Industry Standard
No industry Standard



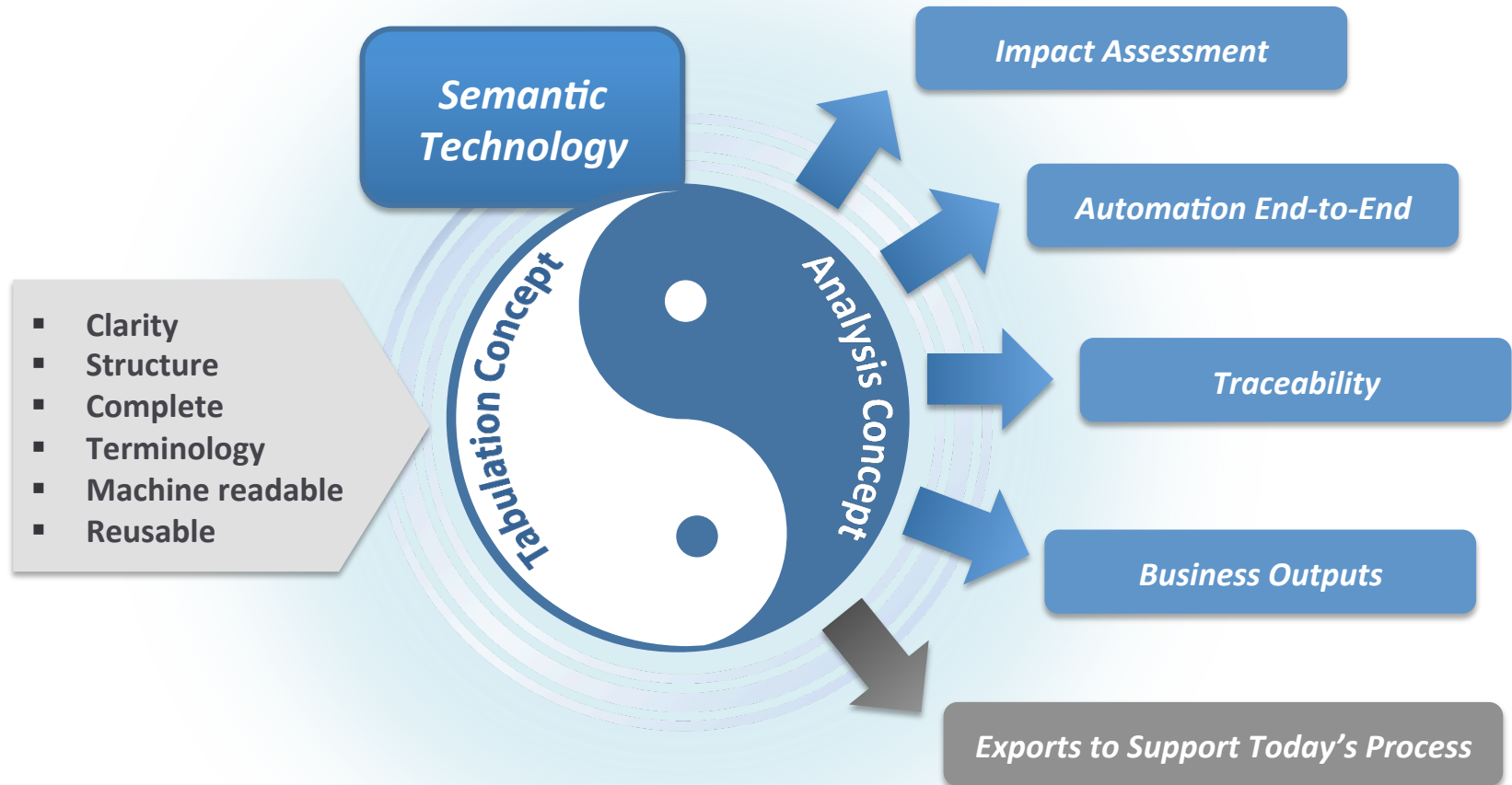
Not everything is standardized (yet)

 **We need concept metadata**



Gap Analysis 3

Conclusion



■ Is this something the industry **wants**?

■ **Effort** is needed on an industry scale



Thank you



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