



Easing Your Pain with Biomedical Concepts

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Outline

Biomedical Concepts

- Challenges in study setup
- Biomedical Concepts: What – is it?
- Why – bother about it?
- How – can it help?

Study Setup

Translating study specifications in the protocol to actual implementations of data collection and reporting

Which units to use – do we allow for multiple units or just one? Which ones are applicable for the test?

Which SDTM domains are needed for this study – do we need a new or where does this information belong in SDTM domains? Do we need a new annotation?

Is the blood pressure to be measured STANDING, SITTING or SUPINE – what should be on the CRF? Do we need a new CRF?

Which tests are being measured in BLOOD, SERUM, or PLASMA

Protocol				
Measurements	V1	V2	V3	V4
Demographics	x			
Vital signs	x			x
CT Scan		x		
Dosing		x	x	x
EQ-5D	x			x
Lipids	x			x
Haemoglobin	x			x
Adverse Events	x	x	x	x

VS=Vital Signs

CDISC
Study: CDISC01

Assessment Date:
VSDTC

VITAL SIGNS

VSTEST

VSPOS

Height

Sitting Blood Pressure

Weight

Radial Pulse Rate

Body Frame Size

cm

in

kgs

lbs

Small

Medium

Large

mmHg

bpm

VSORRES / VSORRESU when VSTESTCD = HEIGHT

VSORRES / VSORRESU when VSTESTCD = WEIGHT

VSORRES / VSORRESU when VSTESTCD = PULSE

VSORRES when VSTESTCD = FRMSIZE



Annotations	Case Report Form
Reviewers	Guides
Value Level	Metadata
Computational	Algorithms
Controlled	Terms

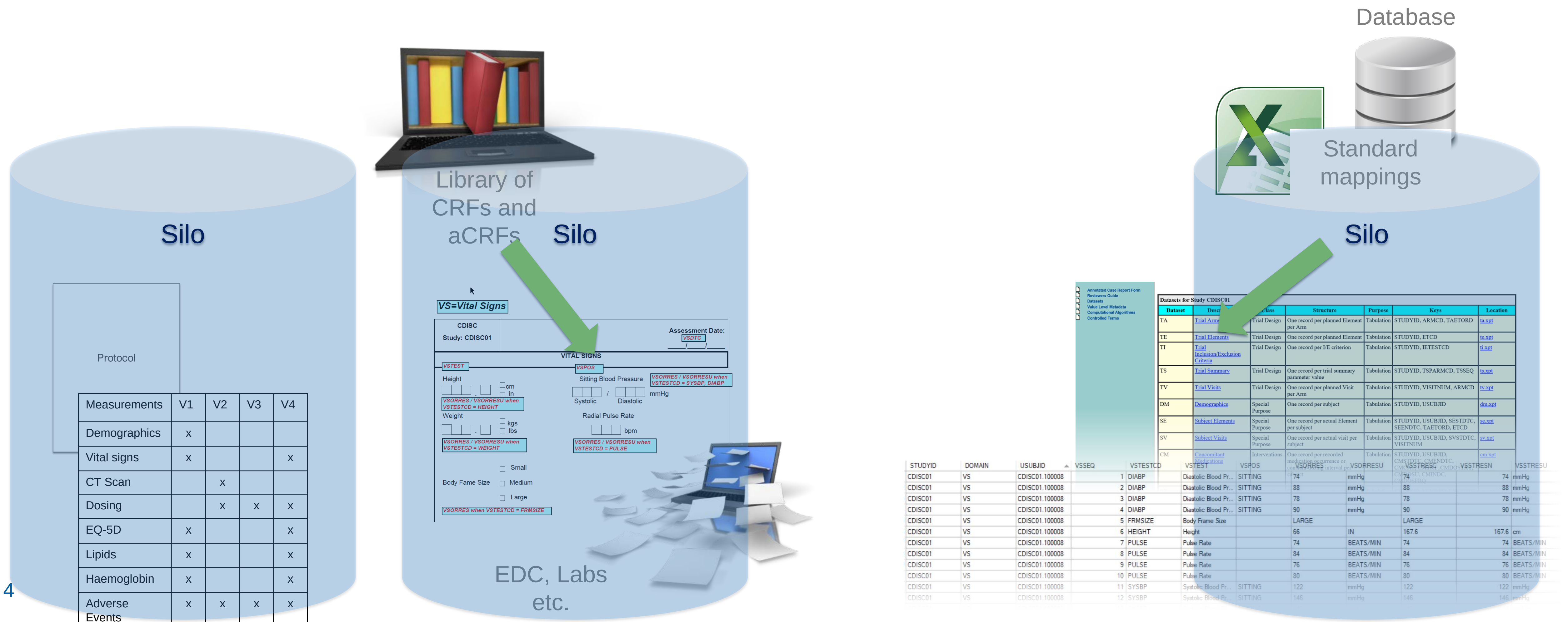
Datasets for Study CDISC01					
Dataset	Description	Class	Structure	Purpose	Keys
TA	Trial Arms	Trial Design	One record per planned Element per Arm	Tabulation	STUDYID, ARMCD, TAETORD
TE	Trial Elements	Trial Design	One record per planned Element	Tabulation	STUDYID, ETCD
TI	Trial Inclusion/Exclusion Criteria	Trial Design	One record per I/E criterion	Tabulation	STUDYID, IETESTCD
TS	Trial Summary	Trial Design	One record per trial summary parameter value	Tabulation	STUDYID, TSPARMCD, TSSEQ
TV	Trial Visits	Trial Design	One record per planned Visit per Arm	Tabulation	STUDYID, VISITNUM, ARMCD
DM	Demographics	Special Purpose	One record per subject	Tabulation	STUDYID, USUBJID
SE	Subject Elements	Special Purpose	One record per actual Element per subject	Tabulation	STUDYID, USUBJID, SESTDTC, SEENDTC, TAETORD, ETCD
SV	Subject Visits	Special Purpose	One record per actual visit per subject	Tabulation	STUDYID, USUBJID, SVSTDTC, VISITNUM
CM	Concomitant Medications	Interventions	One record per recorded medication occurrence or interval per subject	Tabulation	STUDYID, USUBJID, CMSTDTC, CMENDTC, CMDOSE, CMDOSEUNIT, CMFREQ

STUDYID	DOMAIN	USUBJID	VSSEQ	VSTESTCD	VSTEST	VSPOS	VSORRES	VSORRESU	VSTRESC	VSTRESN	VSTRESU
CDISC01	VS	CDISC01.100008	1	DIABP	Diastolic Blood Pr...	SITTING	74	mmHg	74		74 mmHg
CDISC01	VS	CDISC01.100008	2	DIABP	Diastolic Blood Pr...	SITTING	88	mmHg	88		88 mmHg
CDISC01	VS	CDISC01.100008	3	DIABP	Diastolic Blood Pr...	SITTING	78	mmHg	78		78 mmHg
CDISC01	VS	CDISC01.100008	4	DIABP	Diastolic Blood Pr...	SITTING	90	mmHg	90		90 mmHg
CDISC01	VS	CDISC01.100008	5	FRMSIZE	Body Frame Size		LARGE		LARGE		
CDISC01	VS	CDISC01.100008	6	HEIGHT	Height		66	IN	167.6		167.6 cm
CDISC01	VS	CDISC01.100008	7	PULSE	Pulse Rate		74	BEATS/MIN	74		74 BEATS/MIN
CDISC01	VS	CDISC01.100008	8	PULSE	Pulse Rate		84	BEATS/MIN	84		84 BEATS/MIN
CDISC01	VS	CDISC01.100008	9	PULSE	Pulse Rate		76	BEATS/MIN	76		76 BEATS/MIN
CDISC01	VS	CDISC01.100008	10	PULSE	Pulse Rate		80	BEATS/MIN	80		80 BEATS/MIN
CDISC01	VS	CDISC01.100008	11	SYSBP	Systolic Blood Pr...	SITTING	122	mmHg	122		122 mmHg
CDISC01	VS	CDISC01.100008	12	SYSBP	Systolic Blood Pr...	SITTING	146	mmHg	146		146 mmHg

EDC, Labs
etc.

Study Setup

Standards in place – but not connected



Study Setup

Standards in place – but not connected

No link to terminology



Library of CRFs and aCRFs

Code	Codelist Code	Codelist Extensible (Yes/No)	Codelist Name	CDISC Submission Value
C66770		Yes	Units for Vital Signs Results	VSRESU
C25613	C66770		Units for Vital Signs Results	%
C49673	C66770		Units for Vital Signs Results	beats/min
C49674	C66770		Units for Vital Signs Results	breaths/min
C42559	C66770		Units for Vital Signs Results	C
C49668	C66770		Units for Vital Signs Results	cm
C44277	C66770		Units for Vital Signs Results	F

No link to terminology



Database



Standard mappings

No link to annotation

Measurements	V1	V2	V3	V4
Demographics	x			
Vital signs	x			x
CT Scan		x		
Dosing		x	x	x
EQ-5D	x			x
Lipids	x			x
Haemoglobin	x			x
Adverse Events	x	x	x	x

VS=Vital Signs

CDISC Study: CDISC01

Assessment Date:

VITAL SIGNS

VSTEST

Height ☐ cm ☐ in

VSORRES / VSORRESU when VSTESTCD = HEIGHT

Weight ☐ kgs ☐ lbs

VSORRES / VSORRESU when VSTESTCD = WEIGHT

☐ Small ☐ Medium ☐ Large

VSORRES when VSTESTCD = FRMSIZE

VSPOS

Sitting Blood Pressure / mmHg

Systolic Diastolic

Radial Pulse Rate bpm

VSORRES / VSORRESU when VSTESTCD = PULSE

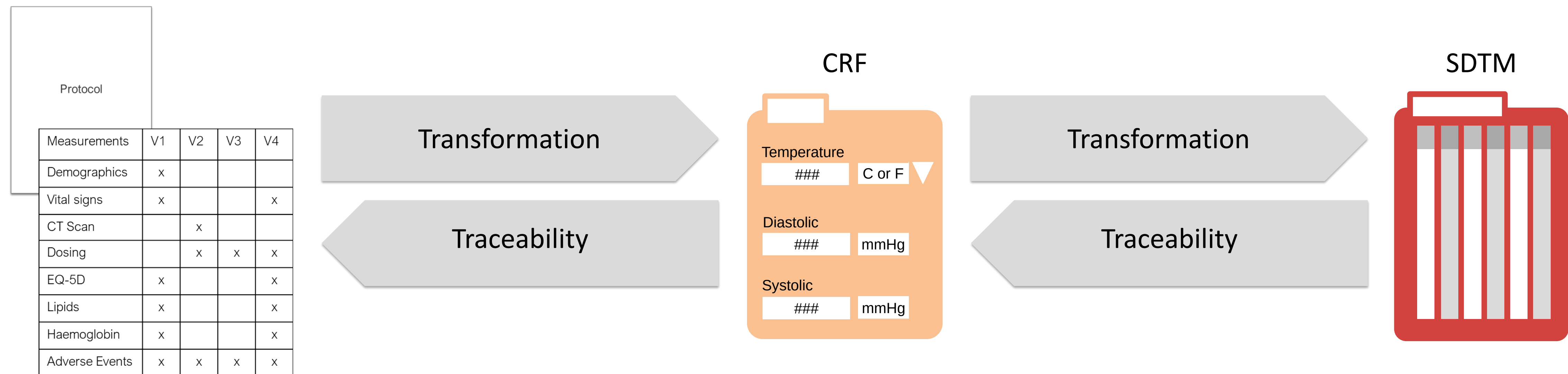
VSORRES / VSORRESU when VSTESTCD = SYSBP, DIABP

EDC, Labs etc.

STUDYID	DOMAIN	USUBJID	VSSEQ	VSTESTCD	VSTEST	VSPOS	VSORRES	VSORRESU	VSSTRES	VSSTRESU
CDISC01	VS	CDISC01.100008	1	DIABP	Diastolic Blood Pr...	SITTING	74	mmHg	74	mmHg
CDISC01	VS	CDISC01.100008	2	DIABP	Diastolic Blood Pr...	SITTING	88	mmHg	88	mmHg
CDISC01	VS	CDISC01.100008	3	DIABP	Diastolic Blood Pr...	SITTING	78	mmHg	78	mmHg
CDISC01	VS	CDISC01.100008	4	DIABP	Diastolic Blood Pr...	SITTING	90	mmHg	90	mmHg
CDISC01	VS	CDISC01.100008	5	FRMSIZE	Body Frame Size		LARGE		LARGE	
CDISC01	VS	CDISC01.100008	6	HEIGHT	Height		66	IN	167.6	cm
CDISC01	VS	CDISC01.100008	7	PULSE	Pulse Rate		74	BEATS/MIN	74	BEATS/MIN
CDISC01	VS	CDISC01.100008	8	PULSE	Pulse Rate		84	BEATS/MIN	84	BEATS/MIN
CDISC01	VS	CDISC01.100008	9	PULSE	Pulse Rate		76	BEATS/MIN	76	BEATS/MIN
CDISC01	VS	CDISC01.100008	10	PULSE	Pulse Rate		80	BEATS/MIN	80	BEATS/MIN
CDISC01	VS	CDISC01.100008	11	SYSBP	Systolic Blood Pr...	SITTING	122	mmHg	122	mmHg
CDISC01	VS	CDISC01.100008	12	SYSBP	Systolic Blood Pr...	SITTING	146	mmHg	146	mmHg

Study Setup

Challenge – maintaining transformations and traceability effectively

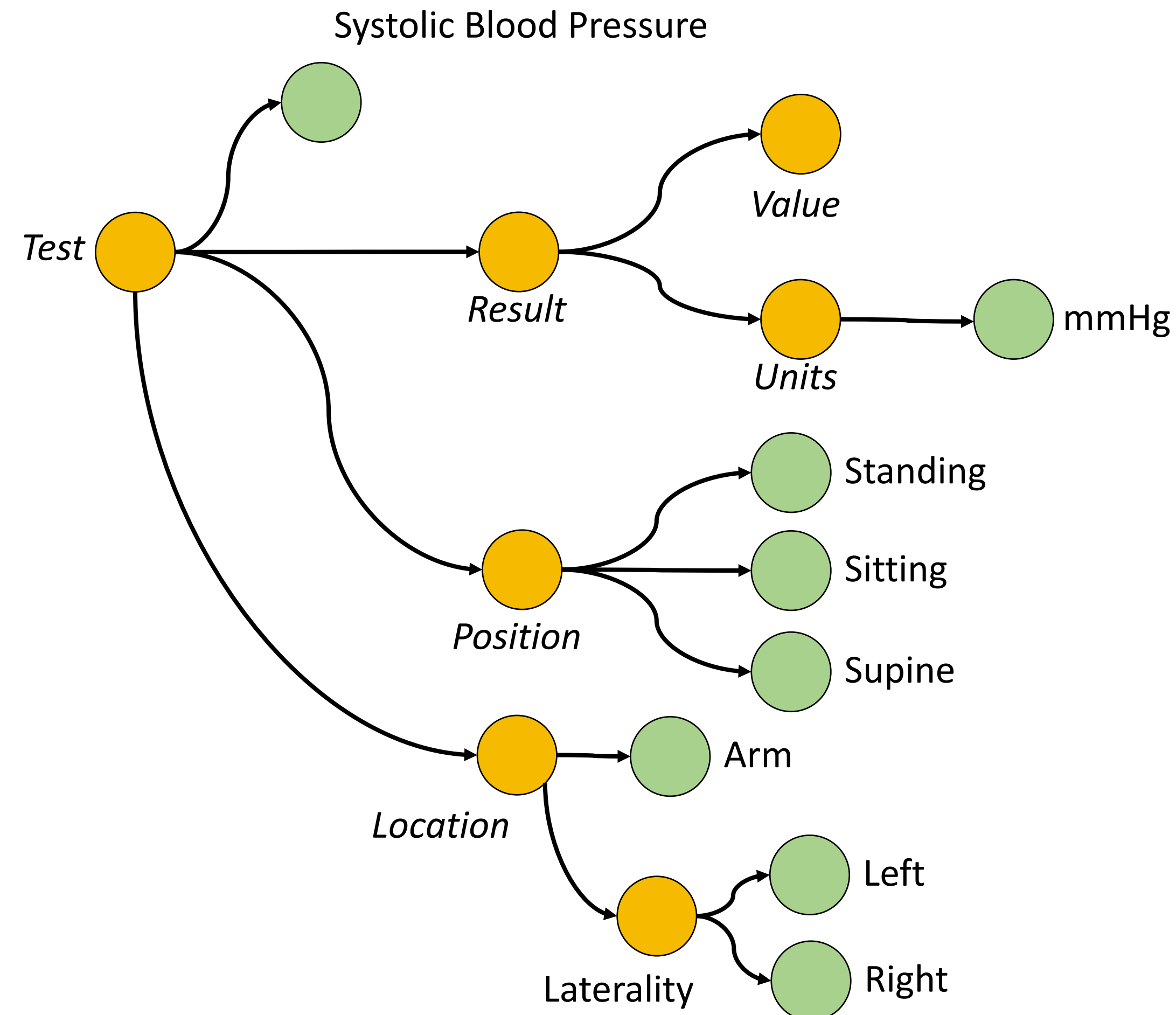


Biomedical Concept (BC) ties the standard 'silos' together and facilitates a consistent way of collecting the data across studies



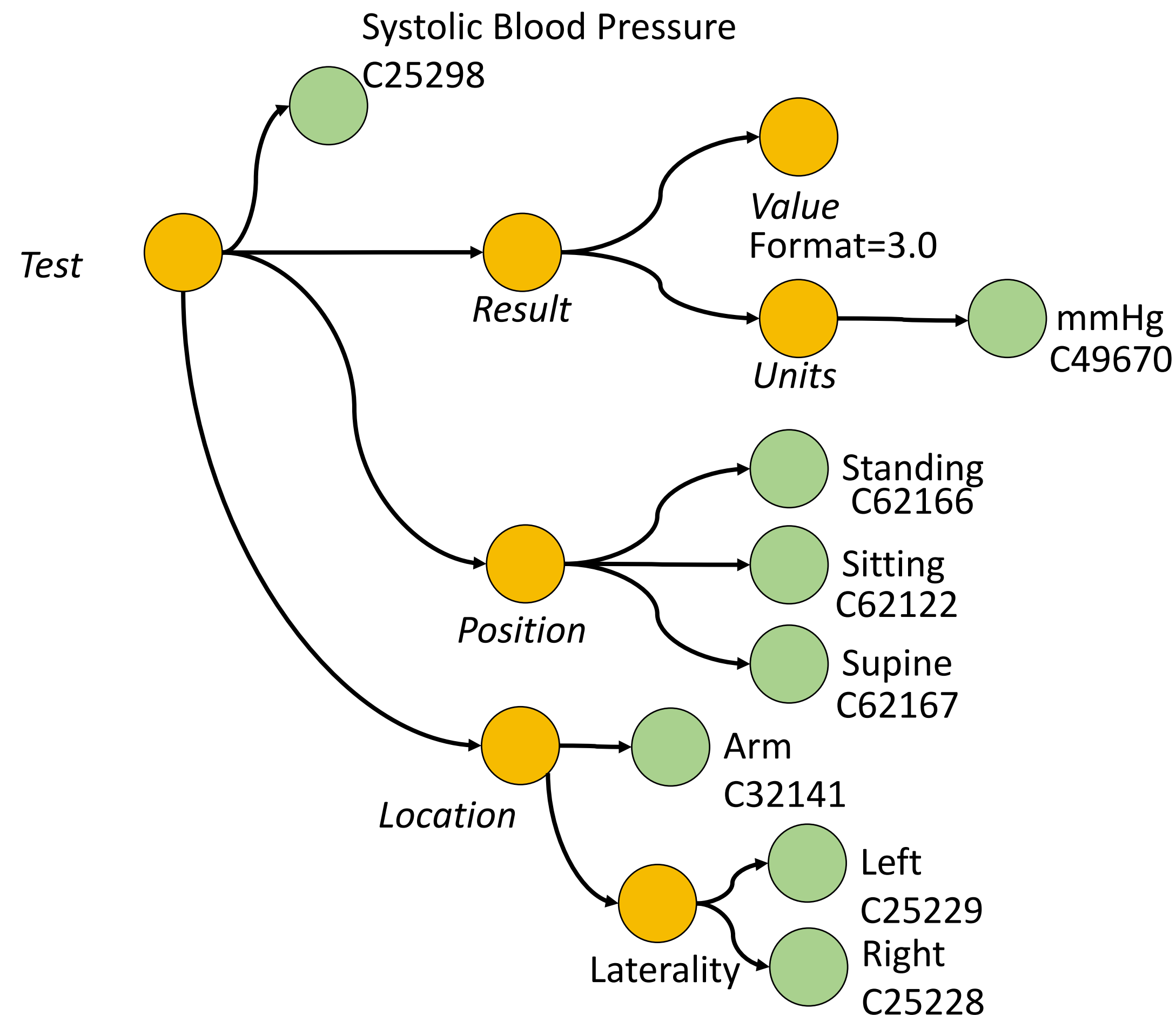
What is a Biomedical Concept?

Clinical view – systolic blood pressure



What is a Biomedical Concept?

Data Manager/Programmer view – systolic blood pressure



SDTM view - BC is a topic that would generate a record in SDTM

Biomedical Concepts

An example of an implementation

Show: Systolic Blood Pressure (BC C25298) BC C25298 (V3.1.0, 4, Incomplete)

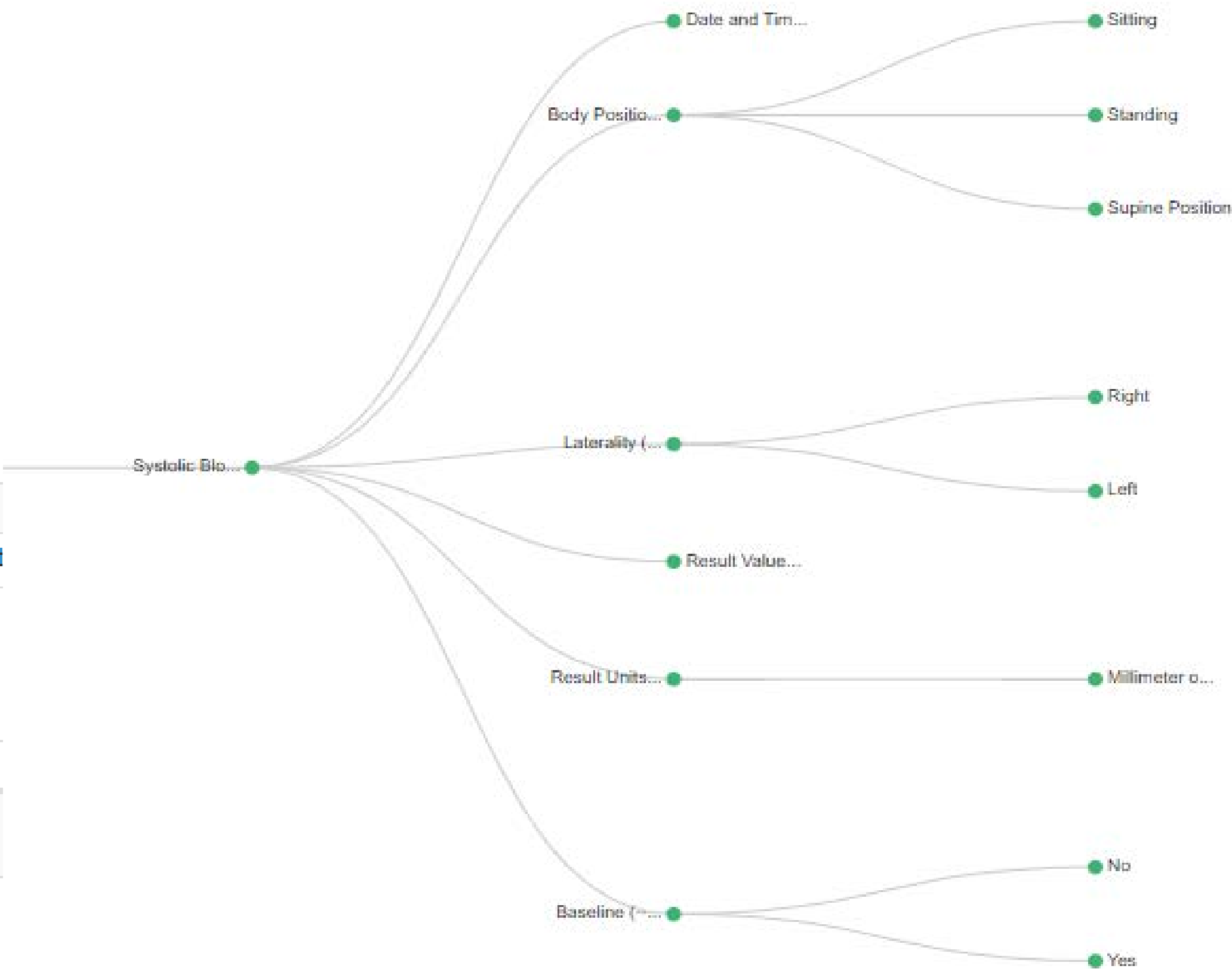
Details

Identifier	Label	Owner	Status
BC C25298	Systolic Blood Pressure (BC C25298)	ACME	Incomplete

Items

Show 10 entries

Alias	Question Text	Prompt Text	Enabled				
Baseline (--BLFL)	Is this a baseline value?	Baseline	✓				
Body Position (--POS)	In what position was the subject during the measurement?	Position	✓				
Date and Time (--DTC)	On what date were the measurement performed?	Date	✓				
Laterality (--LAT)	Which arm?	Arm	✓	✓	string		RIGHT (C25228) LEFT (C25229)
Location (--LOC)	The location of the measurement	Location	✓	✗	string		ARM (C32141)
Method Code (--METHOD)			✗	✗	string		
Result Units (--ORRESU)	The unit of the measurement	Units	✓	✓	string		mmHg (C49670)
Result Value (--ORRES)	What was the result of the measurement?	Result	✓	✓	float	3	
Test Code (--TESTCD)			✓	✗	string		SYSBP (C25298)
Test Name (--TEST)			✓	✗	string		Systolic Blood Pressure (C25298)



Refer domains to Biomedical Concepts

Where does the collected information belong?

Show: Vital Signs VS Domain (V1.0.0, 2, Standard)

Details

Identifier	Label	Owner	Internal Version	Version
VS Domain	Vital Signs	ACME	1.0.0	

Notes

Used Variables

Show 10 entries

Search:

Ordinal	Name	Label	Datatype	CT	Format	Role	Sub Role	IG Notes	Notes	Core
1	STUDYID	Study Identifier	Char			Identifier		Unique identifier for a study.		Required
2	DOMAIN	Domain Abbreviation	Char	DOMAIN		Identifier		Two-character abbreviation for the domain.		Required
3	USUBJID	Unique Subject Identifier	Char			Identifier		Identifier used to uniquely identify a subject across all studies for all applications or submissions involving the product.		Required
4	VSSEQ	Sequence Number	Num			Identifier		Sequence Number given to ensure uniqueness of subject records within a domain. May be any valid number.		Required
5	VSGRPID	Group ID	Char			Identifier		Used to tie together a block of related records in a single domain for a subject.		Permissible
6	VSSPID	Sponsor-Defined Identifier	Char			Identifier		Sponsor-defined reference number. Perhaps pre-printed on the CRF as an explicit line identifier or defined in the sponsor's operational database.		Permissible
7	VSTESTCD	Vital Signs Test Short Name	Char	VSTESTCD		Topic		Short name of the measurement, test, or examination described in VSTEST. It can be used as a column name when converting a dataset from a vertical to a horizontal format. The value in VSTESTCD cannot be longer than 8 characters, nor can it start with a number (e.g. "1TEST"). VSTESTCD cannot contain characters other than letters, numbers, or underscores. Examples: SYSBP, DIABP, BMI.		Required
8	VSTEST	Vital Signs Test Name	Char	VSTEST		Qualifier	Synonym Qualifier	Verbatim name of the test or examination used to obtain the measurement or finding. The value in VSTEST cannot be longer than 40 characters. Examples: Systolic Blood Pressure, Diastolic Blood Pressure, Body Mass Index.		Required
9	VSCAT	Category for Vital Signs	Char			Qualifier	Grouping Qualifier	Used to define a category of related records.		Permissible
10	VSSCAT	Subcategory for Vital Signs	Char			Qualifier	Grouping Qualifier	A further categorization of a measurement or examination.		Permissible

Showing 1 to 10 of 32 entries

Previous 1 2 3 4 Next

Unused Variables

Show 10 entries

Search:

Ordinal	Name	Label	Datatype	CT	Format	Role	Sub Role	IG Notes	Notes	Core
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No data available in table

Showing 0 to 0 of 0 entries

Previous Next

Biomedical Concepts

Show 10 entries

Search: pressure

Identifier	Label	Owner	Version	Version Label
BC C25298	Systolic Blood Pressure (BC C25298)	ACME	2.0.0	0.2
BC C25298	Systolic Blood Pressure (BC C25298)	ACME	3.0.0	0.3
BC C25299	Diastolic Blood Pressure (BC C25299)	ACME	2.0.0	0.2

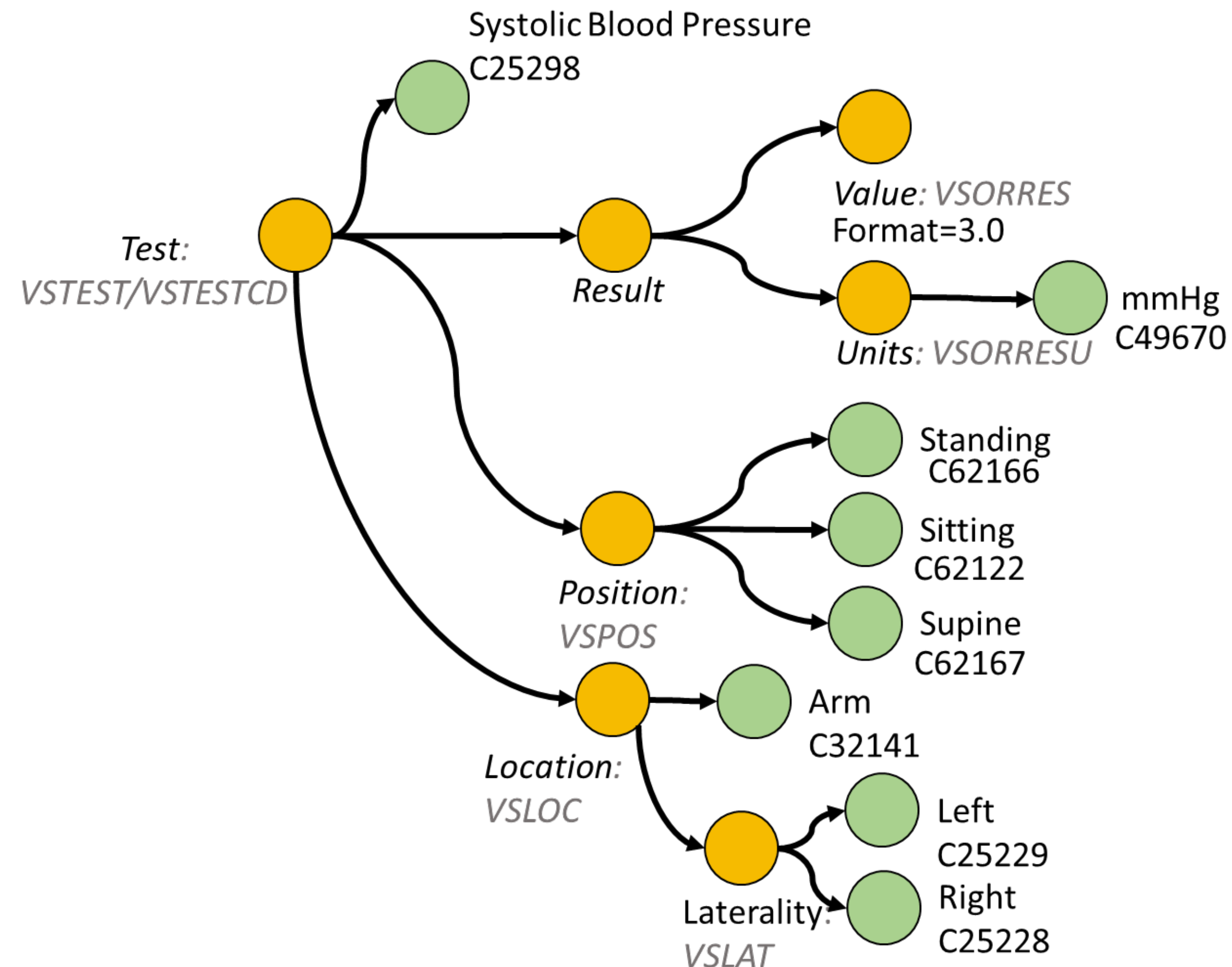
Multiple domains can refer to the same BC.

The context of the study will then determine which domain is used



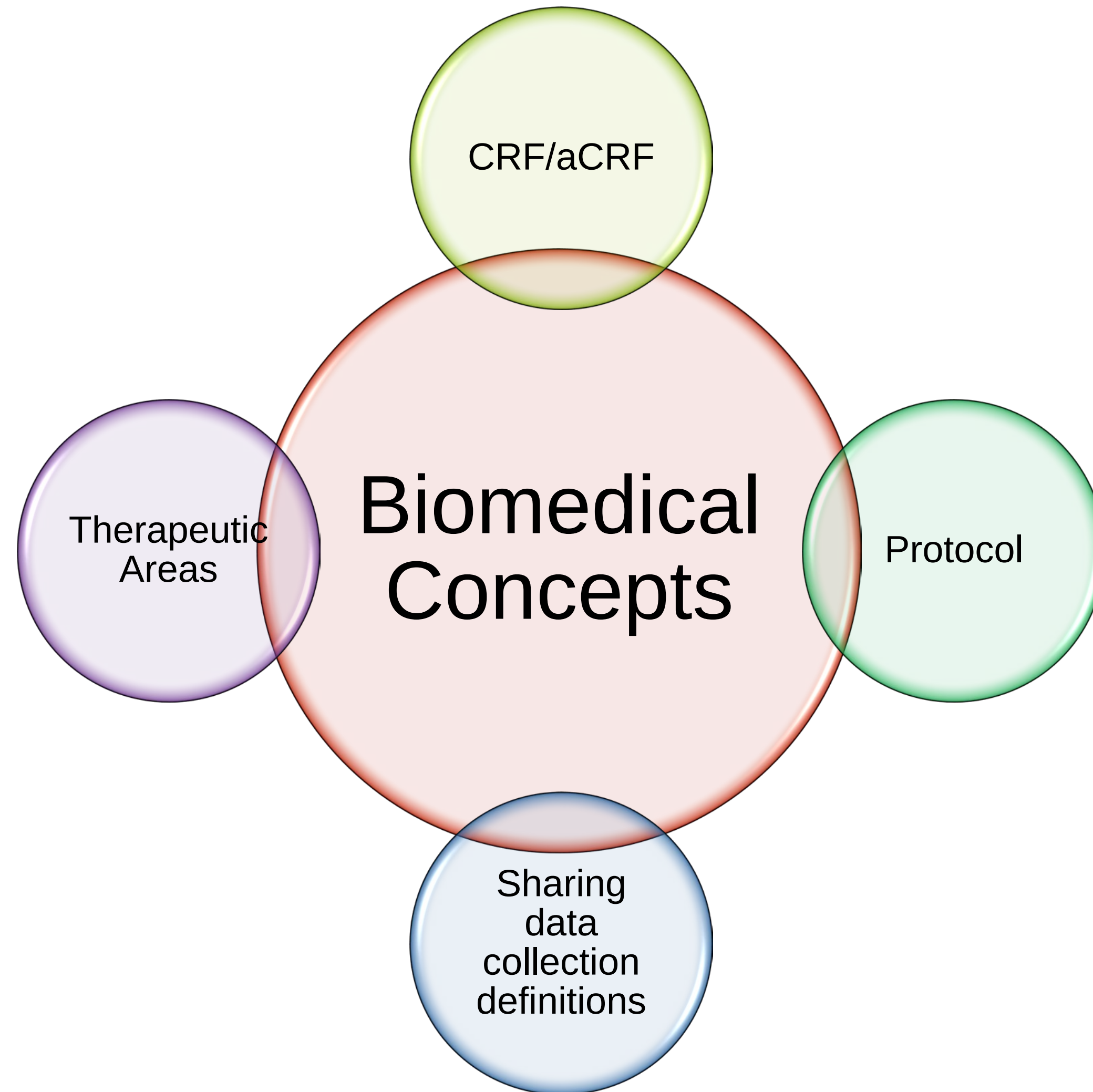
Biomedical Concepts

Relationship to domain



Why bother?

BC is a standardised definition that can be used for various purpose and facilitates faster and more flexible study setup

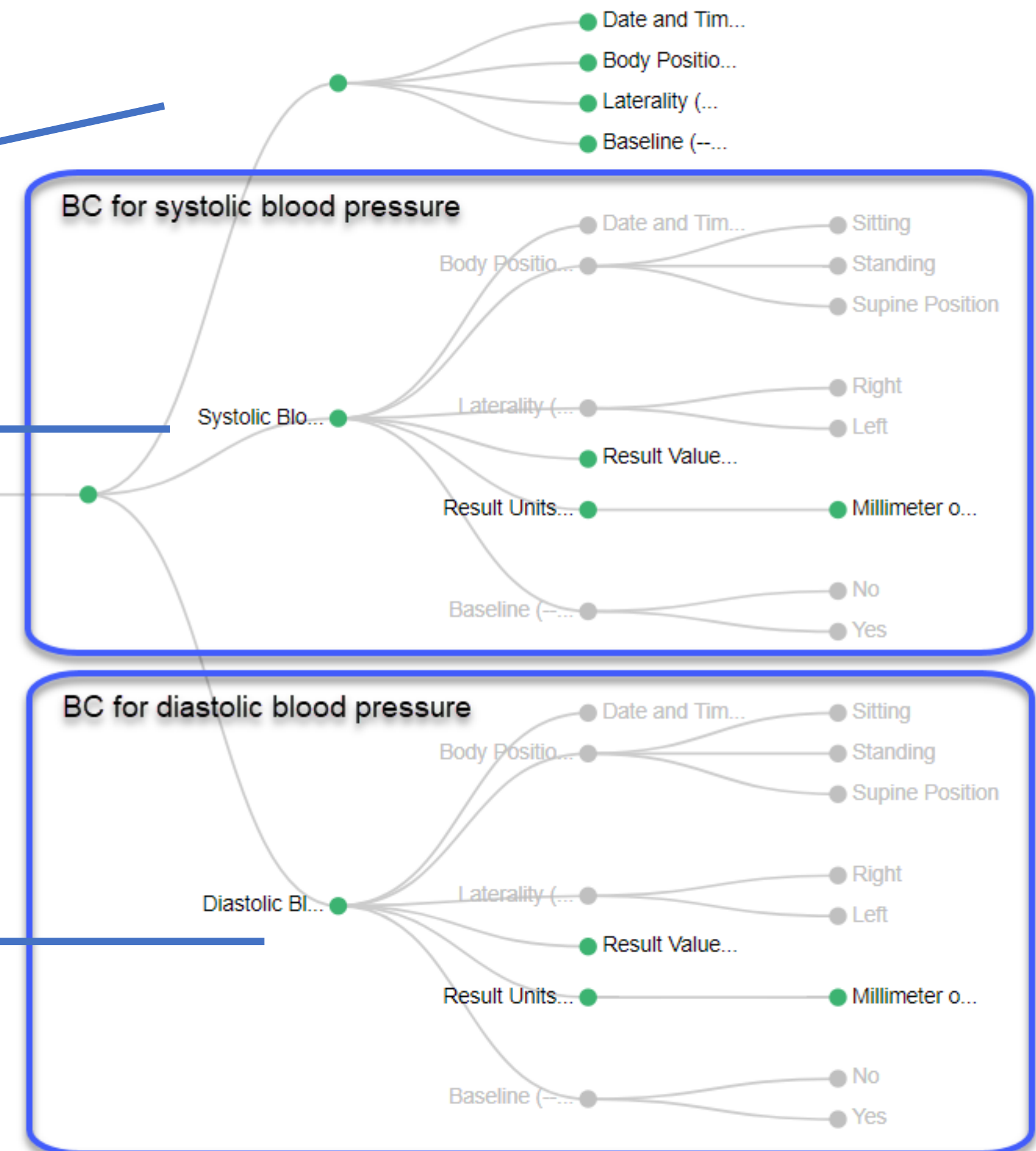


Standardisation - From Forms to BCs

Flexible form creation while still ensuring adherence to CDISC standards

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

Vital Signs		VS=Vital Signs
Vital Signs		
On what date were the measurement performed?	VSDTC where VSTESTCD=DIABP VSDTC where VSTESTCD=SYSBP	
In what position was the subject during the measurement?	VSPOS where VSTESTCD=DIABP VSPOS where VSTESTCD=SYSBP	☐ Sitting ☐ Standing ☐ Supine Position
Which arm?	VSLAT where VSTESTCD=DIABP VSLAT where VSTESTCD=SYSBP	☐ Right ☐ Left
Is this a baseline value?		☐ No ☐ Yes
Systolic Blood Pressure (BC C25298)		
What was the result of the measurement?	VSORRES where VSTESTCD=SYSBP	
The unit of the measurement	VSORRESU where VSTESTCD=SYSBP	☐ Millimeter of Mercury
Diastolic Blood Pressure (BC C25299)		
Result of the measurement	VSORRES where VSTESTCD=DIABP	
Result units	VSORRESU where VSTESTCD=DIABP	☐ Millimeter of Mercury

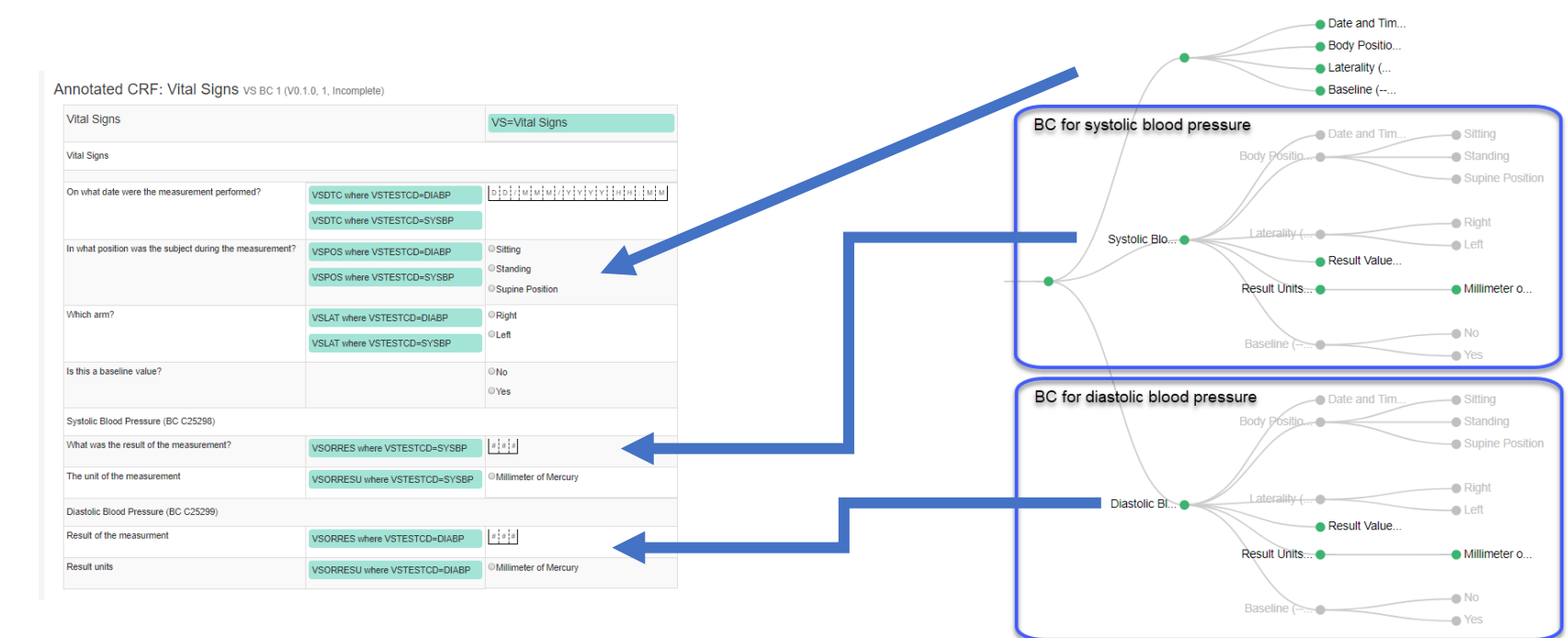


Standardisation - From Forms to BCs

Flexible form creation while still ensuring adherence to CDISC standards

The flexibility is achieved on 3 levels:

1. The user can decide which BCs to add to a Vital Signs form, i.e. which questions are included in the vital sign page
2. The user can enable/disable data elements in a BC, e.g. decide not to use the baseline flag question if not relevant, i.e. what the level of response is needed for the question
3. The user can decide if questions and/or responses are optional/mandatory



Upstream Standardisation

BCs used in protocols
- Protocol metadata – machine readable

Assessments	Screening	Baseline	Treatment	EndOfTrial
Demographics	x			
Vital signs	x			x
CT Scan		x		
Dosing		x	x	x
EQ-5D	x			x
Lipids	x			x
Haemoglobin	x			x
Adverse Events	x	x	x	x

Assessments	BC	Screening	Baseline	Treatment	EndOfTrial
Demographics	Age Race Date of Birth Sex	x			
Vital signs	Height Weight Heart Rate Temperature Systolic Blood Pressure Diastolic Blood Pressure	x			x
CT Scan	CT scan timing		x		
Dosing	Number of dosing units		x	x	x
EQ-5D	Mobility	x			x
Lipids	LDL HDL Total Cholesterol	x			x
Haemoglobin	Haemoglobin	x			x
Adverse Events	Adverse Events	x	x	x	x

Upstream Standardisation

BCs used in protocols

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

Vital Signs VS=Vital Signs

Vital Signs

On what date were the measurement performed? VSOTC where VSTESTCD=DIABP

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

In what position? Vital Signs VS=Vital Signs

Vital Signs

Which arm? On what date were the measurement performed? VSOTC where VSTESTCD=DIABP

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

Is this a baseline? In what position was the subject? Vital Signs VS=Vital Signs

Vital Signs

On what date were the measurement performed? VSOTC where VSTESTCD=DIABP

Which arm? VSOTC where VSTESTCD=SYSBP

In what position was the subject during the measurement? VSPOS where VSTESTCD=DIABP

VSPOS where VSTESTCD=SYSBP

Is this a baseline value? VSPOS where VSTESTCD=SYSBP

VSPOS where VSTESTCD=SYSBP

Which arm? VSLAT where VSTESTCD=DIABP

VSLAT where VSTESTCD=SYSBP

Is this a baseline value? VSLAT where VSTESTCD=SYSBP

Systolic Blood Pressure (BC C25298)

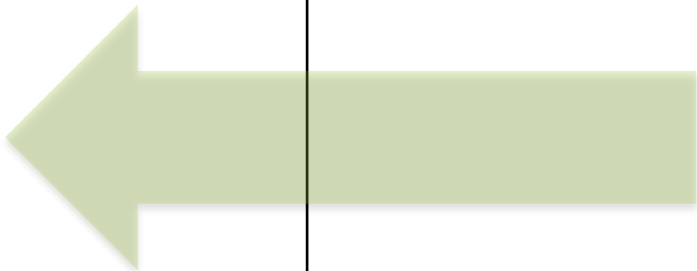
What was the result of the measurement? VSORRES where VSTESTCD=SYSBP

The unit of the measurement VSORRESU where VSTESTCD=SYSBP

Systolic Blood Pressure (BC C25299)

Result of the measurement VSORRES where VSTESTCD=DIABP

Result units VSORRESU where VSTESTCD=DIABP



Assessments	BC	Screening	Baseline	Treatment	EndOfTrial
Demographics	Age Race Date of Birth Sex	X			
Vital signs	Height Weight Heart Rate Temperature Systolic Blood Pressure Diastolic Blood Pressure	X			X
CT Scan	CT scan timing		X		
Dosing	Number of dosing units		X	X	X
EQ-5D	Mobility	X			X
Lipids	LDL HDL Total Cholesterol	X			X
Haemoglobin	Haemoglobin	X			X
Adverse Events	Adverse Events	X	X	X	X

Forms containing these BCs will then be listed and the CRF designer would then pick the appropriate CRF.

CRF reviewed early by the study group allowing for adjustments to the protocol if needed.

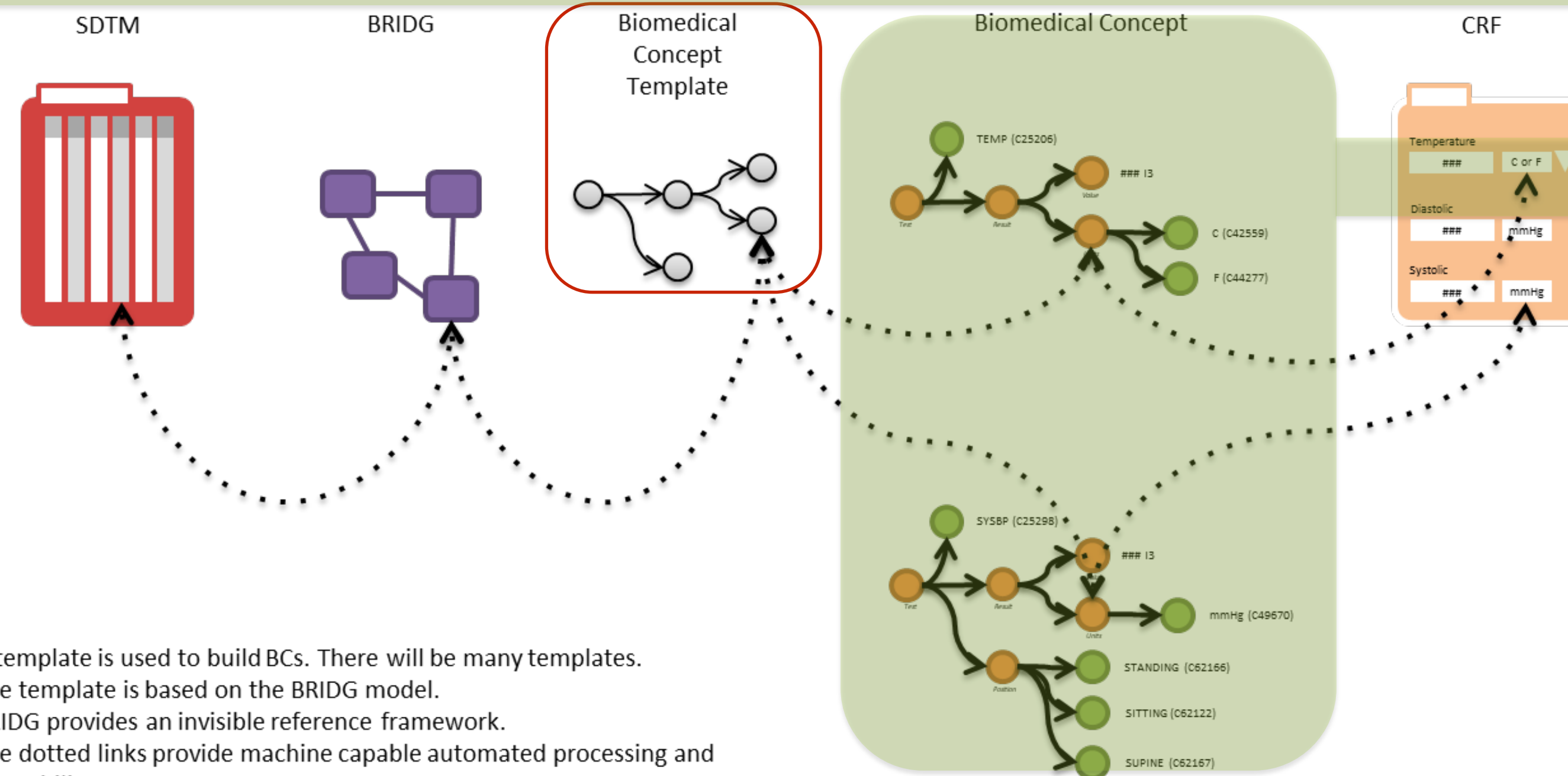


Sharing BCs

Common definitions based on templates – various implementations

BCs should be made based on templates to ensure consistency.

Contributors could be both pharmaceutical companies, CROs as well as regulators.
Sharing the definition of a BC does not disclose any intellectual property or any sensitive data that needs de-identification



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

BCs For Defining Therapeutic Areas (TAs)

Current metadata for TAs – a BC template

Doesn't define the possible/required tests for the TA

Domain	Question Text	Prompt	SDTM or CDASH Variable Name	BRIDG	Definition	Codelist	CRF Completion Instructions	Core	Data Type
VS	What is the vital sign test name?	<Test>	VSTEST	PerformedActivity.PerformedObservation > PlannedActivity > StudyActivity > DefinedActivity.DefinedObservation.name Code.CD.originalText	Verbatim name of the test or examination used to obtain the measurement or finding. {VSTEST} (See Section 2.2.)	VSTEST	Record the name of the vital sign test if not pre-printed on the CRF.	Highly Recommended	Char
VS	What was the unit of the measurement?	<Units>	VSORRESU	PerformedObservation > PerformedObservationResult.value.ANY=> PQ.translation.PQR.code	Original units in which the data were collected. {VSRESU} (See Section 2.2.)	VSRESU	'Record or select the unit of measure associated with the test, if not pre-printed on the CRF.'	Recommended /Conditional	Char

Doesn't define the possible/required units for the test

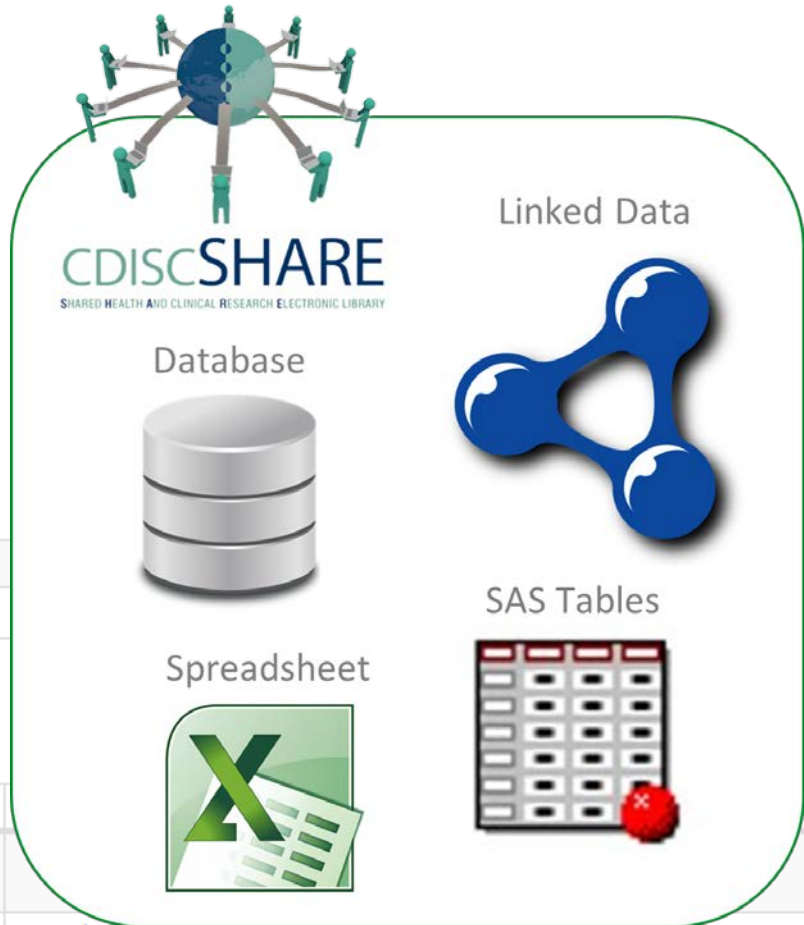
BCs For Defining Therapeutic Areas (TAs)

TAs could be defined as a set of BCs and relationship to domain

Assessments	Domain	BC	Screening	Baseline	Treatment	EndOfTrial
Demographics	DM	Age Race Date of Birth Sex	X			
Vital signs	VS	Height Weight Heart Rate Temperature Systolic Blood Pressure Diastolic Blood Pressure	X			X
CT Scan	PE	CT scan timing		X		
Dosing	EX	Number of dosing units		X	X	X
EQ-5D	QS	Mobility	X			X
Lipids	LB	LDL HDL Total Cholesterol	X			X
Haemoglobin	LB	Haemoglobin	X			X
Adverse Events	AE	Adverse Events	X	X	X	X

Show: Systolic Blood Pressure (BC C25298) BC C25298 (V3.1.0, 4, Incomplete)

Details		Owner	Status
Identifier	Label	ACME	Incomplete
BC C25298	Systolic Blood Pressure (BC C25298)		
Items			
Show	10 entries		
Alias	Question Text	Prompt Text	Enabled
Baseline (--BLFL)	Is this a baseline value?	Baseline	✓
Body Position (--POS)	In what position was the subject during the measurement?	Position	✓
Date and Time (--DTC)	On what date were the measurement performed?	Date	✓
Laterality (--LAT)	Which arm?	Arm	✓
Location (--LOC)	The location of the measurement	Location	✗
Method Code (--METHOD)			✗
Result Units (--ORRESU)	The unit of the measurement	Units	✓
Result Value (--ORRES)	What was the result of the measurement?	Result	✓
Test Code (--TESTCD)			✗
Test Name (--TEST)			✗



No data available in table				
Showing 0 to 0 of 0 entries				
Biomedical Concepts				
Show	10 entries	Search: pressure		
Identifier	Label	Owner	Version	Version Label
BC C25298	Systolic Blood Pressure (BC C25298)	ACME	2.0.0	0.2
BC C25298	Systolic Blood Pressure (BC C25298)	ACME	3.0.0	0.3
BC C25299	Diastolic Blood Pressure (BC C25299)	ACME	2.0.0	0.2

BCs added to the VS domain



Conclusion

A BC is defined once and can be reused for various purposes

- Protocol specification – facilitating early data flow decisions.
- CRF build – facilitating flexible and distributed CRF build while still ensuring adherence to SDTM standards.
- Definition of Therapeutic Areas (TAs) – facilitating more precise guidance on the content to the users.
- To ensure consistent definition of BCs a set of templates can be defined.
- BCs should also be shared which would expand the reuse beyond a single company and hereby minimise the variance in SDTM implementations.

Thank you

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