



The Transcelerate Hack: Transforming and
Automating the Future of Clinical Research

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PHUSE EU Connect, November 9-13 2020

Abstract

In 2018, Transcelerate launched the Digital Data Flow (DDF) initiative with the objective to make the clinical start up process more digital. In November 2019, they announced the 30 day Hackathon for transforming Clinical Trial Start Up. The goal for participants was ambitious: to create a workflow for automating study setup from protocol content including e.g. objectives, endpoints, study design, assessments and visit matrix, and be able to version manage it. The industry has been discussing this topic for years, so it was a great opportunity to really test the feasibility. Having a 30 day limit challenges your perspective and you have some fun! This presentation will cover, Project rationale and the approach taken, What we did and results, What we should have done. The presentation will conclude with a discussion on how the overall approach simplifies the problem space, leads to automation gains and accelerates clinical study start up.

Transcelerate Virtual Hackathon

Digital Data Flow initiative (DDF) - Digitizing Clinical Study Design

TransCelerate Hackathon: Digitizing Clinical Study Design

🕒 March 09, 12:00 AM - April 07, 11:59 PM

📍 TransCelerate Hackathon -

The TransCelerate Digital Data Flow initiative (DDF) will conduct a virtual Hackathon from March 9 to April 7 to:

- Evaluate feasibility of the published Solution Framework and Conceptual Design
- Assess vendor readiness to build such a solution, and bring visibility to DDF
- During the Hackathon, multiple vendors will develop technical demonstrations of components of a study builder, design repository, and/or exchange platform
- The learnings from the Hackathon will be used to inform design elements as well as the future direction of the DDF project

The organization is inviting creative problem solvers to address one of the most vexing challenges in clinical research operations. Clinical study methods have long been stuck in the past, and we need you to give them a digital transformation. Clinical study planning is currently done through a series of manual activities accomplished in a document-based environment. This results in significant duplication of efforts and numerous inefficiencies. We are looking for solutions to transform the document-based to a content driven-data, design, workflow and management system.

The Spark

November 2019. A paragraph

*“For example, using the TA Library for Asthma, a study in severe asthma could have as its **Primary Objective** “To evaluate the effect of drug x in participants with severe asthma.” The primary endpoints linked to this objective are limited to “absolute change in percent of **predicted FEV1** from **baseline** to **[Week X]**” OR “increase [magnitude of change] in FEV1 from baseline to [Week X].” This also implies that the **FEV1 biomedical concept** will require spirometry assessments to be scheduled at baseline (CDM: **primary timepoint**) and week X visits (CDM: **secondary timepoint**), and that FEV1 measurements will need to be captured in the study database, either by EDC or via data transfer. Further, options for Secondary Objectives include FVC or FEV1/FVC ratio (spirometry), reduction in symptoms (questionnaire data) or fewer Clinical Exacerbations (medical history or diary data) or reduction in the use of rescue medication (diary, dosing device or medication count data). As each objective is chosen, the appropriate choice of linked assessments and measures would also be assembled in the tool using the latest available standards for that assessment.”*



EXECUTIVE SUMMARY DIGITAL DATA FLOW
SOLUTION FRAMEWORK AND CONCEPTUAL DESIGN

Appendix A: User Process Supported by Study Builder and Data Flow Schematics

Future State Narrative

Purpose

This appendix describes a technology-enabled business process for defining a clinical study design supported by a Study Builder platform. This narrative lays out the activities and functionality the tool should support. The final section of this appendix consists of schematics which explain the data flows implied by the business process.

The Study Builder will constitute the central component of a broader application ecosystem. Study Builder will articulate the study design by accessing centrally stored definitions from a Study Design Repository; it will enable the automated use/reuse of design elements in downstream applications by leveraging clinical data standards and study design metadata. The use of industry standards (e.g., CDISC, HL7), or company-specific standards and metadata, will enable structured protocol elements to be “prepared” for presentation to Application Programming Interfaces (APIs) that will in turn automate configuration of those downstream systems. The system configuration APIs themselves are out of scope for this document.

Fast Forward

March 2020 – The World Changed

- Transcelerate had initially scheduled the Hackathon for March 9th to April 7th
- We thus scheduled a week to focus on the hackathon from 16th to 20th March
- On March 12th we held a partners meeting where we decided to get people to work from home
- Friday March 13th Denmark shut down
- That Friday was spent getting people setup at home, keyboards, monitors etc.
- We quickly started using Microsoft Teams

[corona | covid-19]

Recommendations for travellers using public transport

Hotline: +45 7020 0233 | coronasmitte.dk

 Walk or cycle If you are planning a short journey, please consider whether it would be possible to walk or bike. This way, you avoid coming into close contact with others during your journey and will allow more room for others, who do not have any alternatives, when taking public transport.	 Travel outside rush hours During rush hour, passengers using public transport might have to stand very close to each other on busses, trains and the metro. Consider if it would be possible to travel outside rush hour by, for instance, re-scheduling your appointment or coming in to work a bit earlier or later than usual.	 Show consideration for other passengers Do not cough or sneeze in the direction of other passengers. If you need to cough or sneeze, please cover your face with your sleeve or a paper handkerchief. Please be particularly careful not to cough or sneeze near elderly passengers.	 Remember good hand hygiene Observing good and thorough hand hygiene is an effective way to prevent infections. Please be aware of this when having been in direct contact with touch surfaces in common areas, such as handles, straps, stop buttons, etc.	 Do not use public transport if you are ill or suspect that you might be infected If you are ill, or you suspect that you might be infected, do not use public transport.
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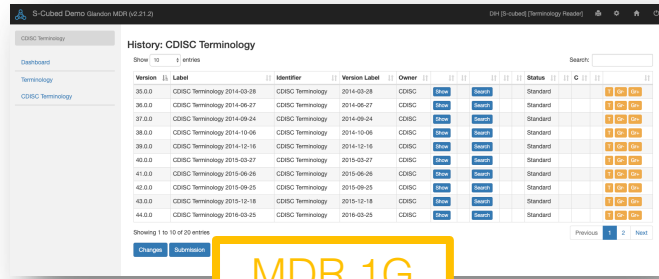
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Product Development

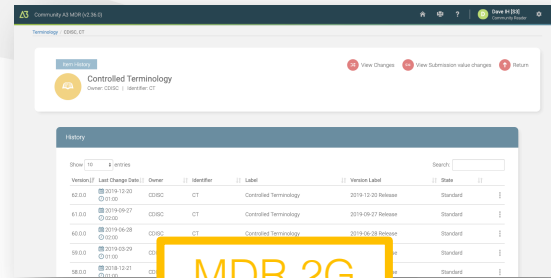
State at start of Hackathon

At the start of the Hackathon the products were

- 1st Generation Metadata Repository (MDR)
- 1st Generation Study Work Bench (SWB)
- 2nd Generation MDR containing full terminology support for Sponsor & CDISC Terminology

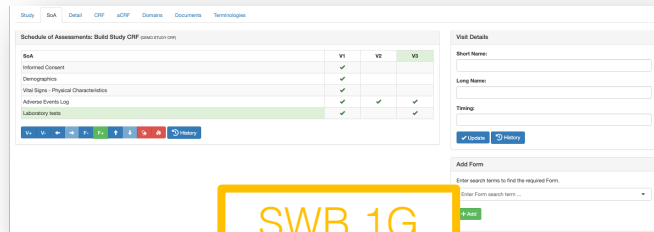


MDR 1G

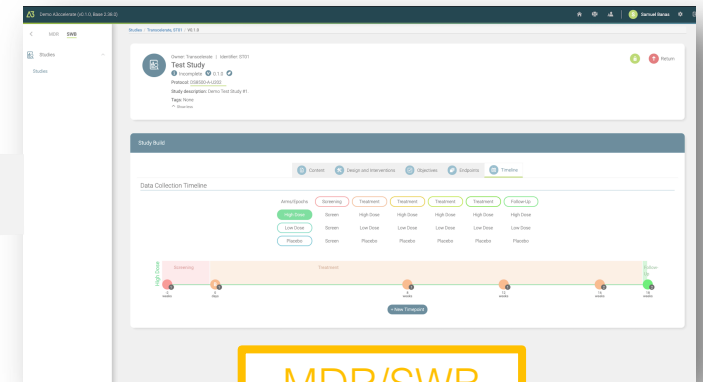


MDR 2G

Transcelerate Digital Data Flow (DDF)



SWB 1G



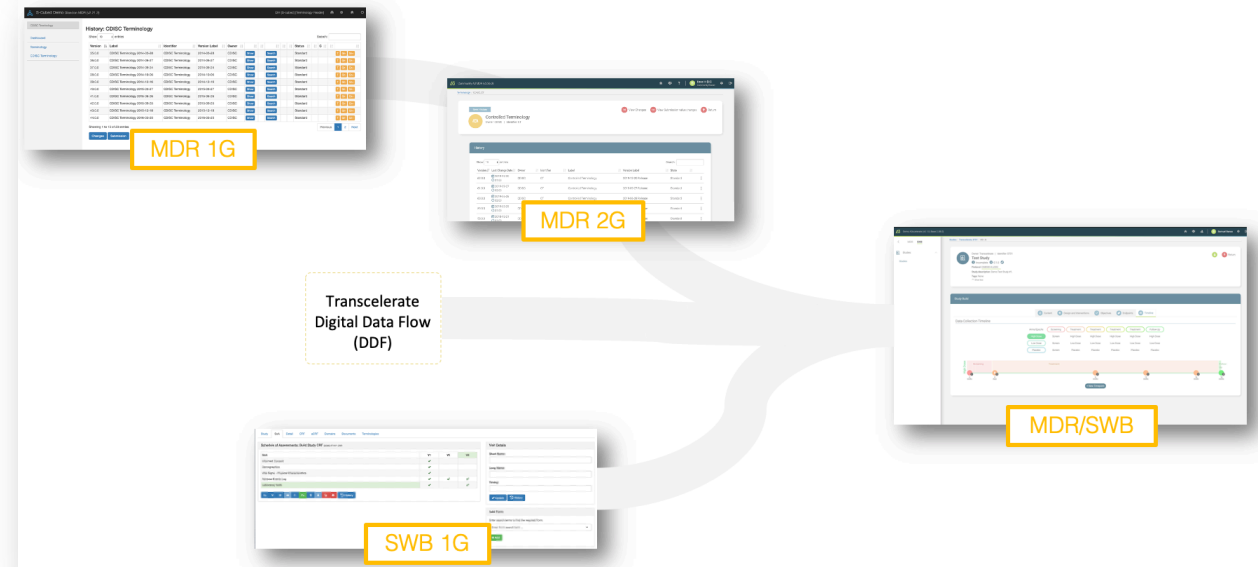
MDR/SWB

Approach

From idea to reality

We decided to:

- Focus on the key pieces, the more technically demanding and not the easy tasks.
- Time-box our activity limiting the time we spent on the project and doing what we could within that period
- Take our 2nd generation MDR and add in a new Study Build component to form a unified, single MDR/SWB cloud application
- Develop a prototype that auto-generates the Schedule of Assessments (SoA) from Study Objectives, Study Endpoints and a Study Timeline
- Link Study Endpoints to BCs
- This provides the link to the existing functionality implemented within the 1st Generation Study Work Bench



Approach Combine

- The 1st Generation SWB already demonstrates the ability to take a manually entered SoA and dynamically show domain use, export aCRF, ALS, ODM and Define.xml using definitions from the MDR.
- Add the Study Objectives, Endpoints, Timepoints and Timeline to show it is possible to build from Protocol through Study Design, Study Timeline, SoA, aCRF, EDC exports and onto define.xml in an efficient automated manner

NEW MDR/SWB

Menu from protocol to SoA developed for Hackathon

Existing 1st Generation SWB menu from study SOA to aCRF, SDTM domains, EDC export and define.xml

SWB 1G

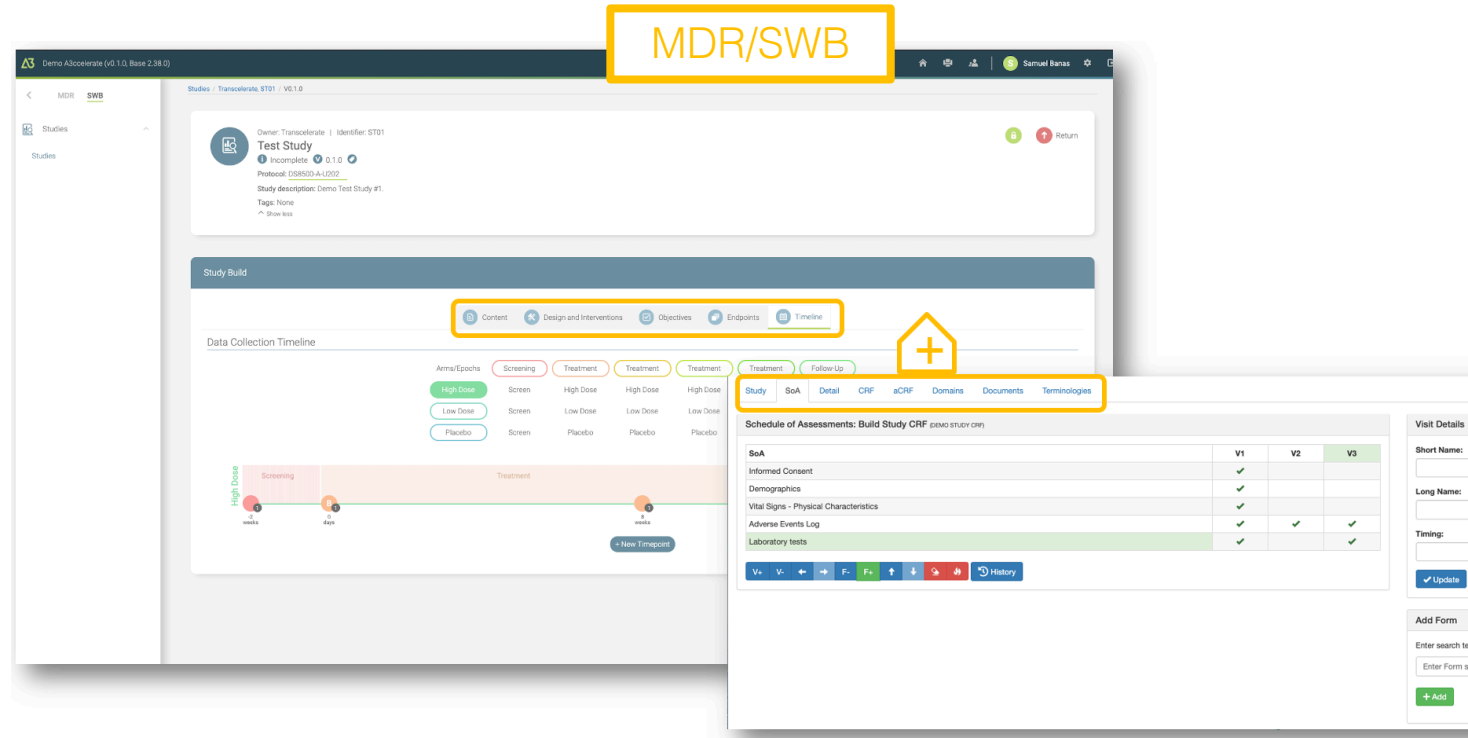
The screenshot displays the S-CUBED SWB 1G interface. The top navigation bar includes 'MDR' and 'SWB' tabs. The main content area is titled 'Test Study' and shows a 'Study Build' section with a 'Data Collection Timeline' and a 'Schedule of Assessments: Build Study CRF' table. The timeline shows a sequence of events: Screening (High Dose, Low Dose, Placebo) and Treatment (High Dose, Low Dose, Placebo). The 'Schedule of Assessments' table lists various assessments and their timing across visits V1, V2, and V3. The interface also includes a 'Visit Details' section on the right and a 'New Timepoint' button at the bottom.

Assessment	V1	V2	V3
Informed Consent	✓		
Demographics	✓		
Vital Signs - Physical Characteristics	✓		
Adverse Events Log		✓	✓
Laboratory tests	✓		✓

Approach

Seamless Integration

- Show it is possible to seamlessly link from Protocol through Study Design, Study Timeline, SoA, aCRF, EDC exports and onto define.xml



Protocol

Design &
Interventions

Objectives

Endpoints

Timeline

+

SoA

Detail

CRF

aCRF

Domains

Documents

Terminologies

Approach

Seamless Integration

- Show it is possible to seamlessly link from Protocol through Study Design, Study Timeline, SoA, aCRF, EDC exports and onto define.xml

The screenshot displays the MDR/SWB (Monitoring Data Repository/Study Web Browser) interface. A yellow box labeled "MDR/SWB" is positioned at the top. The main window shows a "Test Study" overview with fields for Owner, Identifier, and Protocol. Below this is the "Study Build" section, which includes a "Data Collection Timeline" and a "Schedule of Assessments: Build Study CRF" table. The timeline shows various study phases (Screening, Treatment, Follow Up) with associated interventions (High Dose, Low Dose, Placebo). The assessment table lists various data points (V1, V2, V3) and their corresponding status (e.g., Informed Consent, Demographics, Vital Signs). A yellow box highlights the "Content" tab in the "Study Build" section, and another yellow box highlights the "Study" tab in the "Schedule of Assessments" table. A yellow house icon with a plus sign is also visible.

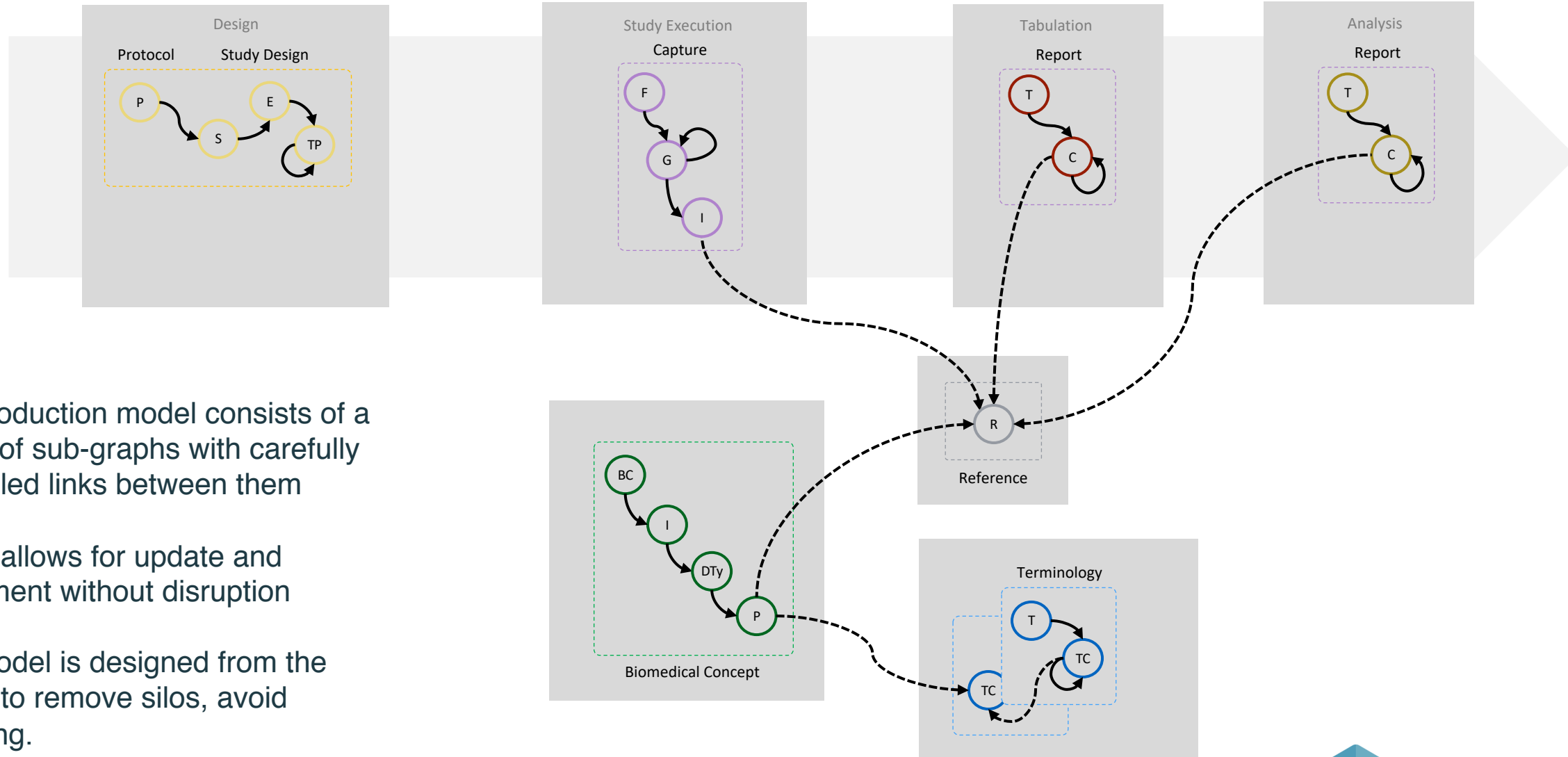
Study	SoA	Detail	CRF	aCRF	Domains	Documents	Terminologies
V1	V2	V3					
✓	✓	✓					
✓	✓	✓					
✓	✓	✓					
✓	✓	✓					

Protocol Design & Interventions Objectives Endpoints Timeline SoA Detail CRF aCRF Domains Documents Terminologies

The Model

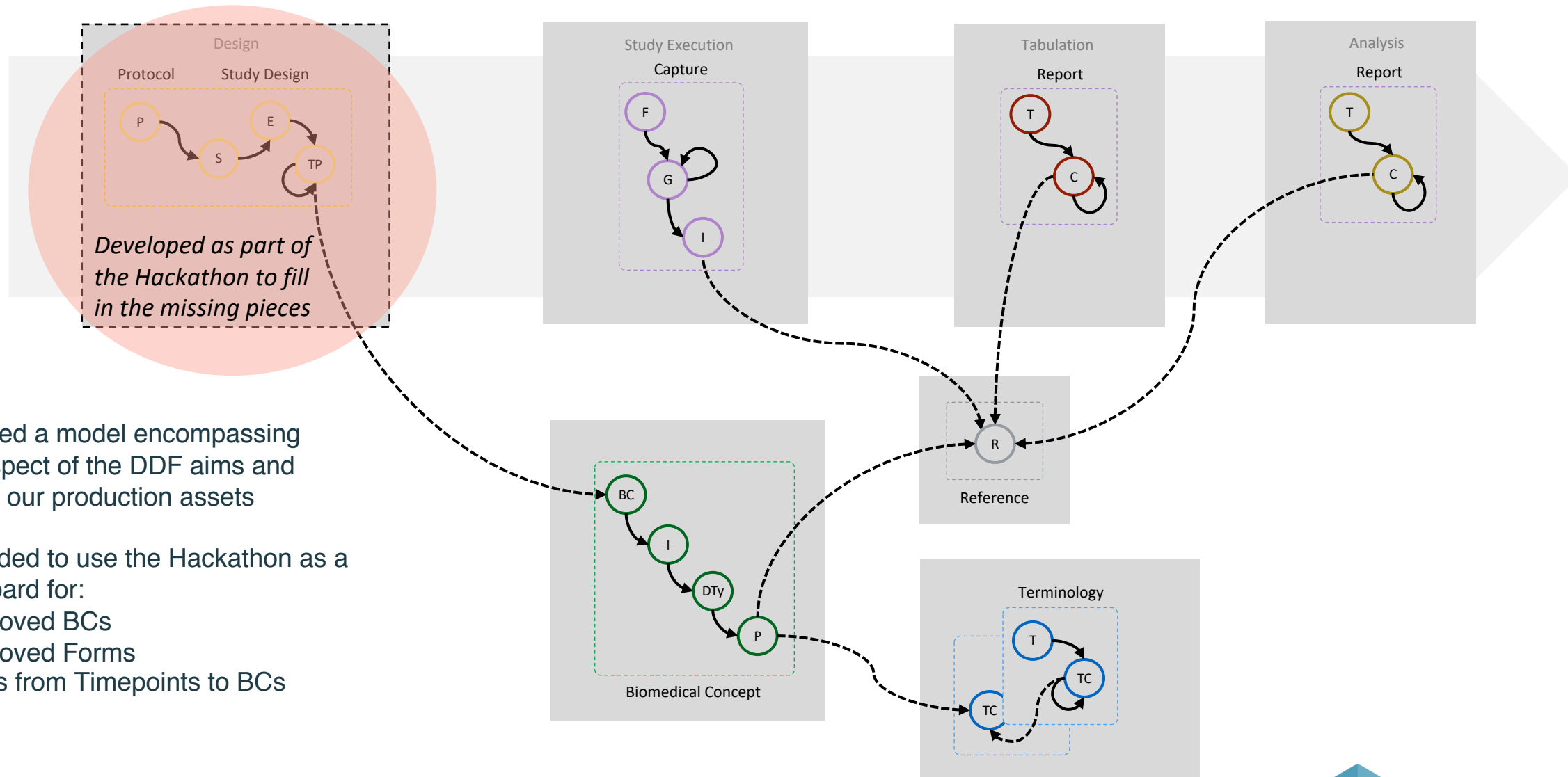
Complete, Flexible, Upgradable

- Our production model consists of a series of sub-graphs with carefully controlled links between them
- Model allows for update and refinement without disruption
- The model is designed from the outset to remove silos, avoid mapping.



The Model

Complete, Flexible, Upgradable



- Developed a model encompassing every aspect of the DDF aims and linked to our production assets
- We decided to use the Hackathon as a springboard for:
 - Improved BCs
 - Improved Forms
 - Links from Timepoints to BCs

The protocol



Owner: Transcelerate | Identifier: TLDEMO

Timeline Demo

Incomplete

0.1.0

Show more



Return

Study Build

Content

Design and Interventions

Objectives

Endpoints

Timeline

SoA

Study Content

<u>Acronym</u>	H2Q-MC-LZZT
<u>Title</u>	Safety and Efficacy of the Xanomeline Transdermal Therapeutic System (TTS) in Patients with Mild to Moderate Alzheimer's Disease.
<u>Short Title</u>	
<u>Study Phase</u>	Phase II Trial
<u>Study Type</u>	Interventional Study
<u>Intervention</u>	Parallel Study
<u>Masking</u>	Double Blind Study
<u>Indication</u>	Alzheimer's Disease
<u>Therapeutic Area</u>	Nervous system disorders

View Raw Triples

Objectives and Endpoints



Owner: Transcelerate | Identifier: TLDEMO
Timeline Demo
Incomplete 0.1.0
[Show more](#)

Return

Sets of pre-selected Objectives and Endpoints used in the Study.

Study Build

Content

Design and Interventions

Objectives

Endpoints

Timeline

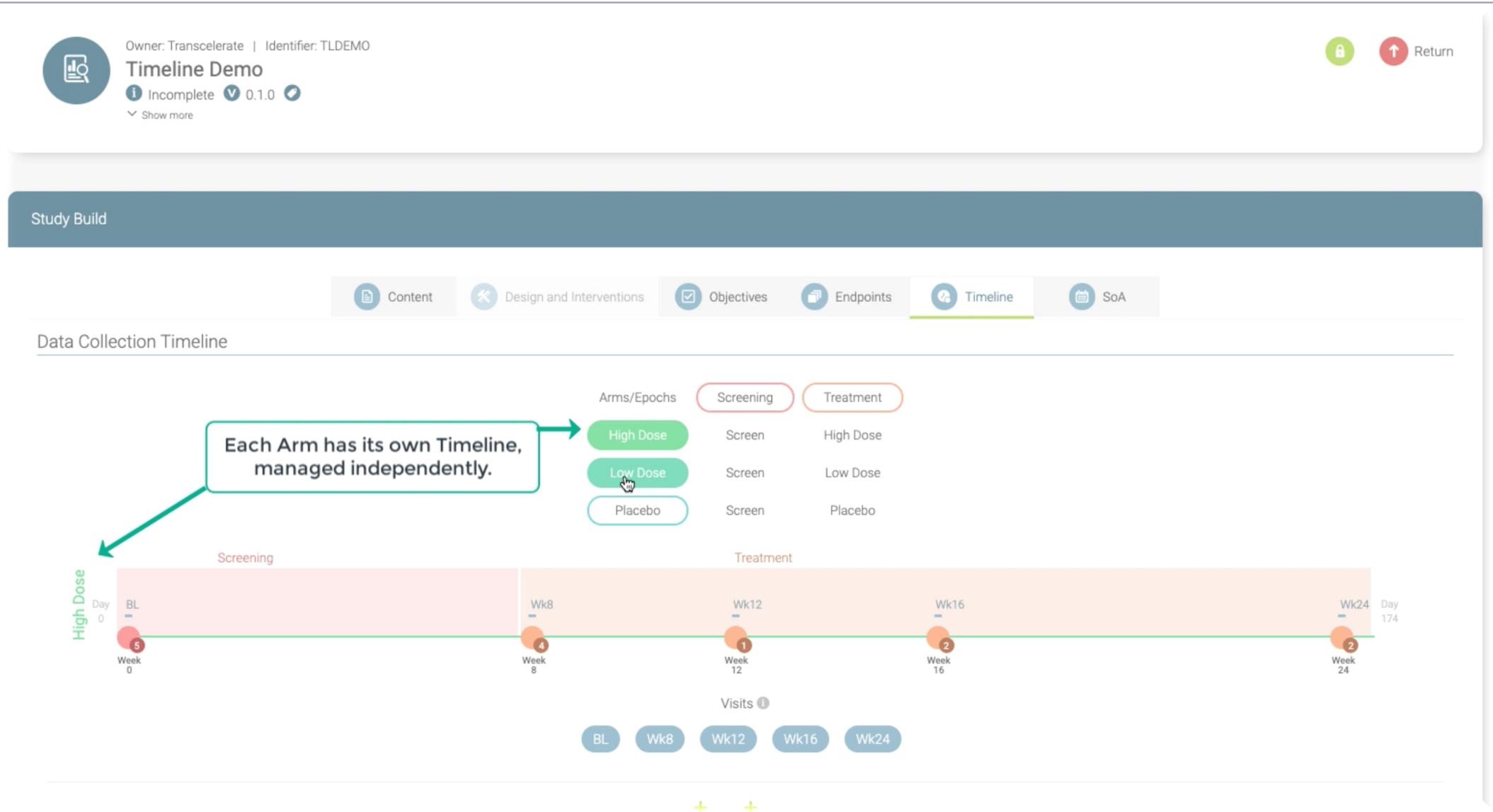
SoA

Study Objectives

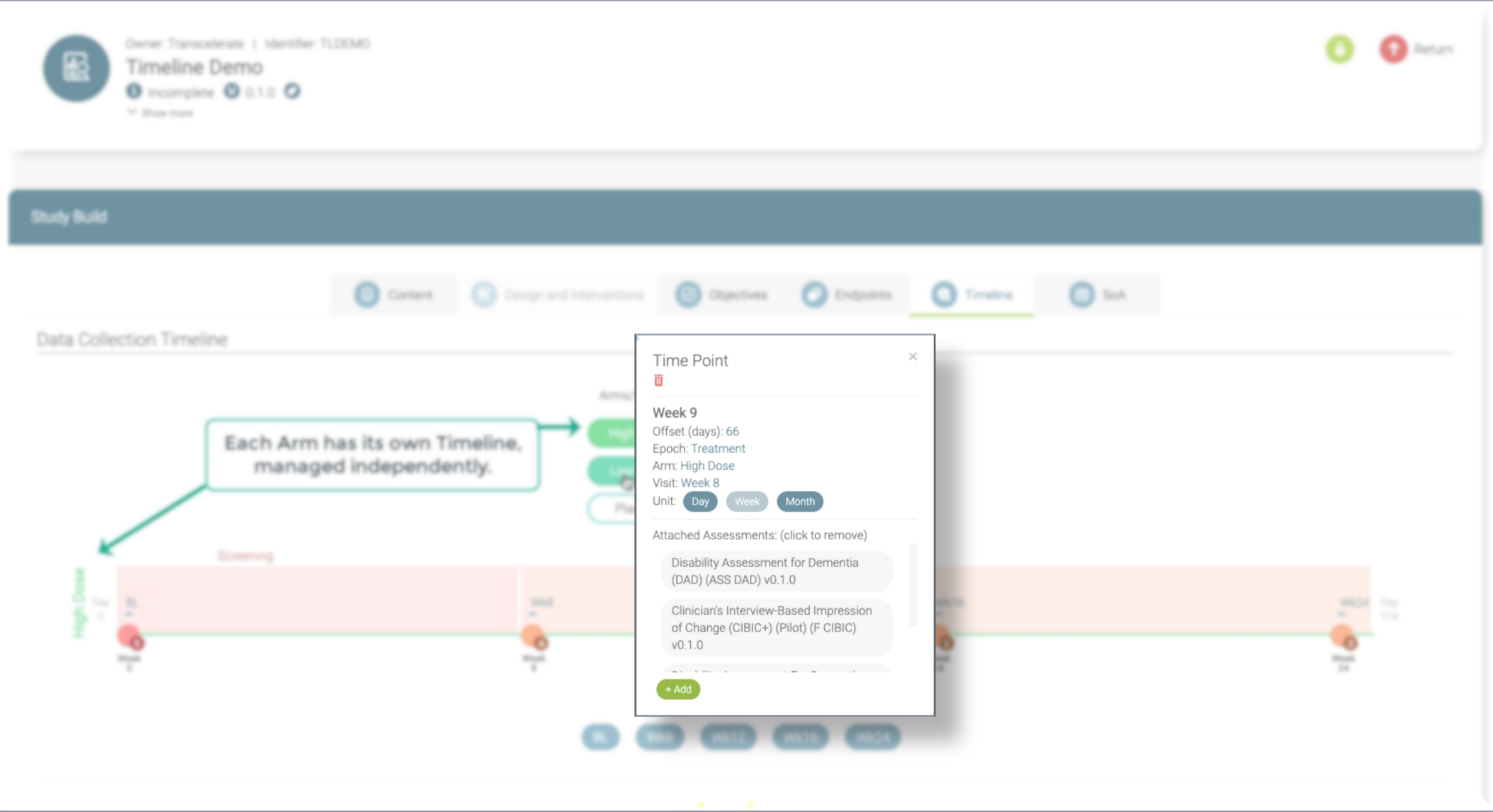
The following is the list of available Study Objectives. The ones being used in this study are marked.

Objective	Type	Used in Study
To assess the effect of Xanomeline Transdermal Therapeutic System (TTS) on the ADAS-Cog and CIBIC+ scores at Week 24 in participants with Mild to Moderate Alzheimer's Disease	Primary	✓
To assess the dose-dependent improvement in behavior. Improved scores on the Revised Neuropsychiatric Inventory (NPI-X) will indicate improvement in these areas	Primary	✓
To document the safety profile of the xanomeline TTS.	Secondary	✓
To assess the effect of xanomeline TTS on the measure of behavioral/neuropsychiatric symptoms in participants with Alzheimer's Disease	Secondary	✓
To assess the dose-dependent improvements in activities of daily living. Improved scores on the [assessment] will indicate improvement in these areas	Not Set	✗

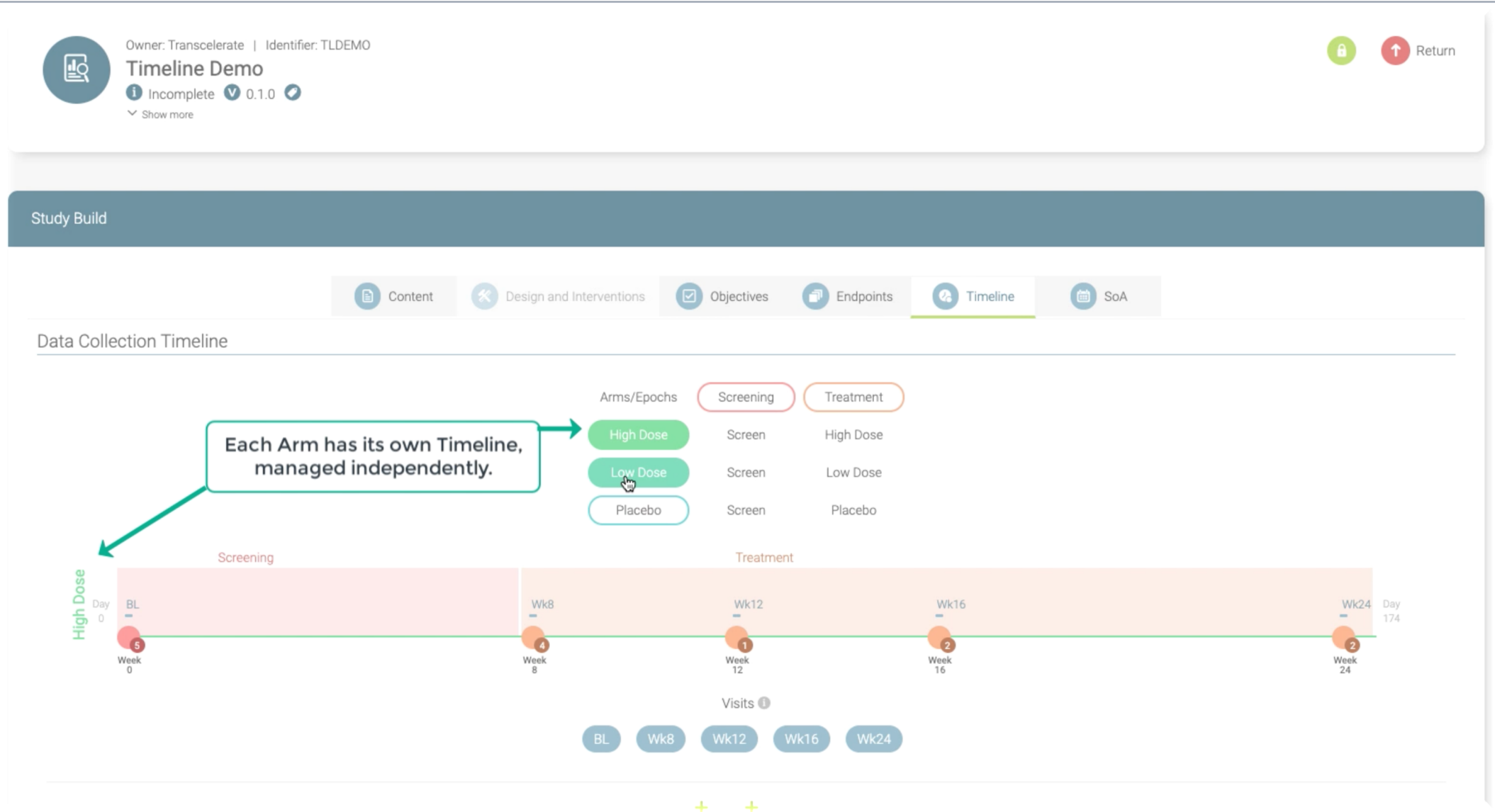
Timeline



Timeline



Timeline



Timeline -> Schedule of Assessments



Owner: Transcelerate | Identifier: TLDEMO
Timeline Demo
Incomplete 0.1.0
[Show more](#)

Return

Study Build

Content

Design and Interventions

Objectives

Endpoints

Timeline

SoA

Schedule of Assessments

Type	Assessment / Visit	BL	Wk8	Wk12	Wk16	Wk24
	ASS DAD Disability Assessment for Dementia (DAD)					
	F DAD Disability Assessment For Dementia (DAD) (Pilot)					
	F LAB SAMPLES Laboratory Samples					
	F ECG ECG Measurements					
	F CIBIC Clinician's Interview-Based Impression of Change (CIBIC+) (Pilot)					
	DIABP Diastolic Blood Pressure					
	SYSBP Systolic Blood Pressure					

The SoA now includes the BCs we selected!

18 | ©2020 S

Removing the silos

Protocol -> Timepoint -> BC -> Data points -> SDTM domain ... But VISIT?

2018
EUROPE
INTERCHANGE
BERLIN
23-27 APRIL



Into the Fire, CDISC & FHIR

SDTM domain generated from data being extracted
from an EHR via FHIR

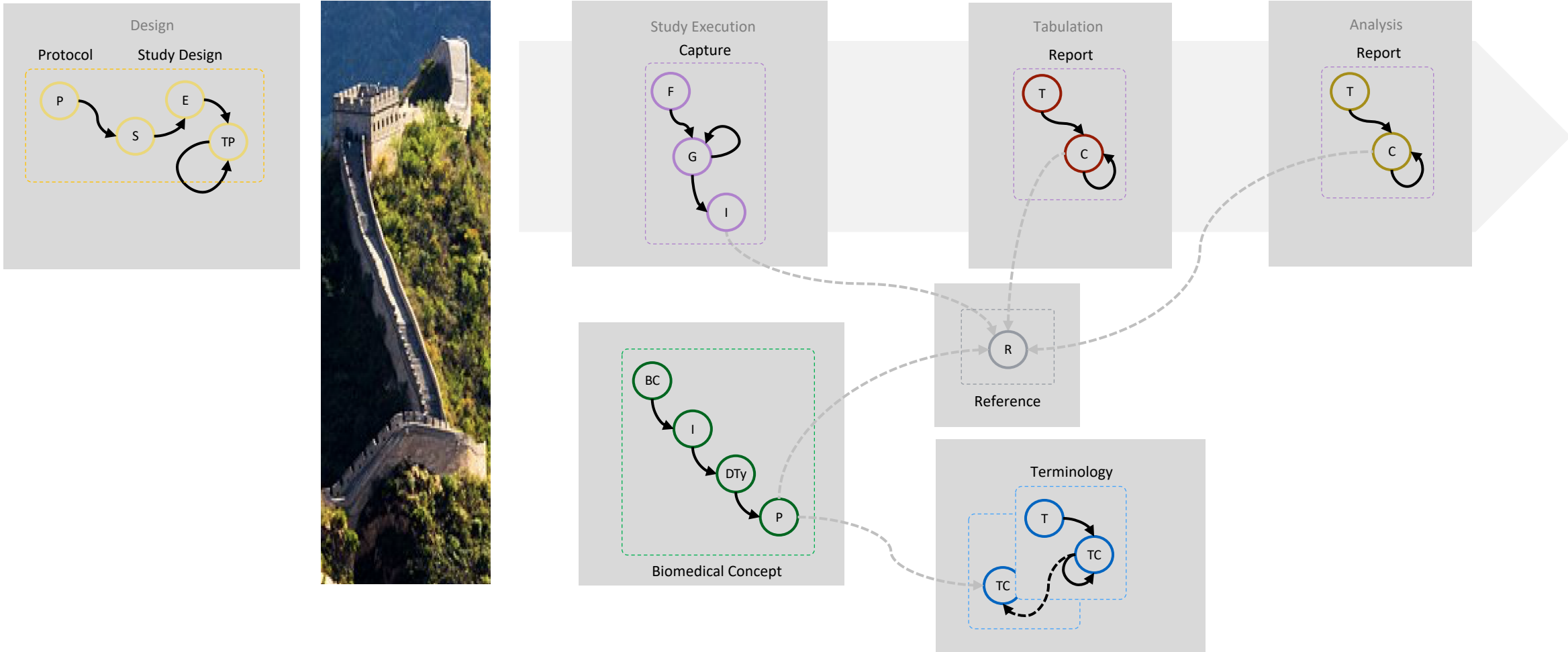


Tabulation

STUDYID	DOMAIN	USUBJID	VSSEQ	VSGRPID	VSSPID	VSTESTCD	VSTEST	VSCAT	VSSCAT	VSPOS	VSORRES	VSORRESU	VSSTRESC	VSSTRESN	VSSTRESU	VSSTAT	VSREASND	VSLOC	VSBLFL	VSDRVFL	VISITNUM	VISIT	VISITDY	VSDTC	VSDY	VSTPT	VSTPTNUM
VSBC2	VS	VSBC2-SMART-1288992	1			HEIGHT	Height				163.068	cm												2009-04-24T00:00:00-06:00			
VSBC2	VS	VSBC2-SMART-1288992	2			WEIGHT	Weight				86.50006	kg												2009-04-23T00:00:00-06:00			
VSBC2	VS	VSBC2-SMART-1272431	3			HEIGHT	Height				174.752	cm												2002-05-20T00:00:00-06:00			
VSBC2	VS	VSBC2-SMART-1272431	4			WEIGHT	Weight				75.47777	kg												2002-05-30T00:00:00-06:00			
VSBC2	VS	VSBC2-SMART-1213208	5			WEIGHT	Weight				114.21456	kg												2003-09-25T00:00:00-06:00			
VSBC2	VS	VSBC2-SMART-1213208	6			HEIGHT	Height				161.036	cm												2003-08-11T00:00:00-06:00			

Removing the silos

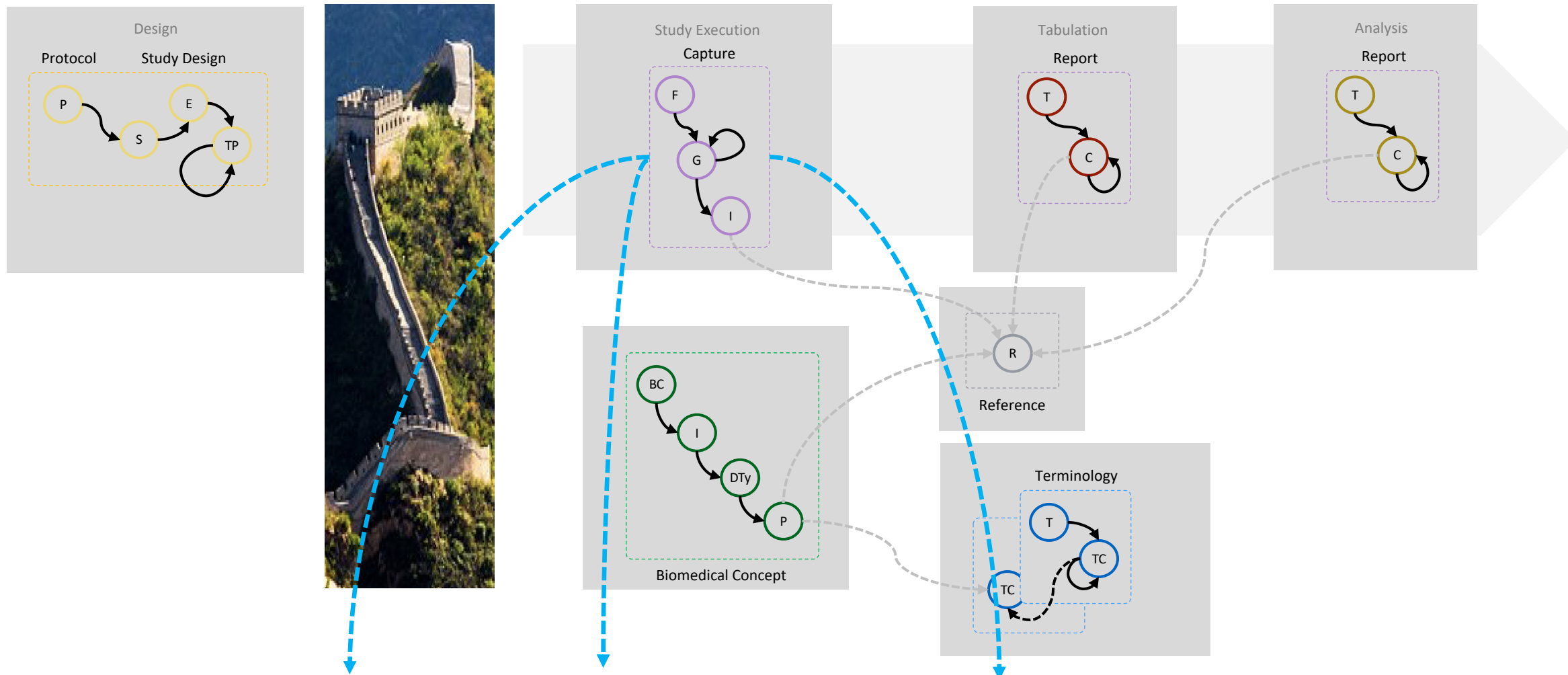
Protocol -> Timepoint -> BC -> Data points -> SDTM domain ... But VISIT?



STUDYID	USUBJID	--TESTCD	--ORRES	--ORRESU	--LOC	--DTC	VISIT	--TPT

Removing the silos

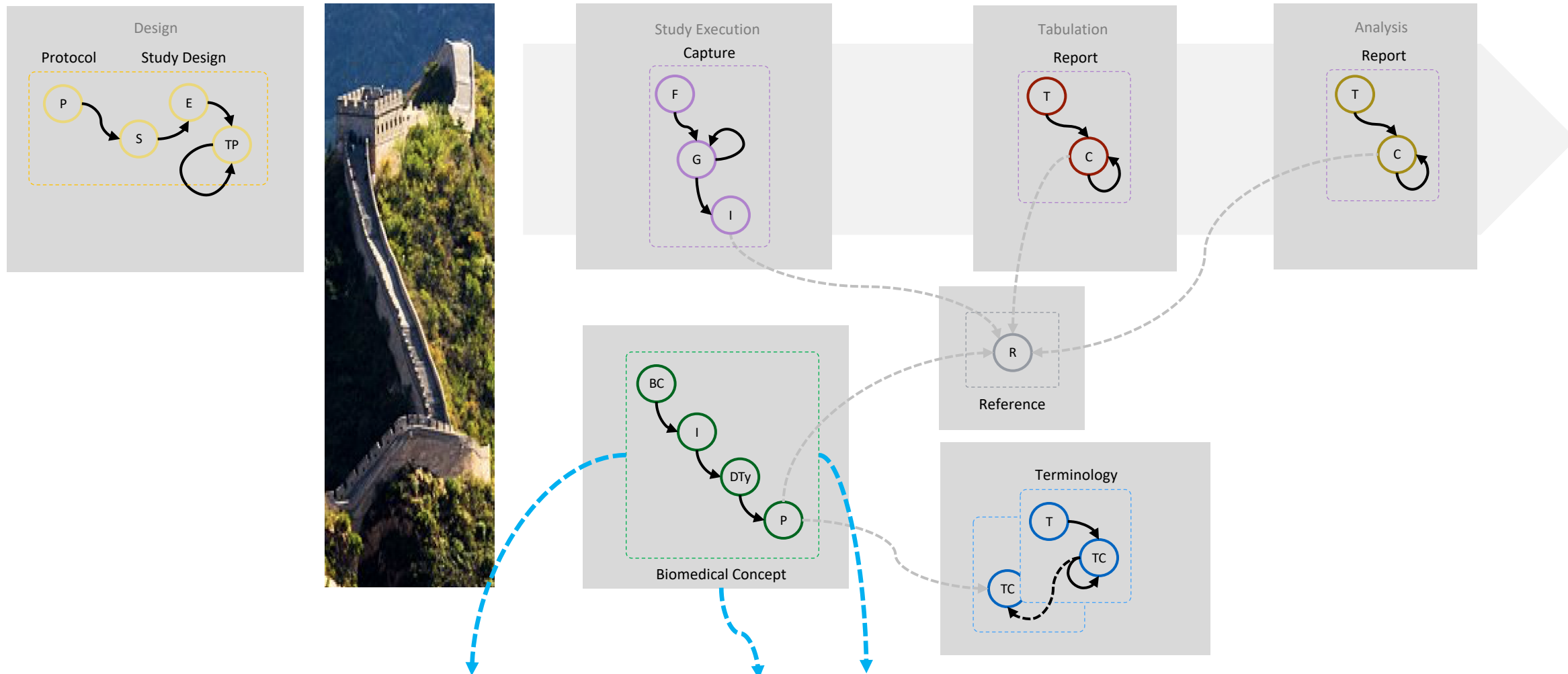
Protocol -> Timepoint -> BC -> Data points -> SDTM domain ... But VISIT?



STUDYID	USUBJID	--TESTCD	--ORRES	--ORRESU	--LOC	--DTC	VISIT	--TPT
	SUBJ01		36.11			2020-06-23		

Removing the silos

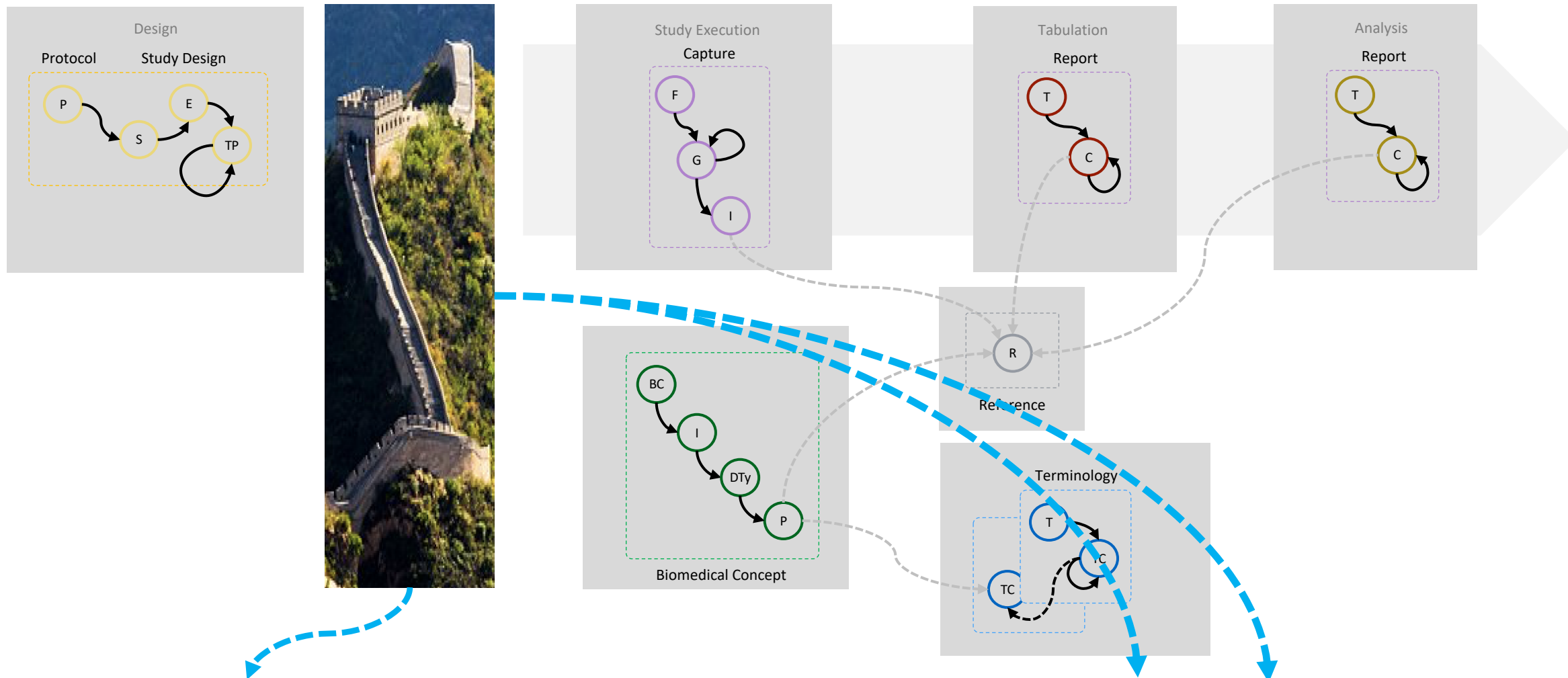
Protocol -> Timepoint -> BC -> Data points -> SDTM domain ... But VISIT?



STUDYID	USUBJID	--TESTCD	--ORRES	--ORRESU	--LOC	--DTC	VISIT	--TPT
		TEMP		C	ORAL CAVITY			

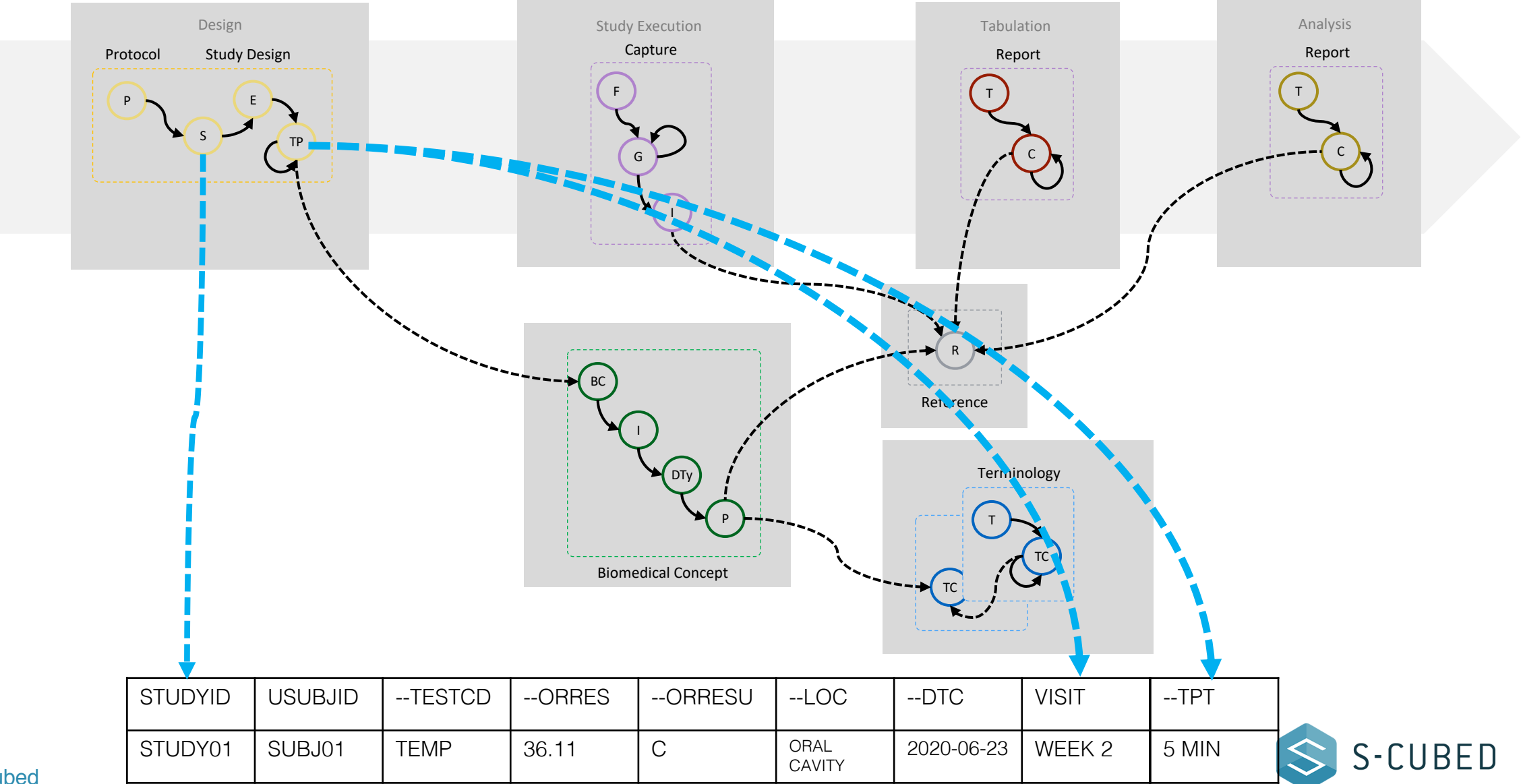
Removing the silos

Protocol -> Timepoint -> BC -> Data points -> SDTM domain ... But VISIT?

[illegible]

Removing the silos

Protocol -> Timepoint -> BC -> Data points -> SDTM domain ... But VISIT?



Conclusions

- We achieved a lot in the short period we allowed ourselves to participate in the Hackathon but you never get as far as you would like!
- We demonstrated the core purpose; we can link Protocol to Study Design and onto Study Build, SoA, aCRFs, define.xml and EDC exports. We can automate.
- The work has been very beneficial to us and will strongly flavour our next phase of development
- The linked model removes silos and allows access to the desired information when it is needed

For Further Information Contact:
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S-CUBED

Thanks for listening

For Further Information Contact:

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