COST BENEFIT ANALYSIS FOR IMPLEMENTATION OF DATA STANDARDS

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29 May 2018

- *ANALYSIS PROCESS & METHODOLOGY*
- *OBSERVATIONS*
- *ROI CALCULATIONS*
- *CONCLUSIONS*

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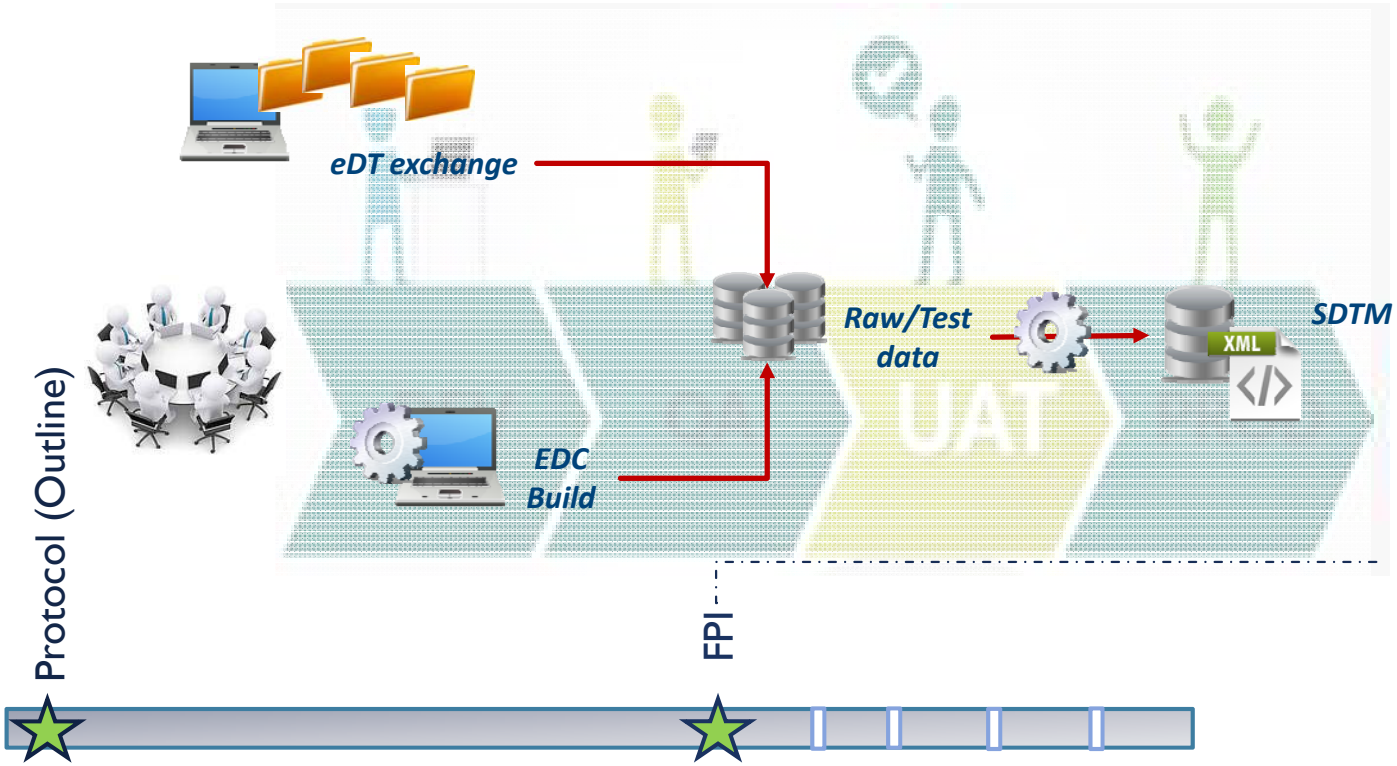
Scope of activities included in Cost-Benefit analysis



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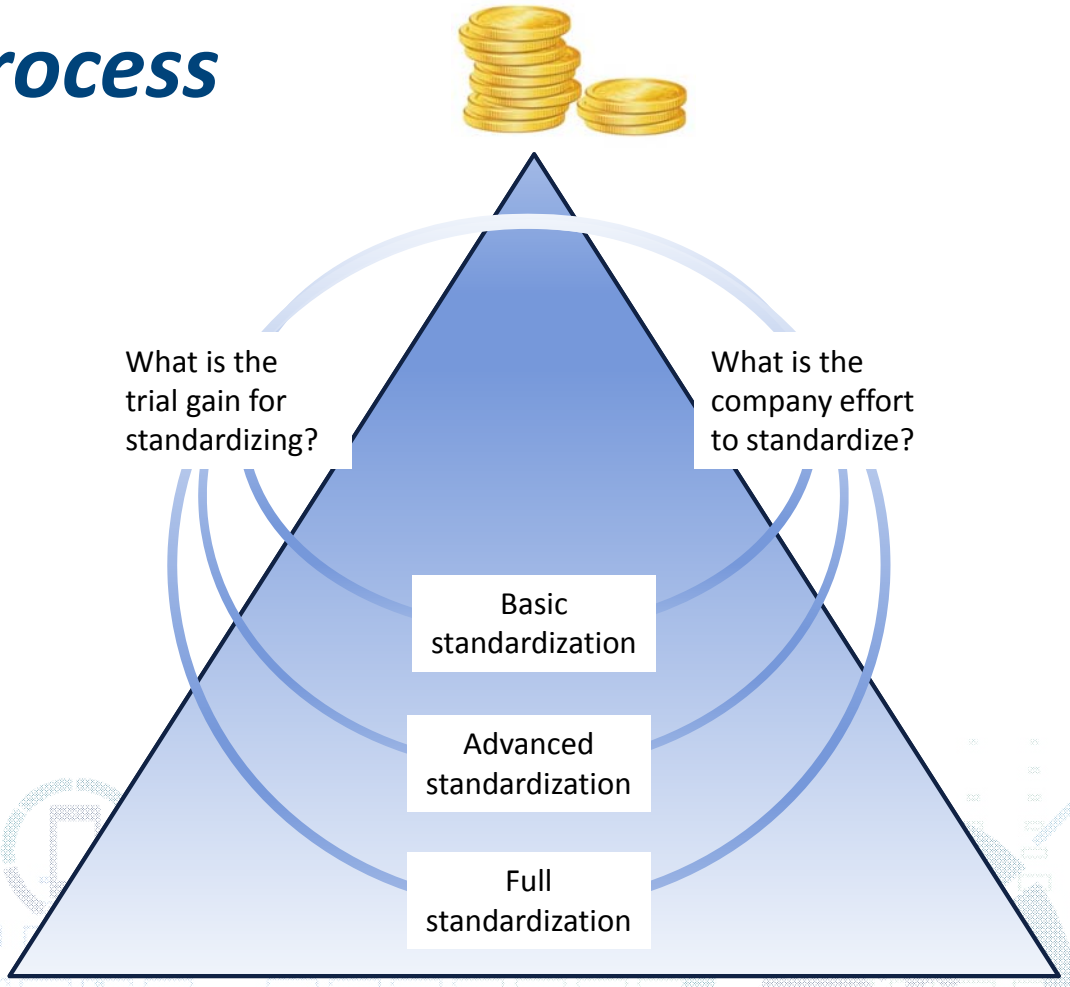
Analysis Process



Methodology – data gathering

Analysis of cost proposals across multiple sponsors/multiple CROs/across TAs

- ❑ *Compilation of data since 2005*
  - Widespread Industry recognition of CDISC and EDC as a standards
- ❑ *Exclude regional variability*
  - All labour done with 'standard rate per profile'
- ❑ *Exclude EDC hosting fees*
- ❑ *Assume SDTM was deliverable*
  - No post-trial conversion costs taken into account

Fixed parameters

Phase

 # Sites

 # Subjects

Trial duration

Comparator values

Study complexity (# unique collection points)

Level of standardization

ANALYSIS PROCESS & METHODOLOGY

OBSERVATIONS

ROI CALCULATIONS

CONCLUSIONS

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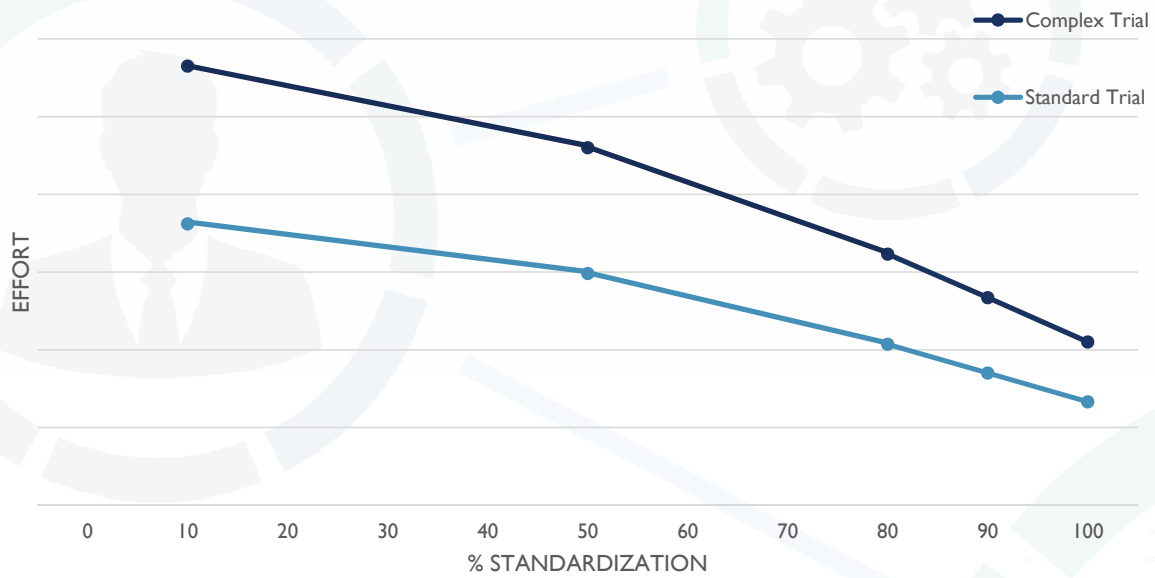
Impact of standardization on trial set-up effort



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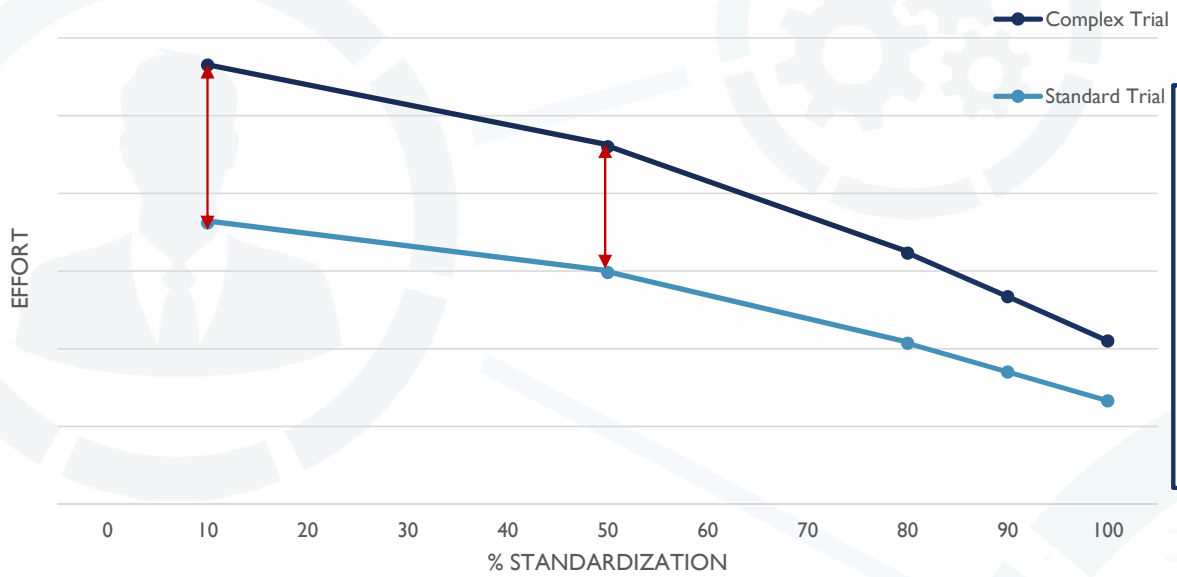
Impact of standardization on trial set-up effort



Conclusion 1:

- ❑ *Any level of standardization has a positive impact on study set-up effort*
- ❑ *Impact of standardization on study set-up effort is higher for complex trials*

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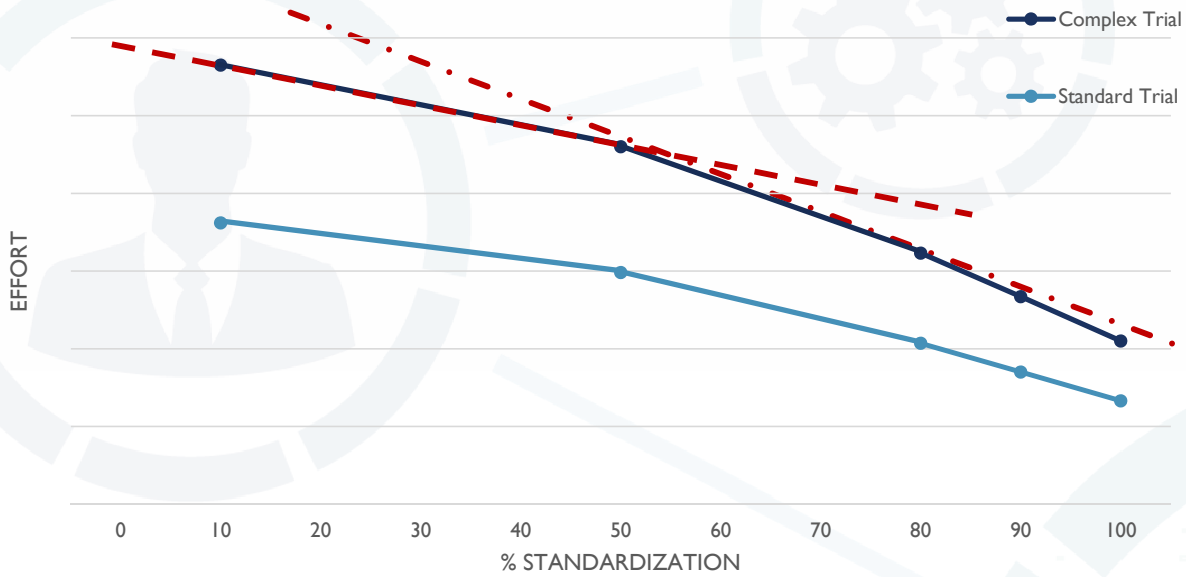
Impact of standardization on trial set-up effort



Conclusion 2:

- *A higher level of standardization has a bigger impact in reducing the set-up effort*

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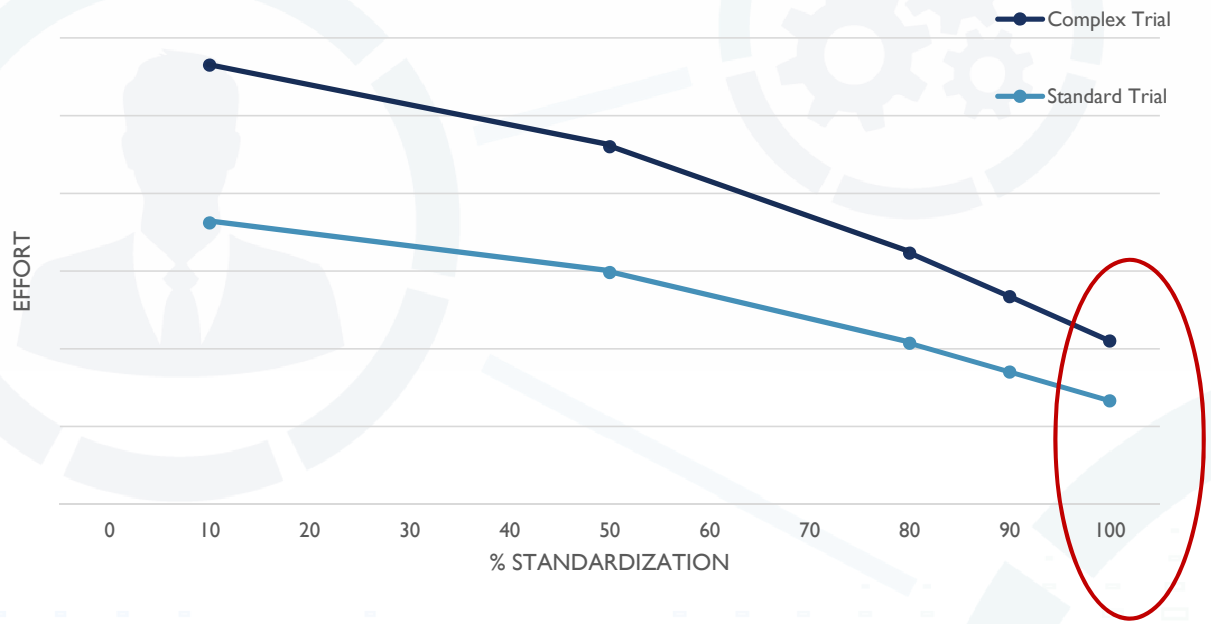
Impact of standardization on trial set-up effort



Conclusion 3:

- *There is a finite benefit to implementation of standards*

"Effort will not reduce to 0 with 100% standardization"

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Approach

- ANALYSIS PROCESS & METHODOLOGY
- OBSERVATIONS
- **ROI CALCULATIONS**
- CONCLUSIONS

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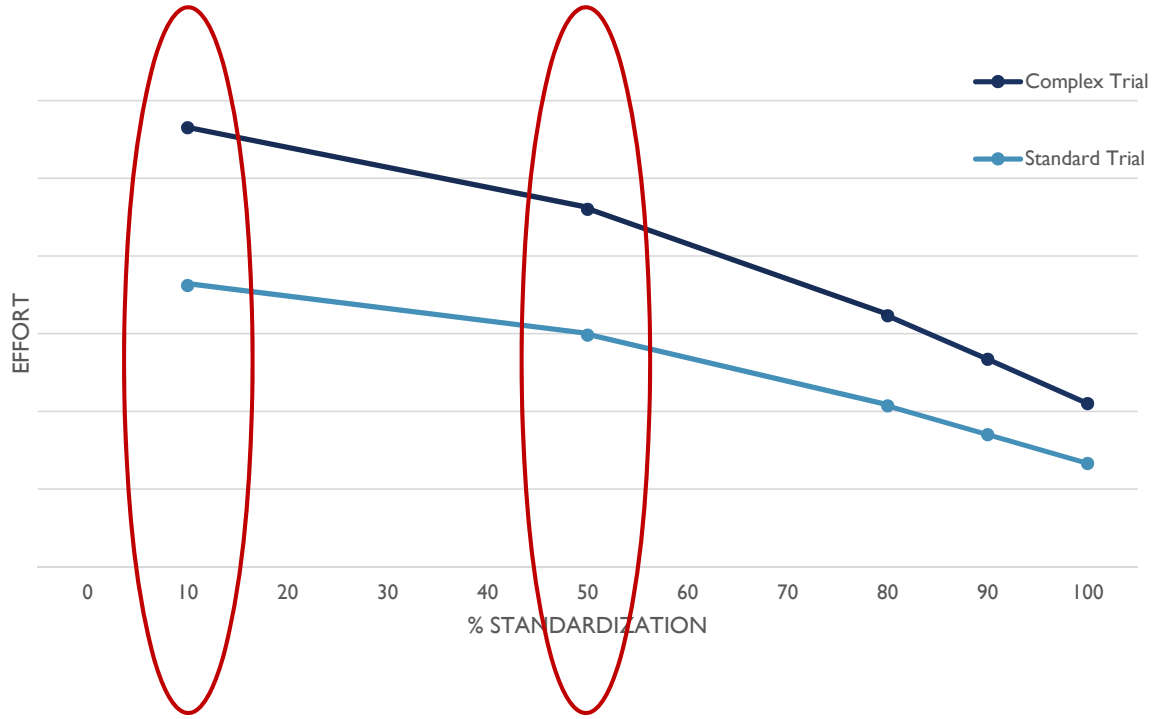
Methodology - Analysis

- *Determine Break-even Point where*

Cost of trial set-up with Standardization	=	Cost of trial without standardization
+ Trial cost		+ Trial cost
+ Investment		-
+ Standards build + Governance + Technology Investment + Maintenance + Process Updates + Training		

LEVELS OF STANDARDIZATION – NONE vs BASIC



No Standardization

Basic Standardization

- Data Collection Modules
- Define conventions for recurring Methods, Computational Algorithms

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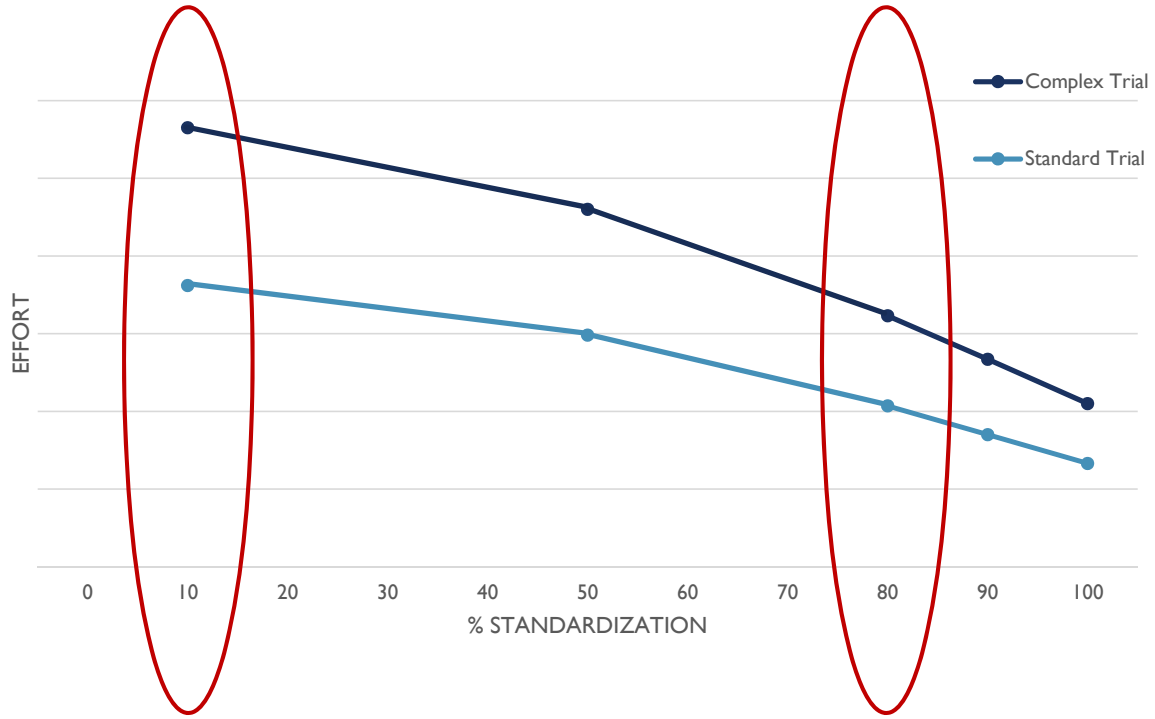
LEVELS OF STANDARDIZATION – NONE vs ADVANCED



No Standardization

Advanced Standardization
- Study endpoints defined
- Provide expectations

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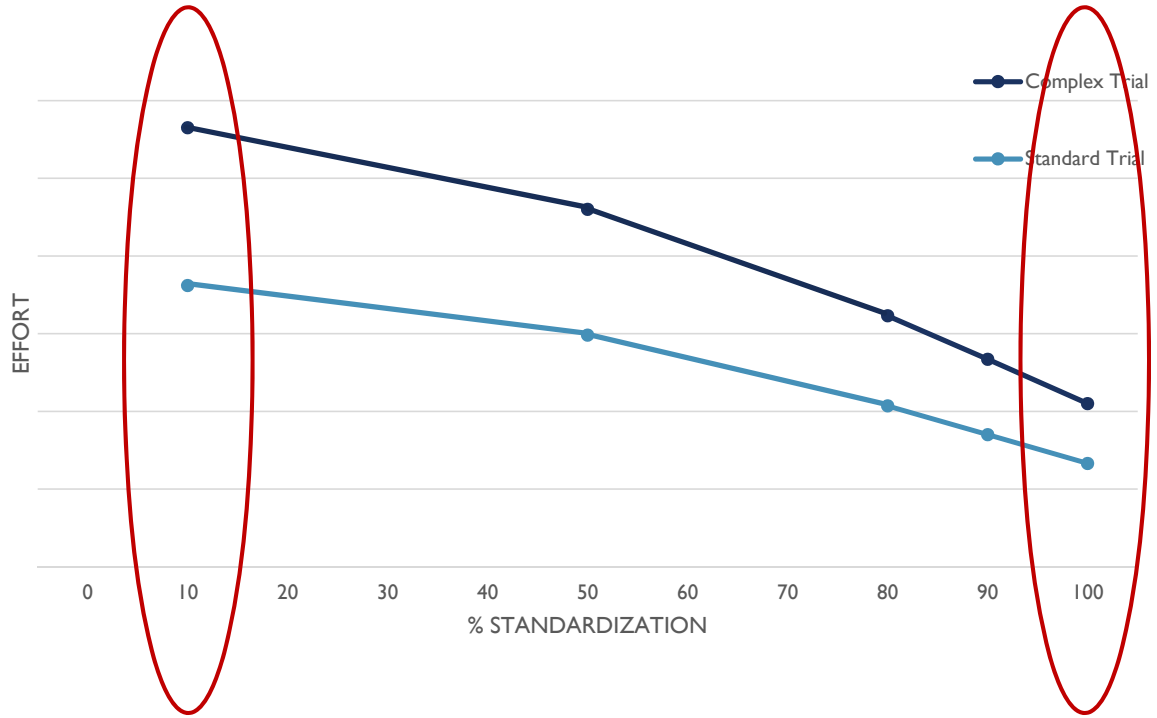
LEVELS OF STANDARDIZATION – NONE vs FULL



No Standardization

Full Standardization
- CRF layouts / define.xml
- Provide study specifications

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BASIC STANDARDIZATION (Define Conventions): Impact on Oversight and Quality Control

- *Effort*
  - ***Translate CDISC SDTM IG in Data Collection Modules***

- *Goals:*
  - ***Have consistent definitions across common domains***
    - **E.g. Reference dates, controlled terminology**
  - ***Minimal standardization Effort (Cost and/or Time)***

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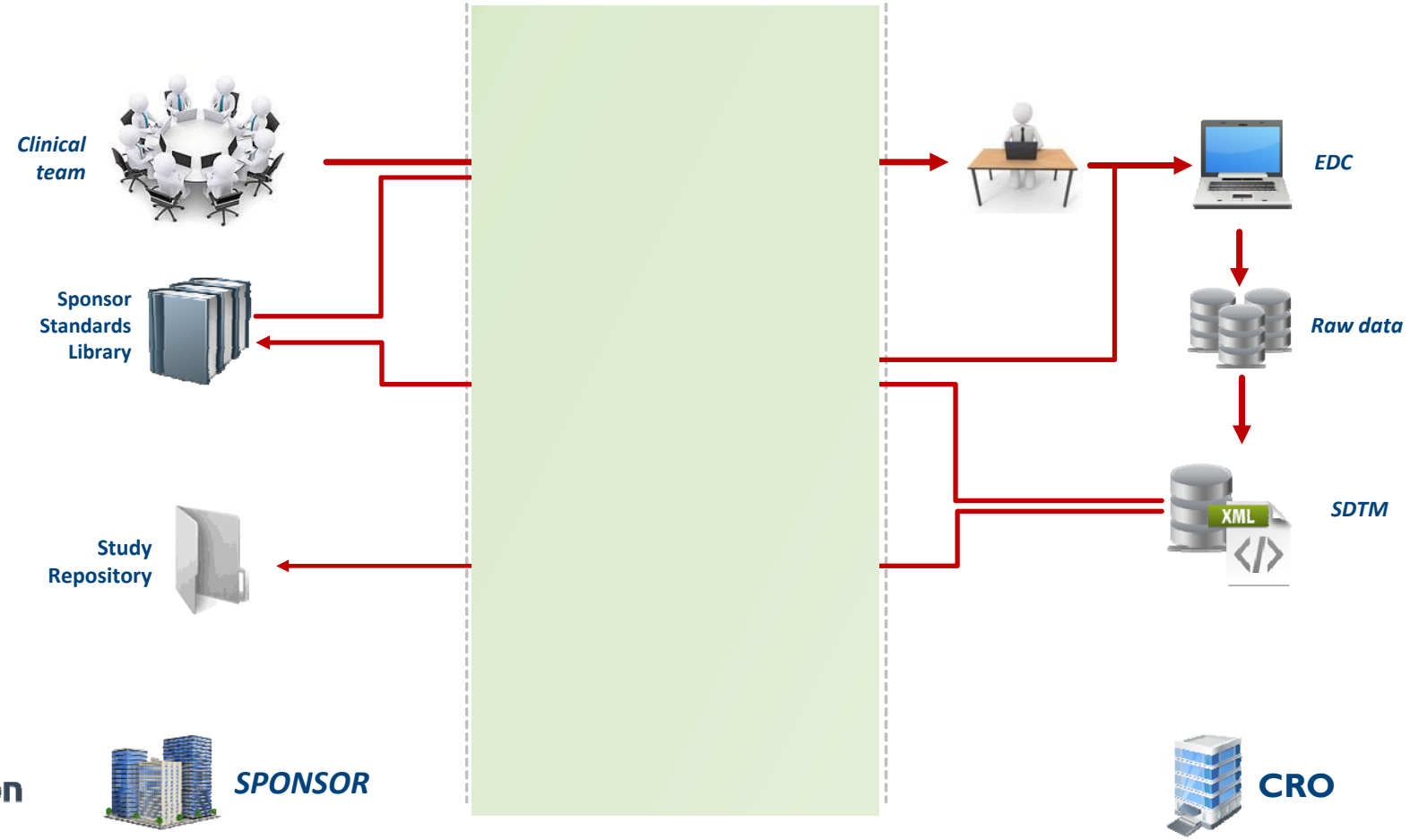
BASIC STANDARDIZATION (define Conventions)

AE		ADVERSE EVENTS	DCM ID: AE_GL_001	
STUDYID	STUDYID	Study	[Free text]	[Preprinted]
SITEID	SITEID	Site	[Free text]	[Preprinted]
SUBJID	SUBJID	Subject	[Free text]	[Preprinted]
Adverse Events				
[Not Submitted]	AEYN	Were any adverse events experienced?	[Radiobutton {Yes; No}]	NY
AESPID	AESPID	AE number	[Numeric field]	[Preprinted]
AETERM	AETERM	What is the adverse event term?	[Free text]	
AESTDTC	AESTDAT	Start Date	[Date {DD-MMM-YYYY}]	
	AESTTIM	Start Time	[24 hr clock]	
AEENDTC	AEENDAT	End Date	[Date {DD-MMM-YYYY}]	
	AEENTIM	End Time	[24 hr clock]	
If Yes, AEENRTPT = ONGOING	AEONGO	Is the adverse event still ongoing?	[Radiobutton {Yes; No}]	NY
AESEV	AESEV	Severity	[Radiobutton {Mild; Moderate; Severe}]	AESEV
AESER	AESER	Is the adverse event serious?	[Radiobutton {Yes; No}]	NY
		If Yes:		
AEREFID	AEREFID	SAE Number	[Free text]	
AESCONG	AESCONG	Congenital Anomaly	[Radiobutton {Yes; No}]	NY
AESDISAB	AESDISAB	Significant Disability	[Radiobutton {Yes; No}]	NY
AESDTH	AESDTH	Death	[Radiobutton {Yes; No}]	NY
AESHOSP	AESHOSP	Hospitalization	[Radiobutton {Yes; No}]	NY
AESLIFE	AESLIFE	Life Threatening	[Radiobutton {Yes; No}]	NY
AESMIE	AESMIE	Other Medically Important Event	[Radiobutton {Yes; No}]	NY
AEREL	AEREL	Relationship to Study Treatment	[Radiobutton {Not related; Unlikely Related; Possibly Related; Probably Related}]	REL
AEACN	AEACN	Action taken with Study Treatment	[Radiobutton {Dose Not Changed; Drug Withdrawn; Dose Reduced}]	ACN

SDTM **CDASH** **CRF questions** **eDC build instructions** **Controlled terminology**

Impact on Oversight and Quality Control



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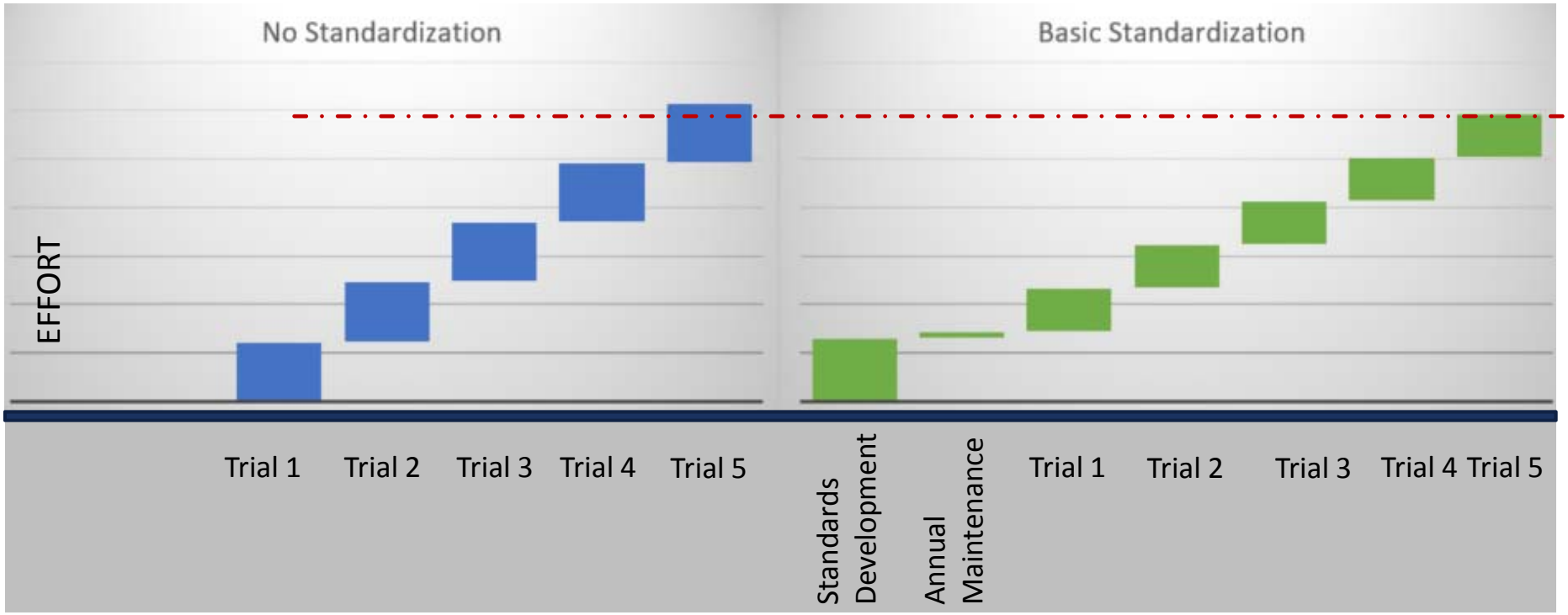
Cost Break-even point for "Complex Trials"



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ADVANCED STANDARDIZATION (Define Expectations):

- *Effort*
  - ***Define Standards for Study Endpoints and Disease Area assessments***
  - ***Store Metadata***
- *Goals:*
  - ***Re-Use of library templates across studies***
  - ***Define Expectations - Unambiguous communication between Sponsor and Vendor***
  - ***Submission preparation***
    - **Consistency across trials**
    - **Facilitate Data Pooling**

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Example Standards Library - metadata

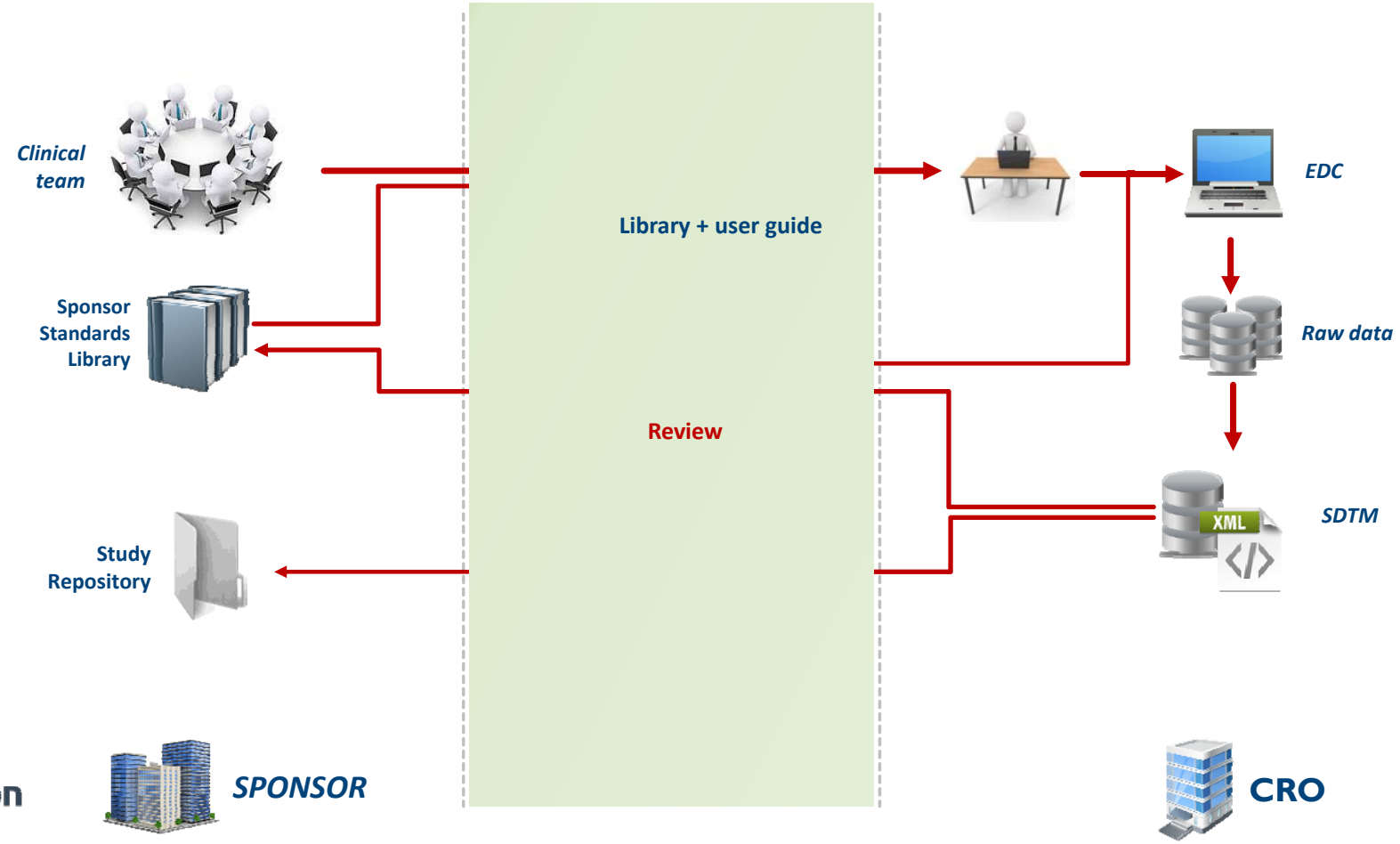
AE	ADVERSE EVENTS		DCM ID: AE_GL_001	
STUDYID	STUDYID	Study	[Free text]	[Preprinted]
SITEID	SITEID	Site	[Free text]	[Preprinted]
SUBJID	SUBJID	Subject	[Free text]	[Preprinted]

Adverse Events	Dataset	Description	Class	Structure	Purpose	Key Variables	Repeating	Reference Data
[Not Submitted]	AE	Adverse Events	EVENTS	One record per adverse event per subject	Tabulation	STUDYID,USUBJID,AECAT,AEDECOD,AESTDTC	Yes	No

Dataset	Variable	Label	Data Type	Length	Significant Digits	Format	Mandatory	Codelist	Origin	Pages	Method	Predecessor	Role	Comment	Core
AE	STUDYID	Study Identifier	text	12			Yes		Protocol				Identifier		Req
AE	DOMAIN	Domain Abbreviation	text	2			Yes	AE.DOMAIN	Assigned				Identifier		Req
AE	USUBJID	Unique Subject Identifier	text	18			Yes		Derived		USUBJID		Identifier		Req
AE	AESEQ	Sequence Number	integer	8			Yes		Derived		SEQ		Identifier		Req
AE	AEGRPID	Group ID	text	20			No		Derived		AEGRPID		Identifier		Perm
AE	AEREFID	Reference ID	text	20			No		CRF				Identifier		Perm
AE	AESPID	Sponsor-Defined Identifier	text	20			No		CRF				Identifier		Perm
AE	AETERM	Reported Term for the Adverse Event	text	200			Yes		CRF				Topic		Req
AE	AEMODIFY	Modified Reported Term	text	200			No		Assigned				Synonym Qualifier		Perm
AE	AELLT	Lowest Level Term	text	200			No	MedDRA	Assigned				Variable Qualifier		Exp
AE	AEDECOD	Dictionary-Derived Term	text	200			No	MedDRA	Assigned				Variable Qualifier		Exp
AE	AEPTCD	Preferred Term Code	integer	8			No	MedDRA	Assigned				Variable Qualifier		Exp
AE	AEHLT	High Level Term	text	200			No	MedDRA	Assigned				Variable Qualifier		Exp
AE	AEHLTCD	High Level Term Code	integer	8			No	MedDRA	Assigned				Variable Qualifier		Exp
AE	AEHLGT	High Level Group Term	text	200			No	MedDRA	Assigned				Variable Qualifier		Exp
AE	AEHLGTCD	High Level Group Term Code	integer	8			No	MedDRA	Assigned				Variable Qualifier		Exp
AE	AEBDSYCD	Body System or Organ Class Code	integer	8			No	MedDRA	Assigned				Variable Qualifier		Exp
AE	AESOC	Primary System Organ Class	text	200			No	MedDRA	Assigned				Variable Qualifier		Exp
AE	AESOCCD	Primary System Organ Class Code	integer	8			No	MedDRA	Assigned				Variable Qualifier		Exp
AE	AELOC	Location of Event	text	200			No	LOC	CRF				Record Qualifier		Perm
AE	AESEV	Severity/Intensity	text	20			No	AESEV	CRF				Record Qualifier		Perm
AE	AESER	Serious Event	text	1			No	NY_YN	CRF				Record Qualifier		Exp
AE	AEACN	Action Taken with Study Treatment	text	40			No	ACN	CRF				Record Qualifier		Exp
AE	AEACNOTH	Other Action Taken	text	200			No		CRF				Record Qualifier		Perm
AE	AEREL	Causality	text	20			No	REL	CRF				Record Qualifier		Exp
AE	AERELNST	Relationship to Non-Study Treatment	text	40			No		CRF				Record Qualifier		Perm

ID	Name	NCI Codelist Code	Data Type	Order	Term	NCI Term Code	Decoded Value	Extensible
ACN	Action Taken with Study Treatment	C66767	text		DOSE INCREASED	C49503	Dose Increased	N
ACN	Action Taken with Study Treatment	C66767	text		DOSE NOT CHANGED	C49504	Dose Not Changed	N
ACN	Action Taken with Study Treatment	C66767	text		DOSE REDUCED	C49505	Dose Reduced	N
ACN	Action Taken with Study Treatment	C66767	text		DRUG INTERRUPTED	C49501	Drug Interrupted	N
ACN	Action Taken with Study Treatment	C66767	text		DRUG WITHDRAWN	C49502	Drug Withdrawn	N
ACN	Action Taken with Study Treatment	C66767	text		NOT APPLICABLE	C48660	Not Applicable	N
ACN	Action Taken with Study Treatment	C66767	text		UNKNOWN	C17998	Unknown	N

Impact on Oversight and Quality Control



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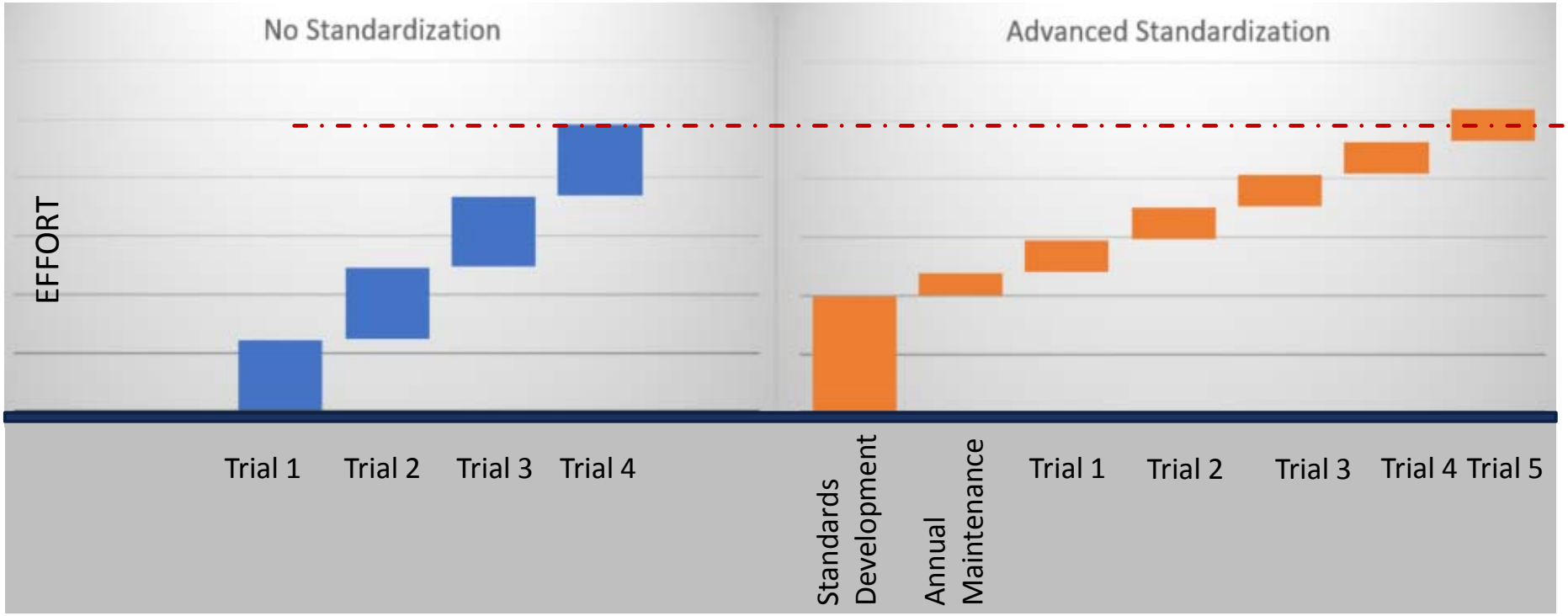

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FULL STANDARDIZATION (Provide Specifications):

- *Effort*
  - ***Implement Metadata Repository***
  - ***End-End data standards creation (CDASH/SDTM/Define.xml)***
  - ***Study Specific standards selection and modification Interface***
- *Goal :*
  - ***Data specifications 100 % defined***
  - ***Automation of study build and QC***

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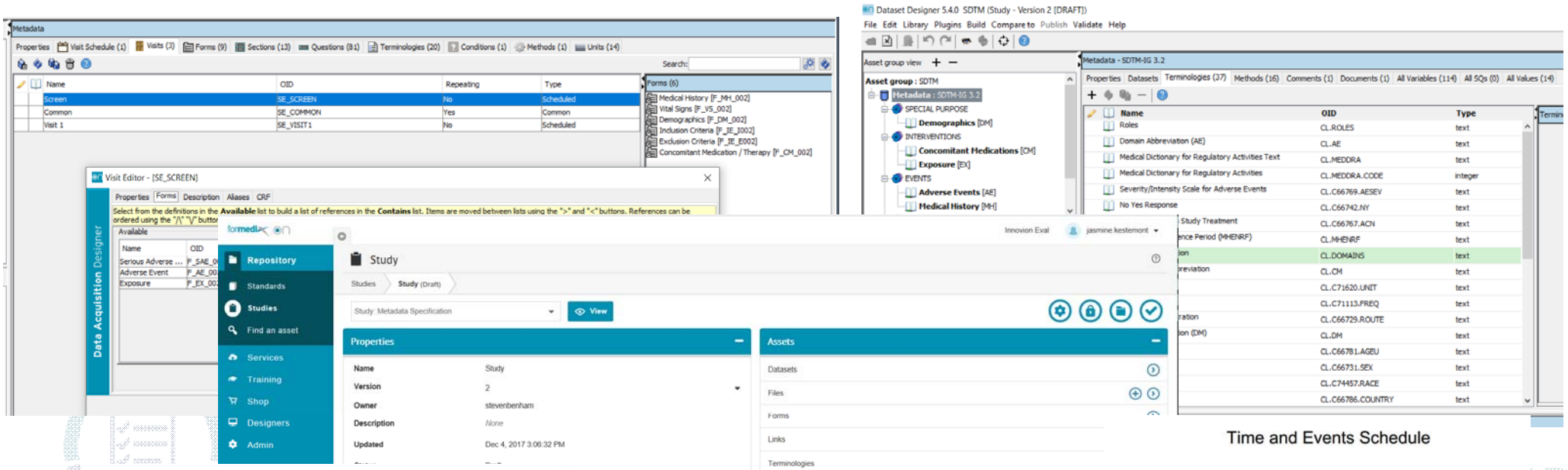
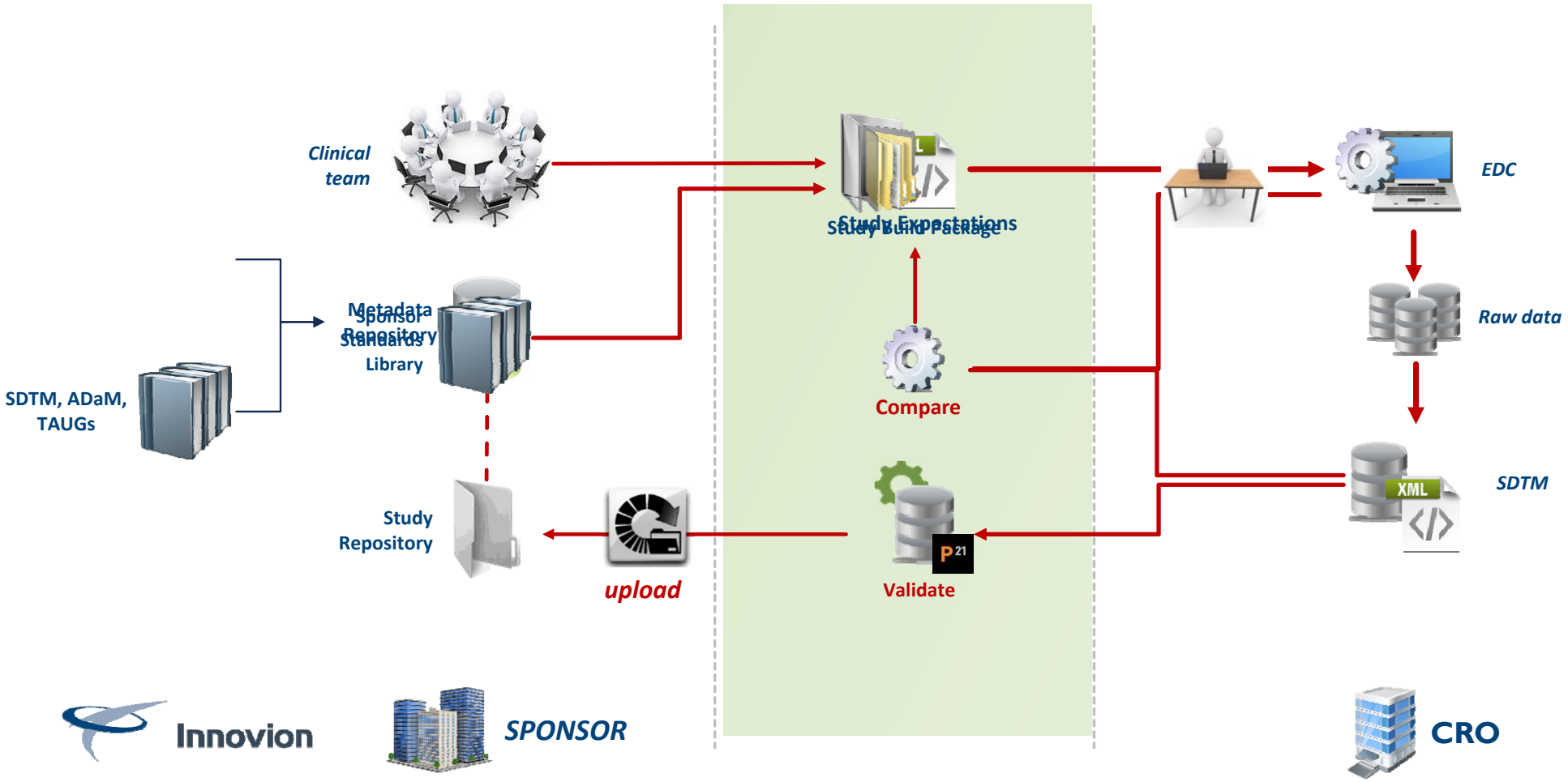
Example Metadata Repository



Impact on Oversight and Quality Control



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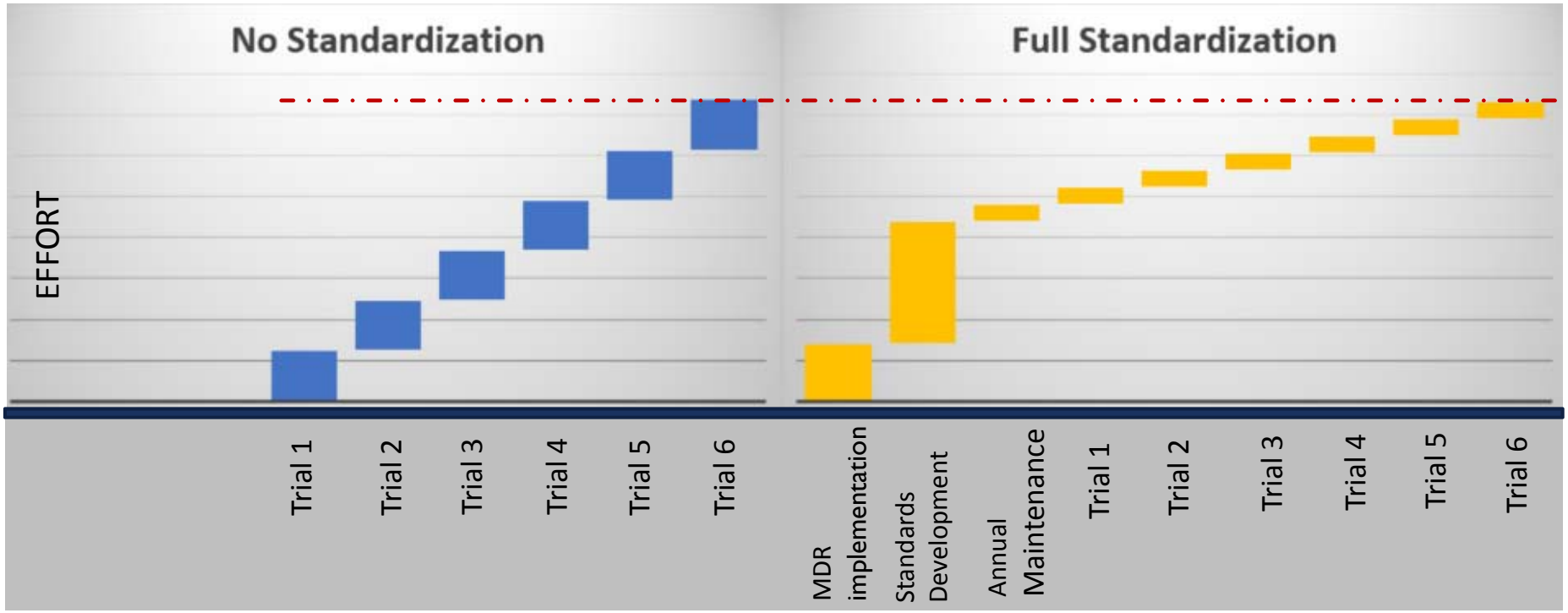

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Summary: achieving Return-on-Investment

Basic Standardization (Defining Conventions)		Advanced Standardization (Expectations)		Full Standardization (Specifications)	
Standard Trials	Complex Trials	Standard Trials	Complex Trials	Standard Trials	Complex Trials
10	5	7	5	10	6

- *Impact*
  - ***Larger for "complex" trials***

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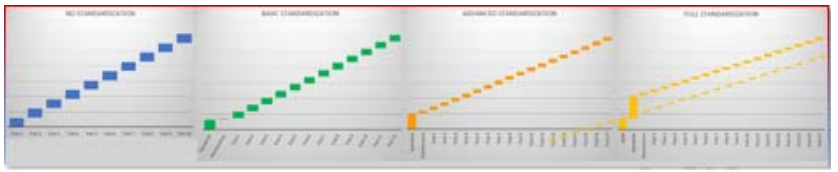
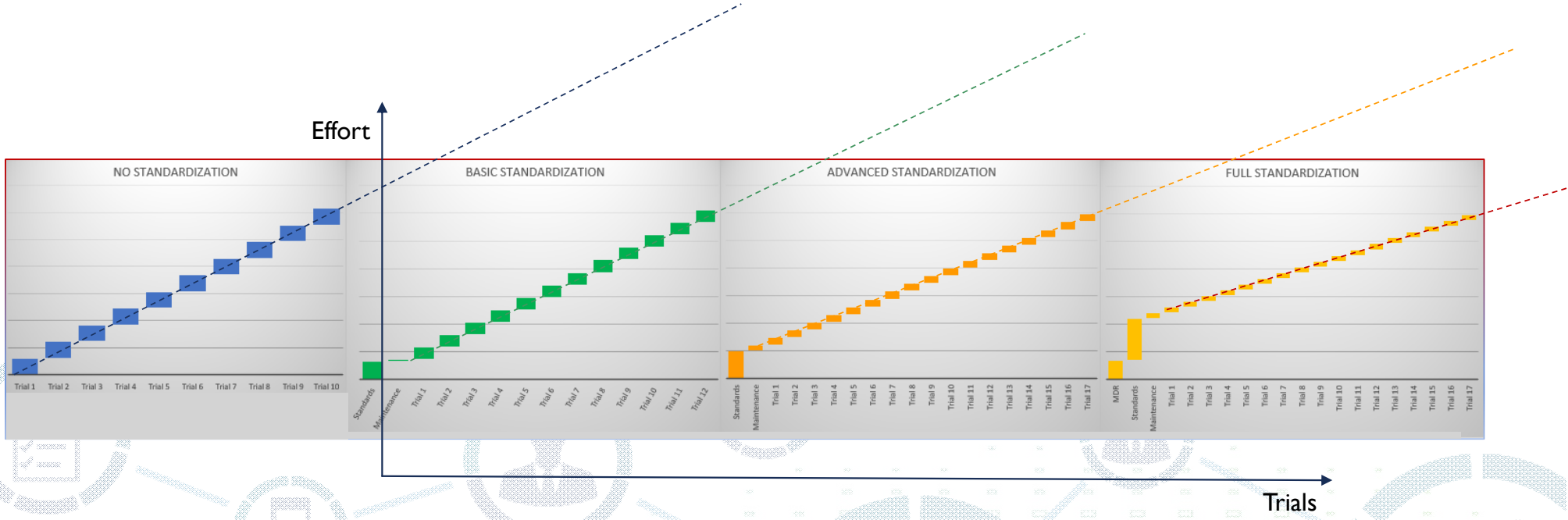
Beyond the Break-even Point





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Conclusion

- *Benefits of Standardization*
  - ***Shortened Set-up Timelines***
  - ***Reduced Quality Control***

  → ***Reduced Cost***
- *ROI depends on*
  - ***Size of Portfolio and Complexity of trials***
- *With any Standards implementation*
  - ***Ensure you have the right skillset and discipline***

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A passion for data