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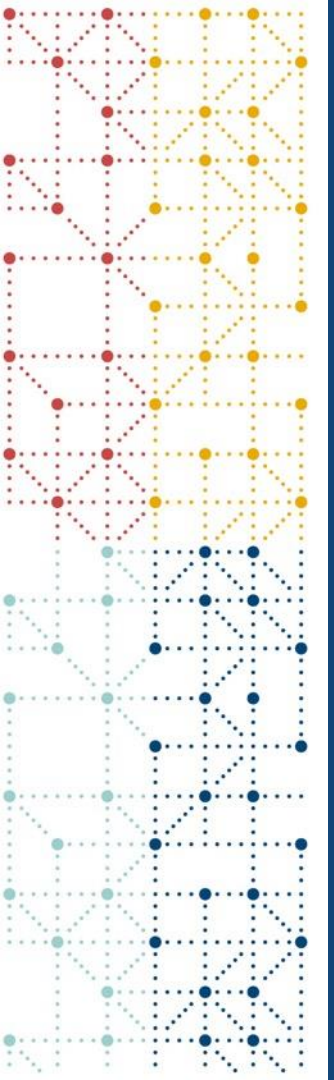
- *The views and opinions expressed in this presentation are those of the author(s) and do not necessarily reflect the official policy or position of CDISC.*

Agenda

1. Introduction
2. Drivers for Change
3. Three Dimensions of Standardization
4. Conclusion



Introduction

One Dimensional Standardization

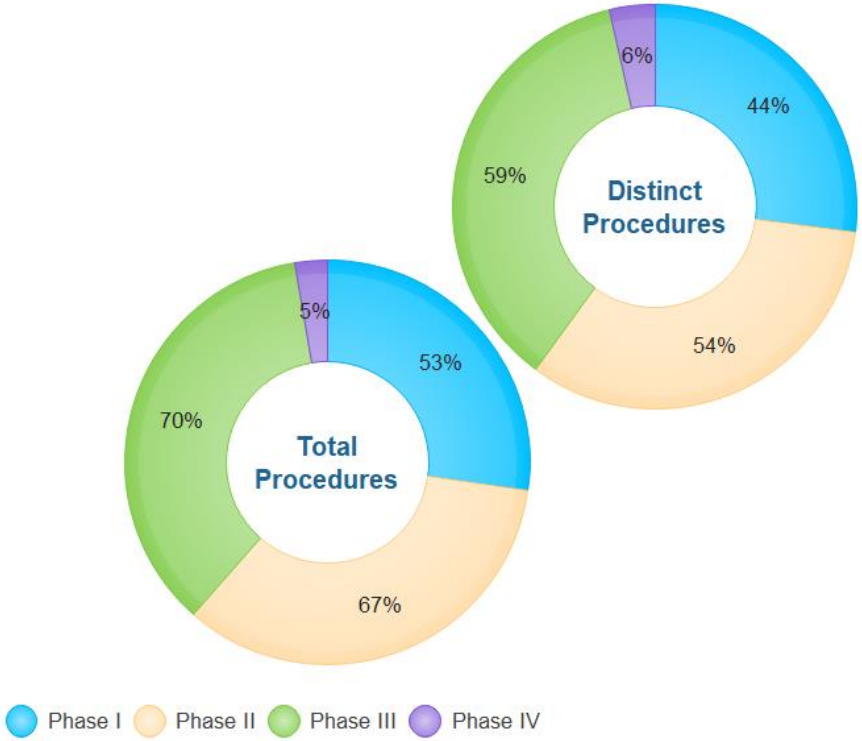
Has the Benefit of Data Standards been fully Realized?

- The bulk of standardization in clinical trials today revolves around the CDISC standards, not least because of regulatory mandates
- End-to-end standardization has focused largely on Data Collection (CDASH) to Tabulation (SDTM)
- Standardization is at the study level with some consideration given to managing consistency across studies in a program
- Standardization is pretty much one-dimensional
- Increasing complexity in study design and data sources continually challenge this one-dimensional approach
- The benefits of data standards cannot be realized with this limited approach

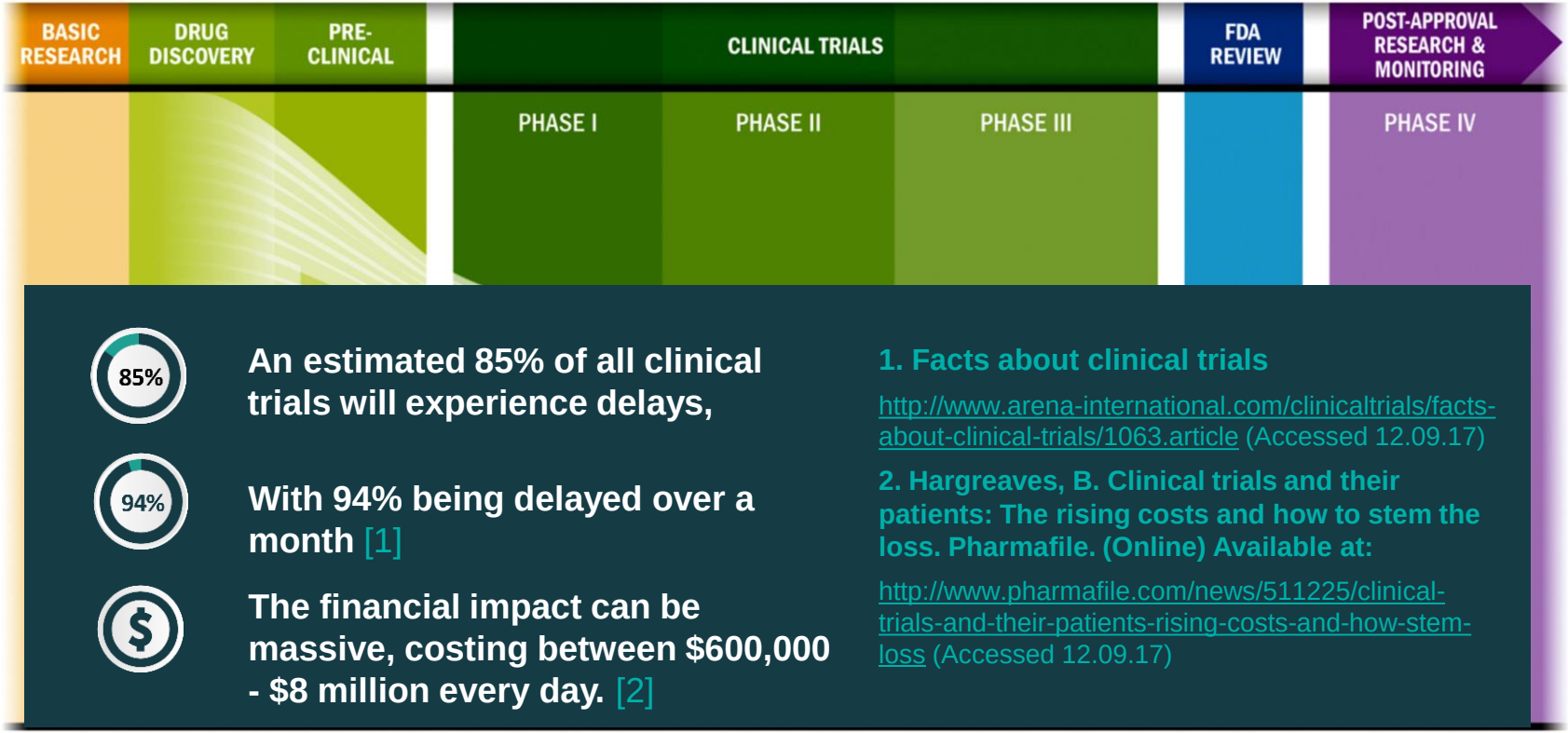
Protocol Design Trends

A Typical Phase III Protocol	2001 - 2005	2011-2015
Total Number of Endpoints	7	13
Total Number of Eligibility Criteria	31	50
Total Number of Procedures	110	187
Total Number of Procedures per visit	10	13
Proportion of Procedures that are ‘Non Core’	18%	31%
Total number of data points collected*	494,236	929,203

Source: K. Getz, Tufts CSDD; *Medidata Solutions



Drivers for Change



Key: IND: Investigational New Drug Application, NDA: New Drug Application, BLA: Biologics License Application

* The average R&D cost required to bring a new, FDA-approved medicine to patients is estimated to be $2.6 billion over the past decade (in 2013 dollars). Including the cost of the many potential medicines that do not make it through to FDA approval.

Source: PhRMA adaptation based on Tufts Centre for the Study of Drug Development (CSDD) Briefing: "Cost of Developing a New Drug," Nov.2014. Tufts CSDD & School of Medicine., and US FDA Infographic, "Drug Approval Process," http://www.fda.gov/downloads/Drugs/ResourcesForYou/Consumers/UCM284393.pdf (accessed Jan.20,2015)

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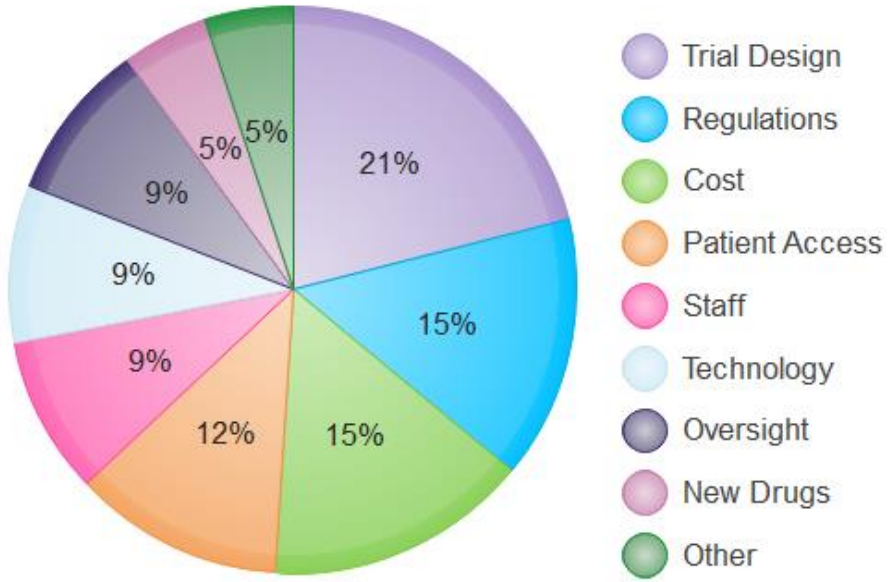
Clinical Operations Challenges



knect365.com, Clinical Trials Innovation, Report: Biggest Challenges Clinical Trials

Clinical trials have been growing increasingly complex for years – under pressure to design trials that:

- Give the right answers
- Simple and unobtrusive for patients
- Acceptable to regulators and payers

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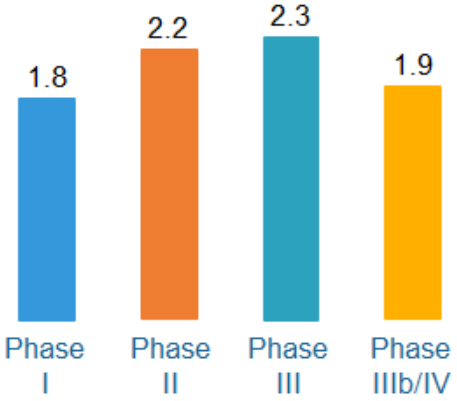
Protocol Amendments Trends

Mean number of amendments per protocol



Implementation cost per amendment:

- On average 3 month of unplanned time
- 141 K$ in direct cost of Phase II protocols
- 535 K$ in direct cost of Phase III protocols

Top reason for amendment

Phase I	New and modified safety assessment (15.4% of total)
Phase II	Change in Eligibility Criteria (17.2%)
Phase III	Change in Eligibility Criteria (15.2%)
Phase IIIb/IV	Change in Eligibility Criteria (17.9%)

Source: K. Getz, Tufts CSDD

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Three Dimensions of Standardization

A Digitized Clinical Development Process

Three Dimensions of Standardization

- End-to-End Clinical Study Standards – starting with structured protocol development, and structured development of the schedule of protocol activities (procedures).
- Project Standardization - alignment of trials within the Clinical Development Project (CDP) and alignment of trials with the Target Product Profile (TPP),
- CDO Process Standardization – covering all aspects of Clinical Development Operations

The Role of TransCelerate's Common Protocol Template

- The protocol must be considered in end-to-end standardization as it is the first point where deviation from standards can occur
- The CPT provides an excellent starting point for protocol standardization, but we require more than a template. It provides the opportunity for development of a common protocol model
- A digitized authoring solution, supported up by an MDR, provides the bridge between study planning and study and study execution
- A digitized schedule of activities (SOA) connected to downstream standards drives automation and consistency
- A digitized protocol connected to downstream standards reduces cycle times on study start up

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The Second Dimension of Standardization

- Standardization of the Clinical Development Plan (CDP)
- Once a digitized end-to-end study standardization (protocol to submission) is in place we can standardize at the program level
- With a metadata model that supports CDP a digitized solution can drive standardization across a program
- A digitized solution with workflow capabilities can capture decisions for changes made to the CDP over time. Stored centrally this provides:
  - A central knowledgebase
  - A system of record for CDP changes
  - A feedback mechanism to refine subsequent studies in a plan

The Third Dimension of Standardization

- Clinical Development Process Standardization
- Digitized end-to-end study standardization with a digitized CDP provides opportunities for standardization and automation of Clinical Development Processes.
- With a digitized protocol solution the protocol authoring task is no longer a linear, or, serial process
- No longer dependent on a final signed protocol “document” multiple processes can run in parallel with a digitized protocol solution
  - Feasibility & Recruitment
  - Clinical Supply Chain
  - EDC build
- The standards driven approach improves overall quality

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Benefits of Digitized 3D Standardization

01 Reduce number of protocols amendments prior First-Patient-First-Visit (FPFV)

02 Reduce number of CRO contract changes due to late change in design or inconsistent usage of medical standards

03 Reduce number of data points being captured

04 Direct access and use of medical standards in Metadata Repository (MDR)

05 Use structured protocol data to fully realize End to End (E2E) efficiency goals

06 Transforming TPP, CDP and Study Definition into an integrated digital platform to leverage the benefits of having this information available in a machine-readable format

80% of all benefits derived from Standards occur in the study startup phase
(**Gartner:** CDISC standards business case)

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Conclusion

It’s Time to Think of Clinical Development Standardization in 3D

Outlook

- Digitized Protocol Solution
  - CPT based
- MDR Integration
  - With downstream system integrations
- CDP/TPP view and alignment
- This is Disruptive Innovation with the capability to significantly improve clinical develop process automation
  - Reduce unnecessary protocol amendments
  - Adapt the CDP with a digitized feedback loop
  - Make critical program decisions early
  - Reduce time to market
  - Bring medicines to patients sooner

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Thank You!