The Interface Between Biostatistics and Clinical Data Management

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Association of Clinical and Translational Statisticians
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Outline

- Rationale for discussion this topic
- Data Management discipline
- Changing landscape of research
- Data management in *Team Science*
- Education and professional development
- Interactions
- Future challenges

Goals

- Gain an appreciation of the importance of data management as a discipline
- Enhance interactions between biostatistics and clinical data management
- Know what to expect in the future

Why discuss data management at a biostatistics meeting?

Data Quality

Criteria for Reproducible Research*

Research Component	Requirement
Data	Analytical data set is available.
Methods	Computer code underlying figures, tables, and other principal results is made available in a human-readable form. In addition, the software environment necessary to execute that code is available.
Documentation	Adequate documentation of the computer code, software environment, and analytical data set is available to enable others to repeat the analyses and to conduct other similar ones.
Distribution	Standard methods of distribution are used for others to access the software, data, and documentation.

*from Peng, Dominici, Zeger. *Am J Epidemiol* 2006;163:783–789

Data Quality

First critical element in the reproducible research chain

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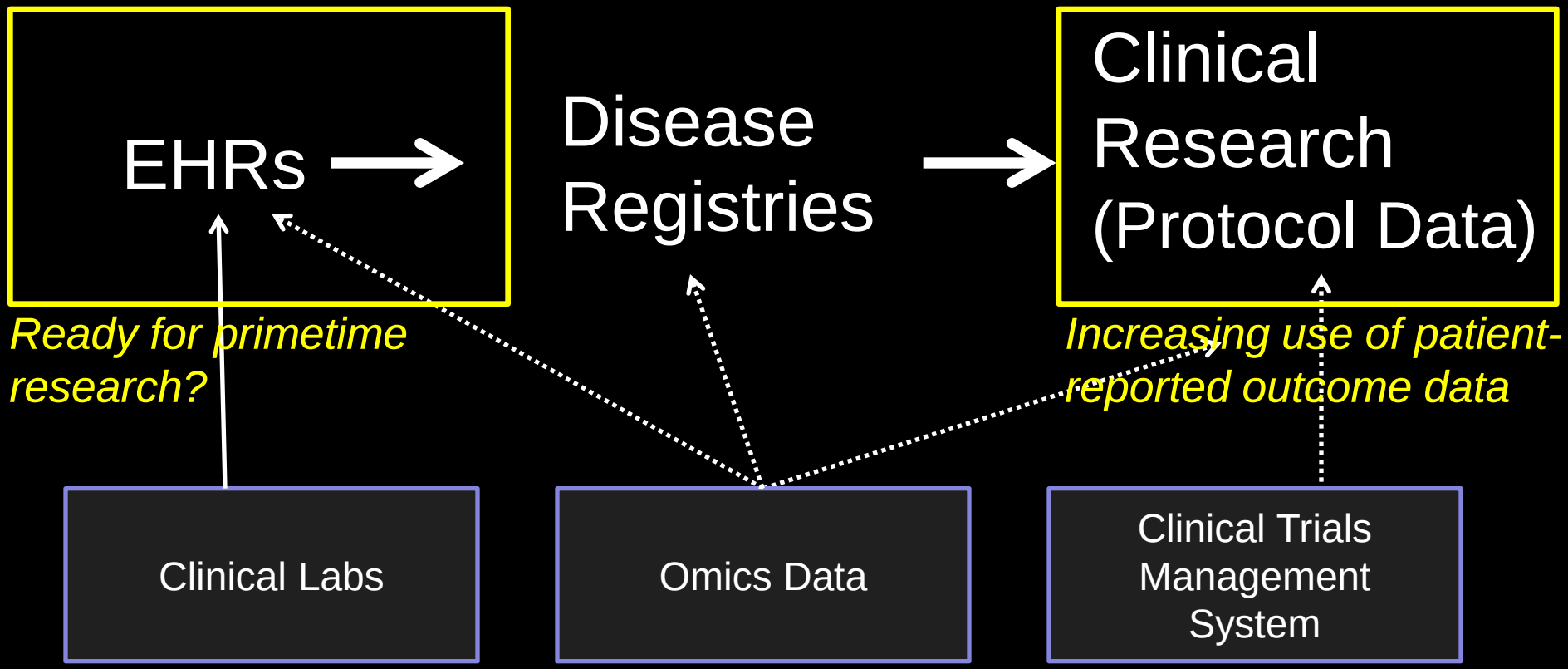
Another reason to discuss the topic...

Much more stringent regulatory climate

Diverse Data Sources



We need a workforce of research professionals who can help define, collect, curate and disseminate data that are of sufficient quality to support human studies research.

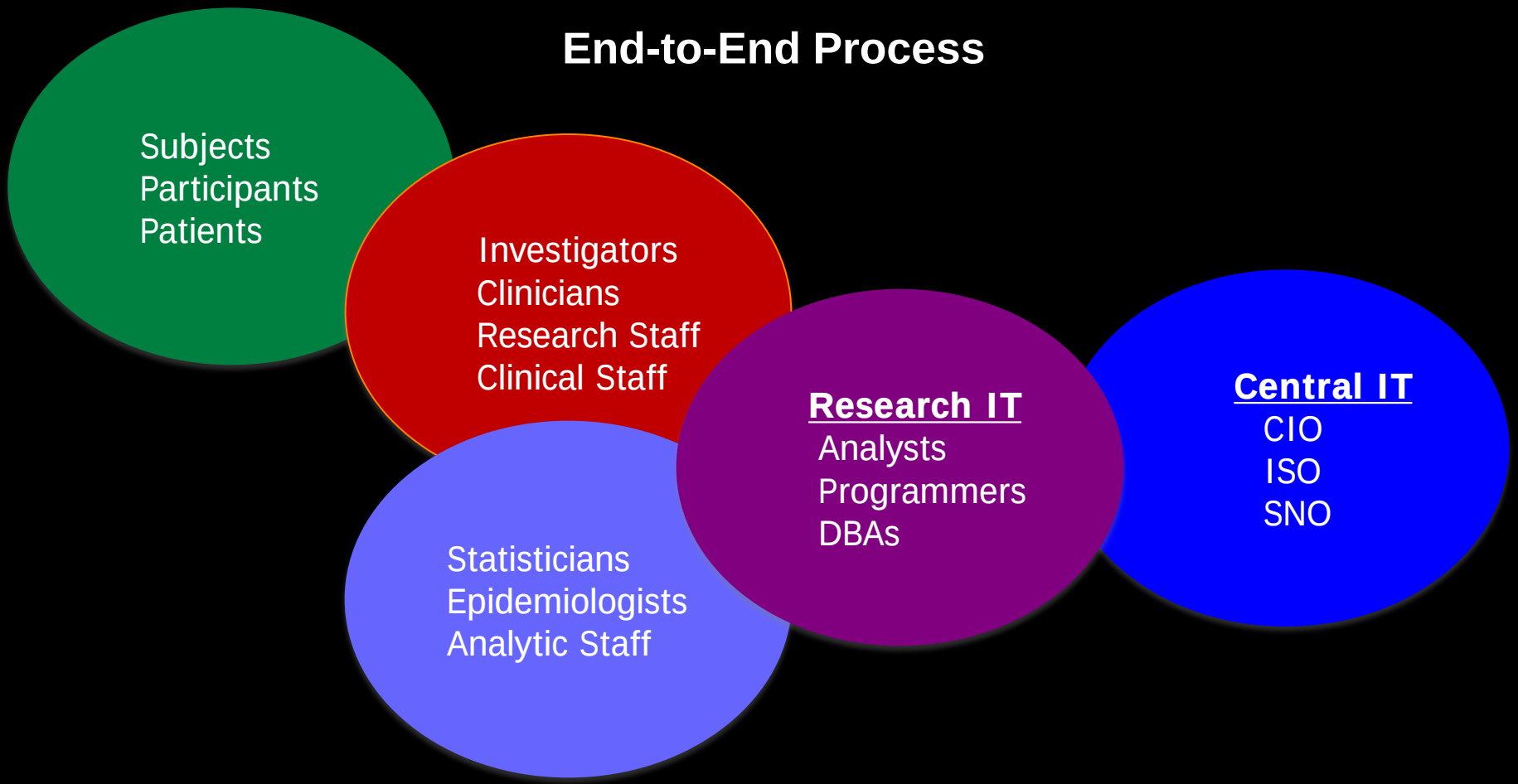
Data Management Definition

Data Management

- The development, execution and supervision of plans, policies, programs and practices that control, protect, deliver, and enhance the value of data and information assets*

*Data Management Association, Data Management Body of Knowledge (DAMA-DMBOK), 2008

Who's Involved in Data Management?



Data Management within the Research Process

Protocol Development

Data Management Process

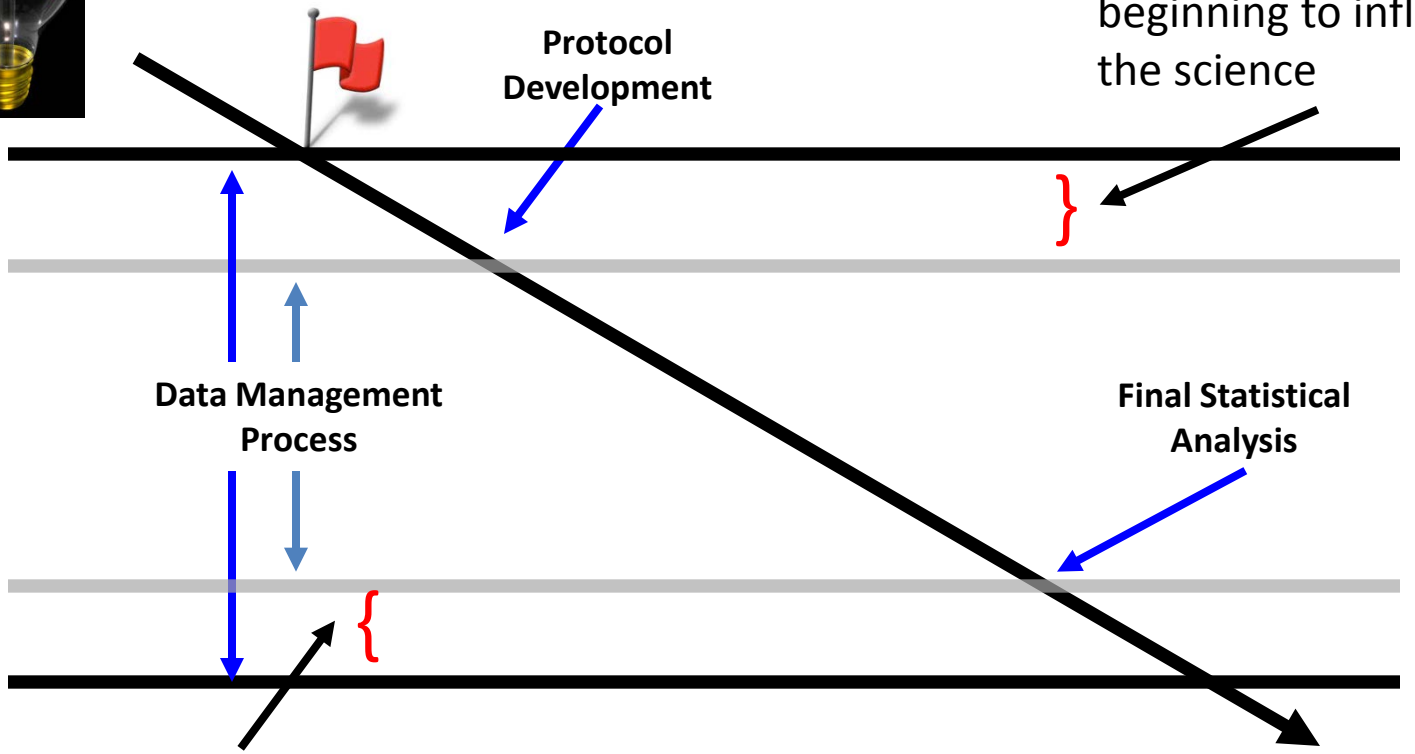
IT Involvement

Final Statistical Analysis

JAMA®
The Journal of the American Medical Association

Data Management Changing Within the Research Process

Data management considerations are beginning to influence the science



Storage and long term utilization affect the data long after the protocol's final analysis

JAMA®
The Journal of the American Medical Association

Changing Landscape of Clinical Research

- Increasing regulatory requirements posing a threat/new opportunities

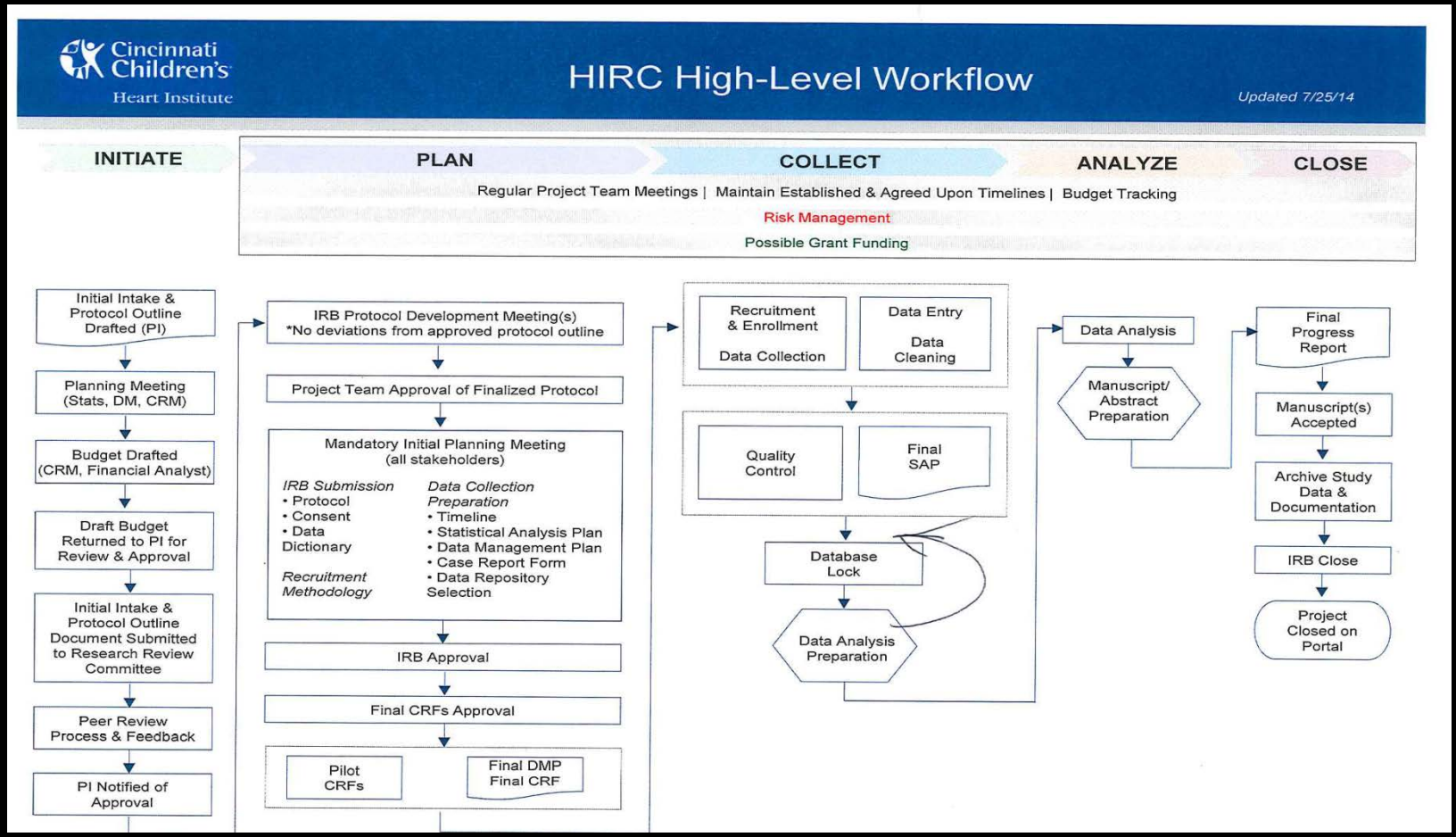
Changing Landscape of Clinical Research

- Increased FDA scrutiny of investigators, sites, and sponsors[1,2,3]
  - Trustworthiness of data, participants safety
  - Clinical breakthroughs = f(confidence in our data) = f(reliability of our data/processes)
- Passage of FDA Safety and Innovation Act (PL 112-144) on July 9, 2012[4]
  - Develop 'standardized clinical data terminology' (e.g., CDISC, CDASH, SDTM)
  - Issue guidance on standards and given authority to enforce standards
  - Begin tracking 'standards compliant' submissions and efficiency by 2015
  - Data standards should be incorporated from the beginning of a study, including Case Report Forms (CRFs), CDM Systems, and Statistical Analysis Plans[5]
- NIH is *not* the FDA, but, many NIH studies end up as an FDA submission
  - NCI, NINDS, NICHD, NIAIDS are actively adopting CDISC Standards
  - NIH Roadmap Projects (TB Roadmap, CV Roadmap)
  - REDCap CDASH Library

Changing Landscape of Clinical Research

- Increasing regulatory requirements posing a threat/new opportunities
- Wild west days of doing whatever the investigator wants are ending

Changing Landscape of Clinical Research



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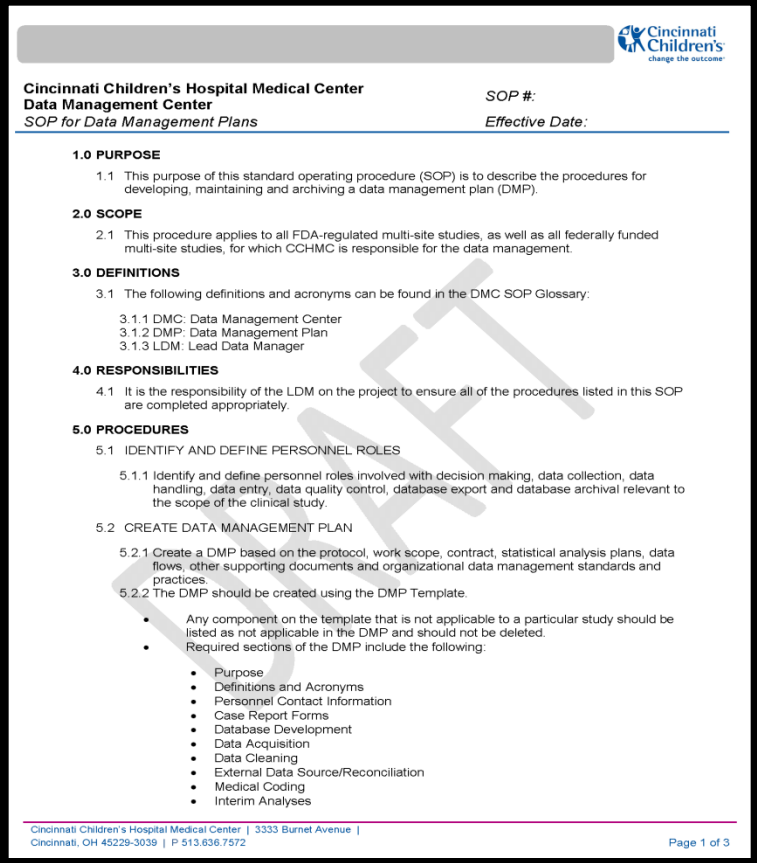
Changing Landscape of Clinical Research

- Increasing regulatory requirements posing a threat/new opportunities
- Wild west days of doing whatever the investigator wants are ending
- Institutional infrastructure investment is even more important
- Investigators can be convinced that they have to use Good Clinical Data Management Practices for legal reasons
- Attitude of someone saying “I know biostatistics there I know data management is simply not valid

Changing Landscape of Clinical Research



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SOP for Data Management Plans

SOP #:
Effective Date:

1.0 PURPOSE

1.1 This purpose of this standard operating procedure (SOP) is to describe the procedures for developing, maintaining and archiving a data management plan (DMP).

2.0 SCOPE

2.1 This procedure applies to all FDA-regulated multi-site studies, as well as all federally funded multi-site studies, for which CCHMC is responsible for the data management.

3.0 DEFINITIONS

3.1 The following definitions and acronyms can be found in the DMC SOP Glossary:

3.1.1 DMC: Data Management Center
3.1.2 DMP: Data Management Plan
3.1.3 LDM: Lead Data Manager

4.0 RESPONSIBILITIES

4.1 It is the responsibility of the LDM on the project to ensure all of the procedures listed in this SOP are completed appropriately.

5.0 PROCEDURES

5.1 IDENTIFY AND DEFINE PERSONNEL ROLES

5.1.1 Identify and define personnel roles involved with decision making, data collection, data handling, data entry, data quality control, database export and database archival relevant to the scope of the clinical study.

5.2 CREATE DATA MANAGEMENT PLAN

5.2.1 Create a DMP based on the protocol, work scope, contract, statistical analysis plans, data flows, other supporting documents and organizational data management standards and practices.
5.2.2 The DMP should be created using the DMP Template.

- Any component on the template that is not applicable to a particular study should be listed as not applicable in the DMP and should not be deleted.
- Required sections of the DMP include the following:
  - Purpose
  - Definitions and Acronyms
  - Personnel Contact Information
  - Case Report Forms
  - Database Development
  - Data Acquisition
  - Data Cleaning
  - External Data Source/Reconciliation
  - Medical Coding
  - Interim Analyses

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Page 1 of 3

DRAFT

Clinical Data Management Standard Operating Procedures

- Archiving Study Data
- Case Report Form Creation, Approval, and Release
- Case Report Form Tracking, Storage, and Archival
- Database Audit
- Database Design and Setup
- Database Lock
- Data Management Plans
- Data Discrepancies
- Data Entry Processes
- Data Exports
- Handling External Electronic Data
- Medical Coding
- Data Management Plan Template

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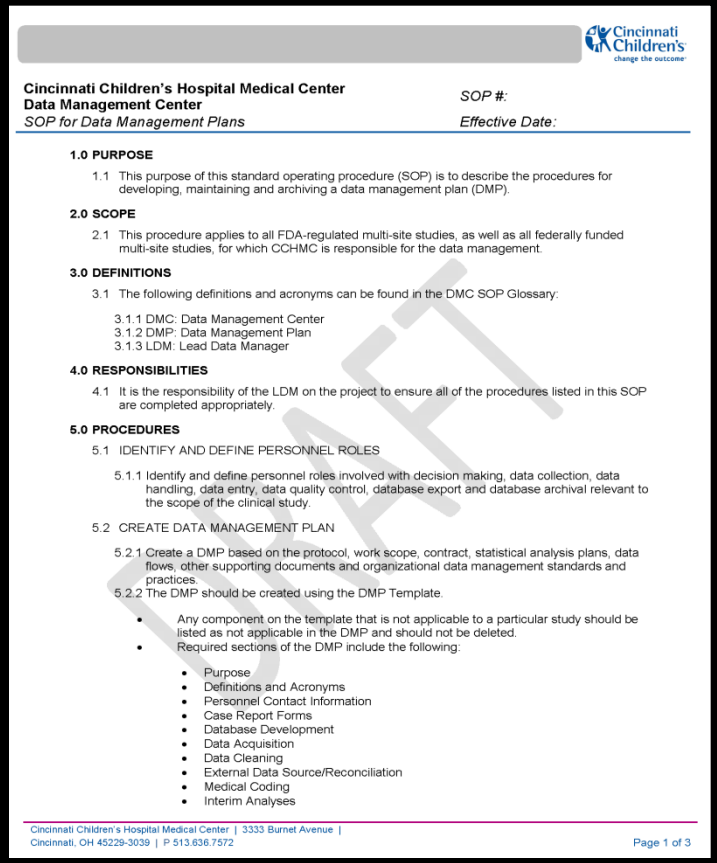
Changing Landscape of Clinical Research



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change the outcome

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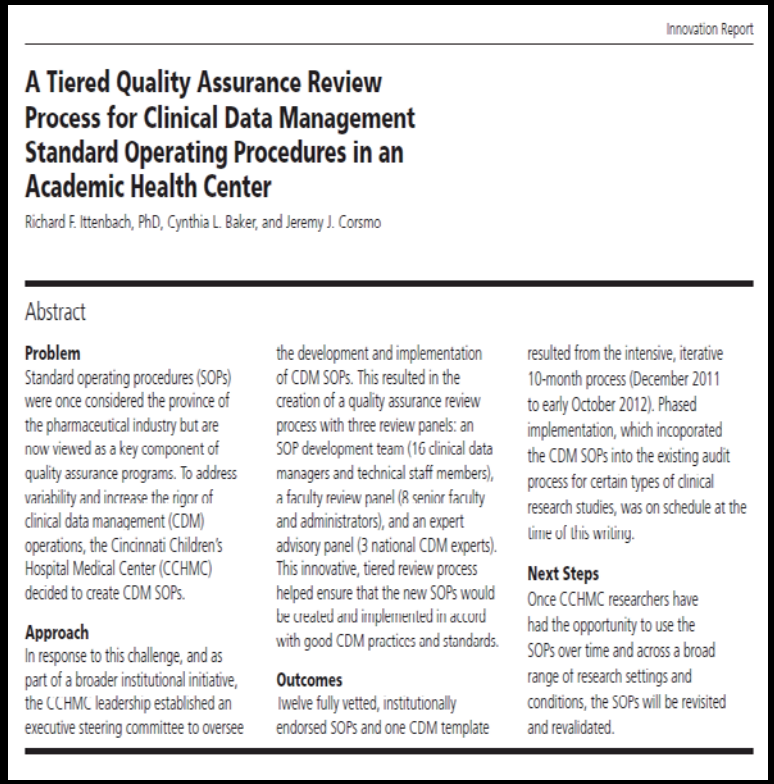

Innovation Report

A Tiered Quality Assurance Review Process for Clinical Data Management Standard Operating Procedures in an Academic Health Center

Richard F. Ittenbach, PhD, Cynthia L. Baker, and Jeremy J. Corsmo

Abstract

Problem
Standard operating procedures (SOPs) were once considered the province of the pharmaceutical industry but are now viewed as a key component of quality assurance programs. To address variability and increase the rigor of clinical data management (CDM) operations, the Cincinnati Children's Hospital Medical Center (CCHMC) decided to create CDM SOPs.

Approach
In response to this challenge, and as part of a broader institutional initiative, the CCHMC leadership established an executive steering committee to oversee the development and implementation of CDM SOPs. This resulted in the creation of a quality assurance review process with three review panels: an SOP development team (16 clinical data managers and technical staff members), a faculty review panel (8 senior faculty and administrators), and an expert advisory panel (3 national CDM experts). This innovative, tiered review process helped ensure that the new SOPs would be created and implemented in accord with good CDM practices and standards.

Outcomes
Twelve fully vetted, institutionally endorsed SOPs and one CDM template resulted from the intensive, iterative 10-month process (December 2011 to early October 2012). Phased implementation, which incoporated the CDM SOPs into the existing audit process for certain types of clinical research studies, was on schedule at the time of this writing.

Next Steps
Once CCHMC researchers have had the opportunity to use the SOPs over time and across a broad range of research settings and conditions, the SOPs will be revisited and revalidated.

Source: Ittenbach et al. (2014) *Acad Med, 89*(5), 745-748.

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Engagement of Clinical Data Managers in Team Science

Strengthening the interface between biostatisticians and clinical data managers is completely consistent with the NIH Roadmap/Common Fund [6, 7, 8]

New Pathways to Discovery

Address the needs of complex biological systems by expanding access to "technologies, databases, and other scientific resources"... more easily adaptable to individual researcher's needs

Research Teams of the Future

Force movement of scientists beyond the confines of their own disciplines into new organizational models ('team science') with more holistic (nontraditional) perspectives and methods

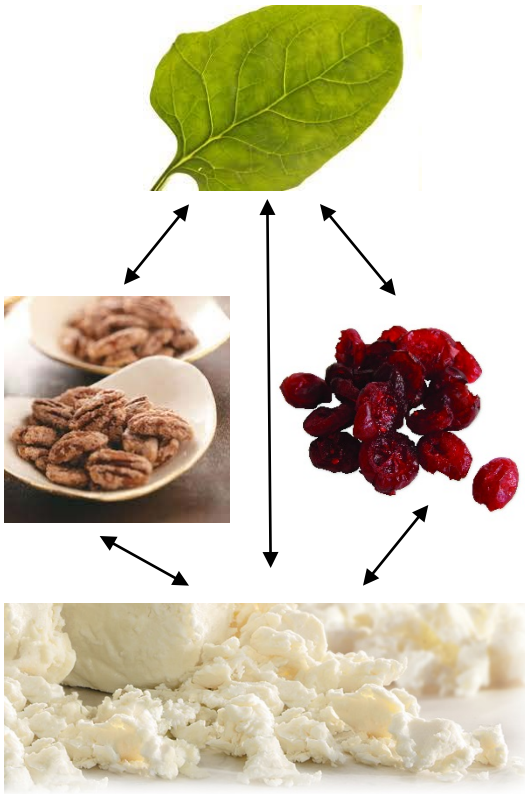
Reengineering the Clinical Research Enterprise

Establishment of better, stronger clinical research networks with better training mechanisms and more consistent standards and database requirements

Team Science

Interdisciplinary, Multidisciplinary, Transdisciplinary

Interdisciplinary **Multidisciplinary** **Transdisciplinary**



Engagement of Clinical Data Managers in Team Science

Who are clinical data mangers?

Rapidly growing professional specialty of health-care knowledge that integrates training from biomedical informatics, biostatistics, clinical operations, and compliance and regulatory affairs (hence, inter/transdisciplinary knowledge base)

Contribution	to manage the flow of data through the data life-cycle of a study
Benefits	better, more efficient data on which to base our findings
Challenges	staying on top of advances in technology and regulatory affairs establish presence alongside other disciplines under-recognized part of investigative process enhanced expectations for all (leadership, delivery/accountability)

Specialty areas

auditing, CRF and protocol development, data collection, database development and testing, electronic/ data entry, project management, SDV, archival of data

Education and Training Opportunities

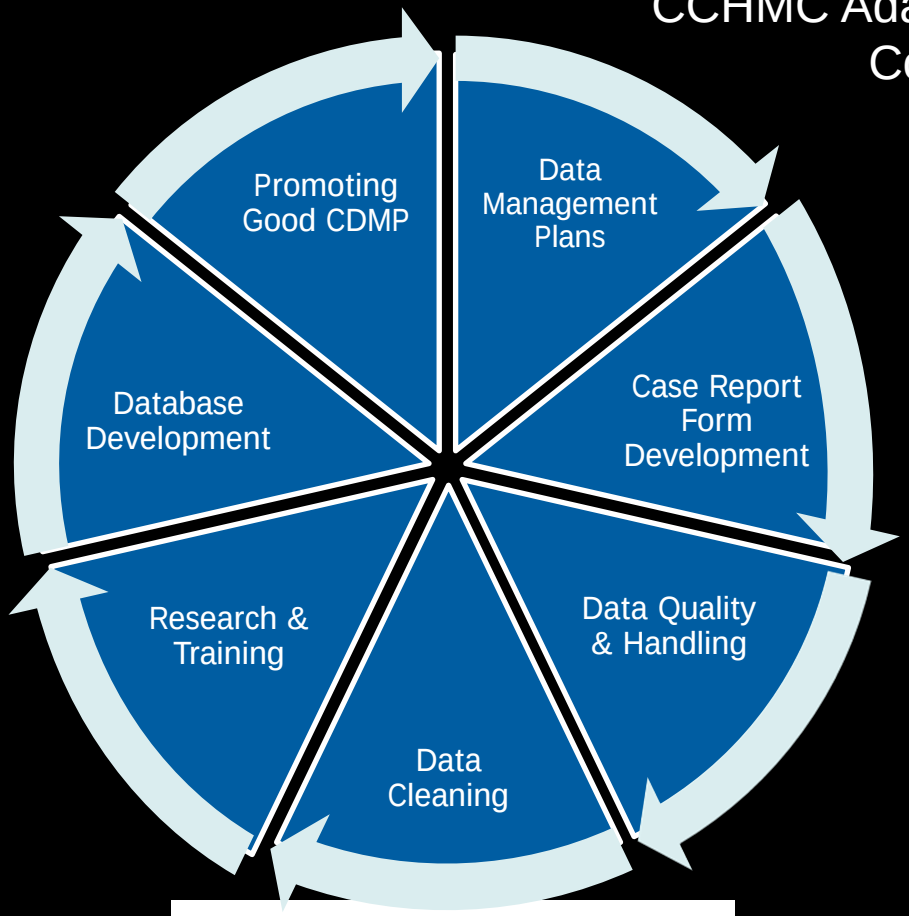
Education and Training Opportunities

- Many opportunities for webinars and short courses are available wrt GCDMP, regulatory, and operations:
  - Society of Clinical Data Management (SCDM), Drug Information Association (DIA)
  - Barnett Educational Services
  - Kestrel Consultants
- Limited number of textbooks are also available:
  - Loshin, D. (2011). *Practitioner´s guide to data quality improvement*. Boston, MA: Elsevier.
  - Prokscha, S. (2007). *Practical guide to clinical data management* (2/e). New York: Taylor and Francis
  - Pryor, G. (2012). *Managing research data*. London: Facet.

Education and Training Opportunities

Education and Training Opportunities

CCHMC Adaptation of GCDMP Core Competencies[10]



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Education and Training Opportunities

ENTRY NUMBER	TOTAL SCORE	TOTAL COUNT	MEASURE	MODEL S.E.	INFIT MNSQ	INFIT ZEMP	OUTFIT MNSQ	OUTFIT ZEMP	PT-MEASURE CORR.	PT-MEASURE EXP.	EXACT MATCH OBS%	EXACT MATCH EXP%	ITEM
29	955	595	.94	.08	1.30	1.1	.96	-.1	.71	.73	67.0	67.9	q_29
28	954	593	.93	.08	1.21	.8	1.13	.2	.71	.73	64.9	67.7	q_28
17	1016	599	.62	.07	.82	-.8	.63	-.9	.78	.75	73.4	65.1	q_17
4	1019	599	.61	.07	1.07	.3	.92	-.2	.75	.75	67.7	65.0	q_04
25	1033	595	.49	.07	.95	-.2	.84	-.4	.77	.76	70.6	64.1	q_25
30	1027	589	.47	.07	.90	-.4	.75	-.6	.78	.76	71.5	63.7	q_30
9	1046	599	.46	.07	1.13	.6	1.01	.0	.75	.76	65.7	63.8	q_09
24	1041	597	.46	.07	1.00	.0	.88	-.3	.77	.76	69.9	64.0	q_24
3	1067	596	.33	.07	1.10	.4	1.04	.1	.76	.77	65.3	62.6	q_03
15	1070	598	.32	.07	.81	-.9	.72	-.8	.79	.77	67.8	62.7	q_15
14	1073	595	.28	.07	.89	-.5	.78	-.6	.79	.77	67.6	62.4	q_14
2	1089	598	.23	.07	1.12	.5	1.12	.3	.76	.78	64.6	62.0	q_02
8	1091	599	.22	.07	.84	-.7	.72	-.8	.79	.78	68.4	62.1	q_08
7	1102	599	.16	.07	.88	-.5	.79	-.6	.79	.78	68.0	61.7	q_07
18	1106	598	.15	.07	.89	-.5	.76	-.7	.80	.78	68.8	61.6	q_18
16	1101	595	.15	.07	.77	-1.1	.64	-1.0	.81	.78	70.5	61.8	q_16
6	1156	599	-.08	.07	.94	-.3	.97	-.1	.80	.79	63.8	59.8	q_06
26	1151	593	-.11	.07	.85	-.7	.90	-.3	.81	.79	66.5	59.6	q_26
31	1157	592	-.17	.07	1.03	.1	1.16	.5	.79	.79	62.2	59.3	q_31
19	1178	600	-.18	.07	.72	-1.4	.67	-1.1	.83	.80	67.7	59.3	q_19
1	1183	600	-.20	.07	1.24	1.0	1.49	1.2	.77	.80	55.5	59.3	q_01
21	1189	599	-.24	.07	.83	-.8	.81	-.6	.82	.80	68.8	59.1	q_21
20	1192	595	-.28	.07	.75	-1.2	.72	-.9	.83	.80	68.0	58.9	q_20
27	1188	591	-.32	.07	.88	-.6	.85	-.5	.82	.80	64.3	58.9	q_27
10	1230	599	-.42	.07	.78	-1.1	.82	-.6	.83	.81	68.1	58.0	q_10
5	1231	597	-.45	.07	1.07	.3	1.01	.0	.80	.81	60.5	57.5	q_05
12	1251	596	-.54	.07	.81	-.9	.86	-.5	.83	.81	65.0	56.8	q_12
23	1274	591	-.66	.07	1.09	.4	1.15	.5	.81	.82	59.5	55.8	q_23
32	1283	588	-.73	.06	2.01	3.7	2.91	4.2	.71	.82	48.2	55.3	q_32
13	1314	598	-.79	.06	.95	-.2	.94	-.2	.83	.82	58.3	54.8	q_13
22	1313	597	-.79	.06	1.46	1.9	1.70	1.9	.77	.82	50.1	55.0	q_22
11	1325	596	-.83	.06	1.11	.5	1.17	.6	.81	.82	53.2	54.7	q_11
MEAN	1137.7	596.1	.00	.07	1.01	.0	.99	-.1			64.7	60.6	
S.D.	102.8	3.2	.49	.00	.25	1.0	.41	1.0			6.0	3.5	

Education and Training Opportunities

Item	Domain	Question	Meas	Std Error	Infit (z)	Outfit (z)	Point-Meas
Q4	Database Development	Implementing change control processes for database validation....	0.61	0.07	0.30	-0.20	0.75
Q13	Data Quality & Handling	Applying data quality methods throughout data handling process...	0.15	0.07	-0.50	-0.70	0.80
Q18	Data Management Plans	Implementing data management plans to provide a consistent...	-0.79	0.06	-0.20	-0.20	0.83

Example: Drexel University Options

- MS in Clinical Research Organization and Management
- MS in Clinical Research for Health Professionals
- MSN in Clinical Trials Research
- Certificate of Study in Clinical Research
- Quantitative Principles for Clinical Research Certificate

Professional Advancement

- Just like academic biostatisticians worrying about faculty development issues, data management professionals need the same consideration:
  - Job opportunities, job stability, seniority, performance metrics to include in résumé
- Institutional recognition of the importance of this discipline is needed


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SCDM Annual Conference 2014: Register now!
For a few days, Las Vegas will be the center of the Clinical Data Management world. A glimpse of the magical atmosphere of Vegas at one of our networking events, and the opportunity to accrue your CDM skills in the relaxing and removed environment of the Conference venue. Save thanks to the early bird fee and your membership! Register now.
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Professional Development

What makes ACRP Professional Development better?

Professional development is about more than contact hours or "checking the training box" — it is about the individual clinical research professional's interest and participation in a comprehensive, sustained and intensive pursuit of maintaining and improving professional competency.

At ACRP, we believe professional development is the intrinsic motivation that comes from within each clinical research professional to recognize his or her responsibility for: safeguarding patient safety; ensuring quality of data; ensuring ethical conduct of clinical trials; ensuring regulatory compliance at all times; and ensuring research projects are completed on time, on target, and on budget.

We support the professional development of clinical research professionals by offering high-quality resources and services that are relevant to the needs, interests, and work of clinical researchers, performance-based, and which allow you to own your success in clinical research.

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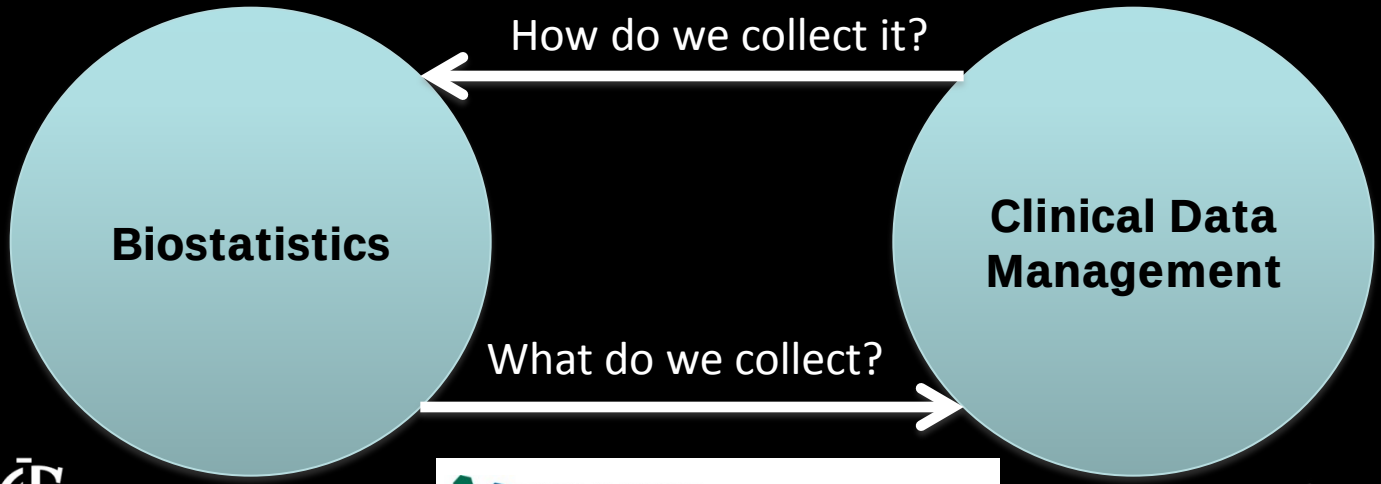
SoCRA Continuing Education

Category of CE	Description of Category	Amount of CE Allowable	Total CE Required
Clinical Research Operations / Regulatory	CE related to clinical research regulations, policy, operations, etc.	Minimum of 22 CEU may be claimed (no maximum)	45 CE per 3 year certification period
Therapeutic / Professional Area	CE related to your specialty in research (therapy, treatment, etc.)	No minimum	
Recertification Quiz	CE for completing the self administered knowledge test	One (1) CE may be claimed	

Biostatistics and Clinical Data Management

- A symbiotic relationship supporting each other through comparative advantage
  - Biostatistics helps define “What we collect?” i.e., endpoints/monitoring
  - Data management defines “How we collect it in the highest quality manner?”



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Close Interactions between Biostatisticians and Clinical Data Managers

- Coordinating centers
- Cores
- Schools of Medicine
  - CRAs
  - Research nurses
- Other clinical research environments
  - CROs

Fostering Better Interactions

- Need a transdisciplinary environment
  - Biostatisticians
  - Epidemiologists
  - Clinical Research Associates / Research Nurses
  - Research IT personnel
  - Domain experts
- Need institutional infrastructure investment
- Interactions across professional societies
  - e.g., SCDM Academic Task Force

Future Challenges

- Keeping up with changing technology platforms:
  - Paper → all electronic
  - Source documents?
  - Platforms (hardware/server, software)
- Patient-reported outcomes (PROs)
- Research data from Electronic Health Records
  - PCORI's PCORnet
  - CTSA's SHRINE pilot

Future Challenges (continued)

- mHealth technologies
  - PRO data collection
  - Mobile sensors for health (e.g., physical activity)
- Long time horizons (e.g., TOUGH)
- Interoperability and federation
  - caTissue Suite, FreezerWorks, REDCap
- Imaging informatics
- Growing “Big Data” sources

Acknowledgments

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[1]Ball, L. K. (2011, June). *Quality by design – Planning clinical trials on multiple fronts: A regulatory perspective. DIA Annual Meeting, Chicago, IL.*

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