Statistical Leadership in the Changing Landscape of Drug Development

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FDA U.S. FOOD & DRUG ADMINISTRATION

Outline

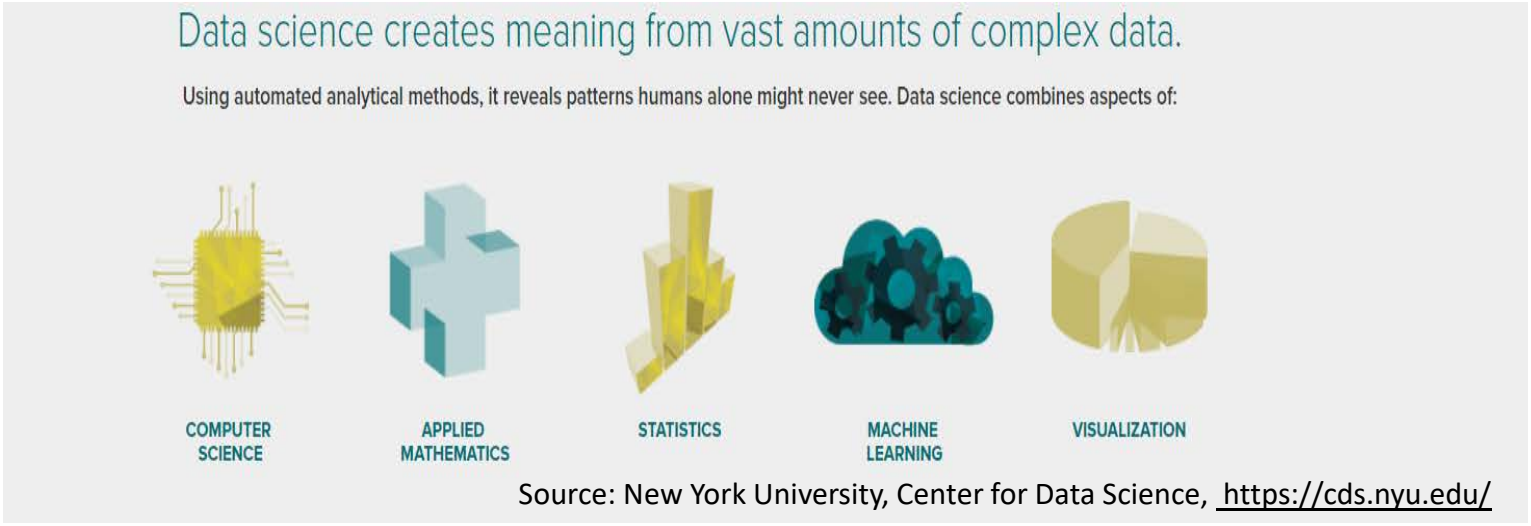
- Initial thoughts
- Statistical Leadership in current FDA initiatives
  - Real World Evidence (RWE)
  - Patient Focused Drug Development (PFDD)
  - Complex Innovative Design (CID) Pilot
  - Model Informed Drug Development
- Closing remarks

Initial Thoughts

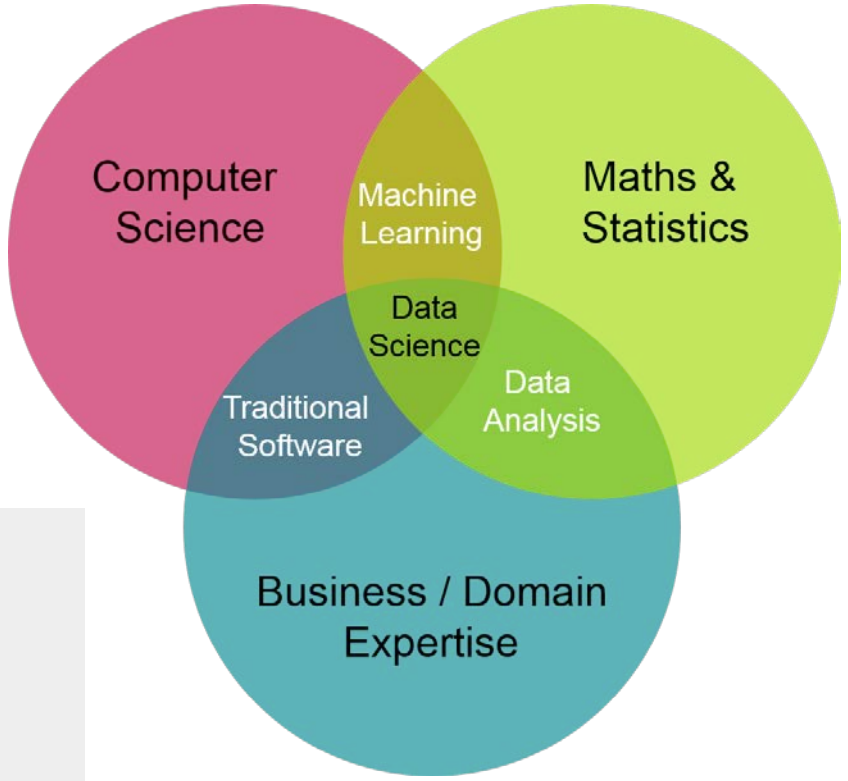
- Statistical leadership is at a unique crossroads

“ The story of how data scientists became sexy is mostly the story of the coupling of the mature discipline of statistics with a very young one—computer science. The term “Data Science” has emerged only recently to specifically designate a new profession that is expected to make sense of vast stories of big data. ”

Source: https://www.forbes.com/sites/gilpress/2013/05/28/a-very-short-history-of-data-science/#441188ef55cf



Source: New York University, Center for Data Science, https://cds.nyu.edu/



Source: https://towardsdatascience.com/introduction-to-statistics-e9d72d818745

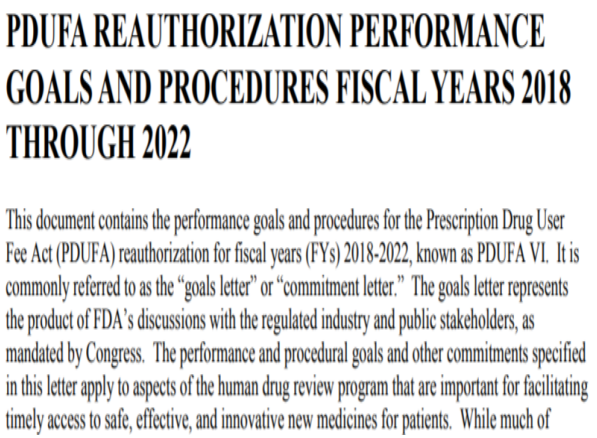
Statistical Leadership in current FDA initiatives

Section 3022	Section 3001	Section 3002	Section 3021
• Real World Evidence	• Patient experience data	• Patient-focused drug development	• Novel clinical trial designs

21st Century Cures Act

The 21st Century Cures Act (Cures Act), signed into law on December 13, 2016, is designed to help accelerate medical product development and bring new innovations and advances to patients who need them faster and more efficiently

PDUFA VI



PDUFA REAUTHORIZATION PERFORMANCE GOALS AND PROCEDURES FISCAL YEARS 2018 THROUGH 2022

This document contains the performance goals and procedures for the Prescription Drug User Fee Act (PDUFA) reauthorization for fiscal years (FYs) 2018-2022, known as PDUFA VI. It is commonly referred to as the "goals letter" or "commitment letter." The goals letter represents the product of FDA's discussions with the regulated industry and public stakeholders, as mandated by Congress. The performance and procedural goals and other commitments specified in this letter apply to aspects of the human drug review program that are important for facilitating timely access to safe, effective, and innovative new medicines for patients. While much of

- Enhancing Use of Real World Evidence for Use in Regulatory Decision-Making
- Enhancing the Incorporation of the Patient's Voice in Drug Development and Decision-Making
- Enhancing Capacity to Review Complex Innovative Designs
- Advancing Model-Informed Drug Development

Real World Evidence (RWE)

CDER Definitions

Real World Data (RWD) are data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources.

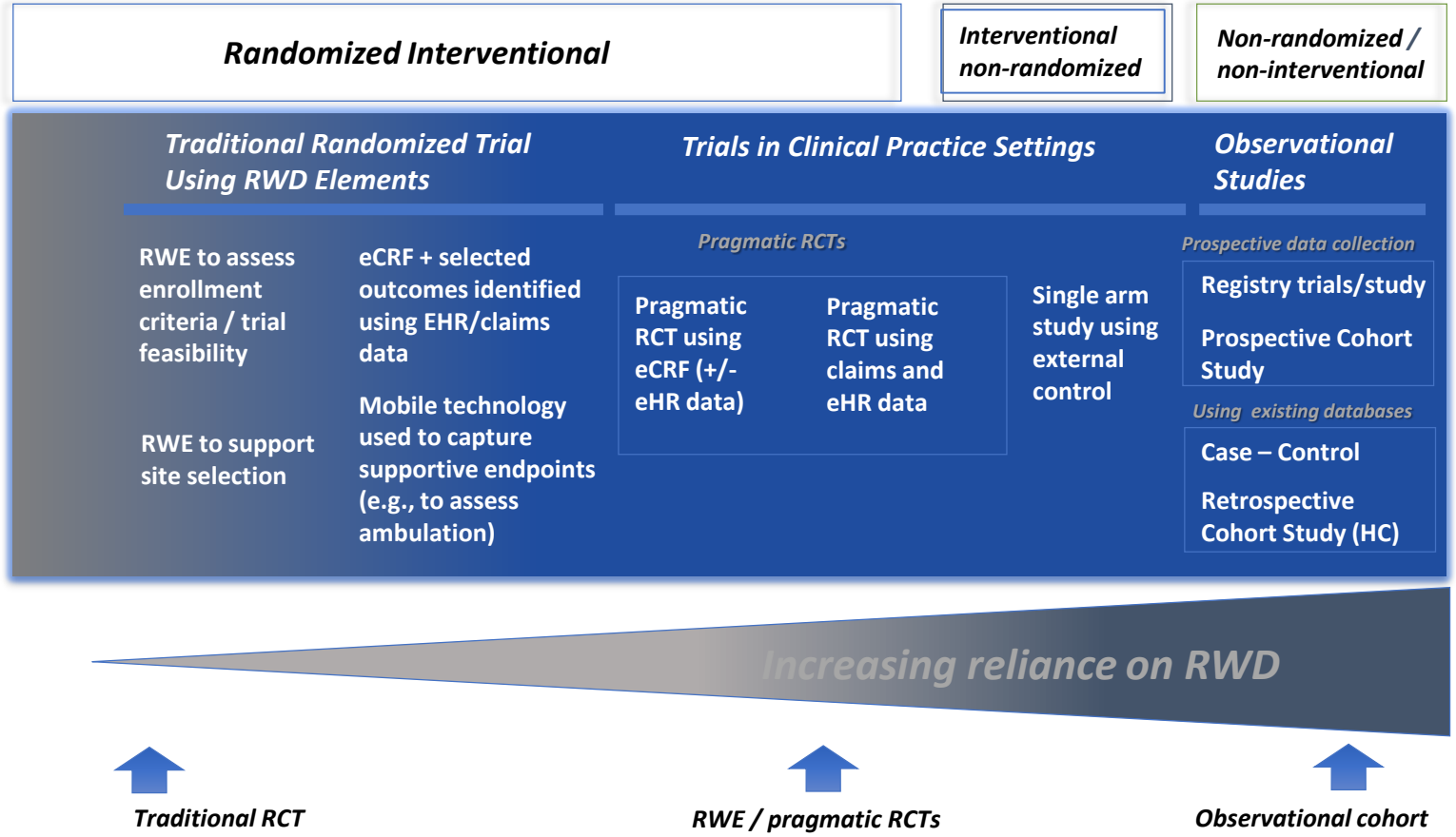
- electronic health records (EHRs)
- claims and billing data
- data from product and disease registries
- patient-generated data including in home-use settings
- data gathered from other sources that can inform on health status, such as mobile devices

Real World Evidence is the clinical evidence regarding the usage and potential benefits or risks of a medical product derived from analysis of RWD.

Generated using many different study designs, including but not limited to, randomized trials, such as large simple trials, pragmatic clinical trials, and observational studies.

- Maximize opportunities to have regulatory decisions incorporate data/evidence from settings that more closely reflect clinical practice
  - Increase the diversity of populations
  - Improve efficiency by incorporating existing data
- Maintain evidentiary standards

Spectrum of potential uses of RWD / RWE in Clinical Studies



Sentinel

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Sentinel is a National Medical Product Monitoring System

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Network of Collaborators

Sentinel brings together public, academic and private organizations that provide access to healthcare data and expertise.

Data at a Glance

The Sentinel Distributed Database is comprised of quality-checked electronic data held by 18 partner organizations.

Statistical Methods

Sentinel explores the application of a wide range of methods to enhance medical product safety assessment.

FDA

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13 Clinical Data Research Networks*

CDRNs are networks that originate in healthcare systems, such as hospitals, health plans, or practice-based networks, and securely collect health information during the routine course of patient care.

20 Patient-Powered Research Networks*

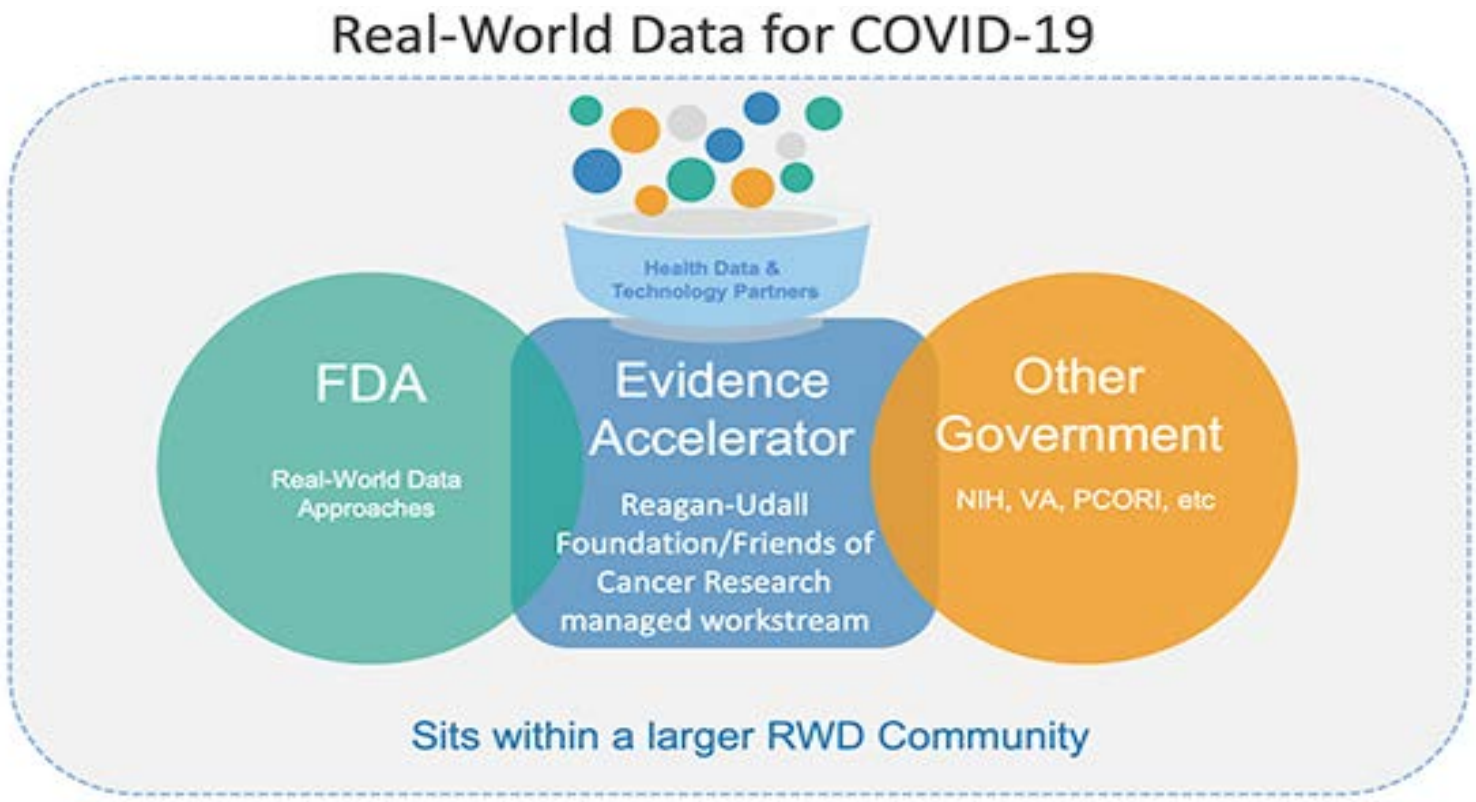
PPRNs are operated by patient groups and their partners, and are focused on a particular condition or population.

2 Health Plan Research Networks (HPRNs)

HPRNS are health plans that cover significant numbers of patients in one or more of the PCORnet CDRNs.

- HealthCore-Anthem Research Network American
- HUMnet: Humana

- About **100 million** patients who have had a medical encounter in the past five years*
- Engaged and collaborating partner networks
- **130+** partnerships with health systems and patient groups
- **150+** common and rare conditions
- **$50 million** in PCORI-approved funding to support demonstration projects



Therapeutic Evidence Accelerator

Diagnostic Evidence Accelerator

The Accelerator brings together the country's leading experts in health data aggregation and analytics in a unified effort to share insights, compare results, and answer key questions about COVID-19 treatment and response as quickly as possible.

https://evidenceaccelerator.org/

COVID-19 EVIDENCE ACCELERATOR PRINCIPLES

Together, we will **create** and **lead**.

C **CONTEXT** — tie data to the question, address bias, explain validation strategies.

R **RESPECT** — for patient privacy and the patient voice is paramount.

E **EARN TRUST** — show processes, analytic approaches, and comparisons. Be open to input. Challenge with productive intent.

A **ACT FAST AND DO GOOD WORK** — act with a sense of urgency, but not at the expense of quality or credibility.

T **TRANSPARENCY** — ruthless transparency.

E **EMBRACE AND EXPLORE** —convergence and discordance to facilitate understanding and generate knowledge.

L **LEARN** — continually integrate best practices from **sharing** process, limitations, pitfalls, and successes.

E **EXERCISE PATIENCE** — state when a question can't be answered right away and institute action to answer it.

A **ACCESSIBILITY AND TRACEABILITY** — document data generation, processing, curation, and analytics.

D **DISSEMINATE WORK** — to show what good looks like. *Teach, Don't Preach.*

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Patient Focused Drug Development

Patient Experience Data (Cures Act)

- Collected by any persons (including patients, family members and caregivers of patients, patient advocacy organizations, disease research foundations, researchers, and drug manufacturers)
- Intended to provide information about patients' experiences with a disease or condition

Patient-focused drug development

- Systematic approach to help ensure patients' experiences, perspectives, needs and priorities are captured and meaningfully incorporated into drug development and evaluation

Patient Focused Drug Development - Guidances

Guidance 1: Collecting Comprehensive and Representative Input	FINAL
Guidance 2: Methods to Identify What is Important to Patients	DRAFT
Guidance 3: Selecting, Developing or Modifying Fit-for-Purpose Clinical Outcomes Assessments	
Guidance 4: Incorporating Clinical Outcome Assessments into Endpoints for Regulatory Decision Making	

Public Workshop to receive input from patients and external stakeholders completed for all four guidances

CID Pilot Meeting Program

- **Goals**
  - Facilitate the use of CID approaches (complex adaptive, Bayesian and other novel clinical trial designs) in late-stage drug development.
  - Promote innovation by allowing FDA to publicly discuss the trial designs considered through the pilot program
- Agency
  - Selects up to 2 submissions per quarter
  - Uses the design as a case study for education and information sharing

CID Pilot Meeting Program

Examples of Complex Innovative Trial Design Features

- Innovative use of external data
- Formal incorporation of prior knowledge
- Inclusion of pre-specified adaptations to multiple aspects of a trial

Disclosure to Facilitate Learning

CIDs accepted into the pilot will serve as educational resources to facilitate the science and adoption of CIDs. Subject to a disclosure agreement, FDA may present elements of the trial designs as case studies before regulatory approval of the medical product.

FDA Evaluation of CID Meeting Requests

- Therapeutic need
- Trial design appropriateness
- Need for simulations
- Level of innovation of the trial design
- Value proposition of the CID

CID Pilot Meeting Program Benefits

- Innovates medical product development
- Increases dialogue and education among stakeholders
- Advances the use of CIDs
- Develops therapeutic options of benefit to patients

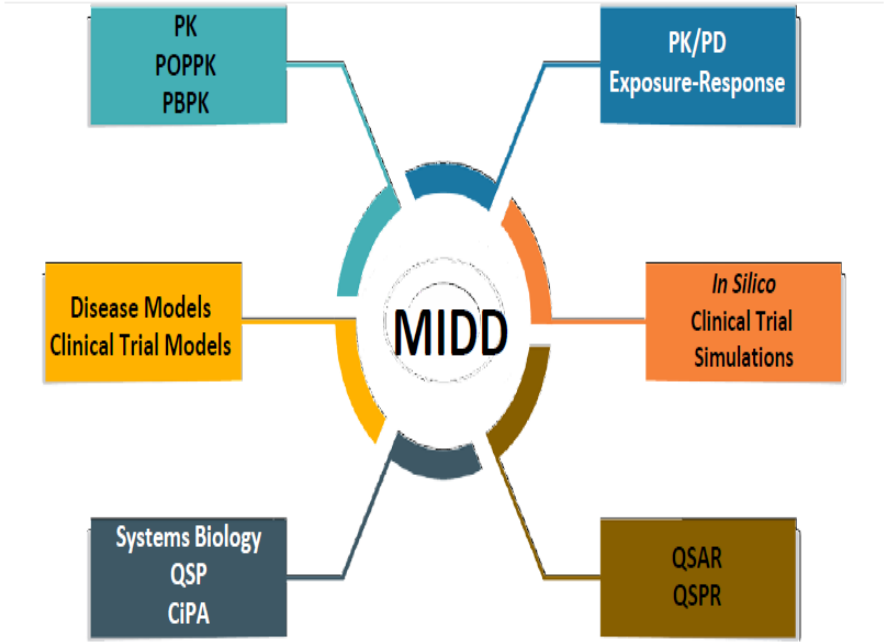
Program Eligibility Criteria

The criteria for eligibility include:

- Sponsor has a pre-Investigational New Drug (IND) or IND number
- Proposed CID is intended to provide substantial evidence of effectiveness to support regulatory approval
- There is sufficient clinical information to inform the CID (not a first-in-human study)
- FDA and Sponsor reach an agreement on the trial design information to be publicly disclosed

Model Informed Drug Development

Development and application of exposure-based, biological, and statistical models derived from preclinical and clinical data sources to address drug development or regulatory issues*



- Eligibility – focus and priority on:
  - Dose selection or estimation
  - Clinical trial simulation
  - Predictive or mechanistic safety evaluation
  - Excludes statistical designs involving complex adaptations, Bayesian methods, or other features requiring computer simulations to determine the operating characteristics of a confirmatory clinical trial
- Led by Office of Clinical Pharmacology (OCP) with OB in a critical role

https://www.fda.gov/drugs/development-resources/model-informed-drug-development-pilot-program

Closing thoughts

- Statisticians should step up to being change agents
- Success can come only from interdisciplinary collaboration
- Regulatory agencies, industry and academia have to play critical roles
- Lessons learnt and early successes should be shared transparently

Thanks to
- Amy Abernethy
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