Applying Lessons Learned from RWE in the Time of COVID-19 to the Future

Virtual (Zoom)

October 1, 2020

1:00-4:00 pm ET

Welcome and Overview of the COVID-19 Response

Mark McClellan
Director, Duke-Margolis Center for Health Policy

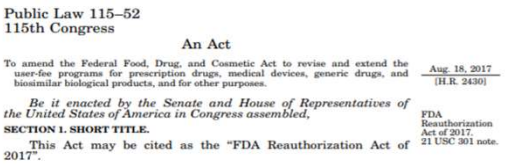
Ongoing FDA RWD/RWE Activity

Examples

Legislative Action	FDA Response	Stakeholder Efforts

- RWD infrastructure continues to grow and be made more robust, including digital health
- Broader industry use and acceptance of RWE to support evidentiary packages
- Pilot projects demonstrating the application of RWD and RWE

Legislative Action



Public Law 115–52
115th Congress

An Act

To amend the Federal Food, Drug, and Cosmetic Act to revise and extend the user-fee programs for prescription drugs, medical devices, generic drugs, and biosimilar biological products, and for other purposes.

Aug. 18, 2017
[H.R. 2430]

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

FDA Reauthorization Act of 2017.
21 USC 301 note.

SECTION 1. SHORT TITLE.

This Act may be cited as the "FDA Reauthorization Act of 2017".

FDA Response

Internal FDA Process

Guidance Development

Submitting Documents Using Real-World Data and Real-World Evidence to FDA for Drugs and Biologics
Guidance for Industry

DRAFT GUIDANCE

Stakeholder Engagement

Event

Leveraging Randomized Clinical Trials to Generate Real-World Evidence for Regulatory Purposes

Public Workshop

Establishing a High-Quality Real-World Data Ecosystem Day 1 & 2

Projects

FDA COVID19

Source Data Capture from Electronic Health Records (EHRs): Using Standardized Clinical Research Data

COVID-19 Requires Us to Disrupt Traditional Evidence Generation Paradigm

RWE from Practical Trials

Large-scale practical trials for COVID-19 therapeutics

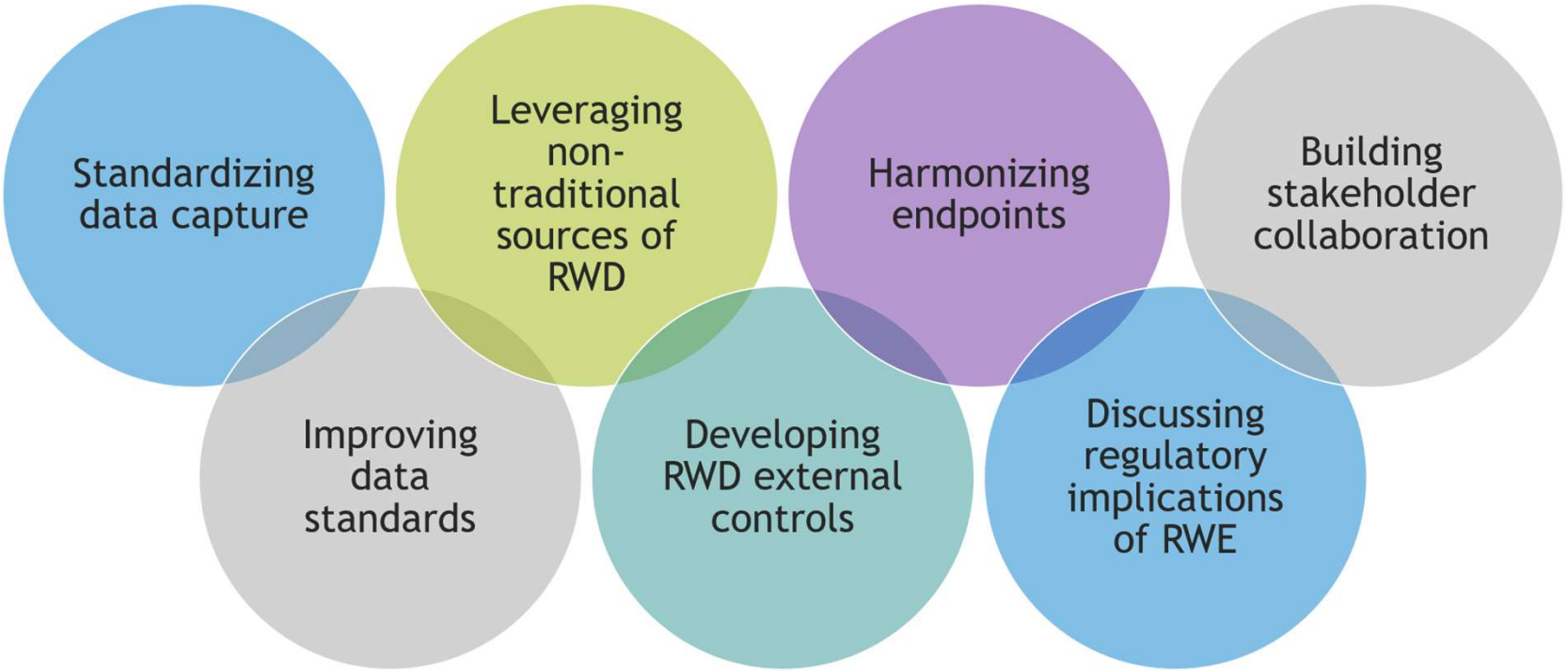
Digital Tools and Technology

Acceleration of adoption of digital tools, remote patient monitoring, and telemedicine in COVID-19

Real-World Data Infrastructure

Stakeholder collaboration to align observational studies for COVID-19 therapeutics

COVID-19 RWE Work Accelerates RWD and RWE Use for Decision-Making



Looking Ahead…

Continue building on and learning from existing efforts as we continue to adapt to the COVID-19 pandemic and beyond

Initiate collaborative pilots to develop use cases to facilitate future learning

Emphasize the importance of creating a shared RWD infrastructure to align and improve data collection efforts

Agenda

1:00 pm Welcome and Overview of the COVID-19 Response

1:10 pm Keynote Address

1:25 pm Session I: Embedding Practical Trials in EHRs: A Critical Approach for Leveraging Randomization, Objective Endpoints, Large Sample Size, and Minimal Data Collection to Deliver Decisive Results

2:10 pm Session II: Transforming Outcome Capture: Advancing Routine Use of Digital Tools and Technology for Study Measurement

2:55 pm Session III: Collaborating to Build a Better Real-World Data Infrastructure for Enhanced Post-Market Evidence

3:35 pm Fireside Chat

3:55 pm Closing Remarks

4:00 pm Adjourn

Virtual Meeting Reminders

- Visit the Duke-Margolis website (https://healthpolicy.duke.edu/events) for meeting materials, including the agenda, speaker biographies, and discussion questions.

- Questions for our panelists? Feel free to submit questions via email to MargolisEvents@duke.edu.

- Join the conversation @Duke-Margolis #RWE2020

Keynote Address

John Concato

Deputy Director, Office of Medical Policy Initiatives, Center for Drug Evaluation and Research,

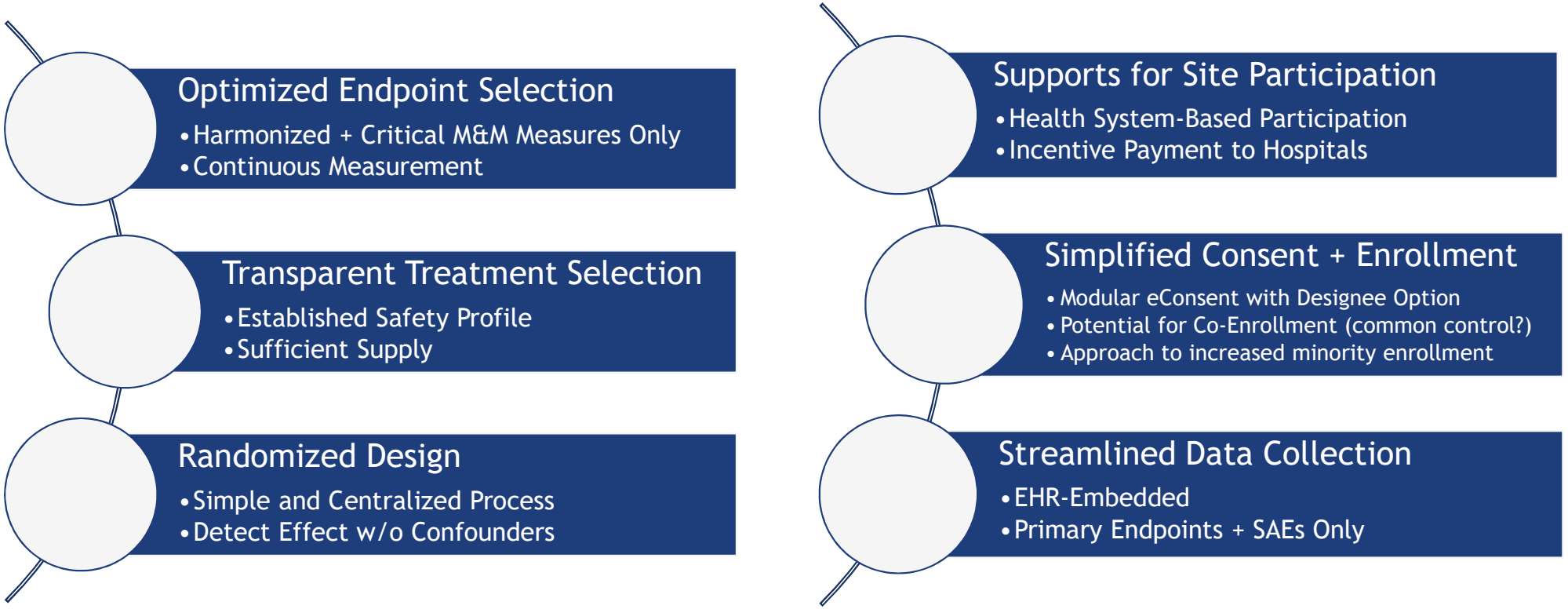
U.S. Food and Drug Administration

Session I: Embedding Practical Trials in EHRs: A Critical Approach for Leveraging Randomization, Objective Endpoints, Large Sample Size, and Minimal Data Collection to Deliver Decisive Results

What is a Practical Trial?

- Enhanced, large simple trial
- Randomization
- Streamlined data collection
  - Few, important endpoints
  - Serious adverse events
- Embedded in routine clinical care (EHRs)

Key Features of Ideal Practical Trial Protocol



Robert Califf

Head, Clinical Policy and Strategy

Verily and Google Health

verily

Practical Trials

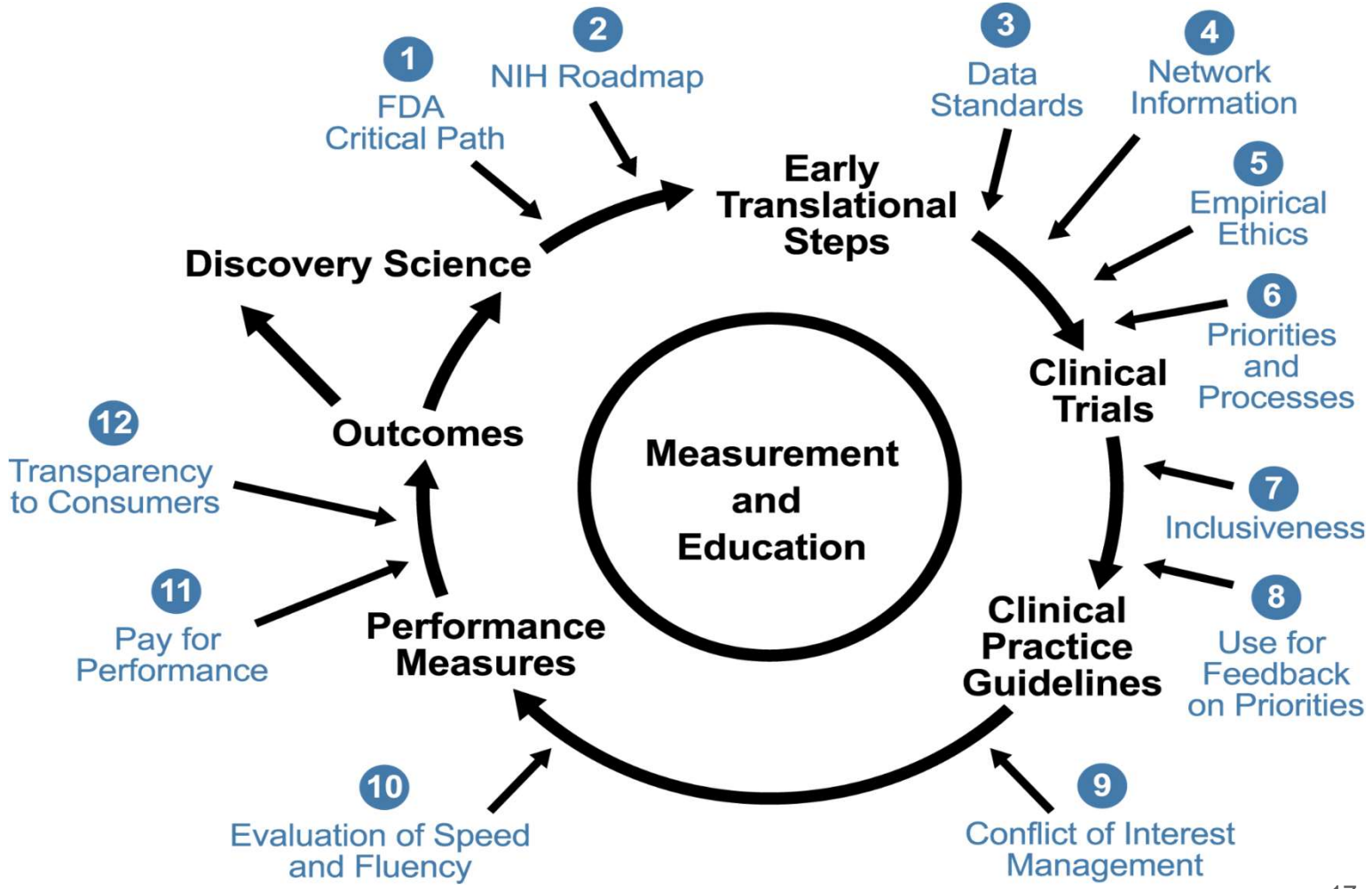
Robert M Califf MD
Head of Clinical Policy and Strategy
Verily Life Sciences and Google Health
October 1st, 2020

A Brief Personal History of Pragmatic Trials

- Polio vaccine trials (1.8 million children)
- Oxford large, simple trials (LST)
- GUSTO brings automation—key role of FDA
- Effectiveness movement leads to pragmatic/practical trials effort and PRECIS
- Efforts to reform trials (Clinical Trials Transformation Initiative)—Quality by Design
- 21st Century Cures and User Fee Agreements push for ”real world data” and “real world evidence”
- PCORnet, NIH Collaboratory, ISPY usher in participant- centered hybrid trials
- The pandemic and NHS/Recovery cause many to ask why we can’t get reliable answers more quickly

If we want to inform patients, families, clinicians and policy makers about which options are best for screening, prevention, diagnosis and treatment we must deal with fragmentation and misaligned incentives to rapidly conduct RCTs

Generating Evidence to Inform Decisions



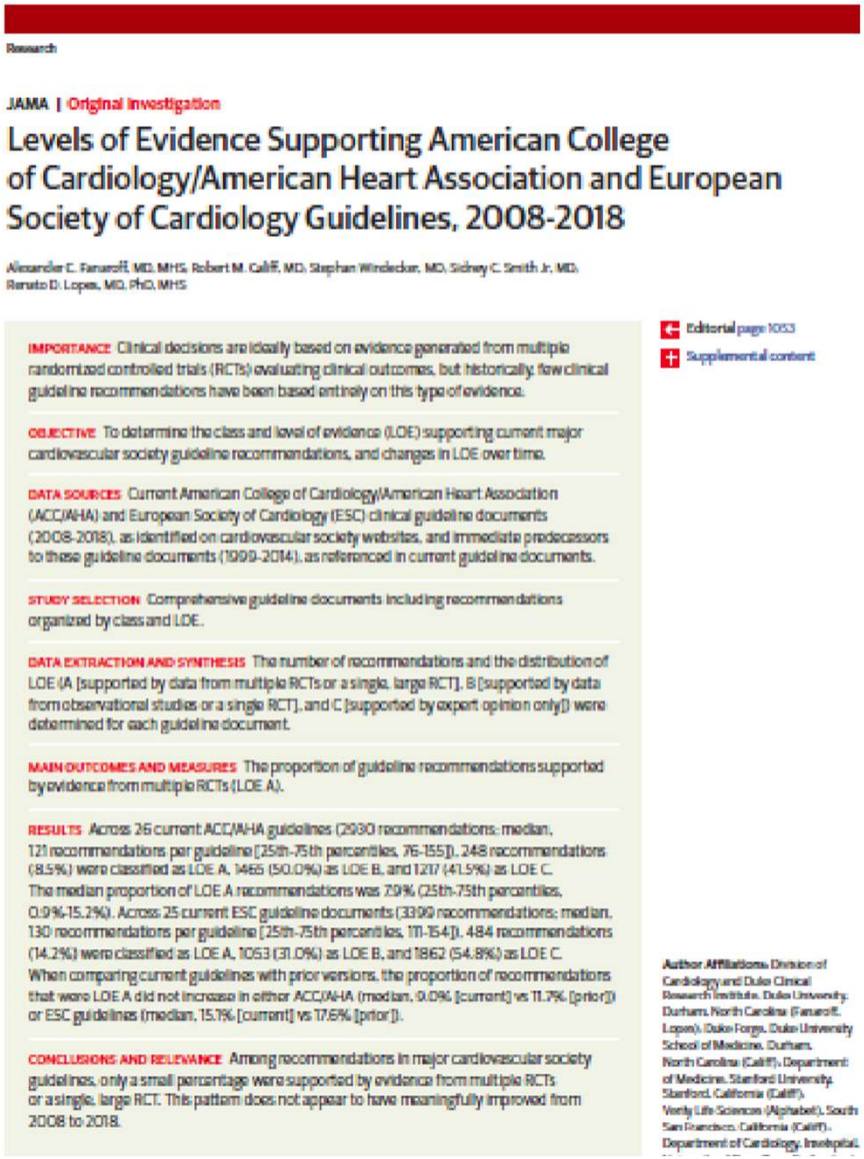
J Am Coll Cardiol. 2002
Dec 4;40(11):1895-901

Our National Clinical Research System is Well-intentioned But Flawed

- High percentage of decisions not supported by evidence*
- Health outcomes and disparities are not improving
- Current system is great **except**:
  - Too slow, too expensive, and not reliable
  - Doesn't answer questions that matter most to patients
  - Unattractive to clinicians & administrators

We are not generating the evidence we need to support the healthcare decisions that patients and their doctors have to make every day.

Tricoci P et al. JAMA 2009;301:831-41



Research

JAMA | Original Investigation

Levels of Evidence Supporting American College of Cardiology/American Heart Association and European Society of Cardiology Guidelines, 2008-2018

Alexander C. Fanaroff, MD, MHS; Robert M. Califf, MD; Stephan Windecker, MD; Sidney C. Smith Jr, MD; Renato D. Lopes, MD, PhD, MHS

Editorial page 1053
Supplemental content

IMPORTANCE Clinical decisions are ideally based on evidence generated from multiple randomized controlled trials (RCTs) evaluating clinical outcomes, but historically, few clinical guideline recommendations have been based entirely on this type of evidence.

OBJECTIVE To determine the class and level of evidence (LOE) supporting current major cardiovascular society guideline recommendations, and changes in LOE over time.

DATA SOURCES Current American College of Cardiology/American Heart Association (ACC/AHA) and European Society of Cardiology (ESC) clinical guideline documents (2008-2018), as identified on cardiovascular society websites, and immediate predecessors to these guideline documents (1999-2014), as referenced in current guideline documents.

STUDY SELECTION Comprehensive guideline documents including recommendations organized by class and LOE.

DATA EXTRACTION AND SYNTHESIS The number of recommendations and the distribution of LOE (A [supported by data from multiple RCTs or a single, large RCT], B [supported by data from observational studies or a single RCT], and C [supported by expert opinion only]) were determined for each guideline document.

MAIN OUTCOMES AND MEASURES The proportion of guideline recommendations supported by evidence from multiple RCTs (LOE A).

RESULTS Across 26 current ACC/AHA guidelines (2930 recommendations; median, 121 recommendations per guideline [25th-75th percentiles, 76-155]), 248 recommendations (8.5%) were classified as LOE A, 1465 (50.0%) as LOE B, and 1217 (41.5%) as LOE C. The median proportion of LOE A recommendations was 7.9% (25th-75th percentiles, 0.9%-15.2%). Across 25 current ESC guideline documents (3390 recommendations; median, 130 recommendations per guideline [25th-75th percentiles, 111-154]), 484 recommendations (14.2%) were classified as LOE A, 1053 (31.0%) as LOE B, and 1862 (54.8%) as LOE C. When comparing current guidelines with prior versions, the proportion of recommendations that were LOE A did not increase in either ACC/AHA (median, 0.0% [current] vs 11.7% [prior]) or ESC guidelines (median, 15.1% [current] vs 17.6% [prior]).

CONCLUSIONS AND RELEVANCE Among recommendations in major cardiovascular society guidelines, only a small percentage were supported by evidence from multiple RCTs or a single, large RCT. This pattern does not appear to have meaningfully improved from 2008 to 2018.

Author Affiliations: Division of Cardiology and Duke Clinical Research Institute, Duke University, Durham, North Carolina (Fanaroff, Lopes); Duke Forge, Duke University School of Medicine, Durham, North Carolina (Califf); Department of Medicine, Stanford University, Stanford, California (Califf); Verily Life Sciences (Alphabet), South San Francisco, California (Califf); Department of Cardiology, Inselspital,

Across 26 current ACC/AHA guidelines, 8.5% of recommendations were LOE A

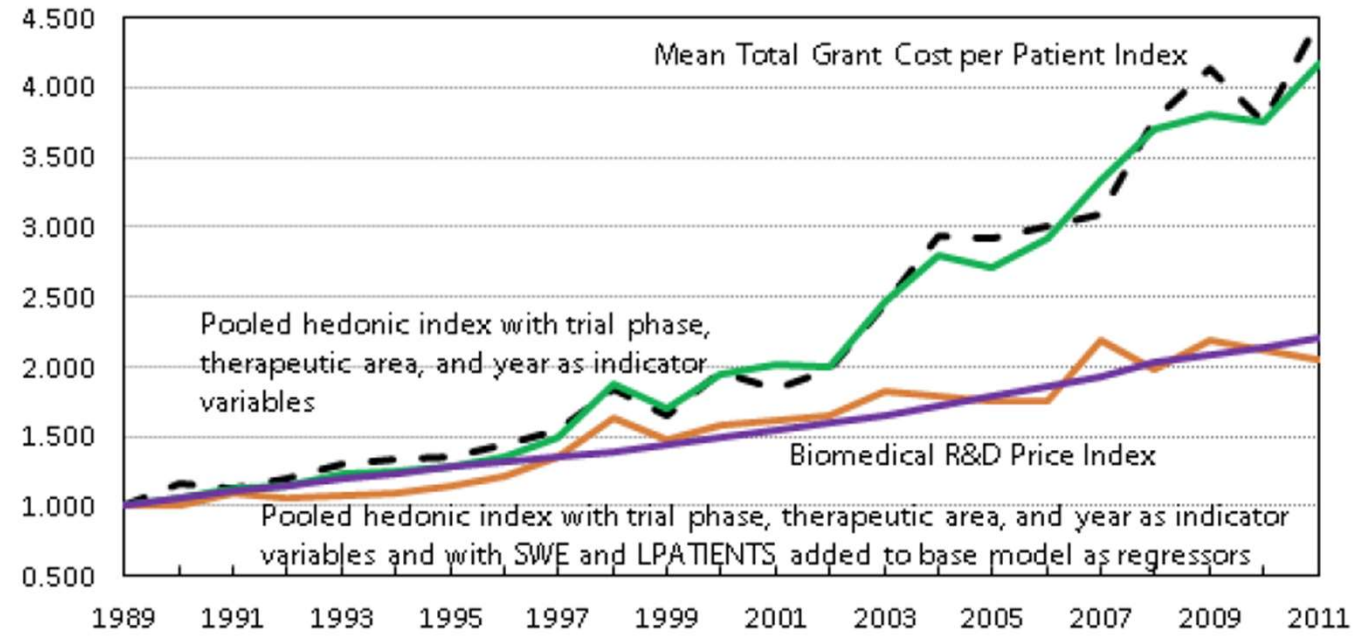
Across 25 ESC guidelines, 14.2% of recommendations were LOE A

This pattern does not appear to have meaningfully improved from 2008 to 2018

Fanaroff AC, Lopes RD, et al. JAMA 2019;321:1069

Trial Hyperinflation

Figure 3. Mean Total Grant Cost per Patient Index, Biomedical R&D Price Index, and pooled hedonic indexes, 1989–2011



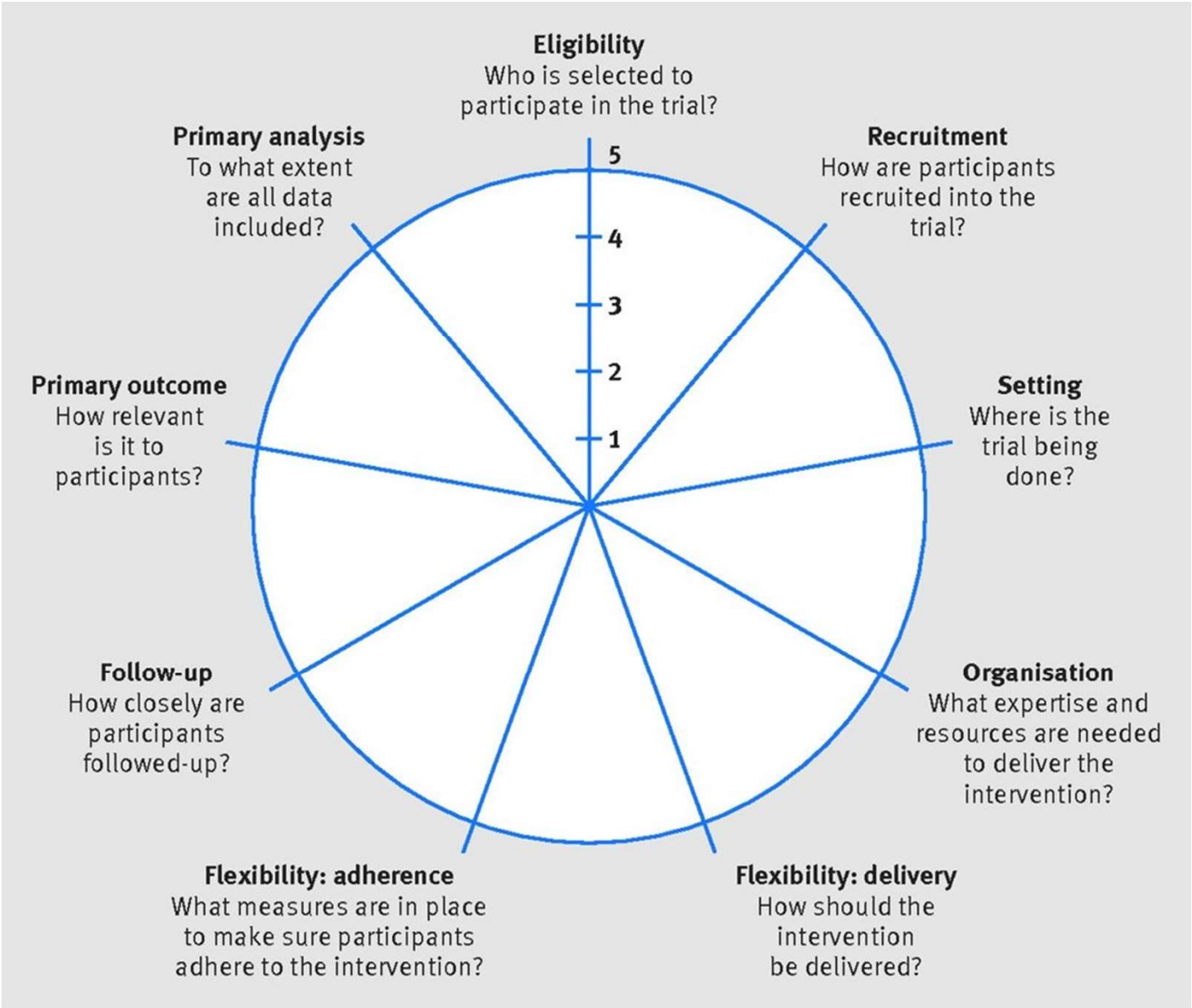
Source: Authors' calculations based on Medidata Solutions, Inc.'s, PICAS® database.

verily

Berndt E, Cockburn I. Monthly Labor Review, June 2014

Some Thoughts on Nomenclature

- Traditional randomized clinical trials (TRCTs)
- Pragmatic trials
- Large simple trials (LSTs)
- Simple trials +


Eligibility
Who is selected to participate in the trial?
Recruitment
How are participants recruited into the trial?
Setting
Where is the trial being done?
Organisation
What expertise and resources are needed to deliver the intervention?
Flexibility: delivery
How should the intervention be delivered?
Flexibility: adherence
What measures are in place to make sure participants adhere to the intervention?
Follow-up
How closely are participants followed-up?
Primary outcome
How relevant is it to participants?
Primary analysis
To what extent are all data included?
5
4
3
2
1

LST+

- **LST**
  - Uncertainty about a clinical/policy decision
  - Primary intention to inform practice for individuals and/or policy
  - Primary data collection as simple as possible to answer the question
  - Don’t confuse precision and reliability
  - Key measures of quality
    - Was the trial designed to answer the crucial question?
    - Were right participants identified and randomized?
    - Was randomization done properly?
    - Was assigned treatment taken as planned?
    - Were primary endpoints identified and measured without bias and complete follow-up for relevant time?
- **Elements of +**
  - EHR and claims data capture
  - Platforms
  - Adaptive designs/Bayesian designs
  - Participant centered rather than treating “subjects” as objects
  - Involve clinicians but don’t burden them (practice based research and research based practice)
  - Alternate forms of randomization
  - Add substudies only if they don’t impair the likelihood of answering the primary question

Simple Trials +

- Intent to inform decision-making as opposed to elucidating a biological or social mechanism
- Intent to enroll a population relevant to the decision in practice and representative of the patients/populations and clinical settings for whom the decision is relevant
- Either an intent to:
  - Streamline procedures and data collection so that the trial can focus on adequate power for informing the clinical and policy decisions OR
  - Measure a broad range of outcomes

Designed for the primary purpose of informing decision-makers regarding the comparative balance of benefits, burdens and risks fo a biomedical or behavioral health intervention at the individual or population level

Laura Esserman

Director, Carol Franc Buck Breast Care Center

The University of California, San Francisco

Platform Trials: Approach to Solving Serious Clinical Problems

- Pre-competitive consortium with common purpose
  - FDA, Academics, Community Hospitals, Industry, Advocates, Investigators
- Efficient: Screening many NEW promising agents, common control
- Look for big impact
  - Fail fast
  - Find winners FAST TO SAVE PEOPLES' LIVES!!!!!
- Scalable from Breast Cancer to COVID
  - Entire trial process replicated in 8 weeks
    - Consortium/ master protocol/ trial specific data checklists with embedded analytics/ agent selection/approval/engagement of investigators and clinicians
    - Entire community across many disciplines working with energy, urgency and purpose
  - 6 agents already approved ready to test, many more in the pipeline

Consider a New Paradigm that Accelerates Progress

Old Gold Standard

- Features
  - Randomized 1:1
  - Double blind
  - Fixed accrual
  - Frequentist
- Data Collection
  - Collect all possible data
  - Data recollected by coordinators
  - Monitor all data entries
  - Report all adverse events to the FDA
  - Assign attribution to all adverse events
  - Research and care are separate systems and both are suboptimal

New Gold Standard

- Features
  - Standing platform
  - Master protocol
  - Accrual based on performance
  - Bayesian
- Data Collection
  - Design data plan
  - Use check list of mission critical data
    - As part of clinical care/ RWE
  - Use source data for primary endpoints
  - Reporting for grade 3, 4 events
  - Attribution based on data of all AEs
  - Research and care is integrated- same system, enter once use many

Breaking down Barriers: Everyone has a role to play

	Today's RCT	Tomorrow/ Master Platforms
Industry	One drug, one trial; pharma sponsored	Platform where many companies participate Take risk on new trial designs
Delivery systems	Contract on hospital by hospital basis	Systems based approach
Delivery Systems	Every site has multiple competing trials	Fewer focused platform trials
Delivery Systems	Huge hurdle for "write back" /data sharing	"Jump Start" package (stds, security) for data sharing
Payors	Never participate in trials; wait for FDA approval and longer	Participate in trials to drive health care value
Regulatory Endpoints	Recurrence free survival and mortality	Early endpoints (residual tumor burden) and survival ; time to recovery and survival
Regulatory Approval	Drug A vs. Drug B; Double Blind	Optimal combinations; Open Label (not Industry sponsored)
Regulation of investigational pharmacies	Each site has investigational pharmacy	Hub and spoke model Pharmacies can be virtually audited
Regulation of investigators	Every investigator takes full training course every year	Supervising site plays role in managing, collection data, Shorter training course for "spoke"investigators
All: Real World Evidence	Not Included	An Essential Comparator, Outcomes as byproduct of care

Silver Lining: COVID is forcing a change to business as usual

- Urgency
- Collaboration
- Focus on what matters most to care and research
  - Insights automated; soul crushing tasks minimized
  - Value much higher
- Accrual strategies adjust and adapt to disease
- Focus on minimum essential data set
  - For Care
  - For Trials
- Focus on what is best for patients
- Willingness to take risk to solve critical health problems

Adrian Hernandez

Vice Dean & Executive Director, Duke Clinical Research Institute

Duke University School of Medicine

Re-engineering Clinical Research

Adrian Hernandez, MD, MHS
Vice Dean and Executive Director
Duke Clinical Research Institute
Duke University School of Medicine

@texhern

Duke Clinical Research Institute | FROM THOUGHT LEADERSHIP TO CLINICAL PRACTICE

The HERO Program

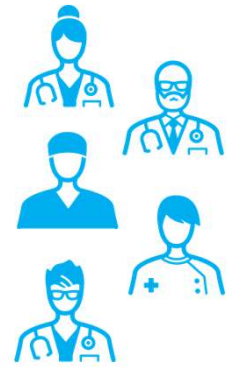
- Designed with multiple stakeholders
  - Healthcare workers –front-line workers
  - Professional Societies
  - Federal Agencies
  - Health systems
- Build a community of thousands of healthcare workers (HCWs)
  - To understand the impact of COVID 19 on HCW health and other outcomes
  - To answer questions – related to COVID19 and beyond – important to HCWs
  - To understand preferences about participation in trials and serve as an engaged community and platform to facilitate trials

HERO

Healthcare Worker Exposure Response & Outcomes

HERO

Together, healthcare workers can ENGAGE to help find answers that will PROTECT and IMPROVE the health and well-being of America's frontline



Join the HERO Registry

1

Answer short surveys + participate in future clinical studies

2

Learn results from HERO research

3

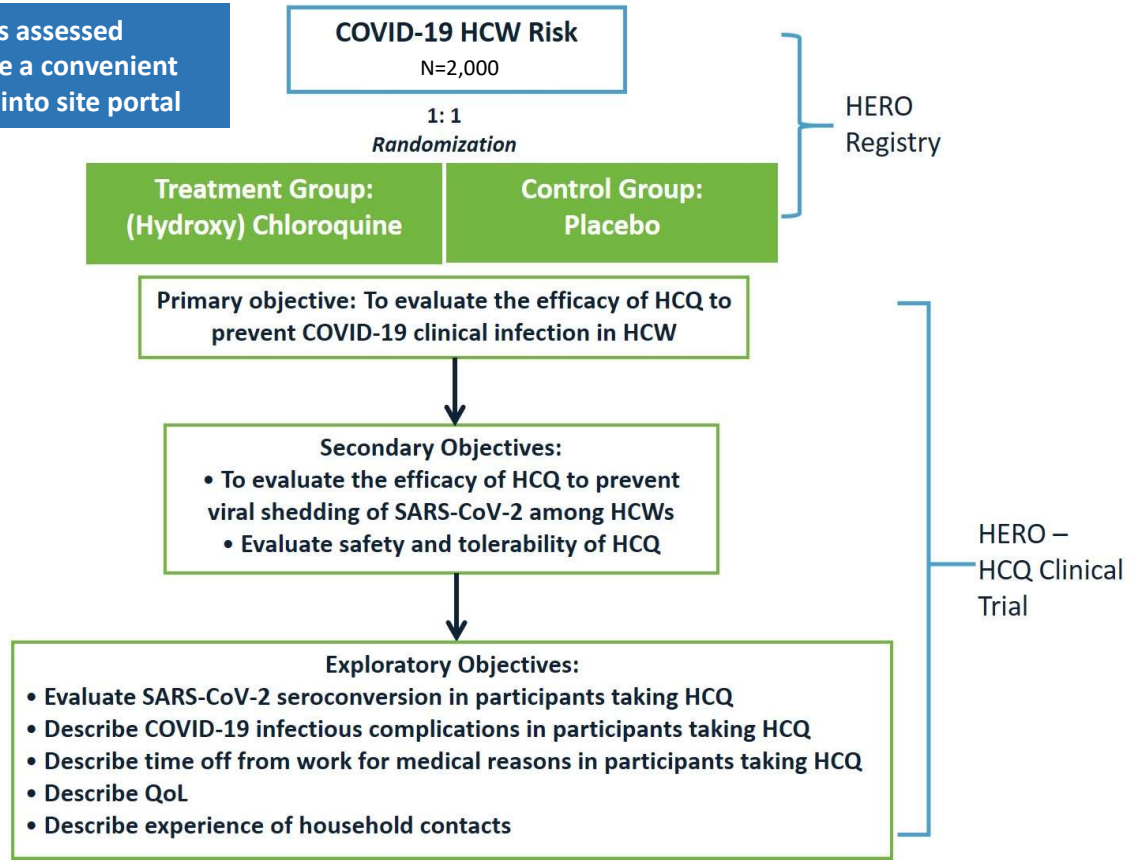
Share ideas for problems to address and research to do

Healthcare workers form a community, indicate preferences, participate and get results returned

- Interest and eligibility for trials assessed
- Pre-screened HCWs can choose a convenient enrolling site to visit and feed into site portal

Features:

- Facilitate rapid enrollment
- Pre-screened off-site
- Enrollment appointments
  - Testing
  - Randomization
  - Drug supply
- Remote follow-up
  - Portal
  - Tele-back-up
- Close-out visit
  - Testing



Pamela Tenaerts

Executive Director

Clinical Trials Transformation Initiative (CTTI)

CTTI vision for clinical trials 2030

Focus

A research study in which one or more participants are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.

https://grants.nih.gov/policy/clinical-trials/definition.htm

CTTI

Clinical Trials Vision 2030

CTTI

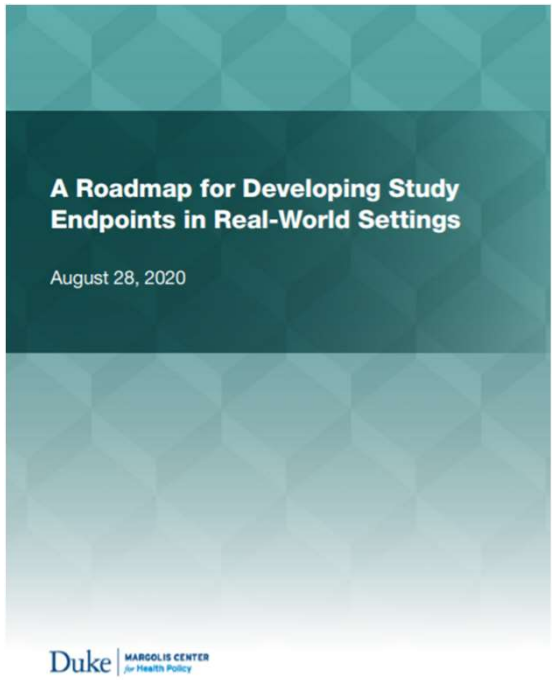
David Soergel

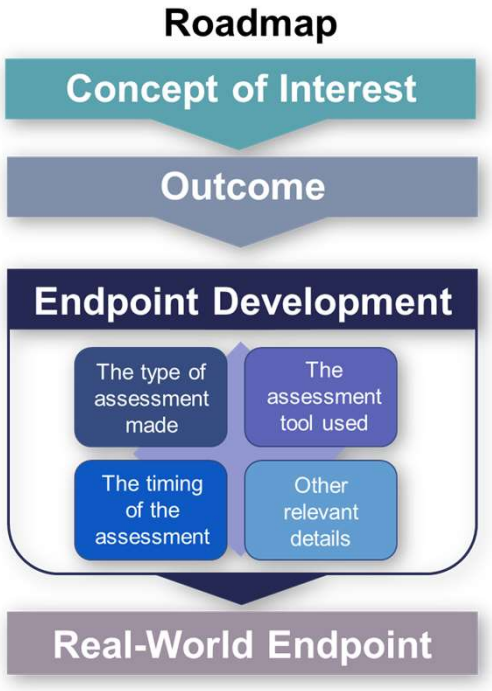
Global Head, Cardio-Renal-Metabolic Development

Novartis

Session II: Transforming Outcome Capture: Advancing Routine Use of Digital Tools and Technology for Study Measurement

A Roadmap for Developing Study Endpoints in Real-World Settings





Nancy Dreyer

Senior Vice President & Chief Scientific Officer, Real World Solutions

IQVIA

IQVIA COVID Active Research Experience (CARE) project

An active, adaptable rapid reporting system designed to study factors that influence symptom severity and progression

Non-prescription and prescription medicines

Vitamins, minerals, herbals

Demographics, underlying health conditions, occupational exposure

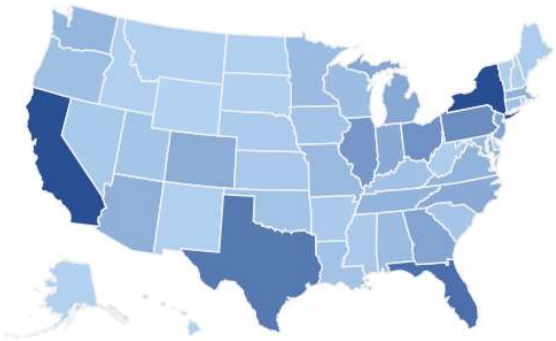
COVID-19 test results, vaccine (coming soon)

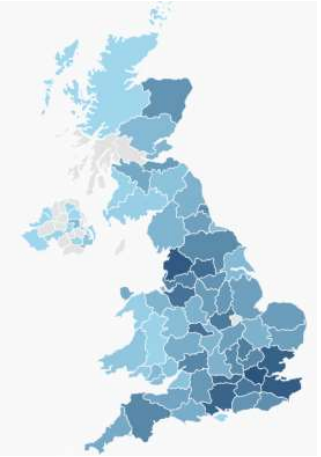
www.helpstopcovid19.com

- Participants come from the community with eligibility based on exposure, not test result
- Evaluates the effects of many factors on symptom severity and change over time
- Alternate contacts can be mobilized for follow-up on hospitalization and death
- Supplementary questions can be sent to participants
- Protocols are available at Clinicaltrials.gov NCT04368065; EU PAS register EUPAS36240

IQVIA COVID Active Research Experience (CARE) Project

Inquiries welcomed at CAREproject@IQVIA.com





www.helpstopCOVID19.com

- **~20,000** participants reporting by smart phone, tablet or PC
- US recruitment started April 2020, UK started July 2020
- Uses adaptive curation with near real-time reporting

LINKAGE — **In the US, a trusted process for tokenization used to link RWD linkage on prescriptions, ambulatory care and hospitalizations**

Leonard Sacks

Associate Director of Clinical Methodology, Office of Medical Policy, Center for Drug Evaluation and Research, U.S. Food and Drug Administration

Digital health technology in mHealth and clinical trials

Biosensors

Continuous glucose monitor

Continuous ECG monitor

Continuous blood pressure monitor

Fall detector

Smart pills

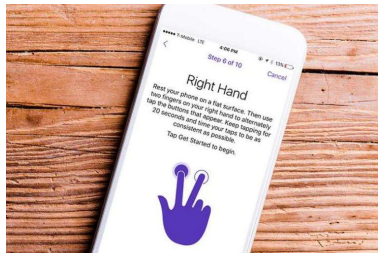
Actigraphy

Interactive mobile applications

Patient reported outcome

Cellphone camera

Coordination test in Parkinson's



Why bother?

Ernesto Ramirez

Design Lead, Research, Analysis, and Learning Team

Evidation Health, Inc.

evidation

Tackling Infectious Disease Research with Decentralized Trials

Ernesto Ramirez, PhD

October 1, 2020

CASE STUDY 1

Home Testing of Respiratory Illness

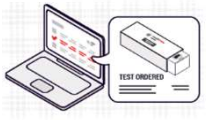
A novel decentralized observational trial exploring symptoms and outcomes related to respiratory illness in adults during 2019-2020 flu season.

- Funded by BARDA and run in collaboration with Audere
- Daily symptom reporting
- Additional recovery and health care experience reports
- Two at-home nasal swabs triggered on symptoms
- Connected wearable data

5,229 participants enrolled over 6½ weeks

527,877 daily surveys completed

606,266 days of wearable data collected



1,006 tests triggered and completed

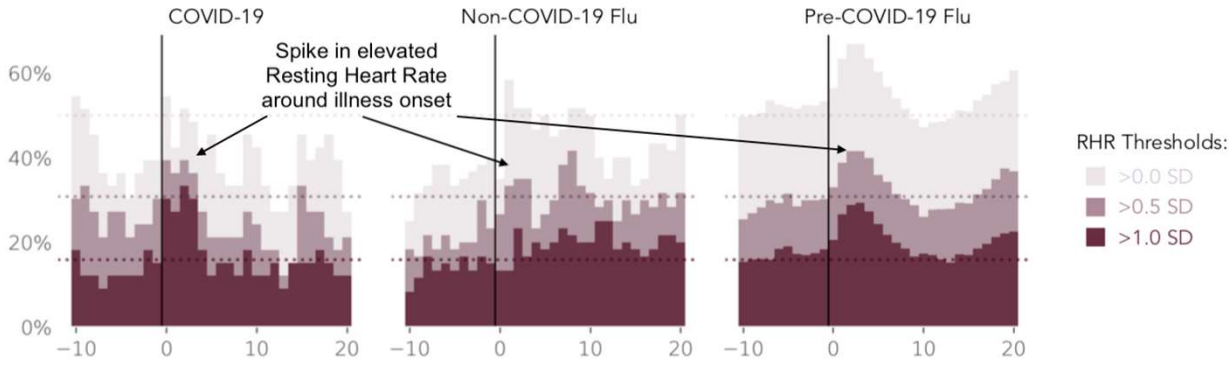
CASE STUDY 2

Measuring COVID-19 in the Real World with PGHD

Large-scale ILI surveillance program updated with assessment of COVID-19 symptoms and outcomes.

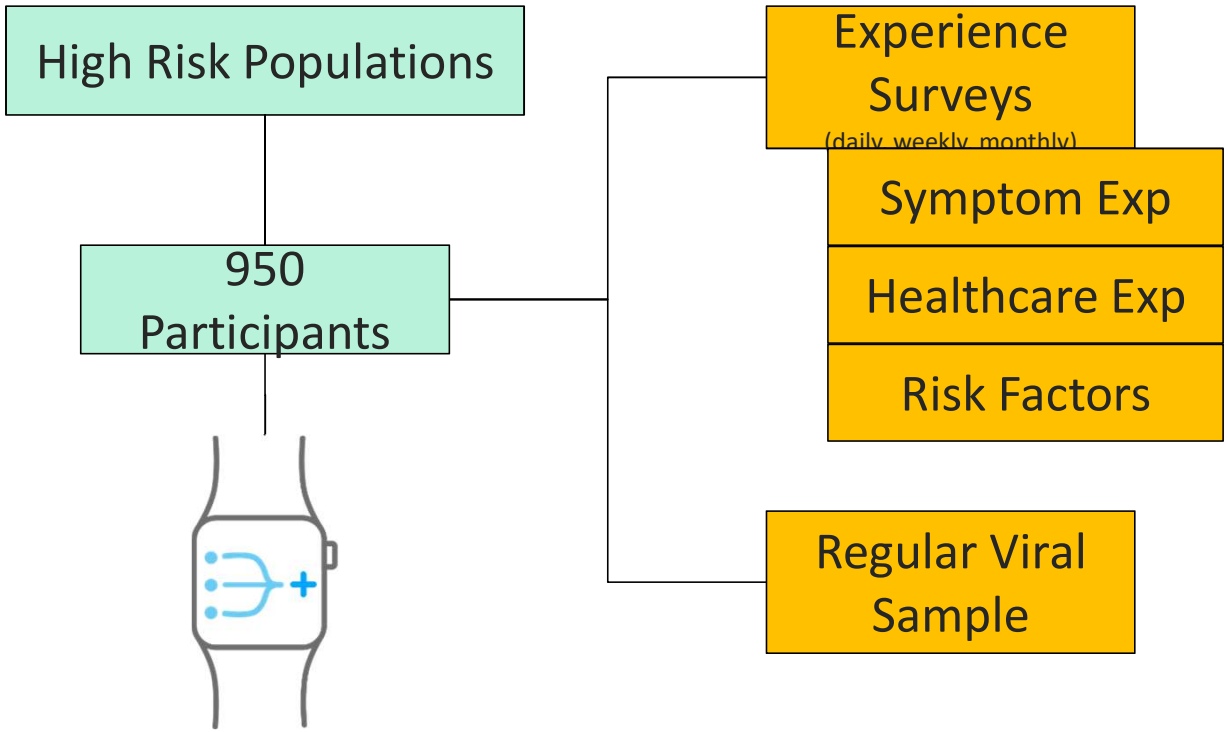
- Weekly symptom assessment on Achievement consumer platform
- 2019-20 flu season + extended through August 2020.
- **1,096,335** weekly survey responses
- **80,274** reported experiencing flu-like symptoms
- Connected wearable data

- Self-reported symptoms of COVID-19 present differently from flu.
- **COVID-19 cases tended to last longer than flu** (median of 12 days vs. 9 days ($p<0.05$) & 7 days ($p<0.01$)) and are characterized by chest pain/pressure, shortness of breath, and anosmia.
- **The fraction of elevated resting heart rate** measurements collected daily from wearable devices **rise significantly in the 2 days surrounding the onset of Covid-19 symptoms** compared to a baseline period.
- Steps lost due to COVID-19 persists for longer than for flu.



CASE STUDY 3

COVID Signals: A multistakeholder program led by BARDA leveraging our platform and expertise to explore potential detection algorithms



- To develop a database of PGHD via wearable and self-reported metrics combined with laboratory confirmation of COVID-19 infection.
- To explore the relationship between PGHD and outcomes among individuals infected with COVID-19
- To build, train, and test preliminary analytical

Crystal Browning

Senior Director, Regulatory Affairs

Pfizer Inc.

Crisaborole
Stasis Dermatitis
'Site-less' Trial Strategy
and
FDA Feedback

October 2020

Breakthroughs that
change patients' lives

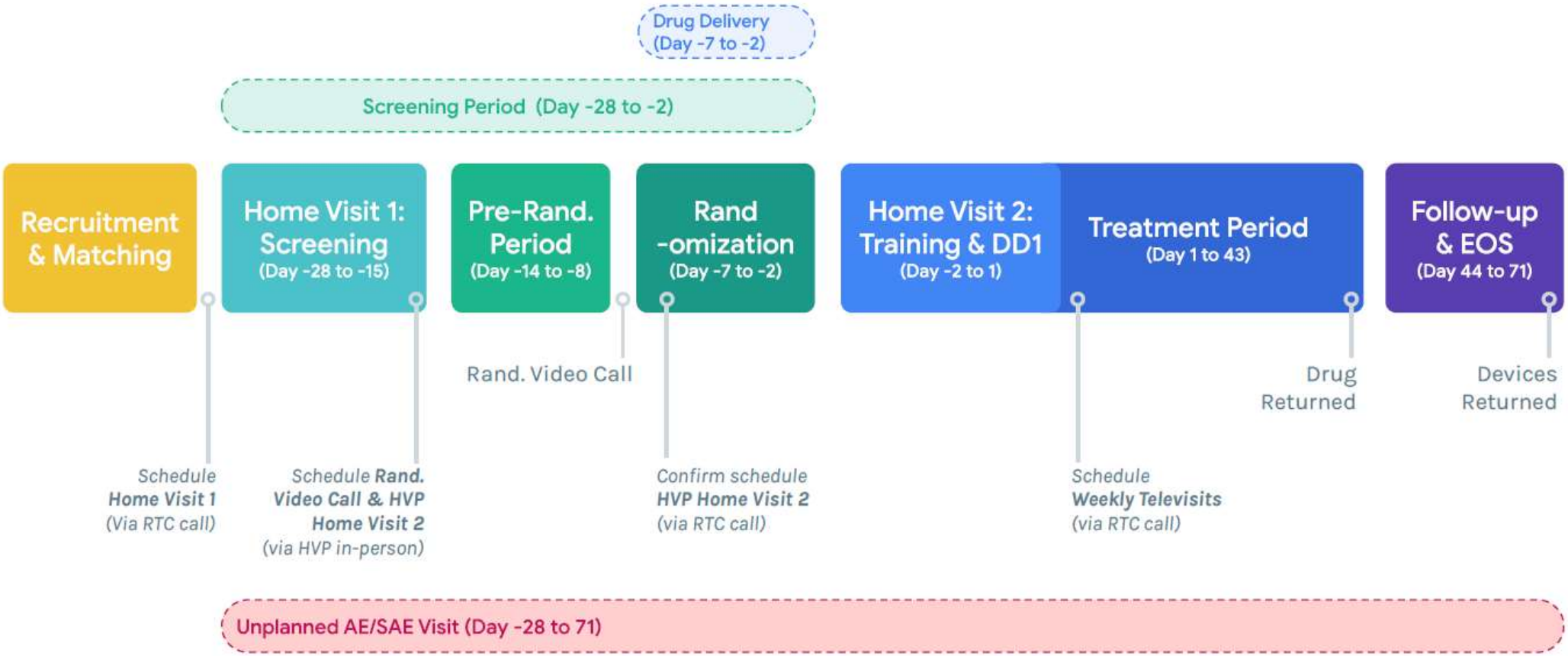
Crisaborole 2% in Stasis Dermatitis Good Context of Use for Site-less Design?

- Disease and population characteristics:
  - Elderly, often with mobility issues
  - Limited body surface area (knees to feet)
- Site-less design
  - Efficacy endpoints measurable by high resolution digital photography and ePROs (pain and itch)
- Drug characteristics:
  - Topical PDE4 inhibitor
  - Approved for Atopic Dermatitis (US, AUS, CAN, EU, China, Israel, etc)
  - Topical, active rapidly metabolized systemically – with limited BSA very little systemic pharmacology
  - Simple and well-known safety profile
  - Simple administration – BID topical
- Place in overall development: Phase 2 proof of concept

Virtual Study C3291038

- No brick-and-mortar investigational sites – ever – and no visits to any 'trial site'
- Central Investigator Group located remotely to subjects location
- Recruited through the internet advertising
- Confirmation of diagnosis and endpoints assessment done by Home Visit Practitioner (HVP) at patient's home
- Three visits at patient's home for lab work, physical examination, endpoint assessment (baseline and screening visits)
- Photos of the lesions taken by patients and read centrally by a group of dermatologists which will be used to validate the remote endpoint capture for future studies Primary Endpoint will use the in-person assessments (bridging remote to in-person)
- Study drug sent directly to subjects from the central pharmacy
- Maintains compliance with the 'fundamentals' of all 21 CFR Part 312 requirements.

Study Phases from Protocol



US FDA Feedback Key Points

- Confirmed Stasis Dermatitis is a viable indication to explore.
- Requested validation of the photographic methodology
  - The validation will be done using the in-person efficacy assessments and the photographic images (bridging concept).
- Provided feedback and guidance regarding the efficacy endpoints for SD and patient reported outcomes measures.
  - The in-person efficacy assessment will be used for the primary endpoint (but will bridge to digital images with central read to support future development with less in person assessment).
  - The team developed a Stasis Dermatitis Symptom Scale which probes on a variety of commonly reported SD symptoms, including pruritus (itch) and pain.
- Requested additional operational details of the study.
  - Drug Supply, vendors roles and oversight, monitoring, participant identity verification, etc.
- Given that this is a proof of concept (POC) trial with no clinical safety concerns, the initiation of the study proceeded without FDA's feedback on the written responses.

Jennifer Goldsack

Co-founder & Executive Director

Digital Medicine Society (DiMe)

TOUR OF DUTY 2020

The Playbook: Digital Clinical Measures

Introducing the essential industry guide for successful remote monitoring across *clinical research*, *clinical care*, and *public health*.

Source: playbook.dimesociety.org

DIGITAL MEDICINE SOCIETY · elektralabs · Genentech A Member of the Roche Group · koneksa health · MYOKARDIA · SageBionetworks · Scripps Research

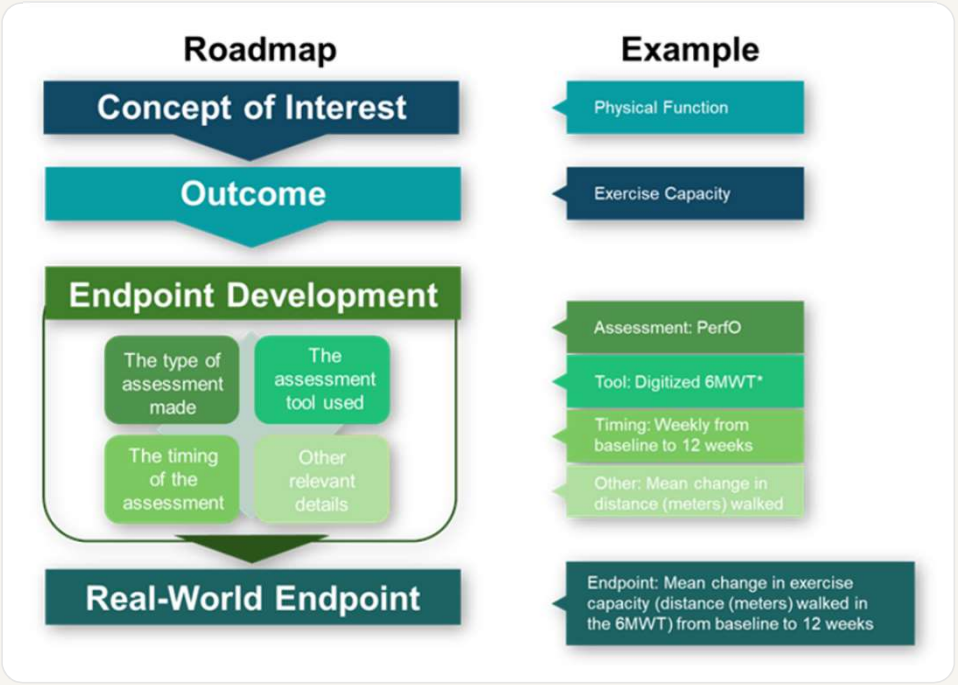
Example: *Real-world setting* endpoint

SPOTLIGHT

A roadmap for developing study endpoints in real-world settings

The example provided by the team at Duke Margolis is consistent with the **MAH > COI > Measure > Endpoint** framework.

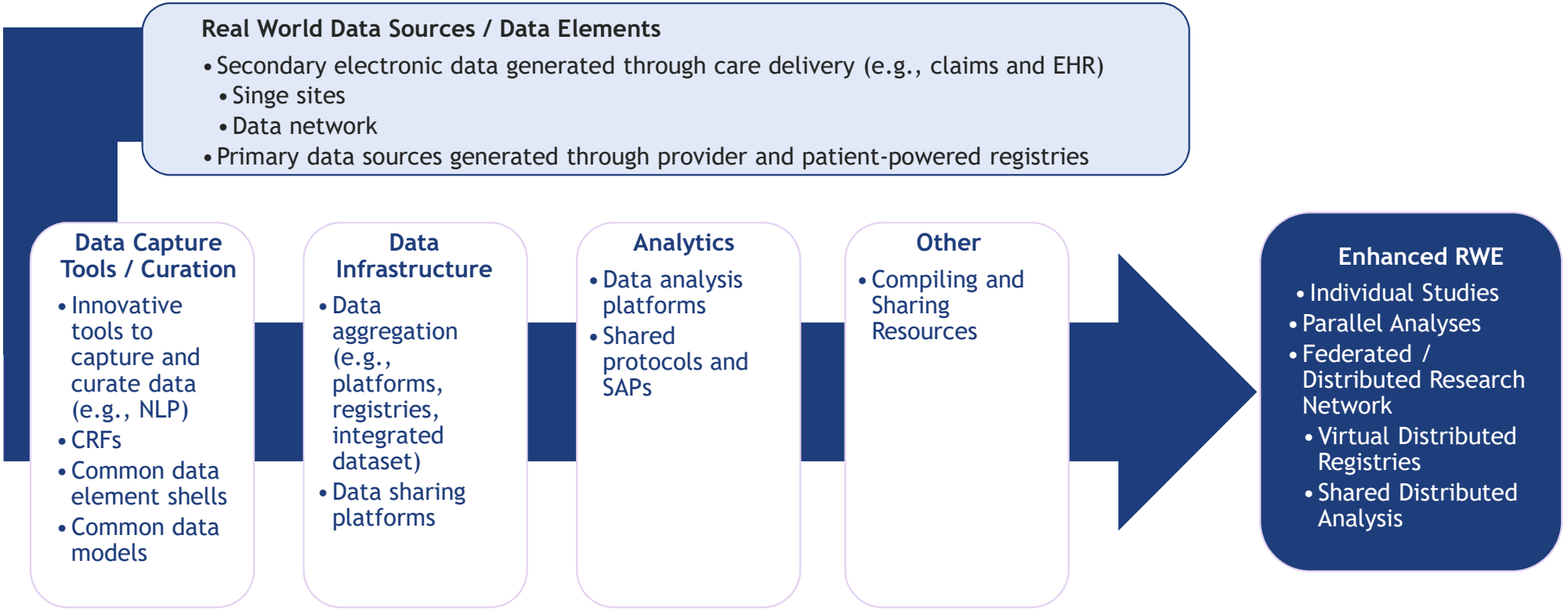
Figure 2. **Roadmap for selecting a feasible and relevant endpoint as illustrated by an example.**



Source: https://healthpolicy.duke.edu/publications/roadmap-developing-study-endpoints-real-world-settings, Playbook team analysis

Session III: Collaborating to Build a Better Real-World Data Infrastructure for Enhanced Post-Market Evidence

Augment Evidence at Product Approval or EUA* by Building on Existing Common Data Models and Data Networks



*EUA: Emergency Use Authorization

Susan Winckler

Chief Executive Officer

Reagan-Udall Foundation for the U.S. Food & Drug Administration

COVID-19 Evidence Accelerator: Community of data & analytic partners ready to urgently address questions

Prioritized research questions

Common data elements and translation tables between common data models

Common protocol for repeated analysis of priority research questions across multiple data partners (the “parallel analysis”)

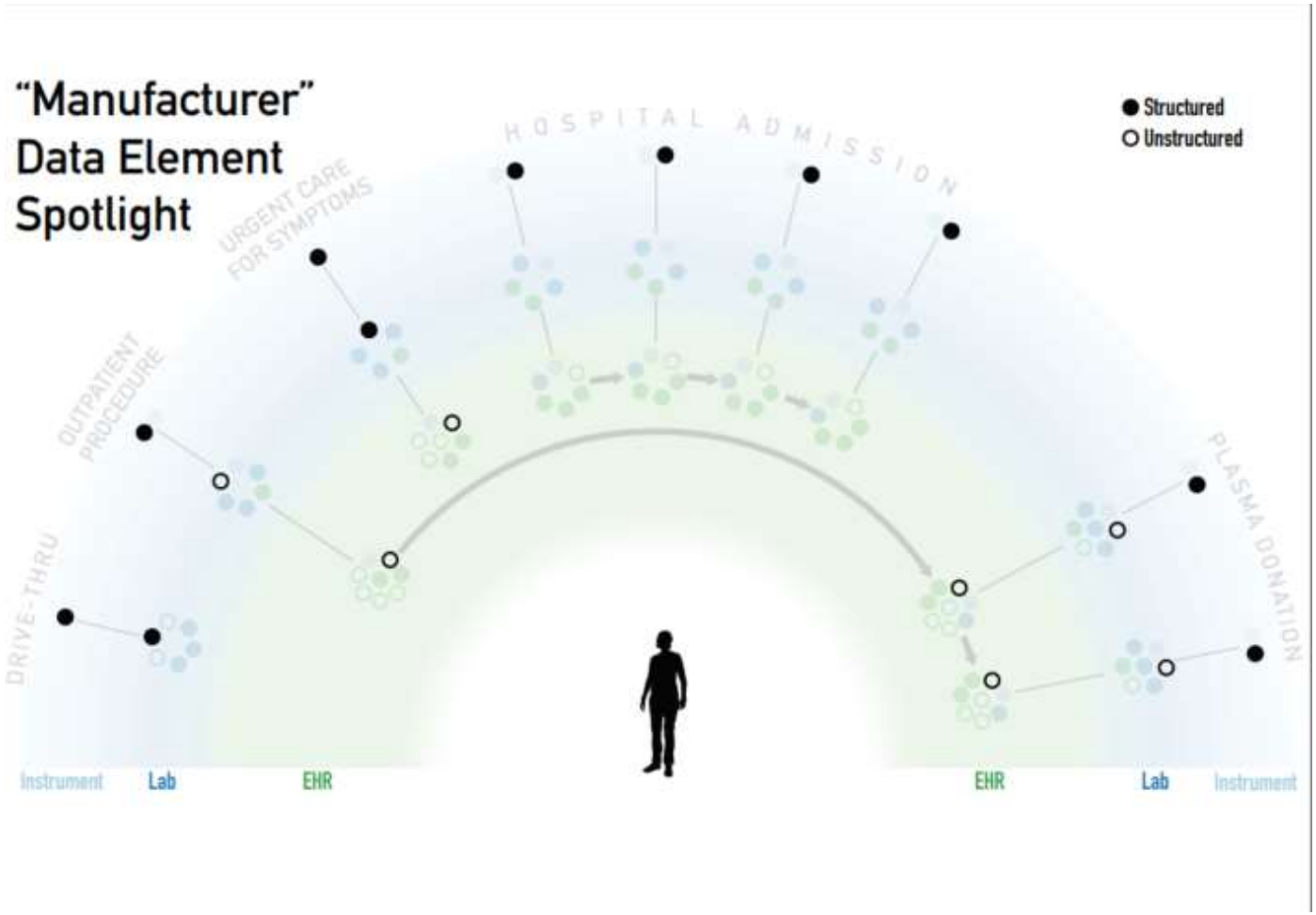
Meetings and forum for rapid cycle feedback and learning

Individual Accelerator communities focused on specific topics (e.g., therapeutics, diagnostics)

REAGAN-UDALL FOUNDATION FOR THE FDA

FRIENDS of CANCER RESEARCH

Sample Data Challenge the Accelerator is Addressing



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.*

REAGAN-UDALL FOUNDATION for the Food and Drug Administration

FRIENDS of CANCER RESEARCH

Brian Anderson

Chief Digital Health Physician

The MITRE Corporation

Griffin Weber

Associate Professor of Medicine & Biomedical Informatics

Department of Medicine, Beth Israel Deaconess Medical Center & Department of Biomedical Informatics, Harvard Medical School

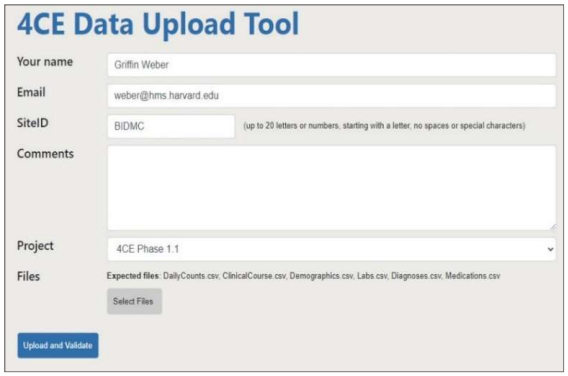
4CE ("foresee") Consortium

https://covidclinical.net

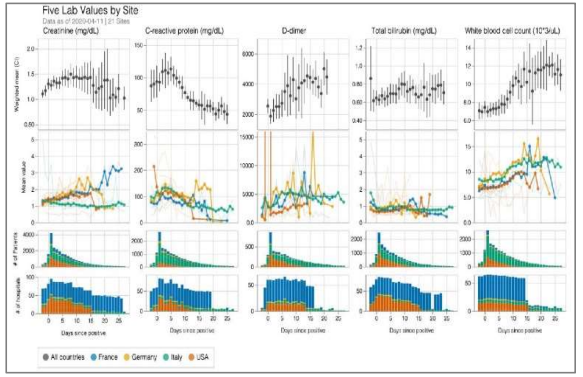
- 200+ hospitals worldwide; organized by i2b2 tranSMART Foundation; Isaac Kohane, PI
- Consortium for Clinical Characterization of COVID-19 by EHR (4CE) Approach:
  - **Move fast**: Early intelligence worth more than complete intelligence later
  - **Reduce barriers**: Run analyses locally, share only aggregate statistics centrally (simple .CSV files)
  - **Share, share, share**: Raw data, visualizations, and methods on public website
  - **Secret sauce**: Engage local informatics experts to iteratively improve sites' data quality (lab units, coding practices, date formats)
- Phase 1: First preprint online in only 4 weeks, with 27,584 COVID-19 patients from 5 countries
- Phase 2: Run more complex patient-level local analyses in R, validate disease severity algorithms

Weekly Zooms, Thousands of Slack Messages

Sites Upload .CSV Files with Aggregate Counts



Review Data with Interactive Visualizations



Brat GA, Weber GM, Gehlenborg N, *et al.* International electronic health record-derived COVID-19 clinical course profiles: the 4CE consortium. *npj Digit. Med.* **3,** 109 (2020). https://doi.org/10.1038/s41746-020-00308-0

Solomon Iyasu

Vice President & Global Head, Pharmacoepidemiology

Merck and Co.

Fireside Chat

Mark McClellan, Director, Duke-Margolis Center for Health Policy

Amy Abernethy, Principal Deputy Commissioner, U.S. Food and Drug Administration

Closing Remarks

Adjournment