Ten Years In: Taking Stock and Looking Forward

Robert M Califf, MD

Vice Chancellor for Health Data Science, Duke University

Advisor, Verily Life Sciences
Motivation for CTTI

Growing frustration that clinical trials were:

- Increasingly expensive
- Increasingly complex
- Often not answering the most important questions
- Not attractive to clinicians

Common discussions involving FDA, industry and academia expressing those same frustrations

Realization that at the core, FDA regulations, guidance and meetings have enormous influence on the entire enterprise

And that FDA needs to have a venue to both listen and participate in improving the system separately from activities related to decisions about specific products

But clinical trials have an impact well beyond the FDA

- Basic mechanisms, clinical practice, health system quality, public health

Accordingly a decision was made to include all sectors in a public private partnership
Overview

- The Clinical Trials Enterprise is robust and productive by any metric

- CTTI has been one of many factors achieving
  - Incremental improvement in clinical trials operations
  - Major step forward in concepts for transformative change

- Major forces are in play that could lead to dramatic change over the next 5-10 years

- There is no substitute for dedicated and passionate people who come together to solve problems

- If transformative change accelerates, CTTI well positioned to be a major positive force
Projects

- Clinical Trial Monitoring and Quality Assurance
- Use of Central IRBs—Advancing the Use
- IND Safety Assessment and Communication
- GCP Training
- Recommendations on Quality by Design
- Effective Engagement with Patient Groups
- Informed Consent
- Electronic Portals for Expedited Safety Reporting
- Efficient and Effective Clinical Trial Recruitment Planning
Projects

- Data Monitoring Committees
- Optimizing operational Efficiency for HABP/VABP Trials/Streamlining protocols
- Improving pediatric Trials in Antibacterial Drug Development
- Registry Trials
- Novel endpoints generated by mobile technology
- Pregnancy Testing
- Strengthening the Investigator Site community
- Improving the value of clinicaltrials.gov
Trend 1: We are close to being able to look at the whole clinical trials enterprise—this will increase peer learning
### Key Clinical Trial Reporting Requirements

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td><strong>What</strong></td>
<td>Registration*</td>
<td>Registration &amp; results reporting</td>
<td>Registration &amp; results reporting</td>
</tr>
<tr>
<td><strong>Scope</strong></td>
<td>Clinical trials (any)</td>
<td>Applicable clinical trials</td>
<td>Clinical trials (NIH-funded)</td>
</tr>
<tr>
<td><strong>Phase</strong></td>
<td>All</td>
<td>Not Phase 1 and device feasibility</td>
<td>All</td>
</tr>
<tr>
<td><strong>Intervention Type</strong></td>
<td>All</td>
<td>Drug, biological, &amp; device products</td>
<td>All (including behavioral interventions)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>regulated by the FDA</td>
<td></td>
</tr>
<tr>
<td><strong>Enforcement</strong></td>
<td>Refusal to publish</td>
<td>Criminal proceedings and civil penalties (up to $10,000/day); loss of HHS funding</td>
<td>Withholding/loss of NIH funding</td>
</tr>
</tbody>
</table>

*ICMJE policy also: (1) expects compliance with results reporting requirements and (2) encourages results reporting for all other trials.
ClinicalTrials.gov Reporting Volume
(as of 5 February 2018)

Registration
- 265,000 study records (including observational)
- 600 submissions/week
- 17,500 data providers (sponsors and investigators)

Summary Results Reporting
- 30,000 records with results posted
- 140 submissions/week
- 3,000 data providers

Usage Stats
- 244M hits per month
- 171M page views per month
- 93K unique visitors per day
Landscape Analysis: Started in CY2017 vs. Registered from Oct 2007-Sep 2010 (Califf et al., 2012)

Records Listing Study Start Date in CY2017 (N = 22,352)

Study Type:
- 4,476 (20%) Observational
- 17,876 (80%) Interventional*

  • Location by Facility Country:
    - 6,105 (34.2%) U.S. Only
    - 8,788 (49.2%) Non-U.S. Only
    - 741 (4.1%) U.S. and Non-U.S.
    - 2,242 (12.5%) Missing

*Subsequent landscape analysis tables limited to Interventional Studies only (N = 17,876)
Landscape Analysis: Started in CY 2017 vs. Registered from Oct 2007-Sep 2010 (Califf et al., 2012)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Started in CY2017</th>
<th>First Registered (Oct 2007-Sept 2010)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lead Sponsor</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Industry</td>
<td>4,135 (23.1%)</td>
<td>15,248 (37.2%)</td>
</tr>
<tr>
<td>NIH</td>
<td>159 (0.9%)</td>
<td>1,106 (2.7%)</td>
</tr>
<tr>
<td>US Federal</td>
<td>158 (0.9%)</td>
<td>547 (1.3%)</td>
</tr>
<tr>
<td>Other</td>
<td>13,424 (75.1%)</td>
<td>24,069 (58.7%)</td>
</tr>
<tr>
<td><strong>Intervention Type (Top 5)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drug and Biological</td>
<td>9,152 (51.2%)</td>
<td>27,699 (67.6%)</td>
</tr>
<tr>
<td>Other</td>
<td>3,670 (20.5%)</td>
<td>5,110 (12.5%)</td>
</tr>
<tr>
<td>Device</td>
<td>2,906 (16.3%)</td>
<td>3,799 (9.3%)</td>
</tr>
<tr>
<td>Behavioral</td>
<td>2,252 (12.6%)</td>
<td>3,307 (8.1%)</td>
</tr>
<tr>
<td>Procedure</td>
<td>1,673 (9.4%)</td>
<td>4,104 (10.0%)</td>
</tr>
</tbody>
</table>
Landscape Analysis: Started in CY 2017 vs. Registered from Oct 2007-Sep 2010 (Califf et al., 2012)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Started in CY2017</th>
<th>First Registered (Oct 2007-Sept 2010)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anticipated Enrollment (# participants)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>3 (&lt;1%)</td>
<td>N/A</td>
</tr>
<tr>
<td>0 (Withdrawn)</td>
<td>238 (&lt;1%)</td>
<td>N/A</td>
</tr>
<tr>
<td>1-100</td>
<td>11,409 (64.7%)</td>
<td>17,726 (62.0%)</td>
</tr>
<tr>
<td>101-1,000</td>
<td>5,586 (31.7%)</td>
<td>9,629 (33.8%)</td>
</tr>
<tr>
<td>&gt;1,000</td>
<td>640 (3.6%)</td>
<td>1,103 (3.9%)</td>
</tr>
<tr>
<td>Number of Arms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>106 (&lt;1%)</td>
<td>N/A</td>
</tr>
<tr>
<td>1</td>
<td>4,624 (25.9%)</td>
<td>N/A</td>
</tr>
<tr>
<td>2</td>
<td>9,732 (54.4%)</td>
<td>N/A</td>
</tr>
<tr>
<td>&gt;2</td>
<td>3,414 (19.1%)</td>
<td>N/A</td>
</tr>
</tbody>
</table>
Landscape Analysis: Started in CY 2017 vs. Registered from Oct 2007-Sep 2010 (Califf et al., 2012)

*Among trials with 2 or more arms (N = 13,146)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Started in CY2017</th>
<th>First Registered (Oct 2007-Sept 2010)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation = “Randomized”</td>
<td>11,540 (64.9%)</td>
<td>27,027 (68.9%)</td>
</tr>
<tr>
<td>Masking = “Yes” (≥1 party)</td>
<td>7,842 (44.1%)</td>
<td>N/A</td>
</tr>
<tr>
<td>DMC = “Yes”</td>
<td>3,157 (40.3%)</td>
<td>N/A</td>
</tr>
</tbody>
</table>
Trend 2: Components of a Previous Disaggregated Evidence Generation System will be increasingly connected
Generating Evidence to Inform Decisions

1. FDA Critical Path
2. NIH Roadmap
3. Data Standards
4. Network Information
5. Empirical Ethics
6. Priorities and Processes
7. Inclusiveness
8. Use for Feedback on Priorities
9. Conflict of Interest Management
10. Evaluation of Speed and Fluency
11. Pay for Performance
12. Transparency to Consumers

Discovery Science → Early Translational Steps → Clinical Trials → Clinical Practice Guidelines → Measurement and Education → Performance Measures → Outcomes → Discovery Science
Industrial Revolutions

First: Water and steam power mechanize production

Second: Electric power to create mass production

Third: Electronics and information technology to automate production

Fourth: Digital revolution characterized by a fusion of technologies that is blurring the lines between the physical, digital and biological spheres
Lessons from Davos

- Massive investment in data and information
- Key components
  - "Big data"
  - Quantitative methods ("AI/Machine learning")
  - Connectedness
- Movement toward value based payment
  - Amazon, Berkshire, JP Morgan
- "Home Inversion" – moving health care to focus on the "other 99%"
Trend 3: Biomolecular, Clinical, Behavioral and Population data will co-exist in common operating systems
WE’VE MAPPED THE WORLD. NOW LET’S MAP HUMAN HEALTH.

www.projectbaseline.com
**DEEP & COMPREHENSIVE DATA CAPTURE WITH STANDARDIZED TOOLS**

<table>
<thead>
<tr>
<th>Category</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Labs</td>
<td>(e.g., CBC, metabolism, liver function)</td>
</tr>
<tr>
<td>Clinical Assessments</td>
<td>(e.g., vitals, physical performance, medical history)</td>
</tr>
<tr>
<td>Cognitive Assessments</td>
<td>(e.g., memory, stress, mood)</td>
</tr>
<tr>
<td>Molecular Labs</td>
<td>(e.g., genomics, proteomics, microbiome)</td>
</tr>
<tr>
<td>Imaging</td>
<td>(e.g., coronary calcium, echocardiogram, chest x-ray)</td>
</tr>
<tr>
<td>Sensor</td>
<td>(e.g., Study Watch, Sleep Sensor)</td>
</tr>
<tr>
<td>Behavior</td>
<td>(e.g., location, activity, social media usage)</td>
</tr>
<tr>
<td>Other</td>
<td>(e.g., health records, claims, environmental)</td>
</tr>
</tbody>
</table>
Learning health care systems

In a learning health care system, research influences practice and practice influences research.

**EVALUATE**
Collect data and analyze results to show what works and what doesn’t.

**IMPLEMENT**
Apply plan in pilot and control settings.

**DESIGN**
Design care and evaluation based on evidence generated here and elsewhere.

**ADJUST**
Use evidence to influence continual improvement.

**DISSEMINATE**
Share results to improve care for everyone.

**INTERNAL AND EXTERNAL SCAN**
Identify problems and potentially innovative solutions.
U.S. Hospitals & physicians in Health Systems

By the end of 2016, there were 626 health systems* in the United States.

<table>
<thead>
<tr>
<th>U.S. hospitals and physicians in health systems</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percentage of U.S. hospital beds in systems</td>
</tr>
<tr>
<td>88.2%</td>
</tr>
<tr>
<td>69.7% of U.S. hospitals are in health systems</td>
</tr>
<tr>
<td>91.6% of U.S. hospital discharges are from system hospitals</td>
</tr>
</tbody>
</table>

| Percentage of U.S. physicians in health systems |
| 44.6%                                         |
| 42.7% of U.S. primary care physicians are in health systems |

Note: The hospital figures represent all non-Federal general acute care hospitals in the United States.

CONTINUOUS MONITORING THROUGH PASSIVE SENSORS

Study watch
Investigational wrist-worn sensor for continuous recording of physiological and environmental data

Sleep sensor
Commercially available, placed under mattress to passively monitor multiple physiologic data parameters

App
Mobile interface for self-reported and passive data acquisitions

Study hub
Safely sends device data to secure, encrypted Baseline database
The Process of Digital Phenotyping

Digital phenotyping involves collecting sensor, keyboard, and voice and speech data from smartphones to measure behavior, cognition, and mood.

Figure Legend:

The Process of Digital Phenotyping

Digital phenotyping involves collecting sensor, keyboard, and voice and speech data from smartphones to measure behavior, cognition, and mood.
1 in 20 of over 3 billion Google searches per day are health related
Categories of information needs
From: Inequalities in Life Expectancy Among US Counties, 1980 to 2014 Temporal Trends and Key Drivers


Figure Legend:
Life Expectancy at Birth by County, 2014
Counties in South Dakota and North Dakota had the lowest life expectancy, and counties along the lower half of the Mississippi, in eastern Kentucky, and southwestern West Virginia also had very low life expectancy compared with the rest of the country. Counties in central Colorado had the highest life expectancies.
Table 1. Variables Included in the Regression Analysis With Summary Statistics and Bivariate Regression Results

<table>
<thead>
<tr>
<th>Variable</th>
<th>Summary Statistics, Mean (SD) [Range]</th>
<th>Bivariate Regression Results</th>
<th>Coefficient (SE)</th>
<th>R²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Socioeconomic and race/Ethnicity factors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Population below the poverty line, %</td>
<td>16.3 (6.4) [3.1-62.0]</td>
<td>-0.24 (0.005)</td>
<td>0.47</td>
<td></td>
</tr>
<tr>
<td>Median household income, log $</td>
<td>10.6 (0.2) [9.8-11.6]</td>
<td>6.06 (0.130)</td>
<td>0.41</td>
<td></td>
</tr>
<tr>
<td>Graduates, age ≥25 y, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High school</td>
<td>83.7 (7.2) [46.3-98.6]</td>
<td>0.20 (0.004)</td>
<td>0.42</td>
<td></td>
</tr>
<tr>
<td>College</td>
<td>19.2 (8.6) [4.2-72.0]</td>
<td>0.15 (0.004)</td>
<td>0.34</td>
<td></td>
</tr>
<tr>
<td>Unemployment rate, age ≥16 y, %</td>
<td>9.1 (3.2) [2.1-27.4]</td>
<td>-0.29 (0.011)</td>
<td>0.18</td>
<td></td>
</tr>
<tr>
<td>Black population, %</td>
<td>9.4 (4.7) [0-85.8]</td>
<td>-0.07 (0.002)</td>
<td>0.24</td>
<td></td>
</tr>
<tr>
<td>American Indian, Native Alaskan, and Native Hawaiian population, %</td>
<td>2.3 (7.9) [0-97.2]</td>
<td>-0.06 (0.005)</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>Hispanic population, %</td>
<td>8.1 (13.1) [0-95.9]</td>
<td>0.02 (0.003)</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>Behavioral and metabolic risk factors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obesity prevalence, age ≥20 y</td>
<td>37.0 (4.3) [18.0-52.0]</td>
<td>-0.39 (0.006)</td>
<td>0.54</td>
<td></td>
</tr>
<tr>
<td>No leisure-time physical activity prevalence, age ≥20 y</td>
<td>27.0 (5.2) [11.7-47.2]</td>
<td>-0.34 (0.005)</td>
<td>0.62</td>
<td></td>
</tr>
<tr>
<td>Cigarette smoking prevalence, age ≥18 y</td>
<td>24.7 (4.1) [7.7-42.1]</td>
<td>-0.40 (0.007)</td>
<td>0.54</td>
<td></td>
</tr>
<tr>
<td>Hypertension prevalence, age ≥30 y</td>
<td>39.5 (3.6) [27.9-56.4]</td>
<td>-0.49 (0.007)</td>
<td>0.62</td>
<td></td>
</tr>
<tr>
<td>Diabetes prevalence, age ≥20 y</td>
<td>14.0 (2.4) [8.1-25.5]</td>
<td>-0.72 (0.011)</td>
<td>0.59</td>
<td></td>
</tr>
<tr>
<td>Health care factors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insured population, age &lt;65 y, %</td>
<td>81.7 (5.7) [57.3-96.7]</td>
<td>0.15 (0.007)</td>
<td>0.14</td>
<td></td>
</tr>
<tr>
<td>Quality index</td>
<td>70.1 (11.5) [0-100]</td>
<td>0.10 (0.003)</td>
<td>0.28</td>
<td></td>
</tr>
<tr>
<td>Physicians per 1000 population, No.</td>
<td>1.1 (1.0) [0-4.4]</td>
<td>0.53 (0.039)</td>
<td>0.06</td>
<td></td>
</tr>
</tbody>
</table>

**Table Title:**
Variables Included in the Regression Analysis With Summary Statistics and Bivariate Regression Results
Trend 4: Patients and Health Care Systems will align to produce needed evidence to guide clinical care and medical product use
National System Paradigm Shift

Passive Surveillance: Challenging to find right pre/post market balance without confidence in post-market data.

Active Surveillance to better protect patients:
- Leverage RWE to support regulatory decisions throughout TPLC
- Embedded in Health Care System (collect data during routine clinical care)
- Shared system to inform the entire Ecosystem (patients, clinicians, providers, payers, FDA, Device Firms)

Current: Parallel track to clinical practice, Inefficient one-off studies.

National System
Post Market Studies, including comparative effectiveness

PCORnet

www.fda.gov
PCORnet® embodies a "network of networks" that harnesses the power of partnerships

20 Patient-Powered Research Networks (PPRNs) + 13 Clinical Data Research Networks (CDRNs) + 1 Coordinating Center = A national infrastructure for people-centered clinical research
PPRNs

- **American BRCA Outcomes and Utilization of Testing Patient-Powered Research Network (ABOUT Network)**
  - University of South Florida

- **Arthritis patient Partnership with comparative Effectiveness Researchers (AR-POウェR PPRN)**
  - Global Healthy Living Foundation

- **CCFA Partners Patient Powered Research Network**
  - Crohn's and Colitis Foundation of America

- **Collaborative Patient-Centered Rare Epilepsy Network (REPA)**
  - Epilepsy Foundation

- **Community and Patient-Partnered Centers of Excellence for Behavioral Health**
  - University of California Los Angeles

- **Community-Engaged Network for All (CENA)**
  - Genetic Alliance, Inc.

- **COPD Patient Powered Research Network**
  - COPD Foundation

- **DuchenneConnect Registry Network**
  - Parent Project Muscular Dystrophy

- **Health eHeart Alliance**
  - University of California, San Francisco (UCSF)

- **ImproveCareNow: A Learning Health System for Children with Crohn’s Disease and Ulcerative Colitis**
  - Cincinnati Children’s Hospital Medical Center

- **Interactive Autism Network**
  - Kennedy Krieger Institute

- **Mood Patient-Powered Research Network**
  - Massachusetts General Hospital

- **Multiple Sclerosis Patient-Powered Research Network**
  - Accelerated Cure Project for Multiple Sclerosis

- **National Alzheimer’s and Dementia Patient and Caregiver-Powered Research Network**
  - Mayo Clinic

- **NephCure Kidney International**
  - Arbor Research Collaborative for Health

- **Patients, Advocates and Rheumatology Teams Network for Research and Service (PARTNERS) Consortium**
  - Duke University

- **Phelan-McDermid Syndrome Data Network**
  - Phelan-McDermid Syndrome Foundation

- **PI Patient Research Connection: PI-CONNECT**
  - Immune Deficiency Foundation

- **Population Research in Identity and Disparities for Equality Patient-Powered Research Network (PRIDEnet)**
  - University of California San Francisco

- **Vasculitis Patient Powered Research Network**
  - University of Pennsylvania
CDRNs

**ADVANCE**
Accelerating Data Value Across a National Community Health Center Network (ADVANCE)
Oregon Community Health Information Network (OCHIN)

**CAPriCORN**
Chicago Area Patient Centered Outcomes Research Network (CAPriCORN)
The Chicago Community Trust

**GPC**
Greater Plains Collaborative (GPC)
University of Kansas Medical Center

**PORTAL**
Kaiser Permanente & Strategic Partners Patient Outcomes Research To Advance Learning (PORTAL) Network
Kaiser Foundation Research Institute

**REACHnet**
Research Action for Health Network (REACHnet)
Louisiana Public Health Institute (LPHI)

**Mid-South CDRN**
Vanderbilt University

**National PEDSnet**
A Pediatric Learning Health System
The Children’s Hospital of Philadelphia

**NYC-CDRN**
New York City Clinical Data Research Network (NYC-CDRN)
Weill Medical College of Cornell University

**OneFlorida Clinical Data Research Network**
University of Florida

**Patient-Centered Network of Learning Health Systems (LHSNet)**
Mayo Clinic

**pSCANNER**
Patient-oriented SCAlable National Network for Effectiveness Research (pSCANNER)
University of California, San Diego (UCSD)

**PaTH**
Towards a Learning Health System
University of Pittsburgh

**Scalable Collaborative Infrastructure for a Learning Healthcare System (SCILHS)**
Harvard University
Resulting in a national evidence system with “research readiness”

PCORnet represents:
~122 million patients
who have had a medical encounter in the past 5 years

*some individuals may have visited more than one Network Partner and would be counted more than once

For clinical trials: 57,000,000
For observational studies: 122,000,000
### Policy efforts underpinning RWE push

<table>
<thead>
<tr>
<th>Cures provisions (Sec. 3022)</th>
<th>PDUFA RWE provisions</th>
</tr>
</thead>
</table>
| - Requires FDA to establish a program to evaluate the potential use of real world evidence to:  
  - Help support the approval of new indications for an approved drug  
  - Help support or satisfy post approval study requirements | - Tracks with Cures Act  
- Requires FDA to establish a program to evaluate the potential use of real world evidence to:  
  - Help support the approval of new indications for an approved drug  
  - Help support or satisfy post approval study requirements |

#### Reinforcing of a Learning Health Care System:
- Doesn’t change approval standards, rather it better supports and enables use of data and evidence on outcomes that are hard to get from traditional RCTs (e.g., outcomes that are too costly, too small populations with particular clinical features, too long follow-up needed, diff impact in diff clinical settings, etc.)
- Learning from real-world patient experiences can support better informed health care decision-making by a range of stakeholders
Payment for value

Sounds simple till you try to do it

But if just ask some simple questions:

- Why doesn’t email work in medicine like other areas?
- Why can’t a person easily get reliable information about health or healthcare on the internet?
- Why do we rely on physical visits to the clinic to try to help people deal with problems that occur at home, work and recreational places?

Defining value has been a complicated and somewhat frustrating pursuit
Berwick’s (ihi) Triple aim has lasting value

- Improved patient/customer experience
- Better outcomes (longevity, function)
- Lower cost
Trend 5: There will be a battle over truth and expertise, just as much in health care as in politics
Technology advances; people stay the same.
Truth and Expertise

We are seeing an erosion in public confidence in:

- Veracity of traditional sources of information
- The value of credentialed expertise
- Science itself

The deluge of information is a key factor
My Major Concern

- Gaps in reliable evidence and scientific truth will be filled in by:
  - Misleading information
  - False information

- The same methods that could get reliable information to the right people at the right time can be used to target susceptible individuals and groups for misleading and untruthful information
Russian Add in Facebook

'LIKE' IF YOU WANT JESUS TO WIN!
Bottom Line

- We live in a continuum of information from home, workplace, health care system...

- Learning is happening continuously with available information—the old divisions (health/non-health; research/clinical care) are breaking down

- We need new constructs to guide the learning enterprise to benefit and away from harmful practices, diagnostic strategies and therapies
Trend 6:
Despite setbacks along the way, the movement towards data sharing and transparency is inevitable
Trialists’ Intent to Share Individual Participant Data as Disclosed at ClinicalTrials.gov

Clinical trials registered between Jan 2016-Aug 2017 (N = 35,621)

- 25,551 (72%) responded to Plan to Share IPD data element
  - 16,317 (63.9%) “No”
  - 6,452 (25.3%) “Undecided”
  - 2,782 (10.9%) “Yes”

- Misunderstanding of “IPD sharing” among sample of free-text descriptions of IPD sharing plans included
  - Via publication or posting on results database
  - Data would be provided to trial participants
  - Data would be shared with select groups (e.g., collaborators)

The New Einsteins Will Be Scientists Who Share
From cancer to cosmology, researchers could race ahead by working together—online and in the open

By MICHAEL NIELSEN

In January 2009, a mathematician at Cambridge University named Tim Gowers decided to use his blog to run an unusual social experiment. He picked out a difficult mathematical problem and tried to solve it completely in the open, using his blog to post ideas and partial progress. He issued an open invitation for others to contribute their own ideas, hoping that many minds would be more powerful than one. He dubbed the experiment the Polymath Project.

Several hours after Mr. Gowers opened up his blog for discussion, a Canadian-Hungarian mathematician posted a comment. Fifteen minutes later, an Arizona high-school math teacher chimed in. Three minutes after that, the UCLA mathematician Terence Tao commented. The discussion ignited, and in just six weeks, the mathematical problem had been solved.
Data Activation and Testing Outcomes

What Impacts Behavior?

A
CONTROL

B
VARIATION
Digital Transformation

2010
Individual Productivity
IT Silos

- Data on premise, hard to access, analyze and use
- Productivity tools built for individual, local usage
- IT focusing on *where* it computes

2020
Collective Intelligence
Distributed Computing

- Data stored in cloud, simple to query
- Collaborative, cloud based productivity applications
- Machine learning drives deep, actionable insights
- IT changing *how* it computes
Asymptotic Goal

People should have access to clear, understandable information about the benefits and risks of medical products, medical interventions and major decisions about their health.
Premise

There is no technological limitation to developing clear, understandable information about the benefits and risks of medical products, healthcare delivery practices and major decisions about people’s health and to giving them access to it.
Ten Questions about CTTI and Clinical Trials

- Are we really making progress, or just treading water?
  - In 2007 (another 10 year anniversary!) the National Academy of Sciences workshop summary noted that the sheer volume of clinical decisions to be made in the absence of support from clinical trials requires that we understand the best alternative methods when traditional, regulated RCTs are unavailable, impractical or inapplicable. Some alternatives to traditional, regulated RCTs may include practical clinical trials, cluster randomized trials, observational treatment trials, interrupted time series and instrumental variable analysis. How far have we come in 10 years? What does CTTI need to do to advance these new methods?

- How do we go from talk to action in “real world data” and “real world evidence”?
  - Real world data and real world evidence are buzz words in our industry right now, but have the potential to transform the way we conduct clinical trials. What do you think is needed to move from talk to action? And/or, how can CTTI move the needle?

- How do we better share learning to accelerate improvements in trials?
  - We’ve made a lot of great incremental improvements to clinical trials. There are still a lot of opportunities to be transformational as we improve efficiency in clinical trials, from study start up processes to data collection. What are those opportunities? In many cases it seems that we re-invent the wheel with each new trial. How can we as an industry better learn from one another’s best practices and cut some of the waste/inefficiency in the system?
Ten Questions about CTTI and Clinical Trials

Patient/Person Engagement
- CTTI has been a leader in promoting patient engagement in clinical trial design and conduct. How must the way we engage with patients, consumers and carers evolve over the next 5 years? How can we leverage the patient voice more effectively, turning it into the science of patient input? Are we talking about “patients” or “people” (patients, consumers, carers, caregivers…)?

Data Sharing and Transparency
- We’ve heard a lot about data sharing and transparency lately. What are some gains we might see through more open data sharing? Through better reporting of results? What keeps us from sharing? What could CTTI do to reduce data blocking and hoarding?

Innovative Trial Designs
- Innovative trial designs (adaptive designs, master protocols, platform trials) will help to change the way we gather and interpret data, and clinical trials that incorporate adaptive designs are becoming more and more common. What are other innovations are you seeing? what others do you need, or are hoping for? how will these new approaches create higher quality, more efficient trials?
Ten Questions about CTTI and Clinical Trials

- Engaging those who fund trials and set the rules for how they are done
  - How do we reach deeper into FDA, NIH and CMS to engage the thousands of experts within the Agencies?

- Assessing Value as well as “Safe and Effective”
  - People, clinicians and health systems want to know the value of treatment (clinical benefit relative to resource use or cost);
  - Does CTTI have a role here?

- Joining the 4th Industrial Revolution
  - *Appropriate* use of technology will be critical to the success of a learning health care system. What are some challenges and opportunities you perceive as technology becomes a normed part of trial conduct?
  - What about trials that can be done completely outside of the regulatory/medical system?

- Defining Quality of Clinical Trials
  - What is quality by design reduced to practice?
  - How do we define high quality and poor quality trials?