Therapeutics in Children: Great Progress, Now Let’s Fill in the Gaps

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Duke University
Advisor, Verily Life Sciences
FDA ADEPT Meeting
September 18th, 2017
Frontiers

• Human biology
  – Growth and development
  – Maternal Fetal systems biology

• Evidence generation with pragmatic outcome studies

• Implementation science

• Social determinants of health

• Ethics of information and data science in children
Historical Milestones and Legislation

- **1902** The Biologics Control Act enacted following the death of 22 children from tainted anti-toxins
- **1938** FD&C Act: Drugs must be Safe: enacted after 100 deaths, many in children, after use of Elixir Sulfanilamide
- **1962** Following thalidomide tragedy in Europe; Kefauver–Harris amendments require effectiveness
- **1962** The FD&C Act amended: Drugs not tested in children should not be used in children
- **1974** AAP Committee on Drugs issues guidelines for evaluating drugs for pediatric use
- **1977** AAP issues guidelines for ethical conduct in pediatric studies
- **1979** FDA requires sponsors to conduct pediatric clinical trials before including pediatric information in the labeling
- **1992** Agency proposed Pediatric Labeling Rule and proposes extrapolation of efficacy from other data
- **1994** Final Rule on Pediatric Labeling. Formalizes Extrapolation of Efficacy; manufacturers to update labeling if pediatric data existed; HOWEVER, it allowed a disclaimer to the labeling for drugs not evaluated in children
- **1994** Pediatric Plan to encourage voluntary development of pediatric data
- **1997** FDAMA creates pediatric exclusivity provision *(voluntary)*, provides 6-month exclusivity incentive
- **1998** Pediatric Rule *(mandatory)*: products are required to include pediatric assessments if the drug is likely to be used in a "substantial number of pediatric patients" (50,000) or if it may provide a "meaningful therapeutic benefit"
- **2002** Pediatric Rule declared invalid by DC Federal Court; the rule exceeded FDA’s authority
- **2002** FDAMA reauthorized as BPCA. Maintains 6-month exclusivity added to patent life of the active moiety. Creates Office of Pediatric Therapeutics (including ethicist). Mandates pediatric focused safety reviews
- **2003** PREA re-establishes many components of the FDA’s 1998 pediatric rule. Orphan products are exempted
- **2007** FDAA Reauthorizes BPCA & PREA for 5 years: Pediatric Review Committee (PeRC) formed. Studies submitted will result in labeling. Negative and positive results of pediatric studies will be placed in labeling
- **2012** FDASIA legislation makes permanent BPCA and PREA
Measures of Success

• 1997-2016: Over 620 products have been studied in pediatrics and have new pediatric information in the label
  – Of these, over 560 involved new pediatric studies
• First products submitted and labeled as a result of the BPCA “Docket” process involving FDA/NIH/investigators
  – 4 products have had a docket opened (sodium nitroprusside, meropenem, lorazepam, and ampicillin)
  – 3 products with finalized labeling (sodium nitroprusside, meropenem, and lorazepam)
The need for actionable evidence generation is urgent in the US
Mortality in the 20th Century

Better treatment of cardiovascular disease, low birth-weight infants

Reduced infectious disease mortality (clean water, sewers, antibiotics, better nutrition)
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.
Figure Legend:

Change in Life Expectancy at Birth by County, 1980 to 2014

Compared with the national average, counties in central Colorado, Alaska, and along both coasts experienced larger increases in life expectancy between 1980 and 2014, while some southern counties in states stretching from Oklahoma to West Virginia saw little, if any, improvement over this same period.
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>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Coefficient (SE)</td>
</tr>
<tr>
<td><strong>Socioeconomic and race/Ethnicity factors</strong></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>
</tr>
<tr>
<td>Median household income, log $</td>
<td>10.6 (0.2) [9.8-11.6]</td>
<td>6.06 (0.130)</td>
</tr>
<tr>
<td>Graduates, age ≥25 y, %</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>
</tr>
<tr>
<td>College</td>
<td>19.2 (8.6) [4.2-72.0]</td>
<td>0.15 (0.004)</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>
</tr>
<tr>
<td>Black population, %</td>
<td>9.4 (14.7) [0-85.8]</td>
<td>-0.07 (0.002)</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>
</tr>
<tr>
<td>Hispanic population, %</td>
<td>8.1 (13.1) [0-95.9]</td>
<td>0.02 (0.003)</td>
</tr>
<tr>
<td><strong>Behavioral and metabolic risk factors, %</strong></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>
</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>
</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>
</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>
</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>
</tr>
<tr>
<td><strong>Health care factors</strong></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>
</tr>
<tr>
<td>Quality index</td>
<td>70.1 (11.5) [0-100]</td>
<td>0.10 (0.003)</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>
</tr>
</tbody>
</table>

Table Title:
Variables Included in the Regression Analysis With Summary Statistics and Bivariate Regression Results

**Abbreviation:** SE, standard error.
Current system of evidence generation is inadequate
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

Outcomes
Performance Measures
Discovery Science
Early Translational Steps
Clinical Trials
Clinical Practice Guidelines
Measurement and Education
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
Organizational substrate for far better system is developing rapidly
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.
Previously Independent Sites now part of large integrated health systems
increasingly sophisticated data warehouses
Nodes are Operational Clusters Using Common Data
Public private partnerships are developing to generate reliable evidence rapidly.
Drug Surveillance and Trials

Coordinating Center

Sentinel
Device Surveillance and Trials

NEST

Coordinating Center
National System Paradigm Shift

Passive Surveillance

Challenging to find right pre/post market balance without confidence in post-market data

Parallel track to clinical practice

Inefficient one-off studies

Current

Active Surveillance to better protect patients

Leverage RWE to support regulatory decisions throughout TPLC

National System

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)
Post Market Studies, including comparative effectiveness

PCORnet

Coordinating Center

www.fda.gov
Demonstration Project Overview-NIH Healthcare Systems Research Collaboratory

10 Demonstration Projects spanning 12 NIH institutes and centers

Major clinical outcome trials

1-year planning phase (UH2)

Implementation phase (UH3)

Using EHRs and minimal additional data collection

Log order reduction in cost

Collaboratory Coordinating Center

- LiRE — Lumbar Image Reporting and Epidemiology
- SPOT — Suicide Prevention Outreach Trial
- TSOS — Trauma Survivors Outcomes and Support
- TIME — Time to Reduce Mortality in End-Stage Renal Disease (sites to be selected from units across all 50 states)
- STOP CRC — Step Colorectal Cancer in Priority Populations
- PPaCT — Collaborative Care for Chronic Pain
- PROVEN—Pragmatic Trial of Video Education in Nursing Homes
- ABATE — Active Bathing to Eliminate Infection
- ICD-Pieces — Improving Chronic Disease Management with Pieces

Additional sites to be determined

22
PCORnet/PCRF as an Example
People-Centered Research Foundation
PCORnet 2.0
PCORnet® : the National Patient-Centered Clinical Research Network

An innovative initiative funded by the Patient-Centered Outcomes Research Institute (PCORI), PCORnet is a large, highly representative, national patient-centered clinical research network.

Our vision is to support a learning U.S. healthcare system and to enable large-scale clinical research conducted with enhanced quality and efficiency.

Our mission is to enable people to make informed healthcare decisions by efficiently conducting clinical research relevant to their needs.
PCORnet® embodies a "network of networks" that harnesses the power of partnerships.
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-PoWER PPRN)
Global Healthy Living Foundation

CCFA Partners Patient Powered Research Network
Crohn’s and Colitis Foundation of America

Collaborative Patient-Centered Rare Epilepsy Network (REN)
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

<table>
<thead>
<tr>
<th>ADVANCE</th>
<th>Accelerating Data Value Across a National Community Health Center Network (ADVANCE)</th>
<th>Oregon Community Health Information Network (OCHIN)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPriCORN</td>
<td>Chicago Area Patient Centered Outcomes Research Network (CAPriCORN)</td>
<td>The Chicago Community Trust</td>
</tr>
<tr>
<td>GPC</td>
<td>Greater Plains Collaborative (GPC)</td>
<td>University of Kansas Medical Center</td>
</tr>
<tr>
<td>PORTAL</td>
<td>Kaiser Permanente &amp; Strategic Partners Patient Outcomes Research To Advance Learning (PORTAL) Network</td>
<td>Kaiser Foundation Research Institute</td>
</tr>
<tr>
<td>REACHnet</td>
<td>Research Action for Health Network (REACHnet)</td>
<td>Louisiana Public Health Institute (LPHI)</td>
</tr>
<tr>
<td>Mid-South CDRN</td>
<td>Vanderbilt University</td>
<td></td>
</tr>
<tr>
<td>National PEDSnet: A Pediatric Learning Health System</td>
<td>The Children's Hospital of Philadelphia</td>
<td></td>
</tr>
<tr>
<td>NYC-CDRN</td>
<td>New York City Clinical Data Research Network (NYC-CDRN)</td>
<td>Weill Medical College of Cornell University</td>
</tr>
<tr>
<td>OneFlorida Clinical Data Research Network</td>
<td>University of Florida</td>
<td></td>
</tr>
<tr>
<td>LHSNet</td>
<td>Patient-Centered Network of Learning Health Systems (LHSNet)</td>
<td>Mayo Clinic</td>
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<tr>
<td>pSCANNER</td>
<td>Patient-oriented SCAlable National Network for Effectiveness Research (pSCANNER)</td>
<td>University of California, San Diego (UCSD)</td>
</tr>
<tr>
<td>PaTH</td>
<td>PaTH: Towards a Learning Health System</td>
<td>University of Pittsburgh</td>
</tr>
<tr>
<td>SCILHS</td>
<td>Scalable Collaborative Infrastructure for a Learning Healthcare System (SCILHS)</td>
<td>Harvard University</td>
</tr>
</tbody>
</table>
Resulting in a national evidence system with “research readiness”

<table>
<thead>
<tr>
<th>Sex</th>
<th>Female</th>
<th>Male</th>
<th>Missing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Race</td>
<td>White</td>
<td>Non-White</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>0–4</td>
<td>5–14</td>
<td>15–21</td>
</tr>
</tbody>
</table>

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

**Pool of patients**

<table>
<thead>
<tr>
<th>For clinical trials</th>
<th>57,000,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>For observational studies</td>
<td>122,000,000</td>
</tr>
</tbody>
</table>
Policy supports this evolution of real world evidence
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
Real World Data vs Evidence

Real World Data and Efficacy

Real-World Evidence — What Is It and What Can It Tell Us?

- Real-world evidence can be used across a wide spectrum of research, ranging from observational studies to studies that incorporate planned interventions, whether with or without randomization at the point of care.

- Incorrect to contrast the term “real-world evidence” with the use of randomization in a manner that implies that they are disparate or even incompatible concepts.

- Must consider the components of such trials that are critical to obtaining valid results and minimizing bias.
Deeper Information about Mechanism will Soon be Available
WE’VE MAPPED THE WORLD. NOW LET’S MAP HUMAN HEALTH.
www.projectbaseline.com
COMPREHENSIVE ONSITE ASSESSMENTS

“Omics”
- Genomics
- Proteomics
- Transcriptomics
- Metabolomics
- Microbiome
- Etc.

Eye exam, audiometry, PFT, etc.

Personal, family history surveys, etc.

Imaging
- Chest x-ray
- Coronary CT
- Echocardiography
- Etc.

Cognitive tests, physical performance tests, etc.

Blood, urine, stool, saliva, microbiome

Continuous monitoring study watch, sleep sensor, app
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
MOBILE APP

Project Baseline

Sleep Poll
1 day poll • 1 minute per day
How you slept yesterday may help us predict how you function today
LEARN MORE START

On site visit
Wed June 24th • 9:00am - 5:30pm
How you slept yesterday may help us predict how you function today
LEARN MORE START

How many times did you wake up?
Select a number

1
2
3
4
5
6
7
NEXT
# Deep Molecular Profiling

## Samples
- Serum
- Whole Blood
- PBMCS
- Plasma
- Stool
- Saliva
- Urine

## Core Platforms
- **Clinical Labs**
- **Genomics** (WGS, DNA arrays)
- **Epigenomics** (Methyl arrays)
- **Transcriptomics** (RNA-seq)
- **Immunophenotyping** (CyTOF)
- **Microbiome** (16S rRNA)
- **Proteomics**
- **Metabolomics**

## Automation

~6TB data per subject

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*Project Baseline*
Novel approaches: examples

- Computational
  - Maternal-fetal physiologically-based pharmacokinetic (PBPK) models

- Non-invasive drug measurements
  - Raman technology

- Developmental fetal pharmacodynamics
Maternal-fetal PBPK models

- Incorporate drug properties and maternal-fetal physiologic changes to predict drug disposition in mother and fetus

- Ex-vivo placental perfusion and animal models inform and help bridge PBPK models to humans

- Observed data is used to confirm predictions and reduce women enrolled in trials
Fetal PBPK model structure
Maternal-fetal drug exposure simulations predicted with PBPK

Changes in maternal (solid) and fetal (dashed) exposure at 20 wk (red) and 40 wk (blue) GA under different placental drug disposition assumptions

Drug Metab Dispos 45:920–938, August 2017
Non-invasive drug concentration: preclinical

Figures shows good correlation between traditional tenofovir porcine vaginal tissue concentration measurements (HPLC/MS/MS) and Raman predictions.
Information is already ubiquitous—how do we help people find accurate, truthful information that is scientifically based?
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
1 in 20 Google searches are health related
Our Mission:
Make health information universally accessible and useful.
Categories of information needs

- Condition
- Treatments
- Local
- Other

- Home Remedies
- Symptoms & Diagnosis
- Nav
- Shopping
- Fitness
- Reproduction
- News

- Expert
How do we help people find their way to useful action and behaviors?
WHY DEPRESSION?

DEPRESSION IS HIGHLY PREVALENT

300M people suffer from depression globally, WHO has declared it a leading cause of disability [WHO]

MANY PEOPLE DON'T GET TREATMENT

50% of people with depression in the US did not get any treatment [JAMA]

TREATMENT IS OFTEN DELAYED

7 YRS average time from onset to treatment in the US [JAMA]

TREATMENT IS EFFECTIVE

70% of patients can improve, often in a matter of weeks [NIMH]

Google has the reach, scale and technology to help
PRODUCT OVERVIEW: What is PHQ-9?

PHQ-9 is a Patient Health Questionnaire, with 9 questions, that is used to measure depression severity.

<table>
<thead>
<tr>
<th>Over the last 2 weeks, how often have you been bothered by any of the following problems?</th>
<th>Not at all</th>
<th>Several days</th>
<th>More than half the days</th>
<th>Nearly every day</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Little interest or pleasure in doing things</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>2. Feeling down, depressed, or hopeless</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3. Trouble falling or staying asleep, or sleeping too much</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>4. Feeling tired or having little energy</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>5. Poor appetite or overeating</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>7. Trouble concentrating on things, such as reading the newspaper or watching television</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>8. Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>9. Thoughts that you would be better off dead or of hurting yourself in some way</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>
PRODUCT OVERVIEW: MVP Design & Demos

go/phq9-demo
We need a massive educational shift at all levels to take this gift of technology and optimize its use for better health for individuals and populations.
For Big-Data Scientists, ‘Janitor Work’ Is Key Hurdle to Insights
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
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
Frontiers

• Human biology
  – Growth and development
  – Maternal Fetal systems biology
• Evidence generation with pragmatic outcome studies
• Implementation science
• Social determinants of health
• Ethics of information and data science in children