Clinical Research Informatics & Implementation Science Year-in-Review

Peter J. Embí, MD, MS, FACP, FACMI, FAMIA, FIAHSI

President and CEO, Regenstrief Institute
Leonard Betley Professor of Medicine
Associate Dean for Informatics and Health Services Research
Vice-President for Learning Health Systems, IU Health

March 24, 2021
AMIA Virtual Informatics Summit

Regenstrief Institute

Disclosures

- **Federal Funding:** NIH: NLM, NCATS; PCORI
- **Academic Consulting:** Yale University, Cleveland Clinic, Virginia Commonwealth University, University of Miami, University of Florida, University of Iowa, University of Pittsburgh, University of Colorado, Georgetown U., Rochester U.
- **Other Boards/Consulting/Honoraria:** American Medical Informatics Association (AMIA)
- **Study Section:** NIH
- **Corporate Institutional Partnerships (no personal compensation):** Lifeomic LLC; Merck; Pfizer; Roche; Cook Medical; Eli Lilly; VenTech.

Approach to this presentation

- Mixed approach to article identification:
  - Started with structured approach
    - (akin to ACP “update” sessions)
  - Solicited recommendations from colleagues
  - Augment with “what seemed interesting” approach
- Learned a lot from doing this last 10 years
  - Tracked manuscripts throughout the year
  - Intended to spread work out…

    …still worked down to the wire

- So, what was my approach…

Source of Content for Session

- Literature review:
  - Initial search by MESH terms and keywords, including:
    - "Biomedical Research"[Mesh] AND "Informatics"[Mesh]
    - NOT ("computational biology"[mesh] OR "genetics"[mesh])
    - Initial searches resulted in **704** articles
    - Further limits: **490**
  - Additional articles found via:
    - Recommendations from colleagues
    - Other keyword searches using terms like:
      - Clinical Trials, Clinical Research Informatics, Translational, Data Warehouse, Research Registries, Recruitment, Learning Health System, etc.
    - Yielding **299** total
  - From those, I've selected **68** representative papers that I'll present here (*briefly*)

Session caveats

What this is not…

- A systematic review of the literature
- An exhaustive review

What this is…

- My best attempt at *briefly* covering *some* of the representative CRI literature from the past year
- A snap-shot of excellent CRI activity over past year+
- What I thought was particularly notable

Topics

- Grouped **68** articles into several CRI categories (not *all* CRI areas)
  - Data Sharing, Re-Use and RWD
  - CRI Methods and Approaches
  - Participant Engagement & Recruitment
  - Learning Health Systems & Delivery Science
  - CRI Ethics
  - Policy & Perspectives
- In each category, I'll highlight a **2-4** key articles and then given a quick(er) "shout out" to others
- Conclude with notable events from the past year+

Apologies up front

- I’m CERTAIN I’ve missed a lot of great work
- I’m REALLY SORRY about that

Clinical Research Informatics

The maturation of clinical research informatics as a subdomain of biomedical informatics
Bakken, S. JAMIA. 2021

Review of Clinical Research Informatics Solomonides, A. Yearbk of Med Info. 2020

Table 1 Results of the literature search for CRI papers.

PRINCIPAL REVIEW CATEGORIES	COUNT
AI (MACHINE-LEARNING, IMAGING, AND NATURAL-LANGUAGE-PROCESSING)	99
ANALYTICS - DATA SCIENCE	13
BLOCKCHAIN	12
CAUSAL INFERENCE	33
COGNITION AND DIAGNOSIS	10
DATA, DATA QUALITY, AND DATA QUERIES	59
DE-IDENTIFICATION AND DISTRIBUTED PARADIGMS	42
ETHICAL, LEGAL, AND SOCIAL ISSUES	23
ECONOMICS, BUSINESS, AND IMPLEMENTATION	19
PHENOTYPING AND COHORT DISCOVERY	67
REAL WORLD EVIDENCE	39
MISCELLANEOUS	24
TOTAL	440

Data Sharing, Re-Use & RWD for Research

The National COVID Cohort Collaborative (N3C): Rationale, design, infrastructure, and deployment

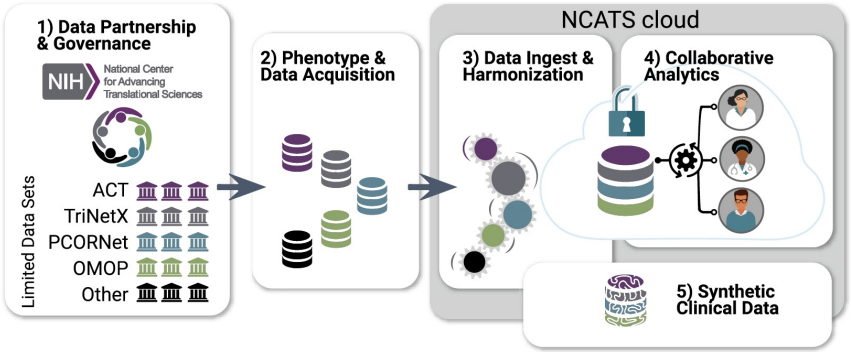
Haendel, M, et al. JAMIA. 2020

- **Objective:** Led by CD2H, effort to bring together a multi-organizationl COVID data resource for enabling research. Enabling statistical, machine learning, and causal analyses on large-scale data beyond what is available in any given organization.
- Here, they introduce National COVID Cohort Collaborative (N3C), an open science community focused on analyzing patient-level data from many centers.
- **Materials and Methods:** The Clinical and Translational Science Award Program and scientific community created N3C to overcome technical, regulatory, policy, and governance barriers to sharing and harmonizing individual-level clinical data. We developed solutions to extract, aggregate, and harmonize data across organizations and data models, and created a secure data enclave to enable efficient, transparent, and reproducible collaborative analytics.

The National COVID Cohort Collaborative (N3C): Rationale, design, infrastructure, and deployment

Haendel, M, et al. JAMIA. 2020

- Multi-network partnership
- Hundreds of organizations involved
- Immense, collaborative effort



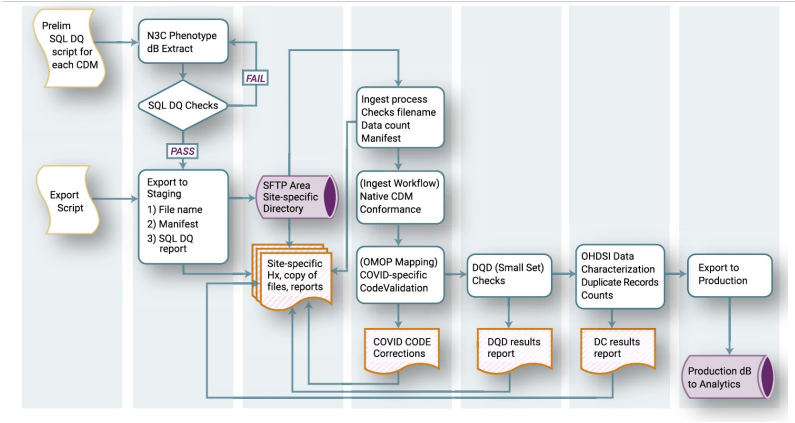
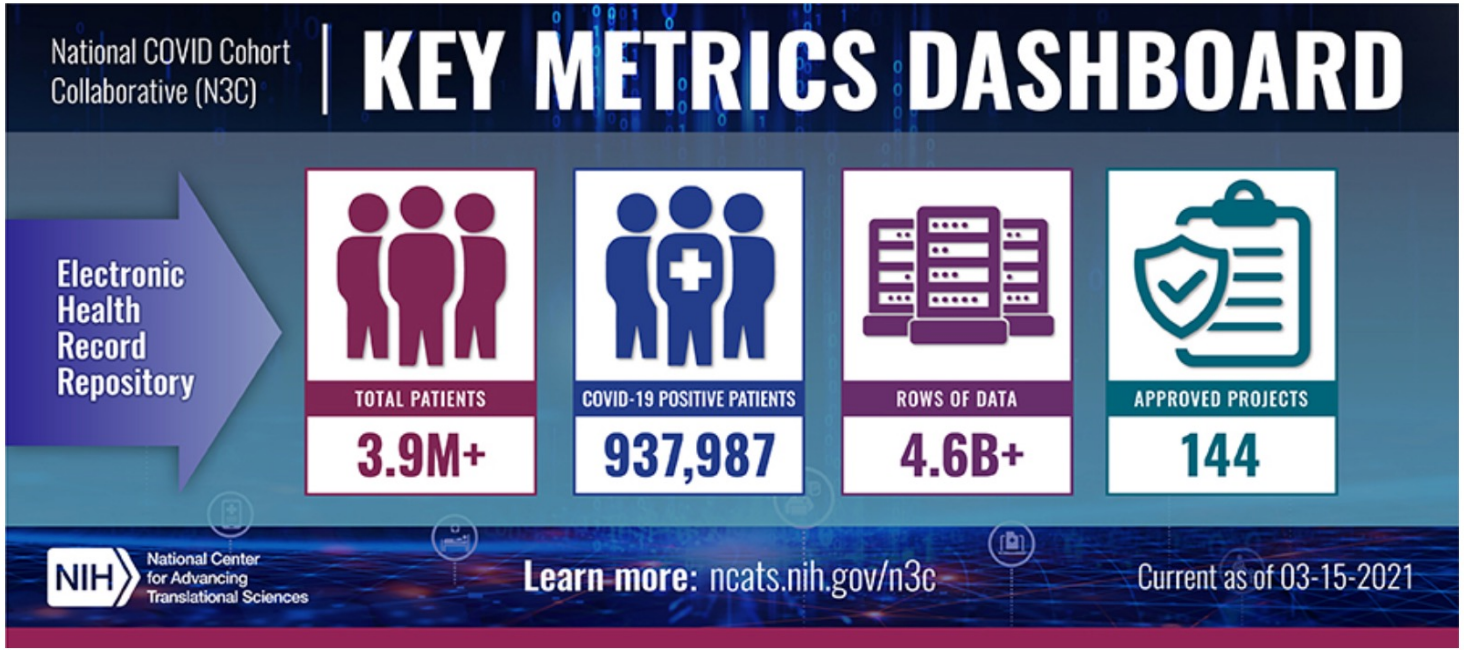


Figure 3. National COVID Cohort Collaborative (N3C) Data Quality Checks. At the sites, the extraction script performs a check for duplicate primary keys; if duplicate keys are found, the extraction fails until the site resolves the error. When extraction is successfully completed, a data "manifest" is created that contains metadata about the site and the payload. Site personnel then sFTP the data to N3C to be queued for ingestion. The first step in the ingestion process checks that the payload is consistent with the formatting requirements and the manifest file. Next, the payload is loaded into a database modeled after the payload's native common data model (CDM), which ensures source data model conformance. Next, a series of data quality checks including a subset of coronavirus disease 2019 (COVID-19)–specific code validations are performed, and if needed, minimal corrections are made. Any corrections are recorded and added to the payload documentation. Next, the payload is transformed to Observational Medical Outcomes Partnership (OMOP) 5.3.1 using the validated maps from the payload's native CDM. Once in OMOP 5.3.1, a subset of the Observational Health Data Sciences and Informatics (OHDSI) Data Quality Dashboard tests are run, and the results of these are added to the payload documentation. The payload is then exported to a merged database containing all the previously harmonized site data payloads, where it is then checked for conformance again before export to the analytics pipeline. DC: Data Characterization; DQD: Data Quality Dashboard.

The National COVID Cohort Collaborative (N3C): Rationale, design, infrastructure, and deployment

Haendel, M, et al. JAMIA. 2020



The National COVID Cohort Collaborative (N3C): Rationale, design, infrastructure, and deployment

Haendel, M, et al. JAMIA. 2020

- **Results:** Organized in inclusive workstreams, we created legal agreements and governance for organizations and researchers; data extraction scripts to identify and ingest positive, negative, and possible COVID-19 cases; a data quality assurance and harmonization pipeline to create a single harmonized dataset; population of the secure data enclave with data, machine learning, and statistical analytics tools; dissemination mechanisms; and a synthetic data pilot to democratize data access.
- **Conclusions:** The N3C has demonstrated that a multisite collaborative learning health network can overcome barriers to rapidly build a scalable infrastructure incorporating multiorganizational clinical data for COVID-19 analytics. We expect this effort to save lives by enabling rapid collaboration among clinicians, researchers, and data scientists to identify treatments and specialized care and thereby reduce the immediate and long-term impacts of COVID-19.
- **CRI Implications:** An extraordinary effort to create a national data resource in record time, spurred by the pandemic. Great promise for the current crisis and as an excellent example of such a data-sharing network for other uses.

International electronic health record-derived COVID-19 clinical course profiles: the 4CE consortium

Brat, GA, et al. Nature Digital Medicine. 2020

- We leveraged the largely untapped resource of electronic health record data to address critical clinical and epidemiological questions about Coronavirus Disease 2019 (COVID-19).
- To do this, we formed an international consortium (4CE) of 96 hospitals across five countries (www.covidclinical.net).
- Contributors utilized the Informatics for Integrating Biology and the Bedside (i2b2) or Observational Medical Outcomes Partnership (OMOP) platforms to map to a common data model.

Table 1. Sites contributing data to the consortium.

Healthcare system	Acronym	City	Country	Population	Hospitals	Be
Assistance Publique—Hôpitaux de Paris	APHP	Paris	France	Adult & Pediatric	39	20
Bordeaux University Hospital	FRBDX	Bordeaux	France	Adult & Pediatric	3	2
Erlangen University Hospital	UKER	Erlangen	Germany	Adult & Pediatric	1	1
Medical Center, University of Freiburg	UKFR	Freiburg	Germany	Adult & Pediatric	1	1
University Medicine Mannheim	UMM	Mannheim	Germany	Adult & Pediatric	1	1
ICSM Pavia Hospital	ICSM1	Pavia	Italy	Adult	1	
ICSM Lumezzane/Brescia Hospitals	ICSM5	Lumezzane/Brescia	Italy	Adult	1	
ICSM Milano Hospital	ICSM20	Milan	Italy	Adult	1	
Policlinico di Milano	POLIMI	Milan	Italy	Adult & Pediatric	1	
ASST Papa Giovanni XXIII Bergamo	HPG23	Bergamo	Italy	Adult & Pediatric	1	
National University Hospital	NUH	Singapore	Singapore	Adult & Pediatric	1	
Boston Children's Hospital	BCH	Boston, MA	USA	Pediatric	1	
Beth Israel Deaconess Medical Center	BIDMC	Boston, MA	USA	Adult	1	
Children's Hospital of Philadelphia	CHOP	Philadelphia, PA	USA	Pediatric	1	
University of Kansas Medical Center	KUMC	Kansas City, KS	USA	Adult & Pediatric	1	
Mayo Clinic	MAYOC	Rochester, MN	USA	Adult & Pediatric	1	2
Mass General Brigham (Partners Healthcare)	MGB	Boston, MA	USA	Adult & Pediatric	10	3
Medical University of South Carolina	MUSC	Charleston, SC	USA	Adult & Pediatric	8	
University of Pennsylvania	UPenn	Philadelphia, PA	USA	Adult	5	2
University of California, LA	UCLA	Los Angeles, CA	USA	Adult & Pediatric	2	
University of Michigan	UMICH	Ann Arbor, MI	USA	Adult & Pediatric	3	
University of North Carolina at Chapel Hill	UNC	Chapel Hill, NC	USA	Adult & Pediatric	11	3
UT Southwestern Medical Center	UTSW	Dallas, TX	USA	Adult	1	
				Total	96	45

International electronic health record-derived COVID-19 clinical course profiles: the 4CE consortium

Brat, GA, et al. Nature Digital Medicine. 2020

- The group focused on temporal changes in key laboratory test values. Harmonized data were analyzed locally and converted to a shared aggregate form for rapid analysis and visualization of regional differences and global commonalities.
- Data covered 27,584 COVID-19 cases with 187,802 laboratory tests. Case counts and laboratory trajectories were concordant with existing literature.
- Laboratory tests at the time of diagnosis showed hospital-level differences equivalent to country-level variation across the consortium partners.
- Despite the limitations of decentralized data generation, we established a framework to capture the trajectory of COVID-19 disease in patients and their response to interventions.

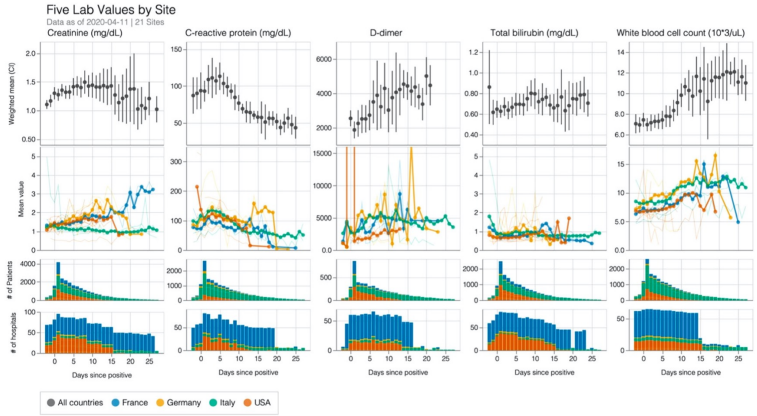
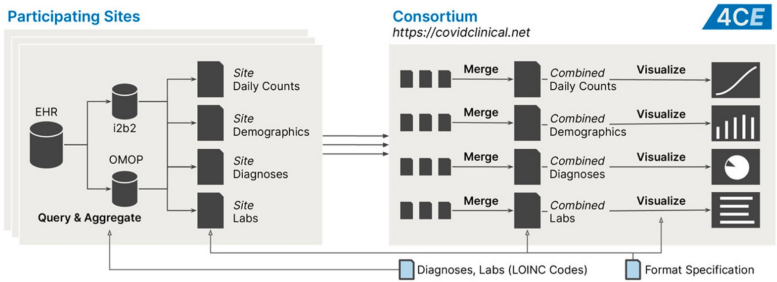


Fig. 3 Laboratory tests representative of renal function (creatinine), systemic inflammation (C-reactive protein), coagulopathy (D-dimer), liver function (total bilirubin), and immune response (white blood cell count) visualized relative to date of diagnosis of COVID-19. The top row shows weighted means and 95% confidence intervals across all patients. The second row shows unweighted country- (thick lines) and site-level (thin lines) means. The third and fourth rows show the number of patients and sites, respectively, contributing laboratory tests of each type on a given day.



Association of Intensive Care Unit Patient Load and Demand With Mortality Rates in US Department of Veterans Affairs Hospitals During the COVID-19 Pandemic

Bravata D, et al. JAMA Network Open. 2020

- **Relevance:** Although strain on hospital capacity has been associated with increased mortality in nonpandemic settings, studies are needed to examine the association between coronavirus disease 2019 (COVID-19) critical care capacity and mortality.
- **Objective:** To examine whether COVID-19 mortality was associated with COVID-19 intensive care unit (ICU) strain.
- **Design, Setting, and Participants** This cohort study was conducted among veterans with COVID-19, as confirmed by polymerase chain reaction or antigen testing in the laboratory from March through August 2020, cared for at any Department of Veterans Affairs (VA) hospital with 10 or more patients with COVID-19 in the ICU. The follow-up period was through November 2020. Data were analyzed from March to November 2020.
- **Exposures** Receiving treatment for COVID-19 in the ICU during a period of increased COVID-19 ICU load, with load defined as mean number of patients with COVID-19 in the ICU during the patient's hospital stay divided by the number of ICU beds at that facility, or increased COVID-19 ICU demand, with demand defined as mean number of patients with COVID-19 in the ICU during the patient's stay divided by the maximum number of patients with COVID-19 in the ICU.
- **Main Outcomes and Measures** All-cause mortality was recorded through 30 days after discharge from the hospital.

Association of Intensive Care Unit Patient Load and Demand With Mortality Rates in US Department of Veterans Affairs Hospitals During the COVID-19 Pandemic

Bravata D, et al. JAMA Network Open. 2020

Figure 1. Coronavirus Disease 2019 (COVID-19) Intensive Care Unit (ICU) Load and Demand at an Example Facility

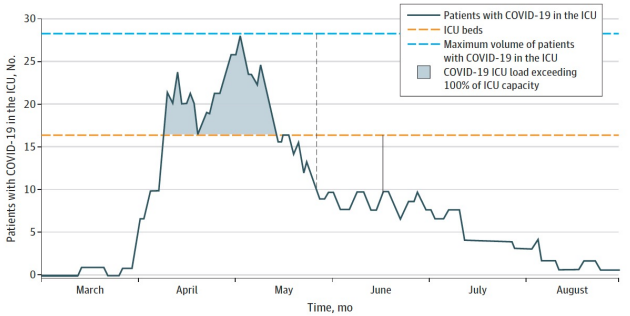


Table 3. Proportional Hazard Results From Admission to 30 Days Postdischarge or Death

	Overall		General ward only		ICU	
Characteristic	Adjusted HR (95% CI)	*P* value	Adjusted HR (95% CI)	*P* value	Adjusted HR (95% CI)	*P* value
COVID-19 ICU load[b]						
≤25%	1 [Reference]	.01	1 [Reference]	.04	1 [Reference]	.049
>25% to 50%	1.19 (0.99-1.43)		1.30 (0.92-1.84)		1.10 (0.88-1.37)	
>50% to 75%	1.03 (0.77-1.40)		0.74 (0.42-1.32)		1.15 (0.81-1.64)	
>75% to 100%	1.63 (1.13-2.35)		1.90 (0.98-3.65)		1.67 (1.08-2.60)	
>100%	2.03 (1.16-3.56)		1.14 (0.29-4.49)		2.35 (1.25-4.39)	
COVID-19 ICU demand[c]						
≤25%	1 [Reference]	<.001	1 [Reference]	.09	1 [Reference]	<.001
>25% to 50%	1.11 (0.94-1.31)		1.41 (1.07-1.84)		0.99 (0.81-1.22)	
>50% to 75%	1.25 (1.05-1.49)		1.30 (0.95-1.79)		1.19 (0.95-1.48)	
>75%	1.67 (1.33-2.11)		1.29 (0.85-1.97)		1.94 (1.46-2.59)	

Association of Intensive Care Unit Patient Load and Demand With Mortality Rates in US Department of Veterans Affairs Hospitals During the COVID-19 Pandemic
Bravata D, et al. JAMA Network Open. 2020

- **Findings:** Cohort study of 8516 patients with COVID-19 admitted to 88 US Veterans Affairs hospitals.
  - Among patients with COVID-19, those treated in the ICU during periods of peak COVID-19 ICU demand had a nearly **2-fold increased risk of mortality** compared with those treated during periods of low demand.
- **Conclusions and Relevance**
  - Although facilities augmented ICU capacity during the pandemic, strains on critical care capacity were associated with increased COVID-19 ICU mortality.
  - Tracking and managing COVID-19 ICU demand across hospitals may be important to optimize outcomes for patients with this illness.
- **Implications:**
  - These findings suggest that public health officials and hospital administrators should consider interventions that reduce COVID-19 ICU demand to improve survival among patients with COVID-19 in the ICU.
- **CRI Implications**:
  - This study would not have been possible without the VA Corporate Data Warehouse, and it demonstrates yet again the importance of such resources and maintaining their quality and accessibility for research.

Risk of hydroxychloroquine alone and in combination with azithromycin in the treatment of rheumatoid arthritis: a multinational, retrospective study

- BACKGROUND:
  - Hydroxychloroquine is commonly used to treat rheumatoid arthritis
  - Much negative publicity and concern for adverse events associated with its authorization for emergency use to treat patients with COVID-19 pneumonia.
  - Studied the safety of hydroxychloroquine, alone and in combination with azithromycin, to determine the risk associated with its use in routine care in patients with rheumatoid arthritis.
- METHODS:
  - Multinational, retrospective study, adult patients with rheumatoid arthritis initiating hydroxychloroquine were compared with those initiating sulfasalazine and followed up over 30 days, with 16 severe adverse events studied.
  - Self-controlled case series were done to further establish safety in wider populations and included all users of hydroxychloroquine regardless of rheumatoid arthritis status or indication.
  - Separately, severe adverse events associated with hydroxychloroquine plus azithromycin (compared with hydroxychloroquine plus amoxicillin) were studied.
  - Data from 14 sources of claims data or electronic medical records from Germany, Japan, the Netherlands, Spain, UK, and USA.
  - **Enabled by the OHDSI-COVID-19 consortium!**

Risk of hydroxychloroquine alone and in combination with azithromycin in the treatment of rheumatoid arthritis: a multinational, retrospective study

- **FINDINGS:**
  - Study included 956,374 users of hydroxychloroquine, 310,350 users of sulfasalazine, 323,122 users of hydroxychloroquine plus azithromycin, and 351.956 users of hydroxychloroquine plus amoxicillin.
  - No excess risk of severe adverse events identified when 30-day hydroxychloroquine and sulfasalazine use were compared.
  - However, long-term use of hydroxychloroquine appeared to be associated with increased cardiovascular mortality (calibrated HR 1.65 [95% CI 1.12-2.44]).
  - Addition of azithromycin appeared to be associated with an increased risk of 30-day cardiovascular mortality (calibrated HR 2.19 [95% CI 1.22-3.95]), chest pain or angina (1.15 [1.05-1.26]), and heart failure (1.22 [1.02-1.45]).
- **INTERPRETATION:**
  - Hydroxychloroquine treatment appears to have no increased risk in the short term among patients with rheumatoid arthritis, but in the long term it appears to be associated with excess cardiovascular mortality.
  - The addition of azithromycin increases the risk of heart failure and cardiovascular mortality even in the short term.
  - Implications – hydroxychloroquine and hcq+azithro is not without risk, so benefits must outweigh
  - **CRI implication: Would not have been possible without the OHDSI-COVID19 consortium!**

Data Sharing, Re-Use, and RWD: Other notable papers

- Burn E, You SC, Sena AG, et al. **Deep phenotyping of 34,128 adult patients hospitalised with COVID-19 in an international network study**. *Nat Commun.* 2020;11(1):5009.
- Geleris J, Sun Y, Platt J, et al. **Observational Study of Hydroxychloroquine in Hospitalized Patients with Covid-19**. *N Engl J Med.* 2020;382(25):2411-2418.
- Foraker RE, Lai AM, Kannampallil TG, Woeltje KF, Trolard AM, Payne PRO. **Transmission dynamics: Data sharing in the COVID-19 era**. *Learn Health Syst.* 2020;5(1):e10235.
- Goldstein BA. **Five analytic challenges in working with electronic health records data to support clinical trials with some solutions**. *Clin Trials.* 2020;17(4):370-376.
- Sass J, Bartschke A, Lehne M, et al. **The German Corona Consensus Dataset (GECCO): a standardized dataset for COVID-19 research in university medicine and beyond**. *BMC Med Inform Decis Mak.* 2020;20(1):341.

Data Sharing, Re-Use, and RWD: Other notable papers

- Dixon BE, Grannis SJ, McAndrews C, et al. **Leveraging Data Visualization and a Statewide Health Information Exchange to Support COVID-19 Surveillance and Response: Application of Public Health Informatics**. *Journal of the American Medical Informatics Association : JAMIA*. 2021.
- Forrest CB, McTigue KM, Hernandez AF, et al. **PCORnet® 2020: current state, accomplishments, and future directions**. *J Clin Epidemiol*. 2021;129:60-67.
- Klann JG, Weber GM, Estiri H, et al. **Validation of an Internationally Derived Patient Severity Phenotype to Support COVID-19 Analytics from Electronic Health Record Data**. *Journal of the American Medical Informatics Association : JAMIA*. 2021.
- Rogers JR, Lee J, Zhou Z, Cheung YK, Hripcsak G, Weng C. **Contemporary use of real-world data for clinical trial conduct in the United States: a scoping review**. *Journal of the American Medical Informatics Association : JAMIA*. 2021;28(1):144-154.
- Campion TR, Craven CK, Dorr DA, Knosp BM. **Understanding enterprise data warehouses to support clinical and translational research.** JAMIA. 2020;27(9):1352-8.

CRI Methods and Approaches

Spot the difference: comparing results of analyses from real patient data and synthetic derivatives

Foraker, R.E., et al. JAMIA Open. 2020

- **Background:** Synthetic data may provide a solution to researchers who wish to generate and share data in sup- port of precision healthcare. Recent advances in data synthesis enable the creation and analysis of synthetic derivatives as if they were the original data; this process has significant advantages over data deidentification.
- **Objectives:** To assess a big-data platform with data-synthesizing capabilities (MDClone Ltd., Beer Sheva, Israel) for its ability to produce data that can be used for research purposes while obviating privacy and confidentiality concerns.
- **Methods:** We explored three use cases and tested the robustness of synthetic data by comparing the results of analyses using synthetic derivatives to analyses using the original data using traditional statistics, machine learning approaches, and spatial representations of the data.
- Designed use cases with the purpose of conducting analyses at the **observation level** (Use Case 1), **patient cohorts** (Use Case 2), and **population-level** data (Use Case 3).

Spot the difference: comparing results of analyses from real patient data and synthetic derivatives
Foraker, R.E., et al. JAMIA Open. 2020

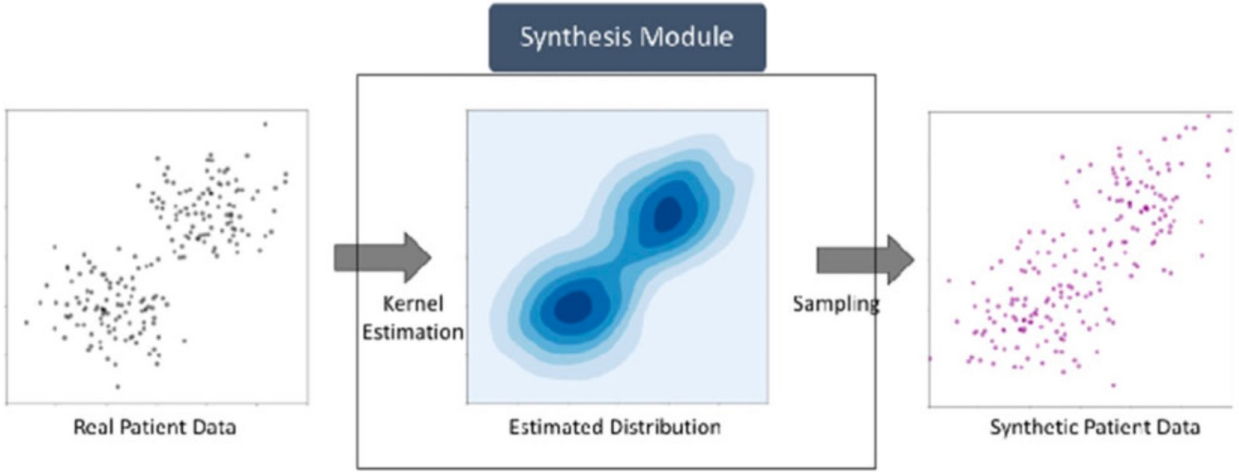


Figure 1. Data synthesis process.

- With this approach, rather than "camouflaging" individuals with shifts or other "noise," models are created based on groups of similar patients in the original set.
- Those models are used to create a new "patients" in the synthetic set, on demand.
- If altered with new features or if variable choices change, then a new synthetic set can be generated.

Spot the difference: comparing results of analyses from real patient data and synthetic derivatives
Foraker, R.E., et al. JAMIA Open. 2020

- Team created and analyzed synthetic derivatives using MDClone platform and validated findings against original data.
  - Use Case 1: pediatric trauma (Top right)
  - Use Case 3: public health dashboard (bottom right)
- Both represent original (left) and synthetic (right) data representations
- For each use case, results of the analyses were sufficiently similar—and statistically nonsignificant—to draw the same conclusions.
- **CRI implications:** These and other synthetic approaches are gaining traction and enabling greater access to data while protecting privacy

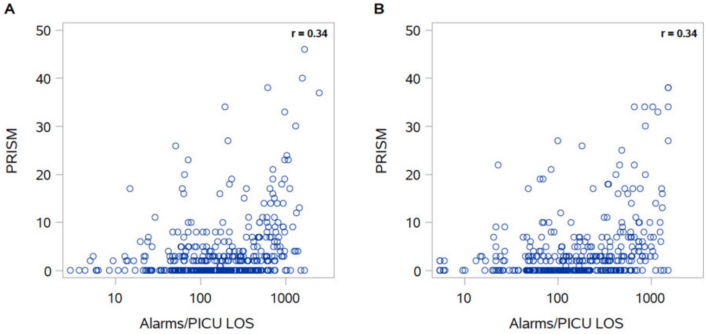


Figure 2. Alarms/PICU length of stay by PRISM III score: real (A) and synthetic (B) data.

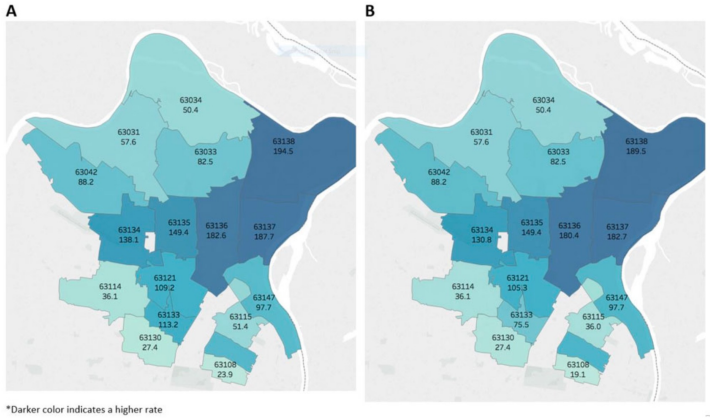
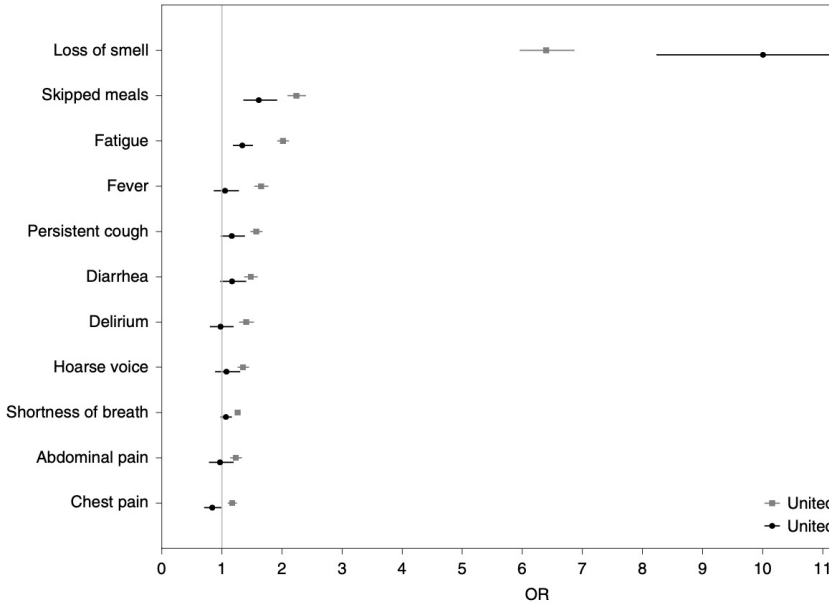


Figure 3. Chlamydia rates (per 100 000 persons) by zip code: real (left) versus synthetic (right) data, 2014. *Darker color indicates a higher rate.

Real-time tracking of self-reported symptoms to predict potential COVID-19
Menni C. et al. Nature Medicine. 2020

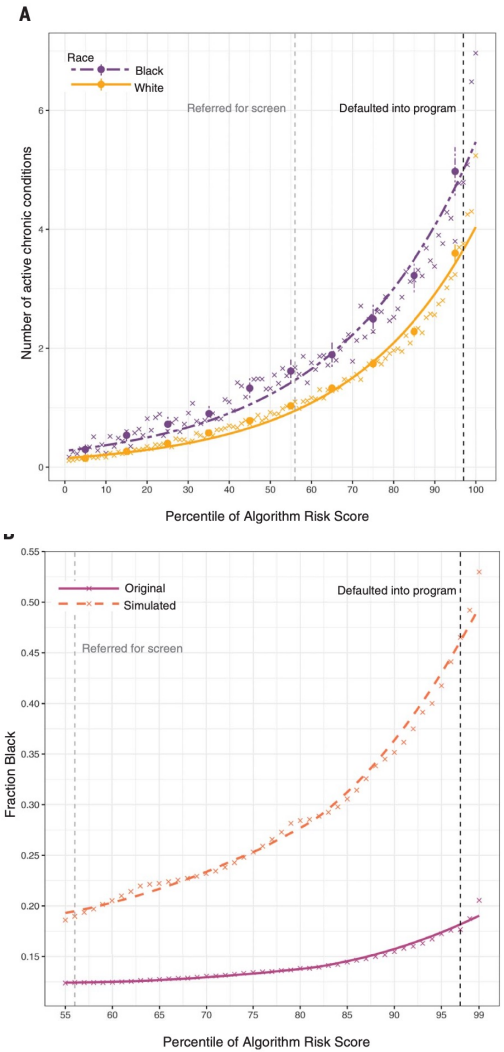
- A total of 2,618,862 participants reported their potential symptoms of COVID-19 on a smartphone-based app.
- Among the 18,401 who had undergone a SARS-CoV-2 test, the proportion of participants who reported loss of smell and taste was higher in those with a positive test result (4,668 of 7,178 individuals; 65.03%) than in those with a negative test result (2,436 of 11,223 participants; 21.71%) (odds ratio = 6.74; 95% confidence interval = 6.31–7.21).
- A model combining symptoms to predict probable infection was applied to the data from all app users who reported symptoms (805,753) and predicted that 140,312 (17.42%) participants are likely to have COVID-19.



Dissecting racial bias in an algorithm used to manage the health of populations

Obermeyer Z., et al. Science. 2019

- Health systems increasingly rely on prediction algorithms to identify and help patients with complex health needs.
- They showed that a widely used algorithm, typical of this industry-wide approach and affecting millions of patients, exhibits significant racial bias:
  - At a given risk score, Black patients are considerably sicker than White patients, as evidenced by signs of uncontrolled illnesses.
  - Remedying this disparity would increase the percentage of Black patients receiving additional help from 17.7 to 46.5%.
  - The bias arises because the algorithm predicts health care costs rather than illness, but unequal access to care means that we spend less money caring for Black patients than for White patients.
- Despite health care cost appearing to be an effective proxy for health by some measures of predictive accuracy, large racial biases arise.
- They rightly suggest that the choice of convenient, seemingly effective proxies for ground truth can be an important source of algorithmic bias in many contexts.



Multiple papers on concerns & proposed approaches to addressing AI bias/errors, need for evaluation and monitoring

- **The Case for Algorithmic Stewardship for Artificial Intelligence and Machine Learning Technologies.** Eaneff S, et al. JAMA. 2020.
  - At Health System level (and beyond), akin to other stewards
- **Evaluating Artificial Intelligence in Medicine: Phases of Clinical Research.** Park Y. et al. JAMIA Open. 2020
- **Artificial Intelligence in Health Care: The Hope, the Hype, the Promise, the Peril.** Matheny et al. Nat Acad of Med. 2019.
- **Regulatory Frameworks for Development and Evaluation of Artificial Intelligence-Based Diagnostic Imaging Algorithms: Summary and Recommendations** Larson D.B, et al. J. Amer. Coll. Radiology. 2021

Figure. Existing and Proposed Processes and Tools to Ensure Appropriate Use of Drugs for Algorithmic Stewardship Efforts

	Existing processes and tools	Proposed processes and tools for algorithmic stewardship
1 Clinical trials	Phase 1, 2, and 3 trials	Assess safety, efficacy, and fairness (potentially via clinical trials)
2 Scale-up and early adoption	Hospital formulary	Algorithm inventory
3 Postmarket use and evaluation	Medication use evaluations	Algorithm use evaluations
4 Ongoing oversight	Antimicrobial steward role	Algorithmic steward role

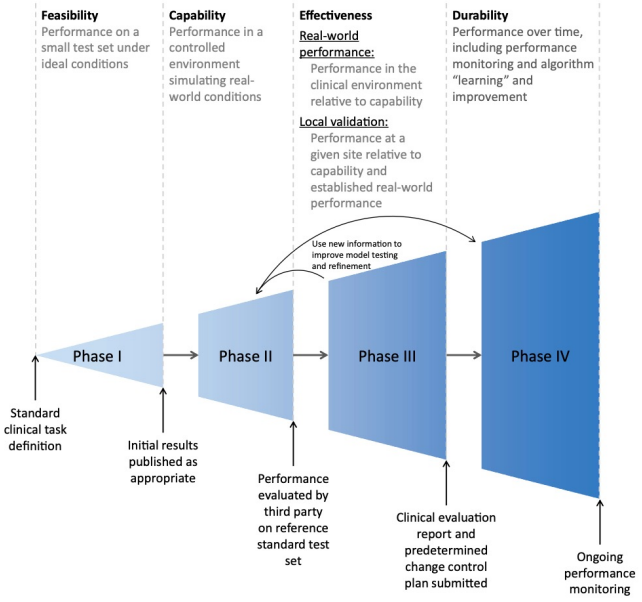


Fig 2. Phased development and evaluation process of diagnostic algorithms.

CRI Methods:
Other notable papers

- **Action-Informed Artificial Intelligence-Matching the Algorithm to the Problem**. Lindsell CJ, et al. *JAMA*. 2020
- **Explainable artificial intelligence model to predict acute critical illness from electronic health records.** Lauritsen SM, et al. *Nat Commun*. 2020
- **Artificial Intelligence and the Future of Primary Care: Exploratory Qualitative Study of UK General Practitioners' Views**. Blease C, et al. *J Med Internet Res*. 2019
- **Precision Health-Enabled Machine Learning to Identify Need for Wraparound Social Services Using Patient- and Population-Level Data Sets: Algorithm Development and Validation**. Kasthurirathne, S. N. *J Med. Internet Res*. 2020
- **Social determinants of health in electronic health records and their impact on analysis and risk prediction: A systematic review**. Chen M, et al. JAMIA. 2020

CRI Methods:
Other notable papers

- **Facilitating phenotype transfer using a common data model**. Hripcsak G, et al. *J Biomed Inform*. 2019;96:103253.
- **Data model harmonization for the All Of Us Research Program: Transforming i2b2 data into the OMOP common data model**. Klann JG, et al. *PloS one*. 2019
- **Evaluation of patient-level retrieval from electronic health record data for a cohort discovery task.** Chamberlin SR, et al. *JAMIA Open*. 2020
- **Transitive Sequencing Medical Records for Mining Predictive and Interpretable Temporal Representations.** Estiri H, et al. *Patterns (Cell)*. 2020.

Participant Engagement and Recruitment

Broad-scale informed consent: A survey of the CTSA landscape
Chandler R. et al. J. Clin & Trans Sci. 2019

- **Introduction:**
  - Research opportunities associated with the proliferation of the electronic health record (EHR), big data initiatives, and innovative approaches to trial design can present challenges for obtaining and documenting informed consent.
  - Broad-scale informed consent (a term used herein to describe institutional models, rather than the Common Rule's strict regulatory definition for "broad consent") may facilitate the use of existing data and samples and speed the pace of research by minimizing barriers to consent.
  - We explored the use of broad- scale informed consent within the Clinical Translational Science Award (CTSA) Program Network.
- **Methods:**
  - We surveyed CTSA Hubs concerning policies, practices, experiences, and needs within three domains of broad-scale informed consent: (1) participant recontact; (2) biospecimens; and (3) clinical data sharing.

Broad-scale informed consent: A survey of the CTSA landscape

Chandler R. et al. J. Clin & Trans Sci. 2019

- Results:
  - Of 61 CTSA Hubs surveyed, 37 (61%) indicated ongoing work related to at least 1 domain of broad-scale informed consent; 18 Hubs (30%) reported work in all 3 domains. The EHR predominated as the implementation system across all three domains. Research and IT leadership and the Institutional Review Board were most commonly endorsed as institutional drivers, while systems/technical issues and impact on clinical workflow were the most commonly reported barriers.

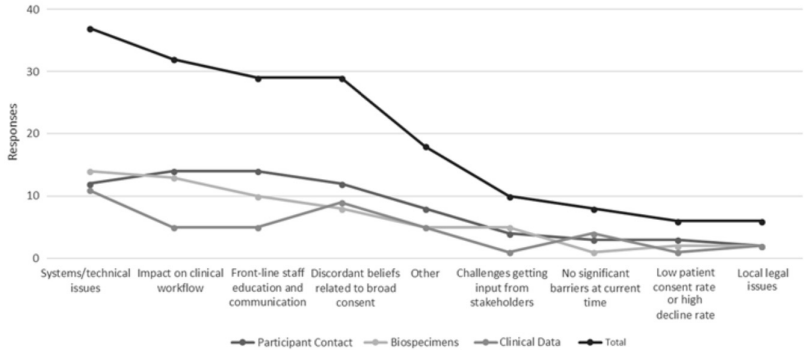


Fig. 2. Key implementation barriers for broad-scale informed consent policies and practices.

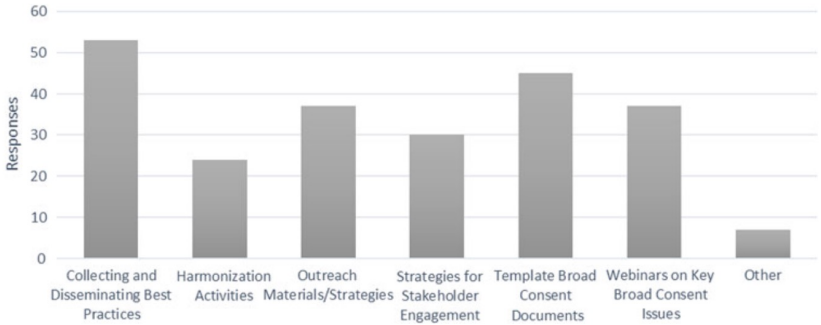


Fig. 3. Recommended areas for collective action by the Clinical Translational Science Award consortium.

Broad-scale informed consent: A survey of the CTSA landscape
Chandler R. et al. J. Clin & Trans Sci. 2019

- **Conclusions:**
  - While survey results indicate considerable variability in the implementation of broad-scale informed consent across the CTSA consortium, it is clear that all CTSA Hubs are actively considering policy and process related to these concepts.
  - Next steps cluster within three areas:
    - training and workforce development,
    - streamlined policies and templates, and
    - implementation strategies that facilitate integration into clinical workflow.

Towards clinical data-driven eligibility criteria optimization for interventional COVID-19 clinical trials

Kim JH, et al. JAMIA. 2021

- **Objective:** This research aimed to evaluate the impact of eligibility criteria on recruitment and observable clinical outcomes of COVID-19 clinical trials using electronic health record (EHR) data.
- **Materials and Methods:** Starting last June, 2020, the group identified frequently used eligibility criteria from all the interventional COVID-19 trials in ClinicalTrials.gov (n=288). They applied the frequently used criteria to the EHR data of COVID-19 patients at their facility (CUIMC) (March 2020–June 2020) and evaluated their impact on patient accrual and the occurrence of a composite endpoint of mechanical ventilation, tracheostomy, and in-hospital death.
- **Results:** There were 3251 patients diagnosed with COVID-19 from the CUIMC EHR included in the analysis. The median follow-up period was 10 days. The composite events occurred in 18.1% (n=587) of the COVID-19 cohort during the follow-up.
- In a hypothetical trial with common eligibility criteria, 33.6% (690/2051) were eligible among patients with evaluable data and 22.2% (153/690) had the composite event.
- **Discussion:** By adjusting the thresholds of common eligibility criteria based on the characteristics of COVID-19 patients, we could observe more composite events from fewer patients.

Towards clinical data-driven eligibility criteria optimization for interventional COVID-19 clinical trials

Kim JH, et al. JAMIA. 2021

- **Authors' Conclusions:** This research demonstrated the potential of using the EHR data of COVID-19 patients to inform the selection of eligibility criteria and their thresholds, supporting data-driven optimization of participant selection towards improved statistical power of COVID-19 trials.

- **CRI implications:**
  - This study represents early progress towards data-driven eligibility criteria optimization for better trial feasibility and patient safety.
  - Given pace and demand, it will be key to determine how eligibility criteria can be broadened and simplified to include diverse clinical trial participants without weakening the statistical power of COVID-19 trials.
  - This approach is a step in that direction.

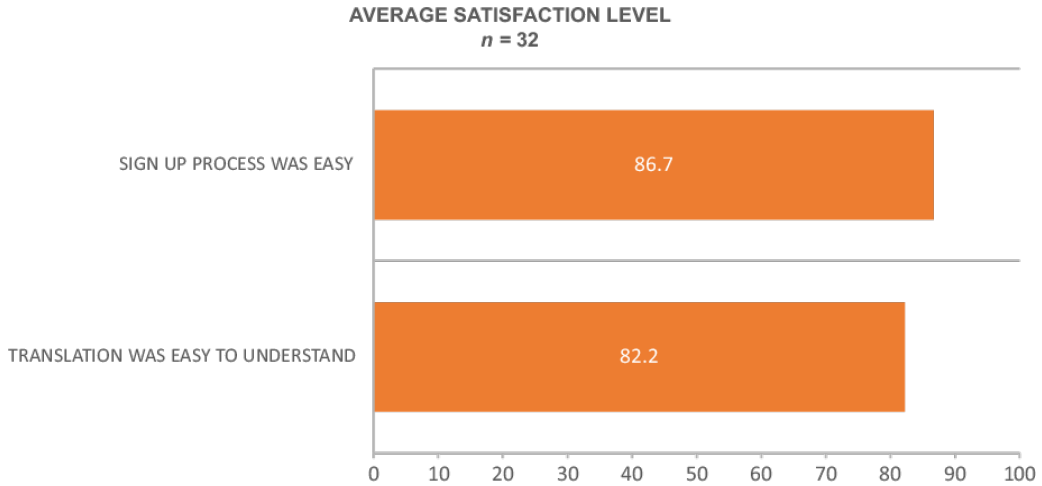
Opening doors to clinical trial participation among Hispanics: Lessons learned from the Spanish translation of ResearchMatch

Byrne, L.M. et al. J Clinical and Translational Science. 2020

- **Objective:** Trial participation among US Hispanics remains low. ResearchMatch has matched >110,000 individuals with trials led by 8700 researchers, 170 institutions. 38% of US Hispanics are estimated to speak Spanish primarily or exclusively. Objective: effectively translate ResearchMatch platform into Spanish.
- **Methods:** Translation of the ResearchMatch site consisted of several activities including:
  - (1) improving the English language site's reading level, removing jargon, and using plain language;
  - (2) obtaining a professional Spanish translation of the site and incorporating iterative revisions by a panel of bilingual community members from diverse Hispanic backgrounds;
  - (3) technical development and launch; and
  - (4) initial promotion and monitoring

Opening doors to clinical trial participation among Hispanics: Lessons learned from the Spanish translation of ResearchMatch
Byrne, L.M. et al. J Clinical and Translational Science. 2020

- **Results:** The Spanish language version launched in August 2018, after 11 months of development. Community input improved the initial translation, and early registration and use by researchers demonstrate the utility of Spanish ResearchMatch in engaging Hispanics.
- Over 12,500 volunteers in ResearchMatch self-identify as Hispanic (8.5%).
- From August 2018 to March 2020, 162 volunteers registered through the Spanish language version of ResearchMatch, and over 500 new and existing volunteers have registered a preference to receive messages about studies in Spanish.



Opening doors to clinical trial participation among Hispanics: Lessons learned from the Spanish translation of ResearchMatch
Byrne, L.M. et al. J Clinical and Translational Science. 2020

- **Study Conclusions:** By applying the principles of health literacy and cultural competence, we developed a Spanish language translation of ResearchMatch. Our multiphase approach to translation included key principles of community engagement that should prove informative to other multilingual web-based platforms.
- **CRI Conclusions:** Addressing disparities in care and research is critical. Meeting people where they are is key to participant engagement and successful research that is applicable to a large and growing population.

Participant Recruitment and Engagement
Other notable papers

- **Understanding What Information Is Valued By Research Participants, And Why.** Wilkins CH, et al. *Health affairs.* 2019.
  - Respondents highly valued results revealing genetic effects on medication response and predicting disease risk as well as information about nearby clinical trials and updates on how their data was used. The information most valued varied by education, race/ethnicity, and age.
  - Policies are needed to enable **return of information in ways that recognize participants' differing informational needs and values**.
- **A REDCap-based model for electronic consent (eConsent): Moving toward a more personalized consent**. Lawrence CE, et al. *J Clin Transl Sci.* 2020.
- **An example of medical device-based projection of clinical trial enrollment: Use of electrocardiographic data to identify candidates for a trial in acute coronary syndromes**. Selker HP, et al. *J Clin Transl Sci. 2019.*

Participant Recruitment and Engagement
Other notable papers

- **Selective recruitment designs for improving observational studies using electronic health records**. Barrett JE, et al. *Stat Med*. 2020
- **Real-time clinical note monitoring to detect conditions for rapid follow-up: A case study of clinical trial enrollment in drug-induced torsades de pointes and Stevens-Johnson syndrome**. DeLozier S, Speltz P, Brito J, et al. *JAMIA*. 2021
- **Patient Cohort Identification on Time Series Data Using the OMOP Common Data Model**. Maier C, et al. *Appl Clin Inform*. 2021
- **Leveraging Real-World Data for the Selection of Relevant Eligibility Criteria for the Implementation of Electronic Recruitment Support in Clinical Trials**. Melzer G, et al. *Appl Clin Inform*. 2021
- **The COVID-19 Trial Finder**. Sun Y, et al. *JAMIA*. 2021

Learning Health Systems and Delivery Science

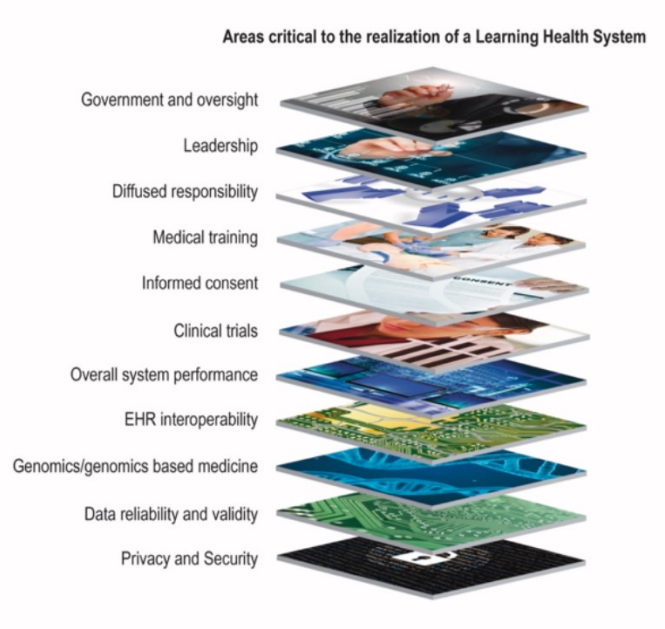
An Analysis of the Learning Health System in Its First Decade in Practice: Scoping Review

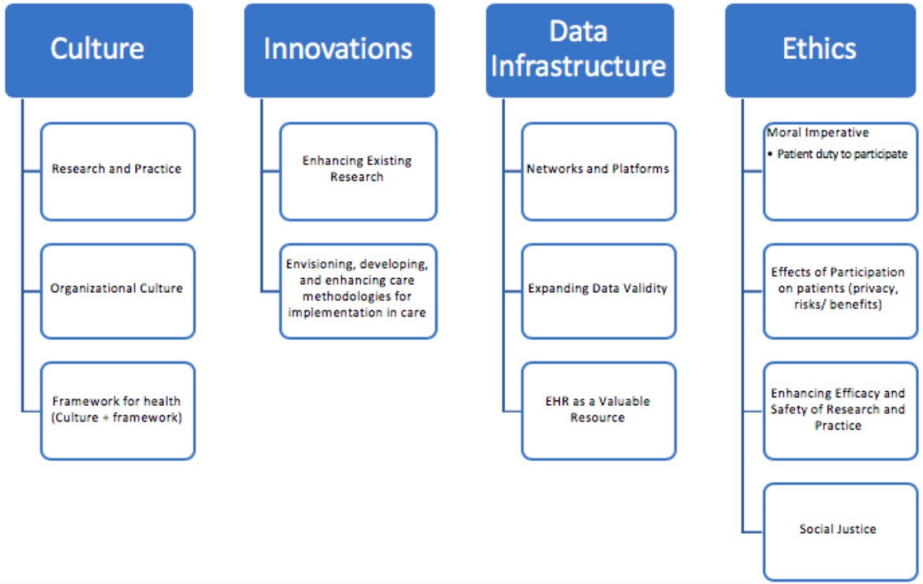
Platt JE, et al. J. Med. Internet Res. 2020

- **Background:** Learning Health System (LHS) has been proposed as an opportunity for increasing the value of health care via rapid learning from data and immediate translation to practice and policy.
- An LHS is defined in the literature as a system that seeks to continuously generate and apply evidence, innovation, quality, and value in health care.
- **Objective:** This review aimed to examine themes in the literature and rhetoric on the LHS in the past decade to understand efforts to realize the LHS in practice and to identify gaps and opportunities to continue to take the LHS forward.
- **Methods:** We conducted a thematic analysis in 2018 to analyze progress and opportunities over time as compared with the initial *Knowledge Gaps and Uncertainties* proposed in 2007.
- **Results:** We found that the literature on the LHS has increased over the past decade, with most articles focused on theory and implementation; articles have been increasingly concerned with policy.

An Analysis of the Learning Health System in Its First Decade in Practice: Scoping Review
Platt JE, et al. J. Med. Internet Res. 2020

- Thorough review leading to confirmation of key areas for realizing a LHS, and thematic topics that emerged from the literature review





An Analysis of the Learning Health System in Its First Decade in Practice: Scoping Review
Platt JE, et al. J. Med. Internet Res. 2020

- Frequency of LHS-focused articles growing in recent years
- Range of topics – limited empirical or implementation focused papers

Figure 3. Frequency of articles published by year (n=542).

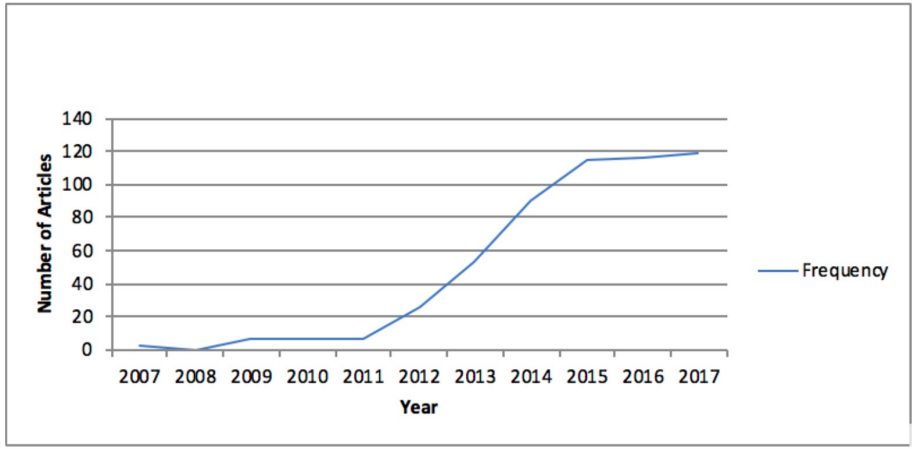
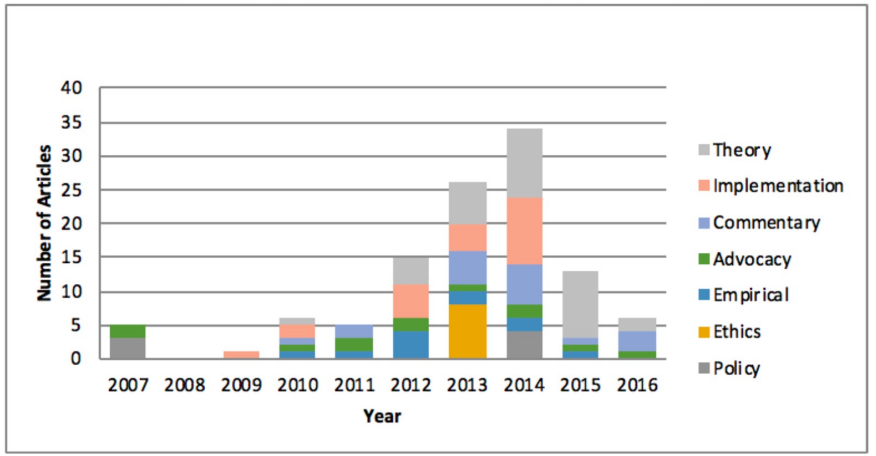


Figure 4. Trends in article categories among frequently cited articles based on review of frequently cited articles (n=85).



Conclusions: There is need for attention to understanding the ethical and social implications of the LHS and for exploring opportunities to ensure that these implications are salient in implementation, practice, and policy efforts.

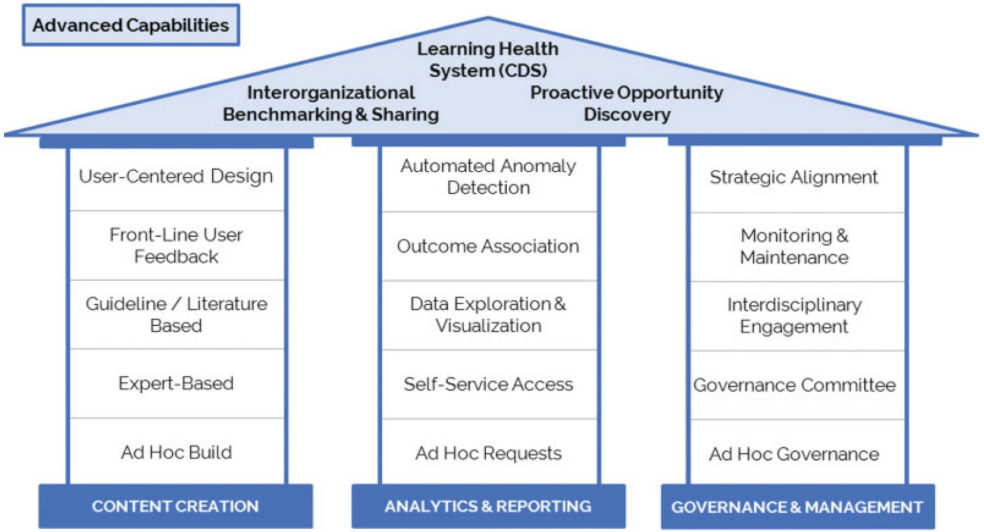
CRI Implication: A useful foundational work to help guide future research.

Towards a Maturity Model for Clinical Decision Support Operations
Orenstein, E. W., et al. Appl Clin Inform. 2019

- Clinical decision support (CDS) is simultaneously critical to improving care and an often-challenging EHR-based feature to manage and leverage.
- Building on recent work in maturity model development, this team sought to develop one that describes a roadmap toward organizational functions and processes that help health care systems use CDS more effectively to drive better outcomes.
- They interviewed health care leaders at 80 organizations, and iteratively developed their model. Excellent qualitative methods, leading to saturation.
- The proposed CDS maturity model includes three main "pillars":
  - Content Creation
  - Analytics and Reporting
  - Governance and Management

Towards a Maturity Model for Clinical Decision Support Operations

Orenstein, E. W., et al. Appl Clin Inform. 2019



ig. 1 Clinical decision support operations maturity model.

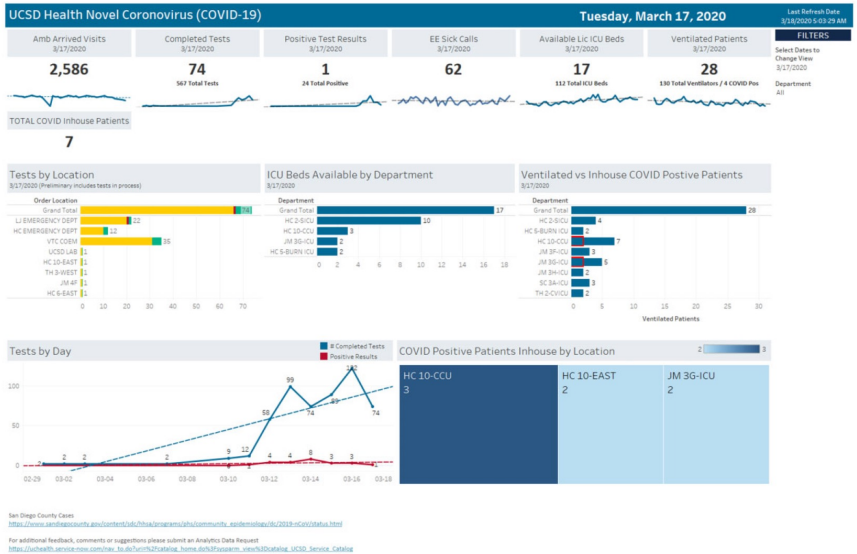
- Each pillar has five levels-advancing along each pillar provides CDS teams a deeper understanding of the processes CDS systems are intended to improve.
- A "roof" represents CDS functions that become attainable after advancing along each of the pillars.
- Organizations need not advance in order and can develop in one pillar separately from another.
- However, optimal deployment of preceding levels and advancing in tandem along the pillars should increase the value of organizational investment in higher levels of CDS maturity.
- Case studies are also presented
- **A good addition to our "maturing" catalogue of informatics "maturity models"**

Rapid response to COVID-19: health informatics support for outbreak management in an academic health system.
Reeves JJ, et al. JAMIA. 2020

- **Objective:** Describe the implementation of technological support important for optimizing clinical management of the COVID-19 pandemic.
- **Materials and Methods:** Upon identifying COVID-19, an Incident Command Center was established early in the crisis and helped identify electronic health record (EHR)-based tools to support clinical care.
- **Results:** One of (certainly in US) to publish their design and implementation of EHR-based rapid screening processes, laboratory testing, clinical decision support, reporting tools, and patient-facing technology related to COVID-19.

Rapid response to COVID-19: health informatics support for outbreak management in an academic health system.
Reeves JJ, et al. JAMIA. 2020

- Examples of early outbreak management dashboard (left)
- Telemedicine video-interface (right)



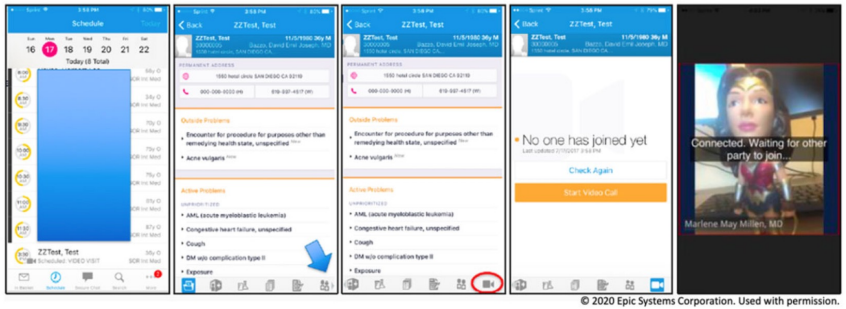


Figure 3. Telemedicine - Video Visit. Graphic displaying the layout of UC San Diego's virtual visit encounter.

Rapid response to COVID-19: health informatics support for outbreak management in an academic health system. Reeves JJ, et al. JAMIA. 2020

- **Discussion:** The EHR became an essential tool for rapid deployment of standardized processes.
- The team at UC San Diego Health built multiple COVID-19-specific tools to support outbreak management, including scripted triaging, electronic check-in, standard ordering and documentation, secure messaging, real-time data analytics, and telemedicine capabilities.
- Challenges included the need to frequently adjust build to meet rapidly evolving requirements, communication, and adoption, and to coordinate the needs of multiple stakeholders while maintaining high-quality, pre-pandemic medical care.
- **Conclusion: One of the earliest examples of leveraging the EHR and its capabilities to respond to the COVID-19 crisis at an academic health center**

Other notable papers in this (LHS/DS) category:

- **Advancing the learning health system by incorporating social determinants**. Palakshappa D, et al. *Am J Manag Care*. 2020
- **Health information technology as a learning health system: Call for a national monitoring system**. *Learn Health Syst.* Colicchio TK, et al. 2020
- **Clinical Performance Feedback Intervention Theory (CP-FIT): a new theory for designing, implementing, and evaluating feedback in health care based on a systematic review and meta-synthesis of qualitative research.** Brown B, et al. *Implement Sci.* 2019
- **A framework for analysing learning health systems: Are we removing the most impactful barriers?** *Learn Health Syst.* McLachlan S, et al. 2019
- **CDS in a Learning Health Care System: Identifying Physicians' Reasons for Rejection of Best-Practice Recommendations in Pneumonia through Computerized Clinical Decision Support**. *Appl Clin Inform.* Jones BE, et al. 2019
- **Creating a Learning Health System through Rapid-Cycle, Randomized Testing**. *N Engl J Med.* Horwitz LI, et al. 2019
- **Leaders' perspectives on learning health systems: a qualitative study.** *BMC health services research.* Enticott J, et al. 2020

Other notable papers in this (LHS/DS) category:

- **Pandemic as a Catalyst for Rapid Implementation: How Our Hospital Became a Learning Health System Overnight**. *Am J Med Qual.* Stefan MS, et al. 2020
- **Learning health systems, embedded research, and data standards-recommendations for healthcare system leaders**. *JAMIA Open.* Richesson RL. 2020
- **Rapid design and implementation of an integrated patient self-triage and self-scheduling tool for COVID-19**. *JAMIA.* Judson TJ, et al. 2020
- **Adoption of Digital Technologies in Health Care During the COVID-19 Pandemic: Systematic Review of Early Scientific Literature**. *J Med Internet Res.* Golinelli D, 2020
- **Building the evidence-base to reduce electronic health record-related clinician burden**. *JAMIA.* Dymek C, et al. 2020.
- **We're not all cut from the same cloth: TAILORing treatments for children with chronic conditions**. *J Patient Rep Outcomes.* Jerome RN, 2019
- **Putting the "why" in "EHR": capturing and coding clinical cognition**. *JAMIA.* Cimino JJ. 2019


CRI Ethics

CRI Ethics

- **Rethinking ethical oversight in the era of the learning health system**. *Healthc (Amst).* Asch DA, et al. 2020
  - Opportunities to advance science increasingly arise through investigations embedded within routine clinical practice in the form of learning health systems. Such activities challenge conventional approaches to research regulation that have not caught up with those opportunities, often imposing burdens generalized from riskier research. We analyze the rules and conventions in the US, demonstrating how even those rules are compatible with a much more flexible approach to participant risk, institutional oversight, participant consent, and disclosure for low-risk learning activities in all jurisdictions.

- **The Ethics of Artificial Intelligence in Pathology and Laboratory Medicine: Principles and Practice**. *Acad Pathol.* Jackson BR, et al. 2021
  - Growing numbers of artificial intelligence applications are being developed and applied to pathology and laboratory medicine. These technologies introduce risks and benefits that must be assessed and managed through the lens of ethics. This article describes how long-standing principles of medical and scientific ethics can be applied to artificial intelligence using examples from pathology and laboratory medicine.

CRI Ethics

- **Building and maintaining trust in clinical decision support: Recommendations from the Patient-Centered CDS Learning Network**. *Learn Health Syst.* Richardson JE, et al. 2020
- **From Return of Information to Return of Value: Ethical Considerations when Sharing Individual-Level Research Data**. *J Alzheimers Dis.* Nebeker C, et al. 2019
- **Ethics in Telehealth: Comparison between Guidelines and Practice-based Experience -the Case for Learning Health Systems**. *Yearbook of medical informatics.* Kuziemsky CE, et al. 2020

Policy & Perspective

Recommendations for the safe, effective use of adaptive CDS in the US healthcare system: an AMIA position paper
Peterson C, et al. JAMIA. 2021

- The development and implementation of clinical decision support (CDS) that trains itself and adapts its algorithms based on new data—here referred to as Adaptive CDS—present unique challenges and considerations.
- Although Adaptive CDS represents an expected progression from earlier work, the activities needed to appropriately manage and support the establishment and evolution of Adaptive CDS require new, coordinated initiatives and oversight that do not currently exist.
- In this AMIA position paper, the authors describe current and emerging challenges to the safe use of Adaptive CDS and lay out recommendations for the effective management and monitoring of Adaptive CDS.

Recommendations for the safe, effective use of adaptive CDS in the US healthcare system: an AMIA position paper
Peterson C, et al. JAMIA. 2021

- Key elements to ensure safe and effective deployment:
  - Clear clinical utility for the Adaptive CDS, using communications standards describing which patients/populations are relevant
  - Transparency metrics describing how the Adaptive CDS was developed and tested
  - The feasibility of successful implementation given available data
  - Expected deployment challenges
  - Anticipated clinical uptake and associated metrics
  - Ongoing maintenance

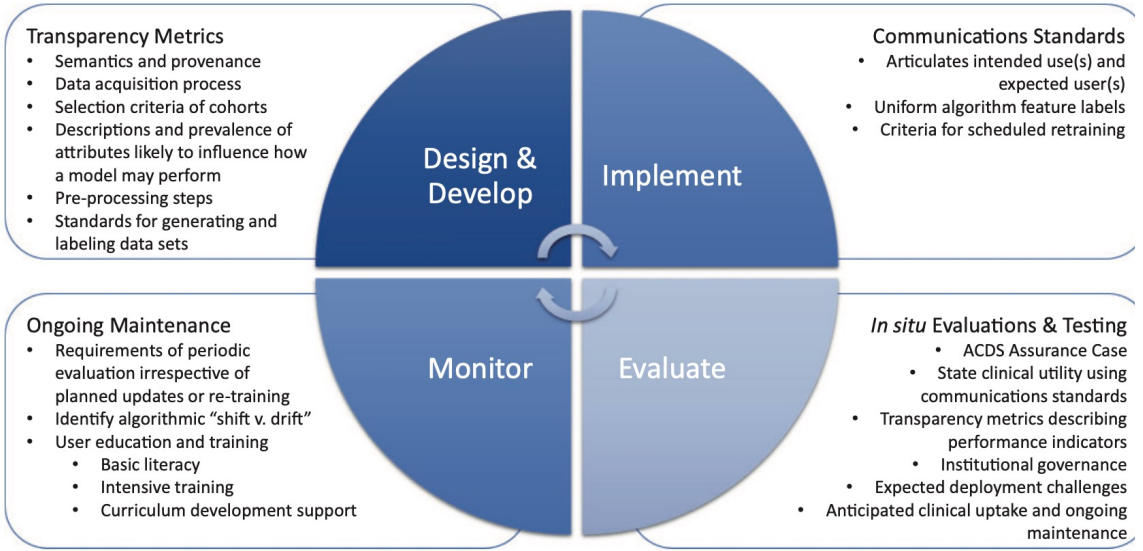


Figure 1. Policy recommendations for all stages of Adaptive CDS (ACDS)—design and development, implementation, evaluation, and ongoing monitoring—quire further development to ensure safe and effective ACDS. A concerted multistakeholder effort to identify key transparency metrics for training datasets a communications standards for AI-driven applications in healthcare is needed to understand how bias can corrupt AI-driven decision support and identify ways mitigate such bias. Additionally, policies that standardize *in situ* testing and evaluation, as well as ongoing maintenance, of ACDS should be established.

Use of electronic health records to support a public health response to the COVID-19 pandemic in the United States: a perspective from 15 academic medical centers

Madhavan, S. et al. JAMIA. 2021

- Objective: To summarize the collective experience of 15 organizations in dealing with unprecedented challenges in understanding, predicting, preparing for, containing, and mitigating the COVID-19 pandemic in the US.
- Catalogued a range of efforts related to collection and analysis of data corresponding to healthcare organizations, public health departments, socioeconomic indicators, as well as additional signals collected directly from individuals and communities.
- Focus on experiences and challenges of leveraging and scaling EHR-data to improve clinical care, research, and inform public health decision-making.
  - Outline challenges in the data ecosystem and the technology infrastructure that are relevant to COVID-19, as witnessed in our 15 institutions.
- Also catalogued range of registries and clinical data networks created
- Proposed a specific set of strategic next steps to increase interoperability, overall organization, and efficiencies.

Use of electronic health records to support a public health response to the COVID-19 pandemic in the United States: a perspective from 15 academic medical centers

Madhavan, S. et al. JAMIA. 2021

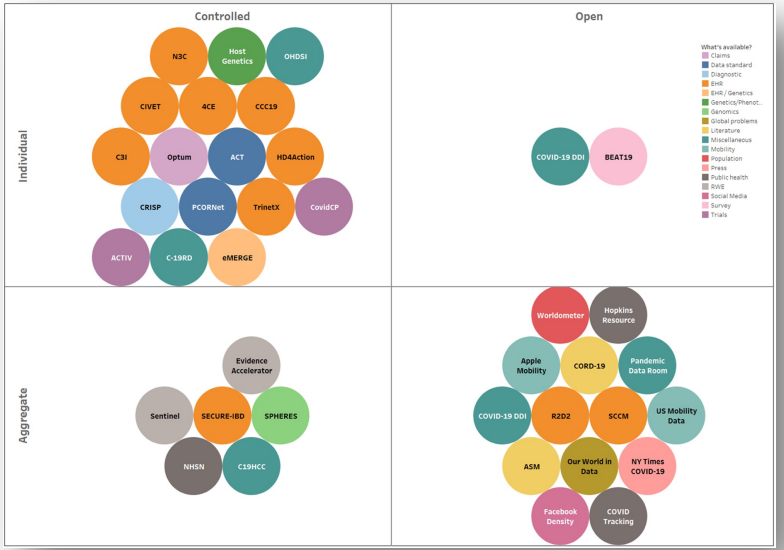


Figure 1. COVID-19 data initiatives

Table 2. Partial list of COVID-19 data initiatives

Scale	Initiative	Resource name	Resource URL
Global	4CE	Consortium for Clinical Characterization of COVID-19 by EHR (4CE)	https://transmartfoundation.org/covid-19-community-project/; https://covidclinical.net/
	Apple Mobility	Apple Mobility Trends Reports	https://www.apple.com/covid19/mobility
	ASM	American Society of Microbiology COVID Research Registry	https://asm.org/COVID/COVID-19-Research-Registry/Home
	C-19RD	COVID-19 research database	https://covid19researchdatabase.org/
	CORD-19	COVID-19 Open Research Dataset Challenge (CORD-19)	https://www.kaggle.com/allen-institute-for-ai/CORD-19-research-challenge
	COVID-19 DDI	COVID-19 Data Discovery Index	www.covid19dataindex.org
	Evidence Accelerator	FDA Evidence Accelerator program	https://www.focr.org/covid19
	Facebook Density	Facebook population density	https://data.humdata.org/dataset/highresolutionpopulationdensitymaps
	Hopkins Resource Center	Johns Hopkins Coronavirus Resource Center	https://coronavirus.jhu.edu/us-map
	Host Genetics	COVID-19 Host Genetics Initiative	https://www.covid19hg.org
	NY Times COVID-19	NY Times COVID-19 Data	https://raw.githubusercontent.com/nytimes/covid-19-data
	OHDSI	OHDSI study-a-thon	https://www.ohdsi.org/covid-19-updates/
	Our World in Data	Our World in Data	https://ourworldindata.org/coronavirus-source-data
	Pandemic Data Room	Flattening the curve: COVID-19 Pandemic Data Room Visualization Challenge	https://cgdv.github.io/challenges/COVID-19/
	R2D2	Reliable Response Data Discovery for clinical COVID-19 consultations using patient observations	https://covid19questions.org
	SECURE-IBD	Surveillance, Epidemiology of Coronavirus (COVID-19) under research exclusion	https://covidibd.org/
	TrinetX	TriNetX network	https://www.trinetx.com/coronavirus/
	Worldometer	Worldometer	https://www.worldometers.info/coronavirus/
National	ACT	ACT Network COVID-19: Developing COVID-19 phenotype and ontology	https://www.amia.org/sites/default/files/AMIA-COVID19-Webinar-Series-ACT-Network-CRI-2.pdf
	ACTIV	ACTIV (Accelerating COVID-19 Therapeutic Interventions and Vaccines): NIH clinical trials network for COVID vaccines testing	https://www.nih.gov/research-training/medical-research-initiatives/activ
	BEAT19	Behavior, Environment and Treatments for Covid-19 (BEAT19)	https://github.com/beat19-org/beat19-public-data
	C19HCC	COVID-19 Healthcare Coalition (C19HCC)	https://mcovid.org/
	C3I	Cancer Center Cessation Initiative (C3I) + COVID	https://sites.google.com/wisc.edu/c3icovidsmoking/grantee-resources
	CCC19	COVID Cancer Consortium (CCC19)	https://ccc19.org/
	CIVET	North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) Corona Infectious Virus Epidemiology Team (CIVET)	https://naaccord.org/covid-19
	COVID Tracking	The COVID Tracking Project	https://covidtracking.com/
	CovidCP	CovidCP clinical trials registry	
	eMERGE	eMERGE network to support COVID research	https://emerge-network.org
	HD4Action	RWJF Health Data 4 Action COVID-19 Registry (with AcademyHealth, Health Care Cost Institute, Care-Journey, and numerous health systems)	https://www.academyhealth.org/blog/2020-04/new-initiative-aims-build-model-open-covid-19-patient-data-registry-network
	N3C	N3C (National COVID Cohort Collaborative): building a nationwide COVID-19 cohort through informatics	covid.cd2h.org/N3C
	NHSN	CDC's National Healthcare Safety Network (NHSN) COVID-19 module	https://www.cdc.gov/nhsn/acute-care-hospital/covid19/index.html
	Optum	Optum	https://www.optum.com/campaign/ls-cb/covid-19-data-dashboard.html
	PCORNet	PCORNet Mini/Thin CDM: Stand-alone, ancillary COVID-19 version of the CDM	https://pcornet.org/news/pcornet-covid-19-common-data-model-launched-enabling-rapid-capture-of-insights/
	SCCM	Society of Critical Care Medicine: Discovery VIRUS COVID-19 registry	https://www.sccm.org/Research/Research/Discovery-Research-Network/VIRUS-COVID-19-Registry

Use of electronic health records to support a public health response to the COVID-19 pandemic in the United States: a perspective from 15 academic medical centers
Madhavan, S. et al. JAMIA. 2021

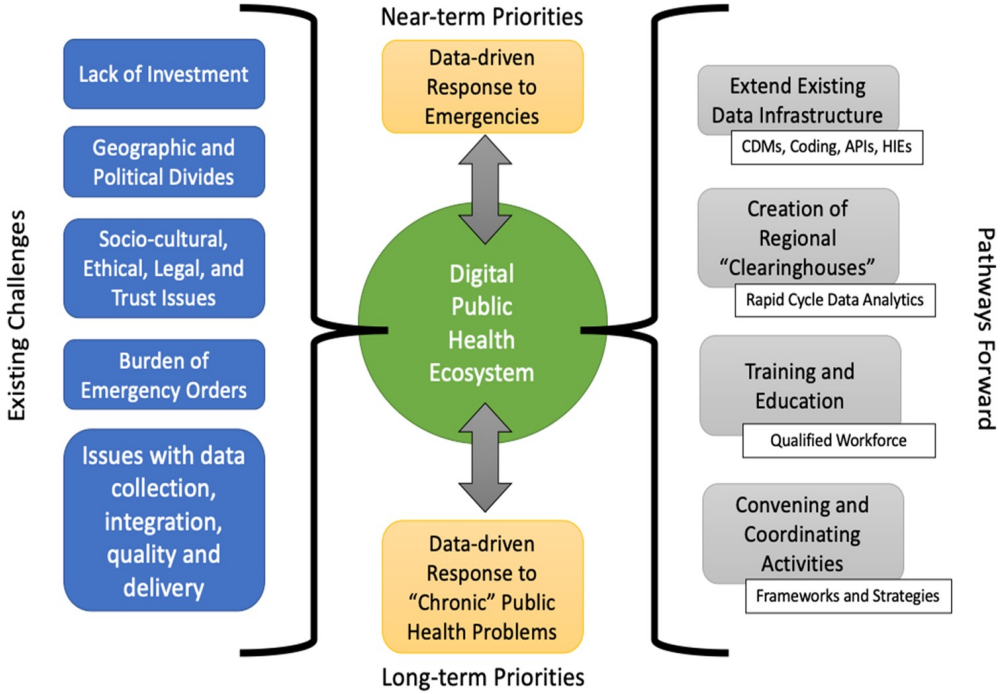


Figure 2. Conceptual model for an evolving digital public health ecosystem. A durable information infrastructure to overcome existing challenges requires careful coordination and leverage of existing resources. Most of the components for a future, integrated system are already in place, with the pathways moving forward requiring agreement or translation among standards, governance structures, and clear definitions of roles and responsibilities. "Chronic" public health issues refer to long-term challenges such as healthcare-acquired infections or prescription overdose.

Reimagining the research-practice relationship: policy recommendations for informatics-enabled evidence-generation across the US health system.
Embi PJ, et al. JAMIA Open. 2019

- The widespread adoption and use of electronic health records and their use to enable learning health systems (LHS) holds great promise to accelerate both evidence-generating medicine (EGM) and evidence-based medicine (EBM), thereby enabling a LHS.
- Report from AMIA's 10th annual Policy Invitational to discuss issues key to facilitating the EGM-EBM paradigm at points-of-care (nodes), across organizations (networks), and to ensure viability of this model at scale (sustainability).
- Synthesis of conference and augments with relevant context to inform ongoing policy development.
- Suggestions for public policies needed to facilitate EGM-EBM activities on a national scale, particularly those policies that can enable and improve clinical and health services research at the point-of-care, accelerate biomedical discovery, and facilitate translation of findings to improve the health of individuals and populations.

Policies for Research from the Office of the National Coordinator for Health IT

- **National health information technology priorities for research: A policy and development agenda**. Zayas-Cabán, T. JAMIA. 2020
  - ONC led a collaborative effort to identify challenges, priorities, and actions to leverage health IT and electronic health data for research. Included: review of literature and programs, key informant interviews, and a stakeholder workshop to identify electronic health data and health IT infrastructure gaps.
  - This effort resulted in the National Health IT Priorities for Research: A Policy and Development Agenda, which articulates an optimized health information ecosystem for scientific discovery.
  - Outlines 9 priorities and recommended actions to be implemented in collaboration with the research and informatics communities for realizing this vision.
- **Leveraging the health information technology infrastructure to advance federal research priorities.** Zayas-Cabán, T. JAMIA. 2020
  - Building upon the policy article above, *this* article describes support for the Agenda from the Food and Drug Administration, the National Institutes of Health, and the Veterans Health Administration. Advancing the Agenda will benefit these agencies and support their missions as well as the entire ecosystem leveraging the health IT infrastructure or using data from health IT systems for research.

NIH Rule on Data Sharing

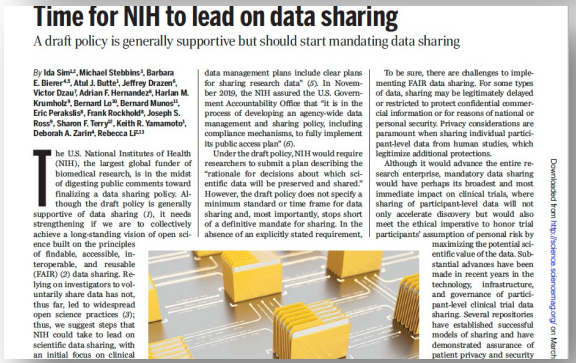
- During comment period, feedback from our community, including AMIA and thought leaders like Sim et al. in Science. 2020
- Final data sharing rule released in October 2020.
  - Takes effect in 2023 – worth a read!

AMIA: NIH Misses Mark on Data Sharing Proposals

Monday, January 13, 2020

Nation's health informatics experts urge NIH to dramatically revise draft data management and sharing policy to maximize the value of scientific data

BETHESDA, MD – Last week the American Medical Informatics Association (AMIA) warned the National Institutes of Health (NIH) that its proposed data management and sharing policy would be detrimental to data-driven discovery and lead to increased compliance burdens for researchers. The organization



Time for NIH to lead on data sharing

A draft policy is generally supportive but should start mandating data sharing

By Ida Sim[1,2], Michael Stebbins[3], Barbara E. Bierer[4,5], Atul J. Butte[6], Jeffrey Drazen[7], Victor Dzau[8], Adrian F. Hernandez[9], Harlan M. Krumholz[9], Bernard Lo[10], Bernard Munos[11], Eric Perakslis[12], Frank Rockhold[13], Joseph S. Ross[9], Sharon F. Terry[14], Keith R. Yamamoto[1], Deborah A. Zarin[4], Rebecca Li[2,3]

The U.S. National Institutes of Health (NIH), the largest global funder of biomedical research, is in the midst of digesting public comments toward finalizing a data sharing policy. Although the draft policy is generally supportive of data sharing (1), it needs strengthening if we are to collectively achieve a long-standing vision of open science built on the principles of findable, accessible, interoperable, and reusable (FAIR) (2) data sharing. Relying on investigators to voluntarily share data has not, thus far, led to widespread open science practices (3); thus, we suggest steps that NIH could take to lead on scientific data sharing, with an initial focus on clinical data management plans include clear plans for sharing research data" (5). In November 2019, the NIH assured the U.S. Government Accountability Office that "it is in the process of developing an agency-wide data management and sharing policy, including compliance mechanisms, to fully implement its public access plan" (6).

Under the draft policy, NIH would require researchers to submit a plan describing the "rationale for decisions about which scientific data will be preserved and shared." However, the draft policy does not specify a minimum standard or time frame for data sharing and, most importantly, stops short of a definitive mandate for sharing. In the absence of an explicitly stated requirement, To be sure, there are challenges to implementing FAIR data sharing. For some types of data, sharing may be legitimately delayed or restricted to protect confidential commercial information or for reasons of national or personal security. Privacy considerations are paramount when sharing individual participant-level data from human studies, which legitimize additional protections.

Although it would advance the entire research enterprise, mandatory data sharing would have perhaps its broadest and most immediate impact on clinical trials, where sharing of participant-level data will not only accelerate discovery but would also meet the ethical imperative to honor trial participants' assumption of personal risk by maximizing the potential scientific value of the data. Substantial advances have been made in recent years in the technology, infrastructure, and governance of participant-level clinical trial data sharing. Several repositories have established successful models of sharing and have demonstrated assurance of patient privacy and security

National Institutes of Health
Office of Science Policy

NIH Data Management and Sharing Activities Related to Public Access and Open Science

Validation and progress in biomedical research – the cornerstone of developing new prevention strategies, treatments, and cures – is dependent on access to scientific data. Sharing scientific data helps validate research results, enables researchers to combine data types to strengthen analyses, facilitates reuse of hard to generate data or data from limited sources, and accelerates ideas for future research inquiries. Central to sharing scientific data is the recognized need to make data as available as possible while ensuring that the privacy and autonomy of research participants are respected, and that confidential/proprietary data are appropriately protected.

Related to Public Access and Open Science

***NEW* Final NIH Policy for Data Management and Sharing and Supplemental Information (October 2020)**

- Federal Register Notice
- NIH Guide Notices:
  - NOT-OD-21-013 – Final NIH Policy for Data Management and Sharing
  - NOT-OD-21-014– Supplemental Information to the NIH Policy for Data Management and Sharing: Elements of an NIH Data Management and Sharing Plan

Scientific Data Sharing

› Genomics and Health

› Scientific Data Management

https://osp.od.nih.gov/scientific-sharing/nih-data-management-and-sharing-activities-related-to-public-access-and-open-science/

Notable CRI News/Events

Changes at ONC

- New administration – new ONC Director
- TEFCA rule now finalized
- Role for HIEs expanding further

Micky Tripathi, Ph.D. M.P.P.

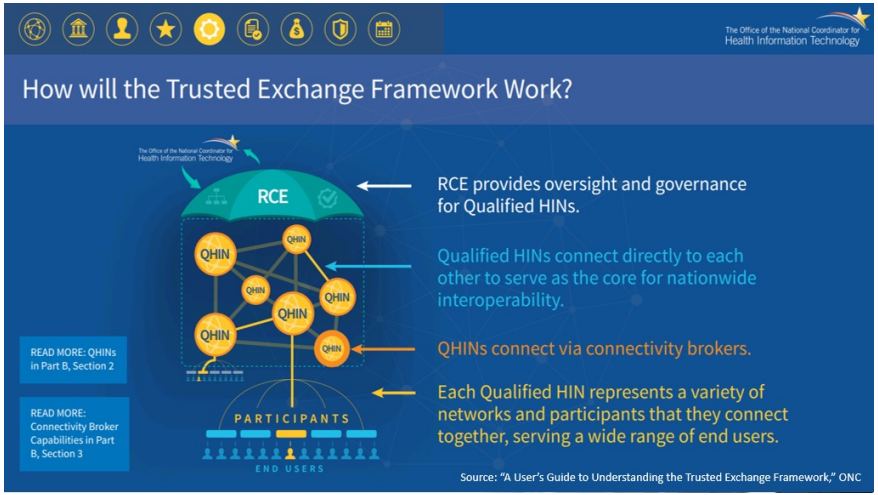
National Coordinator for Health Information Technology

Micky Tripathi is the National Coordinator for Health Information Technology at the U.S. Department of Health and Human Services, where he leads the formulation of the federal health IT strategy and coordinates federal health IT policies, standards, programs, and investments.

Mr. Tripathi has over 20 years of experience across the health IT landscape. He most recently served as Chief Alliance Officer for Arcadia, a health care data and software company focused on population health management and value-based care, the project manager of the Argonaut Project, an industry collaboration to accelerate the adoption of FHIR, and a board member of HL7, the Sequoia Project, the CommonWell Health Alliance, and the CARIN Alliance.

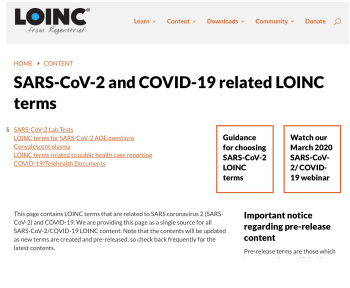
Mr. Tripathi served as the President and Chief Executive Officer of the Massachusetts eHealth Collaborative (MAeHC), a non-profit health IT advisory and clinical data analytics company. He was also the founding President and CEO of the Indiana Health Information Exchange, a statewide HIE partnered with the Regenstrief Institute, an Executive Advisor to investment firm LRVHealth, and a Fellow at the Berkman-Klein Center for Internet and Society at Harvard University.

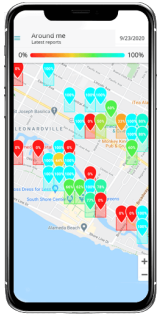
He holds a PhD in political science from the Massachusetts Institute of Technology, a Master of Public Policy from Harvard University, and an AB in political science from Vassar College. Prior to receiving his PhD, he was a Presidential Management Fellow and a senior operations research analyst in the Office of the Secretary of Defense in Washington, DC, for which he received the Secretary of Defense Meritorious Civilian Service Medal.

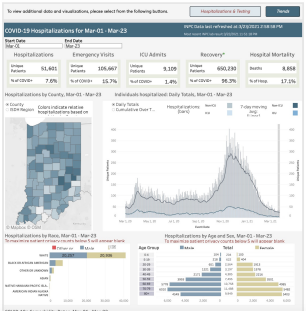


Most notable: COVID

- COVID!
  - It has changed so much, including our field
- Rapid acceleration of Informatics interventions – examples today
- Rapid conduct of studies, papers
- Huge rise in pubs/pre-prints
- Need for rapid innovation, translation, new capabilities
- Breaking down barriers
- Focus on extraordinary collaboration
- Many “networks” doing great work
- Even as we’ve remained ”virtual”







COVID and CRI

- Multiple stimulus packages – significant research funding
- Leveraging our data and capabilities
- Monitor and track, it's not over
- Pivoting now to longer-term…
- Launch of long-covid studies initiative
  - So much work to be done
  - Our specialty at the center
  - We're all counting on each other!

Open Funding Opportunities

Explore COVID-19 funding opportunities from NIH.

Trying to Make Sense of Long COVID Syndrome

Posted on January 19th, 2021 by Dr. Francis Collins

Credit: NIH

NIH National Institutes of Health
Turning Discovery Into Health

Search NIH

NIH Employee Intranet | Staff Directory | En Español

Health Information | Grants & Funding | News & Events | Research & Training | Institutes at NIH | About NIH

COVID-19

- Get the latest public health information from CDC
- NIH staff guidance on coronavirus (NIH Only)
- Get the latest research information from NIH | Español

Home » About NIH » Who We Are » The NIH Director

THE NIH DIRECTOR

The NIH Director
Photo Gallery
Congressional Testimonies
Advisory Groups
Video & Sound Gallery
Articles
Statements

February 23, 2021

NIH launches new initiative to study "Long COVID"

I write to announce a major new NIH initiative to identify the causes and ultimately the means of prevention and treatment of individuals who have been sickened by COVID-19, but don't recover fully over a period of a few weeks. Large numbers of patients who have been infected with SARS-CoV-2 continue to experience a constellation of symptoms long past the time that they've recovered from the initial stages of COVID-19 illness. Often referred to as "Long COVID", these symptoms, which can include fatigue, shortness of breath, "brain fog", sleep disorders, fevers, gastrointestinal symptoms, anxiety, and depression, can persist for months and can range from mild to incapacitating. In some cases, new symptoms arise well after the time of infection or evolve over time. In December, NIH held a workshop to summarize what is known about these patients who do

Notable CRI-Related Events:
Societal events also affect health/research/informatics

- AI Ethics and Bias concerns
  - Examples in major industries, e.g. Google
- Assault on science has also had a great effect
  - Creation of Scientist as president's cabinet position a major event
  - We must do good work to address anti-science
- More specific to CRI…
  - RWD/RWE boom
  - AI/ML boom
  - New capabilities (e.g. synthetic data) to enable democratization of data
  - Continued rrowth in CRIO role
  - Pragmatic research on the rise (e.g. results of major PCORNet study – ADAPTABLE to be announced in May)

In Summary…

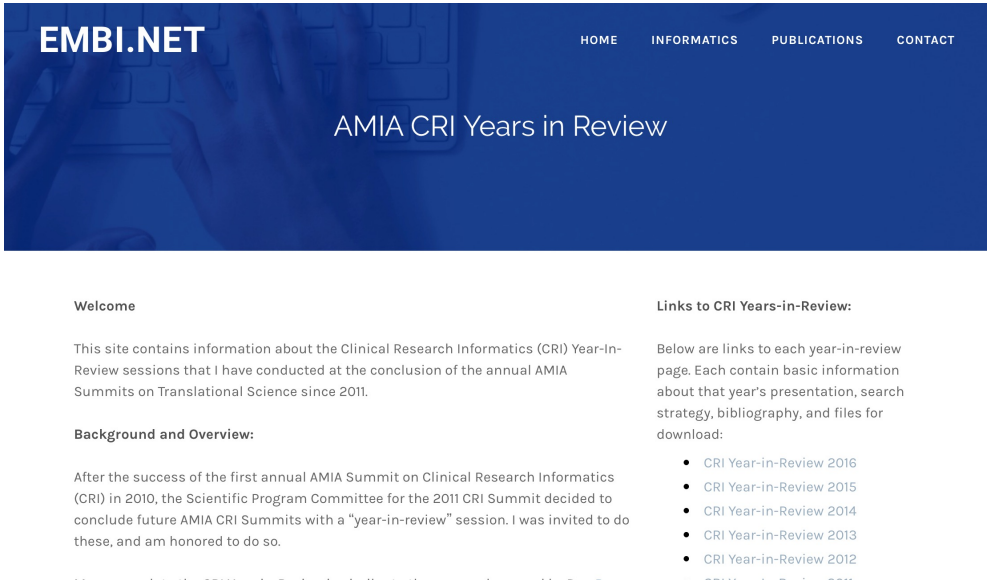
- Informatics and CRI/Implementation Science has never been more important
  - **Much** more activity than in years past
- CRI continues to *mature* and is clearly driving science
- COVID is changing everything – including CRI
- Multiple federal, state and local initiatives continue to advance field
- Initiatives and investments beginning to realize the vision of the "*learning health system*"
- No question CRI is and will remain relevant
- A **very** exciting time to be in CRI!

Thanks!

Special thanks to those who suggested articles/events to highlight, particularly

- Rachel Richesson
- Philip Payne
- Chunhua Weng
- Erin Holve
- Shawn Murphy
- Paul Harris
- David Haggstrom
- Ida Sim
- John Holmes
- Adam Wright
- Bill Hersh
- Mark Weiner
- Chris Longhurst
- Brian Dixon

Thanks!



pembi@regenstrief.org

Twitter: @embimd

Slideshow, files:
http://www.embi.net/

Q&A

Regenstrief Institute