Clinical Research Informatics

Year-in-Review

Peter J. Embí, MD, MS, FACP, FACMI, FAIHSI
Chair, Department of Biomedical Informatics
Professor of Biomedical Informatics and Medicine
Senior Vice-President for Research and Innovation

VANDERBILT UNIVERSITY
MEDICAL CENTER

AMIA Informatics Summit
Boston, MA
March 20, 2024

Disclosures

- **Federal Funding:** NIH: NLM, NHGRI, NCATS; AHRQ; PCORI
- **Foundation Funding:** Gordon & Betty Moore Foundation
- **Academic Consulting:** Yale University, University of Miami, University of Florida, University of Iowa, University of Pittsburgh, University of Colorado, U. Pittsburgh, Rochester U.
- **Study Section:** AHRQ
- **Corporate Institutional Partnerships (no personal compensation):** GE Healthcare

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 13 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:
    - ((“Research”[Mesh]) AND “Informatics”[Mesh] NOT ("genetics"[Mesh])
    - Limited to Dates: 1/1/2023 – 3/15/2024
    - Initial searches resulted in **465** articles
    - Further limits: **428**
  - Additional articles found via:
    - Recommendations from colleagues
    - Other keyword searches using terms like:
      - Clinical Trials, Clinical Research Informatics, Translational, Data Warehouse, Data Network, Recruitment, Learning Health System, Phenotype, Artificial Intelligence etc.
    - Yielding **521** additional
  - From those, I’ve selected **85** 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 **85** articles into several CRI categories (not *all* CRI areas)
  - Data Sharing, Re-Use and RWD
  - CRI Methods and Approaches
  - Participant Recruitment and Retention
  - Learning Health Systems & Pragmatic Trials
  - AI and CRI
  - CRI Ethics & Policy
- 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

ChatGPT… a little help

You

Write a haiku about me giving a year-in-review keynote address to the AMIA Informatics Summit

ChatGPT

Year's wisdom distilled,

AMIA Summit, keen ears,

Insights paint the sky.

Data Sharing, Re-Use & RWD for Research

OHDSI Standardized Vocabularies-a large-scale centralized reference ontology for international data harmonization.

Reich C, et al. JAMIA 2024

- IMPORTANCE: Observational Health Data Sciences and Informatics (OHDSI) is the largest distributed data network in the world w/ more than 331 data sources with 2.1 billion patient records across 34 countries.
- It enables large-scale observational research through standardizing the data into a common data model (CDM) (Observational Medical Outcomes Partnership [OMOP] CDM).
- METHODS: This paper is the first to describe the OHDSI Standardized Vocabularies - a common reference ontology mandatory to all data sites in the network - that enables:
  - Harmonization through assigned domains according to clinical categories,
  - Comprehensive coverage of entities within each domain
  - Support for commonly used international coding schemes
  - Standardization of semantically equivalent concepts.

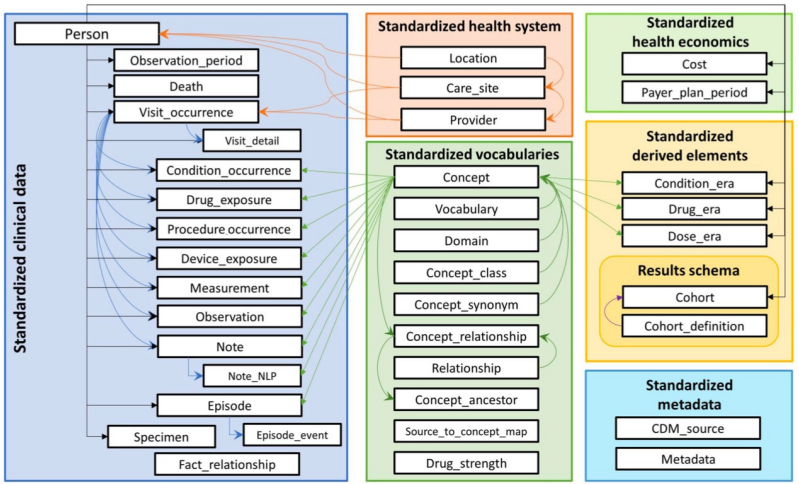
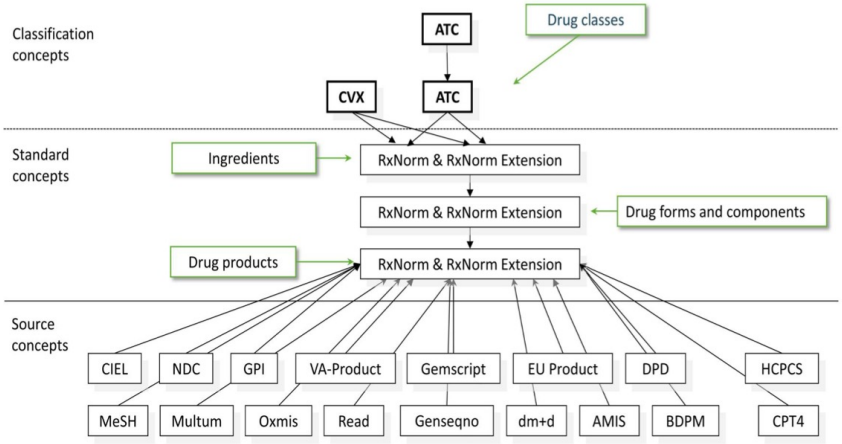


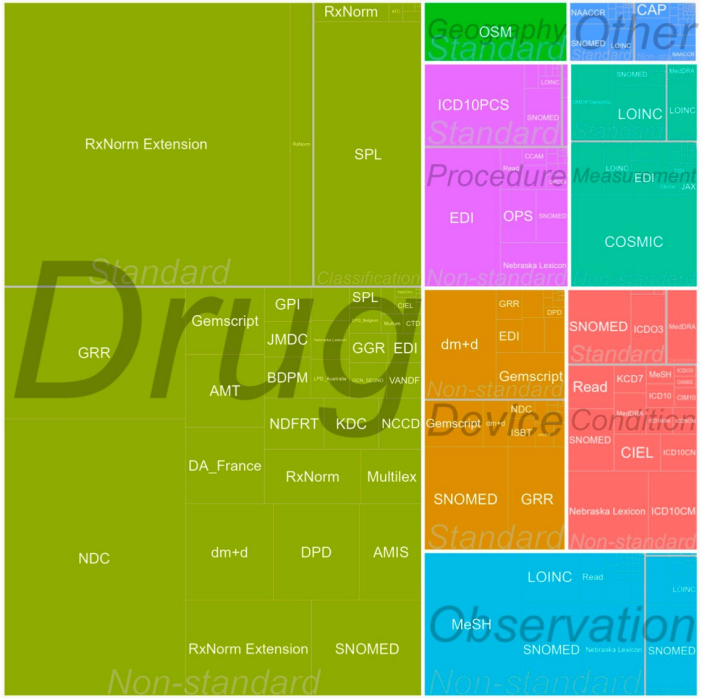
Figure 1. Overview of structure of OMOP CDM and Standardized Vocabularies. Grey arrows indicate foreign key relationships, and orange arrows indicate relationships of concepts, which follow domain-field association.

OHDSI Standardized Vocabularies-a large-scale centralized reference ontology for international data harmonization.

Reich C, et al. JAMIA 2024



Different types of concepts of the OHDSI standardized vocabularies, and the vocabularies they are derived from, in the Drug domain, and the hierarchical system.



Distribution of the concepts in the OHDSI Standardized Vocabularies organized by domain and underlying vocabularies.

OHDSI Standardized Vocabularies-a large-scale centralized reference ontology for international data harmonization.
Reich C, et al. JAMIA 2024

- **FINDINGS:** The OHDSI Standardized Vocabularies comprise over 10 million concepts, 80-million relationships, from 136 vocabularies. Used by hundreds of groups and several large data networks. More than 8,600 users have performed 50,000 downloads of the system.
- **CONCLUSION:** OHDSI has made available a comprehensive, open vocabulary system that supports global observational research. It addresses an impediment of large-scale observational research - the dependence on the context of source data representation.
- **CRI Implications:** The OHDSI Standardized Vocabularies are a mature and reliable resource to power the world's largest distributed data network. It enables the application of standardized large-scale analytical methods in a truly federated setting, leading to the generation of relevant findings and publications of impactful observational research.

Implementation of a commercial federated network of electronic health record data to enable sponsor-initiated clinical trials at an academic medical center

Campion, TR, et al. Int J Med Inform 2024

- A commercial federated network called TriNetX has connected electronic health record (EHR) data from academic medical centers (AMCs) with biopharmaceutical sponsors in a privacy-preserving manner to promote sponsor-initiated clinical trials. Little is reported about how AMCs have implemented TriNetX to support clinical trials.

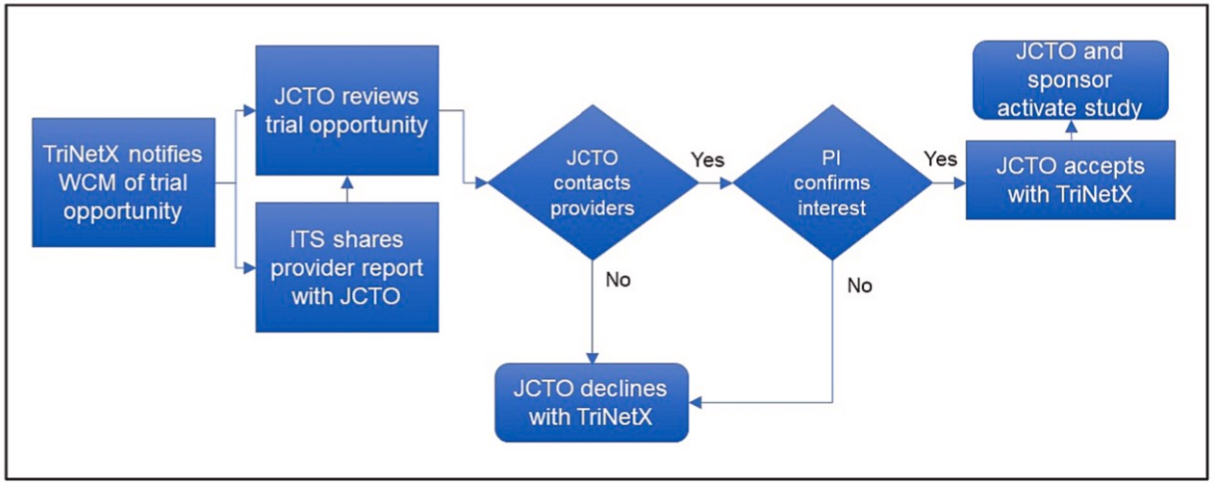


Fig. 1. TriNetX workflow at Weill Cornell Medicine (WCM). JCTO: Joint Clinical Trials Office. ITS: Information Technologies & Services Department. PI: principal investigator.

Implementation of a commercial federated network of electronic health record data to enable sponsor-initiated clinical trials at an academic medical center

Campion, TR, et al. Int J Med Inform 2024

- **Findings:** Over a six-year period, TriNetX enabled 402 requests for sponsor-initiated clinical trials, 14 % (n = 56) of which local investigators expressed interest in conducting.
- Although clinical trials administrators indicated TriNetX yielded unique study opportunities, measurement of impact of institutional participation in the network was challenging due to lack of a common trial identifier shared across TriNetX, sponsor, and our institution.
- **Conclusion:** Among first studies to describe integratio of a federated network of EHR data into institutional workflows for sponsor-initiated clinical trials.
- **CRI Implications:** Potential, but also challenges in assessing value. More work needed by CRI professionals to characterize and ensure such systems lead to valuable impacts.

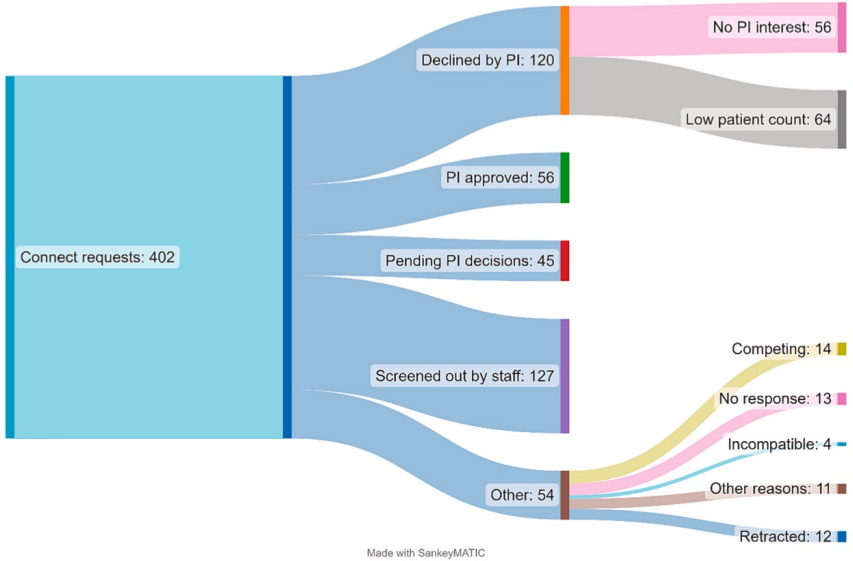


Fig. 2. Sankey diagram illustrating disposition of TriNetX requests 2017–2023. PI: principal investigator.

Long COVID risk and pre-COVID vaccination in an EHR-based cohort study from the RECOVER program

M. D. Brannock, et al. Nat Commun 2023

- EHR-derived data from the N3C or National COVID Cohort Collaborative used to characterize association between SARS-CoV-2 vaccination and Long COVID (LC) diagnosis
- Spanning Aug 1, 2021 – Jan 31, 2022
- >5.4 Million patient cohort to start, >47,000 Dx LC
- Two cohorts with distinct LC definitions

- **CRI Implication: Further demonstrates strength of such large data sets for RWD analyses**

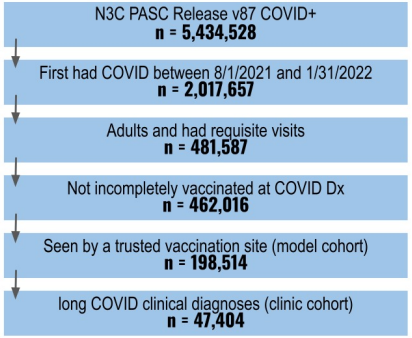
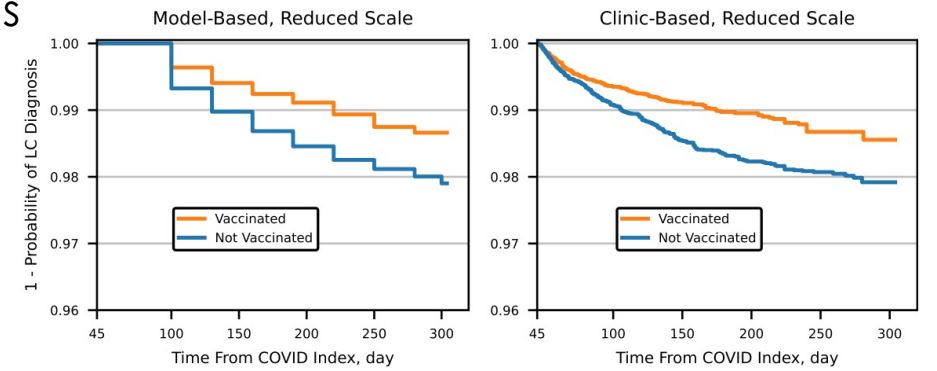


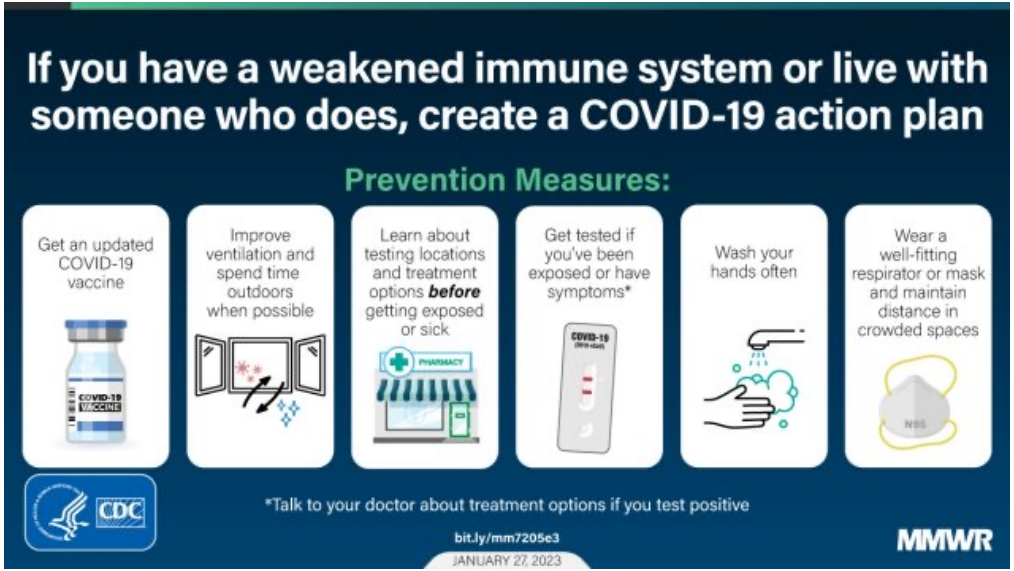
Fig. 3 | Cohort definition flowchart. Cumulative number of patients meeting the study's inclusion criteria.



Real World Evidence to inform prevention and care from large data-sharing networks.

Not possible without efforts from our CRI community

Informatics saves lives!



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

- **Number needed to vaccinate with a COVID-19 booster to prevent a COVID-19-associated hospitalization during SARS-CoV-2 Omicron BA.1 variant predominance, December 2021-February 2022, VISION Network: a retrospective cohort study.** K. Adams, et al. Lancet Reg Health Am 2023
  - VISION VE Network – over 10 states of RWD. Demonstrated, while variable depending on local infection rates and pt factors, NNV with booster to prevent hospitalization (205 median) & ED visit (156 median).
- **Emulation of Randomized Clinical Trials with Nonrandomized Database Analyses: Results of 32 Clinical Trials**. Wang, SV, et al. JAMA. 2023
  - From DUPLICATE-RCT Initiative. When closely emulated, database studies can closely approximate RCTs. Though not a substitute, each offers insights into the validity of other study design and can contribute to knowledge of sufficient causation. “Careful comparisons between RCTs and real-world evidence represent a productive line of research.”
- **Effectiveness of COVID-19 vaccines at preventing emergency department or urgent care encounters and hospitalizations among immunocompromised adults: An observational study of real-world data across 10 US states from August-December 2021.** P. J. Embi, et al. Vaccine 2023

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

- **Genomic data in the All of Us Research Program.** A. G. Bick, et al. Nature 2024
  - Genomic + EHR derived data – excellent description of this resource with great potential.
- **Toward standardization, harmonization, and integration of social determinants of health data: A Texas Clinical and Translational Science Award institutions collaboration.** C. K. Craven, et al. J Clin Transl Sci 2024
  - Variable completeness levels for SDOH data in EHR across Texas CTSA hubs and were low for most measures.
- **Data-driven hypothesis generation among inexperienced clinical researchers: A comparison of secondary data analyses with visualization (VIADS) and other tools.** X. Jing, et al. J Clin Transl Sci 2024
  - (VIADS, a visual interactive analysis tool for filtering and summarizing large datasets coded with hierarchical terminologies) - helped users develop hypotheses more quickly, but seemed to reduce quality. Further studies of such tools needed.

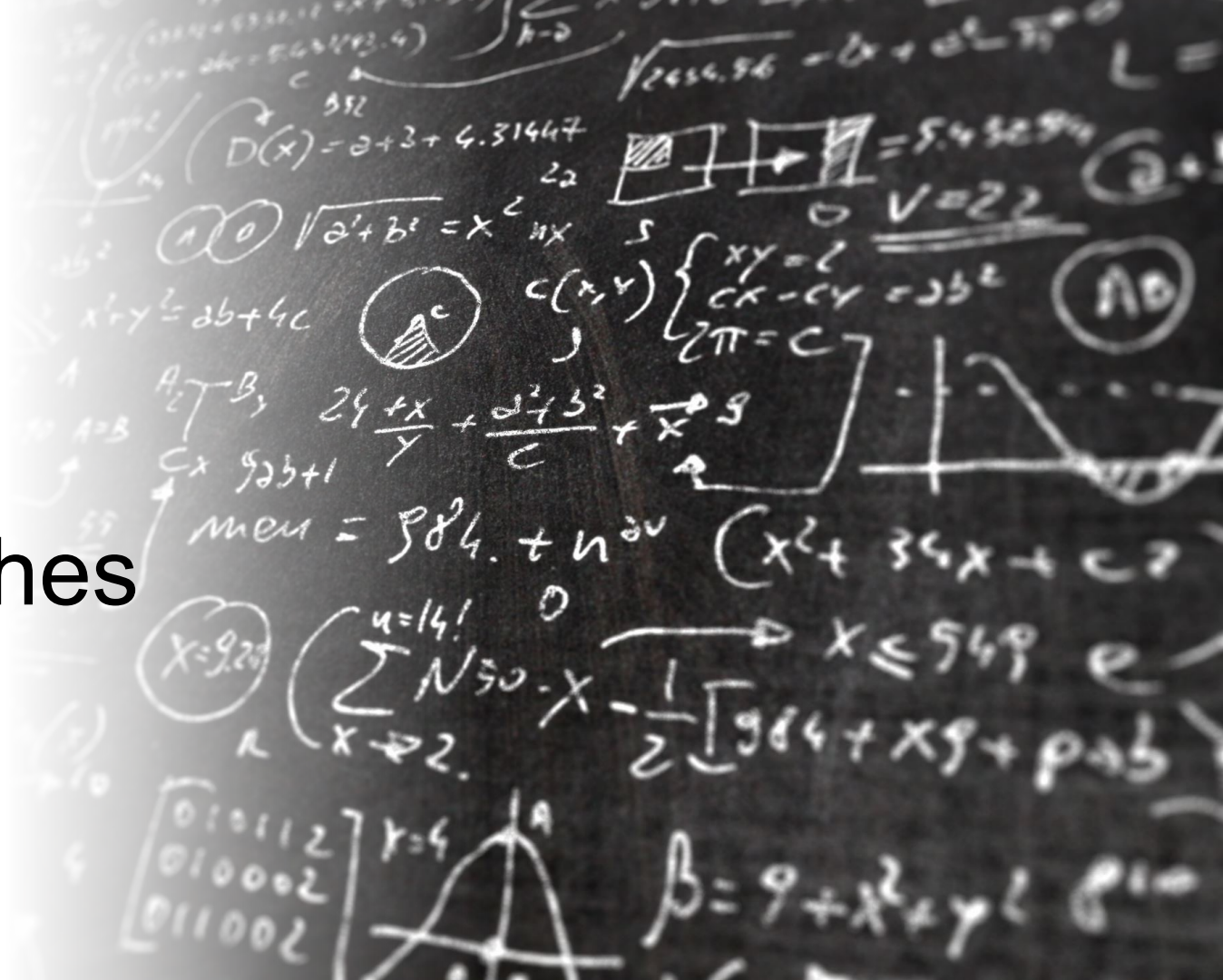
Data Sharing, Re-Use, and RWD: Other notable papers

- **Representing and utilizing clinical textual data for real world studies: An OHDSI approach.** V. K. Keloth, et al. J Biomed Inform 2023
  - Framework for representing and utilizing textual data in real-world evidence generation, including representations of information from clinical text in the OMOP CDM, the workflow and tools to ETL data from clinical notes, current applications and specific use cases described.
- **Scalable and interpretable alternative to chart review for phenotype evaluation using standardized structured data from electronic health records.** A. Ostropolets, et al. J Am Med Inform Assoc 2023
  - OHDSI paper on "Knowledge-Enhanced Electronic Profile Review" (KEEPER) – a phenotype evaluation tool that extracts patient's structured data elements relevant to a phenotype and presents them in a standardized fashion following clinical reasoning principles. Evaluation as alternative to chart review presented and discussed.
- **Improving Diversity in Clinical Trials by Using Real-world Data to Define Eligibility Criteria.** T. J. Royce, et al. JAMA Oncol 2023
  - Viewpoint discusses the need for thoughtful, modernized eligibility criteria with equity prioritization in clinical trials.

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

- **Guidance for reporting analyses of metadata on electronic health record use.** A. Rule, et al. J Am Med Inform Assoc 2024
  - Perspective with guidance to those working with EHR-use metadata – describes 4 common types, how they are recorded, and how they can be aggregated into higher-level measures of EHR use. And guidelines for reporting analyses of EHR-use metadata.
- **Digital Health Data Quality Issues: Systematic Review.** R. Syed, J Med Internet Res 2023
- **Rare Diseases in Hospital Information Systems-An Interoperable Methodology for Distributed Data Quality Assessments.** K. Tahar, et al. Methods Inf Med 2023
- **Ten simple rules for organizations to support research data sharing.** Champieux R, et al. PLoS Comput Biol. 2023.

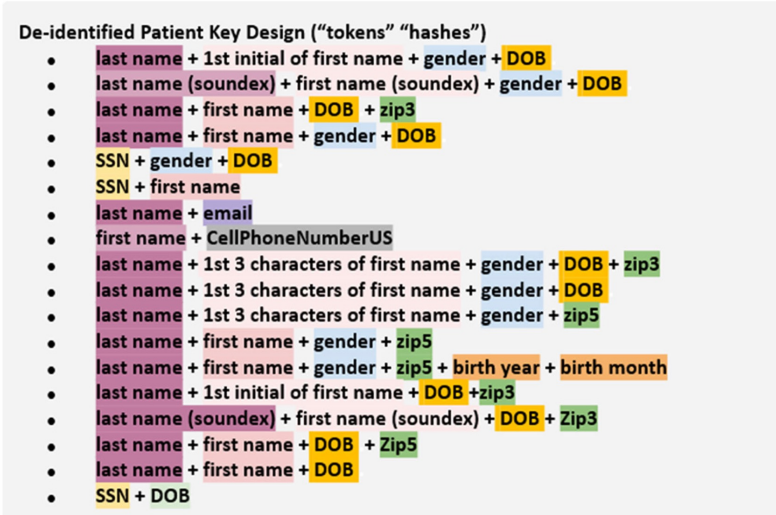
CRI Methods and Approaches



Privacy-preserving record linkage across disparate institutions and datasets to enable a learning health system: The national COVID cohort collaborative (N3C) experience

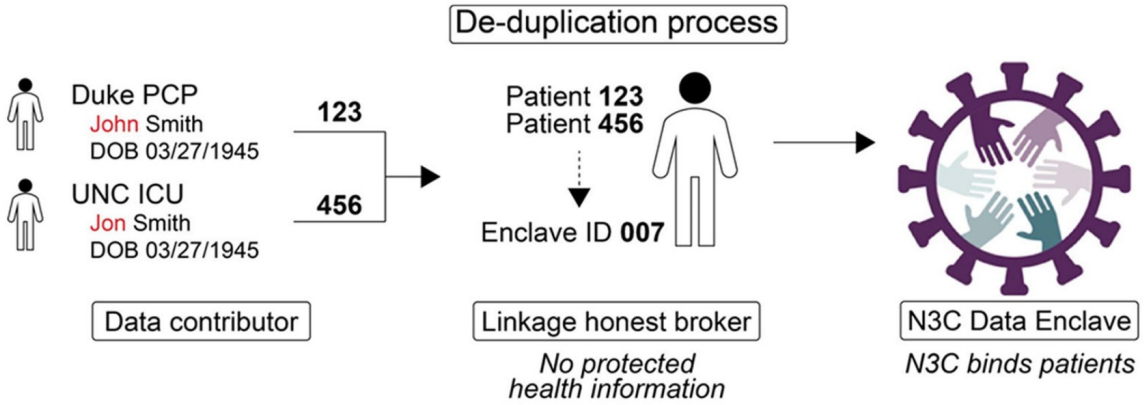
U. Tachinardi, et al. Learn Health Syst 2024

- **Objective:** To establish privacy-preserving record linkage (PPRL) methods for N3C to ensure that patient-level EHR data remains secure and private when governance-approved linkages with other datasets occur.
- **Methods:** Per agreements and approval processes, **The Linkage Honest Broker** (LHB), an independent neutral party, ensures data linkages are robust and secure by adding an extra layer of separation between PHI and clinical data. The LHB's PPRL methods (including algorithms, processes, and governance) match patient records using "deidentified tokens," which are hashed combinations of identifier fields that define a match across data repositories without using patients' clear-text identifiers.
- Eighteen tokens selected for use with N3C datasets. DOB, date of birth; SSN, social security number; zip3, first 3 numbers of zip code; Zip5, first 5 numbers of zip code.



Privacy-preserving record linkage across disparate institutions and datasets to enable a learning health system: The national COVID cohort collaborative (N3C) experience

U. Tachinardi, et al. Learn Health Syst 2024



Deduplication process. Patients with multiple records, both within a single site and across different sites, are identified and linked.

FIGURE 1 Patient linkage statistics for the N3C linkage honest broker process as of March 2023. Privacy preserving record linkage (PPRL) is used to identify and link multiple records for the same person within and across data contributing sites.

Privacy-preserving record linkage across disparate institutions and datasets to enable a learning health system: The national COVID cohort collaborative (N3C) experience

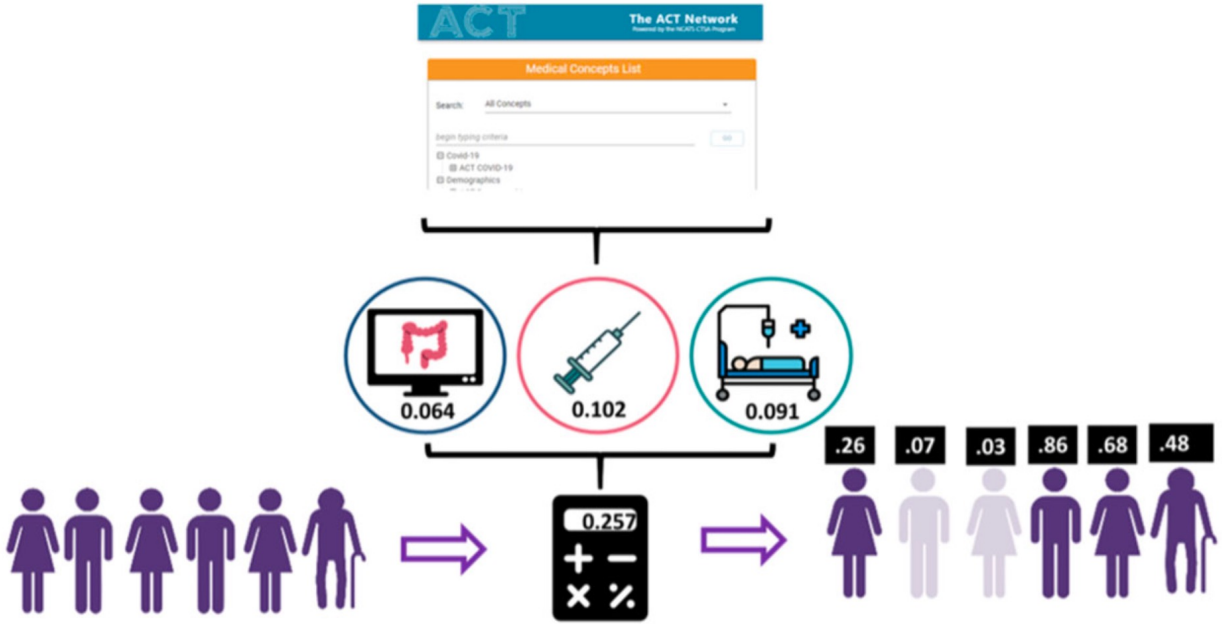
U. Tachinardi, et al. Learn Health Syst 2024

- RESULTS: These methods enabled three linkage functions: Deduplication, Linking Multiple Datasets, and Cohort Discovery.
- As of March 1, 2023, 43 sites had signed the LHB Agreement; 35 sites have sent tokens generated for 9,528,998 patients. In an initial cohort across 2 sites, the LHB identified 135,037 matches and confirmed 68,596 duplicates.
- CONCLUSION: This large-scale linkage study using deidentified datasets of varying characteristics established secure methods for protecting the privacy of N3C patient data when linked for research purposes.
- **CRI Implication:** As data sharing increases, this appraoch has potential for use with other networks.

A broadly applicable approach to enrich electronic-health-record cohorts by identifying patients with complete data: a multisite evaluation.
J. G. Klann, et al. J Am Med Inform Assoc 2023

- **OBJECTIVE:** Patients who receive most care within a single healthcare system (colloquially called a "**loyalty cohort**") have mostly complete data within that organization's EHR.
- Loyalty cohorts have **low data missingness**, which can unintentionally bias research results. Using proxies of routine care and healthcare utilization metrics, they computed a per-patient score that identifies a loyalty cohort.
- **MATERIALS AND METHODS:** They implemented a computable program for the widely adopted i2b2 platform that identifies loyalty cohorts in EHRs based on a machine-learning model, which was previously validated using linked claims data.
- They developed a novel validation approach, which tests, using only EHR data, whether patients returned to the same healthcare system after the training period, and evaluated these tools at 3 institutions using data from 2017 to 2019.

A broadly applicable approach to enrich electronic-health-record cohorts by identifying patients with complete data: a multisite evaluation.
J. G. Klann, et al. J Am Med Inform Assoc 2023



Algorithm uses ENACT's medical concept list to quantify "loyalty" and uses that along with a regression equation to compute a score for each patient. Higher scores indicate more likely to have complete data.

A broadly applicable approach to enrich electronic-health-record cohorts by identifying patients with complete data: a multisite evaluation.
J. G. Klann, et al. J Am Med Inform Assoc 2023

- **Results:** Loyalty cohort calculations to identify patients who returned during a 1-year follow-up yielded a mean area under the receiver operating characteristic curve of 0.77 using the original model and 0.80 after calibrating the model at individual sites.
- Factors such as multiple medications or visits contributed significantly at all sites. Screening tests' contributions (e.g., colonoscopy) varied across sites, likely due to coding and population differences.
- **Discussion:** The open-source implementation of a "loyalty score" algorithm had good predictive power. i2b2 sites can use this approach to select cohorts with mostly complete EHR data.
- **CRI Implications:** Enriching research cohorts by utilizing these low-missingness patients is a way to obtain the data completeness necessary for accurate causal analysis.

Leveraging the Expertise of the CTSA Program to Increase the Impact and Efficiency of Clinical Trials

P. A. Harris, et al. JAMA Netw Open 2023

- Description of the TINs and RIC….
- Focus on conducting multicenter randomized clinical trials (mRCT) which presents challenges.
- The Trial Innovation Network (TIN), established in 2016 to partner with the Clinical and Translational Science Award (CTSA) Consortium of academic medical institutions in the implementation of mRCTs, consists of **3 Trial Innovation Centers (TICs)** and **1 Recruitment Innovation Center (RIC)**.
- Aimed to address critical roadblocks that impede the design and conduct of mRCTs, in expectation of accelerating the translation of novel interventions to clinical practice.
- Challenges and achievements are described, along with examples of innovative resources and processes that may serve as useful models for other clinical trial networks providing operational and recruitment support.

Leveraging the Expertise of the CTSA Program to Increase the Impact and Efficiency of Clinical Trials

P. A. Harris, et al. JAMA Netw Open 2023

- OBSERVATIONS: The TIN has successfully integrated more than 60 CTSA institution program hubs into a functional network for mRCT implementation and optimization.
- Resources and processes span the clinical trial spectrum and enable the TICs and RIC to serve as coordinating centers, data centers, and recruitment specialists to assist trials across the National Institutes of Health and other agencies.
- The TIN's impact has been demonstrated through its response to both historical operational challenges and emerging public health emergencies, including the national opioid public health crisis and the COVID-19 pandemic.

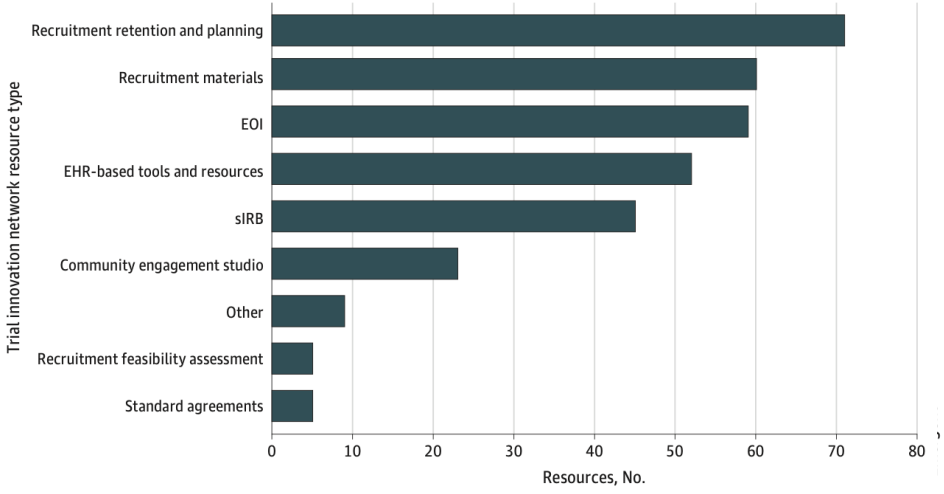
Therapeutic area	Proposals, %
Cardiovascular disease	14
Neurology	8
Infectious diseases	7
Pediatric diseases	6
Pulmonary diseases	4
Oncology	4
Gastroenterology	3
Behavioral medicine (clinical)	2
Trauma	2
Diabetes	2
Other	47

Leveraging the Expertise of the CTSA Program to Increase the Impact and Efficiency of Clinical Trials

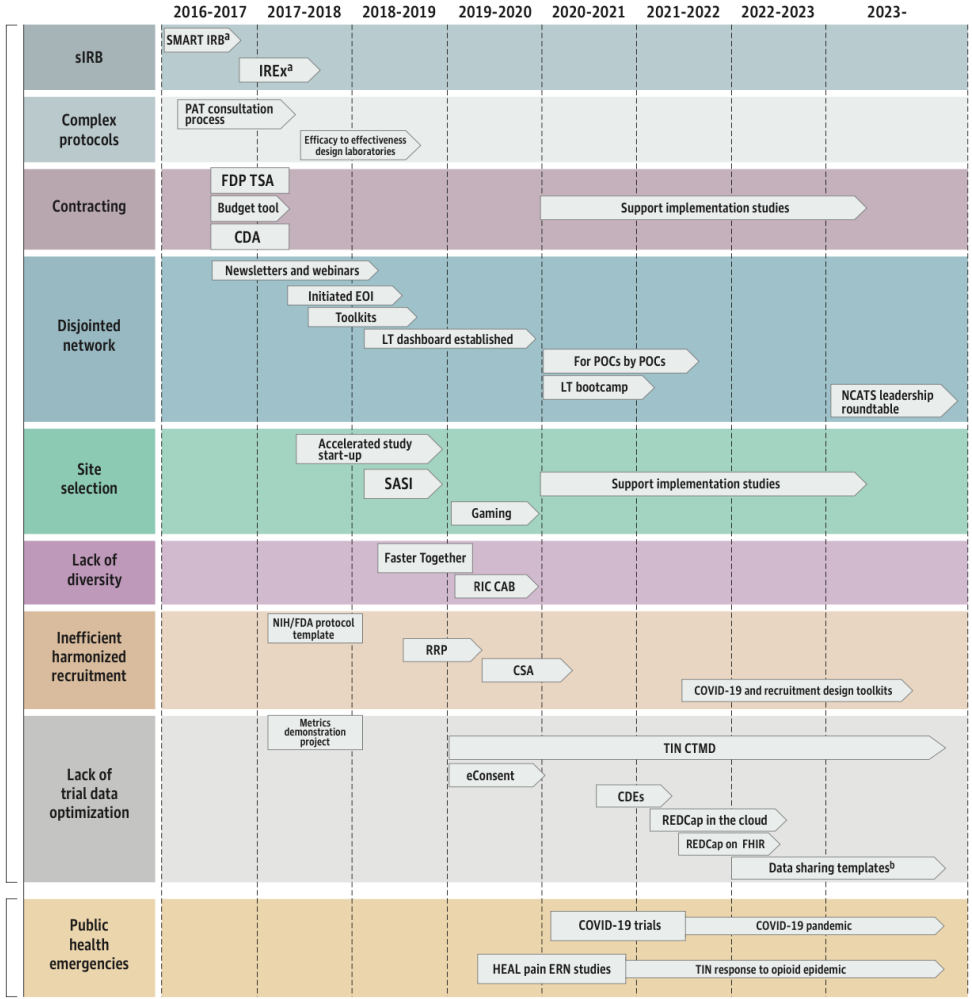
P. A. Harris, et al.
JAMA Netw Open
2023

- **CONCLUSIONS AND RELEVANCE:**
- The TIN has worked to reduce barriers to implementing mRCTs and to improve mRCT processes and operations by providing needed clinical trial infrastructure and resources to CTSA investigators.

Figure 3. Summary of Trial Innovation Network's Consultations and Provided Support



Trial Innovation Network's Response to Historical Operational Challenges and Emerging Landscape



CRI Methods/Approaches: Other notable papers

- **Characterizing variability of electronic health record-driven phenotype definitions.** Brandt PS, et al. J Am Med Inform Assoc. 2023;30(3):427-37.
- **Next-generation phenotyping: introducing phecodeX for enhanced discovery research in medical phenomics.** Shuey MM, et al. Bioinformatics. 2023;39(11).
- **Improving reporting standards for phenotyping algorithm in biomedical research: 5 fundamental dimensions.** Wei WQ, et al. J Am Med Inform Assoc. 2024.
- **Ontologizing health systems data at scale: making translational discovery a reality.** Callahan TJ, et al. NPJ Digit Med. 2023;6(1):89.

CRI Methods/Approaches: Other notable papers

- **Using A Standardized Nomenclature to Semantically Map Oncology-Related Concepts from Common Data Models to a Pediatric Cancer Data Model.** Carlson B, et al. AMIA Annu Symp Proc. 2023;2023:874-83.
- **Knowledgebase strategies to aid interpretation of clinical correlation research.** Stead WW, et al. J Am Med Inform Assoc. 2023;30(7):1257-65.
- **Decentralized research technology use in multicenter clinical research studies based at U.S. academic research centers.** Cummins MR, et al. J Clin Transl Sci. 2023;7(1):e250.
- **The Iowa Health Data Resource (IHDR): an innovative framework for transforming the clinical health data ecosystem.** Davis HA, et al. J Am Med Inform Assoc. 2024;31(3):720-6.

CRI Methods/Approaches: Other notable papers

- **Assessing clinical site readiness for electronic health record (EHR)-to-electronic data capture (EDC) automated data collection.** Eisenstein EL, et al. Contemp Clin Trials. 2023;128:107144.
- **Federated electronic data capture (fEDC): Architecture and prototype.** J Biomed Inform. Ganzinger M, et al. 2023;138:104280.
- **Not all phenotypes are created equal: covariates of success in e-phenotype specification.** Hamidi B, et al. J Am Med Inform Assoc. 2023;30(2):213-21.
- **Electronic health records (EHRs) in clinical research and platform trials: Application of the innovative EHR-based methods developed by EU-PEARL.** Lombardo G, et al. J Biomed Inform. 2023;148:104553.

CRI Methods/Approaches: Other notable papers

- **Automated Electronic Health Record to Electronic Data Capture Transfer in Clinical Studies in the German Health Care System: Feasibility Study and Gap Analysis.** Mueller C, et al. J Med Internet Res. 2023;25:e47958.
- **Leveraging retooled clinical research infrastructure for Clinical Research Management System implementation at a large Academic Medical Center.** Mullen CG, et al. J Clin Transl Sci. 2023;7(1):e127.
- **Decentralized clinical trials in the trial innovation network: Value, strategies, and lessons learned.** Hanley DF, et al. J Clin Transl Sci. 2023;7(1):e170.
- **Target Trial Emulation: A Design Tool for Cancer Clinical Trials.** JCO Clin Cancer Inform. Kwee SA, et al. 2023;7:e2200140.

CRI Methods/Approaches: Other notable papers

- **Identifying the capabilities for creating next-generation registries: a guide for data leaders and a case for "registry science".** Labkoff SE, et al. J Am Med Inform Assoc. 2024.
- **Cite-seeing and reviewing: A study on citation bias in peer review.** Stelmakh I, et al. PLoS One. 2023;18(7):e0283980.
- **Comparing Responses to COVID-19 Across Institutions: Conceptualization of an Emergency Response Maturity Model.** Senathirajah Y, et al. Stud Health Technol Inform. 2023;302:907-8.
- **Development of a social and environmental determinants of health informatics maturity model.** Espinoza JC, et al. J Clin Transl Sci. 2023;7(1):e266.

Participant Recruitment and Retention

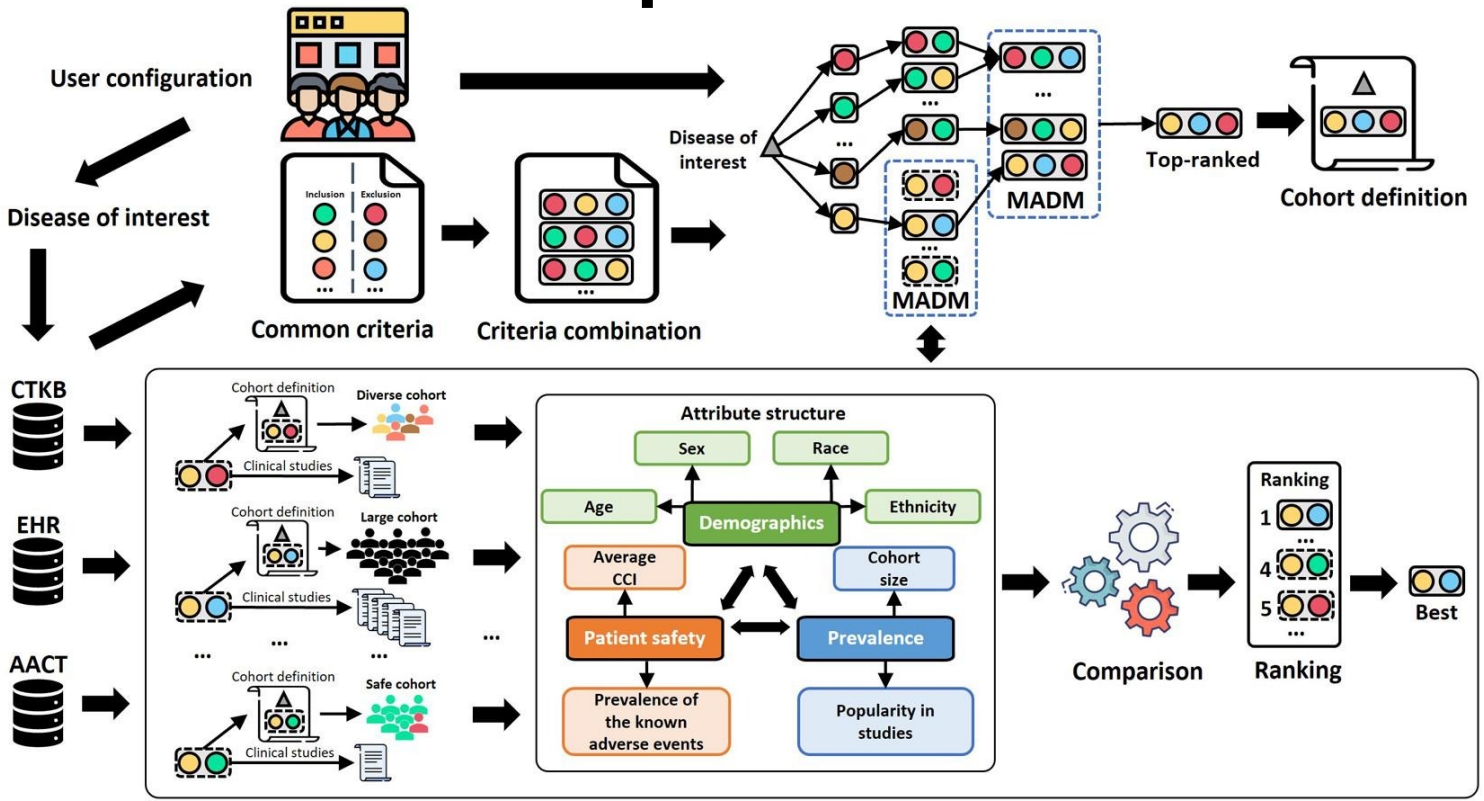
Fang Y, Liu H, Idnay B, Ta C, Marder K, Weng C. A data-driven approach to optimizing clinical study eligibility criteria. J Biomed Inform. 2023 Jun

- **Objective:** Existing expert-centered methods for eligibility criteria selection may not be representative of real-world populations. This paper presents a novel model called **OPTEC (OPTimal Eligibility Criteria)** based on the Multiple Attribute Decision Making method boosted by an efficient greedy algorithm.

- **Methods:** It systematically identifies the best criteria combination for a given medical condition with the optimal tradeoff among feasibility, patient safety, and cohort diversity.

- The model offers flexibility in attribute configurations and generalizability to various clinical domains. The model was evaluated on two clinical domains (i.e., Alzheimer's disease and Neoplasm of pancreas) using two datasets (i.e., MIMIC-III dataset and NewYork-Presbyterian/Columbia University Irving Medical Center (NYP/CUIMC) database).

Multiple Attribute Decision Making for Inclusion Criteria Optimization



This figure displays the process of selecting the top-ranked 3-criteria combination in the scenario that prioritizes the cohort size. Each colored circle represents a common eligibility criterion retrieved from CTKB. The grey triangle represents the initial event (i.e., the occurrence of the disease of interest). The attribute structure is also shown in the figure.

Fang Y, Liu H, Idnay B, Ta C, Marder K, Weng C. A data-driven approach to optimizing clinical study eligibility criteria. J Biomed Inform. 2023 Jun

- **Results:** Simulated process of optimizing eligibility criteria according to user-specified prioritization preferences and generated recommendations based on the top-ranked criteria combination accordingly with OPTEC.
- Also designed an interactive criteria recommendation system and conducted a case study with an experienced clinical researcher using the think-aloud protocol.
- **Conclusions:** The results demonstrated that OPTEC could be used to recommend feasible eligibility criteria combinations, and to provide actionable recommendations for clinical study designers to construct a feasible, safe, and diverse cohort definition during early study design.

CRI implication: Addresses an important need for clinical trial eligibility criteria selection and trial success

The RIC Recruitment & Retention Materials Toolkit - a resource for developing community-informed study materials

S. A. Mayers, et al. J Clin Transl Sci 2023

- Recruitment materials and messaging are key to successful recruitment
- These must be culturally tailored, and professional-looking.
- To address this, the Recruitment Innovation Center (RIC) developed a Recruitment & Retention Materials Content and Design Toolkit, which offers research teams guidance, actionable tips, resources, and customizable templates for creating trial-specific study materials.

- The toolkit is organized into four main sections:
  - Introduction
  - Content & Design
  - Templates
  - Tips & Tutorials

- Template Offerings include:

Table 2. Recruitment and retention materials template offerings

Material type	Recruitment & awareness-raising		Retention
Audience	Potential participants	Clinicians	Enrolled participants
Templates	• Brochures • Flyers • Posters • Study information sheet/consent aid • Flip chart/ presentation	• Flyers • Posters • Clinician study information sheet	• "Thank you" cards • Birthday cards • Holiday cards • "Thinking of you" cards • Newsletters

The RIC Recruitment & Retention Materials Toolkit - a resource for developing community-informed study materials

S. A. Mayers, et al. J Clin Transl Sci 2023

- All sections also contain: Notes, tips, and recommendations to help research teams create recruitment and retention materials, including guidance on content and design, engaging potential participants for feedback, and developing an appropriate budget; Community expert advice is also available
- A useful resource for the research community

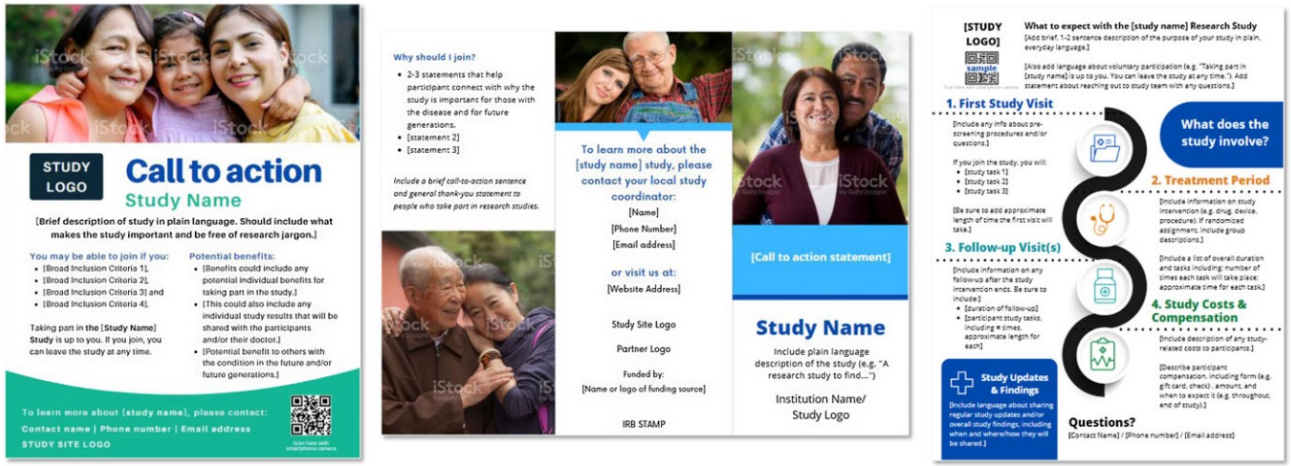


Figure 1. Example recruitment materials templates – flyer, brochure, and study information sheet.

Recruitment: Other notable papers

- **Direct-to-Consumer Recruitment Methods via Traditional and Social Media to Aid in Research Accrual for Clinical Trials for Rare Diseases: Comparative Analysis Study**. Applequist J, et al. J Med Internet Res. 2023;25:e39262.
- **Implementation of inclusion and exclusion criteria in clinical studies in OHDSI ATLAS software.** Blasini R, et al. Sci Rep. 2023;13(1):22457.
- **Development and utility of a clinical research informatics application for participant recruitment and workflow management for a return of results pilot trial in familial hypercholesterolemia in the Million Veteran Program.** Brunette CA, et al. JAMIA Open. 2024;7(1):ooae020.
- **Beyond Participation: Evaluating the Role of Patients in Designing Oncology Clinical Trials.** Farah E, et al. Curr Oncol. 2023;30(9):8310-27.

Recruitment: Other notable papers

- **Count Me In: an inclusive approach towards patient recruitment for clinical research studies in the NHS.** Hinze V, et al. BMJ Ment Health. 2023;26(1).
- **Uncovering key clinical trial features influencing recruitment**. Idnay B, et al. J Clin Transl Sci. 2023;7(1):e199.
- **Sociotechnical feasibility of natural language processing-driven tools in clinical trial eligibility prescreening for Alzheimer's disease and related dementias.** Idnay B, et al. J Am Med Inform Assoc. 2024.
- **Piloting an automated clinical trial eligibility surveillance and provider alert system based on artificial intelligence and standard data models.** Meystre SM, et al. BMC Med Res Methodol. 2023;23(1):88.

Recruitment:
Other notable papers

- **Undertaking Studies Within A Trial to evaluate recruitment and retention strategies for randomised controlled trials: lessons learnt from the PROMETHEUS research programme**. Parker A, et al. Health Technol Assess. 2024;28(2):1-114.

- **Improving Diversity in Clinical Trials by Using Real-world Data to Define Eligibility Criteria.** Royce TJ, et al. JAMA Oncol. 2023;9(4):455-6.

- **Enrollment of underrepresented racial and ethnic groups in the Rare and Atypical Diabetes Network (RADIANT).** Tosur M, et al. J Clin Transl Sci. 2023;7(1):e47.


AI and CRI

A Bibliometric Analysis of the Rise of ChatGPT in Medical Research. Med Sci (Basel).

Barrington NM, et al. 2023;11(3).

- Sudden increase in publications re: LLMs in Health. Performed analysis of ChatGPT literature in medicine and science.
- After screening, 267 articles were included in the study, most of which were editorials or correspondence with an average of 7.5 +/- 18.4 citations per publication.
- Published articles on ChatGPT were authored largely in the United States, India, and China.

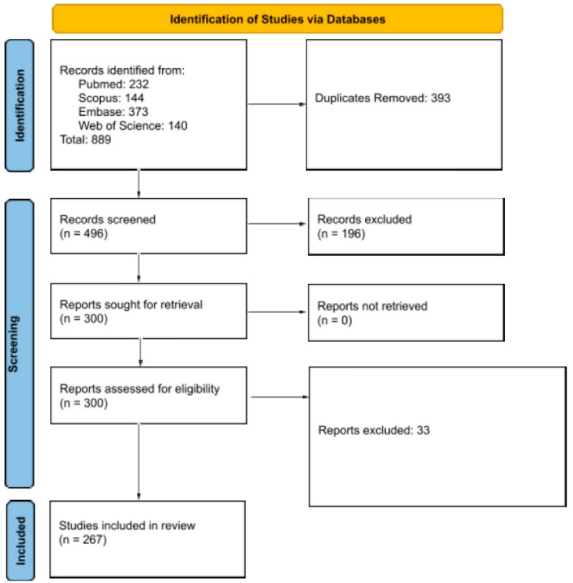


Figure 1. PRISMA diagram demonstrating screening strategy for inclu

A Bibliometric Analysis of the Rise of ChatGPT in Medical Research. Med Sci (Basel).
Barrington NM, et al. (Sep) 2023;11(3).

- The topics discussed included use and accuracy of ChatGPT in research, medical education, and patient counseling.
- Non-surgical specialties: radiology #1
  Surgical: plastic surgery #1

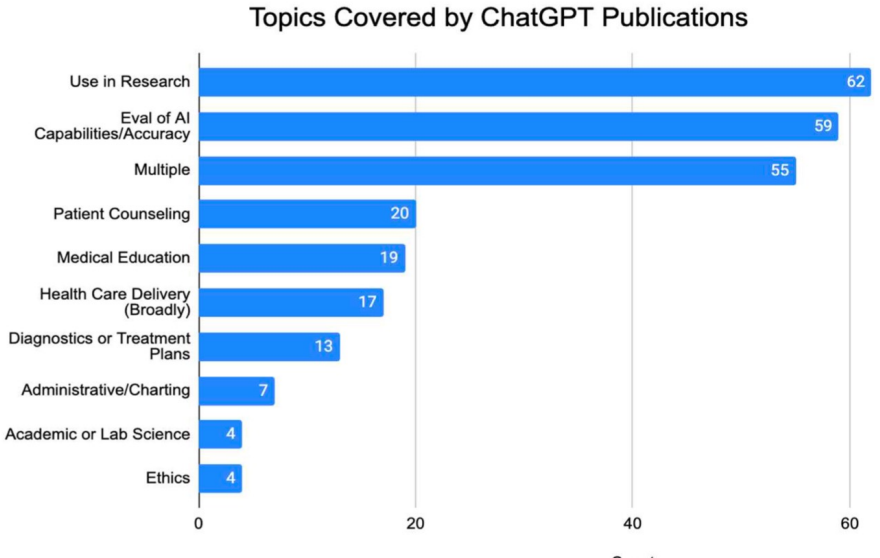


Table 1. Number of publications produced by surgical and non-surgical specialties.

Medical Specialty	Number of Publications
Non-Surgical	**N (%)**
Radiology	21 (25.3%)
Internal Medicine/Primary Care	10 (12.0%)
Oncology	6 (7.2%)
Gastroenterology	5 (6.02%)
Rheumatology	5 (6.02%)
Dermatology	4 (4.8%)
Emergency Medicine	4 (4.8%)
Endocrine	4 (4.8%)
Pediatrics	4 (4.8%)
Psychiatry	4 (4.8%)
Neurology	3 (3.6%)
Anesthesia	2 (2.4%)
Infectious Disease	2 (2.4%)
Pathology	2 (2.4%)
Pulmonology/Critical Care	2 (2.4%)
Cardio	1 (1.2%)
Fam Med	1 (1.2%)
Hepatology	1 (1.2%)
Sports Med	1 (1.2%)
Toxicology	1 (1.2%)
Surgical Specialties	**N (%)**
Plastic Surgery	18 (26.9%)
General Surgery	15 (22.4%)
Orthopedic Surgery	7 (10.4%)
Ophthalmology	6 (9.0%)
Obstetrics and Gynecology	5 (7.5%)
Neurosurgery	4 (6.0%)
Otolaryngology	4 (6.0%)
Oral and Maxillofacial Surgery	2 (3.0%)
Surgical Oncology	2 (3.0%)
Urology	2 (3.0%)
Bariatric Surgery	1 (1.5%)
Colorectal Surgery	1

A Bibliometric Analysis of the Rise of ChatGPT in Medical Research. Med Sci (Basel). Barrington NM, et al. 2023;11(3).

- The average citation number among the top 20 most-cited articles was 60.1 +/- 35.3.
- Among journals with the most ChatGPT-related publications, there were on average 10 +/- 3.7 publications.
- Just the start, and many since performed. Tracking trends as matures will be of interest.

Table 2. Top 20 most-cited publications regarding the use of ChatGPT in medicine.

Rank	Article Name	Number of Citations	Journal of Article
1	How Does ChatGPT Perform on the United States Medical Licensing Examination? The Implications of Large Language Models for Medical Education and Knowledge Assessment.	147	*JMIR Medical Education*
2	A Conversation on Artificial Intelligence, Chatbots, and Plagiarism in Higher Education	119	*Cellular and Molecular Bioengineering*
3	Artificial Hallucinations in ChatGPT: Implications in Scientific Writing	118	*Cureus Journal of Medical Science*
4	ChatGPT: the future of discharge summaries?	94	*The Lancet Digital Health*
5	Can artificial intelligence help for scientific writing?	87	*Critical Care*
6	Evaluating the Feasibility of ChatGPT in Healthcare: An Analysis of Multiple Clinical and Research Scenarios.	68	*Journal of Medical Systems*
7	Role of Chat GPT in Public Health	61	*Annals of Biomedical Engineering*
8	ChatGPT: evolution or revolution?	57	*Medicine, Health Care, and Philosophy*
9	Generating scholarly content with ChatGPT: ethical challenges for medical publishing	56	*The Lancet Digital Health*
10	ChatGPT—Reshaping medical education and clinical management.	51	*Pakistan Journal of Medical Sciences*
11	The future of medical education and research: Is ChatGPT a blessing or blight in disguise?	48	*Medical Education Online*
12	Can ChatGPT draft a research article? An example of population-level vaccine effectiveness analysis.	45	*Journal of Global Health*
13	Comparing Physician and Artificial Intelligence Chatbot Responses to Patient Questions Posted to a Public Social Media Forum.	41	*JAMA Internal Medicine*
14	ChatGPT and other artificial intelligence applications speed up scientific writing.	37	*Journal of the Chinese Medical Association*
15	Revolutionizing radiology with GPT-based models: Current applications, future possibilities and limitations of ChatGPT.	32	*Diagnostic and Interventional Imaging*
16	Using ChatGPT to write patient clinic letters.	32	*The Lancet Digital Health*
17	Artificial intelligence bot ChatGPT in medical research: the potential game changer as a double-edged sword.	29	*Knee Surgery, Sports Traumatology, Arthroscopy*
18	ChatGPT and antimicrobial advice: the end of the consulting infection doctor?	28	*The Lancet Infectious Diseases*
19	To ChatGPT or not to ChatGPT? The Impact of Artificial Intelligence on Academic Publishing	26	*The Pediatric Infectious Disease Journal*
20	Assessing the performance of ChatGPT in answering questions regarding cirrhosis and hepatocellular carcinoma.	25	*Clinical and Molecular Hepatology*

Leveraging generative AI to prioritize drug repurposing candidates for Alzheimer's disease with real-world clinical validation.
Yan C, et al. NPJ Digit Med. 2024;7(1):46.

- Drug repurposing represents an attractive alternative to the costly and time-consuming process of new drug development, particularly for serious, widespread conditions with limited effective treatments, such as Alzheimer's disease (AD).
- Emerging generative artificial intelligence (GAI) technologies like ChatGPT offer the promise of expediting the review and summary of scientific knowledge.
- To examine the feasibility of using GAI for identifying drug repurposing candidates, we iteratively tasked ChatGPT with proposing the twenty most promising drugs for repurposing in AD and tested the top ten for risk of incident AD in exposed and unexposed individuals over age 65 in two large clinical datasets:
  - (1) Vanderbilt University Medical Center
  - (2) All of Us Research Program.
- Among the candidates suggested by ChatGPT, metformin, simvastatin, and losartan were associated with lower AD risk in meta-analysis.
- These findings suggest GAI technologies can assimilate scientific insights from an extensive Internet-based search space, helping to prioritize drug repurposing candidates and facilitate the treatment of diseases.

Leveraging generative AI to prioritize drug repurposing candidates for Alzheimer's disease with real-world clinical validation.
Yan C, et al. NPJ Digit Med. 2024;7(1):46.

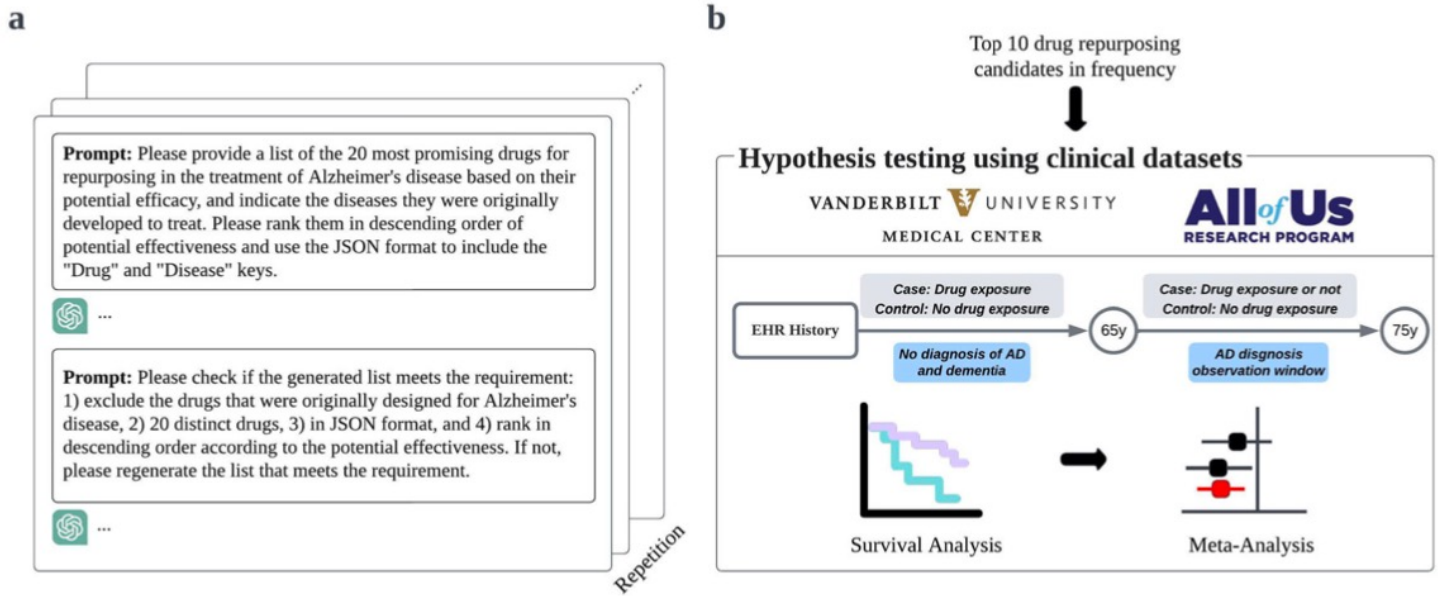


Fig. 1 | An illustration of the study design. a Employing iterative queries of ChatGPT to recommend twenty drugs for AD repurposing. **b** Evaluating the potential efficacy of the ten most frequently suggested drugs using electronic health records (EHR) data from two large clinical databases.

Reporting Use of AI in Research and Scholarly Publication- JAMA Network Guidance.

Flanagin A, et al. JAMA. 2024.

- JAMA network provides guidance for reporting use of AI in manuscript prep or research.
- **AI Used in Manuscript Preparation**
  - When traditional and generative AI technologies are used to create, review, revise, or edit any of the content in a manuscript, authors should report in the Acknowledgment section the following:
  - Name of the AI software platform, program, or tool
  - Version and extension numbers
  - Manufacturer
  - Date(s) of use
  - A brief description of how the AI was used and on what portions of the manuscript or content
  - Confirmation that the author(s) takes responsibility for the integrity of the content generated
  - Note that this guidance does not apply to basic tools for checking grammar, spelling, references, and similar.

Reporting Use of AI in Research and JAMA Network Guidance.

Flanagin A, et al. JAMA. 2024.

- **AI Used in Research**
- "Follow relevant reporting guidelines for specific study designs when they exist (see examples in the Box)…"
- "Avoid inclusion of identifiable patient information in text, tables, and figures."
- "Be aware of copyright and intellectual property concerns if including content (text, images) generated by AI, and indicate rights or permissions to publish that content as determined by the AI service or owner."
- More guidance related to:
  - Methods, Results and Discussion Sections
- **CRI Message:** As we use/guide others, keeping track of these evolving policies is important

Box. Examples of AI-Related Reporting Guidelines

CONSORT-AI for clinical trial reports evaluating interventions with an AI component[15]

SPIRIT-AI for clinical trial protocols evaluating interventions with an AI component[16]

MI-CLAIM for studies including clinical AI modeling[17]

CLAIM for studies describing applications of AI in medical imaging[18]

MINIMAR (MINimumInformation for Medical AIReporting) for studies of AI in health care[19]

DECIDE-AI for studies describing the early-stage live clinical evaluation of AI-based decision support systems[20]

Recommendations for Reporting Machine Learning Analyses in Clinical Research for studies of machine learning analyses[21]

Other AI reporting extensions and guidelines (under development):

STARD-AI for AI-centered diagnostic test accuracy studies[22]

TRIPOD-AI for prediction model studies based on machine learning techniques[23]

PROBAST-AI for risk of bias assessment of machine learning–based prediction model studies[23]

CANGARU for ethical use, disclosure, and reporting of AI in scholarly publication[24]

CHART for studies assessing use of chatbots and LLMs for health information[25]

AI and CRI:
Other notable papers

- **DECIDE-AI: a new reporting guideline and its relevance to artificial intelligence studies in radiology.** Vasey B, et al. Clin Radiol. 2023;78(2):130-6.

- **Reporting and Methodological Observations on Prognostic and Diagnostic Machine Learning Studies.** El Emam K, et al. Jmir Ai. 2023;2.

- **Human-Centered Design to Address Biases in Artificial Intelligence.** Chen Y, et al. J Med Internet Res. 2023;25:e43251.

- **The role of patient-reported outcome measures in trials of artificial intelligence health technologies: a systematic evaluation of ClinicalTrials.gov records (1997-2022).** Pearce FJ, et al. Lancet Digit Health. 2023;5(3):e160-e7.

AI and CRI:
Other notable papers

- **How Academic Medical Centers Govern AI Prediction Tools in the Context of Uncertainty and Evolving Regulation**. Nong P, et al. Nejm Ai. 2024;1(3).
- **Towards a framework for interoperability and reproducibility of predictive models.** Rahrooh A, et al. J Biomed Inform. 2024;149:104551.
- **Foundation models for generalist medical artificial intelligence.** Moor M, et al. Nature. 2023;616(7956):259-65.
- **Entwistle D, Pfeffer MA. Creation and Adoption of Large Language Models in Medicine.** Shah NH, et al. Jama. 2023;330(9):866-9.

AI and CRI:
Other notable papers

- **Sustainable deployment of clinical prediction tools-a 360 degrees approach to model maintenance.** Davis SE, et al. J Am Med Inform Assoc. 2024.

- **How AI is being used to accelerate clinical trials**. Hutson M. Nature. 2024;627(8003):S2-S5.

- **A Nationwide Network of Health AI Assurance Laboratories.** Shah NH, et al. Jama. 2024;331(3):245-9.

- **Organizational Factors in Clinical Data Sharing for Artificial Intelligence in Health Care.** Youssef A, et al. JAMA Netw Open. 2023;6(12):e2348422.

Learning Health Systems and Informatics-enabled Pragmatic Trials

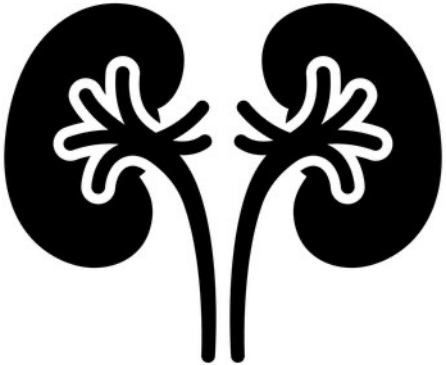
Cefepime vs Piperacillin-Tazobactam in Adults Hospitalized With Acute Infection: The ACORN Randomized Clinical Trial

Qian ET, et al. JAMA 2023

- **Importance** Cefepime and piperacillin-tazobactam are commonly administered to hospitalized adults for empirical treatment of infection. Each hypothesized to cause injury, and widespread recommendation was to select one over other… but safety never compared to other.
- **Objective** To determine whether the choice between cefepime and piperacillin-tazobactam affects the risks of acute kidney injury or neurological dysfunction.
- **Design, Setting, and Participants** The Antibiotic Choice on Renal Outcomes (ACORN) randomized clinical trial
- Compared cefepime vs piperacillin-tazobactam in adults for whom a clinician initiated an order for antipseudomonal antibiotics within 12 hours of presentation to the hospital in the emergency department or medical intensive care unit between November 10, 2021, and October 7, 2022. The final date of follow-up was November 4, 2022.
- **Interventions** Patients were randomized in a 1:1 ratio to cefepime or piperacillin-tazobactam.

Next step: individual patient randomization

Piperacillin-Tazobactam (Zosyn)



Kidney injury?

Cefepime (Maxipime)

Neurotoxicity?

Low quality studies

New: comparative safety trial

Next step: individual patient randomization

Piperacillin-Tazobactam (Zosyn)

Cefepime (Maxipime)

FDA Black Box Warning

5.5 Nephrotoxicity in Critically Ill Patients

The use of ZOSYN was found to be an independent risk factor for renal failure and was associated with delayed recovery of renal function as compared to other beta-lactam antibacterial drugs in a randomized, multicenter, controlled trial in critically ill patients [*see Adverse Reactions (6.1)*]. Based on this study, alternative treatment options should be considered in the critically ill population. If alternative treatment options are inadequate or unavailable, monitor renal function during treatment with ZOSYN [*see Dosage and Administration (2.3)*].

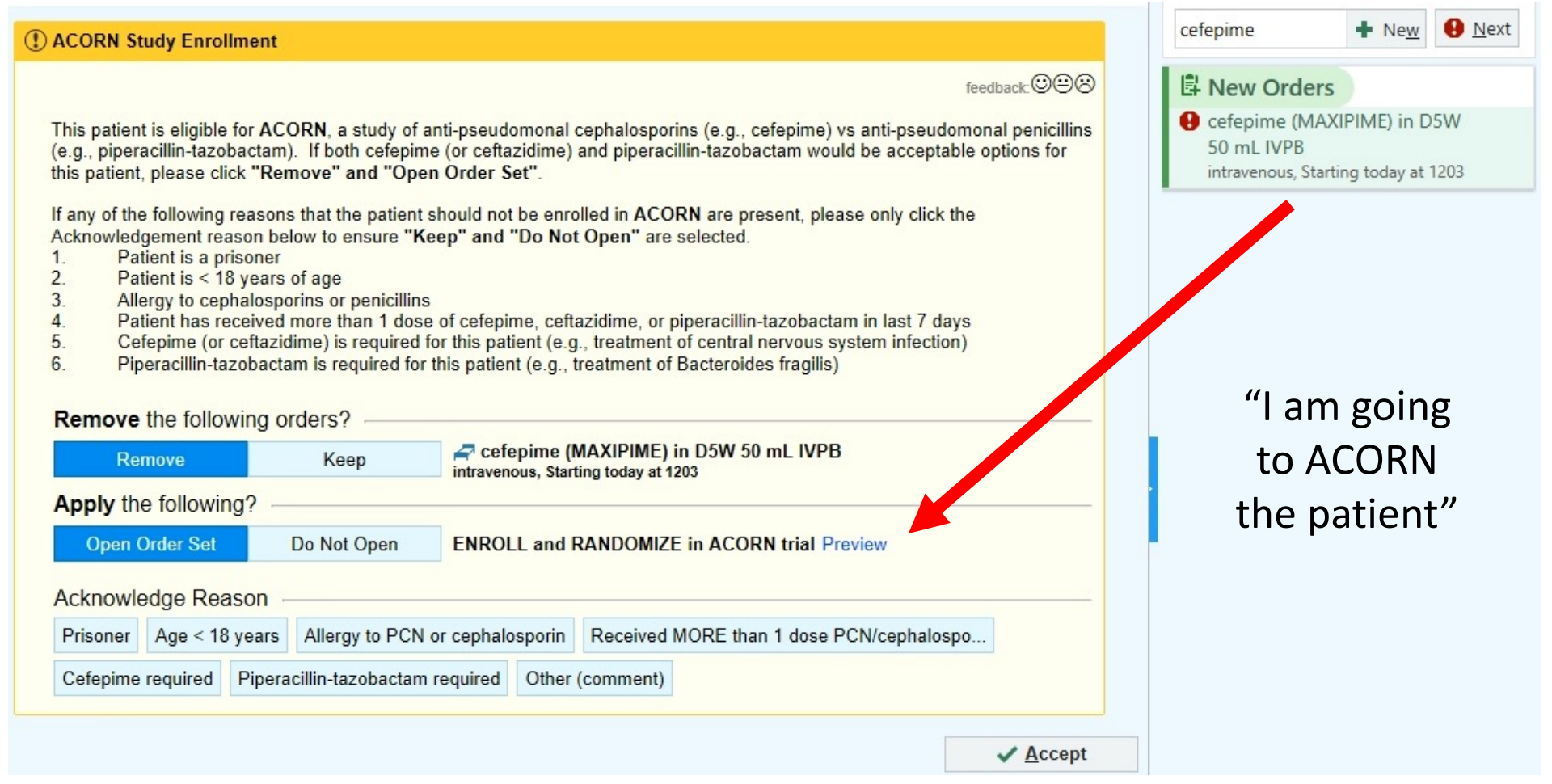
Kidney injury?

Neurotoxicity?

Low quality studies

New: *comparative safety trial*

EHR-embedded randomized trial



"I am going to ACORN the patient"

Vanderbilt ED and MICU patients

- Clinician ordered either cefepime or Zosyn and agreed to randomization

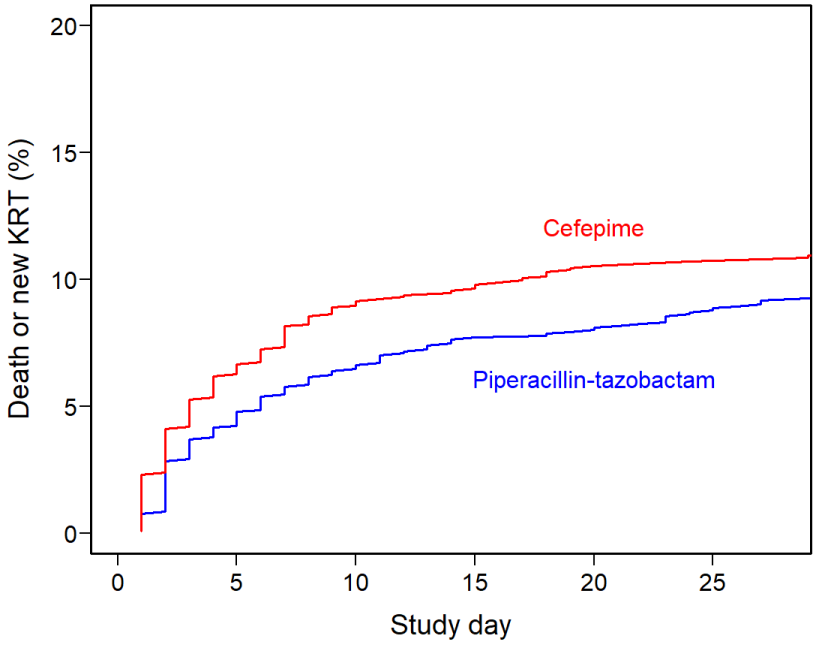
- Nov 10, 2021 – Oct 7, 2022

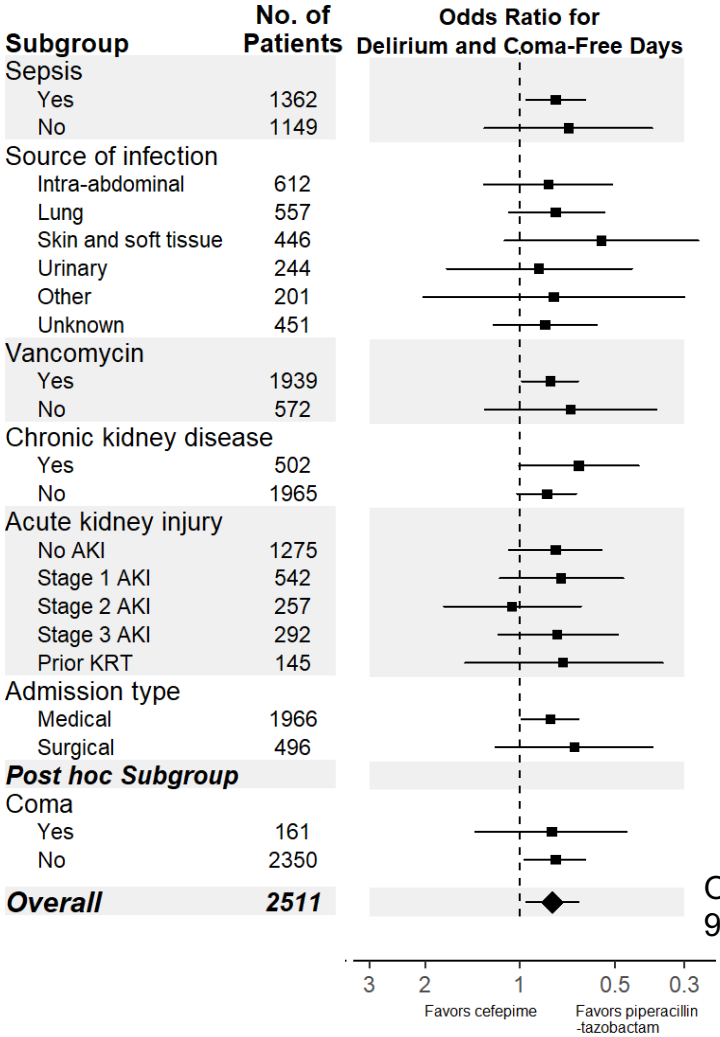
  [11 months]

- N = 2,511

Primary Results

No difference between groups for any kidney outcome.
Cefepime group with more delirium/coma.





OR: 0.79;
95%CI: 0.65, 0.95

EDITORIAL

JAMA Published online October 14, 2023

Acute Kidney Injury With Empirical Antibiotics for Sepsis

Steven Y. C. Tong, PhD; Balasubramanian Venkatesh, MD; Erin K. McCreary, PharmD

On the Results:
"This trial provides *the highest quality evidence to date* to show there is no difference in the incidence of AKI between use of piperacillin-tazobactam and vancomycin vs cefepime and vancomycin."

On the Methods:
". . . provides *a roadmap for embedded randomized clinical trials*. The current study could be replicated using almost identical processes at multiple hospitals."

NEJM Journal Watch

OCTOBER 17TH, 2023

A Brilliant Strategy for Conducting Clinical Trials — The ACORN Study

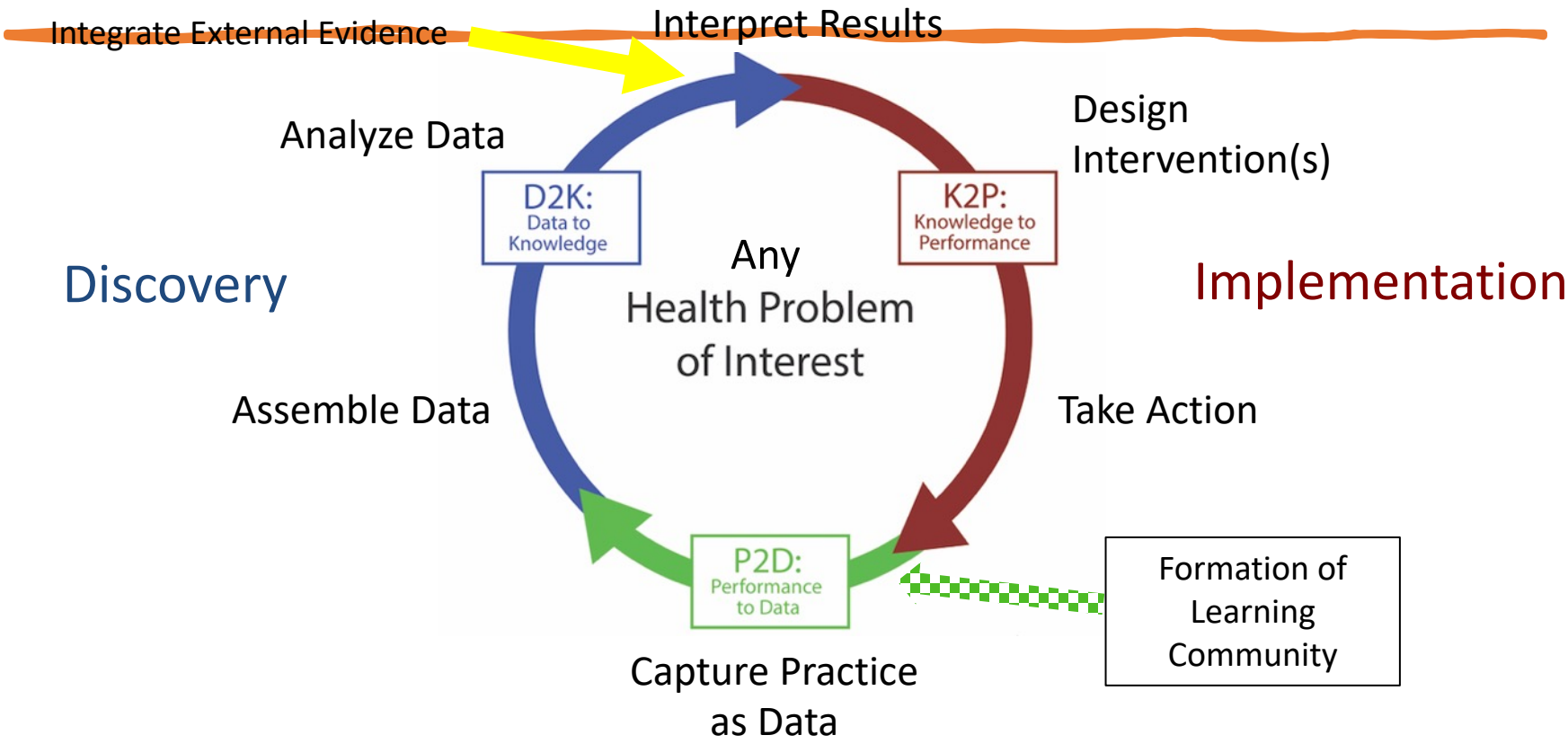
Hey Bing AI, make a cartoon battle between cefepime and pip-tazo.

Paul E. Sax, MD

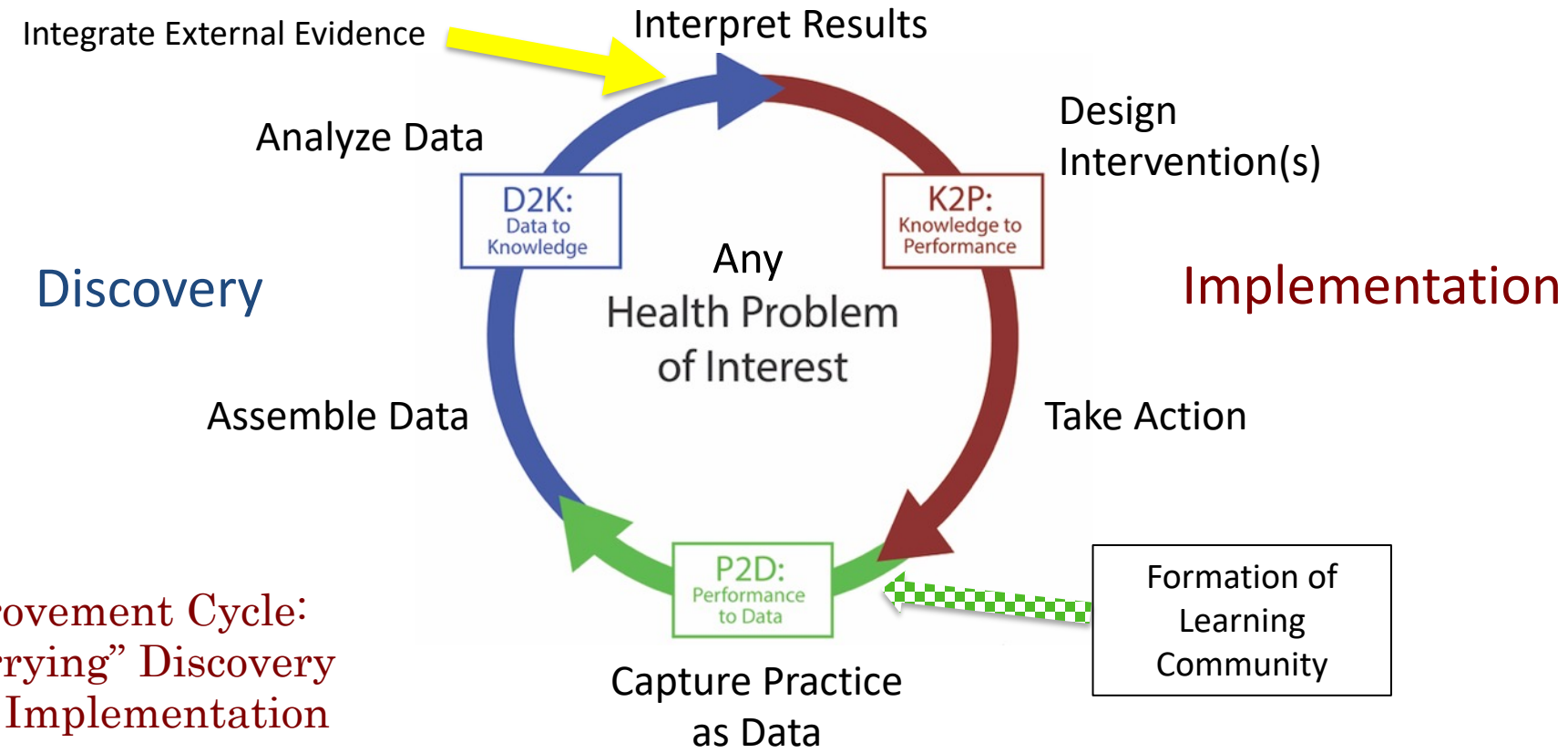
Contributing Editor

NEJM JOURNAL WATCH INFECTIOUS DISEASES

Socio-technical infrastructure for a learning health system.
Friedman CP, et al. Learn Health Syst. 2024;8(1):e10405.

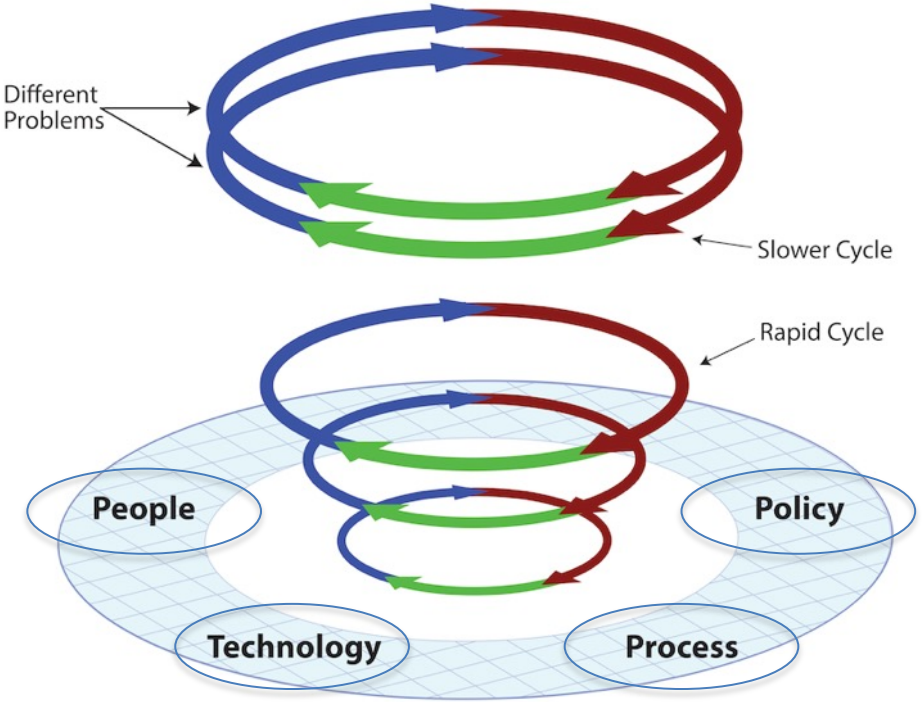


Socio-technical infrastructure for a learning health system.
Friedman CP, et al. Learn Health Syst. 2024;8(1):e10405.

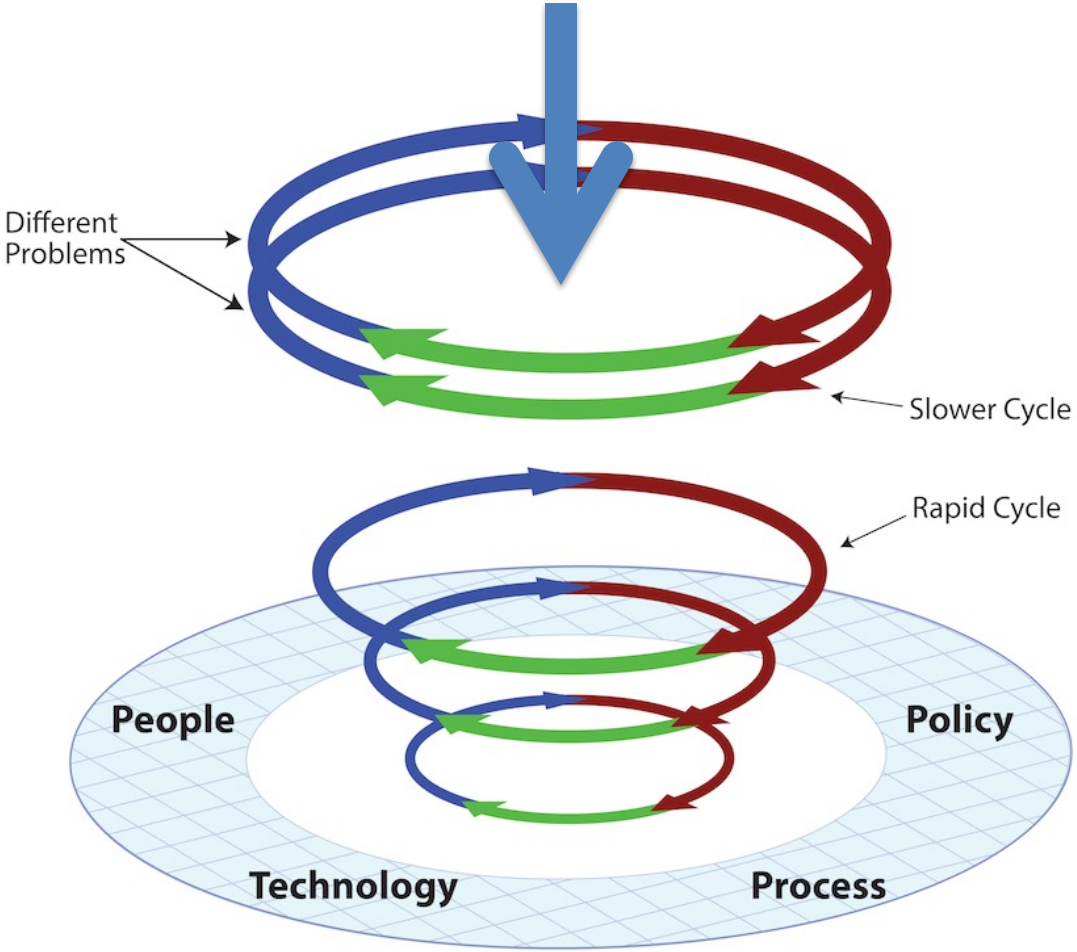


Improvement Cycle: "Marrying" Discovery with Implementation

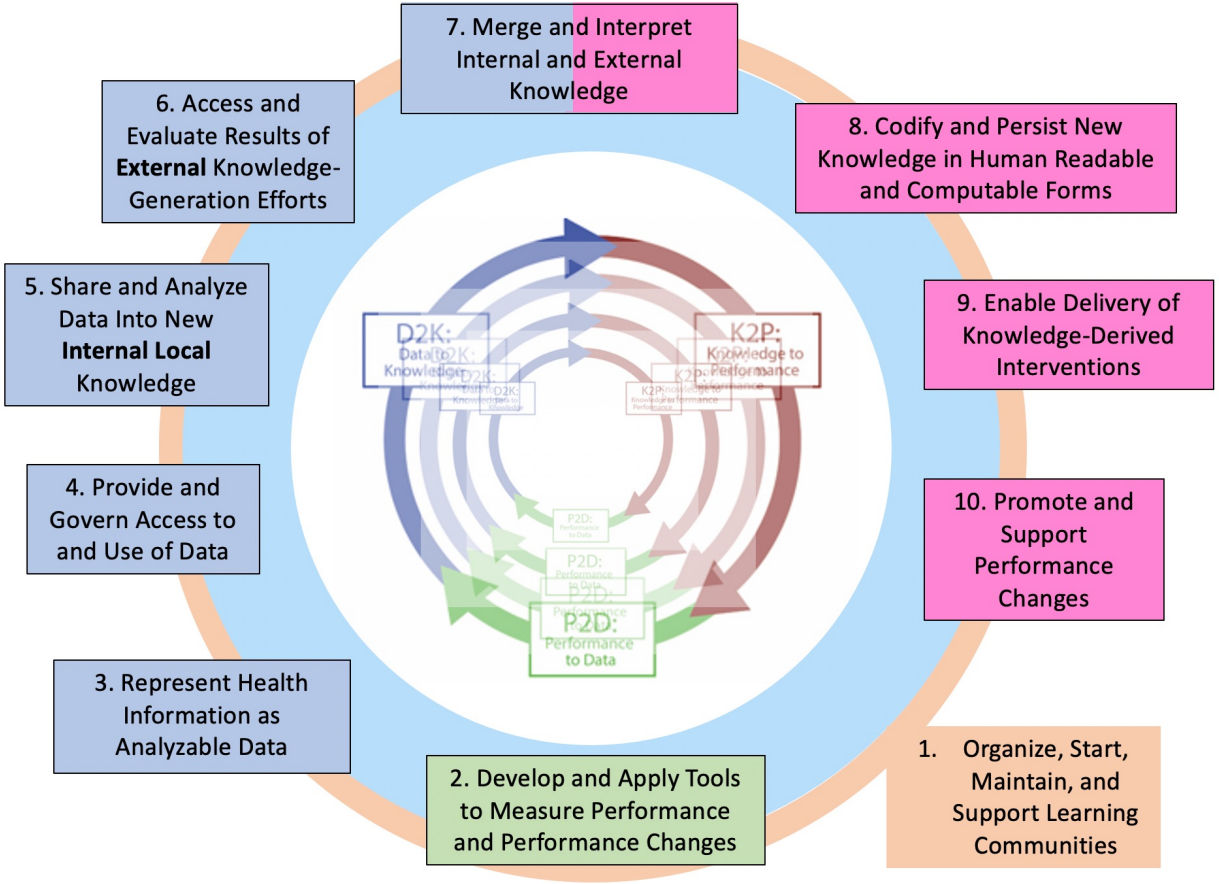
The Infrastructure is Socio-technical



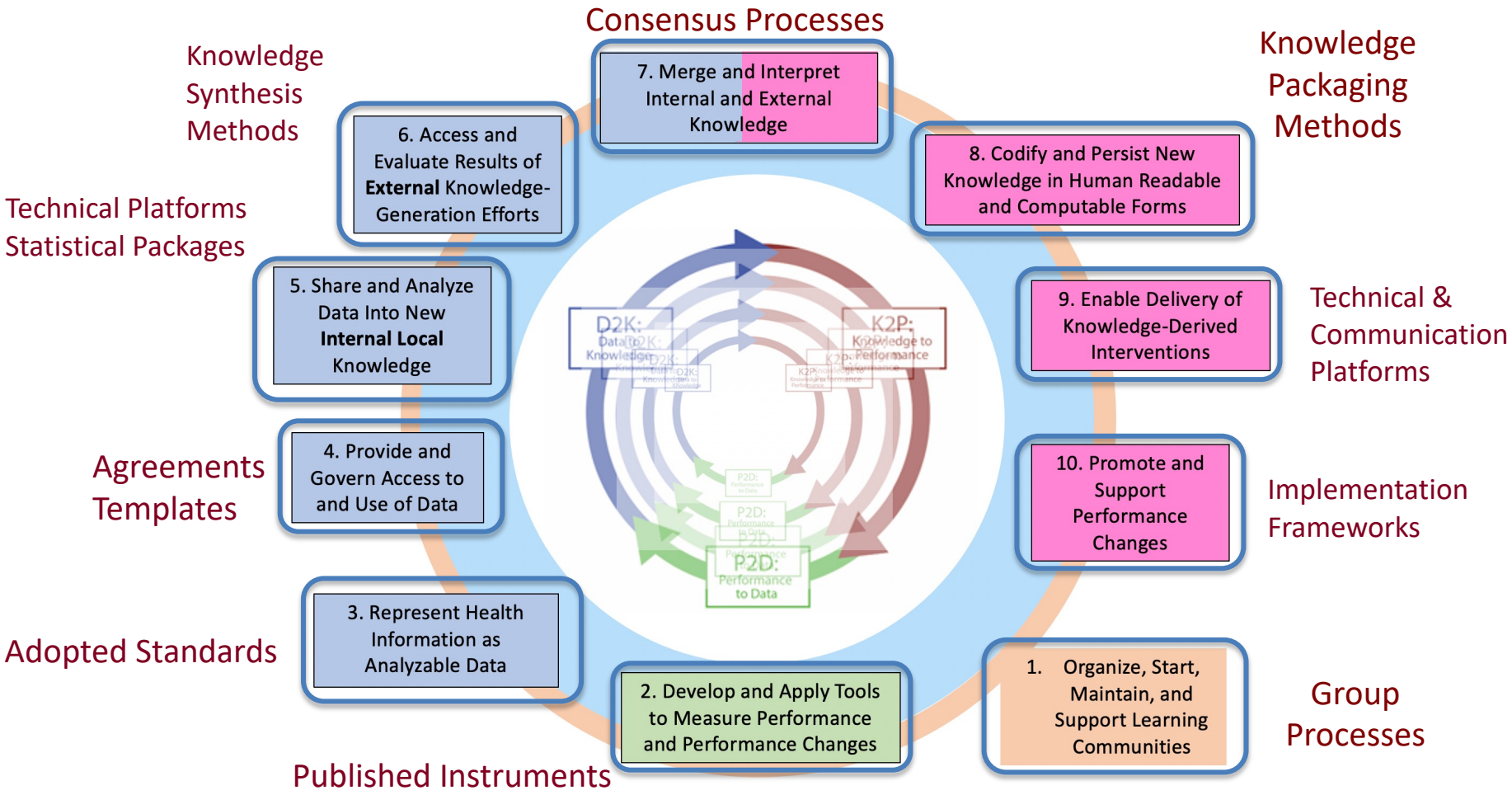
Look Down into the "Tornado"



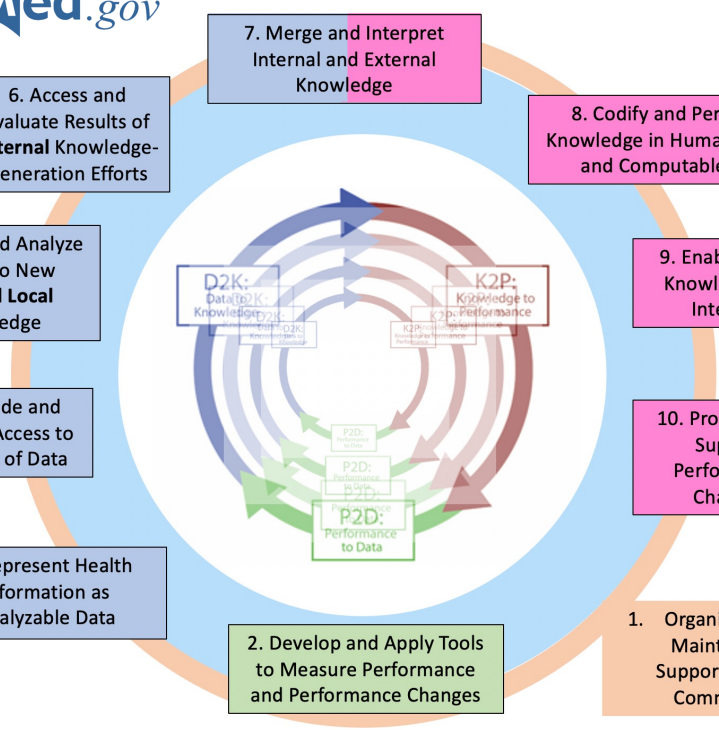
Ten Socio-Technical Infrastructure Services



What Each Service Provides



Many (Open) Infrastructure Components Exist!



1. Organize, Start, Maintain, and Support Learning Communities
2. Develop and Apply Tools to Measure Performance and Performance Changes
3. Represent Health Information as Analyzable Data
4. Provide and Govern Access to and Use of Data
5. Share and Analyze Data Into New **Internal Local** Knowledge
6. Access and Evaluate Results of **External** Knowledge-Generation Efforts
7. Merge and Interpret Internal and External Knowledge
8. Codify and Persist New Knowledge in Human Readable and Computable Forms
9. Enable Delivery of Knowledge-Derived Interventions
10. Promote and Support Performance Changes

THE COMMONS Social Change Library

COMPUTABLE PUBLISHING

PubMed.gov

R

OHDSI Observational Health Data Sciences and Informatics

i2b2

PopMedNet

emerse

Knowledge Grid

TRANSFoRm

SMART IRB

pcornet

RE-AIM: Reach • Effectiveness • Adoption • Implementation • Maintenance

OPERATIONALIZING A LEARNING COMMUNITY FOR A LEARNING HEALTH SYSTEM: A Practical Guide

HL7® FHIR®

SNOMED International

ICHOM

Deliberative Dialogue

Learning Health Systems and PCTs: Other notable papers

- **Higher-Dose Fluvoxamine and Time to Sustained Recovery in Outpatients With COVID-19: The ACTIV-6 Randomized Clinical Trial.** Stewart TG, et al. JAMA. 2023;330(24):2354-63.
- **Progressing from "Whether to" to "How to" Conduct Pragmatic Trials.** Casey JD, et al. Am J Bioeth. 2023;23(8):33-6.
- **Post-trial responsibilities in pragmatic clinical trials: Fulfilling the promise of research to drive real-world change.** Morain SR, et al. Learning Health Systems. 2024.
- **Factors Affecting Post-trial Sustainment or De-implementation of Study Interventions: A Narrative Review.** Green T, et al. J Gen Intern Med. 2024.
- **Gathering speed and countering tensions in the rapid learning health system. Reid RJ, Greene SM.** Learn Health Syst. 2023;7(3):e10358.


CRI Ethics & Policy

Policy Preferences Regarding Health Data Sharing Among Patients With Cancer: Public Deliberations.

Raj M, et al. JMIR Cancer. 2023;9:e39631.

- OBJECTIVE: Aimed to understand the policy preferences of current and former patients with cancer regarding the sharing of health information
- METHODS: 2 public deliberations, including pre-deliberation and post-deliberation surveys, with patients who had a current or former cancer diagnosis (n=61).
- Following informational presentations, the participants engaged in facilitated small-group deliberations to discuss and rank policy preferences related to health information sharing, such as:
  - Use of patient portal, email or SMS text messaging,
  - Signage in health care settings,
  - Opting out of commercial data sharing, payment, and preservation of the status quo.

Figure 1. Scenario A policy options.

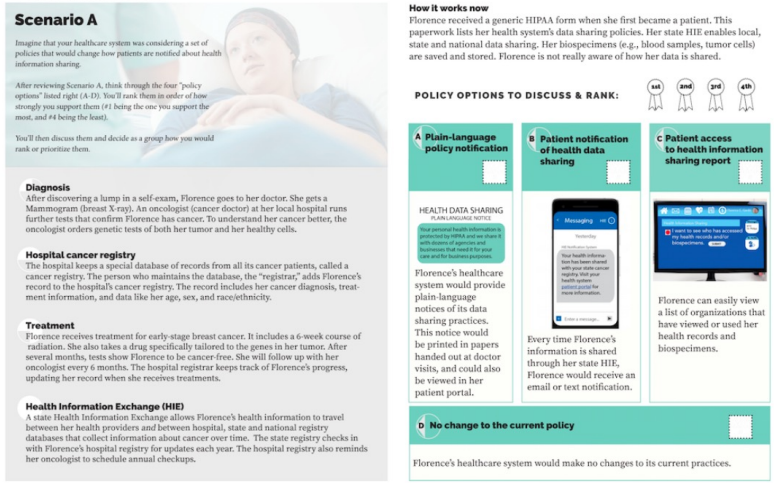
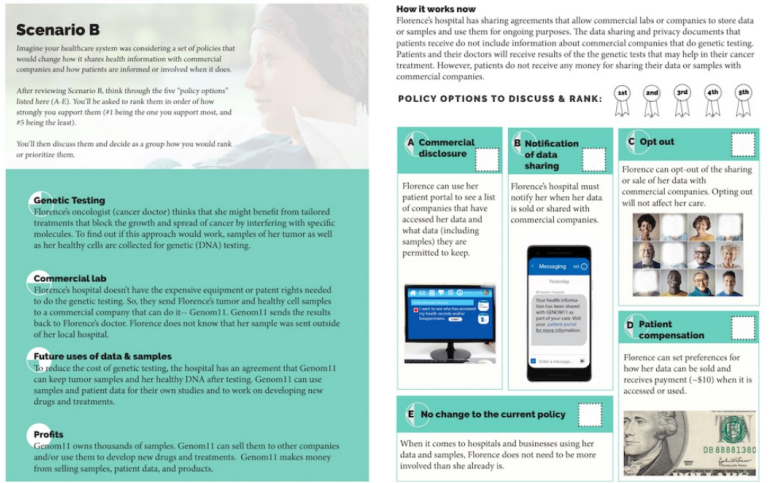


Figure 2. Scenario B policy options.



Policy Preferences Regarding Health Data Sharing Among Patients With Cancer: Public Deliberations.

Raj M, et al. JMIR Cancer. 2023;9:e39631.

- RESULTS: Patient portal was ranked as the most preferred policy choice.
- Participants expressed concerns about transparency and awareness, convenience, and accessibility of information about health data sharing.
- Specifically, the patients were not aware of how, when, or why their data were being used and wanted more transparency in these regards as well as greater control and autonomy around the use of their health data.
- The deliberations suggested that patient portals would be a good place to provide additional information about data sharing practices but that over time, notifications should be tailored to patient preferences.
- CONCLUSIONS: Apparent need for better disclosure of health information sharing practices. Describing health data sharing practices through patient portals or other mechanisms personalized to patient preferences would minimize the concerns expressed by patients about the extent of data sharing that occurs without their knowledge.
- Future research and policies should identify ways to increase patient control over health data sharing without reducing the societal benefits of data sharing.

Public perspectives on the use of different data types for prediction in healthcare.

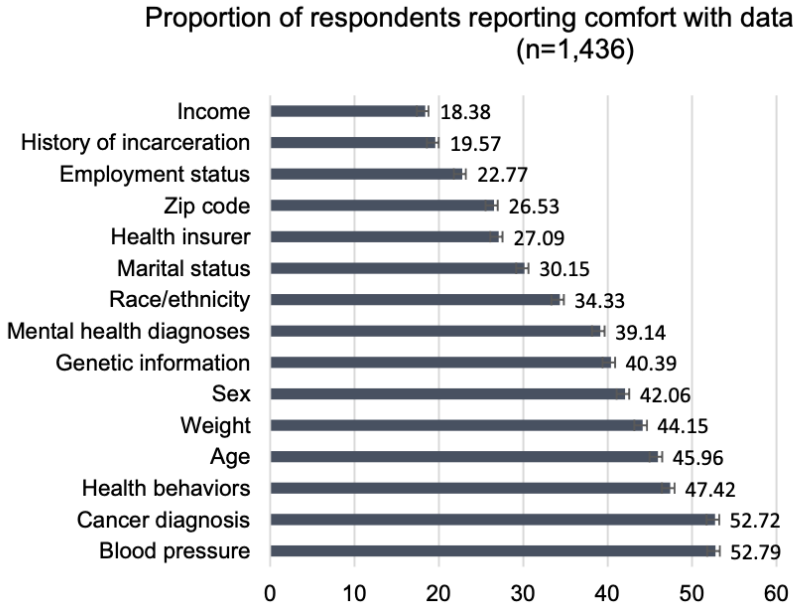
Nong P, et al. J Am Med Inform Assoc. 2024.

- OBJECTIVE: Understand public comfort with the use of different data types for predictive models.
- MATERIALS AND METHODS: They conducted and analyzed data from a national survey of US adults (n = 1436) fielded from November to December 2021.
- For three categories of data (identified using factor analysis), they used descriptive statistics to capture comfort level.

Public perspectives on the use of different data types for prediction in healthcare.

Nong P, et al. J Am Med Inform Assoc. 2024.

- RESULTS: Public comfort with data use for prediction is low.
- For 13 of 15 data types, most respondents were uncomfortable with that data being used for prediction. In factor analysis, 15 types of data grouped into three categories based on public comfort:
  - (1) personal characteristic data,
  - (2) health-related data, and
  - (3) sensitive data.
- Mean comfort was highest for health-related data (2.45, SD 0.84, range 1-4), followed by personal characteristic data (2.36, SD 0.94), and sensitive data (1.88, SD 0.77).
- There was a statistically significant positive relationship between trust in health systems' use of patient information and comfort with data use for prediction.
- DISCUSSION: Although public trust is recognized as important for the sustainable expansion of predictive tools, current policy does not reflect public concerns. Low comfort with data use for prediction should be addressed in order to prevent potential negative impacts on trust in healthcare.
- CONCLUSION: Findings demonstrate a need for realignment of policy around the sensitivity of non-clinical data categories.



CRI Ethics & Policy:
Other notable papers

- **The Limits of Clinician Vigilance as an AI Safety Bulwark.** Adler-Milstein J, et al. JAMA. 2024.
- **The impact of commercial health datasets on medical research and health-care algorithms.** Alberto IRI, et al. Lancet Digit Health. 2023;5(5):e288-e94.
- **Harnessing the Promise of Artificial Intelligence Responsibly**. Dorr DA, et al. Jama. 2023;329(16):1347-8.
- **Digital health interventions for all? Examining inclusivity across all stages of the digital health intervention research process.** Krukowski RA, et al. Trials. 2024;25(1):98.
- **Moving From Idealism to Realism With Data Sharing.** Marsolo KA, et al. Ann Intern Med. 2023;176(3):402-3.

CRI Ethics & Policy:
Other notable papers

- **President Biden's Executive Order on Artificial Intelligence-Implications for Health Care Organizations.** Mello MM, et al. Jama. 2024;331(1):17-8.
- **Think Pragmatically: Investigators' Obligations to Patient-Subjects When Research is Embedded in Care.** Morain S, et al. Am J Bioeth. 2023;23(8):10-21.
- **"I Want to Know Everything ... ": The Return of Research Results and the Importance of Transparency in the Acceptability of Lumbar Punctures for African American Older Adults.** Passmore SR, et al. J Alzheimers Dis. 2023;95(2):663-75.
- **A Privacy Nihilist's Perspective on Clinical Data Sharing: Open Clinical Data Sharing is Dead, Long Live the Walled Garden**. Starren J, et al. Journal of the Society for Clinical Data Management. 2023;3(3).
- **Fifty Years of Trust Research in Health Care: A Synthetic Review**. Taylor LA, et al. Milbank Q. 2023;101(1):126-78.

Notable CRI News/Events

New CMS Data Rule

- https://www.cms.gov/data-research/files-order/data-disclosures-and-data-use-agreements-duas/important-research-data-request-access-policy-changes-0
- Released Feb 12, 2024
- Updated Mar 1, 2024
- Two major changes:
  - Starting in August – new projects must access data through CMS cloud environment, with costs per "seat"
  - New high fees to continue using data stored outside their cloud infrastructure.
- Feedback period ongoing, and some more changes may come, but something to keep an eye on.

FIRST OPINION

New CMS rules will throttle access researchers need to Medicare, Medicaid data

By Rachel M. Werner Feb. 20, 2024 Reprint

NIH Pragmatic Trials Collaboratory

Initiated through the NIH Common Fund in 2012

Goal: Strengthen the national capacity to implement cost-effective, large-scale research studies that engage healthcare delivery organizations as research partners

Vision: Support the design and execution of innovative pragmatic clinical trial Demonstration Projects to establish best practices and proof of concept

Demonstration Projects

- Pragmatic trials embedded in healthcare
  systems to address questions of major public health importance
- Projects span multiple NIH Institutes, Centers, and Offices
- Projects have 1-year planning phase followed by implementation phase
- Coordinating Center supports methods-focused cores

The Living Textbook *of Pragmatic Clinical Trials*

- www.rethinkingclinicaltrials.org

NIH PRAGMATIC TRIALS COLLABORATORY

Rethinking Clinical Trials®

Milestones in the FDA's **Real-World Evidence** Activities

Real-world data (RWD) are data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources. Examples of RWD include data derived from electronic health records, medical claims data, data from product or disease registries, and data gathered from other sources (such as digital health technologies) that can inform on health status.

Real-world evidence (RWE) is the clinical evidence about the usage and potential benefits or risks of a medical product derived from analysis of RWD.

2018

Framework for FDA's Real-World Evidence Program

Created in response to the 21st Century Cures Act, the framework provides guidance on how the FDA will evaluate the use of RWE to support regulatory decisions.

September 2021

DRAFT GUIDANCE:

Real-World Data: Assessing Electronic Health Records and Medical Claims Data To Support Regulatory Decision-Making for Drug and Biological Products

2022

PDUFA VII

The sixth reauthorization of the Prescription Drug User Fee Act (PDUFA) incorporated as part of the FDA User Fee Reauthorization Act of 2022.

September 2022

FINAL GUIDANCE:

Submitting Documents Utilizing Real-World Data and Real-World Evidence to FDA for Drugs and Biologics

October 2022

Advancing Real-World Evidence Program

Fulfills an FDA commitment under PDUFA VII. This seeks to improve the quality and acceptability of RWE-based approaches in support of new intended labeling claims, including approval of new indications of approved medical products or to satisfy post-approval study requirements.

February 2023

DRAFT GUIDANCE:

Considerations for the Design and Conduct of Externally Controlled Trials for Drug and Biological Products

August 2023

FINAL GUIDANCE:

Considerations for the Use of Real-World Data and Real-World Evidence To Support Regulatory Decision-Making for Drug and Biological Products

December 2023

DRAFT GUIDANCE:

Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices

December 2023

FINAL GUIDANCE:

Real-World Data: Assessing Registries to Support Regulatory Decision-Making for Drug and Biological Products Guidance for Industry

December 2023

FINAL GUIDANCE:

Data Standards for Drug and Biological Product Submissions Containing Real-World Data

https://www.evidencebaseonline.com/infographics/infographic-milestones-in-the-fdas-real-world-evidence-activities/

More Notable CRI-Related Events

- Executive Order on the Safe, Secure, and Trustworthy Development and Use of Artificial Intelligence
  - https://www.whitehouse.gov/briefing-room/presidential-actions/2023/10/30/executive-order-on-the-safe-secure-and-trustworthy-development-and-use-of-artificial-intelligence/
  - On heels of White House Blueprint for an AI Bill of Rights - https://www.whitehouse.gov/ostp/ai-bill-of-rights/

WHITE HOUSE

OCTOBER 30, 2023

Executive Order on the Safe, Secure, and Trustworthy Development and Use of Artificial Intelligence

BRIEFING ROOM › PRESIDENTIAL ACTIONS

By the authority vested in me as President by the Constitution and the laws of the United States of America, it is hereby ordered as follows:

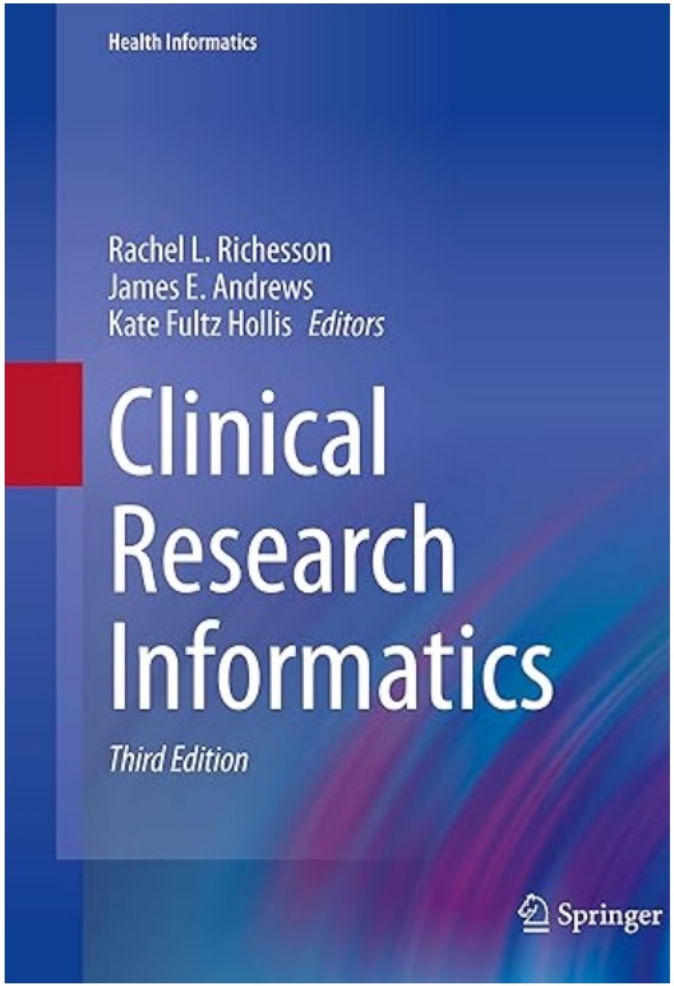
Section 1. Purpose. Artificial intelligence (AI) holds extraordinary potential for both promise and peril. Responsible AI use has the potential to help solve urgent challenges while making our world more prosperous, productive, innovative, and secure. At the same time, irresponsible use could exacerbate societal harms such as fraud, discrimination, bias, and disinformation; displace and disempower workers; stifle competition; and pose risks to

More Notable CRI-Related Events

- 3rd edition of CRI textbook is out!

- New NEJM AI journal – adding to others
  - Focus on pragmatic research in AI, including to advance discovery.
- Growing impacts of Informatics across health and biomedicine

- And so much more…



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

AI Ethics and Bias concerns

- Examples in major industries, including health
- Opportunities for us to lead and address concerns we understand best

Politicization of science has had an effect

- Trust in our institutions continues to be a concern
- Must continue do good work to address anti-science sentiment
- Financial issues plaguing heathcare can affect academy

More specific to CRI…

- RWD/RWE boom
- AI/ML boom
- New capabilities to enable democratization of data
- Continued growth in CRI leadership roles (e.g. CRIO)
- Pragmatic research on the rise
- Continued focus at intersection with LHS

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 and… translation into practice!
- COVID changed a LOT – 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

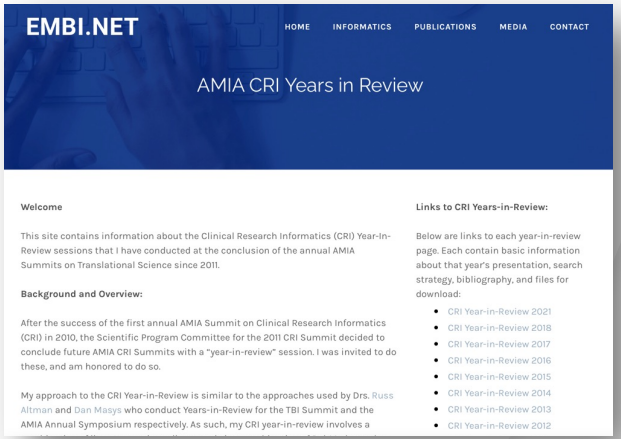
- Rachel Richesson
- Shawn Murphy
- Paul Harris
- Adam Wilcox
- Dave Dorr
- Melissa Haendel
- Boyd Knosp
- Matt Semler
- Michael Matheny
- Christel Daniel
- George Hripcsak
- Chris Lindsell
- Jessica Ancker
- Sean Mooney

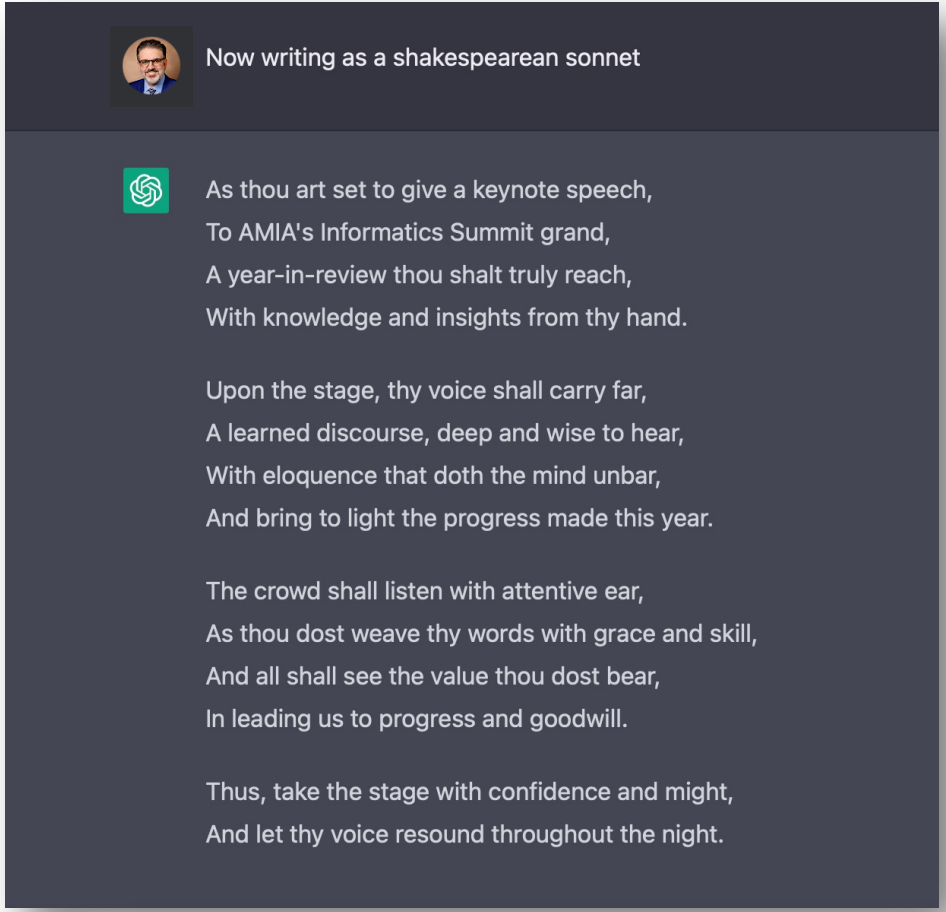
Thanks!

peter.embi@vumc.org

Twitter: @embimd

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





Q&A