Beth Israel Deaconess Medical Center

HARVARD MEDICAL SCHOOL TEACHING HOSPITAL

DIVISION OF CLINICAL INFORMATICS™

An Academic Division of the Dept of Medicine
at Harvard Medical Faculty Physicians at BIDMC, Inc.

Bioinformatics for Discovery and Global Collaborations: Approaches and Lessons Learned

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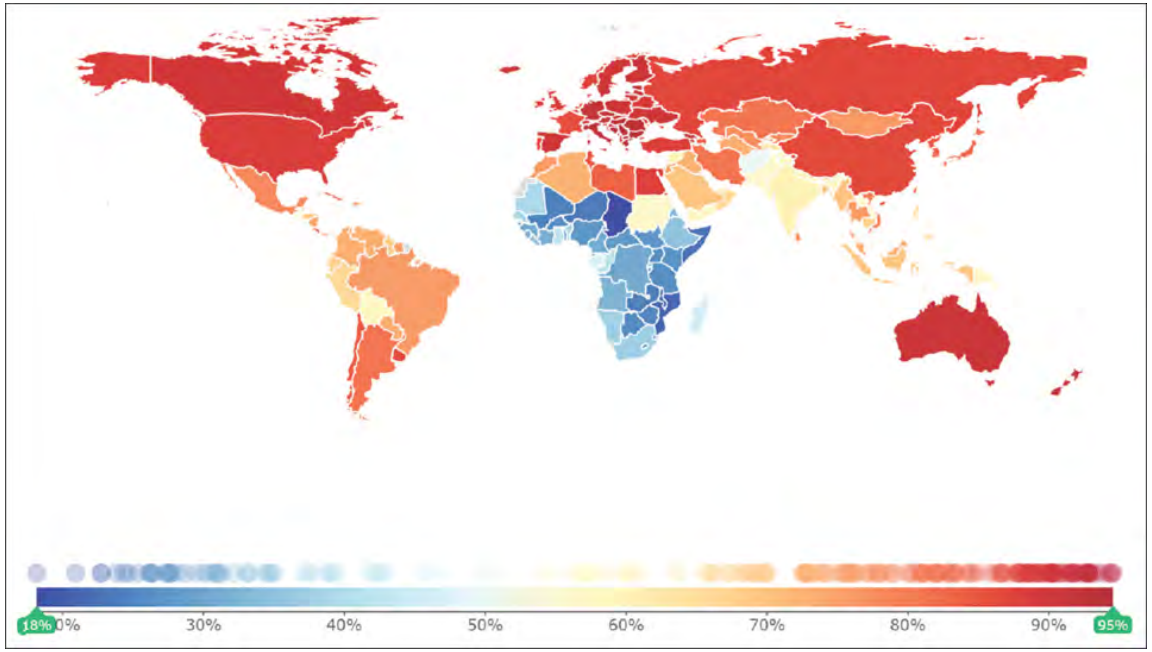
Why do we need Bioinformatics?

Rise of Chronic Diseases

- NCDs are the leading causes of death (63%) in all regions except Africa.
- NCDs projected to cost more than US$30 trillion (48% of global GDP in 2010)
- Respiratory diseases and allergies are a major global problem



Percentage of deaths from non-communicable diseases by country, 2013 (DOI: 10.4103/1658-600X.179820 Institute for Health Metrics and Evaluation

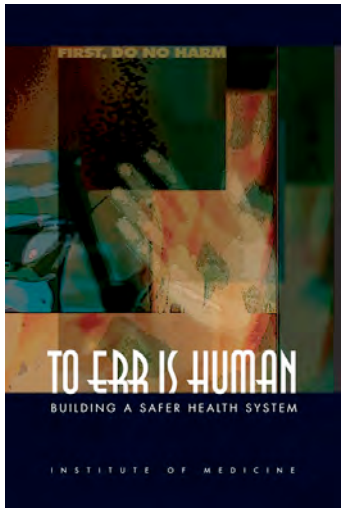
Diversity of Patients

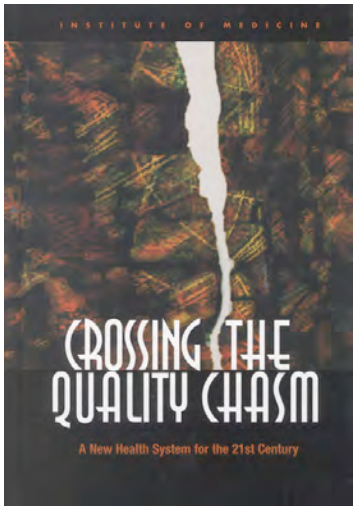
- People are moving from countries and regions (lost health records)
- Most clinical research has been done in USA and Europe (biased sample)
- Personalized treatment optimized to genetics requires global approach

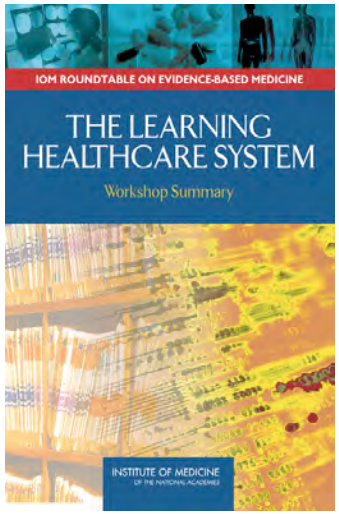
Source: The global flow of people - Migration flows between and within regions for five-year periods http://www.global-migration.info

Evolution of Putting Research into Practice

We need not only better data and evidence-based science but better learning networks and research communities







Vision: Our vision is for a healthcare system that draws on the best evidence to provide the care most appropriate to each patient, emphasizes prevention and health promotion, delivers the most value, adds to learning throughout the delivery of care, and leads to improvements in the nation's health.

Goal: By the year 2020, 90 percent of clinical decisions will be supported by accurate, timely, and up-to-date clinical information, and will reflect the best available evidence. We feel that this presents a tangible focus for progress toward our vision, that Americans ought to expect at least this level of performance, that it should be feasible with existing resources and emerging tools, and that measures can be developed to track and stimulate progress.

"The Learning Healthcare System", Institute of Medicine. The National Academies Press **2007** http://www.nap.edu/read/11903/chapter/1#ix .

Optimizing Healthcare

- Most clinical systems have incomplete data due to problems with data collection, interoperability, and data sharing
- Many centers have challenges integrating clinical and genomic data due to complexity and cost
- Many centers do not integrate family history or environmental history
- Research has largely been focused on populations in high income countries due to funding sources, biased genetic pool

- Future personalized treatments will need to be tailored to genetics, clinical, family history and environmental factors

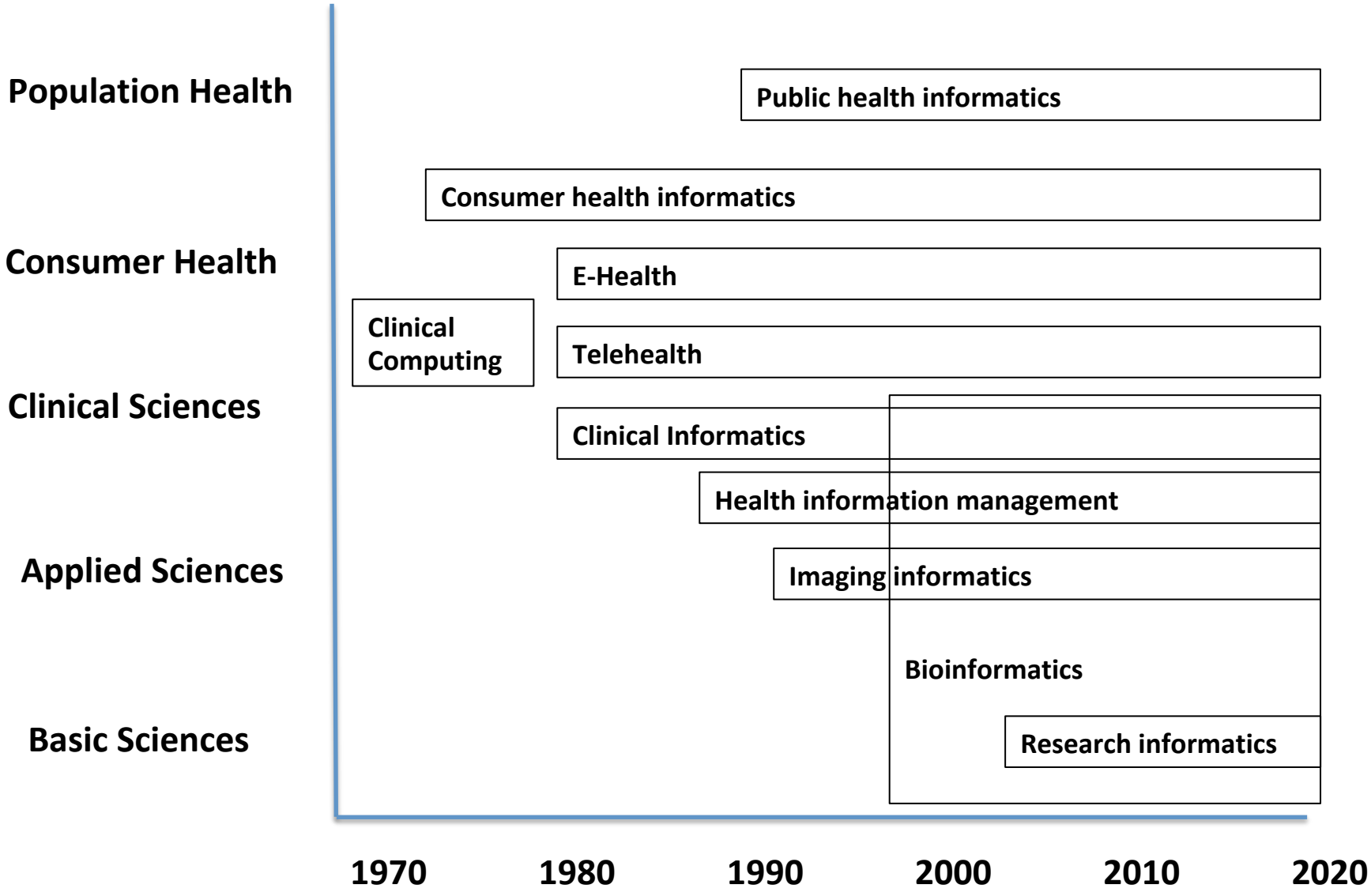
What is Bioinformatics?

Biomedical Informatics

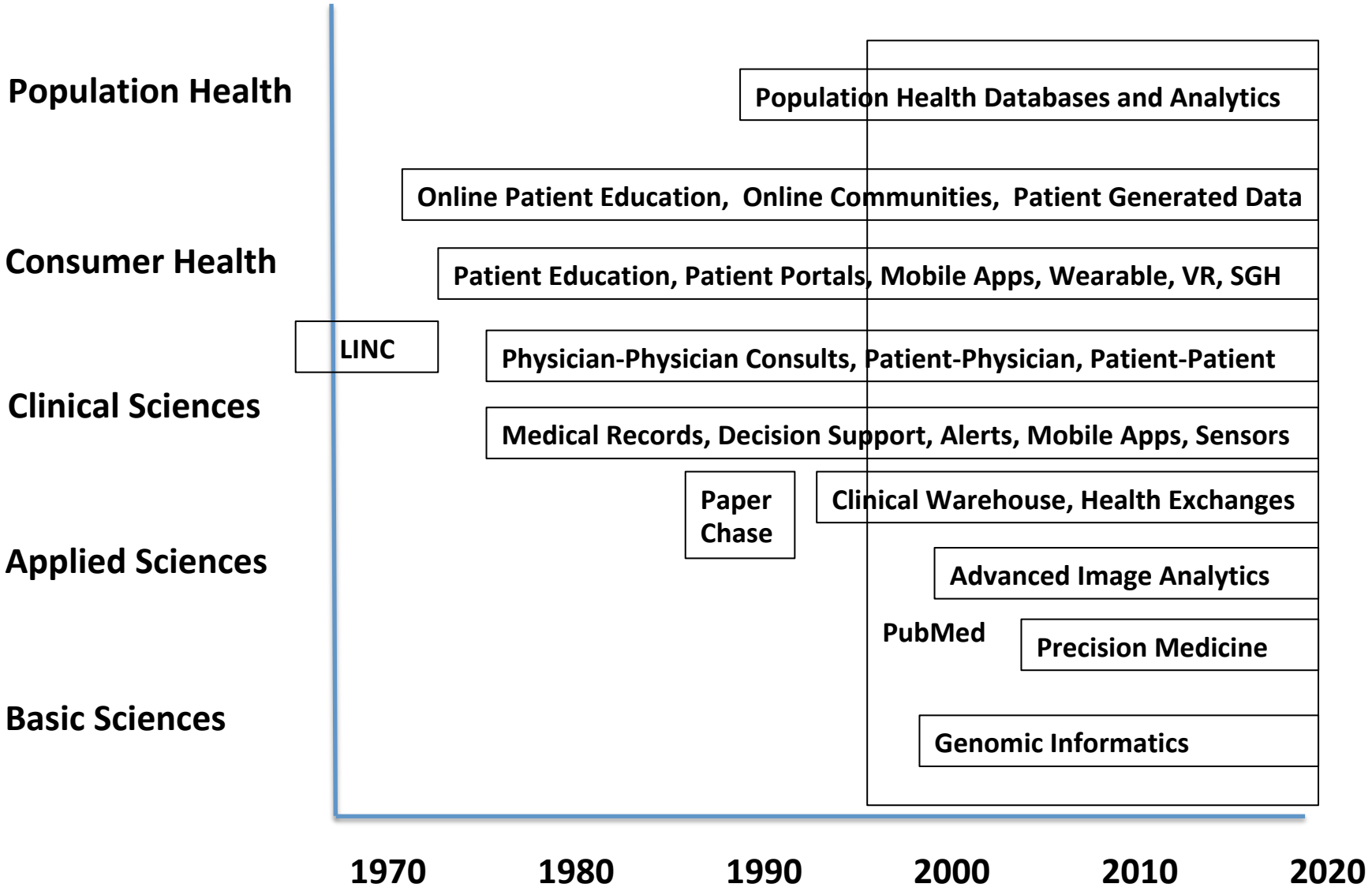
Biomedical informatics is an interdisciplinary field that develops analytical methods and software tools for understanding clinical and biological data. It combines elements from the fields of basic sciences, biology, computer science, mathematics, and engineering.

References: Biomedical Informatics: Computer Applications in Health Care and Biomedicine, Shortliffe and Cimino (editors), Springer, 2013
AMIA Board white paper: definition of biomedical informatics and specification of core competencies for graduate education in the discipline. Kulikowski 2012 DOI: 10.1136/amiajnl-2012-001053

Evolution of Field



Applications



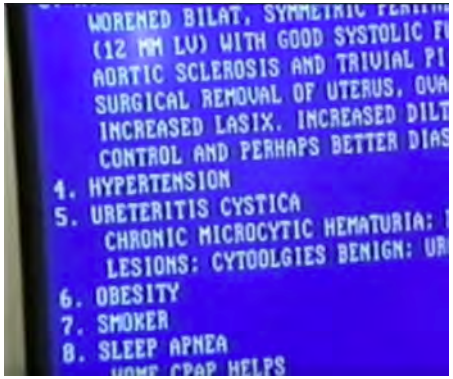
Contributions to the field by DCI

http://www.hmfpinformatics.org

Connecting healthcare providers to clinical data and literature

"LINC with Tomorrow" Dr. Warner Slack on national TV, 1967

PaperChase, the first search engine for biomedical literature, Dr. Howard Bleich, 1977, precursor to PubMed



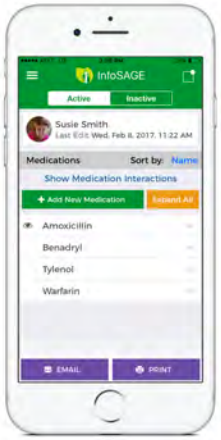
The Online Medical Record (OMR), Dr. Charles Safran, 1989

Connecting patients and families to their data and care network

Baby CareLink telemedicine application, Dr. Charles Safran, Dr. Jim Gray, et. al. 1996

PatientSite
my health journey
Beth Israel Deaconess Medical Center

PatientSite (2000), OpenNotes (2010), patient access to medical records and physician notes, Dr. Tom Delbanco, Jan Walker, Dr. Henry Feldman, et. al.



InfoSAGE
Mobile care coordination and communication for elders and families, C Safran, Y, Quintana B Crotty, et. al.

Complexity of Data

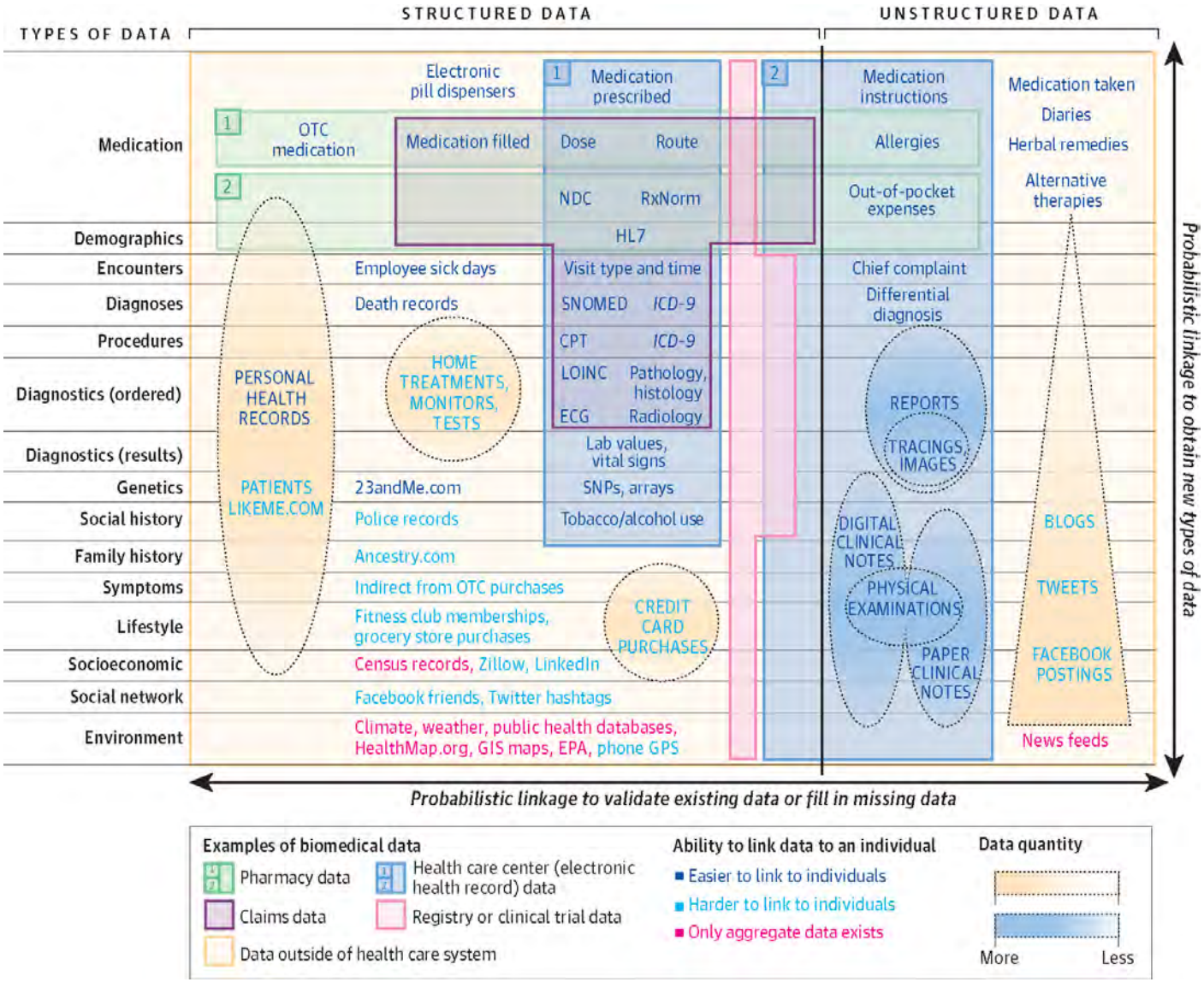


Image Source: Finding the Missing Link for Big Biomedical Data. JAMA. 2014;311(24):2479-2480. doi:10.1001/jama.2014.4228

De-Identification Levels

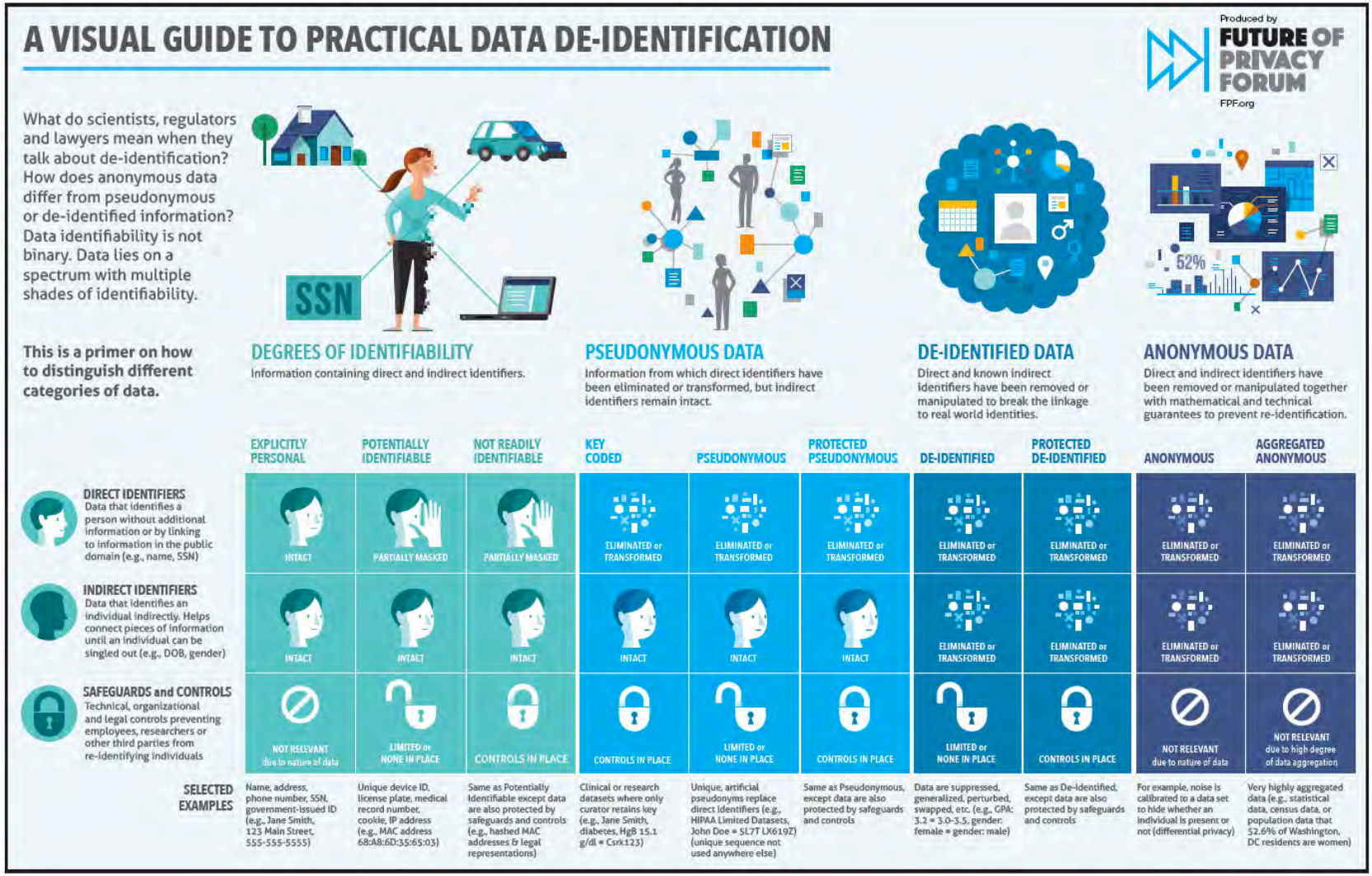


Image Source: https://fpf.org/2016/04/25/a-visual-guide-to-practical-data-de-identification/
and Shades of Gray: Seeing the Full Spectrum of Practical Data De-Identification. published in the Santa Clara Law Review.

Human Genome Project Timeline

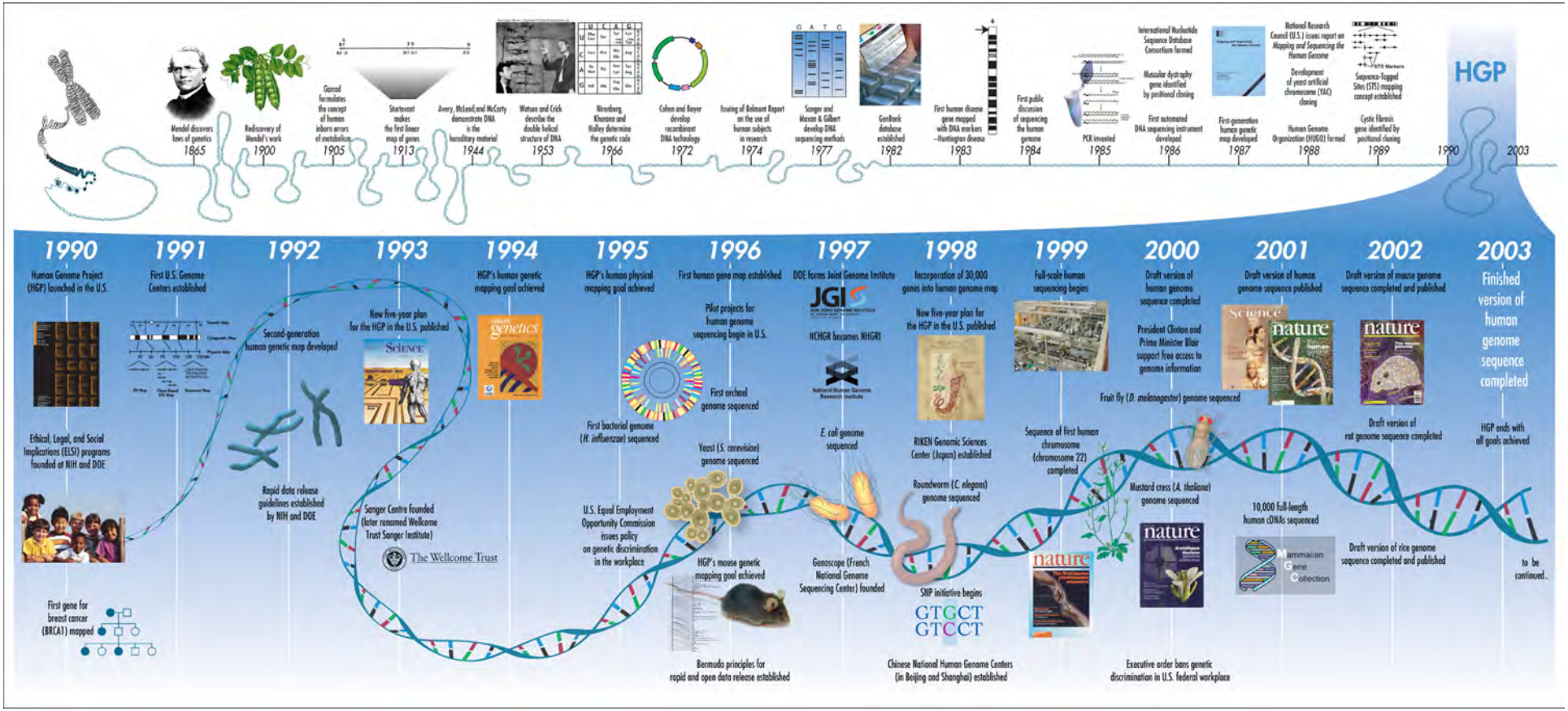
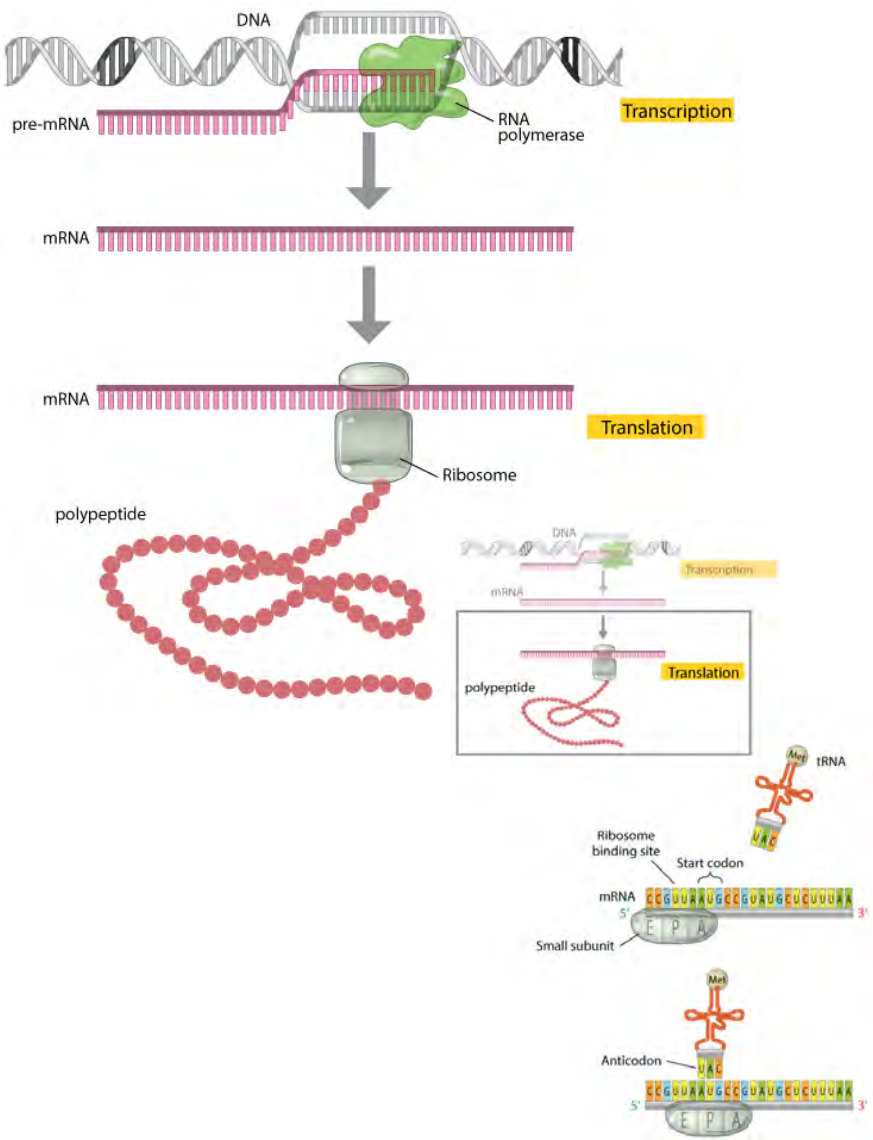


Image Source: NIH https://www.genome.gov/imagegallery/viewimage/?imageID=26964377742

Complexity of Data



genome

genomics

transcriptome

transcriptomics

proteome

proteomics

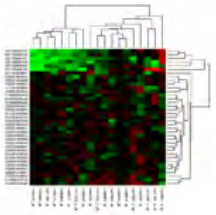
metabolome

metabolomics

DNA Sequencer

DNA sequencers Manufacturers Roche, Illumina, Life Technologies, Beckman Coulter, Pacific Biosciences

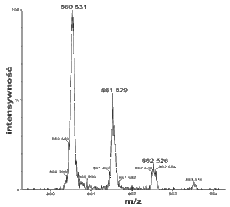
DNA microarray



Gene expression heat maps

Affymetrix chips

Mass spectrometer



Mass spectrum of a peptide

Orbitrap mass spectrometer

Image Sources: Nature https://www.nature.com/scitable/topicpage/translation-dna-to-mrna-to-protein-393 and Wikimedia

The Cost of Sequencing a Human Genome

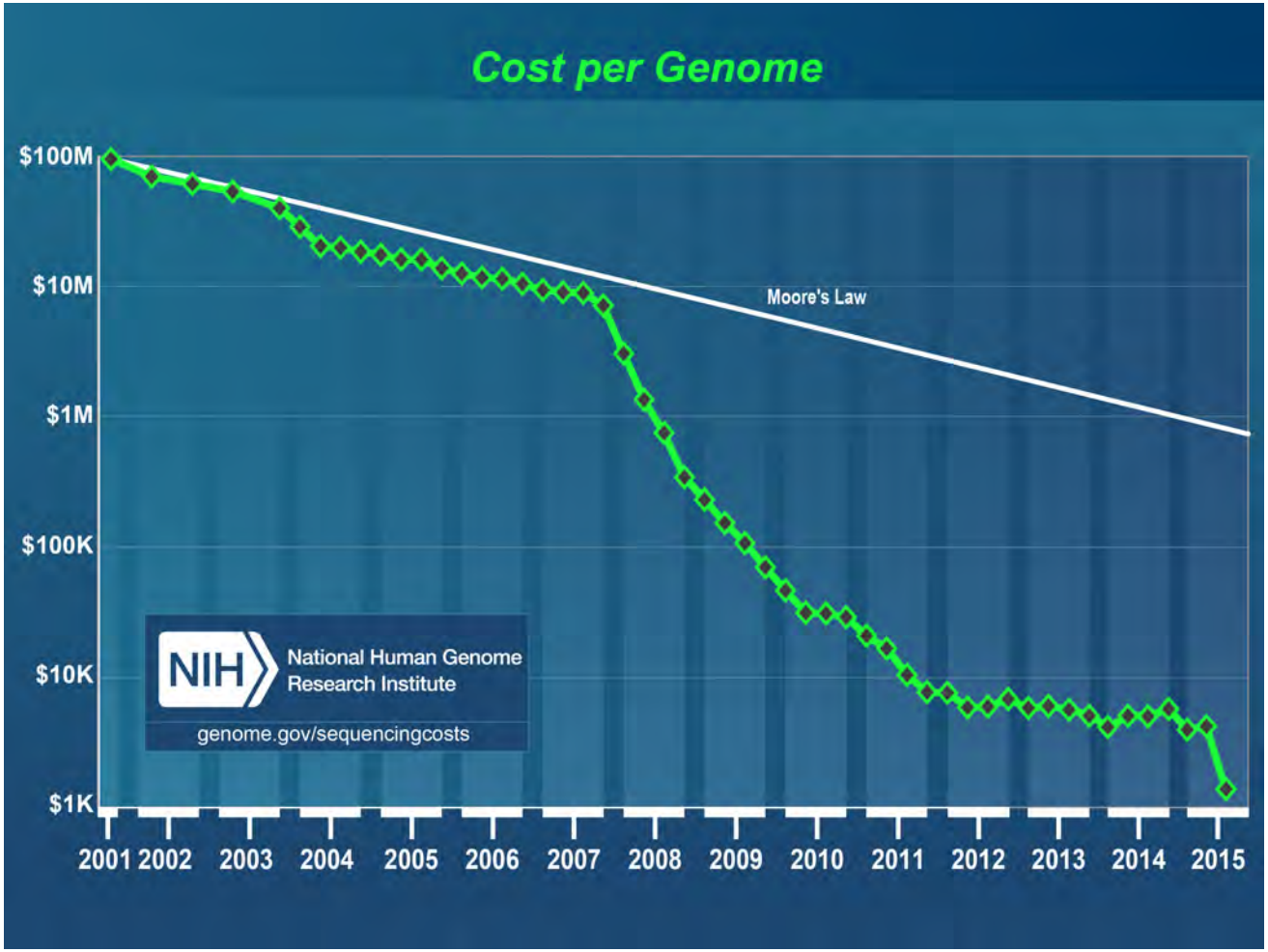
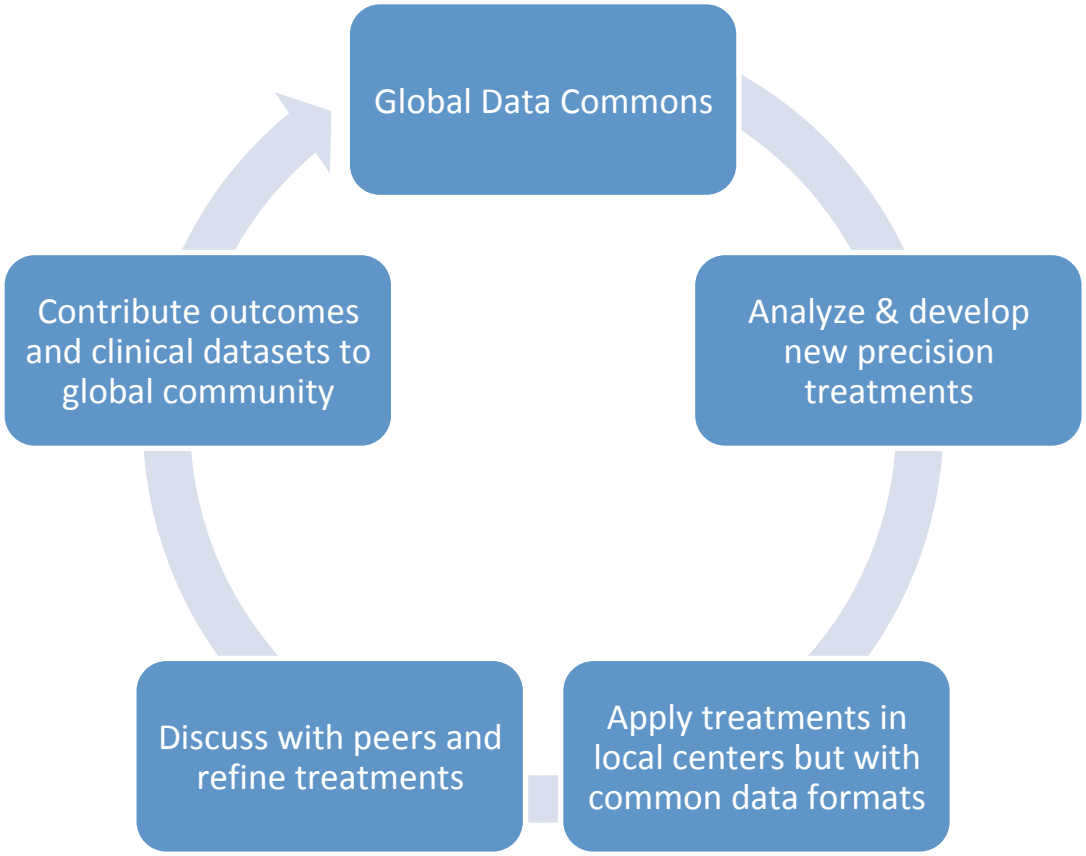


Image Source: https://www.genome.gov/27565109/the-cost-of-sequencing-a-human-genome/

Networks for Collaboration and Learning with Bioinformatics Data

Global Learning Health System



Global Pediatric Cancer Network

Cure4Kids.org – Global Education and Collaboration on Pediatric Oncology

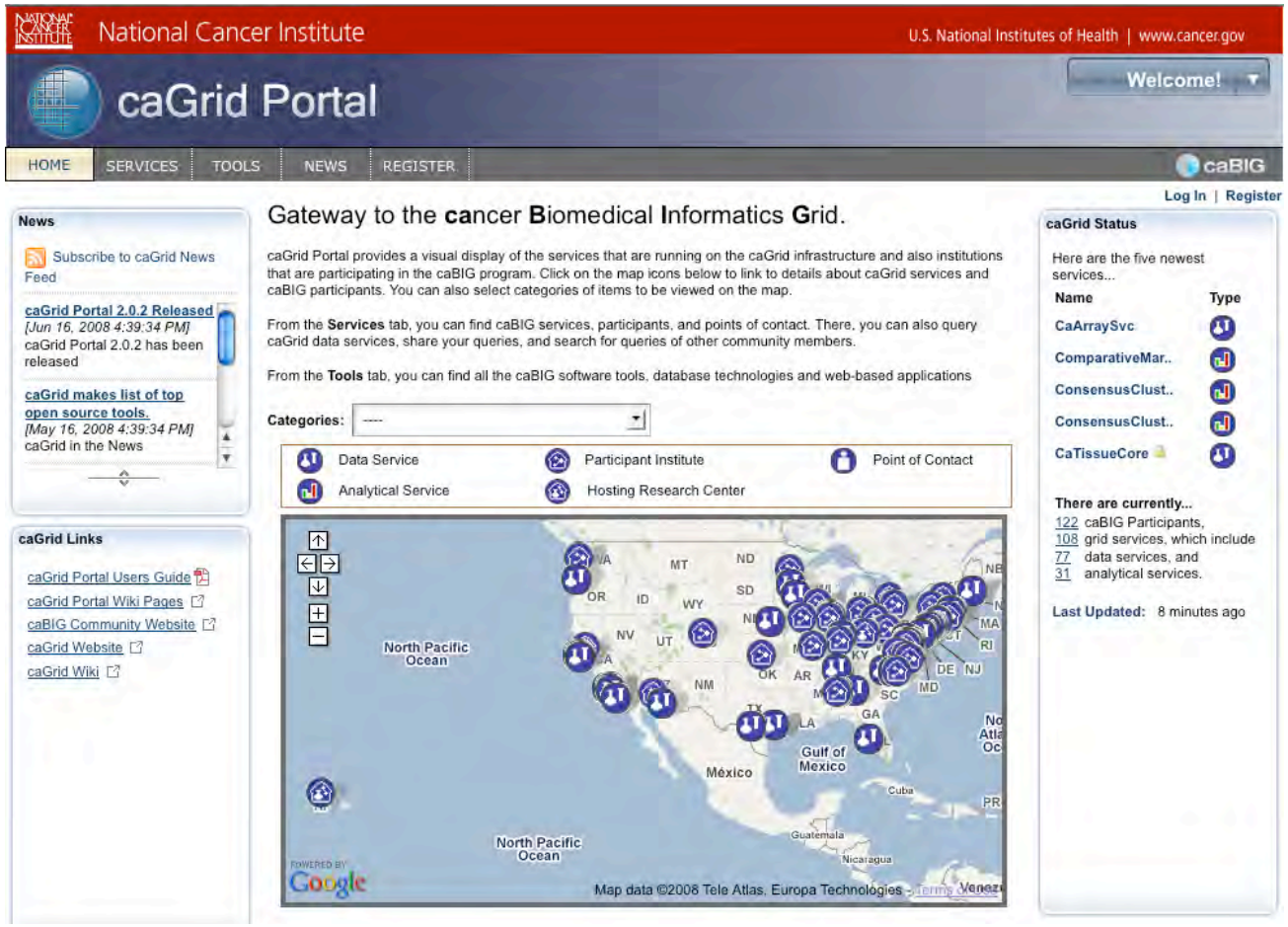
POND4Kids.org – Global Shared Clinical Protocols and Outcomes Database

Richardson, S., Banks, M.S., Kettinger, W., and Quintana, Y. IT and Agility in the Social Enterprise: A Case Study of St. Jude Children's Research Hospital's 'Cure4Kids' IT-Platform for International Outreach. Journal of the Association of Information Systems. 2014: 15(1), pp 1-32.

Quintana Y, Patel AN, Arreola M, Antillon FG, Ribeiro RC, Howard SC. POND4Kids: A Global Web-based Database for Pediatric Hematology and Oncology Outcome Evaluation and Collaboration. Stud Health Technol Inform. 2013;183:251-6.

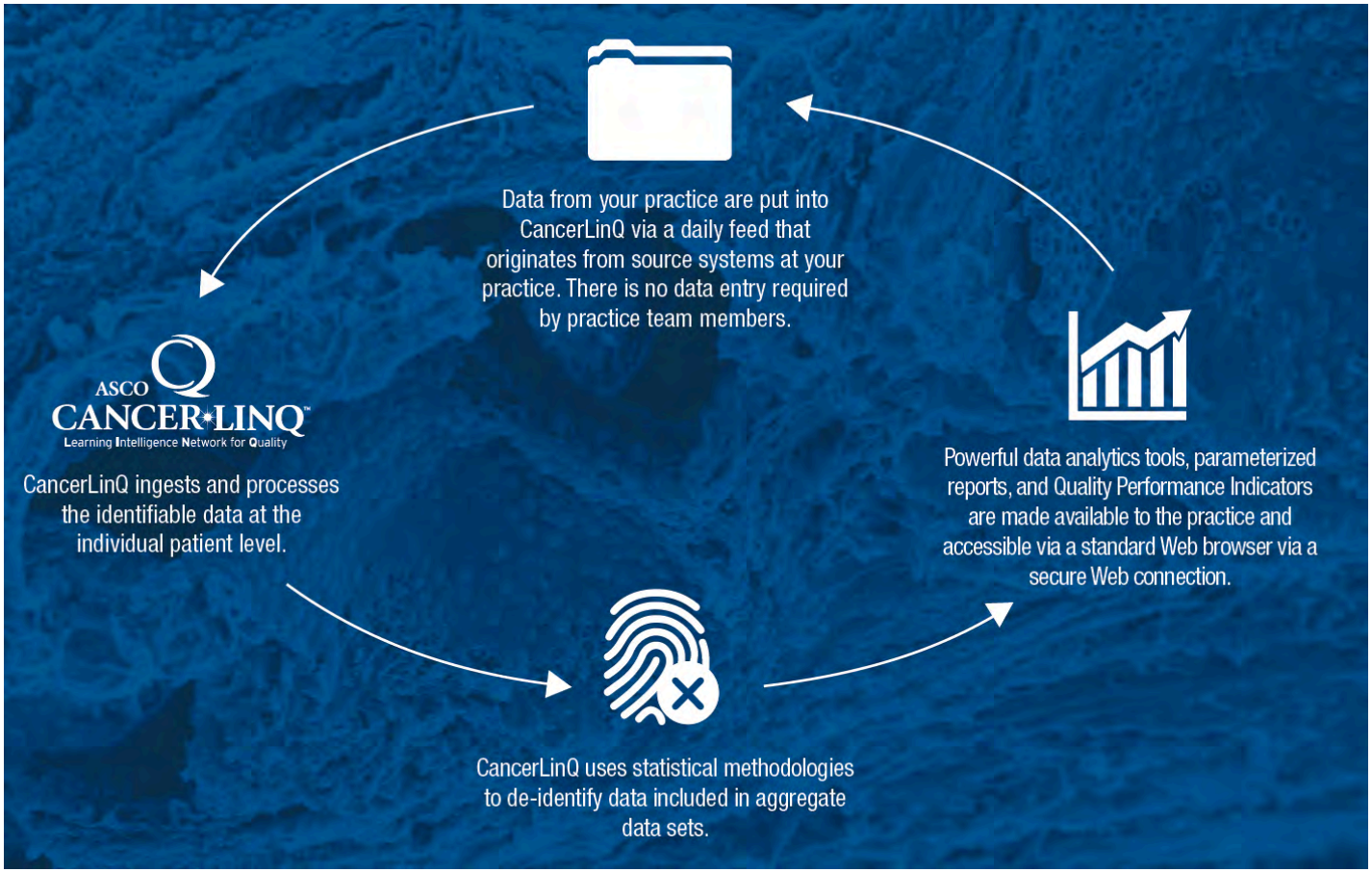
Quintana Y, O'Brien R, Patel A, Becksfort J, Shuler A, Nambayan A, Ogdon D, Chantada G, Howard SC, Ribeiro RC. Cure4Kids: Research challenges in the design of a website for global education and collaboration. Information Design Journal 2008; 16:3, 243-249.

CaBIG



- Cancer Biomedical Informatics Grid (caBIG) was a USA government program from 2004-2011 to develop an open source, open access information network called caGrid for secure data exchange on cancer research.
- NCI published review of CaBIG that included a long list of problems with the program, and recommended that most projects should be discontinued. Kenneth Buetow (April 1, 2008). "Heading for the BIG Time" (PDF). The Scientist. 22 (4), and
- Board of Scientific Advisors Ad Hoc Working Group (March 3, 2011). "An Assessment of the Impact of the NCI Cancer Biomedical Informatics Grid (caBIG®)" (PDF). National Cancer Institute.

CancerLinQ™ by ASCO

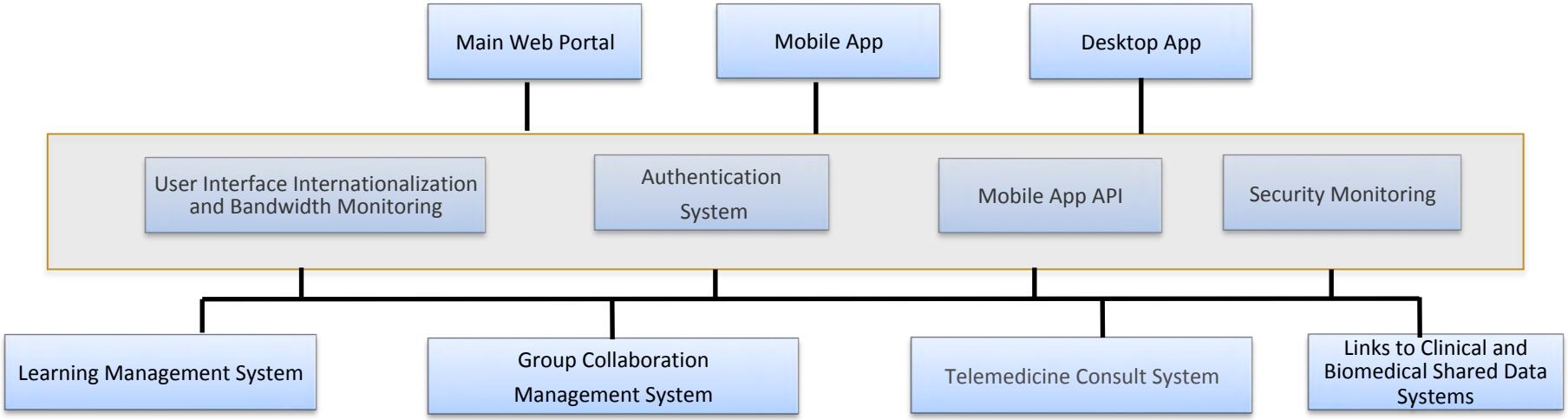


CancerLinQ™ (2015-) aggregates Clinical Records from oncology practices, gives insights from de-identified data on hundreds of thousands of patients, potentially identifying important trends and increasing the confidence of care decisions, visualizes patients' medical histories in powerful new ways

As of Dec 2017, 100 oncology practices in 40 states, 12 source systems, 600K cancer Records, 2,500 oncologists
Image Source: https://cancerlinq.org/

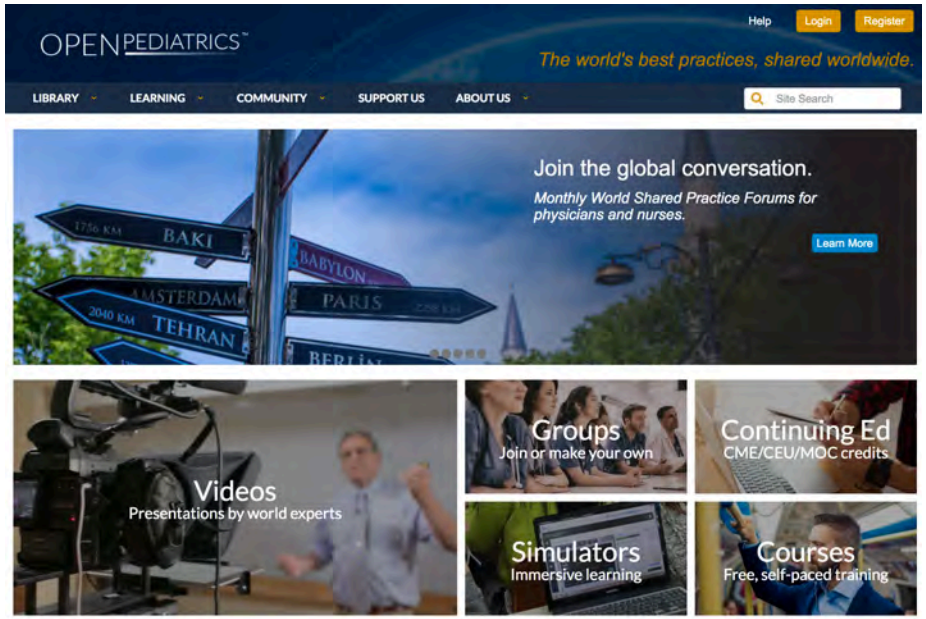
Alicanto™ – Global Communities of Practice

An Integrated Platform for Education, Communication and Data Sharing

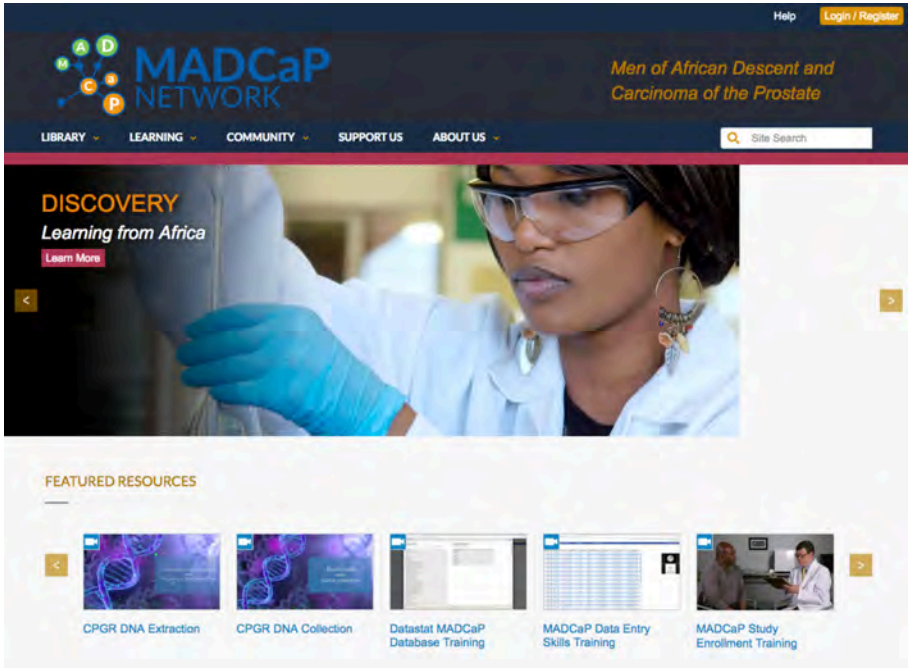


http://www.alicantocloud.com

Alicanto™ Networks

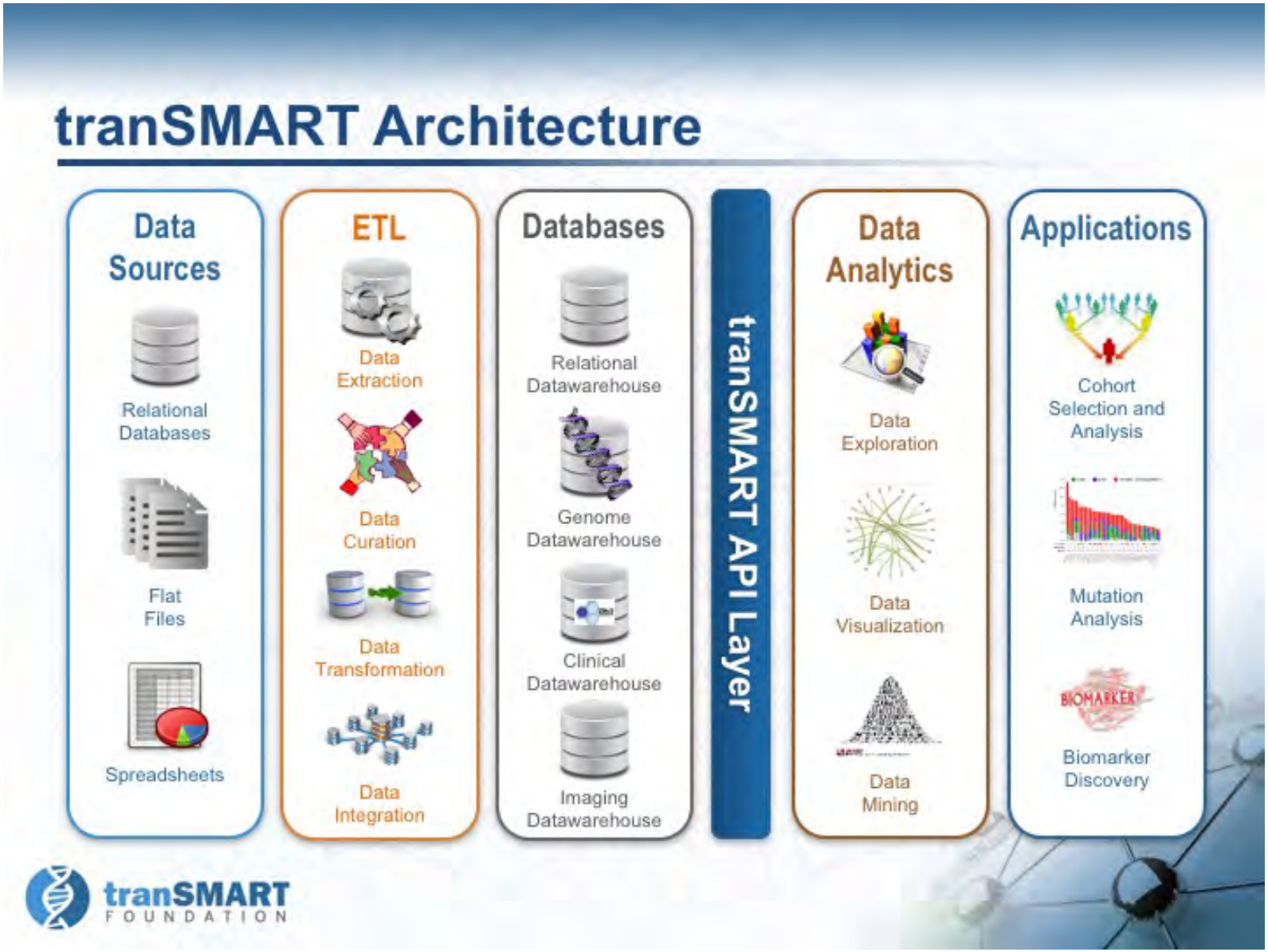


OPENPediatrics™ from Boston Children's Hospital
https://www.openpediatrics.org



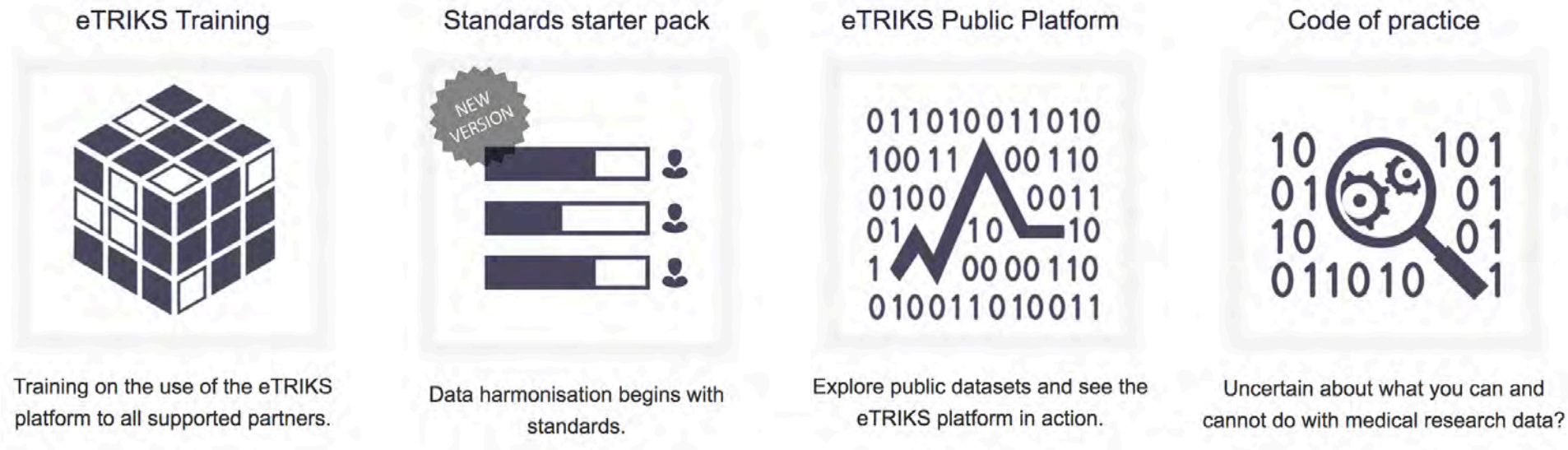
MADCAP Network from Dana-Farber Cancer Center
https://www.madcapnetwork.org

i2b2 and Transmart



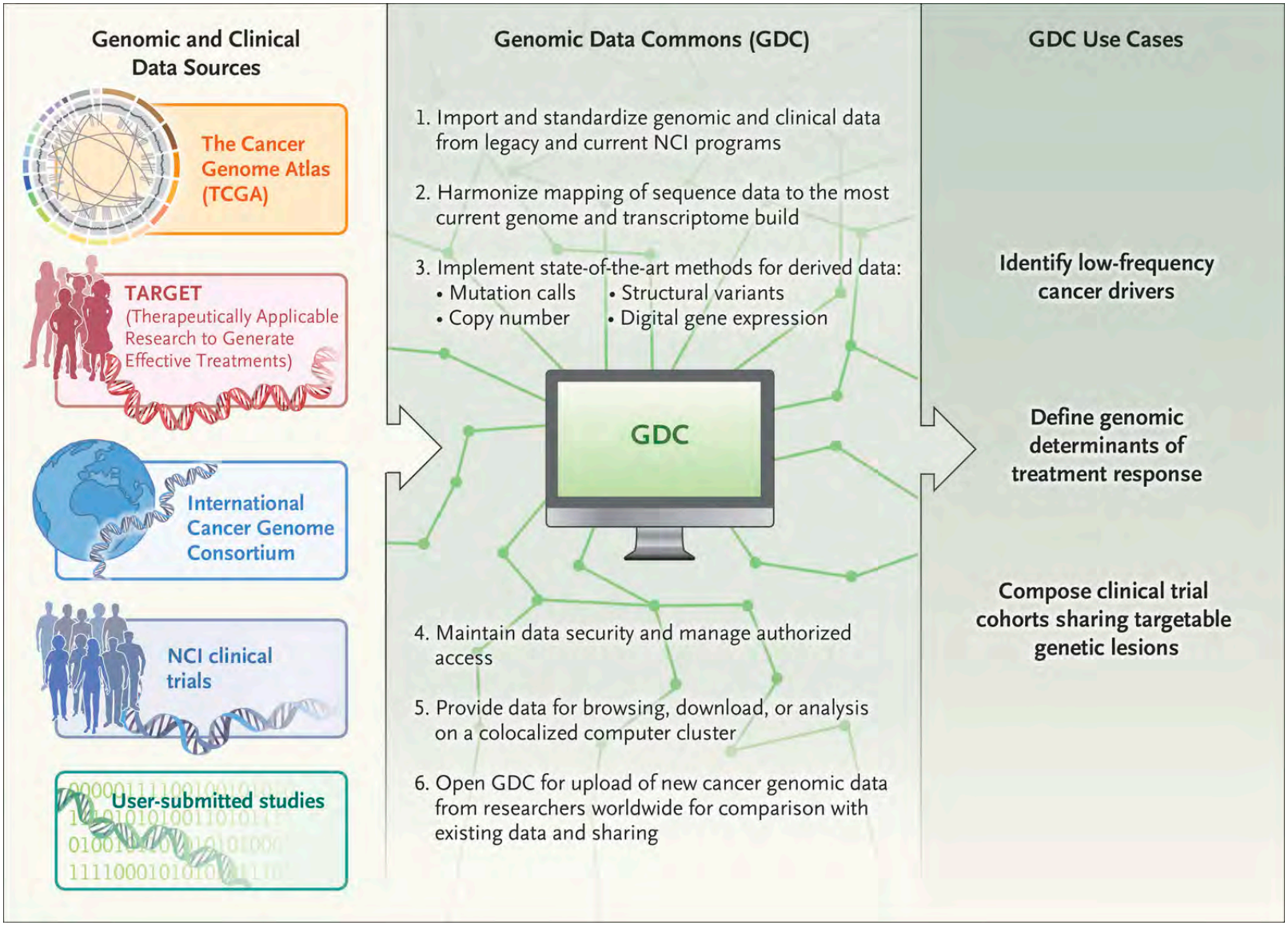
tranSMART is a knowledge management platform that enables scientists to develop and refine research hypotheses by investigating correlations between genetic and phenotypic data, and assessing their analytical results in the context of published literature and other work. I Source: http://transmartfoundation.org

eTricks – European Union



eTRIKS is the result of a collaboration between 17 different partners. Each combining their strengths in the development of a platform and services for data staging, exploration and use in translational research. https://www.etriks.org/

NIH Genomic Data Commons (USA)



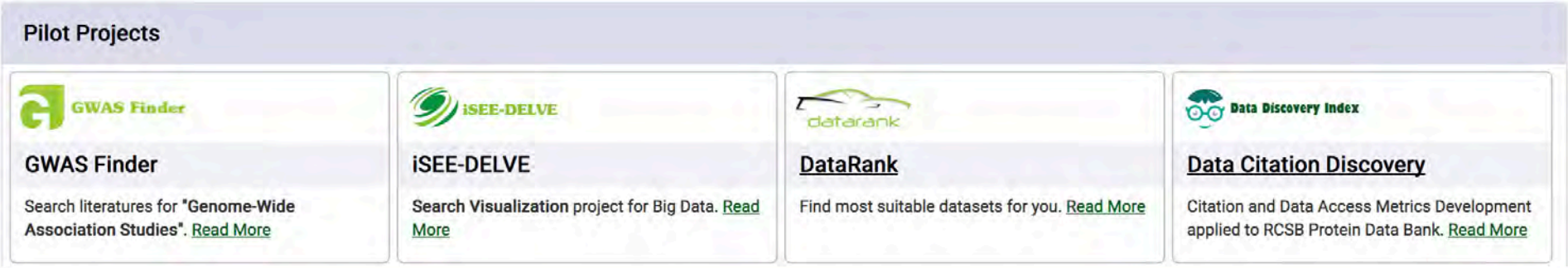
https://gdc.cancer.gov/ Image Source: Toward a Shared Vision for Cancer Genomic Data Grossman RL et al. N Engl J Med 2016;375:1109-1112. www.nejm.org/doi/full/10.1056/NEJMp1607591

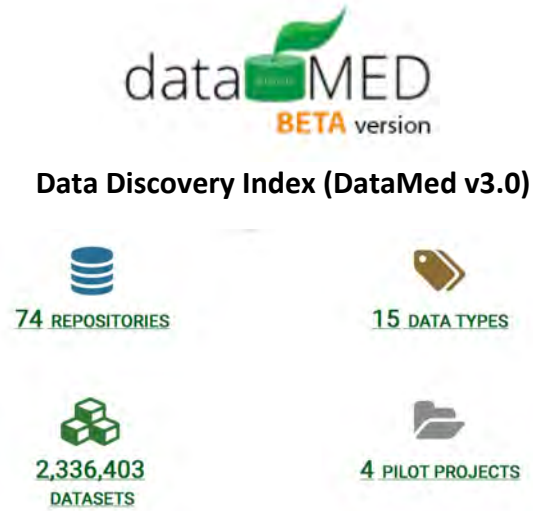
Biobanking and BioMolecular Resource Research Infrastructure (Europe)

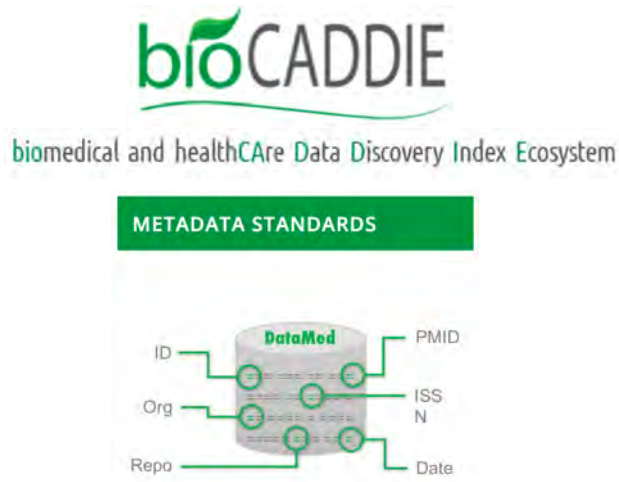
Informatics Tools

CDSKB | Catalogs and shares clinical decision support implementation artifacts and designs consideration for genomic medicine programs
eleMAP | Harmonizes local phenotype data dictionaries to existing metadata and terminology standards
eRecordCounter | Provides exploratory data figures for research planning purposes and feasibility assessment
PheKB | Offers a collaborative environment to build and validate electronic algorithms to identify characteristics of patients within health data
PheWAS Catalog | Functions as a platform for analysis of phenotypes against a single gene variant
SPHINX | Operates as a tool for exploring data for hypothesis generation, especially around drug response implications of genetic variation across the eMERGE PGx cohort
Clinical Report File Formats | Lists clinical reports and research materials (e.g. consent forms)
Genotyping Tools | PennCNV, Biofilter, Biobin, PLATO, ATHENA, Synthesis-View, PheWAS-View, and Phenogram
Phenotyping Tools | PheKB, eleMAP, and PheWAS

USA NIH Big Data to Knowledge (BD2K)

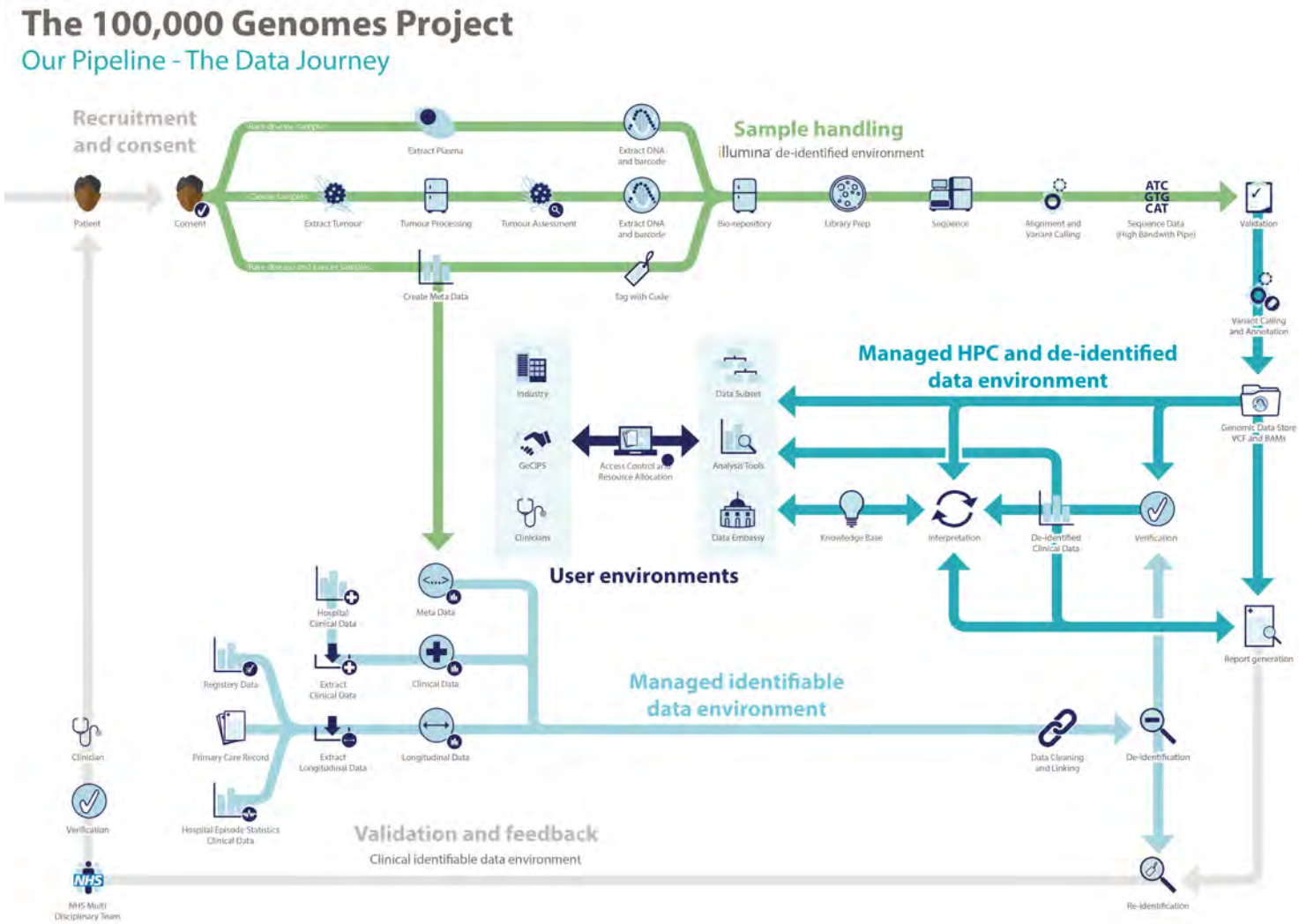






The Big Data to Knowledge (BD2K) program is a trans-NIH initiative that was launched in 2013 to support the research and development of innovative and transformative approaches and tools to maximize and accelerate the integration of big data and data science into biomedical research. The BD2K Program also supported initial efforts toward making data sets "**FAIR" Findable, Accessible, Interoperable, and Reusable**. In its first phase (FY2014-FY2017), BD2K invested $200 million in grant awards to address some major data science challenges and to stimulate data-driven discovery https://commonfund.nih.gov/bd2k and https://datamed.org/ and https://biocaddie.org/

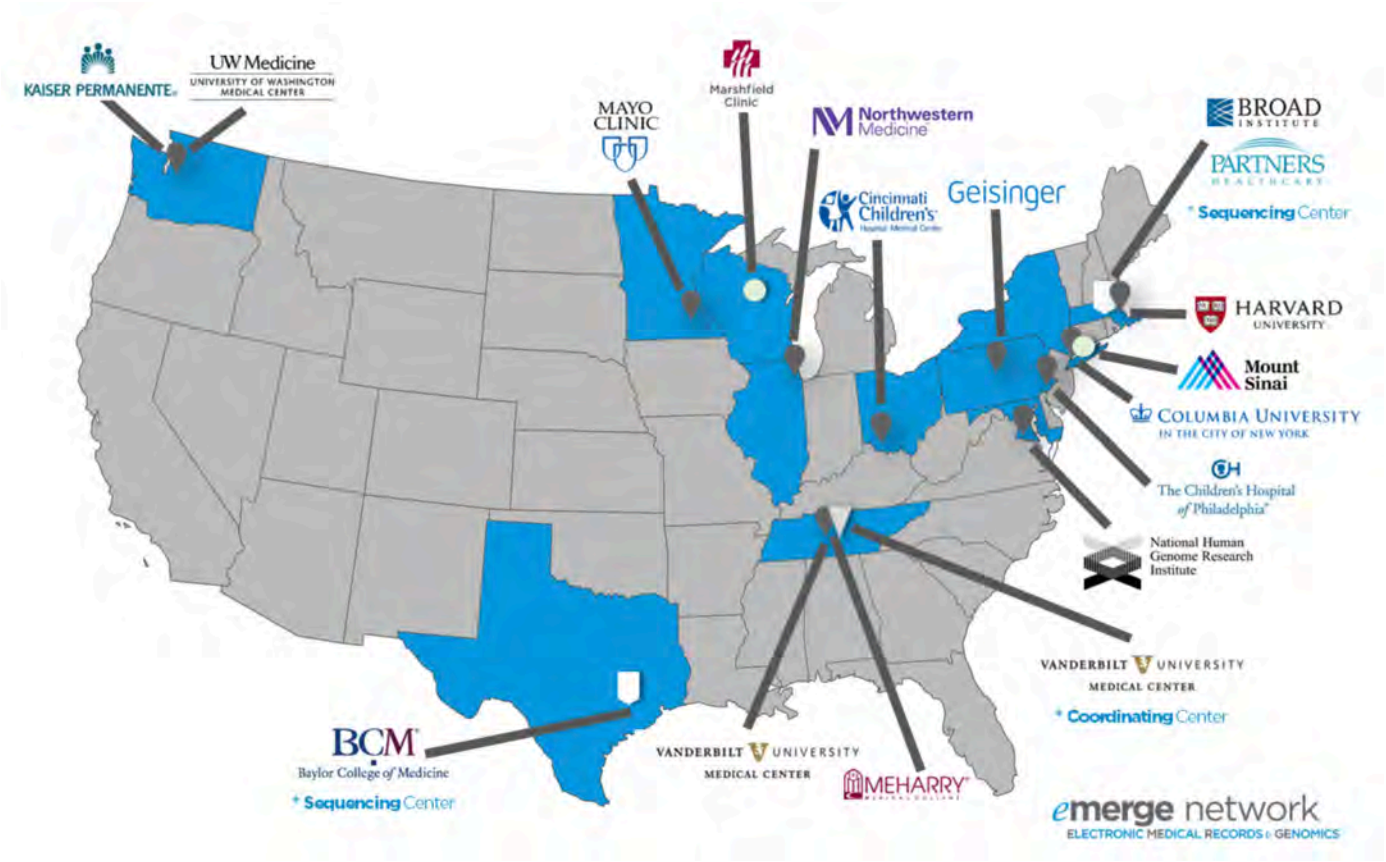
Genomics England - 100,000 Genomes Project



Genomics England, with the consent of participants and the support of the public, is creating a lasting legacy for patients, the NHS and the UK economy, through the sequencing of 100,000 genomes. Objectives: 1) To bring benefit to patients 2) To create an ethical and transparent programme based on consent 3) To enable new scientific discovery and medical insights 4) To kickstart the development of a UK genomics industry

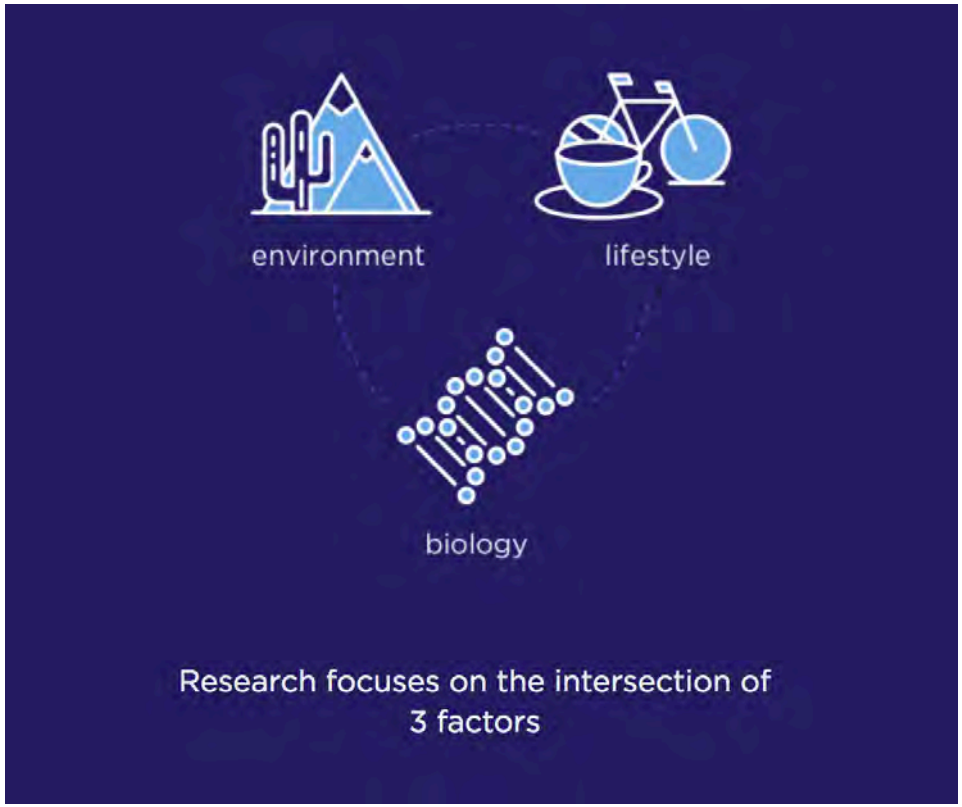
Image Source: https://www.genomicsengland.co.uk

eMERGE Network (USA)



eMERGE is a national network organized and funded by the National Human Genome Research Institute (NHGRI) that combines DNA biorepositories with electronic medical record (EMR) systems for large scale, high-throughput genetic research in support of implementing genomic medicine. 7 clinical sites 2 pediatric sites in 2012. https://emerge.mc.vanderbilt.edu/

All of US - Precision Medicine Initiative (USA)



The mission of the *All of Us* Research Program is to accelerate health research and medical breakthroughs, enabling individualized prevention, treatment, and care for all of us. Building a repository of data for 1,000,000+ people.

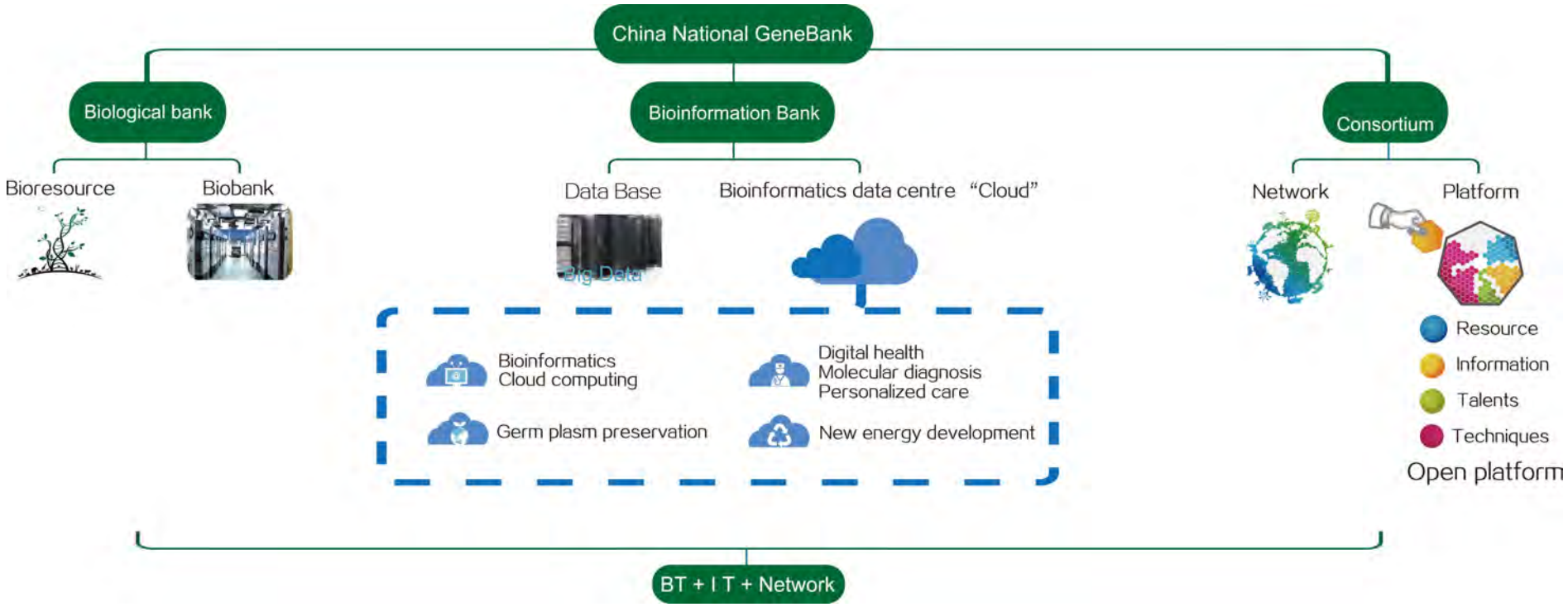
PMI launched in fiscal year 2016 when $130 million was allocated to NIH to build a national, large-scale research participant group, called a cohort, and $70 million was allocated to the National Cancer Institute to lead efforts in cancer genomics as part of PMI for Oncology. Source: https://allofus.nih.gov

USA Veteran Affairs Million Veteran Program

MVP is a national, voluntary research program funded entirely by the Department of Veterans Affairs Office of Research & Development. The goal of MVP is to partner with Veterans receiving their care in the VA Healthcare System to study how genes affect health. To do this, MVP will build one of the world's largest medical databases by safely collecting blood samples and health information from one million Veteran volunteers. Data collected from MVP will be stored in a secure manner and will be coded for researchers so that researchers cannot directly identify participants. Researchers will study diseases like diabetes and cancer, and military-related illnesses, such as post-traumatic stress disorder

Image Source: https://www.research.va.gov/MVP/

BGI-Shenzhen-*China National GeneBank* (China)



Established by BGI-Shenzhen, the China National GeneBank (CNGB) is the first national genebank integrating a large-scale bio-repository and an omics database. It is approved by Chinese government, with the mission of collecting, preserving and exploiting genomics resources, and to build a network fostering global communication and collaboration on biodiversity conservation and genetic resources utilization. In addition, CNGB is supported by BGI's high-throughput sequencing and bio-informatics capacity, and it will not only provide a repository system for biological collection, but more importantly develop a novel platform to further understand genomic mechanisms of life.

Image Source: http://www.genomics.cn

Biomedical Network Key Roles

- Chief Scientist
- Biomedical, Life Sciences, Clinical Scientists
- Research Informatics Director
- Clinical Informatics Director
- Biomedical Platforms Architect
- Biomedical Engineers and Programmers
- Clinical and Genomic Classification Experts
- Quality Assurance Engineers and Analysts
- Data Scientists
- Machine Learning/AI Researchers
- Visualization and User Interface Experts
- Research Ethics and Privacy Directors
- Communication (Internal & External) Directors
- Education and Training Directors
- Cybersecurity Experts
- Cloud Computing Architects and Engineers
- External Partnerships Director

Challenges in Implementation

- Lack of Focus (Feature rich, function poor)
- Lack of Adequate Trained Personnel
- Lack of Multidisciplinary Team
- Poor Governance
- Poor Leadership
- Lack of Adequate Funding (but not the biggest problem)
- Collecting and Managing Data Usage Consents
- Data Use Agreements between institutions
- Lack of diversity in patient data sets
- Agreement on Data formats, taxonomies and indexing needs to support scientific questions
- Usability of tools
- De-identification strategy
- Legal and Compliance Regulations
- Sustainable funding models

Clinical and Bioinformatics Training

- Graduate Programs in Bioinformatics, Clinical Informatics and Bio-Engineering
- American Medical Informatics Association and Journals www.amia.org
- IEEE Life Sciences Societies and Conferences lifesciences.ieee.org
- Clinical Informatics Subspecialty Board Examination - American Board of Preventive Medicine (ABPM)
- American Nurses Credentialing Center (ANCC) offers a board certification in Nursing Informatics
- CIIP (Certified Imaging Informatics Professional) certification by ABII (The American Board of Imaging Informatics)
- American Health Information Management Registered Health Information Administrator and Certified Coding Associate

Roadmap

- Select carefully for key leadership positions
- Assemble a multi-disciplinary team
- Involve patients as true partners
- Start with focused and feasible initial plan, but scalable
- Have clear transparency and ethics

References

Bioinformatics

- Biomedical Informatics: Computer Applications in Health Care and Biomedicine (Health Informatics) 4th ed. 2014 Edition By Edward H. Shortliffe and James J. Cimino(Editors)
- AMIA Board white paper: definition of biomedical informatics and specification of core competencies for graduate education in the discipline. Kulikowski 2012 DOI: 10.1136/amiajnl-2012-001053
- Methods in Biomedical Informatics A Pragmatic Approach. Edited by Neil Sarkar
- Journal of Biomedical Informatics, Springer

Quintana cited work on Global Health Informatics

- Global Health Informatics—An Overview. By Yuri Quintana, Charles Safran. In Heimar de Fátima Marin, Eduardo Massad, Marco Antonio Gutierrez, Roberto J. Rodrigues and Daniel Sigulem, editors: Marin-Global Health Informatics, Oxford: Academic Press, 2017, pp. 1-13.
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- Transmart Foundation http://transmartfoundation.org and i2b2: Informatics for Integrating Biology & the Bedside https://www.i2b2.org
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Related Medical Informatics Specialties

- **Bioinformatics**- Informatics applied to cellular and molecular biology, and genomics.
- **Clinical informatics**- Informatics applied in healthcare or individual health settings. It is related to, such as nursing informatics, dental informatics, pathology informatics.
- **Imaging informatics**- Informatics applied to imaging, systems in health care settings (storage, retrieval, analysis).
- **Consumer health informatics**- Informatics applies to consumer and patient access.
- **Research informatics**- Informatics to support biomedical and health research, with a focus to support translation of knowledge bench to bedside.
- **Public health informatics**- Informatics applied to public health such as health surveillance, reporting, and health promotion.
- **Health information management** -A related field applied to the management of medical records and access.
- **E-Health** – Terms from the 1990s on the application of electronic methods to health care
- **Telehealth** – Study of the distribution of health-related services and information via electronic
- **Clinical Computing** – Early term used by pioneers such as Dr. Warner Slack and Dr. Howard Bleich in 1970s

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