Information Exchange and Data Transformation (INFORMED) Initiative

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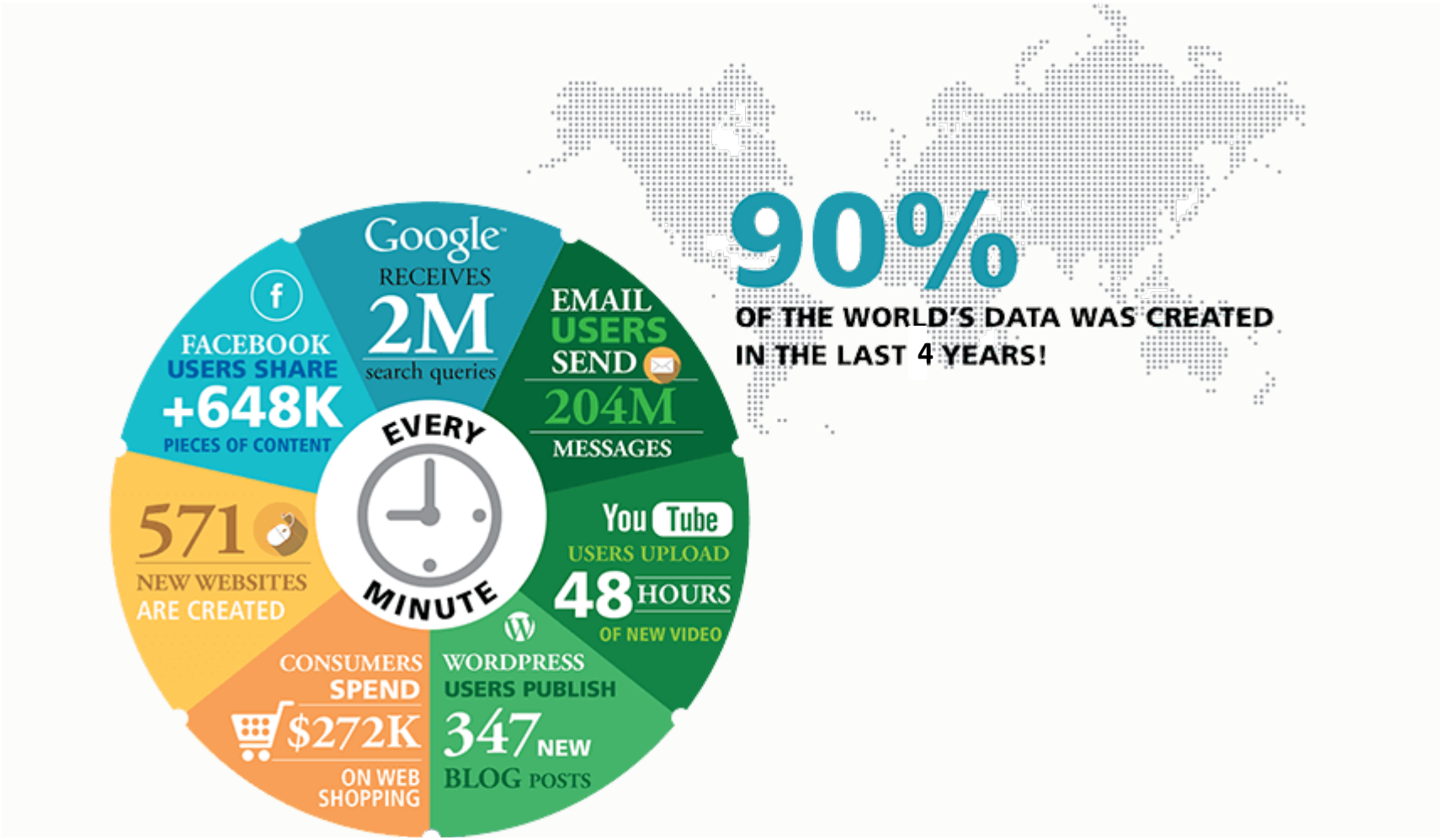
Food and Drug Administration (FDA)

Disclosures

None

#bigdata

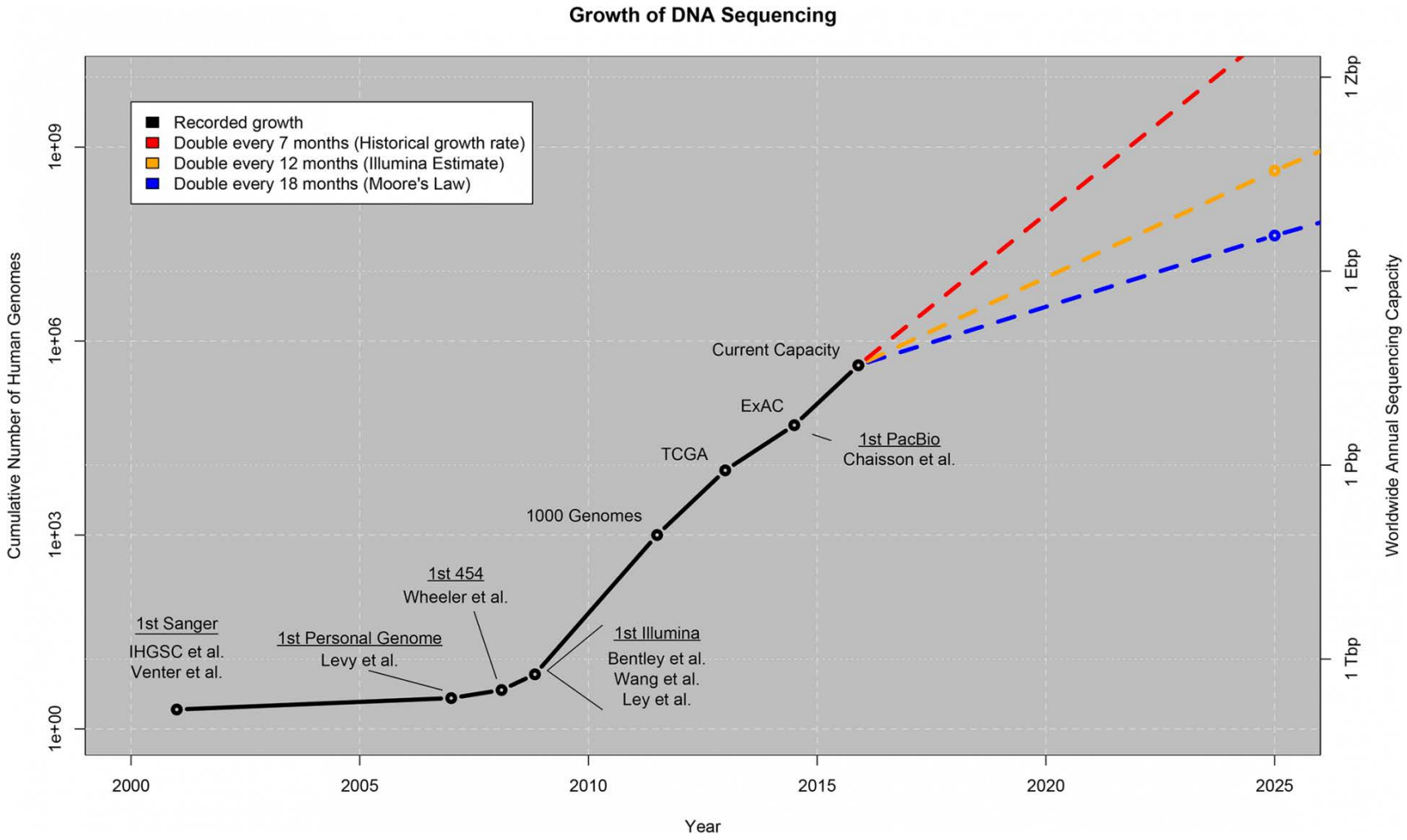


About 3 quintillion bytes of data per day

The 4 v's of #bigdata

Volume	• Large repositories
Velocity	• Increasing trajectory
Variety	• Clinical trials, omics, biometrics, EHRs, unstructured content
Veracity	• Uncertainty re: data quality/integrity

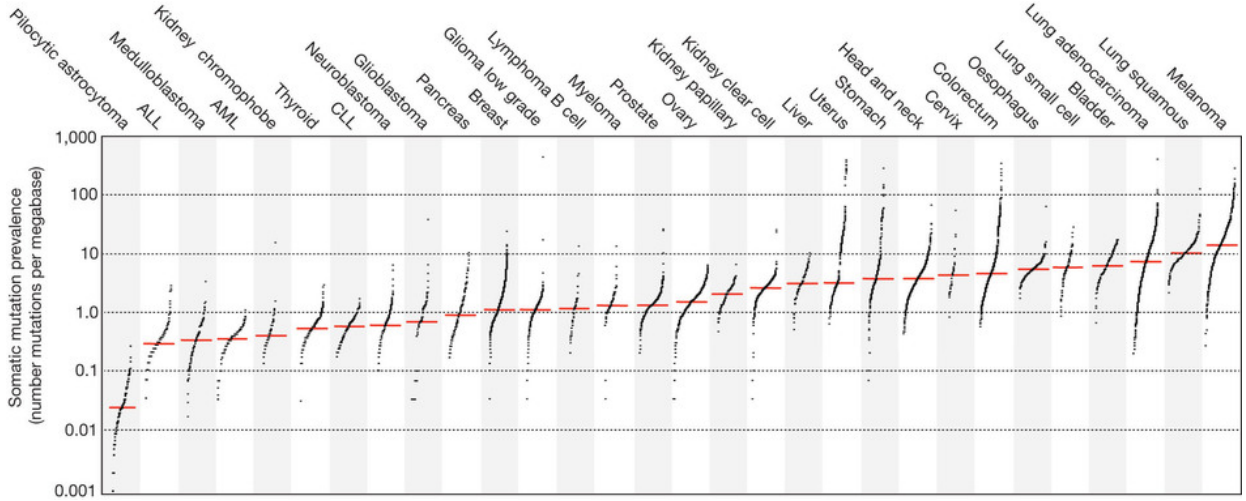
Velocity greater than anticipated



Stephens ZD, et al. PLoS Biol. 2015 Jul; 13(7): e1002195

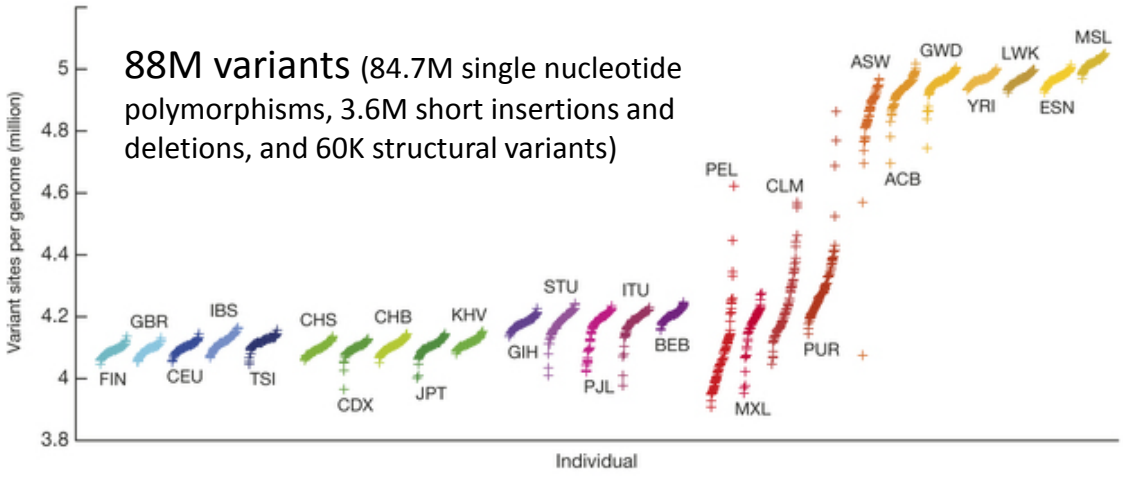
Large amount of diversity

Tumor



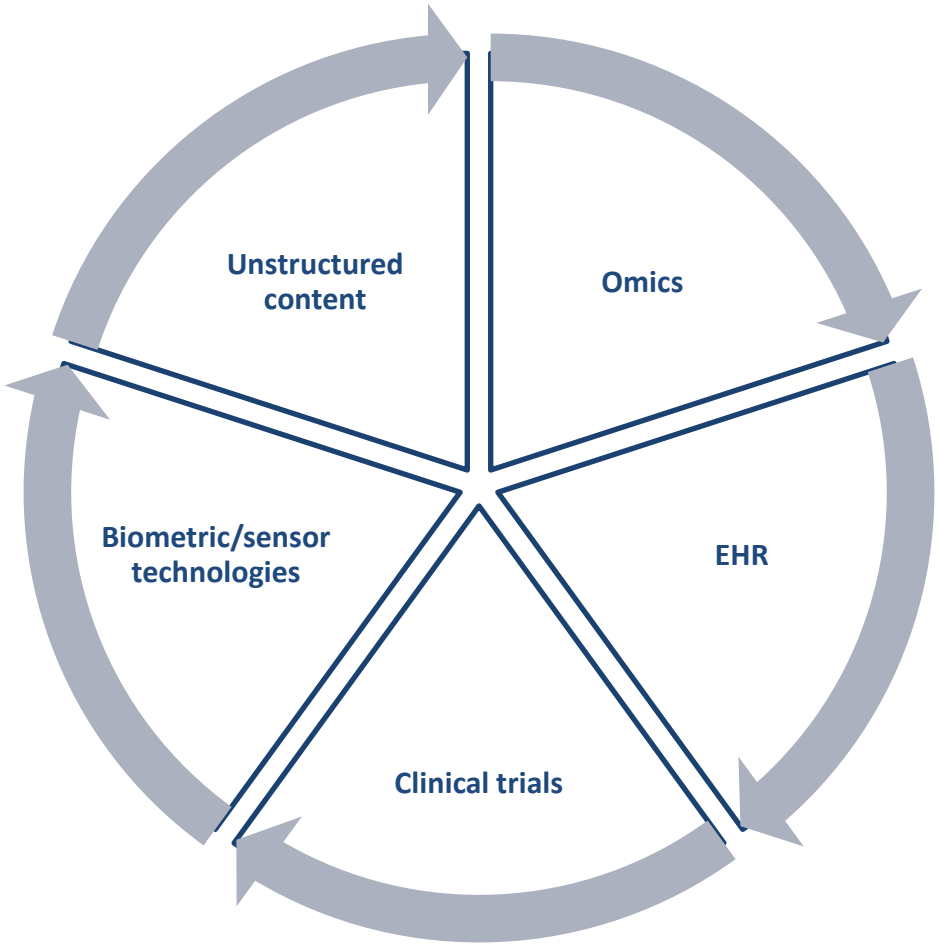
Individual

88M variants (84.7M single nucleotide polymorphisms, 3.6M short insertions and deletions, and 60K structural variants)



Alexandrov LB, et al. Nature. 2013 Aug 22;500(7463):415-21.
The 1000 Genomes Project Consortium. Nature. 2015 Oct 1;526(7571):68-74.

Leveraging #bigdata requires breaking siloes



Why?

We are nearing the limits of siloed approaches

"Driver" mutations in NSCLC:

	Adenocarcinoma	Squamous-cell carcinoma
EGFR	5–15%*	<5%†
ALK	5–15%	<5%
HER2	<5%	0
BRAF	<5%	0
KRAS	>15%	<5%
PIK3CA	<5%	<5%
AKT1	0	<5%
MAP2K1	<5%	0
MET	<5%	<5%

2010

Pao W, et al. Lancet Oncol. 2011 Feb;12(2):175-80.

	Frequency
Mutations	
KRAS	32·2%
EGFR	11·3%
NF1	8·3%
BRAF	7·0%
MET exon 14 skipping	4·3%
RIT1	2·2%
ERBB2	1·7%
HRAS, NRAS, MAP2K1	1·7%
Translocations	
ROS1	1·7%
ALK	1·3%
RET	0·9%
Amplifications	
MET	2·2%
ERBB2	0·9%

2015

Devarakonda S, et al. Lancet Oncol. 2015 Jul;16(7):e342-51.

Clear recognition

Key investments in President's 2016 budget to launch the Precision Medicine initiative

INVESTMENT	AGENCY	OBJECTIVES
$130M	NIH	To develop, in collaboration with other agencies, a voluntary national research cohort of a million or more volunteers. • Sources of information will include medical records, environmental and lifestyle data, patient-generated information, and personal device and biometric sensor data.
$70M	NCI	To scale up efforts to identify genomic drivers in cancer and apply that knowledge in the development of more effective approaches to cancer treatment.
$10M	FDA	To acquire additional expertise and advance the development of high-quality curated databases to support the regulatory structure needed to advance innovation in precision medicine and protect public health.
$5M	ONC	To develop interoperability standards and requirements that address privacy and enable secure exchange of data across systems for the voluntary national research cohort initiative.

M indicates million; NCI, National Cancer Institute; NIH, National Institutes of Health; ONC, Office of the National Coordinator for Health.

Khozin S, Blumenthal GM. *AJMC* Aug 2015

The White House
Office of the Press Secretary

For Immediate Release July 29, 2015

Executive Order -- Creating a National Strategic Computing Initiative

EXECUTIVE ORDER

https://www.whitehouse.gov/the-press-office/2015/07/29/executive-order-creating-national-strategic-computing-initiative

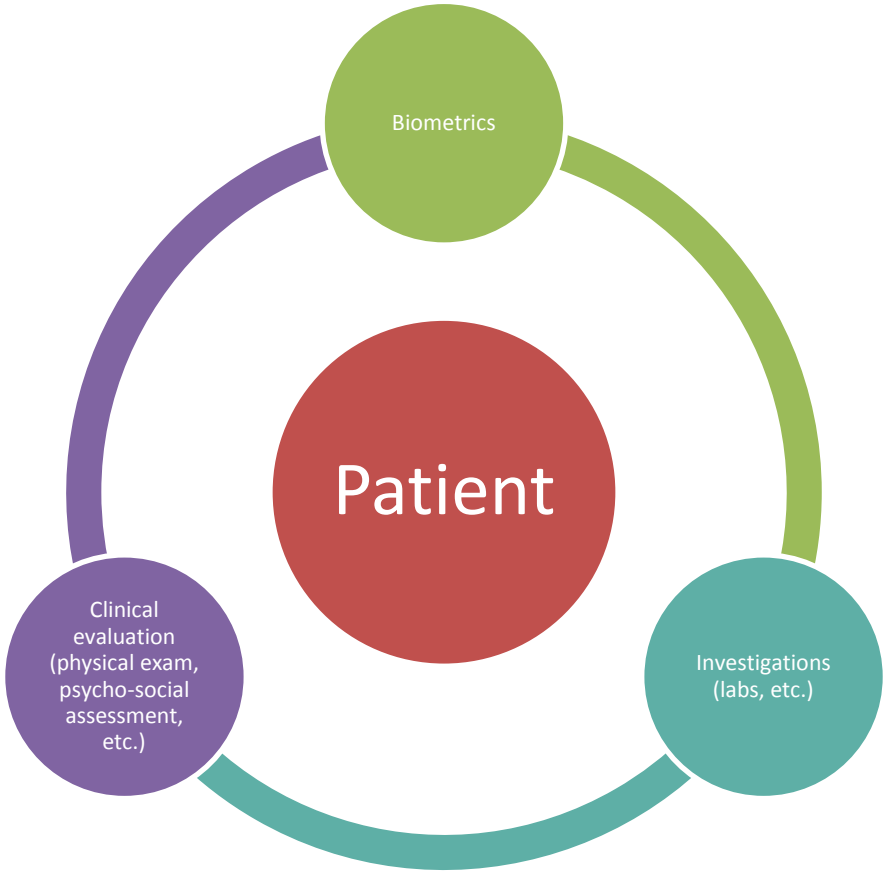
siloed data→ #bigdata → #smartdata

Reductionist

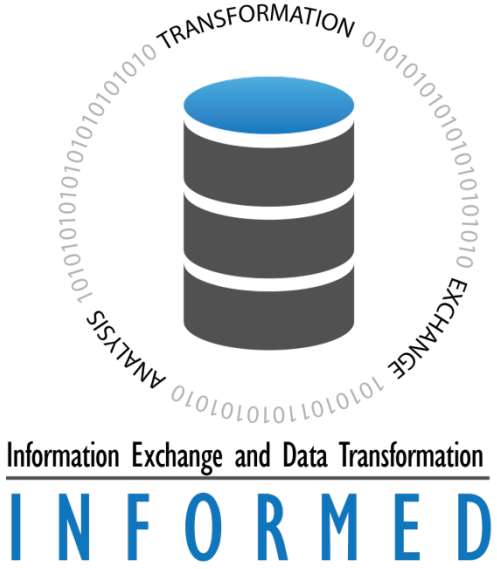
- One-gene one-drug
- Trials with strict eligibility criteria
- Leap of faith clinical development

Holistic

- Pragmatic trials
- Multiomics
- Systems biology
- Predictive analytics


Biometrics
Patient
Clinical evaluation (physical exam, psycho-social assessment, etc.)
Investigations (labs, etc.)

In the near future, #bigdata will simply be called data



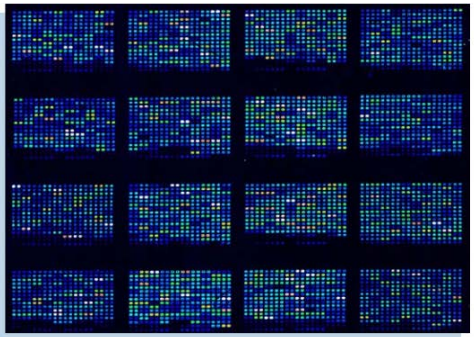
Building capabilities and infrastructure to optimize data analysis, enable new data explorations, and serve as a platform for dialogue and stakeholder engagement to advance regulatory science and FDA's mission of protecting and **promoting** the public health

FDA's strategic priorities for regulatory science

FDA's regulatory scientists have a unique ability to facilitate development of knowledge and clinical evaluation tools needed for successful translation of discoveries into viable products.

FDA will collaborate with others to help develop the new tools and approaches needed to catalyze the development of personalized medicine.

Expansion and improvement of the existing IT infrastructure would enhance and augment these ongoing activities.



http://www.fda.gov/downloads/ScienceResearch/SpecialTopics/RegulatoryScience/UCM268225.pdf

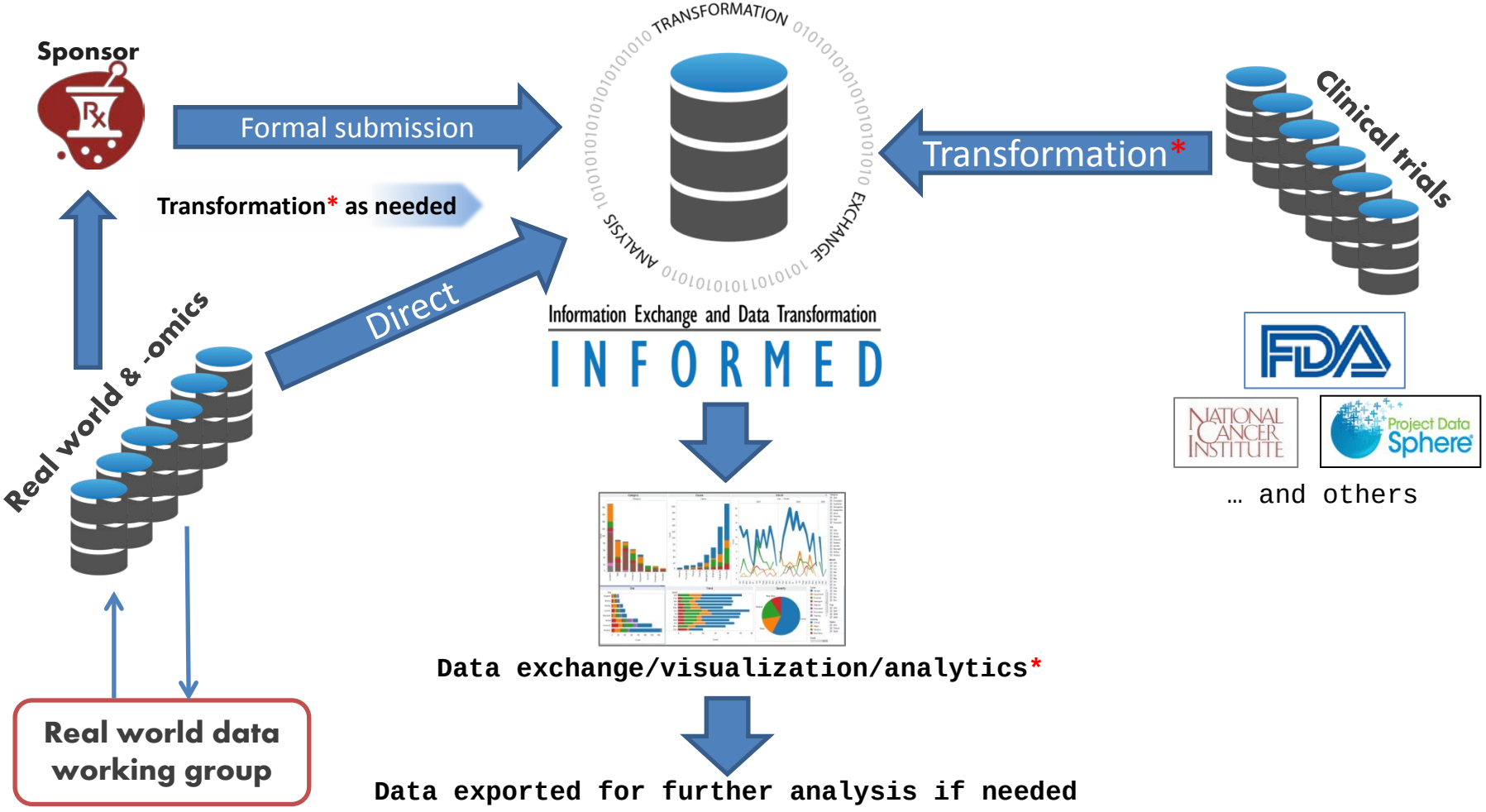
INFORMED: 3 components

1. Transformation of FDA's existing clinical trial datasets into a common standard;

2. Development of a big data environment for storage and mining of transformed datasets; and

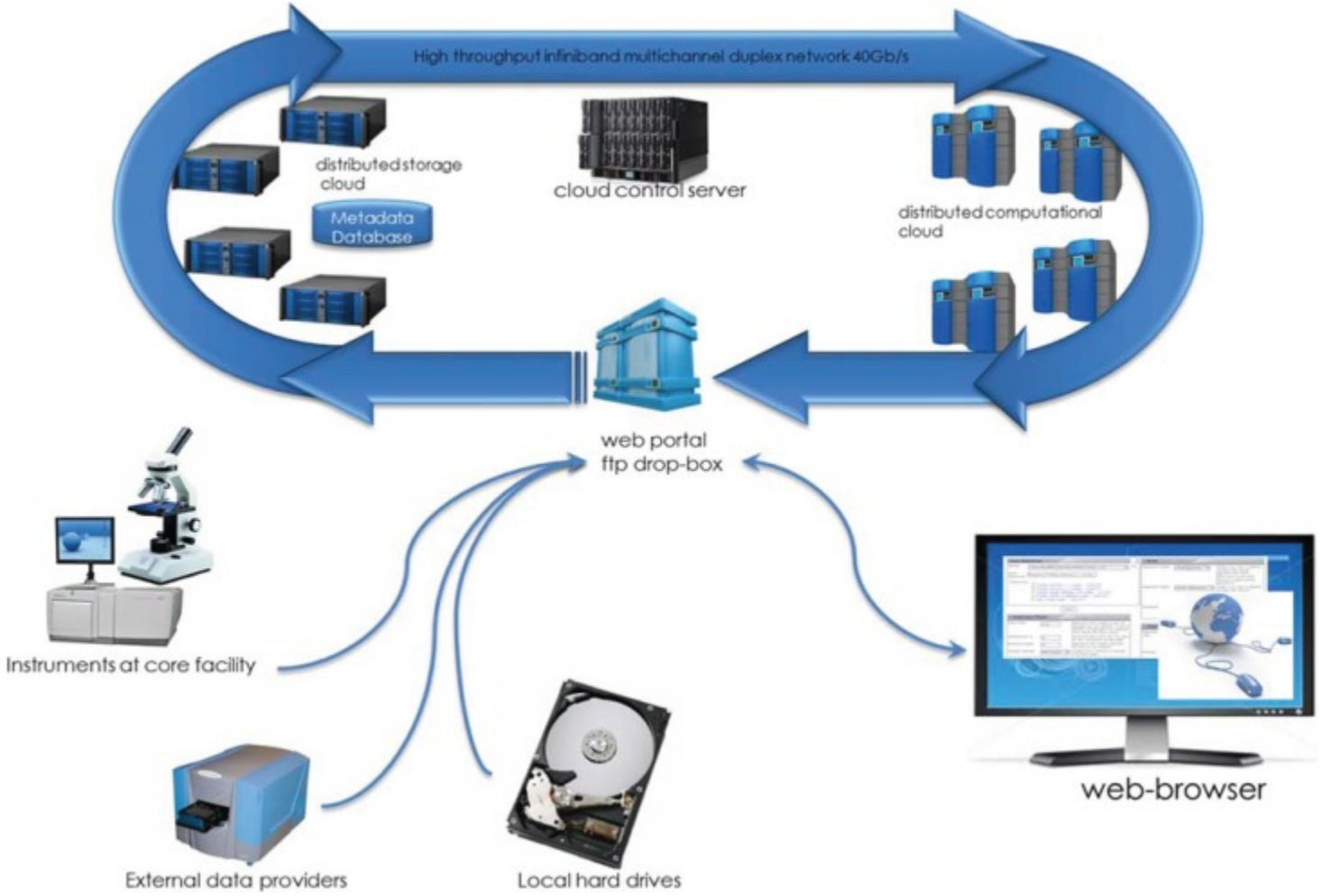
3. Incorporation of diverse pipelines of data (e.g. electronic health records, biometric monitoring devices, unstructured content [e.g. social media], omics) into the big data environment

INFORMED: Framework



*Technology and software development

High-Performance Integrated Virtual Environment (HIVE)

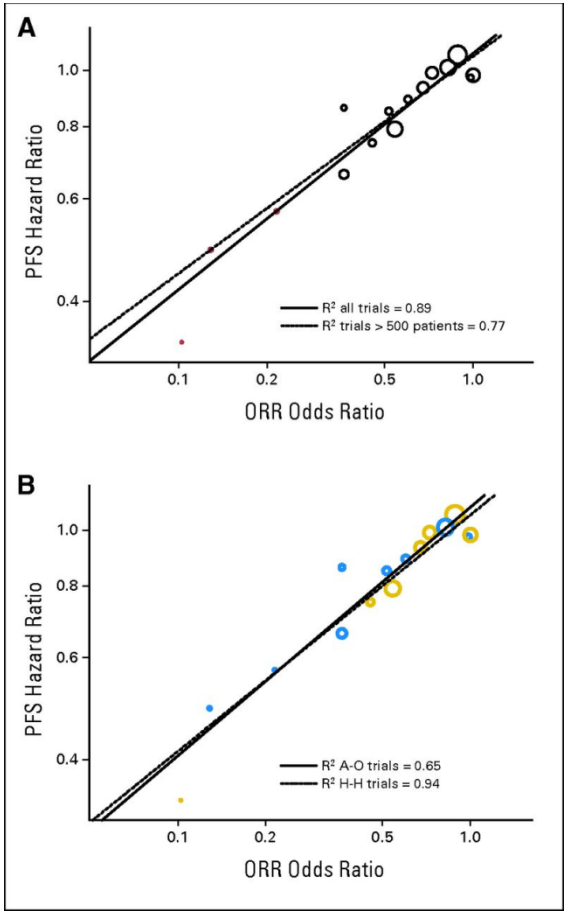


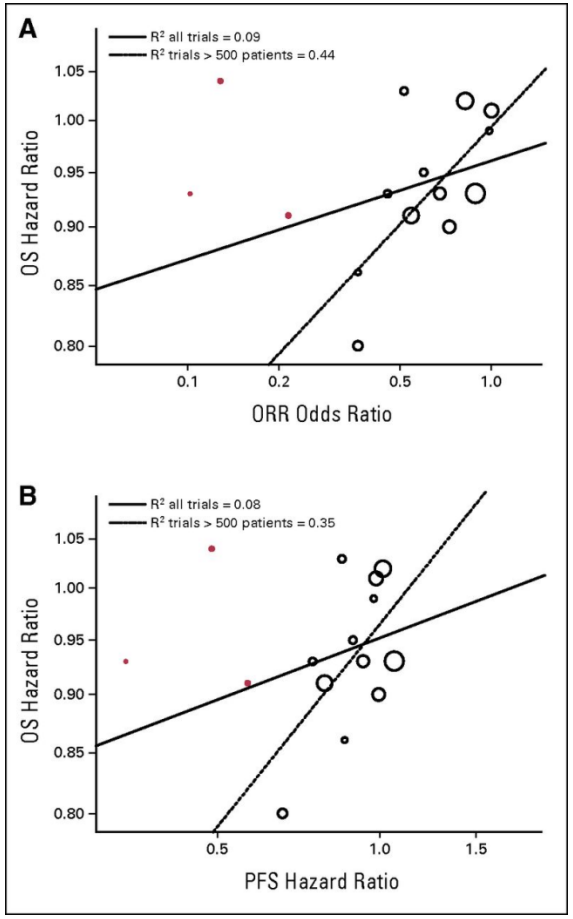
Simonyan V, Mazumder R. Genes (Basel). 2014 Sep 30;5(4):957-81

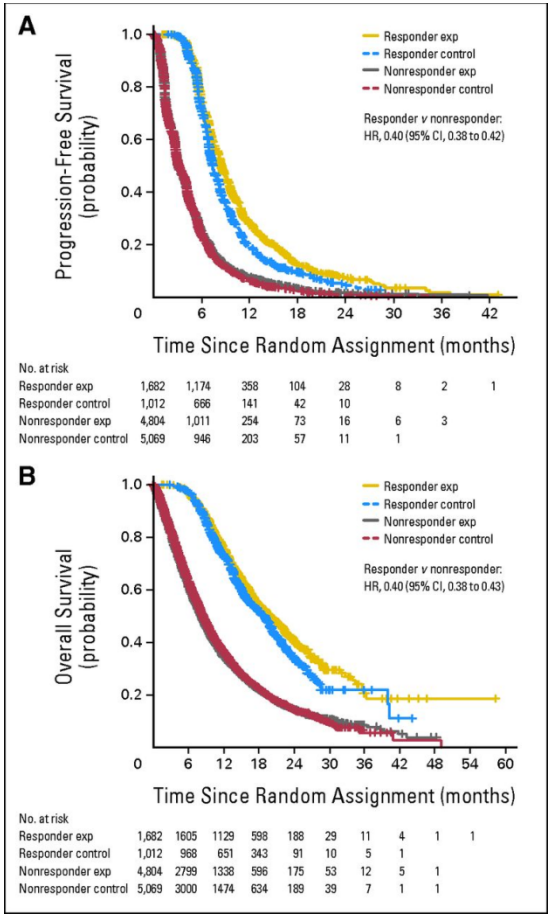
Project examples

Building on pervious experience and developing new hypotheses

Efficacy endpoints in non-small cell lung cancer (NSCLC)



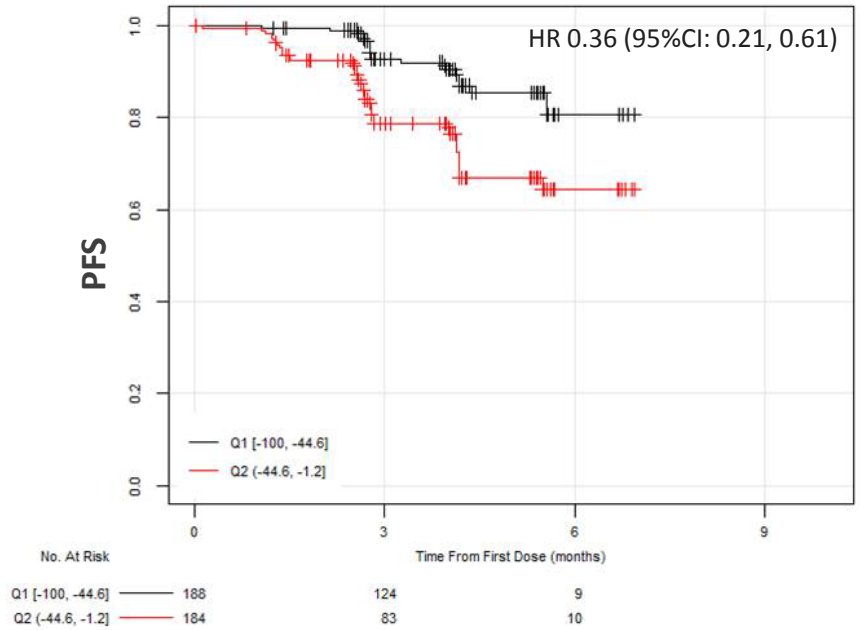




Blumenthal GM, et al. J Clin Oncol. 2015 Mar 20;33(9):1008-14.

Multi-dimensional model to capture tumor kinetics

Depth of tumor response



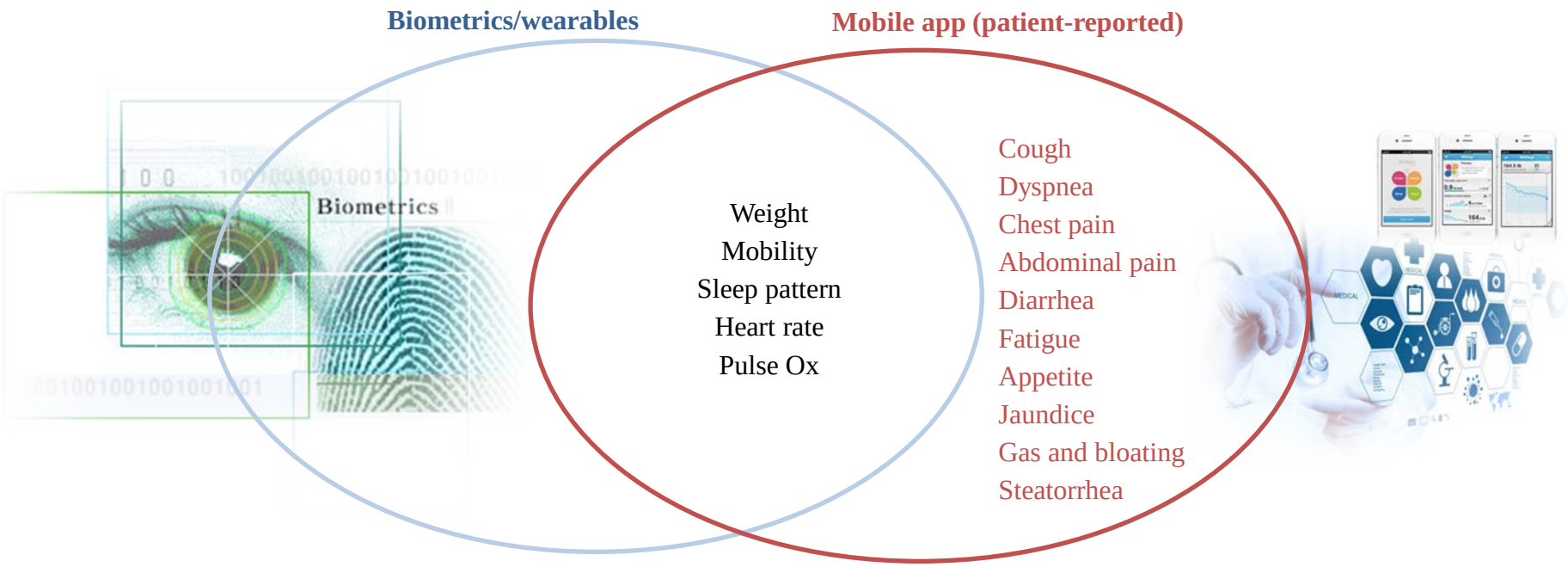
Exploratory pooled analysis of two single arm trials in advanced NSCLC treated with next generation TKI

Patients with >0% decrease in tumor size from baseline based on independent radiology review

Pazdur index

- Response (depth, velocity)
- Time: pre-specified landmarks (t_1, t_2, …)
- Fidelity: % patients on treatment at t_x
- Other (work in progress)

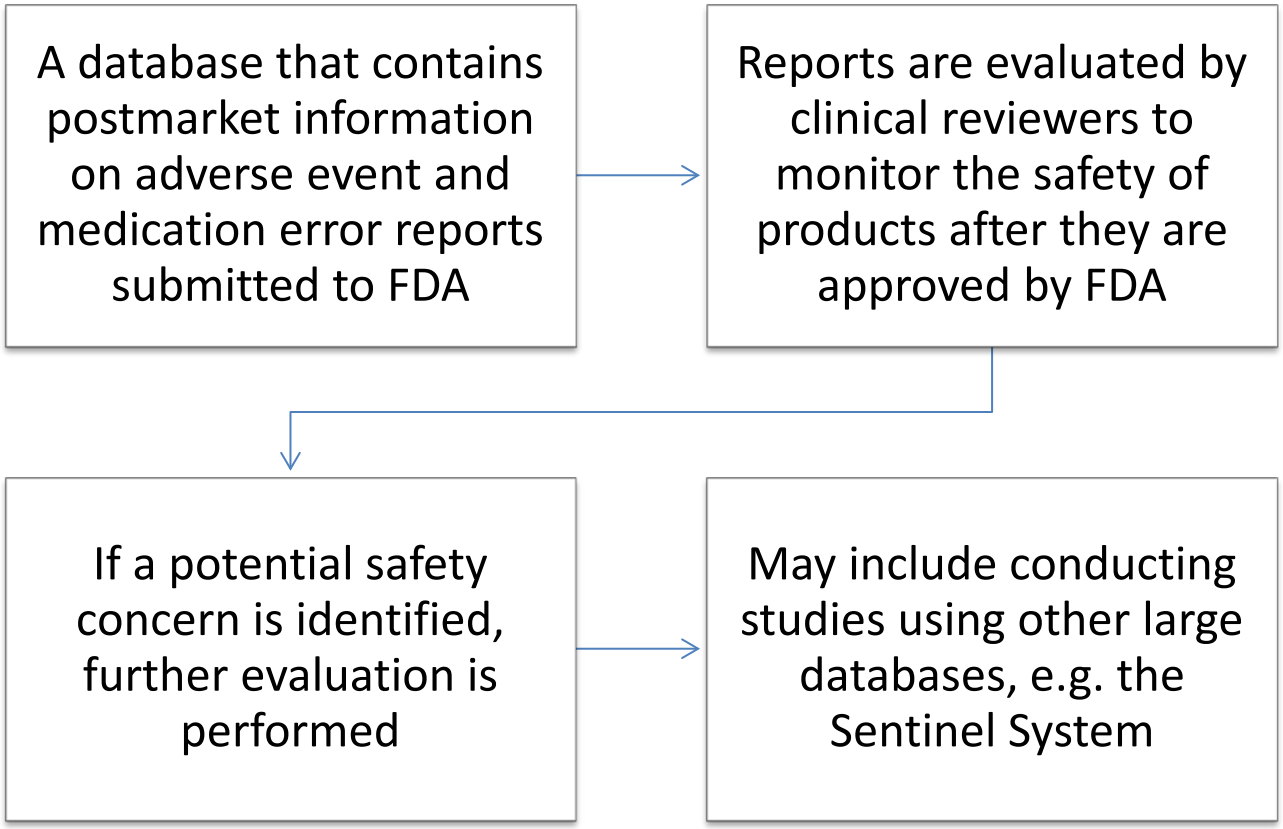
Patient- and biometrically-captured experience in oncology



"Real world" data

- FDA Adverse Event Reporting System (FAERS)
- Sentinal Initiative
- Medicare Claims
- Patient registries
  - Usually via formal submissions

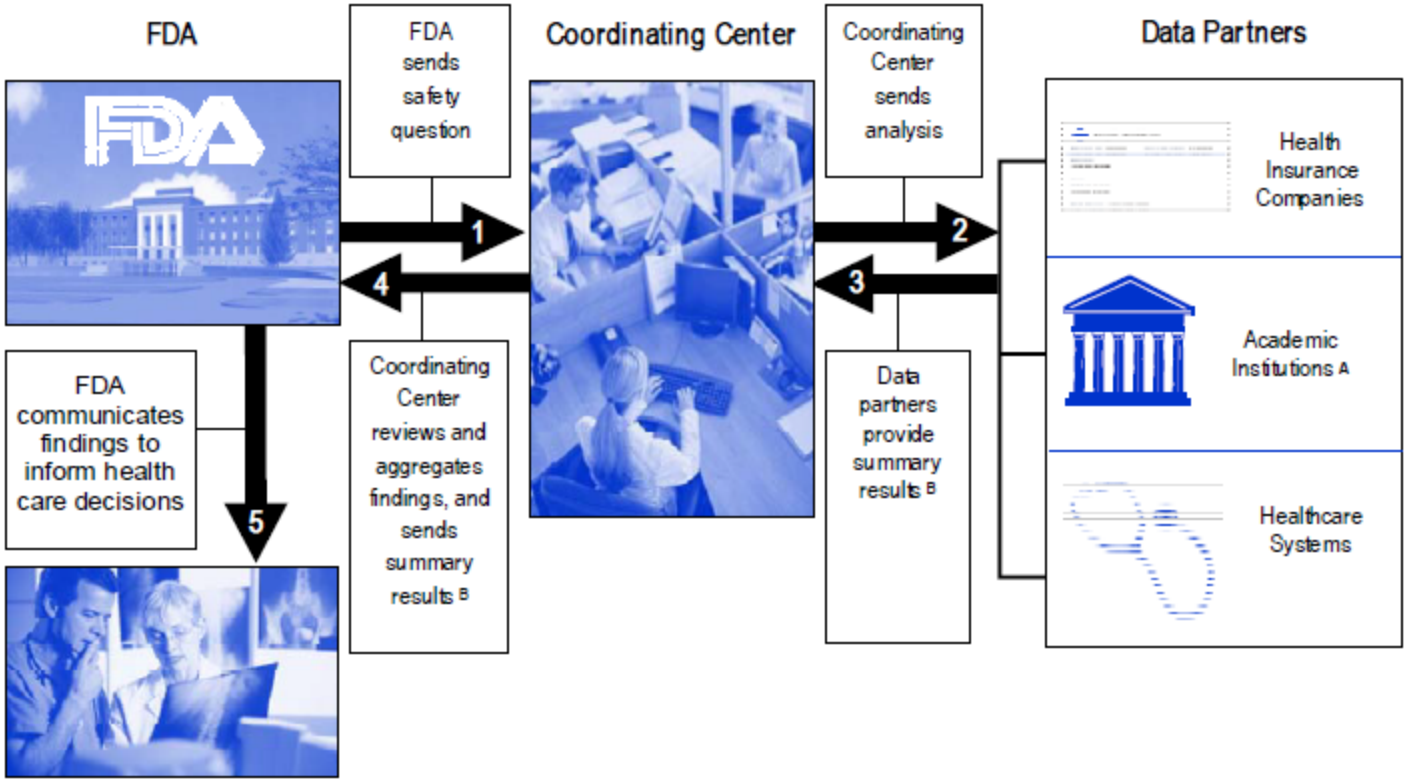
FDA Adverse Event Reporting System (FAERS)



Sentinel Initiative

- Section 905 of the Food and Drug Administration Amendments Act (FDAAA), which became law in September 2007, mandates FDA to develop an enhanced ability to monitor the safety of drugs after these products reach the market using “active surveillance”
- In May 2008, HHS announced the launch of FDA’s Sentinel Initiative
- Based primarily on billing codes
  - International Classification of Disease codes (ICD)
  - The Current Procedural Terminology (CPT) codes

Sentinel Initiative



A. Only those academic institutions with electronic healthcare data will receive safety questions for evaluation.
B. Data partners will provide summary results from analyses conducted within their secure data environments. Those summary results will not include directly identifiable health information.

Challenges with claims-based data

Clinical relevance

Missing data

- Information on disease characteristics (e.g., stage, histology, molecular profile) and clinical outcomes (e.g., toxicity, response to treatment)

http://medicaleconomics.modernmedicine.com/medical-economics/news/20-bizarre-new-icd-10-codes?page=0,0

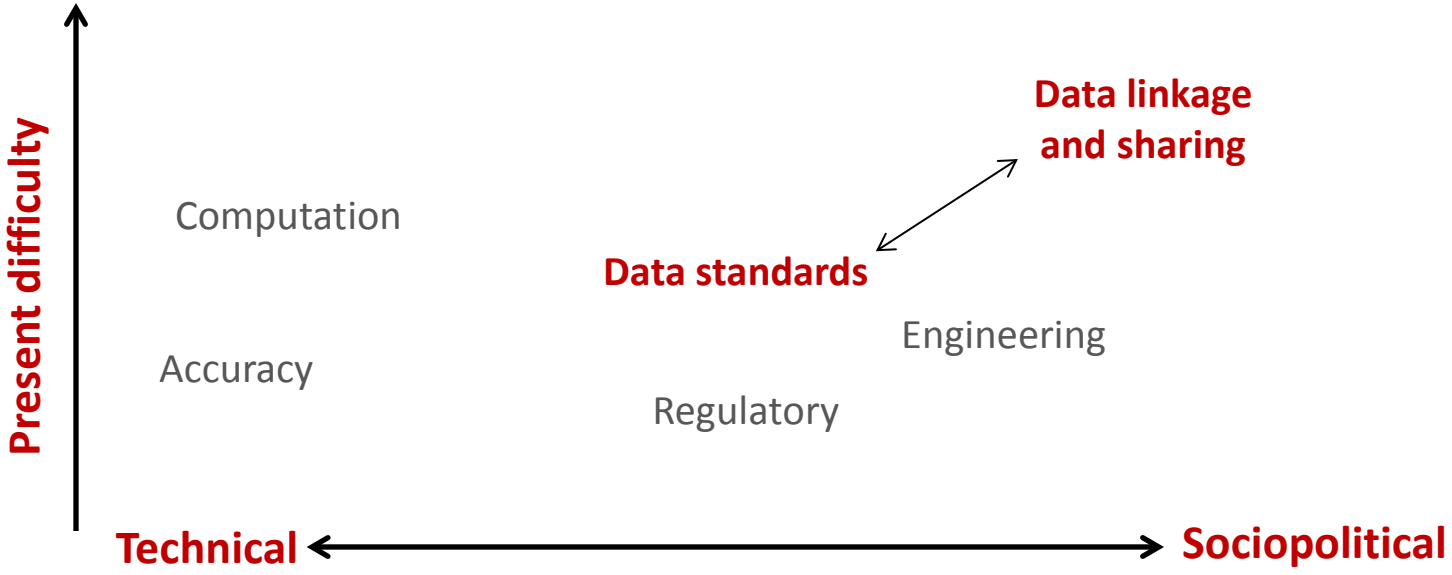
Real world data: beyond postmarket surveillance?

- Data on natural history of disease, available therapy definitions
- Incorporation of randomization into systems collecting population health data
  - Cluster-randomized studies
    - Individuals grouped into “clusters”
    - Can be a factorial design: multiple clusters and interventions
    - Inference made to the individual

OHOP real world data working group
Califf RM, Ostroff S. Sci Transl Med. 2015 Jul 15;7(296):296ed9.

Challenges

More than just technology



Adapted with modification from Kohane IS. Science. Vol. 349 no. 6243 pp. 37-38

Avoid data standards proliferation

Data standards harmonization

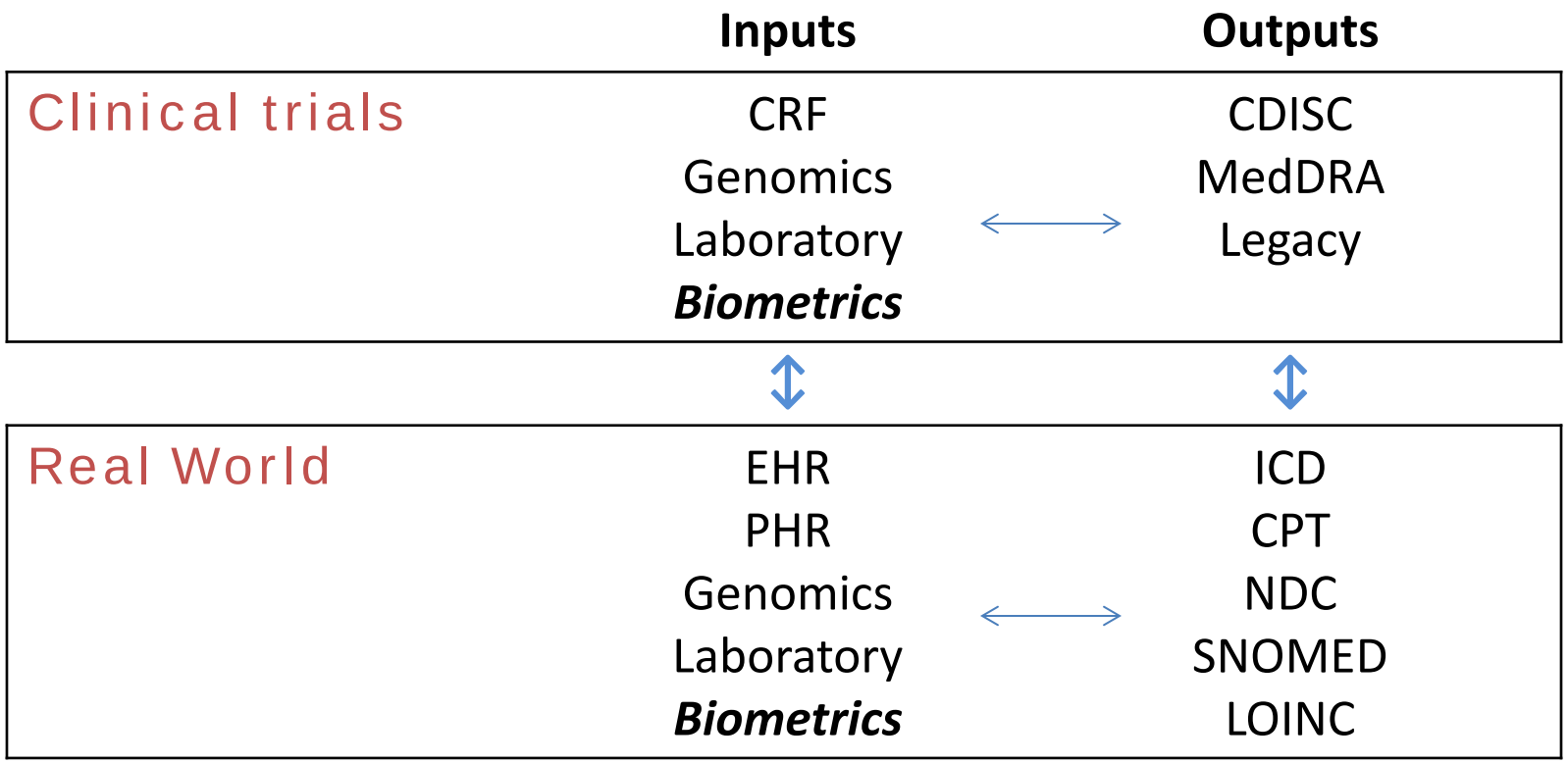
Clinical Trials

- Clinical Data Interchange Standards Consortium (CDISC)
- Coalition For Accelerating Standards and Therapies (CFAST)
  - Therapeutic area standards development with input from FDA and other stakeholders
    - Lung, breast, prostate, brain tumors

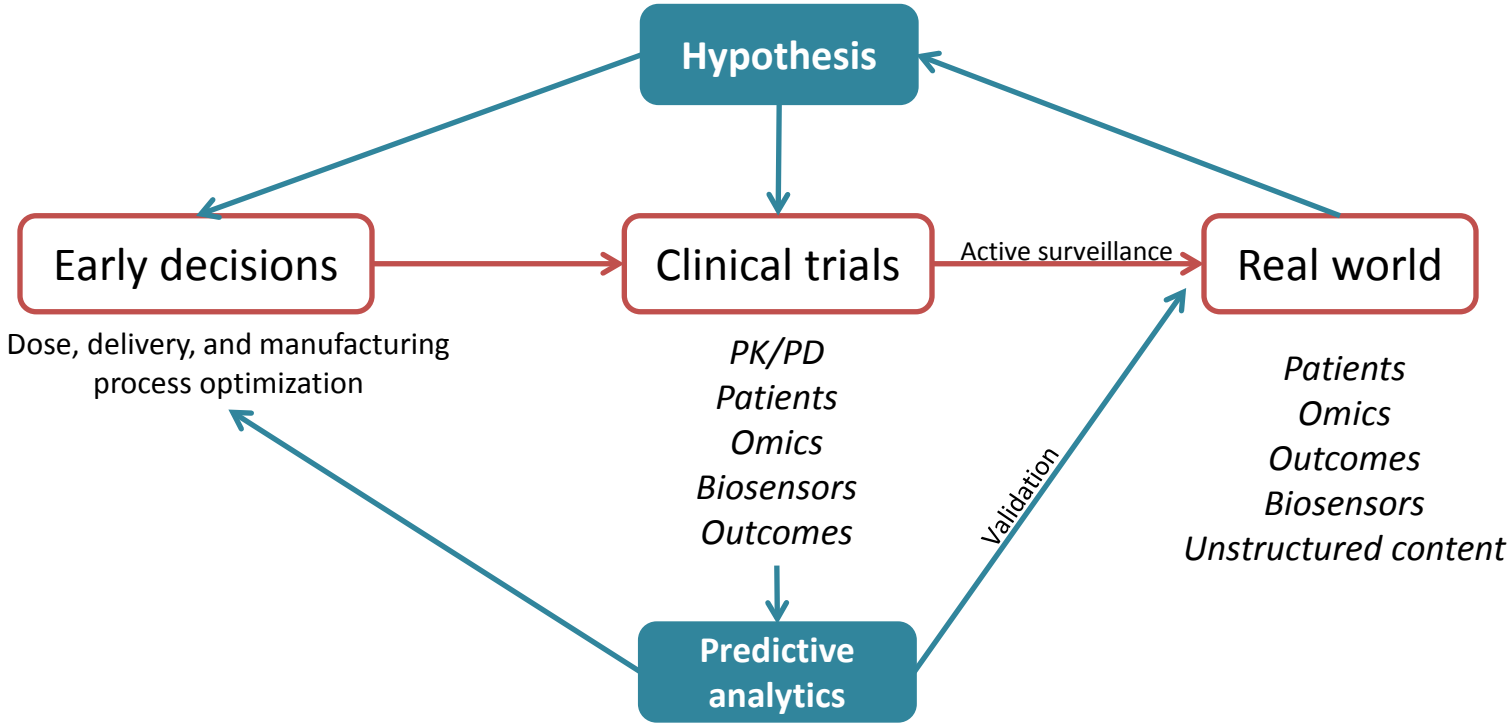
Real World

- Health Level Seven (HL7)
- Biomedical Research Integrated Domain Group (BRIDG) HL7 Work Group is working on developing a shared information model
- BRIDG includes CDISC, HL7, FDA, and NIH among its stakeholders

Harmonization



#bigpicture: product lifecycle

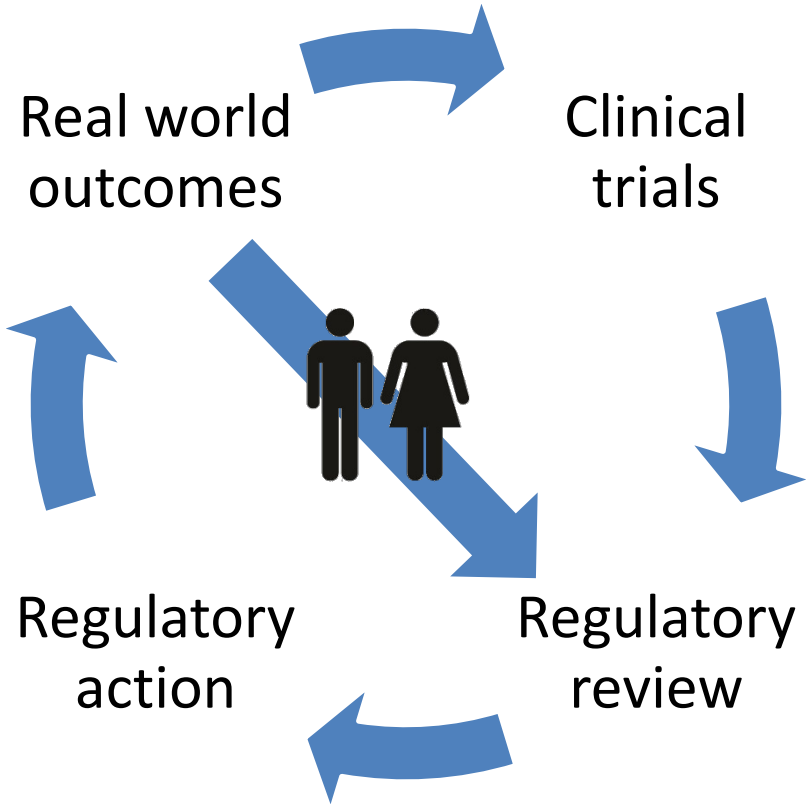


#biggerpicture

The learning health system (IOM)

A system where science, informatics, incentives, and culture are aligned for continuous improvement and innovation

Discovery as a product of the healthcare delivery experience



#thankyou