Real World Evidence
Collaboration and Convergence for Change

Big Data, Digital and Tech—and Real World Applications and Implications for Industry

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48th Annual Conference (Vienna, Austria)

EUROPEAN MEDICAL WRITERS ASSOCIATION

09 May 2019

Ambition of RWE

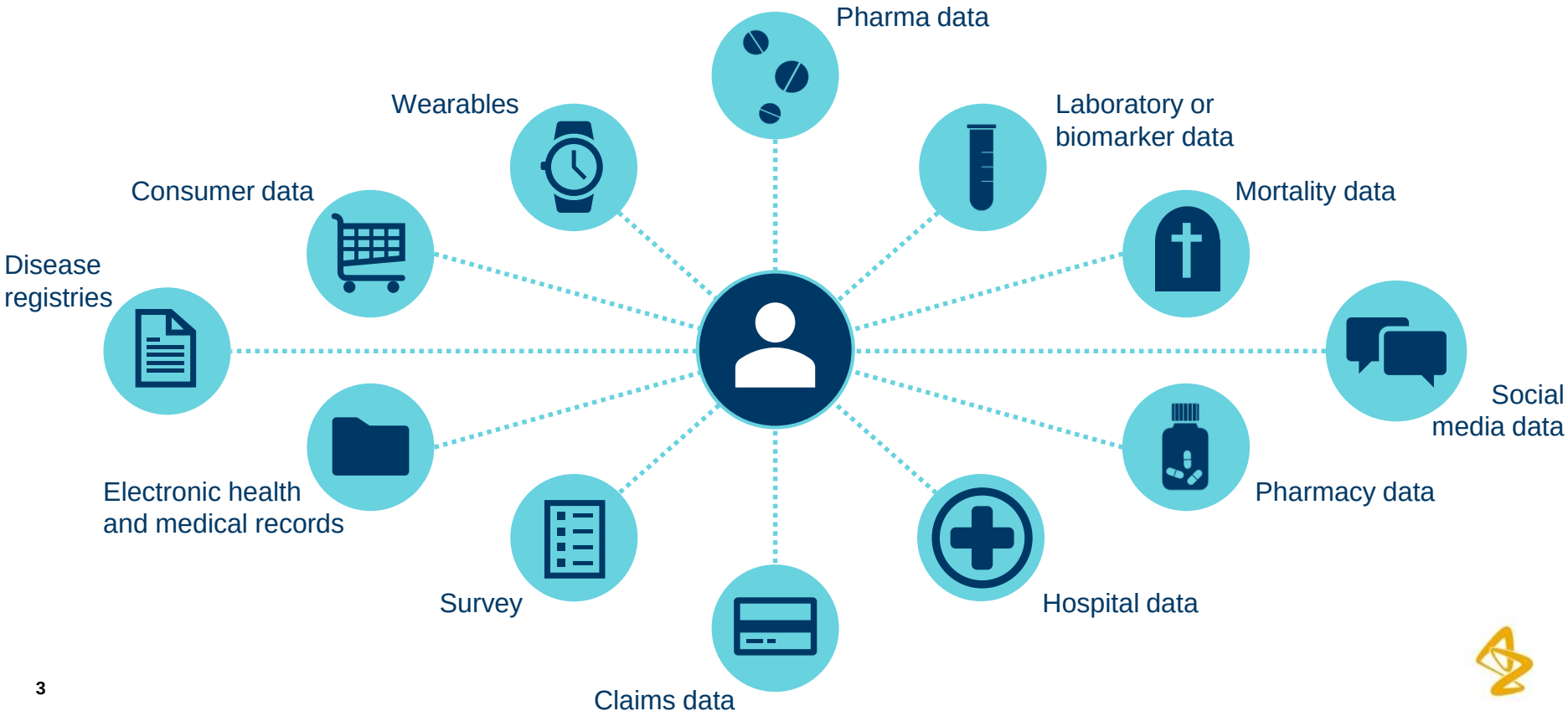
Higher quality and more comprehensive, efficient generation of evidence in order to make faster, better, earlier and more targeted discovery, access, and benefit-risk decisions

Create a holistic picture of the patient journey through the health care system through the collection, generation, utilization and analysis of real-world data to support RCTs

Build ecosystems and innovate through collaborations and strategic alliances to better serve patients, providers, payers, and partners for improved outcomes

Patient-Centered Science

Big Data to ‘N of 1’



Complex, Converging Forces Changing Healthcare

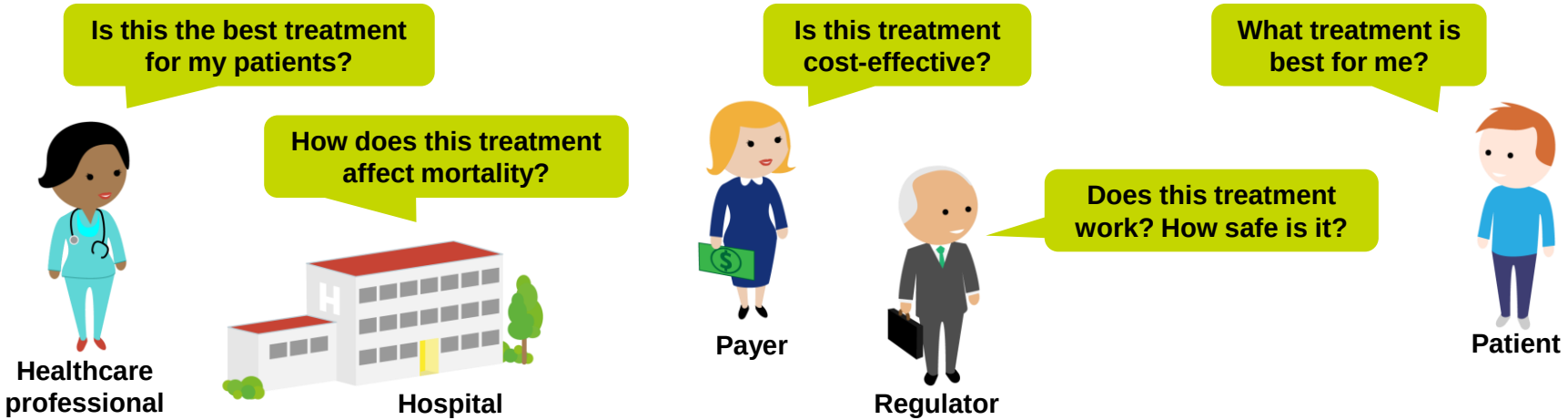
The five disrupters

Source: Bain & Company

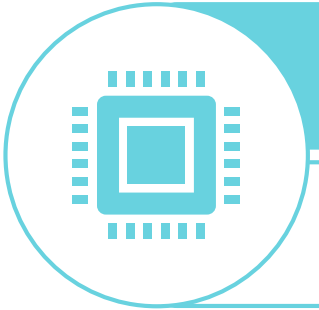
- Changes across entire ecosystem
- Disruption and convergence across people, process, data, technology
  - Data Science, Digital, AI/ML, Blockchain, Analytics, ‘Omics’, Value & Reimbursement
  - Educated and Empowered Patients!
- Need to understand various stakeholder needs, perspectives; generate evidence to improve outcomes, inform value, enable access, better lives

Growing Need to Generate Real-World Evidence

- Healthcare decision-makers are interested in clinical decisions and the evidence supporting those decisions
- Understanding stakeholders and decision-maker perspectives is key to generating the right evidence



Real-World Data vs Real-World Evidence



RWD are data relating to patient health status and/or to the delivery of health care collected from a variety of sources

- Data from observational studies
- Electronic Health Record (EHR)
- Hospital/insurance claims/billing
- Patient-generated/reported information (PRO) (e.g. wearables, mobile, sensors)

RWE is the clinical evidence on the use and potential benefits or risks of a medical product derived from analyses of RWD

- Early Access Programmes
- Post-Authorization safety study
- Pragmatic clinical trials
- Observational studies
- Non-interventional studies
- Registry studies

FDA Framework for RWE: Reliability and Relevance

2016

One Hundred Fourteenth Congress
of the
United States of America
AT THE SECOND SESSION

An Act

2018

2021

Use of Real-World Evidence to Support Regulatory Decision-Making

Guidance for Industry and Food and Drug Administration Staff

"As the breadth and reliability of RWE increases, so do the opportunities for FDA to make use of this information."

Scott Gottlieb, FDA Commissioner
National Academies of Science, Engineering, and Medicine,
Examining the Impact of RWE on Medical Product Development,
September 19, 2017

Is the RWD selected **fit for use** to generate data for product effectiveness decisions?

- ✓ **New or modified indications**, **expand labels** for approved drugs
- ✓ **Post-approval study requirements**

Is the **study design** used to generate RWE able to provide **robust scientific evidence** to help address the regulatory question?

- ✓ Inform **coverage decisions,** develop **guidelines** and **decision-support tools for use in clinical practice**

Is the **execution** of the studies generating RWE able to meet FDA regulatory requirements?

- ✓ Support **clinical trial designs** and **observational studies** for innovative treatment approaches
  e.g. randomized designs using RWD, non-randomized, single-arm with RWD control, etc.

FDA's Guidance on Use of Artificial Intelligence

Oncology Healthcare Environment: Future Challenges

The healthcare environment in the US is changing, with increasing emphasis on ***value*** for the ***patient, provider and payers***.

Oncology drugs often receive regulatory approval based on a limited number of patients and follow-up in registrational trials, making ***the need for RWE even more acute for specialty care portfolios***.

Healthcare providers, patients and payors need to have high-quality data to inform treatment decisions relative to value. This will be critical to ***patient-centric*** value driven care in the future.


The New York Times

Incredible Prices for Cancer Drugs

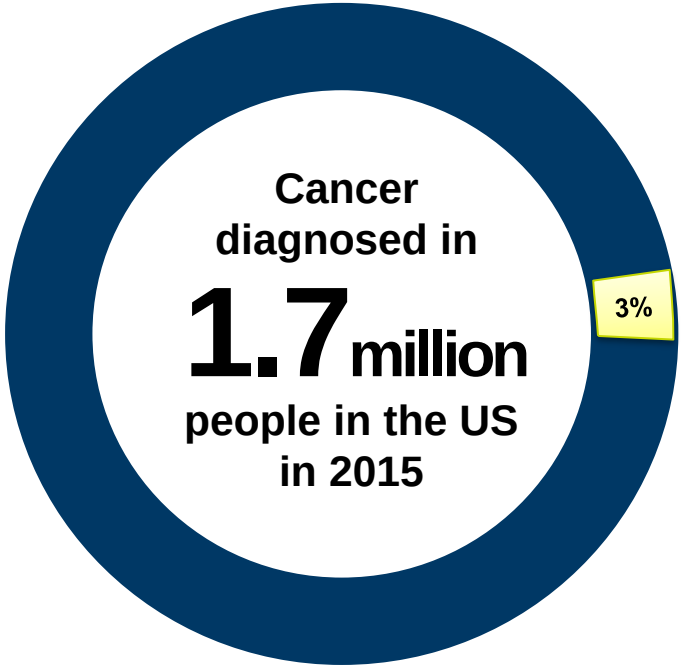
Incredible Prices for Cancer Drugs

NOVEMBER 12, 2012

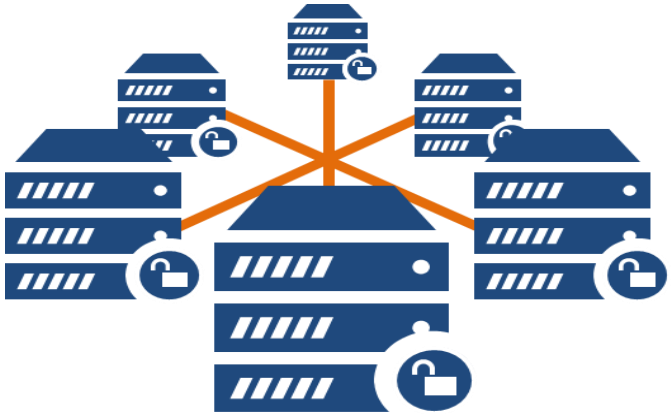
An unusually bold stand by doctors at the Memorial Sloan-Kettering Cancer Center in New York has forced a big drug company to reduce the cost of an

Validity, Generalizability, Reliability and Predictiveness

Only 3% of adult patients with cancer in the US enroll in oncology clinical trials[1]



97% of patient data locked away in unconnected files and servers



1. Unger JM *et al. Am Soc Clin Oncol Educ Book* 2016;35:185–98

Patients enrolled in oncology clinical trials often are not representative of the real world population

25%

of patients in clinical trials are aged

≥ 65 years[1]

61%

of patients in a real world setting are aged

≥ 65 years[1]

40%

of patients with kidney cancer were not healthy enough to qualify for the trials that supported the approval of their treatments[2]

90%

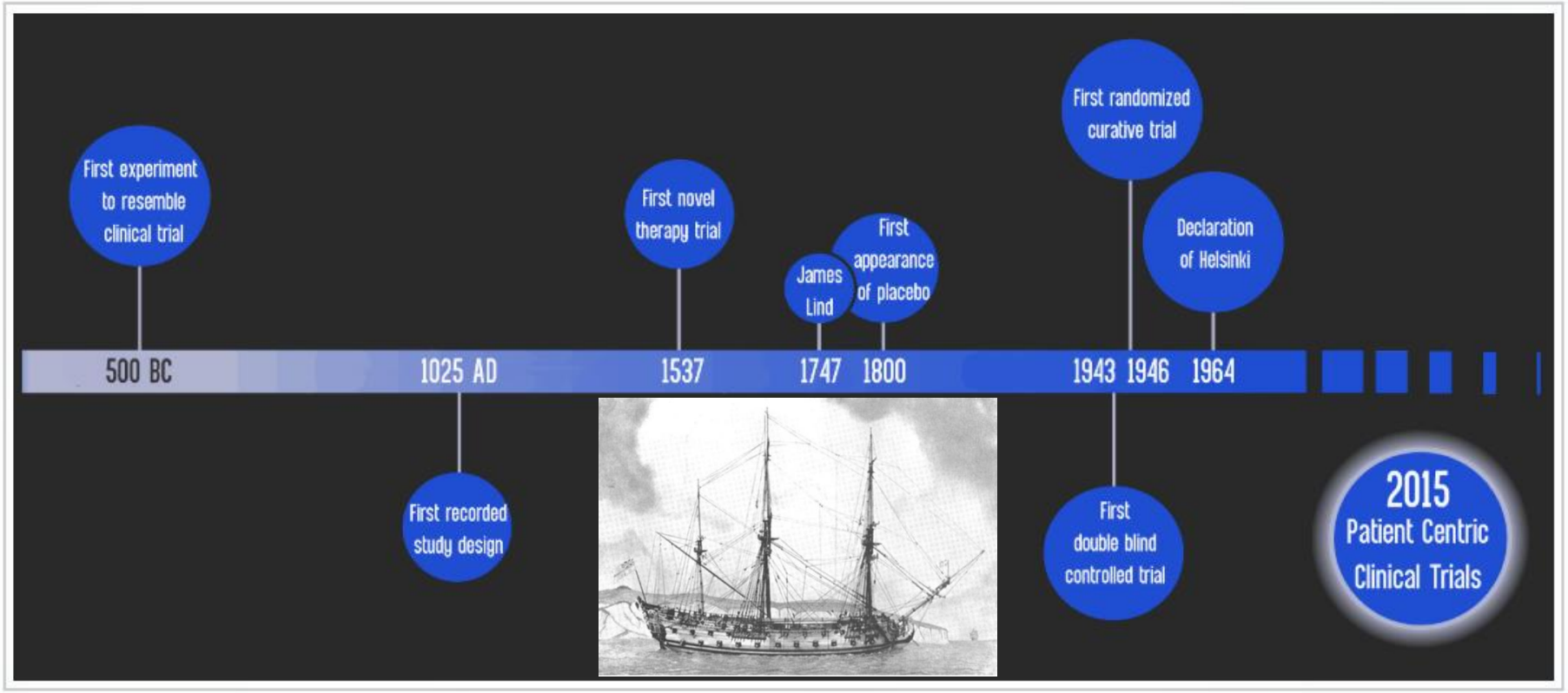
of patients in National Cancer Institute trials are white[3]

77%

of the USA population is white[3]

1. Lewis JH *et al. J Clin Oncol* 2003;21:1383–9; 2. Mitchell AP *et al. J Clin Oncol* 2014;32(suppl):6510;
3. National Cancer Institute. Available from: http://www.cancer.gov/ncicancerbulletin/051810/page7 (Accessed 23 July 2014)

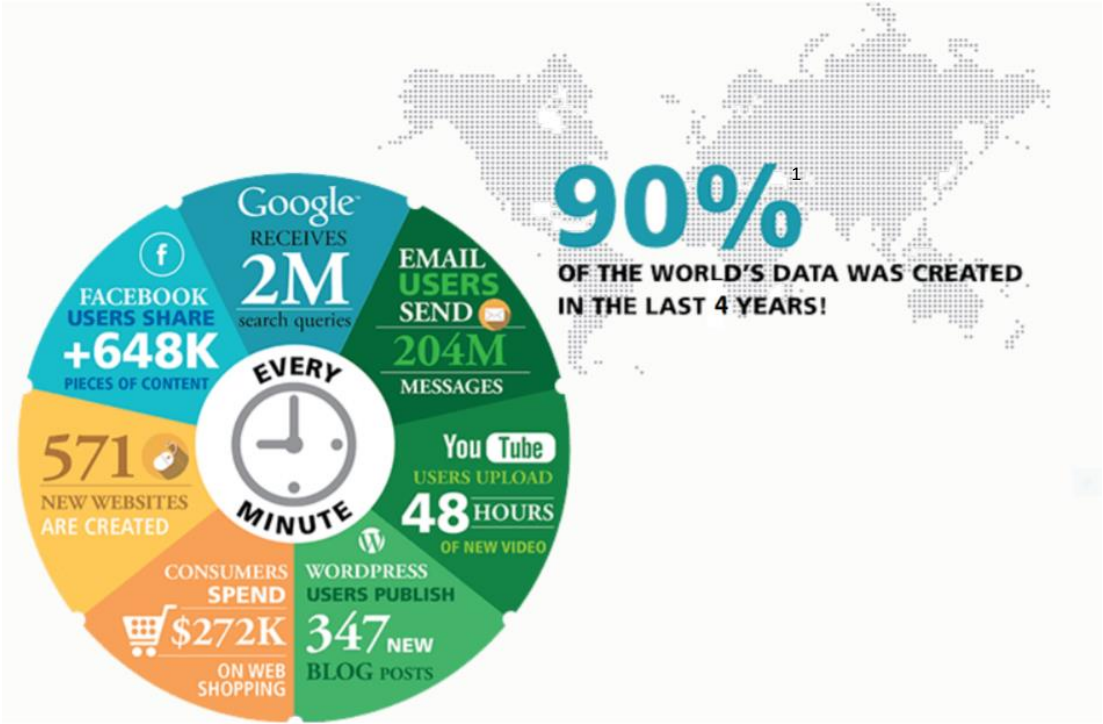
A Call to Action to Modernize our Approaches



Reconstruction of His Majesty's ship Salisbury. Credit: ***Journal of the Royal society of Medicine***

https://www.vinceandassociates.com/blog/a-historical-timeline-of-clinical-trials

Big Data… Grows Bigger by the Day



About 3 quintillion bytes of data per day

1 https://public.dhe.ibm.com/common/ssi/ecm/wr/en/wrl12345usen/watson-customer-engagement-watson-marketing-wr-other-papers-and-reports-wrl12345usen-20170719.pdf

How can RWE enrich RCT design?

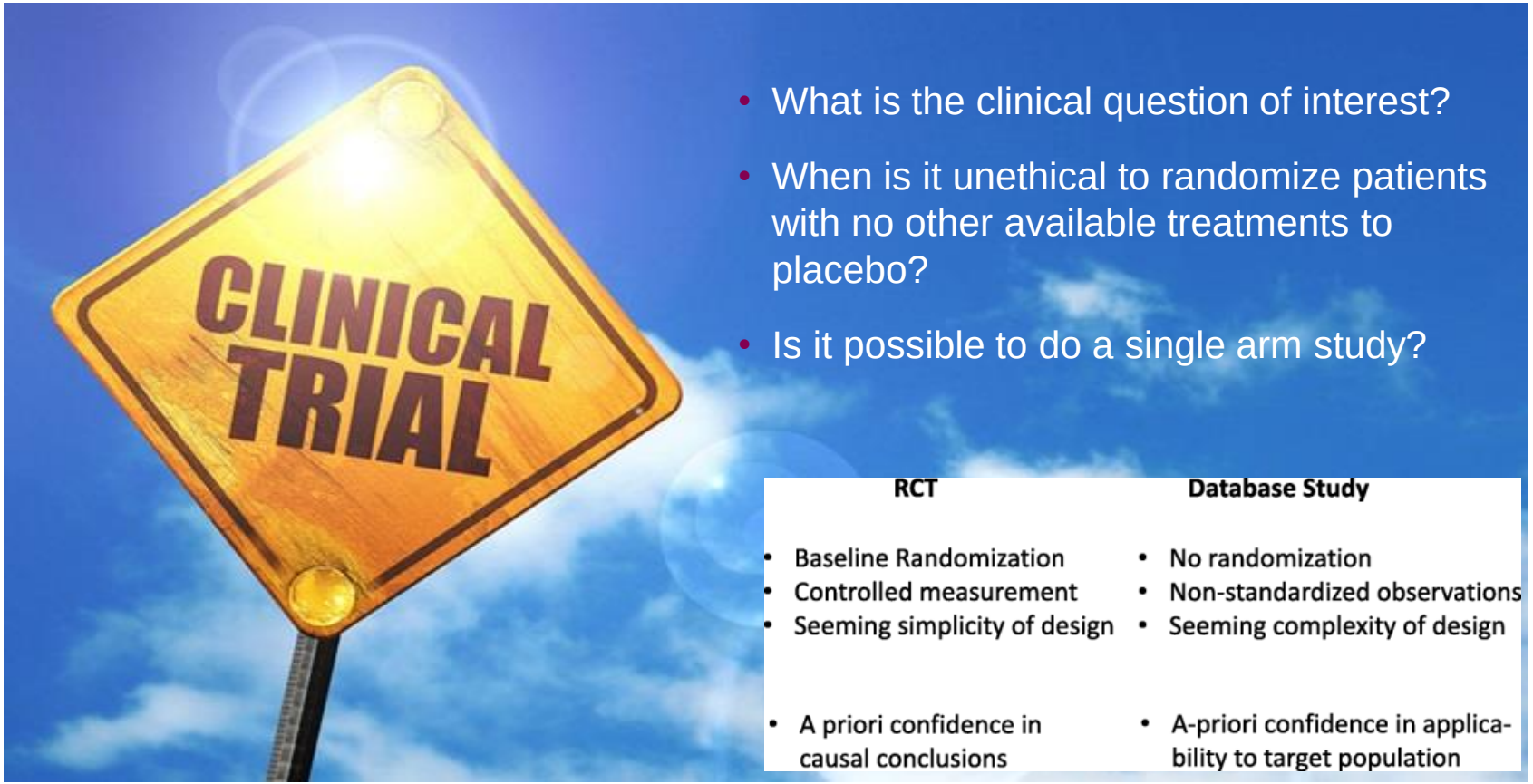
RCTs provide evidence on efficacy and safety, and remain important for securing regulatory approval

RWE can complement RCTs by assessing a wider range of outcomes representative of everyday clinical settings

How can RWE add value to clinical trials?

- Identify diseases or indications that represent a substantial burden
- Characterize patient populations
- Use RWD as a synthetic control arm
- Target and design clinical trials (e.g. optimize inclusion/exclusion criteria)

Fit for Purpose: When and how to rely to RWE

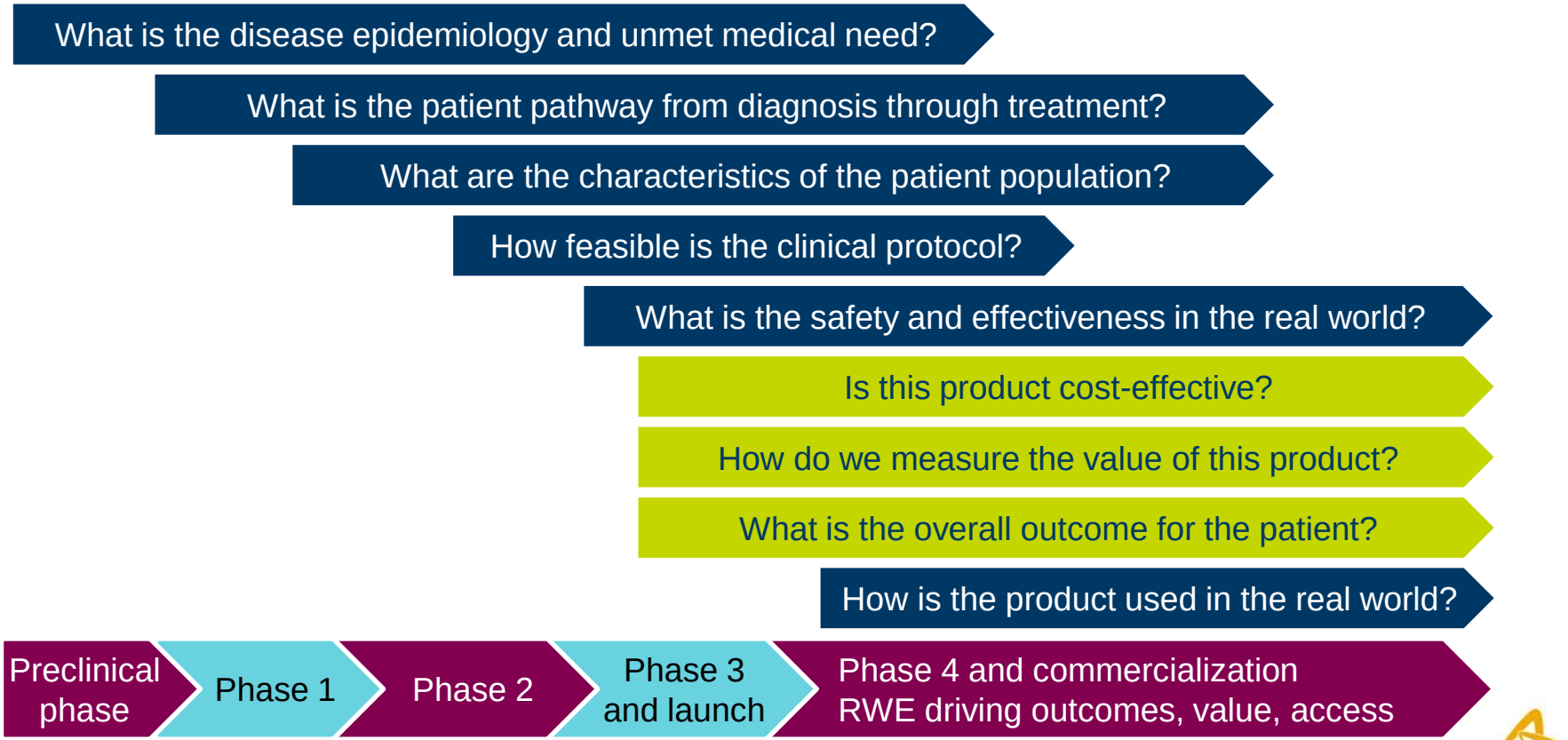


- What is the clinical question of interest?
- When is it unethical to randomize patients with no other available treatments to placebo?
- Is it possible to do a single arm study?

RCT	Database Study
• Baseline Randomization • Controlled measurement • Seeming simplicity of design	• No randomization • Non-standardized observations • Seeming complexity of design
• A priori confidence in causal conclusions	• A-priori confidence in applica-bility to target population

Clinical Pharmacology & Therapeutics, Volume: 102, Issue: 6, Pages: 924-933, First published: 24 August 2017, DOI: (10.1002/cpt.857)

RWE informs decisions across the product life cycle



Adapted from Khosla S *et al*. *F1000Res* 2018;7:111

Real world applications for different stakeholder groups

Clinical Outcomes and Effectiveness

- Outcomes research
- Comparative effectiveness
- Subpopulation evaluation
- Patient-staging/decision trees
- Clinical trial recruitment and modelling

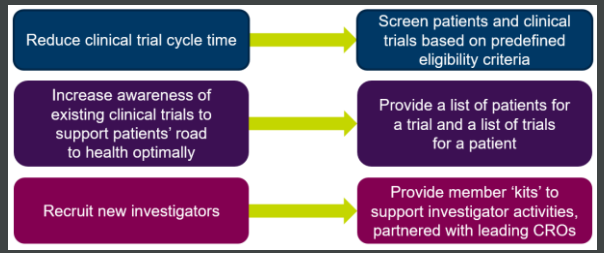
Adoption and Use

- Therapy adoption and diffusion
- Therapy and technology assessment
  - Biomarker testing
- Profiling for providers and patients

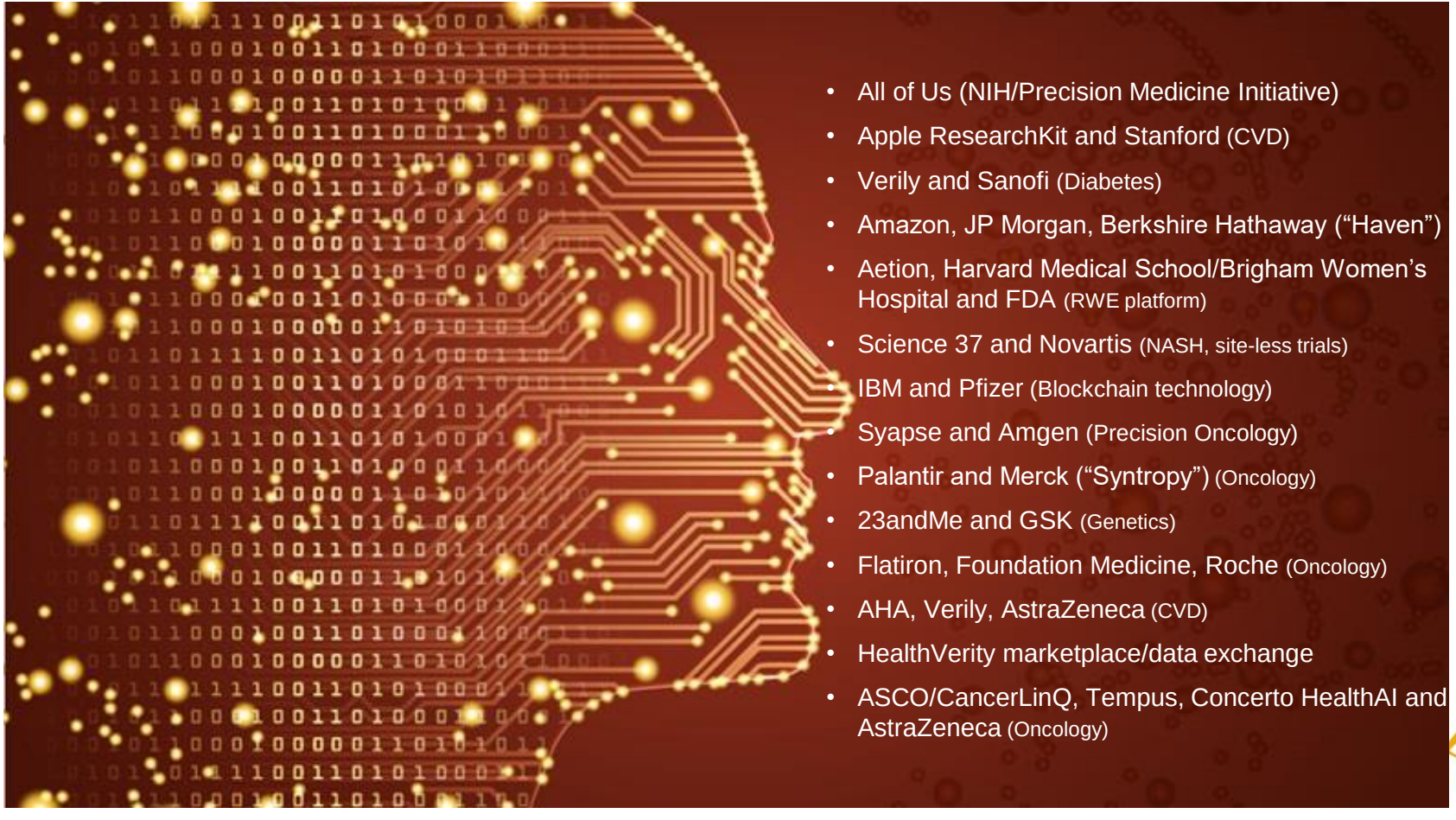
Value and Reimbursement

- Payer value proposition
- Pricing strategy
- Contracting strategy/evaluation
- Payer messaging
- Source of business

Clinical Trial Design and Execution

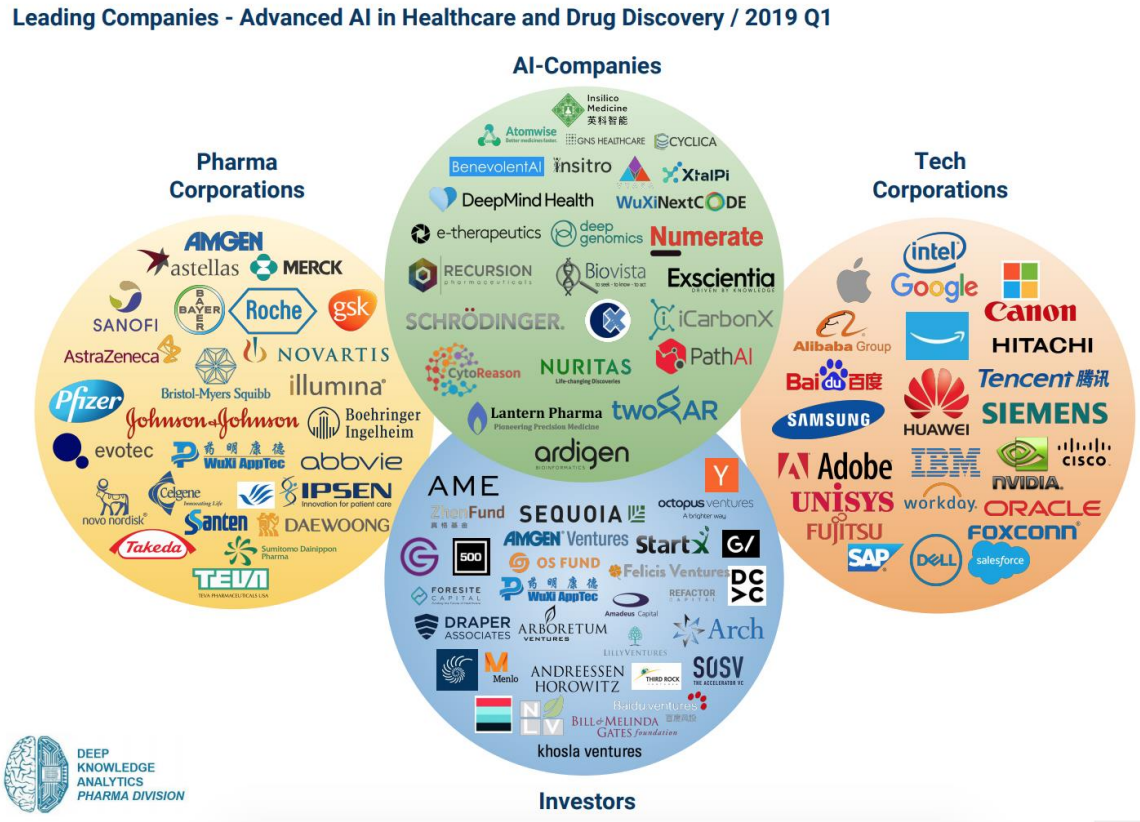


Sample of Real World Data, Digital & Tech Partnerships



- All of Us (NIH/Precision Medicine Initiative)
- Apple ResearchKit and Stanford (CVD)
- Verily and Sanofi (Diabetes)
- Amazon, JP Morgan, Berkshire Hathaway (“Haven”)
- Aetion, Harvard Medical School/Brigham Women’s Hospital and FDA (RWE platform)
- Science 37 and Novartis (NASH, site-less trials)
- IBM and Pfizer (Blockchain technology)
- Syapse and Amgen (Precision Oncology)
- Palantir and Merck (“Syntropy”) (Oncology)
- 23andMe and GSK (Genetics)
- Flatiron, Foundation Medicine, Roche (Oncology)
- AHA, Verily, AstraZeneca (CVD)
- HealthVerity marketplace/data exchange
- ASCO/CancerLinQ, Tempus, Concerto HealthAI and AstraZeneca (Oncology)

Convergence of Titans



https://www.outsourcing-pharma.com/Article/2019/04/16/AI-for-drug-discovery-will-be-driven-by-biopharma-and-the-rise-of-Asian-tigers-Insilico-CEO

Pharma-Tech Collaborations:
Learning Healthcare Ecosystems, Platform-Based Approach

RWE platforms to serve cross-organizational needs at scale

TEMPUS

Concerto HealthAI

“The goal is to get the right treatment to the right patient for the right reason, in order to get the right outcome for the right cost.

Andrew von Eschenbach, former FDA Commissioner