FASTER, BETTER, CHEAPER: THE INCREASING ROLE OF REAL-WORLD EVIDENCE IN DRUG DISCOVERY, DEVELOPMENT, AND COMMERCIALIZATION

The need to effectively utilize real-world evidence derived from big data sources to accelerate the discovery, development, and delivery of 21st century drug therapies in a post-COVID-19 world

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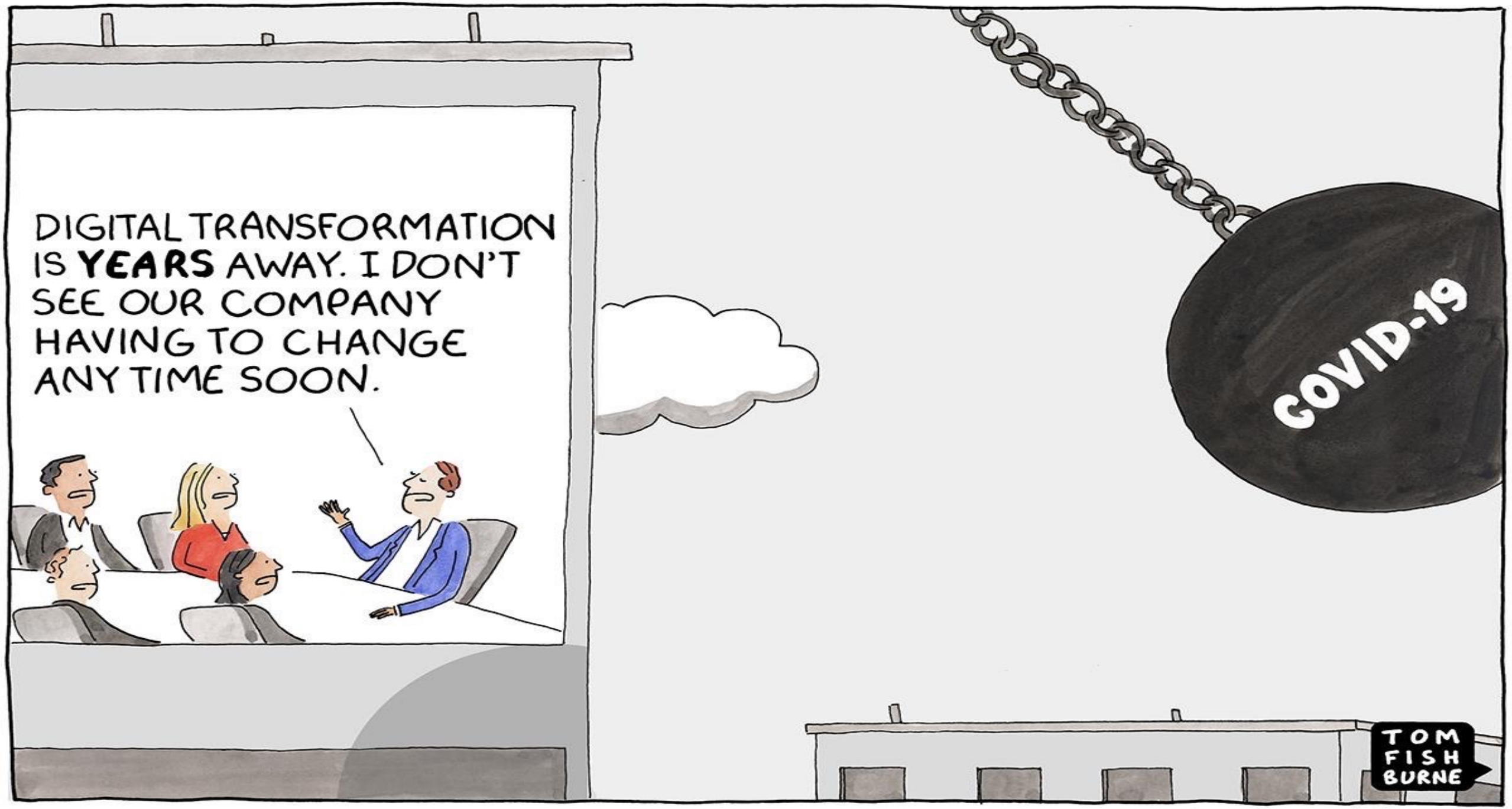


HELLO | A WORD ABOUT ME

- Dallas, TX native born and raised
- Husband & Father
- Dallas Cowboys Fan
- Patient Advocate, Social Scientist, Health Informaticist, Futurist

- Spent the majority of my career in biopharma, health systems, nonprofits, and consulting firms
- Moonlight as a NYU Wagner School professor teaching health informatics, data analytics, and health policy courses
- Serves on several influential boards and committees, including the PCORI Board of Governors

KEY TAKEAWAYS FOR TODAY

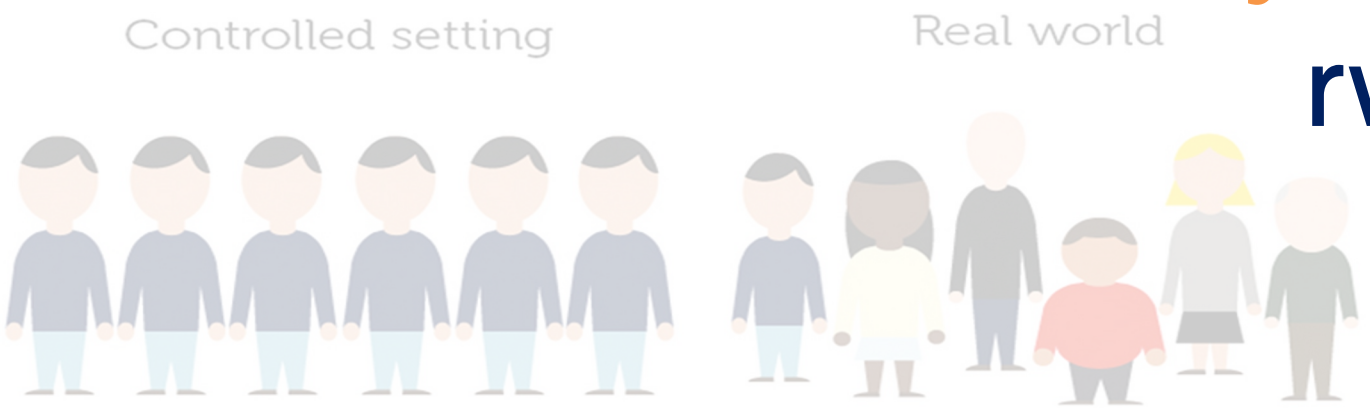
The ability to generate **compelling evidence** throughout the lifecycle of a drug or device therapy is increasingly important…

… as we move from a world where evidence generation is predominately generated from **randomized clinical trials** (RCT) prior to launch…

… to one where ***ongoing* generation of the *right* evidence (Randomized Clinical Trials**, Real-World Evidence, Patient Experience Data) is critical to delivering on the therapy's **full potential**…

…whether that is measured in **safety and effectiveness of therapy, or patient access to the therapy.**

TODAY'S DISCUSSION



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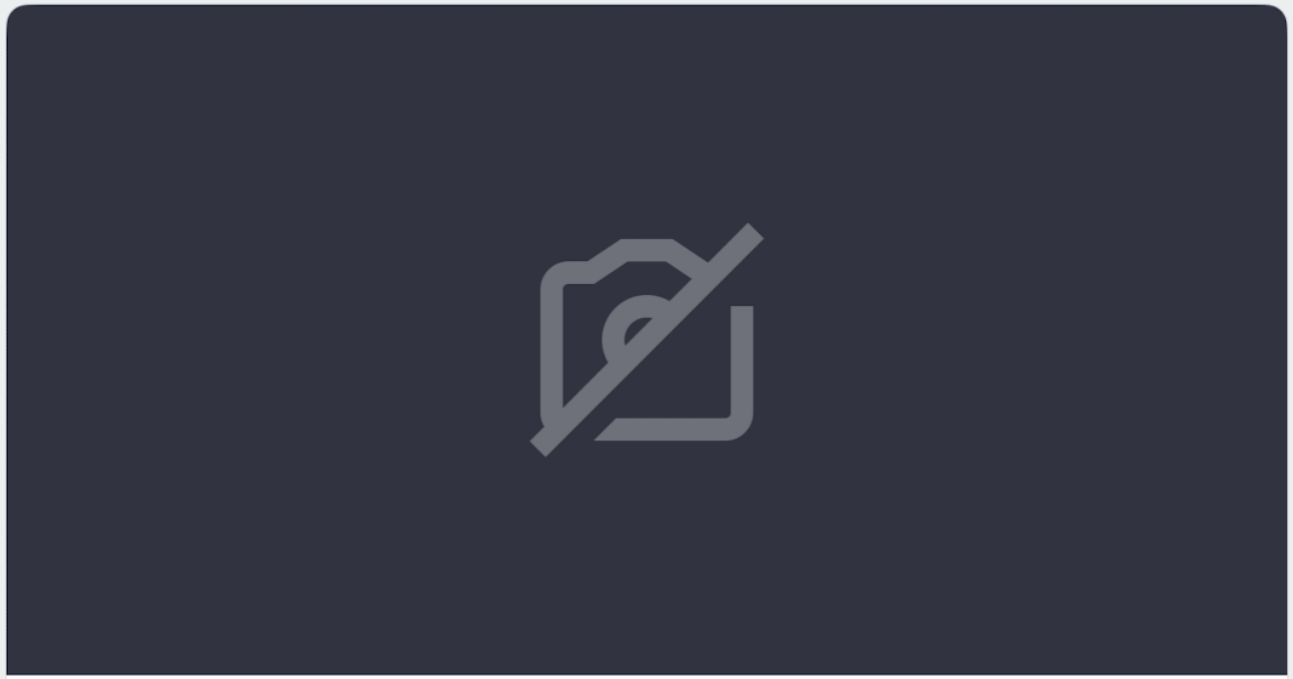
Dr. Robert M. Califf 
@DrCaliff_FDA

Our clinical research (evidence generation) system is too slow and expensive, leading to a vast gap between what we need to know about health interventions and what we actually know.



journals.sagepub.com
Now is the time to fix the evidence generation system - Robert M Califf, 2023

12:51 PM · 1/18/23

DRUG DISCOVERY AND DEVELOPMENT ARE EXPENSIVE AND HIGH-RISK INVESTMENTS

14 YEARS

$2.6 BILLION 

AND LESS THAN

10%

OF THERAPIES THAT ENTER HUMAN TRIALS MAKE IT TO THE PHARMACY

Source 1: https://www.bloomberg.com/news/features/2019-07-15/google-ai-could-challenge-big-pharma-in-drug-discovery
Source 2: https://www.optum.com/business/resources/library/drug-approval-process.html

ONGOING CHALLENGES WITH CLINICAL TRIAL RECRUITMENT AND RETENTION

54%

Of clinical investigators participate in one research study and never participate in another

<5%

Of patients participate in clinical research

49%

Of patients drop out before study completion

48%

Of trial sites miss enrollment targets

50 mi

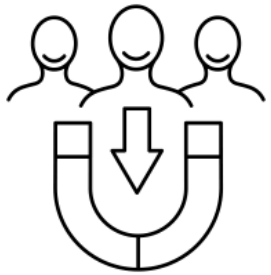
Average distance patient lives from nearest site

Rapid recruitment

Participant Diversity

Hard-to-recruit sub-populations

Patient retention



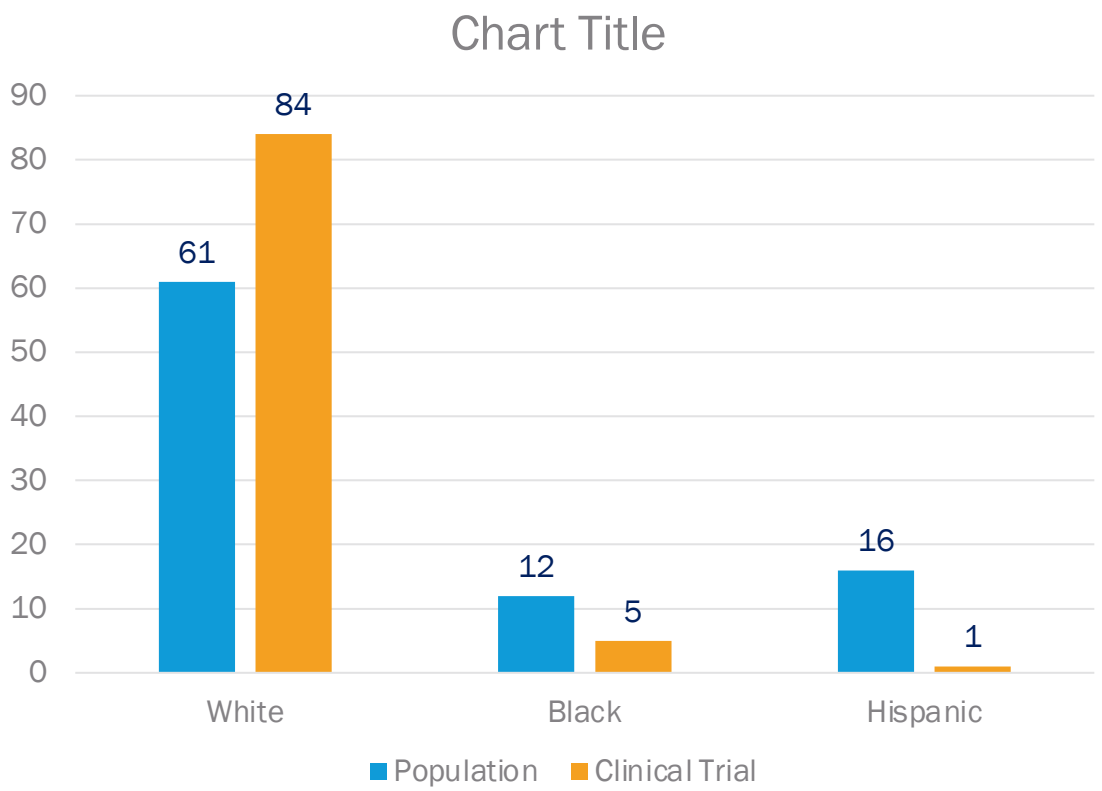
Speed to market

Cost efficiencies

Source: IQVIA

REPRESENTATIVE TRIALS REMAINS AN ISSUE

US Population Relative to Clinical Trial Participation



Key Observations

- White males are the primary participants in trials, while women, people of color, and the elderly are generally underrepresented.
- People of color make up 39% of the U.S. population but represent between 2% and 16% of patients in clinical trials.
- African Americans alone are about 12% of the U.S. population but make up just 5% of trial participants.
- Hispanics are about 16% of the population but only 1% of trial participants.

Source: https://www.clinicalleader.com/doc/steps-to-address-diversity-in-clinical-trials-0001

Pharma

Thumbs down on Lilly, Innovent China trial for lung cancer drug Tyvyt, says FDA AdComm

by Kevin Dunleavy | Feb 10, 2022 3:40pm

When is a clinical trial conducted exclusively in a foreign country enough to support FDA approval?

That was the question before the agency's Oncologic Drugs Advisory Committee (ODAC) on Thursday as it weighed whether to recommend Eli Lilly and Innovent Biologics' application for its PD-1 lung cancer drug Tyvyt (sintilimab).

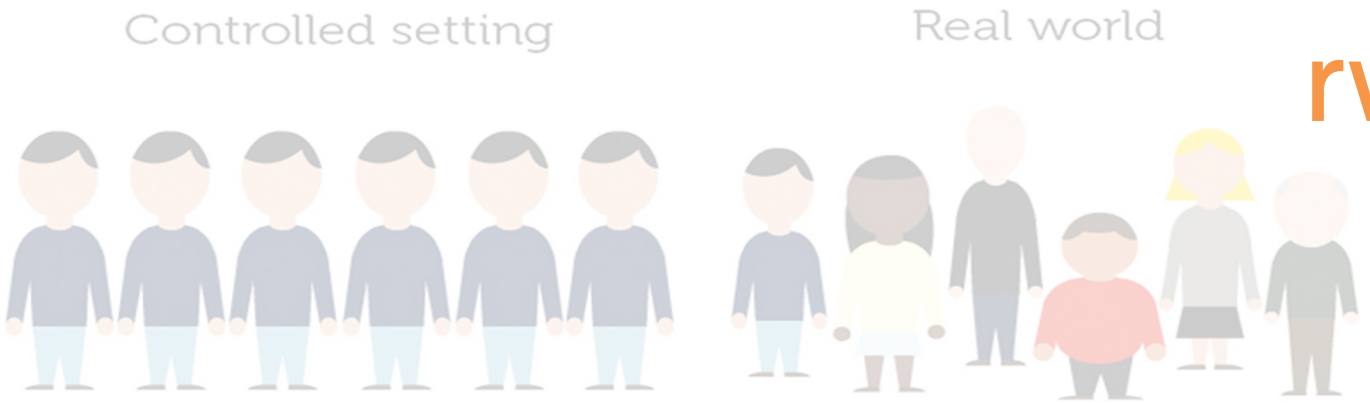
By a vote of 14-1, the independent panel ruled against the companies, declaring that another clinical trial, demonstrating that that the drug works on U.S. patients, should be required before approval.

The decision might have been different had Tyvyt been destined for a market with no good options for patients—or if the trial had used the gold standard of cancer research, overall survival, as its primary endpoint. But it didn't, and Tyvyt was aiming to treat non-small cell lung cancer, a disease with multiple rival drugs that have proven they can extend patients' lives.

Plus, diversity in clinical trials has become more important than ever.

"Over the past two to three years—especially since the pandemic—this country has experienced significant social change," the FDA's cancer drugs chief, Richard Pazdur, said during Thursday's virtual meeting. "And there has been a tremendous outcry for diversity and representation in clinical trials. We as a public agency have to adhere to what patients want in the United States."

TODAY'S DISCUSSION



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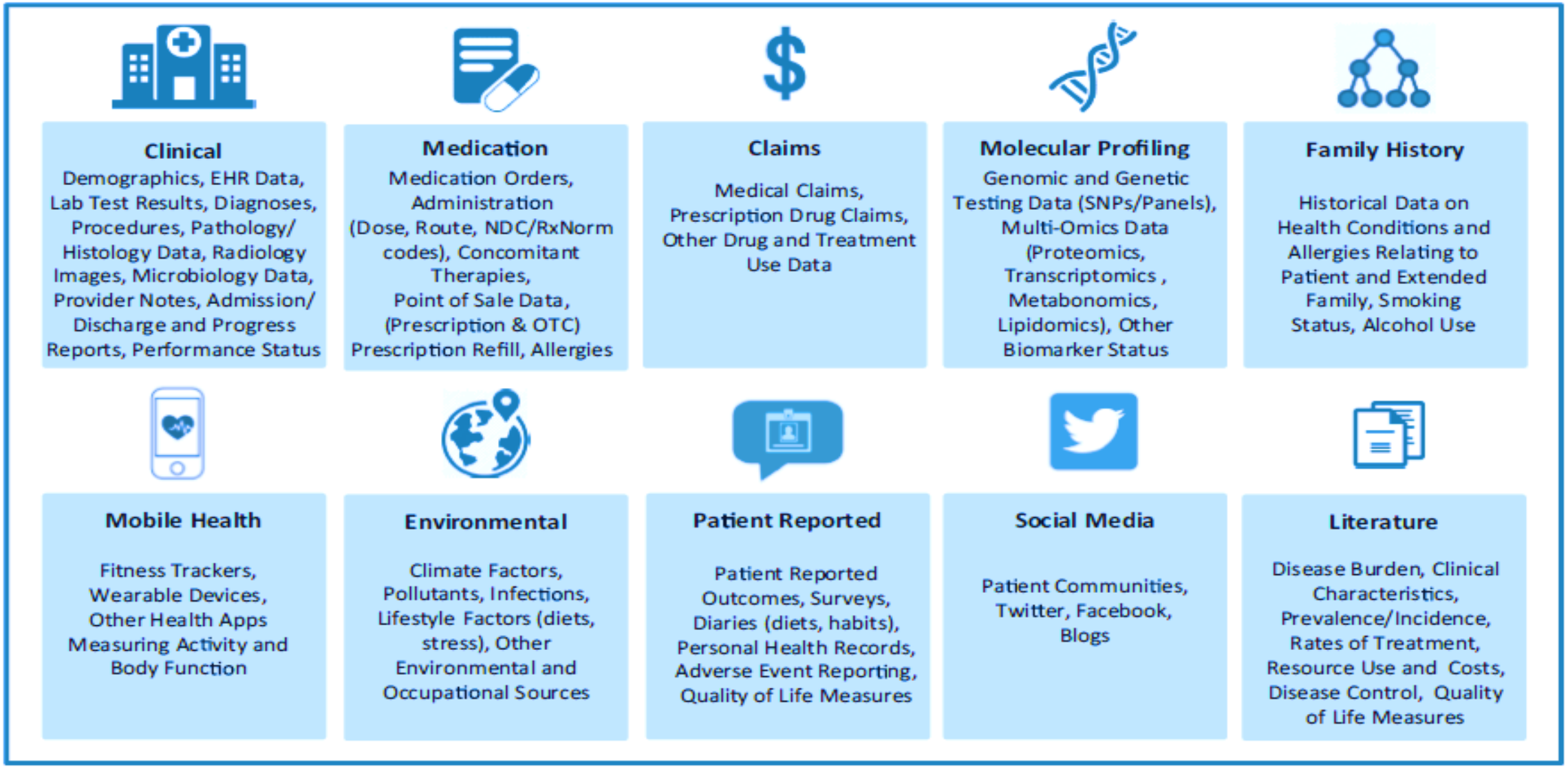
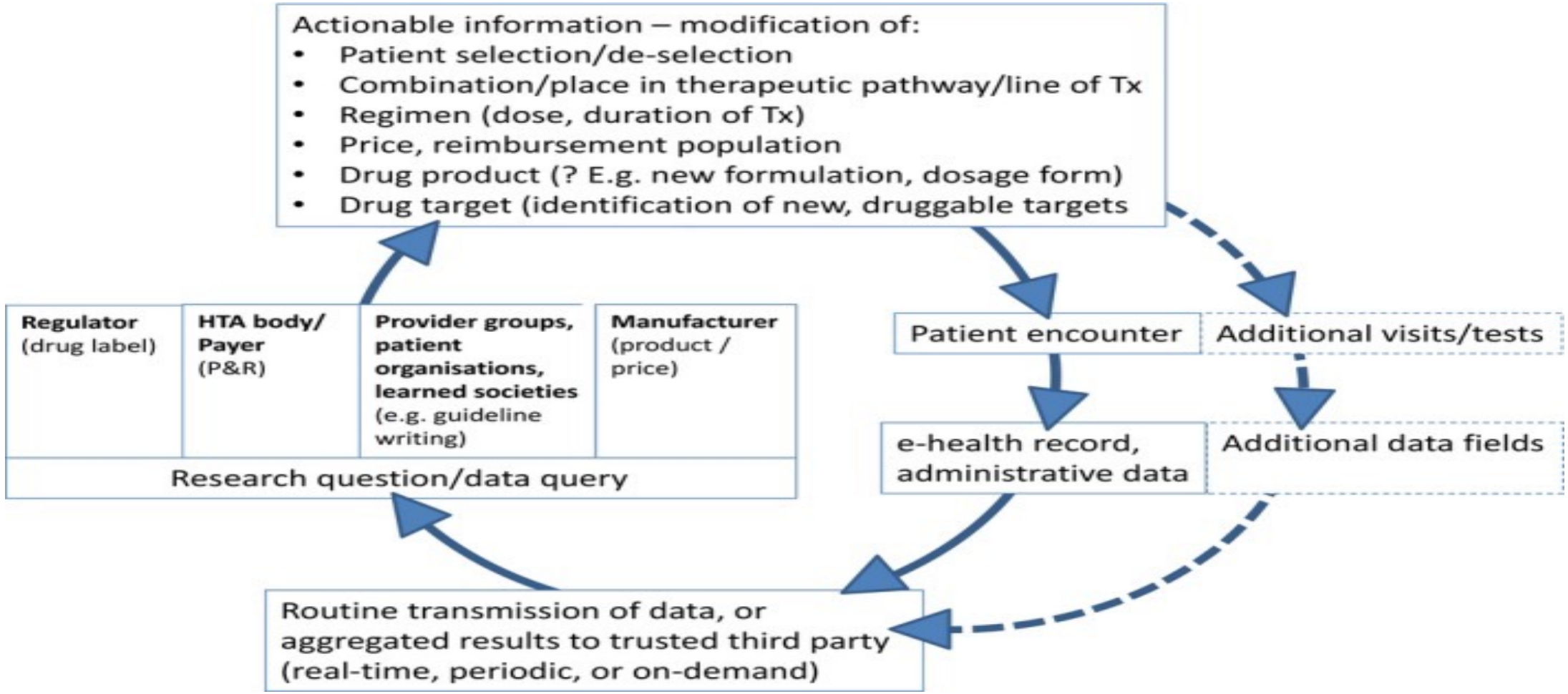
“RWE provides insight about how patients actually respond to treatments in typical care settings, which may differ from responses in the controlled environment of a randomized clinical trial. RWE can be used to show regulators, payers and physicians that a treatment is right for a specific condition and type of patient, and that it is better than available treatments in some way, such as effectiveness, safety or tolerability. RWE can also dash the hopes of once-promising treatments when benefits don’t translate to real-world settings.”

Source: Nancy Dreyer, Chief Scientific Officer, IQVIA - https://www.pharmavoice.com/news/2020-03-rwe-research/612297/

LEADING SOURCES FOR CAPTURING REAL-WORLD DATA



EXAMPLE: USING AN EHR AS A MECHANISM FOR CLINICAL TREATMENT, THERAPY DEVELOPMENT, AND POPULATION STUDIES



WHY IS RWE ESPECIALLY APPEALING TODAY FOR BIG PHARMA?

Pace of scientific innovation

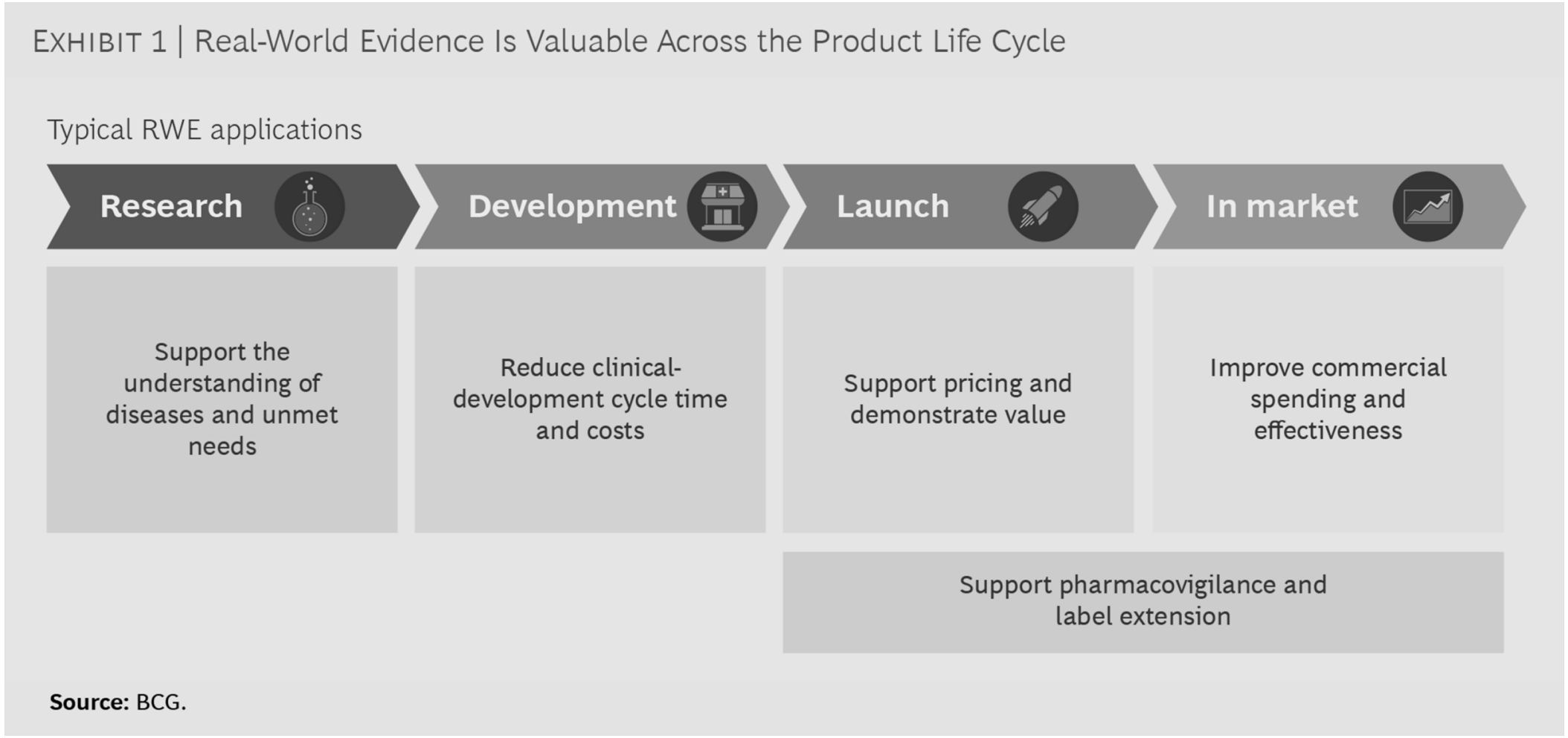
Rising development costs

Increasing availability of data

Importance of patient-centricity

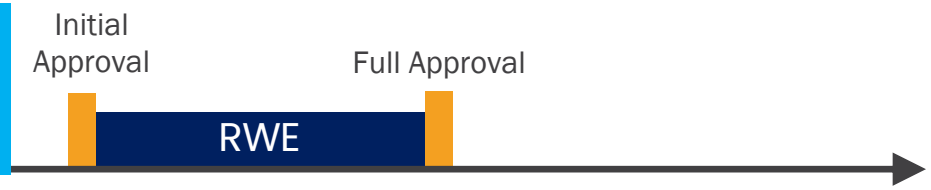
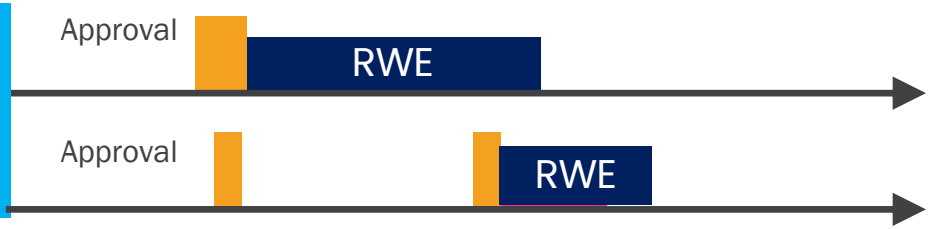
Emphasis on value

HOW DOES BIOPHARMA USE RWE TO SUPPORT THE LIFECYCLE OF DRUG DEVELOPMENT?



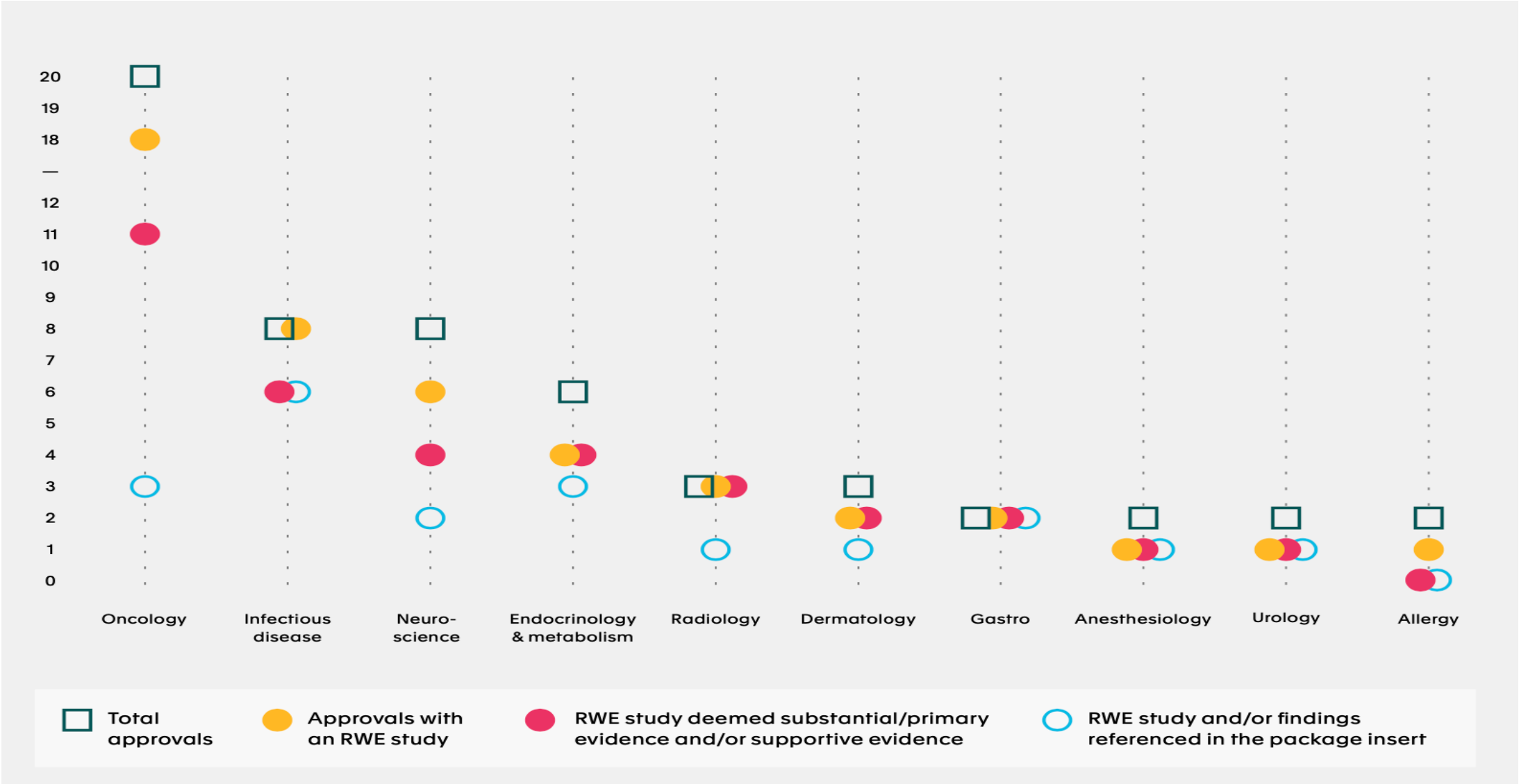
Available online at: https://www.bcg.com/publications/2020/covid-19-opens-a-new-era-for-real-world-evidence-in-pharma

PRIMARY USE CASES FOR INFORMING REGULATORY DECISION-MAKING

Indication Prioritization		Explore indication landscape
Primary Approval		Create historical controls and synthetic comparison groups
Secondary Indications		**Identify new uses and new populations**
Adaptive Pathways		**Add biomarkers to clinical endpoints, broaden populations and learn what happens next**
Post-market studies		**Rapidly identify safety signals and understand comparative effectiveness in the real world**

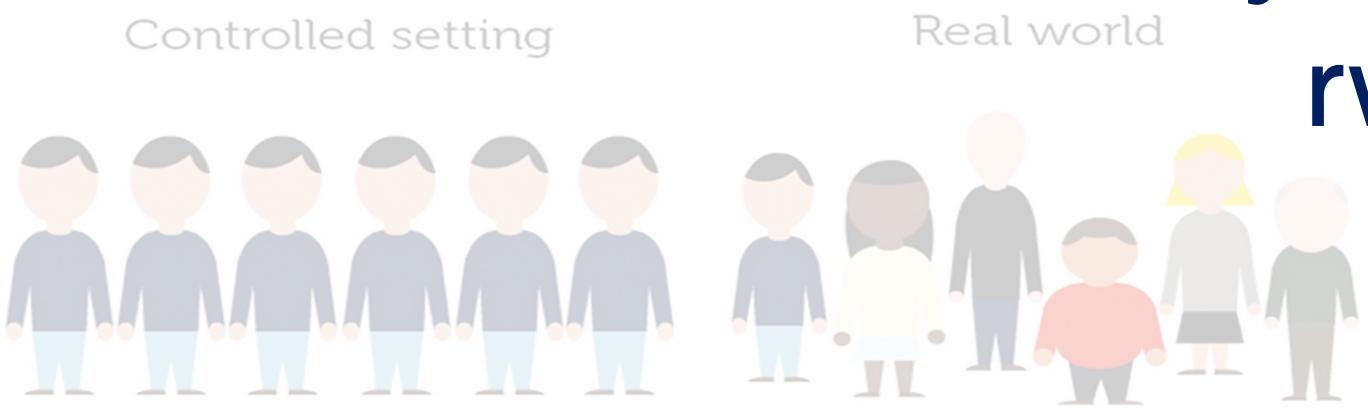
Source: Franklin JM, Glynn RJ, Martin D, Schneeweiss S. Clinical Pharmacology & Therapeutics, Evaluating the Use of Nonrandomized Real-World Data Analyses for Regulatory Decision Making, January 2019

2020 FDA APPROVALS THAT INCLUDED RWE STUDIES SPAN TEN THERAPEUTIC AREAS



Source: Aetion. "The Role of Real-World Evidence in FDA Approvals: 2021 Update" ebook published in 2022. Available online: https://aetion.com/ebook/the-role-of-real-world-evidence-in-fda-approvals-2021-update/

TODAY'S DISCUSSION



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THE EVOLVING GLOBAL POLICY LANDSCAPE FOR LEVERAGING RWE

Food and Drug Administration (FDA)

In 2018, FDA issued its 3-year plan on use of RWE in decision-making. Since then, it issued multiple draft guidances encouraging submissions

European Medicines Agency (EMA)

In 2019, the EMA issued its 5-year plan to promote the use of high-quality RWD in decision-making. In 2020, the EMA, HMA issued its joint 5-year strategy, which builds on EMA's plan. In 2021, the Big Data Steering Group released its 2021-2023 work plan, operationalizing these strategic goals

National Medical Products Administration (NMPA)

In 2019, NMPA released a draft/final guidance on its guiding principles for RWE for development/review.

Health Canada

In 2019, Health Canada issued reports on protocol elements and data quality and optimizing use of RWE. It is also inviting manufacturers to submit high-quality RWE for evaluation. We're awaiting its guidance.

Pharmaceuticals and Medical Devices Agency (PMDA)

In 2021, PMDA researchers published a manuscript discussing seven guidance documents published since 2019 and the increasing use of RWE for regulatory decision-making.

Medicines and Healthcare Products Regulatory Agency (MHRA)

In 2020, the MHRA issued the first in a series of guidances discussing RWE trial designs

Taiwan Food and Drugs Administration (TFDA)

In 2020, the TFDA published RWE guidance use on label changes, premarketing safety profile evaluations, and premarketing effectiveness assessments

NOTABLE U.S. RWE PUBLIC POLICY, REGULATORY, AND TECH DEVELOPMENTS

2007-2008

2007
ISPOR defines RWE

2007
Apple Inc. CEO Steve Jobs unveils the iPhone at the Macworld convention in San Francisco.

2007
Fitbit marketed – increased concept of a wearable device to monitor personal health information

2007
OMOP FDA-led public private partnership focused on drug safety and obtained access to 10-large RWD sources

2008
FDA launches Sentinel Program to monitor post approval safety of drugs, vaccines, and medical devices

2009-2016

2009
American Recovery and Reinvestment Act – incentivized health care providers to support implementation of EHRs

2010
Blue Button Initiative provides electronic access for veterans and Medicare beneficiaries to their clinical data

2010
Affordable Care Act passed which, drove explosion of RWD use through risk-based structures like ACOs

2012
Salford Lung Study – first time a pRCT was conducted before registration of the treatment being investigated

2014
FDA approves Vimizin for treatment of Morquio A Syndrome using RWD

2016
Bipartisan Policy Center issues report calling on FDA to develop guidance on use of RWE in regulatory context

2016
FDA Draft Guidance on RWE in medical device regulatory decisions

2016
21st Century Cures Act – requires FDA to establish a program to evaluate potential for RWE

2017-2019

2017
FDA Guidance on Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices

2018
2018: FDA Framework for Real-World Evidence Program

2018
FDA Guidance on the Use of Electronic Health Records in Clinical Investigations

2019
FDA approves Ibrance for men with breast cancer based on RWE

2019
2019 – June 2021: 116 of 136 FDA approvals (85%) included real-world evidence in some form

2021-2022

2021
FDA issues Guidance on RWD; Assessing EHRs and medical claims to support regulatory decision making

2021
FDA issues Data Standards for Drug and Biological Product Submissions Containing Real-World Data

2021
FDA issues Guidance on Assessing Registries to Support Regulatory Decision-Making for drug and Biological Products

2022
FDA issues Guidance on using RWD and RWE to submit documents to FDA for Drugs and Biologics

2023
FDA issues Final Guidance for Considerations for the use of RWD/RWE to Support Regulatory Decision-Making for Drug & Biologics

Regulatory Policy & Guidance

Changes to Traditional Drug Development

Advancements in RWD/Technology

REGULATORS ACROSS THE GLOBE ARE OFFERING GUIDELINES AND FRAMEWORKS FOR EXPANDED USE OF REAL-WORLD EVIDENCE

DRAs	INPUTS	ACTIVITIES		OUTPUTS	OUTCOMES
	What DRAs invested	What DRAs did	Who DRAs reached	What DRAs got	What DRAs achieved
FDA	**Aim: "Utilizing Real World Evidence.": supporting the approval of new indications for approved drugs and post-approval research requirements**				
	· Staff and experts · Financial · Technology · Equipment and platform. · Community · Domestic and international partners	· Conduct workshops and meetings · Provide project findings · Together stakeholders · Develop reports, curricula, resources · Facilitate access to information · Work with partners	· Industry · Academic institutions · Domestic government institutions · Overseas institutions	· Publications and reports · Regulatory guidelines · Database and data sharing platforms	· Decision-making: • New drugs approved · Awareness · Knowledge · Skills · Motivations · Behavior · Health · Social · Economic
EMA	**Aim: Utilizing the power of big data and improving the application of high-quality RWD to support regulatory decision-making**				
	· Staff and experts · Financial · Committee · Technology · Resources and organization	· Conduct workshops and meetings · Organize initiatives · Together stakeholders · Facilitate access to information · Work with partners from different countries	· Industry · Academia · Agencies and community · Decision-makers · EU country health institutions · Overseas institutions	· Publications and reports · Centers and committees · Tools developed by activities. · Annual conference reports · Database and data sharing platforms	· Decision-making: • New drugs approved and indications added. · Communications · Motivations · Behavior · Health · Social · Economic
NMPA	**Aim: Utilizing the power of big data and improving the application of high-quality RWD**				
	· Financial · Technology · Domestic partners	· Conduct workshops and meetings · Organize projects · Together stakeholders · Facilitate access to information · Leadership in local institutions	· Industry · Academia · Local institutions	· Publications and reports · Regulatory guidelines · Regulatory Science Action Plan	· Decision-making: • New devices approved and indications added. · RWE platform · Motivations · Health · Social · Economic

BIG DATA IN CLINICAL RESEARCH ALLOWS FOR MORE PRECISION BUT RAISES ETHICAL ISSUES

Privacy

Bias

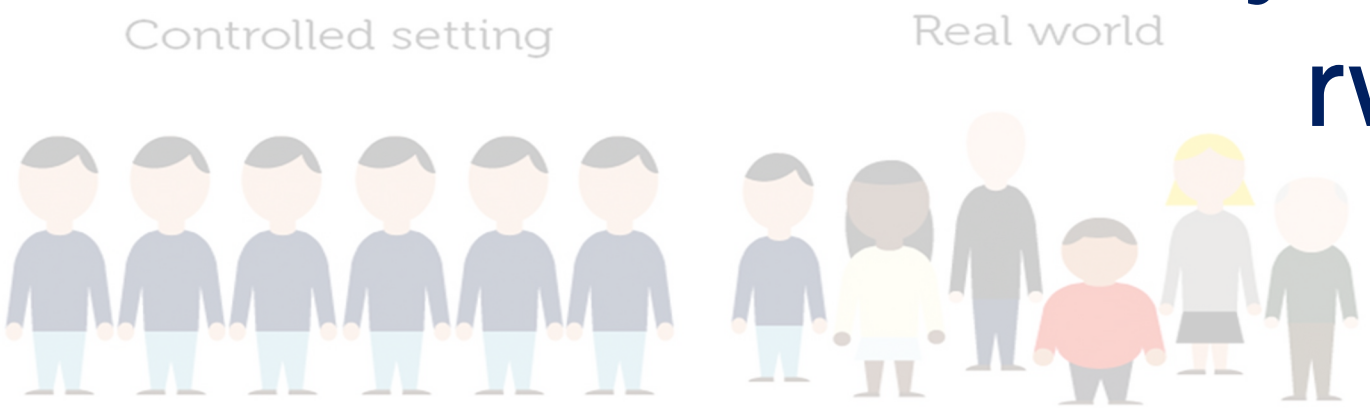
Transparency

Consent

Accountability

Fairness

TODAY'S DISCUSSION



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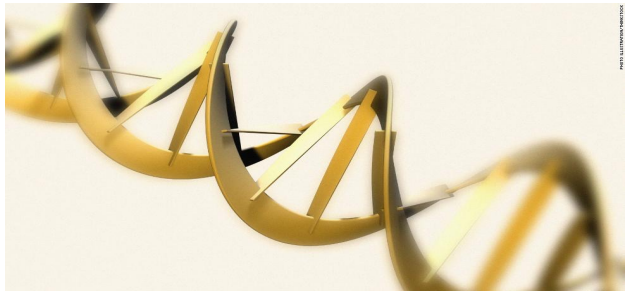
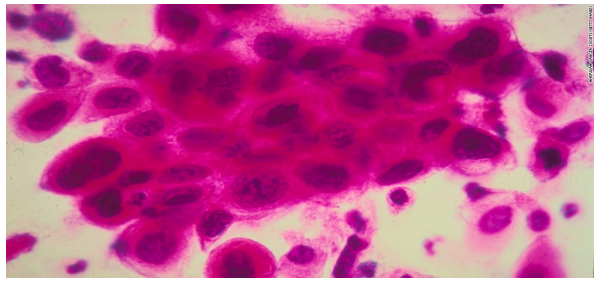
SOME KEY ADVANCES IN CLINICAL RESEARCH OVER THE LAST 25 YEARS

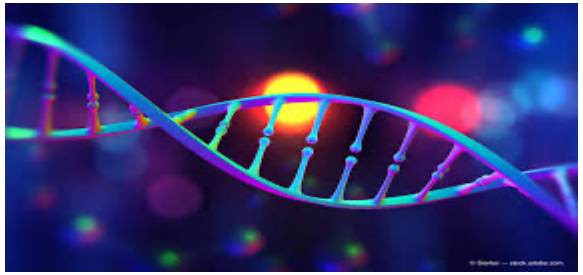
Human Genome Project



Targeted Cancer Therapies



Precision Medicine Revolution



Patient Products Achieved with 3D Printing

Ubiquity of Digital Health and Health Data

Artificial Intelligence in Healthcare

AI Model Enables Alzheimer's Disease Detection from Brain MRIs

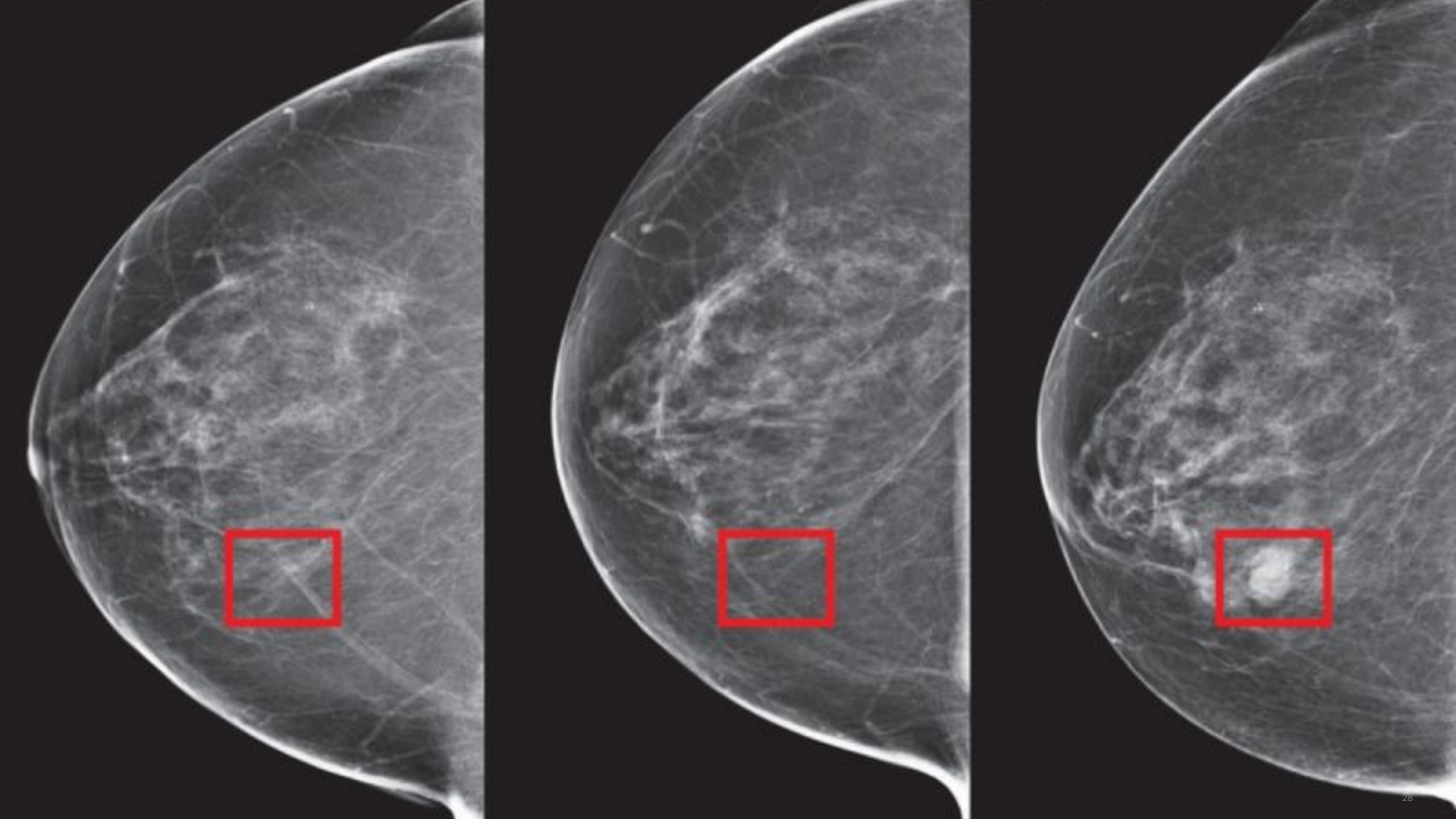
A research team at Massachusetts General Hospital developed an artificial intelligence model that uses routinely collected clinical brain images to detect Alzheimer's disease.

Source: Getty Images

By Mark Melchionna

March 09, 2023 - Published in *PLOS ONE*, a recent study **described** how a team of researchers at Massachusetts General Hospital (MGH) developed and validated an artificial intelligence (AI) model, specifically a deep-learning model, to analyze data from brain magnetic resonance images (MRIs) to detect Alzheimer's disease.

Source: https://healthitanalytics.com/news/ai-model-enables-alzheimers-disease-detection-from-brain-mris



> **The healthcare industry is faced with the challenge of incorporating simultaneous advances in physical, biological, and digital technologies, as the development of new diagnostic approaches and therapies coincides with a push to digitize patient records and capitalize on the wealth of information that can be gathered from wearable devices and implantable technologies.**

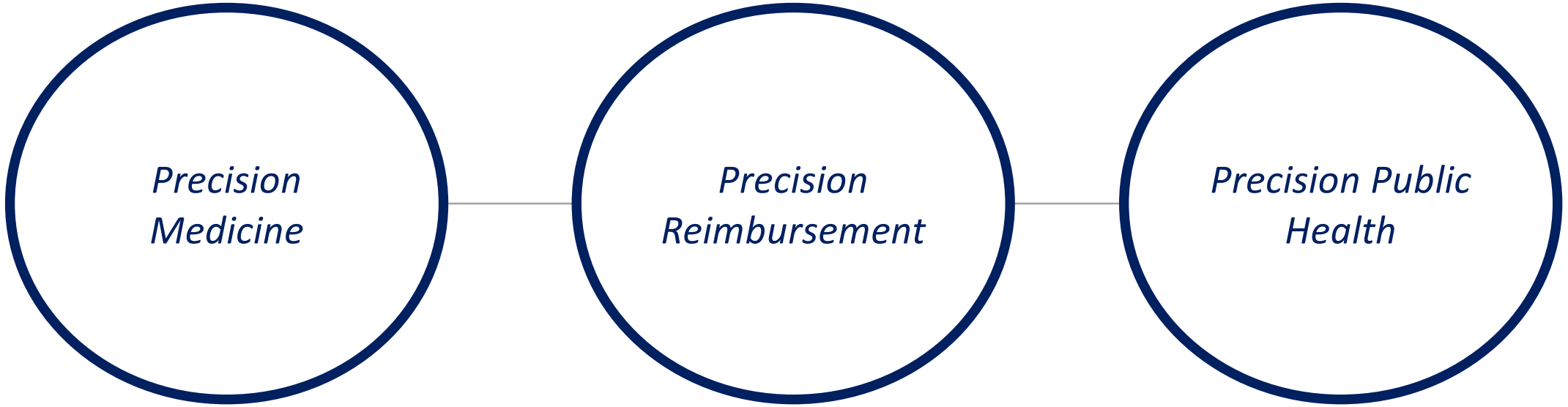
Source: World Economic Forum “Fourth Industrial Revolution”

THE NEXT 25 YEARS: THE CONVERGENCE OF BIOTECH AND HUMAN DATA SCIENCE BENEFITS HUMAN LIFE

- **DNA sequencing of an increasingly representative and diverse slice of the world's population** will be sequenced – approximately 60 million genomes are projected by 2025
- **Expanded use of digital technologies will enable the use of mass phenotyping** – enabling longitudinal data that provides deeper understanding of the effects of nutrition, health, and disease
- **Digitization and virtualization will allow for the storage and democratization** of larger datasets globally
- **Precision therapy will increase significantly** in importance and utility – driven by patients

Source: "The Next 25 Years." Nature Biotechnology, Volume 39, March 2021, Published online at: www.nature.com/naturebiotechnology

THE ERA OF PRECISION IN HEALTHCARE AND LIFE SCIENCES IS UPON US



Tailoring prevention and treatment to individuals

Requires taking into account individual differences in genes, environments, and lifestyles when developing a treatment plan and/or drug therapy

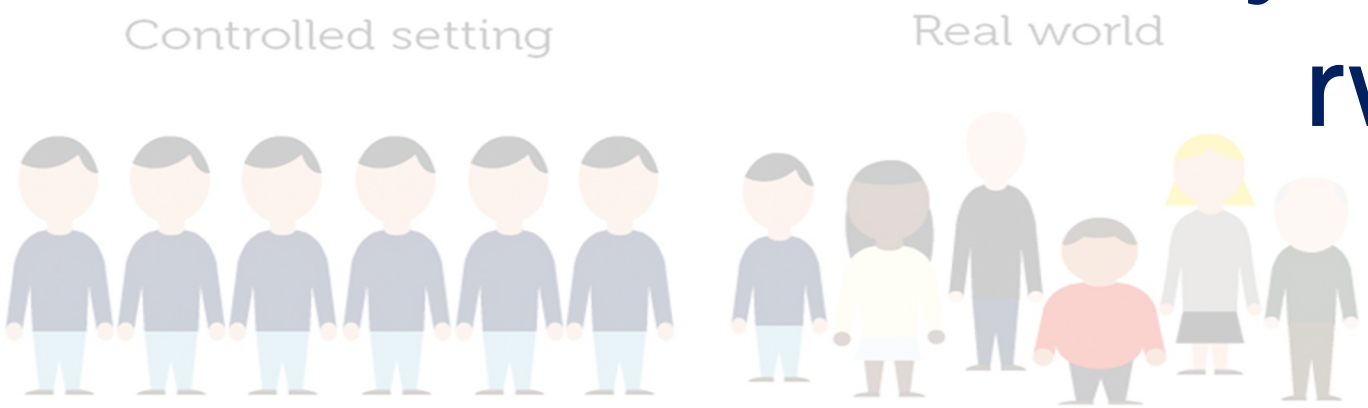
Informing decision-making to specific patient clusters

Integrates economic and clinical value assessment by explicitly discovering distinct clinical and health care utilization phenotypes among patients

Targeting interventions for populations

Requires rapid and iterative collection, analysis, and visualization of genomic, epidemiologic, geospatial, and contact tracing data

TODAY'S DISCUSSION



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HOW THE ROLE OF THE RWE FUNCTION IS EVOLVING

PAST
In the early days, the RWE group was all about…

- **Data sourcing** / the identification and procurement of real world data assets
- **Portfolio management** / tracking RWE projects and identifying synergies for better collaboration and resource utilization
- **Best practices** / trying to reduce duplication of effort and eliminate process roadblocks
- **Pilots and proof cases** / demonstrating the actual value of RWD/E

PRESENT
But, increasingly, it involves…

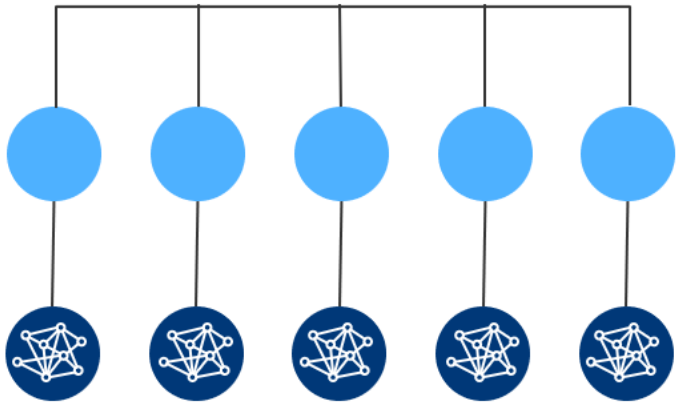
- **Talent and community development** / attracting, developing, and retaining talent
- **Enterprise operating models** / designing and implementing a platform and operating model that are grounded in an enterprise strategy
- **Technology enhancements** / Deployment of central analytics platforms
- **High-value use cases** /

FUTURE
The future resides in its ability to incorporate…

- **Novel partnerships** / Developing a data strategy and organizational capability to engage in external partnerships with health care system stakeholders to gain access to the right data
- **Advanced RWE capabilities** / applying advanced analytics to RWE generation to deliver impact at scale

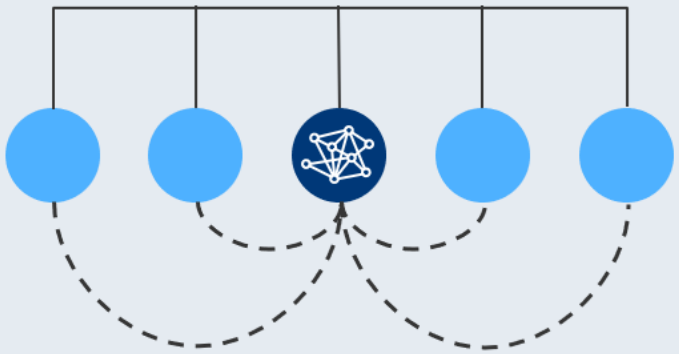
RWE FUNCTIONS COME IN DIFFERENT SHAPES AND SIZES

Federated or decentralized



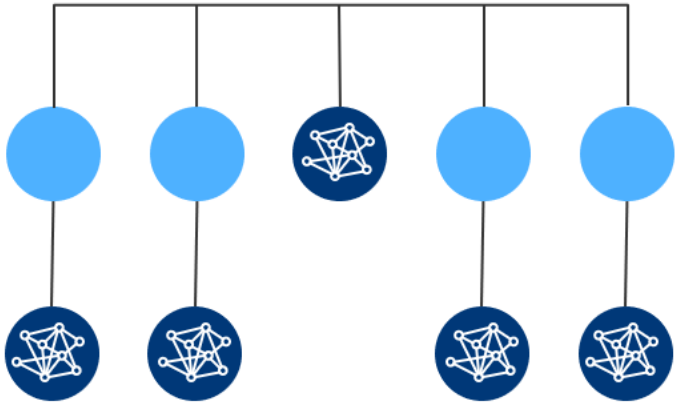
Individual RWE groups are spread across different functions in the organization, reporting to and serving business/function-specific teams. Provides stronger alignment with business priorities and processes.

Centralized



A core RWE organization providing services to the entire enterprise as a center of excellence. Offers greater consistency and knowledge sharing when under one roof.

Hybrid



A core RWE organization that serves as a center of excellence, while specific functions / business units have their own RWE teams – **often referred to as hub-and-spoke**. Offers the best of both worlds.

FIVE STRATEGIES FOR FORWARD-THINKING RWE LEADERS

1. Leaders are actively deploying strategies to elevate understanding, accessibility, and communication of RWE's value drivers to the enterprise with high-value use cases.
2. Leaders are establishing agile operating models that drive adoption and integration of RWE across the pipeline, while developing risk mitigation plans.
3. Leaders are deploying rapid, cost-effective data analytical platforms that can democratize the use of data and analytics at scale.
4. Leaders are focused on developing and/or expanding robust partnership ecosystems.
5. Leaders are thinking about ways to shift to the expanded use of advanced RWE capabilities and the recruitment of high-performing diverse talent to achieve success.

NEXT STEPS FOR BIOPHARMA TO ACCELERATE THE USE OF RWE

1

INCREASE UNDERSTANDING AND COMMUNICATION OF RELEVANT ENDPOINTS USING RWE

Elevation of frontline capabilities across medical affairs, commercial, development, market access, and HEOR/RWE will be required to identify novel data sources that generate evidence for regulators and other stakeholders.

2

CREATE AN ORGANIZATION, OPERATING MODEL, AND CULTURE THAT DRIVES INTEGRATION OF RWE

This should include (1) an enterprise RWE strategy focused on the organizational culture and role of RWE; (2) structure, processes, and resourcing to make it repeatable and sustainable; (3) approach to governance and interface with the other functions within the organization.

3

BUILDING SCALABLE PLATFORMS TO MANAGE AND ANALYZE DATA IN A RAPID, LOW-COST FASHION

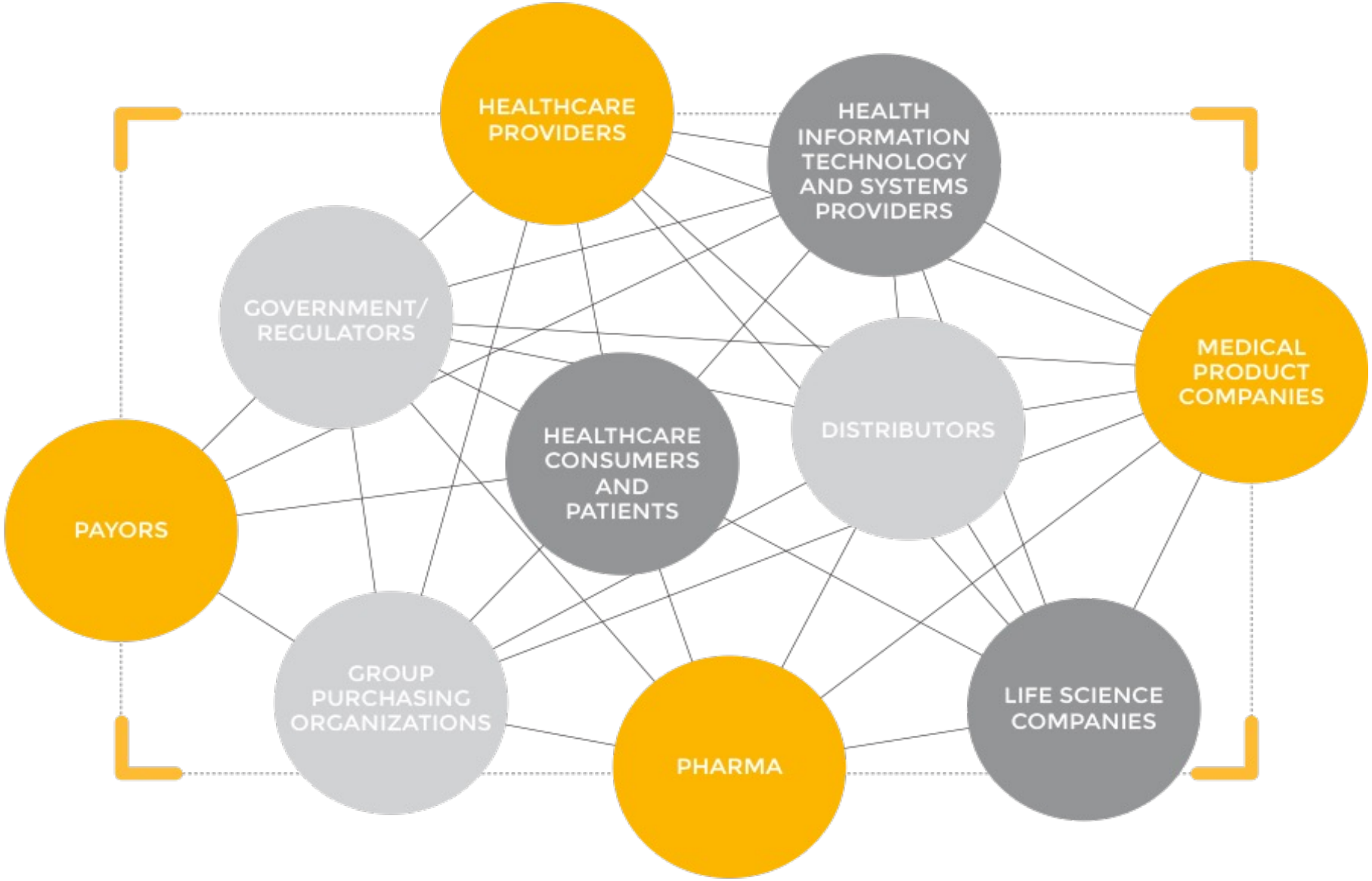
Building platforms and capabilities—including data infrastructure and storage—to increase the turnaround time and decrease the cost of RWE studies is critical to being able to utilize this data for internal business decisions.

4

ADVOCATING FOR GLOBAL HARMONIZATION OF REGULATORY GUIDANCES FOR RWE ACCEPTABILITY

Standardization of regulatory submission processes and availability of clear guidance on submission of evidence packages that include RWE.

THE FUTURE OF EVIDENCE IN PHARMA SHIFTS TO STRATEGIC CROSS-SECTOR PARTNERSHIPS



Every company has big data in its future and every company will eventually be in the data business.

— Thomas H. Davenport —

AZ QUOTES

THANK YOU

Scan me!