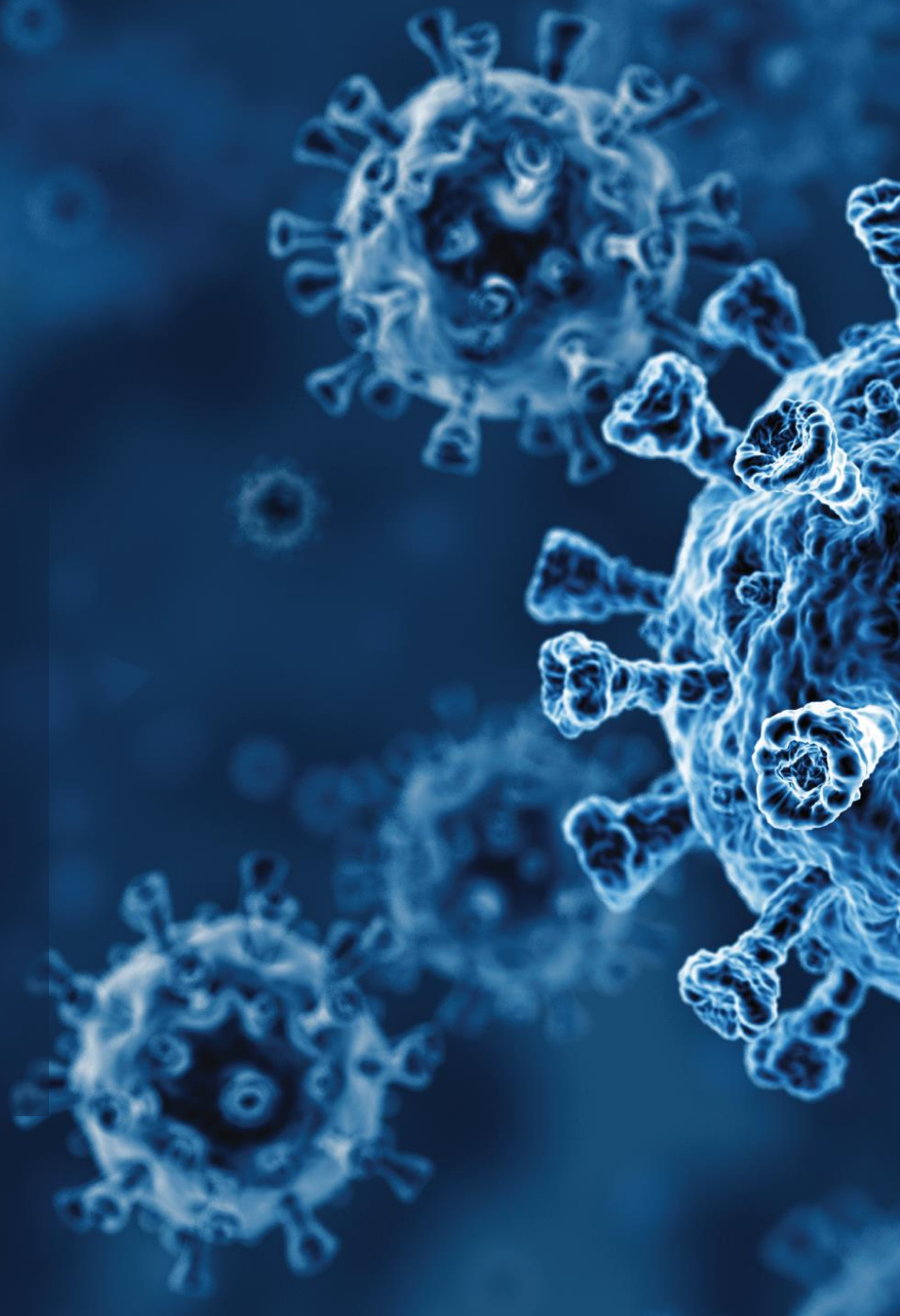
MULTI-REGIONAL CLINICAL TRIALS

THE MRCT CENTER of BRIGHAM AND WOMEN'S HOSPITAL and HARVARD

Reimagining Clinical Trials: Learning from COVID-19

June 16, 2021



The MRCT Center is a research and policy center focused on addressing the conduct, oversight, ethics and regulatory environment for clinical trials.

BRIGHAM AND WOMEN'S HOSPITAL

HARVARD UNIVERSITY

The MRCT Center

Our Vision

Improve the integrity, safety, and rigor of global clinical trials.

Our Mission

Engage diverse stakeholders to define emerging issues in global clinical trials and to create and implement ethical, actionable, and practical solutions.

Reimaging Clinical Trials: Learnings from COVID-19

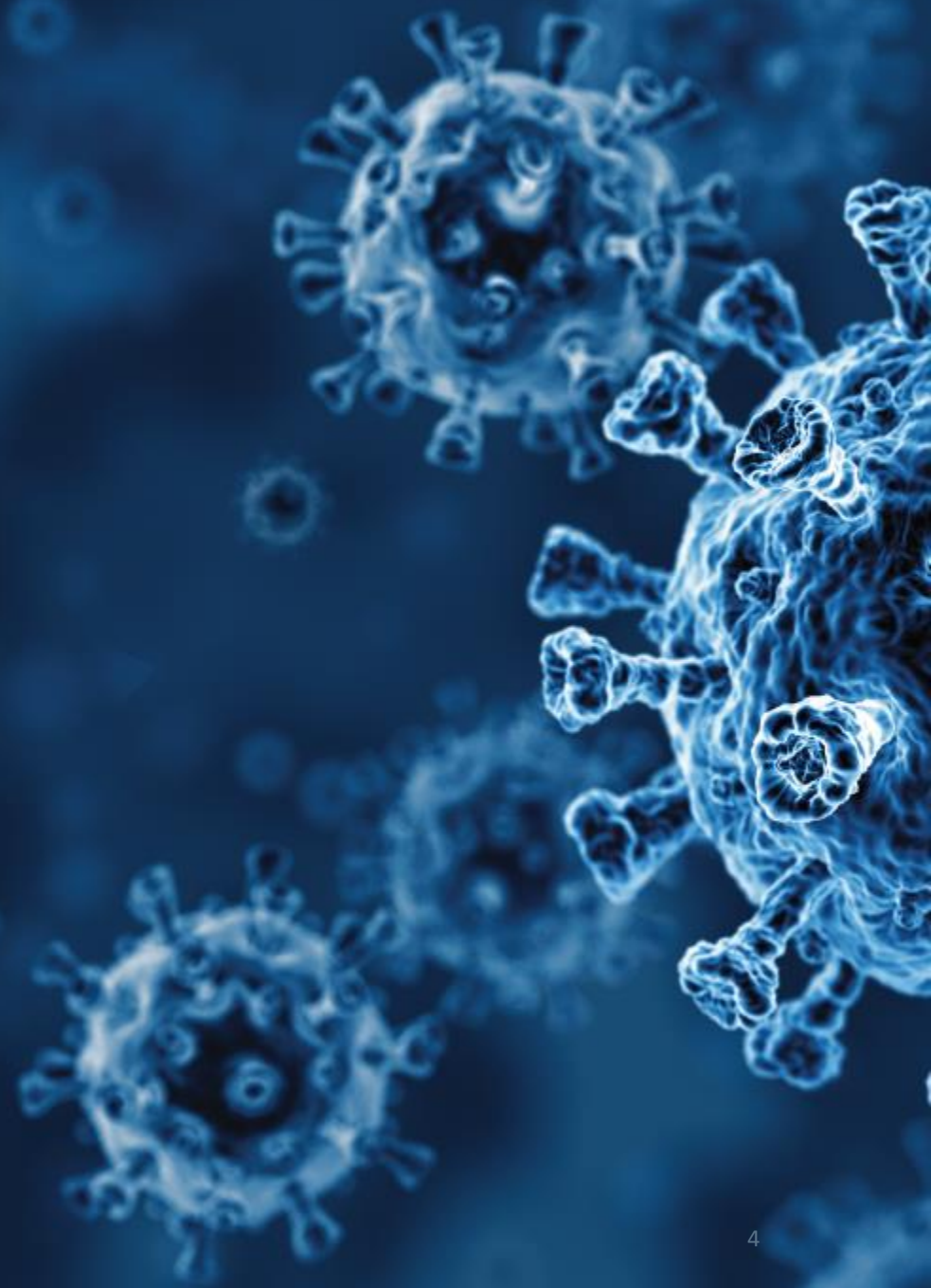
2 Meeting Dates

June 16, 2021, 10AM-1PM EDT

Permissible flexibilities to study conduct and coordination and the implications for the clinical trial workforce in this new environment.

June 24, 2021, 10AM-1PM EDT

Regulatory flexibilities, international cooperativity, and governance.



Reimaging Clinical Trials: Learnings from COVID-19

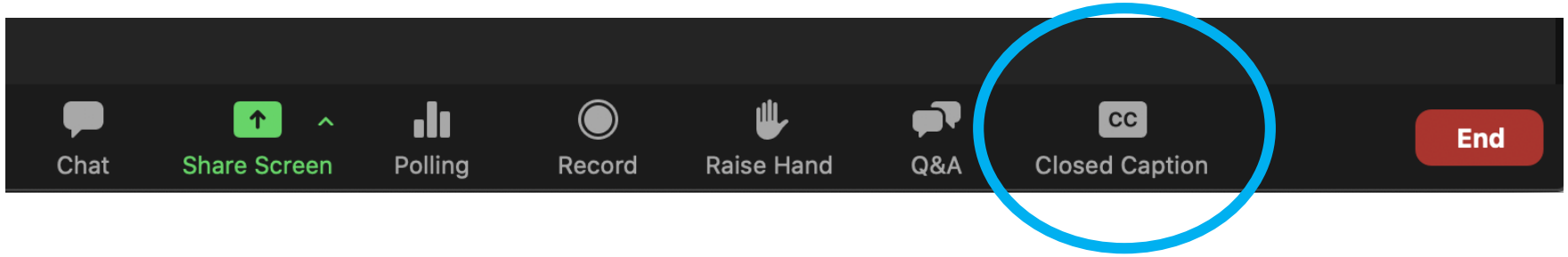
Our Goal

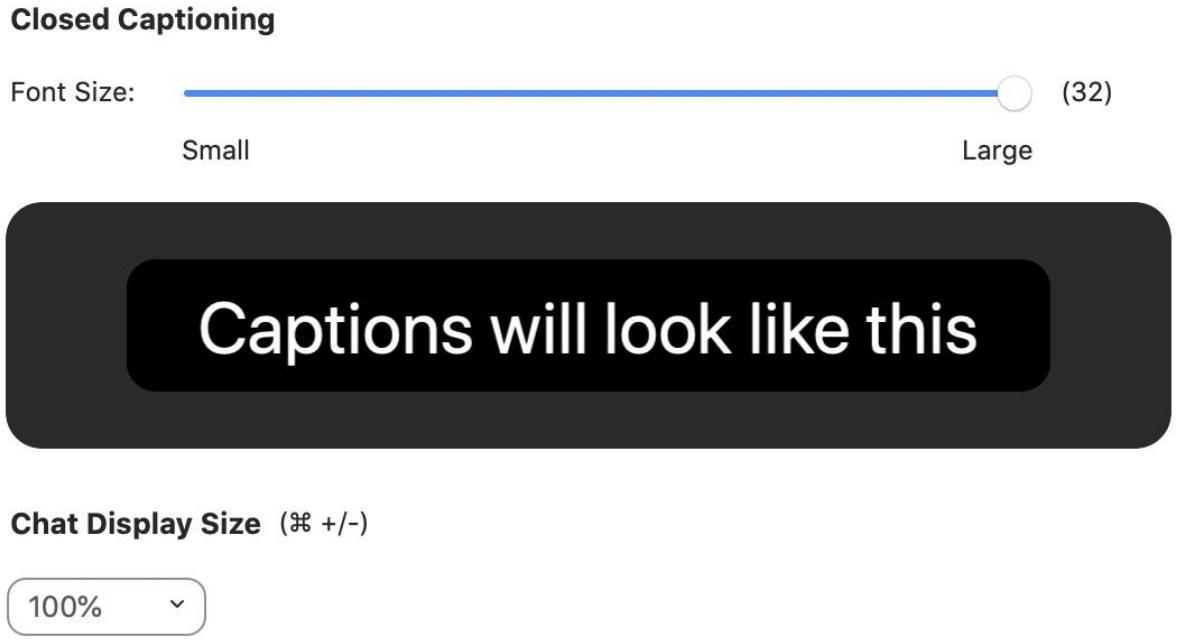
- What is the vision for new ways of conducting clinical trials?
- What worked, what did not work, and what we need to analyze further?
- How do we build upon experiences of clinical trials during the COVID-19 pandemic

June 16, 10:00 AM – 1:00 PM EDT

TIME	TOPIC	SPEAKERS
10:00 AM – 10:30 AM EDT	**Introduction & Keynote speaker:** The Future of Clinical Trials	•**Barbara Bierer**, Faculty Director, MRCT Center •**Sarah White**, Executive Director, MRCT Center •**Esther Krofah**, Executive Director, FasterCures
10:30 AM – 11:30 AM EDT	**First Panel:** Useful and permissible flexibilities: A discussion of regulatory, protocol, and study conduct flexibilities that can and should be sustained in the future, that should be eliminated, and for which further experience is necessary	•**Lindsey Baden**, Division's Director of Clinical Research, Brigham and Women's Hospital/ Dana-Farber Cancer Institute •**Penny Carlson**, Vice President, Head of Global Development Support, Takeda •**Valen Keefer**, Patient Advocate for polycystic kidney disease (PKD) and Organ Donation •**Isaac R. Rodriguez-Chavez**, Head, Global Center of Excellence Strategy for Decentralized Clinical Trials, PRAHealthSciences **Moderator:** •**Paul Kluetz**, Deputy Director, Oncology Center of Excellence, U.S. FDA
11:30 AM – 11:40 AM	**BREAK**	
11:40 AM – 12:40 PM EDT	**Second Panel:** Implications for and need to re-imagine the workforce in a reimagined clinical research enterprise	•**Nicholas Brooke**, Founder & Executive Director of The Synergist, Chief Executive Officer of Patient Focused Medicines Development (PFMD) •**Andrea Ferris**, President and Chief Executive Officer, LUNGEvity •**Andrew (Andy) Lee**, Senior Vice President, Head of Global Clinical Trial Operations, Merck •**Harpreet Singh**, Director of Division of Oncology, U.S. FDA **Moderator:** •**Craig Lipset**, Co-Chair of Decentralized Trials & Research Alliance
12:40 PM – 1:00 PM EDT	**Discussion and wrap-up**	•**Moderators Paul Kluetz** and **Craig Lipset** •**Barbara Bierer,** Faculty Director, MRCT Center •**Sarah White**, Executive Director, MRCT Center

Closed Caption Settings





Closed Caption size can be increased by clicking on the Closed Captions button and viewing the “subtitle settings”.

Thank you to the Planning Committee

Maria Apostolaros, PhRMA

Ginny Beakes-Read, Amgen

David Peloquin, Ropes & Gray

Michele Russell-Einhorn, Advarra

Shona Sanchita Pendse, Kowa

Jessica Scott, Takeda

Moke Sharma, Alexion

Michael Steel, Novartis

Fergus Sweeney, EMA

<u>MRCT Center team</u>

Carmen Aldinger

Barbara Bierer

Sarah White

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Keynote: The Future of Clinical Trials

Esther Krofah,

Executive Director,
FasterCures

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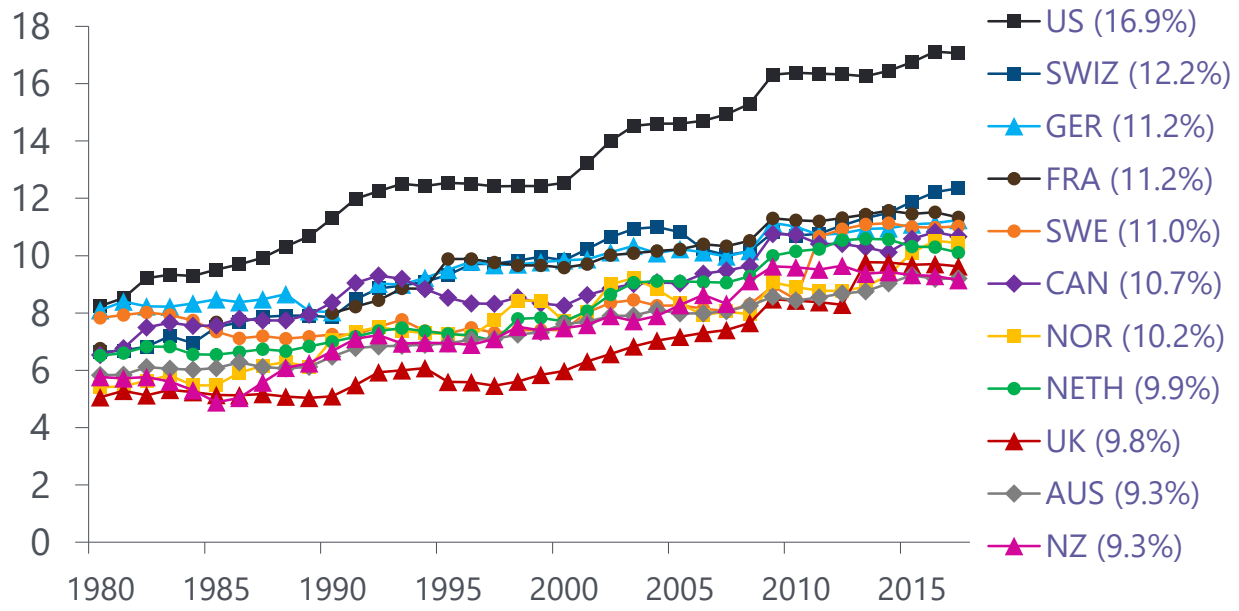
FasterCures

Transforming the Clinical Trials Enterprise: Lessons Learned from COVID 19 and Beyond

JUNE 2021

Context: American Health Care Landscape

Health Care Spending as a Percent of GDP, 1980-2018



Notes: Current expenditures on health. Based on System of Health Accounts methodology, with some differences between country methodologies. OECD average reflects the average of 36 OECD member countries, including ones not shown here.

*2018 data are provisional or estimated.

Source: OECD Health Data 2019.

The U.S. spends nearly **twice as much** as the average OECD country on health care as a share of the economy. This is largely attributed to **greater use of medical technology and higher prices** compared to other high-income countries.

(Source: Commonwealth Fund)

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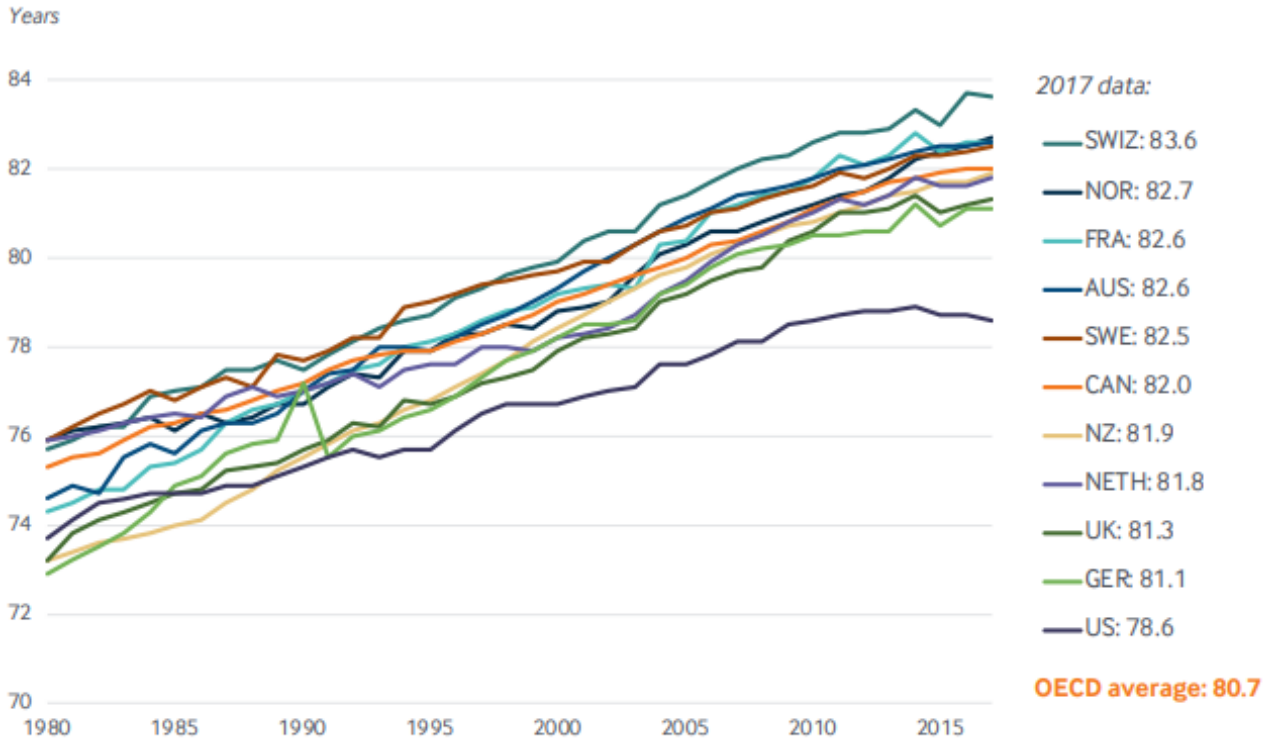
Context: American Health Care Landscape

The U.S. Has the Lowest Life Expectancy, 1980-2017



Note: OECD average reflects the average of 36 OECD member countries, including ones not shown here.

Data: OECD Health Statistics 2017.

Source: Roosa Tikkanen and Melinda K. Abrams, *U.S. Health Care from a Global Perspective, 2019: Higher Spending, Worse Outcomes?* (Commonwealth Fund, Jan. 2020). https://doi.org/10.26099/7avy-fc29

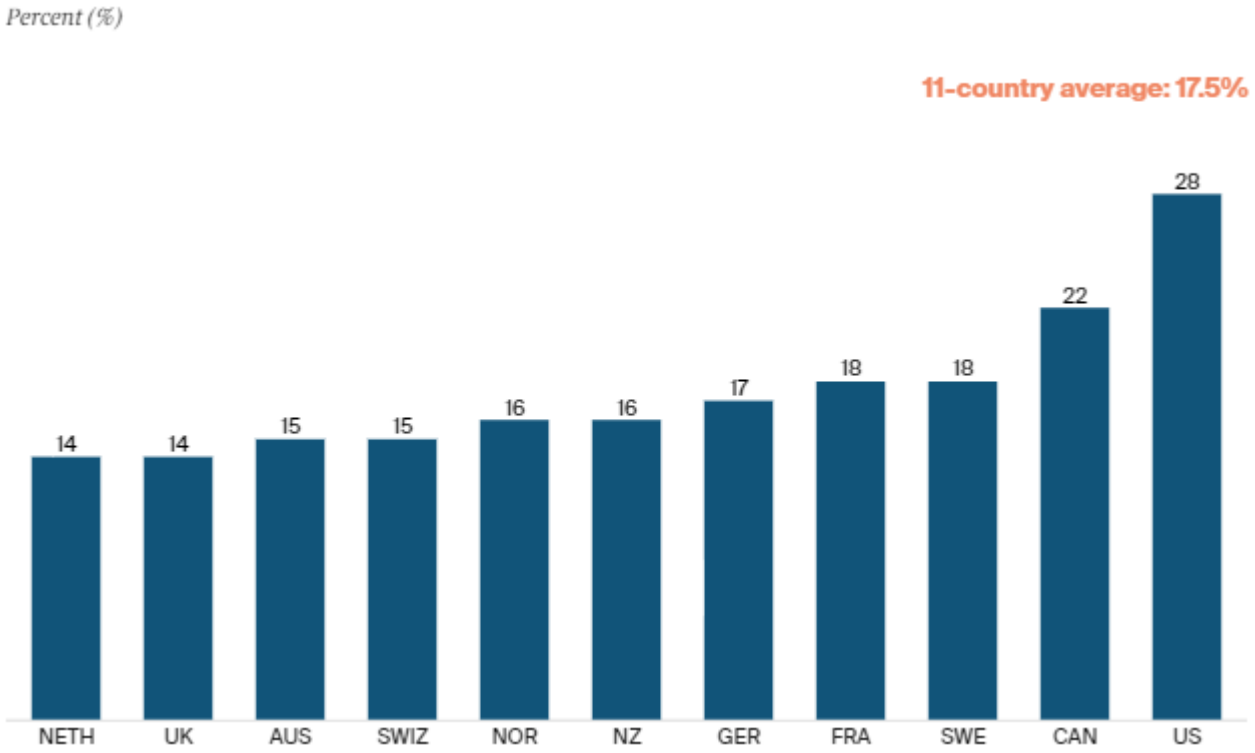
However, despite spending the most on health care, Americans experience the **worst health outcomes** as compared to their international peers.

Life expectancy at birth in the U.S. was 78.6 years in 2017, **two years lower than the OECD average.**

(Source: Commonwealth Fund)

Context: American Health Care Landscape

U.S. Adults Have the Highest Chronic Disease Burden



American adults also have the **highest chronic disease burden** and an obesity rate that is two times higher than the OECD average.

(Source: Commonwealth Fund)

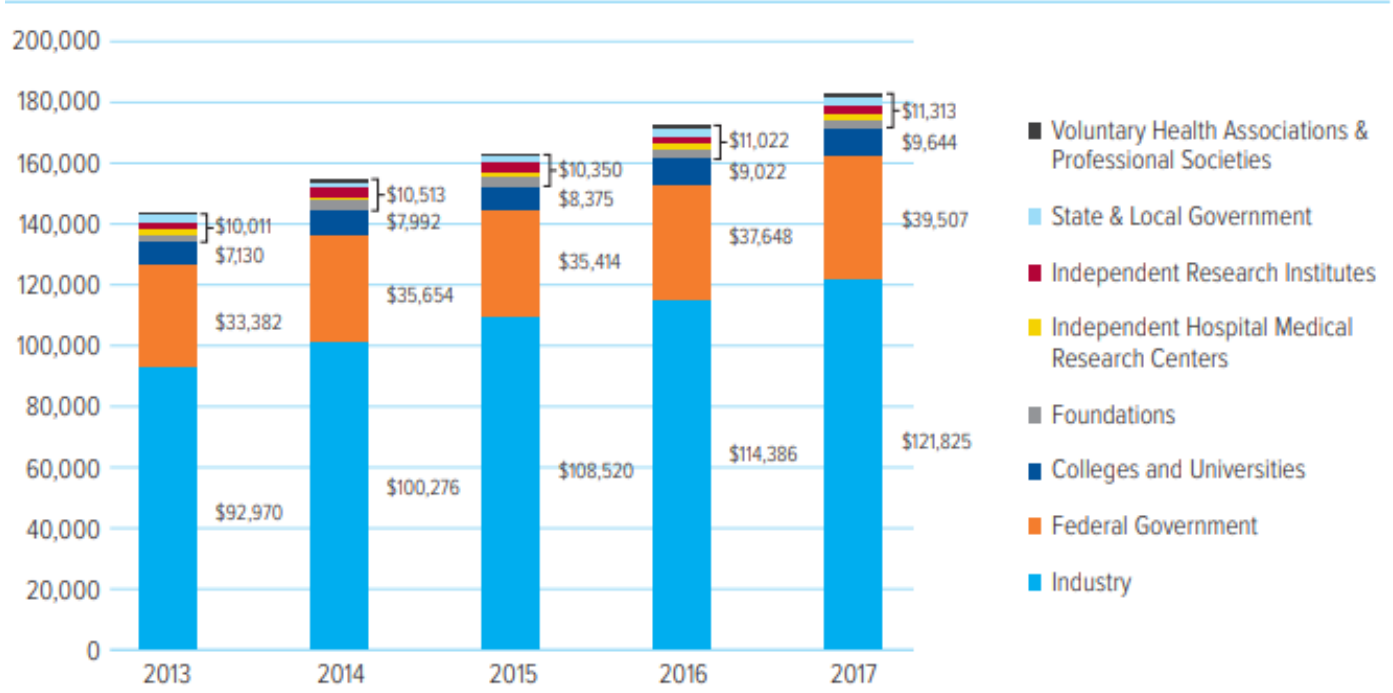
Notes: Chronic disease burden defined as adults age 18 years or older who have ever been told by a doctor that they have two or more of the following chronic conditions: joint pain or arthritis; asthma or chronic lung disease; diabetes; heart disease, including heart attack; or hypertension/high blood pressure. Average reflects 11 countries shown in the exhibit that take part in the Commonwealth Fund's International Health Policy Survey.

Data: Commonwealth Fund International Health Policy Survey, 2016.

Source: Roosa Tikkanen and Melinda K. Abrams, *U.S. Health Care from a Global Perspective, 2019: Higher Spending, Worse Outcomes?* (Commonwealth Fund, Jan. 2020). https://doi.org/10.26099/7avy-fc29

Snapshot of Today's Clinical Trials Enterprise

Estimated U.S. Medical and Health R&D Expenditures ($ in millions)



Source: Research! America, *US Investments in Medical and Health Research and Development 2013-2017*

Furthermore, the U.S. **ranks highest** in public and private spending and investment in biomedical research, but the clinical trials ecosystem remains **inefficient** and **siloed.**

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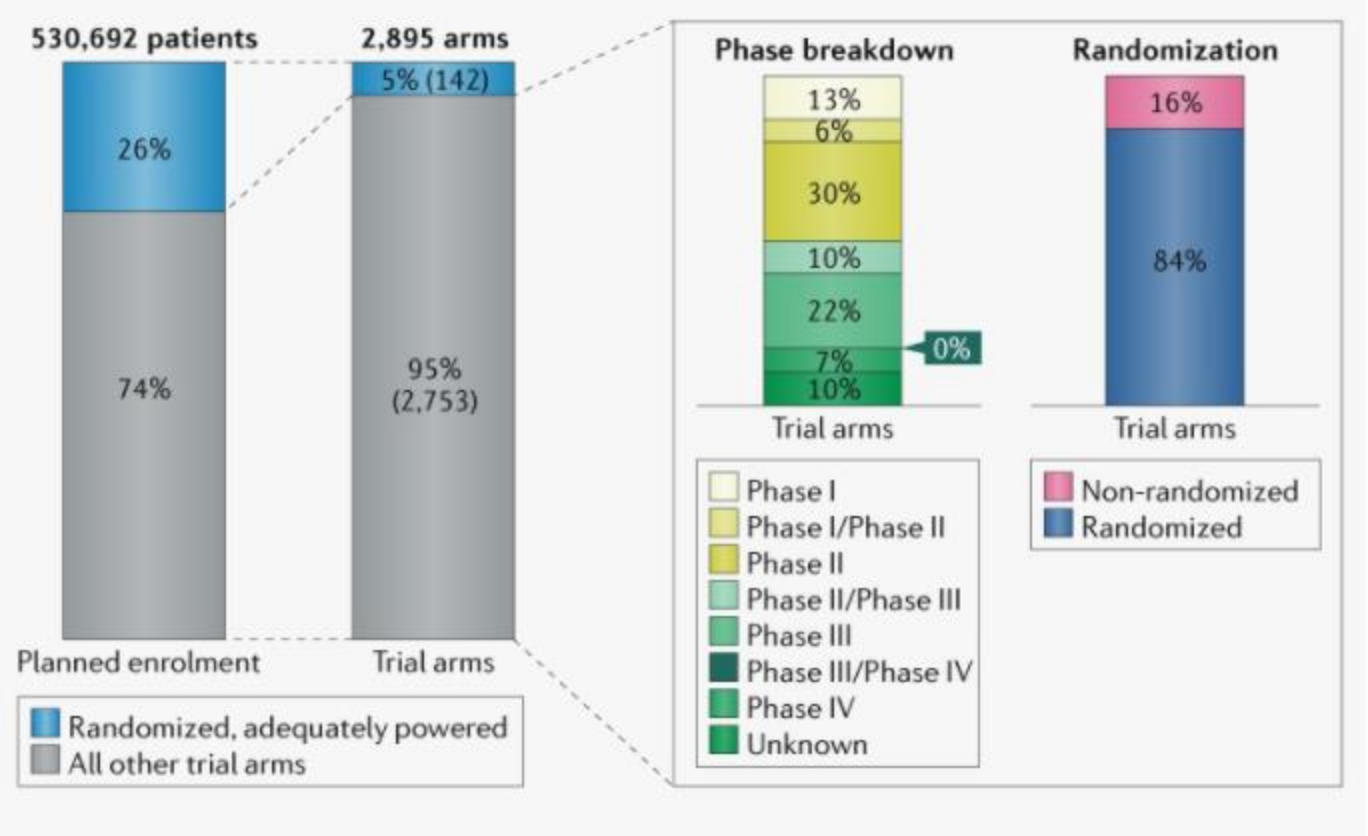
Snapshot of Today's Clinical Trials Enterprise

Trends in COVID-19 Therapeutic Clinical Trials



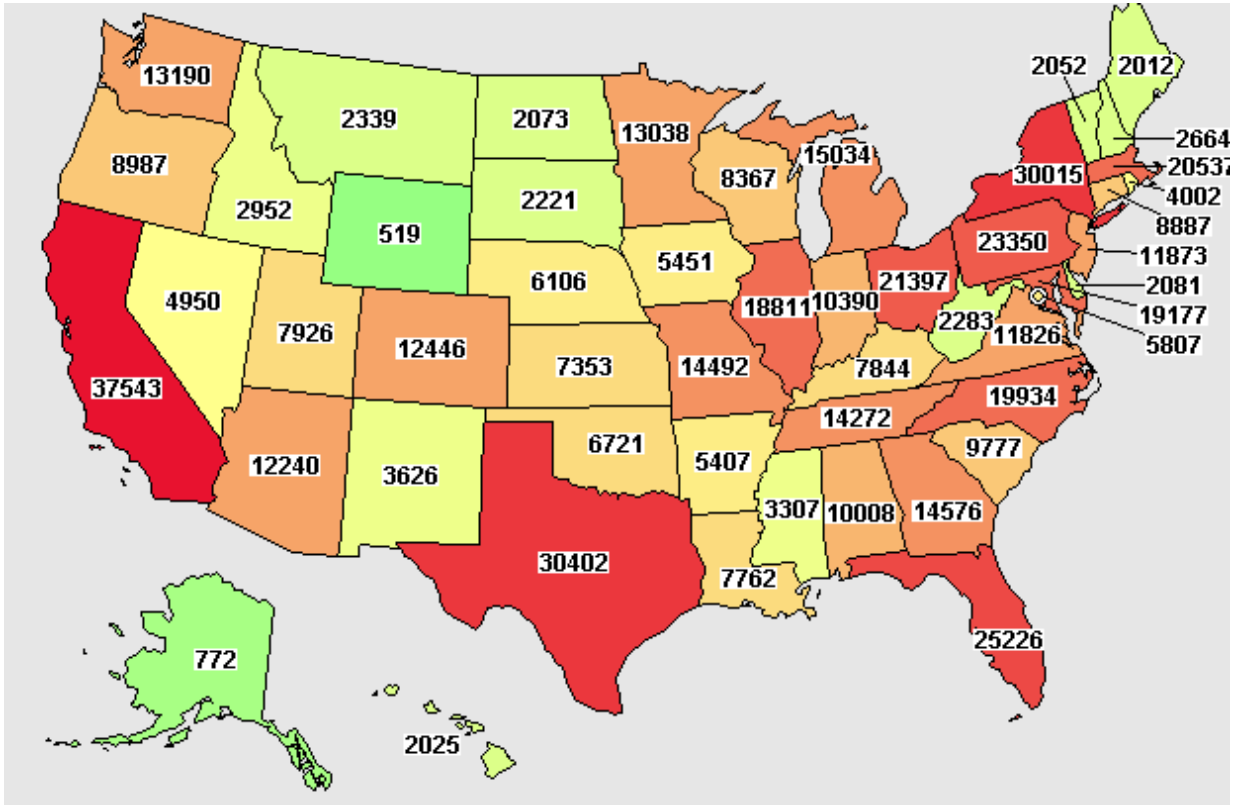
Source: Nature Reviews Drug Discovery, *Trends in COVID-19 Therapeutic Clinical Trials*

The **inefficient** and **siloed** nature of clinical trials in the U.S. – and across the world – has been **extremely detrimental to achieving progress in identifying viable therapeutics for COVID-19**.

According to ClinicalTrials.gov and the WHO clinical trial registry, **there are 2,895 COVID 19 trial arms.** However, **only ~5%** could be considered randomized and adequately powered.

Snapshot of Today's Clinical Trials Enterprise

Map of All Studies on ClinicalTrials.gov



Source: ClinicalTrials.gov, Map of All Studies on ClinicalTrials.gov

Breaking this down further, ClinicalTrials.gov provides this map as an indicator of where trials are taking place.

We know **that few clinical trial networks exist in community-based settings** where most patients – including patients of color – receive care (see next slide).

Existing clinical trial requirements create **high barriers to entry** for new trial sites.

Snapshot of Today's Clinical Trials Enterprise

The data presented in this chart developed by the Milken Institute highlights the starling realities around the lack of diversity in today's clinical trials enterprise.

Disease Condition	Clinical Trial Representation
Cardiovascular Disease	• Between 2006- 2020, the FDA approved 24 new molecular entity drugs for 7 cardiovascular conditions. In related clinical trials supporting FDA drug approval 2.9% were Black participants.
Stroke	• In 2015, roughly 27.1% of stroke clinical trial respondents indicated working exclusively in minority communities.
Diabetes	• In 5 of the 7 diabetes drug trials done pre-2017, Black people were less than 5% of the patients. 13% of Black people in the U.S. have diabetes, compared with 7.6% of White Americans.
COVID-19 (rate ratios)	• Pfizer-BioNTech phase 2/3: 9.8% Black and 26.2% Hispanic • Moderna phase 3: 9.7% Black and 20% Hispanic • J&J phase 3: 17.2% Black and 45.1% Hispanic • Veklury (Remdesivir) phase 3: 20.1% Black and 24.8% Hispanic
Cancers	• In 2019, out of 3,593 oncology trial participants, 4% were Black and 5% were Hispanic. • Less than 5% of participants in trials for 24 of 31 cancer drugs approved since 2015 were Black. • Although 20% of U.S. multiple myeloma patients are Black, they only accounted for 4.5% of participants in multiple myeloma trials since 2003. • In 230 trials leading to FDA oncology drug approvals over the past decade race was reported in only 63%.

However, through the COVID-19 pandemic, hope has emerged.

There is a new focus on designing a better system

The National Academies Forum on Drug Discovery, Development and Translation convened a series of public workshops to Envision a Transformed Clinical Trials Enterprise in 2030.

Three major themes emerged as lessons for the future of the clinical trial enterprise.

Efficiency

The clinical trial enterprise would benefit from **paring away** things that **cost money** and **time without either adding scientific value or protecting research participants**.

Wasted funding and time is a burden on research participants. **Simpler, more pragmatic trials showed their value during COVID-19**.

The RECOVERY Trial in the UK; master protocols and adaptive trial designs throughout the NIH's ACTIV; and Operation Warp Speed are all examples of **efficient, large-scale efforts to help lend answers and drive treatments to mitigate the pandemic.**

Key Approaches

- Streamline trial startup & enrollment
- Simplify contracting, IRP approvals & startup costs
- Simplify data collection from multiple sources
- Enhance the role of routine data capture
- Data, information & knowledge exchange among stakeholders
- Clarify rules governing use of tech in clinical trials

Engagement

If we hope to engage people from underrepresented communities, we must reach further upstream to **ask if we are doing research that will benefit those communities**.

The clinical trial enterprise of the future should be **reflective of the burden of disease** and focus on increasing trial relevance to underrepresented groups.

Diverse racial and ethnic groups, pregnant and lactating women, older adults, rural populations, populations hesitant with or unable to access technologies – **must all be involved in decision-making and defining research in order to improve overall population health.**

Key Approaches

- Enhance "user-friendliness" & bridge the technical divide
- Extend reach, reliability & report-ability of clinical trials
- Process/decision-making tools for participation
- Lower barriers to recruitment
- Enable rural/underserved participation
- Engage a more diverse clinical trials workforce

Coordination

A new vision for a national community-based clinical trial network requires **a cohesive plan with a central entity to oversee massive shifts in the system.**

Increasing trust in science and reconsidering research culture and incentives in academic medicine are pathways to promoting better alignment with the overall enterprise goals.

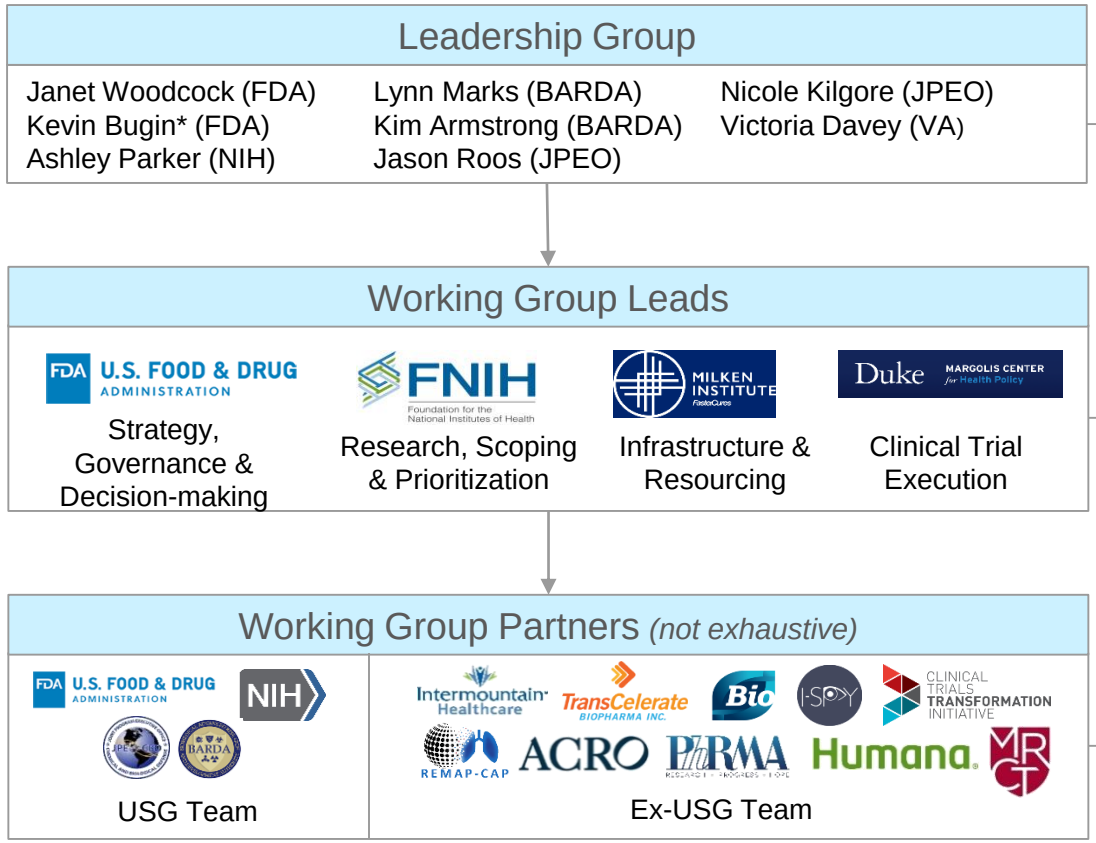
Improving diversity includes building a **diverse clinical trials workforce.**

Key Approaches

- Enable more efficient information sharing
- Collaborative trial design, conduct & analyses
- Develop tools to efficiently allocate resources
- Prioritize trials with robust design/higher public health needs
- Enable community-based partnerships
- Establish infrastructure & training opportunities

A USG effort has also emerged to examine lessons learned from COVID-19 therapeutic trials

Working groups were formed around the key topic areas to ensure robust lessons learned and recommendations, with oversight from a leadership group.



Key roles

Leadership Group: Oversee overall initiative and provide input on cross-agency & stakeholder buy-in

WG Leads: Coordinate and provide input to the development of lessons learned in the topic areas assigned to them based on expertise

WG Partners: Share lessons learned from their organization's experience and support development of recommendations

*Reach out to Kevin Bugin (PM for initiative) with any further questions: Kevin.Bugin@fda.hhs.gov

Key Emerging Themes from This Effort

- ✓ Ensure clear communication and engagement to all stakeholders across the CT landscape, especially researchers, patients, and developers
- ✓ Build clinical trial infrastructure, networks and partnerships and keep them warm working on other critical needs outside of PHE
- ✓ Set strategic principles, tools, and guidelines for clinical trial design that ensure the response can be quickly shaped from PHE inception
- ✓ Develop and disseminate tools and best practices to improve clinical trial execution
- ✓ Establish mechanisms and tools for data collection and sharing across the US CT ecosystem
- ✓ Prioritize and resource partnering with international community in joint effort, including across regulatory bodies

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*Reach out to Kevin Bugin (PM for initiative) with any further questions: Kevin.Bugin@fda.hhs.gov

In Summary: Two "Big Bucket" Issues to be Addressed

Toward a National Network of Clinical Trials in Community Practice

Early in the process, research should be exploratory, innovative, and pursue broad options. But the concept of a national-level network means that limited national resources such as funding and access to infrastructure should be prioritized for the most promising or novel approaches and well-designed studies likely to result in actionable evidence.

What entity should be the one to prioritize this? If it is a new entity, what would it look like? Where will funding and support for this entity come from?

Clear Goals & Metrics

Concrete goals and metrics can help assign a direction to the systemic changes and measure progress. FDA has tracked some of this in terms of diversity and inclusion in clinical trials, but we can do more and do better.

What would these metrics look like, and who could track them to measure progress?

Key Initiatives Already Underway

- Accelerated move to decentralized/hybrid trials
- Industry focus on diversity in clinical trials
- CROs building more diverse trial networks
- NIH UNITE
- USG led evaluation of COVID-19 therapeutic trials
- Public webinars and workshops (DCRI, MRCT, National Academies, etc.)

Thank You.

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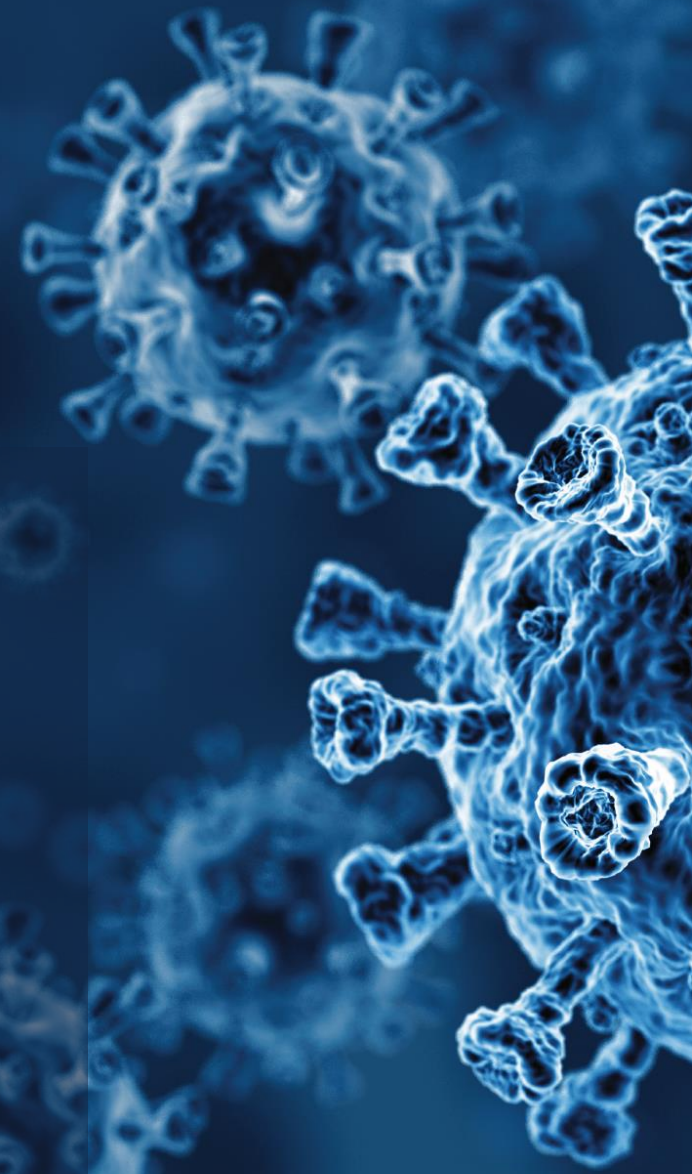

First Panel:

Useful and permissible flexibilities: A discussion of regulatory, protocol, and study conduct flexibilities that can and should be sustained in the future, that should be eliminated, and for which further experience is necessary

10:30 AM – 11:30 AM EDT

Panelists

Dr. Lindsey Baden
Brigham and Women's Hospital

Penny Carlson
Takeda

Paul Kluetz
US FDA

Valen Keefer
Patient Advocate

Dr. Isaac R. Rodriguez-Chavez
PRA Health Services

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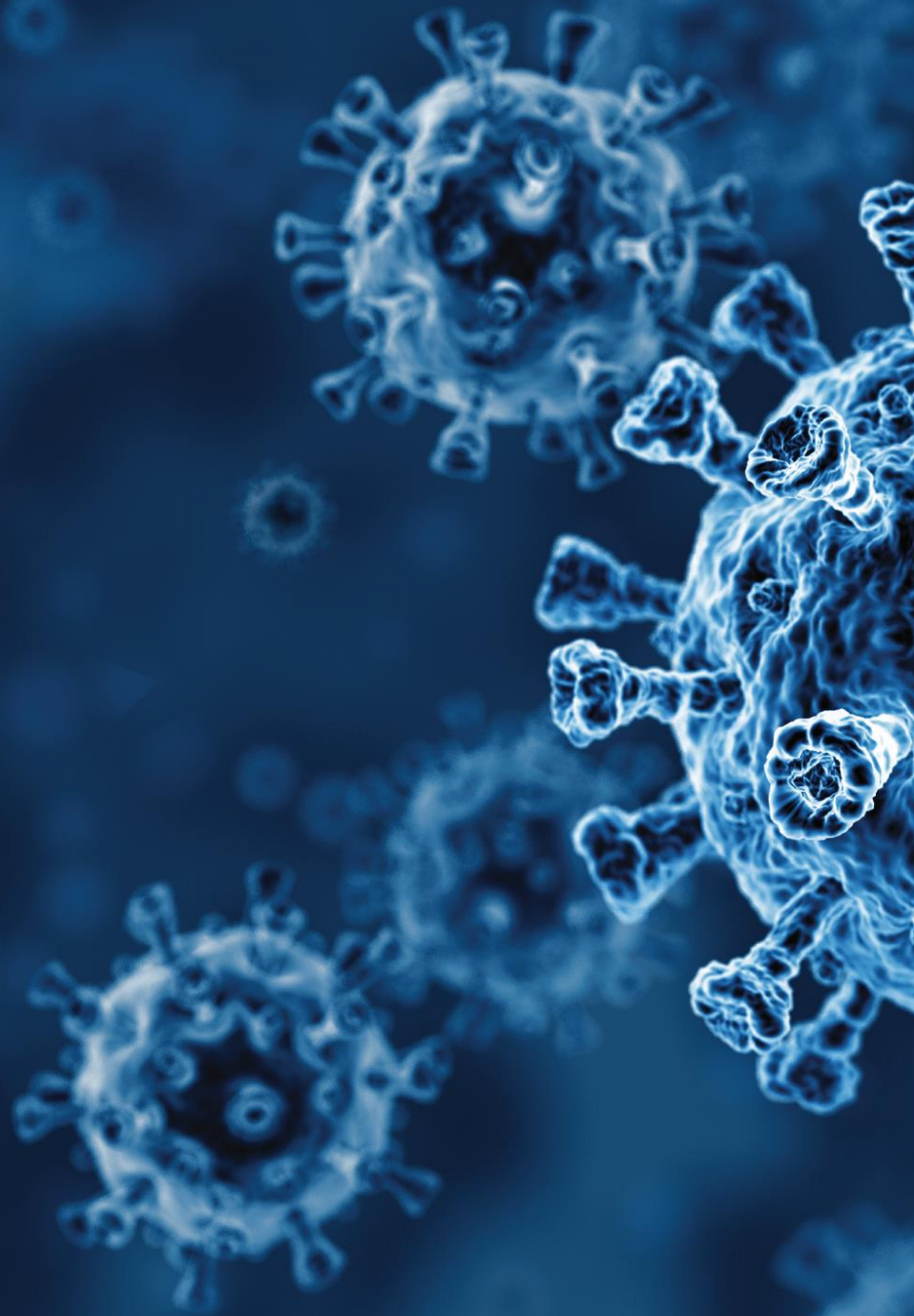

BREAK
10 min

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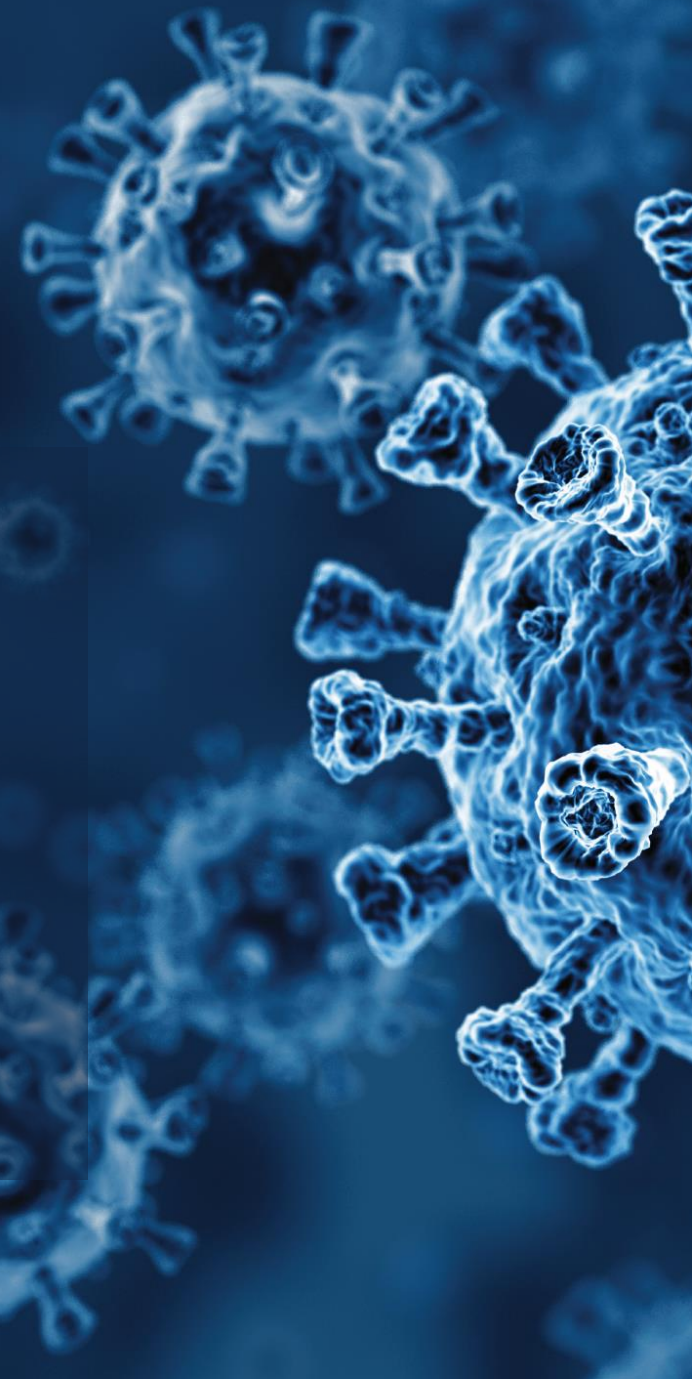

Second Panel:

Implications for and need to re-imagine the workforce in a reimagined clinical research enterprise

11:40 AM – 12:40 PM EDT

Panelists

Nicholas Brooke
Patient-Focused Medicines Development

Andrea Ferris
LUNGevity

Craig Lipset
Decentralized Trials & Research Alliance

Andrew (Andy) Lee
Merck

Harpreet Singh
US FDA

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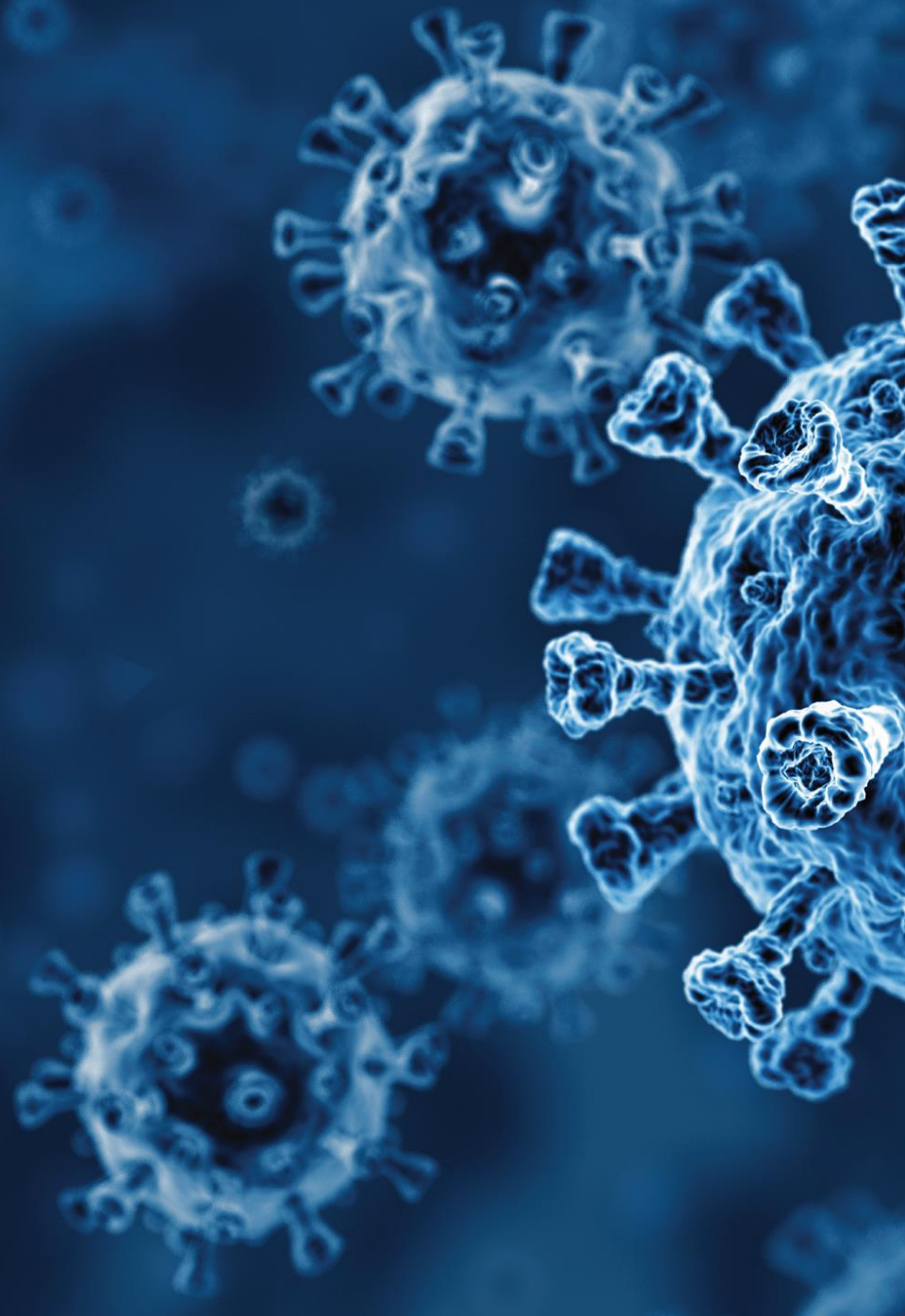
Discussion and Wrap-up



June 24, 10:00 AM – 1:00 PM EDT

TIME	TOPIC	SPEAKERS
10:00 AM - 10:45 AM EDT	**Introduction & Keynote speakers** *Can/should we change the regulatory lens as a result of the pandemic?* – Michael Rosenblatt *Reimagining Clinical Trials: Learning from COVID-19* – Fergus Sweeney *Aligning global clinical trial requirements* – Ginny Beakes-Read	•**Barbara Bierer**, Faculty Director, MRCT Center •**Michael Rosenblatt**, Senior Partner, Flagship Pioneering •**Fergus Sweeney**, Head, Clinical Studies and Manufacturing Taskforce, European Medicines Agency (EMA) •**Ginny Beakes-Read**, Executive Director, Global Regulatory and R&D Policy, Amgen
10:45 AM - 11:40 AM EDT	**First Panel –** Enabling regulatory flexibilities in a global context	•**Taras Carpiac**, Executive Director, Innovation & Process Improvement, Amgen •**Richard Moscicki**, Chief Medical Officer and Executive Vice President of Science and Regulatory Advocacy, PhRMA •**Michele Russell-Einhorn**, Chief Compliance Officer, Advarra •**Névine Zariffa**, Principal and Founder, NMD Group **Moderator:** •**Barbara Bierer**, Faculty Director, MRCT Center
11:40 AM – 11:50 AM	**BREAK**	
11:50 AM - 12:45 PM EDT	**Second Panel** – Regulatory cooperation and communication and issues of governance in a global pandemic	•**M. Khair ElZarrad**, Deputy Director, Office of Medical Policy at Center for Drug Evaluation and Research (CDER), U.S. FDA •**Owen Fields**, Vice President for Regulatory Strategy, Research and Development, Pfizer •**Steven Kern**, Deputy Director of Quantitative Sciences, Bill and Melinda Gates Foundation •**Fergus Sweeney**, Head, Clinical Studies and Manufacturing Taskforce, European Medicines Agency (EMA) **Moderator:** •**Mark Barnes**, Faculty Co-Director, MRCT Center; Partner, Ropes & Gray
12:45 PM – 1:00 PM EDT	**Discussion and wrap-up**	•**Barbara Bierer**, Faculty Director, MRCT Center •**Mark Barnes**, Faculty Co-Director, MRCT Center; Partner, Ropes & Gray

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Thank You