# JAMA Summit Update: Is the Clinical Trials Enterprise Broken? And How Can it be Fixed?

Society for Clinical Trials Annual Meeting
May 21, 2024
Boston, Massachusetts





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## The Speakers

Kirsten Bibbins-Domingo, PhD, MD, MAS, Editor-in-Chief, JAMA and the JAMA Network

Roger J. Lewis, MD, PhD, Senior Statistical Editor, JAMA

Alison J. Huang, MD, MAS, University of California, San Francisco

Kaleab Z. Abebe, PhD, University of Pittsburgh



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## Outline

**Introduction to JAMA and the JAMA Summits** (4:05 pm – 4:20 pm EDT)
Kirsten Bibbins-Domingo, PhD, MD, MAS, Editor-in-Chief, JAMA and the JAMA Network

**Summit on Randomized Clinical Trials (RCTs): Domains and Overarching Theme** (4:20 pm – 4:30 pm EDT)
Roger J. Lewis, MD, PhD, Senior Statistical Editor, JAMA

**Q&A** (4:30 – 4:45 pm EDT) Moderator: Lehana Thabane, PhD, McMaster University

**Three Example Domains: Trial Design, Populations, and Data Sources** (4:45 – 5:00 pm EDT)
Designs, Roger J. Lewis, MD, PhD, Senior Statistical Editor, JAMA
Populations, Alison J. Huang, MD, MAS, University of California, San Francisco
Data Sources, Kaleab Z. Abebe, PhD, University of Pittsburgh

**Audience Discussion and Reaction** (5:00 – 5:20 pm EDT) Moderator: Lehana Thabane, PhD, McMaster University
**Future Directions and Opportunities for Involvement** (5:20 – 5:30 pm EDT) Kirsten Bibbins-Domingo, PhD, MD, MAS





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## Information about JAMA

Lead journal of the JAMA Network, a consortium of 13 peer-reviewed journals

The most widely circulated general medical journal in the world, published in print and online 48 times per year

Led by Kirsten Bibbins-Domingo, PhD, MD, MAS (Editor in Chief) and Gregory Curfman, MD (Executive Editor)

9500 annual submissions across all article types, 12% overall acceptance rate

4800 annual submissions of research manuscripts, 4% acceptance rate

91 clinical trials published in 2023

See https://jamanetwork.com/journals/jama/pages/for-authors



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## Why Publish in *JAMA*?

SPEED

Online First publication of all articles

Median time to first decision:

**3** Days **without** review

**32** Days **with** review


IMPACT

Journal Impact Factor

**120.7**

**One of the highest** in medicine and science

**+57 MILLION**

**Annual article** views and downloads

REACH AND EXPOSURE

Extensive press coverage

**+67,800**

**Media mentions** in 2023

Broad reach through author audio interviews, editor podcasts, email alerts, social media, and multimedia





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EDITORIAL

# Introducing the JAMA Summit

Kirsten Bibbins-Domingo, PhD, MD, MAS; Derek C. Angus, MD, MPH; Hannah Park; Roger J. Lewis, MD, PhD; Rohan Khera, MD, MS; Jennifer Zeis; Annette Flanagin, RN, MA; Gregory Curfman, MD

**Over the past year,** *JAMA* editors have been developing the concept of the JAMA Summit—forums for catalyzing discussion and action on pressing issues in science, medicine, and public health. Over its more than 140-year history, *JAMA* has been a leader in publishing on critical issues related to health. As a forum for eliciting new ideas, facilitating cross-sector dialogue, and identifying opportunities for progress that inspire discussion and action, the JAMA Summit represents the latest iteration of this long tradition of furthering our mission to advance the science and art of medicine and the betterment

the world attended this in-person meeting, including researchers, funders, regulators, patient advocates, policymakers, innovators, and industry representatives. Over 2 days, 3 keynote addresses, and 5 panel presentations and discussions, the challenges and opportunities to improve the design and conduct of randomized clinical trials to be most responsive to the needs in clinical practice were dissected and debated.

This JAMA Summit on integrating clinical trials and practice will soon enter the second phase, and *JAMA* will begin





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## JAMA Summits

Forums for catalyzing discussion and action on pressing issues in science, medicine, and public health

Two phases

- Convening thought leaders from across relevant sectors to discuss and debate, and to identify themes and actionable steps
- Elaboration on themes and next steps through published materials in JAMA and the JAMA Network journals

First Summit held October 2023 on the clinical trials enterprise, attended by 65 individuals over 2 days, 3 keynote addresses, 5 panel presentations and extensive discussion

Second Summit will focus on the integration of artificial intelligence with clinical care, beginning with an in-person assembly



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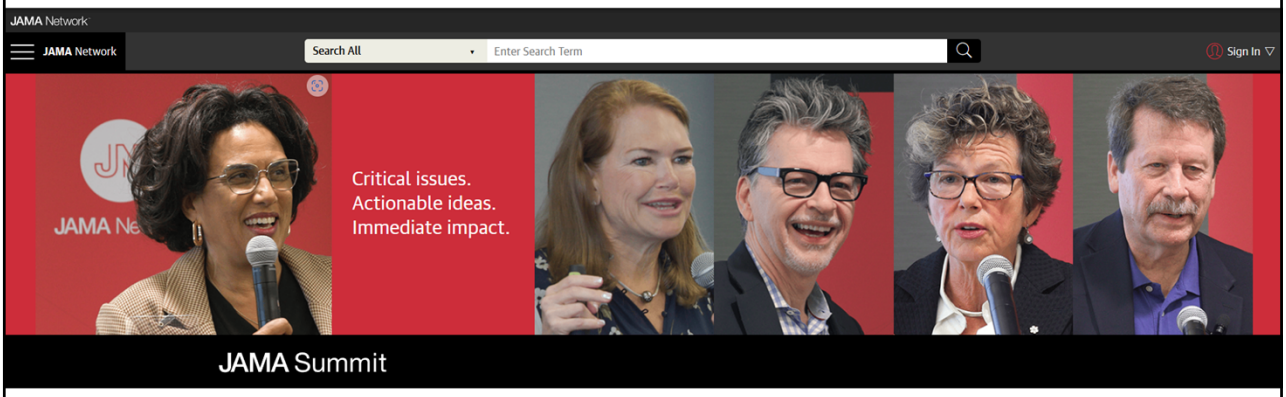
## JAMA Summits




**Learn about the JAMA Summit**

**JAMA Summit**™ is an initiative of *JAMA* and the JAMA Network that convenes leaders from across sectors and around the world to discuss and debate critical issues in medicine, health, and health care.

**JAMA Summit: Clinical Trials**
October 10-11, 2023
JAMA Network Offices
Chicago, IL

**JAMA Summit: Artificial Intelligence**
October 15-16, 2024
JAMA Network Offices

https://jamanetwork.com/pages/jama-summit



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## Why a JAMA Summit Focusing on RCTs?

In general, the RCT enterprise is

- Too slow and expensive, not scalable or sustainable, and unable to meet demand for answers
- Slow to leverage progress in technology and new sources of clinical, behavioral, and other information
- Structured to precisely answer questions of diminished clinical relevance to patients, their healthcare providers, and healthcare systems
- Carefully designed to avoid the complexity and heterogeneity of clinical care

*The net effect is a failure to fully meet our contract with society: to create knowledge that improves the effectiveness of healthcare in ways that matter to patients*



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## JAMA Summit on the Clinical Trials Enterprise

Presentations and discussion organized around 4 initial themes

- Clinical trial design
- Data infrastructure
- Ethics and regulatory oversight
- Financial incentives

**Key theme**

- The challenges facing the clinical trials enterprise and reducing the value of clinical trials for improving the effectiveness and patient-centeredness of care can be traced to the separation of the clinical research enterprise from the delivery of healthcare
- Reactions to this theme?



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## Three Example Domains:

## Clinical Trial Design, Populations, and Data Sources





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## Clinical Trial Design: Challenges

Inferential design versus structural design and operational planning

- Inferential (i.e., statistical) design is simplified to a degree that fails to reproduce key characteristics of clinical care (e.g., heterogeneity of patients, patient diversity, multiple treatments [simultaneously or over time])
- Structural design and operational planning is “trial-centric” rather than “patient-” or “healthcare-centric”

Both characteristics predictably lead to the generation of evidence that

- Is largely or completely silent on many questions facing patients and their caregivers (e.g., treatment of patients with multiple diseases, combination treatment strategies, selection of second-line treatments)
- Has low validity for informing typical treatment decisions, e.g., based on evidence gathered from patients, providers, and healthcare settings qualitatively distinct from usual care settings





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## Clinical Trial Design: Potential Solutions

Inferential Design, e.g.:

- Platform trials, evaluating *multiple* treatments in *heterogeneous* patient populations, with available treatments changing over time, to create a "perpetual" learning system (leveraging COVID-19 experience)
- Sequential multiple assignment randomized trials (SMARTs) to determine the optimal *sequence* of treatments conditional on individual responses to prior therapy

Structural Design and Operational Planning, e.g.:

- Embedding research into the location, structure, and processes of everyday clinical care to enroll representative, heterogeneous, diverse populations
- Decrease the disruption of care and burden associated with research (data sources and population domains)
- Decrease both the financial costs to society to conduct research (e.g., don't rebuild the stadium to play each game) and the opportunity costs to individuals to participate in research





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## Patient and Population Centeredness: Challenges

Narrow perspectives: Despite superficial gestures, few trials are designed and conducted with continuous and meaningful input from end-target populations

Unrepresentative populations: Trials apply inconsistent standards in engaging representative people or communities—and there is no accountability for failure

Limited view of care settings: Most trials ignore factors outside the hospital or clinic that can have a major impact on engagement with health interventions

Focus on "health care" vs "health": Even with integration into healthcare systems, trials reflect the shortcomings and biases of the existing health care enterprise





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# “It’s nobody’s fault”





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## Patient and Population Centeredness: Potential Solutions

Can the trial community develop, disseminate, and incentivize use of standard toolkits and score systems for promoting equity in intervention development and testing?

Can greater and more streamlined integration between disease registries and trials promote more representative trial engagement?

Will more consistent engagement of behavioral and social scientists in trial teams (even for drug or device trials) improve patient centeredness?

Should trial “gatekeepers” (funders, IRBs, journals) establish systematic processes for weighing the relevance of trial questions to patients and communities?

Should approval or payment for interventions be conditional upon proof of relevance to patients or other end-users, via direct engagement or post-research implementation?





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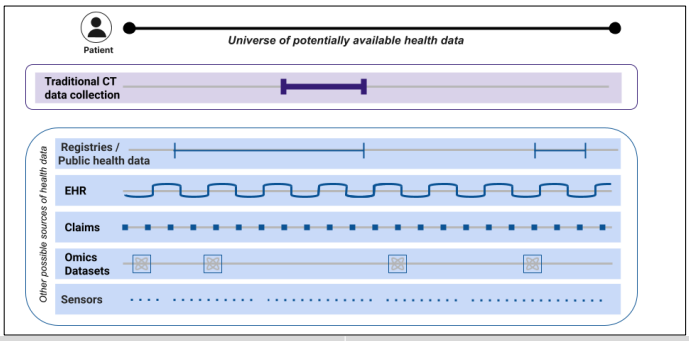
## Data Infrastructure: Challenges

- Current data infrastructure is expensive, labor-intensive, and inefficient
- Typically, RCT data is collected separately from routine health care data
- Only captures a “snapshot” of life, ignoring important non-clinical information, such as social determinants of health
- Once an RCT is completed…we start anew with the next one





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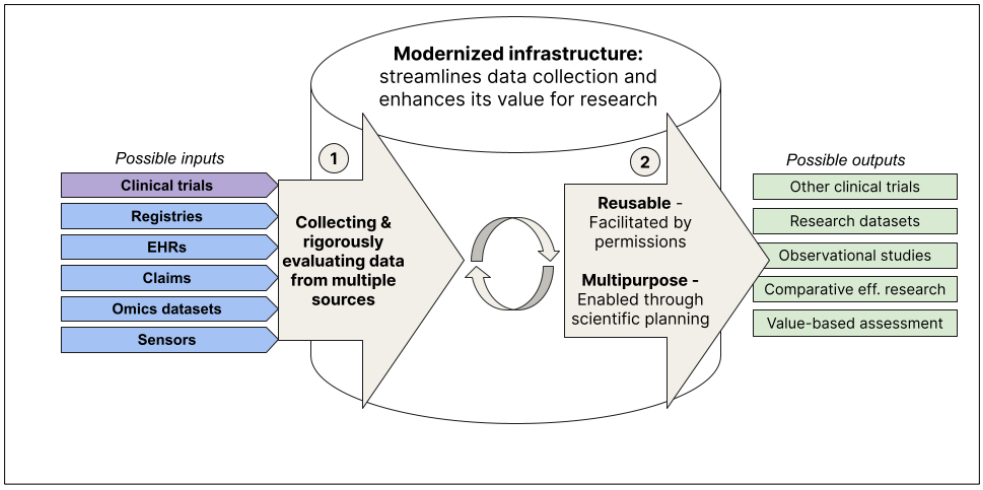
## Data Infrastructure: Potential Solutions

- A modernized data collection infrastructure is sorely needed.





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## Data Infrastructure: Potential Solutions

How to get there? 3 potential initiatives:

- Utilize metadata (how, when, by whom was data collected – and how this changes over time)
- Focus data elements on those routinely collected in clinical care
- Better integration of research and clinical care data systems

Important Considerations

- Ethical – who owns the data and who is able to reuse for what purposes
- Relationship with healthcare providers – how to minimize their role in the burdensome collection of data
- Impact on the global research – should there be an updated ICH?

Multidisciplinary community is needed to solve these problems

- Patients, data coordinating centers, biostatisticians, research and clinical IT, clinicians, health system personnel, government, regulatory, ethics





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## Moderated Discussion





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## Future Directions—for Discussion

- Future directions—where do we go from here?
- How can SCT members become involved?
- How can SCT as a Society become involved?





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