Catalyzing Change How First-in-Patient Trials Can Fix U.S. Clinical Trials

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Vice Dean, Duke University School of Medicine

Duke Clinical Research Institute

Will U.S. clinical trials exist in 10 years?

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How will U.S. clinical trials be globally competitive in 10 years?

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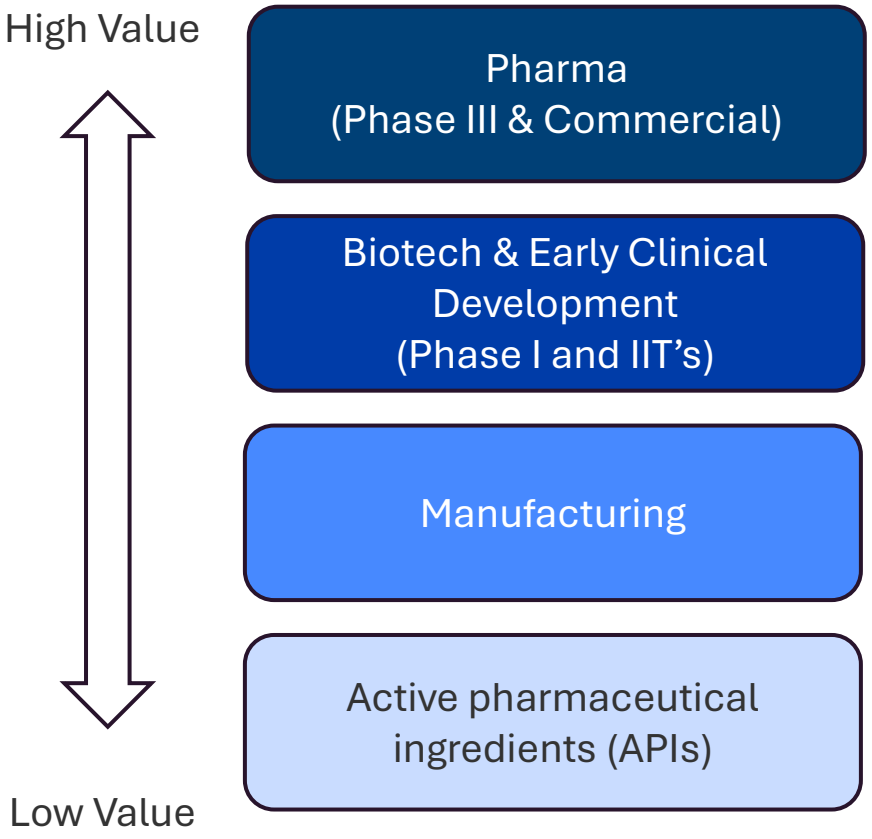
Ask yourself….

Using a range of 0%-100%, what's the probability of the following?

1. >90% are manufactured outside the U.S.
2. >90% of new drugs are discovered outside the U.S.
3. The U.S. is a token requirement for clinical trials, only at the very final stages.
4. U.S. patients must go abroad to access early discoveries.
5. >90% of academic research originates outside the U.S.

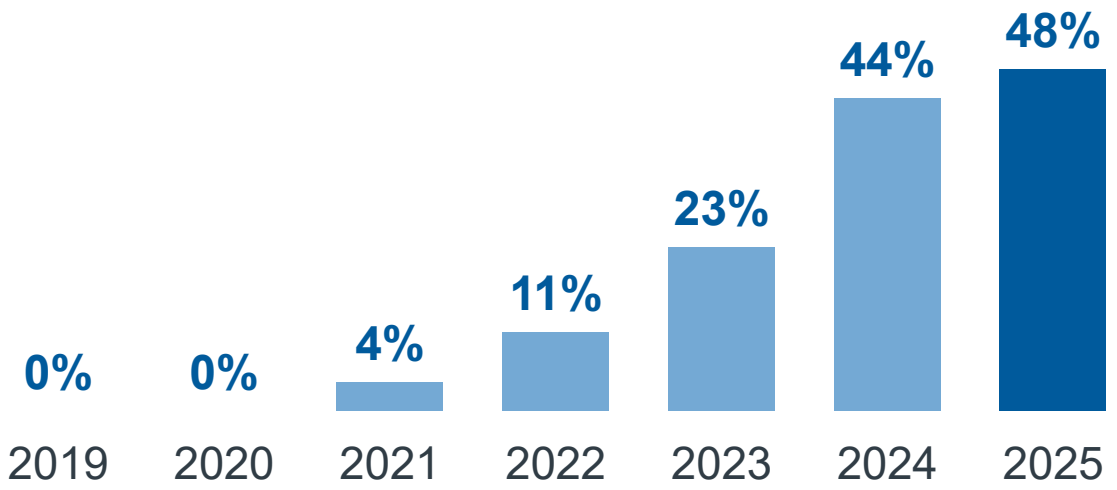
Is it a non-zero probability?

China’s success: biotech policy, infrastructure, and growth



Licensing deals from China

Share of large-pharma deals with ≥$50M upfront



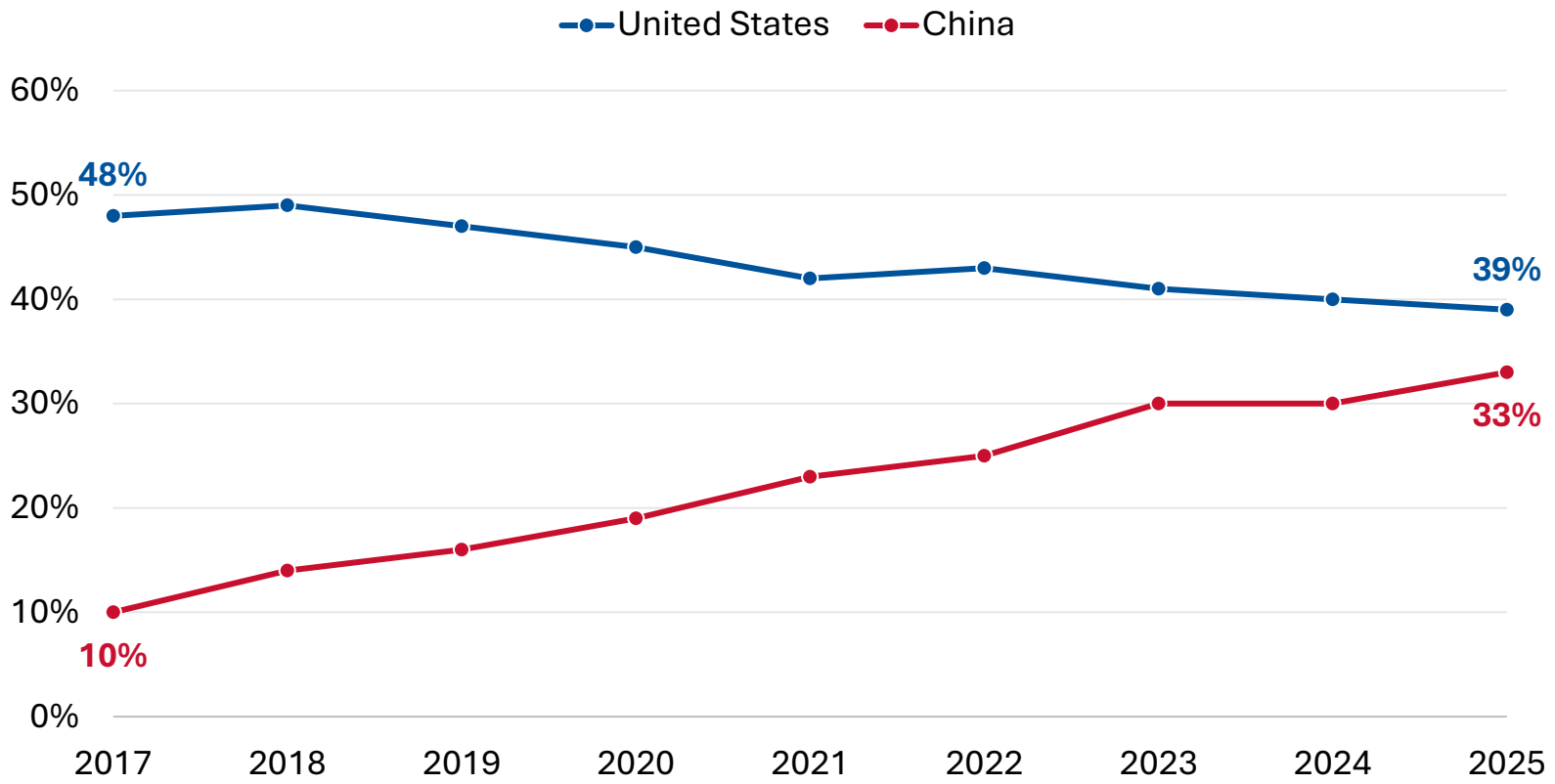
Source: DealForma

China also accounts for >80% of the global supply chain for generic active pharmaceutical ingredients (APIs).

2026 DCRI ThinkTank: Early Phase Research Summit
https://dcri.org/stories/early-phase-trials-move-overseas-experts-urge-us-act

Early-Phase Trial Share Shifts

Share of all industry-sponsored early-phase (Phase 1 or 2) trials worldwide, 2017-2025

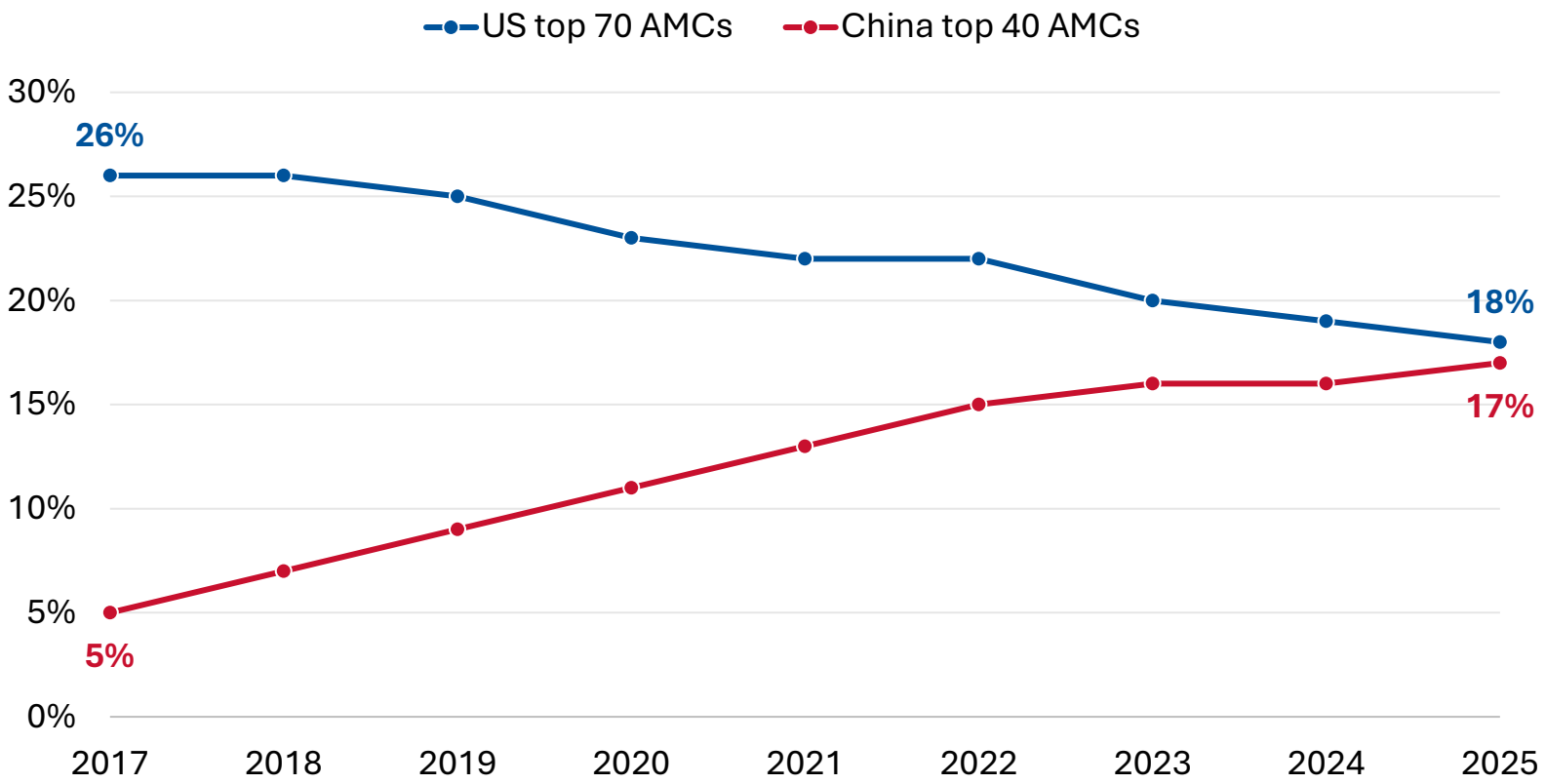


U.S. share fell 48% to 39%
while China rose 10% to 33% — a 23-point swing in nine years.

Source: ClinicalTrials.gov. Industry-sponsored trials (Phase 1 or 2); trials in both countries counted for each.

Shifts in Early-Phase Research in Academic Centers

Each cohort's share of worldwide industry-funded early-stage trials, 2017-2025



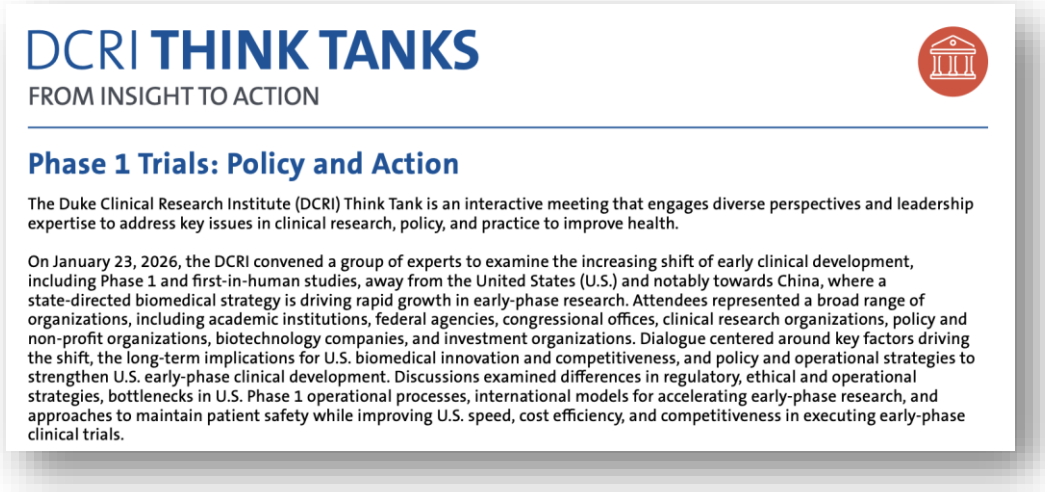
From 5x to near parity

U.S. top 70 AMCs: 26% to 18% (-8 points). China top 40 AMCs: 5% to 17% (+12 points).

Source: ClinicalTrials.gov. Share of worldwide industry-funded early-stage trials (Phase 1, Early Phase 1, Phase 1/2); a trial is credited to a cohort if it lists at least one site at a cohort AMC.
U.S. cohort: 70 AMCs with ≥10 industry-funded early-stage trials in 2017. China cohort: top 40 Chinese AMCs by 2017-2025 cumulative volume. Interim years read from the source figure.

Early Phase Research Summit: Key Takeaways

DCRI Phase 1 Trials: Policy and Action January 23, 2026



DCRI **THINK TANKS**
FROM INSIGHT TO ACTION

Phase 1 Trials: Policy and Action

The Duke Clinical Research Institute (DCRI) Think Tank is an interactive meeting that engages diverse perspectives and leadership expertise to address key issues in clinical research, policy, and practice to improve health.

On January 23, 2026, the DCRI convened a group of experts to examine the increasing shift of early clinical development, including Phase 1 and first-in-human studies, away from the United States (U.S.) and notably towards China, where a state-directed biomedical strategy is driving rapid growth in early-phase research. Attendees represented a broad range of organizations, including academic institutions, federal agencies, congressional offices, clinical research organizations, policy and non-profit organizations, biotechnology companies, and investment organizations. Dialogue centered around key factors driving the shift, the long-term implications for U.S. biomedical innovation and competitiveness, and policy and operational strategies to strengthen U.S. early-phase clinical development. Discussions examined differences in regulatory, ethical and operational strategies, bottlenecks in U.S. Phase 1 operational processes, international models for accelerating early-phase research, and approaches to maintain patient safety while improving U.S. speed, cost efficiency, and competitiveness in executing early-phase clinical trials.

Competitiveness has strategic implications

- Risk of weaker U.S. research capacity
- Greater reliance on development abroad
- Economic, biomedical, and biosecurity threats

Speed influences trial location

- Australia CTN: starts quickly after final protocol
  - No major safety issues since 2015

Costs and incentives matter

- Australia: tax incentives lower costs
- Simpler contracts and predictable activation

U.S. delays extend beyond regulation

- Extensive pre-IND requirements
- Variable local processes delay startup

Source: DCRI, Phase 1 Trials: Policy and Action, January 23, 2026 summit brief, p. 1.

Early Phase Research Summit: Recommendations

Proposals to improve U.S. competitiveness while protecting patients and data integrity

A national strategy

- Align U.S. funding, industry and regulation
- Explore tax credits and rebates

Faster startup processes

- Tailor IND/CMC requirements to phase
- Streamline IRB review and standardize contracts/budgets
- Publicly report startup metrics

Reenforce study standards

- Verify patient-level data, consent and GCP compliance
- Inspect or pre-certify sites in countries of concern
- Use remote monitoring when access is limited

Source: DCRI, Phase 1 Trials: Policy and Action, January 23, 2026 summit brief, p. 2.

Early-phase research in China and Australia

Regional use in industry-sponsored trials

Phase I–III, 2019 compared with H1 2025

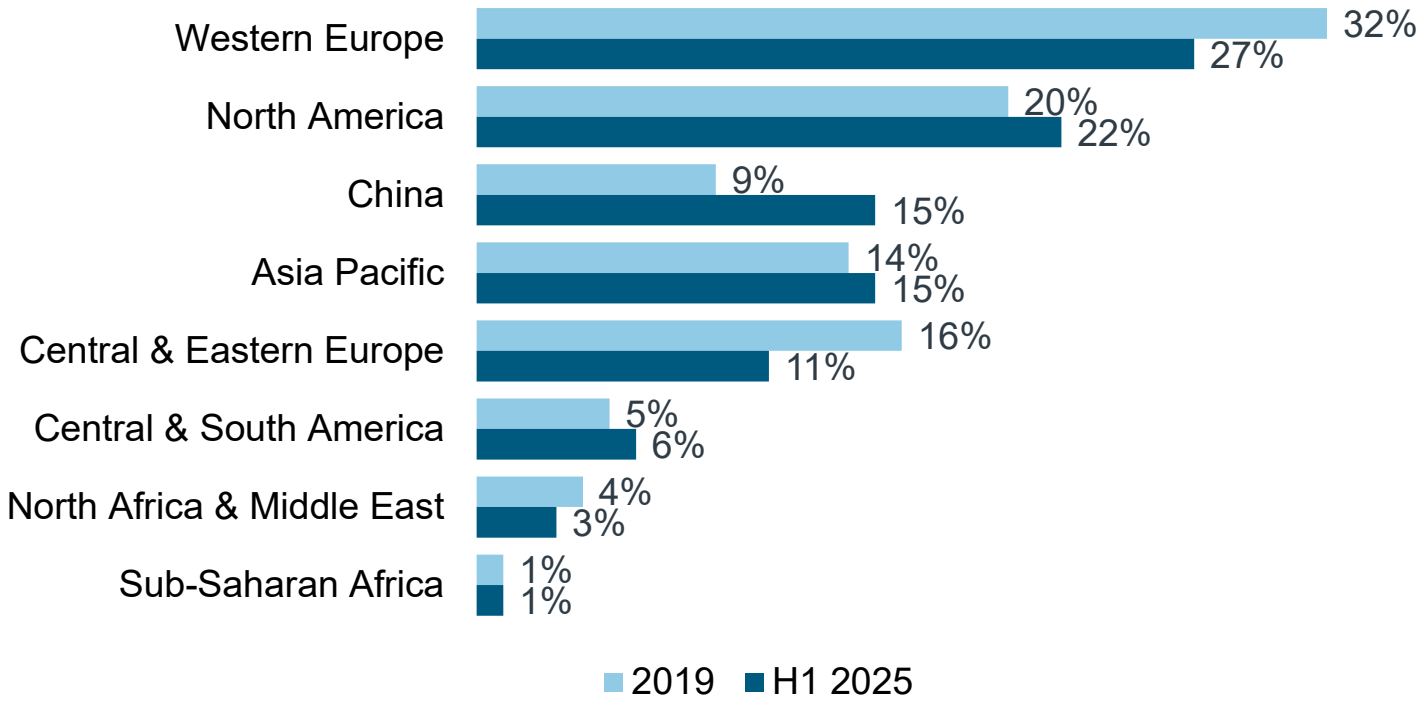


Chart: Citeline Trialtrove, July 2025. Percent of trial country uses.

Australia

<70 days

Protocol to site activation

Clinical trial notification system

China

Growing translational science and first-in-human trials

Lower costs and faster timelines

Proof of concept before U.S. trial start

Australia's CTN pathway: a different regulatory architecture

Responsibility shifts toward ethics review and institutional accountability while national oversight remains.

1. Sponsor prepares protocol

2. HREC scientific and ethics review

Protocol and Investigator's Brochure

Scientific validity, safety and risk–benefit

Consent and participant protections

Specialist input when needed

3. Institution authorizes trial

4. Sponsor notifies TGA

5. Trial may commence

HREC continues review and monitoring

6. TGA retains compliance and enforcement authority

CTN = Clinical Trial Notification HREC = Human Research Ethics Committee
TGA = Therapeutic Goods Administration

NOTIFICATION, NOT NO OVERSIGHT

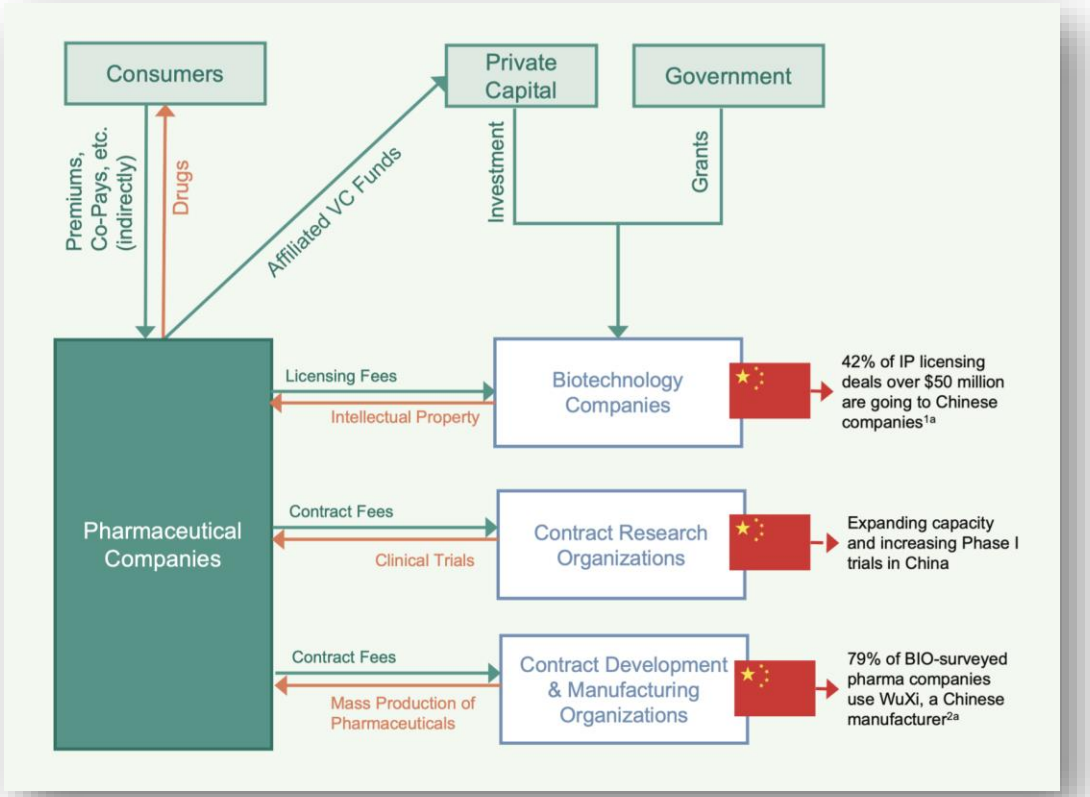
The design principle is sequencing and accountability, not lower standards.

Sources: TGA, CTN scheme (2025) and Australian clinical trial handbook (2024). NHMRC, National Statement (2025).

National Attention to Biotechnology Competitiveness

NSCEB report released December 19, 2025



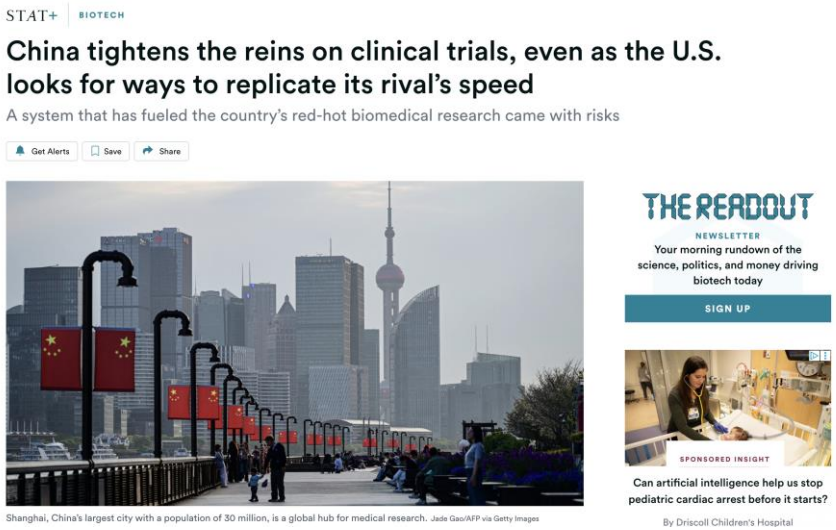


U.S. policymakers have a three-year window to retain, or in some cases regain, biotechnology leadership or risk ceding profound military, geopolitical, and economic advantages to China.

Source: National Security Commission on Emerging Biotechnology. The Future of U.S.–China Biotechnology Competition. December 2025.

Release date: NSCEB official announcement, December 19, 2025.

With Speed Comes Risks…


STAT+ BIOTECH

China tightens the reins on clinical trials, even as the U.S. looks for ways to replicate its rival's speed

A system that has fueled the country's red-hot biomedical research came with risks

Get Alerts Save Share

Shanghai, China's largest city with a population of 30 million, is a global hub for medical research. Jade Gao/AFP via Getty Images

THE READOUT

NEWSLETTER

Your morning rundown of the science, politics, and money driving biotech today

SIGN UP

SPONSORED INSIGHT

Can artificial intelligence help us stop pediatric cardiac arrest before it starts?

By Driscoll Children's Hospital

Risks

Patient safety concerns

Limited transparency

Questions over intellectual property

China's reform response

New biomedical technologies

Order No. 818, effective 1 May 2026

Scientific and ethics review

Required before studies begin, supported by nonclinical safety and efficacy evidence.

National filing

Institutions must file within five working days after scientific and ethics approval.

Institutional accountability

Qualified hospitals, investigators and safeguards for research quality and participants.

Sources: Brian Yang, STAT, 10 Aug 2026. China State Council Order No. 818, Articles 9–15.

Should we be surprised?

Duke Clinical Research Institute

These trends span more than a decade

2014

Published more than a decade ago

Clinical trial research price indexes



U.S. BUREAU OF LABOR STATISTICS

Monthly Labor Review

ARTICLE

JUNE 2014

Price indexes for clinical trial research: a feasibility study

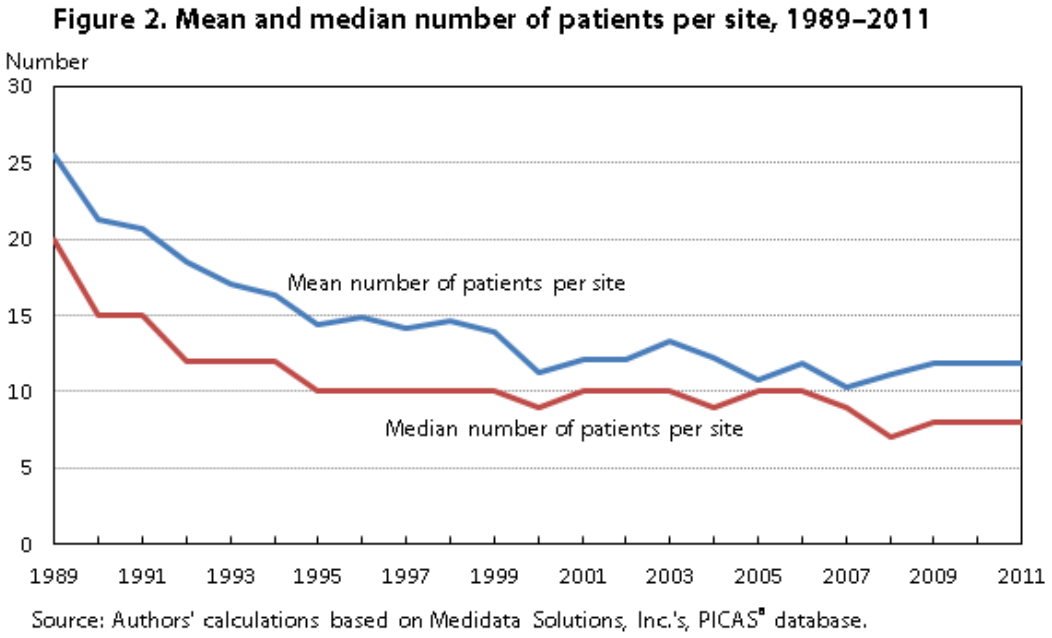
A study using a large sample of agreements between sponsors of clinical trials and clinical investigators produces estimated hedonic price indexes for clinical trial research, an important component of biomedical research and development. Measured as total grant cost per patient, nominal prices grew by a factor of 4.5 between 1989 and 2011, while the U.S. National Institutes of Health Biomedical R&D Price Index, the only published source of information on trends in pricing in the biomedical research-and-development sector, rose only slightly more than twofold. After

Source: Berndt E, Cockburn I. Monthly Labor Review, June 2014.

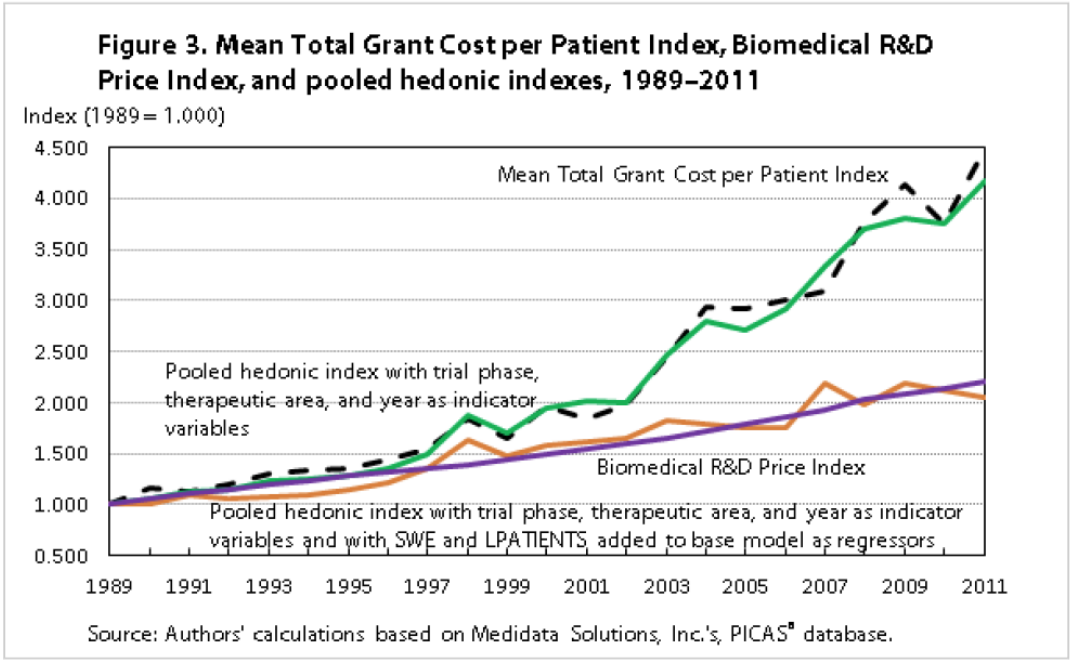
Higher costs, lower productivity

Clinical trial trends, 1989–2011

Fewer patients per site



Higher cost per patient



Source: Berndt E, Cockburn I. Monthly Labor Review, June 2014.

We're losers: Clinical Trial Humility

Research Letter

February 12, 2025

Patient Enrollment for Cardiovascular Clinical Trials in the United States

Muhammad Shahzeb Khan, MD, MSc[1,2,3]; Adeena Jamil, MBBS[4]; Muteia Shakoor, MBBS[4]; et al

» Author Affiliations | Article Information

JAMA Cardiol. 2025;10(3):298-300. doi:10.1001/jamacardio.2024.5537

- **North America:** most sites (1377; 31.4%) but lowest median enrollment (8.0 patients/site)
- **South America:** fewest sites (329; 7.5%) but highest patients per site (24.8)
- **Eastern Europe:** highest median per-site enrollment (16.0 patients/site)

Table 2. Site-Specific Enrollment Characteristics for Trials Reporting Patient-per-Site Data

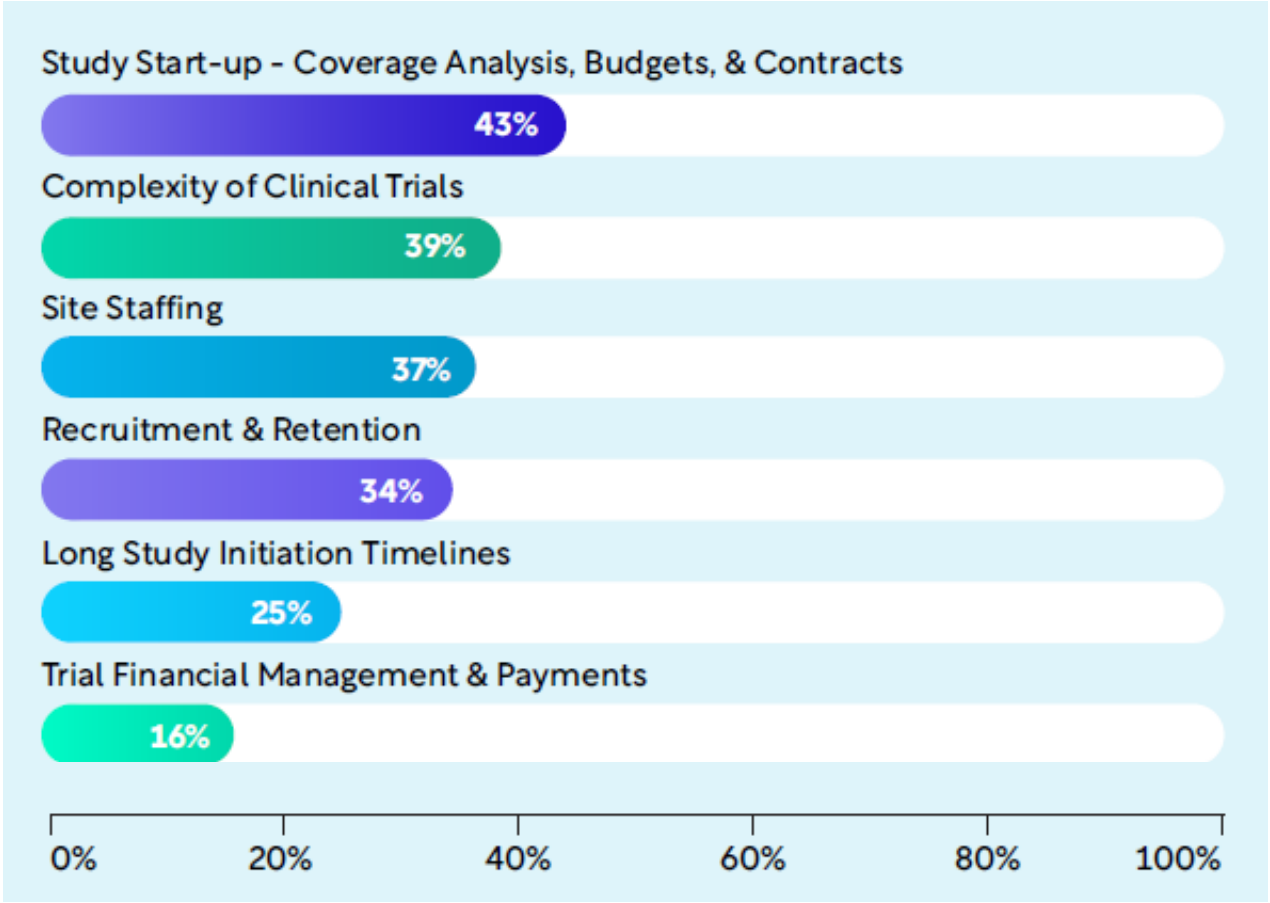
	Patients enrolled			No. (%)		
					Sites enrolling <10 patients	
Trial	Total No.	US, No. (%)	Total sites, No.	US sites	Overall	US[a]
Total	89 172	17 705 (19.9)	4388	1133 (25.8)	2014 (45.8)	659 (58.1)
ISCHEMIA-CKD	777	159 (20.5)	118	36 (30.5)	95 (80.5)	31 (86.1)
COP-AF	3209	355 (11.1)	45	8 (17.8)	12 (26.7)	3 (37.5)
THEMIS	19 220	2266 (11.8)	1297	307 (23.7)	668 (51.5)	228 (74.3)
ILUMIEN IV: OPTIMAL PCI	2487	909 (36.6)	80	35 (43.8)	23 (28.7)	14 (40.0)
PARADISE-MI	5702	454 (8.0)	494	82 (16.6)	284 (57.5)	73 (89.0)
REPRIEVE	7769	3787 (48.7)	145	100 (69.0)	23 (15.9)	18 (18.0)
SELECT	17 604	3652 (20.7)	804	201 (25.0)	220 (27.4)	58 (28.9)
ISCHEMIA	5179	853 (16.5)	319	109 (34.2)	207 (64.9)	88 (80.7)
AEGIS-II	18 219	1993 (10.9)	899	196 (21.8)	450 (50.1)	138 (70.4)
TWILIGHT	9006	3277 (36.4)	187	59 (31.6)	32 (17.1)	8 (13.6)

- **Author's conclusion:** the United States had the **most sites** but enrolled **significantly fewer patients**.
- These trends suggest **underlying legal, regulatory, and cost-related barriers**, highlighting the need for improved clinical trial infrastructure.

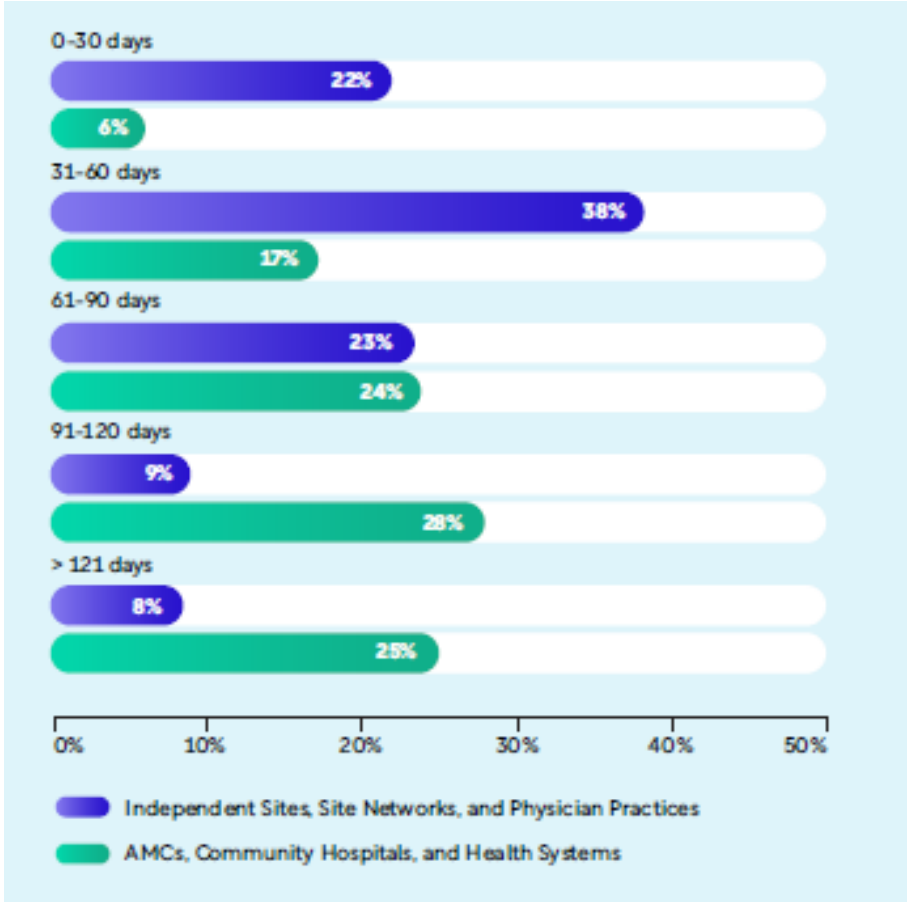
JAMA Cardiol. 2025;10(3):298-300. doi:10.1001/jamacardio.2024.5537

Top issues impacting academic, health system, and community hospital research sites

Top issues impacting ability to conduct research

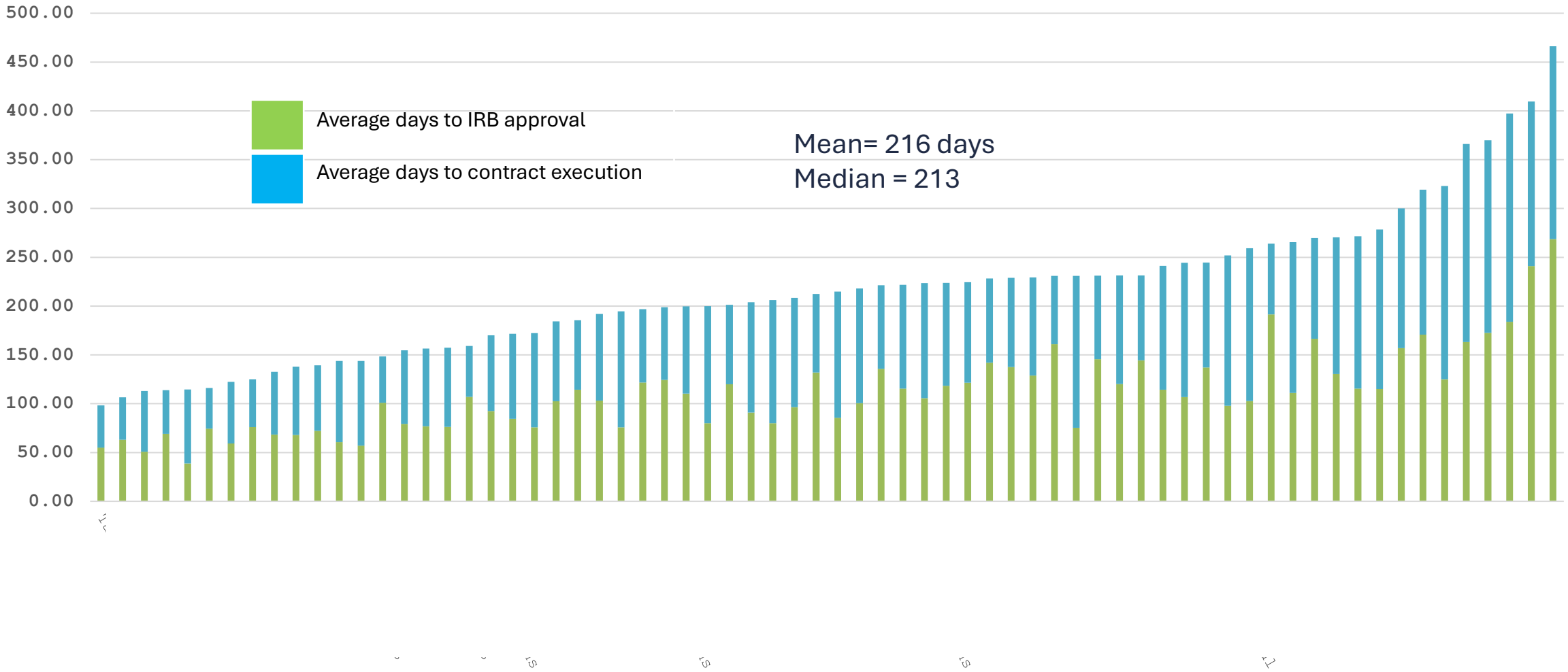


Reported start-up timelines

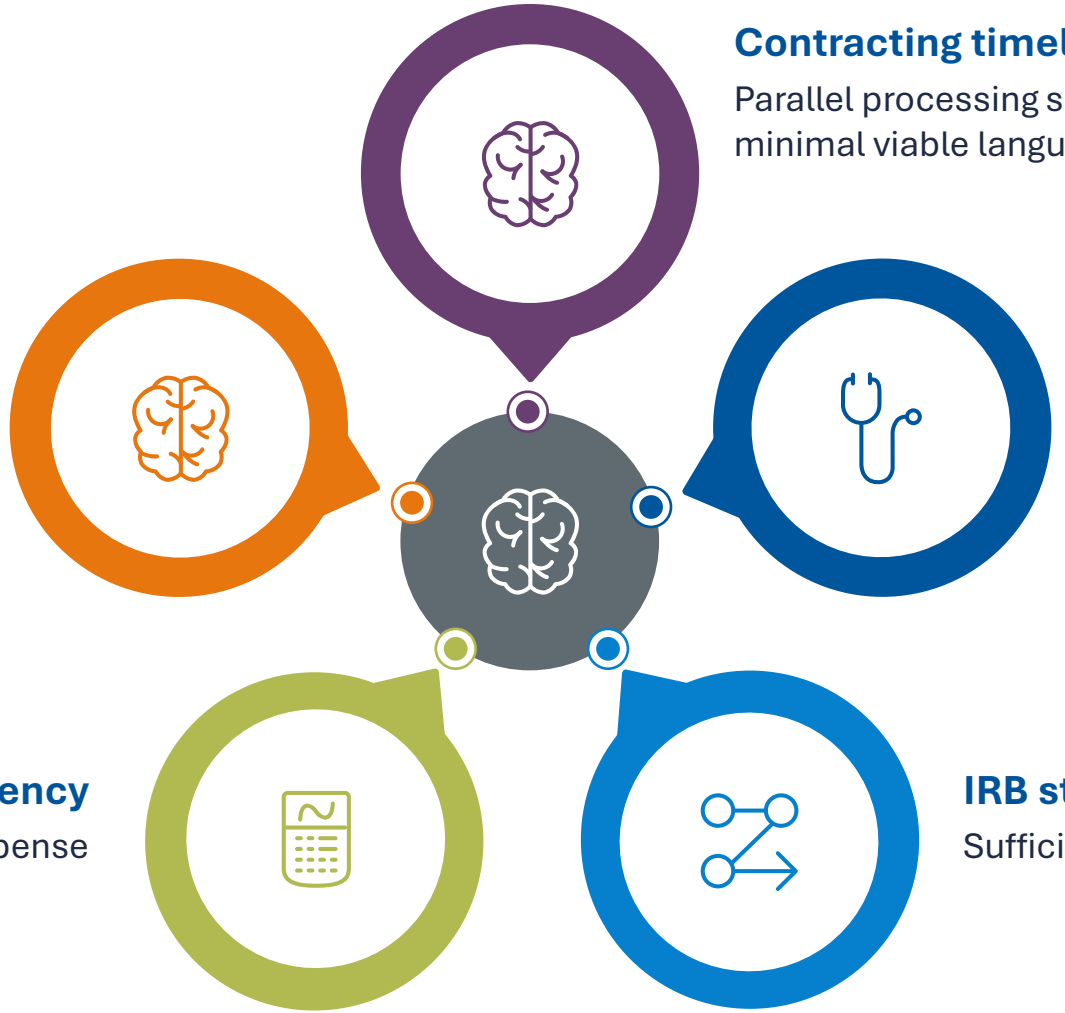


From: WCG Clinical 2024 Clinical Research Site Challenges Survey Report

Site Variability as a Quality Improvement Target



Accelerating industry sponsored research in academic settings



Contracting timelines

Parallel processing suprior to sequential, minimal viable language and acceptance

Prioritization

Availability of Principle Investigators and incentivization

Intellectual property

Signfiicant divergence with non-academic sites

Cost and efficiency

Appropriate value for expense

IRB staffing and responsiveness

Sufficiency of expertise, availability, and focus

Hernandez AF, Spaeder JA. Pivoting Clinical Trials Into a New and Evolving World. NIH Collaboratory Grand Rounds, May 16, 2025.

Delays span the whole operating system

A serial process compounds delays. Parallel review can reduce avoidable waiting.

1 Regulatory review

Pre-IND consultation and IND review

Phase-appropriate manufacturing and nonclinical evidence

Submission and review interactions

2 Contracts

Budget and agreement negotiations

Variable processes across sites

3 IRB review

Ethics review and local requirements

Reliance coordination for multisite studies

4 Institutional reviews

Scientific review and conflicts of interest

Coverage analysis / billing

Pharmacy and ancillary services

Biosafety and radiation safety

5 Activation

Technology and system setup

Staffing and training

Final site-readiness checks

6 Enrollment

Clinical workflow and eligibility

Geography and participant burden

Reviews may run in parallel. Requirements vary by institution and protocol.

IND: investigational new drug. IRB: institutional review board.

In other worlds what can you buy that's complex, and regulated where lives are at risk?

An Italian villa



A home or office anywhere

OUR HOMES

Commercial Modular Buildings by ideabox

Smart Spaces for Ambitious Ideas

Prefab buildings designed to elevate your business, built with the same care and creativity as every ideabox home.



Your private jet



Construction equipment



RITCHIE BROS.®

Car



amazon autos

Reform Approaches for U.S. Early-Phase Research

Duke Clinical Research Institute

Reagan Udall Report



Recommendations report
June 2026

17 recommendations across five priority areas

Modernize investigational new drug (IND) review

Use risk-proportionate requirements and rolling submissions.

Modernize Phase 1 trials and tools

Update early-stage trial approaches and supporting tools.

Improve early FDA–sponsor engagement

Optimize early-stage interactions and review processes.

Build dedicated U.S. Phase 1 infrastructure

Connect it to a coordinated national clinical trial strategy.

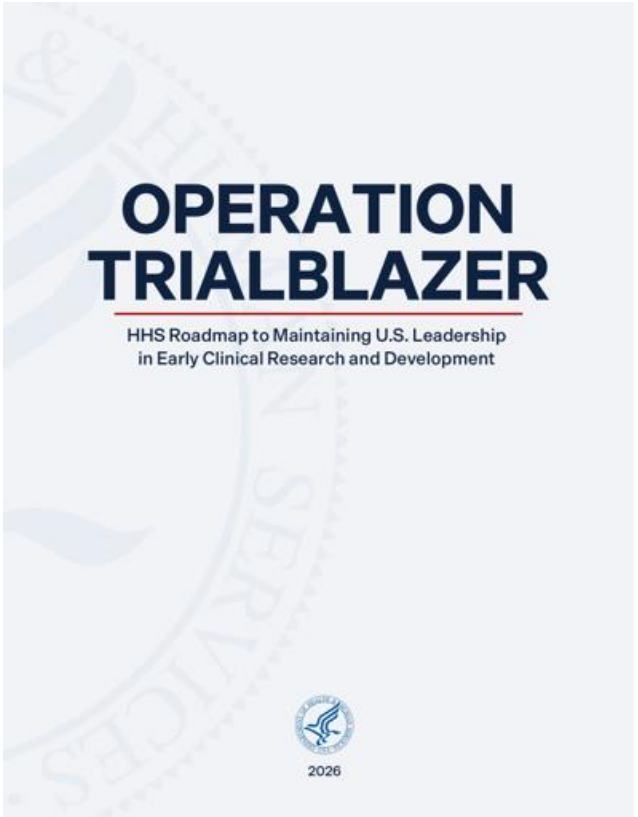
Mitigate litigation risk for trial sites

Address liability exposure in first-in-human and Phase 1 trials.

Source: Enhancing Early-Stage Drug Development in the United States (June 2026). Recommendations, not FDA policy.

Operation TrialBlazer: an HHS-wide roadmap

Regulation, funding, data, technology, access and clinical workflow



Released June 22, 2026

FDA

Phase-appropriate INDs, rolling review, IRB reform

NIH

Metrics, networks, reusable playbooks, real-world data

ARPA-H

Predictive models and platform approaches

ONC

EHR integration and computable protocols

CMS / OIG / OHRP

Patient and clinician participation barriers

Source: HHS launch announcement, June 22, 2026.

Molly Klote’s priorities for faster trial startup

A response to Operation TrialBlazer, July 3, 2026

“Mr. Secretary, Respectfully, the Problem Is Over Here”

Molly Klote, MD
Klote Medical Research Advisors

A complementary proposal

A national no-fault fund for research injuries could protect volunteers and reduce contract disputes.

1 Adopt standard agreements without reopening terms

Use the existing Accelerated Clinical Trial Agreement.

2 Address the local review that single IRB leaves behind

Measure institutional policies and state-law requirements.

3 Reduce avoidable protocol complexity

Limit amendments and the rework they trigger.

4 Make activation and enrollment performance visible

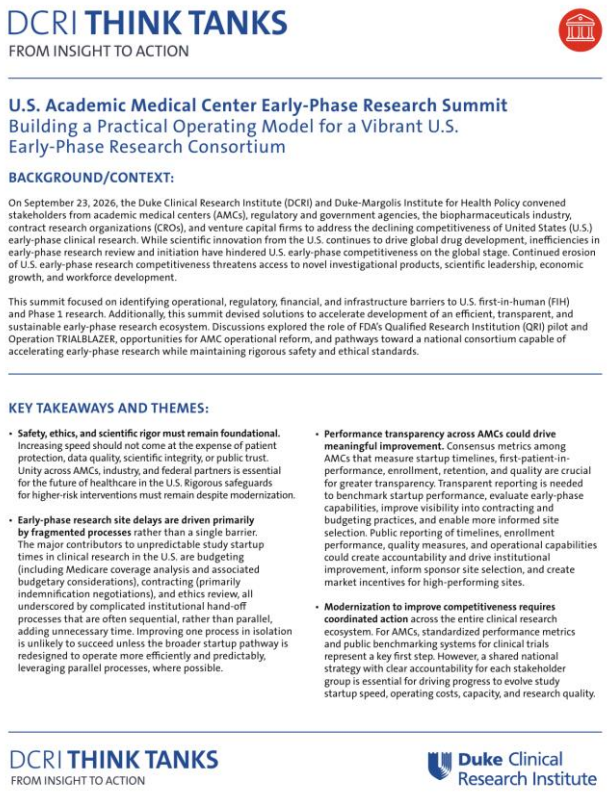
Publish timelines and identify likely non-enrolling sites.

5 Pilot new models with conflict-of-interest safeguards

Separate scientific pre-review, ethics review and sponsor advice.

Source: Molly Klote, July 3, 2026 commentary, pp. 1–3, and LinkedIn screenshot supplied by the presenter.Klote, “Mr. Secretary, Respectfully, the Problem Is Over Here,” July 3, 2026, pp. 1–3..

AMC Early-Phase Research Summit



DCRI THINK TANKS
FROM INSIGHT TO ACTION

U.S. Academic Medical Center Early-Phase Research Summit
Building a Practical Operating Model for a Vibrant U.S. Early-Phase Research Consortium

BACKGROUND/CONTEXT:

On September 23, 2026, the Duke Clinical Research Institute (DCRI) and Duke-Margolis Institute for Health Policy convened stakeholders from academic medical centers (AMCs), regulatory and government agencies, the biopharmaceuticals industry, contract research organizations (CROs), and venture capital firms to address the declining competitiveness of United States (U.S.) early-phase clinical research. While scientific innovation from the U.S. continues to drive global drug development, inefficiencies in early-phase research review and initiation have hindered U.S. early-phase competitiveness on the global stage. Continued erosion of U.S. early-phase research competitiveness threatens access to novel investigational products, scientific leadership, economic growth, and workforce development.

This summit focused on identifying operational, regulatory, financial, and infrastructure barriers to U.S. first-in-human (FIH) and Phase 1 research. Additionally, this summit devised solutions to accelerate development of an efficient, transparent, and sustainable early-phase research ecosystem. Discussions explored the role of FDA's Qualified Research Institution (QRI) pilot and Operation TRIALBLAZER, opportunities for AMC operational reform, and pathways toward a national consortium capable of accelerating early-phase research while maintaining rigorous safety and ethical standards.

KEY TAKEAWAYS AND THEMES:

- **Safety, ethics, and scientific rigor must remain foundational.** Increasing speed should not come at the expense of patient protection, data quality, scientific integrity, or public trust. Unity across AMCs, industry, and federal partners is essential for the future of healthcare in the U.S. Rigorous safeguards for higher-risk interventions must remain despite modernization.
- **Early-phase research site delays are driven primarily by fragmented processes** rather than a single barrier. The major contributors to unpredictable study startup times in clinical research in the U.S. are budgeting (including Medicare coverage analysis and associated budgetary considerations), contracting (primarily indemnification negotiations), and ethics review, all underscored by complicated institutional hand-off processes that are often sequential, rather than parallel, adding unnecessary time. Improving one process in isolation is unlikely to succeed unless the broader startup pathway is redesigned to operate more efficiently and predictably, leveraging parallel processes, where possible.
- **Performance transparency across AMCs could drive meaningful improvement.** Consensus metrics among AMCs that measure startup timelines, first-patient-in-performance, enrollment, retention, and quality are crucial for greater transparency. Transparent reporting is needed to benchmark startup performance, evaluate early-phase capabilities, improve visibility into contracting and budgeting practices, and enable more informed site selection. Public reporting of timelines, enrollment performance, quality measures, and operational capabilities could create accountability and drive institutional improvement, inform sponsor site selection, and create market incentives for high-performing sites.
- **Modernization to improve competitiveness requires coordinated action** across the entire clinical research ecosystem. For AMCs, standardized performance metrics and public benchmarking systems for clinical trials represent a key first step. However, a shared national strategy with clear accountability for each stakeholder group is essential for driving progress to evolve study startup speed, operating costs, capacity, and research quality.

DCRI THINK TANKS
FROM INSIGHT TO ACTION

Duke Clinical Research Institute

September 23, 2026

Key takeaways

1. Safety, ethics and scientific rigor must remain foundational.
2. Fragmented startup processes drive delays, especially budgets, contracts and institutional handoffs.
3. Transparent performance metrics could strengthen accountability and site selection.
4. Modernization requires coordinated action across academic centers, industry and federal partners.
5. TrialBlazer's qualified-institution pilot is promising, but operational barriers remain.
6. Early-phase infrastructure needs reliable funding to maintain readiness.

AMC Summit: recommended solutions

Near term

A shared operating playbook

Standardize milestones, contracts and budgets.
Define dedicated startup and research roles.

Transparency and accountability

Publish activation, enrollment and quality metrics.
Describe site capabilities and performance.

Technology to reduce delays

Use digital tools for feasibility, recruitment and research operations.

Mid term

Sustainable infrastructure

Fund operational readiness and develop accreditation or certification standards.

Regulatory and liability reform

Modernize Form FDA 1572 guidance.
Align indemnification, insurance and liability.

Central IRB and national coordination

Expand central IRB reliance and coordinate procedures within a national research strategy.

Long term: a national early-phase consortium with turnkey processes

Potential Reforms and Enablers

	Guidance and tools	Behavior change	Regulation	Legislation
Priority actions	• Phase I playbook • Qualified institutions • Standard contracts and budgets • IRB reliance	• National consortium • Process measures • Reliance on others for institutional reviews • Public reporting or pay-for-performance	• Risk-proportionate and rolling IND submissions • Broader single-IRB reliance	• Notification pathway • Participant-support safe harbors • Federally chartered first-in-human network
Enablers	FDA, NIH, HHS Sites and sponsors	HHS and federal partners Sites, sponsors, patients	FDA and HHS	Congress, HHS, FDA NIH and OIG

Breaking it down into steps...

	1 Now	2 Near-term	3 Medium-term	4 Long-term
Focus	Clarify and convene	Testing	Scaling	Build lasting capacity
Priority actions	• Phase I playbook • Roundtables and public input • Issue identification • Standard templates	• Rolling IND and qualified-institution pilots • 60-day activation pilots • Expand reliance agreements beyond IRB processes	• Risk-proportionate rulemaking • More effective single-IRB reliance • Voluntary public reporting of process measures	• Legislation for a notification pathway • Participant-support safe harbors • First-in-human network authority
Intended outcome	Shared definitions and startup commitments	Shorter startup and activation times	Consistent operations for eligible studies	Durable capacity for high-quality research

Imagine what could be possible in the coming years

Shared infrastructure enables parallel startup across qualified research institutions.

OLD MODEL: Serial handoffs and repeated site-by-site setup



PROPOSED MODEL: Parallel workstreams with one coordinated readiness check



Common safety standards, activation benchmarks and enrollment commitments

Performance metrics: days from protocol release to each milestone



Voluntary benchmarking supports shared improvement.

Extending early-phase reform to U.S. late-stage trials

Early-phase reform	Potential late-stage application	Late-stage goal
Parallel startup	Run contracts, IRB reliance and site readiness in parallel using shared templates	Less repeated work Faster activation
Qualified site networks	Extend shared training and infrastructure to all sites with appropriate capabilities	Broader patient access More reliable enrollment
Proportionate processes	Simplify procedures and data collection around critical outcomes. Match monitoring to trial risk	Lower burden Reliable results
Shared performance metrics	Track activation, enrollment and retention alongside representation, safety and data completeness	Accountability for speed and quality

Conclusions

- U.S. trial efficiency is declining, with early-phase research at risk of extinction
- FDA and Operation TrialBlazer offers hope…for reforms
- But academic centers need:
  - Predictable activation without duplicate reviews
  - Potential safe harbor or pooled insurance
  - Sufficient study volume for dedicated teams and infrastructure
  - Performance metrics with recognition and rewards
- And successful reforms could extend to later-phase trials