CLINICAL TRIALS TRANSFORMATION INITIATIVE

Assessing U.S. Clinical Trials Site Capacity and Readiness for Public Health Emergencies

CTTI Expert Meeting

July 31, 2025

Lessons Learned from Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) Program

FNIH

ACTIV
Accelerating COVID-19 Therapeutic Interventions and Vaccines

Building Bridges to Breakthroughs

Science has the power to cure, but no single organization can do it alone.

The Foundation for the National Institutes of Health (FNIH) is a non-profit organization chartered by the U.S. Congress and launched in 1996 to support the mission of NIH.

We connect world-leading NIH researchers with the ingenuity and expertise of public and private sector leaders to accelerate medical breakthroughs.

FNIH

LAUNCH

On April 17, 2020, NIH announced the launch of a public-private partnership, **Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV)**

MISSION

Develop a coordinated research response to **speed COVID-19 treatment and vaccine options**

FNIH

ACTIV Private-Public Partnership Stakeholders

8
Government Partners

39
Industry Partners

4
Non-Profits

- Biomedical Advanced Research and Development Authority
- Centers for Disease Control and Prevention
- European Medicines Agency
- National Institutes of Health
- U.S. Army Medical Research and Development Command
- U.S. Department of Veterans Affairs
- U.S. Food and Drug Administration
- White House COVID-19 Response Team

Original ACTIV Partners

- AbbVie Inc.
- Amgen
- AstraZeneca PLC.
- Bristol-Myers Squibb Co.
- Eisai Co.
- Eli Lilly and Co.
- Evotec BioSystems GmbH
- F. Hoffmann-La Roche AG
- Gilead Sciences, Inc.
- GlaxoSmithKline
- Johnson & Johnson, Inc.
- Merck & Co., Inc.
- Moderna, Inc.
- Novartis AG
- Novavax, Inc.
- Pfizer, Inc.
- Rhythm Pharmaceuticals, Inc.
- Sanofi S.A.
- Takeda Pharmaceutical Industries, Ltd.
- Vir Biotechnology, Inc.

Additional Contributing Partners

- Accord Healthcare
- Alexian Pharmaceuticals
- Apotex
- Brii Biosciences
- Constant Therapeutics
- Deloitte
- Humanigen, Inc.
- Ingenus Pharmaceutical
- Molecular Partners
- NeuroRx
- Rhthym Pharmaceutics, Inc.
- Rigel Pharmaceuticals, Inc. (RIGL)
- Rose Li Associates
- SAB Biotherapeutics
- Sagent
- Shionogi, Inc.
- Synairgen
- Teva Pharmaceuticals
- Trevena, Inc.

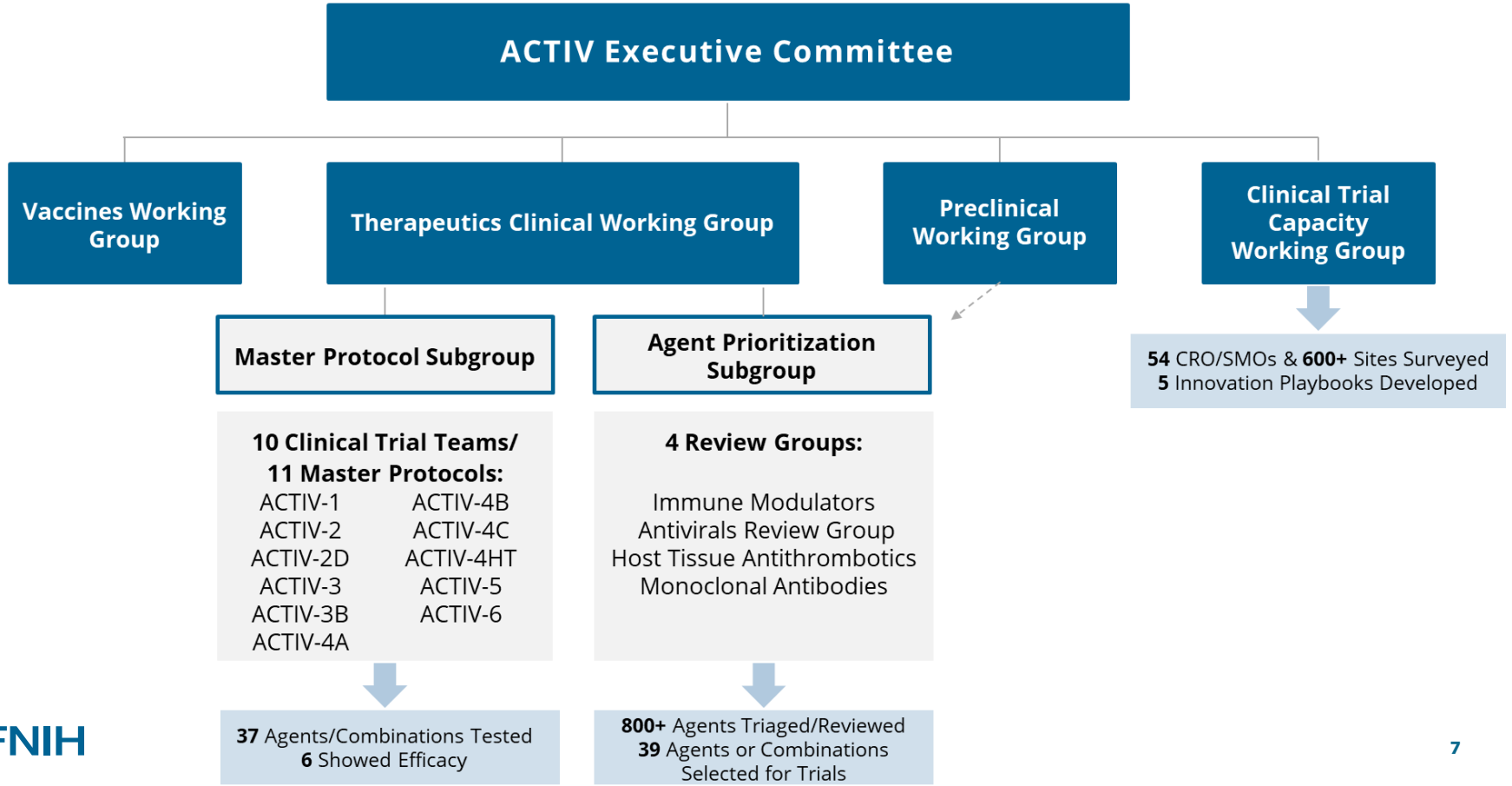
- Bill & Melinda Gates Foundation
- Foundation for the National Institutes of Health
- Fred Hutchinson Cancer Center
- Research Triangle Institute

FNIH

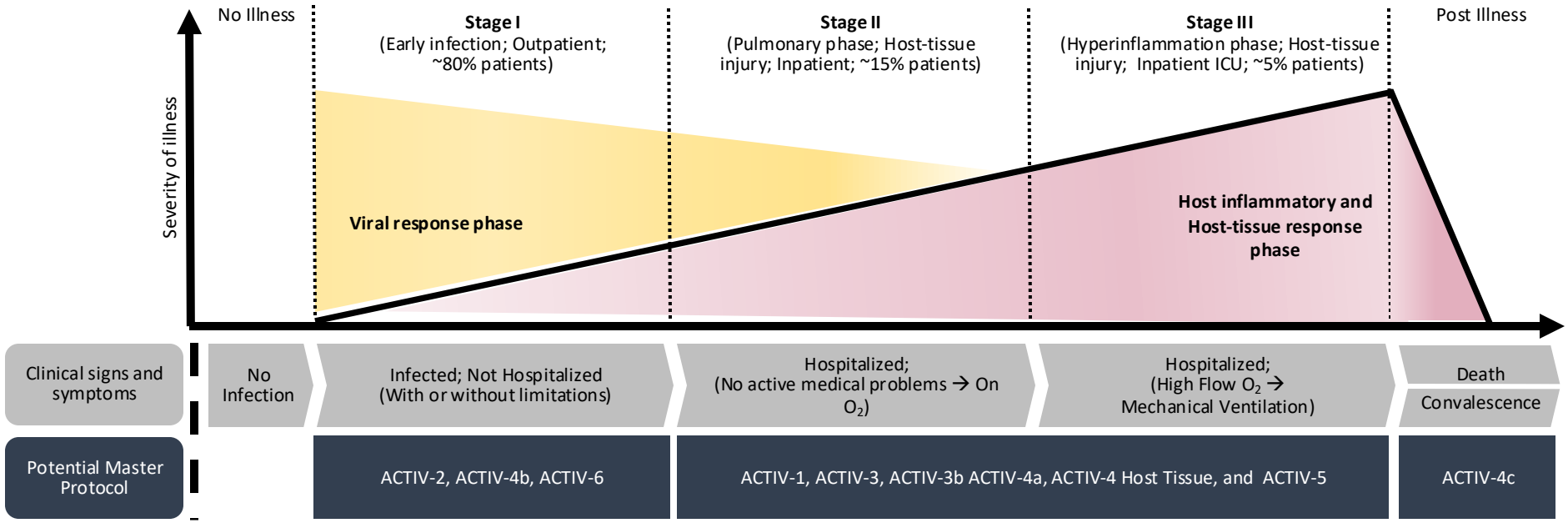
ACTIV Four Major Focus Areas

	Vaccines	Preclinical	Clinical Trial Capacity	Therapeutics – Clinical
Objective	+ Accelerate the evaluation of vaccine candidates to enable rapid authorization or approval	+ Develop a collaborative, streamlined forum to identify preclinical treatments	+ Improve clinical trial capacity and effectiveness	+ Accelerate clinical testing of the most promising COVID treatments
Achievements	+ Developed harmonized protocols for vaccine efficacy trials + Support decision-making for EUA criteria + Recommendations re: controlled human infection trials and threat of immune-associated disease enhancement	+ National strategy for non-human primate research + Inventory of in-vitro and in-vivo resources + SOPs for accelerated preclinical development + Open Data Portal at NIH ↓ TRACE	+ International clinical site survey + (63 networks, 39 CROs/SMOs, 728 sites) + Online geotracking tool + Strategies for enhancing trials in a pandemic (virtual, digital, online solutions)	+ Accelerated clinical testing of the most promising COVID treatments

Working Groups Critical to Protocol Launch



ACTIV Clinical Trials Targeting Different Stages of Disease Pathobiology



ACTIV Therapeutics Launched 11 Master Protocols

Population	Master Protocol	Phase	Drug Class	Networks	Target Sample Size (per arm)	Agents Tested
Inpatient Studies	ACTIV-1	III	Host-targeted Immune Modulators	NCATS TIN + DCRI + TRI + CRO	540	*Abatacept (BMS), Cenicriviroc (AbbVie), Infliximab (Janssen)*
	ACTIV-3	III	mAbs and Antivirals	NIAID INSIGHT + NHLBI PETAL + CTSN + VA + CRO	1,500	*mAbs (Lilly, Brii, GSK-Vir, AZ), DARPin (Molecular Partners), ritonavir/nirmatrelvir (Pfizer)*
	ACTIV-3B	III	Host-targeted Immune Modulators for ARDS	NIAID INSIGHT + NHLBI PETAL + CTSN + VA + CRO	620	*Aviptadil, VIP (NeuroRx)*
	ACTIV-4A	III	Host-tissue Directed Antithrombotics	NHLBI CONNECTS	1000	*LMWH, UFH, P2Y12 Inhibitors (Anti-platelet Agents), Crizanlizumab (Novartis), SGLT2 inhibitors*
	ACTIV-4HT	II/III	Host-tissue Targeted Therapies	NHLBI CONNECTS	300+	*TXA127 (Constant), TRV027 (Trevena), Fostamatinib (Rigel)*
	ACTIV-5	II	Screen Promising Immune Modulators	NIAID + CRO	200 (expansion to 500)	*Risankizumab (AbbVie), Lenzilumab (Humanigen), Danicopan (AZ)*
	STRIVE (severe ARI)	III	All agents relevant to acute viral respiratory diseases	NIAID INSIGHT	600-800	*Ensitrelvir (Shionogi)*
Outpatient Studies	ACTIV-2/2D	II/III	mAbs and Oral Antivirals	NIAID ACTG + CRO	Ph II = 220 Ph III = 1,200	*mAbs (Lilly, Brii Bio, RU-BMS, AZ), IFN-beta (Synairgen), camostat (Sagent), nPAB (SAB), Ensitrelvir (Shionogi)*
	ACTIV-4B	III	Host-tissue Directed Antithrombotics	NHLBI CONNECTS	1750	*Low-dose Aspirin, Prophylactic-dose Apixaban, Therapeutic-dose Apixaban (BMS)*
	ACTIV-6	III	Existing Prescription and OTC Medications	NCATS + DCRI + PCORnet + SignalPath + CRO	600 (expansion to 1200)	*Ivermectin (Ingenus), fluvoxamine (Apotex), fluticasone (GSK), Montelukast, Metformin*
	ACTIV-4C (convalescent)	III	Host-tissue Directed Antithrombotics	NHLBI CONNECTS Network	2660	*Apixaban (BMS)*

Therapeutic Trials Demographics Summary

AGE

Median age of participants was

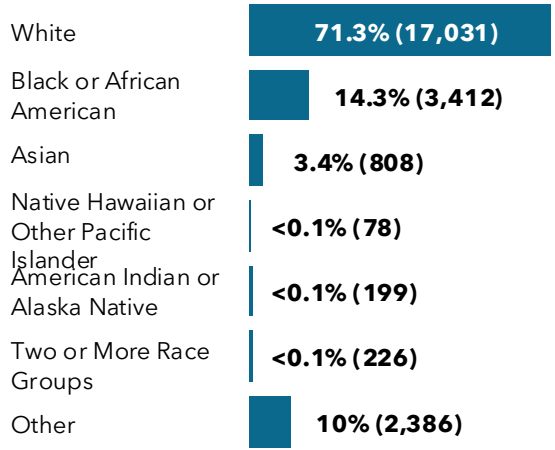
57 years

SEX

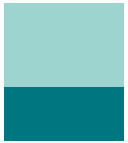
50.45% (12,041) of participants identified as female

49.55% (11,824) of participants identified as male

RACE

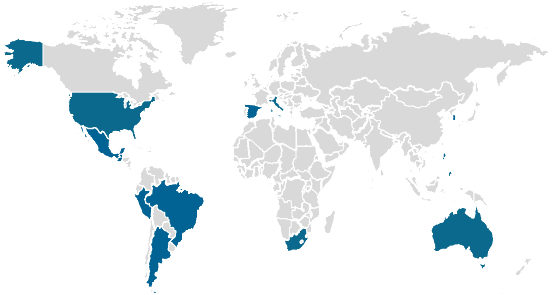


ETHNICTIY



30.72% (7,333)
Hispanic/Latino Ethnicity

COUNTRIES



ACTIV trials enrolled in

11 countries

INCLUDING:

- **United States**
- **Mexico**
- **Italy**
- **Argentina**
- **Guatemala**
- **Philippines**
- **Peru**
- **Brazil**
- **South Africa**
- **Spain**
- **South Korea**

FNIH

ACTIV Therapeutics Clinical Trials Outcomes

ENROLLMENTS & ACTIVATION

26,000+ Participants enrolled into ACTIV trials

600+ Sites enrolled participants into ACTIV trials

PUBLICATIONS

54 Scientific Publications on ACTIV Trials released in **17 Medical Journals**

These publications have been **cited 2038 times** according to Google Scholar with **"Therapeutic Anticoagulation with Heparin in Noncritically Ill Patients with Covid-19"** as the highest cited publication

AGENT REVIEWS & AUTHORIZATIONS

800+	Total agents reviewed by the ACTIV Tx-Clinical WG Agent Review Panel
37	Agents, combinations, dosages, and formulations selected and entered the ACTIV Master Protocols *(Additional 3 compounds selected did not enter trials)*
35	Agents, combinations, dosages, and formulations fully completed testing through the ACTIV Master Protocols
6	Agents proven efficacious against COVID-19 in analysis of data from the ACTIV Trials
25	Agents proven definitively not efficacious against COVID-19 in analysis of data from the ACTIV Trials

- **EUA ACHIEVEMENTS where ACTIV data was included:**
  - Lilly LY-CoV-555 (EUA)
  - Brii Bio Brii-196/Brii-198 (EUA filed/approved in China)
  - AstraZeneca's AZD7442 (IV) (EUA)
- Both **molnupiravir and paxlovid**, which were granted EUA, used the ACTIV protocol designs
- ACTIV-4A's work on heparin and other anticoagulants **changed clinical practice**
- ACTIV-1 and -3's work with **AZD7442, infliximab, and abatacept** all showed **positive benefit on overall mortality** for hospitalized COVID-19 patients

ACTIV Agent Testing Summary

Tested- unsuccessful at interim

- Cenicriviroc
- AZD7442 (IM)# *(Outpatient)*
- AZD7442 (IV)# *(Outpatient)*
- Camostat Mesylate
- BMS-986414/BMS-986413
- LY-CoV-555 *(Inpatient)*
- Brii-196/Brii-198 *(Inpatient)*
- VIR-7831
- DARPin MP0420
- Pfizer PF-07304814#
- Aviptadil + Remdesivir (ARDS patients)
- Remdesivir (ARDS patients)**
- Therapeutic Heparin + P2Y12 Inhibitors in Moderately-ill Pts
- Crizanlizumab
- Aspirin
- Apixaban**
- TRV027
- TXA127
- SGLT2 inhibitors
- Fostamatinib

Tested- unsuccessful at final outcome

- Risankizumab
- Lenzilumab
- Danicopan
- Ivermectin (400)
- Ivermectin (600)
- Fluticasone
- Fluvoxamine (50)
- Fluvoxamine (100)
- Prophylactic Heparin + P2Y12 Inhibitors in Critically-ill Pts
- Montelukast
- Metformin
- Shionogi-217622 (outpatient-low risk)

Tested- successful

- Infliximab
- Abatacept
- Brii-196/Brii-198* *(Outpatient)*
- LY-CoV-555* *(Outpatient)*
- Therapeutic Anticoagulation with Heparin in Non-critically Ill Pts
- AZD7442 (IV)* *(Inpatient)*

Undetermined

- SNG001 IFN-beta (Phase 2)**
- SAB-185**
- Shionogi-217622 (inpatient ongoing)

**Received EUA or data from an ACTIV trial has or will contribute to an EUA filing*
***Ceased due to operational futility*
#Ceased due to company decision

FNIH

Early Lessons Learned of Therapeutics Testing

The ACTIV Therapeutics-Clinical Manuscript Sub Teams have published two sister manuscripts documenting the strategy, process, and lessons learned for **agent prioritization** and **master protocol development**.

TITLE	**Accelerating COVID-19 Treatment Interventions and Vaccines (ACTIV) – Selecting Compounds for Clinical Evaluation in COVID-19 Clinical Trials**	**Accelerating COVID-19 Treatment Interventions and Vaccines (ACTIV) – Designing Master Protocols for Evaluation of Candidate COVID-19 Therapeutics**
OVERVIEW	Overall strategy, process, and evaluation criteria that allowed for a streamlined and standardized assessment of hundreds of therapeutic agents with potential application for COVID-19	Approach and process by which seven master protocols to test investigational agents against COVID-19 were designed, developed, and launched, as well as lessons learned on critical design decisions for future pandemic situations
AUTHORS	*Timothy G. Buchman, Ruxandra Draghia-Akli, Stacey J. Adam, Neil R. Aggarwal, Joshua Fessel, Elizabeth S. Higgs, Joseph Menetski, ACTIV Therapeutics Clinical Working Group, Sarah W. Read, and Eric A. Hughes*	*Lisa LaVange, Stacey J. Adam, Judith S. Currier, Elizabeth S. Higgs, Lora A. Reineck, ACTIV Therapeutics Clinical Working Group, Eric A. Hughes, and Sarah W. Read*
STATUS	**Published in *Critical Care Medicine (CCM)*** **Manuscript Link:** https://journals.lww.com/ccmjournal/Abstract/9000/Accelerating_Coronavirus_Disease_2019_Therapeutic.95104.aspx	**E-published in *Annals of Internal Medicine (AIM)*** **Manuscript Link:** Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV): Designing Master Protocols for Evaluation of Candidate COVID-19 Therapeutics | Annals of Internal Medicine (acpjournals.org).

Start to Finish Lessons Learned from ACTIV for Future Pandemics

- 9 Manuscripts - JCTS Journal Supplement
  - **COVID-19 Therapeutic Platform Trials Lessons Learned**
    Guest Editors: Stacey J. Adam, Sarah Dunsmore, Lisa Merck, Sarah Read, Yves Rosenberg
    Editorial: The Future is Now – Using the Lessons Learned from the ACTIV COVID-19 Therapeutics Trials to Create an Inclusive and Efficient Clinical Trials Enterprise
    Click here for the full issue.

- FNIH was one of four non-profits engaged by OWS in a workshop (hosted by RUF) in September 2021 that resulted in the first comprehensive "lessons learned" document in September 2021

  https://reaganudall.org/sites/default/files/2022-02/020122_COVID%20Response_Final_0.pdf

Summary of Lessons Learned from ACTIV

ACTIV MANUSCRIPTS	KEY CATEGORIES OF LESSONS LEARNED	
Overview of ACTIV Trial-Specific Lessons Learned	• Partnership, collaboration, leadership - recipe for success • Importance of appropriate representation in enrolled populations • Considerations for protocol design and implementation	
Preparing Better: Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) Therapeutics Trials Lessons Learned - A Call to the Future	• Agent prioritization process • Preclinical asset prioritization and tracking • Results communication and data sharing	• Manufacturing and drug scaling • Considerations for protocol design and implementation • Benefits of the Private Public Partnership
ACTIV trials: lessons learned in trial design in the setting of an emergent pandemic	• Sample size and power calculation • Flexible eligibility criteria • Outcome measures and optimal endpoints	• Industry partnership • Trial governance structure and network assembly • Early regulatory interactions
ACTIV Trials Cross Trial Lessons Learned for Master Protocol Implementation	• Building a global trial infrastructure • Contracting and site selection • Challenges with multi-national trials • Investigational products and supplies	• Changing standard of care • Centralized site and investigator support • Role of DSMB • Barriers to participant recruitment and follow-up
Lessons Learned from COVID-19 to Overcome Challenges in Conducting Outpatient Clinical Trials to Find Safe and Effective Therapeutics for the Next Infectious Pandemic	• Limited infrastructure • Availability of staff and study fatigue • Community engagement and recruitment of vulnerable populations	• Institutional variability • Trial confusion • Follow-up of participants
Lessons Learned from the Conduct of Inpatient Clinical Trials in a Pandemic	• Research sponsors and protocol development • Needs from regulatory leadership • Best Practices for investigators and research team	• Investigational Drug Services pharmacy and pharmacy leadership • Critical roles for institutional clinical/research leadership
The statistical design and analysis of pandemic platform trials: implications for the future	• Coordination of the statistical response • Endpoint and outcome selection • Multiplicity in master protocols • Unexpected trial adaptations due to pandemic	• Blinding and DSMB • Considerations for the Statistical Analysis Plan • Data collection and management • Shared controls
Engaging Communities in Therapeutics Clinical Research During Pandemics: Experiences and Lessons from the ACTIV COVID-19 Therapeutics Research Initiative	• Public messaging and research marketing • Peacetime activities	• Early and continuous community outreach and engagement
Practical application of good participatory practices for trials or emerging pathogens (GPEP): Developing materials for use in ACTIV-3, -3b and ACTIV-associated COVID-19 trials	• Implementation of good clinical practice guidelines in COVID-19 inpatient trials • Process for developing and producing materials • Materials for study staff and non-study medical personnel	

Master Protocol Implementation Lessons Learned

Topic	Lessons Learned and Recommendations
Site Selection and Quality Assessment	• Speedy site selection and onboarding with adequate, timely funding is critical when global epidemiology of infection is evolving rapidly. • Site selection requires a multi-disciplinary team evaluating sites based on balanced criteria including infrastructure, capabilities, and evolving pandemic dynamics. • A Quality Assessment (QA) checklist is a resourceful tool for documenting quality oversight and timely comprehensive site activation checklists.
Building a Global Trial Infrastructure	• Global network infrastructure should be established well in advance of pandemics to leverage different expertise globally and efficiently. This could be done through unification of existing clinical trial networks and standardization of their procedures to the best practices from each. • A functioning multinational regulatory consortium with standardized procedures should be in place before the next pandemic. • Compilation of existing regulations on clinical trial operations would help with necessary standardization. • Standards should be established for national ethics and regulatory bodies for pandemic operations, encouraging flexibility in requirements whenever possible, and facilitating collaboration between regulators and ethics committees in evaluating trial applications. • Maintaining continuity of external support during trial is crucial.
Contracts	• Standardized contracting language and contractual flexibilities would lead to more efficient enrollment and data acquisition.
Timeline Expectations	• Clearly defined timeline expectations to sites for activation and regulatory reviews are necessary for swift study start. • Organizations not able to achieve these timelines should not be considered to avoid using limited time and resources in ways that will not be fruitful.
Challenges with Multi-National Trials	• A Trial Master File (TMF) Index must be developed prior to study start to set expectations of required documents to collect, manage, and file.
Investigational Products and Supplies	• Incorporating trained research pharmacists is necessary early on in protocol conception and implementation to identify investigational drug services (IDS) specific challenges and allow communication with investigational product (IP) manufacturers. • Use a standardized pharmacy site checklist at site qualification. • Formalize regular meetings for site pharmacists and network specialist pharmacists to deal with IDS issues to improve efficiency and mitigate negative outcomes.
Changing Standard of Care (SOC)	• Adaptive design of protocols would provide flexibility in maintaining SOC during evolving pandemic.
Centralized Site and Investigator Support	• A centralized, continuous investigator support system would be beneficial in providing help with key protocol questions on a 24-hour/day basis. • Remote site training and weekly discussions are critically important to keep constant connection to sites and address concerns. • Intermittent retraining is important as new sites onboard and due to high staff turnover.
Role of DSMB	• Data Safety Monitoring Boards (DSMBs) provide a critical role in reassuring safety and halting criteria and efficacy signals. • Clarity between the role of the DSMB and the regulatory agencies in IP decisions for a trial should be sought prior to the next pandemic.
Barriers to Participant Recruitment	• Addressing barriers for recruitment of participants is vital to ensuring efficient recruitment of diverse populations.
Participant Follow-Up	• A strategic follow-up plan including home blood draw, transportation, outside hospital follow-up locations (clinics, rehabilitation centers, long-term care facilities, mobile research vans, etc.) should be considered for protocols in advance.

Community Engagement and Outreach Lessons Learned

Topic	Lessons Learned and Recommendations
Public Messaging and Research Marketing	• Utilization of a registry allows for rapid enrollment and focused outreach to registrants from underrepresented and highly impacted groups. • A registry of potential research participants is now being adopted by the ACTG for HIV trials, given successful use by the CoVPN. • Effective use of social media as a recruitment tool should be explored as many ACTIV-6 participants reported that they first became aware of ACTIV-6 through social media advertisements.
Community Outreach, Engagement, and Participant Recruitment	• Sites are critically important in increasing enrollment, especially among historically underrepresented populations. • Researchers can make future platforms stronger and more trustworthy to potential participants by incorporating feedback from partners. • Involving key stakeholders during the formative stages of the research program can ensure desired communities are engaged and invested from the start. • Involving community representatives in study planning, protocol development, and agent prioritization efforts can improve the design and implementation of future studies. • Leaders from highly impacted populations and communities should be invited to the table as the initiative is being formed and protocols drafted. • Including sites as enrollment and communications partners (the IDeA Centers for Translational Research) has the potential to enhance outreach, community engagement, and diversity of enrollment in future studies. • A decentralized approach to evaluating treatment for disease outbreaks is not only feasible, but also has the potential to achieve geographic and demographic diversity of participation. • Future efforts must include relevant, early representation from populations that will be asked to participate.
Peacetime Activities	• Undertaking in community messaging about research importance to individuals, communities, and national well-being during in-between periods is the best time to prepare for a future infectious disease crisis. • Research networks, clinical investigators, and study teams should regularly engage with communities in preparation of a public health emergency, and engagement plans and potential emergency protocols should be ready for rapid implementation. • Efforts must intensify to regain trust of communities among whom it has been chronically deficient. • Preparation should include plans for an infrastructure with flexibility to set up mobile study sites and/or preparation to be deployed to affected communities, as well as the knowledge on transportation and distribution of study material and samples. • Investing in on-going dialogue with respected influencers is necessary to cultivate awareness and understanding of infectious disease threats and the role of healthcare and research responses can combat issues with mistrust in government and academic institutes.

STRIVE

Strategies and Treatments for Respiratory Infections and Viral Emergencies

Professor Gail Matthews,
Infectious Diseases Physician
Head of Therapeutic Vaccine Research Program
Chair Executive Committee **STRIVE**

Kirby Institute, Sydney, Australia

STRIVE ACTIV INSIGHT018

insight

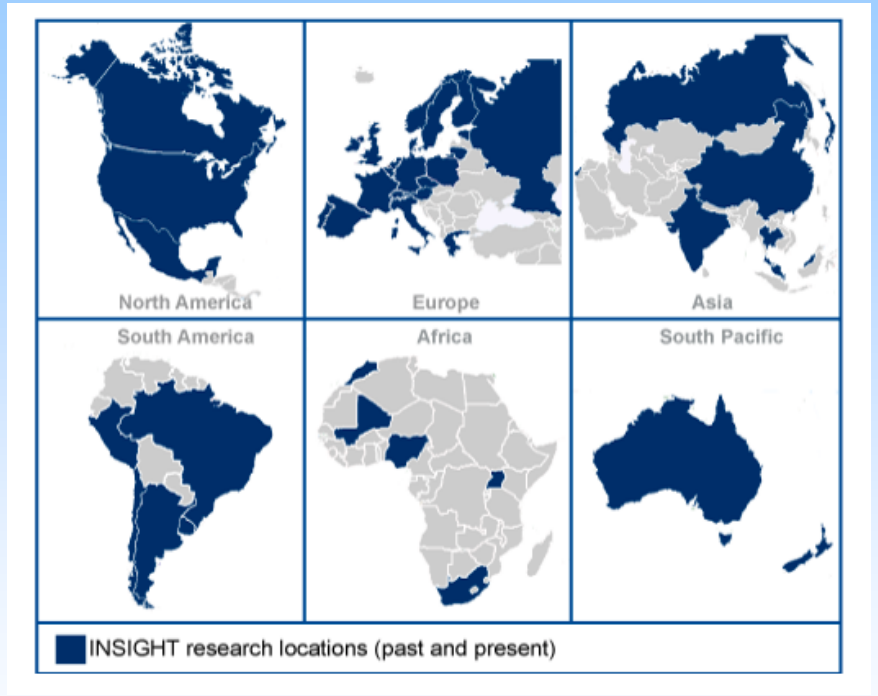
Multiple Networks Combined Efforts with a Global Footprint

ACTIV-1 (NCATS)

ACTIV-3 (NIAID, NHLBI, U.S.VA)

- **INSIGHT:** International Network for Strategic Initiatives in Global HIV Trials
- **PETAL:** Prevention & Early Treatment of Acute Lung Injury Network
- **CTSN:** Cardiothoracic Surgical Trials Network
- **VA:** Department of Veterans Affairs
- **NIH-DCR:** Division of Clinical Research

ACTIV-5/ACTT1-4 (NIAID)



ACTIV STRIVE INSIGHT018

NIH NIAID NCATS

ACTIV-1 IM
Randomized Master Protocol for Immune Modulators for Treating COVID-19

PETAL NETWORK
Prevention & Early Treatment of Acute Lung Injury

CTSN
CARDIOTHORACIC SURGICAL TRIALS network

VA U.S. Department of Veterans Affairs

insight

STRIVE Master Protocol - May 2022

Key principles

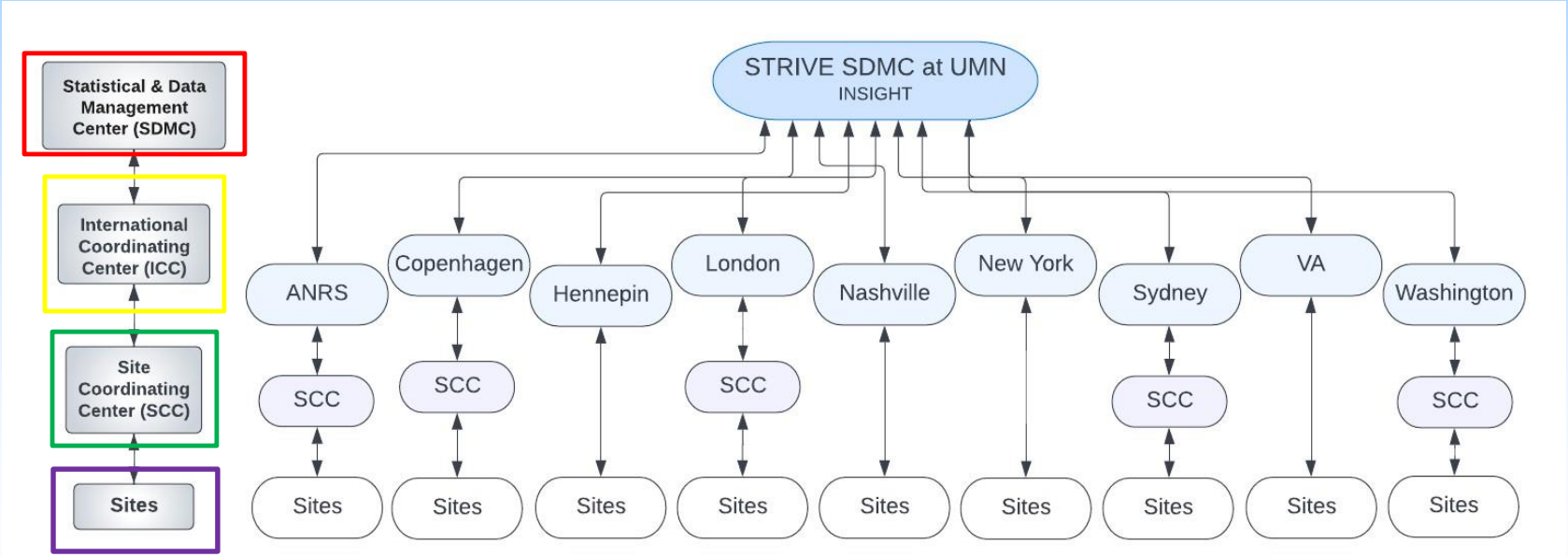
- To evaluate interventions aimed at one or several respiratory pathogens
  - Novel agents ***or*** strategies of using established interventions
- Master protocol
  - Menu-based framework (endpoints, data and sample collection)
  - Simple eligibility criteria: hospitalised inpatients with respiratory infection
- Trial-specific appendices
  - Specifics for each trial (eg COVID-19, influenza)

Mid 2023:STRIVE transitions from protocol to network

From	To
One master protocol platform to study interventions against respiratory infections.	A diverse, broadened research portfolio that could study: ▪ Interventions against COVID ▪ Emerging and re-emerging infectious diseases ▪ In-patient subjects ▪ Out-patient subjects
A protocol being executed by multiple clinical research networks	A global clinical research network executing STRIVE and other protocols
Governance model focused on a protocol	Governance model focused on a Network
Reliant on primarily funding from NIAID	Reliant on funding from multiple sources
Focused on execution of a protocol	Focused on execution of >1 protocol Focused on developing the next generation of researches Focused on building engagement and capacity with LMIC
Focused on responding to COVID	Focused on a complete roadmap to rapidly respond to emerging threats
Pandemic research	Pandemic and “peace-time” research

A consolidated network infrastructure

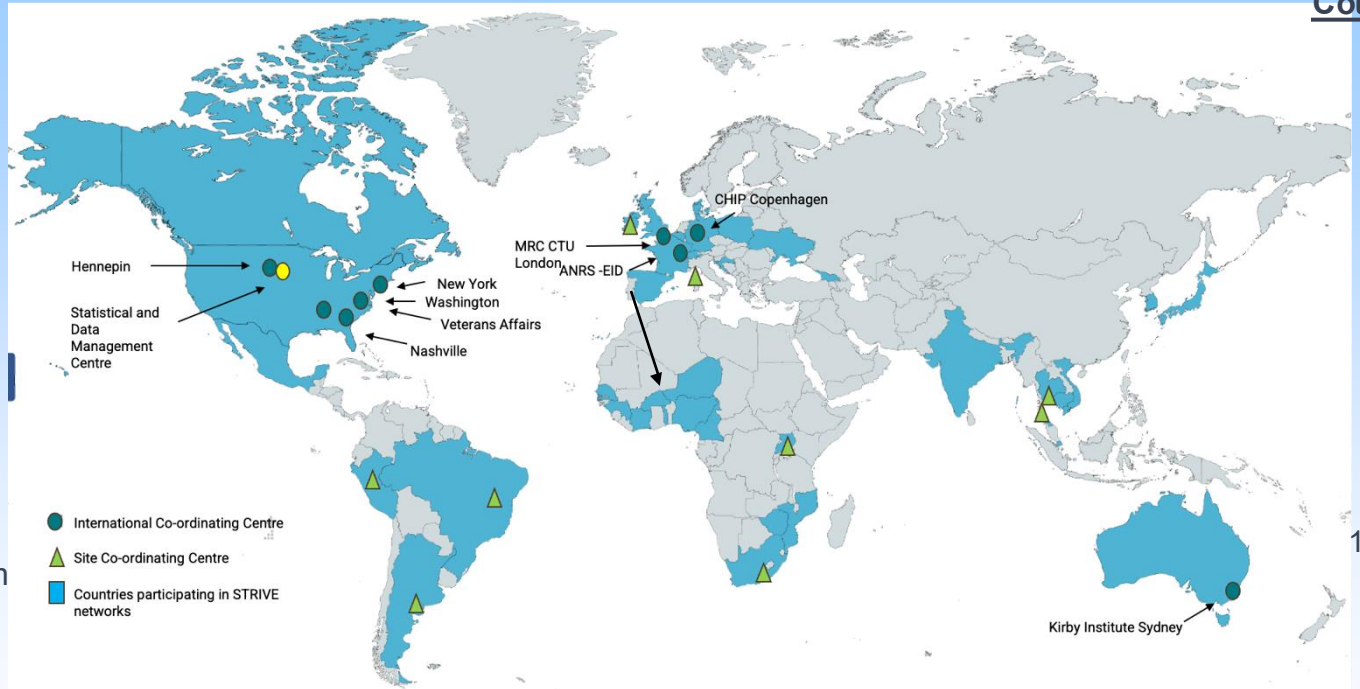
300+ clinical sites in 44 countries across 6 continents coordinated via 9 ICCs



STRIVE Global Reach

High-Income Countries (HICs):

1. Australia
2. Belgium
3. Canada
4. Denmark
5. France
6. Germany
7. Ireland
8. Italy
9. Japan
10. Singapore
11. South Korea
12. Spain
13. Switzerland
14. United Kingdom
15. United States



Low-Income Countries (LICs):

1. Burkina Faso
2. Cameroon
3. Guinea
4. Ivory Coast
5. Madagascar
6. Niger
7. Nigeria
8. Senegal
9. Togo
10. Cambodia
11. Georgia
12. India
13. Mozambique
14. Uganda

Upper Middle-Income Countries (UMICs):

1.Argentina 2.Brazil 3.Cambodia 4.Croatia 5.Greece 6.Mexico 7.Peru 8.Poland 9.South Africa 10.Ukraine 11. Vietnam

STRIVE ACTIV INSIGHT018

insight

A Strategic Vision

STRIVE is a global clinical research consortium aimed at improving the clinical outcomes of patients with infections while being prepared to respond to infectious disease emergencies, through the rapid implementation of clinical trials designed to inform practice guidelines, public health policy, and the delivery of health care.

Aims

- ***To conduct*** *clinical research to the highest ethical and quality standards, using innovative approaches, producing outcomes that are reliable, rigorous, and impactful.*
- ***To respond*** *rapidly and effectively to emerging infectious disease threats.*
- ***To promote*** *diversity, equity, and inclusion internally and in populations we engage in our clinical research.*
- ***To collaborate*** *with diverse stakeholders and organizations and include communities to ensure our research has transformative impact on care.*

A Continuous and Evolving Portfolio of Research

COVID-19 Trials

Past

TICO/TESICO
ITAC
EPOC
VATICO
ICOS

COVID-19 Trials

Here and now

OTAC
Passive immunity
Anti-SARS-CoV2
immunoglobulin

Trial 1
Antiviral agent
Ensitrelvir

Trial 2
Immunomodulation
Abatacept

Observational study

Coming

Understand severe infections better
Warm base research
Prepare for new trials

New Trials

On the horizon

Design and conduct practice-changing trials in the field of emerging and serious infection

Novel antivirals
Strategy trials
Vaccines
Emerging infections

STRIVE ACTIV INSIGHT018

insight

STRIVE Network and Site Operation and Evaluation

STRIVE
Strategies and Treatments for Respiratory Infections and Viral Emergencies

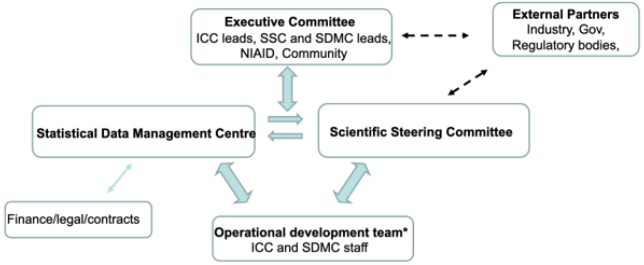
STRIVE Governing Charter

Mission Statement

Strategies and Treatments for Respiratory Infections and Viral Emergencies (STRIVE) is a global clinical research consortium aimed at improving the clinical outcomes of patients with acute severe infections while being prepared to respond to infectious disease emergencies, through the rapid implementation of clinical trials designed to inform practice guidelines, public health policy, and the delivery of health care.

STRIVE Governance

STRIVE is governed by three bodies: the STRIVE Executive Committee (EC), the STRIVE Scientific Steering Committee (SSC), and the Statistical and Data Management Center (SDMC) (Figure). The EC provides operational and strategic oversight. The SSC oversees the design, execution, and dissemination of the science of STRIVE. The SDMC manages the finances, data, and regulatory oversight of STRIVE. Details of each body are described in this document.



STRIVE: Principles for network evaluation

Background/context

The STRIVE network has evolved from INSIGHT (a collaboration between SDMC and 4 ICCs performing trials in the setting of outpatient HIV care) through ACTIV-3 (a collaboration between SDMC and eight ICCs performing inpatient COVID trials in the setting of a pandemic) into STRIVE – a novel collaboration between SDMC and 9 ICCs positioned to conduct infectious disease research both during pandemics and between pandemics with access to a vast number of clinical trial sites. This network stretches across over 300 sites on 6 continents and contains within it a diverse mix of sites with varied expertise, location, speciality interest and ethnicity.

One of the greatest challenges for STRIVE going forward is to maximise the efficiency of the use of the network's resources, and a component of this is appropriately choosing sites that can best deliver on any particular trial. This may vary greatly from a request to establish sites rapidly in response to an emerging threat in a specific geographical location, to a study conducted between pandemics where the goals may be quite different.

Guiding Principles

In INSIGHT, site selection was largely left up to the individual ICCs. Considerable ICC and SDMC resources, and therefore network resources, were frequently invested in working with less efficient sites by some ICCs. This is a source of inefficiency for the network and can reduce expectations for all ICCs and sites. Centralized evaluation of site performance could help identify ICCs and sites with more efficient procedures which could be shared across the network. Moreover, this evaluation could help with selection of sites for some studies. Further, evaluation of ICC and SDMC indicators will also help to guide areas for improvement.

Central evaluation of SDMC, ICC and site performance using a pre-defined set of metrics is a novel concept to STRIVE and needs to be undertaken with clear aims and objectives as well as a transparent process of documentation and feedback. This is not intended to be punitive but rather to: i) identify sites, networks and/or regions that may face specific barriers and benefit from input to help overcome these; ii) help identify sites which have the capacity, expertise and tools to rapidly open (i.e., priority sites); and iii) identify barriers at higher operational levels in the network that may be amenable to additional interventions.

Process

The following table identifies necessary steps at all levels of the network that could promote efficient network operation and facilitate rapid participant enrolment. It is not completely exhaustive and additional steps may be required for some studies, e.g., trials of

Acknowledgements

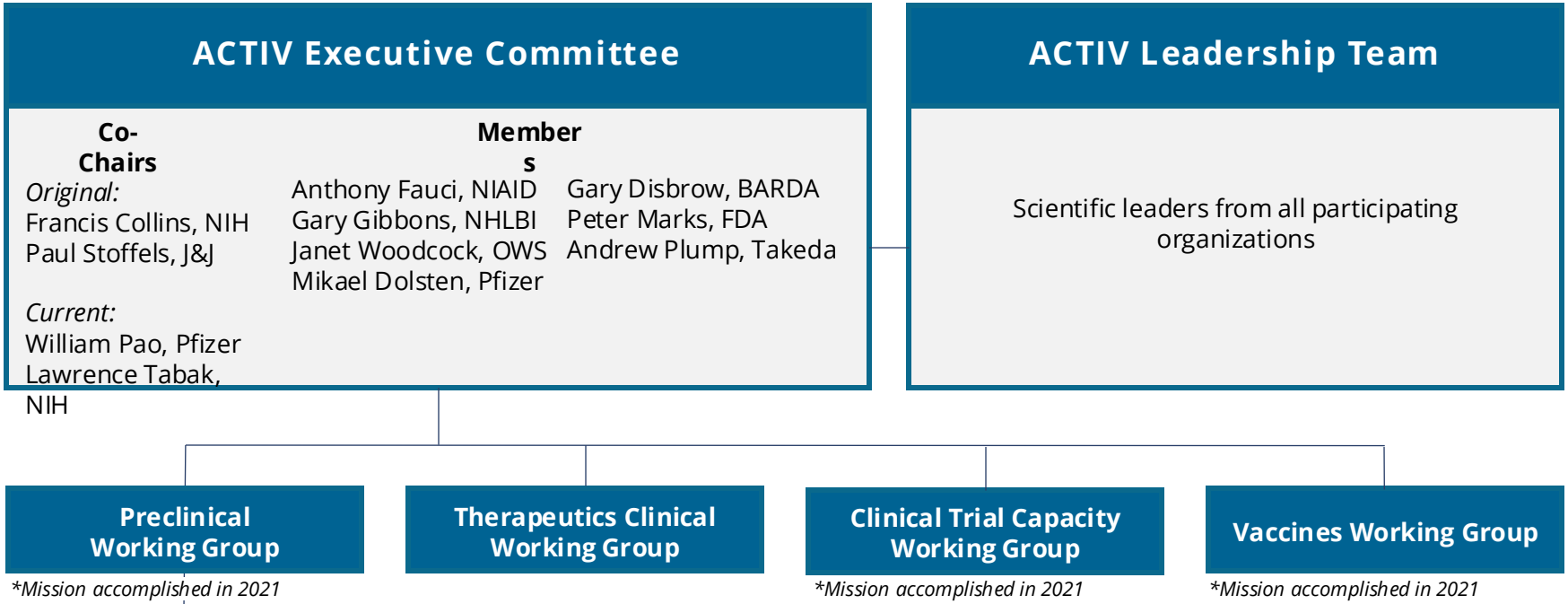
ACTIV-2

ACTIV-5: BIG EFFECTS TRIAL (BET)

Backup Slides
Deep Dive Lessons Learned

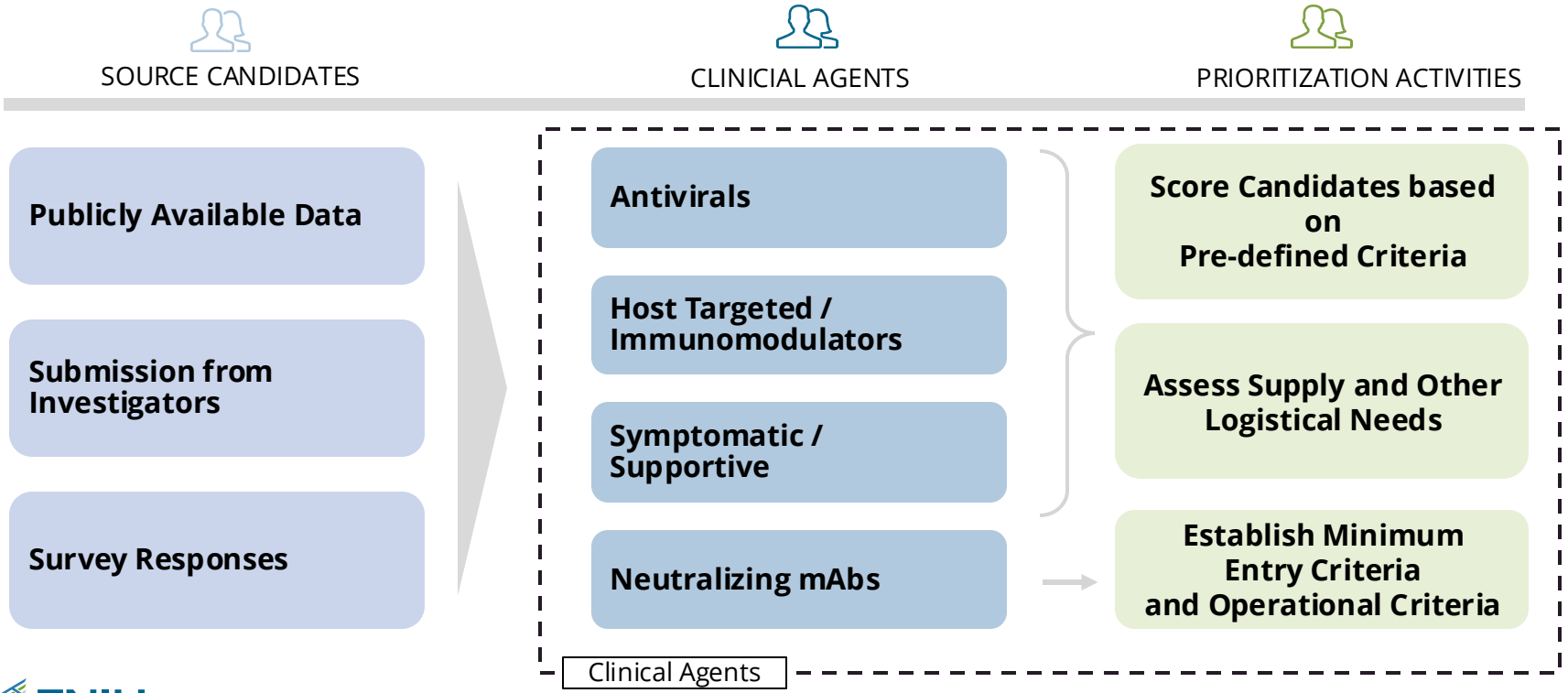
FNIH

ACTIV Governance



Prioritizing Promising Therapeutic Agents for COVID-19

The Working identified agents that stop the virus or that treat its symptoms and placed them in appropriate master protocols for Phase II or III testing – so far ACTIV has reviewed more than 800 agents.



Overall ACTIV Therapeutics Lessons Learned

Topic	Recommendations
Agent Prioritization	• Develop minimum required treatment attributes for the different types of interventions prior to initiating the agent prioritization process. • Employ a use of RWD for review of agents with known MOAs and safety profiles, incorporating emerging variant data, and accounting for long-term viral effects. • Enhance data sharing between groups and endeavor for a standardized selection process across all pandemic respondents.
Preclinical	• Develop repositories with capability and capacity to ensure researchers have rapid access to standardized sequences, viruses, assays, animal models, and appropriate testing facilities. • Ensure the quickest communication of preclinical findings possible with resources like open data platforms, preprint servers, etc.
Master Protocol Use	• Create separate inpatient, outpatient for novel/registration intent agents, and outpatient repurposed drug master protocols but mandate a standardized data collection protocol or platform for all trials. • Engage with the regulators early to sign off on simple, validated endpoints that can evolve with the changing nature of the disease or emergency but be drafted for an off-the-shelf protocol that builds on the successes of more creative trial designs created during pandemics.
Master Protocol Implementation	• Improve international regulatory coordination for global platform protocols. • Establish trigger to initiate US pandemic research response with responsibility assigned for prioritized research agenda and implementation plan development. • Maintain a warm base infrastructure (i.e., a network of sites, an active protocol, etc.) during time between public health emergencies. • Ensure that participants are enrolled in protocols such that trial results are applicable to the majority of affected persons.
Results Communication and Data Sharing	• Develop a consensus on common data elements, formats, and management practices and a mechanism to ensure use by all trials. • Develop during "peacetime" and utilize one structured data repository to ensure quick data readouts. • Consider a centralized repository for samples and data upfront and if capacity is available, a central virology core lab. • Publish rapidly with full data in preprint and share with the Guidelines Committees for review to effect clinical practice. • Establish a communication plan early in the emergency to aid with rapid results dissemination and help combat disinformation.
Manufacturing and Drug Scaling	• Require specific criteria for product supply inventory or scalability to meet demand, but ensure funds are available to help achieve production targets. • Map manufacture and distribution resources to specifically maintain the viability of the most promising scalable therapeutic candidates. • Establish a processes now to allow supply and distribution through the Strategic National Stockpile to support US government trials during a pandemic. • Generate plans, procedures, and contracts in place now with large pharmaceutical production capabilities.
Additional Benefits of the PPP	• Emphasize and maintain a PPP's role and infrastructure in building trust across stakeholders in preparation for the next pandemic.

Master Protocol Design Lessons Learned

Topic	Lessons Learned and Recommendations
Central Design Principles	• Early pandemic trials must adapt to evolving disease context and SOC, allowing for changes in endpoints and study design goals.; study designs must be flexible and when possible agnostic to background clinical milieu. • Adaptations need to occur quickly, requiring active engagement of numerous regulatory bodies, including FDA and others. • Adaptive design techniques facilitate more rapid decisions and the ability to test multiple agents in different patient populations with optimal allocation of resources.
Sample Size Calculation and Power	• Sample size determination and power analyses for master protocols should be consistent with the research and regulatory objectives and incorporate the best information available at the start of a pandemic. • Statistical methods for blinded sample size reassessment and early stopping for futility or evidence of efficacy can be utilized to help counter the uncertainty of important parameters at the time of design, supporting adaptations to an evolving emergency environment.
Flexible Inclusion/Exclusion (eligibility) Criteria	• The application of broad inclusion criteria focusing on the demographics, care setting, and disease manifestations, coupled with agent-specific exclusions for safety purposes, is effective. • Reducing complexity by minimizing between-arm variation in eligibility supports the sharing of control data between study arms and simplifies enrolment among frontline research teams while also avoiding the need to constrain the platform's logical evolution or revise this fundamental aspect of the trial protocol as the platform evolves over time.
Outcome Measure and Optimal Endpoints	• Of particular importance to future pandemics is establishing a framework for outcomes that can track with disease severity and knowledge. • The initial focus on survival, functional status, and subsequently symptomatology allows for progressive decision making. • To facilitate outcome selection in future pandemics, we recommend inclusion of global measures such as mortality and quality of life, and the rapid adoption of existing, repurposable scales and measurements specific to the predominant injuries observed.
Industry Partnership	• Early engagement from industry partners is critical to trial success.
Trial Governance Structure	• Trial governance needed to be nimble in its decision making, but comprehensive in its stakeholder makeup to ensure proper expertise for quick decisions. • Coordination between each master protocol trial in addition to the internal trial coordination is essential. • A strong centralized coordinating entity, such as that performed by FNIH and NIH, is essential to help facilitate trial stand up, regulatory functions, and infrastructure.
Regulatory	• For future RCTs in the context of a health emergency, regulatory agencies should be in closer communication with DSMBs around real time safety reviews. • Both the DSMB and the FDA have significant roles to play in safety oversight.
Assembling Networks	• Including global clinical trial site capacity, updated on an ongoing basis, in pandemic preparedness activities is essential to early trial start up in a pandemic situation.

Inpatient Site-Specific Lessons Learned

Stakeholder	Solutions
Institutional Clinical/Research Leadership	• Develop policies for the procurement, maintenance, and distribution of PPE. • Determine institutional research priorities. • Establish a clinical trial review committee and prioritize research in accordance with research priorities. • Promote awareness of clinical trials among clinical staff through research updates, incorporating research roles into clinical teams, and engaging HCP as site co-investigators. • Refrain from providing unproven treatments under EUA, provide education on SOC availability, prioritize conducting randomized trials.
IDS Pharmacists and Pharmacy Leadership	• Modify research pharmacy staffing models. • Schedule regular meetings for IDS site and sponsor pharmacists. • Incorporate trained research pharmacists at sponsor-level early on in protocol conception and implementation to identify IDS specific challenges and allow communication with IP manufacturers.
Investigators and Research Team	• Prioritize trials between different research teams. • Engage in home health services. • Utilize telehealth.
Regulatory Leadership	• Emphasize the dynamic process of informed consent. • Simplify readability of ICFs to help improve user comprehension and understanding. • Align central/single and local IRBs to reduce the length of consent forms by decreasing the required documentation.
Research Sponsors and Protocol Development Teams	• Careful site selection, community outreach, research teams that reflect the community and training of cross-cultural perspectives, minimize barriers to enrollment; develop more pragmatic protocols including specimen collection schedule.

Outpatient Site Specific Lessons Learned

Topic	Lessons Learned and Recommendations
Limited Infrastructure	• Work with community hospitals and clinics to ensure readiness by providing infrastructure (e.g., personal protective equipment (PPE)). • Address obstacles to study conduct (e.g., transportation for those with respiratory infections requiring isolation) and remote/home enrollment for study visits if feasible. • Develop a lab supply list in parallel with site selection to support sites with planning and procurement or consider lab kits/kit management system. • Share production procedures for 3D printed laboratory supplies and PPE. • Continue to waive Health Insurance Portability and Accountability Act (HIPAA) regulations for pandemic communications. • Deploy federal disaster tents with community aid in all areas, independent of politics.
Availability of Staff and Study Fatigue	• Create a national pool of trained Study Coordinators who can deployed during emergency situations. • Simplify training site investigators and study personnel. • Create video consent and centralized websites with frequently asked questions to help with recruitment and trial information dissemination. • Streamline centralized information about PPE use and supplies. • Standardize practices for site engagement strategies.
Community Engagement and Recruitment of Vulnerable Populations	• Integrate the community early to provide feedback on study design and to help with messaging and outreach. • Storefront with multiple enrollment assistance materials/social media toolkit. • Ensure ongoing education and continually updated website. • Ensure continuous participant education about the trial's progress. • Convert large open public spaces to testing and clinic facilities. • Streamline connections with research referral services without having to establish individual permissions with each entity. • Utilize emergency department waiting rooms to disseminate up to date and accurate information. • Focus on dispelling misinformation (e.g., TV ads, notices, flyers).
Institutional Variability	• Support trial site capacity and infrastructure during institutional shutdowns. • Support local and centralized IRB procedures. • Streamline and standardize instructions for sites (e.g., start-up, monitoring, IRB, isolation procedures). • Maintain pandemic specific local and central IRBs that can function in24-hour capacity. • Create pre-existing agreements about data sharing and trial cooperation between public health entities and research entities such that agreements for referrals and data access are not recreated in real time each time- consider an opt out checkbox on all reportable disease testing about research referral.
Trial Confusion	• Provide simple document(s) with pictures for study staff to explain the study and drugs. • Amend protocols multiple times to allow standard of care as evolved during trial implementation. • Standardize site laboratory procedures. • Describe required biological sampling clearly.
Follow-Up of Participants	• Plan for enrollments when participants present after hours or during weekends and holidays. • Provide a centralized 24-hr/day email and phone service for answering questions by medical officers regarding inclusion and exclusion criteria. • Institute protocol defined criteria for follow-up (e.g., in-person and virtual), like those who were admitted to the hospital. • Use home nursing for study visits and sample collection.

Pandemic Platform Trials Statistical Lessons Learned

Topic	Lessons Learned and Recommendations
Coordination of the Statistical Response	• When mobilizing for a pandemic, it is critical to provide a forum for statisticians to engage with one another to optimize the trials for purpose. • In particular, the shared perspectives of industry, academia, government funding agencies, and regulators, and the willingness to selflessly contribute, was pivotal to the rapid response.
Designing for a Pandemic	• A range of statistical approaches that provide flexibility in the presence of uncertainty were already available in the early days of the pandemic. • As demonstrated by the innovative use of emerging information for decision making in the ACTIV protocols, the statistical design can and should be tailored to the specific research goals and environment. • Interim monitoring of study data is a must, and methods that reduce time-to-decision should be considered so as to rapidly evaluate a large number of potential treatments. • Most importantly, having skilled statisticians on hand to select the optimal approach can help ensure that any master protocol is launched with a fit-for-purpose design.
Endpoint Selection	• Statistical input to the choice of endpoint is critical, with factors such as power, analysis approach, and interpretation of statistical results in terms of clinical meaningfulness at the forefront. • Regulatory buy-in is critical, and flexibility must be accommodated. • Establishing an efficient process to rapidly select, monitor, and update acceptable endpoints prior to the next pandemic would greatly accelerate trial design decisions and limit unplanned adaptations.
Multiplicity in Master Protocols	• The early involvement of statisticians that were highly facile running platform trials was critical to integrating prior knowledge into the trial design, speeding up development decisions by drawing on specialized clinical trials experience.
Unexpected Trial Adaptations	• While trial analysis plans have to be defined prior to trial execution, changes in external context can result in unplanned adaptations and updates to the statistical analysis plan. • A pathway for doing so, blinded to treatment assignment and results, should be available until the conclusion of the trial.
Shared Controls	• Sharing concurrent control data is recommended when an appropriate design to avoid bias is feasible. • In general, we expect the efficiency gains to outweigh the logistical challenges, and careful planning can address the anticipated challenges in advance. • Sharing controls in a platform trial may impact efficiency gains if there is a differential placebo response; platform trials are encouraged to consider comparability of placebo response before proceeding with a shared control strategy.
Blinding	• Overall, the blinding approaches used for platform trials must consider logistics surrounding shared control participants. • The choice to blind may be influenced by pace of implementation, but the benefit of blinding is largely unaffected by pandemic context or uncertainty. • The decision to allow participants to opt-out of a study arm, or to unblind which agent the participant is randomized to, can alter willingness to consent and willingness to proceed with trial procedures.
Other Considerations for the Statistical Analysis Plan	• Efficiency gains from using similar data elements and a similar analysis plan for all agents within a platform start to diminish as differences among the individual study arms expand.
Data and Safety Monitoring	• During a pandemic, data and safety monitoring plans should have enough flexibility to accommodate waves in recruitment without sacrificing data quality or participant safety. • Data and safety monitoring of platform trials during a pandemic requires considerable analysis and reporting by the study team and a large time commitment of the DSMB members, and an experienced DSMB.
Data Collection and Management	• Appropriate planning for changes, including personnel resources for change management, is critical. • Data systems should be configured for flexibility. • Data entry logic checks and branching logic can be used to facilitate appropriate targeting of data collection. • As well as limiting errors in the enrollment process, workflows should also address variations in site-specific data, such as lab reference ranges and validation limits, to reduce errors in real time. • In future pandemics, we recommend careful attention to biospecimen processing so that operational delays to measurements and thus analyses can be addressed early.
Statistical Resources	• A strong recommendation for pandemic preparedness is to pre-identify and maintain statistical resources that can lead without distraction, and that are sufficient to support the magnitude of response needed from the statistical community. • In addition to establishing a forum for rapid communication and cross-education, such a resource could include the development of federated data management and analysis models among those critical experienced and trusted partners, with simplified data sharing agreements for use in a pandemic.

FNIH

Mapping the Evolving Global Landscape of Investigative Site Models

CTTI Project Watchtower Expert Meeting

July 30-31, 2025

Joan A. Chambers

Senior Consultant

Tufts Center for the Study of Drug Development
TUFTS UNIVERSITY

About the Tufts Center for the Study of Drug Development (Tufts CSDD)

Center History: 48-year-old Independent, globally-focused, academic group based within Tufts University School of Medicine (Boston).

Mission: Conduct robust, data-driven assessments and analyses to inform drug development stakeholders committed to optimizing quality, performance, efficiency and economics.

Communities Served: Congress, the National Academies of Science, Foundations, Industry, Regulatory Agencies (e.g., FDA, EMA) EFPIA, PhRMA, BIO, DOD, NIH, CTTI, Capital Markets.

Tufts Center for the Study of Drug Development
TUFTS UNIVERSITY

Agenda

- Insights
- Global Investigative Site Landscape Overview
- New Clinical Trial Execution Models
- Clinical Trials Becoming More Accessible to Participants and Local Communities
- Closing Remarks

Industry Insights

- Patient recruitment is the leading reason most clinical trials fall behind schedule
- Only **2%-5% of U.S. patients** participate in clinical trials, prompting sponsors to enhance their recruitment support
- Just **27% of screened participants** meet the eligibility criteria, increasing screening costs due to high attrition
- Patients are central to clinical trials, driving progress in therapy development and care innovation
- Clinical trial sponsors prioritize patient participation and trial completion
- Research highlights key participation barriers, including access challenges and indirect expenses
- Studies also reveal that lack of support for baseline medications hinders participation and increases drop-out rates, particularly among socio-economically vulnerable populations
- An integrated, ecosystem-wide approach is essential for raising awareness and ensuring efficient, representative trials

Source: L.E.K. Consulting Executive Insights, Feb 2024

Global Investigative Site Landscape

- The global investigative site landscape is evolving rapidly due to market conditions, demand for new and more **accessible** and **convenient** execution models
- New clinical trial execution models that have been introduced include:
  - Site staff embedded within clinical care settings, remote sites (e.g., specialty labs, retail pharmacies, urgent care facilities), mobile sites, and home health services
- Part-time community-based clinical research sites have divested their research operations
- Site networks and academic institutions have scaled and gained market share of pharmaceutical industry study grants

Source: Tufts CSDD Analysis

Global Investigative Site Landscape

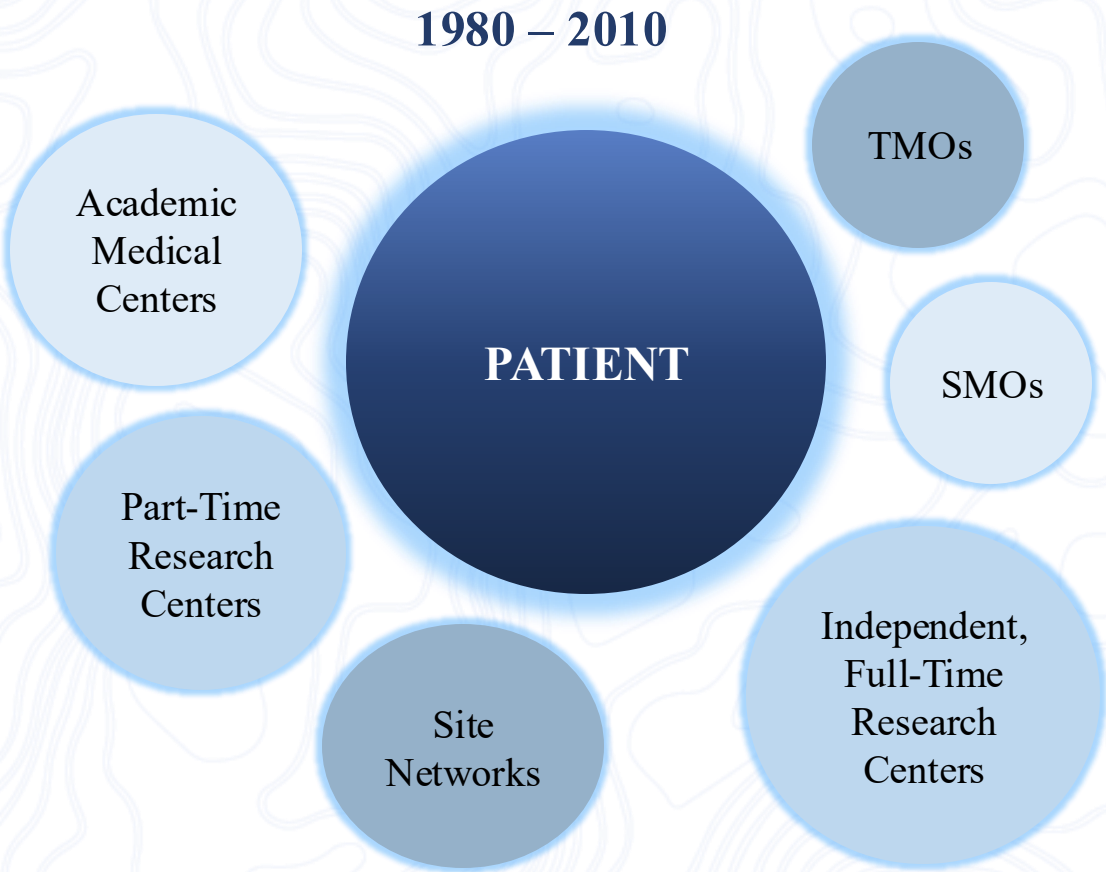
- Most of the larger private site networks have secured investment capital to drive their growth strategies
  - Growing interest from the capital markets in supporting roll-up strategies and ‘transformative’ execution models
- Many companies are reevaluating and modifying the utilization of sites and the different study execution models
- Anecdotally, some sponsors and CROs are evaluating site performance quality, with a specific focus on sites that are part of networks supported by private equity, venture capital, and institutional investors

Source: Tufts CSDD

Global Investigative Site Landscape

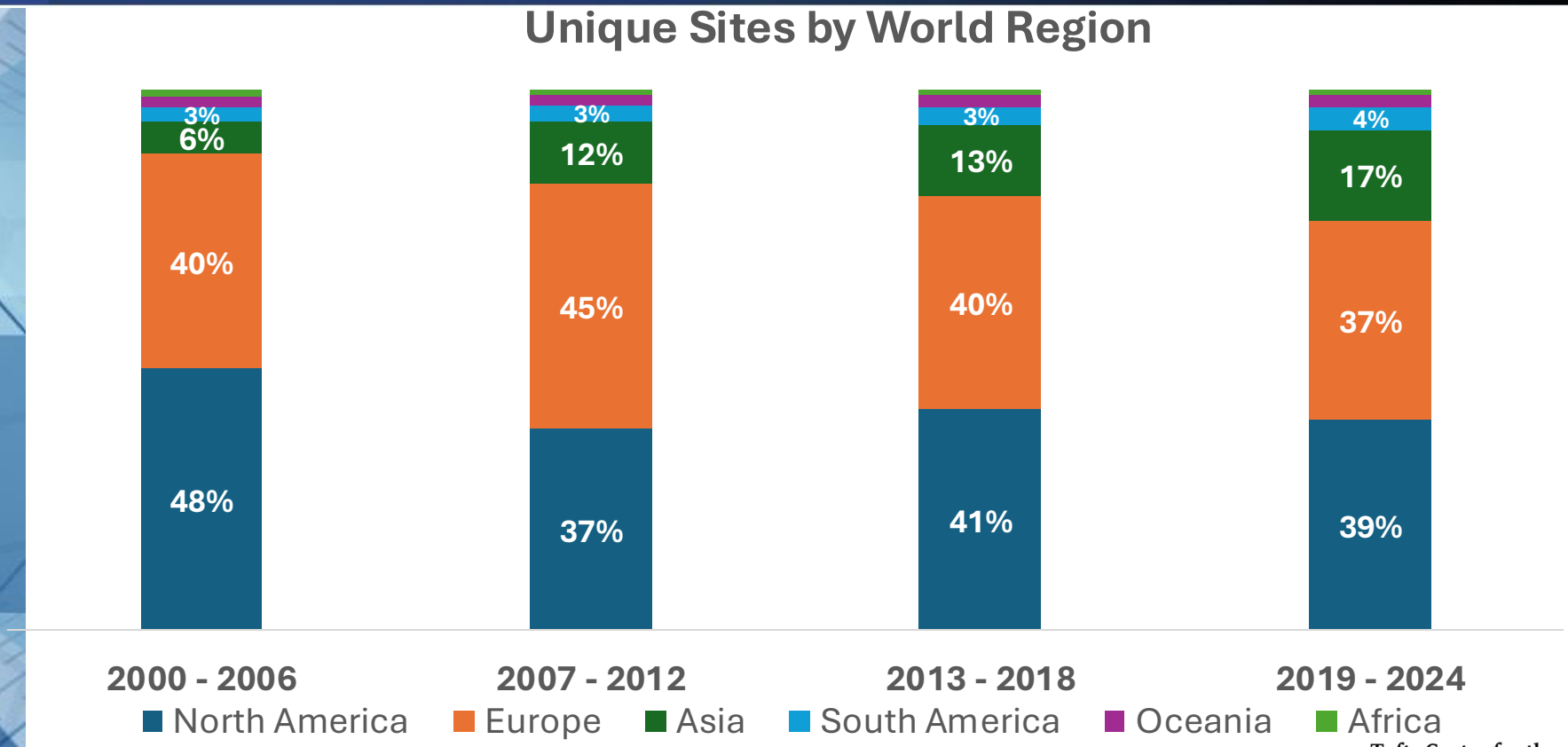
Tufts Center for the Study of Drug Development
TUFTS UNIVERSITY

Investigative Site Landscape: Historic Look



Source: Tufts CSDD

Distribution of Sites by Trial Start Year



Source: clinicaltrials.gov

Tufts Center for the Study of Drug Development
TUFTS UNIVERSITY

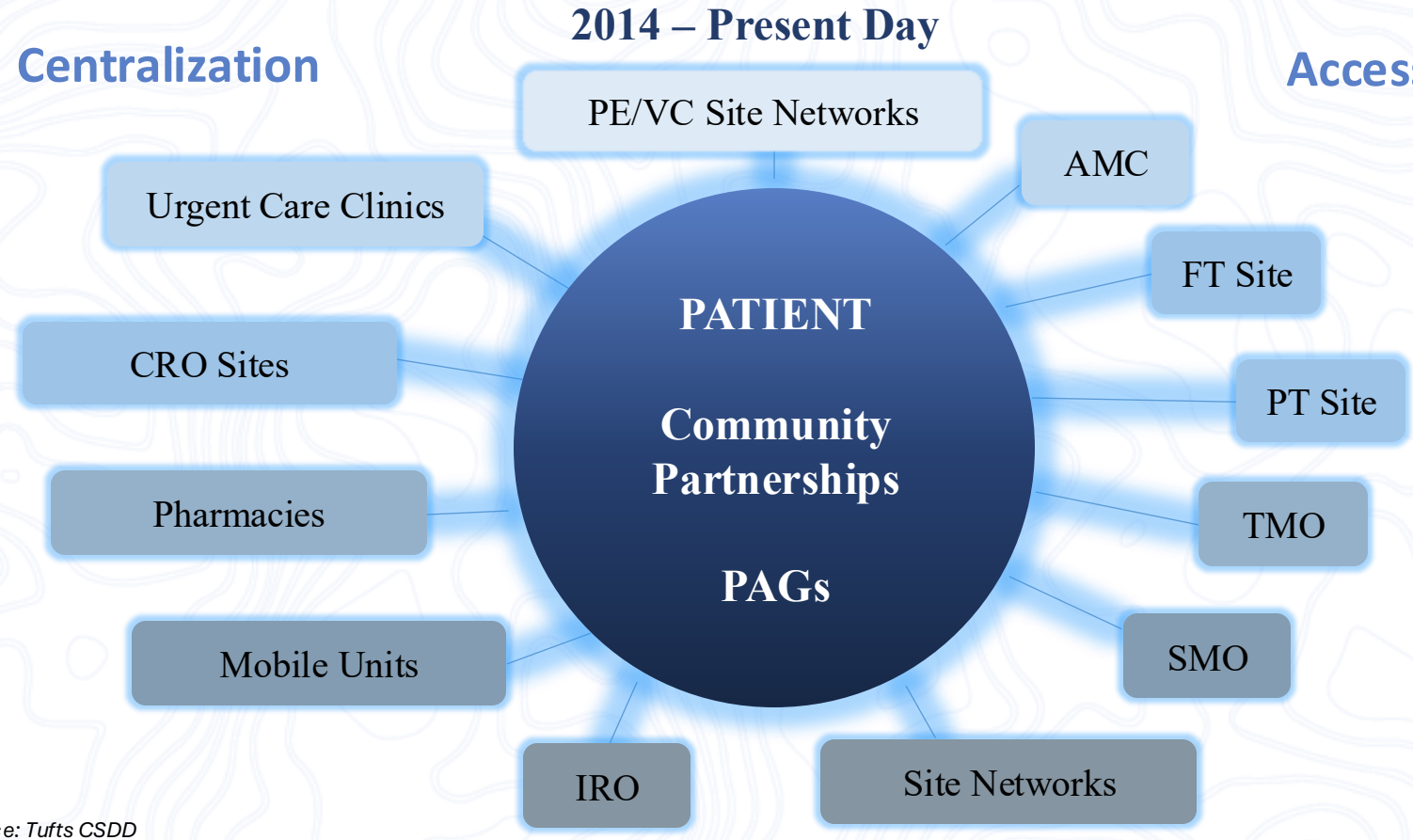
A Maturing Site Landscape

(Share of FDA Regulated Clinical Trials)	2012	2022
Annual Volume		
1 Filing	68%	43%
2-5 Filings	23%	37%
6+ Filings	9%	20%
Setting		
AMC/Hospitals	40%	43%
(PT) Community-Based	52%	45%
Dedicated	8%	12%

Source: FDA, Tufts CSDD Analysis of BMIS Data

Tufts Center for the Study of Drug Development
TUFTS UNIVERSITY

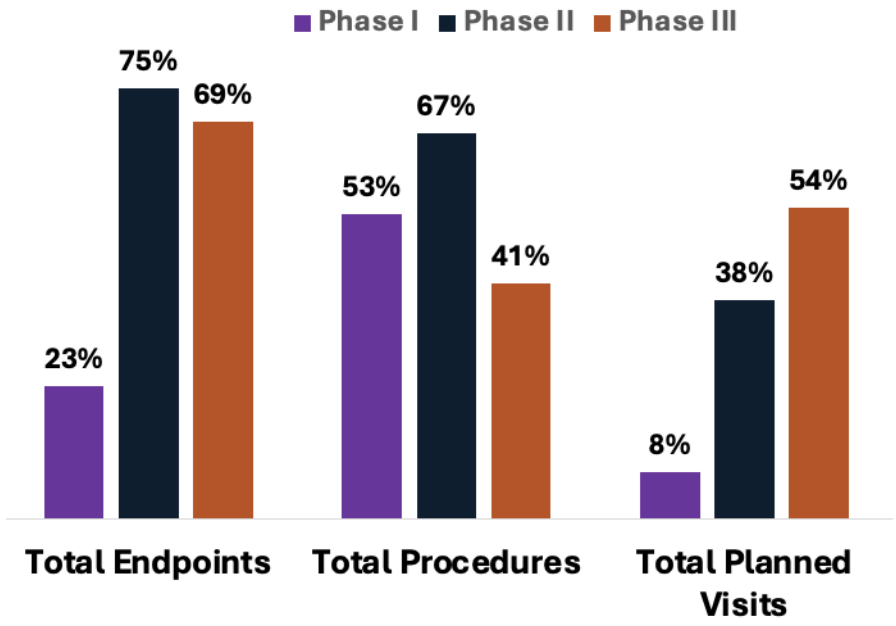
Evolution of the Investigative Site Landscape



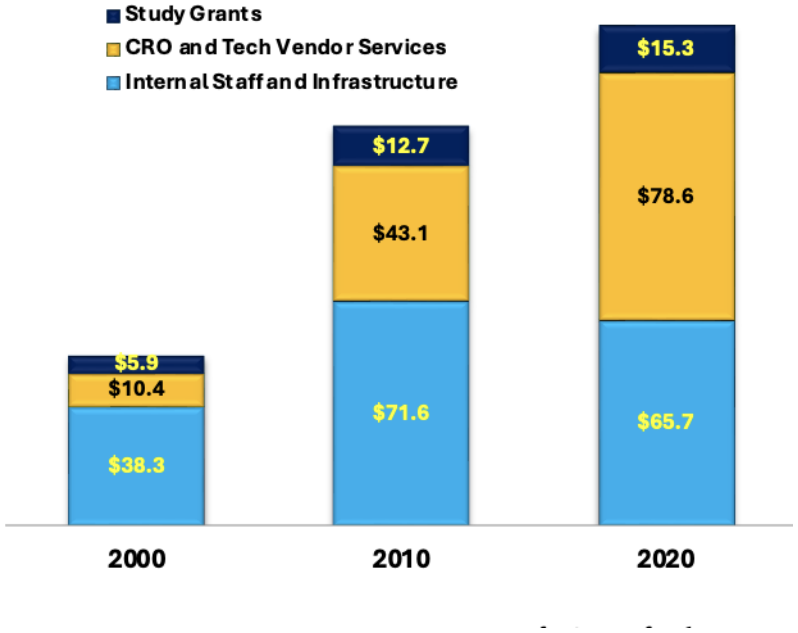
Source: Tufts CSDD Analysis

Design and Executional Customization

10-Yr Growth in Protocol Design Customization
(2010-2020)



Rapidly Rising Executional Fragmentation



Source: Tufts CSDD Analysis

Tufts Center for the Study of Drug Development
TUFTS UNIVERSITY

Customization and Clinical Trial Performance

Protocol Design Practice

Phase III Pivotal Trials *(Means)*	2010	2020	10-Year Change
Total Endpoints	13	22	69.2%
Total Eligibility Criteria	34	30	-11.8%
Total Procedures	187	263	40.6%
Total Countries	9	15	66.7%
Total Investigative Sites	65	104	60.1%
Procedures per Visit	11	13	18.2%
Total Patients Randomized	597	632	5.9%
Total Data Points Collected	929,203	3,560,201	283.2%

Change in Trial Performance – 2010 to 2020

Phase III Pivotal Trials	10-year Change
Initiation Duration (approval to FPFV)	27.2%
Enrollment Duration (FPFV – LPLV)	36.9%
Closeout Duration (LPLV to DBL)	16.3%
Total Substantial Amendments	113.3%
Drop-Out Rates	105.1%

Source: Tufts CSDD Analysis

Tufts Center for the Study of Drug Development
TUFTS UNIVERSITY

Trends in Clinical Trial Durations by Phase

Time Period	Mean Trial Duration (months) (Protocol Approval to DBL)	Coefficient of Variation
Phase I		
2008-2013	13.8	1.59
2014-2018	14.8	1.51
2018 - 2021	20.3	1.29
Phase II		
2008-2013	27.1	.88
2014-2018	30.2	.85
2018 - 2021	40.6	.98
Phase III		
2008-2013	26.8	.83
2014-2018	28.5	.75
2018 - 2021	39.4	.91

Source: Tufts CSDD; N = 1,329 protocol

Tufts Center for the Study of Drug Development
TUFTS UNIVERSITY

Study Volunteer Participation Burden

Pre-Study Experience

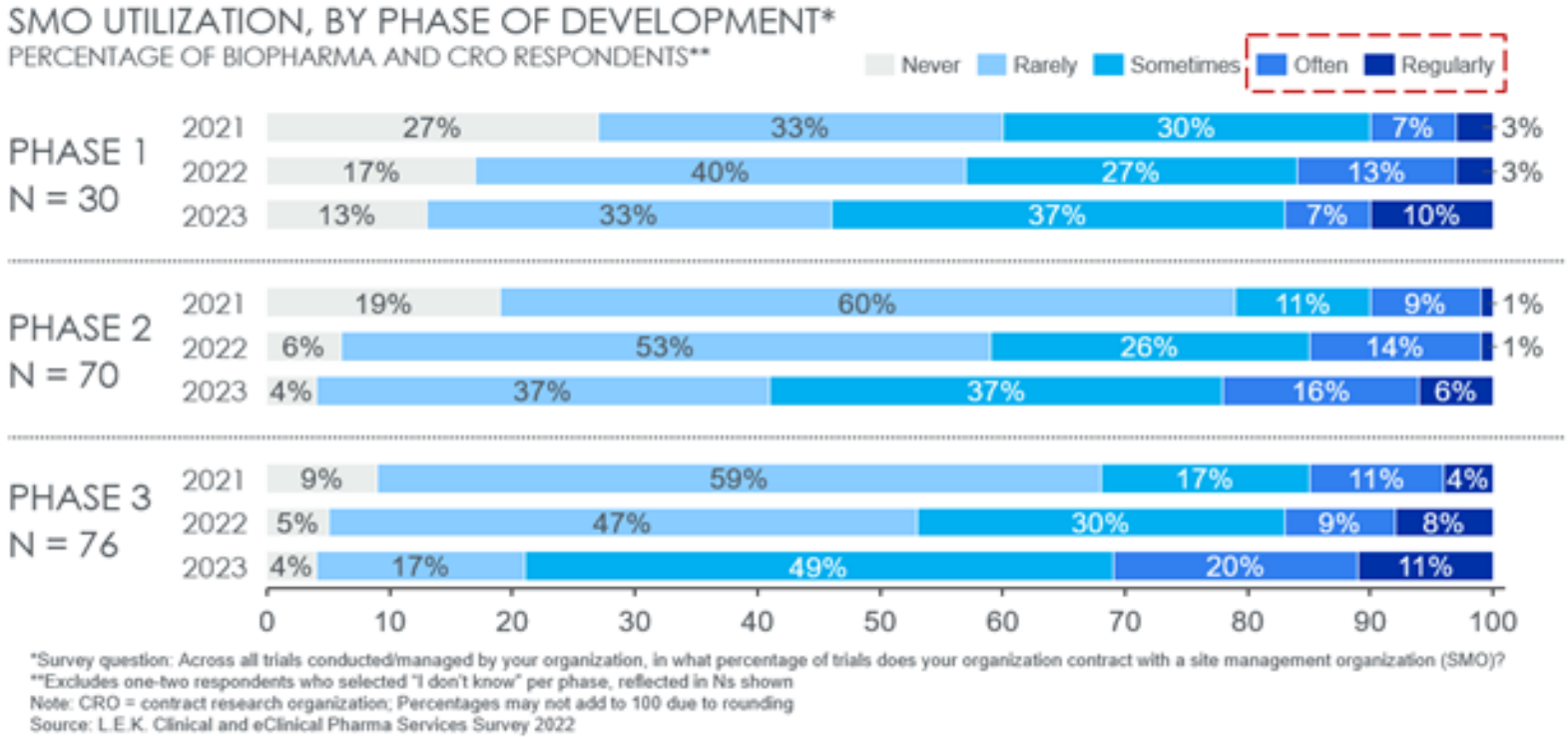
After reviewing the Informed Consent Form, what led you to decide NOT to participate	Percent of Total
Expected burden of participation	54%
Scientific/study risks	25%
Lack of sufficient information	14%
Concerns about privacy and confidentiality	7%

Post-Study Feedback

What did you least like about your participation experience? *(Top 5 mentions)*	Percent of Total
Not knowing whether I was getting the investigational treatment	30%
Location of the research center	22%
Study visits were too time consuming	19%
Compensation was not enough given the demands of the study	16%
Study procedures were too cumbersome	15%

Source: Tufts CSDD Analysis

SMO Utilization Across Development Phases

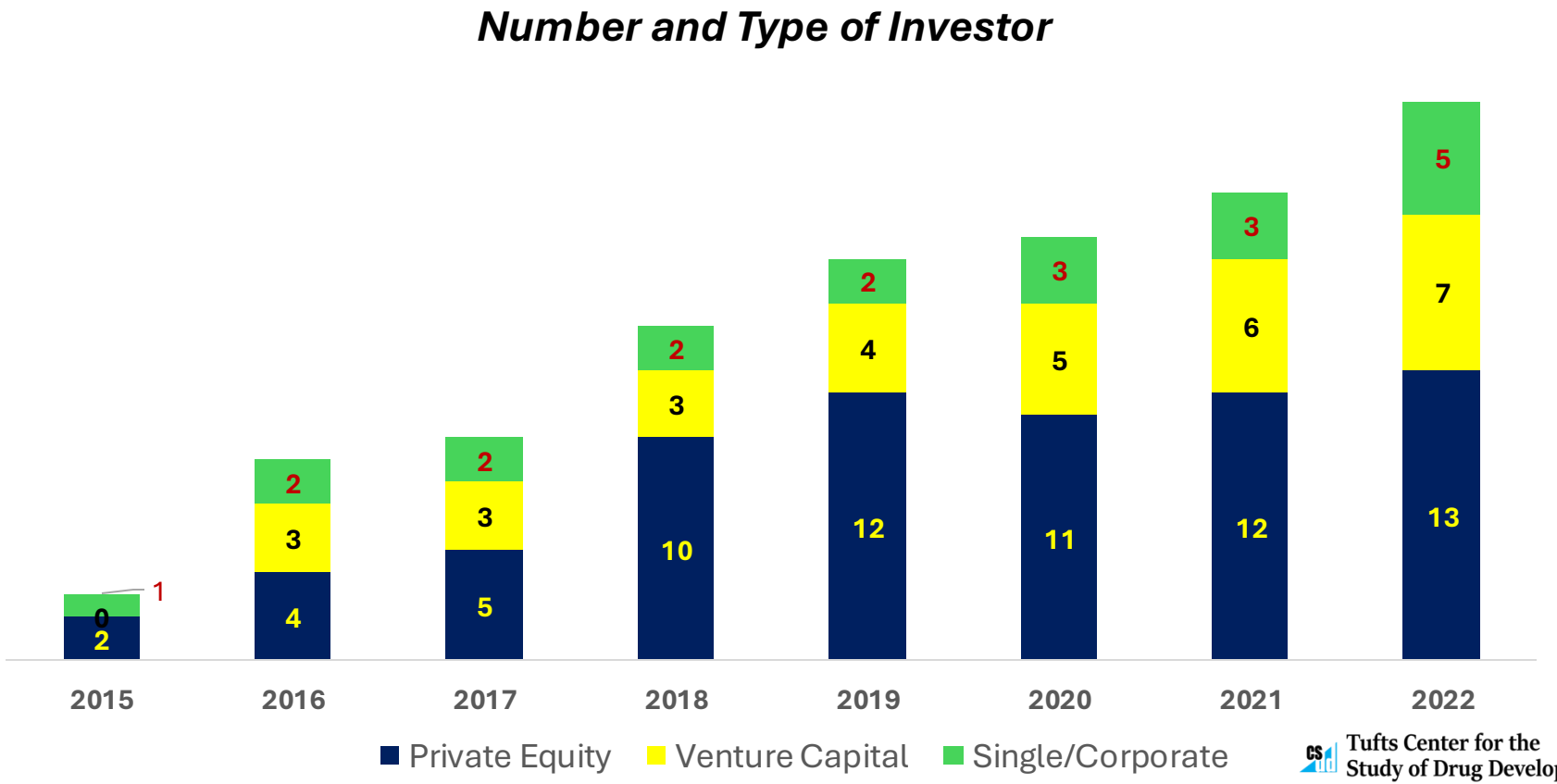


*Survey question: Across all trials conducted/managed by your organization, in what percentage of trials does your organization contract with a site management organization (SMO)?
**Excludes one-two respondents who selected "I don't know" per phase, reflected in Ns shown
Note: CRO = contract research organization; Percentages may not add to 100 due to rounding
Source: L.E.K. Clinical and eClinical Pharma Services Survey 2022

Source: L.E.K. Consulting; Clinical and eClinical Pharma Services Survey 2022

Tufts Center for the Study of Drug Development
TUFTS UNIVERSITY

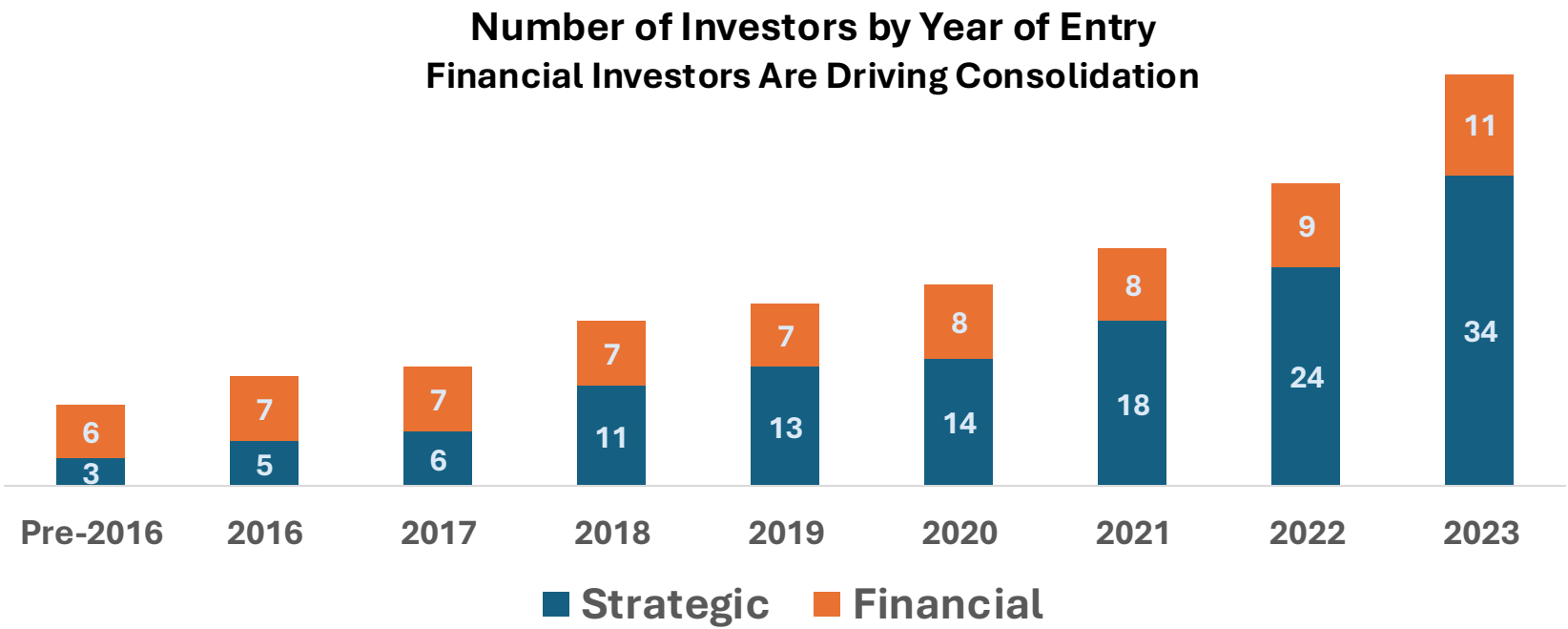
Capital Market Interest in Investigative Sites



Source: CRIO Clinical Research, November 2023

Tufts Center for the Study of Drug Development
TUFTS UNIVERSITY

Investors Focus Strategically and Financially

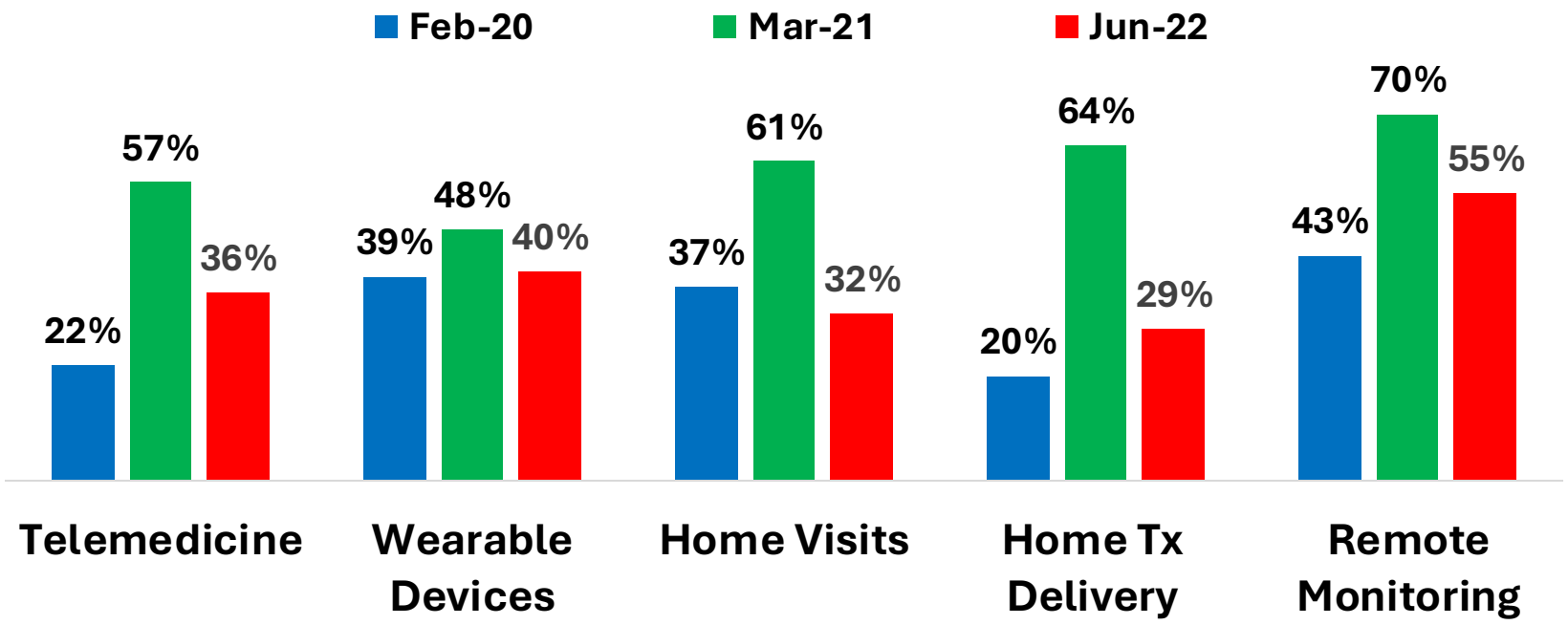


Source: CRIO Clinical Research, November 2023

Tufts Center for the Study of Drug Development
TUFTS UNIVERSITY

Remote and Virtual Solutions Adoption

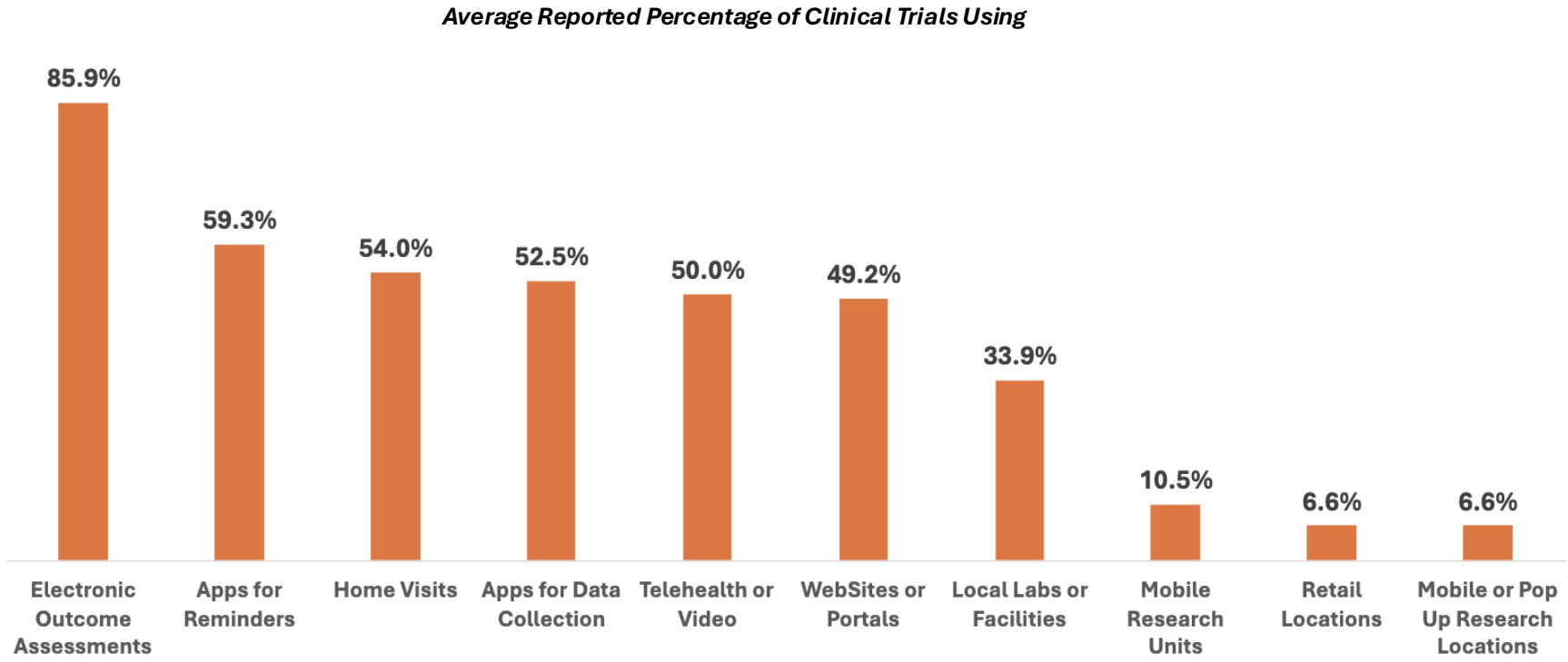
Percent of Companies Report Deploying



Source: Tufts CSDD; N=54 individual companies

Tufts Center for the Study of Drug Development
TUFTS UNIVERSITY

DCT Solutions Use For Study Visit Activities



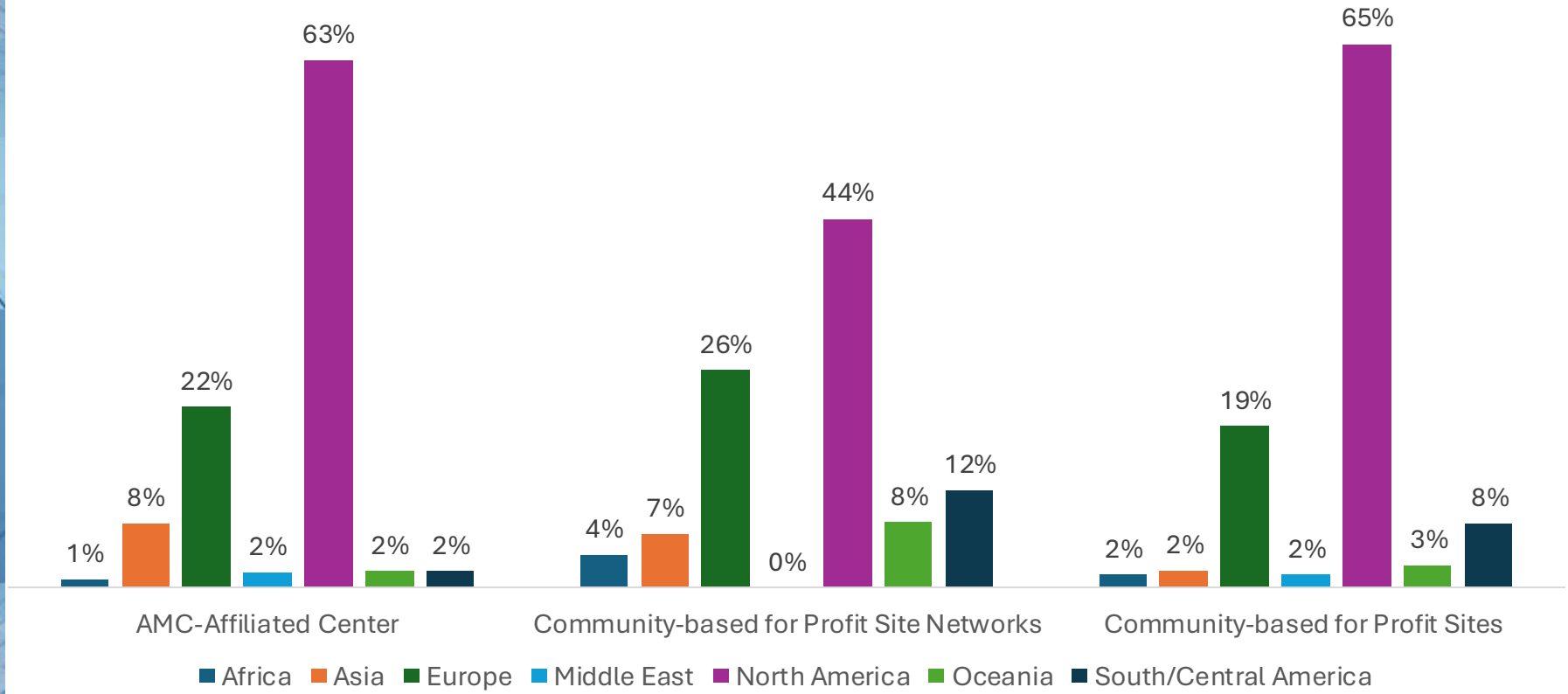
Source: Tufts CSDD PACT Consortium of 30 sponsor and CRO companies; 2023-2024; N = 70 Clinical Trials

Tufts Center for the Study of Drug Development
TUFTS UNIVERSITY

Global Investigative Site Landscape Segmentation

Tufts Center for the Study of Drug Development
TUFTS UNIVERSITY

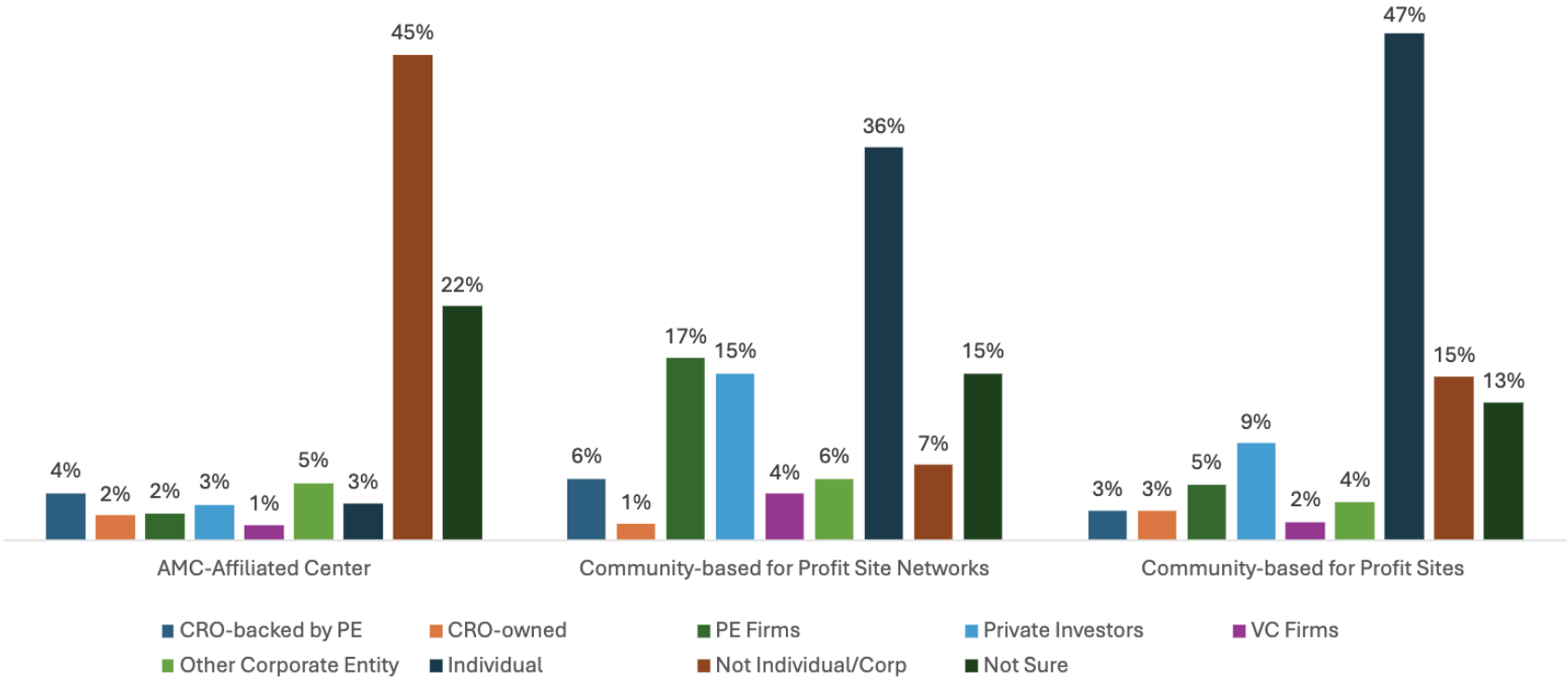
World Region: Site Type



Source: Tufts CSDD Global Investigative Site Landscape Project 2025;
N=1,154

Tufts Center for the Study of Drug Development
TUFTS UNIVERSITY

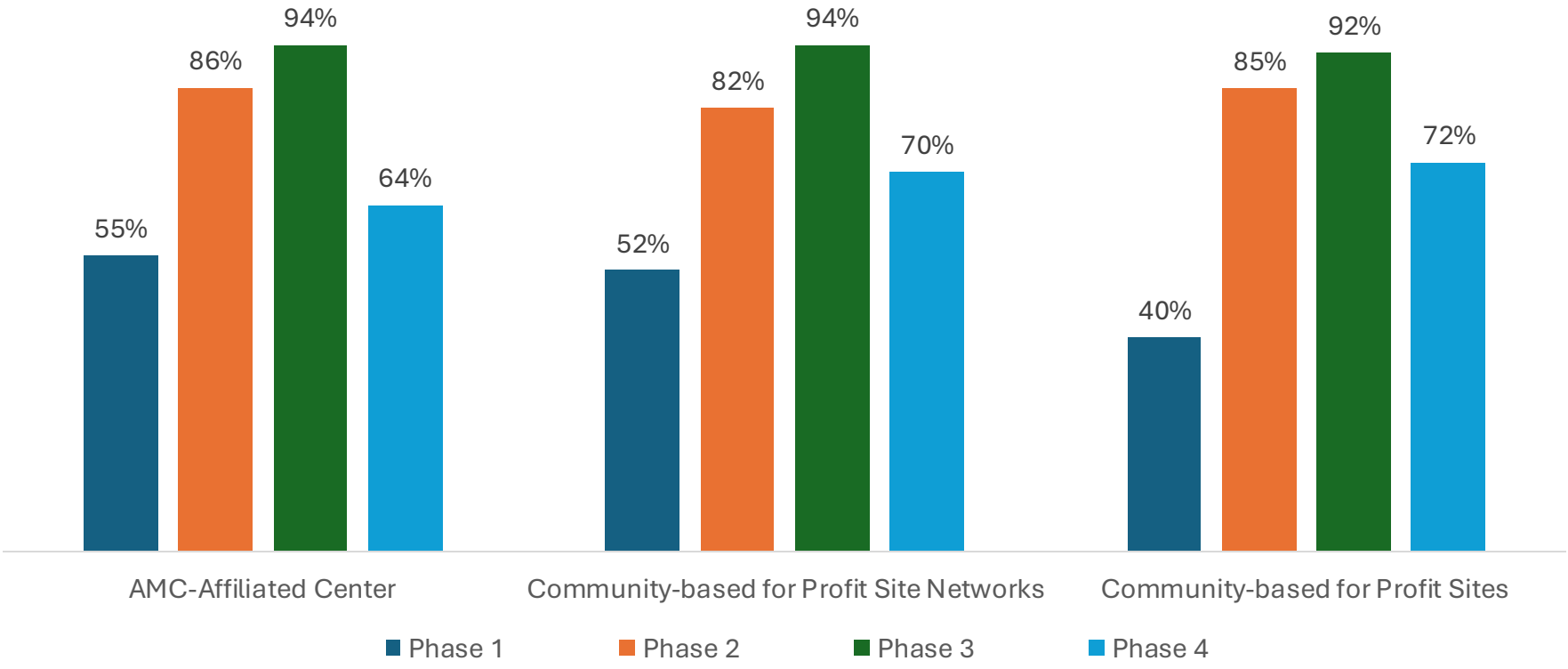
Funding Sources



Source: Tufts CSDD Global Investigative Site Landscape Project 2025;
N=1,154

Tufts Center for the Study of Drug Development
TUFTS UNIVERSITY

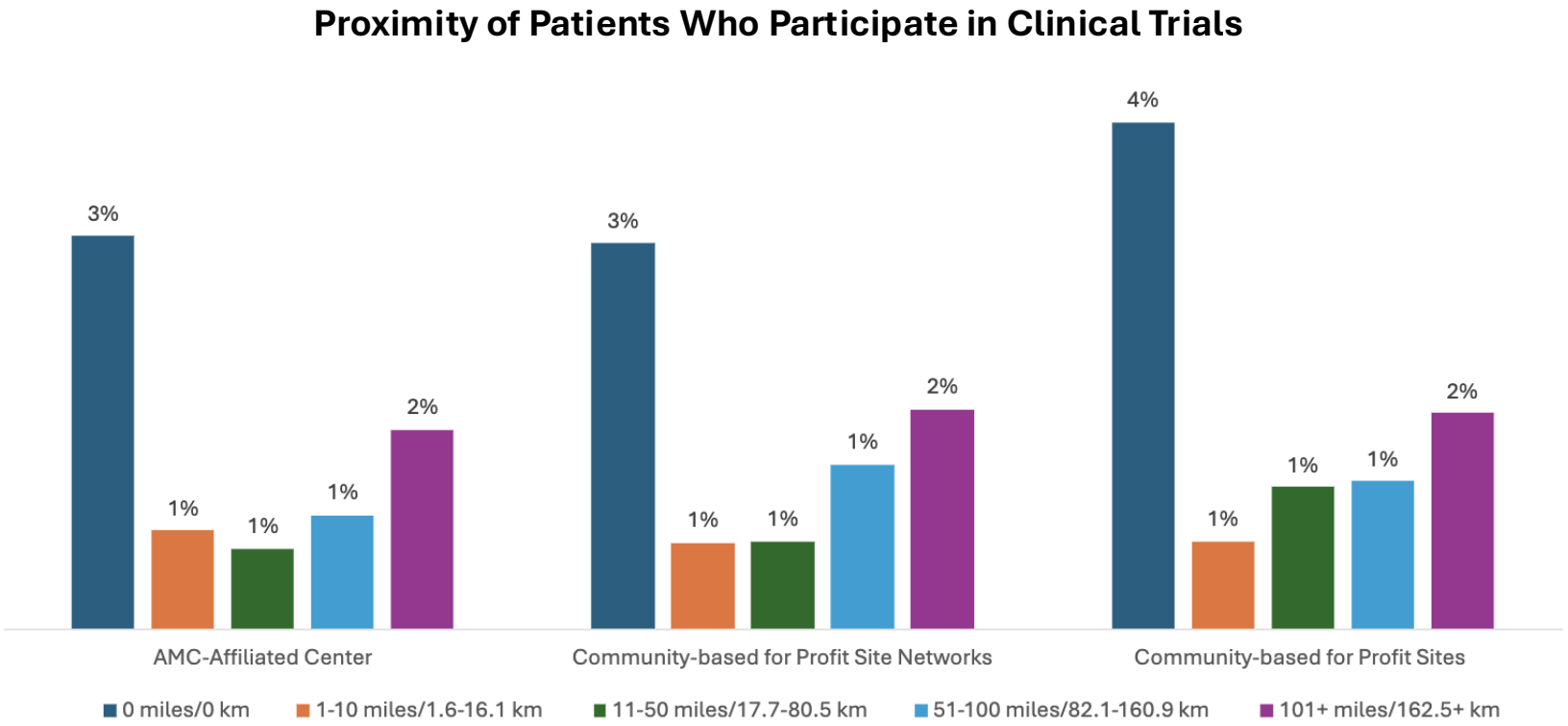
Study Conduct Phase: Site Type



Source: Tufts CSDD Global Investigative Site Landscape Project 2025;

Tufts Center for the Study of Drug Development
TUFTS UNIVERSITY

Proximity of Patient Population

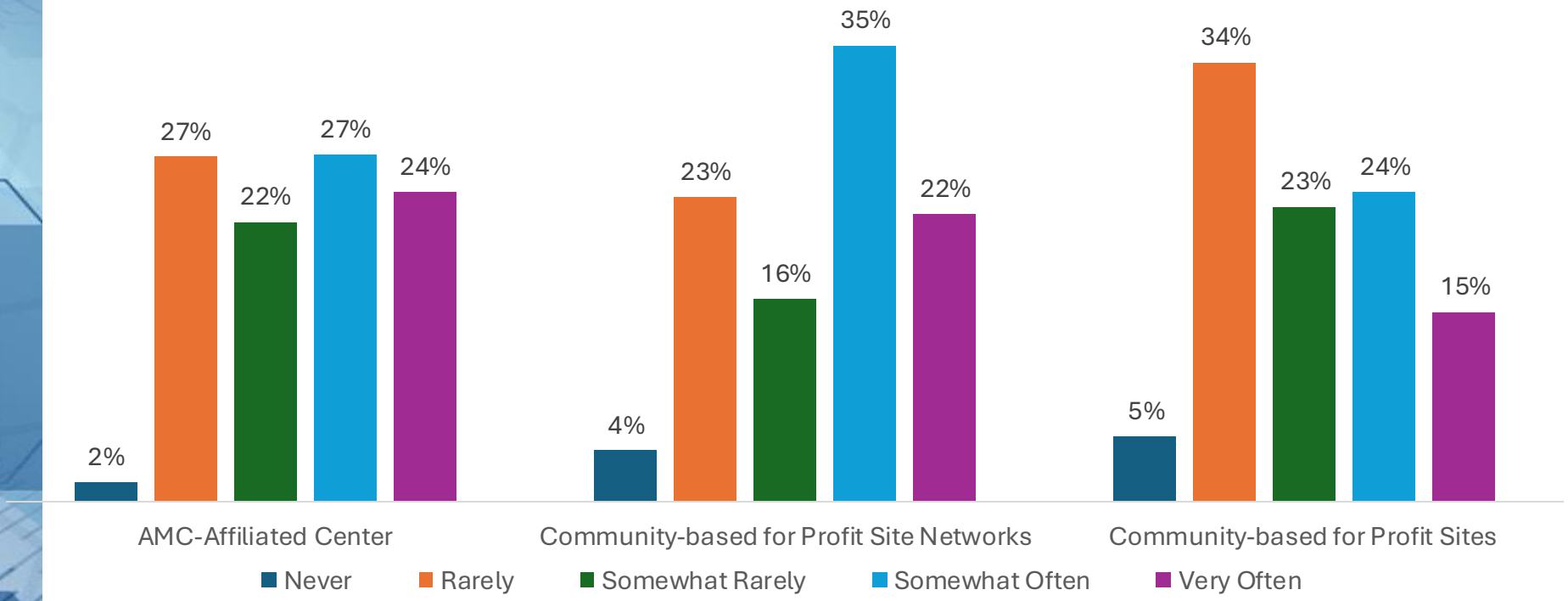


Note: 0 miles / 0 km = patients participate at their home

Source: Tufts CSDD Global Investigative Site Landscape Project 2025; N=1,154

Tufts Center for the Study of Drug Development
TUFTS UNIVERSITY

Public Transportation Availability

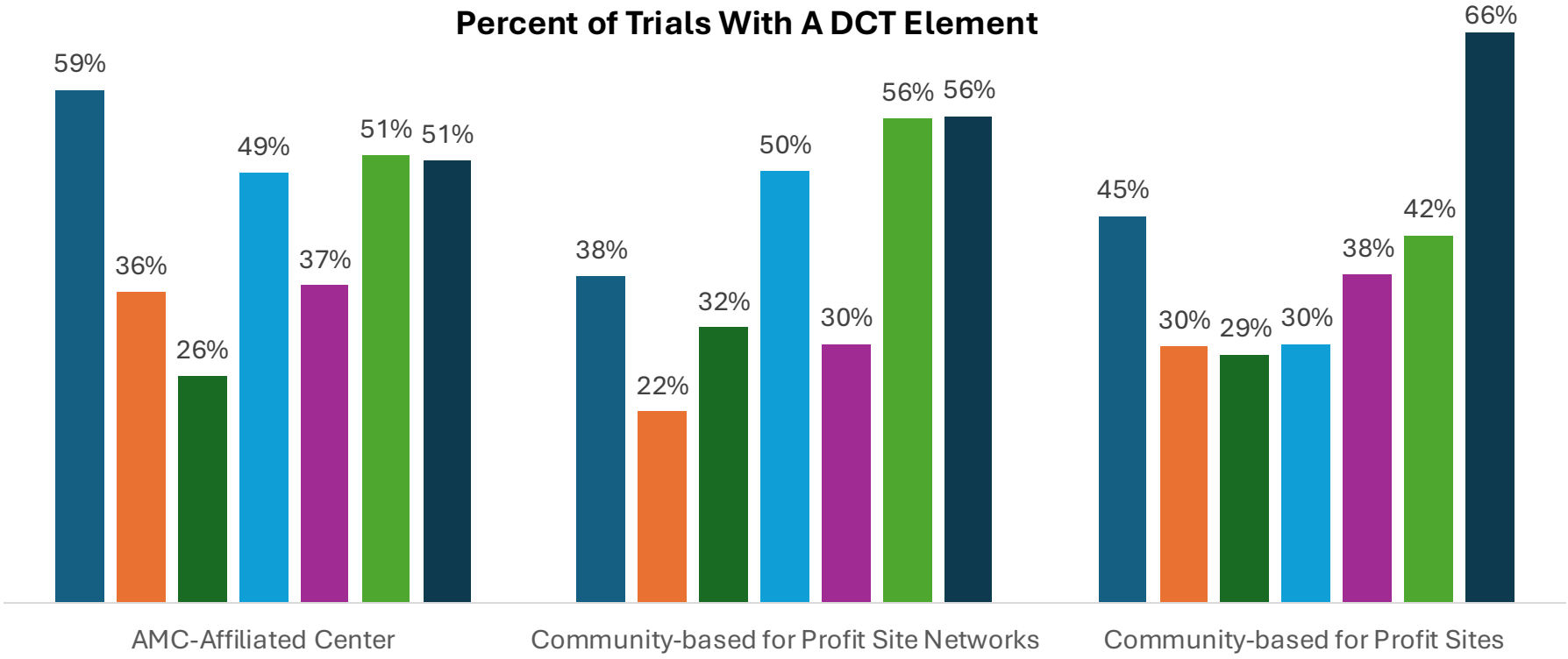


Note: Never = public transportation is not available to the site

Source: Tufts CSDD Global Investigative Site Landscape Project 2025; N=1,154

Tufts Center for the Study of Drug Development
TUFTS UNIVERSITY

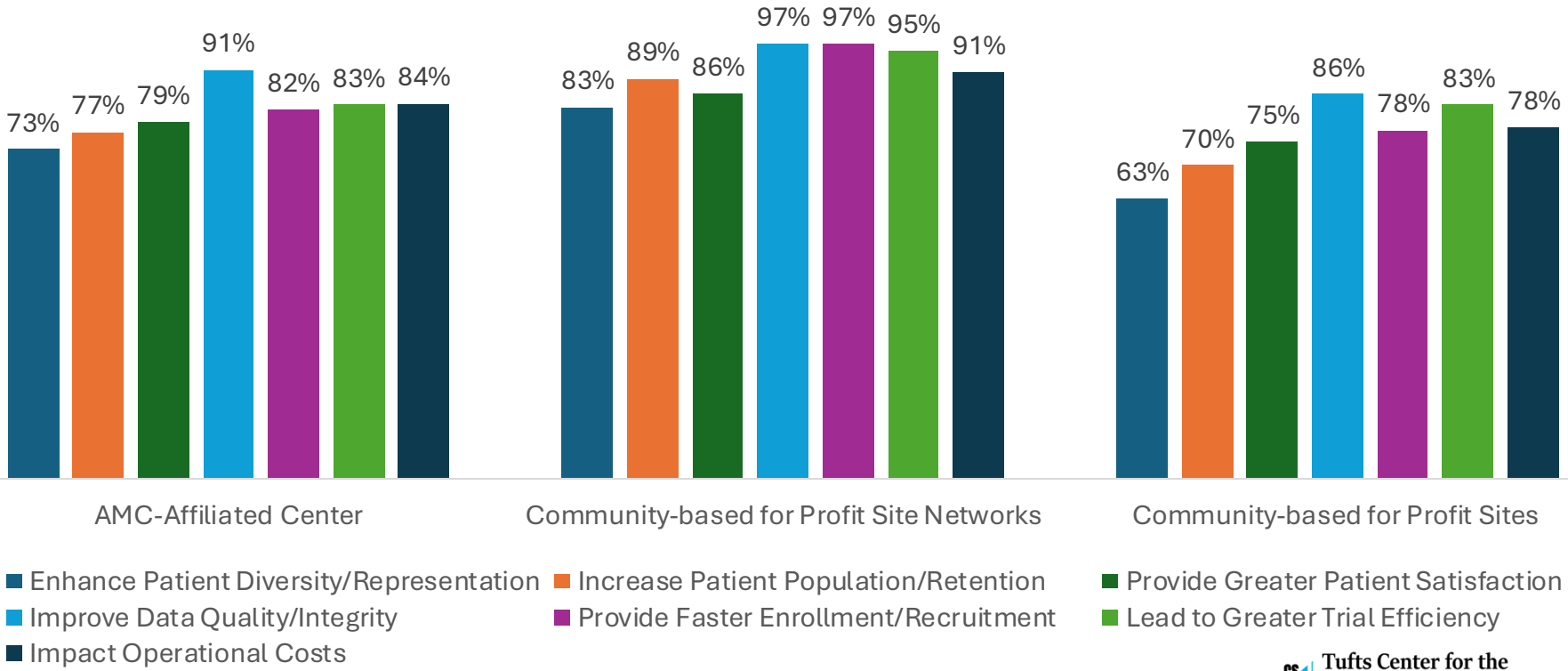
Decentralized Clinical Trial Use: Site Type



Source: Tufts CSDD Global Investigative Site Landscape Project 2025;
N=1,154

Tufts Center for the Study of Drug Development
TUFTS UNIVERSITY

Expected Impact of Technology: Site Type



Source: Tufts CSDD Global Investigative Site Landscape Project 2025; N=1,154

Tufts Center for the Study of Drug Development
TUFTS UNIVERSITY

Top 5 Challenges

Top Challenges	AMC-Affiliated Centers	Community-based for Profit Site Networks	Community-based for Profit Sites
CRO Communication and Relationship	14%	20%	17%
Protocol Complexity	21%	18%	25%
Patient Access and Recruitment	18%	25%	25%
Increased Pressure to make a Profit	12%	22%	16%
Staff Turnover	18%	16%	17%

Source: Tufts CSDD Global Investigative Site Landscape Project 2025;
N=1,154

Tufts Center for the Study of Drug Development
TUFTS UNIVERSITY

Building Relationships With Communities

Creating Convenience and Accessibility For All

Meeting the Patients Where They Are Located

Mutual Trust and Transparency are Central to Community Relationships

Sustainability is Building Relationships; Commitment to Time

Offering Options; “Not One Size Fits All!”

Engagement Approaches with Community Partners

Source: Tufts CSDD

Closing Remarks

- Market pressures are driving the industry to seek solutions that enhance operational efficiency, accessibility, and convenience for both sites and patients.

- In response, new site execution models are emerging to manage complex protocols more effectively and expand patient access by offering diverse participation options.

- Investors are supporting the growth and infrastructure of evolving site models.

- As the global site landscape evolves—with potential consolidation, larger SMOs and site networks, AMCs, and dedicated individual sites—sponsor-CRO interactions may shift based on the site model managing the trial.

- The adoption of technology solutions and DCT components is increasing, with evidence suggesting a shift toward fit-for-purpose implementation, customized to patient needs and site capabilities.

Thank you

Joan A. Chambers
Senior Consultant
Joan.chambers@tufts.edu
Joan Chambers | LinkedIn

Tufts Center for the Study of Drug Development
TUFTS UNIVERSITY

Break

Reconvene at 12:20pm EDT to enter breakout groups

Watchtower

CTTI

CLINICAL TRIALS **TRANSFORMATION** INITIATIVE

@CTTI_Trials

THANK YOU

www.ctti-clinicaltrials.org