CLINICAL TRIALS TRANSFORMATION INITIATIVE

January 15, 2021

How CTTI & the Clinical Trials Community Have Risen to Meet the Challenge of COVID-19

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Introduction to CTTI

CLINICAL TRIALS **TRANSFORMATION** INITIATIVE

Multi-stakeholder,
public-private partnership
co-founded by Duke University & FDA

Participation of 500+ more orgs and
± 80 member organizations

MISSION: To develop and drive adoption of practices that will increase the quality and efficiency of clinical trials

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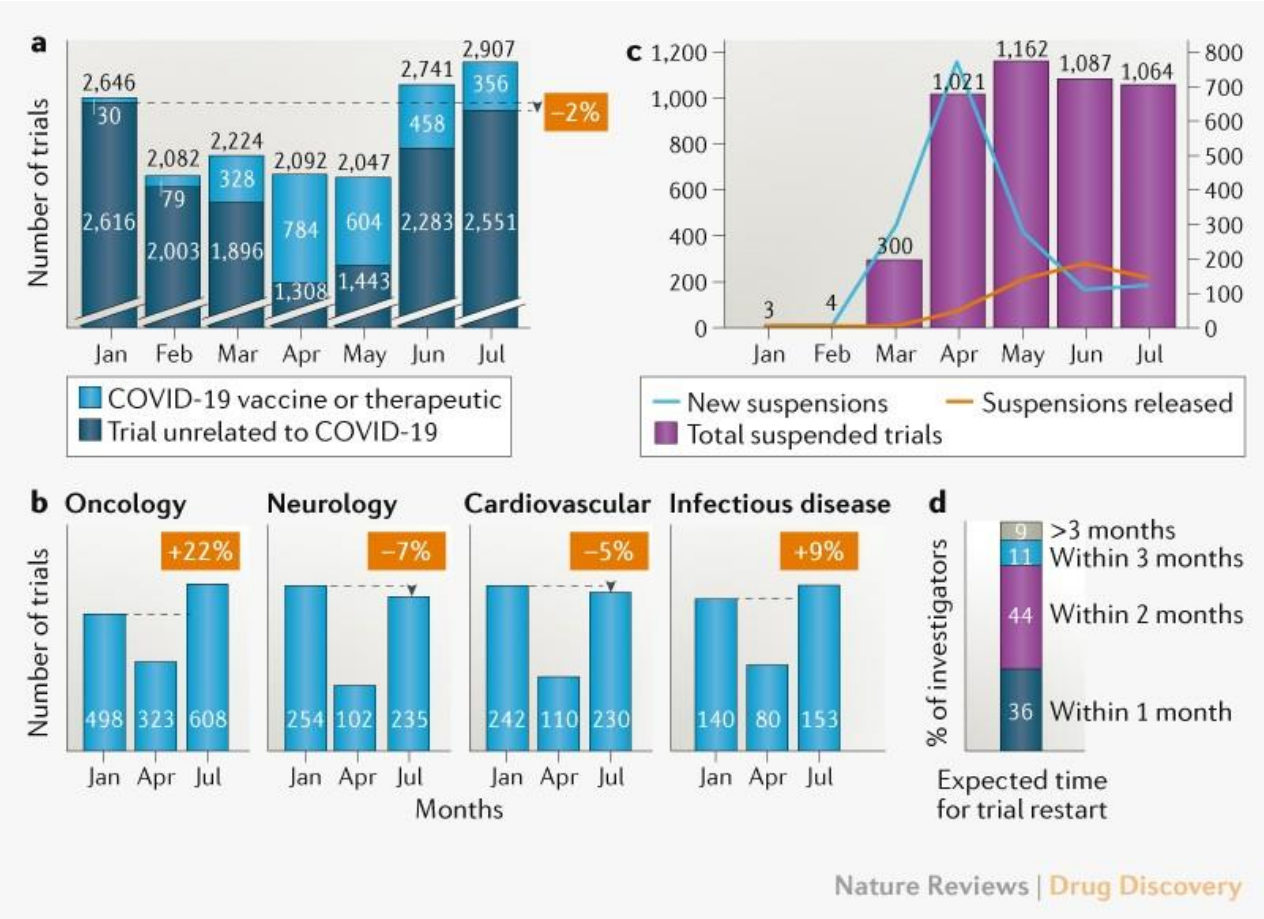
Global Clinical Trial Activity (Sep 2020)



Resumption of global clinical trial activity. **a** | New trial starts recorded in ClinicalTrials.gov, including industry, government and investigator-sponsored trials. **b** | New trial starts in four therapeutic areas with the highest trial volume. **c** | Trials suspended in ClinicalTrials.gov explicitly citing COVID-19. **d** | 245 clinical trial investigators were surveyed on expectation of timing to trial restart between 8–18 May 2020. The countries most represented were the US (104), UK (33), Italy (19), Germany (17), Spain (16), France (12).

https://doi.org/10.1038/d41573-020-00150-9

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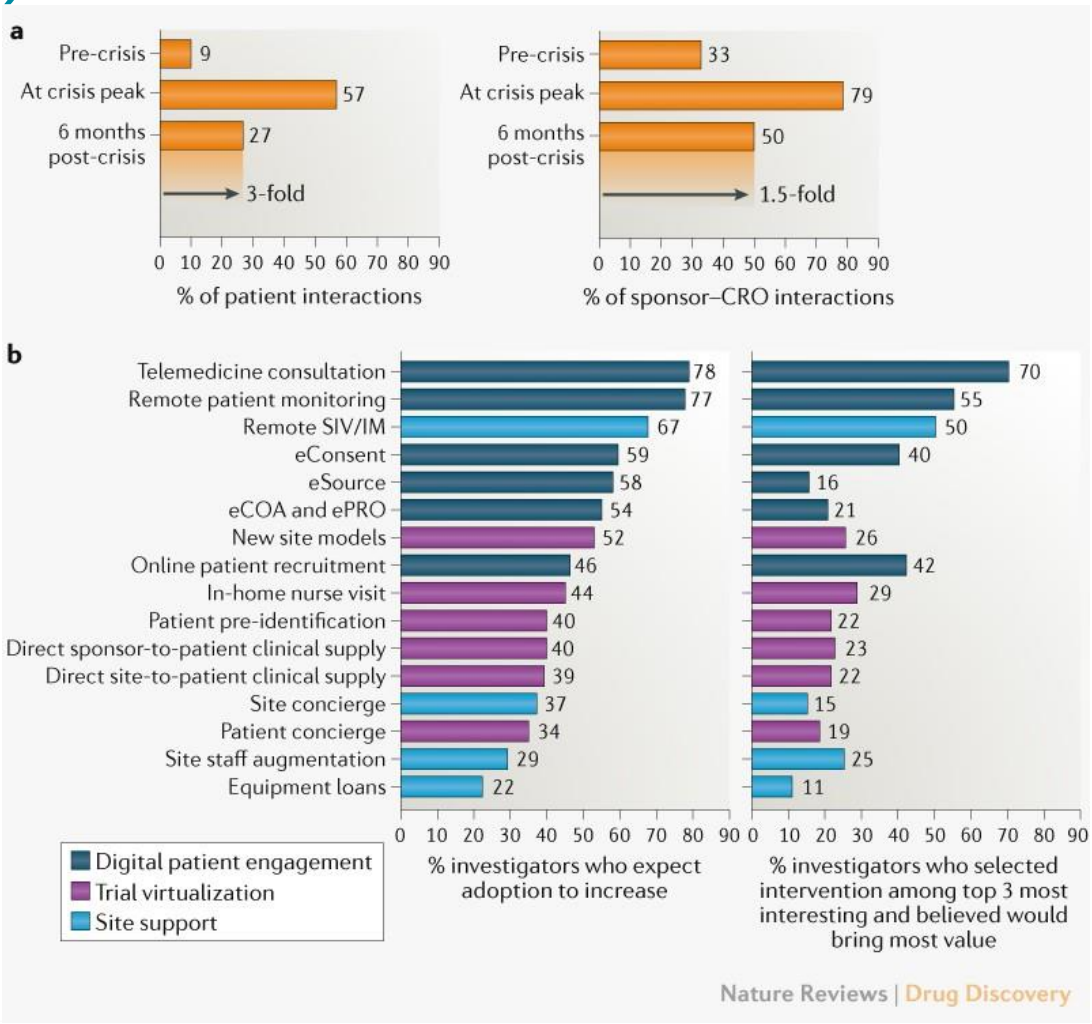
Remote Engagement & Trial Digitization

(Sep 2020)



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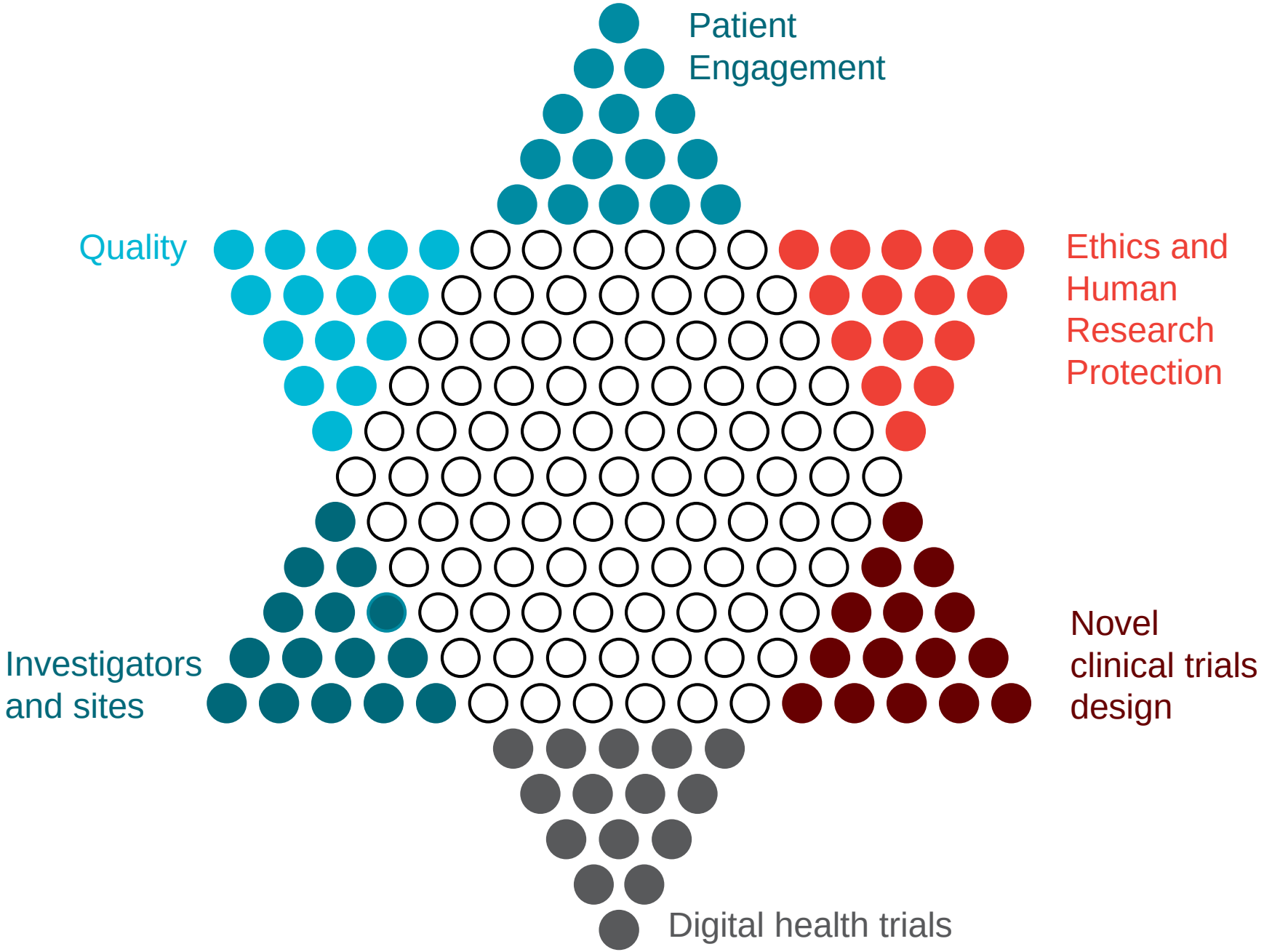
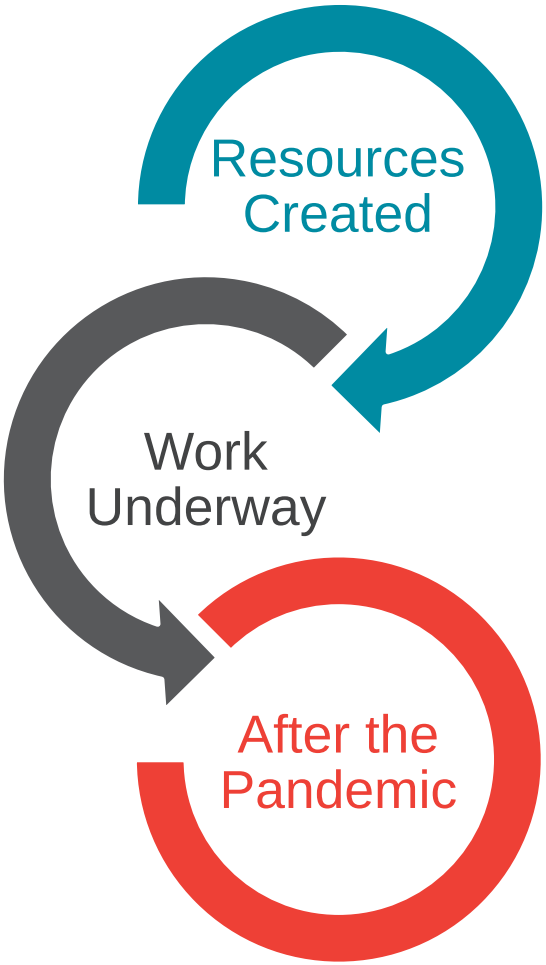

Patient Engagement
Quality
Ethics and Human Research Protection
Investigators and sites
Novel clinical trials design
Digital health trials

CTTI's COVID-19 Work

Overview of COVID-19 Activities



Best Practices: Ongoing Trials

- Conduct of Ongoing Trials in COVID
- Switching to Remote & Virtual Visits

Best Practices: COVID-19 Trials

- Daily ClinicalTrials.gov download
- Designing High-Quality Trials
- Engaging Minority Patients

- Master Protocol Summit
- Lessons learned relative to transforming trials
- COVID-19 treatment trial report

- Analysis of clinical trial ecosystem changes
- Maintaining the transformation

https://www.ctti-clinicaltrials.org/projects/clinical-trials-issues-related-covid-19

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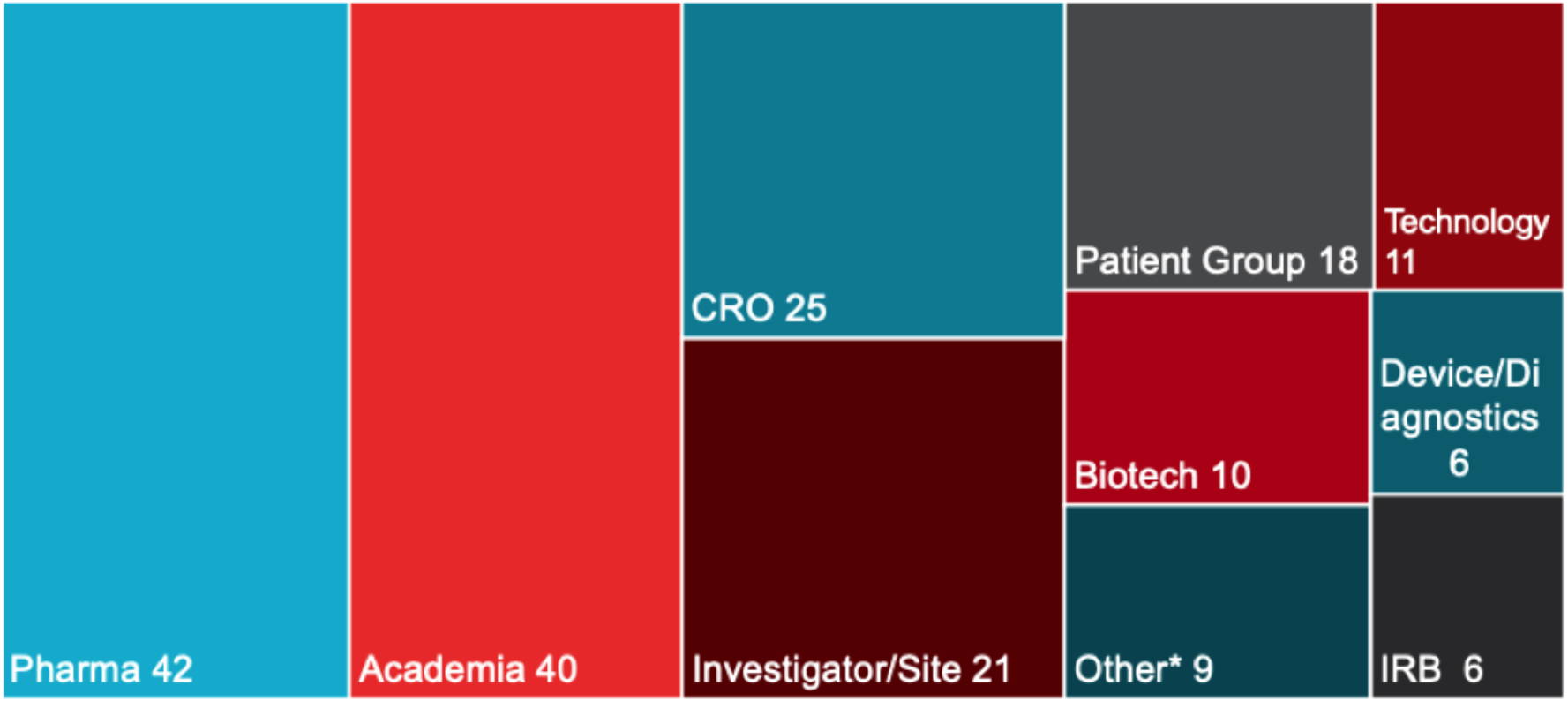
Collected Experiences & Best Practices

- Many informal discussions
- Surveys (N=188)



Adjusting & Adapting: Clinical Trials Conduct during the Pandemic

Best Practices for Clinical Trials Conduct during the Pandemic

1	Keep Participants Informed
2	Perform Ongoing Risk-Benefit Assessment
3	Communicate with IRB/IEC and Regulatory Authorities
4	Adjust New Study Starts and Enrollment Based on Current Risks
5	Pivot to Remote Study Visits
6	Switch to Remote Monitoring
7	Be Flexible
8	Document Everything with COVID-19 Tag

Switching to Remote/Virtual Visits

Site

Think ahead & create a plan

Test run the telehealth platforms

Be flexible

Maintain clear & on-going communication

Industry

Evaluate which assessments can be done remotely

Use mobile HCPs & Local Labs (match to assessments)

Follow regulations: privacy/OCR, local, Ethics/IRB

Be respectful of sites: this is not their only priority

Run a stats analysis to determine validity of remote data

Tech

Deploy privacy compliant tech platforms

Train pts/caregivers & sites on platform

Create an appropriate environment

Know how to handle system failures

As conveyed by 50% of respondents

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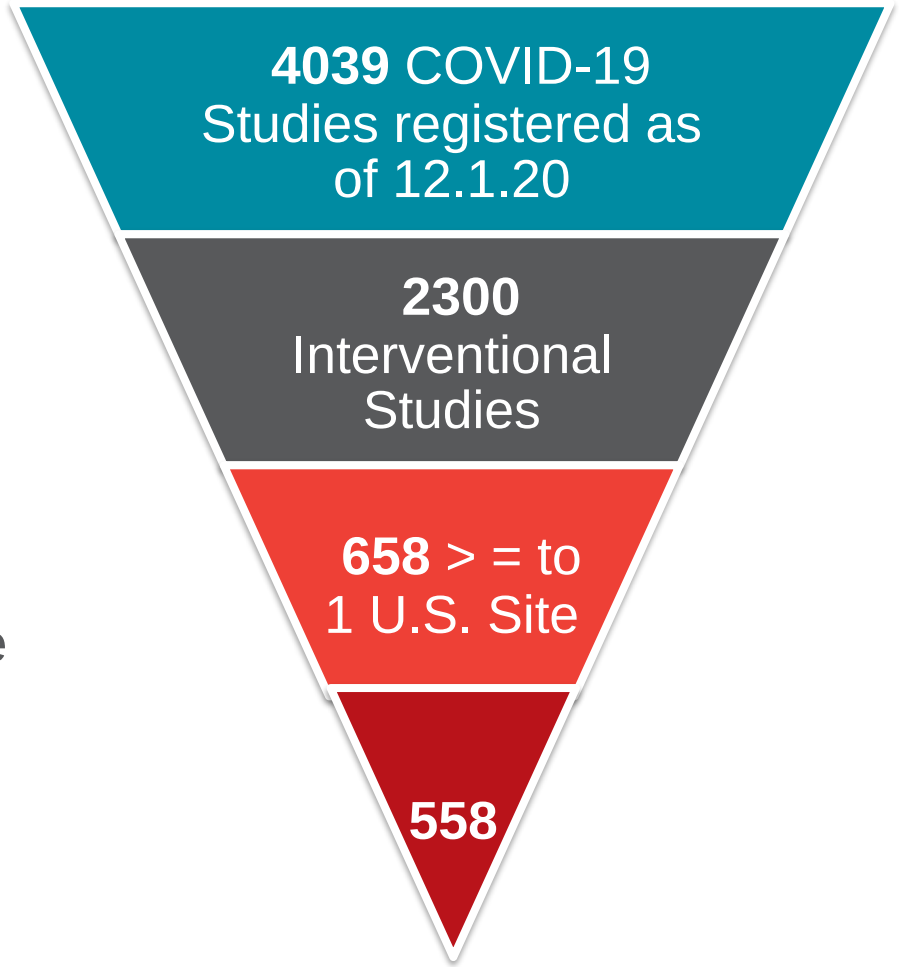
Designing & Running COVID-19 Treatment Trials

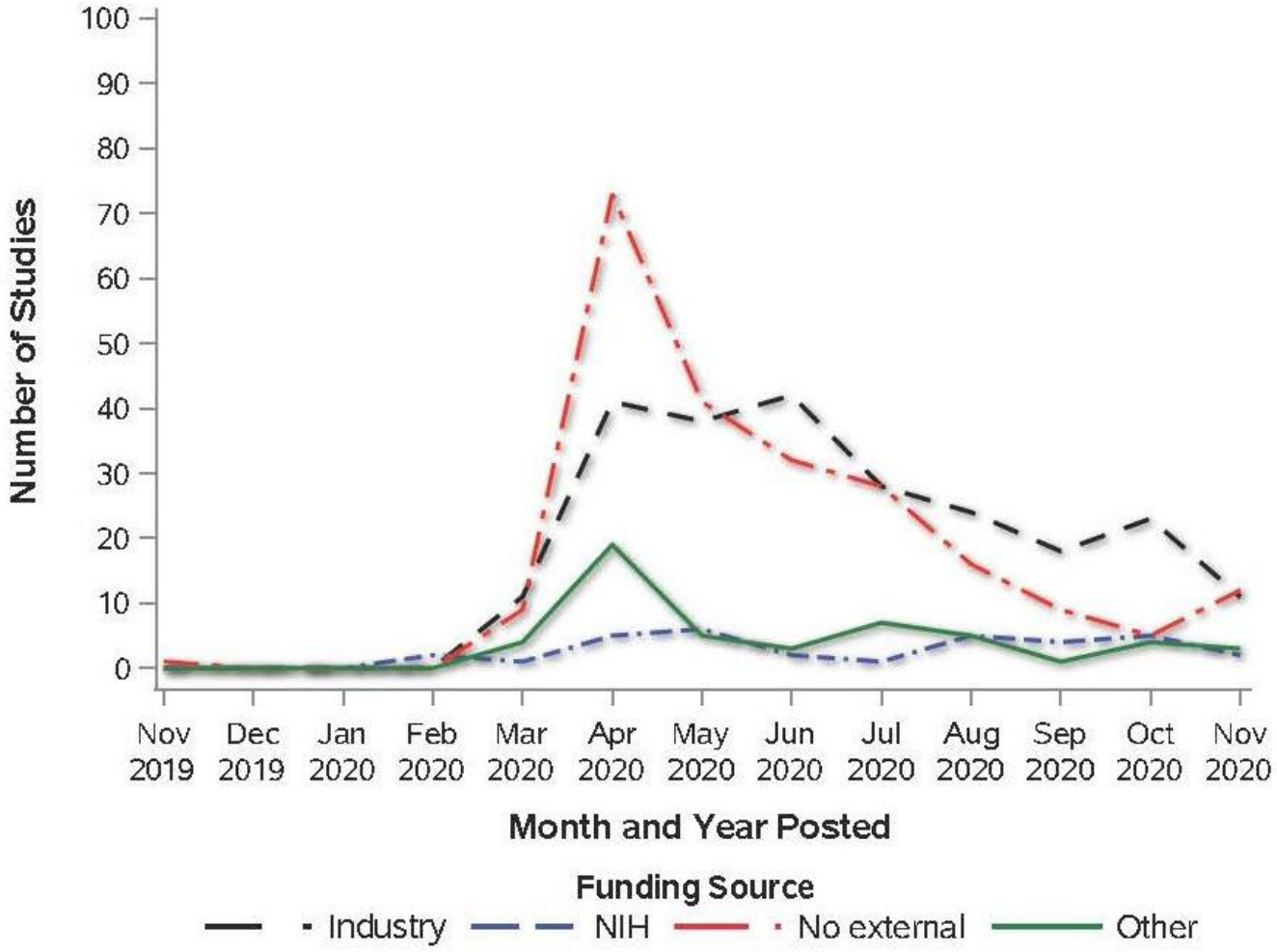
> “Trials must be done during the pandemic if we’re going to make progress. This comes down fundamentally to meticulous planning, quality by design, integrating data collection efforts into the ordinary work flow & determining what constitutes an objective for future trials.”
>
> - Janet Woodcock, FDA, CDER

State of COVID-19 Clinical Trials

- Created Daily COVID-19 Related Clinical Studies Spreadsheet - allows users explore trials in a spreadsheet format
- Analyzing U.S. COVID-19 Treatment or Prevention Clinical Trials
- Using the database for Aggregate Analysis of ClinicalTrials.gov (AACT) (https://aact.ctti-clinicaltrials.org/).



U.S. COVID-19 Prevention or Treatment Trials on ClinicalTrials.gov, by Funder Type



Adapted from graph originally reported at https://califf001.medium.com/complete-rapid-reporting-of-clinical-trials-a-necessary-component-of-the-pandemic-response-aa158eb1a1cb

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Duplication & Many Single Centers

Intervention	# of Studies, % US studies	% Multisite	Median # of sites (Q1, Q3)	No external funder, n(%)
Hydroxychloroquine	50 (9%)	22/50 (44.0%)	**1 (1, 4)**	31/50 (62.0%)
Convalescent plasma	43 (7.7%)	18/43 (41.9%)	**1 (1, 4)**	34/43 (79.1%)
Remdesivir	19 (3.4%)	17/19 (89.5%)	15 (10, 64)	1/19 (5.3%)
Azithromycin	19 (3.4%)	9/19 (47.4%)	**1 (1, 4)**	11/19 (57.9%)
Tocilizumab	12 (2.2%)	7/12 (58.3%)	4 (1, 64)	5/12 (41.7%)

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Best Practices for Designing & Running COVID-19 Treatment Trials

1	Use Large Randomized Clinical Trials (Master Protocols)
2	Include Racial & Ethnic Minorities
3	Quality Does Not Slow You Down
4	Focus on What Matters
5	Communicate, Collaborate, & Plan

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Diversity Best Practices

Site

Build trust

Partner with community stakeholders

Provide information

Hire diverse staff & raise awareness

Industry

Partner with racial and ethnic minority communities early

Develop accessible site networks

Commitment & reinforcement from executive leadership

Example: Using Master Protocols
RECOVERY trial

Differentiating moderate benefits from no benefit/harm requires:

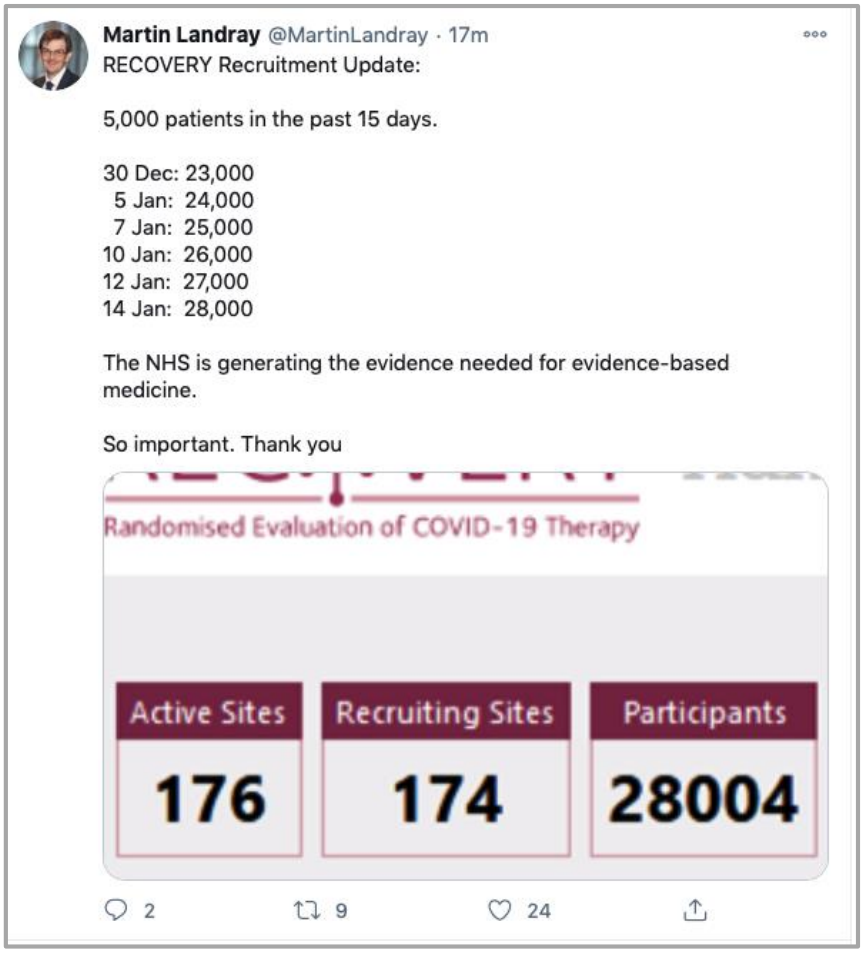
- Randomization
- Comparison vs. control group not receiving the drug
- Large numbers

Three key principles:

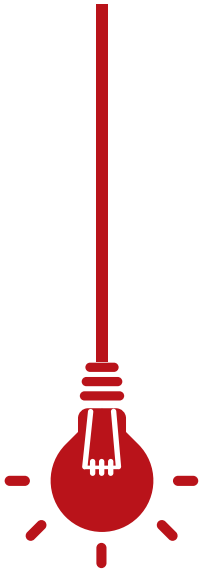
- Obtain robust results that can rapidly impact care
- Consider well-being of patients
- Consider well-being of staff

Focus only on what matters (Quality by Design)

- Leave orthodoxy, habits, & traditional practices behind
- Communicate & collaborate
- Transparency



Strategies to Successfully Start Up Sites

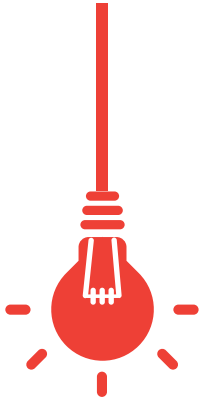


CONTRACTING

Being flexible

Take it or leave it

Leverage existing contracts

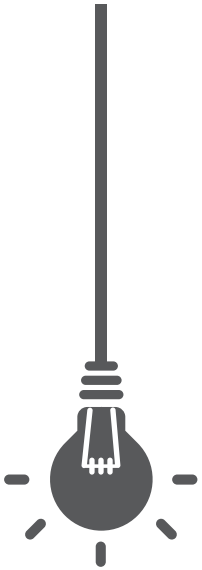


STAFFING

Reallocate

Supplement

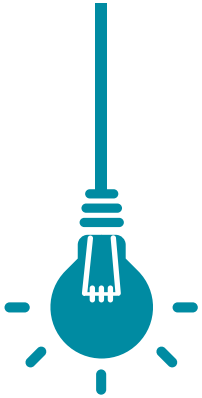
Training



IRB

Expedited

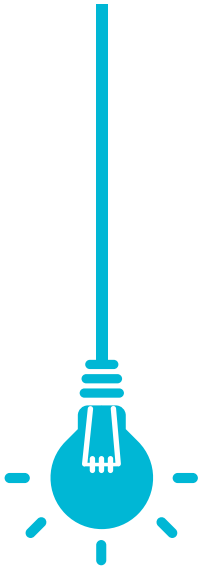
Select sites based on timely review



FEASIBILITY

Streamline Protocol

Single point of contact site management



TRIAL BUDGET

Increase Budgets

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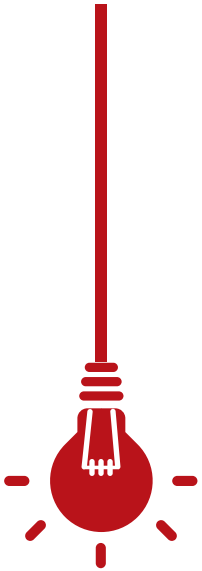
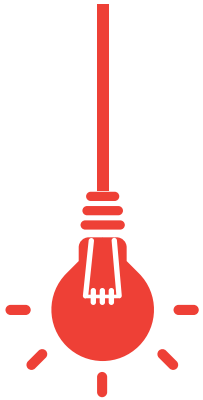
Strategies to Successfully Enroll Participants



SITES

Communication

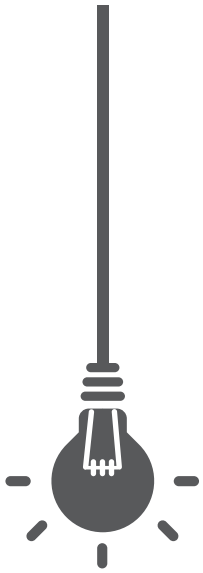
New sites
Domestically
Non-US



PROTOCOL DESIGN

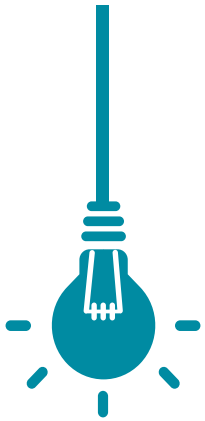
Amendments

Streamline protocol



CONSENT

Simplify

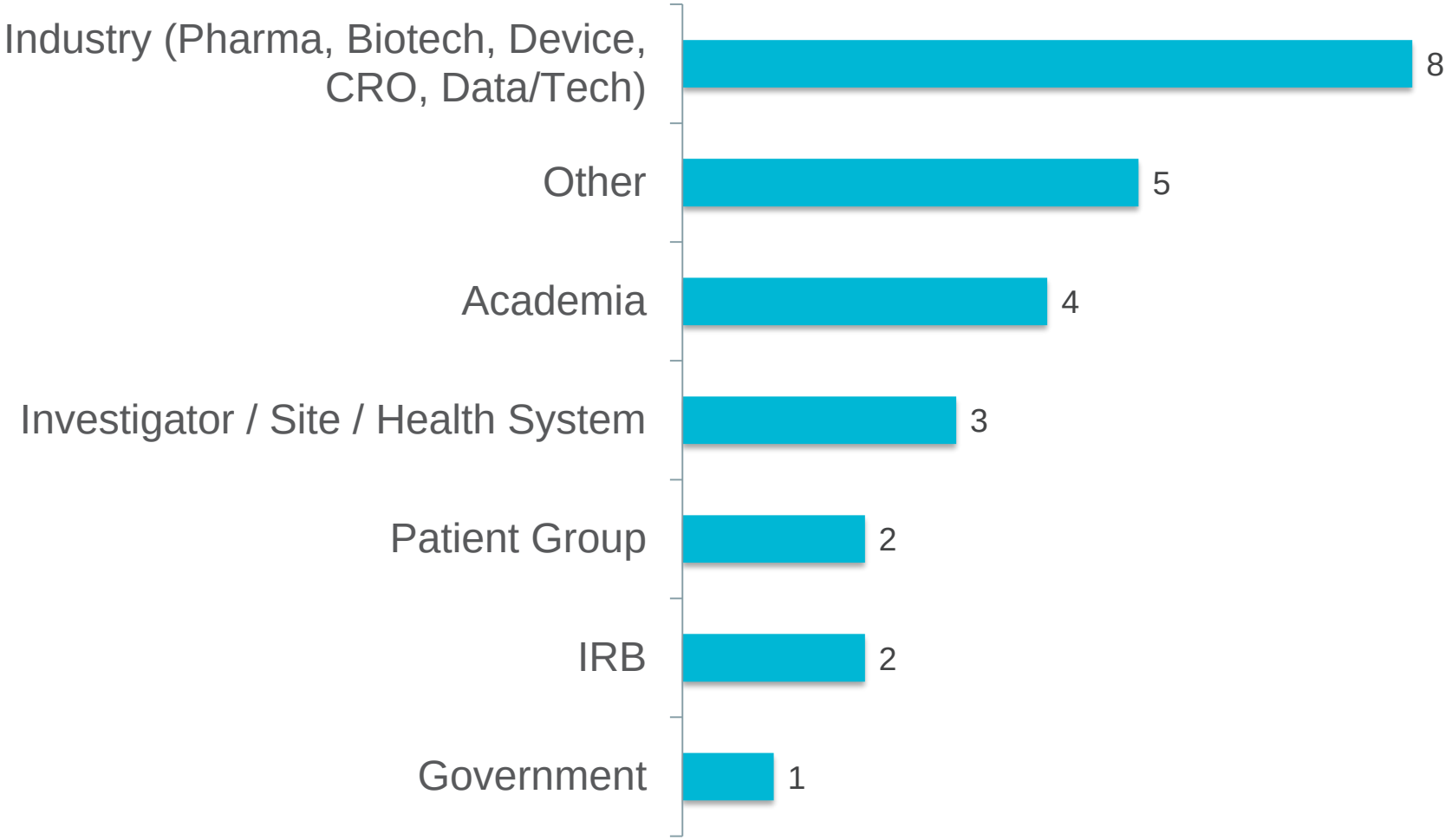


CO-ENROLLMENT

Transformative Opportunities for Clinical Trials Based on Experiences during COVID-19*

*Survey responses from 27 CTTI member organizations

Survey Participants



Findings: Research Site Adaptations

Change in how trials are designed/conducted	Lessons learned from change
Temperature and symptom screening is performed at each location prior to building entrance	Screening is effective
COVID-19 screening of all patients prior to study entry or any treatment cycle start	Not every change was funded via site budget

Findings: Digital Health & Decentralized Trials

Change	Selected Lessons Learned
Switched to e-consent	Need to be sure of identity Compliance is better, it is recorded
Protocol Simplification	Preplanning is beneficial
Virtual & Remote Visits	Demonstrated feasibility of telemedicine trials Right incentives were in place Facilitate research, more widespread participation
Supplement (Local Labs & HealthCare Providers)	Participants could stay locally Some labs/imaging were easier set up than others Logical extension of where we were going
Investigational Medical Product	IP needs to be appropriate for shipping & self administration Geographic differences drive site receptiveness
Monitoring	Increased appreciation of what could be done off-site Setting up pro-actively would help

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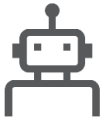
Conclusion

Real momentum towards DHT & decentralized clinical trials

60% of respondents express changes will continued to be implemented in trials going forward



About 60% of those implementing changes going forward are evaluating the changes they are implementing

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Closing

CTTI COVID-19 Resources

- For Ongoing Trials
  - Playbook of Best Practices
  - Webinar: Conduct of Ongoing Trials in COVID
  - Webinar: Switching to Remote & Virtual Visits
- For COVID-19 Trials
  - Daily ClinicalTrials.gov download
  - Master Protocol Summit
  - Webinar: Designing High-Quality Trials
  - Webinar: Engaging Minority Patients

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Next Steps

- **There's still much more to be done**
  - Applying lessons learned to treatment trials
  - Transitioning to a new norm & making lessons learned "stick"
  - Continue to communicate, collaborate, & evolve

- **Upcoming CTTI efforts:**
  - A call to join Transforming Trials 2030
  - New work on DCT (2.0), diversity, trials in health settings, the State of Clinical Trials & more

THANKS

CLINICAL TRIALS **TRANSFORMATION** INITIATIVE

Stay in touch!

Sign up for CTTI's e-newsletter and follow us to hear more about our ongoing COVID-19 efforts, as well as our Transforming Trials 2030 initiative.

www.ctti-clinicaltrials.org

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