Orientation to the Trial Innovation Network

What is the Trial Innovation Network (TIN) and how can IDeA investigators access TIN services

Dan Hanley PI JHU TIC

Morgantown, West Virginia

November 9, 2023

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Disclosures of Conflict

- Rt-PA in Brain Clot Lysis is a non-approved use IND # 8523
- NIH funds support my salary and staff
- FDA funds, FDA external consultant, FDA applicant
- Pharma
- Device companies
- Professional, patient, NGO, public corporate and NIH boards
- Karen Lane, Nichol McBee, Lindsay Eyzaguirre & Andrew Mould = **BIOS /TIN**

mRCTs at NIH

Some Problems Recognized by External Oversight

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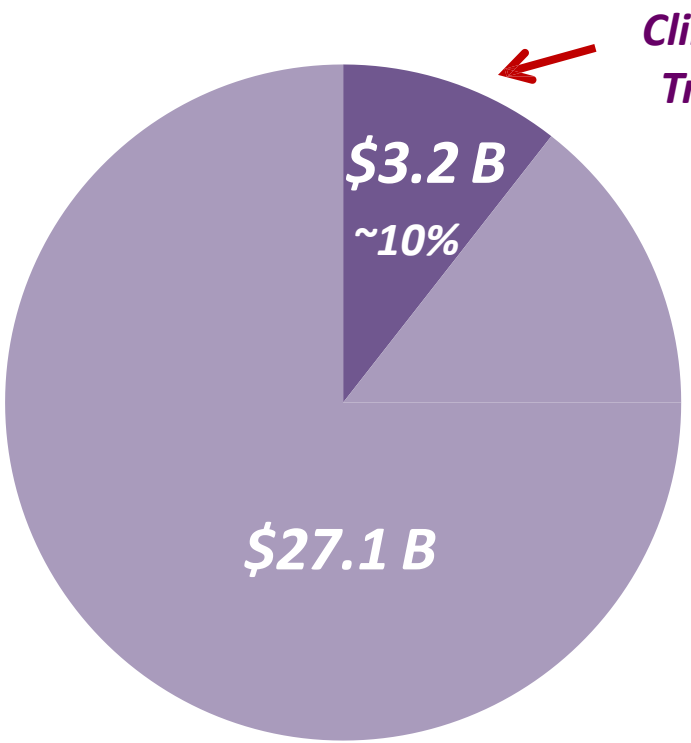
NIH Changes in Multisite Clinical Trials Operations

NIH Budget – FY 2015



NIH tackles clinical trial shortcomings

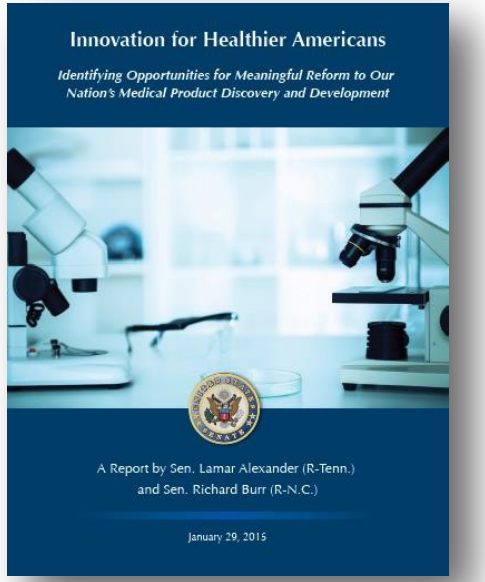
The NIH is developing new tools, and overhauling its clinical trial funding system, to improve the stewardship of NIH-funded clinical trials

GAO

United States Government Accountability Office

Report to Congressional Committees

Additional Data Would Enhance the Stewardship of Clinical Trials across the Agency



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NIH Budget Office; Mullard A. Nature Reviews Drug Disc 2016; GAO Report, 2016; *Innovation for Healthier Americans*, 2015

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VIEWPOINT

Toward a New Era of Trust and Transparency in Clinical Trials

Kathy L. Hudson, PhD
National Institutes of Health, Bethesda, Maryland.

Michael S. Lauer, MD
National Institutes of Health, Bethesda, Maryland.

Francis S. Collins, MD, PhD
National Institutes of Health, Bethesda, Maryland.

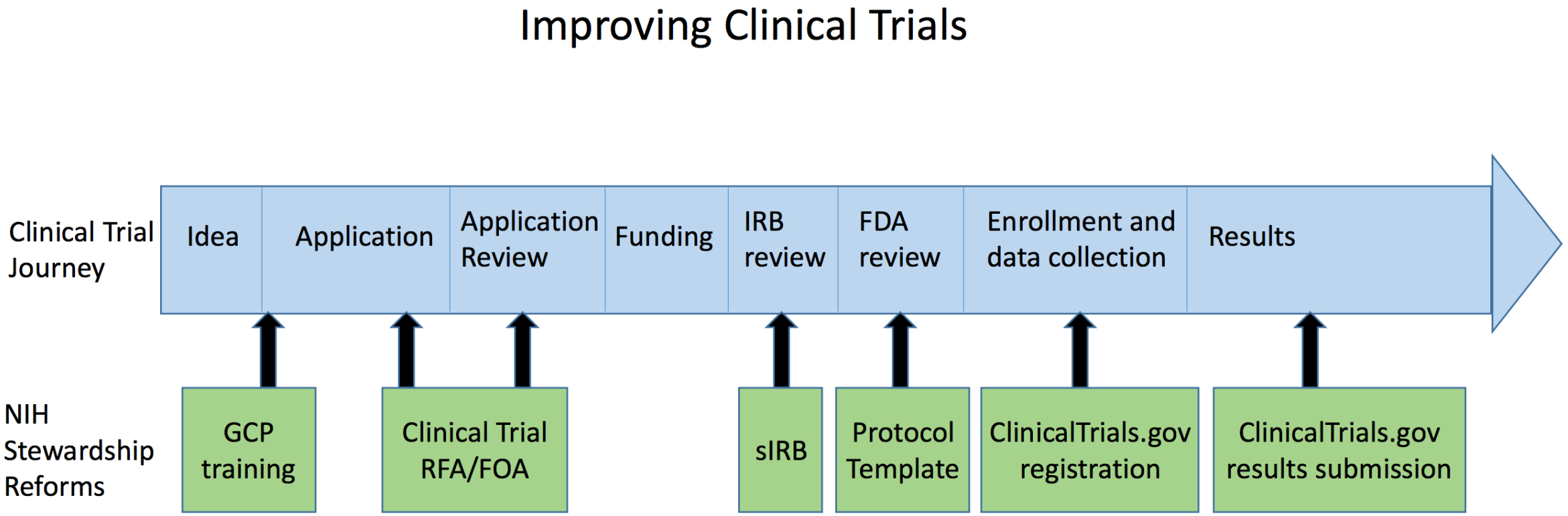
Supplemental content

Clinical trials are the most publicly visible component of the biomedical research enterprise, from the potential human application of novel laboratory findings to the generation of robust evidence about treatments or preventive interventions in routine clinical care. These trials are also the point at which biomedical research most directly engages human participants—dedicated volunteers who trust investigators to uphold the highest standards of scientific rigor and ethical oversight. While clinical trials have evolved and improved over time—producing impressive advances in diagnosis, treatment, and prevention—there are still major challenges. Therefore, fundamental changes are needed to reflect science and society's movement to increase efficiency, accountability, and transparency in clinical research.

As the largest public funder of clinical trials in the United States, currently investing more than $3 billion each year, the National Institutes of Health (NIH) takes its stewardship of the nation's clinical trial enterprise very seriously. The aim is to help ensure that all involved in the clinical trial enterprise have the appropriate knowledge about the design, conduct, monitoring, recording, analysis, and reporting of clinical trials. While GCP training on its own may not be sufficient, it provides a consistent and high-quality standard.

Another important change at the beginning of the clinical trial lifecycle is a new NIH policy that will require all applications for clinical trials to be submitted in response to clinical trial–specific Funding Opportunity Announcements (FOAs). This will mean that applications including one or more clinical trials will no longer be accepted in response to parent funding announcements, which are broad FOAs that allow researchers to submit investigator-initiated applications without specific elements appropriate to describe and evaluate a trial. Under this policy, NIH trial applications will need to contain specific information about protocols and other information necessary for effective peer and program-

2016: NIH Stewardship & "…the new era"



VIEWPOINT

Toward a New Era of Trust and Transparency in Clinical Trials —JAMA 2016;316(13):1353-1354

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mRCTs in the world

A View from the Moon

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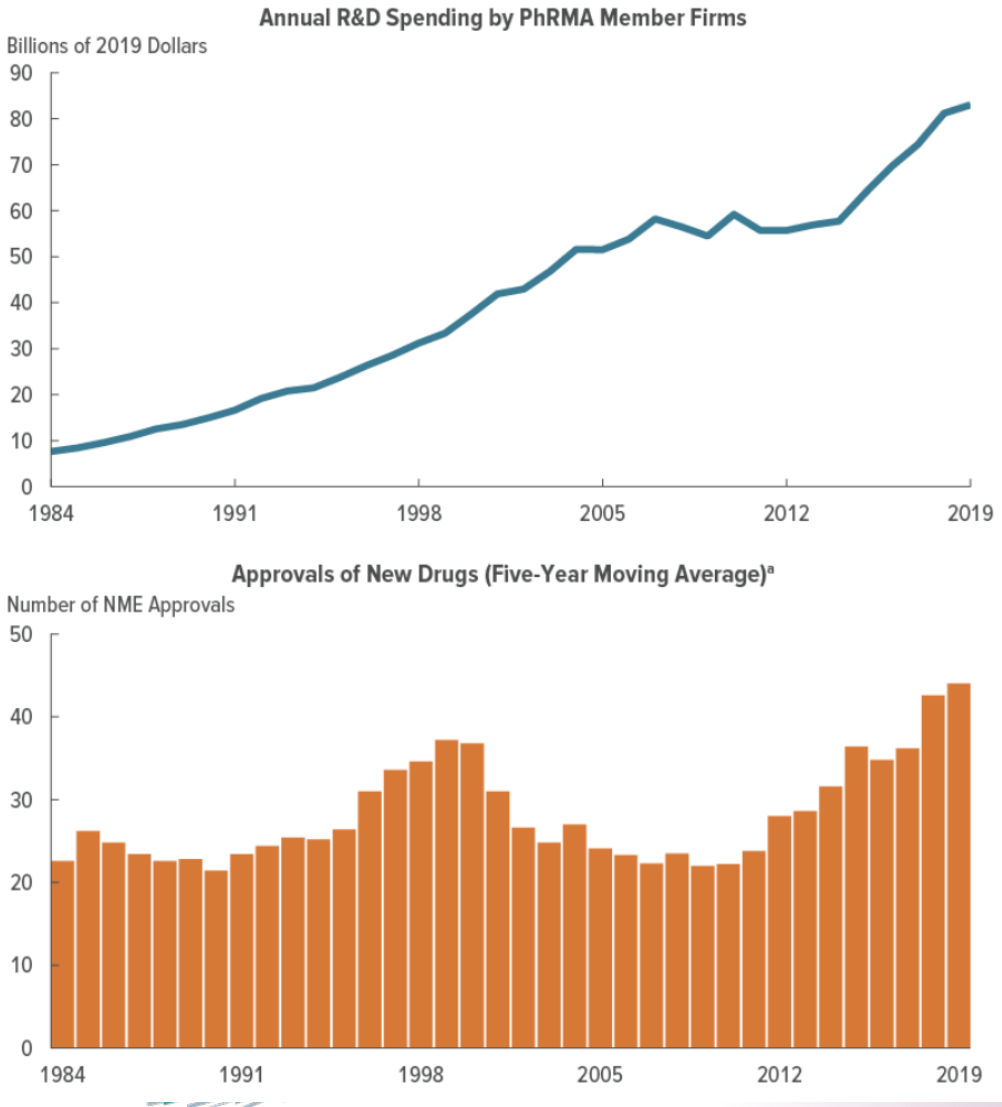
Pharma Spending vs New Drug Approvals

R&D Spending and New Drug Approvals



Sustained increases in pharmaceutical R&D spending do not necessarily lead to rising numbers of new drugs. R&D spending also reflects rising costs of labor (skilled researchers) and capital (laboratory technologies).

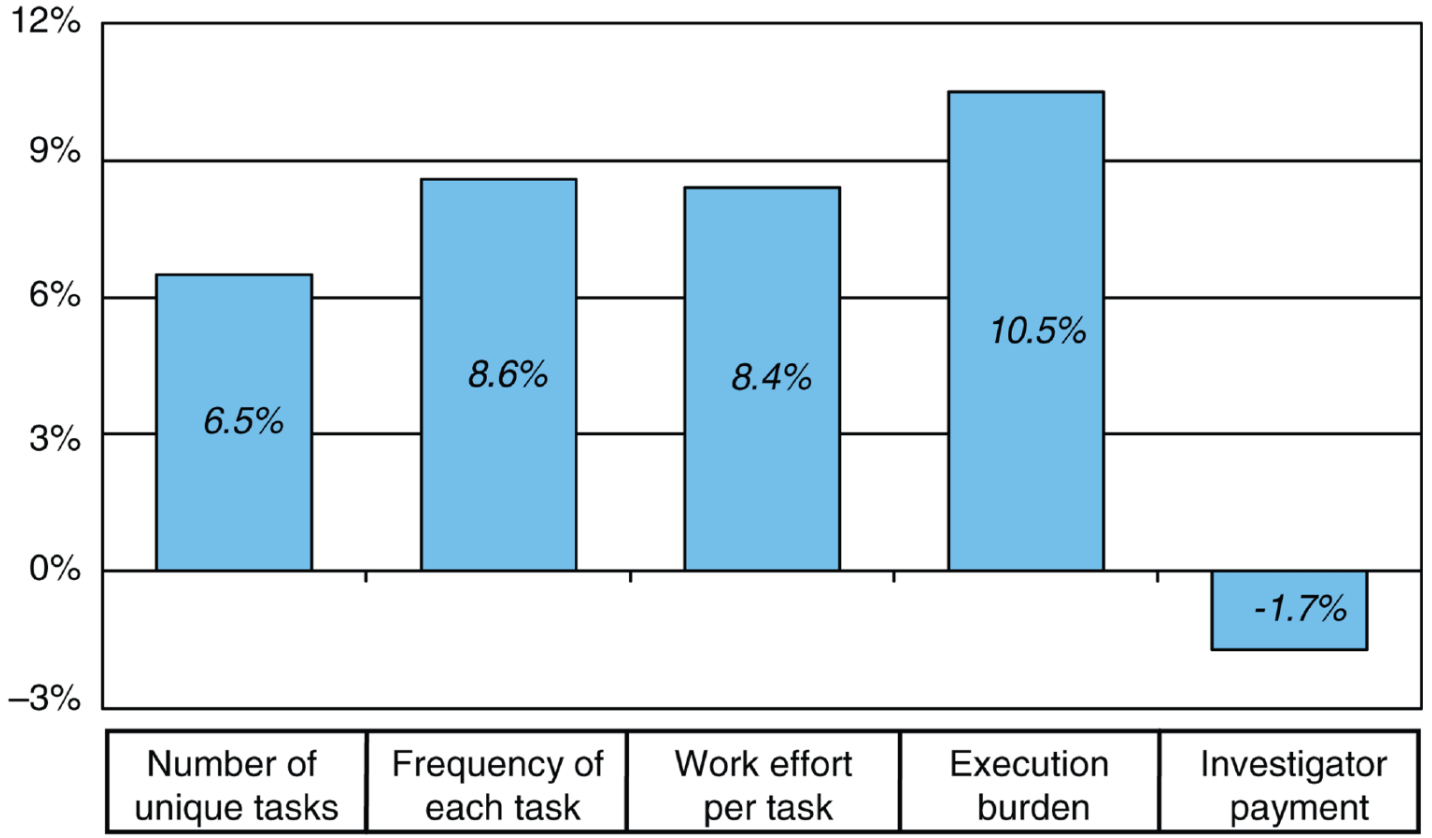
Research and Development in the Pharmaceutical Industry. Congressional Budge Office; 2021. Accessed September 8, 2021. https://www.cbo.gov/publication/57126

2017 Survey of Global Public Attitudes

- 12,427 individuals
  - Mean age 55 years; 59% female; 81.2% white
  - 17.7% had participated in previous clinical research studies
- 84.5% perceived clinical research to be very important to the discovery and development of new treatments
- 59.0% were unable to name a place where studies were conducted
- 90.0% believed that clinical research is generally safe
  - 44.9% reported that clinical trials are rarely discussed with their physicians
  - Clinical trial participation was perceived as inconvenient and burdensome
- 49.0% of previous research participants said clinical trial participation disrupted their daily routine

Anderson A, Borfitz D, Getz K. Global Public Attitudes About Clinical Research and Patient Experiences With Clinical Trials. *JAMA Netw Open.* 2018;1(6):e182969. doi:10.1001/jamanetworkopen.2018.2969

Changes in Design Requirements of Clinical Trials



Kaitin KI. Deconstructing the drug development process: the new face of innovation [published correction appears in Clin Pharmacol Ther. 2011 Jan;89(1):148]. *Clin Pharmacol Ther*. 2010;87(3):356-361. doi:10.1038/clpt.2009.293

Federal Funding for NIH: Fiscal years 1995-2020

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Research and Development in the Pharmaceutical Industry. Congressional Budget Office; 2021. Accessed September 8, 2021. https://www.cbo.gov/publication/57126

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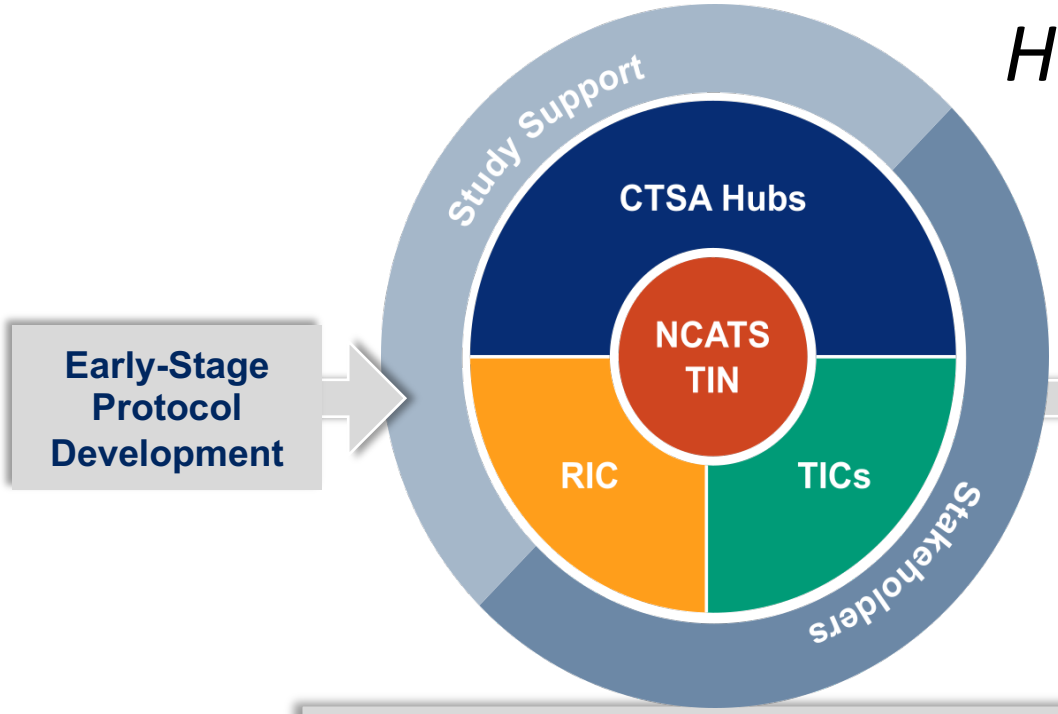
Trial Innovation Network

How It Works



Early-Stage Protocol Development

Robust Clinical Trials

Scientific Questions
NIH Institutes
Other Partners
Operational Questions
NCATS

Operational Performance
Doing Trials Better, Faster, & More Efficiently
Operational Innovation Activities
Testing Novel Clinical Trial Designs, Precise Interventions, Engagement, & Retention

Result
Scientific Evidence to Change Practice
Operational Results
New Operational Methods
Trials on Time & On Budget

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Goals of the 1st Trial Innovation Network (TIN)

- Focus on ***operational innovation***, ***excellence*** and ***collaboration*** and leverages the expertise and resources of the 60+ hubs of the CTSA Program and 30+ affiliates.
- The TIN employs a single IRB system, master contracting agreements, quality by design approaches, and development and utilization of evidence-based strategies for recruitment and patient engagement.
- The TIN pursues better, faster, and more cost-efficient trial execution
- The TIN will be a national laboratory to facilitate evidence-based innovations related to the process of conducting clinical trials.
- 2nd TIN actively seeks broader collaborations with IDeA Net, HBCUs, PCORI, and others.

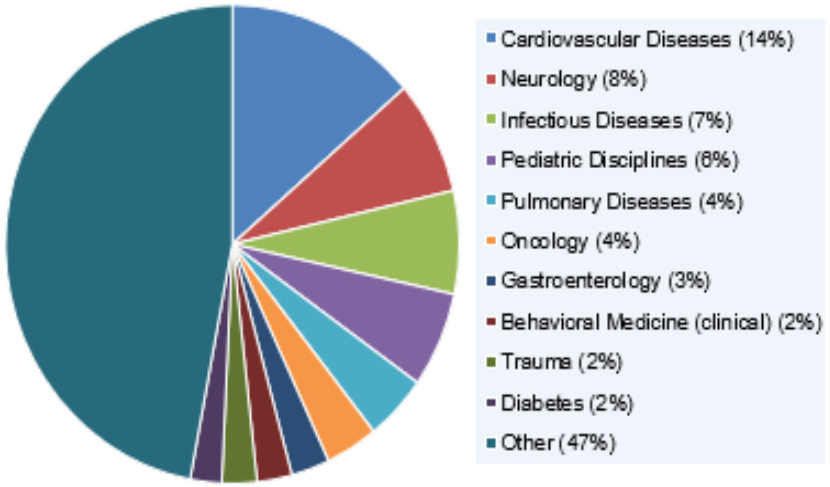
Reporting of the TIN efforts over the last 7 years

NETWORK PROPOSALS

401	76	62 (94%)	31	20
REQUESTED NETWORK SUPPORT	THERAPUETIC AREAS REPRESENTED	NUMBER (%) OF CTSA SUBMITTED PROPOSALS	NUMBER OF NON-CTSA SUBMITTED PROPOSALS	NIH I/Cs ENGAGED

- NHLBI
- NINDS
- NIDDK
- NCATS
- NICHD
- NIA
- NCI
- NIAMS
- NIAID
- NIDCD
- NEI
- NIAAA
- NIMH
- NIDA
- NIDCR
- NIBIB
- NCCIH
- NINR
- NIMHD
- NHGRI

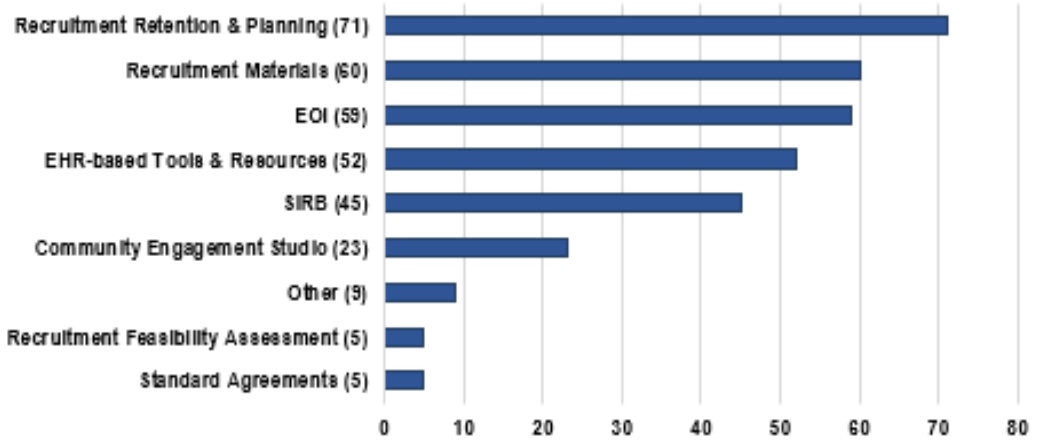
Top 10 Therapeutic Areas Represented (%)



NETWORK SUPPORT

365	83	37
INITIAL CONSULTATIONS	COMPREHENSIVE CONSULTATIONS	FUNDED TRIALS

Types of TIN Support



NETWORK DISSEMINATION

TIN's Publications Across Clinical Trial Lifecycle (n=60)

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21	6	24	3	6
PLANNING & DEVELOPMENT	STARTUP	RECRUITMENT & RETENTION	IMPLEMENTATION	DISSEMINATION

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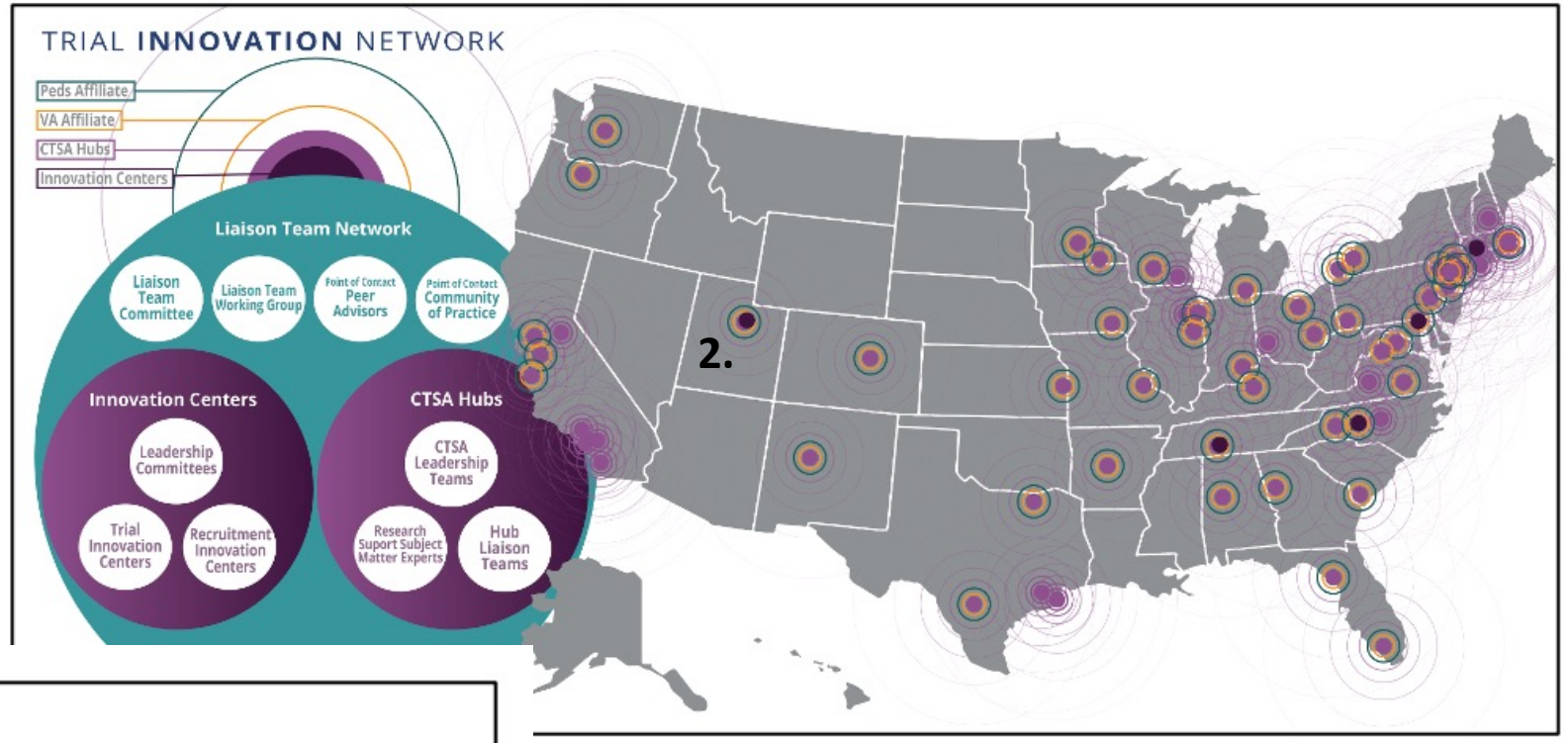
Networking

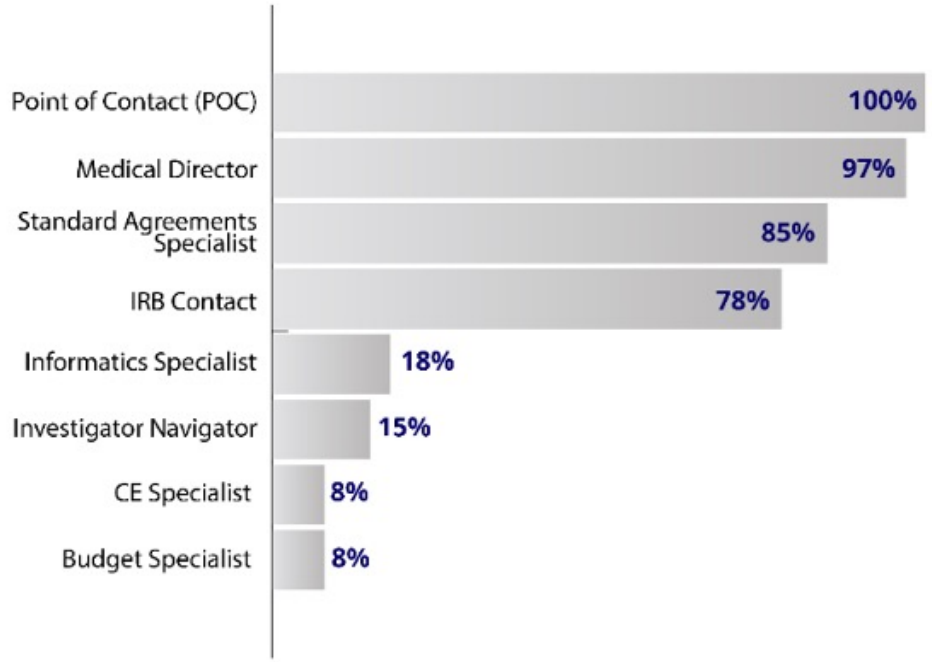
Expansive reach and diversity of HLT members



Most HLTs Include
Regulatory Experts
Recruitment Experts
Contract Experts

Some HLTs Include
Informatics Experts
Biostatistics Experts
Community Engagement Experts

A Few HLTs Include
Education Experts
Protocol Development Experts
Evaluations Experts
Budgeting Experts
Marketing Experts
Compliance Experts



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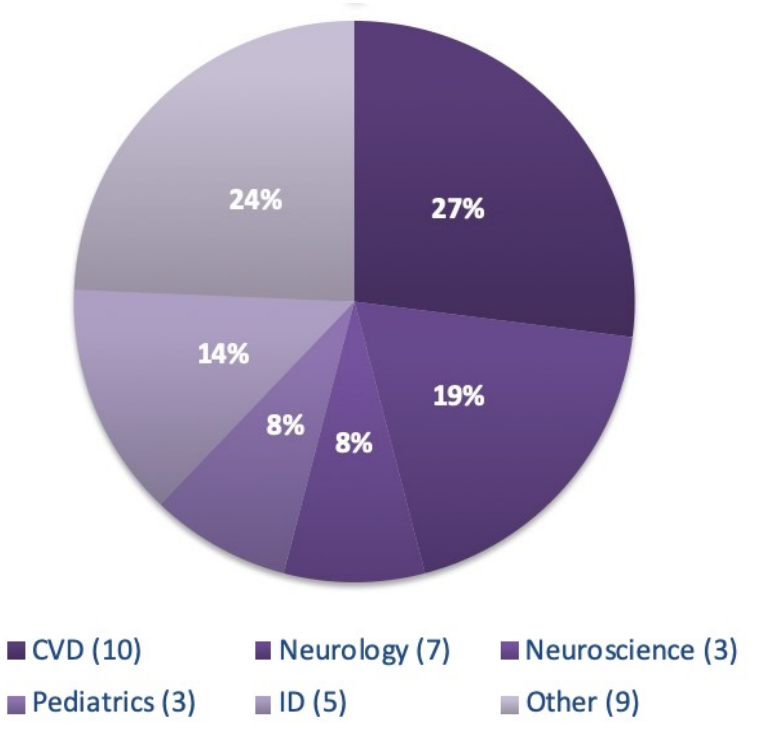
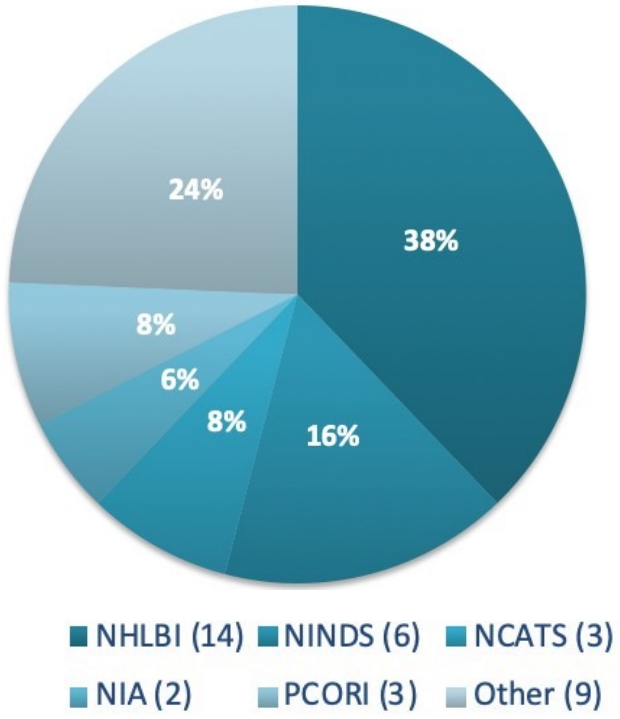
Consult Demographics*

37 PAT-Approved Comprehensive Consultations - Nov. 2016 – June 30, 2023

JHU/Tufts TIC
Comprehensive Consultation
Therapeutic Areas



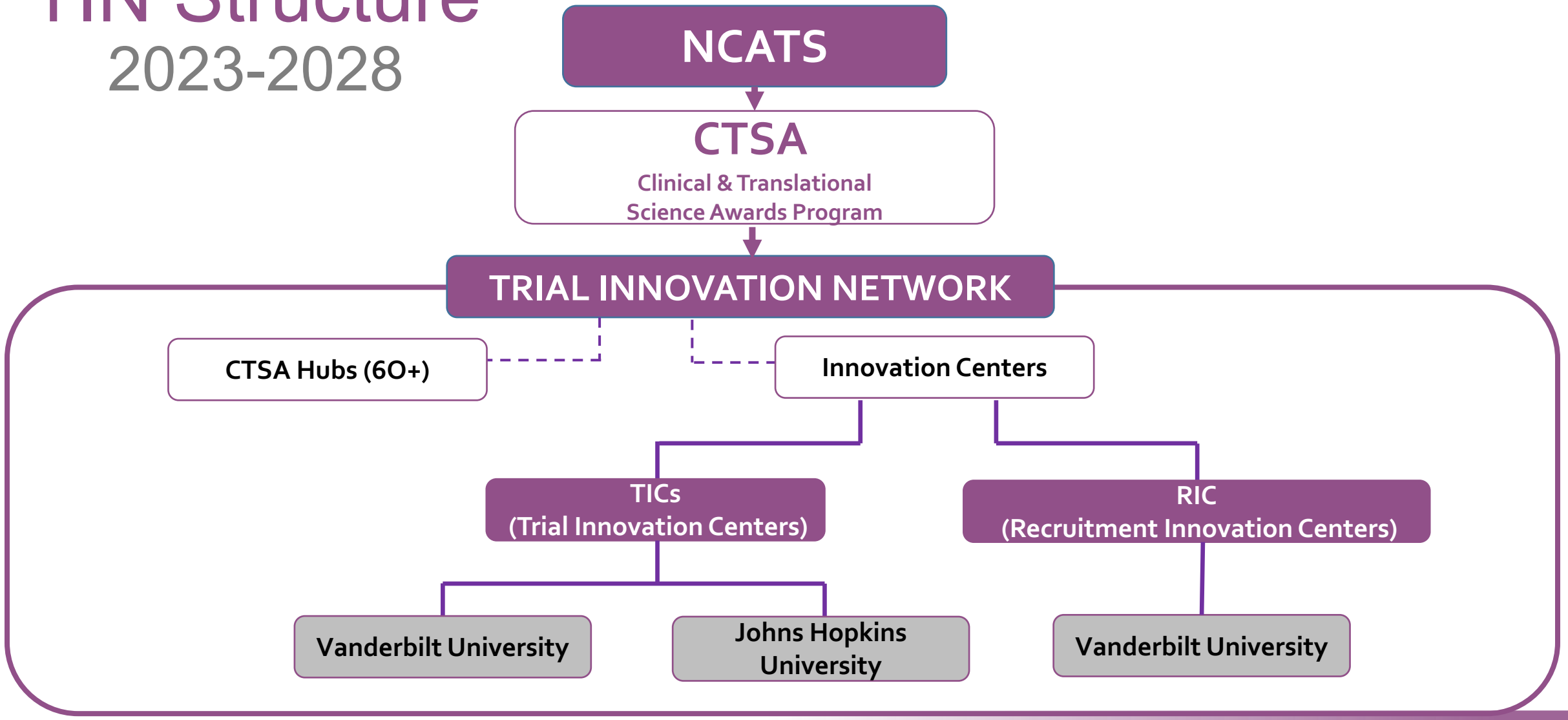
JHU/Tufts TIC
Comprehensive Consultation
Primary Funding Sources



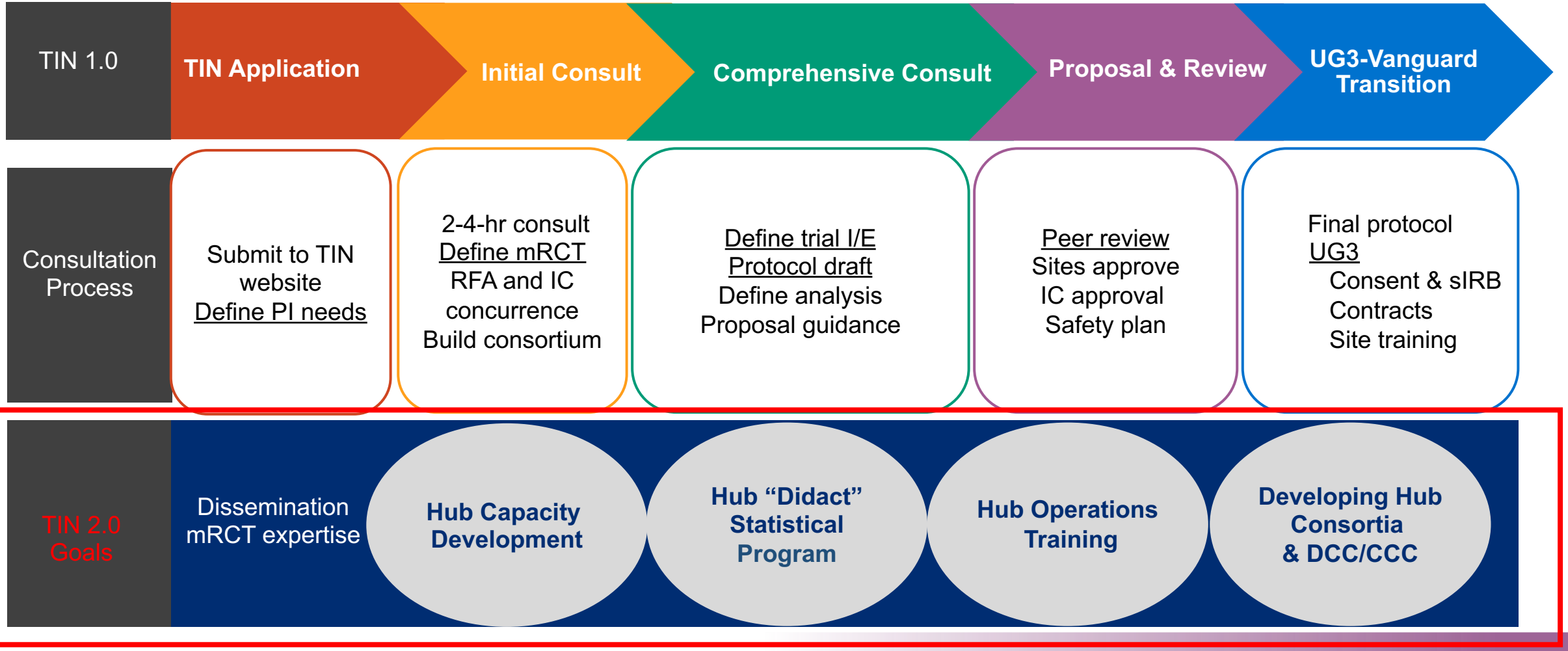
- **20** different institutions/CTSAs
- **18** utilized sponsor IC/PO discussion prior to TIN submission
- **21** budgets >$500,000 DC/year
- **33** adult, **3** pediatric populations; **1** adult and pediatric population
- Planned subjects range: 36 - 10,000
- Planned sites range: 2 - 120

*REDCap Dashboard -

TIN Structure
2023-2028



TIN Consultation Processes



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TIN Consult Process – Initial Consult Topics - Deliverables

Submitting Investigator

Seek local CTSA support

Assigned within 5 business days

Submit through the TIN website

TIC/RIC Assigned
- JHU TIC
- Vanderbilt TIC
- Vanderbilt RIC

30-60 min kick off call, then 1-3 hour topic specific discussions as needed

Initial Consultation
- Protocol Design
- Study Budget Estimate
- Projected Timelines
- Recruitment & Retention Strategy
- Assessment of Study Feasibility

Proposal Assessment Team Review
Letter is sent to the submitting PI with one of the following three outcomes:

- **No further support**
- **Approved for resources**
  - Begin discussions/implementation of the resources approved
- **Approved for comprehensive consultation**
  - Assist with getting the proposal ready for submission
    - **Grant is submitted to funders**

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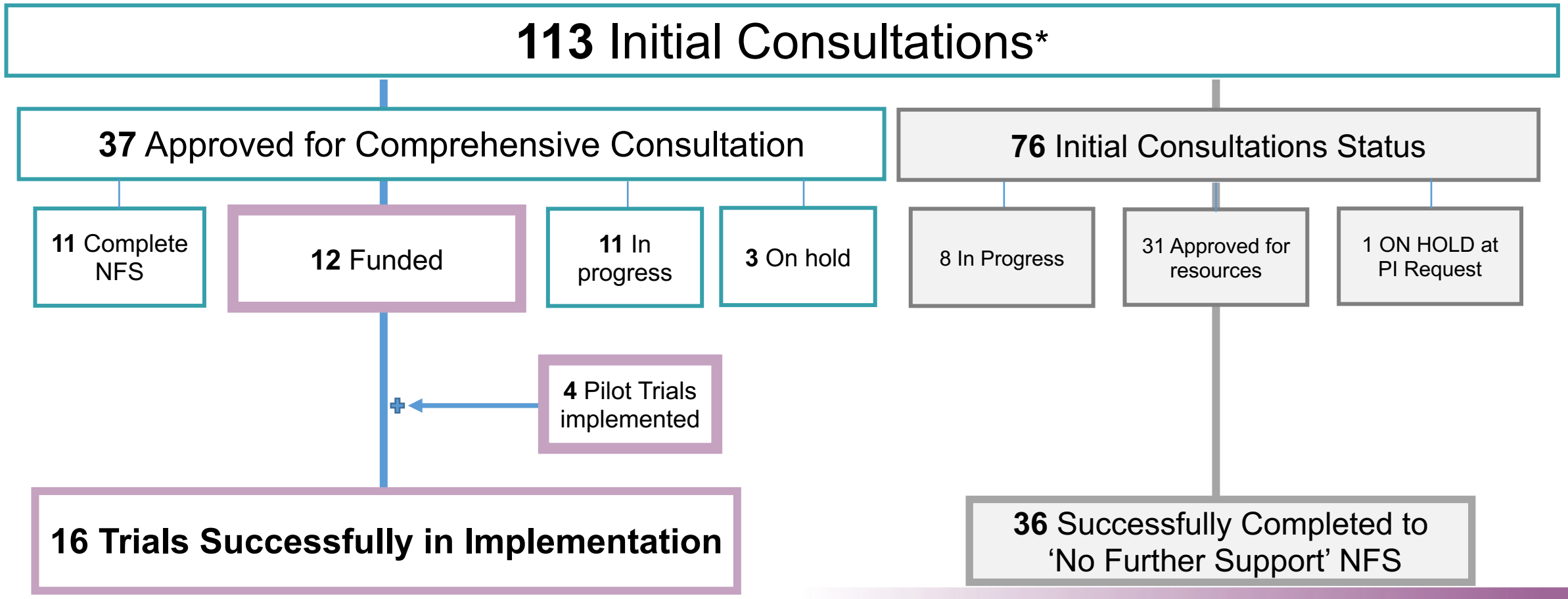
Consort Diagram: Nov. 2016 - June 2023

JHU-Tufts TIC Trials in Implementation



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*2 **TIN 1.0** Joint consults assigned to Duke (1) and Utah (1); 111 to JHU

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TIN 1.0 Timeline

Years 1 - 7

HEAL PILOT

HEAL

COVID

06/16 — 06/20 — 06/23

0 1 2 3 4 5 6 7

Sponsors	
NIA	2
NINDS	1
NICD	1
DOD	2
NIDDK	1
NHLBI	2
AHA	1
NY State	1
NCATS	1

Kids MoD PAH partners: JH, U of Colorado, Columbia, PAHNET, Duke

MAP partners: Columbia, JH

REACT-AF partners: NU, STANFORD, UCSF, JH

RAFT partners: JH, NAFTNET

NeuroNYCures partners: Cornell, U Rochester, NY state lab, JH

BEACH partners: U of K, JH

PENS partners: JH, U of BC, U of Wash, Utah

CSSC-001 partners: JH, 20 TIN sites

CSSC-004 partners: JH, 20 TIN sites

C-19 Collab partners: JH, Vanderbilt, Harvard, Duke

Technology to Manage Celiac Disease (U34) partners: Columbia, JH

mTECH partners: JH

Key:

- Implementation stage
- End of implementation
- Implementation ongoing

4 Stages of the Consult Process

1. Consult - to build partnership

2. Team Plan - mRCT

3. Operate - mRCT

JHU TIC Activities

Employed in Consults

Areas of Expertise

- Site Initiation, Selection & Activation
- Clinical Site Monitoring
- Effectiveness Trials
- Neurological Research
- Cardiovascular Research
- Perinatal and Neonatal Research
- Stakeholder Engagement
- Clinical Trial Metrics
- Imaging Center & Management
- Strategies for Drug/Device Development

Research Methodology

- Study Design
- Protocol/CRF Development
- Feasibility Studies
- IDE / IND Regulatory Requirements
- Manuals of Procedures
- Teaching & Training
- Data Reporting
- Safety Programs
- Biostatistics
- Quality Assurance
- Risk Management

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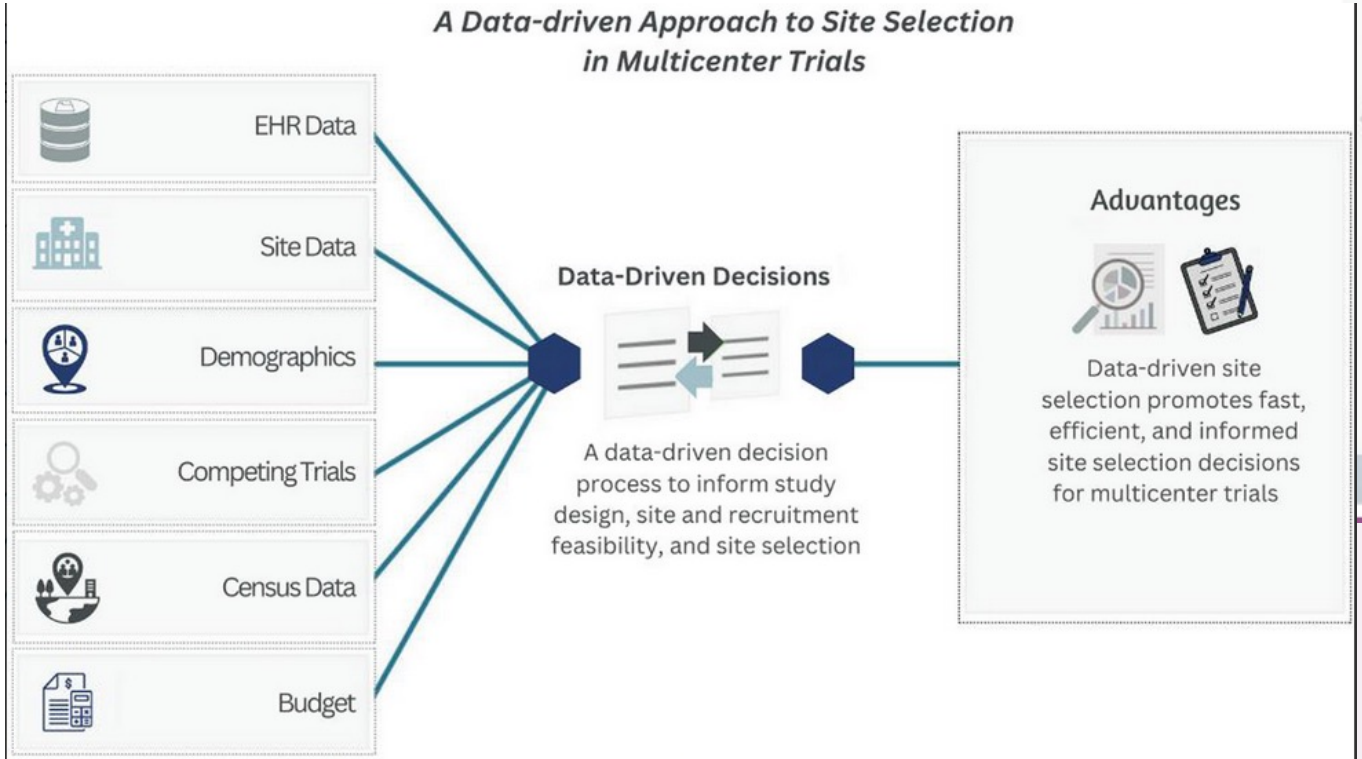
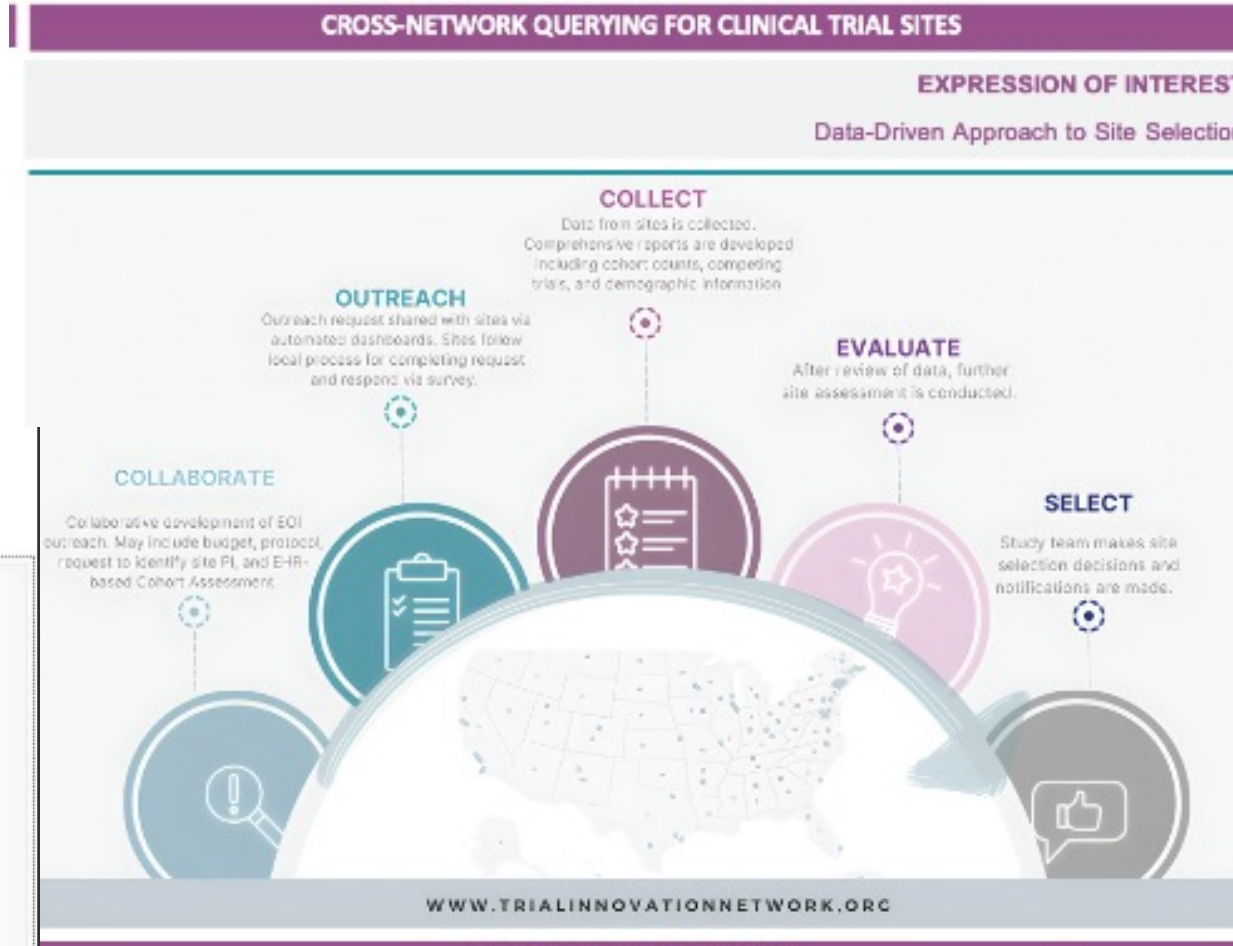
Start Up – Site identification (EOI) and selection

The Expression of Interest (EOI) can include:

- EHR-based cohort assessment
- Site PI identification
- Protocol review/feasibility
- Budget review/feasibility





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Top 4 recruitment and retention recommendations from the RIC

- Proactively assess R&R barriers and develop mitigation strategies
- Prioritize participants experience- minimize burden and returning value
- Data driven site selection
- Engage stakeholders at every step

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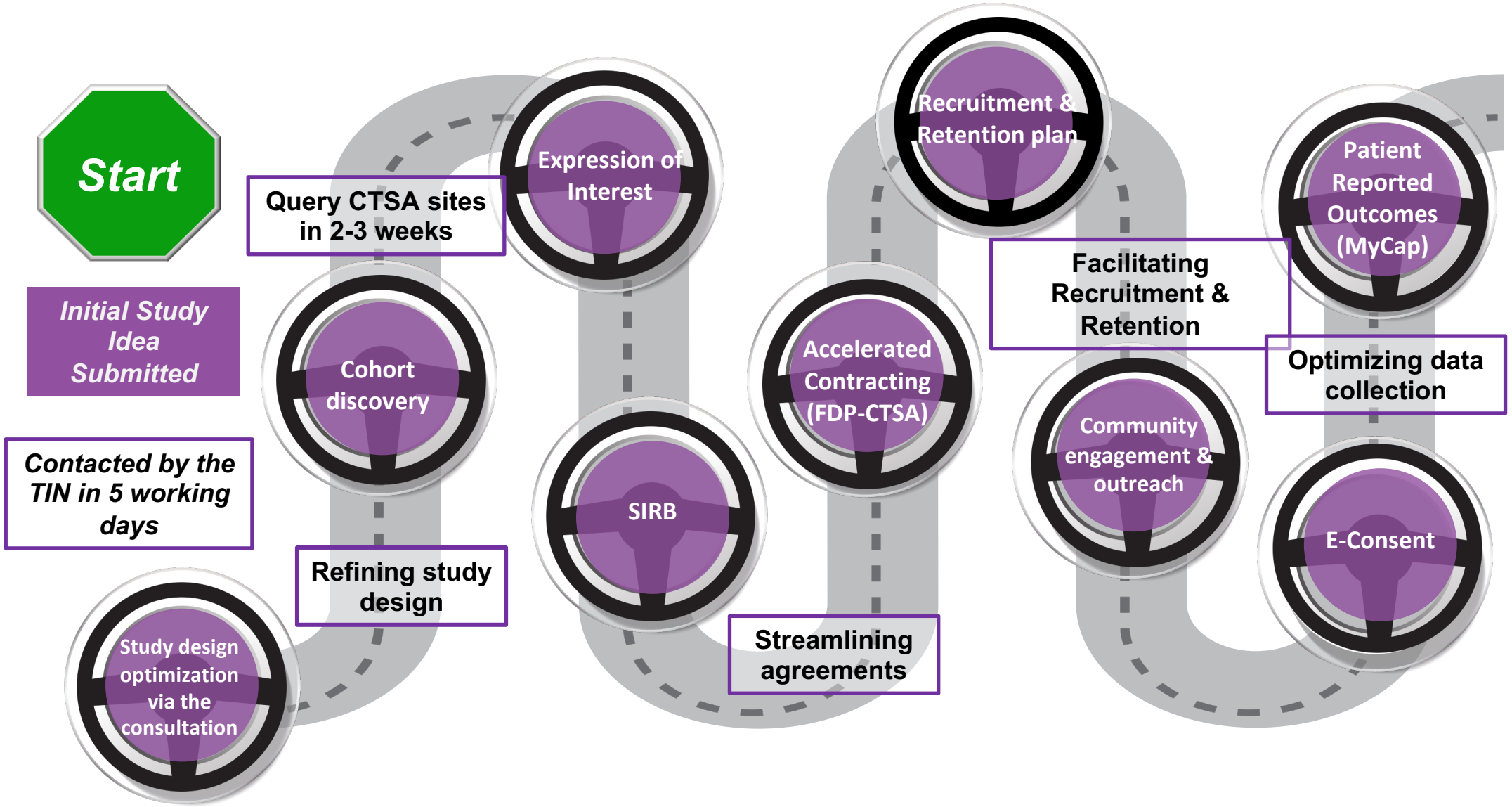
Infrastructure Available for Efficient Quality Study Conduct



Open Floor for Q & A