Avoiding the Fumble: Building on a Decade of Lessons from Pragmatic Clinical Trials

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What is a fumble?

In Merriam Webster:

"To grope for or handle something clumsily or aimlessly."

In American Football:

"To drop or lose control of (the ball), sometimes causing a turnover."

On social media:

"When one is given a chance and somehow messes up."

The Fumble: 1987 AFC Championship (Broncos vs. Browns)

If other industries were like healthcare...

Banking

ATM transactions **would take not seconds but perhaps days or longer** as a result of unavailable or misplaced records.
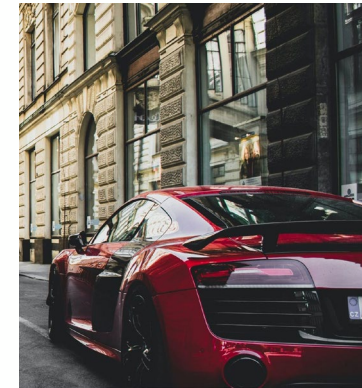
Home building

Carpenters, electricians, and plumbers **each would work with different blueprints**, with very little coordination.
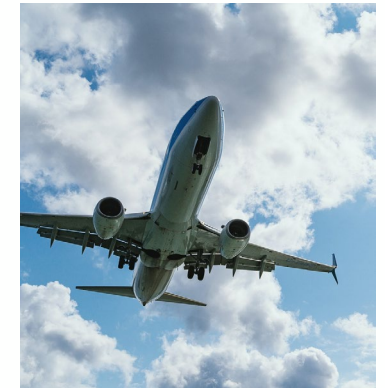
Shopping

Product prices would not be posted, and the price charged would vary widely within the same store, depending on the source of payment

Car manufacturing

Warranties covering defects would not exist...so few factories would seek to **monitor and improve production** line performance and product quality

Airline travel

Each pilot would be free to **design their own preflight safety check, or not to perform one at all**

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But what if…

- ✓ **Records were immediately updated** and available for use by patients
- ✓ Care delivered was **proven reliable at the core** and tailored at the margins
- ✓ **Patient and family needs and preferences** were a central part of the decision process
- ✓ All team members were fully **informed in real time** about each other's activities

- ✓ Prices and total costs were **fully transparent** to all participants
- ✓ Payment incentives were structured to **reward outcomes and value**, not volume
- ✓ Errors were promptly **identified and corrected;** and
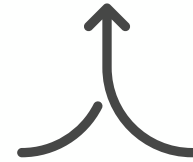- ✓ Results were routinely captured and used for **continuous improvement**.

National Academies of Sciences, Engineering, and Medicine. 2013. Best Care at Lower Cost: The Path to Continuously Learning Health Care in America. Washington, DC: The National Academies Press. https://doi.org/10.17226/13444.

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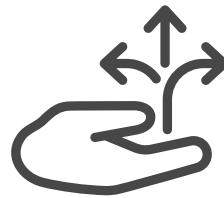
Why should we bother?

Conducted within the healthcare system

Not disruptive to clinical workflow

Streamlined procedures and infrastructure

Makes use of existing data
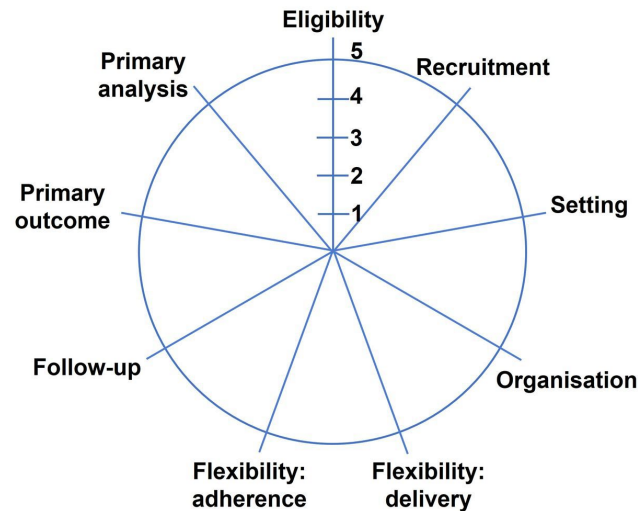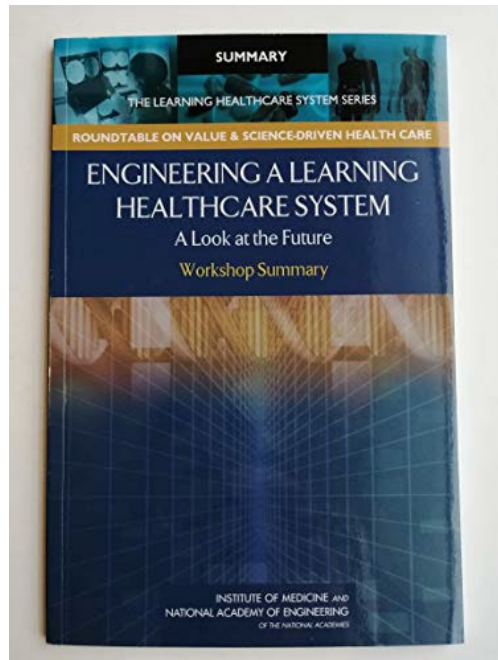
Answer questions with major public health importance

Outcomes important to decision-makers

Diverse, representative study population

Highly generalizable results

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A Decade Ago: The High Hopes for PCTs

"Pragmatic clinical trials are having a moment— actually, a decade."
-Platt, Bosworth, Simon?

- 80% of PCT PubMed hits in last 10 years
- PRECIS-2 ~700 citations

Platt R, Bosworth HB, Simon GE. *JAMA.* 2024;332(22):1875–1876.

Fast Forward to 2025: Are We Still Fumbling?

"Protocol complexity has steadily risen, increasing site workload and patient burden rather than reducing them. The industry tends to point out that simplifying protocols could reduce patient burden, but **without a fundamental shift in trial design philosophy, the industry's cautious approach will continue to slow progress.**"
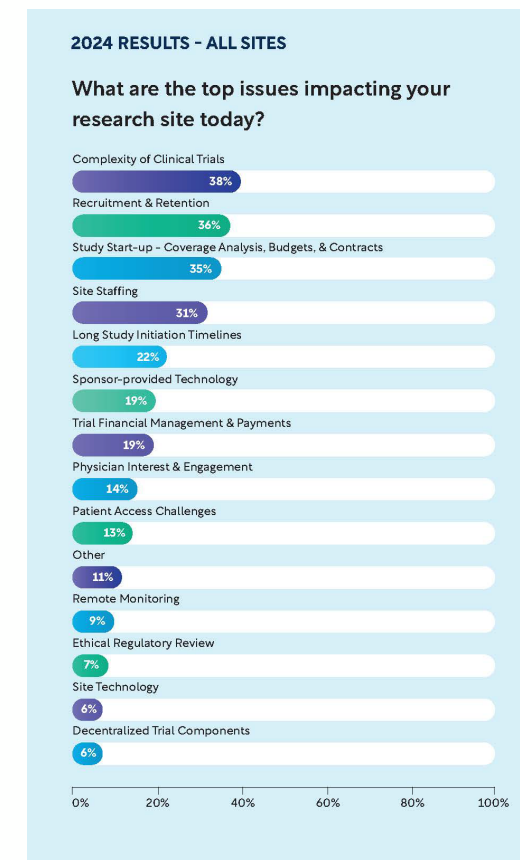
3x

# of datapoints

2x

# of endpoints

Vs. 2015

2024 RESULTS – ALL SITES

What are the top issues impacting your research site today?

Issue	%
Complexity of Clinical Trials	38%
Recruitment & Retention	36%
Study Start-up – Coverage Analysis, Budgets, & Contracts	35%
Site Staffing	31%
Long Study Initiation Timelines	22%
Sponsor-provided Technology	19%
Trial Financial Management & Payments	19%
Physician Interest & Engagement	14%
Patient Access Challenges	13%
Other	11%
Remote Monitoring	9%
Ethical Regulatory Review	7%
Site Technology	6%
Decentralized Trial Components	6%

Source: WCG 2024 Clinical Research Site Challenges Report

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Fast Forward to 2025: Are We Still Fumbling?

113%

↑ in substantial amendments

27%

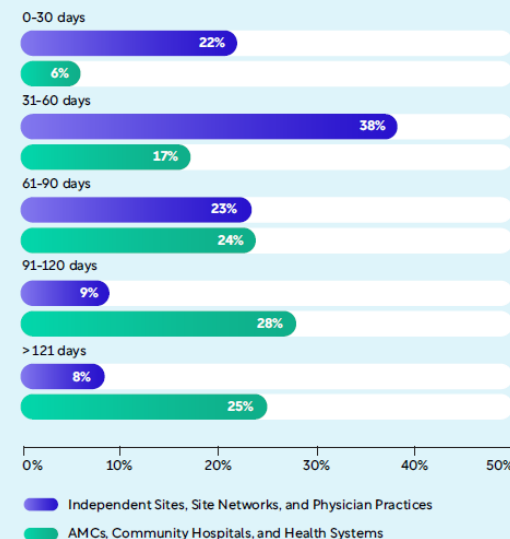↑ in time from protocol approval to FPV

105%

↑ in dropout rates

Vs. 2015

ACADEMIC MEDICAL CENTERS, HEALTH SYSTEMS, AND COMMUNITY HOSPITALS VS INDEPENDENT SITES, PHYSICIAN PRACTICES, AND SITE NETWORKS

How long did your site's average study start-up process take last year?

Duration	Independent Sites, Site Networks, and Physician Practices	AMCs, Community Hospitals, and Health Systems
0-30 days	22%	6%
31-60 days	38%	17%
61-90 days	23%	24%
91-120 days	9%	28%
>121 days	8%	25%

Legend:
- Independent Sites, Site Networks, and Physician Practices
- AMCs, Community Hospitals, and Health Systems

Source: WCG 2024 Clinical Research Site Challenges Report

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Fast Forward to 2025: Are We Still Fumbling?

- Not all "positive" trials adopted by health systems
- Some "negative" trials were adopted (subgroup effects, patient/staff satisfaction, optics)
- Trial success ≠ system priorities

Table 1. Intervention *Not Sustained* When Intervention *Did* Improve Primary Outcome

Primary Endpoint	Post Hoc/Secondary Findings	Implementation
PPACT		
Significant: Reduction in pain	Significant: Reduction in pain-related disability and benzodiazepine use	Not sustained: None of the participating health systems fully sustained the intervention, largely due to upfront staffing costs and feasibility considerations
TSOS		
Significant: Reductions in PTSD symptoms at 6 months (but not at 12 months)	Significant: Secondary stratified analyses showed significant 3, 6 and 12-month PTSD intervention treatment effects at sites with good/excellent implementation, but no significant intervention treatment effects at sites with fair/poor implementation.	Trauma centers must have protocols to identify and refer patients at high risk for psychological sequelae; no trauma center-based intervention required.

Table 2. Intervention *Sustained* When Intervention *Did Not* Improve Primary Outcome

Primary Endpoint	Post Hoc/Secondary Findings	Implementation
ABATE		
Null: No significant reduction in infections in the non-critical care population	In patients with medical devices, intervention was associated with reductions in all-cause bloodstream infections and multi-drug resistant organism cultures	Sustained: Health system sustained the intervention for patients with a medical device in participating hospitals that were in the intervention arm. Expanded: Adopted intervention for patients with a medical device in all other health system hospitals
LIRE		
Null: No decrease in spine-related healthcare utilization after imaging	Slightly reduced subsequent opioid prescriptions	Sustained (partially): Half of participating systems sustained the intervention based on its potential to reduce opioid use; no additional resources were required to

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Why the Disconnect?

- Different audiences require different kinds of evidence.
  - <u>Systems</u>: want timely, actionable signals (often subgroup- or cost-driven)
  - <u>Funders/guidelines:</u> want $p<0.05$, prespecified endpoints
- NIH-style 5-10 year studies misaligned with systems' 2-3 year decision horizons
- Cost and EHR infrastructure rarely factored in

"Researchers often have a tail-wagging-the-dog problem. We assume if we think something is a good idea, the healthcare system will too... We need to remember that we're the tail and the healthcare system is the dog."
-Greg Simon, MD, MPH

Platt R, Bosworth HB, Simon GE. *JAMA*. 2024;332(22):1875–1876.

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Not-so-easy lessons for the next decade

Collect sustainability data from the start

Align outcomes with system priorities (*Ask: what would motivate systems to adopt*?)

Health system-friendly timelines (2-3 years)

Flexibility in design and implementation

"Fumbles" are part of the game

- Progress takes time
- We can't improve if we only share wins
- Transparency + teamwork helps us bounce back faster

GROWTH MINDSET

- Analyze mistake
- Accept challenges
- Ability to learn new things
- Inspired by others success

FIXED MINDSET

- Unchangeable aptitude
- Avoid challenges
- Avoid failure
- Give up easily

The Playbook

- Inspired by the Collaboratory Living Textbook + PCORnet lessons
- Practical "drills" for avoiding common fumbles (recruitment, workflow, outcome capture)
- Tool for sharing, refining, and learning

It's not "failing faster," it's learning sooner.

Instead of a new stadium for every game…

- ✓ **Research networks develop analysis-ready data**
  - Standard format
  - Harmonized definitions
  - Quality checked in advance

- ✓ **Reusable analysis tools**

- ✓ **Simple, pragmatic studies integrated into routine care**

- ✓ **Administrative simplicity**

- ✓ **Efficient clinical trial enrollment and follow up mechanisms**

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The PCORnet Track Record

50+
PCORnet® Studies
Received over $500 million in funding

FUNDED BY
- PCORI 53%
- Federal 29%
- Industry 18%

75+
PCORnet® Network Partners
8 PCORnet® Clinical Research Networks across the U.S.

50
States
PCORnet is linked to patients in every state in the U.S.

47+
Million People
PCORnet represents data from everyday healthcare encounters with more than 47 million people annually across the U.S.

145+
Publications
About PCORnet® Studies

400+
Publications
Supported by PCORnet resources

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Goal

Develop a user guide and instruction manual to catalyze and support national-scale research

Learn how to engage with the PCORnet community

Design projects that appropriately leverage infrastructure

Know what to expect when working with Network Partners

Playbook Development

User-centered design process: Engage PCORnet groups, partners, and members of the Playbook's intended audience to inform and guide the content
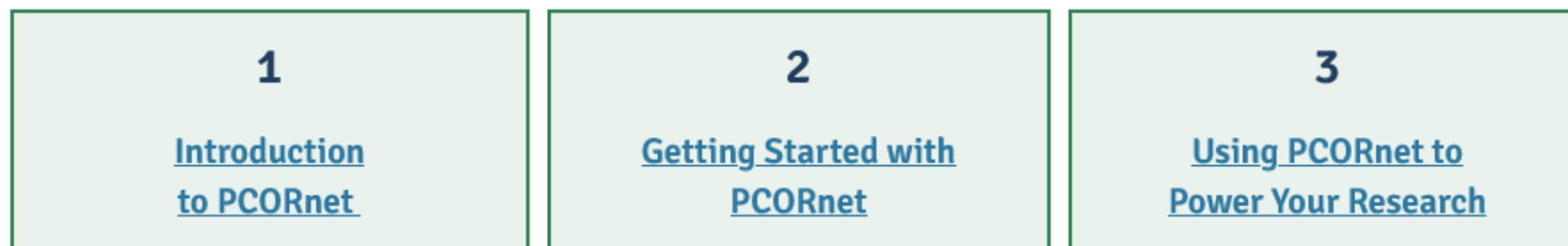

Innovation Workgroup

Patient partners

PCORnet® CRNs and CRN sites
Investigators, project managers, data and technology specialists, etc

Playbook Project Team

Network Governing Committees

The Coordinating Center for PCORnet®

PCORnet "naïve" panel

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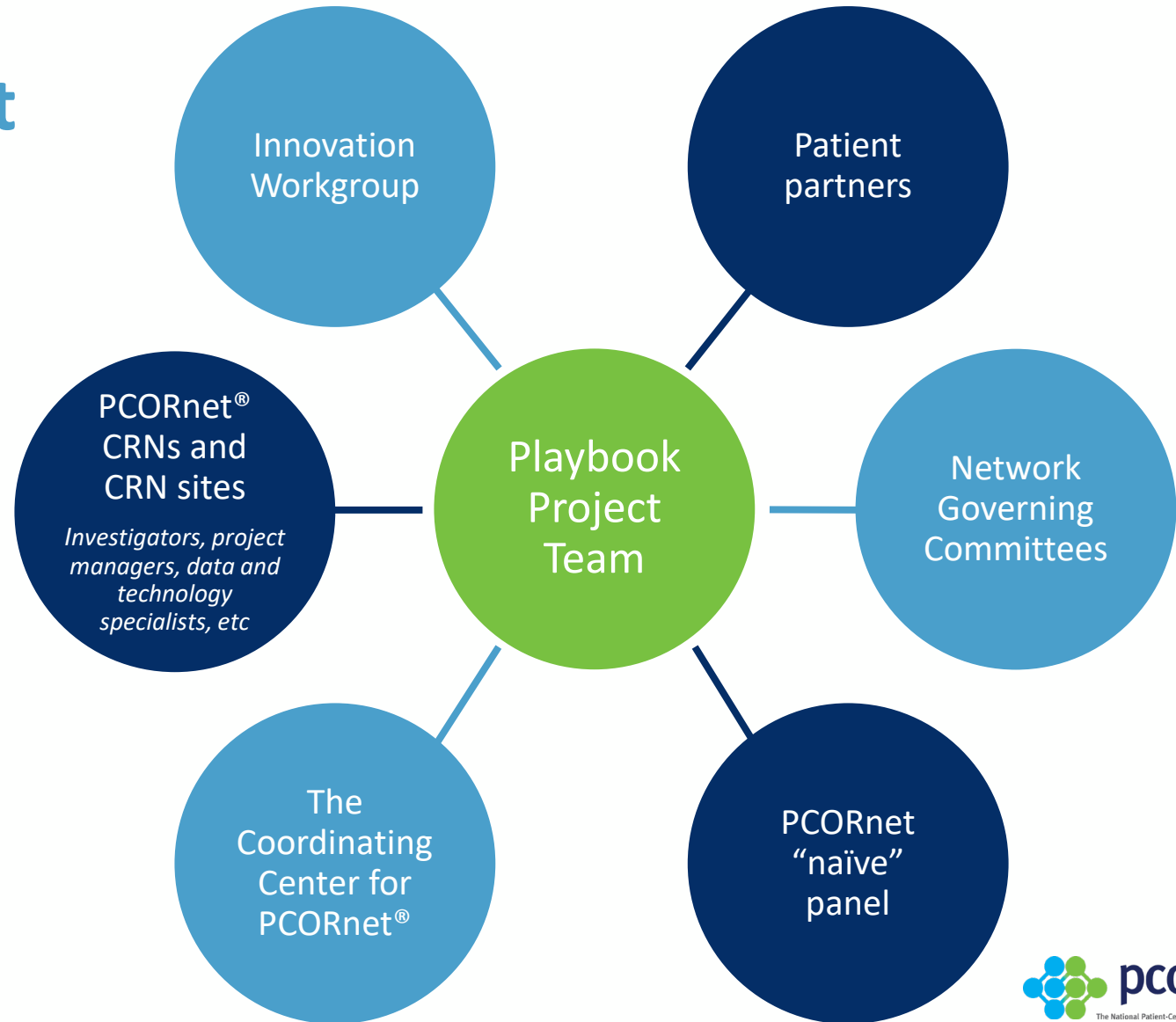
Topic Prioritization
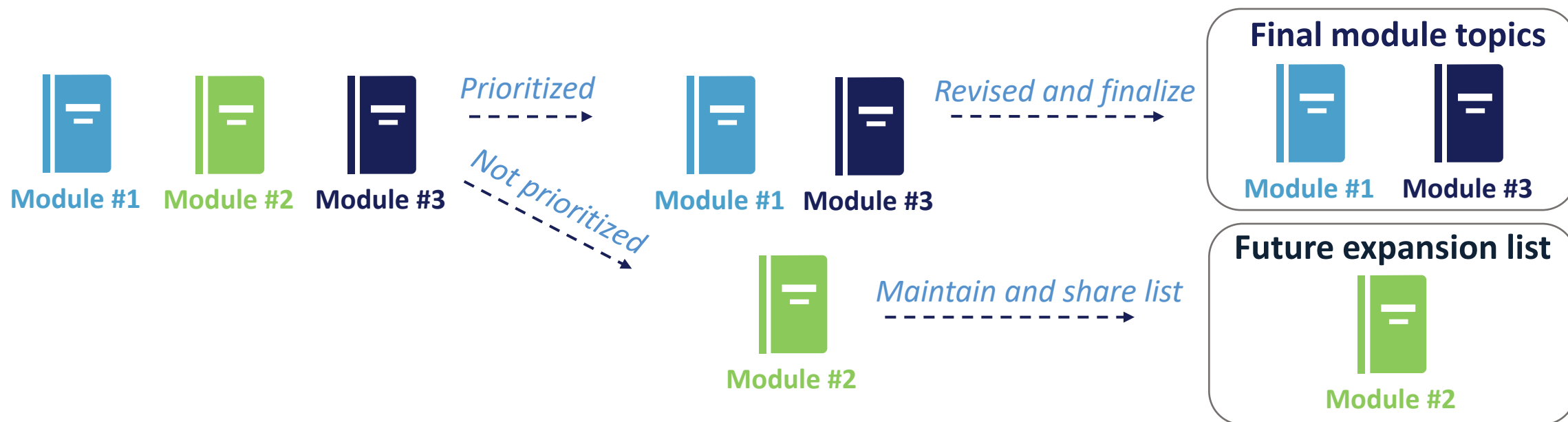
Launching 2025

Modules	Content Includes
1: Introduction	• Benefits of using PCORnet • Types of research PCORnet can support
2: Getting Started in PCORnet	• How PCORnet supports research teams • What is a PCORnet® Study?
3: Using PCORnet to Support Your Research	• What to expect: process, timing, and pricing • Types of requests
4: Dissemination and Implementation	• Expectations for PCORnet® Studies • Sharing opportunities through PCORnet
5: Case Studies	• Examples of a variety of PCORnet® Studies

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Playbook Overview

Getting to know the Playbook

| PLAYBOOK HOME | MODULE 1 | MODULE 2 | MODULE 3 |

1

Introduction to PCORnet

- Introduction
- What Kind of Research Can the PCORnet Infrastructure Support?
- Frequently Asked Questions

2

Getting Started with PCORnet

- Knocking on the PCORnet® Front Door
- What is a PCORnet® Study?

3

Using PCORnet to Power Your Research

- What to Expect
- Administrative Simplicity
- Pricing Guidance

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Playbook Overview

Getting to know PCORnet

Module 1: Introduction to PCORnet

Sharing the vision
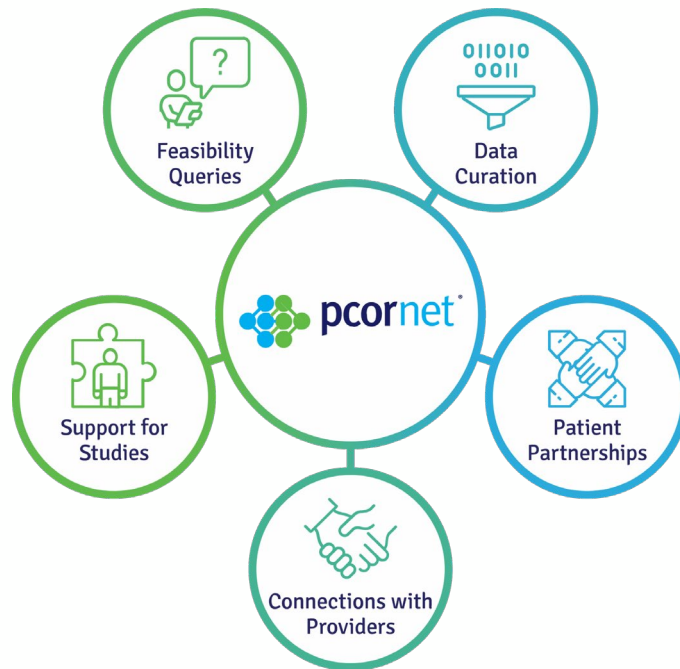
Other large-scale research infrastructures offer some of these capabilities, but only the PCORnet infrastructure offers them all.

"Innovating in clinical research means we need to embrace new technologies, new ways of contacting and following participants... and working together to push the envelope to do research in new ways."

Russell Rothman
Principal Investigator at STAR, a PCORnet® Clinical Research Network

Module 1: Introduction to PCORnet

Illustrating study diversity

Real-World Evidence Research
Using data collected from routine clinical practice

Comparative Clinical Effectiveness Research
Assessing the benefits and harms of different interventions

Population Health Research
Understanding health outcomes of groups and influencing factors

Pragmatic Research
Evaluating intervention effectiveness in real-world practice settings

Health Systems Research
Studying how healthcare delivery systems function

Implementation Science Research
Examining how to help healthcare settings implement interventions or practices

Studies may fall into multiple categories

Module 1: Introduction to PCORnet

Links to external resources

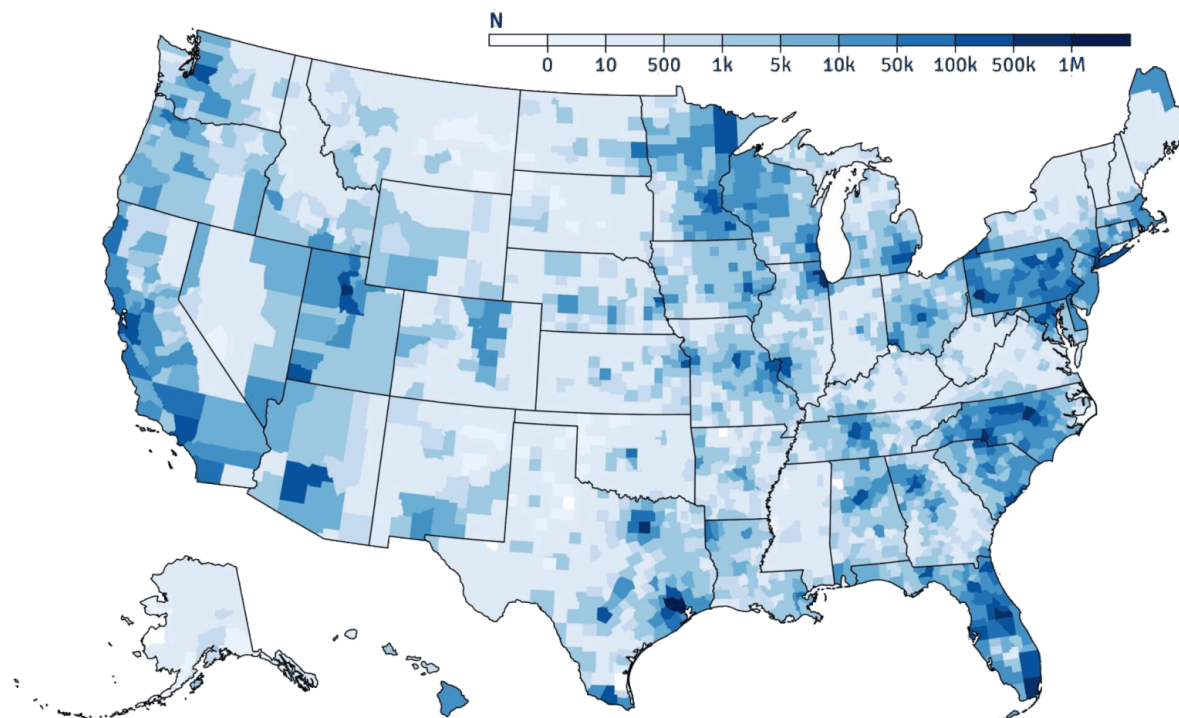The Big Picture: Healthcare Data and Interoperability

Common Data Models

Module 1: Introduction to PCORnet

Highlighting Partnerships

Module 1: Introduction to PCORnet

Answering FAQs

Frequently Asked Questions

Are all PCORnet® Studies funded by PCORI?	**+**
Can PCORnet® Studies include sites outside PCORnet?	**+**
Am I able to access raw data through PCORnet?	**+**
Is PCORnet only for multi-center studies?	**+**
What does PCORnet offer other than data?	**+**
How do I use the PCORnet infrastructure?	**+**

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Module 2: Getting Started with PCORnet

How to access the Front Door

Knock on the PCORnet® Front Door to access PCORnet

1 **Tell us** about your study via a short intake form

2 **Discuss** your study with the PCORnet® Front Door team

3 **Learn how** PCORnet can support your research goals with a Study Feasibility Review

4 **Determine** next steps with the PCORnet® Front Door team

If PCORnet is able to support your study, you may choose one or both services.

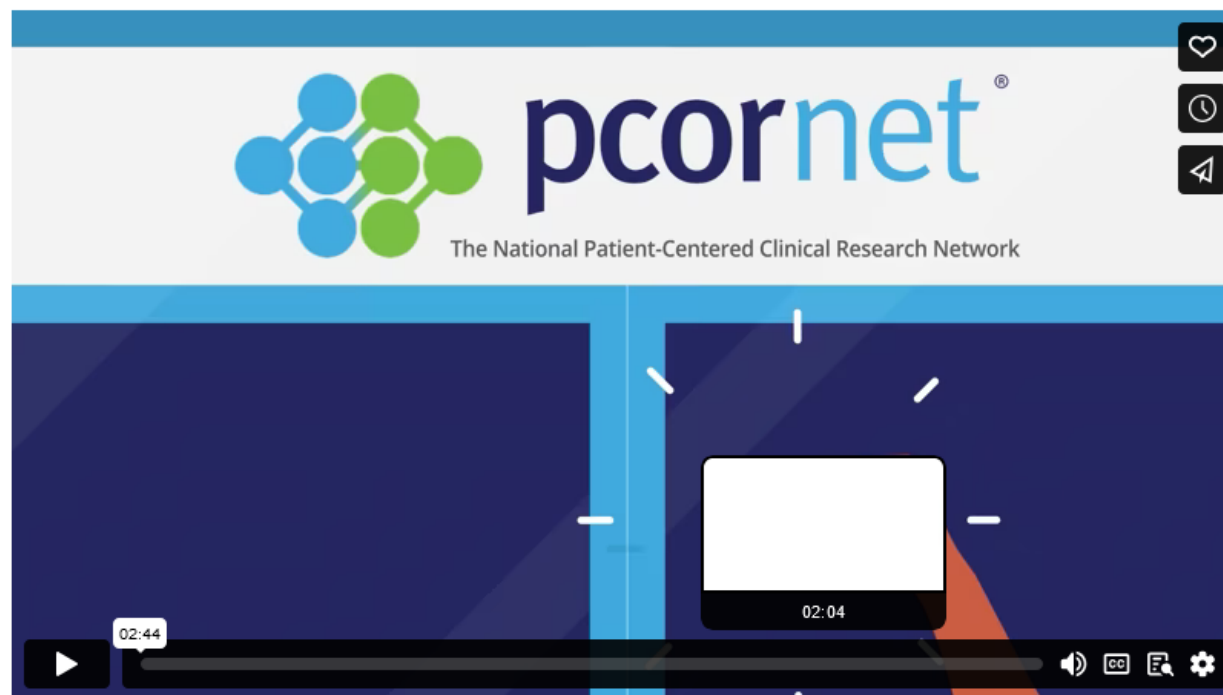**Get data insights** from PCORnet® Clinical Research Networks with a Data Network Request

Build your study team with a Network Collaborator Request

Module 2: Getting Started with PCORnet

How to access the Front Door

Watch this video to learn more about the PCORnet® Front Door

Module 2: Getting Started with PCORnet

Defining "PCORnet Study"

What is a PCORnet® Study?

" PCORnet® Studies are designed specifically in service to the patient, from engagement in the design and conduct to dissemination of results. It is one way we help ensure research that matters to patients continues to progress—and, at the end of the day, that's what the PCORnet is all about.

Russell Rothman
Principal Investigator at STAR, a PCORnet® Clinical Research Network

To be designated a PCORnet® Study, your project must:

- Include at least two PCORnet® Clinical Research Networks (CRNs). Sites that are not partnered with the network may participate in PCORnet® Studies.
- Demonstrate how participants and patients are engaged throughout the study.
- Be committed to returning results to participants.
- Agree to regularly share study progress and best practices.
- Leverage the PCORnet® Common Data Model, as applicable.

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Module 3: Using PCORnet® to Power Your Research

Demystifying the process

3 Main Service Types within a Consultation

Consultation with the
PCORnet® Front Door

↓

Study Feasibility Review

Network Collaborator
Request

Data Network
Request
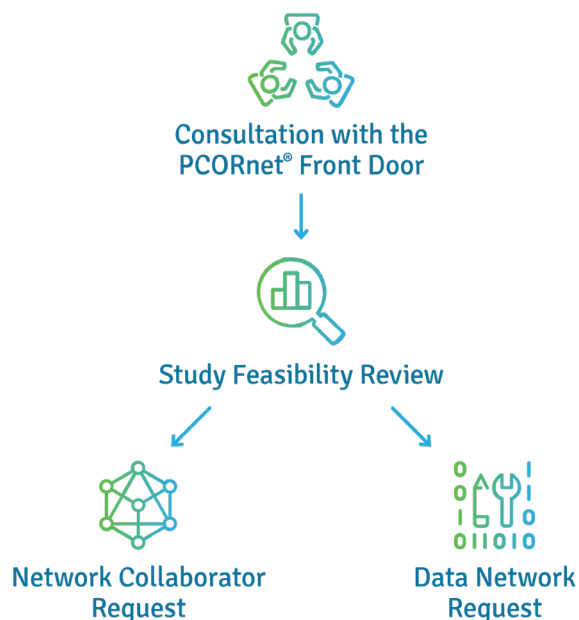
"We really appreciated the PCORnet® Front Door team, who explained everything to us and helped us navigate the process, including timelines (ours was short!), and connections with CRNs (regional networks) and individual sites."

— *Brendan Everett, Principal Investigator, PRECIDENTD, a PCORnet® Study*

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Module 3: Using PCORnet® to Power Your Research

"What does PCORnet offer besides data"?

Key Tools

Data Sharing Agreement

Clinical Research Collaboration Agreement

SMART IRB and IREx List

Data Study Flow Templates

Data Sharing Agreement	+
Clinical Research Collaboration Agreement	+
SMART IRB	+
IREx List	+
Data Study Flow Templates	+

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Module 3: Using PCORnet® to Power Your Research

"What is a feasibility review?"

Steps in a Study Feasibility Review

Step 1
Submit a brief intake form through the PCORnet® Front Door

Step 2
Within 1 business day, someone from the PCORnet® Front Door team will contact you

Step 3
Discuss your study with a team of PCORnet research experts
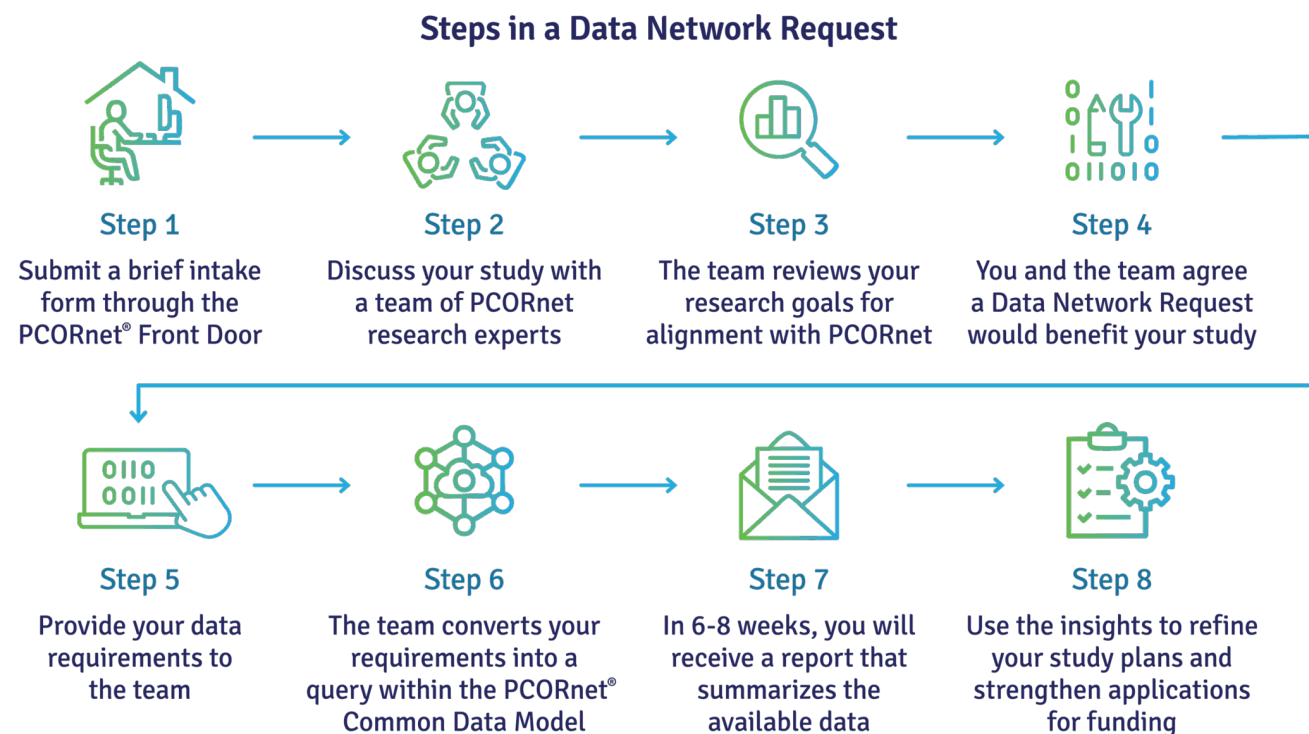
Step 4
The team reviews your research goals for alignment with PCORnet
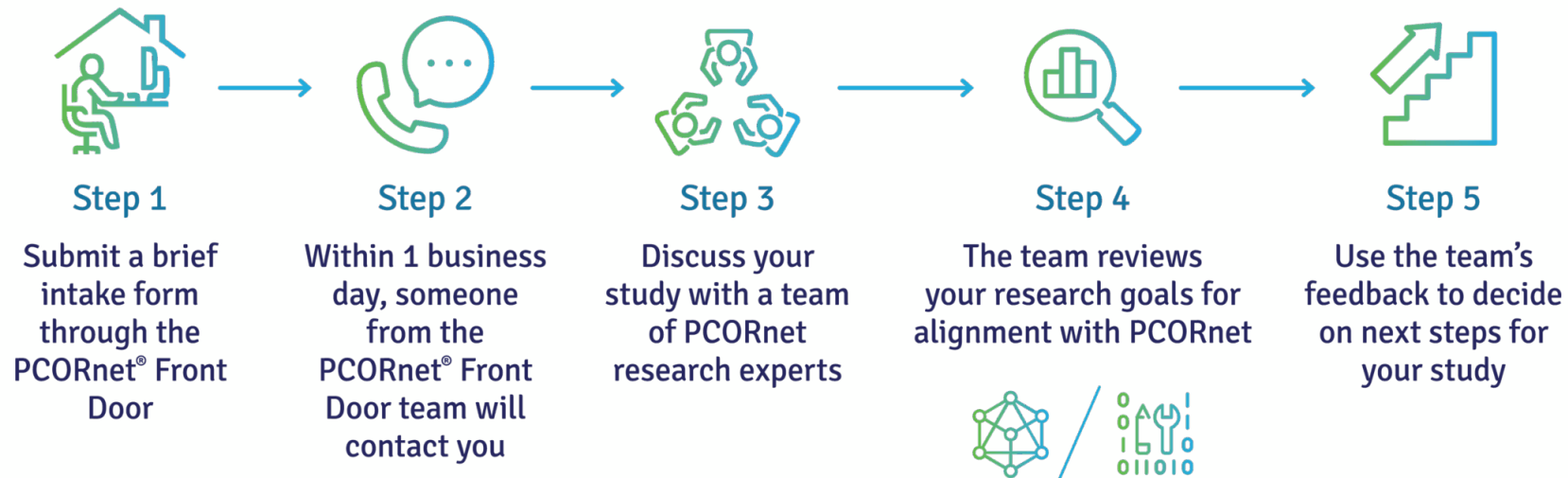
If PCORnet is able to support your study, the team may recommend a Network Collaborator Request and/or a Data Network Request

Step 5
Use the team's feedback to decide on next steps for your study

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Module 3: Using PCORnet® to Power Your Research

"What is a Data Network Request?"

Steps in a Data Network Request

Step 1
Submit a brief intake form through the PCORnet® Front Door

Step 2
Discuss your study with a team of PCORnet research experts

Step 3
The team reviews your research goals for alignment with PCORnet

Step 4
You and the team agree a Data Network Request would benefit your study

Step 5
Provide your data requirements to the team

Step 6
The team converts your requirements into a query within the PCORnet® Common Data Model

Step 7
In 6-8 weeks, you will receive a report that summarizes the available data

Step 8
Use the insights to refine your study plans and strengthen applications for funding

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Module 3: Using PCORnet® to Power Your Research

Pricing Guidance

Planning services provided at no cost
- Study Feasibility Reviews
- Data Network Requests
- Network Collaborator Requests

Study Costs
- Site-Specific Activities
- Query Costs

"Costs **depend on the needs of a study** and vary across different PCORnet® CRNs, so this module doesn't include specific amounts. However, it provides **general guidance** and describes the various factors that influence cost and how to account for them."

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Links to other resources

Connecting to other PCORnet tools

Data Reports

Data Reports Powered by PCORnet®

Data reports provide a valuable starting point for understanding how the PCORnet infrastructure can be leveraged to investigate key health topics prioritized by PCORI for research. These reports offer topic-specific snapshots of the extensive, real-world patient data collected across PCORnet® Clinical Research Networks (CRNs), helping researchers gain a deeper understanding of the rich data resources available within the network. This allows research teams to refine research questions, identify relevant data elements, and design more informed, impactful studies.

All modules are available for PDF download

DOWNLOAD MODULE 1
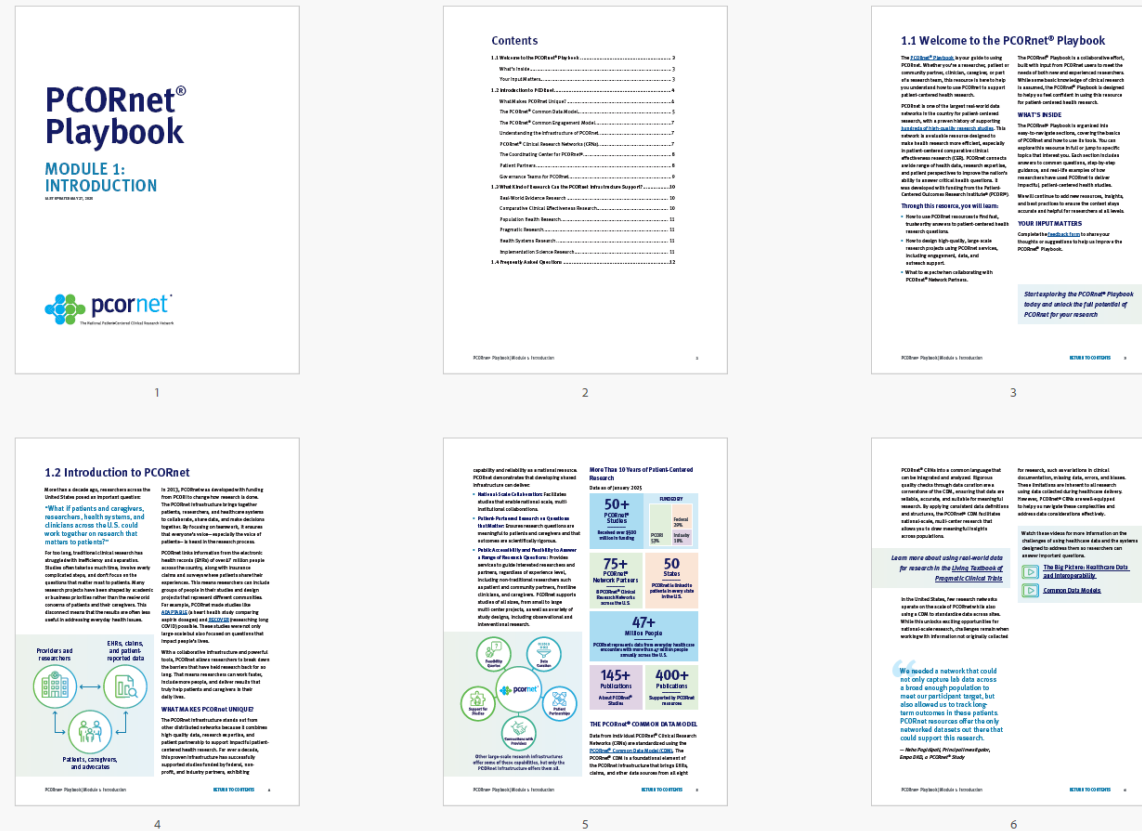
Quotes from Collaborators

Making it personal

"We needed a network that could not only capture lab data across a broad enough population to meet our participant target, but also allowed us to track long-term outcomes in these patients. PCORnet resources offer the only networked datasets out there that could support this research."

Neha Pagidipati
Principal Investigator, Empa DKD, a PCORnet® Study

"The PCORnet® Front Door team was exceptionally helpful. During the initial consult, the team identified the types of PCORnet resources most directly related to my proposal, and provided me with resources to better frame our request and understand the data model used by sites and networks."

Keith Feldman,
PCORnet® Front Door requestor, Children's Mercy Research Institute

"In its first decade, the PCORnet infrastructure has made great strides in helping researchers embed the patient voice at every level. We are not experts at clinical research, but we are experts in what it is like to be a patient considering participation in a clinical trial—and for a research team designing a study, that expertise can be quite valuable.

— *Greg Merritt, Patient Partner on the PCORnet® Steering Committee*

Where is the Playbook?

The Playbook is publicly available on Pcornet.org under "Resources"
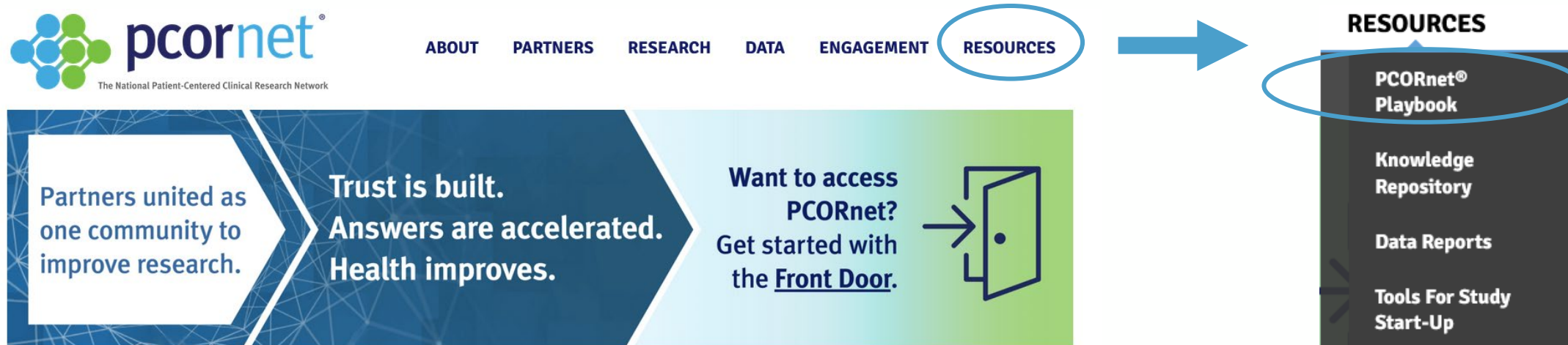
Feedback Form

Long-Term Vision

○ Regular review and maintenance

○ Ongoing enhancement and expansion

○ Similar to NIH Pragmatic Trials Collaboratory's Living Textbook (rethinkingclinicaltrials.org)

What's Next

Module Topic	Target Date
Engagement *(partnership with Vanderbilt team)*	2026
Dissemination and Implementation	Q3 2025
Case Studies	Q4 2025
Representativeness *(possible integration with existing module)*	Q4 2025
Digital Toolkit *(possible integration with existing module)*	Q1 2026 *(tentative)*

Q&A