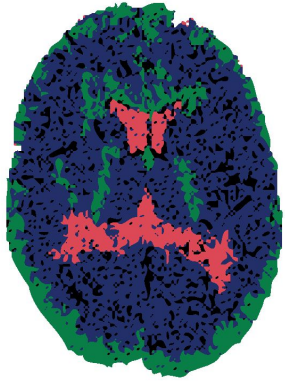
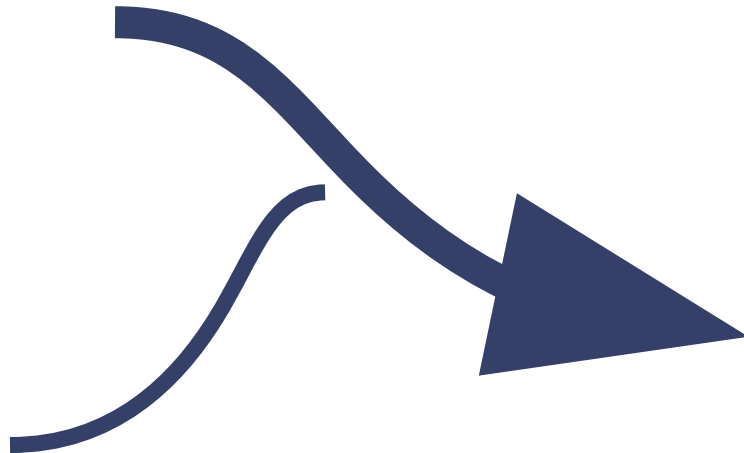


NIH SIREN Emergency Trials Network



Neurological Emergencies Treatment Trials

Evolution not creation



NIH SIREN Emergency Trials Network



National Heart, Lung,
and Blood Institute



National Institute of
Neurological Disorders
and Stroke

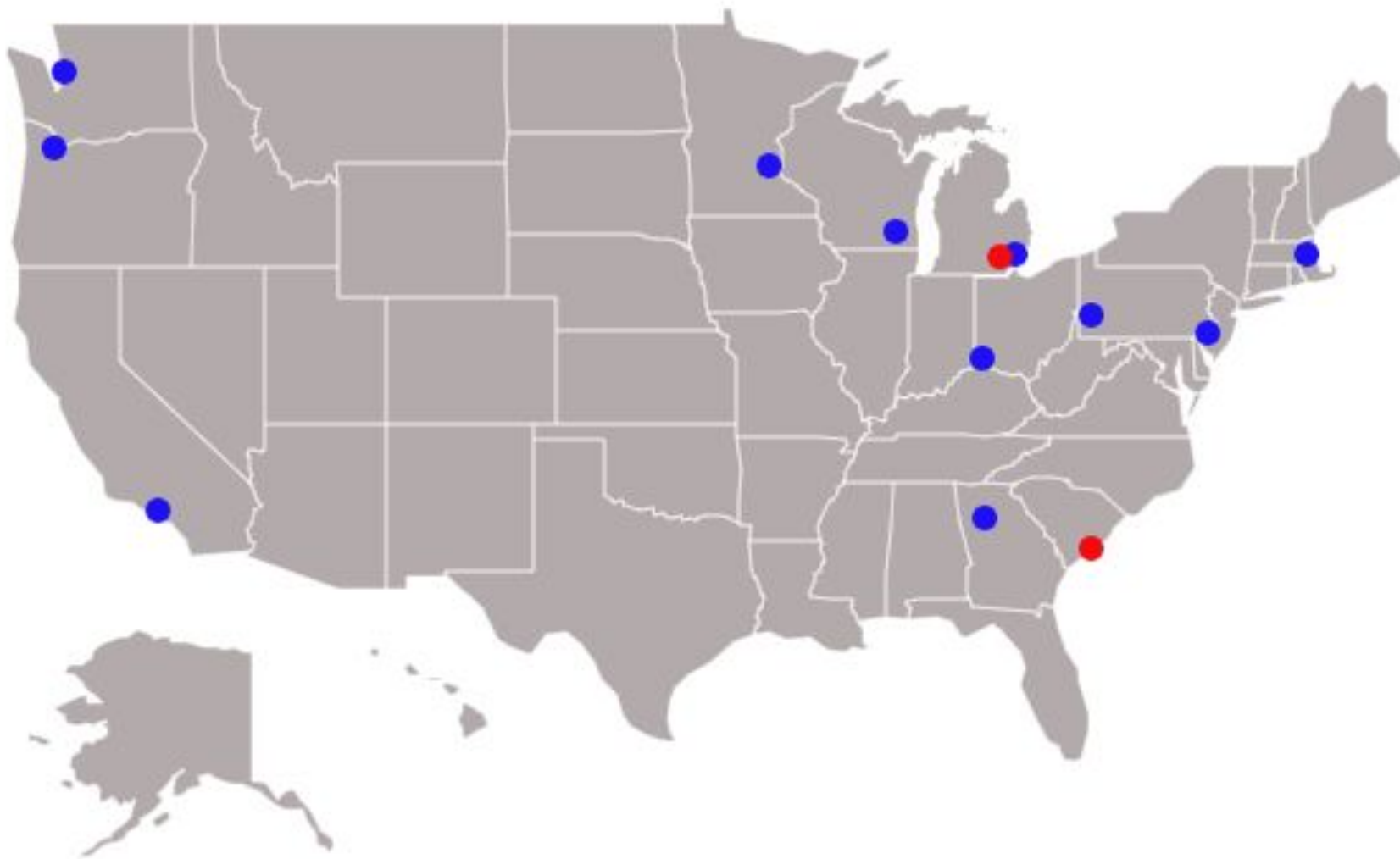


National Center
for Advancing
Translational Sciences



Investigator Meeting
February 2018





● Hub-Award
 ● Coordinating Center

SIREN Grant Awards

- Massachusetts General Hospital
- Temple University
- University of Pittsburgh
- Wayne State University
- University of Cincinnati
- Emory University
- Medical College of Wisconsin
- University of Minnesota
- University of Washington
- Oregon Health Sciences University
- University of California Los Angeles

Coordinating Centers

- University of Michigan
- Medical University of South Carolina

Specific aims

1. Diligently recruit, efficiently perform, and widely disseminate the most scientifically and **clinically important trials in emergency patient care**
2. Create a **culture of clinical trials that is collaborative**, multidisciplinary, diverse and inclusive through leadership, openness, and engagement
3. **Transform the emergency research enterprise** through innovative design, patient stakeholder engagement, better operational strategies

Design principles and organizational values

- Focus on **early treatment**.
- Focus on **meaningful outcomes for patients**.
- Focus on **efficiency**.
- Focus on **collaboration**.
- Focus on **transforming the clinical trials enterprise**.

Innovations in trial design

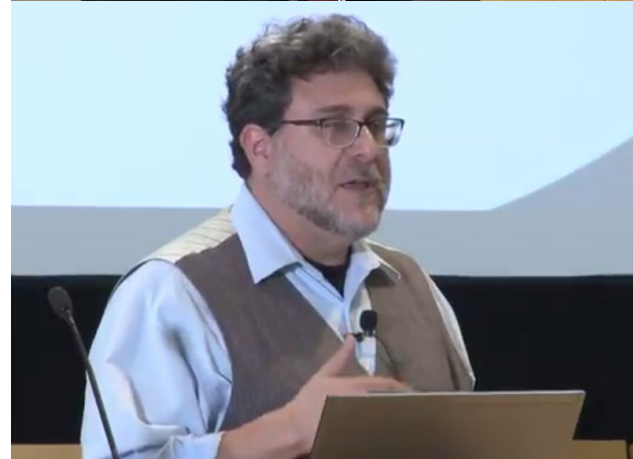
- Answering the most important questions with the most appropriate trial design for that question
 - Adaptive Designs
 - Registry Based RCT's (AHA and ACS/COT)
- Good Trial Design Affects Subject Accrual

Innovations in trial operations

- Study Teams Affect Trial Success
- Creating a Culture of Service
- Engaging Community Stakeholders

Multiple PI Leadership Plan - CCC

- Barsan
- Silbergleit
- Callaway



Multiple PI Leadership Plan - DCC

- Palesch
- Durkalski

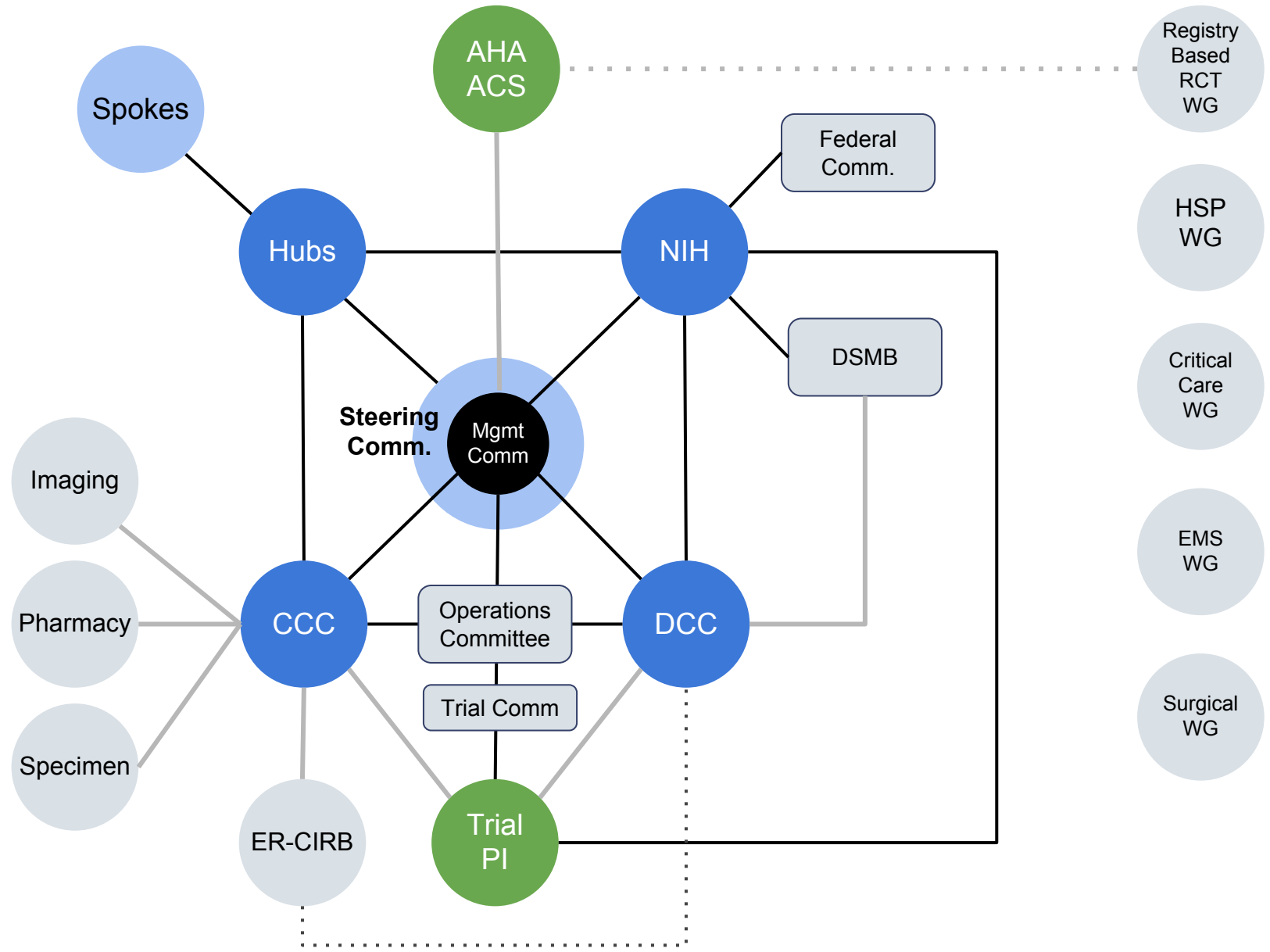


NIH Program Leadership

- Brown (NINDS)
- Mendoza-Puccini (NINDS)
- Sopko (NHLBI)
- Tinsley (NHLBI)
- Lupe Aquino (NCATS)

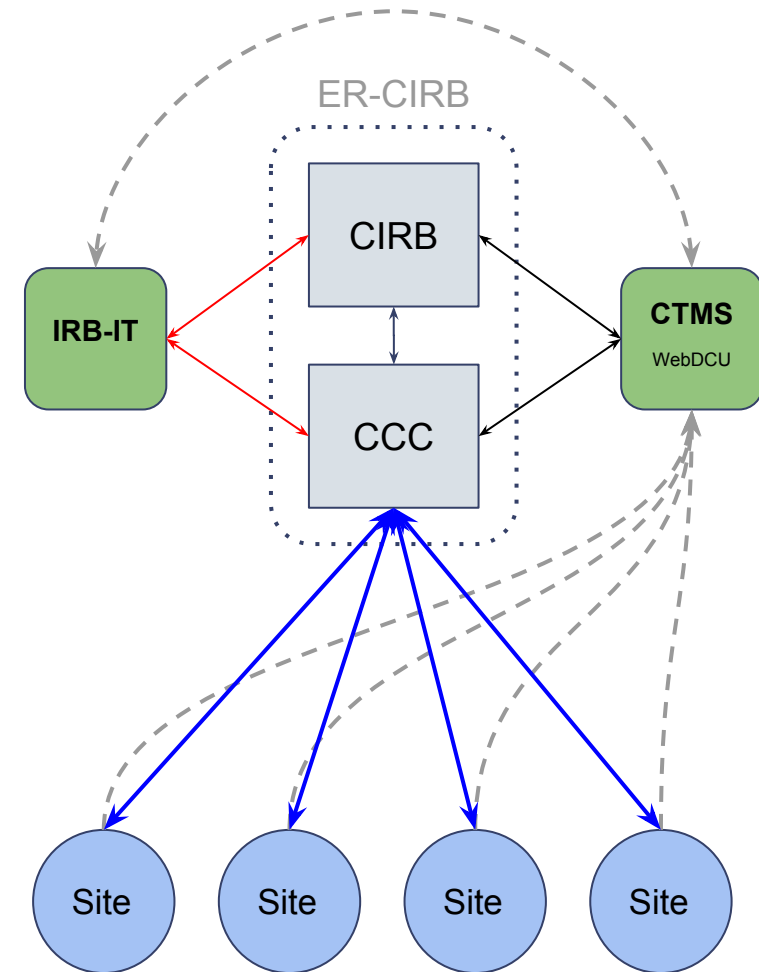


Organizational Structure



Emergency Research Central IRB (ER-CIRB)

- Close collaboration with vendor (ADVARRA)
- Mostly existing reliance agreements
- IRB communication all through CCC
- Info all submitted through WebDCU



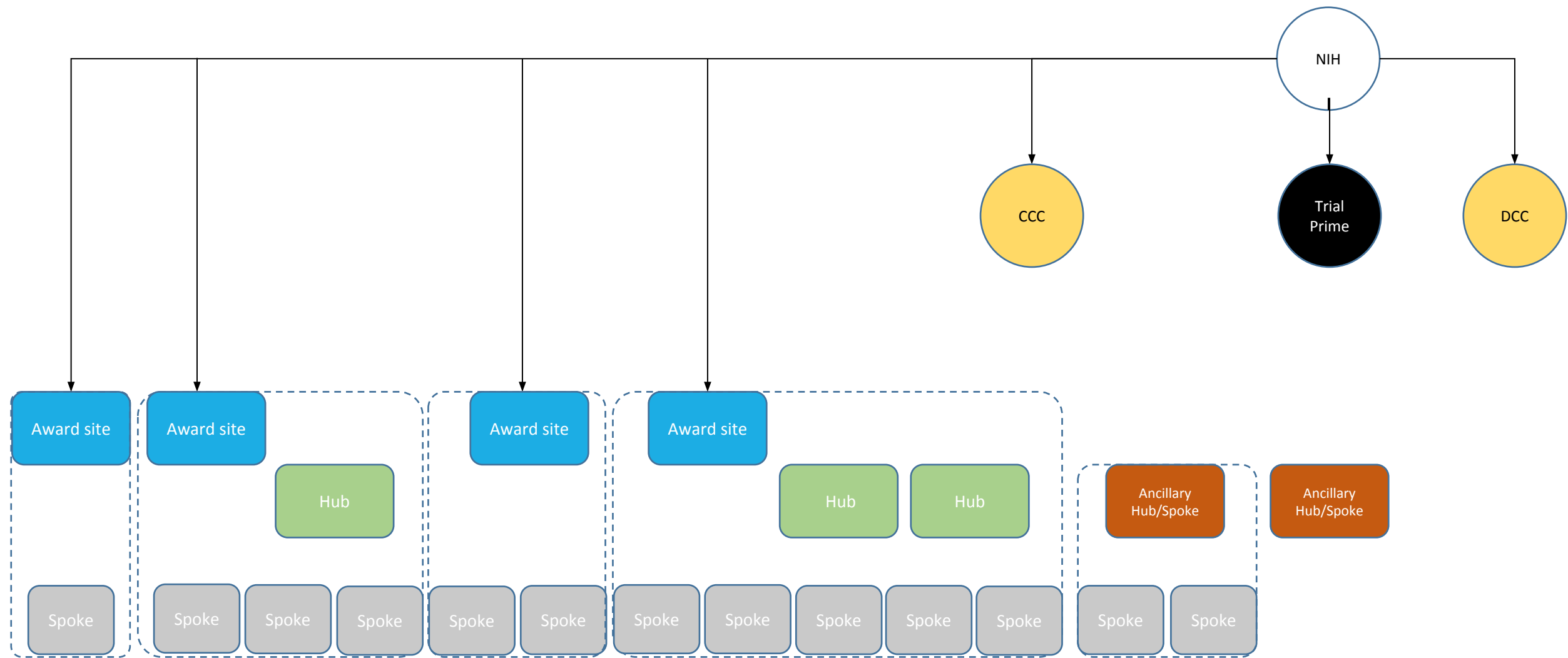


Illustration of grant relationships in SIREN

Hubs and spokes (designated by rectangles) represent enrollment sites. Circles are coordinating entities.

Hubs and spokes (designated by rectangles) represent enrollment sites. Circles are coordinating entities. Dotted lines represent optional relationships. Dashed lines represent Hub-spoke complexes. Number of blue "award sites" is established by number of individual NIH enrollment hub awards. Steering Committee includes all "award site" PI's (including multiple PI's) with only one vote per award site. Green "hubs" are affiliated with "award sites" but have their own master agreement with the CCC. Which sites within a hub-spoke complex are "hubs" is determined locally, but are typically distinguished by the "hub" being an institution that has its own spokes. Ancillary Hub/spokes are typically contracted by the Trial Prime if brought on for a single trial, or by the CCC if expected to participate in multiple trials (including those already participating in multiple trials).

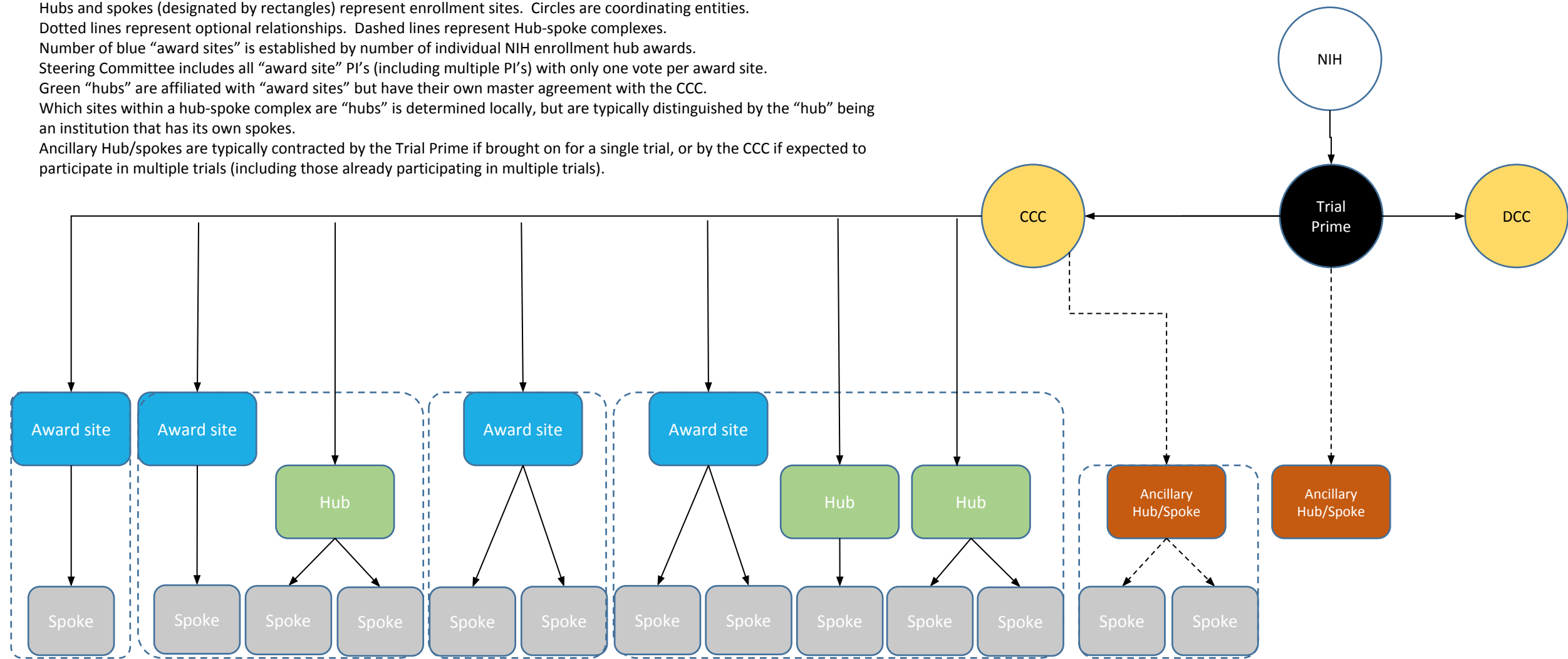


Illustration of proposed contractual relationships in SIREN

Key assets

- People
- Streamlined Financial Management
- Patient Recruitment and Enrollment
- Outstanding Data Management
- Quality Assurance

Trial Recruitment and Pipeline

Adaptable open clinical trial infrastructure

Collaborative leadership (typically multiple PI)

Respectful of investigators' ownership and control of the science

Sharing of operational and statistical responsibilities

Facilitating successful implementation and data integrity

Scientifically and Clinically Important Questions and Observations

Begin discussions with NIH program officers early

NIH Study Section



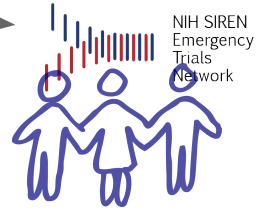
Clinical Trial Summary and Rough Budget

Institute Pre-approval to submit

Revise

Grant application(s)

Grant Award



Collaborative Grant Application and Protocol Development with input from Sites, Patients, and Others



Grant Award to Scientific PI's Institution with major subaward to CCC

DCC may be paired grant or subaward depending on IC

Begin discussions with SIREN leadership early as well.

SIREN leadership will evaluate fit for the network, contribute to concept, and relay to site PI's

SIREN will NOT be a layer of scientific peer review



Trial Recruitment and Pipeline

Effectiveness and efficiency from consistent re-use of:

- established skilled research teams and interpersonal relationships
- pre-existing contractual, regulatory, administrative frameworks
- familiar and consolidated clinical trial management technology.

Optimal strategy for working with the network is:

- contact prior to requesting permission from the institute to submit
- collaborative development of trial, grant application, and budget

Scope of Portfolio

Late learning phase or confirmatory phase trials

Patient oriented outcomes

Controlled efficacy to registry based RCT

Appropriate sized for our scalable network

Primary focus on neurological, cardiac, lung and blood (NINDS/NHLBI)

Secondary focus on other IC portfolios, and health services

Potential Sources of Trials

Early referrals from program officers at NIH

Investigators contacting us directly

SIREN initiated/generated trials

(addressing needs, portfolio gaps, IC priorities)

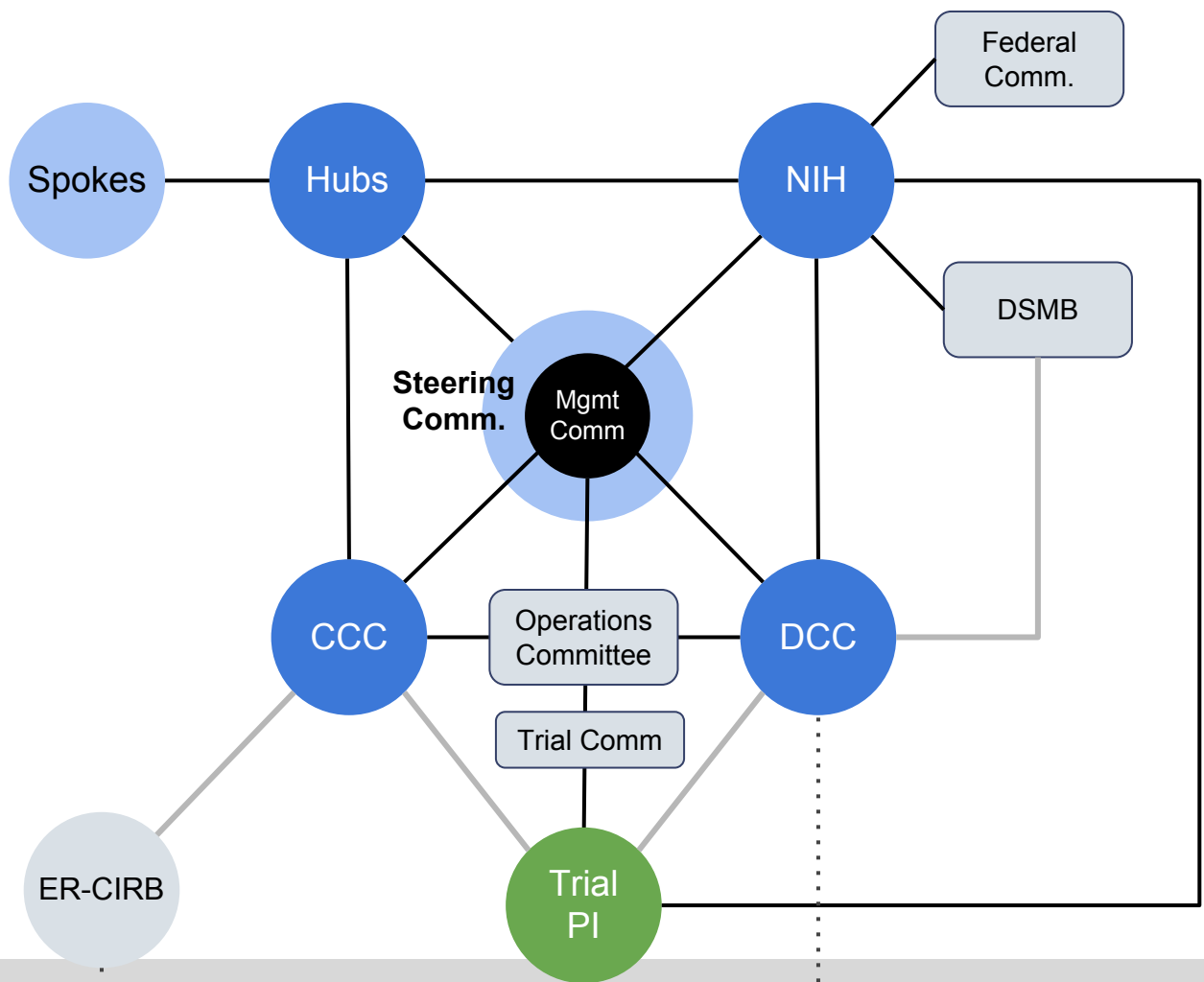
(retreats/workshops)

Industry partnerships (SBIRs)

Outreach

- Network Collaboration
 - PECARN
 - PETAL
 - LITES
 - StrokeNET
 - Others
- Stakeholder Engagement

QUESTIONS?



- HSP WG
- Critical Care WG
- EMS WG
- Ancillary WG

