

Neurological Emergencies Treatment Trials

NETT-SIREN CCC
Vision - Transition

Steering Committee Meeting
Baltimore, March 2017

Multiple PI Leadership Plan

- Barsan
- Silbergleit
- Callaway

Specific Aim 1

To diligently recruit, efficiently perform, and widely disseminate the most scientifically and clinically important trials necessary to advance the emergency care of patients with neurologic, cardiac, respiratory, hematologic and trauma emergencies. We will organize and conduct at least 4 large, simple trials in the ED and prehospital setting over the 5 year grant period.

Specific Aim 2

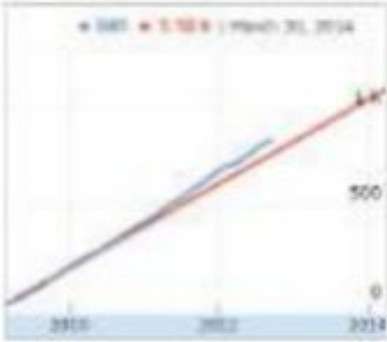
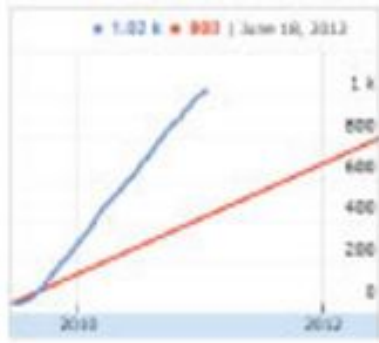
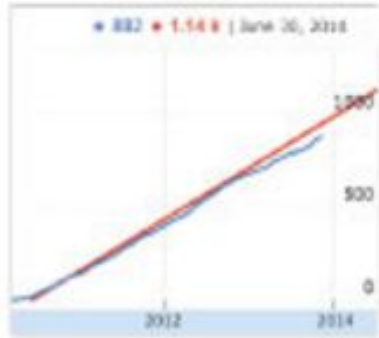
To create a coherent, collaborative, multidisciplinary emergency clinical trials community that is diverse and inclusive. Through leadership, openness, and engagement, SIREN will promote a culture of acute care investigation that ensures success within the network and provides collateral benefits to investigation, dissemination and translation beyond the network.

Specific Aim 3

To transform the emergency research enterprise, by exploring innovations in clinical trial designs (including adaptive and registry-based methods), by better and earlier engagement of patient stakeholders in trial planning, and by creative improvements in implementing and performing trials (using newer better strategies for planning, screening, collecting data, contracting, quality assurance, and compliance).

Guiding design principles and organizational values essential to the success of the NETT

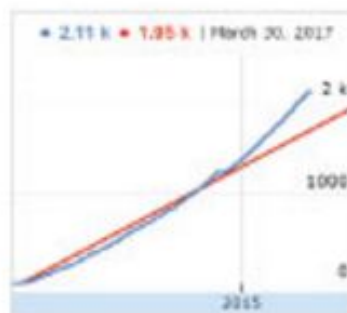
- Focus on **early treatment**.
- Focus on **meaningful outcomes for patients**.
- Focus on **efficiency**.
- Focus on **collaboration**.
- Focus on **transforming the clinical trials enterprise**.

Trial Acronym	(location of sites)	Enrollment Rate	Proportion	Award to CCC IRB
Intervention studied		red is expected blue is actual	Lost to f/u	Award to 1st site IRB
Funder, clinicaltrials.gov #, sponsor			Missing data	Award to 1st subject
# sites, local v. CIRB, follow up period, Journal pub			Eligibility dev.	Last subj to DB lock
				DB lock to prim pub
ALIAS	(North America)		2.8% 5.0% 3.1%	n/a n/a n/a 119 days 58 days
High dose albumin versus placebo in acute ischemic stroke				
NINDS, NCT00235495, U of Miami				
25 sites, local IRB, 12 mo follow up, Lancet Neurol				
RAMPART	(United States)		0% 0% 8.1%	n/a n/a n/a 12 days 65 days
IV lorazepam versus IM midazolam in prehospital status epilepticus				
NINDS, NCT00809146, Silbergleit				
17 hubs, local IRB, followed to hosp dc, NEJM				
ProTECT	(United States)		2.0% 5.9% 22.3%	61 days 208 days 304 days 82 days 39 days
Very early progesterone versus placebo infusion in moderate to severe traumatic brain injury				
NINDS, NCT00822900, Wright				
36 sites, local IRB, 12 mo follow up, NEJM				

POINT (North America, Overseas)

Clopidogrel plus aspirin versus aspirin alone for secondary stroke prevention after TIA or minor stroke

NINDS, NCT00991029, UCSF
110 sites*, local IRB, 90 day follow up



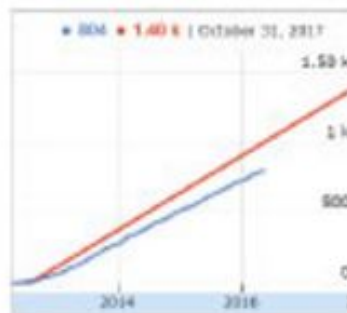
4.1%
n/a
11.0%

114 days
176 days
238 days
ongoing
ongoing

SHINE (United States)

Intensive versus standard glucose control in acute ischemic stroke complicated by hyperglycemia

NINDS, NCT01369069, U Virginia
62 sites, local IRB, 90 day follow up



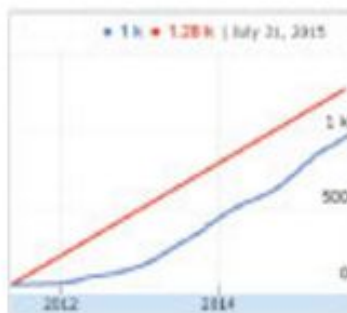
1.1%
n/a
0.8%

133 days
103 days
259 days
ongoing
ongoing

ATACH (North America, Overseas)

Intensive versus standard early blood pressure reduction in acute ICH complicated by hypertension

NINDS, NCT01176565, U Minnesota
110 sites, local IRB, 90 day follow up, NEJM



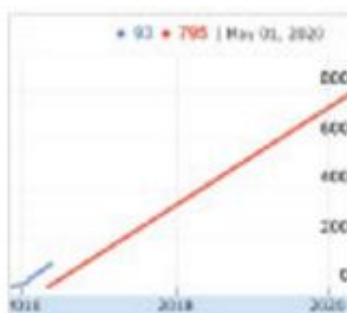
2.8%
3.9%
7.4%

17 days
14 days
284 days
77 days
21 days

ESETT (United States)

Effectiveness of fosphenytoin versus valproate versus levetiracetam in established status epilepticus

NINDS, NCT01960075, Kapur
56 sites, local IRB, followed to hosp dc



0%
n/a
19.4%

109 days
104 days
394 days
ongoing
ongoing

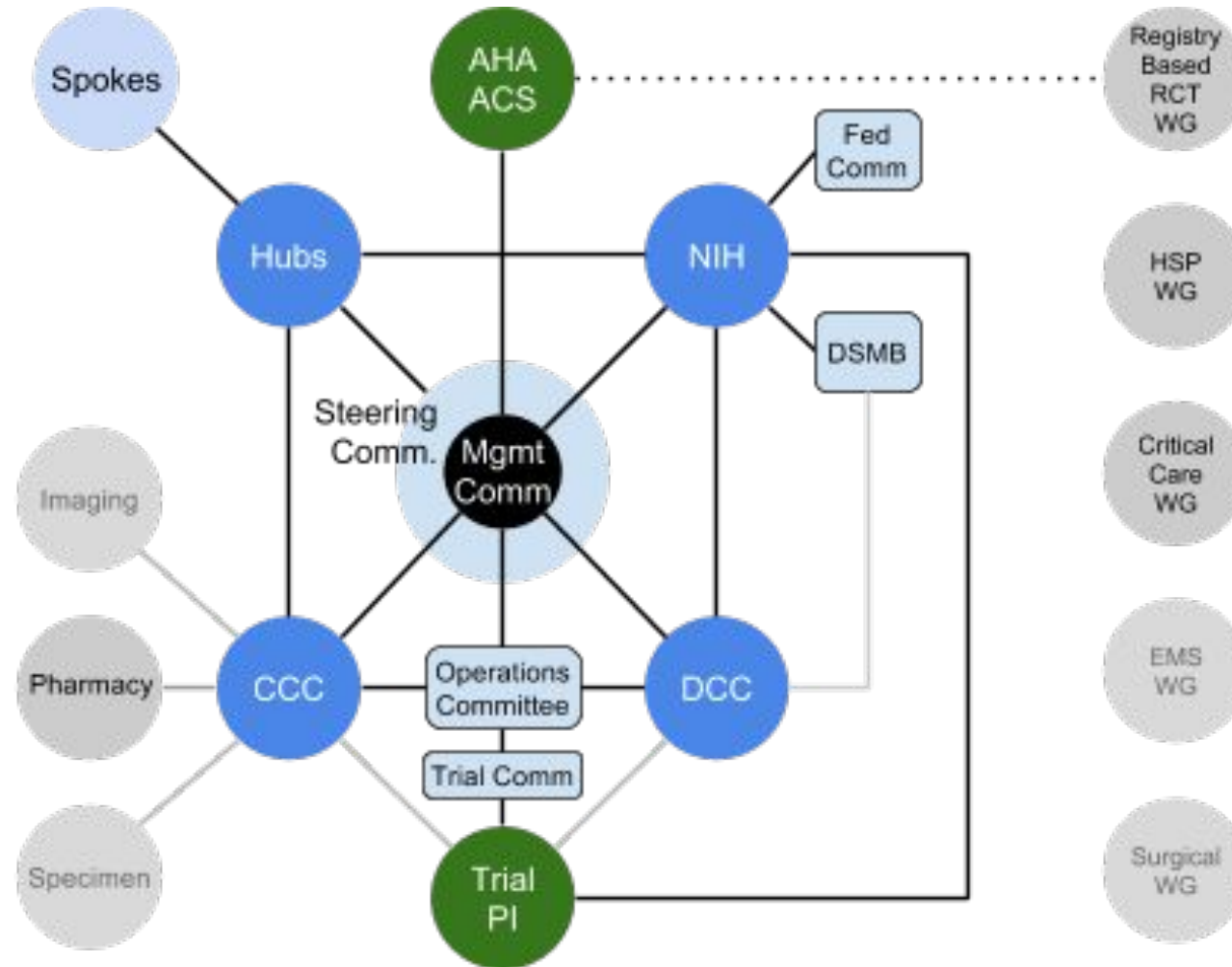
Innovations in trial design

- The most important questions utilizing the most appropriate trial design
 - 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

Organizational Structure



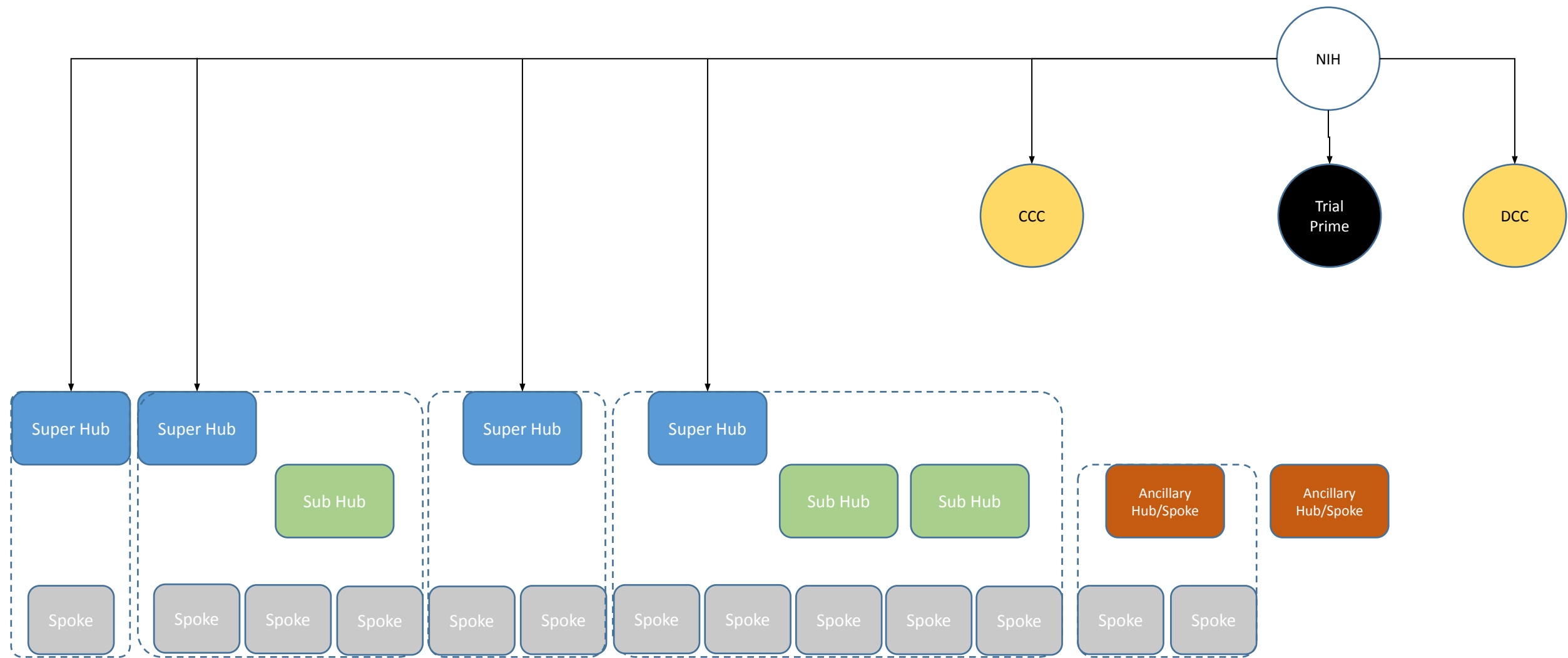
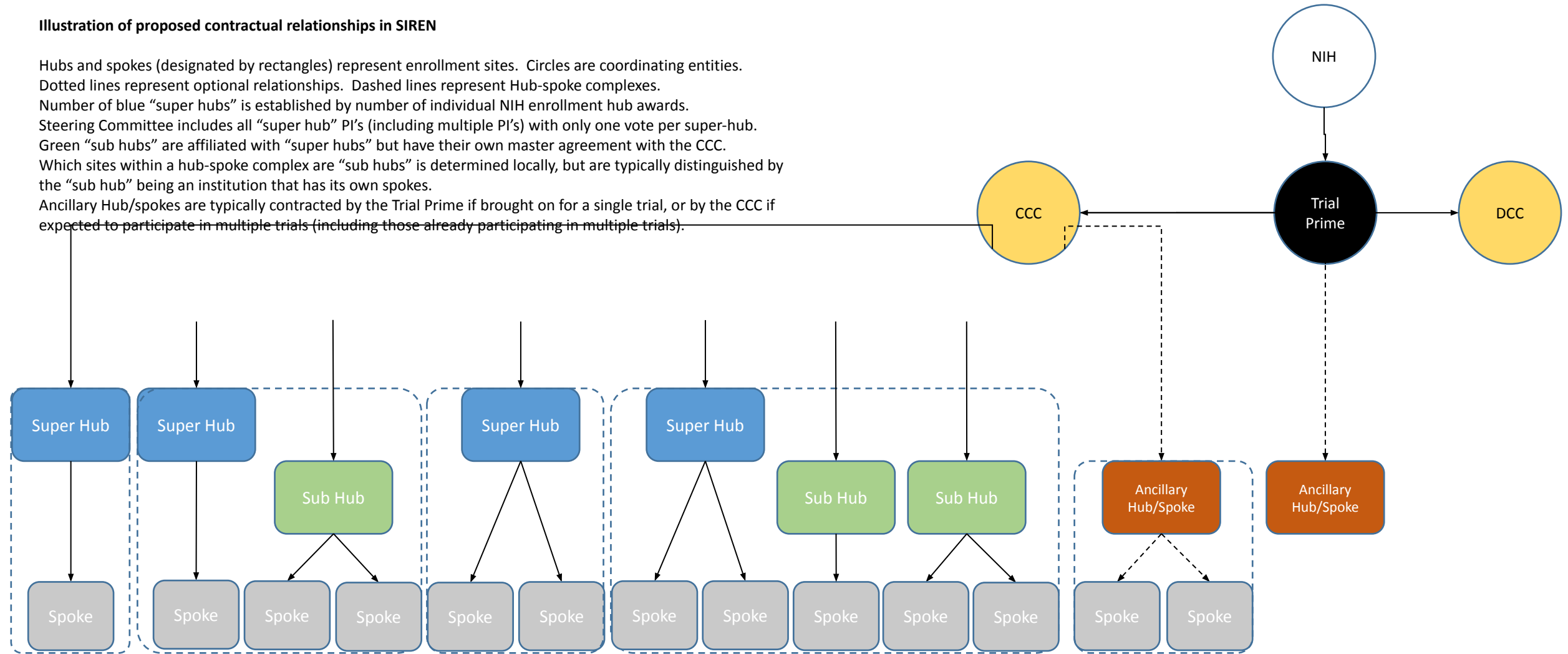


Illustration of grant relationships in SIREN

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

Illustration of proposed contractual relationships in SIREN

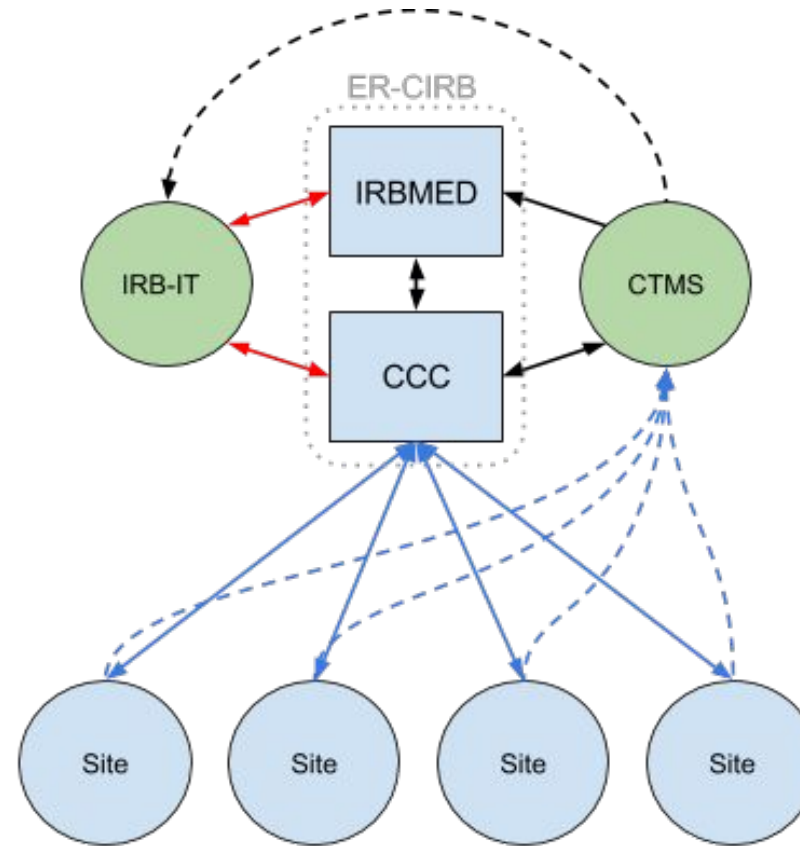
Hubs and spokes (designated by rectangles) represent enrollment sites. Circles are coordinating entities. Dotted lines represent optional relationships. Dashed lines represent Hub-spoke complexes. Number of blue “super hubs” is established by number of individual NIH enrollment hub awards. Steering Committee includes all “super hub” PI’s (including multiple PI’s) with only one vote per super-hub. Green “sub hubs” are affiliated with “super hubs” but have their own master agreement with the CCC. Which sites within a hub-spoke complex are “sub hubs” is determined locally, but are typically distinguished by the “sub 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).



Key elements

- People
- Streamlined Financial Management
- Quality Assurance
- Trial Recruitment and Pipeline
- Patient Recruitment and Enrollment

Emergency Research Central IRB (ER-CIRB)



ER-CIRB = Emergency Research Central IRB
IRBMED = University of Michigan Medical IRB
CCC = SIREN Clinical Coordinating Center
CTMS = Clinical Trial Management System
IRB-IT = IRB Information Technology System
Site = SIREN Clinical Enrollment Sites

Master & Reliance Agreements
Master IRB Application & Protocol
Site Application / ICD Submission
Data Transfer
Other Close Coordination/Read/Write



Core resources

- Planning and Design
- Education and Training
- Human Subjects Protection
- Outcomes Assessment
- Communications

Outreach

- Network Collaboration
- Stakeholder Engagement

Grant application available for viewing.....

<https://goo.gl/zUfgAK>