

# Experiences with an investigator-initiated clinical trial during COVID-19: transitioning from single- to multi-center

Clinical Research Seminar

Nick Bosch

4-14-2021

No disclosures

# Learning objectives

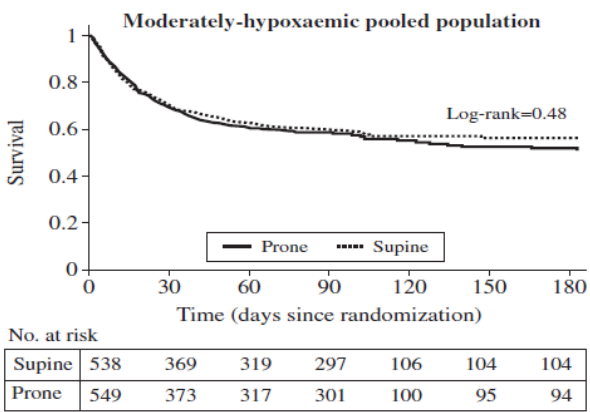
- Discuss mechanisms to identify potential collaborators
- Explore issues related to converting to a multi-center trial
- Identify strengths and weaknesses of decentralized IRB review

# Timeline

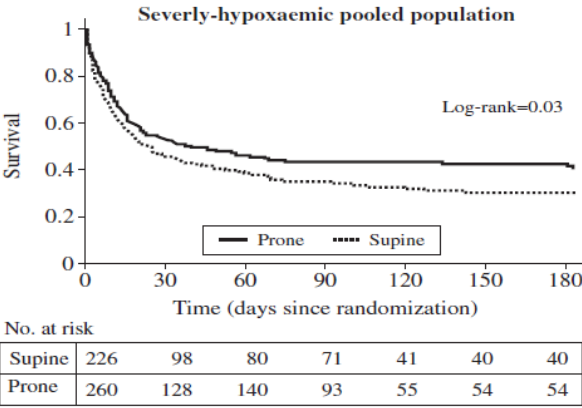


March 2020

*“Doing something”*



B

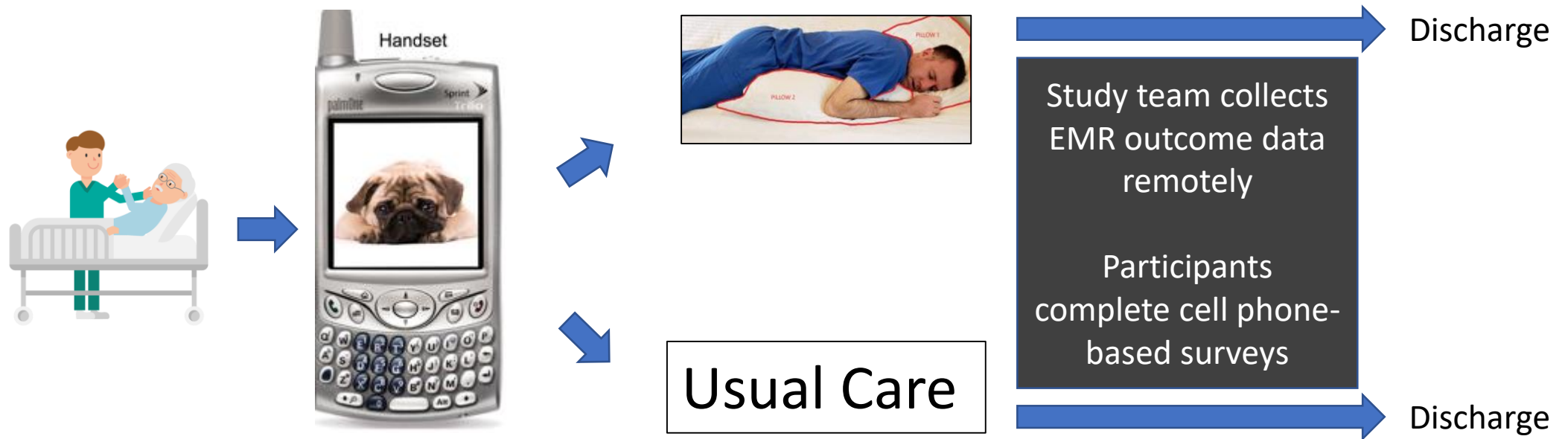


Gattinoni et al. Minerva Anestesiologica. 2010

# COVID-19 smArtphone-based Trial of Non-ICU Admission Prone Positioning - CATNAP



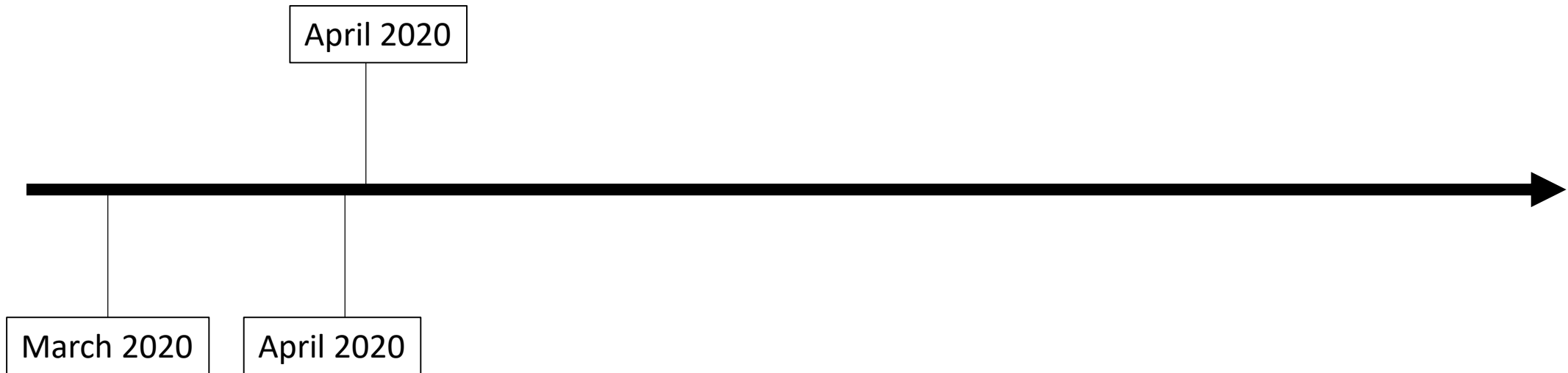
# COVID-19 smArtphone-based Trial of Non-ICU Admission Prone Positioning



30 eligible patients per day

0-1 consent per day

What happens when the surge ends?



# Identifying additional potential study sites

- Sites without a protocol
  - Social media
  - Collaboration platforms
- Sites with a protocol
  - Clinicaltrials.gov
  - CTSI





*“Hey Friends, we are starting a protocol for proning non-ICU COVID-19 patients twice a day for 3 hrs. Composite endpoints of HFNC, intubation, NIPPV, mortality. Not enough power on our own, based on published data. Anyone interested in a multi-site trial? Direct msg me. @accpchest”*

- Steven Q. Simpson





## Awake Prone Positioning in Early hypoXemia in COVID-19 (APPEX-19)

Principal Investigator(s):	Nicholas Bosch (Boston University) Garrett Rampon (University of Kansas Medical Center)
Location:	Boston, MA, United States
Study Type:	randomized
Status:	<b>IN PROGRESS</b>
Eligibility Criteria:	<ul style="list-style-type: none"><li>- Adult age &gt; 18</li><li>- COVID-19 confirmed or suspected</li><li>- admitted to a medical ward or planned admission to the medical ward within the next 24 hours</li><li>- has access to own functional smartphone</li><li>- English or Spanish speaking</li><li>- able to read simple instructions and answer simple written questions</li></ul>
Intervention Arms:	<p>Patients will receive a text message instruction linking them to a study website that contains:</p> <ol style="list-style-type: none"><li>1. Welcome message</li><li>2. Brief educational review on prone positioning</li><li>3. A text reminder to self prone 4 times daily for up to 2 hours at a time and at night for up to 9 hours at a time (texting reminder sent twice daily)</li><li>4. A survey collecting amount of time spent in prone position</li></ol>
Outcomes:	<ul style="list-style-type: none"><li>• ICU admission</li><li>• supplemental oxygen</li><li>• mechanical ventilation</li><li>• death</li></ul>

[Request to collaborate on this protocol](#)

ClinicalTrials.gov is a database of privately and publicly funded clinical studies conducted around the world.

Explore 374,155 research studies in all 50 states and in 220 countries.

See [listed clinical studies](#) related to the coronavirus disease (COVID-19)

ClinicalTrials.gov is a resource provided by the U.S. National Library of Medicine.

**IMPORTANT:** Listing a study does not mean it has been evaluated by the U.S. Federal Government. Read our [disclaimer](#) for details.

Before participating in a study, talk to your health care provider and learn about the [risks and potential benefits](#).

### Find a study (all fields optional)

#### Status ⓘ

Recruiting and not yet recruiting ☐ All studies ☒

#### Condition or disease ⓘ (For example: breast cancer)

#### Other terms ⓘ (For example: NCT number, drug name, investigator name)

#### Country ⓘ

[Search](#)[Advanced Search](#)[Help](#) | [Studies by Topic](#) | [Studies on Map](#) | [Glossary](#)

Row	Saved	Status	Study Title	Conditions
1		Recruiting	<a href="#">Prone Position and Respiratory Outcomes in Non-Intubated COVID-19 Patients: The "PRONE" Study</a>	<ul style="list-style-type: none"><li>Covid19</li><li>Pneumonia, Viral</li></ul>
2	<input type="checkbox"/>	Not yet recruiting	<a href="#">Prone Position in Non-Invasive Ventilation and High-Flow Oxygen Therapy</a>	<ul style="list-style-type: none"><li>Evaluation of <b>Prone</b> Position Effect During NI Respiratory Failure</li></ul>
3	<input type="checkbox"/>	Unknown <sup>†</sup>	<a href="#">Prone Versus Prone-Flexed Position For Percutaneous Nephrolithotomy (PCNL)</a>	<ul style="list-style-type: none"><li>Percutaneous Nephrolithotomy (PCNL)</li><li><b>Prone</b> Position</li><li><b>Prone</b>-Flexed Position</li><li>Complication of Surgical Procedure</li></ul>
4	<input type="checkbox"/>	Recruiting	<a href="#">Prone Position to Improve Oxygenation in COVID-19 Patients Outside Critical Care</a>	<ul style="list-style-type: none"><li>Pneumonia</li><li>Covid19</li></ul>
5	<input type="checkbox"/>	Completed	<a href="#">Early <b>Prone</b> Position on Coronavirus Disease 2019 Pneumonia</a>	<ul style="list-style-type: none"><li>Coronavirus Infection</li><li>Acute Respiratory Failure</li></ul>
6	<input type="checkbox"/>	Completed	<a href="#">Awake <b>Prone</b> Positioning and Oxygen Therapy in Patients With COVID-19</a>	<ul style="list-style-type: none"><li>COVID</li><li>ARDS</li><li>Pneumonia</li></ul>



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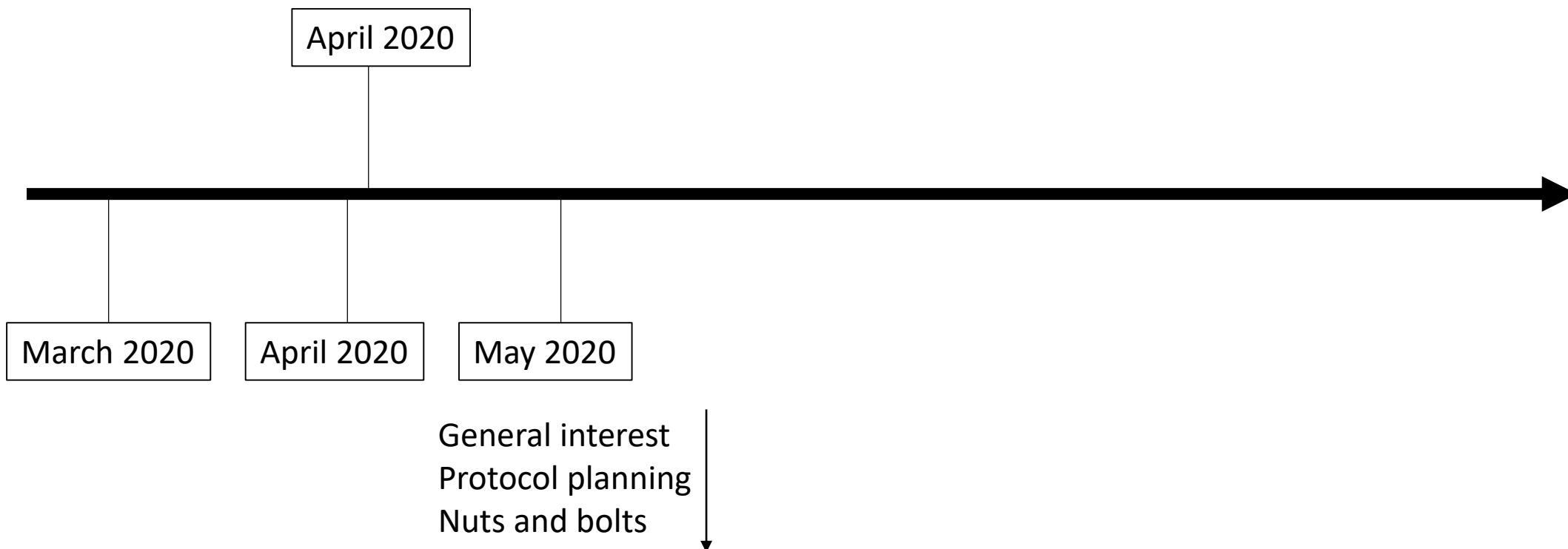
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# Accelerating Discoveries Toward Better Health

The BU-CTSI is a center of expertise providing tools, services and resources to clinical investigators, maximizing the impact of discoveries & speeding the translation of research into improved patient care



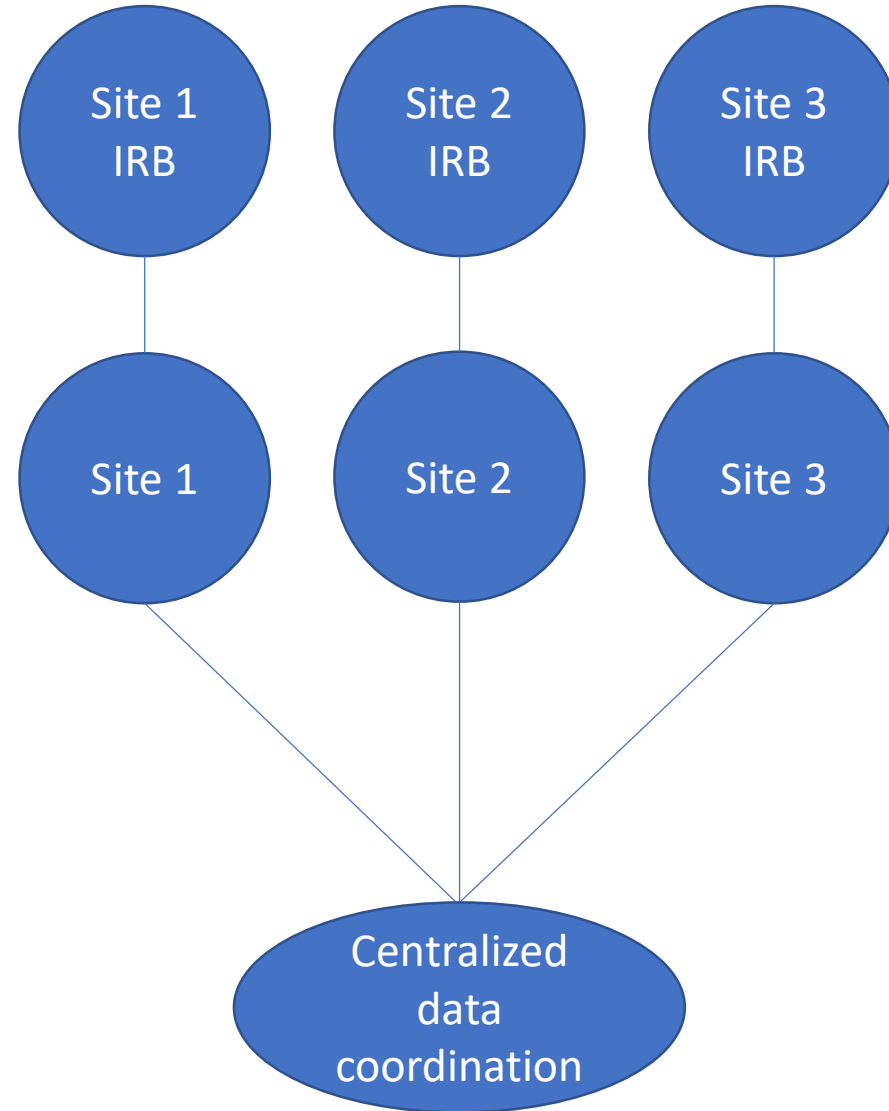
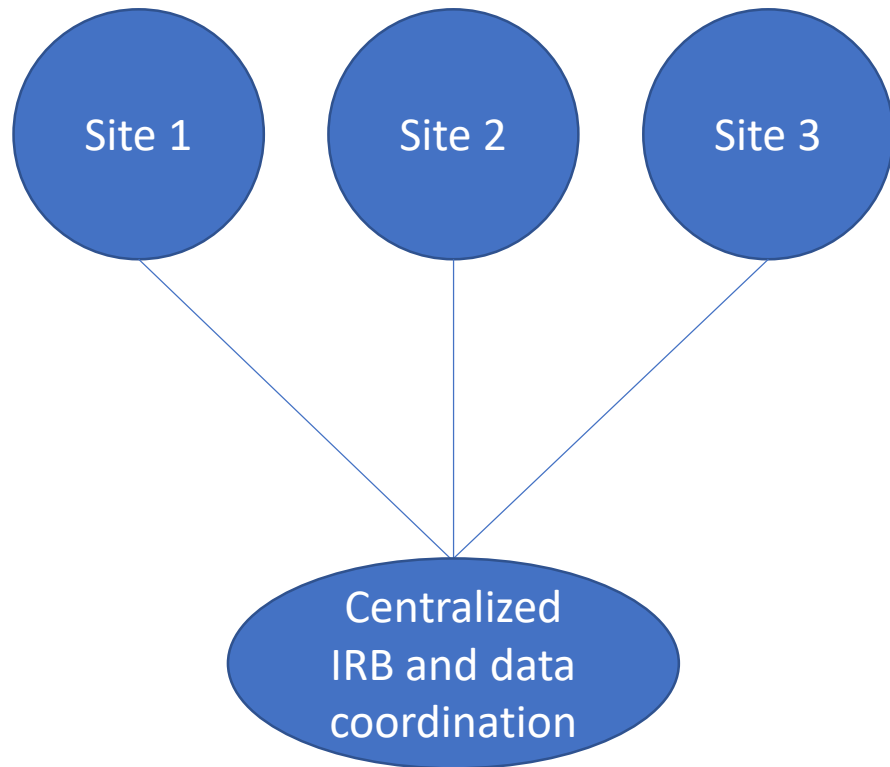


# Lessons learned from meeting with prospective sites

- Set agenda and deadlines early on for gauging interest
- Balancing new ideas/enthusiasm with practicality to facilitate buy-in and foster engagement
  - Protocol changes
  - Name change
  - Related studies
- Establish a core team to make decisions
- Transparency – the good and maybe bad
- Establish authorship expectations early
- Sites with existing protocols less likely to collaborate

# Nuts and Bolts

- Centralized vs institutional (decentralized) IRB



# Approach to IRB in multicenter studies

- Centralized IRB (required for NIH-funded US-based multicenter trials)
  - Advantages:
    - efficiency (especially for protocol amendments)
    - homogenous study procedures
  - Disadvantages:
    - **limitations of IRBs to act as centralized IRB especially during COVID-19 and for unfunded studies**
    - site specific requirements may be more difficult to address
- Institutional IRB
  - Advantage:
    - **faster uptime for some study sites, especially if sites have varying readiness to start**
    - **stronger knowledge about local study requirements/needs/patients/customs/community**
    - **Potentially more control over the speed of review**
  - Disadvantage:
    - potentially slower uptime for some study sites
    - still needs a data coordinating center
    - Small sites may not have IRBs
    - **Protocol amendments are slow**



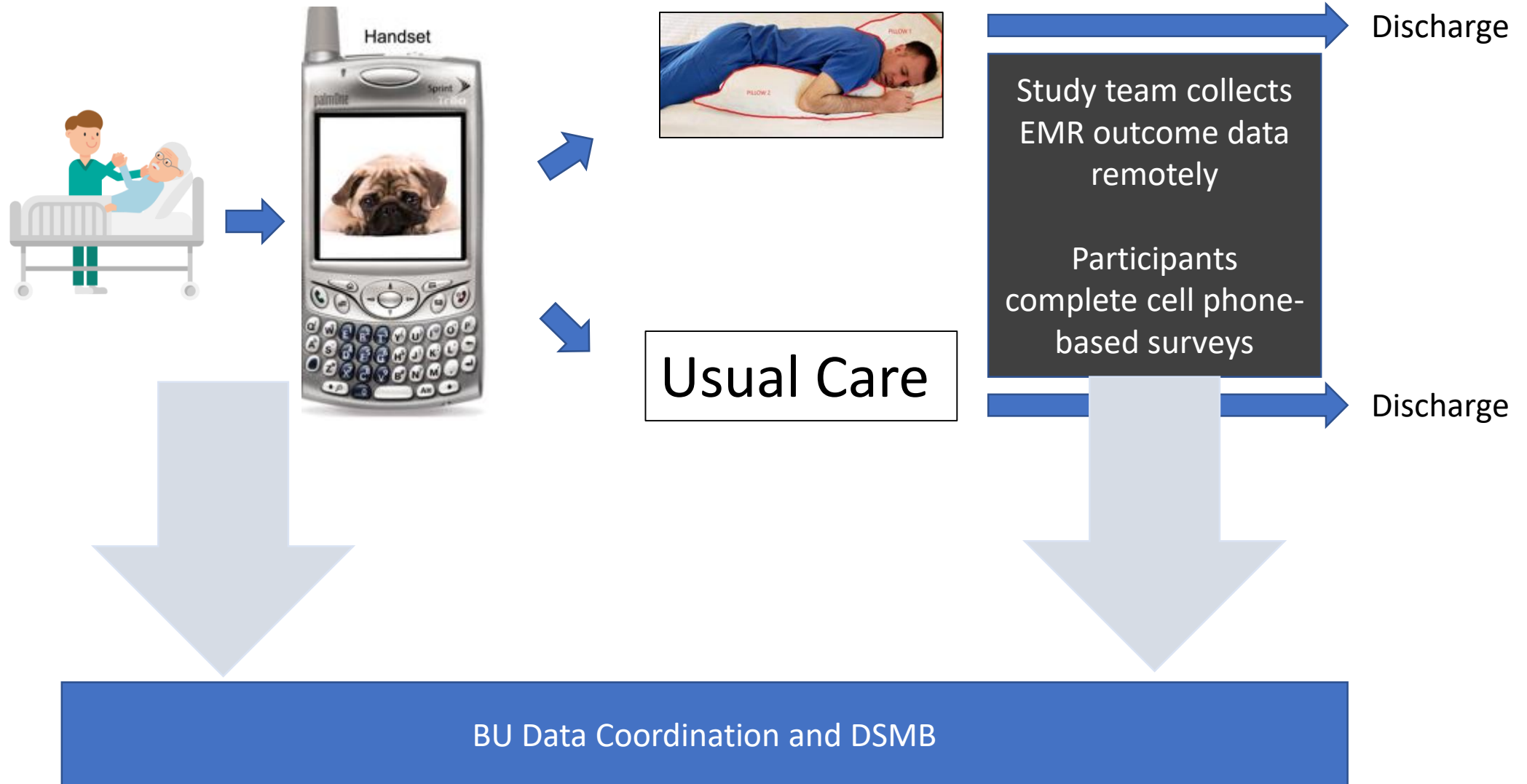
# Nuts and bolts discussions

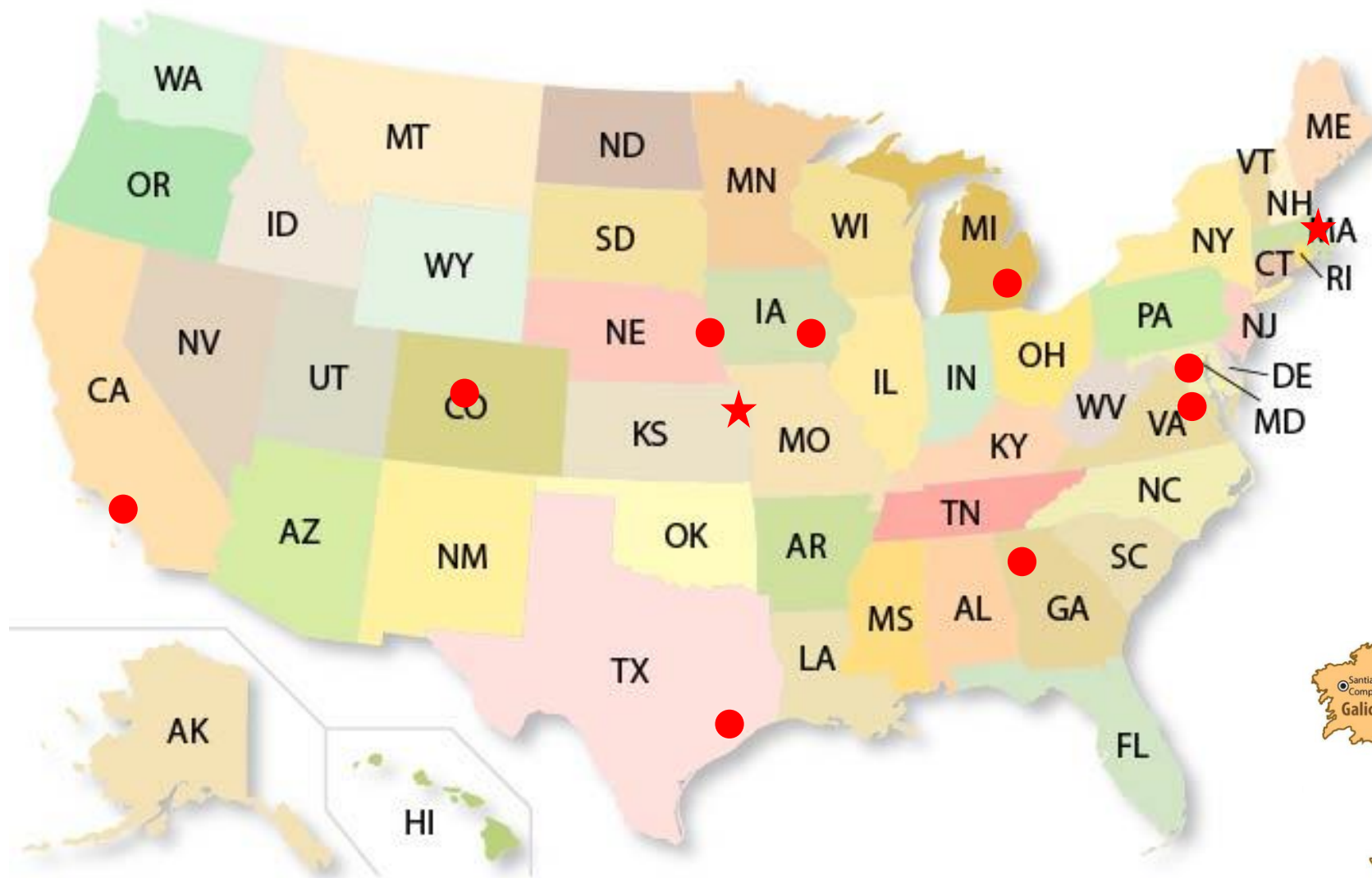
- Data use agreements
  - Limited
  - De-identified
- Data coordination and workflow mapping
  - REDCap/Qualtrics
    - DAGs
  - DSMB Review
  - Adverse event reporting
- Site specific issues
  - Double IRB review at VA sites
  - COVID-19 study order priority
  - Translating study materials into multiple languages
  - Remote consent platforms
- Pragmatic protocol focus minimizes site specific issues
- Repository of study site information
  - BMC box
  - BU Google Drive

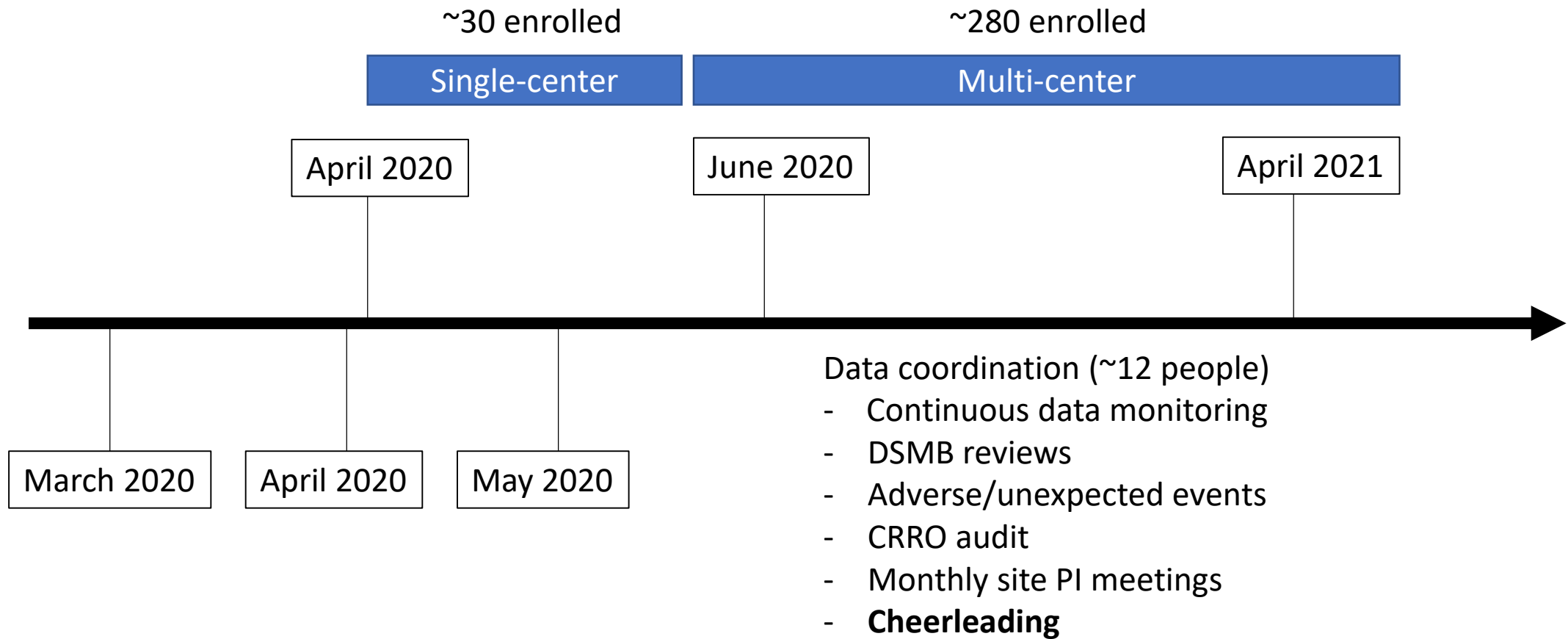
# Continuous on-boarding of new sites (1-2 months on average)

- Sites express interest
- Site credentials reviewed
- Protocol sharing
- Site specific IRB review
- Data use agreement
- Training and access to study data platforms
- Begin enrollment
- Audit of initial participant workflow at each site

# Awake Prone Position for Early Hypoxemia in COVID-19







# Team/tasks

- Twice daily data coordination/enrollment tracking
  - Nick, Katie, Kari
- Twice daily survey tracking
  - Nick G, Chas
- Weekly DSMB contact
  - Justin
- Bimonthly interim analysis data preparation and periodic REDCap servicing
  - Mike
- Monthly site PI meetings
  - Nick, Garrett
- Periodic adverse event reporting
  - Nick, Garrett, Justin

- Site specific unplanned issues
  - Nick, Garrett

- BMC enrollment and data collection
  - Katie, Kari, Nick

- Interim analyses
  - Gheorghe, Mike
- DSMB board
  - Art, Hasmeena, Bob

- Protocol amendments and site administrative tasks/onboarding, cheerleading
  - Nick

# Ending the study

- Plan ahead
  - Contributor list
  - Author order/writing committee
    - settle disputes
  - Data cleaning
- Analysis/manuscript
  - Sharing results with the study sites
- Future projects
  - Don't let the collaborations end!


# Overall lessons learned

- It is hard to oversee enrollment at your own institution and lead a multicenter study
- Audit, audit, audit
- Limit protocol amendments with decentralized IRB review
- Sites are willing (at least during the pandemic) to contribute despite little to no funding, but they need lots of cheerleading and thanking



# Thanks!


- Allan Walkey
- Steven Simpson
- Karla Damus
- Gheorghe Doros
- Michael Garcia
- Kari Gillmeyer
- Nick Griffiths
- Jung Hyun Lee
- Katherine Modzelewski
- Garrett Rampon
- Craig Ross
- Mary-Tara Roth
- Justin Rucci
- APPEX-19 site research teams

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