THRIVE

We will begin shortly.

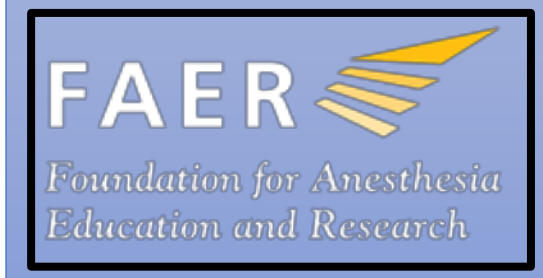
For those in-person wifi access information below

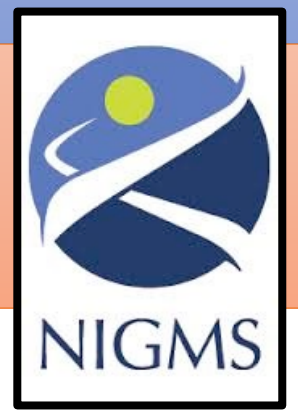
Network = JWMarriot-conference

Password: meeting2022

WELCOME ALL

Acknowledgements



I have no conflicts of interest to declare.

Kevin K. Tremper Research Professor,
Department of Anesthesiology

CONGRATULATIONS

Sachin Kheterpal, MD, MBA

ELECTED TO

National Academy of Medicine

UNIVERSITY OF MICHIGAN
MEDICAL SCHOOL
MICHIGAN MEDICINE

Funding Opportunities

All Funding Opportunities

What & Who We Fund +

What You Need To Know To Apply +

Merit Review +

Closed

Phased Large Awards for Comparative Effectiveness Research – Cycle 3 2020

RESEARCH Cycle 3 2020

Research Initiative Highlights

This PCORI funding announcement invites applications for high-quality comparative effectiveness research (CER) projects that will examine a critical patient-centered research question that is also relevant to decision makers and other stakeholders. For this PFA, investigators should propose an individual-level or cluster randomized controlled trial of significant scale and scope, requiring funding in excess of $10 million in direct costs. The proposed trials should address important decisional dilemmas that require important new evidence about the comparative effectiveness of available interventions. Proposed studies should compare interventions that already have established evidence of efficacy or are in widespread use. Clinical interventions (such as medications, diagnostic tests, or procedures) and delivery system interventions are appropriate for study.


THRIVE

Research In progress; Not yet recruiting

THRIVE: Trajectories of Recovery after Intravenous Propofol vs inhaled VolatilE anesthesia

Sign Up for Updates

JUMP TO SECTION

https://www.pcori.org/research-results/2021/thrive-trajectories-recovery-after-intravenous-propofol-vs-inhaled-volatile-anesthesia


UW Medicine
UW SCHOOL OF MEDICINE
OREGON HEALTH & SCIENCE UNIVERSITY
UCSF
Stanford MEDICINE
UCLA Health
UNIVERSITY OF UTAH HEALTH CARE
Medicine
Medicine
ST. MARY MERCY LIVONIA
Frederick Memorial Hospital
THE UNIVERSITY OF CHICAGO MEDICINE
BRONSON
Hollands Hospital
Beaumont
Spectrum Health
Sparrow
Cleveland Clinic
University of Vermont MEDICAL CENTER
Dartmouth-Hitchcock
MASSACHUSETTS GENERAL HOSPITAL
BRIGHAM AND WOMEN'S HOSPITAL
Yale University School of Medicine
COLUMBIA UNIVERSITY MEDICAL CENTER
Memorial Sloan Kettering Cancer Center
Weill Cornell Medicine
NYU Langone MEDICAL CENTER
Penn Medicine
UVAHealth
DukeHealth
UNC SCHOOL OF MEDICINE
Wake Forest School of Medicine
VANDERBILT UNIVERSITY MEDICAL CENTER
UFHealth
Washington University in St. Louis SCHOOL OF MEDICINE
UAMS
THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
EMFAS.IS

THRIVE

MPOG
MULTICENTER PERIOPERATIVE OUTCOMES GROUP

Dashboard Login

About | Join | Research | Quality | Tools | Downloads | Events / News

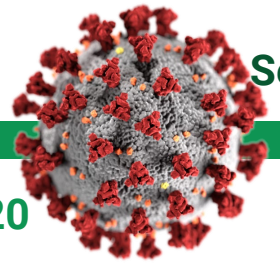
Clinical Trials Network (IMPACT)

This award was established by leaders of academic anesthesiology organizations that recognized there was a need to conduct large pragmatic trials in order to answer important questions in anesthesiology-related research

Welcome

Our journey here

Michael & Sachin discuss ideas for LOI



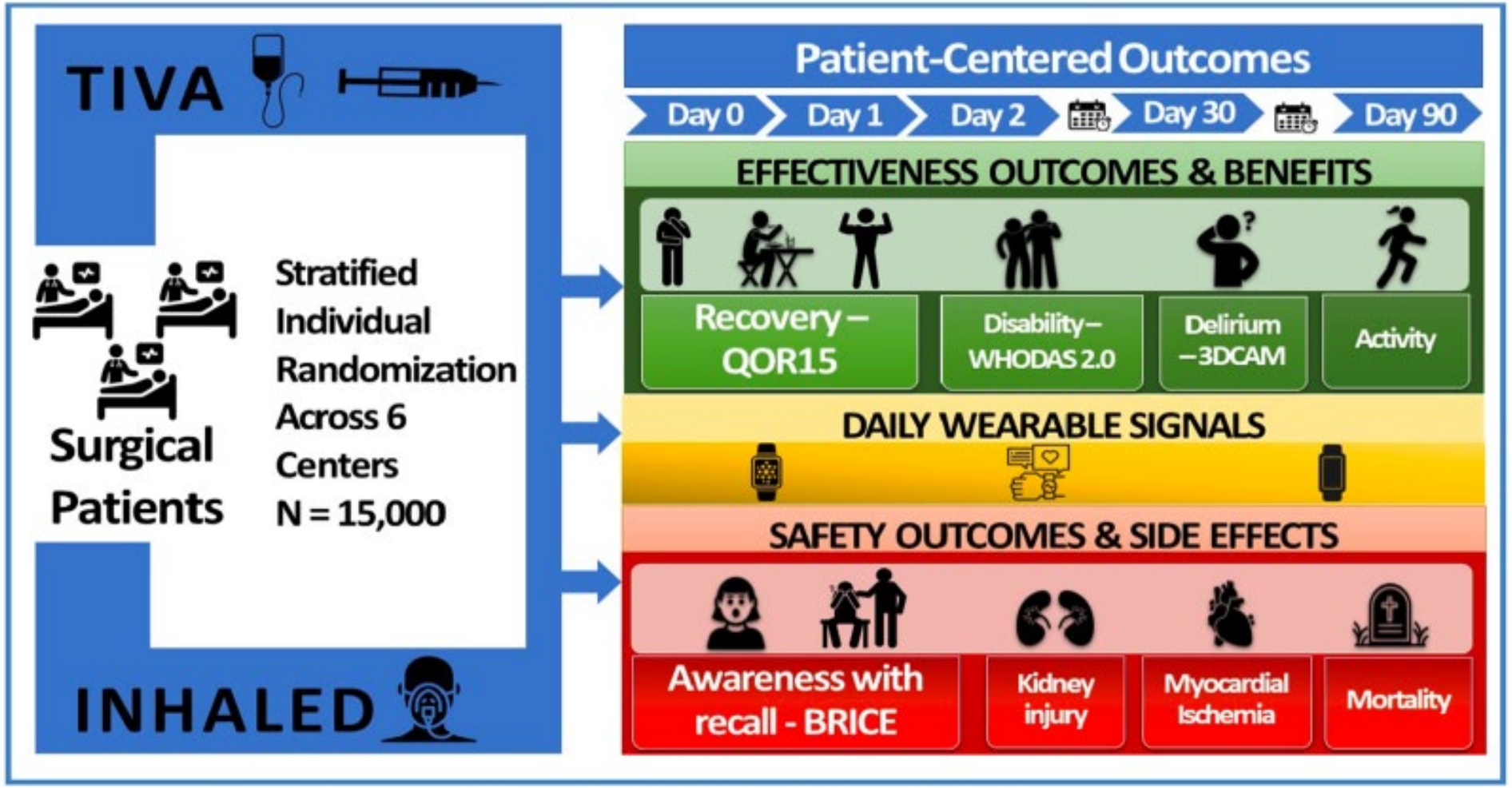
Mar 7, 2020

Sep 29

Oct 27

LOI submitted, then approved

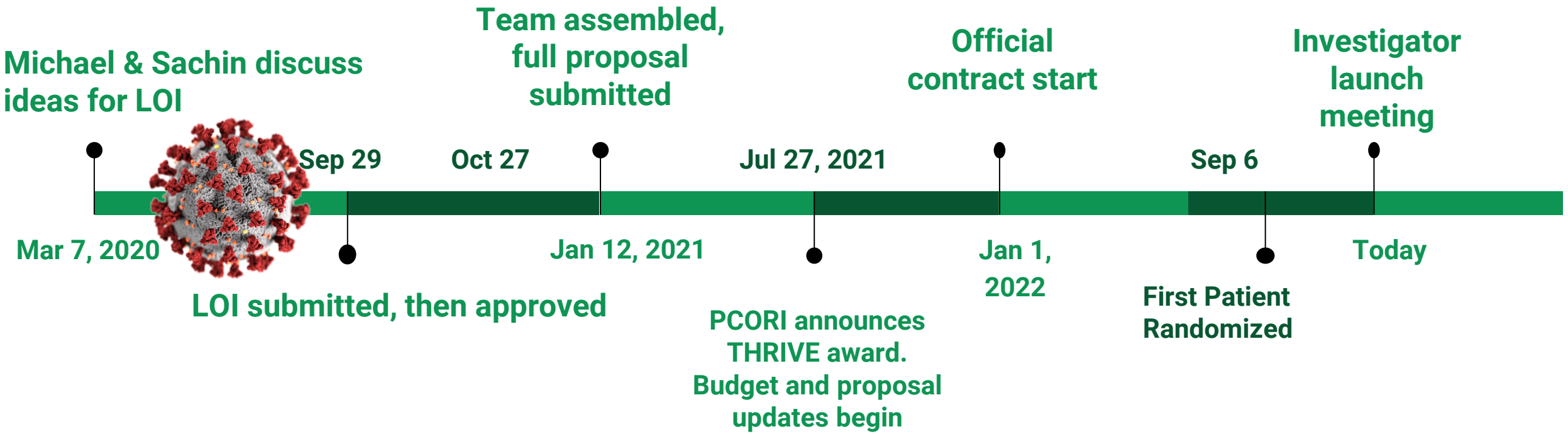
THRIVE - Version 1.0

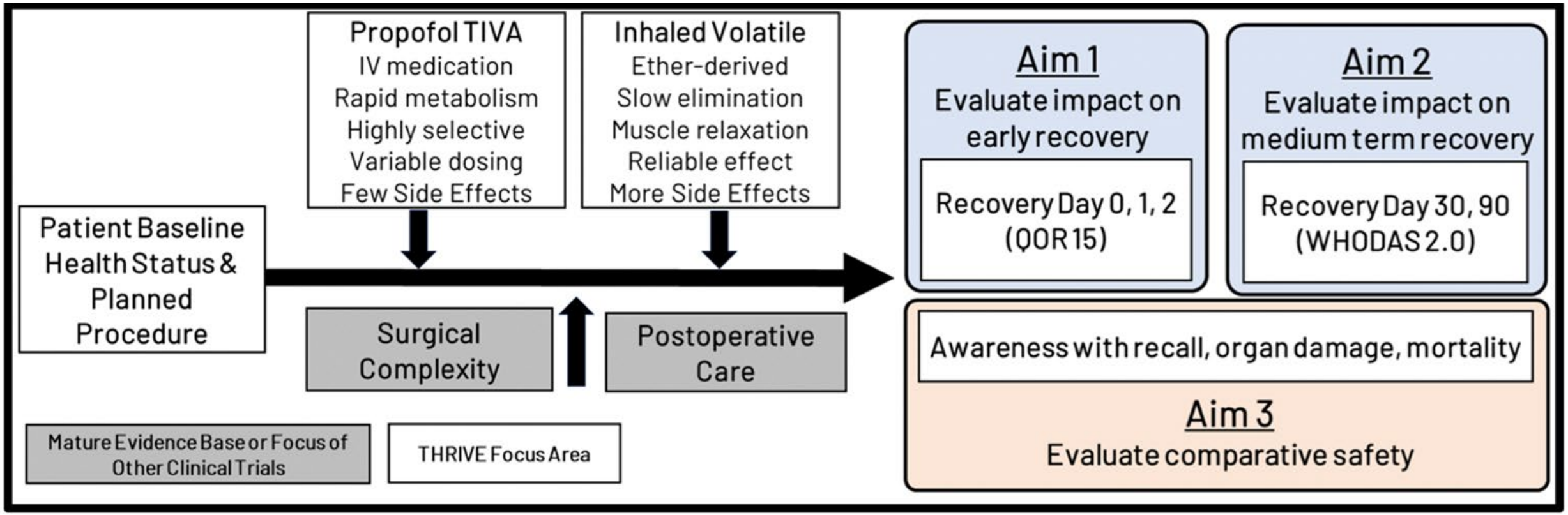


LOI: September 29th 2020

Figure 1: THRIVE trial study design

Our journey here




Propofol TIVA
IV medication
Rapid metabolism
Highly selective
Variable dosing
Few Side Effects
Inhaled Volatile
Ether-derived
Slow elimination
Muscle relaxation
Reliable effect
More Side Effects
Patient Baseline Health Status & Planned Procedure
Surgical Complexity
Postoperative Care
Aim 1
Evaluate impact on early recovery
Recovery Day 0, 1, 2 (QOR 15)
Aim 2
Evaluate impact on medium term recovery
Recovery Day 30, 90 (WHODAS 2.0)
Awareness with recall, organ damage, mortality
Aim 3
Evaluate comparative safety
Mature Evidence Base or Focus of Other Clinical Trials
THRIVE Focus Area

THRIVE team members

Here today in person

Michael Avidan
Mara Bollini
Michael Burns
Hugo Campos
Chelsea Cloyd
Nicole Eyrich
Allison Janda
Sathish Kumar
Sachin Kheterpal
Mark Neuman
Bethany Pennington
Amy Price
Nirav Shah
Laura Swisher

Here in spirit (or digitally)

Arbi Ben Abdallah
Sarah Buday
Jennifer Carron
Larry Chu
David Clark
Douglas Colquhoun
Ralph Dacey
Mark Dehring
Stephen Gregory
Bruce Hall
Melissa Hicks
Katie Holzer
Rose Ignacio
Heidi Klosterman
Amy Krambrink
Meghan Lane-Fall

Here in spirit (or digitally)

George Mashour
Bernadette Peters
Mary Politi
Christie Ramirez Rodriguez
Linda Robison
Michelle Romanowski
Anik Sinha
Cathie Spino
Steve Thelen Perry
Brian Torres
Shelly Vaughn
Phil Vlisides
Zhenke Wu
Andrew Zittleman

Thank you for..

Your commitment and support since the beginning of this journey

Your frank feedback

Your impact on the protocol

Your trust

Your resources

Your local political capital

The Clinical Coordinating Center (CCC) and the Data Coordinating Center (DCC)

Laura Swisher and Chelsea Cloyd

THRIVE

The Clinical Coordinating Center (CCC)

Washington University School of Medicine

THRIVE

Clinical Coordinating Center: Study Support

1. General Oversight of site performance and clinical issues
2. sIRB management and coordination with performance sites
3. Management of SAE reporting and review, in conjunction with the DCC
4. Maintenance of documentation (DOA, Licensure, training certificates, etc.)
5. Continued training for new study members
6. Escalation of unexpected issues and performance concerns
7. Will guide site adoption of any protocol or process changes

THRIVE

Clinical Coordinating Center: Study Support

- Monthly calls to sites after activation will cover
  - Enrollment numbers and demos
  - Regulatory
  - Protocol adherence (study arm compliance, withdrawal #s, deviations, etc.)
  - Help troubleshooting issues as needed
- Available on an “as needed” basis to help site achieve study goals
- Laura Swisher, Program Manager, goodl@wustl.edu

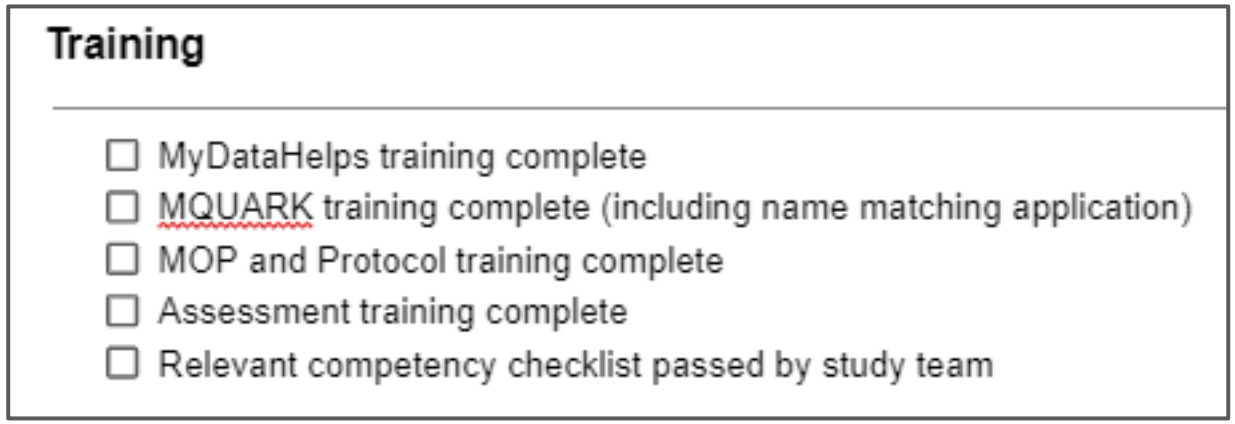
THRIVE

Clinical Coordinating Center: Activation Support

- The CCC can provide suggestions on clinical stakeholder educational and informational session outreach
  - Template slide decks for clinician educational and informational sessions available

THRIVE

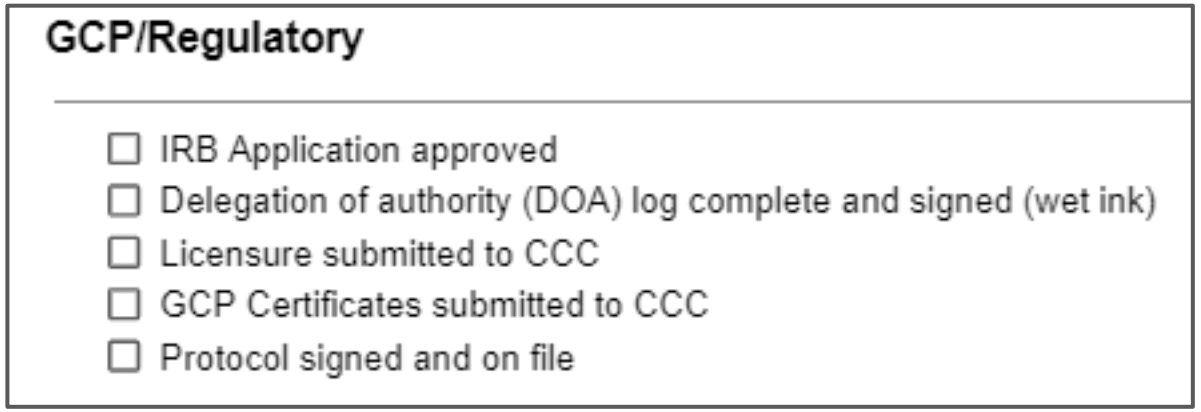
Clinical Coordinating Center: Activation Support



- Will provide MOP and Protocol training for relevant, engaged study team members
- Will track training and work with the DCC to schedule MQUARK and MyDataHelps training
- Will ensure all training is complete and help sites meet this goal

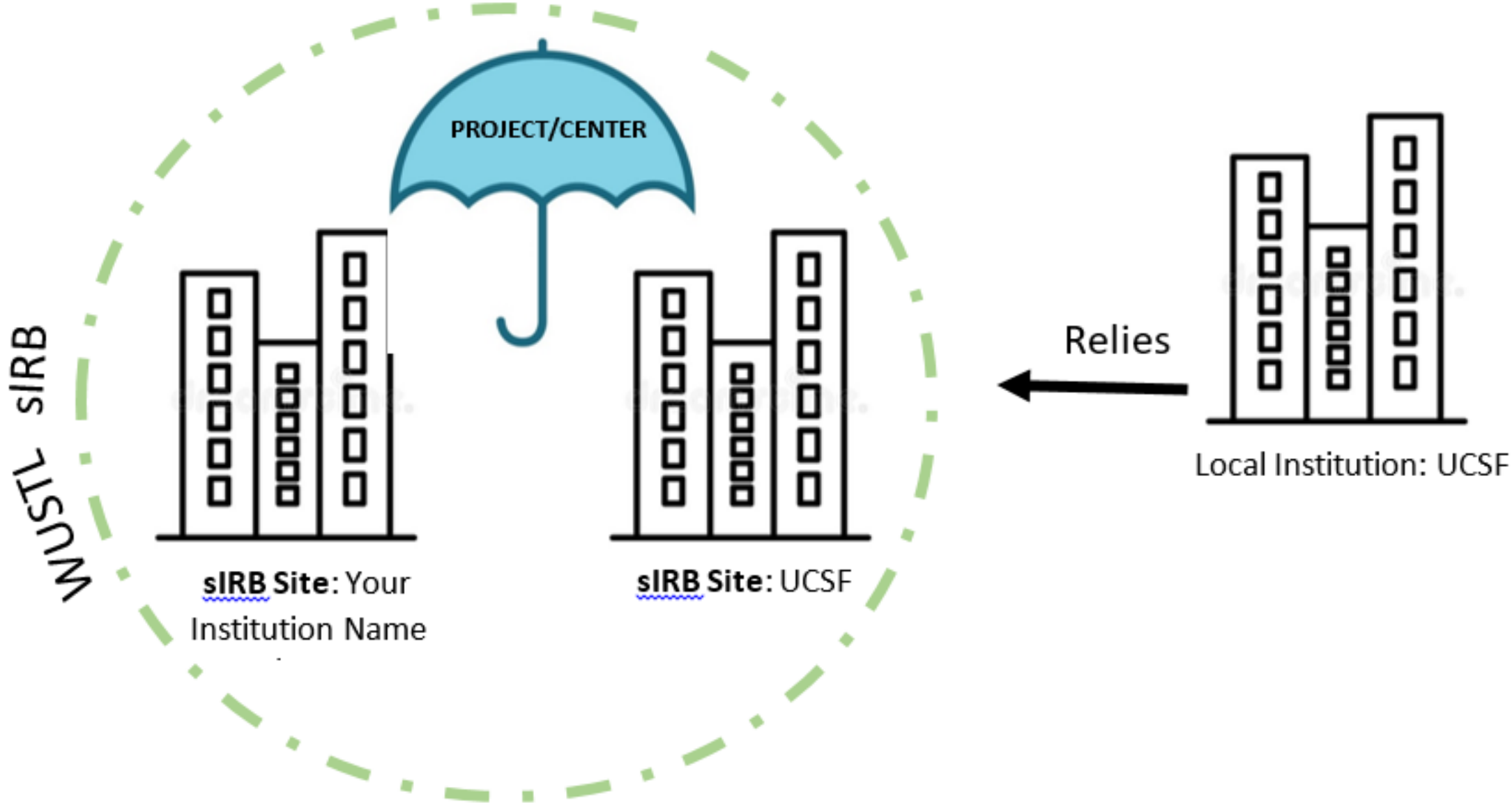
THRIVE

Clinical Coordinating Center: Activation Support



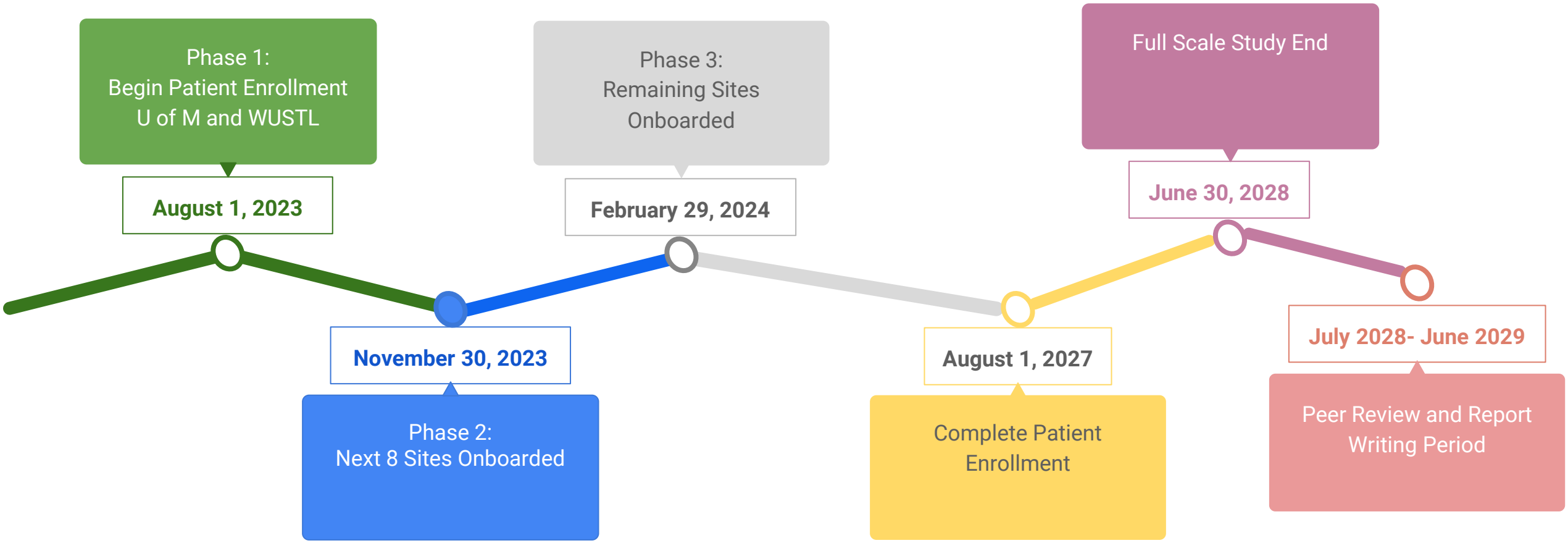
- The CCC will help manage and troubleshoot site application to WUSTL single IRB (sIRB)
- Collection of documents required for GCP will be overseen by the CCC

THRIVE


PROJECT/CENTER
WUSTL sIRB
sIRB Site: Your Institution Name
sIRB Site: UCSF
Relies
Local Institution: UCSF

THRIVE

Site Onboarding and Study Timeline



The Data Coordinating Center (DCC)

THRIVE

DCC Components

DCC Core Responsibilities

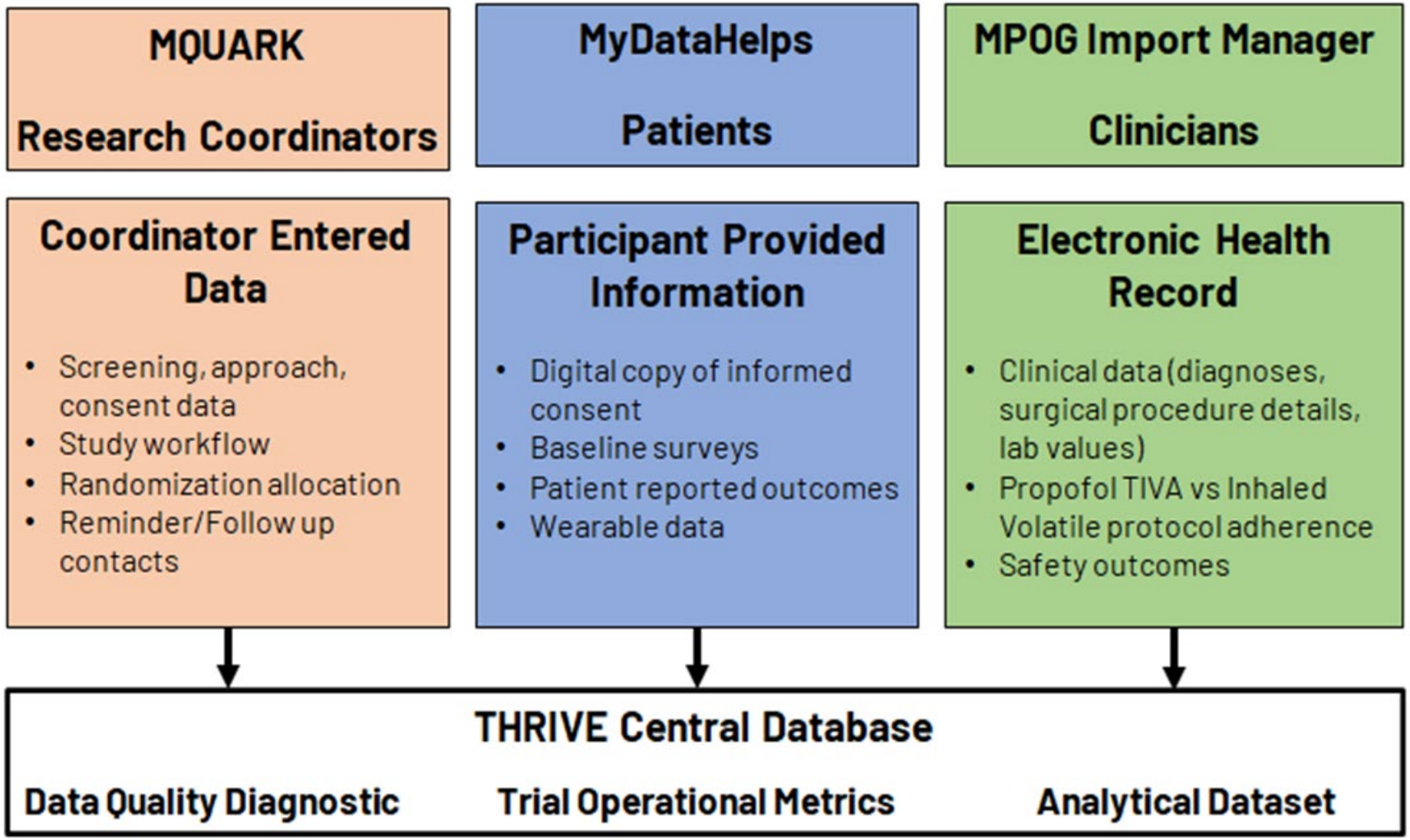
1. Data collection software
2. Support, training, and access
3. Operational Reports
4. Data validation and quality assessment
5. MPOG data flow

In partnership with SABER:

1. DSMP and DSMB
2. Randomization mechanism
3. Statistical analysis plans

THRIVE

Data Sources



MQUARK
MPOG QUALITY & RESEARCH KIT

Potential Patients	Faculty Review Needed	Contacted (unidirectional)
84	10	172

Approached (bidirectional)	Consented/Enrolled	Randomized	Withdrawn
95	72	46	5

MQUARK

Research Coordinators

Coordinator Entered Data

- Screening, approach, consent data
- Study workflow
- Randomization allocation
- Reminder/Follow up contacts

Patient General Info

Email	Participant Identifier	Secondary Identifier	Surgery Date	First Name
None	10100335	1234567890	2022-08-31	Ruby
Last Name	**DOB**	**Sex**	**Site**	**Randomized By**
Dog	1993-02-11	Female	University of Michigan	Chelsea Cloyd

Add Contact Log | Contact Logs | Approach Screening | Consent/Enrollment | Pre Op | POD 0

Anesthesia Clinician Checklist | SAE Reporting | Withdrawal | Shipping and Tracking | Patient Info

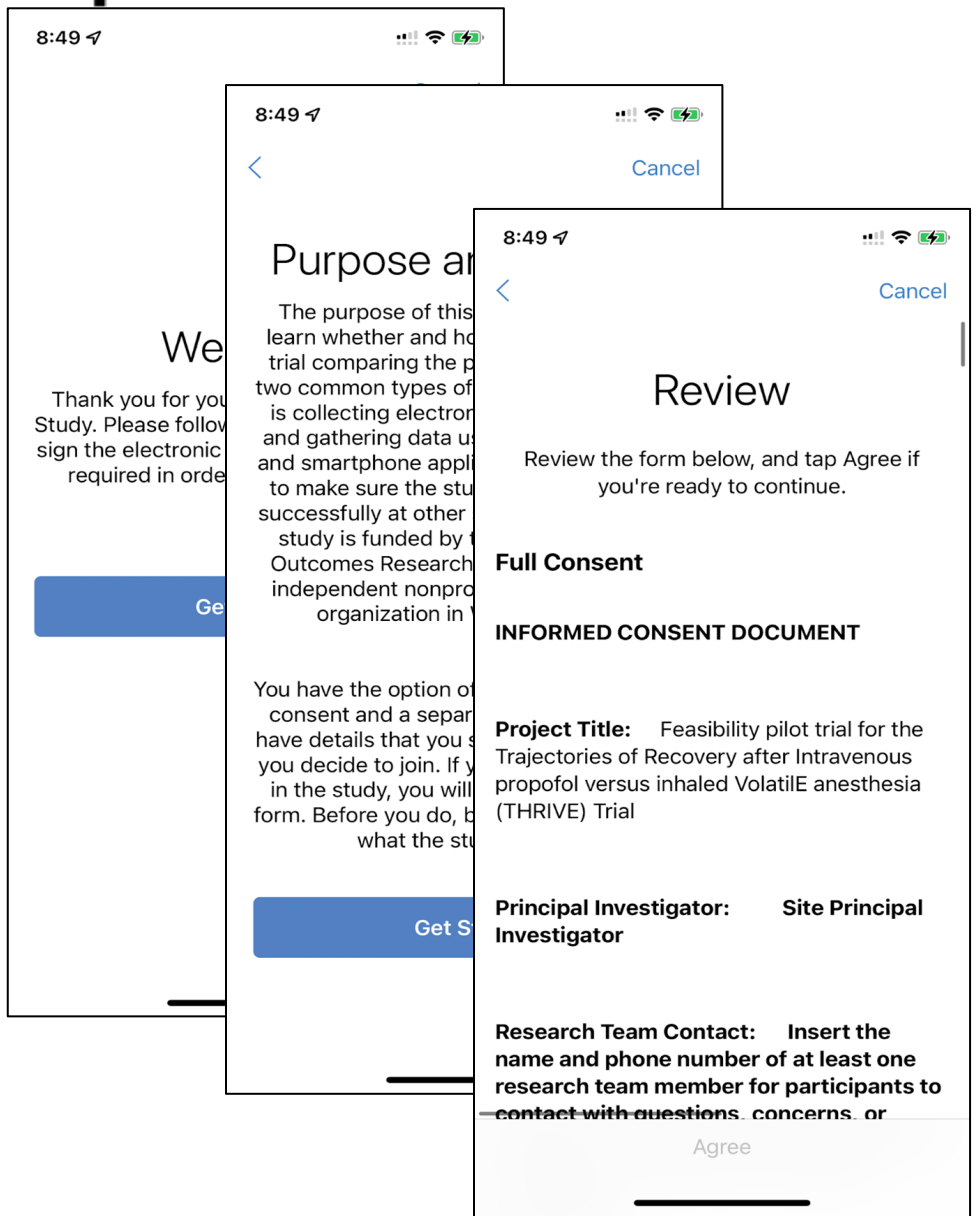
mydatahelps™

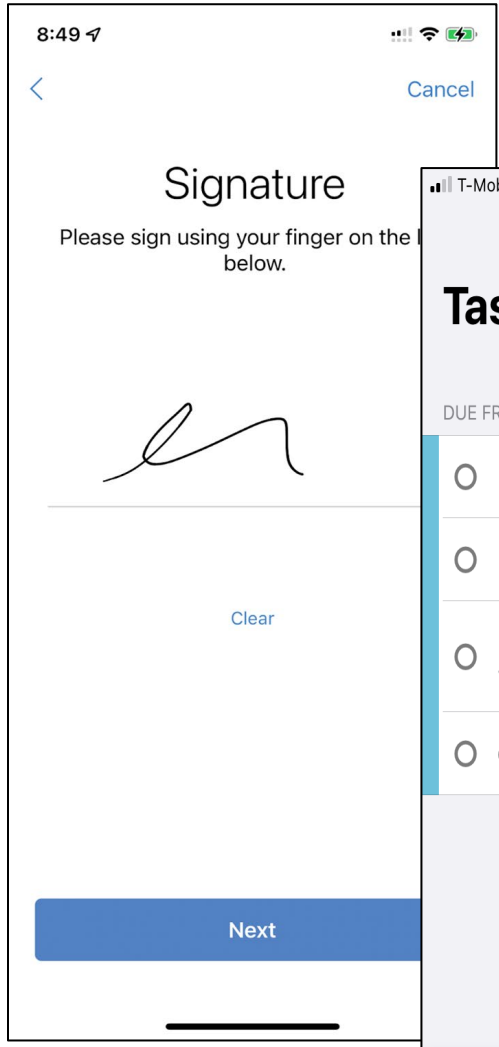
MyDataHelps

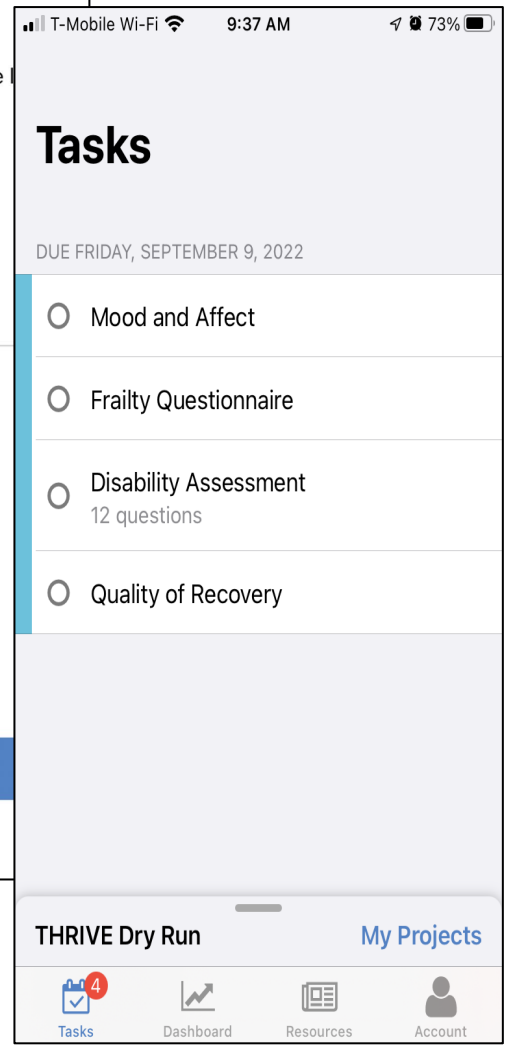
Patients

Participant Provided Information

- Digital copy of informed consent
- Baseline surveys
- Patient reported outcomes
- Wearable data







MPOG Patient Matching App

MPOG Import Manager

Clinicians

Electronic Health Record

- Clinical data (diagnoses, surgical procedure details, lab values)
- Propofol TIVA vs Inhaled Volatile protocol adherence
- Safety outcomes

THRIVE Patient Matching App

Outstanding patients !

Date	Name	Status
2021-10-12	Appleseed, Johnny	Matched
2022-07-28	Bird, Big	Not Matched

Patient Identifiers from MQUARK

Last Name	First Name	Sex	Date of Birth	MRN	Date of Surgery	Procedure
Appleseed	Johnny	Male	1944-07-12	123456789	2021-10-12	Otolaryngology

Possible Matches from MPOG

Exact Match

Appleseed	Johnny	Male	1944-07-12	123456789	2021-10-12	DIRECT LARYNGOSCOPY AND BRONC

Upload Matched Patients | Unmatch | Confirm Match

THRIVE

Data Coordinating Center: Technical Support

Technical

- [ ] MPOG EHR interface active
- [ ] MPOG patient matching software loaded to system
- [ ] Access granted in MQUARK and MyDataHelps (see DOA for who requires access)
- [ ] Site number assigned

THRIVE

Data Coordinating Center: Technical Support

Training

- ☐ MyDataHelps training complete
- ☐ MQUARK training complete (including name matching application)
- ☐ MOP and Protocol training complete
- ☐ Assessment training complete
- ☐ Relevant competency checklist passed by study team

Questions?

askthrive@umich.edu

THRIVE

Site Expectations

Bethany Pennington
Allison Janda

Overview Site Expectations

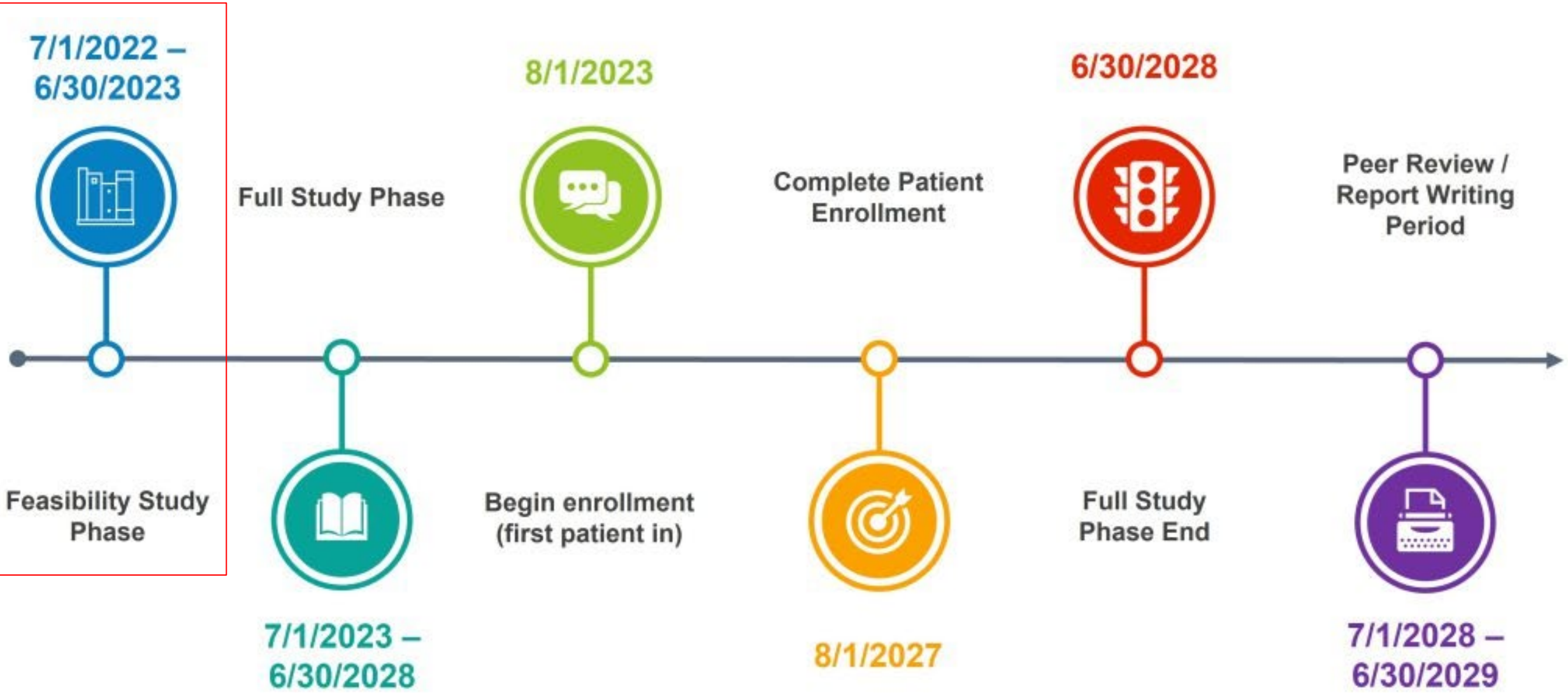
- **Feasibility Protocol Overview**
- **Full Phase Overview**
- **Participation Considerations**

THRIVE

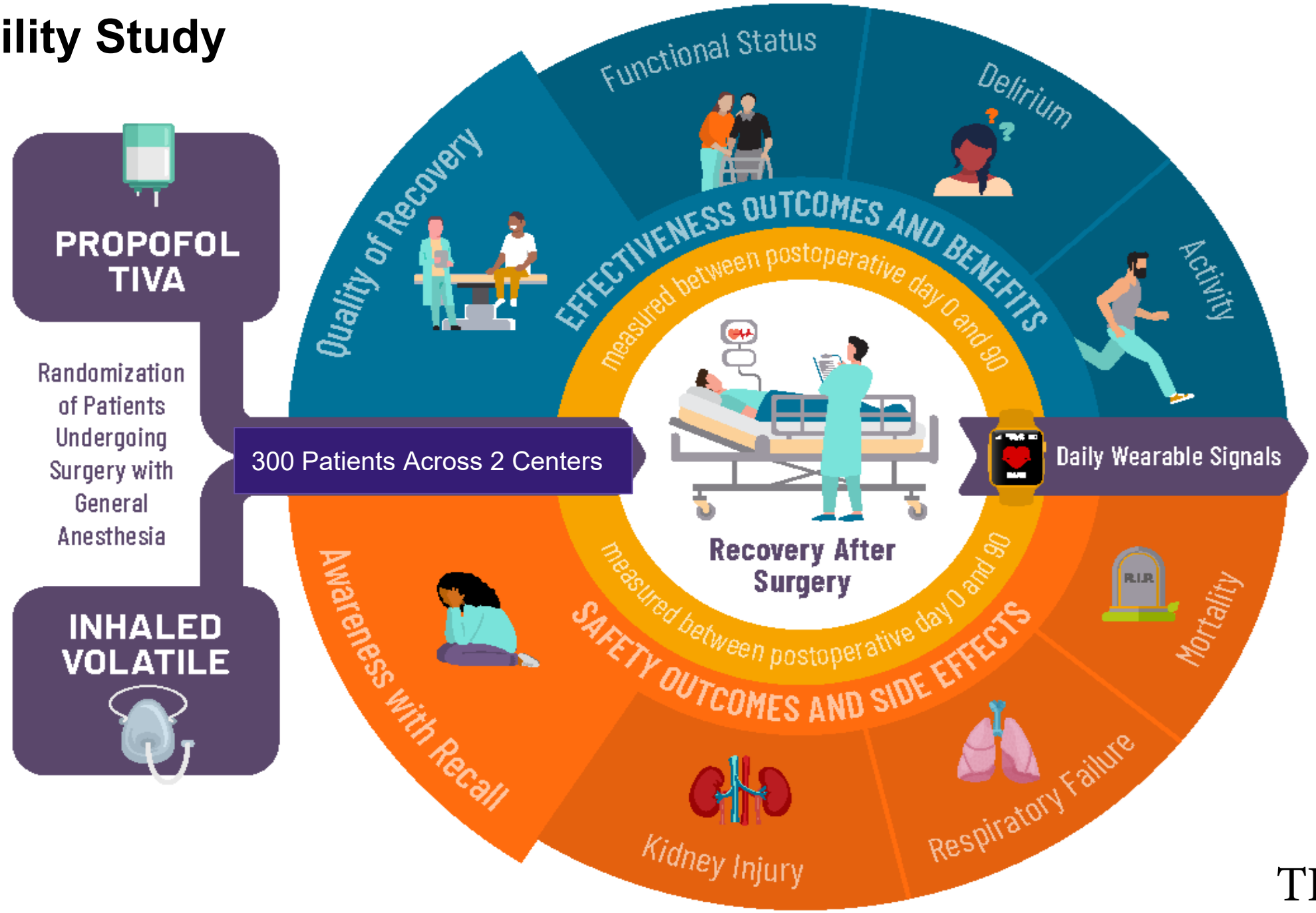
Feasibility Phase

THRIVE

Projected Timeline



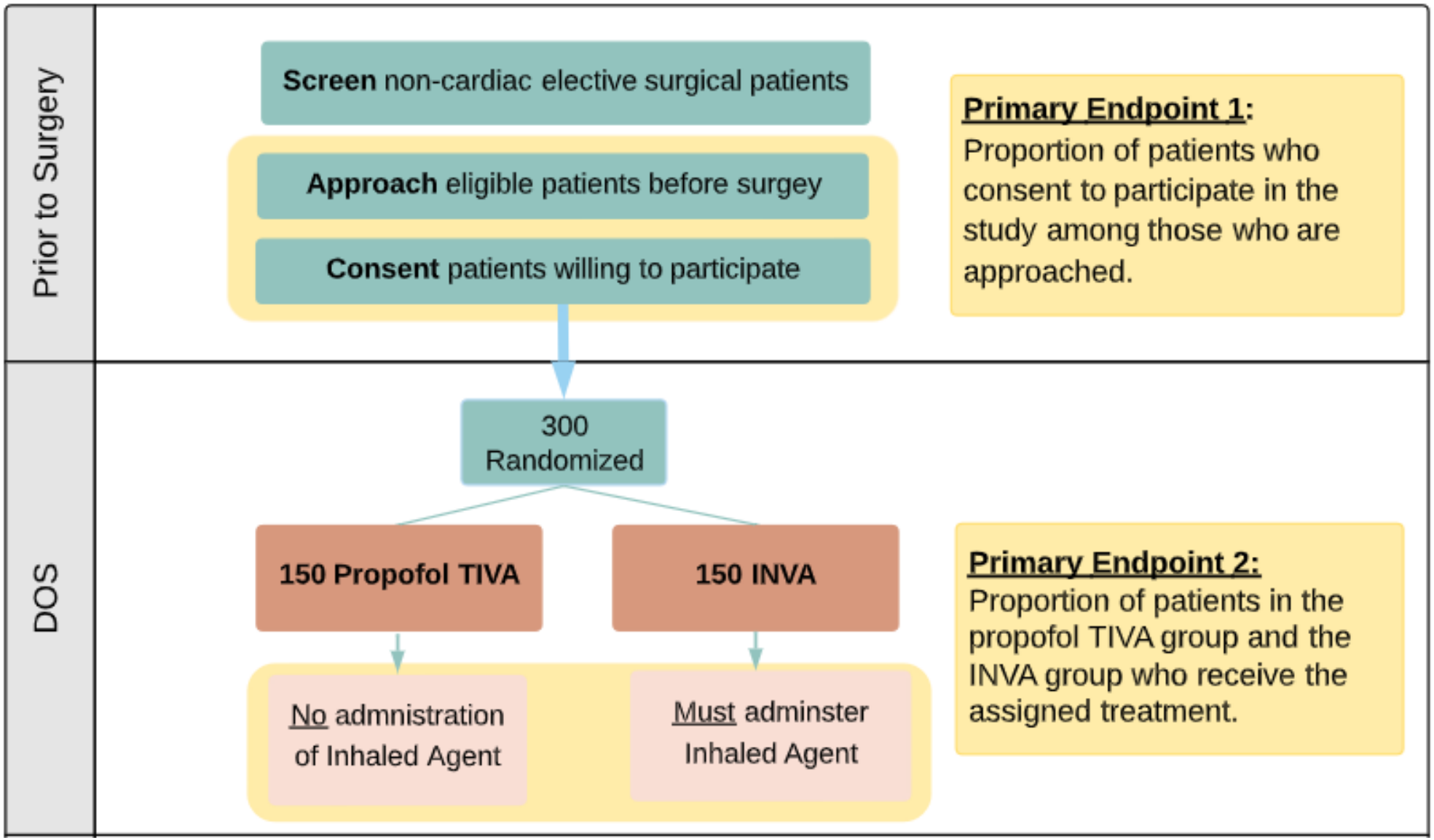
Feasibility Study



THRIVE

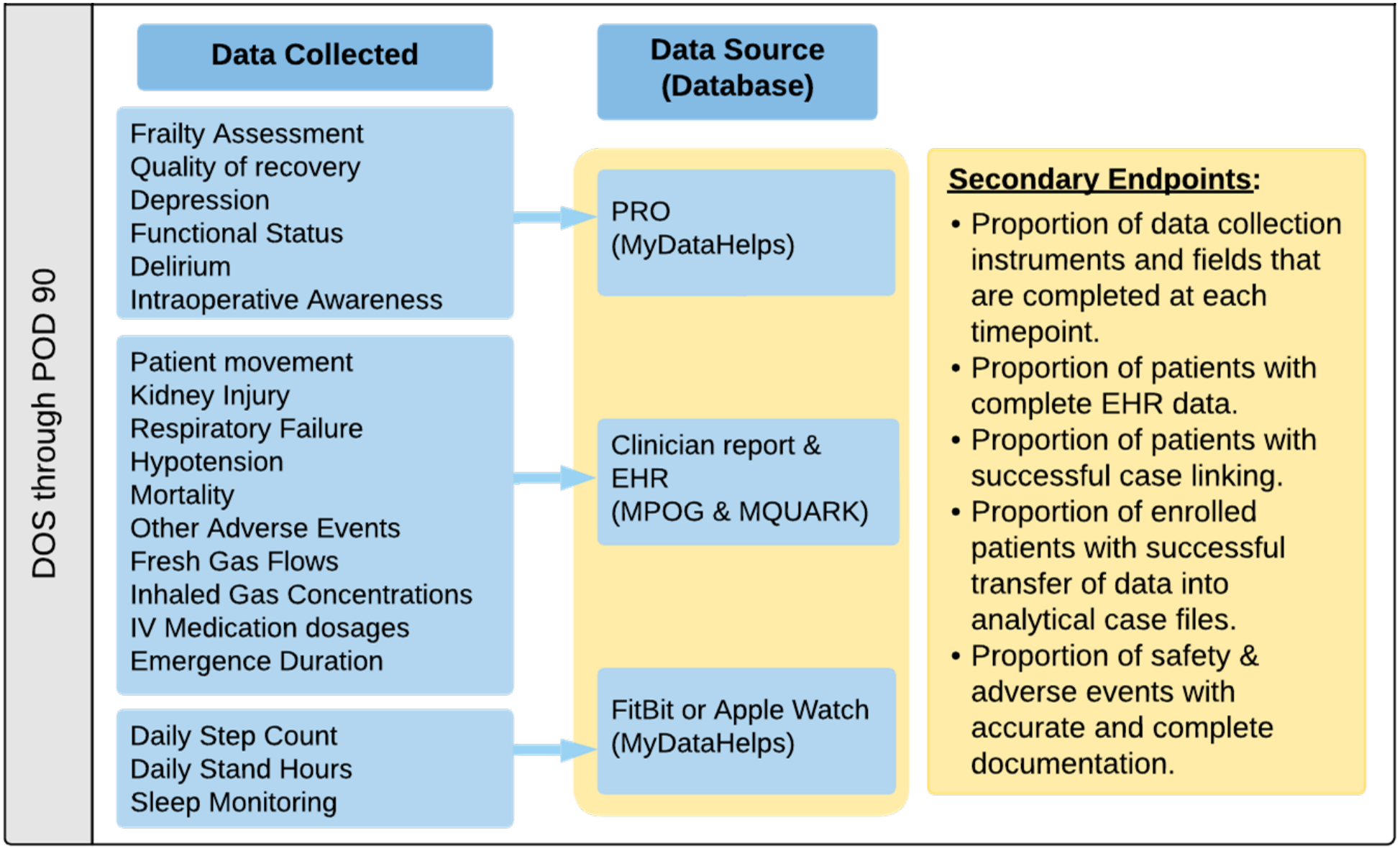
THRIVE

FEASIBILITY PILOT TRIAL: Primary Endpoints



THRIVE

FEASIBILITY PILOT TRIAL: Secondary Endpoints



Goals

Enroll enough patients

> 10% of patients who are approached consent

Administer the assigned anesthetic successfully

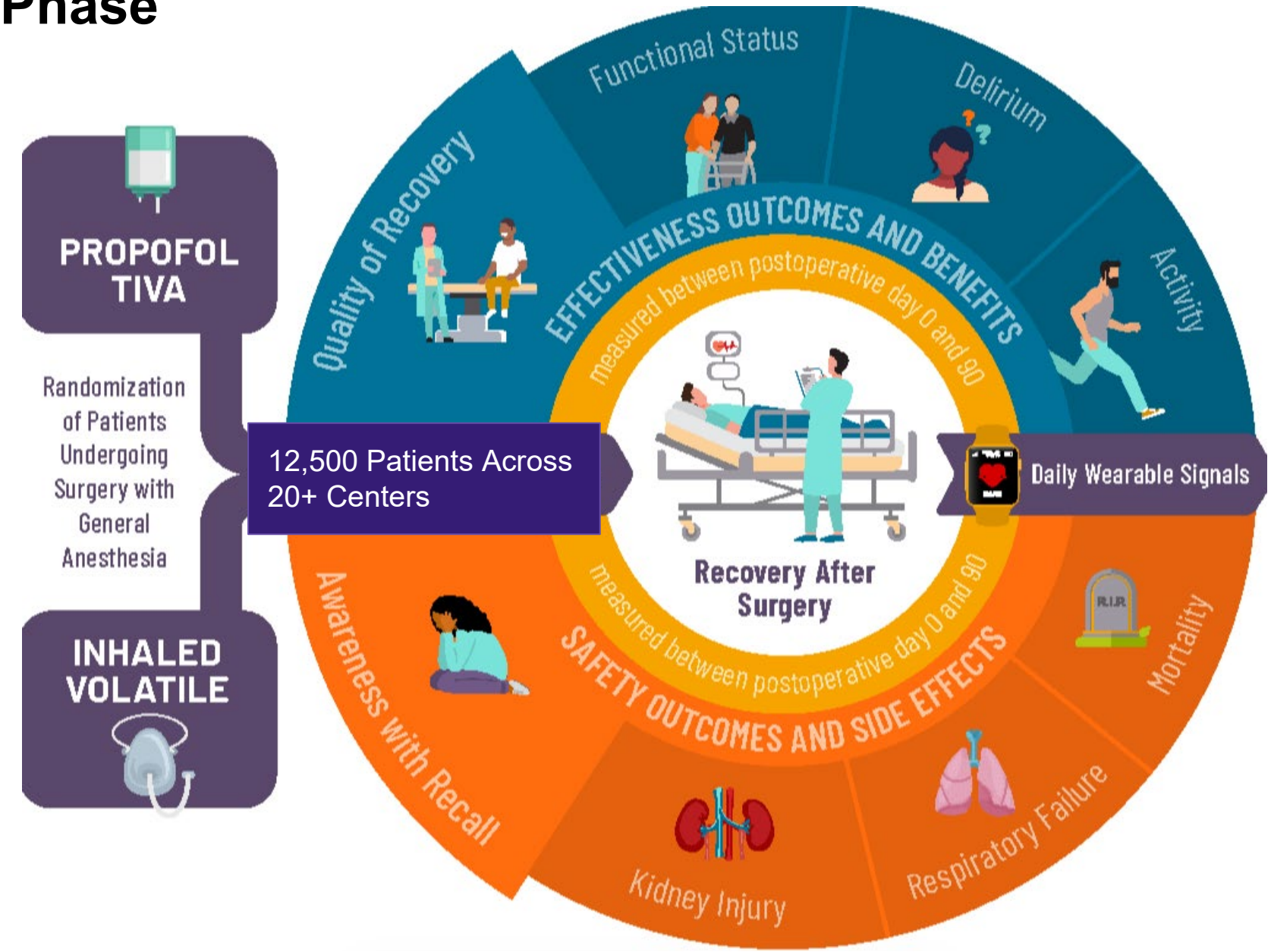
> 80% compliance with each treatment allocation

Complete data collection

>90% obtainment of complete data from EHR and questionnaires

Full Study Phase

Full Study Phase



Inclusion & Exclusion Criteria

Expected patient enrollment	Inclusion criteria*	Exclusion criteria#
<u>12,500 patients at 23 sites</u> ~544 patients enrolled/site over 5 years ~109 patients/year ~9 patients/month	1. Aged 18 years or older 2. Undergoing elective non-cardiac surgery expected to last ≥ 60 min requiring general anesthesia with a tracheal tube or laryngeal mask airway (or similar supra-glottic device)	1. Inability to provide informed consent in English or Spanish 2. Pregnancy (based on patient report or positive test on the day of surgery) 3. Surgical procedure requiring general, regional, neuraxial anesthesia administered by an anesthesia clinician (anesthesiologist, CRNA, anesthesiology assistant) occurring within 30 days prior to or planned to occur within 30 days after surgery date 4. Contraindication to propofol TIVA or inhaled volatile (for example, documented allergy to propofol, history of severe postoperative nausea or vomiting, concern for or history of malignant hyperthermia) based on self-report 5. Surgical procedures requiring a specific general anesthesia technique (for example, TIVA required for neuromonitoring). 6. Locally approved, written protocol mandating a particular anesthetic technique 7. History of intraoperative awareness during general anesthesia based on patient self-report 8. Planned postoperative intubation

*Patients must meet all eligibility criteria to participate, #Patients may meet any one or more of the exclusion criteria to become ineligible to participate

Primary Objectives & Endpoints

Primary Objectives	Endpoints
Compare the early patient quality of recovery after anesthesia and surgery following TIVA with propofol and INVA.	Mean patient reported Quality of Recovery-15 (QOR15) score on POD1.
Determine whether intraoperative awareness is similarly uncommon with propofol TIVA and INVA.	Incidence of unintended intraoperative awareness with recall at either POD1 or POD30.

Primary & Secondary Outcomes

Type	Outcome	Specific measure or definition	Source or Data System	Timepoints
***Primary (effectiveness)**	**Quality of Recovery**	**Quality of Recovery 15 Instrument**	**Patient reported outcome**	**Day 1**
***Primary (safety)**	**Intraoperative Awareness**	**Modified Brice Interview**	**Interview or Patient reported outcome**	**Day 1 and/or 30**
Secondary (effectiveness)	Delirium	UBCAM	Interview	Day 1
Secondary (effectiveness)	Quality of Recovery	Quality of Recovery 15 Instrument	Patient reported outcome	Day 0, 2, 7
Secondary (effectiveness)	Functional status	Change from preoperative baseline in World Health Organization Disability Assessment	Patient reported outcome	Day 30 & 90
Secondary (safety)	Stage 1 Acute kidney injury	Creatinine increase of 50% or 0.3 mg/dl from preoperative baseline (KDIGO)	MPOG EHR interface	Day 7
Secondary (safety)	Respiratory failure	Reintubation within 6 hr or continued intubation 6 hr after surgery	Coordinator	Day 0
Secondary (safety)	Mortality	All-cause mortality	MPOG EHR interface &	Day 30, 90

Primary & Secondary Outcomes (Continued)

Type	Outcome	Specific measure or definition	Source or Data System	Timepoints
Secondary (safety)	Intraoperative hypotension	Duration of mean arterial pressure < 65 mmHg (minutes)	MPOG EHR interface	During surgery
Secondary (safety)	Intraoperative hypotension	Cumulative duration of mean arterial pressure < 55 mmHg of 20 or more minutes	MPOG EHR interface	During surgery
Secondary (safety)	Intraoperative movement	Moderate to severe intraoperative movement reported	Clinician Report	During surgery
Secondary (safety)	Unplanned admission	Hospital admission no later than 24 hours after surgery performed at an ambulatory care center.	MPOG EHR interface	Day 0-1
Secondary (safety)	Propofol related infusion syndrome or Malignant hyperthermia	See full phase protocol	Clinician Report	During surgery
Secondary (effectiveness)	Daily step count, Daily stand hours, Total sleep time, sleep onset latency, wake after sleep onset, sleep efficiency, midpoint of sleep	Fitbit or Apple Watch	MyDataHelps	Day 7, 30
EHR = electronic health record				

Recruitment, Screening, Enrollment

- Patient-facing website *(coming soon)*
- Multiple complementary enrollment strategies:
  - Individualized outreach to participants at home via telephone or email
  - In-clinic enrollment during preoperative assessment
  - Surgical patient community engagement
- Electronic Consent:
  - Patients will complete written informed consent via 1) study coordinator-mediated eConsent on a study tablet or computer; or 2) self-consent using modules on a personal smartphone, tablet, or website
- Subset of patients will be offered a study-provided wearable device (Apple Watch or Fitbit) or the option to use their own wearable device.
  - Participation in this aspect of the study is optional.

THRIVE

Protocol Adherence

Administering the assigned method of anesthesia per protocol is essential for success

Propofol TIVA:

- Administer IV propofol
- Do NOT administer inhaled anesthetics (sevoflurane, isoflurane, desflurane, nitrous oxide) during any part of the anesthetic care.

INVA:

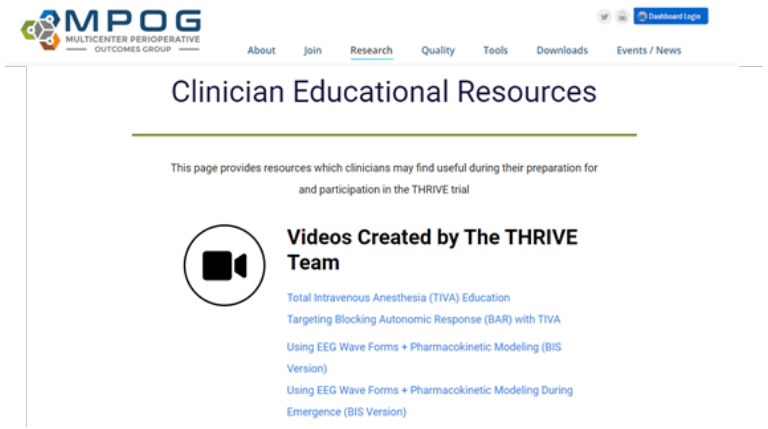
- Administer inhaled volatile anesthetic (sevoflurane, isoflurane, desflurane) as the mainstay of anesthetic maintenance.
- Propofol is permitted for induction or as an adjunct.

Patients in both groups may receive any additional IV adjuncts as deemed appropriate by the clinical team

THRIVE

EEG Monitoring

- Each site will be expected to ensure EEG monitoring is consistent in both treatment arms
- Number of EEG monitors available
- Training study staff or clinicians setup process
- Clinician EEG Educational Resources Available on the MPOG website: https://mpog.org/thrive-clinician-educational-resources/



THRIVE

Blinding

- **Patients**
  - EPIC patient portal does not reveal intraoperative anesthesia details
  - Patients will be asked which intervention they believe they received at day 90 and will be informed of what they received
- **Study team**
  - Study personnel collecting and analyzing outcome data
  - Designated healthcare workers administering the post-Brice questionnaires
  - Intraoperative awareness classification team
- **Surgeons**
  - Email reminder
  - Pre-trial education
- **Postoperative nurses**
  - Signs in room
  - Pre-trial education

THRIVE

Participation Considerations

THRIVE

Research Coordinator & Site-PI

- Research Coordinator
  - Training
    - MQUARK, MyDataHelps, MPOG Patient Matching, UBCAM
    - Establish relationship with patients
    - OR familiarity and etiquette if new to this space
    - Setting up room, providing resources, collecting items after case
    - EEG setup
- Site-PI and THRIVE site clinicians
  - Available to provide hands-on support and education in OR
  - Troubleshooting issues that arise during the case

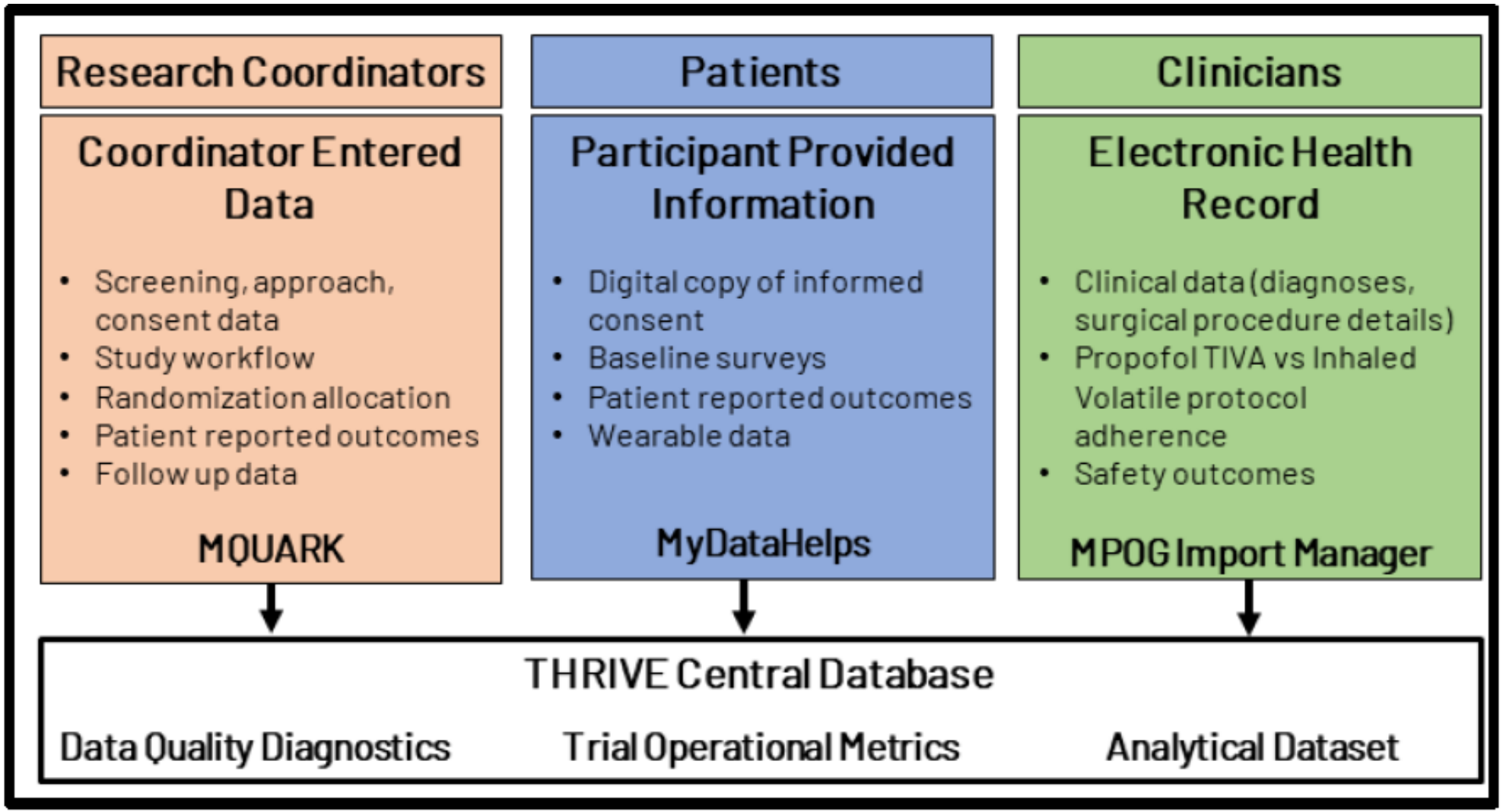
Intraoperative Awareness Protocol

- **Modified Brice Questions**
  - Released to the patient for self-administration on POD1
  - If Brice screen is positive, a THRIVE team member will be notified within 24 hours to perform the follow up questionnaire.
- **Follow up questionnaire**
  - THRIVE team member will perform an audio-recorded interview within 7 days of the + Brice
  - Offer to contact, or provide contact information for, a licensed psychologist or psychiatrist

    <u>*This will be in accordance with the local process established for referring patients who experience intraoperative awareness for counseling at each participating institution*</u>

- **Michigan Awareness Classification**
  - Three independent experts on awareness will listen to the audio-recording and adjudicate whether the awareness report was a definite awareness event, possible awareness event, or related to something else.
  - Apply the Michigan Awareness Classification

3 Data Platforms



MQUARK

- MQUARK (MPOG Quality and Research Kit) will be used to manage patient screening, enrollment and randomization eCRFs

- This existing research system has been customized to the needs of the THRIVE trial and provides integration with data collected from the other systems

- Patient enrollment details, patient demographics, per protocol treatment delivered and clinician report of intraoperative patient movement, SAEs, and AEs will be entered into MQUARK

MyDataHelps

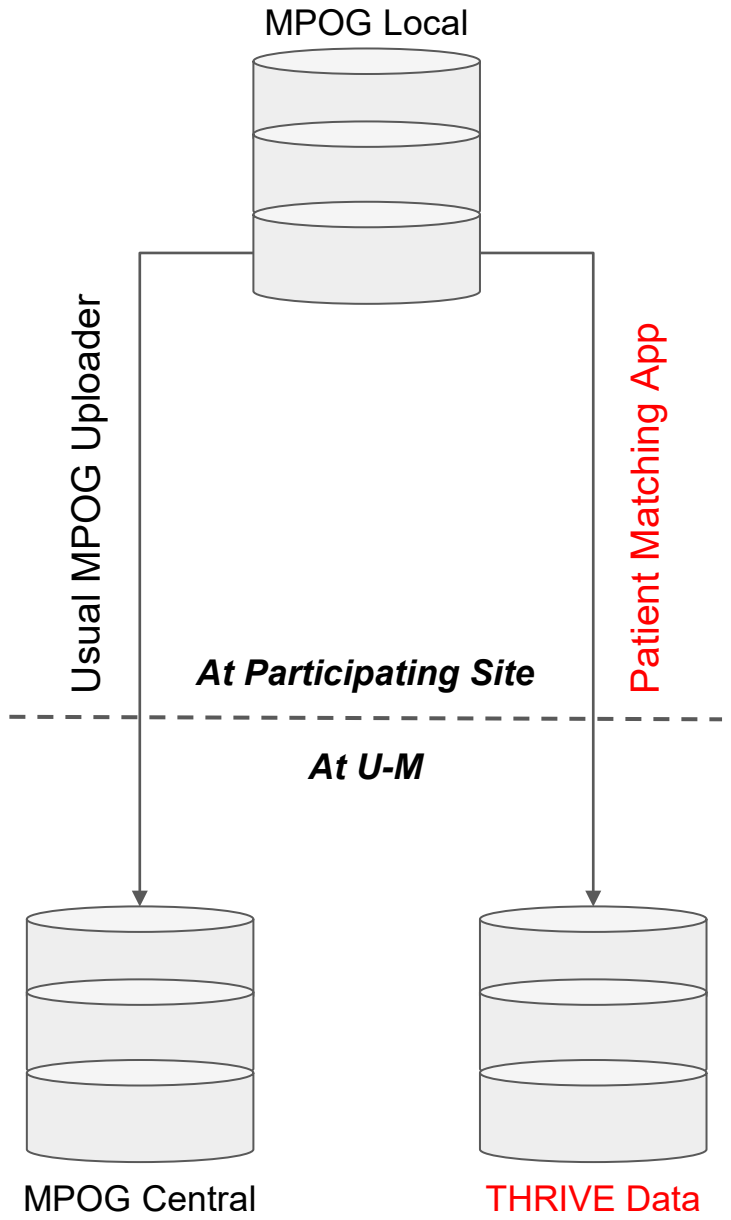
- MyDataHelps is a patient-facing application that allows the collection of patient reported outcome data via the administration of surveys

- Surveys can be completed by dedicated smartphone application, email or web

- Additionally, data will be obtained from wearable devices (Apple Watch or Google FitBit or compatible “bring your own device [BYOD]”) using the MyDataHelps application

MPOG & THRIVE

- THRIVE is embedded within MPOG
- At U-M there is a parallel, trial specific infrastructure for handling THRIVE patients
- THRIVE study data is uploaded and processed separately from existing MPOG processes
- New tool: ***MPOG Patient Matching Application***
  - Joins MPOG Record to Trial Data
  - Handles uploads of THRIVE study data



MPOG - Data Quality Matters

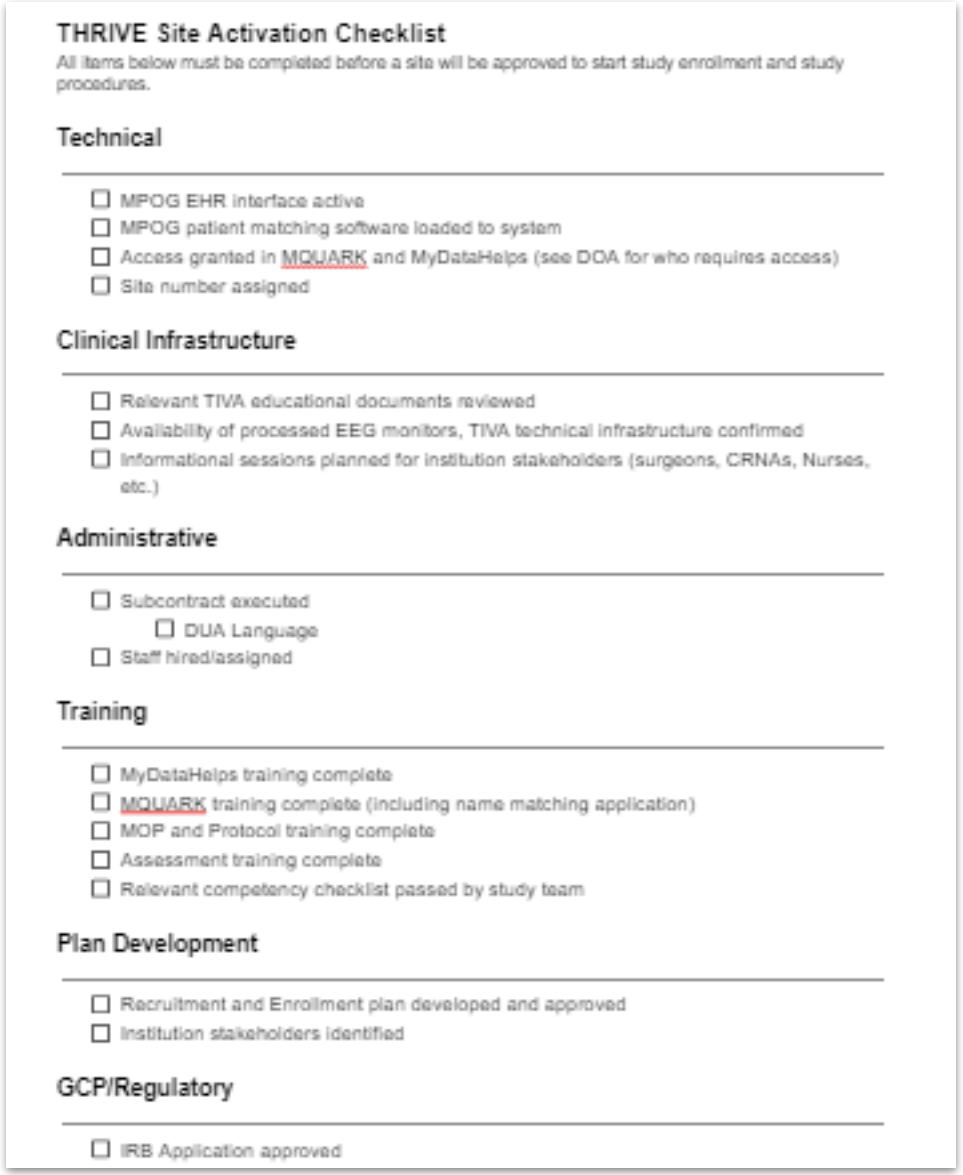
- THRIVE is an EHR (MPOG) embedded clinical trial
  - Active MPOG participation is required for THRIVE participation
  - At a site the THRIVE and MPOG teams work collaboratively for effective participation

- Emphasis on Data Quality Control:
  - Site activation activities - Checking mappings, data diagnostics, case level validation
  - Ongoing site maintenance - Data Diagnostics, Case Validation, Reports from DCC etc
  - Specific to THRIVE, but familiar from MPOG tools.

- Things will happen… planning is key:
  - New monitors, anesthesia machines, EHRs etc will all potentially impact THRIVE participation
  - DCC will be partner in planning for these

Site Activation Checklist

- Summarizes actions sites need to complete before approval to start study enrollment and study procedures
  - *Technical (MPOG, MQUARK, MyData Helps)*
  - *Clinical (Education, Stakeholder outreach, EEG)*
  - *Administrative (Subcontracts, staff)*
  - *Training (study personale, competency checklist)*
  - *Plan Development (Recruitment, Stakeholders)*
  - *Regulatory (IRB, Delegation of Authority)*
  - *Process Overview (payment, wearables)*



THRIVE Site Activation Checklist

All items below must be completed before a site will be approved to start study enrollment and study procedures.

Technical

- ☐ MPOG EHR interface active
- ☐ MPOG patient matching software loaded to system
- ☐ Access granted in MQUARK and MyDataHelps (see DOA for who requires access)
- ☐ Site number assigned

Clinical Infrastructure

- ☐ Relevant TIVA educational documents reviewed
- ☐ Availability of processed EEG monitors, TIVA technical infrastructure confirmed
- ☐ Informational sessions planned for institution stakeholders (surgeons, CRNAs, Nurses, etc.)

Administrative

- ☐ Subcontract executed
  - ☐ DUA Language
- ☐ Staff hired/assigned

Training

- ☐ MyDataHelps training complete
- ☐ MQUARK training complete (including name matching application)
- ☐ MOP and Protocol training complete
- ☐ Assessment training complete
- ☐ Relevant competency checklist passed by study team

Plan Development

- ☐ Recruitment and Enrollment plan developed and approved
- ☐ Institution stakeholders identified

GCP/Regulatory

- ☐ IRB Application approved

Questions?

Lessons Learned in Feasibility

University of Michigan
Washington University St.Louis

10/21/2022

Allison Janda
Sathish Kumar
Laura Swisher

Before Beginning Recruitment and Enrollment

Plan enough lead time to accomplish:

- Clinician Education and Study Information
  - CRNAs, Nurses, Clinicians, Surgeons
  - Grand Rounds
  - Present study at clinician regular weekly meetings
  - THRIVE Developed Slide Decks can be made available
- Single IRB Application (sIRB)
  - Submission to WUSTL sIRB successful
  - ~8 weeks
  - Reliance agreement
  - Allows for differences between institutions
- MPOG Interface Status
  - Complete any Outstanding issues with MPOG data transfer and/or contracting

Before Beginning Recruitment and Enrollment cont.

Equipment and Pharmaceutical needs

- Make sure you have an adequate number of infusion channels available
- Ensure necessary medications & equipment readily available regardless of study arm
- Familiarize CRCs and engaged clinicians with the use of Epic secure chat or some other group messaging system (Teams, Slack, etc) to potentially help with surgery team communication day of surgery
- Site co-Is need to be available to discuss any concerns the surgery team may have related to existing protocols (e.g. opioid avoidance when randomized to TIVA)

Before Beginning Recruitment and Enrollment cont.

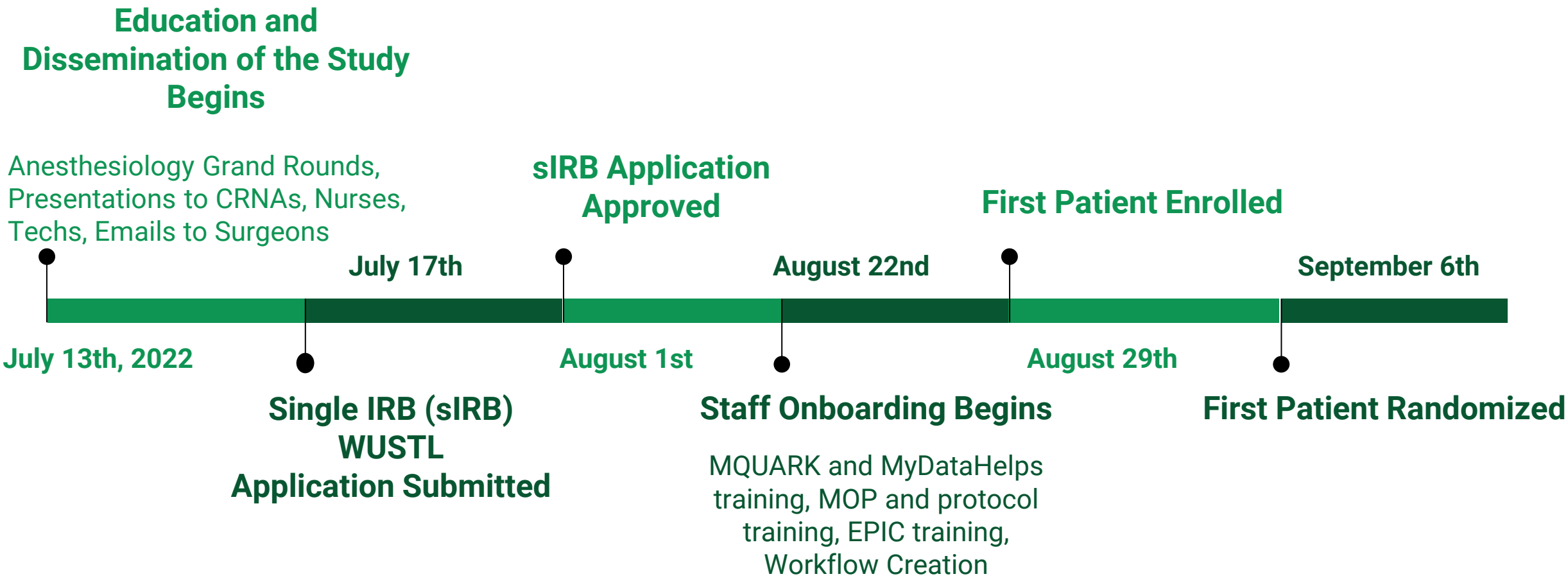
EEG Considerations

- Inventory of available EEG monitors, confirm adequate for study use
- Training coordinators for use and troubleshooting of EEG monitoring devices
- Ensure data from EEG monitors is captured
- Spare leads, cables.
- Education – providers in the room, coordinators, preop and post nursing teams

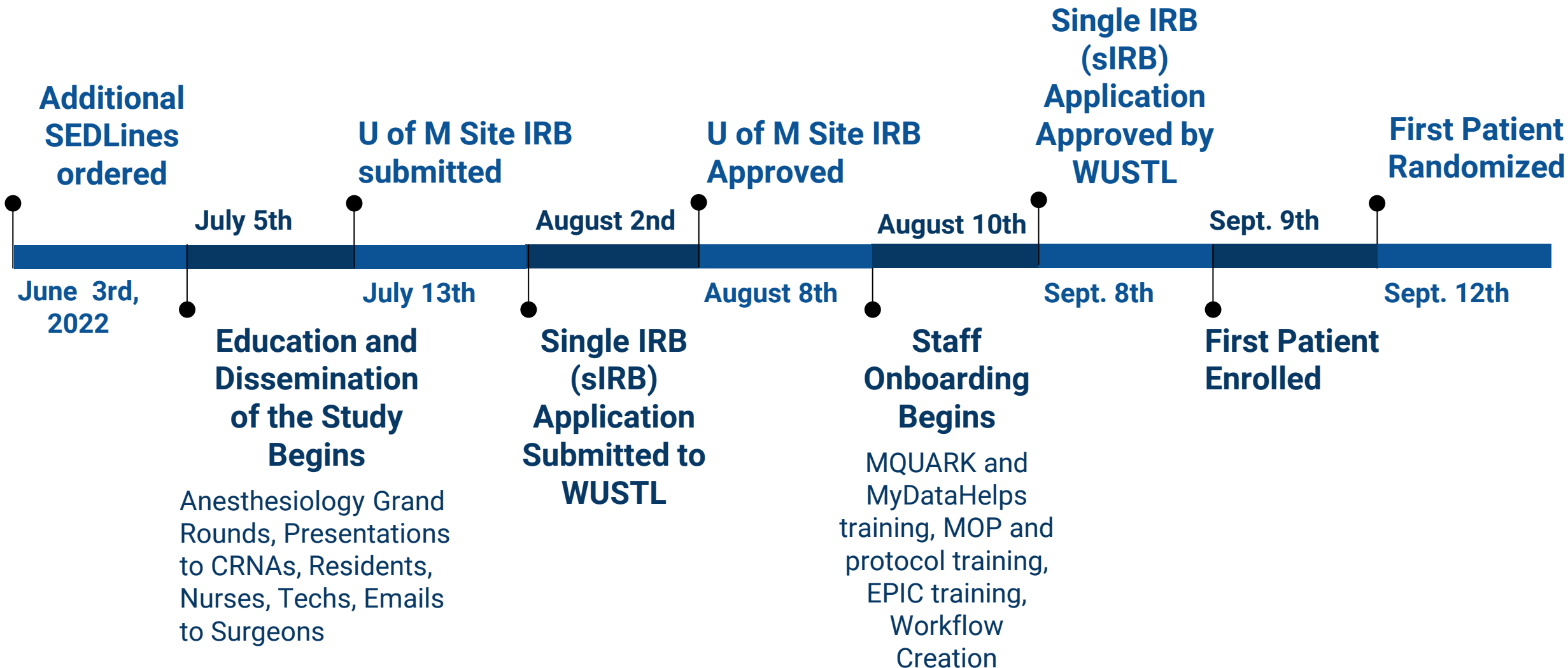
Before Beginning Recruitment and Enrollment cont.

- Create an EPIC search tool that accurately reflects inclusion/exclusion criteria and become familiar with where the criteria can be found within Epic
  - Real time surgery start and stop times, Surgery complexity, Family history
- Establish recruitment strategy that fits your team
  - Assign blinded versus unblinded CRCs
  - Assign CRCs to recruit based on day of surgery to control surgery/day volume
- Ramp Up
  - Consider only recruiting patients with surgeries that occur Monday - Wednesday, no first starts, and only inpatient surgeries in the first week or two

Study Start-up Timeline: Washington University School of Medicine



Study Start-up Timeline: University of Michigan



Recruitment and Enrollment

- Appropriate Surgical Site, Procedure and Supportive Surgical Team
- Helps Ascertain Workflow and understand nuances
- Screening Tools (more diligent screening in the initial period)
- Email, Follow up Calls, Set limits on follow up Calls
- Check for overlapping research studies

Day of Surgery and Postoperative Period

- Randomize after all checks including survey, communication to the team to prepare for the type of anesthetic
- **Avoid unblinding the patient and the coordinator involved in survey postop**
- Continually checking the EHR to monitor completion of surgery
  - Tracking surgery for early start times/end times
  - Asking a clinician to page you when patient enters phase 2

Day of Surgery and Postoperative Period cont.

- Patient may be very groggy or nauseated when waking up which may delay administering/directing completion of POD 0 surveys and evaluations.
  - If patient is not able to answer the POD 0 surveys this may mean they are CAM+ and the rest of the questionnaires may be skipped
- UBCAM cannot be completed over the phone which may impact outpatients
- TAKE AWAY LESSONS
  - Timing of performing surveys
  - Collecting the checklist at the end of the case/including feedback

After POD 0

- Continuous checking to make sure all surveys are complete
- Do not be afraid to reach out to patients to ask them to complete surveys throughout the 90 days of study involvement

MQUARK
MPOG QUALITY & RESEARCH KIT

Potential Patients	Approached	Enrolled	Screening Complete	Withdrawn
38	69	27	43	2

2 Days Preop	1 Day Preop	7 Days Preop
0	0	0

Patients who Need Surveys Administered	Patients with Past Due Surveys	Check for SAEs
0	0	0

Enrollment and Randomization as of October 20th, 2022

	University of Michigan	WUSTL	Total
Approached (bidirectional)	43	52	95
Enrolled	28	46	**74**
Ratio of consented versus approached	65%	88%	78%
Withdrawn before randomization	2	3	**5**
Withdrawn after randomization	0	0	0
Randomized	19	28	**47**
Protocol adherence*	100%	100%	100%

* “Protocol adherence” defined by clinician self-report and coordinator manual review. Detailed MPOG EHR phenotypes may change this percentage.

Summary

- Overall a Very Positive Experience
- **Certainly A Feasible Study**
- Our Experience and Learning Opportunities would help prepare for the full phase study
- Will continue to Share our Experience to future sites
- Teamwork,Communication and Collaboration is Key
- Surgeon and Anesthesiology team feedback

Contracting & Financials

Contracting

- University of Michigan is prime awardee for THRIVE
- All site enrollment contracts will occur through University of Michigan
- Builds upon existing MPOG site contracts
- Single contract that includes
  - Statement of work
  - Financial terms
  - Data use agreement language
  - Confidentiality, IP
  - All PCORI THRIVE contract obligations and language
- Contracts can be signed, but not “active” until full scale approved by PCORI

Financials

- Budget reviewed extensively with PCORI prior to Feasibility Phase
- Goal is to maximize $ allocated to enrollment sites while staying within PCORI PLACER limits
- 56% of all funds flow to enrollment sites

- Initial financial model built upon 12 enrollment sites
- Remains stable, with some CC adjustments, at 20+ sites

- PCORI indirect limit of 40%

Reimbursement model

- Per patient randomized
- Between $950 - $1000 per patient
- Inclusive of indirect costs
- Participant receives additional up to $75 incentive
- Lump sum start-up payment upon first patient randomized

Reimbursement model

- Additional non-participant reimbursement
- Annual incentives for excellent performance
  - Representative population demographics
  - Pace of enrollment
  - Intervention adherence
- Small grant program for stakeholder engagement activities

Questions & feedback

MPOG Retreat

Patient & Stakeholder Engagement Strategies

Mark Neuman

Hugo Campos

Bethany Pennington

Mara Bollini

- In PCORI-funded research, patients and other healthcare stakeholders are equitable partners—as opposed to research subjects—who leverage their lived experience and expertise to influence research to be more patient centered, relevant, and useful.
- *Engagement* is the meaningful involvement of patients, caregivers, clinicians, and other healthcare stakeholders throughout the entire research process—from planning the study, to conducting the study, and disseminating study results.

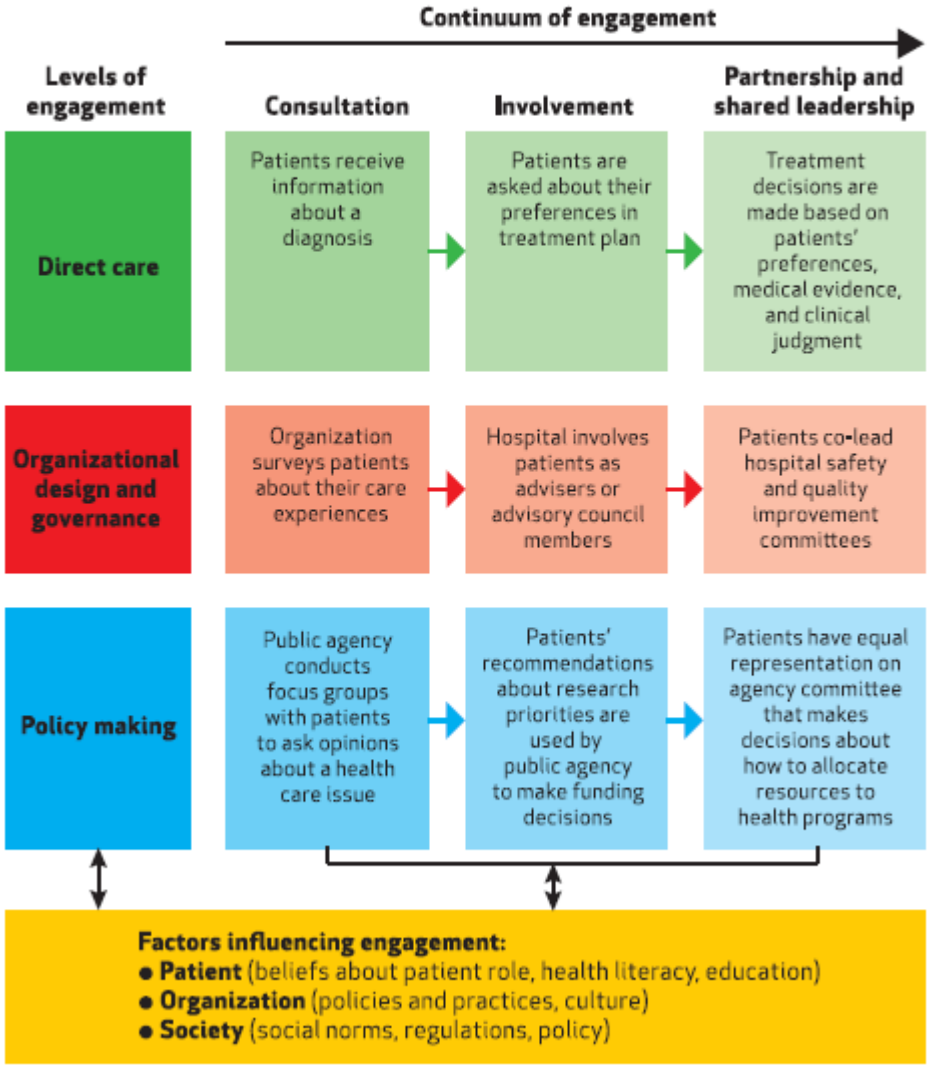
https://www.pcori.org/engagement/value-engagement

By Kristin L. Carman, Pam Dardess, Maureen Maurer, Shoshanna Sofaer, Karen Adams, Christine Bechtel, and Jennifer Sweeney

Patient And Family Engagement: A Framework For Understanding The Elements And Developing Interventions And Policies

EXHIBIT 1

A Multidimensional Framework For Patient And Family Engagement In Health And Health Care



Engagement in THRIVE

- Proposal development
- Feasibility phase
  - Patient engagement
  - Internal stakeholder engagement
  - External stakeholder engagement
- Plans for full study phase

Patient Partners During Proposal Prep

Hugo Campos

Melissa Hicks

Ralph Dacey

Heidi Klosterman

Donna Penner

Linda Robison

- Reviewed potential outcome measures and helped select QOR15 as primary outcome
- Successfully advocated for choice of awareness with recall as primary safety outcome
- Participated in determining meaningful effect size for awareness power calculation

Patient partner Donna Penner has had several surgeries with general anesthesia, including an abdominal surgery with inhaled volatile anesthesia during which she experienced prolonged and distressing intraoperative awareness. Penner states, "The THRIVE research project that we are conducting is compelling, especially when you include the part about how devastating it is to experience awareness... and how it impacts us in our daily living. It cost me my career... I'll take a few sleepless nights any day to prevent someone from going through what I've been through. Any day. In a heartbeat."

Patient partner Linda Robison has had several surgeries with general anesthesia, including spine surgery with propofol TIVA 11 years ago. Robison states, "As an intraoperative awareness victim, being invited to participate in THRIVE is profoundly meaningful. With my continued struggle with PTSD caused by the event, I am hopeful my input will be of value and used in the prevention of awareness. This opportunity will allow me to be heard globally by medical professionals and aid in my healing. I dedicate my participation to all those victims who've gone before me and suffered in silence."

Sara Solomon, a patient partner in THRIVE who has had general anesthesia three times in the last 15 years, states, "If I had a choice of general anesthesia that improved recovery but with a small risk of waking up during surgery, I don't think I'd take it. From what I hear, that's traumatic, and I'd like to keep my love affair with anesthesia alive! If, however, I could choose a type of anesthesia that improved my chance of a faster and higher quality recovery, I'd take it."

THRIVE Revised Engagement Plan

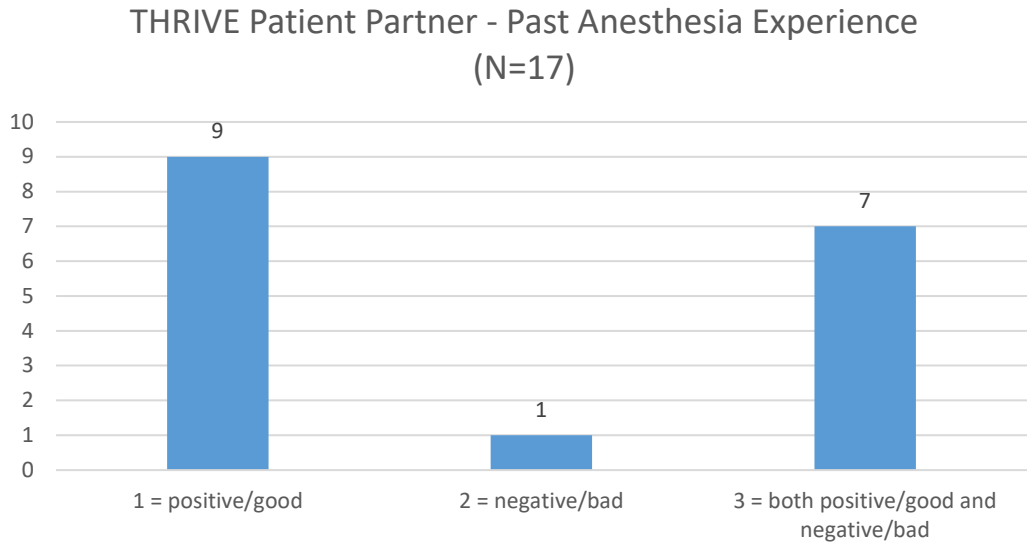
1. To establish mechanisms and resources for patient and stakeholder input and consultation on key study decisions over the lifespan of THRIVE;
2. To demonstrate feasibility of patient and stakeholder collaboration and shared leadership within the *central management structure* of the THRIVE trial;
3. To generate and curate resources and tools to support meaningful patient and stakeholder engagement at the level of *individual THRIVE recruiting sites*;
4. To complete necessary staff training and other preparatory work at the level of individual recruiting sites to support successful site-level patient and stakeholder engagement within the THRIVE full study phase.

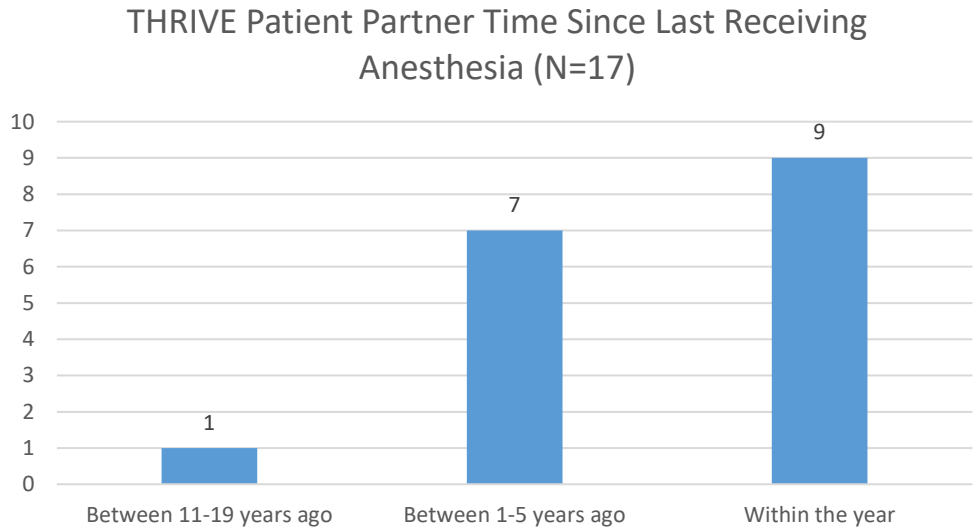







Patient Partner Panel









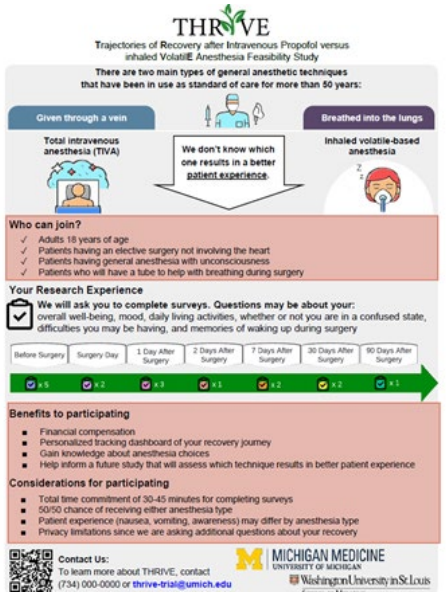



Patient Partner Panel – Monthly Meetings

Structured agenda:

- *Learning to THRIVE* – educational offering
- Presentation related to agenda theme
- Bi-directional discussion/feedback/deliverables for the meeting

Reviewed version


THRIVE

Trajectories of Recovery after Intravenous Propofol versus inhaled VolatilE Anesthesia Feasibility Study

There are two main types of general anesthetic techniques that have been in use as standard of care for more than 50 years:

Given through a vein | Breathed into the lungs

Total intravenous anesthesia (TIVA) | We don't know which one results in a better patient experience. | Inhaled volatile-based anesthesia

Who can join?

- ✓ Adults 18 years of age
- ✓ Patients having an elective surgery not involving the heart
- ✓ Patients having general anesthesia with unconsciousness
- ✓ Patients who will have a tube to help with breathing during surgery

Your Research Experience

We will ask you to complete surveys. Questions may be about your: overall well-being, mood, daily living activities, whether or not you are in a confused state, difficulties you may be having, and memories of waking up during surgery

Before Surgery | Surgery Day | 1 Day After Surgery | 2 Days After Surgery | 7 Days After Surgery | 30 Days After Surgery | 90 Days After Surgery

x5 | x2 | x3 | x1 | x2 | x2 | x1

Benefits to participating

- Financial compensation
- Personalized tracking dashboard of your recovery journey
- Gain knowledge about anesthesia choices
- Help inform a future study that will assess which technique results in better patient experience

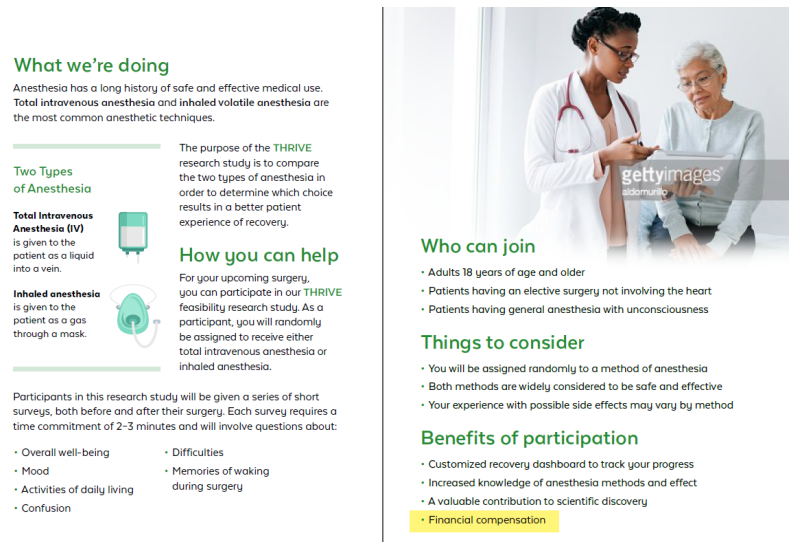
Considerations for participating

- Total time commitment of 30-45 minutes for completing surveys
- 50/50 chance of receiving either anesthesia type
- Patient experience (nausea, vomiting, awareness) may differ by anesthesia type
- Privacy limitations since we are asking additional questions about your recovery

Contact Us:
To learn more about THRIVE, contact
(734) 000-0000 or thrive-trial@umich.edu

MICHIGAN MEDICINE
UNIVERSITY OF MICHIGAN
Washington University in St. Louis

Most recent version – still in draft


What we're doing

Anesthesia has a long history of safe and effective medical use. **Total intravenous anesthesia** and **inhaled volatile anesthesia** are the most common anesthetic techniques.

The purpose of the THRIVE research study is to compare the two types of anesthesia in order to determine which choice results in a better patient experience of recovery.

Two Types of Anesthesia

Total Intravenous Anesthesia (IV) is given to the patient as a liquid into a vein.

Inhaled anesthesia is given to the patient as a gas through a mask.

How you can help

For your upcoming surgery, you can participate in our THRIVE feasibility research study. As a participant, you will randomly be assigned to receive either total intravenous anesthesia or inhaled anesthesia.

Participants in this research study will be given a series of short surveys, both before and after their surgery. Each survey requires a time commitment of 2-3 minutes and will involve questions about:

- Overall well-being
- Mood
- Activities of daily living
- Confusion
- Difficulties
- Memories of waking during surgery

Who can join

- Adults 18 years of age and older
- Patients having an elective surgery not involving the heart
- Patients having general anesthesia with unconsciousness

Things to consider

- You will be assigned randomly to a method of anesthesia
- Both methods are widely considered to be safe and effective
- Your experience with possible side effects may vary by method

Benefits of participation

- Customized recovery dashboard to track your progress
- Increased knowledge of anesthesia methods and effect
- A valuable contribution to scientific discovery
- Financial compensation

Learning to THRIVE

May	What is a Clinical Trial? – NIH Module
June	What is Informed Consent? NIH Module
August	Intro to PCORI Approach to Patient Centered Outcomes Research – PCORI Research Fundamentals
Sept	Sampling, Recruiting & Retaining Study Participants – PCORI Research Fundamentals

Patient Engagement Working Group

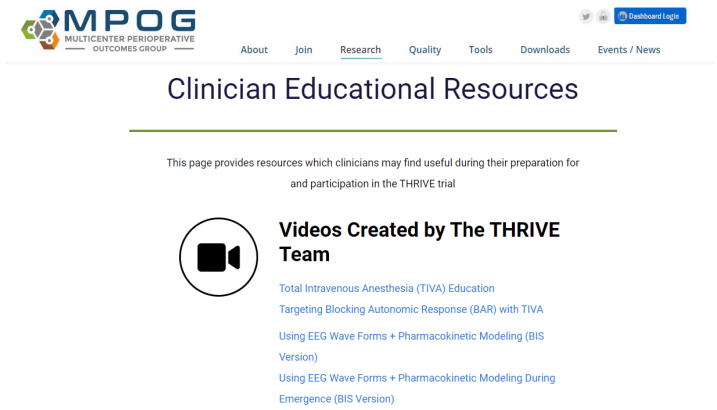
- Alignment of leadership & facilitation for both patient engagement groups – Mark Neuman, Hugo Campos & Mara Bollini
- Provides operational oversight of patient and caregiver engagement activities within THRIVE
- Manages relationships with patient partners and ensures integration of patient and caregiver voice throughout the study
- Oversees patient & caregiver engagement measures of success

Last Name	First Name	Location	Organization	Role
Avidan	Michael	Missouri	WU	Co-Principal Investigator
Bollini	Mara	Missouri	WU	Program Mgr/Staff
Campos	Hugo	California	Unaffiliated	Patient Partner
Carron	Jen	Missouri	BJC/WU	Patient Experience/Staff
Chu	Larry	California	Stanford	Co-Investigator
Eyrich	Nicole	Michigan	U of Michigan	Program Mgr/Staff
Kheterpal	Sachin	Michigan	U of Michigan	Co-Principal Investigator
Neuman	Mark	Pennsylvania	UPENN	Co-Investigator/Site PI
Pennington	Bethany	Missouri	WU	Co-Investigator
Price	Amy	Florida	Stanford	Co-Investigator
Swisher	Laura	Missouri	WU	Program Mgr/Staff

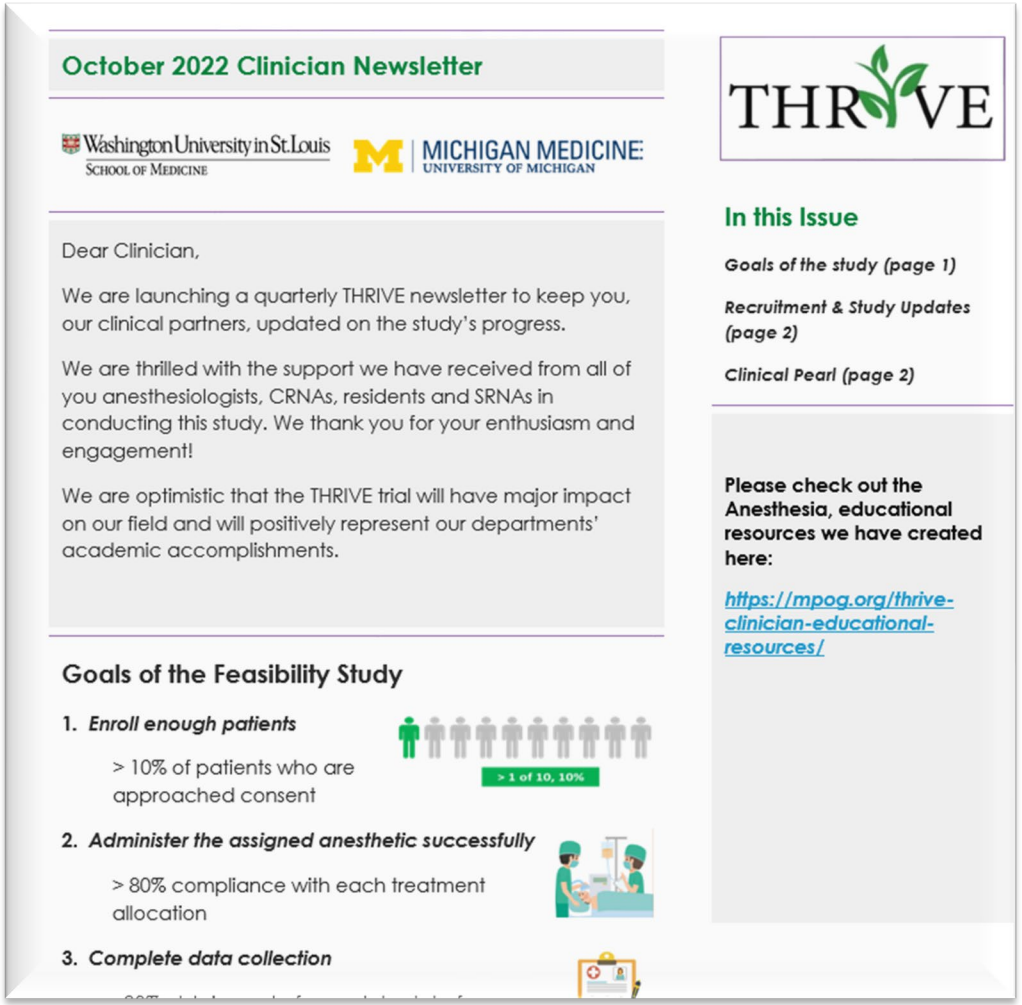
Internal Stakeholder Activities

Clinician Education and Intervention Adherence Working Group:

- **Anesthesia Clinician Education**
  - Grand Rounds presentation
  - Website created with educational videos, tips and resources: https://mpog.org/thrive-clinician-educational-resources/
  - One-on-one clinician education and support during the THRIVE feasibility study

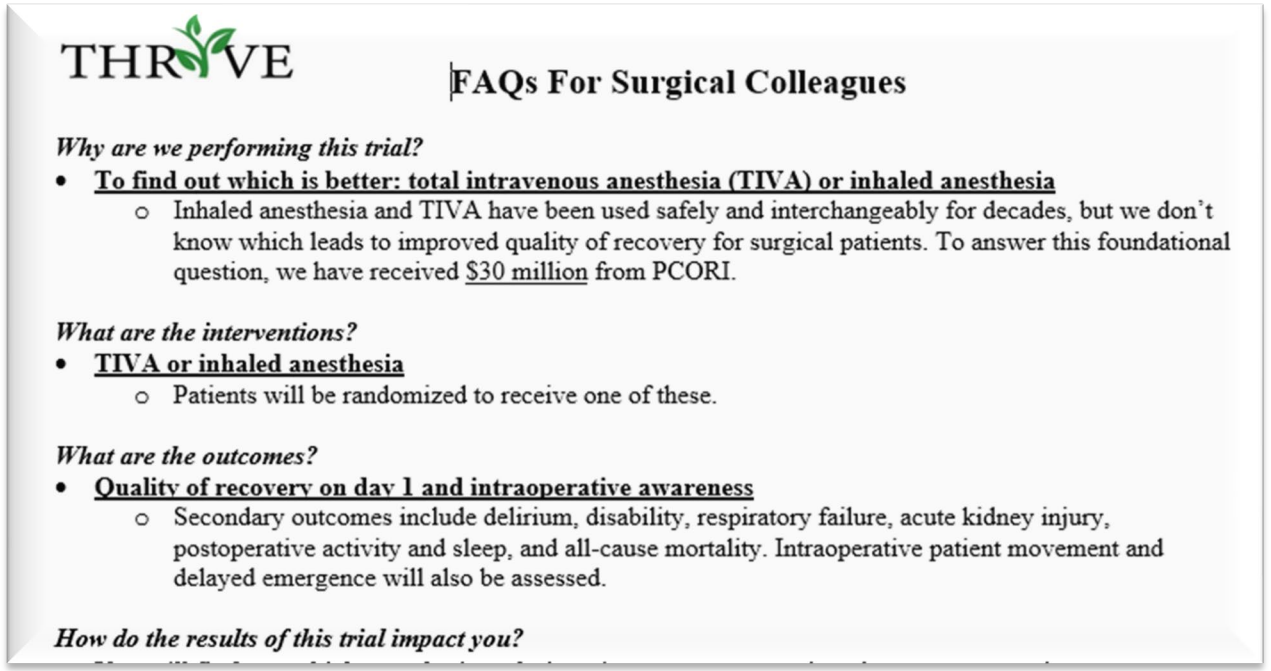


- Quarterly Clinician newsletter



Internal Stakeholder Activities (continued)

- **Non-anesthesia Clinician/Perioperative Education**
  - Personalized THRIVE study overview, FAQs and defined roles presented at multidisciplinary group meetings in August 2022:
    - Surgeons
    - Perioperative nursing
    - Anesthesia Technicians



THRIVE

FAQs For Surgical Colleagues

Why are we performing this trial?

- **To find out which is better: total intravenous anesthesia (TIVA) or inhaled anesthesia**
  - Inhaled anesthesia and TIVA have been used safely and interchangeably for decades, but we don't know which leads to improved quality of recovery for surgical patients. To answer this foundational question, we have received $30 million from PCORI.

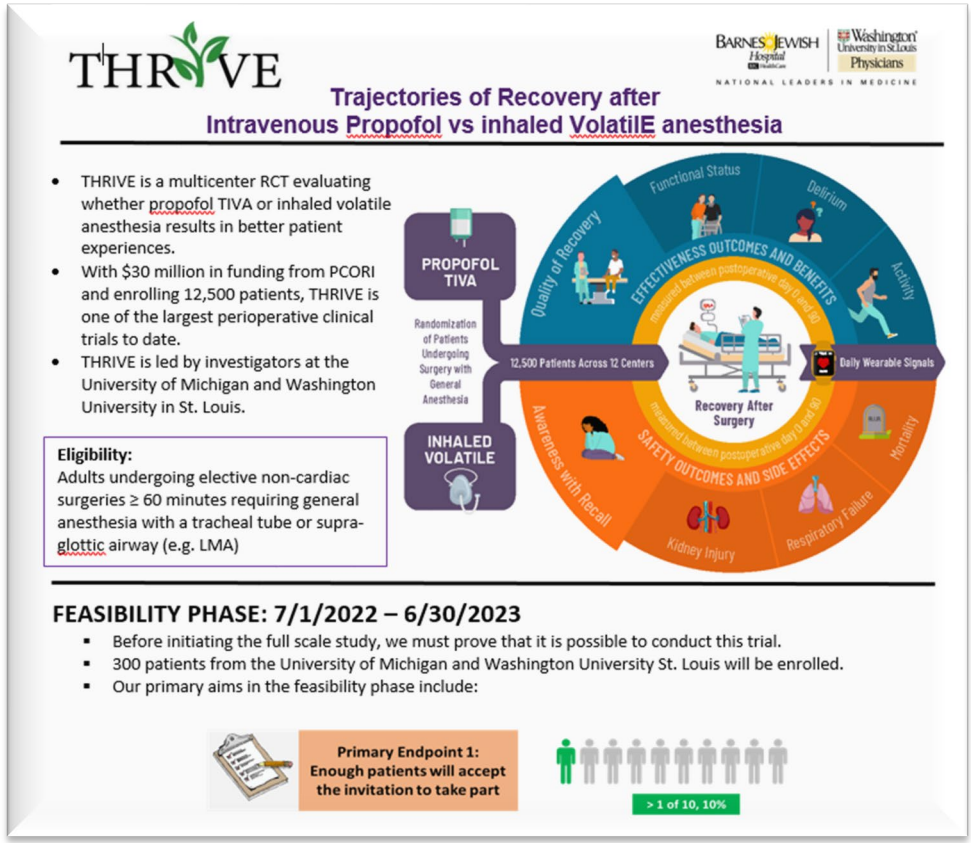
What are the interventions?

- **TIVA or inhaled anesthesia**
  - Patients will be randomized to receive one of these.

What are the outcomes?

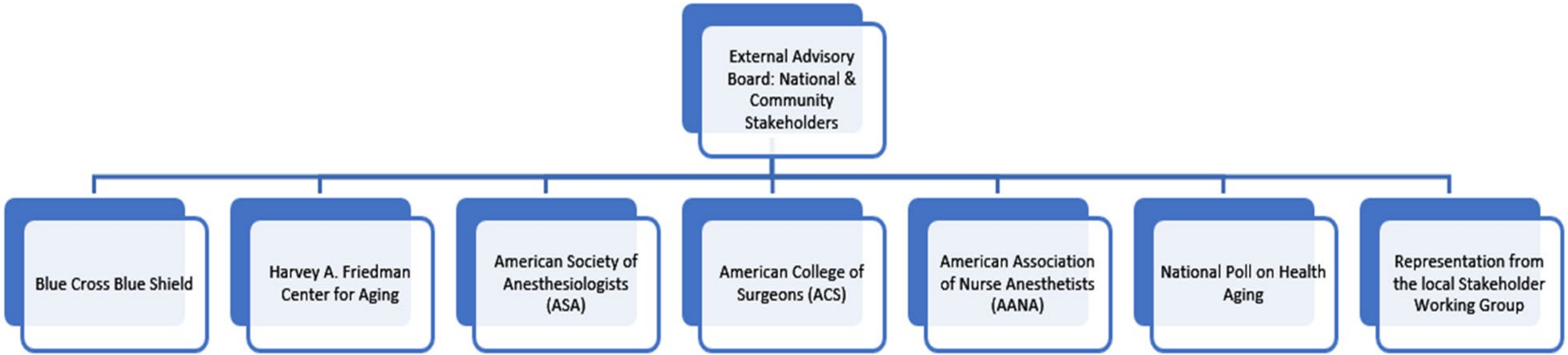
- **Quality of recovery on day 1 and intraoperative awareness**
  - Secondary outcomes include delirium, disability, respiratory failure, acute kidney injury, postoperative activity and sleep, and all-cause mortality. Intraoperative patient movement and delayed emergence will also be assessed.

How do the results of this trial impact you?



External Advisory Board

- Payer, Public health, National Specialty Organizations, Community groups



Stakeholder Experience

- THRIVE should ensure that all stakeholders have a ***positive experience***
- Ensure **ALL** voices are heard
  - ***Patient Partners***
    - Ongoing education throughout the trial
    - Opportunities to extend their role into other working groups, expanding projects related to THRIVE
    - Re-assessment of needs, interest, experience and opportunity to provide feedback
  - ***Internal Stakeholders***
    - Clinician support and education throughout the trial
    - Ongoing communication and follow up
    - Thank you cards and tokens of appreciation
  - ***External Advisory Board***

Engagement goals: site activities

- Overall
  - Completion of selected PCORI-developed training in partnered research principles over the course of the study
  - Interval “engagement rounds discussions” on investigator calls
  - https://research-teams.pcori.org/engaging-stakeholders
- Internal stakeholder engagement: integrated into startup/launch process
  - Onboarding/orientation of local clinical teams
  - Establishment of buy-in from institutional leaders
  - Feedback on study processes from local stakeholders
  - Collection of surgeon satisfaction/operating conditions info

Engagement goals: site activities

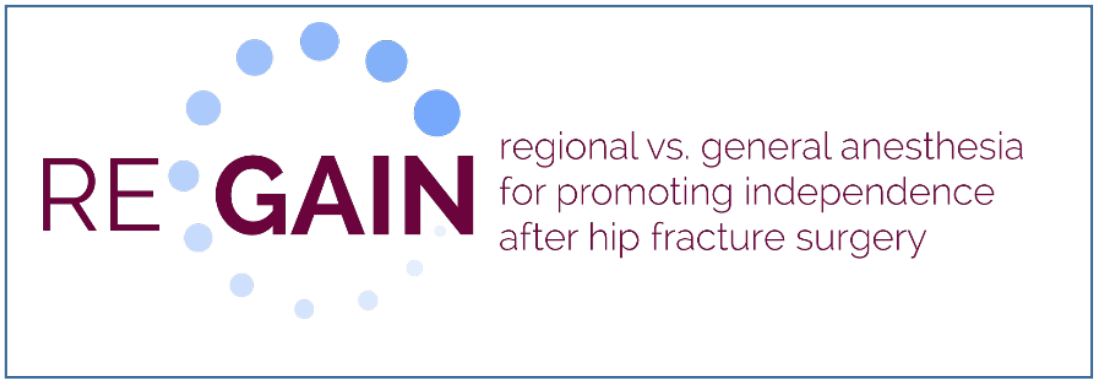
- Patient engagement
  - Goal to conduct 6-12 focus groups over the course of the study to represent site-level patient voices
  - Goal for each site to identify 2-4 patient participants, plus PI and lead coordinator
    - Individuals who have completed THRIVE and agreed to be contacted for additional projects
    - Other local patient partners (e.g., patient/family advisory board members)
  - Focus groups to be organized centrally by Wash U, UM, or Penn teams
- Patient/external stakeholder engagement
  - All sites invited to submit proposals for additional engagement activities focused on patients or external local stakeholder groups (e.g., churches, government, community groups)
  - THRIVE team will fund approved engagement activities at site level up to $5,000/site

Discussion

REGAIN: Top 5 Lessons Learned for THRIVE

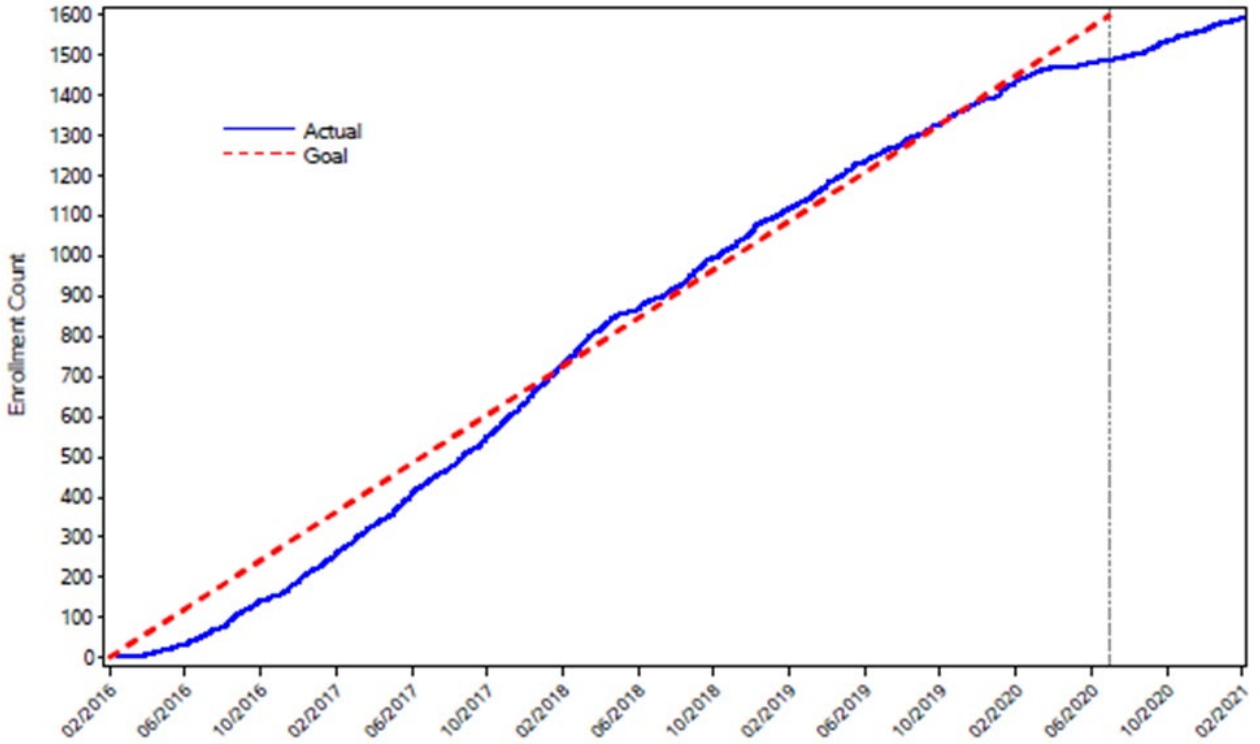
Mark D. Neuman, MD, MSc

University of Pennsylvania

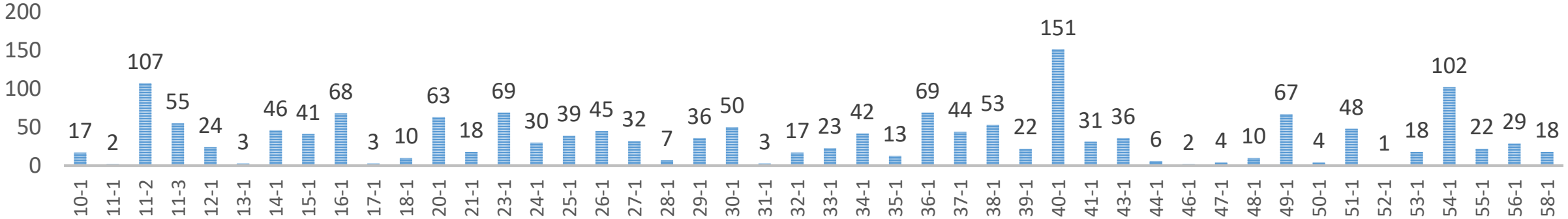


- Pragmatic RCT of spinal versus general anesthesia for hip fracture surgery
- Enrollment (targeted & actual): 1,600 patients enrolled 2/2016-2/2021
  - 22,022 patients screened!
- 46 centers in US & Canada
- Primary outcome: recovery of independence in walking at 60 days after randomization
- Funding: Patient Centered Outcomes Research Institute, $11.8M/5Y

1. It’s accrual world out there



REGAIN FINAL COUNTS BY SITE (PATIENTS RANDOMIZED)



2. Time is the enemy

Short Communication

CLINICAL TRIALS

Clinical Trials
2018, Vol. 15(1) 107–111

DOI: 10.1177/1740774517735536
journals.sagepub.com/home/ctj
SAGE

Time to institutional review board approval with local versus central review in a multicenter pragmatic trial

Mark D Neuman[1,2,3,4], Lakisha J Gaskins[1], Tracy Ziolek[5] and the REGAIN Investigators

Time to selected IRB approval milestones via central vs local IRB review for initial site approval for 34 REGAIN trial sites approved before May 1, 2017

	Central review (N=9)	Local review (N=25)	P value
Time in days from receipt of IRB materials to local IRB submission (median, IQR)	39 (35, 134)	58 (41, 105)	0.711
Time in days from local IRB submission to final IRB approval (median, IQR)	27 (14, 32)	66 (29, 138)	0.026
Time in days from receipt of IRB materials to final IRB approval (median, IQR)	100 (71, 148)	132 (87, 209)	0.191

3. Anesthesia practice is chaotic

Case study: Site 431

- PID 4310028: Anesthesia team unable to place spinal after multiple attempts by 2 providers; patient received general anesthesia.
- PID 4310029: Patient requested general anesthesia while being positioned for spinal. Patient received general anesthesia
- PID 4310036: Patient began vomiting after arrival in the operating room. Anesthesia provider opted for general anesthesia due to potential aspiration risk with sedation.

Managing crossovers: distinguishing "clinical" from "logistical" events

- Site detailing & coaching to minimize logistical crossovers
- Site-level troubleshooting for issues with provider performance
- 1 site suspended for non-adherence (6 crossovers RA→GA w/in 1st 20 patients randomized)

Reason for crossover	n (%)
Spinal attempted, unable to place	52 (43.7)
Clinician selected general anesthesia	29 (24.4)
Patient/proxy request	18 (15.1)
Block failure or intraoperative event necessitating conversion to GA	12 (10.1)
Miscommunication/scheduling	7 (5.9)
No reason	1 (0.8)
Total	119 (100)

4. Docs gonna doc

Well, I mean there I think the patient 100 percent takes precedence….So I'm sorry I'm breaking your – I'm basically going to the other arm and basically breaking protocol. But I strongly believe that this is the best for my patient right now. So I will do this regardless of whether they've been involved in the study or not. –REGAIN Clinician

5. Every successful trial represents the solution to its own specific collective action problem

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Spinal Anesthesia or General Anesthesia for Hip Surgery in Older Adults

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Annals of Internal Medicine

ORIGINAL RESEARCH

Pain, Analgesic Use, and Patient Satisfaction With Spinal Versus General Anesthesia for Hip Fracture Surgery

A Randomized Clinical Trial

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- The Patient –Centered Outcomes Research Institute
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- The Foundation for Anesthesia Education and Research
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THANK YOU!!!

Next Steps

Thank You!

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