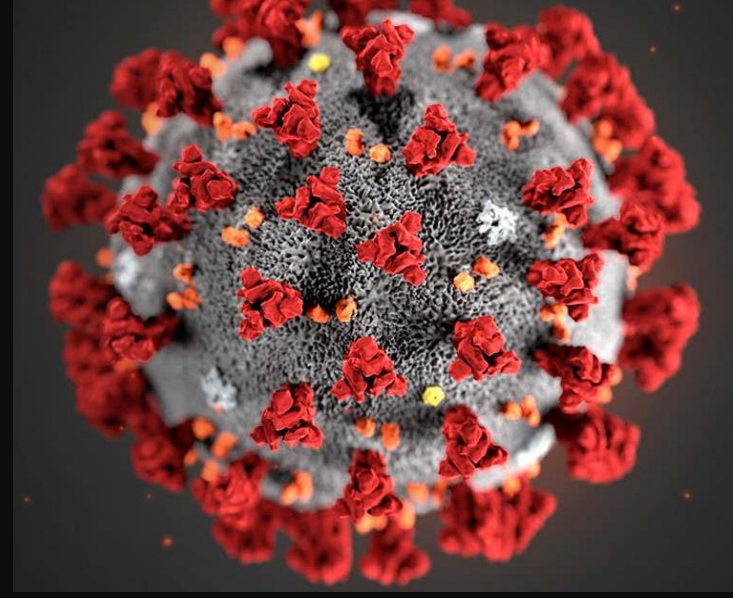
Taking Research to the Participant:

Experiences with TREAT NOW, a No-Touch COVID-19 Trial



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Disclosures

TREAT NOW funding

- **Department of Defense/USAF**
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TREAT NOW: The no touch challenge

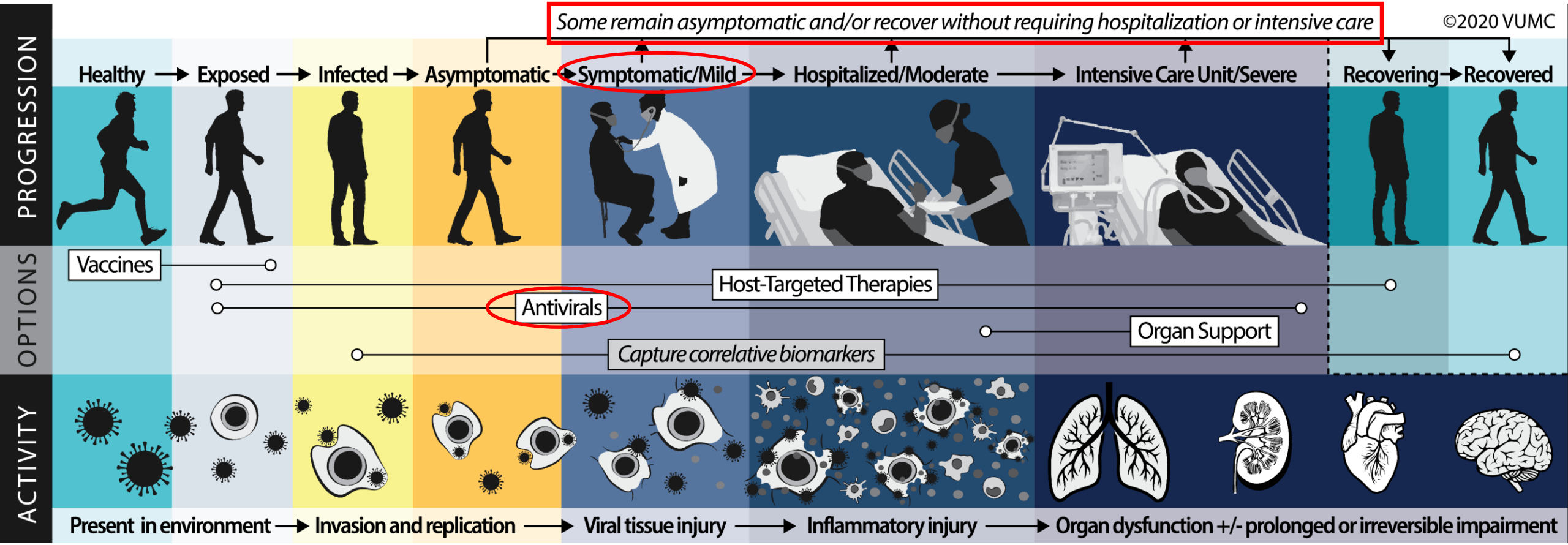
The entire trial has to be completed without ever having any physical interaction with the participant

TREAT NOW: Trial of Early Antiviral Therapies during Non-hospitalized Outpatient Window

- **Objective**: Determine the effectiveness and safety of early treatment with lopinavir/ritonavir in outpatient adults with COVID-19
  - Adaptive, platform trial with ability to add (and remove) additional agents
  - Focus on (repurposed) FDA-approved, rapidly scalable/easily deployed therapies

- **Hypothesis:** Outpatient adults with COVID-19, early initiation of lopinavir/ritonavir will:
  - Reduce disease progression to hospitalization
  - Improve clinical outcomes/recovery

Early Intervention for Mild COVID-19 in Outpatient Setting to Prevent Hospitalization



Rationale for TREAT NOW

- Early intervention in outpatient setting
- Impacts disease progression and recovery
  - Prevent severe disease
  - Reduce long duration of symptoms (PASC)
- High disease prevalence
- Relatively understudied population
- Focus on **repurposed drugs –** can add other drugs, adaptive approach, IND exemption (typically), faster time to clinical use or EUA
- Pragmatic, hands-off design

Rationale for Lopinavir/ritonavir

- FDA approved for Human Immunodeficiency Virus Type 1 (HIV-1)
- Extensive *in vitro* efficacy for severe coronaviruses
  - Potent antiviral activity against SARS-CoV-2
- Endorsed by WHO in their candidate treatment guidelines
- Early clinical data mixed
  - Small sample sizes
  - Hospitalized patients only

TREAT NOW Trial

- **Design:** Investigator-initiated, multicenter, blinded, placebo-controlled, randomized clinical trial
- **Population:** Outpatient (non-hospitalized) adults with COVID-19 (positive SARS-CoV-2) with ≤6 days of symptoms
- **Setting:** 5 enrolling sites (Colorado, Tennessee, Massachusetts, Wisconsin, Mississippi); Vanderbilt Coordinating Center (VCC)
- **Interventions:** Lopinavir/ritonavir or Placebo (hydroxychloroquine dropped early)
- **Pharmacy:** Up to 14 days of therapy, central pharmacy model
- **Recruitment Strategies:** emergency departments/urgent care, outpatient testing centers, advertising (social media, website)
- **Sample Size:** ~300 patients per arm (90% power for OR 1.75)
  - Bayesian adaptive approach

Primary Endpoint

Modified COVID Ordinal Scale to Day 15

Level	Description
1	Death
2	Hospitalized on MV or ECMO
3	Hospitalized on supplemental O2
4	Hospitalized not on supplemental O2
5	Not hospitalized with symptoms and limitation in activity
6	Not hospitalized with symptoms, no activity limitation
7	Not hospitalized without limitation in activity

- Patient-centered
- Collectable in pandemic
- Widely used for COVID-19 trials
- Enhanced power compared with binary outcome

TREAT NOW: The no touch challenge

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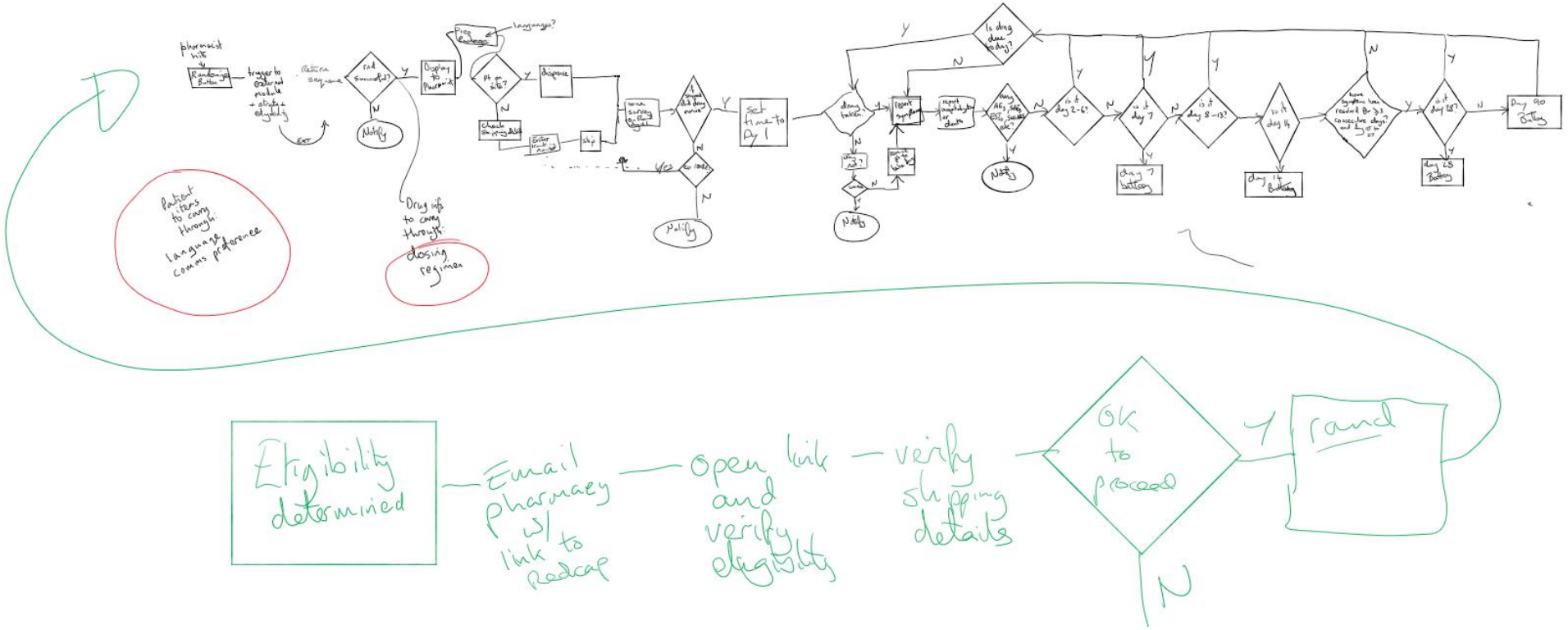
TREAT NOW: Meeting the no touch challenge

- **Recruitment:** How do you find patients and get them into the screening process when they are not on site or in your practice, or even in your state?
  - Equity/diversity, language, technology considerations
- **Eligibility:** How do you verify inclusion and exclusion criteria, including SARS-CoV-2 test results?
- **Investigational drug:** How does the participant get study drug?
- **Evaluations:** How will the outcome be measured?
- **Safety:** How to manage safety without baseline EKG and labs? How will AEs, SAEs and other events of interest be handled?
- **Adherence:** How will we know if the participant took their medications or completed their assessments?

TREAT NOW: Converting the EDC into a smart system



At every step and with every data form, it is essential to think though the possible failures and how the technology can trap them to maintain trial integrity

IN REAL TIME

TREAT NOW: General approach

- Recruitment by phone outreach, social media and advertising
- Site-based, coordinator-assisted enrollment to verify/validate eligibility
- eConsent and/or electronic copies of paper consent
- Integrated pharmacy workflow with an adaptive randomization system
- Text, e-mail, and app-based participant-facing data collection
- Incorporation of multiple fail safes in the electronic data capture systems

TREAT NOW: Data Collection Strategy

- Initial collection via phone at time of consent and entered into REDCap
- Multimodal data collection
  - Text/email link sent with REDCap survey (primary)
  - MyCap app loaded onto phone (primary)
  - Phone survey (secondary)
- Daily symptom/safety check for 16 days
- Final assessment at Study Day 29
  - Chart review if hospitalized

TREAT NOW: Progress to date

Pre-Screened	Declined Screening	Contacted	Eligible	Consented	Randomized
847	184	797	26	21	21
3730	467	1276	64	62	62
61	27	40	22	3	3
167	55	123	9	8	8
2451	339	1249	154	112	112
7256	**1072**	**3485**	**275**	**206**	**206**

- >200 patients enrolled
- Participants from across the country
- Smart data system being repurposed for other trials

TREAT NOW: Key findings

- Data system must accommodate many different levels of technical skill, different languages, and different modes of communication
- Calibrating communication frequency with urgency and impact of an event is essential to minimize alert fatigue
  - Research team never touches patient
  - Research team does not contact patient unless triggered
- Automated communication needs to go to the right people through right method at the right time
- Every request for flexibility has consequences for the “smart” technology
- Some data (SAE or hospitalization) requires deeper access to information about the health condition of the participant than can be solicited via a survey, phone call, or chart review

TREAT NOW: Communication

TS

TREAT-NOW Study <noreply@vumc.org>

Ginde, Adit;

TREAT-NOW: Survey Review Needed!!

TREAT-NOW Subject: 03-063 submitted a survey with the following issues:

- day_5_survey and day_6_survey are missing

["day_5_survey and day_6_survey are missing"]

TREAT-NOW Subject: 03-064 submitted a survey with the following issues:

- Contact requested

["Contact requested"]

TREAT-NOW Subject: 03-055 submitted a survey with the following issues:

- Did not take medication

["Did not take medication"]

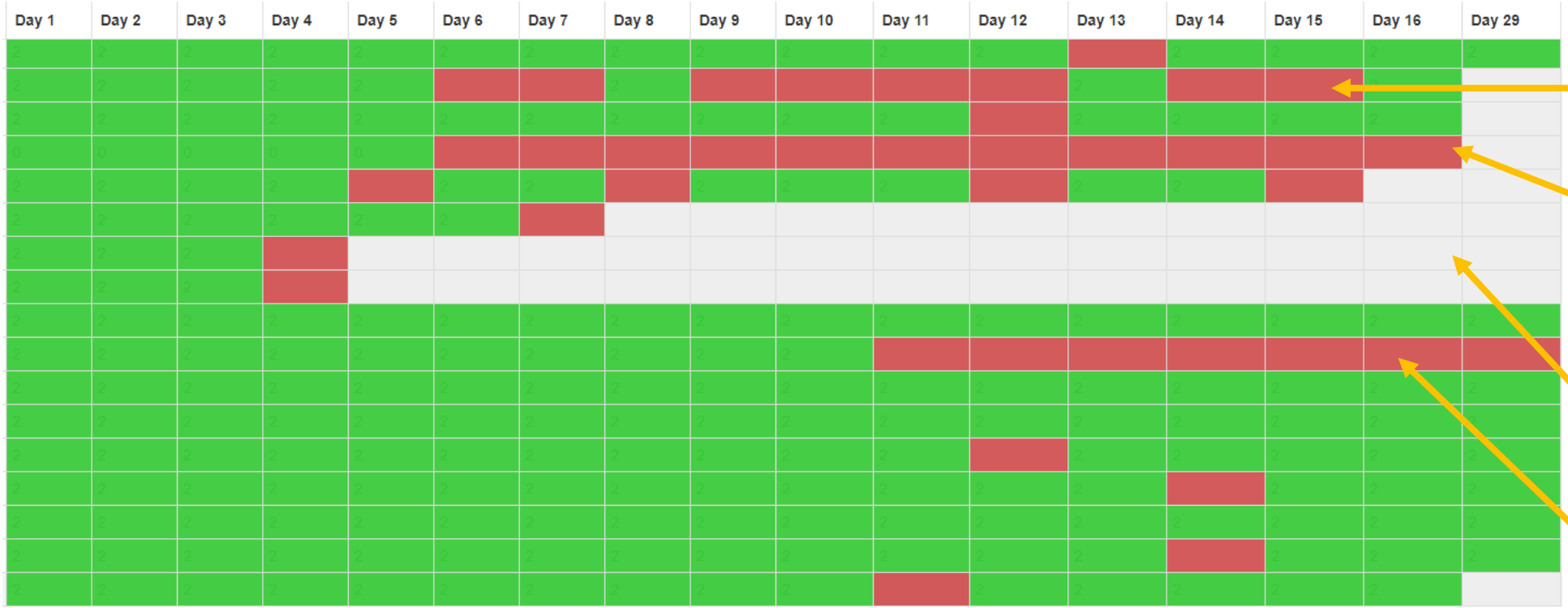
TREAT-NOW Subject: 03-062 submitted a survey with the following issues:

- Received medical care
- Did not take medication
- Contact requested

["Received medical care", "Did not take medication", "Contact requested"]

TREAT NOW: Study design implications

- More data = more information = more power = less participants



- Missingness is not at random

TREAT NOW: Summary

- No touch trials are not just feasible, they are effective
- Expect to spend considerable effort getting the smart data systems right
- Efficiencies emerge after initial build
- There are new methodological challenges to solve
- There is an incredible opportunity for making research accessible to all

Thank you!

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Vanderbilt Coordinating Center (Dr. Chris Lindsell)
Collaborators, Colleagues, Research Staff, Regulatory/Admin Teams, Participants, Patients/Families

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