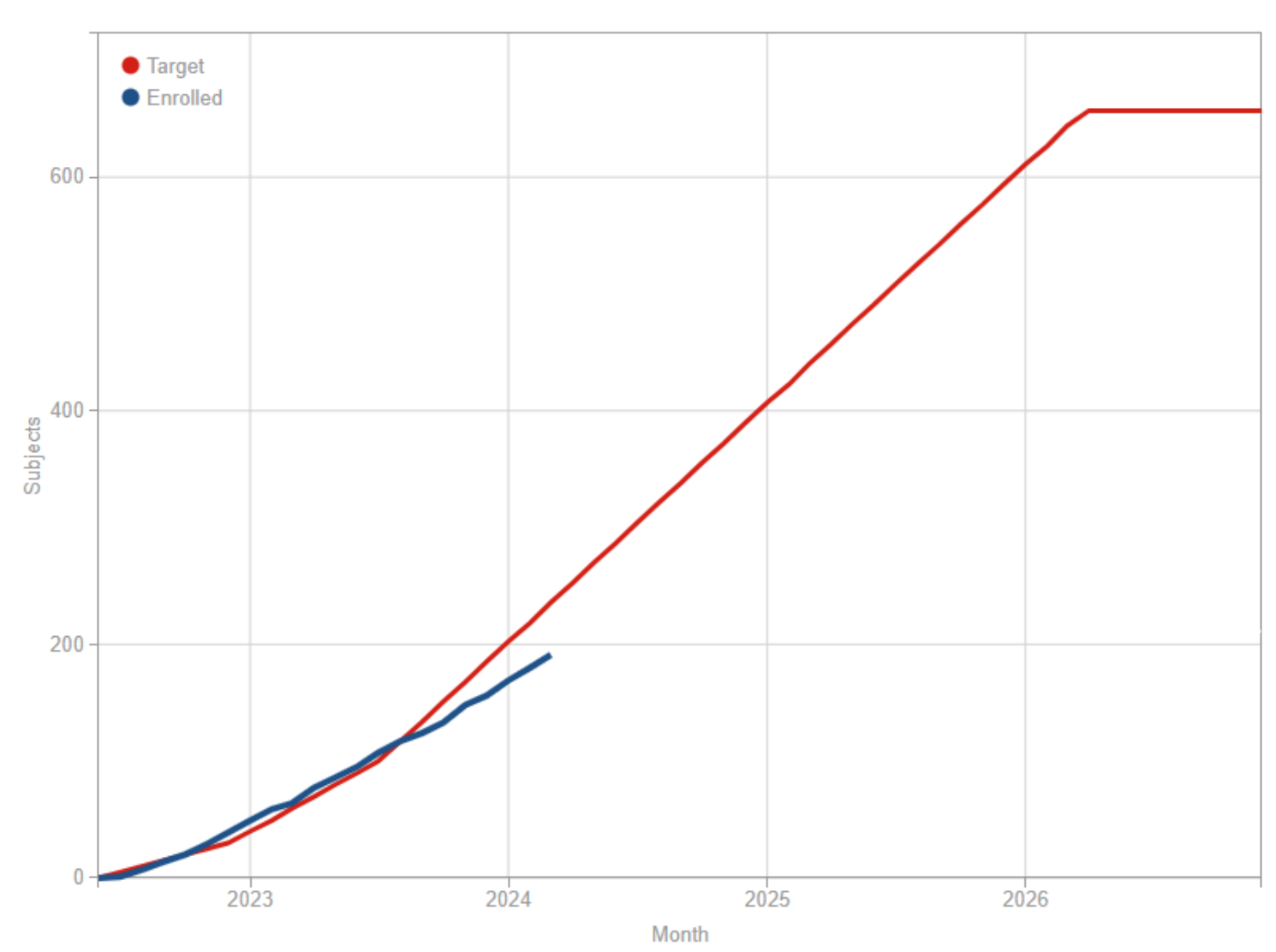
Validation of **E**arly Prognostic Data for **R**ecovery Outcomes after Stroke for **F**uture, Higher **Y**ield Trials: A Biomarker Validation Study

CRC Webinar Agenda
Tuesday, March 26, 2024
12:00pm- 1:00pm ET

1. Welcome, Study Updates/Reminders
2. Screening
3. Pre-Screen Log
4. Consent/eConsent
5. Recruitment Tools
6. Remaining Q&A and Closing Remarks (All)

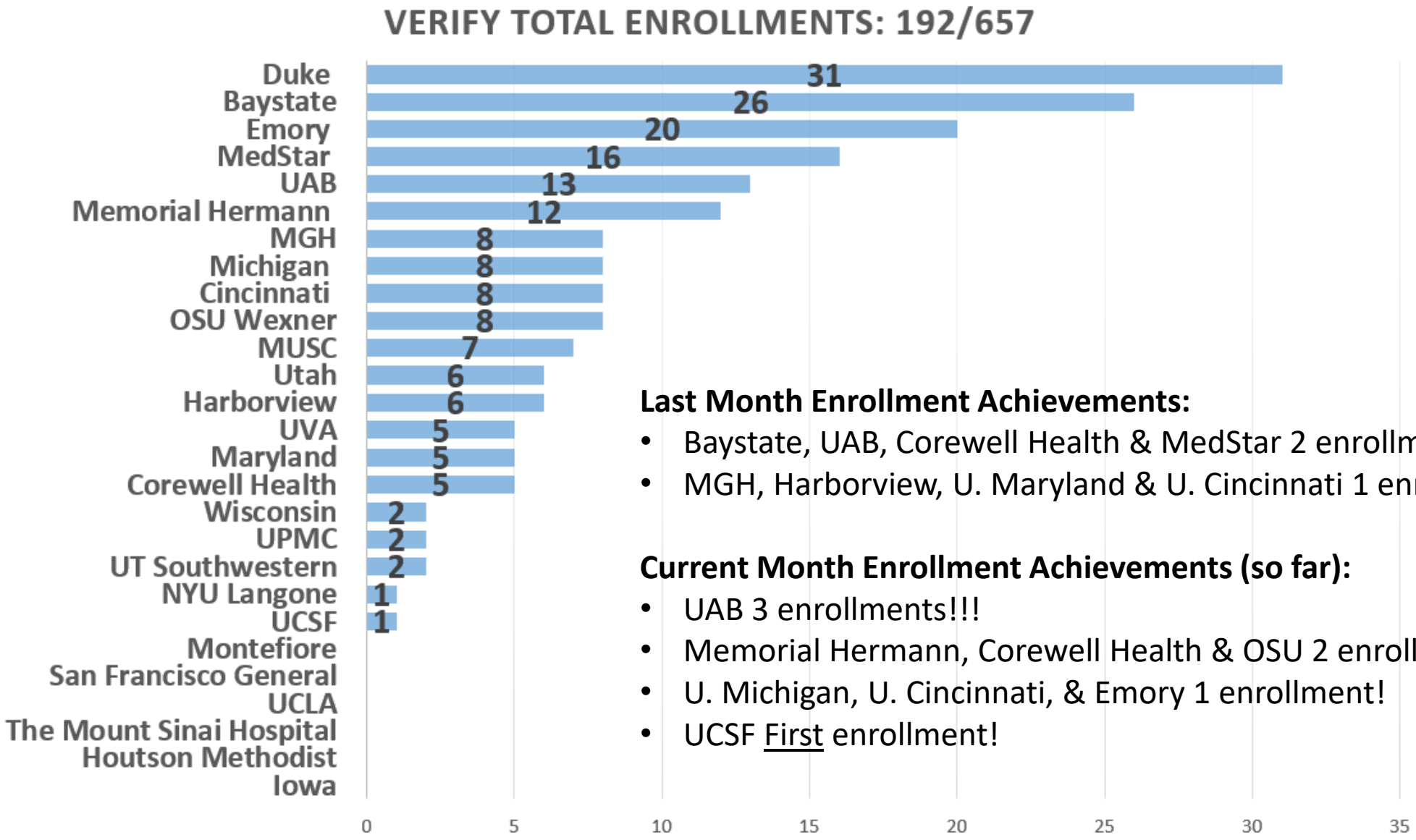
Projection Curve: Target vs Actual Enrollment



Monthly Goal:

17

- Last patient to be enrolled by 10/31/2025
  - February 2024 Enrollments: 12
  - March 2024 Enrollment (so far): 13



Last Month Enrollment Achievements:

- Baystate, UAB, Corewell Health & MedStar 2 enrollments!!
- MGH, Harborview, U. Maryland & U. Cincinnati 1 enrollment!

Current Month Enrollment Achievements (so far):

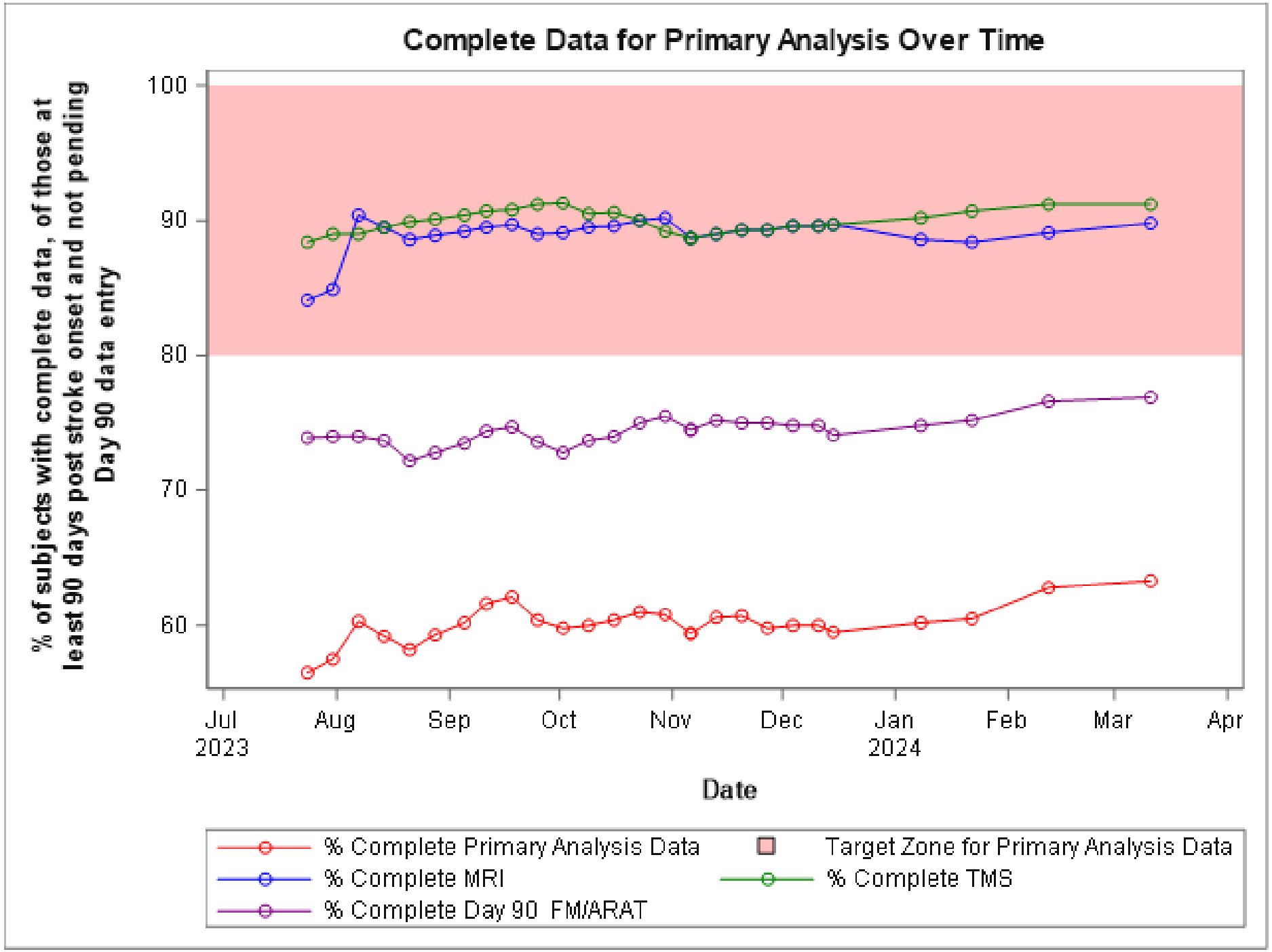
- UAB 3 enrollments!!!
- Memorial Hermann, Corewell Health & OSU 2 enrollments!!
- U. Michigan, U. Cincinnati, & Emory 1 enrollment!
- UCSF First enrollment!

Site Activation Status

Race to Activation Tracker															
Site Name	CTA Executed	CIRB Approved	DOA Approved	Investigator agreement form's uploaded	TMS Shipping Address entered	TMS Machine obtained	At least 1 TMSO online training Completed	Greenlighted to start TMS HV Training	Uploaded TMS HV data to RedCAP	TMS HV Training Completed for at least 1 TMSO	TMS Technique Check	MRI Phantom Approved	All WebDCU Documents uploaded	Site Activation Meeting Completed	Site Activated
Lahey Hospital & Medical Center															
Penn State Hershey Medical Center															
Prisma Health Richland Hospital															
Pennsylvania Hospital															
Strong Memorial Hospital															
Froedtert & Medical College of Wisconsin															
Birmingham VA Medical Center															
Keck Hospital of USC															
Wake Forest Baptist Health															

Missing Primary Data Update

PROGRESS!

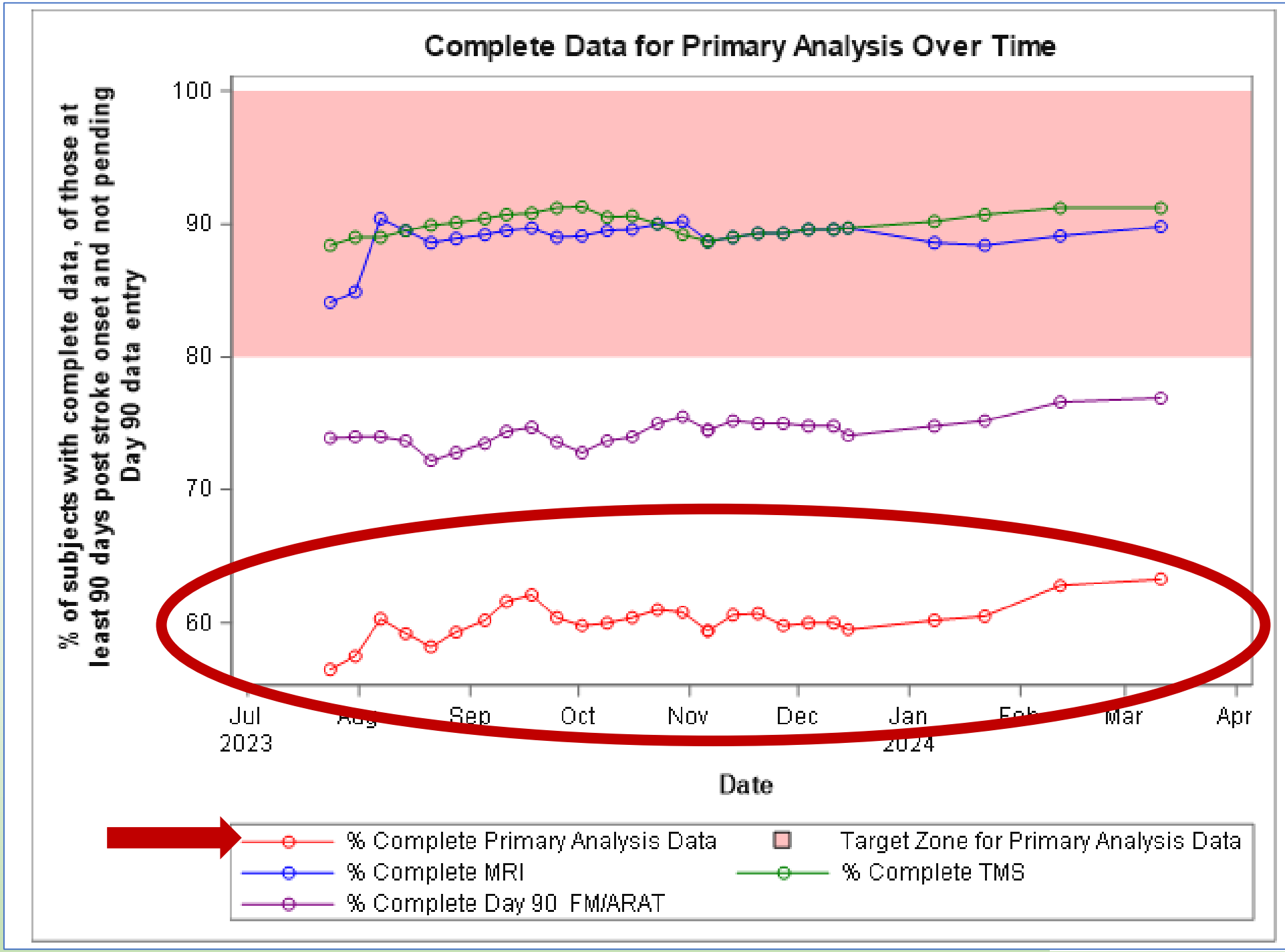


Missing Primary Data Update

93 (63.3%) enrolled pts have complete data

Denominator=147 patients who have reached 90 days post stroke onset without pending Day 90 data

Main driver is FM/ARAT collection at 90 days



In-person Investigator Meeting - CANCELED

Replaced with:

Virtual- Investigator Meeting 2024

- **Dates: June 4th 2PM EST to 5 PM EST**
- Who should attend? Site PI, PSC, TMS operators, ARAT/FM assessors, and any other team members who wish to attend.
- A placeholder calendar invite has been sent out and the webinar calendar invite will be coming soon
- Stay tuned for more details to come

Also plans for individual sites visits at selected sites

Sites with Challenges

Please help us help you!

Activated Sites:

- Team will be scheduling meetings with sites who have not enrolled in the past 3 months to review the following:
  - Screening process
  - Consenting methods

- Plans for in-person sites visits and trainings at selected sites
  - Sites will be contacted directly

Non-activated Sites:

- Team will be in contact with each site to formulate an individualized plan for timeline to activation

All VERIFY Site:

- Is your site having issues that do not apply to those above? Reach out to the team!
  - We can help troubleshoot any issues your site may be facing!

Screening

Screening/Consent Workflow

1. **Daily Chart Screening**
   - Identify all stroke patients (ischemic and ICH) in EMR with the following:
     - <96 hours of onset at admission
     - Alert and able to consent themselves
     - No TMS & MRI contraindications
   - NO→ do not move forward with screening
   - YES→proceed to next step

2. **Ask clinical team if patient has any upper limb symptoms?**
   - NO→enter as a Pre-screen failure
   - YES→proceed to next step

3. **Patient is eligible based on full eligibility criteria?**
   - NO→enter as a Pre-screen failure
   - YES→proceed to next step

4. **Patient consents?**
   - NO→enter as a Pre-screen failure
   - YES→proceed to next step

5. **SAFE score ≤ 8?**
   - NO→enter as a screen failure
   - YES→proceed to next step

6. **Remains eligible and 1st TMS stimulation or study-specific MRI is started?**
   - NO→enter as a screen failure
   - YES→participant is now enrolled!

Screening Tips

- **PreConsent potential subjects.**
  - You can approach a potential subject prior to the 24-hour window!
  - Obtain verbal confirmation they are interested in signing the consent once in the study window.

- **Go to stroke rounds daily!**
  - Print out current stroke patient list from EMR- pre-screen subject prior to rounds.
  - By having the SOC stroke team recognize you- they will be more likely to refer potential enrollments to you without you asking over time.
  - New to your site or stroke clinical research? Start going to rounds prior to study activation at your site!

- **Make friends with stroke fellow (if site has them)**
  - Ask to see if they would be interested in being a Sub-I for screening purposes.
  - Looks good for them on their CV and helps your team in the long run!

- **When patients are located in the ED:**
  - Do not assume the patient does not qualify for VERIFY study or that they are going to be discharged soon:
    - Hospital may be at capacity, and they are unable to be brought to the floor.
    - Some patients can spend several days in the ED prior to being discharged
    - If they had a stroke- they will be followed by the neurology team regardless if they are in the ED, whether is it is inpatient ward, Neuro ICU or Neuro step down unit physicians
    - Talk to the stroke attending, fellow, or neurology residents on service! **Communication** is Key!

- **Consider which inpatient services take care of stroke patients for screening for VERIFY study.**
  - Neurology/stroke ward admissions
  - Stroke admissions into neurocritical care/ICU (ie, post tPA or thrombectomy)
  - Step-down units (may be a separate team)

- **If a participant is being discharged, see if they would be willing to come back in the next day or two of the study window to complete study assessments, imaging, and or TMS.**
  - They do not have to be inpatient at the time of study windows!

Screening a patient:

- Looking into the EMR you come across a patient with the following:
  - LKW 5am 3/25
  - NIHSS 10
  - Went for thrombectomy

1. Do you move forward with screening?

Yes

No

Screening a patient:

- You attend rounds and ask the stroke team if the patient has any upper limb symptoms. They say aren't sure yet.

2. What should you do next?
    A. Wait around and bug the fellow/resident/attending until they can provide you with an answer
    B. Go examine the patient yourself and if confirm if they have symptoms
    C. Go ahead and review the patient for the full inclusion/exclusion criteria to confirm outside of any upper limb symptoms, they may still qualify for the study

Screening a patient:

- The clinical team FINALLY gets back to you and says the patient has some limited range of motion.

  3. Do you move forward with screening?

  Yes
  No

Screening a patient:

- You had already confirmed that the patient (per the EMR) has any medical history that would exclude them from the study, so you approach them for consent. The patient asks that their wife be present before they consent for the study, because she is a former nurse and knows about these things.

4. What do you do next?
    A. Attempt to convince the patient to move forward with the consent, while assuring them that they will explain everything to their wife later.
    B. Wait for wife to be in-person at the hospital and leave a copy of the consent with the patient to review in the meantime.
    C. Ask if they can just call their wife now and go over the study with them both at the same time.

Screening a patient:

- The patient consents, and the official SAFE score is:

Shoulder Abduction		Finger Extension					
		0	1	2	3	4	5
	0						
	1						
	2						
	3						
	4						
	5						

5. Do you move forward with enrollment?

Yes
No

Screening a patient:

- The patient is unexpectantly discharged from the hospital. The SOC MRI included the 3D-T1 sequence (thankfully), but TMS has not been conducted, because the window opens tomorrow.

6. What should you do?
    A. Attempt to see if the patient can come back within window to conduct the TMS
    B. Complete TMS early, so that the biomarker is collected regardless of timing
    C. Move forward with enrollment, since the 3D-T1 sequence was at least obtained

Screening a patient:

- The patient was unable to come back to have TMS performed.

7. Was this patient enrolled in the VERIFY study or were they deemed a screen failure (consented but not enrolled)?

Enrolled
Screen failure

Pre-Screen Fail Log

A02	Site ID	[redacted]
A03	Site name *Assigned by WebDCU.*	[redacted]
A04	Screening date	25-Mar-2024
	Demographic Information	
A05	Birth sex	(●) *Male* ( ) Female
A06	Ethnicity	( ) Hispanic or Latino (●) *Not Hispanic or Latino* ( ) Unknown
A07	Race *Check all that apply*	[ ] American Indian or Alaska Native [ ] Asian [■] *Black or African American* [ ] Native Hawaiian or other Pacific Islander [ ] White [ ] Unknown
A08	Age	[redacted] *years*
A09	Informed consent	(●) *Not approached* ( ) Declined ( ) Obtained
A10	Reason consent not approached or declined	Global Aphasia
A11	Date of informed consent	
A12	Patient withdrew consent prior to enrollment	
A13	Reason consent withdrawn	
B01	Reason patient was not enrolled	(●) *Patient eligibility issues* ( ) Other
B02	Reason patient was not enrolled is 'Other'	
	Inclusion Criteria	
Q14	Age 18 years or older	( ) No (●) *Yes*
Q15	Unilateral stroke due to ischemia or intracerebral hemorrhage *Protocol version 1.6 and above require the stroke to be symptomatic.*	( ) No (●) *Yes*
Q16	Motor deficits in the acutely affected Upper Extremity *For those who were consented, this is defined as SAFE score <= 8 within 48 to 96 hours of stroke onset or last time known well. For those who are NOT consented, this is defined by clinical assessment.*	( ) No (●) *Yes*
Q17	Provision of signed and dated informed consent form by subject within 48 to 96 hours of stroke onset *Or time last known well.*	(●) *No* ( ) Yes
Q18	Stated willingness to comply with all study procedures and availability for the duration of the study	(●) *No* ( ) Yes
Q19	Speaks English or Spanish	(●) *No* ( ) Yes

	Exclusion Criteria	
Q51	Upper Extremity injury or conditions that limited use prior to the stroke	◉ *No* ○ Yes
Q52	Visual impairment that prevents ability to perform ARAT assessment	○ No ◉ *Yes*
Q53	Dense sensory loss indicated by a score of 2 on NIHSS sensory item	◉ *No* ○ Yes
Q54	Unable to abduct the shoulder or extend the fingers of the non-paretic Upper Extremity on verbal command	◉ *No* ○ Yes
Q55	Isolated cerebellar stroke	◉ *No* ○ Yes
Q56	Bilateral acute strokes or symptomatic stroke in any location within 30 days prior to index stroke	◉ *No* ○ Yes
Q57	Co-enrollment in a trial of an intervention targeting the incident stroke *Acute treatment or rehabilitation/recovery intervention after baseline assessments for VERIFY are initiated.*	◉ *No* ○ Yes
Q58	Known or expected inability to maintain follow-up with study procedures through 90 days	○ No ◉ *Yes*
Q59	Cognitive or communication impairment precluding informed consent by the participant	○ No ◉ *Yes*
Q60	Major medical, neurological, or psychiatric condition that would substantially affect functional status	○ No ◉ *Yes*
Q61	Non-cerebrovascular diagnosis associated with unlikely survival at 90 days	◉ *No* ○ Yes
Q62	Pregnancy	◉ *No* ○ Yes
Q63	Contraindication to non-contrast MRI *Certain metallic implants, metallic foreign bodies or severe claustrophobia.*	◉ *No* ○ Yes
Q64	Contraindication to TMS *Cardiac pacemaker or other electronic devices in the body at or above the level of the seventh cervical vertebra (such as cochlear implant, cortical stimulator, deep brain stimulator, vagus nerve stimulator, cervical spine epidural stimulator, or ventriculoperitoneal shunt); Skull defect related to current stroke; Seizure after onset of current stroke; Seizure within the last 12 months while taking anti-epileptic medications; Previous serious adverse reaction to TMS.*	◉ *No* ○ Yes
Q65	Unable to perform behavioral assessments within 48-120 hours of symptom onset *Or time last known well*	○ No ◉ *Yes*
Q66	Unable to receive TMS or get MRI within 72-168 hours of symptom onset *Or time last known well*	○ No ◉ *Yes*
Q67	Anticipated inability to perform study procedures within 168 hours of symptom onset	○ No ◉ *Yes*
Q69	Stated willingness to comply with all study procedures and availability for the duration of the study, including Day 90 visit which must occur in-person	○ No ◉ *Yes*
GC	General comments	

Consenting/eConsent

TMS-Related Seizure Risk Info for Consenting:

- When communicating with patients and families it is safe to say that the risk of seizure is very low.
  - In routine clinical care (ie, without TMS)
    - Around 5% of patients experience a seizure within 2 weeks of their stroke.
  - In contrast, the added risk of seizure with TMS is much lower, at around 0.08%.
    - The risks are extremely low when people are screened using the checklist, to rule out anyone who could have an elevated likelihood of seizure.

- When speaking with patients and families, you could let them know that:
  - *"TMS is safe, painless, and non-invasive. There is a small risk of a seizure, but this risk is extremely low, at **less than one tenth of one percent**. When TMS is performed under published guidelines in patients with stroke, the incidence is 0.08% (8 in 10,000). We will screen you with a checklist to make sure it's ok for you to have TMS".*
  - *Talk about your experience with TMS as a HV volunteer (if you were one)*

Consenting Tips:

- (Coordinators) Present yourself as a resource:
  - The patient is able to contact you with any questions or concerns.
  - Be a listening ear- sometimes patients/families just like to feel like they matter.

- Explain that being apart of research means there are more eyes and hands involved with their care (coordinator, PI and other site study personnel)
  - With studies that do not appear to directly benefit the subject- this is a way to show that they still benefit, just in a different way.

- After the patient is approached for the and you (coordinator) feel like they need SOC topics explained more thoroughly by a PT/OT or physician to obtain the consent make that plan:
  - Some patients/families feel more comfortable with research when a Resident, Fellow or Attending is present during the consent process.
  - This does not have to be someone who is on the DOA- but they can speak to SOC questions while you are able to answer study specific questions.

- Include the family in the conversation:
  - Some patients/families like to make a group decision when it comes to medical/research decisions.

REDCap Training and Resources:

- All sites that are using the RedCAP eConsent should ensure that all consenters have completed the network training:
  - https://redcap.link/StrokeNet_eConsent_Training
  - This training certificate should be filed appropriately and easily assessable upon request

- The VERIFY specific eConsent guide is provided in the toolbox
  - Please review prior to your first eConsent

VERIFY REDCap E-Consent Guide

RedCAP eConsent Access:

- To obtain access to the REDCap VERIFY eConsent each user must request a CCHMC specific REDCap user ID by following the below instructions:
  - Cincinnati Children's CCHMC REDCap Access:
    - For individuals who do not have access to CCHMC REDCap, a self-request survey can be filled out here: https://redcap.research.cchmc.org/surveys/?s=RE8EHCK9YH
    - When asked, 'Would you like to inform another person of your REDCap Account Creating and REDCap Username', please respond 'Yes' and enter verifystudy@ucmail.uc.edu
      - this will allow us to add you as a user to your VERIFY eConsent project.
  - For individuals who have CCHMC REDCap access, you can login at the following link:
    - https://redcap.research.cchmc.org
      - Ensure Cincinnati Children's Hospital Medical Center is selected under the Select your identity provider section, then click Go to Login page button. REDCap will redirect you to the CCHMC federated login page. Enter your CCHMC credentials (individual's email address) and click Login.
      - As of January 2022, CCHMC REDCap will use Multi Factor Authentication (MFA) and users will be prompted to use Duo for authentication. Sites will need to set up Duo MFA Registration to get their account ready: https://mfa.research.cchmc.org (please refer to step by step instructions here: https://confluence.research.cchmc.org/display/RESITHUB/Duo+MFA+Registration).
      - Once authenticated with CCHMC, users will be redirected back to REDCap.
- Email PMs Max Mays and Kalli Beasley to be manually added to the VERIFY specific eConsent projects
  - Note: to be provided access the user must be delegated the consenting task on the DOA in WebDCU

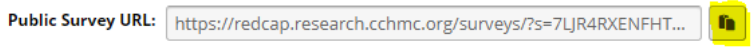
REDCap eConsent Process

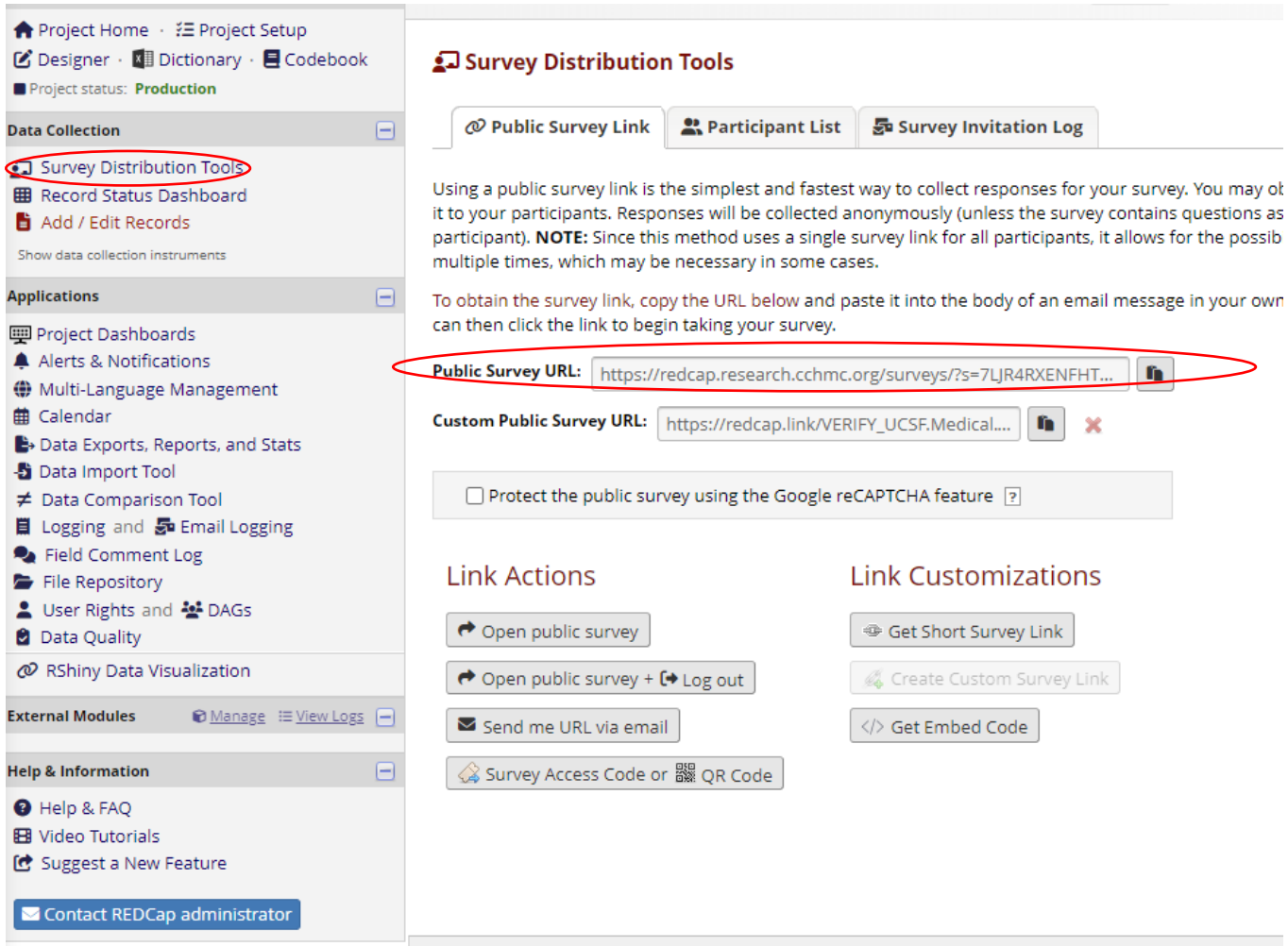
1. Each site will be assigned a static URL to share with the patient when consenting them

https://redcap.research.cchmc.org/surveys/?s=4YKLJC7AYY

- This URL can be found by clicking:

- Then clicking the copy to click board button next to the link:





Recruitment Tools

Recruitment Tools

- Patient-Facing Website: https://theverifystudy.com (includes study informational videos in both English and Spanish)

Questions During Consent/Enrollment

- TMS questions
  - Urgent (during procedure)
    - Call or text hotline at : (833)337-2227
      - Monday – Friday 0800 – 2100h ET
  - Non-urgent questions
    - Email us at verify.study.tms@gmail.com

- Other consent/enrollment questions?
  - Email PMs (Max & Kalli) and VERIFY PIs (Pooja, Steve, Cathy, & Achala)
  - verifystudy@ucmail.uc.edu

    Please include “VERIFY Enrollment Question” in the subject line!!!

Q & As

THANK YOU