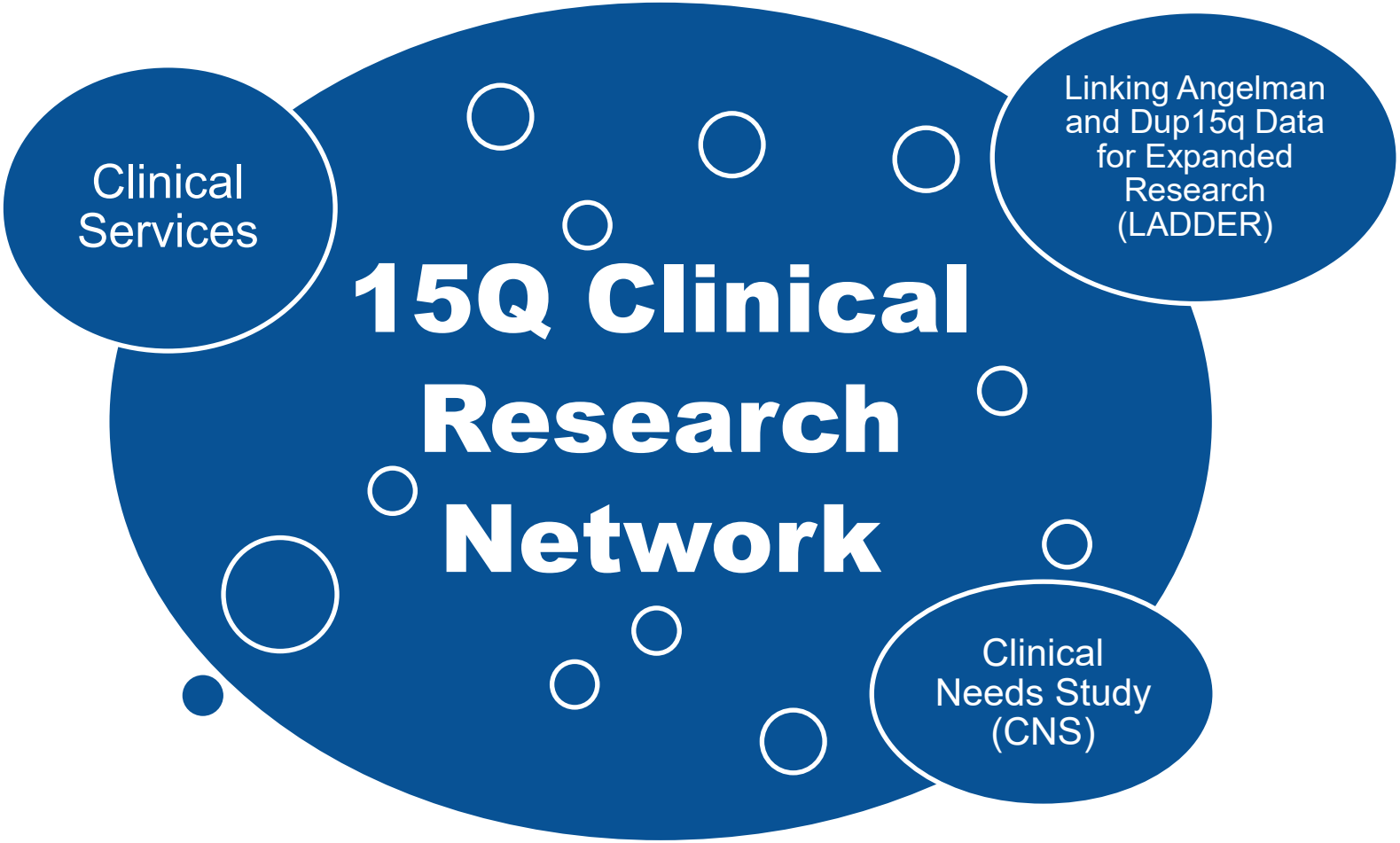
15q Clinical Research Network: Clinic Participation Training

Anne Edwards & Casey Okoniewski
RTI International

CRN 15Q Clinical Research Network

LADDER
Linking Angelman and Dup15q Data for Expanded Research

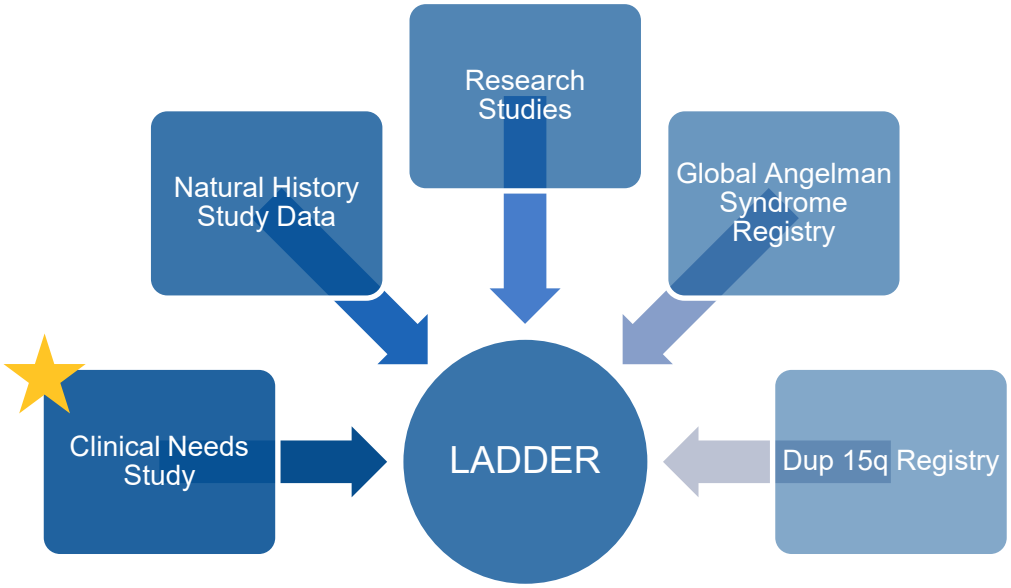

Clinical Services
Linking Angelman and Dup15q Data for Expanded Research (LADDER)
15Q Clinical Research Network
Clinical Needs Study (CNS)

Clinical Services

- Standard clinical care services offered by the Clinic team
  - Genetic Counseling
  - Neurology
  - Psychology/Psychiatry
  - Speech Language
  - Physical/Occupational Therapy
- Connections to Clinical Trials and treatment opportunities
- Patients do NOT need to be enrolled in LADDER or the CNS to access clinical services

Linking Angelman and Dup15q Data for Expanded Research (LADDER)

The objective of LADDER is to develop a comprehensive platform and system to link data on individuals with Angelman or Dup15q syndromes collected from multiple sources, such as research studies, registries, caregiver reports, and clinic visits, with the goal of providing a comprehensive database to expand research and accelerate the development of interventions and treatments.



LADDER Forms? Clinical Needs Surveys?

THEY'RE THE SAME THING!

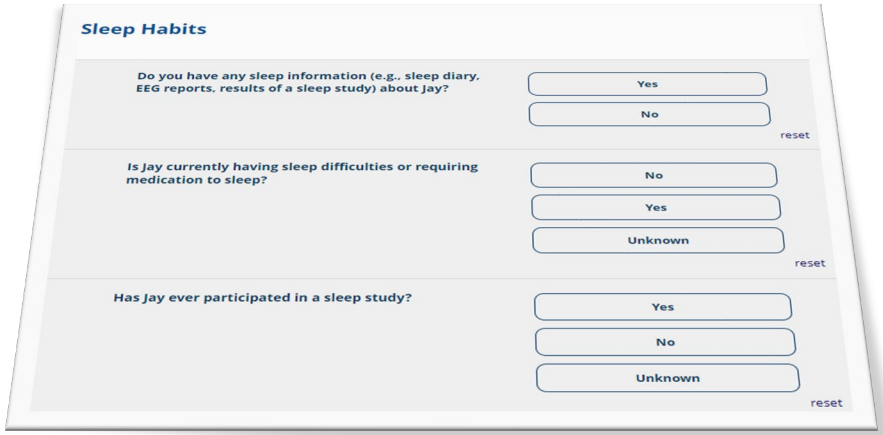
- Clinical Needs Survey = LADDER forms
  - Enrollment in the LADDER Database allows previously collected data to be linked and stored in the database.
  - The LADDER forms were developed as part of the LADDER project as a data collection tool to streamline and standardize data collected from caregivers/clinicians and stored in the LADDER Database.
    - Following discussions with the IRB, the Clinical Needs study was created to allow the clinics, as part of a research study, to use the LADDER clinician form to collect clinical research data and to have access to the LADDER caregiver survey data.
    - Enrollment in LADDER is separate from, but a prerequisite for Clinical Needs study enrollment.
    - **Because there has been confusion between the LADDER Database and the Clinical Needs Study, the LADDER forms will now be referred to as the Clinical Needs Study Caregiver and Clinician surveys.**

Clinical Needs Study

- LADDER as a data repository is exempt from IRB; however, active data collection does require IRB oversight.
- The Clinical Needs Study is currently approved through Advarra as a central IRB.
- There are some steps your site will need to follow to participate in the study which helps to facilitate this streamlined data collection across clinics and for clinical trials.

Standardized Clinic Data Elements

- Questions consolidated from various sources (e.g., active clinic intake forms, existing registries, ongoing research studies) and reviewed by stakeholders, clinicians, and researchers across network
  - Parent/caregiver report
- Additional clinician form that is completed after the patient's visit with clinician gathered data during the appointment



LADDER
Linking Angelman and Dup15q Data for Expanded Research

Clinical Needs Study Data Elements

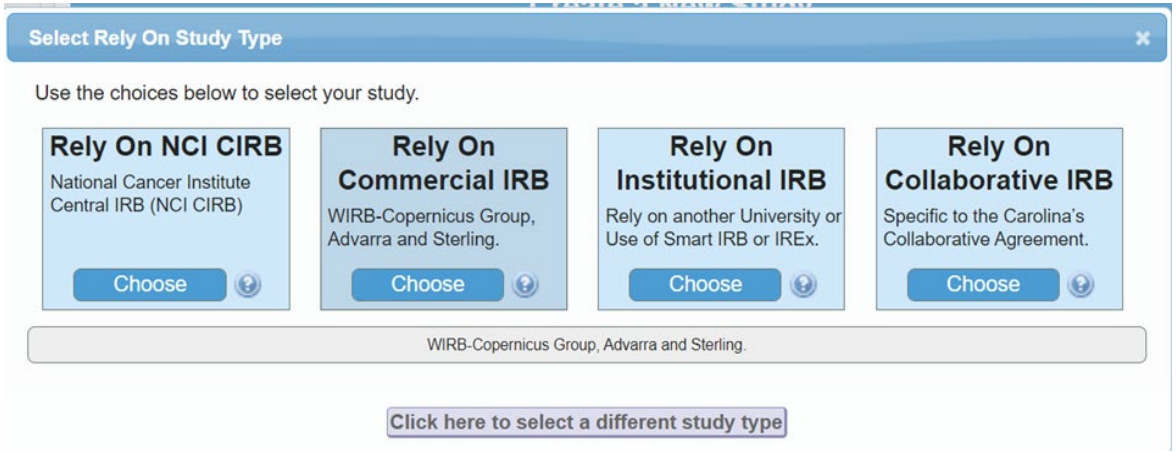
- Intake Information
- Family Composition and Relevant History
- Patient Medical History
- Diagnostic Confirmation (including Genetic report upload)
- Educational and Therapeutic Support
- Seizures
- Sensory
- Language and Communication
- Behavior
- Sleep Motor Needs
- Feeding/Eating/GI concerns
- Other Concerns/Needs
- Research Experience and Interests

Getting Set Up

- **Steps for getting IRB approval**
  1. **Determine whether your institution will consider ceding oversight to Advarra.**
     - **If Yes, you will need to follow your IRB's procedures to initiate a reliance agreement (for Smart IRB submissions, see screen shots below from UNC submission).**
     - **If No, you will need to submit the study to your IRB independently.**
  2. **Submit to your IRB**
     - We will provide:
       - Advarra submission and approval notice
       - Study protocol
       - Approved consent and assent forms (if your institution requires site specific consent language, we will need to submit these changes to Advarra)
       - RTI LADDER exempt determination notice (if needed)
     - LADDER study team information will be provided if needed.
     - Advarra study coordinator: Cheryl Rogers: cheryl.rogers@advarra.com (480)553-8484
     - You will need to provide names, roles, and contact information for clinic staff who will be conducting study activities.
  3. **Send us contact info for person coordinating the IRB submission and feel free to contact us for help with this**.

Screenshots from UNC IRB Application for CNS

- The following screenshots from UNC's IRB submission contain information which may be helpful for your own IRB Application. If additional information is needed, feel free to contact the LADDER team.



UNC Screenshots (cont.)

2. **Brief Summary. Provide a brief non-technical description of the study, which will be used in IRB documentation as a description of the study. Typical summaries are 50-100 words. Please reply to each item below, retaining the subheading labels already in place, so that reviewers can readily identify the content. PLEASE NOTE: THIS SECTION MAY BE EDITED BY THE IRB FOR CLARITY OR LENGTH.** *

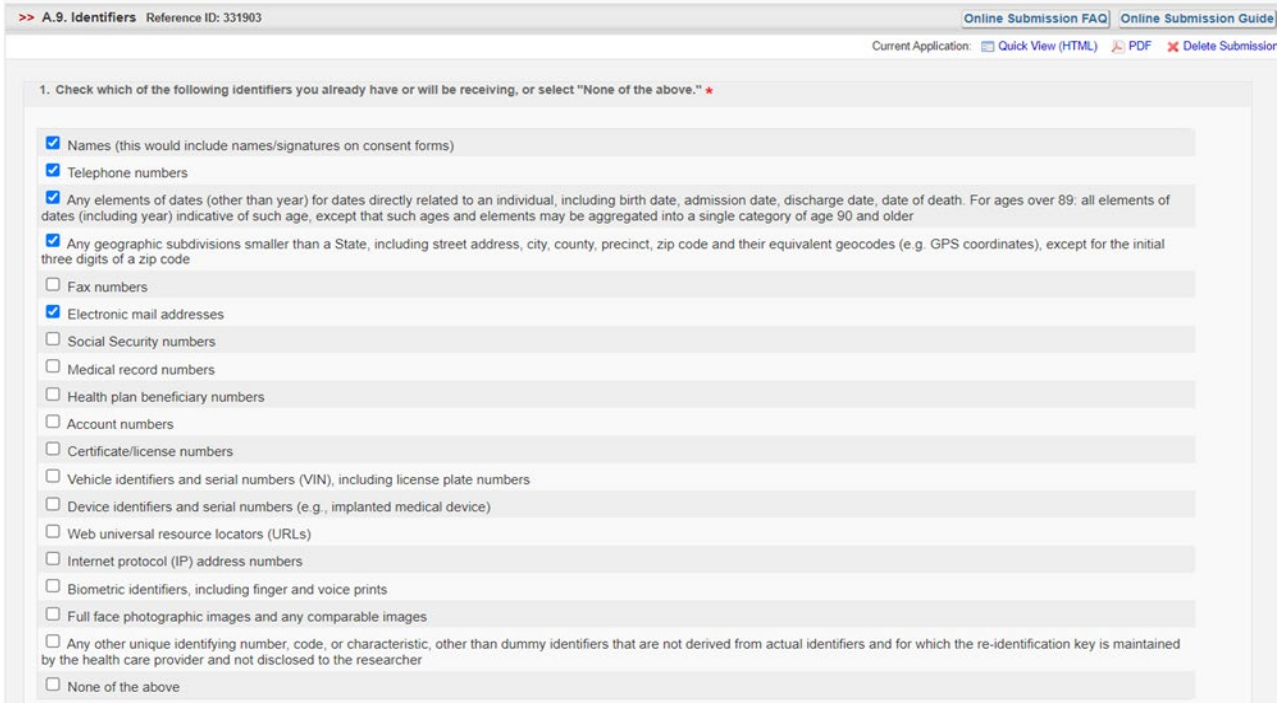
Purpose: The overall goal of the project is to expand knowledge about the nature and consequences of two conditions resulting from changes on chromosome 15 (Angelman Syndrome and Dup15q Syndrome), both for affected individuals and their families, and to use this information to inform clinical practice and policy development.

Participants: Subjects will be individuals with a chromosome 15 condition (Angelman syndrome or Dup15q syndrome) and their caregivers living in the US who have enrolled in the LADDER database and agree to participate in this study.

Procedures (methods):

1. Collect data via REDCap surveys on patients with a chromosome 15 condition from caregivers and from a clinical consortium that is already providing comprehensive medical evaluations and ongoing care to these individuals with the purpose of improving care, treatment and outcomes for these individuals. Participation in the Clinical Needs study will be entirely voluntary.
2. House the data in a central database, Linking Angelman and Dup15q Data for Expanded Research (LADDER), with data collected from 15q Clinical Research Network (CRN) Clinics around the country. Data from the study will be entered into a REDCap database on GovCloud and long-term storage will be in the HIPAA compliant ESN at RTI International and curated by the RTI study team for the purposes of future analysis and characterization of this population. Data will be linked to participant's data (from LADDER enrollment form, other research studies, registries) currently held in LADDER. De-identified data will be shared with researchers who are approved by the LADDER Data Access Committee. Researchers using de-identified LADDER data in human subjects research will be covered by their own institutional IRB.

UNC Screenshots (cont.)



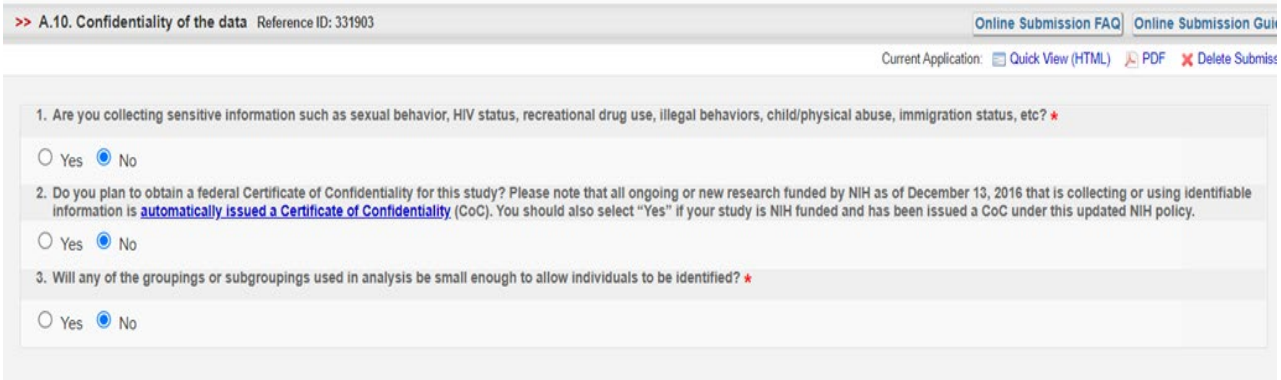
>> A.9. Identifiers Reference ID: 331903

Online Submission FAQ | Online Submission Guide

Current Application: Quick View (HTML) | PDF | Delete Submission

1. Check which of the following identifiers you already have or will be receiving, or select "None of the above." *

- [x] Names (this would include names/signatures on consent forms)
- [x] Telephone numbers
- [x] Any elements of dates (other than year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death. For ages over 89: all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 and older
- [x] Any geographic subdivisions smaller than a State, including street address, city, county, precinct, zip code and their equivalent geocodes (e.g. GPS coordinates), except for the initial three digits of a zip code
- [ ] Fax numbers
- [x] Electronic mail addresses
- [ ] Social Security numbers
- [ ] Medical record numbers
- [ ] Health plan beneficiary numbers
- [ ] Account numbers
- [ ] Certificate/license numbers
- [ ] Vehicle identifiers and serial numbers (VIN), including license plate numbers
- [ ] Device identifiers and serial numbers (e.g., implanted medical device)
- [ ] Web universal resource locators (URLs)
- [ ] Internet protocol (IP) address numbers
- [ ] Biometric identifiers, including finger and voice prints
- [ ] Full face photographic images and any comparable images
- [ ] Any other unique identifying number, code, or characteristic, other than dummy identifiers that are not derived from actual identifiers and for which the re-identification key is maintained by the health care provider and not disclosed to the researcher
- [ ] None of the above



>> A.10. Confidentiality of the data Reference ID: 331903

Online Submission FAQ | Online Submission Gui

Current Application: Quick View (HTML) | PDF | Delete Submiss

1. Are you collecting sensitive information such as sexual behavior, HIV status, recreational drug use, illegal behaviors, child/physical abuse, immigration status, etc? *

○ Yes ◉ No

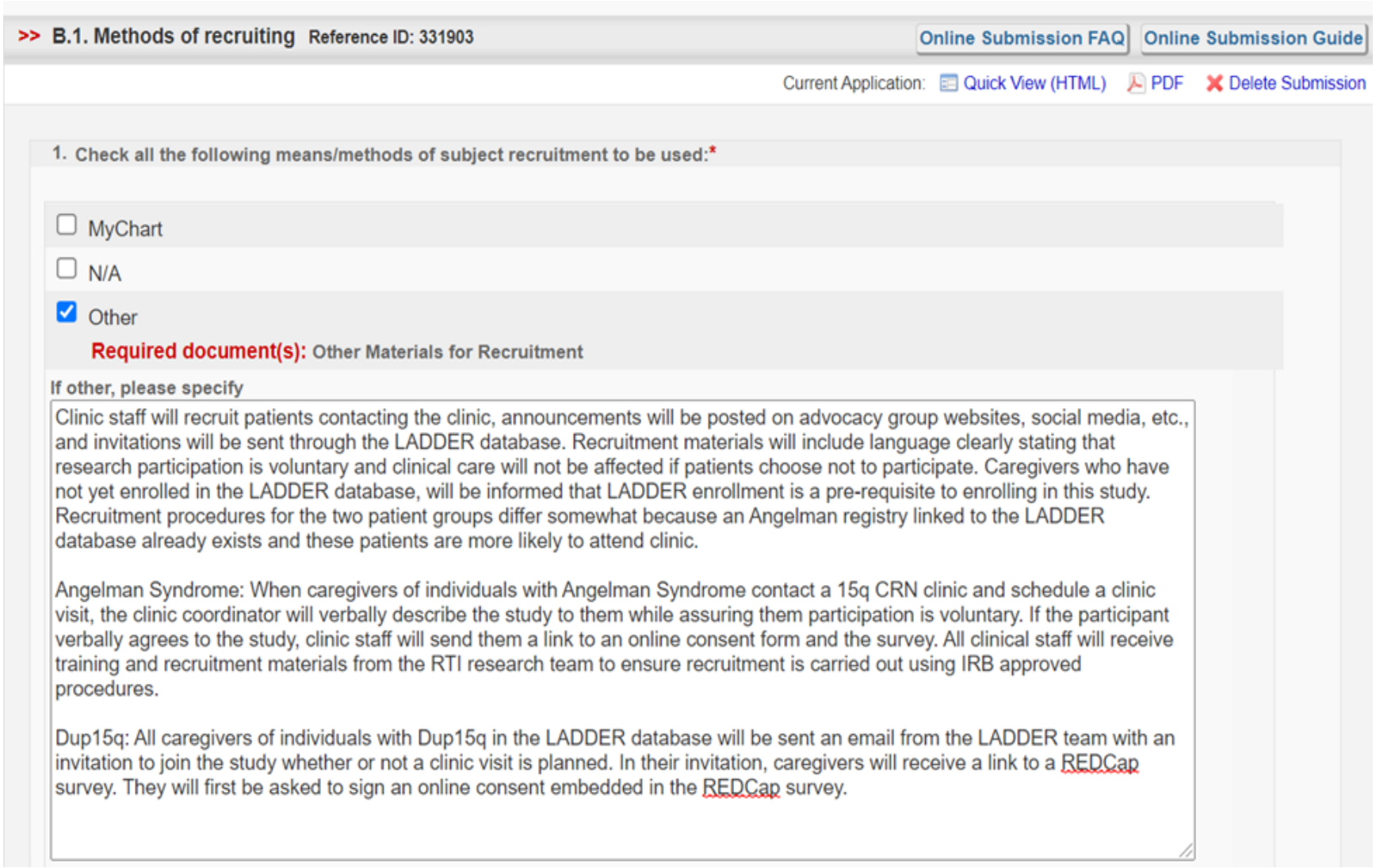
2. Do you plan to obtain a federal Certificate of Confidentiality for this study? Please note that all ongoing or new research funded by NIH as of December 13, 2016 that is collecting or using identifiable information is automatically issued a Certificate of Confidentiality (CoC). You should also select "Yes" if your study is NIH funded and has been issued a CoC under this updated NIH policy.

○ Yes ◉ No

3. Will any of the groupings or subgroupings used in analysis be small enough to allow individuals to be identified? *

○ Yes ◉ No

UNC Screenshots (cont.)



>> B.1. Methods of recruiting Reference ID: 331903

Online Submission FAQ | Online Submission Guide

Current Application: Quick View (HTML) | PDF | Delete Submission

1. Check all the following means/methods of subject recruitment to be used:*

- [ ] MyChart
- [ ] N/A
- [x] Other

Required document(s): Other Materials for Recruitment

If other, please specify

Clinic staff will recruit patients contacting the clinic, announcements will be posted on advocacy group websites, social media, etc., and invitations will be sent through the LADDER database. Recruitment materials will include language clearly stating that research participation is voluntary and clinical care will not be affected if patients choose not to participate. Caregivers who have not yet enrolled in the LADDER database, will be informed that LADDER enrollment is a pre-requisite to enrolling in this study. Recruitment procedures for the two patient groups differ somewhat because an Angelman registry linked to the LADDER database already exists and these patients are more likely to attend clinic.

Angelman Syndrome: When caregivers of individuals with Angelman Syndrome contact a 15q CRN clinic and schedule a clinic visit, the clinic coordinator will verbally describe the study to them while assuring them participation is voluntary. If the participant verbally agrees to the study, clinic staff will send them a link to an online consent form and the survey. All clinical staff will receive training and recruitment materials from the RTI research team to ensure recruitment is carried out using IRB approved procedures.

Dup15q: All caregivers of individuals with Dup15q in the LADDER database will be sent an email from the LADDER team with an invitation to join the study whether or not a clinic visit is planned. In their invitation, caregivers will receive a link to a REDCap survey. They will first be asked to sign an online consent embedded in the REDCap survey.

UNC Screenshots (cont.)

- [x] Medical records in any format.

ALERT: You must check both boxes: 1) Medical records in any format and 2) Electronic medical record using Epic, or you/your study team will not be granted access to Epic for research purposes.

Check all that apply: *

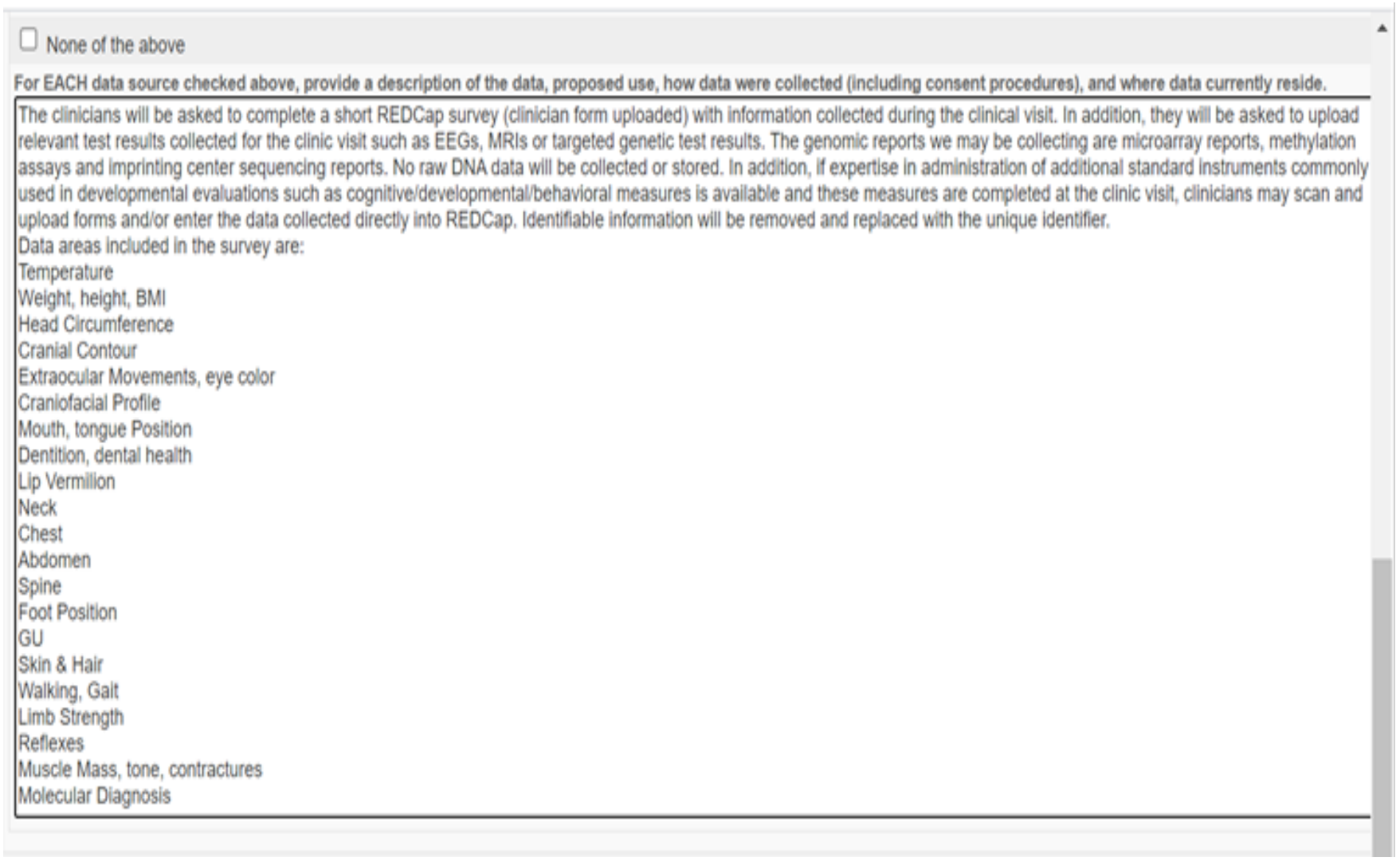
- [x] Electronic medical records using Epic, WebCIS or other electronic system
- [ ] Carolina Data Warehouse for Health (CDW-H) (for UNC and its affiliates only)
- [ ] Carolinas Collaborative Data Request and Review Committee (DRRC)
- [x] Paper medical records

If you access the medical records of fewer than 50 patients under a full or limited waiver of HIPAA, submit a copy of your IRB approval letter and a completed Research Disclosure Form to Health Information Management (HIM). Do not submit this information to the IRB. For additional information about this process, you should contact HIM directly at : 919-595-5591 or 919-966-1225 or 919-595-5580.

- [ ] Data already collected from another research study
- [ ] Patient specimens (tissues, blood, serum, surgical discards, etc.)
- [ ] Data already collected for administrative purposes
- [ ] Student records (You will need to satisfy FERPA requirements: see SOP 3101, section 3.1 for guidance)
- [ ] UNC Dental Records
- [ ] Data coming directly from a health plan, health care clearinghouse, or health care provider?
- [ ] Publicly available data
- [ ] Other
- [ ] None of the above

For EACH data source checked above, provide a description of the data, proposed use, how data were collected (including consent procedures), and where data currently reside.

UNC Screenshots (cont.)

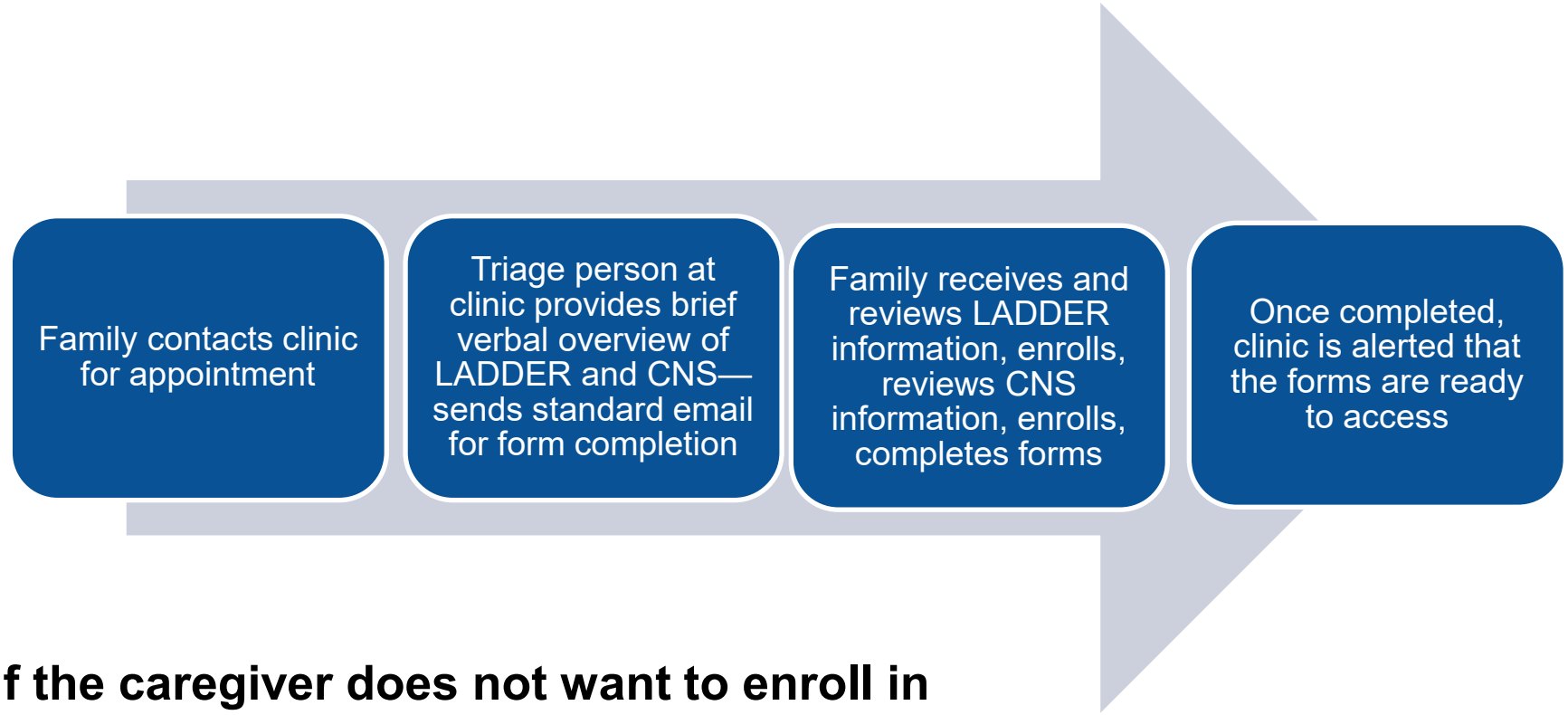


None of the above

For EACH data source checked above, provide a description of the data, proposed use, how data were collected (including consent procedures), and where data currently reside.

The clinicians will be asked to complete a short REDCap survey (clinician form uploaded) with information collected during the clinical visit. In addition, they will be asked to upload relevant test results collected for the clinic visit such as EEGs, MRIs or targeted genetic test results. The genomic reports we may be collecting are microarray reports, methylation assays and imprinting center sequencing reports. No raw DNA data will be collected or stored. In addition, if expertise in administration of additional standard instruments commonly used in developmental evaluations such as cognitive/developmental/behavioral measures is available and these measures are completed at the clinic visit, clinicians may scan and upload forms and/or enter the data collected directly into REDCap. Identifiable information will be removed and replaced with the unique identifier.
Data areas included in the survey are:
Temperature
Weight, height, BMI
Head Circumference
Cranial Contour
Extraocular Movements, eye color
Craniofacial Profile
Mouth, tongue Position
Dentition, dental health
Lip Vermilion
Neck
Chest
Abdomen
Spine
Foot Position
GU
Skin & Hair
Walking, Gait
Limb Strength
Reflexes
Muscle Mass, tone, contractures
Molecular Diagnosis

Proposed Clinic Study Procedures Flow



If the caregiver does not want to enroll in LADDER, they will be instructed to reach back out to the Clinic coordinator. Clinics can still use the CNS forms either in their institutional REDCap system or an alternative method (e.g., paper).

Email Template for Potential Participants

- Template for those who have not enrolled in LADDER:

Dear _____,

Thank you for your interest in the **LADDER** database and the LADDER Clinical Needs Study!

Linking **A**ngelman and **D**up15q **D**atabases for **E**xpanded **R**esearch (**LADDER**) will allow information about individuals with Angelman syndrome which has been gathered from families, clinics, registries, and research studies to be housed in one place. The information held in LADDER is private and no information that could identify you or your family is shared with anyone outside of the LADDER team.

Information collected for the Clinical Needs Study will be stored in the LADDER database so you must enroll in LADDER before you sign up for the study! The study will collect the same information required for a clinic visit but will store it in the LADDER database. Your doctors will be able see your information for the visit and the information can be linked to the other information about your individual with AS stored in the database! You only need to complete these forms once and they can be used for both your visit and for the study! The clinic will also be asked to provide some basic medical information collected by the doctor during the visit.

By combining all this information, LADDER will provide a wealth of new information to researchers, clinicians, and families. We are confident LADDER will lead to improved treatment and care for individuals living with a Chromosome 15 condition!

Joining LADDER should only take about 10 minutes. To join follow these steps:

1. Click here to register for an account.
2. Check your email! You will receive a welcome email with a randomly generated password you can change once you sign in.
3. Return to your account page https://laddertotreatment.org/user/account and complete the Enrollment form.
4. You have enrolled in LADDER and will receive your personal link to the Clinical Needs Study permission form and survey!
5. If you don't want to join, please contact your clinic coordinator to learn how to complete the clinic survey so the information is stored at the clinic only.

Sincerely,

Email Template for Potential Participants

- Template for those who have enrolled in LADDER:

Dear _____,

Thank you for enrolling in LADDER and for your interest in participating in the Clinical Needs Study!

LADDER allows information gathered about individuals with Angelman syndrome to be housed in one place. Participating in the Clinical Needs study allows you to reduce time spent completing forms and maximizes knowledge to help researchers develop better interventions and treatments!

The Clinical Needs study will collect the same information required for a clinic visit but will store it in the LADDER database. Your doctors will be able see your information for the visit and the information can be linked to the other information about your individual with AS stored in the database! You only need to complete these forms once and they can be used for your visit and for the study! The clinic will also be asked to provide some basic medical information collected by the doctor during the visit.

Click here to learn more about the Clinical Needs Study!

Sincerely,

Frequently Asked Questions

- What about the LADDER Forms?
  - The Clinical Needs Study surveys ARE THE LADDER FORMS!
- What if the client does not want to participate in LADDER?
  - They can complete the standard Clinical Needs Study survey questions through the clinic's own REDCap (or similar electronic or paper intake procedures)
- Can we make changes to questions on the CNS forms?
  - You can submit requests to the LADDER team and these requests will be reviewed for consideration/integration quarterly

Frequently Asked Questions

- What about HIPAA forms?
  - Enrollment in LADDER includes completion of a HIPAA form; however, each clinic/site can use their own HIPAA form as required by their IRB.
- Our IRB says we need to use the clinic/site specific consent language, what now?
  - We will work with each site to get specific language approved with Advarra
- How is the data transferred?
  - Each clinic will have their own sign in and access to their client's data ONLY via a secure server
- I have a question about the CRN Contract…
  - Great! Please contact Zoe Dannenberg (15qnetworkcoordinator@dup15q.org)

Helpful Information and Resources

General Questions	contact@laddertotreatment.org Anne Wheeler: acwheeler@rti.org Christine Hill: christineh@rti.org Zoe Dannenberg: zoe.Dannenberg@dup15q.org
Clinical Needs Study/IRB	Anne Edwards anneedwards@rti.org
Clinic Forms/Clinical Needs Study	Casey Okoniewski kokoniewski@rti.org
LADDER Website & Portal	Martin Duparc mduparc@rti.org

LADDER Participant Enrollment	https://laddertotreatment.org/Security/login
LADDER Data Access for Researchers	https://laddertotreatment.org/for-researchers/
LADDER Information for Families	https://laddertotreatment.org/for-families/