STEERING COMMITTEE CHARTER

REDCap Turner Syndrome Clinical Research Registry

3/11/2020

Version 1.0.1

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INTRODUCTION / OVERVIEW OF THE PROJECT

Background: Turner syndrome (TS) is a genetic condition that arises when there is one normal X chromosome and the second sex chromosome is abnormal or missing. TS affects approximately 1 in 2,000 females, some of which are identified and diagnosed prenatally, some in childhood or adulthood, and others not at all. As a rare disease, evaluating clinical outcomes in meaningful numbers from individual institutions is often not possible. In other rare disease populations, clinical registries have served an important role in quantifying clinical outcomes that can be targeted for improvement, recognizing disparities in outcomes, identifying variables or approaches that result in better or worse outcomes, establishing a recruitment pool for studies, and ultimately studying the effect of interventions on meaningful clinical outcomes. A clinical registry does not currently exist for TS. Turner Syndrome Global Alliance (TSGA) has established a clinical network of institutions that provide multidisciplinary care for girls with TS, and this is an ideal foundation to launch a national clinical registry and build research collaborations.

Overarching Goal: Establish a national, multicenter, prospective, longitudinal clinical data registry to improve clinical outcomes in individuals with TS

Specific Aims: In the first five years of the project we aim to:

1. Build a collaborative network of centers with a sustainable, unified, and centralized data repository comprised of a large, nationally-representative, diverse cohort of patients with TS.
2. Quantify the prevalence of prematurity, congenital heart disease, renal malformations, feeding difficulties/failure to thrive, hypertension, autoimmune conditions (thyroid disease, celiac disease, etc), cardiometabolic conditions (obesity, dyslipidemia, diabetes, etc), recurrent otitis media, sleep apnea, hearing loss, vision/eye diagnoses, neurodevelopmental and psychological conditions, and musculoskeletal problems in a large, national cohort of girls with TS. We will explore associations of these outcomes with karyotype, comorbidities, family history, socioeconomic status, and location, as well as management.
3. Quantify the mortality and morbidity as measured by number of chronic illnesses, number of medications, and healthcare utilization (number of outpatient visits/yr, emergency room visits, hospitalizations, surgeries, etc) associated with childhood TS.
4. Describe treatment practice variations and provide preliminary evidence for future comparative effectiveness studies.
5. In depth study of specific outcomes of importance to patients and families using objective and subjective data collection methods to allow intensive descriptive and inferential analysis in the following priority areas:
    a. Anxiety and mental wellbeing
    b. Fertility and fertility preservation
    c. Hearing loss
    d. Obesity, metabolic syndrome and related cardiovascular disease markers
6. Support quality improvement and research proposals by establishing a baseline outcome statistics, generating preliminary data, and serving as a resource pool of potential participants.

Beyond the five year timeframe, aims will focus on practices and interventions that will improve the baseline findings identified in Aims 2 and 3 above. New aims will be developed as the project advances.

Lead Center: The University of Colorado at Anschutz Medical Campus will serve as the lead site under the direction of Dr. Shanlee Davis (PI). Responsibilities of the lead site include: protocol development, create and maintain the registry database, data management and validation, onboard new sites, train study personnel, prepare progress reports, and provide data as requested/approved. In addition, the lead site will oversee all regulatory processes and apply for the Colorado Multiple Institutional Review Board (COMIRB) to serve as the Single IRB in accordance with NIH's new policy.

Participating Sites: A participating site is an institution that clinically cares for patients with TS and has the interest and capacity to conduct human subjects research, enroll and contribute data for a minimum of 5 subjects annually, and comply with all regulatory processes. An institution must request approval to be added as a site, sign a data sharing agreement with the lead center, and be a member of SMART IRB. Responsibilities of participating sites include enrolling and consenting eligible participants, entering data, validating local data, and maintaining local study documentation.

Participants: Participating sites will be encouraged to approach and offer enrollment to all eligible participants with the goal of having >80% of eligible patients approached and >50% of eligible participants enrolled. To establish a meaningful database, the goal would be to have >500 participants with TS enrolled with data collected within 5 years. In addition, limited data will be requested for ALL patients with TS seen at each site regardless of enrollment in the study (number of individual patients seen, demographics, and reason for not participating in the registry if available) to allow comparison between those enrolling and those not enrolling. This will help us to recognize and rectify any disparities contributing to selection bias in the registry.

Inclusion criteria (all of the following):

- Individuals with TS as defined by the 2017 Clinical Practice Guidelines (Gravholt et al)
- Clinic visit at a participating site within the past 12 months (any specialty acceptable)
- All ages
- Informed consent/assent as appropriate

Exclusion criteria:

- Lack of a karyotype or microarray on record confirming TS diagnosis

Data Collection Tool (Database): REDCap is a widely used, HIPAA/research compliant, web-based application for managing databases. All data collection tools will be built within REDCap and either be completed as a survey by the patient or as a form for study staff to complete. Efforts will be made to export discrete elements directly from the Electronic Health Record (Epic, Cerner) into REDCap to minimize burden of data entry, however validation by study staff will still be required. Study staff at participating sites will be trained, have access for data entry in REDCap, and will maintain full access to their own site's data. To access de-identified data from other sites, a proposal process will be established by the Steering Committee.

ORGANIZATION OF THE STEERING COMMITTEE

Composition of the Committee: The REDCap TS Clinical Research Registry steering committee will be made up of a minimum of 8 and no more than 14 stakeholders with the goal of representation from multiple disciplines, institutions, and perspectives.

Selection of Committee Members: The Steering Committee Members and Chair will be appointed by TSGA leadership. Initial members will be recommended and approved by TSGA leadership. If additional members are needed due to attrition or recognition of a gap in expertise they can be recommended by any committee member and voted in by a majority vote of the committee members.

Committee Membership: Members will serve a two year term at which point the roles and need for the committee will be reevaluated. Members will follow conflict of interest guidelines and be cleared of any real or potential conflicts of interest prior to agreeing to serve on the committee. If new conflicts of interest arise, the member is required to promptly inform the chair. Members serve at will and can elect to leave the steering committee at any time. There is no renumeration for this service.

RESPONSIBILITIES AND FUNCTIONS OF THE STEERING COMMITTEE

The role of the Steering Committee is to provide consensus and oversite for the project that will then be carried out by the study team. The responsibilities of the Steering Committee will include:

1. Finalize the Charter for the Steering Committee
2. Review, modify, and approve the proposed study protocol
3. Review, modify, and approve the data collection instrument(s) and determine the process for future modification or addition of data collection instruments
4. Determine the minimum criteria and process for approving new sites interested in participating in the clinical registry
5. Determine the process for data use requests and approvals
6. Provide quarterly progress reports to TSGA, site investigators, and other stakeholders

CONDUCT OF THE STEERING COMMITTEE MEETINGS

Scheduled Meetings: Meetings will be held via teleconference every 4-6 weeks in the first year of the project. Timing and duration of subsequent meetings will be determined by the committee dependent on needs. If feasible, an in-person meeting will be held annually.

Quorum: A minimum of 4 committee members constitutes a quorum for scheduled meetings.

Agenda: The agenda will be provided prior to the meeting by the Study Coordinator. The final agenda will be approved and managed by the Chair.

Voting: Any proposals, motions, or recommendations that require a committee vote will be announced prior to the meeting. Material that requires discussion and voting should be sent via email to all members at least one week ahead of time to allow sufficient time for review, unless urgent/unexpected.

All members present in person or on the conference call are eligible to vote. A simple majority of members present is required to pass a proposal, motion, or recommendation.

Minutes: Meeting minutes will be kept for each meeting by the chair or an individual appointed by the chair. Minutes will be sent out to all committee members within one week of the meeting.

STEERING COMMITTEE REPORTS

Quarterly Reports: Steering committee quarterly reports containing progress updates will be prepared, reviewed and approved during scheduled meetings and/or via email. Reports will be intended for TSGA, site investigators, and other stakeholders.

Additional Reports/Documents: In addition to quarterly progress reports, the following documents should be developed and approved by the Steering Committee:

1. Protocol for modification or addition of data collection instruments and/or new aims
2. Protocol for data use requests and approvals

CONTACT INFORMATION FOR STEERING COMMITTEE MEMBERS

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CONTACT INFORMATION FOR STEERING COMMITTEE MEMBERS

TEMPLATE FOR MEETING MINUTES

Date:

Attendance:

Old Business:

Approval of last meeting's minutes

New Business:

Protocol Updates –

Regulatory Updates –

Enrollment Updates –

Data Management Updates –

Other Subcommittee Updates -

Next Meeting Date/Time: