Collaboration with Midwest Pediatric Nephrology Consortium (MWPNC) and CNOS: Childhood Nephrotic Syndrome Observational Study (CNOS) .

Childhood Nephrotic Observational Syndrome (CNOS)

- STUDY SUMMARY DOCUMENT
- Sponsor: Midwest Pediatric Nephrology Consortium (MWPNC). The MWPNC is a translational research consortium of more than 50 pediatric nephrology divisions throughout the USA and Canada, and includes more than 200 members. Since our founding in 2004, the MWPNC has published over 20 manuscripts, facilitated the awarding of 11 federal or regional grants to its members, and currently has over 25 clinical trials in progress. In all of these efforts, collaboration is integral to the success of our mission.
- Co-Principal Investigators: William E. Smoyer, MD; John Mahan, MD; Larry Greenbaum, MD, PhD; Michelle Rheault, MD
- Summary: This study is a prospective registry study. The Childhood Nephrotic Syndrome Observational Study (CNOS) seeks to improve the care of children with idiopathic nephrotic syndrome through prospective data collection and targeted collection of biological samples for a bio-repository and defined studies. All children will receive routine care as prescribed by the local treating pediatric nephrologists. Salient information from the clinical course of the patient will be abstracted from the medical record. In addition, families and patients will be asked a limited number of targeted questions (e.g., socioeconomic status, birth history).
- Centers can participate at one of two levels: Level 1 involves only the prospective web-based collection of clinical data from the date of presentation, using treatment with local protocols; Level 2 involves an additional commitment to treat children from the time of presentation with a standardized, published protocol. In addition, we hope to roll out a Level 3 within the next two years which will include the addition of periodic biological sample collections to participation at Levels 1 and/or 2.

Specific Aims:

1. To identify and characterize the features, including race, socioeconomic status, disease characteristics that contribute to the variability in the clinical response to routine therapies in children with idiopathic nephrotic syndrome.

2. To define short-term and long-term morbidity and mortality in children with idiopathic nephrotic syndrome and to identify risk factors for increased morbidity and mortality.

Inclusion/Exclusion:

Inclusion: 1) New diagnosis of Idiopathic Nephrotic Syndrome

2) 1 to 18 years of age

Exclusion: 1) Subject previously diagnosed with Idiopathic Nephrotic Syndrome

Primary Endpoint: 5000 subjects with new onset Idiopathic Nephrotic Syndrome will be enrolled in the CNOS Registry/Database

Visits/Data Collected:

Visit 1	Baseline visit, General history and healthcare utilization, Birth history, patient education, family history, physical examination, labs (C3 ,C4, HBSAg, ANA, Hep C, HIV, PPD Skin Test, Creatinine, cholesterol, urine protein, urine blood)
Biopsy	Indication of biopsy (SR, FR, SD, etc.) histologic diagnosis, immunofluorescence, tubular atrophy and/or interstitial fibrosis
Visit 2 – Month 3	Remission data, steroid usage data, treatment data, number hospitalization, ER visits or biopsy
Visit 3 - Annual Review	Clinic/Chart review/ or telephone contact, current status, transplant information, treatment history, medication history, hospitalization history, patient education, physical examination, labs
Hospitalizations	Hospitalization data, clot data, management data
Termination	Reason for termination: death, moved, parent withdraw, lost to follow-up, etc.

1. *Describe how the data is maintained in a secure manner:*

Data Security and Responsibility:

The data is maintained in the OpenClinica web-based electronic data capture (EDC) system. The OpenClinica system (database and web server) is maintained in a highly secure data center at Nationwide Children's Hospital.

The OpenClinica system contains layers. In the OpenClinica system, each user is assigned a User Type. For each Study or Site a user is assigned to, the user is also assigned a Role that relates to the work they do in the OpenClinica system at that Study or Site. The User Type and Role determine the OpenClinica modules and features the user can access. This is supported with a secure user name and password. All user credentials are passed (over the network) via Hypertext Transfer Protocol Secure (**HTTPS**) using strong encryption (128 bit or higher).
The term secure has multiple layers. We secure the data via the OpenClinica application and its associated controls (which are also 21 CFR 11 compliant). The environment the OpenClinica resides in has multiple levels of security (ex. Physical data center accompanied by biometric controls). All security layers are supported by Standard Operation Procedures (exs. Disaster Recovery Plan, Network Security, Information Security Strategy, etc.) and policies to accompany the computer systems to support the study/studies.

The OpenClinica System is secured on an externally hosted server guarded with an application firewall called WebDefend.

2. *Describe the database products you are using to store data (Excel, Access, SharePoint, Filemaker Pro, SQL server, RedCap),*

The OpenClinica system is supported by a PostgreSQL 8.4.x object-relational database. The system is running in an Ubuntu Linux environment with Apache Tomcat 6.0.x as the application server. The environment described is also monitored with the Zabbix monitoring agent.

3. *Identify who is responsible for maintaining the computer system:*

The Research Data Center at the Research Institute at Nationwide Children's Hospital is responsible for the OpenClinica configuration and daily application database backups. The Nationwide Children's Hospital Information Service Departments are responsible for the Disaster Recovery, Network Security and Firewall Security.

4. *Identify who is responsible for entering and maintaining the data:*

The participating sites are responsible to enter their own data and maintain updates for their participants (subjects) in the system.

Levels of participation

Participation in the Childhood Nephrotic Syndrome Observational Study (CNOS) can be done at one of three levels. Participating sites will be requested to select the level(s) at which they wish to participate. Sites will be permitted to increase their level of participation with the understanding that this will require additional agreements to be executed between institutions prior to the enrollment of any subjects into the next level of the study.

LEVEL 1

Entry level, at minimum all sites will participate at this level. Requirements for this level:

- IRB approved protocol, consent, assent
- **Data Agreement** between institution and Nationwide Children's Hospital (location of registry)
- Register and train to enter data into the CNOS registry
- Enroll all new Nephrotic Syndrome patients (at initial visit)
- Collect and enter patient data into registry (requested within one week of visit)

LEVEL 2

In addition to Level 1, Level 2 sites agree to initiate treatment with the "**CNOS Treatment Protocol**" for all new Nephrotic Syndrome patients. Requirements for this level:

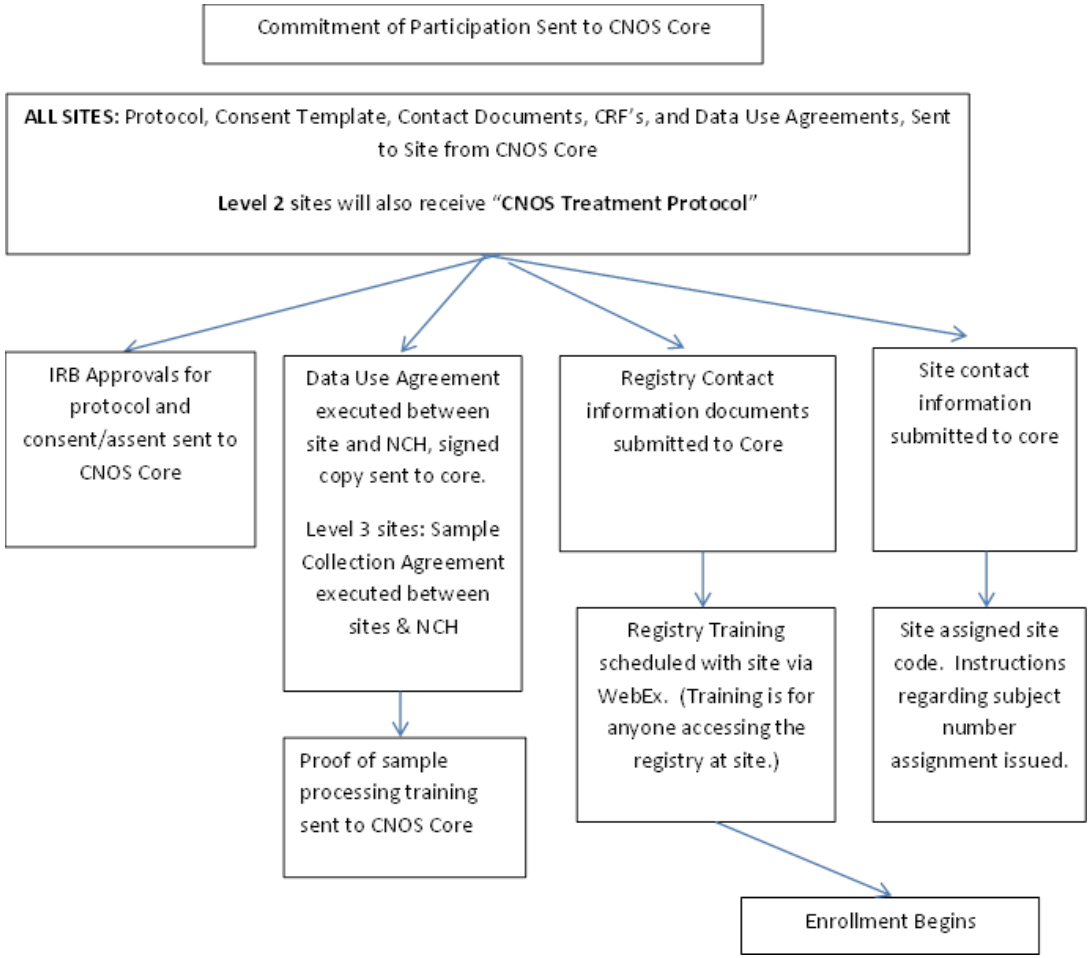
- IRB approved protocol, consent, assent
- **Data Agreement** between institution and Nationwide Children's Hospital (location of registry)
- Initiate treatment of all new Nephrotic Syndrome patients according to the "**CNOS Treatment Protocol**"
- Register and train to enter data into the CNOS registry
- Enroll all new Nephrotic Syndrome patients (at initial visit)
- Collect and enter patient data into registry (requested within one week of visit)

LEVEL 3 (Not currently enrolling)

In addition to Levels 1 and 2, Level 3 sites agree to collect Biological Samples (Blood & Urine) according to the "**CNOS Sample Collection Protocol**" and to submit these samples according to the Protocol to the Bio Repository at Nationwide Children's Hospital. Requirements for this level:

- IRB approved protocol, consent, assent
- **Data Agreement** and **Sample Collection Agreement** between institution and Nationwide Children's Hospital (location of registry and bio repository)
- Register and train to enter data into the CNOS registry
- Enroll all new Nephrotic Syndrome patients (at initial visit)
- Collect and enter patient data into registry (requested within one week of visit)
- Collect and ship biological samples according to "**CNOS Sample Collection Protocol**"

Start up


Commitment of Participation Sent to CNOS Core
ALL SITES: Protocol, Consent Template, Contact Documents, CRF's, and Data Use Agreements, Sent to Site from CNOS Core
Level 2 sites will also receive "**CNOS Treatment Protocol**"
IRB Approvals for protocol and consent/assent sent to CNOS Core
Data Use Agreement executed between site and NCH, signed copy sent to core.
Level 3 sites: Sample Collection Agreement executed between sites & NCH
Proof of sample processing training sent to CNOS Core
Registry Contact information documents submitted to Core
Registry Training scheduled with site via WebEx. (Training is for anyone accessing the registry at site.)
Site contact information submitted to core
Site assigned site code. Instructions regarding subject number assignment issued.
Enrollment Begins