Protocol:

Pediatric Longitudinal Glomerular Disease: a PNRC Multi-Institutional Cohort Study

NCT: Not Yet Assigned

August 7, 2026



Pediatric **L**ongitudinal **G**lomerular **D**isease: a PNRC Multi-**In**stitutional Cohort Study

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Title:	Pediatric Longitudinal Glomerular Disease: a PNRC Multi-Institutional Cohort Study
Short Title:	PLUGGED IN
PNRC Co-Investigators:	Lead PI: Carla Nester, MD, MSA, FASN Stead Family Children's Hospital University of Iowa Co-PI: William E. Smoyer, MD, FASN Nationwide Children's Hospital Ohio State University
Pathology Lead Investigator:	Joseph Gaut MD, PhD Washington University in St. Louis
Current Version:	V2.0 8/7/2026
Original Version:	V1. 5/11/2026

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Protocol Synopsis

Title/Short Title:	Pediatric Longitudinal Glomerular Disease: a PNRC Multi-Institutional Cohort Study (PLUGGED IN)
Overall (Multicenter) Protocol PI:	Carla Nester, MD, MSA, FASN
PNRC Co-Investigators: Pathology Lead Investigator:	Carla Nester, MD, MSA, FASN William E. Smoyer MD, FASN Joseph Gaut MD, PhD
PNRC Sites:	PNRC U.S. sites
Study Type:	Mixed retrospective-prospective cohort study (longitudinal, observational, non-interventional study)
Study Rationale:	Evaluate the natural history of glomerular disease in children and adolescents in the United States.
Study Objectives:	1) To investigate and determine important relationships among patient/disease characteristics, natural history, treatments, histopathology, and outcomes among pediatric patients with glomerular disease, both across and within pre-specified disease cohorts (see below), by means of multicenter collection, storage and analysis of longitudinal clinical data. 2) To provide a platform for and facilitate, with participant consent, rapid assessment of potential participant eligibility for planned and/or ongoing investigator-initiated and/or industry-sponsored clinical trials of pediatric glomerular disease.
Main Study Inclusion and Exclusion Criteria:	Inclusion: • Incident or prevalent, objectively diagnosed (via biopsy and/or clinical diagnosis*) glomerular disease *Clinical diagnosis limited to suspected PIGN, INS and Alport Syndrome with genetic diagnosis • Birth to $\leq$ 17 years and 364 days (at time of diagnosis) • Signed and dated written informed consent provided by the participant's parent(s) or legal guardian) and the participant's assent

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	Exclusion: • Failure to meet the defined objective criteria for “pediatric glomerular disease” • Inability to sign informed consent (+ informed assent of minors)
Endpoints	Primary: 1. Proteinuria, and change over time thereof (urine protein-creatinine ratio) Secondary: 1. eGFR slope 2. eGFR, and change (from baseline) overtime thereof 3. Growth trajectory, derived from height and weight 4. Developmental trajectory derived from QOL survey of caregiver 5. Educational attainment trajectory, derived from QOL survey of caregiver 6. Caregiver effect: Missed days of school and work for caregiver a. (i.e., “How many days did you miss as a caregiver related to your child’s disease?”) 7. Unplanned Hospitalization – a. duration and frequency including AKI (reason for admission) 8. Infections a. Urine, Blood, Ear, Skin/Tissue, URI and others 9. Histopathological Response – Serial biopsy reports and images 10. Renal failure a. including dialysis-dependence 11. Renal transplantation 12. Death

1) PROTOCOL TITLE

Pediatric Longitudinal Glomerular Disease: a PNRC Multi-Institutional Cohort Study

2) OBJECTIVE, AIMS AND ENDPOINTS:

Objective: Evaluate the natural history of glomerular disease in children in the United States.

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Aim 1: To investigate and determine important relationships among patient/disease characteristics, natural history, treatments, histopathology, and outcomes among pediatric patients with glomerular disease, both across and within pre-specified disease cohorts (see below), by means of multicenter collection, storage, and analysis of longitudinal data.

Aim 2: To provide a platform for and facilitate, with participant consent, rapid assessment of potential participant eligibility for planned and/or ongoing investigator-initiated and/or industry-sponsored clinical trials of pediatric glomerular disease.

Primary Endpoints:

Proteinuria, and change over time thereof (urine protein-creatinine ratio)

Secondary Endpoints:

1. eGFR slope
2. eGFR, and change (from baseline) overtime thereof
3. Growth trajectory, derived from height and weight
4. Developmental trajectory derived from QOL survey of caregiver
5. Educational attainment trajectory, derived from QOL survey of caregiver
6. Caregiver effect: Missed days of school and work for caregiver
    a. (i.e., "How many days did you miss as a caregiver related to your child's disease?")
7. Unplanned Hospitalization –
    a. duration and frequency including AKI (reason for admission)
8. Infections
    a. Urine, Blood, Ear, Skin/Tissue, URI and others
9. Histopathological Response – Serial biopsy reports and images
10. Renal failure
    a. including dialysis-dependence
11. Renal transplantation
12. Death

Exploratory Endpoint:

Health-related Quality of Life (HR-QOL, employing the PROMIS QOL instrument validated in children)

3) BACKGROUND

3.1 Glomerular Disease in Children

There is a paucity of natural history data for virtually all pediatric glomerular diseases (GD). Recent literature in IgAN[1] and FSGS[2] suggests that outcomes in children may be similar to adults with regards to GFR decline and proteinuria reduction. Traditionally there has been an assumption that glomerular diseases in children had a benign course associated with favorable outcomes – however this perception through emerging data is being challenged. It is imperative to obtain prospective data on kidney outcomes in children to better define risk of attaining adverse outcomes, ideal points for positive management interventions and given the escalating advances in therapeutics in this area, improve pathways for participation of children in clinical trials. Children are a particularly vulnerable population, because they live longer with their underlying glomerular disease than adults, making the application of optimal management approaches critical.

In recent years however, there has been a dramatic increase in the number of FDA approvals of drugs for GD, though almost all the FDA approvals to date have been only for adults. To date, only one drug for GD has been approved by the FDA for children with GD, leaving the vast majority of children with GD without access to approved treatments for their disease.

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Many forms of GD could benefit from enhanced efforts to study them in children, including but not limited to those listed below:

- IgA Nephropathy
- IgA Vasculitis
- Idiopathic Immune Complex Glomerulonephritis (ex: IC-MPGN, Full house GN without diagnosis of Lupus, etc.)
- C3 Glomerulopathy
- Membranous Nephropathy
- Focal and Segmental Glomerulosclerosis
- Minimal Change Disease
- Anti-Neutrophilic Cytoplasmic antibody-GN (ANCA)
- Lupus Nephritis
- Alport Syndrome
- Infection-related or post-infectious Glomerulonephritis (with or without biopsy)
- Idiopathic Nephrotic Syndrome (with or without biopsy)

An important aspect of achieving FDA approval for novel treatments for any GD is a solid understanding of the natural history of disease allowing a comparison of a potential new treatment effect to the natural history of each GD. Unfortunately, most data collected to date for children with GD have been collected in settings where databases historically have lacked the rigor required for natural history data that is acceptable to regulatory agencies for consideration for regulatory approval. In addition, these databases have tended to exclude robust measures of patient reported outcomes, which are best captured through prospective data collection.

3.2 Cohort Study for Collection of Data Adequate to Achieve FDA Approval

A cohort study is designed to study a group of individuals with a common disease or a common risk factor within a defined time period. Participants are followed longitudinally after their exposure (defined as disease onset or risk factor identification), and monitored for outcomes of interest (such as death, disability, or new disease onset). Hence, a prospective cohort study can consist of a “healthy” cohort, an “at-risk” cohort (sometimes with challenging distinction between the two), or a “diseased” cohort.[3,4]

Population-based cohorts are best suited for identifying risk factors for incident disease (healthy cohorts), whereas institution-based cohorts are well-positioned for determining natural history and outcome predictors among those with established disease (disease cohorts). These latter objectives require capture of treatment variables, markers of disease activity, and other modifying factors not usually available by the large epidemiologic design of a population-based cohort.[3,4]

In rare diseases, institution-based retrospective cohort studies and case series are common. Prospective cohort studies, however, collect data forward in time from the point of enrollment, adding cost and time-intensiveness to the study planning and execution. Data quality is superior in the prospective design, in which data fields are uniformly defined and collected, rather than relying upon available records and non-standardized disease and outcome definitions. When data collection occurs during a participant encounter, recall bias and missing data are minimized. In a non-inception cohort study, however, the time after exposure at which patients begin their prospective follow-up on study is variable, limiting the ability to investigate the relationship between early/acute post-exposure factors and longer-term outcomes. For this reason, an inception cohort provides an additional enhancement in

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data quality. In a prospective inception-type disease cohort such as PLUGGED IN, participants who will be followed for long-term outcomes are enrolled within a limited time period post-presentation or post-diagnosis of disease.[3,4]

Given the high quality of the institution-based prospective inception-type disease cohort study, its findings are worthy of direct application in an expanded multicenter cohort for substantiation of findings, culminating in the design of risk-stratified (i.e., prognostically-stratified) randomized controlled clinical trials.

Through the successful execution of PLUGGED IN, we will be able to better explain apparent discrepancies among various GDs, and to derive more clinically meaningful and accurate prognostic assessments, toward better risk-stratification in pediatric GD. Hence, PLUGGED IN will facilitate development of, and improvement in, risk-stratified and more-personalized therapeutic approaches, thereby leading ultimately to improved outcomes in these pediatric GDs.

3.3 Methods:

Study Type: Mixed, prospective-retrospective cohort study (longitudinal, observational, non-interventional study

Duration: 5+ years

The **P**ediatric **L**ongit**u**dinal **G**lomerular **D**isease a PNRC Multi-**In**stitutional cohort study is a mixed prospective-retrospective cohort study that will enroll children (wherein childhood is defined as birth through 17years and 364 days of age), diagnosed with glomerular disease in July 2023 or forward and are receiving care at multiple pediatric nephrology participating institutions across the United States[5]).

This research is characterized by a mixed retrospective-prospective cohort study design.[6] This design signifies that eligible incident and prevalent “cases” of glomerular diseases (i.e., patients) are enrolled while under the care of pediatric nephrologists and followed forward in time from present to future, with simultaneous collection of data. Because both incident and prevalent cases are eligible, such that patients may be enrolled with various lag times following the time of initial diagnosis of glomerular disease, data of interest that have been generated through routine clinical care between the time of diagnosis and the time of enrollment will be retrospectively collected. In both phases of data collection for a given participant (prospective and retrospective), data will be abstracted from the medical record and entered into a REDCap database for the study. Any data collected from study-specific source records (e.g., patient reported outcomes or Quality of Life instruments not obtained/utilized in routine clinical care) will be designated as such in the cohort-specific Schedule of Assessments (Appendix A).

The total target accrual for the study is estimated in the several thousands of patients over time. The estimated enrollment in the first 2 years is 1,000 participants based on historical data from participating sites. Each study participant will be followed to a maximum age of ≤ 21 years old.

Data collection scope and timing for enrolled patients are summarized in the cohort-specific Schedules of Assessments.

This study will have optional patient self-assessment/parent proxy surveys to assess fatigue, anxiety, and peer relationships. These assessments can be completed during the wait for a clinic visit or can be emailed to participant after visit. These assessments are to collect the patient perspective of their daily life while living with kidney disease. These surveys will be

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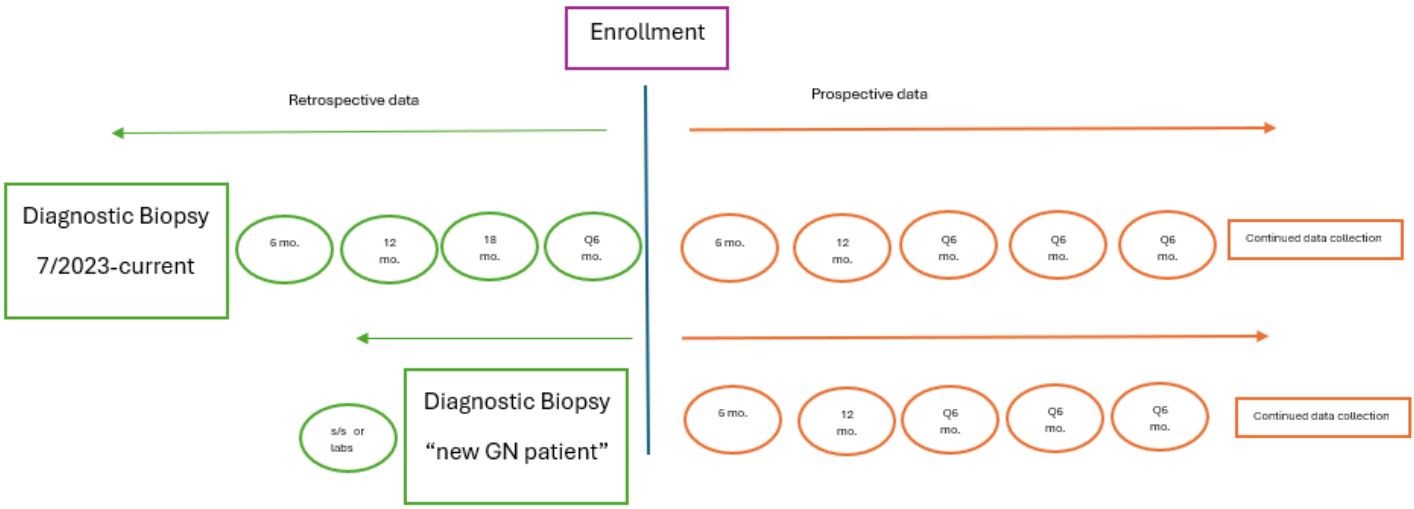
administered to patients, parents or guardians at entry into PLUGGED IN and then once every 12 months, ±3 months in hopes that will be able to obtain statistically significant results.

The study will also involve generation of biopsy images by sharing clinical biopsy slides from the clinical pathology departments at participating centers and scanning the slides to create images for long-term secure storage at the Digital Pathology Repository for the study, to facilitate additional characterization of histopathological features and their investigation as putative prognostic factors of the prespecified outcomes in the study, in alignment with Aim 1. Therefore, the informed consent form will include permission for biopsy image sharing. (see section 12 Digital Pathology Repository)

Patients may dually enroll on this cohort study and existing/future interventional trials.

A schematic of the mixed retrospective-prospective cohort study design is presented in Figure 1.

Figure 1: Mixed prospective-retrospective cohort study design



3.4 INCLUSION AND EXCLUSION CRITERIA

The target population for this study is children who have been diagnosed at ≤ 18 years of age with incident or prevalent documented glomerular disease at participating PNRC U.S. sites.

The population will include children with biopsy-proven glomerular disease or populations with a clinical diagnosis of glomerular disease [ex. Post-Infectious Glomerulonephritis or Post-Streptococcal Glomerulonephritis (PIGN) and Idiopathic Nephrotic Syndrome (INS), Alport Syndrome]

3.4.1 Main Inclusion Criteria (common to all disease cohorts):

1. Incident or prevalent (earliest diagnostic date 2023), objectively diagnosed (via biopsy and/or clinical diagnosis) glomerular disease

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2. Birth to 17 years, 364 days at time of diagnostic biopsy and/or diagnosis and are ≤ 18 years of age at enrollment.
3. Post-renal transplant patients with post-transplant biopsy proven GD compatible with one of the selected cohorts will be eligible.
4. Signed and dated written informed consent provided by the participant's parent(s) (or legal guardian) and the participant's assent in accordance with International Council for Harmonization Good Clinical Practice (ICH-GCP) and local site laws/regulations prior to admission to the trial.

   Assent will be sought according to the participant's age, level of maturity, competence and capacity.

3.4.2 Main Exclusion Criteria (common to all disease cohorts):

1. Declined (or unable to provide informed consent, + informed assent of minors) to participate
2. End Stage Kidney Disease (Stage 5 CKD, eGFR ≤ 15mL/min/1.73m^2)

The study population will be further categorized into the following prespecified disease cohorts:

1. IgA Nephropathy
2. IgA Vasculitis
3. Idiopathic Immune Complex Glomerulonephritis (ex: IC-MPGN, Full house GN without diagnosis of Lupus, etc.)
4. C3 Glomerulopathy
5. Membranous Nephropathy
6. Focal and Segmental Glomerulosclerosis
7. Minimal Change Disease
8. Anti-Neutrophilic Cytoplasmic antibody-GN (ANCA)
9. Lupus Nephritis
10. Alport Syndrome
11. Infection-related or post-infectious Glomerulonephritis (with or without biopsy)
12. Idiopathic Nephrotic Syndrome (with or without biopsy)

Additional cohort-specific eligibility criteria are delineated below.

3.5 IgA Nephropathy Cohort

3.5.1 IgA Nephropathy Cohort-specific Inclusion Criteria:

1. Incident or prevalent, objectively diagnosed (via biopsy) glomerular disease
   a. Predominant or codominant IgA deposits on kidney biopsy
2. Birth to 17 years 364 days at time of biopsy and/or diagnosis and are ≤ 18 years of age at enrollment.

3. Signed and dated written informed consent provided by the participant's parent(s) (or legal guardian) and the participant's assent in accordance with International Council for Harmonization Good Clinical Practice (ICH-GCP) and local site laws/regulations prior to admission to the trial.

   Assent will be sought according to the participant's age, level of maturity, competence and capacity.

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3.5.2 IgA Nephropathy Cohort-specific Exclusion Criteria:

1. Declined (or unable to provide informed consent, + informed assent of minors) to participate
2. End Stage Kidney Disease (Stage 5 CKD, eGFR ≤ 15mL/min/1.73m^2)
3. Skin lesions c/w IgA Vasculitis
4. Associated gastrointestinal lesions (i.e. Crohn's)
5. Staph or strep infection immediately prior (i.e. c/w IgA dominant PIGN)
6. Any other reason to think that the disease is a secondary form of GN

3.6 IgA Vasculitis Cohort

3.6.1 IgA Vasculitis Cohort-specific Inclusion Criteria:

1. Incident or prevalent, objectively diagnosed (via biopsy) glomerular disease
    a. Predominant or codominant IgA deposits on kidney biopsy associated with a clinical diagnosis of skin and/or joint lesions classically seen in IgA vasculitis
2. Birth to 17 years 364 days at time of biopsy and/or diagnosis and are ≤ 18 years of age at enrollment
3. Signed and dated written informed consent provided by the participant's parent(s) (or legal guardian) and the participant's assent in accordance with International Council for Harmonization Good Clinical Practice (ICH-GCP) and local site laws/regulations prior to admission to the trial.

   Assent will be sought according to the participant's age, level of maturity, competence and capacity.

3.6.2 IgA Vasculitis Cohort-specific Exclusion Criteria:

1. Declined (or unable to provide informed consent, + informed assent of minors) to participate
2. End Stage Kidney Disease (Stage 5 CKD, eGFR ≤ 15mL/min/1.73m^2)
3. Associated gastrointestinal lesions (i.e. Crohn's)
4. Staph or strep infection immediately prior (i.e. c/w IgA dominant PIGN)
5. Any other reason to think that the disease is a secondary form of GN

3.7 Idiopathic Immune Complex Glomerulonephritis

3.7.1 Idiopathic Immune Complex Glomerulonephritis (ex: IC-MPGN, Full house GN without diagnosis of Lupus, etc.) Cohort-specific Inclusion Criteria:

1. Incident or prevalent, objectively diagnosed (via biopsy) glomerular disease
    a. Proliferative glomerulonephritis (mesangial or membranoproliferative) without an associated cause
2. Birth to 17 years 364 days at time of biopsy and/or diagnosis and are ≤ 18 years of age at enrollment.
3. Signed and dated written informed consent provided by the participant's parent(s) (or legal guardian) and the participant's assent in accordance with International Council for Harmonization Good Clinical Practice (ICH-GCP) and local site laws/regulations prior to admission to the trial.

   Assent will be sought according to the participant's age, level of maturity, competence and capacity.

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3.7.2 Idiopathic Immune Complex Glomerulonephritis (ex: IC-MPGN, Full house GN without diagnosis of Lupus, etc.) Cohort-specific Exclusion Criteria:

1. Declined (or unable to provide informed consent, + informed assent of minors) to participate
2. End Stage Kidney Disease (Stage 5 CKD, eGFR ≤ 15mL/min/1.73m^2)
3. Evidence of diseases with recognized diagnostic criteria
4. Documented, Infection associated disease[1]

3.8 C3 Glomerulopathy Cohort

3.8.1 C3 Glomerulopathy Cohort-specific Inclusion Criteria:

1. Incident or prevalent, objectively diagnosed (via biopsy) glomerular disease
    a. C3 glomerulonephritis on biopsy (Isolated C3 deposition or C3 deposition of 2 orders of magnitude higher than any other immunoreactant accompanied by evidence of proliferation (either of cells or of membrane, when infection has been reasonably ruled out
2. Birth to 17 years 364 days at time of biopsy and/or diagnosis and are ≤ 18 years of age at enrollment.
3. Signed and dated written informed consent provided by the participant's parent(s) (or legal guardian) and the participant's assent in accordance with International Council for Harmonization Good Clinical Practice (ICH-GCP) and local site laws/regulations prior to admission to the trial.

    Assent will be sought according to the participant's age, level of maturity, competence and capacity.

3.8.2 C3 Glomerulopathy Cohort-specific Exclusion Criteria:

1. Declined (or unable to provide informed consent, + informed assent of minors) to participate
2. End Stage Kidney Disease (Stage 5 CKD, eGFR ≤ 15mL/min/1.73m^2)
3. Evidence of infection
4. Monoclonal gammopathy, infection related C3 dominant glomerulonephritis, late-stage kidney disease with no evidence of underlying complement dysregulation

3.9 Membranous Nephropathy Cohort

3.9.1 Membranous Nephropathy Cohort-specific Inclusion Criteria:

1. Incident or prevalent, objectively diagnosed (via biopsy) glomerular disease
    a. Diffuse GBM thickening w/o hypercellularity; "spikes" of GBM on silver stain IF: IgG & C3 staining along the GBM
2. Birth to 17 years 364 days at time of biopsy and/or diagnosis and are ≤ 18 years of age at enrollment.
3. Signed and dated written informed consent provided by the participant's parent(s) (or legal guardian) and the participant's assent in accordance with International Council for Harmonization Good Clinical Practice (ICH-GCP) and local site laws/regulations prior to admission to the trial.

    Assent will be sought according to the participant's age, level of maturity, competence and capacity.

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3.9.2 Membranous Nephropathy Cohort-specific Exclusion Criteria:

1. Declined (or unable to provide informed consent, + informed assent of minors) to participate
2. End Stage Kidney Disease (Stage 5 CKD, eGFR ≤ 15mL/min/1.73m^2)
3. Evidence of secondary cause i.e. malignancy, medications, infection, other autoimmune diseases

3.10 Focal and Segmental Glomerulosclerosis Cohort

3.10.1 Focal and Segmental Glomerulosclerosis Cohort-specific Inclusion Criteria:

1. Incident or prevalent, objectively diagnosed (via biopsy) glomerular disease
2. Birth to 17 years 364 days at time of biopsy and/or diagnosis and are ≤ 18 years of age at enrollment.
3. Signed and dated written informed consent provided by the participant's parent(s) (or legal guardian) and the participant's assent in accordance with International Council for Harmonization Good Clinical Practice (ICH-GCP) and local site laws/regulations prior to admission to the trial.

   Assent will be sought according to the participant's age, level of maturity, competence and capacity.

3.10.2 Focal and Segmental Glomerulosclerosis Cohort-specific Exclusion Criteria:

1. Declined (or unable to provide informed consent, + informed assent of minors) to participate
2. End Stage Kidney Disease (Stage 5 CKD, eGFR ≤ 15mL/min/1.73m^2)
3. Evidence of secondary FSGS (viral infection, drug-induced, obesity, diabetes, reflux, dysplasia, other primary glomerular disease)

3.11 Minimal Change Disease Cohort

3.11.1 Minimal Change Disease Cohort-specific Inclusion Criteria:

1. Incident or prevalent, objectively diagnosed (via biopsy (MCD)) glomerular disease
2. Birth to 17 years 364 days at time of biopsy and/or diagnosis and are ≤ 18 years of age at enrollment.
3. Signed and dated written informed consent provided by the participant's parent(s) (or legal guardian) and the participant's assent in accordance with International Council for Harmonization Good Clinical Practice (ICH-GCP) and local site laws/regulations prior to admission to the trial.

   Assent will be sought according to the participant's age, level of maturity, competence and capacity.

3.11.2 Minimal Change Disease Cohort-specific Exclusion Criteria:

1. Declined (or unable to provide informed consent, + informed assent of minors) to participate
2. End Stage Kidney Disease (Stage 5 CKD, eGFR ≤ 15mL/min/1.73m^2)
3. Evidence of secondary MCD (i.e. malignancy)

3.12 Anti-Neutrophilic Cytoplasmic antibody-GN (ANCA) Cohort

3.12.1 Anti-Neutrophilic Cytoplasmic antibody-GN (ANCA) Inclusion Criteria:

1. Incident or prevalent, objectively diagnosed (via biopsy) glomerular disease

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a. Pauci-immune lesion on biopsy

2. Birth to 17 years 364 days at time of biopsy and/or diagnosis and are ≤ 18 years of age at enrollment.
3. Signed and dated written informed consent provided by the participant's parent(s) (or legal guardian) and the participant's assent in accordance with International Council for Harmonization Good Clinical Practice (ICH-GCP) and local site laws/regulations prior to admission to the trial.

   Assent will be sought according to the participant's age, level of maturity, competence and capacity.

3.12.2 Anti-Neutrophilic Cytoplasmic antibody-GN (ANCA) Exclusion Criteria:

1. Declined (or unable to provide informed consent, + informed assent of minors) to participate
2. End Stage Kidney Disease (Stage 5 CKD, eGFR ≤ 15mL/min/1.73m^2)
3. Evidence of secondary ANCA ruled out (drug or infection-related)

3.13 Lupus Nephritis Cohort

3.13.1 Lupus Nephritis Inclusion Criteria

1. Incident or prevalent, objectively diagnosed (via biopsy) glomerular disease
   a. WHO Class I-IV renal biopsy findings
2. Birth to 17 years 364 days at time of biopsy and/or diagnosis and are ≤ 18 years of age at enrollment.
3. Signed and dated written informed consent provided by the participant's parent(s) (or legal guardian) and the participant's assent in accordance with International Council for Harmonization Good Clinical Practice (ICH-GCP) and local site laws/regulations prior to admission to the trial.

   Assent will be sought according to the participant's age, level of maturity, competence and capacity.

3.13.2 Lupus Nephritis Exclusion Criteria

1. Declined (or unable to provide informed consent, + informed assent of minors) to participate
2. End Stage Kidney Disease (Stage 5 CKD, eGFR ≤ 15mL/min/1.73m^2)
3. Evidence of secondary cause i.e. malignancy, medications, infection, other autoimmune diseases

3.14 Alport Syndrome Cohort

3.14.1 Alport Syndrome Inclusion Criteria

1. Incident or prevalent, objectively diagnosed (via biopsy and/or clinical diagnosis) glomerular disease associated variants in genes encoding the alpha-3, alpha-4, and/or alpha-5 chains of collagen
2. Birth to 17 years, 364 days at time of biopsy and/or diagnosis and are ≤ 18 years of age at enrollment.
3. Signed and dated written informed consent provided by the participant's parent(s) (or legal guardian) and the participant's assent in accordance with International Council

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for Harmonization Good Clinical Practice (ICH-GCP) and local site laws/regulations prior to admission to the trial.

Assent will be sought according to the participant's age, level of maturity, competence and capacity.

3.14.2 Alport Syndrome Exclusion Criteria

1. MYH9
2. P3H2
3. MYO1E
4. TRIM8
5. Declined (or unable to provide informed consent, + informed assent of minors) to participate
6. End Stage Kidney Disease (Stage 5 CKD, eGFR $\leq$ 15mL/min/1.73m^2)
7. Evidence of secondary cause i.e. malignancy, medications, infection, other autoimmune diseases

Non-Biopsy Cohort: the following diagnosis may or may not have a biopsy associated with the diagnosis.

3.15 Infection-related or post-infectious Glomerulonephritis (PIGN) (with or without biopsy) Cohort

3.15.1 Infection-related or post-infectious Glomerulonephritis (with or without biopsy) Cohort-specific Inclusion Criteria:

1. Incident or prevalent, objectively diagnosed (via biopsy and/or clinical diagnosis) glomerular disease
    a. Clinical history consistent with PIGN without another noted suspected cause
2. Birth to 17 years 364 days at time of biopsy and/or diagnosis and are $\leq$ 18 years of age at enrollment.
3. Signed and dated written informed consent provided by the participant's parent(s) (or legal guardian) and the participant's assent in accordance with International Council for Harmonization Good Clinical Practice (ICH-GCP) and local site laws/regulations prior to admission to the trial.

   Assent will be sought according to the participant's age, level of maturity, competence and capacity.

3.15.2 Infection-related or post-infectious Glomerulonephritis (with or without biopsy) Exclusion Criteria:

1. Declined (or unable to provide informed consent, + informed assent of minors) to participate
2. End Stage Kidney Disease (Stage 5 CKD, eGFR $\leq$ 15mL/min/1.73m^2)
3. An otherwise specified GN

3.16 Idiopathic Nephrotic Syndrome Cohort

3.16.1 Idiopathic Nephrotic Syndrome Cohort-specific Inclusion Criteria:

1. Incident or prevalent, objectively diagnosed (via biopsy and/or clinical diagnosis) glomerular disease

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2. Birth to 17 years 364 days at time of biopsy and/or diagnosis and are ≤ 18 years of age at enrollment.
3. Signed and dated written informed consent provided by the participant's parent(s) (or legal guardian) and the participant's assent in accordance with International Council for Harmonization Good Clinical Practice (ICH-GCP) and local site laws/regulations prior to admission to the trial.

   Assent will be sought according to the participant's age, level of maturity, competence and capacity.

3.16.2 Idiopathic Nephrotic Syndrome Cohort-specific Exclusion Criteria:

1. Declined (or unable to provide informed consent, + informed assent of minors) to participate
2. End Stage Kidney Disease (Stage 5 CKD, eGFR ≤ 15mL/min/1.73m^2)
3. Clinical history not consistent with alternative diagnosis

3.17 Alport Syndrome: refer to section 3.14

4) VULNERABLE POPULATIONS

Assent will be obtained for children whose maturity and psychological state make it possible for them to make an independent decision to participate in a study.
Since biopsy images and data will remain after minors turn 18 years old, we will seek re-consent from minor participants once they reach the age of majority, in order to continue to use their data and images.

5) RESOURCES

The PNRC is the regulatory sponsor of the study. The lead physicians of the study are responsible for coordinating investigators at the different sites participating in the study. Each site is required to comply with the IRB approved protocol and the terms of their site agreement in the conduct of the study.
The PLUGGED IN Steering Committee consisting of pediatric nephrology experts and stakeholder representatives has been established to support the lead investigators who are also part of the Steering Committee.

The PNRC has assigned Project Managers responsible for coordinating all required activities, in order to:

- Manage the study in compliance with U.S. regulations
- Direct the clinical study teams in preparation, conduct and reporting of the study
- Ensure appropriate training of sites and their staff
- Monitor site enrollment, study conduct, data collection and query resolution management
- Provide central communication to sites from the Steering committee and Steering Committee communications to the sites.

6) NUMBER OF PARTICIPANTS

The estimated total enrollment in the first 2 years is 1000 (500 per year) participants across all participating sites, based on historical data from participating sites. Enrollment goals for the site are 2 participants per month.

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7) MULTI-SITE RESEARCH

The PNRC has over 400 members representing over 125 sites across North America. US sites will be selected to support enrollment of pediatric participants. We expect to recruit 500 participants per year.

- The Lead Co-Principal Investigators in coordination with the PNRC will ensure communication to all of the sites:
    - All sites will have the most current version of the study plan (protocol), IRB approved consent document, and HIPAA authorization (per site specific template).
    - All required approvals will have been obtained from each site (including approval by the site's IRB of record) and filed in the trial master file.
    - All modifications will be communicated to sites and approved (including approval by the site's IRB of record) before the modification is implemented.
    - All engaged participating sites will safeguard data as required by local information security policies.
    - All local site investigators conduct the study appropriately.
    - All non-compliance with the study plan (protocol) or applicable requirements will be reported in accordance with local policy.
- The following methods will be used for communicating to engaged participating sites:
    - Collection of essential study records for the coordinating center master file
    - Ongoing site (PI and Coordinator) meetings and engagement
    - Monitoring of study milestones (i.e. start up, enrollment, remote monitoring)
    - Risk Management – regular communication with sites.
    - Issue Resolution: Tracking of site issues. All sites will be emailed and/or phoned with any problems in any of the following categories:
        - Consent documents reviewed and errors noted
        - Data: queries, resolution to queries
        - Protocol compliance concerns
    - Interim reporting: prepare regular updates for the study steering committee
    - Interim results- collated data metrics will routinely be shared with the lead PIs and coordinators at sites and at PNRC meetings
    - Closure of a study- while we aim to have the Multi-Institutional Cohort Study for long term data entry, we would notify all sites if funding was depleted and study closure was necessary.

8) RECRUITMENT METHODS

PNRC sites will recruit from their Pediatric Nephrology clinics and hospitalized patients by their clinical or research staff. Personnel will be overseen by the site Principal Investigator or sub-investigator(s). Each site will submit their specific recruitment plan and recruitment may include:

- Patient/family communication (if sites utilize family newsletters or clinic updates)
- Hospital/Division website or social media (if sites utilize web-based IRB approved ads)
- Discussing the study during clinic visits or hospitalizations
- Electronic Health Record query using ICD9/10 codes to identify potential participants at the site.
- Each site will describe their recruitment plan upon submission to the IRB of record, including any visuals used for website/social media
- The PI/Sub-I, clinic staff and research staff will review the potential participant for inclusion and exclusion criteria.
- The study will be posted on clinicaltrials.gov to ensure that any participant/family that wants to be involved in the study will have opportunity to explore options to enroll.

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9) STUDY TIMELINES

Duration of participant's study participation: Each participant will be followed to a maximum age of 21 years old.

Duration of the overall study: The duration of the study will be 5 years. Given the study's landmark status as the first and only North American multi-disease multi-institutional longitudinal cohort study in the field of pediatric nephrology, there is no planned end date to the study at this time.

10) PROCEDURES INVOLVED

This Multi-Institutional Cohort Study will be observational only with no treatment changes or additional treatments offered.

10.1 Data collection from clinical data

Participants, once providing consent, will have their clinical data entered into the study REDCap EDC. Upon enrollment, each participant will be assigned a study ID number. This study ID number will be used on pathology reports and pathology slides/images that will be used for the study.

Data abstracted from the EHR or captured in study-specific source records is described in detail in Appendix B.

10.2 Quality of Life Questionnaires and Social Determinants of Health

Participants will be asked to complete quality of life questionnaires using the PROMIS (Patient-Reported Outcomes Measurement Information System) at enrollment and then annually. PROMIS is a set of person-centered measures that evaluates and monitors physical, mental, and social health in adults and children. It can be used with the general population and with individuals living with chronic conditions. These validated tools will assess the impact of kidney disease on daily functioning, enabling participants and their caregivers (parents/guardians) to meaningfully contribute their perspectives to the study.

The questionnaires are optional and the participant would not be disenrolled if either the participant or the parent/guardian is unable or unwilling to complete the questionnaires. The PROMIS tools are available in translations including Spanish, Traditional Chinese, Japanese, Korean and Portuguese* (Portuguese translations are limited in the adult tools).

The following measures will be utilized:
Peds patient forms (ages 8-17 years):
PROMIS® Pediatric Item Bank GenPop v3.0 – Anxiety – Short Form 8a
PROMIS® Pediatric Item Bank GenPop v3.0 – Fatigue – Short Form 10a
PROMIS® Pediatric Item Bank GenPop v3.0 – Peer Relationships – Short Form 8a

Parent Proxy forms (Parent-Report for participants (ages 5-17 yrs):
PROMIS® Parent Proxy Item Bank GenPop v3.0 – Fatigue – Short Form 10a
PROMIS® Parent Proxy Item Bank GenPop v3.0 – Anxiety – Short Form 8a
PROMIS® Parent Proxy Bank GenPop v3.0 – Peer Relationships – Short Form 7a

Early Childhood (Parent-Report for participants (ages 1-5 yrs):
PROMIS® Early Childhood Parent Report Item Bank v1.0 – Anxiety – Short Form 4a
PROMIS® Early Childhood Parent Report Item Bank v1.0 – Social Relationships – Peer Relationships –Short Form 4a

Adult participant (ages 18+)
PROMIS Item Bank v1.0-Anxiety-Short form 8a

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PROMIS Item Bank v1.0-Fatigue-Short Form 10a (FACIT-Fatigue-10)
PROMIS Item Bank v2.0-Satisfaction with Social Roles and Activities-Short Form 8a

Social Determinates of Health also have potential to impact children with kidney disease[9]. An annual questionnaire to assess education and resources, missed days of school or work, zip code, insurance type, employment status and mode of transportation to clinic will be completed at the same time as the PROMIS questionnaires.

10.3 Estimated Glomerular filtration rate (GFR)

GFR will be calculated using the eGFR $U25_{crea}$ (which includes the patient height in centimeters) to assess kidney function at the timepoints indicated in the Schedule of Events (Appendix A).

$$eGFRCrea = \kappa * \left(\frac{ht\ (\text{meters})}{SCrea\ \text{mg/dL}}\right)$$

10.4 Providing biopsy slides and images

Sites without conforming scanning capabilities will, in consultation with their Pathology Department, package diagnostic Renal biopsy slides and ship them to a centralized laboratory for scanning and uploading into the digital pathology repository (DPR). Staff at each site will need to retrieve and select slides from existing patient materials, de-identify the slides using a label provided in the kit, label it with the study ID number and transfer de-identified immunofluorescence and electron microscopy images, and redacted pathology report with only the study ID assigned to the participant (on the image) to a secure FTP site. Slides and a copy of the redacted report will be shipped in provided shipping kits to Washington University in St. Louis. All biopsy slides will be shipped back within a month to the study site once imaging is complete to maintain clinical biopsy materials at the site. Sites will remove the label from the slide upon receipt of the slides and return it to their routine storage area of clinical biopsy material. Alternatively, sites that have whole slide image capabilities using a Leica GT450 scanner at 40x magnification may scan the kidney biopsy slides locally and upload into the Halo Link database directly along with the electron microscopy and immunofluorescence images. The same deidentification procedure applies to digital whole slide images.

10.5 Pregnancy occurrence during the study

During the course of the study, if a participant becomes pregnant, we would like to continue to collect clinical data relating to their glomerular disease. Our goal is retention in the study to better understand the natural history of their disease.

11) PLUGGED IN Digital Pathology Repository

11.1 Purpose

The purpose of the study Digital Pathology Repository (DPR) is to store and make available to PNRC users digital images of all pathology materials used to confirm the histology diagnosis for study participants. Access to patient biopsy materials is critical to determine the histopathologic response and impact of histopathologic findings in natural disease course (Aim 1). The DPR also serves to facilitate enrollment of patients into future clinical trials

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where confirmation of histopathologic diagnosis is essential for enrollment. The study DPR is located at Washington University School of Medicine in St. Louis, MO and is under the direction of the study's Pathology Core Lead. The images that will be included in the DPR are listed below:

- Whole-slide digital images (.svs) of glass slide-mounted sections (2-3 microns) of formalin-fixed, paraffin-embedded (FFPE) tissue stained with H&E, PAS, Jones silver, and trichrome.
- Digital images from immunofluorescence tissue (jpeg).
- Digital images from electron microscopy tissue (jpeg).
-

11.2 Digital Pathology Repository

Centrally operated HALO Link® digital pathology repository (DPR) to securely manage, share, and analyze whole slide images and pathology data.

- The DPR will design and develop the pathology EDC
- Stained glass slides will be scanned in the Washington University School of Medicine Department of Pathology and Immunology Digital Imaging Center (DIC) to generate whole-slide images. Slides will be scanned using a Leica GT450 high throughput scanner at 40x magnification. Whole slide images will be generated as .SVS format files.
- Sites with a local Leica GT450 high throughput scanner may scan biopsy slides locally at 40x magnification to generate. SVS format files for uploading into the DPR.
- Each digital image with the assigned study ID number (slides, immunofluorescence, and electron microscopy) will be uploaded to the HALO Link® platform.
- Histology data/annotation will be documented on the pathology worksheet and entered into the EDC.
- Upon completion of scanning and QC processing, the glass slides are mailed back to the PNRC Site pathology laboratory. A return shipping manifest is completed prior to mailing, and an automated email is generated to inform the PNRC Site of the incoming return of pathology material.
- Images obtained with the scanning and shared images will be stored for future use in the HALO Link® for a period of up to 20 years with anticipation of extending for future research purposes.
- PNRC members, scientists, researchers and industry may request access to the images through an application to the BCDUC (Biospecimen & Clinical Data Use Committee) of the PNRC. Upon review of the request and if approval is obtained, a data query will be sent from the PNRC to WUSTL for the requested and approved images.

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12) DATA MANAGEMENT

12.1 Study Primary Endpoint

This natural cohort study will evaluate change in proteinuria (urine protein-creatinine ratio) over time – as a marker of kidney health.

12.2 Data Quality

The Data Coordinating Center (DCC) will track incomplete data and issue routine reports ("missingness reports and /or queries) to the PNRC. Project managers for the PLUGGED IN Study will issue site specific reports on data fields that need to be reviewed and addressed. Monitoring of data will include unusual/out of range data entry as well with ultimate review, verification and/or correction at the site level in the database. Documentation of all communication of queries by the PNRC will be maintained and EDC audit trail of any corrections serve to ensure validity of the study data.

12.3 Confidentiality

All participants will be issued a unique identifier via the Data Coordinating Center (DCC).

Clinical data (including radiologic, histologic and clinical laboratory results) will be extracted from the medical record into electronic Case Report Forms (eCRFs) via the use of the electronic data capture (EDC) system, REDCap, comprised of a secure, password-protected, web-based front end and a Johns Hopkins University-based SQL server back end within the Johns Hopkins Health System IT firewall, with nightly back-up procedures in place.

Protected Health Information (PHI) collected will be restricted to a HIPAA-limited dataset, and the patient will be given a unique study ID. Data entered into EDC will include information like dates and geographic data (zip code). PHI will be marked/tagged in the EDC and stripped from a data report.

User access to the EDC will be restricted by the DCC database administrator to research personnel involved with the study. The EDC and its user access will adhere to 21CFR part 11 requirements for audit trails.

Biopsy slides and images will be labeled with the same unique identifier. Biopsy slides will be scanned into a central HALO Link EDC where these images/data will be maintained separately from the EDC in a Digital Pathology Repository EDC that houses biopsy data for this study, as well as all others maintained by the Digital Pathology Repository at WUSTL.

Any reports and datasets from the EDC and the Digital Pathology Repository EDC will be provided to investigators with the PNRC (note that identifiers are limited to the HIPAA limited data set) per the Data Use Policy. Similarly, biopsy images and annotations to be used for research, and associated confirmatory diagnostic criteria, will be provided to study investigators using the unique specimen ID, in lieu of any PHI. Access to biopsy images and data collected under this protocol will not be granted to individuals other than study investigators, except when executed via a specific Data Use Agreement (DUA) and/or Materials Transfer Agreement (MTA) under a collaborative research effort with one of the investigators. With IRB approval, under DUAs and/or MTAs, investigators may transfer biopsy images and data to outside entities for analysis. As disclosed in the informed consent process and the informed consent form, this may include an industry-sponsored (whether industry-driven or investigator-driven) research addressing the specific

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population/condition of interest, pertaining to the aforementioned cohorts. Any use of the images/data for purposes beyond those specified in this protocol and the accompanying informed consent/assent document will require separate IRB protocols and approvals.

12.4 Future Use of Data

Data from this study will be stored in the REDCap database maintained and supported by the Data Coordinating Center. The data will be stored for more than 20 years and there is the potential that storage may be extended beyond this if there is continued use. Data requests will be submitted to the PNRC Data Use Committee per the policy. Upon review and approval with the appropriate data use agreement in place, the data request will be sent to the DCC and a query of the database performed. The resulting data set will be sent to the PNRC DUC who will provide it to the requester. Consented blinded or aggregate subject data may be shared with PNRC members, collaborators and industry for future research uses. This release of data would require each requester to submit a data request. Per the agreement (see policy) the requestor must abide by the policy in terms of use, reporting back to the DUC, acknowledgment in publication and appropriate destruction of the dataset when work is completed.

13) STATISTICAL CONSIDERATIONS

13.1 Analysis

Different statistical methods suitable for the analysis of a longitudinal cohort study will be used to address specific scientific questions that will use data from this study. The methods will take into account correlation of repeated measures, minimize the effect of bias and confounding on effect estimates, address missing data. Baseline demographics and clinical characteristics will be summarized with descriptive statistics by age group, sex, and disease subtype using means and standard deviations or medians and IQRs for continuous variables and counts and percentages for categorical variables. We will compare characteristics by age group using t-test (parametric) or Mann- Whitney U (non-parametric) tests for continuous variables and $\chi 2$ tests for categorical variables. Prevalence and incidence will be estimated with their corresponding 95% confidence intervals. Time-to-event variables will be evaluated by Kaplan-Meier analysis and groups will be compared with log-rank tests. Trajectories of different outcomes and the association between salient exposure variables (putative risk factors, including disease cohort) and the prespecified primary, secondary and exploratory outcomes of interest will be evaluated using mixed models (e.g. trajectories of eGFR), Poisson models (e.g. rate of proteinuria relapse), Cox proportional hazard models and joint longitudinal and survival models. The findings of the study will be reported following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

- *Handling of missing data*
- The primary analysis for all the Aims will be a complete case analysis. However, if the proportion of missing data on the outcomes is more than 5%, we will examine the frequency and patterns of missing data and, if deemed appropriate, the potential impact of missing data will be evaluated using sensitivity analyses with multiple imputation. Multiple imputation models will include outcome and baseline variables in a single

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imputation model and 50 complete data sets will be imputed using chained equations.

Methods for specific analyses (non-limiting examples) are summarized below.

The trajectories of eGFR will be compared by age category using linear mixed-effects models. The outcome for the models will be eGFR with an interaction term between time and age category to evaluate whether trajectories of eGFR differ by age category.

The association between clinical factors and eGFR will be evaluated using mixed-effects models and the association between clinical factors and disease progression will be evaluated with Cox regression models. The time from diagnosis/biopsy to first treatment, percentage decline in eGFR, kidney failure, or renal replacement will be analyzed using Kaplan-Meier method with 95% confidence intervals and groups will be compared with log-rank tests. Growth, development, educational attainment, and HRQoL trajectories over time, overall and by disease cohort and by salient subgroups within/among disease cohorts, will be summarized using descriptive statistics and visualized by plots with 95% confidence intervals to illustrate trends.

Prespecified subgroup analyses for each of the aforementioned analyses will include age group, sex and disease type.

13.2 Sample Size Justification

The pediatric population (age 0-17 yrs.) in the United States is estimated at 74 million. It is estimated that 0.5% of U.S. children (0-17 yrs.) have moderate chronic kidney disease (CKD) (NHANES Annual Data Report | USRDS[7]), resulting in ~370,000 children with CKD. In children, it is estimated that 14% of CKD (eGFR <75) cases are glomerular[8]. Therefore, it has been estimated that approximately 52,000 children have glomerular disease with CKD in the U.S. We conservatively estimate to enroll 1000 patients in the first two years of the study and continue to enroll afterwards.

14) PROTECTING THE PRIVACY OF PARTICIPANTS

The rights of the study participant to privacy and protection of the data obtained during the study must be ensured in accordance with U.S. regulations. All participants will be assigned a unique study identification number (ID) at the time of enrollment. Any participant records or data that are sent to the DPR or entered into the REDCap EDC will be labeled with the study ID. Any data that are exported from the EDC will contain identifier only: participant Protected Health Information (PHI) or any information which would make the participant identifiable will not be transmitted/exported.

The participant/parent/legal guardian must be informed that the participant's medical records may be examined by authorized personnel appointed by the PNRC, members of the IRB and inspectors from regulatory authorities.

The agreement between the PNRC and trial sites specifies the responsibilities of the parties related to data protection, including the handling of data security breaches and respective communication and cooperation of the parties.

15) DISCONTINUATION OF STUDY PARTICIPANTS FROM THE STUDY

15.1 WITHDRAWAL OF PARTICIPANTS

Participation in this study is voluntary. Study participants and /or their parent or legal guardian may withdraw their assent/consent to study participation at any time without the need to provide a reason.

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If a study participant and/or their parent/legal guardian wants to withdraw consent the study principal investigator or sub-investigator should be involved in the discussion and explain that unless otherwise requested data that has been collected up to the time of withdrawal will be maintained (still deidentified) and will continue to be used for the study purposes.

15.2 Discontinuation of the study by the Coordinating Center

The PNRC reserves the right to discontinue the study overall or at a particular study site at any time for the following reasons:

- Failure to meet expected enrollment goals overall or at a particular study site
- Deviations from GCP/non-compliance, the study protocol, or concerns of site conduct of the study
- Termination of study funding to support the ongoing study

The study site will be reimbursed for reasonable expenses incurred in the case of trial termination (except in the case of number 2)

15.3 Lost to follow up

If a study participant is lost to follow-up, a reasonable effort must be made to by the investigator and clinical research staff to contact and locate the participant before they are declared lost to follow up. The following steps are suggested:

- Follow routine outpatient clinic procedures in which staff attempt to contact the participant's parents/legal guardian to reschedule clinic appointments as routine for their age, diagnosis and treatment.
- If more than 2 years has passed since the last visit to the site (either inpatient or outpatient), and there are no future site outpatient clinic visits, complete the lost to follow up case report form.

16) RISKS TO PARTICIPANTS

The risks associated with this protocol pertain to breach of confidentiality, for which protections are described above in the Data Confidentiality section.

17) POTENTIAL BENEFITS TO PARTICIPANTS

There is no direct benefit to the participant. However, we anticipate that critical knowledge gained from this study will help advance multiple pediatric fields addressed by the cohorts of interest, ultimately benefiting future patients with these conditions. There is also a potential benefit that the Multi-Institutional Cohort Study participant may be identified and approached for enrollment into a clinical trial(s) for their kidney disease.

18) SHARING OF RESULTS WITH PARTICIPANTS

All results utilized for study purposes will have been already generated as part of routine clinical care, and those results will have been communicated as part of routine clinical care to the patient by their treating nephrologist or other appropriate clinician. The overall study findings, based on research reports published in peer-reviewed medical/scientific journals, will be communicated in lay terms to the participants through the PNRC website and by letters sent to participant/family by the local study team overseeing their study participation both of which will be IRB-approved prior to any posting/dissemination.

19) PRIOR APPROVALS

All PNRC studies must be reviewed and approved by the Protocol Review Committee (PRC) prior to IRB submission.

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Local sites relying on the central IRB will have completed local context review and the approval letters provided following completion of same will be provided to the central IRB as well as maintained by the local study team in their site regulatory binder and by the PNRC in the study master file.

Local sites who do not rely on the central IRB will have obtained local governing IRB approval prior to commencing study activities, and the approval letters will be maintained by the local study team in their site regulatory binder and by the PNRC in the study master file.

The study will be carried out in compliance with the protocol, Good Clinical Practice and FDA Code of Federal Regulations guidelines, local institutional policies, as well as local institutional Standard Operating Procedures. The study will be initiated only after all legal documentation has been reviewed and approved by the respective site IRB and/or central IRB.

The Site investigator will be responsible for providing a documented approval of the study by either the local IRB or the central IRB to the Coordinating Center. In addition, the site investigator will be responsible for submitting an annual status update of the study to the IRB or more frequently as required by the IRB and provide the approval letter for ongoing study activities to the Coordinating Center.

Prior to participation in the study, informed consent (written or e-Consent) must be obtained from participants or the parent(s)/legal guardian according to ICH GCP and the U.S. Regulatory authorities.

20) COMPENSATION FOR RESEARCH-RELATED INJURY

N/A- minimal risk study, observational

21) ECONOMIC BURDEN TO PARTICIPANTS

There are no anticipated costs that a participant and/or family would incur as a result of their participation in this study.

22) CONSENT PROCESS AND DOCUMENTATION

Consent will be obtained by the study investigators, clinical staff, clinical research nurses, or clinical research coordinators, all of whom have obtained at minimum basic training in human subjects research and training in HIPAA. The cohort study design, visit schedule, and nature of the research versus routine clinical care will be described during the informed consent process, and the consent document will be reviewed in detail, with the patients/parents/legal guardians when they present for evaluation, treatment, or consultation in inpatient and outpatient settings at participating sites. The informed consent process will be conducted and documented in addition to the informed consent/assent form, in compliance with Good Clinical Practice and FDA Code of Federal Regulations guidelines, local institutional policies, as well as local institutional Standard Operating Procedures for research informed consent. All participants will be given a copy of the signed informed consent form. The original, signed informed consent will be stored at the site.

A signed informed consent will be obtained from a minor participant’s parent or legally appointed guardian prior to any collection of data for the study. Each signature must be personally dated by each signatory. The participant and/or their parent or legally acceptable representative will be permitted time and opportunity to inquire about the details of the study and to decide whether or not to participate. The decision by the participant and/or parent or legally appointed guardian is entirely voluntary. The

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investigator or delegated staff member will obtain written or e-consent of the study participant/parent/legal guardian after confirming that the study participant/parent/legal guardian understands the contents. The investigator or designate staff will ensure documentation of the consent discussion is entered into the participant's medial record/source records.

For children, where applicable, the participant will be provided with an age-adapted assent form. Assent will be collected for children ages 12 years to 17 years, 364 days.

Re-consenting may be necessary if there are any changes to the study protocol or if a child reaches the age of majority, which is the age at which a person is legally considered an adult. In most U.S. states, the age of majority is 18 years, but age of majority should be determined by each site according to their state laws.

Subjects may disenroll at any time simply by contacting study staff.

Local sites will be asked to have their consent and assent forms translated into Spanish once their English consent/assent documents have been approved by the IRB. If a Spanish speaking participant/family is identified for the study, an approved interpreter will be utilized to obtain consent/assent with IRB approved translated documents.

23) STUDY MONITORING

The Coordinating Center and/or a designee are responsible for monitoring the study with the requirements of ICH/GCP and in accordance with the study Monitoring Plan.

Monitoring will include all stages of study conduct from site initiation to close-out. The investigator and staff will allow adequate time for such monitoring activities. This monitoring will be done remotely in which staff will need to assist with remote access to: Original source records, consent/assent forms and documentation of the consent process, investigator site file and other documents as requested to ensure site compliance with the protocol and federal regulations for research.

24) Pharmacovigilance Requirements

If during the study, participants share any adverse events (AE) or serious adverse events (SAE) that are thought or possibly related to a medication, coordinators and PI will reference the adverse event reporting form, indicate and notify the Primary Coordinating Center (PCC) within 5 days for further instruction.

See AE reporting form

Details to be collected will include: Identification of the participant or guardian who reported the AE or SAE; details of the safety event and its outcome; investigational study ID if available; study title; name of sponsor; and the date of the report.

25) REFERENCES

1. Pitcher D, Braddon F, Hendry B, Mercer A, Osmaston K, Saleem MA, Steenkamp R, Wong K, Turner AN, Wang K, Gale DP, Barratt J. Long-Term Outcomes in IgA Nephropathy. Clin J Am Soc Nephrol. 2023 Jun 1;18(6):727-738. doi: 10.2215/CJN.0000000000000135. Epub 2023 Apr 13. PMID: 37055195; PMCID: PMC10278810.
2. Pitcher D, Braddon F, Hendry B, Mercer A, Barratt, J, Steenkamp R, Wong K, Turner N, Gong W, Gale D, Saleem M. Long-Term Outcomes in Nephrotic Syndrome b Kidney Biopsy Diagnosis and Proteinuria. JASN. 2025 July: 36(7): 1398-1416. doi:10.1681/ASN.0000000610.

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3. Armstrong-Wells J, Goldenberg NA. Institution-based prospective inception cohort studies in neonatal rare disease research. Semin Fetal Neonatal Med. 2011 Dec;16(6):355-8.
4. Bernard TJ, Armstrong-Wells J, Goldenberg NA. The institution-based prospective inception cohort study: design, implementation, and quality assurance in pediatric thrombosis and stroke research. Semin Thromb Hemost. 2013 Feb;39(1):10-4.
5. International Council for Harmonisation (ICH) E11 (R1) Addendum: Clinical Investigation of Medicinal Products in the Pediatric Population. (18 August 2017) section 2.5
6. Szklo M and Nieto EJ. Epidemiology: Beyond the Basics (Jones and Bartlett, Sudbury, MA, USA), 2004, pp. 27-29.
7. United States Renal Data System. Chronic Kidney Disease: Chapter 5. Kidney disease among children and adolescents. *2024 USRDS Annual Data Report: Epidemiology of kidney disease in the United States*. Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 2024.
8. Harambat, J., van Stralen, K.J., Kim, J.J. *et al.* Epidemiology of chronic kidney disease in children. *Pediatr Nephrol* **27**, 363–373 (2012). https://doi.org/10.1007/s00467-011-1939-1Pediatr Nephrol. 2011 Jun 29;27(3):363–373. doi:10.1007/s00467-011-1939-1
9. Seo-Mayer P, Ashoor I, Hayde N, Laster M, Sanderson K, Soranno D, Wigfall D, Brown D. Seeking justice, equity, diversity and inclusion in pediatric nephrology. Front Pediatr. 2022 Dec 12;10:1084848. doi: 10.3389/fped.2022.1084848. PMID: 36578658; PMCID: PMC9791125.

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Appendix A: Schedule of Events

The goal is to have Enrollment/ICF, demographic, Social Determinants of Health (SDOH), clinical baseline data + two more data entries per year after the diagnostic biopsy until the date of informed consent (retrospective data). The study goal is for two data entry points/year, ideally 6-month and 12-month intervals prospectively.

Data collection	Enrollment	Visit 1 6 months ± 1 month after diagnosis (retrospective) or ICF (prospective)	Visit 2 12 months ±1 month (& ongoing every 6-month intervals)	Visit 3 18 months ±1 month (& ongoing every 6-month intervals)
Enrollment/ICF	X			
Historical data (from initial biopsy to current/enrollment)	X			
Demographics	X			
SDOH	X			
Clinical				
Glom Disease	X	X	X	
Biopsy	X	X (If applicable)	X (If applicable)	
Family hx/comorbidity	X	X	X	
Treatment/con meds	X	X	X	
Procedures/Hospitalization	X	X	X	
Pregnancy	X	X	X	
LTF/Death	X	X	X	
Labs	X	X	X	
Patient Reported Outcomes	X		X (annual)	

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Appendix B: General data collection

CRF name	sub name	Description of data fields
Demographic (enrollment & annual updates)	Patient demographics	DOB, biological sex, race, ethnicity, development-grade if school aged, date of diagnosis*
SDOH (enrollment & annual)	SDOH	Zip code, insurance type (private, Medicaid, self-pay). Employment status of parent (s), mode of transportation to clinic (car, rides w/ other, ride share (taxi/uber), public
Clinical	Glomerular disease	Primary diagnosis, date of diagnosis*, diagnostic test name/result, genetic or other testing,
	Vital signs/measurements	blood pressure (manual or electronic cuff) height/weight/ BMI
	Biopsy	Initial biopsy date w/ Path report (grade, severity) Date slides sent to Core (name slides sent) Date images sent to Core (name images sent) Any Re-biopsy date w/ path report
	Patient & family history/comorbidities	Patient conditions other than kidney disease, Family history Hypocomplementemia Blood disorder Heart disease HTN Diabetes T1-insulin Diabetes T2 Celiac/gluten intolerance Lupus RA Gout Thyroiditis Scleroderma Hypothyroid DeafnessCrohn's IBS NOS kidney disease Hematuria Proteinuria FSGS IgA

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		C3G Membranous MPGN Eczema Psoriasis Unexplained rashes Age-related Macular degen Partial/total blindness Drusen Glaucoma (Genetic) Factor H mutation MCP mutation Factor I mutation Other:
	Treatment	Disease specific medications, concomitant medications indicate date started (prescribed by HCP) ACEi ARB SGLT2i Sparsentan Finerenone Belimumab Other: Hydroxychloroquine Prednisone Other steroid: Mycophenolate mofetil (MMF) Pegcetacoplan Iptacopan B Cell Therapy (name) Cyclophosphamide Calcineurin Inhibitor Prophylaxis yes/no If yes specify:
	Procedures/hospitalizations	Date & length of stay, admission diagnosis, treatment during stay, Plasma Exchange (yes/no) if yes, #, biopsy, ultrasound, imaging (CT, MRI) Dialysis (yes or no)
	Pregnancy	Date, outcome
	LTF/Death	Last known visit
	Laboratory tests	eGFR ($U25_{crea}$ formula) C3 level C4 level CH50 (CAE) Uric acid Hgb

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		Hct CR (mg/dL) Cystatin C (mg/L) BUN Albumin Na K+ Cl- CO2 Bili, total AST ALT GGT (urine) Urine blood dip Urine protein dip Urine WBC/hpf Urine RBC/hpf UA Cr UA Protein UA Albumin Urine P/C ratio (mg/mg) Urine Microalbumin/Cr ratio PEP urine random PEP serum IFE Kappa/Lambda K/L Kappa Free light chain Lambda free Light chain
Special testing	Genetic testing	(list)
		Serum Novel Antigen THS7A PLA2R Other: _____ Tissue Novel Antigen
	Complement biomarkers	ADAMTS13
	Infectious disease evaluation	Hep A,B,C, HIV, BCx, No on RVP, ECHO, EBV, CMV
	Antibody testing	ANA, ANCA, Anti-cardiolipin ab, Anti- B2GP1 ab, Lupus anti-coagulant, Anti dsDNA, Anti Smith Ab
Annual data	Demographic	Educational attainment
	SDOH	Update if changes
	Patient & family history/comorbidities	Update if changes from enrollment
	Procedures/Hosp	Detail and biopsy, hospital admissions
	Labs	UPCR – list all done in the last year
		All serum creatinine testing done in the last year

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